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Cobalt-Catalyzed Reductive Cross-Coupling between C-Heteroatom (S, N, O, X) Electrophiles to Build Csp³-Csp² and Csp³-Csp³ Bonds

Mengyu Gao

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Cobalt-Catalyzed Reductive Cross-Coupling between C- Heteroatom (S, N, O, X) Electrophiles to Build Csp^3 - Csp^2 and Csp^3 - Csp^3 Bonds

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*We are on a stage we did not choose, playing a play we
did not choose.*

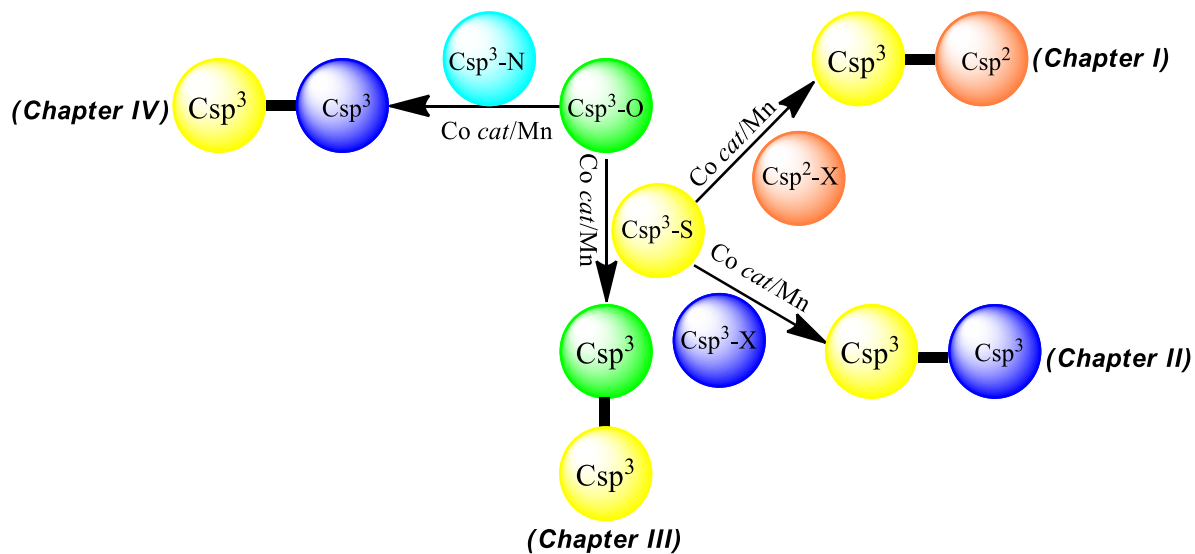
-Epictetus

But we can choose how to work on our script.

Résumé thèse

Ces travaux de recherches ont permis de mettre en avant la versatilité des applications catalytiques d'un métal de transition non-noble : le cobalt, pour former des liaisons Carbone-Carbone. Nous avons voulu remplacer les composés halogénés utilisés généralement comme produits de départ par d'autres composés électrophiles plus éco-compatibles. Différentes liaisons Carbone-Carbone ont pu être créées dans des conditions douces en une seule étape grâce à la catalyse au cobalt sans qu'il soit nécessaire de préformer un organométallique stœchiométrique. Ces couplages croisés ont pu être réalisés directement à partir de deux électrophiles possédant des liaisons Carbone-Halogène, Carbone-Oxygène, Carbone-Azote ou Carbone-Soufre. Parmi les différents catalyseurs de métaux de transition, les catalyseurs au cobalt largement utilisés dans notre laboratoire, présentent une toxicité relativement faible, sont peu onéreux et offrent une alternative aux complexes de palladium, en particulier pour éviter la génération de produits secondaires de β -élimination lorsqu'un partenaire halogénure d'alkyle est impliqué. L'emploi de ce catalyseur présente également une réactivité complémentaire par rapport à d'autres métaux de transition. Dans ce travail de recherche, nous nous sommes intéressés à la formation de diverses liaisons Csp^3-Csp^2 et Csp^3-Csp^3 par couplage réducteur catalysé au cobalt en essayant de remplacer au moins un des deux électrophiles par un composé qui ne rejette pas de déchets halogénés. Le premier chapitre décrit le couplage croisé catalysé au cobalt à partir d'électrophiles Csp^3-S représentés par des sels de benzyle sulfonium et des composés aromatiques Csp^2-X (Br, Cl)/ Csp^2-OTf pour former des diarylmethanes. Les sels de sulfonium sont obtenus à partir de l'alcool correspondant. De plus, c'est la première utilisation de ces composés en présence d'une catalyse au cobalt alors qu'ils ont déjà été utilisés en présence d'une catalyse au nickel. Cette nouvelle méthodologie emploie des conditions opératoires douces rendant cette procédure directe et simple d'utilisation tout en permettant la présence de nombreux groupements fonctionnels. Le second chapitre est consacré à la construction de liaisons Csp^3-Csp^3 à partir de liaison Csp^3-S toujours sous forme de sels de benzylsulfonium et d'halogénures (I, Br) d'alkyle inactivés par couplage réducteur. Les meilleurs rendements sont obtenus à partir d'iodure d'alkyle primaires non activés ou de chlorures benzyliques. Le troisième chapitre est consacré à l'allylation de sels de benzylsulfonium. Des liaisons Csp^3-Csp^3 ont pu être formées à partir de Csp^3-S représentée par des sels de benzylsulfonium et des électrophiles Csp^3-O tels que des acétates d'allyle, carbonates d'allyle ou éthers d'allyle. C'est le premier couplage cobalta-catalysé utilisant des éthers allyliques et le premier couplage réducteur qui a été décrit avec ces composés. Enfin dans le quatrième chapitre, les mêmes composés que ceux formés dans le troisième chapitre ont pu être synthétisés par couplage réducteur. Cependant, ces composés sont obtenus ici par couplage de liaisons Csp^3-N et des électrophiles Csp^3-O (acétates d'allyle, carbonate d'allyle et éther d'allyle). Les composés azotés sont sous forme de sels de benzylpyridinium obtenus à partir de l'amine correspondante.

A l'issue de chacun des chapitres, afin de mieux comprendre les processus mis en jeu dans ces différentes réactions de couplages croisés, une étude mécanistique a été réalisée pour chacune des réactions montrant l'implication de radicaux lorsqu'un composé aliphatique est utilisé.



Couplages réducteurs étudiés par catalyse au cobalt

Acknowledgment

First of all, thanks to the China Scholarship Council and Dr. Gosmini gave me the chance to study at École Polytechnique, Institut Polytechnique de Paris. After four years of guidance and supervision of Dr. Gosmini, I finished four projects and obtained lots of good results, which have been published and other parts are still ongoing. Based on these explorations and achievements, I finished my Ph.D. defense successfully. As a minority part of the lab, the foreign students, I felt kindness from the students and permanent staff, and got lots of help from students, such as Pauline, Thibault, and Paul-Alexis, who are really good colleagues, shared lots of writing thesis practice to me. Moreover, I also thank Grégory Danoun, Thomas Simler, and Sophie Bourcier who helped me with GC, GC-MS, and HRMS, as well as the exploration of the reaction mechanism. Thanks to the support from Dr. Cédric Tard and Dr. Audrey Auffrant. There are so many nice students and permanent staff worth introducing. Meeting them and working at the Molecular Chemistry laboratory (LCM) is my luck and pleasure. At the same time, thanks to Dr. Sylvie Coussot, maybe for her, I am a part of her daily job, but for me, she is like sunshine in my suffering period, gave me support, and directed me.

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Abbreviations

Ac	Acetyl
Acac	Acetylacetonate
Ad	Adamantyl
Alk	Alkyl
aq.	Aqueous
Ar	Aryl
Bipy	2,2'-bipyridine
EDG	Electron-donating group
Bn	Benzyl
Boc	Tert-butoxy carbonyl
BPin	Boronic pinacol ester
BPhen	Bathophenanthroline
Bu	Butyl
EWG	Electron-withdrawing group
C	Concentration
Cat.	Catalyst
Cbz	Carbobenzyloxy (BnOC=O)
Cy	Cyclohexane
d	Doublet
de	Diastereomeric excess
DMA	Dimethylacetamide
DMAP	4-Dimethylaminopyridine
DMBA	2,6-dimethyl benzoic acid
DME	Dimethoxyethane
DMF	Dimethylformamide
DMO	Dimethyl oxalate
DMSO	Dimethyl sulfoxide
dppe	Bis(diphenylphosphino)ethane)
dppbe	1,2-Bis(diphenylphosphanyl)benzene
dppf	1,1'-Ferrocenediyl-bis(diphenylphosphine)
dtbbpy	4,4'-Di-tert-butyl-2,2'-dipyridyl

EC	Ethyl crotonate
ee	Enantiomeric excess
eq.	Equation
equiv	Equivalent
er	Enantiomeric ratio
Et	Ethyl
FG	Functional group
GC	Gas chromatography
GC-MS	Gas chromatography-mass spectrometry
glyme	Dimethoxyethane
Het	Heterocycle
hp	Heptane
HR-MS	High-resolution mass spectrometry
hx	Hexane
<i>i</i> Bu	Iso-butyl
<i>i</i> Pr	Iso-propyl
L	Ligand
LG	Leaving group
<i>m</i> -	<i>Meta</i>
[M]	Metal
Me	Methyl
MS	Mass spectrometry
Ms	Mesylate
<i>n</i> Bu	Normal- butyl
NHC	N-heterocyclic carbene
NHP	N-hydroxyphthalimide
NMP	N-Methylpyrrolidone
NMR	Nuclear magnetic resonance
<i>n</i> Pr	Normal- propyl
<i>o</i> -	<i>Ortho</i>
Oct	Octahedral
<i>p</i> -	<i>Para</i>

Ph	Phenyl
Phen	1,10-Phenanthroline
PG	Protected groups
ppm	Part-per-million
Pr	Propyl
Py	Pyridine
Pybox	Two enantiomeric oxazoline rings containing a bulky substituent at the 4- and/or the 5-carbon positions are bridged with the pyridine.
R	An organic group
rt	Room temperature
s	Singlet
SET	Single-electron-transfer
t	Time/triplet
T	Temperature
TBAB	Tetrabutylammonium bromide
TBS	Tert-butyldimethylsilyl
<i>t</i> Bu	Tert-butyl
TDAE	Tetrakis(dimethylamino)ethylene
Terpy	Terpyridine
TEA	Triethylamine
TEMPO	Tetramethylpiperidinyloxy
Tf	Triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TM	Transition metal
TMHD	2,2,6,6-Tetramethyl-3,5-heptanedione
TMS	Trimethylsilyl
Tol	Toluene
TS	Tosylate
V	Volume
X	Halides
XEC	Cross-electrophile coupling
4-Me-bipy	4,4'-Dimethyl-2,2'-dipyridyl

5-Me-bipy

5,5'-Dimethyl-2,2'-dipyridyl

4-MeO-bipy

4,4'-Dimethoxy-2,2'-bipyridine

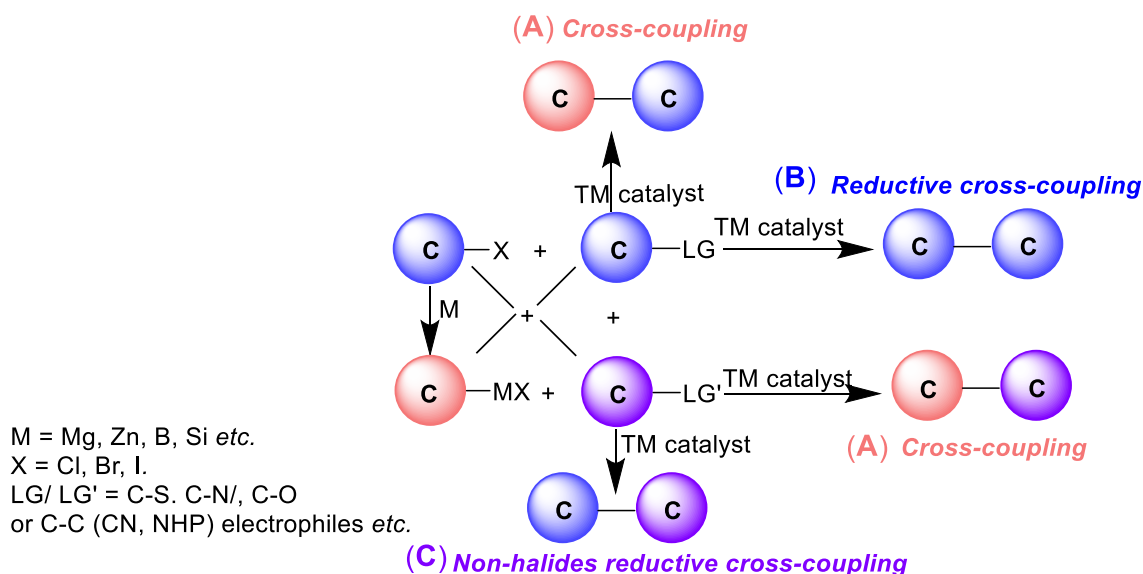


Introduction

1. General Introduction.

1.1. Background introduction.

Carbon–carbon bonds are the most important and pervasive units in pharmaceuticals, plastics, and natural products.¹ Their formation is the critical element to build the carbon framework of organic molecules and timeless topics for organic synthesis². Transition metal-catalyzed cross-couplings have become one of the most important tools in carbon-carbon bond formation since the pioneering works of Suzuki, Heck, and Negishi, which were awarded by the Nobel Prize in Chemistry in 2010 for palladium-catalyzed cross-coupling reactions.³ With the development of transition metal-catalyzed cross-couplings, more and more strategies for C-C bond formation were reported (*Scheme 1*). One of the most significant parts is the cross-coupling of an electrophile bearing an active leaving group, like halides, sulfonates, carboxylate derivatives, and ammonium salts, *etc.*, with organometallic reagents, such as organomagnesium, organoboron, organostannane or organozinc reagents, via a transition metal catalyst, particularly palladium or nickel catalysts.^{3a} (*Scheme 1, A*) Most of these reactions undergo a cascade of oxidative addition, transmetalation, and reductive elimination processes or single-electron-transfer (SET) processes to deliver the C-C bond-forming compounds.⁴



Scheme 1. Transition metal-catalyzed C-C bond formation

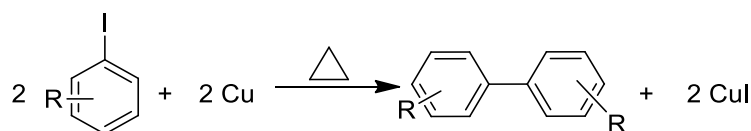
¹ Selected review: (a) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang. *Chem. Soc. Rev.* **2011**, *40*, 5068. (b) A. Alexakis, J. E. Backvall, N. Krause, O. Pamies, M. Dieguez. *Chem. Rev.* **2008**, *108*, 2796–2823. (c) B. M. Trost, F. D. Toste, A. B. Pinkerton. *Chem. Rev.* **2001**, *101*, 2067.

² (a) J. Gu, X. Wang, W. Xue, H. Gong. *Org. Chem. Front.* **2015**, *3*, 1411. (b) D. A. Everson, D. J. Weix. *J. Org. Chem.* **2014**, *79*, 4793. (c) D. J. Weix. *Acc. Chem. Res.* **2015**, *48*, 1767. (d) T. Moragas, A. Correa, R. Martin. *Chem. Eur. J.* **2014**, *20*, 8242. (e) J.-Y. Ne'de'lec, J. Pe'richon, M. Troupel. *Top. Curr. Chem.* **1997**, *185*, 141.

³ (a) J.; Marsden, M. Haley, A. de Meijere, F. Diederich. In *Metal-Catalyzed Cross-Coupling Reactions*, WILEY-VCH: Weinheim, (2004). (b) P. Knochel, In *Handbook of Functionalized Organometallics. Applications in Synthesis*, Wiley-VCH: Weinheim, Germany, (2005). (c) C. C. C. Johansson-Seechurn, M. O. Kitching, T. J. Colacot, V. Snieckus, *Angew. Chem. Int. Ed.*, **2012**, *51*, 5062.

⁴ (a) C. Liu, H. Zhang, W. Shi, A. Lei. *Chem. Rev.* **2011**, *111*, 1780. (b) D.-Y. Gu, B.-J. Li, Z.-J. Shi. *Acc. Chem. Res.* **2010**, *43*, 1486. (c) R. Jana, T. P. Pathak, M. S. Sigman. *Chem. Rev.* **2011**, *111*, 1417.

Another rapidly developing method corresponds to transition metal-catalyzed reductive cross-coupling reactions between two electrophilic reagents, which will be introduced deeply in this thesis. The transition metal-catalyzed reductive cross-coupling focus on chemical methods (no report about electrochemical and photocatalysis will be mentioned), notably concerning the construction of Csp³-Csp² and Csp³-Csp³ bonds. (**Scheme 1, B, C**). In fact, early in 1901, the Ullmann reaction was reported as one of the earliest reductive cross-coupling reactions to construct C-C bonds from two aryl halides using stoichiometric copper.⁵ (**Scheme 2**) The reductive cross-coupling reactions avoid the preparation of organometallic species, most of which are mentioned to be unstable, sensitive to moisture and oxygen, challenging to synthesize, and limiting the presence of functional groups. In the reductive cross-coupling reactions, most electrophilic coupling partners, such as widely used organohalides⁶, sulfonates⁷, carboxylate derivatives⁸, and esters⁹, as well as oxalates¹⁰, pyridinium salts¹¹, ammonium salts¹², and so on, are commercially available, easy to store and handle (that do not have to deal with under anhydrous anaerobic conditions), and can be used on larger scales, These reactions have been reported gradually and achieved significant breakthroughs in C-C bond formation in recent years.



Scheme 2. Ullmann reaction

While excellent work has been reported by chemists worldwide, they always insist on the exploration of sustainable protocols with cheap and benign catalytic systems and environment-friendly reaction partners under mild conditions. Thus, non-noble metals, like iron, copper, nickel, and cobalt, are more and more applied in constructing Csp³-Csp² and Csp³-Csp³ bonds due to their lower cost and natural abundance. Among various transition metal catalysts, cobalt catalysts have always been the main

⁵ F. Ullmann, J. Bielecki, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 2174.

⁶ (a) E. Lucas, E. Jarvo *Nat. Rev. Chem.*, **2017**, *1*, 0065. (b) H. Xu, C. Zhao, Q. Qian, W. Deng, H. Gong. *Chem. Sci.* **2013**, *4*, 4022. (c) X. Yu, T. Yang, S. Wang, H. Xu, H. Gong. *Org. Lett.* **2011**, *13*, 8, 2138. (d) S. Pal, S. Chowdhury, E. Rozwadowski, A. Auffrant, and C. Gosmini, *Adv. Synth. Catal.*, **2016**, *358*, 2431. (e) A. Moncomble, C. Gosmini. *Isr. J. Chem.*, **2010**, *50*, 568. (f) M. Amatore, C. Gosmini. *Chem. Eur. J.*, **2010**, *16*, 5848. (g) M. Amatore, C. Gosmini. *Angew. Chem. Int. Ed.*, **2008**, *47*, 2089.

⁷ (a) L. K. G. Ackerman, L. L. Anka-Lufford, M. Naodovic, D. J. Weix. *Chem. Sci.*, **2015**, *6*, 1115. (b) B. R. P. Reddy, S. Chowdhury, A. Auffrant, C. Gosmini. *Adv. Synth. Catal.* **2018**, *360*, 3026. (c) K. Komeyama, T. Michiyuki, I. Osaka. *ACS Catal.* **2019**, *9*, 10, 9285. (d) J-H. Liu, C-T. Yang, X-Y. Liu, Y. Fu, L. Liu. *Chem. Eur. J.* **2014**, *20*, 15334. (e) W-Y. Ma, G-Y. Han, S. Kang, X. Pang, Liu, X-Y. X-Z Shu. *J. Am. Chem. Soc.* **2021**, *143*, 15930.

⁸ For selected review: (a) S. Karmakar, A. Silamkoti, N. A. Meanwell, A. Mathur, A. K. Gupta. *Adv. Synth. Catal.* **2021**, *363*, 3693. (b) Y. Li, L. Ge, M. T. Muhammad, H. Bao. *Synthesis*, **2017**, *49*, 5263. (c) H. Chen, X. Jia, Y. Yu, Q. Qian, H. Gong. *Angew. Chem. Int. Ed.* **2017**, *56*, 13103.

⁹ (a) M. O. Konev, L. E. Hanna, E. R. Jarvo. *Angew. Chem. Int. Ed.* **2016**, *55*, 6730. (b) X. Qian, A. Auffrant, A. Felouat, C. Gosmini. *Angew. Chem. Int. Ed.*, **2011**, *50*, 10402. (c) R.-D. He, Bai, G.-Y. Han, Z.-Z. Zhao, X. Pang, X. Pan, Liu, X.-Y. X.-Z. Shu. *Angew. Chem. Int. Ed.* **2022**, *61*, e202114556. (d) M. Amatore, C. Gosmini, J. Périchon. *Eur. J. Org. Chem.*, **2005**, 989.

¹⁰ (a) Y. Ye, H. Chen, J. L. Sessler, H. Gong, *J. Am. Chem. Soc.* **2019**, *141*, 820. (b) M. Gao, D. Sun, H. Gong. *Org. Lett.* **2019**, *21*, 1645. (c) Y. Pan, Y. Gong, Y. Song, W. Tong, H. Gong. *Org. Biomol. Chem.* **2019**, *17*, 4230. (d) Y. Ye, H. Chen, G. Ma, H. Gong, *Org. Lett.* **2020**, *22*, 2070.

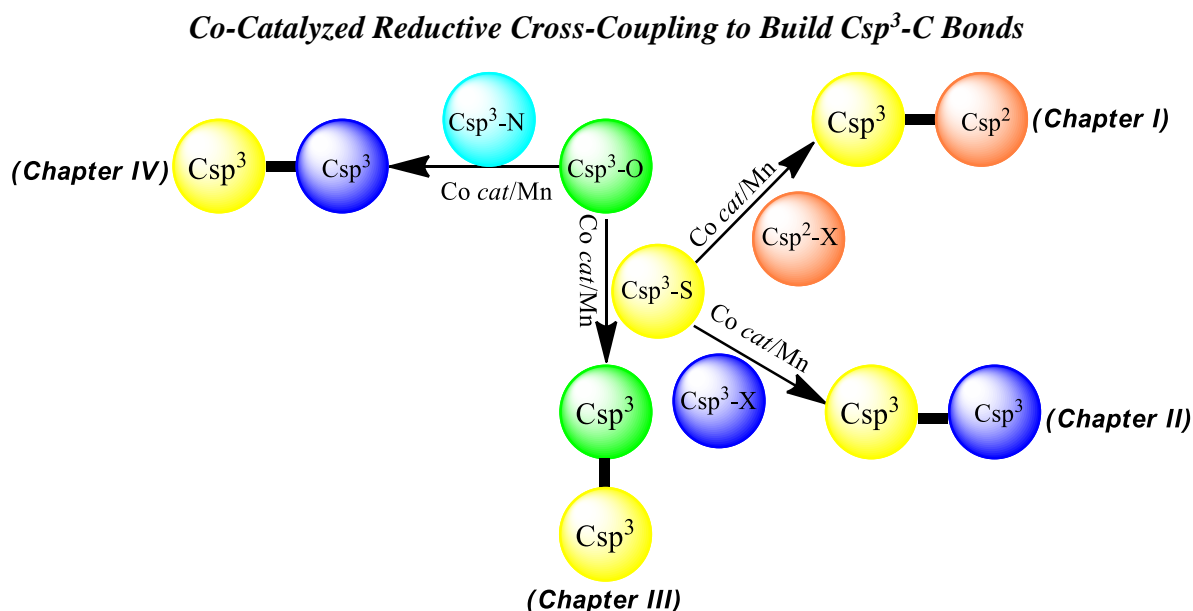
¹¹ (a) J. Liao, C. H. Basch, M. E. Hoerrner, M. R.; Talley, B. P. Boscoe, J. W. Tucker, M. R. Garnsey, M. P. Watson. *Org. Lett.* **2019**, *21*, 2941. (b) R. Martin-Montero, V. R. Yatham, H. Yin, J. Davies, R. Martin. *Org. Lett.* **2019**, *21*, 2947. (c) H. Yue, C. Zhu, L. Shen, Q. Geng, K. J. Hock, T. Yuan, L. Cavallo, M. Rueping. *Chem. Sci.* **2019**, *10*, 4430. (d) S. Ni, C.-X. Li, Y. Mao, J. Han, Y. Wang, H. Yan, Y. Pan. *Sci. Adv.* **2019**, *5*, eaaw9516

¹² R.-D. He. C.-L. Li. Q.-Q. Pan, P. Guo, X.-Y. Liu, X.-Z. Shu, *J. Am. Chem. Soc.* **2019**, *141*, 12481.

research topic in our lab: they feature relatively low toxicity, and are more suitable for sustainable, large-scale production. Moreover, they offer a useful alternative and show a complementary reactivity to palladium complexes, particularly in avoiding the generation of β -elimination side products when an alkyl halide partner is used in the cross-coupling. As mentioned above, excellent work related to environment-friendly and easily accessible electrophiles, like C-O and C-N electrophiles, have been reported and studied over the past few years. These two years, C-S electrophiles, represented by sulfonium salts, attracted chemists' interest again more than 20 years after Liebeskind's seminal reports¹³. Thus, the achievements of cross-electrophile couplings to construct $\text{Csp}^3\text{-Csp}^2$ and $\text{Csp}^3\text{-Csp}^3$ bonds will be introduced deeply, employing C-O, C-N, C-S, as well as C-X as electrophilic partners in this chapter.

1.2. Content and outline of this thesis

As mentioned, our group has been committed to the Co-catalyzed reductive cross-couplings to achieve all types of C-C bond formation via two C-X electrophiles, C-O and C-X electrophiles, and C-O and C-C (CN) electrophiles.^{6d-g, 14} Thus, we envisioned that $\text{Csp}^3\text{-S}$ electrophiles (alkyl sulfonium salts), $\text{Csp}^3\text{-N}$ electrophiles (alkyl pyridinium salts), $\text{Csp}^3\text{-O}$ electrophiles, at least one non-halogenated electrophiles could be ideal radical precursors to form $\text{Csp}^3\text{-Csp}^2$ or $\text{Csp}^3\text{-Csp}^3$ bonds via cobalt-catalyzed reductive cross-coupling. As shown in **Scheme 3**, we will present our work in the following aspects:



Scheme 3. Work-related to this thesis

¹³ (a) J. Srogl, G. D. Allred, L. S. Liebeskind. *J. Am. Chem. Soc.* **1997**, *119*, 12376. (b) S. Zhang, D. Marshall, L. S. Liebeskind. *J. Org. Chem.* **1999**, *64*, 2796.

¹⁴ C. Dorval, M. Tricoire, J.-M. Begouin, V. Gandon, C. Gosmini. *ACS Catal.* **2020**, *10*, 12819.

- In *Chapter I*, Co-catalyzed reductive construction of Csp³-Csp² bonds from Csp³-S electrophiles represented by benzyl sulfonium salts and Csp²-X (Br, Cl)/Csp²-OTf electrophiles.
- In *Chapter II*, Co-catalyzed reductive construction of Csp³-Csp³ bonds from Csp³-S electrophiles represented by benzyl sulfonium salts and unactive Csp³-X (I, Br) electrophiles.
- In *Chapter III*, the Co-catalyzed reductive construction of the Csp³-Csp³ bond from Csp³-S represented by benzyl sulfonium salts and active Csp³-O electrophiles (allyl acetates, allyl carbonate, and allyl alkyl ether).
- In *Chapter IV*, the Co-catalyzed reductive construction of the Csp³-Csp³ bond from Csp³-N represented by benzyl pyridinium salts and Csp³-O electrophiles (allyl acetates, allyl carbonate, and allyl alkyl ether)

2. Transition Metals-Catalyzed Reductive Cross-Coupling to Construct Csp³-Csp² Bonds

Csp³-Csp² bonds are essential linkages in organic molecules, and their synthesis is one of the most attractive topics in the chemical sciences world. More and more methods have been reported to build Csp³-Csp² bonds with the development of transition metal-catalyzed cross-couplings.^{8a, 15} However, compared to the cross-coupling of an electrophile with an organometallic reagent to build Csp³-Csp² bonds¹⁶, the cross-electrophile reactions leading to Csp³-Csp³ bond formation was developed relatively slowly due to the robust competition of β -hydride elimination and dimerization with cross-coupling processes of the Csp³-electrophiles during the catalytic cycle. They received much attention and were explored widely decades ago since the pioneering work of Gosmini, Gong, and Weix, which used a cobalt /nickel -Mn/Zn catalyzed system to achieve the construction of Csp³-Csp² bonds.

The construction of Csp³-Csp² bonds via cross-electrophile coupling reactions started with two C-X electrophiles (organic halides) due to their abundance and commercial availability. However, the challenge for this method was the inherent difference in reactivity between Csp²- hybrid electrophiles and Csp³- hybrid electrophiles. As a result, the more reactive Csp³- electrophile prefers to form the homo-coupling product. Then the less reactive one conducts the cross-coupling process leading to its symmetric dimer, finally resulting in product mixtures^{2c}. Thus, the exploration of different types of electrophile partners has always aroused general interest in this field. More electrophiles, such as those mentioned above, C-O electrophiles, C-N electrophiles, carboxylate derivatives, *etc.*, were employed to build Csp³-Csp² bonds because of the unremitting effort of chemists in recent years.

2.1. Cross-coupling with two C-X electrophiles.

2.1.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp² bonds.

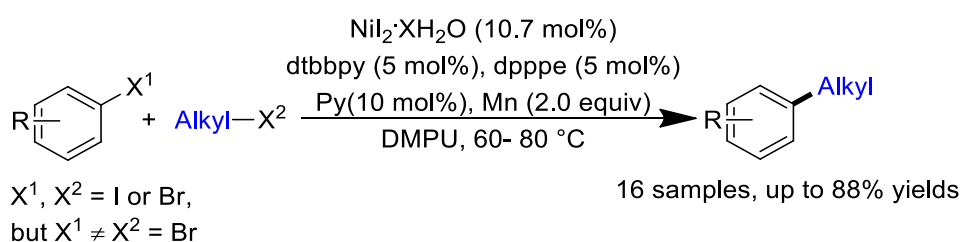
Transition metals-catalyzed reductive cross-coupling between two C-X electrophiles is an essential strategy for constructing Csp³-Csp² bonds. In this field, Ni or Co-catalyzed cross-electrophile coupling developed rapidly. Early in 2010, the Weix group reported a reductive cross-coupling of aryl halides with alkyl halides to build Csp³-Csp² bonds via a dual-ligand nickel catalytic system.¹⁷ (*Scheme 4*) This reaction avoided the intermediacy of a stoichiometric organometallic reagent during the Ni- catalyzed

¹⁵ Selected reviews: (a) X. Pang, R.-D. He, X.-Z. Shu. *Synlett* **2020**, 31, 635. (b) X. Pang, P.-F. Su, X.-Z. Shu. *Acc. Chem. Res.* **2022**, 55, 2491. (c) W. Xue, X. Jia, X. Wang, X. Tao, Z. Yin, H. Gong. *Chem. Soc. Rev.*, **2021**, 50, 4162.

¹⁶ Selected reviews: (a) D. Haas, J.M Hammann, R. Greiner, P. Knochel, *ACS Catal.* **2016**, 6, 3, 1540. (b) R. Jana, T.P. Pathak, M.S. Sigman, *Chem. Rev.* **2011**, 111, 3, 1417. (c) C. Gosmini, J.-M. Bégouin, A. Moncomble, *ChemComm.* **2008**, 28, 3221. (d) G. Cahiez, A.Moyeux. *Chem. Rev.* **2010**, 110, 3, 1435. (e) T. Shu, J. Cossy, *Chem. Eur. J.* **2021**, 27, 43, 11021.

¹⁷ D. A. Everson, R. Shrestha, D. J. Weix. *J. Am. Chem. Soc.* **2010**, 132, 920.

process. The keys to overcoming the challenge that competition of homo-coupling and β -hydride elimination of Csp^3 - electrophiles are: (a) a combination of two ligands, 4,4'-di-*tert*-butyl-2,2'-bipyridine (dtbbpy) and 1,2- bis(diphenylphosphino)benzene (dppbe) improved yields. The addition of bisphosphine (dppbe) as a co-ligand avoided the generation of an aryl dimer, (b) the use of pyridine (Py) diminished β -hydride elimination, (c) 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU) as the solvent raised the yield of cross-coupling efficiently. Moreover, this reaction tolerated various functional groups, such as hydroxy, acetyl, cyano, protected amines, and Bpin, leading to high yields with only 1 equivalent of each coupling partner. On the other hand, alkyl halides, either with unhindered primary, secondary, or neopentyl, could also be coupled with aryl iodides.

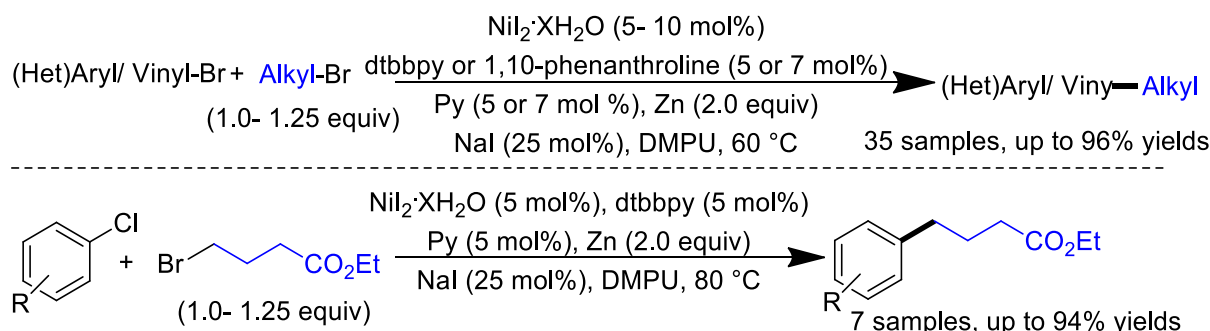


Scheme 4. Nickel-catalyzed reductive cross-coupling of aryl halides (I, Br) with alkyl halides (I, Br).

Later, the Weix group extended the scope of the nickel-catalyzed reductive cross-coupling of aryl halides with alkyl halides to aryl bromides and aryl chlorides with alkyl bromides (*Scheme 5*) under slightly different conditions of the above report.¹⁸ (*Scheme 4*) As shown in *Scheme 5*, aryl and vinyl bromides are coupled with alkyl bromides in high yields via nickel catalysis, when Zn was used as the reductant and sodium iodide as the additive. Under similar conditions but with higher temperature, aryl chlorides with EWG could also be coupled with small excess alkyl bromides (1.25 equivalents), leading to moderate to excellent yields. The experimental results showed that adding NaI reduced the generation of the homo-coupling products of aryl compounds, while replacing Mn with Zn decreased the generation of both the homo-coupling products of aryl compounds and the alkyl halides. The pyridine did not dramatically affect the yield but enhanced the reaction rate. This Ni-catalyzed reductive alkylation of aryl bromides and chlorides with alkyl bromides tolerated highly functional groups (-OH, -NHTs, -OAc, -OTs, -OTf, -COMe, -NHBoc, -NHCbz, -CN, -SO₂Me) and was easily handled (could be conducted in air or moisture atmosphere). Moreover, the mechanistic studies indicated that: (a) oxidative addition of the bromoarene did not play a decisive role in the process, (b) the higher concentration of alkyl bromides and catalyst was beneficial to the reaction, which was the opposite of aryl halide concentration, (c) using an organic reductant (TDAE) instead of metal reductants demonstrated no organozinc reagents were generated in the catalytic cycle. Later, this group extended the nickel-

¹⁸ D. A. Everson, B. A. Jones, D. J. Weix, *J. Am. Chem. Soc.* **2012**, *134*, 6146.

catalyzed reductive cross-electrophile coupling to 2-chloropyridines with alkyl bromides.¹⁹ The difference is that the new method used 4,7-diphenyl-1,10-phenanthroline as the ligand and was conducted in a high concentration of DMF (1.7 M) at slightly lower temperature (40 °C). In recent two years, the Vaidyanathan group reported a nickel-catalyzed reductive cross-electrophile coupling reaction from a substituted 2-chloropyridine and ethyl 3-chloropropanoate with Mn as the reductant activated by chlorotriethylsilane (TESCl).²⁰ This reaction could be scaled up to 7 kg successfully to afford the cross-coupling product in 64% yield.



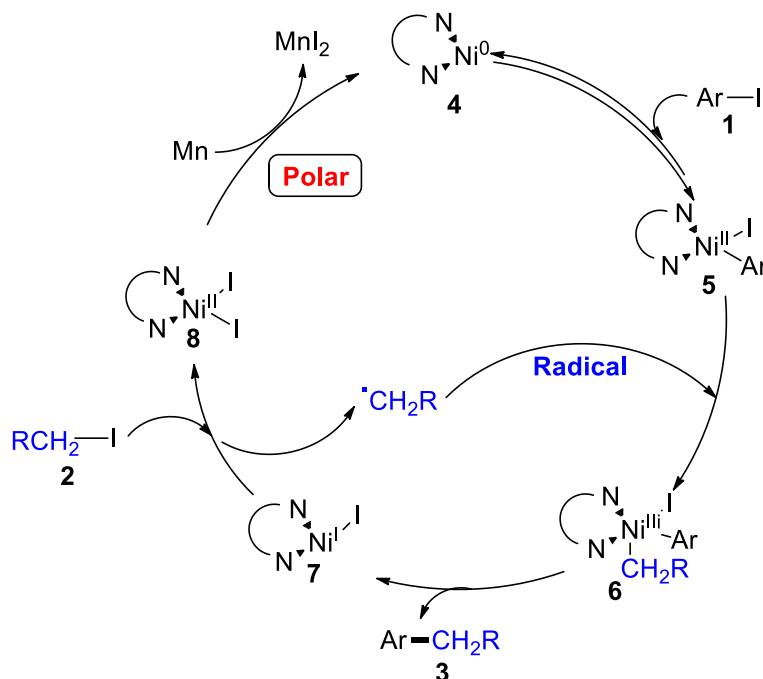
Scheme 5. Nickel-catalyzed reductive alkylation of aryl bromides and chlorides with alkyl bromides

Two years later, Weix uncovered the mechanism and demonstrated that the reaction selectivity arises from the Ni catalytic cycle combining polar and radical steps to generate the new Csp³-Csp² bond.²¹ The experiments showed that: (a) a Ni(0) (L_N)₂ species preferred to form a more stable aryl nickel(II) intermediate **5** with aryl iodide than alkyl nickel(II) species, (b) alkyl-I **2** reacted with complex Ni(I)I(L_N)₂ **7** to lead to an alkyl radical and a Ni(II)I₂(L_N)₂ species **8** during the process, (c) a stoichiometric amount of aryl-nickel(II) intermediate **5** reacted with alkyl-I **2** and delivered the desired product in the absence of a metal reductant. As shown in [Scheme 6](#), the proposal mechanism begins with Ni(II) species **8** reduced by Mn to release Ni(0) species **4**. Then the one underwent oxidative addition with an aryl iodide **1**, resulting in an aryl-Ni(II) species **5**. Next, species **5** reacted with an alkyl radical generated from alkyl-I **2** to form a diorganoNi(III) intermediate **6**, which then released the cross-product **3** via reductive elimination and gave a reactive Ni(I) species **7**. While species **7** reacted with the alkyl-I **2** to generate the alkyl radical mentioned above, along with regenerated Ni(II)I₂(L_N)₂ species **8**.

¹⁹ Everson, D. A.; Buonomo, J. A.; Weix, D. J. *Synlett*, **2014**, 25, 233.

²⁰ S. K. Nimmagadda, S. Korapati, D. Dasgupta, N. A. Malik, A. Vinodini, A. S. Gangu, S. Kalidindi, P. Maity, S. S. Bondigela, A. Venu, W. P. Gallagher, S. Aytar, F. González-Bobes, R. Vaidyanathan. *Org. Process Res. Dev.* **2020**, *24*, 1141.

²¹ S. Biswas, D. J. Weix. *J. Am. Chem. Soc.* **2013**, *135*, 16192.



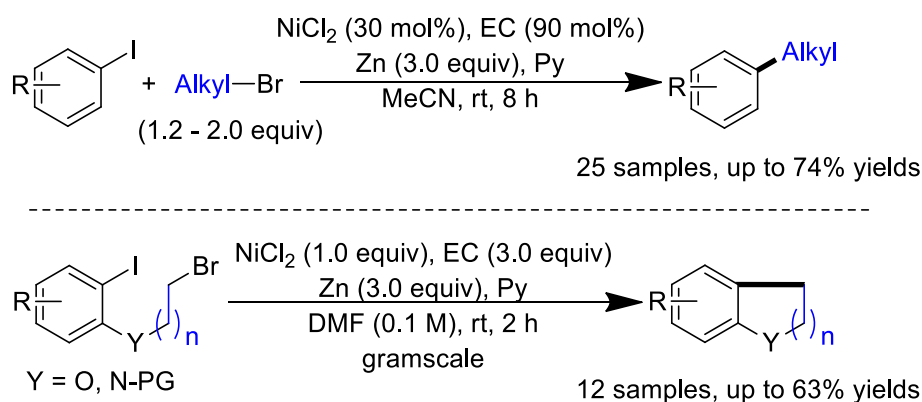
Scheme 6. Proposed mechanism for cross-electrophile coupling of aryl halides with alkyl halides.

Inspired by the work of Weix and Gosmini (which will be introduced in 2.1.2, p20) that Ni or Co catalyzed directly reductive cross-couplings of alkyl halides with aryl halides to build Csp³-Csp² bonds, Peng and his colleagues reported inter- and intramolecular reductive cross-coupling reactions with organohalides.²² Different from the reductive Csp³-Csp² cross-coupling reaction reported by Weix, Peng reported a reductive cross-coupling between substituted iodobenzene and 2-phenyl ethyl bromide (1.2 equivalents) with moderate to good yields. This cross-coupling reaction employed [Ni(0)·2EC·Py] complex, which was generated *in-situ* from a mixture of Zn/NiCl₂/pyridine/ethyl crotonate (EC), as the catalyst in MeCN at rt. (Scheme 7) 30 mol% of NiCl₂ were used to generate the [Ni(0)·2EC·Py] complex. In comparison, 50 mol% of NiCl₂ and 2 equivalents of alkyl bromides were necessary to get moderate yields for some aryl iodides bearing acetyl, hydroxy functional groups, or alkyl bromides with hydroxy, ester phenyl groups. In addition, the scope of this Ni-catalyzed reductive cross-coupling was extended to the intramolecular counterpart. As shown in Scheme 7, the intramolecular reductive coupling with 1 equivalent of Ni catalyst led to indoline and tetrahydroquinoline derivatives with model rate yields on a gram scale. When DMF was used as the solvent instead of acetonitrile, the yields of the desired products increased slightly. Although this Ni-catalyzed intramolecular reductive coupling required a sub-stoichiometric amount of catalyst, the synthesis of the Ni catalyst avoided using volatile, flammable, and highly toxic [Ni(CO)₄], which was reported by Corey and Semmelhack²³. This intramolecular

²² C.-S. Yan, X.-B. Xu, Y.-W. Wang, Y Peng. *Chem. Eur. J.* **2012**, *18*, 6039.

²³ (a) E. J. Corey, M. F. Semmelhack, *J. Am. Chem. Soc.* **1967**, *89*, 2755; For reviews, see: (b) M. F. Semmelhack, *Org. React.* **1972**, *19*, 115. (c) D. C. Billington, *Chem. Soc. Rev.* **1985**, *14*, 93.

C-C cross-coupling strategy provided an approach to these functional, structural motifs that complement those based on C-N and C-O coupling reactions with organometallic reagents, often requiring rather harsh conditions²⁴.

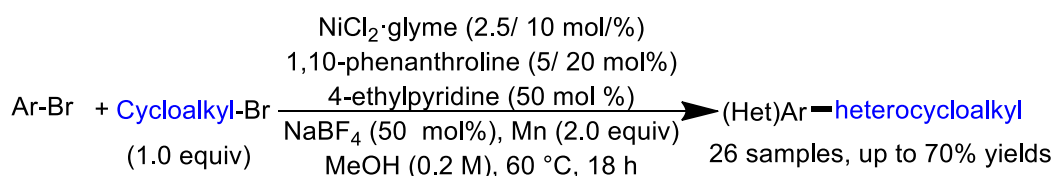


Scheme 7. Ni-catalyzed inter-/ intramolecular reductive cross-coupling of alkyl bromides and aryl iodides

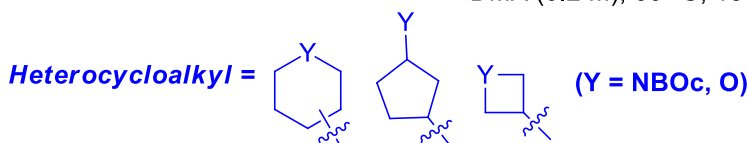
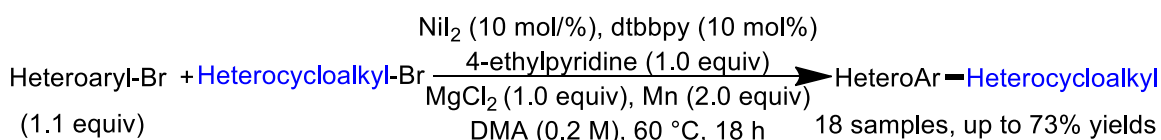
The incorporation of saturated, heteroatom-containing ring systems can occupy a large amount of three-dimensional space, potentially permitting more excellent selectivity toward a druggable target while maintaining good physical properties for sound absorption and selectivity. In 2014, the Molander group developed a method to synthesize the incorporation of nonaromatic heterocycles by Ni-catalyzed reductive cross-coupling of nonaromatic, heterocyclic bromides with aryl or heteroaryl bromides.²⁵ Compared to the methods introduced above, as shown in [Scheme 8](#), the conditions involved air-stable Ni(II) catalyst coordinated with a phenanthroline or dtbbpy ligand, Mn as the reductant, an inorganic salt (NaBF₄), and pyridine derivative as additives in MeOH or DMA at 60 °C. These conditions were suitable for the cross-coupling of N-containing cyclic bromides with (het)aryl bromides, O-containing cyclic bromides with aryl bromides, and heterocyclic alkyl bromides with heteroaryl bromide. Experimental results demonstrated that using 4-ethyl pyridine decreased the amounts of protodehalogenation of the alkyl bromide (Alkyl-H) and avoided biaryl homo-coupling (Ar-Ar). Under these three slightly different conditions, nonaromatic heterocycles were incorporated in moderate to good yields through the direct cross-coupling of nonaromatic heterocyclic structures with (hetero) aryl bromides bearing various functional groups.

²⁴ S. V. Ley, A. W. Thomas, *Angew. Chem.* **2003**, *115*, 5558; *Angew. Chem. Int. Ed.* **2003**, *42*, 5400.

²⁵ K. M. Traister, B. T. O'Neill, G. A. Molander. *J. Org. Chem.* **2014**, *79*, 5771.

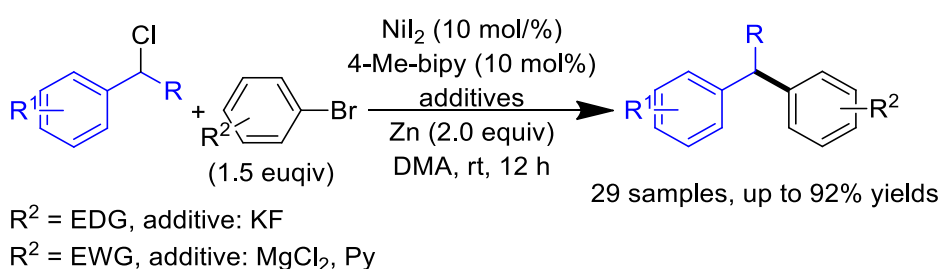


- (a) N-containing cycloalkyl bromides and (het)aryl bromides:
NiCl₂·glyme (10 mol%), *1,10-phenanthroline* (20 mol%).
- (b) O-containing cycloalkyl bromides and aryl bromides:
NiCl₂·glyme (2.5 mol%), *1,10-phenanthroline* (5 mol%).



Scheme 8. Reductive cross-coupling of nonaromatic, heterocyclic bromides with aryl and heteroaryl bromides

In addition to alkyl bromides and alkyl iodides, in 2016, the Gong group presented a method to build Csp³-Csp² bonds via Ni-catalyzed reductive cross-coupling of benzyl chlorides with aryl halides.²⁶ Initially, aryl bromides bearing EDG and EWG were incompatible with the conditions. However, when the former used KF as the additive, and the latter employed MgCl₂ and Py, moderate to good yields were obtained. (**Scheme 9**) On the other hand, the substituted groups on the benzene moieties of benzyl chlorides did not significantly impact the coupling yields. Similar results were also obtained with substituents at the α-position on the benzyl chlorides.



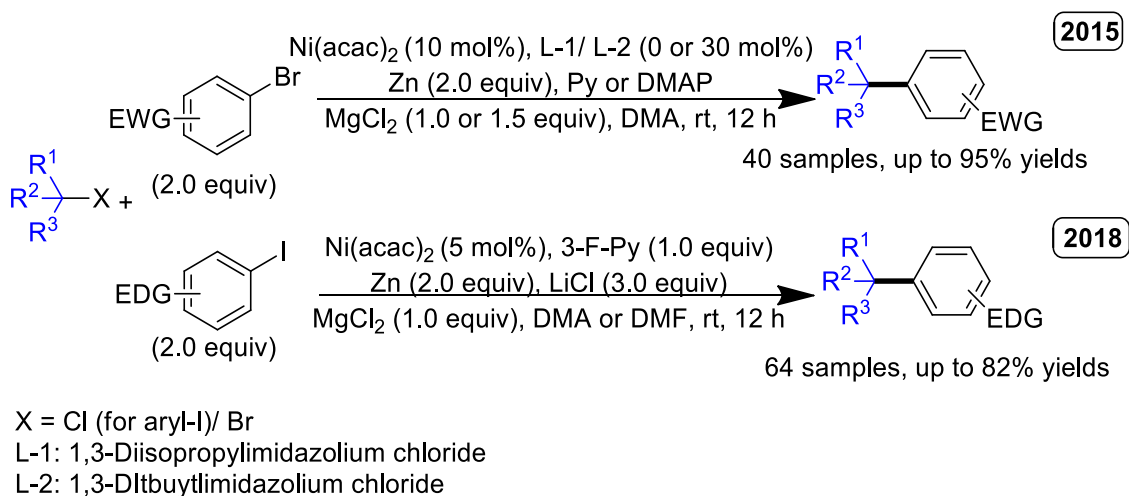
Scheme 9. Nickel-catalyzed reductive cross-coupling of benzyl halides with aryl halides.

Furthermore, the Gong group also described mild reductive arylation reactions between tertiary alkyl halides with aryl halides via Ni catalyst to construct all-carbon quaternary centers, which are widespread in biologically active natural products and pharmaceutical compounds.²⁷ As shown in **Scheme**

²⁶ Q. Zhang, X. Wang, Q. Qian, H. Gong. *Synthesis* **2016**, 48, 2829.

²⁷ (a) X. Wang, S. Wang, W. Xue, H. Gong. *J. Am. Chem. Soc.* **2015**, 137, 11562. (b) X. Wang, G. Ma, Y. Peng, C. E. Pitsch, B. J. Moll, T. D. Ly, X. Wang, H. Gong. *J. Am. Chem. Soc.*, **2018**, 140, 14490.

10, when alkyl bromides are coupled with aryl bromides bearing electron-withdrawing groups, the tertiary alkyl-aryl products were obtained in moderate to excellent yields with excellent functional group tolerance, and good retention to isomerization ratios (R: I) in the Ni(acac)₂/imidazolium salt /Zn / MgCl₂ catalytic system.^{27a} Wherein, the addition of MgCl₂, DMAP, and pyridine was crucial for the catalytic process, without them, only trace or no desired product was detected. The role of DMAP or pyridine needed to be clarified. In contrast, imidazolium salts were demonstrated to act as additives rather than ligands. However, these conditions for tertiary alkyl-aryl compound formation were not compatible with aryl halides with electron-donating groups due to their low coupling efficiency and severe isomerization. To circumvent this problem, Gong described the tertiary alkyl-aryl products formation from alkyl chlorides/ bromides with aryl iodides involving electron-donating groups and applied this strategy to synthesize many natural products, like (+)-asperazine and its analogues.^{27b} As depicted in **Scheme 10**, it was clearly shown that the reaction gave excellent yields with slight modifications, such as employing 3-F-Py as the ligand and LiCl as the additive. In the absence of 3-F-Py, LiCl, or MgCl₂, the yield decreased significantly. It was found that heteroaromatic iodides and chlorocryptamines with either vinyl and dienyl groups or endo and exoesters were compatible with the new conditions.

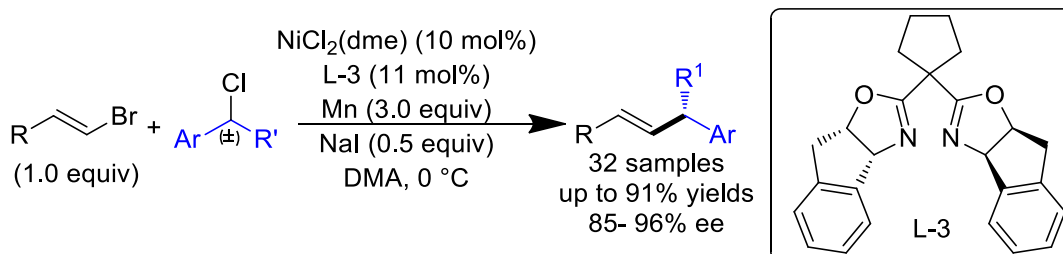


Scheme 10. Nickel-catalyzed reductive coupling of aryl halides with tertiary alkyl halides.

Vinyl halides were also employed as electrophiles to achieve Csp³-Csp² bond formation by Ni or Co-catalyzed (which will be introduced in **2.1.2, p20**). In 2014, the Reisman group first demonstrated a Ni-catalyzed asymmetric reductive cross-coupling of vinyl bromides and benzyl chlorides to synthesize alkenes bearing stereogenic, aryl-substituted tertiary allylic centers.²⁸ This selective alternative approach provided direct access to various enantioenriched alkenyl products in good yields with high

²⁸ A. H. Cherney, S. E. Reisman. *J. Am. Chem. Soc.* **2014**, 136, 14365.

enantiomeric excess under mild conditions (*Scheme 11*). This method avoided the use of organometallic reagents and solved the regioselectivity issues. The cyclopentyl-linked chiral ligand L-3 and low temperature are crucial elements to achieve the high ee value. Furthermore, NaI was used again as an additive since it is known to enhance reactivity in reductive cross-couplings. Its role allowed either the acceleration of electron transfer between Mn and Ni or *in-situ* formation of organic iodide electrophiles²⁹. The mechanistic experiments (the addition of radical inhibitor, radical clock experiment, and using TDAE instead of a metal reductant) demonstrated the presence of the alkyl radicals in this Ni-catalyzed asymmetric reductive cross-coupling. Few years later, Fu and co-workers described an approach for monofluoroalkenylation via nickel-catalyzed defluorinated reductive cross-coupling of *gem*-difluoro alkenes with alkyl halides, employing bis(pinacolato)diboron [(BPin)₂] as a terminal reductant. A large variety of functionalized monofluoroalkenes were obtained under mild reaction conditions with good functional group compatibility and excellent *Z*-selectivity³⁰.



Scheme 11. Ni-catalyzed asymmetric synthesis of alkenes bearing aryl substituted allylic stereogenic centers.

It is also worth mentioning the application of the Ni-catalyzed asymmetric reductive cross-coupling to synthesize enantioenriched acyclic α, α -disubstituted ketones, which are essential synthetic intermediates to generate natural products and pharmaceutical agents. The Reisman group achieved the synthesis of enantioenriched α, α -disubstituted ketones from acid chloride and racemic benzyl chlorides³¹. Earlier than Reisman's report, the Weix group had described the synthesis of racemic functionalized dialkyl ketones from carboxylic acid derivatives and alkyl halides using the combination of NiCl₂(DME), dtbbpy, Mn, and DMA at 0 °C.³² The Gong group also reported a method to form ketone derivatives by Ni-catalyzed reductive coupling of unactivated alkyl halides with aryl acid anhydrides employing Zn as the reductant or by direct coupling of alkyl iodides with aryl acids in the presence of Boc₂O and MgCl₂.³³ In the asymmetric electrophilic version developed by Reisman³¹, similar conditions were used, but in the presence of a chiral ligand L-4, 2,6-dimethyl benzoic acid (DMBA), THF as a co-solvent, and

²⁹ (a) I. Colon, D. R. Kelsey. *J. Org. Chem.* **1986**, *51*, 2627. (b) M. R. Prinsell, D. A. Everson, D. J. Weix. *Chem. Commun.* **2010**, 46,5743.

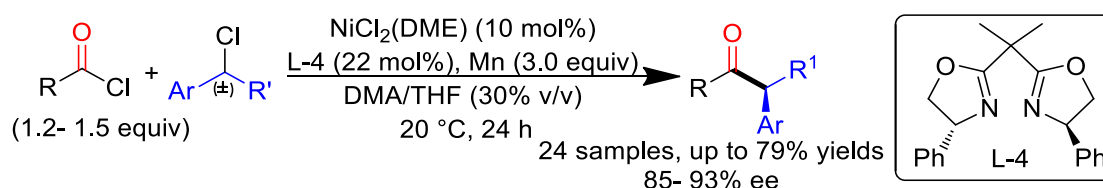
³⁰ X. Lu, Y. Wang, B. Zhang, J.-J. Pi, X.-X Wang, T.-J. Gong, B. Xiao, Y. Fu. *J. Am. Chem. Soc.* **2017**, *139*, 12632.

³¹ A. H. Cherney, N. T. Kadunce, S. E. Reisman. *J. Am. Chem. Soc.* **2013**, *135*, 7442.

³² A. C. Wotal, Weix D. *J. Org. Lett.* **2012**, *14*, 1476.

³³ H. Yin, C. Zhao, H. You, Q. Lin, H. Gong. *Chem. Commun.* **2012**, *48*, 7034.

3 Å molecular sieves to obtain high yield and ee value of α , α -disubstituted ketones at 20 °C. (**Scheme 12**) Adding extra carboxylic acids (DMBA) restrained the homo-coupling of benzyl chlorides and increased the yield of the desired α , α -disubstituted ketones. Notably, no tertiary center isomerization product was produced by the reduced acyl group during the reaction. The proposed mechanism described that a Ni(II)-acyl complex was generated by the oxidative addition of Ni(0) into the acid chloride, and this species was reduced by Mn to give the low valent Ni(I)-acyl species. Then, the Ni(I)-acyl species were subsequently added into benzyl chloride by oxidative addition via a radical process to lead to a Ni(III) complex. Next, this high valent Ni(III) complex underwent reductive elimination to release the desired α , α -disubstituted ketone, and a low valent Ni(I)-chloride complex, which closed the catalytic cycle.



Scheme 12. Ni-catalyzed reductive synthesis of enantioenriched acyclic α , α -disubstituted ketones.

One year later, the Gong group developed a Ni-catalyzed direct reductive coupling of alkyl acids with sterically hindered unactivated tertiary alkyl halides to generate all carbon quaternary ketones. Moreover, this method was suitable to synthesize saturated, fully oxygenated C-acyl glycosides from readily available glycosyl halides and alkyl acids.³⁴ In this reaction, Zn was still used as the reductant, and the addition of MgCl₂ was proposed to promote the reduction of Ni(II) complexes. Mechanistic exploration disclosed that the alkyl radical could be generated from the reaction of the halide with the low-valent of the Ni(I) species to give the alkyl-Ni(II)X species.

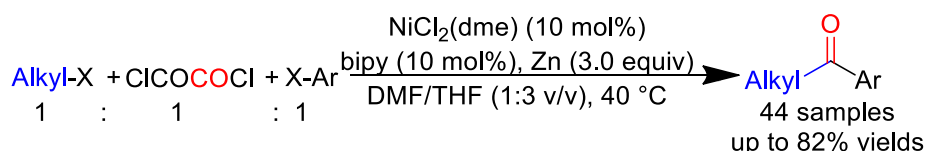
Besides acid chlorides used as electrophilic partners to synthesize the disubstituted ketones, inserting CO into organic molecules is also one of the most popular methods to get various carbonyl derivatives. However, CO gas is hazardous and typically coordinates with Ni catalysts to generate a poisonous, volatile, and inert metal carbonyl complex during carbonylation.³⁵ Thus, Shi and Bai reported a nickel-catalyzed reductive carbonylation using oxalyl chloride as a readily available CO surrogate since oxalyl chloride is a cheap, commercially available, and very common organic reagent in chemical reactions.³⁶ In this report, only a 1:1:1 ratio of aryl iodides, alkyl halides, and oxalyl chloride under mild conditions could achieve high chemoselectivity. (**Scheme 13**) In addition, primary and secondary alkyl iodides

³⁴ C. Zhao, X. Jia, X. Wang, H. Gong. *J. Am. Chem. Soc.* **2014**, *136*, 17645.

³⁵ (a) T. Morimoto, K. Kakiuchi. *Angew. Chem., Int. Ed.* **2004**, *43*, 5580. (b) D. U. Nielsen, K. T. Neumann, T. Skrydstrup. *Chimia* **2018**, *72*, 606. (c) J.-B. Peng, H.-Q. Geng, X.-F. Wu. *Chem* **2019**, *5*, 526.

³⁶ J. Wang, Y. Yin, X. He, Q.-L. Duan, R. Bai, H.-W. Shi, R. Shi. *ACS Catal.* **2023**, *13*, 8161.

were also compatible with the conditions. Mechanistic studies indicated that the reaction between oxalyl chloride and Zn released the same amount of CO₂ and CO under mild reaction conditions. Compared to using oxalyl chloride as a CO surrogate, Hu and coworkers described nickel-catalyzed carbonylation of alkyl halides using ethyl chloroformate as a CO source³⁷ which was also used in the previous cobalt-catalyzed synthesis of symmetrical diaryl ketones reported by Gosmini³⁸.



Scheme 13. Nickel-catalyzed reductive carbonylation by oxalyl chloride as the carbonyl source.

In addition, some metallaphotoredox-catalyzed cross-electrophile couplings to construct Csp³-Csp² bonds were also reported. For example, in 2016, the MacMillan group developed a strategy for the cross-coupling of alkyl bromides with aryl or heteroaryl bromides in the presence of commercially available tris(trimethylsilyl)silane and the metallaphotoredox catalysis NiCl₂(dtbbpy) and [Ir[dF(CF₃)ppy]₂(dtbbpy)]PF₆ in excellent yields.³⁹ Last year, Barham also described a cross-electrophile coupling between two different organic halides catalyzed by the combination of NiCl₂·(glyme) and an organophotocatalysis (1,2,3,5-Tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (4-CzIPN)) to form C-C bonds, not only Csp³-Csp² but also Csp³-Csp³/ Csp²-Csp²/ Csp²-Csp³ bonds.⁴⁰ It is worth mentioning that cheap triethylamine was used as a precursor to provide α-aminoalkyl radicals, which were employed as halogen atom transfer (XAT) agents.

2.1.2. Co-catalyzed reductive cross-coupling to construct Csp³-Csp² bonds

As introduced above, halides are widely studied and frequently used as electrophiles in organic synthesis due to their relatively high reactivity. In transition metals-catalyzed reductive cross-coupling field, Co catalysts which are more eco-compatible than Ni catalysts, have also shown excellent performance in reductive cross-couplings of C-X electrophiles to build Csp³-Csp² bonds with various sensitive functional groups.

In 2010, the Gosmini group reported a cobalt-catalyzed alkylation of aryl halides under simple and mild conditions^{6f}. Compared to Weix 's work²¹, this Co-catalyzed alkylation reaction required only the *i*Pr₂PhP or bipy as the ligands (depending on the nature of the alkyl halides) associated with CoBr₂ to synthesize various cross-coupling products in good to excellent yields. (Scheme 14) In this CoBr₂/ligand

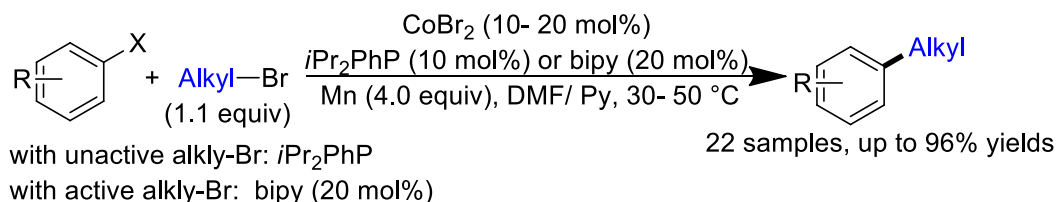
³⁷ R. Shi, X. Hu, *Angew. Chem. Int. Ed.* **2019**, *58*, 7454; *Angew. Chem.* **2019**, *131*, 7532.

³⁸ A. Rérat, C. Michon, F. Agbossou-Niedercorn, C. Gosmini. *Eur. J. Org. Chem.* 2016, 4554.

³⁹ P. Zhang, C. Le, D. W. C. MacMillan. *J. Am. Chem. Soc.* **2016**, *138*, 8084.

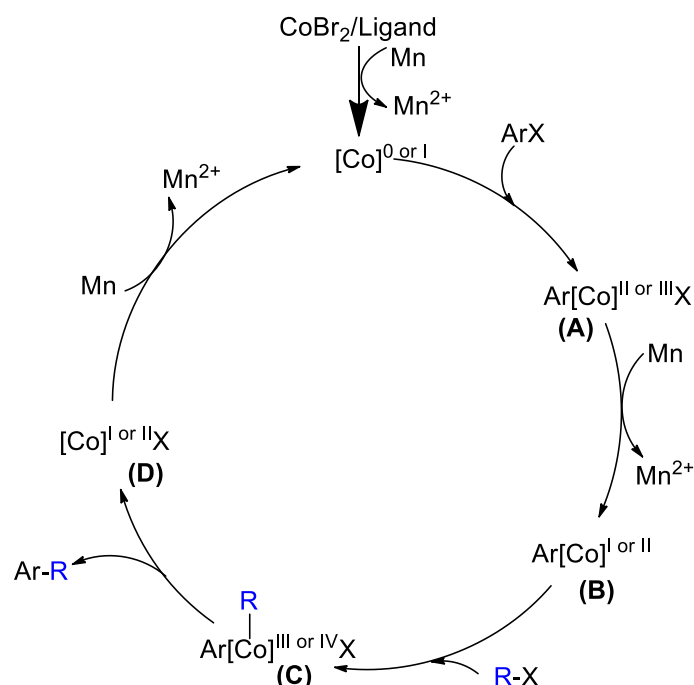
⁴⁰ X. Tian, J. Kaur, S. Yakubov, J. P. Barham. *ChemSusChem* **2022**, e202200906.

/Mn catalytic system, aryl bromides bearing EWG or aryl chlorides with EWG coupled well with unreactive primary or secondary alkyl bromides bearing a β -hydrogen atom. Moreover, some sensitive functional groups such as esters, nitriles, or ketones could be tolerated on both coupling partners. With more reactive alkyl halides, like benzyl chlorides, or ethyl 3-bromopropionate, bipy was employed as the ligand to deliver the desired product in good yields.



Scheme 14. Cobalt-catalyzed direct alkylation of aryl halides.

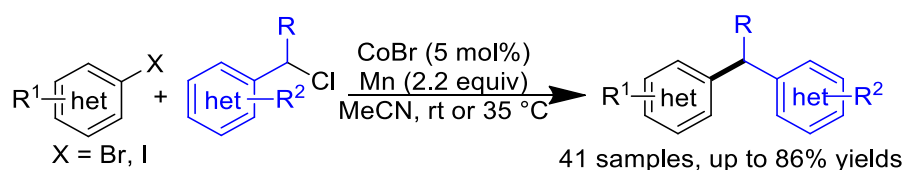
Refereeing to the previously reported Co-catalyzed synthesis of biaryl compounds⁴¹, the proposed mechanism was shown in **Scheme 15**. Initially, low valent Co (0 or I) species generated from the reduction of the Co(II) complex by Mn underwent oxidative addition to the aryl halide giving an aryl cobalt intermediate (**A**). Next, the intermediate (**A**) was reduced by Mn again, leading to the ArCo(I or II) species (**B**), which reacted with the Csp³-X partner to form an Ar-Co-R complex (**C**) that displayed sufficient stability towards unproductive β -hydride elimination. The cross-coupling product was obtained by reductive elimination and regenerated an active Co species.



Scheme 15. The postulated mechanism for the direct alkylation of aryl halides.

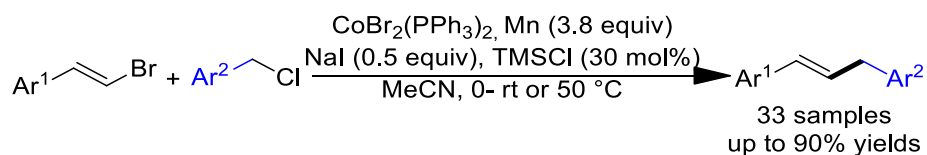
⁴¹ (a) M. Amatore, C. Gosmini, J. Perichon, *J. Org. Chem.* **2006**, *71*, 6130. (b) C. Amatore, A. Jutand, *Organometallics* **1988**, *7*, 2203.

Several years later, the Gosmini group improved the cobalt-catalyzed direct arylation of benzyl chlorides to form functionalized diarylmethanes.⁴² As shown in *Scheme 16*, diarylmethanes were obtained from reductive cross-coupling between benzyl chlorides and aryl halides bearing either EWG or EDG in pretty simple conditions: only low equivalents of Co catalyst, Mn as the reductant in acetonitrile as a sole solvent without the presence of ligand and pyridine at rt or 35 °C. It should be mentioned that adding secondary benzylic chlorides dropwise led to the cross-coupling product in good yield in a one-step procedure due to the increased reactivity of α -position substituted benzyl chlorides. Moreover, heteroaryl rings either on the aryl or the alkyl partners were compatible with these conditions for this cobalt-catalyzed reductive synthesis of diarylmethanes.



Scheme 16. Cobalt-catalyzed reductive cross-coupling between benzyl chlorides and aryl halides.

One year later, the Co-catalyzed reductive cross-coupling involving benzyl halides was extended to alkenyl halides to construct Csp^3-Csp^2 bonds by this group.⁴³ (*Scheme 17*) Like Reisman's work²⁸, this Co-catalyzed alkylation reaction proceeded smoothly in acetonitrile in the presence of $[CoBr_2(PPh_3)_2]$ as the catalyst and TMSCl as the activator to Mn. Both EDG and EWG on phenyl moieties of both electrophilic partners were tolerated, leading to moderate to excellent yields. However, the reaction conditions were not suitable for secondary benzyl halides using either TMSCl or TFA. Furthermore, a stereochemical investigation demonstrated the retention of the double-bond configuration.



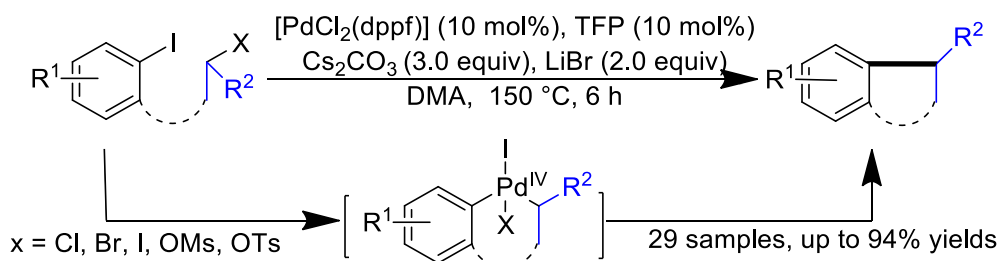
Scheme 17. Cobalt-catalyzed reductive cross-coupling between styryl and benzyl halides.

⁴² S Pal, S. Chowdhury, E. Rozwadowski, A. Auffrant, C. Gosmini. *Adv. Synth. Catal.* **2016**, *358*, 2431.

⁴³ Y. Cai, A. D. Benischke, P. Knochel, C. Gosmini. *Chem. Eur. J.* **2017**, *23*, 250.

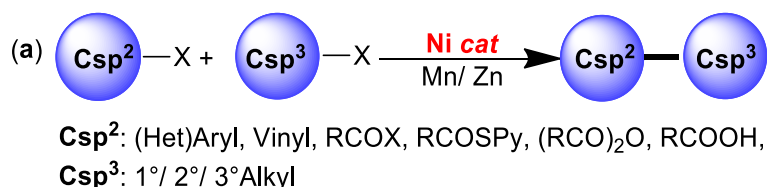
2.1.3. Pd-catalyzed reductive cross-coupling to construct Csp³-Csp² bonds.

Pd catalysts are generally associated with cross-coupling reactions with organometallic derivatives. In 2006, Wang and coworkers reported a palladium-catalyzed synthesis of symmetrical and unsymmetrical biaryls from the direct coupling of aryl halides in poly(ethylene glycol).⁴⁴ It is known that the use of palladium catalysts easily results in β -hydrogen elimination. Thus, Pd-catalyzed reductive Csp³-Csp² cross-coupling is relatively rare reported. In 2014, Jiang and co-workers described a palladium-catalyzed intramolecular cross-coupling of Csp²-I and Csp³-X bonds through double oxidative addition and reductive elimination via a Pd(IV) intermediate.⁴⁵ (Scheme 18) Compared to the mentioned Ni-catalyzed intramolecular cross-coupling of two C-X electrophiles²², in this reaction, additional ligand tri(2-furyl)phosphine (TFP) increased the yield of the desired products; DMA acted as an essential element to provide reductive atmosphere by reduced Pd(II) complex to the Pd(0) active species; while the use of two equivalents of LiBr as the additive was speculated further to prohibit the β -hydrogen elimination of the Csp³-X bond. This reaction showed good functional group tolerance, and various indoline derivatives were synthesized in moderate to excellent yields. Moreover, replacing Csp³-X with Csp³-OMs/OTs was also compatible with these intermolecular reductive conditions. In addition, intramolecular cross-couplings of vinyl iodides and alkyl iodides were also possible, giving moderate to good yields.



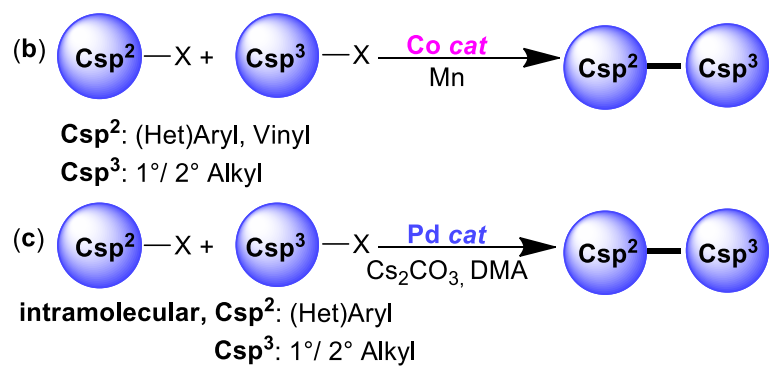
Scheme 18. Palladium-catalyzed intramolecular reductive cross-coupling of Csp³-Csp² bond formation.

According to the above introductions of reductive cross-coupling to construct Csp³-Csp² bonds, it can be summarized as follows (Scheme 19):



⁴⁴ (a) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire. *Chem. Rev.* **2002**, *102*, 1359. (b) L. Wang, Y. Zhang, L. Liu, Y. Wang. *J. Org. Chem.* **2006**, *71*, 3, 1284.

⁴⁵ H. Liu, J. Wei, Z. Qiao, Y. Fu, X. Jiang. *Chem. Eur. J.* **2014**, *20*, 8308.



Scheme 19. Ni/ Co/ Pd reductive cross-coupling to construct Csp³-Csp² bonds.

2.2. Cross-coupling with C-X and C-O electrophiles

As introduced above, C-halide electrophiles have been widely employed as convenient electrophilic partners in reductive cross-coupling reactions to build Csp³-Csp² bonds over the last decades. However, the high price, environmental toxicity, and sluggish preparation of organohalides often limit their application in industrial synthesis.⁴⁶ Thus, exploring other environmentally-friendly electrophiles is always a hot topic in transition metal-catalyzed reductive cross-coupling. To date, with the effort of the chemist, a number of electrophiles other than alkyl halides have been investigated and applied to realize Csp³-Csp² cross-electrophile couplings. In this part, the investigation of C-X electrophiles and C-O electrophiles derived from abundant alcohols or phenols will be described in transition metals-catalyzed reductive cross-couplings.

2.2.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp² bonds.

In 2016, Jarvo and co-workers developed an inter- and intramolecular reductive cross-coupling reaction between benzylic pivalate esters (OPiv) and aryl halides (Br) in the presence of the catalytic NiBr₂(glyme), bathophenanthroline (BPhen) as ligand, and Zn as the reductant in DMA at rt or 50 °C. The reaction tolerated a range of heterocycles and functional groups to generate various indanes, tetralins, or diarylmethanes.⁴⁷ In recent years, the Shu group reported Ni-catalyzed cross-couplings between C_{vinyl}-O electrophiles and alkyl halides to form a Csp³-Csp² bond (**Scheme 20**).^{9c, 48} As known, allyl boronates are essential reagents in organic synthesis for the allylation of carbonyl compounds and in cross-coupling reactions.⁴⁹ In 2020, the Shu group demonstrated an approach to the synthesis of cyclically allyl boronates from vinyl triflates and α-chloroboronates in the presence of NiBr₂ as the catalyst, bipy as the ligand, Mn as the reductant, and NaBr as the additive in DMF at -15 °C.⁴⁸ (**Scheme 20. eq 1**). NaBr is proposed to act similarly to NaI mentioned in the above reports (for example, ref 29), generating more reactive α-bromoboronates via *in-situ* halide exchange of α-chloroboronates with NaBr. Thus, the yield of the desired product was increased, and the vinyl dimerization process was partly inhibited. The reaction had to be conducted at a relatively low temperature (-15 °C) due to the formation of a significant amount of vinyl dimer at room temperature. Last year, this group reported a Ni-catalyzed reductive alkylation of alkenyl acetates with alkyl bromides.^{9c} It should be pointed out that alkenyl acetates obtained from ketones were already used in Co-catalyzed reductive cross-coupling to form Csp²-Csp² bonds by Gosmini⁵⁰. Compared to these two alkylation reactions

⁴⁶ D.-G. Yu, B.-J. Li, Z.-J. Shi. *Acc. Chem. Res.* **2010**, *43*, 12, 1486.

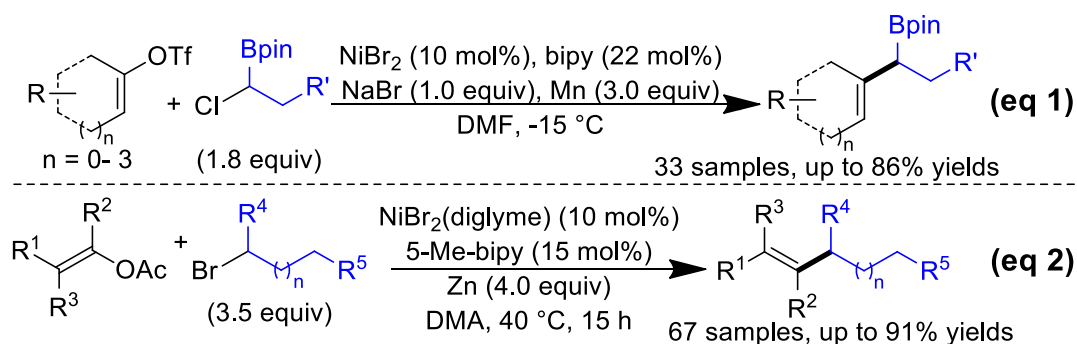
⁴⁷ M. O. Konev, Luke E. Hanna, and Elizabeth R. Jarvo. *Angew. Chem.* **2016**, *128*, 6842.

⁴⁸ (a) J.-B. Qiao, Z.-Z. Zhao, Y.-Q. Zhang, K Yin, Z.-X. Tian, X.-Z. Shu. *Org. Lett.* **2020**, *22*, 5085.

⁴⁹ M. Raducan, R. Alam, K. J. Szabó. *Angew Chem.* **2012**, *51*, 13050.

⁵⁰ M. Amatore, J. Périchon, C. Gosmini. *Eur. J. Org. Chem.* **2005**, 989.

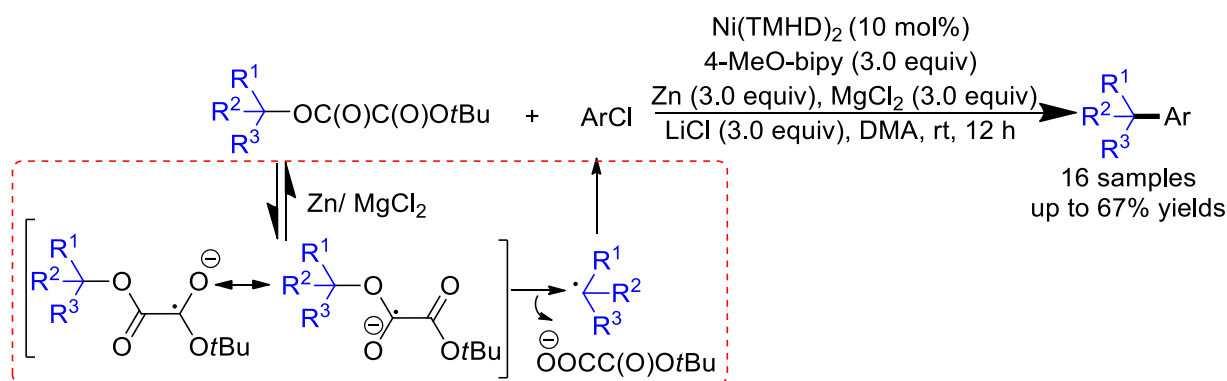
depicted in *Scheme 20*, it is obvious that in the case of the coupling with the more stable alkenyl C-O electrophiles (alkenyl acetates), more excess amount of alkyl bromide (3.5 equivalents) had to be employed. Zn instead of Mn was more suitable for the alkylation process of alkenyl acetates (*Scheme 20*, *eq 2*). Various functionalities, such as aldehyde, amide, and cyano group, were well tolerated under mild conditions with organometallic reagents. This reaction complemented the established method for the alkylation of stable alkenyl C-O electrophiles. Moreover, the mechanistic studies proved that the alkenyl acetate was activated by Ni(I) species in these conditions, different from the introduced pathway of Csp^2-X electrophiles activated by Ni(0) species²¹



Scheme 20. Ni-catalyzed cross-couplings between $C_{\text{vinyl-O}}$ electrophiles and alkyl halides.

In addition to the Csp^3-X as an alkyl radical source, the Gong group extended the cross-coupling of tertiary Csp^3-X electrophiles²⁷ to the C-O electrophiles, which were not based on esters⁵¹, carbonates, or sulfonate but on oxalates.^{10a} In this reaction, tertiary alkyl radicals were formed from C-O bond cleavage, which of alkyl oxalate was activated by Zn/ $MgCl_2$. (*Scheme 21*) A wide range of $3^\circ R_{\text{alkyl-Ox-tBu}}$ coupled with aryl chlorides bearing EWG led to moderate yields. Both open-chain and cyclic tertiary oxalates were compatible with these conditions. Except for the construction of quaternary carbon center compounds, his group also reported a reductive cross-coupling of α -hydroxycarbonyl compounds modified with oxalyl groups and aryl halides^{10b}, as well as iron-catalyzed reductive vinylation of tertiary alkyl oxalates with vinyl bromides^{10d}.

⁵¹ X. Tao, Y. Chen, J. Guo, X. Wang, H. Gong. *Chem. Sci.* **2021**, *12*, 220.



Scheme 21. Arylation of tertiary alkyl oxalates with aryl chlorides.

Carboxylic acids and their derivatives used as the C-O electrophiles, which are mainly employed to synthesize a variety of ketones in the former part (2.1.1, p11), were also used to achieve Csp³-Csp² bond formation in recent years. Acyl fluorides rather than acyl chlorides as coupling partners via decarboxylation were described to build Csp³-Csp² bonds with alkyl bromides via a nickel-catalyzed reductive cross-coupling by Nishihara and co-workers last year.⁵² At the same time, abundant alkyl alcohols were directly employed as electrophilic partners and coupled with aryl bromides to synthesize alkylation products. Because of the strong C-O bond strength, the hydroxy group is always defined as a poor leaving group; thus, when alcohols were used as electrophiles in Ni-catalyzed reductive cross-couplings, they always underwent an alcohol transformation process through metal reagents (usually Ti species)⁵³ or organic reagents^{54, 55} (halides resources or carbonyl derivatives) in a one-pot reaction.

In 2018, the Shu group reported a combination of NiCl₂(dppp) and ZrCl₄ as the catalytic system used for the cross-electrophile coupling of aryl halides with allylic alcohols to form linear allylarenes selectively, with Mn as the reductant and bipy as the ligand. Preliminary mechanistic experiments proposed that allylic alcohols were activated by ZrCl₄ and then coupled with ArNi(I) species.⁵⁶ While in Suga and Ukaji's work⁵³, low-valent titanium reagents were used to incorporate carbon radicals from the homolytic C-O bond cleavage of benzyl alcohols via Ni catalysis (Scheme 22, eq 3). The reaction between benzyl alcohols and aryl halides in the presence of a Ni catalyst, TiCl₄(lutidine), 2,6-lutidine, and Mn as the reductant in THF at reflux temperature afforded the cross-coupling products in high yields. The use of 2,6-lutidine could cause a significant positive effect for parts of benzyl alcohols. Their later report also demonstrated that these reaction conditions were also suitable for the coupling of benzyl alcohols and alkenyl bromides with TiCl₄(collidine) and additional collidine.⁵⁷ Rahaim reported that

⁵² Q. Chen, J. You, T. Tian, Z. Li, M. Kashiara, H. Mori, Y. Nishihara. *Org. Lett.* **2022**, *24*, 9259.

⁵³ T. Suga, Y. Ukaji. *Org. Lett.* **2018**, *20*, 7846.

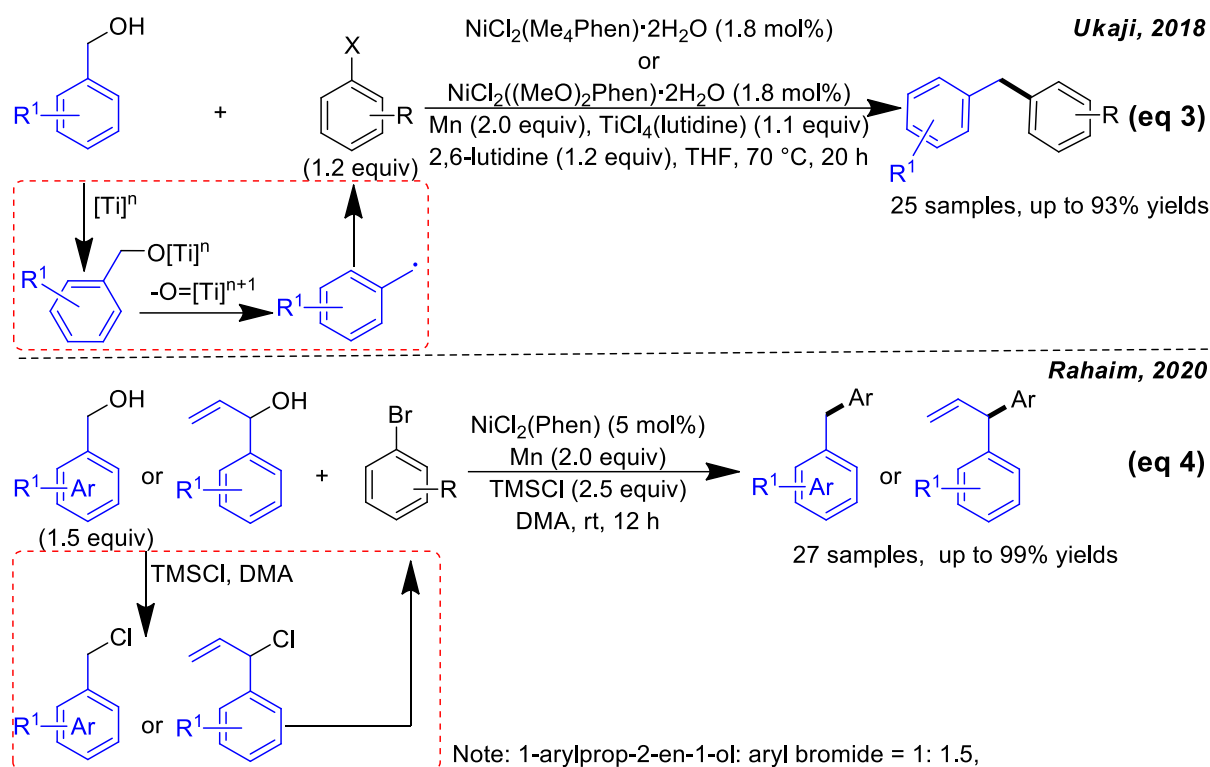
⁵⁴ V. K. Chenniappan, D. Peck, R. Rahaim. *Tetrahedron Lett.* **2020**, *61*, 151729.

⁵⁵ P. Guo, K. Wang, W.-J. Jin, H. Xie, L. Qi, X.-Y. Liu, X.-Z. Shu. *J. Am. Chem. Soc.* **2021**, *143*, 513.

⁵⁶ X.-G. Jia, P. Guo, J. Duan, X.-Z. Shu. *Chem. Sci.*, **2018**, *9*, 640.

⁵⁷ T. Suga, Y. Takahashi, Y. Ukaji. *Adv. Synth. Catal.* **2020**, *362*, 5622.

TMSCl was used as an additive to convert benzyl alcohols to benzyl chlorides *in-situ*.⁵⁴ (Scheme 22, eq 4) Notably, when substituted carbon of 1-arylprop-2-en-1-ols were employed as the partner, the linear product was the major one. This reaction also showed high stereoselectivity favoring the formation of the *E*-isomer.



Scheme 22. Nickel-catalyzed cross-electrophile coupling between benzyl alcohols and aryl halides

Moreover, in 2021, Wang reported a Ni-catalyzed reductive allylation reaction between activated alcohols and challenging aryl chlorides, in which 1.0 equivalent of $MgCl_2$ acted as a Lewis acid to activate alcohols and Zn as the metal reductant.⁵⁸ In the same year, Wang and Liang described a Ni-catalyzed dehydroxylation C-C coupling of phenyl-phosphonium salts and allylic alcohols. In this reaction, Lewis acids- $ZrCl_4$ (10 mol%) and $LaCl_3$ (100 mol%) were used to activate alcohols.⁵⁹ In addition to the activated alcohol, the dihydroxylation of non-activated alcohols was also developed. The Gong group disclosed that a combination of *2-chloro-3-ethylbenzo[d]oxazol-3-ium salt (CEBO)* and *tetra butyl ammonium bromide (TBAB)* could transfer various non-activated alkyl alcohols into their corresponding bromide counterparts rapidly in the MeCN, and then coupled with aryl halides via Ni catalysis in mild condition.⁶⁰ In contrast, Weix and co-workers used a combination of *Hendrickson's POP reagent* ($[(Ph_3P)_2O](OTf)_2$) and *TBAB* as an alternative to achieve the activation through alcohol bromination.⁶¹

⁵⁸ H. Yu, Z.-X Wang. *Org. Biomol. Chem.* **2021**, *19*, 9723.

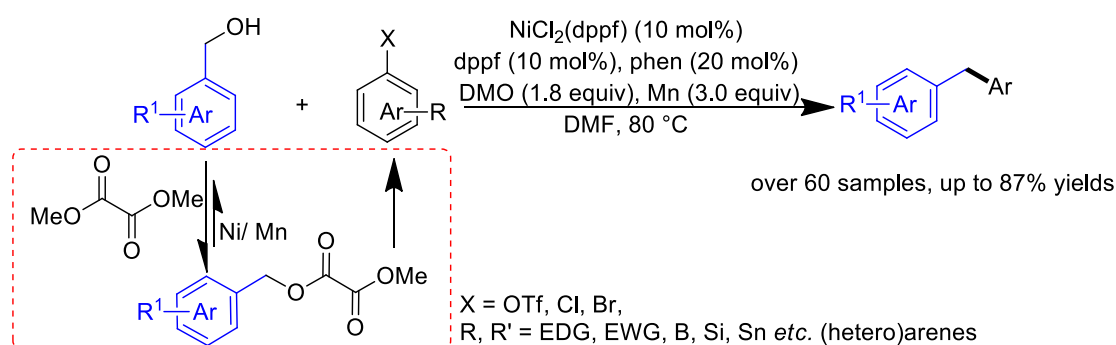
⁵⁹ H. Wang, M. Yang, Y. Wang, X. Man, X. Lu, Z. Mou, Y. Luo, H. Liang. *Org. Lett.* **2021**, *23*, 8183.

⁶⁰ Q. Lin, G. Ma, H. Gong. *ACS Catal.* **2021**, *11*, 14102.

⁶¹ B. K. Chi, J. K. Widness, M. M.; Gilbert, D. C. Salgueiro, K. Garcia, D. J. Weix. *ACS Catal.* **2022**, *12*, 580.

Except for the reactions involving Ni catalysis mentioned above, metallaphotoredox-based cross-coupling of tertiary alcohols and heteroaryl bromides was also developed, which used *N-heterocyclic carbene salts* to activate free alcohols and then subsequently achieved C-O bond homolytic cleavage.⁶²

In recent years, oxalates have demonstrated to be great leaving groups for the deoxygenated functionalization of alcohols⁶³ (part of the work related to oxalates will be introduced in 3.1.1, p43). After reporting a reductive coupling of benzyl oxalates with highly functionalized alkyl bromides by nickel catalysis (which will be introduced in 3.2.1, p45), the Shu group demonstrated a nickel-catalyzed dynamic kinetic cross-coupling directly from functionalized alcohols and (hetero) aryl electrophiles under mild condition⁵⁵. (Scheme 23) The presence of additional dppf increased yield by 30%. The 1,10-Phenanthroline (phen) was not mandatory for the reaction but helped to raise the yield and performed better than other nitrogen ligands. This reaction could achieve C-O bond cleavage to build Csp³-Csp² bonds by the Ni/Mn catalytic system. Wherein adding *dimethyl oxalate (DMO)* as an activator which is proposed to form benzyl oxalates *in-situ*, and then rerelease a radical species. Moreover, this reaction demonstrated excellent advantages in substrate tolerance, functional group compatibility, unique chemoselectivity, and application in the synthesis of biologically active molecules, and peptide modification. It should be noticed that with heterobenzyl alcohols, pyridine (10 mol %) and AlCl₃ (10 mol %) were added additionally. AlCl₃ not only slowed down the process that the alcohol transferred into the oxalates but enhanced the reactivity of aryl triflates to improve the yield and selectivity for the cross-products. One year later, his group reported a Ti-catalyzed dehydroxylation alkenylation of tertiary alcohols with alkenyl halides to construct the vinylated all-carbon quaternary centers. The reaction showed good tolerance in various functionalities under mild conditions.⁶⁴



Scheme 23. Ni-catalyzed dynamic kinetic cross-electrophile arylation of benzyl alcohols.

⁶² Z. Dong, D. W. C MacMillan. *Nature* **2021**, 598, 451.

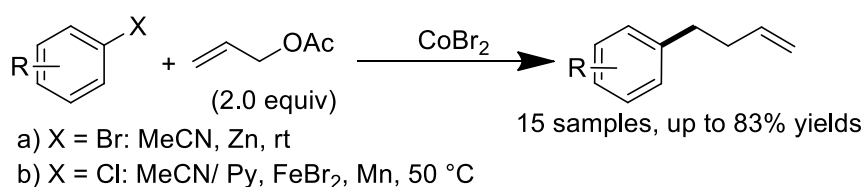
⁶³ Photoredox-Catalyzed examples with oxalates: (a) G. L. Lackner, K. W. Quasdorf, L. E. Overman. *J. Am. Chem. Soc.* **2013**, 135, 15342. (b) C. C. Nawrat, C. R. Jamison, Y. Slutskyy, D. W. C. MacMillan, L. E. Overman. *J. Am. Chem. Soc.* **2015**, 137, 11270. (c) Y. Slutskyy, C. R. Jamison, P. Zhao, J. Lee, Y. H. Rhee, L. E. Overman. *J. Am. Chem. Soc.* **2017**, 139, 7192.

⁶⁴ H. Xie, S. Wang, Y. Wang, P. Guo, X.-Z. Shu, *ACS Catal.* **2022**, 12, 1018.

During the development of the transition metals-catalyzed process, some dual metal-catalyzed reductive cross-couplings of C-O electrophiles and C-X electrophiles to construct Csp³-Csp² bonds were also disclosed in this field. Like in 2017, Komeyama and co-workers reported a reductive coupling of aryl halides and non-activated alkyl tosylates catalyzed by NiBr₂, assisted with nucleophilic vitamin B₁₂ (VB₁₂: cyanocobalamin).⁶⁵ The role of VB₁₂ was to activate the tosylate and provided alkyl-Co(III) species. Then, this species reacted with ArNi(I) species to generate Ar-alkylNi(III) species, which released Csp³-Csp² cross-coupling products through reductive elimination.

2.2.2. Co-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

In the early 2000s, the Gosmini group successively reported Co-catalyzed electroreductive arylation from allyl acetates and aryl halides⁶⁶ and reductive arylation cross-coupling in DMF or acetonitrile associated with the pyridine⁶⁷. In reductive cross-coupling reaction (**Scheme 24**), the Co-Zn catalytic system was required for the coupling of allyl acetates and aryl bromides. To decrease the amount of the reduced product (ArH), a catalytic amount of bromobenzene was added to limit the hydrogenation of aryl bromide. In comparison, the Co-Fe-Mn reductive system was employed for less active aryl chlorides. This method was compatible with several substituents, such as -CN, -CF₃, and led to moderate to good yields.



Scheme 24. Co-catalyst cross-coupling between aryl halides and allylic acetates.

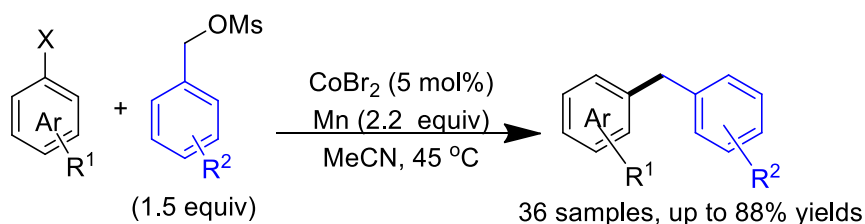
In addition to employing an allyl acetate as a C-O electrophilic partner, the Gosmini group described a method to synthesize functionalized diarylmethanes from benzyl mesylates and aryl halides in 2018.^{7b} Compared to the synthesis of diarylmethanes already introduced by the same group⁴², this method used a straightforward catalytic system involving only CoBr₂ and Mn as a reductant in acetonitrile at 45 °C, realizing the reductive Csp³-Csp² cross-coupling in the absence of any additives or ligands. (**Scheme 25**) Besides the aryl halides, heteroaryl halides were also applied under the condition, leading to moderate to good yields. In the case of α -substituted benzyl mesylate, good yields were obtained with aryl bromides if benzyl mesylates were added dropwise. It is worth highlighting that this procedure could also be carried out directly from the benzyl alcohol without isolating benzyl mesylate,

⁶⁵ R Ohata, S. Kiguchi, I. Osaka, K. Komeyama. *Chem. Commun.*, **2017**, 53, 6401.

⁶⁶ P. Gomes, C. Gosmini, J. Périchon, *J. Org. Chem.* **2003**, 68, 1142.

⁶⁷ P. Gomes, C. Gosmini, J. Périchon. *Org. Lett.* **2003**, 5, 7, 1043.

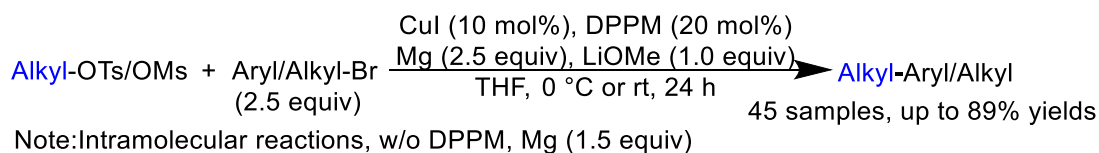
leading to slightly lower yields of coupling products. Preliminary mechanistic studies proposed a benzyl radical likely involved in this reductive cross-coupling.



Scheme 25. Cobalt-catalyzed diarylmethanes from benzyl mesylates and aryl halides.

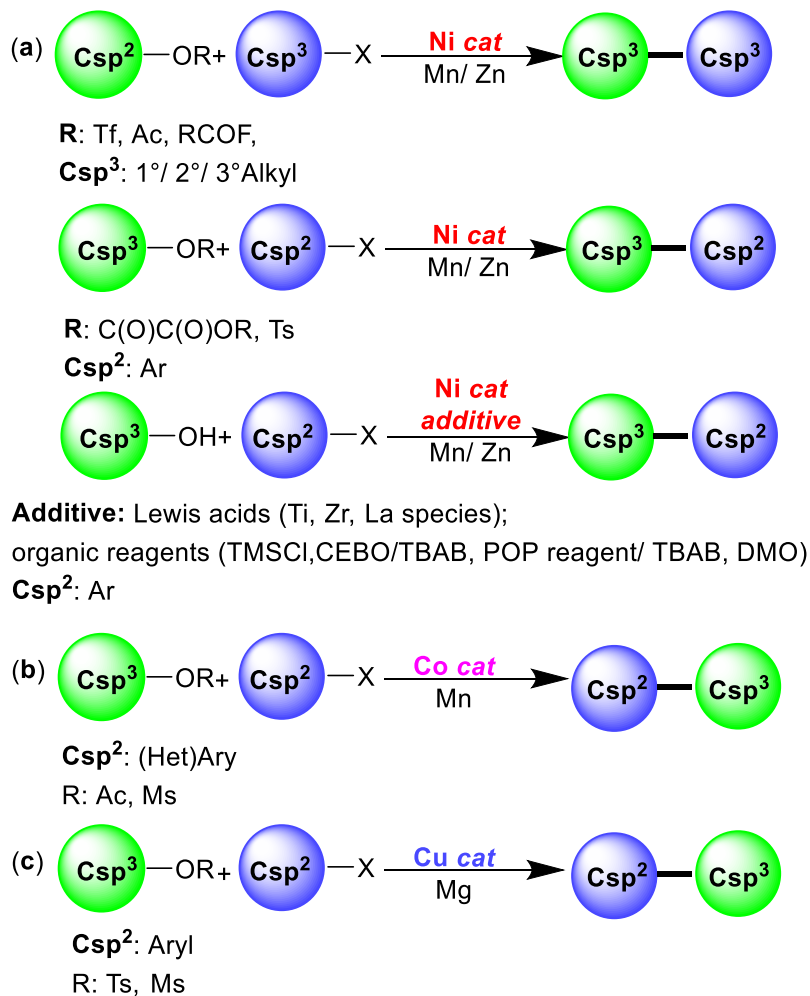
2.2.3. Cu-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

Besides Ni or Co catalyzed reductive cross-coupling to build Csp³-Csp² bonds between C-O electrophiles and C-X electrophiles, in 2014, a copper-catalyzed reductive cross-coupling of non-activated alkyl tosylates/ mesylates with alkyl/ aryl bromides was published by Liu and Fu.^{7d} In this work, the combination of CuI as the catalyst, LiOMe as the additive, Mg powder as the reductant, and bis(diphenylphosphino)methane (DPPM, a bidentate phosphine ligand) allowed the cross-coupling of alkyl-OTs/OMs and aryl bromides to form alkyl-aryl products in good yields. In addition, intramolecular reductive cross-coupling was also described to deliver cyclization products. Furthermore, the formation of Csp³-Csp³ cross-coupling products was obtained in moderate to good yields with this catalytic system from a primary or secondary alkyl bromide and a primary or secondary alkyl-OTs/OMs. (**Scheme 26**)



Scheme 26. Copper-catalyzed reductive cross-coupling of nonactivated alkyl tosylates and mesylates with alkyl and aryl bromides

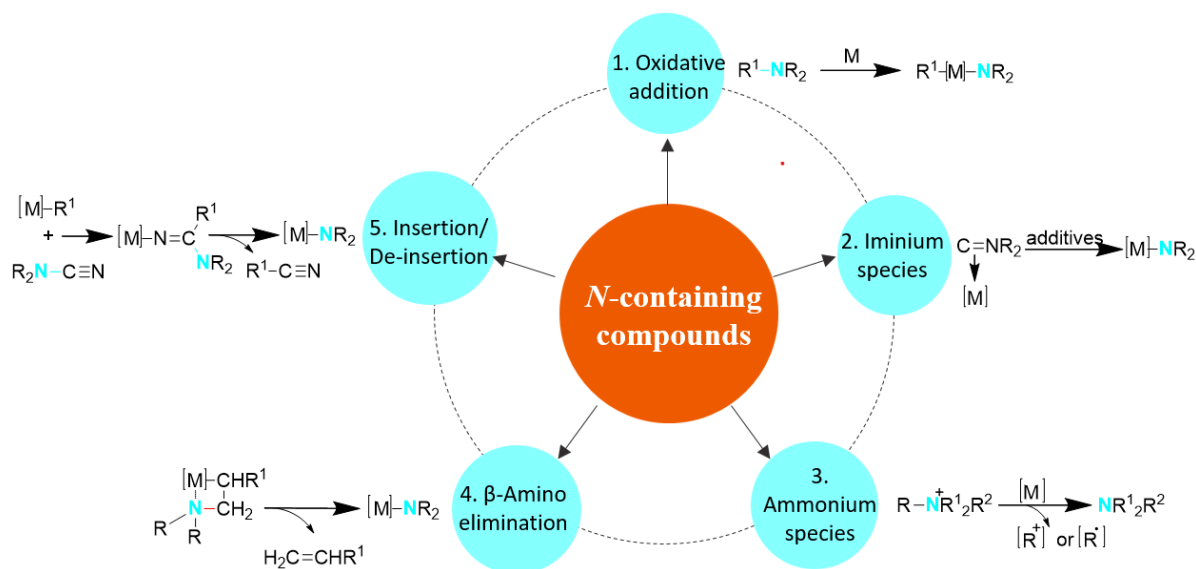
To summarize reductive cross-couplings of C-X and C-O electrophiles to construct Csp³-Csp² bonds, we can learn that (Scheme 27):



Scheme 27. Reductive of C-X and C-O electrophiles to construct Csp³-Cs² bonds.

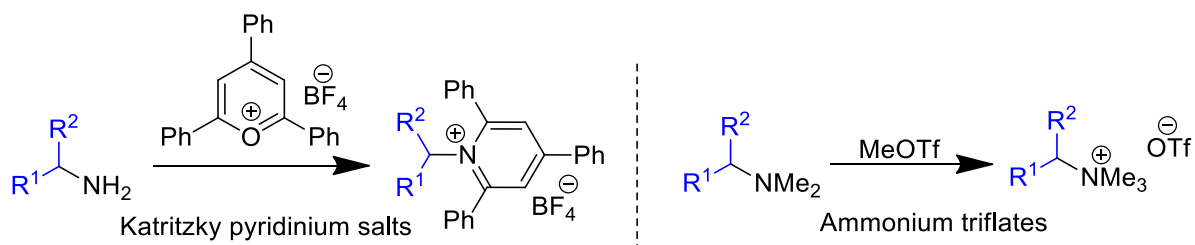
2.3. Cross-coupling with C-X and C-N electrophiles

Amino compounds are prevalent in biomolecules, drugs, and natural products⁶⁸. The transformation of C–N bonds catalyzed by transition metals dates back to 1980. The main pathways of their transformation are as follows⁶⁹: (1) via oxidative addition of transition-metal catalysts into the C–N bond, (2) via imine or iminium species, (3) via ammonium species, (4) via β -amino elimination, (5) via insertion/de-insertion, etc. (Scheme 28)



Scheme 28. Main pathways of transition metal-catalyzed cleavage of C–N bond

Here the third method aims to increase the reactivity of the C–N bond by transforming unactivated amino groups (NH_2) into the corresponding ammonium species. It has been widely reported by Watson et al. since 2010 because the amino group (NH_2) is easy to convert to ammonium triflates or Katritzky pyridinium salts in one step. (Scheme 29) After decades of development and exploration, C–N electrophiles represented by ammonium triflates, particularly Katritzky pyridinium salts, have been commonly used to construct C–C bonds in transition metal-catalyzed reactions.



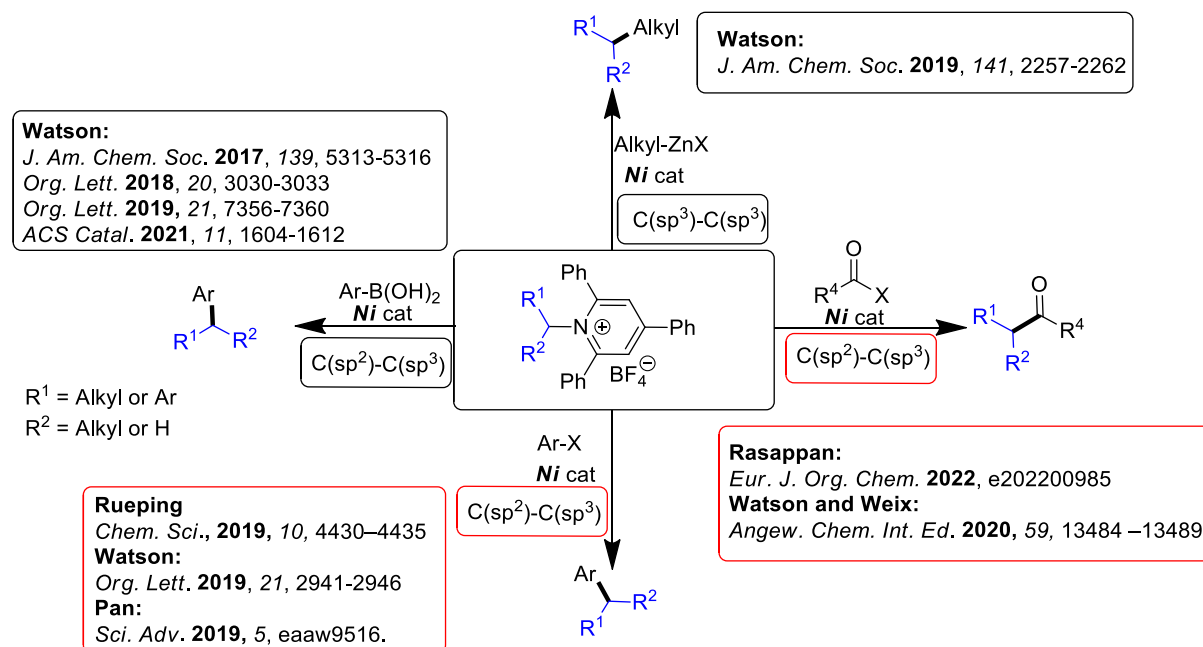
Scheme 29. The amino group (NH_2) converted to ammonium triflates or Katritzky pyridinium salts in one step

⁶⁸ C. H. Basch; J. Liao; J. Xu; J. J. Piane; M. P. Watson. *J. Am. Chem. Soc.* **2017**, *139*, 5313.

⁶⁹ K. Ouyang; W. Hao; W.-X. Zhang; Z. Xi. *Chem. Rev.* **2015**, *115*, 12045.

2.3.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

As shown in *Scheme 30*, either Ni-catalyzed Suzuki cross-coupling or Negishi cross-coupling has been reported to construct Csp³-Csp² and Csp³-Csp³ bonds by the Watson group.⁷⁰ Subsequently, Ni-catalyzed reductive cross-couplings were studied by Watson and other groups.

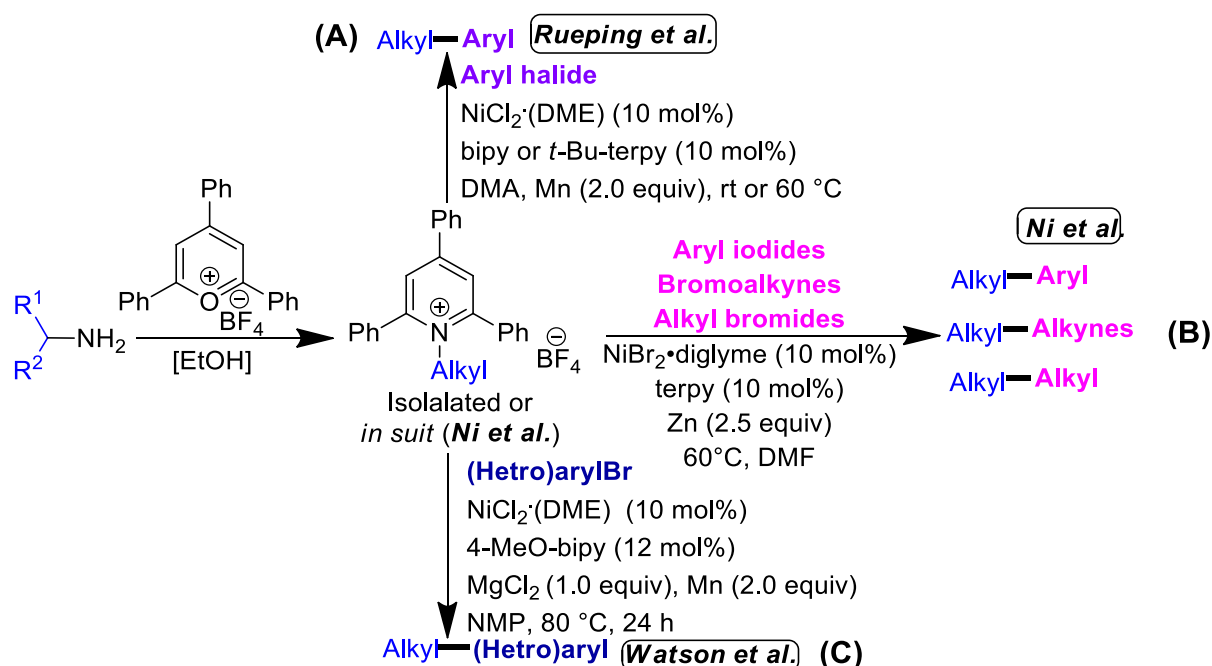


Scheme 30. Nickel-catalyzed C–N bond activation by pyridinium salts.

In the same year, three groups: Watson, Ni and Li, and Rueping reported Ni-catalyzed the reductive cross-coupling of alkyl Katritzky pyridinium salts with aryl halides, respectively. (*Scheme 31*) The Rueping group reported the nickel-catalyzed reductive cross-coupling of activated primary alkyl amines with aryl halides (Br, I) under mild reaction conditions for the first time.^{11c} In his report, primary and secondary alkyl pyridinium salts coupled with aryl halides in the combination of 10 mol% of NiCl₂·(DME), 10 mol% of dtbbpy or 4,4',4''-tri-tert-butyl-2,2':6',2''-terpyridine (*t*-Bu-terpy), and 2 equivalents of Mn as the reductant in DMA at rt or 60 °C (for primary alkyl pyridinium salts) leading to the cross-coupling products up to 99% yield. (*Scheme 31, A*) His method is also efficiently used for some natural products and drugs, like tryptamine, mexiletine, amphetamine, Lipitor intermediate, and dopamine. Compared to Rueping's work, Watson also used 10 mol% of NiCl₂·(DME) as the catalyst, slightly more nitrogen-based ligand (12 mol% of 4-MeO-bipy), and Mn, but added MgCl₂ as the additive and used an NMP as the solvent to achieve the cross-coupling of primary and secondary alkyl pyridinium salts with (hetero)aryl bromides at high temperature (80 °C)^{11a}. (*Scheme 31, C*) Watson's reaction tolerated heterocycles, including protic groups. The mechanistic studies proved the presence

⁷⁰ Watson' work: (a) *Org. Lett.* **2018**, 20, 3030. (b) *Org. Lett.* **2019**, 21, 7356. (c) *ACS Catal.* **2021**, 11, 1604. (d) *J. Am. Chem. Soc.* **2019**, 141, 2257.

of alkyl radicals in the process, which played a critical role in the reaction. Later, Ni and Li reported a cross-electrophile coupling reaction to construct: (1) Csp-Csp³ bond from alkyl pyridinium salts and bromoalkynes, (2) Csp²-Csp³ bond from alkyl pyridinium salts and aryl iodides, (3) Csp³-Csp³ bond from alkyl pyridinium salts and alkyl bromides.⁷¹ (**Scheme 31, B**) In contrast to Rueping's and Watson's work, they used Zn as the reductant instead of Mn, and their reactions also succeeded in achieving the cross-coupling in a one-pot procedure without isolating alkyl pyridinium tetrafluoroborate salts.



Scheme 31. Ni-catalyzed deamination reductive cross-electrophile couplings of alkyl pyridinium salts.

In addition to the Csp²-halides employed as electrophiles in the reductive cross-coupling of alkyl pyridinium tetrafluoroborate salts, the carboxylic acid derivatives like acid chlorides⁷² and acid fluorides⁷³ mentioned above, as well as 2-pyridyl esters instead of halides as acyl substituted groups, were also described as electrophilic partners with alkyl pyridinium tetrafluoroborate salts to build Csp³-Csp² bonds.

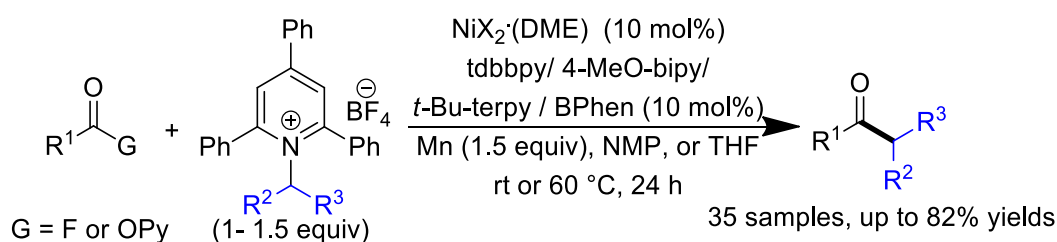
In 2020, Watson and Weix reported together a new method to synthesize dialkyl ketones with acid chlorides⁷². They used alkyl pyridinium tetrafluoroborate salts as electrophilic partners instead of alkyl halides^{31, 32, 33}, which avoided the halide wasters. As shown in **Scheme 32**, the new reaction uncovered the cross-coupling of N-alkyl pyridinium salts with *in-situ* formed carboxylic acid fluorides or 2-pyridyl esters using NiX₂·(DME) (X = Cl, Br) associated with bipy or terpyridine as ligand and Mn as the

⁷¹ Y Mao, J Han, Y Wang, H Yan, Y Pan, S. Ni, C.-X. Li. *Sci. Adv.* **2019**; 5: eaaw9516

⁷² R Pilli, B. Chindan, R. Rasappan. *Eur. J. Org. Chem.* **2022**, e202200985.

⁷³ J. Wang, M. E. Hoerrner, M. P. Watson, D. J. Watson. *Angew. Chem. Int. Ed.* **2020**, 59, 13484.

reductant. It was proposed that the role of Mn was to increase the reduction process of the catalyst, or to reduce directly pyridinium salts which were critical in the product formation. Moreover, it was found that the secondary alkyl pyridinium salts were easier to generate dihydropyridine byproduct. Thus, the experimental conditions used for the cross-coupling of primary alkyl pyridinium salts and 2-pyridyl esters were modified: THF as the solvent, rt, and bathophenanthroline (BPhen) as the ligand instead of terpyridine. Using $\text{NiBr}_2(\text{DME})$ and increasing the amount of pyridinium salt to 1.5 equivalents also enhanced the coupling efficiency between secondary alkyl pyridinium salts and 2-pyridyl esters.



Scheme 32. The deamination coupling of pyridinium salts with carboxylic acid derivatives.

In the same year, Matsuo et al. reported nickel-catalyzed deamination of activated alkyl pyridinium salts with aromatic amides.⁷⁴ Furthermore, very recently, the Weix group reported the synthesis of aryl-alkyl products from 2-pyridyl aryl carboxylic acid esters and alkyl radical donors, the latter generated from alkyl halides or alkyl pyridinium salts using a Ni-ligand-Mn catalytic reductive system.⁷⁵

Compared to the cross-coupling of two C-X electrophiles and C-X with C-O electrophiles, the development of C-N electrophiles (pyridinium salts) is relatively late. The Csp³-Csp² bond-forming reactions mainly occurred between alkyl pyridinium salts and aryl halides/ aromatic amides/ carboxylic acid esters.

⁷⁴ C.-G. Yu, Y. Matsuo. *Org. Lett.* **2020**, *22*, 950.

⁷⁵ J. Wang, L. E. Ehehalt, Z. Huang, O. M. Beleh, I. A. Guzei, D. J. Weix. *J. Am. Chem. Soc.* **2023**, *145*, 9951.

2.4. Cross-coupling between C-X and C-S electrophiles

Like the O-containing and N-containing compounds, S-containing compounds also widely exist in natural products, agricultural chemicals, and protein structures. Studies about their activation, cleavage, and transformation dates back to the early stage of synthetic organic chemistry.⁷⁶ Compared to other C-heteroatom compounds, which have been extensively engaged in transition metal-catalyzed cross-coupling reactions, S-containing compounds were less studied because of their strong complexing ability; sulfur atoms can poison transition metals. Moreover, the unpleasant odor of most sulfur-containing compounds sometimes discourages researchers from exploring them as reaction partners.⁷⁷

The reactions involving S-containing compounds have been investigated since last century, and there is a wide range of well-known named reactions based on sulfoxides, sulfur ylides, sulfonium salts so on. Recently, the C-S bond cleavage was reported with stoichiometric transition metal complexes like Pt, Ru, Fe, Ni, Co, *etc.*⁷⁸. Nevertheless, compared to the use of stoichiometric transition metal complexes, the catalytic activations of C-S bonds were scarcely reported. Especially, cobalt-catalyzed reductive cross-coupling of C-S bond cleavage has not been studied yet.

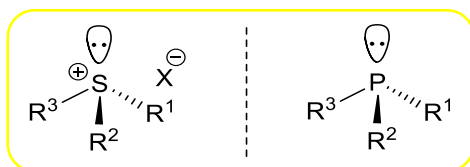
Sulfonium ions ($[R_3S]^+X^-$, X^- is a non-coordinated counter anion) have a positive charge on center sulfur ions and are bonded to three organic substituents. Compared to their oxonium salts analogs, they are easier to handle under atmospheric conditions and are more bench-stable compounds. Many sulfonium salts can be purified by traditional silica gel column chromatography.⁷⁹ (*Scheme 33*) Due to the positive charge of the center sulfur ions, they show a strong tendency to form an uncharged sulfide. As organohalides or other excellent leaving groups, sulfonium salts can act as electrophilic partners to easily undergo oxidative addition into one of their R-S bonds in transition metals-catalyzed cross-coupling, mainly employing palladium and nickel catalysts. In addition, sulfonium salts can also be used as radical precursors to generate a thioether as well as a carbon-centered radical through a single electron transfer among one of the C-S bonds, we were interested in exploring if sulfonium salts can be used as C-X/ C-O/ C-N electrophiles in transition metal-catalyzed reductive cross-coupling to construct C-C bond.

⁷⁶ D. Kaiser; I. Klose; R. Oost; J. Neuhaus; N. Maulide. *Chem. Rev.* **2019**, *119*, 8701.

⁷⁷ S. G. Murray; F. R. Hartley. *Chem. Rev.* **1981**, *81*, 365.

⁷⁸ (a) T. A. Ateşin; S. Kundu; K. Skugrud; K. A. Lai; W. D. Jones. *Organometallics* **2011**, *30*, 4578. (b) D. Benito-Garagorri; L. G. Alves; L. F. Veiros; Karl. Kirchner. *Organometallics* **2010**, *29*, 4923. (c) M. Li ; A. Ellern, J. H. Espenson. *J. Am. Chem. Soc.* **2005**, *127*, 10436. (d) M. R. Grochowski; T. Li; W. W. Brennessel; W. D. Jones. *J. Am. Chem. Soc.* **2010**, *132*, 12412.

⁷⁹ S. I. Kozhushkov; M. Alcarazo. *Eur. J. Inorg. Chem.* **2020**, 2486.

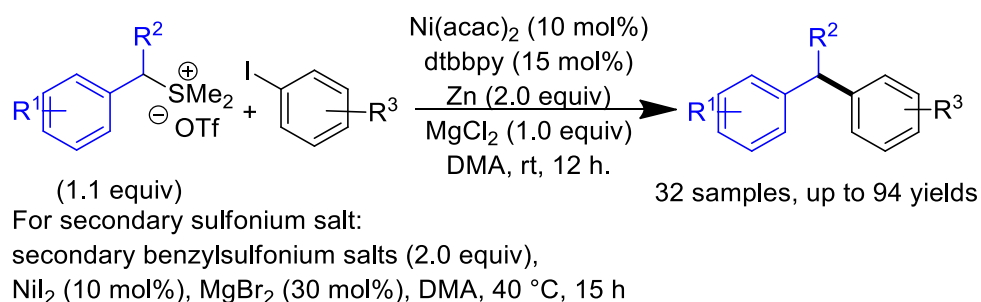


- Pyramidal geometry.
- Higher thermodynamic stability.
- Easier to handle under atmospheric conditions.

Scheme 33. Sulfonium ions

2.4.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

In 2022, Wu et al. developed a cross-electrophile coupling of benzylic sulfonium salts with aryl iodides with the Ni/ligand/Zn catalytic system to provide various diarylmethanes.⁸⁰ As shown in **Scheme 34**, either primary or secondary benzylic sulfonium salts coupled with aryl iodides leading to the cross-coupling products in good yields. In contrast, when secondary benzylic sulfonium salts were used as electrophilic partners, the conditions were modified: NiI₂ as the catalyst, MgBr₂ as the additive at 40 °C for 15 h, and because of the higher reactivity of secondary benzylic sulfonium salts, 2.0 equivalents of secondary benzyl sulfonium salts had to be added to get good yields. On the other hand, this reaction was not compatible with benzyl sulfonium salts bearing electron-withdrawing groups. Thus, the extension to other sulfonium salts, different from benzyl sulfonium salts, still needs to be studied. Moreover, the cross-electrophile coupling of sulfonium salts and other more accessible electrophiles to construct C-C bonds is also attractive.



Scheme 34. Nickel-catalyzed reductive cross-coupling of benzylic sulfonium salts with aryl iodides.

⁸⁰ W. Wang, K Yao, F. Wu. *Synlett* **2022**, 33, 361.

2.5. Cross-coupling with two non-halides electrophiles

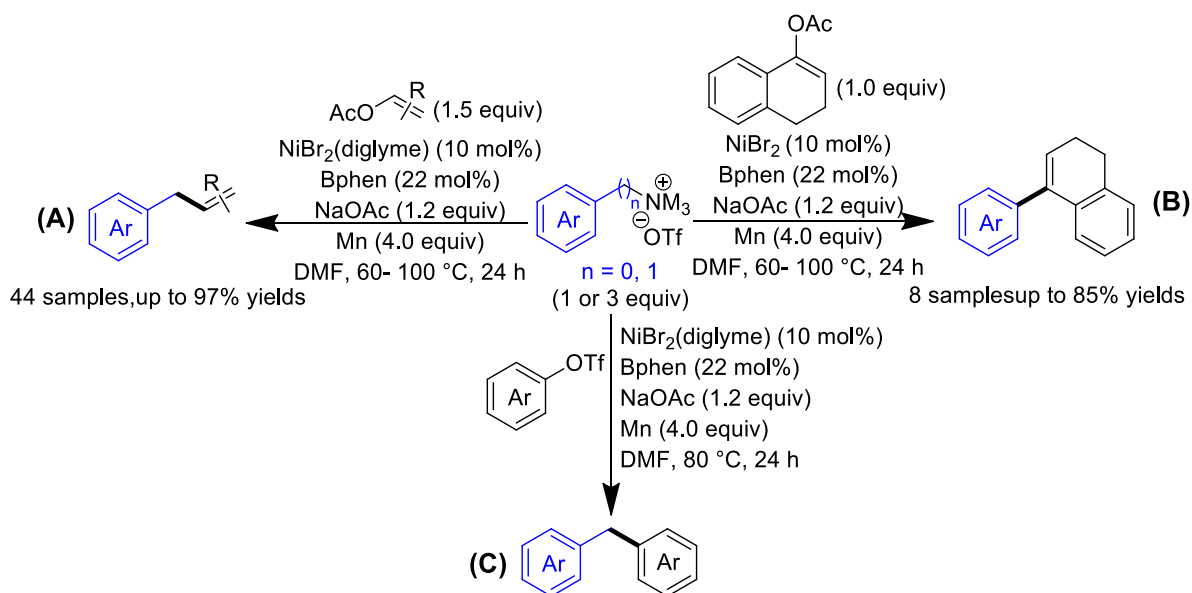
Excellent works on the cross-electrophile coupling between either two organic halides or one organic halide with one C-O/ C-N/-C-S electrophile have been developed these last decades. Nevertheless, as we know, organic halides have some disadvantages, such as (1) their high cost and relative toxicity, (2) environmental pollution caused by halogenated wastes, (3) the difficulty of preparing and limiting their application in large-scale syntheses, and (4) restricted the design space for new reactions and achieved new reactivities. Thus, exploring other types of cross-couplings between two non-halide electrophiles is highly desirable, and the application in transition metal-catalyzed cross-electrophile coupling still needs to be developed.

2.5.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

The group of Shu has made excellent efforts in this field. Since 2019, Shu has successively developed the reductive cross-couplings: (1) between benzyl/aryl ammonium salts and vinyl/aryl C-O electrophiles (vinyl acetates and aryl triflates);¹²(2) between vinyl/aryl triflates and alkyl sulfonate electrophiles to synthesize cycloalkenes and modify peptides;⁸¹(3) between aryl ammonium salts and vinyl acetates to build Csp²-Csp² bonds^{15a}

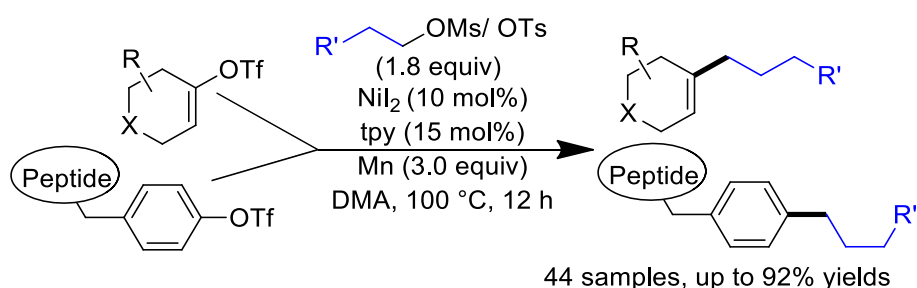
The possibility of Csp²-Csp²/Csp³-Csp² bond formation via C-N and C-O cleavage was demonstrated by Shu in 2019., through the reductive coupling of benzyl/aryl ammonium salts with substituted vinyl acetates and aryl triflates using the Ni/ligand/ Mn catalytic system⁸¹, In **Scheme 35**, benzyl ammonium salt derivatives, in the presence of NiBr₂(diglyme) as the catalyst, BPhen as the ligand, NaOAc as the additive, and Mn as the metal reductant at 80 °C, coupled with styryl acetates, heterocycle substituted vinyl acetates, and alkyl-substituted vinyl acetates efficiently, leading to the desired products in good yields.¹² (**Scheme 35, A**) The coupling of aryl ammonium salts generally requires strong organic nucleophiles due to the high C-N bond strength of aryl ammonium salts. Thus, the reaction conditions for the coupling of aryl ammonium salts and cyclic vinyl acetates needed to be slightly modified: NiBr₂ as the catalyst with an excess amount of aryl ammonium salts (3.0 equivalents) to obtain the target products in moderate to good yields.^{15a} (**Scheme 35, B**) Moreover, aryl triflates could also perform well with benzyl ammonium salts to generate various diarylmethanes under these conditions. Preliminary mechanistic studies demonstrated that a radical was produced from ammonium salts activated by Ni catalysts. (**Scheme 35, C**) Later, this group extended the scope of C-O electrophiles to aryl tosylate/ mesylate and aryl acetate.⁸¹

⁸¹ J. Duan, Y.-F. Du, X. Pang, X.-Z. Shu. *Chem. Sci.*, **2019**, *10*, 8706.



Scheme 35. Ni-catalyzed reductive coupling between C–N and C–O electrophiles

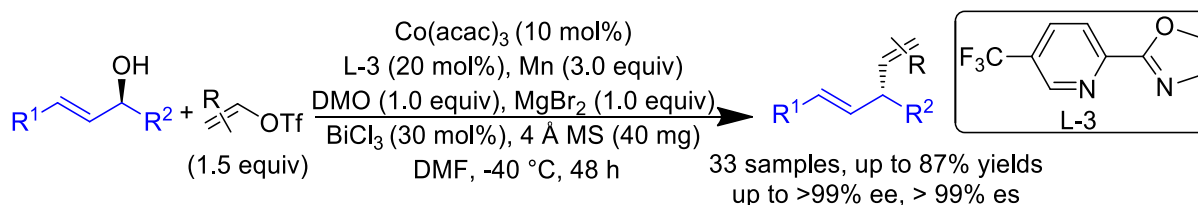
As mentioned above, in addition to the cross-coupling of C–N and C–O electrophiles, Shu also reported cross-coupling reactions between two C–O electrophiles to synthesize cycloalkenes and modify selectively tyrosine in peptides⁸¹ (**Scheme 36**). In this Ni-catalyzed reductive cross-coupling, highly reactive cyclic vinyl triflates and unactivated alkyl mesylates were employed as C–O electrophilic partners between two C–O electrophiles. Owing to the high reactivity discrepancy of both partners, some difficulties were encountered in controlling the selectivity in the formation of the cross-products. For some samples, NaI (0.5 equiv) was used to promote the transformation of the alkyl mesylate under the condition. Replacing NiI₂ with NiCl₂ or NiBr₂ resulted in a significant decline in the yield of the desired product, along with most of the alkyl mesylates remaining. On the other hand, NiBr₂ catalysis combined with NaI (0.5 equiv.) improved the yield of the desired product compared to NiBr₂ catalysis without NaI, along with a large amount of alkyl–alkyl homo-coupling product. These results indicated the importance of the catalytic amount of iodide to activate the alkyl mesylate.



Scheme 36. Ni-catalyzed cross-electrophile coupling between vinyl/aryl and alkyl sulfonates.

2.5.2. Co-catalyzed reductive cross-coupling to construct Csp³-Csp² bond

In addition to the Ni-catalyzed reductive cross-coupling of two non-halides electrophiles to construct a Csp³-Csp² bond, Shu also reported a Co-catalyzed enantiospecific cross-electrophile vinylation of allylic alcohols with vinyl triflates which could not be realized by nickel catalysts.^{7e} This procedure provided a new method to obtain enantioenriched cyclic compounds in moderate to good yields and high ee/es values. Similar to the strategy for the dynamic kinetic coupling of the reductive arylation of benzyl alcohols by Ni-catalysis in the presence of dimethyl oxalate (DMO),⁵⁵ as shown in *Scheme 37*, in this vinylation process, dimethyl oxalate (DMO) was also employed to activate allyl alcohols and generate allyl oxalates. The latter would participate in the reductive cross-coupling once they were formed. Furthermore, this vinylation also employed 2-(4,5-dihydro-2-oxazolyl)-5-(trifluoromethyl)pyridine (CF₃-Pybox, L-3) as the ligand, 4 Å MS, MgBr₂, and BiCl₃ as additives. In the absence of MgBr₂, the yield of the cross-coupling product decreased, along with most of the vinyl triflate remaining, and the addition of the Lewis acid-BiCl₃ improved the generation of allyl oxalates. Increasing the temperature to 0 °C did not affect the yield significantly but caused a sharp decline in ee/es values. Finally, mechanistic experiments showed that the Co catalyst reacted with *in-situ* generated allyl oxalates first and then coupled with the vinyl triflate.



Scheme 37. Cobalt-catalyzed cross-electrophile vinylation of allylic alcohols with vinyl triflates.

From these reports related to transition metal-catalyzed reductive cross-coupling with two no-halides electrophiles, we can learn that the strategies used for Csp³-Csp² bonds mainly concerned the C-N electrophiles with Csp²-O electrophiles, and two C-O electrophiles, not yet extend to C-S electrophiles. Also, almost the reported Csp²-O/Csp³-O electrophiles are ester and sulfonate derivatives.

As mentioned in this part (2, p11), transition metal-catalyzed C-C bond-forming cross-couplings have been essential and timeless topics in the synthesis of pharmaceuticals and natural products.⁸² The construction of Csp³-Csp² bonds via transition metals- catalyzed reductive cross-couplings was presented:

(1) with two C-X electrophiles;

⁸² (a) J. A. Marsden, M. M. Haley, A. de Meijere, F. Diederich. In *Metal-Catalyzed Cross-Coupling Reactions*, WILEY-VCH: Weinheim, (2004).
 (b) P. Knochel, In *Handbook of Functionalized Organo-metallics. Applications in Synthesis*, Wiley-VCH: Weinheim, Germany, (2005).

(2) with C-X and C-O electrophiles;

(3) with C-X and C-N electrophile;

(4) with C-X and C-S electrophiles;

(5) with two non-halides electrophiles.

It can learn about the rapid development in this field these last decades. Excellent improvements and strategies have been reported for the synthesis of compounds containing all kinds of Csp^3 - Csp^2 bonds.

3. Transition Metals-Catalyzed Reductive Cross-Coupling to Construct Csp³-Csp³ Bonds

It is known that Csp³-Csp³ bonds are ubiquitous linkages in a range of natural products and pharmaceuticals. However, their formation remains challenging compared to well-developed Csp³-Csp² (introduced in the former part) and Csp²-Csp² bond (not mentioned in this thesis) formation⁸³. Indeed, it is rather difficult to control the selectivity between two radical-based electrophiles exhibiting the same hybridization and to avoid the competitive β-hydride elimination pathway. Thus, to overcome these problems, various C-O/C-N electrophiles, *etc.*, have been developed as alternative coupling partners of C-X electrophiles in transition metals-catalyzed reductive reactions, mainly using Ni species as catalysts.

3.1. Cross-coupling with two C-X electrophiles

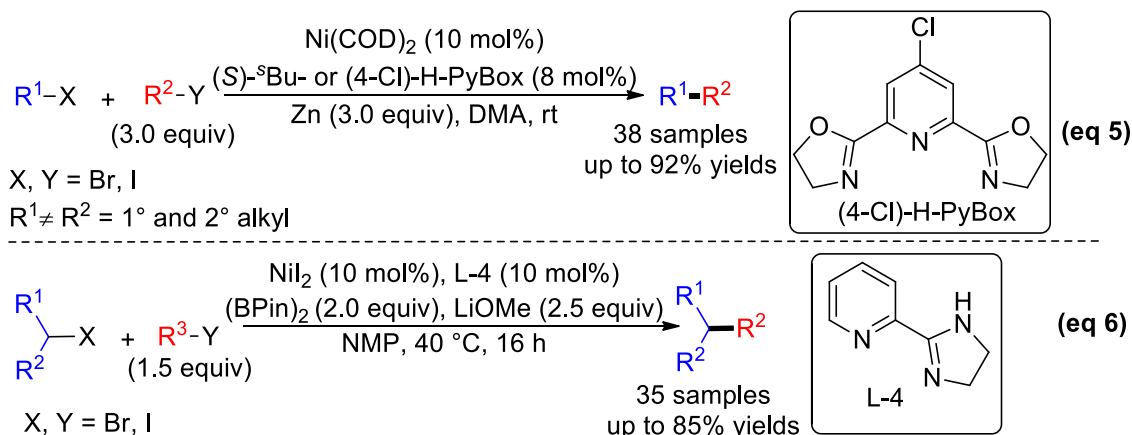
3.1.1. Ni-catalyzed reductive cross-coupling to construct Csp³-Csp³ bonds

Cross-electrophile coupling reactions (XEC) to construct Csp³-Csp³ bonds with two C-X electrophiles, practically via Ni catalysis, have been almost the most essential components in organic synthesis. As introduced, Csp³-Csp³ bond formation remains challenging³ due to the generation of two radical-based electrophiles exhibiting the same hybridization and the competitive β-hydride elimination. Thus, most of these reactions related to two C-X electrophiles are limited to the coupling between secondary and primary halides, aiming to avoid a competitive homo-coupling.

The Gong group first described a Ni-catalyzed reductive cross-coupling of two unactivated alkyl halides to build Csp³-Csp³ bonds.^{6c} The reaction was compatible with primary and secondary halides (at least one being a bromide) under mild reaction conditions, leading to moderate to excellent yields. (*Scheme 38, eq 5*) On the other hand, although Zn was used as the reductant, the mechanistic experiments demonstrated that no Negishi-type process happened under these reductive coupling conditions and indicated the generation of the two alkyl radical intermediates during the coupling reaction using a radical clock experiment. Later, the Gong group improved this cross-coupling reaction to inhibit the generation of homo-coupling side products.^{6b} This new reaction also employed unactivated secondary, primary alkyl halides and Ni catalysis to synthesize the Csp³-Csp³ coupling products in good yields. However, bis(pinacolato)diboron (BPin)₂ was used as the terminal reductant instead of metal reductants, with low equivalents of primary bromides (1.5 equivalents) (*Scheme 38, eq 6*). Although (BPin)₂

⁸³ For selected reviews: (a) C. E. I. Knappke, S. Grupe, D. Gärtner, M. Corpet, C. Gosmini, A. Jacobi von Wangelin. *Chem. Eur. J.*, **2014**, *20*, 6828-6842. (b) J. Liu, Y. Ye, J. L. Sessler, H. Gong. *Acc. Chem. Res.* **2020**, *53*, 9, 1833.

is usually used as a borylation reagent, mechanistic investigations ruled out the possibility of an *in-situ* organoborane/Suzuki process during mechanistic explorations. Moreover, the reaction was proved to proceed through the double oxidative addition of alkyl halides to Ni(I). The bases and ligands significantly affected the selectivity of this reductive coupling process. These conditions were suitable for the cross-coupling of primary and primary alkyl halides, and primary and secondary alkyl halides. Still, it did not produce good results between secondary and secondary alkyl halides. In recent years, his group published a nickel-catalyzed reductive cross-coupling between tertiary alkyl halides and benzyl chlorides/ chloroformates to construct benzylated quaternary carbon centers in moderate to excellent yields with high functional group tolerance, either EWG or EDG.⁸⁴



Scheme 38. Nickel-catalyzed reductive cross-coupling of unactivated alkyl halides.

In addition to Gong's achievements in the nickel-catalyzed reductive cross-coupling between unactivated alkyl halides, Shu and co-workers also developed a ligand-controlled regio-divergent alkylation reaction via nickel-catalyzed cross-electrophile coupling of two distinct alkyl bromides.⁸⁵ In this reaction, the secondary alkyl bromides reacted with primary alkyl bromides leading to non-migrated or migrated alkyl-alkyl products, which occurred at three similar positions in the case of secondary alkyl bromides with excellent chemo- and regioselectivity, via different Ni/ligand catalytic systems. Moreover, Gong also reported a Ni-catalyzed reductive methylation reaction to build the Csp³-Csp³ bond from methyl p-tosylates.⁸⁶

In the case of Ni-catalyzed reductive cross-coupling to construct Csp³-Csp³ bonds, the scope of the C-X electrophiles is limited to the coupling between secondary and primary halides, using common Zn, (Bpin)₂, Mn as reductants.

⁸⁴ J. Wang, Y. Gong, D. Sun, H. Gong. *Org. Chem. Front.*, **2021**, *8*, 2944.

⁸⁵ W.-T. Zhao, H. Meng, J.-N. Lin, W. Shu. *Angew. Chem. Int. Ed.* **2023**, *62*, e202215779.

⁸⁶ . Z. Liang, W. Xue, K. Lin, H. Gong, *Org. Lett.* **2014**, *16*, 5620.

3.2. Cross-coupling with C-X and C-O electrophiles

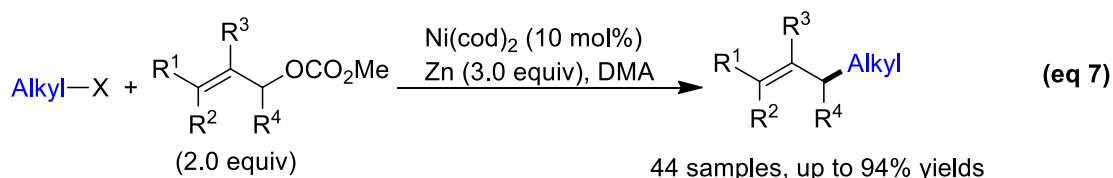
Although the Ni-catalyzed reductive cross-coupling of two C-X electrophiles has been developed, mainly by the Gong group, the competition of the homo-coupling process of an alkyl halide with the expected cross-coupling cannot be efficiently avoided, and an excess of one alkyl halides have to be employed to obtain higher yields. Thus, chemists were inspired to explore more ideal strategies to improve the efficiency of reductive Csp^3 - Csp^3 cross-couplings. One of the methods is to employ different electrophiles that try to distinguish easily two Csp^3 hybridized electrophiles.

3.2.1. Ni-catalyzed reductive cross-coupling to construct Csp^3 - Csp^3 bonds

Gong's work related to the direct cross-couplings of two different unactivated alkyl halides under Ni-catalyzed reductive conditions has been introduced above. In 2012, his group also developed an allyl alkylation reaction between secondary alkyl halides and allyl carbonates, which are considered more active than unactivated alkyl halides.⁸⁷ In the allyl alkylation reaction, Zn was used as the reductant to provide *E*-alkenes in good to excellent yields and regioselectivities. The conditions were slightly different when alkyl bromides and alkyl iodides were employed as partners of allyl carbonates. (**Scheme 39, eq 7**) For alkyl bromides, 10 mol% of *t*Bu-Terbpy were used as ligand and 1.5 equivalents of $MgCl_2$ as an additive at 80 °C for 12 h, but when the latter was used, (*S*)-*i*Pr-PyBox acted as the ligand, CuI (30 mol%) instead of $MgCl_2$ was used as the additive at a lower temperature (35 °C) for a shorter time (6 h). Moreover, the reaction showed excellent regioselectivities and functional group tolerance. The mechanistic experiments demonstrated the impossibility of the *in-situ* alkyl zinc/Negishi pathway.

Several years later, the Gong group extended this allyl alkylation reaction to tertiary alkyl halides with allyl carbonates to form all Csp^3 quaternary centers by Ni-catalyzed cross-electrophile coupling.^{8c} This allylic alkylation method also performed well in functional-group compatibility, leading to products with high *E* selectivity. It should be noted that the reaction conditions were modified slightly when the substitutes were at different positions on allyl carbonates. (**Scheme 39, eq 8**) A combination of $NiBr_2 \cdot glyme$ /*i*Pr-Pybox /Zn and pyridine/ $MgCl_2$ as additives in DMA at rt was used as conditions with methyl (2-phenylallyl) carbonate as starting materials. In contrast, with un-substituted allyl carbonates or analogues bearing substituents at the terminal position, *t*dbbpy, and pyridine-2,6-diamine were employed as the ligands and/or additives, improving significantly the coupling efficiency with $Ni(COD)_2$ as the catalyst.

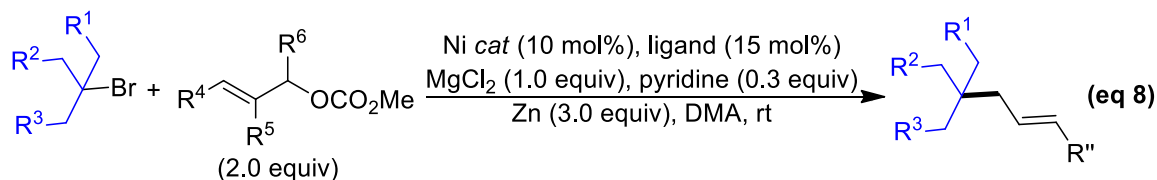
⁸⁷ Y. Dai, F. Wu, Z. Zang, H. You, H. Gong. *Chem. Eur. J.* **2012**, *18*, 808.



X = Br: *t*Bu-Terbpy (10 mol%), MgCl₂ (1.5 equiv), 80 °C, 12 h

X = I: (*S*)-*i*Pr-PyBox (10 mol%), CuI (30 mol%), 35 °C, 6 h

Alkyl = 1° and 2°



R⁴, R⁶ = H, R⁵ = Ph: NiBr₂·glyme/ *i*Pr-Pybox

R⁵, R⁶ = H: Ni(COD)₂, dtbbpy, pyridine 2,6-diamine instead of Py

Scheme 39. Nickel-catalyzed reductive allylation of alkyl halides with allylic carbonates.

As mentioned in 2.2.1 (p25), the Shu group reported a Ni-catalyzed reductive cross-coupling of benzyl oxalates with highly functionalized alkyl bromides to form Csp³-Csp³ bonds.⁵⁵ In this study, the oxalate was employed as the leaving group and released a benzyl radical via C-O bond activation; DMSO was used to increase the yield since it effectively inhibited the reduction of benzyl oxalate product formation. Moreover, P(4-CF₃Ph)₃ instead of nitrogen ligands (in Gong's report⁵¹) was used as the ligand. This reaction tolerated a variety of functional groups, such as chloride, alcohol, aldehyde, amine, amide, boronated ester, ether, ester, heterocycle, phosphonate, strained ring, *etc.*, on the alkyl halides. One year later, Wang and co-workers reported a Csp³-Csp³ bond-forming reaction via a Ni-catalyzed reductive C-F and C-O bond cleavage. This reaction used α -trifluoromethyl alkenes and aryl/alkyl aldehyde dimethyl acetal to synthesize gem-difluoro alkenes.⁸⁸

Furthermore, in 2019, Komeyama and Osaka developed a Csp³-Csp³ cross-coupling of alkyl halides with alkyl tosylates in a combination of Ni and VB₁₂ catalytic system with Mn as reductant under mild conditions. The mechanistic studies demonstrated the presence of alkyl radicals from both alkyl halides and alkyl tosylates in the reductive cross-coupling process.^{7c}

In addition, tosylates and carbonates were also employed as leaving groups in reductive cross-couplings. Carboxylic acids⁸⁹ and their derivatives have also been reported as electrophiles in recent years. Last year, the Weix group reported a two-step, one-pot method for the formation of Csp³-Csp³ bonds from the *in-situ* generated primary N-hydroxyphthalimide esters and unactivated primary alkyl

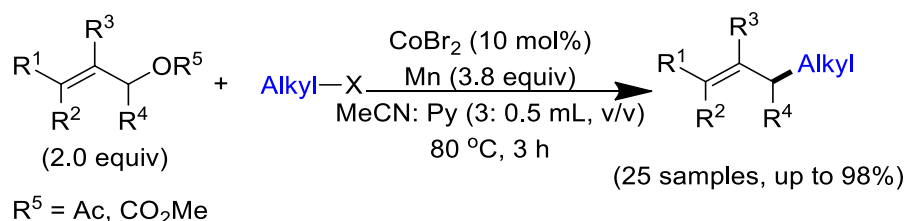
⁸⁸ Z. Lin, Y. Lan, C. Wang. *ACS Catal.* **2019**, *9*, 775.

⁸⁹ C. Johnston, R. Smith, S. Allmendinger, D. W. C. MacMillan. *Nature* **2016**, *536*, 322.

bromides by the Nickel-catalyzed cross-electrophile coupling. The mechanistic studies proved that alkyl radicals were released from two substrates during the reaction.⁹⁰

3.2.2. Co-catalyzed reductive cross-coupling to construct Csp³-Csp³ bond

In addition to Ni-catalyzed C_{allyl}- electrophiles reductive cross-coupling to construct Csp³-Csp³ bonds, allyl acetates were also used in Co-catalyzed reductive cross-coupling. Previous works involving cobalt-catalyzed allylic alkylation mainly focused on using alkyl zinc or Grignard reagents, which limited functional group tolerance.⁹¹ To avoid handling sensitive organometallic reagents, in 2011, the Gosmini group reported a direct reductive cross-coupling of alkyl halides with allylic acetates or carbonates to form Csp³-Csp³ bond with the Co/ Mn catalytic system in a mixture of acetonitrile and pyridine in the absence of any ligand.⁹² (Scheme 40) This Co-catalyzed allyl alkylation showed excellent functional group tolerance. Good to excellent yields were obtained for the cross-coupling of substituted allyl acetates or carbonates with primary, secondary, or tertiary alkyl halides under simple and mild conditions. Moreover, in the case of substituted allyl acetates, the linear products were the major or the only products.



Scheme 40. Cobalt-catalyzed reductive allylation of alkyl halides with allylic acetates or carbonates.

Compared to the reports about Csp³-Csp² bonds by transition metal-catalyzed reductive cross-coupling of C-X and C-O electrophiles, the methods developed for Csp³-Csp³ bond formation in this field are relatively limited, the Csp³-O electrophiles are mainly allyl ester/carbonates, alkyl tosylate, and NHP esters.

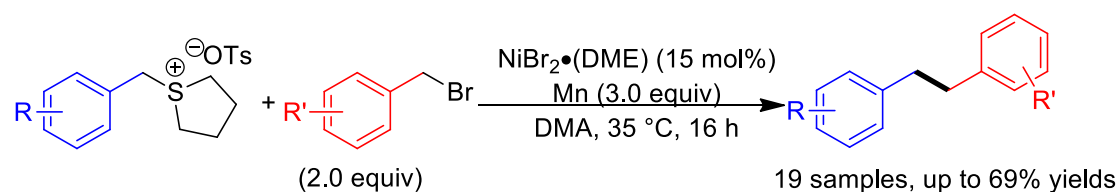
⁹⁰ K. Kang, D. J. Weix. *Org. Lett.* **2022**, 24, 2853.

⁹¹ (a) C. Kishan Reddy, P. Knochel, *Angew. Chem.* **1996**, 108, 1812; *Angew. Chem. Int. Ed. Engl.* **1996**, 35, 1700. (b) T. Tsuji, H. Yorimitsu, K. Oshima, *Angew. Chem.* **2002**, 114, 4311; *Angew. Chem. Int. Ed.* **2002**, 41, 4137. (c) H. Ohmiya, T. Tsuji, H. Yorimitsu, K. Oshima, *Chem. Eur. J.* **2004**, 10, 5640.

⁹² X.Qian, A. Auffrant, A. Felouat, C. Gosmini. *Angew. Chem. Int. Ed.* **2011**, 50, 10402.

3.3. Cross-coupling with C-X and C-S electrophiles

C-S electrophiles have been introduced in 2.4 (p37). Even though they have lots of advantages, their application in transition metal-catalyzed reductive cross-coupling is rarely reported. Last year, the Alemán group reported a reductive cross-coupling reaction between benzyl sulfonium salts and benzyl bromides bearing EDG using a Ni/Mn catalytic system.⁹³ This report demonstrated the ability of sulfonium salts as the leaving groups in cross-electrophile couplings. Besides, this method can be applied as an alternative to synthesizing various interesting dihydrostilbene derivatives. The reaction also described the possibility of benzyl tosyl derivatives *in-situ* formation of the corresponding sulfonium salts in reductive cross-coupling to build Csp³-Csp³ bonds. (Scheme 41). In addition, Novák reported a method to synthesize 2-benzyl pyrrolidines via a Ni-Ir dual photocatalytic system. The benzyl sulfonium salts coupled with proline are excited by the photocatalyst to form radicals through CO₂ extrusion.⁹⁴



Scheme 41. Nickel-catalyzed cross-electrophile coupling of benzyl bromides and sulfonium salts

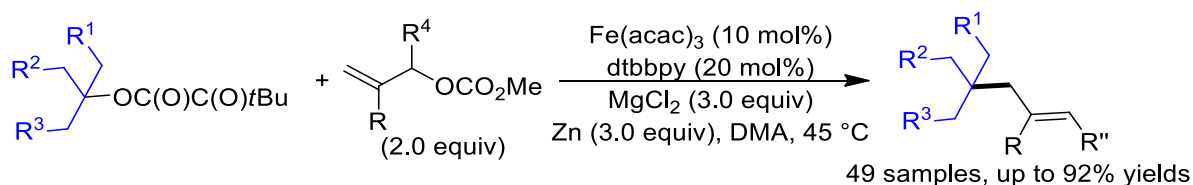
Until now, no reductive cross-coupling involving C-halides and Csp³-sulfonium salts was reported with other catalysts to construct Csp³-Csp³ bonds.

⁹³ R. del Río-Rodríguez, L. Blanco, A. Collado, J. A. Fernández-Salas, J. Alemán. *Chem. Eur. J.* **2022**, *28*, e202201644.

⁹⁴ B. Varga, Z. Gonda, B. L. Tóth, A. Kotschy, Z. Novák. *Eur. J. Org. Chem.* **2020**, 1466.

3.4. Cross-coupling with two non-halides electrophiles

The development of Ni-catalyzed reductive cross-couplings with two C-X electrophiles or between C-O and C-X electrophiles to build Csp³-Csp² and Csp³-Csp³ bonds has been extensively introduced a lot by Gong's group. In 2020, he described a reductive cross-coupling with two different C-O electrophiles to form Csp³-Csp³ bonds.⁹⁵ In this work, tertiary alkyl oxalates and allyl carbonates were employed as C-O electrophilic partners to lead to all Csp³-quaternary centers mediated by Zn/MgCl₂ and promoted by a Fe catalyst. (**Scheme 42**) Without Fe(acac)₃ as the catalyst and dtbbpy as the ligand, the yield of allyl alkyl products decreased significantly to 38%. In comparison, the cross-coupling reaction was inhibited completely in the absence of Zn or MgCl₂. Wherein the MgCl₂ acted as a Lewis acid to promote the C-O bond cleavage of oxalates, but also played a key role in allylic C-O bond cleavage. Moreover, this Zn/MgCl₂ mediated and Fe-promoted cross-coupling condition is also compatible with a three-component radical reaction with the addition of activated alkenes.



Scheme 42. C–O/C–O bond fragmentation of oxalates and allyl carbonates to form alkylated quaternary carbon centers

Later, Kojima and Matsunaga reported a method to construct Csp³-Csp³ bonds from alkyl Katritzky salts and allyl esters with good linear-/*E*-selectivity, but in this reaction, cobalt/organophotoredox dual catalysis was employed.⁹⁶ The same year, Suga and Ukaji described a Ti-mediated homolytic C-O bond cleavage to synthesize (*E*)-selective trisubstituted alkenes. Benzyl alcohols were transformed into the corresponding benzyl radicals using 1 equivalent of TiCl₄(col) (col = 2,4,6-collidine) and Mn. Under these reaction conditions, 2-carboxyallyl acetates were used as coupling partners, and the subsequent elimination of the acetoxy group produced α , β -unsaturated carbonyl compounds with exclusive (*E*)-stereoselectivity.⁹⁷ In 2021, the Alexanian group reported a nickel-catalyzed allylation of alkyl tosylates with allyl alcohols under mild conditions.⁹⁸ In these reactions, 2.2 equivalents of vinyl magnesium chloride as a reductant and hexamethyldisilazane (HMDS) were employed to improve the stereospecificity of the reaction.

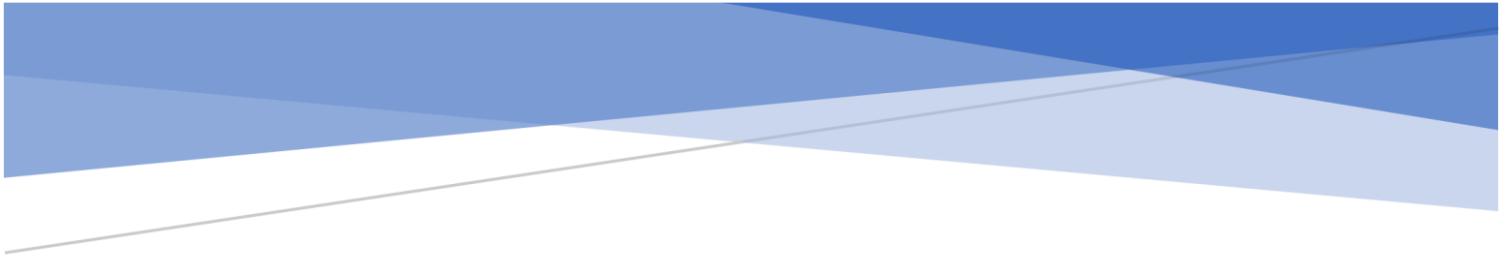
⁹⁵ H. Chen, Y. Ye, W. Tong, J. Fang H. Gong, *Chem. Commun.*, **2020**, 56, 454.

⁹⁶ T. Sekino, S. Sato, T. Yoshino, M. Kojima, S. Matsunaga. *Org. Lett.* **2022**, 24, 2120.

⁹⁷ R. Takada, S. Shimazu, M. Sakata, T. Suga, Y. Ukaji. *J. Org. Chem.* **2022**, 87, 7487.

⁹⁸ Q. D. Tercenio, E. J. Alexanian. *Org. Lett.* **2021**, 23, 721.

As described at the beginning of this part (3, p43), the Csp^3-Csp^3 bond formation remains challenging compared to the well-developed Csp^3-Csp^2 and Csp^2-Csp^2 bonds, and developed slowly. Up to now, transition metal-catalyzed reductive cross-couplings to construct Csp^3-Csp^3 bonds via two C-X electrophiles generally employ secondary and primary halides, using Zn, $(Bpin)_2$, or Mn as reductants with a Ni catalyst. For reductive cross-coupling of C-X and C-O electrophiles to build Csp^3-Csp^3 bonds, the Csp^3-O electrophiles are mainly allyl ester/carbonates, alkyl tosylate, and NHP esters. Moreover, no reductive cross-coupling involving C-halides and Csp^3 -sulfonium salts was reported with other catalysts to construct Csp^3-Csp^3 bonds, except a Ni catalyst. Finally, in the case of cross-coupling with two non-halide electrophiles, $C_{allyl}-O$ electrophiles are mainly employed as electrophilic partners



**Chapter I: Cobalt-Catalyzed Reductive
Cross-coupling of Benzyl Sulfonium
Salts and Aryl Halides to Form Csp³-
Csp² Bonds**

1. Sulfonium Salts in Transition Metal-Catalyzed Reductive Cross-Coupling

Sulfonium ions ($[\text{R}_3\text{S}]^+\text{X}^-$; X⁻ is a non-coordinated counter anion) have a positive charge on the center sulfur ion and are bonded to three organic substituents. Compared to their oxonium salts analogs, they are easier to handle under atmospheric conditions and are more bench-stable compounds. Moreover, many sulfonium salts can be purified by traditional silica gel column chromatography.⁷⁹ Due to the positive charge on the center sulfur ions, they show a strong tendency to form an uncharged sulfide. Same as C-X / C-O / C-N electrophiles, sulfonium salts can act as electrophilic partners to easily undergo either oxidative addition into one of their R-S bonds in transition metal-catalyzed cross-coupling or as radical precursors to generate a thioether as well as a carbon-centered radical through a single electron transfer among one of the C-S bonds.⁹⁹ Although the sulfonium salt shows good performance in C-S bond activation, cleavage, and transformation, it was less reported in the transition metal-catalyzed cross-coupling fields, particularly in the reductive cross-coupling aspect, compared to C-X / C-O / C-N electrophiles, the sulfur atom can poison transition metals due to its strong complexing ability, as well as the unpleasant odor of most sulfur-containing compounds.¹⁰⁰

As introduced in the [Introduction \(2.4, p37\)](#), the study of sulfonium salt in transition metal-catalyzed cross-coupling started with Liebeskind's excellent works in the last century¹³. However, its employment in transition metal-catalyzed reductive cross-coupling to build C-C bonds has been only published recent two years.^{80, 93}

Our group has developed various Co-catalyzed cross-couplings to achieve the C-C bond formation via the reductive cross-coupling of C-O/C-X/C-CN electrophiles with C-X electrophiles^{6, 14, 42, 67}. Thus, we envisioned that sulfonium salts could be excellent radical precursors to form Csp³-Csp² or Csp³-Csp³ bonds in the presence of other electrophilic partners via cobalt-catalyzed reductive cross-coupling.

2. Results and Discussions between Benzyl Sulfonium Salt and Ar-X

2.1. Optimization of reaction conditions

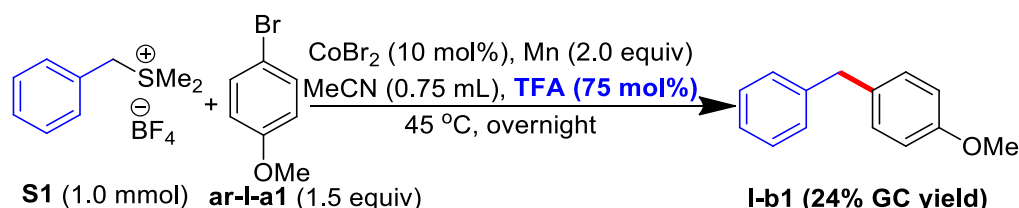
Our exploration began with the synthesis of diarylmethanes from benzyl sulfonium salts. These compounds are essential in pharmacologically active compounds, agrochemicals, and, more generally,

⁹⁹ (a) P. S. Engl; A. P. Häring; F. Berger; G. Berger; T. Ritter. *J. Am. Chem. Soc.* **2019**, *141*, 13346. (b) M. H. Aukland, F. J. T. Talbot; D. J. Procter. *Angew. Chem.* **2018**, *130*, 9933-9937.

¹⁰⁰ S. G. Murray; F. R. Hartley. *Chem. Rev.* **1981**, *81*, 365.

organic synthesis.^{9a, 101} Earlier, their synthesis by cobalt-catalyzed reductive cross-coupling from aryl halides and either a benzyl chloride or a benzyl mesylate or from an organozinc reagent have been reported in our group.^{6e, 7b, 42} However, the application of C-S electrophile represented by sulfonium salt in the Co-Mn catalytic system has yet to be developed. Thus, benzyl sulfonium salt (**S1**), synthesized from the corresponding benzyl alcohol, was engaged as a new electrophile due to its higher reactivity and stability and is easily handling.

Table I- 1. Optimizing the activator and ligands of the reaction.



Entry	Conditions	Results ^a		
		ar-I-a1/%	Bibenzyl/%	I-b1/%
1	none	Trace	Trace	24
2	TMSBr instead of TFA	Trace	Trace	32
3	bipy (10 mol%)	44	×	31 ^b
4	4-Me-bipy (10 mol%)	Trace	Trace	54^b
5	dtbbpy (10 mol%)	..	8	47 ^b
6	4-MeO-bipy (10 mol%)	..	trace	54 ^b
7	5-Me-bipy (10 mol%)	51 ^b
8	1,10-phenanthroline (10 mol%)	42 ^b
9	Imidazole (10 mol%)	22	..	48 ^b
10	PPh ₃ (10 mol%)	×	12	37 ^b

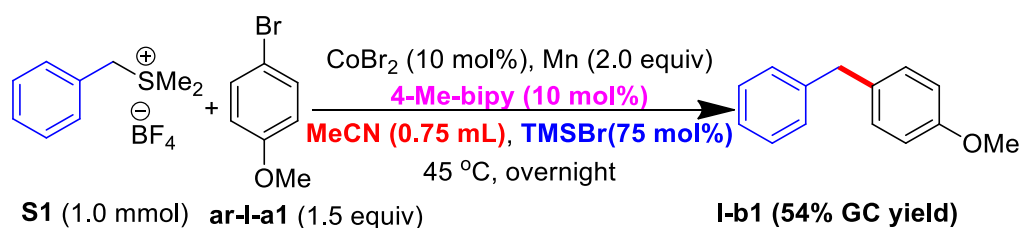
^a GC yields using hexadecane as an internal standard. ^b TMSBr was used as an activator. × = Not detected

As a model, the cross-coupling of benzyl dimethyl sulfonium salt (**S1**) and 4-bromoanisole (**ar-I-a1**) was conducted as the previous report with benzyl-OMs and Ar-X^{7b} with 10 mol% CoBr₂ and 2 equivalents of Mn activated by TFA in acetonitrile leading to the desired product **I-b1** in a 24% GC yield (**Table I- 1**, entry 1). In contrast, the yield of **I-b1** increased by about 10% using TMSBr as an activator instead of TFA (**Table I- 1**, entry 2). Different N-containing ligands and triphenylphosphine (PPh₃) were screened. The yield of the cross-coupling **I-b1** did not improve with bipy (**Table I- 1**, entry 3) but increased to around 50% with substituted bipy ligands, and only a trace amount of bibenzyl was detected (**Table I-**

¹⁰¹ (a) S. Mondal, G. Panda. *RSC Adv.*, **2014**, *4*, 28317. (b) K. E. Poremba, N. T. Kadunce, N. Suzuki, A. H. Cherney, S. E. Reisman. *J. Am. Chem. Soc.* **2017**, *139*, 5684. (c) L. L. Anka-Lufford, K. M. M. Huihui, N. J. Gower, L. K. G. Ackerman, D. J. Weix. *Chem. Eur. J.* **2016**, *22*, 11564. (d) M. Amatore, C. Gosmini. *Chem. Commun.* **2008**, 5019. (e) L. K. G. Ackerman, L. L. Anka-Lufford, M. Naodovic, D. J. Weix. *Chem. Sci.*, **2015**, *6*, 1115.

1, entries 4- 7). Using 1,10-phenanthroline as the ligand led to 42% of the yield (**Table I- 1**, entry 8). Although the use of Imidazole gave a slightly higher yield than 1,10-phenanthroline, 22% of 4-bromoanisole **ar-I-a1** remained after the reaction (**Table I- 1**, entry 9). The yield of the desired product **I-b1** did not increase obviously with PPh₃ as a ligand, but much more bibenzyl was detected compared to using other ligands (**Table I- 1**, entry 10). Similar GC yields (54%) of the desired product **I-b1** were obtained with 4-Me-bipy and 4-MeO-bipy, but considered the price of these ligands, 4-Me-bipy was used in further optimization experiments. (4-Me-bipy, 179,00 € /5 G; 4-MeO-bipy, 206,00 € /5 G from sigmaaldrich.com).

Table I- 2. Optimizing the reaction with TMSBr as the activator.

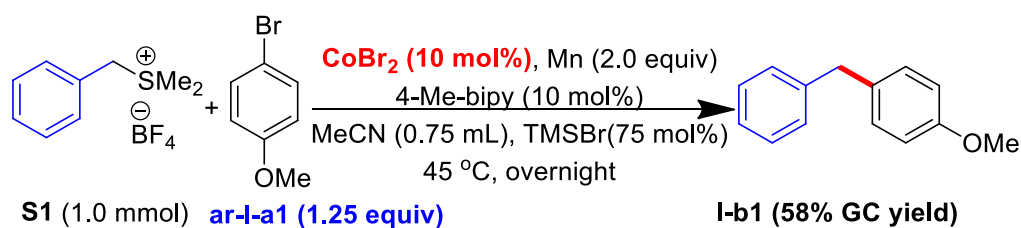


Entry	Variations			Results in ^a		
	4-Me-bipy/ mol%	S1:ar-I-a1	MeCN/ mL	ar-I-a1/%	Bibenzyl/%	I-b1/%
1	15	1.0: 1.5	0.75	7	Trace	50
2	20	Trace	..	50
3	10	1.0: 1.25	..	Trace	..	58
4	..	1.0: 1.0	..	×	..	51
5	..	1.25:1.0	..	×	9	56
6	..	10: 1.25	1.0	15	Trace	50
7	1.5	29	..	42

^a GC yields using hexadecane as an internal standard. ×= Not detected.

In the next step, the amount of 4-Me-bipy and the ratio of two starting materials were screened. As shown in **Table I- 2**, no improvement was observed when the ligand amount increased (entries 1- 2). Ranging the ratio of two electrophilic partners (**S1: ar-I-b1**) from 1.0: 1.5 to 1.25:1.0 did not cause apparent variation in the yield. But when the concentration of the medium decreased (1.25 equivalents of 4-bromoanisole **ar-I-a1** was used) in the reaction, 58% GC yield was obtained (entries 3- 5). On this base, the yield of the cross-coupling product **I-b1** decreased gradually, and the amount of remaining aryl bromide increased (entries 6- 7).

Table I- 3. Optimizing the Co catalysts.

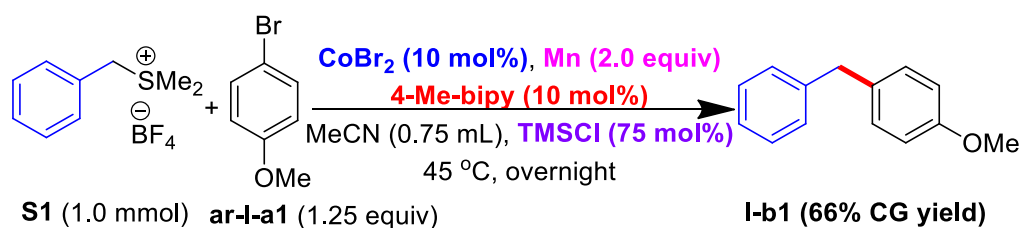


Entry	CoX2	Results ^a		
		ar-I-a1/%	Bibenzyl/%	I-b1/%
1	CoCl ₂	Trace	Trace	58
2	Co(OAc) ₂	×	..	60
3	Co(acac) ₂	Trace	5	58

^a GC yields using hexadecane as an internal standard. ×= Not detected

Moreover, various Co salts were employed in further experiments (**Table I- 3**). Similar yields were obtained with all these simple Co salts, such as CoCl₂, Co(OAc)₂, and Co(acac)₂, to that of CoBr₂ as catalyst under the condition (**Table I- 3**, entries 1-3). Under this condition, it was found that TMSCl was used instead of TMSBr, delivering a 66% yield of the desired product **I-b1**. Additionally, the price of TMSCl is lower than TMSBr, so TMSCl was chosen to activate to Mn in this arylation reaction (**Table I- 4**, entry 1).

Table I-4. Optimizing the reaction condition with TMSCl as the activator.

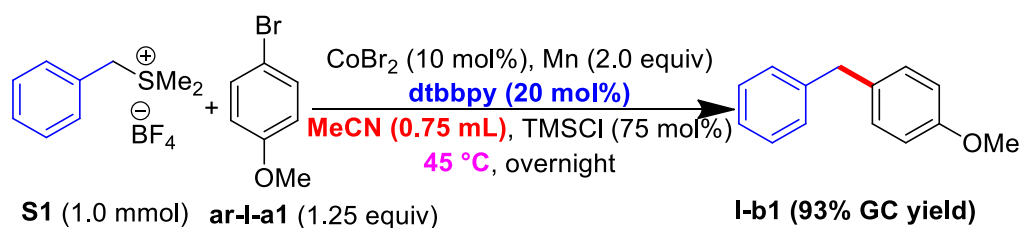


Entry	Variations				Results ^a		
	TMSCl /mol%	Ligand/ mol%	Mn/ equiv	ar-I-a1/%	Bibenzyl/%	I-b1/%	
1	None				×	5	66
2	25	4-Me-bipy	10	2.0	Trace	Trace	61
3	50	×	7	63
4	100	×	13	53
5	150	×	10	46
6	75	..	20	..	×	5	63
7	..	dtbbpy	10	..	Trace	5	58
8	20	2.0	Trace	Trace	93^b
9	1.5	22	..	50
10	2.5	×	..	72
11	3.0	×	..	69
12	4.0	×	..	60

^a GC yields using hexadecane as an internal standard. ×= Not detected. ^b 77 isolated yield.

As shown in the table **Table I-4**, the yield of the desired product **I-b1** increased slightly as the amount of TMSCl increased from 25% to 75% (**Table I-4**, entries 1- 3) but declined obviously with more TMSCl added (from 75% to 150%), along with increased bibenzyl (**Table I-4**, entries 4- 5). Adding 20 mol% of 4-Me-bipy affected slightly on the reaction efficiency (**Table I-4**, entry 6); however, replacing 4-Me-bipy with dtbbpy (20 mol%) caused a significant improvement in the yield of **I-b1** (93% CG yield, 77% isolated yield) (**Table I-4**, entry 8). Then the amount of Mn was screened with dtbbpy as a ligand (**Table I-4**, entries 9- 12). Whatever the amount of Mn, the cross-coupling efficiency did not get further enhanced.

Table I- 5. Optimizing the temperature and solvents.

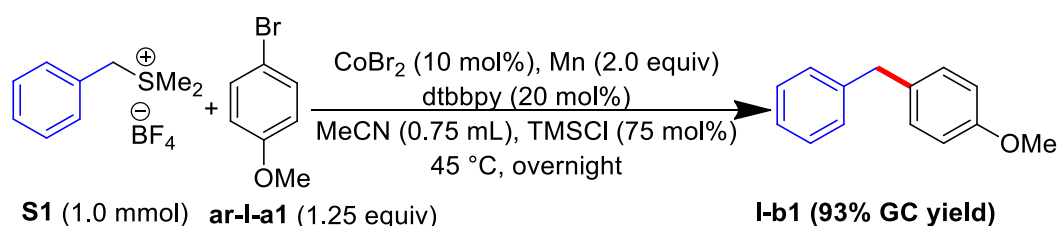


Entry	Variations			Results ^a		
	T/ °C	Solvent/ mL		ar-I-a1/%	Bibenzyl/%	I-b1/%
1	rt	MeCN	0.75	×	Trace	77
2	60	×	..	89
3	45	MeCN: Py	0.7: 0.05	×	..	86
4	0.65: 0.10	×	..	52
5	0.6: 0.15	×	..	32
6	..	DMF	0.75	√	√	Trace
7	..	DMA	..	√	√	Trace
8	..	THF	..	√	9	6
9	..	Toluene	..	√	×	×
10	..	DME	..	√	√	Trace

^a GC yields using hexadecane as an internal standard. √ =detected ×= Not detected

Although the cross-coupling of benzyl sulfonium salt **S1** and 4-bromoanisole **ar-I-a1** gave a 93% GC yield at 45 °C, the temperature was screened in order to further improve the yield. (Table I- 5, entries 1- 2). The yield of **I-b1** decreased slightly when the reaction was conducted at rt or 60 °C. Next, the mixed solvent of MeCN and Py was tried in the reaction, which is commonly used in our reported Co-Mn catalytic system. It could see that the yield of the cross-coupling product decreased as the ratio of Py in the mixed solvent increased because the addition of pyridine accelerated the homo-coupling process of the aryl bromide (Table I- 5, entries 3- 5). Finally, different solvents instead of MeCN were tried under the condition, as shown from entries 6- 10 in the table, poor results were obtained with either polar solvents, like DMF, DMA, or non-polar solvents, such as THF, Toluene, and DME, along with some remained **ar-I-a1** and bibenzyl after the reaction.

Table I- 6. Control experiments.

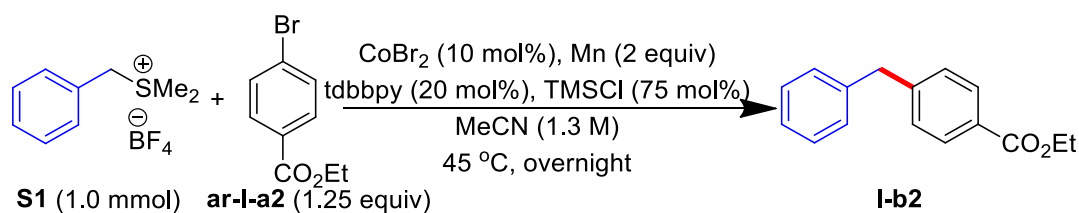


Entry	Variations	Results ^a		
		ar-I-a1/%	Bibenzyl/%	I-b1/%
1	CoBr ₂ (5 mol%), dtbbpy (10 mol%)	5	trace	49
2	Zn instead of Mn		..	23
3	w/o CoBr ₂	√	..	×
4	w/o dtbbpy	×	..	27
5	w/o t Mn	√	..	×
6	w/o TMSCl	√	..	×
7		√	12	30
8				79% ^b
9				49

^a GC yields using hexadecane as an internal standard. √ =detected ×= Not detected

Decreasing the amounts of Co catalyst and ligand to half resulted in a significant decline in the yield of the cross-coupling product (Table I- 6, entry 1). Replacing Mn with Zn as the reductant, a lower yield was obtained, along with a large amount of unreacted 4-bromoanisole **ar-I- a1** left, and trace amounts of both homo-coupling products were detected (Table I- 6, entry 2). Control experiments demonstrated that the presence of the cobalt catalyst, Mn, and the activator was essential for this reductive cross-coupling (Table I- 6, entries 3, 5, 6), while the presence of dtbbpy made a significant improvement in this Csp³-Csp² bond forming process (Table I- 6, entry 4). Moreover, the cross-coupling 1-benzyltetrahydrothiophenium tetrafluoroborate salt instead of **S1** as the C-S electrophile with aryl bromide **ar-I-1** led to a lower yield than using **S1** (Table I- 6, entry 7). For a substituted benzyl sulfonium salts with a methyl and an ester group, under the optimization condition (10 mol% of CoBr₂, 2.0 equivalents of Mn activated by 75 mol% TMSCl in 0.75 mL of MeCN), the cross-coupling led to the desired products in a 79% isolated yield and a 50% GC yield, respectively (Table I- 6, entries 8- 9). A lower yield of the latter was obtained due to the higher reactivity of aryl bromide bearing EWG.

Table I- 7. Optimizing the reaction conditions with ethyl 4-bromobenzoate.

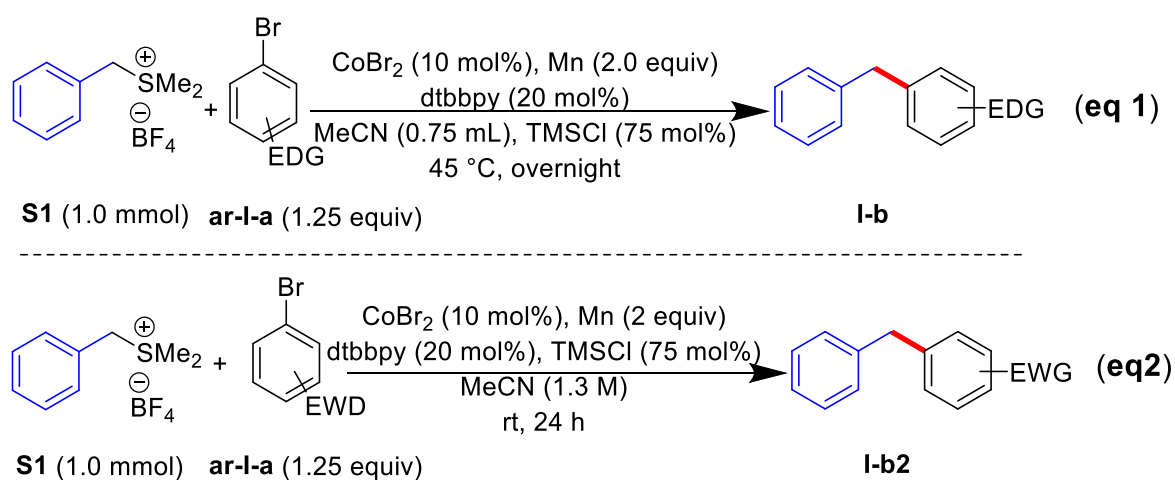


Entry	Variations	I-b2 ^a /%
1	None	49
2	rt, 24h	89 (88 ^b)
3	S1: ar-I-a2=1.25: 1.0, rt	62
4	30 °C	29

^a GC yields using hexadecane as an internal standard. ^b isolated yield.

To improve the efficiency of the cross-coupling between benzyl sulfonium salts and aryl bromide bearing electron-withdrawing groups, some experiments were conducted (Table I- 7). To our delight, an 89% GC yield (88% isolated yield) was obtained when the reaction was conducted at rt for 24 h (Table I- 7, entry 2). Whereas the yield of the cross-coupling decreased to 62% with a different ratio of **S1** and **ar-I-a2** (Table I- 7, entry 3). Increasing the temperature from rt to 30 °C decreased the yield significantly (Table I- 7, entry 4).

Thus, for the cross-coupling between benzyl sulfonium salt **S1** and aryl bromide, the optimized conditions are as following (Scheme I- 1):

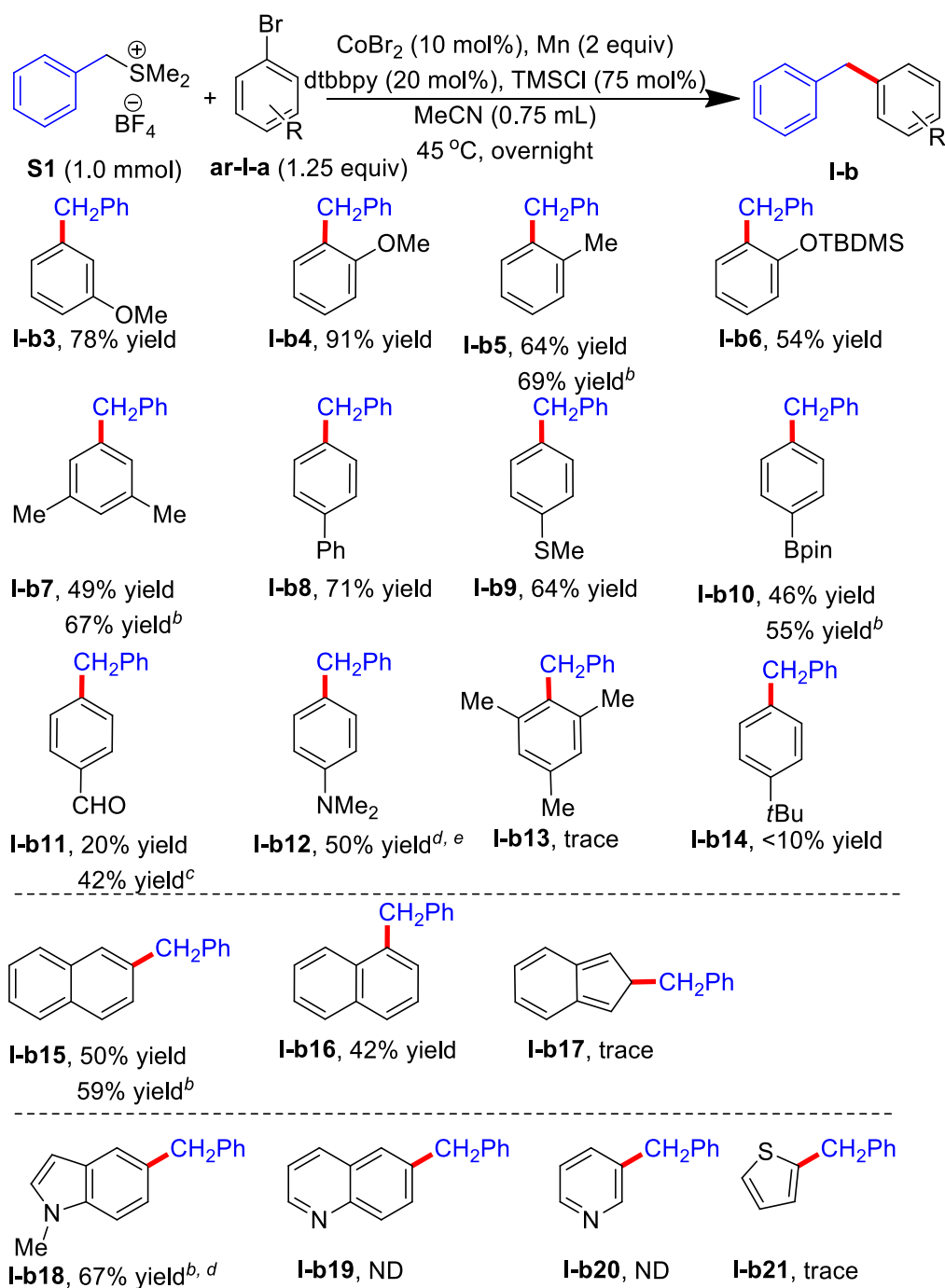


Scheme I- 1. Optimized conditions for the cross-coupling between benzyl sulfonium salt **S1** and aryl bromide.

2.2. The scope of arylation reaction between benzyl sulfonium salts and aryl bromides.

With these optimized conditions in hand (*Scheme I-1*), the scope of this reductive arylation cross-coupling was set out with (het)aryl bromide derivatives.

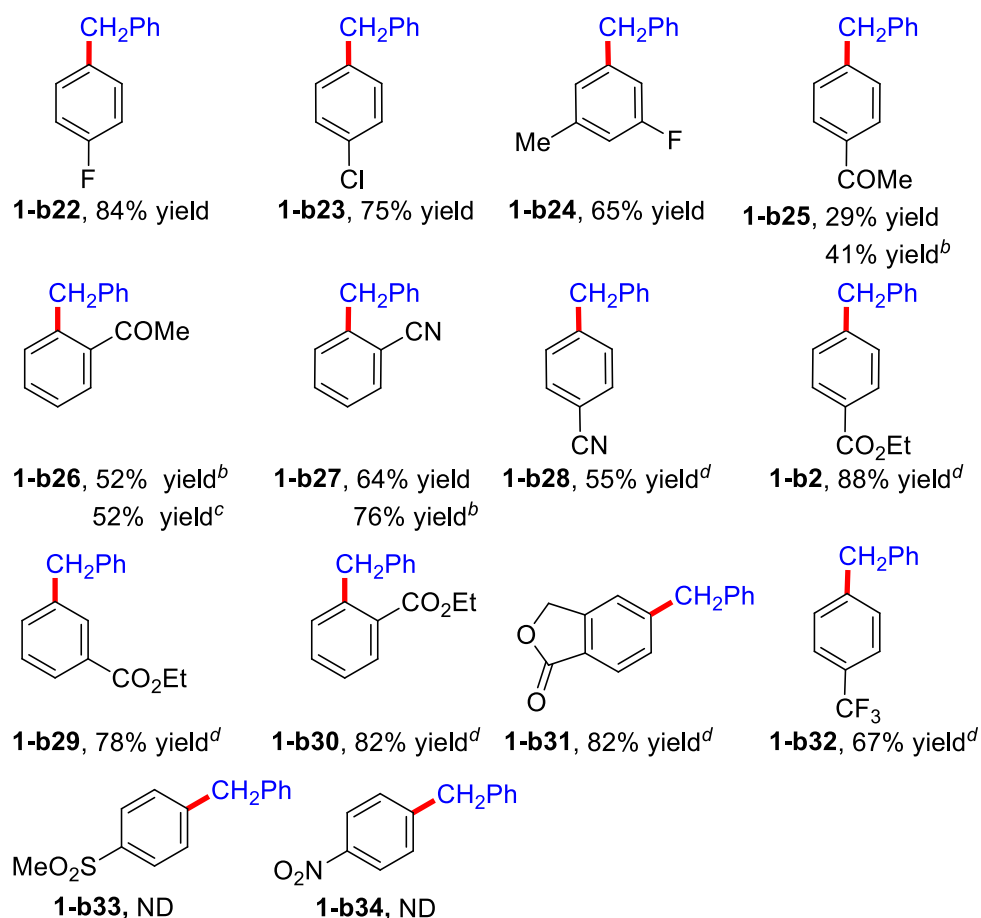
Table I-8. Scope of the Reaction of Benzyl dimethyl sulfonium Salt (S1) with (het) Aryl Bromides.^a



^a Isolated yield. ^b MeCN (0.7 mL) / Py (0.05 mL). ^c 2-(4-bromophenyl)-1,3-dioxolane was used. ^d NMR yield. ^e dtbbpy (30 mol%).

As shown in **Table I-8**, a wide range of aryl bromides bearing EDG were successfully coupled with **S1** leading to diarylmethanes in moderate to excellent yields (from **I-b3** to **I-b12**). Functional groups, such as methoxy (**ar-I-a3**, **ar-I-a4**), methyl (**ar-I-a5**, **ar-I-a7**), silane (**ar-I-a6**), phenyl (**ar-I-a8**), thioether (**ar-I-a9**), boron (**ar-I-a10**) were compatible with the reaction conditions. The efficiency of this arylation reaction did not affect by the steric hindrance on the aryl bromides, whether the ortho substituent is methoxy (**ar-I-a4**), methyl (**ar-I-a5**), tert-butyldimethylsilyl (**ar-I-a5**). The cross-coupling products (**I-b4** to **I-b6**) were obtained in 54% to 91% yields, which decreased as the electron-donating ability of the substituents decreased. Two methyl on the aryl bromide **ar-I-a7** was tolerated and afforded corresponding diarylmethanes in a 49% yield. However, the yield of **I-b7** increased to 67% when the mixed solvent of MeCN/Py was used. In contrast, no desired product was detected when three methyl groups were on the aryl bromide due to the huge steric hindrance of **ar-I-a13**. With 4-bromo-benzaldehyde as a coupling partner, only a 20% yield of 4-benzyl benzaldehyde (**I-b11**) was isolated. However, protecting the carbonyl function (2-(4-bromophenyl)-1,3-dioxolane) led to a higher yield (42%). Unexpectedly, only a 10% yield of the desired product was detected when aryl bromide bearing the *t*-Butyl group (**I-b14**). For some aryl fused ring compounds, like naphthyl bromides, and 2-bromoindene, a moderate yield of **I-b15** was obtained when bromide is at the 2-position of the naphthene, while a bit lower yield of the cross-coupling product (**I-b16**) was obtained with Br at 1-position. The protected bromoindole led to a 67% NMR yield of **I-b17** in the mixed solvent (MeCN/Py). Whereas 2-bromoindene was used as a partner, only a trace amount of the cross-coupling product (**I-b18**) and indenenes were detected. Moreover, heteroaryl bromides were also tried in this Co-catalyzed Csp³-Csp² bond-forming reaction. Disappointingly, bromoquinoline, bromopyridine, or bromothiophene were not tolerated in the condition (**I-b19** to **I-b21**), even using the mixed MeCN/Py as solvent. It is worth mentioning that, in some cases, for some less reactive aryl bromides (**ar-I-a5**, **ar-I-a7**, **ar-I-a10**, **ar-I-17**), the addition of pyridine proved beneficial, probably because it stabilizes the low valent cobalt active species.

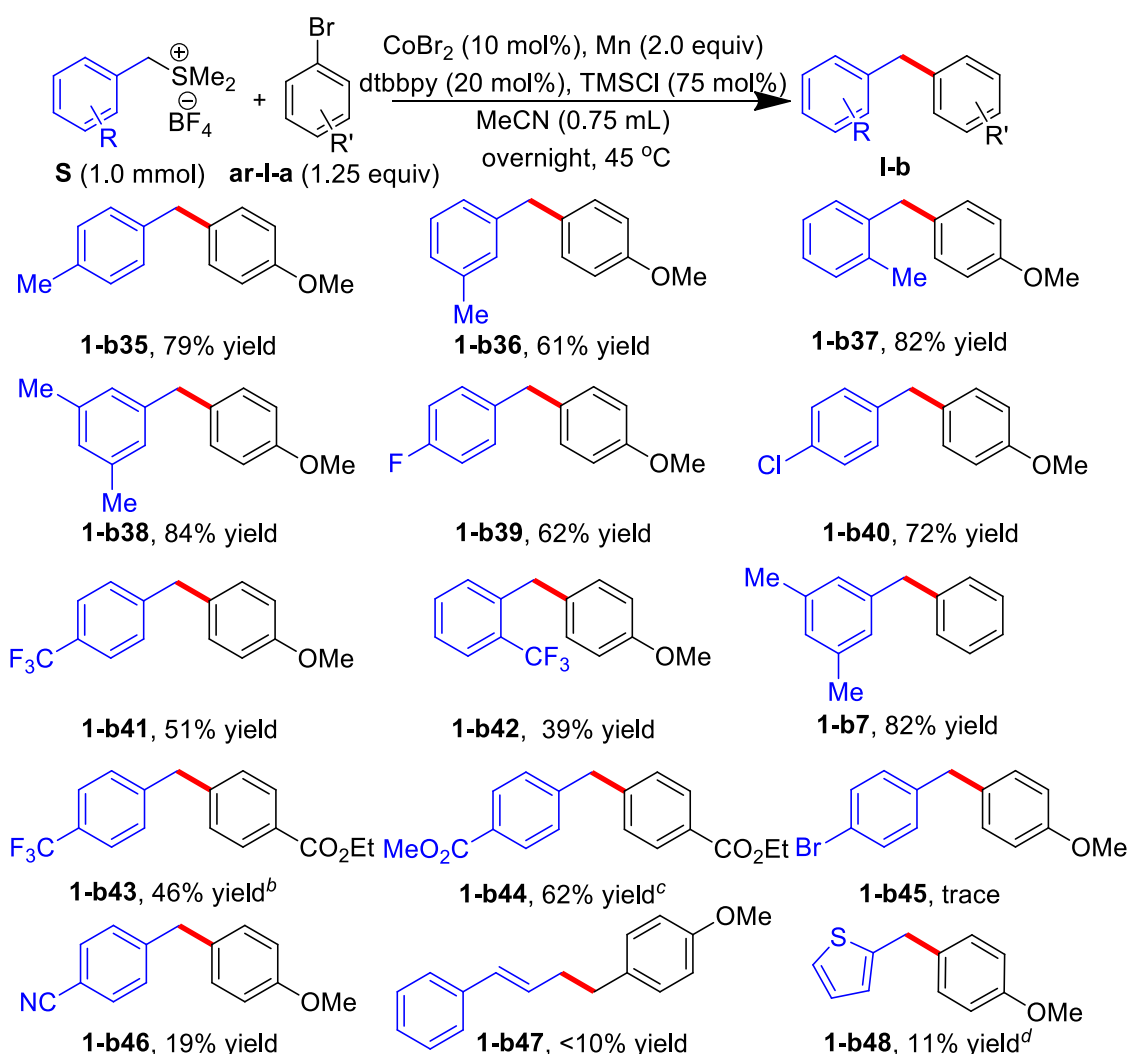
Table I-9. Scope of the reaction of benzyl dimethyl sulfonium Salt (S1) with aryl bromides with EWG.^a



^a Standard condition as **Table I-8**, Isolated yield. ^b MeCN (0.7 mL)/ Py (0.05 mL). ^c dtbbpy (30 mol%). ^d rt, 24 h.

For aryl bromides bearing halides (fluorine, chlorine), even two different substitutes, moderate to good yields were obtained as shown in **Table I-9**, entries **I-b22**, **I-b23**, **I-b24**. The acetyl group on the *o*-position of aryl bromides led to better yield in the solvent of MeCN/ Py than at the *p*-position (**I-b25**, **I-b26**). With aryl bromides bearing higher reactivity electron-withdrawing groups like nitriles (**ar-I-a27**, **ar-I-a28**), esters (**ar-I-a2** to **ar-I-a31**), and trifluoromethyl (**ar-I-a32**), the reaction could be conducted at room temperature but for a longer time (24 h) to deliver good yields (55% -58%). As described, the reactions of **S1** with aryl bromides involving EDG were insensitive to the steric hindrance on the aryl bromides, as **ar-I-a27**, **ar-I-a3**, and the cross-coupling products proceeded efficiently (**I-b27**, **I-b30**). Moreover, for the **ar-I-a27**, the cross-coupling product was obtained in a 76% yield in a mixture of MeCN/ Py as the solvent and about 10% higher than in MeCN alone. However, when 4-bromophenyl methyl sulfone (**ar-I-a33**) and 1-bromo-4-nitrobenzene (**ar-I-a34**) were used as the partners, no desired product was detected with either **S1** or benzyl sulfonium salt bearing an ester group.

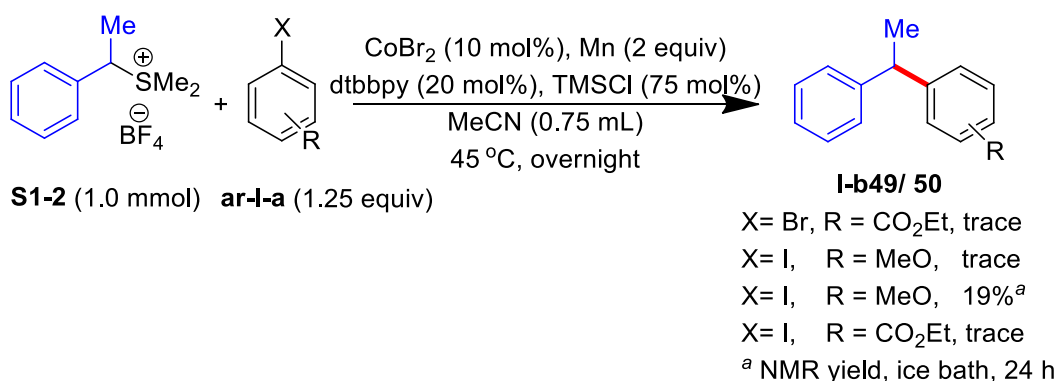
Table I- 10. Scopes of substituted benzyl dimethyl sulfonium salt derivatives (S) with aryl bromides.^a



^a Isolated yield. ^b rt, 24 h. ^c Ethyl 4-iodobenzoate was used, MeCN (0.7 mL) / Py (0.05 mL), rt, 24 h. ^d NMR yield.

For benzyl dimethyl sulfonium salts, various functional groups were also well tolerated on their aromatic moieties and led to moderate to good yields (Table I- 10), irrelevant to whether they were in *para*- (ar-I-a35, ar-I-a39 to ar-I-a41, ar-I-a43- ar-I-a44), *meta*- (ar-I-a36, ar-I-a38, ar-I-b7), or *ortho*-position (ar-I-a27, ar-I-a42). Benzyl dimethyl sulfonium salts bearing a halogenated group, such as F or Cl, coupled well with 4-bromoanisole ar-I-a1 and provided I-b39 and I-b40 in 62% and 72% yield, respectively, while only a trace amount of the desired product was detected with bromo group, along with the reduced aryl bromide and the dimers of benzyl sulfonium salts (I-b45). With a trifluoromethyl group in the *para*- or *ortho*- position, moderate yields of the desired product were obtained (I-b31, I-b42) because of the detrimental formation of bibenzyl derivatives. In addition, substituted benzyl sulfonium salts were coupled with bromobenzene (I-b43) or aryl halides bearing an ester group (I-b43, I-b44) and provided 82% yields at room temperature. Furthermore, benzyl sulfonium salts bearing cyano group or generated from cinnamyl alcohol were used in the optimized condition; as shown, the

yields of the cross-coupling products were poor (**I-b46**, **I-b47**). The former mainly generated the reducing product from the substituted benzyl sulfonium salt, while the latter generated many homo-coupling products of both electrophiles. Thus, to improve the reactivity of the aryl halides, ethyl 4-bromobenzoate **ar-I-a2** or 4-iodoanisole were used with the latter. However, the results still needed improvement. The sulfonium salt generated from heteroaryl methyl alcohol was also tried in the reaction, while only 11% NMR yield of the cross-coupling product was detected (**I-b48**).



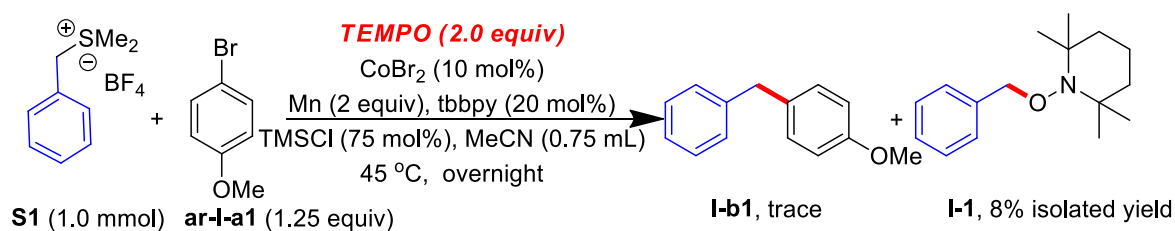
Scheme I- 2. Secondary benzyl dimethyl sulfonium salt with aryl halides.

In addition to the cross-coupling of primary benzyl sulfonium salts with aryl bromides, an α -substituted secondary benzyl sulfonium salt (**S1-2**) was explored under the optimized condition (**Scheme I- 2**). However, the reaction did not succeed between **S1-2** and aryl halides (Br, I) either with EDG or EWG. The reduced and homo-coupling products of aryl halides were detected as products, along with the homo-coupling product of benzyl sulfonium salt **S1-2**. In comparison, a 19% NMR yield of the cross-coupling product between **S1-2** and 4-iodoanisole was detected under decreased reaction temperature and extended reaction time. In this case, α -substituted secondary benzyl sulfonium salt (**S1-2**) was added dropwise, and the yield of the cross-coupling did not improve.

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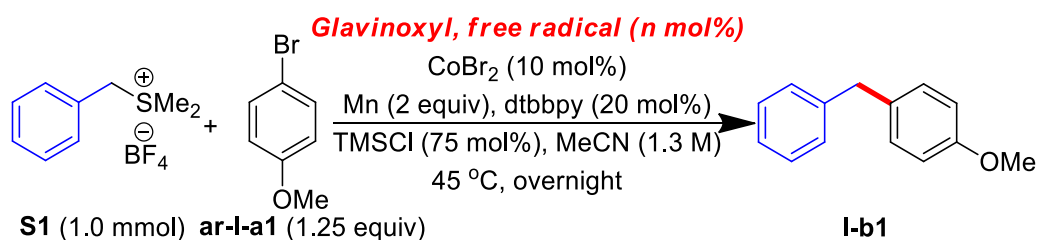
2.3. Exploration of the Mechanism.

2.3.1. Trapping experiments



Scheme I-3. TEMPO trapping experiments with aryl bromide.

To understand deeply the mechanism of this Co-catalyzed reductive arylation formation process, a few experiments were conducted. As shown, in the presence of 2 equivalents of 2,2,6,6-tetramethylpiperine-1-oxyl (TEMPO), the reactions were inhibited significantly using aryl bromides as coupling partners (*Scheme I-3*). To our delight, the cross-coupling product (**I-b1**) of **S1** with TEMPO was obtained in an 8% isolated yield, demonstrating that benzyl sulfonium salt acted as a benzyl radical precursor in this Co-catalyzed arylation reaction.



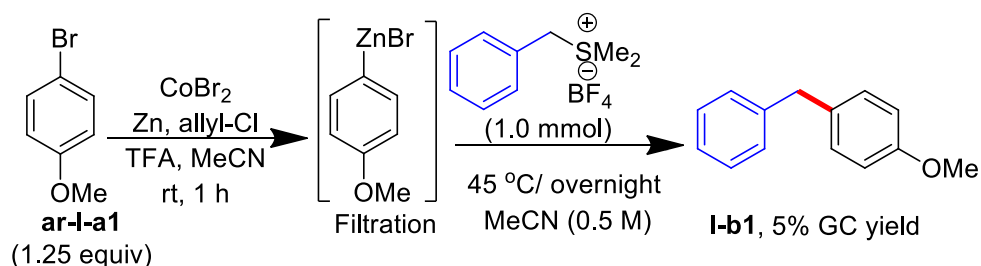
Entry	n (mol%)	I-b1 ^a /%
1	/	93
2	50	66
3	100	24
4	125	14

^a GC yields using hexadecane as an internal standard.

Scheme I-4. Radical trapping experiment with glavinoyl, free radical.

On the other hand, glavinoyl, free radical (n mol %) was performed with **S1** and **ar-I-a1** under the standard arylation condition (*Scheme I-4*). As the amount of free radical reagent increased, the yield of **I-b1** decreased from 93% to 14%. The Co-catalyzed reductive cross-coupling of benzyl sulfonium salts and aryl bromide process was inhibited significantly.

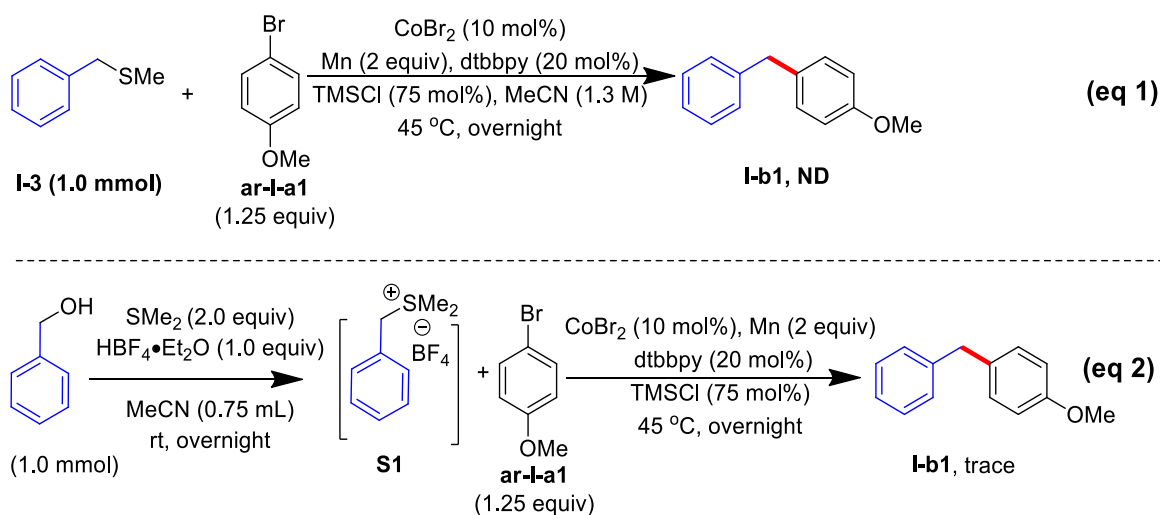
2.3.2. Organozinc experiments



Scheme I-5. Organozinc experiments

On the other hand, 23% of the cross-coupling product was obtained when Zn instead of Mn was used as the reductant metal (*Table I-6*, entry 2). Thus, the above experiment was conducted to investigate if organozinc species can be coupled with benzyl sulfonium salts (*Scheme I-5*). The aryl organozinc reagent was synthesized according to the reported procedure¹⁰², filtrated, and injected into an acetonitrile mixture at 45 °C coupling with the benzyl sulfonium salt **S1** and stirred overnight. Finally, only a 5% GC yield of the desired product **I-b1** was detected. Without filtering the organozinc, a trace amount of the desired product was detected with the homo-coupling of the organozinc; even dtbbpy was added at the second step.

2.3.3. One-pot reaction to construct Csp³-Cp² bond.



Scheme I-6. One-pot reaction with benzyl sulfide or benzyl alcohol

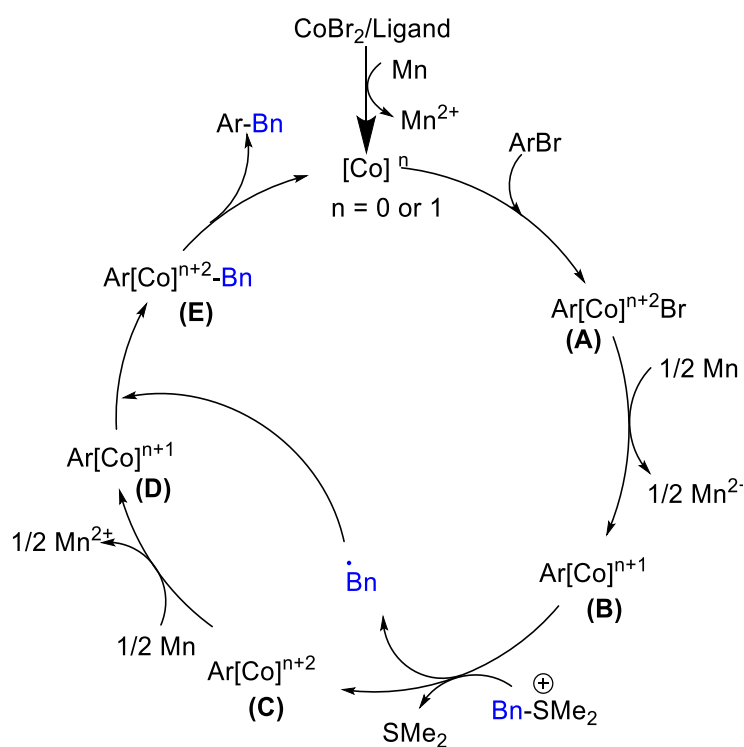
To explore if the presence of benzyl sulfonium is necessary in this Co-catalyzed reductive arylation reaction, benzyl methyl sulfide and benzyl alcohol as starting materials were directly employed in the reaction, respectively (*Scheme I-6*). As shown in **eq1**, no desired product was detected when benzyl

¹⁰² J. M. Begouin, C. Gosmini, *J. Org. Chem.* **2009**, *74*, 3221.

methyl sulfide was used as the starting material under the optimized condition, along with the two remaining electrophiles detected after the reaction. When benzyl sulfonium salt **S1** was synthesized from benzyl alcohol and used directly without filtration with **ar-1-a1**, a trace amount of **I-b1** was detected, as well as the remaining aryl bromide and homo-coupling product of **S1** (*Scheme I-6, eq 2*). These results demonstrated that it is mandatory to synthesize benzyl sulfonium salts before using them in the reductive arylation reaction.

2.3.4. Proposed Mechanism.

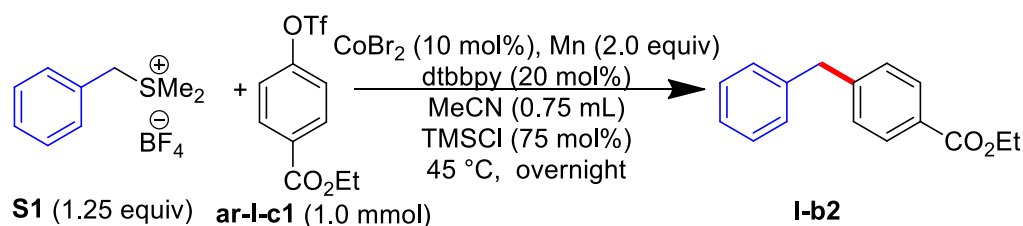
Based on these results, a mechanism depending on the nature of the organic halide was proposed (*Scheme I-7*). Similar to our previous reports on cobalt-catalyzed C-C bond formation of diarylmethanes^{7b, 42}, the initiation step is the reduction of the Co(II) precatalyst into the active low-valent Co species by the manganese. Subsequent oxidative addition to the aryl bromide forms an aryl Co intermediate **A**, which is reduced into **B** by Mn. Then this species **B** undergoes one electron transfer to benzyl sulfonium salt, delivering a Co complex **C**, a benzyl radical together with a thioether, due to the positive charge of benzyl sulfonium salt, which results in undergoing easily homolytic fragmentation of its C_{benzyl}-S bonds via electron reduction⁷⁹. Finally, the benzyl aryl Co complex **E**, generated from a combination of the benzyl radical and a reduced low-valent Co complex **D**, provides the cross-coupling product by reductive elimination along with the regeneration of the active species.



Scheme I-7. Proposed Mechanism

2.4. Exploration with other Csp²-electrophiles- aryl triflate.

Table I- 11. Exploration of benzyl sulfonium salt with aryl triflate.



Entry	Variations	Results ^a		
		ar-I-c1/%	Bibenzyl/%	I-b2/%
1	none	✓	Trace	✗
2	80 °C instead of 45 °C	✓	✓	✗
3	MeCN/ Py (0.65 /0.15 mL) instead of MeCN	✓	✓	✗
4	MeCN/ Py (0.65 /0.15 mL) instead of MeCN	✓	✓	✗ ^b
5	DMF/ Py (0.65 /0.15 mL) instead of MeCN	✓	✓	Trace
6	PPh ₃ instead of dtbbpy	✓	✓	Trace
7	TFA instead of TMSCl	✓	✓	Trace
8	Mn (4.0 equiv) instead of Mn (2.0 equiv)	✓	✓	Trace
9	PhSM ₂ ⁺ BF ₄ ⁻ instead of ar-I-c1	✗	✓	✗
10	Methyl 4-chlorobenzate instead of ar-I-c1	✓	✓	Trace

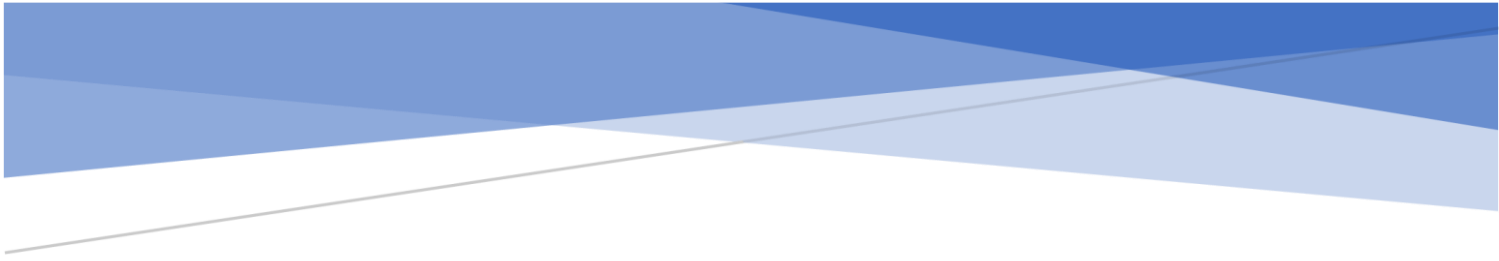
^a GC yields using hexadecane as an internal standard. ✓ =detected ✗= Not detected. ^b 80 °C

Except for the cross-coupling of benzyl sulfonium salts and aryl bromide, other Csp²-electrophiles were also studied in this Co-Mn-catalyzed Csp³-Csp² bond formation reaction. As shown in [Table I- 11](#), replacing aryl bromide **ar-I-a1** with benzene triflate derivative **ar-I-c1** under the optimized arylation condition, no desired product was detected by GC, and the **ar-I-c1** remained after the reaction due to its low reactivity (entry 1). Increasing the temperature from 45 °C to 80 °C, the result was the same with more bibenzyl (entry 2). Furthermore, the solvent was screened (entries 3- 5). Pyridine was added in MeCN, usually used in cross-coupling involving Csp² electrophiles^{6f, g}, but no cross-coupling was obtained, either at 45 °C or 80 °C. At the same time, DMF/ Py was used as the solvent, and a trace amount of the cross-coupling product was detected (entry 5). Using PPh₃ instead of dtbbpy, which was used for the cross-coupling of benzene triflate and benzene bromide cross-coupling^{6f} (entry 6), or changing activator (entry 7), as well as increasing the amount of Mn (entry 8), no improvement was observed. Finally, the cross-coupling of benzene sulfonium salt or the substituted benzene chloride with benzyl sulfonium salt **S1** under the reaction condition (entries 9- 10), no desired product was detected in the cross-coupling with benzene sulfonium salt, but a bit of thioanisole was observed. A trace amount of

the cross-coupling product was detected, along with remained methyl 4-chlorobenzoate and the homo-coupling of the benzyl sulfonium salt **S1**.

3. Conclusion and Perspectives.

In conclusion, benzyl sulfonium salts, which are stable and readily available from alcohols, have demonstrated the potentiality for the construction of Csp³-Csp² bonds with various functionalized aryl bromides via a Co-catalyzed reductive cross-coupling. A large variety of functionalized diarylmethanes were synthesized from different benzyl sulfonium salts and aryl bromides bearing EDG and EWG in good to excellent yields under mild conditions. This Co-catalyzed reductive arylation reaction is a simple and new alternative method to the synthesis of diarylmethanes by C-S bond cleavage. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl sulfonium salts. Although excellent results have been obtained to construct Csp³-Csp² bonds from benzyl sulfonium salts and aryl bromides, the reactions between benzyl sulfonium salts and Csp²-O electrophiles (Csp²-OTf) or aryl chloride need to be improved. Moreover, this Co-Mn catalyzed system was unsuitable for heteroaryl halides and heteroaromatic benzyl sulfonium salts. Thus, extending the scope of the sulfonium salts and aryl halides is still interesting to explore. We have demonstrated that the Co-catalyzed reductive cross-coupling of benzyl sulfonium salts and aryl bromides was possible and showed benefit to synthesize diarylmethane composed to the Ni-catalyzed cross-coupling, which employed more expensive aryl iodides⁸⁰.



**Chapter II: Co-Catalyzed Construction
of Csp³- Csp³ Bonds via Benzyl Sul-
fonium Salts and Unactivated C-X (I,
Br) Electrophiles**

1. Benzyl Sulfonium Salts with Unactivated Alkyl Iodides

Inspired by the good results of Co-catalyzed arylation via the cross-coupling of sulfonium salts and aryl bromides, the research field with these active C_{Bn}-S electrophiles was considered to build Csp³-Csp³ bonds. As introduced in **Introduction- 3**, the Csp³-Csp³ bonds are ubiquitous linkages in a range of natural products and pharmaceuticals. However, their formation remains challenging compared to well-developed Csp³-Csp² and Csp²-Csp² bond formation^{15,83}. Indeed, it is rather challenging to control the selectivity between two radical-based electrophiles exhibiting the same hybridization and to avoid the competitive β-hydride elimination pathway. Thus, the critical aspect is finding a suitable electrophile for this C_{Bn}-S electrophile to achieve Csp³-Csp³ bond formation.

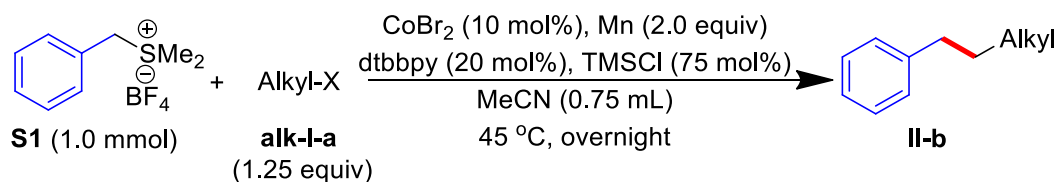
This chapter studied the Co-catalyzed cross-electrophile coupling of benzyl sulfonium salts with inactivated alkyl compounds. This reaction was never studied, regardless of the transition metal catalysis.

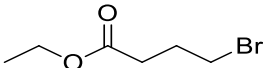
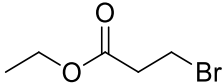
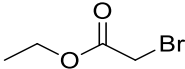
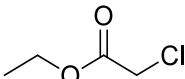
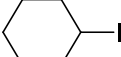
2. Results and Discussions between Benzyl Sulfonium Salts with Unactivated Alkyl Iodides

2.1. Optimization of reaction conditions

2.1.1. Iodocyclohexane as an electrophilic partner with benzyl sulfonium salt (S1).

Table II- 1. The cross-coupling of alkyl halides with S1 under the arylation conditions.



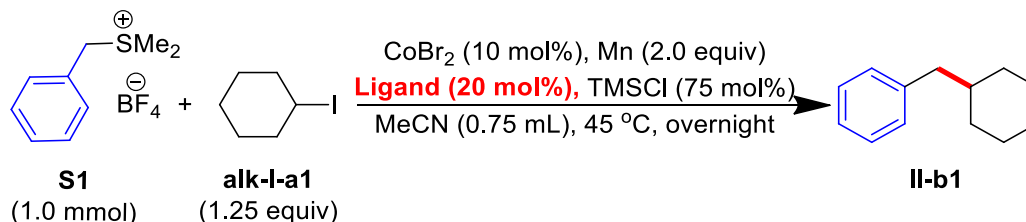
Entry	Alkyl-X	Results ^a		
		Alkyl-X	Bibenzyl	II-b
1		√	√	Trace
2		×	√	×
3		×	√	×
4		×	√	×
5		×	√	√

^a was detected by GC-MS. √ =detected, ×= Not detected.

Our investigation of Csp³-Csp³ bond formation started with the cross-coupling of benzyl sulfonium salt **S1** and ethyl 4-bromobutyrate under the conditions for diarylmethane formation from benzyl sulfonium salts and aryl halides which were described in [Chapter I](#). However, only a trace amount of the desired product was detected, along with the remaining ethyl 4-bromobutyrate and homo-couplings of two starting materials. Thus, to search for a suitable Csp³-X electrophile, various alkyl halides were applied in the conditions with **S1** ([Table II- 1](#)). As shown, no alkyl-Br remained as the reactivity of alkyl-Br increased. However, the desired product was not detected either ([Table II- 1](#), entries 1-3), even after replacing the alkyl bromide with the corresponding alkyl chloride ([Table II- 1](#), entry 4). While using Iodocyclohexane (**alk-I-1**) as another partner with benzyl sulfonium salt **S1**, a small amount of the cross-coupling product was detected by GC-MS ([Table II- 1](#), entry 5). As the reactivity of Iodocyclohexane (**alk-I-a1**) is higher than ethyl 4-bromobutyrate but lower than α-halides acetic acid ethyl

ester, thus, **alk-I-a1** was considered an electrophilic partner in the Co-catalyzed reductive construction of the Csp³-Csp³ bond cross-coupling reaction.

Table II- 2. Screening the ligands of reaction between S1 and alk-I-a1.

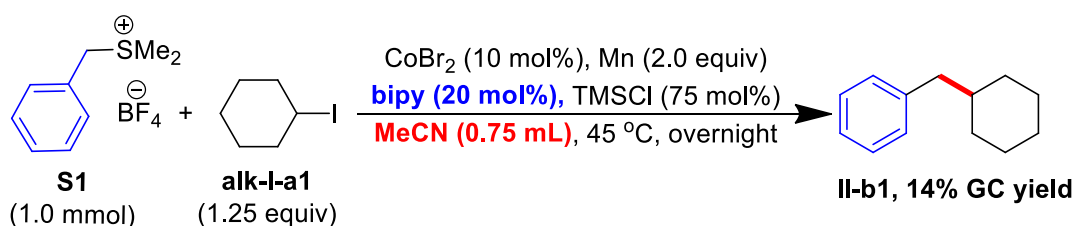


Entry	Ligand	Results ^a		
		alk-I-a1	Bibenzyl/%	II-b1/%
1	bipy	×	5	14
2	4-Me-bipy	×	5	11
3	5-Me-bipy	×	5	Trace
4	4-MeO-bipy	×	10	9
5	1.10-phenanthroline	×	13	10
6	PPh ₃	×	13	6
7	dppe	×	5	9

^a GC yields using n-hexadecane as a standard reference. × = Not detected

The optimization process began with screening ligands. As shown in **Table II- 2**, **alk-I-a1** was consumed completely whatever ligands were added under the condition, and the yield of cross-coupling product **II-b1** ((cyclohexylmethyl)benzene) decreased slightly as substituted bipy ligands used (**Table II- 2**, entries 1- 5). The addition of 4-MeO-bipy, 1.10-phenanthroline, as well as PPh₃ generated more bibenzyl product, which means that their use improved the C-S bond cleavage but still is not good enough for the cross-coupling process (**Table II- 2**, entries 4- 6). When a bidentate organophosphorus ligand (dppe) was used, the yield of this Co-catalyzed cross-coupling declined (**Table II- 2**, entry 7).

Table II- 3. Optimizing reaction condition of S1 with alk-I-a1.

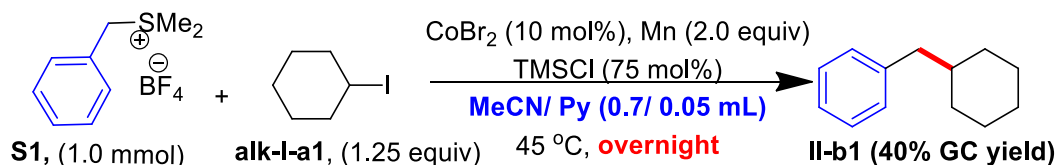


Entry	Variations	Results ^a		
		alk-I-a1	Bibenzyl/%	II-b1/%
1	bipy (10 mol%)	×	4	19
2	MeCN/Py = 0.7 mL/0.05 mL	×	14	27
3	MeCN/Py = 0.7 mL/0.05 mL	×	14	40^b
4	MeCN/Py = 0.65 mL/0.1 mL	×	21	38 ^b
5	MeCN (0.75 mL)	×	15	28 ^b
6	Py (10 mol%)	×	16	26 ^b
7	Py (50 mol%)	×	10	28 ^b
9	Py (75 mol%)	×	7	30 ^b
10	Py (100 mol%)	×	10	37 ^b

^a GC yields using n-hexadecane as a standard reference. ^b Without bipy as a ligand. × = Not detected

Then, a series of optimizing experiments were conducted in the presence of pyridine. Decreasing the amount of bipy to 10 mol% gave a 19% yield of cross-coupling product **II-b1**, and a bit higher yield was obtained by adding a small amount of Py as a co-solvent (**Table II- 3**, entry 1, 2). Nevertheless, removing bipy from the condition with MeCN-Py as a co-solvent, the yield of **II-b1** increased to 40%, along with a significant amount of bibenzyl (**Table II- 3**, entry 3). Increasing the ratio of Py in the co-solvent did not cause an improvement in yield but gave more bibenzyl (**Table II- 3**, entry 4). Adding MeCN as a single solvent without bipy as the ligand led to a noticeable decline in the cross-coupling efficiency (**Table II- 3**, entry 5). In this case, using Py as a ligand did not lead to improvement in **II-b1** yield, but the homo-coupling product-bibenzyl decreased slightly (**Table II- 3**, entries 6- 10). However, this yield of cross-coupling **II-b1** remained around 30- 40%, regardless of changing the activator, screening the ratio of **S1** and **alk-I-a1**, or modifying the TMSCl and Py adding time. These results made us consider whether the **alk-I-a1** is a suitable electrophilic partner in this Co-catalyzed reductive Csp³-Csp³ bond formation reaction.

Table II- 4. Following reactions of S1 with alk-I-a1.



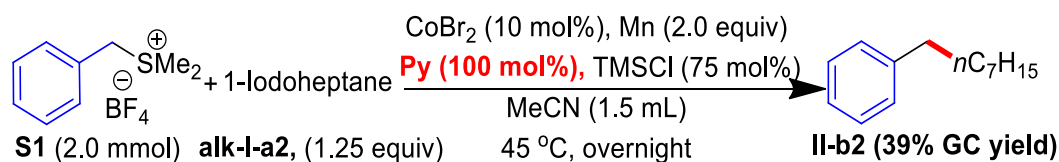
Entry	Time	Results ^a		
		alk-I-a1	Bibenzyl/%	II-b1/%
1	30 min	√	×	12
2	1 h	√	×	21
3	3h	√	Trace	21
4	6h	√	6	25

^a GC yields using n-hexadecane as a standard reference. √ =detected, ×= Not detected

The following-up reactions showed that the homo-coupling of **alk-I-a1** was generated formerly than bibenzyl, and after 1 h, the yield of the cross-coupling product, **II-b1** rose slowly (Table II- 4). To inhibit the homo-coupling products of the two electrophiles, particularly the alkyl electrophiles, the reactivity of primary alkyl iodides (**alk-I-2**) were considered. Thus 1-Iodoheptane (**alk-I-a2**) was used as the other partner ultimately.

2.1.2. Iodoheptane as an electrophilic partner with benzyl sulfonium salt (S1).

Table II- 5. Optimizing pyridine of S1 with alk-I-a2.

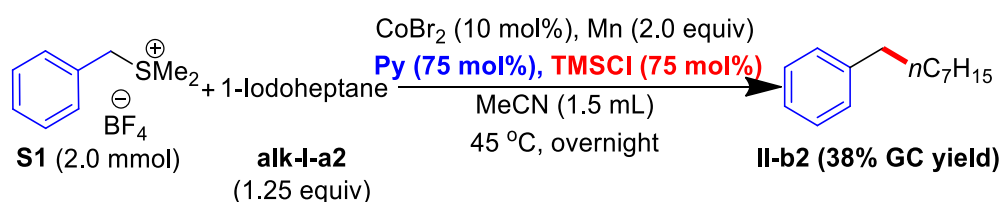


Entry	Variations		Results ^a		
	Py / n mol%		alk-I-a2/%	Bibenzyl/%	II-b2/%
1	None		×	19	39
2	w/o Py	/	13	18	14
3	2-MePy	100	×	22	23
4	3-MePy	..	×	18	36
5	4-MePy	..	×	19	34
6	DMAP	..	×	22	29
7	Py	25	×	18	28
8	..	75	×	34	38
9	..	125	×	18	38

^a GC yields using n-hexadecane as a standard reference. ×= Not detected.

Given the previous Co-catalyzed reductive cross-coupling reported by the Gosmini group, the optimization reactions between **S1** and **alk-I-a2** were set up with 2 mmol of **S1** as standard. As shown, a similar yield (39%) was obtained when the scale of this reaction was doubled (*Table II-5*, entry 1 compared to *Table II-3*, entry 10). In contrast to the reaction with Iodocyclohexane **alk-I-a1**, removing Py from the reaction mixture led to a noticeable decline in the yield of the cross-coupling product **II-b2**; nevertheless, 13% of the starting material **alk-I-a2** remained, which means that the Py is beneficial to increase the reaction rate of alkyl iodides in this Csp³-Csp³ bond formation process (*Table II-5*, entry 2). And then, several substituted pyridines with methyl group were employed in the reaction, and these results demonstrated that Py accelerated the reaction rate of the alkyl electrophile. Still, the yield of the desired product **II-b2** did not improve at all (*Table II-5*, entries 3- 6). Based on the obtained results, the amount of Py was optimized (*Table II-5*, entries 7- 9). The yield of **II-b2** was increased with the amount of Py from 25 to 75 mol% but kept steady when its amount was over 75%. Thus 75 mol% of Py was used in further exploration.

Table II- 6. Optimizing the ratio of S1 with alk-I-a2 and the amount of TMSCl.



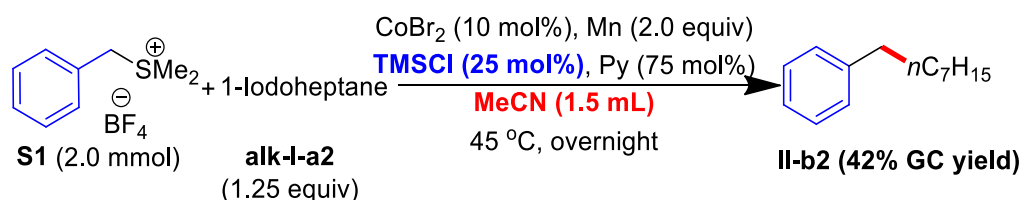
Entry	Variations		Results ^a		
	S1: alk-I-a2 (equiv)	TMSCl/ mol%	alk-I-a2 /%	Bibenzyl/%	II-b2 /%
1	1.0: 1.5	75	×	13	43
2	1.0: 2.0	..	10	11	43
3	1.0: 1.0	..	×	18	36
4	1.25: 1.0	..	×	20	39
5	1: 1.25	25	×	16	42
6	..	50	×	13	43
7	..	100	×	15	35

^a GC yields using n-decane as a standard reference. ×= Not detected

Changing the ratio of two electrophiles did not improve the cross-coupling efficiency (*Table II-6*, entries 1- 4); thus, the ratio (1: 1.25) of **S1**: **alk-I-a2** was kept. Then, decreasing the amount of **TMSCl** from 75 to 25 mol% gave 42% of the desired product **II-b2**, while adding 100 mol% of **TMSCl** resulted in a lower yield (*Table II-6*, entries 5- 7). So far, under the condition of 10 mol% of **CoBr₂**, 2 equivalents of **Mn**, 25 mol% of **TMSCl**, and 75 mol% of **Py** in 1.3 M (1.5 mL) of **MeCN** at 45 °C overnight, the cross-coupling of **S1** with **alk-I-a2** gave 42% of **II-b2**. Compared to the initial result, the efficiency of this Co-

catalyzed reductive Csp³-Csp³ bond-forming reaction via a sulfonium salt and an unactivated alkyl iodide had improved a lot but not enough. Numerous experiments were conducted continually to explore the development possibilities of this Csp³-Csp³ bond-forming reaction.

Table II- 7. Optimizing the reaction solvents of S1 with alk-I-a2.



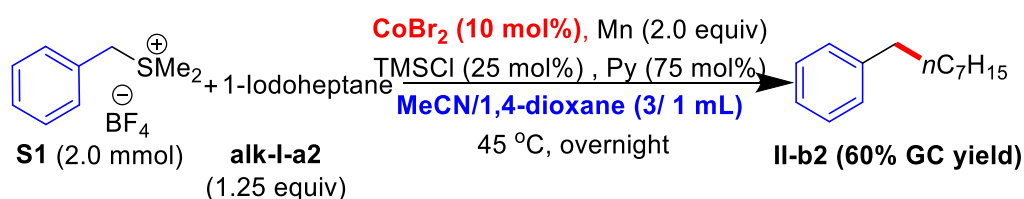
Entry	Variations		Results ^a		
	Solvent	MeCN/dioxane/ mL	alk-I-a2/%	Bibenzyl/%	II-b2/%
1	MeCN (2 mL)	/	×	15	46
2	MeCN (3 mL)	/	×	17	41
3	MeCN (4 mL)	/	×	11	49
4	MeCN (5 mL)	/	×	18	48
5	THF (4 mL)	/	×	18	36
6	DME (4 mL)	/	×	23	34
7	1,4-dioxane (4 mL)	/	90	13	11
8	DMF (4 mL)	/	√	Trace	Trace
9	DMA (4 mL)	/	√	Trace	Trace
10	MeOH (4 mL)	/	×	21	25
11	/	3.75: 0.25	×	15	49
12	/	3.50: 0.50	×	18	56
13	/	3.0: 1.0	×	16	60
14	/	2.5: 1.5	×	26	34
15	/	2.0: 2.0	×	14	30

^a GC yields using n-decane as a standard reference. √ =detected ×= Not detected

As shown in **Table II- 7**, decreasing the concentration of this Csp³-Csp³ bond formation reaction, the yield of the desired product **II-b2** did not change markedly (entries 1- 4). Increasing the amount of MeCN to 5 mL did not improve the yield. When other solvents were used instead of MeCN, like non-polar solvents THF, DME, and 1,4-dioxane, the yields of **II-b2** decreased by about 10% (entries 5- 6). It was found that the yield of **II-b2** was reduced significantly by using 1,4-dioxane, but 90% of the starting material **alk-I-a2** remained, which means that 1,4-dioxane inhibited the reactivity of alkyl iodide sharply (entry 7). While with polar solvents, such as DMF and DMA, either **II-b2** or bibenzyl was detected as trace, along with the remained alkyl iodide. Similar to the results of benzyl sulfonium salts with aryl halides (in **Chapter I**), polar solvents are unsuitable for this Co-catalyzed C-S bond cleavage

reaction (entries 8- 9). Interestingly, employing methanol as the solvent obtained a 25% yield of **II-b2** and 21% of bibenzyl, which was never used in our previously reported Co-catalyzed reductive cross-couplings (entry 10). Since the 1,4-dioxane can depress the reactivity of the alkyl iodide, a mixture of MeCN and 1,4-dioxane was proposed. To our delight, the cross-coupling yield of **S1** with **alk-I-a2** was increased from 49- 60% with the ratio of 1,4-dioxane to MeCN increasing to 1:3 mL (entries 11- 13), while extending the proportion of 1,4-dioxane in the co-solvent resulted in the desired product yields decreasing (entries 14- 15).

Table II- 8. Optimizing the reaction catalysts of S1 with alk-I-a2.

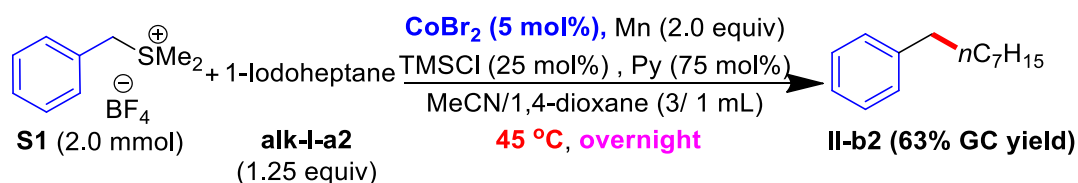


Entry	Variations		Results ^a		
	CoX ₂ /10 mol%	CoBr ₂ /mol%	alk-I-a2/%	Bibenzyl/%	II-b2/%
1	CoCl ₂	/	×	15	33
2	Co(OAc) ₂	/	×	15	58
3	Co(acac) ₂	/	×	8	19
4	CoBr ₂ (bipy) ₂	/	×	25	8
5	CoBr₂	5	×	9	63
6	..	7.5	×	7	30
7	..	12.5	×	14	45

^a GC yields using n-decane as a standard reference. ×= Not detected

Types and amounts of Co catalysts were optimized after screening the solvent (**Table II- 8**). Co(OAc)₂ in the reaction condition gave a similar yield, other Co catalysts, like CoCl₂, Co(acac)₂, caused the decline in yield, particularly the Co complex- CoBr₂(bipy)₂ led to half of **S1** to generate the homo-coupling product (**Table II- 8**, entries 1- 4). Keeping CoBr₂ as the catalyst, its amount was screened in the next step. The result showed that adding only half amount (5 mol%) of CoBr₂ gave a similar yield (**Table II- 8**, entry 5) to 10 mol% of Co catalyst, while adding either 7.5 mol% or 12.5 mol% of CoBr₂ gave a bit lower yield (**Table II- 8**, entries 6, 7).

Table II- 9. Optimizing the reaction temperature and reaction time of S1 with alk-I-a2.

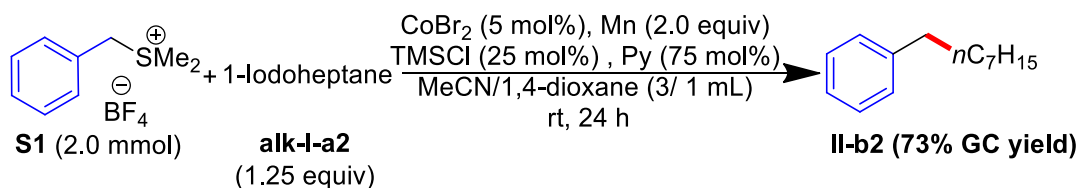


Entry	Conditions		Results ^a		
	T	t	alk-I-a2/%	Bibenzyl/%	II-b2 /%
1	rt	overnight	43	×	40
2	rt	24 h	×	6	73 (57 ^b)
3	60	overnight	×	19	43

^a GC yields using n-decane as a standard reference. ×= Not detected. ^b Isolated yield

Moreover, the temperature and reaction time were screened. The experiments showed that the yield of the desired product was decreased to 40% at rt, but extending reaction time to 24 h led to a 73% yield of **II-b2** in this case, along with few bibenzyl (**Table II- 9**, entries 1, 2). Raising the temperature to 60 °C gave a lower yield (43%) than the reaction conducted at 45 °C (**Table II- 9**, entry 3).

Table II- 10. Control experiment of S1 and alk-I-a2.



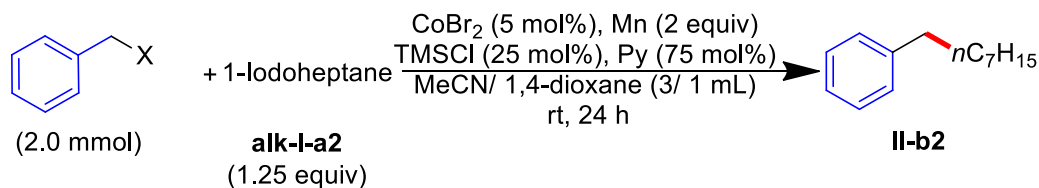
Entry	Variations	Results ^a		
		alk-I-a2/%	Bibenzyl/%	II-b2/%
1	w/o CoBr ₂	√	×	9
2	w/o Mn	√	×	×
3	w/o py	53	Trace	33
4	S1 (10 mmol)	×	√	78 (66 ^b)
5	Zn instead of Mn	Trace	×	9
6	NiBr ₂ instead of CoBr ₂	√	×	×

^a GC yields using n-decane as a standard reference. ×= Not detected. ^b Isolated yield

Defined the condition in **Table II- 9** (entry 2), the control experiments proved the necessity of Co catalyst and Mn in this Csp³-Csp³ bond-forming reaction; without their presence, this reaction almost shut down. The interesting point is that 9% of the cross-coupling product **II-b2** and a trace amount of tetradecane (the homo-coupling product of **alk-I-a2**) were obtained without Co catalyst, which demonstrated these alkyl radicals could be generated through Mn reducing (**Table II- 10**, entries 1, 2).

Removing Py from the medium, the desired product **II-b2** was obtained in 33% yield (*Table II-10*, entry 3). The yield increased much compared to the initial condition (*Table II-5*, entry 2). Scaling up the reaction to 10 mmol (**S1**) led to a 78 % yield (65% isolated yield) (*Table II-10*, entry 4). Replacing Mn with Zn or using NiBr₂ instead of CoBr₂ caused the significant yield decline of **II-b2**, which demonstrated the advantage of this Co-Mn reductive cross-coupling system in constructing Csp³-Csp³ bonds via sulfonium salts and unactivated alkyl iodides.

Table II-11. Cross-Coupling of Benzyl derivatives with alk-I-a2.



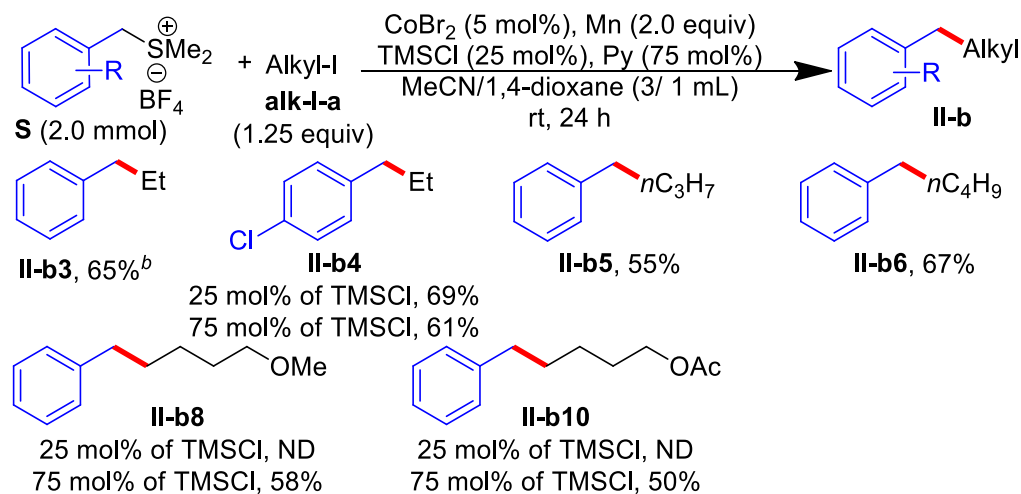
entry	X	II-b2 yield ^a / %	entry	X	II-b2 yield ^a / %
1		10	5	OTs	Trace
2		56	6		Trace
3	Cl	84 (63 ^b)	7	OMs	17
4	Br	Trace	8	OAc	×

^a GC yields using n-decane as a standard reference. ×= Not detected. ^b Isolated yield.

In addition to the cross-coupling of **S1** with 1-iodoheptane **alk-I-a2**, the reaction between various benzyl derivatives and **alk-I-a2** was explored under the optimized alkylation condition. As shown in *Table II-11*, the nature of the sulfonium salts was initially studied in this Co-catalyzed reductive cross-coupling (entries 1, 2). Other sulfonium salts, such as benzyl dimethyl sulfonium bromide and 1-benzyl tetrahydro-1H-thiophen-1-ium hexafluorophosphate, were employed under the optimized condition leading to 10% and 56% yield, respectively. The coupling was also performed with benzyl halides to compare with other benzylic electrophiles. For example, benzyl chloride gave a similar yield as benzyl sulfonium salt **S1**, while only a trace amount of **II-b2** was detected with the more reactive benzyl bromide (entries 3, 4). In addition, some C_{Bn}-O electrophiles were also applied in this reaction. Experimental results showed that benzyl acetate was unreactive; benzyl sulfonates (benzyl tosylate and mesylate) gave trace and a low yield of the desired product, respectively (entries 5-8).

2.1.3. Reaction scopes of benzyl sulfonium salts (S) and alkyl iodides (alk-I-a).

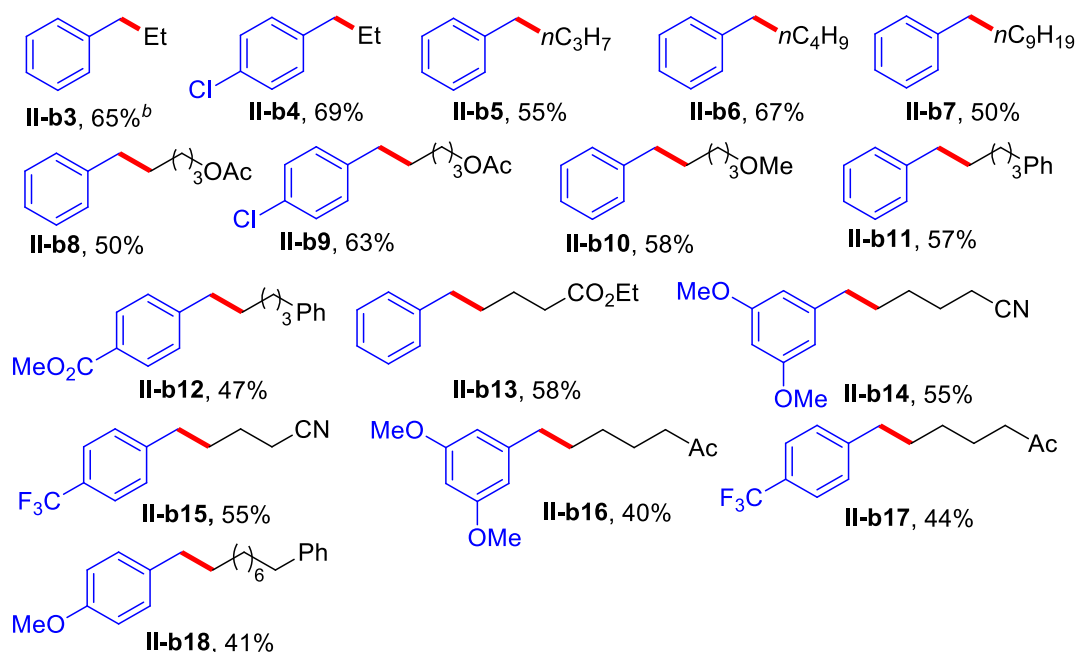
Table II- 12. Effect of the amount of TMSCl on some cross-coupling reactions of S and alk-I-a^a



^a Standard condition: S (2.0 mmol), alk-I-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield. ^b GC yield.

With the optimized conditions ([Table II- 9](#), entry 2) in hand, various functionalized alkyl iodides (**alk-I-a**) were employed to construct Csp³-Csp³ bonds by Co-catalyzed ([Table II- 12](#)). However, the process did not go smoothly at the beginning of the expansion under the optimized condition. Some cross-coupling experiments gave very low yields or did not react at all ([Table II- 12](#)). To find out what caused cross-coupling inefficiencies, the type of solvents, the materials adding sequence, as well as the time gap adding TMSCl and Py were tested gradually. Eventually, it was found that the problem was the amount of TMSCl; even though adding 25 mol% of TMSCl could obtain a yield similar to adding 75 mol%, it could not ensure the Mn was activated every time. Thus, 75 mol% of TMSCl was used for some samples.

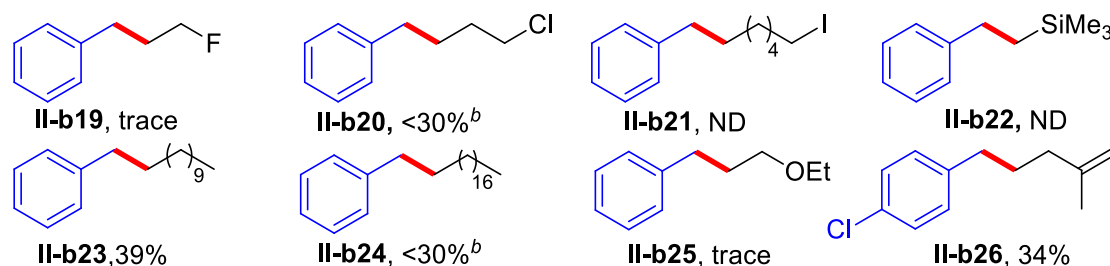
Table II- 13. Scopes of benzyl sulfonium salt derivatives (S) with primary alkyl iodides (alk-I-a)^a



^a Standard condition: S (2.0 mmol), alk-I-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield. ^b GC yield.

A large number of substituted unactivated alkyl iodides and functionalized benzyl sulfonium salts were applied under the condition either with 25 or 75 mol% of TMSCl. Experimental results indicated that this method is general for primary alkyl iodides, providing a wide range of cross-coupling products in moderate to good isolated yields (**Table II- 13**). For unsubstituted primary linear alkyl iodides, 50% to 69% of yields were obtained (**II-b3** to **II-b7**). 4-Chlorobenzyl sulfonium salt reacted with small molecule-ethyl iodide gave a 69% isolated yield of **II-b4**. While longer linear 1-iodononane coupled with **S1** also delivered the desired product **II-b7** in 50% yield. Alkyl iodides with various functionalities, such as ester (**II-b8**, **II-b9**, **II-b13**), ether (**II-b10**), and phenyl (**II-b11**, **II-b12**), were tolerated well under this Co-catalyzed Csp³-Csp³ bond-forming condition. Higher yields were obtained from chlorobenzyl sulfonium salt than unsubstituted **S1** (**II-b4**, **II-b9**). Moreover, alkyl iodides with a cyano- or keto- group reacted with either benzyl sulfonium salts with electron-donating (methoxy) or electron-withdrawing (trifluoromethyl) groups gave similar moderate to good yields (55- 55%, **II-b14**- **II-b15**; 40- 44%, **II-b16**- **II-b17**, respectively).

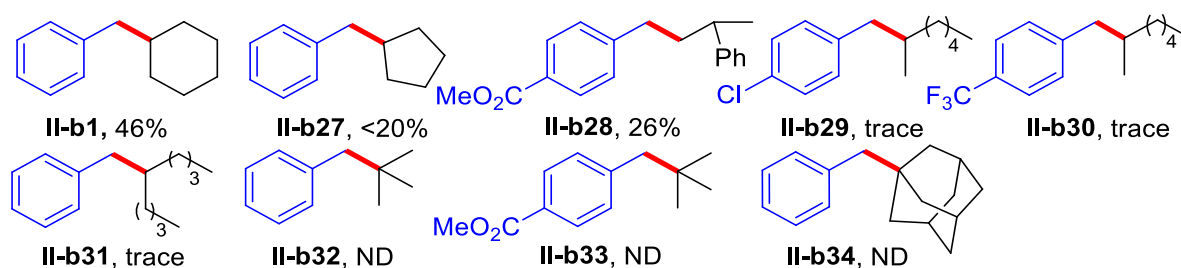
Table II- 14. Failed scopes of benzyl sulfonium salt derivatives (S) with primary alkyl iodides (alk-I-a)^a



^a Standard condition: S (2.0 mmol), alk-I-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield. ^b GC yield.

However, when alkyl iodides bearded an ether halide like F- and Cl-, the experimental results were not satisfying (**Table II- 14**). Only a trace amount or a low yield of desired products were obtained (**II-b19** and **II-b21**), while the substituted groups on alkyl iodides are I- or Si(Me)₃- (**II-b22** and **II-b23**), no cross-coupling products were detected, but lots of diaryl ethanes were detected by GC. Compared to the application of 1-Iodononane (**II-b7**), the reaction of 1-Iodoundecane and a larger linear alkyl iodide with benzyl sulfonium salt **S1** led to much lower yields (**II-b23**, **II-b24**) because alkyl iodides with a longer carbon chain were not the completely suitable in the MeCN/1,4- dioxane co-solvent. On the other hand, it was found that the efficiency of the cross-coupling was also affected by the nature and position of the functional groups, for example, while an ether group at the β-position of alkyl iodide, only a trace amount of **II-b25** was detected, or the yield of the cross-coupling product **II-b26** was lower than 40%.

Table II- 15. Scopes of benzyl sulfonium salt derivatives (S) with secondary/ tertiary alkyl iodides (alk-I-a)^a

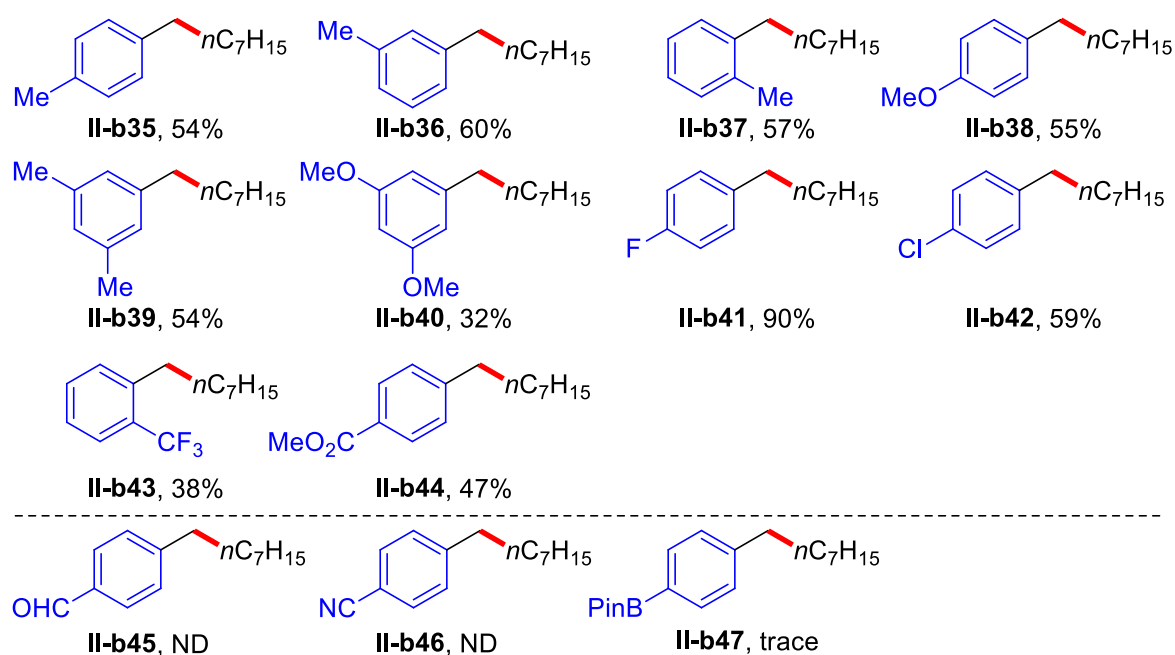


^a Standard condition: S (2.0 mmol), alk-I-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield. ^b GC yield.

Next, the scope of alkyl iodides was extended to secondary and tertiary alkyl iodides under the optimized condition (**Table II- 15**). Firstly, the iodocyclohexane **alk-I-a1**, which was used as this optimized starting material at the beginning of the project, coupled with **S1**, delivered the desired product **II-b1** in 46% isolated yield under this optimized condition. While applying iodocyclopentane as a partner obtained a yield lower than 20% (**II-b27**). And then, the cycloalkanes were replaced with secondary

linear alkanes, and only the α -methyl benzyl iodide gave the cross-coupling product **II-b28** in 26% isolated yield with more reactive 4-(methoxycarbonyl) benzyl sulfonium salt and an enormous amount of homo-coupling product of α -methyl benzyl iodide was detected, along with a reduced product of 4-(methoxycarbonyl)benzyl sulfonium salt. Other secondary linear alkyl iodides without functional groups, like 2-iodoheptane, reacted with benzyl sulfonium salts bearing either Cl- or CF₃- group, and only a trace amount of the desired product was detected (**II-b29**, **II-b30**), along with homo-coupling products of both starting materials. The same result was also detected with 5-iodononane (**II-b31**). Moreover, tertiary alkyl iodides are not compatible with this Co-catalyzed Csp³-Csp³ bond-forming reaction condition. Neither simple (CH₃)₃I nor 1-iodoadamantane led to the cross-coupling products (**II-b32**- **II-b34**) due to their high reactivity and large steric hindrance. With 1-iodoadamantane as an electrophile, only its reduced product was obtained. Given the high reactivity of tertiary iodides, two or three tertiary bromides were tried under the conditions, but no satisfying results were obtained.

Table II- 16. Scopes of benzyl sulfonium salt derivatives (S) with alkyl iodides (alk-I-a)^a



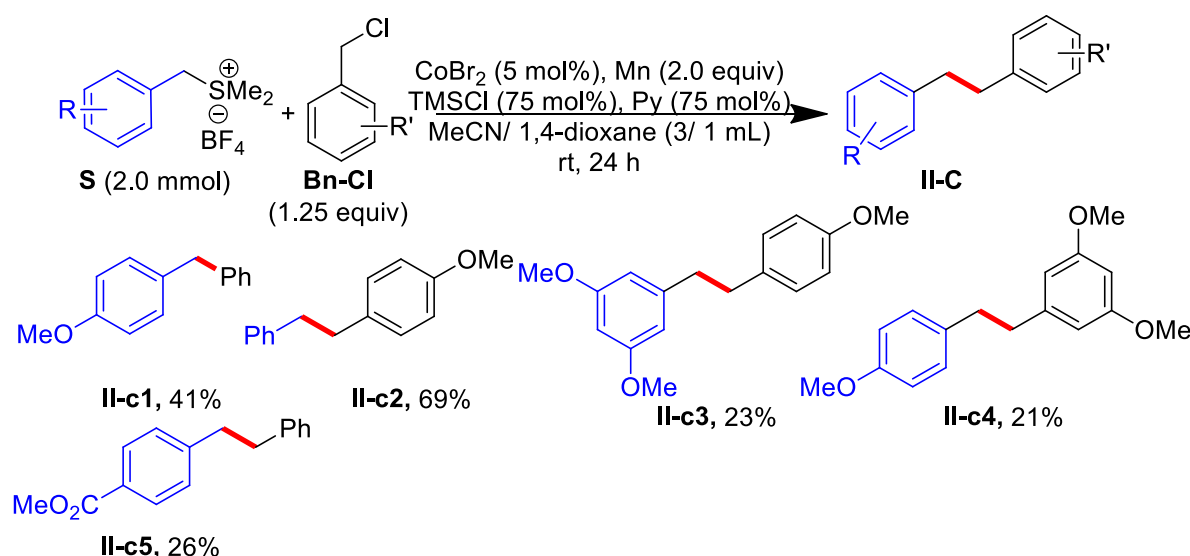
^a Standard condition: S (2.0 mmol), alk-I-a1 (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield.

In addition to the scope of alkyl iodides, the tolerance of the functionalized groups on benzyl moiety of sulfonium salts was also tested under this optimized alkylation condition (**Table II- 16**). The reaction of benzyl sulfonium salts bearing electron-donating groups, like methyl, and methoxy groups, gave better yields with 1-iodoheptane **alk-I-a2** (54- 60%, **II-b35**- **II-b38**). The steric hindrance on the benzyl sulfonium salts did not affect the cross-coupling efficiency, and a moderate yield was obtained (**II-b37**). The presence of several electron-donating groups was also allowed to be tolerated in this Co-catalyzed reductive cross-coupling (**II-b39**, **II-b40**), but when the electron-donating ability of functional groups

increased, the yields of the desired products decreased from 54% to 32%. Fluor and chloro groups on the aryl ring of sulfonium salts were also compatible with this alkylation reaction condition, leading to the cross-coupling products in good yields (**II-b41**, 90%; **II-b42**, 59%). However, the presence of electron-withdrawing groups on benzyl moieties of sulfonium salts, like trifluoromethyl or ester groups, gave lower yields (**II-b43**, **II-b44**), compared to ones with EDG, due to the competitive homo-coupling of the benzyl sulfonium salts. The benzyl sulfonium salt with aldehyde did not deliver the cross-coupling product (**II-b45**). Unexpectedly, the cyano-group used commonly in our previous reports^{7b, 67} was incompatible with the condition. No desired product was detected except its reduced and homo-coupling products (**II-b46**). Moreover, benzyl sulfonium salt with the Bpin group also did not perform well with **alk-I-a1** under the optimized condition (**II-b47**).

2.1.4. Reaction scopes of benzyl sulfonium salts (S) and benzyl chlorides (Bn-Cl).

Table II- 17. Co-catalyzed cross-coupling between benzyl sulfonium salt derivatives (S) with benzyl chlorides (Bn-Cl)^{a, b}



^a Standard condition: S (2.0 mmol), Bn-Cl (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), pyridine (75 mol%), TMSCl (25 or 75 mol%) in MeCN (3.0 mL) and 1,4-dioxane (1.0 mL) at rt, 24 h under N₂. Isolated yield.

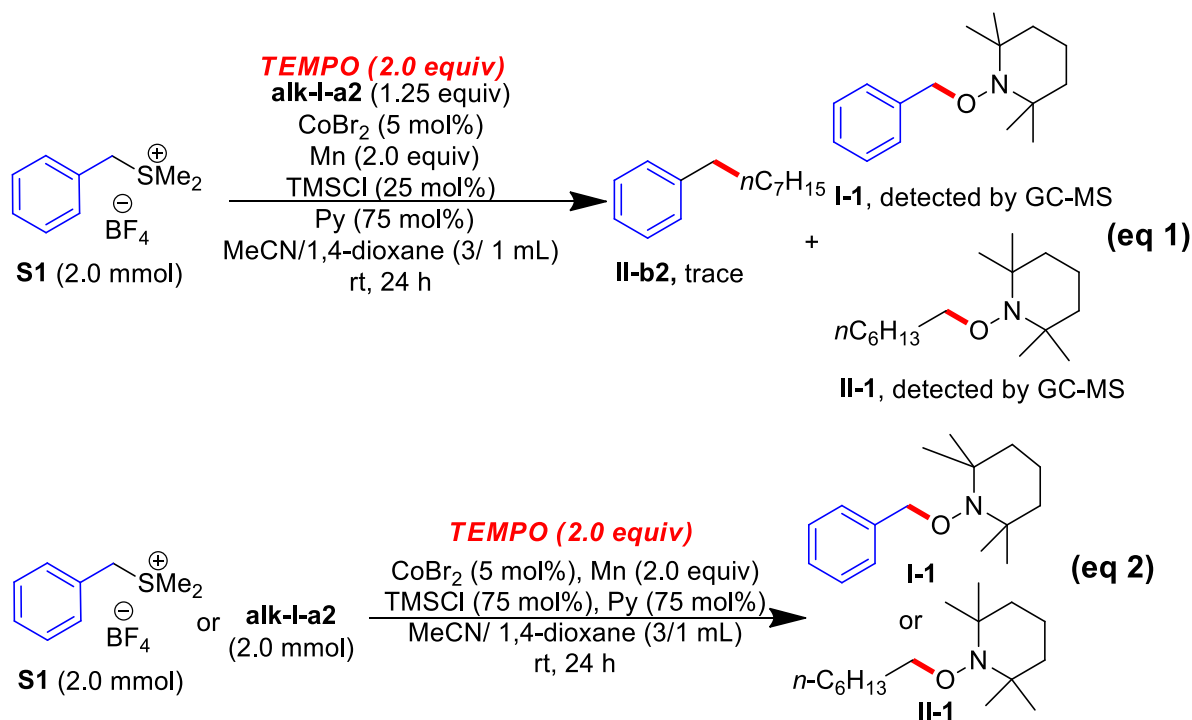
As mentioned above, after optimizing the conditions of **S1** with **alk-I-a2**, other benzyl derivatives (**Table II- 11, p84**) were also applied in this alkylation condition. The cross-coupling of benzyl chloride with 1-iodoheptane **alk-I-a2** was performed well, and 63% isolated yield was obtained (**Table II- 11**, entry 3), which showed better compatibility of benzyl chloride in this Co-catalyzed Csp³-Csp³ bond-forming reaction. Then benzyl chlorides were used as the other electrophile with sulfonium salts in this Co-catalyzed Csp³-Csp³ bond-forming reaction to generate diaryl ethane derivatives (**Table II- 16**). Without surprise, in contrast to the work carried over by Alemán⁹³, benzyl chloride showed good and even better efficiency than benzyl bromide under the optimized condition used with alkyl iodides. When a methoxy group was on the benzyl chloride, the yield increased significantly compared to the same

substituent on benzyl sulfonium salt (**II-c1**, **II-c2**). These results prompted us to attempt the synthesis of a dihydro resveratrol precursor (**II-c3**) - a key intermediate in the inhibition of pancreatic oxidative damage. However, the yield of the cross-coupling products was around 20%, regardless of whether the dimethoxy group was on the sulfonium salt or the Bn-Cl (**II-c4**). Moreover, benzyl sulfonium salt bearing EWG, such as an ester group, coupled with benzyl chloride and gave a poor yield (**II-c5**), along with the reduced product of the sulfonium salt and bibenzyl from benzyl chloride.

2.2. Exploration of the Mechanism

To investigate deeply the mechanism of this Co-catalyzed reductive Csp³-Csp³ bond-forming process, a few experiments were conducted.

2.2.1. TEMPO trapping experiments with alkyl iodide.

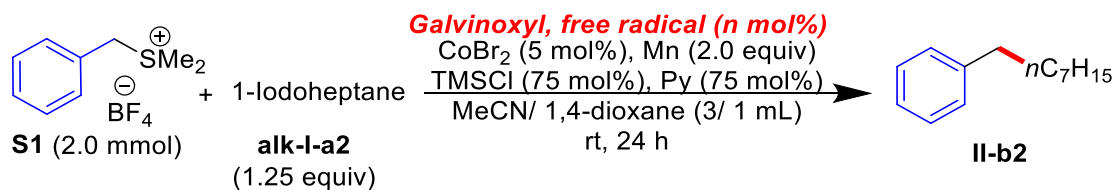


Entry	S1	alk-I-a2	I-1 ^a	Bibenzyl ^b	II-1 ^a	nC ₁₄ H ₂₈ ^b
1	+	/	Trace	32%	/	/
2	/	+	/	/	Trace	16%

^a detected by GC-MS. ^b GC yields using decane as an internal standard.

Scheme II-1. TEMPO trapping experiments with alkyl iodide.

At the outset, 2 equivalents of 2,2,6,6-tetramethylpiperine-1-oxyl (TEMPO) were performed with **S1** and **alk-I-a2** under the optimized alkylation condition. The alkylation reaction was inhibited significantly. As shown in [Scheme II-1](#); only a trace amount of the cross-coupling product **II-b2** was detected by GC-MS, along with trace amounts of the TEMPO-trapped products **I-1**, **II-1** of two electrophilic partners in this benzyl alkylation reaction process ([Scheme II-1, eq 1](#)). Moreover, the cross-coupling reaction of **S1** or **alk-I-a2** with TEMPO was also tried ([Scheme II-1, eq 2](#)). When only **S1** was employed with TEMPO in this alkylation reaction condition, a trace amount of **II-1** was detected by GC-MS, as well as a 32% GC yield of bibenzyl. Likewise, a trace amount of 1-(heptyloxy)-2,2,6,6-tetramethylpiperidine (**II-1**) by GC-MS was detected if only **alk-I-a2** was added into the condition, and the homo-coupling product - tetradecane was detected by 16% GC yield.



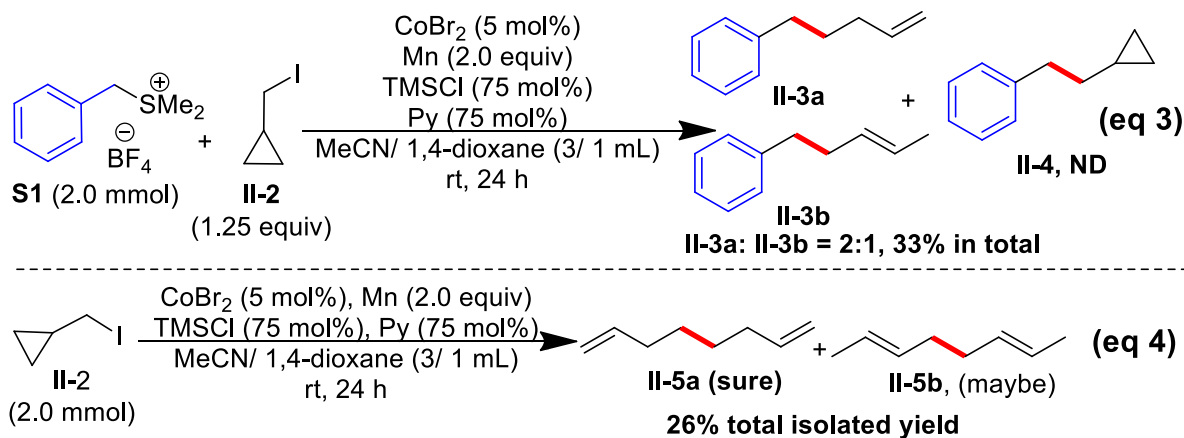
Entry	galvinoxyl, free radical / <i>n</i> mol%	alk-I-a2	Bibenzyl	II-b2 ^a /%
1	/	✓	✓	73
2	50	✓	✓	50
3	100	✓	✓	43
4	150	Trace	✓	16

^a GC yields using *n*-decane as a standard reference.

Scheme II- 2. Radical experiments between alkyl iodide and galvinoxyl free radical

On the other hand, galvinoxyl free radical was performed with **S1** and **alk-I-a2** under these optimized alkylation conditions (Scheme II- 2). Experimental results showed that the yield of **II-b2** decreased significantly with the amount of free radical reagent increasing (from 73% to 16%). These experiments demonstrated preliminarily that benzyl and alkyl radicals were involved in this alkylation reaction.

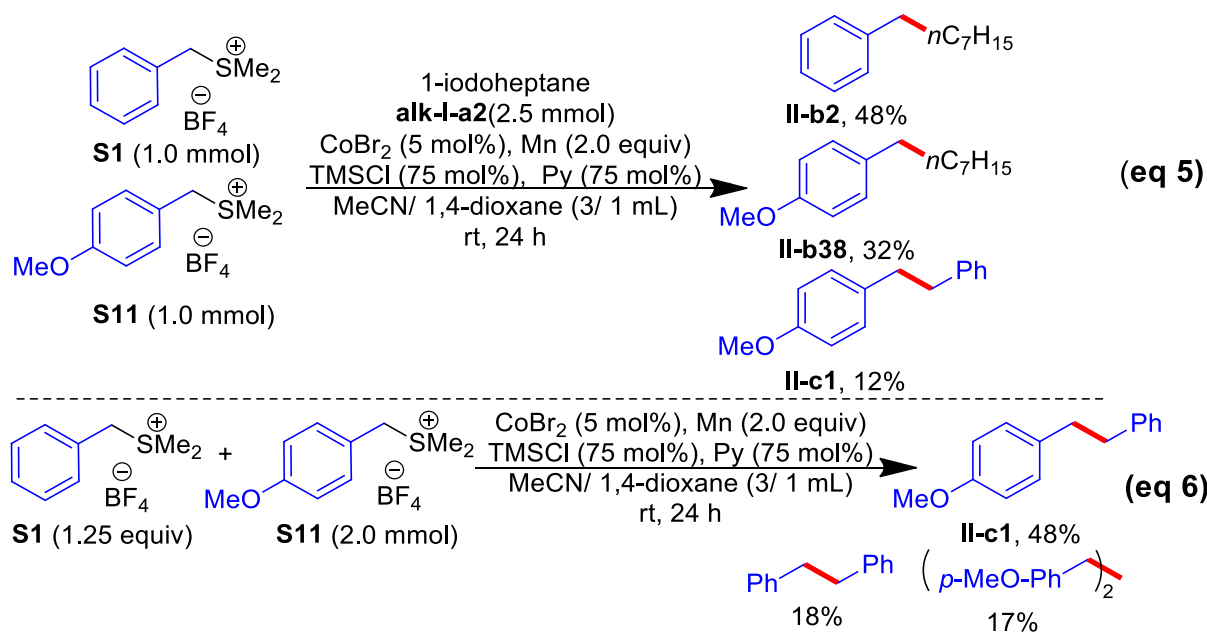
2.2.2. Radical clock trapping experiments.



Scheme II- 3. Radical clock trapping experiments.

To further explore if both electrophilic partners can form alkyl radicals in the alkylation reaction, iodomethylcyclopropane (**II-2**) was coupled with **S1** under the alkylation conditions (Scheme II- 3, eq 3). A mixture of ring-opened products **II-3** (5-phenylpent-1-ene **II-3a** and (*E*)-3-pentenyl benzene **II-3b**) was obtained in 33% isolated yield, without unrearranged cross-coupling product detected (**II-5**). Moreover, it was found when only compound **II-2** was added in this condition, two ring-opening products were obtained in 26% isolated yield in total. However, it was difficult to confirm if **II-5b** was generated during the process; but it can be distinguished easily the presence of **II-5a** by the NMR spectrum (Scheme II- 3, eq 4).

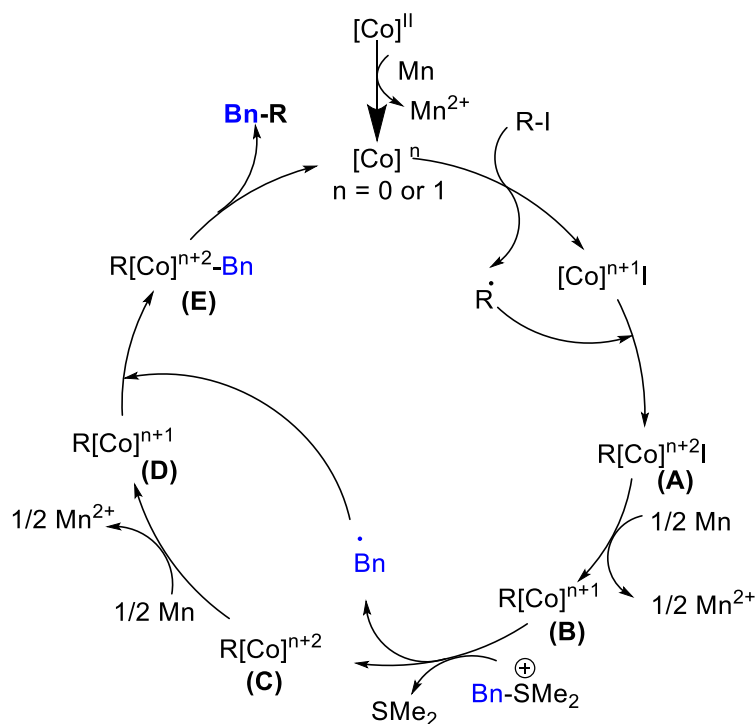
2.2.3. The cross-coupling between different benzyl sulfonium salts and alk-I-a.



Scheme II- 4. The reactions between different benzyl sulfonium salts and alkyl iodide

Additionally, the competitive reactions of two different benzyl sulfonium salts with **alk-I-a2** were also conducted. As shown in **Scheme II- 4**, the reaction provided the cross-coupling products **II-b2** and **II-b38** in 48% and 32% yield, respectively, along with the cross-coupling product of the two benzyl sulfonium salts (**II-c1**) in 12% yield (**Scheme II- 4**, **eq 5**). At the end of the exploration, only two benzyl sulfonium salts (**S1** with **S11** (4-methoxy benzyl sulfonium salt)) were applied in the condition. The experimental result showed that two benzyl sulfonium salts not only carried out the homo-coupling reaction but mainly afforded the cross-coupling product **II-c1** in 48% yield (**Scheme II- 4**, **eq 6**), as well as a small amount of diarylethene.

2.2.4. Proposed mechanism



Scheme II- 5. Proposed mechanism.

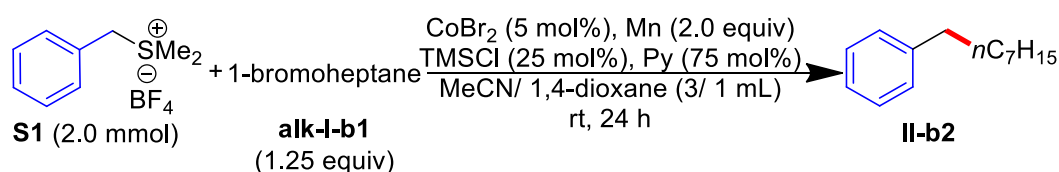
Based on the mechanistic exploration of experimental results and the reactivities of **S1**, benzyl chloride, and alkyl iodide, a mechanism was proposed according to our previous reports related to the Csp³-Csp³ homocoupling¹⁰³. According to the cross-coupling of benzyl sulfonium salts and benzyl chlorides, we can see that the reactivity of benzyl sulfonium salts is lower than BnCl. Thus, we proposed that alkyl radical was generated former than benzyl radical as shown in **Scheme II- 5**. The initiation step is the reduction of the Co(II) precatalyst by the manganese into an active low-valent Co species. Subsequently, an alkyl radical generated from the alkyl iodide went through oxidative addition to the low-valent Co species to form a cobalt complex **A**, which is again reduced into the alkyl complex **B** by Mn. Then, this species **B** underwent one electron transfer to benzyl sulfonium salt, delivering a Co complex **C**, a benzyl radical together with a thioether, due to the positive charge of benzyl sulfonium salt, which resulted in undergoing easily homolytic fragmentation of its C_{Bn}-S bonds via electron reduction. Finally, the benzyl alkyl Co complex **E**, generated by the combination of the benzyl radical and a reduced low-valent Co complex **D**, provides the cross-coupling product by reductive elimination along with the regeneration of the active Co species.

3. Unactivated Alkyl Bromides as Electrophilic Partners

In addition to the alkyl iodides as electrophilic partners in this Co-catalyzed Csp³-Csp³ bond-forming reaction, less reactive alkyl bromides used to build Csp³-Csp³ bond with benzyl sulfonium salts were explored in this project. As displayed in the [Table II- 1](#), the cross-coupling of **S1** and alkyl bromides under the condition of diaryl methane formation (in [Chapter I](#)) only gave a trace amount of the desired product. To calculate the yield of the cross-coupling product from an alkyl bromide conveniently, **S1** and 1-bromoheptane (**alk-I-b1**) were employed as standard starting materials to conduct the optimizing experiments.

3.1. Optimization of reaction conditions

Table II- 18. The cross-coupling of **alk-I-b1** with **S1**.

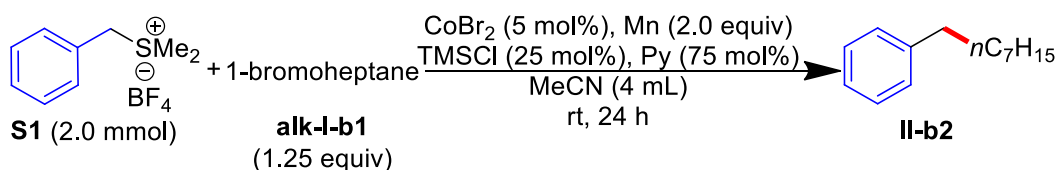


Entry	Conditions	Results ^a		
		alk-I-b1/%	Bibenzyl/%	II-b2/%
1	None	√	√	ND
2	45 °C instead of rt	√	√	6
3	w/o 1,4-dioxane	√	√	9 ^b
4	S1 : alk-I-b1 (1.25 :1)	√	√	5 ^b

^a GC yields using n-decane as a standard reference. √ =detected. ^b at 45 °C.

Under the optimized alkylation condition of benzyl sulfonium salts and alkyl iodides, applying 1-bromoheptane **alk-I-b1** as the other electrophile did not detect the desired product **II-b2**, unsurprisingly, due to the low reactivity of the alkyl bromide ([Table II- 18](#), entry 1). To improve its reactivity, the temperature was increased to 45 °C, 6% of **II-b2** was detected by GC at this time ([Table II- 18](#), entry 2). Even though the yield was poor, it exhibited the possibility that 1-bromoheptane **alk-I-b1** replaced 1-iodoheptane **alk-I-a2** as an electrophilic partner. As known, alkyl bromides are more commercially available and abundant than alkyl iodides. Thus, it is more convenient to use alkyl bromides as electrophiles. Then, the optimization was further conducted at 45 °C. Removing 1,4-dioxane, which was mentioned above to decrease the reaction rate of alkyl iodides, gave **II-b2** with 9% yield ([Table II- 18](#), entry 3). Changing the ratio of **S1** and **alk-I-b1** did not improve the yield of **II-b2** at 45 °C ([Table II- 18](#), entry 4).

Table II- 19. Optimizing the cross-coupling condition of alk-I-b1 with S1.

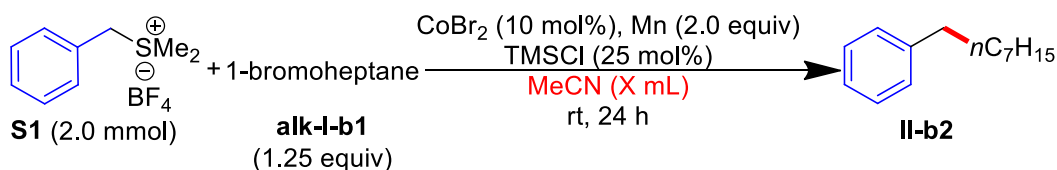


Entry	Conditions	Results ^a		
		alk-I-b1/%	Bibenzyl/%	II-b2/%
1	w/o Py	✓	✓	12
2	CoBr ₂ (10 mol%)	✓	✓	8
3	CoBr ₂ (10 mol%) and w/o Py	✓	✓	17/7

^a GC yields using n-decane as a standard reference. ✓ =detected.

When only MeCN was used as the solvent, the yield of II-b2 increased slightly without pyridine (Table II- 19, entry 1). Increasing the amount of Co catalyst to 10 mol% did not result in any improvement in yield (Table II- 19, entry 2). While combining the former two conditions, a 17% GC yield of II-b2 was detected for the first time. Disappointingly, repeating the experiment got only a 7% yield of II-b2 (Table II- 19, entry 3).

Table II- 20. Optimizing the reaction concentration of alk-I-b1 with S1.

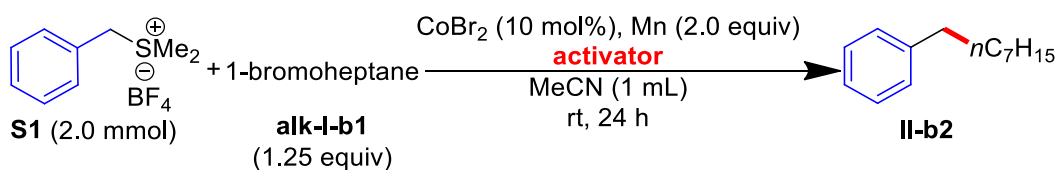


Entry	MeCN/X mL	Results ^a		
		alk-I-b1/%	Bibenzyl/%	II-b2/%
1	1.0	✗	✓	13
2	1.5	✗	✓	6
3	2.0	✗	✓	4
4	3.0	✓	✓	5

^a GC yields using n-decane as a standard reference. ✓ =detected, ✗ = Not detected.

Next, by screening the concentration of the reaction in the absence of pyridine, it was found that the yield of the cross-coupling product decreased when the concentration increased in Table II- 20. On the other hand, the alk-I-b1 remained from 3 mL of MeCN used in the condition. However, although adding 1 mL of MeCN gave the best yield in the Table II- 20, it was lower than 17%. Thus, the stability of this reaction is urgent to solve.

Table II- 21. Optimizing the activator of the reaction between alk-I-b1 and S1.

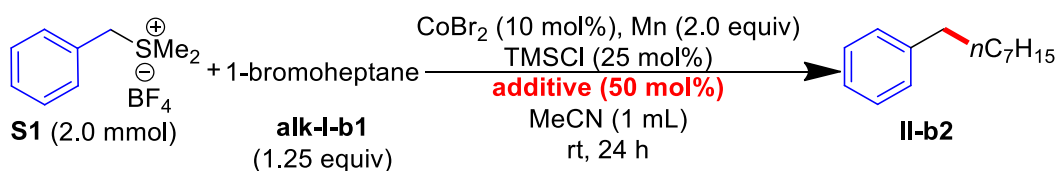


Entry	Activator	Results ^a		
		alk-I-b1/%	Bibenzyl/%	II-b2/%
1	TMSCl (50 mol%)	×	√	6
2	TMSCl (75 mol%)	×	√	11
3	TMSCl (100 mol%)	×	√	13
4	TMSBr (25 mol%)	×	√	4
5	TFA (25 mol%)	×		trace

^a GC yields using n-decane as a standard reference. √ =detected.

To confirm if the amount of TMSCl affects the reaction, different amounts of TMSCl were added to the reaction. The results showed that increasing the amounts of TMSCl was not beneficial for this cross-coupling process (**Table II- 21**, entries 1- 3). Replacing TMSCl with TMSBr or TFA did not give better results, even though the 1-bromoheptane **alk-I-b1** had been consumed completely (**Table II- 21**, entries 4- 5).

Table II- 22. Optimizing the additives of the reaction between alk-I-b1 and S1.



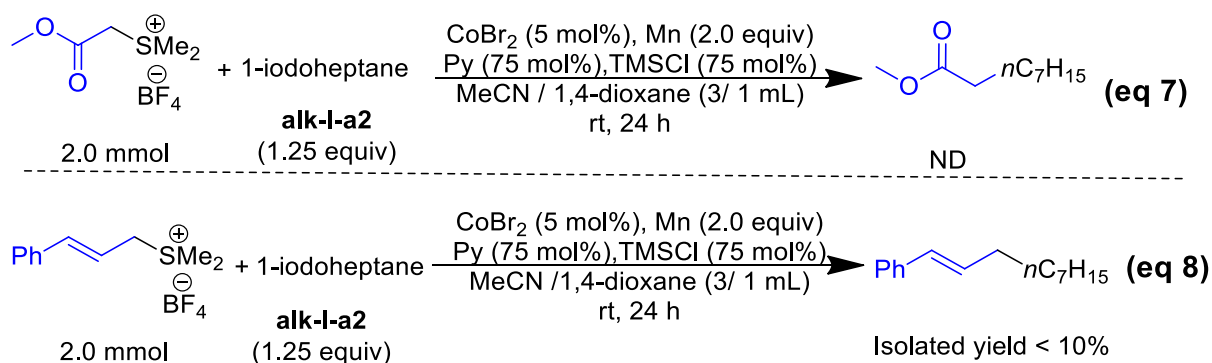
Entry	Additive	Results ^a		
		alk-I-b1/%	Bibenzyl/%	II-b2/%
1	KI	√	√	17
2	NaI	√	√	trace
3	TBAI	√	√	12

^a GC yields using n-decane as a standard reference. √ =detected.

Given the difference in reactivity of the two electrophiles, some iodide salts were added to the mixture to form 1-iodoheptane **alk-I-a2** from 1-bromoheptane **alk-I-b1** (**Table II- 22**). It showed that KI used gave a 17% yield of **II-b2** while adding NaI only gave a trace amount of the desired product **II-b2**, and the use of TBAI gave a similar yield with no additive, along with the remaining **alk-I-b1**

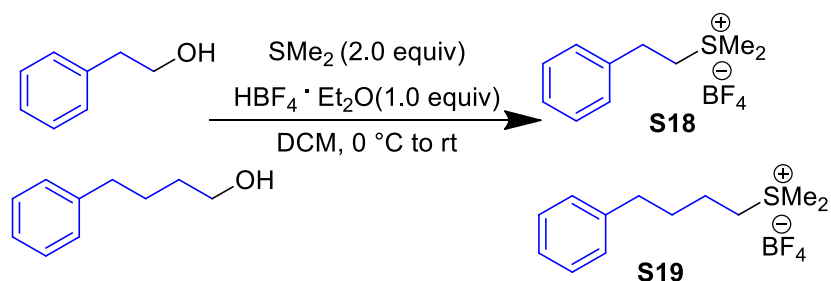
Ultimately, the emphasis on improving the efficiency of the cross-coupling between sulfonium salts and alkyl bromides is to determine the reactivity-matched electrophiles. Later, the substituted benzyl sulfonium salts with a methoxy (**S11**) or two methoxy groups (**S12**) were applied to continue the optimization experiments. Unfortunately, the yields of the cross-coupling did not improve obviously.

4. Exploration of Active and Unactive Alkyl Sulfonium Salts in Constructing Csp³-Csp³ Bond



Scheme II- 6. Cross-coupling of other sulfonium salts with alk-I-a2

Different types of activated alkyl sulfonium salts were also tried to construct Csp³-Csp³ bond under the condition, like the (carbomethoxy-methyl) dimethyl sulfonium salt and 3-phenylprop-2-enyl-dimethylsulfonium salt in *Scheme II- 6*. Adding the (carbomethoxy-methyl) dimethyl sulfonium salt as the electrophile, no desired product was detected except the homo-coupling product of the alkyl iodide (*Scheme II- 6, eq 7*). In contrast, the use of 3-phenylprop-2-enyl-dimethylsulfonium salt gave a poor yield of the desired product, along with an enormous amount of two homo-coupling products (*Scheme II- 6, eq 8*).



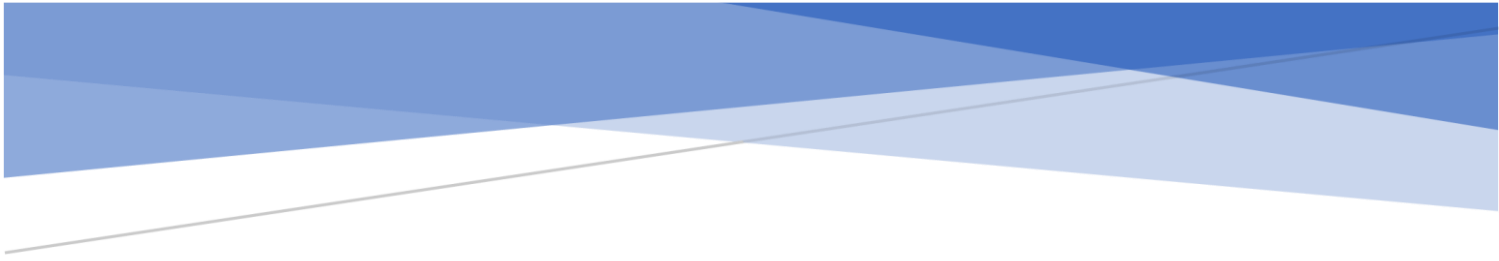
Scheme II- 7. Synthesis of unactivated alkyl sulfonium salts

On the other hand, unactivated alkyl sulfonium salts were considered to achieve the Csp³-Csp³ bond. However, disappointingly, no targeted unactivated alkyl sulfonium salts (**S18**, **S19**) were obtained according to the method used to synthesize benzyl sulfonium salts (*Scheme II- 7*).

5. Conclusion and Perspectives

In this chapter, benzyl sulfonium salts have demonstrated their suitability to construct Csp³-Csp³ bonds with unactivated alkyl iodide via a Co-catalyzed reductive cross-coupling. A large variety of functionalized primary or secondary alkyl iodides were coupled with different benzyl sulfonium salts with electron-donating or electron-withdrawing groups leading to desired products in moderate to good yields under mild conditions. To our knowledge, it is the first report using sulfonium salts in Co-catalyzed reactions to construct Csp³-Csp³ bonds with alkyl halides. Moreover, this reaction was not limited to the benzyl sulfonium salts as reported with Ni catalysis. The mechanistic studies demonstrated the generations of benzyl and alkyl radicals from both benzyl sulfonium salts and alkyl iodides, respectively. On the hand, other C-X electrophiles, such as benzyl chlorides and alkyl bromides, were also explored to build Csp³-Csp³ bonds in the Co-Mn catalytic system. However, the cross-coupling of benzyl sulfonium salts with alkyl bromide has yet to be improved.

Thus, the optimized condition of benzyl sulfonium salts with alkyl bromide will be attractive to explore. On the hand, the cross-couplings of sulfonium salts with secondary or tertiary alkyl iodides are also important, particularly in constructing quaternary carbon centers. Finally, the mechanism still needs to be clarified; thus, it is essential to gain detailed mechanistic insight, for example, trying to isolated or detect the alkyl Co complex, which is still a big challenge.



**Chapter III: Co-Catalyzed Construction
of Csp³- Csp³ Bonds via Benzyl Sul-
fonium Salts and C_{allyl}-O Electrophiles**

1. C_{allyl}-O Electrophiles with Benzyl Sulfonium Salts in Co-Catalyzed Construction of Csp³-Csp³ Bonds.

C-X electrophiles are one of the most critical segments in the transition metals-catalyzed Csp³-Csp³ bond formation, particularly since the development of the Suzuki, Heck, and Negishi reactions in the 1970s.¹⁰⁴ While with perseverance in the exploration of chemists, more and more electrophiles are developed to build Csp³-Csp³ bonds, C-O electrophiles are excellent alternatives in this field. Compared to organohalides, alcohol/phenol compounds present some obvious advantages: (1) widely exist in nature and synthetic systems, (2) commercial availability and lower price sometime, (3) more environmentally benign, without the production of halide waste, thus lowering the environmental impact in the cross-coupling, (4) lower toxicity.¹⁰⁵ Despite these advantages, the use of alcohol/phenol compounds is still more challenging than organohalides in reductive cross-coupling due to the higher C-O bond strength compared to the C-X bond (Br, I).¹⁰⁶ (**Table III- 1**) Thus, the active C_{allyl}-O electrophiles, used to constructive Csp³-Csp³ bonds with alkyl bromide by Co catalyst in our group's previous report^{9b} is selected as the other partner for benzyl sulfonium salts to extend the exploration of Co-catalyzed construction of Csp³-Csp³ Bonds.

Table III- 1. Average Bond Energies.

C-X	Average Bond Energies (kJ/mol)	C-X	Average Bond Energies (kJ/mol)
C-C	346	C-F	485
C-O	358	C-Cl	327
C-N	305	C-Br	285
C-S	272	C-I	213

¹⁰⁴ (a) F. Diederich, P. J. Stang, Eds.; Wiley-VCH: Weinheim, Germany, 1998. (b) Cross-Coupling Reactions. A Practical Guide; N. Miyaura, Ed.; Springer-Verlag: Berlin, 2002. (c) Metal-Catalyzed Cross-Coupling Reactions; A. de Meijere, F. Diederich, Eds.; Wiley-VCH: Weinheim, Germany, 2004.

¹⁰⁵ B.J. Li; D-G Yu, C-L. Sun; Z-J Shi; *Chem. Eur. J.* **2011**, *17*, 1728-1759.

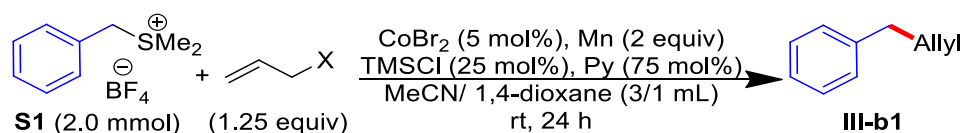
¹⁰⁶ J. B. Pedley, R. D. Naylor, S. P. Kirby. *Thermochemical Data of Organic Compounds*, 2nd ed.; Chapman and Hall: New York, 1986.

2. Results and Discussions between Benzyl Sulfonium Salts and C_{allyl}-O Electrophiles.

2.1. Allyl acetate derivatives as electrophiles with sulfonium salts

2.1.1. Optimization of reaction conditions.

Table III- 2. Cross-coupling of **S1** with allyl derivatives.

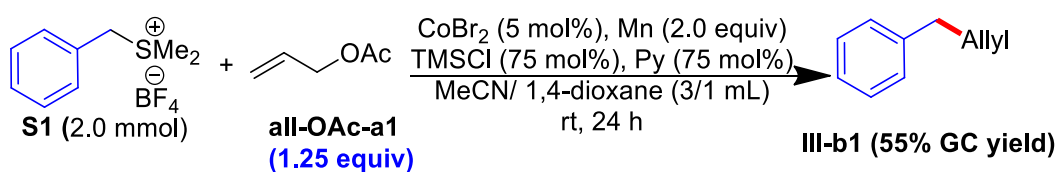


Entry	X	Results ^a	
		Bibenzyl/%	III-b1/%
1	OAc	Trace	55
2	OMe	✓	8
3	Br	✓	5
4	Cl	✓	5

^a GC yields using dodecane as an internal standard. ✓ =detected.

The exploration started with the screen of allyl derivatives with benzyl sulfonium salt **S1** under the optimized alkylation condition (in the former chapter), as shown in [Table III- 2](#). Surprisingly, replacing 1-iodoheptane **alk-I-a2** with allyl acetate (**all-OAC-a1**) delivered the desired allylation product- 4-phenyl-1-butene (**III-b1**) in 55% GC yields. (entry 1), This means constructing Csp³-Csp³ bonds by Co-catalyzed cross-coupling of sulfonium salts and C_{allyl}-O electrophiles is feasible. At the same time, allyl methyl ether (**all-OMe**) and allyl halides were also applied under the alkylation condition. However, poor yields of **III-b1** were detected due to the low reactivity of the **all-OMe**, and the high reactivity of the latter two (entries 2- 4). Thus, the allylation optimization reactions represented by the benzyl sulfonium salt (**S1**) and allyl acetate (**all-OAC-a1**) were kicked off.

Table III- 3. Optimization of the amounts of allyl acetate.

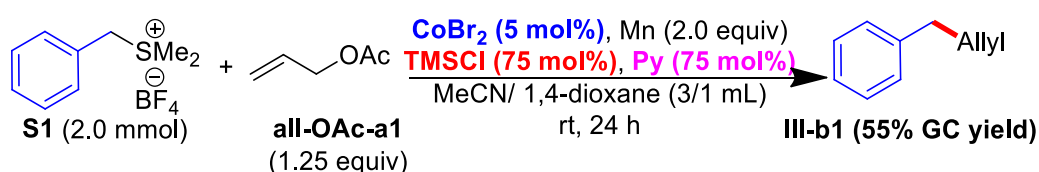


Entry	all-OAc-a1/ equiv	Results ^a	
		Bibenzyl/%	III-b1/%
1	1.5	Trace	56
2	1.75	Trace	54
3	2.0	Trace	47

^a GC yields using dodecane as an internal standard.

Increasing the amount of **all-OAc-a1**, the yield of 4-phenyl-1-butene **III-b1** did not vary obviously, and always kept around 50% yield (**Table III- 3**). Compared to the alkylation reaction, **S1** coupled with **all-OAc-a1** led to a trace amount of homo-coupling product-bibenzyl. When the added amount of **all-OAc-a1** increased, the yield of **III-b1** started to decrease slightly.

Table III- 4. Optimizing catalysts, activators, and the amount of Py of S1 with all-OAc-1.



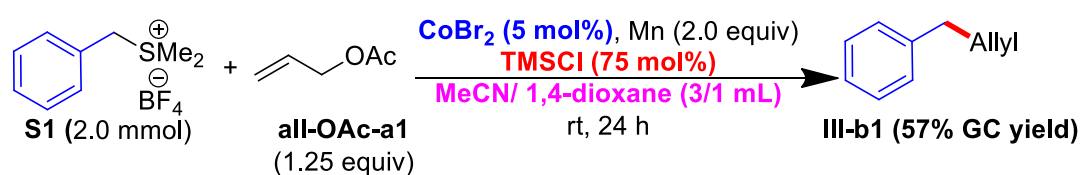
Entry	Variations			Results ^a	
	CoBr ₂ /X mol%	Activator	Py/ mol%	Bibenzyl/%	III-b1/%
1	5	TMSBr	75	Trace	54
2	..	TFA	..	✓	Trace
3	10	TMSCl	..	16	44
4	15	10	46
5	5	..	/	6	57
6	25	7	60
7	50	6	55
8	100	7	56

^a GC yields using dodecane as an internal standard.

Based on the ratio of **all-OAc-a1** to **S1** is 1.25:1, the amount of Co catalyst, the type of activator, and the amount of pyridine were optimized. As shown in **Table III- 4**, changing TMSBr to TMSCl gave a similar yield, but it is known that the price of TMSBr is higher than TMSCl, so TMSCl was used in further

optimizing experiments (entry 1). While using TFA to activate Mn, only a trace amount of the cross-coupling product **III-b1** was detected (entry 2). Then, increasing the amount of CoBr₂ resulted in the yield decline of **III-b1**, but the amount of bibenzyl did not increase significantly. Maybe **S1** remained or was transformed to the reduced product (entries 3- 4). Moreover, it showed that the presence of Py had little impact on the yields of **III-b1**, which is significantly different from the alkylation reaction between benzyl sulfonium salts and alkyl iodides and the published work concerning allylation reaction of alkyl halides with allyl acetates or carbonates^{9b} The pyridine is not mandatory for this allylation reaction between allyl acetate and benzyl sulfonium salts (entries 5- 8).

Table III- 5. Optimization of solvent of S1 with all-OAc-1.



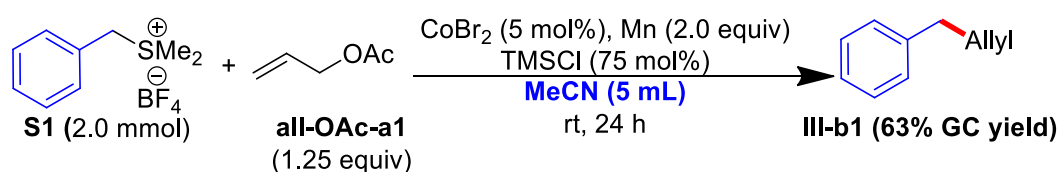
Entry	Variations		Results ^a	
	Solvent	Amount / mL	Bibenzyl/%	III-b1/%
1	MeCN: 1,4-dioxane	4: 0	8	54
2	..	2.5: 1.5	Trace	59
3	..	2.0: 2.0	7	50
4	..	1.0: 3.0	Trace	14
5	THF	4:0	9	21
6	Toluene	..	NR	NR
7	DME	..	14	Trace
8	DMA	..	20	×
9	DMF	..	17	×
10	Acetone	..	6	6
11	MeCN	1.0	22	in
12	..	2.0	15	47
13	..	3.0	5	52
14	..	5.0	6	63
15	..	10	6	69
16	..	15	Trace	67

^a GC yields using dodecane as an internal standard. ×= Not detected, NR: No reaction.

Without pyridine, different solvents were screened in the next step. It showed that the yield of the cross-coupling process was not affected by using MeCN as solvent alone (**Table III- 5**, entry 1). However, the yield of the desired product **III-b1** changed obviously as the ratio of 1,4-dioxane increased in

co-solvent. For example, when the ratio of MeCN and 1,4-dioxane was 1: 3 mL, only 14% of GC yield was obtained since the solubility of the benzyl sulfonium salt decreased in the co-solvent when the amount of 1,4-dioxane increased (**Table III- 5**, entries 2- 4). With only MeCN without dioxane, 54% of the cross-coupling product **III-b1** could be obtained. Other kinds of solvents were tested in the reaction alone. However, no-polar solvents, like THF, DME, or toluene, or polar solvents, such as DMF, DMA, and acetone, gave poor yields of the desired product. For the former solvents, benzyl sulfonium salt **S1** has poor solubility in non-polar solvents, which resulted in low efficiency of the cross-coupling (**Table III- 5**, entries 5- 7). However, the cross-coupling of **S1** with **all-OAc-a1** in polar solvent did not lead to the desired product but generated lots of bibenzyl. The use of acetone gave low yields of both products (**Table III- 5**, entries 8- 10). Further exploration showed that increasing the reaction concentration resulted in more bibenzyl compound and lower yield of the cross-coupling product (**Table III- 5**, entries 11- 14). The lower concentration decreased the generation of bibenzyl, and the yield of **III-b1** increased slightly to 69% (**Table III- 5**, entries 14- 16). Because adding 5 mL and 10 mL did not lead to a noticeable difference in yield, and given the economic efficiency, 5 mL of MeCN were used.

Table III- 6. Optimization the ligands and the amount of Mn of S1 with all-OAc-1.



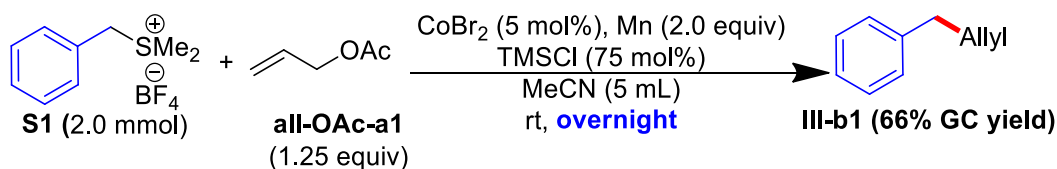
Entry	Variations	Results ^a	
		Bibenzyl/%	III-b1/%
1	bipy	Trace	53
2	dtbbpy	Trace	56
3	1,10- phenanthroline	Trace	53
4	PPh ₃	47	Trace
5	Mn (1.5 equiv) instead of Mn (2.0 equiv)	Trace	67
6	Mn (2.5 equiv) instead of Mn (2.0 equiv)	Trace	69
7	Reacted 5.5 h instead of 24 h	×	33
8	Reacted overnight instead of 24 h	Trace	66
9	TMSCl (50 mol%) instead of TMSCl (75 mol%)	Trace	61 ^b

^a GC yields using dodecane as an internal standard. ×= Not detected. ^b reacted overnight.

Some ligands associated with the Co catalyst were also tried in the condition. As shown in **Table III- 6**, the use of N-containing ligands, like bipy, dtbbpy, and 1,10- phenanthroline, could lead to moderate yields but did not improve the cross-coupling efficiency (entries 1- 3), while using the PPh₃ as ligand,

led to a trace amount of **III-b1** along with a considerable amount of bibenzyl (entry 4). Modifying the amount of Mn did not improve the yield (entries 5, 6). However, a similar yield (66%) was obtained by decreasing the reaction time from 24 h to overnight (entry 7). This means this allylation reaction rate is faster with the same C-S electrophiles than the alkylation process.

Table III- 7. Control experiments



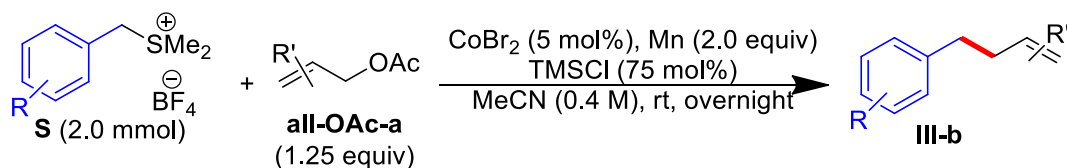
Entry	Variations	Results ^a	
		Bibenzyl/%	III-b1/%
1	w/o CoBr_2	7	×
2	Zn instead of Mn	×	8
3	w/o TMSCl	×	×
4	1.0 mmol of S1 as standard	Trace	27
5	CoCl_2 instead of CoBr_2	Trace	54
6	Allyl carbonate	√	8
7	Allyl methyl ether	10	31

^a GC yields using dodecane as an internal standard. ×= Not detected.

Defining the optimized condition as 5 mol% CoBr_2 , 2 equivalents of Mn activated by 75 mol% of TMSCl in MeCN (5 mL), **S1**, and **all-OAc-a1** (1.25 equiv) reacted at rt overnight, control experiments were carried out. The experimental results showed that Co catalyst, Mn, and activator to Mn are necessary for this alkyl allylation reaction (**Table III- 7**, entries 1- 3). Replacing Mn with Zn caused a sharp decline in the yield of **III-b1**. When the scale of **S1** decreased to 1 mmol, the yield of the cross-coupling product was only obtained in 27% yield (entry 4). Using CoCl_2 instead of CoBr_2 as a catalyst, the yield of the cross-coupling product **III-b1** decreased by 10 % (entry 5). Moreover, other allyl derivatives, like allyl carbonate and allyl methyl ether, were also applied in the reaction and gave lower yields (8% and 31%, respectively) (entries 6- 7), but the yield with allyl methyl ether increased obviously compared to it was applied in the condition above that described for alkyl iodides (from 8% to 31%).

2.1.2. Scope of reaction with allyl acetate derivatives

Table III- 8. Scopes of benzyl dimethyl sulfonium salt derivatives (S) with allyl acetate derivatives (all-OAc-a)^{a, b}



Entry	R	All-OAc-a	III-b	Yield/ %
1	4-MeO (S11)	all-OAc-a1		III-b2, 64%
2	4-Me (S2)			III-b3, 61%
3	2-Me (S4)			III-b4, 56%
4	2-CF ₃ (S9)			III-b5, 20%
5	2-CF ₃ (S9)	all-OCO ₂ Me		III-b5, 53%
6	4-CF ₃ (S8)			III-b6, 36%
7	4-CO ₂ Me (S10)			III-b7, 45%
8	3,5-diOMe (S12)	all-OAc-a1		III-b8, 58%
9	4-MeO (S11)	 all-OAc-a2		III-b9, 34%
10		 all-OAc-a3	 (major)	III-b10, 48% (>9: 1)
11	4-H (S1)	 all-OAc-a4		III-b11, 27% ^c
12	4-MeO (S11)			III-b12, 21% ^c
13	4-MeO (S11)			III-b13, 44%
14	3,5-diOMe (S12)	 all-OAc-a5		III-b14, 49%
15	4-Me (S2)			III-b15, 70%
16	2-Me (S4)			III-b16, 33% (>9: 1)
17	4-Me (S2)	 all-OAc-a6		III-b17, 33%
18	2-Cl (S14)	 all-OAc-a7	 (major)	III-b18, 31% (>99%)
19	4-CF ₃ (S8)	 all-OAc-a9	 (major)	III-b19, 49% (>9: 1)

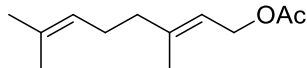
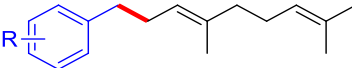
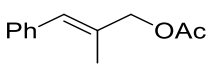
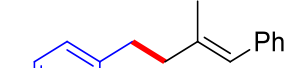
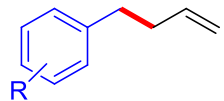
20	4-F (S7)			III-b20 , 41% (>9: 1)
21	4-MeO (S11)			III-b21 , 75% (1: 2)
22	4-CF ₃ (S8)			III-b22 , 32%
23	4-CO ₂ Me (S10)			III-b23 , 37%
24	4-H (S1)			III-b24 , 54% ^c
25	4-OMe (S11)			III-b25 , 58% ^c
26		all-OAc-a1		III-b26 , Trace

^a Standard condition: **S** (2.0 mmol), All-OAc-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), TMSCl (75 mol%) in MeCN (5.0 mL) at rt under N₂, overnight (~15 h). ^b Isolated yield. ^c reacted 24 h.

With the optimized condition in hand, the cross-couplings of various benzyl sulfonium salts and different allyl acetates were conducted to generate alkyl olefin derivatives. As shown in [Table III- 8](#), allyl acetate without substitutes (**all-OAc-a1**), coupled with benzyl sulfonium salts with electron-donating groups, and delivered higher yields of the desired products than those bearing electron-withdrawing groups ([Table III- 8](#), entries 1- 4, **III-b2- III-b5**). However, in this case, employing allyl carbonate (**all-OCO₂Me**) and benzyl sulfonium salts with EWG gave better yields. As shown, the yield of 2-(trifluoromethyl) benzyl sulfonium salt **S9** reacted with **all-OCO₂Me** was double with **all-OAc-a1** ([Table III- 8](#), entry 4, 5, **III-b5**). At the same time, when benzyl sulfonium salts bearing other substituted groups, such as 4-trifluoromethyl (**S8**) or ester (**S10**) coupled with **all-OCO₂Me**, moderate yields could also be obtained ([Table III- 8](#), entry 6, 7, **III-b6- III-b7**). The results demonstrated that this Co-catalyzed alkyl allylation was not affected by the steric hindrance of functional groups and multiple functional groups on the benzyl sulfonium salts ([Table III- 8](#), **III-b4**, **III-b5**, **III-b8**). Compared to the position of the substitutes on benzyl sulfonium salts, it was found that their position on the double bond of allyl acetate derivatives could lead to a significant difference in yield in this reductive Csp³-Csp³ cross-coupling ([Table III- 8](#), **III-b9- III-b12**). When the methyl group was at the terminal position of the double bond, the desired product (**III-b10**) was obtained in 48% yield with mainly the linear product. This yield was better than the ones from **all-OAc-a2** and **all-OAc-a4** bearing two methyl groups at the terminal position (**III-b11**, **III-b12**). With longer linear alkyl at the terminal position of allyl acetates (**all-OAc-a5**), the efficiency of this allylation reaction was impacted by the functional groups and their positions on benzyl moiety of sulfonium salt, and the yields ranged from 33% to 70% ([Table III- 8](#), **III-b15**, **III-b16**). In

contrast, for the coupling of 4-methyl benzyl salt **S2** with (2*E*,4*E*)-2,4-hexadien-1-yl acetate (**all-OAc-a6**), the yield declined to 33% (**III-b17**) due to the conjugation of allene group making its-C-O bond more stable, compared to the yield with **all-OAc-a5** (**III-b15**). For some allyl acetate derivatives, which substituted groups at α -position (from **III-b18** to **III-b23**), linear alkyl groups performed better than cycloalkyl because of the steric hindrance (**III-b18** - **III-b20**). Benzyl sulfonium salts with an electron-withdrawing group were usually used as partners of α -substituted allyl acetate derivatives in this reaction because their reactivities matched more. Almost linear cross-coupling products were obtained (**III-b18**, **III-b19**). Based on the mechanism proposed in our previous paper^{9b}, the allyl Co(II) complex was proposed during this Co-catalyzed alkyl allylation process. For **all-OAc-a10**, its reactivity is lower than **all-OAc-a9** due to the substituent at the terminal position of the double bond. Thus, it was coupled with 4-methoxybenzyl sulfonium salt **S11**, leading to a 75% yield of mixed cross-coupling products (**III-b21**). However, benzyl sulfonium salts with different electron-withdrawing groups reacted with **all-OAc-a11** delivering about 30% yields of the desired products. Applying nopyl acetate (**all-OAc-12a**) in the reaction led to moderated yields either with **S1** or 4-methoxybenzyl sulfonium salt **S11**, even if the reaction time was extended to 24 h. A thiophenylmethylenyl sulfonium salt was also employed in this allylation reaction condition. To our disappointment, only a trace amount of the cross-coupling product **III-b26** was detected.

Table III- 9. Failed scopes of benzyl dimethyl sulfonium salt derivatives (S) with all-OAc-a^a

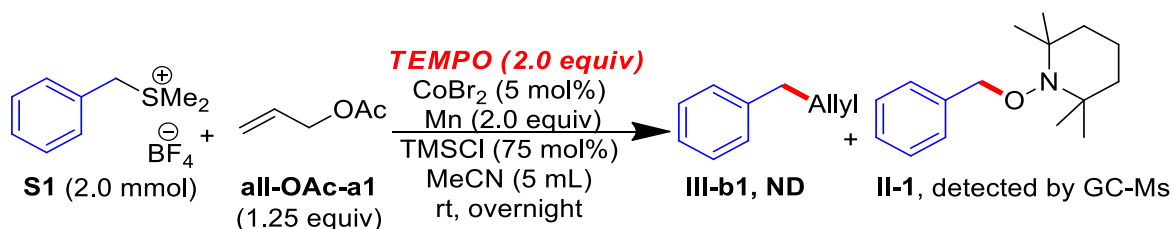
Entry	R	all-OAc-a	III-b	Yield/ %
1	3,5-diOMe	 all-OAc-a13		III-b27 , ND
2	3,5-diOMe			III-b27 , Trace
3	4-H			III-b28 , Trace
4	4-H	 all-OAc-a14		III-b29 , Trace
5	4-CF ₃			III-b30 , Trace
6	4-BPin	all-OAc-a1		III-b31 , ND
7	4-SO ₂ Me			III-b32 , Trace
8	4-CHO			III-b33 , Trace

^a Standard condition: S (2.0 mmol), all-OAc-a (2.5 mmol), CoBr₂ (5 mol%), Mn (2.0 equiv), TMSCl (75 mol%) in MeCN (5.0 mL) at rt under N₂, overnight (~15 h).

In addition to the samples mentioned above, other allyl acetate derivatives or benzyl sulfonium salts were employed in the condition, but only a trace amount of the desired products was detected (**Table III- 9**). As shown, using the geranyl acetate with benzyl sulfonium salts under the condition, only a trace amount of the desired products was detected, along with a considerable amount of remaining

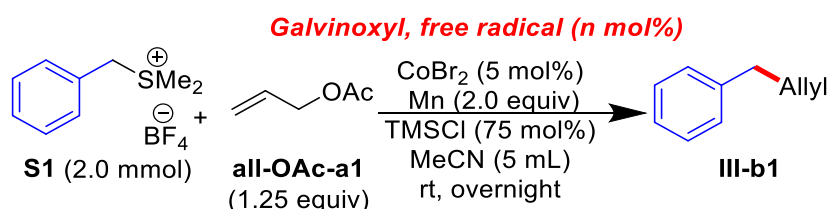
geranyl acetate (**III-b27**- **III-b28**). The same results were obtained when **all-OAc-a14** was used as an electrophile with benzyl sulfonium salts, but the difference is that the latter one generated more homo-coupling products in the reaction process (**III-b29**- **III-b30**). Moreover, benzyl sulfonium salts with Bpin, mesylate, as well as aldehyde groups were tested with **all-OAc-a1**, similar to the results of the alkylation reaction, and these sulfonium salts are not compatible with this allylation reaction condition (**III-b31**- **III-b33**).

2.1.3. Exploration of the mechanism.



Scheme III- 1. Radical trapping experiments with TEMPO.

To gain insight into the mechanism of this allylation process, a few experiments were conducted. In the presence of 2 equivalents of TEMPO, the cross-coupling of **S1** and **all-OAc-a1** performed under the optimized condition, and the reaction completely shut down. No **III-b1** was detected after the reaction, and a trace amount of 1-Benzyloxy-2,2,6,6-tetramethylpiperidine (**II-1**) was detected by GC-MS, which demonstrated that this allylation reaction involved benzyl radical in the process (**Scheme III- 1**).



Entry	n (mol %)	GC yield of III-b1/ %
1	0	66
2	50	48
3	100	19
4	200	7

^adodecane was used as a GC standard reference.

Scheme III- 2. Radical trapping experiments with galvinoxyl, free radical.

Moreover, galvinoxyl, free radical (n mol %), was used with **S1** and **all-OAc-a1** under optimized conditions. It was shown that the yield of the cross-coupling product **III-1** decreased significantly as the amount of free radical reagent increased (**Scheme III- 2**). The yield ranged from 66% to 7%.

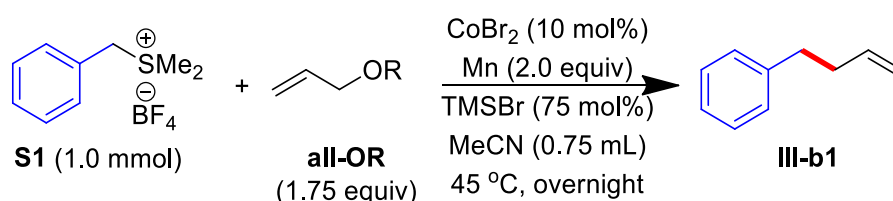
Based on these results, we proposed a mechanism for the cross-coupling of C_{allyl}-O electrophiles with sulfonium salts that was similar to the previous report of alkyl halides with allyl acetate and allyl carbonates^{9b}. A generated allyl Co complex reacted with benzyl sulfonium salts to give an allyl benzyl Co complex through forming a benzyl radical. And then, the complex provides the cross-coupling product by reductive elimination along with the regeneration of the active Co species.

2.2. Allyl Methyl Ether as Electrophiles with Sulfonium Salts

Allyl methyl ether (**all-OMe**), the simplest allyl ether compound, is rarely reported as C_{allyl}-O electrophiles in transition metal-catalyzed reductive cross-coupling, compared to allyl acetates or allyl carbonate derivatives. The most significant challenge to employ allyl methyl ether in constructing the Csp³-Csp³ bonds is the activation of its stable C-O bond. To our knowledge, the coupling with allyl ether derivatives as C-O electrophiles were mainly described with organometallic species^{4b}. Moreover, in most cases, allyl aryl ethers were employed as coupling partners to achieve C_{allyl}-O bond cleavage by Co catalyzed¹⁰⁷ or electrocatalysis (Co, Ni) due to their higher reactivity than allyl alkyl ether. While these reports show the possibility of C_{allyl}-O bond cleavage, particularly, Opsenica reported the deprotection of allyloxyarenes reaction¹⁰⁷. However, during our investigation, we have found that allyl methyl ether (**all-OMe**) could react with sulfonium salts either under the alkylation condition (**Table III-2, p104**) or under the allylation condition (**Table III-7**), as described in **Chapter II** and **Chapter III**. They gave 8% and 31% yield, respectively. To our delight, in high reaction concentration, the cross-coupling of **S1** and **all-OMe** was obtained in a 65% yield of the desired product **III-b**. This demonstrated the possibility that **all-OMe** is used as an electrophilic partner in Co-catalyzed reductive cross-coupling. Thus, with this inspiring result, the exploration of the cross-coupling of sulfonium salts and allyl methyl ether to build Csp³-Csp³ bonds was undertaken.

2.2.1. Optimization of reaction conditions.

Table III- 10. The reactions between S1 and allyl-OR derivatives.



Entry	R	Results ^a	
		Bibenzyl/%	III-b1/%
1	Me	13	65
2	Ac	36	22
3	Co ₂ Me	32	32

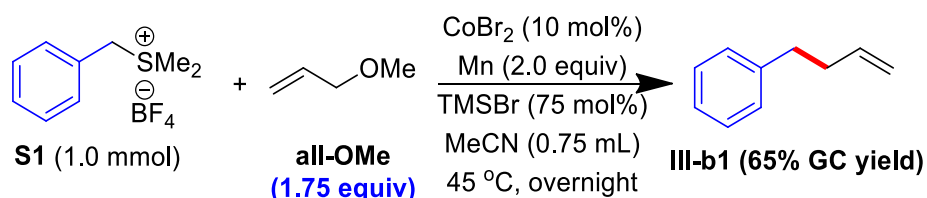
^a GC yields using dodecane as an internal standard.

Our study started with the cross-coupling of sulfonium salt **S1** and allyl methyl ether (**all-OMe**) under the conditions that combined by 10 mol% CoBr₂, 2 equivalents of Mn, and 75% of TMSBr to activate Mn in 0.75 mL of MeCN at 45 °C overnight. As illustrated in **Table III- 10**, in these conditions, allyl

¹⁰⁷ B. Kokić, Ž. Selaković, A. M. Nikolić, A. Andrijević, B. Anđelković, V. Ajdačić, I. M. Opsenica. *Eur. J. Org. Chem.* **2022**, e202201112

methyl ether **all-OMe** coupled with **S1** and delivered the desired allylation product- 4-phenyl-1-butene (**III-b1**) in 65% GC yield (entry 1). In these conditions, allyl acetate and allyl carbonate, which are commonly used as C_{allyl}-O electrophiles in transition metal-catalyzed reductive cross-coupling, performed poorly and led to the desired product **III-b1** in 22% and 32% of GC yield, respectively, along with a considerable amount of bibenzyl (entries 2- 3).

Table III- 11. The screen of the ratio of S1 and all-OMe.

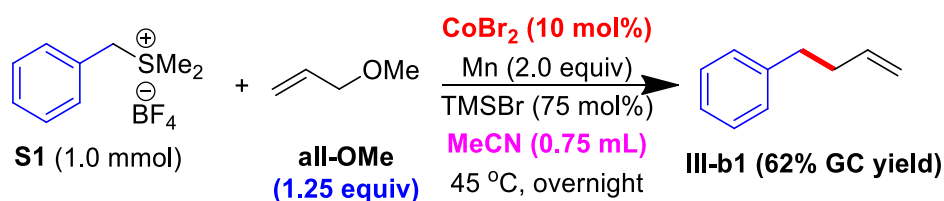


Entry	S1: all-OMe/ equiv	Results ^a	
		Bibenzyl/%	III-b1/%
1	1.0: 1.0	16	54
2	1.0: 1.25	15	62
3	1.0: 1.5	15	63
4	1.0: 2.0	15	63
5	1.0: 2.5	13	23
6	1.25: 1.0	27	60
7	1.5: 1.0	37	62

^a GC yields using dodecane as an internal standard.

The ratio of these two starting materials was screened first to obtain the optimized condition. As seen in **Table III- 11**, increasing the amount of **all-OMe** led to the yield rising from 54% to 63% (entries 1- 4). When the amount of **all-OMe** was from 1.25 to 2.0 equivalents, the yield of desired allylation product **III-b1** maintained steady and even decreased to 23% as 2.5 equivalents of **all-OMe** was used (entry 5). In contrast, using an excess amount of benzyl sulfonium salt **S1** did not cause any improvement in the cross-coupling efficiency (entries 6- 7).

Table III- 12. Optimizing the catalysts, solvents and ligands of S1 and all-OMe.



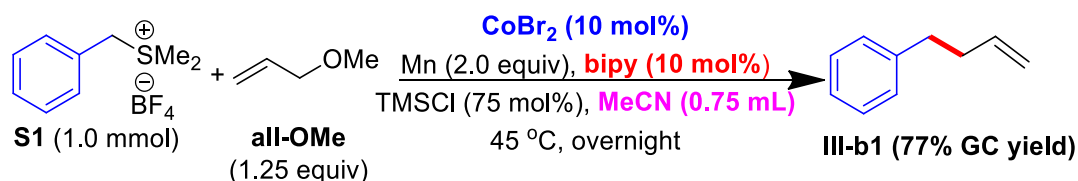
Entry	Variations				Results ^a	
	CoX ₂	Solvent	The amount/ mL	Ligand/ 10 mol%	Bibenzyl/%	III-b1/%
1	CoBr ₂	MeCN	1.0	/	16	63
2	1.5	/	21	47
3	Co(OAc) ₂	..	0.75	/	18	46
4	CoCl ₂	/	15	62
5	Co(acac) ₂	/	18	42
6	CoBr ₂	Dioxane	..	/	Trace	Trace
7	..	Toluene	..	/	Trace	Trace
8	..	DMA	..	/	√	Trace
9	..	DMF	..	/	√	Trace
10	..	DMPU	..	/	√	Trace
11	..	NMP	..	/	√	Trace
12	..	MeCN	..	bipy	trace	77
13	4-Me-bipy	8	76
14	Imidazole	7	71
15	Py	14	45

^a GC yields using dodecane as an internal standard.

Since using 1.25 equivalents of all-OMe got a similar yield to 1.75 equivalents, the former one was chosen in further optimization for the reaction economic efficiency. The results in the Table III- 12 showed that decreasing the reaction concentration slightly did not affect the cross-coupling efficiency (entry 1), but adding more amount (1.5 mL) of MeCN caused the yield of the desired product III-b1 decrease to 47% (entry 2). Thus, in 0.75 mL of MeCN, different Co catalysts were screened (entries 3- 5). The use of CoCl₂ led to a similar yield to CoBr₂, but considering its small mass effect on the adding accuracy, as well as the poorer performance of Co(OAc)₂ and Co(acac)₂ in the reaction, CoBr₂ continued to be used as the catalyst. And then, various solvents instead of MeCN were used in the reaction. To our surprise, only a trace amount of the desired product III-b1 was detected either using non-polar or other polar solvents. At the same time, the latter yielded more bibenzyl (entries 6- 11). To increase the efficiency of this reductive cross-coupling, various ligands were added to the condition. Using bipy or 4-Me-bipy as a ligand the reaction, the yield of the desired product III-b1 increased by about 10%,

but compared to the price of these two kinds of bipy ligands, the bipy is more beneficial (entries, 12-13. bipy, 107 € /25 g; 4-Me-bipy, 419 € /25. g, data from.sigmaaldrich.com). Imidazole as the ligand led to a lower yield than bipy (entry 14, 71% GC yield) but much better than using Py, which gave a 45% yield of the cross-coupling product (entry 15).

Table III- 13. Optimizing the activators, Mn and temperature of S1 and all-OMe.

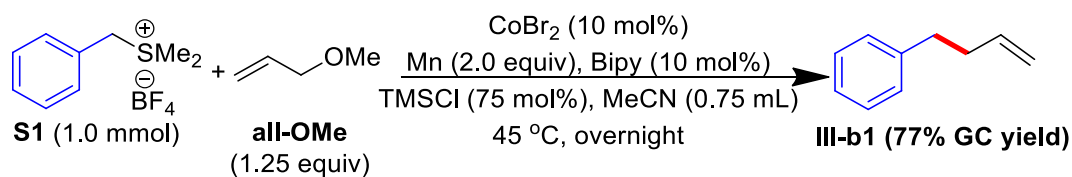


Entry	Variations				Results ^a	
	TMSCl/ mol%	Mn/ equiv	CoBr ₂ / mol%	T/ °C	Bibenzyl/%	III-b1/%
1	25	2.0	10	45	Trace	19
2	50	9	19
3	100	9	68
4	75	1.5	5	62
5	..	3.0	8	72
6	..	4.0	8	70
7	..	2.0	5	..	Trace	67
8	15	70
9	10	30	..	61
10	60	..	65

^a GC yields using dodecane as an internal standard.

While bipy was used as the ligand, the activator was screened. Replacing the TMSBr with TMSCl delivered a similar yield (74% GC yield), but the TMSCl was employed in further experiments due to its lower price. Using TFA instead of TMSCl or TMSBr to activate the Mn led to poorer yield of the desired product **III-b1**. As shown in **Table III- 13**, with TMSCl as an activator, either decreasing or increasing the amount of TMSCl decreased the yield of **III-b1**; notably, when 25 mol% and 50 mol% of TMSCl were used, the yield decreased to 19% (entries 1- 3). Changing the amount of Mn did not make any significant improvement in the yield (entries 4- 6). Changing the amounts of Co catalyst did not improve results (entries 7- 8). Either at 30 °C or increasing the temperature to 60 °C, the efficiency of this reductive cross-coupling was not enhanced (entries 9- 10).

Table III- 14. Control experiments.



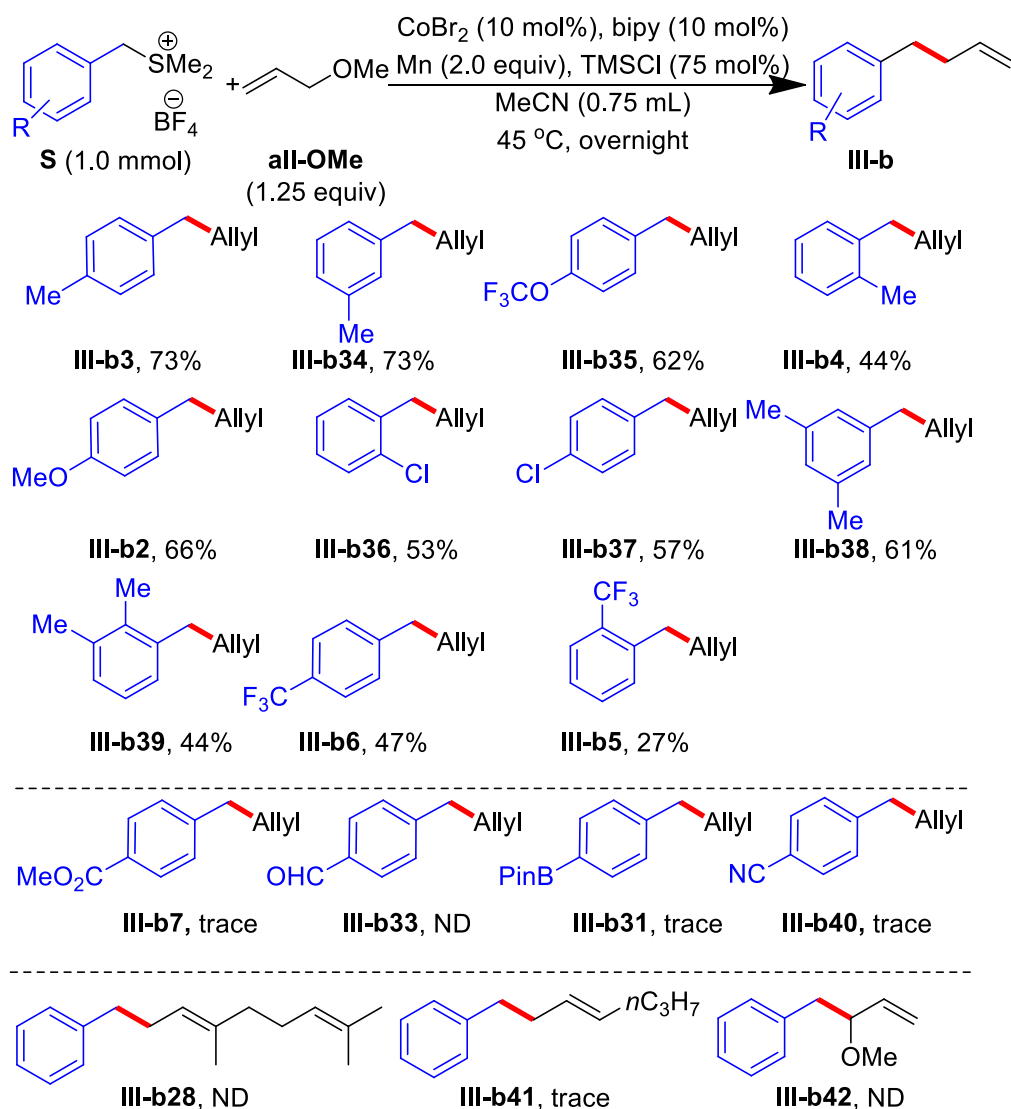
Entry	Conditions	Results ^a	
		Bibenzyl/%	III-b1/%
1	w/o CoBr_2	×	×
2	Zn instead of Mn	6	3 ^b
3	w/o Mn	×	Trace
4	CoBr_2 (5 mol%)/ bipy (5mol%)	Trace	70

^a GC yields using dodecane as an internal standard.

Defining the optimized condition as 10 mol% CoBr_2 , 2 equivalents of Mn activated by 75 mol% TMSCl in 0.75 mL of MeCN , sulfonium salts **S** (1.0 mmol), and **all-OMe** (1.25 equiv) reacted at 45 °C overnight. Control experiments were carried out (Table III- 14). Experimental results showed that the Co catalyst and Mn were mandatory for this cross-coupling (entries 1- 3). And decreasing the amount of Co catalyst and ligand to 5% resulted in a slightly lower yield of **III-b1** (entries 4).

2.2.2. Reaction Scopes of benzyl dimethyl sulfonium salt derivatives (S) with all-OMe.

Table III- 15. Scopes of benzyl dimethyl sulfonium salt derivatives (S) with all-OMe ^{a,b}

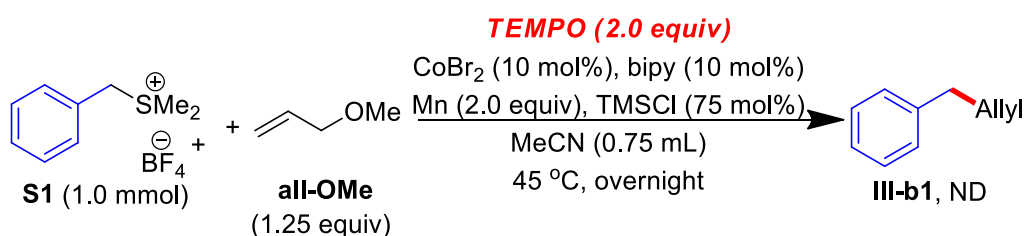


^a Standard condition: S (1.0 mmol), all-OMe (1.25 mmol), CoBr_2 (10 mol%), bipy (10 mol%), Mn (2.0 equiv), TMSCl (75 mol%) in MeCN (1.3 M) at 45 °C, overnight (~15 h) under N_2 . ^b Isolated yield.

With this optimized condition in hand, the scope of benzyl sulfonium salts with allyl methyl ether derivatives was explored. As shown in [Table III- 15](#), benzyl sulfonium salts bearing an electron-donating group performed better than those with electron-withdrawing groups due to the lower reactivity of the former, which showed similar results to the reaction with alkyl iodides. Moderate to good yields were obtained when benzyl sulfonium salts bearing methyl ([Table III- 15](#), III-b3- III-b4, III-b34), trifluoromethoxy ([Table III- 15](#), III-b35), and methoxy ([Table III- 15](#), III-b2). However, the steric hindrance of sulfonium salts affected this cross-coupling efficiency. When the methyl group is at the *o*-position, the yield of desired product III-b4 decreased to 44%, whereas with chlorine, this effect is not obvious ([Table III- 15](#), III-b36- III-b37). Benzyl sulfonium salts with multiple functional groups were also added

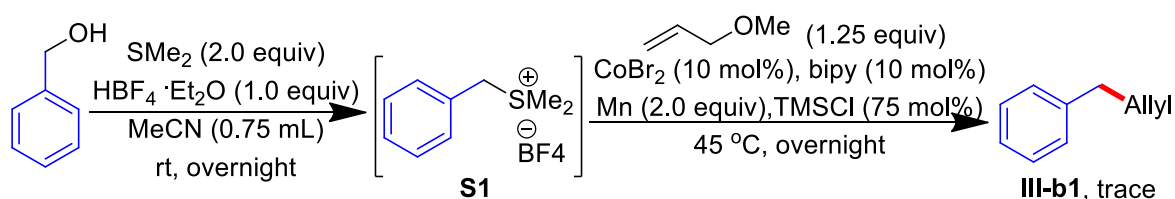
in this reaction (**Table III- 15**, **III-b38**, **III-b39**). Due to the steric hindrance, functional groups at the 2,3-position of benzyl moiety gave a 27% yield, lower by about 20% than those on the 3,5-position. Benzyl sulfonium salts with a trifluoromethyl group and **all-OMe** led to lower yield (**Table III- 15**, **III-b6**, **III-b5**), especially the one at *o*-position. However, as described in the cross-coupling of sulfonium salts with alkyl iodides, benzyl sulfonium salts bearing several functional groups, such as cyano, dihydride Bpin, and mesylate, were not tolerant to this reaction (**Table III- 15**, **III-b7**, **III-b33**, **III-b31**, **III-b40**). After the scope of various benzyl sulfonium salts with **all-OMe**, different substituted allyl methyl ethers as partners were tried in this allylation reaction. To our disappointment, no or trace of cross-coupling products were obtained (**Table III- 15**, **III-b28**, **III-b41- III-b42**). Further explorations of benzyl sulfonium salts with substituted allyl methyl ether will be continued in our lab.

2.2.3. Exploration of the mechanism.



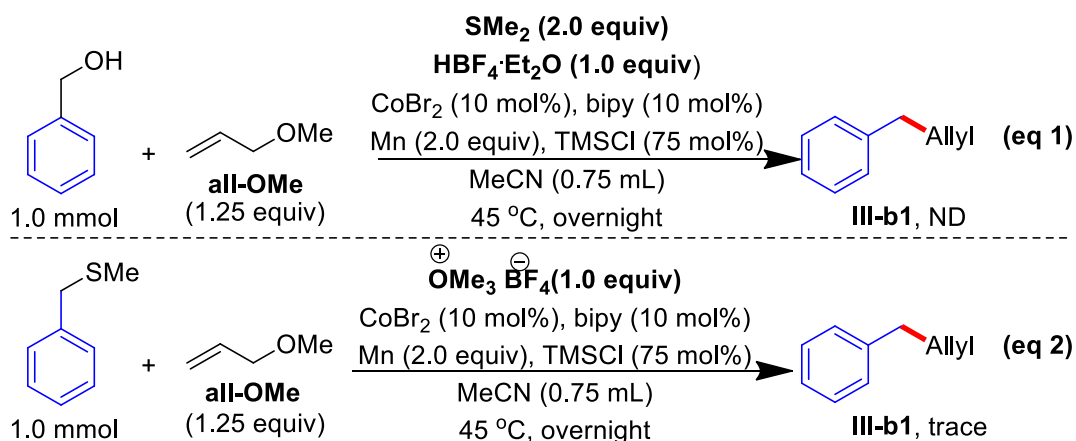
Scheme III- 3 Radical trapping experiments with TEMPO

To understand the allylation mechanism of the cross-coupling between sulfonium salts and **all-OMe**. A radical trapping experiment with TEMPO was conducted. In these conditions, the cross-coupling of **S1** and **all-OMe** showed that no target product was detected when 2 equivalents of TEMPO were added under the optimized condition. This reaction supported the proposal that benzyl radical was generated from the C_{Bn}-S bond cleavage of sulfonium salts in this Co-catalyzed allylation reaction (**Scheme III- 3**).



Scheme III- 4 Synthesis **III-b1** without filtration of **S1**

The cross-coupling of **S1** with **all-OMe** without isolating benzyl sulfonium salt was also tried to get a benzyl allylation products. However, only a trace amount of the cross-coupling product **III-b1** was detected, as well as the homo-coupling product of **S1** (**Scheme III- 4**).



Scheme III- 5. One-pot reaction to synthesize III-b1 from benzyl alcohol or benzyl sulfide.

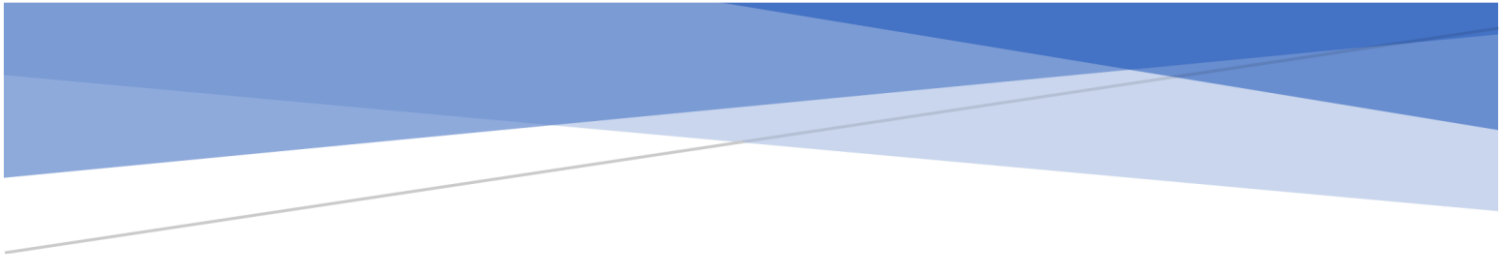
A one-pot reductive cross-coupling allylation reaction starting from benzyl alcohol directly, used as the partner of **all-OMe**, was also studied. The dimethyl sulfide and tetrafluoroboric acid·diethyl ether complex were added into the mixture to form benzyl sulfonium salt **S1**. However, no desired product was detected (**Scheme III- 5, eq1**). In contrast, in another experiment used the method reported by Berchtold¹⁰⁸ to synthesize sulfonium salts from benzyl methyl sulfide as starting material, with trimethyloxonium tetrafluoroborate, a trace amount of **III-b1** was detected (**Scheme III- 5, eq2**).

¹⁰⁸ A. L. Maycock, G. A. Berchtold, *J. Org. Chem.* **1970**, 35, 8, 2532–2538

3. Conclusion and Perspectives

In this chapter, benzyl sulfonium salts were demonstrated to be suitable for constructing Csp³-Csp³ bonds with either allylic acetates or allylic ether via a Co-catalyzed reductive cross-coupling. Various functionalized alkyl olefinic compounds were obtained under mild conditions in moderate to good yields from benzyl sulfonium salts bearing electron-donating or electron-withdrawing groups. These reactions employed two non-halogenated electrophiles for the first time in C-C bond formation in Co-catalyzed reductive cross-coupling. It is also the first report using allyl alkyl ether to construct a C-C bond in reductive cross-coupling. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl sulfonium salts. Further studies to apply sulfonium salts in cobalt-catalyzed C-C bond formation is currently underway in our laboratory.

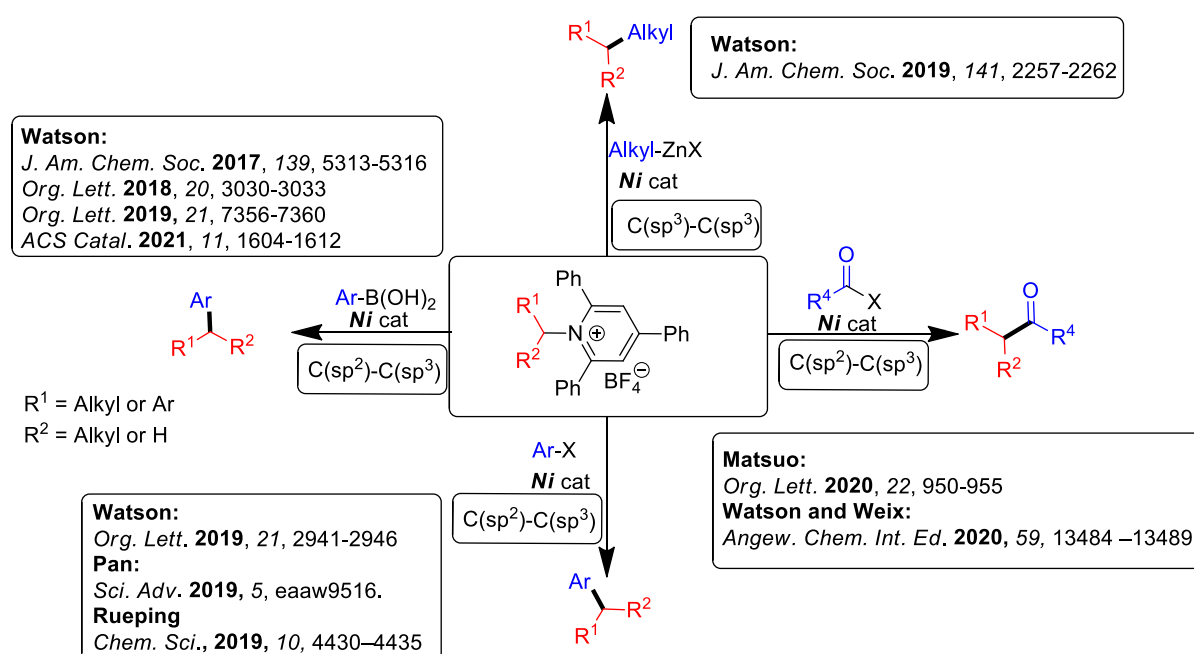
Although excellent improvements have been obtained in Csp³-Csp³ bond formation by Co-catalyzed reductive cross-coupling, the scope of allyl acetates or allyl methyl ether remains a big challenge. Thus, searching for a suitable method to extend the scope of allyl methyl ether to substituted ones is a priority study in future research.



**Chapter IV: Co-Catalyzed $C_{sp^3}-C_{sp^3}$
Cross-Coupling of Benzyl Pyridinium
Salts with $C_{allyl}-O$ Electrophiles**

1. Pyridinium Salts in Forming C-C Bonds

Amino compounds are prevalent in biomolecules, drugs, and natural products⁶⁸. The transformation of the C–N bonds by transition metals catalyzed can be dated back to 1980; as introduced in the **Introduction**, there are several main pathways to its transformation⁶⁹. Among them, the ammonium species increase the activity of the C–N bond, which can generate alkyl radicals via transition metal-catalyzed. This deamination pathway has been widely reported by Watson et al. since 2010 because the amino group (NH₂) is easily converted to ammonium triflates or Katritzky pyridinium salts in one step¹¹ (**Scheme IV-1**). In this chapter, the reductive cross-coupling of the ammonium species, represented by Katritzky pyridinium salts, with C_{allyl}-O electrophiles to construct Csp³-Csp³ bonds by Co-catalyzed was presented.

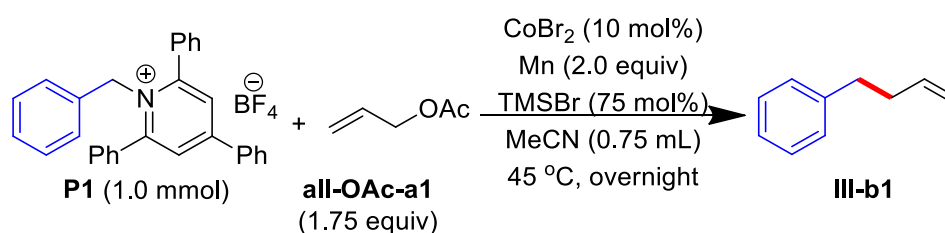


Scheme IV-1. Nickel-catalyzed C–N bond activation by Katritzky pyridinium salts

2. Results and discussions between Benzyl Pyridinium Salts and C_{allyl}-O Electrophiles

2.1. Optimization of reaction conditions.

Table IV- 1. Co-catalyzed reductive cross-coupling of benzyl Katritzky pyridinium salt and allyl acetate.

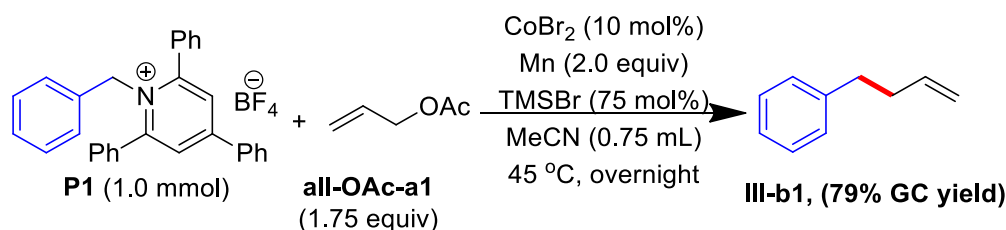


Entry	Variations	Results ^a	
		Bibenzyl/%	III-b1/%
1	None	Trace	79
2	Zn instead of Mn	..	21
3	TFA instead of TMSBr	14	37

^a GC yields using dodecane as an internal standard.

The investigation started with the cross-coupling of the benzyl Katritzky pyridinium salt (**P1**) and allyl acetate (**all-OAc-a1**) under the condition involving 10 mol% CoBr_2 , 2 equivalents of Mn activated by 75 mol% TMSBr in MeCN at 45 °C overnight. A 79% GC yield of the cross-coupling product-4-phenyl-1-butene (**III-b1**) was obtained (**Table IV- 1**, entry 1) in these conditions. However, replacing Mn with Zn as a reductant metal led to a sharp decline in the yield of the cross-coupling product **III-b1** (**Table IV- 1**, entry 1). A similar low yield of the cross-coupling product was obtained when TFA was used as the activator instead of TMSBr, but 14% of homo-coupling product-bibenzyl was detected, higher than using TMSBr (**Table IV- 1**, entry 3).

Although 79% GC yield of the cross-coupling product **III-b1** has been obtained, we studied different parameters of this reaction, such as the temperature, the ratio of two electrophiles, the reaction concentration, the ligand screen, *etc.* The experimental results are as follows.

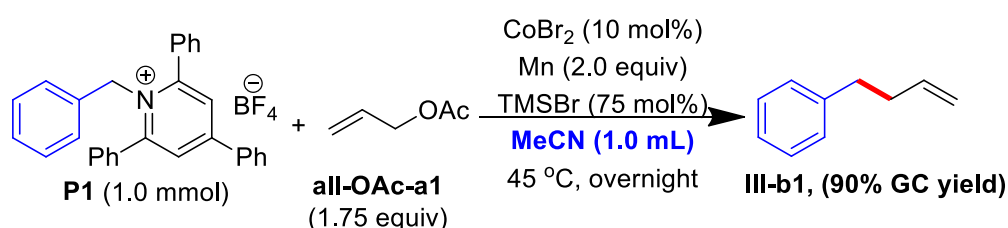
Table IV- 2. Optimizing the temperature, the ration of starting materials, solvent, and ligands.

Entry	Variations				Results ^a	
	T/ °C	P1: all-OAc-a1	MeCN/ mL	Ligand/ 10 mol%	Bibenzyl/%	III-b1/%
1	rt	1: 1.75	0.75	/	Trace	47
2	60	14	57
3	45	1: 1.5	9	66
4	..	1: 2.0	Trace	67
5	..	1:1.75	1.0	90
6	1.5	88
7	1.0	bipy	9	86
8	4-Me-bipy	Trace	82
9	dtbbpy	..	84

^a GC yields using dodecane as an internal standard.

Changing the reaction temperature to rt or 60 °C resulted in a noticeable decline in the yield of the cross-coupling product **III-b**, and the yield of bibenzyl increased to 14% at 60 °C (**Table IV- 2**, entries 1- 2). On the other hand, 1.75 equivalents of allyl acetate **all-OAc-a1** were most suitable for the reaction condition compared to 1.5 and 2.0 equivalents of **all-OAc-a1** used (**Table IV- 2**, entries 3- 4). When the reaction construction decreased to 1 M (1 mL of MeCN), the yield of **III-b** raised to 90% GC yield, higher by about 20% than using 0.75 mL of MeCN, while increasing the amount of MeCN continuously, a similar yield was obtained (**Table IV- 2**, entries 5- 6). Thus, 1.0 mL of MeCN was used in further exploration (**Table IV- 2**, entry 5). Then several bipyridyl ligands were employed in the condition. However, no improvement was observed (**Table IV- 2**, entries 7- 9), and the yield of the desired product was kept at 82- 84%.

The experiment demonstrated that a 90% GC yield of the cross-coupling product between benzyl Katritzky pyridinium salt (**P1**) and allyl acetate (**all-OAc-a1**) was obtained, which is a bit better than the results of benzyl sulfonium salt (**S1**) with **all-OAc-a1**. This Co-catalyzed reductive cross-coupling was also optimized to construct Csp³-Csp³ bonds from C-N and C-O electrophiles by screening solvents, the amounts of activator, reductant, etc.

Table IV-3. Optimization of activator, Mn, and allyl derivatives.

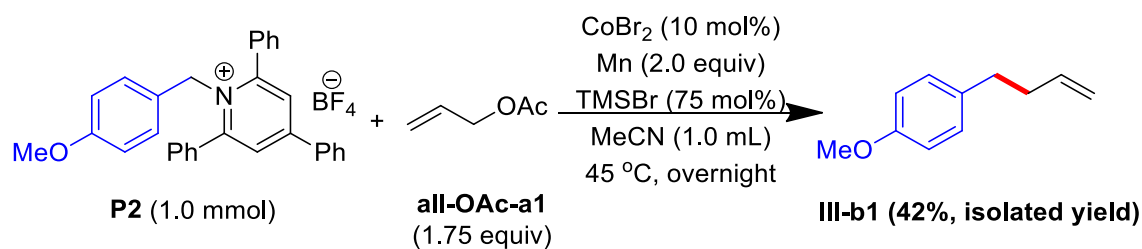
Entry	Variations				Results ^a	
	TMSBr/mol%	Mn/ equiv	Solvent	Ally-OR	Bibenzyl/%	III-b1/%
1	25	2	MeCN	Ac (all-OAc-a1)	Trace	83
2	50	85
3	75	92
4	75	9	75 ^b
5	100	Trace	83
6	75	1.5	×	60
7	..	2.5	9	75
8	..	3.0	×	85
9	..	2	THF	..	11	Trace
10	Dioxane	..	Trace	..
11	Toluene
12	DMA	..	22	..
13	DMF	..	24	..
14	MeCN	CO ₂ Me	×	88
15	Me	×	75
16	H	×	8

^a GC yields using dodecane as an internal standard. × = Not detected. ^b TMSCl instead of TMSBr.

As shown in **Table IV-3**, the yield of the desired allylation product **III-b1** increased first and then decreased with the amount of TMSBr increasing (entries 1- 3, 5). Repeating the reaction of **Table IV-2**, entry 5, led to a 92% yield of the **III-b1**, demonstrating the stability of this allylation reaction from benzyl Katritzky pyridinium salt (**P1**) (entry 3). In contrast to the allylation reaction with benzyl sulfonium salts, the efficiency of activating Mn by TMSCl did not have any advantage over TMSBr in this Co-Mn catalytic system (**Table IV-3**, entry 4). Screening the amount of Mn did not help enhance the cross-coupling yield (**Table IV-3**, entries 6- 7). Various solvents were applied under these conditions. Unsurprisingly, as the observed cross-coupling of benzyl sulfonium salts and allyl acetate, poor yields were detected with non-polar solvents, like THF, dioxane, and toluene, due to the low solubility of benzyl Katritzky pyridinium salt in these solvents (**Table IV-3**, entries 9- 11). In polar solvents, the

bibenzyl was still detected as the main product (*Table IV- 3*, entries 12- 13). Finally, allyl carbonate and allyl methyl ether were employed under these optimized allylation reaction conditions; unexpectedly, excellent yields (75% and 88% yield, respectively) were obtained when these two C_{allyl}-O electrophiles were used instead of allyl acetate. In contrast, low yields (8% with allyl carbonate and 31% yield allyl methyl ether) were obtained in the condition of benzyl sulfonium salts and allyl acetate (*chapter III, Table III- 7*, entries 6- 7, p108).

Table IV- 4. Control experiments.

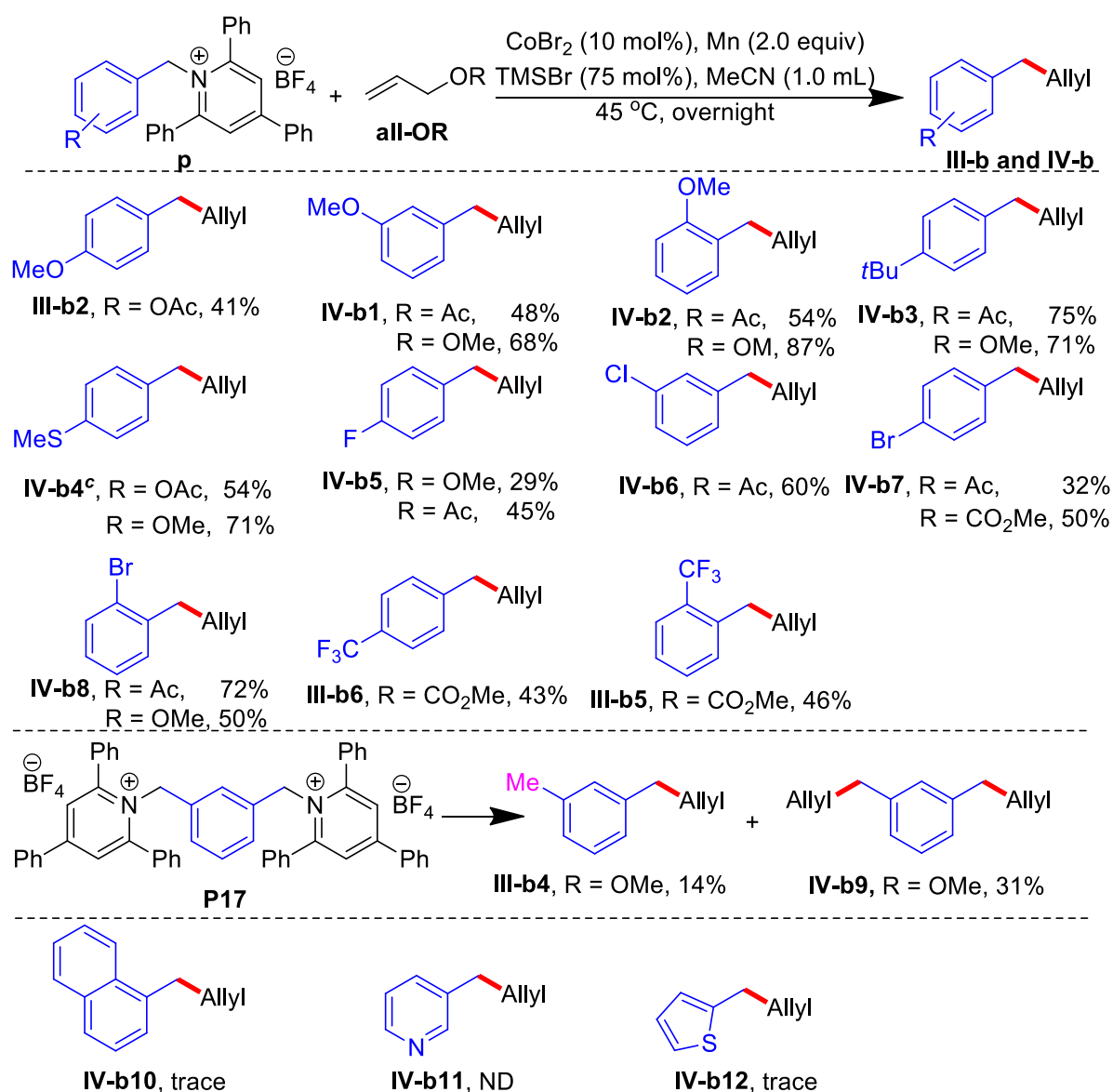


Entry	Variations	III-b1 ^a /%
1	w/o CoBr ₂	×
2	w/o Mn	×
3	w/o TMSBr	Trace

^a GC yields using dodecane as an internal standard. ×= Not detected

Conformed the optimization conditions of benzyl Katritzky pyridinium salt **P2** with allyl acetate **all-OAc-a1**; some control experiments were carried out. As shown in *Table IV- 4*, the results demonstrated that Co catalyst, Mn, and TMSBr to activate Mn are mandatory for this Co-catalyzed Csp³-Csp³ cross-coupling of benzyl pyridinium salts with allyl derivatives (*Table IV- 4*, entries 1- 3).

2.2. Scopes of benzyl pyridinium salts with allyl acetate.

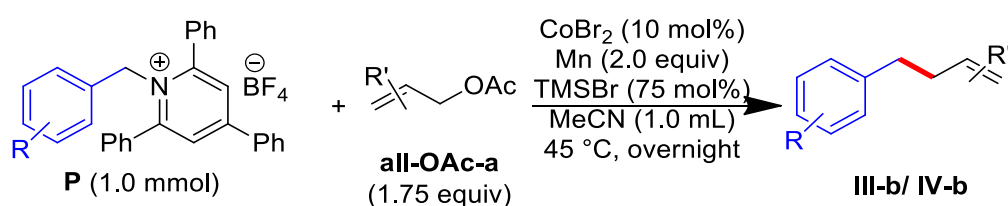
Table IV-5. Scopes of benzyl pyridinium salts with allyl acetate by Co-catalyzed. ^{a, b}

Note: III-b are these products obtained in Chapter III. IV-b: are new products obtained in this Chapter

^a Standard condition: **P** (1.0 mmol), All-OR (1.75 mmol), CoBr₂ (10 mol%), Mn (2.0 equiv), TMSBr (75 mol%) in MeCN (1.0 mL) at 45 °C, overnight (~15 h) under N₂. ^b Isolated yield. ^c MeCN (0.75 mL)

Under the optimized allylation condition of benzyl Katritzky pyridinium salt **P1** and allyl acetate **all-OAc-a1**, the scope of the various benzyl Katritzky pyridinium salts with allyl acetate/methyl ether/carbonate was illustrated in **Table IV-5**. The experimental results regularly were similar to the cross-coupling of benzyl sulfonium salts and C_{allyl}-O electrophiles (**Chapter III**). Better yields were obtained with benzyl pyridinium salts bearing electron-donating groups than ones with electron-withdrawing groups. When methoxy, *t*-Butyl, and thioether groups are on benzyl moieties of benzyl pyridinium salts, the yields of the cross-coupling products with allyl methyl ether **all-OMe**, which has lower

reactivity, were overall better than with **all-OAc-a1 (IV-b1 to IV-b4)**. In this case, the yields of desired allylation products with **all-OMe** increased about 20%, compared to **all-OAc-a1**, except **IV-b3**. Moreover, the steric hindrance on the benzyl pyridinium salts did not affect the cross-coupling efficiency; in contrast, higher yields were obtained with substituents at the *o*-position due to their less homo-coupling products of benzyl pyridinium salts (**IV-b2, IV-b8**). The cross-coupling of benzyl pyridinium salts bearing halides with **all-OMe** led to moderate yields. As the reactivity of benzyl pyridinium salts increased, more reactive C_{allyl}-O electrophiles were applied in the reaction (**IV-b5- IV-b7, IV-b7- IV-b8**). When the bromide on the *o*-position of benzyl pyridinium salt reacted with **all-OAc-a1**, compared to the one on the *p*-position (**IV-b8**: 32% yield, 50% yield with allyl carbonate), the yield of the desired product (**IV-b8**) increased to 72%, due to the higher steric hindrance and lower reactivity of 2-bromide substituted benzyl pyridinium salt. While with a CF₃ substituted group, only moderate yields were obtained, even with allyl carbonate (**III-b7, III-b5**). When the benzyl with two pyridinium salts **P17** was employed in the cross-coupling reaction with **all-OMe**, two products-the two-substituted product **IV-b9**, and the mono-substituted **III-b4** were obtained. In addition, naphthyl and heteroaryl benzyl pyridinium salts were also tried under these allylation conditions, but yields were not good and showed that naphthyl/heteroaryl benzyl pyridinium salts were not compatible with these conditions (**IV-b10 to IV-b12**).

Table IV- 6. Scopes of benzyl Katritzky pyridinium salts with allyl acetate derivatives (all-OAc-a) ^{a, b}

Entry	R	All-OAc-a	III-b /V-b	Yield/ %
1	4-MeO (P2)			III-b9 , 55% ^c
2	3-MeO (P3)	all-OAc-a2		IV-b13 , 61%
3	4-H (P1)			IV-b14 , 72%
4	4-MeO (P2)	all-OAc-a3		III-b10 , 55%
5	4-H (P1)			III-b11 , 48%
6	4-MeO (P2)	<i>n</i> C ₃ H ₇ -allyl acetate all-OAc-a5		III-b13 , 62% ^c
7	4-MeO (P2)	<i>n</i> C ₅ H ₁₁ -allyl acetate all-OAc-a15		IV-b15 , 44% ^c
8				IV-b16 , 44% ^c

^a Standard condition: **P** (1.0 mmol), all-OR (1.75 mmol), CoBr₂ (10 mol%), Mn (2.0 equiv), TMSBr (75 mol%) in MeCN (1.0 mL) at 45 °C, overnight (~15 h) under N₂. ^b Isolated yield. ^c MeCN (0.75 mL)

On the other hand, the cross-couplings of different benzyl Katritzky pyridinium salts with various substituted allyl acetates were also conducted to construct Csp³-Csp³ bonds. As shown in [Table IV- 6](#), different substituted groups on different positions of allyl acetates (**all-OAc-a**), coupled with benzyl Katritzky pyridinium salts (**P**) and delivered moderate to good yields of the desired products (entries 1- 8, the yields ranged from 44% to 72%). Compared to the cross-couplings of benzyl sulfonium salts with substituted allyl acetates (**all-OAc-a**) (In [chapter III, Table III- 8, p109](#)), better yields were obtained when benzyl Katritzky pyridinium salts (**P**) coupled with allyl acetates bearing methyl group at either the middle or terminal position of double bonds ([Table IV- 6](#), entries 1- 4). Moreover, compared **III-b9** to **IV-b13**, and **IV-b14** to **III-b10** ([Table IV- 6](#)), yields of the cross-coupling products increased as the reactivity of the benzyl pyridinium salts (**P**) increased. When there are two methyl groups at the terminal position of allyl acetate **all-OAc-a4**, a 48% isolated yield of the cross-coupling product **III-b11** was obtained ([Table IV- 6](#), entry 5). These results demonstrated: (1) the higher efficiency of Csp³-Csp³ bond formation via benzyl Katritzky pyridinium salts (**P**) than benzyl sulfonium salts (**S**) via Co-catalyzed reductive cross-coupling and (2) a lower effect of substituents on the double bond of allyl acetate

derivatives. With more extended linear alkyl groups at the terminal position of allyl acetates (**all-OAc-a5**, **all-OAc-a15**), the efficiency of this allylation reaction was impacted by the length of functional groups. When **all-OAc-a5** was employed in the cross-coupling with 4-methoxyl benzyl pyridinium salt **P2**, a higher yield was obtained than **all-OAc-a15** (**III-b13** vs. **IV-b15**, 62% vs. 44%). When (2*E*,4*E*)-2,4-hexadien-1-yl acetate (**all-OAc-a6**) was used as the partner with **P2**, the yield of **IV-b16** declined about 20% due to the conjugation of the alkene making its C-O bond more stable, compared to **III-b13**.

Table IV- 7. Scopes of benzyl Katritzky pyridinium salts with allyl acetate derivatives (all-OAc-a) ^{a, b}

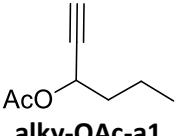
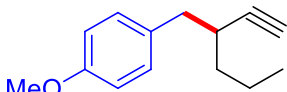
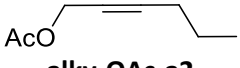
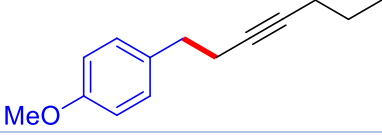
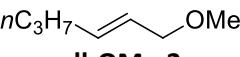
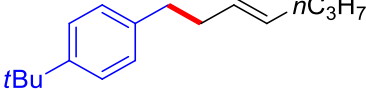
Entry	R	All-OAc-a	III-b/ V-b	Yield/ %
1	4-H (P1)			IV-b17 , 60%
2	3-Cl (P8)	all-OAc-a16		IV-b18 , 61%
3	4-H (P1)			IV-b19 , 49% ^c
4	4-CF ₃ (P11)	all-OAc-a17		IV-b20 , 63% ^c
5	3-MeO (P3)			IV-b21 , 61%
6				IV-b22 , 47%
7	4-CF ₃ (P11)			III-b24 , 33%
8				IV-b23 , ND
9	4-H (P1)			IV-b24 , <20%

^a Standard condition: P (1.0 mmol), all-OR (1.75 mmol), CoBr₂ (10 mol%), Mn (2.0 equiv), TMSBr (75 mol%) in MeCN (1.0 mL) at 45 °C, overnight (~15 h) under N₂. ^b Isolated yield. ^c MeCN (0.75 mL)

Secondary allyl acetate derivatives substituted in α -position (**Table IV- 7**), like **all-OAc-a16**, **all-OAc-a17**, and **all-OAc-a9**, led to moderate yields with almost linear cross-coupling products (from 49% to 63%, **IV-b17** to **IV-b20**). From comparing **IV-b19** with **IV-b20** and **IV-b20** with **IV-b21**, benzyl pyridinium salts with an electron-withdrawing group performed better than those with an electron-donating group. On the other hand, similar results could be obtained when the pyridinium salts with either EDG

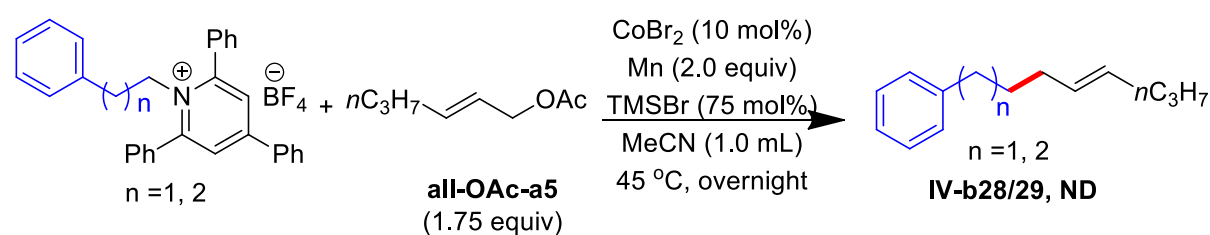
or EWG have longer linear substituents at the α -position. It showed that reactivities of benzyl pyridinium salts with an electron-withdrawing group match more with α -position substituted secondary allyl acetate derivatives. For the allyl acetate derivative **all-OAc-a7** substitute at α -position with a cycloalkyl delivered 47% yield of the cross-coupling product **IV-b22** with 4-trifluoromethyl benzyl pyridinium salt **P11**, along with a bit of homo-coupling products. When 4-trifluoromethyl benzyl pyridinium salt **P11** reacted with **all-OAc-11a**, the yield of desired product **III-b24** decreased to 33%, as well as a lot of both homo-coupling products. When the α -position substituted group was a phenyl group, no cross-coupling product **IV-b23** was detected, except the reduced product of the allyl acetate **all-OAc-a18**. Replacing the substituent with the 3-pentyl group, the yield of the cross-coupling decreased significantly (**IV-b24**).

Table IV- 8. Scopes of benzyl Katritzky pyridinium salts with C-O derivatives (all-OAc-a) ^{a, b}

Entry	R	All-OAc-a	IV-b	Yield/ %
1	4-MeO (P2)	 alky-OAc-a1		IV-b25, ND
2		 alky-OAc-a2		IV-b26, ND
3	4-tBu(P5)	 all-OMe-2		IV-b27, ND

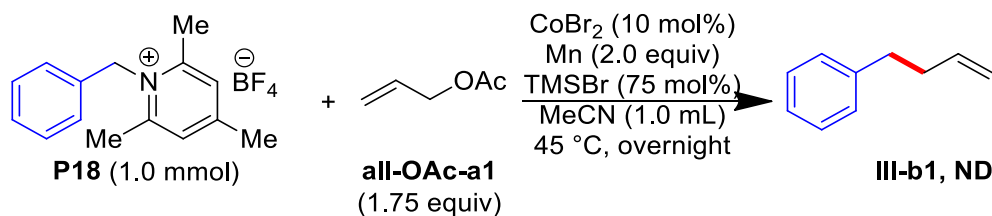
^a Standard condition: P (1.0 mmol), all-OR (1.75 mmol), CoBr₂ (10 mol%), Mn (2.0 equiv), TMSBr (75 mol%) in MeCN (1.0 mL) at 45 °C, overnight (~15h) under N₂.

In addition to the allyl acetate derivatives, propargyl acetates were also tried under the optimized allylation reaction condition with 4-methoxy benzyl pyridinium salt **P2** (Table IV- 8). However, the propargyl acetates remained after the reaction, and no desired products were detected (**IV-b25, IV-b26**). The same result was obtained when allyl methyl ether derivative **all-OMe-2** was used in the reaction; no desired product **IV-b27** was detected.



Scheme IV- 2. Alkyl pyridinium salts with allyl acetate by Co-catalyzed.

Furthermore, less reactive alkyl pyridinium salts were synthesized and used in reductive cross-coupling as the C-N electrophiles with **all-OAc-a5** under the optimized condition, shown as *Scheme IV-2*; no desired products were detected, and only the homocoupling product of allyl acetate was detected by GC-MS.

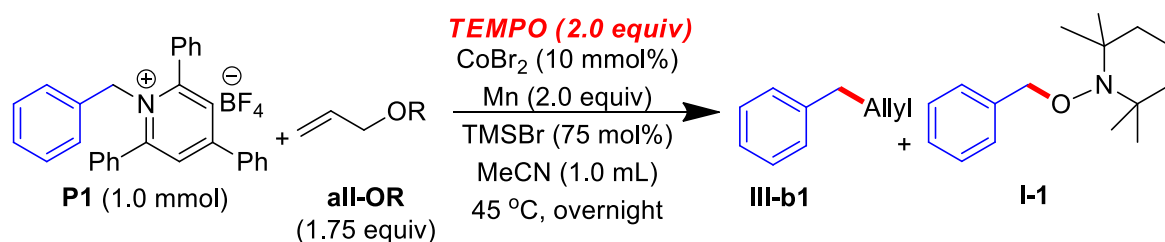


Scheme IV-3. Another pyridinium salt with allyl acetate by Co-catalyzed.

To learn deeply about this Co-catalyzed Csp³-Csp³ cross-coupling of benzyl Katritzky pyridinium salts with C_{allyl}-O electrophiles, as well as increasing the molecular economy, benzyl pyridinium salt **P18**, which replaces the phenyl group on pyridinium salt with the methyl group (*Scheme IV-3*). However, the desired product was not detected overnight due to the lower reactivity of the C-N bond of **P18**

2.3. Exploration of the mechanism

2.3.1. Radical trapping experiments

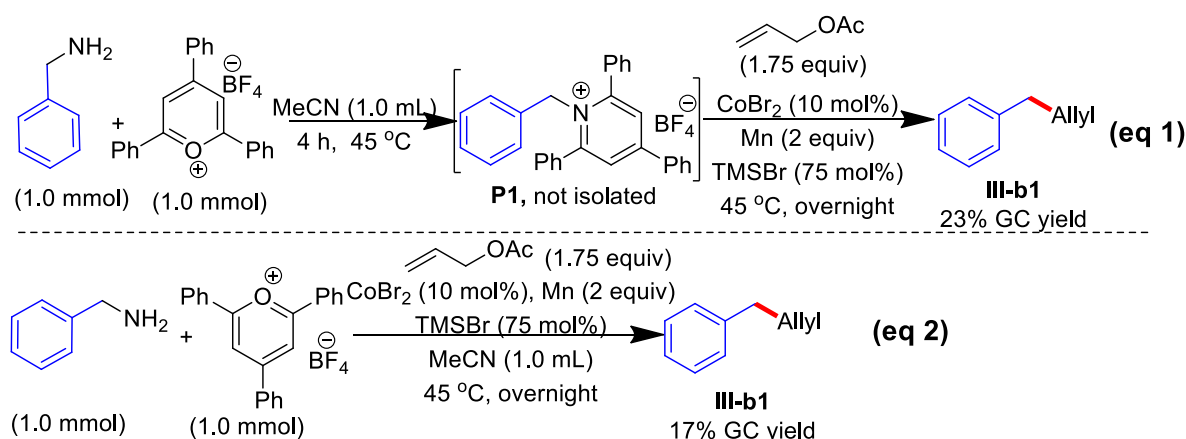


Entry	R	Results ^a	
		I-1 ^b / %	III-b1 / %
1	Ac	Trace	×
2	Me		

^a dodecane was used as a GC standard reference. × = Not detected. ^b Detected by GC-MS.

To gain insight into the mechanism of this Co-catalyzed allylation reaction between benzyl Katritzky pyridinium salts and C_{allyl}-O electrophiles, radical trapping experiments with TEMPO were conducted. The results showed that the cross-couplings of **P1** with **all-OAc-a1/all-OMe** were inhibited completely when 2 equivalents of TEMPO were added to the reaction under the optimized condition and a trace amount of **I-1** was detected by GC-MS. These results supported the proposal that benzyl radical was generated from benzyl Katritzky pyridinium salts in this Co-catalyzed allylation reaction, as previous reports using a Ni catalysis¹⁰⁹.

2.3.2. One-pot experiments of P1 with A-OAc-1a



Scheme IV-4. One-pot experiments

¹⁰⁹ Y.-N. Li, F. Xiao, Y. Guo, Y.-F. Zeng *Eur. J. Org. Chem.* **2021**, 1215–1228

To understand the reaction process and achieve the Csp³-Csp³ bond-forming process directly from benzylamine by Co catalysis, benzylamine, and 2,4,6-triphenylpyrylium tetrafluoroborate were used as the starting materials (*Scheme IV- 4*). Similar to the exploration of the one-pot allylation reaction from benzyl alcohol or benzyl sulfide in *Chapter III*, benzylamine and 2,4,6-triphenylpyrylium tetrafluoroborate was used to synthesize **P1** without filtration and added with **all-OAc-a1** under optimized condition, surprisingly, 23% GC yield of **III-b1** was detected (*Scheme IV- 4, eq 1*). Inspired by the result, the reaction was conducted directly from benzylamine, 2,4,6-triphenylpyrylium and allyl acetate as starting materials, 17% GC yield of the desired product was obtained (*Scheme IV- 1, eq 2*). Although the yield is not satisfactory, the possibility to use directly benzylamine as an electrophile to build a Csp³-Csp³ bond via Co-catalyzed reductive cross-coupling was demonstrated.

3. Conclusion and Perspectives

Benzyl Katritzky pyridinium salts, widely used as C-N electrophiles, have achieved all types of C-C bond formation. In this chapter, they have demonstrated to be an excellent alternative for constructing Csp³-Csp³ bonds with C_{allyl}-O electrophiles via a Co-catalyzed reductive cross-coupling. Various functionalized benzyl Katritzky pyridinium salts coupled with substituted allyl acetates and led to allyl benzyl derivatives under mild conditions in moderate to good yields. This method provides a convenient way to construct Csp³-Csp³ bonds with two non-halogenated electrophiles with only a Co catalyst. It was worth mentioning that benzyl Katritzky pyridinium salts can also couple with allyl methyl ether and deliver good yields as described work with benzyl sulfonium salts. It is also the first report using allyl alkyl ether in cross-coupling to construct a Csp³-Csp³ bond with benzyl Katritzky pyridinium salts in transition metal-catalyzed reductive cross-coupling. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl Katritzky pyridinium salts.

Although good results have been obtained in Csp³-Csp³ bond formation by Co-catalyzed reductive cross-coupling of benzyl Katritzky pyridinium salts and C_{allyl}-O electrophiles, the scope extension of allyl methyl ether derivatives remains a big challenge. Moreover, this Co-Mn catalyzed allylation is limited with benzyl Katritzky pyridinium salts. Thus, exploring cross-couplings of unactivated alkyl Katritzky pyridinium salts or ammonium salts with C_{allyl}-O electrophiles is a priority study in future research.



General Conclusion and Perspectives

First, C-S electrophiles represented by benzyl sulfonium salts which are stable and readily available from alcohols, have demonstrated the potentiality for constructing $\text{Csp}^3\text{-Csp}^2/\text{Csp}^3\text{-Csp}^3$ bonds in Co-Mn catalyzed reductive cross-coupling system.

In **Chapter I**, various functionalized diarylmethanes was synthesized by different benzyl sulfonium salts and aryl bromides in good to excellent yields under mild conditions. This method provides a simple alternative way to get diarylmethane compounds via C-S bond cleavage by a Co catalyst. In our procedure, the diarylmethanes formation involves a cheaper coupling partner (aryl bromides vs aryl iodides), a less toxic metal (Co vs Ni). It tolerates a wide variety of functionalities with electron-donating and electron-withdrawing groups. While compared to well-developed $\text{Csp}^3\text{-Csp}^2$ and $\text{Csp}^2\text{-Csp}^2$ bond formation, the $\text{Csp}^3\text{-Csp}^3$ bonds, as ubiquitous linkages in a range of natural products and pharmaceuticals, remain challenging in synthesis.

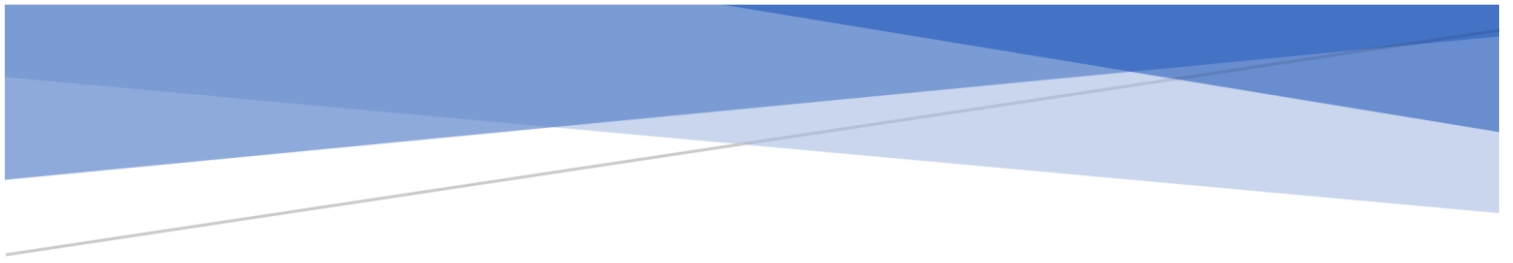
Thus, in **Chapter II**, the benzyl sulfonium salts were used to explore the $\text{Csp}^3\text{-Csp}^3$ bond formation and overcome this challenge. Experimental results have demonstrated that various benzyl sulfonium salts were good partners for constructing $\text{Csp}^3\text{-Csp}^3$ bonds with unactivated alkyl iodides via a Co-catalyzed reductive cross-coupling. Various functionalized primary or secondary alkyl iodides were coupled with different benzyl sulfonium salts bearing electron-donating or electron-withdrawing groups leading to desired products in moderate to good yields under mild conditions. To our knowledge, it is the first report using sulfonium salts in Co-catalyzed reactions to build $\text{Csp}^3\text{-Csp}^3$ bonds with unactivated alkyl iodides. Moreover, the mechanistic studies demonstrated the generations of benzyl and alkyl radicals from both benzyl sulfonium salts and alkyl iodides, respectively.

Given the high price and low abundance of alkyl iodides (compared to other halides) and the halide pollution caused during the reaction process, non-halogenated electrophilic partners were used to achieve the $\text{Csp}^3\text{-Csp}^3$ bond formation. In **Chapter III**, the active $\text{C}_{\text{allyl}}\text{-O}$ electrophiles, which were used to construct $\text{Csp}^3\text{-Csp}^3$ bonds with alkyl bromides by Co catalyst, was used instead of alkyl halides. Either allylic acetates or ether could be coupled with benzyl sulfonium salts leading to various functionalized alkyl olefinic compounds through Co-catalyzed reductive cross-coupling. The experiments were conducted under mild conditions and delivered the cross-coupling products in moderate to good yields. These reactions employed two non-halogenated electrophiles for the first time in C-C bond formation by Co-catalyzed reductive cross-coupling. It is also the first report using allyl alkyl ether to construct a C-C bond in reductive cross-coupling. It was worth mentioning that sulfonium salts can also couple with allyl methyl ether, never used as electrophiles in reductive cross-coupling. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl sulfonium salts.

In addition to the application of C-S electrophiles in the Csp³-Csp³ bond formation, C-N electrophiles like benzyl Katritzky pyridinium salts well developed by Watson *et al.* since 2010, were also employed as an excellent alternative for constructing Csp³-Csp³ bonds with C_{allyl}-O electrophiles via a Co-catalyzed reductive cross-coupling in **Chapter IV**. Various functionalized benzyl Katritzky pyridinium salts coupled with substituted allyl acetates led to allyl benzyl derivatives under mild conditions in moderate to good yields only by a Co catalyst. It was worth mentioning that benzyl Katritzky pyridinium salts could react with substituted allyl acetates either at the terminal or α- position. Moreover, benzyl Katritzky pyridinium salts could also couple with allyl methyl ether and deliver good yields. It is the first report using allyl alkyl ether in cross-coupling to build a Csp³-Csp³ bond with benzyl Katritzky pyridinium salts in transition metal-catalyzed reductive cross-coupling. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl Katritzky pyridinium salts.

Although excellent results have been obtained in the construction of Csp³-Csp²/Csp³-Csp³ bonds from C-S with C-X electrophiles, C-S with C-O electrophiles, and C-N with C-O electrophiles, these reactions remain challenges to overcome.

- The cross-coupling between benzyl sulfonium salts and Csp²-O electrophiles or aryl chloride has yet to progress. Moreover, this Co-Mn catalyzed arylation reaction was limited to the scope of benzyl sulfonium salts with aryl bromides and was also unsuitable for heteroaryl halides. Thus, extending the scope of the sulfonium salts and aryl chlorides/ triflates is still an interesting project.
- For Csp³-Csp³ bond formation from Csp³-sulfonium salts with alkyl halides, the cross-coupling of benzyl sulfonium salts with alkyl bromide has yet to improve significantly. On the other hand, the synthesis of unactivated sulfonium salts has yet to be achieved. Extending the scope of unactivated alkyl sulfonium salts or halides will be a significant development in Co-catalyzed reductive cross-coupling to build Csp³-Csp³ bonds
- As the development of C-S/C-N with C-O electrophiles to achieve Csp³-Csp³ bond formation by Co-catalyzed reductive cross-coupling, the scope of allyl acetates or allyl methyl ether remains a big challenge, particularly for the allyl alkyl ether derivatives. Thus, searching for a suitable method to extend the scope of allyl methyl ether to substituted ones is a priority study in future research.
- Moreover, the Co-Mn catalyzed allylation is limited to benzyl Katritzky pyridinium salts, so exploring suitable cross-coupling conditions of unactivated alkyl Katritzky pyridinium salts or ammonium salts with C_{allyl}-O electrophiles to synthesize alkyl olefins will be more meaningful and attractive.



1. General Information

1.1. Materials

All reactions were performed under an atmosphere of nitrogen using anhydrous solvents unless otherwise mentioned. All glassware was stored 24 h in a pre-heated oven prior to use. CoBr₂ salt and Mn were stored in a pre-heated oven. Dry THF, Toluene was purified with a M-Braun MB-SPS 800 solvent purification system. Anhydrous MCN, DMF, DMA, and DME were purchased from Across Organics. 1,4-dioxane and pyridine were from Carlo Erba Reagents. Chloroform-d was stored on activated 4Å molecular sieves. Starting materials, like benzyl alcohols and aryl halides¹¹⁰, alkyl halides¹¹¹, allyl acetate derivatives¹¹², and allyl methyl ether derivatives¹¹³ were obtained from commercial suppliers (Acros Organics, Alfa Aesar, Fluorochem, Sigma Aldrich, and TCI) without further purification or prepared according to literature procedures.

1.2. Analytical methods.

- NMR spectra were recorded on a Bruker AC-300 SY spectrometer operating at 300.0 MHz for ¹H, 75.0 MHz for ¹³C and 282 MHz for ¹⁹F. Chemical shifts (H, C) are reported in δ units, parts per million (ppm) relative to the chemical shift of residual solvent. Reference peaks for Chloroform-d in ¹H NMR and ¹³C NMR spectra were set at 7.26 ppm and 77.0 ppm, respectively. The abbreviations used to indicate the multiplicity of signals are s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiple), or a combination of the above. The coupling constants J were expressed in hertz. The spectra were analyzed with MestReNova software.
- Gas Chromatography (GC) was performed on a Brucker Scion 436-GC equipped with a split-mode, capillary injection system, and flame ionization detectors using an SGE apolar IDBP5 (15m x 0.25mm (0.25µm)) column.
- Column chromatography was performed on Biotage IsoleraPrime with Biotage SNAP cartridge KP-Sil 10g/25g as silica gel column.
- High-Resolution Mass Spectrometry (HRMS) experiments were performed on a Tims-TOF mass spectrometer (Bruker, France). Two API sources (ESI and APPI) have been used in a positive mode according to the structure of the studied compound.

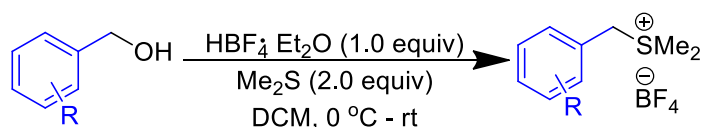
¹¹⁰ (a) É. Rochette, V. Desrosiers, Y. Soltani, F.-G. Fontaine. *J. Am. Chem. Soc.* **2019**, *141*, 12305. (b) F. Labre, Y. Gimbert, P. Bannwarth, S. Olivero, E. Duñach, P. Y. Chavant. *Org. Lett.*, **2014**, *16*, 2366.

¹¹¹ H. Zhao, A. J. McMillan, T. Constantin, R. C. Mykura, F. Julia, D. Leonori. *J. Am. Chem. Soc.* **2021**, *143*, 36, 14806.

¹¹² X.-L. Xu, Z. Li, *Angew. Chem. Int. Ed.* **2017**, *56*, 8196.

¹¹³ R. Matsubara, T. F. Jamison. *J. Am. Chem. Soc.* **2010**, *132*, 20, 6880–6881.

2. General Procedure and Characterization of Benzyl Sulfonium Salts

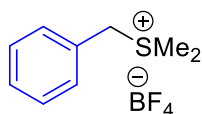


→ General procedure (**GP-S**):

To a solution of dry dichloromethane (30 mL) in a 100 mL dry round bottom flask was added the appropriate alcohol (1 equiv) followed by dimethyl sulfide (2 equiv) and placed under nitrogen gas. A solution of tetrafluoroboric acid (tetrafluoroboric acid diethyl ether complex) (1 equiv) was added dropwise for 5 minutes at 0 °C. The mixture was stirred overnight at room temperature. Evaporation of the solvent under reduced pressure gave a thick oil precipitated with diethyl ether to obtain the desired salt as a solid.¹¹⁴

• Characterization data of benzyl sulfonium salts

Benzyl dimethylsulfonium tetrafluoroborate salt (**S1**)



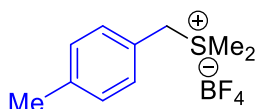
Following **GP-S** with benzyl alcohol (5.4 g, 50 mmol) was used, affording the corresponding sulfonium salt **S1** as a white solid (9.2 g, 77%).

¹H NMR (300 MHz, DMSO-d₆) δ 7.88 – 7.17 (m, 5H), 4.61 (s, 2H), 2.76 (s, 6H).

¹³C NMR (75 MHz, DMSO-d₆) δ 131.84, 130.86, 130.55, 129.42, 46.97, 25.01.

The spectroscopic data match the reported one in the literature.¹¹⁴

4-Methylbenzyl dimethylsulfonium tetrafluoroborate salt (**S2**)



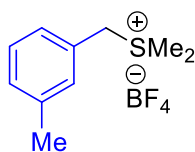
Following **GP-S** with 4-methyl benzyl alcohol (3.05 g, 25 mmol) was used, affording the corresponding sulfonium salt **S2** as a white solid (4.9 g, 77%).

¹H NMR (300 MHz, DMSO-d₆) δ 7.54 – 7.20 (m, 4H), 4.58 (s, 2H), 2.76 (s, 6H), 2.33 (s, 3H).

¹³C NMR (75 MHz, DMSO-d₆) δ 140.50, 131.79, 131.10, 126.17, 46.67, 24.77, 22.02.

HRMS (ESI⁺) m/z: [M-BF₄⁻] calculated for (C₁₀H₁₅S⁺) 167.0889; Found 167.0883.

3-Methylbenzyl dimethylsulfonium tetrafluoroborate salt (S3)



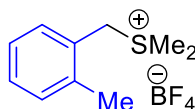
Following **GP-S** with 3-methyl benzyl alcohol (1.2 g, 10 mmol) was used, affording the corresponding sulfonium salt **S3** as a white solid (1.5 g, 59%).

^1H NMR (300 MHz, DMSO- d_6) δ 7.35 (m, 1H), 7.26 (m, 3H), 4.56 (s, 2H), 2.75 (s, 6H), 2.32 (s, 3H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 139.93, 132.25, 131.50, 130.43, 129.28, 128.91, 46.90, 24.96, 22.10.

HRMS (ESI $^+$) m/z : [M-BF $_4^-$] calculated for (C $_{10}$ H $_{15}$ S $^+$) 167.0889; Found 167.0882.

2-Methylbenzyl dimethylsulfonium tetrafluoroborate salt (S4)



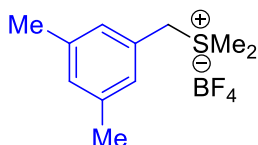
Following **GP-S** with 3-methyl benzyl alcohol (1.2 g, 10 mmol) was used, affording the corresponding sulfonium salt **S4** as a white solid (1.9 g, 75%)

^1H NMR (300 MHz, DMSO- d_6) δ 7.47 – 7.12 (m, 4H), 4.65 (s, 2H), 2.83 (s, 6H), 2.38 (s, 3H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 139.35, 132.88, 132.35, 131.06, 127.99, 127.83, 45.62, 25.22, 20.17.

HRMS (ESI $^+$) m/z : [M-BF $_4^-$] calculated for (C $_{10}$ H $_{15}$ S $^+$) 167.0889; Found 167.0882.

(3,5-dimethyl benzyl)dimethyl sulfonium tetrafluoroborate salt (S5)



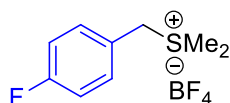
Following **GP-S** with 3,5-dimethyl benzyl alcohol (1.4 g, 10 mmol) was used, affording the corresponding sulfonium salt **S5** as a white solid (1.8 g, 67%).

^1H NMR (300 MHz, DMSO- d_6) δ 7.09 (s, 1H), 7.02 (s, 2H), 4.51 (s, 2H), 2.75 (s, 6H), 2.28 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 139.77, 132.25, 129.39, 129.19, 46.92, 24.99, 22.00.

HRMS (ESI $^+$) m/z : [M-BF $_4^-$] calculated for (C $_{11}$ H $_{17}$ S $^+$) 181.1045; Found 181.1038.

4-Fluorobenzyl dimethylsulfonium tetrafluoroborate salt (S6)



Following **GP-S** with 4-fluorobenzyl alcohol (1.3 g, 10 mmol) was used, affording the corresponding sulfonium salt **S6** as a white solid (2.0 g, 87%).

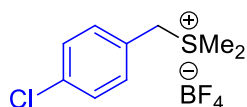
^1H NMR (300 MHz, DMSO- d_6) δ 7.62 – 7.43 (m, 2H), 7.40 – 7.28 (m, 2H), 4.60 (s, 2H), 2.75 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 165.59, 162.32, 134.19 (d, J = 8.8 Hz), 125.69 (d, J = 3.1 Hz), 117.53 (d, J = 21.8 Hz), 46.07, 24.83.

^{19}F NMR (282 MHz, DMSO- d_6) δ -111.54 – -111.69 (m), -147.89.

The spectroscopic data match the reported one in the literature.¹¹⁴

4-Chlorobenzyl dimethylsulfonium tetrafluoroborate salt (**S7**)



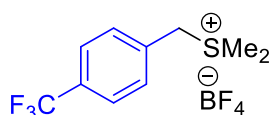
Following **GP-S** with 4-chlorobenzyl alcohol (1.4 g, 10 mmol) was used, affording the corresponding sulfonium salt **S7** as a white solid (1.9 g, 69%).

^1H NMR (300 MHz, DMSO- d_6) δ 7.54 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.5 Hz, 2H), 4.60 (s, 2H), 2.76 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 135.69, 133.73, 130.57, 128.45, 46.06, 24.90.

HRMS (ESI⁺) m/z : [M-BF₄⁻] calculated for (C₉H₁₂ClS⁺) 187.0343; Found 187.0335.

4-(Trifluoromethyl)benzyl sulfonium tetrafluoroborate salt (**S8**)



Following **GP-S** with 4-(trifluoromethyl)benzyl alcohol (1.4 g, 8 mmol) was used, affording the corresponding sulfonium salt **S8** as a white solid (1.8 g, 58%).

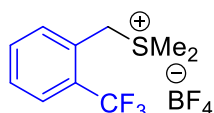
^1H NMR (300 MHz, DMSO- d_6) δ 7.86 (d, J = 8.0 Hz, 2H), 7.67 (d, J = 7.8 Hz, 2H), 4.70 (s, 2H), 2.80 (s, 3H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 134.41, 132.78, 127.39 (d, J = 3.9 Hz), 46.18, 25.19.

^{19}F NMR (282 MHz, DMSO- d_6) δ -61.39, -147.88 (d, J = 15.8 Hz).

The spectroscopic data match the reported one in the literature.¹¹⁴

2-(Trifluoromethyl)benzyl sulfonium tetrafluoroborate salt (**S9**)



Following **GP-S** with 2-(trifluoromethyl) benzyl alcohol (1.7 g, 10 mmol) was used, affording the corresponding sulfonium salt **S9** as a white solid (1.1 g, 36%).

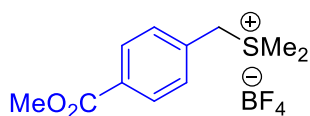
^1H NMR (300 MHz, DMSO- d_6) δ 7.86 (m, 1H), 7.79 (m, 2H), 7.73 – 7.65 (m, 1H), 4.80 (s, 2H), 2.94 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 134.91, 134.67, 131.60, 127.99, 44.57, 25.77.

^{19}F NMR (282 MHz, DMSO- d_6) δ -57.35, -148.01 (d, J = 18.4 Hz).

HRMS (ESI $^+$) m/z : $[\text{M-BF}_4^-]$ calculated for $(\text{C}_{10}\text{H}_{12}\text{F}_3\text{S}^+)$ 221.0606; Found 221.0604.

(4-(Methoxycarbonyl)benzyl)dimethyl sulfonium tetrafluoroborate salt (**S10**)



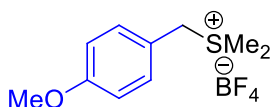
Following **GP-S** with methyl 4-(hydroxymethyl) benzoate (2.5 g, 15 mmol) was used, affording the corresponding sulfonium salt **S10** as a white solid (2.7 g, 91%).

^1H NMR (300 MHz, DMSO- d_6) δ 8.02 (dd, J = 8.1, 2.9 Hz, 2H), 7.79 – 7.41 (m, 2H), 4.68 (d, J = 2.9 Hz, 2H), 3.84 (d, J = 2.9 Hz, 2H), 2.79 (d, J = 2.9 Hz, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 166.92, 134.71, 132.24, 131.72, 131.19, 53.56, 46.32, 25.03.

HRMS (ESI $^+$) m/z : $[\text{M-BF}_4^-]$ calculated for $(\text{C}_{11}\text{H}_{15}\text{O}_2\text{S}^+)$ 211.0787; Found 211.0779.

4-Methoxybenzyl dimethyl sulfonium tetrafluoroborate salt (**S11**)



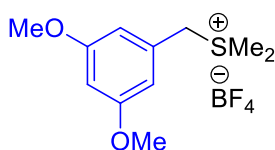
Following **GP-S** with 4-methoxybenzyl alcohol (2.76 g, 20 mmol) was used, affording the corresponding sulfonium salt **S11** as a white solid (5.0 g, 92%).

^1H NMR (300 MHz, DMSO- d_6) δ 7.42 – 7.28 (m, 2H), 7.07 – 6.80 (m, 2H), 4.54 (s, 2H), 3.76 (s, 3H), 2.71 (s, 3H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 161.42, 133.36, 120.55, 115.93, 56.45, 46.72, 24.62.

HRMS (ESI $^+$) m/z : $[\text{M-BF}_4^-]$ calculated for $(\text{C}_{10}\text{H}_{15}\text{OS}^+)$ 183.0838; Found 183.0831.

(3,5-dimethoxybenzyl) dimethyl sulfonium tetrafluoroborate salt (**S12**)



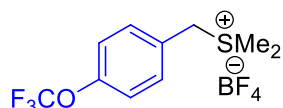
Following **GP-S** with 3,5-dimethoxy benzyl alcohol (3.4 g, 20 mmol) was used, affording the corresponding sulfonium salt **S12** as a white solid (4.0 g, 66%).

^1H NMR (300 MHz, DMSO- d_6) δ 6.60 (s, 3H), 4.49 (s, 2H), 3.74 (s, 6H), 2.76 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 162.11, 131.28, 109.68, 102.32, 56.57, 47.14, 25.12.

HRMS (ESI $^+$) m/z : $[\text{M}-\text{BF}_4^-]$ calculated for $(\text{C}_{11}\text{H}_{17}\text{O}_2\text{S}^+)$ 213.0944; Found 213.0945.

4-(Trifluoromethoxy) benzyl sulfonium tetrafluoroborate salt (**S13**)



Following **GP-S** with 4-trifluoromethoxy benzyl alcohol (1.9 g, 10 mmol) was used, affording the corresponding sulfonium salt **S13** as a white solid (2.2 g, 68%).

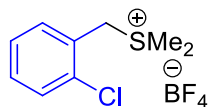
^1H NMR (300 MHz, DMSO- d_6) δ 7.61 (d, $J = 8.7$ Hz, 1H), 7.55 – 7.43 (m, 1H), 4.67 (s, 1H), 2.82 (s, 3H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 149.59, 133.27, 128.25, 122.18, 45.35, 24.38.

^{19}F NMR (282 MHz, DMSO- d_6) δ -56.76, -148.10.

HRMS (APPI-P): m/z : $[\text{M}-\text{BF}_4^-]$ calculated for $(\text{C}_{10}\text{H}_{12}\text{F}_3\text{O}_2\text{S}^+)$ 237.0555; Found 237.0556.

2-Chlorobenzyl dimethylsulfonium tetrafluoroborate salt (**S14**)



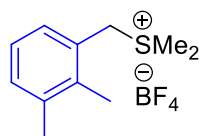
Following **GP-S** with 2-chlorobenzyl alcohol (1. g, 10 mmol) was used, affording the corresponding sulfonium salt **S14** as a white solid (2.07 g, 75%).

^1H NMR (300 MHz, DMSO- d_6) δ 7.63 (dt, $J = 7.5, 1.8$ Hz, 2H), 7.59 – 7.37 (m, 2H), 4.79 (s, 2H), 2.91 (s, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 134.58, 133.79, 132.23, 130.71, 128.59, 127.08, 44.45, 24.84.

The spectroscopic data match the reported one in the literature.¹¹⁴

(2,3-dimethylbenzyl) dimethyl sulfonium tetrafluoroborate salt (**S15**)



Following **GP-S** with 2,3-dimethyl benzyl alcohol (1.4 g, 10 mmol) was used, affording the corresponding sulfonium salt **S15** as a white solid (2.0 g, 75%).

¹¹⁴ J. Forrester, R. V. Jones, L. Newton, P. N. Preston, *Tetrahedron*. **2001**, 57, 2871-2884

^1H NMR (300 MHz, DMSO- d_6) δ 7.43 – 7.05 (m, 3H), 4.70 (s, 2H), 2.84 (s, 6H), 2.29 (d, J = 2.3 Hz, 6H).

^{13}C NMR (75 MHz, DMSO- d_6) δ 138.50, 137.24, 131.74, 130.11, 127.03, 126.47, 45.53, 24.55, 15.86.

HRMS (ESI $^+$) m/z : $[\text{M}-\text{BF}_4^-]$ calculated for ($\text{C}_{11}\text{H}_{17}\text{S}^+$) 181.1045; Found 181.1045.

3. General Procedure for Benzyl Sulfonium Salts and Aryl Halides

3.1. The cross-coupling of benzyl sulfonium salts and aryl bromides

3.1.1. General Procedure of diaryl methane.

▪ **For aryl bromides with electron-deficient groups (GP-I-A):**

In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt derivative (**S**) (1.0 mmol, 1.0 equiv), dtbbpy (53 mg, 0.2 mmol, 20 mol%), Mn powder (110 mg, 2.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N₂ three times and added the MeCN (0.75 mL), aryl halide (**ar-I-a**) (1.25 equiv, if it is liquid) under N₂. The mixture was stirred for 3 min, and then TMSCl (95 μ L, 0.75 mmol, 75 mol%) was added at rt. Then the mixture was allowed to stir overnight (around 15 h) at 45 °C. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with EtOAc. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether) afforded the corresponding product characterized by NMR (¹H, ¹³C, ¹⁹F).

▪ **For aryl bromides electron-withdrawing group (GP-I-B):**

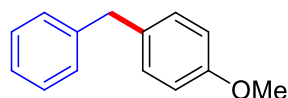
The same procedure was used as above, except the reaction mixture was allowed to stir at rt for 24 h.

▪ **Note:**

For several aryl halides, MeCN (0.7 mL)/ Py (0.05 mL) was used as the solvent instead of MeCN (0.75 mL) (Py was added to accelerate its reaction rate), and Py was added after TMSCl in 3min.

• **Characterization Data of diaryl methane**

1-Benzyl-4-methoxybenzene (I-b2) [834-14-0]



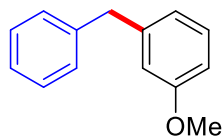
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and ar-I-a2 (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (152 mg, 77% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.54 – 7.38 (m, 2H), 7.37 – 7.30 (m, 3H), 7.26 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.3 Hz, 2H), 4.07 (s, 2H), 3.89 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.16, 141.76, 133.39, 130.03, 128.98, 128.60, 126.15, 114.05, 55.32, 41.21.

The spectroscopic data match the reported one in the literature.¹¹⁵

1-Benzyl-3-methoxybenzene (I-b3) [23450-27-3]



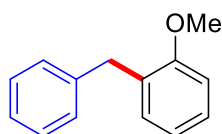
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 3-bromoanisole (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (154 mg, 78% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.51 – 7.32 (m, 2H), 7.32 – 7.22 (m, 4H), 6.96 – 6.73 (m, 3H), 4.03 (s, 2H), 3.83 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 159.82, 142.81, 141.03, 129.53, 129.03, 128.58, 126.22, 121.49, 114.90, 111.40, 55.19, 42.08.

The spectroscopic data match the reported one in the literature.¹¹⁶

1-Benzyl-2-methoxybenzene (I-b4)



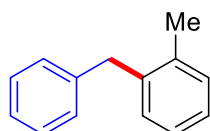
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 2-bromoanisole (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (180 mg, 91% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.37 – 7.20 (m, 6H), 7.12 (d, *J* = 7.0, 1H), 6.98 – 6.87 (m, 2H), 4.04 (s, 2H), 3.86 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.52, 141.23, 130.53, 129.83, 129.18, 128.47, 127.63, 125.99, 120.68, 110.57, 55.46, 36.10.

The spectroscopic data match the reported one in the literature.¹¹⁶

1-Benzyl-2-methylbenzene (I-b5) [713-36-0]



¹¹⁵ Z. He, F. Song, H. Sun, Y. Huang, *J. Am. Chem. Soc.* **2018**, *140*, 2693

¹¹⁶ T. Wang, J. Guo, X. Wang, H. Guo, D. Jia, H. Wang, L. Liu, *RSC Adv.*, **2019**, *9*, 5738

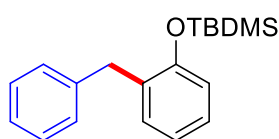
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 2-bromotoluene (214 mg, 1.25 mmol) were used, and MeCN (0.7 mL)/ Py (0.05 mL) was used as the solvent, affording the title compound as a colorless oil (126 mg, 69% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.43 (m, 2H), 7.32 (m, 6H), 4.14 (s, 2H), 2.40 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) ¹³C NMR (75 MHz, Chloroform-d) δ 140.54, 139.09, 136.78, 130.46, 130.13, 128.92, 128.56, 126.64, 126.18, 126.10, 39.64, 19.87.

The spectroscopic data match the reported one in the literature.¹¹⁶

2-Benzylphenoxy(tert-butyl)dimethylsilane (I-b6) [1417315-87-7]



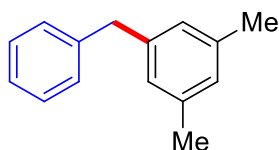
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and (2-bromophenol) (tert-butyl) dimethylsilane (359 mg, 1.25 mmol) were used, affording the title compound as a white solid (162 mg, 54% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.34 (m, 2H), 7.29 – 7.20 (m, 3H), 7.20 – 7.05 (m, 2H), 6.93 (m, 2H), 4.07 (s, 2H), 1.05 (s, 9H), 0.30 (s, 6H).

¹³C NMR (75 MHz, Chloroform-d) δ 153.65, 141.07, 131.69, 131.00, 129.03, 128.40, 127.27, 125.92, 121.20, 118.51, 36.18, 25.92, 18.40, -3.96.

HRMS (ESI⁺) m/z: [(M+H)]⁺ calculated for (C₁₉H₂₇OSi⁺) 299.1826; Found 299.1826.

1-Benzyl-3,5-dimethylbenzene (I-b7) [28122-27-2]



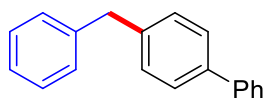
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 1-bromo-3,5-dimethylbenzene (231 mg, 1.25 mmol) were used, and MeCN (0.7 mL)/ Py (0.05 mL) was used as the solvent, affording the title compound as a colorless oil (131 mg, 67% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.61 – 7.21 (m, 5H), 7.00 (s, 3H), 4.08 (s, 2H), 2.45 (s, 6H).

¹³C NMR (75 MHz, Chloroform-d) δ 142.28, 141.89, 138.80, 129.83, 129.32, 128.65, 127.72, 126.87, 42.77, 22.19.

The spectroscopic data match the reported one in the literature.¹¹⁶

4-Benzylbiphenyl (I-b8) [613-42-3]



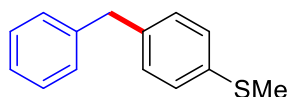
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 4-bromobiphenyl (291 mg, 1.25 mmol) were used, affording the title compound as a white solid (174 mg, 71% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.80 – 7.58 (m, 4H), 7.52 (t, *J* = 7.5 Hz, 2H), 7.46 – 7.25 (m, 8H), 4.13 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 141.21 (d, *J* = 2.8 Hz), 140.47, 139.23, 129.58, 129.21, 128.97, 128.76, 127.44, 127.32, 127.23, 126.39, 41.82.

The spectroscopic data match the reported one in the literature.¹¹⁵

1-Benzyl-4-methylsulfanyl-benzene (I-b9) [484649-59-4]



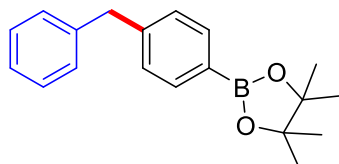
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 4-bromothioanisole (254 mg, 1.25 mmol) were used, affording the title compound as a light-yellow solid (137 mg, 64% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.36 – 7.28 (m, 2H), 7.27 – 7.18 (m, 5H), 7.14 (d, *J* = 8.1 Hz, 2H), 3.97 (s, 2H), 2.48 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 141.09, 138.26, 135.86, 129.56, 128.97, 128.60, 127.16, 126.24, 41.47, 16.26.

The spectroscopic data match the reported one in the literature.¹¹⁵

2-(4-benzylphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (I-b10) [911708-01-5]



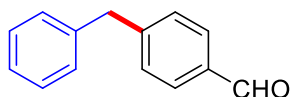
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 1-bromo-3,5-dimethylbenzene (252 mg, 1.25 mmol) were used, and MeCN (0.7 mL)/ Py (0.05 mL) was used as the solvent, affording the title compound as a white solid (162 mg, 55% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether)

^1H NMR (300 MHz, Chloroform- d) δ 7.78 (d, J = 7.8 Hz, 2H), 7.53 – 6.86 (m, 7H), 4.02 (s, 2H), 1.36 (s, 12H).

^{13}C NMR (75 MHz, Chloroform- d) δ 144.50, 140.92, 135.12, 128.99, 128.53, 128.53, 126.18, 83.73, 42.22, 24.95.

The spectroscopic data match the reported one in the literature.¹¹⁵

4-Benzylbenzaldehyde (I-b11) [67468-65-9]



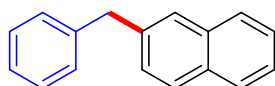
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 2-(4-bromophenyl)-1,3-dioxolane (286 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (82 mg, 42% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 9.98 (s, 1H), 7.82 (d, J = 8.1 Hz, 2H), 7.34 (m, 4H), 7.28 – 7.23 (m, 1H), 7.23 – 7.11 (m, 2H), 4.07 (s, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 192.00, 148.44, 139.76, 134.65, 130.06, 129.57, 128.98, 128.70, 126.53, 42.10.

The spectroscopic data match the reported one in the literature.¹¹⁷

2-Benzyl-naphthalene (I-b15) [613-59-2]



Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and 2-bromonaphthalene (259 mg, 1.25 mmol) were used, and MeCN (0.7 mL)/ Py (0.05 mL) was used as the solvent, affording the title compound as a white solid (134 mg, 59% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

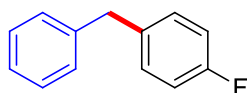
^1H NMR (300 MHz, Chloroform- d) δ 7.93 – 7.74 (m, 3H), 7.68 (s, 1H), 7.57 – 7.41 (m, 2H), 7.40 – 7.17 (m, 6H), 4.18 (s, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 141.00, 138.62, 133.61, 132.09, 129.06, 128.53, 128.11, 127.66, 127.58, 127.12, 126.18, 126.01, 125.38, 42.14.

The spectroscopic data match the reported one in the literature.¹¹⁶

¹¹⁷ J. Khamraj, I. Ghosh, A. Savateev, M. Antonietti, B. König, *ACS Catal.* **2020**, *10*, 3526

1-Benzyl-4-fluorobenzene (I-b22) [587-79-1]



Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 1-bromo-4-fluorobenzene (219 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (156 mg, 84% yield) after purification by flash chromatography (SiO₂ 5% EtOAc in petroleum ether).

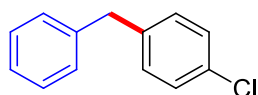
¹H NMR (300 MHz, Chloroform-d) δ 7.33 (m, 2H), 7.28 – 7.11 (m, 5H), 7.00 (m, 2H), 3.98 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 163.14, 159.91, 141.06, 136.88 (d, J = 3.2 Hz), 130.40 (d, J = 7.8 Hz), 128.95, 128.65, 126.32, 115.45, 115.17, 41.17.

¹⁹F NMR (282 MHz, Chloroform-d) δ -117.15 (d, J = 9.0 Hz).

The spectroscopic data match the reported one in the literature.¹¹⁶

1-Benzyl-4-chlorobenzene (I-b23) [831-81-2]



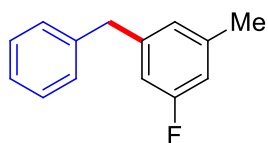
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 1-bromo-4-chlorobenzene (239 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (151 mg, 75% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.42 – 7.26 (m, 5H), 7.25 – 7.20 (m, 2H), 7.17 (m, 2H), 4.00 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 140.65, 139.69, 131.98, 130.37, 128.97, 128.67, 126.41, 41.34.

The spectroscopic data match the reported one in the literature.¹¹⁸

1-Benzyl-3-fluoro-5-methylbenzene (I-b24)



Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 1-bromo-3-fluoro-5-methylbenzene (236 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (130 mg, 65% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.37 (dd, J = 7.9, 6.4 Hz, 2H), 7.32 – 7.22 (m, 3H), 6.87 (s, 1H), 6.84 – 6.71 (m, 2H), 3.99 (s, 2H), 2.37 (s, 2H).

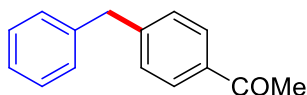
¹¹⁸ L. Lv, D. Zhu, JTang, Z. Qiu, C.-C. Li, J. Gao, C.-J. Li. *ACS Catal.* **2018**, *8*, 4622.

^{13}C NMR (75 MHz, Chloroform- d) δ 164.68, 161.44, 143.36 (d, J = 7.6 Hz), 141.28 – 139.68 (m), 128.83 (d, J = 26.8 Hz), 126.39, 125.43 (d, J = 2.4 Hz), 113.74 (d, J = 21.0 Hz), 112.90 (d, J = 21.3 Hz), 41.73 (d, J = 1.8 Hz), 21.39.

^{19}F NMR (282 MHz, Chloroform- d) δ -114.51 (dd, J = 9.8, 3.5 Hz).

HRMS (APPI) m/z : calculated for ($\text{C}_{14}\text{H}_{13}\text{F}$) 200.0996; Found 200.0991.

4'-Benzylacetophenone (I-b25) [782-92-3]



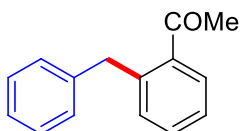
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 4-bromoacetophenone (249 mg, 1.25 mmol) were used, and *MeCN* (0.7 mL)/ *Py* (0.05 mL) was used as a solvent, affording the title compound as a light-yellow oil (86 mg, 41% yield) after purification by flash chromatography (SiO_2 : 10% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 7.90 (d, J = 8.3 Hz, 2H), 7.37 – 7.27 (m, 4H), 7.27 – 7.23 (m, 1H), 7.23 – 7.15 (m, 2H), 4.05 (s, 2H), 2.59 (s, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 197.81, 146.85, 140.07, 135.25, 129.14, 128.97, 128.68, 126.45, 41.93, 26.62.

The spectroscopic data match the reported one in the literature.¹¹⁷

1-(2-Benzylphenyl)ethenone (I-b26) [61608-94-4]



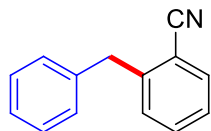
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 2-bromoacetophenone (249 mg, 1.25 mmol) were used, and *MeCN* (0.7 mL)/ *Py* (0.05 mL) was used as a solvent, affording the title compound as a light-yellow oil (109 mg, 52% yield) after purification by flash chromatography (SiO_2 : 10% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 7.66 (dd, J = 7.7, 1.5 Hz, 1H), 7.48 – 7.35 (m, 1H), 7.35 – 7.21 (m, 4H), 7.20 – 7.14 (m, 2H), 4.31 (s, 2H), 2.47 (s, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 202.39, 140.95, 140.58, 138.32, 131.83, 131.43, 129.15, 129.05, 128.35, 126.25, 125.98, 39.27, 29.83.

The spectroscopic data match the reported one in the literature.^{6f}

2-Benzylbenzonitrile (I-b27) [56153-61-8]



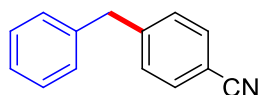
Following **GP-I-A**, the corresponding S1 (240 mg, 1.0 mmol) and 4-bromobenzonitrile (228 mg, 1.25 mmol) were used, and MeCN (0.7 mL)/ Py (0.05 mL) was used as a solvent, affording the title compound as a light brown oil (146 mg, 76% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.64 (d, *J* = 7.7 Hz, 1H), 7.50 (m, 1H), 7.29 (m, 7H), 4.22 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 144.97, 138.83, 132.95 (d, *J* = 2.6 Hz), 130.10, 129.02, 128.77, 126.81 (d, *J* = 7.2 Hz), 118.26, 112.56, 40.23.

The spectroscopic data match the reported one in the literature.¹¹⁸

4-Benzylbenzonitrile (I-b28) [23450-31-9]



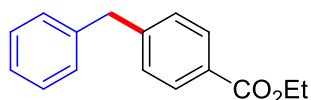
Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and 4-bromobenzonitrile (228 mg, 1.25 mmol) were used, affording the title compound as a yellow oil (106 mg, 55% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.40 – 7.25 (m, 5H), 7.22 – 7.15 (m, 2H), 4.05 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 146.79, 139.40, 132.32, 129.68, 129.01, 128.81, 126.71, 119.06, 110.03, 42.00.

The spectroscopic data match the reported one in the literature.¹¹⁸

Ethyl 4-benzylbenzoate (I-b2) [18908-74-2]



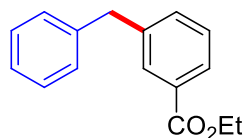
Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and ethyl 4-bromobenzoate (286 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (210 mg, 88% yield) after purification by flash chromatography (SiO₂: 10% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.98 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.22 (m, 5H), 7.18 (d, *J* = 7.4 Hz, 2H), 4.37 (qd, *J* = 7.2, 1.1 Hz, 2H), 4.04 (s, 2H), 1.39 (td, *J* = 7.1, 1.2 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 166.59, 146.42, 140.21, 129.82, 128.96, 128.96, 128.63, 128.47, 126.39, 60.86, 41.94, 14.40.

The spectroscopic data match the reported one in the literature.¹¹⁸

Ethyl 3-benzylbenzoate (I-b29) [134752-72-0]



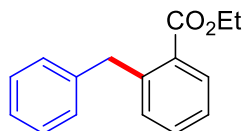
Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and ethyl 3-bromobenzoate (286 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (187 mg, 78% yield) after purification by flash chromatography (SiO_2 : 10% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 8.19 – 7.78 (m, 2H), 7.40 – 7.36 (m, 2H), 7.35 – 7.28 (m, 2H), 7.27 – 7.17 (m, 3H), 4.39 (q, $J = 7.2$ Hz, 2H), 4.05 (s, 2H), 1.40 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 166.69, 141.46, 140.58, 133.50, 130.74, 130.07, 128.93, 128.63, 128.56, 127.46, 126.34, 60.99, 41.77, 14.41.

The spectroscopic data match the reported one in the literature.^{110d}

2-Benzylbenzoic acid ethyl ester (I-b30) [1585-99-5]



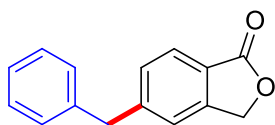
Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and ethyl 2-bromobenzoate (286 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (197 mg, 82% yield) after purification by flash chromatography (SiO_2 : 10% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 7.93 (dd, $J = 7.8, 1.7$ Hz, 1H), 7.57 – 7.39 (m, 1H), 7.37 – 7.23 (m, 3H), 7.19 (m, 4H), 4.43 (s, 2H), 4.31 (qd, $J = 7.1, 1.4$ Hz, 2H), 1.32 (td, $J = 7.1, 1.5$ Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 167.76, 141.95, 141.00, 131.87, 131.58, 130.60, 130.45, 128.93, 128.35, 126.28, 125.94, 60.92, 39.62, 14.26.

The spectroscopic data match the reported one in the literature.^{110d}

5-Benzyl-3H-isobenzofuran-1-one (I-b31) [945740-86-3]



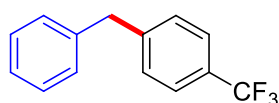
Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and 5-bromophthalide (266 mg, 1.25 mmol) were used, affording the title compound as a white solid (185 mg, 82% yield) after purification by flash chromatography (SiO₂: 10% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.82 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.34 – 7.23 (m, 4H), 7.22 – 7.16 (m, 2H), 5.24 (s, 2H), 4.11 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 171.07, 148.43, 147.34, 139.66, 130.07, 129.02, 128.80, 126.67, 125.61, 123.71, 122.41, 69.57, 42.16.

HRMS (ESI⁺) *m/z*: [(M+H)]⁺ calculated for (C₁₅H₁₃O₂)⁺ 225.0910; Found 225.0907.

4-benzylbenzotrifluoride (I-b32) [34239-04-8]



Following **GP-I-B**, the corresponding S1 (240 mg, 1.0 mmol) and 4-trifluoromethylphenyl bromide (281 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (158 mg, 67% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

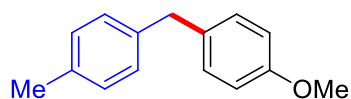
¹H NMR (300 MHz, Chloroform-d) δ 7.61 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.29 (m, 5H), 7.29 – 7.20 (m, 2H), 4.09 (s, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 145.33, 140.08, 129.28 (d, *J* = 1.7 Hz), 129.03 (d, *J* = 1.7 Hz), 128.76 (d, *J* = 1.8 Hz), 126.57 (d, *J* = 1.8 Hz), 125.47 (d, *J* = 4.3 Hz), 41.79.

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.23 (d, *J* = 6.0 Hz).

HRMS (APPI⁺) *m/z*: [(M-H)]⁺ calculated for (C₁₄H₁₀F₃)⁺ 235.0729; Found 235.0719.

1-(4-Methoxybenzyl)-4-methylbenzene (I-b35) [22865-60-7]



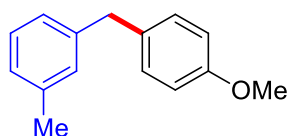
Following **GP-I-A**, the corresponding 4-methylbenzyl dimethyl sulfonium tetrafluoroborate salt (S2) (254 mg, 1.0 mmol) and ar-I-a2 (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (168 mg, 79% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.21 (m, 6H), 6.94 (d, *J* = 8.3 Hz, 2H), 4.00 (s, 2H), 3.86 (s, 3H), 2.43 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.05, 138.67, 135.51, 133.66, 129.90, 129.24, 128.81, 113.97, 55.30, 40.74, 21.12.

The spectroscopic data match the reported one in the literature.¹¹⁵

1-(4-Methoxybenzyl)-3-methylbenzene (I-b36) [53039-51-3]



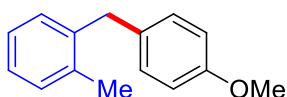
Following **GP-I-A**, the corresponding 3-methyl- benzyl dimethyl sulfonium tetrafluoroborate salt (S3) (254 mg, 1.0 mmol) and ar-I-a2 (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (129 mg, 61% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.44 – 7.13 (m, 3H), 7.09 (m, 3H), 6.91 (m, 2H), 3.96 (s, 2H), 3.84 (s, 3H), 2.39 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.06, 141.64, 138.10, 133.50, 129.98, 129.73, 128.47, 126.88, 126.01, 113.97, 55.31, 41.12, 21.56.

The spectroscopic data match the reported one in the literature.¹¹⁸

1-(4-Methoxybenzyl)-2-methylbenzene (I-b37) [53039-52-4]



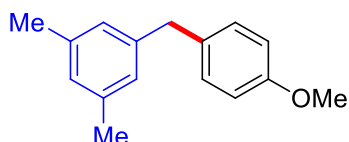
Following **GP-I-A**, the corresponding 2-methyl- benzyl dimethyl sulfonium tetrafluoroborate salt (S4) (254 mg, 1.0 mmol) and ar-I-a2 (233 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (174 mg, 82% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.31 – 7.23 (m, 2H), 7.21 (m, 1H), 7.15 (d, J = 8.6 Hz, 2H), 6.93 (d, J = 8.6 Hz, 2H), 4.03 (s, 2H), 3.86 (s, 3H), 2.35 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.71, 140.21, 137.37, 133.26, 131.11, 130.63, 130.51, 127.21, 126.82, 114.67, 56.04, 39.42, 20.49.

The spectroscopic data match the reported one in the literature.¹¹⁸

1-(4-Methoxybenzyl)-3,5-dimethylbenzene (I-b38) [1818350-34-3]



Following **GP-I-A**, the corresponding 3,5-dimethyl- benzyl dimethyl sulfonium tetrafluoroborate salt (S5) (268 mg, 1.0 mmol) and ar-I-a2 (233 mg, 1.25 mmol) were used, affording the title compound as

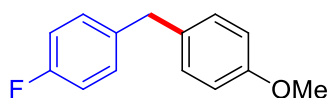
a colorless oil (190 mg, 84% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.36 – 7.15 (m, 2H), 7.08 – 6.78 (m, 5H), 3.96 (s, 2H), 3.87 (s, 3H), 2.39 (s, 6H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.04, 141.60, 138.00, 133.62, 129.97, 127.80, 126.82, 113.96, 55.30, 41.07, 21.44.

The spectroscopic data match the reported one in the literature.¹¹⁸

1-(4-Fluorobenzyl)-4-methoxybenzene (I-b39) [38695-26-0]



Following **GP-I-A**, the corresponding 4-fluoro benzyl dimethyl sulfonium tetrafluoroborate salt (S6) (268 mg, 1.0 mmol) and ar-I-a2 (258 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (135 mg, 62% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

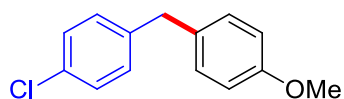
¹H NMR (300 MHz, Chloroform-d) δ 7.27 – 7.06 (m, 4H), 7.06 – 6.92 (m, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 3.93 (s, 2H), 3.81 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 161.97 (m), 158.13, 138.34 – 136.75 (m), 133.13, 130.23 (dd, *J* = 7.7, 1.4 Hz), 129.86, 115.24 (d, *J* = 21.1 Hz), 114.01 (d, *J* = 1.4 Hz), 55.28, 40.25.

¹⁹F NMR (282 MHz, Chloroform-d) δ -117.34 (m).

The spectroscopic data match the reported one in the literature.¹¹⁵

1-Chloro-4-(4-methoxybenzyl) benzene (I-b40) [37155-52-5]



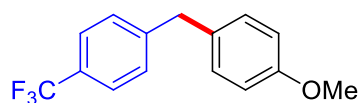
Following **GP-I-A**, the corresponding 4-chlorobenzyl dimethyl sulfonium tetrafluoroborate salt (S7) (275 mg, 1.0 mmol) and ar-I-a2 (258 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (168 mg, 72% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

¹H NMR (300 MHz, Chloroform-d) δ 7.27 (d, *J* = 8.4 Hz, 2H), 7.11 (m, 4H), 6.86 (d, *J* = 8.6 Hz, 2H), 3.91 (s, 2H), 3.80 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.19, 140.18, 132.72, 131.83, 130.23, 129.90, 128.60, 114.05, 55.28, 40.42.

The spectroscopic data match the reported one in the literature.¹¹⁵

1-Methoxy-4-(4-(trifluoromethyl)benzyl)benzene (I-b41) [398126-85-7]



Following **GP-I-A**, the corresponding 4-(trifluoromethyl) benzyl dimethyl sulfonium tetrafluoroborate salt (S8) (308 mg, 1.0 mmol) and ar-I-a2 (258 mg, 1.25 mmol) were used, affording the title compound as a light-yellow oil (137 mg, 51% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

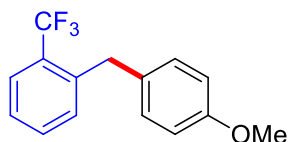
¹H NMR (300 MHz, Chloroform-d) δ 7.57 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.5 Hz, 2H), 6.90 (d, J = 8.6 Hz, 2H), 4.01 (s, 2H), 3.82 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.28, 145.78 (d, J = 1.5 Hz), 132.11, 129.95, 129.11, 128.16 (t, J = 32.3 Hz), 125.39 (q, J = 3.8 Hz), 114.09, 55.24, 40.85.

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.24.

HRMS (ESI⁺) m/z : [(M+H)]⁺ calculated for (C₁₅H₁₄F₃O⁺) 267.0991; Found 267.0986.

1-(4-Methoxybenzyl)-2-(trifluoromethyl)-benzene (I-b42) [1394225-93-4]



Following **GP-I-A**, the corresponding 2-(trifluoromethyl) benzyl dimethyl sulfonium tetrafluoroborate salt (S9) (308 mg, 1.0 mmol) and ar-I-a2 (258 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (104 mg, 39% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

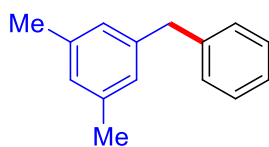
¹H NMR (300 MHz, Chloroform-d) δ 7.73 – 7.62 (m, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.30 (m, 1H), 7.19 (d, J = 7.7 Hz, 1H), 7.10 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.15 (s, 2H), 3.81 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.17, 140.06 (d, J = 1.7 Hz), 131.92, 131.79 (d, J = 1.2 Hz), 131.60, 130.16, 128.58 (q, J = 29.6 Hz), 126.13, 125.84 (q, J = 5.8 Hz), 113.96, 55.22, 36.91 (d, J = 2.2 Hz).

¹⁹F NMR (282 MHz, Chloroform-d) δ -59.52.

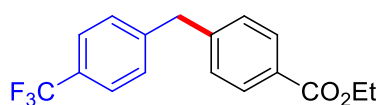
HRMS (ESI⁺) m/z : [(M+H)]⁺ calculated for (C₁₅H₁₄F₃O⁺) 267.0991; Found 267.0984.

1-Benzyl-3,5-dimethylbenzene (I-b7) [28122-27-2]



Following **GP-I-A**, the corresponding 3,5-dimethyl- benzyl dimethyl sulfonium tetrafluoroborate salt (S5) (268 mg, 1.0 mmol) and bromobenzene (196 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (161 mg, 82% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

Ethyl 4-(4- trifluoromethyl benzyl) benzoate (I-b43)



Following **GP-I-B**, the corresponding 4-(trifluoromethyl) benzyl dimethyl sulfonium tetrafluoroborate salt (S8) (308 mg, 1.0 mmol) and ethyl 4-bromobenzoate (286 mg, 1.25 mmol) were used, affording the title compound as a colorless oil (143 mg, 46% yield) after purification by flash chromatography (SiO₂: 5% EtOAc in petroleum ether).

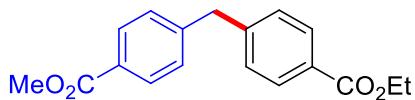
¹H NMR (300 MHz, Chloroform-d) δ 8.00 (d, *J* = 8.1, 2H), 7.55 (d, *J* = 8.3, 2H), 7.26 (m, 4H), 4.61 – 4.25 (m, 2H), 4.14 – 3.96 (s, 2H), 1.39 (t, *J* = 7.2 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 166.42, 145.14, 144.28 (d, *J* = 1.4 Hz), 129.97, 129.22, 128.93, 128.85, 128.52, 126.04, 125.53 (q, *J* = 3.8 Hz), 122.43, 60.93, 41.62, 14.32.

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.35 (d, *J* = 7.8 Hz).

HRMS (ESI⁺) *m/z*: [(M+H)]⁺ calculated for (C₁₇H₁₆F₃O₂)⁺ 309.1097; Found 309.1095.

Ethyl 4-[(4-methoxycarbonylphenyl)methyl]benzoate (I-b44)



Following **GP-I-A**, the corresponding (4-(Methoxycarbonyl)benzyl) dimethyl sulfonium tetrafluoroborate salt (S10) (240 mg, 1.0 mmol) and ethyl 4-iodobenzoate (345 mg, 1.25 mmol) were used, and *MeCN* (0.7 mL)/ *Py* (0.05 mL) was used as the solvent, affording the title compound as a light-yellow oil (192 mg, 62% yield) after purification by flash chromatography (SiO₂: 10% EtOAc in petroleum ether).

^1H NMR (300 MHz, Chloroform- d) δ 7.95 (dd, $J = 8.1, 3.8$ Hz, 4H), 7.22 (d, $J = 7.9$ Hz, 4H), 4.34 (q, $J = 7.3$ Hz, 2H), 4.04 (s, 3H), 3.87 (s, 2H), 1.36 (t, $J = 7.0$ Hz, 3H).

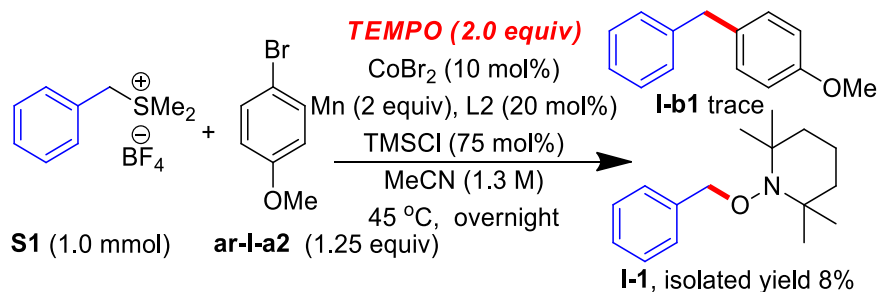
^{13}C NMR (75 MHz, Chloroform- d) δ 167.65, 167.17, 146.26, 146.06, 130.90, 130.67 (t, $J = 1.6$ Hz), 129.68 (d, $J = 1.4$ Hz), 129.46, 129.08, 127.93, 61.64, 52.81, 42.57, 15.10.

HRMS (ESI $^+$) m/z : $[(\text{M}+\text{H})]^+$ calculated for $(\text{C}_{18}\text{H}_{19}\text{O}_4^+)$ 299.1278; Found 299.1272.

3.2. Mechanistic experiments

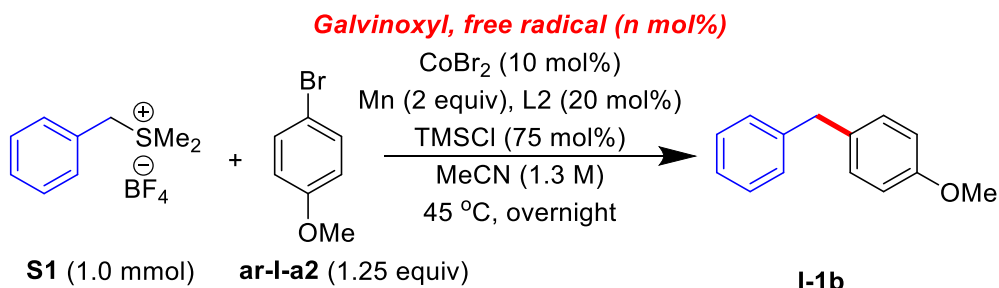
3.2.1. Radical trapping experiment

◆ The reaction with TEMPO.



In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt S1 (240 mg, 1.0 mmol, 1.0 equiv), tdbbpy (53 mg, 0.2 mmol, 20 mol%), Mn powder (110 mg, 2.0 mmol, 2.0 equiv), TEMPO (314 mg, 2.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N₂ three times, and added the MeCN (0.75 mL), ar-I-a2 (233 mg, 1.25 mmol, 1.25 equiv, if it is liquid) under N₂. The mixture was stirred for 3 min and then TMSCl (95 μL, 0.75 mmol, 75 mol%) was added at rt. After the reaction mixture was allowed to stir overnight (around 15 h) at 45 °C. After completion, the reaction mixture was added 250 μL hexadecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS. And then, the crude product was worked-up and concentrated under reduced pressure before being purified by flash chromatography.

◆ The reaction with galvinoxyl, free radical.



Entry	n (mol %)	Yield of I-1b ^a / %
1	50	66
2	100	24
3	125	14

^a GC yields using hexadecane as an internal standard.

In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt S1 (240 mg, 1.0 mmol, 1.0 equiv), tdbbpy (53 mg, 0.2 mmol, 20 mol%), Mn powder (110 mg, 2.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 10 mol%) galvinoxyl, free radical (211 mg, 0.5 mmol, 5 mol %; 422 mg, 1 mmol, 100 mol%; 633 mg, 1.5 mmol, 150 mol%, respectively) were added. The tube was filled with N₂ thrice, and the MeCN (0.75 mL), ar-I-a2 (233 mg, 1.25 mmol, 1.25 equiv) was added under N₂. The

mixture was stirred for 3 min and then TMSCl (95 μ L, 0.75 mmol, 75 mol%) was added at rt. After the reaction mixture was allowed to stir overnight (around 15 h) at 45 $^{\circ}$ C After completion, the reaction mixture was added 250 μ l hexadecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

4. General Procedure for Benzyl Sulfonium Salts and Alkyl Iodides

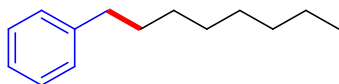
4.1. The cross-coupling of Benzyl Sulfonium Salts and Alkyl iodides

♣ General Procedure of Alkylation with Alkyl iodides (GP-II-A).

In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt derivative (S) (2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) were added. The tube was filled with N₂ three times and added MeCN (3.0 mL), 1-4 dioxane (1.0 mL), and alkyl iodides (1.25 equiv, if it is liquid) under N₂. The mixture was stirred for the 30s and then TMSCl (25 mol%, or 75 mol%, to be sure that the reaction was triggered) was added at rt. After 3 min, pyridine (125 μL, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir at rt for 24 h. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with diethyl ether. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether) afforded the corresponding product characterized by NMR (¹H, ¹³C, ¹⁹F)

• Characterization data of products

Octylbenzene (II-b1) [2189-60-8]



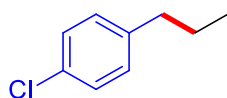
Following *GP-II-A*, S1 (480 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (217 mg, 57% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.38 (m, 2H), 7.28 (m, 3H), 2.71 (t, *J* = 7.8 Hz, 2H), 1.73 (m, 2H), 1.41 (m, 10H), 1.01 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 143.74, 129.21, 129.03, 126.36, 32.77, 32.42, 30.37, 30.23, 30.15, 23.55, 14.95.

The spectroscopic data match the reported one in the literature.¹⁷

1-Chloro-4-propylbenzene (II-b4) [52944-34-0]



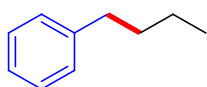
Following **GP-II-A**, the 4-chlorobenzyltrimethylsulfonium tetrafluoroborate salt (**S7**) (548 mg, 2.0 mmol) and 1-iodoethane (390 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (228 mg, 69% yield) after purification by flash chromatography (SiO₂: pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.28 (d, *J* = 8.3, Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 2.59 (t, *J* = 7.7 Hz, 2H), 1.65 (m, 2H), 0.97 (t, *J* = 7.4, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 141.82, 132.08, 130.57, 129.07, 38.14, 25.28, 14.49.

The spectroscopic data match the reported one in the literature.¹¹⁶

1-butylbenzene (II-b5) [104-51-8]



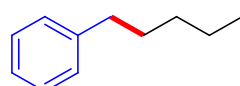
Following **GP-II-A**, **S1** (480 mg, 2.0 mmol) and 1-iodopropane (244 μL, 2.5 mmol) were used, affording the title compound as a colorless oil (150 mg, 55% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.35 (t, *J* = 7.5 Hz, 2H), 7.26 (d, *J* = 7.3 Hz, 3H), 2.70 (t, *J* = 7.8 Hz, 2H), 1.69 (m, 2H), 1.45 (m, 2H), 1.02 – 0.87 (m, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 143.67, 129.16, 128.96, 126.29, 36.44, 34.45, 23.15, 14.73.

The spectroscopic data match the reported one in the literature.¹¹⁹

Pentylbenzene (II-b6) [538-68-1]



Following **GP-II-A**, **S1** (480 mg, 2.0 mmol) and 1-iodobutane (287 μL, 2.5 mmol) were used, affording the title compound as a colorless oil (199 mg, 67% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.53 – 7.37 (m, 2H), 7.33 (d, *J* = 7.3 Hz, 3H), 3.47 – 2.56 (m, 2H), 1.85 – 1.71 (m, 2H), 1.63 – 1.37 (m, 4H), 1.25 – 0.95 (m, 3H).

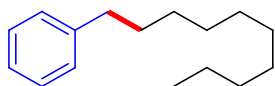
¹³C NMR (75 MHz, Chloroform-d) δ 143.78, 129.27, 129.09, 126.43, 36.88, 32.45, 32.13, 23.47, 14.91.

The spectroscopic data match the reported one in the literature.¹²⁰

Decylbenzene (II-b7) [104-72-3]

¹¹⁹ Y Zhao, X. Feng, S. Zhang, Y. Yamamoto, M. Bao, *ChemCatChem*.**2020**, *12*, 4951

¹²⁰ B. A. F. Le Bailly, M. D. Greenhalgh, S. P. Thomas. *Chem. Commun.*, **2012**, *48*, 1580



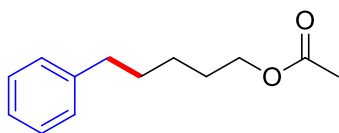
Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and 1-iodononane (635 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (292mg, 50% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.37 – 7.24 (m, 2H), 7.20 (d, J = 7.1 Hz, 3H), 2.62 (t, J = 7.8 Hz, 2H), 1.62 (m, 2H), 1.31 (m, 14H), 0.90 (t, J = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 143.76, 129.26, 129.08, 126.42, 36.95, 32.87, 32.49, 30.59, 30.49, 30.31, 23.64, 15.03.

The spectroscopic data match the reported one in the literature.¹²¹

5-Phenylpentyl acetate (II-b8) [75553-28-5]



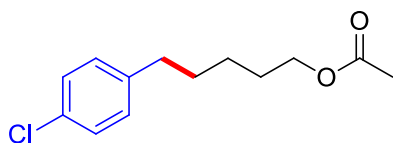
Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and 4-isobutyl acetate (378 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (206 mg, 50% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.31 (t, J = 7.8 Hz, 2H), 7.22 (m, 2H), 4.09 (t, J = 6.7 Hz, 2H), 2.66 (t, J = 7.7 Hz, 2H), 2.06 (s, J = 1.3 Hz, 3H), 1.69 (m, 4H), 1.53 – 1.31 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 171.82, 143.14, 129.16, 129.07, 126.50, 65.21, 36.58, 31.87, 29.27, 26.34, 21.73.

The spectroscopic data match the reported one in the literature.⁹

5-(4-Chlorophenyl)Pentyl acetate (II-b9)



Following **GP-II-A**, the 4-chlorobenzyltrimethylsulfonium tetrafluoroborate salt (S7) (548 mg, 2.0 mmol) and 4-isobutyl acetate (378 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (304 mg, 63% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

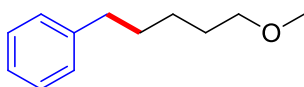
¹²¹ S. K. Ghorai, M. Jin, T. Hatakeyama, M. Nakamura, *Org. Lett.* **2012**, *14*, 1066.

^1H NMR (300 MHz, Chloroform- d) δ 7.20 (d, J = 8.3 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 4.02 (t, J = 6.7 Hz, 2H), 2.55 (t, J = 7.7 Hz, 2H), 2.00 (s, 3H), 1.77 – 1.49 (m, 4H), 1.43 – 1.25 (m, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 171.91, 141.53, 132.14, 130.46, 129.11, 65.13, 35.85, 31.67, 29.17, 26.19, 21.75.

HRMS (ESI $^+$) m/z : [(M+H)] $^+$ calculated for (C $_{13}$ H $_{18}$ ClO $_2$) $^+$ 241.0990; Found 241.0983.

ϵ -Methoxypropylbenzene (II-b10) [52692-50-9]



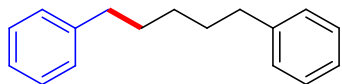
Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and 1-iodo-5-methoxy-pentane (570 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (206 mg, 58% yield) after purification by flash chromatography (SiO $_2$: 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.41 – 7.31 (m, 2H), 7.25 (d, J = 7.1 Hz, 3H), 3.53 – 3.24 (m, 5H), 2.70 (t, J = 7.7 Hz, 2H), 1.99 – 1.59 (m, 4H), 1.56 – 1.38 (m, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 143.42, 141.90, 130.01, 129.07, 126.45, 73.58, 59.33, 36.76, 32.23, 30.39, 26.70.

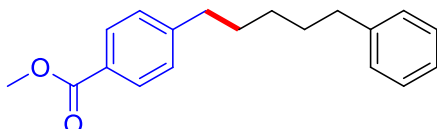
HRMS (ESI $^+$) m/z : [(M+H)] $^+$ calculated for (C $_{12}$ H $_{19}$ O $^+$) 179.1430; Found 179.1427.

1,5-Diphenylpentane (II-b11) [1718-50-9]



Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and 4-phenyl-1-iodobutane (650 mg, 2.5 mmol) were used, affording a light-yellow oil mixture (362 mg, which contained the title compound 255 mg, 57% yield) after purification by flash chromatography (SiO $_2$: pentane).¹²²

Methyl 4-(5-phenylpentyl)benzoate (II-b12)



Following **GP-II-A**, the (4-(methoxycarbonyl)benzyl) dimethyl sulfonium tetrafluoroborate salt (S10) (596 mg, 2.0 mmol) and 4-phenyl-1-iodobutane (650 mg, 2.5 mmol) were used, affording a colorless

¹²² H. Wang, X. Li, Y. Jiang, M. Li, Q. Xiao, T. Zhao, S. Yang, C. Qi, P. Qiu, J. Yang, Z. Jiang, W. Luo, *Angew. Chem. Int. Ed.* **2022**, *61*, e202200465; *Angew. Chem.* **2022**, *134*, e202200465

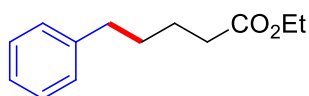
oil mixture (305 mg, which contained the title compound 0.94 mmol, 47% yield) after purification by flash chromatography (SiO₂: 10% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 8.01 (dd, *J* = 8.0, 6.0 Hz, 2H), 7.55 – 7.05 (m, 7H), 3.94 (s, 3H), 2.67 (dt, *J* = 10.8, 7.6 Hz, 4H), 1.86 – 1.60 (m, 4H), 1.55 – 1.30 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 167.91, 149.07, 143.37, 130.46, 129.22, 129.18, 129.07, 128.50, 126.47, 52.69, 36.69, 36.65, 32.09, 31.79, 29.66.

The spectroscopic data match the reported one in the literature.³⁹

Ethyl 5-phenylpentanoate (II-b13) [17734-38-2]



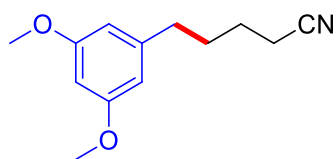
Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and ethyl 4-isobutyrate (605 mg, 2.5 mmol) were used, affording the title compound as a light-yellow oil (239mg, 58% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.34 – 7.26 (m, 2H), 7.23 – 7.15 (m, 3H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.79 – 2.56 (m, H), 2.44 – 2.25 (m, 2H), 1.85 – 1.57 (m, 4H), 1.27 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 174.35, 142.92, 129.14, 129.07, 126.53, 60.97, 36.36, 34.96, 31.69, 25.39, 15.03.

The spectroscopic data match the reported one in the literature.¹²³

5-(3,5-Dimethoxyphenyl)valeronitrile (II-b14)



Following **GP-II-A**, the 3,5-dimethylbenzyltrimethylsulfonium tetrafluoroborate salt (S8) (600 mg, 2.0 mmol) and 4-iodobutyronitrile (488 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (241mg, 55% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

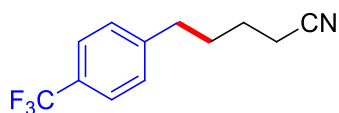
¹H NMR (300 MHz, Chloroform-d) δ 6.33 (d, *J* = 1.6 Hz, 3H), 3.78 (s, 6H), 2.60 (t, *J* = 7.3 Hz, 2H), 2.34 (t, *J* = 6.9 Hz, 2H), 2.01 – 1.47 (m, 4H).

¹²³ R. Rory Devlin, D. J. Jones, G. P. McGlacken, *Org. Lett.* **2020**, *22*, 5223

^{13}C NMR (75 MHz, Chloroform-*d*) δ 160.86, 143.60, 119.61, 106.45, 97.90, 55.24 (d, $J = 4.2$ Hz), 35.25, 29.96, 24.81, 17.03.

HRMS (APPI-P): $[\text{MH}]^+$ calculated for $(\text{C}_{13}\text{H}_{18}\text{NO}_2^+)$ 220.1332; Found 220.1334.

5-(4-Trifluoromethylphenyl) valeronitrile (II-b15)



Following **GP-II-A**, the 4-(trifluoromethyl) benzyl dimethyl sulfonium tetrafluoroborate salt (S8) (619 mg, 2.0 mmol) and 4-iodobutyronitrile (488 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (244mg, 55% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

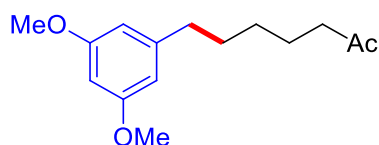
^1H NMR (300 MHz, Chloroform-*d*) δ 7.55 (d, $J = 8.1$ Hz, 2H), 7.29 (d, $J = 8.0$ Hz, 2H), 2.72 (t, $J = 7.4$ Hz, 2H), 2.37 (t, $J = 6.9$ Hz, 2H), 1.81 (m, 2H), 1.75 – 1.63 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 145.35, 128.65, 126.08, 125.37 (d, $J = 3.9$ Hz), 122.48, 119.40, 34.79, 29.93, 24.77, 17.00.

^{19}F NMR (282 MHz, Chloroform-*d*) δ -62.35.

HRMS (APPI-P): $[\text{M}]^+$ calculated for $(\text{C}_{12}\text{H}_{12}\text{F}_3\text{N}^+)$ 227.0916; Found 227.0915.

7-(4-methoxyphenyl)heptan-2-one (II-b16)



Following **GP-II-A**, the 4-methoxybenzyl dimethyl sulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and 6-iodohexan-2-one (565 mg, 2.5 mmol) were used, affording the title compound as a light-yellow oil (176 mg, 40% yield) after purification by flash chromatography (SiO_2 : 5%-10% diethyl ether in pentane).

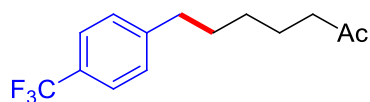
^1H NMR (300 MHz, Chloroform-*d*) δ 7.07 (d, $J = 8.6$ Hz, 2H), 6.80 (d, $J = 8.6$ Hz, 2H), 3.75 (s, 3H), 2.53 (t, $J = 7.7$ Hz, 2H), 2.39 (t, $J = 7.4$ Hz, 2H), 2.09 (s, 3H), 1.58 (p, $J = 7.6$ Hz, 4H), 1.43 – 1.18 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-*d*) δ 208.92, 157.67, 134.53, 129.19, 113.66, 55.15 (d, $J = 4.0$ Hz), 43.59, 34.77, 31.44, 28.69, 23.63.

The spectroscopic data match the reported one in the literature.¹²⁴

¹²⁴ H. Seo, F. Timothy, T. F. Jamison, *Org. Lett.* **2019**, *21*, 24, 10159.

7-(4-Trifluoromethylphenyl)heptan-2-one (II-b17)



Following **GP-II-A**, the 4-(trifluoromethyl) benzyl dimethyl sulfonium tetrafluoroborate salt (S8) (619 mg, 2.0 mmol) and 6-iodohexan-2-one (565 mg, 2.5 mmol) were used, affording the title compound as a light-yellow oil (225 mg, 44% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

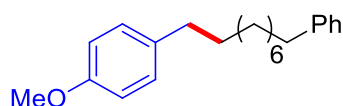
¹H NMR (300 MHz, Chloroform-d) δ 7.50 (d, *J* = 8.0 Hz, 2), 7.33 – 7.15 (m, 2 H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.41 (t, *J* = 7.3 Hz, 3H), 2.10 (s, 1H), 1.72 – 1.50 (m, 4H), 1.40 – 1.16 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 208.81, 160.74, 146.62, 128.63, 125.12 (d, *J* = 3.9 Hz), 122.57, 43.46, 35.48, 30.88, 29.77 (d, *J* = 3.9 Hz), 28.61, 23.46.

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.32.

HRMS (ESI⁺) *m/z*: [MH⁺] calculated for (C₁₄H₁₈F₃O⁺) 259.1304; Found 259.1307.

1-methoxy-4-(9-phenylnonyl)benzene (II-b18)



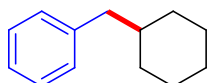
Following **GP-II-A**, the 4-methoxybenzyl dimethyl sulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and 8-phenyloctyl iodide (790 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (225 mg, 44% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.35 – 7.26 (m, 2H), 7.24 – 7.17 (m, 2H), 7.15 – 7.08 (m, 2H), 6.94 – 6.79 (m, 2H), 3.81 (s, 3H), 2.59 (dt, *J* = 17.7, 7.7 Hz, 4H), 1.72 – 1.51 (m, 4H), 1.45 – 1.15 (m, 10H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.60, 142.93, 135.03, 129.22, 128.38, 128.20, 125.53, 113.65, 55.21, 35.99, 35.04, 31.74, 31.50, 29.50, 29.32, 29.25.

The spectroscopic data match the reported one in the literature.¹²⁵

(Cyclohexylmethyl)benzene (II-b1) [4410-75-7]



Following **GP-II-A**, S1 (480 mg, 2.0 mmol) and iodocyclohexane (323 μL, 2.5 mmol) were used, affording the title compound as a colorless oil (161 mg, 46% yield) after purification by flash chromatography (SiO₂: pure pentane).

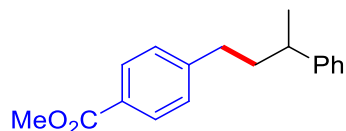
¹²⁵ K. Kundu, S. K. Nayak, *J. Nat. Prod.* **2017**, *80*, 6, 1776.

^1H NMR (300 MHz, Chloroform- d) δ 7.39 – 7.31 (m, 2H), 7.29 – 7.17 (m, 3H), 2.56 (d, J = 7.1 Hz, 2H), 1.89 – 1.63 (m, 5H), 1.59 (m, 1H), 1.34 – 1.19 (m, 3H), 1.04 (m, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 142.14, 129.98, 128.83, 126.36, 44.98, 40.61, 33.99, 27.41, 27.15.

The spectroscopic data match the reported one in the literature.¹²⁶

Methyl 4-(2-phenylpropyl)benzoate (II-b28)



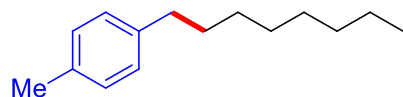
Following **GP-II-A**, the (4-(methoxycarbonyl)benzyl) dimethyl sulfonium tetrafluoroborate salt (S10) (596 mg, 2.0 mmol) and (1-iodopropan-2-yl)benzene (615 mg, 2.5 mmol) were used, affording a colorless oil mixture (208 mg, which contained the title compound 0.52 mmol, 26% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.97 (dd, J = 8.2, 1.7 Hz, 2H), 7.49 – 7.28 (m, 2H), 7.28 – 7.06 (m, 5H), 3.91 (s, 3H), 2.73 (h, J = 7.0 Hz, 1H), 2.58 (t, J = 8.4 Hz, 2H), 1.95 (m, 2H), 1.31 (d, J = 7.0 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 167.11 (d, J = 1.7 Hz), 148.09, 146.89, 129.63 (d, J = 4.0 Hz), 129.06, 128.43 (d, J = 6.0 Hz), 127.73, 127.03, 126.10, 51.89 (d, J = 4.7 Hz), 39.54, 34.01, 22.47.

The spectroscopic data match the reported one in the literature.¹²⁷

1-Methyl-4-octylbenzene (II-b35) [7686-25-1]



Following **GP-II-A**, the 4-methylbenzyl dimethyl sulfonium tetrafluoroborate salt (S2) (508 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (220 mg, 54% yield) after purification by flash chromatography (SiO₂: pure pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.18 (s, 5H), 2.67 (t, J = 8.8 Hz, 2H), 2.42 (s, 3H), 1.70 (m, 1H), 1.57 – 1.31 (m, 10H), 1.00 (t, J = 6.4 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 140.70, 135.72, 129.77, 129.13, 36.47, 32.82, 30.43, 30.29, 30.21, 23.61, 21.85, 15.00.

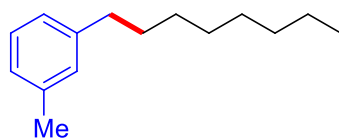
The spectroscopic data match the reported one in the literature.¹²⁸

¹²⁶ Y. Wang, Zhang, W.-X. Z. Xi, *Chem. Soc. Rev.*, **2020**, *49*, 5810.

¹²⁷ H. Li, S. Li, H. Hu, R. Sun, M. Liu, A. Ding, H. Cai, *Chem. Commun.*, **2023**, *59*, 1205.

¹²⁸ R. B. Bedford, M. Betham, D. W. Bruce, A. A. Danopoulos, R. M. Robert M. Frost, M. Hird, *J. Org. Chem.* **2006**, *71*, 1104.

***m*-Octyl-toluol (II-b36) [51918-84-4]**



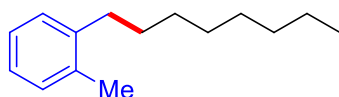
Following **GP-II-A**, the 3-methylbenzyltrimethylsulfonium tetrafluoroborate salt (S3) (508 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (240 mg, 60% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.28 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 3H), 2.68 (t, *J* = 8.8 Hz, 2H), 2.45 (s, 3H), 1.71 (m, 2H), 1.60 – 1.28 (m, 11H), 1.01 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 143.74, 138.52, 130.09, 128.99, 127.17, 126.29, 36.88, 32.85, 32.54, 30.45, 30.36, 30.23, 23.62, 22.28, 15.02.

The spectroscopic data match the reported one in the literature.¹²⁹

1-Methyl-2-octylbenzene (II-b37) [79835-99-7]



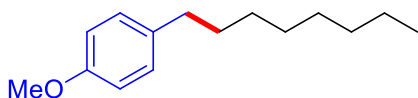
Following **GP-II-A**, the 2-methylbenzyltrimethylsulfonium tetrafluoroborate salt (S4) (508 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (234 mg, 57% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.27 (d, *J* = 3.5 Hz, 4H), 2.82 – 2.64 (m, 2H), 2.45 (s, 3H), 1.71 (q, *J* = 7.4 Hz, 2H), 1.62 – 1.33 (m, 10H), 1.05 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 141.96, 136.62, 130.98, 129.68, 126.75, 126.62, 34.32, 32.90, 31.30, 30.72, 30.54, 30.30, 23.67, 20.17, 15.05.

The spectroscopic data match the reported one in the literature.

1-(4-Methoxyphenyl)octane (II-b38) [3307-19-5]



Following **GP-II-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and Alk-a1 (540 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (240 mg, 55% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

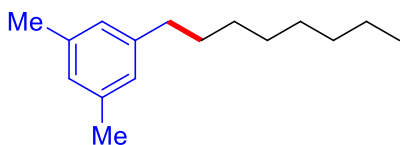
¹H NMR (300 MHz, Chloroform-d) δ 7.19 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 3.86 (s, 3H), 2.64 (t, *J* = 7.7 Hz, 2H), 1.68 (m, 2H), 1.48 – 1.29 (m, 10H), 1.15 – 0.92 (m, 3H).

¹²⁹ Z. Mo, Q. Zhang, L. Deng, *Organometallics*, **2012**, 31, 6518.

^{13}C NMR (75 MHz, Chloroform- d) δ 158.45, 135.80, 130.04, 114.44, 55.90, 35.93, 32.79, 32.67, 30.40, 30.19, 23.56, 14.96.

The spectroscopic data match the reported one in the literature.

1,3-Dimethyl-5-octylbenzene (II-b39) [177969-48-1]



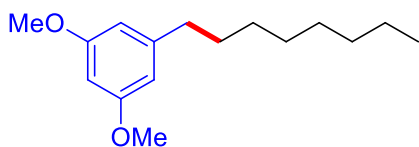
Following **GP-II-A**, the 3,5-dimethylbenzyl dimethylsulfonium tetrafluoroborate salt (S5) (536 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (237 mg, 54% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform- d) δ 6.94 (s, 1H), 2.66 (t, $J = 7.9$ Hz, 1H), 2.42 (s, 2H), 1.72 (td, $J = 7.6$, 4.3 Hz, 1H), 1.53 – 1.32 (m, 4H), 1.03 (t, $J = 6.5$ Hz, 1H).

^{13}C NMR (75 MHz, Chloroform- d) δ 143.74, 138.45, 128.06, 127.11, 36.78, 32.83, 32.56, 30.41 (d, $J = 3.0$ Hz), 30.20, 23.60, 22.14, 15.00.

HRMS (ESI $^+$) m/z : $[M^+]$ calculated for ($\text{C}_{16}\text{H}_{26}^+$) 218.2029; Found 218.2019.

1,3-Dimethoxy-5-octylbenzene (II-b40) [41497-46-5]



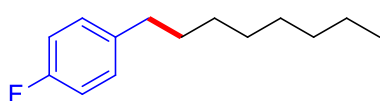
Following **GP-II-A**, the 3,5-dimethyl benzyl dimethylsulfonium tetrafluoroborate salt (S12) (600 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (170 mg, 32% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 6.41 (d, $J = 2.3$ Hz, 2H), 6.36 (t, $J = 2.3$ Hz, 1H), 3.82 (s, 6H), 2.60 (m, 2H), 1.83 – 1.57 (m, 2H), 1.47 – 1.20 (m, 10H), 1.07 – 0.79 (m, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 161.53, 146.10, 107.24, 98.33 (d, $J = 1.5$ Hz), 55.85, 37.14, 32.74, 32.13, 30.34, 30.21, 30.12, 23.51, 14.90.

HRMS (ESI $^+$) m/z : $[(M+H)]^+$ calculated for ($\text{C}_{16}\text{H}_{27}\text{O}_2^+$) 251.2006; Found 251.1997.

1-Fluoro-4-octylbenzene (II-b41) [28593-20-6]



Following **GP-II-A**, the 4-florobenzyl dimethylsulfonium tetrafluoroborate salt (S6) (516 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (375 mg, 90% yield) after purification by flash chromatography (SiO₂: pure pentane).

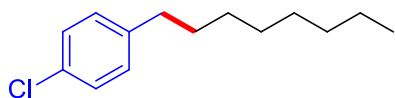
¹H NMR (300 MHz, Chloroform-d) δ 7.18 (dd, *J* = 8.5, 5.6 Hz, 2H), 7.08 – 6.90 (m, 3H), 2.63 (dd, *J* = 8.7, 6.8 Hz, 2H), 1.66 (t, *J* = 7.7 Hz, 2H), 1.49 – 1.29 (m, 10H), 1.08 – 0.75 (m, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 163.57, 160.35, 139.23 (d, *J* = 3.2 Hz), 130.40 (d, *J* = 7.7 Hz), 115.67 (d, *J* = 20.9 Hz), 35.96, 32.72, 32.45, 30.29, 30.10, 30.06, 23.50, 14.87.

¹⁹F NMR (282 MHz, Chloroform-d) -133.09 (m).

HRMS (APPI) *m/z*: calculated for (C₁₄H₂₁F) 208.1622; Found 208.1619.

1-Chloro-4-octylbenzene (II-b42)



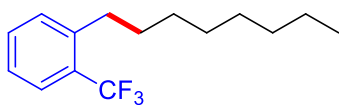
Following **GP-II-A**, the 4-chlorobenzyl dimethylsulfonium tetrafluoroborate salt (S6) (548 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a light-yellow oil (263 mg, 59% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.28 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.1 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H), 1.64 (t, *J* = 7.4 Hz, 2H), 1.46 – 1.29 (m, 10H), 0.95 (t, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 142.06, 132.04, 130.50, 129.09, 36.12, 32.71, 32.23, 30.27, 30.08, 30.06, 23.50, 14.92.

The spectroscopic data match the reported one in the literature.¹³⁰

2-Perfluorooctyl benzotrifluoride (II-b43) [1104602-68-7]



Following **GP-II-A**, the 2-(trifluoromethyl)benzyl dimethyl sulfonium tetrafluoroborate salt (S9) (619 mg, 2.0 mmol) and Alk-a1 (565 mg, 2.5 mmol) were used, affording the title compound as a light-yellow oil (196 mg, 38% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.65 (d, *J* = 7.9 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 2.83 (t, *J* = 8.1 Hz, 2H), 1.68 (p, *J* = 7.3 Hz, 2H), 1.53 – 1.25 (m, 10H), 0.95 (t, *J* = 6.4 Hz, 3H).

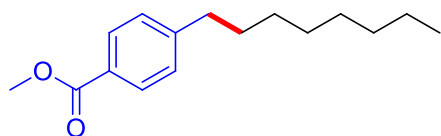
¹³⁰ L. Jin, Y. Zhao, L. Zhu, H. Zhang, A. Lei, *Adv. Synth. Catal.* **2009**, 351, 630. <https://doi.org/10.1002/adsc.200800703>

^{13}C NMR (75 MHz, Chloroform- d) δ 142.60, 132.30, 131.68, 129.12 (q, J = 29.5 Hz), 126.70 – 126.42 (m), 126.37, 123.68, 33.55, 32.69, 32.61, 30.55, 30.21, 30.05, 23.48, 14.83.

^{19}F NMR (282 MHz, Chloroform- d) δ -59.58 (d, J = 4.4 Hz).

GC-MS (EI+) m/z (% rel. int., ion): 258.2 (23.50%, M^+), 201.3 (23.59%, M^+ - C_4H_9), 160.4 (100%, M^+ - C_7H_{15}).

Methyl 4-octylbenzoate (II-b44) [54256-51-8]



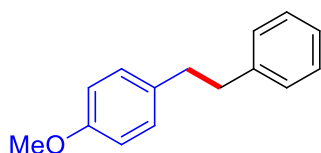
Following **GP-II-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S10) (596 mg, 2.0 mmol) and Alk-a1 (540 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (233 mg, 47% yield) after purification by flash chromatography (SiO_2 : 5% to 10% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.95 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 3.88 (s, 3H), 2.64 (t, J = 7.7 Hz, 2H), 1.84 – 1.48 (m, 2H), 1.52 – 1.16 (m, 10H), 0.88 (t, J = 6.5 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 167.86, 149.20, 131.65, 129.13, 128.34, 52.59, 36.75, 32.62, 31.90, 30.19, 30.02, 30.00, 23.42, 14.84.

The spectroscopic data match the reported one in the literature.¹³¹

1-(4-Methoxyphenyl)-2-phenylethane (II-c1) [14310-21-5]



Following **GP-II-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and benzyl chloride (316 mg, 2.5 mmol) were used, affording the title compound as a white solid (176 mg, 41% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.47 -7.37 (m, 2H), 7.35 -7.28 (m, 3H), 7.22 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.6 Hz, 2H), 3.89 (s, 3H), 3.01 (s, 4H).

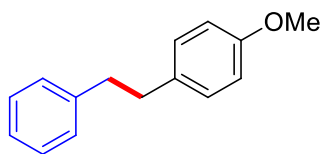
^{13}C NMR (75 MHz, Chloroform- d) δ 158.77, 142.74, 134.74, 130.25, 129.39, 129.21, 126.78, 114.65, 56.07, 39.11, 37.93.

The spectroscopic data match the reported one in the literature.¹³²

¹³¹ J. Sheng, H.-Q. Ni, H.-R. Zhang, K.-F. Zhang, Y.-N. Wang, X.-S. Wang, *Angew. Chem. Int. Ed.* **2018**, *57*, 7634

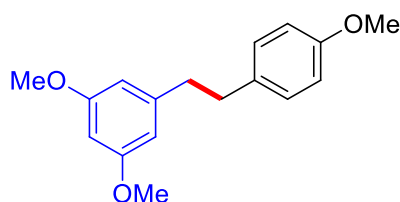
¹³² C.-S. Yan, Y. Peng, X.-B. Xu, Y.-W. Wang, *Chem. Eur. J.*, **2012**, *18*, 6039

1-(4-Methoxyphenyl)-2-phenylethane (II-c2) [14310-21-5]



Following **GP-II-A**, S1(480 mg, 2.0 mmol) and 4-methoxy benzyl chloride (392 mg, 2.5 mmol) were used, affording the title compound as a white solid (274 mg, 69% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

1-(3,5-Dimethoxyphenyl)-2-(4-methoxyphenyl)ethane (II-c3) [83638-45-3]



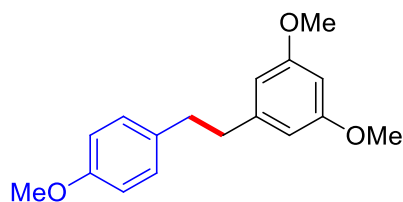
Following **GP-II-A**, the 3,5-dimethylbenzyl dimethylsulfonium tetrafluoroborate salt (S12) (600 mg, 2.0 mmol) and 4-methoxy benzyl chloride (392 mg, 2.5 mmol) were used, affording the title compound as a white solid (119 mg, 23% yield) after purification by flash chromatography (SiO₂: 10% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.15 (d, $J = 7.7$ Hz, 2H), 6.87 (d, $J = 7.7$ Hz, 2H), 6.39 (s, 3H), 3.80 (s, 9H), 2.89 (s, 4H).

¹³C NMR (75 MHz, Chloroform-d) δ 161.52, 158.66, 145.05, 134.60, 130.13, 114.54, 107.32, 98.72, 56.01, 39.27, 37.57.

The spectroscopic data match the reported one in the literature.¹³³

1-(3,5-Dimethoxyphenyl)-2-(4-methoxyphenyl)ethane (II-c4) [83638-45-3]



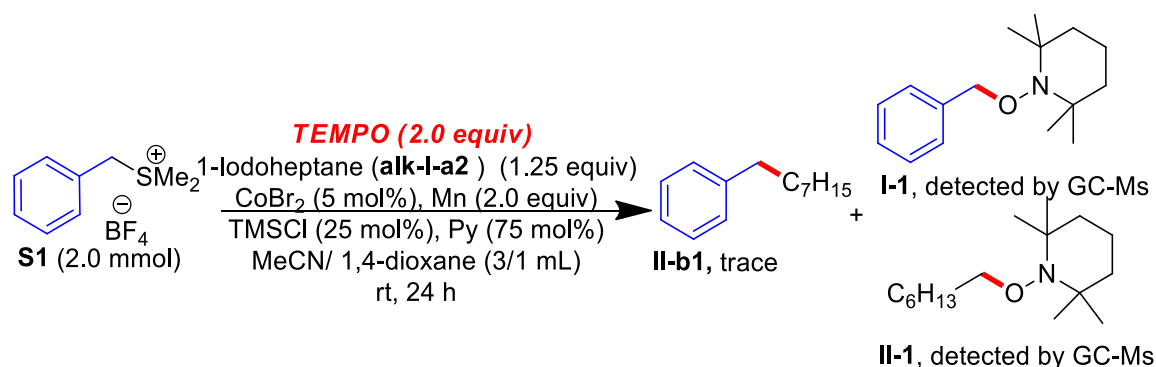
Following **GP-II-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and 3,5-dimethyl benzyl chloride (466 mg, 2.5 mmol) were used, affording the title compound as a white solid (112 mg, 21% yield) after purification by flash chromatography (SiO₂: 10% diethyl ether in pentane).

¹³³ R. del Río-Rodríguez, L. Blanco, A. Collado, J. A. Fernández-Salas, J. Alemán, *Chem. Eur. J.* **2022**, e202201644.

4.2. Mechanistic experiments of S1 with Alk-1a

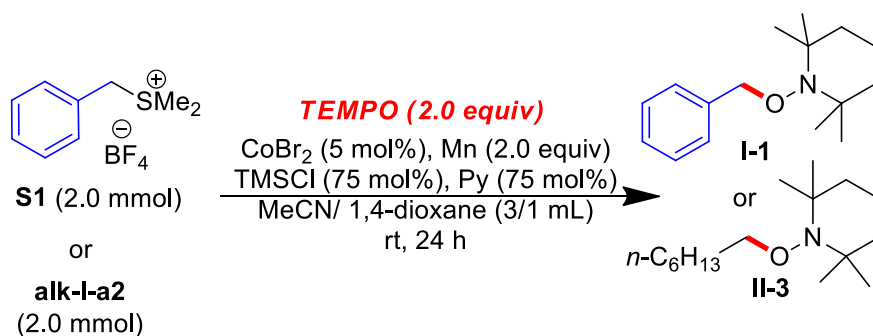
4.2.1. Radical trapping experiments

a) The reaction with TEMPO.



In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and TEMPO (628 mg, 4.0 mmol, 2.0 equiv) were added. The tube was filled with N₂ three times, and added the MeCN (3.0 mL), 1,4 dioxane (1.0 mL), and alk-I-a2 (410 μL, 2.5 mmol, 1.25 equiv) under N₂. The mixture was stirred for the 30s and then TMSCl (25 mol%, to be sure that the reaction was triggered) was added at rt. After 3 min, pyridine (125 μL, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir for 24 h at rt. After completion, the reaction mixture was added 250 μL decane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-Ms.

b) The reaction of S1 or Alk-1a with TEMPO:



Entry	S1	alk-I-a2	I-1 ^a	bibenzyl ^b	II-3 ^a	n-C ₁₄ H ₂₈ ^b
1	+	/	trace	32%	/	/
2	/	+	/	/	trace	16%

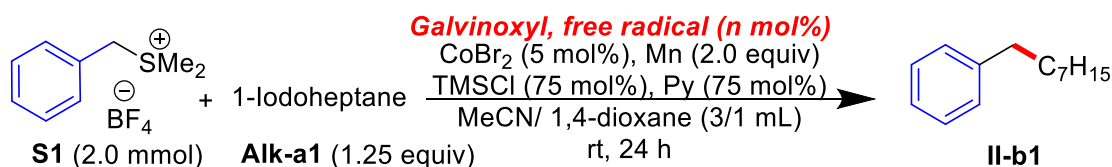
^aDetected by GC-Ms. ^bGC yield with 250 μL decane as reference

♣ In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and TEMPO (2.0 equiv, 628 mg) were added.

The tube was filled with N₂ thrice, and the MeCN (3.0 mL), 1-4 dioxane (1.0 mL) under N₂, was added.

- ♣ Or In an oven-dried, 20-mL reaction tube, Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and TEMPO (2.0 equiv, 628 mg) were added. The tube was filled with N₂ three times, and added the MeCN (3.0 mL), 1-4 dioxane (1.0 mL), and alk-I-a2 (410 μL, 2.5 mmol, 1.25 equiv) under N₂
- ♣ The mixture was stirred for 30s and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. After 3 min, pyridine (125 μL, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir for 24 h at rt. After completion, the reaction mixture was added 250 μL decane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

c) The reaction of S1 or Alk-a1 with galvinoxyl, free radical.



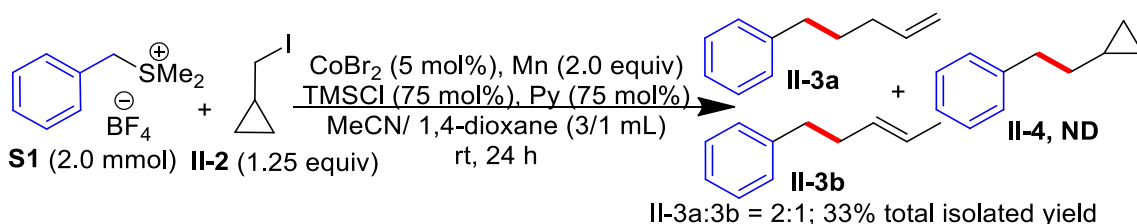
Entry	n (mol %)	GC yield of II-b1/ %
1	50	50
2	100	43
3	150	16

^aGC yields using decane as an internal standard.

In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and galvinoxyl, free radical (422 mg, 1 mmol, 50mol%; 844 mg, 2 mmol, 100 mol%; 1.27 g, 3 mmol, 150 mol% respectably) were added. The tube was filled with N₂ three times, and added the MeCN (3.0 mL), 1-4 dioxane (1.0 mL), and alk-I-a2 (410 μL, 2.5 mmol, 1.25 equiv) under N₂. The mixture was stirred for the 30s and then TMSCl (190 μL, 1.5 mmol, 75 mol%, to be sure that the reaction was triggered) was added at rt. After 3 min, pyridine (125 μL, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir for 24 h at rt. After completion, the reaction mixture was added 250 μl decane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

4.2.2. Radical ring-opening experiment

a) S1 with cyclopropyl methyl iodide (II-2)



In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), and CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%). The tube was filled with N₂ three times and added the MeCN (3.0 mL), 1-4 dioxane (1.0 mL), cyclopropyl methyl iodide (II-2) (455 mg, 2.5 mmol, 1.25 equiv) as the starting materials. The reaction was quenched according to the general procedure **GP-II-A** After stirring at rt for 24 h. Then the crude material was purified by flash chromatography on silica gel (100% hexanes) to afford a colorless oil (95 mg) containing compound 5-phenylpent-1-ene **3a** and (*E*)-3-pentenyl benzene **3b** whose ratio is 2:1 in 33% yield. The unrearranged compound was not detected.

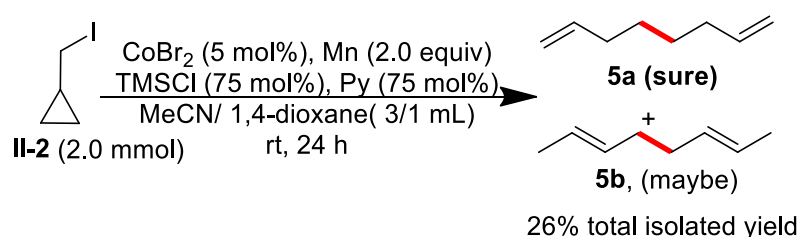
♣ For compounds **3a** and **3b**:

¹H NMR (300 MHz, Chloroform-*d*) δ 7.35 (m, 3H), 7.28 – 7.09 (m, 4.5H), 5.91 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.55 (td, *J* = 3.6, 1.8 Hz, 1H), 5.21 – 4.81 (m, 2H), 2.89 – 2.61 (m, 3H), 2.42 – 2.28 (m, 1H), 2.27 – 2.08 (m, 2H), 1.86 – 1.76 (m, 2H), 1.73 (dq, *J* = 2.7, 1.3 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-*d*) δ 143.24, 142.98, 139.38, 131.39, 129.24, 129.07, 129.03, 128.96, 126.48, 126.17, 115.50, 36.92, 36.13, 35.26, 34.10, 31.43, 18.71.

The spectroscopic data match the reported one in the literature.¹³⁴

b) Cyclopropylmethyl iodide (4) as only electrophiles

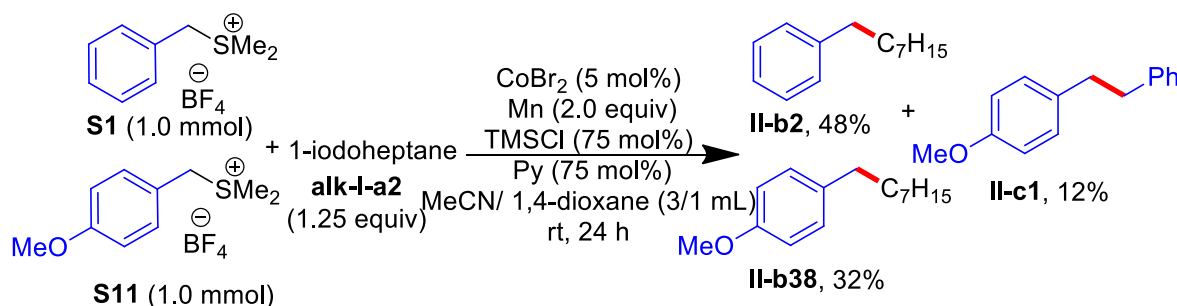


In an oven-dried, 20-mL reaction tube, Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%). The tube was filled with N₂ three times, and added the MeCN (3.0 mL), 1-4 dioxane (1.0 mL), cyclopropylmethyl iodide (II-2) (364 mg, 2.0 mmol, 1 equiv) as only electrophilic partner. The reaction was quenched according to the general procedure after stirring at rt for 24 h. Then the crude

¹³⁴ a) Q.-Y. Meng, T. E. Schirmer, K. Katou, B. König, *Angew. Chem. Int. Ed.* **2019**, *58*, 5723. b) R. J. Armstrong, C. García-Ruiz, E. L. Myers, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2017**, *56*, 786.

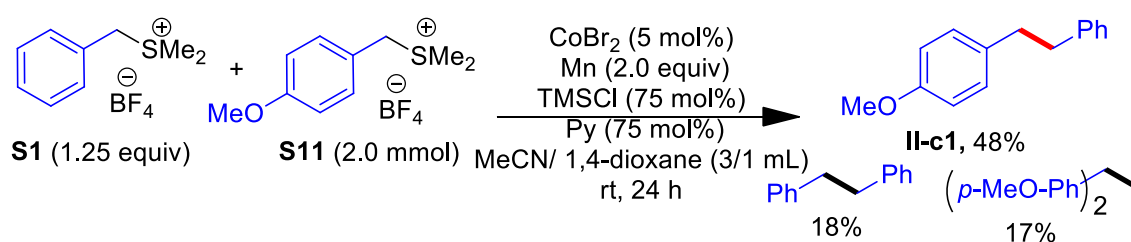
material was purified by flash chromatography on silica gel (100% hexanes) to afford to mix ring-open products **5a** and **5b** (29 mg, 26 % total isolated yield).¹³⁵

4.2.3. Co-catalyzed cross-coupling between different benzyl sulfonium salts and Alk-1.



In an oven-dried, 20-mL reaction tube, S1 (240 mg, 1.0 mmol) and S11 (270 mg, 1.0 mmol), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), and CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) were added. The tube was filled with N₂ three times and added the MeCN (3.0 mL), 1-4 dioxane (1.0 mL), and alk-1a (565 mg, 2.5 mmol, 1.25 equiv) under N₂. The mixture was stirred for the 30s, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. After 3 min, pyridine (125 μL, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir for 24 h at rt. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with diethyl ether. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel afforded **II-b2** in 48% yield, **II-b38** in 32% yield, and **II-c1** in 12% yield, respectively.

4.2.4. Co-catalyzed cross-coupling of two different benzyl sulfonium salts



In an oven-dried, 20-mL reaction tube, S1 (600 mg, 2.5 mmol, 1.25 equiv) and S11 (540 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) were added. The tube was filled with N₂ thrice, and the MeCN (3.0 mL), 1-4 dioxane (1.0 mL) under N₂, was added. The mixture was stirred for the 30s and then TMSCl (75 mol%, to be sure that the reaction was

¹³⁵ a) T. Nishino, T. Watanabe, M. Okada, Y. Nishiyama, N. Sonoda. *J. Org. Chem.* **2002**, *67*, 3, 966–969. b) D. J. Pasto, G. L'Hermine. *Tetrahedron*. **1993**. *49*. 16, 3259-3272.

triggered) was added at rt. After 3 min, pyridine (125 μ L, 1.5 mmol, 75 mol%) was injected. Then the reaction mixture was allowed to stir for 24 h at rt. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with diethyl ether. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel afforded **II-c1** in 48% yield and homo-coupling products of two benzyl sulfonium salts.

5. General Procedure of Allylation with Allyl Derivatives

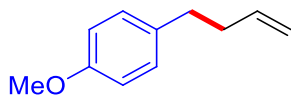
5.1. The cross-coupling of benzyl sulfonium salts and allyl acetate derivatives.

5.1.1. General Procedure of Allylation (GP-III-A).

In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt derivative (S) (2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv) and CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) were added. The tube was filled with N₂ three times and added the MeCN (5.0 mL), allyl acetate derivatives (all-OAc-a) (1.25 equiv) by syringe under N₂. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to stir overnight at rt. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with diethyl ether. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether) afforded the corresponding product characterized by NMR (¹H, ¹³C, ¹⁹F).

- Characterization data of products

4-(p-Methoxyphenyl)but-1-ene (III-b2) [20574-98-5]



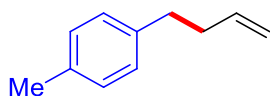
Following **GP-III-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with A-OAc-1a (270 μL, 2.5 mmol) was used, affording the title compound as a colorless oil (207 mg, 64% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.12 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.2 Hz, 2H), 5.87 (m, 1H), 5.18 – 4.88 (m, 2H), 3.80 (s, 3H), 2.66 (dd, *J* = 8.9, 6.7 Hz, 2H), 2.35 (q, *J* = 7.2 Hz, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.78, 145.42, 134.30, 129.19, 113.74, 110.20, 55.21 (d, *J* = 4.2 Hz), 39.88, 33.37, 22.62 (d, *J* = 3.3 Hz).

The spectroscopic data match the reported one in the literature.^{134a}

1-(But-3-en-1-yl)-4-methylbenzene (III-b3) [20574-99-6]



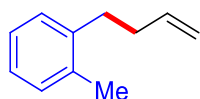
Following **GP-III-A**, the 4-methylbenzyl dimethylsulfonium tetrafluoroborate salt (S2) (508 mg, 2.0 mmol) and with A-OAc-1a (270 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (178 mg, 61% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.16 (s, 4H), 5.94 (ddt, J = 16.8, 10.1, 6.5 Hz, 1H), 5.17 – 4.78 (m, 2H), 2.75 (dd, J = 9.1, 6.6 Hz, 2H), 2.50 – 2.17 (m, 5H).

¹³C NMR (75 MHz, Chloroform-d) δ 139.61, 139.01, 136.02, 129.81, 129.13, 115.65, 36.51, 35.78, 21.84.

The spectroscopic data match the reported one in the literature.

1-(But-3-en-1-yl)-2-methylbenzene (III-b4) [45892-60-2]



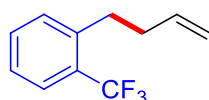
Following **GP-III-A**, the 2-methylbenzyl dimethylsulfonium tetrafluoroborate salt (S4) (508 mg, 2.0 mmol) and with All-OAc-a1 (270 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (164 mg, 56% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.47 – 6.92 (m, 4H), 6.06 (m, 1H), 5.52 – 4.98 (m, 2H), 3.08 – 2.77 (m, 2H), 2.66 – 2.34 (m, 5H).

¹³C NMR (75 MHz, Chloroform-d) δ 140.10, 138.34, 135.92, 130.23, 128.86, 126.06, 126.01, 114.89, 34.44, 32.84, 19.38 (d, J = 2.8 Hz).

The spectroscopic data match the reported one in the literature.¹³⁶

1-Allyl-2-(trifluoromethyl)benzene (III-b5) [1417514-27-2]



Following **GP-III-A**, the 2-(trifluoromethyl) benzene benzyl dimethyl sulfonium tetrafluoroborate salt (S9) (619 mg, 2.0 mmol) and with A-OCO₂Me (284 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (246 mg, 53% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.74 – 7.54 (m, 1H), 7.49 (td, J = 7.7, 1.4 Hz, 1H), 7.38 – 7.14 (m, 2H), 5.92 (m, 1H), 5.34 – 4.55 (m, 2H), 3.16 – 2.72 (m, 2H), 2.62 – 2.17 (m, 2H).

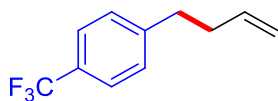
¹³C NMR (75 MHz, Chloroform-d) δ 140.61 (d, J = 1.8 Hz), 137.59, 131.59, 131.01, 128.49 (q, J = 29.7 Hz), 125.92 (d, J = 2.2 Hz), 122.84, 115.21, 35.53, 32.07 (d, J = 2.0 Hz).

¹⁹F NMR (282 MHz, Chloroform-d) δ -59.71.

¹³⁶ R. Liu, Z.-H. Lu, X.-H. Hu, J.-L. Li, X.-J. Yang, *Org. Lett.* **2015**, *17*, 6, 1489.

The spectroscopic data match the reported one in the literature.¹³⁷

4-(4-Trifluoromethylphenyl)-1-butene (III-b6)



Following **GP-III-A**, the 4-(trifluoromethyl) benzene benzyl dimethyl sulfonium tetrafluoroborate salt (S8) (619 mg, 2.0 mmol) and with *A-OCO₂Me* (284 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (143 mg, 36% yield) after purification by flash chromatography (SiO₂: pure pentane).

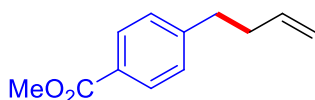
¹H NMR (300 MHz, Chloroform-d) δ 7.58 (d, J = 8.1 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 5.88 (m, 1H), 5.29 – 4.84 (m, 2H), 2.81 (t, J = 7.8 Hz, 2H), 2.60 – 2.25 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 145.93, 137.32, 132.11 – 126.85 (m), 125.18 (q, J = 3.9 Hz), 115.39, 35.10 (d, J = 6.3 Hz).

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.35.

The spectroscopic data match the reported one in the literature.¹³⁸

Methyl 4-(but-3-en-1-yl) benzoate (III-b7) [15451-34-0]



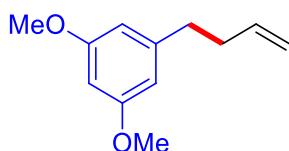
Following **GP-III-A**, the 4-methoxybenzyl dimethyl sulfonium tetrafluoroborate salt (S10) (596 mg, 2.0 mmol) and with *A-OCO₂Me* (284 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (172 mg, 45% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.95 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 8.2 Hz, 2H), 5.82 (m, 1H), 5.21 – 4.84 (m, 2H), 3.88 (s, 3H), 2.74 (dd, J = 8.8, 6.7 Hz, 2H), 2.50 – 2.24 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 166.98, 147.26, 137.41, 129.62, 128.42, 127.86, 115.29, 51.83 (d, J = 4.8 Hz), 35.31, 35.00.

The spectroscopic data match the reported one in the literature.^{134a}

4-(3,5-Dimethoxyphenyl)-1-butene (III-b8) [111540-02-4]



¹³⁷ X. Yang, G. C. Tsui, *Org. Lett.* **2018**, *20*, 4, 1179.

¹³⁸ Y.-F. Wang, Y.-R. Gao, S. Mao, Y.-L. Zhang, D.-D. Guo, Z.-L. Yan, Y.-Q. Wang, *Org. Lett.* **2014**, *16*, 6, 1610.

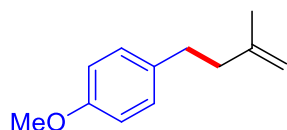
Following **GP-III-A**, the 3,5-dimethyl benzyl dimethylsulfonium tetrafluoroborate salt (S12) (600 mg, 2.0 mmol) and with All-OAc-a1(270 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (221 mg, 58% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 6.43 (d, J = 2.3 Hz, 2H), 6.38 (t, J = 2.3 Hz, 1H), 5.93 (m, 1H), 5.20 – 4.99 (m, 2H), 3.82 (s, 6H), 2.72 (dd, J = 9.1, 6.5 Hz, 2H), 2.60 – 2.36 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 160.78, 144.25, 138.03, 114.89, 106.50, 97.79 (d, J = 2.1 Hz), 65.83, 55.13 (d, J = 4.2 Hz), 35.70, 35.29, 15.28.

The spectroscopic data match the reported one in the literature.¹³⁹

4-(4-Methoxyphenyl)-2-methyl-1-butene (III-b9) [18491-21-9]



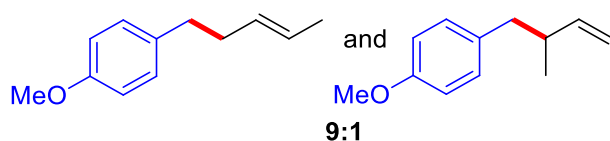
Following **GP-III-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with methyl acetate (310 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (119 mg, 34% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.16 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 4.88 – 4.68 (m, 2H), 3.83 (s, 3H), 2.87 – 2.60 (m, 2H), 2.35 (dd, J = 9.6, 6.6 Hz, 2H), 1.82 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.78, 145.42, 134.30, 129.19, 113.74, 110.20, 55.21 (d, J = 4.2 Hz), 39.88, 33.37, 22.62 (d, J = 3.3 Hz).

The spectroscopic data match the reported one in the literature.¹⁴⁰

5-(4-Methoxyphenyl)-2-pentene (III-b10) [140836-82-4]



Following **GP-III-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with trans-2-butenyl acetate (191 μ L, 2.5 mmol) was used, affording the title compound as a colorless oil (169 mg, 48% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹³⁹ H. Deguchi, K. Hanaya, T. Sugai, S. Higashibayashi, *Chem. Commun.*, **2023**, 59, 748.

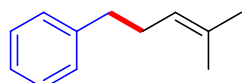
¹⁴⁰ G. Onodera, E. Yamamoto, S. Tonegawa, M. Iezumi, R. Takeuchi, *Adv. Synth. Catal.*, **2011**, 353: 2013.

^1H NMR (300 MHz, Chloroform- d) δ 7.18 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 5.56 (td, J = 3.6, 1.8 Hz, 2H), 5.13 – 4.96 (m, 3H), 3.85 (s, 2H), 2.70 (dd, J = 9.1, 6.6 Hz, 2H), 2.43 – 2.07 (m, 2H), 1.93 – 1.55 (m, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 157.80, 134.31, 130.76, 129.33, 125.32, 113.72, 55.18 (d, J = 4.1 Hz), 35.26, 34.78, 17.96 (d, J = 3.2 Hz).

The spectroscopic data match the reported one in the literature.¹⁴¹

(4-Methylpent-3-en-1-yl)benzene (III-b11) [33501-90-5]



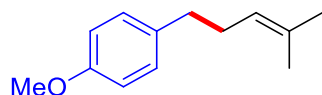
Following **GP-III-A**, S1 (480 mg, 2.0 mmol) and 3-methylbut-2-enyl acetate (310 μL , 2.5 mmol) were used and reacted for 24 h, affording the title compound as a colorless oil (64 mg, 20% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.39 – 7.31 (m, 2H), 7.29 – 7.22 (m, 3H), 5.26 (m, 1H), 2.72 (dd, J = 9.1, 6.7 Hz, 2H), 2.38 (q, J = 7.9 Hz, 3H), 1.78 (s, 3H), 1.65 (s, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 142.43, 132.10, 128.47, 128.24, 125.68, 123.79 (d, J = 1.6 Hz), 36.20, 30.11, 25.70 (d, J = 3.3 Hz), 17.66 (d, J = 3.1 Hz).

The spectroscopic data match the reported one in the literature.¹⁴²

1-Methoxy-4-(3-methylbut-3-en-1-yl)benzene (III-b12) [4586-91-8]



Following **GP-III-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with 3-methylbut-2-enyl acetate (310 μL , 2.5 mmol) were used, affording the title compound as a colorless oil (78 mg, 21% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.13 (d, J = 8.5 Hz, 2H), 6.85 (d, J = 8.5 Hz, 2H), 5.40 – 5.05 (m, 1H), 3.81 (s, 3H), 2.61 (dd, J = 9.0, 6.6 Hz, 2H), 2.29 (q, J = 7.6 Hz, 2H), 1.94 – 1.65 (m, 3H), 1.60 (d, J = 1.4 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 157.70, 134.53, 132.00, 129.29, 123.83, 113.65, 55.22 (d, J = 4.3 Hz), 35.21, 30.29, 25.67 (d, J = 3.5 Hz), 17.65 (d, J = 3.2 Hz).

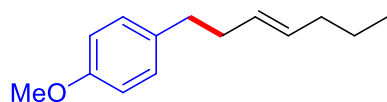
The spectroscopic data match the reported one in the literature.¹⁴³

¹⁴¹ T. Satoh, A. Kondo, J. Musashi, *Tetrahedron*. **2004**, *60*, 5453.

¹⁴² D. A. Everson, B. A. Jones, D. J. Weix, *J. Am. Chem. Soc.* **2012**, *134*, 14, 6146.

¹⁴³ D. C. Braddock, J. S. Marklew, A. J. Thomas, *Chem. Commun.*, **2011**, 47, 9051.

(4E)-7-(4-Methoxybenzyl)-4-heptene (III-b13)



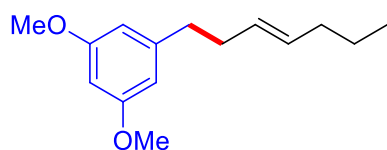
Following **GP-III-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with (*E*)-2-hexen-1-yl acetate (316 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (179 mg, 44% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 5.65 – 5.24 (m, 2H), 3.80 (s, 3H), 2.62 (dd, *J* = 8.9, 6.6 Hz, 2H), 2.43 – 2.16 (m, 2H), 2.03 – 1.81 (m, 2H), 1.37 (q, *J* = 7.3 Hz, 2H), 0.88 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.66, 134.31, 130.83, 129.56, 129.29, 113.62, 55.20, 35.24, 34.66, 22.65, 13.61.

HRMS (APCI-P): [MH]⁺ calculated for (C₁₄H₂₁O)⁺ 205.1587; Found 205.1584.

(4E)-7-(3,5-Dimethoxyphenyl)-4-heptene (III-b14)



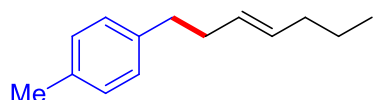
Following **GP-III-A**, the 3,5-dimethyl benzyl dimethylsulfonium tetrafluoroborate salt (S12) (600 mg, 2.0 mmol) with (*E*)-2-hexen-1-yl acetate (316 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (228 mg, 49% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 6.37 (dd, *J* = 14.1, 2.3 Hz, 3H), 5.60 – 5.41 (m, 2H), 3.80 (s, 6H), 2.65 (dd, *J* = 9.2, 6.5 Hz, 2H), 2.45 – 2.27 (m, 2H), 2.06 – 1.92 (m, 2H), 1.41 (h, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 160.73, 144.57, 130.88, 129.49, 106.50, 97.74, 55.11 (d, *J* = 4.0 Hz), 36.51, 34.69, 34.27, 22.68, 13.62.

HRMS (APPI-P): [MH]⁺ calculated for (C₁₅H₂₃O₂)⁺ 235.1693; Found 235.1689.

(4E)-7-(4-Methylphenyl)-4-heptene (III-b15)



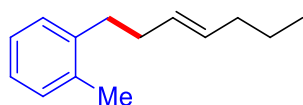
Following **GP-III-A**, the 4-methylbenzyltrimethylsulfonium tetrafluoroborate salt (S2) (508 mg, 2.0 mmol) with (*E*)-2-hexen-1-yl acetate (316 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (262 mg, 70% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.22 (s, 4H), 5.78 – 5.50 (m, 2H), 2.79 (dd, *J* = 9.1, 6.6 Hz, 2H), 2.47 (s, 5H), 2.20 – 2.02 (m, 2H), 1.68 – 1.48 (m, 2H), 1.18 – 0.93 (m, 4H).

¹³C NMR (75 MHz, Chloroform-d) δ 139.21, 135.09, 130.87, 129.76, 129.00, 128.42, 35.90, 34.79 (d, *J* = 5.5 Hz), 22.81, 21.06 (d, *J* = 3.1 Hz), 13.73.

HRMS (APPI-P): [MH]⁺ calculated for (C₁₄H₁₉O₂⁺) 187.1481; Found 187.1474.

(4*E*)-7-(2-Methylphenyl)-4-heptene (III-b16)



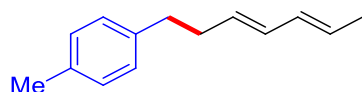
Following **GP-III-A**, the 2-methylbenzyltrimethylsulfonium tetrafluoroborate salt (S4) (508 mg, 2.0 mmol) with (*E*)-2-hexen-1-yl acetate (316 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (125 mg, 33% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.35 – 6.91 (m, 4H), 5.58 (qd, *J* = 3.7, 2.1 Hz, 2H), 2.82 – 2.65 (m, 2H), 2.53 – 2.25 (m, 5H), 2.09 (ddd, *J* = 8.6, 7.1, 5.2 Hz, 2H), 1.68 – 1.39 (m, 2H), 1.00 (t, *J* = 7.4 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 140.40, 135.89, 130.87, 130.13, 129.74, 128.89, 125.90, 34.78, 33.59, 33.35, 22.75, 19.37 (d, *J* = 3.1 Hz), 13.74.

HRMS (APPI-P): [M-H]⁺ calculated for (C₁₄H₁₉⁺) 187.1481; Found 187.1474.

(2*E*,4*E*)-7-(4-Methylphenyl) hepta-2,4-diene (III-b17)



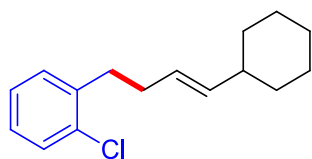
Following **GP-III-A**, the 4-methylbenzyltrimethylsulfonium tetrafluoroborate salt (S2) (508 mg, 2.0 mmol) with (*E*)-2-hexen-1-yl acetate (316 μ L, 2.5 mmol) were used, affording the title compound as a colorless oil (123 mg, 33% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.26 – 6.98 (m, 4H), 6.27 – 6.07 (m, 2H), 5.85 – 5.62 (m, 2H), 2.80 (dd, *J* = 9.2, 6.7 Hz, 2H), 2.66 – 2.34 (m, 5H), 1.87 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 138.94, 135.24, 131.78, 131.08, 130.90, 129.10 (d, *J* = 1.3 Hz), 128.40, 127.18, 37.75, 35.61, 34.68, 21.10 (d, *J* = 2.9 Hz).

HRMS (APCI-P): [MH]⁺ calculated for (C₁₄H₁₉⁺) 187.1481; Found 187.1478.

((E)-5-Cyclohexyl-pent-3-enyl)- 2-chloro-benzene (III-b18)



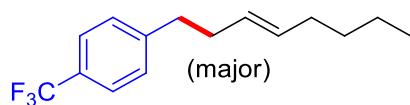
Following **GP-III-A**, the 2-chlorobenzyl dimethylsulfonium tetrafluoroborate salt (S14) (548 mg, 2.0 mmol) with 1-acetoxy-1-cyclohexyl-2-propene (455 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (153 mg, 31% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.37 (d, *J* = 7.5 Hz, 1H), 7.26 – 7.10 (m, 3H), 5.43 (d, *J* = 5.1 Hz, 2H), 2.83 (t, *J* = 7.8 Hz, 2H), 2.37 – 2.29 (m, 2H), 1.95 (tt, *J* = 11.4, 5.7 Hz, 1H), 1.77 – 1.64 (m, 5H), 1.41 – 1.18 (m, 3H), 1.16 – 1.00 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 139.66, 137.43, 133.98, 130.53, 129.37, 127.14, 126.53, 126.30, 40.66, 33.88, 33.16, 32.70, 26.28, 26.14.

HRMS (APCI-P): [MH]⁺calculated for (C₁₆H₂₂Cl)⁺ 249.1405; Found 249.1401

(5E)-8-(4-Trifluoromethylphenyl)-5-heptene (III-b19)



Following **GP-III-A**, the 4-(trifluoromethyl) benzyl dimethyl-sulfonium tetrafluoroborate salt (S8) (619 mg, 2.0 mmol) with 3-acetoxy-1-heptene (390 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (216 mg, 42% yield) after purification by flash chromatography (SiO₂: pure pentane).

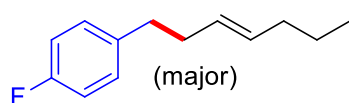
¹H NMR (300 MHz, Chloroform-d) δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.60 – 5.38 (m, 2H), 2.77 (dd, *J* = 8.7, 6.7 Hz, 2H), 2.37 (tdd, *J* = 7.6, 5.1, 2.3 Hz, 2H), 2.10 – 1.94 (m, 2H), 1.54 – 1.25 (m, 4H), 0.94 (t, *J* = 7.0 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 146.23, 131.78, 128.77, 128.55, 127.09 (d, *J* = 127.7 Hz), 125.09 (q, *J* = 3.8 Hz), 122.64, 35.92, 34.05, 32.20, 31.67, 22.11, 13.83.

¹⁹F NMR (282 MHz, Chloroform-d) δ -62.34.

HRMS (APPI-P): [MH]⁺calculated for (C₁₅H₂₀F₃)⁺ 257.1512; Found 257.1522.

(4E)-7-(4-Methphenyl) -4-heptene (III-b20)



Following **GP-III-A**, the 4-florobenzyl dimethylsulfonium tetrafluoroborate salt (S6) (516 mg, 2.0 mmol) with 3-acetoxy-1-hexene (355 mg, 2.5 mmol) was used, affording the title compound as a colorless oil (156 mg, 41% yield) after purification by flash chromatography (SiO₂: pure pentane).

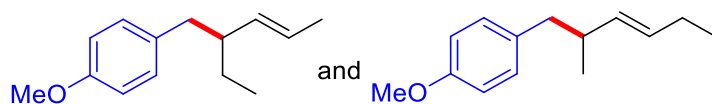
¹H NMR (300 MHz, Chloroform-d) δ 7.18 (dd, *J* = 8.5, 5.6 Hz, 2H), 7.10 – 6.98 (m, 2H), 5.49 (dd, *J* = 4.5, 2.9 Hz, 2H), 2.71 (m, 2H), 2.48 – 2.28 (m, 2H), 2.14 – 1.96 (m, 2H), 1.43 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 162.88, 159.66, 137.72 (d, *J* = 3.2 Hz), 131.21, 129.77 (d, *J* = 7.7 Hz), 129.20, 114.90 (d, *J* = 21.1 Hz), 35.35, 34.71, 34.59, 22.69, 13.61.

¹⁹F NMR (282 MHz, Chloroform-d) δ -117.91 (d, *J* = 8.0 Hz).

HRMS (APCI-P): [2MH]⁺ calculated for (C₂₆H₃₅F₂)⁺ 385.2701; Found 385.2690.

(*E*)-2-Ethyl-1-(4-methoxyphenyl)-3-pentene and 2-methyl-(4-methoxyphenyl)-hex-3-ene (III-b21)



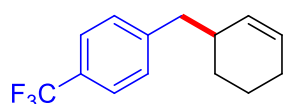
Following **GP-III-A**, the 4-methoxybenzyl dimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) with (*E*)-4-hexen-3-yl acetate (355 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (306 mg, 75% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.15 (dd, *J* = 8.7, 2.3 Hz, 2H), 6.91 (dd, *J* = 8.7, 2.4 Hz, 2H), 5.52 – 5.47 (m, 1H), 5.44 – 5.28 (m, 1H), 3.91 – 3.75 (m, 3H), 2.80 – 2.62 (m, 1H), 2.60 – 2.39 (m, 1H), 2.29 – 2.05 (m, 2H), 1.88 – 1.79 (m, 1H), 1.79 – 1.66 (m, 1H), 1.63 – 1.45 (m, 1H), 1.39 – 1.28 (m, 1H), 1.21 – 1.01 (m, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.75 (d, *J* = 6.1 Hz), 135.07, 134.60, 133.13 (d, *J* = 2.9 Hz), 130.27 (d, *J* = 15.3 Hz), 124.94, 113.44 (d, *J* = 3.0 Hz), 55.11 (d, *J* = 4.5 Hz), 46.41, 43.00, 41.13, 38.53, 27.16, 25.67, 19.95, 14.03.

HRMS (APCI-P): [MH]⁺ calculated for (C₁₄H₂₁O)⁺ 205.1587; Found 205.1581

4-(Cyclohex-2-en-1-ylmethyl)-trifluoromethyl-benzene (III-b22)



Following **GP-III-A**, the 4-(trifluoromethyl) benzyl dimethyl-sulfonium tetrafluoroborate salt (S8) (619 mg, 2.0 mmol) with cyclohex-2-enyl acetate (280 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (179 mg, 32% yield) after purification by flash chromatography (SiO₂: pure pentane).

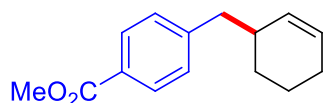
^1H NMR (300 MHz, Chloroform- d) δ 7.57 (d, J = 8.1 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 5.75 (dt, J = 6.4, 2.8 Hz, 1H), 5.58 (tt, J = 7.8, 3.8 Hz, 1H), 2.68 (qd, J = 13.3, 7.6 Hz, 2H), 2.43 (m, 1H), 2.11 – 1.93 (m, 2H), 1.74 (dq, J = 6.9, 3.9, 3.4 Hz, 2H), 1.54 (m, 1H), 1.42 – 1.22 (m, 1H).

^{13}C NMR (75 MHz, Chloroform- d) δ 145.00, 130.60, 129.37, 128.04 – 127.20 (m), 125.05 (d, J = 3.8 Hz), 42.50, 36.99, 28.82, 25.29, 21.18.

^{19}F NMR (282 MHz, Chloroform- d) δ -62.37 (d, J = 66.4 Hz).

The spectroscopic data match the reported one in the literature.¹⁴⁴

Methyl 4-(cyclohex-2-en-1-ylmethyl)-benzoate (III-b23)



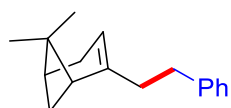
Following **GP-III-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S10) (596 mg, 2.0 mmol) with cyclohex-2-enyl acetate (280 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (232 mg, 37% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 8.08 – 7.82 (m, 2H), 7.29 – 7.04 (m, 2H), 5.66 (m, 1H), 5.57 – 5.40 (m, 1H), 3.85 (d, J = 1.8 Hz, 3H), 2.59 (qd, J = 13.2, 7.6 Hz, 2H), 2.01 – 1.84 (m, 2H), 1.76 – 1.60 (m, 2H), 1.57 – 1.37 (m, 1H), 1.36 – 1.06 (m, 1H).

^{13}C NMR (75 MHz, Chloroform- d) δ 166.96, 146.36, 143.38, 130.69, 129.48, 129.07, 127.82, 51.78 (d, J = 5.0 Hz), 42.64, 36.94, 28.81, 25.26, 21.17.

HRMS (APPI-P): $[\text{MH}]^+$ calculated for ($\text{C}_{15}\text{H}_{19}\text{O}_2^+$) 231.1380; Found 231.1385.

Nopyl-benzene (III-b24)



Following **GP-III-A**, S1(480 mg, 2.0 mmol) and mystery acetate (485 mg, 2.5 mmol) were used and reacted for 24 h, affording the title compound as a colorless oil (244 mg, 54% yield) after purification by flash chromatography (SiO_2 : pure pentane).

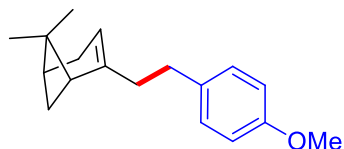
^1H NMR (300 MHz, Chloroform- d) δ 7.43 – 7.35 (m, 2H), 7.30 (m, 3H), 5.38 (dt, J = 2.7, 1.4 Hz, 1H), 2.87 – 2.76 (m, 2H), 2.54 – 2.47 (m, 1H), 2.44 – 2.33 (m, 3H), 2.22 (dt, J = 5.6, 1.6 Hz, 2H), 1.43 (s, 3H), 1.32 (d, J = 8.5 Hz, 1H), 1.00 (s, 3H).

¹⁴⁴ E. Le Saux, M. Zanini, P. Melchiorre, *J. Am. Chem. Soc.* **2022**, *144*, 3, 1113.

^{13}C NMR (75 MHz, Chloroform- d) δ 147.97, 142.54, 128.38, 128.28, 125.70, 116.25 (d, $J = 2.6$ Hz), 46.03, 40.99, 38.97, 38.07, 34.02, 31.75, 31.38, 26.47 (d, $J = 1.9$ Hz), 21.31.

HRMS (APPI-P): $[\text{MH}]^+$ calculated for ($\text{C}_{17}\text{H}_{23}^+$) 227.1794; Found 227.1789.

4-Nopyl-anisole (III-b25)



Following **GP-III-A**, the 4-methoxybenzyltrimethylsulfonium tetrafluoroborate salt (S11) (540 mg, 2.0 mmol) and myrtenyl acetate (485 mg, 2.5 mmol) were used, affording the title compound as a colorless oil (263 mg, 58% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.17 (d, $J = 8.6$ Hz, 2H), 7.03 – 6.87 (m, 2H), 5.31 (dt, $J = 3.0, 1.6$ Hz, 1H), 3.84 (s, 3H), 2.75 – 2.61 (m, 2H), 2.46 (dt, $J = 8.4, 5.6$ Hz, 1H), 2.37 – 2.25 (m, 4H), 2.17 (dd, $J = 5.9, 1.5$ Hz, 2H), 1.38 (s, 3H), 1.26 (d, $J = 8.4$ Hz, 1H), 0.94 (s, 3H).

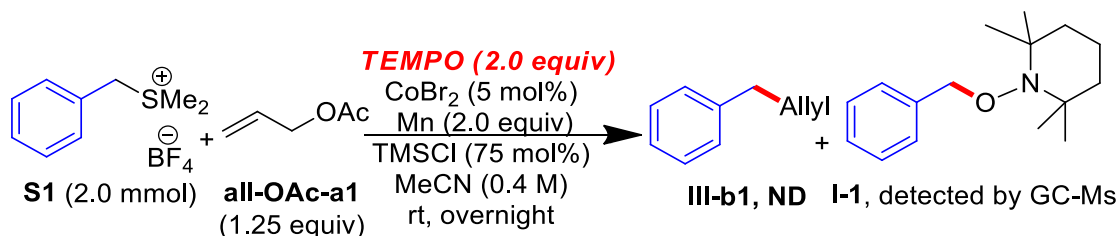
^{13}C NMR (75 MHz, Chloroform- d) δ 157.74, 148.03, 134.60, 129.21, 113.71, 55.19 (d, $J = 4.5$ Hz), 45.99, 40.96, 39.21, 38.04, 33.06, 31.73, 31.35, 26.46 (d, $J = 1.8$ Hz), 21.30.

HRMS (APPI-P): $[\text{MH}]^+$ calculated for ($\text{C}_{18}\text{H}_{25}\text{O}^+$) 257.1900; Found 257.1895.

5.2. Mechanistic experiments

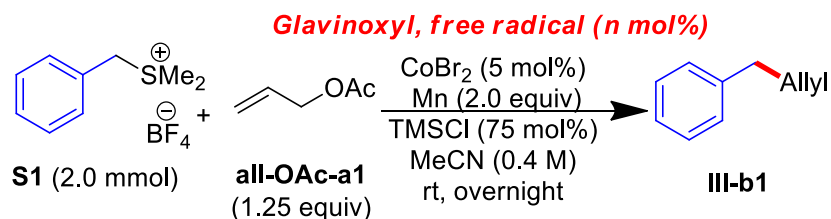
5.2.1. Radical trapping experiments of S1 with allyl acetate (A-OAc-a1)

a) The reaction with TEMPO.



In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and TEMPO (628 mg, 4.0 mmol, 2.0 equiv) were added. The tube was filled with N₂ three times, and the MeCN (5.0 mL), all-OAc-a1 (270 μL, 2.5 mmol, 1.25 equiv) was added by syringe under N₂. The mixture was stirred and then TMSCl (190 μL, 1.5 mmol, 75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to stir overnight at rt. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

b) The reaction of S1 and all-OAc-a1 with glavinoyl, free radical



Entry	n (mol %)	GC yield of III-b1 ^a / %
1	50	48
2	100	19
3	200	7

^aGC yields using dodecane as an internal standard.

In an oven-dried, 20-mL reaction tube, S1 (480 mg, 2.0 mmol, 1.0 equiv), Mn powder (220 mg, 4.0 mmol, 2.0 equiv), CoBr₂ (21.8 mg, 0.1 mmol, 5 mol%) and glavinoyl, free radical (422 mg, 1 mmol 50 mol%; 844 mg, 2 mmol, 100 mol%; 1.67 g, 4 mmol, 200 mol% respectively) were added. The tube was filled with N₂ three times, and the MeCN (5.0 mL), all-OAc-a1 (270 μL, 2.5 mmol, 1.25 equiv) was added by syringe under N₂. The mixture was stirred and then TMSCl (190 μL, 1.5 mmol, 75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to stir overnight at rt. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

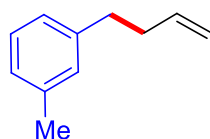
5.3. The cross-coupling of benzyl sulfonium salts and allyl methyl ether

5.3.1. General Procedure of Allylation with Allyl methyl ether (GP-III-B).

In an oven-dried, 20-mL reaction tube, benzyl dimethyl sulfonium tetrafluoroborate salt derivative (S) (1.0 mmol, 1.0 equiv), Mn powder (110 mg, 2.0 mmol, 2.0 equiv), bipyridine (15.6 mg, 0.1 mmol, 10 mol%) and CoBr₂ (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N₂ three times, and added the MeCN (0.75 mL) and allyl methyl ether (all-OMe) (1.25 equiv) by a syringe under N₂. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to heat to 45 °C and stirred overnight. After completion, the reaction mixture was poured into a solution of 2N HCl and extracted with diethyl ether. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether) afforded the corresponding product characterized by NMR (¹H, ¹³C, ¹⁹F).

- Characterization data of products

4-(3-Methylphenyl)-1-butene (III-34) [20574-99-6]



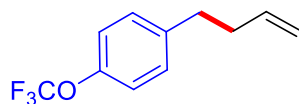
Following **GP-III-B**, the 4-methylbenzyl dimethyl sulfonium tetrafluoroborate salt (S2) (274 mg, 1.0 mmol) with all-OMe (117 μL, 1.25 mmol) was used, affording the title compound as a colorless oil (107 mg, 73% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.16 (s, 4H), 5.94 (m, 1H), 5.17 – 4.78 (m, 0H), 2.75 (dd, *J* = 9.1, 6.6 Hz, 2H), 2.50 – 2.17 (m, 5H).

¹³C NMR (75 MHz, Chloroform-d) δ 139.61, 139.01, 136.02, 129.81, 129.13, 115.65, 36.51, 35.78, 21.84.

The spectroscopic data match the reported one in the literature.¹³⁶

4-(4-Trifluoromethoxy phenyl)-1-butene (III-35)



Following **GP-III-B**, the 4-trifluoromethoxy benzyl dimethyl sulfonium tetrafluoroborate salt (S13) (324 mg, 1.0 mmol) with all-OMe (117 μL, 1.25 mmol) was used, affording the title compound as a colorless oil (134 mg, 62% yield) after purification by flash chromatography (SiO₂: pure pentane).

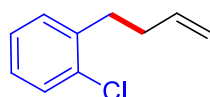
^1H NMR (300 MHz, Chloroform-d) δ 7.43 – 7.02 (m, 4H), 5.87 (m, 1H), 5.37 – 4.75 (m, 2H), 2.74 (dd, J = 8.9, 6.6 Hz, 2H), 2.53 – 2.17 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-d) δ 148.15, 141.30, 138.28, 130.38, 123.77 – 118.48 (m), 116.02, 36.12, 35.41.

^{19}F NMR (282 MHz, Chloroform-d) δ -58.00.

HRMS (APPI-P): $[\text{MH}]^+$ calculated for $(\text{C}_{11}\text{H}_{12}\text{F}_3\text{O}^+)$ 217.0835; Found 217.0833.

1-Allyl-2-chlorobenzene (III-b36) [3047-25-4]



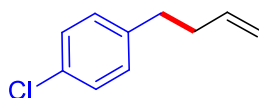
Following **GP-III-B**, the 2-chlorobenzyltrimethylsulfonium tetrafluoroborate salt (S14) (274 mg, 1.0 mmol) with all-OMe (117 μL , 1.25 mmol) was used, affording the title compound as a colorless oil (88 mg, 53% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform-d) δ 7.36 (dd, J = 7.5, 1.8 Hz, 1H), 7.25 – 7.12 (m, 3H), 5.90 (m, 1H), 5.29 – 4.95 (m, 2H), 2.92 – 2.72 (m, 2H), 2.55 – 2.12 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-d) δ 140.12, 138.48, 134.71, 131.19, 130.23, 128.10, 127.45, 115.96, 34.50, 33.88.

The spectroscopic data match the reported one in the literature.¹⁴⁵

1-(But-3-en-1-yl)-4-chlorobenzene (III-b37) [3047-24-3]



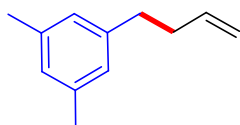
Following **GP-III-B**, the 4-chlorobenzyltrimethylsulfonium tetrafluoroborate salt (S6) (274 mg, 1.0 mmol) with all-OMe (117 μL , 1.25 mmol) was used, affording the title compound as a colorless oil (95 mg, 57% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform-d) δ 7.28 (d, J = 8.3 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 5.86 (m, 1H), 5.30 – 4.79 (m, 2H), 2.71 (dd, J = 8.8, 6.7 Hz, 2H), 2.53 – 2.31 (m, 2H).

^{13}C NMR (75 MHz, Chloroform-d) δ 140.26, 137.65, 131.55, 129.84, 128.41, 115.32, 35.43, 34.73.

The spectroscopic data match the reported one in the literature.¹³⁶

1-Allyl-3,5-dimethylbenzene (III-b38)



¹⁴⁵ F.-P. Wu, D. Li, J.-B. Peng, X.-F. Wu, *Org. Lett.* **2019**, *21*, 14, 5699.

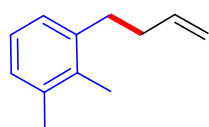
Following **GP-III-B**, the 3,5-dimethylbenzyltrimethylsulfonium tetrafluoroborate salt (S5) (268 mg, 1.0 mmol) with all-OMe (117 μ L, 1.25 mmol) was used, affording the title compound as a colorless oil (92 mg, 61% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 6.92 (d, J = 3.1 Hz, 3H), 5.97 (m, 1H), 5.46 – 4.77 (m, 2H), 2.73 (dd, J = 9.4, 6.5 Hz, 2H), 2.39 (s, 8H).

¹³C NMR (75 MHz, Chloroform-d) δ 142.63, 139.11, 138.54 (d, J = 1.1 Hz), 128.28, 127.09, 115.53, 36.48, 36.12, 22.11.

The spectroscopic data match the reported one in the literature.¹⁴⁵

1-But-3-enyl-2,3-dimethylbenzene (III-b39)



Following **GP-III-B**, the 2,3-dimethylbenzyltrimethylsulfonium tetrafluoroborate salt (S15) (268 mg, 1.0 mmol) with all-OMe (117 μ L, 1.25 mmol) was used, affording the title compound as a colorless oil (71 mg, 44% yield) after purification by flash chromatography (SiO₂: pure pentane).

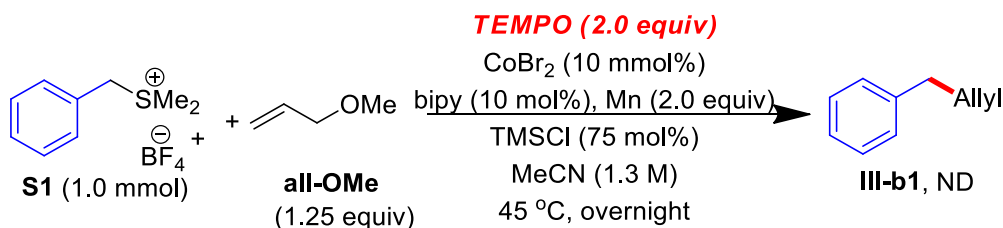
¹H NMR (300 MHz, Chloroform-d) δ 7.10 (d, J = 1.2 Hz, 3H), 5.98 (ddt, J = 16.8, 10.1, 6.6 Hz, 1H), 5.42 – 4.82 (m, 2H), 2.85 – 2.72 (m, 2H), 2.46 – 2.32 (m, 5H), 2.29 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 139.98, 138.41, 136.83, 134.44, 127.80, 126.92, 125.37, 114.72, 34.76, 33.58, 20.75 (d, J = 3.3 Hz), 15.03 (d, J = 3.6 Hz).

HRMS (APCI-P): [MH]⁺ calculated for (C₁₂H₁₇)⁺ 161.1325; Found 161.1318.

5.3.2. Mechanistic experiments of S1 with allyl methyl ether (all-OMe).

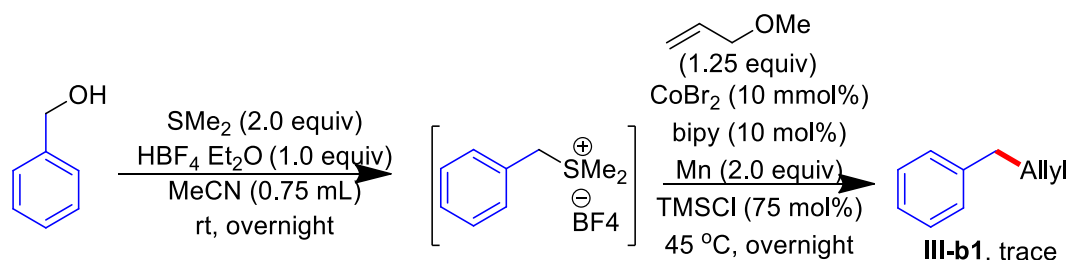
5.3.2.1. Radical trapping experiments of S1 with all-OMe



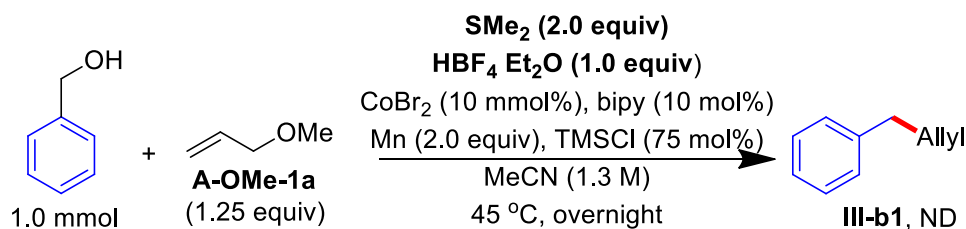
In an oven-dried, 20-mL reaction tube, S1 (240 mg, 1.0 mmol, 1.0 equiv), Mn powder (110 mg, 2.0 mmol, 2.0 equiv), bipyridine (15.6 mg, 0.1 mmol, 10 mol%), CoBr₂ (21.8 mg, 0.1 mmol, 10 mol%) and TEMPO (312 mg, 2.0 mmol, 2.0 equiv) were added. The tube was filled with N₂ three times, and the MeCN (0.75 mL) and all-OMe (117 μ L, 1.25 equiv) were added) by syringe under N₂. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to heat to 45 °C and stirred overnight. After completion, the reaction

mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

5.3.2.2. One-spot experiments of S1 with All-OMe

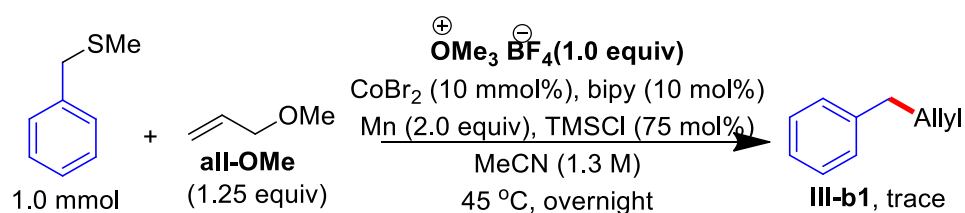


- a)** In an oven-dried, 20-mL reaction tube, in the solution MeCN (0.75 mL) with benzyl alcohol (108 mg, 1.0 mmol, 1.0 equiv), dimethyl sulfide (124 mg, 2.0 mmol, 2.0 equiv), the tetrafluoroboric acid diethyl ether complex ($\text{HBF}_4 \cdot \text{O}(\text{CH}_2\text{CH}_3)_2$) (162 mg, 1 mmol, 1.0 equiv) was added dropwise at 0 °C. And the mixture was allowed to be stirred at rt overnight. Then Mn powder (110 mg, 2.0 mmol, 2.0 equiv), bipyridine (15.6 mg, 0.1 mmol, 10 mol%), and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added to the former mixture without work-up under N_2 . Then all-OMe (117 μL , 1.25 equiv) was injected by syringe. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. The reaction mixture was allowed to heat to 45 °C and stirred overnight. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.



- b)** In an oven-dried, 20-mL reaction tube, Mn powder (110 mg, 2.0 mmol, 2.0 equiv), bipyridine (15.6 mg, 0.1 mmol, 10 mol%), and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N_2 three times and added MeCN (0.75 mL), benzyl alcohol (108 mg, 1.0 mmol, 1.0 equiv), dimethyl sulfide (124 mg, 2.0 mmol, 2.0 equiv), the tetrafluoroboric acid diethyl ether complex ($\text{HBF}_4 \cdot \text{O}(\text{CH}_2\text{CH}_3)_2$) (162 mg, 1 mmol, 1.0 equiv) and all-OMe (117 μL , 1.25 equiv) by syringe. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to heat to 45 °C and stirred overnight. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

c) Using the method reported by Berchtold.¹⁰⁸



In an oven-dried, 20-mL reaction tube, Mn powder (110 mg, 2.0 mmol, 2.0 equiv), bipyridine (15.6 mg, 0.1 mmol, 10 mol%), CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) and trimethyloxonium tetrafluoroborate (148 mg, 1.0 mmol, 1.0 equiv) were added. The tube was filled with N_2 three times and added MeCN (0.75 mL), benzyl methyl sulfide (138 mg, 1.0 mmol, 1.0 equiv), and all-O-Me (117 μL , 1.25 equiv) by syringe. The mixture was stirred, and then TMSCl (75 mol%, to be sure that the reaction was triggered) was added at rt. Then the reaction mixture was allowed to heat to 45 °C and stirred overnight. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

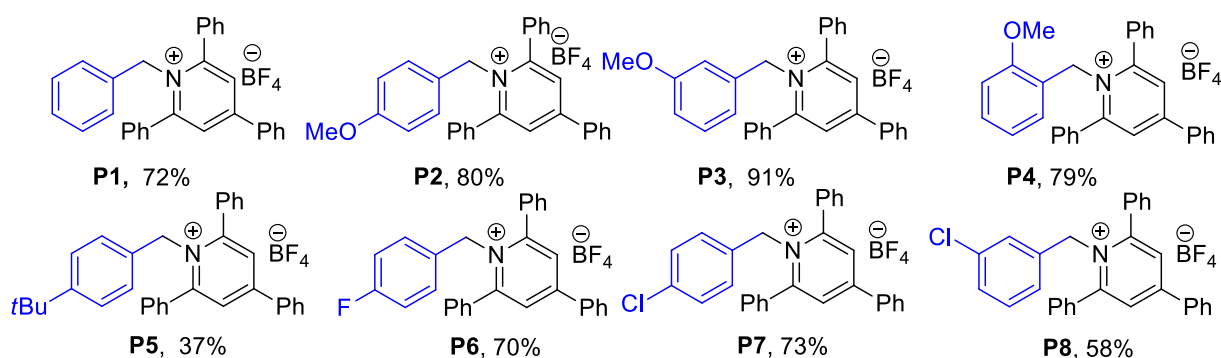
6. General Procedure for Benzyl Katritzky Pyridinium Salts and C-O Electrophiles

6.1. General procedure for benzyl Katritzky pyridinium salts

- a) **GP-IV-A**¹⁴⁶: The amine (1.2 - 1.4 equiv) was added to a suspension of 2,4,6-triphenylpyrylium tetrafluoroborate in EtOH (1 M), which led to an immediate color change to deep red, and dissolving of the material. Then, the solution was refluxed for the indicated time and cooled to rt. Then, Et₂O was added. If a precipitate formed, the suspension was stirred for 1 h; the material was filtered off and washed with Et₂O. After drying under a vacuum, the product was obtained. In cases of no precipitate, sticky material had formed, all solvents were removed under vacuum, and the crude material was dissolved in DCM. and purified by column chromatography (0 – 10% MeOH /DCM).
- b) **GP-IV-B**¹⁴⁷: 2,4,6-triphenylpyrylium tetrafluoroborate (1.0 equiv.) was added to a stirred solution of the primary amine (1.2 - 1.4 equiv.) in CH₂Cl₂ (0.5 M) in a round bottom flask. And then, AcOH (2.0 equiv) was added after 15 min. The reaction mixture was stirred at room temperature overnight. If product precipitation occurred, the solid was filtered, washed with Et₂O, and dried under a high vacuum. If product precipitation did not occur, the solvent was removed in vacuo. It was subjected to flash column chromatography, eluting with 0 – 10% MeOH /DCM.

P1¹⁴⁶, **P6**¹⁴⁶, **P8**¹⁴⁶, **P9**¹⁴⁶, **P10**¹⁴⁸, **P11**¹⁴⁶, **P12**¹⁴⁹, **P13**¹⁵⁰, and **P15**¹⁴⁸ were synthesized according to **GP-IV-A**. Their spectroscopic data match the reported one in the literature.

P2¹⁴⁸, **P3**¹⁴⁷, **P4**¹⁴⁹, **P5**¹⁵⁰, **P7**¹⁴⁷, **P14**¹⁴⁸, and **P16**¹⁴⁸ were synthesized according to **GP-IV-B**. Their spectroscopic data match the reported one in the literature.



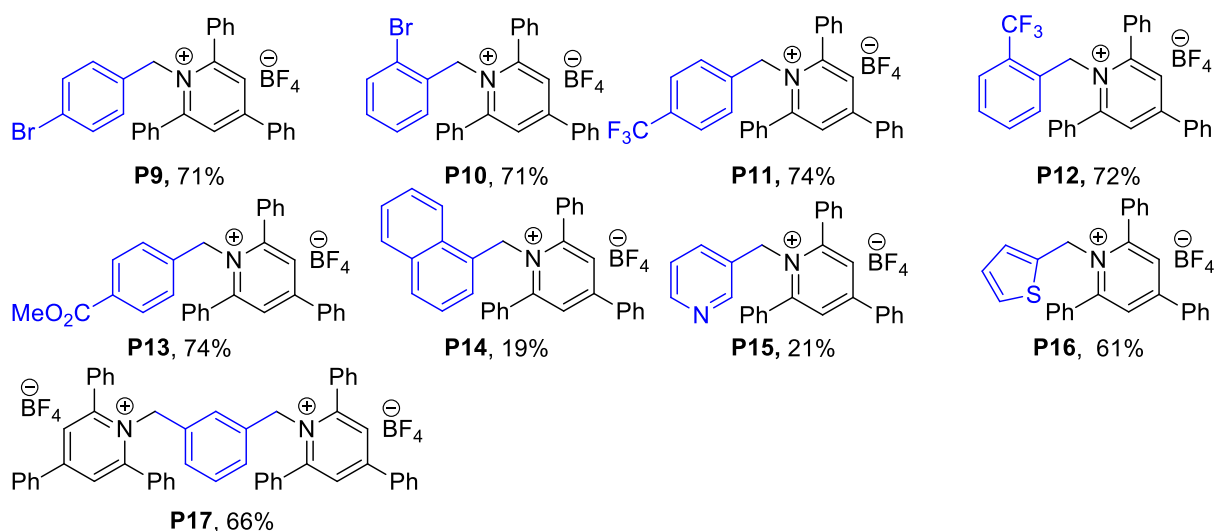
¹⁴⁶ D. Schönbauer, C. Sambaglio, T. Noël, B. M. Schnürch. *J. Org. Chem.* **2020**, *16*, 809. doi:10.3762/bjoc.16.74.

¹⁴⁷ J. A. Andrews, L. R. E. Pantaine, C. F. Palmer, D. L. Poole, M. C. Willis. *Org. Lett.* **2021**, *23*, 21, 8488.

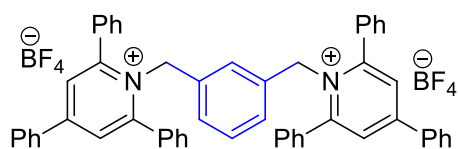
¹⁴⁸ F. J. R. Klauk, H. Toon, M. J. James, M. Lautens and F. Glorius, *ACS Catal.*, **2019**, *9*, 236

¹⁴⁹ Y. Huang, J. Jia, Q. P. Huang, L. Zhao, P. Wang, J. Gu, C. Y. He. *Chem. Commun.*, **2020**, *56*, 14247.

¹⁵⁰ D. J. Charboneau, H. Huang, E. L. Barth, C. C. Germe, N. Hazari, B. Q. Mercado, M. R. Uehling, S. L. Zultanski. *J. Am. Chem. Soc.* **2021**, *143*, 49, 21024.



- **Characterization data of P17**



Following **GP-IV-A** with 1,3-di(aminomethyl)benzene (1 g, 7.5 mmol) was used, affording the corresponding benzyl Katritzky pyridinium salt **P17** as a light-yellow solid (4.4 g, 66%).

^1H NMR (300 MHz, Chloroform- d) δ 7.83 (s, 4H), 7.81 – 7.74 (m, 4H), 7.52 (dt, J = 5.9, 2.0 Hz, 14H), 7.43 – 7.32 (m, 12H), 6.83 (t, J = 7.8 Hz, 1H), 6.22 (dd, J = 7.9, 1.7 Hz, 2H), 5.81 (d, J = 1.7 Hz, 1H), 5.63 (s, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 157.37, 156.65, 134.55, 133.64, 132.51, 130.95, 129.76, 129.26, 129.13, 128.22, 126.73.

^{19}F NMR (282 MHz, Chloroform- d) δ -152.17 (d, J = 2.5 Hz).

HRMS (ESI $^{2+}$) m/z : [M^{2+}] calculated for ($\text{C}_{54}\text{H}_{42}\text{N}_2^{2+}$) 359.1678; Found 359.1669.

6.2. The cross-coupling of benzyl Katritzky pyridinium salts and allyl derivatives

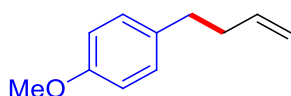
6.2.1. General procedure of allylation from benzyl pyridinium salts and allyl derivatives (GP-IV-A)

In an oven-dried, 20-mL reaction tube, benzyl Katritzky pyridinium salt (**P**) (1.0 mmol, 1.0 equiv), Mn powder (110 mg, 2.0 mmol, 2.0 equiv) and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N_2 three times, and added the MeCN (1.0 mL) and allyl derivatives (**All-OR**) (1.75 equiv, if it is liquid) were under N_2 . The mixture was stirred at rt, and then TMSBr (100 μL , 0.75 mmol, 75

mol%) was added. After the reaction mixture was allowed to stir overnight (around 15 h) at 45 °C., the mixture was poured into a solution of 2N HCl and extracted with DCM. The organic layer was washed with a saturated solution of NaCl and dried over MgSO₄. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether) afforded the corresponding product characterized by NMR (¹H, ¹³C, ¹⁹F).

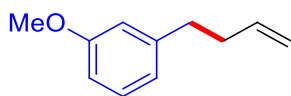
- **Characterization data of products**

4-(p-Methoxyphenyl)but-1-ene (III-b2) [20574-98-5]



Following **GP-IV-A**, the 4-methoxybenzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with All-OAc-a1(189 μL, 1.75mmol) was used, affording the title compound as a colorless oil (66 mg, 41% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

4-(3-Methoxyphenyl)-1-butene (IV-b1) [1199-90-2]



Following **GP-IV-A**, the 3-methoxybenzyl Katritzky pyridinium salt (P3) (515 mg, 1.0 mmol)

- ♣ with all-OMe (164 μL, 1.75mmol) was used, affording the title compound as a colorless oil (111 mg, 68% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).
- ♣ with all-OAc-a1(189 μL, 1.75mmol) was used, affording the title compound as a colorless oil (78 mg, 48% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.29 – 7.15 (m, 1H), 6.94 – 6.70 (m, 3H), 4.84 – 4.66 (m, 2H), 3.82 (s, 3H), 2.90 – 2.66 (m, 2H), 2.47 – 2.23 (m, 2H), 1.80 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 160.36, 146.11, 144.65, 130.00, 121.52, 114.89, 111.77, 110.97, 55.88, 40.25, 35.07, 23.40.

The spectroscopic data match the reported one in the literature.¹⁵¹

4-(2-Methoxyphenyl)-1-butene (IV-b2) [63667-83-4]



¹⁵¹ A. Nouaille, X. Pannecoucke, T. Poisson, S. Couve-Bonnaire, *Adv. Synth. Catal.* **2021**, 363, 2140.

Following **GP-IV-A**, the 2-methoxybenzyl Katritzky pyridinium salt (P4) (515 mg, 1.0 mmol)

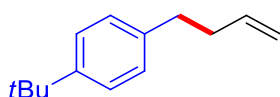
- ♣ with all-OMe (164 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (150 mg, 87% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).
- ♣ with all-OAc-a1(189 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (87 mg, 54% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.33 – 7.12 (m, 2H), 7.08 – 6.75 (m, 2H), 5.94 (ddtd, J = 16.8, 10.2, 6.6, 0.8 Hz, 1H), 5.35 – 4.81 (m, 2H), 3.86 (d, J = 0.9 Hz, 3H), 2.77 (dd, J = 9.1, 6.5 Hz, 2H), 2.55 – 2.25 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 157.48, 138.77, 130.28, 129.87, 127.09, 120.34, 114.51, 110.22, 55.25, 33.96, 29.85.

The spectroscopic data match the reported one in the literature.¹⁵¹

1-(But-3-en-1-yl)-4-(tert-butyl)benzene (IV-b3)



Following **GP-IV-A**, the 4-(tert-butyl) benzyl Katritzky pyridinium salt (P5) (541 mg, 1.0 mmol)

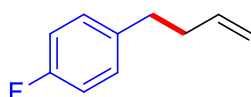
- ♣ with all-OMe (164 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (123 mg, 71% yield) after purification by flash chromatography (SiO₂: pure pentane).
- ♣ with all-OAc-a1(189 μ L, 1.75mmol) were used, affording the title compound as a colorless oil (141 mg, 75% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.42 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 5.98 (ddt, J = 16.8, 10.2, 6.5 Hz, 1H), 5.48 – 4.86 (m, 2H), 2.79 (dd, J = 9.3, 6.5 Hz, 2H), 2.49 (td, J = 6.9, 3.1 Hz, 2H), 1.42 (s, 9H).

¹³C NMR (75 MHz, Chloroform-d) δ 148.63, 138.91, 138.40, 128.15, 125.28, 114.87, 35.63, 34.95, 34.46, 31.54.

The spectroscopic data match the reported one in the literature.¹⁵¹

1-(But-3-en-1-yl)-4-fluorobenzene (IV-b5)



Following **GP-IV-A**, the 4-fluorobenzyl Katritzky pyridinium salt (P6) (503 mg, 1.0 mmol)

- ♣ with all-OMe (164 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (44 mg, 29% yield) after purification by flash chromatography (SiO₂: pure pentane).

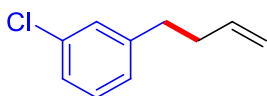
- ♣ with all-OAc-a1(189 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (67 mg, 45% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.14 (dd, J = 8.3, 5.4 Hz, 2H), 6.97 (t, J = 8.5 Hz, 2H), 5.85 (ddt, J = 16.8, 10.2, 6.5 Hz, 1H), 5.02 (t, J = 13.9 Hz, 2H), 2.69 (t, J = 7.8 Hz, 2H), 2.36 (q, J = 7.4 Hz, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 162.85, 159.63, 137.79, 137.42 (d, J = 3.2 Hz), 129.75 (d, J = 7.7 Hz), 116.02 – 113.65 (m), 35.65, 34.55.

The spectroscopic data match the reported one in the literature.¹⁵¹

1-(But-3-en-1-yl)-3-chlorobenzene (IV-b6) [91426-46-9]



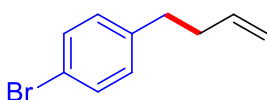
Following **GP-IV-A**, the 3-chlorobenzyl Katritzky pyridinium salt (P7) (503 mg, 1.0 mmol) with all-OAc-a1(189 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (100 mg, 60% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.22 (d, J = 7.1 Hz, 3H), 7.09 (dt, J = 6.5, 1.8 Hz, 1H), 5.86 (ddt, J = 16.7, 9.9, 6.6 Hz, 1H), 5.31 – 4.73 (m, 2H), 2.71 (dd, J = 9.0, 6.5 Hz, 2H), 2.52 – 2.28 (m, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 144.62, 138.25, 134.80, 130.28, 129.34, 127.41, 126.77 (d, J = 3.1 Hz), 35.96 (d, J = 2.4 Hz), 35.77.

The spectroscopic data match the reported one in the literature.¹⁵¹

1-(3-Butenyl)-4-bromobenzene (IV-b7) [15451-32-8]



Following **GP-IV-A**, the 4-bromobenzyl Katritzky pyridinium salt (P9) (564 mg, 1.0 mmol)

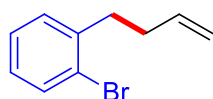
- ♣ with all-OAc-a1(189 μ L, 1.75mmol) was used, affording the title compound as a colorless oil (67 mg, 32% yield) after purification by flash chromatography (SiO₂: pure pentane).

- ♣ with all-OCO₂Me (199 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (105 mg, 50% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.41 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.1 Hz, 2H), 5.84 (ddt, J = 16.9, 10.2, 6.6 Hz, 1H), 5.30 – 4.75 (m, 2H), 2.68 (dd, J = 8.9, 6.7 Hz, 2H), 2.49 – 2.24 (m, 2H).

The spectroscopic data match the reported one in the literature.¹⁵¹

1-bromo-2-(but-3-en-1-yl)benzene (IV-b8) [71813-50-8]



Following **GP-IV-A**, the 2-bromobenzyl Katritzky pyridinium salt (P10) (564 mg, 1.0 mmol)

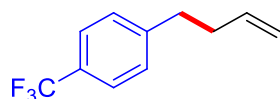
- ♣ with all-OAc-a1 (189 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (151 mg, 72% yield) after purification by flash chromatography (SiO₂: pure pentane).
- ♣ with all-OMe (164 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (99 mg, 50% yield) after purification by flash chromatography (SiO₂: pure pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.59 (d, J = 8.0 Hz, 1H), 7.35 – 7.22 (m, 2H), 7.11 (ddd, J = 7.1, 4.3, 1.5 Hz, 1H), 6.06 – 5.83 (m, 1H), 5.22 – 4.95 (m, 2H), 2.89 (dd, J = 9.2, 6.6 Hz, 2H), 2.44 (dtd, J = 7.9, 6.5, 1.4 Hz, 2H).

¹³C NMR (75 MHz, Chloroform-d) δ 141.07, 137.66, 132.81, 130.42, 127.61, 127.36, 124.49, 115.23, 35.68, 33.88.

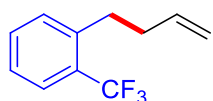
The spectroscopic data match the reported one in the literature.¹⁵¹

4-(4-Trifluoromethylphenyl)-1-butene (III-b6)



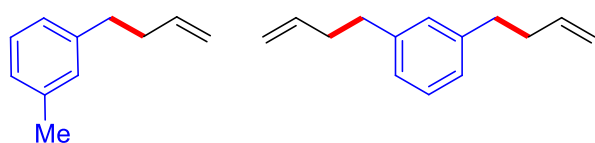
Following **GP-IV-A**, the 4-(trifluoromethyl) benzyl Katritzky pyridinium salt (P11) (553 mg, 1.0 mmol) and with all-OCO₂Me (199 μ L, 1.75 mmol) were used, affording the title compound as a colorless oil (87 mg, 43% yield) after purification by flash chromatography (SiO₂: pure pentane).

1-(But-3-en-1-yl)-2-(trifluoromethyl)benzene (III-b5)



Following **GP-IV-A**, the 4-(trifluoromethyl) benzyl Katritzky pyridinium salt (P12) (553 mg, 1.0 mmol) and with All-OCO₂Me (199 μ L, 1.75 mmol) were used, affording the title compound as a colorless oil (92 mg, 46% yield) after purification by flash chromatography (SiO₂: pure pentane).

4-(3-Methylphenyl)-1-butene (III-b4) and 1,3-Bis(but-3-enyl)benzene (IV-b9)



Following **GP-IV-A, P17** (892 mg, 1.0 mmol) and all-OMe (374 μ L, 3.5 mmol) were used, affording the title compound as a colorless oil 4-(3-Methylphenyl)-1-butene (III-b4) (21mg, 14% yield) and 1,3-Bis(but-3-enyl)benzene (IV-b9) (57 mg, 31% yield) after purification by flash chromatography (SiO₂: pure pentane).

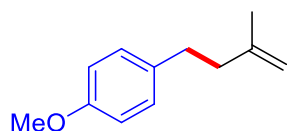
1,3-Bis(but-3-enyl)benzene (IV-b9):

¹H NMR (300 MHz, Chloroform-d) δ 7.42 – 7.12 (m, 1H), 7.17 – 6.92 (m, 3H), 6.07 – 5.65 (m, 1H), 5.39 – 4.79 (m, 4H), 2.71 (dd, J = 9.3, 6.3 Hz, 4H), 2.44 – 2.17 (m, 4H).

¹³C NMR (75 MHz, Chloroform-d) δ 142.61 (d, J = 1.2 Hz), 129.39, 128.99, 126.67 (d, J = 1.2 Hz), 115.59, 36.34, 36.15 (d, J = 1.3 Hz).

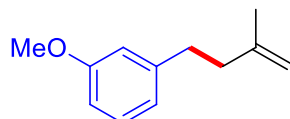
HRMS (APCI-P): [MH]⁺ calculated for (C₁₄H₁₉⁺) 187.1478; Found 187.1481.

4-(4-Methoxyphenyl)-2-methyl-1-butene (III-b9) [18491-21-9]



Following **GP-IV-A**, the 4-methoxybenzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with methylallyl acetate (217 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (97 mg, 55% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

5-(3-methoxyphenyl)-2-pentene (IV-b13) [162707-40-6]



Following **GP-IV-A**, the 3-methoxybenzyl Katritzky pyridinium salt (P3) (515 mg, 1.0 mmol) with methylallyl acetate (186 μ L, 1.5 mmol) was used, affording the title compound as a colorless oil (106 mg, 60% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.29 – 7.15 (m, 1H), 6.94 – 6.70 (m, 3H), 4.84 – 4.66 (m, 2H), 3.82 (s, 3H), 2.90 – 2.66 (m, 2H), 2.47 – 2.23 (m, 2H), 1.80 (s, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 160.36, 146.1, 144.65, 130.00, 121.52, 114.89, 111.77, 110.97, 55.88, 40.25, 35.07, 23.40.

HRMS (APCI-P): [MH]⁺ calculated for (C₁₂H₁₇O⁺) 177.1270; Found 177.1274.

(E)-3-Pentenylbenzene (IV-b14)



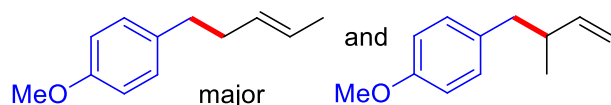
Following **GP-IV-A**, P1 (480 mg, 1.0 mmol) with trans-2-butenyl acetate (134 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (106 mg, 72% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.42 – 7.34 (m, 2H), 7.33 – 7.24 (m, 3H), 5.58 (td, J = 3.6, 1.9 Hz, 2H), 2.77 (dd, J = 9.1, 6.6 Hz, 2H), 2.61 – 2.29 (m, 2H), 1.76 (dq, J = 2.7, 1.4 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 142.98, 131.39, 129.25, 129.03, 126.48, 126.18, 36.93, 35.30, 18.73.

The spectroscopic data match the reported one in the literature.¹⁵²

5-(4-Methoxyphenyl)-2-pentene (III-b10) [140836-82-4]



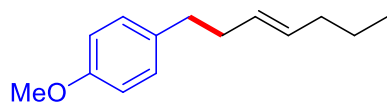
Following **GP-IV-A**, the 4-methoxybenzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with trans-2-butenyl acetate (134 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (96 mg, 55% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

(4-Methylpent-3-en-1-yl)benzene (III-b11)[33501-90-5]



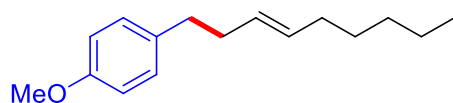
Following **GP-IV-A**, P1 (480 mg, 1.0 mmol) with 3-methylbut-2-enyl acetate (217 μ L, 1.75 mmol) was used, affording the title compound as a colorless oil (77 mg, 48% yield) after purification by flash chromatography (SiO₂: pure pentane).

(4E)-7-(4-Methoxybenzyl)-4-heptene (III-b13)



Following **GP-IV-A**, the 4-methoxybenzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with (E)-2-hexen-1-yl acetate (190 μ L, 1.5 mmol) were used, affording the title compound as a colorless oil (127 mg, 62% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

(E)-1-(4'-methoxyphenyl)non-3-ene (IV-b15)



¹⁵²Y.-L. Lai, J.-M. Huang, *Org. Lett.* **2017**, *19*, 8, 2022

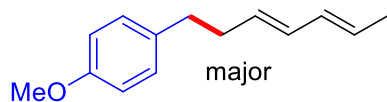
Following **GP-IV-A**, the 4-methyl benzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with (*E*)-2-octen-1-yl acetate (256 mg, 1.5 mmol) was used, affording the title compound as a colorless oil (125 mg, 51% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.14 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.48 (q, *J* = 4.1, 3.2 Hz, 2H), 3.82 (s, 3H), 2.66 (dd, *J* = 9.0, 6.6 Hz, 2H), 2.45 – 2.26 (m, 2H), 2.12 – 1.95 (m, 2H), 1.57 – 1.17 (m, 6H), 0.95 (t, *J* = 6.9 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.45, 135.07, 131.89, 130.12 (d, *J* = 4.0 Hz), 114.39, 55.96, 36.04, 35.51, 33.34, 32.15, 30.04, 23.35, 14.86.

The spectroscopic data match the reported one in the literature.¹⁵³

(2*E*,4*E*)-7-(4-Methoxyphenyl) hepta-2,4-diene (IV-b16)



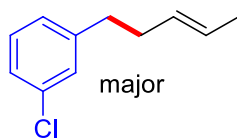
Following **GP-IV-A**, the 4-methyl benzyl Katritzky pyridinium salt (P2) (515 mg, 1.0 mmol) with (*E*)-2-hexen-1-yl acetate (190 μL, 1.5 mmol) was used, affording the title compound as a colorless oil (89 mg, 44% yield) after purification by flash chromatography (SiO₂: 5% diethyl ether in pentane).

¹H NMR (300 MHz, Chloroform-d) δ 7.22 – 7.04 (m, 2H), 6.88 (dd, *J* = 8.6, 2.2 Hz, 2H), 6.15 – 5.94 (m, 2H), 5.85 – 5.51 (m, 2H), 3.82 (s, 3H), 2.69 (dd, *J* = 9.1, 6.7 Hz, 2H), 2.42 (dd, *J* = 16.3, 9.1 Hz, 2H), 1.78 (d, *J* = 6.5 Hz, 3H).

¹³C NMR (75 MHz, Chloroform-d) δ 158.53, 134.79, 132.38, 131.75, 131.56, 130.06, 127.95, 114.48, 55.99, 35.79, 35.48 (d, *J* = 1.9 Hz), 18.81.

HRMS (APCI-P): [MH]⁺ calculated for (C₁₄H₁₉O⁺) 203.1427; Found 203.1430.

1-Chloro-3-[(*Z*)-pent-3-enyl]benzene (IV-b18)



Following **GP-IV-A**, the 2-chlorobenzyl Katritzky pyridinium salt (P8) (519 mg, 1.0 mmol) with 2-acetoxy-3-butene (224 μL, 1.5 mmol) was used, affording the title compound as a colorless oil (110 mg, 61% yield) after purification by flash chromatography (SiO₂: pure pentane).

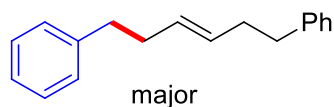
¹H NMR (300 MHz, Chloroform-d) δ 7.31 – 7.13 (m, 3H), 7.08 (dt, *J* = 6.7, 1.8 Hz, 1H), 5.48 (td, *J* = 3.7, 1.9 Hz, 2H), 2.66 (dd, *J* = 9.1, 6.6 Hz, 2H), 2.43 – 2.18 (m, 2H), 1.68 (dd, *J* = 3.4, 1.3 Hz, 3H).

¹⁵³ S. E. Denmark, A. Jaunet. *J. Org. Chem.* **2014**, *79*, 140.

^{13}C NMR (75 MHz, Chloroform- d) δ 144.95, 134.74, 130.80, 130.23, 129.35, 127.42, 126.67, 126.61, 36.51, 34.93, 18.69.

HRMS (APCI-P): $[\text{M}-\text{H}]^+$ calculated for $(\text{C}_{11}\text{H}_{12}\text{Cl}^+)$ 179.0619; Found 179.0622.

(*E*)-1,6-Diphenyl-3-hexene (IV-b19) [52772-46-0]



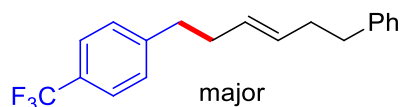
Following **GP-IV-A**, P1 (480 mg, 1.0 mmol) with 5-phenylpenten-3-yl acetate (306 μL , 1.5 mmol) was used, affording the title compound as a colorless oil (117 mg, 49% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.39 (t, $J = 7.2$ Hz, 4H), 7.28 (td, $J = 6.5, 1.7$ Hz, 6H), 5.65 – 5.39 (m, 2H), 2.77 (td, $J = 8.6, 7.9, 4.1$ Hz, 4H), 2.54 – 2.34 (m, 4H).

^{13}C NMR (75 MHz, Chloroform- d) δ 142.91, 130.93, 129.32, 129.08, 126.57, 36.92, 35.27.

The spectroscopic data match the reported one in the literature.¹⁵⁴

(*E*)-1-(4-TrifluoromethylPhenyl)-6-phenyl-3-hexene (IV-b20)

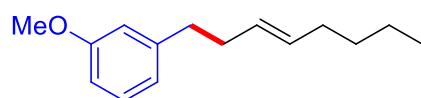


Following **GP-IV-A**, the 4-(trifluoromethyl) benzyl Katritzky pyridinium salt (P11) (553 mg, 1.0 mmol) with 5-phenylpenten-3-yl acetate (357 μL , 1.75 mmol) were used, affording the title compound as a colorless oil (192 mg, 63% yield) after purification by flash chromatography (SiO_2 : pure pentane).

^1H NMR (300 MHz, Chloroform- d) δ 7.59 (d, $J = 8.0$ Hz, 1H), 7.40 – 7.05 (m, 3H), 5.53 (td, $J = 5.3, 3.8$ Hz, 1H), 2.98 – 2.61 (m, 2H), 2.38 (dt, $J = 11.3, 5.7$ Hz, 2H).

^{13}C NMR (75 MHz, Chloroform- d) δ 146.15, 141.96, 130.69, 129.44, 128.82, 128.49, 128.28, 125.80, 125.17 (d, $J = 3.6$ Hz), 35.93 (d, $J = 11.3$ Hz), 34.16 (d, $J = 24.2$ Hz).

(*E*)-1-(3'-Methoxyphenyl) oct-3-ene (IV-b21)



Following **GP-IV-A**, the 3-methoxybenzyl Katritzky pyridinium salt (P3) (515 mg, 1.0 mmol) with 3-Acetoxy-1-heptene (273 mg, 1.75 mmol) was used, affording the title compound as a colorless oil (132 mg, 61% yield) after purification by flash chromatography (SiO_2 : 5% diethyl ether in pentane).

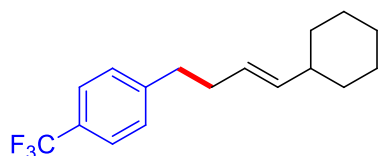
¹⁵⁴ T. Nakagiri, M. Murai, K Takai. *Org. Lett.* **2015**, *17*, 13, 3346.

^1H NMR (300 MHz, Chloroform- d) δ 7.24 (tt, J = 7.2, 1.8 Hz, 1H), 6.92 – 6.67 (m, 3H), 5.69 – 5.30 (m, 2H), 3.84 (s, 3H), 2.70 (td, J = 7.8, 2.0 Hz, 2H), 2.44 – 2.23 (m, 2H), 2.16 – 1.78 (m, 2H), 1.47 – 1.24 (m, 4H), 0.94 (dt, J = 8.4, 4.0 Hz, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 159.59, 143.85, 131.15, 129.28, 129.15, 120.91, 114.24, 111.00, 55.08 (d, J = 4.6 Hz), 36.25, 34.37, 32.26, 31.75, 22.18, 13.97.

HRMS (APCI-P): $[\text{MH}]^+$ calculated for ($\text{C}_{14}\text{H}_{19}\text{O}^+$) 203.1427; Found 203.1430.

4-(*E*-4-cyclohexylbut-3-en-1-yl)- trifluoromethyl-benzene (IV-b22)



Following **GP-IV-A**, the 4-(trifluoromethyl) benzyl Katritzky pyridinium salt (P11) (553 mg, 1.0 mmol) with 1-acetoxy-1-cyclohexyl-2-propene (319 mg, 1.75 mmol) were used, affording the title compound as a colorless oil (132 mg, 47% yield) after purification by flash chromatography (SiO_2 : pure pentane).

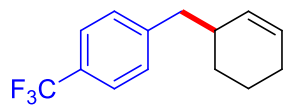
^1H NMR (300 MHz, Chloroform- d) δ 7.55 (d, J = 7.9 Hz, 2H), 7.30 (d, J = 7.9 Hz, 2H), 5.40 (s, 2H), 2.74 (t, J = 7.7 Hz, 3H), 2.40 – 2.27 (m, 2H), 1.92 (tt, J = 11.6, 4.8 Hz, 1H), 1.79 – 1.58 (m, 5H), 1.46 – 1.18 (m, 3H), 1.13 – 0.94 (m, 3H).

^{13}C NMR (75 MHz, Chloroform- d) δ 146.23, 137.74, 136.67, 128.79, 127.10, 125.97, 125.07 (d, J = 3.8 Hz), 40.65, 35.99, 34.11, 33.27, 33.13, 26.36 – 25.89 (m).

^{19}F NMR (282 MHz, Chloroform- d) δ -62.26.

HRMS (APCI-P): $[\text{MH}-\text{H}_2]^+$ calculated for ($\text{C}_{17}\text{H}_{20}\text{F}_3^+$) 281.1506; Found 281.1512.

4-(Cyclohex-2-en-1-ylmethyl)-trifluoromethyl-benzene (III-b24)

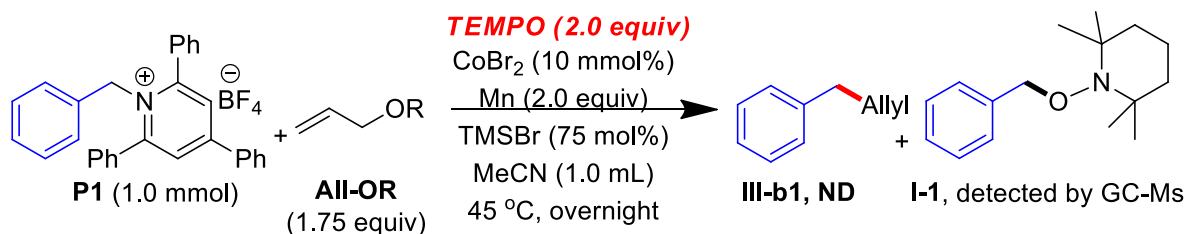


Following **GP-IV-A**, the 4-(trifluoromethyl) benzyl Katritzky pyridinium salt (P11) (553 mg, 1.0 mmol) with cyclohex-2-enyl acetate (196 mg, 1.75 mmol) were used, affording the title compound as a colorless oil (79 mg, 33% yield) after purification by flash chromatography (SiO_2 : pure pentane).

6.3. Mechanistic experiments

6.3.1. Radical trapping experiments of P1 with allyl acetate (A-OAc-a1)

a) The reaction with TEMPO.

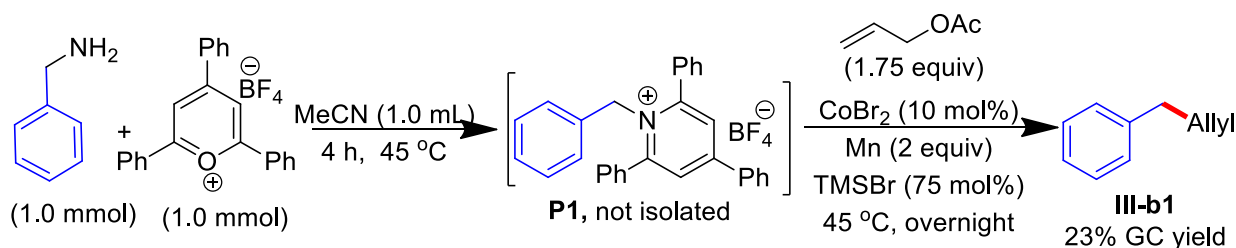


Entry	R	I-1 ^a / %	III-b1 ^b / %
1	Ac	Trace	ND
2	Me		

^adetected by GC-MS. ^bGC yield with 250 μL dodecane as reference.

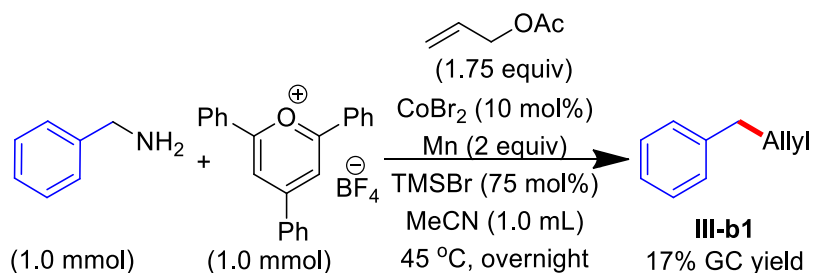
In an oven-dried, 20-mL reaction tube, **P1** (480 mg, 1.0 mmol, 1.0 equiv), Mn powder (110 mg, 2.0 mmol, 2.0 equiv), and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N_2 three times and added the MeCN (1.0 mL), all-OAc-a1 (189 μL , 1.75 mmol)/ all-OMe (164 μL , 1.75 mmol) under N_2 . The mixture was stirred at rt, and then TMSBr (100 μL , 0.75 mmol, 75 mol%) was added. After the reaction mixture was allowed to stir overnight (around 15 h) at 45 $^\circ\text{C}$. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

6.3.2. One-spot experiments of P1 with All-OAc-a1



a) In an oven-dried, 20-mL reaction tube, in the solution MeCN (1.0 mL) with benzylamine (109 μL , 1.0 mmol, 1.0 equiv), 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv) was added. And then, the mixture was allowed to be stirred at 45 $^\circ\text{C}$. After reacting for 4 h, the mixture was stopped and cooled down to rt, Mn powder (110 mg, 2.0 mmol, 2.0 equiv), and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added to the mixture without work-up under N_2 . Then all-OAc-a1 (189 μL , 1.75 equiv) was injected by syringe. The mixture was stirred, and TMSBr (100 μL , 75 mol%, to be sure that the reaction was triggered) was added at rt. Finally, the reaction mixture was heated to 45 $^\circ\text{C}$ and stirred overnight. After completion, the reaction mixture was added 250

μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.



- b)** In an oven-dried, 20-mL reaction tube, 2,4,6-triphenylpyrylium tetrafluoroborate (396 mg, 1.0 mmol, 1.0 equiv), Mn powder (110 mg, 2.0 mmol, 2.0 equiv), and CoBr_2 (21.8 mg, 0.1 mmol, 10 mol%) were added. The tube was filled with N_2 three times. And then, MeCN (1.0 mL), benzylamine (109 μL , 1.0 mmol, 1.0 equiv), and all-OAc-a1(189 μL , 1.75 equiv) were injected by syringe. The mixture was stirred, and TMSBr (100 μL , 75 mol%, to be sure that the reaction was triggered) was added at 45 °C overnight. After completion, the reaction mixture was added 250 μL dodecane as a reference and filtered by flash chromatography. The filtrate was analyzed by GC and GC-MS.

Titre : Couplage réducteur catalysé au cobalt entre C- hétéroatome(S, N, O, X) électrophiles à construire Obligations Csp^3-Csp^2 et Csp^3-Csp^3 Couplage réducteur catalysé au cobalt entre C- hétéroatome (S, N, O, X) électrophiles à construire Obligations Csp^3-Csp^2 et Csp^3-Csp^3 .

Mots clés : Catalysé au Cobalt, Couplage réducteur, Activation de liaison C-S, Activation de liaison C-N, Activation de liaison C-O, Formation de liaison C-C

Résumé : Les liaisons carbone-carbone sont les unités les plus importantes et les plus répandues dans les produits pharmaceutiques, les plastiques et les produits naturels. Nous avons imaginé que les électrophiles non halogéné « Csp^3-X » ($X=S, N, O$) pourraient être des précurseurs de radicaux idéaux pour former des liaisons Csp^3-Csp^2 ou Csp^3-Csp^3 via un couplage réducteur catalysé par le cobalt. Divers diarylméthanés fonctionnalisés ont été synthétisés, dans des conditions douces, par différents sels de benzylsulfonium et des bromures d'aryle avec des rendements bons à excellents. Puis plusieurs iodures alkyliques primaires ou secondaires fonctionnalisés ont été couplés à différents sels de benzylsulfonium contenant des groupes donneur ou attracteur d'électrons, conduisant aux produits désirés avec des rendements modérés à bons dans des conditions.

Douces. D'autre part, des acétates allyliques ou d'éther ont pu être couplés avec des sels de benzylsulfonium conduisant à la formation de divers composés alkyl-oléfiniques fonctionnalisés dans des conditions douces et avec des rendements modérés à bons. En plus de l'application d'électrophiles C-S, des électrophiles C-N -benzylpyridinium ont également été employés pour construire des liaisons Csp^3-Csp^3 avec des électrophiles $C_{allyl}-O$ par un couplage réductif co-catalysé conduisant à des dérivés allylbenzyliques dans des conditions douces avec des rendements modérés à bons. Il convient de mentionner que les sels de benzyl pyridinium pourraient également s'associer à l'éther allylméthyle et donner de bons rendements. Des études mécanistiques ont démontré la formation de radicaux benzyliques à partir de sels de benzyl sulfonium/ pyridinium.

Title: Cobalt-Catalyzed Reductive Cross-Coupling between C- Heteroatom (S, N, O, X) Electrophiles to Build Csp^3-Csp^2 and Csp^3-Csp^3 Bonds Cobalt-Catalyzed Reductive Cross-Coupling between C- Heteroatom (S, N, O, X) Electrophiles to Build Csp^3-Csp^2 and Csp^3-Csp^3 Bonds

Keywords: Cobalt-Catalyzed, Reductive Cross-Coupling, C-S Bond Activation, C-N Bond Activation, C-O Bond Activation, C-C bond Formation

Abstract: C-C bonds are the most important and pervasive units in pharmaceuticals, plastics, and natural products. We described that Csp^3-S electrophiles, Csp^3-N electrophiles, Csp^3-O electrophiles, and at least one non-halogenated electrophiles as ideal radical precursors to form Csp^3-Csp^2 or Csp^3-Csp^3 bonds via cobalt-catalyzed reductive cross-coupling. Various functionalized diarylmethanes were synthesized by different benzyl sulfonium salts and aryl bromides in good to excellent yields under mild conditions. Then functionalized primary or secondary alkyl iodides were coupled with different benzyl sulfonium salts bearing electron-donating or electron-withdrawing groups leading

to desired products in moderate to good yields under mild conditions. On the other hand, either allylic acetates or ether could be coupled with benzyl sulfonium salts leading to various functionalized alkyl olefinic compounds under mild conditions in moderate to good yields. In addition, C-N electrophiles were also employed to construct Csp^3-Csp^3 bonds with $C_{allyl}-O$ electrophiles via a Co-catalyzed reductive cross-coupling leading to allyl benzyl derivatives under mild conditions in moderate to good yields. It was worth mentioning that benzyl pyridinium salts could also couple with allyl methyl ether and deliver good yields. Mechanistic studies demonstrated the generations of benzyl radicals from benzyl sulfonium /pyridinium salts.