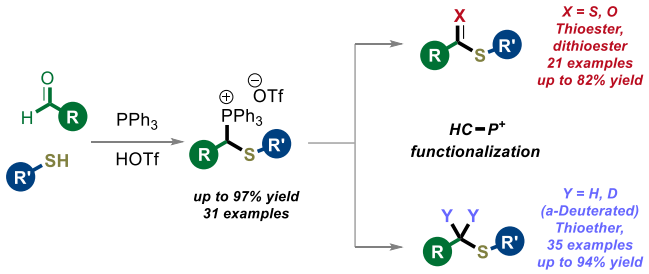
Practical Synthesis and Functionalization of Thiophosphonium Salts: A Divergent Approach to Access Thioether, Thioester, and Dithioester Derivatives

Gurupada Hazra, and Ahmad Masarwa*

Institute of Chemistry, The Center for Nanoscience and Nanotechnology, and Casali Center for Applied Chemistry, The Hebrew University of Jerusalem, Jerusalem, 9190401, (Israel)

***Corresponding Author:** *E-mail:* Ahmad.Masarwa1@mail.huji.ac.il*

TOC GRAPHIC



ABSTRACT: Herein, we report a straightforward method for efficiently obtaining a diverse range of thiophosphonium salts. This method involves the direct coupling of commercially available thiols and aldehydes with Ph_3P and TfOH. The setup is simple and carried out in a metal-free manner. The synthetic utility of these salts is demonstrated through various examples of C–$^+$P bond functionalizations, enabling the synthesis of thioether, deuterated-thioether, thioester, and dithioester derivatives. These products, which serve as valuable building blocks, are obtained in high yields.

Organophosphonium salts containing C—$^+$P moieties, in particular organophosphorus-based Wittig salts, are among the most utilized reagents in organic synthesis for constructing C—C double bond. In recent years, new methods for C—$^+$P bond functionalization have been developed that use organophosphonium compounds in novel ways enabling new bonds formation. For example, there are few examples of selective C—$^+PPh_3$ group functionalization to give products featuring new C—O, C—N, C—S, and C—C bonds. Despite these advancements, there are still limitations that need to be addressed. Therefore, it is important to investigate additional methods by synthesizing new variants of organophosphonium species and their functionalizations. Such exploration is expected to greatly enhance the existing approaches for derivatizing noble organophosphonium salts and enable the creation of new connections.

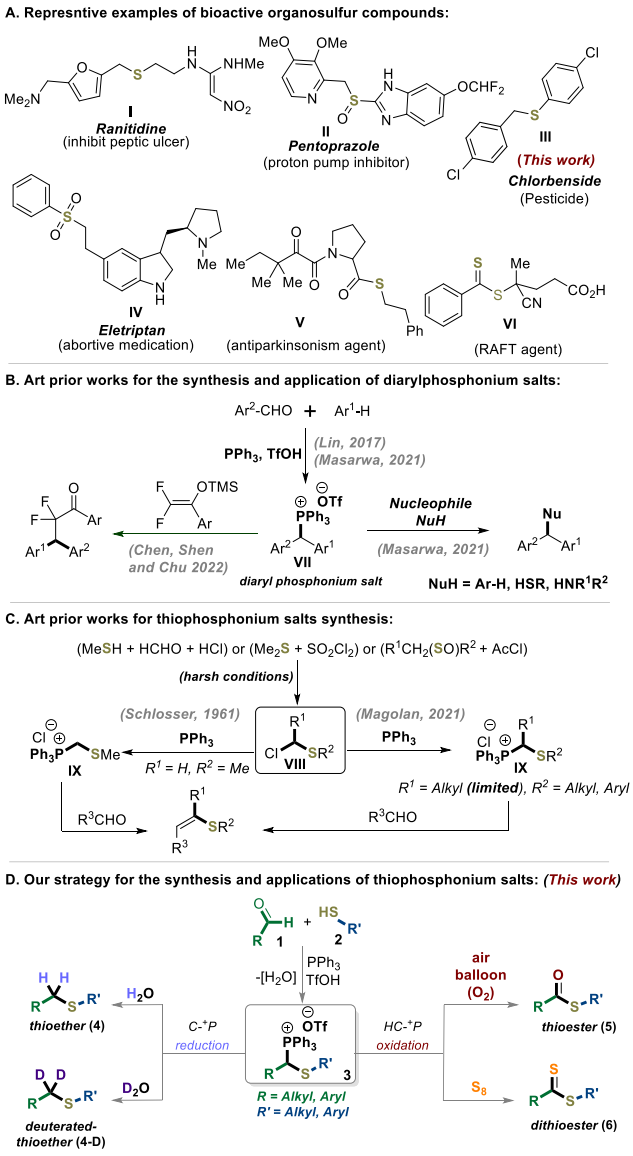
In this regard, our research group has successfully described a versatile method for synthesizing benzhydryl triarylphosphonium salts (**VII**) through a convenient one-pot, regioslective four-component coupling reaction using readily available starting materials (Scheme 1B). The resulting benzhydryl phosphonium salt building blocks exhibited excellent utility, as demonstrated by their selective post-functionalization of C-selective electrophilic benzylic C(sp^3)—$^+PPh_3$ groups. This allowed for a range of transformations including aminations, thiolations, and arylations, leading to the creation of bioactive arylated scaffolds (Scheme 1B). In this method, benzhydrylamines, benzhydrylthioethers, and triarylmethanes, structural motifs that are present in many pharmaceuticals and agrochemicals, are respectively readily accessed. Furthermore, Chu and coworkers have developed an efficient metal-free difluoroalkylation reaction of these organophosphonium salts (**VII**) with difluoroenol silyl ethers (Scheme 1B).

As part of our overarching strategies to synthesize a diverse range of thio-based bioactive compounds (**I-VI**), encompassing thioether, thioester, and dithioester derivatives, we recognized the potential of thiophosphonium salts as versatile core scaffolds for these molecules (Scheme 1A).

However, the synthesis and application of thiophosphonium salts have been relatively uncommon, with few reports addressing their exploration (Scheme 1C). Notably, in 1961, Schlosser described the use of α-chloro sulfides (**VIII**) as transient intermediates in the synthesis of thiophosphonium salts (Scheme 1C). More recently, in 2021, Magolan

utilized a similar approach, utilizing α-chloro sulfides (**VIII**) as a starting point for the synthesis of thiophosphonium salts **IX** (Scheme 1C). These salts (**IX**) were subsequently converted to vinyl sulfides, which further underwent transformations leading to the formation of ketones and indoles. It is important to highlight that the synthesis of α-chloro sulfides (**VIII**) necessitates the use of demanding reaction conditions. Moreover, it should be noted that the versatility of these reactions is predominantly limited to thioalkyl phosphonium salts (**IX**). Therefore, it is imperative that a complementary, general, milder, and diversifiable method for thio-phosphonium salts will be developed.

Scheme 1: Overview of This Work

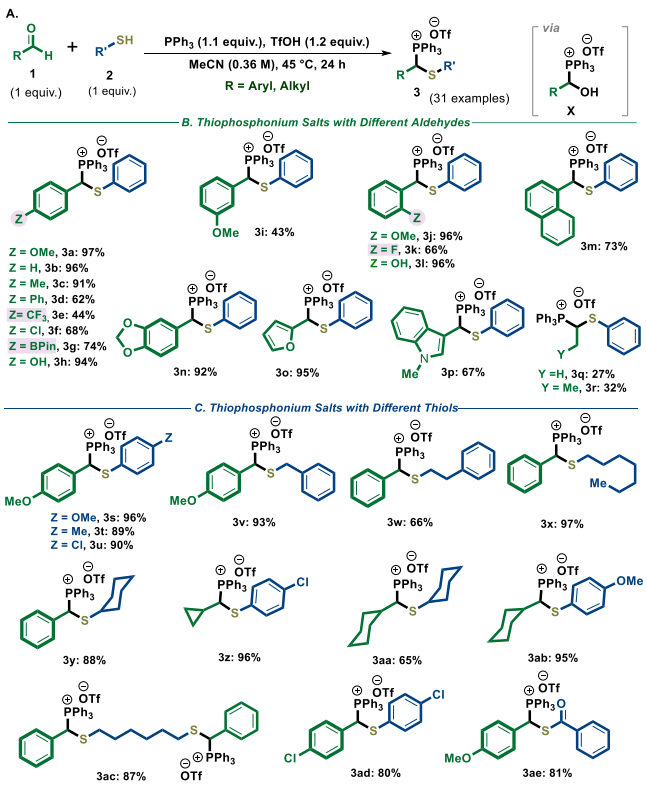


With this goal in mind, we envisioned an operationally simple strategy to synthesize thiophosphonium salts **3** and convert them into valuable thio-based motifs (**4-6**, **III**) through C(sp^3)–$^+$P transformation (Scheme 1D). In fact, drawing inspiration from our recent report and Lin's work (Scheme 1B), our method involves a simple four-component reaction utilizing readily accessible and commercially available starting materials, i.e. aldehydes **1** and thiols **2** (Scheme 1D).

To test our hypothesis, we first treated *p*-anisaldehyde (**1 a**) with thiophenol (**2 a**), triphenylphosphine (PPh_3), and triflic acid in CH_3CN for 24h at 45 °C to obtain the desired phosphonium salt **3 a** in 97 % isolated yield (Scheme 2A-B). Notably, no conversion was observed in the absence of either PR_3 or TfOH. (for full details, see the SI, pages S8, S47-48)

Next, a series of thiophosphonium salts (**3a–3u, 3ab**) were synthesized from thiophenol **2a** coupling different aldehyde derivatives (**1**) bearing aromatic moieties which substituted with electron-donating groups (EDG; e.g., **1a - c**), with electron withdrawing groups (EWG; e.g., **1d-g**, **1k**), phenolic derivatives (**1a, 1h**, **1j**, **1l**, **1n**) as well as *N*-methylindole-based derivatives (**1p**). The reaction showed high functional group tolerance as evidenced by fluorine- (**3k**), chlorine- (3**f**), boron- (3**g**), and hetro-arene-containing (**3o-p**) substrates (Scheme 2). In addition, different types of aliphatic aldehydes both cyclic and acyclic (3**z-ab**, **3q**, **3r**, Scheme 2A-C) were explored. The reaction also demonstrated fruitful applicability to a diverse range of aromatic and aliphatic thiols as well (**3a-3ad**, Scheme 2B-C). Importantly, the utilization of thiobenzoic acid (**2j**) has proven to be effective in the formation of the fascinating benzoylthio-phosphonium salt (**3ae**).

Scheme 2: The Synthesis of Thiophosphonium Salts (3)



[a]Reaction conditions: **1** (1.46 mmol), **2** (1.46 mmol), PPh_3 (1.6 mmol), TfOH (1.75 mmol) in 4 mL MeCN at 45 ˚C for 24 h. All the yield of the reactions are isolated after diethyl ether washed.

In all cases, the phosphonium thio-alkylation-type reaction occurs selectively via nucleophilic-substitution-type scenario of hydroxy-triphenylphosphonium intermediate **X** (for more details on this thio-alkylation-type Friedel–Crafts mechanism, see the mechanistic studies in the SI, pages S47-48). Moreover, most of these products (**3**) were purified by simple precipitation—an additional advantage. The one-pot, four-component, coupling approach can be carried out on gram-scale (see **3a**, Scheme 2). Using the same approach, di-thiophosphonium salt **3ac** was prepared from benzaldehyde (**1b**) and 1,6-hexanedithiol (**2i**).

We next explore the synthetic usefulness of these thiophosphonium products (**3**), we aimed to demonstrate their synthetic utility in selective transformations of the C–$^{+}$P bonds and the synthesis of bioactive chemicals. To this end, various representative applications were conceived for these valuable salts **3** as depicted in Schemes **3-4**. For instance, we conducted selective reduction and oxidation protocols of the C–$^{+}$P, enabling the synthesis of the valuable thioether, deuterated-thioether, thioester, and dithioester derivatives.

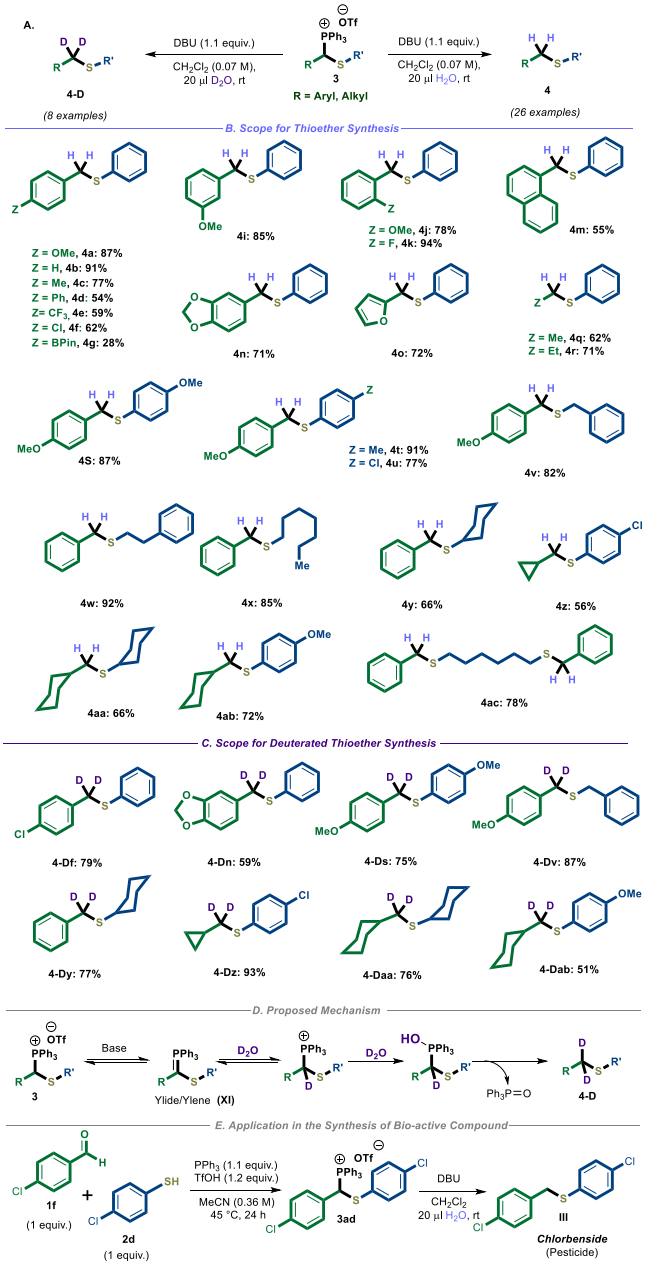
In this regard, a hydrolysis-based reduction protocol has been developed for thiophosphonium salts **3** using H_2O (Scheme 3A-B). In this method, we explored the reduction of a thiophosphonium salt, specifically utilizing **3a** as a standard salt for reaction optimization. Various organic and inorganic bases were employed for the reaction, and the supporting information provides further details on these bases (See SI pages 23-24). Ultimately, DBU was identified as the optimal base for the hydrolytic reduction of the thiophosphonium salt, leading to the formation of thioether **4a** with an isolated yield of 87% (Scheme 3A-B).

Subsequently, we successfully synthesized a variety of thioether derivatives by adapting the standard reaction conditions outlined in Scheme 3. The reaction exhibited a broad scope, encompassing with aryls with substituents such as -OMe, -F, -Cl, -Ph, -Bpin, and -Me, with good yields. Notably, even alicyclic and cyclic aliphatic substituents on the thiol part yielded the desired thioether derivatives with good yields. Furthermore, replacing water with D_2O provided a valuable opportunity to produce fully α-deuterated thioether (**4-D**), exhibiting excellent deuterium labeling and good yields (Scheme 3A, C).

A possible mechanism for hydrolysis-based reduction pathway is proposed in Scheme 3D. On the basis of reports in the literature, this mechanistic process involves the formation of ylide/ylene **XI**, followed by protonation/deuteration of ylene **XI**. Subsequently, the cleavage of the C(sp_3)–$^{+}$P bond takes place through P-selective nucleophilic substitution, resulting in the liberation of triphenylphosphine oxide (Ph_3P=O).

Finally, we also successfully prepared the pesticide chemical chlorbenside **III** from the commercially available 4-chlorobenzaldehyde **1f** and 4-chlorothiophenol **2d** in only two steps. This was achieved through the selective coupling reaction of **1f** and **2d** to generate thiophosphonium salt **3ad**, which was then reacted with DBU and water through CH–$^{+}$P group hydrolysis-based reduction reaction in a single operation (Scheme 3E).

Scheme 3: Reduction of Thiophosphonium Salts to Thioethers and α-Deuterated Thioethers[a]



[a]Reaction conditions: **3** (0.2 mmol), **DBU** (0.22 mmol) and 20 µL H_2O or D_2O in 3 mL CH_2Cl_2 at room temperature. All the yield of the reactions are isolated after column chromatography.

Encouraging by these results of the reduction methodology, we were contemplating the possibility of synthesizing important thioester and dithioester motifs using the thiophosphonium salt **3**. We imagined that this could be achieved by the generation of phosphorus ylide (**XI**) from salt **3** flowing by a direct oxidation of this ylide (**XI**).

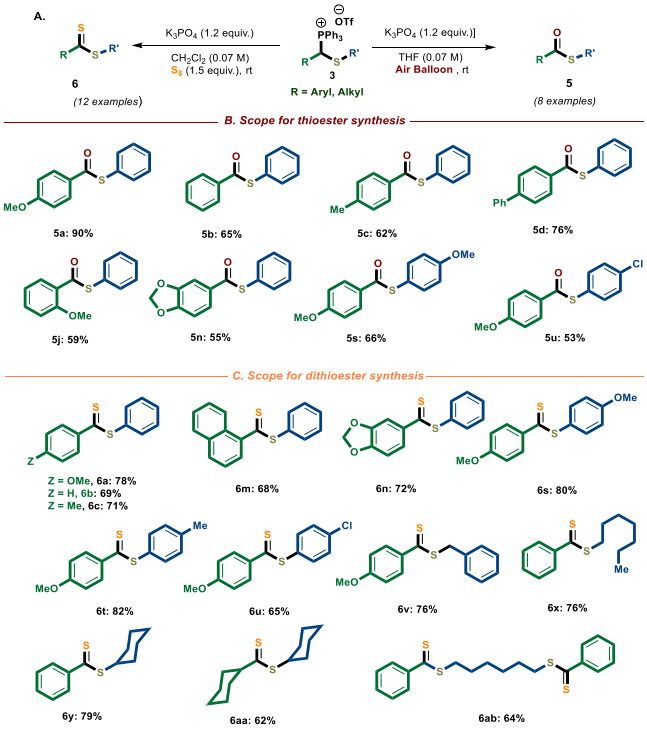
Our initial optimization efforts focused on the formation of thioester **5a** from thiophosphonium salt **3** and a base under air (a source of O_2), via the corresponding ylide **XI**. After

many experiments, the use of K_3PO_4 in dry THF were found to be the best reaction condition to obtain the thioester product **5a** with yield of 90%.

Next, we explored the reaction's scope, we employed identical reaction conditions. Consequently, thiophosphonium salt **3** effectively participated in the reaction, resulting in the formation of the desired product **5** with good yields, as depicted in Scheme 4A-B, were satisfactory.

To further showcase the synthetic utility of salts **3**, we developed their transformation into dithioesters **6** (Scheme 4A, C). To this end, we employed basic reaction conditions to treat thiophosphonium salt 3 with elemental sulfur (S_8). We conducted a thorough exploration of the optimal reaction conditions and determined that employing dry CH_2Cl_2 and K_3PO_4 as the standard reaction conditions resulted in the highest yield of dithioester **6a**, with approximately 78% (For more details, see the supporting information). Additionally, we shown that various thiophosphonium salts **3** could tolerate these reaction conditions, leading to the formation of the desired dithioester **6** with good yields, as depicted in Scheme 4C.

Scheme 4: Oxidation of Thiophosphonium Salts to Thioesters and Dithioesters[a]



[a]Reaction conditions: **3** (0.2 mmol), **K_3PO_4** (0.24 mmol) and air balloon in 3 mL dry THF at room temperature (for thioester synthesis) or **3** (0.2 mmol), **K_3PO_4** (0.24 mmol) and S_8 (0.30 mmol) in 3 mL dry CH_2Cl_2 at room temperature (for dithioester synthesis) All the yield of the reactions are isolated after column chromatography.

In conclusion, we have developed a simple and broadly, straightforward protocol for the direct synthesis of a diverse range of thiophosphonium salts. This protocol involves the one-pot, four-component coupling reaction of commercially available thiols and aldehydes with Ph_3P and TfOH. The utility of the resulting phosphonium salt building blocks was demonstrated by the chemoselective post-functionalization of C(sp^3)–$^+PPh_3$ groups to achieve divergent reduction and oxidations protocols. In this way, thioether, deuterated-thioether, thioester, and dithioester derivatives, structural motifs that are present in many important chemicals, are readily accessed. This includes the synthesis of the pesticide chemical chlorbenside from the simple commercially available materials in only two steps. The setup of these C-P group post-functionalization is simple and the products were obtained in good yields. These protocols should greatly simplify access to pharmaceutically relevant compounds, and further advance their use in a variety of new applications.

ACKNOWLEDGMENT

This research was supported by a grant from the Israel Science Foundation (Grant No. 287/21).

REFERENCES

(1) Sundaravelu, N.; Sangeetha, S.; Sekar, G. Metal-catalyzed C–S bond formation using sulfur surrogates. *Organic & Biomolecular Chemistry* **2021**, *19* (7), 1459-1482, 10.1039/D0OB02320E. DOI: 10.1039/D0OB02320E. Shen, C.; Zhang, P.; Sun, Q.; Bai, S.; Hor, T. S. A.; Liu, X. Recent advances in C–S bond formation via C–H bond functionalization and decarboxylation. *Chemical Society Reviews* **2015**, *44* (1), 291-314, 10.1039/C4CS00239C. DOI: 10.1039/C4CS00239C. Bhunia, S.; Pawar, G. G.; Kumar, S. V.; Jiang, Y.; Ma, D. Selected Copper-Based Reactions for C–N, C–O, C–S, and C–C Bond Formation. *Angewandte Chemie International Edition* **2017**, *56* (51), 16136-16179. DOI: https://doi.org/10.1002/anie.201701690. Chauhan, P.; Mahajan, S.; Enders, D. Organocatalytic Carbon–Sulfur Bond-Forming Reactions. *Chemical Reviews* **2014**, *114* (18), 8807-8864. DOI: 10.1021/cr500235v. Li, J.; Yang, S.; Wu, W.; Jiang, H. Recent developments in palladium-catalyzed C–S bond formation. *Organic Chemistry Frontiers* **2020**, *7* (11), 1395-1417, 10.1039/D0QO00377H. DOI: 10.1039/D0QO00377H. Kondo, T.; Mitsudo, T.-a. Metal-Catalyzed Carbon–Sulfur Bond Formation. *Chemical Reviews* **2000**, *100* (8), 3205-3220. DOI: 10.1021/cr9902749.

(2) Bautista, D. M.; Movahed, P.; Hinman, A.; Axelsson, H. E.; Sterner, O.; Högestätt, E. D.; Julius, D.; Jordt, S.-E.; Zygmunt, P. M. Pungent products from garlic activate the sensory ion channel TRPA1. *Proceedings of the National Academy of Sciences* **2005**, *102* (34), 12248-12252. DOI: doi:10.1073/pnas.0505356102. Robert, M. M.; Rajesh, N.; Bhushan, S. Organosulfur Compounds in Cancer Chemoprevention. *Mini-Reviews in Medicinal Chemistry* **2007**, *7* (8), 827-838. DOI: http://dx.doi.org/10.2174/138955707781387939.

(3) Bhalerao, D. S.; Kondaiah, G. C. M.; Dwivedi, N.; Mylavarappu, R. K.; Reddy, L. A.; Roy, A.; Nagaraju, G.; Reddy, P. P.; Bhattacharya, A.; Bandichhor, R. Novel Approach to the Synthesis of Omeprazole: An Antipeptic Ulcer Agent. *Synthetic Communications* **2010**, *40* (20), 2983-2987. DOI: 10.1080/00397910903341171.

(4) Guo, W.; Wang, D.-Y.; Chen, Q.; Fu, Y. Advances of Organosulfur Materials for Rechargeable Metal Batteries. *Advanced Science* **2022**, *9* (4), 2103989. DOI: https://doi.org/10.1002/advs.202103989. Shadike, Z.; Tan, S.; Wang, Q.-C.; Lin, R.; Hu, E.; Qu, D.; Yang, X.-Q. Review on organosulfur materials for rechargeable lithium batteries. *Materials Horizons* **2021**, *8* (2), 471-500, 10.1039/D0MH01364A. DOI: 10.1039/D0MH01364A.

(5) Devendar, P.; Yang, G.-F. Sulfur-Containing Agrochemicals. *Topics in Current Chemistry* **2017**, *375* (6), 82. DOI: 10.1007/s41061-017-0169-9.

(6) Liu, B.; Lim, C.-H.; Miyake, G. M. Visible-Light-Promoted C–S Cross-Coupling via Intermolecular Charge Transfer. *Journal of the American Chemical Society* **2017**, *139* (39), 13616-13619. DOI: 10.1021/jacs.7b07390. Kim, J.; Kang, B.; Hong, S. H. Direct Allylic C(sp3)–H Thiolation with Disulfides via Visible Light Photoredox

Catalysis. *ACS Catalysis* **2020**, *10* (11), 6013-6022. DOI: 10.1021/acscatal.0c01232.
(7) Guo, S.-r.; Yuan, Y.-q.; Xiang, J.-n. Metal-Free Oxidative C(sp3)–H Bond Thiolation of Ethers with Disulfides. *Organic Letters* **2013**, *15* (18), 4654-4657. DOI: 10.1021/ol402281f. Cheng, Y.; Peng, H.-Y.; Dong, Z.-B. Synthesis of alkyl dithiocarbamates by using thiuram disulfide reagents: A metal-free C(sp3)-S bond formation. *Tetrahedron Letters* **2019**, *60* (8), 617-620. DOI: https://doi.org/10.1016/j.tetlet.2019.01.044. Wu, M.; Yan, C.; Zhuang, D.; Yan, R. Metal-Free C–S Bond Formation in Elemental Sulfur and Cyclobutanol Derivatives: The Synthesis of Substituted Thiophenes. *Organic Letters* **2022**, *24* (29), 5309-5313. DOI: 10.1021/acs.orglett.2c01907.
(8) Kelleman, A.; Mattern, R.-H.; Pierschbacher, M. D.; Goodman, M. Incorporation of thioether building blocks into an αvβ3-specific RGD peptide: Synthesis and biological activity. *Peptide Science* **2003**, *71* (6), 686-695. DOI: https://doi.org/10.1002/bip.10586. Zhang, Y.; Li, H.; Chang, J.; Guan, X.; Tang, L.; Fang, Q.; Valtchev, V.; Yan, Y.; Qiu, S. 3D Thioether-Based Covalent Organic Frameworks for Selective and Efficient Mercury Removal. *Small* **2021**, *17* (22), 2006112. DOI: https://doi.org/10.1002/smll.202006112.

(9) Pankau, W. M.; Verbist, K.; Kiedrowski, G. v. Phase-transfer synthesis of novel water-soluble gold clusters with tripodal thioether based ligands. *Chemical Communications* **2001**, (6), 519-520, 10.1039/B008967M. DOI: 10.1039/B008967M.
(10) Levason, W.; Reid, G.; Zhang, W. The chemistry of the p-block elements with thioether, selenoether and telluroether ligands. *Dalton Transactions* **2011**, *40* (34), 8491-8506, 10.1039/C1DT10317B. DOI: 10.1039/C1DT10317B. Villuendas, P.; Urriolabeitia, E. P. Ru-Catalyzed Regioselective CH-Hydroarylation of Alkynes with Benzylthioethers Using Sulfur as Directing Group. *Organic Letters* **2015**, *17* (12), 3178-3181. DOI: 10.1021/acs.orglett.5b01552.
(11) Baud, M. G. J.; Leiser, T.; Petrucci, V.; Gunaratnam, M.; Neidle, S.; Meyer-Almes, F.-J.; Fuchter, M. J. Thioester derivatives of the natural product psammaplin A as potent histone deacetylase inhibitors. *Beilstein Journal of Organic Chemistry* **2013**, *9*, 81-88. DOI: 10.3762/bjoc.9.11. Reed, K. A.; Manam, R. R.; Mitchell, S. S.; Xu, J.; Teisan, S.; Chao, T.-H.; Deyanat-Yazdi, G.; Neuteboom, S. T. C.; Lam, K. S.; Potts, B. C. M. Salinosporamides D–J from the Marine Actinomycete Salinispora tropica, Bromosalinosporamide, and Thioester Derivatives Are Potent Inhibitors of the 20S Proteasome. *Journal of Natural Products* **2007**, *70* (2), 269-276. DOI: 10.1021/np0603471.
(12) Hirschbeck, V.; Gehrtz, P. H.; Fleischer, I. Metal-Catalyzed Synthesis and Use of Thioesters: Recent Developments. *Chemistry – A European Journal* **2018**, *24* (28), 7092-7107. DOI: https://doi.org/10.1002/chem.201705025.
(13) Jabarullah, N. H.; Jermsittiparsert, K.; Melnikov, P. A.; Maseleno, A.; Hosseinian, A.; Vessally, E. Methods for the direct synthesis of thioesters from aldehydes: a focus review. *Journal of Sulfur Chemistry* **2020**, *41* (1), 96-115. DOI: 10.1080/17415993.2019.1658764. Yi, C.-L.; Huang, Y.-T.; Lee, C.-F. Synthesis of thioesters through copper-catalyzed coupling of aldehydes with thiols in water. *Green Chemistry* **2013**, *15* (9), 2476-2484, 10.1039/C3GC40946E. DOI: 10.1039/C3GC40946E. Tang, H.; Zhang, M.; Zhang, Y.; Luo, P.; Ravelli, D.; Wu, J. Direct Synthesis of Thioesters from Feedstock Chemicals and Elemental Sulfur. *Journal of the American Chemical Society* **2023**, *145* (10), 5846-5854. DOI: 10.1021/jacs.2c13157.
(14) Moad, G. Dithioesters in RAFT Polymerization. In *RAFT Polymerization*, 2021; pp 223-358.
(15) Duréault, A.; Taton, D.; Destarac, M.; Leising, F.; Gnanou, Y. Synthesis of Multifunctional Dithioesters Using Tetraphosphorus Decasulfide and Their Behavior as RAFT Agents. *Macromolecules* **2004**, *37* (15), 5513-5519. DOI: 10.1021/ma030420j. Takayama, R.; Yamada, A.; Fuchibe, K.; Ichikawa, J. Synthesis of Sulfanylated Difluoroalkenes: Electrophilic Difluoromethylidenation of Dithioesters with Difluorocarbene. *Organic Letters* **2017**, *19* (19), 5050-5053. DOI: 10.1021/acs.orglett.7b02222. Cerda, Matthew M.; Newton, T. D.; Zhao, Y.; Collins, B. K.; Hendon, C. H.; Pluth, M. D. Dithioesters: simple, tunable, cysteine-selective H2S donors. *Chemical Science* **2019**, *10* (6), 1773-1779, 10.1039/C8SC04683B. DOI: 10.1039/C8SC04683B.
(16) Maryanoff, B. E.; Reitz, A. B. The Wittig olefination reaction and modifications involving phosphoryl-stabilized carbanions. Stereochemistry, mechanism, and selected synthetic aspects. *Chemical Reviews* **1989**, *89* (4), 863-927. DOI: 10.1021/cr00094a007. Byrne, P. A.; Gilheany, D. G. The modern interpretation of the Wittig reaction mechanism. *Chemical Society Reviews* **2013**, *42* (16), 6670-6696, 10.1039/C3CS60105F. DOI: 10.1039/C3CS60105F.
(17) Levy, J. N.; Alegre-Requena, J. V.; Liu, R.; Paton, R. S.; McNally, A. Selective Halogenation of Pyridines Using Designed Phosphine Reagents. *Journal of the American Chemical Society* **2020**, *142* (25), 11295-11305. DOI: 10.1021/jacs.0c04674. Zhang, X.; McNally, A. Phosphonium Salts as Pseudohalides: Regioselective Nickel-Catalyzed Cross-Coupling of Complex Pyridines and Diazines. *Angewandte Chemie International Edition* **2017**, *56* (33), 9833-9836. DOI: https://doi.org/10.1002/anie.201704948. Dolewski, R. D.; Hilton, M. C.; McNally, A. 4-Selective Pyridine Functionalization Reactions via Heterocyclic Phosphonium Salts. *Synlett* **2018**, *29* (01), 08-14. DOI: 10.1055/s-0036-1591850. Gasnot, J.; Botella, C.; Comesse, S.; Lakhdar, S.; Alayrac, C.; Gaumont, A.-C.; Dalla, V.; Taillier, C. Taming the Reactivity of Phosphiranium Salts: Site-Selective C-Centered Ring Opening for Direct Synthesis of Phosphinoethylamines. *Angewandte Chemie International Edition* **2020**, *59* (29), 11769-11773. DOI: https://doi.org/10.1002/anie.201916449.
(18) Babu, K. N.; Massarwe, F.; Shioukhi, I.; Masarwa, A. Sequential Selective C−H and C(sp3)−+P Bond Functionalizations: An Entry to Bioactive Arylated Scaffolds. *Angewandte Chemie International Edition* **2021**, *60* (50), 26199-26209. DOI: https://doi.org/10.1002/anie.202111164.
(19) Yu, Z.-L.; Chen, J.-W.; Chen, Y.-L.; Zheng, R.-J.; Ma, M.; Chen, J.-P.; Shen, Z.-L.; Chu, X.-Q. DMSO-Promoted Difluoroalkylation of Organophosphonium Salts with Difluoroenol Silyl Ethers. *Organic Letters* **2022**, *24* (30), 5557-5561. DOI: 10.1021/acs.orglett.2c02088.
(20) Guo, M.-M.; Qin, G.-Q.; Jiang, X.-Y.; Xu, H.; Ma, M.; Shen, Z.-L.; Chu, X.-Q. Aerobic Coupling of Organophosphonium Salts with Alkenes: Catalyst-Free C(sp3)−C(sp2) Bond Formation. *Advanced Synthesis & Catalysis n/a* (n/a). DOI: https://doi.org/10.1002/adsc.202300259.
(21) Wittig, G.; Schlosser, M. Über die Herstellung von Vinyläthern, Vinylthioäthern und Vinylhalogeniden auf der Phosphylen-Basis; IV. Mitteil. über Phosphin-alkylene als olefinbildende Reagenzien. *Chemische Berichte* **1961**, *94* (5), 1373-1383. DOI: https://doi.org/10.1002/cber.19610940532. Fragis, M.; Deobald, J. L.; Dharavath, S.; Scott, J.; Magolan, J. Aldehyde to Ketone Homologation Enabled by Improved Access to Thioalkyl Phosphonium Salts. *Organic Letters* **2021**, *23* (12), 4548-4552. DOI: 10.1021/acs.orglett.1c01189.
(22) Pal, P.; Fragis, M.; Dharavath, S.; Johnson, J. W.; Magolan, J. Use of Vinyl Sulfides in Fischer Indole Reactions. *Synthesis* **2022**, *54* (22), 4917-4931. DOI: 10.1055/a-1868-4148.
(23) Byrne, P. A.; Gilheany, D. G. The Mechanism of Phosphonium Ylide Alcoholysis and Hydrolysis: Concerted Addition of the O−H Bond Across the P=C Bond. *Chemistry – A European Journal* **2016**, *22* (27), 9140-9154. DOI: https://doi.org/10.1002/chem.201600530.
(24) Kupwade, R. V.; Khot, S. S.; Lad, U. P.; Desai, U. V.; Wadgaonkar, P. P. Catalyst-free oxidation of sulfides to sulfoxides and diethylamine catalyzed oxidation of sulfides to sulfones using Oxone as an oxidant. *Research on Chemical Intermediates* **2017**, *43* (12), 6875-6888. DOI: 10.1007/s11164-017-3026-0.
(25) Burhardt, M. N.; Taaning, R. H.; Skrydstrup, T. Pd-Catalyzed Thiocarbonylation with Stoichiometric Carbon Monoxide: Scope and Applications. *Organic Letters* **2013**, *15* (4), 948-951. DOI: 10.1021/ol400138m.
(26) Devi, N. S.; Singh, S. J.; Singh, O. M. An efficient transesterification of β-oxodithioesters catalyzed by stannous chloride under solvent-free conditions. *Tetrahedron Letters* **2013**, *54* (11), 1432-1435. DOI: https://doi.org/10.1016/j.tetlet.2013.01.001.
(27) Lee, S.; Kim, S. A.; Jang, H.-Y. Aerobic Oxidation of Benzylic Carbons Using a Guanidine Base. *ACS Omega* **2019**, *4* (18), 17934-17938. DOI: 10.1021/acsomega.9b03064.
(28) Nguyen, T. B. Recent Advances in Organic Reactions Involving Elemental Sulfur. *Advanced Synthesis & Catalysis* **2017**, *359* (7), 1066-1130. DOI: https://doi.org/10.1002/adsc.201601329.