

SYNLETT Spotlight 405

Umemoto's Reagent

Compiled by Huiqin Li



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

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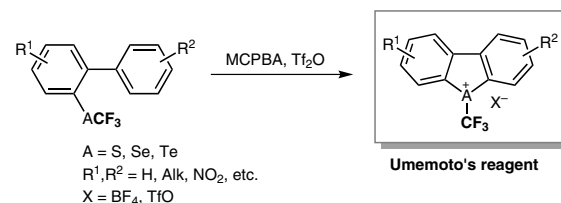
Introduction

The trifluoromethyl group is an important structural moiety in diverse organic molecules due to the significant unique features that trifluoromethylated compounds have in pharmaceuticals, agricultural chemicals, and functional materials.¹

The first electrophilic trifluoromethylating reagent, diaryl(trifluoromethyl) sulfonium salt, $\text{Ar}_2\text{S}^+\text{CF}_3\text{SbF}_6^-$, was achieved by Yagupolskii and co-workers in 1984.² In 1990, Umemoto and co-workers developed a new series of electrophilic trifluoromethylating reagents, for example, (trifluoromethyl)dibenzoheterocyclic salts with fine tuning of their electrophilicity.^{3–5} The reagents are achieved via an oxidation of the starting materials (sulfides, selenides or telluride) followed by a cyclization or a direct fluorination (Scheme 1). As an efficient electrophilic trifluoromethylating agent, Umemoto's reagent has been successfully applied in the trifluoromethylation of a wide

range of nucleophiles including carbanions, silyl enol ethers, enamines, phenols, anilines, phosphines and thioates. The combination of Umemoto's reagent with a chiral base provided a useful entry to the enantioselective electrophilic trifluoromethylation. More recently, the direct C–H bond trifluoromethylation has been achieved by using the Umemoto's reagent and transition-metal catalysis, thus expanding the scope of current popular C–H bond activations.

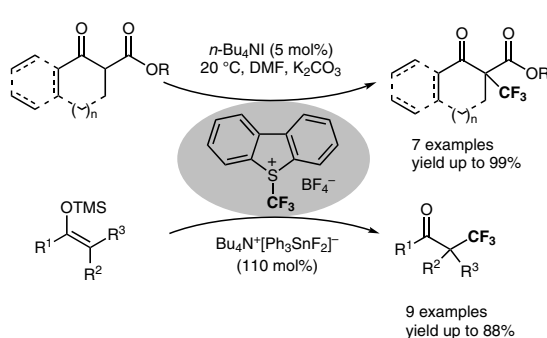
Umemoto's reagents are operational simple, high stable at ambient conditions and commercially available.



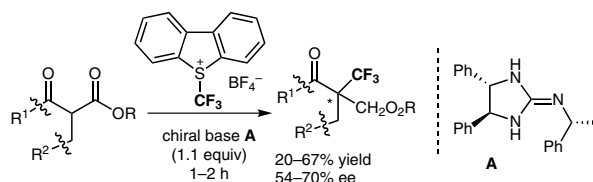
Scheme 1 Umemoto's reagent

Abstracts

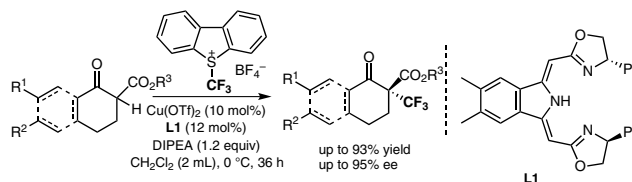
(A) Ma and Cahard⁶ reported the efficient trifluoromethylation of cyclic and acyclic β -keto esters with Umemoto's reagent in the presence of a phase-transfer catalyst to give the corresponding α -substituted α -trifluoromethyl β -keto esters in good to excellent yields. Similarly, the Umemoto's reagents, such as *S*-trifluoromethyldibenzothiophenium tetrafluoroborate, were applied to the electrophilic trifluoromethylation of various silyl enol ethers and gave the corresponding α -trifluoromethyl ketones in good to high yields.



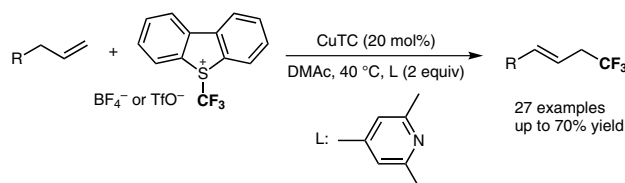
(B) Enantioselective electrophilic trifluoromethylation continues to be a stimulating area of research. In the presence of chiral nonracemic guanidines, acting as Brønsted bases to produce guanidinium enolates, the enantioselective electrophilic trifluoromethylation of β -keto esters has been realized by means of *S*-(trifluoromethyl)dibenzothiophenium tetrafluoroborate (Umemoto's reagent).⁷ Even though the ee's are not satisfying at all, this result would spark the imagination of chemists to design new chiral bases to improve the stereochemical outcome.



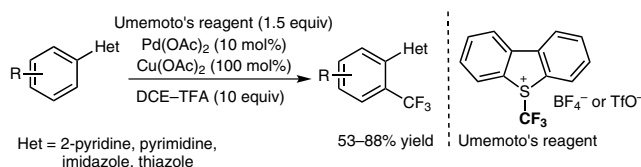
(C) Recently, the breakthrough in the enantioselective electrophilic trifluoromethylation of β -keto esters was made by Gade and co-workers,⁸ who reported a range of α -CF₃ β -keto esters obtained with up to 95% ee by use of a copper catalyst and chiral pincer ligands in the presence of Umemoto's reagent.



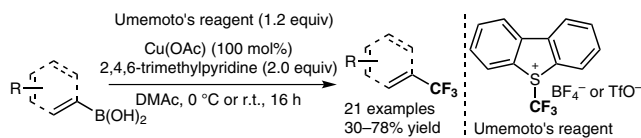
(D) Very recently, Liu and co-workers developed a copper-catalyzed trifluoromethylation of terminal alkenes through allylic C–H bond activation.⁹ Using these methods, a new Csp³–CF₃ bond could be constructed under the practical and mild reaction conditions. Based on theoretical calculations, Liu and co-workers proposed that the reaction may proceed through a Heck-like four-membered ring transition state.



(E) The direct C–H bond functionalization has attracted great attention in recent years. A chelating group was generally employed to install the functional group to a specific position on the aromatic ring, such as the 2-pyridyl group. A directed ortho-trifluoromethylation of aromatics has been realized by Yu and co-workers,¹⁰ who used Pd(OAc)₂ and Cu(OAc)₂ as co-catalyst to convert 2-pyridine and other heterocycles such as thiazoles, imidazole, or pyrimidine with Umemoto's reagent into the corresponding ortho-trifluoromethylated arenes in good yields.



(F) The incorporation of a CF₃ group into aromatics, for example, aryl, heteroaryl, and vinylboronic acids under mild conditions using Umemoto's reagent was accomplished by Liu and co-workers.¹¹ This work shows good functional group compatibility as well as good moisture tolerance.



References

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