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(Trifluoromethyl)trimethylsilane
Compiled by Thi Minh Ha Vuong

Thi Minh Ha Vuong was born in Vietnam, in 1985. She completed her B.Sc. degree in chemistry at the University of Science in Ho Chi Minh City, in Vietnam. Then, she obtained her M.Sc. degree in organic chemistry from the University of Maine in France. She is currently working towards her PhD at the University of Toulouse III Paul Sabatier under the supervision of Professor K. I. Moineau-Chane Ching (co-supervision: Dr. B. Garreau de Bonneval). Her research interests focus on the synthesis of neutral metal bis-dithiolene complexes and their organic electronic applications.

Laboratoire de Chimie de Coordination du CNRS, 205 Route de Narbonne, 31078 Toulouse, France
E-mail: ha.vuong@lcc-toulouse.fr

Introduction

(Trifluoromethyl)trimethylsilane (TMSCF3) is a flammable liquid with a boiling point of 54–55 °C, a flash point of −17 °C and density of 0.926 g/mL at 20 °C. It may be harmful if inhaled, swallowed, absorbed through skin and may cause respiratory tract, skin and eye irritation. TMSCF3 was firstly synthesized by Rupert1 in 1984 via the condensation reaction of CF3Br and TMSCl with (Et2N)3P. Nowadays, there are various synthetic methodologies to yield this compound. Among them, the approach of Pawelke is considered as the most efficient method.2 Following this method, the reaction of CF3I and tetrakis(dimethylamino)ethylene formed an in situ mediated complex which reacted directly with TMSCl to afford TMSCF3 in 94% yield. TMSCF3 is a versatile reagent for trifluoromethylation, such as transition-metal-catalyzed reaction, miscellaneous trifluoromethylation, and addition to carbonyl and imine groups. These reactions are extremely useful approaches in the pharmaceutical and agrochemical industry,3 because they enhance metabolic stability (metabolic blocking) and alter the compound properties (lipophilicity, binding selectivity).

Abstract

(A) Oxidative Trifluoromethylation of Terminal Alkynes and Heteroarenes:
Qing and co-worker described a powerful method for the synthesis of a broad range of trifluoromethylated acetylenes in good yields by using the copper-mediated protocol.4 Recently, they have developed an alternative copper-catalyzed trifluoromethylation.5 This method is also applied to the oxidative trifluoromethylation of heteroarenes and highly electron-deficient arenes via C–H activation.6

(B) Oxidative Trifluoromethylation of Boronic Acids:
Copper-mediated or -catalyzed oxidative cross-couplings of aryl- and alkenylboronic acids with TMSCF3 under mild condition have been reported.5,7 This procedure can be employed in the various ranges of functionalized aryl, heteroaryl and alkenyl boronic acids.

(C) Cu-Catalyzed Reaction of Arylboronic Acid with TMSCF3 and S8:
This study provides an efficient and convenient protocol for the synthesis of aryl trifluoromethyl thioethers.8

(D) Cu-Mediated Nucleophilic Trifluoromethylation of Allyl Halides:
The trifluoromethylated allylic products have been synthesized in good yields.9

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Ag-Mediated Trifluoromethylation of Arenes:
The innovative procedures for silver-mediated CH trifluoromethylation of aromatic substrates were developed by Melanie S. Sanford and co-workers.10 The mechanism of these reactions is suggested to proceed via an AgCF₃ intermediate.

Pd-Catalyzed Trifluoromethylation of Aryl Halides and Vinyl Sulfonates:
Hartwig,¹¹ Sanford,¹² Grushin¹³ and Buchwald¹⁴,¹⁵ have contributed to a notable feature of this reaction.

Pd-Catalyzed Intermolecular Oxidative Aryltrifluoromethylation of Activated Alkenes:
The powerful synthesis of oxidole derivatives containing CF₃ was explored by Liu and colleagues.¹⁶ The desired products were obtained via initial arylpalladation of alkenes, continued by sequential oxidation and reductive elimination of Csp² PdIVCF₃ species.

A powerful strategy for the synthesis of precursors of biologically important unnatural cyclic amino acids and fluorinated N-heterocycles was reported. The addition to related carbonyl compounds (enones, amides, esters sulfonic, sulfinic, selenic esters and α-keto esters) was also described.¹⁸

Synthesis of α-CF₃ N-Heterocycles Through Tandem Nucleophilic Additions:
Addition catalyzed by AgF was reported by Hammond.¹⁷ The formation of activated alkenes by tandem reactions based on amination and trifluoromethylation is a notable feature of this reaction.

Addition to the Carbonyl Group:
The catalytic nucleophilic enantioselective trifluoromethylation of carbonyls, including aldehydes, ketones (alkynylketones and aryl ketones), acyl trifluoromethane, acylphosphonates and acylsilanes was reported. The addition to related carbonyl compounds (enones, amides, esters sulfonic, sulfinic, selenic esters and α-keto esters) was also described.¹⁸

Addition to Imines, Nitrones, Thiocyanate and Selenocyanate:
This series of trifluoromethylation by addition allows for generating promising candidates for the pharmaceutical and agrochemical industry.¹⁸

References
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