Togni Reagent: A Hypervalent Iodine Based Electrophilic Trifluoromethylation Reagent

Compiled by Deepak Kumar Yadav

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Dedicated to my honourable mentor Associate Professor Geeta Watal and to Professor Antonio Togni’s research group, the inventors of this reagent

Introduction

Antonio Togni and co-workers have reported a new electrophilic trifluoromethylation reagent based on a 10-I-3 hypervalent iodine, 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole known as Togni reagent, which nicely complements the nucleophilic Ruppert–Prakash reagent. The Togni reagent has the ability to transfer a CF₃ moiety electrophilically to a wide range of substrates and functionalities, including C=C and C–H bonds in hydrocarbons as well as atoms containing lone pairs, such as sulfide, primary and secondary alcohols. This electrophilic CF₃ transfer agent is the reagent of choice for most trifluoromethylation reactions (better than Yagupol’skii, Umemoto, and Shreeve reagents) due to its substrate-induced selectivity, specificity, high reactivity under mild conditions (at 0–25 °C and neutral pH), and applicability to acid- or base-sensitive substrates. It is easy to handle and can be exposed to moist air for short periods of time without any apparent alteration.

The Togni reagent is commercially available [CAS: 887144970] and can be easily prepared starting from iodo benzonic acid in a few-step synthesis.

Abstracts

(A) Trifluoromethylation of β-Keto Esters:

Antonio Togni and co-workers have reported that β-keto esters were found to react with 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole under phase-transfer catalysis to yield the α-trifluoromethylated derivatives.

(B) Electrophilic Trifluoromethylation of Aromatic and Aliphatic Thiols:

Aromatic and aliphatic thiols undergo S-trifluoromethylation in the presence of the Togni reagent without formation of the corresponding disulfide. The reaction is remarkably tolerant of various functional groups and does not show significant solvent dependence.

**Figure 1**

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(C) Trifluoromethylation of Alkyl and Aryl Phosphene P(III) Centers:
A direct, mild, and efficient trifluoromethylation of primary and secondary phosphenes is achieved with Togni reagent 1 acting as electrophilic CF₃ transfer reagent.¹¹

(D) Selective C-Functionalization of Phenols:
The Togni reagent 2 behaves as soft reagent and undergoes C-trifluoromethylation of phenol derivatives instead of the corresponding trifluoromethyl ethers.¹⁵

(E) Trifluoromethylation of Sulfonic Acids:
A variety of sulfonic acids have been trifluoromethylated using the Togni reagent 1 under mild conditions in good to excellent yields. Initial mechanistic investigations of this reaction show a clean second-order kinetics and only very weak substrate electronic effects.¹³

(F) Electrophilic Trifluoromethylation of α-Nitroesters:
α-Nitroesters were found to react with the Togni reagent 1 yielding trifluoromethylated α-nitroesters which are precursors of α-trifluoromethyl α-amino acids.¹⁰

(G) Zinc-Mediated Formation of Trifluoromethyl Ethers from Alcohols:
The hypervalent iodine Togni reagent 1 reacts with primary alcohols to give the corresponding trifluoromethylated ethers in excellent yield under mild conditions in the presence of zinc(II) bis(trifluoromethylsulfonyl)imide.¹⁴

References
(10) Kieltsch, I.; Eisenberger, P.; Togni, A. Angew. Chem. Int. Ed. 2007, 46, 754.