

SYNLETT Spotlight 329

Togni Reagent: A Hypervalent Iodine Based Electrophilic Trifluoromethylation Reagent



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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Deepak Kumar Yadav was born in 1986 in Balepur Khurd, Deoria, Uttar Pradesh, India. He received his M.Sc. (2007) in Organic Chemistry from the D.D.U. Gorakhpur University, Uttar Pradesh, India. He worked for two years as a research chemist at Chembiotek Research International Pvt. Ltd. in Kolkata before joining the research group of Associate Professor Geeta Watal at the University of Allahabad for his doctoral studies. His current research interest is focused on the development of new synthetic methodologies for discovering novel antidiabetic and antioxidant biodynamic agents of high potential with special reference of green chemistry principles.

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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 have¹ reported a new electrophilic trifluoromethylating reagent based on a 10-I-3 hypervalent iodine, 3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole known as Togni reagent **1**, which nicely complements the nucleophilic Ruppert–Prakash reagent.² 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,³ Umemoto,^{4–8} and Shreeve⁹ 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 iodobenzoic acid in a few-step synthesis.¹

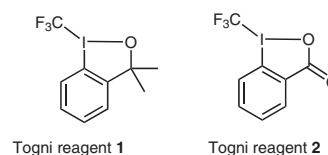
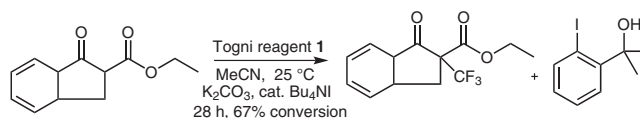


Figure 1

Abstracts

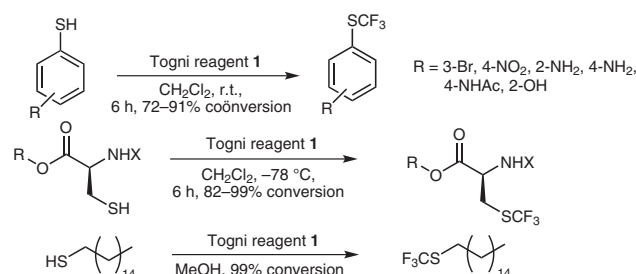
(A) Trifluoromethylation of β -Keto Esters:

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.¹



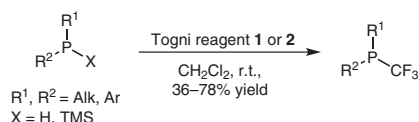
(B) Electrophilic Trifluoromethylation of Aromatic and Aliphatic Thiols:

Aromatic and aliphatic thiols undergo S-trifluoromethylation in the presence of the Togni reagent **1** without formation of the corresponding disulfide. The reaction is remarkably tolerant of various functional groups and does not show significant solvent dependence.¹⁰

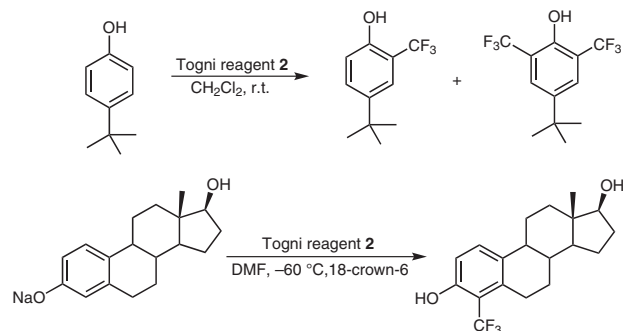


(C) *Trifluoromethylation of Alkyl and Aryl Phosphene P(III) Centers:*

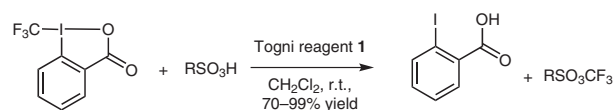
A direct, mild, and efficient trifluoromethylation of primary and secondary phosphenes is achieved with Togni reagent **1** acting as electrophilic CF₃ transfer reagent.¹¹

(D) *Selective C-Functionalization of Phenols:*

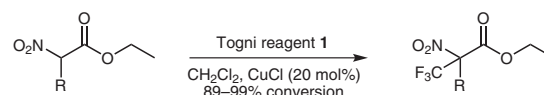
The Togni reagent **2** behaves as soft reagent and undergoes C-trifluoromethylation of phenol derivatives instead of the corresponding trifluoromethyl ethers.¹²

(E) *Trifluoromethylation of Sulfonic Acids:*

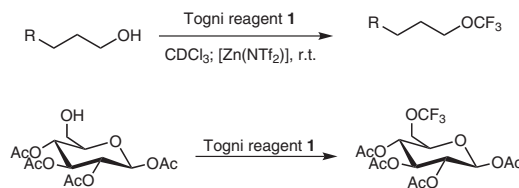
A variety of sulfonic acids have been trifluoromethylated using the Togni reagent **1** under mild conditions in good to excellent yields. Initial mechanistic investigations of this reaction show a clean second-order kinetics and only very weak substrate electronic effects.¹³

(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

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