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HYPERVALENT IODINE OXIDATION OF TRIMETHYLSILYL ENOL ETHERS OF KETONES: A DIRECT SYNTHESIS OF α-KETO TRIFLATES

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Summary α-Trifluoromethanesulfonoxy ketones (α-keto triflates) have been synthesized under very mild conditions by the reaction of silyl enol ethers of ketones and trimethylsilyl trifluormethanesulfonate/iodosobenzene in dichloromethane.

The trifluormethanesulfonic ester (triflate)[1] group positioned α to the carbonyl group represents an increasingly important entity in both mechanistic[2] and synthetic[3] organic chemistry. One of the reasons for this is the very high leaving group ability (nucleofugacity) of the triflate group[1, 4] and this accounts for the considerable synthetic utility associated with these groups in functionalization of carbonyl compounds.

Presently, among the most common methods available for synthesis of α-keto triflates are i) esterification of the α-hydroxy carbonyl compound with triflic anhydride[5,6] in the presence of a base,, and ii) reaction of an α-diazo carbonyl compound in SO_2 with triflic acid[6]. Both methods entail the obvious disadvantage of having to synthesize the precursor α-hydroxy or diazo compounds.

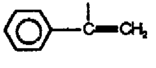
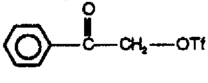
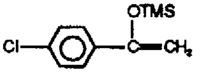
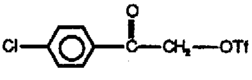
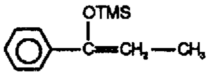
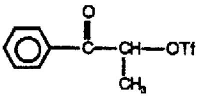
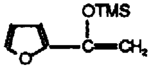
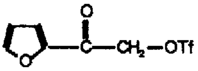
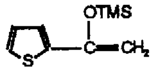
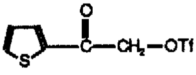
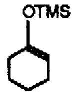
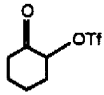
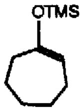
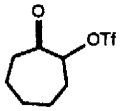
Recent studies have shown that hypervalent iodine oxidation[7] can be used to functionalize the α position of carbonyl compounds. For example, α-tosyloxy,[8] mesyloxy,[9] alkoxy,[10] hydroxy,[11] phosphoryloxy,[12] fluro,[13] and perfluoro[14] ketones have been synthesized using hypervalent iodine reagents.

In this preliminary communication we report a new and direct method of synthesis for α-keto triflates *via* hypervalent iodine oxidation of trimethylsilyl enol ethers of ketones in the presence of trimethylsilyl trifluoromethane sulfonate (TMSOTf). Our method employs the addition of TMSOTf (2) to a suspension of iodosobenzene (1)[15] in CH_2Cl_2 at -78°C followed by the addition of trimethylsilyl enol ether of the ketones (4a-g) to afford the α-keto triflates (6a-g) after usual workup in fair to good yields. (Table 1)

A possible mechanism includes initial activation of iodosobenzene (1) by TMSOTf (2) to give the hypervalent iodine electrophilic intermediate (3). This in turn may react with the trimethylsilyl enol ether (4a-g) to give intermediate 5. Nucleophilic[16] attack by the OTf anion and reductive elimination of iodobenzene then leads to the products 6a-g. Here in fact, the hypervalent iodine acts as a reverse polarity synthon.[18]

Table 1

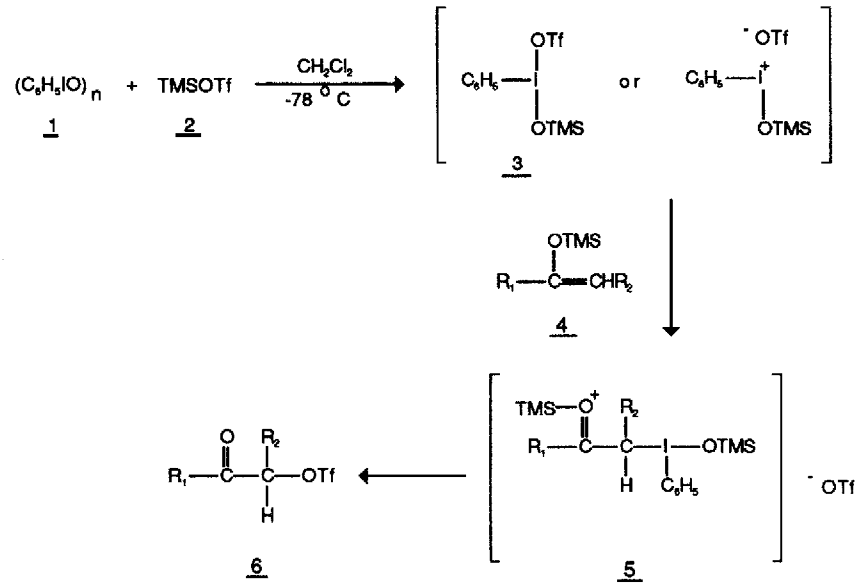
Synthesis[a] of α keto triflates

	Silyl enol ethers (4a-g)	Products[b, c] (6a-g)	M.P. (C°)	Isolated Yield %
a)			53-55 (Lit. 55.5-56)[6]	70
b)			128-130	53
c)			36-37	77
d)			79-80	70
e)			85-86	69
f)			61-63 (Lit. 59-62)[5]	64
g)			32-33	74

a) In a typical reaction, to a cooled (-78°C) suspension of 1 (2.64 g, 0.012 mol) in dry CH_2Cl_2 (50 ml), TMSOTf (2) (2.66 g, 0.012 mol) was added and stirred for 10-15 min under N_2. The trimethylsilyl enol ether (0.01 mol) in CH_2Cl_2 (30 ml) was added dropwise and stirred for 1.5 hrs at -78°C. The mixture was then brought to room temperature and the reaction mixture was stirred for 1 additional hr for 6a-e and for 15-20 min for 6f-g. Immediately, the reaction solution was washed with cold H_2O (2x50 ml), sat. aq. $NaHCO_3$ (1x25 ml), dried ($MgSO_4$) and evaporated in vacuum. Products 6a,b,d and e gave crystalline solids directly on evaporation which were washed with hexane and recrystallized with hexane or ether. Products 6c,f and g gave liquids on evaporation. Addition of hexane and cooling to 0°C overnight afforded crystalline solids.

b) All the products are best stored at or below 0°C.

c) Products were identified through IR, ^1H and ^{13}C NMR, mass spectra and elemental analysis (for C and H, in case of new compounds). Satisfactory analysis (± 0.3 %) were obtained for all new compounds, except 6g which decomposed easily. This, for carbon, had a difference of -0.6%.



The α-keto triflates 6a-g thus formed are readily identified through IR, ^1H and ^{13}C NMR spectra. The proton attached to the α carbon atom experiences a downfield shift in the range of $\delta = 5.0\text{-}6.5$. The ^{13}C NMR shows the presence of a quartet for the triflate carbon atom around 117-119 ppm. The IR spectrum shows distinct bands at $\nu = 1400\text{-}1430$, 1200-1250 and 1130-1190 cm^{-1}, due to symmetric and asymmetric SO_2 vibrations.[1]

We plan to extend our method for esters and lactones. Studies are currently going on in this direction.

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