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DIMETHYL SULFIDE DITRIFLATE: A NEW REAGENT FOR THE FACILE OXIDATION OF ALCOHOLS

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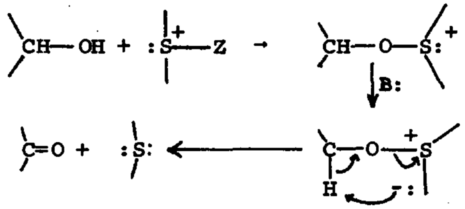
In view of the recent report on sulfoxonium salt oxidants,[1] we wish to report our investigations concerning dimethylsulfide ditriflate, which grew out of recent work in our laboratory centered on the exceptionally strong electron-withdrawing capabilities of the trifluoromethane sulfonyl ("trifyl") group.[2,3]

Dimethylsulfide-derived reagents have a long history as oxidizing agents for alcohols.[4-9] All such reagents oxidize in a similar manner proceeding through an ylide intermediate[10-12] (Equation 1).

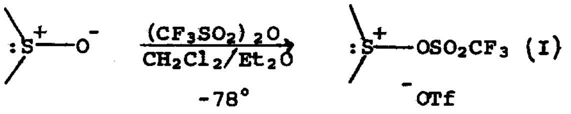


(1)

The triflate ($-OSO_2CF_3$) group should therefore be eminently suited to the role of -Z in equation (1) owing to its stability and low nucleophilicity.

Dimethyl sulfoxide was found to react with trifluoromethane sulfonic anhydride at -78° C producing the complex I which could be precipitated as a white solid from methylene chloride/ethyl ether (m.p. 85-90° C, dec.). The NMR of I ($CDCl_3$) displayed a singlet at 3.2 δ showing a pronounced downfield shift in comparison with dimethylsulfoxide (2.5 δ). The complex I decomposed overnight at room temperature or upon exposure to air or water. Therefore all reactions with I were performed by preparing the complex in situ under a nitrogen atmosphere at -78° C.

While the oxidation of "activated" alcohols (benzoins) appeared to work well using methylene chloride as a solvent, considerable amounts of the typical methylthiomethyl ether side product (II) was obtained with other substrates.



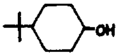
(I)

$$RCH_2OH + (I) \longrightarrow RCHO + RCH_2OCH_2SCH_3 \quad (II)$$

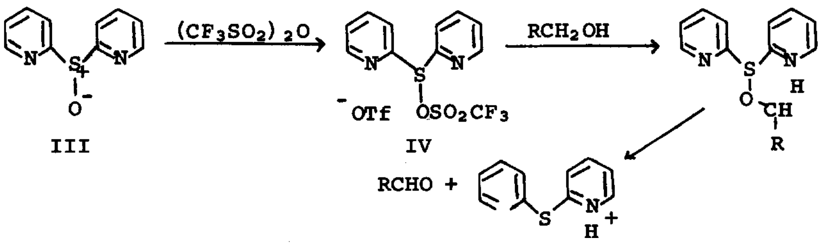
Since it was previously found that the proportion of II present in the reaction mixture was dependent on solvent polarity,[7] a systematic study of yield vs. solvent polarity was undertaken. The results are summarized in Table I.

Table I. Oxidation of alcohols with Dmso-Triflic Anhydride (2 eq.)

A) - Effect of Solvent Polarity

Substrate	Solvent System	Solvent Ratio	Time (min.)	Temp. (° C)	Yield Ketone	Yield $ROCH_2SCH_3$	Yield
Cholestanol	CH_2Cl_2/CH_3CN	1:1	10	-78	20	57	10
"	CH_2Cl_2	-	10	-78	45	40	15
"	CH_2Cl_2/CCl_4	1:1.25	15	-25	36	36	12
"	CH_2Cl_2/CCl_4	1:4.3	15	-25	53	20	--
"	CH_2Cl_2/hexanes	1:3.3	30	-78	64	12	--
"	CH_2Cl_2/hexanes	1:9	30	-78	73	10	5
	CH_2Cl_2	-	10	-78	6	84	--
"	CH_2Cl_2/hexanes	1:9	30	-78	50	50	--

In an effort to eliminate the methylthiomethyl ether side product, we investigated a reagent designed to serve the same oxidizing function without the structural option of elimination. To this end we prepared III and IV, in which the pyridine nitrogen is intended to serve as the internal base.



III IV

α,α'-Dipyridyl sulfide[13] was converted by periodate oxidation[14] to the sulfoxide III (m.p. 86-87° C) and then to IV with triflic anhydride at low temperature as before.

However reaction of IV with benzoin resulted in no reaction, even after prolonged periods at room temperature. Conducting the same reaction at -78° C (30 minutes) followed by quenching with triethylamine brought about partial oxidation, benzil being isolated in 36% yield. Cholestanol was likewise unreactive towards IV, unless quenched by external base, in which case, with pyridine as external base, elimination to cholestene proceeded in 21% yield. Thus reagent IV did not serve as expected in these oxidations and this may be a result of inadequate basicity on the reagent pyridine ring for internal removal of the requisite hydrogen.

A procedural example is as follows: 8.05 x 10^{-2} ml triflic anhydride (0.52 mm) in 0.5 ml methylene chloride was added dropwise to 3.64 x 10^{-2} ml dimethyl sulfoxide (0.5 mm) (distilled from calcium hydride) in 1 ml of methylene chloride at -78° C under a nitrogen atmosphere. After 5 minutes, 100 mg of cholestanol (0.26 mm) in 1 ml methylene chloride was added dropwise, stirred for 15 minutes, and followed by the addition of 20 ml of hexanes. After stirring for 15 minutes, 3.0 x 10^{-1} ml of triethylamine (2.08 mm) in 2.5 ml hexanes was added. The solution was allowed to warm to room temperature, and stirred for 15 minutes. The solution was diluted with 50 ml ethyl ether, washed with 10% hydrochloric acid solution (3 x), saturated sodium chloride solution (2 x), dried over sodium sulfate and evaporated leaving 95 mg clear oil. Preparative TLC ($CHCl_3$) provided 73 mg of cholestanone as white crystals (m.p. 121-23° C).

The results of similar oxidations are summarized in Table II.

Table II. Results of Dimethyl Sulfide-Ditriflate Oxidations

Alcohol	Solvent system (Ratio)	Product	Yield (%, Isolated)
Benzoin	CH_2Cl_2	Benzil	97
1,2 Diphenylethylene Glycol	CH_2Cl_2	Benzil	66
M,M′-Dimethoxybenzoin	CH_2Cl_2	M,M′-Dimethoxy-Benzil	51
Cyclohex-2-enol	CH_2Cl_2	Cyclohexeneone	46
Cholestanol	CH_2Cl_2/Hexanes (1:9)	Cholestenone (By NMR)	73
4-t-Butylcyclohexanol	"	4-t-Butylcyclo-Hexanone	50
Cholesterol (30 min RXN)	"	Δ^4Cholestenone	51
Cholesterol (10 min RXN)	"	Δ^5Cholestenone	60

It is apparent that dimethyl sulfide ditriflate is a mild oxidant which possesses the ability to rapidly oxidize alcohols in the presence of various other functionality (i.e. α,β and β,γ unsaturated alcohols, glycols, α hydroxy ketones) at low temperature.

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