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TRIFLUOROACETIC ANHYDRIDE: A NEW ACTIVATING AGENT FOR DIMETHYL SULFOXIDE IN THE SYNTHESIS OF IMINOSULFURANES

Ashok K. Sharma and Daniel Swern

Fels Research Institute and Department of Chemistry
Temple University, Philadelphia, Pennsylvania 19122

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Simple, general, high speed, high yield methods of preparation of iminosulfuranes (II) by activation of dimethyl sulfoxide (DMSO) with highly reactive electrophilic substances (AE), in which the intermediate reaction product (I) also contains an efficient leaving group and is therefore readily susceptible to facile nucleophilic attack by suitable nitrogen compounds, has been an important objective of our research program. A general iminosulfurane synthesis based on these principles is outlined below:

$$(CH_3)_2\overset{+}{S}\text{-}\overset{-}{O} + AE \longrightarrow [(CH_3)_2\overset{+}{S}\text{-O-E}]\ A^- \xrightarrow{RNH_2} [(CH_3)_2\overset{+}{S}\text{-NH-R}]\ A^- \xrightarrow{B:} (CH_3)_2\overset{+}{S}\text{-}\overset{-}{N}\text{-R}$$

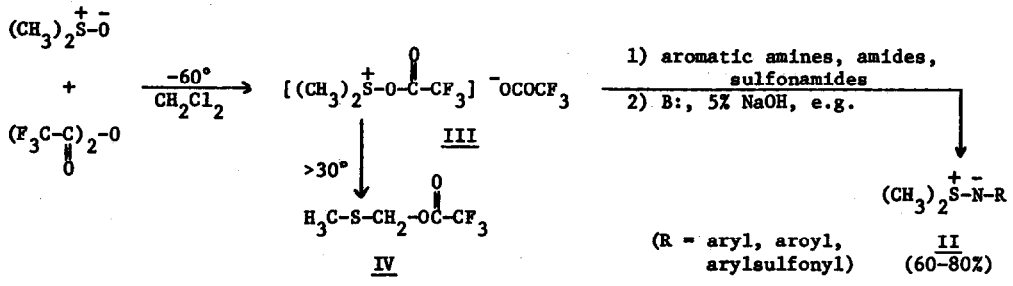
I II

A number of electrophilic substances have been used previously to activate DMSO (typically, chlorine,[1] acetic anhydride,[2] and alkyl chloroformate[3]) for the oxidation of alcohols, whereas other electrophiles (SO_3,[4,5] P_4O_{10},[4,6,7] and DCC[8,9]) have also been used for iminosulfurane preparation. Use of the latter group of activating substances presents certain problems, notably formation of side products, somewhat limited scope and applicability, and often long reaction times.

Reaction of DMSO with certain acid derivatives (halides and some anhydrides) at room temperature is extremely exothermic and can result in explosions. We therefore correctly anticipated that it would be necessary to carry out DMSO reaction with very active electrophiles under carefully controlled conditions at low temperatures. We have examined several reactive electrophiles and we find that trifluoroacetic anhydride (TFAA) is not only an extremely reactive activating agent for DMSO but it also provides an intermediate III containing an excellent leaving group. Subsequent in situ reaction of III with certain

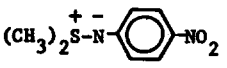
nitrogen-containing nucleophiles (aromatic amines, amides, sulfonamides) provides a high speed, high yield preparative method for iminosulfuranes II. This method has two other advantages over prior methods: (a) we have not detected any side products and (b) reaction rates for both activation and nucleophilic displacement are high.

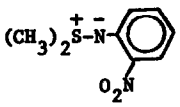
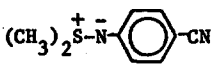
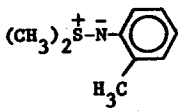
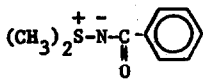
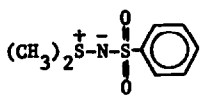
DMSO and TFAA appear to react almost instantaneously and exothermically at -60° in CH_2Cl_2 to yield a white precipitate which, for convenience, is written as structure III. This precipitate is stable at low temperatures (below -30°) but the solution becomes homogeneous on warming, resulting in the formation of IV, the Pummerer Rearrangement product of III. Formation of IV is readily observed by nmr (δ 5.35, 2H, s; 2.28, 3H, s).



Although we have no direct evidence for the structure of III (attempts to isolate it have failed) we can intercept and trap it with various nitrogen-containing nucleophiles, such as aromatic amines (in particular those with electron-withdrawing groups on the ring), carboxylic acid amides, and sulfonamides. All of these nucleophiles react rapidly; the crude products, after basification, are almost pure iminosulfuranes isolated in 60-80% yields. With amines, the reaction is complete within a few minutes (tlc); with benzenesulfonamide reaction takes about 30 min but with carboxylic acid amides about 90 minutes are required. Reaction of the corresponding nitrogen species with DMSO activated by SO_3 or P_4O_{10} usually takes about 20-30 times as long.

Some of the iminosulfuranes we have prepared, and their yields, are shown below:

	nmr[a], (δ)	mp (°C)	Yield, (%)
	2.84, 6H, s 7.60, 2H, d 8.28, 2H, d	166-7 (lit 164-6;[10] 170-1[11])	65

	nmr[a], (δ)	mp (°C)	Yield, (%)
	2.64, 6H, s 7.50, 1H, m 7.90, 1H, m 8.16, 1H, m 8.56, 1H, m	73-4[b]	60
	2.80, 6H, s 7.1, 2H, d 7.7, 2H, d	108-9 (lit 110-11;[11] 108-12[12])	66
	2.40, 3H, s 3.60, 6H, s 7.10, 4H, m	132-2.5[c]	60
	2.8, 6H, s 7.3, 3H, m 8.0, 2H, m	108-10 (lit 106-8[13])	60
	2.7, 6H, s 7.35, 3H, m 7.85, 2H, m	129-31 (lit 131[14])	80

[a] s = singlet, m = multiplet, d = doublet; $CDCl_3$ solution with XL-100 NMR Spectrometer

[b] New compound; correct elemental analysis obtained

[c] New compound; correct elemental analysis could not be obtained owing to the instability of the compound

Other noteworthy features of this new procedure are its apparent generality and the facile, high yield preparation of iminosulfuranes not readily accessible by other routes, such as S,S-dimethyl-N-(o-nitrophenyl)iminosulfurane and S,S-dimethyl-N-(benzoyl)iminosulfurane. These could not be obtained from DMSO activated by SO_3 upon reaction with o-nitroaniline or benzamide, respectively. Also, attempts to react intermediate III with aliphatic amines have not yielded iminosulfurane II but salts of the amines.

GENERAL PROCEDURE: DMSO (0.018 mol) was dissolved in CH_2Cl_2 (5 ml) in a three-necked flask fitted with a mechanical stirrer, thermometer and drying tube. Dry nitrogen was passed through the system and it was cooled to -60°. TFAA (0.01 mol) was then added slowly while maintaining the temperature below -40° throughout. The reaction was highly exothermic and a white precipitate appeared immediately. p-Nitroaniline (0.01 mol dissolved in 5 ml of

CH_2Cl_2 + 3 ml of DMSO) was slowly added while maintaining the temperature between -40 and -60°. By the time all the amine had been added, the white precipitate had disappeared. Aqueous 10% NaOH solution (5 ml) was added and the stirred reaction mixture was allowed to warm up to room temperature. The solution was extracted with CH_2Cl_2 (2 x 20 ml) and the combined CH_2Cl_2 extracts were washed with water (2 x 10 ml) and dried over anhydrous $MgSO_4$. The filtrate was evaporated to dryness at room temperature under vacuum. The residue, usually obtained in almost quantitative yield, was recrystallized from CH_2Cl_2-ether using decolorizing charcoal; the pure product, S,S-dimethyl-N-(p-nitrophenyl)iminosulfurane, was obtained in 65% yield (mp, nmr, ir, tlc identical with those of an authentic sample).[11]

Besides nitrogen nucleophiles, we are studying the reaction of other nucleophiles, such as alcohols, with the DMSO-TFAA intermediate and have achieved facile oxidation. The scope and limitations of the oxidations are currently being worked out.[15]

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