Synthetic Methods and Reactions; 52[1]. Preparation of Nitriles from Aldoximes via Dehydration with Trimethylamine/Sulfur Dioxide Complex

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Trialkylamines form 1:1 complexes with sulfur dioxide[2-5]. The relative stability of these complexes depends upon the specific amine. Amongst various amines, trimethylamine forms the strongest, the solid complex[6] with sulfur dioxide melting at 77°, whereas triethylamine gives a liquid complex showing some equilibrium SO_2 vapor[3] pressure at room temperature. None of these complexes has so far been utilized as a synthetic reagent.

We wish to report now the use of the trimethylamine/sulfur dioxide complex for the facile dehydration of aldoximes to nitriles. The well known Karl-Fischer[7,8] reagent consisting of iodine, pyridine, and sulfur dioxide in a 1:10:3 molar ratio has been widely used for the quantitative analysis of water content in various substances, but generally, no dehydration of the organic compound occurs with this reagent. More recently Nojima et al.[9] reported that iodine, pyridine, and sulfur dioxide in a 1:3:100 molar ratio can be used to carry out dehydrative condensation reactions as to obtain amides from carboxylic acids and amines. Although such systems could also be used to carry out dehydration of aldoximes into nitriles, use of the trimethylamine/sulfur dioxide complex described herein does not necessitate the use of free sulfur dioxide or iodine, can be easily handled, and refluxed in dichloromethane (or related solvents) without decomposition. Further, although various methods[10-13] are known to convert aldoximes into nitriles, yields are not generally high, frequently forceful reaction conditions are needed, and methods frequently are not general for both aryl and alkyl substitution of aldoximes. In contrast, the present method is uniformly applicable under mild conditions. Also, the reagent can be readily prepared and is a very inexpensive dehydrating agent for such a conversion. Results of the dehydration of aldoximes to nitriles are summarized in the Table. The reaction proceeds through the following mechanism.

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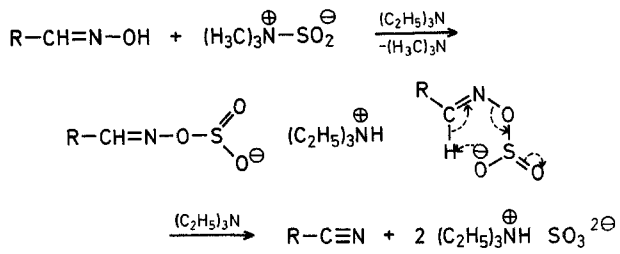

The use of an equivalent amount of triethylamine (or related base) is necessary to bind the sulfurous acid produced in the reaction, since otherwise it may destroy the nitrile. It is also possible to use the triethylamine-sulfur dioxide complex with a molar excess of triethylamine. The yields of nitriles obtained in both cases are comparable.

Preparation of Trimethylamine/Sulfur Dioxide Complex:
Trimethylamine and sulfur dioxide are separately drawn from the commercial cylinders at −78° and dissolved in dichloromethane. Equimolar quantities of the two solutions are then mixed in a flask at −78°. Dichloromethane is pumped off, resulting in a quantitative yield of the trimethylamine/sulfur dioxide complex; m.p. 77°.

General Procedure for Preparation of Nitriles:
To a magnetically stirred solution of the corresponding aldoxime (0.01 mol) and dry triethylamine (0.02 mol) in dry dichloromethane (10 ml) is dropwise added the solution of trimethylamine/sulfur dioxide complex (0.025 mol) in dry dichloromethane (5 ml) at 0° over a period of 10 min. The reaction mixture is then stirred at room temperature for 3 h, and then heated under reflux for 1 h. After being cooled, it is poured into ice/water. The dichloromethane layer is separated and the water layer extracted three times with dichloromethane (3 × 25 ml). The organic layers are combined, washed with water, and dried over anhydrous sodium sulfate. Evaporation of the solvent gives the nitriles, which are purified by distillation or recrystallization. All nitriles prepared were known compounds identified by physical properties (m.p. and b.p., I.R. and N.M.R. spectral characteristics).

Table. Nitriles from Aldoximes using Trimethylamine/Sulfur Dioxide Complex

R	Yield[a] [%]	b.p./torr or m.p. solvent	Lit.[14] b.p./torr or m.p.
n-C_5H_{11}	81	53°/12	47.3°/10
n-C_6H_{13}	83	182–183°/760	183°/760
C_6H_5	84	65°/8	69°/10
4-H_3C—C_6H_4	84	100–102°/12	91°/11
4-H_3CO—C_6H_4	79	60°	61–62°
C_6H_5—CH=CH	74	128–130°/12	134–136°/12
2-furyl	76	144–145°/760	146°

[a] Identity and purity (≥ 99%) of products confirmed by N.M.R. and I.R. spectroscopy and by thin-layer chromatography.

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