# Reagents and Synthetic Methods; 22. 1-Chlorosulfinyl-4-dimethylaminopyridinium Chloride as a New Reagent for the Dehydration of Aldoximes to Nitriles

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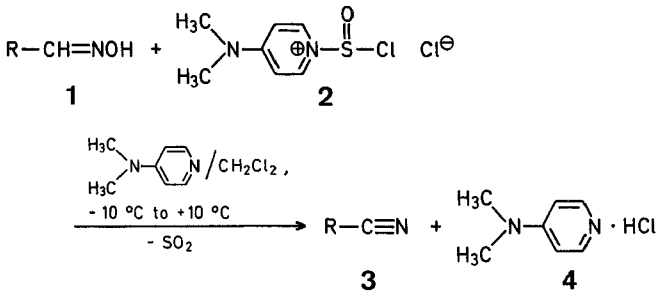
Of the numerous methods for the synthesis of nitriles[1-9] the dehydration of aldoximes[10,11,12] deserves particular attention. Some reagents used for this purpose (see also Ref.[10,11,12]) are benzenesulfenyl chloride and benzeneselenyl chloride[13], *N*-ethylacetonitrilium tetrafluoroborate[14,15], trifluoroacetic anhydride[16,17], orthocarboxylic esters[18,19], hexamethylphosphoric triamide (HMPT)[20], trimethylamine-sulfur dioxide[21], sulfuryl chloride fluoride[22], chlorosulfonyl isocyanate[23], *N,N*-dimethylchloromethaniminium chloride[24], and *N,N*-dimethyldichloromethaniminium chloride[25]. Some of these reagents can be used under mild conditions; however, the reagents are expensive and/or not readily accessible. We have recently reported[26] that 1-chlorosulfinyl-4-dimethylaminopyridinium

chloride (**2**) is more reactive than thionyl chloride or thionyl chloride/pyridine for carboxy group activation. We now report the application of reagent **2** to the dehydration of aldoximes (**1**) to nitriles (**3**).



The reaction is complete within 10–30 min. The isolated crude nitriles **3** are almost pure; they show sharp melting points or narrow melting ranges which are close to those of the purified products. The reaction conditions used are mild so that the method can be applied to sensitive compounds such as 2-hydroxybenzaldoxime (**1d**), cinnamaldoxime (**1g**), and even aldoximes of the types **1h** and **1i**. A further advantages of our method are the use of the relatively inexpensive thionyl chloride as reagent, the easy recovery of 4-dimethylaminopyridine from its hydrochloride **4**, and the easy performance and work-up.

**Nitriles (3) from Aldoximes (1); General Procedure:**
Thionyl chloride (0.20 ml, 2.2 mmol) is added to a stirred solution of 4-dimethylaminopyridine (0.31 g, 2.5 mmol) in dichloromethane (10 ml) at −10 °C. The mixture containing a precipitate is stirred for 5 min. The aldoxime (**1**; 2 mmol) is then added and the mixture is stirred for 1–2 min. Then, 4-dimethylaminopyridine (0.31 g, 2.5 mmol) is added at −10 °C and stirring is continued at room temperature for the time given in the Table. The mixture is washed with water (15 ml), the organic layer is separated and dried with sodium sulfate, and the solvent is evaporated to give the nitrile **3**. The aqueous layer is basified with 40% sodium hydroxide (3 ml) and extracted with dichloromethane (2 × 5 ml). Evaporation of the solvent gives 4-dimethylaminopyridine (**4**); yield: 90–95%; m.p. 110–111 °C (Ref.[29], m.p. 112–113 °C).

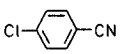
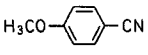
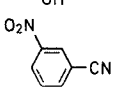
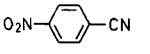
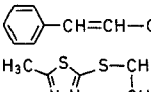
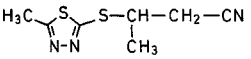
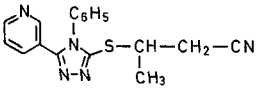
**3-(5-Methyl-1,3,4-thiadiazol-2-ylthio)-butanenitrile (3h); Typical Procedure:**
Thionyl chloride (0.40 ml, 5.5 mmol) is added to a stirred solution of 4-dimethylaminopyridine (0.67 g, 5.5 mmol) in dichloromethane (10 ml) at −10 °C. The mixture containing a precipitate is stirred for 5 min. 3-(5-Methyl-1,3,4-thiadiazole-2-ylthio)-butanal oxime (**1h**; 1.09 g, 5 mmol) is added whereupon the temperature of the mixture rises to 10 °C. Then, 4-dimethylaminopyridine (0.61 g, 5 mmol) is added and the stirring is continued at room temperature (25 °C) for 30 min. Work-up as in the general procedure affords nitrile **3h**; yield: 0.94 g (95%); m.p. 83–87 °C; m.p. upon recrystallization from methanol: 88–89 °C.

| | | | | |
|---|---|---|---|---|
| $C_7H_9N_3S_2$ | calc. | C 42.19 | H 4.55 | N 21.08 |
| (199.3) | found | 42.30 | 4.00 | 21.20 |

$^1$H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 5.6$–$5.1$ (m, 1H, CH); 2.76 (d, 2H, $CH_2$); 2.40 (s, 3H, $CH_3$); 1.56 ppm (d, 3H, $CH_3$).

**3-[4-Phenyl-5-(3-pyridinyl)-1,2,4-triazol-3-ylthio]-butanenitrile (3i); Typical Procedure:**
Thionyl chloride (0.2 ml, 2.2 mmol) is added to a stirred solution of 4-dimethylaminopyridine (0.31 g, 2.5 mmol) in dichloromethane (10 ml) at −10 °C. The mixture which contains a precipitate is stirred for 5 min. 3-[4-Phenyl-5-(3-pyridinyl)-1,2,4-triazole-3-ylthio]-butanal oxime (**1i**; 0.66 g, 1.94 mmol) is added whereupon the temperature of the mixture rises to 10 °C. Then, 4-dimethylaminopyridine (0.24 g, 2 mmol) is added and stirring is continued at room temperature (25 °C) for 30 min. Work-up as in the general procedure affords nitrile **3i**;

**Table.** Nitriles (**3**) from Aldoximes (**1**) and 1-Chlorosulfinyl-4-dimethylaminopyridinium Chloride (**2**)

| 3[a] | Reaction time [min] | Yield[b] [%] | m.p. (solvent) or b.p./torr [°C] | | Molecular formula or Lit. Data [°C] |
|---|---|---|---|---|---|
| | | | crude | distilled or recrystallized | |
| **a**  | 10 | 98 | — | b.p. 146–147°/760 | b.p. 144–146°[27] |
| **b**  | 10 | 95 | m.p. 87–89° | m.p. 91–92° (hexane/benzene) | m.p. 89–90°[27] m.p. 91°[10] |
| **c**  | 30 | 90 | m.p. 56–58° | m.p. 59–60° (hexane/benzene) | m.p. 58–60°[17] |
| **d**  | 10 | 70 | m.p. 86–87° | m.p. 90–92° (benzene) | m.p. 98°[28] |
| **e**  | 30 | 100 | m.p. 115° | m.p. 115–116° (96% ethanol) | m.p. 115–116°[17] |
| **f**  | 30 | 100 | m.p. 140–143° | m.p. 146–147° (96% ethanol) | m.p. 146–148°[17] |
| **g**  | 25 | 90 | — | b.p. 263–264° | b.p. 264°/760[28] |
| **h**  | 30 | 95 | m.p. 83–87° | m.p. 88–89° (methanol) | $C_7H_9N_3S_2$ (199.3) |
| **i**  | 30 | 97 | m.p. 162–165° | m.p. 166–167° (methanol) | $C_{17}H_{15}N_5S$ (321.4) |

[a] The known nitriles **3a–g** were identified by their physical and spectral characteristics.
[b] Yield of isolated product (solid products before recrystallization). Purity of liquid products after distillation: ≥99% as determined by T.L.C. on silica gel using ethyl acetate/hexane (1/1) as eluent, and by $^1$H-N.M.R. spectrometry.

yield: 0.6 g (97%); m.p. 162–165 °C; m.p. after recrystallization from methanol: 166–167 °C.

| | | | | |
|---|---|---|---|---|
| $C_{17}H_{15}N_5S$ | calc. | C 63.53 | H 4.70 | N 21.79 |
| (321.4) | found | 63.40 | 4.20 | 21.80 |

$^1$H-N.M.R. ($CDCl_3/TMS_{int}$): $\delta = 8.35$ (m, $2H_{arom}$); 7.15 (m, $7H_{arom}$); 5.20 (m, 1H, CH); 2.90 (d, 2H, $CH_2$); 1.65 ppm (d, 3H, $CH_3$).

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