

S,S-Dimethyl Dithiocarbonate: A Useful Reagent for Efficient Conversion of Aldoximes to Nitriles

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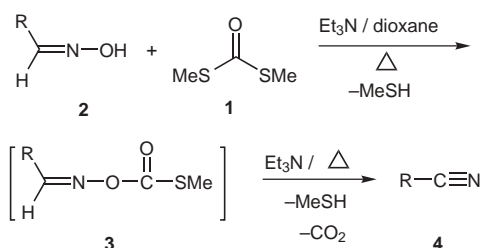
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Received 14 March 2004

Abstract: Dimethyl dithiocarbonate (DMDTC) has been shown to be an efficient dehydrating agent for a range of oximes derived from aliphatic, aromatic and heteroaromatic aldehydes yielding the corresponding nitriles in high yields.

Key words: DMDTC, nitriles, oximes, dehydration

Conversion of aldehydes into nitriles is an important synthetic transformation in organic chemistry¹ since nitriles serve as useful synthetic intermediates for pharmaceuticals, agricultural chemicals, dyes and materials chemistry.² They can be easily converted to amides, carboxylic acids, amines, ketones and esters.^{1c-f} One of the classical methods for the conversion of aldehydes to nitriles involves dehydration of the corresponding aldoximes and several efficient dehydrating agents have been developed for this transformation.³ Among the phosgene derived reagents, chlorosulfonyl isocyanate,^{3q} *N,N'*-carbonyldiimidazole,^{3s} and phenyl chloroformate⁴ have been shown to be mild and effective dehydrating agents for this transformation. During the course of our studies directed towards development of efficient sulfur containing building blocks⁵ and reagents,⁶ we became interested in exploring synthetic transformations of (*S,S*)-dimethyl dithiocarbonate (DMDTC, **1**),⁷ which could be easily prepared in high yield through AlCl₃ induced rearrangement of dimethyl xanthate.⁸ We now wish to report that DMDTC is an efficient dehydrating agent for facile conversion of a wide range of oximes to the corresponding nitriles in high yields (Scheme 1).



Scheme 1

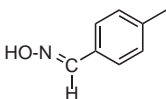
In an initial study, benzaldoxime was reacted with **1** in the presence of triethylamine in refluxing dichloromethane and gave benzonitrile only in moderate yield (50%). We therefore undertook an optimization of the reaction conditions to improve the low conversion of starting material and found that aldoxime **2a** (1.0 mmol) was smoothly converted to nitrile **4a** when heated with **1** (1.1 mmol) in dioxane in the presence of triethylamine (5.0 mmol, Scheme 1). We examined the dehydration of various aldoximes under these conditions and the results are summarized in Table 1 and Scheme 2.

Table 1 shows that electronic variations in the aromatic substituent are equally tolerated. Thus high yields of aromatic nitriles were obtained with electron donating substituents (entries 2–8), whereas the corresponding 4-nitro and 2-hydroxy benzonitriles were obtained in 70% and 63% yields, respectively (entries 9, 10). The corresponding aliphatic aldoximes also gave the respective aliphatic nitriles in high yields (Table 1, entries 11, 12). Aldoximes such as **2m** and **2n** could also be converted into the respective secondary nitriles in good yields (Table 1, entries 13, 14). Similarly, bisaldoxime **2o**, from *p*-phthalaldehyde, was smoothly dehydrated to give 1,2-dicyanobenzene **4o** in excellent yield (92%).

Various heteroaromatic aldoximes were found to be compatible with the employed reaction conditions and the corresponding heteroaromatic nitriles derived from thiophene, furan, pyrrole, indole and pyridine (Table 1, entries 16–22) were obtained in high yields. The synthetic utility of the present method was further demonstrated in the preparation of α,β -unsaturated nitriles **6a,b** and **8** (Scheme 2) which are useful intermediates in organic synthesis.^{9a} Thus, *trans*-cinnamaldoximes **5a,b** were conveniently converted to the corresponding nitriles **6a,b** with stereochemical retention of the double bond. Similarly, the cyclic 3,4-dihydro-2-cyano-6-methoxynaphthalene (**8**) was obtained in 90% yield from the corresponding oxime **7** under identical conditions. The efficiency of the present method was further evident from the facile conversion of citral oxime **9** to geranonitrile **10** (Scheme 2) which is a useful perfumery ingredient in industry.^{9b}

The probable mechanism for the formation of nitriles from aldoximes is shown in the Scheme 1. It is anticipated that the reaction of DMDTC (**1**) with aldoxime should result in displacement of methanethiolate anion to give

Table 1 Dehydration of Aldoximes to Nitriles with DMDTC

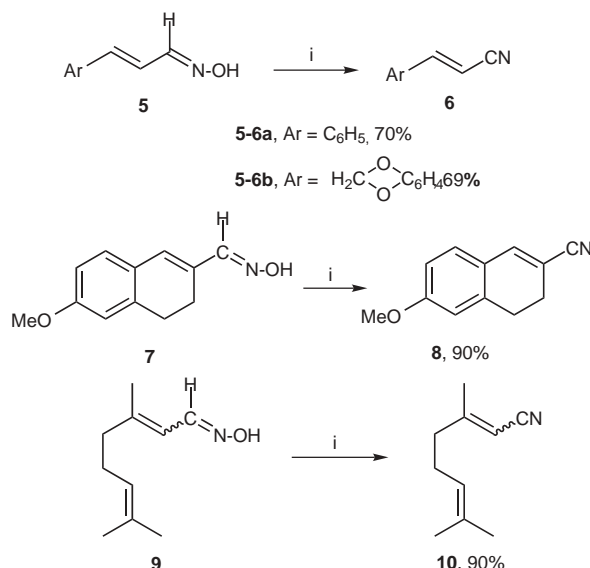
Entry	Oxime	R	Nitrile	Yield (%) ^{10,11}
1	2a	Ph	4a	88
2	2b	4-MeOC ₆ H ₄	4b	92
3	2c	2-MeOC ₆ H ₄	4c	89
4	2d	2,5-(MeO) ₂ C ₆ H ₃	4d	87
5	2e	3,4-(MeO) ₂ C ₆ H ₃	4e	89
6	2f	3,4,5-(MeO) ₂ C ₆ H ₂	4f	93
7	2g	4-ClC ₆ H ₄	4g	80
8	2h	4-(NMe ₂)C ₆ H ₄	4h	93
9	2i	4-NO ₂ C ₆ H ₄	4i	70
10	2j	2-HOC ₆ H ₄	4j	63
11	2k	C ₆ H ₅ CH ₂	4k	81
12	2l	<i>n</i> -C ₇ H ₁₅	4l	80
13	2m	(CH ₃) ₂ CH	4m	85
14	2n	C ₆ H ₅ (CH ₃)CH	4n	75
15	2o		4o	92
16	2p	2-Thienyl	4p	76
17	2q	2-(5-Methyl)furyl	4q	83
18	2r	2-(1- <i>N</i> -Methylpyrrolyl)	4r	84
19	2s	3-(Indolyl)	4s	87
20	2t	3-(1- <i>N</i> -Methylindolyl)	4t	97
21	2u	3-Pyridyl	4u	76

fragmentation prone O-substituted aldoxime thioester **3** which would collapse under reaction conditions to generate nitrile **4**, carbon dioxide and methylmercaptan.

In conclusion, the methodology reported herein demonstrates dimethyl dithiocarbonate to be an efficient dehydrating agent for conversion of a range of aldoximes to the corresponding nitriles and offers a useful alternative to the existing methodologies due to its simplicity and high yields.

Acknowledgment

TAK thanks DST, New Delhi for junior research fellowship. Financial assistance under DST project is also acknowledged.



Scheme 2 Reagents and conditions: (i) DMDTC (1.1 mmol), Et₃N (5.0 mmol), dioxane, 90 °C.

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- (10) All nitriles were characterized by comparison of their physical and spectroscopic data with reported data.
- (11) **General Procedure for Preparation of Nitriles:** To a solution of the appropriate oxime **2** (1 mmol), DMDTC (0.14 g, 1.1 mmol) and Et₃N (0.70 mL, 5.0 mmol) in dioxane (15 mL) were heated with stirring at 90 °C for 8–11 h (monitored by TLC). Concentration under reduced pressure gave crude product, which was filtered through a short silica gel column using hexane–EtOAc as eluent to give the corresponding nitrile **4**.