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$P(RNCH_2CH_2)_3N$: A Versatile and Efficient Catalyst for the Conversion of Aldoximes to Nitriles

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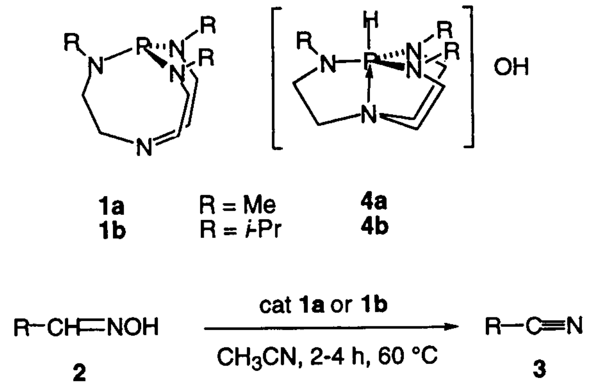
ABSTRACT: *Aldoximes are catalytically dehydrated by the strong nonionic base $P(RNCH_2CH_2)_3N$ to the corresponding nitrile in good yields under mild conditions.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10: 541–543, 1999

INTRODUCTION

The conversion of aldoximes to nitriles is a useful transformation [1] of current interest. Although a wide variety of reagents have been reported for this transformation, many of these methods present disadvantages. For example, dehydration with montmorillonite KSF [2], zeolites [3], and envirocat EPZG [4] requires high reaction temperatures or relatively long reaction times. Reagents such as triethylamine/sulfur dioxide [5] and sulfuryl chloride [6] allow rapid and mild dehydration of aldoximes, but the preparation of these reagents is inconvenient, requiring a low temperature (−78°C). Both Ph_3P/CCl_4 [7] and DBU [8] suffer from limited applicability to aromatic aldoximes. Thus there is a need for a convenient and broadly applicable methodology for this conversion.

The commercially available strong nonionic base **1a** and its analogue **1b** have found a variety of applications as a catalyst and as a stoichiometric base in organic synthesis [9]. Here we report that these phosphine bases function as mild and generally applicable catalysts for the conversion of both aliphatic and aromatic aldoximes to nitriles (Scheme 1). With aliphatic aldoximes the reaction is complete in two hours at room temperature, while the reaction with aromatic aldoximes is achieved in 3 to 4 hours at 60°C (Table 1). After the reaction, the hydroxide of protonated **1a** (Mohan and Verkade, unpublished observations) and **1b**, namely, **4a** and **4b**, respectively, was formed. The preferred amount of **1a** is 0.4 equiv. in these reactions. When less catalyst was employed, for example, 0.1 equiv., the reaction was incomplete in the times given in Table 1 as monitored by thin-layer chromatography (TLC).

The strong nonionic base **1b** functions very well as a catalyst in this reaction with only 0.3 equiv. (Table 2).



SCHEME 1

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Dedicated to Prof. Alfred Schmidpeter on the occasion of his 70th birthday.

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TABLE 1 Dehydration of Aldoximes to Nitriles in the Presence of **1a**

R	T (h)	Yield (%)[a]	M.p. or B.p./Torr [11]	IR[b] (cm^{-1})
Ph	3	93	189–190°C/760 (190.7°C/760)	2225
4-ClC$_6$H$_4$	3	91	91–92°C (92°C)	2226
4-MeOC$_6$H$_4$	4	87	59–60°C (61–62°C)	2220
4-MeC$_6$H$_4$	4	95	27–28°C (27–29°C)	2228
4-O$_2$NC$_6$H$_4$	3	89	148–150°C (149°C)	2231
4-FC$_6$H$_4$	3	90	34–35°C (35°C)	2235
2-Naphthalene	3	86	64°C (66°C)	2214
PhCH=CH	4	90	147°C/21 (263.8°C/760)	2216
PhCH$_2$CH$_2$	3	89	128–129°C/12 (261°C/760)	2255
n-C$_6$H$_{13}$	2	85	181.5°C (183°C/760)	2244
n-C$_7$H$_{15}$	2	87	204–204.5°C (205.2°C/760)	2248
cyclohexyl	2	77	213.5–214°C (215°/760)	2252

[a] Yields of isolated products. All products were identified by comparison of their m.p. or b.p. [11], and by their IR [12] and/or NMR [12b, 12c, 13] spectra with those recorded in the literature.
[a] Neat.

TABLE 2 Dehydration of Aldoximes to Nitriles in the Presence of **1b**

R	T (h)	Yields (%)[a]
4-ClC$_6$H$_4$	3	89
4-O$_2$NC$_6$H$_4$	3	83
PhCH$_2$CH$_2$	3	92
2-Naphthalene	3	95
n-C$_6$H$_{13}$	2	87
n-C$_7$H$_{15}$	2	75
cyclohexyl	2	71

[a] Yields of isolated products. All products were identified by comparison of their m.p. or b.p. [11], and by their IR [12] and/or NMR [12b, 12c, 13] spectra with those recorded in the literature.

TABLE 3 The Dehydration of Aldoximes to Nitriles in the Presence of **4a**

R	T (h)	Yield H (%)[a]
4-ClC$_6$H$_4$	6	90
2-Naphthalene	6	87
PhCH$_2$CH$_2$	7	81
n-C$_7$H$_{15}$	7	75

[a] Yields of isolated products. All products were identified by comparison of their m.p. or b.p. [11], and by their IR [12] and/or NMR [12b, 12c, 13] spectra with those recorded in the literature.

To shed some light on the reaction mechanism, a sample of **4a** was prepared (Mohan and Verkade unpublished observations) for use in this reaction in place of **1a.** Although **4a** also catalyzed the conversion of aldoximes into nitriles, longer reaction times (6–7 hours) were required (Table 3). This suggests that **1a** and **1b** are more catalytically active than **4a** and **4b,** respectively, in deprotonating **2,** a process that is expected to be predominant in the beginning stages of the reaction.

General Procedure for Dehydration of Aldoximes into Nitriles

To a solution of aldoxime [10] (2 mmol) in dry acetonitrile (10 mL) either **1a** (0.8 mmol) or **1b** (0.6 mmol) in dry acetonitrile (10 mL) was added an aldoxime (2 mmol) by syringe under N$_2$. The reaction mixture was stirred at room temperature for 2 hours in the case of the aliphatic aldoximes and was heated at 60°C for 3 to 4 hours in the case of aromatic aldoximes. The solvent was then removed under vacuum, and the residue was extracted with ether (60 mL) and 2 N HCl (20 mL). The organic phase was separated and washed with brine (3 × 10 mL), dried with Na$_2$SO$_4$, and evaporated under reduced pressure. The crude material was purified by column chromatography using ethyl acetate/hexane (1:5) in all cases except for p-O$_2$NC$_6$H$_4$CN, which was eluted with a 1:3 ratio of these solvents to give product that was pure by ^{1}H NMR spectroscopy and that gave a sharp melting point (Table 1).

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