

P(CH₃NCH₂CH₂)₃N: A Nonionic Superbase for Efficient Dehydrohalogenation

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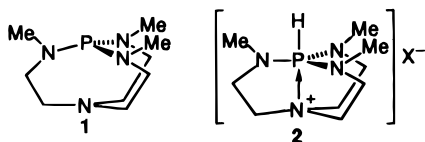
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The commercially available nonionic superbase P(CH₃NCH₂CH₂)₃N (**1**) is far superior to DBU for the conversion of primary and secondary alkyl halides to alkenes. A reason for the efficacy of acetonitrile as a solvent for the halides requiring extended reaction times is presented.

Introduction

In our ongoing search¹ for new synthetic applications of the commercially available proazaphosphatane (**1**) first synthesized in our laboratories, we have discovered that **1** is a superior dehydrohalogenation agent for primary and secondary alkyl halides. The non-nucleo-



philic yet strongly basic **1** is easily regenerated from its solid product **2** by treatment with KO-*t*-Bu.² The introduction of double bonds into organic systems via the elimination of hydrogen halides is a well-known transformation³ that has been applied to the synthesis of a variety of substrates including prostaglandins,⁴ vitamin A,⁵ and polyenes.⁶ Because typical organic bases, such as Et₃N, *N,N*-dimethylaniline, pyridine, and quinoline are often unsatisfactory for such reactions, DBN and DBU have become prominent owing to their non-nucleophilic nature and greater basicity.^{6,7} The efficacy of the latter bases was observed over 30 years ago in the dehydrohalogenation of an intermediate in the synthesis of vitamin A.⁵ However, dehydrohalogenations with DBU or DBN often require heating and excess reagent (2 or more equiv), and yields are often not high. Here, we report the efficient dehydrohalogenation of alkyl halides using only 1.1 equiv of **1** at room temperature in CH₃CN.

Results and Discussion

The isolated yields of olefins obtained in reactions of 1.1 equiv of **1** with a variety of alkyl halides **3–19** under

identical conditions are listed in Table 1. Also listed in Table 1 are conversions of **3–19** to the corresponding olefins as measured by ¹H NMR spectroscopy using DBU. Except for substrate **19**, which afforded no detectable product with either **1** or DBU, the isolated yields (85–98%) of the products formed with the remaining 16 substrates in the presence of **1** exceeded the conversions using DBU (0–87%) by moderate to very substantial margins. In Table 1 it is seen that alkyl halides possessing an electron-withdrawing group β to the halogen (**3–9**) gave high isolated yields of olefins with **1** in 5 min without detectable side reactions. High stereoselectivity was achieved upon HBr elimination from **7** since only *trans*-bromostilbene was formed in 92% yield. The presence of the activating substituents at the β carbon atom in **3–9** apparently facilitates rapid E2 elimination in the presence of strong nonionic bases. Evidence for the formation of **2** (X = Br) in these rapid reactions with **1** came from an NMR experiment involving *p*-nitro-(bromoethyl)benzene (**3**) in CD₃CN. Thus, the proton originally bound to the substrate became bound to the phosphorus in **2**, giving a doublet centered at 5.32 ppm and a one-bond P–H coupling constant of 494.4 Hz, which is characteristic of this cation.⁸ That this reaction does not require a polar solvent was shown by employing C₆D₆ as a solvent instead of CD₃CN. The conversion to *p*-nitrostyrene was again 98%, and the formation of **2** was verified by its characteristic ¹H NMR spectrum.⁸

Rather than olefin formation as the final product from **10**, cyclization to a cyclopropane ring in nearly quantitative yield was observed. Rapid cyclization was also the case for **11** and **12** wherein the presence of acidic protons facilitate epoxide and lactone formation, respectively.

Substrates such as **13–15** required more time to give high yields of the corresponding alkenes. The existence of an electron-releasing substituent at the β carbon in **17** prevents elimination in the presence of DBU, whereas **1**, which is ca. 17 p*K*_a units more basic than DBU,⁹ reacts to give an 85% yield of product, albeit after 72 h.

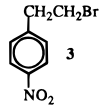
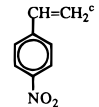







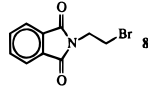
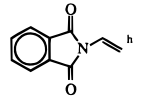


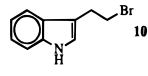

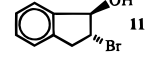
















It is of interest to speculate on a possible dehydrohalogenation pathway for substrates requiring extended reaction times in the presence of **1** in acetonitrile. Earlier, we reported that **1** slowly abstracts a proton from CD₃CN to give the deuterio analogue of **2** and ⁻CD₂CN in an equilibrium reaction.^{1d} Because the deuterio analogue of **2** was the only phosphorus-containing compound isolated in the reaction of **1** with substrates **13–**

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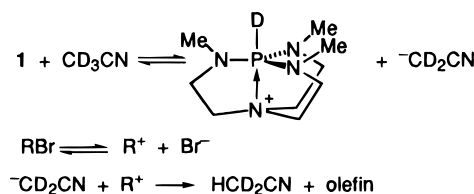
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Table 1. Dehydrohalogenation Reaction of Alkyl Halides with **1^a and DBU**

substrate	product ^b	reaction time (h)	% yield with 1	% conversion with DBU
		1/12	98	87
		1/12	94	83
		1/12	92	80
		1/12	90	18
	<i>trans</i> -PhCH=C(Br)Ph ^f	1/12	92	82
		1/12	85	8
		1/12	94	4, 82 ^j
		1/12	98	87
		1/12	92	85
		1/12	90	60 ⁿ
		20	94	60 ⁿ
		24	85	69
		24	85	50
		20	96	30
		72	85	0
	<i>trans</i> -2-heptene ^t	20	90	20
		120	— ^u	—

^a 1.1 equiv of base in CH₃CN at 25 °C under an atmosphere of N₂. ^b Identification was made by comparing ¹H NMR characteristics with those in the references indicated. ^c Butcher, M.; Mathews, R. J.; Middleton, S. *Aust. J. Chem.* **1973**, *26*, 2067. ^d *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 1358B. ^e *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 973C. ^f *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 1199A. ^g Kropp, P. J.; Crawford, S. D. *J. Org. Chem.* **1994**, *59*, 3102. ^h Benn, M. H.; Mitchell, R. E. *Can. J. Chem.* **1972**, *50*, 2195. ⁱ Rupard, J. H.; Paulis, T. de; Janowsky, A.; Smith, H. E. *J. Med. Chem.* **1989**, *32*, 2261. ^j Because the reaction mixture was a suspension rather than a solution, it was heated to 80 °C for 10 min, whereupon the conversion increased to 82%. ^k Johansen, J. E.; Christie, D.; Rapoport, H. *J. Org. Chem.* **1981**, *46*, 4914. ^l Boyd, D. R.; Sharma, N. D.; Smith, A. E. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2767. ^m Stille, J. K.; Divakaruni, R. *J. Am. Chem. Soc.* **1978**, *100*, 1303. ⁿ This is the product yield using DBU as reported by: Ono, N.; Yamada, T.; Saito, T.; Tanaka, K.; Kaji, A. *Bull. Chem. Soc. Jpn.* **1978**, *50*, 2401. ^o *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **2**, 23A. ^p *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 57c. ^q *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 61c. ^r See Supporting Information. ^s Ireland, R. E.; Habich, D. *Chem. Ber.* **1981**, *114*, 1418. ^t *Aldrich Library of ¹³C and ¹H FT NMR spectra*, **1**, 25A, 25B. ^u No observable reaction.

Scheme 1

17, these reactions in CD₃CN may well take place according to Scheme 1. Furthermore, we reported earlier¹⁰ that the ¹H-decoupled ¹³C NMR spectra of the reaction mixture of 2-bromoheptane (**18**) with **1** in CD₃CN displayed a quintet at 0.84 ppm, which is indicative of the presence of HCD₂CN. This result lends further credence to the pathway shown in Scheme 1. Thus, in the preparative-scale reactions, the ⁻CH₂CN ion (which had time to form during the slower dehydrohalogenations reported here) is apparently the active nucleophile that abstracts a proton from the substrates when **1** is employed as the base. These observations are in accord with the result that *t*-BuBr dehydrobrominates *ca.* three times faster in CH₃CN than in THF.¹⁰

Experimental Section

Unless otherwise noted, materials were obtained from commercial suppliers and were used without purification. Acetonitrile was dried with CaH₂ and distilled under nitrogen. All reactions were carried out at 25 °C under N₂. Although **1** is commercially available (Strem Chemical Co.), we prepared it according to our previously published method⁸ and stored it under N₂. The products were found to be greater than 98% pure by ¹H NMR spectral analysis.

General Procedure for Dehydrohalogenations with **1.** After **1** was dissolved (0.238 g, 1.10 mmol) in 10 mL of acetonitrile at 25 °C under N₂, the appropriate alkyl halide (1.00 mmol) in 5 mL of acetonitrile was added, and the mixture was stirred. After the reaction time stated in Table 1, solvent was removed under vacuum, and the mixture was extracted with 2 × 25 mL of ether or in some cases (i.e., substrates **7**, **8**, and **15**) with ethyl acetate. The extract was washed with 2 × 10 mL of water, and the organic layer was dried with anhydrous sodium sulfate. Concentration of the organic filtrate under vacuum afforded NMR-pure product in the yields indicated in Table 1. Compound **1** was regenerated by our previously reported procedure² from the residue remaining after the extraction.

NMR Monitoring Experiments. A 5 mm NMR tube was charged with **1** (0.048 g, 0.22 mmol) or DBU in CD₃CN (0.5 mL). To the tube was added alkyl halide (0.20 mmol), and the reaction mixture was monitored by ¹H and (in the case of **1**) by ³¹P NMR spectroscopy (see Discussion).

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Supporting Information Available: ¹H and ¹³C NMR spectra data and mass spectral molecular weights (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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