pK_a Measurements of P(RNCH$_2$CH$_3$)$_3$N

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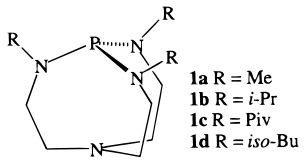
Introduction

The proazaphosphatrane nonionic superbases **1a**[1] and **1b**[2] have been found to be efficient catalysts and promoters for many reactions. Thus, proazaphosphatranes



1a R = Me
1b R = *i*-Pr
1c R = Piv
1d R = *iso*-Bu

catalyze the trimerization of isocyanates;[3] the dehydrohalogenation of alkyl halides;[4] the synthesis of α,*β*-unsaturated nitriles,[5] *β*-hydroxy nitriles,[6] homoallylic alcohols,[7] *β*-nitroalkanols,[8] α,α-dicyano-α,*β*-olefins,[9] glutaronitriles,[10] benzofurans,[11] and oxazolines;[12] the transesterification of esters;[13]the deprotection of acylated alcohols[13] and silylated alcohols;[14] Michael addition reactions;[15] the silylation of hindered alcohols;[16] and the conjugation of methylene-interrupted double bonds.[17] We have also been able to utilize these bases stoichiometrically in other syntheses, such as Wittig products,[18] Stille coupling products,[19] α,*β*-unsaturated esters,[20] and oxazoles.[21] Compound **1a** (available from Strem Chemicals) has been extensively studied and found to be superior to the weaker nonionic bases DBU and Proton Sponge,[22] but a comparison with comparably strong bases[23] was not undertaken. Recent studies with **1a** and **1b** suggest that these bases have somewhat different basicities.[2,3,6] Furthermore, we have found that **1b** is superior to **1a** in a number of reactions as a result of its higher basicity and better stability with respect to oligomerization.[6,7,20] The originally reported pK_a value of 41.2 for **1a** is in the vicinity of that for P_3 and P_4 phosphazene bases, both of which catalyze a rapid self-condensation of MeCN.[23] However, liberation of **1a** with KO-*t*-Bu in MeCN[1,2] did not result in observable MeCN self-condensation. Doubts concerning this discrepancy thus led to the measurement of pK_a values for **1a**H$^+$ by separate techniques in each of our laboratories.

In the Freiburg laboratories, a pK_a value for **1a**H$^+$ of 32.82 in MeCN was determined by UV−vis-monitored titration. In the Ames laboratories, pK_a values for **1a**H$^+$−**1d**H$^+$ were determined in MeCN by ^{31}P NMR spectroscopy. The syntheses of **1c** and **1d** and the chloride salts of their conjugate acids **1c**H$^+$ and **1d**H$^+$, respectively, will be reported elsewhere.[24] Preparations for **1a**,[1] **1b**,[2] and **1c**[3] and the chloride salts of their conjugate acids **1a**H$^+$, **1b**H$^+$, and **1c**H$^+$, respectively, were reported earlier.

Results and Discussion

The proazaphosphatrane base **1c** displayed a ^{31}P NMR signal at 144.3 ppm in C_6D_6 which, upon addition of two drops of nitromethane, rapidly disappeared and was replaced by a single ^{31}P signal at 2.29 ppm. This experiment demonstrates that this proazaphosphatrane has a pK_a value of at least 28 in MeCN, since the pK_a of nitromethane in MeCN should be about 28.[23] The strong basicity of this proazaphosphatrane was confirmed by the ability of its conjugate acid [**1c**H]Cl to equilibrate with P_2-Et in MeCN upon standing at room temperature for 1 h in an experiment monitored in a flame-sealed tube by ^{31}P NMR analysis (eq 1). In the presence of 10 mol %

$$\mathbf{5} + \mathrm{P_2\text{-}E} \rightleftharpoons \mathbf{1} + \mathrm{P_2\text{-}Et\cdot HCl} \qquad (1)$$

of Cr(acac)$_3$ as a relaxagent, this reaction afforded an equilibrium mixture that could be accurately analyzed by ^{31}P NMR spectroscopy to afford a reproducible pK_a value of 32.84 ± 0.03 in MeCN for the conjugate acid [**1c**H]Cl, based on the reported pK_a of P_2-Et.[23] The pK_a values (averages of at least two measurements) similarly obtained for **1a**H$^+$, **1b**H$^+$, and **1d**H$^+$ in MeCN are shown in Table 1. These pK_a values are substantially lower (by ~8 pK_a units) than the value we estimated previously for **1a**.[25] In that report, P_4-*t*-Bu, the only phosphazene base commercially available at that time, was used in a

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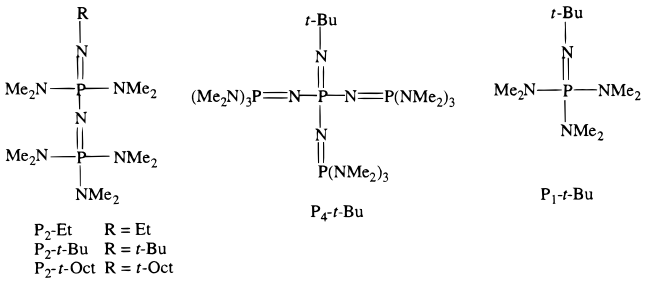
Table 1. The pK_a Values for Conjugate Acids of Proazaphosphatrane Bases in MeCN[a]

base	pK_a in MeCN	base	pK_a in MeCN
1a	32.90 (32.82[b])	**1c**	32.84
1b	33.63	**1d**	33.53

[a] Determined by ^{31}P NMR spectroscopy unless indicated otherwise. [b] Determined by UV−vis-monitored titration.

manner analogous to that described in eq 1. However, for reasons that are not clear, an apparent equilibrium was observed by ^{31}P NMR spectroscopy in an experiment utilizing an equimolar amount each of P_4-*t*-Bu and **1a**H$^+$. In a repetition of that experiment, we have found that a solution of P_4-*t*-Bu in THF completely deprotonates an equimolar amount of either **1a**H$^+$ or **1d**H$^+$ in less than 10 min. On the other hand, P_1-*t*-Bu was unable to deprotonate **1a**H$^+$. Thus, the basicities of proazaphosphatranes **1a**−**1d** are comparable with those of P_2 phosphazene bases such as P_2-Et, P_2-*t*-Bu, and P_2-*t*-Oct.



Experimental Section

The bases **1a**[1] and **1b**[2] were prepared according to previously reported methods, although **1a** is commercially available (Strem). The synthesis of **1c** and **1d** will be reported elsewhere. The MeCN (puriss. absolute) was purchased from Fluka.

Procedure A: Determination of pK_a. To 100 mg (0.30 mmol) of P_2-Et (Aldrich) weighed under nitrogen in an NMR tube was added 0.30 mmol of a proazaphosphatrane hydrochloride salt followed by 0.03 mmol of the relaxagent Cr(acac)$_3$. The NMR tube was sealed with a rubber septum, and 0.75 mL of dry[26] MeCN or CD_3CN was added under nitrogen. The tube was then flame-sealed under reduced pressure (<760 Torr but >5 Torr), and then the mixture was shaken vigorously for 0.3−1 h. NMR integration of the ^{31}P signals representing the four species shown in eq 2 afforded their molar ratios. The pK_a was then

$$\mathbf{K}_{1H^+} = \frac{10^{-32.94}[P_2\text{-}EtH^+][\mathbf{1}]}{[P_2\text{-}Et][\mathbf{1}H^+]} = \frac{10^{-32.94}[\mathbf{1}]^2}{[\mathbf{1}H^+]^2} \qquad (2)$$

calculated from this derived relationship and the definition pK_a = −log K_a. The ^{31}P NMR integration values were substituted for the concentrations of the individual species in eq 2. P_2-Et is hygroscopic and our sample of this base slowly developed a small amount of the corresponding protonated form despite efforts to preserve purity in a nitrogen atmosphere. Therefore, the pK_a value (33.53) calculated for **1d**H$^+$ from its reaction with a fresh sample of P_2-Et was used as a secondary reference to check the pK_a values determined for the other proazaphosphatranes with the aging P_2-Et sample. Like P_2-Et **1d** has been found to be stable with respect to oligomerization, oxidation, and hydrolysis under atmospheric conditions. Unlike P_2-Et, however, the proazaphosphatranes and their hydrochloride salts are not appreciably hygroscopic.

Procedure B: Determination of pK_a. To 103 mg (0.30 mmol) of **1d** weighed under nitrogen in an NMR tube was added 0.30 mmol of a protonated proazaphosphatrane chloride followed by 0.03 mmol of the relaxagent Cr(acac)$_3$. The NMR tube was sealed with a rubber septum, and 0.75 mL of dry[26] MeCN or CD_3CN was added under nitrogen. The tube was then flame-sealed under reduced pressure (<760 Torr but >5 Torr), and the mixture was shaken vigorously for 0.3−1 h. ^{31}P NMR integration of the signals representing the four species shown in eq 2 afforded their molar ratios. The pK_a was then calculated as described in Procedure A.

Procedure C: Determination of pK_a. Approximately 6.5 mg (0.030 mmol) of **1a** was dissolved under nitrogen in 2.3892 g (3.040 mL) of dry MeCN in a 10 mm UV cell. The solution also contained a pre-added quantity of *N*-ethyl-2-methyl-4-nitroaniline such that after the addition of the base the extinction at 480 nm was between 0.5 and 1 (actually 0.86 in the present case). The UV/vis spectrum was monitored after the addition of 0, 2, 6, 12, 20, 30, 40, 50, 60, 70, 72, and 74 μL of a 0.4 M solution of ethyldiisopropylammonium tetraphenylborate in dry MeCN, which was added with a 100 μL syringe in portions of 2 μL by means of a liquid feeder. To favor rapid measurement without significant loss in extinction, no thermostating of the UV cell was employed. From the extinctions at 480 nm (after baseline correction at 650 nm), the individual equilibrium constants were calculated employing the Debye−Hückel approximation (assuming a dielectric constant of 35.77[27] and an average effective ionic diameter of **1a**H$^+$ and BPh_4^- of 8.5 Å) and by adjusting the theoretical extinction (extinction at total deprotonation of the indicator) and the end point of the titration such as to minimize the error obtained by the sum of the squares method. A 4% deviation of the calculated titer of the base from unity was observed, indicating the presence of some impurities. Assuming that these impurities are caused by acid contamination (e.g., water, carbonic acid), the calculated ΔpK_a was reduced by ca. 0.03 pK units. By choosing a ΔpK_a of 0.35 ± 0.01, the titration curve was reproduced, assuming that about one-third of the impurities originated from acid contamination. The standard deviation takes into account this uncertainty. With the absolute ^{MeCN}pK_A value of the indicator (determined by titration with Et-P_2 as a reference),[23] the pK_a of **1a**H$^+$ was found by the titration described here to possess a reproducible value of 32.82 ± 0.01. As expected on steric grounds, the titration curve gave no evidence for hydrogen bonding of **1a**H$^+$ with **1a**.

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