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$P(MeNCH_2CH_2)_3N$: An Efficient Nonionic Superbase for Wittig and Wittig-Horner Reactions

Zhigang Wang and John G. Verkade*

Department of Chemistry, Iowa State University, Ames, IA 50011-3111

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ABSTRACT: *The strong non-ionic base* $P(MeNCH_2CH_2)_3N$ **1** *is an efficient base for conversion of* $[RCH_2PPh_3]X$ *and* $RCH_2P(O)(OEt)_2$ *to their corresponding ylides under mild conditions. Reaction of the ylides (generated in situ) with benzaldehyde give the corresponding alkenes in high yield.* © 1998 John Wiley & Sons, Inc. Heteroatom Chem 9: 687–689, 1998

INTRODUCTION

The exceedingly strong nonionic base $P(MeNCH_2CH_2)_3N$ **1** developed in our laboratory is finding a variety of applications in organic synthesis. For example, it is a superior catalyst for conversion of aryl isocyanates to isocyanurates [1], the protective silylation of alcohols [2], the synthesis of α,β-unsaturated nitriles [3], and as a promoter in the acylation of hindered alcohols [4]. It is also an effective deprotonation agent in base-promoted high-yield syntheses of pyrrols [5], α-C-acylamino acids [5], oxazoles [5], porphyrins [5], olefins (via dehydrohalogenation) [6], monoalkylation of active methylene systems [7], and a fluorescing agent [8].

Here, we report that **1** effectively deprotonates triphenyl phosphonium salts and phosphonates at room temperature or 60°C, allowing the ylides generated to further react with aldehydes to give the corresponding alkenes in high yield (Schemes 1 and 2, and Table 1).

RESULTS AND DISCUSSION

As seen in Table 1, the phosphonium halides **2** are dehydrohalogenated by **1** to afford stabilized (entry 1), semistabilized (entries 2–4) and nonstabilized (entries 5–6) ylides. Upon adding a solution of **1** in THF to a solution of **2** in the same solvent, coloration occurred rapidly (yellow, entries 1, 2, 5, and 6; red, entries 3 and 4) as is typical in ylide formation. ^{31}P NMR chemical shifts in C_6D_6 assignable to ylides [9] were observed for entries 1 (15.23 ppm), 2 (3.81 ppm), 3 (13.27 ppm), 4 (7.45 ppm), 5 (23.45 ppm), and 6 (23.81 ppm). Ylides derived from phosphonate **5** (Scheme 2) reacted with benzaldehyde giving E-alkenes with high selectivity and in high yield (Table 1, entries 7–9). The reaction of phosphonate **5** with *trans*-cinnamaldehyde gave (2E, 4E)-alkene in higher yield (91%, Table 1, entry 9) than that obtained by using NaH (75%) [10]. As can be seen from Table 1, the Wittig-Horner reaction generally required somewhat stronger reaction conditions.

When the THF solvent was not carefully dried for the reactions of pentyltriphenylphosphonium bromide and isoamyltriphenylphosphonium bromide with benzaldehyde in the presence of **1**, their corresponding alkyl diphenylphosphine oxides (see *Experimental*) were formed. This facile hydrolysis is consistent with the presence of nonstabilized ylides [11].

The stereochemistry of the reaction product re-

Correspondence to: John G. Verkade.

Dedicated to Prof. Robert R. Holmes on the occasion of his 70 birthday.

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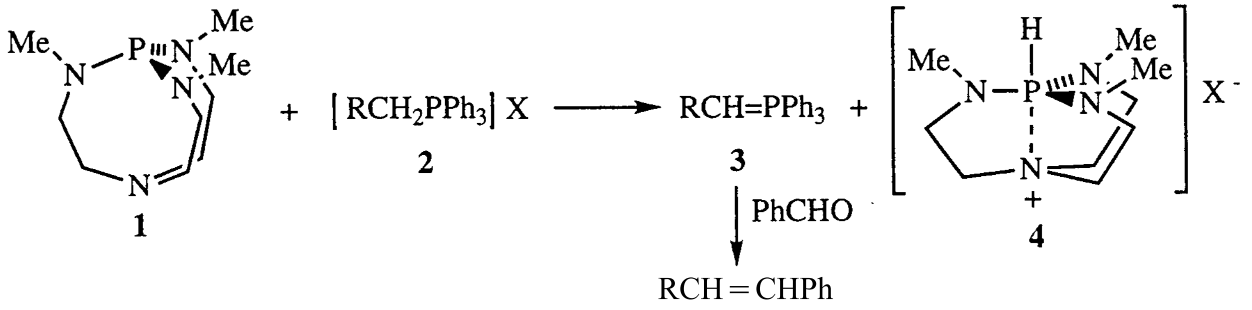

SCHEME 1

TABLE 1 Wittig and Wittig-Horner Reactions Using 1 as the Base[a]

	2		*Conditions*				
Entry	*R*	*X*	*T (°C)*	*t, (h)*	*Olefin R*	*Yield[b] %*	*Ratio E:Z[c]*
1	CH_3CO	Cl	60	4.0	CH_3CO	88	E[d]
2	Ph	Br	60	4.0	Ph	87	56:44[e]
3	$PhCH{=}CH$	Cl	rt	0.5	$PhCH{=}CH$	89	63:37[f]
4	$CH_2{=}CH$	Br	rt	0.5	$CH_2{=}CH$	70	41:59[g]
5	$CH_3(CH_2)_3$	Br	rt	0.5	$CH_3(CH_2)_3$	85	Z[h]
6	$(CH_3)_2CHCH_2$	Br	rt	0.5	$(CH_3)_2CHCH_2$	85	Z[h]
7	Ph		rt	2.0	Ph	82	96:4[e]
8	C_2H_5OCO		60	12	C_2H_5OCO	91	D[i]
9[j]	C_2H_5OCO		60	12	$C_6H_5CH{=}CH-CH{=}CHCOOEt$	92	E[k]

[a] All the reactions were run under argon, **1:2:5** = 1.2:1.2:1.0 mmol

[b] Isolated yield based on aldehyde.

[c] Determined by comparison of the ^1H NMR (300 MHz) of the crude products with those in the cited literature references.

[d] Aldrich Library of ^{13}C and ^1H FT NMR Spectra, 2, 1993, 99C.

[e] Aldrich Library of ^{13}C and ^1H FT NMR Spectra, 2, 1993, 35C-36A.

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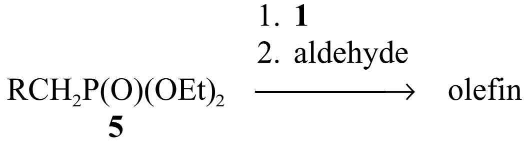
[i] Aldrich Library of ^{13}C and ^1H FT NMR Spectra, 2, 1993, 1232C.

[j] *trans*-cinnamaldehyde was employed.

[k] see Ref. 10.



$$\underset{\mathbf{5}}{RCH_2P(O)(OEt)_2} \xrightarrow[]{\substack{1.\ \mathbf{1}\\ 2.\ \text{aldehyde}}} \text{olefin}$$

SCHEME 2

alized with **1** as a base is the same as that normally observed in the Wittig reaction for the three classes of phosphonium ylides [12]. Thus the nonstabilized ylides in Table 1 quickly react with benzaldehyde to give Z-alkenes (entries 5, 6), whereas semistabilized ylides give a mixture of E and Z alkenes (entries 2–4). Although the reaction of a stabilized ylide with benzaldehyde gave the corresponding E-alkene as expected (entry 1), 4 hours at 60°C was required to complete the reaction. The Wittig-Horner reaction of phosphonates with aldehydes in the presence of **1** gave E-alkenes with high selectivity (entries 8 and 9).

EXPERIMENTAL

The phosphonates **5** and phosphonium salts **2** (both purchased from Aldrich) were reacted with a solution of **1** (0.232 g, 1.20 mmol) in dry THF (1.5 mL). Thus a suspension of alkyl phosphonium salt (1.20 mmol) in dried THF (1.5 mL) was combined with the solution of **1** at 0°C, and the mixture was then stirred at room temperature for 30 minutes, after which benzaldehyde (0.104 g, 1.00 mmol) was added to the resultant solution. The reactions involving the phosphonates **5** were carried out similarly. After the reaction conditions stated in Table 1 had been met, the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and extracted with ether (5 mL). The mixture was separated after stirring for 30 minutes, and the aqueous layer was further extracted with ether (3 × 10 mL). After the organic extracts were combined and dried with $MgSO_4$, the solvent was removed in vacuo to afford the crude alkene, which was purified by flash chromatography (hexane:ethyl acetate = 80:1 for entries 2–7 in Table 1, 30:1 for entries 1, 8, 9).

Pentyldiphenylphosphine oxide [$CH_3(CH_2)_3$-$CH_2P(O)Ph_2$]: mp 76–78°C. The ^{1}H NMR [13] and ^{31}P NMR [14] spectra compared favorably with those in the literature. ^{13}C NMR ($CDCl_3$): δ 133.32 (d, J = 96.75 Hz), 131.68 (d, J = 2.25 Hz), 130.84 (d, J = 9.0 Hz), 128.68 (d, J = 11.25 Hz), 33.21 (d, J = 14.25 Hz), 29.76 (d, J = 72 Hz), 22.22, 21.19 (d, J = 3.75 Hz), 13.90.

(3-Methylbutyl)diphenylphosphine oxide [$(CH_3)_2CHCH_2CH_2P(O)Ph_2$]: mp 98–100°C. The ^{1}H NMR spectrum compared favorably with that found in the literature [13]. ^{13}C NMR ($CDCl_3$): δ 133.32 (d, J = 99 Hz), 131.68 (d, J = 3.0 Hz), 130.87 (d, J = 9.0 Hz), 128.68 (d, J = 12 Hz), 30.02 (d, J = 4.5 Hz), 29.20 (d, J = 15 Hz), 27.76 (d, J = 72 Hz), 22.10; ^{31}P NMR ($CDCl_3$): δ 31.50.

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