

CATALYSIS OF THE MICHAEL REACTION BY TERTIARY PHOSPHINES

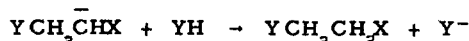
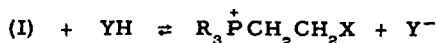
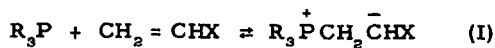
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(Received in USA 16 April 1973; received in UK for publication 31 July 1973)

The Michael addition¹ of carbon acids to activated olefins is usually catalyzed by strong bases such as hydroxide or alkoxide ion. In a few cases¹ weak bases such as Bu_3N ($\text{pK} = 9.93$ in water)² and pyridine ($\text{pK} = 5.25$ in water)³ have been used and more recently reactions catalyzed by fluoride ion⁴ ($\text{pK} = 3.7$ in water)⁵ and Et_3N ⁶ ($\text{pK} = 10.7$ in water)² have been investigated in some detail. It is now reported that this reaction is catalyzed by a group of very weak bases - the tertiary phosphines. For the particular compounds used in this work the following pK values (in 2:1 $\text{EtOH}/\text{H}_2\text{O}$) have been reported⁷ - Bu_3P (6.00), Me_2PhP (4.18), MePh_2P (presumably similar to that of EtPh_2P , i. e. < 2.60), Ph_3P (< 2.60).

The present results (Table 1, reactions 1-5) show that Bu_3P is an effective catalyst for the addition of 2-nitropropane to ethyl acrylate in a variety of solvents. It is noteworthy that both fluoride ion⁴ and Et_3N ⁶ were effective only in polar solvents such as ethanol. In tetrahydrofuran (THF) or dioxane no reaction occurred. Increasing substitution of alkyl groups on the phosphorus atom by aryl ones leads to decreasing activity and yields (Table 1, reactions 6-8). However, even with Ph_3P a good yield can be obtained using excess 2-nitropropane as the solvent (Table 1, reaction 9). Michael adducts are similarly obtained from other activated olefins (Table 1, reactions 10-13). These results with 2-nitropropane are presented as typical examples. Similar reactions have been observed with a variety of carbon acids [e. g., CH_3NO_2 , $\text{CH}_2(\text{CO}_2\text{Me})_2$, $\text{CH}_2(\text{COMe})_2$, Ph_2CHCN]. An example using dimethyl malonate is reported in detail in the Experimental section.

In contrast to the catalytic effect of Me_2PhP , Me_2PhN ($\text{pK} = 4.13$ in 2:1 $\text{EtOH}/\text{H}_2\text{O}$)⁷ is completely ineffective, in spite of the similarity in basicities. However, tertiary phosphines are much stronger nucleophiles than the analogous amines (e. g., the rate of quaternization of Et_2PhP by EtI is > 500 times faster than that of Et_2PhN ⁸). These data suggest that the tertiary phosphines behave as nucleophiles rather than bases in the present systems. The mechanism shown below is consistent with this and since intermediates such as (I) are known to be formed in the tertiary phosphine catalyzed dimerization of activated olefins,⁹ it would appear to be a reasonable interpretation of the present results. Although no strong base is added, it is evident that one is generated in situ with the formation of (I).



It is intriguing to note that initial attack occurs upon the activated olefin, whereas in the normal mechanism¹ it is the carbon acid that is attacked first.

TABLE 1. Michael addition of 2-nitropropane to activated olefins^(a)

Reaction	Olefin	Catalyst (mmoles)	Solvent	Reaction Time (hrs.)	Yield of Adduct (%)
1	CH ₂ =CHCO ₂ Et	PBu ₃ (0.5)	THF	1.5	82
2	"	"	Dioxane	"	89
3	"	"	Benzene	"	88
4	"	"	Cyclohexane	"	90
5	"	"	Hexane	"	86
6	"	PMe ₂ Ph (1)	THF	"	79
7	"	PMePh ₂ (5)	THF	20	80
8	"	PPh ₃ (10)	THF	160	36
9	"	"	excess Me ₂ CHNO ₂	24	78
10	CH ₂ =CHCOMe	PBu ₃ (1)	THF	1.0	70
11	CH ₂ =CHCN	PBu ₃ (0.5)	THF	1.0	21
12	MeCH=CHCN	PBu ₃ (1)	excess Me ₂ CHNO ₂	16	75
13	CH ₂ =C(Me)CN	PBu ₃ (10)	"	20	33

(a) Reactions were carried out by addition of the catalyst (no. of mmoles shown) to a solution of the olefin (100 mmoles) and 2-nitropropane (100 mmoles) in the solvent (20 ml) at room temperature. When excess 2-nitropropane was used as the solvent a total of 25 ml was added. Adducts in the yields shown were isolated by direct distillation after addition of MeI to remove the phosphine.

EXPERIMENTAL

The adducts of 2-nitropropane with ethyl acrylate,¹⁰ methyl vinyl ketone¹¹ and acrylo-, crotono- and methacrylonitriles¹² were identified by comparison with authentic samples made by literature methods and by their nmr spectra (Table 2).

TABLE 2. Nmr spectra of the compounds $\text{Me}_2\text{C}(\text{NO}_2)\text{CH}^\beta\text{R}^\beta\text{CH}^\alpha\text{R}^\alpha\text{X}$

A d d u c t			C h e m i c a l			S h i f t s (a)		
R^β	R^α	X	Me_2C	H^β	R^β	H^α	R^α	X
H	H	CO_2Et	1.60 (s)	2.30 (s)	-	2.30 (s)	-	1.23 (t) 4.11 (q)
H	H	COMe	1.57 (s)	2.0-2.8 (m)	-	2.0-2.8 (m)	-	2.15 (s)
H	H	CN	1.63 (s)	2.37 (m)	-	2.37 (m)	-	-
Me	H	CN	1.57 (s)	2.0-3.0 (m)	1.17 (d)	2.0-3.0 (m)	-	-
H	Me	CN	1.68 (s) 1.73 (s)	2.0-3.1 (m)	-	2.0-3.1 (m)	1.38 (a)	-

(a) In ppm downfield from internal Me_4Si reference, measured in CDCl_3 solution at 60 MHz. Relative areas were those expected. Abbreviations: s = singlet, d = doublet, t = triplet, q = quartet.

The following example is presented as typical of the experimental technique.

Addition of dimethyl malonate to methyl acrylate.

Tributylphosphine (50 mg; 0.25 mmole) was added to a mixture of the malonate (6.6 g; 50 mmoles) and acrylate (8.6 g; 100 mmoles) esters in acetonitrile (25 ml) under a nitrogen atmosphere. Heat was evolved. After 2 h, when the mixture had returned to room temperature a few drops of methyl iodide were added. The mixture was evaporated and distilled giving trimethyl 1,1,3-propanetricarboxylate [2.0 g; 18%; b 85-91° (0.2 mm); found: C 49.1, 49.2; H, 6.3, 6.4. $\text{C}_9\text{H}_{14}\text{O}_6$ requires C, 49.5; H, 6.5%] and tetramethyl 1,3,3,5-pentanetetracarboxylate [12.3 g; b 135-6° (0.2 mm)]. The latter solidified on standing and was recrystallized from cyclohexane/benzene (70/30) to give the pure compound as diamond shaped plates [10.1 g; 66%; m. 58-9°; found: C, 51.1, 51.3; H, 6.4, 6.5. $\text{C}_{13}\text{H}_{20}\text{O}_8$ requires C, 51.3; H, 6.6%]. The former, $(\text{Me}^{\text{A}}\text{OCO})_2\text{CH}^{\text{B}}\text{CH}_2^{\text{C}}\text{CH}_2^{\text{C}}\text{COOMe}^{\text{D}}$, showed nmr bands (in ppm downfield from Me_4Si in CDCl_3 , 60 MHz) at 1.9-2.5 (m, H^{C}), 3.38 (t, H^{B}), 3.63 (s, Me^{D}) and 3.70 (s, Me^{A}) the latter, $(\text{Me}^{\text{A}}\text{OCO})\text{c}(\text{CH}_2^{\text{B}}\text{CH}_2^{\text{B}}\text{COOMe}^{\text{C}})_2$, bands at 2.13 (s, H^{B}), 3.53 (s, Me^{A} or Me^{C}) and 3.63 (s, Me^{C} or Me^{A}).

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5. Both HF and HF_2^- may be formed by reaction with protons, the equilibrium constants $K = [\text{H}^+][\text{F}^-]/[\text{HF}] = \text{ca } 7 \times 10^{-4}$ and $k = [\text{HF}][\text{F}^-]/[\text{HF}_2^-] = \text{ca } 0.3$ having been measured.¹⁴ In the present use the HF_2^- ion is probably formed^{4c} and the relevant equilibrium constant is $K \times k = [\text{H}^+][\text{F}^-]^2/[\text{HF}_2^-] = \text{ca } 2.1 \times 10^{-4}$, giving the pK shown.
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