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NUCLEOPHILIC SUBSTITUTION AT PHOSPHORUS IN TERTIARY PHOSPHINES. EFFECT OF NUCLEOPHILE AND MEDIUM

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The reaction of alkyllithium reagents with tertiary phosphines has been investigated by a number of groups.[1] These reactions have involved the deprotonation of an aryl ring,[1a,b] methyl,[1b,c,d,e] or benzyl[1f,g] groups attached to trivalent phosphorus. We now report that an alternative pathway, nucleophilic substitution at phosphorus (carbon leaving group), is available, and that these reactions have a marked medium dependence. Diphenylmethylphosphine [**1**] was reacted with $\mathrm{Bu^nLi}$ in THF at 25° for 0.25 hr. followed by a D_2O quench to give *n*-butylmethylphenylphosphine [**2**] (31%) and starting phosphine (69%) which had been 27% monodeuterated.[2] Thus in THF (25°) the amount of nucleophilic substitution (*s*) was greater than deprotonation (*d*) [*s*/*d* = 1.7]. Addition of *N*,*N*,*N*´,*N*´-tetramethylethylenediamine (TMEDA) enhanced the basicity but decreased the nucleophilicity significantly. Table 1 outlines the data obtained for other solvents with and without TMEDA and $\mathrm{Bu^nLi}$.

$$\mathrm{Ph_2PCH_3} \xrightarrow[(2)\ \mathrm{D_2O}]{(1)\ \mathrm{RLi}} \mathrm{PhP(R)Me} + \mathrm{Ph_2PCH_2D}$$

1 **2** **1** - d

The more reactive $\mathrm{Bu^tLi}$[3] gave somewhat different results (Table 2). The salient comparative features of these reactions to be extracted from Tables 1 and 2 are as follows: (a) With $\mathrm{Bu^nLi}$ in THF, a large amount of nucleophilic substitution (S_N) occurs (with longer reaction times substitution approaches

TABLE 1. Reaction of Bu^nLi[a] with 1a as a function of medium

Solvent[b]	Reaction Time (hr.)	% Recovered 1 and 1-d		%2a	s/d[c]
THF[d]	0.25	50	19	31	1.7
THF[d] - TMEDA	0.25	53	28	18	0.6
Et_2O	0.50	71	22	<0.1	0
Et_2O - TMEDA	0.50	57	33	8	0.24
C_6H_6	0.50	91	05	<0.1	0
C_6H_6 - TMEDA	0.50	64	28	7	0.24
n-C_6H_{14}	0.50	96	1	<0.1	0
n-C_6H_{14} - TMEDA	0.50	73	25	2	0.09

[a] Introduced at 25° as a ~2M hexane solution in 9-10 fold excess. The resulting concentration of lithium reagent was ca. 0.1 to 0.2M. Values listed are the averages of 2-4 runs. Yields determined by g.l.c. using octadecane as internal standard. Deuterium content was determined mass spectrometrically. [b] TMEDA : Bu^nLi = 2:1. [c] s/d = ratio of substitution to deprotonation of 1a. [d] Appropriate control experiments using THF-d_8 established that the intermediate phosphinocarbanion did not deprotonate THF significantly. The half-life of Bu^nLi in THF at 25° is ca. 20 min. and with TMEDA-THF, ca. 10 min.

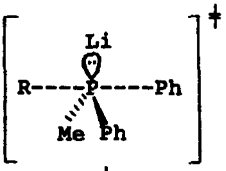
TABLE 2. Reaction of Bu^tLi[a] with 1a as a function of medium

Solvent	Reaction Time (hr.)	% Recovered 1 and 1-d		%2a	s/d
THF[b]	0.25	68	22	3	0.13
THF[b] - TMEDA	0.25	59	28	2.5	0.09
Et_2O	0.50	82	17	1	0.06
Et_2O - TMEDA	0.50	4	38 (9d_2)	45	0.95
C_6H_6	0.50	92	6	1	0.17
C_6H_6 - TMEDA	0.50	69	18	14	0.77
n-C_6H_{14}	0.50	86	12	2	0.17
n-C_6H_{14} - TMEDA	0.50	9	36 (10d_2)	48	1.0

[a] Introduced at 25° as a ~2M pentane solution in 9-10 fold excess. Product determinations, etc., as in footnotes a-d in Table 1. [b] The half-life of Bu^tLi in THF at 25° is ca. 3 min. and with THF-TMEDA, ca. 4 min.

50%), but addition of TMEDA significantly decreases the s/d ratio; (b) With less polar solvents, the S_N reaction is negligible, but addition of TMEDA increases the nucleophilicity of the lithium reagent (much more than the basicity; e.g. in Et_2O, addition of TMEDA increases deprotonation by a factor of 1.5 but S_N by >80) but not up to the level in THF; (c) In THF, Bu^tLi gives an s/d ratio significantly lower than that from Bu^nLi, and this reagent does not respond to the addition of TMEDA significantly; (d) With Bu^tLi in less polar solvents, both deprotonation and S_N respond to the addition of TMEDA, the latter more strongly (e.g. in Et_2O addition of TMEDA increases deprotonation by a factor of 6, but S_N by ~45); (e) In nonpolar solvents and TMEDA, Bu^tLi gives much more S_N than Bu^nLi (e.g. in C_6H_{14}, $S_N(Bu^tLi) = 24S_N\ (Bu^nLi)$.

The data can be rationalized by postulating that the aggregates [$(Bu^nLi)_6$ and $(Bu^tLi)_4$][4] which exist in nonpolar solvents are relatively non-nucleophilic, possibly for steric reasons. These species are still basic, however, since deprotonation would be expected to have lower steric requirements than S_N^P. Addition of TMEDA disrupts[4] the aggregates, giving a less sterically encumbered, more nucleophilic, species, which is better able to participate in a transition state such as $3^{\ddagger}$.



$3^{\ddagger}$

In low polarity solvents - TMEDA, the fact that $S_N(Bu^t) > S_N(Bu^n)$ indicates a higher innate nucleophilicity of Bu^{t-}, despite potentially greater steric interactions in $3^{\ddagger}$. With Bu^nLi in THF it is necessary also to postulate an equilibrium involving lower order, more nucleophilic aggregates. The decrease in s/d (Bu^nLi) upon addition of TMEDA could well be due to the decreased lifetime of Bu^nLi in this medium (Table 1, Footnote d). It is interesting to note that even though $3^{\ddagger}$ appears to have more steric constraints than a transition state leading to deprotonation, S_N^P is quite competitive with deprotonation in the presence of TMEDA.

The scope of the S_N reaction was investigated under standard conditions (*e.g.* entry 1, Table 1), using three additional tertiary phosphines:[5] Ph_2PCH_2Ph gave 30% Ph_2PBu^n exclusively (0.1% $Ph(PhCH_2)PBu^n$ would have been observable); Ph_3P yielded 5% Ph_2PBu^n; finally, $PhPMe_2$ produced no substituion. Apparently 3^{+} derives stabilization from having a phenyl substituent in the equatorial position.

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References

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2. Appropriate control experiments established that H-D exchange was not occurring during the D_2O quench. A similar conclusion had been reached by other workers.[1b] Phosphine **2** was not significantly deuterated.
3. Not surprisingly, there was no evidence for nucleophilic substitution on **1** by the much less reactive Grignard reagents (Bu^nMgBr, Bu^tMgCl) in ether with and without TMEDA.
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5. In all these cases, the yield of starting phosphine plus product phosphine totalled to 100% within experimental error.