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METHOXYMETHYLENE(TRIPHENYL)PHOSPHORANE FROM ALKYLLITHIUM REAGENTS

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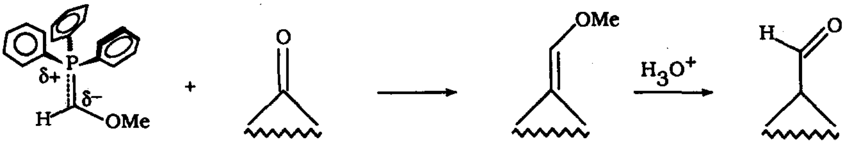
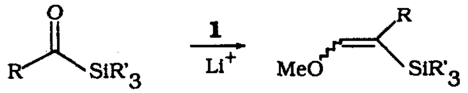
Abstract. *Whereas Li(t-Bu) is an efficient base for the generation of* $Ph_3PCHOMe$, *Li(n-Bu) gives both this ylide and a butylidene ylide which is consistent with a* $Ph_2(MeOCH_2)PCH(n\text{-}Pr)$ *formulation.* ^{31}P *NMR studies and their reactions with acylsilanes are described.*



1

For over three decades, methoxymethylene(triphenyl)phosphorane (**1**) has been extensively employed for the homologation of carbonyl compounds.[2,3] After initial success with LiPh,[2a,b] the wide variety of bases which have been employed for the preparation of **1** from its phosphonium salt include dimsylsodium, alkoxides, amides and a variety of alkyllithiums. We became interested in the generation of **1** with standard alkyllithium bases because the Wittig olefination of acylsilanes is successful only under "Li^+-catalyzed" conditions.[4] While either Li(*n*-Bu) or Li(*t*-Bu) produced comparable results for alkylidene ylides, for **1**, Li(*t*-Bu) proved to be markedly superior to Li(*n*-Bu).[4a] Intrigued by this difference, we were surprised to find that Li(*n*-Bu) is commonly employed to prepare this ylide.[2n-y] We carried out a comparison of these two bases, employing both ^{31}P NMR experiments and product studies with acylsilane substrates (**2**), which clearly illustrate the basic differences between these alkyllithium reagents in this process.



2 **3**

At -90 °C, the slow addition of Li(*t*-Bu) (1 equiv) to a stirred slurry of $(Ph_3PCH_2OMe)Cl$ in THF produces a deep-red solution of **1**, which by ^{31}P NMR, is formed in ≥90% yield (δ 7.9 ppm) along with PPh_3 (δ -5.1 ppm) and several other unidentified species. Upon warming to 25 °C, the signal for **1** shifts to δ 5.8 ppm and its ^1H-coupled ^{31}P NMR spectrum (161.9 MHz) reveals both $^2J_{P\text{-}H}$ (48 Hz) and $^3J_{P\text{-}H}$ (12 Hz) coupling with the αylidic and *o*-phenyl protons, respectively. The decomposition of **1**,[5] which begins during this warm-up, is complete in <24 h at 25 °C, forming mainly PPh_3 (*ca.* 70%)[6] and other phosphorus-containing materials (δ 28.5 and 29.5 ppm). This same procedure using Li(*n*-Bu) as the base produces a *ca.* 2:1 ratio of **1**, and a second ylide, **4**, whose ^1H-coupled signal at δ 7.6 ppm (25 °C) lacks discernable fine structure. This mixture is also unstable at 25 °C giving rise to many new ^{31}P signals. Thus, unlike the stable Ph_3PCHPr (**5**),[7] neither **1** nor **4** could be concentrated for further characterization by ^1H or ^{13}C NMR.

After the generation of **1** with Li(*t*-Bu), pentanoyltrimethylsilane (**2b**) was added at -90 °C which produced a sharp ^{31}P NMR signal at -63.2 ppm indicative of the formation of the oxaphosphetane **6b** (*vide infra*). Also evident were minor signals attributable to PPh_3 (δ -7.5 ppm) and $LiCl{\bullet}(Ph_3PO)_x$ (δ 30.0 ppm) as well as to other species (δ -53.1 and -57.4 ppm). As the temperature rises, the ^{31}P NMR signal for **6b** begins to diminish at -60 °C with the reciprocative production of that for $LiCl{\bullet}(Ph_3PO)_x$, their sum remaining essentially constant at 85±5% throughout the process. GC analysis of the reaction mixture reveals that **3b** is formed as a 79:21 *Z*/*E* mixture in 83% yield (Table 1). Repeating this at -78 °C and adding PhCHO prior to the warm-up, produced no cross-over products, demonstrating the irreversible formation of **6b**. Evidently unresolvable by ^{31}P NMR at 121.4 MHz, the isomeric oxaphosphetanes, **6b**, are calculated to be of essentially equal energy in their MMX-minimized structures, shown below with selected atoms highlighted (0.2 CPK).

6b

(3R*, 4R*) (3R*, 4S*)

AcTMS (**2a**) produces results comparable to those from **2b** (*cf.* Table 1). The yield of **3a** increases only slightly with an excess of **1**, but this excess facilitates its isolation in pure form by avoiding unreacted **2a**. Increasing the size of the silyl groups (AcTES (**2c**)) only slightly increases the *Z* selectivity (84:16) of the olefination at the expense of its efficiency (**3c**, 69%). The enolate of **2c** is formed in a competitive process, and this is trapped with TMSCl to give **7** (*ca.* 30%). For AcTIPS (**2d**), **8** is the sole product, which, like **7**, was independently prepared from **2** by the LDA/TMSCl method.

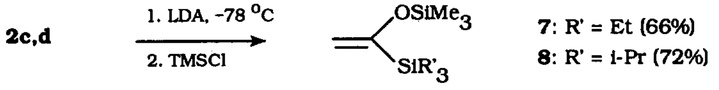
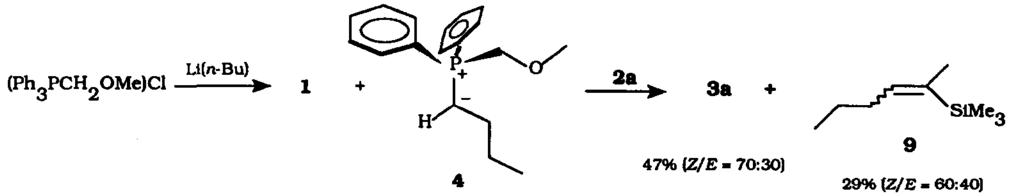


Table 1. β-Silylated Vinyl Ethers from Acylsilanes and **1**.

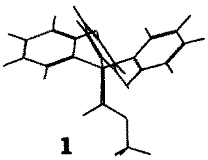
Entry	**2**	R	R'	Yield of **3**[a]	E:Z	bp(Torr)
1	**a**	Me	Me	81(50)[b]	76:24	119-130(760)
2	**b**	*n*-Bu	Me	83(51)	79:21	92-98(39)
3	**c**	Me	Et	69(33)	84:16	102-116(62)
4	**d**	Me	*i*-Pr	0		

[a] GC (Isolated yields of analytically pure material). A 1:1 molar ratio of Li(*t*-Bu)/(Ph_3PCH_2OMe)Cl was used to generate **1** in each case. [b] GC Yields (*Z/E*) with increased equiv of **1**: 83 (75:25), 1.5; 85 (76:24), 2.0; 88 (78:22), 4.0.

We returned to the generation of **1** with Li(*n*-Bu), allowing it to react with **2a** and, as when Li(*t*-Bu) was used, **3a** was produced as a similar *Z/E* mixture (70:30) but in much lower yield (47% *vs.* 81%). Surprisingly, **9** (27%) was also produced as a 60:40 *Z/E* mixture. Each of these products was identified by GC/MS, and **9** was also isolated (prep GC) to firmly establish its 2-TMS-2-hexene composition spectroscopically. This product is readily available (82%) from **5** (LiBr present) and **2a**, but this ylide produces **9** as a 96:4 *Z/E* mixture.[4a]



These observations clearly indicate that the second ylide, **4** (δ 7.6 ppm) while not **5** (δ 12.2 ppm), is a butylidene ylide. Consistent with its mixed ligand composition, it is known[8] that such ylides (*i.e.* $Ph_2(R')PCHR$, R' = Me, allyl) exhibit significantly lower *Z*-selectivity under irreversible conditions than does Ph_3PCHR as was observed for **4**. Also, Pettit's observation[2n] that butylidene products are produced with ((*n*-Bu)$_3$PCH$_2$OMe)Cl/Li(*n*-Bu) can be taken as evidence that in **4**, the butylidene ylide is favored over its methoxymethide alternative. Moreover, Seyferth[9] has observed the displacement of LiPh by Li(*n*-Bu) in the generation of Ph_3PCH_2, but not with alkylidene systems (Ph_3PCHR). These facts suggest that **4** is derived from (Ph_3PCH_2OMe)Cl and Li(*n*-Bu) by the initial displacement of LiPh by Li(*n*-Bu) which, after deprotonation results in **4**. Careful analysis of our reaction mixture by GC and GC/MS, revealed that benzene (MS library match) was produced in ≤47% yield (incomplete resolution). It can be concluded that just as was observed with Ph_3PCH_2, nucleophilic reactions at phosphorus compete with the formation of **1** using Li(*n*-Bu). Therefore, the bulkier Li(*t*-Bu) or other bases[2a,b,3] are preferable. MMX-generated minimum energy structures for the ylene form of ylides **1**, **4**, and **5** are illustrated below.



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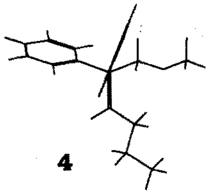

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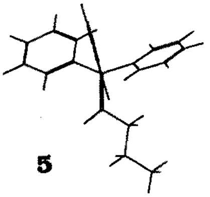

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1. The support of the NIH-MBRS Program (RR08102) is gratefully acknowledged.

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6. PPh_3, previously observed as a reaction by-product,[2n] probably resulted from the decomposition of **1**.

7. **5**: ^{13}C NMR (THF-d_8) δ 11.1 ($^1J_{P\text{-}C}$ = 118.3 Hz); 29.4 ($^2J_{P\text{-}C}$ = 5.8 Hz); 29.6 ($^3J_{P\text{-}C}$ = 11.7 Hz); 14.0; 134.2 ($^1J_{P\text{-}C}$ = 82.9 Hz); 133.0 ($^2J_{P\text{-}C}$ = 9.2 Hz); 128.8 ($^3J_{P\text{-}C}$ = 11.1 Hz); 131.1 ($^4J_{P\text{-}C}$ = 2.5 Hz) ppm. (α-^1H 0.65, dt, J = 17.2, 8.1 Hz). See also: Schlosser, M.; Liu, Z.-P. *Tetrahedron Lett.* **1990**, *31*, 5753.

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