Reactivity of Carbon Anions α to Pentacoordinated Phosphorus: Spirooxyphosphoranyl *C*-Anions as Valuable Intermediates in Olefination Chemistry

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Oxyphosphoranes, *e.g.*, pentaoxyphosphoranes, are well-documented as useful models designed to mimic the structural and electronic features of phosphorous intermediates in phosphate ester hydrolysis.[1] The synthesis and unique geometrical characteristics of many spirooxyphosphoranes have been described previously,[2] and these novel spatial features are envisioned as structural platforms for developing new stereoselective methods.[3]

The spirooxyphosphoranyl substructure (*e.g.*, **1**) was selected because the acyloxy groups are highly electron withdrawing and exhibit a higher apicophilicity (preference for the axial orientation in the trigonal bipyramidal arrangement of substituents attached to phosphorus)[4] than the ethereal P−O−C oxygens.[5] Consequently, the anticipated high barrier attending the stereomutation process, through Berry[6] or turnstile[7] mechanisms, should ensure a strong, if not exclusive, preference for the spirooxyphosphoranyl conformational substructure represented in derivatives of **1**.

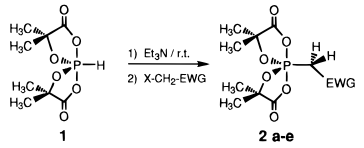
We anticipated that the acidity of the diastereotopic methylene hydrogens in **2** would be influenced by the inductive effects of the ethereal ring oxygens (through the "spiro-linked" phosphorus atom), as well as that of the acyloxy groups. Once formed, the α-"carbanion" might benefit from stabilization caused by possible polarization functions,[8a] d-functions as valence participants,[8b] and/or negative hyperconjugation effects.[9]

The objectives of our investigations were to (a) establish the propensity for the diastereotopic methylene hydrogens in spirooxyphosphorane **2** to exhibit different and measurable kinetic acidities,[10] (b) define the utility of the conjugate base of phosphorane **2** (P^v−CHLi−EWG) for initiating selective alkylations, and (c) demonstrate the feasibility of a new stereoselective olefination procedure through the condensation of the P^v−CHLi−EWG species with benzaldehyde. In this report, we describe our findings on the developments of a new olefination procedure.

Spirooxyphosphoranes **2a**−**e** were obtained by the deprotonation of phosphorane **1** with triethylamine, followed by alkylation as described by Munoz *et al.*[11] (Scheme 1).

A view of the data (Table 1) indicated that the relative ease of substitution and yields of these reactions appeared to be sensitive to the increased steric crowding attending the displacement of the halide ion. The ^{31}P NMR resonances were in accord with the expectations for a substituted pentacoordinate trigonal bipyramidal phosphorane.[12] In addition, two ^{31}P NMR resonances resulted from the *E* and *Z* stereochemistry of the 2-buten-1-yl fragment in **2d**.

Scheme 1. Alkylation of Spirooxyphosphorane **1**

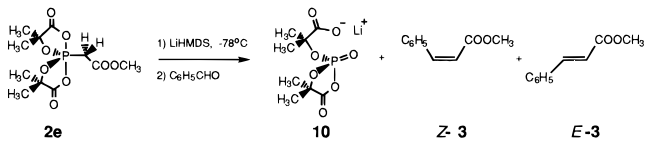


1 **2 a-e**

Table 1. Summary of Alkylation Reactions of Phosphorane **1**

EWG					$-CO_2CH_3$
Alkylated product	**2a**	**2b**	**2c**	**2d**	**2e**
X	Br	Cl	Cl	Br	Br
Rxn. Time (h)	2	10	10	2	2
Yield (%)	80	35	35	55	65
δ ^{31}P NMR ($CDCl_3$)	- 29.5	-29.05	-28.23	(E, Z) -27.06 -27.75	-36.1

Scheme 2. The Olefination Reaction



2e **10** *Z*- **3** *E*-**3**

Viewing the α-phosphoranyl organolithiums derived from the *C*-spirooxyphosphoranes **2a**−**e** as possible candidates for Horner−Wadsworth−Emmons-type olefinations,[13] we examined the lithiation of (methyloxy)carbonyl spirooxyphosphorane **2e** using lithium hexamethyldisilazane (LiHMDS), followed by treatment with benzaldehyde at −78 °C. Under these conditions, a mixture of (*E*)- and (*Z*)-methyl cinnamates **3** was obtained in 81% yield (Scheme 2).

The *E* olefinic stereochemistry was assigned to (*E*)-**3** by comparison of its ^{1}H NMR spectral data with previously reported data,[14] while the stereochemistry of the (*Z*)-**3** was ascertained by correlation of its ^{1}H NMR and MS spectral data with those of (*E*)-**3**.

A more detailed and systematic ^{31}P NMR study provided insights into a probable mechanism for the formation of

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(3) Unpublished results with Powers, T. A., Bojin, M. L., and McKithen, M., University of North Carolina, Chapel Hill, NC.
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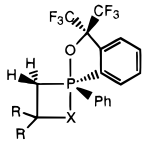
(10) (a) While the acidity (and reactivity of the conjugate base) of the methylene hydrogens α to the pentacoordinate phosphorus atom in **2** have not been explored previously, α-lithiation of 4,4-bis(trifluoromethyl)-1,2λ^5-phosphetanes **11a**,**b** have been reported.



11 a X = O **b** X = N-Ph R = CF_3, Ph

(b) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 869. (c) Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1992**, *114*, 4008. (d) Kawashima, T.; Iwama, N.; Okazaki, R. *Ibid.* **1992** *114*, 7598.
(11) (a) Lamande, L.; Munoz, A. *Phosphorus Sulfur Relat. Elem.* **1987**, *32*, 1. (b) Lamande, L.; Munoz, A. *Tetrahedron* **1990**, *46*, 3527−3534.
(12) (a) Munoz, A.; Lamande, L. *Phosphorus, Sulfur Silicon Relat. Elem.* **1990**, *49/50*, 373−376. (b) Munoz, A.; Lamande, L. *Phosphorus, Sulfur Silicon Relat. Elem.* **1992**, *70*, 263−272. (c) Compounds **2a**−**e** were characterized by employing ^{1}H, ^{13}C, and ^{31}P NMR. For example, **2c** exhibited the following spectroscopic data: ^{31}P NMR ($CDCl_3$) δ −28.23 ppm; ^{1}H NMR δ 1.10 (s, C−CH_3, 6H), 1.55 (s, C−CH_3, 6H), 2.28 (s, aryl-Me, 3H), 2.38 (s, aryl-Me), 3.40 (dd, P−C−H, $^2J_{PH}$ = 17.9 Hz, $^2J_{HH}$ = 12.8 Hz, 1H), 3.65 (dd, P−C−H, $^2J_{PH}$ = 21.9 Hz, $^2J_{HH}$ = 12.8 Hz, 1H), and 6.95−7.15 ppm (m, 3H); ^{13}C NMR ($CDCl_3$) δ 19.07 (s, aryl-Me), 20.73 (s, aryl-Me), 23.86 (d, P−O−C−*C*H$_3$, $^3J_{PC}$ = 7.40 Hz, 2C), 26.07 (s, P−O−C−*C*H$_3$, 2C), 38.64 (d, P−CH_2 $^1J_{PC}$ = 165.26 Hz), 81.01 (d, P−O−C, $^2J_{PC}$ = 6.41 Hz, 2C), 127−136 (m, aryl, 6C), and 172.16 ppm (d, P−O−C(O), $^2J_{PC}$ = 8.55 Hz).
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Scheme 3. Lithiation of **2e** with LiHMDS

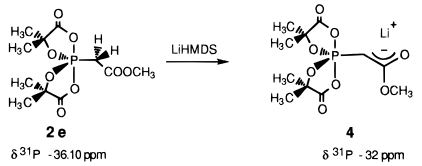


Table 2. Selected NMR Data for Phosphorane **2e** and the Corresponding α-Lithiated Derivative **4**

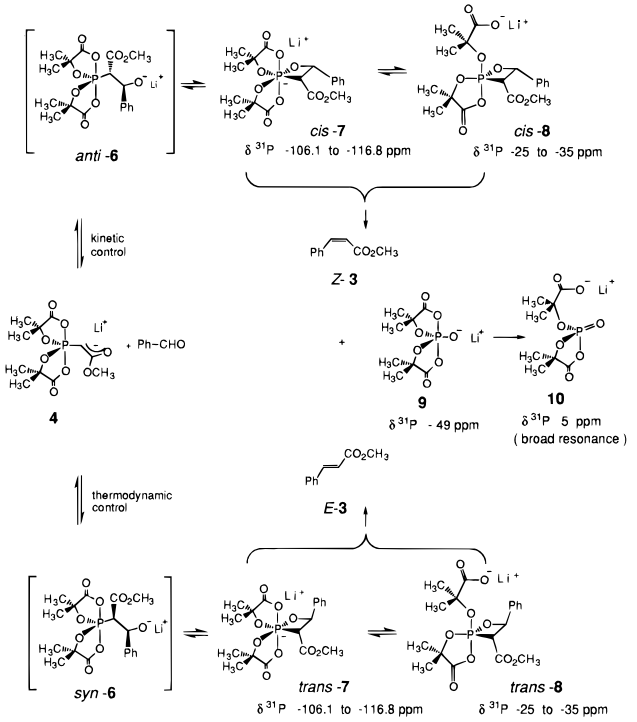
P-substituent	$^1J_{C_\alpha-H}$ (Hz)	δ_{C_α} (ppm)	$^1J_{C_\alpha-P}$ (Hz)
P−**CH$_2$**−CO$_2$CH$_3$ (**2e**)	131.2	40.2	176.5
P−**CH**Li−CO$_2$CH$_3$ (**4**)	154.9	49.5	286.0

cinnamates **3**. After the addition of 1.6 equiv of LiHMDS to 1 equiv of phosphorane **2e** (δ −36 ppm) at −78 °C, a major ^{31}P NMR resonance (δ −32 ppm) was observed. Several minor resonances were also detected (δ −29 to −33 ppm), and their chemical shifts and line shapes were both concentration and temperature dependent. This behavior suggested that this array of minor species (presumably, structurally similar to precursor phosphorane **2e**) reflected different aggregates of lithiophosphorane **4** with the tetrahydrofuran (THF) solvent and HMDS (resulting from the LiHMDS base). Finally, ^{13}C NMR data of the major component (>75%) of the mixture of lithiophosphoranes appeared to be indicative of a highly delocalized, nearly planar α-carbon anion.[15] The schematic representation of the lithiated species as structure **4** is illustrated here (Scheme 3), since we have no firm evidence as to whether the (*E*)- or (*Z*)-enolate dominates.[16a] The trends in the pertinent NMR data (*i.e.*, increases in $^1J_{C\alpha-H}$, $\delta_{C\alpha}$, and $^1J_{C\alpha-P}$ from **2e** to **4** in Table 2) are also in accord with similar observations for analogous β-carbonyl substituted phosphonates.[16b,c]

When 1 equiv of benzaldehyde was added to lithiated oxyphosphorane **4** at −78 °C, trigonal bipyramidal phosphoranes **6** were initially (presumably) formed, but they subsequently collapsed to a diastereomeric mixture of hexavalent oxyphosphoranes **7** according to the ^{31}P NMR chemical shifts (δ −106.1 to −116.8 ppm). These ranges of ^{31}P NMR chemical shifts were consistent with those for similar phosphoranes previously reported (Scheme 4).[17] A rapid equilibration of **7** to isomeric pentacoordinated phosphoranes **8** (^{31}P NMR δ −25 to −35 ppm) occurred. The multiplicities of ^{31}P NMR resonances in the chemical shift regions for hexacoordinated and pentacoordinated phosphoranes were due to (a) a mixture of diastereoisomers arising from the new stereogenic centers in the phosphetane ring and (b) different geometrical configurations of the ligands attached to the phosphorus atom. Eliminative fragmentation of either hexacoordinate phosphorane **7** or pentacoordinate phosphorane **8** afforded the isomeric alkenes. Finally, the slow formation of oxyanionic phosphorane **9** (^{31}P NMR δ −49 ppm) resulting from the extrusion of (*E*)- and (*Z*)-**3** was observed, and phosphorane **9** subsequently isomerized to phosphate **10**.

Variations in the temperature profile after the addition of benzaldehyde have a strong influence on the *E:Z* ratio of cinnamates **3**. For instance, rapid warm-up to ambient temperature (1−2 min) immediately after the addition of benzaldehyde afforded an *E:Z* = 24:76 mixture of olefins, while a rapid warm-up after 3 h at −78 °C yielded an *E:Z* = 64:36 mixture (by GC−MS). These results indicated the potential for an extremely useful kinetic *vs* thermodynamic competitive control of the stereochemical outcome of the olefination.

Scheme 4. Mechanistic Rationale for the Olefination Process



It seems reasonable to speculate that acyloxy-stabilized anion **4** reacts with benzaldehyde through a stepwise two-center pathway to give β-oxido anion *anti*-**6** rather than via an asynchronous cycloaddition[18] directly to oxaphosphetanes *cis*-**7**,**8** and *trans*-**7**,**8** (Scheme 4). It is also reasonable to expect *anti*-**6** to form rapidly, then slowly cyclize to *cis*-**7** and *cis*-**8** because of the inherent ring strain attending the formation of the 1,2-oxaphosphetane, in addition to the increase in the steric congestion due to the *syn* relationship of Ph and CO_2CH_3 substituents attached to the oxaphosphetane ring. Assuming that formation of cinnamates **3** is rate determining, thermal equilibration[19] between *anti*- and *syn*-**6** provides access to the more stable oxaphosphetanes *trans*-**7** and *trans*-**8**. In this way, the thermodynamically more stable (*E*)-**3** can be obtained through equilibration of the requisite intermediates, followed by eliminative fragmentation of *trans*-**7**,**8**.

In summary, we report a new olefination reaction employing spirooxyphosphoranes. Our preliminary mechanistic study shows that the pentacoordinated phosphorus atom is capable of exerting a strong influence on the stereochemistry of carbon−carbon double bond formation in this Horner−Wadsworth−Emmons-type process and that the *E,Z* stereoselectivity can be influenced by both kinetic and thermodynamic control. Additional mechanistic studies as well as investigations to determine the broad synthetic utility of these findings are underway.

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Supporting Information Available: Experimental procedures and spectral data for the previously unreported reaction products (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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