relates to the total dimer concentration, N_2O_4.[18] To our knowledge, there is no work in the literature that would enable us to calculate the relative contributions of the $ONONO_2$ and O_2NNO_2 isomers to the total dimer pool.

The kinetics discussed above are for dilute solutions of hydroperoxide. At the higher concentrations studied, and especially at low temperature, the order of reaction in hydroperoxide falls below unity. This phenomenon is quite common[44] in hydroperoxide chemistry in nonpolar solvents and is attributed to the formation of hydroperoxide dimers. We have chosen not to attempt to correct for dimer formation by using the thermodynamic parameters provided for TBH by Walling and Heaton for example.[45] Rather, we have limited our analysis of rate data to the lower hydroperoxide concentrations and higher temperatures used; i.e., the linear portions of plots such as those in Figure 4.

Summary, Conclusions, and Toxicological Implications

We have shown that N_2O_4 readily nitrosates organic hydroperoxides in solution, giving pernitrite esters that ultimately rearrange to give alkyl nitrates as major products. Nitrates are susceptible to acid-catalyzed decomposition to nitrous acid; the potential for damage by nitrous acid in a biological system is well-known.[46] In addition, a significant fraction of the initially formed pernitrite (ca. 20-30%) appears to decompose to form alkoxyl free radicals. Alkoxyl radicals initiate lipid autoxidation and cause biological damage.[47]

Is the reaction of NO_2/N_2O_4 with lipid peroxides important in the lung for environmental levels of NO_2? There is extensive evidence that NO_2 initiates the autoxidation of unsaturated fatty acids in the lung, forming hydroperoxides.[48] In addition, the lung contains high levels of lipoxygenase and prostaglandin systems, leading to lipid hydroperoxides. The relative rates of attack by NO_2/N_2O_4 on hydroperoxides and olefins can be estimated from our data. Taking the rate constant for nitrosation of hydroperoxides by N_2O_4 as about 10^4 M^{-1} s^{-1} and the rate of addition of NO_2 to an olefin to be about 10^{-1} M^{-1} s^{-1},[49] we obtain a rate constant ratio k_{ROOH}/k_{olef} of 10^5. A 10 ppm level of NO_2 in the gas phase would give a ratio of N_2O_4/NO_2 in solution of about 10^{-3}. Thus, for *equal* concentrations of ROOH and olefin, the ratio of reaction of NO_2/N_2O_4 with these two species equals $(k_{ROOH})/k_{olef})([N_2O_4]/[NO_2]) = 10^5 \times 10^{-3} = 100$; that is, the hydroperoxide is the favored target. If the concentration of ROOH were 1% of the olefin concentration, a ratio that is possible under conditions of high oxidative stress,[50] significant portion of the NO_2/N_2O_4 would react with the hydroperoxide by the mechanism we have outlined.

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Registry No. NO_2, 10102-44-0; N_2O_4, 10544-72-6; cumyl hydroperoxide, 80-15-9; *tert*-butyl hydroperoxide, 75-91-2.

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(50) To our knowledge, there have been no direct measurements of levels of hydroperoxides in lung materials exposed in vivo to NO_2. We calculate the level of conjugated diene found in ref 48 to be about 5% of the total lung lipid isolated. Hydroperoxides will be lower than this value due to decomposition and reduction by peroxidases.

Stereochemistry of the Wittig Reaction. Effect of Nucleophilic Groups in the Phosphonium Ylide[1]

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Abstract: Anionic, nucleophilic groups in the side chain of triphenylphosphonium ylides cause a shift in stereochemistry of the alkene products toward the *E* isomer in reactions with aldehydes. The effect is frequently stronger with aromatic aldehydes than with aliphatic aldehydes. Substituents investigated include oxido, carboxylate, amino, and amido groups. The enhancement of *E* stereoselectivity is highly dependent upon the distance of the anionic group from the phosphorus atom. Also, in the case of oxido ylides, the effect is sensitive to the cation involved. Deuterium-labeling and ^{31}P NMR studies were performed to evaluate possible mechanistic interpretations. An intramolecular Schlosser-type mechanism (as proposed in ref 8a,b) is not chiefly responsible for the anomalous *E* stereoselectivity. It is suggested that the metalloanionic group facilitates oxaphosphetane interconversion via reaction reversal, and it may also perturb the original carbon-carbon bond-forming process.

The Wittig reaction has played a prominent role in synthetic chemistry for several decades, yet a clear mechanistic understanding of its stereochemistry has failed to emerge.[2,3] Non-stabilized triphenylphosphorus ylides generally react with aldehydes to afford mainly *Z* alkenes, by a process suggested to involve betaine and/or oxaphosphetane intermediates.[2-4] The stereochemistry of such reactions can be affected by solvent, cation,

(1) Presented in part at (a) the 185th National Meeting of the American Chemical Society, Seattle, WA, March 1983 ("Abstracts of Papers"; American Chemical Society: Washington, DC, 1983; ORGN-28) and (b) the International Conference on Phosphorus Chemistry, Nice, France, September 1983 (see: Maryanoff, B. E.; Duhl-Emswiler, B. A.; Reitz, A. B. *Phosphorus Sulfur* **1983**, *18*, 187).
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(3) For some recent mechanistic proposals see: (a) Thacker, J. D.; Whangbo, M.-H.; Bordner, J. *J. Chem. Soc., Chem. Commun.* **1979**, 1072. (b) Bestmann, H. J. *Pure Appl. Chem.* **1979**, *51*, 515. (c) Bestmann, H. J. *Ibid.* **1980**, *52*, 771. (d) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823. (e) Schlosser, M.; Schaub, B. *Ibid.* **1982**, *104*, 5821. (f) Olah, G. A.; Krishnamurthy, V. V. *Ibid.* **1982**, *104*, 3987.
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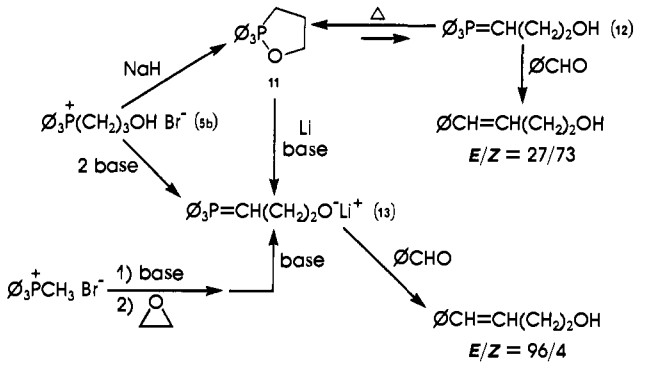
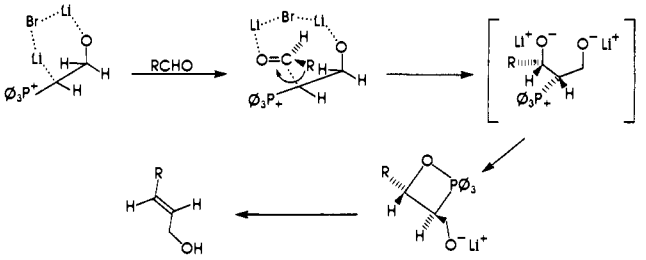
0002-7863/85/1507-0217$01.50/0

Scheme I



Scheme II



temperature, and type of aldehyde.[2-5] *Z* stereoselectivity is maximized by polar aprotic solvents, exclusion of lithium salts, and low reaction temperatures;[2,4,5a] however, a strong preference for *E* alkenes is rarely observed.[2,5]

High *E* stereoselectivity in the reaction of nonstabilized triphenylphosphorus ylides can be induced by the method of Schlosser, which entails metalation of the Wittig intermediate (betaine/oxaphosphetane) at low temperature, to give a lithio β-oxido ylide that undergoes equilibration, followed by quenching with a proton source or other electrophile.[6] Such β-oxido ylides can be generated directly from β-hydroxyalkylphosphonium salts, whereupon they also react with aldehydes to produce a preponderance of *E* alkene.[7] Interestingly, γ-oxido ylides, as well, give large amounts of *E* alkene in their reaction with aromatic and aliphatic aldehydes (e.g., see Scheme I).[8] Since the report of Salmond and co-workers[8a] on the unusual *E* stereoselectivity of γ-oxido ylides, in a synthesis of Δ^{22}-25-hydroxycholesterol, the procedure has been applied in several synthetic enterprises.[8b-f]

The exaggerated *E* stereoselectivity of β-oxido ylides has been discussed in terms of stereoselective formation of a *rac*-dioxido phosphonium adduct (e.g., see bracketed structure in Scheme II), which has a preference for elimination of *E* alkene,[7c] while that of γ-oxido ylides has been rationalized by an internal Schlosser-type "trans-selective wittig" mechanism (e.g., see Figure 4).[8a,8b] In preliminary communications,[9,10] we addressed the applicability of the latter mechanism, which requires proton transfer from carbon to oxygen in the Wittig intermediate (betaine/oxaphosphetane), as an explanation for the special *E* stereoselectivity seen with β- or γ-oxido ylides. Several lines of evidence challenge this possibility: (1) although δ-carboxy ylide **1** has only a weakly basic carboxylate group, it gave anomalously large amounts of *E* alkenes in reactions with aromatic aldehydes;[10] (2) the enhanced production of *E* alkenes with **1** was virtually abolished for aliphatic aldehydes;[10] (3) ε-oxido ylide **2** does not produce accentuated amounts of *E* alkenes in reactions with aliphatic aldehydes,[9,11] although a seven-membered cyclic transition state is suitable for intramolecular protron transfer;[12] and (4) reactions of α-deuterio-γ-oxido ylide **3** with benzaldehyde or hexanal showed only minor exchange of the deuterium label with an external proton source.[9]

$Ph_3P{=}CH(CH_2)_3COO^-M^+$ (**1**) $\quad Ph_3P{=}CH(CH_2)_4O^-M^+$ (**2**)

$Ph_3P{=}CD(CH_2)_2O^-Li^+$ (**3**)

Since the *inducement of abnormal bias for E alkenes by nucleophilic groups*, as in reactions of the oxido and carboxy ylides, has broad significance to Wittig chemistry, we have conducted a systematic study of carboxy, oxido, and amino phosphonium ylides having different distances between the nucleophilic and ylide centers. Our results reveal a remarkable dependency of alkene stereochemistry on chain length in both carboxy and oxido ylides, the trends of which provide a model for predicting final isomer ratios. Abnormal *E* stereoselectivity in the Wittig reaction was found to be maximized when anionic groups are present at certain optimal distances from the ylide site. Also, we describe the use of α-deuterated ylides as mechanistic probes for detection of an intramolecular "trans-selective Wittig" process and discuss ^{31}P NMR spectra of phosphorus ylides bearing nucleophilic groups, as well as their aldehyde adducts (oxaphosphetanes).[13] An attempt is made to collate our various observations into a reasonable mechanistic explanation of the "anionic-group effect".

Results and Discussion

A standard procedure was adopted to evaluate the reaction of phosphorus ylides with aldehydes. Generally, each phosphonium bromide salt (1 mmol) was treated with a strong base (1.1 mol equiv, or 2.1 mol equiv for salts with an auxiliary acidic group) in 3 mL of tetrahydrofuran (THF) at 23 °C (15–30 min). Benzaldehyde or hexanal (0.8 mol equiv) was added, immediately dissipating the ylide color, and the reaction was stirred for 15–60 min.[14] After the mixture was quenched with water, the alkene products were isolated and analyzed. The *Z*/*E* isomer ratios were determined by GLC and corroborated by ^1H NMR. Under these standard and some special related conditions, we studied 19 substituted phosphonium salts **5–10**, as well as phosphonium salt **4** for reference purposes. The results are presented in Table I.

Reference Reactions. For a reference for comparison to be established, **4** was reacted with benzaldehyde or hexanal under standard conditions with a variety of bases: $LiN(SiMe_3)_2$, $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, KO-*t*-Bu (Table I, entries 1–5).[15] We elected to use **4** (instead of $Ph_3P^+CH_2CH_3\,Br^-$, which we had

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(13) In a separate study, we have reported the observation of cis and trans oxaphosphetane intermediates in the Wittig reaction for the first time by ^{31}P NMR spectroscopy (Reitz, A. B.; Mutter, M. S.; Maryanoff, B. E. *J. Am. Chem. Soc.* **1984**, *106*, 1873). These ^{31}P NMR results are an extension of that work and related studies to be reported later.

(14) Several reactions were monitored with time and no change in alkene ratio over the time course of the experiment was observed.

$Ph_3\overset{+}{P}(CH_2)_nOH\ Br^-$

5a, $n = 2$
5b, $n = 3$
5c, $n = 4$
5d, $n = 5$
5e, $n = 6$
5f, $n = 11$

$Ph_3\overset{+}{P}(CH_2)_{n-1}CO_2H\ Br^-$

6a, $n = 3$
6b, $n = 4$
6c, $n = 5$
6d, $n = 7$
6e, $n = 8$
6f, $n = 11$

$Ph_3\overset{+}{P}(CH_2)_2R\ Br^-$

4, R = CH_2CH_3
8, R = NH_2
9, R = $NHCH_3$
10, R = CH_2NH_2

$Ph_3\overset{+}{P}(CH_2)_nN(CH_3)_2\ Br^-$

7a, $n = 2$
7b, $n = 3$
7c, $n = 4$
7d, $n = 6$

used in our earlier work[10]) as a model to establish reference isomer ratios because the longer alkyl chain more closely approximates the length of the aliphatic side chains found in **5–10**. For the reaction of **4** with benzaldehyde, the *Z* isomer predominated with $NaN(SiMe_3)_2$, $KN(SiMe_3)_2$, and KO-*t*-Bu, but not with $LiN(SiMe_3)_2$, which gave a 50:50 *Z*/*E* ratio. The dependence of stereochemistry on cation has extensive literature precedent.[2,4] For hexanal, $LiN(SiMe_3)_2$ gave *Z*-rich alkene in reaction with **4**, as expected; $NaN(SiMe_3)_2$ and $KN(SiMe_3)_2$ (both not run) would presumably give ca. 95% *Z*-rich alkene.[2,5a]

Since we were investigating phosphonium salts with anionic substituents, which could exert a nonspecific effect (e.g., salt or base effect) on the reaction, we also conducted reference reactions of **4** with benzaldehyde and $LiN(SiMe_3)_2$ in the presence of 1 or 5 mol equiv of lithium *n*-pentoxide or lithium *n*-hexanoate (entries 6–9). The *Z*/*E* ratios for these four experiments ranged from 53:47 to 63:37. Thus, such lithium salts, analogous to the intramolecular salts in carboxy and oxido ylides, present in a fairly large quantity, were unable to augment *E* stereoselectivity, by a lithium-salt effect or by a "trans-selective Wittig" mechanism. Indeed, the extraneous salts had a tendency to slightly augment *Z* stereoselectivity. Although this would appear, on first glance, to cast doubt on the validity of the "trans-selective Wittig" mechanism as an explanation for anomalous *E* stereoselectivity in oxido and carboxy ylides, internal proton exchange could be effectively accelerated by intramolecularity.[12]

To examine the effects of small changes in reaction concentration on the alkene isomer ratio, we reacted **4** with benzaldehyde with use of $LiN(SiMe_3)_2$ as base in varying amounts of THF. A modest but detectable dependence of product stereochemistry on the concentration of the reaction was observed. A 4-fold or 2-fold decrease in concentration caused an increase in *Z* isomer by 15% or 7%, respectively (entries 10 and 11), and a 2-fold increase in concentration caused a decrease in *Z* isomer by 15% (entry 12).[16] The concentration dependence alerted us to the necessity of rigorously adhering to a single set of reaction conditions and reinforced the view, previously expressed,[3d] that care must be exercised in extrapolating from Wittig reactions carried out under special conditions. All experiments with salts **5–10** and hexamethyldisilazide bases were performed under identical, carefully controlled conditions.[17] Experiments with KO-*t*-Bu were identical except for the protic *tert*-butyl alcohol generated, and experiments with *n*-butyllithium were identical except for the presence of hexane and *n*-butane.

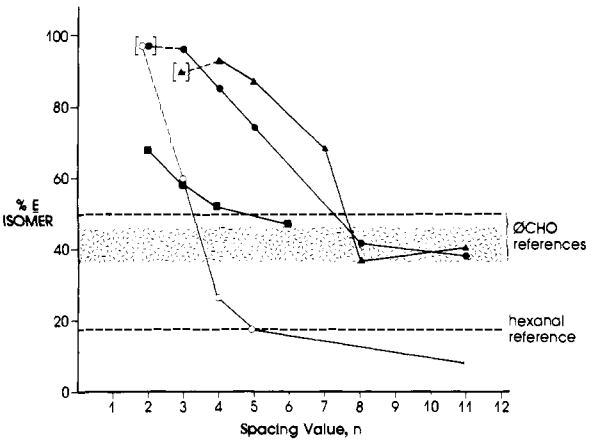


Figure 1. Variation of *Z*/*E* alkene ratio with distance of the nucleophilic site from the ylide center in alkoxy, carboxy, and amino ylides (**5–7**) with $LiN(SiMe_3)_2$. Symbols are assigned as follows: ● for **5a–f**, ▲ for **6a–f**, and ■ for **7a–d** in reaction with benzaldehyde; ○ for **5b–f** in reaction with hexanal. Brackets around a data point indicate a departure from standard conditions (see Table I). The reference reactions with **4** are indicated by the horizontal dashed lines; reference reactions with **4**, benzaldehyde, and added lithium salts are indicated by the shaded area, representing a % *E* isomer between 37 and 47% (Table I, entries 6–9). The lines connecting the data points are present as an aid to the viewer.

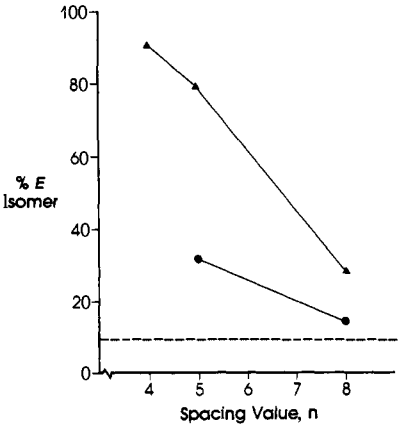


Figure 2. Variation of *Z*/*E* alkene ratio with distance of the anionic site from the ylide center in oxido and carboxy ylides (**5** and **6**) with $NaN(SiMe_3)_2$ in reactions with benzaldehyde. Symbols are assigned as follows: ● for **5d–e**, ▲ for **6b–e**. The reference reaction with **4**, benzaldehyde, and $NaN(SiMe_3)_2$ (Table I, entry 2) is indicated by the horizontal dashed line.

Oxido Ylides.[9,18a] Reactions of oxido ylides derived from phosphonium salts **5a–5f**, and prepared *in situ* by other means, were studied under the standard and some special, related conditions; results are presented in Table I, section B. The influence of chain length on reaction stereochemistry is graphically illustrated by Figures 1–3 for bases in which the cation is lithium, sodium, or potassium, respectively. Abnormal *E* stereoselectivity was observed for ylides with short chain length and, as the ylide chain increased, the *Z*/*E* ratios gradually returned to the reference-reaction values for each base employed. The reaction with benzaldehyde and $LiN(SiMe_3)_2$ showed a tremendous enhancement of *E* stereochemistry, reaching a *Z*/*E* ratio of 4:96 at a spacing value (*n*) of 3 (Table I, entry 18). The *E* amplification

(15) Dimsyl anion in Me_2SO, a popular base system for the Wittig reaction (Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128), was also examined under reference reaction conditions. Contrary to the result reported in our earlier paper (entry 10, Table, ref 10), $Ph_3P^+CH_2CH_3\ Br^-$ reacts with benzaldehyde (using sodium dimsylate in Me_2SO) to give a consistent *Z*/*E* ratio of 52:48 (±2%; three separate experiments). The level of *E* isomer formed was unexpectedly high, particularly for a dipolar, aprotic solvent (cf. the 86:14 *Z*/*E* ratio obtained for the same reaction in HMPA using potassium as the counterion: Bestmann, H. J.; Stransky, W. *Synthesis* **1974**, 798). The amount of *E* isomer was diminished in the reaction of **4** with benzaldehyde using sodium dimsylate in Me_2SO (*Z*/*E* ratio of 70:30 (±1%) in four separate experiments). The 70:30 isomer ratio was found to be constant (±1%) over the time course of the reaction (aliquots taken 5, 15, and 60 min after the addition of benzaldehyde).

(16) (a) This trend was consistent and reproducible. In fact, ^{31}P NMR studies of this reaction confirmed the concentration effect at the stage of the oxaphosphetanes. (b) We have conducted some extensive concentration-effect studies with **4**, benzaldehyde, and $LiN(SiMe_3)_2$ that will be reported in due course.

(17) The fact that small deviations in concentration of the Wittig reaction affect product stereochemistry led us to reexamine the *Z*/*E* ratios reported for the reaction of **6c** with benzaldehyde and different bases (entries 7–9, Table, in ref 10). Under the standard conditions described herein, slightly different *Z*/*E* ratios were determined; these are given in entries 44–46 of Table I.

Table I. Results for Wittig Reactions of **4–10**

entry	phosphonium salt	base (mol equiv)	aldehyde	Z/E ratio	isolated yield, %
		A. Reference Reactions			
1[a]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	50/50	86
2	**4**	$NaN(SiMe_3)_2$ (1.1)	PhCHO	91/9	52
3	**4**	$KN(SiMe_3)_2$ (1.1)	PhCHO	92/8	86
4	**4**	KO-*t*-Bu (1.1)	PhCHO	89/11	70
5[b]	**4**	$LiN(SiMe_3)_2$ (1.1)	hexanal	82/18	
6[c]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	55/45	60
7[d]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	63/37	
8[e]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	63/37	87
9[f]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	53/47	
10[g]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	65/35	
11[h]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	57/43	
12[i]	**4**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	36/64	
		B. Oxido Ylides			
13[j]	**5a**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	28/72	14
14[k]	**5a**	*n*-BuLi (2.1)	PhCHO	3/97	
15	**5b**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	4/96	80
16[l]	**5b**	NaH (1.0)	PhCHO	73/27	50
17[m]	**5b**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	6/94	83
18[n]	**5b**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	4/96	59
19	**5b**	KO-*t*-Bu (2.1)	PhCHO	44/56	34
20	**5c**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	15/85	
21	**5c**	KO-*t*-Bu (2.1)	PhCHO	54/46	
22	**5d**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	26/74	
23	**5d**	$NaN(SiMe_3)_2$ (2.1)	PhCHO	69/31	43
24	**5d**	$KN(SiMe_3)_2$ (2.1)	PhCHO	68/32	57
25	**5d**	KO-*t*-Bu (2.1)	PhCHO	71/29	50
26	**5e**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	59/41	50
27	**5e**	$NaN(SiMe_3)_2$ (2.1)	PhCHO	86/14	84
28	**5e**	$KN(SiMe_3)_2$ (2.1)	PhCHO	87/13	61
29	**5e**	KO-*t*-Bu (2.1)	PhCHO	87/13	73
30	**5f**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	62/38	82
31	**5b**	$LiN(SiMe_3)_2$ (2.1)	hexanal	42/58	82
32[l]	**5b**	NaH (1.0)	hexanal	88/12	63
33[m]	**5b**	$LiN(SiMe_3)_2$ (1.1)	hexanal	48/52	77
34[n]	**5b**	$LiN(SiMe_3)_2$ (2.1)	hexanal	41/59	57
35	**5c**	$LiN(SiMe_3)_2$ (2.1)	hexanal	77/23	
36[b]	**5d**	$LiN(SiMe_3)_2$ (2.1)	hexanal	83/17	
37[b]	**5f**	$LiN(SiMe_3)_2$ (2.1)	hexanal	92/8	
		C. Carboxy Ylides			
38	**6a**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	10/90	
39	**6b**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	7/93	61
40	**6b**	$NaN(SiMe_3)_2$ (2.1)	PhCHO	10/90	53
41	**6b**	$KN(SiMe_3)_2$ (2.1)	PhCHO	14/86	53
42	**6b**	KO-*t*-Bu (2.1)	PhCHO	9/91	69
43[p]	**6c**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	13/87	74
44	**6c**	$NaN(SiMe_3)_2$ (2.1)	PhCHO	21/79	65
45	**6c**	$KN(SiMe_3)_2$ (2.1)	PhCHO	31/69	44
46	**6c**	KO-*t*-Bu (2.1)	PhCHO	35/65	81
47	**6d**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	31/69	48
48	**6e**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	63/37	28
49	**6e**	$NaN(SiMe_3)_2$ (2.1)	PhCHO	73/27	37
50	**6e**	$KN(SiMe_3)_2$ (2.1)	PhCHO	79/21	26
51	**6e**	KO-*t*-Bu (2.1)	PhCHO	81/19	
52	**6f**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	60/40	
53	**6c**	$LiN(SiMe_3)_2$ (2.1)	nonanal	73/27	
		D. Amino Ylides			
54	**7a**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	31/69	70
55	**7b**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	44/56	47
56	**7c**	$LiN(MeSi_3)_2$ (1.1)	PhCHO	47/53	
57[k]	**8**	*n*-BuLi (2.1)	PhCHO	18/82	
58	**9**	$LiN(SiMe_3)_2$ (1.1)	PhCHO	26/74	
59	**9**	*n*-BuLi (1.0)	PhCHO	19/81	45
60	**9**	$LiN(SiMe_3)_2$ (2.1)	PhCHO	17/83	
61	**9**	*n*-BuLi (2.1)	PhCHO	11/89	37
62	**10**	*n*-BuLi (1.0)	PhCHO	27/73	
63	**10**	*n*-BuLi (2.1)	PhCHO	13/87	

[a] Four experiments showed a deviation of ±2% in *Z*/*E* ratio. [b] Analyzed by GLC/MS as the mixture of epoxides (prepared with MCPBA). [c] Standard reaction of **4** but 1.0 mol equiv of lithium hexanoate (from *n*-hexanoic acid and base in situ) was present prior to addition of benzaldehyde. [d] Similar to footnote *c*; 5.0 mol equiv of lithium hexanoate present. [e] Standard reaction of **4** but 1.0 mol equiv of lithium pentoxide (from *n*-pentyl alcohol and base in situ) was present prior to addition of benzaldehyde. [f] Similar to footnote *e*; 5.0 mol equiv of lithium pentoxide present. [g] Similar to the standard reaction except with four times as much THF. [h] Similar to the standard reaction except with two times as much THF. [i] Similar to the standard reaction except with one-half as much THF. [j] Base was added to the phosphonium salt and benzaldehyde at 0 °C, because of ylide instability. [k] Reaction was conducted with *n*-butyllithium (1.6 M in hexane) according to a literature procedure,[7a,b] due to ylide instability. [l] Oxaphospholane **11**, prepared from **5b** with NaH, was heated with the aldehyde in THF at reflux for 15 h. [m] Oxaphospholane **11** (see footnote *l*) was used with 1.1 mol equiv of base. [n] The β-oxido ylide from **5b** was generated by reaction of $Ph_3P^+CH_3\,Br^-$ with 1 mol equiv of $LiN(SiMe_3)_2$, addition of ethylene oxide, then addition of 1.1 mol equiv of base (see ref 8a). [o] Base was added to the phosphonium salt and benzaldehyde at 0 °C because of possible ylide instability, see: Corey, H. S., Jr.; McCormick, J. R. D.; Swensen, W. E. *J. Am. Chem. Soc.* **1964**, *86*, 1884. [p] At least five identical experiments were performed, giving a *Z*/*E* ratio of ±1/1.

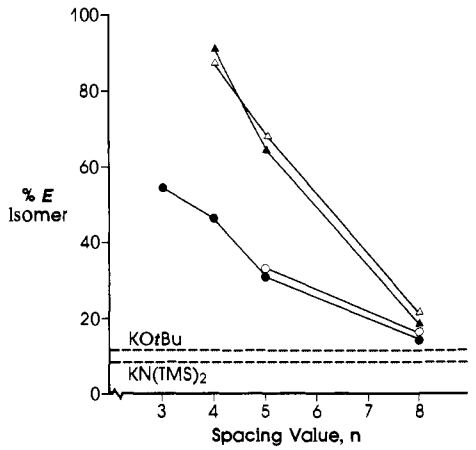
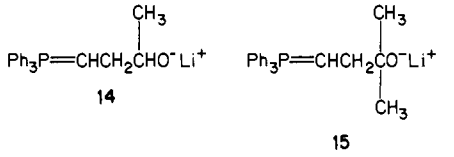


Figure 3. Variation of Z/E alkene ratio with distance of the anionic site from the ylide center in alkoxy and carboxy ylides (**5** and **6**) using K as the cation in reactions with benzaldehyde. Symbols are assigned as follows: ○ for **5b–e** and △ for **6b–e** with KO-*t*-Bu; ● for **5d–e** and ▲ for **6b–e** with $KN(SiMe_3)_2$. The reference reactions with 4, benzaldehyde, and either base (Table I, entries 3 and 4) are indicated by horizontal dashed lines. (TMS = $SiMe_3$).

diminished more rapidly for hexanal and $LiN(SiMe_3)_2$, being completely eliminated at $n = 5$ (entry 36; also see ref 11); however, at short chain lengths ($n = 3$, entry 31) the E amplification (relative to the reference reaction) is comparable to that obtained with benzaldehyde. The experiments in which sodium or potassium is the cation showed a significant but less pronounced E stereoselectivity. Relative to lithium, reactions with Na or K exhibited the same amount of diminished E alkene formation. Even in the reference reactions, no difference was detected between Na and K. Experiments with **5b**, benzaldehyde, and $NaN(SiMe_3)_2$ or $KN(SiMe_3)_2$ yielded little, if any, of the expected alkenols and the reaction products were not analyzed further. Although the reason for lack of reaction with **5b** is unknown, the results indicate that lithium should be employed as cation when using **5b** or related compounds.[18b] A similar cation effect has been observed for diphenylalkylphosphine oxides, whereby lithium stabilizes a γ-oxido functionality, but the use of sodium or potassium promotes decomposition to cyclopropane products.[18c]

Reactions of aldehydes with ylides from **5b** underscore the importance of the anionic group in promoting the increased formation of E alkene. Hydroxy ylide **12**,[19] generated thermally from **11** in the presence of benzaldehyde or hexanal, furnished alkenols without a preponderance of E alkene: Z/E ratios of 73:27 for benzaldehyde[20] and 88:12 for hexanal (see Table I, entries 16 and 32; see Scheme I). Thus, the γ-hydroxy group of **12** is unable to augment E alkene formation (cf. entries 16 and 1; 32 and 5). γ-Oxido ylide **13**, generated by either treatment of **11** with 1 equiv of base, (b) treatment of **5b** with 2 equiv of $LiN(SiMe_3)_2$, or (c) opening of ethylene oxide with methylidenetriphenylphosphorane (see Scheme I) gave anomalous E stereoselectivity with benzaldehyde (Z/E = 4:96) and hexanal (Z/E = ca. 45:55), in comparison to reference reactions (entries 15, 17, 18, 31, 33, and 34). The reaction of hexanal and **13** had a lower E stereoselectivity (Z/E = ca. 45:55) compared with the reaction of an aliphatic aldehyde[8a] with **15** (Z/E = 15:85),[8a] which prompted an investigation of the effect on product stereochemistry of methyl substitution in the ylide side chain. Since **14** and **15** would furnish



at least 95% E alkene with benzaldehyde, hexanal had to be employed. Ylides **14** and **15**, prepared by condensation of propylene or isobutylene oxides with $CH_2{=}PPh_3$ generated by $LiN(SiMe_3)_2$, reacted with hexanal to give 25:75 or 19:81 Z/E alkene ratios, respectively. A trend is evident in the reactions of **13–15** with hexanal, indicating that increased branching of the ylide side chain causes a correspondent increase in E stereoselectivity (56, 75, and 81% E isomer for **13**, **14**, and **15**, respectively).

Carboxy Ylides. Carboxy-substituted ylides also react with benzaldehyde to give exaggerated E stereoselectivity with a dramatic chain-length dependence (Table I, entries 38–52). However, there is only a trivial E enhancement with aliphatic aldehydes (entry 53; also see ref 10). The chain-length dependence can be readily appreciated by inspection of Figures 1–3. Phosphonium salt **6b** reacted with benzaldehyde to give a 10:90 Z/E mixture of 5-phenyl-4-pentenoic acids *irrespective of the base employed*. Thus, in contrast to the results obtained with oxido ylides **5b** and **5c**, carboxy ylides of short-chain length show virtually no stereochemical variation based on the nature of the cation. The enhancement of E alkene is particularly remarkable for the Na and K experiments because the reference reactions in these cases gave a Z/E ratio of ca. 90:10 (entries 2–4), reflecting an overall E enhancement of ca. 80% for **6b**. At longer chain lengths (n = 5, 8), experiments with K displayed the fastest attenuation of E stereoselectivity; the Na reactions were intermediate and the Li reactions were slowest in lessening E isomer formation. In all cases, the Z/E ratios approached reference-reaction values at longer chain lengths (see Figures 1–3).

Amino and Amido Ylides. Three (dimethylamino)alkylphosphonium salts (**7a–c**) were reacted with benzaldehyde by use of $LiN(SiMe_3)_2$; the results are listed in Table I (entries 54–56) and plotted in Figure 1. The shortest ylide (derived from **7a**) exhibited only a 19% increase in formation of E alkene relative to the reference reaction, and the other ylides investigated gave Z/E ratios similar to that of the reference reaction.[21] Thus, although a neighboring amino group can exert an effect (entries 54, 58, 59, 62), E stereoselectivity is greatly attenuated relative to oxido and carboxy groups. The special role of anionic groups is nicely illustrated by the reactions of benzaldehyde with ylides from **10** (entries 62 and 63). The amino ylide (from **10** and 1.0 mol equiv of base) afforded a Z/E ratio of 27:73, indicating the moderate E stereoselectivity of an amino group, whereas the amido ylide (from **10** and 2.1 mol equiv of base) afforded a 13:87 Z/E ratio, indicating strong E selectivity for the anionic amide group. Augmented E selectivity for an amido group vs. an amino group is less evident for ylides from **9** (cf. entries 58 and 59; 60 and 61). A recent report by Meyers also indicated unusually high levels of E alkene product in reactions of lithiated amidoethylphosphonium salts with aromatic aldehydes.[22]

Mechanistic Analysis. Several possible explanations can be envisioned to account for the unusual E stereoselectivity of ylides bearing anionic groups. It has been proposed that a base-induced "trans-selective Wittig" equilibration, involving intramolecular proton exchange in an intermediate betaine/oxaphosphetane, is responsible (Figure 4).[8a] Although it is difficult to imagine a carboxylate group having sufficient basicity to effect proton exchange, intramolecularity may substantially facilitate such a process.[12] If the relatively nonbasic groups were effective in an intramolecular situation, one could expect chain-length dependence, as observed.

(18) (a) Schlosser and co-workers have proposed that the term oxido ylide be replaced by "lithio-oxy ylide" or "metallo-oxy ylide" (Schlosser, M.; Tuong, H. B.; Respondek, J.; Schaub, B. *Chimia* **1983**, *37*, 10). However, we have chosen to use the trivial names oxido, carboxylate, and amido ylides with the understanding that each of these ylides bears an accompanying cation, related to the way in which the ylide was prepared. (b) We have experienced similar difficulties with **5c**, when employing $NaN(SiMe_3)_2$ or $KN(SiMe_3)_2$. (c) Horner, L.; Hoffmann, H.; Toscano, V. G. *Chem. Ber.* **1962**, *95*, 536.

(19) (a) Hands, A. R.; Mercer, A. J. H. *J. Chem. Soc. C* **1968**, 2448. (b) Hands, A. R.; Mercer, A. J. H. *J. Chem. Soc. C* **1967**, 1099.

(20) At 0.25 M a 50:50 Z/E ratio was obtained. The experiment reported in the text was conducted at 0.17 M (as was its hexanal counterpart). Performance of this reaction with LiBr (1 mol equiv) present resulted in no alkene formation.

(21) A similar result has been reported for reaction of **7a** with *p*-chlorobenzaldehyde: Marxer, A.; Leutert, T. *Helv. Chim. Acta* **1978**, *61*, 1708.

(22) Linderman, R. J.; Meyers, A. I. *Tetrahedron Lett.* **1983**, *24*, 3043.

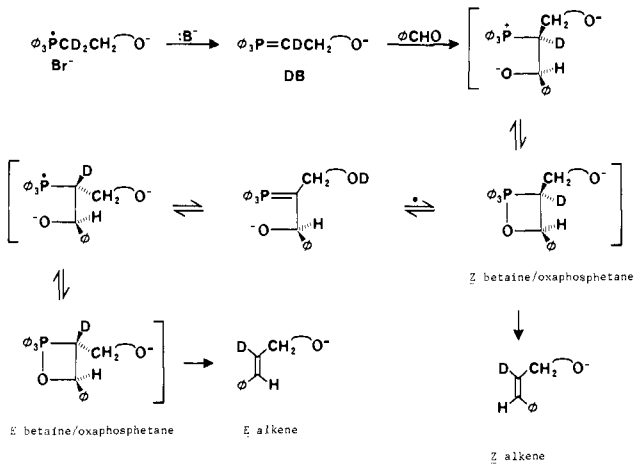


Figure 4. Mechanistic scheme for the Wittig reaction showing the internal, base-induced "trans-selective Wittig" process. A nucleophilic oxygen residue is attached to the deuterated phosphonium ylide via a chain of atoms. Initially formed betaine/oxaphosphetane has predominantly erythro/cis stereochemistry. ^{31}P NMR evidence suggests that oxaphosphetanes are preferred (see text). The asterisk denotes where the trans-selective Wittig process begins.

Corey has postulated a "lithium-bridging" mechanism to account for the *E* stereoselectivity of β-oxido ylides.[7c] Addition of the aldehyde to the oxido ylide with minimal steric interaction would result in an intermediate which, upon decomposition, would generate the *E* olefin (Scheme II).[7c] As an addition to Corey's model, we suggest coordination of the incoming aldehyde with a lithium atom, to define a cyclic transition state (Scheme II), which would strongly favor the more stable anti-addition product. The Li-bridging model would also presumably be subject to a chain-length dependence.

Another possibility is that the ylides are really in a dynamic equilibrium as shown in Scheme III, in which the cyclic form of the ylide reacts to give the *E* olefin due to steric constraints. The chain-length dependence would result from lower amounts of the cyclic ylide as the nucleophilic group is moved away from the phosphorus atom and intramolecular association is less favored.

An additional explanation has been offered for amidoethylphosphorus ylides.[22] Intramolecular donation of electrons from nitrogen would increase the electron density at phosphorus, resulting in more *E* alkene.[2b] This view is supported by the increase in *E* isomer observed with (1) triphenylphosphonium ylides bearing electron-rich substituents on the phenyl rings that can undergo 2p–3d overlap with phosphorus[23] and (2) ylides having alkyl groups as P substituents,[24] both cases involving a concentration of electron density at phosphorus.

As a further possiblity, nucleophilic groups, besides altering the energetics of the cyclocondensation that produces oxaphosphetanes, could influence relative rates of oxaphosphetane decomposition to products or reversion to starting materials. Oxaphosphetanes from aromatic aldehydes and nonstabilized triphenylphosphorus ylides are known to revert to ylide and aldehyde competitive with alkene formation; the relative rates of these processes could be affected by the metalloanionic group in some manner.[3d,25] Since Wittig intermediates from aliphatic aldehydes have been shown not to undergo reversible dissociation,[3d,4,26] we were inclined to disregard this latter mechanism. We thought that perhaps more than a single mechanism could be responsible for the effects of anionic groups on reaction stereoselectivity. Indeed, since oxido ylides give large amounts of *E* alkenes at short-chain length with aliphatic aldehydes, whereas carboxylate ylides do not, doubt arose relative to the existence of a single mechanistic process. However, the reversibility process surprisingly turns out to be a major factor, as described below.

Table II. Proton–Deuterium Exchange Experiments

$$Ph_3P{=}CD(CH_2)_nX \xrightarrow[-78\ ^\circ C]{RCHO} \xrightarrow[5\ equiv]{HN(SiMe_3)_2} RCH{=}CD(CH_2)_nX$$

R	phosphonium salt	base (equiv)	*E*/*Z* ratio	% D in alkenes[a]
Ph	$Ph_3P^+CD_2(CH_2)_2CH_3\ Br^-$	*n*-BuLi (1.0)	38/62	85
Ph	$Ph_3P^+CD_2(CH_2)_2OH\ Br^-$	*n*-BuLi (2.1)	88/12	70
Ph	$Ph_3P^+CD_2(CH_2)_3CO_2H\ Br^-$	*n*-BuLi (2.1)	80/20	75
n-C_5H_{11}	$Ph_3P^+CD_2(CH_2)_2OH\ Br^-$	*n*-BuLi (2.1)	61/39	70

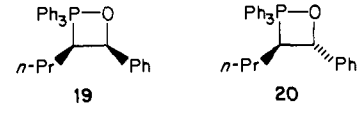
[a] Statistical H/D distribution: 17% D, 83% H.

We conducted the following experiments to limit the number of viable alternatives and to ascertain the main mechanisms.

To probe an intramolecular "trans-selective Wittig" process (Figure 4), three α-deuterated ylides—$Ph_3P{=}CD(CH_2)_2CH_3$ (**16**), $Ph_3P{=}CD(CH_2)_2O^-Li^+$ (**17**),[9] and $Ph_3P{=}CD(CH_2)_3CO_2^-Li^+$ (**18**)—were investigated. The deuterated ylides were prepared from deuterated phosphonium salts with *n*-butyllithium, rather than $LiN(SiMe_3)_2$, to completely dispose of the first deuterium atom. Ylides **16–18** were reacted with benzaldehyde or hexanal at low temperature (−78 °C), to generate the Wittig intermediate (betaine/oxaphosphetane), and then treated with 5 equiv of hexamethyldisilazane, as a proton source. After 45 min at −78 °C, the reaction was rapidly warmed to liberate the alkenes. In separate control experiments, we demonstrated that hexamethyldisilazane was a suitable proton source: (1) it freely exchanges with O-deuterated alcohols at low temperature, (2) it freely exchanges with ylides at low temperature, and (3) it does not interfere with the stereochemical outcome of the reaction. The results of the deuterium-exchange experiments are exhibited in Table II. The amount of deuterium in the alkene products was determined by GLC/MS and ^1H NMR.

If the process depicted in Figure 4 were operative, then the deuterium in the rapidly equilibrating intermediates should be exchanged with the extraneous proton source. In these experiments, complete exchange between the deuterium atom in the ylide and the proton of the hexamethyldisilazane would result in ca. 17% D ($^1/_6 \times 100\%$) in the alkenes. Instead, 70–75% D content was observed (Table II), equally distributed for both isomers. The small level of exchange in the reference reaction (15%) may be due to reversible formation of ylide competitive with alkene formation,[3d] as the solution was warmed. The ylide could suffer D–H exchange and reenter the reaction path. Such a process could account for the 25–30% D loss in the oxido and carboxy cases, especially if one considers facilitated reaction reversal (vide infra). At this point, given the results in Table II, the intramolecular base-induced "trans-selective mechanism", which depends on proton exchange, can be excluded as a major contributing factor to anomalous *E* stereoselectivity for oxido and carboxy ylides.

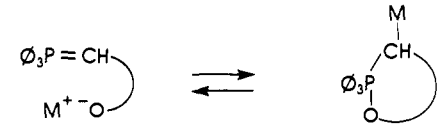
We have also examined 145.8-MHz proton-decoupled ^{31}P NMR spectra of ylides and of the intermediates formed upon treatment of them with aldehydes at low temperature.[13] In a standard case, reaction of butylidenetriphenylphosphorane (**24**) with benzaldehyde (Li present) gave two ^{31}P NMR resonances at −61.4 and −63.8 ppm corresponding to **1.** and **20**, respectively.[13] These



signals were also produced on deprotonation of the corresponding *erythro*- and *threo*-hydroxyphosphonium salts (from **19**/**20** and HBr) with $NaN(SiMe_3)_2$.[13] We have extended our pilot studies[13] to the reactions of anionic-group ylides to establish the stereochemistry of oxaphosphetanes, not just alkenes. This information could allow one to determine whether or not the anionic-group effect is largely manifested in the initial formation of oxaphos-

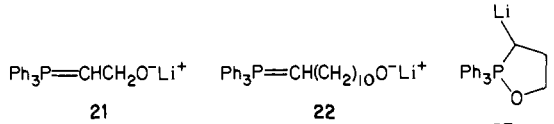
(23) McEwen, W. E.; Cooney, J. V. *J. Org. Chem.* **1983**, *48*, 983 and references cited therein.
(24) (a) Meyers, A. I.; Lawson, J. P.; Carver, D. R. *J. Org. Chem.* **1981**, *46*, 3119. (b) Bissing, D. E. *Ibid.* **1965**, *30*, 1296.
(25) (a) Speziale, A. J.; Bissing, D. E. *J. Am. Chem. Soc.* **1963**, *85*, 3878. (b) Bissing, D. E.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 2683. (c) Schlosser, M.; Christmann, K. F. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 689.
(26) Anderson, R. J.; Henrich, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 4327.

Scheme III



phetanes (i.e., during C–C bond formation).

Carboxylate ylide **1**, with either Li, Na, or K as the cation, appears as a singlet in the proton-decoupled ^{31}P NMR spectrum at 11.0–11.8 ppm (relative to external 85% H_3PO_4), consistent with ^{31}P NMR chemical shifts for other nonstabilized phosphorus ylides.[3d,27] γ-Oxido ylide **13**, however, appears as a multitude



of unresolved peaks between 0 and 20 ppm. Vedejs and co-workers have observed similar ^{31}P NMR behavior for β-oxido ylide **21**.[28] Ylide **2** (M = Li) displayed three closely spaced, sharp lines (centered at 10.6 ppm) but when the oxido group was far removed from the phosphorus atom, as with **22**, the ylide appeared as a normal, sharp singlet (11.5 ppm). This suggests that, with close proximity between the oxido and ylide centers as in **13** and even **2**, an assortment of slowly (NMR time scale) interconverting structures exists, perhaps as a consequence of variously interacting aggregates. Nevertheless, *no* pentavalent phosphorus signals were detected for **13**, **2** (M = Li), or **22**, ruling out cyclic metallo-oxaphosphoranes as major contributing species (Scheme III). Indeed, a species such as **23** could not be observed even on direct deprotonation (with *n*-BuLi) of oxaphospholane **11**; rather, a spectrum similar to that for **13** (above) was observed. Treatment of the ylides with benzaldehyde at ca. −80 °C resulted in the formation of signals in the pentavalent phosphorus region (−55 to −65 ppm) indicative of oxaphosphetane formation. In the proton-decoupled, 145.8-MHz ^{31}P NMR spectra, the oxaphosphetanes from **1** (M = Na, Li),[29] **2** (M = Li), and **13** appeared as two partially or completely resolved singlets, presumably representing the cis and trans diastereomers.[30a]

Reaction of ylides bearing anionic groups with benzaldehyde or hexanal at −78 °C was often accompanied by some precipitate formation. Thus, the oxaphosphetane peaks were not as sharp, even at −40 °C, as those for oxaphosphetanes from simple ylides, which generally give homogeneous solutions and sharp oxaphosphetane signals at −50 °C.[13] However, useful information could still be gained since (alleged) cis and trans oxaphosphetanes bearing anionic groups were cleanly observed in a concentration range of 0.1–0.5 M (THF). Carboxy ylide **1** with either Li, Na, or K as the cation reacted with benzaldehyde to give two signals in the region between −59 and −62 ppm, separated by 2.0–2.5 ppm. By analogy to peak assignments obtained from butylidenetriphenylphosphorane (**24**),[13] we have designated the downfield peak as the cis oxaphosphetane and the upfield peak as the trans oxaphosphetane. We have shown[13] that the initial ratio of oxaphosphetanes is affected by both the cation and the concentration[16b] and that drift can occur during the reaction course to give more *E* alkene in the product than reflected in the oxaphosphetanes (we term this "stereochemical drift").[30b] These trends also apply to reactions of **1**.

The reaction of **1** at 0.25 M, as the lithium salt, with benzaldehyde at −78 °C followed by warming to −45 °C provided a pair of oxaphosphetane resonances at −59.5 and −62.0 ppm in a 1:1.2 ratio (presumably cis/trans, respectively). Whether this ratio represents the ratio of the original condensation or incorporates some shift induced by reversibility is unclear. An experiment performed in the same way at half the concentration (0.125 M) gave an 8:1 mixture of peaks at −59.5 and −62.0 ppm. Although more dilute solutions give more cis oxaphosphetane with standard ylide **24**,[16b] such a large shift (1:1.2 to 8:1) with **1** suggests some variability associated with performing each experiment, such as the exact time before observation of spectra, during which the ratios could change. The use of sodium and potassium as cations gave cis/trans oxaphosphetane mixtures of 2.2:1 (−55 °C) and 6:1 (−80 °C). From these observations we suggest that ylide **1** combines with benzaldehyde, at low temperature, to give predominantly the cis oxaphosphetane which, upon warming, becomes enriched in the trans oxaphosphetane via equilibration due to reaction reversal (prior to substantial production of alkenes). Thus, a principal cause of the *E* stereoselectivity is tentatively assigned to a large amount of stereochemical drift at the oxaphosphetane stage prior to formation of alkenes. In the reaction of **1** (M = Li) with hexanal at 0.125 M, a pair of peaks in a 2.7:1 ratio (tentatively cis:trans) at −59.8 and −64.5 ppm was observed (−80 °C). This is consistent with the lack of *E* stereoselectivity in this reaction at the stage of initial C–C bond formation. Oxido ylides **13** and **2** (M = Li) reacted with benzaldehyde to give variable results, largely due to the problems of precipitate formation. However, the reaction mixture from **13** (at 0.5 M) displayed two peaks tentatively attributed to cis and trans oxaphosphetanes at −61 and −63.6 ppm with an initial ratio of 1:2.2 at −80 °C, which changed to a ratio of 1:14 on standing at −55 °C for 30 min. Reaction of **2** (M = Li) at 0.17 M (−78 to −55 °C) gave an 8:1 mixture of peaks at −59.5 and −62.0 ppm, the higher cis/trans ratio reflecting the longer chain length of the ylide. As with the reactions of **1**, it appears that the oxido ylides facilitate *E* alkene formation by enhancing the stereochemical drift of the oxaphosphetane intermediates, although there could also be a contribution from a slightly enhanced *E* oxaphosphetane level after the initial condensation.

Substantiation of facilitated stereochemical drift for **13** came from HBr quenching experiments. Ylide **13** was combined with 1.2 mol equiv of benzaldehyde at −78 °C, stirred for 15 min, and quenched with dry HBr.[4,13] A mixture of erythro and threo β-hydroxyphosphonium bromide salts was obtained, in a 2:1 ratio [δ ^{31}P ($CDCl_3$) 27.8 and 26.5; δ ^{13}C (4° P-C_6H_5) 118.89 ($^1J_{PC}$ = 84.0 Hz) and 119.34 ($^1J_{PC}$ = 84.0 Hz)].[30c] On standing for 20 min at −45 °C (a temperature too low to allow stereochemical drift in reactions of **24**) and quenching with HBr, the reaction of **13** gave a 1:1 ratio of salts. At −30 °C for 20 min the reaction gave a 1:4 erythro/threo mixture.

If the shift to *E* isomer were due primarily to reversibility-induced "stereochemical drift", which allows for some measure of thermodynamic control during the reaction, then free ylide should be present to some extent. Even if ylide only attained a minute concentration, its presence might be detected by trapping it with a different aldehyde in a crossover experiment. Such experiments have already established that Wittig intermediates derived from aromatic aldehydes are freely reversibly, whereas those from aliphatic aldehydes are not.[3d,4,26] Since short-chain oxido ylides exhibit anomalous *E* stereoselectivity with aliphatic aldehydes, we sought to determine if this is associated with reversibility via crossover experiments.[30d] As a model, the ylide from **4** and $LiN(SiMe_3)_2$ (0.25 M in THF) was treated with 2 mol equiv of hexanal at −65 °C, and the reaction was stirred at −50 °C for 5 min (formation of Wittig intermediates under these conditions was verified by ^{31}P NMR[13]). Then, 5 mol equiv of heptanal were

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(28) Vedejs, E.; Meier, G. P. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 56.

(29) Sodium was preferred over lithium with **1** in oxaphosphetane generation for NMR studies because of occasional precipitation problems with lithium cation present.

(30) (a) We have reproducibly observed two singlets between −60 and −65 ppm in the $^{31}P\{^1H\}$ NMR spectra of oxaphosphetanes from non-stabilized ylides without nucleophilic groups, using aromatic and aliphatic aldehydes (see ref 13). (b) Stereochemical drift is caused by interconversion of reaction adducts (oxaphosphetanes) by reaction reversal to ylide and aldehyde (ref 13). (c) These assignments were made by analogy with ^{13}C NMR data for related erythro and threo triphenyl-(1-butyl-2-hydroxy-2-phenethyl)phosphonium bromides (identified by X-ray analysis[13]). (d) For a preliminary report on these crossover experiments, see: Reitz, A. B.; Maryanoff, B. E. *J. Chem. Soc., Chem. Commun.*, in press. In this paper, ^{31}P NMR data and the question of complete ylide reaction are discussed.

added followed by slow warming to 23 °C. Confirming earlier reports,[3d,4,26] no crossover was observed. In an analogous experiment, the carboxy ylide derived from **6c**, which does not give enhanced *E* alkene levels with aliphatic aldehydes,[10] also demonstrated minimal (less than 1%) crossover. However, in a similar manner, the oxido ylide derived from **5b** (i.e., **13**), which shows strong anomalous *E* stereoselectivity with aliphatic aldehydes, repeatedly exhibited close to statistical crossover, based on the relative amounts of the different aldehydes used. For example, preforming the oxaphosphetane with 2 equiv of hexanal and adding 5 equiv of octanal produced an alkene mixture (59% yield) containing 42% of the hexanal-derived alkenes (*Z*/*E* = 45:55) and 58% of the octanal-derived alkenes (*Z*/*E* = 33:67). Thus, the oxido group appears to facilitate reversible dissociation of oxaphosphetane to ylide, providing the *first observation of a reversible Wittig intermediate derived from an aliphatic aldehyde and a nonstabilized triphenylphosphorus ylide.*[30d] This finding supports the view that anomalous *E* stereoselectivity induced by anionic substituents in the phosphonium ylide is associated with the reversible dissociation of oxaphosphetane to ylide and aldehyde, a process which introduces a degree of thermodynamic control. Since carboxy ylides are unable to enhance reversibility of aliphatic aldehyde-derived Wittig intermediates, their failure in this instance to give exaggerated amounts of *E* alkene is obvious.

Conclusion

Regardless of the mechanistic source of enhanced *E* stereoselectivity, this phenomenon has indisputable significance for synthetic planning. The results that we have accumulated in this work, and elsewhere,[9,10] establish a pronounced dependence of the product stereochemistry upon the distance between the anionic end group and the ylide center. Oxido, carboxy, and amido ylides give high *E* stereoselectivity in reaction with benzaldehyde. Oxido ylides also react with hexanal to give increased *E* isomer levels, such enhancement being highest for ylides with branched side chains. The *E* alkene enhancement seen for carboxy ylides is independent of the cation (Li, Na, or K), whereas oxido ylides show a dramatic dependence on the cation, lithium giving the highest level of *E* alkene. This unifying analysis of what to expect in Wittig reactions involving ylides bearing nucleophilic substituents should foster applications in organic synthesis.

Although the results presented here (i.e., the trends outlined in Figures 1–3) should have general significance, Wittig reactions done under other, special conditions may give somewhat different results. The dependence of the stereochemistry upon concentration (vide supra) and added salts,[2] for example, underscores the caveat that carefully controlled conditions are required for reproducible stereochemical results.

Various mechanisms can be put forward to rationalize the influence of anionic substituents on the stereochemistry of the Wittig reaction (vide supra). Equilibration of Wittig intermediates by a proton-exchange process induced by intramolecular base turns out *not* to be of prime importance, given our results from deuterium-washout experiments. We found that ylides bearing anionic groups have ^{31}P NMR spectra with no cyclic pentavalent species, which, if present in substantial amounts, might promote abnormal stereochemistry. ^{31}P NMR studies of oxaphosphetanes from ylides with anionic groups reveal the existence of "stereochemical drift" at lower temperatures (−78 to −40 °C) than that (−30 °C) at which drift occurs in a model system (**24** + benzaldehyde). In fact, it was difficult to assess the initial cis/trans oxaphosphetane ratios from reactions of γ-oxido ylide **13** or carboxy ylide **2** with benzaldehyde because of the facile shift in the isomer ratios... timing became very critical. We, necessarily, acquired the impression that anionic groups influence stereochemistry by facilitating oxaphosphetane interconversion by reversibility, rather than by greatly affecting initial carbon–carbon bond formation. The enhancement of equilibration by reversibility is substantiated by the HBr quenching experiments with **13** and benzaldehyde, as well as the crossover experiment with **13**, hexanal, and octanal (see Experimental Section). This is the first observation of crossover with a Wittig intermediate derived from an aliphatic aldehyde and a nonstabilized triphenylphosphorus ylide.

At this point, we feel that an adequate explanation for anomalous *E* stereoselectivity in the Wittig reaction of phosphonium ylides possessing anionic groups is at hand. However, we have not been able to exclude a significant contribution to anomalous *E* stereoselectivity from effects of anionic groups in the initial carbon–carbon bond-forming process. An understanding of the precise mechanism underlying facilitated reversibility is a goal for future studies.

Table III. Data on Phosphonium Salts

P^+ salt	mp,[a] °C	lit. mp, °C	ref
5a	212–213	214	31
5b	226–229	222–224	31
5d	186–187	190–191	11
5e	(95–105) 105–110	110[b]	32
5f	91–95	90–91	33
6a	192–195	196–198	30
6b	241–243	245–248	34
6d	180–183	185–187	35
6e	104–105	116–120	36
6f	95–99	93–96	37
7a	195–197 dec	196–199	21
		204–206	38
7b[c]	270–280 dec	280.5–282.5	39
7c	(190–198) 199–202	212–214	40
9	221–226	235.5–237.5	21
		226	41
10	265–272	260–262.5	42

[a] Softening ranges given in parentheses. [b] Began to shrink at 90 °C. [c] As an HBr salt of the amine.

Experimental Section

General Procedures. Proton NMR spectra were recorded on a JEOL FX60Q, Varian EM-360, or Bruker AM-360 (360 MHz) spectrometer with $CDCl_3$ as solvent, chemical shifts being reported as ppm downfield from Me_4Si. Carbon-13 NMR spectra were obtained on a JEOL FX60Q or Bruker AM-360 instrument also with Me_4Si as an internal standard. Phosphorus-31 NMR spectra were obtained at 145.8 MHz on a Bruker AM-360 with THF as solvent; chemical shifts are referenced to 85% H_3PO_4 (external). GLC analyses were conducted on a Perkin-Elmer 3920B instrument with a flame-ionization detector, using a Hewlett-Packard Model 3352 data system and 18652 A/D converter. The GLC columns employed were the following: 3% SE-30 on Chromasorb Q (1/8 in. × 6 ft); 1.75% OV-17 on Chromosorb W/AQ/DMCS (1/8 in. × 6 ft); and 10% or 1% Carbowax on Chromosorb (1/8 in. × 6 ft), specified as columns A–D, respectively. Mass spectra (chemical ionization) were obtained on a Finnigan 3300-6100 system typically with CH_4 as the carrier gas. Electron-impact mass spectra were recorded on a VG Micromass 7035 instrument. Melting points are corrected; melting points may be preceded by softening ranges contained in parentheses. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

Preparation of Phosphonium Salts. Many of the phosphonium salts used in this study are known compounds and were prepared by literature procedures (if not available commercially). The salts were analyzed by ^1H NMR; mp data were compared with literature values. Compounds prepared in this manner are listed in Table III. Phosphonium salt **6c** was purchased from the Aldrich Chemical Co. The syntheses of new salts used in this work are presented below.

(4-Hydroxybutyl)triphenylphosphonium Bromide (5c). A solution of 4-bromobutanol (8.15 g, 53.3 mmol), triphenylphosphine (14.0 g, 1 equiv), and 7.0 g of K_2CO_3 in 45 mL of CH_3CN was heated at reflux under nitrogen for 7 h. The presence of the K_2CO_3 inhibits the formation of $Ph_3P^+(CH_2)_4P^+Ph_3\ 2Br^-$, a side product which occurs readily in this reaction by the mechanism shown in ref 11. Even using K_2CO_3, varying amounts of the bisphosphonium salt shown above were obtained when preparing **5c**, although ^1H NMR integration indicated **5c** was obtained in >90% purity. After the reflux period, the K_2CO_3 was filtered and rinsed with CH_3CN. The filtrate was treated with ether, and the solution was allowed to stand, during which time crystallization occurred. The product was collected as white crystals: 4.6 g (21%); mp 203–206 °C; ^1H NMR ($CDCl_3$) δ 1.6–2.5 (m, 4 H), 3.5–4.2 (m, 4 H), 7.5–8.0 (m, 15 H).[43a] Because the elemental analysis for **5c** did not check, we

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prepared a sample by a different route, involving triphenylphosphine·HBr and THF.[43b] The recrystallized white solid [33%; mp 220–222 °C; ^{13}C NMR (D_2O) δ 21.0 (C_2, $^2J_{CP}$ = 3.9 Hz), 23.8 (C_1, $^1J_{CP}$ = 51.8 Hz), 34.7 (C_3, $^3J_{CP}$ = 16.7 Hz), 63.0 (C_4), 120.6 (4° P-Ph, $^1J_{PC}$ = 86.9 Hz), etc.] did not analyze correctly for C (−1.8%) or Br (+1.3%), even though it was clean by high-field ^1H and ^{13}C NMR. Results obtained with this second sample of **5c** were similar to those with the first.

(2-Aminoethyl)triphenylphosphonium Bromide (8).[43c] A solution of (2-bromoethyl)amine hydrobromide (7.81 g, 38.1 mmol) and triphenylphosphine (10 g, 1 equiv) in CH_3CN (50 mL) was stirred at reflux for 15 h. The precipitate was filtered, dissolved in H_2O, and treated with saturated aqueous K_2CO_3 until the pH was 11. The product was extracted into 2 vol of $CHCl_3$, dried ($MgSO_4$), filtered, and triturated with ether, giving a white precipitate, which was recrystallized from ethanol/ether (3.0 g, 19%): mp 227–233 °C; ^1H NMR ($CDCl_3$) δ 1.90 (s, 2 H), 3.2 (m, 2 H), 4.0 (m, 2 H), 7.8 (m, 15 H); the resonance at 1.90 ppm fully exchanged with D_2O. Anal. Calcd for $C_{20}H_{21}BrNP$: C, 62.19; H, 5.48; Br, 20.69. Found: C, 61.97; H, 5.50; Br, 20.51.

Typical Wittig Reaction Conditions. To 1 mmol of phosphonium salt suspended in 3 mL of THF under N_2 was added 1.1 equiv of base (2.1 equiv of base for salts bearing auxiliary acidic protons). After 15 min, the reaction mixtures were subjected to an extractive workup. Carboxylic acids were converted to their methyl esters with CH_2N_2 prior to further analysis. Purification was effected by using standard distillation or chromatographic techniques. Isolated yields are generally for material distilled by Kugelrohr (>95% pure by GLC). Analysis of the alkene isomer ratios was accomplished by using GLC/MS and ^1H NMR. The GLC data in Table I were acquired on column A for all entries except 13, 14, and 31–37; entries 13 and 14 were analyzed on column B, entries 31–35 on column C, and entries 36 and 37 on column D. In the case of styrene products, integration of one cis olefinic proton relative to a multiplet downfield containing the other cis proton with the two trans protons was consistent with the GLC integration value. In the instances in which concentration was varied, different amounts of THF were added as indicated in Table I.

Reactions of 2,2,2-Triphenyl-1,2-oxaphospholane (11). Compound **11** was prepared by the literature method.[19b] In the base-promoted reaction, **11** (107 mg, 0.33 mmol) was dissolved in THF and treated with $LiN(SiMe_3)_2$ (61 mg, 1.1 equiv). After the mixture was stirred for 15 min, benzaldehyde (27 μL, 0.8 equiv) was added, dissipating the red color of the solution. After 15 min, the solution was subjected to an extractive workup and purified on a $LiN(SiMe_3)_2$ silica gel plate (EtOAc/hexane, 1/4), giving 33 mg (83%) of a 6:94 *Z*/*E* ratio (GLC column A) of homocinnamyl alcohols. Alternatively, heating **11** (107 mg, 1 mmol) in the presence of benzaldehyde (27 μL, 0.8 equiv) in refluxing THF for 15 h gave a 50% yield of a 73:27 *Z*/*E* ratio (GLC column A) of homocinnamyl alcohols.

***(Z)*- and *(E)*-4-Decen-2-ol.** The procedure for opening different epoxides with methylidenetriphenylphosphorane was kept constant; one representative example is given here. To a suspension of 1.0 g of methyltriphenylphosphonium bromide (2.8 mmol, 1.05 equiv) in 5 mL of THF was added a solution of 490 mg of $LiN(SiMe_3)_2$ in 5 mL of THF. After 15 min, the clear, red solution was cooled to −78 °C and propylene oxide (191 mL, 1.0 equiv) was added. After 20 min, the solution was warmed to 23 °C and a second equivalent of $LiN(SiMe_3)_2$ (490 mg) was added. After 15 min, hexanal (980 mL, 1.05 equiv) was added and, after an additional 15 min, the solution was subjected to an extractive workup. The product was purified by distillation (40–65 °C (0.11 torr)), giving an analytically pure 24:76 mixture of *Z*/*E* isomers (GLC column C); 265 mg (61%); ^{13}C NMR ($CDCl_3$) δ 14.1 (q, 1, C_{10}), 22.6 (q and t, 2, C_1 and C_9), 27.4 (*Z*), 29.1, 29.3, 31.4, 32.6 (*Z*) (t, 3, C_6–C_8), 37.1 (t, 0.25, *Z*-C_3), 42.6 (t, 0.75, *E*-C_3), 67.19 (d, 0.75, *E*-C_2), 67.71 (d, 0.25, *Z*-C_2), 124.99 (d, 0.25, *Z*-C_5), 125.71 (d, 0.75, *E*-C_5), 133.56 (d, 0.25, *Z*-C_4), 134.80 (d, 0.75, *E*-C_4). Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.67; H, 12.90.

Butyl-*1,1-d*$_2$-triphenylphosphonium Bromide. To a suspension of methyl-d_3-triphenylphosphonium bromide (Aldrich, 540 mg, 1.5 mmol) in 1.5 mL of THF was added 1.53 mL of a 1 M $LiN(SiMe_3)_2$/THF solution. After 25 min, *n*-propyl bromide (143 μL, 1.05 equiv) was added by syringe. After 35 h the precipitate was filtered and dissolved in $CHCl_3$, washed with water, dried ($MgSO_4$), filtered, and treated with ether. The precipitate was filtered and dried under high vacuum to give 300 mg (52%) of a white powder: mp 219–223 °C (darkened); ^1H NMR (360 MHz, $CDCl_3$) δ 7.7 (m, 15 H), 1.70 (m, 2 H), 1.57 (m, 2 H), 0.91 (t, 3 H). Anal. Calcd for $C_{22}H_{22}BrD_2P$: C, 65.84; H/D, 6.53. Found: C, 66.19; H/D, 6.16.

(4-Carboxybutyl-*1,1-d*$_2$)-triphenylphosphonium Bromide.[44] A solution of NaH (430 mg of a 50% oil dispersion, 3.5 equiv) in 7.5 mL of Me_2SO-d_6 (99.5% D, Merck) was heated at 80 °C for 1 h and cooled to 23 °C and (4-carboxybutyl)triphenylphosphonium bromide (1.1 g, 2.5 mmol) was added. The solution was stirred for 105 min and DOAc (520 μL, 3.6 equiv) was added, dissipating the red color. Ethyl acetate was added to a total volume of 70 mL, and the precipitate was filtered and dissolved in $CHCl_3$. The solution was washed with a 1 M HBr solution saturated with KBr. The aqueous layer was extracted four times with $CHCl_3$. The $CHCl_3$ layers were combined, dried ($MgSO_4$), filtered, concentrated, and then treated with ether, causing the product to crystallize after sitting overnight; this gave 550 mg (50% yield) of the desired product: ^1H NMR ($CDCl_3$) δ 7.8 (m, 15 H), 2.82 (t, 2 H), 1.97 (m, 2 H), 1.73 (m, 2 H). Anal. Calcd for $C_{23}H_{22}BrD_2O_2P$: C, 62.11; H/D, 5.61; Br, 17.84. Found: C, 62.04; H/D, 5.61; Br, 17.94.

(3-Hydroxypropyl-*1,1-d*$_2$)-triphenylphosphonium Bromide.[44] To a suspension of (3-hydroxypropyl)triphenylphosphonium bromide (1.5 g, 3.7 mmol) in 10 mL of THF was added 1.15 equiv of *n*-BuLi (1.55 M in hexane, 2.75 mL). After 15 min, Me_2SO-d_6 (5 g, 99.5% D) was added; 4 mL of HMPA was added to dissolve all solid material. After 18 h, 1.25 equiv of 47% DBr/D_2O (800 μL) was added at 0 °C, followed by 50 mL of 5% HBr/H_2O. The product was extracted into $CHCl_3$ (6 × 50 mL); the combined organics were dried ($MgSO_4$), filtered, and evaporated. Trituration with ether gave crystalline material, which was recrystallized from ethanol, giving 810 mg (54%) of white powder: ^1H NMR (360 MHz, $CDCl_3$) δ 7.8 (m, 15 H), 3.87 (m, 2 H), 2.80 (br s, OH), 1.82 (m, 2 H). Anal. Calcd for $C_{21}H_{20}BrD_2OP$: C, 62.54; H/D, 5.50; Br, 19.81. Found: C, 62.77; H/D, 5.58; Br, 19.87.

Typical Deuterium-Exchange Conditions. The experiments listed in Table II were run in the same manner; typical conditions follow. To a suspenion of 0.25 mol of salt in 1 mL of THF at −78 °C was added *n*-BuLi/hexane (1.6 M, 2.1 equiv for salts bearing an auxiliary acidic group and 1.1 equiv for the reference salt). The solution was allowed to warm to 20 °C for 10 min and recooled to −78 °C. Benzaldehyde (30 μL, 1.2 equiv) was added, followed in 20 min by hexamethyldisilazane (5 equiv, 265 μL). After an additional 45 min at −78 °C, the solution was rapidly warmed to ca. 40 °C (steam bath), H_2O was added, and the product was subjected to an extractive workup and examined by GLC/MS. In separate experiments we found that addition of the hexamethyldisilazane prior to the addition of the benzaldehyde caused a statistical exchange of hydrogens presumably due to exchange of the hexamethyldisilazane protons with the deuterio ylide. Also, slowly warming the solution from −78 °C (over ca. 10 min) caused roughly 50% exchange of the deuterium atoms, possibly because of exchange with the deuterio ylide, known to be formed reversibly from Wittig intermediates at temperatures competitive with decomposition to alkene.[3d] A low-temperature (−40 °C) ^1H NMR experiment established that hexamethyldisilazane freely exchanges with methanol-d_1.

$^{31}P\{^1H\}$ NMR Spectroscopic Experiments. The ylides were prepared in the standard way by treatment of the appropriate phosphonium salts with the requisite amount of hexamethyldisilazide base (Li, Na, or K) in THF at 22 °C under argon. After 15 min, the red ylide solutions were carefully transferred to a 10-mm NMR tube (under Ar) fitted with a coaxial tube containing THF-d_8. The solutions were cooled to −78 °C, and the ^{31}P NMR spectrum was examined under conditions of broad-band proton decoupling. Typically, concentrations of greater than 0.05 M allowed for sufficient sample to obtain a good signal-to-noise ratio after a minimal number of scans (<50). The aldehydes were added at −78 °C, and the solutions were warmed to slightly higher temperatures, if desired. Where precipitates were encountered, the NMR tubes were centrifuged in a tube surrounded by pulverized dry ice to obtain clear supernatant solutions, which were then examined.

Crossover Experiments with Aliphatic Aldehydes. A. With Salt 4.[30d] A suspension of salt **4** (200 mg, 0.5 mmol) in 1.45 mL of THF under

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(43) (a) A correct C, H analysis (±0.4%) was not obtained for **5c**. (b) Schmidt, U.; Lieberknecht, A.; Griesser, H.; Bartkowiak, F. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 318. (c) Although **8** is reported (McAllister, P. R.; Dotson, M. J.; Grim, S. O.; Hillman, G. R. *J. Med. Chem.* **1980**, *23*, 862) as the hydrobromide salt, no analytical or spectroscopic data are presented.
(44) See also: Reitz, A. B.; Maryanoff, B. E. *Synth. Commun.* **1983**, *13*, 845. This paper contains more information on this type of deuterium-exchange procedure.

nitrogen was treated with 0.55 mL of 1 M $LiN(SiMe_3)_2$/THF (1.1 equiv). After 15 min, the clear, red solution was cooled to −65 °C and 120 μL of hexanal was added (2 equiv). The solution was warmed to −50 °C and stirred for 5 min, during which time the red color went away and a white precipitate emerged. Heptanal was carefully added (336 μL, 5 equiv), and the solution was stirred an additional 5 min at −50 °C and then allowed to slowly warm to 23 °C. After 15 min at 23 °C, water was added and the product was subjected to an extractive workup. Analysis of the isomer levels was conveniently achieved by preparation of the corresponding epoxides (10 equiv of MCPBA, $ClCH_2CH_2Cl$, trace of 3-*tert*-butyl-4-hydroxy-5-methylphenyl sulfide, reflux, 2 h) and a comparison to known materials by GLC. A 80:20 *Z*/*E* mixture of 4-decenes was determined with no observable 4-undecene (<0.5%, GLC column A).

B. With Carboxy Salt 6c.[30d] A suspension of **6c** (220 mg, 0.5 mmol) in 0.9 mL of THF under nitrogen was treated with 1.1 mL of 1 M $LiN(SiMe_3)_2$/THF (2.2 equiv). After mixture was stirred for 15 min, the red, clear solution was cooled to −55 °C and nonanal (172 μL, 2 equiv) was added slowly. The solution was warmed to −50 °C and stirred an additional 10 min. Octanal (390 μL, 5 equiv) was then added and the solution stirred for 10 min at −45 to −50 °C, during which time a precipitate came out of solution. The mixture was allowed to warm to 23 °C slowly and subjected to an extractive workup. Methyl esters were formed by treatment with ethereal diazomethane and they were purified by preparative TLC (EtOAc/hexane, 1/4), being careful not to fractionate any alkene component (50% yield of alkene esters). GLC analysis (column A) by comparison with materials of known composition prepared independently established that only the product of reaction with nonanal was present (>99%, *Z*/*E* = 74:26).

C. With Hydroxy Salt 5b.[30d] To a suspension of salt **5b** (200 mg, 0.5 mmol) in 0.9 mL of THF was added 1.1 mL of 1 M $LiN(SiMe_3)_2$/THF (2.2 equiv) under nitrogen. After 15 min, the red, clear solution was cooled to −55 °C and hexanal was slowly added (125 μL, 2 equiv). The red color of the ylide was largely dissipated; a small amount of precipitate formed. After 10 min, octanal (390 μL, 5 equiv) was added and the solution was stirred at −50 °C for 5 min and allowed to warm slowly to 23 °C. After addition of water and extraction with ether, the products were analyzed by GLC (column C), by comparison with authentic materials, which were prepared as isomeric mixtures by individual Wittig reactions. Identification of the GLC peaks was supported by GLC/MS analysis. The results are presented in the text.

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Registry No. 1 (M = Li), 65011-73-6; **1** (M = Na), 41723-91-5; **1** (M = K), 39647-97-7; **2** (M = Li), 93111-01-4; **4**, 1779-51-7; **5a**, 7237-34-5; **5b**, 51860-45-8; **5c**, 87436-78-0; **5d**, 34626-52-3; **5e**, 65734-62-5; **5f**, 19101-00-9; **6a**, 51114-94-4; **6b**, 17857-14-6; **6c**, 17814-85-6; **6d**, 50889-30-0; **6e**, 52956-93-1; **6f**, 7530-96-3; **7a**, 21331-80-6; **7b**, 18355-96-9; **7c**, 83299-97-2; **8**, 89996-00-9; **9**, 34477-69-5; **10**, 89996-01-0; **11**, 14580-93-9; **13**, 89995-99-3; **19**, 89121-74-4; **20**, 89121-77-7; **22**, 93085-36-0; **24**, 3728-50-5; (*Z*)-$PhCH{=}CH(CH_2)_2CH_3$, 7642-18-4; (*E*)-$PhCH{=}CH(CH_2)_2CH_3$, 16002-93-0; (*Z*)-$C_5H_{11}CH{=}CH(CH_2)_2CH_3$, 19398-88-0; (*E*)-$C_5H_{11}CH{=}CH(CH_2)_2CH_3$, 19398-89-1; (*Z*)-$PhCH{=}CHCH_2OH$, 4510-34-3; (*E*)-$PhCH{=}CHCH_2OH$, 4407-36-7; (*Z*)-$PhCH{=}CH(CH_2)_2OH$, 20047-19-2; (*E*)-$PhCH{=}CH(CH_2)_2OH$, 770-36-5; (*Z*)-$PhCH{=}CH(CH_2)_3OH$, 29374-64-9; (*E*)-$PhCH{=}CH(CH_2)_3OH$, 13159-16-5; (*Z*)-$PhCH{=}CH(CH_2)_4OH$, 87436-86-0; (*E*)-$PhCH{=}CH(CH_2)_4OH$, 17924-66-2; (*Z*)-$PhCH{=}CH(CH_2)_7OH$, 87436-87-1; (*E*)-$PhCH{=}CH(CH_2)_7OH$, 87436-88-2; (*Z*)-$PhCH{=}CH(CH_2)_{10}OH$, 87436-89-3; (*E*)-$PhCH{=}CH(CH_2)_{10}OH$, 87436-90-6; (*Z*)-$C_5H_{11}CH{=}CH(CH_2)_2OH$, 10340-23-5; (*E*)-$C_5H_{11}CH{=}CH(CH_2)_2OH$, 10339-61-4; (*Z*)-$C_5H_{11}CH{=}CH(CH_2)_4OH$, 64275-76-9; (*E*)-$C_5H_{11}CH{=}CH(CH_2)_4OH$, 64275-77-0; (*Z*)-$C_5H_{11}CH{=}CH(CH_2)_{10}OH$, 73461-68-4; (*E*)-$C_5H_{11}CH{=}CH(CH_2)_{10}OH$, 87436-91-7; (*Z*)-$PhCH{=}CHCH_2CO_2H$, 59744-46-6; (*E*)-$PhCH{=}CHCH_2CO_2H$, 1914-58-5; (*Z*)-$PhCH{=}CH(CH_2)_3CO_2H$, 81077-22-7; (*E*)-$PhCH{=}CH(CH_2)_3CO_2H$, 16424-56-9; (*Z*)-$PhCH{=}CH(CH_2)_5CO_2H$, 93085-37-1; (*E*)-$PhCH{=}CH(CH_2)_5CO_2H$, 93085-38-2; (*Z*)-$PhCH{=}CH(CH_2)_6CO_2H$, 93085-39-3; (*E*)-$PhCH{=}CH(CH_2)_6CO_2H$, 93085-40-6; (*Z*)-$PhCH{=}CH(CH_2)_9CO_2H$, 93085-41-7; (*E*)-$PhCH{=}CH(CH_2)_9CO_2H$, 93085-42-8; (*Z*)-$CH_3(CH_2)_7CH{=}CH(CH_2)_3CO_2H$, 5684-70-8; (*E*)-$CH_3(CH_2)_7CH{=}CH(CH_2)_3CO_2H$, 5684-69-5; (*Z*)-$PhCH{=}CHCH_2N(CH_3)_2$, 75712-94-6; (*E*)-$PhCH{=}CHCH_2N(CH_3)_2$, 42817-44-7; (*Z*)-$PhCH{=}CH(CH_2)_2N(CH_3)_2$, 93085-43-9; (*E*)-$PhCH{=}CH(CH_2)_2N(CH_3)_2$, 93085-44-0; (*Z*)-$PhCH{=}CH(CH_2)_3N(CH_3)_2$, 93085-45-1; (*E*)-$PhCH{=}CH(CH_2)_3N(CH_3)_2$, 55666-16-5; (*Z*)-$PhCH{=}CHCH_2NH_2$, 4226-59-9; (*E*)-$PhCH{=}CHCH_2NH_2$, 4335-60-8; (*Z*)-$PhCH{=}CHCH_2NHCH_3$, 93085-46-2; (*E*)-$PhCH{=}CHCH_2NHCH_3$, 83554-67-0; (*Z*)-$PhCH{=}CH(CH_2)_2NH_2$, 93085-47-3; (*E*)-$PhCH{=}CH(CH_2)_2NH_2$, 7515-38-0; (*E*)-$PhCH{=}CD(CH_2)_2CH_3$, 87436-83-7; (*Z*)-$PhCH{=}CD(CH_2)_2CH_3$, 87436-82-6; (*E*)-$PhCH{=}CD(CH_2)_2OH$, 87436-85-9; (*Z*)-$PhCH{=}CD(CH_2)_2OH$, 87436-84-8; (*E*)-$PhCH{=}CD(CH_2)_3CO_2H$, 87600-09-7; (*Z*)-$PhCH{=}CD(CH_2)_3CO_2H$, 87600-08-6; (*E*)-$C_5H_{11}CH{=}CD(CH_2)_2OH$, 87600-13-3; (*Z*)-$C_5H_{11}CH{=}CD(CH_2)_2OH$, 87600-12-2; (*Z*)-$CH_3(CH_2)_6CH{=}CH(CH_2)_2OH$, 66348-46-7; (*E*)-$CH_3(CH_2)_6CH{=}CH(CH_2)_2OH$, 66348-45-6; (*Z*)-$C_5H_{11}CH{=}CHCH_2CH(OH)CH_3$, 93085-49-5; (*E*)-$C_5H_{11}CH{=}CHCH_2CH(OH)CH_3$, 93085-50-8; (*Z*)-$PhCH{=}CH(CH_2)_2CO_2H$, 73850-25-6; (*E*)-$PhCH{=}CH(CH_2)_2CO_2H$, 17920-83-1; PhCHO, 100-52-7; $C_5H_{11}CHO$, 66-25-1; $CH_3(CH_2)_7CHO$, 124-19-6; $CH_3(CH_2)_6CHO$, 124-13-0; $Ph_3P^+CH_3Br^-$, 1779-49-3; $Ph_3P^+CD_2(CH_2)_2CH_3Br^-$, 1779-50-6; $Ph_3P^+CD_2(CH_2)_2OHBr^-$, 87436-81-5; $Ph_3P^+CD_2(CH_2)_3CO_2HBr^-$, 93085-48-4; $Ph_3P^+(CH_2)_4P^+Ph_{32}Br^-$, 15546-42-6; $Ph_3P^+CO_3Br^-$, 1787-44-6; $Br(CH_2)_4OH$, 33036-62-3; $Ph_3P{=}CH(CH_2)_2CH_3$, 3728-50-5; Ph_3P, 603-35-0; $Br(CH_2)_2NH_2{\cdot}HBr$, 2576-47-8; $CH_3(CH_2)_2Br$, 106-94-5; ethylene oxide, 75-21-8; propylene oxide, 75-56-9; lithium *cis*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-51-9; lithium *trans*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-52-0; sodium *cis*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-53-1; sodium *trans*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-54-2; potassium *cis*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-55-3; potassium *trans*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butanoate, 93085-56-4; lithium *cis*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-ethoxide, 93085-57-5; lithium *trans*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-ethoxide, 93085-58-6; lithium *cis*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butoxide, 93085-59-7; lithium *trans*-2,2,2,4-tetraphenyl-1,2-oxaphosphetane-3-butoxide, 93085-60-0.