(m, 21 H), 6.6 (d, 1 H, J = 3.7 Hz), 6.12 (t, 1 H, J = 9.9 Hz), 6.0 (d, 1 H, J = 9.9 Hz), 5.96 (dd, 1 H, J = 4.5, 1.0 Hz), 5.9 (m, 1 H), 5.78 (t, 1 H, J = 10.0 Hz), 5.52 (dd, 1 H, J = 11.5, 2.0 Hz), 4.45 (t, 1 H, J = 11.1 Hz), 4.35 (dt, 1 H, J = 10.2, 3.25 Hz), 4.01 (dd, 1 H, J = 11.2, 3.0 Hz), 3.8 (dd, 1 H, J = 11.2, 3.5 Hz), 3.62 (s, 3 H), 2.72 (dd, 1 H, J = 13.1, 4.9 Hz), 2.11 (s, 3 H), 2.05 (dd, 1 H, J = 13.1, 11.5 Hz), 1.85 (s, 3 H).

Disaccharide 82. Via the general procedure, the reaction of **52** with alcohol **63** afforded disaccharide **81** (41%) with 39% recovery of starting material. Following the general oxidation procedure afforded methyl ester **82** (75%): ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.0 (m, 7 H), 7.8 (m, 7 H), 7.2–7.6 (m, 21 H), 5.90 (m, 2 H), 5.78 (m, 3 H), 5.60 (dd, 1 H, J = 10.4, 3.2 Hz), 5.27 (m, 1 H), 4.81 (d, 1 H, J = 9.8 Hz), 4.70 (d, 1 H, J = 7.9 Hz), 4.53 (dd, 1 H, J = 12.2, 5.2 Hz), 4.28 (m, 1 H), 3.97 (m, 1 H), 3.81 (m, 1 H), 3.66 (s, 3 H), 3.59 (s, 3 H), 2.43 (m, 2 H).

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Registry No. 1, 19342-33-7; **5**, 10149-14-1; **5**·NH_3, 90461-30-6; **9R**, 94292-14-5; **15**, 114027-47-3; **17**, 113892-48-1; **18**, 113892-49-2; **19**, 92622-29-2; **20**, 92622-30-5; **21**, 113892-50-5; **22**, 113892-51-6; **23**, 113974-03-1; **24**, 113974-04-2; **25**, 113974-05-3; *ent*-**25**, 113974-15-5; **26**, 113924-25-7; *ent*-**26**, 113924-27-9; **27**, 113892-52-7; **28**, 113892-53-8; **30**, 113892-54-9; **31**, 113974-06-4; **32**, 113974-07-5; **33**, 114027-54-2; **39**, 113974-08-6; **40**, 113974-09-7; **41**, 113974-10-0; **42**, 113892-55-0; **43**, 113892-56-1; **44**, 113974-11-1; **45**, 113974-12-2; **46**, 6730-43-4; **47**, 113974-13-3; **48**, 114031-35-5; **49**, 113892-57-2; **50**, 113892-58-3; **52**, 113892-59-4; **53**, 113974-14-4; **55**, 73650-02-9; **62**, 4064-06-6; **63**, 53182-61-9; **64**, 88037-32-5; **65**, 113892-60-7; **65** (furyl precursor), 113892-74-3; **66**, 113892-61-8; **66** (furyl precursor), 113892-75-4; **67**, 113892-62-9; **67** (furyl precursor), 113892-76-5; **68**, 113924-26-8; **69**, 113892-63-0; **70**, 113892-64-1; **70** (triflate derivative), 113892-77-6; **71**, 113892-65-2; **72**, 113892-66-3; **73**, 113892-67-4; **76**, 113892-68-5; α-**77**, 113892-69-6; β-**77**, 113892-78-7; **78**, 113892-70-9; α-**80**, 113892-71-0; β-**80**, 113892-79-8; **81**, 113892-72-1; **82**, 113892-73-2; $(CF_3CH_2O)_2P(O)CH_2CO_2Me$, 88738-78-7; cholesterol, 57-88-5.

Substituent Effects and the Wittig Mechanism: The Case for Stereospecific Oxaphosphetane Decomposition

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Abstract: A search for reversible Wittig reactions of the ylides **a**–**d** has been made by using the method of independent oxaphosphetane generation. Four pairs of diastereomeric oxaphosphetanes have been synthesized, and those corresponding to the Wittig reactions of **b**–**d** with tertiary aldehyde **18** decompose to alkenes with >98% stereospecificity. In the case of ylide **a**, the oxaphosphetane **20a**-*trans* also decomposes without detectable reversal or loss of stereochemistry. The isomer **19a**-*cis* is the only system studied that undergoes measurable equilibration. The kinetic selectivity of $Et_3P{=}CHCH_3$ favors **19a** by a ratio of ca. 3:1. A variety of phosphorus ylides have been studied in the Wittig reaction. Depending on phosphorus substituents, a range of *kinetic* cis or trans selectivity is observed. Although the one example of extensive Wittig reversal (**19a**-*cis*) is associated with a trans-selective empirical result, there is no connection with retro-Wittig reaction in several other examples of *E*-olefin-selective Wittig reactions.

The first systematic attempts to explain Wittig reaction stereochemistry placed emphasis on reversibility in the step leading to the initial adduct.[1,2] Although the adduct proved to be an oxaphosphetane[3] and not a betaine as suggested in the early rationales, the notion that adduct stereochemistry need not correspond to olefin Z/E ratios was widely accepted. The reversibility argument was invoked for E alkene selective Wittig reactions (for example, those of carbonyl-stabilized ylides, presumed thermodynamic control). Conversely, Z-selective Wittig reactions of nonstabilized $Ph_3P{=}CHR$ were assumed to involve relatively minor reversal (kinetic control), and moderated ylides were believed to occupy a middle ground between these extremes.[1,2]

Few of the above assumptions have been tested, but some important studies have partially clarified the situation. Schlosser and Christmann (1967) demonstrated that $Ph_3P{=}CHCH_3$-PhCHO adducts decompose with good stereospecificity and minor, but significant, Wittig reversal, judging from crossover experiments.[2] Although independent proof of adduct stereochemistry in the $Ph_3P{=}CHR$ series was based only on evaluation of NMR J values, a syn-cycloreversion mechanism for the olefin-forming step was correctly assumed, a proposal that has subsequently been confirmed in related systems by X-ray analysis of a β-hydroxyphosphonium salt obtained by acid quenching of the low-temperature adduct.[4]

Deoxygenation of epoxides by phosphines has often been cited to support arguments for Wittig reversal.[5] Although the mechanisms may be related, the conditions are harsh, and the extrapolation to typical Wittig conditions is difficult at best. The first method for unequivocal generation of Wittig adducts of known stereochemistry under more representative conditions was reported by Jones and Trippett (1966), who also demonstrated the conversion of **1**/**2** into stilbenes upon treatment with base.[6] Most of the experiments were done under protic conditions, which favored loss of stereochemistry, and formation of crossover

(1) For early reviews, see: Trippett, S. *Q. Rev., Chem. Soc.* **1963**, *17*, 406. Maercker, A. *Org. React. (N.Y.)* **1965**, *14*, 270. Johnson, A. W. *Ylide Chemistry*; Academic: New York, 1966. Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1.

(2) (a) Schlosser, M.; Christmann, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1. (b) Schlosser, M.; Schaub, B.; de Oliveira-Neto, J.; Jeganathan, S. *Chimia* **1986**, *40*, 244 (see footnotes).

(3) (a) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778. (b) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823.

(4) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664 and references therein.

(5) (a) Bissing, D. E.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 2683. (b) Boskin, M. J.; Denney, D. B. *Chem. Ind. (London)* **1959**, 330.

(6) Jones, M. E.; Trippett, S. *J. Chem. Soc. C* **1966**, 1090.

0002-7863/88/1510-3940$01.50/0

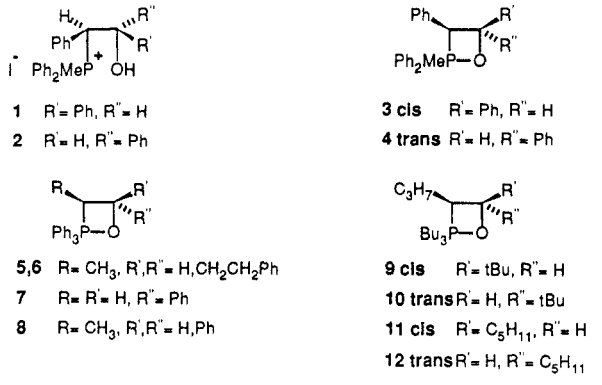

Figure 1.

products was observed with ClC_6H_4CHO. However, this paper also reported some examples where use of ether solvents gave considerably increased retention of stereochemistry.

Subsequent experiments in our laboratory developed a related, more direct route to oxaphosphetanes **3**-*cis* or **4**-*trans* with known stereochemistry.[7] Even though **3**/**4** are the adducts of a moderated ylide ($Ph_2MeP{=}CHPh$), they decomposed to *Z* or *E* stilbenes with ≥98% retention provided that aprotic conditions were used. Analogous **3**/**4** with R′ or R″ = branched or unbranched alkyl gave nearly total retention in many cases. These results proved for the first time that decomposition of Wittig adducts under *typical* Wittig conditions (Li salts present) occurs with high stereospecificity and with the stereochemistry expected from the syn-cycloreversion process that had been assumed earlier.

We did observe a single case of reversal under aprotic conditions in a system where normal olefin formation was prevented by geometric constraints.[7a] We also encountered related examples where loss of oxaphosphetane stereochemistry was due to reversible deprotonation α to phosphorus in the corresponding betaine–lithium halide adduct and did *not* involve Wittig reversal.[7a] However, these were all exceptional cases involving equilibration of stereochemistry in precursors of strained cycloalkenes.

The extrapolation from $Ph_2MeP{=}CHR$ derivatives to the more typical $Ph_3P{=}CHR$ adducts was based partly on analogy and partly on direct evidence. Both ^{31}P and ^1H NMR spectroscopy indicated that oxaphosphetanes were formed from aldehydes at −70 °C, and negative crossover experiments in the representative case of **5**/**6** argued against Wittig reversal for the unbranched aldehyde-derived oxaphosphetanes.[3b] Reversal was also ruled out in the case of **7**. The ethylide adduct **8** did give crossover products, but only at temperatures where olefin formation was relatively fast. We concluded that Wittig reversal plays no significant role in the Wittig reactions between *aliphatic* aldehydes and salt-free nonstabilized ylides $Ph_3P{=}CHR$ (R = alkyl).[3b] More recent papers by Maryanoff et al. have renewed interest in the issue of Wittig reversal[4] and have questioned the use of olefin ratios to deduce kinetic oxaphosphetane geometry in certain cases.[8] The bulk of their evidence pertains to aromatic aldehydes or to ylides containing alkoxide or carboxylate anions with lithium salts present. However, the reported conversion of the *salt-free* adduct of $Bu_3P{=}CHC_3H_7$ + pivaldehyde from an initial 1:2 ratio of **9**-*cis*:**10**-*trans* to an eventual ratio of < 1:10 raises questions.[4] From our earlier findings,[3b] there is no basis to believe that **5**/**6** equilibrate, nor did Maryanoff et al. observe stereochemical changes in the analogous unbranched aldehyde adducts **11**-*cis*/**12**-*trans*.[4] However, we had not specifically tested any oxaphosphetanes from nonstabilized ylides + tertiary aldehydes, which would correspond to Maryanoff's example in aldehyde substitution. Could any of the experiments in our 1981 study of the preparatively important $Ph_3P{=}CHR$ reactions involve undetected oxaphosphetane equilibration? To answer this question, and to probe the role of phosphorus ligands[9] as well as of aldehyde substituents, we have studied four isomeric pairs of tertiary aldehyde derived oxaphosphetanes in detail as described below. The examples were chosen to allow systematic comparisons over a broad range of ylide reactivity, oxaphosphetane stability, and olefin *Z*/*E* selectivity. Although equilibration was detected in one of the eight examples, the oxaphosphetanes derived from $Ph_3P{=}CHCH_3$ were found to decompose with >98% retention of stereochemistry.

Methods. There are drawbacks and subtleties in each of the techniques available for the study of oxaphosphetane equilibration. The crossover method[2,5,6,3b] is a perturbation of the system (excess ClC_6H_4CHO) and is conclusive only in the negative sense (no crossover = no reversal, *provided* that the normal alkene forms efficiently, and that the original Wittig adduct *can be proved to survive at the point where crossover aldehyde is added*). Observation of oxaphosphetane diastereomers by NMR methods (resolution of ^{31}P signals has been reported for a ketone adduct[3a] and for several aldehyde adducts[4]) is better suited for the purpose, but only if equilibration is slow compared to acquisition time and "setup time" and if the intermediates are soluble. Low-temperature acid-quenching experiments can also provide useful information,[2,3b,4] but by themselves cannot distinguish between oxaphosphetanes, betaines, or oxidoylides.

To avoid ambiguities, we have used a combination of the above techniques together with the method of independent generation[7] of oxaphosphetanes via stereospecific cleavage of epoxides by reaction with $LiPPh_2$ and subsequent base treatment of β-hydroxyphosphonium salts **13**/**14**. This does introduce one complication, which may not be an issue in the Wittig reaction. Salts **13**/**14** are obliged to form betaines before they can form oxaphosphetanes while the Wittig reaction may proceed directly to the oxaphosphetanes by cycloaddition.[3] As a result, the independent oxaphosphetane generation experiments encounter opportunities for equilibration at the betaine stage, and loss of stereochemistry would not necessarily apply to the corresponding Wittig reaction. However, a stereospecific conversion from **13** or **14** to the *Z* or *E* alkene would rule out all mechanisms for stereochemical equilibration, including Wittig reversal to ylide and aldehyde.

Salts **13**/**14** correspond to adducts of the tertiary aldehyde **18**. This system was chosen because isolation of the relatively nonvolatile alkene products (**21**, **22**) is more convenient than in the case of pivaldehyde. There is no change in Wittig *Z*/*E* selectivity from pivaldehyde to **18** in reactions with $Ph_3P{=}CHCH_3$ or $Et_3P{=}CHCH_3$ where direct comparisons have been made.

Three of the required β-hydroxyphosphonium salt diastereomer pairs were prepared from epoxides **15**-*trans* or **16**-*cis* as shown in Figure 2. Nucleophilic cleavage (S_N2)[6] with the appropriate lithium phosphide followed by quaternization with C_2H_5I gave each of the isomers **13**/**14a**–**c** without significant cross contamination by its diasteromer. Epoxide **15**-*trans* proved considerably less reactive than **16**-*cis* to S_N2 cleavage, and the synthesis of **13a** in particular was complicated by extensive conversion of **15**-*trans* into the elimination product **17** upon treatment with Et_2PLi. Nevertheless, **13a** was obtained free of the isomeric **14a** after P-ethylation of the intermediate phosphine.

The fourth pair of isomers **13d**/**14d** was prepared via Wittig reaction of $Ph_3P{=}CHCH_3$ + tertiary aldehyde **18**. Essentially one adduct **19d**-*cis* was formed at −40 °C, and an acid quench gave a single salt **13d**. The isomeric **14d** was obtained by treatment of **19d**-*cis* + BuLi in the presence of Li^+, followed by acid quenching of the presumed oxido ylide intermediate. Since the geometry of this specific pair of diastereomers is not necessarily defined by the method of synthesis, the assignment of stereochemistry was confirmed by nuclear Overhauser effect (NOE) experiments on the corresponding oxaphosphetanes. These results are described in the section titled NMR Spectra of Oxaphosphetanes and in Table I.

(7) (a) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178. (b) Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc.* **1973**, *95*, 822. (c) For a recent stereospecific example involving a hindered α-branched system, see: Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1981**, *46*, 4272.

(8) Maryanoff et al. did not intend this generalization (last sentence in ref 4) to apply to all Wittig intermediates, but only to stabilized ylide adducts: Maryanoff, B. E., private communication.

(9) Schlosser, M.; Schaub, B. *J. Am. Chem. Soc.* **1982**, *104*, 5821.

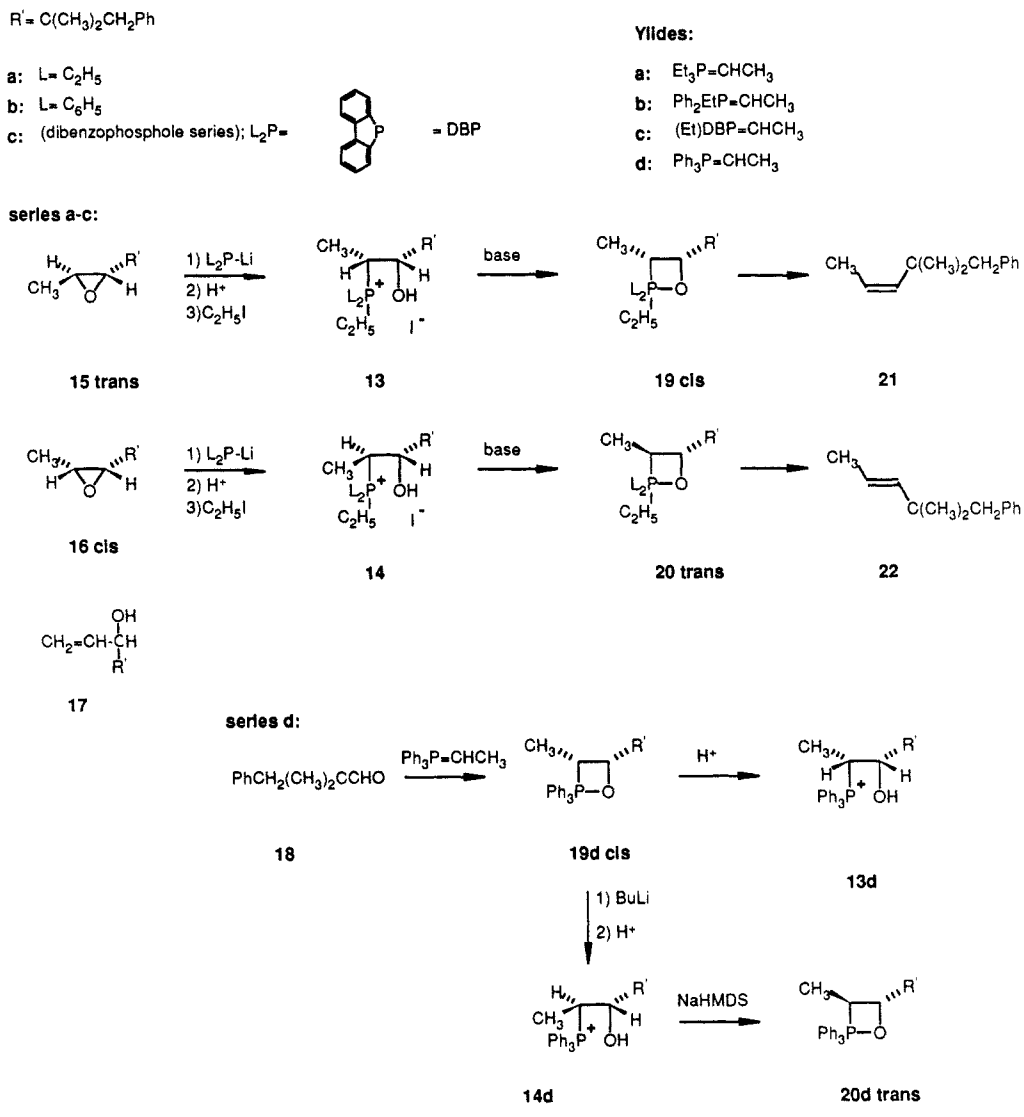

Figure 2.

Table I. NMR Spectral Data of Oxaphosphetanes[a]

compd	δ H_3	δ H_4	$J_{3,4}$ Hz	J_{P-H_4}, Hz	J_{P-H_3}, Hz	$\delta^{31}P$
19a-*cis*	(^{1}H not resolved)					−66.7[c]
20a-*trans*	3.65	2.91	5	<1	18	−68.1[c]
19b-*cis*	4.10	3.45	8	11	21	−64.7[b]
20b-*trans*	4.09	2.92	6	<1	21	−63.4[b]
19c-*cis*	3.72	3.49	6	6	16	−65.5[b]
20c-*trans*	3.86	3.04	7	2	18	−64.4[b]
19d-*cis*	4.09	3.52	6	6	16	−62.9[b]
20d-*trans*	4.56	3.05	8	1	22	−62.2[b]

[a] All ^{1}H NMR spectra in toluene-d_8, −30 to −40 °C; ^{31}P spectra in solvent indicated. [b] Toluene-d_8. [c] Tetrahydrofuran.

With the four pairs of diastereomeric β-hydroxyphosphonium salts **13**/**14** in hand, independent oxaphosphetane generation was examined. Each salt was treated with sodium or potassium bases in inert solvents. Seven of the eight examples gave a single distinct oxaphosphetane according to NMR analysis (Table II), and ^{1}H or ^{31}P signals for the diastereomers were readily distinguished (Bruker AM-500 spectrometer). However, **13a** proved to be exceptional. In this case, the initial NMR spectrum at −70 °C could not be resolved due to line broadening, but at −43 °C, the sample already contained 20% of the isomerized oxaphosphetane **20a**-*trans* in addition to **19a**-*cis*. Warming the sample to −5 °C (±3 °C) caused an increase in the signal of **20**-*trans* while **19**-*cis* disappeared over ca. 30 min. A minor signal corresponding to $Et_3P{=}O$ (from conversion to alkene) also appeared, indicating 10–20% alkene formation by the time that all of the cis oxaphosphetane had decomposed. Further warming to >30 °C was required to complete the conversion to alkenes at a convenient rate, final Z/E ratio = 17:83 of **21**/**22** (72% yield). In addition, 13% of the tertiary aldehyde **18** was isolated.

The above results point to Wittig reversal in the specific case of **13a**.[10,11] Supporting evidence was obtained by repeating the experiment in the presence of 3 equiv of ClC_6H_4CHO, which gave a ratio of 1:0.7:0.5 of $ClC_6H_4CH{=}CHCH_3$/**22**/**21**. We do not know whether the addition of ClC_6H_4CHO perturbs this system relative to the Wittig reaction in the absence of aromatic aldehyde. Qualitatively, these results are consistent with extensive but not total reversal and also suggest that some of the conversion from **19a**-*cis* to **20a**-*trans* occurs via unknown mechanisms. Since the

(10) The closely related reaction of pivaldehyde + $Et_3P{=}CHCH_3$ affords a 9:1 ratio of E/Z alkene. This is *not a kinetic product ratio* as implied in ref 9.

(11) Maryanoff et al. have detected "drift" in the related reaction of pivaldehyde + $Bu_3P{=}CH_3H_7$ (ref 4).

Table II. Wittig Reaction: Salt-Free Ylides + Aldehydes

		Z/E ratio (yield, %)[a]		
ylide	$L_2YP{=}CHCH_3$	1° $PhCH_2CH_2CHO$	2° $PhCH_2CH(CH_3)CHO$	3° $PhCH_2C(CH_3)_2CHO$ (**18**)
a	L = Y = C_2H_5	1:2 (53)	1:3.3 (48)	1:9 (97)
b	L = Ph, Y = C_2H_5	1:2.3 (72)	1:2.7 (76)	5.7:1 (85)
c	L = DBP, Y = C_2H_5	1:18 (83)[b,c]		1:9 (62)[c]
d	L = Y = Ph	16:1 (92)	32:1 (85)	>99:1 (98)
e	L = DBP, Y = Ph	1:1 (75)[b]		9:1 (60)
f	L = Ph, Y = *t*-Bu	17:1 (74)	49:1 (80)	99:1 (96)
g	L = *i*-Pr, Y = Ph	2.6:1 (57)		2.6:1 (98)
h	L = Ph, Y = *i*-Pr	1:4.6 (83)		1:1 (98)
i	L = Et, Y = Ph	1:1.8 (86)		1.3:1 (90)
j	L = DBP, Y = NMe_2	4.6:1 (31)		24:1 (92)
k	L = Y = NMe_2	(<10% yield)		1:>50 (86)

[a] Isolated yield after chromatography unless indicated otherwise. [b] Yield by GLPC, internal standard, DBP = dibenzophosphole. [c] For best results, the ylide was generated by using KHMDS in THF at 20 °C.

starting hydroxyphosphonium salt **13a** has not been obtained in crystalline form, we cannot rule out the intervention of impurities in this experiment. However, all indications point to significant retro-Wittig cleavage starting from **13a**. In contrast, similar experiments with the diastereomer **14a** occurred without any detectable isomerization or reversal. Only the *E* alkene **22** was formed in this case, and crossover experiments were negative.

In all the other examples (**13b–d/14**) there was no significant loss of oxaphosphetane stereochemistry according to the results from independent oxaphosphetane generation. These findings require that salt-free ylides **b–d** must undergo the Wittig reaction without significant (≤2%) equilibration. Olefin Z/E ratios for these three systems therefore correspond to the kinetic cis/trans selectivity in the step leading to oxaphosphetanes.

NMR Spectra of Oxaphosphetanes. Isomeric pairs of oxaphosphetanes could be distinguished by simple ^1H NMR techniques. Initial efforts were complicated by line broadening due to conformational phenomena in the highly congested adducts, but good results could be obtained by adjusting the probe temperature to about 20 °C below the decomposition temperature of the more sensitive adducts. Special care was necessary for all of the cis isomers **19**, which consistently decomposed faster than did the trans isomers **20** and which also were more subject to line broadening problems. In general, **19**-*cis* decomposed at temperatures at least 15 °C below those required for similar decomposition rates for **20**-*trans*. After careful temperature optimization, good ^1H spectra were obtained for each isomer except **19a**-*cis*.

In all examples, oxaphosphetane H_3 (*H*CP) occurs at *lower* field than H_4 (*H*CO), an effect that can be attributed to the hybridization of the basal P–C bond in trigonal–bipyramidal phosphorus. The usual preference for apical oxygen is assumed, with the small ring spanning an apical-basal site. The chemical shift range for H_3 can be significant (δ 3.86–4.56; Table I), but there is no predictable correlation between cis- or trans-disubstituted oxaphosphetanes. On the other hand, the relative chemical shifts of H_4 are highly characteristic of oxaphosphetane stereochemistry, as are the relevant P–C–C–H coupling constants. In each case studied, the H_4 signal of **20**-*trans* is observed near 3 ppm, about 0.5 ppm upfield relative to the corresponding signal of **19**-*cis*. Minimal (0–2 Hz) three-bond coupling between H_4 and phosphorus is seen in each of the **20**-*trans* systems, indicating a similar geometry for the trans oxaphosphetanes. The small H–C–C–P J value is consistent with a dihedral angle in the range 70–90°,[12] suggesting modest distortion away from a planar 4-membered ring to reduce eclipsing interactions. In the **19**-*cis* series, the P–C–C–H coupling is consistently larger (J_{P-H_4} = 6–12 Hz).

The similarity in relative chemical shifts and J values for H_4 provides reassuring support for the stereochemical assignments, especially in the case of **19d**-*cis* and **20d**-*trans* where the geometry is not defined by independent synthesis. Further support for this assignment derives from difference NOE experiments. As expected, H_3 and H_4 experience significant mutual enhancement in **19d**-*cis* but not in **20d**-*trans*. The trans isomer (but not the cis) also has an NOE effect at H_4 (3% enhancement) upon irradiation of the C_3-methyl group. The stereochemistry of these oxaphosphetanes is not in doubt.

NMR Comparison with Low-Temperature Wittig Reactions. Ylides **b** and **c** reacted with aldehyde **18** to give a mixture of oxaphosphetane isomers. The signals corresponded to those seen from the independent generation experiments starting with **13/14**, and the ratios of cis/trans oxaphosphetanes were the same as the final olefin Z/E ratios. Ylide **d** + **18** gave an exceptionally clean spectrum of **19d**-*cis*, and decomposition produced a 99:1 ratio of Z/E alkenes. All of these Wittig reactions therefore occur under kinetic control.

As expected, the Wittig reaction of $Et_3P{=}CHCH_3$ (**a**) + **18** was exceptional and did not take place under kinetic control. The first ^{31}P NMR spectrum obtained (within 6 min at −70 °C) indicated both **19a**-*cis* and **20a**-*trans*, but there was severe line broadening of the cis isomer. In an attempt to increase precision and to minimize the temperature and time variables, $Et_3P{=}CHCH_3$ and **18** were frozen sequentially in separate layers of THF in the same reaction flask (liquid N_2 temperature). The layers were mixed within ca. 1 min by thawing the solvent (−95 °C), and the solution was immediately quenched into methanol/acid at −78 °C by rapid cannula transfer. This experiment gave a 3.1:1 ratio of the same salts **13a/14a**, which had been independently synthesized. In a separate experiment, the initial mixture of oxaphosphetanes was warmed to ca. −5 °C, and the same conversion of **19a** into **20a** and alkene + $Et_3P{=}O$ took place as observed with **13a** + base as starting materials. Direct monitoring by ^1H NMR spectroscopy indicated a > 15:1 Z/E ratio for the small amount of olefin formed at −5 °C due to the fast decomposition of **19a** relative to **20a**. However, the *final* olefin ratio after warming to >30 °C was 1:9 Z/E, identical with that reported for $Et_3P{=}CHCH_3$ + pivaldehyde.[9] On the other hand, the reaction of $Et_3P{=}CHCH_3$ + **18** does *not* involve a true reversible equilibrium between **19a**-*cis* and **20a**-*trans*. If this were the case, control experiments from **14a** to **20**-*trans* and eventually to **22** should have given some of the *Z* olefin **21** because **19a**-*cis* decomposes considerably faster than does **20**-*trans*. Since this was not observed and since reversal of **20a**-*trans* was not detected by crossover experiments, an equilibrium between **19a**-*cis* and **20a**-*trans* is ruled out. Only **19a**-*cis* undergoes significant isomerization, and **20a**-*trans* accumulates.

The only other reported example of substantial oxaphosphetane isomerization involving an aliphatic aldehyde under representative salt-free Wittig conditions is the previously mentioned reaction between $Bu_3P{=}CHC_3H_7$ and pivaldehyde.[4] To establish the analogy, we have briefly investigated the reaction of distilled $Bu_3P{=}CHC_3H_7$ with aldehyde **18**. Low-temperature NMR experiments confirmed conversion to trans oxaphosphetane at ca. −20 °C from an initial ratio of 1:1, determined by the technique

(12) Analogous pentacordinated structures have not been studied extensively. For a review of the dihedral angle dependence for vicinal coupling constants in Phosphorus(III) and Phosphorus(IV) systems, see: Samitov, Yu-Yu. *J. Gen. Chem. USSR (Eng. Transl.)* **1982**, *2*, 1967.

of mixing reactants at −95 °C and quenching into acid at −78 °C. This was somewhat different from the 2:1 trans/cis oxaphosphetane ratio reported from $Bu_3P{=}CHC_3H_7$ + pivaldehyde,[4] but the final olefin ratios were similar with both aldehydes (94:6 *E*/*Z* from **18**). As in the $Et_3P{=}CHCH_3$ reaction, the cis oxaphosphetane decomposed below 0 °C while the more stable trans isomer required ca. 20 °C for a convenient rate of conversion to the *E* alkene.

Discussion

Wittig reversal, or stereochemical isomerization of salt-free oxaphosphetanes by any other mechanism in aprotic solvents, remains a rare phenomenon. There is still no recorded example where a true equilibrium between both isomers, the cis and trans oxaphosphetanes, can be demonstrated in the absence of catalysts.

Earlier studies have ruled out measurable oxaphosphetane isomerization in the adducts corresponding to ylide **b** and a variety of unbranched aldehydes.[7] Strong evidence against equilibration in the corresponding adducts of **d**[3b] and $Bu_3P{=}CHC_3H_7$[4] had also been reported. Furthermore, there has never been proof for Wittig reversal in reactions of salt-free nonstabilized ylides with *unbranched* aliphatic aldehydes under typical Wittig conditions.

The situation is more suspect in the case of tertiary aldehydes. In those reactions involving phosphorus ylides with three alkyl groups as the "inert ligands", such as $Bu_3P{=}CHC_3H_7$[4] or $Et_3P{=}CHCH_3$ (ylide **a**), the cis disubstituted oxaphosphetanes do undergo isomerization. Retro-Wittig reaction is strongly implicated as the mechanism in these exceptional systems. Another logical candidate is ylide **k** ($[Me_2N]_3P{=}CHCH_3$, Table II), but we have not attempted to study this unusual system because of low yields with enolizable aldehydes. To date *no example* of any nonstabilized ylide–aldehyde combination has been found where the trans-disubstituted oxaphosphetane undergoes preparatively significant reversal. This observation allows an important generalization that, so far, applies to *all Wittig reactions*: *the kinetic cis/trans preference for disubstituted oxaphosphetane formation is at least as high as the olefin Z/E ratio.* In other words, Wittig reactions that are highly selective for *Z* olefin are under dominant or total kinetic control.

There are also many *E* olefin selective Wittig reactions that are under kinetic control. Among the entries of Table II involving the unbranched aldehyde $PhCH_2CH_2CHO$, there are six examples of predominant *E* selectivity. Previous studies prove that ylides **a** and **b** react without stereochemical equilibration with the unbranched aldehydes.[3,7] We have also investigated the reaction of the remarkably *E* selective[13] ylide **c** by ^{31}P methods. The adduct signals obtained with $PhCH_2CH_2CHO$ at low temperature do not change until the temperature for olefin formation is reached, and the final alkene ratio (95:5 *E*/*Z*) is the same as the ratio of ^{31}P oxaphosphetane signals.[13] In the absence of *any* contradicting evidence, we conclude that *all* of these Wittig reactions of unbranched aldehydes are kinetically controlled, regardless of product olefin geometry. The singly branched aldehyde entries in Table II have not been studied in detail,[7c] but empirically, they appear similar to the unbranched aldehydes.

Conversion of cis into trans oxaphosphetanes in those isolated systems where it does occur is not simply the result of relatively slow olefin formation. This can be seen clearly with the dibenzophosphole-derived oxaphosphetanes, which decompose stereospecifically even though they are by far the most resistant to olefin formation among the four systems studied in detail. The isomerization process is also not related to any single variable but to a combination of factors. Those factors that are implicated include the presence of donor groups at phosphorus (three alkyl substituents as "inert ligands"; donor amino groups, as in ylide **k**, may have a similar effect, but this remains unproven) and steric congestion in the oxaphosphetane. The steric effect presumably reflects nonbonded interactions in the cis oxaphosphetane and need not be restricted to tertiary aldehydes. However, so far, there are no other known examples of uncatalyzed stereochemical isomerization of oxaphosphetanes derived from aliphatic aldehydes, with the possible exception of a crossover example.[2b] Far less is known about ketone-derived oxaphosphetanes although ^{31}P detection of representative adducts, as well as resolution of oxaphosphetane diastereomer ^{31}P NMR signals, is feasible.[3b] However, there are several clearly established examples of stereospecific oxaphosphetane decomposition in the ketone series as well.[7]

It is misleading to extrapolate from the behavior of aromatic aldehydes to the aliphatic analogues. Much of the early work on Wittig intermediates emphasized benzaldehyde adducts, which are clearly more sensitive to equilibration[2,3b,4,6] than are the aliphatic aldehydes normally used in synthetic applications. Since seven out of eight tested examples of the sterically congested Wittig reactions in Table II involve no significant equilibration, we plan no further evaluation of the remaining entries. It is logical to expect that some of the borderline oxaphosphetane cases will undergo measurable loss of stereochemistry, and we do not suggest that this possibility can be ignored. We do, however, strongly disagree with the use of stereochemical equilibration in any general rationale for the Wittig reaction. Here, the question is not the *possibility* of Wittig reversal but the *extent*. Retro-Wittig cleavage (or equilibration by any other means) is certainly real, but it is rare and must not be invoked without specific proof. A comprehensive discussion of the origins of kinetic Wittig selectivity appears in the accompanying paper.

Experimental Section

Wittig Reactions. Standard Conditions. (A) THF/Potassium *tert*-Butoxide (or KHMDS). The dry phosphonium salt (1.1 equiv) was suspended in THF (to make a 0.2 M solution), and 1.0 equiv of base (*tert*-butoxide or KHMDS) in THF was added. The mixture was allowed to stir for 1 h at room temperature under N_2 and was cooled with a dry ice/acetone bath to −78 °C. The aldehyde (1.1 equiv in 0.5 mL of THF) was added slowly via cannula. After 5 min the reaction mixture was slowly warmed and stirred at room temperature for 12 h. For aqueous workup, 1.0 mL of H_2O was added to dissolve salts, and pentane extractions (3 × 3 mL) were performed. The extracts were combined, dried over $MgSO_4$, and filtered, and the solvent was removed on a rotary evaporator. To remove the remaining polar material, the residue was eluted with pentane through a silica gel plug into a tared 10-mL flask. All pentane was removed to leave behind pure alkene.

(B) THF/Sodamide. The dry phosphonium salt (1.0 equiv) and a large excess of commercial sodamide powder (Aldrich), ca. 5 equiv, were transferred inside a glovebag to a dry 40-mL centrifuge tube with stir bar. The tube was sealed with a septum and parafilm, and enough THF was added via syringe to form a 0.2 M solution. The reaction mixture was allowed to stir for 1–2 h under nitrogen. After the ylide was formed, the N_2 line was removed, and the septum hole was covered with silicone grease, and the solution was clarified by centrifugation. The supernatant solution containing the salt-free ylide was transferred via cannula to a dry round-bottom flask at −78 °C, and a THF solution of the aldehyde (0.95 equiv) was slowly added. The reaction mixture was stirred for 5 min at −78 °C and was slowly warmed to room temperature. After 2–12 h, the reaction mixture was worked up either by using the standard aqueous workup described above or by nonaqueous workup as follows: 2 volumes of pentane were added to precipitate most of the phosphine oxide, and the reaction mixture was filtered. The solvent was removed by rotary evaporation (or by distillation in the case of volatile alkenes), with residual solvent removed by brief exposure to high vacuum. To remove the remaining polar material, the residue was eluted with pentane through a silica gel plug into a tared 10-mL flask. All pentane was removed to leave behind pure alkene.

For the dibenzophosphole derivatives, the following changes were made: a 0.1 M ylide solution and 0.7 equiv of aldehyde relative to the phosphonium salt were used. After reaction at −78 °C, the solution was transferred into a thick-walled tube and sealed, and the sealed tube was heated for 30 min at 110 °C to decompose the oxaphosphetane.

(C) Distilled Ylide $Et_3P{=}CHMe$ or $Bu_3P{=}CHPr$. The neat ylide was measured into a flask with THF (0.2 M), and the aldehyde (0.95 equiv) in THF was added at −78 °C. The reaction mixture was stirred for 5 min, allowed to warm to room temperature, and stirred overnight. The alkenes were isolated as described above.

Alkene Analysis. All alkenes were identified by ^1H NMR spectroscopy at 200, 270, or 500 MHz. *Z*/*E* ratios were determined by NMR integration of appropriate base line resolved signals or by capillary column GLPC analysis. Assignments were verified by independent synthesis of

(13) Vedejs, E.; Marth, C. *Tetrahedron Lett.* **1987**, *28*, 3445.

Z alkenes by using standard salt-free Wittig reactions of appropriate triphenylalkylphosphonium salts. Coupling constants of the olefinic protons confirmed stereochemical assignments.

Distillation of Ylides $Et_3P{=}CHCH_3$[14] and $Bu_3P{=}CHC_3H_7$.[4] The tetraethyl- or tetrabutylphosphonium chloride (50 mmol, 1.0 equiv), first dried at high vacuum, was suspended in ether or THF, respectively, and treated with 0.9 equiv of *n*-BuLi at room temperature, and the ylide was allowed to form overnight. The solution was cooled to −78 °C, high vacuum was applied, the cooling bath was removed, and most of the solvent was removed as the reaction slowly warmed. The butyl ylide was then distilled as previously described.[4] The ethylide was obtained as follows: contrary to literature reports,[14] the LiCl salts did not precipitate from the reaction and could not be removed, which greatly hindered distillation. Remaining solvent from the reaction mixture was removed at high vacuum in a bulb-to-bulb apparatus to leave behind a thick mass of ylide–LiCl complex. This material was heated rapidly with a small Bunsen flame under high vacuum (0.05 mm) to distill over the ylide. Redistillation of the ylide proceeded smoothly at a pot temperature of 75–85 °C and 0.1 mm of pressure to produce pure salt-free ylide.

4,4-Dimethyl-5-phenylpent-2-enes 21 and 22. The pure cis alkene **21** was formed in 98% yield by standard salt-free Wittig reaction of ethylidenetriphenylphosphorane with the aldehyde **18**.[15] (*Z*)-4,4-Dimethyl-5-phenylpent-2-ene (**21**): oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.70; MS, exact mass calcd for $C_{13}H_{18}$ 174.1404; found 174.1406, error 1.1 ppm; IR ($CDCl_3$, cm^{-1}) 1650 (C=C); 500-MHz NMR ($CDCl_3$) δ 7.30–7.10 (5 H, m), 5.37 (1 H, dq, *J* = 12.0, 7.2 Hz), 5.27 (1 H, dq, *J* = 12.0, 1.6 Hz), 2.66 (2 H, s), 1.63 (3 H, dd, *J* = 7.2, 1.6 Hz), 1.12 (6 H, s).

The pure trans alkene **22** was formed via a Wittig reaction with the same aldehyde and the phosphorus ylide $(Me_2N)_3P{=}CHCH_3$[16] as follows: $(Me_2N)_3PEt^+I^-$ (5.0 mmol) was suspended in 25 mL of THF, KHMDS (0.96 equiv) was added via syringe, and the reaction mixture was stirred for 4 h. The solution was cooled to −78 °C, and 0.95 equiv of aldehyde **18** in 4 mL of THF was added to the ylide. The reaction mixture was slowly warmed and stirred overnight at room temperature and was finally heated at reflux for 3 h. An aqueous workup, to remove the salts and the HMPA, was performed as described above to give 86% of trans alkene **22** as a single isomer (>98%) by NMR. (*Z*)-4,4-Dimethyl-5-phenylpent-2-ene (**22**): oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.70; MS, exact mass calcd for $C_{13}H_{18}$ 174.1404, found 174.1400, error 2.3 ppm; IR ($CDCl_3$, cm^{-1}) 1610 (C=C), 1460 (C=C); 500-MHz NMR ($CDCl_3$) δ 7.23–7.08 (5 H, m), 5.45 (1 H, dq, *J* = 15.5, 1.6 Hz), 5.23 (1 H, dq, *J* = 15.5, 6.4 Hz), 2.54 (2 H, s), 1.65 (3 H, dd, *J* = 6.4, 1.6 Hz), 0.96 (6 H, s).

Epoxidations. 1-(1,1-Dimethyl-2-phenylethyl)-2-methyloxiranes 15 and 16. The pure cis or trans alkene (3.0 mmol) was dissolved in 15 mL of methylene chloride and cooled to 0 °C, and 1.4 equiv of solid mCPBA was added directly to the alkene solution. After being stirred at room temperature for 20 min, the reaction mixture was extracted (2 × 20 mL) with aqueous Na_2SO_3 and $NaHCO_3$, dried ($MgSO_4$), and passed through a silica gel plug (10% ether/hexane) to give a 90–96% yield of the cis (**16**) or trans (**15**) epoxide. *cis*-1-(1,1-Dimethyl-2-phenylethyl)-2-methyloxirane (**16**): oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.33; MS, exact mass calcd for $C_{13}H_{18}O$ 190.1353, found 190.1358, error 2.6 ppm; IR ($CDCl_3$, cm^{-1}) 1230 (C—O), 3010 (=C—H); 270-MHz NMR ($CDCl_3$) δ 7.31–7.14 (5 H, m), 2.95 (1 H, qd, *J* = 5.9, 4.4 Hz), 2.72 (1 H, d, *J* = 13.3 Hz), 2.70 (1 H, d, *J* = 4.4 Hz), 2.64 (1 H, d, *J* = 13.3 Hz), 1.18 (3 H, d, *J* = 5.9 Hz), 1.06 (3 H, s), 0.92 (3 H, s). *trans*-1-(1,1-Dimethyl-2-phenylethyl)-2-methyloxirane (**15**): oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.35; MS, exact mass calcd for $C_{13}H_{18}O$ 190.1353, found 190.1354, error 0.6 ppm; IR ($CDCl_3$, cm^{-1}) 1275 (C—O), 3020 (=C—H); 270-MHz NMR ($CDCl_3$) δ) 7.31–7.12 (5 H, m), 2.73 (1 H, qd, *J* = 5.2, 2.4 Hz), 2.69 (1 H, d, *J* = 13.1 Hz), 2.55 (1 H, d, *J* = 13.1 Hz), 2.49 (1 H, d, *J* = 2.4 Hz), 1.23 (3 H, d, *J* = 5.2 Hz), 0.94 (3 H, s), 0.78 (3 H, s).

Epoxide Cleavages. (A) Ph_2PLi. The reactions with Ph_2PLi and epoxides **15** and **16** were performed as described earlier.[7]

(B) Et_2PLi. Diethylphosphine[17] (1.1 mmol) was measured into a dry round-bottom flask (N_2 atmosphere throughout) with 2 mL of THF via syringe and cooled to 0 °C, and *n*-BuLi (1.0 mmol) was added to form the bright yellow phosphide anion. The solution was stirred for 15 min, and the epoxide (1.1 mmol) in THF (1 mL) was added via cannula to the phosphide. The cis epoxide experiment was mildly exothermic at −78 °C while the trans epoxide example was run at −23 °C. Both reactions were stirred at that temperature for 4 h. The reaction was warmed to room temperature and worked up as described under (C) (below) except with water instead of aqueous NH_4Cl. The crude organic residue was redissolved in freshly distilled toluene and evaporated again to remove excess Et_2PH. No attempt was made to purify the hydroxyphosphines, and the crude products were alkylated directly (next section).

(C) DBP-Li.[18] The phosphide anion was prepared and used as follows: 2.10 mL of a 1 M solution of 5*H*-dibenzophosphole[19] in THF (1.05 equiv) was introduced into a dry 10-mL round-bottom flask via syringe, the solution was cooled to −50 °C, and 1.0 equiv of *n*-BuLi was slowly added. The reaction mixture, which turned an orange-red color (phosphide anion) almost immediately, was stirred for 0.5 h at −50 °C. A THF solution of the epoxide (2.0 mmol, 1.0 equiv) in 2 mL of THF was added via cannula to the phosphide anion at 0 °C, and the reaction mixture was warmed to room temperature and stirred overnight. The workup was performed under nitrogen with deoxygenated solutions as follows: aqueous NH_4Cl (2 mL) was added via cannula to quench the reaction, and the aqueous layer was extracted in the round-bottom flask with ether (3 × 5 mL). The organic layers were combined and dried under N_2 by cannula addition into a flask with $MgSO_4$. The solvents were removed under vacuum at low temperature to give the pure product as a thick oil, sufficiently pure for use in the next step.

β-Hydroxyphosphine precursor to **13c**: oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.16; MS, exact mass calcd for $C_{25}H_{27}OP$ 374.1793, found 374.1773, error 5.4 ppm; IR (CH_2Cl_2, cm^{-1}) 3500 (—OH); 270-MHz NMR ($CDCl_3$) δ 7.71–7.50 (4 H, m), 7.23–6.93 (9 H, m), 3.34 (1 H, br dd, *J* = 10.5, 2.5 Hz), 2.67 (1 H, d, *J* = 12.6 Hz), 2.19 (1 H, d, *J* = 12.6 Hz), 2.18–2.13 (1 H, m), 1.16 (3 H, dd, *J* = 15.0, 7.0 Hz), 1.05 (1 H, br s), 0.76 (3 H, s), 0.47 (3 H, s); ^{31}P NMR (benzene-d_6) δ 1.8.

β-Hydroxyphosphine precursor to **14c**: oil; analytical TLC (silica gel F254), 10% ether/hexane, R_f 0.18; MS, exact mass calcd for $C_{25}H_{27}OP$ 374.1793, found 374.1805, error 3.2 ppm; IR ($CDCl_3$, cm^{-1}) 3620 (—OH); 500-MHz NMR ($CDCl_3$, −23 °C) δ 8.01–7.24 (13 H, m), 3.41 (1 H, br s), 2.84 (1 H, d, *J* = 12.8 Hz), 2.80 (1 H, br d, *J* = 6.2 Hz), 2.74 (1 H, d, *J* = 12.8 Hz), 2.52–2.48 (1 H, m), 1.10 (3 H, s), 0.98 (3 H, s), 0.44 (3 H, dd, *J* = 7.0, 7.0 Hz); ^{31}P NMR ($CDCl_3$) δ −7.0.

Preparation of the Dibenzophosphole System. *P*-Phenyldibenzophosphole (PhDBP) was prepared by the method of Cornforth[23] from tetraphenylphosphonium bromide and lithium diethylamide in 80–85% yield.

***P*-Ethyl-*P*-phenyldibenzophospholium Iodide.** *P*-Phenyldibenzophosphole (1.0 g, 3.7 mmol) was dissolved in a fivefold excess of neat ethyl iodide, which had been passed through an alumina plug. The reaction mixture was stirred under N_2 at room temperature, during which time the phospholium salt fell out of solution. After 2 days the EtI was evapoarted, and solid was washed with ether and recrystallized to give the salt in 61% yield. *P*-Ethyl-*P*-phenyldibenzophospholium iodide: solid; mp 191–194 °C (crystallized from acetonitrile/ether); formula $C_{20}H_{18}IP$; 200-MHz NMR ($CDCl_3$) δ 8.49 (2 H, dd, *J* = 8.5, 8.5 Hz), 8.24 (2 H, dd, *J* = 13.7, 7.0 Hz), 8.03 (2 H, dd, *J* = 7.7, 3.0 Hz), 7.86 (2 H, dd, *J* = 7.7, 7.7 Hz), 7.70–7.62 (5 H, m), 3.93 (2 H, dq, *J* = 13.4, 7.5 Hz), 1.15 (3 H, dt, *J* = 22.3, 7.5 Hz); ^{31}P NMR ($CDCl_3$) δ 32.7. Anal. Calcd: C, 57.71; H, 4.36. Found: C, 57.96; H, 4.43.

***P*-Ethyldibenzophosphole.** The title compound was prepared by adaptation of a procedure of Freedman and Ezzell.[24] Phenyldibenzophosphole (3.10 g, 12.0 mmo6) was placed in a 100-mL round-bottomed flask fitted with a reflux condenser. THF (50 mL) and lithium wire (170 mg, 25.0 mmol) were added, and the reaction mixture was stirred and refluxed under N_2 for 4 h. The solution was cooled to room temperature, and ethyl iodide (2.0 mL, 25.0 mmol) was slowly added via syringe as the reaction changed from a dark to light red. The reaction mixture was stirred for 15 min at room temperature, and when quenched with aqueous NH_4Cl, the solution cleared. Workup under nitrogen (see above) and distillation gave the pure phosphole. *P*-Ethyldibenzophosphole: pale yellow liquid; bp 150–160 °C (0.05 mm, bulb-to-bulb distillation); MS, exact mass calcd for $C_{14}H_{13}P$ 212.0752, found 212.0759, error 3.3 ppm;

(14) Schmidbaur, H.; Tronich, W. *Chem. Ber.* **1968**, *101*, 595.
(15) Brannock, K. C.; Dietl, H. K. *Tetrahedron Lett.* **1973**, 1273.
(16) Issleib, K.; Lischewski, M.; Zschunke, A. *Org. Magn. reson.* **1973**, *5*, 401.
(17) Issleib, K.; Tzschach, A. *Chem. Ber.* **1959**, *92*, 704.
(18) Whitham, G.; Roberts, T. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1953.
(19) Braye, E. H.; Caplier, I.; Saussez, R. *Tetrahedron* **1971**, *27*, 5523.
(20) Schlosser, M.; Tuong, H. B.; Schaub, B. *Tetrahedron Lett.* **1985**, *26*, 311 and references therein.
(21) Shaka, A. J.; Keeler, J.; Frenkiel, T.; Freeman, R. *J. Magn. Reson.* **1983**, *52*, 335.
(22) Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694.
(23) Cornforth, J.; Cornforth, R. H.; Gray, R. *J. Chem. Soc., Perkin Trans. 1* **1982**, 2289.
(24) Freedman, L. D.; Ezzell, B. R. *J. Org. Chem.* **1969**, *34*, 1777. Allen, D. W.; Millar, I. *J. Chem. Soc. C* **1967**, 1869.

IR ($CDCl_3$, cm^{-1}) 3030 (=C—H); 1440 (C=C); 200-MHz NMR ($CDCl_3$) δ 7.98–7.29 (8 H, m), 1.85 (2 H, qd, J = 7.6, 2.0 Hz), 0.93 (3 H, dt, J = 14.0, 7.6 Hz); ^{13}P NMR ($CDCl_3$) δ −10.9.

***P,P*-Diethyldibenzophospholium Iodide.** The phosphole was alkylated at room temperature with neat ethyl iodide (ca. 3 equiv) under N_2 for 24 h. The solids were washed with ether, and the product was recrystallized from THF/methylene chloride to give a 61% yield for the two steps: solid; mp 186–187 °C (crystallized from THF/CH_2Cl_2); formula $C_{16}H_{18}IP$; 200-MHz NMR ($CDCl_3$) δ 8.68 (2 H, dd, J 8.0, 8.0 Hz), 8.00–7.62 (6 H, m), 3.66 (4 H, dq, J = 15.0, 7.5 Hz), 0.97 (6 H, dt, J = 21.6, 7.5 Hz); ^{31}P NMR ($CDCl_3$) δ 43.5. Anal. Calcd: C, 52.19; H, 4.93. Found: C, 52.02; H, 4.93.

***P*-Ethyl-*P*-(dimethylamino)dibenzophospholium Iodide.** The phosphine was prepared from 2,2′-dibromobiphenyl[25] and (dimethylamino)-dichlorophosphine by a variation of a procedure by Wittig.[26] The dibromide (6.38 g, 20.0 mmol) in 60 mL of ether was placed in a 100-mL round-bottomed flask fitted with a reflux condenser, the system was flushed with N_2, and n-BuLi (40 mmol) was added via syringe at 0 °C. The reaction mixture was stirred at room temperature for 0.5 h and refluxed for 1 h, and Me_2NPCl_2 (2.22 mL, 19 mmol) in 20 mL ether was added to the refluxing reaction mixture. The reaction mixture was stirred at reflux for 1 h, the solution was allowed to cool and settle, and the supernatant was removed. Solvents were removed under vacuum, and a bulb-to-bulb distillation was performed on the aminophosphole, 180 °C (0.1 mm) to give a distillate, which solidified upon cooling. This material was alkylated with neat ethyl iodide (5 equiv) overnight, and the EtI was evaporated. The residue was washed with ether and recrystallized to give a 55% yield of the salt. *P*-Ethyl-*P*-(dimethylamino)dibenzophospholium iodide: solid; mp 198–200 °C (crystallized from acetonitrile); formula $C_{16}H_{19}INP$; 200-MHz NMR ($CDCl_3$) δ 8.43 (2 H, dd, J = 10.0, 7.5 Hz), 7.93 (2 H, dd, J = 7.5, 3.1 Hz), 7.81 (2 H, dd, J = 7.5, 7.5 Hz), 7.63 (2 H, ddd, J = 7.5, 7.5, 4.0 Hz), 3.60 (2 H, dq, J = 14.0, 7.5 Hz), 2.94 (6 H, d, J = 11.4 Hz), 1.05 (3 H, dt, J = 22.5, 7.5 Hz); ^{31}P NMR ($CDCl_3$) δ 58.7. Anal. Calcd: C, 50.15; H, 5.00. Found: C, 50.05; H, 5.16.

Alkylation of β-Hydroxyphosphines. Salts 13 and 14. (A) 13a and 14a. The β-hydroxyphosphines were each alkylated in neat ethyl iodide (passed through an alumina plug, ca. 10 equiv) for 0.5 h, resulting in precipitation of an oil. Excess ethyl iodide was evaporated, and the crude products were dissolved in hot THF, cooled, and precipitated with dry ether. The trans precursor was recrystallized from THF/ethanol to give a 63% yield (based on the epoxide) of pure **14a**. The isomer **13a**, produced in 18% yield, did not form crystals, and the supernatant liquid after precipitation contained signals in the olefinic region due to **17**. The noncrystalline **13a** was free of **14a** according to NMR analysis: 500-MHz NMR ($CDCl_3$) δ 7.27–7.18 (5 H, m), 4.30 (1 H, br s), 4.01 (1 H, d, J = 13.7 Hz), 2.80 (1 H, dq, J = 14.0, 7.0 Hz), 2.77 (1 H, d, J = 12.7 Hz), 2.63 (1 H, d, J = 12.7 Hz), 2.5–2.46 (6 H, m), 1.47 (3 H, dd, J = 18.1, 7.0 Hz), 1.27 (9 H, dt, J = 18.1, 7.0 Hz), 0.99 (3 H, s), 0.91 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 43.5. **14a**: solid; mp 146–152 °C (crystallized from ethanol/THF); formula $C_{19}H_{34}OIP$; 500-MHz NMR ($CDCl_3$) δ 7.28–7.13 (5 H, m), 5.44 (1 H, d, J = 7.0 Hz), 3.94 (1 H, ddd, J = 7.5, 7.0, 1.7 Hz), 2.95 (1 H, ddq, J = 15.0, 7.5, 7.5 Hz), 2.69 (1 H, d, J = 13.0 Hz), 2.65 (1 H, d, J = 13.0 Hz), 2.51–2.43 (6 H, m), 1.42 (3 H, dd, J = 19.1, 7.4 Hz), 1.31 (9 H, dt, J = 17.8, 7.5 Hz), 0.88 (3 H, s), 0.86 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 39.3. Anal. Calcd: C, 52.30; H, 7.85. Found: C, 52.42; H, 7.99.

(B) Salts 13b and 14b. The β-hydroxyphosphine was added to an excess of ethyl iodide and a small amount of acetonitrile. After the mixture was stirred for 24 h, the solvent and ethyl iodide were evaporated. The residue was taken up in warm THF, precipitated with ether, and recrystallized to give the salt in a 45–55% yield based on epoxide. β-Hydroxyphosphonium salt **13b**: solid; mp 218–220 °C (crystallized from ethanol/ethyl acetate); formula $C_{27}H_{34}OIP$; 500-MHz NMR ($CDCl_3$) δ 7.94–7.65 (10 H, m), 7.23–7.10 (5 H, m), 4.47 (1 H, d, J = 6.8 Hz), 4.08 (1 H, ddd, J = 14.7, 6.8, 1.4 Hz), 3.61 (1 H, ddq, J = 15.9, 12.4, 7.5 Hz), 3.49 (1 H, ddq, J = 15.9, 12.5, 7.5 Hz), 3.41 (1 H, dqd, J = 14.4, 7.2, 1.4 Hz), 2.73 (1 H, d, J = 12.7 Hz), 2.52 (1 H, d, J = 12.7 Hz), 1.54 (3 H, dd, J = 19.5, 7.2 Hz), 1.23 (3 H, dt, J = 19.1, 7.4 Hz), 0.93 (3 H, s), 0.83 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 35.2. β-Hydroxyphosphonium salt **14b**: solid; mp 199–200 °C (crystallized from ethyl acetate/THF); formula $C_{27}H_{34}OIP$; 500-MHz NMR ($CDCl_3$) δ 7.94–7.63 (10 H, m), 7.27–7.12 (5 H, m), 4.91 (1 H, d, J = 6.4 Hz), 3.84–3.76 (2 H, m), 3.36 (1 H, ddq, J = 15.4, 12.4, 7.7 Hz), 3.08 (1 H, ddq, J = 15.4, 12.4, 7.7 Hz), 2.69 (2 H, s), 1.43 (3 H, dd, J = 20.1, 7.0 Hz), 1.12 (3 H, dt, J = 19.8, 7.7 Hz), 0.94 (3 H, s), 0.89 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 36.9. Anal. Calcd: C, 60.91; H, 6.45. Found: C, 60.81; H, 6.41.

(C) DBP Salts 13c and 14c. The β-hydroxyphosphines were alkylated in neat ethyl iodide (passed through an alumina plug, ca. 10 equiv) for 24 h at room temperature, and the solid products were washed with ether to remove excess alkylating agent. Isomer **13c** was recrystallized from acetonitrile to produce the pure β-hydroxyphosphonium salt, 52% yield, based on the epoxide. The DBP salt **14c**, formed in 65% yield, did not crystallize. **14c**: amorphous solid, free of **13c** as determined by NMR analysis; 500-MHz NMR ($CDCl_3$) δ 8.45 (2 H, dt, J = 27.6, 8.1 Hz), 7.98–7.59 (6 H, m), 7.20–7.14 (5 H, m), 4.08 (1 H, br dd, J = 7.0, 7.0 Hz), 3.46 (1 H, ddq, J = 15.0, 12.3, 7.5 Hz), 3.28 (1 H, ddq J = 14.0, 7.0, 7.0 Hz), 3.02 (1 H, ddq, J = 15.2, 12.3, 7.5 Hz), 2.71 (2 H, s), 1.70 (1 H, br s), 1.39 (3 H, dd, J = 22.4, 7.2 Hz), 0.86 (3 H, s), 0.85 (3 H, dt, J = 22.8, 7.5 Hz), 0.84 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 42.8. **13c**: solid; mp 196–200 °C (crystallized from acetonitrile); formula $C_{27}H_{32}OIP$; 500-MHz NMR ($CDCl_3$) δ 8.58–8.46 (2 H, m), 7.90–7.78 (4 H, m) 7.65–7.57 (2 H, m), 7.28–7.20 (5 H, m), 4.47 (1 H, dd, J = 9.4, 2.5 Hz), 3.74 (1 H, ddq, J = 15.3, 13.0, 7.5 Hz), 3.66 (1 H, dqd, J = 14.0, 7.1, 2.5 Hz), 3.44 (1 H, ddq, J = 15.3, 13.0, 7.5 Hz), 2.84 (1 H, d, J = 13.0 Hz), 2.76 (1 H, d, J = 13.0 Hz), 1.82 (1 H, br s), 1.10 (3 H, dd, J = 21.6, 7.1 Hz), 1.06 (3 H, s), 1.04 (3 H, s), 0.82 (3 H, dt, J = 21.3, 7.5 Hz); ^{31}P NMR ($CDCl_3$) δ 50.5. Anal. Calcd: C, 61.14; H, 6.08. Found: C, 61.44; H, 6.04.

β-Hydroxyphosphonium Salts 13d and 14d. Salt **13d** was isolated from a low-temperature quench of the standard salt-free Wittig reaction of $Ph_3PEt^+ I^-$ as follows: $NaNH_2$ in THF was used to form the ylide under standard conditions. The aldehyde (10.0 mmol, 1 equiv) was added to the ylide solution (THF, 50 mL) at −78 °C, and the condensation was effected by warming the reaction to −40 °C for 15 min. The oxaphosphetane solution was then cooled to −78 °C and transferred via cannula into concentrated HCl (2 equiv in methanol), also at −78 °C. The methanol and THF were evaporated, 50 mL of CH_2Cl_2 was added, and the organic layers were washed with 25 mL of $NaHCO_3$ and dried over $MgSO_4$. Solvents were removed, and the resulting oil was washed with ether and recrystallized from acetonitrile to give the pure salt **13d** (67%). Even though chloride was present in the quenching solution, the product was isolated as the iodide (from the original phosphonium salt), according to the $AgNO_3$ test and elemental analysis. Salt **13d**: solid; mp 234–235 °C (crystallized from acetonitrile); formula $C_{31}H_{34}OIP$; 500-MHz NMR ($CDCl_3$) δ 7.84–7.62 (15 H, m), 7.15–7.01 (5 H, m), 4.02 (1 H, br s), 3.90 (1 H, d, J = 16.1 Hz), 3.75 (1 H, dq, J = 14.0, 7.0 Hz), 2.79 (1 H, d, J =13.0 Hz), 2.45 (1 H, d, J = 13.0 Hz), 1.64 (3 H, dd, J = 20.6, 7.0 Hz), 1.01 (3 H, s), 0.88 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 33.7. Anal. Calcd: C, 64.14; H, 5.90. Found: C, 64.06; H, 6.03.

Salt **14d** was produced by isomerization of the initial oxaphosphetane mixture with base.[20] The ylide was formed from $Ph_3PEt^+I^-$ (6.5 mmol, 1.05 equiv) in 30 mL of THF and n-BuLi (1.0 equiv) at 0 °C. The aldehyde (1.0 equiv) in THF was added at −78 °C, and the reaction mixture was stirred at −40 °C for 30 min. A second equivalent of n-BuLi was then added to the solution at −78 °C, the deep red oxido-ylide was warmed and stirred at room temperature for 30 min, and the reaction was quenched and worked up as described above. The ^{31}P NMR spectrum of the crude mixture showed the desired β-hydroxyphosphonium salt **14d** plus about 10% of the isomer **13d**. Recrystallization from ethanol produced **14d** (with a large loss of material) free of **13d** according to NMR analysis: 500-MHz NMR ($CDCl_3$) δ 7.87–7.63 (15 H, m), 7.23–7.08 (5 H, m), 5.13 (1 H, br s), 4.16 (1 H, ddd, J = 7.0, 7.0, 1.8 Hz), 4.11 (1 H, dqd, J = 14.4, 7.2, 7.0 Hz), 2.68 (1 H, d, J = 12.7 Hz), 2.64 (1 H, d, J = 12.7 Hz), 1.59 (3 H, dd, J = 21.3, 7.2 Hz), 0.90 (3 H, s), 0.89 (3 H, s); ^{31}P NMR ($CDCl_3$) δ 31.5.

NMR Spectra. General Instrumental Procedures. (A) ^{31}P NMR. All variable-temperature NMR work was performed on a Brucker AM-500 instrument, operating at 200 MHz for phosphorus, with a 5-mm or 10-mm broadband probe. Samples were run in 5-mm NMR tubes (unless noted otherwise) in toluene-d_8, $CDCl_3$, THF-d_8, or THF. For deuteriated solvents, the spectra were run locked on deuterium and tuned with the lock signal. For nondueteriated solvents, high resolution could be achieved by tuning on the ^1H FID (observed with the decoupler coils), and spectra were run unlocked. All ^{31}P NMR spectra were run with proton decoupling, with the composite pulse decoupling (CPD) sequence WALTZ-16[21] at a power level of 20H, which minimized line widths and sample heating. ^{31}P chemical shifts were referenced relative to triphenylphosphine oxide at δ +28.7 in $CDCl_3$ (room temperature) or at δ +23.4 in THF (room temperature), based on 85% H_3PO_4 at δ 0.

(B) ^1H NMR. All variable-temperature NMR work was performed on a Brucker AM-500 instrumemt, 500-MHz proton frequency, with a 5-mm proton or broad-band probe. Samples were run in toluene-d_8.

β-Hydroxyphosphonium Salt Deprotonation. Oxaphosphetane Observation. All oxaphosphetanes were air-sensitive and/or temperature-sen-

(25) Gilman, H.; Gaj, B. *J. Org. Chem.* **1957**, *22*, 447.
(26) Wittig, G.; Maercker, A. *Chem. Ber* **1964**, *97*, 747. Allen, D. W.; Millar, I. *J. Chem. Soc. C* **1969**, 252.

Table III.

oxaphosphetane	temp, °C	time, min	% decomp
19a-*cis*	−15	20	5 (30% conversion to **20a**)
20a-*trans*	+20	60	55
19b-*cis*	−10	15	70
20b-*trans*	+15	25	60
19c-*cis*	+55	45	70
20c-*trans*	+65	7 h	50
19d-*cis*	−3	32	100[a]
20d-*trans*	−3	32	25[a]

[a] Temperature held to ± 1 °C, integration accurate to ± 2%.

sitive compounds. They were generated in solution as described below and were observed by variable-temperature NMR techniques.

19a. The salt **13a** was placed in a dry 8-mm NMR tube flask with THF (0.2 M solution), and potassium *tert*-butoxide solution (0.96 equiv) was added via syringe at −78 °C. The tube was quickly shaken and placed in the NMR probe at −60 °C. Precipitated KI caused some loss of resolution at low temperature. Upon warming to −43 °C over 15 min, two oxaphosphetane signals at −66.7 and −68.1 ppm were already present, and equilibration could be observed as the temperature was raised. After warming, workup of the reaction mixture gave alkenes in a 17:83 *Z*/*E* ratio, 72% yield. The ^{1}H NMR spectrum of **19a** could not be resolved below the decomposition temperature, ^{31}P NMR (THF, −13 °C) δ −66.7.

20a. The salt **14a** (0.15 mmol) was suspended in 1.5 mL of THF, and 1.1 equiv of potassium *tert*-butoxide was added to the stirred solution at −78 °C. After 5 min the entire reaction was transferred via cannula into an 8-mm NMR tube. This reaction was also done in toluene-d_8 as described below. In both instances a single low-temperature ^{31}P NMR peak for trans oxaphosphetane **20a** was recorded, and pure trans alkene was produced in the reaction upon warming: 500-MHz NMR (toluene-d_8, −40 °C) δ 7.31–7.11 (5 H, m), 3.65 (1 H, dqd, *J* = 18.4, 7.5, 5.5 Hz), 2.91 (1 H, d, *J* = 5.5 Hz), 2.89 (1 H, d, *J* = 12.4 Hz), 2.54 (1 H, d, *J* = 12.4 Hz), 1.38 (3 H, br s), 1.29 (3 H, br s), 1.07 (9 H, dt, *J* = 17.1, 7.5 Hz), 1.02 (3 H, s), 0.90 (3 H, dd, *J* = 25.0, 7.5 Hz), 0.80 (3 H, s); ^{31}P NMR (toluene-d_8, −40 °C) δ −68.5.

19c and 20c. Each salt (**13c** or **14c**) and a large excess of commercial sodamide (ca. 5 equiv) was stirred in toluene-d_8 at room temperature for 0.5–1 h. The solutions were allowed to settle and were transferred via cannula into thick-walled NMR tubes. If necessary, the samples could be further clarified with a centrifuge. Variable-temperature ^{31}P and ^{1}H NMR showed each sample to contain a single, pure oxaphosphetane (*cis*-**19c** or *trans*-**20c**), which survived at room temperature under nitrogen. Decomposition of the intermediate oxaphosphetane and workup of the reaction resulted in formation of pure cis or trans alkene (GLPC and NMR analysis).

19c: 500-MHz NMR (toluene-d_8, −33 °C) δ 7.52–6.97 (13 H, m), 3.72 (1 H, br ddq, *J* = 16, 8, 6 Hz), 3.49 (1 H, br dd, 6.0, 6.0 Hz), 3.06 (1 H, d, *J* =12.0 Hz), 2.45 (1 H, d, *J* = 12.0 Hz), 2.15–2.09 (1 H, m), 1.80–1.74 (1 H, m), 1.12 (3 H, s), 0.99 (3 H, dt, *J* = 21.1, 7.6 Hz), 0.90 (3 H, s), 0.86 (3 H, dd, *J* = 27.0, 8.1 Hz); ^{31}P NMR (toluene-d_8, +25 °C) δ −65.5.

20c: 500-MHz NMR (toluene-d_8, −30 °C) δ 7.58–7.10 (13 H, m), 3.86 (1 H, dqd, *J* = 18.1, 7.4, 7.1 Hz), 3.04 (1 H, dd, *J* = 7.1, 2.3 Hz), 2.85 (1 H, d, *J* = 12.6 Hz), 2.67 (1 H, d, *J* = 12.6 Hz), 2.30–2.19 (1 H, m), 1.98–1.88 (1 H, m), 1.12 (3 H, s), 0.88 (3 H, dt, *J* = 22.8, 7.4 Hz), 0.82 (3 H, s), 0.43 (3 H, dd, *J* = 27.8, 7.4 Hz); ^{31}P NMR (toluene-d_8, −30 °C) δ −64.4.

Oxaphosphetanes 19b, 19d and 20b, 20d. The *cis* precursor salt (**13b**, **13d**) or the trans precursor salt (**14b**, **14d**) was suspended in toluene-d_8 (0.1 M) at −78 °C, and NaHMDS[22] (0.95 equiv) in toluene-d_8 was added by syringe. The reaction mixture was stirred at −20 to −40 °C for 2–4 h (depending on oxaphosphetane stability), solids were allowed to settle at −78 °C, and the supernatant was transferred via cannula into a thick-walled NMR tube, which was sealed. If necessary, the sample could be further clarified by centrifugation of the NMR tube packed in dry ice. Variable-temperature ^{31}P and ^{1}H NMR showed each sample to be a single oxaphosphetane, at least 95% pure. Warming the sample to room temperature followed by workup gave the pure (>99% by GLPC or NMR) cis or trans alkene.

19b: 500-MHz (toluene-d_8, −30 °C) δ 7.38–7.01 (15 H, m) 4.10 (1 H, dqd, *J* = 20.8, 7.7, 7.7 Hz), 3.45 (1 H, dd, *J* = 11.2, 7.8 Hz), 2.91 (1 H, br d, *J* = 12.1 Hz), 2.42 (1 H, d, *J* = 12.1 Hz), 2.29–2.21 (1 H, m), 2.08–2.00 (1 H, m), 1.25 (3 H, dt, *J* = 20.8, 7.2 Hz), 1.20 (3 H, s), 0.98–0.85 (3 H, m), 0.79 (3 H, s); ^{31}P NMR (toluene-d_8, −30 °C) δ −64.7.

20b: 500-MHz NMR (toluene-d_8, −30 °C) 7.71–6.97 (15 H, m), 4.09 (1 H, dqd, *J* = 20.8, 7.4, 6.1 Hz), 2.92 (1 H, br d, *J* = 6.1 Hz), 2.85 (1 H, d, *J* = 12.4 Hz), 2.53 (1 H, d, *J* = 12.4 Hz), 2.33–2.23 (1 H, m), 2.07–2.01 (1 H, m), 1.20 (3 H, dt, *J* = 21.1, 7.4 Hz), 1.13 (3 H, s), 0.82 (3 H, dd, *J* = 27.2, 7.4 Hz), 0.77 (3 H, s); ^{31}P NMR (toluene-d_8, −43 °C) δ −63.4.

19d: 500-MHz NMR (toluene-d_8, −40 °C) δ 7.66–7.50 (5 H, m), 7.14–6.93 (15 H, m), 4.09 (1 H, br dqd, *J* = 16, 8, 6 Hz), 3.52 (1 H, br dd, *J* = 6.0, 6.0 Hz), 2.81 (1 H, d, *J* = 12.5 Hz), 2.33 (1 H, d, *J* = 12.5 Hz), 1.25 (3 H, dd, *J* = 26.8, 8.0 Hz), 1.07 (3 H, s), 0.87 (3 H, s); ^{31}P NMR (toluene-d_8, −43 °C) δ −62.9.

20d: 500-MHz NMR (toluene-d_8, −40 °C) δ 7.67–7.02 (20 H, m), 4.56 (1 H, ddq, *J* = 22.1, 8.1, 7.2 Hz), 3.05 (1 H, br dd, *J* = 8.1, 1.5 Hz), 2.89 (1 H, d, *J* = 12.7 Hz), 2.44 (1 H, d, *J* = 12.7 Hz), 1.21 (3 H, s), 0.88 (3 H, dd, *J* = 27.5, 7.2 Hz), 0.77 (3 H, s); ^{31}P NMR (toluene-d_8, −40 °C) δ −62.2.

Low-Temperature Observation of the Wittig Reaction. The distilled ylide $Et_3P{=}CHCH_3$ (**a**, 0.12 mmol), was placed in 1.2 mL of THF-d_8 in a 5-mm NMR tube, cooled to −84 °C, and aldehyde **18** in a small amount of THF-d_8 was added via cannula to the ylide. The NMR tube was quickly shaken and placed in the NMR probe (Bruker AM-500) at −70 °C. The first ^{31}P spectrum, taken within 6 min, showed complete reaction and gave a peak at −68 ppm for the trans oxaphosphetane and a very broad signal slightly downfield for the cis oxaphosphetane. The broad cis peak became sharper and decreased in size relative to the trans oxaphosphetane signal as the sample was warmed to −15 °C, disappearing near 0 °C. The trans peak increased in size over the same temperature range until decomposition to trans alkene occurred near room temperature.

Low-Temperature Quenches of Wittig Reactions. A solution of the triethyl ylide **a** (either distilled or formed from KHMDS) in THF (0.2 M) was frozen at −196 °C (liquid N_2), and a solution of the tertiary aldehyde **18** in THF was added and frozen on top of the frozen ylide solution. The layers were thawed and mixed at −96 °C (hexane/liquid N_2 bath) within 1–2 min, and an aliquot was immediately quenched by cannula transfer into HCl/methanol (ca. 2 equiv of concentrated HCl) at −78 °C, producing a mixture of β-hydroxyphosphonium salts **13a** and **14**, which were isolated as described above. The ratio of **13a**/**14a** in the optimized experiment was 3.1:1. Assignments were made by comparison to the independently synthesized salts with ^{31}P and ^{1}H NMR at 500 MHz. The remaining portion of the reaction was allowed to warm to room temperature, and standard workup gave alkenes in a 1:9 *Z*/*E* ratio. A similar experiment with the primary aldehyde hydrocinnamaldehyde gave β-hydroxyphosphonium salts in a 1:2 ratio and final alkene products in a *Z*/*E* ratio of 37:63, indicating no equilibration in the primary aldehyde system.

Crossover Experiments with β-Hydroxyphosphonium Salts. Triethyl Derivative 13a. The salt (40 mg, 0.09 mmol) was suspended in 1 mL of THF, and 1.0 equiv of potassium *tert*-butoxide in THF was added via syringe at −78 °C. The reaction was stirred for 3 min, and 3 equiv of crossover aldehyde (*p*-chlorobenzaldehyde) in THF was added at −78 °C. The reaction was stirred for 5 min at this temperature, the cold bath was removed, and the solution was slowly warmed and stirred overnight at room temperature. After workup, ^{1}H NMR analysis showed a 1:1.2 *Z*/*E* mixture of alkenes, plus 45% crossover alkenes. Similar results were obtained when the crossover aldehyde was added to the β-hydroxyphosphonium salt prior to deprotonation with base. The same experiment was performed with the triethyl salt **14a** and showed no crossover.

Oxaphosphetane Decomposition Rates. Each of the oxaphosphetanes was generated from the corresponding β-hydroxyphosphonium salt as described above and found to be a single oxaphosphetane by ^{31}P NMR (except **19a**-*cis*) (Table III). The NMR tubes containing each of the oxaphosphetane solutions were allowed to decompose at the indicated temperature (±3 °C) for the stated time. ^{31}P NMR integration was used to determine the extent of decomposition, and is accurate within ±5%.

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Registry No. 13a, 113686-89-8; **13b**, 113686-94-5; **13c**, 113686-96-7; **13d**, 113686-98-9; **14a**, 113686-90-1; **14b**, 113686-95-6; **14c**, 113686-97-8; **14d**, 113686-99-0; **15**, 113460-15-4; **16**, 113460-14-3; **17**, 113686-91-2; **18**, 1009-62-7; **19a**, 113687-00-6; **19b**, 113687-01-7; **19c**, 113460-16-5; **19d**, 113687-03-9; **20a**, 113773-47-0; **20b**, 113687-02-8; **20c**, 113477-40-0; **20d**, 113773-48-1; **21**, 113460-12-1; **22**, 113460-11-0; a, 17847-85-7; b, 113686-81-0; c, 113686-82-1; d, 1754-88-7; $(Me_2N)_3PEt^+I^-$, 14129-99-8; $(Me_2N)_3P(Et)I$, 113687-04-0; $CH_3CH(PEt_2)CH(OH)C(CH_3)_2CH_2Ph(R^*,S^*)$, 113686-83-2; $CH_3CH(PEt_2)CH(OH)C(CH_3)_2CH_2Ph(R^*,R^*)$, 113686-84-3; $CH_3CH(DBP)CH(OH)C(CH_3)_2CH_2Ph(R^*,S^*)$, 113686-85-4; $CH_3CH(DBP)CH(OH)C(CH_3)_2CH_2Ph(R^*,R^*)$, 113686-86-5; $CH_3CH(PPh_2)CH(OH)C(CH_3)_2CH_2Ph(R^*,S^*)$, 113686-92-3; $CH_3CH(PPh_2)CH(OH)C(CH_3)_2CH_2Ph(R^*,R^*)$, 113686-93-4; $Bu_3P{=}CHPr$, 43216-19-9; Et_2PH,

627-49-6; Me_2NPCl_2, 683-85-2; tetraethylphosphonium chloride, 7368-65-2; tetrabutylphosphonium chloride, 2304-30-5; 5*H*-dibenzophosphole, 244-87-1; *P*-phenyldibenzophosphole, 1088-00-2; *P*-ethyl-*P*-phenyldibenzophospholium iodide, 113686-87-6; *P*-ethyldibenzophosphole, 16523-77-6; *P*,*P*-diethyldibenzophospholium iodide, 113460-10-9; *P*-ethyl-*P*-(dimethylamino)dibenzophospholium iodide, 113686-88-7; *P*-ethyl-*P*-(dimethylamino)iodo dibenzophosphorane, 113687-05-1; 2,2'-dibromobiphenyl, 13029-09-9.

Mechanism of the Wittig Reaction: The Role of Substituents at Phosphorus

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Abstract: The variation in Wittig reaction stereochemistry is attributed to dominant kinetic control in nearly all cases. Formation of cis or trans oxaphosphetanes is the decisive step, and this occurs by an asynchronous cycloaddition. An interplay of 1,2 and 1,3 steric interactions decides which diastereomeric oxaphosphetane will be favored. For $Ph_3P{=}CHCH_3$, the best transition state is the puckered four-center arrangement **2a** having a pseudoequatorial aldehyde alkyl group R' and pseudoaxial α-methyl. This geometry results from the unusual steric consequences associated with having an sp^3-hybridized atom (phosphorus) as one of the reacting centers in a cycloaddition process and is increasingly favored when R' is bulky. A trend toward the trans diastereomer **5** occurs if the nearest phosphorus ligand can orient a compact face toward the aldehyde, or if the aldehyde R' group has at least one α-hydrogen. These conditions are satisfied in the exceptionally trans selective ylide **10**, even for tertiary aldehydes, as a result of bond angle preferences and geometric constraints due to the 5-membered ring. In contrast, **7** is constrained to react via the cis-selective puckered geometry and affords exclusively the *Z* alkene. Nonstabilized or "moderated" ylide reactions involve early transition states having phosphorus in a distorted square-pyramidal geometry. Stabilized ylides react via a productlike geometry, and kinetic trans selectivity is easily understood on the basis of oxaphosphetane-like steric interactions.

We have reported several striking examples of contrasting kinetic cis/trans selectivity in the Wittig step leading to oxaphosphetanes.[1-3] The steric factors that control selectivity will now be considered, together with an overall mechanistic interpretation of the Wittig reaction. The discussion is based on a number of experimental observations summarized under the generalizations in Table I. Most of this information is recent and comes from the accompanying paper[1] or from related studies by Maryanoff et al.[5] The rest is included to facilitate the evaluation of mechanistic proposals in this paper and elsewhere. (See Table I.)

Background. The old ionic mechanism (betaine intermediates assumed) for the Wittig reaction was proposed on the basis of reasonable analogy and the limited experimental evidence available at the time regarding Wittig intermediates.[14a] However, the two-step mechanism is difficult to reconcile with generalizations 1, 3, and 5, as well as with the results of recent theoretical investigations,[15] or with the absence of substantial solvent effects on cis/trans selectivity in the reactions of nonstabilized ylides.[6]

The alternative mechanistic category involves asynchronous cycloadditions. The first recognizable depiction of a four-center addition process (involving $Ph_3P{=}CPh_2$ and a carbonyl group of ketenes or isocyanates) was published by Staudinger and Meyer and predates the betaine mechanism by more than 30 years.[16] Much later, a cycloaddition process was proposed for the reactions of stabilized ylides + aldehydes, based on the results of kinetic studies.[17] Details of stereochemistry or transition-state geometry were not discussed in this work. The notion that a four-center transition state could explain kinetic selectivity for cis-disubstituted oxaphosphetanes first appeared in the communication that also described the detection of oxaphosphetanes (1973).[18] The most important feature of the proposed geometry was the nonplanar arrangement of ylide and aldehyde π-systems. A subsequent full

(1) Vedejs, E.; Marth, C. F.; Ruggeri, R. *J. Am. Chem. Soc.*, preceding paper in this issue.
(2) Vedejs, E.; Marth, C. *Tetrahedron Lett.* **1987**, *28*, 3445.
(3) Vedejs, E.; Huang, W. F. *J. Org. Chem.* **1984**, *49*, 210. Kinetic selectivity has now been proved for salt-free conditions (ref 4).
(4) Vedejs, E.; Fleck, T., unpublished results.
(5) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, 7664 and references therein.
(6) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823.
(7) Schlosser, M.; Christmann, K. F. *Justus Liebigs Ann. Chem.* **1967**, *708*, 1. For recent refinements in stereocontrol, see: Schaub, B.; Jeganathan, S.; Schlosser, M. *Chimia* **1986**, *40*, 246.
(8) Jones, M. E.; Trippett, S. *J. Chem. Soc. C* **1966**, 1090.
(9) Vedejs, E.; Fleck, T.; Hara, S. *J. Org. Chem.* **1987**, *52*, 4637.
(10) (a) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178. (b) Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc.* **1973**, *95*, 822. (c) α-branched example: Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1981**, *46*, 4272.
(11) (a) Maryanoff, B. E.; Reitz, A. B.; Duhl-Emswiler, B. A. *J. Am. Chem. Soc.* **1985**, *107*, 217. (b) Reitz, A. B.; Nortey, S. O.; Jordan, A. D., Jr.; Mutter, M. S.; Maryanoff, B. E. *J. Org. Chem.* **1986**, *51*, 3302.
(12) Anderson, R. J.; Henrick, C. A. *J. Am. Chem. Soc.* **1975**, *97*, 4327. Li^+ present may obscure oxaphosphetane stability issues in this case.
(13) Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 650. Schlosser, M.; Christmann, F. K.; Piskala, A.; Coffinet, D. *Synthesis* **1971**, 29. Schlosser, M.; Tuong, H. B.; Schaub, B. *Tetrahedron Lett.* **1985**, *26*, 311. Li^+ may obscure oxaphosphetane stability in these examples.
(14) (a) Wittig, G.; Schollkopf, U. *Chem. Ber.* **1954**, *87*, 1318. Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654. Trippett, S. *Q. Rev., Chem. Soc.* **1963**, *17*, 406. Maercker, A. *Org. React. (N.Y.)* **1965**, *14*, 270. Johnson, A. W. *Ylide Chemistry*; Academic: New York, 1966. Reucroft, J.; Sammes, P. G. *Q. Rev., Chem. Soc.* **1971**, *25*, 135. Schlosser, M. *Top. Stereochem.* **1970**, *5*, 1. (b) McEwen, W. E.; Beaver, B. D. *Phosphorus Sulfur* **1985**, *24*, 259.
(15) Volatron, F.; Eisenstein, O. *J. Am. Chem. Soc.* **1987**, *109*, 1.
(16) Staudinger, H.; Meyer, J. *Helv. Chim. Acta* **1919**, *2*, 635.
(17) Froyen, P. *Acta Chem. Scand.* **1972**, *26*, 2163. Aksnes, G.; Khalil, F. Y. *Phosphorus Relat. Group V Elem.* **1973**, *3*, 37 and 79. Giese, B.; Schoch, J.; Ruchardt, C. *Chem. Ber.* **1978**, *111*, 1395.
(18) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778.

0002-7863/88/1510-3948$01.50/0