Observation of Pseudorotamers of Two Unconstrained Wittig Intermediates, (3*RS*,4*SR*)- and (3*RS*,4*RS*)-4-Cyclohexyl-2-ethyl-3,4-dimethyl-2,2-diphenyl-1,2λ^5-oxaphosphetane, by Dynamic ^{31}P NMR Spectroscopy: Line-Shape Analyses, Conformations, and Decomposition Kinetics

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Abstract: The two typical, that is unstabilized and unconstrained, oxaphosphetane diastereomers (3*RS*,4*SR*)-(**3**) and (3*RS*,4*RS*)-4-cyclohexyl-2-ethyl-3,4-dimethyl-2,2-diphenyl-1,2λ^5-oxaphosphetane (**5**) have been prepared selectively by deprotonation of (1*RS*,2*SR*)- (**6**) and (1*RS*,2*RS*)-(2-cyclohexyl-2-hydroxy-1-methylpropyl)-ethyldiphenylphosphonium iodide (**7**). The X-ray structure analysis of **7** established the relative configurations of **6** and **7** and consequently those of **3** and **5**. Pseudorotation of the 1,2-oxaphosphetanes **3** and **5** and their alkene formations have been studied by ^{31}P NMR spectroscopy. The conformations of the resolved pseudorotamers at the pentacoordinate trigonal bipyramidal phosphorus atom are identified by ^{1}H, ^{13}C, and ^{31}P NMR data. For both diastereomers, the two rotamers with equatorial position of the ethyl substituent dominate in pseudorotation. Line-shape analyses provided the rate constants and activation parameters of pseudorotations. The results represent the first experimental data for pseudorotation of unstabilized and unconstrained 1,2-oxaphosphetanes. Oxaphosphetanes **3** and **5** stereoselectively decompose to (*Z*)- and (*E*)-2-cyclohexylbut-2-ene, respectively. At −30 °C, pseudorotations are faster than alkene formations by a factor of ca. 10^{11}, and at −20 °C, the half-life of the trans isomer **5** in alkene formation is approximately 8 times longer than that of the cis isomer **3**.

Introduction

The Wittig reaction for the synthesis of alkenes remains an important tool of the chemist, not only in the laboratory, but also for the production of alkenes on an industrial scale. In recent reviews, Vedejs and Peterson have collected a wealth of empirical data and have sought and followed unbroken threads concerning mechanistic and selectivity aspects.[1]

A central theme of mechanistic studies was and still is the detection and analysis of so-called Wittig intermediates.[2] 1,2-Oxaphosphetanes as intermediates in typical Wittig reactions were detected by ^{31}P NMR spectroscopy as early as 1973.[3] With the exception of stabilized betaines,[1,4] they are the only intermediates to be identified. The analysis of the role of 1,2-oxaphosphetanes comprises their formation, their reversal or equilibration, their pseudorotation, and their decomposition to alkenes for the purpose of elucidating the origin of the stereochemistry in the Wittig reactions. The latest work involves investigation of the thermolysis of 1,2-oxaphosphetanes, independently of their formation, by the synthesis of isolable oxaphosphetanes.[5,6]

The pseudorotation of 1,2-oxaphosphetanes has been studied by ^{1}H, ^{13}C, and ^{31}P NMR spectroscopy at low temperatures, but to date, individual pseudorotamers have been resolved only for stabilized[7] or constrained[8] oxaphosphetanes.[9] Many of these

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(1) (a) Vedejs, E.; Peterson, M. J. In *Advances in Carbanion Chemistry*, Vol. 2; Snieckus, V., Ed.; JAI Press Inc.: Greenwich, 1996; pp 1−85. (b) Vedejs, E.; Peterson, M. J. *Top. Stereochem.* **1994**, *21*, 1−157. (c) The reader is also referred to the comprehensive review article with more than 550 references by Maryanoff and Reitz: Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927.

(2) Vedejs, E.; Marth, C. F. In *Phosphorus-31 NMR Spectral Properties in Compound Characterization and Structural Analysis*; Quin, L. D., Verkade, J. G., Eds.; VCH Publishers: New York, 1994; pp 297−313.

(3) (a) Vedejs, E.; Snoble, K. A. J.; Fuchs, P. L. *J. Org. Chem.* **1973**, *38*, 1178−1183. (b) Vedejs, E.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1973**, *95*, 5778−5780. For the first oxaphosphetane detected from an unusual ylide, see: Birum, G. H.; Matthews, C. N. *J. Chem. Soc., Chem. Commun.* **1967**, 137−138.

(4) Recent examples: (a) Geletneky, C.; Försterling, F.-H.; Bock, W.; Berger, S. *Chem. Ber.* **1993**, *126*, 2397−2401. (b) Neumann, R. A.; Berger, S. *Book of Abstracts: International Symposium: The Research of Georg Wittig—Relevance to Chemistry Today*, Heidelberg, July 15−18, 1997; p 42.

(5) (a) Kawashima, T.; Kato, K.; Okazaki, R. *J. Am. Chem. Soc.* **1992**, *114*, 4008−4010. (b) Kawashima, T.; Kato, K.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 869−870. Review: Kawashima, T.; Okazaki, R. *Synlett* **1996**, 600−608.

(6) Isolable 1,2-oxaphosphetanes have been reported much earlier. See refs 39 and 41 in ref 1a and ref 4 in ref 5a.

(7) For example: (a) Ramirez, F.; Smith, C. P.; Pilot, J. F. *J. Am. Chem. Soc.* **1968**, *90*, 6726−6732. (b) Ramirez, F.; Pfohl, S.; Tsolis, E. A.; Pilot, J. F.; Smith, C. P.; Ugi, I.; Marquarding, D.; Gillespie, P.; Hoffmann, P. *Phosphorus* **1971**, *1*, 1−16.

(8) (a) Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1989**, *111*, 1519−1520. (b) Vedejs, E.; Marth, C. F. *J. Am. Chem. Soc.* **1990**, *112*, 3905−3909. (c) Marth, C. F. Ph.D. Dissertation (Order No. 8826058), University of Wisconsin, Madison, WI, 1988.

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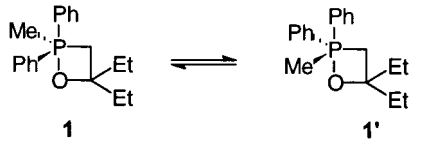
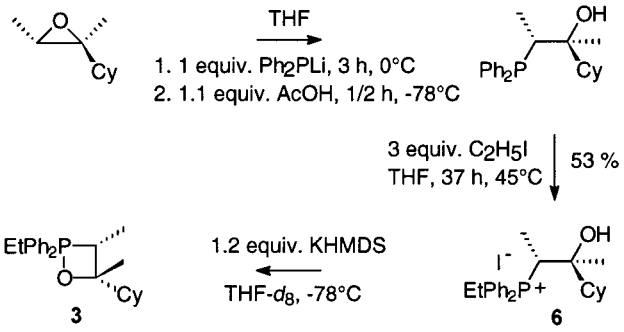
Published on Web 10/06/1998

Scheme 1. Pseudorotation of **1** and **1′** [a]



[a] Estimated minimum rate constant at −83 °C, $\geq 3 \times 10^3$ s^{-1}).[8a]

Scheme 2. Synthesis of 1,2-Oxaphosphetane **3** via Deprotonation of the (1*RS*,2*SR*)-Hydroxyphosphonium Salt **6**[a]



[a] Cy = cyclohexyl. KHMDS = potassium hexamethyldisilazide. *R*,*S* Configurations are shown. The diastereomer **5** was obtained in an analogous manner from the (1*RS*,2*RS*)-hydroxyphosphonium salt **7**.

oxaphosphetanes have been prepared as model compounds. For the typical 4,4-diethyl-2-methyl-2,2-diphenyl-1,2λ^5-oxaphosphetanes (**1**,**1′**) (Scheme 1), typical in the sense of not being stabilized by substituents which are either part of another ring and therefore put constraints in the oxaphosphetane or are electron-withdrawing, a minimum pseudorotation rate constant between **1** and **1′** has been estimated.[8a] We now report what is, to our knowledge, the first kinetic analysis of the pseudorotation of two typical, that is unstabilized and unconstrained, 1,2-oxaphosphetanes. The compounds studied were the diastereomers (3*RS*,4*SR*)- (**3**) and (3*RS*,4*RS*)-4-cyclohexyl-2-ethyl-3,4-dimethyl-2,2-diphenyl-1,2λ^5-oxaphosphetane (**5**) (as enantiomeric pairs). For pseudorotation analysis as well as for the kinetic analysis of the decomposition of oxaphosphetanes **3** and **5**, they have been prepared independently[10] from (1*RS*,2*SR*)- (**6**) and (1*RS*,2*RS*)-(2-cyclohexyl-2-hydroxy-1-methylpropyl)ethyldiphenylphosphonium iodide (**7**) (see Scheme 2 for **3**).

Results and Discussion

^{31}P DNMR: Line-Shape Analyses. In the course of our study[11] of the Wittig reactions of ethylidenetriphenylphosphorane and ethylideneethyldiphenylphosphorane with cyclohexyl methyl ketone, the respective diastereomeric intermediates, the *cis*- (**2** and **3**) and *trans*-oxaphosphetanes[12] (**4** and **5**), have been identified by ^{31}P{^{1}H} NMR spectroscopy (202.46 MHz, in THF-d_8; **2** and **4** at −50 °C, −64.0 and −64.7 ppm; **3** and **5** at −30 °C, −65.6 and −66.8 ppm). As a consequence of the substituents at C_3 and C_4 barriers of pseudorotation higher than between **1** and **1′** were to be expected. Thus the significantly greater temperature dependence of the line widths of oxaphosphetanes **3** and **5** (e.g., at −50 °C, 19 and 21 Hz) compared to ca. 2−14 Hz (0 to −110 °C) of **2** and **4** indicated dynamics accessible on the ^{31}P NMR time scale.

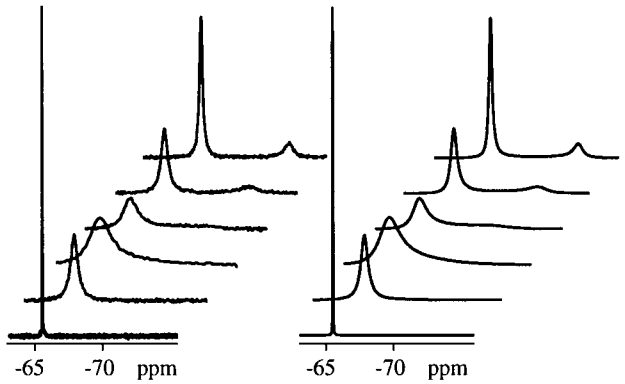
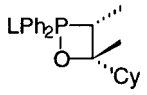
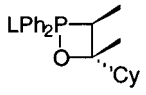


Figure 1. Measured (left, 202.46 MHz, 128 fids, 38.46 kHz sweep width in 64k data points, in THF-d_8 at −30, −70, −80, −85, −90, and −95 °C, bottom to top) and calculated[13] (right) ^{31}P NMR spectra of **3**.





2 L = Ph **3** L = Et **4** L = Ph **5** L = Et

To obtain diastereomerically pure oxaphosphetanes for DNMR investigations, **3** and **5** were synthesized independently (Scheme 2 for **3**).[10] The relative configurations of the precursors **6** and **7** and consequently of the 1,2-oxaphosphetanes **3** and **5** were confirmed by an X-ray structure analysis of **7**. Deprotonation of the phosphonium salts **6** or **7** at −78 °C in THF-d_8 with potassium hexamethyldisilazide (KHMDS) yields stereoselectively solutions of **3** or **5**.

For 1,2-oxaphosphetane **3** the experimental ^{31}P DNMR spectra together with the calculated spectra from line-shape analysis[13] are shown in Figure 1. At −110 °C two peaks of isomers A and B (A dominating) for **3** as well as for **5** are observed (**3**, −63.0 (A) and −69.9 ppm (B); **5**, −63.5 (A) and −70.5 ppm (B)). We interpret these observations as the result of pseudorotation at the oxaphosphetane phosphorus atom entailing resolvable syn and anti isomers[14] (Scheme 3) at low temperature. The exchange rates and populations (for **3** between −95 and −30 °C, for **5** between −95 and −50 °C) were used to obtain the pseudorotation rate constants (Table 1) and activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ (Table 2).[15]

Conformations. ^{1}H (Table 3) and ^{31}P NMR data[16] of **3** and **5**, as well as ^{13}C NMR data[17] as far as accessible for **3** (Table 4), are in complete agreement with data from similar 1,2-oxaphosphetanes.[9] The $^1J_{C3,P}$ coupling constant of **3**, averaged between A and B, is 86.7 Hz, indicating equatorial P−C_3 bonds in the trigonal bipyramidal (*tbp*) configuration of the phosphorus atom. With the exception of oxaphosphetanes bearing electron-

(9) For reviews, see refs 1 and 2.

(10) For the elaboration of this stereoselective method starting from oxiranes, see: Vedejs, E.; Fuchs, P. L. *J. Am. Chem. Soc*. **1973**, *95*, 822−825.

(11) Meier, L. A. Ph.D. Thesis No. 12315, ETH, 1997.

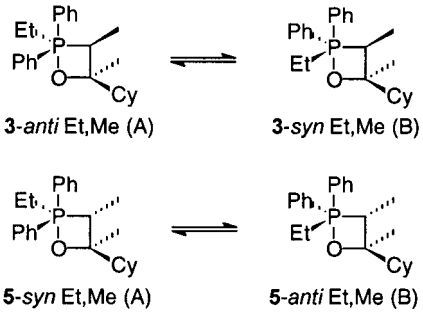
(12) Cis and trans refer to the positions of C_3-CH_3 and C_4-cyclohexyl. The diastereomeric ratio **2**:**4** (at −75 °C) is 95:5 and that for **3**:**5** (at −73 °C) is 4:96 (in THF, with potassium hexamethyldisilazide). For the first resolutions of diastereomeric 1,2-oxaphosphetanes, see: Reitz, A. B.; Mutter, M. S.; Maryanoff, B. E. *J. Am. Chem. Soc*. **1984**, *106*, 1873−1875. See also: ref 1a, pp 34−36.

(13) With WIN-KUBO, Version 951208, Bruker-Franzen Analytik GmbH, Bremen, BRD (Kubo, R.; Tomita, K. *J. Phys. Soc. Jpn.* **1954**, *9*, 888−919. Kubo, R. *J. Phys. Soc. Jpn.* **1954**, *9*, 935−944. Sack, R. A. *Mol. Phys.* **1958**, *1*, 163−167. Johnson, C. S., Jr.; Moreland, C. G. *J. Chem. Educ*. **1973**, *50*, 477−483).

(14) Syn and anti refer to the positions of P-CH_2CH_3 and C_3-CH_3.

(15) Linear regression analyses of the Eyring equation gave squared correlation coefficients of 0.9999 for **3** and 0.9993 for **5**. To avoid potential problems due to the viscosity of the solutions or to the lower solubility of **3** and **5**, spectra obtained below −95 °C have been excluded from line-shape analyses.

Scheme 3. Pseudorotational Isomers of **3** and **5**[a] and Tentative Assignment of Rotamers A and B



[a] Cy = cyclohexyl. Only the 3*S*,4*R*- and 3*R*,4*R* pair, respectively, are shown.

Table 1. Pseudorotation Rate Constants k_A and k_B (10^3 s^{-1}, A is the Main Isomer) and Population of A (p_A) of **3** and **5** (*T* in °C)

	3			**5**		
T	k_A	k_B	p_A	k_A	k_B	p_A
−95	0.284	0.986	0.776	1.06	1.56	0.594
−90	0.667	2.23	0.770	2.51	3.63	0.592
−85	1.64	5.32	0.764	5.40	7.73	0.589
−80	3.51	11.06	0.759	11.5	16.3	0.587
−75				23.8	33.5	0.585
−70	15.6	46.4	0.748	43.2	60.3	0.583
−50				599	809	0.575
−30	1997	4960	0.713			

withdrawing substituents on the P atom, $^1J_{C3,P}$ coupling constants of 76−88 Hz have been reported.[2]

From the $^1J_{C,P}$ coupling constants in $CH_3[^{13}C]H_2$-labeled **3**, obtained with $CH_3[^{13}C]H_2I$ (^{13}C = 99.4%, Scheme 2), it is deduced that in both rotamers of **3** the ethyl substituent is also in the equatorial *tbp* position. The $^1J_{C,P}$ coupling constants at −110 °C are 106.8 Hz in the dominating (A at δ_C = 35.6 ppm) and 92.4 Hz in the minor rotamer (B at 21.5), both values being in the typical range found for equatorial sp^3 carbons.[2,8b] At −30 °C an averaged value of 95.6 Hz (30.5 ppm) is observed. The calculated population averaged value (p_A = 0.713, Table 1), however, is 102.7 Hz. The difference of ca. 7 Hz could indicate that the third rotamer with the ethyl group in apical *tbp* position, which is not populated to a detectable extent at low temperature, makes a minor contribution[18] at temperatures above the fast exchange limit.

It is reasonable to assume an analogous disposition of the oxaphosphetane ring in the diastereomer **5**, and the very close resemblance of the essential ^{1}H NMR data of oxaphosphetanes **3** and **5** (Table 3) suggests that the ethyl group in the rotamers of **5** is also in the equatorial position. Accordingly, pseudorotation between the diastereomeric *syn*/*anti*-Et,Me isomers is proposed (Scheme 3). The equatorial Et positions of **3** and **5** parallel the equatorial Me groups observed for the dominating 1,2-oxaphosphetane rotamers **1** and **1′** (Scheme 1), the pseudorotation of which is still fast at −83 °C and rotamers have not been resolved (averaged $^1J_{C,P}$ = 96.4 Hz, Table 4), and for their dibenzophosphole (DBP) analogues **8a** (slow exchange at −53 °C: $^1J_{C,P}$ = 98.1 Hz), which show coalescence of the C_3 methylene protons near room temperature.[8a] With the help of the coalescence criterion,[19] we have calculated ^{31}P coalescence temperatures of −89 and −92 °C for **3** and **5**, respectively.

The rotamers A of **3** and **5** dominate at low field in the ^{31}P spectra. Only a tentative assignment of A and B to the syn and anti rotamers can be made according to Scheme 3, since neither any relevant ^3J coupling constants from ^{1}H or ^{13}C spectra[20] nor any NOE enhancements[21] in the ^{1}H spectra are accessible. Force field geometry optimizations,[22] however, starting from 50−100 conformations (generated[23] by random walk) to avoid local minima, suggest assigning the major rotamers A to the **3**-anti and **5**-syn pairs: the calculated energy differences (3.1 kJ mol^{-1} for **3** and 1.0 for **5**) between syn and anti pairs (3*S*,4*R* and 3*R*,4*S* of **3**, 3*R*,4*R* and 3*S*,4*S* of **5**) with regard to trend correspond to the experimental energy differences obtained from line-shape analysis ($\Delta\Delta H^{\ddagger}$ of 1.8 kJ mol^{-1} for **3** and 0.6 for **5** (Table 2)).

Pseudorotation. From kinetic and thermodynamic arguments it follows that the isomerizations of 1,2-oxaphosphetanes **3** and **5** are the consequence of pseudorotations in *turnstile*[7b,24] or *Berry*[25] permutation processes and not of acid-catalyzed ring opening ("irregular process" [7b,24] via the protonated betaine). First, isomerizations via the polar protonated betaines would be expected to exhibit negative $\Delta S^{\ddagger}$ values due to the reduction of freedom of the solvent induced by its reorientation toward the polar protonated betaines.[26] Second, the available acid

(16) All NMR data were taken in THF-d_8, chemical shifts (δ, ppm) relative to internal TMS (^{1}H, ^{13}C) and external 85% aqueous H_3PO_4 (^{31}P), coupling constants in hertz; for ^{31}P data, see text. All ^{1}H coupling patterns have been analyzed by iteration with the program WIN-DAISY, Version 3.0, Bruker-Franzen Analytik GmbH, Bremen, BRD, 1995.

(17) Owing to the limited solubility of **6** and **7** and therefore relatively low concentrations of **3** (saturated and filtered solution, <49 mM) and **5** (7 mM), the essential ^{13}C data have been obtained only for **3** at −30 °C, for the dominating rotamer **3**A at −100 °C (minor rotamer B not observable), and for both rotamers of $CH_3[^{13}C]H_2$-labeled **3** (20 mM) at −110 °C.

(18) Assuming a typical apical coupling constant $^1J_{C,P}$ of 15 Hz,[2] the contribution of the population of the third rotamer at −30 °C would be ca. 8%. Additional indications for a small contribution also come from small differences between measured and calculated population averaged chemical shifts of the ethyl-$[^{13}C]H_2$ group (30.5−31.6 = 1.1 ppm) and of ^{31}P (−65.6 − −65.0 = 0.6 ppm). Temperature effects on the ^{31}P shifts are negligible (e.g., the ^{31}P shift of **2** is constant from −110 to −30 °C within 0.1 ppm) but cannot be excluded for ^{13}C shifts because at low temperature a distinction between temperature shifts and shifts which are due to observation of the dominating rotamer only (concentration of **3**[17] too low to observe the minor rotamer except its CH_2 group in ^{13}C-labeled **3**) is impossible. Since the third rotamer is not detectable at low temperature, a three-site exchange analysis is not possible. Nevertheless, this uncertainty does not call into question the principal results presented herein.

(19) Shanan-Atidi, H.; Bar-Eli, K. H. *J. Phys. Chem.* **1970**, *74*, 961−963. Martin, M. L.; Delpuech, J.-J.; Martin, G. J. *Practical NMR Spectroscopy*; Heyden & Son, Ltd.: London, 1980; pp 295−297.

(20) At −110 °C in the ^{1}H spectrum, the lines are too broad, and in the accessible ^{13}C spectra, the concentrations are too low to observe ^{1}H,^{13}C or even ^{13}C,^{13}C ^3J coupling constants in the rotamers of $CH_3[^{13}C]H_2$-labeled **3**.

(21) ^{1}H,^{1}H-NOE enhancements have contributed to the identification of the pseudorotamers of the dibenzophosphole-oxaphosphetane **8b**.[8b] The ^{1}H lines of the oxaphosphetanes **3** and **5** at −90 to −110 °C, however, are too broad for NOE experiments (and in part there is overlap of the relevant resonances with cyclohexyl signals). For the same reasons ^{1}H chemical shift arguments, as applied to **8b**, also cannot be used for **3** and **5**. But the following argument regarding the ^{1}H chemical shifts observed at −30 °C supports the tentative assignment. The only significant difference between the ^{1}H spectra of **3** and **5** is an upfield shift of 0.44 ppm observed for the CH_3-C_4 group in **5** (1.21 and 0.77 ppm, respectively). Since the CH_3-C_4 groups in **3**B and **5**B clearly are positioned in the shielding region of the equatorial free rotor P-phenyl substituent (force field geometry optimizations[22,23]), this upfield shift is likely to reflect the higher population of the rotamer **5**B compared to **3**B (Table 1).

(22) For MM+ force fields in the program HyperChem 5.0 (Hypercube Inc., Waterloo, Canada) the MM2 parameters and atom types (Allinger, N. L., 1991) with the 1977 functional form (Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127−8134. Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph 177; American Chemical Society: Washington, DC, 1982) are used.

(23) In the program ChemPlus (Version 1.5, Hypercube Inc., Waterloo, Canada), an Extension for HyperChem.[22]

(24) Ramirez, F.; Ugi, I. *Adv. Phys. Org. Chem.* **1971**, *9*, 25−126.

(25) Berry, R. S. *J. Chem. Phys.* **1960**, *32*, 933−938.

(26) As negative activation entropies (ca. −24 and −44 J mol^{-1} K^{-1}) have been observed for the second step of the Wittig reaction, the first-order thermolysis of the isolable oxaphosphetanes **9a**[5a] and **9b**,[5b] slightly polar transition states have been postulated.

Table 2. Activation Parameters of Pseudorotation of **3** and **5** ($\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ in kJ mol^{-1}, $\Delta S^{\ddagger}$ in J mol^{-1} K^{-1})

	$\Delta H^{\ddagger}_A$	$\Delta H^{\ddagger}_B$	$\Delta S^{\ddagger}_A$	$\Delta S^{\ddagger}_B$	$\Delta G^{\ddagger}_A$[a]	$\Delta G^{\ddagger}_A$[b]
3	47.3 ± 0.6	45.5 ± 0.6	72.0 ± 3.2	72.0 ± 3.2	35.6 ± 1.1	29.1 ± 1.4
5	44.5 ± 1.4	43.9 ± 1.4	66.9 ± 7.1	66.8 ± 7.0	33.6 ± 2.6	27.5 ± 3.2

[a] At −110 °C. [b] At −20 °C.

Table 3. Essential ^{1}H NMR Data (500.14 MHz, at −30 °C, in THF-d_8) of **3** and **5** (Multiplicities in Brackets)[16]

	H-C$_3$ (dq)[a]			H$_3$C-C$_3$ (dd)			H$_A$CH$_B$-P (ethyl, ddq)[a]				H$_3$C (ethyl, ddd)		
	δ	$^2J_{H,P}$	$^3J_{H,H}$	δ	$^3J_{H,P}$	$^3J_{H,H}$	δ	$^2J_{H,P}$	$^2J_{H,H}$	$^3J_{H,H}$	δ	$^3J_{H,P}$	$^3J_{H,H}$
3	4.31	22.8	7.9	1.07	27.0	7.9	1.95	6.5	12.3	7.8	1.07	20.2	7.8
							2.35	13.8	12.3	7.7			7.7
5	4.18	22.2	7.8	0.92	26.9	7.8	2.08	7.0	13.0	7.6	1.05	20.3	7.6
							2.48	13.0	13.0	7.3			7.3

[a] For comparison, **1** and **1′** at −83 °C, in toluene-d_8: H$_2$C$_3$ (δ = 3.56, $^2J_{H,P}$ = 16.4), CH$_3$-P (δ = 1.91, $^2J_{H,P}$ = 13.7).[8a]

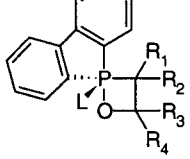
Table 4. ^{13}C{^{1}H} NMR Data[16,17] of **3** (125.77 MHz, at −30 °C, in THF-d_8), of Rotamer **3**A (at −100 °C) and Available Data of **1**,**1′**[8a] (at −53 °C, in Toluene-d_8)

	C$_3$		C$_4$		P−C$_{Ph}$		P−CH$_2$[a]	
	δ	$^1J_{C,P}$	δ	$^2J_{C,P}$	δ	$^1J_{C,P}$	δ	$^1J_{C,P}$
1, **1′**	60.3	83.0	66.9[b]	15[b]	148.8	70.5	24.4	96.4
3[c]	68.7	86.7	69.3	14.0	—[d]	—[d]	30.5	95.6
3A[e]	64.9	ca. 91	70.2	ca. 12	—[d]	—[d]	35.6[f]	106.8[f]

[a] In **1** and **1′**: P-CH$_3$. [b] Reference 1a, p 19 and ref 2, p 302. [c] **C**H$_3$-C$_4$, **C**H$_3$-C$_3$, **C**H$_3$-CH$_2$: δ 24.6, 11.2, 8.5 ($J_{C,P}$ = 15.0, 7.1, 5.9). Cyclohexyl: CH$_2$ δ 27.4, 27.7, 27.8, 27.9, and 30.9 and CH 45.5. [d] For the C$_{Ph}$ atoms, neither the slow (very broad not assignable lines at −100 °C) nor the fast exchange limit has been reached. At −30 °C: six sharp C$_{Ph}$ δ 127.7−133.8 ($J_{C,P}$ = 1.8−10.8) and two broad P-C$_{Ph}$ δ ca. 148.5 and 144.5 (partly averaged $^1J_{C,P}$ of ca. 45 and 80). [e] **C**H$_3$-C$_4$, **C**H$_3$-C$_3$, **C**H$_3$-CH$_2$: δ 24.6, 11.8, 7.2 ($J_{C,P}$ not resolved). Cyclohexyl: CH$_2$ δ 27.1, 27.3, 27.6, 27.7, and 30.7 and CH 44.6. [f] At −110 °C, ^{13}C-labeled **3**, B at 21.5 ($^1J_{C,P}$ = 92.4).

(hexamethyldisilazane from KHMDS, see Scheme 2) is a relatively weak acid (p$K_{a,THF}$ = 25.8[27]) and therefore catalytically inefficient.

The positive $\Delta S^{\ddagger}$ values of pseudorotation of **3** and **5** (Table 2) are in accord with the positive, but smaller $\Delta S^{\ddagger}$ values of 5.5 and 18.0 (± 16.7) J mol^{-1} K^{-1}, respectively, for the pseudorotations of the 1,2-oxaphosphetanes **8a**[8c] and **8b**,[8b] both



8a L = Me, R_1 = R_2 = H, R_3 = R_4 = Et
8b L = Ph, R_1 = R_2 = Me, R_3 = C_2H_4Ph, R_4 = H
8c L = Me, R_1 = CO_2Et, R_2 = R_3 = H, R_4 = Cy
8d L = Et, R_1 = Me, R_2 = H, R_3 = CMe_2CH_2Ph, R_4 = H
8e L = Et, R_1 = Me, R_2 = H, R_3 = R_4 = Et

with the dibenzophosphole ring incorporated as a stabilizing bidentate ligand.[28] However, a number of negative activation entropies (−26.4 J mol^{-1} K^{-1} in *n*-octane to −101.7 in pyridine) have been reported for the permutation process between two diastereomeric 10-Sb-5 stiboranes.[29,30] These negative activation entropies have been attributed either to the "unfavorable, but inevitable equatorial−equatorial disposition" of one of the two bidentate ligands in the transition state or to hexacoordinate transition states (i.e., permutation in an "irregular process" [7b,24]), depending on the donative properties of the solvents. But similar solvent effects have not been observed for corresponding pentacoordinate phosphorus compounds.[31] The common structural feature of the oxaphosphetanes **8a**,**b**, of the stiborane, and of bis(2,2′-biphenylylene)selenurane and -tellurane,[32] in which nearly zero or negative $\Delta S^{\ddagger}$ values (5.9 to −43.9 J mol^{-1} K^{-1}) have also been observed for the pseudorotations, is the presence of one or two bidentate ligands. Therefore, it is likely that the smaller positive (or nearly zero) to negative $\Delta S^{\ddagger}$ values of pseudorotations of oxaphosphetanes **8a**,**b** and of the selenurane and telurane have to be attributed to strain induced by the diequatorial position of a bidentate ligand in the intermediate rotamer[33] of pseudorotation, which has to be traversed in the equilibrium between the populated rotamers.[34] Since there is no bidentate ligand in the 1,2-oxaphosphetanes **3** and **5**, their positive $\Delta S^{\ddagger}$ values do not contradict the observed smaller or negative activation entropies of the other permutation processes.

Comparison of the rate constants k_A and k_B of pseudorotation of **3** and **5** at −85 and −80 °C (1.64 to 16.3 × 10^3 s^{-1}, Table 1) with the estimated minimum rate constant (≥3 × 10^3 s^{-1}) at −83 °C of oxaphosphetanes **1** and **1′**[8a] suggests that pseudorotation between **1** and **1′** might be at least a power of 10 faster. The pseudorotation rate constant of **8a**, the DBP analogue of **1** and **1′**, at 43 °C (5.6 × 10^3 s^{-1}) is very close to the rate constants k_B of **3** and k_A of **5** at −85 °C, that is at a temperature ca. 120° lower. The activation enthalpies $\Delta H^{\ddagger}$ of **8a** (56.5 kJ mol^{-1})[8c] and **8b** (66.5)[8b] compared to 43.9−47.3 kJ mol^{-1} of **3** and **5** in part reflect the stabilization by the bidentate ligand, again understood in terms of the strained intermediate rotamer with a diequatorial disposition of the phosphole ring.[33,34] Considering

(27) Fraser, R. R.; Mansour, T. S.; Savard, S. *J. Org. Chem.* **1985**, *50*, 3232−3234.

(28) The bidentate DBP ligand stabilizes the oxaphosphetanes **8a**,**b** by increasing the activation barriers of pseudorotations as well as of decompositions.[1a]

(29) Kojima, S.; Doi, J.; Okuda, M.; Akiba, K.-y. *Organometallics* **1995**, *14*, 1928−1937.

(30) We thank a reviewer for drawing our attention to this paper. For pseudorotation of 10-P-5 spirophosphoranes, see: Kojima, S.; Kajiyama, K.; Nakamoto, M.; Akiba, K.-y. *J. Am. Chem. Soc.* **1996**, *118*, 12866−12867. For hexacoordinate 1,2-oxaphosphetanides, see: Kojima, S.; Akiba, K.-y. *Tetrahedron Lett.* **1997**, *38*, 547−550, and Kawashima, T.; Watanabe, K.; Okazaki, R. *Ibid.* **1997**, *38*, 551−554. For pseudorotation of a 1,2λ^5-azaphosphetidine, see: Kawashima, T.; Soda, T.; Okazaki, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1096−1098.

(31) Footnote 18 in ref 29: Kojima, S.; Nakamoto, M.; Kajiyama, K.; Akiba, K.-y. Unpublished results.

(32) Ogawa, S.; Sato, S.; Erata, T.; Furukawa, N. *Tetrahedron Lett.* **1992**, *33*, 1915−1918.

(33) Assuming the *turnstile* mechanism, in 1,2-oxaphosphetanes this less stable rotamer has the P−O bond in the unfavorable equatorial position. Originally it had been postulated as a necessary intermediate in the alkene formation step: Bestmann, H. J. *Pure Appl. Chem.* **1979**, *51*, 515−533. See, however, the discussions in refs 1a and 8a.

(34) Reference 1a, pp 46−48.

Table 5. Rate Constants of Alkene Formation of **3** and **5** (T in °C)

T	$k_{(3)}{}^a$	$k_{(5)}{}^b$	T	$k_{(3)}{}^a$	$k_{(5)}{}^b$
−30	4.38×10^{-5}		−15		7.74×10^{-5}
−25	1.09×10^{-4}		−10		1.82×10^{-4}
−20	2.64×10^{-4}	3.18×10^{-5}			

[a] $s^{-1} \pm 1.2-1.9\%$. [b] $s^{-1} \pm 2.0-3.0\%$.

Table 6. Activation Parameters of Alkene Formation of **3** and **5** ($\Delta H^{\ddagger}$ and $\Delta G^{\ddagger}$ in kJ mol^{-1}, $\Delta S^{\ddagger}$ in J mol^{-1} K^{-1})

	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}{}^a$	$t_{1/2}{}^{a,b}$
3	89.7 ± 1.5	42.5 ± 5.8	78.96 ± 0.04	44
5	94.3 ± 1.2	43.1 ± 4.5	83.40 ± 0.06	363

[a] At −20 °C. [b] In minutes.

the different substitution patterns at P, C_3, and C_4 in oxaphosphetanes **1**, **1′**, **3**, **5**, and **8a**,**b**, the stabilization by the DBP ring in two otherwise identically substituted oxaphosphetanes such as **1**, **1′**, and **8a** is expected to be even more apparent.

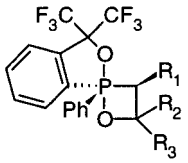
In the ^{13}C spectra of oxaphosphetanes **8d**,**e** at −83 °C or above only one set of signals has been observed, indicating either a single pseudorotamer or rapid interconversion.[8a] In view of the available data of **3**, **5**, and **8a**,**b** the detection of one strongly dominating pseudorotamer of **8d** and of **8e** seems to be more plausible.[35]

Decomposition Kinetics. The decomposition rates were measured independently from the formation of the oxaphosphetanes via deprotonation of **6** and **7** at −78 °C and following the decrease of **3** and **5** by ^{31}P NMR spectroscopy. Alkene formations from *cis*- (**3**) and *trans*-1,2-oxaphosphetane **5** are first-order in **3** and **5** and stereoselective: **3** decomposes (within the detection limit of ^1H and ^{31}P spectroscopy) exclusively to (*Z*)- and **5** exclusively to (*E*)-2-cyclohexylbut-2-ene.[36] With regard to the selectivity of alkene formation in the lithium-free Wittig reaction we have verified by ^1H and ^{31}P spectroscopy (and by crossover experiments[11] with [1,1,2,2,2-$^2H_5$]diethyldiphenylphosphonium bromide) that the diastereomers **3** and **5** do not equilibrate. The kinetically formed **3**/**5** ratio determines the *Z*/*E* ratio[37] (ca. 1:9) of 2-cyclohexylbut-2-ene.

Since only three temperature points are available for **3** as well as for **5** (allowing only one degree of freedom for the Student factor), the error in the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ from conventional linear regression analysis of the Eyring equation would be large and the differences between the activation parameters of alkene formation from **3** and **5** not significant. Therefore, to obtain activation parameters as precise as possible for comparison with available data of constrained and stabilized or isolable 1,2-oxaphosphetanes, the rate constants and activation parameters (Tables 5 and 6) have been evaluated by iterative nonlinear modeling of the Eyring equation with the rate constant substituted from the first-order rate equation (40 and 53 degrees of freedom for **3** and **5**, respectively).[38]

In agreement with the findings for all the oxaphosphetane cis−trans pairs investigated,[39] the *cis*-oxaphosphetane **3** decomposes faster than the *trans*-oxaphosphetane **5** (Table 5). At −20 °C the half-life of the trans isomer **5** is approximately 8 times longer than that of the cis isomer **3** (Table 6). The activation entropies are identical within the confidence limits, a result which is plausible for two diastereomers. $\Delta H^{\ddagger}$ is 4.6 kJ mol^{-1} higher for the trans isomer **5**, understood in terms of stronger nonbonded interactions in the cis isomer **3**.

The isomers **3** and **5** (in THF-d_8) at −20 °C have a 25.6 and 21.2 kJ mol^{-1} lower $\Delta G^{\ddagger}$ than the dibenzophosphole−oxaphosphetane **8a**[8a] at 43 °C (104.6, in CD_2Cl_2), since **8a** is stabilized by the bidentate DBP ligand. The activation enthalpies $\Delta H^{\ddagger}$ of the isolable oxaphosphetanes **9a** (121.8 kJ mol^{-1})[5a] and **9b**



9a R_1= H, R_2 = R_3 = Ph
9b R_1= CO_2Me, R_2 = R_3 = CF_3

(102.1,[5b] both in toluene-d_8) with the Martin ligand are 32.1 and 12.4 kJ mol^{-1} higher than $\Delta H^{\ddagger}$ of oxaphosphetane **3** and 27.5 and 7.8 kJ mol^{-1} higher compared to **5**. The stability of the oxaphosphetanes **9** is due to the CF_3 groups, to the Martin ligand, or to both as electron-withdrawing substituents. The oxaphosphetane **9b** is less stable owing to the ester group in the 3-position. By analogy with the arguments regarding the positive activation entropies of pseudorotation, the positive $\Delta S^{\ddagger}$ values of alkene formation from **3** and **5** indicate nonpolar transition states. Considering the Martin ligand and the electron-attracting substituents in the oxaphosphetanes **9** in comparison to the methyl and cyclohexyl groups in **3** and **5**, this is in understandable contrast to the negative $\Delta S^{\ddagger}$ values of slightly polar transition states as postulated for **9a**,**b**.[26]

Pseudorotation versus Decomposition. In typical 1,2-oxaphosphetanes pseudorotation is much faster than decomposition. For example, the rate constants (partly extrapolated, Tables 1 and 5) at −30 °C of oxaphosphetane **3** differ by approximately 5×10^{10} (k_A) and 1×10^{11} (k_B) and of **5** by 9×10^{11} (k_A) and 1×10^{12} (k_B). Therefore, as in the case of other oxaphosphetanes reported,[8,34] the pseudorotations of **3** and **5** do not control the alkene formation steps. For **1** and **1′** at −10 °C a factor of 10^8 has been estimated by a comparison with the decomposition rate of the *cis*-diphenyl analogue of **8d** (Ph_2 instead of DBP).[8c] Extrapolations of the rate constants of **3** and **5** to −10 °C give

(35) For **8d** this has been suggested to explain the temperature dependence of the ^1H spectra between −78 and 63 °C. A second rotamer was also not detected in the ^{31}P spectra. Reference 8c, pp 155−157.

(36) Both isomers are known compounds. (a) *E* isomer: Danheiser, R. L.; Nowick, J. S. *J. Org. Chem.* **1991**, *56*, 1176−1185. (b) *Z* and *E* isomers: Vedejs, E.; Cabaj, J.; Peterson, M. J. *J. Org. Chem.* **1993**, *58*, 6509−6512.

(37) The initial diastereomeric oxaphosphetane ratio **3**:**5** is 4:96. Stereochemical equilibration during alkene formation is not significant: the *Z*/*E* ratio of the alkene after 100% conversion is 8:92 (reaction time 45 h at −73 °C and 1 h during warming to room temperature). In analogy to our observations ($Ph_3P{=}CHCH_3$ is *Z*-selective, $EtPh_2P{=}CHCH_3$ is *E*-selective; see footnote 12), the reagent control of the *Z*/*E* selectivity in the lithium-free Wittig ethylidenation of a variety of ketones, including cyclohexyl methyl ketone, has been reported by Vedejs and co-workers for the ylides $Ph_3P{=}CHCH_3$ and $EtDBP{=}CHCH_3$ (*Z*/*E* of 2-cyclohexylbut-2-ene 78:22 and 4:96, respectively).[36b]

(38) Available experimental data: 15 data points at each temperature (−30, −25, −20 °C) for **3**; 25 data points (−20 °C), 13 (−15), 20 (−10) for **5**. The experimental errors of the ^{31}P peak integrals have been assumed to be normally distributed with a variance independent of time and temperature. In addition to the enthalpies and entropies of activation, the initial integral value at each temperature has been treated as adjustable parameter (allowing 45 − 5 degrees of freedom for **3**, 58 − 5 for **5**). The confidence intervals for the adjusted parameters have been obtained according to a scheme extending the classical linear approach to an iterative nonlinear approach. For one of the first applications to NMR spectroscopic data, see: Leipert, T. K.; Marquardt, D. W. *J. Magn. Reson.* **1976**, *24*, 181−199 and references therein. Supporting Information is available.

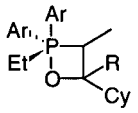
(39) Maryanoff, B. E.; Reitz, A. B.; Mutter, M. S.; Inners, R. R.; Almond, H. R., Jr.; Whittle, R. R.; Olofson, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 7664−7678. See also: ref 1a, pp 37−39. Recent examples: Yamataka, H.; Takatsuka, T.; Hanafusa, T. *J. Org. Chem.* **1996**, *61*, 722−726.

factors between ca. 9×10^9 (k_A of **3**) and 2×10^{11} (k_B of **5**) by which pseudorotations are faster than alkene formation. Since the decomposition rate constants of **3** and the above analogue of **8d** at −10 °C are nearly identical (1.39×10^{-3} and 1.3×10^{-3}) and the pseudorotation rate constant between **1** and **1′** is at least an order of magnitude greater than the rate constants of **3** and **5**, it is very likely that the pseudorotation of **1** and **1′** is approximately 10^{12} times faster than decomposition.

Bidentate ligands, as for example in dibenzophosphole−oxaphosphetanes, increase the activation barriers of both processes to different extents. A typical case is the constrained DBP analogue **8a**[8a] of **1** and **1′** with a ratio of rate constants of pseudorotation to decomposition of ca. 10^8 at 43 °C. The very unstable dibenzophosphole−oxaphosphetane **8c**[40] (Cy = cyclohexyl), an ester-substituted analogue of **8a**, exemplifies the critical influence of this type of substituent and demonstrates that decomposition can become faster than pseudorotation. For **8c**, which could not be detected at a temperature below −80 °C, decomposition at −70 °C has been estimated to be at least 10 times faster than pseudorotation.[34]

The bidentate Martin ligand in constrained and stabilized oxaphosphetanes such as **9a,b** is a special case with respect to activation barriers of decomposition as well as of pseudorotation. Analogous to the monodentate $(CF_3)_2CHO$ group,[24] in combination with additional electron-withdrawing (e.g., CF_3) or conjugating (e.g., Ph) groups, it stabilizes the oxaphosphetanes to such an extent that they may become isolable. At the same time the activation barrier of pseudorotation of such oxaphosphetanes increases since the higher-energy intermediate rotamer has the Martin ligand in a strained diequatorial location and both P−O bonds are thus in an unfavorable equatorial position.[33] And as for **8c**, the activation barrier of decomposition may be decreased to below the barrier of pseudorotation by an ester group at C_3. But decomposition for its part occurs in a far higher temperature region. One typical case is the 3-methoxycarbonyl−oxaphosphetane **9b**,[5b] for which between ca. 69 and 111 °C only alkene formation has been observed.[41,42] The important common feature of **8c** and **9b** is the ester substitution in the 3-position, which is known to facilitate bond cleavage in decomposition.[1a]

The comparison of the oxaphosphetanes **3** and **5** with **1**, **1′** and its DBP analogue **8a** and with the very unstable oxaphosphetane **8c** exemplifies that particularly the separation of constraint by bidentate ligands from stabilization or destabilization by substituents in pairs of closely related 1,2-oxaphosphetanes will provide further insight into the dependence of the relative heights of pseudorotation and decomposition barriers. In this respect the DBP analogue **10a**[36b] of **3** and **5** and the two 1,2-oxaphosphetanes **10b,c**[40] (Cy = cyclohexyl) are very interesting candidates. To our knowledge, **10b** is the structurally closest analogue mentioned in the literature of the oxaphosphetanes **3** and **5**, and **10c** is its DBP analogue. Apart from the alkene *E*/*Z* ratios formed from **10a**[36b] and **10c**,[43] no data seem to be available. The results of Vedejs and Marth for the 1,2-oxaphosphetanes **1**, **1′** and **8a** and our results for **3** and **5**



10a Ar,Ar = DBP, R = Me
10b Ar = Ar = Ph, R = H
10c Ar,Ar = DBP, R = H

suggest that for the 1,2-oxaphosphetanes **10** it may be possible to obtain kinetic data for both pseudorotations and decompositions. A comparison with the data for **3** and **5** would then make it possible to quantify the effects of constraints imposed by the dibenzophosphole ring on both activation barriers in the oxaphosphetanes.[44]

Conclusions

In summary, apart from the estimations for the intermediates **1** and **1′,** the rate constants and activation parameters provided for the pseudorotation of the diastereomeric 1,2-oxaphosphetanes **3** and **5** and for their alkene formation constitute the first experimental data for two typical, that is unconstrained and unstabilized, Wittig intermediates. They reveal the order of magnitude that the rate constant of pseudorotation can be greater than that of decomposition. The comparison with available data of constrained, stabilized, or destabilized 1,2-oxaphosphetanes demonstrates the different extents to which the activation barriers of both processes independently become increased or decreased by substituents.

The conformations of two dominating rotamers in both pseudorotations have been identified, and the stereoselective alkene formation from oxaphosphetanes **3** and **5** has been ascertained by NMR spectroscopy.

Experimental Section

NMR Spectroscopy. All experiments were performed on a Bruker AMX-500 spectrometer with samples in dry, peroxide-free THF-d_8 under argon. Temperature control and calibrations were achieved with a Bruker variable-temperature Unit B-VT 1000E and a Pt-100 sensor (±0.1 °C, Degussa AG). See the Supporting Information for key original spectra and details.

Syntheses. The preparations of **3**, **5**, **6**, **7**, and precursors, including spectroscopic data, are described in the Supporting Information.

Acknowledgment. We thank Dr. Martin Badertscher (Laboratorium für Organische Chemie, Department of Chemistry, ETH) for the nonlinear modeling, Dr. Michael Hennig and Peter Schönholzer (F. Hoffmann-La Roche AG) for the X-ray structure analysis, and F. Hoffmann-La Roche AG for financial support.

Supporting Information Available: X-ray structural information on **7** (crystal data, ORTEP drawing, table of bond lengths and bond angles), details of NMR spectroscopy (THF-purification, T_1 relaxation times, sample preparations, typical sample concentrations and acquisition parameters, parameters of the analyses of decomposition kinetics of **3** and **5**, calculation of coalescence temperatures, complete lists of ^{1}H NMR data of **3**, **5**, and (*E*)- and (*Z*)-2-cyclohexylbut-2-ene), synthetic procedures for **6**, ^{13}C-labeled **6**, **7**, and the 2-cyclohexyl-2,3-dimethyloxiranes (including general methods and analytical data), key

(40) Vedejs, E.; Fleck, T. J. *J. Am. Chem. Soc*. **1989**, *111*, 5861−5871.
(41) Reference 5b, footnote 11.
(42) For decomposition at 120 °C of two stable $(CF_3)_2CHO$-substituted 1,2-oxaphosphetane rotamers without pseudorotation (except by an irregular, catalyzed process), see: Ramirez, F.; Smith, C. P.; Pilot, J. F. *J. Am. Chem. Soc*. **1968**, *90*, 6726−6732. See also: refs 7b and 24. However, fast pseudorotation at room temperature and a slow one at −30 °C of an analogous oxaphosphetane with a second $(CF_3)_2CHO$ group has been observed since one of the three P−O bonds is always in an apical position: Gibson, J. A.; Röschenthaler, G.-V.; Schmutzler, R. *Z. Naturforsch. B* **1977**, *32*, 599−600.
(43) Vedejs, E.; Marth, C. *Tetrahedron Lett*. **1987**, *28*, 3445−3448.
(44) C. F. Marth has discussed ring and steric effects on the pseudorotation of a large number of pentacoordinate phosphorus compounds, but experimental data of 1,2-oxaphosphetanes are still scarce. See ref 8c, pp 171−179.

original NMR spectra (^{1}H of **3** and **5** at 243 K; ^{31}P of **3**, **5**, and ^{13}C-labeled **3** at 163 K; ^{13}C of labeled **3** at 163 K; ^{31}P DNMR of **3** and **5** measured and calculated in the line-shape analyses), and comparison of rate constants and activation parameters of decomposition of **3** and **5**, obtained by linear regression analyses and by iterative nonlinear modeling (in all 21 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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