was chromatographed with silica gel column using $CHCl_3$ as an eluent. *S*-Phenyl-*S*-(α,α-dichlorobenzyl)-*N*-tosylsulfoximine and *S*-benzyl-*S*-phenyl-*N*-tosylsulfoximine were obtained in 61% and 10% yields, respectively. *S*-Phenyl-*S*-(α,α-dichlorobenzyl)-*N*-tosylsulfoximine, mp 120.5–121.5 °C (lit.[14] mp 120–121 °C); *S*-benzyl-*S*-phenyl-*N*-tosylsulfoximine, mp 151.0–152.0 °C (lit.[1] mp 151–152 °C).

Reaction of *S*-Benzyl-*S*-phenyl-*N*-tosylsulfoximine. The title sulfoximine was prepared by oxidation of the corresponding sulfilimine with *m*-chloroperbenzoic acid in CH_2Cl_2 (yield 90%). To a solution of *S*-benzyl-*S*-phenyl-*N*-tosylsulfoximine (400 mg, 1.0 mmol) and Bu_4NBr (150 mg, 0.5 mmol) in 10 mL of AcOEt and 10 mL of CH_2Cl_2 was added an eightfold excess of aqueous NaOCl solution (6.2 g). The mixture was stirred vigorously at room temperature and the reaction was monitored by HPLC and TLC. After the reaction was complete, the mixture was separated by addition of H_2O. The organic layer was separated and dried ($MgSO_4$). After the solvent was removed, the residue was chromatographed with silica gel column using $CHCl_3$ as an eluent. *S*-Phenyl-*S*-(α,α-dichlorobenzyl)-*N*-tosylsulfoximine was obtained in 86% yield.

Registry No. **1a**, 38764-58-8; **1a** (sulfilimine), 13150-76-0; **1b**, 80816-37-1; **1b** (sulfilimine), 24702-38-3; **1c**, 80816-38-2; **1c** (sulfilimine), 24702-37-2; **1d**, 80816-39-3; **1d** (sulfilimine), 80816-33-7; **1e**, 80816-40-6; **1e** (sulfilimine), 24698-06-4; **1f**, 80816-41-7; **1f** (sulfilimine), 80816-34-8; **1g**, 89923-37-5; **1g** (sulfilimine), 89923-38-6; **2a**, 42153-74-2; **2a** (sulfilimine), 10330-22-0; **2b**, 80816-43-9; **2b** (sulfilimine), 60121-20-2; **2c**, 80816-44-0; **2c** (sulfilimine), 38492-27-2; **2d**, 28832-82-8; **2d** (sulfilimine), 24702-26-9; **2e**, 38764-57-7; **2e** (sulfilimine), 15436-21-2; **2f**, 35539-97-0; **2f** (sulfilimine), 24702-28-1; **2g**, 69765-77-1; **2g** (sulfilimine), 10330-18-4; **2h**, 80816-45-1; **2h** (sulfilimine), 53799-63-6; **2i**, 80816-46-2; **2i** (sulfilimine), 58463-53-9; **2j**, 33332-99-9; **2j** (sulfilimine), 69765-76-0; **2k**, 33367-88-3; **25** (sulfilimine), 56561-39-8; **2l**, 80816-47-3; **2l** (sulfilimine), 80816-36-0; **2m**, 57872-24-9; **2m** (sulfilimine), 13553-70-3; **2n**, 35188-38-6; **2n** (sulfilimine), 13553-73-6; **2o**, 22236-45-9; **2o** (sulfilimine), 13150-75-9; **2p**, 70975-35-8; **2p** (sulfilimine), 42787-33-7; **2q**, 38764-59-9; **2q** (sulfilimine), 24702-30-5; **2q** (α,α-dichloro deriv.), 80824-64-2; Ph_2S, 139-66-2; Ph_2SO, 945-51-7; Ph_2SO_2, 127-63-9; Bu_4NBr, 1643-19-2; Bu_4NCl, 1112-67-0; Bu_4NClO_4, 1923-70-2; Bu_4NHSO_4, 32503-27-8; $CH_3(CH_2)_{15}N(CH_3)_3Br$, 57-09-0; $PhCH_2NEt_3Cl$, 56-37-1; $C_{12}H_{25}NMe_3Cl$, 112-00-5; 18-crown-6, 17455-13-9; dibenzo-18-crown-6, 14187-32-7; 15-crown-5, 33100-27-5.

(11) Oae, S.; Harada, K.; Tsujihara, K.; Furukawa, N. *Int. J. Sulfur Chem., Part A* **1972**, *2*, 491.
(12) Horner, L.; Christmann, A. *Chem. Ber.* **1963**, *96*, 388.
(13) Mixan, C. E.; Bailey, D. S. *J. Am. Chem. Soc.* **1972**, *94*, 208.
(14) Johnson, C. R.; Tangerman, A. *Synthesis* **1982**, 286.
(15) Akasaka, T.; Furukawa, N.; Oae, S. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1257.

Bicyclic Dioxaphosphorane. 4.[1] A Kinetic Investigation of the Reactions of Trivalent Phosphorus Compounds with Bicyclic Endoperoxides

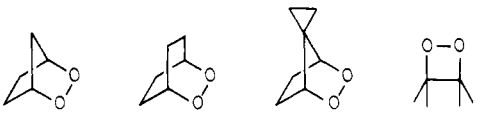
Edward L. Clennan* and Poh Choo Heah

Department of Chemistry, University of Wyoming, Laramie, Wyoming 82071

Received November 30, 1983

The deoxygenation of peroxides by trivalent phosphorus was first reported in 1927 by Challenger and Wilson.[2] Since that initial report, nucleophilic,[3] free-radical,[4] and biphilic[5] mechanisms have been suggested for these reactions.

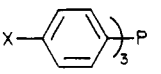
We[1] have recently reported the formation of several phosphoranes by insertion of trivalent phosphorus compounds into the oxygen–oxygen bond of 2,3-dioxabicyclo[2.2.1]heptane (1). We suggested a biphilic mechanism



1 2 3 4

for these reactions based upon the absence of a solvent effect on the rate of reaction of **1** with triphenylphosphine. We now report a more extensive kinetic study of this reaction and the reactions of bicyclic endoperoxides **2** and **3** with several phosphorus compounds. We will also compare these results to the most extensively studied peroxide, tetramethyldioxetane **4**,[6] and discuss their mechanistic implications.

The pseudo-first-order rates of reaction of **5a** with **3** were conveniently measured at five different temperatures by following the disappearance of the phosphine at 290 nm.



5a, X = H
b, X = CF_3
c, X = F
d, X = Cl
e, X = Me
f, X = OMe

The excellent linear correlations observed verify that the reactions are first order in phosphine. The second-order rate constants in Table I were determined by dividing the pseudo-first-order values by the concentrations of the peroxides. Verification that the reactions were also first order in peroxides was obtained by observing the fluctuation in the pseudo-first-order rate constants as a function of peroxide concentration. These results and the activation barriers for all four peroxides, which are typical of those observed for many bimolecular reactions,[7] are consistent with our earlier suggestion of a biphilic mechanism.

These reactions are visibly exothermic. Addition of 1 equiv of phosphine **5a** to a 0.2 M solution of **1** in a NMR tube generates enough heat to make it uncomfortable to hold the sample. This is not surprizing since a considerable amount of ring strain[8] present in the peroxides is relieved in the reaction and two stronger phosphorus–oxygen bonds (45 kcal/mol)[11] are formed at the expense of a weaker

(1) For parts 1–3, see: (a) Clennan, E. L.; Heah, P. C. *J. Org. Chem.* **1981**, *46*, 4105. (b) Clennan, E. L.; Heah P. C. *Ibid.* **1982**, *47*, 3329. (c) Clennan, E. L.; Heah, P. C. *Ibid.* **1983**, *48*, 2621.
(2) Challenger, F.; Wilson, V. K. *J. Chem. Soc.* **1927**, 213.
(3) Horner, V. L.; Jurgeleit, W. *Liebigs Ann. Chem.* **1955**, *591*, 138.
(4) Walling, C.; Rabinowitz, R. *J. Am. Chem. Soc.* **1959**, *81*, 1243.
(5) (a) Denney, D. B.; Jones, D. H. *J. Am. Chem. Soc.* **1969**, *91*, 5821. (b) Denney, D. B.; Denney, D. Z.; Hall, C. D.; Marsi, K. L. *Ibid.* **1972**, *94*, 245.
(6) (a) Baumstark, A. L.; McClosky, C. J.; Williams, T. E.; Chrisope, D. R. *J. Org. Chem.* **1980**, *45*, 3593. (b) Baumstark, A. L.; Barrett, M.; Kral, K. M. *J. Heterocycl. Chem.* **1982**, *19*, 201.
(7) Jarvis, B. B.; Marien, B. A. *J. Org. Chem.* **1976**, *41*, 2182.
(8) We suggest that the relative strain energies of these peroxides parallel those of their hydrocarbon analogues.[9] The dihedral angles between the carbon–oxygen bonds[10] and consequently the lone-pair–lone-pair interactions do not change dramatically from compound to compound.
(9) (a) Goldfarb, V. I.; Belenkii, L. I. *Russ. Chem. Rev.* **1960**, *29*, 214. (b) Allinger, N. L. In "Advances in Physical Organic Chemistry"; Vol. 13. Academic Press: New York, 1978; p 48. (c) Martella, D. J.; Joner, M., Jr.; Scheleyer, P. v. R.; Maier, W. F. *J. Am. Chem. Soc.* **1979**, *101*, 7634. Supplementary material.
(10) Coughlin, D. J.; Brown, R. S.; Salomon, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 1533.

0022-3263/84/1949-2284$01.50/0

Table I. Rate Constants and Activation Barriers for the Reaction of Phosphine 5d with Bicyclic Endoperoxides 1–3

compd[a]	T,[b] °C	10^3k,[c,d] M^{-1} s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	$\Delta H\ddagger$, kcal/mol (T, °C)
1	24	1.58 ± 0.04			
	29	2.26 ± 0.05			
	33.5	2.80 ± 0.10			
	38.0	3.88 ± 0.23			
	43.0	5.21 ± 0.22			19.9 ± 0.02 (25)
			11.0 ± 0.67	−29.6 ± 2.2	20.2 ± 0.02 (35)
2	33.5	0.46 ± 0.02			
	38.0	0.64 ± 0.02			
	43.0	0.95 ± 0.05			
	47.0	1.37 ± 0.09			
	50.0	1.66 ± 0.06			21.1 ± 0.07 (25)
			14.9 ± 1.2	−20.6 ± 3.9	21.3 ± 0.04 (35)
3	15.0	6.11 ± 0.40			
	19.0	9.47 ± 0.30			
	24.0	11.83 ± 0.20			
	29.0	14.96 ± 0.20			
	35.0	23.34 ± 1.11			18.7 ± 0.06 (25)
			10.4 ± 2.6	−27 ± 8.7	19.0 ± 0.10 (35)
4[e]			9.2	−28	17.6 (25)

[a] The reactions of 1–3 were quantitative. The phosphoranes and products of phosphorane decompositions were the only components of the reaction mixture. [b] The temperatures are controlled to ±0.5 °C. [c] Obtained by dividing the pseudo-first-order rates by the concentration of the peroxide. [d] *n*-Decane was utilized as the solvent. [e] Reference 6a.

Table II. Rate Constants and Hammett Reaction Constants for the Reactions of 5a–f with Peroxides 1, 2, and 4

compd	phosphine	10^2k,[a,b] M^{-1} s^{-1}	ρ^+[c]	r[d]
1	**5a**	2.77 ± 0.03		
	5b	1.68 ± 0.26		
	5c	2.48 ± 0.07		
	5d	2.34 ± 0.08		
	5e	3.76 ± 0.11		
	5f	6.71 ± 0.14	−0.44 ± 0.01	0.974
2	**5a**	0.40 ± 0.01		
	5b	0.28 ± 0.01		
	5c	0.51 ± 0.01		
	5d	0.49 ± 0.01		
	5e	0.67 ± 0.01		
	5f	0.92 ± 0.04	−0.38 ± 0.01	0.969
4[e]			−0.82	0.98

[a] Measured in *n*-decane. [b] Value is the average of three independent kinetic determinations. [c] Slope of the line from a plot of σ^+ vs. log (k_X/k_H). [d] Linear regression coefficient. [e] From ref 6b.

oxygen–oxygen bond (35 kcal/mol).[12] Examination of Table I also reveals that the activation free energies and enthalpies for these reactions decrease with increasing ring strain in the peroxide substrates.[8]

The rates of reaction of phosphines **5b–f** with peroxides 1 and 2 were also measured and are reported in Table II. The Hammett reaction constants (ρ^+) for both peroxides 1 and 2 are small and negative. Attempted correlations with $\sum\sigma$ produce regression coefficients for both 1 (r = 0.913) and 2 (r = 0.885) which reflect a decrease in the quality of the fit in comparison to $\sum\sigma^+$. Baumstark[6a] had previously noted the same trend in a study of 4. He suggested that the lack of correlation with $\sum\sigma$ could be due to changing importance of the electrophilic and nulceophilic components of the reaction as the substituents on the phosphines are changed.

The ρ^+ values for these biphilic reactions are much smaller than those observed for nucleophilic reactions of phosphines.[7] This observation is also consistent with a biphilic mechanism in which both nucleophilic and electrophilic components contribute to the character of the transition state. The ρ^+ values for 1 (−0.44) and 2 (−0.38) demonstrate that the nucleophilic components in the transition states for these reactions are less pronounced than those in the reaction of the more strained peroxide 4 (0.82). It is tempting to suggest that the nucleophilic component is most important in those reactions in which the transition state is early on the reaction coordinate. We view the transition states of these reactions as complexes in which the phosphorus lone pair has overlapped with the σ^* orbitals on the peroxide linkages with varying degrees of back bonding from oxygen to the low-lying 3d orbitals on phosphorus.

In summary the data reported here support the suggestion that these reactions are biphilic in nature. The similarity between these data and those reported for the reaction of triphenylphosphine with tetramethyldioxetane 4[6] and alkyl hydroperoxides[13] suggests that the biphilic mechanism may well be a general phenomenon observed in many trivalent phosphorus–peroxide reactions.

Experimental Section

Materials. Tris[(4-fluoro-, -chloro-, -bromo-, and -methoxy)phenyl]phosphines were obtained from Alfa Products and utilized without further purification. Triphenyl phosphine was obtained from Aldrich and also utilized without further purification. The *n*-decane used in the kinetic studies was fractionally distilled twice at 5 mmHg from EDTA. The syntheses of bicyclic peroxides 1,[14] 2,[14] and 3[15] were accomplished as previously reported.

Tris(4-methylphenyl)phosphine, synthesized by the method of Marr and Chaplin:[16] ^{31}P NMR (CH_2Cl_2) δ −7.78; ^{13}C NMR

(11) (a) Drowart, J.; Myer, C. E.; Szwarc, R.; Vander Auwera-Mahieu, A.; Uy, O. M. *J. Chem. Soc., Faraday Trans. 2* **1972**, *68*, 1749. (b) "Handbook of Chemisry and Physics", 62nd ed.; CRC Press: Boca Raton, FL, 1981–82.

(12) Benson, S. W.; Shaw, R. In "Organic Peroxides"; Swern, D., Ed.; Wiley Interscience: New York, 1970; Vol. I, Chapter 2.

(13) Hiatt, P.; Smythe, P. J.; McColemen, C. *Can. J. Chem.* **1971**, *49*, 1707.

(14) (a) Porter, N. A.; Gilmore, D. W. *J. Am. Chem. Soc.* **1977**, *99*, 3503. (b) Salomon, R. G.; Salomon, M. F. *Ibid.* **1977**, *99*, 3501. (c) Coughlin, D. J.; Brown, R. S.; Salomon, R. G. *Ibid.* **1979**, *101*, 1533.

(15) (a) Adam, W.; Erden, J. *J. Org. Chem.* **1978**, *43*, 2738. (b) Adam, W.; Eggelte, H. J. *Ibid.* **1977**, *42*, 3987.

(16) Marr, F. G.; Chaplin, E. J. *J. Chem. Soc.* **1937**, 527.

($CDCl_3$) δ 138.5, 133.8, 128.3, 129.2, 133.5, 21.3; ^1H NMR ($CDCl_3$) δ 7.08–7.26 (m, 4 H), 2.35 (s, 3 H).

Tris[4-(trifluoromethyl)phenyl]phosphine, synthesized by the method of Miller and Grim:[17] mp 69–70 °C (lit.[17] mp 68–70 °C).

NMR Measurements. The ^{31}P NMR measurements were made on a JEOL-FX270 MHz instrument at 109.13 MHz. A total of 16 384 points were collected over a spectral width of 50 000 Hz, utilizing a pulse delay of 5 or 10 s. All the chemical shifts are reported relative to 85% H_3PO_4 by substitution. The proton and ^{13}C NMR data were also collected on a JEOL-FX270 MHz instrument and the data referenced to tetramethylsilane.

Kinetic Method. The rates of the reactions were determined by monitoring the disappearance of the phosphines at 290 nm on a Cary 14R UV spectrophotometer. The absorbances of the corresponding phosphine oxides were negligible at this wavelength. The peroxides were purified by five sublimations immediately before use, but the phosphines were used without further purification. Fresh 10-mL solutions of 2×10^{-2} M peroxide and 2×10^{-4} M phosphine were made up for each kinetic run. A 1.7-mL sample of each solution was added to a 1-cm cuvette thermostated at the desired temperature. The disappearance of the phosphine was monitored for 3 half-lives. Each reported rate is the average of three independent determinations.

Data Treatment. Each rate constant was determined by following the decrease in absorbance of PPh_3 at 290 nm for at least 3 half-lives and plotting ln $(A_0 - A_\infty)$ vs. time. All of the rate constants were obtained by linear regression analysis and the second-order rate constants by dividing the pseudo-first-order rate constants by the concentration of the peroxide. The activation parameters were determined by plotting ln (k/T) vs. $1/T$ and the confidence limits were calculated by the method of Bennett and Franklin[18] and propagated into the activation parameters at the 95% confidence level. For the Hammett studies, plots of log (k_X/k_H) vs. σ^+ were plotted and the confidence limits in the slope were determined by using a least-square fit to a straight line as described by Bevington.[19]

Acknowledgment. We thank the University of Wyoming and the Wyoming Affiliate of the American Heart Association for support of this Research.

Registry No. 1, 279-35-6; 2, 280-53-5; 3, 67105-55-9; 5a, 603-35-0; 5b, 13406-29-6; 5c, 18437-78-0; 5d, 1159-54-2; 5e, 1038-95-5; 5f, 855-38-9.

(17) Miller, G. R.; Grim, S. O. *J. Chem. Phys.* **1969**, *51*, 3185.
(18) Gordon, A. J.; Ford, R. A. In "The Chemist's Companion"; Wiley Interscience: New York, 1972; p 491.
(19) Bevington, P. R. In "Data Reduction and Error Analysis for the Physical Sciences"; McGraw-Hill: New York, 1969.

An Efficient Synthesis of Ethyl LL-3-Amino-2-piperidone-6-carboxylate

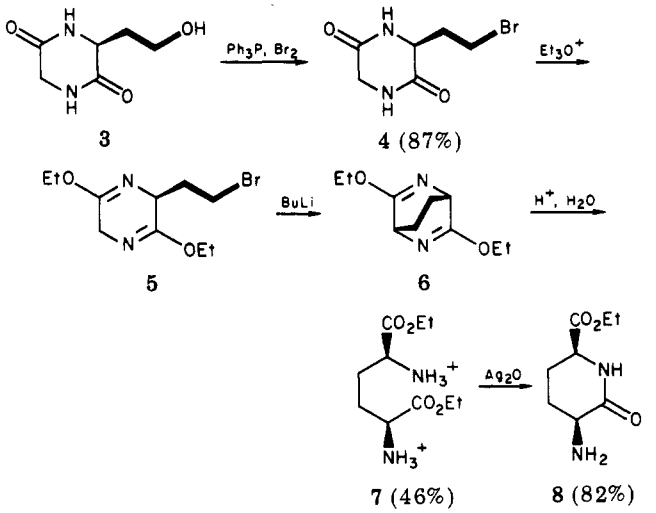
D. S. Kemp* and Paul E. McNamara

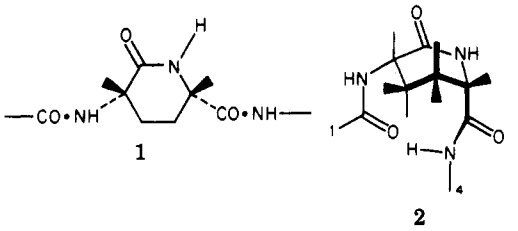
Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received January 27, 1984

Control of the local conformations of the backbones of polypeptides and proteins offers new approaches to fundamental problems ranging from studies of mechanisms of protein folding[1] to developing useful pharmacological mimics of the peptide hormones.[2] As one of the commonest and simplest elements of secondary structure, the β-turn is a natural candidate for conformational control.[3] Elsewhere we have shown[4] that the 3-amino-2-piperidone-6-carboxylic acid residue (Acp, 1), when incorporated into short peptides, adopts conformation 2 in which the 3-acylamino substituent adopts a *pseudo* equatorial and the 6-carboxamido substituent a *pseudo* axial orientation. Thus, the α-carbon atoms of amino acid residues 1 and 4 are within the 6–7 Å of a generalized turn conformation.

Scheme I





Although we have previously reported a synthesis of LL-Acp from L-homoserine involving a high-temperature copper-catalyzed decarboxylation of 3,6-dioxo-2,5-diazabicyclo[2.2.2]octane-1-carboxylic acid,[5] variable racemization attends large-scale execution of this step. We report an alternative synthesis from L-homoserine outlined in Scheme I and based on the chiral amino acid synthesis of Schöllkopf.[6]

Diketopiperazine 3 is available in two steps (70%) from Cbz-Gly-OSu and L-homoserine lactone, followed by hydrogenation. Although NBS–phosphine could be used for conversion to 4, a cleaner preparation of crystalline 4 was achieved by means of bromine and triphenylphosphine.[8] The next three steps could be carried out without purification of intermediates, giving 7 in 46% yield, based on 4. No chromatographic separations are required in this reaction sequence which has been used to generate tens of grams of 7, a conveniently storable precursor of 8.

The efficiency of chiral induction at the second asymmetric center generated in 5 → 6 is in the range of 99.5%,

(1) Kim, P. S.; Baldwin, R. L. *Ann. Rev. Biochem.* **1982**, *51*, 461–484.
(2) Freidinger, R. M.; Veber, D. F.; Perlow, D. S.; Brooke, J. R.; Saperstein, R. *Science (Washington, D.C.)* **1980**, *210*, 656–660.
(3) Nutt, R.; Veber, D. F.; Saperstein, R. *J. Am. Chem. Soc.* **1980**, *102*, 6539–6541.
(4) Kemp, D. S.; McNamara, P. *Tetrahedron Lett.* **1982**, *23*, 3761–3764.
(5) Kemp, D. S.; Sun, E. T. *Tetrahedron Lett.* **1982**, *23*, 3759–3760.
(6) Schöllkopf, U.; Hartwig, W.; Groth, U. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 863–864.
(7) Anderson, G. W.; Zimmerman, J. E.; Callahan, F. M. *J. Am. Chem. Soc.* **1964**, *86*, 1839–1845.
(8) Wiley, G. A.; Hershkowitz, R. L.; Rein, B. M.; Chung, B. C. *J. Am. Chem. Soc.* **1964**, *86*, 964–965.

0022-3263/84/1949-2286$01.50/0