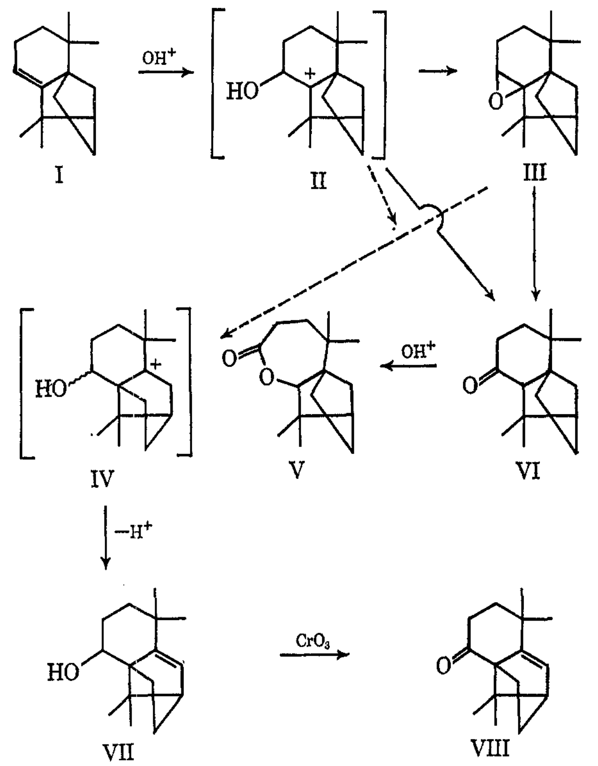
SCHEME I



Experimental Section[3]

Reaction of Isolongifolene (I) with Peracetic Acid.—In a 500-ml flask fitted with stirrer, condenser, and addition funnel was placed 100 g (0.5 mol) of isolongifolene and 12.5 g (0.15 mol) of sodium acetate. The mixture was heated to 60° and 95 g (0.5 mol) of 40% peracetic acid was added dropwise over a period of 45 min, while the temperature was maintained at 60°. After the addition, the mixture was stirred at 60° for 3 hr. It was then cooled, washed with water and 1% sodium sulfite solution, and extracted with toluene. The organic layer was washed once with water and dried over magnesium sulfate. The solvent was removed *in vacuo*. After 65 g of the starting material had been recovered *in vacuo*, the product obtained in an overall yield of 30% consisted of a mixture of previously unknown alcohol VII, ketone VI,[2] and lactone V[2] in a ratio of 4:14:1, respectively.[4] The compounds were isolated by preparative glpc using an 8 ft × 0.25 in., 20% SE-30 column at 200°. Alcohol VII had a melting point of 143–144°.

Anal. Calcd for $C_{15}H_{24}O$: C, 81.57; H, 10.90. Found: C, 81.37; H, 10.89.

Ketone VIII.—In a flask fitted with stirrer, condenser, and addition funnel was placed 42.0 g (0.19 mol) of alcohol VII and 300 ml of acetone. To this mixture was added 85 ml (0.18 mol) of Jones reagent at 15° during a period of 45 min, and the solution was then further stirred at the same temperature for 45 min. After the solids had been filtered off, the acetone was removed *in vacuo* and the crude product was distilled to give 29.0 g of the ketone VIII, 70% yield, bp 106–107° (3.7 mm).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.50; H, 10.10. Found: C, 82.31; H, 9.90.

The 2,4-dinitrophenylhydrazone had mp 181–182°.

Anal. Calcd for $C_{21}H_{26}N_4O_4$: C, 62.29; H, 6.51; N, 14.10. Found: C, 62.89; H, 6.48; N, 13.90.

Reaction of Isolongifolene Epoxide (III) with Peracetic Acid.—Isolongifolene oxide, 1.1 g, mixed with 0.28 g of sodium acetate, was treated with 0.96 g of 40% peracetic acid. The mixture was heated slowly to 60°, and stirred at 60° for 3 hr. The mixture was cooled and extracted with chloroform, and the extract was washed with water and dried over magnesium sulfate. The solvent was removed *in vacuo*, and the products were separated by preparative glpc (8 ft × 0.25 in., SE-30 column, 20%, 200°). The three products were shown by spectral analysis to be V, VI, and VII.

Registry No.—Peracetic acid, 79-21-0; I, 1135-66-6; VII, 22979-29-9; VIII, 22979-30-2; VIII-2,4-dinitrophenylhydrazone, 22979-31-3.

Acknowledgment.—The authors express their thanks to Dr. W. I. Taylor for his helpful suggestions and continued interest. We are also thankful to the Analytical Group for running various spectra and for their help in gas chromatography.

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[3] All the nmr spectra were run on a Varian HA-100 spectrometer. Tetramethylsilane was used as an internal standard. The C and H analyses were run by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

[4] The ratio of the products varies with the varying amounts of sodium acetate used.

The Reactions of Organophosphorous Compounds with α- and β-Diphenylacyl Bromides

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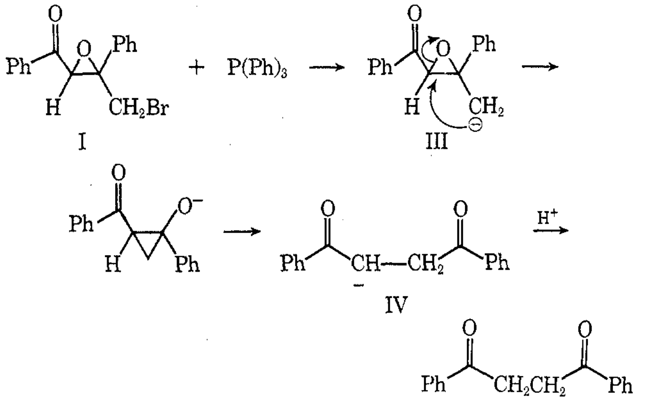
Relatively little attention has been directed to the preparation and reactions of organophosphorous compounds that possess an epoxide function in the β,γ position.[2] In the course of a study on the reactivity of small-membered rings, we investigated the reactions of *cis*- and *trans*-1,3-diphenyl-2,3-epoxy-4-bromo-1-butanone (I and II) with several organophosphorous compounds in an attempt to prepare a β,γ-epoxy phosphorous ylide.



In our studies, we have found that the reaction of *cis*-1,3-diphenyl-2,3-epoxy-4-bromo-1-butanone (I) with triphenylphosphine in refluxing toluene affords dibenzoylethane (55%), *trans*-dibenzoylethylene (5%), phenacyltriphenylphosphonium bromide (30%), benzoylmethylenetriphenylphosphorane (8%), and some triphenylphosphine oxide. Similar results were obtained with the *trans* epoxide (II).

A plausible explanation for the formation of dibenzoylethane involves attack of triphenylphosphine on bromine leading to anion III, which then rearranges to

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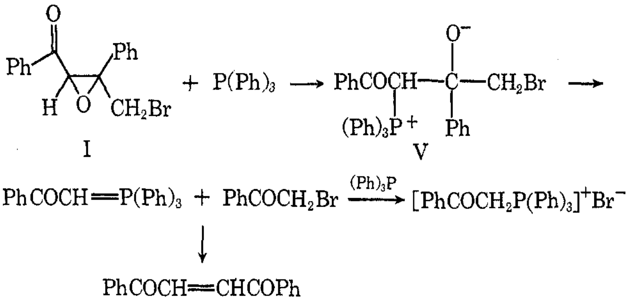
[1] Alfred P. Sloan Foundation Fellow, 1968–1970

[2] For some pertinent references, see C. E. Griffin and S. K. Kundu, *J. Org. Chem.*, **34**, 1532 (1969).

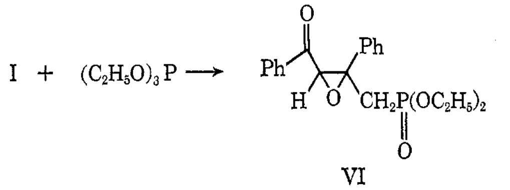
the more stable anion IV.[3] This transformation is related to the debromination of I with zinc in methanol.[4]

The formation of the remaining products can be pictured as proceeding through the intermediacy of an internal phosphonium alkoxide (V), produced by initial displacement at carbon. This intermediate subsequently collapses to phenacyl bromide and benzoylmethylenetriphenylphosphorane which are known to react to form *trans*-dibenzoylethylene.[5,6] It is also known that primary α-bromo ketones such as phenacyl bromide react with triphenylphosphine in aprotic solvents to give α-keto phosphonium bromides.[7] This would account for the isolation of phenacyltriphenylphosphonium bromide in the above reaction.



The formation of an intermediate of type V finds confirmation in work by Speziale and Bissing in their studies on the opening of epoxides with tertiary phosphines.[8] The fact that dibenzoylethane is the major product in this reaction can be attributed to the preference of trivalent phosphorous compounds to carry out displacements at a halogen center as opposed to attack at a sp^3-hybridized carbon atom.[9]

In contrast to the results outlined above, we find that reaction of I with triethyl phosphite at 120° goes to completion and gives diethyl *cis*-1,3-diphenyl-2,3-epoxybutan-1-one phosphonate (VI) as the only isolable material. Similarly, reaction of II with triethyl phosphite gives diethyl *trans*-1,3-diphenyl-2,3-epoxybutan-1-one phosphonate (VII) in high yield. The spectral data obtained for these compounds are summarized in the Experimental Section.



VI

With the expectation that the reaction of VI (or VII) with base would generate a phosphonate anion which could be used for further reaction,[10] we treated VI with sodium hydride. The reaction was carried out at room temperature in dimethoxyethane as solvent. Addition of benzaldehyde or acetone to the mixture gave a dark brown solution. The reaction mixture, upon work-up, gave black tars with ill-defined spectra, unresolved by careful chromatography. In view of the difficulty of isolating characterizable products from this reaction, we abandoned further study on the generation of phosphonate carbanions from these systems.

Experimental Section[12]

***cis*- and *trans*-1,3-diphenyl-2,3-epoxy-4-bromo-1-butanone** were prepared by the method of Wasserman, Aubrey, and Zimmerman using phenacyl bromide and sodium ethoxide in ethanol.[4]

Reaction of *cis*-1,3-Diphenyl-2,3-epoxy-4-bromo-1-butanone (I) with Triphenylphosphine.—A mixture of triphenylphosphine (8.4 g) and I (5.0 g) in toluene (330 ml) was heated at reflux for 36 hr. The resultant precipitate which separated was triturated with boiling acetone to give phenacyltriphenylphosphonium bromide as a white solid, mp 279–280 (lit.[13] mp 279–280°). To the solvent was added benzophenone (1.0 g) and the mixture was heated at reflux for 8 hr. At the end of this time the solvent was removed and the residue was chromatographed on a Florisil column. The column was eluted with benzene and then with 1% ethyl acetate–benzene. The eluent, in 50-ml fractions, was concentrated and dried *in vacuo*. Benzophenone was recovered from elution of the column with benzene. Three major fractions were obtained from elution with 1% ethyl acetate–benzene and were identified as dibenzoylethane (55%), *trans*-dibenzoylethylene (5%), and β-phenylbenzalacetophenone (8%) by comparison with authentic samples.

The isomeric epoxide II gave similar results when it was treated under comparable reaction conditions.

Preparation of Diethyl *cis*-1,3-Diphenyl-2,3-epoxybutan-1-one Phosphonate (VI).—A mixture of *cis* epoxide I (5.0 g) and triethyl phosphite (18 ml) was heated at 120° for 3 hr. During this time ethyl bromide was allowed to distil from the reaction flask. The excess triethyl phosphite was removed *in vacuo* and the crude residue obtained was chromatographed on a Florisil column to give 5.1 g of VI as a colorless oil.

Anal. Calcd for $C_{20}H_{23}PO_5$: C, 64.16; H, 6.19. Found: C, 64.42; H, 6.28.

The infrared spectrum showed bands at 5.9, 8.0, 8.52, 9.6, and 10.25 μ. The nmr spectrum (CCl_4) showed multiplets at τ 1.93 (2 H) and 2.67 (8 H), a singlet at τ 5.15 (1 H), two overlapping quartets at τ 5.92 (4 H), a double doublet at τ 7.37 (J = 20, 5.3 Hz, 2 H), and two overlapping triplets at τ 8.72 (6 H).

Preparation of Diethyl *trans*-1,3-Diphenyl-2,3-epoxy-butan-1-one Phosphonate (VII).—A mixture of *trans* epoxide II (1.8 g) and triethyl phosphite (6 ml) was heated at 110° for 3 hr. During this time ethyl bromide distilled from the reaction mixture. The excess triethyl phosphite was removed by distillation and the crude residue was chromatographed on a Florisil column to give 1.5 g of VII as a mobile oil.

Anal. Calcd for $C_{20}H_{23}PO_5$: C, 64.16; H, 6.19. Found: C, 63.97; H, 6.24.

The infrared spectrum showed strong bands at 5.89, 8.10, 8.53, 9.65, and 10.20 μ. The nmr spectrum ($CDCl_3$) showed multiplets at τ 1.95 (2 H) and 2.42 (8 H), a doublet at τ 5.70 (J = 1.7 Hz, 1 H), two overlapping quartets at τ 6.12 (4 H), a double doublet at τ 7.48 (J = 19.5, 9.0 Hz, 2 H), and two overlapping triplets at τ 8.95 (6 H).

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(3) *Anion IV is presumably protonated* by the small amount of water present in the solvent.

(4) H. H. Wasserman, N. E. Aubrey, and H. E. Zimmerman, *J. Amer. Chem. Soc.*, **75**, 96 (1953).

(5) M. Slemiatycki and H. Strzelecka, *Compt. Rend.*, **250**, 3489 (1960).

(6) Another possible route to dibenzoylethylene is the following.

$$Ph\overset{-}{C}OCHCH_2COPH + Ph_3\overset{+}{P}Br \longrightarrow PhCOCHBrCH_2COPh \xrightarrow{-HBr} PhCOCH{=}CHCOPh$$

(7) I. J. Borowitz, K. C. Kurby, and R. Virkhaus, *J. Org. Chem.*, **31**, 4031 (1966).

(8) D. E. Bissing and A. J. Speziale, *J. Amer. Chem. Soc.*, **87**, 2683 (1965).

(9) A. J. Kurby and S. G. Warren, "The Organic Chemistry of Phosphorous," Elsevier Publishing Co., New York, N. Y., 1967, p 111.

(10) The reaction of phosphonate carbanions with aldehydes or ketones in an aprotic solvent is a useful supplement to the well-known "Wittig" reaction.[11]

(11) W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1732 (1961).

(12) All melting points are uncorrected. The infrared absorption spectra were determined on a Perkin-Elmer Infracord spectrometer, Model 137. The nuclear magnetic resonance spectra were determined at 60 MHz with the Varian Associates high-resolution spectrometer. Tetramethylsilane was used as an internal standard.

(13) F. Ramirez and S. Dershowitz, *J. Org. Chem.*, **22**, 41 (1957).

Registry No.—I, 23265-28-3; II, 23265-29-4; VI, 23265-30-7; VII, 23265-31-8; triphenylphosphine, 603-35-0; triethyl phosphite, 122-52-1.

Acknowledgment.—Support of this work by the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

Base-Catalyzed Deuterium Exchange in Pyridine N-Oxides[1]

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In connection with another study, we observed that 4-benzylpyridine N-oxide (I), recovered after a reflux period of 24 hr in equimolar triethylamine and excess deuterium oxide, exchanged hydrogen for deuterium in excess of the calculated amount for the two benzylic hydrogens.[2] The nuclear magnetic resonance spectrum of the deuterated compound compared well with that of the reference compound, differing only in that a small peak appeared at τ 6.06 replacing the sharp singlet for the benzylic hydrogens. Integration of the peak areas, however, indicated that the doublet at τ 1.89 for the two α hydrogens of the pyridine ring and the multiplet with a sharp peak at τ 2.76 for the two β hydrogens and five phenyl hydrogens were not in a 2:7 ratio. By assuming nonexchange of the β and the phenyl hydrogens, we calculated 95% exchange of the benzylic hydrogens and 17% exchange of the α hydrogens from the integration of the respective peak areas (this is consistent with the elemental analysis of an exchange of 21.00 atom % excess deuterium).[3]

Considerable attention of late has been given to H–D exchange in heterocyclic N-oxide systems. Substituted pyridine N-oxides and similar compounds exchange rapidly in the α position of the ring under basic conditions; for a review of the literature see ref 5. Under acidic conditions similar systems exhibited exchange at the β position when the species reacting was in the conjugate acid form.[6]

In this note we wish to report H–D exchange in the aromatic ring and the side chain of alkylpyridine N-oxides[7] and, qualitatively, the dependence of the exchange on base strength; this is readily seen from the data in Table I for the benzylpyridine N-oxides. Our investigation of the isomeric picoline N-oxides revealed ring-proton exchange as well as side-chain exchange. Prior studies of Zatsepina[8] reported exchange of the protons of the side chains of 2- and 4-picoline N-oxides (III and IV) but not ring-proton exchange. For 2-picoline N-oxide (III), α-proton exchange accompanied methyl-proton exchange in the presence of sodium carbonate and sodium deuteroxide. The relative amount of ring- and side-chain exchange varied with reaction time and base. Typical results follow: for sodium carbonate, 0.5-hr reaction time, α-proton exchange, 12%, 2-methyl proton, 66%; 5-hr reaction time, α-proton exchange, 45%, 2-methyl proton, 97%; for sodium deuteroxide, 0.5 hr, 86% for both ring and methyl protons. The 4 isomer, 4-picoline N-oxide (IV), presented an interesting contrast insofar as the amount of ring exchange exceeded side-chain proton exchange in the presence of triethylamine and sodium carbonate. Typical results follow: for triethylamine, 72 hr, α-proton exchange, 40%, 4-methyl proton exchange, 20%; for sodium carbonate, 0.5 hr, 80 and 50%, respectively, for α-proton and 4-methyl proton exchange; for sodium deuteroxide the amount of side chain and ring exchange was equivalent. As reported previously,[8] 3-picoline N-oxide (V) exhibited both ring- and methyl-proton exchange. Since ring exchange for 2- and 4-picoline N-oxides (III and IV) was not taken into account in the prior publications,[8] the velocity constants given for III and IV are in error in those references; exchange, however, was noted for V and appropriate corrections were made in the velocity constant.

TABLE I

DATA FOR BASE-CATALYZED EXCHANGE OF BENZYLPYRIDINE N-Oxides in Heavy Water[a]

N-Oxide	Expt	Base	Time, hr	Exchange,[b] % α protons	 Side-chain protons
4-Benzylpyridine N-oxide (I)	1	Et_3N[c]	20	17	95
	2	Na_2CO_3[d]	0.5	18	94
	3[e]	Na_2CO_3	5	100	100
2-Benzylpyridine N-oxide (II)	4	Et_3N	21	3	100
	5	Na_2CO_3	0.5	3	78
	6	Na_2CO_3	5	30	100

[a] All nmr spectra were determined in deuteriochloroform solutions. [b] Calculated on the basis of the assumption that only the α protons of the hetero ring readily exchange. Electronic integration of peak intensities was used for the calculations. [c] Reflux temperature, 76°. [d] Reflux temperature, 100°. [e] Good correlation of 2–5 intensity ratio was obtained in the case of 4-benzylpyridine N-oxide (I); the singlet at τ 2.98 and the singlet at τ 2.76, representing the β and the phenyl protons, respectively, were the only signals in the nmr spectrum.

The conditions used for the exchange reactions were mild and yields were good (87%, average). Since deoxygenation of the N-oxides under specific conditions is reported to be facile,[9] deuterated pyridine derivatives may be conveniently prepared by this procedure.

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(1) A preliminary report of this work was presented: Abstracts, Second Middle Atlantic Regional Meeting, of the American Chemical Society, New York, N. Y., Feb 1967, p 65.

(2) V. J. Traynelis and S. A. I. Gallagher, unpublished results. *Anal.* Calcd for $C_{12}H_9D_2NO$: D, 18.18 atom % excess deuterium. Found: D, 21.00 atom % excess deuterium. This analysis was performed by Josef Nemeth, Urbana, Ill.

(3) We were prompted to make this assumption on the evidence of results obtained in expt 3, Table I, footnote *e*. Also, extremely slow or no exchange in the β position has been reported for 3-bromopyridine N-oxide in the presence of sodium deuteroxide at 150°[4] and deuterated 3-chloropyridine N-oxide in the presence of sodium methoxide–methanol.[5]

(4) R. A. Abramovitch, G. M. Singer, and A. R. Vinutha, *Chem. Commun.*, 55 (1967).

(5) J. A. Zoltewicz and G. M. Kauffman, *J. Org. Chem.*, **34**, 1405 (1969).

(6) P. Bellingham, C. D. Johnson, and A. R. Katritzky, *J. Chem. Soc.*, *B*, 1226 (1967), and references cited therein.

(7) A referee called to our attention the kinetic studies of Zatsepina, *et al.*,[8] on the H–D exchange of methyl derivatives of pyridine N-oxide. Qualitatively, our findings are in agreement with the reported data except where noted below.

(8) (a) N. N. Zatsepina, I. F. Tupitsyn, and L. S. Efros, *J. Gen. Chem. USSR*, **33** (8), 2636 (1963); (b) *ibid.*, **34** (12), 4124 (1964).

(9) E. Ochiai, "Aromatic Amine Oxides," Elsevier Publishing Co., New York, N. Y., 1967, p 184.