ring contraction,[3] the bicyclo[3.2.0] system as in **3**, or the diazepinium betaine **4**, in which a driving force for 2 → 5 bridging is absent. In reactions of **1** in basic media, the anion **5** is the reactive nucleophile, and 2-substitution is observed. It may be noted that the diazepinone can be regarded as a vinylogous amide, and as such an ambident system would be expected to undergo these two types of electrophilic attack at the carbonyl oxygen and N-2, respectively.[7] The highly nucleophilic character of N-1, however, precludes the usual substitution at oxygen.

Experimental Section

Methylation of 1 with Diazomethane.—To a solution of 2.00 g (0.01 mole) of the diazepinone **1** in methylene chloride containing 0.8 ml of freshly distilled boron trifluoride etherate was added 125 ml of 0.4 *M* ethereal diazomethane. Nitrogen was evolved and a red oil separated. The mixture was then evaporated and the residue was treated with 12 ml of methanol and 18 ml of 2 *N* HCl. The resulting yellow solid was collected, washed, and dried to give 0.57 g of unreacted **1**, mp 125–130°. Recrystallization raised the melting point to 145–149°; tlc showed no spot corresponding to **2**. Addition of excess 40% KOH to the chilled acidic filtrate produced a red precipitate of betaine **4**, 1.05 g, mp 92–94° dec.

Methylation with Dimethyl Sulfate and Strong Base.—A solution of 200 mg (1 mmole) of **1** in 6 ml of *t*-butyl alcohol containing 2.8 mequiv of potassium *t*-butoxide (MSA Research Corp.) was treated with 0.16 ml of dimethyl sulfate. The solution remained clear, and the color did not deepen perceptibly. After dilution with water the mixture was extracted with ether and the ether solution was washed, dried, and evaporated to give 218 mg of red oil which showed two yellow spots, corresponding to **1** and **2**, on tlc. Chromatography on neutral alumina from hexane solution gave two yellow bands. The first band eluted gave 96 mg of yellow crystals of **2**, mp 72–73°, infrared and ultraviolet spectra being identical with those of an authentic sample. The slower moving zone gave 46 mg of yellow crystals of unreacted **1**, mp 147–150°.

2,3-Dihydro-2-(β-cyanoethyl)-5-methyl-6-phenyl-4H-1,2-diazepin-4-one (6).—Addition of 0.4 ml of acrylonitrile to a solution of 200 mg of **1** in 1.5 ml of 10% KOH solution at 0° gave, after brief stirring and rubbing, 253 mg of yellow-orange solid, mp 113–116°. Recrystallization from ether gave yellow needles of **6**: mp 120–121°; ν^{KBr} 1640 cm^{-1}; nmr δ^{CDCl_3} 1.87 (s, 3), 2.78 (t, 2, J = 7.0 cps), 3.78 (t, 2, J = 7.0 cps), 3.82 (s, 2), 6.98 (s, 1), 7.33 ppm (m, 5).

Anal. Calcd for $C_{15}H_{15}NO_3$: C, 71.12; H, 5.97; N, 16.59. Found: C, 70.75; H, 6.15; N, 16.70.

2,3-Dihydro-2-(β-carboxyethyl)-5-methyl-6-phenyl-4H-1,2-diazepin-4-one (7).—A solution of 500 mg of **1** in 3 ml of 10% aqueous KOH was treated with 0.67 ml of methyl acrylate. After standing for 5 hr at 25° the solution was acidified with 6 *N* HCl and extracted with ether. Evaporation of the dried ether solution gave 225 mg of orange prisms, mp 130–132°. Recrystallization from ether gave deep yellow needles of **7**: mp 133–134°; ν^{KBr} 1740, 1590 cm^{-1}; δ^{CDCl_3} 1.87 (s, 3), 2.83 (t, 2, J = 7 cps), 3.87 (s, 2), 3.93 (t, 2, J = 7 cps), 6.97 (s, 1), 7.38 (m, 5), 9.52 ppm (s, 1, exchanged by D_2O).

Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 65.93; H, 6.22; N, 10.23.

2-(β-Carboxyethylamino)-3-hydroxy-4-methyl-5-phenylpyridine (8).—A mixture of 100 mg of the cyanoethyldiazepinone **6** and 2 ml of 5% aqueous NaOH was heated at 90° for 2 min. After cooling, the solution was neutralized by addition of 6 *N* HCl and a white precipitate (89 mg, mp 110–120°) was collected. Recrystallization from ethanol gave 62 mg of **8** as a microcrystalline powder: mp 155–156°; ν^{KBr} 3480, 2976 (broad), 1661 cm^{-1}; λ_{max}^{MeOH} 263 mμ (ε 7560), 311 mμ (9900); $\lambda_{max}^{MeOH + acid}$ 258 mμ (ε 7620), 313 mμ (ε 11,000); $\lambda_{max}^{MeOH + base}$ 320 mμ (ε 12,700); pK_A' = 4.3, 6.4, and 10.5.

Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92; N, 10.29. Found: C, 65.83; H, 6.01; N, 10.25.

(7) R. Gompper, *Angew. Chem.*, **76**, 412 (1964).

In a similar procedure, 130 mg of the pyridine was obtained from 154 mg of the diazepine acid (**7**).

Benzoylation of 1 in Aqueous Base.—To a solution of 200 mg of the diazepinone **1** in 1.5 ml of 10% aqueous KOH at 20° was added 0.15 ml of benzoyl chloride. After a few minutes the resulting orange oil crystallized. The solid was worked up with methanol and ether to give 150 mg of the 2-benzoyldiazepinone,[2] mp 147–148°.

Registry No.—**1**, 1706-26-9; **2**, 4084-21-3; **4**, 10137-58-3; **6**, 10137-59-4; **7**, 10137-60-7; **8**, 10137-61-8.

Stereochemistry of a Nucleophilic Displacement at Phosphorus

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There has been wide spread interest in the stereochemistry of displacement reactions involving nucleophilic attack at the phosphorus atom.[1] The majority of the work has involved nucleophilic displacements at asymmetric phosphoryl centers which in the case of the phosphono analogs suffer from partial racemization during the reaction or work-up.[2] Therefore, although it is generally agreed that nucleophilic displacements at phosphorus proceed with predominate inversion, partial racemization has led to inconclusive results. In the present work a simple system which does not depend upon optical activity and purity has been developed.

In a previous publication[3] it was shown that bicyclic phosphites undergo an Arbuzov ring opening with an alkyl halide to give a single isomer whose formation is a consequence of the bridged structure of the phosphite and the mechanism of the reaction. Advantage is taken of this phenomena to study the steric course of a substitution at phosphorus by replacing chloride in a cyclic phosphorochloridate whose configuration as a consequence of ring opening is known.

2-Chloromethyl-2-ethyl-1,3-propanediol phosphorochlorochloridate (I, Scheme I) was prepared by treating ethyl bicyclic phosphite with chlorine gas as previously described.[3] The distilled product darkened on standing but upon redistillation gave the same infrared spectrum and index of refraction as freshly prepared material. Treatment of the phosphorochloridate with piperidine using methylene chloride as solvent gave after removal of the hydrochloride and solvent a white crystalline solid, II. Treatment of the bicyclic phosphite with N-chloropiperidine in CCl_4 also gave a sharp melting solid, III. The reaction of phosphites with chloroamines to give an Arbuzov reaction is well documented.[4]

The infrared spectra of II and III were as expected and identical except for the fingerprint region where

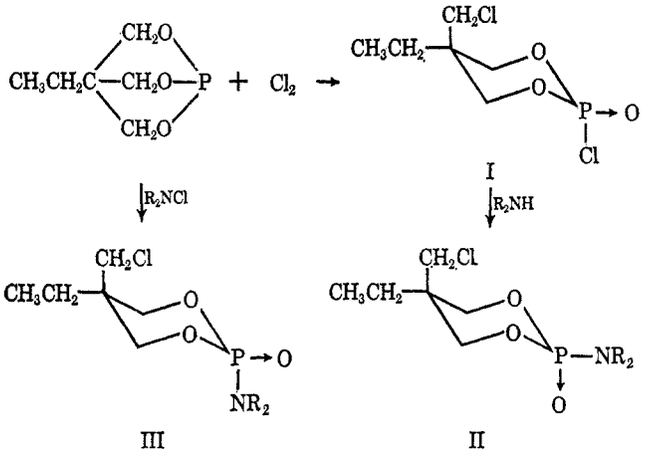
(1) R. F. Hudson and M. Green, *Angew. Chem. Intern. Ed. Engl.*, **2**, 11 (1963); W. E. McEwen, in "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1965, Chapter I.

(2) H. S. Aaron, R. T. Vyeda, H. F. Frack, and J. I. Miller, *J. Am. Chem. Soc.*, **84**, 617 (1962).

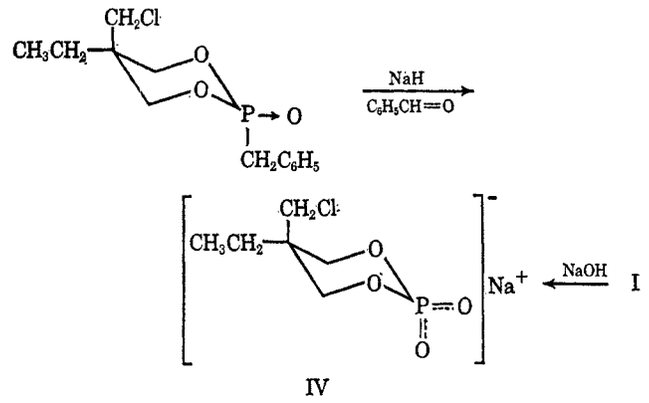
(3) W. S. Wadsworth, Jr., and W. D. Emmons, *ibid.*, **84**, 610 (1962).

(4) K. A. Petrov and G. A. Sokol'skii, *Zh. Obshch. Khim.*, **26**, 3378 (1956).

SCHEME I



there was little similarity. Thin layer chromatography showed both materials to be pure and uncontaminated by the other isomer. Heating both II and III independently to 200° produced no change in physical properties in either case. Treatment of I with 2 equiv of NaOH in CCl_4 gave the sodium salt of the cyclic phosphate, IV. An identical compound was ob-



tained by treating *cis*-2-chloromethyl-2-ethyl-1,3-propanediol benzylphosphonate with sodium hydride and benzaldehyde[5] further excluding the possibility that the different physical properties of II and III are due merely to conformational effects. In the first case inversion would be expected while in the second, if the accepted mechanism for the phosphonate–olefin reaction is correct, retention should predominate.

Westheimer[6] has postulated either a trigonal bipyramid or a square pyramid as likely transition states for the acid hydrolysis of cyclic phosphate esters, and similar transition states can be drawn for the present system. Since in our compounds inversion takes place exclusively and a square pyramid would lead to retention, a trigonal bipyramid where displacement takes place in the radial plane at a mutual angle of 120° would most likely represent the transition state. The ring would span one apical and one radial position. Further work with other nucleophiles and a study of solvent effects is currently in progress and will be reported at a later date.

(5) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).

(6) P. C. Haake and F. H. Westheimer, *ibid.*, **83**, 1102 (1961); E. A. Dennis and F. H. Westheimer, *ibid.*, **88**, 3432 (1966).

Experimental Section

2-Chloromethyl-2-ethyl-1,3-propanediol-N-cyclopentylene Phosphoramide (II).—Ethyl bicyclic phosphite (16.2 g, 0.1 mole) was dissolved in 100 ml of dry methylene chloride. Chlorine gas was bubbled into the solution at 20–30° until the solution took on the characteristic green color of chlorine. The solution was warmed to expel excess chlorine, and piperidine (17.0 g, 0.2 mole) dissolved in 50 ml of dry methylene chloride was added slowly at 20–30°. The solution was suction filtered and the filtrate was stripped under reduced pressure. The residue was recrystallized twice from heptane to give 14.35 g of a white crystalline solid, mp 161–162°.

Anal. Calcd for $C_{11}H_{21}ClNO_3P$: C, 46.89; H, 7.46; N, 4.97. Found: C, 47.09; H, 7.30; N, 4.96.

2-Chloromethyl-2-ethyl-1,3-propanediol-N-cyclopentylene Phosphoramide (III).—N-Chloropiperidine (0.2 mole), prepared from sodium hypochlorite, was dissolved in 100 ml of CCl_4 and the solution was added dropwise at 20–30° with stirring to ethyl bicyclic phosphite (24.3 g, 0.15 mole) dissolved in 100 ml of carbon tetrachloride. After standing overnight, solvent was removed under reduced pressure and the residue was recrystallized twice from heptane to give a white crystalline solid, 32.8 g, mp 99–100°.

Anal. Calcd for $C_{11}H_{21}ClNO_3P$: C, 46.89; H, 7.46; N, 4.97. Found: C, 46.73; H, 7.40; N, 5.04.

Registry No.—II [R = $(CH_2)_5$], 10212-39-2; III [R = $(CH_2)_5$], 10212-40-5.

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The Attempted Conversion of 1-Alkyl-4-(2-hydroxyethyl)-4-phosphorinanols into Bicylic Phosphonium Salts by a Quinuclidine Synthesis[1]

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The cyclic phosphine (Ia) was recently subjected[2] to conditions used by Grob and Brenneisen[3] for converting the analogous nitrogen compound to a quinuclidine derivative (II). By analogy to II, the product of the first step (12 hr in 62% hydrobromic acid at 50–55°) should have been the dibromide (III). To effect cyclization, the product without isolation was placed in refluxing benzene;[3] a salt did indeed precipitate, but it contained hydroxyl and ionic bromine and could not be the phosphorus counterpart of II. The salt was assigned the bicyclic structure (IVa), which seemed best to fit the available data.[2] However, this structure would require the survival of a tertiary alcoholic function in 62% hydrobromic acid, and it was pointed out that such a unique event required further investigation. An alternative structure (V), which avoided this feature, was rejected on the basis of the proton magnetic resonance (pmr) spectrum, which failed to show a signal for CH_2CH_2OH.

(1) Supported by Research Grant CA-05507 from the National Cancer Institute, U. S. Public Health Service. Taken in part from the Ph.D. dissertation of H. E. Shook, Jr., 1966.

(2) L. D. Quin and D. A. Mathewes, *Chem. Ind.* (London), 210 (1963).

(3) C. A. Grob and P. Brenneisen, *Helv. Chim. Acta*, **41**, 1184 (1958).