2,3,4-Tri-*O*-methyl-D-galactose was identified as its characteristic anilide derivative. After recrystallization from absolute ethanol, the m.p. was 167–168°.

Anal. Calcd. for $C_{15}H_{23}O_5N$: N, 4.7. Found: N, 4.7.

An X-ray diffraction pattern of the crystals was identical with that of an authentic specimen.

Test for Reversion.—On paper chromatography of a solution of D-galactose and L-rhamnose in equimolar concentrations which had been subjected to the same conditions used in the hydrolysis of okra mucilage no oligosaccharide spots were observed, showing that the aldobiouronic acid arising upon hydrolysis of okra mucilage is not a reversion product.

Characterization of Aldotriouronic Acids.—Bromine oxidation of a small amount of component II followed by acid hydrolysis and paper chromatography of the hydrolysate indicated that galactose is at the reducing end of this trisaccharide since galactose, having been oxidized to galactonic acid, did not appear on the chromatograms of the hydrolysate when sprayed with *p*-anisidine hydrochloride. Component II was methylated and reduced as described for the aldobiouronic acid. Paper chromatography in solvent D of a hydrolysate of a small amount of the reduced product showed the presence of two trimethylgalactoses and a dimethylrhamnose. The main quantity of the reduced sirup was remethylated and then hydrolyzed to yield tetramethylgalactose, a trimethylgalactose and a dimethylrhamnose as shown by paper chromatography in solvents D and E. Attempts to isolate these derivatives were unsuccessful because of the small amounts present.

By using the bromine oxidation procedure described above, rhamnose was shown to be at the reducing end of component III. Paper chromatography of a hydrolysate of completely methylated component III indicated the presence of a dimethylrhamnose, a dimethylgalacturonic acid and tetramethylgalactose.

Acknowledgment.—The authors wish to express their thanks to Dr. L. Hough for supplying the authentic specimen of 2,3,4-tri-*O*-methyl-D-galactose anilide used for X-ray comparison.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM DEFENCE RESEARCH CHEMICAL LABORATORIES, OTTAWA]

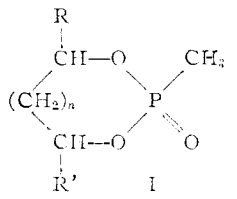
Organic Phosphorus Compounds. III. Reactions of Methanephosphonyl Dichloride with Diols[1]

BY A. F. McKAY, R. A. B. BANNARD, R. O. BRAUN AND R. L. BENNESS

RECEIVED FEBRUARY 11, 1954

Glycols combined with methanephosphonyl dichloride to give heterocyclic structures containing the phosphonate group. Methanephosphonyl dichloride on treatment with D-(−)-2,3-butanediol in the presence of ether and pyridine gave 2,4,5-trimethyl-2-oxo-1,3-dioxa-2-phosphacyclopentane and an optically active compound. The latter compound was identified by degradation with phosphorus pentachloride as 1-methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate.

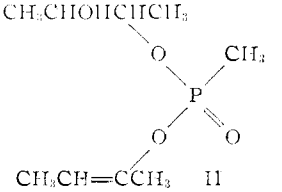
A continuation of the studies[2] of the reaction of glycols with methanephosphonyl dichloride has shown that 2,4-pentanediol, 1,3-butanediol and 1,4-butanediol give the cyclic structures 2,4,6-trimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane (I, R and R′ = CH_3, n = 1), 2,6-dimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane (I, R = CH_3, R′ = H, n = 1) and 2-methyl-2-oxo-1,3-dioxa-2-phosphacycloheptane (I, R and R′ = H, n = 2), respectively. In each run some methanephosphonic acid and/or methanephosphonic anhydride was also produced.



I

Ethylene chlorohydrin combined with methanephosphonyl dichloride giving a mixture of β-chloroethyl hydrogen methanephosphonate and di-β-chloroethyl methanephosphonate.

Recently[2] it was shown that D-(−)-2,3-butanediol and methanephosphonyl dichloride in methylene chloride and in the presence of pyridine gave a 75% yield of the cyclic product 2,4,5-trimethyl-2-oxo-1,3-dioxa-2-phosphacyclopentane (I, R and R′ = CH_3, n = 0). Now it has been found that replacement of the solvent methylene chloride by ether lowered the yield of cyclic product to 53%. Moreover a new optically active compound was formed in 38% yield. This new compound had a rotation of −103° and it gave analytical values in good agreement with the empirical formula $C_9H_{19}O_4P$. Its infrared spectrum has a band at 3400 cm.$^{-1}$ due to O–H stretching vibrations. A medium band at 1710 cm.$^{-1}$ is assigned to C=C stretching vibrations or an associated ester group because C–O stretching vibrations would be expected to give a stronger absorption band. The strong absorption band at 1282 cm.$^{-1}$ with an absorption band on the shoulder at 1265 cm.$^{-1}$ is assigned to stretching vibrations of the P=O group[3–5] and 983 cm.$^{-1}$ is assigned[4,5] to the P–O–C linkage. Since the infrared spectrum of the optically active compound indicated the presence of a double bond, a hydroxy group and P–O–C linkages and the absence of the group C=O, structure II was assigned to it. This structure was confirmed by degradation with phosphorus pentachloride. Previously[6] the structure of dichlorophosphorylmethanephosphonyl



II

(1) Issued as D.R.C.L. Report No. 131.

(2) A. F. McKay, R. O. Braun and G. R. Vavasour, THIS JOURNAL, **74**, 5540 (1952).

(3) R. C. Gore, *Disc. Faraday Soc.*, **9**, 138 (1950).

(4) L. J. Bellamy and L. Beecher, *J. Chem. Soc.*, 728 (1953).

(5) M. Halmann and S. Pinchas, *ibid.*, 626 (1953).

(6) R. A. B. Bannard, J. R. Gilpin, G. R. Vavasour and A. F. McKay, *Can. J. Chem.*, **31**, 976 (1953).

dichloride was proved by an examination of the products from its reaction with phosphorus pentachloride. The products to be expected from the reaction of 1-methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate (II) with phosphorus pentachloride are shown in the equation

$$II + 3PCl_5 \longrightarrow CH_3POCl_2 + CH_3CH{=}CClCH_3 + CH_3CHClCHClCH_3 + 3POCl_3 + HCl$$

When the optically active compound II was heated with three mole equivalents of phosphorus pentachloride at 70–80°, all of the products indicated in the above equation were obtained. The presence of a small amount of phosphorus trichloride together with a 113% yield of hydrogen chloride indicated that some substitutive chlorination occurred as a side reaction. The yields of products were: hydrogen chloride, 113%; 2-chlorobutene-2, 55.5%; methanephosphonyl dichloride, 58.2%; D-(−)-2,3-dichlorobutane, 64.0%; phosphorus oxychloride, 96.7% and phosphorus trichloride (0.031 mole). There was a total of 9% loss during the several distillations. These results firmly establish the structure of the optically active compound as II. Also hydrolysis of 1-methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate (II) with 10% sulfuric acid gave one mole equivalent of D-(−)-2,3-butanediol which was isolated as D-(−)-4,5-dimethyl-1,3-dioxolane.[7]

The high negative rotation (−13.9°) of the D-(−)-2,3-dichlorobutane obtained from the reaction of phosphorus pentachloride with II showed that a double Walden inversion occurred during the chlorination of the 1-methyl-2-hydroxypropyl group.

Experimental[8]

2,4,6-Trimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane.—A stirred solution of 62.8 g. (0.472 mole) of methanephosphonyl dichloride[9] in 245 g. of methylene chloride was brought to reflux and 50 g. (0.481 mole) of 2,4-pentanediol was added over a period of 16 minutes. The refluxing was continued for a further four hours after which the solvent was removed *in vacuo*. The residue was fractionated under reduced pressure to give 62.9 g. (87%) of product, b.p. 99° (0.85 mm.) This material solidified in the receiver to a white crystalline solid.

Anal. Calcd. for $C_6H_{13}O_3P$: C, 43.90; H, 7.92; P, 18.90. Found: C, 43.92; H, 7.95; P, 18.95.

2,6-Dimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane.—1,3-Butanediol (42.8 g., 0.475 mole) was added to a refluxing solution of 62.3 g. (0.470 mole) of methanephosphonyl dichloride in 244 g. of methylene chloride. This reaction was carried out in the same manner as the above preparation of 2,4,6-trimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane. The clear white product (b.p. 71° (0.25 mm.)) crystallized on standing; yield 46.1 g. (69.7%). The crystalline 2,6-dimethyl-2-oxo-1,3-dioxa-2-phosphacyclohexane melted at 40° (capillary tube method).

Anal. Calcd. for $C_5H_{11}O_3P$: C, 39.79; H, 7.94; P, 20.52. Found: C, 39.58; H, 7.64; P, 20.41.

2-Methyl-2-oxo-1,3-dioxa-2-phosphacycloheptane.—To a refluxing solution of 33.3 g. (0.25 mole) of methanephosphonyl dichloride in 100 cc. of dry methylene chloride was added 22.5 g. (0.25 mole) of 1,4-butanediol over a period of 15 minutes. The reaction mixture was refluxed for a further period of 20 hours and then the solvent was removed *in vacuo*. A yellow oil (38.7 g.) was obtained. This oil was distilled *in vacuo* from a distilling flask having a wide side arm a few millimeters above the surface of the liquid. The first distillation gave a yellow solid (b.p. 72–76° (0.5 mm.)), yield 20.8 g. (55.5%). A brown oil (17.5 g.) remained in the distillation flask. This residue was identified as a mixture of methanephosphonic acid and methanephosphonic anhydride by hydrolysis of a portion with water as previously described. The hydrolysis product was crystallized from methyl ethyl ketone and decolorized with charcoal to give pure methanephosphonic acid melting at 108–109°. This product did not depress the melting point of an authentic sample of methanephosphonic acid.

The yellow solid (20.8 g.) was redistilled *in vacuo*. A white crystalline solid was obtained which melted at 68.5–70°, yield 17.0 g. (45.3%).

Anal. Calcd. for $C_5H_{11}O_3P$: C, 40.00; H, 7.82; P, 20.65. Found: C, 40.56; H, 7.72; P, 20.9, 21.1.

Reaction of Methanephosphonyl Dichloride with Chlorohydrin.—Chlorohydrin (161.0 g., 2.0 moles) was added over a period of 25 minutes to a refluxing solution of 133.0 g. (1.0 mole) of methanephosphonyl dichloride in 300 cc. of dry methylene chloride. The reaction mixture was stirred at reflux temperature overnight and then the solvent was removed under vacuum (water-pump) at a temperature of 65°. A light yellow oil remained, yield 215.1 g. This residue was separated into two fractions by distillation *in vacuo;* fraction 1, b.p. 90° (0.1 mm.), yield 46.8 g., and fraction 2, b.p. 90–100° (0.05 mm.), yield 150.9 g. Both these fractions were carefully refractionated *in vacuo* using an 8-inch Vigreux column fitted with a variable take-off distillation head. Fraction 1 gave 10.6 g. (6.3%) of pure β-chloroethyl hydrogen methanephosphate, b.p. 68–69° (0.1 mm.), $n^{24.8}D$ 1.4196, $d^{23.5}_4$ 1.355. A test for ionic chlorine was negative.

Anal. Calcd. for $C_3H_8ClO_3P$: C, 22.72; H, 5.05; Cl, 22.38; P, 19.56. Found: C, 22.55; H, 4.95; Cl, 22.80; P, 19.70, 19.85.

Fraction 2 gave 135.2 g. (61.3%) of pure di-(β-chloroethyl) methanephosphonate, b.p. 98–100° (0.075 mm.), $n^{24.8}D$ 1.4655, $d^{25.8}_4$ 1.355.

Anal. Calcd. for $C_5H_{11}Cl_2O_3P$: C, 27.14; H, 4.97; Cl, 32.12; P, 14.02. Found: C, 26.95; H, 5.20; Cl, 32.00; P, 13.8, 13.7.

1-Methyl-2-hydroxypropyl 1-Methyl-1-propenyl Methanephosphonate (II).—A solution of 238 g. (3 moles) of dry pyridine and 200 g. (1.5 moles) of methanephosphonyl dichloride in 400 cc. of anhydrous ether was prepared in a 2-l. 3-necked flask protected from moisture. This vigorously stirred solution was brought to reflux and 135 g. (1.5 moles) of D-(−)-2,3-butanediol in 100 cc. of anhydrous ether was added over a period of 70 minutes. The reaction mixture was heated at reflux temperature for a further period of 1.5 hours and then allowed to stand at room temperature overnight. The precipitate of pyridine hydrochloride was filtered off in a dry-box and washed with ether (6 × 100 cc.). The filtrate and ether washings were combined and evaporated to dryness. A pale yellow oily residue (191 g.) was obtained. This oil was carefully fractionated using a 15-inch vacuum-jacketed Vigreux column equipped with a variable take-off fractionation head. Fraction 1 was a colorless oil, yield 60.1 g. (38.7%), b.p. 58–68° (0.03 mm.), d^{26}_4 1.080, $n^{24.8}D$ 1.4372, $[\alpha]^{24.8}D$ −98.4°. Fraction II (b.p. 82–84°) (0.3 mm.) came over as a colorless oil which soon solidified, yield 120 g. (53.3%). This material melted at 43–45° alone and on admixture with an authentic sample of 2,4,5-trimethyl-2-oxo-1,3-dioxa-2-phosphacyclopentane. A residue of 3.5 g. was obtained and 8.0 g. of volatiles was present in the cold-trap.

Fraction 1 was refractionated. All of the physical constants remained unchanged with the exception of the optical rotation ($[\alpha]^{24.8}D$ −103.0°). Further fractionation failed to change the optical activity. This fraction gave good analysis for 1-methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate.

Anal. Calcd. for $C_9H_{19}O_4P$: C, 48.63; H, 8.55; P, 13.95. Found: C, 48.37, 48.95; H, 8.45, 8.64; P, 13.85.

Hydrolysis of 1-Methyl-2-hydroxypropyl 1-Methyl-1-propenyl Methanephosphonate (II).—A sample (4.9 g., 0.022 mole) of 1-methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate was refluxed with 25 cc. of 10% aqueous sulfuric acid solution for 20 minutes. Three grams of

(7) H. K. Garner and H. J. Lucas, THIS JOURNAL, **72**, 5497 (1950).

(8) All melting and boiling points are uncorrected. Microanalyses by Micro-Tech Laboratories, Skokie, Ill., and Defence Research Chemical Laboratories.

(9) A. M. Kinnear and E. A. Perrin, *J. Chem. Soc.*, 3437 (1952).

trioxymethylene were added and the formal derivative of D-(−)-2,3-butanediol was removed as formed by use of an esterification apparatus. The aqueous phase was saturated with potassium carbonate and the layer of D-(−)-4,5-dimethyl-1,3-dioxolane was separated, yield 1.9 g. (103%). This material was moist which accounts for the slightly high yield. Several runs gave crude yields of 100–105%. This crude material was dried over anhydrous potassium carbonate and distilled. The final product had the following physical constants: $n^{25}D$ 1.3952, d^{25}_4 0.933, $[\alpha]^{25}D$ −24.30°; b.p. 94–96° (760 mm.). Garner and Lucas[7] report $n^{25}D$ 1.3959, d^{25}_4 0.9346, $[\alpha]^{25}D$ −25.01, b.p. 95° (760 mm.).

Reaction of 1-Methyl-2-hydroxypropyl 1-Methyl-1-propenyl Methanephosphonate with Phosphorus Pentachloride.—1-Methyl-2-hydroxypropyl 1-methyl-1-propenyl methanephosphonate (33.2 g., 0.15 mole) was placed in a 200-cc. four-neck, round-bottom flask. The flask was equipped with a Trubore stirrer, thermometer, reflux condenser, nitrogen inlet tube and a worm-feed addition tube containing 93.5 g. (0.45 mole) of phosphorus pentachloride under anhydrous conditions. The reflux condenser was connected through a calcium chloride tube to a trap immersed in ice-water and then through a U-tube filled with calcium chloride to two gas washing bottles containing standardized 1 *N* sodium hydroxide solution. During the reaction, the equipment was swept with dry nitrogen.

Phosphorus pentachloride was added to the stirred solution at a sufficient rate to maintain a temperature of 50–60°. After the addition period of 55 minutes, the reaction mixture was held at 70° for a further period of 2.5 hours. This solution was allowed to stand overnight at room temperature.

Titration of the residual alkali in the gas washing bottles showed that 6.2 g. of hydrogen chloride was evolved from the reaction. The ice-water trap contained 5.5 g. of colorless liquid, which was identified as 2-chlorobutene-2, while the main liquid product in the reaction flask weighed 115 g. Fractionation of the latter product in a Todd column employing a stainless steel spiral packing and a reflux ratio of 10:20 gave 2.04 g. of 2-chlorobutene-2, 4.26 g. of phosphorus trichloride and 80.2 g. of a mixture of phosphorus oxychloride and 2,3-dichlorobutane.

2-Chlorobutene-2 was obtained as a colorless liquid, b.p. 62–68°, $n^{25}D$ 1.4231. The total yield was 7.54 g. (55.5%).

Anal. Calcd. for C_4H_7Cl: C, 53.07; H, 7.79; Cl, 39.16. Found: C, 53.43; H, 7.62; Cl, 38.80.

Gutner and Tischenko[10] reported the following physical properties for a mixture of *cis* and *trans* isomers of 2-chlorobutene-2, b.p. 62–67° and $n^{15}D$ 1.4232.

The phosphorus trichloride fraction (b.p. 73–77°) was hydrolyzed and oxidized to phosphoric acid. Then the aqueous solution was analyzed for phosphoric acid by the ammonium phosphomolybdate method.[11] This analysis confirmed the identity of this fraction.

In the third fraction phosphorus oxychloride and 2,3-dichlorobutane codistilled, b.p. 105–112°. This solution was hydrolyzed by addition of water and the 2,3-dichlorobutane extracted with ether. The ethereal extract was dried over anhydrous sodium sulfate and fractionated in the Todd column. This procedure gave 12.2 g. (64.0%) of D-(−)-2,3-dichlorobutane, b.p. 117–119.5°, $n^{25}D$ 1.4407, d^{25}_4 1.092 and $[\alpha]^{25}D$ −13.9°.

Anal. Calcd. for $C_4H_8Cl_2$: C, 37.83; H, 6.35; Cl, 55.84. Found: C, 38.11; H, 6.30; Cl, 56.07.

The aqueous fraction on analysis for phosphoric acid by the ammonium phosphomolybdate method[11] was found to contain phosphorus equivalent to 66.6 g. (96.7%) of phosphorus oxychloride.

The still residue (20.1 g.) from the original distillation in the Todd column on fractionation *in vacuo* gave 11.6 g. (58.2%) of methanephosphonyl dichloride, b.p. 49.5–53° (9 mm.) and $d^{25.3}_4$ 1.445. The methanephosphonyl dichloride was identified by a quantitative hydrolysis to methanephosphonic acid. After purification from methyl ethyl ketone, it melted at 108–109° alone and on admixture with an authentic sample of methanephosphonic acid.[2]

Acknowledgment.—The authors are grateful to Messrs. B. Sells and J. R. Gilpin for assistance with some of the experimental work. We also wish to thank Mr. L. J. Blondin of Defence Research Chemical Laboratories for measuring the infrared spectrum.

(10) B. A. Gutner and D. V. Tischenko, *J. Gen. Chem. (U.S.S.R.)*, **6**, 1729 (1936).

(11) Scott's "Standard Methods of Chemical Analysis," Fifth Edition, Vol. I, D. Van Nostrand Co., Inc., New York, N. Y., 1939, p. 694.

OTTAWA, ONTARIO, CANADA

[CONTRIBUTION NO. 1203 FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Nitrogen-substituted-3,4-dihydroxypyrrolidines[1a]

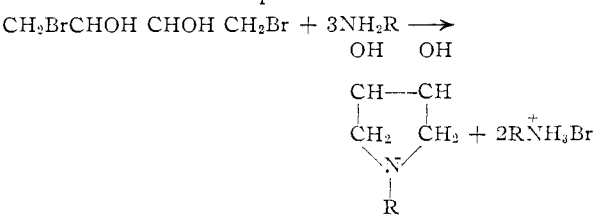
BY ARTHUR J. HILL AND MARY-GERTRUDE MCKEON[1b]

RECEIVED FEBRUARY 1, 1954

A series of nitrogen alkyl-, aryl- and arylalkyl-substituted 3,4-dihydroxypyrrolidines has been prepared by the action of *meso*-1,4-dibromobutanediol-2,3 with primary amines. Two methods of closure have been used, and derivatives, particularly dibenzoates, have been prepared for pharmacological testing.

The β-aminoethanol grouping appears frequently in a variety of pharmacologically active compounds. This fact suggested preparation of a series of N-substituted-3,4-dihydroxypyrrolidines, a type of amino alcohol which has received scant attention. Search of the literature made at the start of this investigation disclosed no reference to this type of pyrrolidine. A subsequent patent describes the preparation of some nitrogen aryl and nitrogen arylalkyl substituted 3,4-dihydroxypyrrolidines.[2]

Ring closure between a 1,4-dihalo entity and a primary amine is a common method for preparing pyrrolidines; in the study here reported, *meso*-1,4-dibromobutanediol-2,3 was treated with alkyl, aryl and alkylaryl primary amines to form N-substituted-3,4-dihydroxypyrrolidines. None of the compounds obtained has been reported previously, although certain of the aromatic and mixed alkyl-aryl series are stereoisomers of 3,4-dihydroxypyrrolidines described in the patent referred to above.



A satisfactory method for the preparation of the dibromobutanediol was developed by modification

(1) (a) Abstracted from the Dissertation submitted by Mary-Gertrude McKeon in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Yale University. (b) Connecticut College for Women, New London, Conn.

(2) German Patent 805,522 (March 15, 1951).