The distillate, b.p. 75–80° (0.3 mm.), 0.19 g., was analyzed by n.m.r. spectroscopy, which indicated 46.7 ± 4.1% of IV and 53.3 ± 4.1 % of III.

(B).—To 3.5 g. of iodine and 6.8 g. of potassium iodide in 60 ml. of water was added the sodium salt of XII (from 1.0 g. of XII and 1.73 g. of sodium bicarbonate) in 30 ml. of water. A heavy oil which separated was extracted with ether. The extracts were washed with sodium bisulfite solution until colorless, sodium bicarbonate solution, and water and dried. Removal of ether furnished 1.5 g. (82%) of an undistillable (dec.) noncrystallizable oil which represented the iodolactone (infrared spectrum). Hydrogenolysis with W-2 Raney nickel in ethanol and triethylamine was only partially successful, whereas hydrogenolysis with nickel and sodium bicarbonate completed removal of iodine. Infrared and n.m.r. spectra of the product indicated that it was composed of III and IV; n.m.r. analysis indicated the presence of 54.2 ± 2% III and 45.8 ± 2% IV.

1-Cycloheptene-1-acetic Acid (XV) and Cycloheptane-$\Delta^{1,\alpha}$-acetic Acid (XVI).—Dehydration of the hydroxy ester, obtained in 67% yield by the Reformatsky reaction of cycloheptanone and ethyl bromoacetate, with thionyl chloride furnished a mixture of α,β- and β,γ-unsaturated ester; b.p. 71–82° (1.5 mm.); yield, 51%; infrared bands at 1740 (ester), 1715 (conjugated ester), and 1635 cm.$^{-1}$ (conjugated double bond) which contained 60% of the β,γ-unsaturated compound (v.p.c.). Hydrolysis gave a mixture of the title compounds, b.p. 110–114 (18 mm.), 74% yield, which was used directly for the following reactions.

(A).—Cyclization of the mixture with dilute sulfuric acid–acetic acid for 11 hr. and work-up in the usual manner gave 57% of a neutral fraction, b.p. 68–73° (0.15 mm.), whose n.m.r. analysis indicated that it was composed of 73.7 ± 1.6% *cis*-lactone III and 26 ± 1.6% *trans*-lactone IV.

(B).—Iodolactonization of the mixed acids yielded 26% of a noncrystallizable oil which decomposed on attempted distillation but was a mixture of iodolactones (infrared spectrum). W-2 Raney nickel hydrogenolysis in ethanol with sodium bicarbonate gave a mixture of lactones III and IV, b.p. 88–92° (0.6 mm.), 44% yield, which contained 66 1% of III ± and 34 ± 1% of IV.

The Reactions of Phosphonic Acid Esters with Acid Chlorides. A Very Mild Hydrolytic Route

ROBERT RABINOWITZ

Chemical Research Department, Central Research Division, American Cyanamid Company, Stamford, Connecticut

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The reaction of trimethylchlorosilane with a number of dialkyl esters of phosphonic acids and the hydrolysis of the resultant silyl phosphonates was studied as a means of preparing the phosphonic acids under very mild conditions. 2-Vinyloxyethylphosphonic acid, β-cyanovinylphosphonic acid, and vinylphosphonic acid were successfully prepared and characterized as their dicyclohexylamine salts. The reaction of primary, secondary, and tertiary alcohols with bis(trimethylsilyl) methylphosphonate results in an equilibrium mixture containing starting materials, acidic products, and mixed ethers [$ROSi(CH_3)_3$]. Mercaptans do not react. The reaction of excess acetyl chloride with dimethyl methylphosphonate yields methyl chloride, acetic anhydride, and dimethyl dimethylpyrophosphonate. The stability of the latter in excess acetyl chloride is discussed. Mechanistic interpretations of all reactions are presented.

The conventional means of converting a phosphonic acid ester into the corresponding phosphonic acid is by refluxing in concentrated aqueous acid.[1] However, this method is not applicable to phosphonates containing acid or water sensitive groups like nitriles, vinyl ethers, acetals, etc. During an investigation of the preparation and reactions of bis(trimethylsilyl) benzylphosphonate it was noted that this compound was hydrolyzed in high yield to benzylphosphonic acid when shaken in water at room temperature. Furthermore, the liquid bis(trimethylsilyl) ethylphosphonate slowly dissolved in water to give a strongly acidic solution. This suggested that conversion of phosphonates of the general formula $RP(O)(O\text{-alkyl})_2$ where R contains an acid labile group, to the corresponding bistrimethylsilyl phosphonates and subsequent hydrolysis should result in the preparation of phosphonic acids which ordinarily would be difficult to obtain.

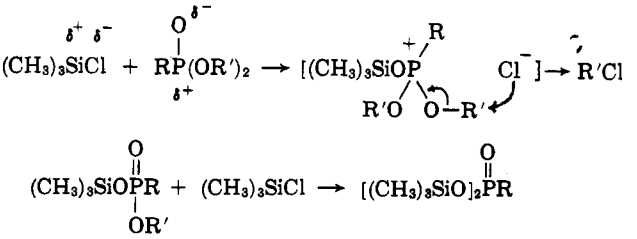
Diethyl β-cyanovinylphosphonate was converted in high yield to bis(trimethylsilyl) β-cyanovinylphosphonate. This was hydrolyzed in water, and a 30% yield of the β-cyanovinylphosphonic acid was isolated and characterized as the crystalline dicyclohexylamine salt. When the bis(trimethylsilyl) compound reacted with methanol, a quantitative yield of the phosphonic acid was obtained. Diethyl 2-vinyloxyethylphosphonate was converted in good yield into the corresponding bistrimethylsilyl compound which, upon reaction with methanol, gave the phosphonic acid as an oil. It was characterized as the crystalline dicyclohexylamine salt. Finally bis(β-chloroethyl) vinylphosphonate and diethyl vinylphosphonate were converted, using this procedure, to vinyl phosphonic acid. Vinyl phosphonic acid has been a rather elusive compound and was reported only recently.[2]

$$2ClSi(CH_3)_3 + NCCH{=}CHP(O)(OC_2H_5)_2 \longrightarrow 2C_2H_5Cl + NCCH{=}CHP(O)[OSi(CH_3)_3]_2$$

$$NCCH{=}CHP(O)[OSi(CH_3)_3]_2 \xrightarrow[\text{or } CH_3OH]{H_2O} NCCH{=}CHP(O)(OH)_2$$

Discussion

The reaction of trimethylchlorosilane with phosphonates as well as phosphates to yield the corresponding trimethylsilyl derivatives has been described.[3] Although no mechanism is proposed it appears likely



(1) G. M. Kosalapoff, "Organophosphorus Compounds," John Wiley and Sons, Inc., New York, N. Y., 1950.

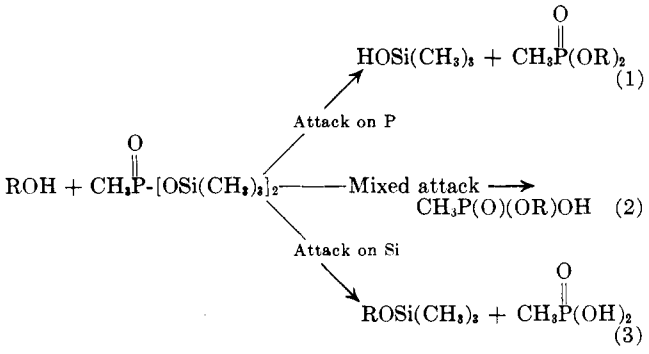
(2) M. I. Kabachnik and T. Ya. Medved, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 2142 (1959).

(3) H. W. Kohlschutter and H. Simoleit, *Kunststoffe—Plastics*, **6**, 9 (1959).

that a phosphonium-type Arbuzov intermediate is involved. (See p. 2975, col. 2, bottom.)

The reactions of the various phosphonates of this work with trimethylchlorosilane were all carried out by heating the phosphonate to approximately 120° and then adding trimethylchlorosilane until the reflux temperature of the system dropped to 70°. Additional quantities of trimethylchlorosilane were added periodically until it appeared that the reaction was complete. Even using a minimum temperature of 70°, the reaction in a number of cases required several days of attention. Dimethyl methylphosphonate was synthesized since it was presumed, on steric grounds, that this would be converted to the corresponding bistrimethylsilyl compound faster than any of the higher esters. Actually the reaction was complete in less than six hours, and a greater than 90% yield of product was obtained.

Aqueous hydrolysis of the bistrimethylsilyl phosphonates, whether water attack is on silicon or phosphorus, will yield the phosphonic acid. However, reaction with alcohols can lead to a phosphonate or a phosphonic acid or a mixed product depending on the position of attack (equations 1–3). The reaction of



bis(trimethylsilyl) methylphosphonate with a number of alcohols was studied with the aid of a Perkin-Elmer 154D gas chromatography apparatus. Qualitatively the results are as follows. Primary and secondary alcohols like methanol, ethanol, 1-butanol, 1-heptanol, cyclohexanol, and phenol react *instantaneously* to give an equilibrium mixture containing the alcohol and the mixed ether (reaction 3). The existence of an equilibrium was postulated on the basis that significant amounts of the alcohol and the mixed ether were present when less than half of the stoichiometric amount of alcohol was added to the phosphonate. Tertiary alcohols like *t*-butyl and *t*-amyl alcohol react very slowly at room temperature; however, when heated for a few minutes at 80–110°, equilibrium is rapidly established. Although the equilibrium must involve both the half-acid ester and the full acid, it is convenient to simply express the over-all equilibrium as shown.

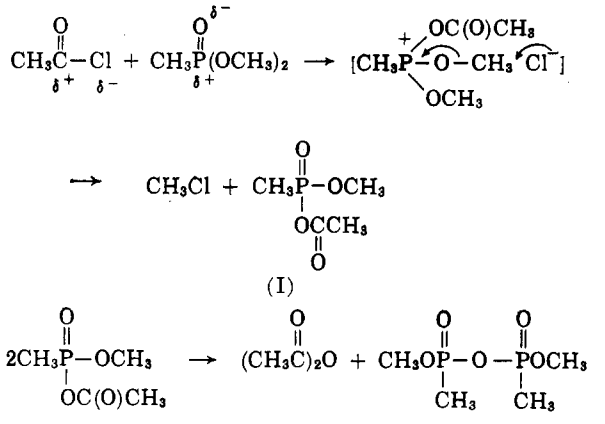
$$CH_3P(O)[OSi(CH_3)_3]_2 + 2ROH \rightleftharpoons 2ROSi(CH_3)_3 + CH_3P(O)(OH)_2$$

Further evidence for the existence of this equilibrium was obtained by adding *n*-propylamine to the reaction mixtures at equilibrium. This serves to remove the phosphonic acid or the half-acid ester as the salt, and as anticipated, the ratio of mixed ether to alcohol increased markedly as a result of the forward reaction proceeding in order to re-establish an equilibrium. Separately it was shown that *n*-propylamine does not react with bis(trimethylsilyl) methylphosphonate even at 100°.

Although the reaction of methanol or ethanol with a bistrimethylsilyl phosphonate reaches an equilibrium before complete reaction, this reaction can be used to convert the phosphonate completely to the phosphonic acid. This is possible by using a reasonable excess of the alcohol while taking advantage of the fact that the alcohol-mixed ether azeotrope always boils at a lower temperature than does the free alcohol.[4]

Amyl mercaptan and benzyl mercaptan do not react with bis(trimethylsilyl) methylphosphonate at room temperature. This was not surprising in view of the fact that the driving force of the reaction of alcohols with the phosphonate is the formation of the strong O–Si bond (89.1 kcal.)[5] while the corresponding S–Si bond is considerably weaker (60.9 kcal.).[5]

The scope of the reaction of acid chlorides like trimethylchlorosilane with phosphonates was investigated by studying the reaction of acetyl chloride with dimethyl methylphosphonate. The reaction was carried out in a large excess of acetyl chloride. The only products identified, besides methyl chloride, were acetic anhydride and dimethyl dimethylpyrophosphonate (49%). The course and proposed mechanism are the following.



These results are in agreement with recent studies[6] on the action of acetyl bromide, acetyl chloride, and benzoyl chloride on diethyl ethylphosphonate. This work was carried out on a mole-to-mole basis and the survival of the pyrophosphonate against further acid chloride attack is understandable. However, the isolation of significant amounts of dimethyl dimethylpyrophosphonate after having carried out the reaction using a large excess of acetyl chloride was, at first, difficult to rationalize. It is now felt that the stability of the mixed ester anhydride (I) and of the pyrophosphonate toward further rapid acetyl chloride attack is due to the fact that, according to the proposed mechanism, phosphorus must accept a positive charge in the transition state. This is not a favorable situation when the electron withdrawing –OC(O)– or OP(O)– groups are also attached to this phosphorus.

(4) R. O. Sauer, *J. Am. Chem. Soc.*, **66**, 1707 (1944).
(5) N. V. Sidgwick, "The Chemical Elements and Their Compounds," Vol. I, XXXI, Claredon Press, Oxford, 1950, p. 551.
(6) A. N. Pudovik, A. A. Muratova, T. I. Konnova, T. Feoktistova, and L. N. Levkova, *Zh. Obshch. Khim.*, **30**, 2624 (1960).

Experimental

Materials.—Dimethyl methylphosphonate and diethyl benzylphosphonate were prepared in high yields by treating trimethyl phosphite and triethyl phosphite with methyl iodide and benzyl chloride, respectively. Diethyl β-cyanovinylphosphonate[7] and diethyl 2-vinyloxyethylphosphonate[8] were available at this laboratory. Bis(2-chloroethyl) vinylphosphonate was obtained from the Monsanto Chemical Company. Trimethylchlorosilane was Anderson's "pure" grade. Diethyl vinylphosphonate was prepared by triethylamine dehydrobromination of diethyl 2-bromoethylphosphonate, the reaction product of triethyl phosphite and an excess of 1,2-dibromoethane.

Preparation of Bis(trimethylsilyl) Benzylphosphonate.—A solution of 35.8 g. (0.155 mole) of diethyl benzylphosphonate and 16.9 g. (0.155 mole) of trimethylchlorosilane was heated under a reflux condenser which was connected to a Dry Ice–trichloroethylene trap. The initial reflux temperature was 72°. Periodically during the next 4 days, when the reflux temperature was above 95°, a total of 29.4 g. (0.27 mole) of trimethylchlorosilane was added. Fractionation of the reaction mixture led to the recovery of 5 g. of trimethylchlorosilane and the isolation of 45.6 g. (93%) of bis(trimethylsilyl) benzylphosphonate, b.p. 96.5–98° (8 mm.).

Anal. Calcd. for $C_{13}H_{25}O_3PSi_2$: C, 49.4; H, 7.91; P, 9.80. Found: C, 50.2; H, 7.89; P, 10.10.

Hydrolysis of Bis(trimethylsilyl) Benzylphosphonate.—A mixture of 9.6 g. (0.030 mole) of bis(trimethylsilyl) benzylphosphonate and 75 ml. of water was shaken for 1 hr. At this point an oil floated on the water, whereas in the original mixture the bis(trimethylsilyl) benzylphosphonate was the lower layer. The mixture was extracted with three 50-ml. portions of chloroform, and the water layer was evaporated to dryness. The residue was a white solid, 4.1 g. (80%), which was recrystallized from 20 ml. of water. The crystalline product was collected and dried, m.p. 169–171°. This was identified as benzylphosphonic acid by comparison with an authentic sample.

Preparation of Bis(trimethylsilyl) Vinylphosphonate. A. From Bis(2-chloroethyl) Vinylphosphonate.—Using the procedure described for the synthesis of bis(trimethylsilyl) benzylphosphonate, 37.8 g. (0.162 mole) of bis(2-chloroethyl) vinylphosphonate reacted with a total of 56.1 g. (0.51 mole) of trimethylchlorosilane during a 30-day addition period. Fractionation yielded 32.6 g. (78%) of bis(trimethylsilyl) vinylphosphonate, b.p. 102.3–104° (14 mm.).

Anal. Calcd. for $C_8H_{21}O_3PSi_2$: C, 37.9; H, 8.3; P, 12.20; Si, 22.4. Found: C, 37.8; H, 8.65; P, 12.31; Si, 19.6.

B. From Diethyl Vinylphosphonate.—Using the procedure described previously, 42.3 g. (0.26 mole) of diethyl vinylphosphonate reacted with a total of 76.2 g. (0.70 mole) of trimethylchlorosilane during a five-day addition period. Fractionation yielded 60 g. (92%) of bis(trimethylsilyl) vinylphosphonate, b.p. 103–104° (14 mm.).

Anal. Calcd. for $C_8H_{21}O_3PSi_2$: C, 37.9; H, 8.3; P, 12.20. Found: C, 37.8; H, 8.7; P, 12.3.

Preparation of Vinylphosphonic Acid and Dicyclohexylamine Salt.—A solution of 7.0 g. (0.028 mole) of bis(trimethylsilyl) vinylphosphonate in 50 ml. of water was shaken for 16 hr. at room temperature. The oil floating on the water layer was extracted with three 50-ml. portions of chloroform. The water layer was devolatilized leaving 2.77 g. (93%) of very slightly yellow liquid residue, vinylphosphonic acid. One gram (0.0090 mole) of the vinylphosphonic acid was dissolved in 6 ml. of benzene and 4 ml. of acetone. This was added to a solution of 3.6 g. of dicyclohexylamine in 6 ml. of benzene and 4 ml. of acetone. Immediately a white solid precipitated which was collected and air-dried, 2.63 g. (100%). A portion of this was recrystallized from dilute water in acetone, and a white crystalline product was obtained, m.p. 210–215°.

Anal. Calcd. for $C_{14}H_{28}NO_3P$: C, 58.2; H, 9.7; N, 4.9; P, 10.7. Found: C, 58.0; H, 9.7; N, 4.9; P, 10.7.

Preparation of Bis(trimethylsilyl) 2-Vinyloxyethylphosphonate.—Using the procedure described previously, 50.0 g. (0.24 mole) of diethyl 2-vinyloxyethylphosphonate reacted with 89.5 g. (0.82 mole) of trimethylchlorosilane during a 48-hr. period. Fractionation of the reaction mixture gave 50 g. (72%) of bis(trimethylsilyl 2-vinyloxyethylphosphonate, b.p. 124–126° (5 mm.).

Anal. Calcd. for $C_{10}H_{26}O_4PSi_2$: C, 40.5; H, 8.43; P, 10.45. Found: C, 39.2; H, 7.83; P, 9.49.[9a]

Preparation of 2-Vinyloxyethylphosphonic Acid and Dicyclohexylamine Salt.—A solution of 12 g. (0.038 mole) of bis(trimethylsilyl) 2-vinyloxyethylphosphonate in 30 ml. of methanol was fractionally distilled,[9b] thus preferentially removing trimethylsiloxymethane and shifting the equilibrium continuously toward products. Finally all the remaining methanol was removed under reduced pressure leaving 5.5 g. (95%) of the phosphonic acid. A solution of 1.8 g. (0.012 mole) of the phosphonic acid in 5 ml. of methanol was added to a solution of 3.0 g. of dicyclohexylamine in 5 ml. of methanol. The temperature rose to 46°. The volume was reduced to 2–3 ml. and then the solution was diluted with 25 ml. of acetone. The solid which precipitated was collected and air-dried, 4.23 g. (106%). This was recrystallized from dilute methanol in acetone, m.p. 184–185°.

Anal. Calcd. for $C_{16}H_{32}NO_4P$: C, 57.8; H, 9.61; N, 4.21; P, 9.34. Found: C, 55.7; H, 9.63; N, 4.48; P, 10.0.[9a]

Reaction of Trimethylchlorosilane with Dimethyl Methylphosphonate. Preparation of Bis(trimethylsilyl) Methylphosphonate.—Using the procedure already outlined, 52.5 g. (0.423 mole) of dimethyl methylphosphonate reacted with 95.4 g. (0.88 mole) of trimethylchlorosilane during a 6-hr. period. Fractionation of the reaction mixture gave 92.0 g. (91%) of the desired product, b.p. 105–107.5° (27 mm.).

Anal. Calcd. for $C_7H_{21}O_3PSi_2$: C, 35.0; H, 8.73. Found: C, 35.6; H, 8.57.

Reactions of Bis(trimethylsilyl) Methylphosphonate with Alcohols.—The majority of these reactions were run on a qualitative basis using a Perkin-Elmer Model 154D gas chromatography (g.c.) apparatus for analysis. Usually the conditions were 180°, 20 lb./sq. in. He, silicone ("O") column (on Celite). The elution times for the silyl phosphonate, pure alcohol, trimethylsiloxymethane,[10] and trimethylsiloxyethane[10] were determined separately. The silyl phosphonate and the alcohol were mixed at room temperature and a sample immediately examined by g.c. The relative peak heights of the starting phosphonate, alcohol, and product ether were measured. Although the elution times of the majority of trimethylsiloxy compounds were not independently determined, the major new peak that appeared in the g.c. pattern of the alcohol–silyl phosphonate reaction mixture was presumed to be the ether. In this manner it was shown that methanol, ethanol, 1-butanol, cyclohexanol, 1-heptanol, and phenol *rapidly* equilibrated with bis(trimethylsilyl) methylphosphonate.

A. Demonstration of an Equilibrium.—When 0.33 cc. of bis(trimethylsilyl) methylphosphonate and 5 drops of cyclohexanol were mixed, the ratio of silyl ether to cyclohexanol peak heights was 1.58. Addition of 5 drops of *n*-propylamine resulted in the immediate increase of this ratio to 4.7.

B. Tertiary Alcohols.—When 0.33 cc. of the silyl phosphonate was contacted with 15 drops of *t*-butyl alcohol, the ratio of product ether to *t*-butyl alcohol was <0.0025. When this solution was heated for 10 min. at 110° this ratio increased to 0.30. An additional 8-min. heating at 110° had no further effect on the ratio.

When 0.33 cc. of the silyl ether was contacted with 15 drops of Eastman Practical *t*-amyl alcohol the ratio of product ether to *t*-amyl alcohol was 0.016. When the solution was heated for 15 min. at 80° the ratio increased to 0.25. An additional 27 min. at 80° and 10 min. at 110° had no effect on the ratio. When 9 drops of *n*-propylamine was added and the solution heated for 8 min. at 100°, the ratio increased to 0.56.

Attempted Reaction of Amines with Bis(trimethylsilyl) Methylphosphonate.—Examination of a solution of the phosphonate and diethylamine by g.c. indicated no reaction had occurred. Starting materials were the only peaks noted. Likewise, no reaction was evident between the phosphonate and *n*-propylamine even after heating at 100° for 20 min.

Reaction of Acetyl Chloride and Dimethyl Methylphosphonate.—A total of 122.2 g. (1.56 moles) of acetyl chloride was slowly

(7) This was prepared by Dr. F. Scotti of this laboratory by reacting triethylphosphite with β-chloroacrylonitrile.

(8) R. Rabinowitz, *J. Org. Chem.*, **26**, 5152 (1961).

(9) (a) Efforts to obtain a more satisfactory analysis were unsuccessful. (b) The first distillate boiled at 50°, the reported[4] boiling point of the methanol–trimethylsiloxymethane azeotrope. When a large-scale reaction of ethanol and the silyl phosphonate was carried out, the first fraction boiled at 67°. The reported[4] boiling point of the ethanol–trimethylsiloxyethane azeotrope is 66°.

(10) Samples were kindly supplied by Dr. Stanley H. Langer of this laboratory; see S. H. Langer, S. Connell, and I. Wender, *J. Org. Chem.*, **23**, 50 (1958).

added to 74.9 g. (0.534 mole) of the phosphonate during a 5-hr. addition period while refluxing. The condenser was attached to a Dry Ice trap, which, after a total of 24 hr. of refluxing had condensed 51.7 g. (1.02 moles) of methyl chloride. Fractionation of the reaction mixture gave acetic anhydride and 26.4 g. (0.13 mole) of a liquid, b.p. 100–101.5° (0.4 mm.), which was identified as dimethyl dimethylpyrophosphonate. The infrared spectrum showed P–CH_3 at 1325 and 900, P–OCH_3 at 1190 and 1050, P–O–P at 960, and P=O at 1265 cm.$^{-1}$.

Anal. Calcd. for $C_4H_{12}O_5P_2$: C, 23.7; H, 5.93. Found: C, 24.2; H, 6.25.

The residue in the distillation flask was a brown tacky immobile material which reacted rapidly with water.

Acknowledgment.—We wish to thank Drs. Joseph Pellon and Richard W. Young for their helpful suggestions and interest.

The Ammonolysis of 1,6-Anhydro-2,4-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranose and the Synthesis of 2,4-Diamino-2,4-dideoxy-D-glucose[1]

ROGER W. JEANLOZ AND ANNETTE M. C. RAPIN

Laboratory for Carbohydrate Research, Departments of Biological Chemistry and Medicine, Harvard Medical School and the Massachusetts General Hospital, Boston, Massachusetts

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Ammonolysis of 1,6-anhydro-2,4-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranose afforded one diamino and two monoamino derivatives. The structure of the first product was established as a 2,4-diamino-2,4-dideoxy derivative of D-glucose by its independent synthesis from 2-acetamido-1,6-anhydro-3-*O*-benzoyl-2-deoxy-4-*O*-methylsulfonyl-β-D-galactopyranose. One of the two monoamino compounds is presumably a derivative of 4-amino-4-deoxy-D-glucose.

Numerous diamino derivatives of hexoses have been isolated from antibiotics in the last few years. In all these compounds, the amino groups are located at positions C-2 or C-3 and at position C-6 of the carbon chain. The recent isolation by Sharon and Jeanloz,[2] from a polysaccharide of *Bacillus subtilis*, of a diamino hexose in which the two amino groups are probably located at positions C-2 and C-4 of the carbon chain has aroused interest in this type of derivative. The synthesis of 2,4-diamino-2,4-dideoxy-D-glucose was, therefore, investigated.

Numerous studies on the opening of epoxide rings of carbohydrates with ammonia have shown that the transdiaxal conformation was greatly favored when the spacial configuration of the starting material was stabilized by the presence of a 1,6-anhydro or a 4,6-*O*-benzylidene ring. During ammonolysis of 1,6-anhydro-2,4-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranose (II), transdiaxal opening resulted in the preponderant formation of 2,4-diamino-1,6-anhydro-2,4-dideoxy-β-D-glucopyranose isolated as the fully acetylated derivative VII. The formation of this diamino product VII could proceed *via* either monoepoxide intermediate, 1,6;3,4-dianhydro-2-*O*-*p*-tolylsulfonyl-β-D-galactopyranose (I) or 1,6;2,3-dianhydro-4-*O*-*p*-tolylsulfonyl-β-D-mannopyranose (III). The presence of traces of water could result in the hydrolytic splitting of the *p*-tolylsulfonyl groups. Since the newly formed hydroxyl groups would be in *trans* position to the epoxide groups, a second nucleophilic displacement would result in the formation of 1,6;2,3-dianhydro-β-D-gulopyranose (V) from I and 1,6;3,4-dianhydro-β-D-altropyranose (IV) from III, respectively.[3] Formation of the epoxide III seems, however, not to be favored, since reaction of II with sodium methoxide, even for prolonged periods of time, gives a monotosyl–monoepoxide product, which has been shown by Černý and Pacák[4] to be 1,6;3,4-dianhydro-2-*O*-*p*-tolylsulfonyl-β-D-galactopyranose (I). Additional evidence for the stability of I in the presence of alkali is shown by its formation during the reaction of 1,6-anhydro-2,3,4-tri-*O*-*p*-tolylsulfonyl-β-D-glucopyranose with a very large excess of barium hydroxide.[5]

In order to ascertain the *gluco* configuration of the diacetamido derivative VII, 2-acetamido-1,6-anhydro-3-*O*-benzoyl-2-deoxy-4-*O*-methylsulfonyl-β-D-galactopyranose (IX)[6] was treated with sodium azide, and the resulting azido compound VIII was hydrogenated and acetylated to give a compound VII inentical to the one obtained by ammonolysis of II. The displacement by an azide group of a sulfonyloxy group located in a pyranose ring in vicinal position to a *cis* hydroxyl group, with concomittant Walden inversion, has been reported recently.[7–9] Saponification of the 3-*O*-acetyl group gave crystalline VI.

Attempts to obtain 2,4-diamino-2,4-dideoxy-D-glucose as the dihydrochloride derivative by direct hydrolysis of VI were not successful. As had already been observed by Sharon and Jeanloz with the diamino sugar isolated from *Bacillus subtilis*[2] and more recently by Reist, *et al.*,[7] with derivatives of 4-amino-4-deoxy-D-glucose, hydrolysis of 4-amino-4-deoxy sugars results in extensive degradation. The hydrolysis of VI also was accompanied by much degradation and the hydrolyzate gave multiple spots on paper chromatograms. These

(1) Amino Sugars XXXV. This is publication no. 339 of The Robert W. Lovett Memorial Unit for the Study of Crippling Disease, Harvard Medical School at the Massachusetts General Hospital, Boston 14, Mass. This investigation has been supported by research grants from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, United States Public Health Service (Grant A-3564). This work was presented before the Division of Carbohydrate Chemistry, at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962.

(2) N. Sharon and R. W. Jeanloz, *J. Biol. Chem.*, **235**, 1 (1960).

(3) W. H. G. Lake and S. Peat, *J. Chem. Soc.*, 1069 (1939); J. G. Buchanan, *Chem. Ind.* (London), 1484 (1954); F. H. Newth, *J. Chem. Soc.*, 441 (1956).

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(5) R. M. Hann and N. K. Richtmyer, personal communication of Dr. N. K. Richtmyer.

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(7) R. D. Guthrie and D. Murphy, *Chem. Ind.* (London), 1473 (1962).

(8) E. J. Reist, R. R. Spencer, B. R. Baker, and L. Goodman, *ibid.*, 1794 (1962).

(9) M. L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, **27**, 4505 (1962).