filtrate was chromatographed over 1300 g. of Florisil. Fractions 20–27 (ethylene chloride:acetone 5:1) were recrystallized from ethyl acetate–Skellysolve B to give an additional 2.92 g. (30.2%), m.p. 206–210° of 3α,11β,17α-trihydroxypregnan-20-one.

Fractions 32–34 (acetone) were recrystallized from ethyl acetate–Skellysolve B to give 1.05 g. (10.9%) of 3α,11α,17α-trihydroxypregnan-20-one, melting at 157–158°.

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

Steroid Homologs Containing Pyridazinone and Related Nuclei[1]

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Heterocyclic analogs of cholesterol and testosterone in which the A ring of these compounds is replaced by a pyridazinone ring have been prepared. The synthesis involved degradation of the A ring of these steroids by removal of carbon atoms 3 and 4 to form γ-keto acids which were then allowed to react with hydrazine. In cholesterol the A ring was also replaced by the tetrahydropyridazone nucleus.

Steroids in which one or more of the rings of the cyclopentanoperhydrophenanthrene system have been replaced by heterocyclic nuclei may be expected to have interesting physiological properties. Compounds of this kind, especially where the heterocyclic ring contains nitrogen,[2-4] are rare and none containing pyridazine, pyridazinone or related systems are known. This paper describes the preparation of cholesterol and testosterone derivatives in which the A ring has been replaced by the pyridazinone or tetrahydropyridazone nucleus. The accompanying chart details the steps in the syntheses of these compounds and the yields realized in the cholesterol series [R = $CH_3CHCH_2CH_2CH_2CH(CH_3)_2$].

Route I → IX → VI was superior to the alternative Barbier–Wieland degradation (II → III → IV → V → VI) in the cholesterol series and the latter was therefore not carried out with testosterone (I, R = OH). However, II (R = OH) was obtained in 75% yield without difficulty by ozonization of testosterone. Lower yields of II (R = OH) were reported from ozonization of testosterone acetate.[2]

Keto acid II (R = C_8H_{17}) which is well known[5] gave ketal ester III as a glass, presumably a mixture of the mono- and di-esters of ethylene glycol. III was used directly to prepare crystalline IV. Hydrolysis of ketal IV and simultaneous dehydration gave a crude product which was converted without difficulty to VI. Keto acid VI showed no characteristic carbonyl absorption in the ultraviolet and gave a single carbonyl band at 5.67 μ in the infrared. Such a band is characteristic of a five-membered lactone and indicates that VI exists in the lactol form.

No crystalline product could be isolated from the hydrolysis mixture, which presumably contained mainly V (R = C_8H_{17}), but a crystalline 2,4-dinitrophenylhydrazone of the correct composition was obtained in high yield. V was regenerated almost quantitatively from this derivative as an oil which had the expected ultraviolet absorption.

Ozonization of V (R = C_8H_{17}) and reductive decomposition of the ozonide gave an oil from which a bis-2,4-dinitrophenylhydrazone corresponding in composition to a derivative of a ketoaldehyde was obtained. Treatment of the oil with hydrazine hydrate produced a complex reaction mixture from which was isolated by chromatography very low yields of several crystalline compounds. None of these proved to be the desired dihydropyridazine and structures were not determined. This reaction and alternative methods for preparing the dihydropyridazine are being examined and will be reported at a later time.

Although hydroxymethylenecholestenone[6] and hydroxymethylenetestosterone[7,8] are known, the latter has never been described carefully, and no report of the ozonization of either has appeared. In the cholestenone series lactol VI (R = C_8H_{17}) was isolated without difficulty when three molecular equivalents of ozone were allowed to react with hydroxymethylenecholestenone and the reaction mixture treated with hydrogen peroxide. No attempt was made to obtain diacid X (R = C_8H_{17}). The same procedure was applied to hydroxymethylenetestosterone, but water-soluble material made up most of the product and only a very low yield of pyridazinone VII (R = OH) was isolated from the hydrazine hydrate reaction on the portion insoluble in water. Diacid X (R = OH) was the only easily isolable product when less ozone was used, but reaction of the residue with hydrazine hydrate gave somewhat better yields of the pyridazinone. Lactol VI (R = OH) was isolated in crystalline form by chromatographing the mixture of crude acids from the ozonization.

An attempt was made to synthesize lactol VI (R = C_8H_{17}) by ozonization of the condensation product of cholestenone and ethyl oxalate[7-9]; crystalline material was not readily obtained from the product, and the infrared spectrum of the crude

(1) Taken in part from a thesis submitted by David C. Remy in partial fulfillment of the requirements for the M.S. degree, University of California, Los Angeles, August, 1952. Presented before the Organic Division of the American Chemical Society, Chicago, Illinois, September, 1953.

(2) C. C. Bolt, *Rec. trav. chim.*, **57**, 905 (1938).

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(4) St. Kaufman, *ibid.*, **73**, 1779 (1951).

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(6) J. G. Burr, W. F. Holton and G. N. Webb, *ibid.*, **72**, 4903 (1950).

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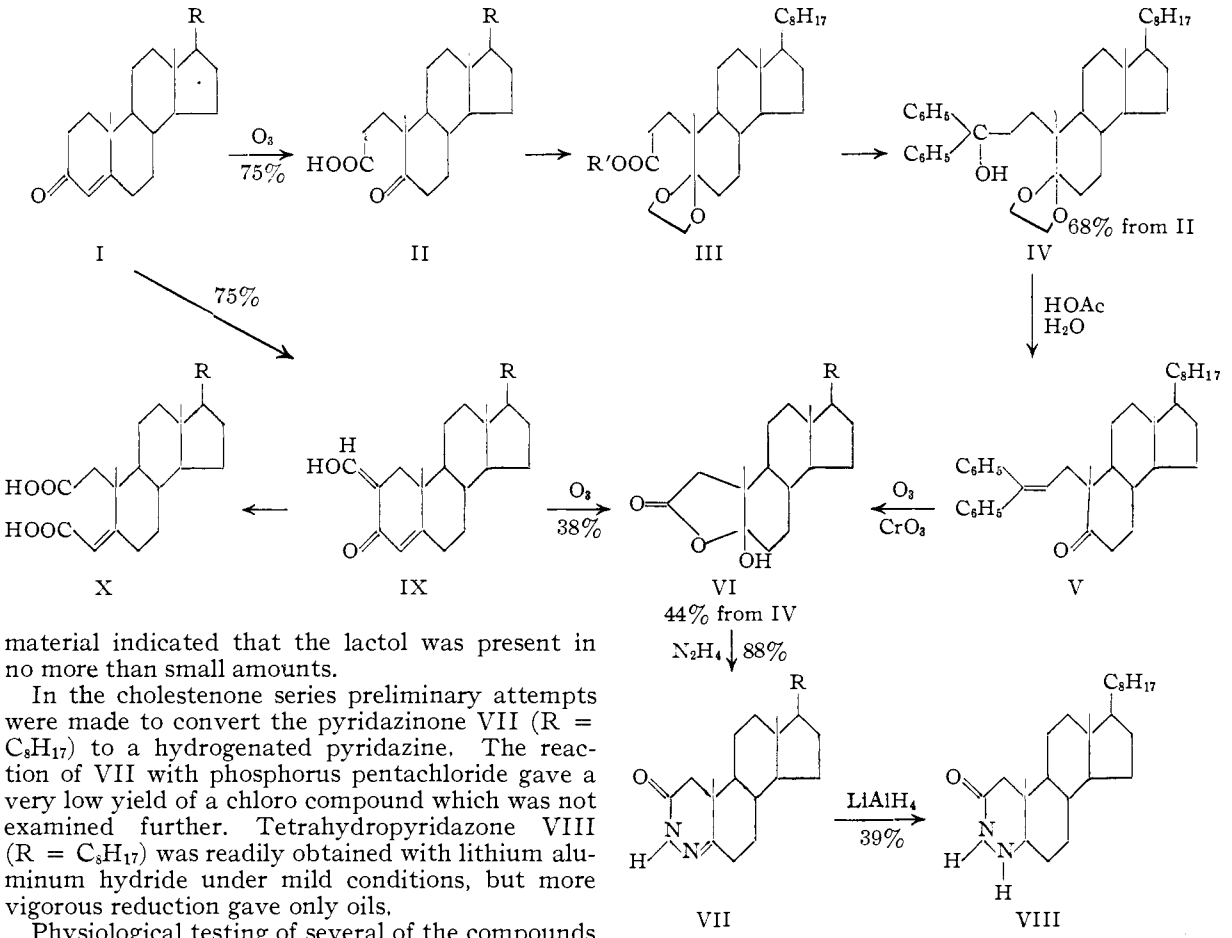

material indicated that the lactol was present in no more than small amounts.

In the cholestenone series preliminary attempts were made to convert the pyridazinone VII (R = C_8H_{17}) to a hydrogenated pyridazine. The reaction of VII with phosphorus pentachloride gave a very low yield of a chloro compound which was not examined further. Tetrahydropyridazone VIII (R = C_8H_{17}) was readily obtained with lithium aluminum hydride under mild conditions, but more vigorous reduction gave only oils.

Physiological testing of several of the compounds described is underway and will be reported elsewhere.

Experimental[10]

Preparation of Ethylene Ketal III (R′ = —CH_2CH_2O—).—Keto acid II[5] (R = C_8H_{17}) (9.0 g.) was dissolved in a mixture of benzene (200 ml.) and ethylene glycol (6.0 ml.) containing *p*-toluenesulfonic acid (150 mg.). The solution was heated under reflux for five hours and the water formed was removed continuously by azeotropic distillation. The benzene solution was washed with water, then sodium bicarbonate solution to remove unreacted acid, dried over magnesium sulfate and concentrated. The neutral light yellow glassy residue (10.5 g.) was not obtained in crystalline form. It was taken up in benzene (50 ml.), diluted with ether (200 ml.) and used directly in the Grignard reaction described below.

Preparation of Diphenylcarbinol Ketal (IV).—The ether-benzene solution of the ethylene ketal (III) (10.5 g.) described above was added dropwise with stirring at 0° during one hour to a solution of phenylmagnesium bromide prepared from magnesium (5.3 g.) and bromobenzene (25 ml.) in ether (150 ml.). The mixture was stirred at room temperature overnight and then the carbinol was liberated by dropwise addition of saturated ammonium chloride solution (38 ml.). The clear ether layer was decanted and the precipitated magnesium salts were washed with ether by decantation. The combined extracts were steam distilled and alcohol (75 ml.) and 6 *N* sodium hydroxide (50 ml.) were added to the residue of crystalline solid and water (150 ml.). This mixture was heated under reflux two hours to saponify any unreacted ester. The alcohol was removed by distillation and the organic material extracted into ether. Concentration of the ether extracts gave an oily residue (12.17 g.). The oil was taken up in ether (40 ml.) and pentane (150 ml.) and concentrated until precipitation began. The precipitate of colorless needles weighed 8.92 g. (68.4%), m.p. 152–153.5°. Recrystallization from petroleum ether gave an analytical sample, m.p. 154–154.5°, $[\alpha]^{23}D$ +10.8° (chloroform).

Anal. Calcd. for $C_{40}H_{58}O_3$: C, 81.86; H, 9.96. Found: C, 81.81; H, 9.97; ultraviolet spectrum $\lambda_{max}^{cyclohexane}$ 259 mμ (log ε 2.7).

Preparation of Diphenylethylene Ketone (V).—Ketal diphenylcarbinol (IV) (0.50 g.) was dissolved in 30 ml. of glacial acetic acid and 0.5 ml. of water and the solution refluxed for six hours. The acetic acid was removed by distillation and the oily residue taken up in ether, washed with sodium carbonate solution, water, dried over sodium sulfate and concentrated. The resultant oil could not be obtained crystalline. The ultraviolet spectrum showed $\lambda_{max}^{cyclohexane}$ 251 mμ (log ε 4.20).

The 2,4-dinitrophenylhydrazone prepared in alcoholic sulfuric acid solution had m.p. 150–151°, $[\alpha]^{24}D$ +41° (chloroform).

Anal. Calcd. for $C_{44}H_{56}O_4N_4$: C, 74.96; H, 8.01. Found: C, 75.05; H, 8.04.

The diphenylethylene ketone (V) prepared by the method described above was always contaminated with a small amount of diphenylethylene ketal. The pure ketone V was obtained by regeneration from the 2,4-dinitrophenylhydrazone using the method of Mattox and Kendall.[11]

The 2,4-dinitrophenylhydrazone of V (2.54 g.) was dissolved in 160 ml. of chloroform and treated under nitrogen with a solution of 40 ml. of pyruvic acid, 40 ml. of acetic and 3.6 ml. of 48% hydrobromic acid in 10 ml. of acetic acid. The mixture was maintained at 45° for six hours and then diluted with 300 ml. of chloroform and 200 ml. of water, the layers separated and the aqueous layer extracted twice with 100-ml. portions of chloroform. The combined ex-

(10) All melting points are corrected.

(11) V. R. Mattox and E. C. Kendall, *J. Biol. Chem.*, **188**, 287 (1951).

tracts were washed with water, 5% sodium bicarbonate solution (until the aqueous solution was colorless), again with water, dried over magnesium sulfate and concentrated leaving a yellow oil. This material was then chromatographed on neutral alumina to remove a small amount of unreacted 2,4-dinitrophenylhydrazone and the pure, colorless ketone V was eluted with 20% benzene-ligroin. It weighed 1.85 g. (98%), $[\alpha]^{25}D$ +90 (chloroform). It could not be induced to crystallize.

Hydroxymethylenecholestenone (IX, R = C_8H_{17}).—This was prepared by a modification of the procedure of Burr, Holton and Webb.[6] Cholestenone (20 g.) was dissolved in a mixture of dry benzene (250 ml.) and ethyl formate (20 ml.) and treated with sodium hydride (3.0 g.). Reaction commenced immediately with precipitation of the enolate salt and after two days the remaining sodium hydride was decomposed by the addition of a solution of methanol (20 ml.), in ether (100 ml.) and the salt filtered off. It weighed 25.4 g. The free enol was obtained by suspending the salt in ether (350 ml.) and 150 ml. of 2 *N* hydrochloric acid and shaking the mixture until the salt dissolved. The layers were separated and the ether solution was washed with water, saturated sodium chloride solution, dried over magnesium sulfate and concentrated. The oily residue crystallized from pentane as yellow prisms, m.p. 109.5–111.5°, 15.99 g. (74.5%) (reported[6] m.p. 112–113°); ultraviolet spectrum $\lambda_{max}^{alc.}$ 252 mμ (log ε 4.05) and 306 mμ (log ε 3.76).

Preparation of Lactol (VI, R = C_8H_{17}). (A) **By Ozonization of Hydroxymethylenecholestenone.**—Hydroxymethylenecholestenone (4.0 g.) dissolved in 40 ml. of acetic acid and 40 ml. of ethyl acetate was cooled in an ice–salt-bath and treated with three molecular equivalents of ozone. The nearly colorless solution was diluted with 40 ml. of water and 10 ml. of 30% hydrogen peroxide and on standing 48 hours deposited 1.43 g. (37.8%) of acidic material, m.p. 157–159°. Two recrystallizations from ether–pentane gave an analytical sample of the lactol (VI, R = C_8H_{17}), as colorless needles, m.p. 166.5–167.5°, $[\alpha]^{24}D$ −29.8° (chloroform).

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 76.87; H, 10.84. Found: C, 76.70; H, 10.56.

The ultraviolet spectrum showed no characteristic carbonyl absorption and the infrared spectrum showed only a single carbonyl band at 5.67 μ characteristic of a five-membered lactone. Thus the keto acid must exist in the lactol form VI.

Although isolation of the remaining organic material from the mother liquors showed that all the hydroxymethylenecholestenone had been converted to acidic substances no more of the lactol could be isolated and an infrared spectrum of this crude acidic material showed only slight absorption at 5.67 μ indicating that only a small amount of lactol was present.

(B) **By Ozonization of the Diphenylethylene Ketone** (V). —Ketal diphenylcarbinol (IV) (1.35 g.) was dissolved in 50 ml. of acetic acid containing 4.0 ml. of water and the solution refluxed for three hours. The acetic acid was removed under vacuum and the residue taken up in 15 ml. of ethyl acetate and 15 ml. of acetic acid and treated with two molecular equivalents of ozone at 0°. The solution of ozonide was diluted with 15 ml. of water and allowed to stand overnight and then evaporated to dryness under reduced pressure. The residue was dissolved in 50 ml. of acetic acid and oxidized at 45–50° with 0.50 g. of chromic acid in 2 ml. of water during one half hour. The excess chromic acid was reduced with sulfur dioxide and the solution concentrated under reduced pressure. Water (100 ml.) was added, and the aqueous solution extracted with ether. The combined ether extracts were extracted with three 50-ml. portions of 0.25 *N* sodium hydroxide. The combined basic extracts were then acidified with 3 *N* hydrochloric acid and the precipitate again extracted into ether. The extracts were washed with water, saturated sodium chloride solution, dried over sodium sulfate and concentrated. The residue was crystallized from ether–petroleum ether to give 394 mg. (44%) of lactol, m.p. 152–154°. Two recrystallizations from ether–petroleum ether raised the melting point to 163.5–164.5°, undepressed on admixture with a sample prepared as in (A).

Preparation of Pyridazinone (VII, R = C_8H_{17}). The lactol (VI, R = C_8H_{17}) (1.53 g.) was dissolved in 10 ml. of ethanol and 0.7 ml. of hydrazine hydrate and heated under reflux for four hours. The solution was diluted with 10 ml. more ethanol and on cooling deposited large, brilliant, colorless plates, 0.93 g., m.p. 211–212°. Dilution of the mother liquors with water gave a second crop of 0.40 g., m.p. 211–212° (total yield 88%). Recrystallization from methanol raised the melting point to 212.0–212.5°, $[\alpha]^{24}D$ +37.9° (chloroform).

Anal. Calcd. for $C_{25}H_{42}ON_2$: C, 77.66; H, 10.95. Found: C, 77.55; H, 10.67; ultraviolet spectrum $\lambda_{max}^{methanol}$ 244 mμ (log ε 3.92).

Hydroxymethylenetestosterone (IX, R = OH).—Sodium hydride (3.0 g.) was added to a solution of testosterone[12] (10.0 g.) in benzene (200 ml.) and ethyl formate (10 ml.) and the reaction mixture was allowed to stand under nitrogen for three days. Methanol (10 ml.) was added to decompose the excess hydride and the solution was then diluted with 300 ml. of water. The layers were separated and the basic solution extracted with ether to remove neutral material. The aqueous layer was then acidified with 80 ml. of 3 *N* hydrochloric acid and the liberated enol extracted with benzene and ether. The combined organic extracts were washed with water, saturated sodium chloride solution, dried over magnesium sulfate and concentrated. The residue of reddish-yellow oil was taken up in 10 ml. of ether and on standing deposited small light yellow crystals (9.12 g., 83%), m.p. 162–162.5°. Recrystallization from chloroform–ether gave an analytical sample, m.p. 165–165.5°, $[\alpha]^{24}D$ +52.5 (alcohol).

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.99; H, 8.73; ultraviolet spectrum $\lambda_{max}^{alc.}$ 252 mμ (log ε 4.06) and 307 mμ (log ε 3.76).

Ozonization of Hydroxymethylenetestosterone (IX, R = OH). **Preparation of Diacid (X) and Pyridazinone** (VII, R = OH).—Hydroxymethylenetestosterone (3.00 g.) was dissolved in 30 ml. of ethyl acetate and 30 ml. of acetic acid and ozonized (2.2 molar equivalents) at −10 to −15°. The resulting light yellow solution was diluted with 30 ml. of water and 7.5 ml. of 30% hydrogen peroxide and allowed to stand 48 hours. The colorless solution was diluted with 400 ml. of ether and the organic layer washed eight times with 75-ml. portions of water to remove the acetic acid. The ether solution was extracted with three 30-ml. portions of 1 *N* sodium hydroxide, the basic extracts acidified with 20 ml. of 6 *N* hydrochloric acid and the precipitate again extracted with ether. The combined ether extracts were washed with water, saturated sodium chloride solution, dried over magnesium sulfate and concentrated leaving a residue of 2.14 g. of amorphous solid. The residue was taken up in a small amount of ether and on standing deposited 0.475 g. of colorless crystals. Recrystallization from methanol–ether gave colorless prisms of the diacid X, softening at 200–205° with change in crystal form and melting sharply at 262–263°, $[\alpha]^{24}D$ +82.8° (alcohol).

Anal. Calcd. for $C_{19}H_{28}O_5$: C, 67.83; H, 8.29. Found: C, 67.56; H, 8.23; ultraviolet spectrum $\lambda_{max}^{alc.}$ 222 mμ (log ε 4.06).

The mother liquors from which the crystalline diacid was obtained were concentrated. An infrared spectrum of this amorphous solid showed strong carbonyl absorption at 5.67 μ indicating that the lactol (VI, R = OH) was present.

The amorphous residue (1.66 g.) was dissolved in 10 ml. of ethanol and 0.75 ml. of hydrazine hydrate and heated on the steam-bath for three hours. The solution was diluted with 5 ml. of water and the alcohol removed under vacuum. The aqueous solution was extracted with ether, the ether extracts washed with potassium bicarbonate, dried over magnesium sulfate and concentrated. The residue crystallized from methanol–water to give 298 mg. (11%) of pyridazinone (VII, R = OH), which softened about 100°, resolidified and melted at 177-179°. For analysis a sample was recrystallized from ethyl acetate–ether and then from tetrahydrofuran–water. This sample softened at 105-120°, resolidified and melted sharply at 181–182°, $[\alpha]^{24}D$ +42.0° (chloroform).

Anal. Calcd. for $C_{17}H_{26}O_2N_2$: C, 70.31; H, 9.02. Found: C, 70.39; H, 8.99; ultraviolet spectrum $\lambda_{max}^{alc.}$ 244 mμ (log ε 3.90).

The bicarbonate extracts from above were acidified and

(12) We wish to thank Dr. Franz Sondheimer of Syntex, S. A., for a gift of the testosterone used in this work.

extracted with ethyl acetate to give 0.260 g. more of the di-acid X, m.p. 256–258° (total yield 23.1%).

In another run the lactol (VI, R = OH) was isolated by chromatography of the crude amorphous acidic material on acetic acid washed alumina. The lactol (VI, R = OH) was eluted with chloroform and crystallized from methanol–ether as colorless prisms, m.p. 178–179°, $[\alpha]^{24}D$ +27° (chloroform).

Anal. Calcd. for $C_{17}H_{26}O_4$: C, 69.35; H, 8.93. Found: C, 69.40; H, 9.18.

The infrared spectrum showed a single carbonyl band at 5.69 μ characteristic of a five-membered lactone.

Preparation of Tetrahydropyridazone (VIII).—To the pyridazinone (VII, R = C_8H_{17}) (200 mg.) dissolved in 20 ml. of ether was added 2 ml. of a 0.9 *M* lithium aluminum hydride solution and after one minute the excess hydride was decomposed with ethyl acetate. Ethyl acetate (50 ml.) and a solution of 3 g. of Rochelle salt in 20 ml. of water were then added, the layers separated, and the aqueous layer extracted with chloroform. The combined extracts were washed with water, saturated sodium chloride solution and concentrated. The crystalline residue was triturated with ether and the colorless crystals filtered off to give 78 mg. (39%) of the tetrahydropyridazone (VIII). For analysis a sample was recrystallized from benzene–ether, m.p. 274–276°, $[\alpha]^{24}D$ +104.2° (chloroform).

Anal. Calcd. for $C_{25}H_{44}ON_2$: C, 77.26; H, 11.41. Found: C, 77.09; H, 11.34.

Preparation of Keto Acid II (R = OH).—Testosterone (4.0 g.) was dissolved in 40 ml. of ethyl acetate and 40 ml. of acetic acid and ozonized (2 molar equivalents) at −10°. The resulting colorless solution was diluted with 25 ml. of water and 4 ml. of 30% hydrogen peroxide and allowed to stand three days. After addition of ether, the organic layer was washed six times with 50-ml. portions of water and then extracted with 160 ml. of 1 *N* sodium hydroxide in five portions. The basic extracts were acidified, and the precipitate again extracted into ether. The ether extracts were washed with water, saturated sodium chloride solution, dried over magnesium sulfate and concentrated leaving a crystalline solid. Recrystallization from acetone–ether gave 3.20 g. (75%) of the keto acid, m.p. 197–199°. Recrystallization from acetone–water gave an analytical sample, m.p. 204–205.5°, $[\alpha]^{24}D$ −30.0° (chloroform). Further recrystallization from acetone did not raise the m.p. although Bolt[2] reported 206.5–207° for this compound.

Anal. Calcd. for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15. Found: C, 70.17; H, 9.32.

Reductive Cleavage of the Ozonide of Diphenylethylene Ketone (V).—Diphenylethylene ketone (0.95 g.) (regenerated from the 2,4-dinitrophenylhydrazone) was dissolved in 40 ml. of ethyl acetate and 30 ml. of methanol and ozonized (2.5 molar equivalents) at −10°. Zinc (3 g.) and 20 ml. of 75% acetic acid were added to the resulting ice-cold solution and the mixture was stirred for 15 minutes. The zinc was filtered off and the solvents removed under vacuum. The residue was taken up in ether and water, the layers separated, the organic layer washed with water, 5% sodium bicarbonate solution, water, dried over magnesium sulfate and concentrated leaving 1.00 g. of colorless oil which could not be induced to crystallize.

This oil (0.10 g.) was treated with an alcoholic sulfuric acid solution containing 0.10 g. of 2,4-dinitrophenylhydrazine. An orange-red precipitate (90 mg.) so obtained was chromatographed on 9.0 g. of neutral alumina. Benzophenone 2,4-dinitrophenylhydrazone was eluted first with 50% benzene–ligroin and recrystallized from chloroform–ethanol as orange-red prisms, m.p. 242–242.5°.

A second compound was obtained by elution with 20% chloroform–benzene and recrystallization from chloroform–benzene gave yellow fluffy crystals, m.p. 166–168° (35 mg.). Recrystallization again from chloroform–ligroin gave orange clusters, m.p. 213–214°, apparently another crystalline form. Analysis indicated it was a bis-2,4-dinitrophenylhydrazone.

Anal. Calcd. for $C_{37}H_{56}O_8N_8$: C, 60.38; H, 6.86. Found: C, 60.36; H, 6.95.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE ROBERT W. LOVETT MEMORIAL FOUNDATION FOR THE STUDY OF CRIPPLING DISEASES, MASSACHUSETTS GENERAL HOSPITAL, AND THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, HARVARD MEDICAL SCHOOL, BOSTON]

4,6-Di-*O*-methyl-D-glucosamine Hydrochloride (2-Amino-2-deoxy-4,6-di-*O*-methyl-D-glucose Hydrochloride)[1,2]

BY ROGER W. JEANLOZ

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4,6-Di-*O*-methyl-D-glucosamine hydrochloride (2-amino-2-deoxy-4,6-di-*O*-methyl-D-glucose hydrochloride) has been prepared *via* two independent routes and transformed to the crystalline N-(2′-hydroxynaphthylidene) derivative.

Synthesis of the various methylated 2-amino-2-deoxy-D-glucopyranoses has been undertaken[3] with the purpose of using them as reference compounds in the elucidation of the structure of complex natural polysaccharides by the methylation procedure.

Synthesis of 2-amino-2-deoxy-4,6-di-*O*-methyl-D-glucose was of special interest, since this compound should result from the degradation of methylated hyaluronic acid[4] if a 1,3-glucuronido–glucosamine linkage exists. Evidence for such a linkage has been advanced as a result of periodate oxidation studies[5] and definitely established by study of a degradation product.[6]

Synthesis of the dimethyl compound has been accomplished *via* two routes starting from methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside[7] (I) as shown in the accompanying diagram.

Protection of the hydroxyl group in position 3 was obtained by benzoylation (III) or tosylation

(1) Studies on hyaluronic acid and related substances VIII. This is publication No. 142 of the Robert W. Lovett Memorial Foundation for the Study of Crippling Diseases, Harvard Medical School, Boston, Massachusetts. This investigation has been supported by research grants from Eli Lilly and Company and from the National Institute of Arthritis and Metabolic Diseases, of the National Institutes of Health, Public Health Service.

(2) Presented before the Division of Sugar Chemistry at the 122nd Meeting of the American Chemical Society, Atlantic City, New Jersey, September, 1952.

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