very potent hypotensive action. Most of these compounds were active in doses of 3 mg./kg. We will publish a fuller account of the pharmacology of these compounds separately.

Experimental

General Preparation of N-Dialkylaminoalkyl Imides and Their Reduction.—The preparation of diethylaminoethyl hexahydrophthalimide and its reduction will illustrate the procedure followed.

(a) **Diethylaminoethyl Hexahydrophthalimide.**—Into a flask fitted with a reflux condenser was placed 0.40 mole of hexahydrophthalic anhydride. With cooling and intermittent shaking 0.41 mole of diethylaminoethylamine was slowly added. After the reaction had subsided, the reaction mixture was allowed to cool to room temperature and then was heated in an oil-bath maintained at 175° for two hours. The resulting crude product was fractionated in vacuum and the pure imide was obtained as a colorless oil which boiled at 132–135° (2 mm.) in 81% yield.

(b) **Reduction.**—In a 2-liter 3-necked flask fitted with a mercury sealed stirrer, dropping funnel and a long condenser to which a calcium chloride tube was attached were placed 19 g. of lithium aluminum hydride and 1 liter of absolute ether. After solution had been effected, a solution of 50 g. of diethylaminoethyl hexahydrophthalimide dissolved in 200 ml. of absolute ether was added dropwise with rapid stirring. The rate of addition was adjusted so that the reaction mixture refluxed gently. During the addition a fine suspension of solid precipitated. After the addition was completed, the stirring was continued under reflux for two hours and the mixture allowed to stand overnight. The flask was cooled in an ice-bath and, with vigorous stirring, the reaction mixture was decomposed by the dropwise addition of water. The addition of the water was regulated so that reflux was just maintained; and then 10 cc. in excess was added at the end. After decomposition the mixture was stirred an additional hour and filtered with suction. The inorganic precipitate was well pressed and washed with 3 portions of ether. After drying over sodium sulfate, the ether was stripped and the residue distilled in vacuum. There was obtained 41 g. (92%) of material boiling at 77–80° (2 mm.).

The methiodides were prepared in the usual way employing absolute alcohol as a solvent.

The hydrochlorides were produced in the usual way by means of alcoholic hydrogen chloride.

Acknowledgment.—We are indebted to the Schwarzkopf Microanalytical Laboratories, Middle Village, Long Island, N. Y., for the microanalyses. We wish to express our thanks to Carbide and Carbon Chemicals Company for generous supplies of materials and to the Sharples Chemicals, Inc., for a generous gift of 3,6-endoxyhexahydrophthalic anhydride.

WASHINGTON 7, D. C.

[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

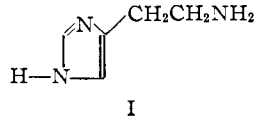
1,2,4-Triazole Analogs of Histamine

BY C. AINSWORTH AND R. G. JONES

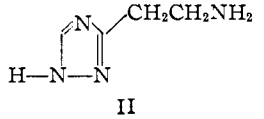
RECEIVED JUNE 11, 1953

3-β-Aminoethyl-1,2,4-triazole and several of its derivatives have been synthesized and tested for pharmacological activity. The parent compound and, to a lesser degree, 3-β-benzylaminoethyl-, 3-β-isopropylaminoethyl- and 3-β-acetamidoethyl-1,2,4-triazole have typical histamine-like activity. Furthermore, these compounds are effective orally.

A number of compounds patterned after histamine (I) have been synthesized and tested in this Laboratory.[1] The object of this work has been to find substances possessing useful physiological activities without the undesirable effects of histamine. The compounds so far examined have been nitrogen heterocycles carrying the β-aminoethyl side chain.[2] Most activity has been found in compounds with small, unsubstituted rings (*e.g.*, thiazole and pyrazole).[1,2c,3] In this paper we describe the preparation and properties of 3-β-aminoethyl-1,2,4-triazole (II) and some of its derivatives.

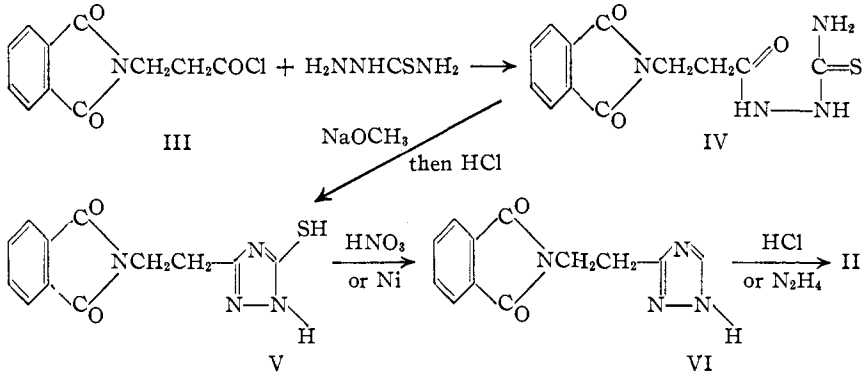


I



II

The method of synthesizing II is outlined by the accompanying series of reactions



The acyl thiosemicarbazide IV was obtained from the readily available acid chloride III[4] and thiosemicarbazide in dry pyridine.[5] Compound IV was cyclized with sodium methylate in alcohol and V was isolated in good yields after acidification of the reaction mixture. Removal of the mercapto group of V was best accomplished by oxidation with nitric acid.[6] Raney nickel desulfurization proved less satisfactory. For optimum yields in the nitric

(1) H. M. Lee and R. G. Jones, *J. Pharmacol. Exptl. Therap.*, **95**, 71 (1949).

(2) (a) R. G. Jones, THIS JOURNAL, **71**, 383 (1949); (b) R. G. Jones, E. C. Kornfeld and K. C. McLaughlin, *ibid.*, **72**, 3539 (1950); (c) R. G. Jones, E. C. Kornfeld and K. C. McLaughlin, *ibid.*, **72**, 4526 (1950).

(3) R. G. Jones and M. J. Mann, *ibid.*, **75**, 4048 (1953).

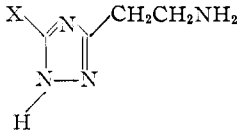
(4) S. Gabriel, *Ber.*, **41**, 242 (1908).

(5) This method of synthesis was described by E. Hoggarth, *J. Chem. Soc.*, 1160 (1949).

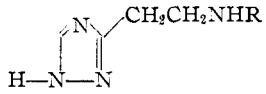
(6) R. G. Jones, THIS JOURNAL, **71**, 644 (1949).

acid conversion of V to VI it was essential that V be carefully purified.

In the course of the present work several derivatives and analogs of II were synthesized. Compounds VII, VIII and IX were obtained from V by appropriate and well known reactions.



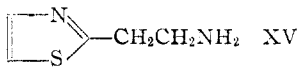
VII, X = SH
VIII, X = SCH_3
IX, X = SO_2NH_2



X, R = $CH(CH_3)_2$
XI, R = $CH_2C_6H_5$
XII, R = $CONH_2$
XIII, R = COC_6H_5
XIV, R = $COCH_3$

Reductive alkylation of II using acetone and benzaldehyde in the presence of hydrogen and a platinum catalyst led to derivatives X and XI, respectively. The urea compound XII and the benzoyl compound XIII were obtained by standard procedures. The acetyl derivative XIV was prepared by the Schotten–Baumann method under carefully controlled conditions. Heating II with acetic anhydride and acetic acid, or heating XIV with aqueous base, gave a compound of unknown structure with an analysis corresponding to the formula $C_{13}H_{10}N_4O_2$.

3-β-Aminoethyl-1,2,4-triazole (II) has been tested for physiological activity, and, although the test results will be reported in detail elsewhere, some of the interesting findings are mentioned here. This compound produces a typical histamine-like responce on an isolated guinea-pig ileum strip and on a weight basis is about one-sixth as active as histamine. Thus, on the isolated tissue, II is among the most potent histamine analogs so far examined and is of the same order of activity as 2-β-aminoethylthiazole (XV).[1,2c]



XV

In the anesthetized cat, compound II acts as a powerful stimulant of gastric secretion. It appears to be even more active than histamine itself in this test. In the dog, however, II appears to have about one-twenty-fifth the activity of histamine,[7] and indications are that it also stimulates gastric acid secretion in the human.

The effect of II on the blood pressure of mammals is of considerable interest. It is about one-fiftieth as active as histamine in lowering the blood pressure of an anesthetized cat. The duration of action, however, is much longer than that of histamine. In the hypertensive dog, hypertensive rat and the human, II has a profound and extended blood-pressure-lowering effect. Furthermore, in contrast with histamine, it is highly effective orally.

Compound II is considerably more active physiologically than the isomeric 4-β-aminoethyl-1,2,3-triazole.[8] Of particular interest is the fact that some of the derivatives of II, notably the isopropyl X, benzyl XI and acetyl XIV compounds retain the pharmacological activity.

(7) Private communication from Dr. M. I. Grossman, University of Illinois Medical School.

(8) J. C. Sheehan and C. A. Robinson, THIS JOURNAL, **71**, 1436 (1949).

Acknowledgment.—The authors are grateful to W. L. Brown, H. L. Hunter and G. M. Maciak for the microanalyses. The pharmacological tests were carried out by Dr. H. M. Lee and associates and by Drs. O. M. Helmer, R. E. Shipley and associates.

Experimental[9]

1-β-Phthalimidopropionylthiosemicarbazide (IV).—A stirred mixture of 102 g. (1.1 moles) of thiosemicarbazide and 700 ml. of thoroughly dry pyridine in a 2-l. flask was cooled to −5°. Portionwise, 237 g. (1.0 mole) of β-phthalimidopropionyl chloride[4] was added, over a one- to two-hour period, at such a rate that the temperature did not exceed 0°. The mixture, after standing overnight, during which time it attained room temperature, was poured with stirring into 2 l. of ice-water. The heavy white solid which formed was collected on a large buchner funnel and was washed successively with 1 l. of ice-water, 1 l. of 50% aqueous acetic acid and finally with 1 l. of ice-water. The product (235–250 g., 80–85% yield) was obtained after recrystallization from acetic acid as white needles; m.p. 238–239° dec.

Anal. Calcd. for $C_{12}H_{12}N_4O_3S$: C, 49.31; H, 4.14; S, 10.97. Found: C, 49.26; H, 4.29; S, 10.62.

3-β-Phthalimidoethyl-1,2,4-triazole-5-thiol (V).—A mixture of 292 g. (1.0 mole) of 1-β-phthalimidopropionylthiosemicarbazide, 60 g. (1.1 moles) of sodium methylate and 2.5 l. of absolute ethanol was heated under reflux overnight. About 2 l. of the solvent was removed by evaporation under reduced pressure, and the residue was added with stirring to 2 l. of ice-water containing 125 ml. of concentrated hydrochloric acid. After standing, the thiol was collected and was washed successively with 500 ml. of water, 200 ml. of 50% aqueous acetic acid and finally with 200 ml. of glacial acetic acid. The 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol (140 g., 50% yield) was recrystallized from acetic acid and obtained as white needles; m.p. 295–297°.

Anal. Calcd. for $C_{12}H_{10}N_4O_2S$: C, 52.55; H, 3.67; N, 20.43; S, 11.68. Found: C, 52.40; H, 3.83; N, 20.67; S, 11.66.

3-β-Aminoethyl-1,2,4-triazole-5-thiol (VII).—To a suspension of 13.7 g. (0.05 mole) of 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol in 50 ml. of water was added 10 ml. (0.20 mole) of hydrazine hydrate. Solution was complete within five minutes, and, after standing at room temperature overnight, a heavy precipitate had formed. The solid was collected and recrystallized from 200 ml. of hot water. It separated as needles; m.p. 296–298° dec. The yield was 4.5 g. (61%).

Anal. Calcd. for $C_4H_8N_4S$: C, 33.32; H, 5.59; N, 38.85; S, 22.23. Found: C, 33.58; H, 5.52; N, 38.55; S, 22.12.

The hydrochloride was formed by dissolving the base in dilute hydrochloric acid and concentrating the solution to dryness under reduced pressure. The 3-β-aminoethyl-1,2,4-triazole-5-thiol hydrochloride separated from methanol, after the addition of ether, as needles; m.p. 270°.

Anal. Calcd. for $C_4H_8N_4S \cdot HCl$: C, 26.59; H, 5.02; Cl, 19.63. Found: C, 26.36; H, 5.10; Cl, 19.33.

3-(β-Phthalimidoethyl)-5-methylmercapto-1,2,4-triazole.—To the suspension, resulting from addition of 27.4 g. (0.1 mole) of 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol and 5.4 g. (0.1 mole) of sodium methylate to 200 ml. of ethanol, was added 6.2 ml. (0.1 mole) of methyl iodide. After heating under reflux for two hours, the solvent was removed by evaporation under reduced pressure. The residue was extracted with 150 ml. of hot ethanol which upon cooling deposited 20 g. of 3-(β-phthalimidoethyl)-5-methylmercapto-1,2,4-triazole; m.p. 170–172°. A small sample was recrystallized from water. It separated as dendritic crystals; m.p. 170–172°.

Anal. Calcd. for $C_{13}H_{12}N_4O_2S$: C, 54.15; H, 4.20; S, 11.12. Found: C, 53.94; H, 4.31; S, 11.20.

3-(β-Aminoethyl)-5-methylmercapto-1,2,4-triazole Dihydrochloride (VIII).—To a suspension of 5.8 g. (0.02 mole) of 3-(β-phthalimidoethyl)-5-methylmercapto-1,2,4-triazole and

(9) Melting points, unless otherwise indicated, were taken on a Fisher–Johns block.

50 ml. of water was added 3 ml. (0.06 mole) of hydrazine hydrate. After standing at room temperature overnight, the solvent was removed by evaporation under reduced pressure, and the residue was extracted with 100 ml. of hot benzene. The benzene was evaporated, and the resulting solid was dissolved in ethanol. Addition of hydrogen chloride caused 3.2 g. (70% yield) of white solid to separate. After recrystallization from methanol–ether mixture, the product melted with decomposition at 218° (capillary).

Anal. Calcd. for $C_5H_{10}N_4S\cdot 2HCl$: N, 24.24; Cl, 30.66. Found: N, 23.92; Cl, 30.51.

Alternatively, a solution of 5.8 g. (0.02 mole) of 3-β-(phthalimidoethyl)-5-methylmercapto-1,2,4-triazole and 50 ml. of 6 *N* hydrochloric acid was heated under reflux for six hours. The phthalic acid which formed on cooling was removed and the filtrate was evaporated to dryness under reduced pressure. The residue consisting of 3.5 g. (76% yield) of 3-(β-aminoethyl)-5-methylmercapto-1,2,4-triazole dihydrochloride was recrystallized from methanol–ether mixture.

3-β-Phthalimidoethyl-1,2,4-triazole-5-sulfonamide.[10]—A suspension of 2.7 g. (0.01 mole) of 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol and 100 ml. of 10% aqueous acetic acid was cooled to 0°. Chlorine was bubbled into the stirred mixture at such a rate that the temperature did not exceed 10°. After one hour, the resulting white solid was collected on a buchner funnel and was added directly to 100 ml. of concentrated ammonium hydroxide. The solution, after evaporation on the steam-cone overnight, left a solid which was slurried with 50 ml. of 1 *N* hydrochloric acid. The product was collected and recrystallized from water to yield 1.3 g. (40%) of 3-β-phthalimidoethyl-1,2,4-triazole-5-sulfonamide; m.p. 280–282° dec.

Anal. Calcd. for $C_{12}H_{11}N_5O_4S$: N, 21.79; S, 9.98. Found: N, 21.57; S, 9.92.

3-β-Aminoethyl-1,2,4-triazole-5-sulfonamide Hydrochloride (IX).—A solution of 3.2 g. (0.01 mole) of 3-β-phthalimidoethyl-1,2,4-triazole-5-sulfonamide, 3 ml. (0.06 mole) of hydrazine hydrate and 50 ml. of methanol was heated under reflux for one-half hour during which time a solid separated. The solvent was removed under reduced pressure, and the resulting residue was dissolved in 50 ml. of water. Phthalhydrazide, which precipitated upon the addition of 6 *N* hydrochloric acid, was removed by filtration. The filtrate was taken to dryness, treated with 50 ml. of 1 *N* sodium hydroxide and again was evaporated to dryness under reduced pressure to remove any remaining hydrazine. Fifty ml. of 6 *N* hydrochloric acid was added, and the resulting solution was evaporated under reduced pressure. The residue was extracted with 50 ml. of absolute ethanol, and addition of dry ether to the filtered extract gave 3-β-aminoethyl-1,2,4-triazole-5-sulfonamide hydrochloride as irregular white prisms; m.p. 170° dec.

Anal. Calcd. for $C_4H_9N_5O_2S\cdot HCl$: C, 21.10; H, 4.43; N, 30.76. Found: C, 21.77; H, 4.50; N, 30.49.

Hydrolysis of the phthalimido compound with 6 *N* hydrochloric acid also gave 3-β-aminoethyl-1,2,4-triazole-5-sulfonamide hydrochloride.

3-β-Phthalimidoethyl-1,2,4-triazole (VI).—To a stirred solution of 100 ml. of concentrated nitric acid, 200 ml. of water and 1 g. of sodium nitrite was added in small portions 100 g. (0.36 mole) of 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol. The temperature was maintained below 45° by a water-bath. Toward the end of the addition a solid separated. The mixture was cooled to 0° and was cautiously neutralized with saturated sodium carbonate solution. The resulting precipitate of 3-β-phthalimidoethyl-1,2,4-triazole was collected by filtration and washed with water. The yield was 40 g. (43%). It was recrystallized from water and obtained as needles; m.p. 215°.

Anal. Calcd. for $C_{12}H_{10}N_4O_2$: C, 59.50; H, 4.16; N, 23.13. Found: C, 59.40; H, 4.12; N, 23.15.

The hydrochloride salt was recrystallized from methanol–ether; m.p. 245° (capillary).

Anal. Calcd. for $C_{12}H_{10}N_4O_2\cdot HCl$: C, 51.71; H, 3.98. Found: C, 51.95; H, 4.28.

When 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol was dissolved in dilute sodium hydroxide solution and reprecipitated with acid the phthalimide ring apparently was opened, for the product, after oxidation with nitric acid, gave none of the desired 3-β-phthalimidoethyl-1,2,4-triazole.

Alternatively, a mixture of 1 g. of 3-β-phthalimidoethyl-1,2,4-triazole-5-thiol, three teaspoonfuls of Raney nickel and 200 ml. of ethanol was heated under reflux for four hours. The hot mixture was filtered and the filtrate was evaporated to dryness under reduced pressure. After recrystallization from water the product was obtained as white needles; m.p. 214–215°. The melting point was not depressed when mixed with 3-β-phthalimidoethyl-1,2,4-triazole described above.

3-β-Aminoethyl-1,2,4-triazole Dihydrochloride.—A solution of 40 g. (0.16 mole) of 3-β-phthalimidoethyl-1,2,4-triazole and 500 ml. of 6 *N* hydrochloric acid was heated under reflux for eight hours. The mixture was cooled in an ice-bath for several hours and the phthalic acid which formed was removed by filtration. The filtrate was evaporated to dryness under reduced pressure, and the resulting solid was dissolved in 500 ml. of methanol (charcoal) followed by 1 l. of dry ether. 3-β-Aminoethyl-1,2,4-triazole dihydrochloride (25–30 g., 84–97% yield) which separated was collected and air dried for one hour. The compound decomposed at 215° when heated in an open capillary tube.

Anal. Calcd. for $C_4H_8N_4\cdot 2HCl$: C, 25.96; H, 5.45; N, 30.28. Found: C, 26.22; H, 5.38; N, 30.23.

3-β-Aminoethyl-1,2,4-triazole (II).—A solution of 18.5 g. (0.1 mole) of 3-β-aminoethyl-1,2,4-triazole dihydrochloride in 100 ml. of absolute ethanol was treated with 10.8 g. (0.02 mole) of sodium methylate. After heating under reflux for one hour the salt was removed by filtration, the solvent was evaporated, and the residual 3-β-aminoethyl-1,2,4-triazole was distilled under reduced pressure. It came over at 158–160° (0.1 mm.) as a colorless liquid, which crystallized after cooling; m.p. 83–85°. The yield was 9 g. (80%).

Anal. Calcd. for $C_4H_8N_4$: C, 42.84; H, 7.19. Found: C, 42.60; H, 7.34.

The dipicrate crystallized from alcohol as yellow cubes; m.p. 190°.

Anal. Calcd. for $C_{16}H_{14}N_{10}O_{14}$: C, 33.69; H, 2.47. Found: C, 33.58; H, 2.53.

3-β-Isopropylaminoethyl-1,2,4-triazole Dihydrochloride (X).—A mixture of 11.2 g. (0.10 mole) of 3-β-aminoethyl-1,2,4-triazole, 5.1 g. (0.11 mole) of acetone, 0.1 g. of platinum oxide catalyst and 100 ml. of ethanol was shaken with hydrogen at 40 lb. pressure. The theoretical amount of hydrogen was absorbed in about six hours, and the process was hastened by heating with an infrared lamp. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The residue in 50 ml. of ethanol was added to 46 g. (0.2 mole) of picric acid dissolved in 300 ml. of 95% ethanol. The solid which separated after cooling was recrystallized twice from 300-ml. portions of 95% ethanol. A small quantity of the dipicrate of 3-β-aminoethyl-1,2,4-triazole remained insoluble in the first recrystallization. The yield of 3-β-isopropylaminoethyl-1,2,4-triazole dipicrate was 45 g. (72%); m.p. 142–144°.

Anal. Calcd. for $C_{19}H_{20}N_{10}O_{14}$: C, 37.26; H, 3.29. Found: C, 37.54; H, 3.31.

The above picrate was suspended in 200 ml. of nitrobenzene and the mixture was extracted with three 100-ml. portions of concentrated hydrochloric acid. The combined acid solution was washed with chloroform and then was evaporated under reduced pressure to yield 3-β-isopropylaminoethyl-1,2,4-triazole dihydrochloride. It was recrystallized by dissolving in methanol and adding ether; m.p. 186° (capillary).

Anal. Calcd. for $C_7H_{14}N_4\cdot 2HCl$: C, 37.01; H, 7.10; N, 24.67. Found: C, 36.68; H, 7.07; N, 24.65.

3-β-Benzylaminoethyl-1,2,4-triazole Dihydrochloride (XI).—A solution of 3.4 g. (0.03 mole) of 3-β-aminoethyl-1,2,4-triazole and 3.2 g. (0.03 mole) of freshly distilled benzaldehyde in 50 ml. of ethanol was heated under reflux for two hours. Platinum oxide catalyst was added and the mixture was reduced at 40 lb. pressure until theoretical hydrogen was absorbed. The catalyst was removed and the filtrate was added to 13.8 g. (0.06 mole) of picric acid dissolved in 100 ml. of hot ethanol. 3-β-Benzylaminoethyl-1,2,4-triazole dipicrate was obtained in 70% yield after re-

(10) Prepared according to the procedure of R. O. Roblin and J. W. Clapp, THIS JOURNAL, **72**, 4890 (1950).

crystallization from 50% alcohol–water mixture; m.p. 115–117°.

Anal. Calcd. for $C_{22}H_{20}N_{10}O_{14}$: N, 21.21. Found: N, 21.34.

The dihydrochloride was obtained from the picrate in the manner described above for 3-β-isopropylaminoethyl-1,2,4-triazole dihydrochloride; m.p. 220° (capillary).

Anal. Calcd. for $C_{11}H_{14}N_4 \cdot 2HCl$: N, 20.36; Cl, 25.77. Found: N, 20.61; Cl, 25.51.

3-β-Ureidoethyl-1,2,4-triazole (XII).—A solution of 5.6 g. (0.03 mole) of 3-β-aminoethyl-1,2,4-triazole dihydrochloride, 2.4 g. (0.03 mole) of potassium cyanate and 2.5 g. (0.03 mole) of sodium bicarbonate in 100 ml. of water was evaporated on the steam-bath. The resulting solid was extracted with 50 ml. of ethanol from which 3-β-ureidoethyl-1,2,4-triazole crystallized after the addition of 500 ml. of dry ether; m.p. 188–190°.

Anal. Calcd. for $C_5H_9N_5O$: C, 38.70; H, 5.85. Found: C, 38.49; H, 5.88.

3-β-Benzamidoethyl-1,2,4-triazole (XIII).—To a solution of 5.5 g. (0.03 mole) of 3-β-aminoethyl-1,2,4-triazole dihydrochloride and 100 ml. of 2 *N* sodium hydroxide, cooled to 0°, was added with stirring 2.8 g. (0.02 mole) of benzoyl chloride. After two hours, 25 g. of ice was added and then concentrated hydrochloric acid to *p*H 5. The solid which formed was collected, washed with sodium bicarbonate solution and recollected by filtration. Recrystallized from water the solid gave 3.8 g. (55% yield) of 3-β-benzamidoethyl-1,2,4-triazole as feathery plates; m.p. 189–190°.

Anal. Calcd. for $C_{11}H_{12}N_4O$: C, 61.09; H, 5.59; N, 25.91. Found: C, 60.99; H, 5.45; N, 25.71.

3-β-Acetamidoethyl-1,2,4-triazole Hydrochloride (XIV).—A solution of 5.5 g. (0.03 mole) of 3-β-aminoethyl-1,2,4-triazole dihydrochloride and 50 ml. of 2 *N* sodium hydroxide solution, cooled to 0°, was treated with 2 ml. (0.02 mole) of acetic anhydride. After 30 minutes the solution was acidified with 6 *N* hydrochloric acid and was evaporated to dryness under reduced pressure. The organic hydrochloride was extracted with 100 ml. of warm absolute ethanol and to this was added 400 ml. of ether. 3-β-Acetamidoethyl-1,2,4-triazole hydrochloride precipitated on cooling as a white solid; m.p. 160°.

Anal. Calcd. for $C_6H_{10}N_4O \cdot HCl$: C, 37.80; H, 5.82; Cl, 18.60. Found: C, 37.94; H, 5.77; Cl, 18.94.

Condensation of 3-β-Aminoethyl-1,2,4-triazole and Acetic Anhydride.—A solution of 1.7 g. (0.015 mole) of 3-β-aminoethyl-1,2,4-triazole and 2 g. (0.020 mole) of acetic anhydride in 50 ml. of glacial acetic acid was heated on the steam-bath for three hours. Water (25 ml.) was added, and after standing for 15 minutes, the solution was concentrated to dryness under reduced pressure. The resulting solid was recrystallized from ethanol and obtained as needles; m.p. 215–216°.

Anal. Calcd. for $C_{13}H_{10}N_4O_2$: C, 61.41; H, 3.96; N, 22.04; mol. wt., 254.2. Found: C, 61.31; H, 4.28; N, 22.08; mol. wt. (Rast), 255.

INDIANAPOLIS, INDIANA

[CONTRIBUTION FROM DEPARTMENT OF BIOCHEMISTRY, PURDUE UNIVERSITY]

Two Further Aldobiouronic Acids from Hemicellulose-B of Corn Cob[1,2]

BY ROY L. WHISTLER AND L. HOUGH

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Further investigation of the uronic acid-containing oligosaccharides produced by partial hydrolysis of corn cobs has shown that two of the four aldobiouronic acids present are 2-O-(α-D-glucopyranosyluronic acid)-D-xylose and 4-O-(α-D-glucopyranosyluronic acid)-D-xylose.

Structural characterization of hemicelluloses can be approached through an examination of oligosaccharide fragments obtained on partial hydrolysis. This approach has been used successfully with other polysaccharides and is particularly suitable since charcoal[3] and cellulose chromatography[4,5] allow clean-cut separations of oligosaccharides from complex sugar mixtures. In an attempt to apply the procedure to the soluble hemicelluloses of corn cob (B-fraction) there have been obtained five components containing uronic acids. One of these has been shown[5] to be 2-O-(4-O-methyl-α-D-glucopyranosyluronic acid)-D-xylose. Further work has been done on a second chromatographically separated fraction which is shown to be a mixture of two different unmethylated aldobiouronic acids. These two aldobiouronic acids are found together as one spot on paper chromatography and no combination of eluants have been found to separate them. Consequently the mixture was investigated to determine whether structural information could be elicited without separation of the individual disaccharides. The mixture was methylated and the fully methylated products reduced with lithium aluminum hydride. Cleavage of the resultant methylated glucosylxyloses gave a mixture of three products, 2,3,4,6-tetra-O-methyl-D-glucose, 3,4-di-O-methyl-D-xylose and 2,3-di-O-methyl-D-xylose which were separated by paper chromatography and converted into crystalline derivatives. This evidence conclusively identifies one of the components as 2-O-(α-D-glucopyranosyluronic acid)-D-xylose, the unmethylated derivative of the mono-O-methylaldobiouronic acid found previously[5] in corn cob hemicellulose-B. This aldobiouronic acid is thus identified in nature for the first time. The other component is probably 4-O-(α-D-glucopyranosyluronic acid)-D-xylose which has been previously characterized in part.[6] The remote possibility that this aldobiouronic acid contains the 1 → 5 linkage is not eliminated.

3-O-(α-D-Glucopyranosyluronic acid)-D-xylose has been found in wheat straw hemicellulose[7,8] and pear cell wall xylan.[9]

(1) Journal Paper No. 721 of the Purdue Agricultural Experiment Station.

(2) Paper presented before the Division of Carbohydrate Chemistry at the 123rd Meeting of the American Chemical Society at Los Angeles, California, March, 1953.

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(6) Paper presented by R. L. Whistler and R. F. Serro before the Division of Sugar Chemistry at the 118th Meeting of the American Chemical Society, Chicago, Ill., 1950.

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