melibiose dihydrate, chemical storehouses at the present time evidently supply what is sometimes referred to as a "monohydrate" or a "hydrate," but there is no evidence as to its anomeric form.

We have recently repeated the preparation of melibiose by the above method[9] using yeast, expecting to obtain the dihydrate, but instead we have obtained a monohydrate, m.p. 179–181°. This monohydrate of melibiose is evidently the α anomer since it shows $[\alpha]_D^{23}$ +157° changing to +137° in water (C, 1.0).

Anal. Calcd. for $C_{12}H_{22}O_{11} \cdot H_2O$: C, 40.00; H, 6.71. Found: C, 39.95; H, 6.60.

When allowance was made for the change in molecular weight, the equilibrium rotation of +137° found for the new monohydrate agreed well with the value of +129.5° reported for the dihydrate.

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(9) "Polarimetry Saccharimetry and the Sugars," Circular C440 of the Natl. Bur. Standards, by Frederick J. Bates and Associates, 1942, p. 473.

Some Derivatives of *p*-Bis(β-hydroxyethyl)-aminobenzaldehyde

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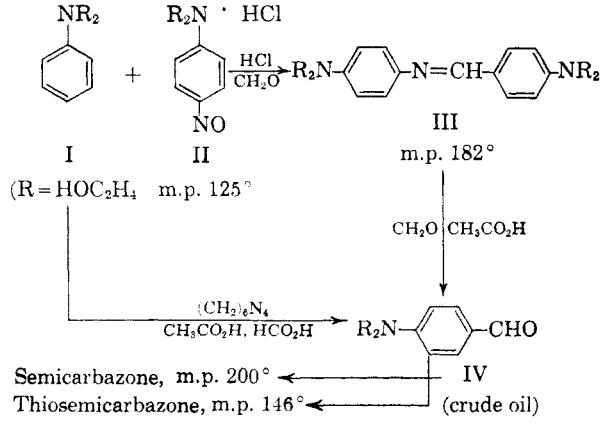
Although several *p*-dialkylaminobenzaldehyde derivatives are reported in the literature, including the butyl- and ethyl-β-hydroxyethyl- compounds,[2] the bis(β-hydroxyethyl) analog apparently has not been reported. Using a procedure similar to that for the preparation of *p*-dimethylaminobenzaldehyde,[3] it has not been possible to obtain a purified sample of the bis(β-hydroxyethyl) compound, although several derivatives of it have been isolated and identified.



(1) Supported by U. S. Public Health Service Grant No. CY-2189.

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EXPERIMENTAL[4]

p-Nitroso-bis(β-hydroxyethyl)aminobenzene hydrochloride (II). A stirred solution of 36.2 g. of bis(β-hydroxyethyl)-aniline in a mixture of 20 ml. of water and 40 ml. of concentrated hydrochloric acid was cooled in an ice-salt bath and a solution of 14.6 g. of sodium nitrite in 25 ml. of water was added, care being taken that the temperature did not rise above 5°. After stirring for a further period of 30 min., the orange crystalline nitroso compound was collected, washed with 40 ml. of cold 1:1 hydrochloric acid and dried first in air and then in a desiccator. On recrystallization from ethanol the compound melted with decomposition at 123–125°.

Anal. Calcd. for $C_{10}H_{15}N_2O_3Cl$: C, 48.68; H, 6.13; N, 11.36. Found: C, 48.33; H, 6.30; N, 11.16.

The nitroso compound seemed to be sensitive to light. The original color soon changed to greenish yellow and finally to black within a few days.

N-[p'-Bis(hydroxyethyl)aminobenzylidene]-p-[bis(hydroxyethyl)amino]-aniline (III). Wet nitroso hydrochloride, from a preparation using four times the quantities described above, was added all at once to a 5-liter beaker containing a solution made by warming for 10 min. on a steam bath a mixture of 173.6 g. of bis(β-hydroxyethyl)aniline, 192 ml. of concentrated hydrochloric acid and 100 ml. of 40% formaldehyde solution. The initial vigorous reaction soon subsided. After allowing the mixture to stand for an hour, about 1600 g. of crushed ice was added to the mixture and it was cautiously neutralized with a very slight excess of 40% sodium hydroxide solution. The aqueous portion was poured off from the plastic mass, which was washed by trituration and decantation with four 3.5-l. portions of cold water, care being taken to see that the wash liquor before decantation was neutral. The temperature throughout the latter operation was maintained below 15°. The plastic mass was warmed with 400 ml. of hot ethanol, seeded (a portion of the solution, diluted with 2–3 times its volume of ether, on cooling, scratching, and washing with cold ethanol gave the desired material for seeding) and cooled thoroughly, when yellow crystalline material separated. This was collected and washed with cold ethanol to yield 105 g., m.p. 176–178°. One recrystallization from ethanol raised the melting point to 181–182°.

Anal. Calcd. for $C_{21}H_{29}N_3O_4$: C, 65.09; H, 7.54; N, 10.86. Found: C, 64.77; H, 7.67; N, 10.83.

p-Bis(β-hydroxyethyl)aminobenzaldehyde semicarbazone. Compound III (27 g., 0.7 mole) was stirred at room temperature with a mixture of 42 ml. of glacial acetic acid and 40% formaldehyde for 4 hr. This mixture was then diluted with 70 ml. of water, cooled thoroughly, cautiously basified with a slight excess of ammonia, and extracted with chloroform in a liquid-liquid extractor for 16 hr. After drying and evaporation of solvent, the residual oil, containing some high-melting by-product, weighed 15.6 g. This oil, presumably the crude aldehyde (IV), could not be crystallized and did not distill at 285° (0.05 mm.). The *semicarbazone*, prepared in the usual way using sodium acetate, readily recrystallized from ethanol, m.p. 199–200°, dec.

Anal. Calcd. for $C_{12}H_{18}N_4O_3$: C, 54.12; H, 6.81; N, 21.04. Found: C, 54.08; H, 7.16; N, 21.32.

p-Bis(β-hydroxyethyl)aminobenzaldehyde thiosemicarbazone. (a) To a solution of 11 g. of the crude oil containing the aldehyde (IV) in 20 ml. of 95% ethanol and 60 ml. of water, 4.8 g. of thiosemicarbazide was added. After heating under reflux for 4 hr., the mixture was cooled and the supernatant liquor was decanted from the oily precipitate. After addition of 200 ml. of hot water, the mixture was heated to boil-

(4) Analyses by Midwest Microanalytical Lab., Indianapolis.

ing. On slow cooling to room temperature, the thiosemicarbazone crystallized; yield, 4.5 g., m.p. 144–146°. After recrystallization from ethanol, the compound melted at 146–147°.

Anal. Calcd. for $C_{12}H_{18}N_4O_2S$: C, 51.05; H, 6.42; N, 19.85; S, 11.33. Found: C, 51.12; H, 6.65; N, 19.72; S, 10.65, 10.57.

(b) A mixture of 18.1 g. of bis(β-hydroxyethyl)aniline, 20 g. of hexamethylenetetramine and 10 ml. of ethanol was heated under reflux. After 15 min., 15 ml. of a mixture of 22.5 ml. of acetic acid and 22.5 ml. of formic acid was added. The remainder was added at 30-min. intervals in 5-ml. portions. After heating for another 3 hr., the reaction mixture was poured into a solution of 12.5 ml. of concentrated hydrochloric acid and 300 ml. of water. After standing overnight, the green solution was cooled, basified with a slight excess of concentrated sodium hydroxide solution and extracted with one 100-ml. and one 50-ml. portion of chloroform. The aqueous portion was saturated with sodium chloride and again extracted with three 50-ml. portions of chloroform. The combined extract was dried with magnesium sulfate and the chloroform was removed. The residual viscous material weighed 17.5 g. This was converted to the thiosemicarbazone essentially as described above; yield, 5.2 g. The two products were identical.

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Synthesis of 2,3-Cyclopenteno-7*H*-benzo[*c*]fluorene

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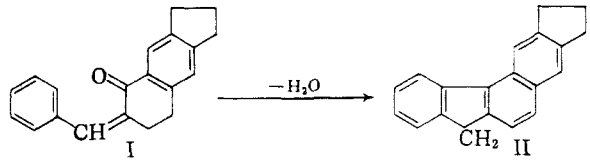
It is well known that whereas benz[*a*]anthracene is at the most only weakly carcinogenic,[1] 9,10-cyclopentenobenz[*a*]anthracene shows pronounced carcinogenic activity.[2] Hence it was of interest to synthesize 2,3-cyclopenteno-7*H*-benzo[*c*]fluorene (II) for biological testing, although the parent compound, 7*H*-benzo[*c*]fluorene had already proved inactive.[3] A further point of interest is the possibility for polycyclic fluorenes of this type to act as antagonists of carcinogens as is the case with 13*H*-dibenzo[*ag*]fluorene.[4]

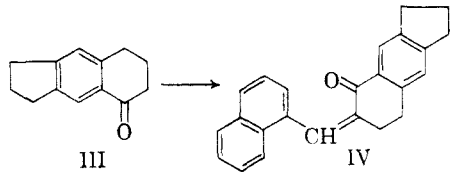
Hydrocarbon II was now readily prepared by cyclodehydration by means of phosphorus pentoxide,[5] of 2-benzylidene-6,7-cyclopenteno-1-tetralone (I).

This last compound was readily prepared by alkali-catalyzed condensation of benzaldehyde with



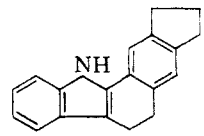
I II

6,7-cyclopenteno-1-tetralone (III), which was obtained from hydrindene by means of the succinic anhydride method.[6] Similar condensation of ketone III with 1-naphthaldehyde furnished 2-(1-naphthylmethylene)-6,7-cyclopenteno-1-tetralone (IV), which, on treatment with phosphorus pentoxide, gave a compound m.p. 249°, in insufficient quantity for analytical determination.



III IV

Fischer indolization of the phenylhydrazone of ketone III afforded 5,6-dihydro-2,3-cyclopenteno-11*H*-benzo[*a*]carbazole (V).



V

Compounds II and V are undergoing biological tests in this Institute, and results will be reported later.

EXPERIMENTAL

Preparation of ketone III. The succinoylation of hydrindene[6] was performed with 50 g. of the hydrocarbon, 42.3 g. of succinic anhydride, and 85 g. of aluminum chloride in 250 ml. of nitrobenzene, and the mixture left for 18 hr. at room temperature prior to the usual treatment. The yield of the γ-keto acid, m.p. 128°, was 60 g. Reduction to the corresponding γ-(5-hydrindyl)butyric acid, b.p. 210–215°/15 mm., m.p. 51°, was effected with hydrazine hydrate and potassium hydroxide in diethylene glycol, and cyclization of the acid chloride (prepared from thionyl chloride) was performed with aluminum chloride in carbon disulfide in the cold (48 hr. standing), giving an 80% yield of ketone III, b.p. 182–183°/12 mm.

2-Benzylidene-6,7-cyclopenteno-1-tetralone (I). A solution of 3.5 g. of the above ketone and 2 g. of freshly redistilled benzaldehyde in 20 ml. of warm ethanol was shaken with a few drops of 20% aqueous potassium hydroxide. The crystalline mass which rapidly formed was filtered off after cooling, washed with water, and recrystallized from ethanol. Yield: 2.8 g. of shiny yellowish prisms, m.p. 128°, giving an orange halochromism with sulfuric acid.

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.6; H, 6.6. Found: C, 87.4; H, 6.6.

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