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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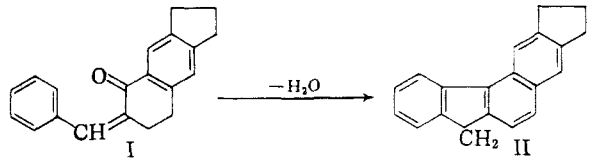
It is well known that whereas benz[*a*]anthracene is at the most only weakly carcinogenic,[1] 9,10-cyclopentenobenz[*a*]anthracene shows pronounced carcinogenic activity.[2] Hence it was of interest to synthesize 2,3-cyclopenteno-7*H*-benzo[*c*]fluorene (II) for biological testing, although the parent 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]

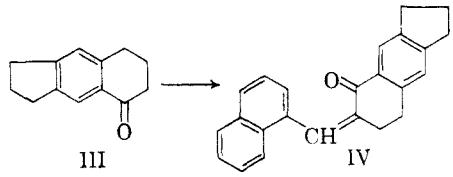
Hydrocarbon II was now readily prepared by cyclodehydration by means of phosphorus pentoxide,[5] of 2-benzylidene-6,7-cyclopenteno-1-tetralone (I).

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



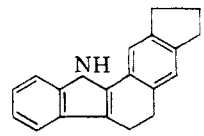
I II

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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2,3-Cyclopenteno-7H-benzo[c] fluorene (II). To a solution of 2.5 g. of the foregoing ketone in 30 ml. of anhydrous xylene, 2.6 g. of finely powdered phosphorus pentoxide was added in small portions, and the mixture was refluxed for 30 hr. After cooling, water was added, and the dark fluorescent xylene solution was washed with aqueous sodium hydroxide, then with water, and dried over sodium sulfate; the solvent was then distilled off and the residue vacuum-fractionated. The thick yellow oil, b.p. 220–225°/0.4 mm. was taken up in ethanol containing some drops of benzene, and the solid precipitate obtained was recrystallized from ethanol, giving shiny colorless needles, m.p. 140° (no coloration with cold sulfuric acid). Yield: 30%.

Anal. Calcd. for $C_{26}H_{16}$: C, 93.7; H, 6.3. Found: C, 93.4; H, 6.3.

The corresponding picrate crystallized from ethanol in orange-red prisms, m.p. 184°.

Anal. Calcd. for $C_{26}H_{19}N_3O_7$: N, 8.7. Found: N, 8.4.

2-(1-Naphthylmethylene)-6,7-cyclopenteno-1-tetralone (IV). A solution of 0.35 g. of ketone III and 0.3 g. of 1-naphthaldehyde in 3 ml. of warm ethanol was treated with one drop of 20% aqueous potassium hydroxide; the solid precipitate formed on cooling crystallized from ethanol in shiny yellowish prisms (0.35 g.), m.p. 115°, giving a deep red halochromism with sulfuric acid.

Anal. Calcd. for $C_{24}H_{20}O$: C, 88.9; H, 6.2. Found: C, 88.6; H, 6.3.

Treatment of this ketone with phosphorus pentoxide in xylene as for the above hydrocarbon, afforded a compound which crystallized from a mixture of ethanol and benzene in shiny colorless leaflets, m.p. 249°, which gave no picrate.

5,6-Dihydro-2,3-cyclopenteno-11H-benzo[a]carbazole (V). A mixture of 3.5 g. of ketone III and 3 g. of phenylhydrazine was heated at 120° until steam had ceased to be evolved; on cooling, 30 ml. of acetic acid saturated with hydrogen chloride was added. The mixture was brought to the boil, poured into water, and the indolization product taken up in benzene; the benzene solution was washed with dilute aqueous sodium hydroxide, then with water, dried over sodium sulfate, the solvent removed, and the residue vacuum-distilled. The portion boiling above 250°/12 mm. crystallized from ethanol in colorless prisms (2.5 g.), m.p. 204°.

Anal. Calcd. for $C_{19}H_{17}N$: N, 5.4. Found: N, 5.2.

The corresponding picrate crystallized from ethanol in shiny, deep violet prisms, m.p. 194°.

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Selective Reduction of a Benzyloxyamino Group in the Presence of a Nitro Group[1]

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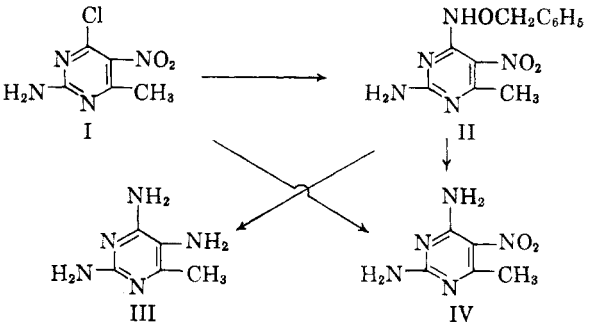
In the course of experiments directed towards the synthesis of purine-9-oxides, selective reduction of



the nitro group in 2-amino-4-benzyloxyamino-5-nitro-6-methylpyrimidine (II) was attempted. This could not be achieved, but conditions have been found for the selective reduction of the benzyloxyamino group.

Reaction of II with hydrazine in the presence of Raney nickel, with ferrous hydroxide or with hydrogen in the presence of palladium catalyst resulted in complete reduction to 2,4,5-triamino-6-methylpyrimidine (III). Unexpectedly, however, reduction with aqueous ethanolic ammonium sulfide gave 2,4-diamino-5-nitro-6-methylpyrimidine (IV), identical with the reaction product of 2-amino-4-chloro-5-nitro-6-methylpyrimidine (I) with ethanolic ammonia.

The steric environment of the nitro group in II probably contributes to the selectivity of the latter reduction. These experiments emphasize the ease of reduction of the benzyloxy grouping under neutral or alkaline conditions where hydrolysis of the group does not occur.

EXPERIMENTAL[2]

2-Amino-4-benzyloxyamino-5-nitro-6-methylpyrimidine (II). To a solution of 9.5 g. of 2-amino-4-chloro-5-nitro-6-methylpyrimidine[3] in 200 ml. of ethanol was added 8.0 g. of benzyloxyamine[4] and 8.5 g. of powdered anhydrous sodium acetate. The mixture was heated under reflux for 1 hr., the solvent removed under reduced pressure and the residue triturated with water. The yellow solid which separated was collected by filtration and recrystallized from ethanol to give 12.0 g. (78%) of fine yellow needles, m.p. 191–192°.

Anal. Calcd. for $C_{12}H_{13}N_5O_3$: C, 52.4; H, 4.7; N, 25.45. Found: C, 52.6; H, 4.9; N, 25.3.

2,4,5-Triamino-6-methylpyrimidine (III). Method *a*. A suspension of 2 g. of powdered 2-amino-4-benzyloxyamino-5-nitro-6-methylpyrimidine in 200 ml. of ethanol was treated with 2 ml. of 96% hydrazine followed by a small amount of Raney nickel catalyst. The resulting mixture was heated under reflux for 20 min., filtered, and the filtrate evaporated to dryness. Recrystallization of the residue from ethanol yielded 0.65 g. (64%) of small tan prisms, m.p. 242–244°. This material is reported to melt at 243°[5] and 241–243°.[6]

(1) This investigation was supported by a grant from the American Cancer Society.

(2) We are indebted to Dr. Joseph F. Alicino, Metuchen, N. J., for the microanalyses. All melting points are corrected.

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