

An examination of the table shows that with one or two exceptions the results are in good agreement with those reported by the National Bureau of Standards. The low percentages obtained on the alloys undoubtedly were due to the experimental difficulties of separating small amounts of iron from relatively large amounts of elements such as tin and antimony. These low results can hardly be attributed to any inherent weakness of the colorimetric method since no tendency of this sort is apparent in the other results obtained. Also, it is of interest to note that in the two cases where the Bureau reports analyses by a colorimetric method, the results obtained by the Ferron method checked the latter closer than the average value reported by the Bureau.

### Summary

A study has been made of 7-iodo-8-hydroxyquinoline-5-sulfonic acid and its reaction with ferric ions. The solubility of the reagent has been determined in water, alcohol, acetic acid and in mixtures of these solvents. The color reaction has been investigated and a probable mechanism for it has been postulated. Cupric ions and salts that hydrolyze easily, or yield colored ions,

interfere with the reaction and should not be present except in very low concentration. The sensitivity of the reaction has been determined. The reagent will measure quantitatively one part of iron in ten million parts of solution, when the observation is made in 50-ml. Nessler tubes (tall form). The color has been found to obey the Lambert-Beer law over the range of concentration examined. The effect of hydrogen-ion concentration has been studied and the optimum pH range for the color reaction determined. Aging and temperature have been found to have no effect on the color reaction. The optimum experimental conditions for the determination of iron have been established.

The iron content of a wide variety of materials has been determined colorimetrically, using 7-iodo-8-hydroxyquinoline-5-sulfonic acid. With one or two exceptions, the results obtained are in good agreement with the values reported by the National Bureau of Standards.

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[CONTRIBUTION FROM THE JOHN HARRISON LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

## Condensations of Aromatic Amines with Formaldehyde in Media Containing Acid. V. Substituted Dihydroquinazolines from *p*-Chloroaniline and *p*-Bromoaniline

BY E. C. WAGNER AND ABNER EISNER<sup>1</sup>

The condensations of *p*-substituted amines with formaldehyde in aqueous acid solution have been studied for *p*-toluidine by Maffei and by the writers,<sup>2</sup> for *p*-phenetidine and *p*-nitroaniline by Maffei,<sup>3</sup> and by Cairncross and Bogert for *p*-aminobenzoic acid and ester<sup>4</sup> and for *p*-bromoaniline.<sup>5</sup> The reported products included the corresponding 3,6-disubstituted-3,4-dihydroquinazolines except in the case of *p*-bromoaniline, from which Cairncross and Bogert<sup>5</sup> obtained as the main product (19%) a base of m. p. 257° identified as 3-(*p*-bromophenyl)-6-bromo-3,4-dihydroquinazolinone-4, and smaller amounts of two other bases (m. p. 204° and 193-196°), neither examined further. At the time these

results were published the writers had practically completed a study of the condensation of *p*-chloroaniline with formaldehyde in dilute hydrochloric acid solution. The principal product was the expected substituted quinazoline. These contrasting results with two compounds so similar led to extension of the work to include *p*-bromoaniline. Condensation of this amine with formaldehyde in dilute hydrochloric acid solution at or below room temperature gave as the main product (26%) a base of m. p. 205.8° (corr.), found to be 3-(*p*-bromophenyl)-6-bromo-3,4-dihydroquinazoline. No base of m. p. 257° was isolated. Comparison of the two sets of conditions which yielded these unlike results shows that Cairncross and Bogert used less acid, more water, and considerably higher temperature (70°); the separation and purification of the several products involved a laborious and lengthy procedure. In the writers' experiments the isolation of the quinazoline offered no difficulty.

(1) Present location: U. S. Bureau of Mines, Pittsburgh, Pa.

(2) (a) Lepetit and Maimeri, *Atti accad. Lincei*, [5] **26**, 558 (1917); (b) Lepetit, Maffei and Maimeri, *Gazz. chim. ital.*, **57**, 867 (1927); (c) Maffei, *ibid.*, **58**, 261 (1928); (d) Eisner and Wagner, *THIS JOURNAL*, **56**, 1938 (1934).

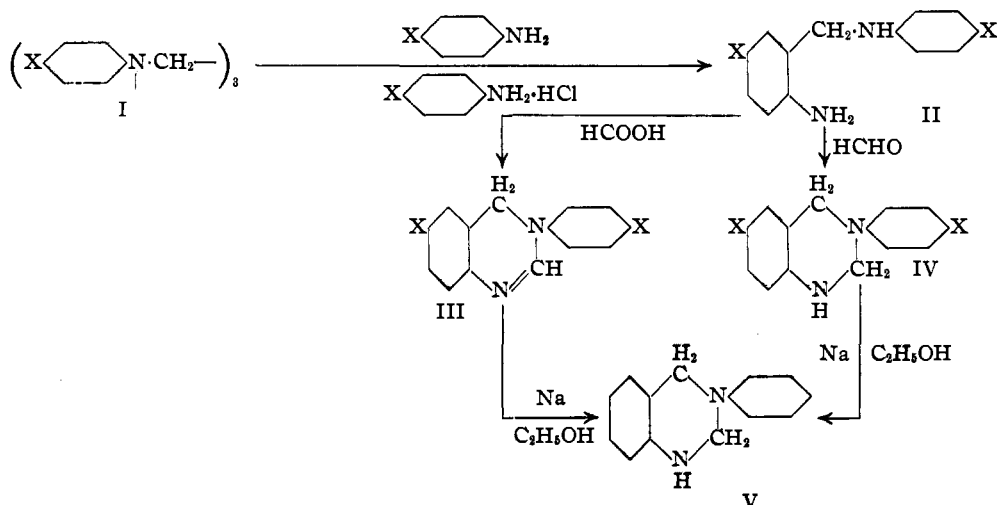
(3) Maffei, *Gazz. chim. ital.*, **59**, 3 (1929).

(4) Cairncross and Bogert, *Collection Czechoslov. Chem. Commun.*, **7**, 58 (1936).

(5) Cairncross and Bogert, *ibid.*, **7**, 548 (1936).

This paper describes the results of condensations of *p*-chloroaniline and of *p*-bromoaniline with formaldehyde in aqueous solutions containing hydrochloric acid, and the experiments by which the main reaction products were identified as the 3,6-disubstituted dihydroquinazolines. From both amines there were obtained also somewhat smaller amounts of lower-melting bases (135° and 134–135°, respectively), which have not been identified. The condensations were accompanied by methylation of part of the original amines, as has been reported also in the cases of *p*-toluidine and *p*-phenetidine.

The identifications of the substituted quinazolines were effected by the syntheses and transformations shown in the reaction scheme.



In the case of each starting compound (*p*-chloroaniline and *p*-bromoaniline) the trimeric Schiff base (I), prepared by the method of Miller,<sup>6</sup> was converted to the aminobenzylarylamine base (II) by the customary procedure,<sup>7</sup> and II was changed to the dihydroquinazoline (III) by ring-closure with formic acid.<sup>7b</sup> The dihydroquinazolines thus obtained were found to be identical with the main products of the condensations of the halogenated amines with formaldehyde. The structure of II, upon which the proof depends, may be inferred from the method of preparation used, and was supported by the characteristic behavior of the compound with formaldehyde to yield the tetrahydroquinazoline (IV), by the fact that II gave with benzaldehyde a monobenzal derivative from which benzaldehyde

was split out by acid hydrolysis, and by the analytical values obtained for II, its benzal derivative, and IV. Hydrogenation of III to IV, apparently a simple way to establish the relationship of the two, was not effected,<sup>8</sup> but III was treated with excess sodium and alcohol under conditions which detached halogen quantitatively,<sup>9</sup> by which treatment both dihydroquinazolines yielded the same product (V), namely, 3-phenyl-1,2,3,4-tetrahydroquinazoline.<sup>10</sup> Further the tetrahydroquinazoline (IV) from *p*-bromoaniline was dehalogenated by sodium and alcohol yielding V, identical with the compound obtained from the two halogenated dihydroquinazolines (III). In the cases of the bromine compounds (III and IV) the bromine split

off was recovered as silver bromide and weighed, with results close to the theoretical.

The foregoing evidence, together with analytical values, identify the two condensation products as 3-(*p*-chlorophenyl)-6-chloro-3,4-dihydroquinazoline (m. p. 192°, corr.) and 3-(*p*-bromophenyl)-6-bromo-3,4-dihydroquinazoline (m. p. 205.8°, corr.). Apparently both compounds have been obtained previously as unidentified reaction products, *viz.*, a base of m. p. 188° from *p*-chloroaniline, reported in a German patent,<sup>11</sup> and the

(8) No method came to hand by which the 1,2-double bond could be hydrogenated without cleavage of halogen. Alcohol and a moderate amount of sodium split off part of the halogen, as found also by Paal and Koch [*J. prakt. Chem.*, [2] 48, 554 (1893)]. Hydrogen under 30 pounds (2 atm.) pressure and in presence of Raney nickel was found, in trials with other dihydroquinazolines, to be ineffective. Hydrogen in presence of palladized calcium carbonate [Busch and Stöve, *Ber.*, 49, 1063 (1916); ref. 5] removes halogen without hydrogenating the double bond.

(9) Drogin and Rosanoff, *THIS JOURNAL*, 36, 711 (1916).

(10) Busch, *J. prakt. Chem.*, [2] 53, 420 (1896).

(11) German Patent 122,474; *Friedl.*, 6, 82.

(6) Miller and Wagner, *THIS JOURNAL*, 54, 3703 (1932).

(7) (a) German Patent 105,797; *Friedl.*, 5, 84; (b) v. Walther and Bamberg, *J. prakt. Chem.*, [2] 73, 209 (1906).

base of m. p. 204° obtained from *p*-bromoaniline by Cairncross and Bogert.<sup>5</sup>

### Experimental

**Condensation of *p*-Chloroaniline and *p*-Bromoaniline with Formaldehyde in Aqueous Acid Solution.**—The amine (0.1 mole) was dissolved in 100 cc. of water and 18 cc. of concd. hydrochloric acid. To the cold solution was added 10 cc. of 37% formalin (0.12 mole), and the mixture was stirred. A white precipitate appeared after some minutes, and increased steadily, while the liquid and precipitate acquired a gradually deepening red color. The separated hydrochlorides were filtered off after several hours. The filtrate was allowed to stand at room temperature, with removal of the further precipitate when it had become considerable, and this was continued until the final precipitate was negligible (eight to eleven days). The combined crops of colored hydrochlorides were dissolved in boiling water, filtered hot, and while still hot (to prevent separation of hydrochloride) the solution was made alkaline. The precipitate of bases was stirred until well granulated, and was filtered cold and washed with water. The yield from *p*-chloroaniline was 9.9 g., and from *p*-bromoaniline 11.2 g. The crude product was crystallized from 95% alcohol. In each case there separated first a crystalline base only slightly soluble in cold alcohol. After recrystallization from alcohol the base from *p*-chloroaniline melted at 186–187°, obsd., and that from *p*-bromoaniline at 201°, obsd. These bases were the dihydroquinazolines. The mother liquors were diluted while hot, and on chilling gave a second product more soluble than the first. The base from *p*-chloroaniline, after recrystallization from dilute alcohol, melted at 135°, obsd., and that from *p*-bromoaniline at 134–135°, obsd. The yields from *p*-bromoaniline were 4.74 g. of the 201° base (25.9%) and 3.34 g. of the 134° base.

After removal of the crude hydrochlorides in an experiment with *p*-bromoaniline the final filtrate was made alkaline and was steam-distilled, yielding 1.38 g. of steam-volatile oil, which was examined by the Hinsberg-Kessler procedure. There were obtained 0.29 g. of primary amine derivative (m. p. 127°), 0.31 g. of secondary amine derivative (brown oil), and 0.27 g. of tertiary base (diazotization and coupling test negative) whose crystallization was not feasible, but which gave a picrate of m. p. 139°, found to be identical (mixed melting point test) with the picrate of dimethyl-*p*-bromoaniline.

**3 - (*p*-Chlorophenyl) - 6 - chloro - 3,4 - dihydroquinazoline.**—Colorless needles from alcohol slightly diluted; m. p. 187°, obsd., or 192°, corr.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>Cl<sub>2</sub>: C, 60.67; H, 3.61; N, 10.11; Cl, 25.62; mol. wt., 277. Found: C, 60.71; H, 3.69; N, 9.96, 9.95; Cl, 25.47, 25.47; mol. wt. (benzene), 294, 295; (camphor), 268, 270. Picrate: small yellow needles from alcohol; m. p. 233°, obsd., or 239°, corr.

**3 - (*p*-Bromophenyl) - 6 - bromo - 3,4 - dihydroquinazoline.**—Small elongated prisms from slightly diluted alcohol; m. p. 201°, obsd., or 205.8°, corr.

*Anal.* Calcd. for C<sub>14</sub>H<sub>10</sub>N<sub>2</sub>Br<sub>2</sub>: C, 45.92; H, 2.73; N, 7.65; Br, 43.66; mol. wt., 366. Found: C, 46.11; H, 2.72; N, 7.60, 7.41, 7.44; Br, 43.59; mol. wt. (cam-

phor), 380, 376. Picrate: small bright yellow needles from hot alcohol; m. p. 235°, obsd., or 242°, corr.

**Trimeric Methylene-*p*-chloroaniline.**—This compound was reported by Bischoff and Reinfeld,<sup>12</sup> who found the m. p. to be 157° and the molecular weight 437, but gave no analytical values. Specimens made for this work by the method of Miller,<sup>6</sup> and crystallized from ligroin, melted at 151°, obsd., a value not raised by another crystallization. This compound was examined further in order to make certain of its identity.

*Anal.* Calcd. for (C<sub>7</sub>H<sub>6</sub>NCl)<sub>3</sub>: Cl, 25.44; mol. wt., 417.5. Found: Cl, 25.25, 25.22; mol. wt. (benzene), 422, 420.

Reduction by zinc dust and hot dilute sulfuric acid<sup>6,13</sup> split the compound into bases recognized by the Hinsberg-Kessler procedure to be primary, secondary and tertiary. The evidence given establishes the compound as the trimeric Schiff base, as claimed by Bischoff and Reinfeld.

In molten camphor this base gave molecular weight values of 287 and 290, indicating partial depolymerization at 175°, as with similar compounds studied previously.<sup>6</sup>

**Trimeric Methylene-*p*-bromoaniline.**—This compound, not previously reported, was prepared by the method of Miller.<sup>6</sup> The reaction mixture, at first kept in an ice-bath, deposited initially a solid product which soon became viscous, and on standing overnight set to an amorphous mass; 17.2 g. of *p*-bromoaniline gave 11.4 g. of crude product (61.7%). The base crystallized from ligroin or alcohol in long thin flexible needles clumped in loose bulky masses. The compound melted at 166° obsd., or 168.8°, corr., to a turbid liquid.

*Anal.* Calcd. for (C<sub>7</sub>H<sub>6</sub>NBr)<sub>3</sub>: C, 45.68; H, 3.26; N, 7.61; mol. wt., 552. Found: C, 45.80; H, 3.38; N, 7.64, 7.54; mol. wt. (benzene), 563, 546. In molten camphor the molecular weight results were 378, 389 and 374, showing partial depolymerization at 175°.

Cleavage of 2.95 g. of the compound by reduction<sup>6</sup> gave 2.28 g. of steam-volatile oil, which by the Hinsberg procedure was shown to contain primary and secondary bases, and yielded also 0.48 g. of a solid tertiary base. This melted at 54–55°, and was found by mixed melting point test to be identical with dimethyl-*p*-bromoaniline (m. p. 54°). The picrates (m. p. 140–141°) also were identical.

**N-(2-Amino-5-chlorobenzyl)-*p*-chloroaniline (II).**—This aminobenzylarylamine was made<sup>14</sup> by heating a mixture of 10 g. of crude methylene-*p*-chloroaniline, 23 g. of *p*-chloroaniline hydrochloride, 50 g. of *p*-chloroaniline and 5 cc. of nitrobenzene for six hours at 80–90°. The mixture was made alkaline and all steam-volatile material was removed. The somewhat gluey residue in the flask was extracted with ligroin (70–90°), yielding a yellow granular product (8.9 g., or 46.5%). Several crystallizations from ligroin gave small imperfect prisms with a slight yellow tinge, and a good melting point of 92°, obsd., or 93°, corr.

(12) Bischoff and Reinfeld, *Ber.*, **36**, 47 (1903).

(13) Wagner, *This Journal*, **54**, 660 (1932).

(14) The procedure used was based on German Patent 105,797 (ref. 7) and will be reported in a later paper.

*Anal.* Calcd. for  $C_{11}H_{12}N_2Cl_2$ : C, 58.45; H, 4.49; N, 10.49; mol. wt., 267. Found: C, 58.67, 58.74; H, 4.45, 4.57; N, 10.34, 10.45; mol. wt. (camphor), 272, 265.

**N-(2-Amino-5-bromobenzyl)-*p*-bromoaniline (II).**—A mixture of 10.0 g. of methylene-*p*-bromoaniline, 10 g. of *p*-bromoaniline hydrochloride and 100 g. of *p*-bromoaniline was heated in an oil-bath at 85° for four hours.<sup>14</sup> After removal of *p*-bromoaniline by steam distillation, the crude product in the flask solidified on cooling. It was partially dried, dissolved in hot alcohol, and recovered in several crops by progressive dilution with water. The crude yield was 10.7 g., or 55.3%. After two crystallizations from ligroin the substance was crystalline, though still yellowish, and melted well at 116°, obsd., or 117.6°, corr.

*Anal.* Calcd. for  $C_{13}H_{12}N_2Br_2$ : C, 43.84; H, 3.37; N, 7.87; mol. wt., 356. Found: C, 44.08, 44.12; H, 3.51, 3.63; N, 7.59, 7.58, 7.63; mol. wt. (camphor), 340, 348.

The resinous material obtained from the alcoholic mother liquors was worked up and yielded a small amount of the picrate of 3-(*p*-bromophenyl)-6-bromo-3,4-dihydroquinazoline (m. p. 232°; identified by mixed m. p. test), a normal by-product of the main reaction, as shown by Simons.<sup>15</sup>

**N-(2-Benzalamino-5-chlorobenzyl)-*p*-chloroaniline.**—To 0.50 g. of 2-amino-5-chlorobenzyl-*p*-chloroaniline in 10 cc. of hot alcohol was added 0.5 cc. of benzaldehyde. The liquid soon set to a mass of crystals. Alcohol was then added in portions to the heated mixture until the product just dissolved. On cooling the filtered solution there separated 0.48 g. of needle-shaped crystals, and from the filtrate after concentration 0.06 g. more, a total yield of 80.6%. The benzal derivative melted at 137°, obsd., or 139°, corr. Heated with dilute sulfuric acid it yielded benzaldehyde.

*Anal.* Calcd. for  $C_{20}H_{16}N_2Cl_2$ : N, 7.89. Found: N, 7.80, 7.84.

**N-(2-Benzalamino-5-bromobenzyl)-*p*-bromoaniline.**—Prepared by the method described for the corresponding chlorine compound this derivative was obtained in 86.6% yield. After recrystallization from alcohol it melted at 142°, obsd., or 144.6°, corr.

*Anal.* Calcd. for  $C_{20}H_{16}N_2Br_2$ : N, 6.31. Found: N, 6.37, 6.27.

#### Conversion of Aminobenzylarylamines (II) to the Corresponding Tetrahydroquinazolines (IV)

Ring-closure by introduction of the methylene group was effected by formaldehyde in alcohol containing potassium hydroxide, as described previously.<sup>2d,16</sup>

**3-(*p*-Chlorophenyl)-6-chloro-1,2,3,4-tetrahydroquinazoline.**—This compound was obtained as small needles and in 72.7% yield. After crystallization from slightly diluted alcohol it melted at 155°, obsd., or 158° corr.

*Anal.* Calcd. for  $C_{14}H_{12}N_2Cl_2$ : N, 10.00. Found: N, 9.92, 10.03, 9.85.

**3-(*p*-Bromophenyl)-6-bromo-1,2,3,4-tetrahydroquinazoline.**—The yield of small plates was 92.9%; m. p. 170°, obsd., or 173°, corr. Recrystallization from hot al-

cohol appeared to deteriorate this compound both in appearance and melting point; better results were obtained when alcohol containing a small amount of potassium hydroxide was used.<sup>17</sup>

*Anal.* Calcd. for  $C_{14}H_{12}N_2Br_2$ : N, 7.61. Found: N, 7.67, 7.59.

#### Conversion of Aminobenzylarylamines (II) to the Corresponding Dihydroquinazolines (III)

Ring closure through =CH— was effected by heating the base with 90% formic acid on the water-bath.<sup>7b</sup> The mixture was made alkaline with sodium hydroxide, and steam-volatile material was removed. The residue was dried, and resins were dissolved by extraction with a little ether in a beaker, assisted by manipulation with a stirring rod with flattened end. The crystalline mass of nearly white dihydroquinazoline was filtered off, washed with a little chilled ether, and recrystallized from slightly diluted alcohol.

**3-(*p*-Chlorophenyl)-6-chloro-3,4-dihydroquinazoline** was thus obtained from aminochlorobenzyl-*p*-chloroaniline as fine needles; after crystallization from alcohol the base melted at 186–187°, obsd. Mixed with the base of m. p. 187°, obsd., obtained by the *p*-chloroaniline-formaldehyde condensation, the m. p. was 186–187°, obsd.

**3-(*p*-Bromophenyl)-6-bromo-3,4-dihydroquinazoline** was obtained, after crystallization from alcohol, as a yellow-tinted crystal meal of m. p. 200°, obsd. Mixed with the base of m. p. 202°, obsd., obtained from the condensation of *p*-bromoaniline and formaldehyde the compound melted at 201°, obsd.

#### Hydrogenation of the Halogenated Dihydroquinazolines

Saturation of the 1,2-double bond, and replacement of halogen by hydrogen, were effected in one operation by drastic reduction with sodium and absolute alcohol, using for 0.5 g. of the dihydroquinazoline about 2.5 g. of sodium and 25 cc. of alcohol. After the sodium had dissolved water was added and the alcohol was taken off under reduced pressure. The precipitated solid was crystallized from dilute alcohol. Both the chlorine and bromine compounds (III) gave the same product: colorless needles of m. p. 121–122°, a mixture of the two had the same melting point. In an experiment with 3-bromophenyl-6-bromodihydroquinazoline the bromine was recovered and weighed as AgBr: 0.50 g. of dihydroquinazoline gave 0.51 g. of silver bromide, corresponding to 43.4% bromine, that calculated being 43.7%. The product, 3-phenyl-3,4-dihydroquinazoline (V), made synthetically by Paal and Busch,<sup>18,18</sup> was reported to melt at 119°.

*Anal.* Calcd. for  $C_{14}H_{14}N_2$ : C, 80.00; H, 6.67; N, 13.33; mol. wt., 210. Found: C, 79.82; H, 6.64; N, 13.21, 13.36, 13.33; mol. wt. (camphor), 211, 218.

**Debromination of 3-(*p*-Bromophenyl)-6-bromo-1,2,3,4-tetrahydroquinazoline.**—Treatment with sodium and alcohol as outlined above gave from 0.50 g. of this compound

(17) The relative instability of the structural condition >N—CH<sub>2</sub>—N< in acid media is familiar. A striking example is afforded by the conversion of bis-(*p*-anisyl)-methane to the trimeric Schiff base on crystallization from alcohol.<sup>12</sup>

(18) Paal and Busch, *Ber.*, **22**, 2693 (1889).

(15) Simons, *This Journal*, **59**, 518 (1937).

(16) Busch and Dietz, *J. prakt. Chem.*, [2] **58**, 420 (1896).

0.20 g. of fine needles of m. p. 118°, obsd. A mixture of the product with that obtained by similar treatment of the dihydroquinazoline (m. p. 121°) melted well at 120°. The bromine split out was weighed as silver bromide: 0.50 g., corresponding to 42.6% bromine, that calculated being 43.5%.

Grateful acknowledgment is made to the Faculty Research Committee of the University of Pennsylvania for a grant to aid this study, and to the following for most of the analytical results reported: W. S. Young (molecular weights), F. W. Landau (nitrogen), and Wm. McClellan (carbon and hydrogen).

### Summary

Condensation of *p*-chloroaniline and of *p*-bromoaniline with formaldehyde in cold aqueous solution containing hydrochloric acid yielded as main products the corresponding 3-(halogenophenyl)-6-halogeno-3,4-dihydroquinazolines, of m. p. 192° (corr.) and m. p. 206° (corr.), respectively. The identities of these bases were experimentally established. Formation of these products was accompanied by that of unidentified bases and by methylation of part of the original amines.

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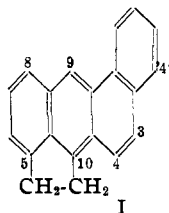
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

## 4,10-Ace-1,2-benzanthracene

BY LOUIS F. FIESER AND ARNOLD M. SELIGMAN

The powerfully carcinogenic hydrocarbon cholanthrene<sup>1,2</sup> is the 5,10-ace- (or dimethylene-) derivative (I) of 1,2-benzanthracene and it is one



of four possible ace- derivatives of this hydrocarbon. Two of the remaining isomers already have been synthesized and submitted to biological tests. The 8,9-ace- compound (8,9-dimethylene-1,2-benzanthracene<sup>2</sup>) has carcinogenic properties, but it produces tumors less than half as rapidly as cholanthrene.<sup>3</sup> The 3,4'-isomer (acenaphthanthracene<sup>4</sup>), in which both meso positions are unsubstituted, has given only negative results.<sup>5</sup> The synthesis of the fourth isomer, 4,10-ace-1,2-benzanthracene (VIII, below), is described in the present paper. The hydrocarbon is of particular interest because of the indications that substitution at the 10-position in the 1,2-benzanthracene molecule often is particularly favorable for the development

of cancer-producing properties,<sup>6</sup> but tests with the new hydrocarbon which are being conducted by Dr. M. J. Shear are not yet complete. The compound produces severe ulceration in mice as rapidly as cholanthrene, but thus far no tumors have been obtained. It is interesting that the three isomeric ace-1,2-benzanthracenes in which the five-membered ring is joined to a meso position of the aromatic system all show some biological activity, while the 3,4'-isomer is completely inactive.

The initial step in the synthesis consisted in the condensation of hydrindene with succinic anhydride. As in other Friedel and Crafts reactions, substitution occurred exclusively in the  $\beta$ -position, giving  $\beta$ -(5-hydrindoyl)-propionic acid (II). Reduction to III, cyclization, and reduction to V all proceeded smoothly, and the structure of the tricyclic compounds was established by oxidation of the ketone IV to pyromellitic acid. The structure of the keto acid II follows from that of the ketone. The condensation of 6,7-cyclopentenotetralin (V) with benzoyl chloride gave a liquid product for which only the structure VI is possible, and dehydrogenation of the ketone with selenium gave a liquid of approximately the composition of 1-benzoyl-2,3-cyclopentenonaphthalene, VII. The final step in the synthesis consists in a modified Elbs condensation of the type employed for the preparation of methyl-

(1) Cook, Haslewood and Robinson, *J. Chem. Soc.*, 667 (1935); Cook and Haslewood, *ibid.*, 767, 770 (1935).

(2) Fieser and Seligman, *THIS JOURNAL*, **57**, 2174 (1935).

(3) Shear, *Am. J. Cancer*, **28**, 334 (1936).

(4) Nicodemus, Eng. Patent 251,270 (1926), Ger. Patent 481,819 (1929); Nicodemus and Berndt, U. S. Patent 1,776,925 (1930); Cook, *J. Chem. Soc.*, 1087 (1930); Geyer and Zuffanti, *THIS JOURNAL*, **57**, 1787 (1935).

(5) Cook, *Proc. Roy. Soc. (London)*, **B111**, 495 (1932).

(6) L. F. Fieser, Mary Fieser, Hershberg, Newman, Seligman and Shear, *Am. J. Cancer*, **29**, 260 (1937).