[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Benzacridines. II. Synthesis of Chlorinated 5,6-Dimethylbenz[c]acridines

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The generality of the synthesis of benz[c]acridines reported in the first paper of this series has been established by the preparation of 9-chloro-5,6-dimethylbenz[c]acridine and 10-chloro-5,6-dimethylbenz[c]acridine. The Pfitzinger-Borsche reaction was used to prepare 11-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine, which was converted to 11-chloro-5,6-dimethylbenz[c]acridine. An abbreviated series of reactions leading to the parent compound, 5,6-dimethylbenz[c]acridine, has also been devised.

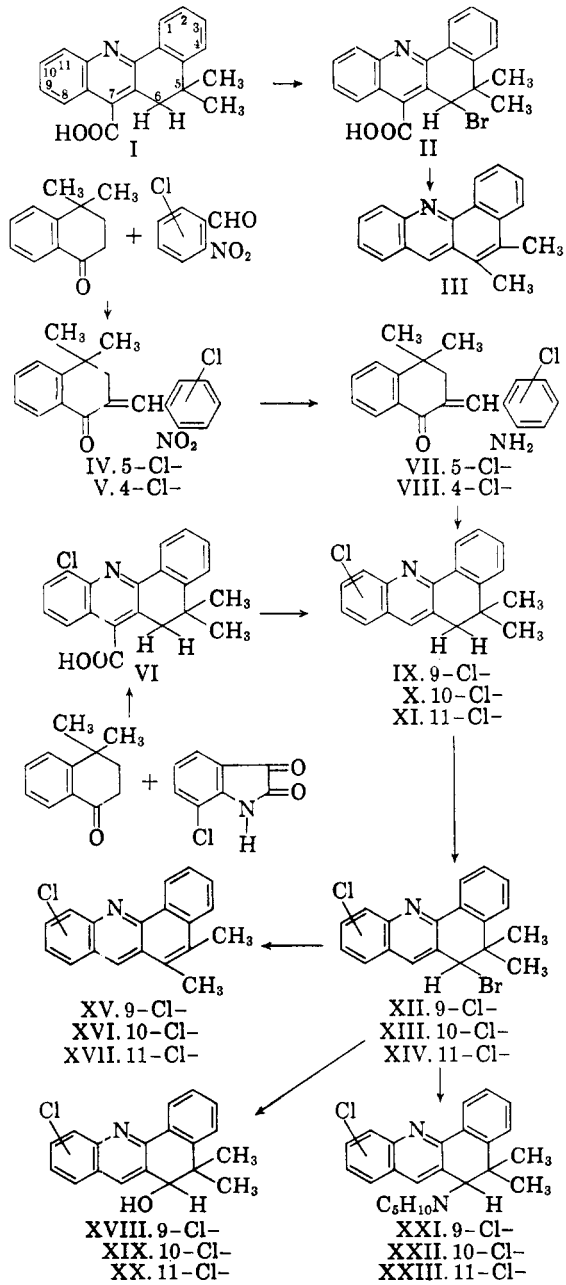
The first paper of this series[3] reported a new synthetic route leading to benz[c]acridines which are of interest as potential carcinogenic agents. In extending this work it was of considerable interest to prepare chlorinated benz[c]acridines, not only from the standpoint of the potential effect of the chlorine substituent on the carcinogenicity of the parent 5,6-dimethylbenz[c]acridine, but also as a test of the general utility of the new route to the preparation of substituted benz[c]acridines.

9-Chloro-5,6-dimethylbenz[c]acridine (XV) and 10-chloro-5,6-dimethylbenz[c]acridine (XVI) were prepared starting with suitably substituted aldehydes, using the general procedure reported previously[3] for the unsubstituted parent benzacridine. Both 5-chloro-2-nitrobenzaldehyde and 4-chloro-2-nitrobenzaldehyde condensed with 4,4-dimethyl-1-tetralone in acetic acid–sulfuric acid solvent to give 80% yields of the nitrobenzal tetralones IV and V. Reduction with iron and acetic acid gave a 90% yield of 4,4-dimethyl-2-(2-amino-5-chlorobenzal)-1-tetralone (VII) and 94% of the corresponding 4-chloro amino tetralone (VIII). Each was ring-closed in nearly quantitative yield to the chlorinated dihydrobenz[c]acridine derivatives IX and X.

A Pfitzinger-Borsche reaction of 7-chloroisatin and 4,4-dimethyl-1-tetralone was less satisfactory than the same reaction carried out with isatin,[3] but a 53% yield of the desired acid VI was obtained. This acid was then readily decarboxylated to 11-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (XI).

Bromination of the dihydrobenz[c]acridines IX, X, and XI was accomplished with *N*-bromosuccinimide in the manner reported previously for the unchlorinated compound. Thermal decomposition, involving a combined "α-dehydrobromination–Wagner rearrangement," gave the desired aromatized benzacridines XV, XVI, and XVII.

Hydrolysis of all three bromo compounds was effected with an aqueous sodium bicarbonate–dioxane solution to give the 6-hydroxy chlorinated



dihydrobenz[c]acridines XVIII, XIX and XX in yields of 73–83%. Loss of the 9-chloro substituent[4]

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(3) V. L. Bell and N. H. Cromwell, *J. Org. Chem.*, **23**, 789 (1958).

(4) R. M. Acheson, *Acridines*, Interscience Publishers, Inc., New York, N. Y., 1956, p. 311.

was not realized under the mild conditions of hydrolysis. However, the ready displacement of the *p*-chlorine group was confirmed in preparing the 6-piperidino derivatives XXI, XXII, and XXIII. If an excess of piperidine was reacted with 6-bromo-9-chloro-5,5-dimethyl-5,6-dihydrobenz[*c*]acridine (XII), not only was the reactive bromine substituent replaced, but also much of the chlorine in the 9- position. Thus, the preparation of 9-chloro-5,5-dimethyl-6-*N*-piperidino-5,6-dihydrobenz[*c*]acridine (XXI) had to be carried out using only two molar equivalents of piperidine. Yields of the piperidino derivatives varied from 46–73% and considerable charcoal treatment was necessary to secure oil-free products.

An alternative route to the parent 5,6-dimethylbenz[*c*]acridine, somewhat simpler than the procedure reported previously,[3] was found to be quite satisfactory. Although 7-carboxy-5,5-dimethyl-5,6-dihydrobenz[*c*]acridine[3] (I), which was prepared via the Pfitzinger-Borsche reaction, appeared to be essentially insoluble in carbon tetrachloride, it was brominated in an 81% yield by refluxing a slurry of *N*-bromosuccinimide and the acid I in carbon tetrachloride. Upon melting the bromo acid II, decarboxylation along with "α - dehydrobromination" and methyl group rearrangement resulted, giving a 61% yield of 5,6-dimethylbenz[*c*]acridine (III). This offers a possibility for preparation of benz[*c*]acridines with substituents in the 8-, 9-, 10- and 11- positions where the suitably substituted isatin is more available than the *o*-nitrobenzaldehyde with the necessary substituent.

Discussion of ultraviolet spectra. A tabulation of the ultraviolet spectra of the benzacridines and intermediates is given in the Experimental section. Little change was noted upon introduction of chlorine into the parent 5,6-dimethylbenz[*c*]acridine.[3] Essentially identical spectra, regardless of substituents, were noted for the dihydro benzacridine derivatives and an extremely simplified spectral pattern was found for all dihydrobenzacridines bearing the 6-bromosubstituent. Thus, it appears that the completely aromatic benz[*c*]acridines can be readily distinguished from the dihydro benz[*c*]-acridines. However, differences in spectra between members of each class having different substituents are too subtle to be of value in identification.

EXPERIMENTAL[5]

6-Bromo-7-carboxy-5,5-dimethyl-5,6-dihydrobenz[c]acridine (II). A slurry of 7.15 g. (0.0236 mole) of the acid I,[3] 4.20 g. (0.0236 mole) of *N*-bromosuccinimide, 0.10 g. of benzoyl peroxide and 350 ml. of carbon tetrachloride was refluxed for 3.5 hr. At the end of this time all of the heavy NBS had changed to the light weight succinimide, which floated with the bromo acid on top of the solvent. The mixture was chilled and the solid was collected. The crude product was triturated thoroughly with cold water to remove the succinimide, after which the remaining solid was dissolved in acetone and the solution was treated with charcoal. Water was added to precipitate the bromo acid II in the form of colorless crystals, m.p. 196–198° (dec.). The yield was 7.30 g. (81%).

Anal. Calcd. for $C_{20}H_{16}NO_2Br$: C, 62.84; H, 4.22; N, 3.66. Found: C, 63.30; H, 4.77; N, 3.63.

5,6-Dimethylbenz[c]acridine (III). One g. (0.0026 mole) of the bromo acid II was melted in a small Erlenmeyer flask and heated carefully (200–210°) until the evolution of carbon dioxide and hydrogen bromide had ceased. The residue was cooled and extracted thoroughly with hot aqueous dioxane. The solution was neutralized with dilute sodium bicarbonate solution and cooled. The tan crystals were collected and recrystallized from aqueous acetone, with charcoal treatment. The yellow plates, 0.41 g. (61%), melted at 159–160°. A mixed melting point determination with authentic 5,6-dimethylbenz[*c*]acridine[3] showed the two products to be identical.

4,4-Dimethyl-2-(5-chloro-2-nitrobenzal)-1-tetralone (IV). A solution of 9.5 g. of 4,4-dimethyl-1-tetralone, 10.5 g. (0.0567 mole) of 5-chloro-2-nitrobenzaldehyde and 15 ml. of 95% sulfuric acid in 75 ml. of glacial acetic acid was allowed to stand at room temperature for 4 days. The precipitated crystals were recrystallized from glacial acetic acid to give 14.9 g. (80% yield) of light yellow crystals of the nitro ketone IV, m.p. 121–122°; λ_{max} 206, 275 mμ; ($\epsilon \times 10^{-3}$ 25.8, 23.7).

Anal. Calcd. for $C_{19}H_{16}NO_3Cl$: C, 66.76; H, 4.72; N, 4.10. Found: C, 66.76; H, 4.60; N, 4.08.

4,4-Dimethyl-2-(4-chloro-2-nitrobenzal)-1-tetralone (V). Using the same procedure outlined above for the 5-chloro isomer, a solution of 17.07 g. of 4,4-dimethyl-1-tetralone, 18.2 g. (0.0981 mole) of 4-chloro-2-nitrobenzaldehyde and 27 ml. of 95% sulfuric acid in 180 ml. of glacial acetic acid gave 26.9 g. (80% yield) of pale yellow crystals of the nitro ketone V, m.p. 150.5–151.5°; λ_{max} 206, 275 mμ; ($\epsilon \times 10^{-3}$ 25.0, 19.0).

Anal. Calcd. for $C_{19}H_{16}NO_3Cl$: C, 66.76; H, 4.72. Found: C, 66.66; H, 4.90.

7-Carboxy-11-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (VI). A solution of 7.55 g. (0.0416 mole) of 7-chloroisatin, 7.25 g. (0.0416 mole) of 4,4-dimethyl-1-tetralone, 8 g. of potassium hydroxide, 40 ml. of methanol and 20 ml. of water was refluxed for 24 hr. The solution was then cooled, diluted with 100 ml. of water, and acidified to methyl orange with hydrochloric acid. The crude acid was recrystallized once from ethanol and once from aqueous acetone, with charcoal treatment, to give 7.5 g. (53% yield) of pale yellow crystals of the acid VI, m.p. 240.5–242° (dec.); λ_{max} 213, 215, 227 (sho.), 265 (sho.), 272, 307, 320, 333, 349 mμ; ($\epsilon \times 10^{-3}$ 36.2, 35.8, 22.8, 32.2, 42.6, 8.40, 9.86, 12.0, 11.6).

Anal. Calcd. for $C_{20}H_{16}NO_2Cl$: C, 71.11; H, 4.77; Cl, 10.50. Found: C, 71.09; H, 4.88; Cl, 10.41.

4,4-Dimethyl-2-(2-amino-5-chlorobenzal)-1-tetralone (VII). A solution of 13.5 g. (0.0395 mole) of the nitro ketone IV in 250 ml. of glacial acetic acid and 40 ml. of water was heated on a steam bath and 5.5 g. of powdered iron was added over a period of 45 min. After heating an additional 15 min., the solution was cooled and poured over 1 l. of ice and water with rapid stirring. The yellow solid was collected, washed, and triturated thoroughly with water. Two recrystallizations from aqueous ethanol gave 11.1 g. (90% yield) of bright yellow crystals of the amino ketone VII, m.p. 151–153°.

Anal. Calcd. for $C_{19}H_{18}NOCl$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.10; H, 5.70; N, 4.37.

4,4-Dimethyl-2-(2-amino-4-chlorobenzal)-1-tetralone (VIII). The procedure described above for the preparation of the 5-chloro isomer (VII) was also used to prepare the 4-chloro isomer (VIII). Reduction of 25.8 g. (0.0755 mole) of the nitro ketone V in 500 ml. of glacial acetic acid and 75 ml. of

(5) Ultraviolet spectral determinations were made at about 25° using a Cary recording spectrophotometer, model 11 MS, using 95% ethanol solutions unless otherwise indicated.

water with 10.4 g. of powdered iron gave 22.05 g. (94% yield) of bright yellow crystals of the amino ketone VIII, m.p. 162–163°.

Anal. Calcd. for $C_{19}H_{18}NOCl$: C, 73.19; H, 5.82; N, 4.49. Found: C, 73.01; H, 5.79; N, 4.52.

9-Chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (IX). A solution of 11.5 g. (0.0369 mole) of the amino ketone VII in 150 ml. of ethanol and 15 ml. of concentrated hydrochloric acid was heated for 1 hr. on a steam bath. The hot solution was treated with charcoal, filtered, and neutralized with dilute sodium hydroxide solution. The solution was diluted with water and cooled, precipitating pale yellow crystals. Recrystallization from aqueous acetone, with charcoal treatment, gave 10.0 g. (92% yield) of colorless plates of 9-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine, m.p. 147–148°; λ_{max} 216, 226, 260 (sho.), 268, 319, 333, 349 mμ; ($\epsilon \times 10^{-3}$ 40.0, 37.8, 29.1, 38.3, 8.74, 14.5, 18.1).

Anal. Calcd. for $C_{19}H_{16}NCl$: C, 77.67; H, 5.49; N, 4.77; Cl, 12.07. Found: C, 77.79; H, 5.70; N, 4.71; Cl, 12.30.

10-Chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (X). Ring closure of the amino ketone VIII was carried out using the procedure described above. From 22.05 g. (0.0707 mole) of VIII was obtained 20.0 g. (96% yield) of 10-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine in the form of colorless plates, m.p. 131–132.5°; λ_{max} 213, 215, 230, 258 (sho.), 265, 299, 320, 335, 350 mμ; ($\epsilon \times 10^{-3}$ 41.7, 41.7, 32.0, 32.6 40.3, 9.00, 8.00, 13.4, 16.5).

Anal. Calcd. for $C_{19}H_{16}NCl$: C, 77.67; H, 5.49; N, 4.77. Found: C, 77.71; H, 5.68; N, 4.79.

11-Chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (XI). The acid VI (8.8 g., 0.026 mole) was melted in a small Erlenmeyer flask and maintained at 245° until the evolution of carbon dioxide had ceased. After cooling, the residue was triturated with 10% potassium hydroxide solution and the alkaline mixture was extracted with ether. The ether layer was washed with water and the ether was evaporated. Two recrystallizations of the residue from aqueous acetone, with charcoal treatment, gave 6.1 g. (80%) of nearly colorless crystals, of XI, m.p. 124–125°; λ_{max} 211, 215, 227 (sho.), 263 (sho.), 270, 319, 332, 348 mμ; ($\epsilon \times 10^{-3}$ 35.5, 36.6, 25.5, 33.0, 43.6, 10.3, 13.4, 13.5).

Anal. Calcd. for $C_{19}H_{16}NCl$: C, 77.67; H, 5.49. Found: C, 77.70; H, 5.43.

6-Bromo-9-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (XII). A mixture of 5.87 g. (0.02 mole) of IX, 3.65 g. (0.02 mole) of *N*-bromosuccinimide and 0.05 g. of benzoyl peroxide in 75 ml. of carbon tetrachloride was refluxed for 2 hr. After cooling, the succinimide was removed by filtration and the solvent was removed under reduced pressure. The solid residue was recrystallized twice from aqueous acetone *at room temperature*, with charcoal treatment, to give 7.1 g. (95%) of colorless crystals of XII. The compound melted at 167.5–170° to a light yellow liquid, which decomposed to a bright red solid over the range 170–190°; λ_{max} (iso-octane) 211, 223, 235 (sho.), 273, 341, 355 mμ; ($\epsilon \times 10^{-3}$ 26.3, 29.2, 26.5, 36.7, 8.50, 8.34).

Anal. Calcd. for $C_{19}H_{15}NClBr$: C, 61.23; H, 4.06. Found: C, 61.44; H, 4.18.

6-Bromo-10-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (XIII). The procedure described above for the 9-chloro isomer was employed to brominate the 10-chloro isomer, giving a yield of 80% of colorless crystals of XIII, m.p. 155–157°. The molten yellow liquid changed sharply to a bright red solid at 166°. λ_{max} (iso-octane) 212, 219, 239, 267, 338, 346, 354 mμ; ($\epsilon \times 10^{-3}$ 27.7, 29.0, 25.0, 46.2, 9.00, 7.02, 10.0).

Anal. Calcd. for $C_{19}H_{15}NClBr$: C, 61.23; H, 4.06. Found: C, 61.72; H, 4.21.

6-Bromo-11-chloro-5,5-dimethyl-5,6-dihydrobenz[c]acridine (XIV). Use of the general bromination procedure resulted in a 90% yield of nearly colorless crystals of XIV, m.p. 180–182°; λ_{max} (iso-octane): 225, 275, 338, 354 mμ; ($\epsilon \times 10^{-3}$ 29.6, 43.8, 7.80, 6.48).

Anal. Calcd. for $C_{19}H_{15}NClBr$: C, 61.23; H, 4.06. Found: C, 61.13; H, 4.09.

9-Chloro-5,6-dimethylbenz[c]acridine (XV). The bromo compound XII, 1.50 g. (0.004 mole) was melted in a 10 ml. Erlenmeyer flask and kept at 200° for 10 min. The red solid was cooled and triturated with hot aqueous dioxane. The dioxane extract was neutralized with dilute sodium carbonate solution and cooled. The resulting solid was collected and recrystallized twice from acetone, with charcoal treatment. Another recrystallization, from benzene and petroleum ether, gave 0.80 g. (68% yield) of yellow needles of XV, m.p. 169–170°; λ_{max} 212, 224, 235, 279, 297, 372, 390 mμ; ($\epsilon \times 10^{-3}$ 25.0, 32.1, 34.8, 53.1, 49.1, 6.09, 5.56).

Anal. Calcd. for $C_{19}H_{14}NCl$: C, 78.21; H, 4.84. Found: C, 77.52, H, 4.90.

10-Chloro-5,6-dimethylbenz[c]acridine (XVI). Thermal decomposition of 1.50 g. of the bromo compound XIII at 165–175° resulted in a yield of 0.90 g. (77%) of 10-chloro-5,6-dimethylbenz[c]acridine (XVI) in the form of yellow needles, m.p. 170–171°; λ_{max} 212, 223, 230 (sho.), 272 (sho.), 281, 294, 324, 339, 357, 377, 394 mμ; ($\epsilon \times 10^{-3}$ 27.0, 35.6, 33.0, 43.2, 55.5, 58.0, 5.00, 5.36, 4.80, 5.60, 5.56).

Anal. Calcd. for $C_{19}H_{14}NCl$: C, 78.21; H, 4.84. Found: C, 78.01; H, 4.93.

11-Chloro-5,6-dimethylbenz[c]acridine (XVII). Thermal decomposition of the bromo compound XIV at 200° resulted in a 77% yield of bright yellow crystals of 11-chloro-5,6-dimethylbenz[c]acridine (XVII), m.p. 197–198°; λ_{max} 212, 224, 229 (sho.), 283, 293, 344, 374, 393 mμ; ($\epsilon \times 10^{-3}$ 28.4, 40.1, 38.4, 57.2, 54.9, 5.88, 5.92, 4.72).

Anal. Calcd. for $C_{19}H_{14}NCl$: C, 78.21; H, 4.84. Found: C, 78.07; H, 4.88.

9-Chloro-5,5-dimethyl-6-hydroxy-5,6-dihydrobenz[c]acridine (XVIII). A solution of 1.50 g. (0.004 mole) of the bromo compound XII in 20 ml. of dioxane and 10 ml. of 5% sodium bicarbonate solution was heated on a steam bath for 1 hr. Ten ml. of water was added and the solution was cooled. The oil which separated slowly solidified. The crude product was recrystallized, once from aqueous acetone with charcoal treatment, and once from ethanol. Colorless crystal, 1.03 g. (83% yield), were obtained, m.p. 190–192°; λ_{max} 218, 227, 262 (sho.), 269, 297, 310, 333, 348 mμ; ($\epsilon \times 10^{-3}$ 40.6, 38.1, 28.9, 33.8, 12.5, 10.0, 13.8, 17.2).

Anal. Calcd. for $C_{19}H_{16}NOCl$: C, 73.66; H, 5.21. Found: C, 73.52; H, 5.13.

10-Chloro-5,5-dimethyl-6-hydroxy-5,6-dihydrobenz[c]acridine (XIX). Treatment of 1.50 g. (0.004 mole) of the bromo compound XIII, as described for the 9-chloro isomer, gave 0.90 g. (73% yield) of the hydroxy compound XIX as colorless crystals, m.p. 166–167.5°; λ_{max} 212, 214, 228, 259 (sho.), 265, 318, 334, 349 mμ; ($\epsilon \times 10^{-3}$ 37.9, 38.7, 31.5, 33.6, 36.2, 7.96, 12.5, 15.2).

Anal. Calcd. for $C_{19}H_{16}NOCl$: C, 73.66; H, 5.21. Found: C, 73.35; H, 5.34.

11-Chloro-5,5-dimethyl-6-hydroxy-5,6-dihydrobenz[c]acridine (XX). Treatment similar to that described above for the 9- and 10-chloro isomers, using 1.50 g. of the bromo compound XIV, gave 1.0 g. (81% yield) of nearly colorless crystals of the hydroxy compound XX, m.p. 177–179°; λ_{max} 212, 216, 265 (sho.), 272, 319, 331 (sho.), 332, 347 mμ; ($\epsilon \times 10^{-3}$ 33.6, 34.8, 32.0, 38.6, 10.0, 12.2, 12.3, 11.4).

Anal. Calcd. for $C_{19}H_{16}NOCl$: C, 73.66; H, 5.21. Found: C, 73.73; H, 5.37.

9-Chloro-5,5-dimethyl-6-N-piperidino-5,6-dihydrobenz[c]acridine (XXI). To a solution of 1.50 g. (0.004 mole) of the bromo compound XII in 10 ml. of benzene was added a solution of 0.70 g. (0.008 mole) of piperidine in 5 ml. of benzene. The solution was refluxed for 2 hr. on a steam bath. After cooling the reaction mixture, the piperidine hydrobromide was removed, the filtrate extracted with water, and the benzene evaporated under reduced pressure. The solid residue was recrystallized once from aqueous acetone and once from ethanol, with charcoal treatment. Colorless crystals of the piperidino derivative XXI, 0.90 g. (60%

yield), were obtained, m.p. 139–140°; λ_{max} 217, 228 (sho.), 270, 336, 351 mμ; ($\epsilon \times 10^{-3}$ 43.3, 36.2, 36.0, 13.6, 14.2).

Anal. Calcd. for $C_{24}H_{25}N_2Cl$: C, 76.47; H, 6.69. Found: C, 76.56; H, 6.72.

10-Chloro-5,5-dimethyl-6-N-piperidino-5,6-dihydrobenz[c]-acridine (XXII). Treatment similar to that described for the 9-chloro isomer, but using an excess of piperidine, gave a 73% yield of the piperidino derivative XXII as pale yellow crystals, m.p. 148–150°; λ_{max} 217, 230 (sho.), 267, 337, 352 mμ; ($\epsilon \times 10^{-3}$ 44.0, 30.9, 37.5, 12.2, 13.0).

Anal. Calcd. for $C_{24}H_{25}N_2Cl$: C, 76.47; H, 6.69. Found: C, 76.05; H, 6.87.

11-Chloro-5,5-dimethyl-6-N-piperidino-5,6-dihydrobenz[c]-acridine (XXIII). This preparation was similar to that used for the 9-chloro isomer. However, three recrystallizations from acetone, with charcoal treatment, were necessary to obtain a pure product. From 1.50 g. of the bromo compound XIV was obtained 0.70 g. (46% yield) of colorless crystals of the piperidino derivative XXIII, m.p. 121.5–123°; λ_{max} 216, 273, 322, 335, 350 mμ; ($\epsilon \times 10^{-3}$ 40.9, 41.8, 10.0, 12.3, 11.1).

Anal. Calcd. for $C_{24}H_{25}N_2Cl$: C, 76.47; H, 6.69. Found: C, 76.73; H, 6.91.

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LINCOLN, NEB.

[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORIES, MICHIGAN STATE UNIVERSITY]

A Study of Factors Influencing Catalytic Hydrogenation Kinetics[1]

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The rate of disappearance of hydrogen in the catalytic hydrogenation of benzene is found to obey the pseudo-first order rate law

$$-\frac{dp}{dt} = \frac{Rkp}{V_1/T_1 + V_2/T_2}$$

in which p is hydrogen pressure, t is time, R is the gas constant, V_1 and T_1 are the volume and absolute temperature of the reaction chamber, V_2 and T_2 are the volume and absolute temperature of the remainder of the apparatus, and k is the pseudo-first order rate constant. When $T_1 = T_2$ and $V_1 + V_2 = V$ (total volume of the apparatus), the expression reduces to

$$-dp/dt = RTkp/V$$

The rate of disappearance of benzene obeys the zero-order expression

$$c_0 - c = k_0 t$$

in which c_0 is the initial concentration of benzene, c is the concentration of benzene at time t, and k_0 is the zero-order rate constant. The relationship between k and k_0 is examined.

The rate of a catalytic hydrogenation is first-order with respect to hydrogen pressure, zero-order with substrate concentration, and directly proportional to the weight of the catalyst,[3] apparently conforming to the simple, pseudo-first order rate equation,

$$-dp/dt = k_{app}p \text{ or } \log p_0/p = k_{app}t/2.303 \quad (1)$$

in which p is the hydrogen pressure at time t, p_0 is the initial hydrogen pressure, and k_{app} is the apparent rate constant. In order to relate the rate constants to a unit quantity of catalyst, their experimental values are customarily divided by the weights of catalyst used.

When measured in terms of hydrogen pressure, the rate of catalytic hydrogenation also shows an apparent inverse relationship to the volume of the hydrogenation apparatus. In order to obtain rate constants which are independent of the apparatus volume, Fuzek and Smith[4] have suggested, on empirical grounds, a revised rate equation which includes this volume V:

$$-dp/dt = k'p/V \text{ or } \log p_0/p = k't/2.303V \quad (2)$$

This revised equation gives satisfactory comparisons of rate constants for low-pressure hydrogenations carried out in apparatus of different volumes but at similar pressures, and at or near room temperature. Recent investigations[5] have shown, however, that Equation 2 becomes less and less applicable as the reaction temperatures are increased; moreover, puzzling discrepancies arise when attempts are made to use Equation 2 for comparison of rates of the same hydrogenation measured in different pressure ranges under otherwise similar conditions.

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(1) Abstracted in part from the doctoral dissertation of Lyman R. Caswell, Michigan State University, 1956.

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(3) H. A. Smith, D. L. Alderman, and F. W. Nadig, *J. Am. Chem. Soc.*, **67**, 272 (1945).

(4) J. F. Fuzek and H. A. Smith, *J. Am. Chem. Soc.*, **70**, 3743 (1948).

(5) L. Ciporin, Master's Thesis, Michigan State University, 1952.