ml. of water, whereupon a pasty mass, that solidified on standing, separated. This precipitate was warmed on a steam-bath with 80 ml. of 5% sulfuric acid and after cooling the insoluble crystalline acid filtered off. This acid was dissolved in 80 ml. of 5% sodium hydroxide solution, filtered, and the filtrate poured into 150 ml. of a 10% sulfuric acid solution. The acid slowly crystallized from this aqueous acid solution and was filtered off in several crops. Repetition of this solution in alkali and reprecipitation by sulfuric acid gave an acid that melted at 85–86°; neut. equiv., 103; mol. wt. (in camphor), 200 (calcd. 200).

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 60.00; H, 8.00. Found: C, 59.81; H, 8.07.

Nepetalic Acid Acetate (XI).—A mixture of 1 g. of nepetalic acid, m. p. 74–75°, and 1.2 g. of acetic anhydride was heated for four hours at 100° and then fractionally distilled. After the acetic acid and unchanged anhydride were removed, the nepetalic acid acetate distilled at 124–126° (0.1 mm.). It solidified in the receiver. After recrystallization from an ether–petroleum ether mixture it melted at 68–69°; $\alpha^{23}\text{D}$ +72.2°. The yield was practically quantitative. This acetate is insoluble in aqueous sodium hydroxide and shows no reaction with bromine in carbon tetrachloride.

Anal. Calcd. for $C_{12}H_{18}O_4$: C, 63.69; H, 8.01. Found: C, 63.61; H, 8.21.

Summary

The acidic constituent of the volatile oil of catnip, to which the name nepetalic acid is assigned, is found to be a tri-substituted cyclopentane with $-CH_3$, —COOH and $-CH(CH_3)CHO$ as the substituent groups. This aldehydo-acid appears to have two tautomeric forms (a) an enol form in which the aldehyde-containing substituent exists as $-C(CH_3){=}CHOH$, and (b) a bicyclic hydroxylactone that yields a neutral acetate with acetic anhydride.

Distillation at atmospheric pressure converts nepetalic acid into an unsaturated lactone, nepetalactone, a compound which is found to make up about half of the oil of catnip. This lactone is rapidly saponified and taken into solution by aqueous sodium hydroxide and together with nepetalic acid comprises the 85% of the oil that dissolves in this solvent.

Nepetalic acid is oxidized by hydrogen peroxide in alkaline solution to formic and nepetonic acids. The latter acid contains an acetyl group in the place of the $-CH(CH_3)CHO$ substituent of nepetalic acid. Sodium hypoiodite converts nepetonic acid into nepetic acid, a methyldicarboxycyclopentane. Oxidation of nepetalic acid with chromic acid converts the aldehyde group to a carboxyl and produces the dibasic nepetalinic acid. A number of derivatives of these various acids are described.

MADISON, WISCONSIN RECEIVED MARCH 8, 1941

[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Selective Hydrogenation of Derivatives of Pyrrole, Indole, Carbazole and Acridine

BY HOMER ADKINS AND HARRY L. COONRADT

The phenylpyrroles, indoles, carbazoles and acridines offer many possibilities for partial and selective hydrogenation. The yield of compounds produced is determined by the catalyst and other conditions of reaction as well as by the structure of the particular hydrogen acceptor involved. This paper presents the experimental results obtained in the partial and complete hydrogenation of twenty-one heterocyclic compounds over copper chromite and Raney nickel. An attempt has been made to correlate the behavior of these compounds toward hydrogenation with their electronic structure.

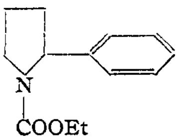
The pyrrole nucleus requires more drastic conditions for hydrogenation than does the benzenoid nucleus. However substitution of a carbethoxy group on the nitrogen of pyrrole so decreases resonance that the ring may be hydrogenated under very mild conditions.[1,2] The phenyl group has a somewhat similar effect for 1-phenylpyrrole was converted under mild conditions to 1-phenylpyrrolidine over Raney nickel.[1] However either a carbethoxy or a phenyl group in the 2-position is very much less effective in decreasing ring resonance than when it is in the 1-position. 2-Phenylpyrrole I underwent hydrogenation in both rings over nickel at 165°, 27% 2-cyclohexylpyrrolidine (II), 15% 2-phenylpyrrolidine (III), and 40% unchanged 2-phenylpyrrole being isolated after a typical two-hour run. Nickel was there-

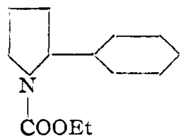
[1] Signaigo and Adkins, THIS JOURNAL, **58**, 709 (1936).

[2] Rainey and Adkins, *ibid.*, **61**, 1104 (1939).

fore useful only for the complete hydrogenation of I to II, 69% of the latter being obtained after shaking for 2.5 hours at 200°. On the other hand, copper chromite showed its preferential action for the hydrogenation of a heterocyclic ring as contrasted with a benzenoid nucleus: over this catalyst for 4.5 hours at 200°, I was converted to a mixture from which 55% of the 2-phenylpyrrolidine was isolated in addition to 20% unchanged I.

In 1-carbethoxy-2-phenylpyrrole the additional decrease in resonance due to the carbethoxy group is such that even nickel brought about a preferential hydrogenation of the pyrroloid ring and 1-carbethoxy-2-phenylpyrrolidine (IV) was readily obtained in good yield. Nickel was of course the preferred catalyst for the complete hydrogenation to give 1-carbethoxy-2-cyclohexylpyrrolidine (V).


IV
Ni, 155°, 80%[3]


V
Ni, 250°, 83%

1-Benzylpyrrole (VI), whose phenyl group is not conjugated with the pyrrole nucleus, is no more readily hydrogenated than pyrrole itself. In fact hydrogenation was so slow over nickel that cleavage occurred and pyrrolidine and toluene were produced: after eight hours at 260°, the sole product was pyrrolidine (70%), while after six and one-half hours at 230°, pyrrolidine (24%), 1-benzylpyrrole (43%) and 1-benzylpyrrolidine (3%) were obtained. After five hours at 200°, the same products were formed in comparable amounts (27%, 48% and 9%, respectively). On the other hand, copper chromite was again an effective catalyst for selective hydrogenation, 1-benzylpyrrolidine being produced in 67% yield after six hours at 200°; only small amounts of pyrrolidine (6%) and unchanged benzylpyrrole (9%) were found.

Von Braun and Bayer[4] reported that the hydrogenation of indole at 200° gave 2-ethyl-cyclohexylamine; 2-methyl- and 3-methylindoles gave the corresponding octahydroindoles at 200° and 2-alkylcyclohexylamines at 240°; 3-ethylindole at 235° gave 2-*s*-butylcyclohexylamine; and 1,2-dimethylindole gave the octahydro compound along with 20% of products resulting from the rupture of a ring. The formation of tetrahydroindoles was reported but neither amounts nor derivatives[3] were mentioned. The preparation of dihydroindoles in 95% yield using a copper-containing catalyst has been claimed.[5] Willstätter and Jacquet[6] reported the hydrogenation of indole over platinum to dihydro- and octahydroindole. Hadano and Matsumo[7] claimed that 2-methylindole over platinum gave 2-methyloctahydroindole and 4,5,6,7-tetrahydro-2-methylindole. However, the properties and derivatives reported for the latter are very similar to those of 2,3-dihydro-2-methylindole.[8,9]

However, we have found that indoles upon hydrogenation behaved like 2-phenylpyrrole in that the pyrrole ring was readily and preferentially hydrogenated over copper chromite to 2,3-dihydroindoles. Apparently the availability of an alternate path for the electrons into the benzene nucleus, isolates the double bond in the 2,3-position and renders it susceptible to hydrogenation. The hydrogenation of indoles with copper chromite at 170–190° ceased after about 70–80% of the indole had reacted. Tests indicated that the catalyst was as active at the end of the period of reaction as at the beginning. It seems probable that there is an equilibrium, indole + $H_2 \rightleftarrows$ dihydroindole, and that even at pressures of about 250 atm. the indole is present in the equilibrium mixture in rather considerable amounts. Thus from indole after an hour at 170°, 57% 2,3-dihydroindole was obtained, while from 2-methylindole (190°), 3-ethylindole (160°) and 1,2-dimethylindole (170°) after 15 min., the corresponding 2,3-dihydroindoles were produced in yields of 55%, 56%, and 48%, respectively, along with, in the first two cases, the unchanged indoles in yields of 18% and 10%.

Using nickel under mild conditions (0.5 hour at 170°) 2-methylindole gave 2-methyl-2,3-dihydroindole (23%) and 2-methyloctahydroindole (30%) in addition to 15% unchanged material. It is evident that nickel is of little value for the selective hydrogenation of the pyrroloid ring. On the other hand, indole, 2,3-dihydroindole, 2-methylindole, 2-methyl-2,3-dihydroindole, 3-ethylindole and 3-ethyl-2,3-dihydroindole all were completely

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[3] Yields of 80 to 85%, as reported in this paper, indicate that only a single product was formed, as the mechanical and distillation losses usually amounted to about 15% of the quantities submitted to hydrogenation.

[4] Von Braun and Bayer, *Ber.*, **58**, 387 (1925).

[5] *Chem. Abst.*, **30**, 4874 (1936); German Patent 623,693 (1935)

[6] Willstätter and Jacquet, *Ber.*, **51**, 767 (1918).

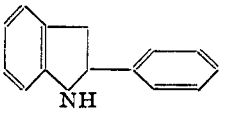
[7] Hadano and Matsumo, *J. Pharm. Soc. Japan*, **48**, 904 (1924).

[8] Von Braun and Steindorf, *Ber.*, **37**, 4729 (1904).

[9] Wenzing, *Ann.*, **239**, 244 (1887).

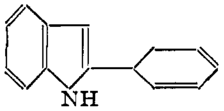
hydrogenated to the corresponding octahydroindoles in 79–81% yield over nickel at 220–250°. Only 1,2-dimethylindole was exceptional, an as yet unidentified product being obtained under these conditions.

The phenyl group in 2-phenylindole apparently greatly decreases resonance in the pyrroloid ring. Thus hydrogenation to the dihydro compound, VII occurred over copper chromite at 155°.



$CuCr_2O_4$, 155°, 43%

VII



VIIa

After only a half hour at that temperature a 14% yield of VII was isolated along with a recovery of 68% of the starting material. The yield of VII was thus 43% based upon the amount of 2-phenylindole not recovered. The double bond in the 2,3-position in this compound thus underwent hydrogenation over copper chromite under conditions almost as mild as those required for a simple alkene linkage or for the 9,10-position in phenanthrene.[10]

The further hydrogenation of 2-phenylindole or VII over copper chromite at 190° produced a rather striking result. Hydrogenation of the phenyl group occurred and there was produced in almost equal amounts 2-cyclohexylindole, and 2-cyclohexyldihydroindole. The hydrogenation of a benzenoid nucleus over copper chromite at a temperature as low as 190° is unusual and suggests that the mechanism is different from that usually followed in the hydrogenation of an aromatic nucleus.

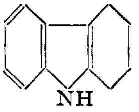
This anomaly disappears if it is assumed that the first formed 2,3-dihydrophenylindole, VII, rearranges to a compound of the structure VIIa, which would be readily further hydrogenated over copper chromite since the double bonds reacting in VIIa are of a non-aromatic type. The rearrangement postulated is the same as that which must occur when 9,10-dihydrophenanthrene is converted into tetrahydro or *sym*-octahydrophenanthrene. The similarity of the 9,10-position in phenanthrene to the 2,3-position in indoles with respect to the acceptance of hydrogen has been noted above, so that the postulation of a rearrangement similar to that of 9,10-dihydrophenanthrene seems reasonable. A similar migration of hydrogen is noted below in the discussion of the hydrogenation of acridine.

The presence of 2-cyclohexylindole along with 2-cyclohexyldihydroindole in the reaction products is probably due to the existence of an equilibrium between these two compounds, similar to that between simple indoles and their dihydro derivatives noted above.

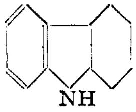
The hydrogenation of 2-phenylindole to 2-cyclohexyl-octahydroindole was complete in less than an hour over Raney nickel at 230°, to give a yield of 81%.

In carbazole there are apparently no structural factors which tend to reduce the resonance of the pyrroloid ring as contrasted with pyrrole itself. In fact von Braun was unable to hydrogenate carbazole and obtained only rather poor yields of 1,2,3,4-tetrahydro- and 1,2,3,4,5,6,7,8-octahydro-9-methylcarbazole from 9-methylcarbazole.[11,12] The complete hydrogenation of carbazole has been reported in a patent, but the temperature required was 400°.[13] However, we have had no difficulty in hydrogenating carbazoles over either nickel or copper chromite under conditions similar to those for the hydrogenation of pyrroles.

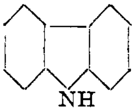
Over nickel at 230° for 15 min., carbazole was hydrogenated to a mixture from which 1,2,3,4-tetrahydrocarbazole (VIII, 33%), 1,2,3,4,10,11-hexahydrocarbazole (IX, 14%) and dodecahydrocarbazole (X, 28%) were isolated in addition to unchanged carbazole (3%). When the hydrogenation is allowed to run for a longer period (seven hours at 230°) or at a higher temperature (one hour at 260°), (X) is the sole isolable product (83% and 87%, resp.). Similar results were obtained with 9-methyl- and 9-ethylcarbazole. After fifteen min. at 200°, the former gave 8% tetrahydro derivative, 53% dodecahydro derivative, with 11% unchanged, while the corresponding figures for the 9-ethyl compound were 10%, 33% and 11%. Under more vigorous conditions, 9-methyl- (230°, two and one-half hours, 85%) and 9-ethyl- (200°, one hour 80%) dodecahydro-



VIII



IX



X

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[10] Durland and Adkins, THIS JOURNAL, **60**, 150 (1938).

[11] Von Braun and Ritter, *Ber.*, **55**, 3792 (1922).

[12] Von Braun and Schoring, *ibid.*, **58**, 2156 (1925).

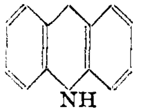
[13] *Chem. Abst.*, **25**, 2157 (1931); German Patent 514,822 (1929).

carbazole were obtained to the exclusion of other products. Moreover, the partially hydrogenated carbazoles were easily reduced to the corresponding dodecahydro derivatives, *e. g.*, VIII → X (250°, 3 hrs., 87%), IX → X (250°, 1.5 hrs., 81%), 1,2,3,4-tetrahydro-9-methylcarbazole → 9-methyldodecahydrocarbazole (200°, 0.25 hr., 84%) and 1,2,3,4-tetrahydro-9-ethylcarbazole → 9-ethyldodecahydrocarbazole (200°, 0.25 hr., 82%).

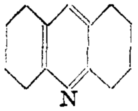
Using copper chromite qualitatively similar results were obtained. After one hour at 220°, carbazole gave VIII (55%), IX (17%) and X (1%) in addition to 2% unchanged material. After ten hours under the same conditions the corresponding figures were: VIII (36%), IX (9%), X (20%). On raising the temperature to 230° after two and one-half hours there was obtained 72% VIII, 12% IX and 3% X with 7% unchanged carbazole, while after fifteen hours at this temperature the sole isolable product was the dodecahydro derivative (82%). In like manner 9-methylcarbazole (240°, 2 hrs.) and 9-ethylcarbazole (240°, 1.5 hrs.) over copper chromite gave, respectively, 24 and 46% 1,2,3,4-tetrahydro derivative, 47% and 20% dodecahydro derivative with 4 and 9% unchanged starting product. It is interesting that the 9-substituted carbazoles gave no hexahydro derivatives with either catalyst. Finally, 1,2,3,4-tetrahydrocarbazole over copper chromite for an hour at 230° was converted to a mixture from which IX (16%), and X (12%) were isolated as well as 58% unchanged material.

Acridine has been reported as very resistant to hydrogenation as Padoa and Febris[14] broke one of the benzenoid rings when they attempted to hydrogenate acridine in the vapor phase. Von Braun[15] obtained the two octahydroacridines, XII and XIII, but was unable to carry the hydrogenation further.

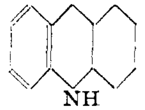
In contrast with these results we have found acridine to be one of the most reactive compounds toward hydrogen ever encountered in this Laboratory. Acridine took up one mole of hydrogen within ten minutes at room temperature over Raney nickel with the formation of 9,10-dihydroacridine, XI. After thirty minutes at 100° acridine or 9,10-dihydroacridine over Raney nickel was converted into a mixture of octa and dodecahydroacridines, XII, XIII and XIV. This extraordinary reactivity points to a quinoid type of structure in acridine and an almost complete lack of resonance in two of the rings.



Ni, 25°, 85%
$CuCr_2O_4$, 150°, 90%
XI



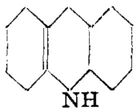
Ni, 100°, 16%
XII



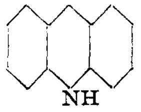
$CuCr_2O_4$, 190°, 70%
Ni, 100°, 38%
XIII

Copper chromite, like nickel, catalyzed under mild conditions in four minutes a smooth hydrogenation of acridine to 9,10-dihydroacridine. Unlike nickel it brought about the formation of the *as*-octahydroacridine, XIII, in an excellent yield, no *sym*-octahydroacridine being formed. This result is apparently due to the selective or preferential action of copper chromite against pyridinoid rings as contrasted with benzenoid nuclei. Nickel gave both of the octahydroacridines and was the preferred catalyst for the preparation of the octahydro compound, XII, although the yield was poor. The formation of the *sym* compound from acridine or dihydroacridine over nickel involves the migration of hydrogen from the 9,10-positions just as does the formation of octahydrophenanthrene from 9,10-dihydrophenanthrene.

The complete hydrogenation of acridine to tetradecahydroacridine, XV, went well over nickel at 240°. Over either nickel or copper chromite at lower temperatures the reaction tended to stop with the formation of a dodecahydroacridine which presumably has the structure indicated in formula XIV. This result is remindful of the hydrogenation of phenanthrene where reaction also tends to stop while there is yet one double bond shared by two rings.[10]



Ni, 100°, 22%
$CuCr_2O_4$, 190°, 13%
XIV



Ni, 240°, 81%
XV

Preparation of Compounds

1-Phenylpyrrole[16] was made through the reaction of aniline with mucic acid. Aniline (1210 g.) was heated to 150° in a 3-liter three-necked flask fitted with a mechanical stirrer and reflux condenser, and mucic acid (1260 g.) added. After three to four hours of refluxing the hot reaction product was transferred to a 5-liter flask, and 3000 ml. of material distilled. The distillate was extracted with ether, the ether solution washed with 10 to 20% hydro-

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[14] Padoa and Febris, *Gazz. chim. ital.*, **38**, I, 233 (1908).

[15] Von Braun, Petzold and Schultheiss, *Ber.*, **56**, 1347 (1923).

[16] Allen, Gilbert and Young, *J. Org. Chem.*, **2**, 230 (1937).

chloric acid, and then with a dilute sodium carbonate solution and finally with water. After drying over calcium chloride the ether was distilled and 360 to 430 g. of product, b. p. 110–116° (9 mm.) or 127–135° (30 mm.), m. p. 55–60°, was obtained. This crude product was satisfactory for the preparation of 2-phenylpyrrole, but the pure compound (m. p. 60–61°) was obtained by two crystallizations from a mixture of 3 parts alcohol and 1 part water.

2-Phenylpyrrole was made by the rearrangement of 1-phenylpyrrole. The process was developed after it was ascertained that the method recently described was unsatisfactory except for small quantities.[16]

1-Phenylpyrrole (286 g.) was refluxed for about two hours around a red hot nichrome wire while the boiling point rose from 230 to 275°. The crude product was distilled and the fraction b. p. 175–183° (30 mm.) or 160–166° (18 mm.), m. p. 80–110° was recrystallized three or four times from 500–700 ml. of 70% alcohol. The solid (m. p. 125–126°) was added to 200 ml. of boiling toluene and then precipitated by the addition of 400 ml. of petroleum ether (b. p. 60–70°). The solid obtained was retreated in the same manner until the m. p. was 129–130°. The yield was 130–160 g. of silvery crystals which were obtained white if the product was again distilled.

A satisfactory apparatus for the preparation of 2-phenylpyrrole was set up as follows. The nichrome wire was in the form of a helix 15 cm. in length and 5 mm. in diameter made from a 3-meter length of number 20 wire. The wire helix, surrounded by a close-fitting Pyrex glass tube, was suspended perpendicularly by copper wires in the neck of a liter flask, and within the lower end of a reflux condenser attached to the flask with a ground glass joint. The flask was provided with a side arm so that a thermometer could be inserted to measure the temperature of the vapors ascending around the helix. The wire was heated by a current of 5.5 to 6 amperes which was controlled by a rheostat or transformer so that the wire was quite red. The current was not turned on until the wire was surrounded by vapors of the pyrrole and was turned off before the refluxing was allowed to stop. This precaution was taken to avoid the possibility of the ignition of an explosive mixture of the pyrrole with air. It was necessary to replace the wire after two or three runs.

1-Carbethoxy-2-phenylpyrrole (24 g., b. p. 166–167° (19 mm.)) was prepared from the potassium derivative of 2-phenylpyrrole (31 g.) and chloroformic ester as previously described for similar compounds.[2]

1-Benzylpyrrole was made from mucic acid (214 g.) by essentially the same procedure as 1-phenylpyrrole, except that benzylamine (218 g.) was substituted for the aniline, and glycerol (300 ml.) was used as a reaction medium. The distillate (600 ml.) from the reaction mixture was acidified with hydrochloric acid before it was extracted with ether. The product (51 g.) obtained distilled at 122–124° (10 mm.), m. p. 14–15°, n^{25}_D 1.5655.[17]

Indole was prepared by dehydrogenation. 2,3-Dihydroindole (21 g.), palladium (1.7 g.), and xylene (100 ml.) were heated under reflux, with stirring, for twenty-four hours. The mixture was centrifuged to remove the catalyst, and fractionated under reduced pressure. The yield of indole was 13 g. (m. p. 51–52°, b. p. 252–254°, 130–133° (12 mm.)) (62% of the theoretical).

2,3-Dihydroindole was prepared as follows. *o*-Nitrophenylethyl bromide[18] (46 g.) dissolved in ethanol (200 ml.) was added to a solution of hydrated stannous chloride (181 g.), concentrated hydrochloric acid (168 ml.), and water (100 ml.) which had been heated to 60°. After the reaction was completed (clear solution), the beaker was placed in an ice-bath, and a cold solution of sodium hydroxide (400 g.) in water (500 ml.) was added. The temperature of the mixture was kept below 10–20° during the addition. The solution was extracted with ether, the ether distilled, and the residue heated to 150° to effect the cyclization of the *o*-aminophenethyl bromide. The residue was cooled, made alkaline with 20% sodium hydroxide solution, and the oil extracted with ether. The solvent was evaporated, and the residue distilled (b. p. 229–231°). The yield was 14 g. (60% of the theoretical).

Four indoles, 2-methyl- (b. p. 269–271°), 3-ethyl- (b. p 131–133° (7 mm.)), 2-phenyl- (m. p. 188–189°), and 2-cyclohexylindole (m. p. 104–105°) were prepared from phenylhydrazine and acetone, butyraldehyde, acetophenone, and methyl cyclohexyl ketone, respectively, according to Fischer's method.[19] The yields were 39, 32, 77, and 18% of the theoretical, respectively. The scale of operation involved approximately one mole of phenylhydrazine and carbonyl compound except with methyl cyclohexyl ketone where only 0.05 mole of the ketone was used.

1,2-Dimethylindole[20] (21 g., b. p. 126–130° (9 mm.), m. p. 55–56°) was prepared from phenylmethylhydrazine (61 g.) and acetone (61 g.).

2-Cyclohexyl-2,3-dihydroindole (0.26 g., m. p. 66–67°) was prepared from 2-cyclohexylindole (0.35 g.) by reduction with zinc (4 g.) in 20 ml. of 20% hydrochloric acid.

Acridine and carbazole were obtained from the Eastman Kodak Company. Acridine was purified as by Graebe.[21] However, the last precipitation and solution of the hydrochloride described by him was omitted. The acridine (100 g.) in a saturated dioxane solution was then refluxed twice with 5% of its weight of Raney nickel. After each treatment with nickel, the metal was centrifuged out of the hot solution. The acridine was then allowed to crystallize (80 g., m. p. 110–111°).[21]

The carbazole, after recrystallization from dioxane, was refluxed twice in dioxane solution with nickel as described above for acridine. The dioxane solution was then shaken for two hours at 60° under a pressure of 65 atm. of hydrogen in the presence of nickel. The carbazole so obtained melted at 242–243°.

All compounds which had not been prepared by hydrogenation were submitted to methods of purification over Raney nickel for the removal of halides and sulfides similar to those described above before any attempt was made to carry out a hydrogenation on them.

9-Methyl- (m. p. 84–85°)[22] and 9-ethylcarbazole (m. p. 67–68°) were obtained in yields of 60 to 68% through the reaction of dimethyl or diethyl sulfate upon potassium carbazole.

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[17] Ciamician and Silber, *Ber.*, **20**, 1368 (1887).

[18] Foreman and McElvain, THIS JOURNAL, **62**, 1436 (1940).

[19] E. Fischer, *Ann.*, **236**, 126 (1886).

[20] Degen, *Ann.*, **236**, 153 (1886).

[21] Graebe, *ibid.*, **158**, 265 (1891).

[22] Ehrenreich, *Monatsh.*, **32**, 1104 (1911).

Hydrogenations.—In most instances 0.06 to 0.10 mole of compound, in 70 ml. of dioxane, with 3 to 4 g. of catalyst, was hydrogenated in a steel reaction vessel (270 ml. void), under a pressure of 250 to 300 atm., for periods of fifteen minutes to two hours. Dioxane was purified over sodium and the catalysts were prepared as usual in this Laboratory.

The data for various hydrogenations not referred to in detail in the discussion, are given below. The name of the hydrogen acceptor, the temperature, the catalyst, the acceptor recovered (a_r), and the percentage yields of products are stated in that order: 2-phenylpyrrole; 165°, Ni, (a_r 40%), 27% 2-cyclohexylpyrrolidine, 15% 2-phenylpyrrolidine. 2-Phenylpyrrole; 200°, $CuCr_2O_4$, (a_r 20%), 55% 2-phenylpyrrolidine. 1-Benzylpyrrole; 260°, Ni, 70% pyrrolidine. 1-Benzylpyrrole; 230°, Ni, (a_r 43%), 24% pyrrolidine, 3% 1-benzylpyrrolidine. 1-Benzylpyrrole; 200°, Ni, (a_r 48%), 27% pyrrolidine, 9% 1-benzylpyrrolidine. 1-Benzylpyrrole; 200°, $CuCr_2O_4$, (a_r 9%), 6% pyrrolidine, 67% 1-benzylpyrrolidine. 2,3-Dihydroindole; 220°, Ni, 80% octahydroindole. 2-Methylindole; 190°, $CuCr_2O_4$, (a_r 18%), 55% 2-methyl-2,3-dihydroindole. 2-Methylindole; 230°, Ni, 80% 2-methyloctahydroindole. 2-Methylindole; 170°, Ni, (a_r 15%), 23% 2-methyl-2,3-dihydroindole, 30% 2-methyloctahydroindole. 2-Methyl-2,3-dihydroindole; 230°, Ni, 80% 2-methyloctahydroindole. 1,2-Dimethylindole; 170°, $CuCr_2O_4$, 48% 1,2-dimethyl-2,3-dihydroindole. 1,2-Dimethylindole; 240°, Ni, products not identified. 3-Ethylindole; 160°, $CuCr_2O_4$, (a_r 10%), 56% 3-ethyl-2,3-dihydroindole. 3-Ethylindole; 250°, Ni, 81% 3-ethyloctahydroindole. 3-Ethyl-2,3-dihydroindole; 250°, Ni, 79% 3-ethyl-octahydroindole. Carbazole; 230° (7 hr.), Ni, 83% dodecahydrocarbazole. Carbazole; 260° (1 hr.), Ni, 87% dodecahydrocarbazole. Carbazole; 230° (15 hr.), $CuCr_2O_4$, 82% dodecahydrocarbazole. Carbazole; 230° (2.5 hr.), $CuCr_2O_4$ (a_r 7%), 72% 1,2,3,4-tetrahydrocarbazole, 12% 1,2,3,4,10,11-hexahydrocarbazole, 3% dodecahydrocarbazole. Carbazole, 220° (1 hr.), $CuCr_2O_4$ (a_r 2%), 55% 1,2,3,4-tetrahydrocarbazole, 17% 1,2,3,4,10,11-hexahydrocarbazole, 1% dodecahydrocarbazole. Carbazole; 220° (10 hr.) $CuCr_2O_4$, 36% 1,2,3,4-tetrahydrocarbazole, 9% 1,2,3,4,10,11-hexahydrocarbazole, 20% dodecahydrocarbazole. Carbazole; 230° (15 min.), Ni, (a_r 3%), 33% 1,2,3,4-tetrahydrocarbazole, 14% 1,2,3,4,10,11-hexahydrocarbazole, 28% dodecahydrocarbazole. 9-Methylcarbazole; 230°, Ni, 85% 9-methyldodecahydrocarbazole. 9-Methylcarbazole; 240°, $CuCr_2O_4$, (a_r 4%), 24% 1,2,3,4-tetrahydro-9-methylcarbazole, 47% 9-methyl-dodecahydrocarbazole. 9-Methylcarbazole; 200°, Ni, (a_r 11%), 8% 1,2,3,4-tetrahydro-9-methylcarbazole, 53% 9-methyldodecahydrocarbazole. 9-Ethylcarbazole; 200°, Ni, 80% 9-ethyldodecahydrocarbazole. 9-Ethylcarbazole; 240°, $CuCr_2O_4$, (a_r 9%), 46% 1,2,3,4-tetrahydro-9-ethylcarbazole, 20% 9-ethyldodecahydrocarbazole. 9-Ethylcarbazole; 200°, Ni, (a_r 11%), 10% 1,2,3,4-tetrahydro-9-ethylcarbazole, 33% 9-ethyldodecahydrocarbazole. 1,2,3,4-Tetrahydrocarbazole; 230°, $CuCr_2O_4$, (a_r 58%), 16% 1,2,3,4,10,11-hexahydrocarbazole, 12% dodecahydrocarbazole. 1,2,3,4-Tetrahydrocarbazole; 250°, Ni, 87% dodecahydrocarbazole. 1,2,3,4,10,11-Hexahydrocarbazole; 250°, Ni, 81% dodecahydrocarbazole. **1,2,3,4-Tetrahydro-9-methylcarbazole**; 200°, Ni, 84% 9-methyldodecahydrocarbazole. 1,2,3,4-Tetrahydro-9-ethylcarbazole; 200°, Ni, 82% 9-ethyldodecahydrocarbazole. Acridine or 9,10-dihydroacridine; 190°, $CuCr_2O_4$, (a_r trace), 90% *as*-octahydroacridine, 13% dodecahydroacridine isolated as benzoyl derivative. Acridine or 9,10-dihydroacridine; 100°, Ni, 38% *as*-octahydroacridine isolated as benzoyl derivative, 16% *s*-octahydroacridine, 22% dodecahydroacridine.

Separation and Identification of Products.—In general the products were separated by fractional distillation using a Widmer or modified Widmer column. In numerous instances products were separated on the basis of differences in basicity, as for example in the separation of 1-benzylpyrrolidine from 1-benzylpyrrole. In most instances the identity of the various products was sufficiently indicated by the physical properties and analyses of the compounds and their derivatives, taken in conjunction with the structure of the compound and the amount of hydrogen taken up in their formation or on further hydrogenation. Neutral equivalents were determined for certain bases. Benzene sulfonyl chloride was used frequently, not only for the formation of derivatives, but also to demonstrate the absence of primary or secondary amines, and in a number of instances to remove traces of such compounds present in a product.

The products of the hydrogenation of 2-phenylindole were separated as follows. The solvent, dioxane, was distilled and the residue dissolved in benzene. The solution was extracted with 15% hydrochloric acid until all basic material had been removed. The benzene was evaporated and the residue, which may consist of 2-phenylindole and 2-cyclohexylindole, was separated into its components by repeated crystallizations from alcohol. The acid solution of the bases obtained as above was made alkaline with ammonium hydroxide and the bases extracted with benzene. Three bases may be present, *i. e.*, 2-cyclohexyloctahydroindole, 2-phenyl-2,3-dihydroindole and 2-cyclohexyl-2,3-dihydroindole. These were separated from one another by fractional distillation. 2-Cyclohexylindole and 2-cyclohexyl-2,3-dihydroindole were characterized by mixed melting points with authentic specimens prepared as indicated above. 2-Phenyl-2,3-dihydroindole was identified by its m. p., 46–47°,[23] and the m. p. of its chloroplatinate.[24]

If the hydrogenation of 2-phenylindole was carried to completion a simple fractionation was sufficient for the isolation and purification of 2-cyclohexyloctahydroindole. The latter was characterized on the basis of analysis, refractive index, formation of a derivative of a secondary amine, and by analysis of its hydrochloride.

Fractional distillation was unsatisfactory for the separation of the products of the hydrogenations of the carbazoles, except where the completely hydrogenated compound was the sole product. In general the mixture of products, after the evaporation of the dioxane, was treated with 33% hydrochloric acid in which carbazole was not soluble. The acid solution was diluted with water to give a 20% hydrochloric acid solution. The tetrahydrocarbazole separated out as a solid and was recrystallized from alcohol and characterized by analysis, m. p. and the m. p. of its picrate.[25]

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[23] Fischer and Schmidt, *Ber.*, **21**, 1075 (1888).

[24] Pictet, *ibid.*, **19**, 1065 (1886).

[25] Perkin and Plant, *J. Chem. Soc.*, **119**, 1825 (1921).

TABLE I

PHYSICAL PROPERTIES AND ANALYSES OF PRODUCTS AND DERIVATIVES

Compound	B. p., °C. (mm.)	M. p., °C.	$n^{25}\mathrm{D}$	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
2-Phenylpyrrolidine[28]	115–116 (15)	.....	1.5390	147 (m. w.)	149		
2-Phenylpyrrolidine, hydrochloride of	...	163 –164	....	65.40	65.20	7.68	7.80
2-Cyclohexylpyrrolidine[29]	95–97 (9)	.....	1.4829	153 (m. w.)	154		
2-Cyclohexylpyrrolidine, hydrochloride of	...	190 –192	....	63.30	63.20	10.63	10.67
1-Carbethoxy-2-phenylpyrrole	165–166 (19)	.....	1.5703	72.54	72.31	6.09	6.11
1-Carbethoxy-2-phenylpyrrolidine	178–180 (25)	.....	1.5189	71.20	71.28	7.81	7.68
1-Carbethoxy-2-cyclohexylpyrrolidine	170–173 (22)	.....	1.4830	69.29	69.25	10.29	10.25
1-Benzylpyrrolidine[32]	234–236	.....	1.5220				
2,3-Dihydroindole[33]	228–231	.....	1.5891				
Octahydroindole[34]	68– 70 (13)		1.4835				
2-Phenyl-2,3-dihydroindole[23]	184–186 (10)	46 – 47	1.6186	86.12	86.27	6.71	6.76
2-Cyclohexylindole	...	103 –105	....	84.37	84.18	8.60	8.37
2-Cyclohexyl-2,3-dihydroindole	168–170 (8)	65 – 67	....	83.53	83.28	9.52	9.43
2-Cyclohexyl-2,3-dihydroindole, HCl	...	202 –204	....	70.75	71.01	8.50	8.72
2-Cyclohexyloctahydroindole	147–149 (7)		1.4952				
2-Cyclohexyloctahydroindole, HCl	...	290 –293	....	68.96	68.91	10.75	10.59
1,2,3,4-Tetrahydrocarbazole[25]	...	115 –115.5	....	84.17	84.31	7.65	7.42
cis - 1,2,3,4,10,11 - Hexahydrocarbazole[26]	...	98 – 99	....	...	...	...	...
cis - 1,2,3,4,10,11 - Hexahydrocarbazole, 9-acetyl derivative of	...	97 – 98	....	78.10	78.25	7.69	7.93
Dodecahydrocarbazole[27]	124–125 (10)	73 – 74.5	1.5010	...	...	...	...
Dodecahydrocarbazole, HCl	...	208 –209	....	66.81	66.78	10.28	10.19
9,10-Dihydroacridine[21]	...	169 –169.5	....				
sym-Octahydroacridine[15]	163–164 (8)	73.5– 74	....				
as-Octahydroacridine[30]	163–164 (8)	.....	....	83.37	83.16	9.15	9.23
Dodecahydroacridine	...	63.5– 64.5	....	81.60	81.28	11.07	11.24
Tetradecahydroacridine[15]	138–139 (11)	90.5– 91.5	....				
Tetradecahydroacridine, HCl	...	.....	....	67.94	67.79	10.53	10.28
2-Methyl-2,3-dihydroindole[8]	227–230	.....	1.5689				
2-Methyloctahydroindole[35]	191–192	.....	1.4722				
3-Ethyl-2,3-dihydroindole	109–110 (7)	.....	1.5583				
3-Ethyl-2,3-dihydroindole, benzenesulfonamide of	...	97 – 97.5	....	66.87	66.73	5.96	6.16
3-Ethyloctahydroindole	80– 82 (7)	.....	1.4787				
3-Ethyloctahydroindole, benzenesulfonamide of	...	51 – 52	....	65.49	65.32	7.90	7.89
1,2-Dimethyl-2,3-dihydroindole	227–229	.....	1.5482				
1,2,3,4-Tetrahydro-9-methylcarbazole[25]	...	49 – 50	....				
Dodecahydro-9-methylcarbazole[27]	126–128 (8)	.....	1.4980				
1,2,3,4-Tetrahydro-9-ethylcarbazole[31]	168–170 (8)	.....	1.5498	84.37	84.53	8.60	8.56
Dodecahydro-9-ethylcarbazole[27]	124–125 (8)	.....	1.4952				

The 20% acid solution was made alkaline with ammonium hydroxide. Hexahydrocarbazole separated as a solid while the dodecahydrocarbazole was an oil. The former was recrystallized from dilute alcohol and proved to be the *cis* isomer as indicated by its m. p. and the m. p. of its picrate and acetyl derivative.[26]

The crude dodecahydrocarbazole which separated, as indicated above, was extracted with benzene and distilled after the removal of the benzene. Dodecahydrocarbazole obtained after the complete hydrogenation of carbazole over nickel at 260° apparently consisted of two geometrical isomers. Two products were obtained which showed the same boiling point and analysis for carbon and hydrogen, yet one was a solid, m. p. 73–74° (from petroleum ether), while the other was a liquid. The picrate of the solid form had a m. p. 167–168°. The dodecahydrocarbazole previously reported had a m. p. of 65°, with a picrate m. p. 187°.[27]

The products of the hydrogenation of 9-methyl- and 9-ethylcarbazole were separated as in the case of the products from carbazole, except that the tetrahydro-9-ethylcarbazole was a liquid, so it was extracted from the 20% hydrochloric acid with benzene.

A semi-solid mixture of octahydroacridines was obtained by fractionation at 165–167° (11 mm.). The mixture was treated with benzoyl chloride in 10% sodium hydroxide solution. The reaction mixture was extracted with ether

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[26] Cartwright and Plant, *J. Chem. Soc.*, 1898 (1931).

[27] Perkin and Plant, *ibid.*, **125**, 1503 (1924).

[28] Gabriel and Colman, *Ber.*, **41**, 521 (1908).

[29] Starr, Bulbrook and Hixon, THIS JOURNAL, **54**, 3971 (1932).

[30] Perkin and Sidgwick, *J. Chem. Soc.*, **125**, 2437 (1924).

[31] *Chem. Cent.*, **94**, IV, 724 (1923), German Patent 374,098 (1923).

and the latter washed with water and then extracted with 10% hydrochloric acid. The acid layer was made alkaline with ammonium hydroxide and the solid *s*-octahydrohydroacridine obtained. The compound was identified by its b. p., m. p. and m. p. of its picrate.[15] The ether layer after evaporation gave the benzoyl derivatives of the two geometrical isomers of *as*-octahydroacridine. Both geometrical isomers were produced but with copper chromite the higher melting one (m. p. 82°), was predominant and was readily separated in a pure form as its benzoyl derivative, m. p. 186–187°.[26]

9,10-Dihydroacridine and dodecahydroacridine were each recrystallized from ethanol. The dodeca- and tetradecahydroacridine had almost the same boiling point, but the dodecahydroacridine had a sharp melting point 27° lower than the tetradeca compound, and its benzoyl derivative and benzene sulfonamide melted distinctly higher than the corresponding derivatives of the tetradecahydroacridine. When the two compounds were mixed the melting point was depressed to below 45°. These facts are stated so that it will be clear that the substance called the dodecahydroacridine was not merely a mixture of the tetradeca with some less hydrogenated acridine.

Tetradecahydroacridine was readily separated in a pure state after a hydrogenation of acridine at 240° over Raney nickel. It was recrystallized from petroleum ether (b. p. 40–60°). The m. p. of the compound (90.5–91.5°) and its derivatives was considerably higher than those previously reported.[15] It is possible that the differences in properties are due to geometrical isomerism but from the description given by Von Braun and associates it seems more probable that they did not have a pure sample of the tetradecahydroacridine.

The physical properties of the products of hydrogenation and of certain of their derivatives, and the analytical figures for various compounds are given in Table I.

In addition to those listed in Table I derivatives of various products were obtained. They had the melting points indicated: picrates of 1-benzylpyrrolidine 127–128°,[32] 1,2,3,4-tetrahydrocarbazole 145–145.5°,[25] *cis*-1,2,3,4,10,11-hexahydrocarbazole 155–156°,[26] dodecahydrocarbazole 167–168°,[27] *s*-octahydroacridine 200–201.5°,[15] tetradecahydroacridine 193–195°,[15] 1,2,3,4-tetrahydro-9-methylcarbazole 114–114.5°,[25] dodecahydro-9-methylcarbazole 142.5–143.5°,[27] and 1,2,3,4-tetrahydro-9-ethylcarbazole 92–92.5°; benzenesulfonamides of 2,3-dihydroindole 132–132.5°,[33] octahydroindole 69.5–70.5°,[34] 2-cyclohexyloctahydroindole, 165–166°, dodecahydroacridine 147.5–149°, tetradecahydroacridine 89–90°, 2-methyl-2,3-dihydroindole 88–89°,[8] and 2-methyl-octahydroindole 118–119°[35]; benzoyl derivatives of *as*-octahydroacridine 186.5–187°,[26] dodecahydroacridine 123–124°, and tetradecahydroacridine 69–70°; methiodides of tetradecahydroacridine above 360°,[15] 1,2-dimethyl-2,3-dihydroindole 208–210°[36] and dodecahydro-9-ethylcarbazole 218.5–219.5°[27]; and the chloroplatinate of 2-phenyl-2,3-dihydroindole 184–186°.[24]

Summary

The partial and complete hydrogenation of several phenylpyrroles, indoles, carbazoles and acridines over copper chromite and Raney nickel catalysts has been investigated. The complete hydrogenation of all of these compounds was best achieved over Raney nickel, the yields being of the order of 80%.

2-Phenylpyrrole and 1-benzylpyrrole were hydrogenated preferentially in the pyrroloid ring in the presence of either catalyst, but copper chromite was the more effective for the selective hydrogenation.

Indole and simple alkyl substituted indoles were hydrogenated to the corresponding 2,3-dihydroindoles over both nickel and copper chromite but the latter gave the better results. There is evidence that the indoles and dihydroindoles were in equilibrium with each other under the conditions used for hydrogenation.

2-Phenylindole gave products of the same type as those from indole and alkylindoles and in addition cyclohexylindole and cyclohexyldihydroindole. The formation of these compounds suggests that the 2,3-dihydro-2-phenylindole undergoes a rearrangement similar to that of 9,10-dihydrophenanthrene and of 9,10-dihydroacridine.

The facile hydrogenation of the pyrroloid ring in indoles and phenylpyrroles is attributed to the decrease in resonance brought about by the benzenoid ring.

Carbazoles were much more resistant to catalytic hydrogenation than the indoles and phenylpyrroles. However, tetra-, hexa- and dodecahydrocarbazoles were obtained in yields of 72, 16 and 85%, respectively.

Acridine was hydrogenated at room temperature to dihydroacridine. *sym*- and *as*-octahydroacridines were obtained at 100–150°, the latter being produced over copper chromite in 70% yield. The dodeca- and the tetradecahydroacridines were obtained by hydrogenation over Raney nickel.

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(32) Schlink, *Ber.*, **32**, 953 (1899).

(33) Ferber, *ibid.*, **62**, 189 (1929).

(34) Willstätter, Seitz and v. Braun, *ibid.*, **58**, 385 (1925).

(35) *Chem. Abs.*, **23**, 144 (1929).

(36) Bamberger and Sternitzki, *Ber.*, **26**, 1294 (1893).