

R74-57

Chemistry of Isoindolines. The Synthesis of
1,2,3,5,6,7-Hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole and
1,2,3,4,5,6-Hexahydrobenzo[1,2-*c*:3,4-*c'*]dipyrrole

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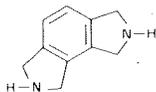
The preparation and properties of 1,2,3,5,6,7-hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole (I) and its isomer, 1,2,3,4,5,6-hexahydrobenzo[1,2-*c*:3,4-*c'*]dipyrrole (II), are described. Contrary to the claims of earlier investigators, compound I and its 2,6-diacetyl and 2,6-dicarboxamide derivatives VI and IX are easily preparable, readily isolable, stable substances.

In the course of our study of the chemistry of isoindoles (1) and isoindolines (2) it occurred to us that 1,2,3,5,6,7-hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole (I) and 1,2,3,4,5,6-hexahydrobenzo[1,2-*c*:3,4-*c'*]dipyrrole (II) might be useful for the preparation of thermally stable polyamides, polysulfonamides, and polyureas. Examination of the literature revealed that Shono and his co-workers (3), in their quest for high temperature-resistant polymers, had prepared by reaction of 1,2,4,5-tetrakis-(chloromethyl)benzene with various diamines, a series of polyamines containing repeating units of hexahydrobenzo-dipyrrole I. Their procedure was, in effect, an extension of the method used earlier by Ruggli and Geiger (4) to prepare 2,6-dialkylated and diarylated derivatives of I.

1,2,3,4,5,6-Hexahydrobenzo[1,2-*c*:3,4-*c'*]dipyrrole (II)



I

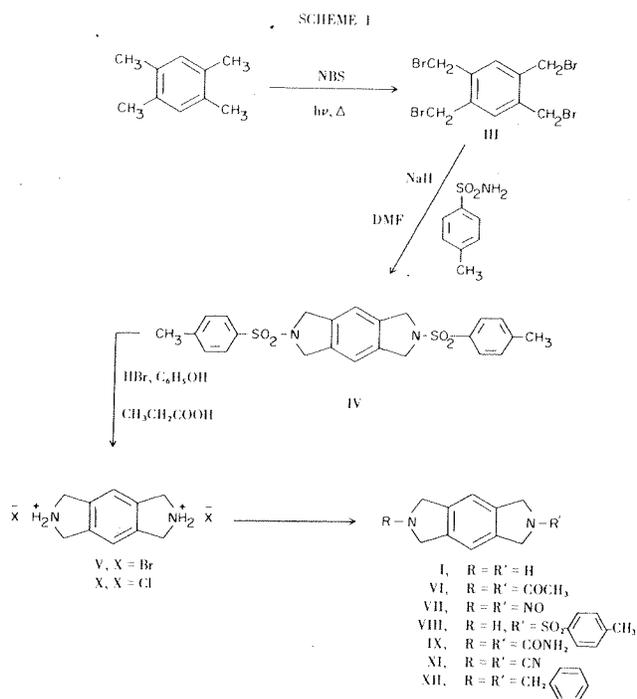


II

has not been described previously, but isomer I was reported by Ruggli and Geiger (4) to be unstable and incapable of isolation from its dihydrochloride X. Furthermore, these workers claimed that the heterocyclic rings of the 2,6-diacetyl and 2,6-dicarboxamide derivatives VI and IX were especially susceptible to hydrolytic cleavage and they attributed this behavior to an unexplained labilizing effect of the carbonyl groups. This alleged instability of compound I and its carbonyl-containing derivatives was surprising since our experience with iso-

indolines would have led us to expect these substances to be stable. We now wish to report that hexahydrobenzodipyrroles I and II are readily preparable by the procedure originally developed by us for the synthesis of isoindolines of simpler structure (2) and that these compounds, including the forenamed derivatives of I, are in fact quite stable.

The synthesis of 1,2,3,5,6,7-hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole (I) from durene is shown in Scheme I. Conversion of durene to 1,2,4,5-tetrakis(bromomethyl)benzene (III) was effected with *N*-bromosuccinimide in 35-45% yield; a 300-watt photoflood lamp served both as photochemical activator and as a source of heat. The procedure of Ried and Bodem (5), which utilizes benzoyl peroxide as catalyst in this bromination, gave substantially lower yields of III in our hands. Treatment of III with *p*-toluenesulfonamide in the presence of sodium hydride and dimethylformamide afforded 1,2,3,5,6,7-hexahydro-2,6-bis(*p*-tolylsulfonyl)benzo[1,2-*c*:4,5-*c'*]dipyrrole (IV) in 94% yield. Reductive cleavage of IV in propionic acid by a mixture of phenol and 48% hydrobromic acid readily furnished dihydrobromide V (88% yield), which was smoothly converted by aqueous sodium hydroxide to the free base I in 97% yield. Vacuum sublimation or recrystallization from benzene gave analytically pure I as long, white needles, m.p. 166-167° dec., which could be stored indefinitely at room temperature over a 1:1 mixture of Drierite and Ascarite in a nitrogen atmosphere. The infrared spectrum (potassium bromide pellet) of 1,2,3,5,6,7-hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole (I) ex-

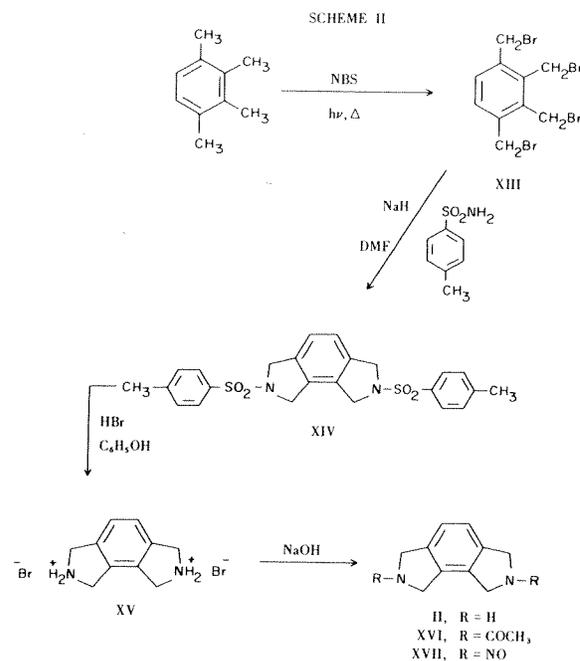


hibited a band at 3330 cm^{-1} attributable to N-H stretching vibrations and the nmr spectrum (deuteriochloroform) of I showed signals at δ 2.15 (s, 2H, NH), 4.18 (s, 8H, CH_2), and 7.07 (s, 2H, ArH). Compound I, as described in the Experimental Section, was further characterized by its mass spectrum, neutralization equivalent, salt formation (dihydrochloride X and dipicrate XX), and by preparation of its diacetyl VI, dinitroso VII, *p*-tolylsulfonyl IV and VIII, and dicarboxamide IX derivatives.

1,2,3,4,5,6-Hexahydrobenzo[1,2-*c*:3,4-*c'*]dipyrrole (II) was synthesized from prehnite by the reaction sequence outlined in Scheme II. Since the procedure was essentially the same as that used for the preparation of isomer I, details of the method as well as properties of intermediates will be restricted to the Experimental Section except for a comment on the preparation of 1,2,3,4,5,6-hexahydro-2,5-bis(*p*-tolylsulfonyl)benzo[1,2-*c*:3,4-*c'*]dipyrrole (XIV). Owing to the possibility of multiple reaction pathways during the alkylation of *p*-toluenesulfonamide with tetrabromide XIII some difficulties were anticipated, but none actually materialized and compound XIV was cleanly formed in nearly quantitative yield.

Cyclic diamine II is a white, slightly hygroscopic, crystalline solid, m.p. $102\text{--}103^\circ\text{ dec.}$, which is somewhat more reactive than compound I toward carbon dioxide of the atmosphere. Compound II could be stored indefinitely at room temperature under the same conditions used with isomer I. The infrared spectrum (potassium bromide pellet) of II showed the expected band for the N-H functions at 3155 cm^{-1} and the nmr spectrum

(deuteriochloroform) of II displayed signals at δ 2.20 (s, 2H, NH), 4.15 (s, 4H, CH_2), 4.22 (s, 4H, CH_2), and 7.10 (s, 2H, ArH). The diacetyl XVI, dinitroso XVII, and dipicrate XXI derivatives of II were readily prepared by essentially the same procedure used for the corresponding derivatives of isomer I.



The failure of Ruggli and Geiger (4) to prepare hexahydrobenzodipyrrole I and its 2,6-diacetyl and 2,6-dicarboxamide derivatives VI and IX prompted us to re-examine their procedures with special care. These investigators also utilized 1,2,3,5,6,7-hexahydro-2,6-bis(*p*-tolylsulfonyl)benzo[1,2-*c*:4,5-*c'*]dipyrrole (IV) as an intermediate in their attempted synthesis of I. Because of difficulties encountered in removing the *p*-tolylsulfonyl groups by the usual methods, they devised a procedure which employed a mixture of sulfuric acid and acetyl chloride as cleaving agent. On the basis of the formation of *p*-toluenesulfonyl chloride from the reaction of IV with this mixture, Ruggli and Geiger believed that an exchange of groups had occurred and that 1,2,3,5,6,7-hexahydro-2,6-diacetylbenzo[1,2-*c*:4,5-*c'*]dipyrrole (VI) had been produced. However, elemental analysis of the product indicated the presence of approximately two moles of water which successfully resisted all attempts at removal. For this reason they assumed that both heterocyclic rings of VI had undergone hydrolytic cleavage and they assigned structure XVIII to the product.



Reinvestigation of the foregoing experiment now has revealed that the action of the sulfuric acid-acetyl chloride system on IV actually does afford diacetyl derivative VI in 85% yield; we found no evidence of ring cleavage. Moreover, when VI was heated for an extended period of time with 33% aqueous sodium hydroxide or in a sealed tube with concentrated hydrochloric acid for 18 hours, hexahydrobenzodipyrrole I and its corresponding dihydrochloride X were formed in 92 and 68% yield, respectively. Again, no indication of ring opening was given by these experiments. Additional verification of the structure of diacetyl derivative VI was furnished by elemental analysis and by comparison with an authentic specimen prepared from the reaction of acetic anhydride with dihydrobromide V. Contrary to the report of Ruggli and Geiger (4), we found that hexahydrobenzodipyrrole I was liberated (96% yield) in high purity when the above dihydrochloride X was treated with aqueous sodium hydroxide according to the procedure used with the analogous dihydrobromide V.

Hydrolytic opening of the pyrroline rings of dicarboxamide IX was also believed by Ruggli and Geiger (4) to have occurred during their attempted preparation of the compound from 1,2,3,5,6,7-hexahydro-2,6-dicyanobenzo[1,2-*c*:4,5-*c'*]dipyrrole (XI) by heating with 25% aqueous sulfuric acid. On the basis of elemental analysis they proposed structure XIX for the product. We found no evidence of such lability when XI, prepared by reaction of cyanogen bromide with 1,2,3,5,6,7-hexahydro-2,6-dibenzylbenzo[1,2-*c*:4,5-*c'*]dipyrrole (XII) (4), was subjected to their experimental conditions. The expected dicarboxamide IX was obtained in 70% yield and its identity was established by comparison with an authentic sample prepared by the action of potassium cyanate on hexahydrobenzodipyrrole dihydrobromide V.

We believe that the failure of Ruggli and Geiger (4) to assign the correct structures to the diacetyl and dicarboxamide derivatives of I was caused by poor elemental analyses (6) since our study has established that these investigators actually had these compounds in hand. We cannot account for their inability to isolate cyclic diamine I from its dihydrochloride X. In this connection, it is interesting to note that the melting point (172-175° dec.) of the material obtained by them from alkaline treatment of salt X is close to that of pure I.

A description of the polymers prepared from compounds I and II will appear elsewhere in the near future.

EXPERIMENTAL

Melting points were determined in capillary tubes with a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were carried out by Midwest Microlab, Inc., Indianapolis, Indiana. Infrared spectra were obtained on a Perkin-Elmer 521 spectro-

meter. Nmr spectra were recorded on Varian A-60 and HA-100 spectrometers with tetramethylsilane as internal standard. Mass spectra were run on a Consolidated Electro Dynamics 110B instrument.

1,2,4,5-Tetrakis(bromomethyl)benzene (III).

A vigorously stirred slurry of durene (16.8 g., 0.125 mole) and *N*-bromosuccinimide (89.1 g., 0.50 mole) in 275 ml. of carbon tetrachloride was illuminated with a Westinghouse RFL-2 300-watt photoflood lamp, which was placed sufficiently close to the reaction flask to induce reflux. After a 30-minute period of reflux the succinimide which had formed was removed by filtration of the hot reaction mixture. Chilling the filtrate overnight afforded a light yellow solid which was recrystallized from chloroform to give 22.8 g. (40%) of III as colorless granules, m.p. 156-160°; lit. m.p. 160° (5).

1,2,3,5,6,7-Hexahydro-2,6-bis(*p*-tolylsulfonyl)benzo[1,2-*c*:4,5-*c'*]dipyrrole (IV).

To a stirred suspension of sodium hydride (54% dispersed in mineral oil, 22.22 g., 0.50 mole) in 163 ml. of purified dimethylformamide, at room temperature and under dry nitrogen was added dropwise a solution of *p*-toluenesulfonamide (85.61 g., 0.50 mole) in 303 ml. of dimethylformamide over a period of 75 minutes. Stirring of the suspension was continued for 1 hour at room temperature and then for an additional hour with warming in a water bath at 65°. A solution of III (44.99 g., 0.10 mole) in 636 ml. of dimethylformamide was then added dropwise to the vigorously stirred mixture while the bath temperature was maintained at 65-70°. Upon completion of the addition the resulting light grey suspension was stirred at room temperature for an additional 3 hours before being poured into 2 l. of ice water. After standing overnight the grey precipitate was collected by suction filtration and washed successively 3 times with 200-ml. portions of warm acetone and 3 times with 500-ml. portions of hot water. The crude, light grey solid weighed 43.8 g. (94%) after being air dried and had m.p. 236-242° dec.; it was sufficiently pure for use in the next step. The analytical sample was prepared by dissolving IV in the minimum amount of *m*-cresol at elevated temperature (but not exceeding 138°) and then adding an equal volume of methanol to precipitate the compound. The almost colorless solid was collected, washed several times with methanol, and dried *in vacuo* (90°/2 mm); m.p. 246-248° dec.; ν max (potassium bromide): 1335 and 1155 cm^{-1} .

Anal. Calcd. for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_4\text{S}_2$: C, 61.51; H, 5.16; N, 5.98; S, 13.69. Found: C, 61.70; H, 5.41; N, 6.09; S, 13.47.

1,2,3,5,6,7-Hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole Dihydrobromide (V).

A stirred mixture of IV (39.6 g., 0.085 mole), phenol (50.3 g.), 48% hydrobromic acid (616 ml.), and propionic acid (264 ml.) was heated under reflux for 52 hours during which time the reaction mixture changed from red to dark brown. The mixture was set aside at room temperature overnight after which the resulting precipitate was collected, air dried, and then taken up in 250 ml. of boiling water; filtration was necessary to remove ca. 1.5 g. of insoluble material (mostly unchanged IV). The filtrate was decolorized with charcoal and treated with 100 ml. of 48% hydrobromic acid. Refrigeration overnight, followed by filtration and drying (90°/2 mm), gave V (24.0 g., 88%) as long needles, m.p. 268-270° dec.; ν max (potassium bromide): 2800 cm^{-1} (NH_2).

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2 \cdot 2\text{HBr}$: C, 37.30; H, 4.38; Br, 49.63; N, 8.69. Found: C, 37.33; H, 4.50; Br, 49.40; N, 8.61.

The time required to effect the above reaction could be shortened with only slight decrease in yield of product by substituting *m*-cresol for phenol. In a typical run a reaction mixture consisting of IV (8.42 g., 0.018 mole), *m*-cresol (104 ml.), 48% hydrobromic acid (24 ml.), and propionic acid (24 ml.) gave, after being heated at reflux for 4 hours, 4.65 g. (82%) of V.

1,2,3,5,6,7-Hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole (I).

A solution of 5.0 g. (0.015 mole) of V in 15 ml. of water at ca. 90° was stirred vigorously while an excess (about 3.2 ml.) of 33% aqueous sodium hydroxide was added. A white solid precipitated and immediately thereafter the flask was stoppered and chilled in an ice bath for 30 minutes. The precipitate was collected by filtration, washed 5 times with 15-ml. portions of ice-cold, carbon dioxide-free water, and then dried on the funnel for 30 minutes under a stream of purified nitrogen. Final drying of I (2.33 g., 97%), m.p. 166-167° dec., was effected over phosphorus pentoxide in a desiccator purged with nitrogen. The gradual decomposition of I which occurred when it was stored over phosphorus pentoxide could be avoided by storage over a 1:1 mixture of Drierite and Ascarite in a nitrogen atmosphere. Analytically pure I could be obtained either by sublimation (111°/5 mm) or by recrystallization from dry benzene (long white needles, m.p. unchanged). For ir and nmr data, see text. Mass spectrum (70 eV) *m/e* (rel. intensity) 160 (92, M), 159 (97, M-1), 132 (68), 131 (83), 130 (100), 117 (78), 103 (69), 102 (45), 91 (20), 78 (58), 77 (86), 63 (80), 52 (62), 50 (81), 41 (35), 39 (82), 28 (95).

Anal. Calcd. for C₁₀H₁₂N₂: C, 74.97; H, 7.55; N, 17.48; neut. equiv., 80.11. Found: C, 74.65; H, 7.77; N, 17.53; neut. equiv., 80.13.

Regeneration of IV from I.

A solution of I (1.0 g., 6.24 mmoles) in 100 ml. of pyridine was stirred at room temperature while a solution of *p*-toluenesulfonyl chloride (2.3 g., 12.48 mmoles) in 20 ml. of acetone was added dropwise over a period of 5 minutes. The light yellow precipitate which formed was collected after 1 hour and washed with acetone. Recrystallization from a mixture of *m*-cresol and methanol, as described above, gave 2.9 g. (97%) of IV, m.p. 246-248° dec. This material was shown by ir spectral comparison and mixture melting point determination to be identical with the compound prepared above from the reaction of III with *p*-toluenesulfonamide.

1,2,3,5,6,7-Hexahydro-2-(*p*-tolylsulfonyl)benzo[1,2-*c*:4,5-*c'*]dipyrrole (VIII).

Dihydrobromide V (11.22 g., 0.035 mole) was added to a stirred solution of 412 ml. of a 2:1 acetone-water mixture in 262 ml. of sodium acetate-acetic acid buffer solution (pH 4.58). The pH, monitored with a pH meter, was adjusted to 5.2 (the equivalence point) by the dropwise addition of 48% hydrobromic acid at which value all crystals of V completely dissolved. A solution of *p*-toluenesulfonyl chloride (6.7 g., 0.035 mole) in 113 ml. of acetone was added dropwise over a 70-minute period while the pH value of 5.2 was maintained by addition of a drop or two of 33% aqueous sodium hydroxide as required. A white precipitate appeared after 5 minutes. After all of the *p*-toluenesulfonyl chloride had been added, the pH of the reaction mixture was held constant for an additional 0.5 hour. The volume of the reaction mixture was reduced to one half by heating and the hot mixture was filtered by suction through hardened filter paper to remove the bis(*p*-tolylsulfonyl) coproduct IV (4.27 g., 26%).

Concentration of the filtrate to approximately one half its volume followed by refrigeration overnight gave the monohydrobromide monohydrate of VIII as pearly plates which were collected by filtration (with some difficulty). Drying at 90°/5 mm afforded 4.27 g. (30%) of a lusterless, white powder, m.p. 240-248° dec.; ir ν max (potassium bromide): 2930 (NH₂), 1160 cm⁻¹ (C-SO₂-N). The analytical sample was recrystallized from 95% ethanol; m.p. unchanged.

Anal. Calcd. for C₁₇H₁₈N₂O₂S·HBr·H₂O: C, 49.40; H, 5.12; Br, 19.33; N, 6.78; O, 11.61; S, 7.76. Found: C, 49.67; H, 4.95; Br, 19.64; N, 6.72; O, 11.57; S, 7.52.

Treatment of a 0.66-g. sample of the above monohydrobromide monohydrate of VIII in 30 ml. of hot water with 33% sodium hydroxide according to the procedure used above to liberate I from its dihydrobromide (V) afforded 0.49 g. (97%) of VIII as a white crystalline solid, m.p. 184-185° dec.; ir ν max (potassium bromide): 3375 (NH), 1330 and 1155 cm⁻¹ (C-SO₂-N); nmr (deuteriochloroform) δ : 2.15 (s, 1H, NH), 2.39 (s, 3H, CH₃), 4.15 (s, 4H, CH₂), 4.56 (s, 4H, CH₂), 7.00 (s, 2H, ArH), 7.26-7.74 (m, 4H, ArH).

Anal. Calcd. for C₁₇H₁₈N₂O₂S: C, 64.94; H, 5.77; N, 8.91; O, 10.18; S, 10.20. Found: C, 64.62; H, 5.87; N, 8.95; O, 10.47; S, 10.09.

1,2,3,5,6,7-Hexahydro-2,6-diacetylbenzo[1,2-*c*:4,5-*c'*]dipyrrole (VI).

(a) From Dihydrobromide V and Acetic Anhydride.

A stirred solution of dihydrobromide V (3.2 g., 0.01 mole) in 20 ml. of cold water was treated dropwise with 1.91 ml. (0.02 mole) of acetic anhydride. A precipitate formed slowly and was collected after 2 hours. Recrystallization of the air-dried material from 1:1 methanol-ethanol followed by drying at 90°/5 mm afforded 2.2 g. (92%) of VI as fine, white needles, m.p. 252-314° dec.; ir ν max (potassium bromide): 1610 cm⁻¹ (C=O).

Anal. Calcd. for C₁₄H₁₆N₂O₂: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.81; H, 6.63; N, 11.42.

(b) From IV and Acetyl Chloride in the Presence of Sulfuric Acid.

Treatment of 6.0 g. (0.013 mole) of IV with a mixture of sulfuric acid and acetyl chloride by the procedure of Ruggli and Geiger (4) afforded 2.70 g. (85%) of VI, m.p. 252-314° dec. Spectral and elemental analysis showed that this material was identical with that prepared above from V and that no cleavage of the pyrrole rings had occurred.

Anal. Calcd. for C₁₄H₁₆N₂O₂: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.87; H, 6.65; N, 11.14.

Conversion of VI to I by Aqueous Sodium Hydroxide.

A suspension of VI (20.0 mg., 0.082 mmole) in 50 ml. of 33% aqueous sodium hydroxide was heated under reflux in a nitrogen atmosphere for 44 hours; during this period the solid dissolved and the resulting solution assumed a greenish color. Cooling the reaction mixture in an ice bath afforded a white solid which was purified by the procedure used above for I. The product (12 mg., 92%) had m.p. 166-167° dec. and was shown by mixture melting point determination and spectral comparison to be identical in all respects with a sample of I prepared from V.

1,2,3,5,6,7-Hexahydrobenzo[1,2-*c*:4,5-*c'*]dipyrrole Dihydrochloride (X).

Heating of diacetyl derivative VI (1.0 g., 4.10 mmoles) with 40 ml. of concentrated hydrochloric acid in a sealed tube for 18 hours according to the method of Ruggli and Geiger (4) gave, on

work-up, 0.67 g. (68%) of dihydrochloride X as white crystals, m.p. 268-270° dec.; ν max (potassium bromide): 3430 cm^{-1} (NH_2). The analytical sample was recrystallized from concentrated hydrochloric acid.

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2 \cdot 2\text{HCl}$: C, 51.52; H, 6.05; Cl, 30.41; N, 12.02. Found: C, 51.67; H, 6.30; Cl, 30.35; N, 11.68.

This substance was spectrally identical with an authentic sample of X which was prepared in 86% yield by cooling overnight a solution of 1.0 g. (6.2 mmoles) of hexahydrobenzodipyrrole I in 30 ml. of concentrated hydrochloric acid, m.p. 268-270° dec.

Conversion of Dihydrochloride X to I by Aqueous Sodium Hydroxide.

The procedure used was identical to that described above for the liberation of I from dihydrobromide V. Dihydrochloride X (0.214 g., 0.92 mmole) afforded I (0.139 g., 96%) with m.p. 166-167° dec.; ν spectrum (potassium bromide) superimposable on that of I prepared from V.

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.89; H, 7.88; N, 17.73.

1,2,3,5,6,7-Hexahydro-2,6-dinitrosobenzo[1,2-c:4,5-c']dipyrrole (VII).

Dihydrobromide V (3.20 g., 0.01 mole) was dissolved in 100 ml. of water containing 12 drops of 48% hydrobromic acid. Sodium nitrite (1.4 g., 0.02 mole) in 7 ml. of water was added dropwise to the stirred solution at room temperature over a period of 10 minutes. A magma of fine crystals formed which, after being set aside overnight, was collected and recrystallized from 150 ml. of 50% ethanol to give 1.72 g. (79%) of VII, m.p. 222-225° dec.; ν max (potassium bromide): 1445 cm^{-1} (N-NO).

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_4\text{O}_2$: C, 55.04; H, 4.62; N, 25.68; O, 14.66. Found: C, 54.95; H, 4.89; N, 25.41; O, 14.76.

1,2,3,5,6,7-Hexahydrobenzo[1,2-c:4,5-c']dipyrrole Dipicrate (XX).

A solution of dihydrobromide V (3.2 g., 0.01 mole) in 10 ml. of water was treated with 10 ml. of a saturated ethanolic solution of picric acid at room temperature. The yellow needles which formed were collected the following day, washed 3 times with 5-ml. portions of cold ethanol, and dried (90°/5 mm) to give 5.1 g. (82%) of XX, m.p. 220-240° dec.

Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2 \cdot 2\text{C}_6\text{H}_3\text{N}_3\text{O}_7$: C, 42.73; H, 2.93; N, 18.12; O, 36.22. Found: C, 42.99; H, 3.19; N, 17.89; O, 35.92.

1,2,3,5,6,7-Hexahydrobenzo[1,2-c:4,5-c']dipyrrole-2,6-dicarboxamide (IX).

(a) From Hydrolysis of 1,2,3,5,6,7-Hexahydro-2,6-dicyanobenzo[1,2-c:4,5-c']dipyrrole (XI).

Hydrolysis of a 1.0-g. quantity of dinitrile XI was carried out with 50 ml. of 25% sulfuric acid containing 0.5 ml. of ethanol according to the procedure of Ruggli and Geiger (4). The light grey, highly insoluble crystalline dicarboxamide IX (0.83 g., 70%) was best purified by recrystallization from a large volume of water (0.435 g. of IX in 1400 ml. of water), m.p. 250-360° dec. This material was identical in all respects with the comparison sample prepared below from dihydrobromide V.

Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{N}_4\text{O}_2$: C, 58.53; H, 5.73; N, 22.75. Found: C, 58.23; H, 5.88; N, 22.58.

(b) From Dihydrobromide V and Potassium Cyanate.

A stirred solution of V (2.0 g., 6.2 mmoles) in 150 ml. of

water was adjusted to pH 7.0 by addition of 1N potassium hydroxide and then placed in a water bath at 50°. A solution of 1.0 g. (12.4 mmoles) of potassium cyanate in 5 ml. of water was added and after 5 minutes a precipitate appeared. The reaction mixture was stirred for an additional 90 minutes, refrigerated overnight, and the solid collected and dried (90°/10 mm). Recrystallization of the crude product (1.2 g., 79%) from water yielded analytically pure IX as light grey crystals, m.p. 250-360° dec.; ν max (potassium bromide): 1640 and 1600 cm^{-1} (CONH_2).

Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{N}_4\text{O}_2$: C, 58.53; H, 5.73; N, 22.75; O, 12.99. Found: C, 58.18; H, 5.93; N, 22.62; O, 13.27.

1,2,3,4-Tetrakis(bromomethyl)benzene (XIII).

Prenhitene (134.2 g., 1.0 mole) was allowed to react with *N*-bromosuccinimide (712 g., 4.0 moles) in 2.20 l. of carbon tetrachloride under the same conditions used previously for the conversion of durene to III. The crude product (330 g., 74%), m.p. 95-108°, was recrystallized once from *n*-butyl alcohol to give 258 g. (58%) of XIII, m.p. 104-114°, sufficiently pure for use in the preparation of compound XIV. For elemental analysis, a sample was recrystallized from 95% ethanol (6.0 g. in 100 ml. of solvent) and dried overnight at 61°/10 mm; the colorless crystals had m.p. 124-126°.

Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{Br}_4$: C, 26.70; H, 2.24; Br, 71.06. Found: C, 26.41; H, 2.31; Br, 71.20.

1,2,3,4,5,6-Hexahydro-2,5-bis(*p*-tolylsulfonyl)benzo[1,2-c:3,4-c']dipyrrole (XIV).

To a stirred suspension of sodium hydride (54% in mineral oil, 22.22 g., 0.5 mole) in 163 ml. of purified dimethylformamide was added dropwise, at room temperature and in a nitrogen atmosphere, a solution of *p*-toluenesulfonamide (85.6 g., 0.5 mole) in 303 ml. of dimethylformamide during the course of 75 minutes. The resulting mixture was stirred for an additional hour at room temperature and then for 1 hour on a water bath whose temperature was 50-55°. A solution of XIII (44.99 g., 0.10 mole) in 636 ml. of dimethylformamide was then added dropwise over a 1-hour period while vigorous stirring and heating at 50-60° were maintained. Toward the end of the addition all the solid had dissolved. The bath was removed and stirring was continued until the reaction mixture was at room temperature. The mixture was filtered by suction and the filtrate poured into 2 l. of ice water. The resulting precipitate was collected by filtration and washed successively 5 times with 500-ml. portions of cold water and 5 times with 500-ml. portions of warm (50°) water before being air dried. The faint yellow crystals of XIV, sufficiently pure for use in the next step, weighed 46.1 g. (98.5%); m.p. 228-240° dec.; ν max (potassium bromide): 1345 and 1160 cm^{-1} ($\text{C-SO}_2\text{-N}$); nmr (deuteriated dimethyl sulfoxide) δ : 2.35 (s, 6H, CH_3), 4.59 (s, 8H, CH_2), 7.09 (s, 2H, ArH), 7.34-7.78 (m, 8, ArH). Recrystallization from 3:1 *n*-butyl alcohol-95% ethanol afforded an analytical sample of XIV as fine, white crystals after drying at 120°/10 mm; m.p. unchanged.

Anal. Calcd. for $\text{C}_{24}\text{H}_{24}\text{N}_2\text{O}_4\text{S}_2$: C, 61.51; H, 5.16; N, 5.98; S, 13.69. Found: C, 61.40; H, 5.27; N, 5.93; S, 13.60.

1,2,3,4,5,6-Hexahydrobenzo[1,2-c:3,4-c']dipyrrole Dihydrobromide (XV).

A stirred mixture of 4.68 g. (0.01 mole) of XIV, 6.4 g. of phenol, 77 ml. of 48% hydrobromic acid, and 33 ml. of propionic acid was heated under reflux for 55 hours. The reaction mixture was evaporated *in vacuo* to dryness and the resulting residue was

dissolved in the minimum amount of water to give an orange-red solution, which could not be decolorized with charcoal. Five washings of the solution with ether removed both the residual phenol and color. Concentration of the aqueous solution to ca. one third its original volume followed by refrigeration overnight afforded a brown solid which was collected by filtration. This substance was taken up in hot methanol and the resultant solution decolorized with charcoal before being treated with 10 ml. of 48% hydrobromic acid. Refrigeration overnight afforded, after drying (61°/10 mm), 1.23 g. (38%) of compound XV as fine white crystals, m.p. 268-274° dec.

Anal. Calcd. for $C_{10}H_{12}N_2 \cdot 2HBr$: C, 37.30; H, 4.38; Br, 49.63; N, 8.69. Found: C, 36.99; H, 4.28; Br, 49.62; N, 8.74.

1,2,3,4,5,6-Hexahydrobenzo[1,2-c:3,4-c']dipyrrole (II).

An excess of 33% aqueous sodium hydroxide (12 drops) was added quickly with shaking to a solution of 0.717 g. (2.2 mmoles) of dihydrobromide XV in 1 ml. of carbon dioxide-free water; a white precipitate formed. Collection of this substance by suction filtration proved difficult owing to a tendency to liquefy on the funnel. For this reason, the reaction mixture was diluted by addition of 50 ml. of water and the product extracted with 10 100-ml. portions of ether. The combined extracts, after being dried over potassium carbonate, yielded, upon concentration, compound II as a light yellow solid. Sublimation (98°/2 mm) afforded analytically pure II (0.204 g., 57%) as white crystals, m.p. 102-103° dec.; ir and nmr: see text. Mass spectrum (70 eV) m/e (rel. intensity) 161 (87, M+1), 160 (100, M), 133 (50), 131 (79).

Anal. Calcd. for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.72; H, 7.46; N, 17.50.

1,2,3,4,5,6-Hexahydro-2,5-diacetylbenzo[1,2-c:3,4-c']dipyrrole (XVI).

This preparation was carried out in an atmosphere of dry nitrogen. To a stirred solution of 1.60 g. (0.01 mole) of diamine II in 30 ml. of purified chloroform was added dropwise over a period of 10 minutes a solution of 1.57 g. (0.02 mole) of acetyl chloride in 30 ml. of chloroform; a precipitate slowly formed. Stirring was continued at room temperature for an additional two hours at the end of which time was added 100 ml. of hexane to complete the precipitation of the crude, hygroscopic product (2.31 g., 95%). Recrystallization from 95% ethanol yielded XVI as a grey solid which, after drying in a nitrogen atmosphere, had m.p. 218-220° dec.; ir ν max (potassium bromide): 1623 cm^{-1} (C=O).

Anal. Calcd. for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.88; H, 6.52; N, 11.23.

1,2,3,4,5,6-Hexahydro-2,5-dinitrosobenzo[1,2-c:3,4-c']dipyrrole (XVII).

Dihydrobromide XV was converted in 92% yield to XVII by the procedure used above for VII. The light yellow crystals (from 95% ethanol) had m.p. 205-240° dec.; ir ν max (potassium bromide): 1450 cm^{-1} (N-NO).

Anal. Calcd. for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.62; N, 25.68; O, 14.66. Found: C, 55.01; H, 4.63; N, 25.40; O, 14.96.

1,2,3,4,5,6-Hexahydrobenzo[1,2-c:3,4-c']dipyrrole Dipicrate (XXI).

Treatment of a solution of diamine II (1.6 g., 0.01 mole) in 1.5 ml. of water with saturated ethanolic picric acid by the procedure used above for the dipicrate of I yielded 4.3 g. (70%) of XXI as yellow plates, darkening at 210° and melting explosively at 267°.

Anal. Calcd. for $C_{10}H_{12}N_2 \cdot 2C_6H_3N_3O_7$: C, 42.73; H, 2.93; N, 18.12. Found: C, 42.81; H, 2.87; N, 18.33.

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