Synthesis of 1,2,3,4,8,9,10,11-Octahydro-[1,4]diazepino[6,5,4-*jk*]carbazole and Related Compounds

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1,2,3,4,8,9,10,11-Octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (VIa) was synthesized from 2,3,4,5-tetrahydro-1*H*-benzodiazepine (Ia) *via* the route shown in Scheme I. Other compounds which were prepared similarly are 3-acetyl-6-chloro-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino-[6,5,4-*jk*]carbazole (Vb) and 3-methyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (VIII). Chemical transformations which were carried out with VI and 3-acetyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (Va) are also described.

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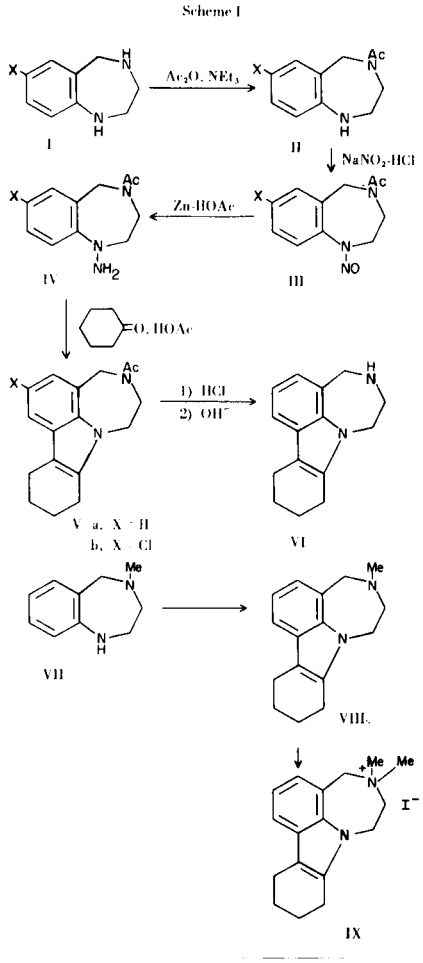
1,4-Benzodiazepines have received extensive attention by medicinal chemists in the last several decades, and proven to be a very fruitful area of research resulting in numerous therapeutically important drugs (1). Lately, the work in this area has been expanded to the synthesis of benzodiazepins fused to other heterocyclic nuclei (2). In continuing our work on the evaluation of benzodiazepine derivatives as potential antihypertensive agents (3), we have synthesized a few examples of the 1,4-diazepino-[6,5,4-*jk*]carbazole, a ring system in which a benzodiazepine is fused to indole (4).

The synthetic approach used in obtaining the examples of the novel ring system is shown in Scheme I. The approach consists of blocking the N_4-position of the tetrahydro-1,4-benzodiazepine by acetylation, and subsequent construction of a tetrahydroindole nucleus under the conditions of the Fisher indole synthesis. The tetrahydrobenzodiazepine Ia was acetylated selectively at the N_4-position by treatment with an equivalent amount of acetic anhydride in the presence of triethylamine in ether. Treatment of 4-acetyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (IIa) thus obtained with sodium nitrite in the presence of hydrochloric acid at 0° gave 4-acetyl-1-nitroso-tetrahydro-1,4-benzodiazepine, IIIa as an oil. The latter was reduced with zinc-acetic acid to give IVa which was then directly subjected to the reaction with cyclohexanone under the conditions of the Fisher indole synthesis. Thus there was obtained 3-acetyl-1,2,3,4,8,9,10,11-octahydro [1,4]diazepino[6,5,4-*jk*]carbazole (Va) in an overall yield of 45% calculated from IIa. The product Va gave a satis-

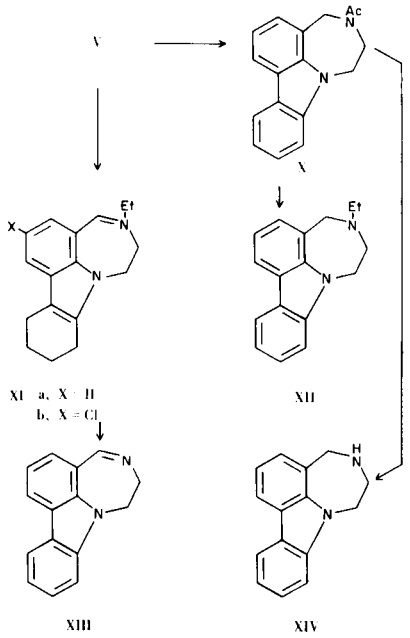
Scheme I



factory combustion analytical result, and showed an ir carbonyl absorption band at 6.10 μ. The nmr spectrum (deuteriochloroform) of the compound showed signals at δ 2.10 (s, 3H, CH_3), 1.90 and 2.70 (m, m, 8H, CH_2CH_2-CH_2CH_2), 4.00 (s, 4H, NCH_2CH_2N), 4.73 and 4.98 (s, s, $ArCH_2N$), and an aromatic multiplet at 6.92~7.50 ppm (3H). In a similar fashion, 3-acetyl-6-chloro-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (Vb) was prepared from IIb in a 40% overall yield. 3-Methyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (VIII), which was prepared from 4-methyltetrahydro-1,4-benzodiazepine following the above sequence, was characterized as the quaternary salt IX resulted by treatment with methyl iodide. The removal of the acetyl group in Va was effected by heating a solution of Va in concentrated hydrochloric acid on a steam bath for 6 hours, giving VI as a hydrochloride salt in a 95% yield. The free base was obtained by extraction of the alkaline solution of the hydrochloride salt with ether.

Treatment of Va with palladium-charcoal (10%) in refluxing xylene for 24 hours resulted in aromatization of the tetrahydrocarbazole system, giving 3-acetyl-1,2,3,4-tetrahydro[1,4]diazepino[6,5,4-*jk*]carbazole X in a 68% yield. The same aromatization was also effected with DDQ, but the yield was much inferior. Reduction of Va and Vb with lithium aluminum hydride proceeded smoothly to give, in good yields, XIa and XIb, respectively. It is worth noting that the treatment of XIa with palladium-charcoal in refluxing xylene caused elimination of the ethyl group at the N_3-position as well as aromatization

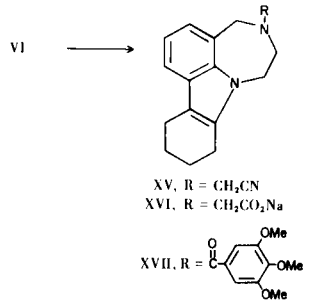
Scheme II



of the carbazole system, yielding 1,2-dihydro[1,4]diazepino[6,5,4-*jk*]carbazole (XIII). The nmr spectrum (deuteriochloroform) of XIII showed proton resonance signals at δ 4.30 (s, 4H, NCH_2CH_2N), an aromatic multiplet at 7.10 ~ 8.18 (7H), and a broad singlet at 8.65 ppm (1H, Ar-C*H*=N). A new absorption band shown at 6.15 μ in the ir spectrum of XIII was ascribed to the C=N bond. Removal of the acetyl group in X was effected by heating with 20% sulfuric acid for 4 hours (Scheme II).

The compound VI was used as a starting point to obtain derivatives of potential pharmacological interest. The reaction of VIa with chloroacetonitrile was carried out in ethanol medium in the presence of sodium bicarbonate to give XV in a 87% yield. The acetic acid derivative XVI was prepared by the treatment of VIa with ethyl bromoacetate in DMF again using sodium bicarbonate as an acid scavenger, and subsequent hydrolysis with dilute aqueous sodium hydroxide solution. The treatment of VIa with 3,4,5-trimethoxybenzoyl chloride in ether in the presence

Scheme III

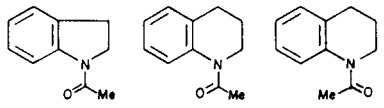


of triethylamine afforded XVII (Scheme III).

In the nmr spectrum of IIa the methylene protons at the 5-position appeared as two singlets at δ 4.40 and 4.50 in the ratio of approximately 3:2. Similarly, the corresponding methylene protons of V and X were shown in two peaks. Thus compound Va exhibited its methylene signals at δ 4.73 (86%) and 4.98 (14%), and in X they appeared at δ 4.70 (72%) and 4.95 (28%). The signals of the methyl protons of the acetyl group in IIa were also shown in two singlets at δ 2.02 and 2.15 in approximately 2:5 ratio. When the acetyl group was removed or reduced to the ethyl group, the methylene protons then appeared as a singlet (see Experimental).

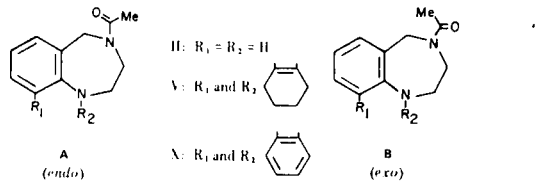
It is well known that an amide may exist in several rotamers (5-8). The existence of such conformational forms are known to be due to the partial double-bond character arising from the contribution of resonance structure $-\overset{O}{\overset{\|}{C}}-N= \longleftrightarrow -\overset{O^-}{\overset{|}{C}}=\overset{+}{N}=$, consequently leading to a large rotational energy barrier around the amide bond and a stiff, approximately planar framework (9). Thus in the case of 1-acetylindoline, the molecule is known to exist in

the almost entirely *endo* conformational form XVIII (5), whereas 1-acetyl-1,2,3,4-tetrahydroquinoline consists of about equal quantities of the *endo* (XIXA) and the *exo* conformers (XIXB) (6). These conclusions were derived from the nmr spectral data demonstrated by the considerable deshielding effect of the acetyl carbonyl group, and also confirmed by measurements of dipole moments (10).



XVIII XIXA XIXB

Analogously, two rotamers, **A** and **B** can be envisioned for compounds II, V, and X. The small resonance peak shown in the downfield may then be attributed to the rotamer **A** in which the methylene protons between the phenyl nucleus and the nitrogen are under the influence of the deshielding effect of the acetyl carbonyl double bond. The large peak is attributed to the rotamer **B** (11,12). Apparently, these compounds exist predominantly in the *exo* conformational form.



Although this report describes only the syntheses of a few simple examples of 1,4-diazepino[6,5,4-*jk*]carbazole including the parent compound, we believe that the synthetic method described here is generally applicable to the synthesis of variously substituted 1,4-diazepino[6,5,4-*jk*]-carbazoles when started with appropriately substituted tetrahydro-1,4-benzodiazepines and cyclohexanones.

EXPERIMENTAL

The melting points were determined in capillary tubes using a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were obtained in potassium bromide disks using a Perkin-Elmer (Model 21) spectrophotometer. Nuclear magnetic resonance spectra were obtained with a Varian A-60 spectrometer. Elemental analyses were obtained with a Perkin-Elmer (Model 24) elemental analyzer.

4-Acetyl-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (IIa).

Acetic anhydride (18 g.) was added dropwise to an ether solution (450 ml.) containing 2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (Ia) (13) (26.4 g.) and triethylamine (27 g.) at room temperature. The resulting mixture was refluxed gently for 4 hours. The precipitate which separated was removed by filtration, and the filtrate was concentrated under reduced pressure to about a half of the original volume. Chilling of the concentrated solution in a freezer overnight caused separation of a precipitate which was collected on a filter, washed with ether several times, then with water 5 times giving 21.5 g. (63.5%) of the product, m.p. 84-86°. An analytical sample, m.p. 84-86°, was obtained by recrystallization from ether; ir μ 3.05, 3.45, and 6.20; nmr (deuteriochloroform): δ 2.02 and 2.15 (s, s, 3H, CH_3), 3.13 and 3.78 (m, m, 4H, CH_2-CH_2), 4.13 (broad s, 1H, NH), 4.40 and 4.55 (s, s, 2H, CH_2), and aromatic multiplet centered at 6.95 ppm.

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.44; H, 7.42; N, 14.73. Found: C, 69.60; H, 7.50; N, 14.59.

4-Acetyl-7-chloro-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (IIb).

Acetic anhydride (6 g.) was added dropwise to an ether solution (200 ml.) containing 7-chloro-2,3,4,5-tetrahydro-1*H*-1,4-benzodiazepine (Ib) (9.1 g.), triethylamine (12 ml.), and pyridine (1 ml.). The resulting mixture was heated under gentle reflux for 4 hours. Organic salts formed during the reaction were removed by filtration. The filtrate was evaporated under reduced pressure to give an oil. The oil was treated with dilute aqueous sodium hydroxide solution, and extracted with ether several times. The combined ether extracts was washed with water, then dried over potassium carbonate. Evaporation of the ether solution under reduced pressure on a rotary evaporator afforded an oil which crystallized to give 6.7 g. (60%) of the product, m.p. 95-96°; ir μ 3.05, 3.55, and 6.16; nmr (deuteriochloroform) δ: 2.07 and 2.17 (s, s, 2H, CH_3), 3.22 and 3.82 (m, m, 4H, NCH_2CH_2N), 4.25 (broad s, 1H, NH), 4.43 and 4.53 ppm (s, s, 2H, CH_2).

Anal. Calcd. for $C_{11}H_{13}ClN_2O$: C, 58.80; H, 5.83; N, 12.47. Found: C, 58.66; H, 5.82; N, 12.58.

3-Acetyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]-carbazole (Va).

An aqueous sodium nitrite solution obtained by dissolving 4.2 g. of sodium nitrite in 10 ml. of water was added dropwise with stirring to a cold aqueous solution of IIa under chilling in ice. The latter solution was obtained by dissolving 11.6 g. of IIa in 100 ml. of water and 6 ml. of concentrated hydrochloric acid. The stirring was continued for an additional 10 minutes after the completion of the addition at room temperature. A product deposited as an oil which was extracted with chloroform several times. The combined extract was washed with water, then dried over potassium carbonate. Removal of the chloroform by evaporation on a rotary evaporator under reduced pressure gave an oil. The oil was dissolved in 140 ml. of glacial acetic acid. Zinc dust (30 g.) was added in small portions with stirring to the acetic acid solution. The temperature of the reaction mixture was kept under 30°, preferably between 30-25° by chilling in ice. After the addition of zinc dust, the mixture was allowed to stir at 25° for an additional hour. The reaction mixture was filtered under suction into a 500 ml. round bottom flask which contained 7.0 g. of cyclohexanone. The mixture thus obtained was heated on a steam bath for 1.5 hour. The original yellow color of the solution turned into brown. Acetic acid was removed *in vacuo* to give a resinous material which solidified on treatment with water. The product was collected on a filter, washed with water several times, then recrystallized from ether with a small amount of tetrahydrofuran to give 7.3 g. (45%) of Va, m.p. 129-131°. An analytical sample which was obtained by recrystallization from ether melted at 130-132°; ir μ 3.50 (broad), and 6.10; uv max (95% ethanol): 234 (ϵ, 3.10 x 10^4), 287 (ϵ, 6.85 x 10^3) and 2.97 mμ (shoulder) (ϵ, 5.75 x 10^3).

Anal. Calcd. for $C_{17}H_{20}N_2O$: C, 76.08; H, 7.51; N, 10.44. Found: C, 76.24; H, 7.64; N, 10.22.

3-Acetyl-6-chloro-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino-[6,5,4-*jk*]carbazole (Vb).

This compound was prepared, by a procedure analogous to that for Va, starting with 12 g. of IIb. Amounts of all other reagents used for this preparation were the same as those used for the preparation of Va. The heating period of acidic acid solution in the last step was extended to 2 hours. Removal of the acetic acid *in vacuo* afforded a resinous material which was washed with water repeatedly, then allowed to set in water for 2 days. A crystalline product thus separated was collected on a filter. Recrystallization of the product from a mixture of tetrahydrofuran and ether afforded 6.4 g. (40%) of the product, m.p. 135-137°; ir μ 3.25 (broad) and 6.12; nmr (deuteriochloroform): 2.11 (s, 3H, CH_3), 1.90 and 2.65 (m, m, 8H, $CH_2CH_2CH_2CH_2$), 4.05 (s, 4H, CH_2CH_2), 4.75 and 4.90 (s, s, 2H, CH_2), and 6.90 and 7.35 (m, m, 2H, aromatic).

Anal. Calcd. for $C_{17}H_{19}ClN_2O$: C, 67.43; H, 6.32; N, 9.25. Found: C, 67.26; H, 6.60; N, 9.20.

3-Methyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]-carbazole (VIII).

This compound was prepared by the same procedure as used for the synthesis of Va starting with 10 g. of VII (10). The compound was obtained as an oil in a 50% yield (7.5 g.), and used directly for the preparation of IX; nmr (deuteriochloroform): δ 2.50 (s, 3H, CH_3) and 4.05 ppm (s, 2H, CH_2).

1,2,3,4,8,9,10,11-Octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (VI).

Seven g. of Va was dissolved in 100 ml. of concentrated hydrochloric acid in a 250 ml. round bottom flask to give a brown solution. The flask was equipped with a water condenser, and heated on a steam bath for 4 hours, then for an additional 2 hours without the condenser. A precipitate was separated during the last hour of the heating. Chilling of the reaction mixture in ice caused separation of an additional precipitate. The precipitate was collected on a filter and washed with water to give 6.5 g. (95%) of the product as a hydrochloride salt, m.p. 318° dec. An analytical sample was obtained by recrystallization from water, m.p. 326° dec.; ir μ 3.85 (broad).

Anal. Calcd. for $C_{15}H_{18}N_2 \cdot HCl$: C, 68.55; H, 7.29; N, 10.66. Found: C, 68.59; H, 7.14; N, 10.49.

Treatment of the hydrochloride salt with aqueous sodium hydroxide solution, extraction with ether, then evaporation after drying over potassium carbonate gave VIa as a free base. An analytical sample which was recrystallized from ether and petroleum ether melted at 113-115°; ir μ 3.05; nmr (deuteriochloroform): δ 1.63 (s, 1H, NH), 1.88 and 2.65 (m, m, 8H, CH_2CH_2-CH_2CH_2), 3.22 and 3.78 (m, m, 4H, NCH_2CH_2N), 4.17 (s, 2H, CH_2) and aromatic multiplet at 6.70 ~ 7.40 (3H).

Anal. Calcd. for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.60; H, 8.09; N, 12.34.

1,2,3,4,8,9,10,11-Octahydro-3,3-dimethyl-[1,4]diazepino[6,5,4-*jk*]carbazolium Iodide (IX).

Methyl iodide (4.1 g.) was added dropwise to an ether solution obtained by dissolving VIII (7.0 g.) in ether (150 ml.). The resulting solution was allowed to stir at room temperature overnight. A precipitate was collected on a filter and washed with ether several times to give 10.5 g. (94%) of the product, m.p. 245-248°. Recrystallization from ethanol improved the m.p. to 249-251°.

Anal. Calcd. for $C_{17}H_{23}IN_2$: C, 53.41; H, 6.08; N, 7.33. Found: C, 53.19; H, 6.07; N, 7.44.

3-Acetyl-1,2,3,4-tetrahydro[1,4]diazepino[6,5,4-*jk*]carbazole (X).

A mixture of Va (6.0 g.), palladium-charcoal (10%) (5.0 g.), and xylene (400 ml.) was refluxed under nitrogen atmosphere for 24 hours, then filtered using a sintered glass filter while hot. Removal of xylene in a rotary evaporator *in vacuo* gave an oily residue. Treatment of the oil with tetrahydrofuran afforded 4.05 g. (68%) of the product, m.p. 113-115°; ir μ 6.14; nmr (deuteriochloroform): δ 1.99 and 2.10 (s, s, 3H, CH_3), 4.10 (m, 4H, NCH_2CH_2N), 4.70 and 4.95 (s, s, 2H, CH_2), and aromatic multiplet at 7.10 ~ 8.10 ppm (7H); uv max (95% ethanol): 236 (ϵ, 4.05 x 10^4), 262 (ϵ, 1.67 x 10^4), and 2.91 mμ (ϵ, 1.49 x 10^4).

Anal. Calcd. for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 76.97; H, 6.20; N, 10.48.

1,2,3,4-Tetrahydro[1,4]diazepino[6,5,4-*jk*]carbazole (XIV).

A mixture of X (0.6 g.) and 20% sulfuric acid (40 ml.) was heated under reflux for 4 hours. Chilling of the reaction mixture in ice caused separation of a precipitate which was collected on a filter and recrystallized from water, giving the product as a hemisulfate, hemihydrate, m.p. 258-260° dec.

Anal. Calcd. for $C_{15}H_{14}N_2 \cdot \frac{1}{2}H_2SO_4 \cdot \frac{1}{2}H_2O$: C, 64.27; H, 5.75; N, 10.00. Found: C, 64.19; H, 5.44; N, 9.68.

The sulfuric acid salt was dissolved in water. The aqueous solution was made alkaline with an addition of dilute aqueous sodium hydroxide, and extracted with ether several times. The ether extract was dried over potassium carbonate. Addition of ether-hydrogen chloride solution to the ether extract caused separation of a precipitate which was collected on a filter and recrystallized from ethanol with charcoal treatment to give XIV as a hydrochloride, m.p. 286-288° dec.; ir μ 3.25 and 3.80 (broad); uv max (95% ethanl): 237 (ϵ, 3.90 x 10^4), 262 (ϵ, 1.65 x 10^4), and 291 mμ (ϵ, 1.47 x 10^4).

Anal. Calcd. for $C_{15}H_{14}N_2 \cdot HCl$: C, 69.62; H, 5.84; N, 10.83. Found: C, 69.29; H, 5.87; N, 10.69.

3-Ethyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (XI).

Eight and one-tenth g. of Va was reduced with 2.3 g. of lithium aluminum hydride using tetrahydrofuran as a reaction medium by a conventional method to give the product (6.5 g., 85%) as an oil. A small portion of the oily product was dissolved in anhydrous ether, then treated with ether-hydrogen chloride solution. The precipitate thus separated was collected on a filter and dried over phosphorus pentoxide *in vacuo*. Recrystallization from isopropanol with charcoal treatment gave an analytical sample, m.p. 149-151°; ir μ 4.05 (broad); nmr (deuteriochloroform): δ 1.10 (t, 3H, CH_3), 1.83 and 2.63 (m, m, 8H, $CH_2CH_2CH_2CH_2$), 3.13 (m, 2H, NCH_2Me), 3.73 (m, 4H, NCH_2CH_2N), 4.10 (s, 2H, $PhCH_2N$), and aromatic multiplet at 6.80 ~ 7.10 ppm (3H).

Anal. Calcd. for $C_{17}H_{22}N_2 \cdot HCl$: C, 70.20; H, 7.98; N, 9.64. Found: C, 70.59; H, 8.04; N, 9.63.

3-Ethyl-1,2,3,4-tetrahydro[1,4]diazepino[6,5,4-*jk*]carbazole (XII).

Three g. of X were reduced with 0.86 g. of lithium aluminum hydride by a conventional method using tetrahydrofuran as a reaction solvent, giving the product as an oil. The oil was converted into a hydrochloride salt by treatment of the oil as an ether solution with dry hydrogen chloride gas. The precipitate was collected and recrystallized from absolute ethanol to give 2.0 g. (61.5%) of the product as a hydrochloride salt, m.p. 237-239°; nmr (DMSO-d_6): δ 1.40 (t, 3H, CH_3), 3.34 (q, 2H, NCH_2Me), 3.34 (s, 1H, NH), 3.93 and 4.83 (m, m, 4H, NCH_2CH_2N), 4.95 (s, 2H, $Ph\text{-}CH_2N$) and aromatic multiplet at 7.12 ~ 8.32 ppm (7H).

Anal. Calcd. for $C_{17}H_{18}N_2 \cdot HCl$: C, 71.19; H, 6.68; N, 9.77.

Found: C, 70.83; H, 6.87; N, 9.31.

6-Chloro-3-ethyl-1,2,3,4,8,9,10,11-octahydro[1,4]diazepino[6,5,4-*jk*]carbazole (XIb).

Three g. of Vb were reduced with 0.8 g. of lithium aluminum hydride using tetrahydrofuran as a reaction medium by a conventional method, giving XIb as an oil. The oil was dissolved in anhydrous ether, and treated with ether-hydrogen chloride solution. Hydrochloric acid salt thus separated was collected on a filter under nitrogen atmosphere and dried over phosphorus pentoxide *in vacuo*. The product melted at 229-231° and amounted to 3.2 g. (99%); ir: μ 3.25 and 4.06.

Anal. Calcd. for $C_{17}H_{21}ClN_2 \cdot HCl$: C, 62.77; H, 6.82; N, 8.61; Cl, 21.80. Found: C, 62.88; H, 6.92; N, 8.48; Cl, 21.85.

1,2-Dihydro-[1,4]diazepino[6,5,4-*jk*]carbazole (XIII).

A mixture of XIa (2.5 g.), palladium-charcoal (10%) (2.5 g.), and xylene (250 ml.) was refluxed under nitrogen atmosphere for 30 hours. The catalyst was removed by filtration while hot, and washed with hot xylene several times. Removal of xylene *in vacuo* on a rotary evaporator afforded an oil. The oil was dissolved in warm ether, treated with charcoal and filtered. Chilling of the filtrate in dry ice-acetone mixture caused separation of a precipitate which was collected on a filter, m.p. 114-116°; ir μ 3.50 (broad) and 6.15 (C=N); nmr (deuteriochloroform): δ 4.30 (s, 4H, NCH_2CH_2N), aromatic multiplet at 7.10 ~ 8.18 (7H), and 8.65 ppm (s, 1H, Ar-CH=N); mass spectrum, m/e: 220 (M^+).

Anal. Calcd. for $C_{15}H_{12}N_2$: C, 81.79; H, 5.49; N, 12.72. Found: C, 81.41; H, 5.73; N, 12.40.

1,2,3,4,8,9,10,11-Octahydro[1,4]diazepino[6,5,4-*jk*]carbazole-3-acetonitrile (XV).

Aqueous solution of VIa hydrochloride (2.4 g.) was made alkaline by addition of dilute aqueous sodium hydroxide solution, then extracted with ether several times. The combined extract was dried over potassium carbonate and evaporated on a rotary evaporator under reduced pressure. The free base thus obtained as an oil was dissolved in ethanol (50 ml.). To the ethanol solution was added anhydrous sodium bicarbonate (0.8 g.) and subsequently chloroacetonitrile (0.8 g.) dilute with ethanol while stirring. The resulting mixture was allowed to stir at room temperature for 0.5 hour, then heated under refluxing conditions for 3 hours. It was then allowed to set at room temperature overnight. Approximately 20 ml. of water was added to the mixture, and the mixture was chilled in ice. The precipitate thus separated was collected on a filter and washed with water, then with ethanol, giving 2.2 g. (91%) of product, m.p. 122-124°. Recrystallization from ethanol improved the m.p. to 124.5-126°.

Anal. Calcd. for $C_{17}H_{19}N_3$: C, 76.94; H, 7.22; N, 15.84. Found: C, 77.00; H, 7.15; N, 15.92.

1,2,3,4,8,9,10,11-Octahydro[1,4]diazepino[6,5,4-*jk*]carbazole-3-acetic Acid Sodium Salt (XVI).

A mixture of VIa hydrochloride (2.5 g.), ethyl bromoacetate (1.9 g.), sodium bicarbonate (0.95 g.), and DMF (50 ml.) was heated under reflux for 3.5 hours. The DMF was then evaporated in a rotary evaporator under reduced pressure. Twenty-five ml. of 15% aqueous sodium hydroxide solution was added to the residue, and heated under reflux for 1.5 hours. A precipitate started to separate in *ca.* 40 minutes. After the reaction mixture was chilled, the precipitate was collected on a filter and recrystallized from water with charcoal treatment. The product did not melt below 360°, yield, 0.8 g. (27%); ir: μ 6.27.

Anal. Calcd. for $C_{17}H_{19}N_2O_2Na$: C, 66.64; H, 6.25; N, 9.15. Found: C, 66.85; H, 6.54; N, 9.34.

1,2,3,4,8,9,10,11-Octahydro-3-(3,4,5-trimethoxybenzoyl)[1,4]-diazepino[6,5,4-*jk*]carbazole (XVIII).

Four and two-tenth g. of VIa hydrochloride were dissolved in water. The aqueous solution was made alkaline with addition of 50% aqueous sodium hydroxide solution, then extracted with ether 5 times. The combined extract was washed with water twice, then dried over anhydrous potassium carbonate. After removing the drying agent by filtration, 3,4,5-trimethoxybenzoyl chloride (3.7 g.), then triethylamine (1.6 g.) was added in small portions to the ether solution. The resulting mixture was allowed to stir at room temperature for 4 hours, then chilled in ice. The precipitate which deposited was collected on a filter and washed with water several times, then recrystallized from ethanol, giving 1.7 g. of product, m.p. 164-166°. Concentration of the ether mother liquor and subsequent chilling in ice afforded an additional quantity (1.9 g.) of the product, total yield, 3.6 g. (54%); ir: μ 3.50 and 6.08.

Anal. Calcd. for $C_{25}H_{28}N_2O_4$: C, 71.41; H, 6.71; N, 6.66. Found: C, 71.23; H, 7.10; N, 6.46.

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