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Studies on 1-Azabicyclo Compounds. XII.[1] Synthesis of 5,6,8,9,10,11,11a,12-Octahydroindolo[3,2-*b*]quinolizine and Related Compounds

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Monoester of benzylmalonic acid (I) and 3-carboxy-4-octahydroquinolizinone (V) were coupled with benzenediazonium salt to yield labile phenylhydrazones, IIa and VII, respectively. IIa was kept standing in chloroform or heated to give another phenylhydrazone (IIb). VIa was similarly converted into VIb. The condensed four-cyclic compound (VIIIa) derived from VIa or VIb was heated with hydrochloric acid and the resulting product (IXa) was subjected to Pictet-Spengler reaction by formalin to afford octahydroindolo[3,2-*b*]quinolizine (Xa). Xa was also obtained by reduction of VIIIa with LAH. Treatment of IXa with benzaldehyde in aqueous hydrochloric acid produced XII. Some methoxyl derivatives (VIIIb, Xb) were obtained according to the same route as mentioned above.

There exist six kinds of four-cyclic systems which are possibly formed by condensation of octahydroquinolizine with an indole ring. Syntheses of 1,2,3,4,6,7-hexahydroindolo-[2,3-*a*]quinolizine and its derivatives possessing the skeleton of corynantheane alkaloids have been reported in large numbers, but a few reports[3] concerning the other systems have appeared so far in the literatures. It is also expected that any physiological active compounds may be found in these systems. Therefore, the authors have attempted to synthesize a number of compounds belonging to these systems in order to examine their physiological activity. This paper deals with synthesis of 5,6,8,9,10,11,11a,12-octahydroindolo[3,

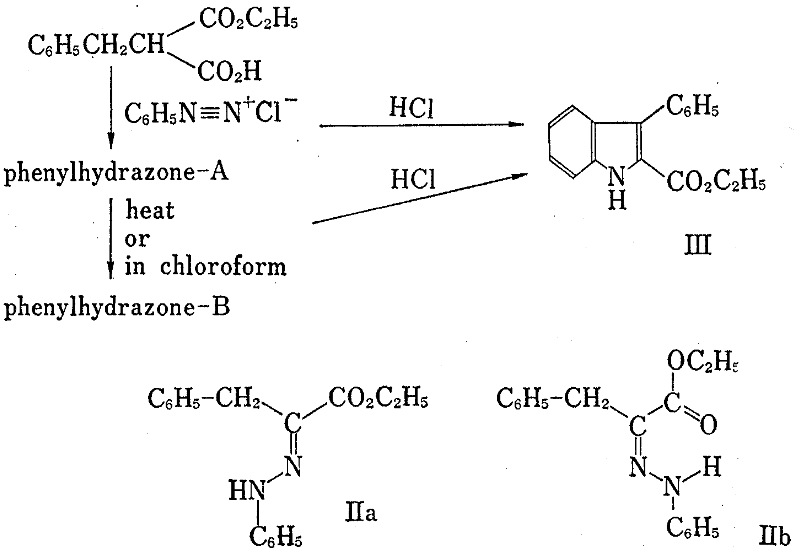

Chart 1

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[1] Part XI: Y. Arata and T. Shioda, *Chem. Pharm. Bull.* (Tokyo), **20**, 783 (1972).

[2] Location: *13-1, Takara-machi, Kanazawa.*

[3] *a*) J. Keufer, *Ann. Pharm. Franc.*, **8**, 816 (1950), [*Chem. Abst.*, **45**, 10246 (1951)]; *b*) G.R. Clemo and J.C. Seaton, *J. Chem. Soc.*, **1954**, 2582; *c*) H. Bader and W. Oroshnik, *J. Am. Chem. Soc.*, **79**, 5686 (1957); *d*) F. Kebrle, A. Rossi and K. Hoffman, *Helv. Chim. Acta*, **42**, 907 (1959); *e*) N.V. Koninklijke, *Chem. Abst.*, **65**, 7179 (1966).

2-*b*]quinolizine (X) and related compounds.

As a preliminary experiment, monoester of benzylmalonic acid (I) was allowed to react with benzenediazonium salt and the resulting product was developed over alumina column chromatography to afford the known phenylhydrazone (A),[4] mp 92—94° in 16% yield. The phenylhydrazone-A was heated at 100° to isomerize into phenylhydrazone-B, mp 56.5—58°. The infrared (IR) spectrum of the latter phenylhydrazone showed bands at 1600, 1500, 750 (phenyl) and 1675 cm^{-1} (ester), being different from that (ester: 1700 cm^{-1}) of the former.

The nuclear magnetic resonance (NMR) spectrum[5] of the latter in deuteriobenzene was assigned as follows: τ 9.21 (3H, triplet, J=7.1 cps, $-CH_2C\underline{H}_3$), 6.25 (2H, quartet, J=7.1 cps, $-C\underline{H}_2CH_3$), 6.20 (2H, singlet, $C_6H_5-C\underline{H}_2-$), 2.7—2.95 (10H, $-C_6-\underline{H}_5$) and −2.45 (1H, singlet, $N\underline{H}$), whereas that of the former indicated signals at τ 8.90 (3H, triplet, J=7.1 cps, $-CH_2C\underline{H}_3$), 5.81 (2H, quartet, J=7.1 cps, $-C\underline{H}_2CH_3$), 6.20 (2H, singlet, $C_6H_5-C\underline{H}_2-$), 2.8—3.0 (10H, $-C_6-\underline{H}_5$) and 2.05 (1H, singlet, $N\underline{H}$). In addition, NMR spectrum of the latter in deuteriochloroform exhibited $C_6H_5-C\underline{H}_2-$ signal at τ 6.20 and $C_6H_5-N\underline{H}-N=$ signal at τ −1.90 (Fig. 1-1) and that of the former in the same solvent, on the other hand, indicated $C_6H_5-C\underline{H}_2-$ signal at τ 5.97 and $C_6H_5-N\underline{H}-N=$ signal at τ 2.03, accompanied with the faint signals of the latter (Fig. 1-2).

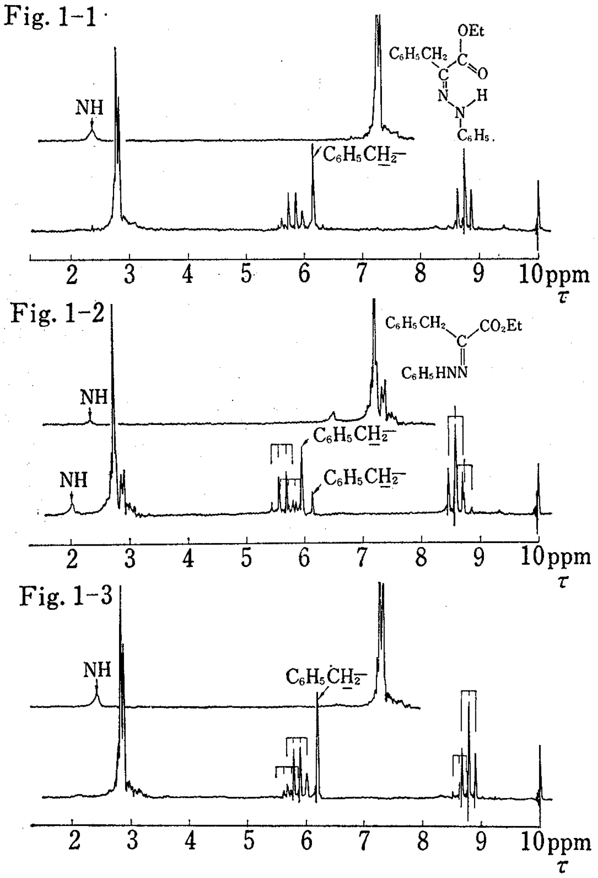

Fig. 1. The NMR Spectra of *syn*- and *anti*-Ethyl 2-Phenylhydrazono-3-phenylpropionate in Deuteriochloroform.

These signals, changing in process of time (Fig. 1-3), were finally in accordance with those of the latter. In fact, phenyl hydrazone-A, when kept standing for 48 hr in chloroform, was readily converted into the isomer B. The facts that the $N\underline{H}$ signal appeared at the exceedingly lower field than that of the other in the NMR spectrum of phenylhydrazone-B, and that the frequence of the carbonyl band showed considerably low for that of the other in its IR spectrum seem to be caused by intramolecular interaction of the NH group with the carbonyl oxygen of the ester. Thus, the structures IIa and IIb were, respectively, postulated for phenylhydrazone-A and -B. When heated with hydrochloric acid in acetic acid, IIb afforded III,[6] mp 137—138°, in 20% yield, so did IIa in 75% yield.

Hereupon, 3-ethoxycarbonyl-4-octahydroquinolizinone (IV)[7] was hydrolized with aqueous potassium hydroxide and the resulting carboxylic acid (V) was coupled with benzenediazonium salt in an aqueous solution adjusted to pH 3—4 with sodium acetate giving

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[4] H. Gault and R. Weick, *Bull. Soc. Chim. France*, [4], **31**, 890 (1922), [*Chem. Abst.*, **17**, 1222 (1923)].

[5] *a*) G.J. Karabatsos and R.A. Taller, *J. Am. Chem. Soc.*, **85**, 3624 (1963); *b*) S. Inaba, K. Ishizumi, K. Mori and H. Yamamoto, *Chem. Pharm. Bull.* (Tokyo), **19**, 722 (1971).

[6] R.H.F. Manske, W.H. Perkin and Robert Robinson, *J. Chem. Soc.*, **1927**, 1.

[7] Y. Arata, T. Shioda, J. Yamada and Y. Hayashi, *Yakugaku Zasshi*, **89**, 389 (1969).

3-phenylhydrazono-4-octahydroquinolizinone (VIa), mp 197—198°, IR cm^{-1}: 1630, in 91% yield. Heating of the phenylhydrazone (VIa) was effected to give the other one (VIb), mp 109.5—110.5°, IR cm^{-1}: 1603. The NMR spectra of VIb and VIa in deuteriochloroform showed C_6H_5-N$\underline{H}$-N= signals at τ −3.0 and 2.02, respectively. The signals of the former were invariable in process of time, while those of the latter were gradually changing and finally coincident with the former signals after the lapse of 48 hr, as mentioned in the case of IIa. From the facts, phenylhydrazones VIa and VIb would be represented by formulae VIa and VIb, respectively. VIa and VIb, when heated with hydrochloric acid in acetic acid, produced, as expected, the condensed four-cyclic compound VIIIa, mp 289°, IR cm^{-1}: 3260 (NH), 1630 (lactam); UV mμ (ε): 229 (22200), 241 (17100), 303 (18000), in good yield.

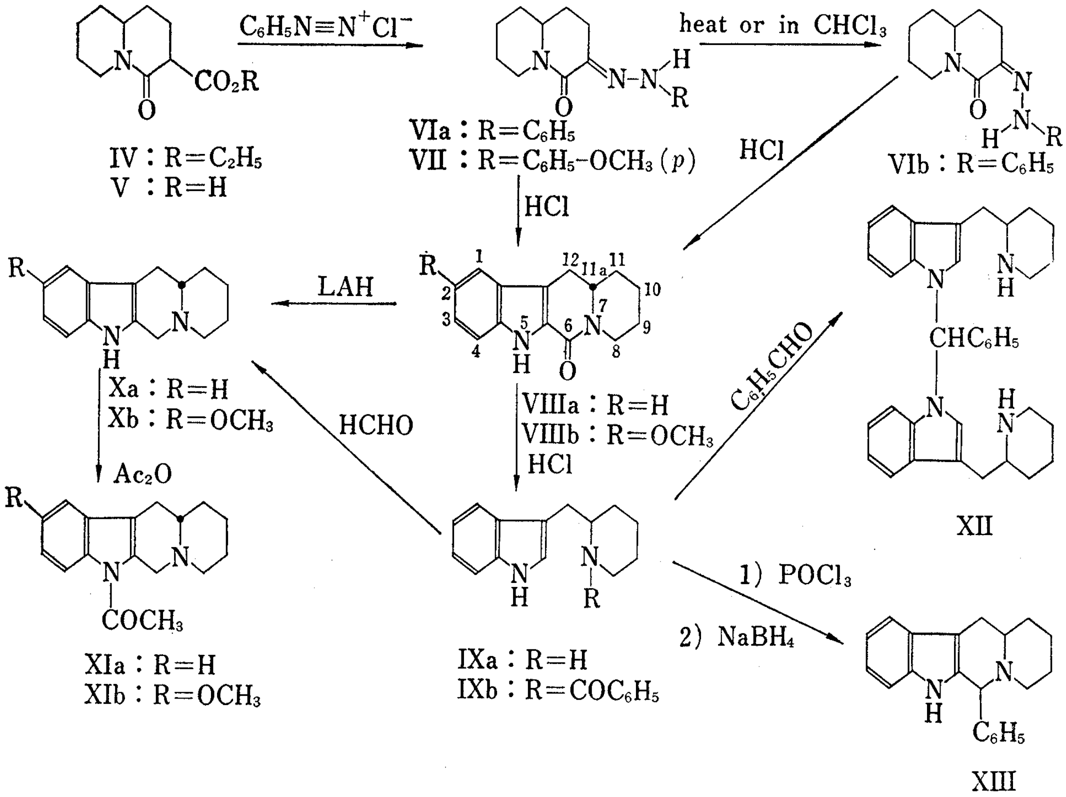

Chart 2

In addition, the corresponding methoxyphenylhydrazone (VII), mp 92—94° was obtained by the similar coupling reaction of V with *p*-methoxybenzenediazonium salt. However, VII was so unstable that it easily changed its color into brown, and thus the stereochemical elucidation of VII remained as the unsettled problem. VII was subjected to heating with hydrochloric acid in acetic acid to afford VIIIb, mp 255—256° (decomp.), IR cm^{-1}: 3290 (indolic NH), 1630 (lactam); UV mμ (ε): 224 (23400), 313 (20200), in 71% yield. Lithium aluminum hydride (LAH) reduction of VIIIa and VIIIb gave 5,6,8,9,10,11,11a,12-octahydroindolo[3,2-*b*]quinolizine (Xa),[3c] mp 227° (decomp.), and its methoxy derivative (Xb), mp 210—211° (decomp.), respectively. Both Xa and Xb showed broad bands at 2800—2400 cm^{-1} in the IR spectra, respectively, which suggested that both compounds would exist as inner salts formed by the indolic NH and the tertiary amine. Hereupon, conformations of the octahydroquinolizine rings in Xa and Xb were confirmed by the following procedure. Both Xa and Xb were refluxed in acetic anhydride giving the respective N-acetyl derivatives, XIa, mp 129—129.5° and XIb, mp 142—143°. The IR spectra of XIa and XIb indicated Bohlmann bands at 2760 and 2730, and 2770 and 2750 cm^{-1}, respectively. From the data, Xa and Xb as well as VIIIa and VIIIb were clarified to be *trans*-octahydroquinolizine derivatives. Heating of VIIIa in hydrochloric acid–acetic acid led to the formation of IXa, mp 160—161°, IR cm^{-1}: 3340 (indolic NH), in 85% yield. On the other hand, similar treatment of VIIIb with hydrochloric acid in acetic acid, gave only a resinous product. Pictet-Spengler reaction of IXa[3c] with formalin in the presence of hydrochloric acid produced, as expected, Xa, which was identified with the product (Xa) from reduction of VIIIa with LAH by the direct comparison.

Furthermore, when IXa was treated with benzaldehyde in aqueous hydrochloric acid, a product XII, mp 237—239°, was obtained. The structure of XII was confirmed by spectral data as well as elemental analysis. The NMR spectrum of XII in dioxane showed two protons (τ 3.78, singlet) at α-position of two indole rings and no indolic NH protons. The mass spectrum showed peaks at the following positions, *m/e* 516 (parent peak), 433, 350, 220, 130, and 84, and the main fragmentation was illustrated in Chart 3. Since an attempt to synthesize 6-phenyl-octahydroindolo[3,2-*b*]quinolizine (XIII) through reaction of VIIIa with phenylmagnesium bromide was unsuccessfully carried out, we followed the following route. The N-benzoyl derivative (IXb) of IXa was subjected to Bischler-Napieralski reaction by phosphorous oxychloride followed by sodium borohydride reduction to afford XIII, mp 174—175°, IR cm^{-1}: 3480 (indolic NH), 2800, 2750 (*trans*-octahydroquinolizine) in a poor yield.

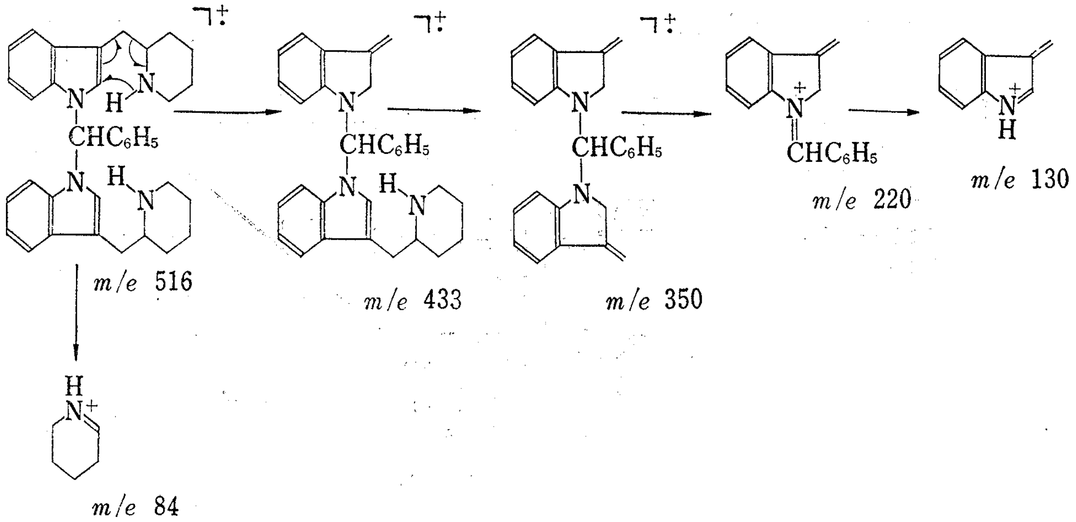

Chart 3

Experimental[8]

***anti*-Ethyl 2-Phenylhydrazono-3-phenylpropionate(IIa)**——To a solution of ethanol (70 ml) dissolved potassium hydroxide (6.9 g) was added diethyl benzylmalonate (31 g). The solution was kept standing for 20 hr at room temperature, and then evaporated *in vacuo*. The residue was dissolved in water, and the solution was shaken with ether. The water layer was acidified with hydrochloric acid, and shaken with ether. From the ether layer, monoester(I) (25 g) was obtained. To a solution of 25 g of I in 1.8% aqueous sodium hydroxide (300 ml) was added aqueous benzenediazonium chloride (prepared from 10.8 g of aniline, 7.8 g of sodium nitrite and 30 ml of conc. hydrochloric acid) under cooling, followed by addition of sodium acetate (60 g). The solution was stirred for 7 hr under cooling at 0—5°, and then kept standing overnight at room temperature. An oily product deposited was extracted with ether. The ether layer was washed with water and desiccated, followed by the evaporation of the solvent. The residue was subjected to alumina column cnromatography by elution with petroleum ether to afford 5.5 g (yield: 16%) of a crystalline product (IIa). Recrystallized from isopropylether to give yellow plates, mp 92—94° (lit.[4] mp 89°). *Anal.* Calcd.

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[8] All melting points were measured with a Yanagimoto Micro Melting Point Apparatus and uncorrect. IR spectra were measured with a Spectrophotometer IR-G, Japan Spectroscopic Co., UV with a Spectrophotometer EPS-2U of Hitachi Co., and NMR with a H-60-C of Japan Electron Lab. Co., using tetramethylsilane as an internal standard.

for $C_{17}H_{18}O_2N_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.30; H, 6.55; N, 10.09. IR ν_{max}^{Nujol} cm^{-1}: 1700 (ester), 1600, 1500, 740 (phenyl). NMR (10% solution in C_6D_6) τ: 8.90 (3H, triplet, $J=7.1$ cps, $-CH_2C\underline{H}_3$), 6.20 (2H, singlet, $C_6H_5-C\underline{H}_2-$), 5.81 (2H, quartet, $J=7.1$ cps, $-C\underline{H}_2CH_3$), 2.8—3.0 (10H, $-C_6\underline{H}_5$), 2.05 (1H, singlet, N$\underline{H}$). (10% solution in $CDCl_3$): 8.60 (triplet, $J=7.1$ cps, $-CH_2C\underline{H}_3$), 8.76 (triplet, $J=7.1$ cps, $-CH_2C\underline{H}_3$), 6.20 (singlet, $C_6H_5-C\underline{H}_2-$), 5.97 (singlet, $C_6H_5-C\underline{H}_2-$), 5.84 (quartet, $J=7.1$ cps, $-C\underline{H}_2CH_3$), 5.64 (quartet, $J=7.1$ cps, $-C\underline{H}_2CH_3$), 2.7—2.95 ($-C_6\underline{H}_5$), 2.03 (singlet, NH), −1.90 (singlet, N$\underline{H}$).

***syn*-Ethyl 2-Phenylhydrazono-3-phenylpropionate(IIb)**——1) 0.5 g of IIa was heated at 100° for 1 hr. The reaction product was recrystallized from ethanol to give yellow plates(IIb), mp 56.5—58°. Yield: quantitative. *Anal.* Calcd. for $C_{17}H_{18}O_2N_2$: C, 72.32; H, 4.63; N, 9.92. Found: C, 72.61; H, 6.71; N, 10.02. IR ν_{max}^{Nujol} cm^{-1}: 1675 (ester), 1600, 1500, 750 (phenyl). NMR (10% solution in C_6D_6) τ: 9.21 (3H, triplet, $J=7.1$ cps, $-CH_2C\underline{H}_3$), 6.25 (2H, quartet, $J=7.1$ cps, $-C\underline{H}_2CH_3$), 6.20 (2H, singlet, $C_6H_5-C\underline{H}_2-$), 2.7—2.95 (10H, $-C_6\underline{H}_5$), −2.45 (1H, singlet, N$\underline{H}$). (10% solution in $CDCl_3$) τ: 8.76 (3H, triplet, $J=7.1$ cps, $-CH_2C\underline{H}_3$), 6.20 (2H, singlet, $C_6H_5-C\underline{H}_2-$), 5.84 (2H, quartet, $J=7.1$ cps, $-C\underline{H}_2CH_3$), 2.65—2.85 (10H, $-C_6\underline{H}_5$), −1.90 (1H, singlet, N$\underline{H}$).

2) A solution of 0.5 g of IIa in chloroform was kept standing for 48 hr. The solvent was removed *in vacuo*. The residue was recrystallized from ethanol to give yellow plates, mp 56.5—58°. Yield: quantitative. No depression of melting point was observed by the admixture of the compound with the phenylhydrazone mentioned above and the IR spectra of both compounds were completely in accordance.

Ethyl 3-Phenylindole-2-carboxylate(III)——1) A mixture of 2.0 g of IIb, 4 ml of conc. hydrochloric acid and 4 ml of acetic acid was refluxed for 3 hr. The reaction solution was evaporated to dryness *in vacuo*, and the residue was shaken with ether. The ether layer was washed with aqueous sodium carbonate, and then with water. The ether layer was desiccated, followed by the evaporation of the solvent to afford the residue(III). Yield: 0.4 g (20%). Recrystallized from ethanol to give colorless plates, mp 137—138°. *Anal.* Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.84; H, 5.84; N, 5.31. IR ν_{max}^{Nujol} cm^{-1}: 3300 (indolic NH), 1670, 1260 (ester), 1600, 1540, 750 (aromatic ring).

2) A mixture of 2.0 g of IIa, 4 ml of conc. hydrochloric acid and 4 ml of acetic acid was refluxed for 3 hr. The reaction solution was treated in the same way as mentioned above. The product was recrystallized from ethanol to give colorless plates, mp 137—138°. Yield: 1.5 g (75%). This compound was in accordance with III obtained from IIb in the IR spectra, and no depression of melting point was observed by the admixture of both compounds.

***anti*-3-Phenylhydrazono-4-octahydroquinolizinone(VIa)**——A mixture of 3-ethoxycarbonyl-4-octahydroquinolizinone(IV) (30 g) and 10% aqueous potassium hydroxide (300 ml) was stirred for 24 hr at room temperature. To the reaction solution was added benzenediazonium chloride solution (prepared from 37.8 g of aniline, 28.5 g of sodium nitrite and 102 ml of conc. hydrochloric acid) under cooling. The reaction mixture was adjusted the pH value to 3—4 with aqueous sodium acetate, and kept standing for 24 hr under cooling at 0—5°. The precipitate(VIa) was collected by filtration. Yield: 31 g (91%). Recrystallized from ethyl acetate to give yellow needles, mp 197—198°. *Anal.* Calcd. for $C_{15}H_{19}ON_3$: C, 70.00; H, 7.44; N, 16.33. Found: C, 69.93; H, 7.54; N, 16.02. IR ν_{max}^{Nujol} cm^{-1}: 1630 (lactam), 1601, 1500, 753 (phenyl). NMR (3% solution in $CDCl_3$) τ: 2.76 (5H, singlet, $-C_6\underline{H}_5$), 2.02 (1H, singlet, N$\underline{H}$).

***syn*-3-Phenylhydrazono-4-octahydroquinolizinone(VIb)**——0.5 g of VIa was heated for 1 hr at 200—205°. The reaction product was recrystallized from ethanol giving yellow plates, mp 109.5—110.5°. Yield: quantitative. *Anal.* Calcd. for $C_{15}H_{19}ON_3$: C, 70.00; H, 7.44; N, 16.33. Found: C, 69.78; H, 7.60; N, 16.22. IR ν_{max}^{Nujol} cm^{-1}: 1603 (lactam), 1500, 750 (phenyl). NMR (6% solution in $CDCl_3$) τ: 2.95 (5H, singlet, $-C_6\underline{H}_5$), −3.0 (1H, singlet, N$\underline{H}$).

5,6,8,9,10,11,11a,12-Octahydroindolo[3,2-*b*]quinolizin-6-one(VIIIa)——1) A mixture of 31 g of VIa, 120 ml of acetic acid and 100 ml of conc. hydrochloric acid was refluxed for 3 hr. To this was added water to deposite the precipitate(VIIIa) which was collected by filtration. Yield: 20 g (69%). Recrystallized from ethanol to afford colorless needles, mp 289°. *Anal.* Calcd. for $C_{15}H_{16}ON_2$: C, 74.97; H, 6.71; N, 11.67. Found: C, 74.99; H, 6.80; N, 11.57. IR ν_{max}^{Nujol} cm^{-1}: 3260 (indolic NH), 1630 (lactam) 1615, 1500, 745 (aromatic ring). UV λ_{max}^{EtOH} mμ (ε): 229 (22200), 241 (17100), 303 (18000).

2) A mixture of 1.8 g of VIb, 25 ml of acetic acid and 3 ml of conc. hydrochloric acid was refluxed for 5 hr. To the solution was added water and the precipitate(VIIIa) was collected by filtration. Yield: 1.5 g (89%). Recrystallized from ethanol to yield colorless needles, mp 289°. No depression of melting point was observed by the admixture of the compound with VIIIa mentioned above and the IR spectra of both compounds were completely in accordance.

5,6,8,9,10,11,11a,12-Octahydro-2-methoxy-indolo[3,2-*b*]quinolizin-6-one(VIIIb)——A mixture of 2.0 g of IV and 3% aqueous potassium hydroxide solution (65 ml) was stirred for 24 hr at room temperature. To this solution was added aqueous diazonium salt (prepared from 3.3 g of *p*-anisidine, 1.9 g of sodium nitrite and 6.8 ml of conc. hydrochloric acid). The reaction mixture was adjusted the pH value to 3—4 with aqueous sodium acetate and kept standing for 24 hr at 0—5°. The precipitate(VII) was collected by filtration. Yield: 1.2 g (46.2%). Recrystallized from ethyl acetate to yeild white needles, mp 92—94°. The phenylhydrazone(VII) was so unstable that it changed its color into brown. Conformation of this phenylhydrazone was unable to determine. A mixture of 1.2 g of VII, 6 ml of acetic acid and 25 ml of conc. hydrochloric acid was refluxed for 3 hr. The precipitate(VIIIb) was collected by filtration and recrystallized from ethanol to give colorless needles, mp 255—256° (decomp.). Yield: 0.8 g (71%). *Anal.* Calcd. for $C_{16}H_{18}O_2N_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.23; H, 6.92; N, 10.30. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3290 (indolic NH), 1630 (lactam), 1500, 775 (aromatic ring). UV $\lambda_{\max}^{\text{EtOH}}$ mμ (ε): 224 (23400), 313 (20200).

3-(2-Piperidylmethyl)indole(IXa)——A mixture of 1.0 g of VIIIa, 20 ml of 17% hydrochloric acid and 30 ml of acetic acid was heated in a sealed tube for 24 hr at 145—150°. The reaction solution was evaporated to dryness *in vacuo*. To the residue was added water and then shaken with ether. The water layer was made alkaline with sodium carbonate, and then shaken with ether. The ether solution was washed with water and desiccated, followed by the evaporation of the solvent. The residue (IXa) was recrystallized from ethyl acetate to give white needles, mp 160—161°. Yield: 0.7 g (85%). (lit.3c) mp 156—156.5°.) *Anal.* Calcd. for $C_{14}H_{18}N_2$: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.70; H, 8.67; N, 12.86. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3340 (indolic NH), 1500, 745 (aromatic ring). UV $\lambda_{\max}^{\text{EtOH}}$ mμ (ε): 222 (36600), 276 (6100), 282 (6200), 291 (5800).

5,6,8,9,10,11,11a,12-Octahydroindolo[3,2-*b*]quinolizine(Xa)——1) To a suspension of 0.2 g of LAH in tetrahydrofuran (10 ml) was added dropwise a solution of 0.2 g of VIIIa in tetrahydrofuran (10 ml). The suspension solution was stirred for 5 hr at room temperature and then added water to decompose an excess of LAH. The solvent was removed *in vacuo* and the residue was shaken with ethyl acetate. The residue (Xa) obtained from ethyl acetate layer was recrystallized from methanol to give colorless sands, mp 227° (decomp.). Yield: 0.18 g (96%). (lit.3c) mp 218—219°). *Anal.* Calcd. for $C_{15}H_{18}N_2$: C, 79.60; H, 8.02; N, 12.38. Found: C, 79.62; H, 7.90; N, 12.22. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2800—2400 (-N$^+$H), 1600, 1500, 725 (aromatic ring). UV $\lambda_{\max}^{\text{EtOH}}$ mμ (ε): 226.5 (36800), 284 (7400), 291 (6000).

2) To a solution of 100 mg of IXa in N-hydrochloric acid (25 ml) was added 0.5 ml of 35% formaldehyde solution. The reaction mixture was adjusted the pH value to 5.5 with aqueous sodium acetate and kept standing for 5 days at room temperature. The solution was made alkaline with ammonia, and shaken with ethyl acetate. The residue (Xa) obtained from the ethyl acetate layer was recrystallized from methanol to give colorless sands, mp 227° (decomp.). Yield: 89 mg (85%). No depression of melting point was observed by the admixture of this compound with Xa obtained by reduction of VIIIa with LAH, and the IR spectra of both compounds were in accordance.

5,6,8,9,10,11,11a,12-Octahydro-2-methoxyindolo[3,2-*b*]quinolizine(Xb)——To a suspension of 0.5 g of LAH in tetrahydrofuran (15 ml) was added dropwise a solution of 0.5 g of VIIIb in tetrahydrofuran (15 ml). The reaction mixture was stirred for 7 hr at room temperature and to this was added water to decompose an excess of LAH. The solvent was removed *in vacuo*, and the residue was shaken with ether. The residue (Xb) from the ether layer was recrystallized from methanol to give coloress needles, mp 210—211° (decomp.). Yield: 0.4 g (82%). *Anal.* Calcd. for $C_{16}H_{20}ON_2$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.98; H, 7.90; N, 10.67. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2800—2400 (-N$^+$H), 1600, 1500, 820, 795 (aromatic ring). UV $\lambda_{\max}^{\text{EtOH}}$ mμ (ε): 228.5 (27100), 282 (8400), 294 (7600).

Phenylmethano-1,1′-bis[3-(2-piperidinylmethyl)indole](XII)——To a solution of 0.2 g of IXa in N-hydrochloric acid (60 ml) was added benzaldehyde (4 ml). The mixture was kept standing 5 days under nitrogen atomsphere and shaken with ether to take off an excess of benzaldehyde. The water layer was made alkaline with 10% aqueous sodium hydroxide and then shaken with ether. The residue(XII) from the ether layer was recrystallized from ethyl acetate yielding white needles, mp 237—239°. Yield: 0.2 g (83%). *Anal.* Calcd. for $C_{35}H_{40}N_4$: C, 81.35; H, 7.80; N, 10.84. Found: C, 81.37; H, 7.86; N, 10.39. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 1600, 1495, 740 (aromatic ring). NMR (5% solution in dioxane) τ: 3.78 (2H, singlet, H at α-position of indole). Principal peaks in mass spectrum were shown in Table I.

TABLE I. The Principal Peaks in Mass Spectrum of the Compound XII

m/e	Observed	Calculated	Assignment
516	0.322	0.325	$C_{35}H_{40}N_4$ (M$^+$)
433	0.251	0.252	$C_{30}H_{31}N_3$
350	0.178	0.178	$C_{25}H_{22}N_2$
335	0.154	0.155	$C_{24}H_{19}N_2$
332	0.130	0.131	$C_{24}H_{16}N_2$
302	0.177	0.178	$C_{21}H_{22}N_2$
257	0.108	0.108	$C_{18}H_{13}N_2$
220	0.111	0.113	$C_{16}H_{14}N$
206	0.095	0.097	$C_{15}H_{12}N$
130	0.067	0.066	C_9H_8N
116	0.051	0.050	C_8H_6N

3-[2-(1-Benzoyl)piperidinylmethyl]indole(IXb)——To a solution of 0.1 g of IXa in pyridine (10 ml) was added benzoyl chloride (0.1 g) under cooling. The reaction solution was kept standing for 1.5 hr at room temperature and to this was added water and then extracted with ether. The ether layer was washed with 5% hydrochloric acid and then with aqueous sodium carbonate. The residue(IXb) from the ether layer was recrystallized from a mixed solvent of methanol and isopropylether (1:1) to give colorless needles, mp 203.5—204°. Yield: 0.14 g (95%). *Anal.* Calcd. for $C_{21}H_{22}ON_2$: C, 79.21; H, 6.96; N, 8.80. Found: C, 79.44; H, 7.02; N, 8.82. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3160 (indolic NH), 1610 (lactam), 740 (aromatic ring).

8,9,10,11,11a,12-6*H*-Hexahydro-5-acetylindolo[3,2-*b*]quinolizine(XIa)——A mixture of 351 mg of Xa, anhydrous sodium acetate (254 mg) acetic anhydride (15 ml) was refluxed for 3 hr. The reaction solution was evaporated *in vacuo*. The residue was made alkaline with sodiun carbonate and then shaken with ether. The ether layer was washed with water, desiccated, and then evaporated. The residue(XIa) was recrystallized from ethanol to give white needles, mp 129—129.5°. Yield: 324 mg (78%). *Anal.* Calcd. for $C_{17}H_{20}ON_2$: C, 76.08; H, 7.51; N, 10.44. Found: C, 75.83; H, 7.52; N, 10.69. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2760, 2730 (trans-qunclizidine), 1700 (amide), 1615, 745 (aromatic ring).

8,9,10,11,11a,12-6*H*-Hexahydro-5-acetyl-2-methoxyindolo[3,2-*b*]quinolizine(XIb)——A mixture of 1.0 g of Xb, anhydrous sodium acetate (1.0 g) and acetic anhydride (20 ml) was refluxed for 3 hr. The reaction mixture was treated in the same way as mentioned above. The residue(XIb) from the ether layer was recrystallized from ethyl acetate to give colorless needles, mp 142—143°. Yield: 650 mg (56%). *Anal.* Calcd. for $C_{18}H_{22}O_2N_2$: C, 72.45; H, 7.43; N, 9.39. Found: C, 72.21; H, 7.46; N, 9.28. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 2770, 2750 (*trans*-qunolizidine), 1680 (amide), 770 (aromatic ring).

5,6,8,9,10,11,11a,12-Octahydro-6-phenylindolo[3,2-*b*]quinolizine(XIII)——To a solution of 2.4 g of IXb in 100 ml of toluene was added dropwise 15 ml of phosphorous oxychloride and then refluxed for 3 hr. To this was added petroleum ether to deposite the gummy precipitate. The precipitate obtained by decantation was dissolved in 80% aqueous alcohol and to this solution was added sodium borohydride (2.0 g) and the solution was kept standing overnight. The solution was evaporated to dryness *in vacuo*. To the residue was added aqueous sodium hydroxide, and the solution was shaken with ethyl acetate. The residue(XIII) from the ethyl acetate layer was recrystallized from isopropylether to give pale yellow needles. mp 174—175°. Yield: 0.7 g (31%). *Anal.* Calcd. for $C_{21}H_{22}N_2$: C, 83.40; H, 7.33; N, 9.26. Found: C, 83.55; H, 7.43; N, 9.21. IR $\nu_{\max}^{\text{Nujol}}$ cm^{-1}: 3480 (indolic NH), 1490, 740 (aromatic ring), 2800, 2750 (*trans*-quinolizidine).

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