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A NOVEL INDOLE REARRANGEMENT

THE INTERCONVERSION OF 2-(3-INDOLYL)-1-[2-(1-PYRROLINYL)]INDOLES AND 2,3,5,6-TETRAHYDRO-5-(3-INDOLYL)-1H-PYRROLO-[2,1-b][1,3]-BENZODIAZEPINES

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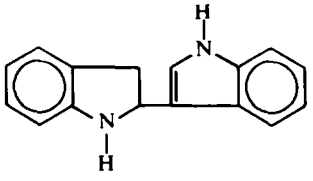
Abstract—The reaction of 2-(3-indolyl)indoline with 2-pyrrolidinone-$POCl_3$ adducts results in the formation of 2-(3-indolyl)-1-[2-(1-pyrrolinyl)]indoles (**3**) which rearrange to 2,3,5,6-tetrahydro-5-(3-indolyl)-1H-pyrrolo[2.1-b] [1,3]benzodiazepines (**4**). The structures have been determined by NMR, MS and chemical evidence. The rearrangement proceeds in a base-catalyzed equilibrium process. Structural prerequisites for the rearrangement are discussed in terms of a proposed mechanism.

IN THE course of synthetic work involving the reaction of indole dimer **1** with 2-pyrrolidinone–$POCl_3$ adduct **2a**, we isolated two different crystalline materials of the same molecular formula as that of the expected product, 2-(3-indolyl)-1-[2-(1-pyrrolinyl)]indole **3a**. During subsequent investigation of their structures we dis-



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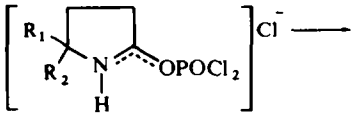
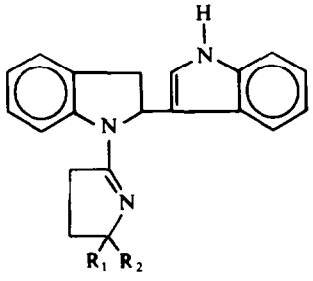


2a $R_1 = R_2 = H$
2b $R_1 = H, R_2 = CH_3$
2c $R_1 = R_2 = CH_3$



3a $R_1 = R_2 = H$
3b $R_1 = H, R_2 = CH_3$
3c $R_1 = R_2 = CH_3$

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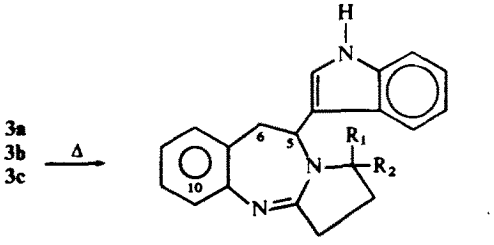
covered a novel rearrangement,* i.e., compound **3a** rearranged to 2,3,5,6-tetrahydro-5-(3-indolyl)-1H-pyrrolo[2,1-b] [1,3-]benzodiazepine **4a** on heating at 180° or on refluxing in EtOH. This paper deals with structural studies, investigation of the rate and reaction conditions of interconversion, and a proposed mechanistic rationale for the rearrangement.

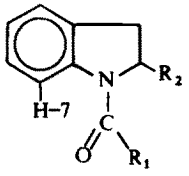


4a $R_1 = R_2 = H$
4b $R_1 = H, R_2 = CH_3$
4c $R_1 = R_2 = CH_3$

RESULTS AND DISCUSSION

Spectroscopic Studies

NMR spectra of **3a** and **4a** revealed significant differences in the δ 5·0–δ 9·0 region (Fig 1). A downfield broad doublet at δ 8·38 in the acetone-d_6 spectrum of **3a** was absent in the spectrum of **4a**. This doublet (J = 7 Hz; ortho-coupling) integrated for one proton. Deuterium exchange (D_2O) with the indole N—H did not cause collapse of the doublet to a single peak. This supported the assignment to the H-7 proton of



5a: $R_1 = CH_3$; R_2 = H
5b: R_1 = H, R_2 = β-indolyl
5c: $R_1 = CH_3$; R_2 = β-indolyl

the indoline moiety. A feature of this type has been reported[1] for the spectra of 1-acylindolines. Thus, in 1-acetylindoline **5a** the H-7 proton appears as a doublet (J = 7 Hz) at δ 8·2 ($CDCl_3$). The considerable downfield shift of the H-7 proton is due to the magnetic anisotropy of the carbonyl group. This deshielding effect on H-7 was also present in 1-acyl-2-(3-indolyl)-indolines **5b**† and **5c**.

* The referee of this paper noted that the rearrangement is related to the acid-catalyzed trimerization of indole, c.f., R. J. Sundberg, "The Chemistry of Indoles", Academic Press, New York and London, 1970, p. 8.

† 1-Formyl-2-(3-indolyl)indoline, **5b** was obtained as a by-product in some related work and will be reported later.

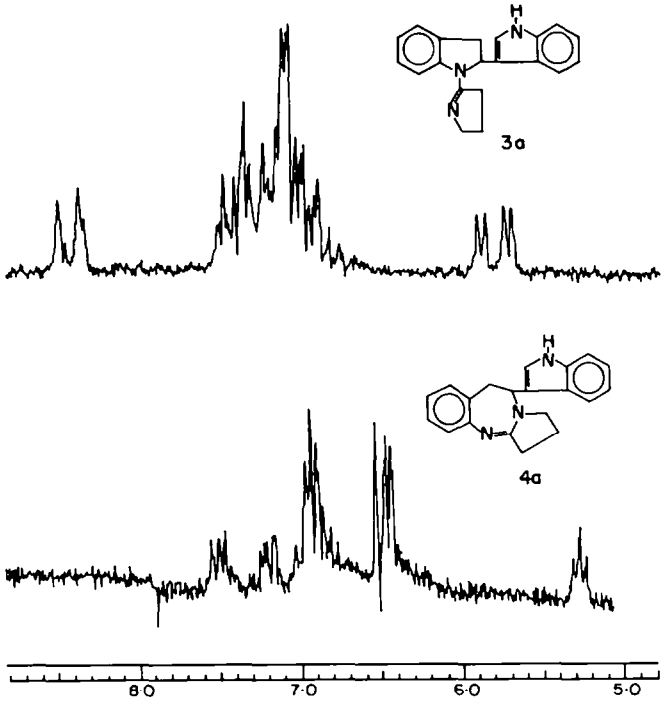
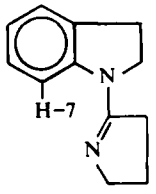


FIG 1. Downfield portion of the NMR spectra of **3a** and **4a** in acetone-d_6

Similarly, 1-(2-pyrrolinyl)-indoline **6** exhibits a doublet at δ 7·64 ($CDCl_3$). The decrease in downfield shift relative to the amides is due to the difference in magnetic anisotropy between C=O and C=N, and the lack of a buttressing group at C-2 of



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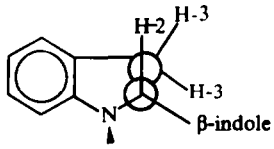
the indoline ring. The buttressing effect is demonstrable. 1-Formylindoline exhibits a doublet at δ 8·0 which integrates for only 25% of one proton. 1-Formyl-2-(3-indolyl) indoline, **5b**, however, shows a doublet at δ 8·2 accounting for nearly one proton. The magnetic anisotropic effect of the imino group can be eliminated by protonation. Thus, in the spectra of the hydrochloride salts of both **6** and **3a**, the downfield proton returns to the aromatic region (δ 7·0–δ 7·7).

A second variance is the one proton "triplet" at δ 5·30 in the spectrum of **4a** which is a doublet of doublets at δ 5·77 for **3a**. A molecular model of **3a** showed that the



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proton on C-2 of the fairly rigid indoline ring was nearly eclipsed with one of the protons on C-3 as depicted in **7**. The effect of this non-equivalence of the two C-3 protons in their interaction with the C-2 proton gives an ABX system[2] which ideally displays the H-2 pattern as a doublet of doublets. The molecular model of the more flexible diazepine structure, **4a**, formed the basis for predicting an AXX′ pattern[2] for the H-5 and H-6 protons. This pattern typically results in a "triplet" for H-5 of the diazepine structure, **4a**.

The chemical shift of the indole α-proton varies with solvent polarity[3] and concentration,[4] while that of the β-proton exhibits little change over the same polarity and concentration ranges. Accordingly, a concentration study on **3a** indicated the presence of an indole α-proton (cf. Fig 2) and the consequent establishment of a

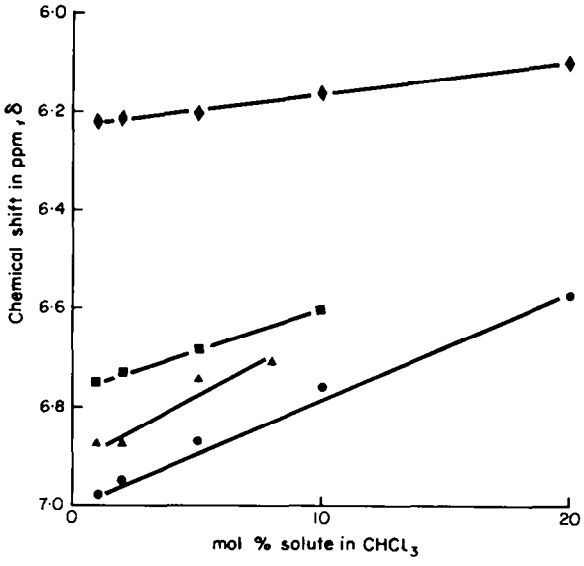
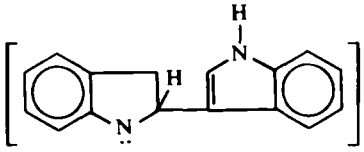


FIG 2. Concentration Dependency of Indole α or β. Proton Chemical Shift. The points are: ●, 3-methyl indole; ▲, 3a; ■, 2-(3-indolyl)indoline; ◆, 2-methylindole

3-indolyl group as part of **3a**. A similar study on **4a** could not be made due to its limited solubility even in quite polar solvents.

Mass spectra of the two products gave limited information due to the ready rearrangement of **3a** to **4a** from the heat of the electron beam or electron impact. Consequently, the fragmentation patterns of **3a** and **4a** were about the same. The differences were in the relative abundances for the same *m/e* peaks. The mass spectrum

of **3a** gave higher relative abundances for *m/e* 233 and 232 than **4a**. The *m/e* 233 fragment corresponds to the indole dimer ion **8** and loss of a hydrogen atom gives *m/e* 232.



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The pertinent data of NMR and MS of molecules **3a–c** and **4a–c** are summarized in Table 1

TABLE 1

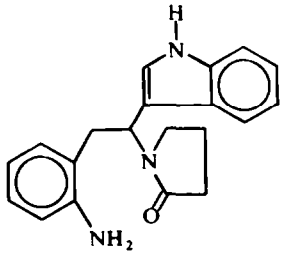
			rel abundance	
Compound	H-2	H-7	*m/e* 233	*m/e* 232
3a	doublet of doublets at δ 5·77[a]	δ 8·38	24	48
3b	doublet of doublets at δ 5·75[b]	δ 8·32	63	100
3c	doublet of doublets at δ 5·70[c]	δ 8·20	73	100
	H-5	H-10		
4a	triplet at δ 5·30[a]	δ 7·0–δ 7·7	8	11
4b	triplet at δ 5·32[b]	δ 7·0–δ 7·7	16	20
4c	triplet at δ 5·38[b]	δ 7·0–δ 7·7	9	10

[a] Acetone-d_6 as solvent [b] DMSO-6_6 as solvent [c] $CDCl_3$ as solvent

Chemical studies

Chemical studies on **3a** were inconclusive due to its facile conversion to **4a**. Base hydrolysis resulted only in conversion to **4a**. Hydrolysis under acidic conditions gave polymeric materials.

Compound **4a** was inert to nitrosation, chloranil dehydrogenation, and acid hydrolysis. Dehydrogenation of **4a** with 10% Pd/C at 240° formed a complex mixture of materials as did treatment of **4a** with $LiAlH_4$. Hydrolysis with ethanolic KOH produced a new compound **9**, which could be reconverted to **4a** by treatment with



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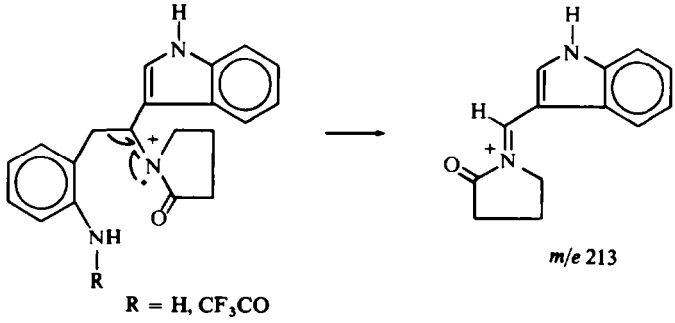
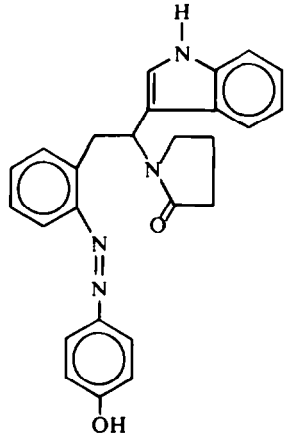
$POCl_3$. Compound **9** and its trifluoroacetyl derivative gave base peaks of *m/e* 213 in their MS.



The presence of a primary amine group in **9** was confirmed by the formation of **10** by a diazotization and coupling reaction.



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Studies of some analogs

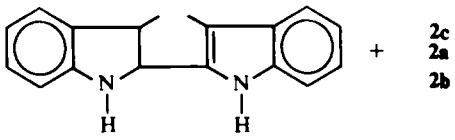
To find the limitations and scope of this rearrangement we extended our work to other formimidoyl derivatives.

Substitution of skatole dimer **11** for indole dimer in the reaction with 2-pyrrolidone–$POCl_3$ complex gave **12**. All attempts to bring about rearrangement failed.

A series of linear amidines **13** was prepared. Again, no rearrangement could be induced.

Study of the rearrangement

NMR spectroscopy is a good method for monitoring the rearrangement. We chose the rearrangement of **3b** to **4b** for our studies because **4b** has the greatest solubility among the generally insoluble diazepines. The presence of two centers of



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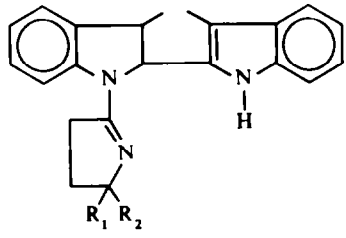
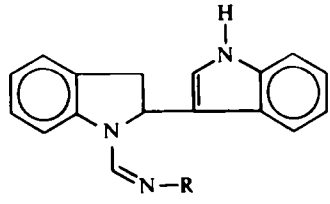


12a $R_1 = R_2 = H$
12b $R_1 = H, R_2 = CH_3$
12c $R_1 = R_2 = CH_3$

12



13
R = alkyl, cycloalkyl

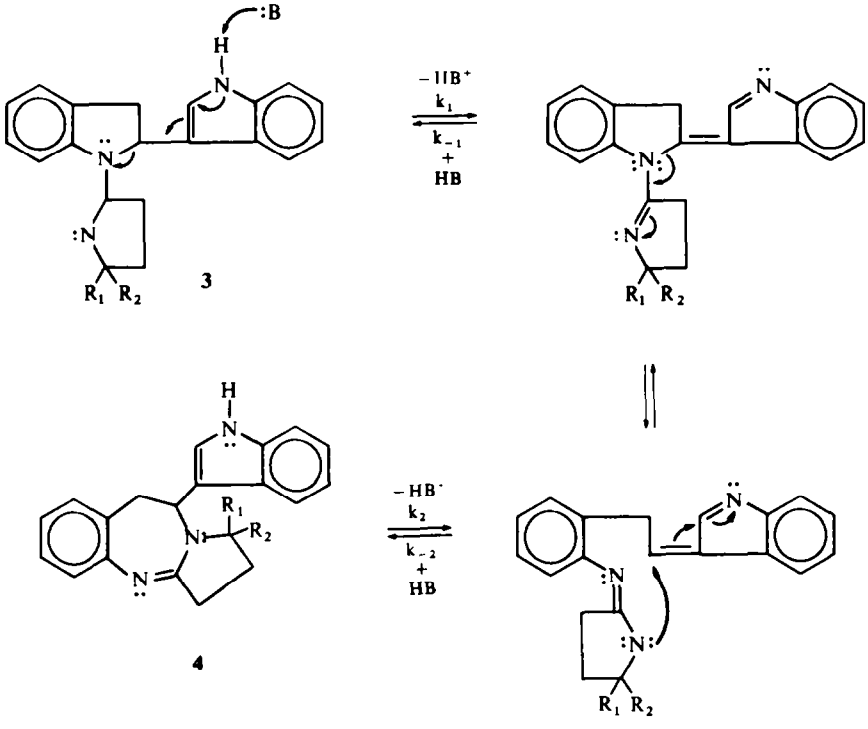
asymmetry, C-2 of the indoline ring and C-5 of the pyrroline ring, incorporates diastereoisomerism in the system to add capability for study. The CH_3 pattern of **3b** has a different chemical shift from the CH_3 pattern of **4b** which allows accurate calculation of the ratio of these species.

The results showed that the free bases rearranged in a base-catalyzed equilibrium process. This is in accord with our earlier finding that the hydrochloride salts of these amidines were inert to rearrangement. We had indeed utilized this feature for the purification of optical isomers. The equilibrium composition of 55% **3b**: 45% **4b**, can be reached by starting with either **3b** or **4b**. Base catalysis of the rearrangement was shown by an enhancement of equilibrium approach either with added pyridine–d_5 (cf. Fig 3) or with added NaOMe to DMSO–d_6 solutions of **3b**. The latter catalyst is less desirable as decomposition developed on continued reaction; consequently, only the early measurements were valid.

When these studies were performed on a sample of **3b** composed mainly of one of the two possible diastereomers,* a 50:50 mixture of the two diastereomers was formed in less than 1 hr. During this period, rearrangement had progressed less than 1%.

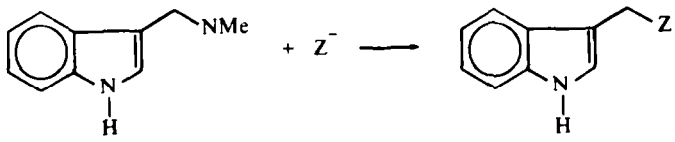
Another useful observation is the racemization of optically active **4a** in refluxing EtOH.

We propose the following mechanism on the basis of the above data:



The ring-opening steps with rate constants k_1 and k_2 are supported by the stereoisomerization of the diastereomers of **3b** and the enantiomers of **4a**. The diastereomer equilibration of **3b** during the time that rearrangement has proceeded less than 1% indicates that k_{-1} is much larger than k_{-2}. A corresponding comparison of stereoisomerization with rearrangement rate for **4** could not be made because of the insolubility of **4a** and **4c** and the exhibition of only a single CH_3 doublet in NMR spectrum of **4b**. Precedents for ths type of bond cleavage are known in the literature,[5] for example the nucleophilic replacement of the dimethylamine moiety, a poor leaving group, of gramine **15**.

* The CH_3 doublet of each diastereomer was observed in most solvents. Pure DMSO–d_6, however, caused a shift resulting in a single doublet. Due to ready interconversion, neither of the **3b** diastereomers could be isolated.



15

We propose that equilibrium favors the seven-membered ring compound because of the severe crowding in species **3**. The fact that the noncyclic amidines, **14**, lack this degree of crowding makes the relief unnecessary. Therefore, the equilibrium favors the indolylindoline structures to the exclusion of isolable amounts of rearranged products.

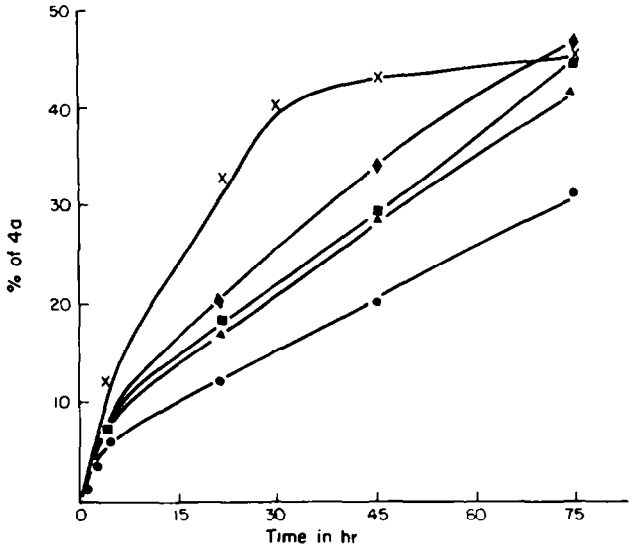
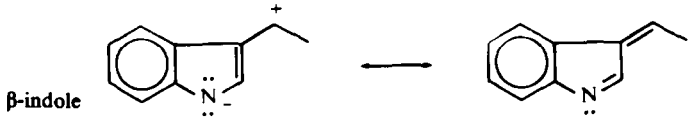


FIG 3. Rearrangement of **3a** to **4a** in DMSO–d_6 with added pyridine–d_5. ●, no pyridine; ▲, 0·1 equiv pyridine; ■, 0·5 equiv pyridine; ◆, 1·0 equiv pyridine; X, DMSO-pyridine (1 : 1)

No rearrangement has been observed for the diskatole analogs **12**. Ring-opening does not occur, and the diastereomers of **12b** are isolable and stable. According to the molecular models, the steric features of the diskatyl amidines are quite similar to those of the indolylindoline amidines. This suggests that electronic factors may be critical. Examining the pertaining valence-bond resonance forms, one expects **16b** to be more significant than **17b**.



16a **16b**

17a **17b**

To obtain a quantifying dimension, molecular orbital calculations were made. The hybrid structures **16a**, **16b** and **17a**, **17b** were suitable models for contrasting the π-electronic effects of the two ring-opened intermediates. The two model matrices were programmed.* The total π-energy parameter for each model was examined to compare the stabilizing influence of the β-indolyl and α-skatyl anions. These values indicate that the ring-opened intermediate (with its implication of the transition

Calculation	β-indolyl Eπ	α-skatyl Eπ	Δ Eπ
HMO	13·44	12·90	0·54β[a] = 9·2 kcal
ω	13·93	13·35	0·58β = 9·8 kcal

[a] β was assigned a value of 17 kcal.

state) is on the order of 9–10 kcal more stable when stabilized by the β-indolyl anion than by the α-skatyl anion.

EXPERIMENTAL

The IR spectra were obtained on KBr pellets of the sample with a Beckman IR-9 spectrophotometer. NMR spectra were taken on Varian A-60 and HA-100 spectrometers using TMS as an internal standard. MS data were obtained from a CEC 21–104 mass spectrometer at 70 ev using the direct introduction probe. The m.ps are corrected and were determined on a Thomas Hoover capillary apparatus. Elemental analyses were run on a F & M model 185 CHN Analyzer.

Rearrangement rate studies. Solutions for the rate studies were 10% (w/v) except for pyridine-d_5, 5% (w/v) solutions were also used. The sample tubes were placed in H_2O baths at 75°. The tubes were withdrawn periodically for NMR scan and returned to the bath. The shrinkage of the CH_3 pattern of **3b** and the pattern growth for **4b** were the primary features to be assayed. Since there was some pattern overlap, peak height was also measured. Auxiliary spectral features in observing the rearrangement were the shift of the indolinyl C-2 proton and the diminution of the downfield H–7 proton pattern.

2-(3-*Indolyl*)-1-[2-(1-*pyrrolinyl*)]*indoline* (**3a**). A solution of $POCl_3$ (15·3 g, 0·1 mole) in dichloroethane 50 ml was added all at once to a stirred mixture of 2-(3-indolyl)indoline† (23·4 g, 0·1 mole) and 2-pyrrolidinone (17·0 g, 0·2 mole) in dichloroethane (150 ml). After an initial exothermic phase (reaction temperature ~55°) the stirred reaction returned to 25° in 1·5 hr. The reaction mixture was cooled to 0° and stirred with ice water (80 ml). The organic layer was separated from an aqueous slurry, dried ($MgSO_4$), filtered, and concentrated to 8·6 g of a residual material which was dissolved in 1:2 MeOH-isopropyl alcohol (30 ml). Crude product as HCl salt (4·4 g, mp 203–207° (dec.)) precipitated on standing at 0°.

The aqueous slurry was filtered. The solid was stirred in dichloroethane (100 ml) at 0° and basified with

* A. Streitweiser, Jr., "Molecular Orbital Theory for Organic Chemists." John Wiley and Sons, Inc., New York, N.Y., 1961, p. 68. The actual program was obtained from C. A. Girard to whom the authors are indebted. For our calculations $H_N = 0·5$, $K_{CN} = 0·8$ and for α-skatyl $H_{C-3} = -0·5$, $K_{C-Me} = 0$.

† Indole and skatole dimerize under acidic conditions. Refer to O. Schmitz-Dumont and B. Nicolojannis, *Ber.*, **63**, 323 (1930); O. Schmitz-Dumont, K. Hamann and K. H. Geller, *Ann.*, **504**, 1 (1933); G. F. Smith, *Chem. and Ind.* (London), 1451 (1954); H. F. Hodson and G. F. Smith, *J. Chem. Soc.*, 3544 (1957); B. Oddo and G. B. Crippa, *Gazz. Chim. ital.*, **54**, 339 (1924); O. Schmitz-Dumont, *Ann.*, **514**, 267 (1934).

cold 29% NH_4OH (100 ml). The organic layer was separated and the aqueous phase extracted with additional dichloroethane (100 ml). The combined dichloroethane solutions were dried ($MgSO_4$), filtered, and concentrated to 25 ml. Skelly B (150 ml) was added, and after 15 hr at 0° 19 g of crude base, mp 124–135°, was obtained. The base was converted to its crude HCl salt (17 g). Recrystallization of combined crude HCl salts (21·4 g) from ethanol (350 ml) yielded 14·7 g (43·5%) of pure **3a** hydrochloride, mp 218–220. Calcd for $C_{20}H_{19}N_3 \cdot HCl$: C, 71·09; H, 5·97; Cl, 10·50; N, 12·44. Found: 71·05; H, 6·02; Cl, 10·49; N, 12·30%.

Pure **3a** was obtained by suspending 1 g of the salt in H_2O (100 ml) and basifying with either aq. NaOH or NH_4OH while keeping cold. Recrystallization from isopropyl ether gave a quantitative yield of **3a**: mp 159–161°; UV max (MeOH) 289 mμ (ε 11,740), 265 mμ (ε 17,850); IR (KBr) 1614 (C=N); NMR ($CDCl_3$) δ 1·87 (m, 2), 2·65 (m, 2), 3·08 (d of d, 1, J = 3·0, 16·0 Hz, Ph—CH—), 3·70 (d of d, 1, J = 9·5, 16·0 Hz, Ph—CH—), 3·81 (t, 2, N—CH_2—), 5·71 (d of d, 1, J = 3·0, 9·5, N—CH) 8·20 (broad d, 1, indoline H-7), 8·70 (broad s, 1, indole N—H); MS (70 eV) *m/e* (rel intensity) 301 (28), 233 (27), 232 (48), 41 (100). Calcd for $C_{20}H_{19}N_3$: C, 79·70; H, 6·36; N, 13·94. Found: C, 79·97; H, 6·22; N, 14·03%.

2-(3-*Indolyl*)-1-[2-(5-*methyl*-1-*pyrrolinyl*)]*indoline* (**3b**). The procedure for the preparation of **3a** was repeated using 5-methyl-2-pyrrolidinone. The reaction mixture was poured into cold concd NH_4OH (29%) (200 ml), and the organic solvent layer separated and dried ($MgSO_4$). Ten grams of crude **3b** were obtained, m.p. 173–178°. This material was converted to the HCl salt, 8·3 g (23·6%), m.p. 194·5–199·5° (dec.). Calcd for $C_{21}H_{21}N_3 \cdot HCl$: C, 71·68; H, 6·30; Cl, 10·08; N, 11·94. Found: C, 71·69; H, 6·31; Cl, 9·78; N, 11·64%.

The HCl salt was converted into the base **3b** in the same manner as for **3a**. Recrystallization from 1,2-dichloroethane gave **3b**, m.p. 176–178°; NMR (DMSO–d_6) δ 1·14 (d, 3, J = 6·2 Hz CH–CH_3), 1·7–4·0 (broad s, 7); 5·75 (d of d, 1, J = 3·5, 10·0 Hz, indoline H-2), 8·32 (broad d, 1, indoline H-7), 10·98 (broad s, 1, indole N–H); MS spectrum 70 eV) *m/e* (rel intensity) 315 (61), 233 (63), 232 (100). Calcd for $C_{21}H_{21}N_3$: C, 79·97; H, 6·71; N, 13·32. Found: C, 79·72; H, 6·69; N, 13·14%.

1-[2-(5,5-*Dimethyl*-1-*pyrrolinyl*)]-2-(3-*indolyl*)*indoline* (**3c**). The general procedure was repeated using 5,5-dimethyl-2-pyrrolidinone. Recrystallization of the HCl salt of **3c** from EtOH-Et_2O gave material melting at 260–261°. Calcd for $C_{22}H_{23}N_3 \cdot HCl$: C, 72·22; H, 6·61; N, 11·48. Found: C, 72·33; H, 6·60; N, 11·41%.

The free base was obtained by the usual conversion of the HCl salt and recrystallization from 20% aq EtOH to give **3c** (65%) m.p. 206–208°; NMR ($CDCl_3$) δ 5·7 (d of d, 1, indoline H-2), 8·2 (d of d, 1, indoline H-7); MS (70 eV) *m/e* (rel intensity) 233 (73), 232 (100). Calcd. for $C_{22}H_{23}N_3$: C, 80·21; H, 7·04; N, 12·75. Found: C, 80·45; H, 7·15; N, 12·65%.

2,3,5,6-*Tetrahydro*-5-(3-*indolyl*)-1H-*pyrrolo*[2,1-b][1,3]*benzodiazepine* (**4a**). **3a** was dissolved in a minimal amount of 80% EtOH and refluxed for several hr. Concentration and chilling caused precipitation. The solid was collected. Recrystallization from abs EtOH gave **4a** (45%), m.p. 234–236°; IR (KBr) 1590 (C=N): NMR (trifluoroacetic acid) δ 2·34 (m, 2, —CH_2—), 3·48 (t, 2, J = 8·3 Hz, —CH_2—), 3·63 (d, 2, J = 4· Hz, —CH_2—) 4·07 (t, 2, J = 7·2 Hz, —CH_2—), 5·63 (t, 1, J = 4·0 —CH) 6·68 (s, 1, —CH=), 7·1 (m, 7), 7·71 (d of d, 1), 9·48 (broad s, 1, N—H), MS (70 eV) *m/e* (rel intensity) 301 (13), 233 (8), 232 (11), 41 (100). Calcd for $C_{20}H_{19}N_3$: C, 79·70; H, 6·36; N, 13·94. Found: C, 79·80; H, 6·67; N, 13·95%.

HCl salt of **4a**, m.p. 262–264°. Calcd for $C_{20}H_{19}N_3 \cdot HCl$: C, 71·09; H, 5·97; Cl, 10·50; N, 12·44. Found: C, 71·38; H, 5·90; Cl, 10·26; N, 12·65%.

Resolution of 2,3,5,6-*Tetrahydro*-5-(3-*indolyl*)-1H-*pyrrolo*[2,1-b][1,3]-*benzodiazepine* (**4a**). An ethanolic solution of **4a** was treated with an equivalent of D-(−)-di-*p*-toluoyltartaric acid causing crystallization of salt of the (−)-enantiomer of **4a**. Repeated crystallization from EtOH gave a salt; m.p. 176·5° (dec.); $[\alpha]^{25}D$ − 118·6 (*c* 1, CH_3OH). Concentration of the combined filtrates and basification with aq NH_4OH gave **4a** enriched in the (+)-enantiomer. Treatment with L-(+)-di-*p*-toluoyltartaric acid in EtOH resulted in the crystallization of the salt of the (+)-enantiomer of **4a**; m.p. 174–175 (dec); $[\alpha]^{25}D$ 119·5 (*c* 1, CH_3OH). These salts were converted to the corresponding HCl salts by treatment with ethanolic HCl. The HCl salts of the **4a** enantiomers had the following physical properties:

HCl salt of 4a	m.p.	$[\alpha]^{25}D$ (c 1, CH_3OH)		Anal C	H	N	Cl
			Calcd.	71·09	5·97	12·44	10·50
(+)-enantiomer	251·5–253·5°	81·0	Found	71·11	5·94	12·25	10·58
(−)-enantiomer	252·5–254·5°	−80·2	Found	71·03	5·88	12·42	10·29

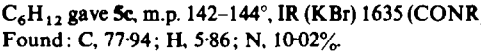
2,3,5,6-*Tetrahydro*-5-(3-*indolyl*)-3-*methyl*-1*H*-*pyrrolo*[2,1-b][1,3]*benzodiazepine* (**4b**). The procedure of **4a** was repeated using **3b**. Recrystallization from 80% aq EtOH gave **4b**, m.p. 190–192°; NMR (DMSO–d_6 δ 1·23 (d, 3, J = 6·2 Hz, —CH_3), 2·05 (m, 2, —CH_2), 2·63 (m, 2, —CH_2), 3·25 (m, 2, CH_2), 3·60 (m, 1, CH), 5·32 (t, 1, CH), 10·67 (broad s, 1, N—H), MS (70 eV) *m/e* (rel intensity 315 (61), 233 (16), 232 (20). Calcd for $C_{21}H_{21}N_3$: C, 79·97; H, 6·71; N, 13·32. Found: C, 79·80; H, 6·87; N, 12·93.

2,3,5,6-*Tetrahedro*-5-(3-*indolyl*)-3,3-*dimethyl*-1H-*pyrrolinyl*[2,1-b]-[1,3]*benzodiazepine* (**4c**). The procedure of **4a** was repeated* starting with **3c** and extending the reflux time to 42 hr. The reaction solution was concentrated to dryness and triturated in hot acetone. Crude **4c** was isolated by filtration of the cooled acetone mixture. Recrystallization from abs EtOH gave **4c**, m.p. 212·5–213·5°, NMR (DMSO–d_6) δ 1·02 (s, 3, —CH_3), 1·31 (s, 3, —CH_3), 1·88 (m, 2, —CH_2), 2·1–3·5 (broad s, 4), 5·38 (t, 1, —CH) 10·48 (broad s, 1, N—H), MS (70 eV) *m/e* (rel intensity 233 (9), 232 (10). Calcd for $C_{22}H_{23}N_2$: C, 80·21; H, 7·04; N, 12·75. Found: C, 80·20; H, 7·04; N, 12·78%.

1-*Acetyl*-2-(3-*indolyl*)*indoline* (**5c**). 2-(3-Indolyl)indoline (2·34 g, 0·01 mole) was dissolved in warm dichloroethane (25 ml) and this solution was treated with Ac_2O (1·5 ml) and refluxed briefly. Concentration gave a brown syrup which solidified in cyclohexane to an off-white solid. Recrystallization from C_6H_6–C_6H_{12} gave **5c**, m.p. 142–144°, IR (KBr) 1635 ($CONR_2$). Calcd for $C_{18}H_{16}N_2O$: C, 78·19; H, 5·84; N, 10·14. Found: C, 77·94; H, 5·86; N, 10·02%.

1-(2-*Pyrrolinyl*)*indoline* (**6**). A solution of indoline (11·9 g, 0·1 mole) and 2-pyrrolidinone (17·0 g, 0·1 mole) in dichloroethane 250 ml was treated dropwise with $POCl_3$ (15·4 g, 0·1 mole) in dichloroethane 50 ml. The reaction mixture was stirred for 15 hr, poured on crushed ice, and basified with 20% aq NaOH. The organic layer was separated and extracted with dilute HCl. The acid extract solution was again basified with 20% aq NaOH and extracted with Et_2O. The Et_2O extracts were concentrated to give crude product. Recrystallization from n-C_6H_{12} gave 16 g (86%) of **6**, m.p. 134–136°. The base was converted to the HCl salt, m.p. 265–266·5° (EtOH–Et_2O). Calcd for $C_{12}H_{14}N_2$·HCl: C, 64·71; H, 6·79; Cl, 15·92; N, 12·58. Found: C, 65·01; H, 6·87; Cl, 15·91; N, 12·31%.

3-[2-(2-*Aminophenyl*)-1-(2-*oxo*-1-*pyrrolidinyl*)*ethyl*]*indole* (**9**). A mixture of **4a** (5 g) in 95% EtOH 500 ml and 56% aq KOH 50 ml was refluxed for 12 hr. The clear yellow solution was concentrated to a residual solid which was stirred in H_2O and filtered. After being dried this white solid was stirred in warm acetone (80 ml) and filtered. The insoluble material was the recovered **4a** (usually ca 10% recovery). The acetone filtrate was concentrated to a residue which was recrystallized from EtOAc to give 2·2 g (41%) of **9**, m.p. 184·5–186·5°; IR (KBr) 3400, 3240 (NH, NH_2), 1660 ($CONR_2$); NMR ($CDCl_3$) δ 1·7 to 3·14 (8), 4·2 (broad s, 2, $ArNH_2$), 5·83 (t, 1, J = 8 Hz, C—H), 6·5 to 7·7 (9), 9·48 (broad s, 1, indole N—H), MS (40 eV) *m/e* (rel intensity) 319 (2·3), 233 (13), 214 (28), 213 (100). Calcd for $C_{20}H_{21}N_3O$: C, 75·21; H, 6·63; N, 13·16. Found: C, 75·02; H, 6·62; N, 12·94%. The trifluoroacetyl derivative of **9** was prepared, m.p. decomp from 125°; IR (Nujol) 1725 (CF_3C—N) 1620 (—CH_2—C—N).



2′-[2-(3-*Indolyl*)-2-(2-*oxo*-1-*pyrrolidinyl*)*ethyl*]-4-*hydroxyazobenzene* (**10**). Conc HCl (0·8 ml) and **9** (1·0 g, 31 mmoles) were slurried in a water–ice mixture and a solution of $NaNO_2$ (0·22 g, 31 mmoles) added. This mixture was stirred until no HONO was detected (starch–iodide paper). Phenol (0·29 g, 31 mmoles) and 40% aq NaOH (1·5 ml) were combined and added to the diazonium mixture. A golden orange solid was obtained. Recrystallization from C_6H_6-trace of MeOH gave orange colored **10**, m.p. 207–209°; IR (KBr) 3315 (N—H), 3250, br (O—H), 1660 ($CONR_2$), 1595 (—N=N—); NMR (DMSO-d_6) δ 1·8 (m, 2, CH_2), 2·5 (m, 2, CH_2), 3·3 (m, 2, CH_2), 3·8 (m, 2, CH_2), 5·8 (m, 1, CH) 6·9 and 7·9 (2d, 4, A_2B_2 pattern), 10·2 and 11·0 (2 broad s, 2, O—H and N—H). Calcd for $C_{26}H_{24}N_4O_2$: C, 73·56; H, 5·70; N, 13·20. Found: C, 73·38; H, 5·55; N, 13·12%.

3-*Methyl*-2-(3-*methyl*-2-*indolyl*)-1-[2-(1-*pyrrolinyl*)]*indoline* (**12a**). 3-Methyl-2-(3-methyl-2-indolyl)indoline (10·5 g, 0·04 mole); 2-pyrrolidinone (3·4 g, 0·04 mole); and triethylamine (4·05 g, 0·04 mole) were dissolved in dichloroethane (125 ml) and stirred while being kept at −20°. $POCl_3$ (6·14 g, 0·04 mole) dissolved in dichloroethane (25 ml) was added dropwise over a period of 45 min. The mixture was allowed to warm to room temperature during 2·5 hr, and stirred into a solution of NaOAc (35 g) in H_2O (100 ml). The pH was adjusted to 14 with KOH to separate 9·7 g (74%) of **12a**, m.p. 253–254 (dec); NMR ($CDCl_3$) δ 8·3 (d of d, 1, indoline H-7). The HCl salt of **12a** melted at 261·5–263·5°. Calcd for $C_{22}H_{17}N_2$·HCl: C, 72·21; H, 6·61; N, 11·49. Found: C, 71·97; H, 6·61; N, 11·25%. **12b** and **12c** and their HCl salts were prepared by using the same procedure with the suitable 5-substituted 2-pyrrolidinone.

* Use of n-BuOH as solvent increases the yield of **4c**

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