68.24; H, 6.87; N, 9.85; Cl, 8.06. Found: 68.28; H, 6.77; N, 9.42; Cl, 8.02.

1,2,3,4-Tetrahydro-1-(3-indolyl)-2-(5,5-dimethyl-1-pyrrolin-2-yl)isoquinoline Hydrochloride (7a). The compound was prepared from **2b** with a procedure similar to the one used for **4a**. Recrystallization from isopropyl alcohol gave a 60% yield of a pink solid, mp 281.5–283.5°. Anal. Calcd for $C_{23}H_{25}N_3 \cdot HCl$: C, 72.71; H, 6.90; N, 11.06; Cl, 9.33. Found: C, 72.60; H, 6.80; N, 10.84; Cl, 9.48.

The 1-Alkylindole Derivatives. Method A. 1,2-Dihydro-1-(1-methyl-3-indolyl)-2-(1-pyrrolin-2-yl)isoquinoline (6a). A solution of 1,2-dihydro-1-(3-indolyl)-2-(1-pyrrolin-2-yl)isoquinoline (**2c**, 4.6 g, 0.015 mol) in 110 ml of DMF (dried over molecular sieves) was first treated under a nitrogen atmosphere, with sodium hydride (57% mineral oil dispersion, 0.70 g, 0.015 mol), then stirred for 3 hr, and finally treated with a solution of iodomethane (2.1 g, 0.015 mol) in 15 ml of DMF (dried over molecular sieves). After being stirred for an additional 24 hr, the reaction mixture was filtered. The clear yellow filtrate was poured into approximately 300 ml of stirred ice water, and the resulting precipitate was filtered, dried (vacuum oven at 65°), and recrystallized from EtOAc to give 3.2 g (65% yield) of an off-white solid, mp 186–189°. Anal. Calcd for $C_{22}H_{21}N_3$: C, 80.70; H, 6.47; N, 12.83. Found: C, 80.89; H, 6.21; N, 12.71.

Method B. 1,2-Dihydro-2-(1-methyl-3-indolyl)-1-(5-methyl-1-pyrrolin-2-yl)quinoline (3a). The compound was prepared from 1-methylindole, 5-methyl-2-pyrrolidinone, and quinoline according to the procedure given for the synthesis of **1c**. Compound **3a**, purified as the free base, had mp 175–177°. Anal. Calcd for $C_{23}H_{23}N_3$: C, 80.90; H, 6.79; N, 12.31. Found: C, 80.75; H, 6.64; N, 12.48.

Acknowledgment. The authors wish to thank P. S. Schrecker and C. I. Kennedy for their contributions to structural analysis and R. E. Yeager for technical assistance. A special thanks is given to C. Combs by the authors for his invaluable aid and helpful suggestions in structural determination.

Registry No.—**1a**, 53159-51-6; **1b**, 53019-08-2; **1c**, 53019-07-1; **1d**, 53018-88-5; **1e**, 53019-04-8; **1f**, 53089-20-6; **2a**, 53018-80-7; **2b**, 53018-83-0; **2c**, 53018-81-8; **3a**, 53019-00-4; **4a**, 53159-52-7; **4b**, 53018-85-2; **5a**, 53881-35-9; **6a**, 53018-99-8; **7a**, 53089-14-8; **8a**, 53019-02-6; quinoline, 91-22-5; isoquinoline, 119-65-3; 5,6-benzoquinoline, 85-02-9; 6-methoxyquinoline, 5263-87-6; 3,4-benzoquinoline, 229-87-8; indole, 120-72-9; 5-methoxyindole, 1006-94-6; *N*-methylindole, 603-76-9; *N*-isopropylformamide, 16741-46-1; *N*-cyclohexylformamide, 766-93-8; 5,5-dimethyl-2-pyrrolidinone, 5165-28-6; 2-pyrrolidinone, 616-45-5; 5-methyl-2-pyrrolidinone, 108-27-0.

References and Notes

(1) Y. H. Wu, W. G. Lobeck, Jr., R. P. Ryan, and A. W. Gomoll, *J. Med. Chem.*, **15**, 529 (1972).
(2) R. P. Ryan, W. G. Lobeck, Jr., C. M. Combs, and Y. H. Wu, *Tetrahedron*, **12**, 2325 (1971).
(3) H. von Dobeneck and W. Goltzsche, *Chem. Ber.*, **95**, 1484 (1962).
(4) J. Bergman, *J. Heterocycl. Chem.*, **7**, 1071 (1970).
(5) This is a feature noted previously for imidoylation of the indolylindolines.[2] Increased ring size or a substituent in the 7 position of the indoline ring prevented imidoylation of the 2-(3-indolyl)indolines.
(6) A. K. Sheinkman, S. G. Potashnikova, and S. N. Baranov, *Khim. Geterotsikl. Soedin*, 1292 (1970); *Chem. Abstr.*, **74**, 125377n (1971); A. K. Sheinkman, A. N. Kost, S. G. Potashnikova, A. O. Ginzburg, and S. N. Baranov, *Khim. Geterotsikl. Soedin*, 648 (1971); *Chem. Abstr.*, **76**, 72342e (1972).
(7) Prepared by the procedures in "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N.Y., 1963, pp 357, 652.

Rearrangement of 1,2-Dihydro-2-(3-indolyl)-1-[2-(1-pyrrolinyl)]quinolines to 9-(3-Indolylvinyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolines[1]

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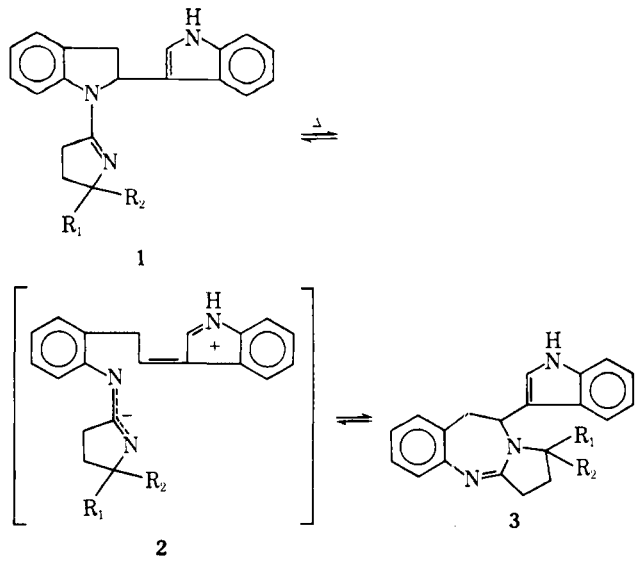
A series of 1,2-dihydro-2-(3-indolyl)-1-[2-(1-pyrrolinyl)]quinolines (**4**) undergoes a novel rearrangement to 9-(3-indolylvinyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolines (**10**). The structures of the rearranged products were assigned spectroscopically and further confirmed by a structure correlation scheme. A mechanism for the rearrangement is proposed and discussed in terms of kinetic and structural data.

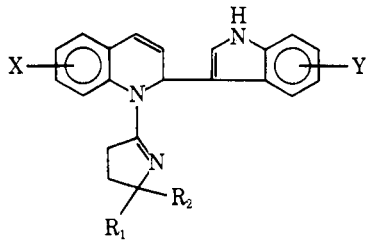
In the course of work with 1-imidoyl-2-(2- and 3-indolyl)indolines,[2a] we reported[2b] the interconversion of 2-(3-indolyl)-1-[2-(1-pyrrolinyl)]indoles, **1**, to 2,3,5,6-tetrahydro-5-(3-indolyl)-1*H*-pyrrolo-[2,1-*b*][1,3]benzodiazepines **3**. The postulated mechanism for this interconversion (Scheme I) involves a reversible ring opening to give the intermediate **2**, which undergoes ring closure after geometric isomerization. Because of the novelty of this rearrangement and a desire to determine its scope, we extended our study to the reactions of 1,2-dihydro-2-(3-indolyl)-1-[2-(1-pyrrolinyl)]quinolines **4** and -isoquinolines **5** and the corresponding tetrahydro derivatives **6** and **7**, the preparations of which are described in the Experimental Section.

Scheme I

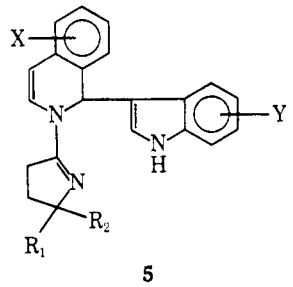


Results

Present in all of the compounds investigated was the structural fragment **8**; yet we found that only the 1,2-dihydro-2-(3-indolyl)-1-[2-(1-pyrrolinyl)]quinolines **4** underwent rearrangement. Moreover, the structures of the rearranged products were not the expected benzodiazocines **9** from analogy to the indolylindoline rearrangement, but were the stable pyrroloquinazolines, **10**.

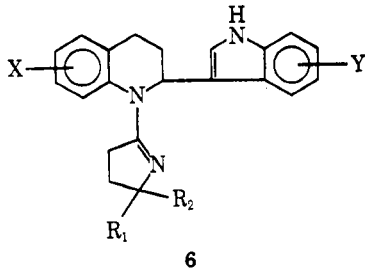


4

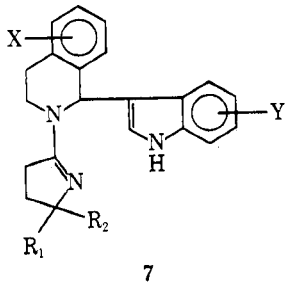


5

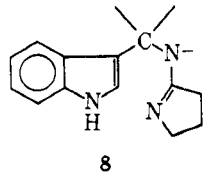
a, $R_1 = R_2 = H$; X = Y = H
b, $R_1 = H$; $R_2 = CH_3$; X = Y = H
c, $R_1 = R_2 = CH_3$; X = Y = H
d, $R_1 = R_2 = CH_3$; X = 7-OCH_3; Y = H
e, $R_1 = R_2 = CH_3$; X = 5,6-benzo; Y = H
f, $R_1 = H$; $R_2 = CH_3$; X = 7-OMe; Y = 5-OMe
g, $R_1 = R_2 = CH_3$; X = 7-OMe; Y = 5-OMe



6

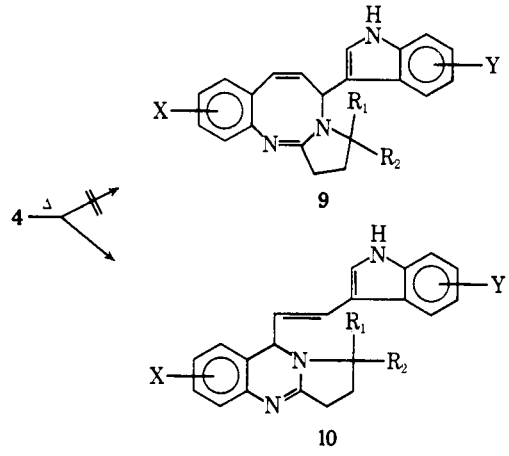


7



8

The NMR and mass spectral data were consistent with this structure assignment. The olefinic protons of the starting dihydroquinoline isomer **4** exhibited a typical cis coupling of 9.5 Hz. The olefinic protons in the rearranged product, however, exhibited a coupling constant of 15.8 Hz, more indicative of a trans double bond than the cis double bond expected in benzodiazocine **9**. The most salient piece of evidence from the mass spectrum of rearranged products was that the 100% peak for each analog corresponded to the ion left after the loss of the indolylvinyl moiety. This would correspond to a predicted fragmentation of the pyrroloquinazoline structure **10** but



9 10

a, $R_1 = R_2 = H$; X = Y = H
b, $R_1 = H$; $R_2 = CH_3$; X = Y = H
c, $R_1 = R_2 = CH_3$; X = Y = H
d, $R_1 = R_2 = CH_3$; X = 7-OCH_3; Y = H
e, $R_1 = R_2 = CH_3$; X = 7,8-benzo; Y = H
f, $R_1 = H$; $R_2 = CH_3$; X = 6-OMe; Y = 5-OMe
g, $R_1 = R_2 = CH_3$; X = 6-OMe; Y = 5-OMe

should not be so abundant in the fragmentation of the benzodiazocine **9**.

Various chemical studies were carried out with the pyrroloquinazoline structure. While treating **10** with ozone caused extensive fragmentation of the molecule, no simple cleavage products were isolated from the ozonized reaction mixture. The milder Lemieux–Johnson oxidation[4] and base hydrolysis also failed to give a meaningful structural fragment. The olefinic bond could be hydrated in acidic media under mild conditions or catalytically hydrogenated. These chemical studies failed to give any confirmatory data for structure assignment. A structure correlation scheme was therefore studied (Scheme II). In this scheme, hydrogenation converted the indolylvinyl group of **10a** to a less troublesome indolylethyl group in the correlation compound **11**. At the other end of the scheme, an indolylchalcone **12**, prepared by condensing *o*-nitroacetophenone with indole-3-carboxaldehyde, was hydrogenated to the hydroxyamino compound **13**, which was allowed to react with the 2-pyrrolidinone–$POCl_3$ adduct. Although the expected hydroxyamidine compound was not isolated, we were able to isolate and identify (TLC, ir, mass spectrum) a small amount of the correlation compound **11** from the tarry reaction mixture.[6] This scheme supported our pyrroloquinazoline structure assignment.

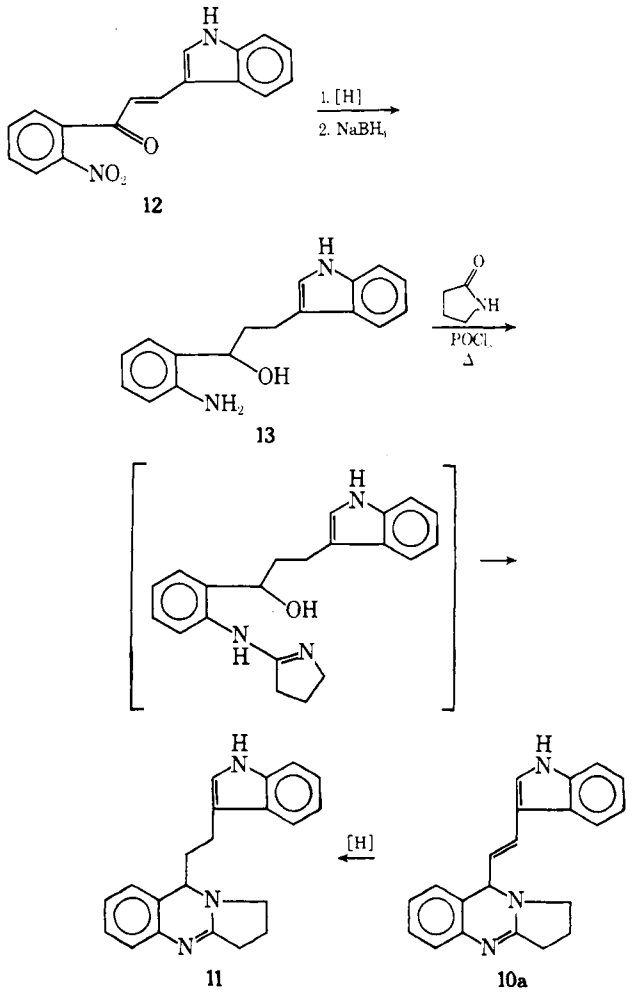
Mechanism

To begin our study of the rearrangement process, we examined the effect of substrate structure on the rearrangement. Only the dihydroquinoline class of analogs rearranged. Table I lists the structural variants which did not rearrange.

We studied the kinetics of the rearrangement with NMR using DMSO-d_6 as the solvent and 5-methylpyrrolinyl analogs as the substrates, e.g., **4b**, because they exist as pairs of diastereomers. Diastereoisomerism gives added capability for study of the reaction mechanism.

Experimentally, we found that the rearrangement is irreversible in contrast to the equilibrium process of the indolylindolines to benzodiazepines.[2b] Although the rearrangement appears to exhibit acidic as well as basic catalysis (Figure 1), the rate enhancement varies inversely with acid strength. Thus, 0.1 equiv of HCl enhanced rearrangement rate to a greater extent than did 1.0 equiv of HCl and the

Scheme II
Structure Correlation Scheme



use of trifluoroacetic acid retarded the reaction. Figure 1 shows that NH_4OAc increased the rate of rearrangement more than acetic acid.

The structural and kinetic data suggest the following

Scheme III
Rearrangement Mechanism

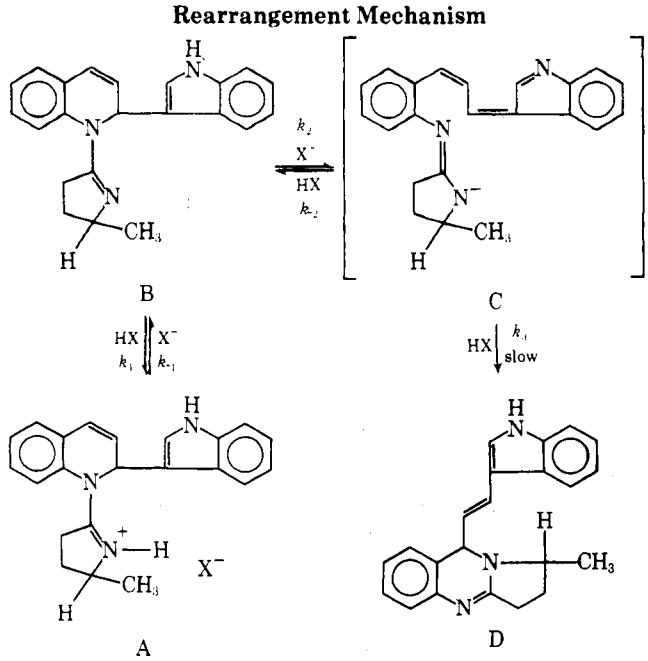
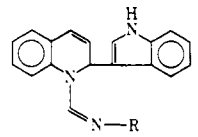
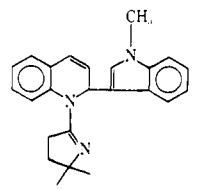
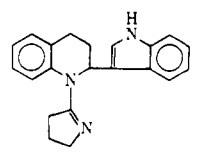
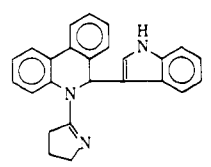
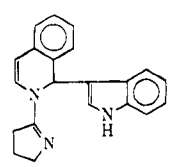
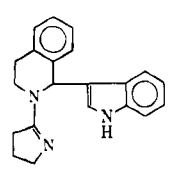


Table I
Imidoylquinolines and -isoquinolines Which Do Not Rearrange

No.	Structure	Variation
1		Linear imidoyl moiety
2		Indole N-methylation
3		1,2,3,4-Tetrahydroquinoline
4		3,4 bond incorporated into benzo ring
5		1,2-Dihydroisoquinoline
6		1,2,3,4-Tetrahydroisoquinoline

mechanism for the rearrangement (Scheme III). When the rearrangement occurs in acidic media, the dihydroquinoline isomer B can be protonated. The extent to which this occurs affects overall reaction rate by depleting the concentration of the dihydroquinoline base B, the species that undergoes ring opening to C. This is supported by the facts that (1) NH_4OAc enhances the rate more than HOAc, (2) 0.1 equiv of HCl enhances more than 1.0 equiv of HCl, and (3) 1.0 equiv of HOAc enhances more than 1.0 equiv of trifluoroacetic acid. In basic media, of course, this equilibrium can be ignored. The primary event leading to rearrangement is base abstraction of the indolic N–H to give the ring-opened intermediate C. This process, denoted by rate constant k_2, seems subject to general base catalysis. The reversibility of the ring-opening process is illustrated by the experiment using only one of the two diasteromeric pairs of **4b** (Table II). The starting dihydroquinoline diastereomer **4b-I** was completely equilibrated with the other in a time span in which only 8% of the rearranged pyrroloquinazoline was formed. The importance of proton abstraction is shown by complete inhibition of rearrangement when the indole nitrogen is methylated. This is in agreement with an earlier report[5] on related work in which indolenine formation is required for elimination of a group from the 3-indolyl α carbon.

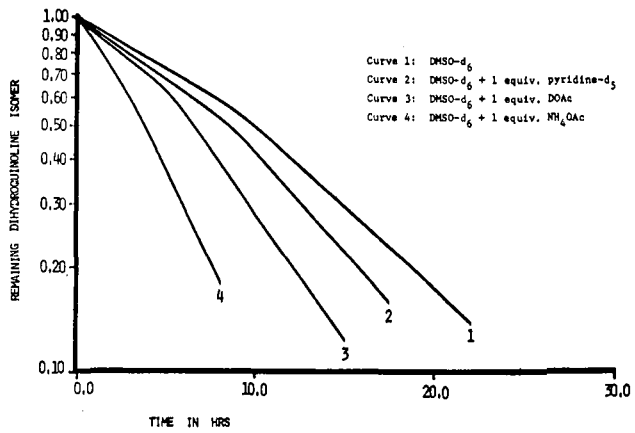
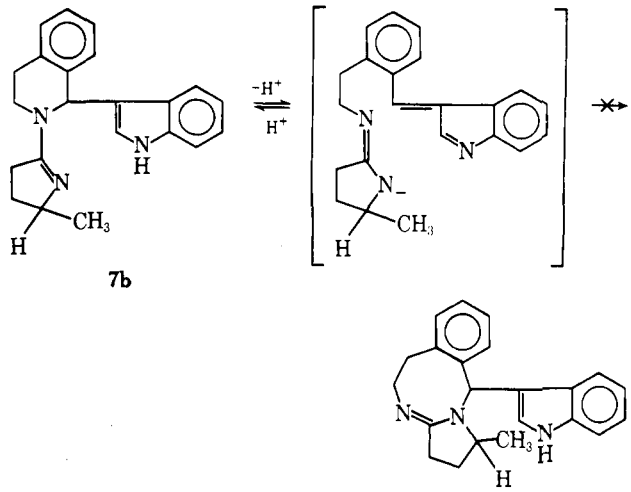


Figure 1. Remaining dihydroquinoline isomer vs. time.

Table II
Rearrangement of 4b Diastereomer I

Time, hr	4b-I, %	4b-II, %	Pyrroloquinazoline product 10b, %
0	100	0	0
1	80	20	0
7	52	40	8

Scheme IV
Isomerization of Tetrahydroisoquinoline Diastereomer



7b

Time, hr	7b-I, %	7b-II, %
0	30	70
2	40	60
4	44	56
7	48	52
15	54	46
30	54	46

Finally, ring closure to D occurs in the slow step, denoted by rate constant k_3. Only the dihydroquinolines are structurally capable of converting to the product indolylvinylpyrroloquinazolines. This class of analogs is still subject to some structural limitations. When the nucleophilicity of the attacking nitrogen in the slow step is lessened, e.g., by greater steric hindrance in linear imidoyl groups[7] (Table I, structure 1), the rearrangement does not proceed. It also fails if the attacked 3,4 double bond is part of an aromatic ring. Dihydroisoquinoline analogs do not possess the requisite structure necessary for this type of rearrangement. This applies also to the tetrahydroquinolines and tetrahydroisoquinolines. These structures could only rearrange to a benzodiazocine, the higher homolog of the indolylindoline rearrangement. No rearrangement has ever been detected in these cases, owing probably to the difficulty of formation and instability of the large ring product. According to our postulated mechanism, nothing should prevent ring opening for any particular amidine **4–7**, since they each have incorporated into their structure fragment 8. This was tested. Heating a diastereomeric mixture enriched in one diastereomer (I) of either a tetrahydroquinoline or tetrahydroisoquinoline, as shown in Scheme IV, resulted in the equilibration of the diastereomer. No rearrangement was observed even under vigorous conditions, while forcing conditions resulted in decomposition.

The fact that this rearrangement is irreversible whereas the indolylindoline–benzodiazepine interconversion is an equilibrium process is explainable in terms of a structural prerequisite for ring opening. The indolylvinylpyrroloquinazoline structure D has lost fragment 8 as a structural feature and ring opening is not favored.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary apparatus and are corrected. Ir spectra were taken on either a Beckman Model IR 8 or IR 18A. NMR spectra were from a Varian A-60 or Varian XL-100 spectrometer. The mass spectra were obtained from either a CEC 21-104 or Varian MAT 311 mass spectrometer. Satisfactory analytical data were obtained on all of the compounds but are not all inclusive in the Experimental Section. Similar experimental procedures are given only for a representative of each class.

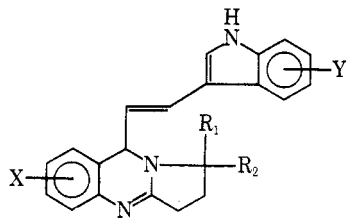
A. Pyrroloquinazoline Compounds (Table III). 1,1-Dimethyl-9-(3-indolylvinyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]benzo[*f*]quinazoline (10e). 3,4-Dihydro-4-(5,5-dimethyl-1-pyrrolin-2-yl)-3-indol-3-ylbenzo[*f*]quinoline hydrochloride[3] (**4e**, 3.0 g, 0.007 mol), 95% EtOH (250 ml), and 56% KOH solution (25 ml) were combined, stirred, and heated to reflux for 1 hr, when a white solid precipitated from the yellow solution. No starting material remained (tlc) and the reaction mixture was chilled and filtered, yielding a solid which gave 2 g (65% yield) of **10e**, mp 262–263.5° dec, upon recrystallization from EtOH.

B. Structure Correlation Compounds (Scheme II). 3-Indolylvinyl 2-Nitrophenyl Ketone (12). The procedure used was essentially that of Venturella, Bellino, and Piozzi.[8] A mixture of indole-3-carboxaldehyde (8.8 g, 0.06 mol), *o*-nitroacetophenone (10.0 g, 0.06 mol), piperidine (18 ml), and EtOH (115 ml) was refluxed for 2 hr, filtered hot, and then chilled to precipitate 10.7 g (61%, after drying at 80°) of **12**, mp 170–172°. Anal. Calcd for $C_{17}H_{12}N_2O_3$: C, 69.85; H, 4.14; N, 9.59. Found: C, 70.06; H, 4.03; N, 9.43; *m/e* 292 (M^+, $C_{17}H_{12}N_2O_3$ requires *m/e* 292).

3-[3-(2-Aminophenyl)-3-hydroxypropyl]indole (13). A solution of ketone **12** in EtOAc–HOAc was hydrogenated (50 psi) over PtO_2, filtered, concentrated, and recrystallized from isopropyl alcohol to give 3.2 g (61%) of 2′-amino-3-(3-indolyl)propiophenone, mp 165–167°. Anal. Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.52; H, 6.02; N, 10.36. A hot stirred solution of this propiophenone (6.5 g, 0.025 mol, in 400 ml of isopropyl alcohol) was first treated portionwise with $NaBH_4$ (1.5 g, 0.033 mol), then refluxed for several hours, and finally chilled. The resulting solid was stirred in 100 ml of H_2O, filtered, and dried (80°) to give 4.0 g (61%) of **13**, mp 164.5–167°. Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.62; H, 6.60; N, 10.55; *m/e* 266 (M^+, $C_{17}H_{18}N_2O$ requires *m/e* 266), 130 (100%, 3-indolyl-CH_2^+), 122 (52%, 2-NH_2^+-benzyl alcohol).

9-(3-Indolylethyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazoline (11). I. A solution of 9-(3-indolylvinyl)-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazoline (**10a**, 0.63 g, 2 mmol) in 50 ml of HOAc was hydrogenated (50 psi) over PtO_2, filtered, and concentrated to an oil. After washing with benzene, the oil was precipitated in water and recrystallized twice from isopropyl alcohol to give 0.1 g (15%) of **11**, mp 236–239°. Anal. Calcd for $C_{21}H_{21}N_3$: C, 79.96; H, 6.71; N, 13.32. Found: C, 79.98; H, 6.74; N, 13.16; *m/e* 315 (M^+, $C_{21}H_{21}N_3$ requires *m/e* 315).

Table III
9-[1-(2-Indol-3-ylvinyl)]-1,2,3,9-tetrahydropyrrolo[2,1-*b*]quinazolines



Compd	X	Y	R_1	R_2	Mp, °C	Yield, %	Molecular formula	Analysis, % Calcd	Analysis, % Found
10a	H	H	H	H	228.5–232 dec (cor)	56.0	$C_{21}H_{19}N_3$	C, 80.48; H, 6.11; N, 13.41	C, 80.44; H, 5.84; N, 13.44
10b	H	H	H	CH_3	229.5–231.5 dec (cor)	13.5	$C_{22}H_{21}N_3$	C, 80.70; H, 6.47; N, 12.83	C, 80.76; H, 6.44; N, 13.00
10c	H	H	CH_3	CH_3	270–270.5 dec (cor)	79.6	$C_{23}H_{23}N_3$	C, 80.90; H, 6.79; N, 12.31	C, 81.13; H, 6.93; N, 12.15
10d	7-MeO	H	CH_3	CH_3	237.5–238.5 dec (cor)	50.8	$C_{24}H_{25}N_3O$	C, 77.60; H, 6.78; N, 11.31	C, 77.60; H, 6.56; N, 11.37
10e	7,8-Benzo	H	CH_3	CH_3	262–263.5 dec (cor)	64.8	$C_{27}H_{25}N_3$	C, 82.83; H, 6.44; N, 10.73	C, 82.94; H, 6.33; N, 10.89
10f	6-MeO	5-MeO	CH_3	H	207.5–209.5 (cor)	2.6	$C_{24}H_{24}N_3O_2$	C, 74.39; H, 6.50; N, 10.85	C, 74.67; H, 6.60; N, 10.92
10g	6-MeO	5-MeO	CH_3	CH_3	244.5–245.5 dec (cor)	72.4	$C_{25}H_{27}N_3O_2$	C, 74.78; H, 6.78; N, 10.47	C, 74.58; H, 6.83; N, 10.49

2. A solution of $POCl_3$ (0.8 g, 5 mmol, in 5 ml of $C_2H_4Cl_2$) was trickled into a stirred solution of **13** (1.4 g, 5 mmol) and 2-pyrrolidinone (0.45 g, 5 mmol) in 25 ml of $C_2H_4Cl_2$. After the initial exotherm subsided, the mixture was refluxed for several hours. The tarry reaction mixture was basified and the organic layer was removed and concentrated to a residual foam. The foam was extracted with benzene, dilution of which with hexane gave 0.5 g of a pink solid which was vacuum sublimed and recrystallized from benzene–hexane twice to give a small amount of solid which exhibited the same tlc behavior, ir, and mass spectrum as **11** prepared above in 1.

C. Rearrangement Rate Studies. Solutions for the rate studies were generally 5% (w/v). The sample tubes were kept in 75° oil baths and withdrawn periodically for NMR scan and returned to the bath. The shrinkage of the methyl peak of **4b** and its analogs and the growth of the methyl peak of **10b** and its analogs were the primary structural features used to evaluate relative concentrations. In certain instances, the methyl peaks of each diastereomer could be seen depending upon the experimental conditions.

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Registry No.—**4a,** 53089-20-6; **4b** isomer I, 53907-00-9; **4b** isomer II, 53907-01-0; **4c,** 53089-17-1; **4d,** 53907-02-1; **4e,** 53907-03-2; **4f,** 53907-04-3; **4g,** 53907-05-4; **10a,** 53907-06-5; **10b,** 53907-07-6; **10c,** 53907-08-7; **10d,** 53907-09-8; **10e,** 53907-10-1; **10f,** 53907-11-2; **10g,** 53907-12-3; **11,** 53907-13-4; **12,** 53907-14-5; **13,** 53907-15-6; 2′-amino-3-(3-indolyl)propiophenone, 53907-16-7.

References and Notes

(1) Presented at the 166th National Meeting of the American Chemical Society, Chicago, Ill., Aug 27, 1973.
(2) (a) Y. H. Wu, W. G. Lobeck, Jr., R. P. Ryan, and A. W. Gomoll, *J. Med. Chem.*, **15,** 529 (1972). (b) R. P. Ryan, W. G. Lobeck, Jr., C. M. Combs, and Y. H. Wu, *Tetrahedron*, **12,** 2325 (1971).
(3) R. P. Ryan, R. A. Hamby, and Y. H. Wu, *J. Org. Chem.*, **40,** 724 (1975).
(4) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Wiley, New York, N.Y., 1967, pp 812–813.
(5) B. G. Gower and E. Leete, *J. Am. Chem. Soc.*, **85,** 3683 (1963).
(6) The remaining bulk of the reaction material was polymeric in nature.
(7) Examination of models demonstrated the greater accessibility of the electron pair of attacking nitrogen when alkyl substituents on the nitrogen were "tied back" in a ring; cf. E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Rinehart and Winston, New York, N.Y., 1959, p 278.
(8) P. Venturella, A. Bellino, and F. Piozzi, *Farmaco (Pavia)*, **26,** 591 (1971).