$n^{25}D$ 1.4780, *Z*, 21.7, $\lambda_{max.}$ 218 mμ, $E_{max.}$ 10,250; 2,4-dinitrophenylhydrazone, m.p. 169–169.5°; 20.8 g. of material was in the intermediate fractions and the undistillable residue amounted to 35.5 g.

(d) **2-Pentanone.**—For this dehydration 258 g. (3.0 moles) of 2-pentanone, $n^{25}D$ 1.3878, was passed over P heated to 450° to produce 19.4 g. (33%) pentenes, b.p. 30–34°, $n^{25}D$ 1.3751–1.3757, *Z*, 18; dibromopentane, b.p. 78–80° (25 mm.); and 42.2 g. of high boiling material, which gave a positive carbonyl test when treated with 2,4-dinitrophenylhydrazine reagent. The yield is based on unrecovered starting material.

(e) **Diisopropyl Ketone.**—Under the same conditions as described above for 2-pentanone, only starting material was recovered after passing 180 g. (1.5 mole) of diisopropyl ketone over P.

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Course and Kinetics of the Acid–Base-Catalyzed Rearrangements of 11-Hydroxytetrahydrocarbazolenine[1]

BY BERNHARD WITKOP AND J. B. PATRICK

11-Hydroxytetrahydrocarbazolenine (III) was prepared (a) by catalytic oxidation of tetrahydrocarbazole in ethyl acetate with platinum catalyst and subsequent gentle hydrogenation, (b) by the action of ethereal hydrogen peroxide on tetrahydrocarbazole. The compound III is remarkable for the ease with which it undergoes rearrangements under the influence of acid, base, heat, refluxing solvents and acetic anhydride. The rearrangement product in all cases was *spiro*-[cyclopentane-1,2′-ψ-indoxyl] (IV), m.p. 79°, which, in the presence of acid, easily added to III yielding Compound A, $C_{24}H_{26}N_2O_2$, m.p. 138–141°, which in turn easily lost water to give Compound B, $C_{24}H_{24}N_2O$, m.p. 227–229°; finally Compound C, $C_{24}H_{22}N_2$, m.p. 255 and 315° (dec.), was formed as a by-product in all rearrangements of III involving acid catalysis, possibly by an independent route.

The acid-catalyzed Wagner–Meerwein rearrangement leading from III to IV (and subsequently to Compounds A, B and C) was measured spectrophotometrically and found to be first order with regard to III and with respect to acid. The rearrangement of III in base, formally analogous to a benzilic acid type of reaction, was first order with respect to III and to base. Further reactions are discussed and a revision of some derivatives of tetrahydrocarbazole is given.

The investigation of the mechanism of oxidation of indole compounds[2] made it necessary to prepare a derivative of a hydroxyindolenine.[3] It was previously shown that the "11-hydroxytetrahydrocarbazolenine" of the literature[4] is in reality *spiro*-[cyclopentane-1,2′-ψ-indoxyl] (Chart II).[5,6] In this paper we describe the preparation of authentic 11-hydroxytetrahydrocarbazolenine,[7] some of its remarkable chemical features, as well as some kinetic observations.

Tetrahydrocarbazole (I) in ethyl acetate over platinum took up one mole of oxygen to yield the peroxide (II) first mentioned in the literature by Robertson, *et al.*[8] In the preparation of 11-hydroxytetrahydrocarbazolenine (III) it was unnecessary to isolate the intermediary II. After the catalytic oxidation the material was hydrogenated and one mole of hydrogen was taken up; III was obtained in beautiful crystals from ethyl acetate in 75% yield. Any other oxidation of tetrahydrocarbazole, *e.g.*, the reaction with absolute ethereal hydrogen peroxide[9] for several days gave much smaller yields (*cf.* Method B, Experimental part). The initial slow uptake of oxygen in the catalytic oxidation of tetrahydrocarbazole seemed to indicate an induction period as is frequently observed in (aut)oxidations.[10] However, this initial delay in oxygen uptake seems to be due to changes occurring at the surface of the catalyst when the freshly reduced platinum catalyst comes into contact with oxygen.[11] Indeed, a steady curve of oxygen uptake was obtained when the catalyst was shaken with oxygen before the solution of tetrahydrocarbazole was added. The well-known 1,3-relationship for indoles, or 9,11-tautomerism of tetrahydrocarbazole, encountered in so many ionic reactions, is demonstrated here in a radical type of reaction. The radical (Ia) produced from I reacts with oxygen rather in the form (Ib)[12] to give a peroxide radical intermediate which reacts with a further molecule of tetrahydrocarbazole to yield 11-hydroperoxytetrahydrocarbazolenine (II) and a new radical (Ia↔Ib). There is no reason to depart from this generally accepted picture of oxidation[13] and to assume, for instance, the formation of a four-membered peroxide ring.[8,14,15]

The structure of III was proven by gentle hydrogenation to 11-hydroxy-1,2,3,4,10,11-hexahydrocarbazole (V). The reduction of indolenines under more vigorous conditions to give dihydroindolenines is known.[16] V is only stable in the

(1) This investigation was supported by a grant-in aid from Research Corporation, New York.

(2) Witkop, THIS JOURNAL, **72**, 1428 (1950).

(3) Witkop and Patrick, *Experientia*, **6**, 183 (1950).

(4) Perkin and Plant, *J. Chem. Soc.*, **123**, 688 (1923).

(5) Witkop, THIS JOURNAL, **72**, 614 (1950).

(6) Plant and Robinson, *Nature*, **165**, 36 (1950), and (added in proof) *ibid.*, **165**, 928 (1950); *J. Chem. Soc.*, 2127 (1950).

(7) Adumbrated in a Communication to the Editor, THIS JOURNAL, **72**, 633 (1950).

(8) Beer, McGrath, Robertson and Woodier, *Nature*, **164**, 362 (1949), and (added in proof) *J. Chem. Soc.*, 2118, 3283 (1950).

(9) Criegee and Richter, *Ann.*, **522**, 94 (1936).

(10) *Cf.* Frank, *Chem. Revs.*, **46**, 156 (1950).

(11) A comprehensive account of such displacement and reorientation reactions occurring at the surface of noble metal catalysts is given by Bacaredda in Schwab, "Handbuch der Katalyse," Vol. VI, Springer, Vienna, 1943, p. 234.

(12) We are at present engaged in an investigation of nitrogenous peroxides. So far, we have not encountered a single case of an >N-O-O- type of organic peroxide. As we shall show in a subsequent paper (*cf. Experientia*, **6**, 461 (1950)) the size of the isocyclic ring C changes the nature and stability of the peroxide and the preceding radical intermediate.

(13) Farmer, Koch and Sutton, *J. Chem. Soc.*, 541 (1943); Cullis and Hinshelwood, *Discussions of the Faraday Society*, **2**, 117 (1947).

(14) Hilditch, *J. Chem. Soc.*, 1022 (1946).

(15) Hilditch, *J. Oil & Colour Chemists' Assoc.*, **30**, 1 (1947).

(16) Ciamician and Plancher, *Ber.*, **29**, 2476 (1896): sodium in ethyl or amyl alcohol Brunner, *Monatsh.*, **16**, 864 (1895); **18**, 115 (1897); zinc and acetic acid, Plancher and Ghigi, *Gazz. chim. ital.*, **59**, 339 (1929). Another method to arrive at indolines from indolenines was shown by Leuchs, Heller and Hoffmann, *Ber.*, **62**, 871 (1929).

absence of any trace of acid. With acid V forms tetrahydrocarbazole (I). Similarly a carbonium ion (VIa) was postulated in the Wagner–Meerwein rearrangement of *spiro*-[cyclopentane-1,2′-dihydroindoxyl] (VI), isomeric with V, leading also to tetrahydrocarbazole (I). Whereas in the latter case it was possible to isolate a yellow picrate stable for about two hours at room temperature, no such transitory picrate could be obtained from the isomeric V even under anhydrous conditions. Red tetrahydrocarbazole picrate resulted always, preceded by a precipitate that was yellow for a fraction of a second only. The isolation and properties of V definitely rule out the structure of a 9-hydroxy derivative for III, a possibility that had to be taken into consideration previously.[5] III with lithium aluminum hydride was quantitatively converted to tetrahydrocarbazole; apparently the intermediate V loses water to give I due to the presence of an aluminum compound acting in this case as a Lewis acid.[17]

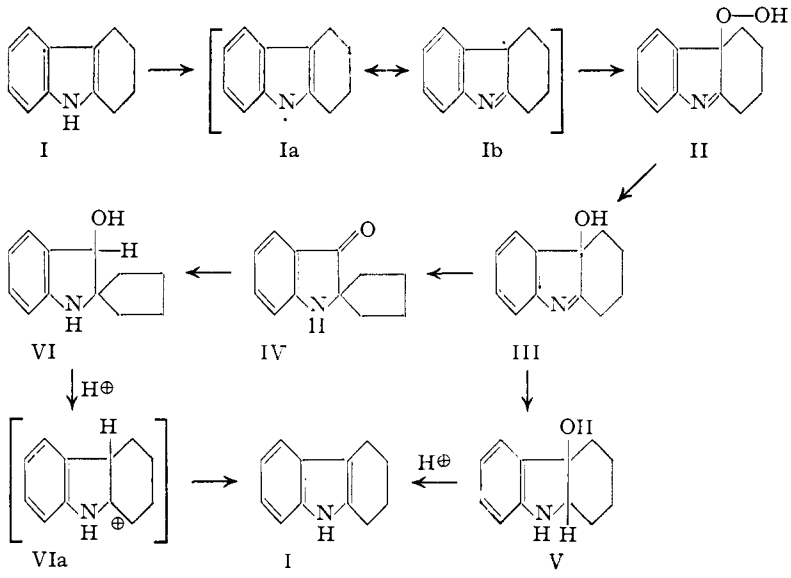
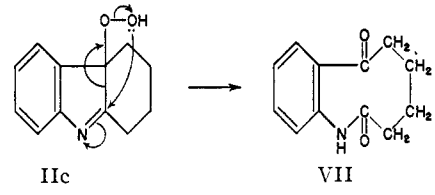


Chart I

The infrared absorption spectra of II and III (Fig. 1, A and B) provide further structural evidence. It is not possible to measure the infrared spectrum of II in chloroform solution fast enough so that the C=O bands of the lactam (VII), both at 6.0 μ, so easily formed by an acid-catalyzed peroxide rearrangement *via* IIc,[2] do not appear. 2-Isopropyl-3,3-dimethylindolenine has a comparable infrared spectrum (Fig. 1C) especially with regard to the strong and characteristic band at 6.15 μ (Ph—N=C<). Similarly the ultraviolet absorption spectrum of the latter indolenine (Fig. 2) is comparable to that of 11-hydroxytetrahydrocarbazolenine (III, Fig. 2; Table I). In the latter case one can recognize a distinct dependence of the extinction on the concentration reminiscent of the same phenomenon observed with gelsemine



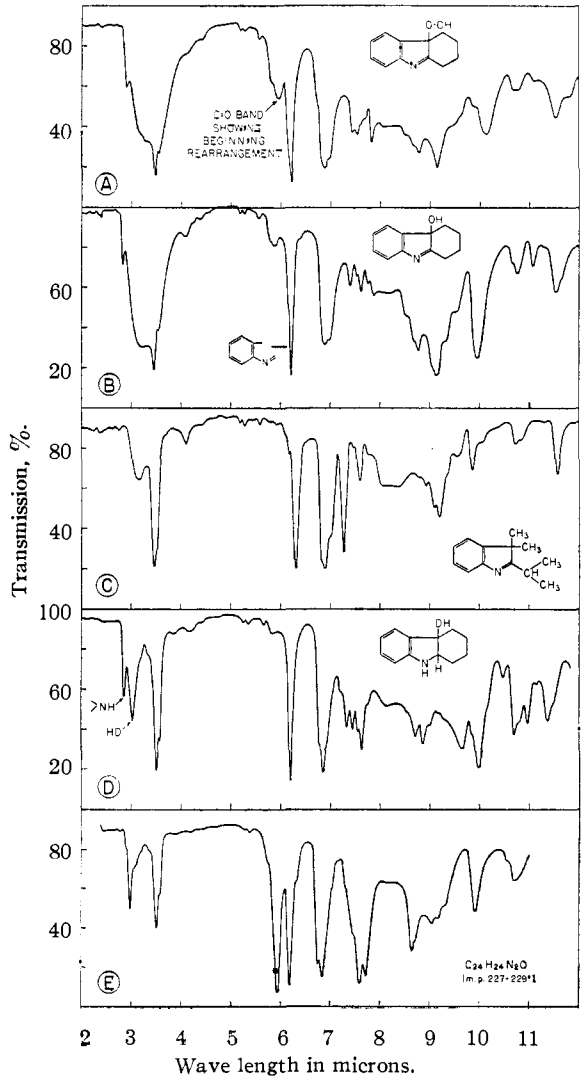


Fig. 1.—Infrared spectra in chloroform.

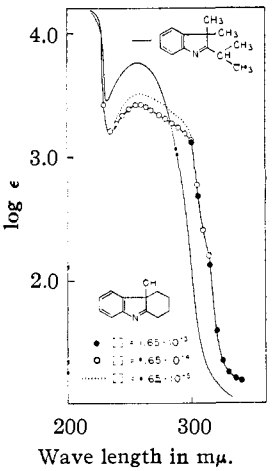


Fig. 2.—Absorption spectra of III (in ethyl alcohol).

(17) A still more striking case of lithium aluminum hydride acting as the rearranging agent in the Wagner–Meerwein shift of an intermediary carbinol was reported previously (Witkop and Patrick, THIS JOURNAL, **73**, 713 (1951)).

and C-curarine-I.[18] The infrared spectrum of hydroxyhexahydrocarbazole (V, Fig. 1D) shows clearly the presence of the hydroxyl and imino bands.

TABLE I

Compound	λMax. mμ	(log ε)	λMin. mμ	(log ε)
11-Hydroxytetrahydrocarbazolenine (III)	260	(3.421)	235	(3.213)
11-Hydroxytetrahydrocarbazolenine (III) after 24 hours + H⁺	392	(1.904)	360	(1.509)
	402	(1.916)	398	(1.812)
	412	(2.114)	404	(1.897)
2-Isopropyl-3,3-dimethylindolenine	258	(3.770)	235	(3.499)
$C_{24}H_{22}N_2$, m.p. 255 (315°) ("Dihydrocarbazole")	290	(4.086)	262	(3.848)
	[355	(2.897)	350	(2.622)]
	[395	(2.505)	375	(2.410)]
$C_{24}H_{24}N_2O$, m.p. 227–220° (Compound B)	225	(4.598)	245	(4.252)
	270	(4.066)	335	(2.483)
	420	(3.670)		
spiro-[Cyclopentane-1,2′-*pseudo*indoxyl] (IV)	235	(4.276)	285	(2.316)
	400	(3.566)		
spiro-[Cyclopentane-1,2′-dihydro-ψ-indoxyl] (VI)	230	(4.040)	240	(3.778)
	249	(3.851)	275	(3.209)
	292	(3.309)		

The ultraviolet spectrum of the isomeric *spiro*-[cyclopentane-1,2′-dihydroindoxyl] (VI) does not differ sufficiently from that of tetrahydrocarbazole so that one could follow the Wagner–Meerwein rearrangement from the former into the latter spectroscopically. The spectrum of the yellow *spiro*-[cyclopentane-1,2′-ψ-indoxy] (IV, Fig. 3) is markedly different from that of its colorless precursor (III). This difference prompted us to follow the acid- and base-catalyzed rearrangements of III into IV spectrophotometrically.

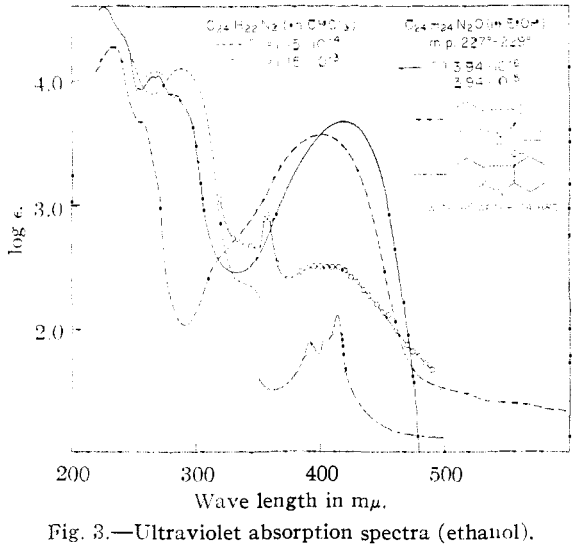


Fig. 3.—Ultraviolet absorption spectra (ethanol).

The Acid-Catalyzed Rearrangements of 11-Hydroxytetrahydrocarbazolenine.—11-Hydroxytetrahydrocarbazolenine could not be recrystallized from alcohol, only from ethyl acetate; likewise, the alcoholic solution used for the determination of the ultraviolet spectrum (Fig. 3) became yellow on standing, a process which could be accelerated by the addition of a drop of alcoholic mineral acid. Such a solution after 24 hours showed three new absorption bands (Fig. 3, Table I). These bands belong to the indoxylic chromophore of spirocyclopentane-1,2′-ψ-indoxyl (Fig. 3; Table I). However, the spirane (IV) is not isolated from such solutions. Instead, under carefully controlled conditions, a compound A, $C_{24}H_{26}N_2O_2$, m.p. 138–141°, is obtained for which we suggest the expression (XIII). The same addition compound can be prepared by letting equimolar quantities of the spirane IV react with III in slightly acidic alcoholic solution, whereupon the low melting spirane IV is entirely consumed. Two further reactions exhibit the great reactivity of the >C=N—bond present in III, *viz.*, the unexpected diazotizability and the ready acid-catalyzed dimerization with loss of water. The diazotization reaction originally prompted Plant and Tomlinson[19,20] to consider III as 10-hydroxy-1,2,3,10-tetrahydrocarbazole (Chart II) and to formulate the diazotizable amine as XIV. We

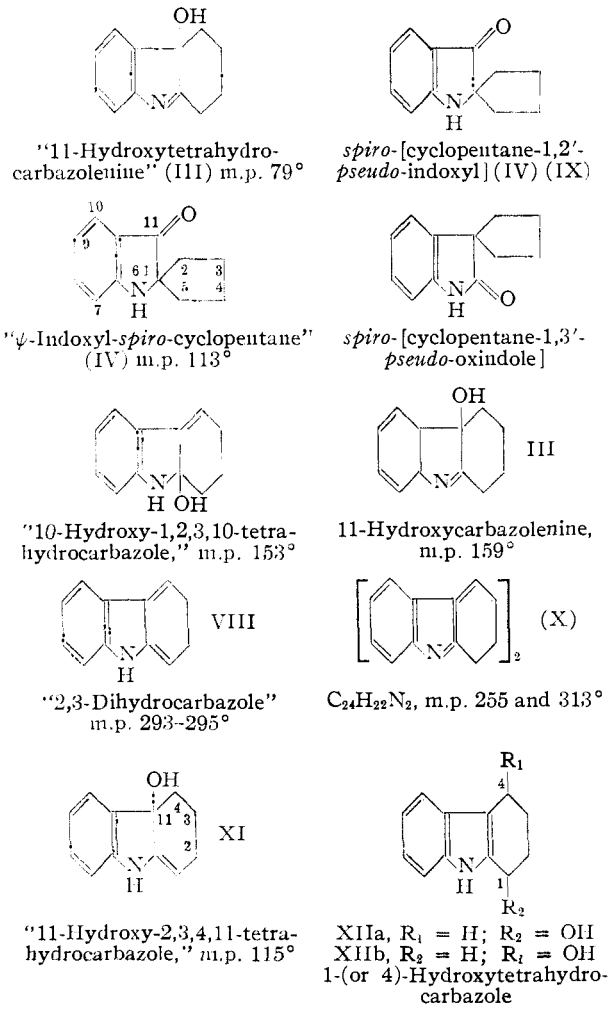


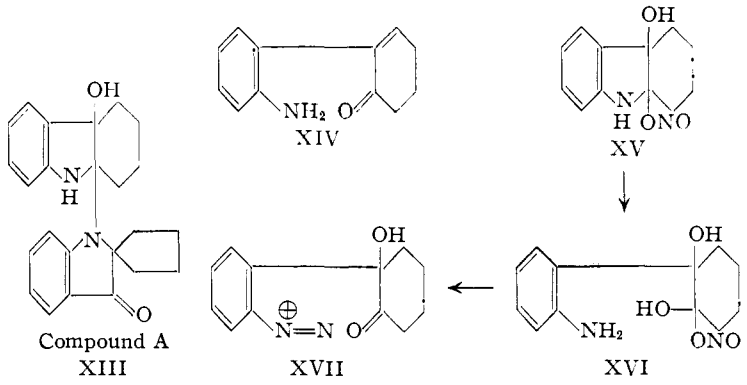
Chart II.—Revisions in the tetrahydrocarbazole series.

(18) Witkop, FIAT Review, 1939-1946, Biochemistry, Part II, 207 (1948); *C. A.*, **43**, 3888 (1949).

(19) Plant and Tomlinson, *J. Chem. Soc.*, 298 (1933).

(20) Plant and Tomlinson, *ibid.*, 3324 (1931).

regard the first step in the diazotization reaction as an addition of nitrous acid to III, leading *via* the intermediates XV and XVI to the diazonium salt XVII. Normal indolenines do not show this reaction. This diazotization test of β-hydroxyindolenines is very important in connection with similarly constituted natural products. Apart from compound A (XIII) another indoxyl derivative B, $C_{24}H_{24}ON_2$, m.p. 229° (Figs. 1E, 3), was



isolated on treatment of III with various reagents (Table II). B contains one molecule of water less than compound A. Whether B results from a simple dehydration of A or whether this process is accompanied by rearrangement has not been ascertained yet. Compound C was obtained as a

TABLE II

THE TRANSFORMATION PRODUCTS OF 11-HYDROXYTETRAHYDROCARBAZOLENINE UNDER THE ACTION OF HEAT, ALKALI, ACID OR ACETIC ANHYDRIDE

11-hydroxytetrahydrocarbazolenine (III) $C_{12}H_{13}NO$, m.p. 159°

HO⊖, EtOH, Heat, H⊕, Ac_2O

spiro-[cyclopentane-1,2'-ψ-indoxyl] (IV) m.p. 79°

H⊕ or EtOH + III

Heat (160°) + III

$C_{24}H_{26}N_2O_2$ (XIII) m.p. 138–141° (Compound A)

H^+ or Ac_2O

$C_{24}H_{24}N_2O$ m.p. 229° (Compound B)

H^+, Ac_2O

$C_{24}H_{22}N_2$ m.p. 255° (315°) (Compound C)

H⊕ (air)

yellowish needles m.p. 210° (deep depression on mixing with Compound B)

by-product in the reaction of III with acid, boiling ethyl alcohol or acetic anhydride (Table II). This substance has been obtained before and named "dihydrocarbazole" (VIII).[19] Actually, it is a dimeric compound $C_{24}H_{22}N_2$, as indicated by its moderate solubility in organic solvents, comparison with the isomeric dihydrocarbazole (XIX)[21] and by a determination of the molecular weight (Rast). The situation in the literature is further confused by the description of a compound named "11-hydroxy-2,3,4,11-tetrahydrocarbazole"[20] (Chart II, XI). This compound is probably 1-(or 4)-hydroxytetrahydrocarbazole (Chart II, XIIa or b).[22] In attempts to repeat the preparation of XIIa (or XIIb) we obtained a new compound $C_{19}H_{15}NO_2$, m.p. 248°, containing two hydrogen atoms less than the benzoyl derivative of XII.

The infrared absorption spectrum of compound C in nujol and in chloroform (Fig. 4) does not show the presence of the characteristic indole-imino bands (2.9μ). The dimerization, therefore, is not likely to have proceeded by a Diels–Alder type of reaction from the hypothetical dienic anhydro indolenine monomer. The reaction is apparently analogous to the dimerization of indolenines occurring on prolonged standing[23,24] or on the catalytic action of Grignard reagent.[25] Compound C is stable to catalytic hydrogenation and has no basic properties.[26]

The ultraviolet spectrum of the compound C is shown in Fig. 3. Here also, as in the case of (III), the spectrum changes in chloroform solution (Table I, figures in parentheses) especially in the presence of acid. A yellow compound m.p. 210° could be isolated from such solutions. The paucity of the material did not allow of further investigation. The compound was not identical with compound B.[27] Table II summarizes these facts and interrelationships.

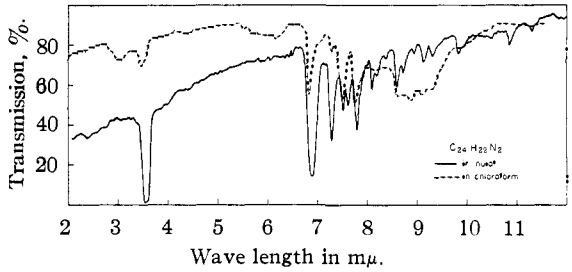


Fig. 4.—Infrared spectrum of anhydroindolenine dimer (X) in nujol and chloroform.

(21) Schmidt and Schall, *Ber.*, **40**, 3227 (1907), give m.p. 229°.

(22) The formation of XIIa or b is in analogy with the formation of 2-hydroxymethyl-3-methylindole from 1-acetyl-2,3-dimethylindole with bromine in acetic acid, Plant and Tomlinson, *J. Chem. Soc.*, 955 (1933); Taylor, *Helv. Chim. Acta*, **33**, 164 (1950).

(23) Plancher and Bonaviva, *Gazz. chim. ital.*, **32**, 11, 422 (1902).

(24) Trimerization is observed with α-unsubstituted indolenines, Brunner, *Monatsh.*, **16**, 854 (1895); Grgin, *ibid.*, **27**, 731 (1906). Whether these trimers are *sym*-triazine derivatives has not been established yet; *cf.* the trimerization of Δ¹-piperideine, Schöpf, *et al.*, *Ann.*, **559**, 1 (1947).

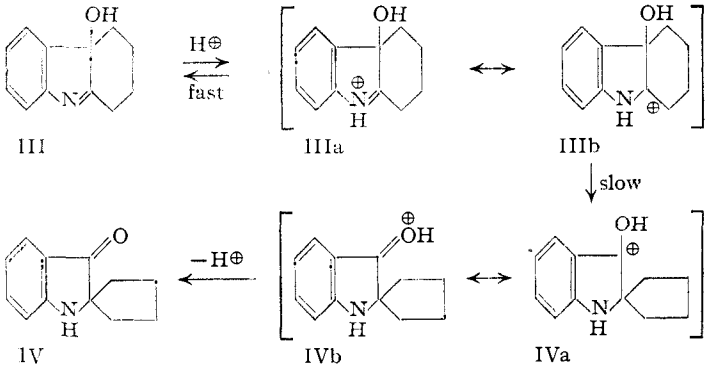
(25) Plancher and Ravenna, *Atti Reali accad. Lincei*, [5] **15**, **11**, 555 (1906); *Chem. Zentr.*, **78**, 1, 107 (1907).

(26) It may be possible that the principle underlying these indolenine dimerizations governs also the formation of dicarbanil [Esafov, *J. Gen. Chem. (U. S. S. R.)*, **14**, 299 (1944); *C. A.*, **39**, 3787 (1945)], of the dimeric indoxylred [Seidel, *Ber.*, **77**, 790 (1944)], of the compound $C_{14}H_{12}N_2$ from indole and sulfur [Madelung and Tencer, *ibid.*, **48**, 953 (1915)], and possibly also the formation of calycanine from calycanthine [Marion and Manske, *Can. J. Research*, **16B**, 432 (1938)].

(27) The strong indolic NH-band (Fig. 2E) of compound B rules out a simple relationship with compound C. For this reason we have not attempted to reduce the indoxyl derivative with lithium aluminum hydride and rearrange it by the action of acid, a route we used before in the structural elucidation of indoxyl derivatives [Witkop and Patrick, THIS JOURNAL, **73**, 713 (1951)].

Kinetic Studies.—11-Hydroxytetrahydrocarbazolenine (III) offers the rare case of a colorless compound rearranging by the action of acid or base to the same primary yellow product. Although, as discussed above, the spirane IV formed by acid catalysis will react further with III to give a mixture of compounds A and B, we have nonetheless obtained some kinetic information on these interesting rearrangements. The rates of the transformations were determined spectrophotometrically using a Beckman quartz spectrophotometer with a thermostated cell holder.

Acid Catalysis.—Solutions of 11-hydroxytetrahydrocarbazolenine and *p*-toluenesulfonic acid in absolute alcohol were thermostated at 30° and pipetted into a small flask, mixed and transferred to a spectrophotometer cell. Optical density readings were taken at 400 mμ (see Fig. 3) using ethanol as a standard. Readings were taken at one-half to five minute intervals (more frequently at the beginning of the run) for a period of 10 to 30 minutes. Zero time was taken as the time of mixing the solutions. The optical densities were plotted as a function of time and the initial slope of the curves determined. These slopes were converted to the change in concentration of *spiro*-[cyclopentane-1,2′-ψ-indoxyl] (IV) with time by using the known molar extinction coefficient of the spirane at 400 mμ (Fig. 3). For runs involving high excess of acid this value for the initial rate of formation of spirane was divided by the initial concentration of 11-hydroxytetrahydrocarbazolenine (III) to obtain the unimolecular rate constants (Table III, runs 1–4). The average of four values for the rate constant obtained in this fashion is 9.5×10^{-3} min.$^{-1}$ with an average deviation of 0.8×10^{-3}. For runs involving comparable concentrations of 11-hydroxytetrahydrocarbazolenine and of acid, the bimolecular rate constants were obtained by dividing the initial rate of spirane formation by the product of the concentrations of III and of acid (Table III, runs 5–11). Since the rearrangement is followed by secondary reactions, it was impossible to determine the rate constant for the formation of IV by the usual plot of logarithm of concentration of III *versus* time.



Evaluation.—By confining the kinetic measurements to the first few minutes of the reaction the percentage of rearrangement observed is small and the effect of the secondary reactions is thus minimized. Furthermore, the absorption maxima of IV, as well as compounds A and B, are close enough to eliminate errors from this source. When the acid concentration was comparable to the concentration of III, variations in the acidity produced changes in the rate of rearrangement which became proportionately greater, approaching first order behavior, as the relative acid concentration was reduced. Table III shows that an increase in relative acid concentration from *e.g.*, one-fourth to one-half of the concentration of III, increases the value of the initial slope from 0.14×10^{-3} to 0.26×10^{-3}, and that the bimolecular rate constant approaches a value of approximately 6×10^{-2} l./mole × min., as the relative acidity is reduced at an ionic strength of 3.2×10^{-3} *M*. A possible

TABLE III

THE REARRANGEMENT OF 11-HYDROXYTETRAHYDROCARBAZOLENINE WITH *p*-TOLUENESULFONIC ACID IN ETHYL ALCOHOL AT 30°[a]

Run	[III] × 10^3	[HTs] × 10^3	(dD/dt) × 10^2	$\left[\frac{(d[III]/dt)_0}{[III]_0}\right]$ × 10^3	$\left[\frac{(d[III]/dt)_0}{[III]_0[HTs]}\right]$ × 10^2
1	0.48	33	19	10.8	
2	0.96	33	32	9.1	
3	0.48	66	15	8.5	
4	0.56	167	21	10.2	
5[b,d]	1.61	1.60	0.48		5.1
6[b,d]	1.61	0.80	0.26		5.5
7[b,d]	1.61	0.40	0.14		5.9
8[b,d]	1.61	3.20	0.64		3.4
9	1.61	1.60	0.48		5.1
10	1.61	0.80	0.28		6.0
11	1.61	0.40	0.16		6.8
12[c]	1.61	0	0	0	

[a] All concentrations are molar. [b] Sufficient lithium *p*-toluenesulfonate added to bring the ionic strength to 3.20×10^{-3} *M*. [c] Run was 1.60×10^{-3} *M* in lithium *p*-toluenesulfonate. [d] Plotted in Fig. 5.

mechanism in agreement with the kinetic data is shown below. The combination of III with a proton to give the resonance hybrid IIIA ↔ IIIB is presumably an equilibrium, so that, in the presence of large excess acid, when III is entirely converted to its conjugate acid, the rearrangement becomes *pseudo* first order, apparently depending solely on the concentration of III. The subsequent rearrangement, followed by release of a proton, is the rate-determining step.

The effect of added salt (lithium *p*-toluenesulfonate) is small and negative. To minimize salt effects some runs (Fig. 5) were made at constant ionic strength. The results of comparable runs without this precaution approach first-order kinetics more slowly. While better accordance with first-order kinetics could be expected in runs utilizing still lower relative acid concentrations, in practice the reaction under such conditions soon becomes too slow for convenient measurement.

The values of the initial slopes (Table III, column 4) were determined by two different methods: The less accurate procedure involved

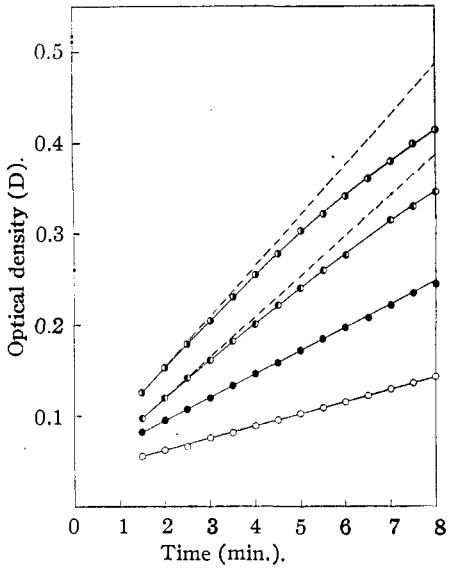


Fig. 5.—Acid-catalyzed rearrangement of 11-hydroxytetrahydrocarbazolenine at constant ionic strength.

drawing of the origin tangent to the curve of optical density *versus* time. Where the quality of the data seemed to justify it, the consecutive increments in optical density were plotted as a function of time in minutes and the resulting best straight line extrapolated to zero time. As the concentration of IV increases, the formation of compounds A and B becomes significant; no kinetic study was made of this reaction.

Base Catalysis.—Analogous rate runs at 40° with sodium ethoxide indicated a similar situation with regard to basic catalysis (Table IV). Under the conditions employed the rearrangement to the spirane was again incomplete, so the method of initial slopes had to be used. However, under basic conditions the spirane after formation does not undergo secondary addition reactions as with acid catalysis. Since the base-catalyzed reaction is too slow to be measured conveniently under the conditions of temperature and concentration used in the acid runs, higher temperature (40°) and concentration were employed. Consequently the rate of purely thermal rearrangement, which had been negligible in the acid runs (Table III, run 12), became significant. The rate of increase of optical density due to thermal rearrangement was deducted from the initial slopes of the density–time curves, and the resulting corrected values were then converted to the bimolecular rate constants by the same method used for the acid-catalyzed runs. For runs at a constant ionic strength of 48 × 10^{-3} *M* with comparable concentrations of III and of base (Fig. 6, Table IV, runs 9–12) the bimolecular rate constant was 11.4 × 10^{-3} with an average deviation of 11%.

Employment of a large excess of base (Table IV, runs 1–6) tends to depress the value for the bimolecular rate constant, but even a 235-fold excess does not make the reaction kinetically first-order.

Runs at constant ionic strength (Fig. 6, Table IV, runs 8–11) were slower than corresponding runs without added salt

TABLE IV

THE REARRANGEMENT OF 11-HYDROXYTETRAHYDROCARBAZOLENINE WITH SODIUM ETHOXIDE IN ETHYL ALCOHOL AT 40°[a]

Run no.	[111] × 10^3	[NaOEt] × 10^3	$(dD/dt)_0$ × 10^3	$\left[\frac{(d[111]/dt)_0}{[111]_0[NaOEt]^b}\right]$ × 10^3
1	2.2	250	15	7.1
2	2.13	250	15	7.3
3	2.13	500	20	5.0
4	4.26	250	30	7.3
5[d]	5.25	125	27.4	10.2
6	5.25	250	38.8	7.7
7[d]	5.25	0	2.5	..
8[c,e,f]	12.00	3.0	4.75	2.8
9[e,f]	12.00	6.0	7.45	11.1
10[e,f]	12.00	12.0	9.25	9.0
11[e,f]	12.00	24.0	16.7	11.8
12[e,f]	12.00	48.0	32.8	13.5
13	12.00	3.0	6.54	16.7
14	12.00	6.0	8.29	15.2
15	12.00	12.0	14.0	18.0
16	12.00	24.0	20.9	15.6
17	12.89	0	4.4	..
18	1.63	0	0.5	..

[a] All concentrations are molar. [b] Corrected for thermal rate. [c] Run 8 is of limited value, since the uncorrected value for the initial rate is of nearly the same magnitude as the rate of the thermal reaction. [d] Sufficient sodium iodide added to bring the ionic strength to 250 × 10^{-3} *M*. [e] Sufficient sodium iodide added to bring the ionic strength to 48.0 × 10^{-3} *M*. [f] Plotted in Fig. 6.

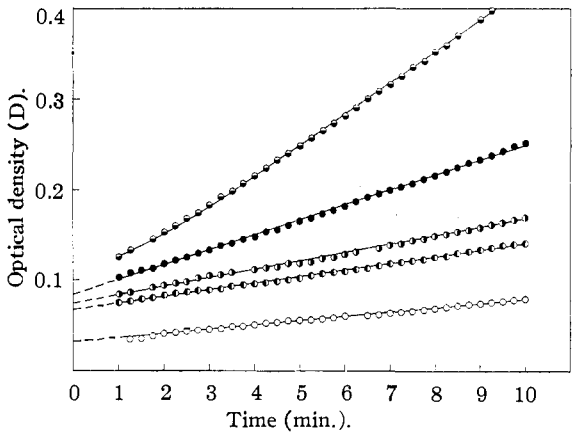
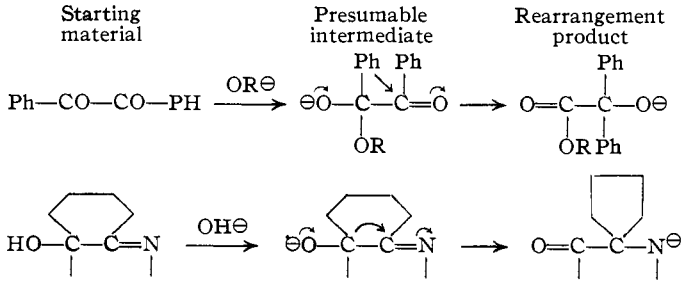


Fig. 6.—Base-catalyzed rearrangement of III at constant ionic strength.

(Table IV, runs 13–16), indicating a small negative salt effect. The bimolecular rate constants obtained from runs of varying ionic strengths were erratic.

Evaluation.—The rearrangement is first order



with regard to III and with respect to base. It is formally a benzilic acid type of shift.[28]

The benzilic acid end product derives its stabilization and irreversibility of the reaction[29] from the resonance energy of the carboxyl group. In the case of the spirane (IV) the gain in energy comes from the resonance of the conjugated lactam system O=C—C=C—NH—. We reported previously[3] on the reversion of this reaction under the action of Grignard reagent on IV; there a unique rearrangement involving a twofold 1,2-shift occurs.

Thermal Rearrangement.—The kinetic data for the thermal rearrangement of III at 40° are presented in Table V. The reaction is approximately kinetically first-order (Table V, column 4) with respect to III.

TABLE V

THERMAL REARRANGEMENT OF 11-HYDROXYTETRAHYDROCARBAZOLENINE IN ETHYL ALCOHOL AT 40°

Run	$[III] \times 10^3$	$(dD/dt)_0 \times 10^3$	$(d[III]/dt)_0/[III]_0 \times 10^4$	$(d[III]/dt)_0/[III]_0^2 \times 10^2$
7	5.25	2.5	1.3	2.5
17	12.89	4.4	0.93	0.7
18	1.63	0.5	0.86	5.3
			Av.	1.03 ±0.18

Experimental[30]

11-Hydroxytetrahydrocarbazolenine (III) A. Catalytic Oxidation Method.—Tetrahydrocarbazole (1.0 g., 5.4 millimoles) in 10 ml. of ethyl acetate containing 200 mg. of reduced platinum catalyst[31] was stirred under oxygen for four hours. Care was taken that no catalyst was splashed up onto the walls of the flask, since it was found that explosive oxidation of the mixture was likely to result, particularly during the first five minutes. The net uptake was 110 cc. (calcd. 121 cc.) of oxygen. The stirring was stopped, the system evacuated, and the oxygen replaced by hydrogen. Stirring was resumed; the initial uptake was so rapid that external cooling was occasionally necessary. After 35 minutes the rate of gas absorption had slowed up considerably; 110 cc. had been taken up. The platinum was filtered off and the solution allowed to evaporate overnight in a vacuum desiccator. The residue, which was already crystalline, was triturated three times with ethyl acetate and twice with ether. The crystals which remained were almost colorless, m.p. 155–159° (sublimation from 90°; clear yellow melt),[32] after two recrystallizations 159°. Such a pure preparation is not indefinitely stable and, after five months, shows m.p. 142–164°. The infrared spectrum of this compound is identical with that of the compound obtained from the peroxide procedure. Methylcyclohexane and glacial acetic acid were also tested as solvents for the catalytic oxidation but were found to be unsatisfactory. Yields up to 75% were obtained by this procedure.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.42. Found: C, 77.21; H, 7.08; N, 7.48.

B. Peroxide Method.—Tetrahydrocarbazole (120 g., 0.7 mole) was treated with 200 ml. of a 3.5 molar solution of hydrogen peroxide in absolute ether.[9] The reaction mixture was allowed to stand for 35 hours and then extracted with consecutive portions of 2 *N* hydrochloric acid, under ice cooling. From the reaction mixture there were obtained two products: 2.5 g. of a high-melting material, not readily soluble in ether, which was identified as carbazole; and 3.2 g. of crude 11-hydroxytetrahydrocarbazolenine which crystallized on seeding. The compound was moderately soluble in cold benzene, easily soluble in hot benzene, and virtually insoluble in petroleum ether. On recrystallization from benzene–petroleum ether 500 mg. of white fluffy needles, m.p. 157–159° (clear yellow melt) were obtained. Attempted recrystallization from methanol was unsuccessful. The material was identical with that obtained by Method A.

Reaction with Picric Acid.—The crystalline product dissolves slowly in warm ether and shows a blue fluorescence. After addition of ethereal picric acid no precipitate is formed, but on evaporation long red needles are obtained; m.p. 162° identical with the picrate of compound C.

Anal. Calcd. for $C_{24}H_{22}N_2 \cdot 2C_6H_3O_7N_3$: C, 54.27; H, 3.56. Found: C, 54.51; H, 3.91.

11-Hydroxy-1,2,3,4,10,11-hexahydrocarbazole (V).—11-Hydroxytetrahydrocarbazolenine (100 mg., 0.54 millimole) in 5 ml. of ethyl acetate was stirred under hydrogen for 20 minutes in the presence of 50 mg. of platinum oxide catalyst. The net uptake was 27.5 cc. (calcd. 12.1 cc. + 10 cc. for the catalyst, 22.1 cc.). The solution was filtered and evaporated to dryness. When the residue was recrystallized from ethyl acetate and washed with ether, glass-clear cubic crystals were obtained; m.p. 109° (sintering 105°; clear colorless melt). The crystals became white and opaque on drying.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99. Found: C, 76.15; H, 7.94.

Reaction with Picric Acid.—11-Hydroxyhexahydrocarbazole in ether treated with picric acid solution yielded a yellow picrate which turned red after a fraction of a second. The red picrate was identical with the picrate of tetrahydrocarbazole

Acid Dehydration of 11-Hydroxy-1,2,3,4,10,11-hexahydrocarbazole.—11-Hydroxyhexahydrocarbazole (20 mg.) dissolved in 2 ml. of methanol was treated with two drops of 2 *N* hydrochloric acid. On evaporation of the solution and recrystallization of the residue from aqueous methanol crystals, m.p. 118°, were obtained which were identical with tetrahydrocarbazole. The infrared spectra were compared and found to be the same.

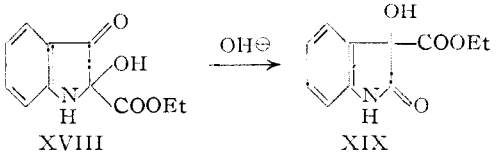
The Reduction of 11-Hydroxytetrahydrocarbazolenine with Lithium Aluminum Hydride.—11-Hydroxytetrahydrocarbazolenine (50 mg.) was slowly added to an ether solution of excess lithium aluminum hydride. A vigorous reaction occurred; the material which stuck to the wall of the flask became yellow in color, while the material falling directly into the suspension dissolved with evolution of hydrogen and no color change. When the reaction was complete, the mixture was decomposed with ice and the ethereal solution dried with anhydrous sodium sulfate and evaporated to dryness. The residue was approximately 45 mg. of colorless crystals easily soluble in ether. The substance was identical in melting point and infrared spectrum with tetrahydrocarbazole.

Diazotization of 11-Hydroxytetrahydrocarbazolenine.—An alcoholic solution of 11-hydroxytetrahydrocarbazolenine was treated with sodium nitrite and hydrochloric acid and added to an alkaline solution of β-naphthol. A brilliant red-colored azo dye resulted. Similar tests on 2-isopropyl-3,3-dimethylindolenine and on 11-ethyltetrahydrocarbazolenine were negative in both cases.

Basic Rearrangement of 11-Hydroxytetrahydrocarbazolenine.—A solution of 50 mg. of 11-hydroxytetrahydrocarba-

(28) Westheimer, THIS JOURNAL, **58**, 2209 (1936); Roberts and Urey, *ibid.*, **60**, 880 (1938).

(29) The rearrangement of camphenylic acid to camphenic acid (Aschan, *Ber.*, **47**, 1121 (1914)) and, somewhat more remote, the conversion of diphenyl glycol aldehyde to benzoin (Danilow, *ibid.*, **60**, 2390 (1927)) form rare examples of a reverse type of benzilic acid rearrangement. The interesting "migration" of a carbethoxy group in the conversion of the ester of the yellow indoxanthinic acid (XVIII) into that of the colorless dioxindole-3-carboxylic acid (XIX) by



XVIII XIX

the action of dilute alkali in the cold [Kalb, *ibid.*, **44**, 1455 (1911)] probably involves ring opening and reclosure with an intermediate *normal* benzilic acid rearrangement.

(30) All melting points are corrected and were taken on a hot-stage in connection with a microscope according to Kofler.

(31) If the catalyst is not shaken with oxygen separately prior to the oxidation, an induction period is always observed before the reaction begins.

(32) The melt, when dissolved in ether, shows the characteristic blue fluorescence associated with ethereal solutions of *spiro*-[cyclopentane-1,2′-*pseudo*indoxyl].

zolenine in methanol was treated with 2 *N* sodium hydroxide and boiled. The solution turned yellow and the characteristic green fluorescence of *spiro*-[cyclopentane-1,2′-*pseudo*-indoxyl] in alcohol appeared. When the solution was extracted with petroleum ether, the extract yielded yellow crystals, m.p. 79°, which showed no melting point depression when mixed with an authentic sample of *spiro*-[cyclopentane-1,2′-*pseudo*indoxyl].

Acid Rearrangement of 11-Hydroxytetrahydrocarbazolenine.—To a solution of 200 mg. of III in 20 ml. of ethanol was added 10 mg. of *p*-toluenesulfonic acid ($^1/_{200}$ *N*). After a few seconds the solution turned yellow and exhibited the characteristic green fluorescence of alcoholic solutions of the spirane (IV). After 5 hours the red brown solution, depositing colorless crystals, was evaporated in a vacuum desiccator; the residue was practically insoluble in petroleum ether (b.p. 20–40°). Ether extracted some yellow material (Compound B). The crystalline residue from the ether extraction (115 mg., m.p. 235–240°) was recrystallized from benzene and gave 75 mg. of Compound C (*vide infra*), m.p. 255 and, after resolidification, 315°.

Compound C.—11-Hydroxytetrahydrocarbazolenine (0.5 g.) was refluxed for 30 minutes in 2 ml. of acetic anhydride. After 10 minutes a colorless crystalline substance separated from the solution. This material was filtered off and recrystallized from benzene. There were obtained 60 mg. of brilliant colorless polyhedra showing a double melting point at 255° and 315° (dec.) (sublimation from 217°; resolidification above 255° to long yellow blade-like needles; progressive darkening above 260°).

Anal. Calcd. for $C_{24}H_{22}N_2$: C, 85.17; H, 6.55; N, 8.28; mol. wt., 338. Found: C, 85.15; H, 6.89; N, 8.40; mol. wt., 363, 325 (Rast).

Picrate.—Treatment of a benzene solution of $C_{24}H_{22}N_2$ with picric acid and recrystallization of the picrate from benzene–petroleum ether (1:2) afforded dark-red short needles, m.p. 165°.

The Influence of Acid on Compound C.—Thirty milligrams of $C_{24}H_{22}N_2$ was dissolved in 5 ml. of ethyl alcohol and treated with three drops of concentrated hydrochloric acid. A yellow color and a strong green fluorescence developed. The mixture was refluxed for four hours. When the solution was evaporated to dryness, a yellow powder was obtained which gave a dark brown solution in chloroform. The solution was filtered through an alumina column; a dark brown ring was produced in the column, and the filtrate had a light yellow color with a green fluorescence. On evaporation a residue was obtained which was easily soluble in ether, soluble in methanol and less soluble in benzene. Recrystallization from methanol afforded a yellow microcrystalline powder, m.p. 206–210°. A mixed melting point with an authentic sample of $C_{24}H_{24}N_2O$, m.p. 227–229°, obtained from the reaction of 11-hydroxytetrahydrocarbazolenine in refluxing acetic anhydride, gave m.p. (mixed) 155°, a depression of 72°.

Compound B. A. From III with Acetic Anhydride.—The acetic anhydride mother liquor from the isolation of compound C was diluted with ether and the ether solution thoroughly extracted with dilute potassium hydroxide solution. The ether solution was then dried over anhydrous sodium sulfate and evaporated. By careful fractionation with ether the low melting spirane was separated from a residue markedly less soluble in ether. Recrystallization of the residue from benzene-petroleum ether yielded yellow polyhedral crystals, m.p. 227–229° (sublimation above 215°).

Anal. Calcd. for $C_{24}H_{22}N_2O$: C, 80.86; H, 6.79; N, 7.86; mol. wt., 356. Found: C, 80.32; H, 6.75; N, 7.74; mol. wt. (Rast), 399, 392.

B. By Thermal Rearrangement from III.—Two hundred milligrams of III was held at 160° (oil-bath) for 90 seconds; the material formed a yellow melt after 30 seconds and then started effervescing (elimination of water). Crystals formed on cooling. The melt was extracted with ligroin (b.p. 60–90°) which dissolved all but about 20 mg. of Compound B, yellow crystals, m.p. 225°. The ligroin extract on slow evaporation gave some more of Compound B and 150 mg. of the yellow spirane (IV), m.p. 79°.

Compound A (Presumably XIII). A. By Refluxing of III in Ethyl Alcohol.[19]—Two hundred milligrams of 11-hydroxytetrahydrocarbazolenine in 20 ml. of ethanol was allowed to reflux for five hours. Within the first five minutes the green fluorescence, characteristic of alcoholic solutions of the spirane IV, was noticed, In cases where the alcohol used was not absolute and free of traces of acid, and moisture was not excluded during refluxing, the mixture on cooling deposited colorless crystals of Compound C; yield 20 mg. (10%), m.p. 255° and 312–315° (dec.). In the experiments carried out under anhydrous conditions, no Compound C was observed and the clear yellow-green fluorescent solution was evaporated *in vacuo*. The residual yellow lacquer crystallized directly on treatment with petroleum ether, yielding 160 mg. of yellow crystals, melting on recrystallization from petroleum ether, 79°, identical with spirane IV. In some experiments it was possible by dissolving the unrecrystallized spirane IV carefully in cold ether to isolate yellow crystals less readily soluble in ether, m.p. 138–141°, melting under effervescence (elimination of water).

Anal. Calcd. for $C_{24}H_{26}O_2N_2$: C, 77.00; H, 7.00. Found: C, 76.42; H, 7.44.

B. By Controlled Acid Rearrangement of III.—When 100 mg. of III was left at room temperature for one hour dissolved in 10 ml. of absolute alcohol containing 5 mg. of *p*-toluenesulfonic acid, the solution showed a pure yellow-green color and fluorescence. After evaporation *in vacuo* at 20° petroleum ether extracted first 60 mg. of the noncrystalline residue. The extraction was repeated with the dry extract and gave then only 30 mg. of material completely soluble in ligroin. This material was obtained crystalline from cold methanol, yielding yellow prisms, m.p. 138°, undepressed on admixture with Compound A as prepared above. The infrared absorption spectrum showed the presence of the following bands: NH, 2.95 μ; OH, 3.11; C=O, 5.86; Ph-N<, 6.16.

C. By Acid-Catalyzed Addition of Spirane IV to 11-Hydroxytetrahydrocarbazolenine (III).—When 30 mg. of III and 20 mg. of the spirane IV were left in a solution of 5 ml. of ethanol containing 2 mg. of *p*-toluenesulfonic acid for 5 hours at 20°, the clear yellow solution on evaporation no longer contained any spirane IV extractable with petroleum ether. The crystalline residue (melting range 125–210°) consisted of a mixture of Compounds A and B which could be separated in quantities sufficient for mixed melting points with authentic material, using slow crystallization from petroleum ether and ether solutions.

Compound $C_{19}H_{15}NO_2$ from 9-Benzoyltetrahydrocarbazole.—When 10 g. of N-benzoyltetrahydrocarbazole was treated with 5.8 g. of bromine in glacial acetic acid as described by Plant and Tomlinson,[19] the petroleum ether extracts of the reaction mixture on slow evaporation eventually gave colorless glossy needles, m.p. 248° (240° sintering).

Anal. Calcd. for $C_{19}H_{15}NO_2$: C, 78.89; H, 5.19; N, 4.84. Found: C, 78.91; H, 5.34; N, 4.96.

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