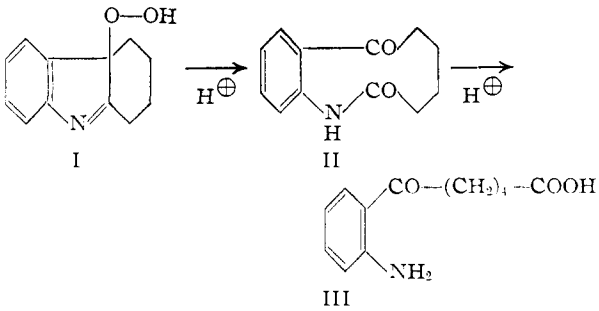
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY AND THE NATIONAL HEART INSTITUTE]

On the Mechanism of Oxidation. I. A New Type of Peroxide Rearrangement Catalyzed by Acid

BY BERNHARD WITKOP[1] AND JAMES B. PATRICK[1]

11-Hydroperoxytetrahydrocarbazolenine (I) in solutions of polar solvents and in the presence of acid rearranges to 1-aza-8,9-benzcyclononadi-2,7-one (II). The rearrangement is discussed and correlated with the autoxidation reactions of hydrazones, anils and a number of heterocyclic representatives. Cyclopentanone, in the Fischer indole synthesis, directly gave some γ-*o*-aminobenzoylbutyric acid, an example illustrative of the generality of this type of oxidation.

The catalytic oxidation of tetrahydrocarbazole[2] with platinum catalyst and molecular oxygen leads to 11-hydroperoxytetrahydrocarbazolenine (I), a new type of indole peroxide previously reported by Robertson and co-workers.[3] This peroxide, fairly stable in a dry state, is very unstable in solutions, especially of polar solvents and, on standing or recrystallization, changes rapidly into a new compound that has lost its peroxide character.[4] The new compound is 1-aza-8,9-benzcyclonona-2,7-dione (II) or the cyclic lactam of δ-*o*-aminobenzoylvaleric acid[5] (III) obtainable from II by acid treatment. This interesting peroxide rearrangement is reminiscent of the transformation of 9-*trans*-decalyl hydroperoxide benzoate[6] into cyclodecanolone-1,6[7,8] favored by ionizing solvents. Criegee[7] and Leffler[9,10] have suggested polar mechanisms for this type of rearrangement and for the decomposition of peroxidic intermediates occurring in such processes as the reactions of Caro's and perbenzoic acids with ketones,[11,12] the Dakin reaction, autoxidation and ozonolysis.



I II III

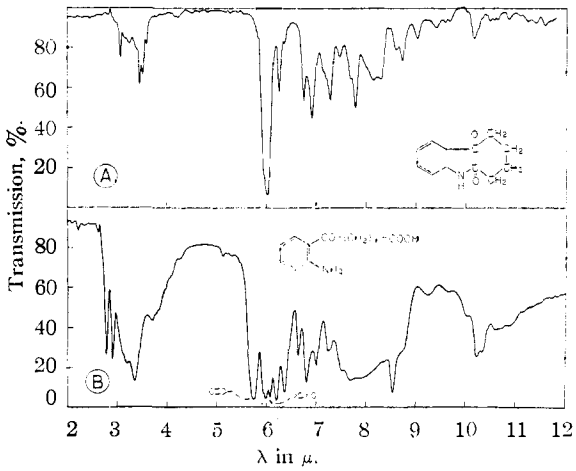


Fig. 1.—Infrared spectra in chloroform.

Since the cyclic lactam II, in contrast to the initial peroxide (I),[13] has a very strong band of absorption in the infrared at 6.0 μ caused by the two carbonyl groups (Fig. 1A), infrared spectrophotometry offers a convenient method of following the peroxide rearrangement *in situ*.[14] Figure 2 gives a direct picture of the rate of rearrangement as a function of the change in per cent. transmission. For our purpose it was not necessary to convert the figures plotted on the ordinate into changes of concentration.[15] When similar runs were taken in the presence of varying amounts of *p*-toluenesulfonic acid in anhydrous chloroform free of alcohol, and plotted as shown in Fig. 3, the catalyzing action of acid in this reaction became apparent. We conclude from these data that the rearrangement of 11-hydroperoxytetrahydrocarbazolenine at room temperature in polar solvents proceeds by an ionic mechanism. The ease of rearrangement is considerably greater here than with 9-*trans*-decalyl hydroperoxide. In the latter case the –O–OH bond is not sufficiently polar alone and a benzoyl group has to be attached to it in order to facilitate the postulated heterolytic cleavage of the peroxide bond. Even then, the half-life time of the peroxide in chloroform at 40° is 13 hours and not about 50 minutes (at 27°) as in the case of I.

This particular ease of rearrangement must be due to the presence in the peroxide molecule of the strongly polar group —N=C<. The scheme underlying the rearrangement of 9-decalyl hydroperoxide must be modified here. After heterolytic cleavage of the peroxide bond (IV), changes that lead, *via* the intermediate stages V or Va, to the lactam II seem possible. However, we prefer to let the driving force of the reaction come from the

(1) National Heart Institute, Bethesda 14, Maryland.

(2) B. Witkop and J. B. Patrick, THIS JOURNAL, **72**, 713 (1950).

(3) R. J. S. Beer, L. McGrath, A. Robertson and A. B. Woodier, *Nature*, **164**, 362 (1949) and (added in proof) *J. Chem. Soc.*, 2118, 3283 (1950).

(4) *Cf.* B. Witkop, THIS JOURNAL, **72**, 1428 (1950).

(5) W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, **123**, 676 (1923); J. R. Keneford and J. C. E. Simpson, *ibid.*, 2318 (1948).

(6) R. Criegee, *Ber.*, **77**, 22, 722 (1944).

(7) R. Criegee, *Ann.*, **560**, 127 (1948).

(8) R. Criegee and W. Schnorrenberg, *ibid.*, **560**, 141 (1948).

(9) J. E. Leffler, Thesis Harvard University, 1948.

(10) J. E. Leffler, *Chem. Revs.*, **45**, 385 (1949).

(11) S. L. Friess, THIS JOURNAL, **71**, 2571 (1949).

(12) *Cf.* R. B. Turner, *ibid.*, **72**, 878 (1950).

(13) See Fig. 2A in Ref. 2.

(14) This very useful method has not been applied too frequently yet, *cf.* G. L. Simard, J. Steger, T. Mariner, D. J. Salley and V. Z. Williams, *J. Chem. Phys.*, **16**, 836 (1948).

(15) The conversion of per cent. transmission into concentration can be done by empirical calibration of the instrument, by planimetric evaluation of the area enclosed by the absorption bands, or with the aid of the simple relation $\ln 100/T = kcd$.

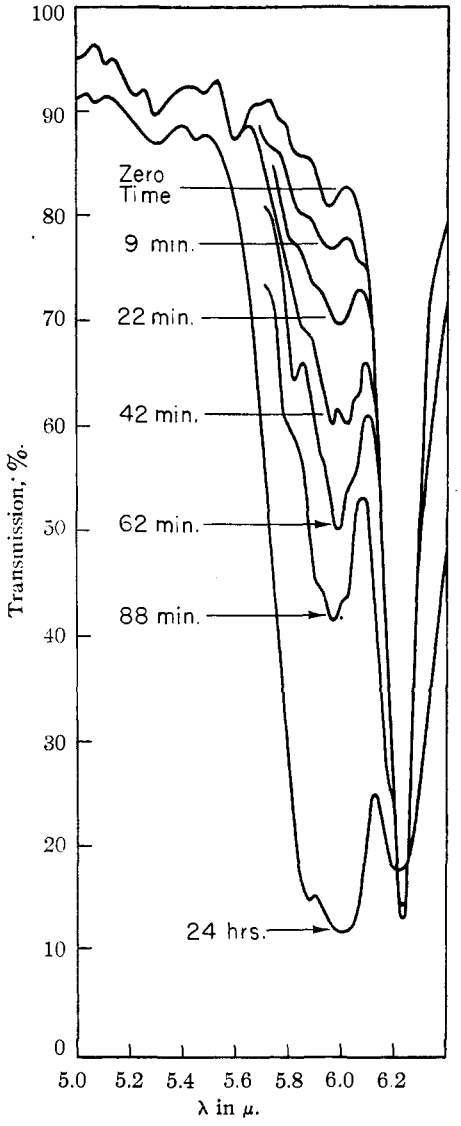
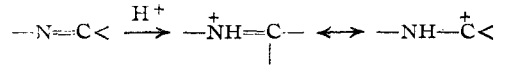


Fig. 2.—The rearrangement of 11-hydroperoxytetrahydrocarbazolenine in chloroform as observed directly in a self-recording double-beam IR-spectrophotometer.

ability of the —N=C< group to attract rather than to donate electrons. We have dealt previously with such addition reactions of the intermolecular type in the indoxyl series[16] and of the intramolecular type, as shown in the conversion of the alkaloid cinchonamine into quinamine *via* a β-hydroxyindolenine intermediate.[17] This additive power of the —N=C< group is especially marked in the presence of acid due to the changes



The polarity of the solvent, or the presence of acid, in the rearrangement of I→II will, therefore, effect a polarization of the —N=C< group. The subsequent internal addition through the *quasi*-four-membered cyclic intermediates[18] VI and VII

(16) B. Witkop and J. B. Patrick, THIS JOURNAL, **73**, 713 (1951).

(17) B. Witkop, *ibid.*, **72**, 2311 (1950).

(18) There is no reason to believe in the existence of *real* four-membered cyclic peroxides. Yet, quasi-four-membered cyclic peroxide intermediates have been used in the interpretation of a number of other reactions, *e.g.*, abnormal ozonizations; W. G. Young, A. V. McKinnis, I. D. Webb and J. D. Roberts, *ibid.*, **68**, 293 (1946).

(19) J. B. Patrick and B. Witkop, *ibid.*, **72**, 633 (1950).

(20) *Cf.* A. A. Morton, "The Chemistry of Heterocyclic Compounds," 1st ed., McGraw-Hill Book Co., Inc., New York, N. Y., and London, 1946, p. 110.

(21) H. Leuchs, D. Philpott, P. Sander, A. Heller and H. Köhler, *Ann.*, **461**, 27 (1928).

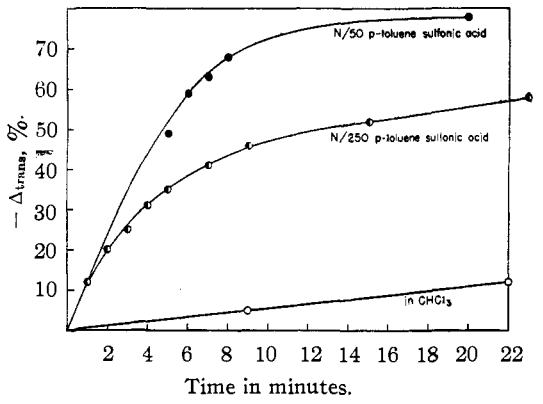
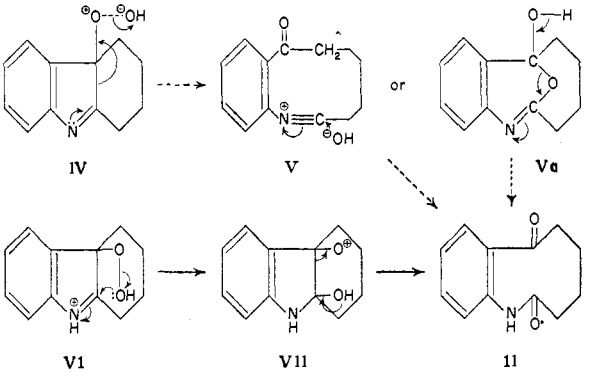
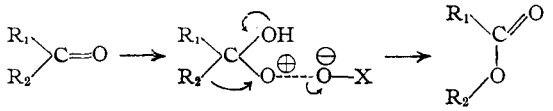


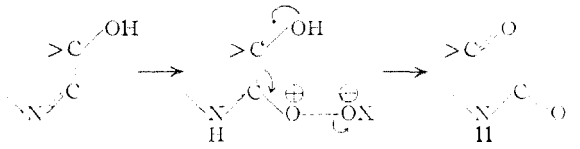
Fig. 3.—The influence of acid on the rate of rearrangement of 11-hydroperoxytetrahydrocarbazolenine into the nine-membered lactam of γ-*o*-aminobenzoylvaleric acid.

leads to the cyclic lactam II. In these changes the breakage, formation and renewed breakage of the various bonds may well be concerted.

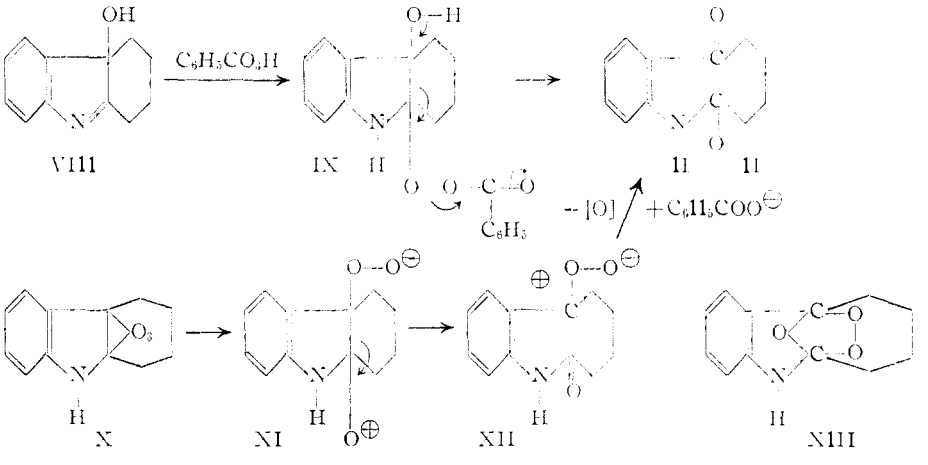


More information with regard to these transformations comes from a study of the reaction of 11-hydroxytetrahydrocarbazolenine[2,19] with perbenzoic acid which leads smoothly and in good yield to the same lactam II. Again the intermediate addition product IX is in analogy with the intramolecular addition compounds VI and VII. This addition reaction is typical of indolenines which are comparable to aldehydes and ketones[20] in their ability of adding amines, ammonia, acetic anhydride and, in this special case, perbenzoic acid.[21] The reaction of perbenzoic acid with 11-hydroxytetrahydrocarbazolenine becomes comparable then to the oxidation of aldehydes and ketones to esters or lactones with peracids





It may be recalled in this connection that the assumption of an addition of the peracid to the carbonyl as the first step in the Baeyer reaction[22,11] has been challenged recently by Criegee.[23] The driving forces for the formation of II from IX



are (i) the "electron push" from the β-hydroxyl group, (ii) the liberation of benzoate ion, and (iii) the energy gained by the formation of the more stable lactam.[24]

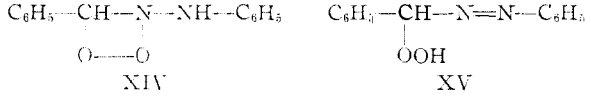
The lactam II was also obtained in excellent yield by ozonolysis of tetrahydrocarbazole. A true ozonide[25] of tetrahydrocarbazole (XIII) cannot exist for sterical reasons. In such cases, ozonolysis in methanol at −79° often furnishes methoxyhydroperoxides,[26] a type of compound which was not formed from tetrahydrocarbazole under these conditions. This fact suggests that the possible intermediate XII forms immediately the lactam II before it can add methanol or dimerize.

We consider the formation of the cyclic lactam II from 11-hydroperoxytetrahydrocarbazolenine (I) by an internal ionic rearrangement, or from 11-hydroxytetrahydrocarbazolenine (VIII) with peracids, as the fundamental model reactions underlying most oxidations of indole compounds in vitro or in vivo that are accompanied by cleavage of the α,β-double bond. The first intermediate in the reaction of indoles with molecular oxygen,[2,3] perbenzoic acid,[27] peracetic acid,[28] peroxidases,[29] *etc.*, is either a β-hydroperoxy- or a β-hydroxyindolenine. Whenever at this stage internal addition can occur leading to β-hydroxydihydroindole derivatives (quinamine,[17] quebrachamine,[30]) no further oxidation occurs.[31]

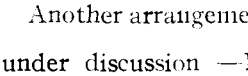
Of the many examples that are illustrations of this concept of oxidation only a few may be discussed here. The isolated system —CH=CH—N< present in methoxymethyldihydroneostrychnine shows the same behavior and is smoothly oxidized by perbenzoic acid to methoxymethylchanodihydrostrychnone.[32,33] A less clear-cut oxidation of an indolenine is described in the Experimental section.

Phenylhydrazones form peroxides very readily.[34,35,36] These peroxides have been misinterpreted (XIV) and are actually hydroperoxides of type XV.[37]

Anils, more closely related to indolenines, are often readily subject to autoxidation.[37a] A peroxide rearrangement strikingly similar to that given by 11-hydroperoxytetrahydrocarbazolenine (I) is shown in the



transformation of phenylindandione-*p*-dimethylaminoanil hydroperoxide[38,10] to an isoquinoline derivative XXI.[39,40]

Another arrangement of the characteristic system under discussion  is found in dihydroyobyrine.[41] This base is remarkable for the ease with which it is oxidized in solution by molecular oxygen to form yobyrone.

(22) M. Stoll and W. Scherrer, *Helv. Chim. Acta*, **13**, 142 (1930); A. Robertson and W. A. Waters, *J. Chem. Soc.*, 1574 (1948).

(23) R. Criegee, *Ann.*, **560**, 131, footnote 12 (1948); *cf.* W. von E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950); S. H. Friess and N. Farnham, *ibid.*, **72**, 5519 (1950).

(24) Although a calculation of the heat contents from the bond energies of I and II shows that II is more stable by about 40 kcal. mole^{-1}, no conclusions regarding the position of the equilibrium between I and II are drawn.

(25) Stable ozonides have only been reported in indole derivatives with an aromatic substituent (phenyl or pyridine) in the α-position: P. Karrer and P. Enslin, *Helv. Chim. Acta*, **32**, 1390 (1949); G. Mentzer, D. Molho and Y. Bergner, *Bull. soc. chim.*, 555 (1950); *cf.* B. Witkop, *Ann.*, **556**, 103 (1944).

(26) R. Criegee and G. Wenner, *ibid.*, **564**, 9 (1949); R. Criegee, "Organic Peroxides," Fortschritte der chemischen Forschung, Springer Verlag, Berlin-Göttingen-Heidelberg, 1950, pp. 528, 529.

(27) B. Witkop and H. Fiedler, *Ann.*, **558**, 91 (1947).

(28) B. Witkop, *ibid.*, **558**, 98 (1947).

(29) W. E. Knox and H. A. Mehler, *J. Biol. Chem.*, **187**, 419, 431 (1950).

(30) B. Witkop, unpublished experiments.

(31) There are indications that β-hydroperoxides of dihydroindoles do not rearrange. More analogous to decalyl hydroperoxide they may require a polarizing acyl group prior to rearrangement. This question is under investigation.

(32) R. Robinson and T. M. Reynold, *J. Chem. Soc.*, 935 (1935).

(33) R. B. Woodward and W. J. Brehm, THIS JOURNAL, **70**, 2107 (1948).

(34) M. Busch and W. Dietz, *Ber.*, **47**, 3277 (1914); H. Bilz and H. Wienands, *Ann.*, **308**, 1 (1899).

(35) G. M. Robinson and R. Robinson, *J. Chem. Soc.*, **125**, 834 (1924).

(36) A. H. Cook and K. J. Reed, *ibid.*, 399 (1945).

(37) *Cf.* ref. 26, p. 512 and (added in proof) K. H. Pausacker, *J. Chem. Soc.*, 3478 (1950); R. Criegée and G. Lobaus, *Chem. Ber.*, **84** 219 (1951).

(37a) The formation of peptides by the oxidation of azomethines is of great interest in this connection: R. V. Oppenauer, *Anz. Akad. Wiss. Wien, Math.-naturw. Klasse*, **84**, 37 (1947); *C. A.*, **44**, 1414 (1950); *Naturwissenschaften*, **34**, 90 (1947).

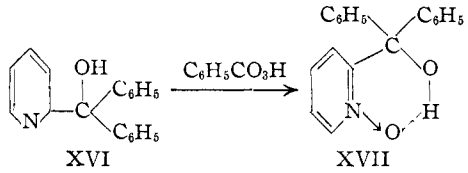
(38) P. Pfeiffer and H. L. de Waal, *Ann.*, **520**, 185 (1935).

(39) A. Schönberg and R. Michaelis, *J. Chem. Soc.*, 109 (1937).

(40) P. Pfeiffer and H. H. Roos, *J. prakt. Chem.*, **169**, 13 (1941).

(41) P. L. Julian, W. J. Karpel, A. Magnani and E. W. Meyer, THIS JOURNAL, **70**, 180 (1948).

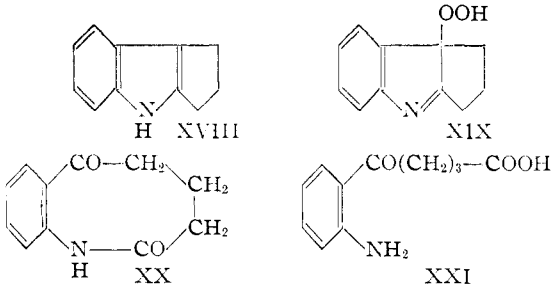
The behavior of the group —N=C—C—OH toward perbenzoic acid in a molecule where this characteristic element forms part of an aromatic system[42] as in α,α-diphenyl-2-pyridinemethanol



XVI XVII

(XVI)[43] was found to be different. No rupture into benzophenone and α-pyridone occurred, only the aminoxide (XVII) was formed, the unusual stability of which suggests a chelated pseudo six-membered ring structure (*cf.* infrared spectra, Fig. 4, A and B).

In all the different cases under discussion the stability of the intermediate peroxides varied greatly. The most active peroxides rearranging instantaneously were obtained from molecules in which some ring strain was present. As a major by-product in the Fischer indole synthesis with cyclopentanone γ-*o*-aminobenzoylbutyric acid (XXI) was identified. The intermediate dihydrocyclopentindole (XVIII) oxidized rapidly to the hydroperoxide (XIX), rearranging to the lactam (XX)[44] which was opened by the acid, present in the reaction mixture, to the amino acid (XXI). This striking example confirms and underlines the significance of this type of oxidation.



XVIII XIX XX XXI

An extension of this concept of oxidation to biochemical problems has led to a series of investigations now in progress at these laboratories.

Experimental[45]

1-Aza-8,9-benzcyclononadi-2,7-one (II)

A. By Rearrangement from 11-Hydroperoxytetrahydrocarbazolenine (I).—When 1 g. (5.4 millimoles) of tetrahydrocarbazole in 10 ml. of ethyl acetate containing 200 mg. of freshly reduced platinum catalyst was shaken under oxygen, 110 cc. (calcd. 121 cc.) of oxygen was taken up after about 4 hours. The peroxide which had mostly crystallized from the solution was collected together with the platinum black. Careful recrystallization from ethyl acetate gives a colorless product, m.p. 132–133° (sintering at 129°); the melt is slightly yellow and evolves oxygen. When the recrystallization is carried out under prolonged heating, or when the peroxide is left in solutions of polar solvents, especially chloroform, a new compound can be isolated, forming slightly yellow prisms, m.p. 156–157°, clear colorless melt, no gas evolution.

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.94; H, 6.40; N, 6.9. Found: C, 70.60; H, 6.54; N, 6.75.

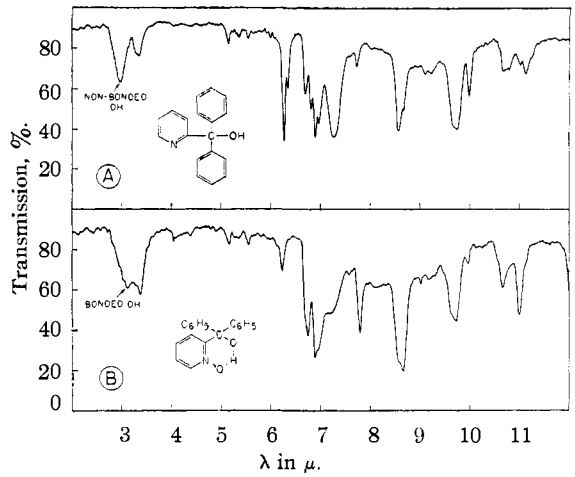


Fig. 4.—Infrared spectra in chloroform: The band of B at 7.8μ (1285 cm.$^{-1}$) could be the N-oxide band [G. R. Clemo and A. F. Daglish, *J. Chem. Soc.*, 1483 (1950)] shifted to longer wave length due to hydrogen bonding.

Kinetic Runs.—The material used for the kinetic studies was recrystallized three times from ethyl acetate at a temperature not exceeding 40°. The product was then absolutely colorless and melted at 134°. Solutions of this hydroperoxide in chloroform were completely colorless, turned slightly yellow after 25 minutes and assumed a strongly yellow brown color after two hours. The stability of solutions increased in the following order of solvents: nitromethane (ϵ = 39.4) < chloroform (5.14) < ethyl acetate (6.11) < carbon tetrachloride (2.25) < pyridine (12.4).[46] The chloroform used for the kinetic studies was freshly distilled from calcium hydride. Chloroform solutions containing 30 mg. of hydroperoxide/cc. of solvent were placed in standard sodium chloride cells (thickness of salt plates 0.635 cm., diameter 4.11 cm., space between plates 0.4 mm.,

Pure chloroform (27°)		In *n*/250 *p*-toluenesulfonic acid soln. in chloroform, 27°		*n*/50 *p*-toluenesulfonic acid soln. in chloroform, 27°	
Time, min.	$-\Delta_{trans.}$, %	Time, min.	$-\Delta_{trans.}$, %	Time, min.	$-\Delta_{trans.}$, %
9	5	1	12	5	49
22	12	2	20	6	59
42	21.5	3	25	7	63
62	32	4	31	8	68
98	39	5	35	20	78
24 hr. (∞)	71	7	41		
		9	46		
		15	52		
		23	58		

(42) Even the extended system —N=C—C=C—CH_2—, although embedded in an aromatic structure, is autoxidizable: N. J. Leonard and J. H. Boyer, *ibid.*, **72**, 2980 (1950). The reaction leading from 9-methylacridine to 1,2-bis-(9-acridyl)-ethylene may well go through the intermediate peroxide and aldehyde.

(43) A. E. Tschitschibabin and S. W. Benewolenskaja, *Ber.*, **61**, 547 (1928): phenylmagnesium bromide and 2-benzoylpyridine; M. R. F. Ashworth, R. P. Daffern and D. L. Hammick, *J. Chem. Soc.*, 809 (1939): using the "Hammick reaction"; C. H. Tilford, R. S. Shelton and M. G. van Campen, Jr., THIS JOURNAL, **70**, 4001 (1948): from α-pyridylmagnesium bromide and benzophenone. We used ethyl picolinate and Grignard reagent analogous to W. Sobecki, *Ber.*, **41**, 4103 (1908).

(44) J. B. Patrick, M. Rosenblum and B. Witkop, *Experientia*, **6**, 461 (1950).

(45) All melting points are corrected and all boiling points are uncorrected. The analyses were carried out by Mr. S. M. Nagy and his associates, Microchemical Laboratory, Massachusetts Institute of Technology.

(46) The solution in pyridine was only slightly yellow after one week at room temperature; this shows that the dielectric constant of the solvent is not so important for the rate of the rearrangement as traces of acid, always present or easily formed, in solvents such as ethyl acetate or chloroform.

approximate capacity 0.55 cc.). The cells were placed in a standard double-beam infrared spectrophotometer. The wave length of the instrument was set for 6.0 μ. The reference cell was filled with the same solvent or the same solution when *p*-toluenesulfonic acid was present. Several runs were made (see table).

B. From 11-Hydroxytetrahydrocarbazolenine with Perbenzoic Acid.—To 1 g. of 11-hydroxytetrahydrocarbazolenine (VIII) in 50 ml. of chloroform was added slowly and under ice-cooling 76 ml. of a 0.134 *M* chloroform solution of perbenzoic acid. The solution became distinctly warm and took on a red color. After 24 hours in the ice box, the solution was extracted with the amount of a 5% solution of sodium bicarbonate necessary to remove the benzoic acid. The chloroform solution was then dried over sodium sulfate and evaporated to dryness *in vacuo*. The residue (1.1 g.) was recrystallized from ether, forming transparent slightly yellow rods, m.p. 156–157°, no depression on admixture with the compound obtained with procedure A.

Anal. Calcd. for $C_{12}H_{13}NO_2$: C, 70.94; H, 6.40; N, 6.9. Found: C, 71.05; H, 6.76; N, 6.8.

δ-*o*-Aminobenzoylvaleric Acid (III).—When 200 mg. of the lactam II was heated on the steam-bath in 8 ml. of 2 *N* hydrochloric acid for 30 minutes, a red solution was obtained. After cooling the *p*H of the solution was brought to 8 by the cautious addition of sodium bicarbonate. When the solution was then made acidic with acetic acid colorless stout prisms crystallized slowly; m.p. 127–129°.

Anal. Calcd. for $C_{12}H_{15}NO_3$: C, 65.15; H, 6.79; N, 6.33. Found: C, 64.85; H, 6.89; N, 6.18.

Azo Test.—To a solution of a few mg. of the acid III in 0.1 *N* alkali was added the necessary amount of sodium nitrite. The ice-cold solution was then made acidic by the cautious addition of a few drops of 2 *N* hydrochloric acid. The addition of a few drops of the solution of this diazonium chloride to a solution of β-naphthol in 2 *N* alkali produced a brilliant red azo dye. When the diazotization was carried out with 200 mg. of the acid under the conditions given by Keneford and Simpson (ref. 5) 3,4′-hydroxy-3′-cinnolyl-*n*-propane-1-carboxylic acid (m.p. 201–203°) could be isolated.

C. By Ozonolysis of Tetrahydrocarbazole.—Five grams of tetrahydrocarbazole, dissolved in 50 ml. of methyl alcohol, were ozonized under cooling with Dry Ice in acetone. The solution was evaporated *in vacuo* and left 5.5 g. of slightly yellowish crystals, m.p. 145–156°, which were washed several times with ether and recrystallized from ether or ethyl acetate. The almost colorless crystals, m.p. 158°, were identical with the lactam II (mixture m.p. infrared spectrum) prepared by methods A and B.

Oxidation of 2-Isopropyl-3,3-dimethylindolenine with Perbenzoic Acid.[47]—To a solution of 0.56 g. (3 millimoles) of 2-isopropyl-3,3-dimethylindolenine in chloroform was added 23.5 ml. of a 0.14 *N* perbenzoic acid solution in chloroform. The mixture was colorless at first, became straw-yellow after three minutes and was red-brown after standing for 15 hours in the refrigerator. The clear solution was then extracted three times with 5% sodium bicarbonate, dried over sodium sulfate and evaporated in the desiccator. The brown gum was taken up in benzene and treated with a solution of picric acid in benzene. Careful addition of petroleum ether and prolonged rubbing induced crystallization. The picrate was recrystallized first from benzene and then from methanol; yellow-green needles, m.p. 187–188°. The mixed melting point with a picrate of the original indolenine (180.5°) was 156–168°.

(47) This experiment was carried out by Mr. Arvid Ek.

Anal. Calcd. for $3[C_{13}H_{17}NO_2]\cdot C_6H_3N_3O_7$: C, 57.60; H, 5.45; N, 10.49. Found: C, 57.74; H, 4.80; N, 10.45.[48]

α,α-Diphenyl-2-pyridinemethanol (XVI).—An ethereal solution of ethyl α-picolinate (30 g., 0.2 mole) was added dropwise to an ice-cooled, well stirred solution of phenylmagnesium bromide (0.7 mole) in the course of one-half hour. The first drops produced a lemon-green colored precipitate, which dissolved on stirring. The solution assumed a cherry red color which gradually darkened to a deep mulberry color. The reaction mixture was refluxed for one hour on the steam-bath, cooled and decomposed with dilute sulfuric acid and ice. The aqueous extract was made strongly alkaline and the oil formed taken up in benzene. The fractional distillation of the dried benzene extract gave 34 g. (64% of the theoretical) of a fraction, b.p. 160–170° (0.3 mm.), solidifying to crystals, m.p. 105° (reported m.p. 104–105°).

α,α-Diphenyl-2-pyridinemethanol Oxide (XVII).—To 0.5 g. of α,α-diphenyl-2-pyridinemethanol in 3 cc. of chloroform was added 6 cc. of a perbenzoic acid solution in chloroform corresponding to 3 millimoles. After 20 hours in the ice-box there was still an excess of perbenzoic acid present. The perbenzoic and benzoic acids were removed by extraction with aqueous sodium bicarbonate solution. The crystalline residue consisting of slightly yellowish square plates was purified by microsublimation at 150° (2 mm.). The colorless sublimate consisted of glass-hard, stout prisms, m.p. 194° (184° sintering, 175° crystalline transformation into small needles).

Anal. Calcd. for $C_{18}H_{15}N_2O_2$: C, 77.97; H, 5.41; N, 5.17. Found: C, 77.74; H, 5.26; N, 5.18.

γ-*o*-Aminobenzoylbutyric Acid from the Preparation of Dihydropentindole.—The ligroin mother liquor from the first crystallization of 2-dihydropentindole, following the directions of Perkin and Plant,[49] was concentrated to approximately half its volume and set aside. About 5 ml. of a red oil separated, which was subjected to steam distillation. Dihydropentindole passed over in the distillate. The aqueous residue from the steam distillation, on standing overnight, contained large yellow needles in addition to a considerable quantity of tar. The liquor was decanted, the needles separated from the tars and recrystallized from hot water. After two recrystallizations light tan needles were obtained, m.p. 127–129° (clear melt) undepressed on admixture with γ-*o*-aminobenzoylbutyric acid obtained by another route.[44] The identity was further confirmed by comparison of the infrared spectra. The acid is insoluble in petroleum ether and cold benzene, soluble in methanol, acetone and hot benzene. Diazotization and coupling with an alkaline solution of β-naphthol shows the presence of an aromatic amino group.

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.24; N, 6.76. Found: C, 63.60; H, 6.26; N, 6.54.

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(48) The unusual composition of the oxidation product could come from an initial attack of the oxidant at the tertiary carbon of the 2-isopropyl group, possibly followed by an addition or condensation reaction.

(49) W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, **123**, 3244 (1923).