(437 mg.) was dissolved in hexane and chromatographed on alumina.[16] Table II summarizes the results.

TABLE II

Compound eluted	Wt., mg.	M.p., °C.	$[\alpha]^{25}D$
V	44	126–127	+41.3° (*c* 1.9)
VIII	269	141–142.5	+22.7° (*c* 3.7)
IX	92	181–183	+24.0° (*c* 1.3)

Normal Lithium Aluminum Hydride Reduction of Coprostanone Enol Acetate.—A solution of 500 mg. (1.2 mmoles) of the enol acetate in 15 ml. of anhydrous ether was added over a period of 30 minutes to an ethereal solution of lithium aluminum hydride (8 mmoles in 15 ml.). The slightly turbid solution was stirred for an additional four hours at room temperature and then processed as described above. Chromatography yielded coprostanone and a mixed stanol fraction. It was possible to separate some epicoprostanol from this mixture by careful elution of the alumina column, but it was more efficient to elute the total stanol fraction and employ digitonin to separate the epimers. The stanols (381 mg.) were dissolved in 40 ml. of hot 90% ethanol and to this solution there was added 0.4 g. of digitonin dissolved in 40 ml. of hot 90% ethanol. The mixture was cooled overnight at ice temperature and the digitonide filtered, dried and then redissolved in 5 ml. of dry pyridine. The pyridine solution was added to 50 ml. of ether and the resulting suspension filtered through supercel. The filtrate was washed with acid, base and water and then dried and evaporated. Crystallization of the residue from ethanol yielded coprostanol. The filtrate from the digitonide preparation was added to a threefold excess of ether, filtered (supercel) and diluted with a large excess of water. The ethereal layer was separated and processed as for the insoluble fraction. A summary of the results is given in Table III.

TABLE III

Compound isolated	Wt., mg.	M.p., °C.	$[\alpha]^{25}D$
X	43	Oil[a]	.....
XIII	60	96–98	+24° (*c* 1.25)
XIV	315	107–109	+30° (*c* 1.67)

[a] The coprostanone isolated by chromatography of the crude reduction mixture frequently defied crystallization until it was evaporatively distilled.

Sodium Borohydride Reduction of Cholestanone Enol Acetate.—A solution of 0.2 g. (5.3 mmoles) of sodium borohydride in 20 ml. of methanol was added dropwise over a period of 20 minutes to a refluxing solution of 500 mg. (1.2 mmoles) of the enol acetate in 20 ml. of methanol and 5 ml. of ether. After heating for three hours, the reaction mixture was decomposed with 3 ml. of concentrated hydrochloric acid and then heated for an additional hour. The mixture was cooled, diluted with 80 ml. of ether, washed with several portions of water, dried over anhydrous sodium sulfate and evaporated. Chromatography of the residue yielded 67 mg. of epicholestanol, m.p. 178–182°, and 357 mg. of cholestanol, m.p. 139–141°.

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(16) Unless otherwise specified, all absorbent used was Merck and Co., Inc., Reagent Aluminum Oxide. Approximately 25 g. of alumina was used per gram of steroid. The solvent sequence employed was hexane, 15% ether (by volume) in hexane and 25% ether in hexane.

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

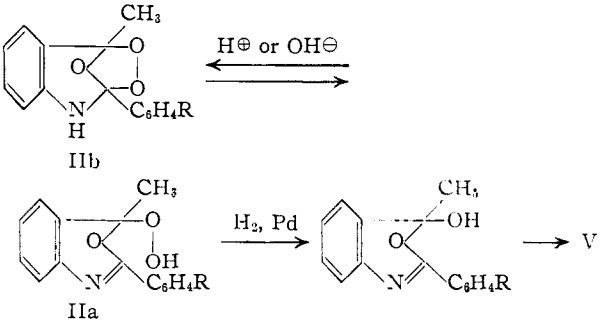
Reductive Cleavages of a Stable Ozonide[1]

BY BERNHARD WITKOP[2] AND JAMES B. PATRICK[2,3]

RECEIVED JULY 9, 1951

The stable ozonide IIa from 2-phenylskatole (I) was studied in its spectral and chemical behavior. The following agents were used for reductive cleavage of the ozonide: hydrogen and palladium, lithium aluminum hydride, sodium boron hydride, alkali metal, phenyl- and *n*-butylmagnesium bromide and methyllithium. For the first time a crystalline ozonide and hydroperoxide (VI), both prepared from the same precursor (I), were correlated *via* their common oxidation product (V) obtained by acid-catalyzed rearrangements from II and VI.

Criegee's recent reinvestigation of certain ozonides has led to a revision of the structure of Hückel's stable "ozonide" from $\Delta^{9,10}$-octalene,[4] established a new course of ozonization for a number of compounds,[5] and thus brought up the question whether the customary formulation of ozonides according to Staudinger[6] is still justified.[7] Especially the ozonides and hydroperoxides derived from 2-(*p*-anisyl)-skatole, [B. Witkop, J. B. Patrick and H. Kissman, Heinrich Wieland Jubilee Volume, *Chem. Ber.*, 85 (1952)] which led to the conclusion that these ozonides are capable of a true *ring-chain tautomerism* (IIa ⇄ IIb:



R = H or OCH_3). All the reactions described in this paper involving the action of acid or base reflect the reactions of the true ozonide (IIb). The reduction with palladium in neutral alcoholic solution starts from the "chain" tautomer IIa leading to the hemiacetal which, lacking the stability of the parent hydroperoxy compound (IIa), isomerizes easily to give *o*-benzaminoacetophenone (V). Also, the decomposition in refluxing benzene without any catalyst is a thermal decomposition of the hydroperoxide tautomer (IIa) involving radical intermediates (formation of diphenyl, etc.).

(1) On the Mechanism of Oxidation. III. Preceding paper in this series; THIS JOURNAL, **73**, 2641 (1951).

(2) National Heart Institute, National Institutes of Health, Bethesda, Md.

(3) Research Corporation Fellow, 1950.

(4) R. Criegee and K. Wenner, *Ann.*, **564**, 9 (1949).

(5) R. Criegee, "Organische Peroxyde, Fortschritte der chemischen Forschung," Vol. I, Springer-Verlag, Berlin, Göttingen, Heidelberg, 1950, pp. 527–530.

(6) Leading literature: A. Rieche, "Alkylperoxyde und Ozonide," T. Steinkopff, Dresden and Leipzig, 1931; L. Long, *Chem. Revs.*, **27**, 437 (1940); A. Rieche, R. Meister and H. Sauthoff, *Ann.*, **553**, 187 (1942).

(7) R. Criegee, European Scientific Notes, Office of Naval Research, London Branch, **4**, 110 (1950).—*Added in proof:* R. Criegee reported on the structure of the ozonide from phenylskatole at the 120th Meeting of the American Chemical Society, New York, N. Y., September 7, 1951, Abstracts 22M. As a result of stimulating discussions with Dr. Criegee, who favored the expression IIa (R = H), we started a more thorough investigation of the spectral and chemical behavior of the

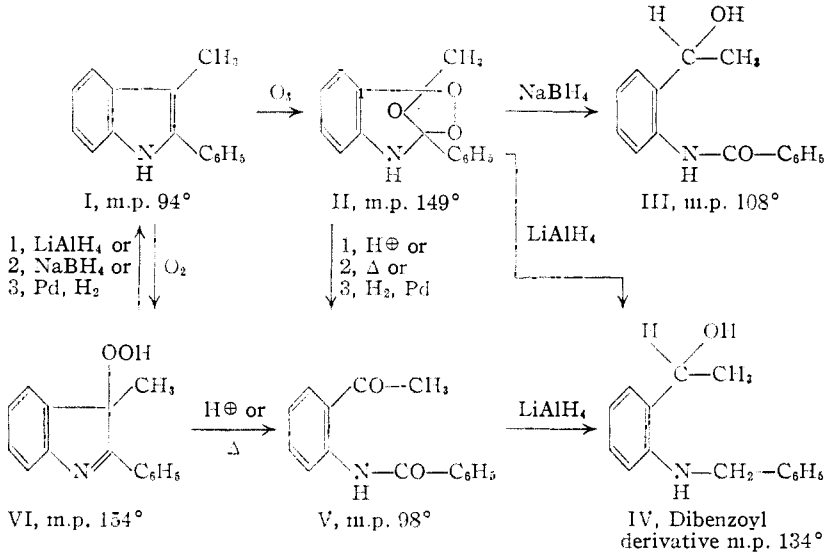
structure of stable ozonides[8-11] seemed to call for revision or reinvestigation. In this and in the following paper we describe the chemical behavior of the ozonide from phenylskatole (I)[12] which is an unusually stable crystalline compound, recrystallizable from boiling ethyl alcohol, and which can be prepared and stored in any quantity. By loss of the indole double bond the ozonide gained enough basicity to furnish a stable hydrochloride, sulfate and picrate (II).

The stability of this ozonide does not result from its being a dimer or polymer[13,14] as the determination of the molecular weight in acetone according to Signer[15] shows. The absence of a band in the carbonyl region of the infrared spectrum[16] rules out the possibility of a ketonic peroxide.[4,5] The ultraviolet spectrum (Fig. 1) differs surprisingly little from that of the parent phenylskatole (I). Whereas the stable "ozonides" from dihydrodicyclopentadiene[8] and from 2-phenyl-3-ethylindone[9] are suspiciously resistant to catalytic hydrogenation, the ozonide from I, on hydrogenation with palladium in ethyl acetate, is smoothly and rapidly converted into *o*-benzaminoacetophenone (V) also obtainable from II by the action of heat (melting) or acid.

The reduction of the ozonide with lithium aluminum hydride is smooth and less vehement than reported for the reduction of a number of hydroperoxides.[17] The oily benzylaminophenylmethylcarbinol[18] (IV) was characterized and isolated as the crystalline dibenzoyl derivative. Sodium boron hydride in alcohol reduced the ozonide to the crystalline *o*-benzaminomethylcarbinol (III).

By autoxidation of phenylskatole in hydrocarbon solvents we prepared the hydroperoxide (VI, ultraviolet spectrum Fig. 1). Peroxides of this kind undergo an acid-catalyzed rearrangement,[19] and the product thus obtained is identical with benzaminoacetophenone (V). *This is the first case reported in which the same oxidation product is obtained by two related acid-catalyzed rearrangements from the crystalline ozonide and hydroperoxide precursors.*[20]

The hydroperoxide of phenylskatole (VI) is more stable than the stablest hydroperoxide in the tricyclic series, *viz.*, 11-hydroperoxytetrahydrocarbazolenine, which rearranges in chloroform solution at room temperature.[21] The reduction of the hydroperoxide (VI) with lithium aluminum hydride gave phenylskatole (I). The milder sodium boron hydride yielded phenylskatole (I) and 2-phenyl-3-methyl-3-hydroxyindolenine (VII), also obtainable from the hydroperoxide by catalytic hydrogenation. Catalytic reduction, though tried in numerous variations, always furnished VII, phenylskatole or unchanged starting material, but not the hydroxyindoline (VIII, *cis* or *trans*). The two isomers of VIII would have been helpful in deciding whether easy dehydration is only observed with the *trans* or also with the *cis* compound. The analogous compound (IX)[21] is easily dehydrated by the action of acid, but the stereochemistry of the molecule is not established. This question is of importance, since the ready dehydration of the strychnone precursor X to give strychnone,[22] together with the evaluation of the



(8) R. Pummerer and H. Richtzenhain, *Ann.*, **529**, 33 (1937): "Ozonide" from dihydrodicyclopentadiene, m.p. 62°; and ozonide from ethyl fumarate, m.p. 43°, also obtainable from diethyl maleate. This latter ozonide is a true stable ozonide (B. Witkop and S. Goodwin, unpublished).

(9) R. L. Frank, H. Eklund, J. W. Richter, C. R. Vanneman and A. N. Wennerberg, THIS JOURNAL, **66**, 1 (1944); "Ozonide" from 2-phenyl-3-ethylindone, m.p. 93°.

(10) M. Tits and A. Bruylants, *Bull. soc. chim. Belg.*, **57**, 50 (1948): Ozonides from α,β-unsaturated amides, and *cf.* (added in proof) K. I. Altman and J. E. Richmond, 12th Intern. Congress of Pure and Applied Chemistry, Abstracts Biol. Chem., 70, September, 1951; H. Fischer and M. Dezelic, *Z. Physiol Chem.*, **222**, 278 (1933).

(11) P. Karrer and P. Enslin, *Helv. Chim. Acta*, **32**, 1390 (1949); ozonide from 2-(3,4-diethylpyridyl)-3-ethylindole, m.p. 134°.

(12) G. Mentzer, D. Molho and Y. Berguer, *Bull. soc. chim.*, 555 (1950).

(13) *Cf.* C. Harries, *Ann.*, **390**, 235 (1912).

(14) A. Rieche, R. Meister and H. Sauthoff, *ibid.*, **553**, 218 (1942).

(15) R. Signer, *ibid.*, **478**, 246 (1930); E. P. Clark, "Semimicro Quantitative Analysis," Academic Press, Inc., New York, N. Y., 1943, p. 78.

(16) The exact location of the significant bands of the free ozonide in chloroform solution between 9 and 12 microns is: 9.24; 9.40; 9.76; 10.93; 11.27; 11.48; 11.97. A definite assignment of these bands to the oxiran and peroxide components in the ozonide structure has to await further infrared studies on ozonides now in progress; *cf.* O. D. Shreve, M. R. Heether, H. B. Knight and D. Swern, *Anal. Chem.*, **23**, 277, 282 (1951).

(17) D. A. Sutton, *Chemistry and Industry*, 272 (1951).

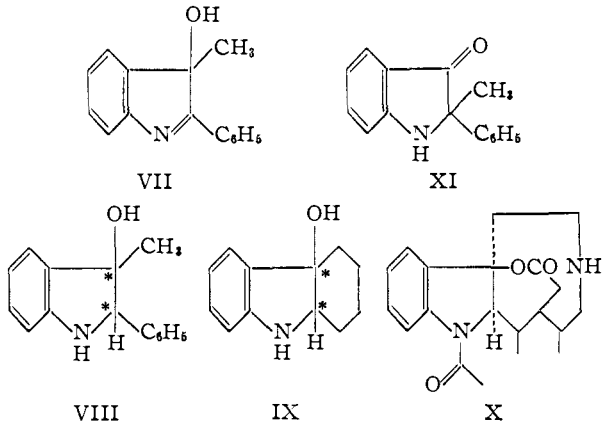
(18) The reduction product proved difficult to purify, possibly due to the presence of *o*-ethylbenzylaniline formed by hydrogenolysis, *cf.* L. H. Conover and D. S. Tarbell, THIS JOURNAL, **72**, 3586 (1950).

(19) B. Witkop and J. B. Patrick, *ibid.*, **73**, 2196 (1951).

(20) Another interesting correlation between autoxidation (a reaction proceeding by a radical mechanism) and ozonization (a reaction obeying the rules of an electrophilic substitution: J. P. Wibaut, F. L. J. Sixma, H. Boer and H. J. Pel, XIIth International Congress of Pure and Applied Chem., New York, N. Y., 1951, Abstracts, p. 435; *Rec. trav. chim.*, **71**, 473 (1952); *cf.* however, G. M. Badger, *ibid.*, **71**, 468 (1952)) is the formation of ozonides by autoxidation of furans (G. O. Schenck, *Angew. Chem.*, **60**, 244 (1948); **64**, 12 (1952)).

(21) B. Witkop and J. B. Patrick, THIS JOURNAL, **73**, 2188 (1951).

(22) H. Leuchs, E. Tuschen and M. Mengelberg, *Ber.*, **77**, 408 (1944); R. B. Woodward, W. J. Brehm and A. L. Nelson, THIS JOURNAL, **69**, 2250 (1947).



VII XI

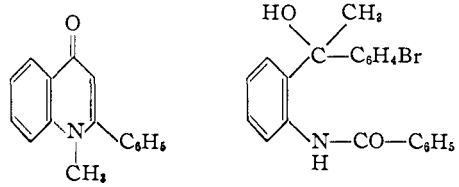
VIII IX X

X-ray diffraction pattern,[23] form the only basis for the formulation of strychnine as a derivative of *cis*-hexahydrocarbazole. On the other hand, anhydrodethiogliotoxin ("Compound F")[24] which, though unlikely, may be a 2,3-dihydroindoxyl derivative, can be sublimed unchanged without dehydration to the corresponding diketopiperazinoindole and may, therefore, have the two hydrogens at positions 2,3 (or 10,11 following the numbering in gliotoxin) in the *trans* position.

The action of acid on the hydroxy compound (VII) produces stable salts; the action of base under conditions that rearrange 11-hydroxytetrahydrocarbazolenine[21] does not form the indoxylspirane (XI), thus demonstrating the small migratory aptitude of methyl compared with the ready constriction of the 6-membered ring.

By the reaction of the ozonide with metallic potassium in boiling benzene[25] and subsequent methylation 1-methyl-2-phenyl-4-quinolone (XII, ultraviolet spectrum Fig. 2) was obtained, probably *via* *o*-benzaminoacetophenone, the major product in this reaction.

In the hope to obtain preferential reaction with either the ether or peroxide part of the ozonide we studied the interaction of the ozonide with lithium



XII XIII

and magnesium organic compounds. While phenylmagnesium bromide fails to react with di-*t*-butyl peroxide,[26] the ozonide gave a definite reaction yielding four different products separated by chromatography: (1) *o*-benzaminoacetophenone (V); (2) *o*-benzaminodiphenylmethylcarbinol (m.p. 145–147°); (3) diphenyl, probably formed in the same way as the olefins in the reactions of di-*t*-butyl peroxide with Grignard reagents[26] as the result of dehydrogenation caused by the ozonide; (4) a compound $C_{21}H_{18}NO_2Br$, m.p. 192–195°, formulated as XIII on the basis of the analysis and the infrared spectrum which is very similar to the bromine-free product. The exact location and origin (by a radical or ionic mechanism) of the bromine has not been ascertained yet.

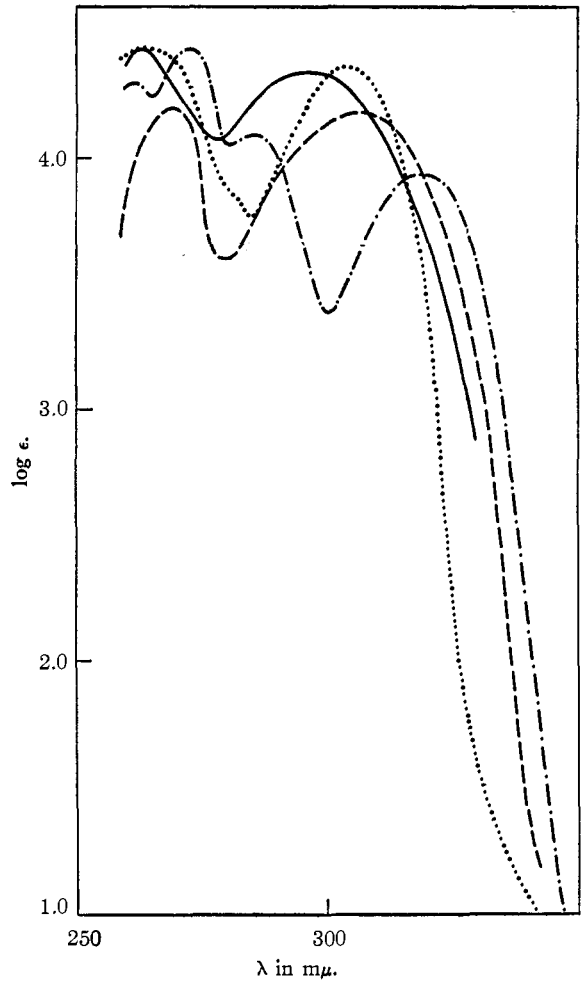


Fig. 1.—Ultraviolet spectra (in absolute ether) of the ozonide from 2-phenylskatole (—), of 2-phenylskatole (.....), of 2-phenyl-3-methyl-3-hydroxy-ψ-indole (----), and of *o*-benzaminoacetophenone (—·—·—·).

Six different products were obtained from the reaction of the ozonide with *n*-butylmagnesium bromide: (1) again *o*-benzaminoacetophenone as the major product; (2) benzoic acid, probably formed by the cleavage of the amide by the action of Grignard reagent; (3) phenol, possibly from the benzene that was used as the solvent; (4) *o*-benzaminophenyl-*n*-butylmethylcarbinol (m.p. 118–120.5°), the normal Grignard addition product to V; (5) a compound $C_{15}H_{15}NO$, m.p. 154.5–156°, showing a carbonyl band at 5.78 μ, not identified yet; (6) *o*-benzaminophenol, whose formation will be discussed in the following paper.

This same *o*-benzaminophenol is also obtained by the decomposition of the ozonide in refluxing benzene, evidently by a radical reaction, since biphenyl,

(23) C. Bokhoven, J. C. Schoone and J. M. Bijvoet, *Koninkl. Nederland. Akad. Wetenschap. Proc.*, **50**, 825 (1947); **51**, 990 (1948); **52**, 120 (1949); J. H. Robertson and C. A. Beevers, *Nature*, **165**, 690 (1950); *Acta Cryst.*, **3**, 164 (1950).

(24) J. A. Elvidge and F. A. Spring, *J. Chem. Soc.*, 2935 (1951).

(25) This reaction was used by N. A. Milas and D. M. Surgenor, THIS JOURNAL, **68**, 205 (1946), for the cleavage of the O–O-bond in di-*t*-butyl peroxide into two molecules of *t*-butyl alcohol.

(26) T. W. Campbell, W. Burney and T. L. Jacobs, *ibid.*, **72**, 2735 (1950); *cf.* W. Treibs, *Ber.*, **84**, 438 (1951).

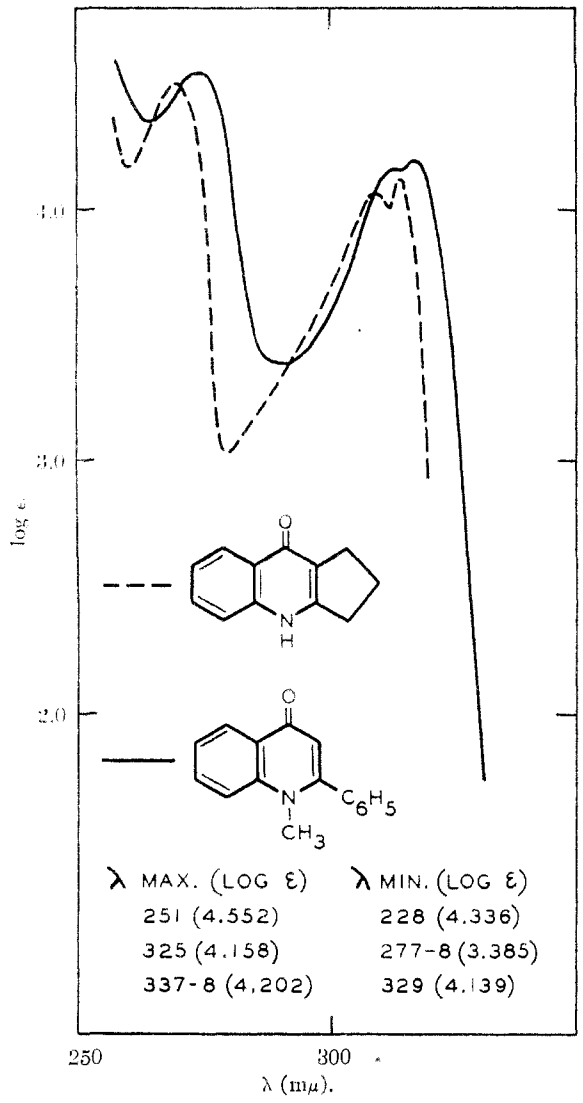


Fig. 2. -Ultraviolet spectra in ethanol.

together with phenol and benzoic acid, are also formed, besides V and a condensation product, m.p. 206–212°. In order to test the possibility of participation of the solvent in this reaction benzene was replaced by methyl benzoate. However, no methyl *p*-salicylate could be isolated from the reaction mixture. This decomposition of the ozonide in benzene is also observed at room temperature in the presence of catalytic amounts of boron trifluoride; benzoic acid and phenol are formed but *no biphenyl*. These results seem to indicate the possibility of an alternative *radical* or *ionic* path for the decomposition of the ozonide in solvents depending on the experimental conditions.

The action of methyllithium on the ozonide producing, besides V, two compounds not identified yet, is described in the Experimental section.

Experimental[27]

2-Phenylskatole.—The following adaptation of the general method described by Snyder and Smith[28] was used: A mixture of propiophenone (67 g., 0.5 mole); phenylhydrazine (54 g., 0.5 mole) and benzene (150 ml.) was refluxed for three hours using a water separator. At the end of this time the theoretical amount of water (9 ml.) had separated. Refluxing was continued and a total of 125 ml. of benzene was removed at intervals by opening the stopcock of the separator. Glacial acetic acid (140 ml.) was then added, all at once, and another 25 ml. of liquid was distilled off through the separator in the same manner as before. The mixture was then allowed to cool, and 64 ml. of boron trifluoride etherate was added all at once. The water separator was removed, the condenser set directly for refluxing, and the flask swirled to mix in the boron trifluoride etherate. Within two minutes boiling commenced and after ten minutes refluxing was so violent that cooling with a water-bath was necessary. A copious precipitate of ammonium boron trifluoride developed. After 20 minutes external heat was applied and refluxing was continued for 15 more minutes. The mixture was then cooled, poured into 3.5 liters of cold water, and stirred. A brown oil formed at first, and then set to a tan crystalline mass. This was filtered under suction, washed five times with a total of 800 ml. of water, thoroughly pressed, and sucked as dry as possible at the pump. The cloudy filtrate contained some tar and was discarded. The moist filter cake was taken up in approximately 250 ml. of boiling methanol, treated with charcoal, filtered, again heated to boiling, and set aside to crystallize. After standing overnight the crystals were collected, washed four times with methanol, and air-dried. There was obtained 41.5 g. (40%) of light tan product, melting 92–94°. The mother liquors and washings were combined, concentrated to half volume and allowed to crystallize furnishing another 13.9 g. of product, bringing the total yield to 53.5%.

2-Phenylskatole Ozonide.—The following procedure was found to be more convenient than the general procedure of Meitzer, Molho and Berguer[12] and seemed to be entirely safe: A current of ozonized oxygen was passed through a solution of 20 g. of 2-phenylskatole in 100 ml. of ethyl acetate. No cooling was applied. From time to time, when the white precipitate in the ozonization vessel threatened to clog the gas entry tube, the flow of ozone was stopped and the reaction mixture filtered. The filtrate was then returned to the ozonization vessel and further treated. When no more precipitate formed, the solution was evaporated *in vacuo* and the small amount of residue added to the combined precipitates. These combined precipitates were then washed several times with ethyl acetate. After drying *in vacuo*, there remained 19.0 g. (75%) of pure white crystalline material, m.p. 148–149°. The substance gives a positive starch–iodide test.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.56; H, 5.13; mol. wt., 255.3. Found: C, 70.84; H, 5.39; mol. wt., 258.5.[29]

The ozonization in absolute methanol at −74°[4] gave the same compound.

Hydrochloride.—Addition of hydrogen chloride in ether to an ether solution of the ozonide caused precipitation of a slightly yellow material which redissolved on standing. Part of the precipitate was washed thoroughly with ether before it could redissolve. The resulting colorless crystalline material melted at 102–104° (sint. 100°). The substance gave a positive starch–iodide test and silver nitrate test for halogen. The free ozonide could also be recovered from the hydrochloride by treatment with base.

Anal. Calcd. for $C_{15}H_{13}NO_3 \cdot HCl$: C, 61.73; H, 4.84. Found: C, 62.11; H, 4.85.

Picrate.—Treatment of an ether solution of the ozonide with ethereal picric acid, followed by rubbing and scratching, caused precipitation of a yellow crystalline picrate; golden yellow needles, dec. 71–115° (loss of gas up to 86°). The picrate was appreciably soluble in ether. The substance did not show any tendency to explode, even when scratched, hammered or melted.

Anal. Calcd. for $C_{15}H_{13}NO_3 \cdot C_6H_3N_3O_7$: C, 52.07; H, 3.33; N, 11.57. Found: C, 53.86; H, 4.52; N, 10.72.

The analytical results indicate partial loss of oxygen.

o-Benzaminoacetophenone (V).—Three hundred milligrams of 2-phenylskatole ozonide in 5 ml. of ethyl acetate was stirred under an atmosphere of hydrogen in the presence of 5

(27) All melting points are corrected, all boiling points are uncorrected. The microanalyses were carried out by Mr. S. M. Nagy and associates, Microchemical Laboratory, M.I.T.

(28) H. R. Snyder and C. W. Smith, THIS JOURNAL, **65**, 2454 (1943).

(29) Signer's method (ref. 15) was used employing acetone as a solvent; the ozonide is insoluble in cyclopentadecanone; *cf.* H. Keller and H. V. Halban, *Helv. Chim. Acta*, **27**, 1439 (1944).

mg. of palladium black. The uptake of hydrogen was 35.3 cc. in 10 minutes. The solution was filtered and evaporated. The crystalline residue, weighing 265 mg., was recrystallized from methanol, yielding 110 mg. of fine greenish needles, m.p. 97–100° (sint. 95°; clear, colorless melt). The crystals were insoluble in 2 *N* sulfuric acid in the cold, but dissolved on heating, while a white film formed on the surface of the solution. The solution then gave a positive azo test with β-naphthol.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.87; H, 5.47. Found: C, 76.09; H, 5.76.

The same product was obtained by melting the ozonide or refluxing it in chloroform in the presence of *p*-toluenesulfonic acid.

***o*-Benzylaminophenylmethylcarbinol (IV).**—An ether solution of 450 mg. of ozonide was slowly added to excess lithium aluminum hydride in ether with ice-bath cooling. The solution was then allowed to come to 25° and to stand for three hours. The mixture was then decomposed with ice and extracted with ether. The ether extract, after drying over sodium sulfate, was evaporated to leave 290 mg. of a yellowish oil. The oil was benzoylated with excess benzoyl chloride in ether, using ten drops of pyridine as catalyst. The ether solution was then washed with 2 *N* hydrochloric acid, 2 *N* potassium hydroxide and water. After drying over sodium sulfate the ether was evaporated, leaving 390 mg. of an oil which was taken up in benzene and filtered through alumina. The colorless glass-hard prisms which were thus obtained melted at 127–129° and could be recrystallized from methanol or benzene–petroleum ether, whereby the melting point was raised to 132–134°. The infrared spectrum clearly showed the ester and amide bands for the dibenzoyl compound.

Anal. Calcd. for $C_{29}H_{25}NO_3$: C, 79.95; H, 5.79; N, 3.37. Found: C, 79.67; H, 5.94; N, 3.59.

***o*-Benzaminophenylmethylcarbinol (III).**—An alcoholic solution of 500 mg. of the ozonide was slowly added to 300 mg. of sodium borohydride in 10 ml. of alcohol at 0°. Mild effervescence was observed during the addition. Ten ml. of alcohol was then added and the mixture was refluxed for an hour. The reaction mixture was then cooled and decomposed with ice and water. Extraction with ether and drying of the extract over sodium sulfate was followed by evaporation of the extract to leave 550 mg. of a yellow oil which crystallized on standing. Recrystallization from carbon tetrachloride produced 440 mg. of hard grayish crystalline nodules, m.p. 109–112° (clear colorless melt).

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.66; H, 6.27. Found: C, 73.95; H, 6.27.

1-Methyl-2-phenyl-4-quinolone (XII).—To 1.1 g. of potassium metal chips in 60 ml. of benzene was added a benzene suspension of 2.5 g. of ozonide (II). The mixture was then refluxed five hours. After standing overnight the remaining pellets of potassium were removed manually, and 1.5 g. of methyl iodide was added. The mixture then stood for three hours, was refluxed for one hour, cooled and filtered. Evaporation of the filtrate left 1.5 g. of dark red oil smelling strongly of *o*-benzoylaminoacetophenone. The oil was taken up in benzene and chromatographed over 45 g. of alumina. Benzene eluted 600 mg. of a colorless crystalline material which was identified as *o*-benzoylaminoacetophenone. Chloroform then eluted a slightly yellow crystalline material, m.p. 136°, which, on the basis of its infrared and ultraviolet spectrum, was identified as 1-methyl-2-phenyl-4-quinolone.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.66; H, 5.57; N, 5.95. Found: C, 81.51; H, 5.77; N, 6.33.

Infrared Spectrum.—The two bands at 6.14 and 6.21 μ (in chloroform) correspond closely to the two similar bands of 2,3-cyclopenteno-4-quinolone, ref. 1, p. 2645, Table I.

2-Phenyl-3-methyl-3-hydroperoxyindolenine (VI).—The crude, dry 2-phenylskatole (30 g.) was recrystallized from benzene–ligroin, the solution being boiled somewhat longer than usual before being set aside to cool. After three days standing, approximately 3 g. of crystals was obtained, melting 125–149° with evolution of gas. Recrystallization from ethyl acetate yielded 2.1 g. of colorless, glossy rods, m.p. 154–156° (gas evolution from 141°; sublimation in droplets from 145°; quiet, slightly yellow melt). The compound gives a positive starch–iodide test.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.27; H, 5.47; N, 5.85. Found: C, 75.21; H, 5.57; N, 5.88.

Hydrochloride.—Treatment of an ethereal solution of the peroxide with hydrogen chloride in ether yielded the hydrochloride as slightly yellow, small, cubic prisms, m.p. 154–157° (droplets from 144°, dark red melt, no gas evolution).

Anal. Calcd. for $C_{15}H_{14}NO_2Cl$: C, 65.34; H, 5.12. Found: C, 65.47; H, 5.34.

Acid Rearrangement.—A few drops of an ether solution of hydrogen chloride was added to a solution of 50 mg. of the hydroperoxide (VI) in 10 ml. of chloroform. After the mixture had been boiled for 15 minutes, the infrared spectrum of the solution was identical with that of a chloroform solution of *o*-benzoylaminoacetophenone.

Thermal Rearrangement.—Fifty milligrams of the hydroperoxide was heated slowly on an oil-bath. Loss of oxygen occurred suddenly at 142°. The infrared spectrum of the resulting dark melt was identical with the infrared spectrum of *o*-benzoylaminoacetophenone (V).

Reduction of the Hydroperoxide (VI) with Lithium Aluminum Hydride.—Fifty milligrams of the hydroperoxide (VI) dissolved in 3 ml. of ether was added dropwise to 20 mg. of lithium aluminum hyride in 3 ml. of ether. There was immediate vigorous reaction. The mixture was allowed to stand for two minutes, then decomposed with ice and extracted with ether. After drying of the ether extract over sodium sulfate, followed by evaporation of the ether on the steam-bath, there remained 42 mg. of a colorless oil with the odor of 2-phenylskatole. On standing, the oil crystallized in characteristic ice-blossom crystals, m.p. 88°. After recrystallization, the material melted at 93–94°, and had an infrared spectrum identical with that of *2-phenylskatole*.

2-Phenyl-3-methyl-3-hydroxyindolenine (VII). A. Reaction of 2-Phenyl-3-methyl-3-hydroperoxyindolenine with Sodium Borohydride.—Two hundred milligrams of VI dissolved in 4 ml. of absolute ethanol was added to 50 mg. of sodium borohydride in 4 ml. of ethanol at 25°. A mild, smooth reaction occurred, with evolution of gas. After 15 minutes, the reaction mixture was evaporated to dryness *in vacuo*. The residue was taken up in ether; the ether solution was dried over sodium sulfate, filtered and evaporated on the steam-bath. A fragrant yellow oil (230 mg.) remained which partly crystallized on standing. On recrystallization from petroleum ether, two types of crystals were obtained: small buttons (A), and one large brilliant crystal (B). A melted at 142–144° (sublimation in small rods from 120°; sintering 135°; resolidification 139°; colorless, quiet melt). The melting point was undepressed by admixture of 2-phenyl-3-methyl-3-hydroxyindolenine obtained by hydrogenation of the hydroperoxide. B, m.p. 94° (sintering 85°) was identical with 2-phenylskatole.

B. **Catalytic Hydrogenation.**—Two hundred milligrams of 2-phenylskatole hydroperoxide (VI) in 5 ml. of ethyl acetate was reduced at 25° with hydrogen at atmospheric pressure, in the presence of 20 mg. of palladium black. In the course of 12 minutes, 21.5 cc. of hydrogen was absorbed. The solution was filtered and evaporated to dryness. The remaining yellow-brown oil was degassed *in vacuo*, then dissolved in ether. Slow evaporation of the ether solution left clusters of brownish needles. After two washings with benzene–petroleum ether there remained colorless crystals, m.p. 138–142° (sintering 128°, sublimation in droplets 135°). The product gave no depression on mixed melting point with a sodium borohydride reduction product of the peroxide (see above).

If the hydrogenation was stopped after uptake of 1 mole of hydrogen, unchanged hydroperoxide was still present in the reaction mixture. When the hydroperoxide was allowed to take up two moles of hydrogen, phenylskatole (I) could be isolated, probably formed *via* the non-isolable indoline (VIII).

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.67; H, 5.87. Found: C, 80.20; H, 6.04.

Hydrochloride.—A solution of 20 mg. of the hydroxy compound in 1 ml. of chloroform was treated with one drop of concentrated hydrochloric acid and heated on the steam-bath. Evaporation of the solution and washing of the residue with chloroform left slightly yellow tiny needles, m.p. 178–182° (sudden gas evolution 184°, dark brown melt).

Anal. Calcd. for $C_{15}H_{14}NOCl$: C, 69.36; H, 5.43. Found: C, 69.07; H, 5.41.

Reaction of the Ozonide with Phenylmagnesium Bromide.—A Grignard reagent prepared from 700 mg. of magnesium

turnings and 3 ml. of bromobenzene in 20 ml. of ether was added to a suspension of 2.8 g. of ozonide in 50 ml. of warm benzene. Vigorous reaction occurred, accompanied by separation of an olive-colored sludge. After standing for 20 minutes, the mixture was decomposed with ice and water and filtered. The layers in the filtrate were separated and the red organic layer dried over sodium sulfate and evaporated on the steam-bath. The residue, 4.5 g. of a dark-red oil, was taken up in benzene and chromatographed over 120 g. of alumina (standardized). Benzene eluted two substances: first 50 mg. of biphenyl (identified by odor and infrared spectrum), and subsequently 450 mg. of *o*-benzoylaminoacetophenone (identified by mixed m.p. with an authentic sample). Chloroform then eluted two more substances. The first crystallized from ether, yielding 60 mg. of magnificent needles, m.p. 192–195° (sintered 187°).

Anal. Calcd. for $C_{21}H_{18}NO_2Br$: C, 63.64; H, 4.58; N, 3.54; Br, 20.16. Found: C, 65.45; H, 4.94; N, 3.57; Br, 16.58. (The analysis indicates contamination by the bromine-free carbinol.)

The second substance, presumably *o*-benzaminophenylmethyl carbinol, eluted by chloroform, crystallized from ether as rectangular prisms, m.p. 145–147°. (A mixed m.p. with the substance from the methyl lithium reaction, m.p. 153–157°, showed deep depression.)

Anal. Calcd. for $C_{21}H_{19}NO_2$: C, 79.46; H, 6.03; N, 4.41. Found: C, 79.18; H, 6.04; N, 4.42.

Reaction of the Ozonide with *n*-Butylmagnesium Bromide.—A Grignard solution prepared from 750 mg. (31.4 millimoles) of magnesium turnings and 4.3 g. (31.4 millimoles) of *n*-butyl bromide in 50 ml. of ether was added to a suspension of 4.0 g. (15.7 millimoles) of ozonide in 50 ml. of benzene. An exothermic reaction occurred, accompanied by formation of an olive-tan sludge. The mixture was allowed to stand for three days, decomposed with ice and water, and filtered. The layers in the filtrate were separated and the aqueous layer discarded. The organic layer was extracted with 5% sodium bicarbonate solution. Acidification of the extract, washing with ether, and drying and evaporation of the ether extract left approximately 1 mg. of crystalline material which was not further investigated. The organic layer was then extracted with 1 *N* sodium hydroxide solution and the extract treated as just described. The residue was a small amount of reddish-brown oil which was not further investigated. The organic layer was then dried over magnesium sulfate, diluted with 30 ml. of petroleum ether and poured on a column of 100 g. of alumina. Benzene eluted 2.28 g. of *o*-benzoylaminoacetophenone (identified by its infrared spectrum). Ether then eluted 1.31 g. of a substance as a green ether solution showing a red fluorescence. After two recrystallizations from benzene–petroleum ether, the substance, presumably *o*-benzamino-*n*-butylmethylcarbinol, was obtained as colorless crystals, m.p. 118–120.5°.

Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.72; H, 7.79; N, 4.71. Found: C, 76.88; H, 7.98; N, 4.84.

Subsequent elution with chloroform yielded 140 mg. of a purple oil, which was taken up in methanol, decolorized with charcoal, filtered and evaporated to dryness. On recrystallization from benzene–petroleum ether colorless prisms were obtained, m.p. 154–156° (clear colorless melt).

Anal. Calcd. for $C_{15}H_{15}NO$: C, 80.13; H, 6.73; N, 6.22. Found: C, 80.13; H, 6.16; N, 6.31.

Infrared Spectrum.—The solution of this compound in chloroform shows the following major bands: 2.94 (sharp imino band); 3.16 (hydroxyl); 5.78; 6.17 (Ph–NH–); 6.81; 7.30; 7.60; 8.52; 8.93.

Reaction of the Ozonide with Lithiummethyl.—An ether solution of lithiummethyl, prepared from 210 mg. of lithium and 4.3 g. of methyl iodide, was added to a suspension of 7 g. of ozonide in 50 ml. of benzene. There was distinct warming and gas evolution during the addition. The mixture was refluxed for three hours, then left at room temperature for 24 hours. The solution was decomposed with water and the organic layer separated and thoroughly washed with water. The deep red solution, exhibiting a powerful green fluorescence, was dried over sodium sulfate and evaporated to dryness. The residual red oil was taken up in benzene and chromatographed over 25 g. of alumina. Benzene first eluted a considerable amount of a crystalline material identified as *o*-benzoylaminoacetophenone. A second material was then eluted by benzene; this substance crystallized from benzene–petroleum ether as glistening red prisms, m.p. 153–157° (sublimed in long needles from 123°; sintered 149.5°; clear pink melt).

Anal. Found: C, 78.67; H, 6.18; N, 6.27.

Infrared Spectrum.—Major bands at 2.87; 3.06; 6.0; 6.32; these bands indicate the structure of some sort of an *o*-benzaminophenylcarbinol.

Chloroform then eluted a crystalline red substance which, after charcoal treatment and two recrystallizations from benzene–ligroin melted at 145–146° (sublimed in colorless rods from 99°; clear red melt).

Anal. Calcd. for $C_{16}H_{15}NO$: C, 81.01; H, 6.35; N, 5.90. Found: C, 80.80; H, 6.16; N, 6.25.

The infrared spectrum of this compound in chloroform showed a characteristic band at 5.76 μ.

Decomposition of 2-Phenylskatole Ozonide in Refluxing Benzene.—Five grams of ozonide was refluxed for 24 hours in benzene. After cooling, extraction of the red benzene solution with 5% sodium bicarbonate, followed by the usual acidification of the extract, yielded 150 mg. of *benzoic acid*. The benzene solution was next extracted thoroughly with 1 *N* sodium hydroxide. The extract, on acidification, yielded 730 mg. of mixed phenolic materials, in which the odor of *phenol* could clearly be detected. When the phenol was removed by washing with benzene, the residue, after purification by dissolution in alkali and reprecipitation, formed colorless platelets, m.p. 168°, the infrared spectrum of which was identical with that of *o-benzaminophenol*. After these extractions, the benzene solution was dried over magnesium sulfate and chromatographed over 100 g. of alumina. Benzene eluted approximately 40 mg. of *biphenyl*, followed by 2.98 g. of *o*-benzoylaminoacetophenone. Ether then eluted approximately 50 mg. of a yellowish crystalline substance, m.p. 206–212° (clear yellowish melt).

Anal. Calcd. for $(C_{13}H_{11}NO_2)_n$: C, 73.23; H, 5.20. Found: C, 73.82; H, 5.25.

The material was not investigated further. Further elution of the column with chloroform yielded only slight amounts of red material.

The same experiment carried out at *room temperature* in the presence of a drop of boron trifluoride etherate (commercial solution) gave a dark red solution from which aqueous sodium bicarbonate extracted 280 mg. of *benzoic acid* and sodium carbonate extracted 0.8 g. of a solid fraction with distinct phenolic odor. Washing of this fraction with ether removed some dark material together with *phenol*. The odorless residue was recrystallized several times from absolute ether, glistening platelets, m.p. 168–170°, identical with *o-benzaminophenol*.

Anal. Calcd. for $C_{13}H_{11}NO_2$: C, 73.24; H, 5.16; N, 6.57. Found: C, 72.95; H, 5.23; N, 6.37.

The ether layer remaining from the extraction with sodium carbonate was dried, evaporated, taken up in benzene, and filtered through an alumina column. *No biphenyl* could be isolated from the initial elutions.

Decomposition of the Ozonide in Methyl Benzoate.—A solution of 4 g. of the ozonide in 125 ml. of methyl benzoate was held at 90° for 24 hours. The yellow cooled solution was then extracted with 2 *N* alkali. The alkaline extract was acidified and extracted with ether. Extraction of the ether layer with sodium bicarbonate gave 465 mg. of benzoic acid, and subsequent extraction with sodium carbonate gave 262 mg. of a phenolic compound containing no methyl *p*-salicylate (absence of carbomethoxy band in the infrared spectrum)[30] and consisting mainly of *o*-benzaminophenol.

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(30) The test for *p*-substituted phenols with α-nitroso-β-naphthol (O. Gerngross, K. Voss and H. Herfeld, *Ber.*, **66**, 435 (1933)) cannot be used for *p*-salicylic acid and its esters.