tered and evaporated under reduced pressure. The residue, presumably the diazoketone, was a pale yellow viscous liquid.

A suspension of 50 mg. of silver oxide in 5 ml. of anhydrous methanol was refluxed on a steam-bath until a silver mirror was formed (15 minutes). Then a solution of the diazoketone in a few ml. of methanol and an additional 50 mg. of silver oxide were added and the whole was refluxed for eight hours. Evaporation of the filtered solution yielded a viscous yellow liquid which could not be made to crystallize.

A solution of the product in 10 ml. of benzene was passed through a column (150 × 7 mm.) of aluminum oxide (Fisher Scientific Co.). A yellow band appeared near the top of the column. Six 10-ml. portions of benzene (eluates collected in separate flasks) served to wash through 100 mg. of colorless liquid. The yellow material on the column was finally eluted by benzene–methanol and methanol.

The colorless liquid (100 mg.), which did not crystallize when seeded with the alpha (m.p. 126°) or beta (m.p. 114°) forms of the dimethyl ester of 7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (XI), was hydrolyzed by refluxing with a solution of 0.28 ml. of *N* sodium hydroxide (sufficient for one ester group) in 2.5 ml. of methanol for three hours. The methanol was removed by evaporation in a current of air, and water and a little alkali were added to dissolve the sodium salt of the acid ester. A small quantity of insoluble material was extracted into ether, the clear aqueous solution was acidified with hydrochloric acid and the precipitated acid ester was extracted with ether. Evaporation of the ether left a colorless liquid which crystallized readily when scratched under ether–petroleum ether. The colorless solid was collected on a filter; weight 50 mg., m.p. 143–145°. The acid ester crystallized from ether–petroleum ether in colorless needles, m.p. 147–148°. The neutral ester, presumably the **dimethyl ester of *cis*-1-carboxy-2-methyl-2-carboxymethyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (X)**, prepared by means of diazomethane crystallized from petroleum ether (60–75°) in colorless needles, m.p. 74–75°.

*Anal.* Calcd. for $C_{21}H_{24}O_5$: C, 70.8; H, 6.7. Found: C, 70.7; H, 6.7.

(b) On ***cis*-1-Carboxy-2-carbomethoxy-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene.**—When 180 mg. of the acid ester (IX, m.p. 156–157°) was added to a solution of 1.2 ml. of oxalyl chloride in 1.2 ml. of benzene a crust of solid formed on the bottom and adhered to the glass. By tapping and swirling, the solid was dislodged and finally (15 minutes) went into solution. After two hours the yellow solution was evaporated under reduced pressure, and the residue treated with 1 ml. of dry benzene, which was then removed under reduced pressure. The residual acid chloride was added to ethereal diazomethane and the diazoketone was rearranged exactly in the manner described for its isomer in the preceding section.

A solution of the product, a viscous yellow liquid, in 5 ml. of benzene and 40 ml. of petroleum ether (60–75°) was passed through a column of alumina (150 × 7 mm.) which had been wet with petroleum ether. The following fractions were collected: (1) 40 ml. p.e. + 5 ml. benzene (nothing on evaporation); (2) 8 ml. p.e. + 2 ml. benzene (nothing); (3) 5 ml. p.e. + 5 ml. benzene (nothing); (4) 5 ml. p.e. + 5 ml. benzene (trace of colorless liquid); (5) 10 ml. benzene (45 mg. colorless liquid); (6) 10 ml. benzene (30 mg. colorless liquid); (7) 10 ml. benzene + 1 ml. methanol (30 mg. viscous yellow liquid); (8) 10 ml. benzene (viscous yellow liquid). Small amounts of methanol were added to each fraction after evaporation and the solutions allowed to evaporate slowly but no crystals appeared except in (7).

The colorless liquids in fractions 4, 5 and 6 were combined and hydrolyzed by boiling with a solution of 0.22 ml. of *N* sodium hydroxide in 2 ml. of methanol for three hours. The acid ester was isolated as described in the preceding preparation; yield 45 mg. of colorless solid, m.p. 144–147°. From ether–petroleum ether it crystallized in needles; m.p. 146–148° alone and when mixed with the product (m.p. 146–148°) obtained from the isomeric acid ester.

Fractions 7 and 8 were combined and dissolved in 10 ml. of benzene and passed through a 25 × 7 mm. column of alumina and washed with two 10-ml. portions of benzene, one of 1:1 benzene–chloroform and finally chloroform. The first 10-ml. fraction contained colorless liquid which crystallized readily on scratching under methanol; the second and third fractions contained nothing and the last ones contained viscous yellow gum. The crystals from the first fraction were collected on a filter; yield 10 mg., m.p. 124–126°. From methanol the product crystallized in clusters of thick colorless plates; m.p. 126–127° alone and when mixed with authentic alpha form (m.p. 126–127°, precursor of isoequilenin) of the dimethyl ester of *cis*-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (XI); the melt solidified readily on cooling and on reheating melted at 126–127°.

**Ultraviolet Absorption Spectra.**—Ethanol was used as the solvent for all of the compounds in the figures with the exception of the anhydrides Ia and Ib for which chloroform was employed.

ANN ARBOR, MICH. RECEIVED DECEMBER 4, 1950

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

# Ring Effects in Autoxidation. A New Type of Camps Reaction[1,2]

BY BERNHARD WITKOP,[3] JAMES B. PATRICK[3,4] AND MYRON ROSENBLUM

2,3-Cyclopentenoindole (I), by catalytic oxidation as well as autoxidation, is readily converted to 1-aza-7,8-benzcyclooctanedi-2,6-one (VII), opened by base (and acid) to yield δ-*o*-aminobenzoylbutyric acid (IX). The homologous lactam (VIII) with base undergoes a new type of Camps reaction to yield 2,3-cyclopenteno-4-quinolone (X), while the homologous 10-membered lactam undergoes intramolecular angular condensation to tetrahydrophenanthridone (XI). 2,3-Cycloöctenoindole (IV) is easily converted to the 2-keto derivative VI by autoxidation. VI was synthesized by applying the Japp–Klingemann reaction to 2-hydroxymethylenecycloöctanone. Attention is directed to the diagnostic value of the infrared and ultraviolet absorption spectra of α- and γ-quinolones, permitting an easy distinction between the two types of compounds.

It has been shown that catalytic oxygenation,[5,6] as well as autoxidation,[7] converts tetrahydrocarbazole (II) into the hydroperoxide V ($n = 6$) which easily rearranges to the lactam (VIII). We have now extended these reactions to homologous tricyclic indole derivatives in which the size of the isocyclic ring C varied from 5 to 8 members. The results are summarized in the chart.[8]

Whilst tetrahydrocarbazole (II) is stable in various solvents (ethyl acetate, chloroform, alcohol, etc.), 2,3-cyclopentenoindole (I)[9] in solution (*e.g.*,

(1) On the Mechanism of Oxidation. II. First paper in this series, THIS JOURNAL, **73**, 2196 (1951).

(2) Presented in part before the Summer Symposium on Natural Products, University of New Brunswick, Fredericton, N. B., August 22–26, 1950.

(3) National Heart Institute, Washington 14, D. C.

(4) Research Corporation Fellow 1950.

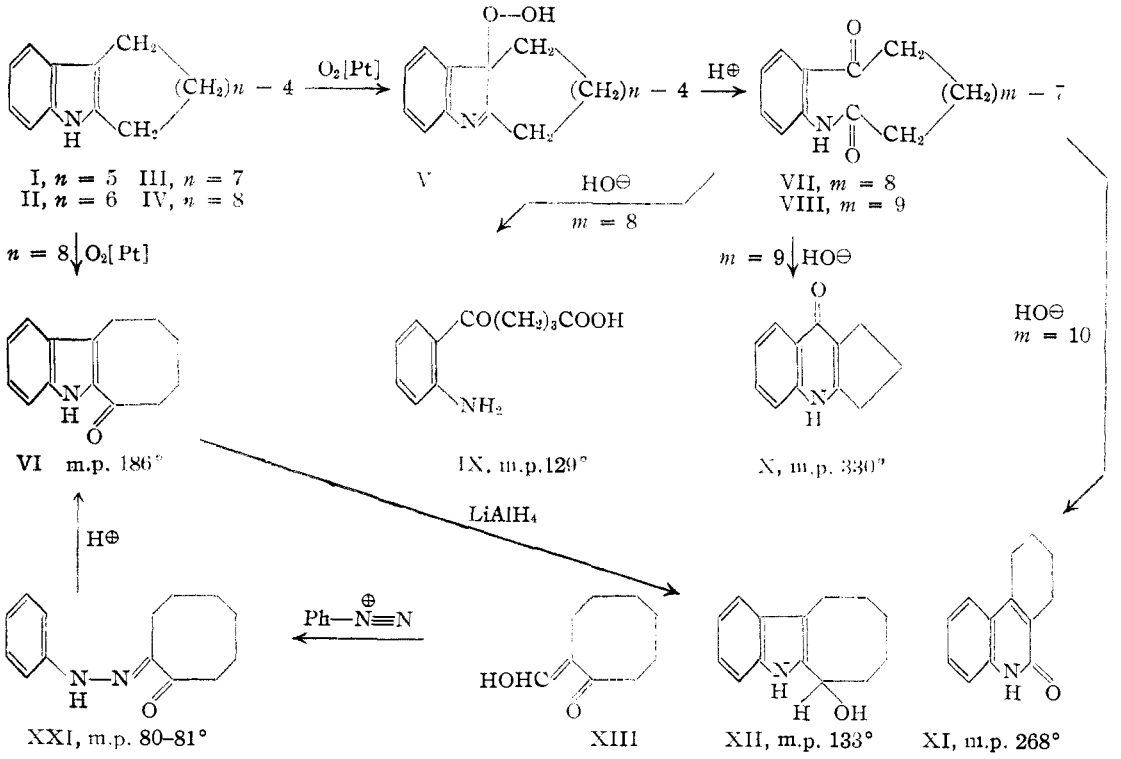
(5) B. Witkop and J. B. Patrick, THIS JOURNAL, **72**, 633, 1428 (1950).

(6) B. Witkop and J. B. Patrick, *ibid.*, **73**, 2188 (1951).

(7) R. J. S. Beer, L. McGrath and A. Robertson, *J. Chem. Soc.*, 2118 (1950).

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

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




chloroform) is very unstable and changes rapidly (10 to 40 hours) into the lactam (VII). The intermediate hydroperoxide was not isolated. Catalytic oxygenation of I, after a short induction period (Fig. 1), directly led to the same lactam (VII). Figure 1 represents the rates of oxygen uptake for the four homologs I–IV.

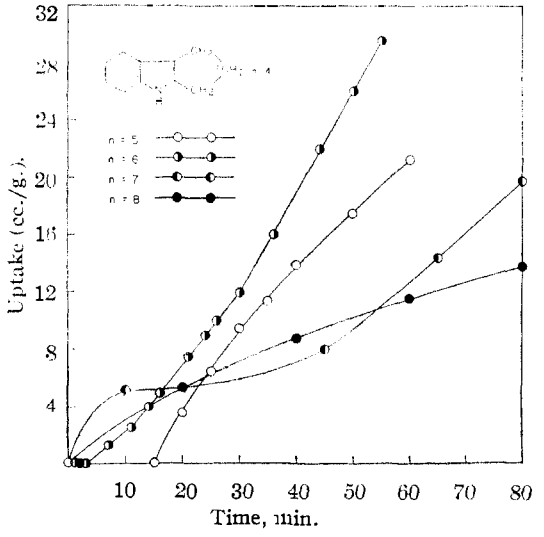



Fig. 1.—Comparative rates of catalytic oxygenation of compounds I–IV under comparable conditions.

The ultraviolet absorption spectrum of the 8-membered lactam (VII, Fig. 2), comparable to that of *o*-acetaminoacetophenone (XIV),[10] shows a distinct *hypsochromic effect*. The 9-membered lactam (VIII) shows this effect to an even greater extent and differs also in the infrared spectrum (Fig. 3; ref. 6, Fig. 1A). Figure 4A shows one of the possible conformations of VIII in a Stuart model. It is impossible to construct a model of VIII which avoids the thermodynamically unfavorable "*opposed*" conformations.[11] Since an ionic excited state of VIII is necessarily planar, the rigidity of the lactam accounts for the hypsochromic effect observed. This rigidity diminishes with increasing size of the lactam ring as the model for an 11-membered lactam (Fig. 4B) clearly demonstrates.

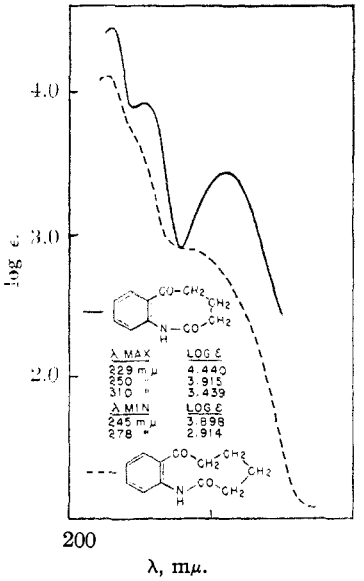



Fig. 2.—Ultraviolet spectra in ether.

A reaction that permits one to assess the importance and nature of this "*medium-size ring effect*"

(10) H. Dannenberg, *Z. für Naturforschung*, **4B**, 342 (1949).

(11) *Cf* V. Prelog, *J. Chem. Soc.*, 420 (1950).

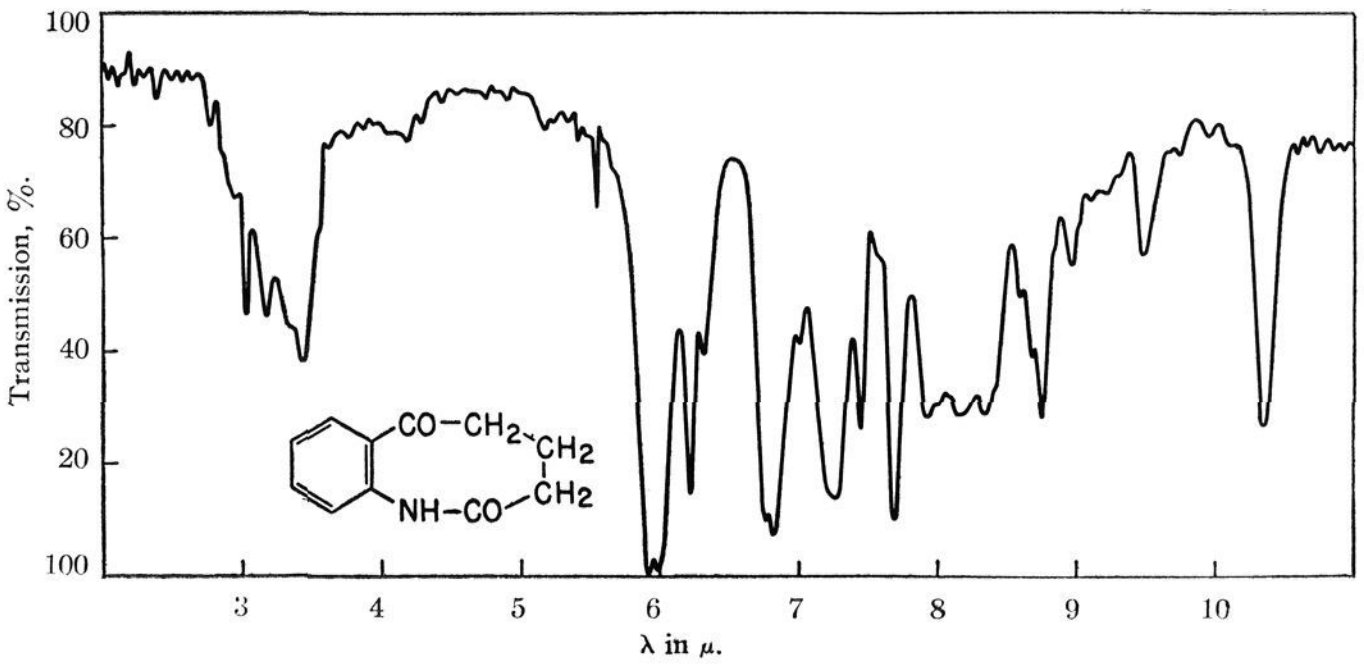



Fig. 3.—Infrared spectrum of VII in chloroform.

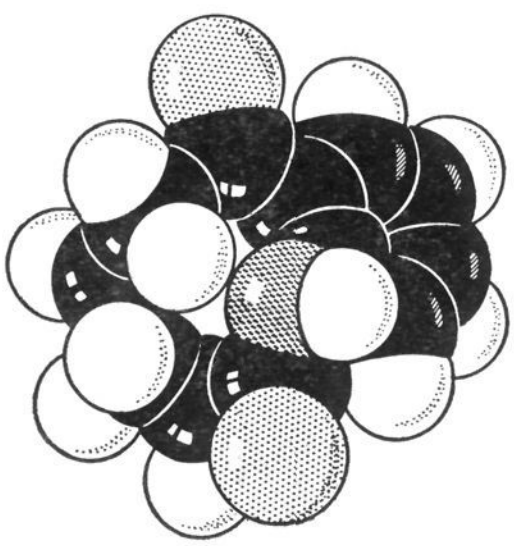


Fig. 4A.—Conformation of the 9-membered lactam (VIII) approaching the transition state XVIII.

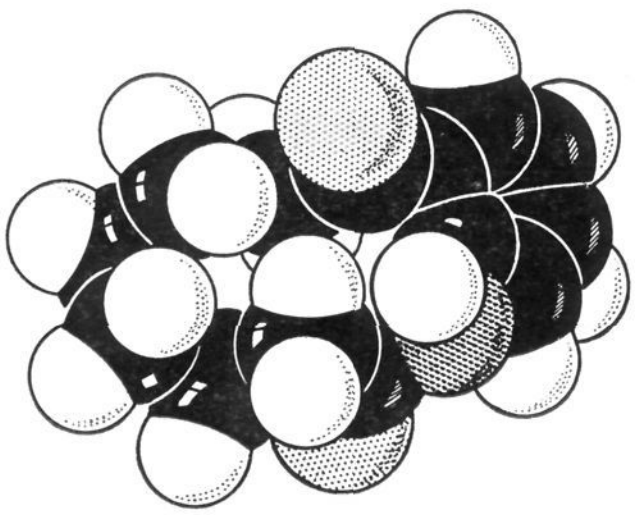
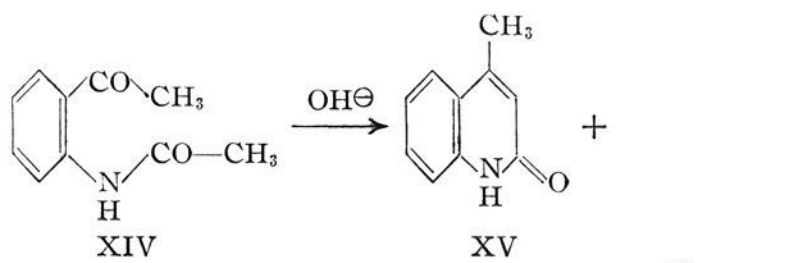


Fig. 4B.—Conformation of an 11-membered lactam approaching the transition state XVII.

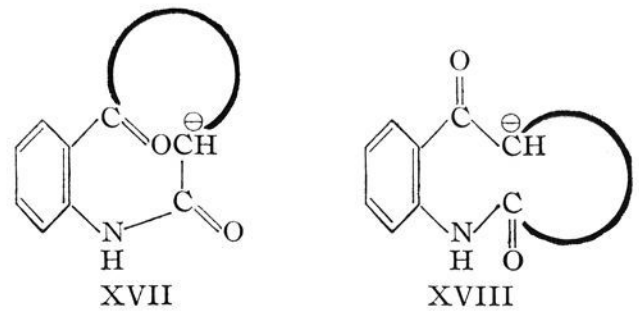
is the intramolecular base-catalyzed condensation of the type first described by Camps[12] in the open series. There, for example, *o*-acetaminoacetophenone (XIV), under the action of base, yields 70% of 4-methylcarbostyril (XV) and 20% of 2-methyl-4-quinolone (XVI).

While the lactam (VII) is opened by base to give the amino acid IX, VIII under these conditions yields exclusively the 4-quinolone derivative (X)

(12) R. Camps, *Ber.*, **32**, 3228 (1899); *Arch. Pharm.*, **237**, 659 (1899).




identified by synthesis.[13] Thus, of the two possible conformations approaching the transition state (XVII, XVIII), only XVIII seems to be favored.




Special models[14] of the two stages preceding XVII and XVIII (Fig. 5) do not disclose a significant reason for this difference.

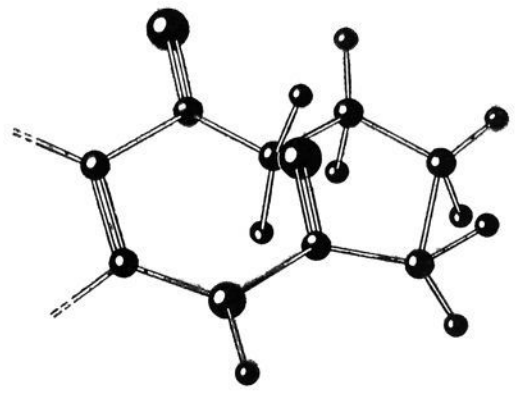


Fig. 5.—Model of the transition state XVIII of the lactam VIII.

(13) B. K. Blount, W. H. Perkin and S. G. P. Plant, *J. Chem. Soc.*, 1975 (1929).

(14) We take pleasure in thanking Dr. D. H. R. Barton for giving us an opportunity to use these individually constructed models.

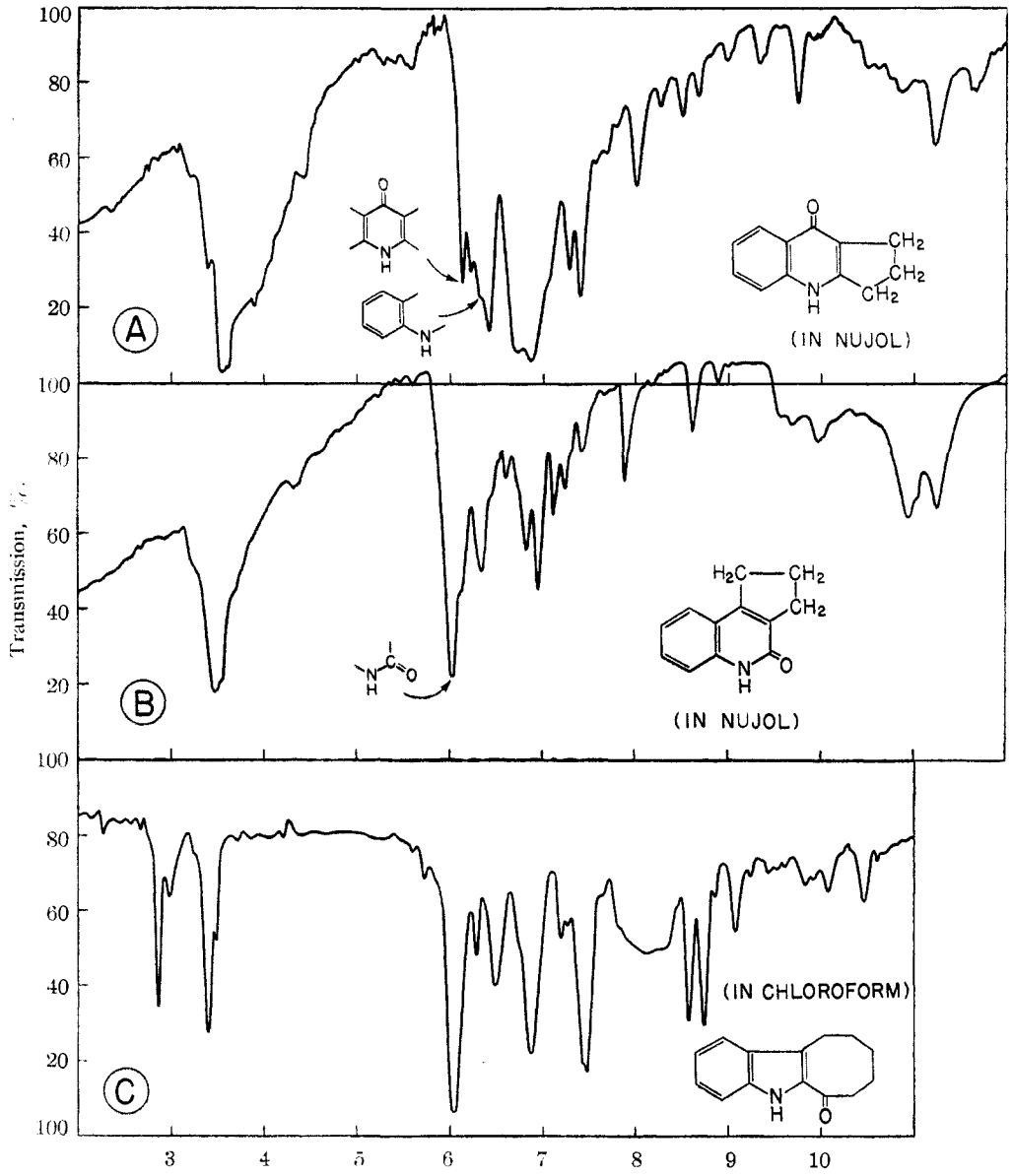



Fig. 6.

When 2,3-cycloheptenoindole (III)[26] was oxygenated catalytically and, without isolation of the intermediate peroxide, subjected to chromatographic purification, the 10-membered lactam, apparently under the action of the basic aluminum oxide in the column, yielded tetrahydrophenanthridone (XI). In this case, the favored conformation of the reactive intermediate corresponds to XVII.

In a case where a complicated lactam of the critical ring size undergoes the Camps reaction, a choice between the α- or γ-quinolone structure of the product can be made on the basis of the ultraviolet and infrared spectra. The ultraviolet spectra of α-quinolones show three outstanding characteristic peaks (Fig. 8, Table I),[15] whereas γ-quinolones show two principal bands of absorption (Fig. 7). Both types of spectra exhibit a characteristic bifurcation of one peak. The diagnostic difference in the infrared spectra is due to the absorption of the two amide systems –NH–CO– (α-quinolone) and —NH—C=C—C=O (γ-quinolone) in the vicinity of 6 microns[16] where γ-quinolones absorb at longer wave lengths (Figs. 6AB; *cf.* Table I).

2,3-Cycloöctenoindole (IV), in which ring C itself approaches the critical ring size, after catalytic oxygenation and chromatographic adsorption, gave a compound of the expected empirical composition $C_{14}H_{15}NO$, m.p. 186°, *not* identical with the α- and γ-quinolone derivatives XIX[13] and XX synthesized for comparison. The attack of oxygen, therefore, must have occurred at a posi-

(15) E. A. Steck, G. W. Ewing and F. C. Nachod, THIS JOURNAL, **71**, 238 (1949); **68**, 2184 (1946).

(16) *Cf.* R. S. Rasmussen, *Fortschritte der Chemie org. Naturstoffe*, Springer Verlag, Wien, 1948, p. 371.

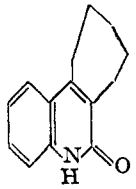
TABLE I

ULTRAVIOLET[a] AND INFRARED ABSORPTION

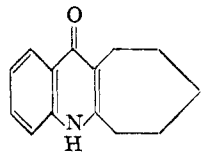
| Compound | λmax. (mμ) | log ε | Peaks in the infrared α- and γ-quinolone region (in μ) |
|---|---|---|---|
| 3,4-Cyclopenteno-2-quinolone or 4-keto-2,3,4,5-tetrahydro-α-quinindene | 228 | 4.526 | 6.03 nujol |
| | 271 | 3.184 | |
| | 281 | 3.870 | |
| | 322 | 3.906 | |
| | 335 | 3.778 | |
| Tetrahydrophenanthridone (XI) | 269 | 3.834 | 6.04 chloroform |
| | (277 | 3.761) | |
| | 321 | 3.992 | |
| | (336 | 3.706) | |
| 3,4-Cycloheptено-2-quinolone (XIX) | 276 | 3.866 | 6.02 chloroform |
| | 285 | 3.804 | |
| | 330 | 3.912 | |
| 2,3-Cyclopenteno-4-quinolone or 9-keto-2,3,4,9-tetrahydro-β-quinindene (X) | 238 | 4.483 | 6.15 |
| | 317 | 4.086 | 6.20 nujol |
| | 331 | 4.126 | |
| 2,3-Cycloheptено-4-quinolone (XX) | 247 | 4.369 | 6.08 |
| | 323 | 3.990 | 6.15 |
| | 334 | 4.001 | 6.23 nujol |
| 2-Keto-1,2,3,4,5,6-hexahydrocyclooctindole (VI) | 212 | 4.192 | 6.05 chloroform |
| | 237 | 4.009 | |
| | 314 | 4.194 | |
| Indole-3-aldehyde | 243 | 4.073 | |
| | 260 | 3.997 | |
| | 296 | 4.072 | |

[a] Ultraviolet spectra were measured using solutions of the compounds in absolute alcohol.

tion different from all the cases discussed so far. Of the two likely positions, 2 and 7, 2 appeared more probable for three reasons: (i) Analogs for



XIX



XX

attack at this position are known in the tetrahydrocarbazole series,[17,18] (ii) while there are five principal resonance structures contributing to the stabilization of the intermediate radical at position 2, there are only two such structures for position 7, (iii) the ultraviolet absorption spectrum of VI (Table I) is more closely related to that of 2-keto-tetrahydrocarbazole than to that of indole-β-aldehyde (Table I). The synthesis of VI, *via* the intermediates XIII and XXI, confirmed these views. 2,3-Cycloöctenoindole (IV), on recrystallization from alcohol or benzene or even on storage in the crystalline state, is autoxidized to the same compound VI.[19] The corresponding alcohol XII

(17) S. G. P. Plant and M. Tomlinson, *J. Chem. Soc.*, 3324 (1931).

(18) S. G. P. Plant, R. Robinson and M. Tomlinson, *Nature*, **165**, 928 (1950).

(19) There is no indication in the infrared spectrum of IV that the 8-membered ring C favors the presence of the indolenine form. Since IV is free of ring strain, the general stereochemistry of the molecule apparently facilitates autoxidation; with regard to the stereochemistry of autoxidation, *cf.* H. Kleinfeller and C. Odefey, *Angew. Chem.*, **62**, 342 (1950).

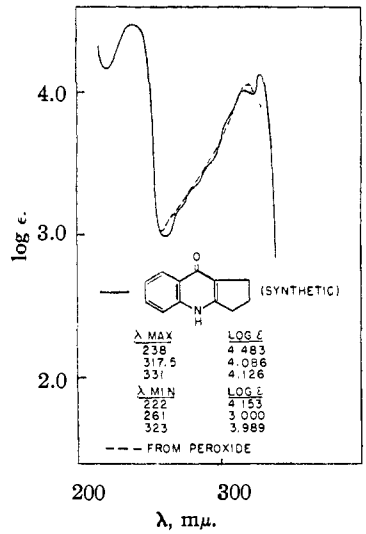



Fig. 7.—Ultraviolet spectrum in ethanol.

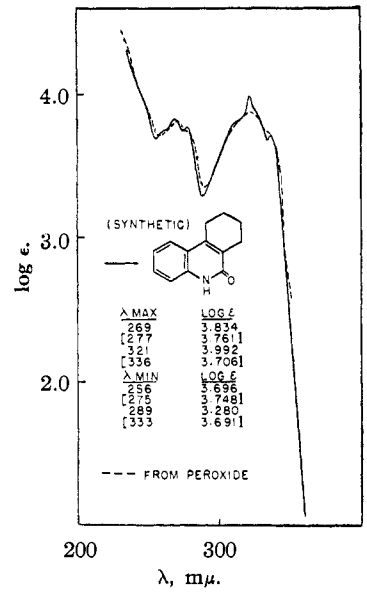



Fig. 8.—Ultraviolet spectrum in ethanol.

is obtained in excellent yield by the reduction of VI with lithium aluminum hydride.[20]

## Experimental[21]

**1-Aza-7,8-benzcycloöctenedi-2,6-one (VII).— A. By Catalytic Oxidation of 2,3-Cyclopentenoindole.**—To a suspension of 100 mg. of reduced platinum oxide in 2 ml. of ethyl acetate was added a solution of 1 g. of freshly prepared 2,3-cyclopentenoindole[9] in 5 ml. of ethyl acetate. The reaction mixture was shaken under oxygen and took up 21 cc. of oxygen during the first hour. After complete oxidation (uptake about 150 cc.) there was a crystalline precipitate which was collected together with the platinum, washed with ethyl acetate and recrystallized from carbon tetrachloride. The solution, on standing overnight in the refrigerator, deposited well-formed cubic, almost colorless crystals, m.p. 170–170.5° (sublimation in colorless rods, starting at 109°). The compound was insoluble in cold 2 *N* alkali or 2 *N* acid.

(20) This method of reduction in this series (*cf.* ref. 7) is far simpler than the reduction using sodium in alcohol (*cf.* ref. 18).

(21) All melting points are corrected, boiling points are uncorrected. The analyses were performed by Mr. S. M. Nagy, Massachusetts Institute of Technology.

*Anal.* Calcd. for $C_{11}H_{11}NO_2$: C, 69.84; H, 5.83; N, 7.36. Found: C, 69.95; H, 6.07; N, 7.34.

**B. By Autoxidation of 2,3-Cyclopentenoindole.**—When a fresh solution of 30 mg. of 2,3-cyclopentenoindole in chloroform was subjected to the determination of the infrared spectrum, the typical indole spectrum was obtained (no absorption bands in the vicinity of 6 $\mu$). After one day there was a marked and growing band at 6 $\mu$. The same solution, after contact with air for two more days, showed the typical absorption spectrum of the lactam VII (Fig. 3A).

**$\gamma$-*o*-Aminobenzoylbutyric Acid (IX).**—When the lactam VII was warmed on the steam-bath either with dilute acid or base a solution was obtained, slightly yellow in the case of base, colorless with acid, which, on neutralization ($p$H 5), deposited glossy needles, m.p. 122–123°, after recrystallization from alcohol, 127–129° (clear colorless liquid). The presence of an aromatic amino group in the acid was proved by diazotization and coupling with an alkaline solution of $\beta$-naphthol.

*Anal.* Calcd. for $C_{11}H_{13}NO_3$: C, 63.77; H, 6.28. Found: C, 63.54; H, 6.12.

**2,3-Cyclopenteno-4-quinolone (X). A. From 1-Aza-8,9-benzcyclononenedi-2,7-one (VIII).**—When 50 mg. of the lactam VIII[1] was dissolved in cold 2 *N* sodium hydroxide, a yellow solution was obtained which after a few seconds warmed up slightly and became colorless. On neutralization a colorless crystalline compound was obtained which melted at 298° under decomposition and progressive charring. On recrystallization from a mixture of benzene and ethanol the crystals decomposed at 325–327°. The material in alcoholic solution gave a red-brown ferric chloride test.

*Anal.* Calcd. for $C_{12}H_{11}NO$: C, 77.88; H, 5.96; N, 7.56. Found: C, 77.73; H, 6.17; N, 7.57.

**B. From 2-Carbethoxycyclopentanone Anil.**—The following modification of the procedure reported by Blount, Perkin and Plant[13] was adopted: ethyl cyclopentanone-2-carboxylate was condensed with aniline. The anil was added rapidly to a large excess of stirred refluxing diphenyl ether at a temperature of 250–260°.[22] The solution darkened considerably after addition. Refluxing was continued for another ten minutes. When the solution was allowed to cool, a crystalline material separated. After the addition of ligroin the solution was filtered, the crude product collected and decolorized with norite. Crystallization from benzene–ethanol yielded colorless plates, m.p. 327° (dec.), undepressed on admixture with the compound obtained by Method A.

**3,4-Cyclopenteno-2-quinolone.**—This compound was prepared according to the method of Blount, Perkin and Plant[13] with the following modifications. Diethyl adipate was obtained in 96% yield by an azeotropic esterification of adipic acid.[23] Cyclization of the diester by a modified Dieckmann reaction[24] gave 2-carbethoxycyclopentanone. Reaction of the latter with aniline in the presence of pyridine[25] gave the anilide which on cyclization in concentrated sulfuric acid yielded the $\alpha$-quinindene, m.p., after recrystallization from ethanol, 256°.

**Tetrahydrophenanthridone (XI). A. By Catalytic Oxygenation of 2,3-Cycloheptenoindole (III).**—To a suspension of freshly reduced platinum oxide (100 mg.) in 2 ml. of ethyl acetate was added a solution of 500 mg. of 2,3-cycloheptenoindole[26] (m.p. 145–147°) in 5 ml. of ethyl acetate. After stirring under oxygen for 10 hours, 65 cc. of oxygen (about 90% of the theory) was taken up. The solution was filtered from the catalyst and evaporated to dryness. The residual dark red oil was substantially free of any indole odor. The oil was taken up in benzene and filtered through a column containing 20 g. of aluminum oxide (standardized according to Brockmann). The first seven fractions were obtained by elution with 10-cc. portions of pure benzene. A small amount of yellowish crystals was obtained from fractions 2 and 3, probably starting material (m.p. 135–142°). Fractions 8 to 13 (elution mixture, 10 cc. of benzene with three drops of ethanol) contained practically no solid material. Fractions 14 to 20 (elution mixture, benzene–ethanol 10:1) were combined and the crude crystalline material, obtained after evaporation of the solvents, was thoroughly washed with ice-cold methyl alcohol. On recrystallization (charcoal) from boiling methanol stout colorless needles were obtained, m.p. 266–268° (clear colorless melt), undepressed on admixture with synthetic tetrahydrophenanthridone.

*Anal.* Calcd. for $C_{13}H_{13}NO$: C, 78.39; H, 6.53. Found: C, 78.12; H, 6.32.

**B. By Synthesis.**—Tetrahydrophenanthridone was prepared according to Blount, Perkin and Plant[13] and yielded colorless plates from ethanol, m.p. 267–268.5°, identical with regard to mixed melting point and infrared spectrum with the material obtained by Method A.

**2,3-Cycloöctenoindole (IV).**—Phenylhydrazine (1.7 g.) was added over a period of 30 min. to a stirred refluxing solution of cycloöctanone (2 g.) in 25 ml. of glacial acetic acid. The solution darkened considerably shortly after the beginning of the reaction. Refluxing was continued for one-half hour after completed addition. The solution was then cooled, the crude crystalline product collected and washed several times with 50% aqueous methanol. Recrystallization from methanol yielded almost colorless crystals, m.p. 72–74°.

*Anal.* Calcd. for $C_{14}H_{17}N$: C, 84.42; H, 8.54; N, 7.03. Found: C, 84.49; H, 8.61; N, 7.11.

**2-Keto-1,2,3,4,5,6-hexahydrocycloöctindole (VI). A. By Catalytic Oxygenation of 2,3-Cycloöctenoindole (IV).**—Oxygenation of IV was carried out in ethyl acetate in the presence of reduced platinum oxide at room temperature and atmospheric pressure. Three separate runs were made, using the proportions

| IV, mg. | $PtO_2$, mg. | Uptake (% of theory) |
|---|---|---|
| 200 | 100 | 68 |
| 1000 | 200 | 77 |
| 1000 | 700 | 63 |

Runs 2 and 3, after evaporation of the solvent, were taken up in benzene and filtered through a column containing 40 g. of aluminum oxide. Twenty-two fractions were obtained when the column was eluted with consecutive portions of 10 ml. of benzene containing 0.01% of ethyl alcohol. Fractions 10 to 13 yielded oily material, easily soluble in aqueous base and displaying a carboxyl band in the infrared absorption spectrum. Fractions 16 to 19 yielded some crystalline material, which, after recrystallization from ethyl alcohol, gave colorless crystals, m.p. 186–187°. The material gave a negative ferric chloride test.

*Anal.* Calcd. for $C_{14}H_{15}NO$: C, 78.88; H, 7.09; N, 6.57. Found: C, 78.43; H, 7.24; N, 6.83.

The compound reacted with an alcoholic aqueous solution of dinitrophenylhydrazine hydrochloride to give a *red* dinitrophenylhydrazone.

**B. By Autoxidation.**—A 2-g. sample of 2,3-cycloöctenoindole after storage in a white glass bottle for three months at room temperature and exposed to daylight showed a strong band near 6 $\mu$ in the infrared absorption spectrum (Fig. 6C). This oxidized product on recrystallization from methyl alcohol gave colorless, rhombic crystals, m.p. 185° (sublimes in long needles at 154°), identical with the compound obtained by Method A (mixed m.p., infrared spectrum).

**C. By Synthesis.**[27] **Cycloöctanedi-1,2-one Monophenylhydrazone (XXI).**—A solution of sodium ethoxide prepared from 1.9 g. of sodium and 27 cc. of absolute alcohol was cooled to −20° and added to a mixture of cycloöctanone (10 g.) and ethyl formate (5.85 g.) also cooled to −20°. A sodium salt precipitated shortly after addition and, on keeping the reaction mixture overnight at 0°, was decomposed with dilute acetic acid (1:8). The aqueous mixture containing the crude hydroxymethylenecycloöctanone (XIII), appearing as a light-orange oil, was added slowly at 0° to a solution of phenyldiazonium hydroxide prepared by diazotization of aniline (5.9 g.) in 5 *N* hydrochloric acid

(22) At this high temperature condensation of the anil to form X supersedes a reaction which sets in at intermediate temperatures where an equilibrium is favored between the anil and the anilide; *cf.* C. R. Hauser and G. A. Reynolds, THIS JOURNAL, **70**, 2402 (1948).

(23) H. Gilman and A. H. Blatt, "Org. Syntheses," Coll. Vol. II, 1943, p. 264.

(24) *Ibid.*, Vol. II, p. 116 (1943).

(25) H. C. Barany and M. Pianka, *J. Chem. Soc.*, 1420 (1947).

(26) W. H. Perkin and S. G. P. Plant, *ibid.*, 2583 (1928).

(27) *Cf.* J. Elk, D. F. Elliot and B. A. Hems, *J. Chem. Soc.*, 625 (1944).

(32 ml.) with sodium nitrite (5.0 g.) 0° and neutralization with a solution of sodium acetate. A deep orange oil separated immediately. After complete addition, when the mixture was brought to room temperature, this oil gradually solidified. The crude product was collected, taken up in ethanol, decolorized with charcoal to give finally bright yellow needles, m.p. 80–81°.

*Anal.* Calcd. for $C_{14}H_{18}N_2O$: C, 73.02; H, 7.86; N, 12.2. Found: C, 72.49; H, 7.91; N, 12.79.

**Cyclization of XIII.**—The phenylhydrazone (0.2 g.) was dissolved in absolute ethanol (15 ml.). The solution was cooled in an ice-bath, saturated with dry hydrogen chloride, and then allowed to come to room temperature and remain there for 15 min. Water was added and the resulting precipitate was collected, taken up in methyl alcohol and decolorized with charcoal. On crystallization from 75% aqueous alcohol one obtained 30 mg. of colorless plates, m.p. 183–185°, identical with the compounds obtained by Methods A and B.

*Anal.* Calcd. for $C_{14}H_{16}NO$: C, 78.88; H, 7.09. Found: C, 79.03; H, 7.10.

**2-Hydroxy-1,2,3,4,5,6-hexahydrocycloöctindole (XII).**—When 200 mg. of the keto compound VI in 5 ml. of tetrahydrofuran was slowly added to an excess of lithium aluminum hydride in 10 ml. of the same solvent, reduction occurred under noticeable warming. The mixture was then refluxed for two hours, decomposed with ice, and extracted with ether. The organic phase was dried over sodium sulfate and left on evaporation 210 mg. of an oil which was obtained from ether solution in colorless needles, m.p. 133° (sintering 128°).

*Anal.* Calcd. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.35; H, 8.17.

**3,4-Cyclohepteno-2-quinolone (XIX).**—Condensation of cycloheptanone with ethyl oxalate[28] gave 2-carbethoxycycloheptanone. Condensation with aniline[13,26] yielded cycloheptanone-2-carboxanilide. Cyclization of the anilide with concentrated sulfuric acid gave XIX, colorless crystals from ethanol, m.p. 270–271°.

*Anal.* Calcd. for $C_{14}H_{15}NO$: C, 78.87; H, 7.04; N, 6.57. Found: C, 78.90; H, 7.00; N, 6.57.

This compound (XIX) was much more soluble in chloroform than the isomeric (XX),[13] which was obtained by the procedure of Perkin and Plant[26] in colorless needles from 50% aqueous acetic acid, showing a m.p. of 344° and a beautiful deep blue fluorescence in solution, which was not exhibited by the angular compound.

(28) Ref. 23, p. 531.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

# Isobornylisothiuronium Salts[1]

BY LEE A. SUBLUSKEY[2] AND L. CARROLL KING

Isobornylisothiuronium *p*-toluenesulfonate (VIIa) was prepared from six different terpenes. Evidence is presented to demonstrate (a) that VIIa has the isobornyl structure and that no detectable quantities of a bornylisothiuronium salt or a camphaneisothiuronium salt were formed as by-products, (b) that the enantiomorphic forms of VIIa are capable of racemic compound formation and (c) that the production of VIIa from an optically active terpene is accompanied by some racemization. Optically pure *l*-isobornylisothiuronium *d*-camphorsulfonate and *l*-isobornylisothiuronium iodide were prepared. Isobornyl mercaptan and some of its derivatives were prepared. A discussion of the reactions involved in the formation of VIIa from the various terpenes is given.

Camphene (I) was found to react with thiourea and *p*-toluenesulfonic acid to give isobornylisothiuronium *p*-toluenesulfonate (VIIa). The same salt VIIa was obtained when thiourea and *p*-toluenesulfonic acid were allowed to react with camphene methyl ether (II), tricyclene (III), isobornyl methyl ether (IV) or isoborneol (V), or when thiourea was allowed to react with bornyl *p*-toluenesulfonate (VI).

Treatment of borneol (VIII) with thiourea and *p*-toluenesulfonic acid failed to give VIIa. All attempts to prepare isobornyl *p*-toluenesulfonate, another possible precursor of VIIa, failed.

When prepared from tricyclene, a symmetrical hydrocarbon, the salt VIIa was optically inactive and was obtained in 96% yield, m.p. 182–183°. When VIIa was prepared from camphene ($[\alpha]^{25}D$ 52.7° in methanol) the initial product (VIIa) was obtained in 96% yield, m.p. 160–170°, and $[\alpha]^{24}D$ −21.4°. The melting point of this optically active salt was increased by repeated recrystallization, but by doing this its rotation was decreased to less than $[\alpha]^{25}D$ −2.2°. This is due to separation of a near racemic compound. When the mother liquors from the above recrystallization process were concentrated, an isomeric salt possessing a higher rotation ($[\alpha]^{25}D$ −33.8°) and lower melting point (163–167°) was obtained. These and related observations are summarized in Table I.

TABLE I

| Reactant Terpene | $[\alpha]^{25}D$ | Crude VIIa Yield, % | M.p., °C. | $[\alpha]^{25}D$ | Racemization,[a] % | Crystallized VIIa M.p., °C. | $[\alpha]^{25}D$ |
|---|---|---|---|---|---|---|---|
| I | 52.7° | 96 | 160–170 | −21.4° | 17[b] | 182–183 | − 2.20° |
| | | | | | | 163–167 | −33.8°[d] |
| II | −3.30° | 96 | 169–174 | −3.09° | 57[c] | 181–183 | 0° |
| III | 0° | 96 | 182–183 | 0° | ... | 182–183 | 0° |
| IV | ..... | 97 | 177–179 | ..... | ... | 181–183 | ..... |
| V | ..... | 97 | 179–181 | ..... | ... | 181–183 | ..... |
| VI | 2.04° | 85 | 177–180 | −2.52° | 43[e] | 181–183 | 0° |

[a] % Racemization = $(1 - rA/aB) \times 100$; where $A$ is the rotation of the optically pure reactant used as a standard, $B$ is the rotation of the corresponding optically pure product used as a standard, $a$ is the rotation of the optically impure reactant, and $r$ is the rotation of the partially racemized product. [b] This calculation is based on the highest known rotation for camphene, $[\alpha]^{25}D$ −111° (in methanol). This value was determined in this laboratory using a sample of pure *l*-camphene supplied by J. P. Bain; J. P. Bain and co-workers, THIS JOURNAL, **72**, 3124 (1950). [c] This calculation is based on the value reported for camphene methyl ether, $[\alpha]D$ −12.7°, prepared from camphene, $[\alpha]D$ 50.8°, J. L. Simonsen "The Terpenes," Vol. II, 2nd ed., Cambridge University Press, London, p. 320. [d] Recovered from mother liquors after separation of Racemate VIIa. [e] This calculation is based on the value reported for bornyl *p*-toluenesulfonate, $[\alpha]^{20}D$ 15.5° in alcohol, prepared from borneol, $[\alpha]^{18}D$ 21.0° in alcohol (J. Ferns and A. Lapworth, *J. Chem. Soc.*, **101**, 276 (1912)) taking into account the highest reported value for borneol, $[\alpha]^{20}D$ 34.1° (R. H. Pickard and W. O. Littlebury, *ibid.*, **91**, 1973 (1907)).

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(2) Hercules Powder Company, Wilmington, Delaware.