

sodium carbonate or concentrated ammonium hydroxide to give clear yellow-brown solutions from which the base is reprecipitated by carbon dioxide.

Aqueous solutions of the salts give with ferric chloride a clear blue color. Diazotization and treatment with alkaline β -naphthol gives a deep red solution.

Test for Chemiluminescence.—The four aminobenzoyleneureas and the two amino-2,3-dihydroxyquinoxalines were tested at 28° for possible chemiluminescence on oxidation by visual observation in a dark room. A 10-ml. sample of a 0.04 molar solution of each compound in 0.5 *N* sodium hydroxide was successively treated with 1 ml. of 3% hydrogen peroxide, 1 ml. of 3% potassium ferricyanide. In a second series of tests each 10-ml. sample was treated first with a trace of the catalytic salicylaldehyde ethylenediimine ferric chloride complex,¹⁴ followed by 1 ml. of 3% hydrogen peroxide. In a third series

(14) Thielert and Pfeiffer, *Ber.*, **71**, 1401 (1938).

of tests each 10-ml. sample was treated with 10 ml. of 8% sodium hypochlorite solution.

Summary

1. All four isomeric aminobenzoyleneureas and both possible amino-2,3-dihydroxyquinoxalines have been prepared by reduction of the corresponding nitro compounds.

2. None of them shows significant chemiluminescence under conditions which with the isomeric 3-aminophthalhydrazide give intense effects.

3. Previous assumption regarding the indisposability of the hydrazine residue for chemiluminescent power has thus been demonstrated.

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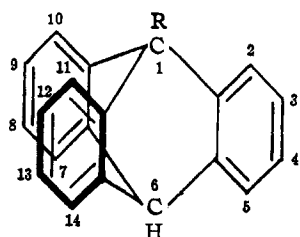
RECEIVED MAY 14, 1942

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Triptycene¹ (9,10-*o*-Benzenoanthracene)

BY PAUL D. BARTLETT, M. JOSEPHINE RYAN AND SAUL G. COHEN

Previous publications from this Laboratory have brought out the special properties of substituents located on the bridgehead of a bicyclic ring system.² These findings would lead us to



I, R absent

II, R = H

predict that the analog (I) of the triphenylmethyl radical in which the ortho positions of the three phenyl groups are united to a common CH should have much less tendency to exist as a free radical than triphenylmethyl itself, as a result of its inability to assume the coplanar form demanded by the usual resonance structures.³ With the eventual purpose of testing this prediction we have prepared the parent hydrocarbon II (9,10-*o*-benzenoanthracene, or tribenzobicyclo(2,2,2)octatriene) and studied some of its chemical properties. For

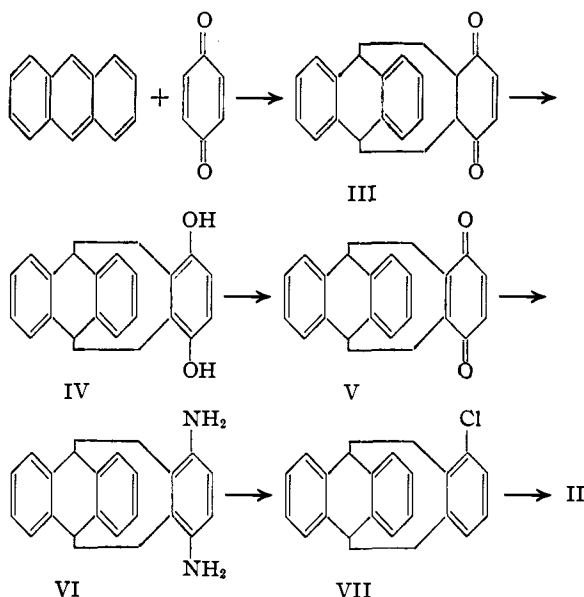
(1) This name is proposed because the shape of this ring system suggests the triptych of antiquity, which was a book with three leaves hinged on a common axis. We are indebted to Professor Mason Hammond of the Harvard Department of Classics for this suggestion.

(2) Bartlett and Knox, *THIS JOURNAL*, **61**, 3184 (1939); Bartlett and Cohen, *ibid.*, **62**, 1183 (1940); Bartlett and Woods, *ibid.*, **62**, 2933 (1940).

(3) Pauling and Wheland, *J. Chem. Phys.*, **1**, 362 (1933).

convenience, the name "triptycene" is suggested for this symmetrical hydrocarbon.¹

The steps in the synthesis of triptycene are as follows



The removal of the functional groups was achieved only after very many unsuccessful attempts. We tried to dehydroxylate the hydroquinone IV with zinc dust, to convert it into a dibromide or diiodide with phosphorus halides, to reduce the quinone by hydrogenation, by the

Clemmensen and Wolff-Kishner procedures, to gain a start in the reduction by replacing benzoquinone with Δ^2 -cyclohexenone in the initial step, as well as several less rational procedures. The hydroxylated ring was successfully reduced, but the hydrogenation product could not be converted to triptycene. Finally, numerous ways were tried for the deamination of the diamine VI, by tetrazotization in dilute and concentrated hydrochloric acid, sirupy phosphoric and concentrated sulfuric acid and mixtures, with nitrous acid and nitrous fumes, followed by attempted reduction with stannous chloride, alkaline formaldehyde, alcohol, and also attempted Sandmeyer reactions. The difficulties appeared to result from the combined facts of the ready nuclear substitution in a diamine and the great tendency of this ring system to yield anthracene under even relatively mild conditions, and especially when the treatment of the substituted ring enabled this to occur irreversibly. Successful deamination of the diamine was accomplished only by tetrazotizing at 10° in a mixture of sulfuric acid, acetic acid and water, destroying the excess nitrous acid, and reducing with hypophosphorous acid.⁴ Control of the temperature proved to be of great importance.

The product of the hypophosphorous acid reduction was not triptycene, but monochlorotriptycene accompanied by a little dichlorination product. Apparently the *p*-diazonium substituent, like the *p*-nitro-, activates the N₂-group toward replacement, at the same time deactivating it toward reductive elimination. The replacement of the first N₂-group by chlorine allows the remaining N₂-group to be eliminated, yielding 2-chlorotriptycene as the principal product. The same treatment using the hydrobromide instead of the hydrochloride of the diamine yielded a small amount of dibromotriptycene. Each of these halogenated products was smoothly reduced to triptycene by the method of Busch.⁵ In each case the deamination was the weak step in the synthesis giving poor yields.

Triptycene crystallizes in fine white rhomboids melting at 254.8–255.2°, and is advantageously crystallized from methanol–water. It is very soluble in benzene, soluble in ethyl alcohol, ether, acetone, chloroform and slightly soluble in methanol.

To the extent to which the central hydrogen atom of triphenylmethane is activated by the

possibility of resonance in the triphenylmethide ion, such activity should be diminished or absent in triptycene. Triptycene in fact yields no exchange with phenylisopropylpotassium under conditions which lead to immediate reaction in the case of triphenylmethane; it is not chlorinated by sulfuryl chloride in the presence of benzoyl peroxide whereas toluene, under identical conditions, gives a high yield of benzyl chloride; and chromic anhydride, under conditions which lead to the formation of triphenylcarbinol from triphenylmethane, gives only anthraquinone and carbon dioxide from triptycene. Moderation of the conditions permitted recovery of only a mixture of unchanged starting material and anthraquinone, showing that if 1-hydroxytriptycene is produced at all under these conditions it is immediately decomposed.

In view of the complete failure of the hydrogen in the 1-position of triptycene to show the reactivity characteristic of the central hydrogen of triphenylmethane, it seems rather likely that the oxidative decomposition of triptycene to anthraquinone is initiated not by attack at the 1-position but by attack upon one of the benzene rings. In seeking a possible reason why these rings should be more susceptible to oxidative attack than normal benzene rings, we observe that the internal bond angles of the bicyclo(2,2,2)octane ring system must always be close to the normal value of 109°28'. This would lead us to expect a Mills–Nixon effect⁶ tending to damp the resonance in each benzene ring by giving preference to the bond structures represented in the formula II. Any such effect would render the oxidative disruption of one of the benzene rings more likely, but would disappear upon opening of the bicyclic ring, system and formation of the dihydroanthracene type. In a quantitative oxidation by chromic anhydride in acetic acid slightly more than enough carbon dioxide was produced to account for the missing benzene ring. The Mills–Nixon effect, if present, is not sufficiently extreme to permit reaction of triptycene with maleic anhydride or with triphenylmethyl, since negative results were obtained with both these compounds.

Experimental

Formation of the Adduct III from Anthracene and Quinone.—The route of Clar⁷ to the quinone IV was

(6) See Fieser in Gilman, "Organic Chemistry—An Advanced Treatise," John Wiley & Sons, Inc., New York, N. Y., 1st ed., pp. 71–73.

(7) Clar, *Ber.*, **64**, 1876 (1931).

(4) Adams and Kornblum, *THIS JOURNAL*, **63**, 188 (1941).

(5) Busch and Stöve, *Ber.*, **49**, 1063 (1916).

modified, yielding, under our conditions, an improved product. Anthracene (108 g.) twice recrystallized from xylene, and 73 g. of reagent grade quinone were heated under reflux in 650 cc. of xylene for two hours.⁷ The solid was collected on a filter and thoroughly washed with hot water to remove quinone and quinhydrone. It was recrystallized from xylene giving 143 g. (83%) of pale yellow rhomboids. This compound has the characteristic melting behavior observed by Clar, which depends on the rate of heating; it is yellow at 207°, red at 210°, and at higher temperatures it carbonizes.

Rearrangement of the Adduct III to the Hydroquinone IV.—To a solution of 11.5 g. of the adduct III in 150 cc. of glacial acetic acid at the boiling point, four drops of 40% hydrobromic acid were added. A vigorous evolution of heat followed and the solution took on an orange color which gradually faded as a fine white solid precipitated out. After another half hour at the boiling point, the reaction mixture was cooled and filtered; yield 10.3 g. (90%); m. p. 338–340° dec.

Hydrogenation of 2,5-Triptycenediol (IV) with Raney Nickel.—A solution of 2 g. of the hydroquinone IV in 38 cc. of warm dioxane was treated with hydrogen at 1140 lb. pressure in the presence of 1 g. of Raney nickel, and the temperature was gradually raised. At 200° hydrogen absorption took place and had ceased after seventeen hours. The mixture was filtered into water, the resulting solid was washed with petroleum ether and recrystallized from benzene. The product, 0.68 g. of white plates, melted at 220–224°. Its solution in alcoholic alkali turned red on shaking in air and the color was discharged by sodium hydrosulfite. Evidently the triptycenediol had become hydrogenated in the two unhydroxylated benzene rings.

Anal. Calcd. for $C_{20}H_{26}O_2$: C, 80.50; H, 8.78. Found: C, 80.20; H, 8.61.

Hydrogenation of the Adduct III with Copper Chromite.—To a solution of 2 g. of the direct addition product III of quinone to anthracene in 35 cc. of dioxane, 0.25 g. of copper chromite was added. The hydrogenation was conducted at 160° under 2200 lb. pressure for ten hours; the solution was filtered in an atmosphere of carbon dioxide and concentrated in a stream of nitrogen. This precaution was found useful in minimizing the dark coloration which always appeared when the hydrogenated solution was exposed to the air. Precipitation with petroleum ether, followed by crystallization from alcohol, yielded 67% of almost colorless crystals melting at 226–228°.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.15; H, 6.90. Found: C, 82.06; H, 7.10.

This pure product was not oxidized in air in the presence of alkali. It yielded a diacetate, m. p. 177–178°. Apparently the action of copper chromite on the non-aromatic ring of the adduct was to hydrogenate this ring preferentially, whereas the nickel catalyst selected from three aromatic rings the two carrying no oxygenated substituents.

Attempts to Dehydrate the Saturated Diol.—Heating of 0.1 g. of the diol under nitrogen at 300° for thirty minutes, followed by vacuum sublimation, led to the isolation of 0.05 g. of anthracene (mixed melting point).

A mixture of 0.1 g. of the diol and 0.5 g. of anhydrous oxalic acid was heated in an atmosphere of nitrogen. The temperature was slowly raised from 110 to 135° in twenty-five minutes and then to 190° in ten minutes. Anthracene sublimed to the top of the tube.

In the same experiment, but with phosphoric acid instead of oxalic, anthracene appeared somewhat above 100°. The use of *p*-toluenesulfonic acid led to no solid products.

Oxidation of the Hydroquinone IV to the Quinone V.—Nineteen grams of the hydroquinone IV was dissolved in a minimum amount of hot glacial acetic acid (app. 1100 cc.) and then a solution of 4 g. of potassium bromate in 300 cc. of hot water was added. A deep orange color developed immediately. The solution was boiled for a minute or two and then 200 cc. more of hot water was added and the boiling continued for a few minutes. The solution was cooled and the orange solid collected. The quinone was washed with acetic acid and then with water; yield 17.5 g. (93%); m. p. 292–296°.

The dioxime was prepared by two hours of boiling of a solution of 0.25 g. of V and 1 g. of hydroxylamine hydrochloride in 25 cc. of ethanol. The dioxime was isolated by pouring into water and was crystallized (78% yield of five yellow rosetts) from acetic acid. Drying *in vacuo* at 100° for twenty-four hours was necessary to remove acetic acid from the product; m. p. 246° dec.

Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49. Found: C, 76.16; H, 4.67.

Reduction of the Dioxime to the Diamine VI.—Twenty grams of the dioxime was dissolved in 750 cc. of alcohol on the steam-bath. When the alcoholic solution was at about 60°, a solution of 88 g. of stannous chloride in 200 cc. of concentrated hydrochloric acid was added to it with stirring. The mixture was heated for a few minutes more and then cooled and filtered. The solid was washed with alcoholic hydrochloric acid and then with ether. Further purification was effected by dissolving in hot water and precipitating again by the addition of concentrated hydrochloric acid. Each successive reprecipitation makes the salt grayer, probably because of oxidation. The yield was 19.8 g. (86%). The hydrochloride gradually decomposed above 210°.

The free base was prepared by dissolving the diamine hydrochloride in hot water and gradually adding 10% sodium hydroxide. This product turns a grayish-purple in air; m. p. 307° dec. The best analysis obtained was still not good but the compound is extremely difficult to burn.

Anal. Calcd. for $C_{20}H_{18}N_2$: C, 84.50; H, 5.64; N, 9.85. Found: C, 83.06; H, 5.99; N, 9.65.

The diacetyl derivative is obtained as small white crystals from acetic acid, dec. 370°.

Anal. Calcd. for $C_{24}H_{20}N_2O_2$: C, 78.23; H, 5.47. Found: C, 78.05; H, 5.62.

Deamination of the Diamine VI.—A suspension of 5 g. of the amine hydrochloride in 150 cc. of glacial acetic acid was cooled to 10° and to it was added a similarly cooled mixture of 100 cc. of concentrated sulfuric acid, 100 cc. of acetic acid, and 60 cc. of water. The temperature was carefully controlled during the reaction because sulfonation takes place above 15°. Five grams of sodium nitrite was dusted in gradually, turning the solution blood red.

After all the nitrite was added the mixture was stirred in the cold for at least an hour and then urea was added until the solution no longer turned starch-iodide paper blue. The thick solution was added to a filtered solution of 12 g. of sodium hypophosphite in 300 cc. of concentrated hydrochloric acid and allowed to stand overnight. The addition of a quantity of water precipitated 3.8 g. of a flaky tan solid melting at 175° with decomposition. All this material was then subjected to sublimation by heating at 195° at a pressure of 2 mm. The best yield obtained was 1.8 g. of shiny white crystals, m. p. 219–221°. After three recrystallizations from methanol the melting point was 222–223°. A quantitative analysis for chlorine indicated that the product was monochlorotriptycene with a small amount of dichlorotriptycene.

Anal. Calcd. for $C_{20}H_{13}Cl$: C, 83.18; H, 5.17; Cl, 12.30. Found: C, 82.16; H, 4.95; Cl, 13.67.

2,5-Dibromotriptycene.—Reduction of the diazonium compound was attempted in the absence of halogen acid and no reaction whatever took place even over a long period of time. Hydrobromic acid had the same effect as hydrochloric and gave dibromotriptycene, m. p. 227–228°, in very poor yield. Debromination of this compound gave the same product as the dechlorination of chlorotriptycene.

Anal. Calcd. for $C_{20}H_{12}Br_2$: C, 58.43; H, 2.95. Found: C, 58.79; H, 2.73.

Triptycene (II).—This reaction was run by the method of Busch and Stöve,⁵ 0.2 g. of the chloro compound was dissolved in 40 cc. of alcohol and 10 cc. of 10% alcoholic potassium hydroxide was added. Four grams of the catalyst, palladium on calcium carbonate, and 12 drops of hydrazine hydrate were added. After refluxing on the steam-bath for one-half hour the mixture was cooled slightly, filtered free of catalyst, and poured into water. There was obtained 0.18 g. of fine white crystals which could be crystallized from methanol-water; m. p. 254.8–255.2°. Like the rest of these compounds the hydrocarbon was hard to burn in a carbon-hydrogen analysis.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.50; H, 5.51. Found: C, 94.13, 93.25, 93.87, 94.01; H, 5.40, 5.62, 5.32, 5.27.

Triptycene and Phenylisopropylpotassium.—Triptycene (0.1 g.) was placed in a round-bottom, long-necked flask with two side arms. The flask was swept out with nitrogen for a short time and then sealed tightly. Ten cc. of 0.055 *N* phenylisopropylpotassium in dry ether, prepared by Dr. J. E. Jones, was added slowly through one of the side arms. After the solution had stood for twenty-one hours with occasional shaking, no color change could be detected. Dry carbon dioxide was bubbled into the solution and the material removed from the flask. After evaporation of the ether and extraction with alkali, 0.08 g. of triptycene was recovered, m. p. 252–253°, mixed m. p. with known sample 253–254°.

Triptycene and Chlorine.—Triptycene (0.2 g.) was dissolved in 50 cc. of purified carbon tetrachloride. The flask was partially evacuated, and then 25 cc. of the chlorine gas was added from a gas buret. The contents of the flask were thoroughly shaken and left in the sunlight for several days. When the carbon tetrachloride was evaporated, there remained a dirty white solid, m. p. 224°.

After sublimation the melting point was 246–248° and a mixed melting point with triptycene was 244–246°. A carbon-hydrogen analysis indicated that a very small amount of chlorine had been taken up.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.50; H, 5.51. Found: C, 91.48; H, 5.10.

In proportions which led to bromination of toluene in good yield⁸ without solvent, sulfuryl chloride and benzoyl peroxide had no action on triptycene in carbon tetrachloride, 85% of the hydrocarbon being recovered unchanged.

Oxidation of Triptycene.—Triptycene was oxidized under conditions which oxidize triphenylmethane to triphenylcarbinol. Triptycene (0.2 g.) was dissolved in 50 cc. of purified glacial acetic acid and 0.5 g. of chromic anhydride was added slowly. The flask was heated very gently on the steam-bath overnight. The green solution was poured into water and a yellow solid precipitated which could be crystallized from benzene; m. p. 283–285°; mixed melting point of the sample with anthraquinone 284–285°.

To determine what became of the rest of the molecule during the oxidation, triptycene was oxidized in a stream of dry air. The air was then passed through an absorption tube containing dehydrite and one containing ascarite. A sample of 0.70 g. of triptycene was heated at 55° with 3.5 g. of chromic anhydride, and 0.782 g. of carbon dioxide was absorbed in the ascarite tube. Since the calculated amount would be 0.726 g. if the third benzene ring were completely oxidized, some other formation of carbon dioxide such as further oxidation of anthraquinone or oxidation of acetic acid must be occurring. Anthraquinone was recovered from the reaction flask in 76% yield.

In an attempt to isolate an intermediate in this oxidation 0.2-g. samples of triptycene were put away for a week at room temperature with 0.05 g. of chromic anhydride and 0.12 g. of potassium permanganate, respectively, in acetic acid solution. From the chromic anhydride only triptycene was recovered, but from the reaction with permanganate both anthraquinone and triptycene were recovered, showing that the intermediate products formed are more susceptible to oxidation than triptycene.

Triptycene and Maleic Anhydride.—Triptycene (0.2 g.) and maleic anhydride (1 g.) in 50 cc. of nitrobenzene were refluxed on a hot-plate for four hours. The nitrobenzene was removed *in vacuo* and the black residue was extracted with alcohol. The alcoholic solution was decolorized with charcoal and poured into water. A white solid weighing 0.13 g. was obtained and recrystallized from methanol. It melted at 253–254° alone and at 254° when mixed with triptycene.

Acknowledgment.—We are indebted to the Associates of Physical Sciences of Harvard University for grants in support of this and related work to be published later.

Summary

The symmetrical hydrocarbon, 9,10-*o*-benzenoanthracene or tribenzobicyclo(2,2,2)octatriene (II)

(8) Kharasch and Brown, *THIS JOURNAL*, **61**, 2142 (1939); Kharasch and Read, *ibid.*, **61**, 3089 (1939).

has been prepared and its properties studied. The name "triptycene" is proposed for this hydrocarbon. Being an analog of triphenylmethane whose symmetrical anion cannot assume the coplanar form demanded by the usual resonance

structures, triptycene is entirely lacking in the activity of its aliphatic hydrogen toward potassium exchange, chlorination, and oxidation which characterizes triphenylmethane.

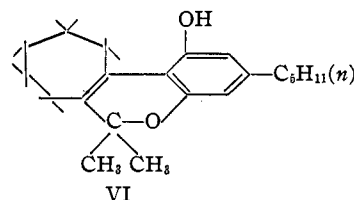
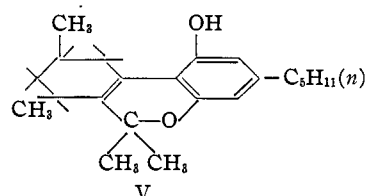
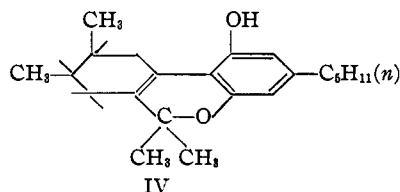
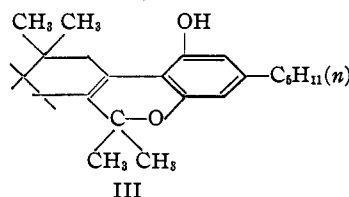
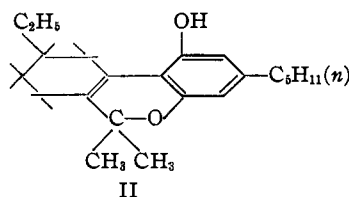
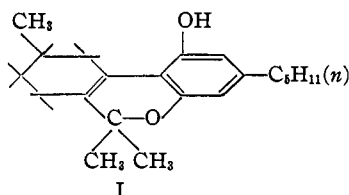
CAMBRIDGE, MASSACHUSETTS RECEIVED JULY 3, 1942

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND FROM THE DEPARTMENT OF PHARMACOLOGY, CORNELL UNIVERSITY MEDICAL COLLEGE, IN COLLABORATION WITH THE TREASURY DEPARTMENT, NARCOTICS LABORATORY, WASHINGTON, D. C.]

Tetrahydrocannabinol Analogs with Marihuana Activity. XV¹

BY ROGER ADAMS, S. LOEWE, C. W. THEOBALD AND C. M. SMITH

The study of analogs of synthetic tetrahydrocannabinol (I) wherein the left-hand ring was modified has comprised those molecules in which the methyl group was eliminated and those in which the methyl group was shifted to the 8- and 10-positions.² This investigation has now been extended, and a variety of products have been synthesized as shown in formulas II-VI.



The pharmacological tests on these molecules by the dog-ataxia method as compared to tetrahydrocannabinol (I) as standard are given in Table I.

TABLE I
PHARMACOLOGICAL ACTIVITY OF TETRAHYDROCANNABINOL ANALOGS

	Expts.	Potency	Mean dev.
1-Hydroxy-3-n-amyloxy-6,6-dimethyl-9-ethyl-7,8,9,10-tetrahydro-6-dibenzopyran II	5	0.22	0.02
1-Hydroxy-3-n-amyloxy-6,6,9,9-tetraethyl-7,8,9,10-tetrahydro-6-dibenzopyran III	7	.10	.02
1-Hydroxy-3-n-amyloxy-6,6,8,9-tetrahydro-7,8,9,10-tetrahydro-6-dibenzopyran IV	10	.11	.03
1-Hydroxy-3-n-amyloxy-6,6,7,9-tetrahydro-7,8,9,10-tetrahydro-6-dibenzopyran V	5	.75	.08
2,2-Dimethyl-3,4-pentamethylene-5-hydroxy-7-n-amyloxy-1,2-benzopyran VI	4	.21	.02

These experiments confirm the results from the study of the previously described compounds that relatively minor changes in the left-hand ring structure reduce by 80 to 90% the activity of the

(1) For previous paper see Adams, Smith and Loewe, *THIS JOURNAL*, **64**, 2087 (1942).

(2) Adams, Smith and Loewe, *ibid.*, **63**, 1973 (1941); see also Russell, Todd, Wilkinson, MacDonald and Woolfe, *J. Chem. Soc.*, 169, 826 (1941).