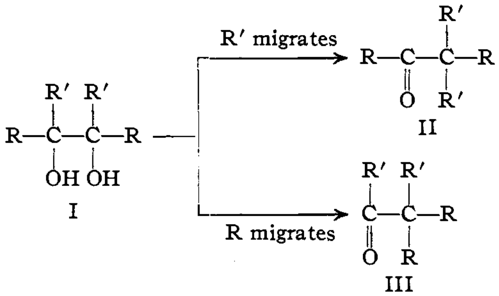
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Studies on the Mechanism of the Pinacol Rearrangement. I. Compounds Related to *meso*- and *dl*-2,3-Butanediol

BY ELLIOT R. ALEXANDER AND DONALD C. DITTMER

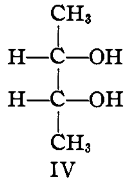
dl-2,3-Butanediol and *cis*-2,3-epoxybutane, when treated with phosphoric acid, produce predominantly methyl ethyl ketone, whereas *meso*-2,3-butanediol and *trans*-2,3-epoxybutane give a mixture of about 75% methyl ethyl ketone and 25% isobutyraldehyde. The reaction of either *threo*- or *erythro*-3-chloro-2-butanol with aqueous silver nitrate, however, gives almost exclusively methyl ethyl ketone. The reactions of the glycols and the epoxides can be rationalized either by assuming that rotation about the central carbon–carbon bond occurs more slowly than rearrangement or by assuming a rapid rotation about this bond coupled with a sterically preferred transition state.

One of the most interesting aspects of the pinacol–pinacolone transformation is the ease with which various groups of a substituted ethylene glycol molecule rearrange. Many experiments have been carried out[1] from which it can be said in summary that the rearrangement of unsymmetrical pinacols is complex[2] but that symmetrical pinacols (I) appear to behave in a manner consistent with the idea that the more electron releasing group (R or R′) will migrate preferentially.



In general, however, compounds of type I exist in *meso* and *dl* forms and in one instance at least the group which migrated was dependent upon the stereochemistry of the glycol rather than the electrical nature of the groups concerned.[3] Accordingly it was the object of this work to study in the pinacol rearrangement the relation between the preferential migration of groups and the stereochemistry of the starting materials.

The first compounds selected for study were the *meso*- and *dl*-2,3-butanediols (IV and V) since their stereochemistry, preparation and characterization are known[4] and since it has been reported that both methyl ethyl ketone and isobutyraldehyde can be isolated from the pinacol rearrangement of the 2,3-butanediol obtained from soy sauce.[5] Similarly the action of acid upon the *cis*- and *trans*-2,3-epoxybutanes (VI and VII) and the effect of silver nitrate on the *threo*- and *erythro*-3-chloro-2-butanols (VIII and IX) was also investigated since these reactions, too, lead to pinacol-type rearrangements.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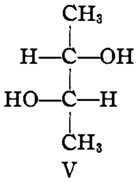
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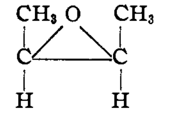
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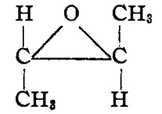
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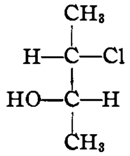
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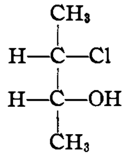
IX

Experimental[6]

***erythro*- and *threo*-3-Chloro-2-butanols.**—These two compounds were prepared by the method described in Lucas and Pressman[7] from the *trans*- and *cis*-2-butenes.[8] After fractionation through an electrically heated 12-inch column packed with glass helices, the *erythro*-3-chloro-2-butanol was obtained as a colorless liquid, b.p. 40–44.5° (16–20 mm.), n^{20}_{D} 1.4393. In three different runs, yields of 23.4, 46.4 and 35.0% were obtained. *threo*-3-Chloro-2-butanol was also a colorless liquid, b.p. 36.5–40° (14 mm.), n^{20}_{D} 1.4403. The yields of this isomer from two runs were 29.8 and 44.5%.

***cis*- and *trans*-2,3-Epoxybutanes.**—These isomers were also prepared by a method described in Lucas and Pressman.[9] Thus from 63.5 g. (0.585 mole) of *erythro*-3-chloro-2-butanol was obtained 37.4 g. (91.5%) of *trans*-2,3-epoxybutane. This material was then fractionated through a 63-plate Podbielniak Heligrid column at 754.8 mm. to separate any of the *cis* isomer which might have been present. The *trans* epoxide was collected at 56.5–56.7°, n^{20}_{D} 1.3739, d^{20}_{20} 0.8025. Similarly from 73.4 g. (0.675 mole) of *threo*-3-chloro-2-butanol was obtained 43.0 g. (88.5%) of *cis*-2,3-epoxybutane. This was also then fractionated through the Podbielniak column, b.p. 61.5–62.8° (749.5 mm.), n^{20}_{D} 1.3825, d^{20}_{20} 0.8301.

***meso*- and *dl*-2,3-Butanediols.**—For these compounds, the perchloric acid hydrolysis of Wilson and Lucas[4] as modified by Grivsky[10] was employed. Thus from 9.6 g. (0.133 mole) of *trans*-2,3-epoxybutane was obtained 8.2 g. (68.5%) of *meso*-2,3-butanediol as a clear, viscous liquid, b.p. 87–89°, n^{20}_{D} 1.4388. From 9.7 g. (0.82 mole) of *cis*-2,3-epoxybutane was obtained 7.4 g. (61%) of *dl*-2,3-butanediol, b.p. 82.5–85°, n^{20}_{D} 1.4336.

Analysis for Isobutyraldehyde and Methyl Ethyl Ketone.—The success of this investigation was dependent upon a satisfactory method for the analysis of methyl ethyl ketone

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[1] For reviews and a number of leading references see *Ann. Repts. Chem. Soc.* (*London*), **27**, 114 (1930); **30**, 181 (1933); **36**, 195 (1939).

[2] See Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 494–519.

[3] Bachmann and Shankland, THIS JOURNAL, **51**, 306 (1929); Bergmann and Schuchardt, *Ann.*, **487**, 234 (1931).

[4] Wilson and Lucas, THIS JOURNAL, **58**, 2396 (1936).

[5] Akabori, *J. Chem. Soc., Japan*, **59**, 1132 (1938); [*C. A.*, **33**, 2106 (1939)].

[6] All melting points and boiling points are uncorrected.

[7] Lucas and Pressman, "Principles and Practice in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 221; see also reference 4.

[8] Obtained in 99% purity from the Phillips Petroleum Company, Bartlesville, Oklahoma.

[9] Lucas and Pressman, ref. 7, p. 265.

[10] Grivsky, *Bull. soc. chim. Belg.*, **51**, 63 (1942).

and isobutyraldehyde when mixed with each other in aqueous solution. It was decided to determine the total amount of carbonyl present by the hydroxylamine hydrochloride method of Bryant and Smith,[11] the aldehyde by the method of Yoe and Reid[12] and the methyl ethyl ketone by difference.

In order to test the method, solutions of methyl ethyl ketone and isobutyraldehyde were prepared in various concentrations by weighing accurately the carbonyl compounds into a 50-ml. volumetric flask containing water and a few crystals of hydroquinone.[13] The solutions were then diluted to volume, and 10-ml. aliquots were analyzed. In the total carbonyl analysis, approximately the same amount of water was added to the titration blank as was in the standard carbonyl solutions. In analyzing these known solutions, more than 95% of the total carbonyl group present could be accounted for. From the aldehyde analysis, at least 92% of the isobutyraldehyde could be found.

Pinacol Rearrangement of the 2,3-Butanediols and 2,3-Epoxybutanes.—To a mixture of 5 ml. (8.5 g., 0.074 mole) of 85% phosphoric acid and 3 ml. of water contained in a 100-ml. round-bottomed flask was added 1.0–1.2 g. (0.011–0.013 mole) of the 2,3-butanediol or 1.5 g. (0.0207 mole) of the 2,3-epoxybutane. A Friedrich reflux condenser was then attached and the mixture was boiled gently for four hours.

At the end of the heating period, the condenser was rinsed thoroughly. The light yellow solutions were diluted to approximately 50 ml. and steam distilled into a 50-ml. volumetric flask completely immersed in an ice-bath. The adapter tube from the condenser reached about a fourth of the way into the volumetric flask and the distillation was conducted so that after about two hours 40–45 ml. of distillate had been collected.[14] The volumetric flask was then removed, diluted to the mark with distilled water, and 10-ml. aliquots were analyzed for total carbonyl and aldehyde as previously described. The results are summarized in Table I.

TABLE I

Run	Cpd. rearranged	Combined yield, aldehyde and ketone, %	Methyl ethyl ketone in product,[a] %	Isobutyraldehyde in product, %
1	*meso*-2,3-Butanediol	60	71	29
2	*meso*-2,3-Butanediol	37	75	25
3	*meso*-2,3-Butanediol	71	79	21
4	*dl*-2,3-Butanediol	48	99	1
5	*dl*-2,3-Butanediol	31	94	6
6	*dl*-2,3-Butanediol	59	98	2
7	*trans*-2,3-Epoxybutane	35	75	25
8	*trans*-2,3-Epoxybutane	44	75	25
9	*cis*-2,3-Epoxybutane	58	93	7
10	*erythro*-3-Chloro-2-butanol	37	97	3
11	*threo*-3-Chloro-2-butanol	50	100	0

[a] Calculated from columns 3 and 5.

The methone derivative of the aldehyde melted at 148–151° and showed no depression on admixture with an authentic sample of the methone derivative of isobutyraldehyde. The ketone was characterized by conversion to a 2,4-dinitrophenylhydrazone[15] which, with the product from the *dl* diol or the *cis* epoxide, melted at 114–115° and showed no depression on admixture with known methyl ethyl ketone phenylhydrazone. With the product from the *meso* diol or the *trans* epoxide, the distillate was first treated dropwise with 2% aqueous potassium permanganate until the color persisted. The solution was then filtered and the ketone converted to the phenylhydrazone as before. Again the derivative melted at 114–115°, and there was no mixed melting point depression with an authentic sample.

Sulfuric acid in various concentrations was also investigated but did not give as good results as boiling 70% phosphoric acid. Cold concentrated sulfuric acid caused no rearrangement of the *meso* diol. Distillation with 25% sulfuric acid produced slight rearrangement while hot concentrated sulfuric acid caused charring.

Reaction of *erythro*- and *threo*-3-Chloro-2-butanol with Silver Nitrate.—To 2 g. (0.018 mole) of the 3-chloro-2-butanol in a 100-ml. round-bottomed flask set for distillation was added a solution of 3.5 g. (0.02 mole) of silver nitrate in 50 ml. of water. The reaction mixture was then heated to boiling and distilled slowly into a 50-ml. volumetric flask, immersed in an ice-bath, at such a rate that after two hours about 40–45 ml. had been collected.[14] After a few minutes silver chloride began to precipitate; and, as the distillation proceeded, a small amount of a greenish-yellow oil came over. Presumably it was a nitrate ester, but this point was not investigated. At the end of the distillation the distillate was diluted to volume, and 10-ml. aliquots were analyzed as before. The results are summarized in Table I. Again the carbonyl components were converted, respectively, to the methone derivative and a 2,4-dinitrophenylhydrazone. There was no melting point depression of either of these solids on admixture with authentic samples.

Attempted Oxidation of Isobutyraldehyde with Nitric Acid.—To determine if isobutyraldehyde was oxidized by the amount of nitric acid formed in the reaction of silver nitrate with the chlorobutanols, a solution containing 0.3 g. (0.0048 mole) of nitric acid, 75 ml. of water, 0.000453 mole (by analysis) of isobutyraldehyde and 2.0 g. (0.012 mole) of silver nitrate was steam distilled in the apparatus used for the analysis of the pinacol rearrangement mixtures. Analysis for isobutyraldehyde showed 0.000454 mole to be present.

Discussion

The results of this investigation (Table I) indicate that *dl*-2,3-butanediol and *cis*-2,3-epoxybutane gave predominantly methyl ethyl ketone when treated with phosphoric acid. Under the same conditions *meso*-2,3-butanediol and *trans*-2,3-epoxybutane gave a mixture of about 75% methyl ethyl ketone and 25% isobutyraldehyde. In contrast, *threo*- and *erythro*-3-chloro-2-butanol gave almost exclusively methyl ethyl ketone when treated with aqueous silver nitrate solution.

It is evident, therefore, that we have, with the glycols and the epoxides, another example of a pinacol rearrangement in which migration is dependent not only upon the electrical nature of the groups concerned but also upon the stereochemistry of the starting materials.[16] The explanation of these results is not yet clear but since we know unequivocally the geometry of our systems, certain stereochemical considerations are of interest.[17] Thus it seems generally agreed that the pinacol rearrangement proceeds through the steps X-XIV or XV to give the protonated form of the pinacolone (XIV or XV). In this work it is the conversion of the oxonium ion (XI) to the ion or transition state (XII or XIII) in which we are particularly interested. Since it is very likely that the migrating group comes in from the side opposite

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(11) Bryant and Smith, THIS JOURNAL, 57, 57 (1935) [Siggia, "Quantitative Organic Analysis via Functional Groups," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 17].

(12) Yoe and Reid, *Ind. Eng. Chem., Anal Ed.*, 13, 238 (1941).

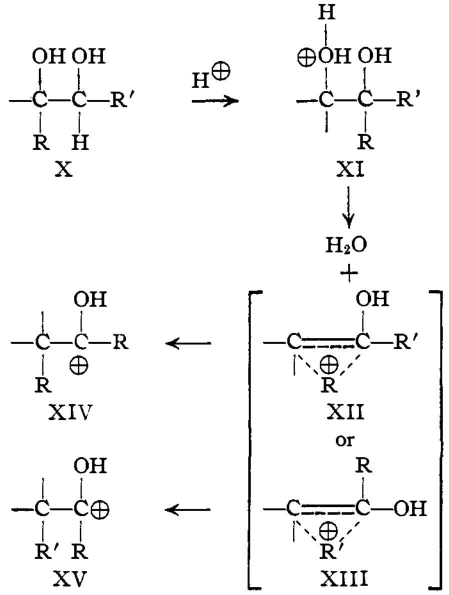
(13) Isobutyraldehyde apparently autoxidizes very rapidly. Accordingly the solutions were always made up from freshly distilled material and stabilized with hydroquinone.

(14) Enough to remove all of the carbonyl components from the reaction mixture. At the end of each run a few drops of the distillate always showed a negative test with 2,4-dinitrophenylhydrazine reagent (ref. 15).

(15) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

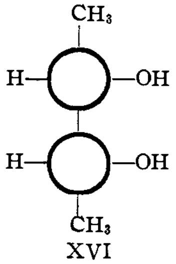
(16) For a similar result in the reaction of nitrous acid with a vicinal aminoalcohol, see Pollak and Curtin, THIS JOURNAL, 72, 961 (1950).

(17) The interpretation of the experiments presented here grew out of a number of helpful discussions with various members of the "Reaction Mechanisms Conference," held at Northwestern University, August, 1950. Particularly helpful were the suggestions of one of the referees.

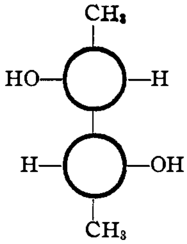


to that from which the water molecule leaves,[18] there are at least three factors which must be considered: First, there is the inherent ability of a group to move (migrational aptitude). Second, there is the ease of formation of the ions or transition states XII and XIII. Certainly, other things being equal, that ion or transition state which provides a *trans* configuration to the more bulky groups is the more comfortable and will be formed with a lower energy of activation. The third factor we must consider in a rearrangement of this type is the rate at which rotation can occur about the central carbon–carbon bond in comparison to the rate at which rearrangement takes place. If rotation about the central carbon–carbon bond can occur more rapidly than rearrangement, then the group which migrates will be determined by a combination of its intrinsic migrational aptitude and the more sterically favored ion or transition state. If rotation about the central carbon–carbon bond occurs more slowly than rearrangement, then it is conceivable that the migrating group will be the one nearest the backside of the atom from which the water molecule is lost regardless of its electrical nature or the stereochemistry of the ion or transition state through which it must pass for rearrangement.

Our data are consistent with either the idea of a slow rotation about the central carbon–carbon bond or of fast rotation about this bond coupled with a sterically preferred transition state. Thus if we assume that the preferred orientation of the 2,3-butanediols is such that the methyl groups (the two largest groups) are as far apart as possible and that rotation about the central carbon–carbon bond is slow, the substituent opposite either of the hydroxyl groups in the *dl* diol (XVI) is a hydrogen atom. Migration of this atom with a pair of electrons or its elimination as a proton[19] would lead to methyl ethyl ketone. This it will be observed was almost the only product obtained. Examination of the *meso* isomer similarly oriented (XVII) reveals that for a migration to occur at the backside of a hydroxyl group some rotation must take place in order to place either a methyl group or a hydrogen atom in an advantageous position for reaction. Consequently, more of a mixture of products would be expected here than from the *dl* isomer. This is again in accord with experiment.

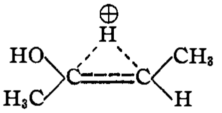


XVI



XVII

Alternatively, if we assume that rotation about the central bond is rapid and that the combined rates of hydride group migration and elimination[19] are inherently more rapid than migration of a methyl group, the results of our experiments can be rationalized in terms of transition state theory. Thus, for the *dl* isomer, formulas XVIII and XIX represent the essential features of the ions or transition states involved in the migration of a methyl group or a hydrogen atom. Formulas XX and XXI represent the corresponding ions or transition states for the *meso* diol. Comparison of formulas XVIII and XIX will show that there is



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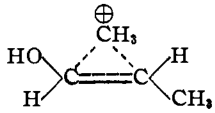

XIX

little choice between the two on the basis of steric repulsions of *cis* oriented groups since in neither case are two methyl groups on the same side of the three-membered ring. Thus the inherently rapid combined rates of hydride group migration and elimination control the situation and methyl

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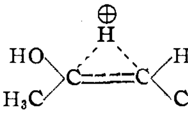
[18] Walden inversion of the atom to which migration occurs has been demonstrated in the closely related reaction of nitrous acid with vicinal aminoalcohols. See Bernstein and Whitmore, *ibid.*, **61**, 1324 (1939).

[19] Methyl ethyl ketone, unlike isobutyraldehyde, could arise either by migration of a hydride group or by simple elimination of a proton. It is not yet possible to determine which of these routes is being followed or whether they are proceeding together. This fact, however, does not alter any of the stereochemical arguments presented in this paper. We are assuming throughout that migration involves a group near the backside of the atom to which migration occurs. It has been shown, at least in cyclic systems, that this is also the hydrogen atom which is preferentially eliminated [Price and Karabinos, THIS JOURNAL, **62**, 1159 (1940)]. Hence a geometry which favors or hinders the formation of methyl ethyl ketone by hydride group migration will similarly favor or hinder the formation of methyl ethyl ketone by elimination.

ethyl ketone is almost the exclusive product. From the *meso* diol, however, structure XXI would be a more stable ion or transition state than XX on the basis of steric considerations alone.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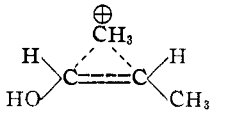
XXI

If, however, the combined rates of hydride group migration and elimination are intrinsically more rapid than the migration of a methyl group, the effects would balance out against each other and a mixture of products would be expected.

Of these two interpretations, we prefer the second since it would seem that rotation about the central carbon–carbon bond in such a simple molecule as a 2,3-butanediol should proceed faster than rearrangement. We feel, however, that the alternative explanation should not be discarded until more experiments have been performed.

The fact that the *cis* and *trans* epoxides gave, within the limits of experimental error, the same proportions of aldehyde and ketone as did the *dl* and *meso* diols, suggests that these reactions involve the same intermediate. It is likely that for both reactions the glycols are the species which actually undergo rearrangement and that the first step in the epoxide rearrangement is simply hydrolysis to the *dl* and *meso* glycols, respectively.[20]

It is not yet clear why less isobutyraldehyde should be formed by the action of silver nitrate on the 3-chloro-2-butanols than from the pinacol rearrangement of the 2,3-butanediols. Seemingly essentially the same transition states should be involved and any steric effects of the large silver ion would appear to be in the direct forcing the methyl group on the adjacent carbon atom nearer the backside of the chlorine atom. This would be expected to result in the formation of more rather than less isobutyraldehyde, but is not in accord with fact. An alternative explanation, namely, that the isobutyraldehyde is oxidized by the nitric acid formed during the reaction, was not supported by experiment. Under the conditions of the experiment, treatment of isobutyraldehyde with the same amount of nitric acid as would be formed during the rearrangement caused no oxidation or consumption of the aldehyde.

[20] See Wheland, ref. 2, pp. 470–473.

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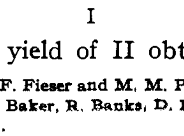
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Cyclic Polyolefins. XIV. 3,7-Dibromo-1,2,5,6-Dibenzcycloöctadiene and 1,2,5,6-Dibenzcycloöctatetraene

BY ARTHUR C. COPE AND STUART W. FENTON

The hydrocarbon 1,2,5,6-dibenzcycloöctadiene (II), previously described by Baker, Banks, Lyon and Mann, has been prepared in an improved yield of 30–46% from α,α'-dibromo-*o*-xylene and sodium under conditions of high dilution Bromination of II with N-bromosuccinimide formed 3,7-dibromo-1,2,5,6-dibenzcycloöctadiene (III) in 70–90% yield. The structure of III was established by conversion to the diol IV by direct hydrolysis, or better through preparation and hydrolysis of the diacetate V, followed by oxidation of IV to 3-hydroxy-1,2,5,6-dibenzcycloöctadien-7-one hemiketal (VII). The structure of VII was determined by comparison with an identical sample obtained by the Meerwein–Ponndorf reduction of 1,2,5,6-dibenz-1,5-cycloöctadiene-3,7-dione (VIII), prepared by the procedure of Wawzonek. Pyrolysis of the diacetate V resulted in the elimination of two equivalents of acetic acid and the formation of 1,2,5,6-dibenzcycloöctatetraene (I) in 70% yield. The hydrocarbon I obtained by this route was identified by reduction to II, and by direct comparison with a sample prepared by the longer original synthesis of I described by Fieser and Pechet.

The synthesis of 1,2,5,6-dibenzcycloöctatetraene (I) by a reaction sequence beginning with the condensation of *o*-phthalaldehyde and *o*-phenylenediacetonitrile has been described by Fieser and Pechet.[1] 1,2,5,6-Dibenzcycloöctadiene (II) has been prepared in 5–6% yield from α,α'-dibromo-*o*-xylene and sodium in dioxane by Baker, Banks, Lyon and Mann.[2] If II could be prepared in better yield, it might be useful as an intermediate in the synthesis of I and other derivatives of cycloöctatetraene. This paper reports an investigation of these possibilities.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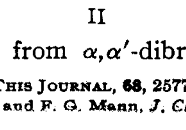
II

The yield of II obtained from α,α'-dibromo-*o*-xylene and sodium was found to be dependent upon the concentration (Fig. 1). With the most dilute solution of the dibromide in dioxane that was studied the yield was 46%, but it was more economical of time and materials to use a simple high-dilution apparatus for the reaction, a procedure which formed II in a yield of 30%. The hydrocarbons 1,2,5,6,9,10-tribenz-1,5,9-cyclododecatriene and 1,2-di-(*o*-tolyl)-ethane, previously described as by-products of this reaction,[2] also were isolated. An examination of the lower boiling fractions gave no evidence that 1,2-benz-1-cyclobutene was present.

The reaction of 1,2,5,6-dibenzcycloöctadiene (II) with one molar equivalent of N-bromosuccinimide proceeded readily but no monobromide was isolated from the product, which proved to be a mixture of a dibromide III and unchanged II. With two molar equivalents of N-bromosuccinimide a 70–90% yield of the dibromide (later proved to be 3,7-dibromo-1,2,5,6-dibenz-1,5-cycloöctadiene

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[1] L. F. Fieser and M. M. Pechet, THIS JOURNAL, **68**, 2577 (1946).

[2] W. Baker, R. Banks, D. R. Lyon and F. G. Mann, *J. Chem. Soc.*, 27 (1945).