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Howard J. Schaeffer

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THE USE OF RADIOACTIVE CARBON IN A STUDY OF 3-PHENYLCYCLOHEXYL AND RELATED SYSTEMS

Howard J. Schaeffer

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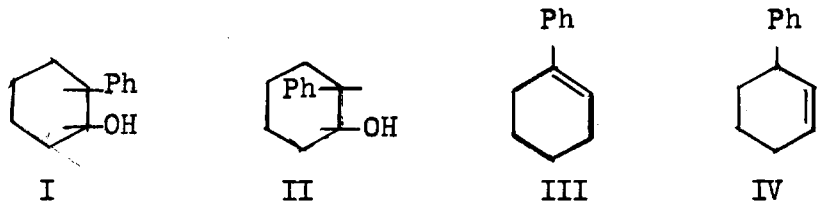
INTRODUCTION AND PRELIMINARY RESULTS

The dehydrations, with phosphoric acid, of cis- and of trans-2-phenylcyclohexanol (I and II, respectively) were reported in 1940 by Price and Karabinos. (1) The results of this study were interpreted as evidence for the trans-elimination of the elements of water in such dehydrations, since the cis-alcohol (I) was reported to yield chiefly 1-phenylcyclohexene (III) whereas the trans-alcohol (II) was said to yield predominantly 3-phenylcyclohexene (IV). It was



suggested (1) that the small amount of isomeric olefin formed in each dehydration was the result either of a) isomerization of the alcohols ($I \rightleftharpoons II$) before dehydration or b) competitive cis-elimination of the elements of water from each carbinol.

The Chugaev reactions of the methyl xanthates, and the thermal decompositions of the acetates of I and II were next studied by Alexander and Mudrak, (2) who showed that in each of these reactions cis-elimination occurred, for the results were the reverse of those reported for the phosphoric acid catalyzed dehydrations of I and II. Thus, both the acetate and the methyl xanthate of the cis-alcohol (I) yielded primarily 3-phenylcyclohexene (IV), whereas the corresponding

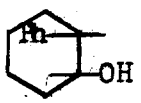
trans-compound yielded principally 1-phenylcyclohexene (III).

The difficulties of determining the yields and identities of liquid, isomeric olefins are indicated by Alexander and Mudrak (2) who measured the refractive indices of the redistilled products from each reaction for this purpose. These authors pointed out that the yields calculated by Price and Karabinos (1) are based upon an incorrect refractive index for 3-phenylcyclohexene, but state that the general conclusions (1) concerning the acid catalyzed dehydrations of I and II remain valid. (2)

By the use of the carbon-14 dilution technique, (4) a method not available to Price and Karabinos (1) at the time of their experiments, it should be possible, by employing carbon-14 labeled reactants, to gain accurate information concerning the yields of olefins III and IV upon dehydration of cis-2-phenylcyclohexanol-2-C^{14} (Ia) and trans-2-phenylcyclohexanol-2-C^{14} (IIa).* It should be possible also to determine whether the small amount of 1-phenylcyclohexene (IIIab) obtained upon dehydration of alcohol IIa is the consequence of cis-elimination of the elements of water, or of participation of the phenyl group during removal of the hydroxyl ion. This latter possibility has been speculated upon by Cram. (3) Thus, in the dehydration

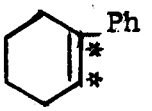
*In this dissertation Roman numerals have been used to designate the names of the various compounds where repetition of their names would be cumbersome. In the case of radioactive compounds, a letter has been appended to the Roman numeral to indicate the position of labeling, thus IIa represents trans-2-phenylcyclohexanol-2-C^{14} discretely labeled in the 2-position whereas IIIab represents 1-phenylcyclohexene-1,2-C^{14}_{1} labeled at both the 1- and 2-positions.

of trans-2-phenylcyclohexanol-2-C^{14} (IIa) the contribution of such an intermediate ion (3) as A, for example, should lead to the formation



IIa

A



IIIab

of 1-phenylcyclohexene-1,2-C_1^{14} (IIIab) in which the radioactive carbon is equally divided between the 1- and 2-positions of the cyclohexene ring.

We have repeated the experiments of Price and Karabinos (1) employing cis-2-phenylcyclohexanol-2-C^{14} (Ia) and trans-2-phenylcyclohexanol-2-C^{14} (IIa), and have determined the yields, for the dehydration of each alcohol, of olefins III and IV. In addition, for the dehydration of IIa, three further olefins have been identified as products, and the extent of phenyl participation in the formation of 1-phenylcyclohexene (IIIab) has been determined. On the basis of our experiments, it has been necessary to modify certain conclusions of the previous investigators. (1) The experimental methods employed, the results of these experiments, and the conclusions drawn from the present work are discussed in the following sections.

Yields of 1-Phenylcyclohexene (IIIa) and 3-Phenylcyclohexene (IVa) on Dehydration of Alcohols Ia and IIa.

The dehydrations of the cis- and the trans-alcohols (Ia and IIa) each labeled with carbon-14 in the 2-position were carried out by

heating under reflux for four hours equal weights of the appropriate alcohol and 85% phosphoric acid. During the first experiments a Glas-Col mantle supplied the source of heat. Later a Woods' metal bath maintained at a temperature of 200-205° C. was employed. The mixture from dehydration of each alcohol was analyzed for olefins IIIa and IVa by means of the radioactivity dilution technique, (4) which is described in detail, (as are the synthetic procedures) later in this dissertation. The results of these experiments are given in Table I, and are compared with those of Price and Karabinos. (1)

Although the results of the dehydration of the cis-alcohol (Ia) are in qualitative agreement with those of Price and Karabinos, (1) the results of dehydration of the trans-compound (IIa) are in disagreement. Thus, in our hand, the trans-alcohol underwent dehydration to produce more 1-phenylcyclohexene (IIIa) than the 3-isomer (IVa) in the ratio of 2:1. In addition, the two olefins (IIIa and IVa) previously reported as the sole products of these reactions, account for only 30% of the material yield in the dehydration of the trans-alcohol (IIa).

Molecular weight determinations of the oil from the dehydration of IIa suggested that this product was a mixture of monomers of the same approximate molecular weight as the olefins IIIa and IVa. The ease of oxidation of this mixture with permanganate suggested the presence of unsaturation.

Our attack on the problem, therefore, was to a) synthesize a number of olefins isomeric with III and IV, which we suspected by

TABLE I

Yields of 1-Phenylcyclohexene (III) and of 3-Phenylcyclohexene (IV) Upon Phosphoric Acid Dehydration of *cis*-2-Phenylcyclohexanol (Ia) and of *trans*-2-Phenylcyclohexanol (IIa).

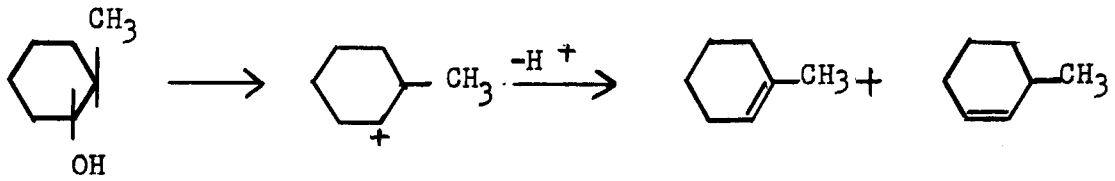
Experiment No.	Reactant	Yield of III%		Yield of IV %	
1	*cis*-alcohol Ia	88		2.4	
Price and Karabinos Ref. 1	*cis*-alcohol I	56 - 62		9 - 17	
2	*trans*-alcohol IIa	18.8	Ave.		
3	*trans*-alcohol IIa	20.8	21.0 ± 1.6	9.6	Ave. 9.3 ± 0.3
4	*trans*-alcohol IIa	23.4		9.0	
Price and Karabinos Ref. 1	*trans*-alcohol II	10 - 18		59 - 68	

reason of our ability to justify them mechanistically might be present in this mixture; b) add a weighed amount of each purified olefin to a separate aliquot of the mixture obtained on dehydration of II; c) reisolate the olefin after homogenizing the solution; d) convert this olefin to a solid derivative and purify to constant radioactivity content; e) calculate, from the foregoing data, the yield of the particular olefin.

HISTORY

Elimination reactions have long been of interest to organic chemists and recently several excellent discussions (5,6,7) have been published. Like substitution reactions, elimination reactions can conveniently be classified into two mechanisms; the unimolecular (E_1) and the bimolecular (E_2) mechanism. The mechanism of the acid-catalyzed dehydration of alcohols has received little attention in these articles, however, and many of the conclusions drawn on the mechanism of elimination reactions of halides, quaternary ammonium compounds, and sulfonium compounds, which are supported by experimental evidence, are merely inferred for the dehydration reactions.

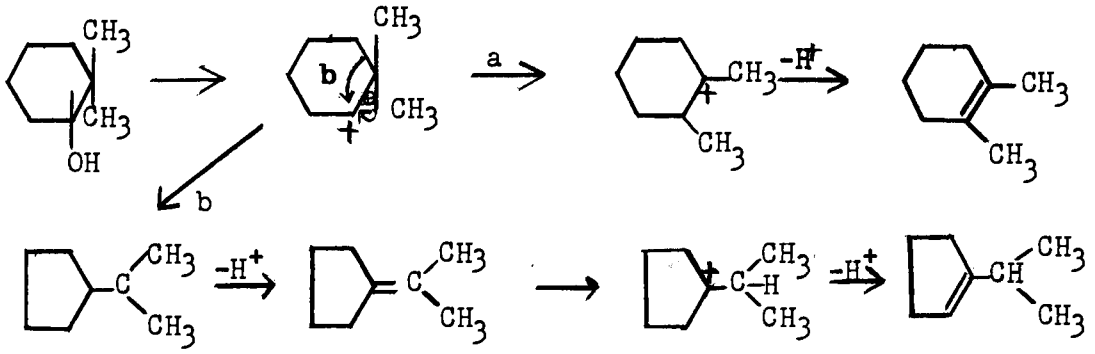
Previously, a carbonium ion mechanism was utilized exclusively to explain the results of acid-catalyzed dehydrations. Thus, the fact that the dehydration of trans-2-methylcyclohexanol (8) produced



approximately equal amounts of 1- and 3-methylcyclohexene could be explained by the formation of a planar carbonium ion which could have equal probability of ejecting a proton from the 2- or the 6-position. Unfortunately the cis-isomer, which should yield the same mixture of isomers upon dehydration if the carbonium ion mechanism is correct, has not as yet been studied.

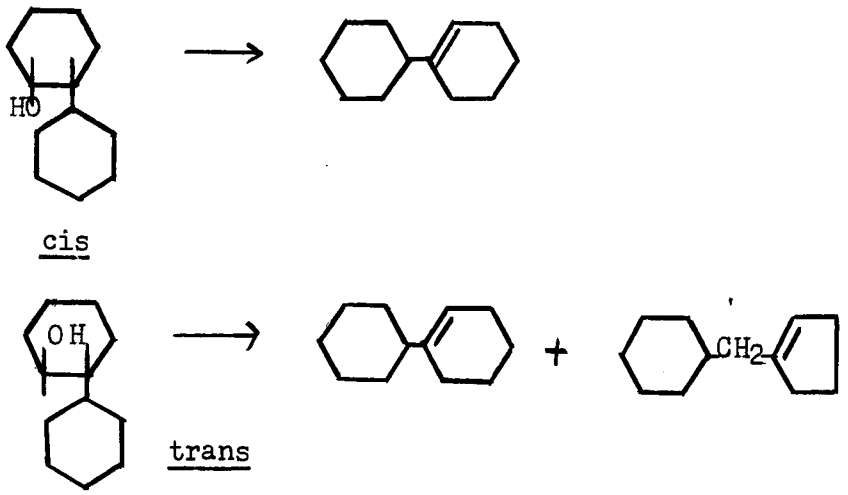
The dehydration of the closely related alcohol, 1,1-dimethyl-

cyclohexanol, (9) was found to yield a mixture of 1,2-dimethylcyclohexene and 1-isopropylcyclopentene in the ratio of 3:1. As is frequently the case in the alicyclic series, the reaction proceeded with migration of a methyl group and with ring contraction. A carbonium ion mechanism was proposed and to account for the formation



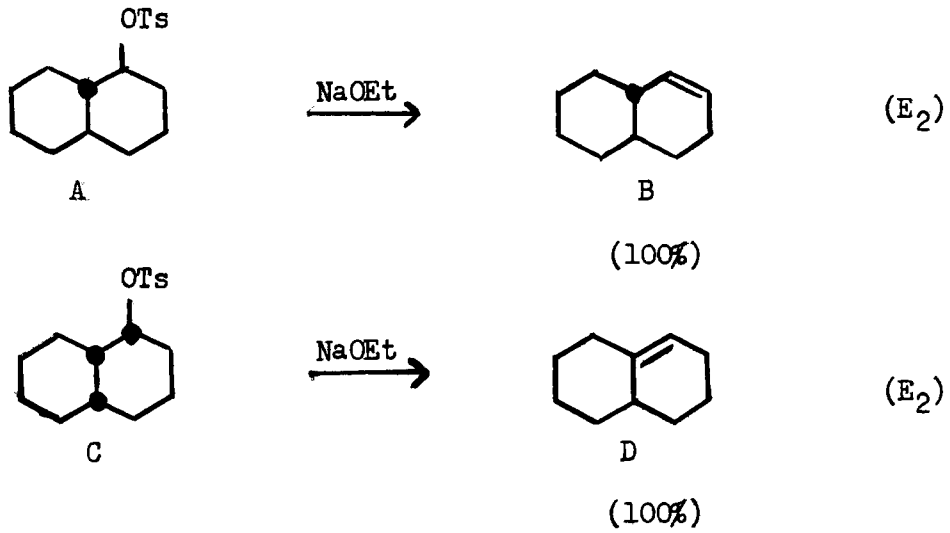
of 1-isopropylcyclopentene, the presence of an unstable intermediate, isopropylidenecyclopentane, was suggested which rearranged in the acidic medium to 1-isopropylcyclopentene as outlined above.

In a study of the dehydration of the two stereoisomers of 2-cyclohexylcyclohexanol, Hückel (10) found that from the <u>cis</u>-isomer a quantitative yield of 1-cyclohexylcyclohexene was obtained whereas

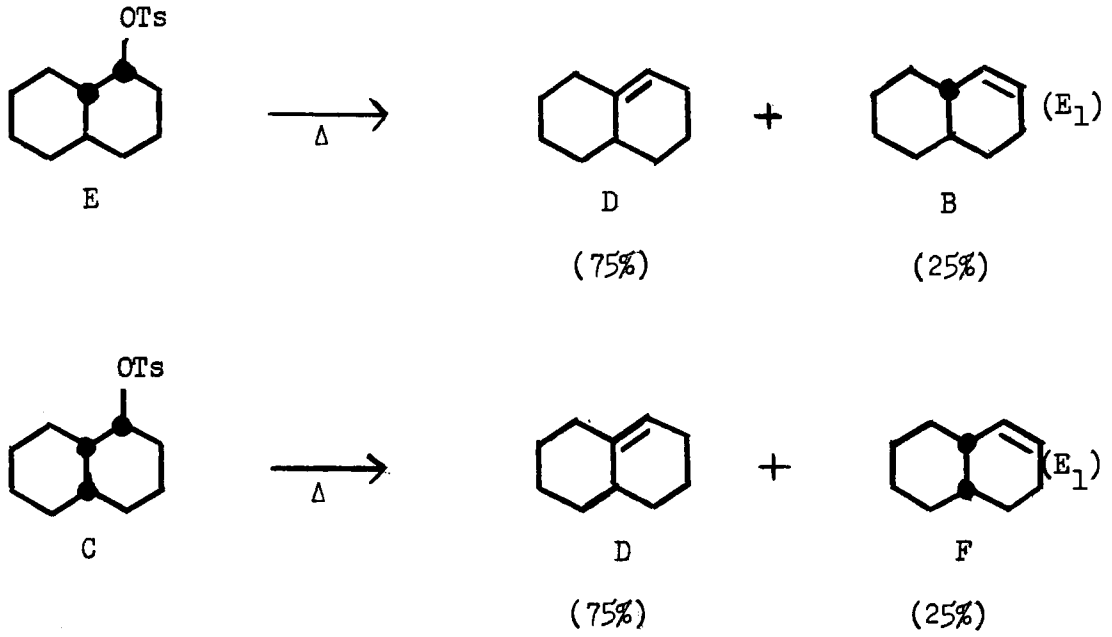


the trans-isomer gave a low yield of a mixture of 1-cyclohexylcyclohexene and 1-hexahydrobenzylcyclopentene. These results suggest that the groups or atoms (H and OH) to be eliminated are most favorably situated for reaction when they bear a trans-relationship to each other.

That the mechanism can greatly influence the products formed in an elimination reaction was demonstrated in the decalol system, whose stereochemistry was recently established by Dauben. (11,12) In this discussion the configurational assignments are in terms of the relative positions of the hydrogen atoms at C_9 and C_{10}, and C_9 and the tosylate group at C_1. Thus, Hückel (13) and co-workers have shown that the bimolecular elimination reaction (E_2) of sodium ethoxide and trans-trans-1-decalyl tosylate (A) yielded entirely trans-$\Delta^{1,2}$-octalin (B) whereas cis-cis-1-decalyl tosylate (C) yielded entirely $\Delta^{1,9}$-octalin (D). The reaction has been shown to be completely stereospecific in that there were no products corresponding to cis-elimination.

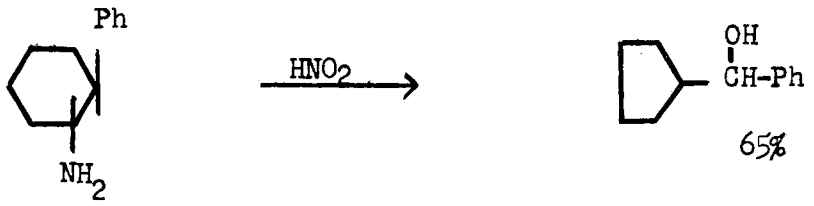


The unimolecular elimination reaction (E_1) of related compounds was carried out by heating the tosylates in the absence of strong base; thus, from trans-cis-1-decalyl tosylate (E) there was obtained a mixture of $\Delta^{1,9}$-octalin (D, 75%) and trans-$\Delta^{1,2}$-octalin (B, 25%) whereas cis-cis-1-decalyl tosylate (C) yielded a mixture of $\Delta^{1,9}$-octalin (D, 75%) and cis-$\Delta^{1,2}$-octalin (F, 25%).

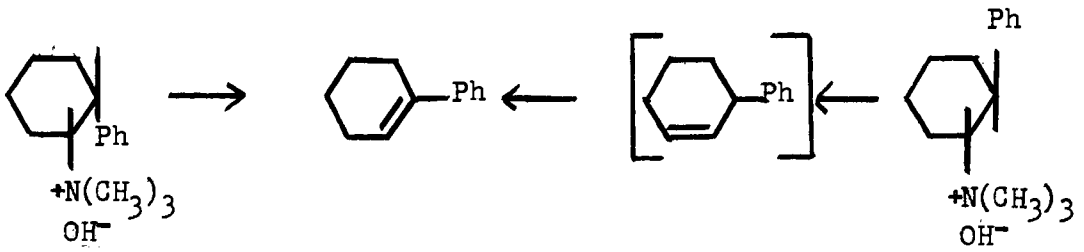


These results suggest that bimolecular elimination reactions (E_2) are dependent upon spatial position and must involve groups or atoms which bear a trans-relationship to each other. However, the unimolecular elimination reactions (E_1) must involve a stage in which the geometrical isomers become equivalent since $\Delta^{1,9}$-octalin (D) was the major product from both C and E. The formation of a free carbonium ion would account for this phenomenon of equivalence of isomers in E_1 reactions.

Two interesting elimination reactions have recently been studied in the 2-phenylcyclohexyl system. Nightengale and Maienthal (14) treated trans-2-phenylcyclohexylamine with nitrous acid and obtained cyclopentylphenylcarbinol whereas Arnold and Richardson (15) obtained



1-phenylcyclohexene by the Hofmann degradation of cis- and trans-2-phenylcyclohexylamines. The latter authors propose a bimolecular trans-elimination indicating that the 3-phenylcyclohexene obtained from the trans-isomer rearranges in the basic medium to 1-phenylcyclohexene as shown:



Results of this kind are further examples of the effect of a changing mechanism. The nitrous acid deamination most certainly reacts by a unimolecular elimination (E_1) and gives ring contraction as the major product but the Hofmann degradation is bimolecular (E_2) and yields the corresponding olefin.

From this discussion it is apparent that application of carbon-14 tracer techniques would give information on the mechanism of the acid-catalyzed dehydration of alcohols. In the following sections some of

these applications will be discussed.

METHODS AND RESULTS

Synthetic and Degradative Methods.

The syntheses of cis- and trans-2-phenylcyclohexanol-2-C^{14} (Ia and IIa) were accomplished as shown in Chart I, the carbon-14

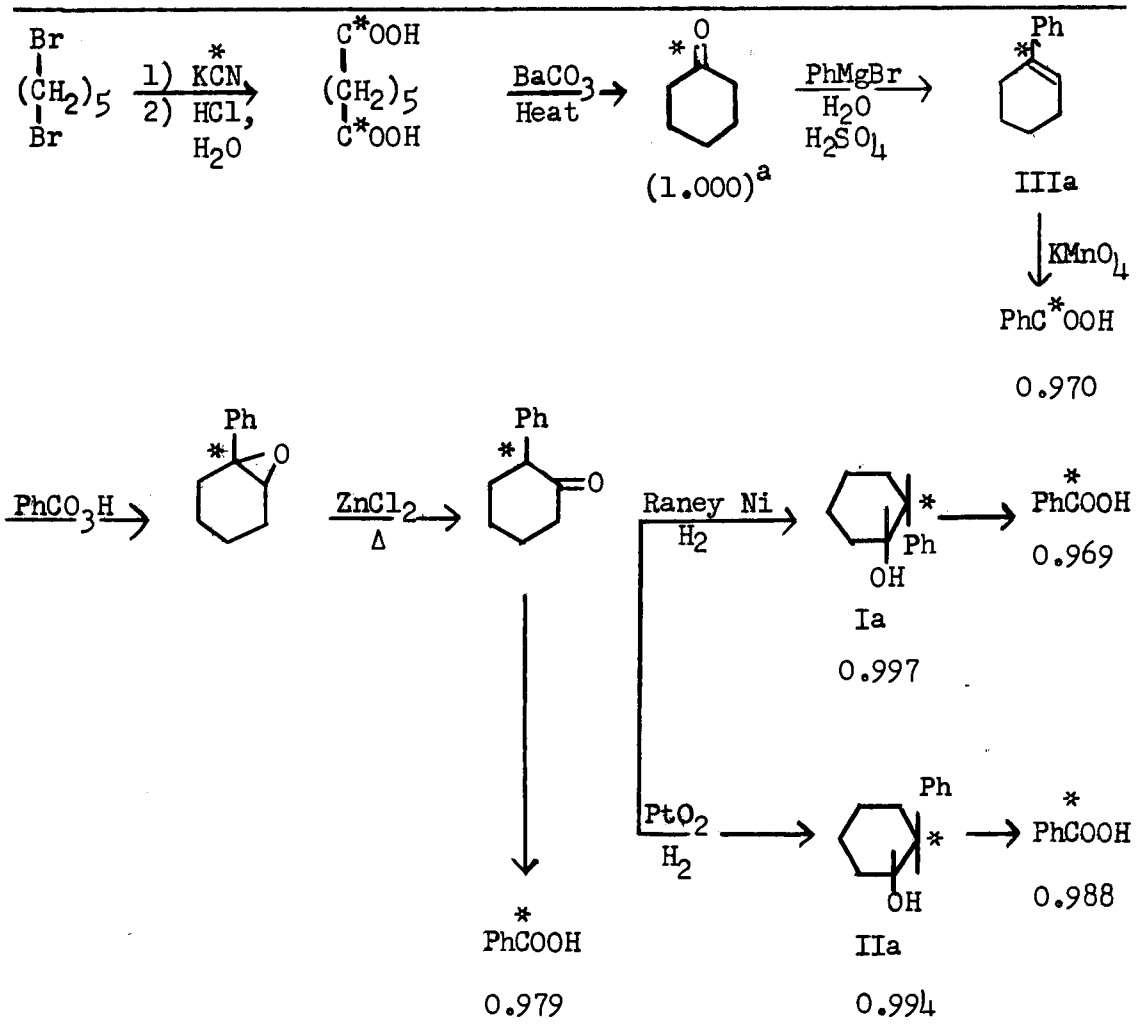


CHART I

a) The molar radioactivity of this compound was taken as 1.000. The molar radioactivity of the other compounds listed in this chart are expressed as the fraction of the original radioactivity of cyclohexanone-1-C^{14}.

being introduced in the preparation of pimelonitrile-1,7-C_2^{14}. The radiochemical structures of the products were established by oxidation of 1-phenylcyclohexene-1-C_1^{14}, of 2-phenylcyclohexanone-2-C^{14} and of alcohols Ia and IIa to benzoic acid. The benzoic acid fractions obtained from these oxidations possessed lower molar radioactivities than the compounds oxidized by about 2-3%. These results indicate that the alcohols Ia and IIa are discretely labeled with carbon-14 in the 2-position at least to the extent of 97-98%. The lower radioactivity assays of the benzoic acid fractions are caused in all probability by an isotope effect occurring during the oxidation of these compounds.

1-Phenylcyclohexene-1-C^{14} (IIIa) was prepared as indicated in Chart I. The degradation of IIIa and conversion of it to a derivative suitable for radioactivity was accomplished in three ways: a) oxidation of the olefin with potassium permanganate to δ-benzoylvaleric acid (VIII); b) preparation of the solid 1-phenylcyclohexene nitrosochloride (X); and c) preparation of 2-phenyl-2-cyclohexenone oxime (XI); followed by oxidation of these derivatives to benzoic acid (IX).

3-Phenylcyclohexene (IV) labeled with carbon-14 was prepared by a modification of the Berlande (16) method. Owing to the fact that the position of labeling was unimportant for the isomerization and stability experiments, the radiochemical structure of 3-phenylcyclohexene was not proven exhaustively. It was shown, however, that 26% of the carbon-14 in the cyclohexene nucleus was adjacent to the phenyl

group (Table VI). In order to obtain a solid derivative suitable for radioactivity assay, 3-phenylcyclohexene was converted to the solid methoxychloromercury derivative (XII), which was also oxidized to benzoic acid (XIII).

The synthesis of 4-phenylcyclohexene (V) was accomplished by the method of Konigsberger and Salmon. (17) This compound was converted to the solid β-phenyladipic acid upon oxidation with chromium trioxide.

1-Benzylcyclopentene (VI) was prepared as described by Denisenko and co-workers. (18,19) This compound was converted to its solid nitrosochloride and the radioactivity content of VI was determined by assay of this derivative.

Benzalcyclopentane (VII) was synthesized by a two-step reaction in which 1-benzylcyclopentene (VI) was used as the starting material. Anhydrous hydrogen bromide was added to VI to give 1-bromo-1-benzylcyclopentene which upon dehydrohalogenation with methanolic potassium hydroxide formed benzalcyclopentane (VII). This compound was degraded by ozonolysis to benzaldehyde whose 2,4-dinitrophenylhydrazone was assayed for radioactivity. This latter assay was taken as a measure of the radioactivity content of olefin VII obtained as a dehydration product of IIa.

In order to insure that the derivatives of the olefins were radiochemically pure, it was necessary to prepare the various derivatives from mixtures of non-radioactive and radioactive olefins whose radioactivity content was known and determine that no

contamination had occurred. For example, (see the Experimental Section) the radiochemical purity of derivative (VIII) of 1-phenylcyclohexene was determined by oxidizing a mixture of 1-phenylcyclohexene-1-C^{14} (IIIa) and 3-phenylcyclohexene (IV) to δ-benzoylvaleric acid (VIII). A 1% decrease in radioactivity was observed, the same decrease observed upon oxidation of pure IIIa, and most probably caused by an isotope effect.

Identification of Further Products in the Dehydration of trans-2-Phenylcyclohexanol-2-C^{14} (IIa).

In order to determine which compounds, other than IIIa and IVa, were formed as a result of the dehydration of trans-2-phenylcyclohexanol, this reaction was repeated using labeled IIa, and the product was divided into several aliquots. To each aliquot a different one of the non-radioactive olefins, 1-phenylcyclohexene (III), 3-phenylcyclohexene (IV), 4-phenylcyclohexene (V), 1-benzylcyclopentene (VI) and benzalcyclopentane (VII) was added. After each of the aliquots had been made homogeneous with the added olefin, the particular aliquot was usually subjected to some initial physical method for separating the compound which had been added (and which now was mixed with the radioactive olefin of identical structure which had been formed on dehydration). After this initial partial purification, the liquid compound in question was converted to its appropriate solid derivative. After repeated crystallization of this derivative until its radioactivity content was constant between crystallizations, the yield could be determined with high accuracy. The results of these

experiments are given in Table II, together with those results included previously in Table I.

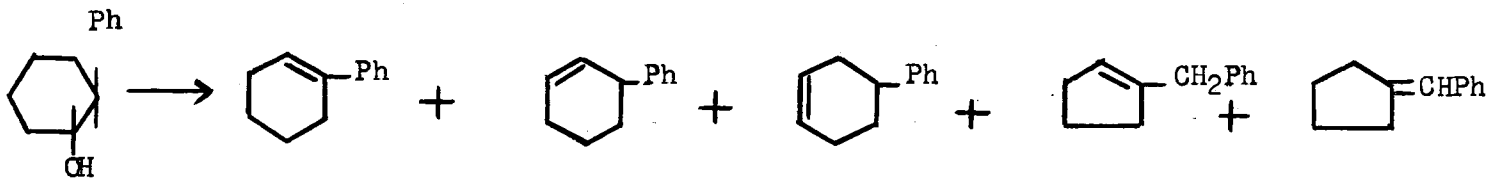
Effect of Dehydrating Conditions on 1- and 3-Phenylcyclohexene (III and IV).

The stability of 1-phenylcyclohexene (III) was determined by subjecting equal weights of the olefin (III) and phosphoric acid to the dehydration conditions. The experiments were performed in two ways: a) by refluxing equal weights of non-radioactive 1-phenylcyclohexene and phosphoric acid for 4 hours, diluting with a known weight of 1-phenylcyclohexene-1-C^{14}, and oxidizing the mixture to δ-benzoylvaleric acid (VIII); and b) by the reverse of the above procedure, that is, by subjecting 1-phenylcyclohexene-1-C^{14} (IIIa) to the dehydrating conditions and diluting with non-radioactive 1-phenylcyclohexene before preparing the derivative. From each of these experiments, the loss of 1-phenylcyclohexene under the dehydration conditions was calculated (Table III).

The stability of a mixture of 1-phenylcyclohexene-1-C^{14} (IIIa) and non-radioactive 3-phenylcyclohexene (IV) was next examined. In this case it was necessary to prepare two derivatives of 1-phenylcyclohexene (III). One derivative of III was prepared from an undiluted aliquot of the olefins and the other was prepared from an aliquot which was diluted with non-radioactive 1-phenylcyclohexene (III). With these two assays both the loss of 1-phenylcyclohexene (III) and the isomerization of 3-phenylcyclohexene (IV) to 1-phenylcyclohexene (III) were then determined. The results of these

TABLE II

Products Formed Upon Dehydration of trans-2-Phenylcyclohexanol (IIa).



Exp. No.	II	III	IV	V	VI	VII
2		18.8%				
3		20.8%	9.6%			
4		23.4%	9.0%	6.0%	31.6%	
5				5.7%	32.5%	29.8%
		Ave.: 21.0%	Ave.: 9.3%	Ave.: 5.85%	Ave.: 32.05%	

experiments also are shown in Table III.

In order to test the stability of 3-phenylcyclohexene (IV), the radioactive olefin (IV) was heated with phosphoric acid under the same conditions used for dehydrating alcohols Ia and IIa. With the aid of the dilution technique the presence as well as the yields of each of the olefins III, IV, V, VI, and VII were determined. It is to be noted that a mixture of the same five isomeric olefins was obtained from the isomerization of radioactive 3-phenylcyclohexene (IV) as was obtained from the dehydration of trans-2-phenylcyclohexanol-2-C^{14} (IIa). All of these stability experiments are summarized in Table III.

That the isomerization of 3-phenylcyclohexene (IV) is not measurably reversible was demonstrated in two ways: a) by subjecting a mixture of 1-phenylcyclohexene-1-C^{14} (IIIa) and non-radioactive 3-phenylcyclohexene (IV) to the dehydrating conditions, diluting with 3-phenylcyclohexene (IV), and preparing the methoxychloromercury derivative (XII) of 3-phenylcyclohexene; and b) by refluxing equal weights of non-radioactive benzalcyclopentane (VII) and phosphoric acid for 4 hours, diluting with radioactive 3-phenylcyclohexene (IV) and preparing the same derivative (XII). Thus, it was found that neither 1-phenylcyclohexene (IIIa) or benzalcyclopentane (VII) is isomerized to 3-phenylcyclohexene. (See Table VI).

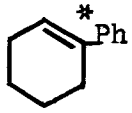
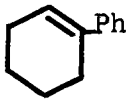
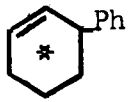
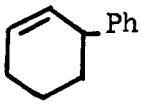
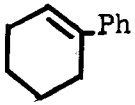
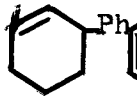
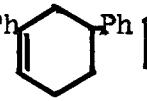
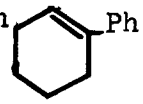
Determination of Phenyl Migration in Reactions Yielding 1-Phenylcyclohexene (III).

cis-2-Phenylcyclohexanol-2-C^{14} (IIa) was dehydrated with

TABLE III

Isomerization Products of 1-Phenylcyclohexene and of

3-Phenylcyclohexene in Refluxing Phosphoric Acid

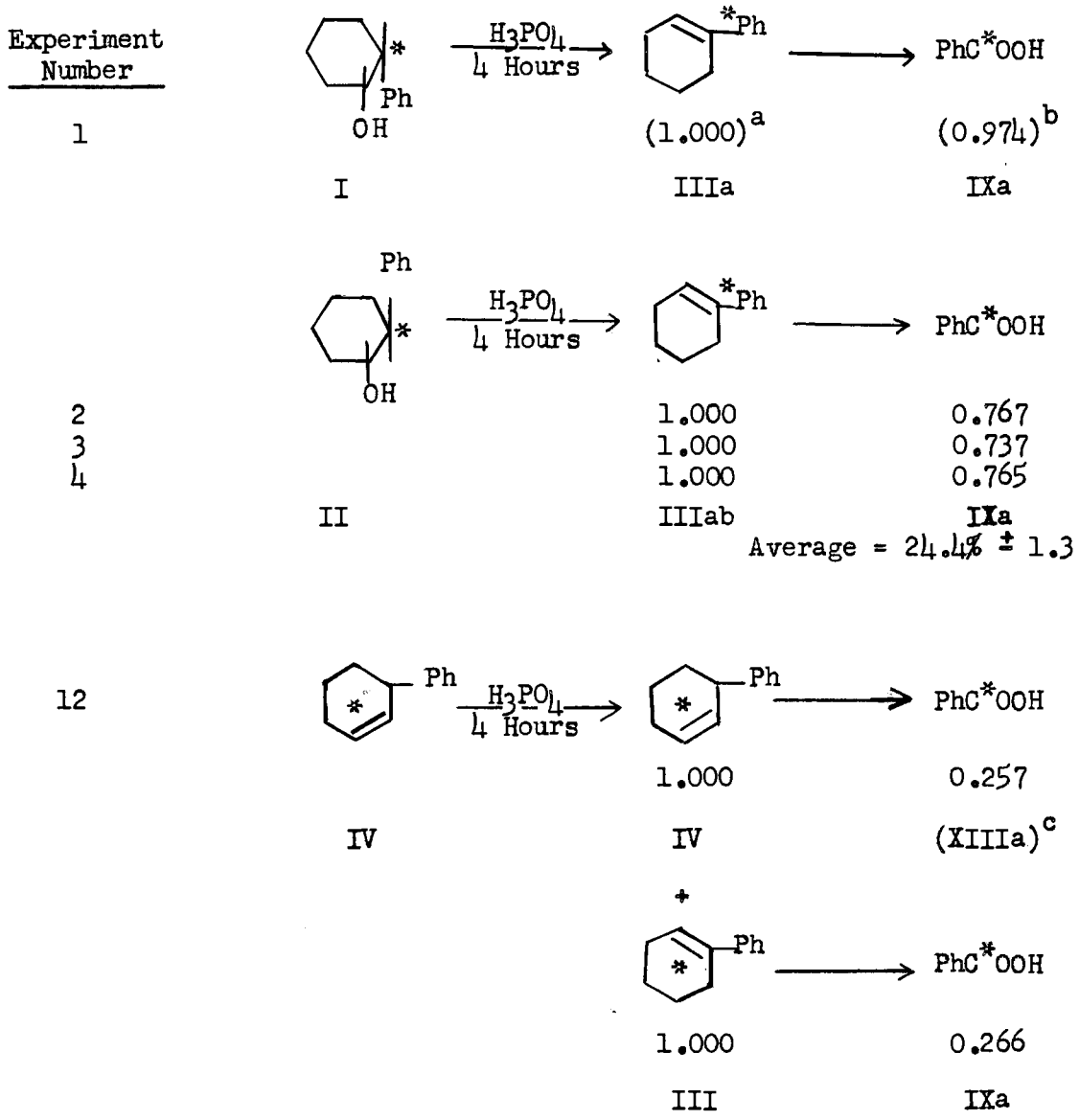
Exp. No.	Mole % Reactant				% Isomerization of IV to Form					% Loss Of
										
6	0.548	-	-	0.452	12.4	-	-	-	-	6.6 Ave. 7.3
7	0.476	-	-	0.524	12.3 Ave. 12.35	-	-	-	-	7.9
8	-	1.00	-	-	-	-	-	-	-	18.3
9	1.00	-	-	-	-	-	-	-	-	11.4
10	-	-	-	1.00	11.2	-	-	-	-	-
11	-	-	1.00	-	17.2	58.6[a]	11.5	5.9	4.4	-
12	-	-	1.00	-	6.8	76.2[a]	-	-	-	-

a) This figure represents the 3-phenylcyclohexene remaining after isomerization.

phosphoric acid as described previously (see Tables I and II) to yield 87.7% of 1-phenylcyclohexene (IIIa). No phenyl migration occurred during this reaction since it was found that the benzoic acid (IXa) obtained on oxidation of IIIa so prepared contained only 2.6% less radioactivity than the parent alcohol (Ia), the same decrease of radioactivity observed on oxidation of both the discretely labeled alcohol and the discretely labeled olefin (IIIa) to benzoic acid, and explainable on the basis of an isotope effect (Chart II). Dehydration of trans-2-phenylcyclohexanol-2-C^{14} (IIa) afforded 1-phenylcyclohexene (IIIab) which was oxidized to benzoic acid containing an average of 24.4% less carbon-14 than the parent alcohol (see Chart II). Radioactive 3-phenylcyclohexene (IV) was isomerized under the dehydration conditions to 1-phenylcyclohexene (III) and subsequent oxidation of III to benzoic acid (IXa) indicated that phenyl migration had not occurred.

CHART II

Determination of Phenyl Migration in 1-Phenylcyclohexene (III).

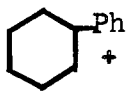


a) The molar radioactivity of product III was taken as 1.000.
b) The molar radioactivity of product IXa was expressed as the fraction of the original radioactivity of product III and represents the amount of radioactivity found in the 1-position of product III.
c) The method of expressing molar radioactivity also applies to product IV and XIIIa.

DISCUSSION

From Tables I, II and III it is apparent that the mechanism of the dehydration of cis- and trans-2-phenylcyclohexanols (I and II) is more complicated than had been previously thought. (1) From these data, however, several obvious conclusions may be reached:

1. From the fact that Ia and IIa yield the same products (III - VII) in widely differing amounts, we may conclude that these two alcohols do not produce, upon dehydration, a common classical carbonium ion intermediate B. At least one of these alcohols, there-



B

fore, must undergo dehydration via a concerted process. Since 3-phenylcyclohexene (IV), when subjected to the same dehydrating conditions as I and II must, in all probability, go through carbonium ion intermediate B to a large extent, we conclude that the portion of the reaction of the trans-alcohol II which produces 1-phenylcyclohexene (III) with phenyl migration must proceed with participation of the phenyl group, probably through either a bridged ion (3) or a symmetrical transition state. If this were not true it would be expected that phenyl migration would take place during the conversion of IV $\rightarrow$ III.

2. If a bridged ion or a symmetrical transition state were the only path of formation of 1-phenylcyclohexene (III) from the trans-

alcohol (IIa), it is obvious that the radioactivity should be distributed equally between the 1- and the 2-positions of the cyclohexene ring. That the observed phenyl migration is only 24% does not, however, invalidate this view nor does it suggest the presence of an unsymmetrical bridged ion. (20) It is readily explainable from the observation of the two paths of formation of 1-phenylcyclohexene during the dehydration of IIa. Let us consider that portion of the 1-phenylcyclohexene (IIIab) which is formed by participation of the phenyl group during dehydration; and assume that it has a 50:50 distribution of radioactivity between the 1- and the 2-positions. We have shown experimentally that the portion which is formed by the isomerization of 3-phenylcyclohexene yields unrearranged 1-phenylcyclohexene (IIIa). With a knowledge of the total yield of 1-phenylcyclohexene (III) from the dehydration of trans-2-phenylcyclohexanol-2-C^{14} (IIa) and of the extent of isomerization of 3-phenylcyclohexene (IV), it is possible to calculate the fraction of radioactivity which should be observed to be lost from the 1-position of the olefin (IIIa and IIIab) produced upon dehydration of the trans-alcohol (IIa). These calculations are given in Table IV. (See the Experimental Section for a sample calculation).

The agreement between the calculated and the observed loss of radioactivity offers good evidence that the assumption concerning the 50:50 distribution of radioactivity in the 1-phenylcyclohexene formed by participation is valid. We conclude, therefore, the intervention of a symmetrical phenonium ion during this step.

TABLE IV

The Observed and Calculated Per Cent Loss of Radioactivity in the Benzoic Acid Obtained from 1-Phenylcyclohexene upon Dehydration of *trans*-2-Phenylcyclohexanol-2-C^{14}.

Experiment Number	Observed Phenyl Migration %		Calculated Phenyl Migration %	
2	23.3	Ave. 24.4 ± 1.3	22.6	Ave. 25.9 ± 2.2
3	26.3		25.9	
4	23.5		29.2	

3. Since the product obtained upon dehydration of the *cis*-alcohol (I) is predominately 1-phenylcyclohexene, (III) whereas this olefin is formed in only small quantity upon isomerization of IV, it is probable that the *cis*-alcohol I undergoes dehydration also *via* a concerted process in which the hydrogen at the 1-position *trans* to the hydroxyl participates in hydroxyl removal. (See discussion in paragraph 1).

4. Nothing can be presumed from the present data as to whether the *trans*-hydrogen of the 6-position of either *cis*- or *trans*-2-phenylcyclohexanol participates in the dehydration by a concerted elimination, since that portion of the dehydration reaction which does not involve phenyl migration from IIa or a concerted hydrogen elimination from Ia is equally explainable if it is assumed that the carbonium ion B is the intermediate. In this respect it is significant that

when labeled 3-phenylcyclohexene (IV) is placed under the same conditions of dehydration employed for the alcohol, the same mixture of olefins is obtained as was produced from the trans-alcohol (Table III). The only important difference in these two mixtures of products is that a portion of the labeled 1-phenylcyclohexene formed from IIa has undergone the previously mentioned phenyl migration (Chart II).

5. Although it cannot be said whether 3-phenylcyclohexene is formed from IIa by a concerted process or through carbonium ion B, 4-phenylcyclohexene (V) must have 3-phenylcyclohexene as a precursor since carbonium ion B can only rearrange to V as outlined in Chart III. A similar situation obtains for the formation of 1-benzylcyclopentene (VI); that is, it must have benzalcyclopentane (VII) as a precursor. It is interesting that benzalcyclopentane (VII) and 1-phenylcyclohexene (III) have been shown not to isomerize to 3-phenylcyclohexene when placed under the dehydrating conditions (Table VI).

6. The reaction mechanism outlined in Chart III is the simplest mechanism for the dehydration which is consistent with all of the facts. Our data do not preclude, however, the formation of 3-phenylcyclohexene by a concerted reaction merely because this olefin (IV) gives the same mixture of products as does trans-2-phenylcyclohexanol-2-C^{14} (IIa) when placed under the dehydrating conditions.

7. From the dehydration of cis-2-phenylcyclohexanol-2-C^{14} (Ia) both 1- and 3-phenylcyclohexene (IIIa and IVa) have been shown to be present. It is obvious, however, that in addition the olefins V, VI,

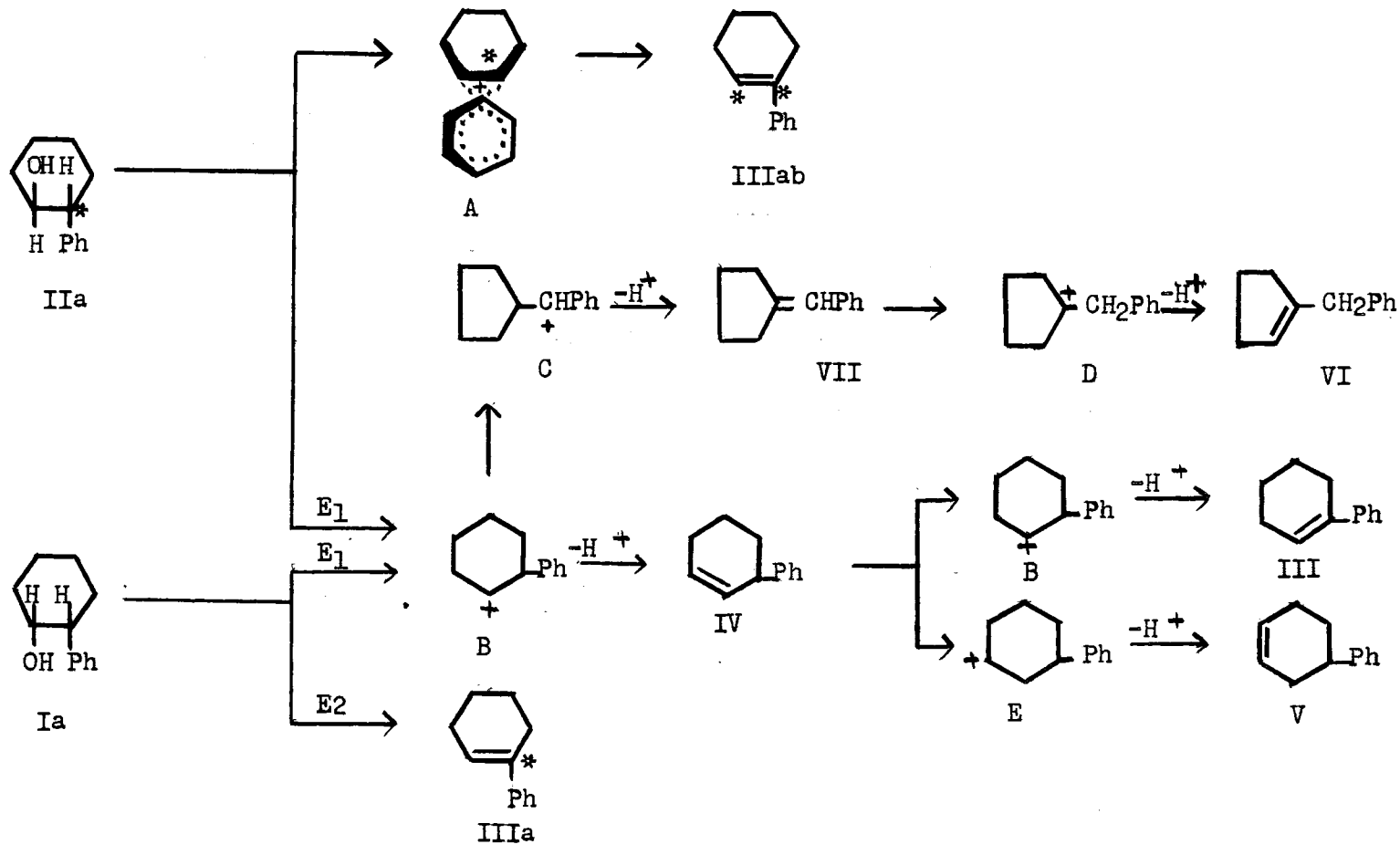


CHART III

Proposed Mechanism for the Phosphoric Acid Catalyzed Dehydration of cis- and trans-2-Phenylcyclohexanol

and VII must be present also, since 3-phenylcyclohexene undergoes isomerization to these products.

EXPERIMENTAL

Cyclohexanone-1-C^{14}.

This compound was prepared by a series of reactions in which pentamethylene dibromide (21) was converted to pimelonitrile-1,7-C_2^{14} followed by hydrolysis to pimelic acid-1,7-C_2^{14}. By the slow distillation of pimelic acid-1,7-C_2^{14} which contained a trace of barium carbonate there resulted a good yield of cyclohexanone-1-C^{14}.

To a solution of 5 gm. (77 mmoles) of non-radioactive potassium cyanide in 20 ml. of water was added 15 millicuries of potassium cyanide-C_1^{14}, 8.5 gm. (36.7 mmoles) of pentamethylene dibromide, and 23 ml. of ethanol. The reaction mixture was heated under reflux on a steam bath for 18 hours. The condenser was replaced with an 18-inch Vigreux column and fitted with a distilling head. The ethanol was removed by slow distillation at atmospheric pressure. The residue was transferred to a continuous extraction apparatus and extracted with ether for 19 hours. The ether was removed from the extract by evaporation and to the residue of pimelonitrile-1,7-C_2^{14} was added 20 ml. of concentrated hydrochloric acid. The mixture was refluxed for 3 hours, cooled, and transferred to a continuous extraction apparatus. The pimelic acid-1,7-C_2^{14} was extracted with ether for 14 hours and the ether was removed from the extract so that a theoretical yield (5.89 gm.) of crude pimelic acid-1,7-C_2^{14} was obtained. (22) The crude acid was dissolved in water, decolorized with Norit, and allowed to crystallize. There was obtained 3.4 gm. of pimelic acid-1,7-C_2^{14}. In order to scavenge the radioactive material from the mother liquor,

two 3 gm. and a 2.2 gm. sample of non-radioactive pimelic acid were crystallized from the mother liquor. Thus, a total of 12.4 gm. of pimelic acid-1,7-C_2^{14} was obtained. This acid was placed in a 50 ml. flask and a 6-inch Vigreux column and a distilling head were added. The flask was lowered into a Woods' metal bath and distillation occurred at a bath temperature of 310° to 365°. The cyclohexanone-1-C^{14} which distilled amounted to 6.5 ml. (81%). The reaction flask was allowed to cool, 3 ml. of non-radioactive cyclohexanone was added and distilled as before. This process was repeated two times using 2 ml. of non-radioactive cyclohexanone for each distillation. In this way, 13.2 ml. of cyclohexanone-1-C^{14} was obtained. Non-radioactive cyclohexanone (160 ml.) was added to the distillate which was dried with anhydrous sodium carbonate, filtered, and distilled. The cyclohexanone-1-C^{14} distilled at 151-154° and amounted to 165 ml. This procedure is a modification of the one described by Boedtker. (23)

A 2,4-dinitrophenylhydrazone was prepared from the cyclohexanone-1-C^{14} and was found to have a radioactivity assay of 2.683 mc/mole.

<u>1-Phenylcyclohexene-1-C^{14} (IIIa).</u>

This olefin was prepared by a method previously described by Sabatier and Mailhe, (24) involving conversion of cyclohexanone-1-C^{14} (ca. 1.00 mc/mole) into 1-phenylcyclohexanol-1-C^{14} with phenylmagnesium bromide (100% excess), followed by dehydration of the alcohol to yield the desired olefin (IIIa).

To a solution of phenylmagnesium bromide (0.88 moles) prepared from 22.2 gm. (0.91 moles) of magnesium and 138 gm. (0.88 moles) of

bromobenzene in 300 ml. of ether was added 42.5 gm. (0.43 moles) of cyclohexanone-1-C^{14} dissolved in 50 ml. of ether. When the addition was completed the mixture was refluxed for 1 hour after which the excess Grignard reagent was decomposed by the addition of a solution of 15 ml. of concentrated sulfuric acid in 300 ml. of water. The organic layer was separated and the aqueous layer was extracted with ether and combined with the original extract. The ether was evaporated and the crude 1-phenylcyclohexanol-1-C^{14} was heated under reflux without prior purification with a solution of 25 ml. of concentrated sulfuric acid in 175 ml. of water for 5 hours. The olefin layer was separated, the aqueous layer was extracted with ether, combined with the olefin extract, washed with water until free of acid, and dried with anhydrous magnesium sulfate. After filtration, the ether was removed by distillation at atmospheric pressure. After two distillations 58.7 gm. (85%) of pure 1-phenylcyclohexene-1-C^{14} was obtained; b. p. 132-134°/20 mm. in agreement with the literature. (24) In several other syntheses of 1-phenylcyclohexene-1-C^{14} (IIIa) the yield varied from 78 to 91%.

The procedures for the preparation of all radioactive compounds reported in this dissertation were previously worked out with the non-radioactive analogs in order to insure the maximum possible yield of the radioactive compounds.

2-Phenylcyclohexanone-2-C^{14}.

This ketone was prepared by a series of reactions in which cyclohexanone-1-C^{14} (1.334 mc/mole) was converted to the desired ketone

without isolation of the intermediate products. Thus, cyclohexanone-1-C^{14} was converted to 1-phenylcyclohexene-1-C^{14} (IIIa) as previously described. Treatment of IIIa with perbenzoic acid for 24 hours at 0° produced the epoxide which was rearranged in the presence of zinc chloride (25) to 2-phenylcyclohexanone-2-C^{14}.

To a solution of 0.91 moles of phenylmagnesium bromide prepared from 22.2 gm. (0.91 moles) of magnesium and 143 gm. (0.91 moles) of bromobenzene was added 45.5 gm. (0.46 moles) of cyclohexanone-1-C^{14}. The alcohol was dehydrated as previously described. The ether solution of the olefin (IIIa) was washed with water, dried with anhydrous magnesium sulfate, filtered, and concentrated to a volume of 255 ml. The ether solution of 1-phenylcyclohexene-1-C^{14} (IIIa) was cooled in an ice bath while a solution of 65 gm. (0.47 moles) of perbenzoic acid (26) in 1050 ml. of chloroform was slowly added. The clear reaction mixture was refrigerated for 24 hours and then extracted with 400 ml. of 10% aqueous sodium hydroxide solution, washed with water, dried with anhydrous sodium sulfate, and filtered. The solvent was removed from the epoxide by vacuum distillation. To the residual epoxide was added 2 gm. of zinc chloride and the mixture was heated gently under reflux until the reaction became quite vigorous, it was then controlled by occasional immersion of the flask in an ice bath until the initial exothermic reaction was completed. The rearrangement of the epoxide was completed after the contents of the flask were heated for an additional hour. The dark residue was distilled so that 51.0 gm. (63%) of 2-phenylcyclohexanone-2-C^{14} was obtained; b. p. 155-

$161^{\circ}/15$ mm. After four recrystallizations from petroleum ether ($30-60^{\circ}$) the pure product was obtained; m. p. $63-64.5^{\circ}$ in agreement with the literature. (25)

cis-2-Phenylcyclohexanol-2-C^{14} (Ia).

2-Phenylcyclohexanone-2-C^{14} (8.0 gm.) was dissolved in 100 ml. of absolute ethanol. Raney nickel catalyst (1.2 gm.) was added and the mixture was hydrogenated at atmospheric pressure until the theoretical amount of hydrogen had reacted (37 hours). The catalyst was removed by filtration, the solvent was removed from the filtrate with the aid of an air stream, and the last traces of the solvent were removed *in vacuo*. The residue partially crystallized on cooling, the oil was removed by filtration, and the solid was recrystallized from petroleum ether ($30-60^{\circ}$) to yield a first crop of the *cis*-alcohol (4.16 gm.); m. p. $42-44^{\circ}$. (1) Concentration of the mother liquor yielded two further crops; m. p. $40-42^{\circ}$ (total yield, 72%).

A phenylurethane of Ia was prepared whose m. p. was $127-128^{\circ}$ in agreement with the literature value. (1)

trans-2-Phenylcyclohexanol-2-C^{14} (IIa).

2-Phenylcyclohexanone-2-C^{14} (16 gm.) was dissolved in 75 ml. of absolute ethanol and 500 mg. of platinum oxide was added. The mixture was reduced overnight in a Parr hydrogenator with an initial pressure of 37.1 p.s.i. of hydrogen. The catalyst was removed by filtration and the solvent was evaporated so that 16.1 gm. of a white solid was obtained. The alcohol was recrystallized from petroleum ether ($30-60^{\circ}$) several times to yield 11.4 gm. (70.5%) of *trans*-2-phenylcyclohexanol-2-C^{14}; m. p. $56-57^{\circ}$ in agreement with the literature

values. The phenylurethane prepared from IIa had a m. p. of 137-138°. (1, 27, 28).

In other preparations of this alcohol, the reduction was also carried out at atmospheric pressure with essentially the same yields of IIa.

3-Phenylcyclohexene-C^{14} (IV).

Cyclohexanone-1-C^{14} (28.4 gm., 0.29 moles) was dissolved in 75 ml. of absolute methanol and 400 mg. of platinum oxide was added. The mixture was reduced overnight in a Parr hydrogenator with an initial pressure of 53.5 p.s.i. of hydrogen. In the morning the theoretical amount of hydrogen had reacted, the catalyst was filtered, and the methanol was removed by distillation through an 18-inch Vigreux column. To the residue (28.4 gm.), which was almost pure cyclohexanol-1-C^{14}, was added 12 gm. of powdered fused potassium hydrogen sulfate and the mixture was distilled through an 18-inch Vigreux column at such a rate that the temperature at the top of the column remained between 75° and 80°. (29) In this way 23.6 ml. (83%) of cyclohexene-C^{14} distilled. Non-radioactive cyclohexene (2 ml.) was added to the residue and it was distilled to scavenge the carbon-14 cyclohexene. The water in the distillate was separated from the cyclohexene-C^{14}, washed once with ether, the ether wash was combined with the cyclohexene-C^{14}, dried with magnesium sulfate, and distilled. Pure cyclohexene-C^{14} (23 ml.) distilled at 81-82°. Non-radioactive cyclohexene (2 ml.) was again added to the residue and distilled until the total volume of cyclohexene-C^{14} was 25 ml. (0.246 moles).

N-Bromosuccinimide (43.8 gm., 0.246 moles), 25 ml. (0.246 moles) of cyclohexene-C^{14}, and 100 ml. of carbon tetrachloride were heated under reflux on a steam bath for 1 hour, cooled, and the succinimide was removed by filtration. (30) The carbon tetrachloride was removed from the filtrate by distillation and 21.4 gm. (0.133 mole) of 3-bromocyclohexene-C^{14} (16) was obtained; b. p. 60-63°/12 mm.

To the phenyl Grignard reagent (0.146 moles, 10% excess) prepared from 3.55 gm. of magnesium and 22.9 gm. of bromobenzene in 100 ml. of ether was added, with cooling, 21.4 gm. (0.133 moles) of 3-bromocyclohexene-C^{14}. After addition was completed the mixture was refluxed for 1/2 hour and decomposed with dilute hydrochloric acid. The ether solution was dried with anhydrous sodium carbonate, filtered, the ether was removed from the filtrate by distillation, and the residue was distilled. 3-Phenylcyclohexene distilled at 76-79°/2 mm. and weighed 14.8 gm. (0.094 moles or 32% based on cyclohexanone-1-C^{14}); n_D^{20} 1.5448.

4-Phenylcyclohexene (V).

This olefin was prepared by a modification of the method of C. Konigsberger and G. Salmon. (17) 1,3-Butadiene (109 gm., 2.2 moles), styrene (68 gm., 0.64 moles), and 40 mg. of N-phenyl-2-naphthylamine were heated in a sealed tube at 100° C. for 120 hours, cooled, and opened. The reactants had formed a plastic which was dissolved in hot benzene and the polystyrene was precipitated with methanol. The clear supernatant liquid was decanted and the process was repeated twice. The solvent was removed from the decanted liquid

by flash distillation and the residue was distilled. There was obtained 23.7 gm. (0.15 moles) of 4-phenylcyclohexene; b. p. 115-116.6/15 mm.; n_D^{20} 1.5412.

1-Benzylcyclopentene (VI).

This olefin was prepared by a method in which cyclopentanone was converted to 1-benzylcyclopentanol followed by dehydration with 20% aqueous oxalic acid to yield 1-benzylcyclopentene as described by Denisenko and co-workers. (18, 19) To 0.57 moles (20% excess) of benzylmagnesium chloride was added 40 gm. (0.48 moles) of cyclopentanone. The excess Grignard reagent was decomposed by the addition of just sufficient water to completely hydrate the magnesium salts. The ether solution was decanted and the ether was removed in an air stream. After removal of the last traces of ether in a vacuum, the residue crystallized, and after repeated crystallizations from hexane 82 gm. (98%) of the pure 1-benzylcyclopentanol obtained; m. p. 58-60°.

Anal.* Calc'd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15; Found: C, 82.04, 82.00; H, 9.13, 9.20.

Denisenko reported that this compound was a liquid; b. p. 129 - 130°/11 mm. but we found it to be a readily crystallizable compound.

1-Benzylcyclopentanol (44.4 gm., 0.25 moles) was refluxed for 4 hours with 200 ml. of 20% aqueous oxalic acid. The two layers were separated and the aqueous layer was extracted with ether, the ether extract was combined with the olefin, washed with water, 5% aqueous

*The elemental analyses were performed by the Huffman Microanalytical Laboratories, Wheatridge, Colorado.

sodium bicarbonate, again with water, and dried with anhydrous magnesium sulfate. The ether was removed by distillation at atmospheric pressure and the residue was distilled through an 18-inch Vigreux column. 1-Benzylcyclopentene (23.9 gm., 66%) distilled at 103-107°/11 mm.; n_D^{20} 1.5367.

Benzalcyclopentane (VII).

This olefin was prepared by the addition of hydrogen bromide to 1-benzylcyclopentene, followed by dehydrohalogenation to yield benzalcyclopentane. To 23.9 gm. (0.15 moles) of 1-benzylcyclopentene at 0° C. was added 14.0 gm. of dry hydrogen bromide over a 30-minute period. The cloudy solution was refluxed with 25% methanolic potassium hydroxide for 1-1/2 hours and allowed to stand overnight. Water (300 ml.) was added and the lighter olefin layer was separated. The aqueous layer was extracted with ether, the ether extract was combined with the olefin layer, washed with water, and dried with anhydrous sodium carbonate. The ether was removed by distillation at atmospheric pressure and the residue was distilled through an 18-inch Vigreux column. There was obtained 7.8 gm. of benzalcyclopentane; b. p. 108-118°/8.5 mm.; n_D^{20} 1.5518.

Preparation of solid Derivaties of Olefins III, IV, V, VI, and VII.

a) Potassium Permanganate Oxidation of 1-Phenylcyclohexene (III) to δ-Benzoylvaleric Acid (VIII).

In a typical experiment, 500 mg. (3.16 mmoles) of 1-phenylcyclohexene was dissolved in 40 ml. of acetone and a solution of 2.5 gm. of potassium permanganate in 80 ml. of water was added. The mixture was

stirred for 15 minutes after which time the oxidation was complete. The maganese dioxide was removed by filtration, and the filtrate was heated on a steam bath to remove most of the acetone. The basic filtrate was extracted with chloroform, made acid with dilute sulfuric acid, and extracted with ether. The ether extract was washed with water and the ether was evaporated leaving 205 mg. (31%) of δ-benzoylvaleric acid which was recrystallized alternately from hexane and water until its melting point was 77-78°. (31)

b) 1-Phenylcyclohexene Nitrosochloride (X).

In one of several experiments 910 mg. (5.77 mmoles) of 1-phenylcyclohexene was dissolved in 2 ml. of glacial acetic acid and 0.6 ml. of hydrochloric acid was added. The flask was cooled in an ice bath while 2.5 gm. of iso-amyl nitrite dissolved in 2 ml. of glacial acetic acid was added, with stirring, over a 15-minute period. The reaction mixture was stirred for an additional 15 minutes at 0°, 5 ml. of methanol was added, and the nitrosochloride (629 mg.) which precipitated was filtered, washed with methanol, with water, and dried; m. p. 128-131° d. Recrystallization from a mixture of methanol and chloroform produced the pure nitrosochloride; m. p. 134-135° d. in agreement with the literature. (32)

c) 2-Phenyl-2-Cyclohexenone Oxime (XI).

To 1-phenylcyclohexene nitrosochloride (629 mg., 2.8 mmoles) prepared as previously described was added 10 ml. of ethanol and 450 mg. of potassium hydroxide dissolved in 2 ml. of water. The mixture was refluxed for 2 hours, poured into 100 ml. of water, cooled, and

filtered. The 2-phenyl-2-cyclohexenone oxime (313 mg. or 60%) obtained had a melting point of 151-153°. After two recrystallizations from methanol, the pure product was obtained; m. p. 156.5-157.5°. (32) This procedure was previously described by Koelsch. (32)

d) Methoxychloromercury Derivative of 3-Phenylcyclohexene (XII).

3-Phenylcyclohexene (300 mg., 1.9 mmoles) was dissolved in 5 ml. of absolute methanol, 606 mg. (1.9 mmoles) of mercuric acetate was added, and the mixture was shaken until solution was complete. It was allowed to stand at room temperature for 46 hours, filtered, and to the filtrate was added 70 ml. of 10% aqueous sodium chloride solution. The resulting cloudy solution was allowed to stand for 4 hours and filtered. The crude derivative was washed with water, dried, and weighed 749 mg. (93%). Two recrystallizations from ethanol gave the pure compound; m. p. 154-155°. The above procedure is a modification of the method of Wright. (33)

Anal. Calc'd for $C_{13}H_{17}OHgCl$: C, 36.71; H, 4.03; Hg, 47.16; Found; C, 36.72, 36.49; H, 4.08, 4.08; Hg, 47.02, 47.20.

e) β-Phenyladipic Acid from 4-Phenylcyclohexene.

In a typical experiment 500 mg. (3.16 mmoles) of 4-phenylcyclohexene was dissolved in 10 ml. of glacial acetic acid and cooled in an ice bath. A solution of chromium trioxide (850 mg.) in 0.5 ml. of concentrated sulfuric acid, 3 ml. of water, and 5 ml. of glacial acetic acid was added dropwise over a 10-minute period while the reaction mixture was being stirred. The reaction mixture was allowed to warm to room temperature and stirred for an additional 15 minutes, poured

into 200 ml. of water and extracted with ether. The ether extract was washed with water and extracted with 10% sodium hydroxide solution. The basic extract was made acid with dilute sulfuric acid and extracted with ether. The ether extract was washed with water and evaporated to dryness. There was obtained by this method 232 mg. (33%) of a solid; m. p. 137-140°. After two recrystallizations from a mixture of ether and benzene, a pure sample of β-phenyladipic acid was obtained; m. p. 147-148°, in agreement with the literature. (34)

f. 1-Benzylcyclopentene Nitrosochloride.

To a stirred solution of 500 mg. (3.16 mmoles) of 1-benzylcyclopentene (VI) in 1 ml. of glacial acetic acid and 1 gm. of iso-amyl nitrite cooled in an ice bath was slowly added 1 ml. of concentrated hydrochloric acid. The mixture was stirred for an additional 15 minutes, 20 ml. of methanol was added, and the mixture was filtered. The white nitrosochloride (96 mg. or 14%) was washed with methanol, water, and again with methanol; m. p. 108-109° d. Two recrystallizations from a mixture of chloroform and methanol gave the pure product; m. p. 109.5 - 110.5° d.

Anal. Calc'd. for $C_{12}H_{14}ONCl$: C, 64.43; H, 6.31; Cl, 15.85; Found; C, 64.15, 63.86; H, 6.40, 6.35; Cl, 16.03, 16.19.

g. Ozonolysis of Benzalcyclopentane to Benzaldehyde 2,4-Dinitrophenylhydrazone.

Benzalcyclopentane (0.9157 gm.) was dissolved in 30 ml. of ethanol and a solution of 2.65 gm. of 2,4-dinitrophenylhydrazine in 9 m. of concentrated sulfuric acid, 5 ml. of water, and 40 ml. of

ethanol was added. The clear solution was ozonized for 45 minutes at room temperature after which the solid was filtered, washed with ethanol, hot water, hot ethanol, and dried. The yield was 1.092 gm. (66%); m. p. 211-218°. Two crystallizations from dioxane gave pure benzaldehyde 2,4-dinitrophenylhydrazone; m. p. 237-238°. (35) The melting point was not depressed when mixed with an authentic sample of benzaldehyde 2,4-dinitrophenylhydrazone.

Oxidation of Various Derivatives of 1-Phenylcyclohexene and 3-Phenylcyclohexene to Benzoic Acid.

a) Oxidation of δ-Benzoylvaleric Acid to Benzoic Acid. In a typical experiment, 400 mg. (1.94 mmoles) of δ-benzoylvaleric acid, 2 gm. of potassium permanganate, 2 ml. of 10% aqueous sodium hydroxide solution, and 30 ml. of water were refluxed for 3 hours, cooled, and the excess potassium permanganate was destroyed with sodium bisulfite. The manganese dioxide was removed by filtration and washed with water. The basic filtrate was extracted with chloroform, made acid with dilute sulfuric acid, and extracted with ether. The ether extract was washed with water and the solvent was evaporated so that 210 mg. (88%) of crude benzoic acid was obtained. Two recrystallizations from water produced the pure compound; m. p. 121-122°.

b) Oxidation of 1-Phenylcyclohexene Nitrosochloride to Benzoic Acid.

To 147 mg. (0.62 mmoles) of 1-phenylcyclohexene nitrosochloride was added a solution of 1 gm. of chromium trioxide in 3 ml. of concentrated sulfuric acid, 3 ml. of water, and 20 m. of glacial

acetic acid. The mixture was refluxed for 1 hour, cooled, poured into 200 ml. of water, and extracted with ether. The ether extract was washed with water and extracted with 10% sodium hydroxide solution The basic extract was made acid with dilute sulfuric acid and extracted with ether. On solvent evaporation there was 70.6 mg. (93%) of crude benzoic acid. One crystallization from water, followed by vacuum sublimation at 100°/12 mm. produced the pure acid; m. p. 121-122°.

c) Oxidation of 2-Phenyl-2-Cyclohexenone Oxime to Benzoic Acid. The oxime (171 mg.) and a solution of 2.5 gm. of potassium permanganate in 40 ml. of water were refluxed for 5 hours, cooled, the excess permanganate destroyed with sodium bisulfite, and the manganese dioxide was filtered. The basic filtrate was extracted with chloroform, made acid with dilute sulfuric acid, and extracted with ether. The ether extract was washed with water and the solvent was evaporated. In this way 53 mg. (47%) of crude benzoic acid was obtained. Crystallization from water followed by vacuum sublimation at 100°/12 mm. produced the pure compound; m. p. 121-122°.

d) Oxidation of the Methoxychloromercury Derivative of 3-Phenylcyclohexene.

The oxidation of this compound was performed in exactly the same way as was the oxidation of 1-phenylcyclohexene nitrosochloride described above. In general, the yields of benzoic acid were 90-95%.

Dehydration of cis- and trans-2-Phenylcyclohexanol-2-C^{14} (Ia and IIa).

Equal weights of Ia or IIa and 85% phosphoric acid were mixed in

a 25 ml. flask and refluxed for 4 hours. In the first experiments a Glas-Col mantle was used as the source of heat but in the remainder of the dehydrations a Woods' metal bath at 200-205° was employed. After the dehydration was complete the contents of the flask were cooled, water and ether were added, the layers separated, and the aqueous layer was extracted with ether which was combined with the original ether extracts. The ether extract was washed with water until it was free of acid and made up to volume with ether in a 100 ml. volumetric flask.

The isolation of the olefins was accomplished by the following method: an accurately measured sample was removed from the volumetric flask and diluted with a known weight of non-radioactive olefin. The mixture was then usually subjected to some preliminary purification and the derivative was prepared as previously described. In the case of olefin III, the crude mixture of olefins was purified by the use of a column of alumina, for olefins IV, V, and VI, the crude mixture of olefins was purified by distillation, and for olefin VII, the derivative was prepared without preliminary purification. Table V summarizes the details of the above-described experiments. The radioactivity assays reported in this dissertation were performed on a vibrating reed electrometer using the wet combustion procedure which was described by Neville (36) and modified by Bonner and Collins. (37)

The calculation of the yields of the olefins may best be illustrated by a sample calculation for 1-phenylcyclohexene in Experiment Number 1 (Table V). In the equation: (6) $A_1(D_1 + X) = A_oX$:

TABLE V

Radiochemical and Dilution Data for the Phosphoric Acid Dehydration of *cis*-2-Phenylcyclohexanol-2-C^{14} (Ia) and of *trans*-2-Phenylcyclohexanol-2-C^{14} (IIa).

Exp. No.	Reactant and Weight in Gms.	Carrier Olefin and Weight in Gms.[a]	Aliquot of Reaction Mixture %	Radioactivity Assay of Derivative mc/mole	% Yield of Added Olefin from Dehydration	Radioactivity Assay of Benzoic Acid mc/mole
1	Ia, 2.8855 gm.	III 0.6606 gm.	10	0.3401 ± 0.0004[b]	87.7	0.3312
	1.330 mc/mole	IV 0.6118 gm.	40	0.0519 ± 0.0002	2.4	
2	IIa, 2.0684 gm.	III 1.4669 gm.	40	0.1161 ± 0.0007[c]	18.8	0.0890 ± 0.00005
	1.334 mc/mole					
3	IIa, 2.1107 gm.	III 0.9204 gm.	50	0.2338 ± 0.0002[c]	20.8	0.1723 ± 0.0012
	1.326 mc/mole	IV 0.8285 gm.	20	0.0554 ± 0.0004	9.6	
4	IIa, 4.9099 gm.	III 0.7128 gm.	40	0.9228 ± 0.0008[c]	23.4	0.7057 ± 0.0022
	2.518 mc/mole	IV 0.7831 gm.	20	0.2315 ± 0.0001	9.0	
		V 1.0533 gm.	11.2	0.0686 ± 0.0004	6.0	
		VI 2.0280 gm.	5.6	0.0933 ± 0.0006	31.6	
5	IIa, 2.5957 gm.	V 0.8810 gm.	30	0.1082 ± 0.00005	5.7	
	2.518 mc/mole	VI 1.0466 gm.	10	0.1700 ± 0.00005	32.5	
		VII 0.8458 gm.	10	0.1908 ± 0.0006	29.8	

(a) The olefin in this column was added to the aliquot of the reaction mixture specified in column four.

(b) Assay as 2-phenyl-2-cyclohexenone oxime. (c) Assayed as 1-phenylcyclohexene nitrosochloride.

A_o = Specific activity of undiluted IIIa = specific activity of starting material (Ia) = 1.330 mc/mole.

A_1 = Measured specific activity of derivative = 0.3401 mc/mole (Column V).

D_1 = Weight of non-radioactive 1-phenylcyclohexene (III) added = 0.6606 gm. (Column III).

X = Weight of 1-phenylcyclohexene-1-C^{14} (IIIa) of specific activity 1.330 mc/mole.

then:

$$(0.3401)\ (0.6606 + X) = 1.330\ (X)$$

$$X = \frac{(0.3401)(0.6606)}{0.990} = 0.227 \text{ gm. of III in 10\% of the reaction mixture (Column IV) or 2.27 gm. of III in total reaction mixture.}$$

Theoretical yield of olefins = 2.59 gm.

$$\frac{2.27}{2.59} \times 100 = 87.7\% \text{ yield of III.}$$

<u>Determination of Phenyl Migration Occurring During the Dehydration of cis- and trans-2-Phenylcyclohexanol-2-C^{14} (Ia and IIa).</u>

The derivatives of 1-phenylcyclohexene (III) obtained from the dehydration of Ia and IIa (Table V) were oxidized to benzoic acid by one of the methods previously described. The radiochemical data are given in Table V along with the observed and calculated per cent decrease radioactivity of the benzoic acid.

The method of calculating the per cent decrease of radioactivity of the benzoic acid may best be described by a sample calculation. (For an explanation of the distribution of radioactivity in

1-phenylcyclohexene (IIIab) obtained from the trans-alcohol (IIa), see Discussion Section.)

For Experiment Number 3 in Table V.

20.8% yield of IIIab = 0.394 gm. of IIIab from the direct dehydration of IIa and from isomerization of carbonium ion B.

7.3% Loss of III - Table VI

$\therefore \frac{0.394}{0.927} = 0.425$ gm. of IIIab before loss.

1.89 gm. = Theoretical Yield of Olefins.

$\frac{0.425}{1.89} \times 100 = 22.5\%$ = Corrected Yield of IIIab

100% - 22.5% = 77.5% - Yield of remaining olefins which pass through carbonium ion B. (Chart III).

0.775 x 1.89 = 1.465 gm. - Weight of olefins which pass through carbonium ion B. (Chart III).

12.3% Isomerization of IV $\longrightarrow$ III (Table VI).

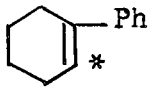
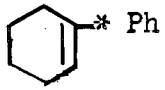
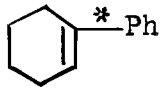
$\frac{1.465}{0.877} = 1.67$ gm. - Real Yield of Olefins which pass Through Carbonium Ion B.

1.89 gm. - 1.67 gm. = 0.22 gm. - Real Yield of IIIab by Direct Dehydration of IIa.

1.67 gm. - 1.465 gm. = 0.205 gm. - Real Yield of IIIa by Isomerization of Olefins which pass Through Carbonium Ion B.

$\frac{0.22}{1.89} \times 100 = 11.6\%$ Yield of IIIab Direct Dehydration (50:50)

$\frac{0.205}{1.89}$ x 100 = 10.8% Yield of IIIa by Isomerization (100:0)

	Parts Rearranged	Parts Unrearranged
	5.8	
		5.8
		10.8
	5.8 +	16.6 = 22.4

$\frac{5.8}{22.4}$ x 100 = 25.9% Calculated Decrease in Specific Activity of Benzoic Acid.

Isomerization of 3-Phenylcyclohexene (IV) and Mixtures of 1- and 3-Phenylcyclohexene (III and IV).

The isomerization experiments of the olefins (III and IV) were performed under the same conditions that were used for the dehydration. Equal weights of the olefin and phosphoric acid were refluxed for 4 hours. The isolation and the derivative preparation of the olefins was accomplished as previously described in this section for the dehydration reactions.

The radiochemical and dilution data are summarized in Table VI.

Purity Determination of 1- and 3-Phenylcyclohexene (III and IV).

In order to insure that the derivatives prepared from the various olefins were not contaminated with high level radioactivity, it was necessary to prepare a number of synthetic mixtures of radioactive and

TABLE VI

Radiochemical and Dilution Data for the Phosphoric Acid Isomerization of 1-Phenylcyclohexene (III), 3-Phenylcyclohexene (IV), and Benzalcyclopentane (VII).

Exp. No.	Reactant and Weight in Gms.	Carrier Olefin and Weight in Gms.[d]	Aliquot of Reaction Mixture %	Radioactivity Assay of Derivative mc/mole	Radioactivity Assay of Benzoic Acid mc/mole	% of Radioactivity in Benzoic Acid
6	IIIa 2.2922 gm. 1.004 mc/mole	III 0.5539 gm.	20	0.4140 ± 0.0025[a]	-	-
	IV 1.8858 gm.		40	0.8973 ± 0.0046[b]	-	-
7	IIIa 1.8946 gm. 1.004 mc/mole	III 0.5316 gm.	20	0.3756 ± 0.0007[a]	-	-
	IV 2.0852 gm.		40	0.8825 ± 0.0025[b]	-	-
		IV 0.5636 gm.	40	0.0004	-	-
8	III 3.8703 gm.	IIIa 0.3737 gm. 1.334 mc/mole	100	0.1409 ± 0.0004[a]	-	-
9	IIIa 3.1477 gm. 1.004 mc/mole	III 2.0729 gm.	100	0.5707 ± 0.0007[a]	-	-
10	IV 1.1580 gm.	IIIa 0.5875 gm. 1.334 mc/mole	100	1.088 ± 0.0010[a]	-	-
11	IVa 4.7652 gm. 2.293 mc/mole	III 0.6340 gm.	15	0.3716 ± 0.0016[c]	-	-
		IV 0.8094 gm.	15	0.7816 ± 0.0024	-	-
		V 0.7874 gm.	15	0.2168 ± 0.0002	-	-
		VI 0.9761 gm.	25	0.1543 ± 0.0006	-	-
		VII 0.3080 gm.	30	0.0990 ± 0.0006	-	-

TABLE VI (Continued)

Radiochemical and Dilution Data for the Phosphoric Acid Isomerization of 1-Phenylcyclohexene (III), 3-Phenylcyclohexene (IV), and Benzalcyclopentane (VII).

Exp. No.	Reactant and Weight in Gms.	Carrier Olefin and Weight in Gms.[d]	Aliquot of Reaction Mixture %	Radioactivity Assay of Derivative mc/mole	Radioactivity Assay of Benzoic Acid mc/mole	% of Radioactivity in Benzoic Acid
12	IVa 4.5558 gm. 2.293 mc/mole	IV 2.0946 gm. III 2.1201 gm.	40 60	0.9143 ± 0.0005 0.1860 ± 0.0008[c]	0.2346 ± 0.0005 0.0495 ± 0.0001	25.7[e] 26.6[f]
13	VII 2.4431 gm.	IV 0.8132 gm. 2.293 mc/mole	100	2.235	-	-

(a) Diluted with carrier olefin - assayed as δ-benzoylvaleric acid.

(b) Undiluted olefin (IIIa) - assayed as δ-benzoylvaleric acid.

(c) Diluted with carrier olefin - assayed as 1-phenylcyclohexene nitrosochloride.

(d) The olefin in this column was added to the aliquot of the reation mixture specified in Column IV.

(e) Per cent radioactivity adjacent to the phenyl group in IV.

(f) Per cent radioactivity adjacent to the phenyl group in III obtained from the isomerization of IV.

non-radioactive olefins, convert them into the corresponding derivatives, and prove that contamination was not a source of error.

The results of these experiments are listed in Table VII and demonstrate that the derivatives are radiochemically pure. That the derivatives of V, VI, and VII are radiochemically pure is supported by the fact that the summation of the yields from both the dehydration of IIa and from the isomerization of 3-phenylcyclohexene (IV) is 98%.

TABLE VII

Radiochemical Data on the Purity of 1- and 3-Phenylcyclohexene and their Derivatives

Experiment Number	Reactant and Weight in Gms.	Derivative	Radioactivity Assay of Derivative, mc/mole	Calculated Radioactivity of Derivative, mc/mole
14	IIIa 4.0 gm. 1.004 mc/mole	VIII	0.9955 ± 0.0016	1.004
15	IIIa 0.9931 gm. 1.004 mc/mole III 1.0139 gm.	VIII	0.4953 ± 0.0011	0.4968
16	IIIa 0.8624 gm. 1.004 mc/mole IV 0.3252 gm.	X	1.004 ± 0.0000	1.004
17	IIIa 0.8665 gm. 1.334 mc/mole IV 0.3201 gm.	VIII	1.320 ± 0.0015	1.334
18	IVa 0.2198 gm. 2.293 mc/mole IV 0.1707 gm.	XII	1.286 ± 0.0090	1.291
19	IIIa 1.8946 gm. 1.004 mc/mole IV 2.0852 gm.	XII	0.0004	0.000

SUMMARY

The dehydration of trans-2-phenylcyclohexanol-2-C^{14} with phosphoric acid has been shown to yield five isomeric olefins: 1-phenylcyclohexene (21%), 3-phenylcyclohexene (9%), 4-phenylcyclohexene (6%), 1-benzylcyclopentene (32%), and benzalcyclopentane (30%). It has also been demonstrated that the portion of the reaction of the trans-alcohol which produces 1-phenylcyclohexene must proceed with participation of the phenyl group.

cis-2-Phenylcyclohexanol-2-C^{14} has been dehydrated under the same conditions and both 1-phenylcyclohexene (88%) and 3-phenylcyclohexene (2%) were isolated. It is evident, however, that 4-phenylcyclohexene, 1-benzylcyclopentene, and benzalcyclopentane are present in the reaction mixture since 3-phenylcyclohexene undergoes isomerization to these five olefins when placed under the dehydrating conditions.

The mechanism of the dehydration and of the isomerization are discussed.

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