Experimental Section

Nmr Analyses.—Neat samples containing tetramethylsilane as an internal standard were run on a Varian A-60 spectrometer at ambient temperature. Infrared spectra were recorded on a Beckman Model IR-10 infrared spectrophotometer.

Starting Materials.—Isoprene, piperylene, and chloroprene (50% solution in xylene) were obtained from Columbia Organic Chemicals Co. and distilled prior to their use. Butadiene from Matheson Co. and 4-methyl-1,3-pentadiene from Chemical Samples Co. were of ~99% purity and used as such. The cyclopentadiene was freshly prepared by destructive distillation of dicyclopentadiene from Enjay Chemical Co. Methane- and benzenesulfenyl chloride were synthesized *via* chlorination of the corresponding disulfides according to previously described procedures.[6]

General Procedure for the Addition of Methane- or Benzenesulfenyl Chloride to Conjugated Dienes.—To a 50% solution of 5 equiv of the respective diene in dry methylene chloride, 1 equiv of methane- or benzenesulfenyl chloride was slowly added. The solution had a small amount of calcium carbonate (~50 mg in a 0.1 *M* reaction) suspended in it. The reaction was carried out under a nitrogen atmosphere, and reaction temperatures were in general maintained at −20 to −25° during the addition. All reactions were strongly exothermic and took place spontaneously. Decolorization of the orange sulfenyl chloride indicated completion of the reaction. Immediately after completion of the addition the solvent and excess unsaturate were removed under reduced pressure at −5 to −10° and the adducts' isomer ratio (Table III) was determined by nmr spectroscopy. All products were pale yellow oils which were formed in essentially quantitative yield. In general, analytical samples of mixtures of the two isomers were obtained by distillation *in vacuo* (Table I).

Acknowledgment.—The authors gratefully acknowledge Mr. W. C. Whitlock for his excellent technical assistance.

Selenium Dioxide Oxidations. III. The Oxidation of Olefins

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Details of the oxidation of 1,3-diphenylpropene with selenium dioxide were studied. In acetic acid at 115° an isotope effect (k_H/k_D) of 3.2 was observed for oxidation at the benzylic position; this indicates that an allylic carbon–hydrogen bond is being broken in the rate-determining step. Oxidation is most rapid for electron-rich olefins and is hindered if the double bond is shielded. A mechanism is proposed that involves the formation of an allylic selenium(II) ester (RCH=CHCHROSeOH) that decomposes to products through a solvolysis reaction. Evidence for a second pathway for oxidation is presented. This proceeds through the addition of selenium dioxide and acetic acid to the double bond, followed by pyrolysis of the selenoxide that is produced to the allylic acetate. The intermediate in this reaction was isolated and characterized. Oxidation of the optically active 3- and 4-methylcyclohexenes in acetic acid and in *n*-butanol was investigated, and products that arise from the introduction of oxygen into the 2, 3, and 4 positions were isolated. For the oxidation of the olefins in *n*-butanol, it was found that the product that is formed is in each case the thermodynamically unstable ether. An analysis of the data suggests that oxidation occurs through addition of selenium dioxide and solvent to the double bond, followed by pyrolytic elimination of selenium in a lower oxidation state to produce allylically oxidized product.

Selenium dioxide is often an attractive reagent for oxidizing olefins since it provides a direct entry into the allylic position. Although the reaction frequently proceeds in moderate to poor yields, its simplicity will usually outweigh this disadvantage. Despite the numerous examples of oxidation that are recorded in the literature,[3] few systematic studies concerned with evaluating the stereochemistry of the reaction, the nature of the intermediates, the effect of asymmetry, and electronic influences on the course of reaction have been reported. In an effort to define the characteristics of the reaction more precisely and to correlate the data that are currently available, we have studied certain details of the oxidation of several olefins and have obtained data that clarify some mechanistic aspects of the reaction.

From an examination of the literature, it is apparent that in many cases the oxidation product that is isolated must result from an allylic rearrangement. For example, oxidation of 1-hexene yields hex-2-en-1-yl acetate as the major product.[4] Although in many instances, rearrangement of the double bond may be an artifact arising from subsequent conversion of a kinetically favored product into one that has a greater thermodynamic stability, we felt that it was critical to obtain data on this point since the results would have important implications relating to the reaction intermediates. Accordingly, our initial studies were focused upon the oxidation of 1,3-diphenylpropene (**1**) and its derivatives.

Oxidation of **1** with selenium dioxide in 99% acetic acid at 115° was rapid and produced 1,3-diphenyl-2-propen-1-yl acetate (**2**) in high yields; no significant quantities of other organic products could be characterized. To elaborate the role of the allylic methylene group in the oxidation process, 1,3-diphenylpropene-3-*d* (**1**-*d*) was prepared. The experimental route to this product is shown in Scheme I. Benzoin was deuterated either by a base-catalyzed exchange with deuterium oxide or by neutralization of its disodium salt (from sodium hydride) with deuterium oxide. The product of these reactions was oxidized to benzaldehyde-1-*d* (**3**-*d*) with lead tetraacetate. Condensation of **3**-*d* with acetophenone yielded the deuterated chalcone (**4**-*d*), which subsequently was reduced to 1,3-diphenylpropan-1-ol-3-*d* (**5**-*d*) by lithium aluminum hydride. Dehydration of **5**-*d* by distillation from potassium acid sulfate yielded **1**-*d* containing 0.87 atom of deuterium per molecule. The nmr spectrum indicated the presence of two vinyl protons and therefore precludes any significant hydride shifts during the dehydration process.

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[1] For paper II in this series, see J. P. Schaefer, *J. Amer. Chem. Soc.*, **84**, 717 (1962).

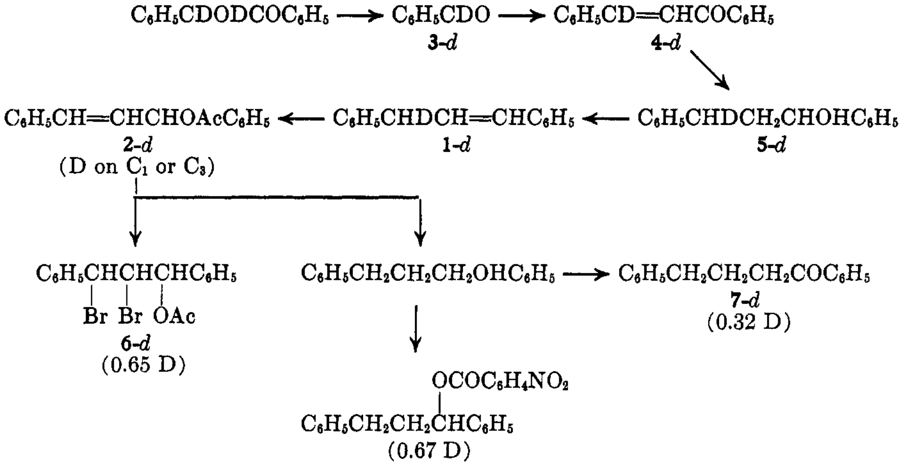
[2] The results of this work are taken in part from the Ph.D. theses of B. Horvath and H. P. Klein as submitted to the Graduate College of the University of Arizona.

[3] N. Rabjohn, *Org. Reactions*, **5**, 331 (1949).

[4] A. Guillemonat, *Ann. Chim.* (Paris), **11**, 143 (1939).

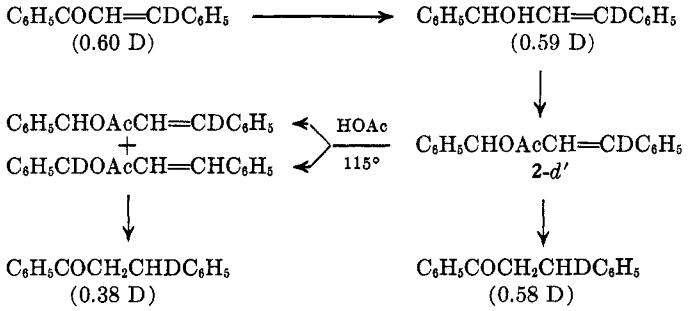
SCHEME I

PREPARATION AND OXIDATION OF 1,3-DIPHENYLPROPENE-3-*d*



SCHEME II

ISOMERIZATION OF 1,3-DIPHENYL-2-PROPEN-1-YL-3-*d* ACETATE



Oxidation of a sample of 1-*d* produced the allylic acetate (2-*d*); a portion of the product was converted into the crystalline dibromide (6-*d*), which was found to contain 0.65 atom of deuterium per molecule. Reduction of 2-*d* with lithium aluminum hydride yielded the saturated alcohol, which gave a *p*-nitrobenzoate containing 0.67 atom of deuterium per molecule. This value is in excellent accord with the results obtained from the dibromide. Since 1-*d* contained 1.13 atom of hydrogen and 0.87 atom of deuterium and was oxidized to product containing 0.34 atom of hydrogen and 0.66 atom of deuterium, it follows that during the course of oxidation of the methylene group 0.79 atom of hydrogen was lost for every 0.21 atom of deuterium. By correcting for the fact that 13% of the starting material contained no deuterium, these values become 0.66 and 0.21, respectively. The ratio of these numbers (3.2) is a measure of the kinetic isotope effect (k_H/k_D) in acetic acid at 115°. This value is sufficiently large to suggest that *the rate-determining step for the oxidation must involve cleavage of an allylic carbon–hydrogen bond.*

Oxidation of the saturated alcohol with chromic acid yielded deuterated 1,3-diphenylpropan-1-one (7-*d*). Analysis of this ketone indicated the presence of 0.32 atom of deuterium per molecule. This observation requires that at some stage of the reaction the two benzylic positions must become equivalent. A decision as to whether this equivalence has its origin in a symmetrical intermediate or is the result of successive allylic rearrangements of the product acetate was reached on the basis of the following experiments.

A sample of 4-*d* containing 0.60 atom of deuterium per molecule (see Scheme II) was reduced to 3-diphenyl-2-propen-1-ol-3-*d* (8-*d*) with sodium borohydride, and the allylic alcohol was converted into 2-*d'* by acetylation. Reduction of 2-*d'* with lithium aluminum hydride followed by oxidation of the saturated alcohol that was produced yielded 7-*d'*, which contained 0.58 atom of deuterium per molecule. This sequence of reactions demonstrates that the degradation scheme used here and in the previous experiments to determine the percentage and position of the deuterium atoms does not involve any rearrangements.

When compound 2-*d'* was refluxed in acetic acid containing phosphoric acid under the reaction conditions used for oxidation of 1 and subsequently converted into 1,3-diphenylpropanone, the latter was found to contain only 0.38 atom of deuterium per molecule. Therefore, although a substantial degree of equilibration of the benzylic positions has taken place, the equilibration is far from complete.

The possibility that partial isomerization of the olefin occurred before oxidation took place was tested by refluxing 1-*d* for an extended period of time in acetic acid containing enough phosphoric acid to simulate the acidity produced by selenous acid. After reisolation of the olefin, the nmr spectrum of this compound was superimposable on that of the starting material. Since neither the starting olefin nor the product acetate isomerizes to a sufficient extent to result in complete equilibration of the benzylic positions, we are forced to conclude that *the oxidation of 1,3-diphenyl-*

propene in acetic acid must involve the formation of a symmetrical intermediate.

In a study of the oxidation of dihydrodicyclopentadiene, Alder and Stern[5] found that the oxidation product was solvent dependent. Oxidation of the olefin in methanol, ethanol, or amyl alcohol produced the allylic methyl, ethyl, or amyl ether whereas oxidation in acetic anhydride yielded the corresponding acetate. When these data are considered in the light of our findings, it appears reasonable to conclude that, in the oxidation of **1**, the structure of the symmetrical intermediate is the allylic carbonium ion. Further support for this conclusion was obtained from a study of the oxidation of the methylcyclohexenes (*vide infra*).

To assess the influence of electronic and steric factors on the rate of reaction, five 1,3-diarylpropenes were synthesized. An equimolar mixture of **1** and a 1,3-diarylpropene was allowed to compete for a limited quantity of selenium dioxide, and the percentages of olefins that remained after reaction were estimated by gas chromatographic analysis. The results of these experiments are summarized in Table I.

TABLE I

COMPETITION OF 1,3-DIARYLPROPENES FOR SELENIUM DIOXIDE

Entry	$ArCH_2CH{=}CHAr'$		$[C_6H_5CH_2CH{=}CHC_6H_5]^a/[ArCH_2CH{=}CHAr']$	Oxidation,^{b} %
	Ar	Ar'		
1	p-$CH_3OC_6H_4$	C_6H_5	0.83	59–68
2	C_6H_5	p-$CH_3OC_6H_4$	0.56	42–47
3	p-ClC_6H_4	C_6H_5	1.18	64–73
4	C_6H_5	p-ClC_6H_4	1.76	65–73
5	C_6H_5	Mesityl	$>13.5^c$	82

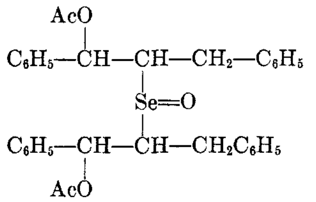
[a] Experiments utilized molar ratios of 1 mol of each olefin and 0.5 mol of selenium dioxide. The ratios reported are the ratios of olefins consumed during reaction. [b] Measured by the weight of selenium precipitated. Reactions were run in duplicate. [c] This represents a minimum value.

The data for entries 2 and 4 are in accord with electrophilic attack of the double bond by selenium dioxide (or its conjugate acid, $HSeO_2^+$). Participation of the double bond in a primary sense, such as through coordination with an attacking electrophile, is further supported by entry 5, which illustrates that shielding the double bond results in a pronounced retardation of the rate of oxidation. Substituent effects observed by varying the environment of the methylene group were small (entries 1 and 3), but they are consistent with the development of an electron-deficient center at that site.

Qualitative observations indicate that the oxidation is acid catalyzed. The rate of formation of selenium was increased markedly by the addition of dichloroacetic acid to the acetic acid solvent. In contrast to these results, oxidation in alcohols at comparable temperatures is much slower than oxidation in acid. The addition of free-radical inhibitors had no detectable effect on the rate or course of the oxidation.

When selenium dioxide (1 mol) and **1** (2 mol) were allowed to stand in acetic acid at room temperature, a white crystalline mass precipitated after several hours. After several days when crystallization was complete, the crystals were collected and purified through repeated recrystallization from hot chloroform and ethanol. An infrared spectrum of this material indicated that it was an acetate ester, and elemental analysis suggested that this compound contains two molecular formulas of **1**, two acetate moieties, a selenium atom, and oxygen.

A structure that appears to be consistent with these data is **8**.



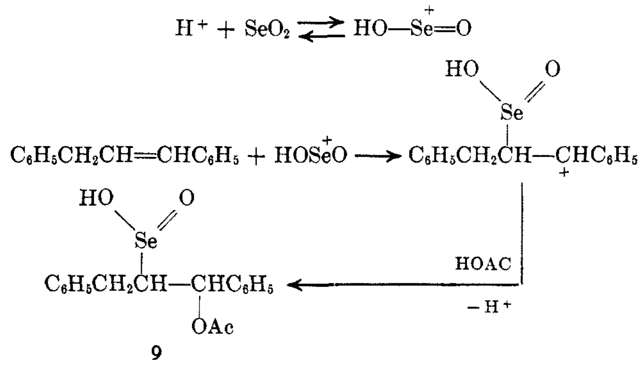
8

When a sample of **8** was dissolved in glacial acetic acid and heated under conditions identical with those used for the oxidations of **1**, a total of 7–8% of the theoretical percentage of selenium precipitated. Pyrolysis of the selenium compound in a test tube at 300° for 3–5 min produced a larger percentage of selenium. Parallel experiments employing **1** and selenium dioxide gave consistent yields of selenium of the order of 65%. Analysis of the products of decomposition of **8** using thin layer chromatography indicated that the product of pyrolysis was a mixture of **1** and **2**. In view of the discrepancy in yields of selenium obtained by heating the intermediate and by reaction of the olefin directly with selenium dioxide, it is apparent that, although **8** can lead to normal oxidation products, it cannot be the major intermediate formed in the experiments previously described.

Mechanistic Considerations.—From a consideration of the data presented above, it is obvious that there are at least two routes through which allylic oxidation of olefins by selenium dioxide can be achieved. As Wiberg and Nielsen[6] pointed out on the basis of a revealing study of the oxidation of some cyclohexenes, one of these pathways has a pyrolytic aspect to it whereas the other involves a solvolysis step.

For the former reaction, it is reasonable to presume that the first step of reaction involves the addition of a selenium dioxide molecule and a solvent molecule across the double bond in the manner shown in Scheme III.

SCHEME III



Reaction of **9** with a second molecule of **1** would yield **8**.

Ample precedents for these reactions are to be found in the literature. When selenium oxychloride comes into contact with an olefin, a vigorous reaction that results in a 1,2 addition across the double bond ensues.

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(5) K. Alder and G. Stern, *Ann.*, **504**, 205 (1933).

(6) K. Wiberg and S. D. Nielsen, *J. Org. Chem.*, **29**, 3353 (1964).

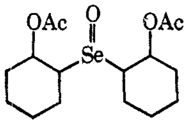
The β-chloroselenoxide that is produced is subsequently converted into a dichloroselenide.[7] More

$$2CH_2{=}CH_2 + SeOCl_2 \longrightarrow (ClCH_2CH_2)_2Se{=}O \longrightarrow (ClCH_2CH_2)_2SeCl_2$$

recently, Olson[8] has been able to isolate a stable addition compound (**10**) from the reaction of ethylene with selenium dioxide. Compound **10** presumably arises

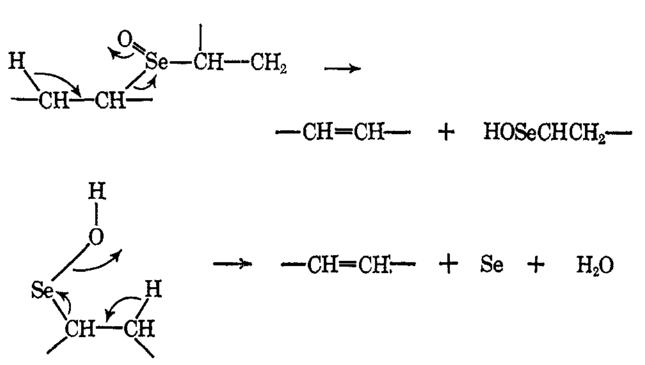
$$2CH_2{=}CH_2 + 2CH_3CO_2H + SeO_2 \longrightarrow \underset{\mathbf{11}}{(CH_3CO_2CH_2CH_2)_2Se{-}O} \longrightarrow \underset{\mathbf{10}}{(CH_3CO_2CH_2CH_2)_2Se}$$

through the preliminary formation of **11** followed by reduction of the latter product by a selenium compound in a similar or lower oxidation state (*e.g.*, Se or SeO). Similarly, Wiberg and Nielsen[6] have isolated an adduct formed from cyclohexene and have found that its properties are consistent wth structure **12**.



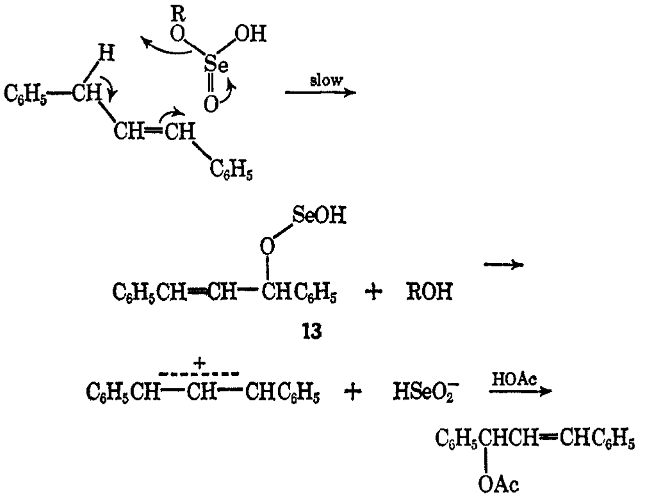
12

Thermal decomposition of **8** should be facile and probably proceeds through a cyclic transition state. Processes similar to these are commonly encountered in the formation of olefins by the pyrolysis of amine oxides, and a reaction of this kind appears to be reasonable in view of the known thermal instability of aliphatic selenoxides.[9,10] The isolation of **1** from the pyrolysis mixture suggests that the formation of **8** is reversible to some degree. In accord with this mechanism is the result of Wiberg and Nielsen[6] who have shown that with cyclohexene the acetate group is introduced into one of the original vinyl positions when cyclohexenyl acetate is formed from the pyrolysis reaction.



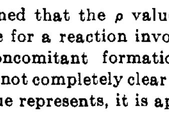
If we consider all of the data presented on the oxidation of **1**, it is clear that the pyrolysis reaction cannot be the major source of product. The reasons for this conclusion follow from the observations that (1) the formation of **2** from **8** is much slower than the formation of **2** from **1** and selenium dioxide, (2) the mechanism provides no route to direct insertion of oxygen at the allylic position, and (3) the substituent effects observed for electrophilic attack at C_2 are too small for this to be a major reaction path.[11,12] A process that appears to be consistent with our results is given in Scheme IV.

SCHEME IV



When selenium is dissolved in water, it is converted into selenous acid. In acetic acid or in an alcoholic solvent, the oxidant will probably exist largely as the mixed anhydride or the half-ester. Attack by the appropriate reagent (R = acetyl, alkyl, or hydrogen) upon the olefin, followed by a molecular reorganization, would lead to a selenium(II) ester (**13**), as we have indicated. The formation of **13** must be rate determining in view of the magnitude of the primary isotope effect that was observed.[13] Solvolysis of **13** would yield an allylic cation that could react with the solvent at either benzylic position. This cationic intermediate provides a satisfactory explanation for the known solvent dependence of the reaction product.[5]

Wiberg and Nielsen[6] have suggested that the structure of the product-producing intermediate should be formulated as a seleninic acid (**14**), which contains a selenium–carbon bond rather than an oxygen–carbon bond. Although there are many examples of inter-



14

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[7] C. E. Frick, *J. Amer. Chem. Soc.*, **45**, 1795 (1923).

[8] D. H. Olson, *Tetrahedron Lett.*, 2053 (1966).

[9] M. L. Bird and F. Challenger, *J. Chem. Soc.*, 571 (1942).

[10] H. Rheinboldt and E. Giesbrecht, *J. Amer. Chem. Soc.*, **69**, 645 (1947).

[11] In a kinetic study of the reaction of α-methylstyrene with selenium dioxide, we have found that at 25° the disappearance of oxidant is rapid and first order with respect to oxidant. However, the consumption of selenium dioxide is not directly related to the production of selenium and organic oxidation products; rather, it appears to be leading to an intermediate similar to **8** under these reaction conditions. Trachtenberg and Nelson[12] have studied in greater detail the kinetics of the reaction of a series of substituted α-methylstyrenes and have determined that the ρ value for the reaction is -2.34, which is a reasonable value for a reaction involving electrophilic attack of the double bond with concomitant formation at an electron-deficient center at C_2. Although it is not completely clear to us what facet of the oxidation of the olefin this ρ value represents, it is apparent that the substituent effects that we have observed are too small to be consistent with a process involving attack of an electrophilic species on **1** at C_2 to produce a benzyl cation.

[12] C. H. Nelson, Ph.D. Thesis, Clark University, Worcester, Mass., 1965.

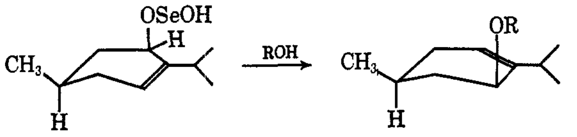
[13] Although the formation of **13** has been formulated for the sake of simplicity as involving a cyclic transition, it is apparent that a two-step process involving addition of the reagent followed by subsequent loss of a proton would accomplish the same result. A two-step process is actually more probable since this would predict the development of a cationic center at one of the vinylic positions, would afford an explanation for the observed[4] selectivity of oxidation sites in unsymmetrical olefins, and also would be in accord with the high ρ value that has been reported.[12]

mediates of this type that arise from the reaction of metallic acetates (*e.g.*, mercuric acetate[14]) with olefins and that undergo facile solvolysis reactions, **14** does not appear to have the structural features necessary to produce an allylic cation. Numerous alkyl seleninic acids [RSe(=O)OH] have been described in the literature and they are uniformly stable compounds. In fact, benzylseleninic acid can be crystallized from water or methanol with decomposition.[15-17] On this basis, we regard **13** as being a more plausible intermediate in the oxidation reaction.

From a consideration of the characteristics of the products that are formed during the reactions of other olefins of a more general type than **1**, it is apparent that there must be a spectrum of pathways available for the decomposition of the selenium(II) ester. The oxidation of (+)-*p*-menth-3-ene (**15**), which has been studied in detail by Suga, Sugimoto, and Matsuura,[18] provides an interesting model for illustrating many facets of these conversions.

In analyzing the details of an olefin oxidation, the first point that must be considered is the stereochemistry of formation of the selenium(II) ester. From an application of stereoelectronic principles, it is evident that in the absence of any abnormal steric effects the transition state of minimum energy would be formed by attack of selenium dioxide upon the double bond in a manner such that oxygen will be inserted into an axial position and the allylic proton in the axial position is the one that is abstracted. In solvents of modest ionizing power but of high nucleophilicity, bimolecular displacement of the selenium(II) ester by a neutral solvent molecule in the cyclohexenyl system occurs through an S_N2' path. In accord with the known stereochemistry of the S_N2' reaction is the fact that the isolated product is also axially substituted. Further confirmation for these suggestions is provided by the observation that, in the oxidation of carvomenthene, oxygen is introduced into the allylic position with retention of optical activity.[6]

15

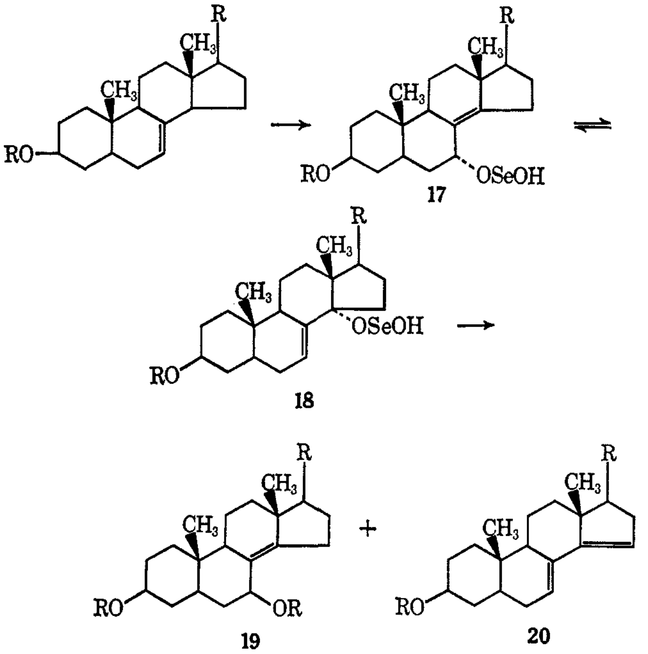


16

If the solvent system used for a reaction medium promotes ion pair formation, allylic rearrangements of the selenium(II) ester can occur. In the case of **16** this would result in racemization, and the oxidation of both **15** and carvomenthene in acetic acid led only to racemic products.[6] Similarly, if the allylic cation is particularly stable as in the case of the 1,3-diarylpropenes, ion-pair formation would be expected to be important. The Δ^7 steroids also provide an instructive example for analysis.

In the Δ^7 steroids, the C_{18} and C_{19} methyl groups and the stability of the tertiary C_8 cation will promote attachment of selenium dioxide to the axial position at C_7 with generation of a Δ^{8-14} double bond. This selenium(II) ester (**17**) can rapidly equilibrate with its C_{14}-substituted counterpart (**18**), which on reaction with solvent would yield **19** (Scheme V). The relative ease of displacement of a secondary *vs.* a tertiary center would result in the isolation of **19** to the exclusion of product that is oxidized at C_{14}. The isolation of considerable amounts of diene **20** suggests that 1,2 or 1,4 eliminations from the selenium(II) ester intermediates provide a favorable alternative route for decomposition.

SCHEME V



In systems with less demanding steric requirements for reaction, a transition from an S_N2' to an S_N2 reaction may be noted. For example, in the oxidation of 1-hexene, the latter type of reaction would be expected to be dominant and, indeed, the product that is isolated is the primary acetate. A difficulty in interpreting

$$C_3H_7CH_2{-}CH{=}CH_2 \longrightarrow C_3H_7CH{=}CH{-}CH_2OSeOH \longrightarrow C_3H_7CH{=}CHCH_2OAc$$

many of these reactions literally is that the products may represent only thermodynamically stable isomers and not the kinetically formed products.

Further Studies.—In the light of the above findings and of our own data, we were surprised to note that the oxidation of (+)-4-methylcyclohexene (**21**) under conditions similar to those used by other investigators[6,12] has been reported[19] to produce optically active 5-methyl-2-cyclohexen-1-yl acetate (**22**). Although the results of Mousseron and Jacquier[19] could have been a manifestation of the differences in the stabilities of the various allylic cations involved, we felt that these observations had sufficiently important mechanistic implications to merit reinvestigation, especially in view of some experimental ambiguities that existed.

Optically active 3-methylcyclohexanone (**23**) ($\alpha^{25}\text{D}$ +13.7°) was reduced with lithium aluminum hydride

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(14) Z. Rappaport, P. D. Sleezer, S. Winstein, and W. G. Young, *Tetrahedron Lett.*, 3719 (1965).

(15) C. L. Jackson, *Ber.*, **7**, 1277 (1874).

(16) C. L. Jackson, *Ann.*, 179 (1875).

(17) R. Lesser and R. Weiss, *Ber.*, **57**, 1077 (1924).

(18) T. Suga, M. Sugimoto, and T. Matsuura, *Bull. Chem. Soc. Jap.*, **36**, 1363 (1963).

(19) M. Mousseron and R. Jacquier, *Bull. Soc. Chim. Fr.*, 467 (1952).

to a mixture of epimeric 3-methylcyclohexanols (**24**), of which about 90% was the *cis* isomer. Using the sulfuric acid dehydration procedure that was previously described,[19] we were unable to obtain olefin that had rotations that were consistently as high as those reported by the French workers. This presumably is due to the partial loss of asymmetry through hydride shifts and should be a sensitive function of the reaction conditions that are employed.

To circumvent this difficulty, the optically active acetate mixture (**25**) was prepared by heating the epimeric alcohols with acetic anhydride in pyridine. Upon pyrolysis of the acetates, an olefin portion ($\alpha^{25}\mathrm{D}$ +110°) that corresponded in physical properties to **21** was obtained. Although we were unable to detect the presence of any other olefin by vapor phase chromatography, it seemed highly unlikely on stereoelectronic grounds that the acetate pyrolysis or the acidic dehydration of the alcohols could have produced a single olefin. Accordingly, the following series of experiments was carried out.

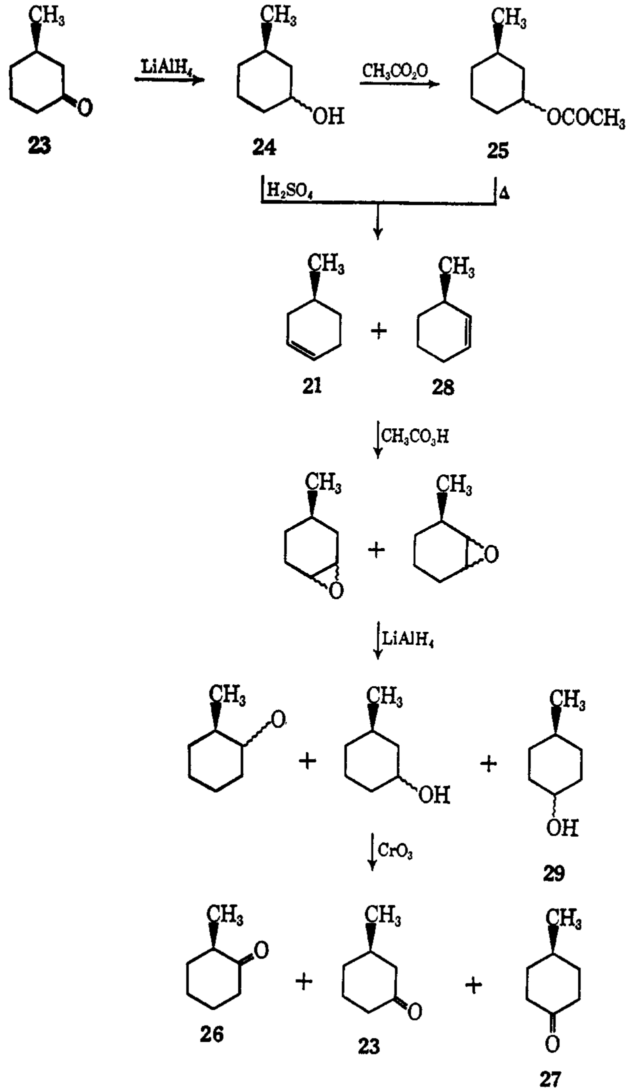
The olefin fraction was allowed to react with peracetic acid, and a mixture of epoxides was obtained in high yield. An examination of the nmr spectrum of this mixture showed two distinct methyl resonances; however, no decision could be reached as to whether these resulted from the presence of a mixture of epimeric epoxides or from isomers that involved formation of an oxide bridge between different carbon atoms. Reduction of the epoxide fraction with lithium aluminum hydride followed by oxidation of the resultant alcohols produced a mixture of 2-methylcyclohexanone (**26**), **23**, and 4-methylcyclohexanone (**27**) in relative yields of 15, 45, and 40%, respectively. The presence of three ketones requires that the olefin starting material must consist of a mixture of 3-methylcyclohexene (**28**) and **21**.

Reduction of **27** with lithium aluminum hydride and acetylation of the epimeric alcohols (**29**) produced a mixture of the epimeric acetates, about 90% of which was the *cis* isomer. Pyrolysis of the acetate mixture yielded an authentic sample of racemic **21**, which was converted into its epoxide by peracetic acid. From a comparison of the nmr spectra of the epoxides produced from the mixture of **21** and **28** with that obtained from pure **21**, it appeared that the ratio of these isomers was about 3:2. Since a separation of these olefins could not be realized, further experiments were carried out on this mixture. A summary of the experiments described above appears in Scheme VI.

Oxidation of the optically active olefins with selenium dioxide in acetic acid containing acetic anhydride[19] produced a mixture of allylic acetates. After hydrogenation of the double bond, the saturated acetates were converted into the corresponding methylcyclohexanols by lithium aluminum hydride. Oxidation of the alcohol mixture with chromic acid yielded a mixture of **26**, **23**, and **27**; these ketones were separated by preparative gas chromatography. The rotation of **26** was $\alpha^{24}\mathrm{D}$ −14.6°; this compound was completely racemized after it had been heated in acetic acid for 3 hr.

In contrast, ketone **23** was virtually optically inactive with $\alpha^{25}\mathrm{D}$ +0.57°. From these observations it is clear that, for the course of selenium dioxide oxidation of olefins, any interpretations based upon the results reported by Mousseron and Jacquier[19] would be in serious error, since the products of reaction were not correctly identified.[20]

Scheme VI



A point of further interest was to determine the stereochemistry of the oxygen that is introduced during the course of the oxidation sequence. Details regarding this feature of the reaction were obtained from a study of the reactions of **21** and **28** with selenium dioxide in *n*-butanol.

Oxidation of the olefin in *n*-butanol at reflux produced a mixture of allylic ethers, allylic alcohols, and α,β-unsaturated ketones; the total yield of products was low and varied from 15 to 20%. Analysis of the products after catalytic hydrogenation of the double bond indicated that 75% of the reaction mixture consisted of the isomeric butyl ethers of the methylcyclohexanols, 15% was a mixture of methylcyclohexanols, and the remainder was an aggregate of methylcyclohexanones.

To identify the various butyl ethers that were formed, ketones **23** and **27** were reduced to the alcohols with lithium aluminum hydride. In agreement with the re-

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[20] An interesting consequence of these experiments is that the absolute configuration of (−)-2-methylcyclohexanone must be the same as that of (+)-3-methylcyclohexanone, since none of the reactions involved could have changed the configuration of the methyl group relative to the oxygen function.

port by Dauben, Fonken, and Noyce[21] was our finding that about 80% of the products in both cases are the thermodynamically favored epimers, namely, *trans*-4-methylcyclohexanol and *cis*-3-methylcyclohexanol. Each pair of epimers was treated with sodium metal and *n*-butyl bromide to give the corresponding epimeric pairs of butyl ethers. A similar sequence of reactions was carried out on a commercial sample of a mixture of the 2-methylcyclohexanols that contained about 80% of the *trans* isomer; it was found that the three isomeric ethers and their epimers could be separated and distinguished by gas chromatography. From a comparison of the retention times of these authentic samples with the products of oxidation, it was immediately apparent that the ether formed during the oxidation is predominantly (~80%) the thermodynamically unstable isomer.

Experimental Section

Benzaldehyde-1-*d*.—To 106 g (0.50 mol) of benzoin were added 200 ml of dry tetrahydrofuran, 10 g (0.50 mol) of deuterium oxide, and 25 g of anhydrous potassium carbonate, The solution was heated at reflux for 24 hr, and the solvent was removed. This cycle was repeated six times. Then the dry residue was mixed with 1 l. of benzene and the slurry was filtered to remove the potassium carbonate. To the filtrate was added 300 ml of absolute ethanol, and the resultant solution was heated to reflux. Freshly prepared lead tetraacetate (300 g) was added in one portion. The solution was heated at reflux for 1 hr and cooled; the lead salts were removed by filtration through a sintered-glass funnel. The filtrate was washed with 50 ml of dilute hydrochloric acid, refiltered, and washed twice with 300-ml portions of water. The filtrate was then neutralized with sodium bicarbonate, washed with water, and dried over anhydrous magnesium sulfate. Distillation yield 50 g (94%) of benzaldehyde, bp 66–66.5° (14 mm). The product contained 0.88 deuterium atom per molecule.

1,3-Diphenylpropene-3-*d*.—The procedures developed by Rondestvedt[22] for the synthesis of 1,3-diarylpropenes were used. Acetophenone and benzaldehyde-1-*d* were condensed to give deuteriochalcone (0.87 deuterium atom per molecule); the latter was reduced to 1,3-diphenylpropan-1-ol with lithium aluminum hydride. Dehydration by distillation from potassium acid sulfate produced the title compound in over-all yields that varied between 40 and 60%. The olefin contained 0.87 deuterium atom per molecule, bp 161–162° (7.5 mm).

Selenium Dioxide Oxidation of Olefins.—A measured quantity of selenium dioxide was dissolved in a few drops of warm water. To this solution was added 100 ml of glacial acetic acid containing the olefin, and the reaction mixture was heated for about 20 min at reflux. The solution was cooled and filtered to remove selenium, which was formed in yields of 70–80%. The filtrate was poured into 1 l. of water and then extracted with three 100-ml portions of ether. The ether extracts were washed with water, base, and water and then dried over magnesium sulfate. The product was distilled rapidly in a small distillation apparatus at pressures of 0.05–0.10 mm at temperatures below 180°; almost no residue remained in the distillation pot under these conditions.

In the case of 1,3-diphenylpropane, chromatography (gas phase and thin layer on silica gel) indicated that about 80% of the product was 1,3-diphenyl-2-propen-1-yl acetate and that the remainder of the material was the starting olefin along with traces of several organoselenium compounds; small quantities of 1,3-diphenylpropanone could be detected. The structures of the identifiable products were confirmed by a comparison of retention times and infrared spectra with those of authentic samples.

Oxidation of 1,3-Diphenylpropene-3-*d*.—To 1.15 g (0.0104 mol) of selenium dioxide was added 7 drops of water, and the paste that was formed was heated to bring about solution. To this was added 100 ml of glacial acetic acid containing 4.00 g (0.0206 mol) of 1,3-diphenyl-1-propene-3-*d*, and the solution was heated at reflux with an open flame for 20 min. The solution was cooled rapidly in an ice bath and filtered to remove selenium (0.52 g, 63%). The product isolation from this point on was the same as that described under the general procedure.

To 100 ml of anhydrous ether were added 3.0 g of lithium aluminum hydride and 2.70 g of the distillate from the oxidation reaction. After the solution had been heated at reflux for 3 hr, water was added to destroy the excess hydride. Isolation of the product in the usual manner yielded 2.5 g of crude 1,3-diphenylpropan-1-ol. From 0.3 g of the crude alcohol the *p*-nitrobenzoate was prepared, mp 88.5° (lit.[23] mp 88–89°), and analysis indicated that the *p*-nitrobenzoate contained 0.67 atom of deuterium per molecule.

To 0.2 g of the crude oxidate in 10 ml of carbon tetrachloride was added a solution of bromine in carbon tetrachloride until the bromine color persisted. After evaporation of the solvent, the yellow residue was recrystallized from ethanol to give a pure sample of 1,2-dibromo-1,3-diphenylpropan-3-yl acetate, mp 177–179° (lit.[24] mp 176–177°). Analysis indicated that the dibromide contained 0.65 atom of deuterium per molecule.

To 2.0 g of the crude deuterated alcohol was added 15 ml of AR grade acetone, and the solution was cooled to 0–5°. The solution was maintained at this temperature while a solution of 1.0 g of chromic acid, 3.0 ml of water, and 1.0 ml of concentrated sulfuric acid was added over a period of 30 min. After having been stirred for 2 hr at room temperature, the solution was poured into 500 ml of water. The ketone was isolated and purified by crystallization from ethanol. The yield of product was 0.91 g, mp 71–72° (lit.[25] mp 71–72°); it was found to contain 0.32 atom of deuterium per molecule.

Attempted Isomerization of 1,3-Diphenyl-1-propene-3-*d*.—To 50 ml of acetic acid was added 0.60 g of 85% phosphoric acid and 2.0 g of 1,3-diphenylpropene-3-*d*. The solution was heated at reflux for 20 min, and the olefin was then reisolated. The nmr spectrum of this material was identical in every respect with that of the starting material.

1,3-Diphenyl-2-propen-1-ol-3-*d*.—To 20.0 g (0.0957 mol) of 1,3-diphenyl-2-propen-1-one-3-*d* containing 0.60 atom of deuterium per molecule was added 200 ml of absolute ether and 1 ml of absolute ethanol. Then 2.0 g of sodium borohydride was introduced, and the mixture was stirred at room temperature for 48 hr. The solution was poured into an iced solution of 4% sulfuric acid and the ether layer was separated, neutralized, and dried with magnesium sulfate. Evaporation of the ether gave 18.2 g of crude product, which after two crystallizations melted at 55–56° (lit.[26] mp 57–58°). Analysis indicated that the alcohol contained 0.59 atom of deuterium per molecule.

1,3-Diphenyl-2-propen-1-yl-3-*d* Acetate.—To 5.0 g (0.024 mol) of the above alcohol was added 15 ml of acetic anhydride and 15 ml of anhydrous pyridine. This mixture was kept at 35–40° for 4 hr. The solution was poured into 100 ml of water and extracted with three 50-ml portions of ether. The combined ether extracts were washed with acid and with base, dried, and distilled; a total of 3.6 g (70%) of acetate was obtained, bp 211° (11 mm) [lit.[24] bp 211° (11 mm)].

Isomerization of 1,3-Diphenyl-2-propen-1-yl-3-*d* Acetate.—To 2.0 g of the acetate were added 50 ml of acetic acid and 0.60 g of 85% phosphoric acid; the solution was heated at reflux for 20 min. Recovery of the acetate was accomplished in the usual manner, and the nmr spectrum indicated that extensive scrambling of deuterium had occurred. Reduction of the acetate with lithium aluminum hydride and chromic acid oxidation of the product produced 1,3-diphenylpropan-1-one, which contained 0.38 deuterium atom per molecule. The same sequence of reactions with acetate that had not been heated in acetic acid yielded ketone containing 0.58 deuterium atom per molecule.

Isolation and Characterization of the Intermediate.—To 1 ml of water was added 4.29 g (0.0386 mol) of selenium dioxide, and to this solution was added 250 ml of glacial acetic acid containing 15.0 g (0.0773 mol) of 1,3-diphenylpropene. The solution was stirred at room temperature, and after 3 days the white crystals that had formed were removed by filtration (6.2 g, 30%).

The product was recrystallized from a 1:1 mixture of chloroform and ethanol. The product melted with decomposition in

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[26] H. H. Wasserman and N. E. Aubrey, *J. Amer. Chem. Soc.*, **77**, 590 (1955).

the range of 199–201°. An infrared spectrum showed strong bands at 1745 and 1200 cm^{-1} indicating the presence of an acetate ester function in the molecule.

Anal. Found: C, 68.63; H, 5.91; Se, 10.46.

A solution of 1.0 g of the intermediate was dissolved in 50 ml of warm glacial acetic acid, and the solution was heated at reflux for 20 min. At the end of this time, a total of 0.01 g (7%) of selenium had precipitated. (In a parallel experiment starting with dioxide and olefin, the yield of selenium after 20 min was 53% of the theoretical). After isolation of the products, thin layer chromatography showed that the product distribution pattern was the same as that obtained for the olefin oxidation.

The crystals (1 g) were placed in a test tube and heated at 300° for 3–5 min. Thin layer chromatography indicated the presence of some undecomposed intermediate along with 1,3-diphenylpropene and 1,3-diphenyl-2-propen-1-yl acetate.

(+)-3-Methylcyclohexanone.—Oil of pennyroyal (Fritzsche), 97% of which was pulegone having $[\alpha]^{25}\mathrm{D}$ +13.7°, was used without further purification. In a 5-l., round-bottomed flask fitted with a reflux condenser were combined 1000 ml of oil of pennyroyal, 650 ml of concentrated hydrochloric acid, and 1950 ml of water. The mixture was heated at reflux for 16 hr, the flask was fitted for distillation, and 327 g of acetone was removed by distillation. The residue was subjected to exhaustive steam distillation. Separation of the organic and aqueous layers of the distillate afforded 620 ml of crude (+)-methylcyclohexanone. From 540 g (4.8 mol) of the crude ketone 895 g (86%) of the sodium bisulfite adduct was prepared. The adduct was stirred for 2 hr with an excess of an aqueous solution of sodium carbonate. The mixture was then extracted several times with diethyl ether. The combined ethereal extracts were dried ($MgSO_4$), concentrated, and distilled to afford 256.4 g (55.3%) of (+)-3-methylcyclohexanone: bp 55–56° (7 mm) [lit.[27] bp 169° (760 mm)]; $[\alpha]^{25}\mathrm{D}$ +13.7° (lit.[28] $[\alpha]^{25}\mathrm{D}$ +13.38°); semicarbazone, mp 178–179° (lit.[29] mp 171–174° dec).

(−)-3-Methylcyclohexanol.—(+)-3-Methylcyclohexanone (224 g, 2.00 mol) was reduced with lithium aluminum hydride in the usual manner. Distillation of the crude alcohol gave 210 g (92.0%) of (−)-3-methylcyclohexanol: bp 70–71° (7 mm) [lit.[30,31] bp 84° (13 mm), 169–170° (748 mm) for *cis*-3-methylcyclohexanol]; $[\alpha]^{25}\mathrm{D}$ −4.63° (lit.[32] $[\alpha]^{25}\mathrm{D}$ −4.15°).

(−)-3-Methylcyclohexyl Acetate.—A mixture of 217 g (1.90 mol) of (−)-3-methylcyclohexanol, 230 g (2.25 mol) of acetic anhydride, 74 g (0.90 mol) of sodium acetate, and 630 ml of dry benzene was stirred and refluxed for 6 hr. The reaction mixture was poured into cold water, and the layers were separated. The organic layer was stirred with sodium carbonate solution, washed once with water, dried, concentrated, and distilled to give 283 g (95.5%) of (−)-3-methylcyclohexyl acetate: bp 66–67° (6 mm) [lit.[33] bp 78–79° (20 mm)]; $[\alpha]^{25}\mathrm{D}$ −25.59°.

(+)-4-Methylcyclohexene and (+)-3-Methylcyclohexene.—(−)-3-Methylcyclohexyl acetate (139 g, 0.891 mol) was passed dropwise in a dry nitrogen atmosphere through a helix-packed Pyrex tube encased by an oven heated to 450–460°. Nine hours were required for the pyrolysis. The products, which were collected in a receiver cooled in a Dry Ice–acetone bath, were dissolved in ether. The ethereal solution was washed with water and sodium carbonate solution until neutrality was achieved. The ether solution was dried ($MgSO_4$) and concentrated. Distillation of the residue through a Vigreux column afforded 51.3 g (60.0%) of olefin: bp 42° (80 mm); $[\alpha]^{25}\mathrm{D}$ +108.9 [lit.[34] bp 102° (760 mm), $[\alpha]^{25}\mathrm{D}$ +106.8° for (+)-4-methylcyclohexene]. This product was shown to be a 3:2 mixture of (+)-4-methylcyclohexene and (+)-3-methylcyclohexene by the series of reactions described below.

Epoxidation of the Optically Active Olefin Mixture.—To a cold, stirred solution of 2.4 g (0.025 mol) of a mixture of (+)-4-methylcyclohexene and (+)-3-methylcyclohexene was added dropwise 10 ml of 40% peracetic acid (Becco) to which 0.4 g of sodium acetate had been added. The temperature was maintained at 0° during the addition and while the mixture was stirred for 2 hr after the addition was complete. Stirring was then continued for 4 hr at room temperature. The reaction mixture was washed with water, 10% potassium hydroxide solution, and water again. The chloroform solution was dried and concentrated to give 2.4 g (86%) of the crude epoxide mixture. An nmr spectrum of the product showed two different methyl groups and thus indicated the possible presence of two different epoxides. However, separation of the compounds by vapor phase chromatography could not be achieved. A sample of 4-methylcyclohexene Comparison of the nmr spectrum of this material with that of the epoxide mixture served to identify 4-methylcyclohexene oxide as the major component of the mixture. The following sequence of reactions identified the other component as 3-methylcyclohexene oxide.

Reduction of the Epoxide Mixture.—The crude epoxide mixture (2.0 g, 0.018 mol) was reduced in the usual manner with lithium aluminum hydride in anhydrous ether to afford a mixture of alcohols in quantitative yield.

Oxidation of the Epoxide Reduction Products.—The crude alcohol mixture (1.5 g, 0.013 mol) obtained by reduction of the epoxide mixture was dissolved in 1.5 ml of glacial acetic acid, and the mixture was cooled to 0°. To this solution was added 1.5 g (0.0050 mol) of sodium dichromated in 2.5 ml of glacial acetic acid. The resultant reaction mixture was heated at 40° for 15 min, cooled, poured into water, and subjected to steam distillation. The distillate was extracted with ether, and the combined extracts were washed with an aqueous solution of sodium bicarbonate until neutrality was achieved. The ethereal solution was dried and concentrated to give 1.16 g (80%) of a mixture of ketones. Vapor phase chromatographic analysis on a Carbowax column was carried out; the components of the mixture were shown to be 2-methylcyclohexanone (15%), 3-methylcyclohexanone (45%), and 4-methylcyclohexanone (40%) by comparison of their retention times with those of commercially available authentic samples.

Selenium Dioxide Oxidation of the Olefin Mixture in Acetic Anhydride.—A stirred mixture of 12.0 g (0.108 mol) of selenium dioxide and 40 g of acetic anhydride was heated to 105°. To this mixture was added rapidly 19.3 g (0.201 mol) of the 3:2 mixture of (+)-4-methylcyclohexene and (+)-3-methylcyclohexene in 50 ml of acetic anhydride. The reaction mixture was heated at 105° for 3 hr, cooled, and filtered. The precipitated selenium that was recovered weighed 1.43 g (16.7%). The filtrate was subjected to steam distillation, and the distillate was extracted with ether. The ethereal extract was washed with water, washed with sodium carbonate solution until the wash solution remained basic, dried, concentrated, and distilled to afford 2.91 g (9.27%) of the allylic acetate mixture: bp 64–66° (6 mm). In order to remove organoselenium impurities, the allylic acetate mixture was treated with 1 g of Raney nickel (W-2) in anhydrous ether. The resultant slurry was refluxed overnight. After filtration and concentration, 2.8 g of product, which was free of organoselenium impurites, was recovered.

Catalytic Reduction of the Allylic Acetates.—The mixture of allylic acetates (2.8 g, 0.018 mol) prepared as described above was reduced at 50 psi of hydrogen in glacial acetic acid in the presence of Adams catalyst. Distillation of the product gave 2.6 g (92%) of a mixture of methylcyclohexyl acetates: bp 63–67° (6 mm).

Hydride Reduction of the Methylcyclohexyl Acetates.—The mixture of 2-, 3-, and 4-methylcyclohexyl acetates (2.5 g, 0.016 mol) was reduced in the usual manner with lithium aluminum hydride in anhydrous ether. Distillation of the product gave 1.7 g (94%) of a mixture of 2-, 3-, and 4-methylcyclohexanols: bp 65–68° (6 mm). The products were identified by comparison of the retention times as determined by vapor phase chromatography (Carbowax) with the retention times of commercially available authentic samples.

Oxidation of the Methylcyclohexanols.—The mixture of alcohols (1.5 g, 0.013 mol) obtained by hydride reduction of the acetate mixture was oxidized with potassium dichromate in acetic acid in a manner similar to that described above. Distillation of the product gave 1.3 g (90%) of the product mixture. This mixture was analyzed by vapor phase chromatography on a 5 ft × 0.25 in 20% Carbowax 20M on 80/100 mesh firebrick column at 120°. The chromatogram showed eight peaks, which corresponded to methylcyclohexane, toluene, the 2-, 3-, and 4-methylcyclohexanones, and small amounts of the 2-, 3-, and

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4-methylcyclohexanols. The hydrocarbons and the ketones were isolated by preparative vapor phase chromatography. Toluene and methylcyclohexane were identified by the nmr spectra. 2-Methylcyclohexanone (35%) had $[\alpha]^{25}\text{D}$ −14.6° (lit.[33] $[\alpha]^{25}\text{D}$ −15.22°) and gave a semicarbazone, which melted at 193–195° (lit.[29] mp 197°). 3-Methylcyclohexanone (30%) had $[\alpha]^{25}\text{D}$ +0.572° (lit.[33] $[\alpha]^{25}\text{D}$ +13.06) and gave a semicarbazone melting at 177–178° (lit.[29] mp 179°). 4-Methylcyclohexanone (35%) appeared as a shoulder on the peak corresponding to 3-methylcyclohexanone and was not separated.

Racemization of (−)-2-Methylcyclohexanone.—A small quantity of the (−)-2-methylcyclohexanone collected by vapor phase chromatography was refluxed in glacial acetic acid for 3 hr. The ketone that was recovered had no measurable optical activity.

Selenium Dioxide Oxidation of the Olefin Mixture in *n*-Butanol.—A stirred solution of 19.8 g (0.206 mol) of the 3:2 mixture of (+)-4-methylcyclohexene and (+)-3-methylcyclohexene in 70 ml of *n*-butanol was heated to reflux and 22.2 g (0.200 mol) of selenium dioxide in 100 ml of *n*-butanol was added dropwise. Reflux of the resultant mixture was continued for 30 hr. The reaction mixture was cooled and filtered to yield 6.2 g (39%) of black selenium. Fractional distillation of the filtrate gave 10 ml of a yellow liquid: bp 130–140° (30 mm). This material was treated with Raney nickel as described above to remove organoselenium impurities. Distillation through a spinning-band column gave 5.2 g of product: bp 90–95° (11 mm). Vapor phase chromatography on a Carbowax column showed five peaks. The material corresponding to the first and largest peak was collected and identified by its nmr spectrum as being a mixture of butoxycyclohexenes. The other peaks corresponded to methylcyclohexenones and methylcyclohexenols. The mixture of products was reduced catalytically in the presence of Adams catalyst in acetic acid. Vapor phase chromatography of the reduction product on a 12 ft × $^3/_8$ in. 23% polyamide on Chromosorb W column was carried out. The butyl ethers of commercially available methylcyclohexanols were prepared. By comparison with these and other commercially available authentic samples, the components of the reduction mixture were determined to be *cis*-2-butoxymethylcyclohexane, *trans*-3-butoxymethylcyclohexane, *cis*-4-butoxymethylcyclohexane, *trans*-2-butoxymethylcyclohexane, *cis*-3-butoxymethylcyclohexane, *trans*-4-butoxymethylcyclohexane, a mixture of methylcyclohexanones, and a mixture of methylcyclohexanols.

Registry No.—Selenium dioxide, 7446-08-4; 1,3-diphenylpropene-3-*d*, 16704-20-4; benzaldehyde-1-*d*, 3592-47-0.

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Bicyclo[3.3.1]nonanes. IV. Dehydration of the Bicyclo[3.3.1]nonane-2,6-diols

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Bicyclo[3.3.1]nonane-2,6-dione (**2**), which was prepared from 1,3,5,7-tetracarbomethoxybicyclo[3.3.1]nonane-2,6-dione (**1**), was reduced with sodium borohydride in methanol to a mixture of epimeric bicyclo[3.3.1]nonane-2,6-diols (**3** and **4**). Dehydration of the diol mixture with sulfuric acid gave bicyclo[3.3.1]nona-2,6-diene (**9**), bicyclo[3.3.1]nona-2,7-diene (**8**), bicyclo[3.3.1]nonan-2-one (**5**), *endo*-bicyclo[3.3.1]non-6-en-2-ol (**10**), *endo*-bicyclo[3.3.1]non-7-en-2-ol (**11**), *endo*-bicyclo[3.3.1]non-3-en-2-ol (**12**), and a mixture of tricyclic oxides, which were tentatively identified as oxaadamantane (**6**) and 10-oxatricyclo[3.3.1.1^{2,7}]decane (**7**).

The first practical route to simply substituted bicyclo[3.3.1]nonanes was developed by Meerwein and Schürmann.[1] In their approach, dimethyl malonate was caused to react with formaldehyde or methylene iodide to produce 1,3,5,7-tetracarbomethoxybicyclo-[3.3.1]nonane-2,6-dione (**1**) in good yield. Since **1** is so readily accessible, it appeared to be an attractive precursor to a number of derivatives that we were interested in preparing.

Upon reinvestigation of Meerwein's work,[1] we found that the preparation of **1** from formaldehyde could be simplified and expedited significantly by carrying out the initial phases of the condensation under anhydrous conditions and removing the water produced during the reaction by azeotropic distillation. Hydrolysis of the ester and decarboxylation of the resultant acid utilizing a procedure similar to that developed by Stetter and his group[2] afforded bicyclo[3.3.1]nonane-2,6-dione (**2**) in over-all yields as high as 38% based upon dimethyl malonate.

Reduction of **2** with sodium borohydride in methanol produced in high yield a mixture of two diols present in approximately equal percentages. In a previous paper,[3] we demonstrated that reduction of bicyclo-[3.3.1]nonan-2-one (**5**) using similar conditions produces *endo*-bicyclo[3.3.1]nonan-2-ol (**14**) almost exclusively. We have also provided data that show that nucleophilic attack on the bicyclo[3.3.1]nonane system occurs almost exclusively from the *exo* face of the molecule. On these grounds, it is reasonable to presume that the first-formed product of reduction is a boron ester of 6-keto-*endo*-bicyclo[3.3.1]nonan-2-ol (**18**). Two routes for the reduction of the second carbonyl group would now be possible.

Bimolecular reduction of the second carbonyl group, initiated by an attack by borohydride ion on the keto alcohol or its boron ester, would be influenced by the same steric effects that were encountered during the reduction of the first carbonyl group. In this instance, the product would be *endo,endo*-bicyclo[3.3.1]nonane-2,6-diol (**4**). Alternatively, an intramolecular path for reduction is also available, but this route would lead to the formation of *endo,exo*-bicyclo[3.3.1]nonane-2,6-diol (**3**). The details of this process merit further discussion.

To allow the initially formed boron ester of **18** to approach sufficiently close to the second carbonyl group so that an interaction can occur, the rings must assume twist-boat conformations. The expenditure of energy required to bring about this conformational change will be compensated for by two factors, namely, the lower activation energy associated with the reduction of ketones by alkoxyborohydrides[4] and the

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