[CONTRIBUTION FROM NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Stereochemistry and Reactions with Hydroxyl Ion and with Silver Oxide of the 2-Bromo-4-phenylcyclohexanols and the 1-Methyl-2-bromo-4-phenylcyclohexanols[1]

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The reactions of the four possible racemic 2-bromo-4-phenylcyclohexanols (I) and of three of the four possible racemic 2-bromo-1-methyl-4-phenylcyclohexanols (II) with potassium hydroxide in isopropyl alcohol and with silver oxide in hexane have been studied. Differences in behavior with silver oxide in hexane of the bromine-equatorial and bromine-axial *trans*-bromohydrins (*trans,trans*-I and *trans,cis*-I) and also of the bromine-equatorial and bromine-axial *cis*-bromohydrins (*cis,cis*-II and *cis,trans*-II) provide examples of a subtle kind of steric control in which the change of configuration of a substituent removed from the reaction site can alter the course of the reaction. *trans*-2-Bromo-4-phenylcyclohexanone (*trans*-III) has been prepared by bromination of 4-phenylcyclohexanone. The *cis* isomer *cis*-III has been prepared by decarboxylation of 2-bromo-2-carboxy-4-phenylcyclohexanone (IV). The ketone *cis*-III with bromine equatorial has been found to give a mixture of bromohydrins *cis,cis*-I and *trans,trans*-I on reduction with isobutylmagnesium bromide or with lithium aluminum hydride. Methylmagnesium iodide gives a mixture also of *cis,cis*-II and *trans,trans*-II. The ketone *trans*-III, on the other hand, with the bromine substituent axial, gives principally a single bromohydrin *cis,trans*-I with isobutylmagnesium bromide and with lithium aluminum hydride and a single methyl bromohydrin *cis,trans*-II with methylmagnesium iodide. 4-Phenylcyclohexene has been found to give on treatment with perbenzoic acid a mixture of approximately equal amounts of *cis*- and *trans*-4-phenylcyclohexene oxide, a result different from that reported in the literature for a peracetic acid oxidation of this olefin. The *trans*-bromohydrins with bromine either axial (*trans,cis*-I and *trans,trans*-VII) or equatorial (*trans,trans*-I and *trans,trans*-II) give epoxides when treated with potassium hydroxide in isopropyl alcohol. With silver oxide in hexane, however, the *trans*-bromohydrins with bromine equatorial (*trans,trans*-I and *trans,trans*-II) undergo ring contraction to give, respectively, 3-phenylcyclopentanecarboxaldehyde (VIII) and 1-acetyl-3-phenylcyclopentane (X), both probably *cis*, whereas the *trans*-bromohydrins with bromine axial (*trans,cis*-I and *trans,trans*-VII) again give epoxides. The stereochemistry of the products *cis*-VIII and *cis*-X is complicated by the possibility of epimerization in the reaction mixture. Both the *cis*-bromohydrins I with bromine equatorial (*cis,cis*-I) and with bromine axial (*cis,trans*-I) either with potassium hydroxide in isopropyl alcohol or with silver oxide in hexane give predominantly 4-phenylcyclohexanone. Both of the *cis*-bromohydrins II with potassium hydroxide in isopropyl alcohol give predominantly 1-acetyl-3-phenylcyclopentane formed by ring contraction. Silver oxide in hexane, however, converts the *cis* isomer with bromine axial (*cis,trans*-II) to 2-methyl-4-phenylcyclohexanone (probably *cis*) whereas the isomer with bromine equatorial (*cis,cis*-II) undergoes ring contraction.

As a continuation of work on stereospecificity of reactions of cyclohexane derivatives[3] it was of interest to examine the behavior of cyclohexane derivatives with the cyclohexane ring locked in one conformation by a large substituent removed as far as possible from the reaction site.[3c,4] For this study, were chosen the stereoisomeric racemates, the *dl*-2-bromo-4-phenylcyclohexanols (I) and the *dl*-2-bromo-1-methyl-4-phenylcyclohexanols (II).[5]

As starting materials *cis*- and *trans*-2-bromo-4-phenylcyclohexanone (*cis*- and *trans*-III) were desired. It was anticipated from work of Corey[6] that *trans*-III (expected to have the phenyl group equatorial and bromine atom axial in the most stable conformation) would be formed in the kinetically controlled bromination of 4-phenyl cyclohexanone. As expected, 4-phenylcyclohexanone reacted with bromine at 0° in ether–chloroform solution to give in 62% yield a bromo ketone, m.p. 116°, shown below to be *trans*-III.[7]

The preparation of the *cis* racemate (*cis*-III) m.p. 77°, was accomplished in 41% yield by the decarboxylation of the bromo keto acid, IV; IV was obtained by the bromination of 2-carboxy-4-phenylcyclohexanone and allowed to undergo decarboxylation without isolation. The choice of this method was based on the presumption that the decarboxylation of the β-keto acid would proceed[8] by way of the enol V which, when it tautomerized to the keto form, should add the proton principally in the axial position.[9] It may be noted that Corey[10] had previously employed a similar decarboxylation procedure to prepare 2,2-dibromocyclohexanone from 2-carboxycyclohexanone.[11]

The configurational assignments to the bromo ketones *cis*- and *trans*-III are based primarily on their infrared and ultraviolet spectra. The axial bromo ketone (*trans*-III) showed its carbonyl absorption (1721 cm.$^{-1}$) in carbon tetrachloride solution at the same frequency as the unbrominated 4-

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(1) Taken from the Ph.D. Thesis of Robert J. Harder, submitted to the University of Illinois, 1956 [*C. A.*, **51**, 12834e (1957)].

(2) National Science Foundation Fellow, 1954–1956. We are, furthermore, indebted to the E. I. du Pont de Nemours Co. for a grant-in-aid which supported this work in 1953–1954.

(3) (a) D. Y. Curtin, *Record Chem. Progr. Kresge-Hooker Sci. Lib.*, **15**, 111 (1954); (b) D. Y. Curtin and S. Schmukler, THIS JOURNAL, **77**, 1106 (1955); (c) D. Y. Curtin, R. D. Stolow and W. Maya, *ibid.*, **81**, 3330 (1959).

(4) For a discussion of general principles and other work in this field see W. G. Dauben and K. S. Pitzer, "Steric Effects in Organic Chemistry," Edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 1.

(5) Throughout this work racemates were employed unresolved. Although the drawings show only one isomer, it should be understood that the mirror image was present in equal amount. The names of the bromohydrins are abbreviated by indicating first the position of the bromine relative to the hydroxyl group and then the position of the phenyl also relative to the hydroxyl group. Thus, "2^{c}-bromo-4^{t}-phenylcyclohexanol (1)" is abbreviated "*cis-trans*-1."

(6) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).

(7) The same bromide, m.p. 115°, has also been obtained in 85% yield by carrying out the bromination in ether solution at 0° (E. J. Corey and Y. L. Yeh, private communication; Y. L. Yeh, Thesis for the Bachelor of Science, University of Illinois, 1954).

(8) K. J. Pedersen, THIS JOURNAL, **58**, 240 (1936).

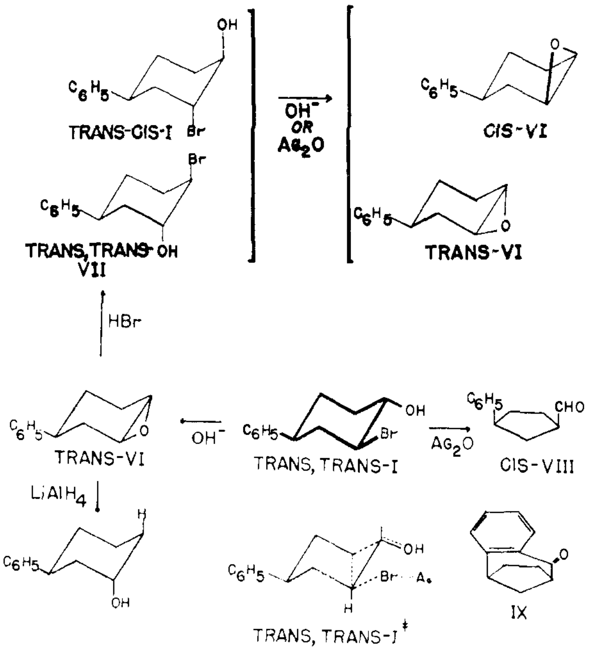
(9) See E. J. Corey and R. A. Sneen, *ibid.*, **78**, 6269 (1956).

(10) E. J. Corey, *ibid.*, **75**, 3297 (1953).

(11) Since the completion of this work the synthesis of a 2-bromo-4-phenylcyclohexanone, m.p. 104-105°, considered to have the bromine equatorial has been reported to be formed in quantitative yield by the bromination of 4-phenylcyclohexanone with N-bromosuccinimide [E. D. Bergmann and S. Yaroslavsky, THIS JOURNAL, **81**, 2772 (1959)]. The yield is uncertain, however, because no weight is reported for the purified product. The only configurational evidence was an assignment of the bromine to an equatorial position on the basis of a comparison of the carbonyl frequencies of the bromo ketone and 4-phenylcyclohexanone (apparently both in potassium bromide pellets). It has been shown [N. L. Allinger, J. Allinger, L. E. Geller and C. Djerassi, *J. Org. Chem.*, **25**, 6 (1960)] that 2-bromo-5-methylcyclohexanone exists predominantly with the bromine axial in the crystalline state but equatorial in solution.

phenylcyclohexanone whereas the equatorial isomer (*cis*-III) had its absorption at 1732 cm.$^{-1}$.[12] The positions and intensities of the ultraviolet maxima also led to this assignment.[13] Further support for the assigned structures comes from the reactions described below.

The addition of Grignard reagents to α-chloro-,[14a] α-hydroxy-[14a] and α-aminocyclohexanones[3b] as well as α-chloro- and α-hydroxycyclopentanones[14b] have been known for some time to occur with preferential addition to give the racemate with the hydroxyl group being formed and the halogen atom *cis* to each other. Reduction of α-chlorocyclohexanone with *t*-butylmagnesium chloride shows similar stereospecificity.[14c] Reduction of the ketones *cis*- and *trans*-III with isobutylmagnesium bromide and also with lithium aluminum hydride was therefore examined. The *cis*-bromo ketone *cis*-III (with bromine equatorial) on reduction with lithium aluminum hydride gave both stereoisomeric reduction products, 2^c-bromo-4^c-phenylcyclohexanol (*cis,cis*-I) and 2^t-bromo-4^t-phenylcyclohexanol (*trans,trans*-I). Separation of the products by chromatography gave 20% of the *cis,cis* isomer and 64% of the *trans,trans*. The *cis,cis* isomer was contaminated with an estimated 3% of a bromine-free ketone, probalby 4-phenylcyclohexanone, which could not be removed. Reduction with isobutylmagnesium bromide also gave a mixture from which 35% of somewhat impure *cis,cis*-I and 21% of *trans,trans*-I could be separated. The positions of the hydroxyl groups in the stereoisomeric bromohydrins were confirmed by catalytic reduction; *cis,cis*-I gave 92% of *cis*-4-phenylcyclohexanol and *trans,trans*-I gave 37% of *trans*-4-phenylcyclohexanol. The *trans*-bromoketone *trans*-III (bromine axial) on reduction either with isobutylmagnesium bromide or with lithium aluminum hydride gave only one isolable reduction product, 2^c-bromo-4^t-phenylcyclohexanol (*cis,trans*-I) (63% yield from the Grignard reduction). The stereochemistry of the hydroxyl group was shown by reduction to *trans*-4-phenylcyclohexanol in 73% yield.



The last racemate of I, 2^t-bromo-4^c-phenylcyclohexanol, since it had not been obtained by reduction of the bromo ketones, was sought by another route. 4-Phenylcyclohexene was oxidized with perbenzoic acid to a mixture of the two stereoisomeric pairs of epoxides in nearly equal amounts.[15] Since attempts to separate epoxides *cis*- and *trans*-VI by crystallization or chromatography were only partially successful, the epoxide mixture was treated with hydrobromic acid. Two bromohydrins were formed and assigned the structures 2^t-bromo-4^c-phenylcyclohexanol (*trans-cis*-I) and 2^t-bromo-5^t-phenylcyclohexanol (*trans-trans*-VII). These structures are consistent with the generalization[16] that opening occurs in such a way that the hydroxyl and bromine substituents are axial in the product (with the phenyl remaining equatorial throughout the reaction). Additional evidence for the structural assignments will be considered below.

Before considering the reactions of the bromohydrins I it is pertinent to consider the stereochemistry of the three substituents, phenyl, bromine and hydroxyl, which are instrumental in determining the conformation of the ring in the starting materials and transition states for the various possible reactions. As a working hypothesis it will be assumed that the cyclohexane ring exists only in the chair conformations during reaction.[17] The equilibrium constants for the equilibria between axial and equatorial bromocyclohexane[18a] and for cyclohexanol[18b] are of the order of 1.2–4 depending on the reaction medium and method of estimation. It would be expected from inspection of molecular models that the steric strain introduced when a phenyl group is moved from an equatorial to an axial position should lead to a considerably larger equilibrium constant for the equilibrium between axial and equatorial phenylcyclohexane than is observed with the bromine atom or hydroxyl group.[19] The position of

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[12] L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., second edition, 1958, pp. 139 ff. See also the study of the 2-bromo-4-*t*-butylcyclohexanones by N. L. Allinger and J. Allinger, THIS JOURNAL, **80**, 5476 (1958).

[13] R. C. Cookson, *J. Chem. Soc.*, 282 (1954).

[14] (a) P. D. Bartlett and R. H. Rosenweld, THIS JOURNAL, **56**, 1990 (1934); (b) P. D. Bartlett and R. V. White, *ibid.*, **56**, 2785 (1934); (c) P. D. Bartlett, *ibid.*, **57**, 224 (1935).

[15] H. Hopff and H. Hoffman [*Helv. Chim. Acta*, **40**, 1585 (1957)] have reported that 4-phenylcyclohexene reacts with anhydrous peracetic acid to give a liquid epoxide believed to be the *trans* isomer. However, the only evidence for its stereochemical homogeneity was that it reacted with water in the presence of boron trifluoride to give a single 4-phenyl-1,2-cyclohexanediol in nearly quantitative yield. It will be seen that if a mixture of *cis*- and *trans*-epoxides have been formed and if each underwent diaxial opening[16] the same glycol should be formed from each epoxide. It will be shown later in this paper that the *trans*-phenylcyclohexane epoxide *trans*-VI is a solid, m.p. 34°. Any conclusions about the steric course of such epoxidations [see, for example, H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 221 (1959)] should be reserved until further data are available.

[16] See D. H. R. Barton and R. C. Cookson, *Quart. Revs.*, **10**, 67 (1956).

[17] See K. E. Howlett, *J. Chem. Soc.*, 4353 (1957).

[18] (a) See E. L. Eliel, *Chemistry & Industry*, 568 (1959); (b) R. A. Pickering and C. C. Price, THIS JOURNAL, **80**, 4931 (1958), and references therein cited.

[19] A. C. Huitric and W. D. Kumler [*ibid.*, **78**, 614 (1956)] have re-

the carbon–hydroxyl stretching frequency has been employed previously as a means of distinguishing between axial and equatorial hydroxyl groups.[18,20] If it is assumed that all the bromohydrins I exist in the conformation with the phenyl group equatorial, the position of the strongest band in the 950–1110 cm.$^{-1}$ region of the infrared spectrum is in general agreement with the expected position. That is, the compounds with the hydroxyl group anticipated to be in an equatorial position have their absorption in the region from 1040–1080 cm.$^{-1}$ while all of those believed to be axial fall in the region from 950–995 cm.$^{-1}$ (Table I).

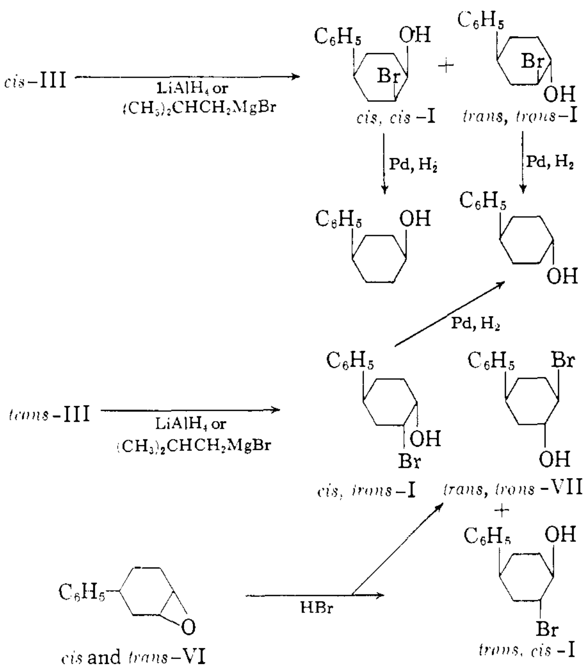
TABLE I

INFRARED CARBON-HYDROXYL FREQUENCIES OF 2° ALCOHOLS

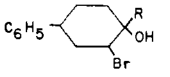
Substance	Substituents	Frequency
trans-4-Phenylcyclohexanol[21]	OH-e	1048[a,b]
cis-3-Phenylcyclohexanol[a]	OH-e	1043[a,b]
trans-4-*t*-Butylcyclohexanol[19]	OH-e	1062[19,c]
2^{t}-Bromo-4^{t}-phenylcyclohexanol[a]	OH-e	1055[a,d]
(*trans,trans*-I)	Br-e	
2^{c}-Bromo-4^{t}-phenylcyclohexanol[a]	OH-e	1077[a,d]
(*cis,trans*-I)	Br-a	
cis-4-Phenylcyclohexanol[21]	OH-a	953[a,b]
trans-3-Phenylcyclohexanol[a]	OH-a	976[a,b]
cis-4-*t*-Butylcyclohexanol[19]	OH-a	955[19,c]
2^{c}-Bromo-4^{c}-phenylcyclohexanol[a]	OH-a	991[a,d]
(*cis,cis*-I)	Br-e	
2^{t}-Bromo-4^{c}-phenylcyclohexanol[a]	OH-a	993[a,d]
(*trans-cis*-I)	Br-a	
2^{t}-Bromo-5^{t}-phenylcyclohexanol[a]	OH-a	972[a,d]
(*trans,trans*-VII)	Br-a	

[a] Present work. [b] Spectra measured in chloroform. [c] Spectra measured in carbon disulfide. [d] Spectra measured in carbon tetrachloride.

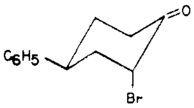
Our data are not sufficiently extensive nor precise to permit a more refined interpretation, but they do serve to confirm the previous structural assignments and also the assumption that the more stable conformation has the phenyl group in an equatorial position in this group of compounds.



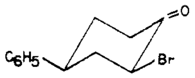
The reactions of the stereoisomeric chlorohydrins, *cis*- and *trans*-2-chloro-1-methylcyclopentanol and *cis*- and *trans*-2-chloro-1-methylcyclohexanol, with 33% aqueous sodium hydroxide had been studied by Bartlett, White and Rosenwald and found to be subject to steric control.[14] Thus, the *trans* isomers underwent epoxide formation, the normal reaction for acyclic halohydrins,[22] but the *cis*-isomers underwent rearrangement to 2-methylcyclopentanone and to acetylcyclopentane. Such rearrangements bear a formal resemblance to the benzilic acid rearrangement. It was hoped that the bromohydrins I and II prepared in the present study would show not only differences in behavior of *cis* and *trans* isomers but also that, if the locking effect of the phenyl group were sufficiently great, there would be differentiation between a *cis* isomer with bromine axial and a *cis* isomer with bromine equatorial. Similarly the behavior of a *trans* isomer with bromine axial might be expected to differ from that of a *trans* isomer with bromine equatorial.



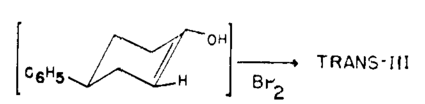
I (R=H)
II (R=CH$_3$)

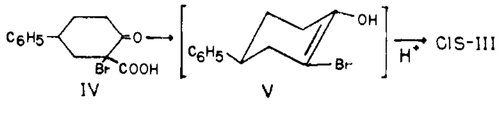


TRANS-III



CIS-III





Initial experiments employing potassium *t*-butoxide as a base were unsatisfactory since the product mixtures appeared to be unnecessarily complicated and, in particular, to contain carboxylic acid fractions which were not identified. Potassium hydroxide in isopropyl alcohol was selected as a more desirable medium. In addition

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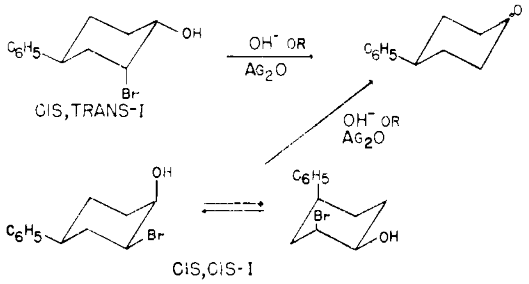
ported evidence from dipole moment studies that α-phenyl- and α-[*p*-halophenyl]-cyclohexanones have the substituent in an equatorial position. E. J. Corey, M. G. Howell, A. Boston, R. L. Young and R. A. Sneen [*ibid.*, **78**, 5036 (1956)] showed with an infrared study that the phenyl group in the 1-deuterio-4-phenylcyclohexanes is largely equatorial. We are particularly indebted to Dr. Ernest Eliel for communication of his work with Rerick [THIS JOURNAL, in press] showing that the value of the free energy difference between equatorial and axial phenyl is approximately 2.6 kcal./mole in agreement with the assumption made in the present work that phenyl has a larger axial effect than a methyl group. We are indebted to Dr. Eliel also for discussion of other aspects of the present work.

(20) A. Nickon, *ibid.*, **79**, 243 (1957).

(21) H. E. Ungnade, *J. Org. Chem.*, **13**, 361 (1948).

(22) S. Winstein and R. B. Henderson, "Heterocyclic Compounds," Vol. 1, Edited by R. C. Elderfield, John Wiley and Sons, Inc., New York, 1948, pp. 9 ff.

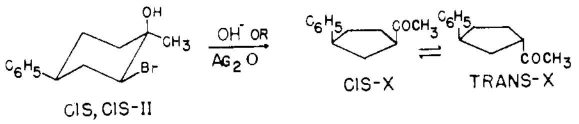
it was desired to study a reaction more analogous to the pinacol family of rearrangements and silver oxide in hexane[3b] was chosen for this purpose. The bromohydrins I and II were therefore subjected to two sets of reaction conditions; treatment with potassium hydroxide in isopropyl alcohol and with silver oxide in hexane. The *trans*-diaxial bromohydrin (*trans,cis*-I), because of the difficulty of separating it from its companion *trans*-diaxial bromohydrin (*trans,trans*-VII), and because of its unspectacular behavior was not studied in pure form, but instead the mixture of the two diaxial bromohydrins *trans,cis*-I and *trans,trans*-VII as they were obtained from the mixture of *cis*- and *trans*-epoxides VI was employed. On treatment with potassium hydroxide in isopropyl alcohol the mixture was converted to a mixture of epoxides (92% yield) shown by a comparison of the infrared spectrum with that of the original mixture of epoxides VI (intensities of the two curves agreed to within 1% at five frequencies compared) to be identical with the epoxide mixture VI from which it had been formed. Such epoxide formation with neighboring group participation of the oxygen (as O^-) which has the optimum geometry is the expected reaction.[15,22] The second reagent, silver oxide in hexane, was chosen in order to facilitate departure of the leaving bromide ion and to discourage neighboring group participation by the alkoxide oxygen. This reagent was chosen rather than silver nitrate in homogeneous solution because previous work[3b] had indicated that the products of the latter reaction were complicated by the formation of by-products. The use of silver oxide in a non-polar solvent is accompanied by some uncertainty in the mechanism of the reactions being studied but was experimentally very satisfactory. Like potassium hydroxide, silver oxide in hexane converted the mixture of diaxial bromohydrins *trans,cis*-I and *trans,trans*-VII to the mixture of *cis*- and *trans*-epoxides VI.

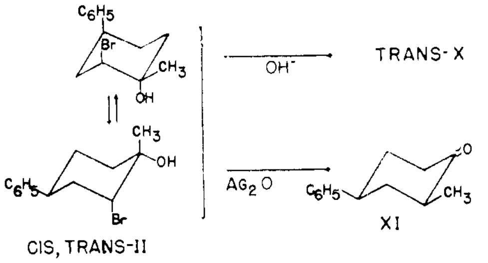


The other *trans*-bromohydrin (*trans,trans*-I) is the most securely conformationally locked bromohydrin of the four racemates I since all three substituents can be equatorial simultaneously. Diequatorial bromohydrins among the steroids have been found to undergo epoxide formation on treatment with base but, as might be expected from steric considerations, at a rate considerably slower than the corresponding diaxial isomers.[23] The diequatorial bromohydrin *trans,trans*-I with potassium hydroxide in isopropyl alcohol was readily converted to the corresponding epoxide, *trans*-VI, which was obtained as a solid, m.p. 34°. With hydrogen bromide the epoxide was converted to the bromohydrin (*trans, trans*-VII) previously obtained from the mixture of *cis*- and *trans*-epoxides VI. This reaction, assuming a diaxial opening of the epoxide ring, serves to strengthen the previous structural assignments to the compounds concerned. Furthermore it suggests strongly that in the previously discussed reaction of the mixture of epoxides *cis*- and *trans*-VI with hydrobromic acid the *trans,cis*-I which was formed originated principally from the *cis*-epoxide *cis*-VI while the *trans,trans*-VII came from *trans*-VI, in agreement with the principle of diaxial opening. It was also shown that partial separation of epoxides *cis*- and *trans*-VI gave fractions, of which one was richer in *trans,cis*-I and the other in *trans,trans*-VII after treatment with hydrobromic acid.

Further evidence for the structure of the *trans*-epoxide VI and also for the principle of diaxial opening was obtained by reduction of the epoxide with lithium aluminum hydride which led mainly to *trans*-3-phenylcyclohexanol. The structure of this substance is based on its oxidation to 3-phenylcyclohexanone, its non-identity with a 3-phenylcyclohexanol prepared by hydrogenation of *m*-phenylphenol under equilibrating conditions and by the infrared evidence that it is an axial alcohol as expected.

The reaction of the *trans*-diequatorial bromohydrin *trans,trans*-I with silver oxide in hexane was of particular interest since it gave no detectable amounts of the epoxides formed from the *trans*-diaxial bromohydrins. Instead there was formed 94% of a colorless oil giving a negative Beilstein test and shown by the infrared spectrum to have an aldehyde carbonyl group (absorption at 1725, 2600 and 2700 cm.$^{-1}$). The infrared absorption showed no evidence of 4-phenylcyclohexanone. Treatment with 2,4-dinitrophenylhydrazine led to the isolation of the dinitrophenylhydrazone of the aldehyde, 3-phenylcyclopentanecarboxaldehyde, tentatively assigned the *cis* configuration (*cis*-VIII).





Oxidation with silver oxide converted the aldehyde *cis*-VIII to a liquid carboxylic acid with an infrared spectrum identical with that of the *trans* isomer to be discussed later except that the *cis*-

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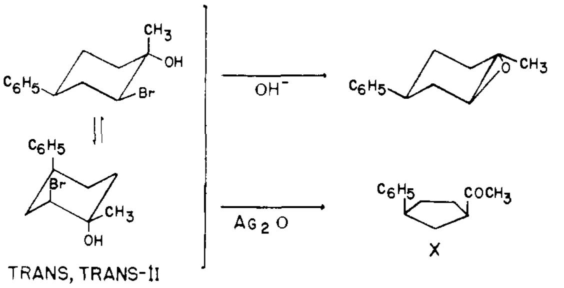
(23) See ref. 16, p. 68.

acid had an additional absorption band in the finger-print region. The 1,3-relationship of the phenyl and carboxyl substituents was shown by closure with polyphosphoric acid to 3,4-benz-2-ketobicyclo[3.2.1]octane (IX). The *cis*-acid gave an amide, m.p. 158°, whereas the amide of the *trans*-acid melted at 149°. This evidence does not exclude the possibility that aldehyde *cis*-VIII contained some of the *trans* isomer but it does suggest strongly that it was largely *cis*. In any case the difference in behavior toward silver oxide of the two *trans*-bromohydrins, *trans,cis*-I and *trans,trans*-I, is striking and is clearly a demonstration of steric control. It is impossible that both reactions proceed through the same identically solvated carbonium ion and it seems probable that in each case there is participation by a neighboring group. Hydroxyl participation in the *trans*-diaxial isomer *trans,cis*-I thus leads to epoxide, and methylene participation in the *trans*-diequatorial isomer *trans,trans*-I leads to ring contraction. In each case the neighboring group winning the competition is that which can participate in such a way that the phenyl group in the 4-position remains equatorial.[24] Consideration of the geometry of the transition state (*trans,trans*-I‡) shows that the aldehyde initially formed should be the *cis* isomer, *cis*-VIII. There remains, however, the problem of whether this isomer was partially isomerized during its isolation.

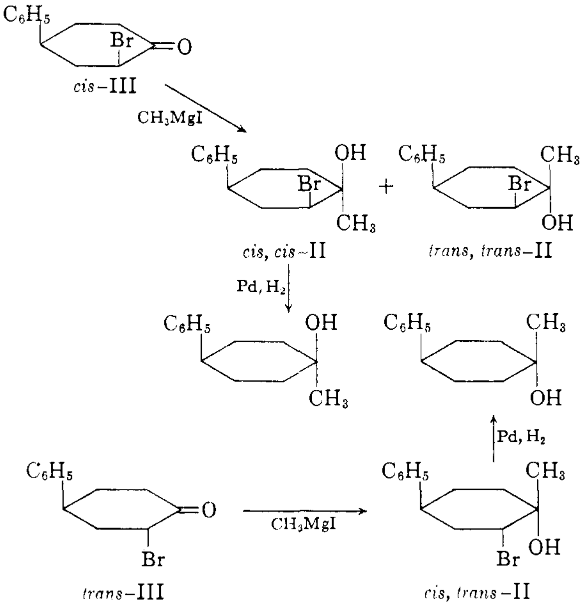
The *cis*-bromohydrin with bromine axial, *cis,trans*-I, has the hydrogen and bromine atoms located such that the transition states for rearrangement with hydrogen-migration or elimination of hydrogen bromide by an E2 mechanism can proceed with the phenyl group equatorial in the transition state. It is not unexpected then that this bromohydrin either with potassium hydroxide in isopropyl alcohol or with silver oxide in hexane was readily converted to 4-phenylcyclohexanone. It is not possible to decide with the data available between an elimination and a hydrogen rearrangement path.

The *cis*-bromohydrin with the bromine atom equatorial, *cis,cis*-I, reacted somewhat less cleanly, but with potassium hydroxide in isopropyl alcohol the major product was clearly 4-phenylcyclohexanone which was isolated in 60% yield as its 2,4-dinitrophenylhydrazone. It had seemed possible that the paths to 4-phenylcyclohexanone might be rendered so unfavorable by the geometry of the ring that alkyl migration leading to ring contraction, a reaction previously observed by Bartlett and Rosenwald,[14a] could become the predominant one. It is clear that cyclohexanone formation has not been sufficiently retarded to permit the ring contraction to become important. By going through a transition state with the phenyl and bromine axial, or possibly by some other means the molecule has still managed to undergo a reasonably rapid reaction to give 4-phenylcyclohexanone. The reaction with silver oxide in hexane gave similar results. Although there was essentially complete reaction, infrared examination of the product suggested that it contained only about 75% of 4-phenylcyclohexanone and the 2,4-dinitrophenylhydrazone was isolated in only 58% yield. The infrared spectrum suggested the presence of a carboxylic acid, but attempts to extract such a product were unsuccessful.



TRANS, TRANS-II

Three of the four possible racemates of the methyl bromohydrins II were synthesized by the addition of methylmagnesium iodide to the bromo ketones III. As was observed with the reduction of the two bromo ketones, addition of methylmagnesium iodide appeared to be more stereospecific when the bromine atom was axial than when it was equatorial. Thus, *trans*-III (bromine axial) gave in 69% yield a single bromohydrin, m.p. 92° assigned the structure 2^{c}-bromo-1-methyl-4^{t}-phenylcyclohexanol (*cis,trans*-II). The racemate *cis*-III gave a mixture of isomers which were separated by chromatography. One, an oil obtained in 53% yield, was assigned the structure 2^{c}-bromo-1-methyl 4^{c}-phenylcyclohexanol (*cis,cis*-II) and the other, a solid (obtained in low yield), m.p. 92°, the structure 2^{t}-bromo-1-methyl-4^{t}-phenylcyclohexanol (*trans,trans*-II). The difference in the steric arrangement of the phenyl, hydroxyl and methyl groups in *cis,trans*-II and *cis,cis*-II was shown by hydrogenolysis. Each bromohydrin gave a different tertiary alcohol in nearly quantitative yield.



It may be highly significant that the reactions of the ketone with bromine axial (*trans*-III)

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(24) For a more elegant analysis of the general problem and for related examples of O *vs.* C participation see S. Winstein and L. L. Ingraham, THIS JOURNAL, **77**, 1738 (1955).

with methylmagnesium iodide, isobutylmagnesium bromide and lithium aluminum hydride are more nearly stereospecific than are the reactions of the racemate with bromine equatorial (*cis*-III). Further investigation of such systems is desirable.[25] A study of the reactions of the methyl bromohydrins II with potassium hydroxide in isopropyl alcohol and with silver oxide in hexane was undertaken, but the results must be regarded as preliminary.

The *cis*-bromohydrin *cis,cis*-II with the bromine atom equatorial can be expected to have the strongest preference for a single conformation of any of the isomers of II since both the phenyl and methyl groups are equatorial in this conformation and the bromine and hydroxyl groups approximately counter-balance each other. The reaction of this isomer with potassium hydroxide in isopropyl alcohol led to an oil estimated by infrared examination to contain some 85% of 1-acetyl-3-phenylcyclopentanone formed by ring contraction. The semicarbazone of this compound isolated in 88% yield was identical with that prepared by the method of Nenitzescu and Gavat.[26] The stereochemistry of this compound had not been determined. It seems likely that the reaction of the bromohydrin *cis,cis*-II with hydroxyl ion involves a concerted displacement of bromide ion by a methylene group of the ring which is in the right position for neighboring group participation when the bromine is equatorial. If this is the case then the initially formed product must have the *cis* configuration. It would almost certainly be equilibrated to a considerable extent if not completely with its *trans* isomer under the reaction conditions however. The *trans* and *cis* isomers may be similar in stability. Thus, *trans*-1,3-dimethylcyclopentane is some 0.5 kcal. less stable than the *cis* isomer[27] and the equilibration of the 1,3-cyclopentanedicarboxylic acids appears to give a mixture with nearly equal amounts of the two acids.[27b] The reaction of bromohydrin *cis,cis*-II with silver oxide led to an oil from which the same semicarbazone as was obtained from the potassium hydroxide reaction could be isolated in a yield of greater than 90%. The relative intensities of certain bands in the infrared spectrum of the ketone product differed in this case from those in the ketone prepared either by the method of Nenitzescu and Gavat[26] or by the potassium hydroxide–isopropyl alcohol reaction of *cis,cis*-II. This suggests that *cis*-X may have survived under these rearrangement conditions, at least in part. However, no final conclusions can be drawn without samples of the *cis*- and *trans*-ketone of unquestioned stereochemical homogeneity.

The *cis*-bromohydrin *cis,trans*-II with bromine axial, on treatment with potassium hydroxide in isopropyl alcohol, gave a ketonic fraction which was supposed from infrared examination to contain about 80% of the ring contraction product, *trans*-X. A semicarbazone fraction, m.p. 163.0–163.5°, was obtained in 94% yield but in spite of its small melting range repeated recrystallization raised the m.p. to 172°, the m.p. of *trans*-X. Although it seems clear that a mixture of ketones is involved, the presence of 2-methyl-4-phenylcyclohexanone (XI) (the product which might have been expected from a concerted displacement by the methyl group located in the rear) appears to be excluded by the infrared spectrum of the crude product since the band at 2960 cm.$^{-1}$ characteristic of this substance was absent. It seems unwise to draw any conclusions from this reaction until a further study of the products is made. Of more interest are the results of the reaction with silver oxide in hexane. In this case the major product was 2-methyl-4-phenylcyclohexanone. A semicarbazone was obtained in 95% yield which was identical with the semicarbazone from the 2-methyl-4-phenylcyclohexanone (probably *cis*) prepared by alkylation of 4-phenylcyclohexanone. In this case the kinetically controlled product should have the *cis* configuration which should also be the more stable isomer, but our work was not sufficient to allow a final conclusion as to the stereochemistry of the semicarbazone isolated. It can be seen that a comparison of the silver oxide reactions of the two *cis*-bromohydrins *cis,cis*-II and *cis,trans*-II provides another example of conformational control since the compound with bromine equatorial underwent primarily ring contraction and that with bromine axial underwent primarily methyl migration.

The single *trans*-bromohydrin *trans,trans*-II, the isomer with bromine equatorial when phenyl is equatorial, behaved like its unmethylated analog *trans,trans*-I. With potassium hydroxide in isopropyl alcohol it gave epoxide and with silver oxide in hexane ring contraction occurred.

The summary in Table II makes easier a comparison of the data just discussed. It will be noted that in the two cases (*trans,trans*-II and *cis,trans*-II) were hydroxyl ion and silver oxide give different products the silver oxide reaction gives the product to be expected from the simple steric considerations previously mentioned and may thus be considered to be less susceptible to disturbing nonsteric influences of the kind discussed. It may be noted also that of the three cases where the methyl series (II) differs from the unmethylated series (I), two (the reactions with hydroxyl ion and with silver oxide of the *cis*-equatorial compounds, *cis,cis*-I and II) are readily explained. Thus, assume that 4-phenylcyclohexanone was formed from *cis,cis*-I by way of a transition state in the conformation with the phenyl group in an axial position. The presence of the extra methyl group which must be axial in the corresponding transition state from *cis,cis*-II might be expected to slow the cyclohexanone-forming reaction relative to ring contraction (where the methyl group remains equatorial) by a factor of about 20. This is sufficient to change the major product to that of ring contraction. A similar effect of the methyl group may be responsible for the difference between the reactions of *cis,trans*-I

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(25) Although extensive studies have been made of the sterochemistry of such Grignard additions and related reactions, particularly in acyclic systems [see D. J. Cram and K. R. Kopecky, THIS JOURNAL, **81**, 2748 (1959), for references] the detailed mechanisms of such reactions are unknown.

(26) C. D. Nenitzescu and I. G. Gavat, *Ann.*, **519**, 260 (1933).

(27) (a) W. G. Dauben and K. S. Pitzer, "Steric Effects in Organic Chemistry," Edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 36. (b) S. F. Birch and R. A. Dean, *J. Chem. Soc.*, 2477 (1953).

TABLE II

Relative positions of bromine and hydroxyl and preferred position of bromine	Prediction from simple steric considerations	Reaction	Principal reaction	
			Found (1)	Found (11)
trans-Axial (*trans,cis*-1 and 11)	Epoxide	OH⁻	Epoxide	....
	Epoxide	Ag$_2$O	Epoxide	....
trans-Equatorial (*trans,trans*-1 and 11)	Ring contrtn.	OH⁻	Epoxide	Epoxide
	Ring contrtn.	Ag$_2$O	Epoxide	Ring contrtn.
cis-Axial (*cis,trans*-1 and 11)	Cyclohexanone	OH⁻	Cyclohex.	Ring contrtn.
	Cyclohexanone	Ag$_2$O	Cyclohex.	Cyclohex.
cis-Equatorial (*cis,cis*-1 and 11)	Ring contrtn.	OH⁻	Cyclohex.	Ring contrtn.
	Ring contrtn.	Ag$_2$O	Cyclohex.	Ring contrtn.

and II with hydroxyl ion, but the reaction of *cis,-trans*-II requires further investigation before any final conclusion can be reached.

Experimental[28]

4-Phenylcyclohexanone was prepared by the method of Ungnade.[21] The m.p. after recrystallization from petroleum ether was 78.5–79.5° and the oxime[21] had m.p. 114–115°.

4-Phenylcyclohexanone 2,4-dinitrophenylhydrazone after recrystallization from ethanol–ethyl acetate had m.p. 194–194.5°.

Anal. Calcd. for $C_{18}H_{18}N_4O_4$: C, 61.0; H, 5.1. Found: C, 61.1; H, 4.9.

cis- **and** ***trans*-4-Phenylcyclohexanol** prepared by the method of Ungnade[21] had m.p. 76–77° and 119.5–120.5°, respectively.

***trans*-2-Bromo-4-phenylcyclohexanone** (*trans*-III).—To a solution of 30.0 g. (0.172 mole) of 4-phenylcyclohexanone in 700 ml. of absolute ether in an ice–salt-bath was added 27.5 g. (0.172 mole) of bromine in 30 ml. of chloroform with vigorous stirring over a period of 1 hr. From the solution 8.2 g. of solid, m.p. 112–114°, separated and was filtered. Removal of the filtrate gave 34 g. of solid, m.p. 100–109°. Recrystallization of the first fraction from petroleum ether gave 6.9 g. of *trans*-III as colorless leaflets, m.p. 115–116°. Three recrystallizations of the second fraction from petroleum ether gave 20 g. of crystals, m.p. 115–116°, λ_{max} 308 mμ, ϵ 100. The total yield was thus 60%.

Anal. Calcd. for $C_{12}H_{13}BrO$: C, 56.9; H, 5.2; Br, 31.6. Found: C, 57.0; H, 5.1; Br, 31.3.

5-Phenylcyclohexan-2-one-1-carboxylic Acid.—To sodium amide prepared by adding 9.0 g. (0.39 mole) of sodium to 500 ml. of liquid ammonia containing a few crystals of iron-(III) nitrate 9-hydrate was added 40 g. (0.23 mole) of 4-phenylcyclohexanone in 400 ml. of absolute ether over a period of 20 min. After removal of the ammonia by evaporation the mixture was poured onto 500 g. of solid carbon dioxide. Extraction with water followed by acidification of the sodium salt and extraction with ether gave, after drying of the ether layer and evaporation of the ether under reduced pressure, 27 g. (54%, 90% based on unrecovered starting material) of 5-phenylcyclohexan-2-one-1-carboxylic acid, m.p. 103° dec. Evaporation of the ether layer after the first aqueous extraction gave 16 g. of starting material, m.p. 74–76°. The β-keto acid was used without further purification for the preparation of the bromo ketone *cis*-III. It was purified for analysis by recrystallization from petroleum ether after which it had m.p. 110° dec. It was relatively stable at 0° but decomposed to 4-phenylcyclohexanone and carbon dioxide on standing for 1 wk. at room temperature.

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.5; H, 6.5. Found: C, 71.8; H, 6.7.

***cis*-2-Bromo-4-phenylcyclohexanone** (*cis*-III).—To a solution of 25.0 g. (0.114 mole) of crude 5-phenylcyclohexan-2-one-1-carboxylic acid in 50 ml. of dioxane and 50 ml. of water containing 18.9 g. (0.230 mole) of sodium acetate was added 18.4 g. (0.115 mole) of bromine in 200 ml. of 5% aqueous potassium bromide over a period of 1 hr. with rapid stirring. The bromine solution decolorized slowly near the end of the addition and bromine was then added only as fast as it reacted. The mixture was warmed to 50° for 15 min. and cooled and extracted with ether. The ether solution was dried over sodium sulfate and the ether distilled under reduced pressure to give 29 g. of colorless oil. Treatment with 300 ml. of petroleum ether and 40 ml. of ether and cooling to −5° gave 13 g. of crystals, m.p. 74–76°, which were filtered. Evaporation of the filtrate to a volume of 100 ml. and cooling to −5° gave an additional 2.5 g. of *cis*-III, m.p. 62–72°. The two fractions were combined and recrystallized from petroleum ether to give 12 g. (41%) of *cis*-III, m.p. 76–77°, λ_{max} 230 mμ, ϵ 20.

Anal. Calcd. for $C_{12}H_{13}BrO$: C, 56.9; H, 5.2; Br, 31.6. Found: C, 57.0; H, 5.3; Br, 31.6.

2^c-Bromo-4^t-phenylcyclohexanol (*cis,trans*-I). **Method A.**—A solution of 10 g. (0.040 mole) of the bromo ketone *trans*-III in 320 ml. of absolute ether was added over a period of 45 min. to a solution of isobutylmagnesium bromide prepared from 11 g. (0.080 mole) of isobutyl bromide and 1.9 g. (0.080 mole) of magnesium in 40 ml. of ether. After 2 hr. at 0° saturated aqueous ammonium chloride was added. The ether layer was separated and the ether evaporated to give 9.1 g. of colorless oil which crystallized on standing. Recrystallization from 125 ml. of hexane after decolorization with activated charcoal gave 6.1 g. (60%) of the bromohydrin *cis,trans*-I, m.p. 90–91.5°. Recrystallization from hexane gave 5.5 g., m.p. 91–92°.

Concentration of the first filtrate and chromatography on acid-washed alumina gave 0.30 g. of additional *cis,trans*-I, a small amount of 4-phenylcyclohexanone and some oil fractions which failed to crystallize. None of the stereoisomeric *trans,cis*-I was found.

Anal. Calcd. for $C_{12}H_{15}BrO$: C, 56.5; H, 5.9; Br, 31.3. Found: C, 56.4; H, 6.1; Br, 31.1.

***cis,trans*-I-Benzoate**, prepared by treatment of the bromohydrin with benzoyl chloride in pyridine and recrystallization from hexane, had m.p. 129–129.5°.

Anal. Calcd. for $C_{19}H_{19}BrO_2$: C, 63.5; H, 5.3; Br, 22.3. Found: C, 63.9; H, 5.5; Br, 22.3.

Method B.—A solution of 0.50 g. (0.0020 mole) of *trans*-III in 20 ml. of absolute ether was added dropwise to a stirred suspension of 0.050 g. of lithium aluminum hydride in 5 ml. of absolute ether. After 15 min. at room temperature the mixture was hydrolyzed, the ether layer separated and dried and the ether removed to give 0.42 g. (83%) of colorless solid, m.p. 75–84°. Recrystallization from petroleum ether gave *cis,trans*-I, m.p. 89–90°. The m.p. of a mixture with a sample prepared by method A was 91–92°.

Oxidation of *cis,trans*-I.—A solution of 0.40 g. (0.0016 mole) of *cis,trans*-I in 10 ml. of glacial acetic acid was added to 1.2 g. of sodium chromate tetrahydrate in 80 ml. of water and 80 ml. of concentrated sulfuric acid at 0.° After 8 min. the mixture was extracted with hexane. The hexane solution was dried over sodium sulfate and the hexane distilled to give 0.36 g. of colorless solid, m.p. 106–110°. Two recrystallizations from petroleum ether gave 0.16 g. of colorless bromoketone *trans*-III, m.p. and mixed m.p. 114.5–115°.

2^t-Bromo-4^t-phenylcyclohexanol (*trans,trans*-I) **and 2^c-Bromo-4^c-phenylcyclohexanol** (*cis,cis*-I). **Method A.**—To a stirred suspension of 0.50 g. of lithium aluminum hydride in 65 ml. of ether was added over a period of 20 min. 9.0 g. (0.036 mole) of *cis*-bromoketone *cis*-III. After 1 hr. the excess hydride was decomposed with wet ether and the ether

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[28] All melting points are corrected. Microanalyses were performed by Mr. Josef Nemeth, Mrs. Esther Fett, Mrs. Lucy Chang, Mr. Rollo Nesset, Mrs. Maria Benassi, Mrs. Ruby Kung-yu Ju and Mrs. Alice Terra. Infrared spectra were obtained by Miss Helen Miklas, Mr. James Brader and Mrs. Louise Griffing with a model 21 Perkin–Elmer double beam spectrophotometer employing 8% carbon tetrachloride solutions in 0.1-mm. matched cells unless otherwise specified. Ultraviolet spectra were obtained by Miss Gerardine Meerman with a Cary model 11 double beam spectrophotometer employing 0.01 molar solutions in a solvent prepared by diluting 1 volume of chloroform to 5 volumes with 95% ethanol. Most of the spectra are reproduced in the thesis of R.J.H.[1] available from Univ. Microfilms [Pub. No. 19829], Ann Arbor, Mich. Infrared frequencies reported here have been corrected using data from calibration curves obtained with water vapor, carbon dioxide, ammonia vapor and polystyrene. The corrections of carbonyl stretching frequencies amounted to 0–1 cm.$^{-1}$; corrections of the hydroxyl frequencies in the region around 1000 cm.$^{-1}$ amounted to 1–8 cm.$^{-1}$.

layer extracted from water and dried over sodium sulfate. Distillation of the ether gave 8.9 g. of colorless oil which was chromatographed on a column 3.1 × 33 cm. containing 270 g. of acid-washed alumina. After elution with 400 ml. of benzene–hexane (1:1) which gave 0.01 g. of an oil, elution with 600 ml. of benzene–hexane (5:1) gave 1.78 g. (20%) of *cis,cis*-I as an oil, $n^{20}D$ 1.5745. The infrared spectrum indicated the presence of a carbonyl compound which could not be removed by further chromatography on acid-washed alumina. If the carbonyl compound is assumed to be 4-phenylcyclohexanone the infrared indicated that it was present to the extent of about 3%. This agrees with the value calculated from the carbon analysis (2.3%) and from the bromine analysis (2.3%). Attempts to crystallize the bromohydrin failed as did attempts to prepare a crystalline benzoate with benzoyl chloride and pyridine.

Anal. Calcd. for $C_{12}H_{15}BrO$: C, 56.5; H, 5.9; Br, 31.3. Found: C, 57.1; H, 6.1; Br, 30.6.

In continuing the chromatography, elution with 20 ml. of benzene–hexane gave 0.94 g. of an intermediate oily solid after which 800 ml. of benzene–hexane, 200 ml. of benzene and 400 ml. of benzene–ether (1:1) gave 5.8 g. (64%) of *trans-trans*-I, m.p. 50.5–52°. Rercystallization from petroleum ether gave long needles, m.p. 51.5–53.5°.

Anal. Calcd. for $C_{12}H_{15}BrO$: C, 56.5; H, 5.9; Br, 31.3. Found: C, 56.6; H, 6.2; Br, 31.2.

***trans,trans*-I-Benzoate**, prepared from benzoyl chloride and pyridine and recrystallized from hexane, had m.p. 135–135.5°.

Anal. Calcd. for $C_{19}H_{19}BrO_2$: C, 63.5; H, 5.3; Br, 22.3. Found: C, 63.7; H, 5.4; Br, 22.3.

Method B.—To isobutylmagnesium bromide prepared from 0.49 g. (0.020 mole) of magnesium and 2.7 g. (0.020 mole) of isobutyl bromide at 0° was added 2.5 g. (0.010 mole) of bromo ketone *cis*-III in 60 ml. of ether at a rate of 4 drops per second. After 2 hours at 0° hydrolysis and removal of the ether gave 2.5 g. of oil which was chromatographed on 150 g. of acid-washed alumina. After preliminary elution with hexane and benzene, 80 ml. of benzene–ether (9:1) gave 0.54 g. of unidentified oil, after which benzene–ether (5:1) gave 0.87 g. (35%) of somewhat impure *cis,cis*-I. The infrared spectrum was identical with the sample prepared in method A except that instead of the absorption at 1725 there were two weak bands at 1700 and 1720 cm.$^{-1}$. After an intermediate cut obtained by elution with 80 ml. of benzene–ether (2:1), there was obtained with 80 ml. more of the same eluent and then 320 ml. of benzene–ether (1:1) 0.52 g. (21%) of impure *trans,trans*-I, of which the main fraction (0.35 g.) had m.p. 49.5–51.5°.

Oxidation of *trans,trans*-I.—To a solution of 0.30 g. of sodium chromate tetrahydrate in 20 ml. of concentrated sulfuric acid and 20 ml. of water was added 0.14 g. of *trans,trans*-I in 6 ml. of glacial acetic acid at 0°. After 10 min. the mixture was extracted with hexane, which after drying was removed by distillation under reduced pressure to give 0.11 g. of yellow oil. Attempts to induce crystallization of the *cis*-bromo ketone *cis*-III were unsuccessful. The oil had intense carbonyl absorption at 1733 cm.$^{-1}$ characteristic of the *cis*-ketone, however.

Epoxidation of 4-Phenylcyclohexene. Mixture of *cis*- and *trans*-VI.—To 9.6 g. (0.061 mole) of 4-phenylcyclohexene[29] in 45 ml. of chloroform at 0° was added 180 ml. of a cold chloroform solution of 8.4 g. (0.061 mole) of perbenzoic acid. After 66 hr. at 0° titration showed that 99.5% of the peracid had been consumed. The solution was then extracted successively with sodium carbonate, potassium iodide and sodium thiosulfate solutions and, after drying, the solvent was removed under reduced pressure to give 10 g. of colorless oil. Distillation through a micro spinning band column gave after a forerun (0.67 g., b.p. 76–112° at 2.8 mm., $n^{20}D$ 1.5459), four main fractions (7.7 g., 73%, b.p. 112–113° at 2.8 mm., $n^{20}D$ 1.5450–1.5452) of the mixture of *cis*- and *trans*-VI. Hopff and Hoffmann[15] reported b.p. 99–101° at 0.3 mm. The infrared spectrum differed from that of *trans*-VI described below in having bands at 998 and 921 cm.$^{-1}$ which are absent in the spectrum of the latter.

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.7; H, 8.1. Found: C, 82.6; H, 8.2.

Attempted chromatographic separation of the epoxides (0.68 g.) on basic alumina (Merck, reagent grade) led to only about 10% recovery by elution with benzene–ether (19:1). Elution with methanol gave 0.5 g. of a crude diol which after recrystallization from hexane and then from carbon tetrachloride had m.p. 125–125.5°.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.0; H, 8.4. Found: C, 74.7; H, 8.5.

Reaction of the Mixture of Epoxides *cis*- and *trans*-VI with Hydrobromic Acid. 2^{t}-Bromo-4^{c}-phenylcyclohexanol (*trans,cis*-I) **and 2^{t}-Bromo-5^{t}-phenylcyclohexanol** (*trans,trans*-VII).—To 2.06 g. (0.0117 mole) of the mixture of epoxides VI in 15 ml. of ether at 0° was added dropwise over 10 min. 5 ml. of 48% hydrobromic acid. The homogeneous solution was allowed to warm to room temperature over a period of 3 hr. during which time two colorless layers formed. The mixture was then brought to *p*H 7 with 5% sodium bicarbonate solution, the organic layer was removed, and after drying over sodium sulfate the solvent was distilled under reduced pressure to give 3.0 g. (99%) of nearly colorless bromohydrins which crystallized on standing at 0°. This mixture, m.p. 54–68°, was used without further purification for the reactions with potassium hydroxide in isopropyl alcohol and silver oxide in hexane.

When 1.0 g. of the epoxide mixture was converted to the bromohydrins as above and the product fractionally crystallized from ether–petroleum ether and petroleum ether there was obtained 0.25 g. of *trans,trans*-VII, m.p. 86–87°; 0.02 g. of *trans,cis*-I, m.p. 69–70°; and opaque prisms, m.p. 56–57°, which proved to be a mixture of the two bromohydrins.

Anal. Calcd. for $C_{12}H_{15}BrO$: C, 56.5; H, 5.9; Br, 31.3. Found for VII: C, 56.5; H, 5.9; Br, 31.0. Found for I: C, 56.4; H, 5.9; Br, 31.4.

As part of the demonstration that the epoxide VI was a mixture, 1.1 g. of epoxide mixture was separated into three fractions by crystallization from petroleum ether at −80°. The first and third fractions were then treated with 48% hydrobromic acid as described above. It was seen from the infrared spectrum that the bromohydrin mixture from the less soluble epoxide fraction was richer in *trans,trans*-VII as shown by the greater intensity of a characteristic absorption at 976 cm.$^{-1}$ relative to the absorption at 998 cm.$^{-1}$ due to *trans,cis*-I. Conversely the more soluble epoxide fraction gave bromohydrin richer in *trans,cis*-I as shown by the relative infrared absorption intensities.

2^{c}-Bromo 1-methyl-4^{t}-phenylcyclohexanol (*cis-trans*-II).—To a solution of methylmagnesium iodide prepared from 5.0 g. (0.035 mole) of methyl iodide in 50 ml. of absolute ether and 0.73 g. (0.030 mole) of magnesium under nitrogen was added 5.1 g. (0.020 mole) of *trans*-bromo ketone *trans*-III in 160 ml. of ether over 1 hr. Addition of aqueous ammonium chloride, separation of the ether layer and distillation of the ether under reduced pressure gave a pale yellow oil which crystallized from ether–petroleum ether solution when cooled in an acetone–dry Ice-bath. The first fraction, 4.3 g., m.p. 91–92°, and the second fraction, 0.41 g., m.p. 87–90°, were combined and recrystallized from petroleum ether to give 3.2 g. of *cis,trans*-II, m.p. 92.5–93°. Concentration of the filtrate gave an additional 0.54 g., m.p. 92–93°, or a total yield of 69%. Further recrystallization from hexane failed to raise the m.p.

Anal. Calcd. for $C_{13}H_{17}BrO$: C, 58.0; H, 6.4; Br, 29.7. Found: C, 58.3; H, 6.4; Br, 29.9.

2^{c}-Bromo-1-methyl-4^{c}-phenylcyclohexanol and **2^{t}-Bromo-1-methyl-4^{t}-phenylcyclohexanol** (*cis,cis*-II and *trans,trans*-II).—To a solution of methylmagnesium iodide prepared from 7.0 g. (0.049 mole) of methyl iodide and 1.2 g. (0.049 mole) of magnesium in 50 ml. of absolute ether was added 10 g. (0.040 mole) of bromo ketone *cis*-III in 160 ml. of absolute ether over 30 min. Treatment of the mixture with aqueous ammonium chloride, washing with aqueous sodium thiosulfate and with water and drying over sodium sulfate gave, after distillation of the solvent under reduced pressure, 9.3 g. of yellow oil. This mixture was quite unstable as indicated by the fact that it turned red on standing even at room temperature for 30 min. It was immediately chromatographed on a 3.1 × 33 cm. column containing 270 g. of acid-washed Merck reagent-grade alumina. Elution with 400 ml. of hexane gave only 0.01 g. of unidentified oil. Elution with 2600 ml. of benzene–hexane (1:1) gave 5.6 g. (53%) of *cis,cis*-II. The middle cuts obtained with 800 ml.

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[29] K. Alder and H. F. Rickert, *Ber.*, **71**, 379 (1938).

of eluent were analyzed (n^{20}_{D} 1.5684) and employed for the rearrangement studies. Although the carbon, hydrogen and bromine analyses were correct, the infrared spectrum indicated that a small amount (about 5%) of a carbonyl compunod (absorption 1715 cm.$^{-1}$) was present both in the crude product before chromatography and after purification. It seems likely that this is due to the rearrangement product, the acetylcyclopentane X.

Anal. Calcd. for $C_{13}H_{17}BrO$: C, 58.0; H, 6.4; Br, 29.7. Found: C, 57.8; H, 6.3; Br, 29.6.

Further elution with 1 l. of benzene–hexane (4:1) and then with 800 ml. of benzene gave 1.2 g. of oily solid as an intermediate fraction which gave a 2,4-dinitrophenylhydrazone, m.p. 182°, but was not further investigated. Finally, elution with 1 l. of benzene and 1 l. of benzene–ether (8:1) gave 1.9 g. of *trans,trans*-II, which after trituration with ether–petroleum ether amounted to 1.7 g., m.p. 80–93°. Recrystallization twice from petroleum ether gave 0.71 g. of *trans,trans*-II, m.p. 97–98°. Further recrystallization of a sample for analysis raised the m.p. to 98.5–99°.

Anal. Calcd. for $C_{13}H_{17}BrO$: C, 58.0; H, 6.4. Found: C, 58.3; H, 6.5.

Hydrogenolysis of the Bromohydrins.—All of the *cis*-bromohydrins and the single isomer, *trans,trans*-I, of the *trans* series were subjected to hydrogenolysis conditions similar to those of Fieser and Huang[30] for the removal of bromine in α-bromosterols. In each case 0.20 g. of palladium chloride on Darco in 10 ml. of ethanol was shaken for 15 min. at 25° under 20 p.s.i. of hydrogen. The bromohydrin in 10 ml. of 95% ethanol and 0.25 g. of potassium hydroxide in 5 ml. of 95% ethanol were added and the mixture was shaken for 40 min. at 25° under 20 p.s.i. of hydrogen. The catalyst was filtered off immediately and the filtrate treated with 0.6 ml. of concentrated hydrochloric acid in 1 ml. of water. Removal of the solvent under reduced pressure and addition of water was followed by extraction of the organic product with ether. After drying of the ether layer the solvent was removed under reduced pressure to leave the product which was treated as described below in each case.

A. *cis-trans*-I.—From 0.30 g. (0.0012 mole) of *cis,trans*-I was obtained 0.20 g. of pale yellow solid, m.p. 106–112°. Recrystallization from hexane afforded 0.15 g. (73%) of *trans*-4-phenylcyclohexanol, m.p. and mixed m.p. with an authentic sample, 119–120°.

B. *trans,trans*-I.—From 0.30 g. (0.0012 mole) of bromohyrin was obtained 0.19 g. of pale yellow solid, m.p. 97–112°. Recrystallization from hexane gave 0.076 g. (37%) of colorless leaflets, m.p. and mixed m.p. with authentic *trans*-4-phenylcyclohexanol, 119–120°.

C. *cis,cis*-I.—From 0.27 g. (0.0010 mole) of bromohydrin was obtained 0.18 g. (97%) of pale yellow solid, m.p. 70–75°. Comparison of the infrared spectrum with that of *cis*-4-phenylcyclohexanol at five frequencies indicated that *cis*-4-phenylcyclohexanol was present to the extent of 95 ± 3%. Recrystallization from petroleum ether gave 0.12 g. of colorless *cis*-4-phenylcyclohexanol, m.p. and mixed m.p. with an authentic sample, 76–77°.

D. *cis,trans*-II. **1-Methyl-*trans*-4-phenylcyclohexanol.**—From 0.40 g. (0.0015 mole) of the bromohydrin was obtained 0.28 g. (99%) of pale yellow solid, m.p. 102–103°. Comparison of the infrared spectrum at six frequencies with that of the substance purified as described below indicated that 95 ± 1% of 1-methyl-*trans*-4-phenylcyclohexanol was present. Recrystallization from hexane gave 0.20 g., m.p. 103–105°. Further recrystallization failed to raise the m.p.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 82.1; E, 9.5.

E. *cis,cis*-II. **1-Methyl-*cis*-4-phenylcyclohexanol.**—From 0.43 g. (0.0016 mole) of bromohydrin was obtained 0.29 g. (95%) of pale yellow solid, m.p. 67–70°. Comparison of the infrared spectrum at six frequencies with that of the purified 1-methyl-*cis*-4-phenylcyclohexanol gave a value of 100 ± 1% of this alcohol present. Recrystallization from petroleum ether gave 0.17 g. of cotton-like crystals, m.p. 71–72°. Further recrystallization failed to raise the m.p.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 82.0; H, 9.3.

Reactions of the Bromohydrins I and II with Potassium Hydroxide in Isopropyl Alcohol.—In each case the bromohydrin was heated with potassium hydroxide in isopropyl alcohol (concentration 5.0 g./100 ml. of solvent unless otherwise specified) under purified nitrogen for the time indicated and then poured into aqueous acid, extracted with diethyl ether and the ether solution washed with aqueous 5% sodium carbonate and with water and dried over sodium sulfate. Removal of the solvent left the product described below in each case. Weights of product at various stages of purification are corrected throughout for samples withdrawn for spectral studies.

A. *cis,trans*-I.—The reaction of 0.50 g. (0.0020 mole) of bromohydrin in 5 ml. of isopropyl alcohol with 10 ml. of potassium hydroxide solution gave a precipitate of potassium bromide immediately after which the reaction was completed by heating at 55° for 70 min. The solid obtained (0.32 g., 94%) had m.p. 66–72° and a comparison of the infrared spectrum at 1166 and 1330 cm.$^{-1}$ with the spectrum of 4-phenylcyclohexanone indicated that there was present 82 ± 1% of this ketone. Treatment with 2,4-dinitrophenylhydrazine gave after recrystallization of the hydrazone from ethyl acetate–ethanol (2:1) 0.48 g. (74%) of orange 4-phenylcyclohexanone 2,4-dinitrophenylhydrazone, m.p. 191–192.5°; mixed m.p. with an authentic sample, 193–194°. Acidification of the sodium carbonate extracts gave only 4 mg. of yellow oil which was not further investigated.

B. *trans,trans*-I. ***trans*-4-Phenylcyclohexene Oxide (*trans*-VI).**—A solution of 0.50 g. (0.0020 mole) of bromohydrin in 5 ml. of isopropyl alcohol added to 10 ml. of potassium hydroxide solution gave an immediate precipitate of potassium bromide but was heated at 55° for 70 min. to complete reaction. The product (0.31 g., 91%) was a colorless oil giving a negative Beilstein test for halogen. On standing for 12 hr. at 0° it crystallized to give the epoxide *trans*-VI, m.p. 33.5–34.5°. Recrystallization from pentane (Dry Ice–acetone-bath) did not change the m.p. No acidic reaction product was obtained.

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.7; H, 8.1. Found: C, 82.4; H, 8.5.

C. *cis,cis*-I.—When 0.20 g. (0.00078 mole) of *cis,cis*-I shown by its infrared spectrum to contain about 5% of a carbonyl compound, probably 4-phenylcyclohexanone, in 2 ml. of isopropyl alcohol was added to potassium hydroxide in isopropyl alcohol (0.22 g., 4 ml.) potassium bromide precipitated after about 15 sec. After 70 min. at 55° there was obtained a neutral fraction of 0.12 g. (88%) with a negative Beilstein test. Calculations based on the absorption at 1165 and 1330 cm.$^{-1}$ indicated that there was present 74% of 4-phenylcyclohexanone. Treatment with 2,4-dinitrophenylhydrazine gave 0.19 g. (75%) of 4-phenylcyclohexanone dinitrophenylhydrazone, m.p. 188–190°. Recrystallization from ethanol–ethyl acetate gave 0.15 g. (60%) of yellow-orange leaflets, m.p. 192.5–193.5°. A m.p. of a mixture with an authentic sample was 193.5–194.5.° Acidification of the basic extracts gave only 11 mg. of an orange oil which was not further investigated.

D. Mixture of *trans,cis*-I and *trans,trans*-VII.—When 0.51 g. (0.0020 mole) of the bromohydrin mixture in 5 ml. of isopropyl alcohol was added to 10 ml. of potassium hydroxide solution, potassium bromide precipitated immediately. After 70 min. at 55° was obtained 0.32 g. (92%) of nearly colorless oil, n^{20}_{D} 1.5453, which gave a negative Beilstein test for halogen. The absorbancies at 855, 904, 952, 980 and 998 cm.$^{-1}$ in the infrared had values of 102, 100, 102, 102 and 101% of the absorbancies of the corresponding bands in the mixture of epoxides *cis*- and *trans*-VI from which the bromohydrins had been prepared. No acidic fraction was obtained.

E. *cis,trans*-II.—When 0.53 g. (0.0020 mole) of bromohydrin in 7 ml. of isopropyl alcohol was heated in a bath at 53° with potassium hydroxide in isopropyl alcohol (0.5 g., 13 ml.) a precipitate of potassium bromide was visible after 3 min. After 2 hr. was obtained 0.34 g. (91%) of pale yellow oil, n^{20}_{D} 1.5318, which possessed the characteristic odor of 1-acetyl-3-phenylcyclopentane (X) and gave a negative Beilstein test. Comparison of the infrared absorption at 1180 and 1365 cm.$^{-1}$ with the corresponding bands of X prepared by the method of Nenitzescu and Gavat[22] indicated that there was present 79± 1% of X (presumably chiefly if not entirely *trans*). The ratio of the absorbance at 1180 cm.$^{-1}$ to that at 1365 cm.$^{-1}$ was 0.80. Treatment of the

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(30) L. F. Fieser and Wei-Yuan Huang, THIS JOURNAL, **75**, 4837 (1953).

product with semicarbazide gave *trans*-X semicarbazone (0.42 g., m.p. 163–163.5°) which when recrystallized twice from 67% ethanol and once from absolute ethanol had m.p. 171.5–172.5°. A mixed m.p. with the semicarbazone described below had m.p. 172–173°.

F. *cis,cis*-II.—When a solution in 7 ml. of isopropyl alcohol of 0.45 g. of slightly impure bromohydrin, estimated as indicated in the description of its preparation to contain 0.43 g. (0.0016 mole) of *cis,cis*-II, was mixed with potassium hydroxide in isopropyl alcohol (0.5 g., 13 ml.) potassium bromide precipitated after 45 sec. at room temperature. After 2 hr. at 53° was obtained 0.29 g. (92% after correction for the 5% of non-bromine-containing impurity in the starting material) of a pale yellow oil, n^{20}D 1.5316, with the distinctive odor of the acetylcylopentane X and which gave a negative Beilstein test. Comparison of the absorbancies at 1180 and 1365 cm.$^{-1}$ with those of the sample prepared by the method of Nenitzescu and Gavat[26] indicated that there was present 85 ± 1% of this ketone. The ratio of the absorbancies at 1180 and 1365 cm.$^{-1}$ was 0.80. Treatment of the product with semicarbazide gave 0.34 g. (88%) of *trans*-X semicarbazone, m.p. 172.5–173.5°.

G. *trans,trans*-II.—When 0.27 g. (0.0010 mole) of the bromohydrin in 3.5 g. of isopropyl alcohol was mixed with potassium hydroxide in isopropyl alcohol (0.27 g., 6.5 ml.) potassium bromide precipitated immediately. After 2 hr. at 53° there was obtained 0.18 g. (96%) of pale yellow oil, n^{20}D 1.5297, which gave a negative Beilstein test for halogen and lacked the characteristic odor of the acetylcyclopentane X. The infrared spectrum showed no absorption in the O–H stretching region nor in the carbonyl region. When 0.13 g. of the product in 10 ml. of absolute ether was treated with 0.06 g. of lithium aluminum hydride suspended in ether for 1.5 hr. at room temperature, there was obtained by the extraction procedure described at the beginning of this section of the Experimental part 0.12 g. of colorless oil of which the infrared spectrum indicated the reaction had not gone to completion. Therefore, 0.10 g. was treated with 0.06 g. of lithium aluminum hydride in ether for 4 hr. at room temperature to give 0.088 g. of colorless oil, n^{25}D 1.5350, an alcohol, as shown by absorption in the O–H region of the infrared spectrum. The infrared spectrum further excluded the presence of either *cis*- or *trans*-4-phenylcyclohexanol in appreciable quantities and the presence of absorption at 992 and its absence at 1050 cm.$^{-1}$ suggested that the product was largely an axial secondary alcohol, probably 2^c-methyl-5^t-phenylcyclohexanol.

Reaction of the Bromohydrins I and II with Silver Oxide in Hexane.—The method was that used by Curtin and Schmukler[3b] with *cis*-2-chloro-1-phenylcyclohexanol. The silver oxide was freshly prepared for each reaction as illustrated by the following description. To 2.0 g. of silver nitrate in 20 ml. of water was added with stirring 0.72 g. of potassium hydroxide in 20 ml. of water. After decantation of the supernatant liquid the oxide was washed successively by decantation with ten portions of water. The oxide was then filtered and washed with water, acetone and ether. After a short period of air-drying it was used immediately. The reaction with the bromohydrin was carried out under nitrogen in an oil-bath at 73°. When reaction was completed the silver salts were filtered and washed with hexane. The filtrate was then shaken with anhydrous sodium sulfate to remove traces of finely divided silver salts and the solvent removed under reduced pressure to give the residue described in each case.

A. *cis,trans*-I.—The reaction of 0.50 g. (0.0020 mole) of bromohydrin in 50 ml. of hexane with 1.1 g. of silver oxide was carried out for 9 min. to give 0.34 g. (100%) of 4-phenylcyclohexanone, m.p. 78–78.5°, and giving a negative Beilstein test for halogen. The mixed m.p. with an authentic sample was 78.5–79°. Absorbancies at 1165 and 1330 cm.$^{-1}$ in the infrared spectrum when compared with the spectrum of the authentic ketone indicated that 100 ± 1% of the ketone was present.

B. *trans,trans*-I. cis(?)-**3-Phenylcyclopentanecarboxaldehyde** (*cis*-VIII).—Reaction of 0.39 g. (0.0015 mole) of bromohydrin with 0.88 g. of silver oxide in 40 ml. of hexane was carried out for 9 min. to give 0.25 g. (94%) of nearly colorless oil, n^{20}D 1.5380, which gave a negative Beilstein test for halogen. Since preliminary work showed that the product had undergone extensive autoxidation when stored at 0° for 48 hr. and then at room temperature for 5 hr., it was in subsequent reactions immediately stored in a sealed vial in a Dry Ice–acetone-bath. Under these conditions the infrared spectrum indicated the absence of *trans*-4-phenylcyclohexene oxide (no absorption at 855 cm.$^{-1}$) and 4-phenylcyclohexanone (no absorption at 1165 nor 1427 cm.$^{-1}$). There was absorption at 1725, 2600 and 2700 cm.$^{-1}$ characteristic of an aldehyde. Treatment with semicarbazide hydrochloride gave a 72% yield of *cis*(?)-VIII **semicarbazone**, m.p. 110–113°. Recrystallization from 25% ethanol brought the m.p. to 114.5–115.5°.

Anal. Calcd. for $C_{13}H_{17}N_3O$: C, 67.5; H, 7.4; N, 18.2. Found: C, 67.5; H, 7.2; N, 17.7.

In another run was obtained 0.40 g. (93%) of the oil, n^{20}D 1.5380, which when treated with 2,4-dinitrophenylhydrazine gave 0.77 g. (94%) of *cis*(?)-VIII **2,4-dinitrophenylhydrazone**, m.p. 86°. Recrystallization from ethanol–ethyl acetate gave 0.63 g. (77%) of yellow-orange lustrous leaflets, m.p. 94–96°. Further recrystallization from 95% ethanol gave 0.566 g. of yellow-orange microcrystals, m.p. 120–121° with previous shrinkage. Recrystallization from methanol–ethyl acetate gave yellow-orange leaflets, m.p. 98.5° with resolidification and remelting at 119.5–120.5°.

Anal. Calcd. for $C_{18}H_{18}N_4O_4$: C, 61.0; H, 5.1; N, 15.8. Found: C, 61.1; H, 5.1; N, 15.4.

C. *cis,cis*-I.—Reaction of 0.41 g. (0.0016 mole) of the bromohydrin (slightly impure as described in its synthesis) and 0.88 g. of silver oxide in 40 ml. of hexane was carried out for 9 min. to give 0.27 g. (97% after correction for the non-bromine-containing impurity in the starting material) of oily crystals giving a negative Beilstein test for halogen and estimated by infrared examination (bands at 1165 and 1330 cm.$^{-1}$) to contain 75 ± 1% of 4-phenylcyclohexanone. Absorption in the 2900–3200 cm.$^{-1}$ region and a shoulder at 1705 cm.$^{-1}$ suggested that a carboxylic acid was present as an impurity, but attempts to extract such an acid from an ether solution of the products with 5% sodium bicarbonate of 5% sodium hydroxide failed. Treatment with 2,4-dinitrophenylhydrazine gave 0.42 g. (75%) of yellow dinitrophenylhydrazone, m.p. 184–190°, which after recrystallization from ethanol–ethyl acetate amounted to 0.33 g., m.p. 192.5–193.5°. A mixed m.p. with authentic dinitrophenylhydrazone showed no depression.

D. *trans,cis*-I **and** *trans,trans*-VII.—The reaction of 0.50 g. (0.0020 mole) of the mixture of bromohydrins described above and 1.1 g. of silver oxide in 50 ml. of hexane was carried out for 9 min. to give 0.32 g. (94%) of pale yellow oil, n^{20}D 1.5455, giving a negative Beilstein test for halogen. The infrared spectrum differed only slightly from that of the mixture of epoxides from which the bromohydrin mixture had been prepared. Slight absorption at 1725 cm.$^{-1}$ suggested that about 3% of an aldehyde was present. Intensities of the absorption maxima at 855, 904, 952, 980 and 998 cm.$^{-1}$ had values which were 95, 98, 98, 100 and 96% of those in the original epoxide mixture. No increase in the carbonyl band was observed when the reaction was carried out for 36 min. instead of 9.

E. *cis,trans*-II.—The reaction of 0.55 g. (0.0020 mole) of bromohydrin with 1.1 g. of silver oxide in 50 ml. of hexane was carried out for 6 hr. to give 0.38 g. (98%) of colorless oil, n^{20}D 1.5346, which lacked the distinctive odor of the acetylcyclopentane X and gave a negative Beilstein test for halogen. The product crystallized on standing at 0°, but remelted on warming to room temperature. The infrared spectrum excludes the presence of more than a few per cent. of the cyclopentane X. Treatment with semicarbazide gave in 95% yield a semicarbazone, m.p. (dec.) 200.5°, identical with that obtained from the methylation of 4-phenylcyclohexanone as described below. Recrystallization from dilute ethanol brought the m.p. to 202° dec. The mixed m.p. with the sample prepared as described below showed no change. A reaction carried out for 24 hr. gave similar results. A middle fraction from chromatography of the product on alumina, eluting with benzene–hexane (1:1), had an infrared spectrum essentially identical with that of the product before chromatography.

F. *cis,cis*-II.—The reaction of 0.61 g. of the somewhat impure bromohydrin described above (estimated to contain 0.58 g. or 0.0022 mole of *cis,cis*-II) with 1.2 g. of silver oxide in 55 ml. of hexane was carried out for 24 hr. to give 0.41 g. (93%, corrected for the 5% non-bromine-containing impurity in the starting material) of pale yellow oil, n^{20}D 1.5318, which gave a weak positive Beilstein test for halogen. Assuming that all of the bromine is present as starting material this would amount to about 1% of unreacted starting material. The infrared spectrum was identical with the spectrum of the acetylcyclopentane X prepared from cyclopentene as described below except that the broad band at 1180 cm.$^{-1}$ in this case had a rather flat maximum and the ratio of the absorbancy at this frequency to that at 1365 cm.$^{-1}$ was 0.64 instead of 0.81. Treatment of the product with semicarbazide gave 0.51 g. (96%) of semicarbazide, m.p. 171–172°, which after recrystallization from 67% ethanol amounted to 0.45 g. with m.p. 172.5–173.5°. The mixed m.p. with *trans*-X semicarbazide was 173–173.5° and the infrared spectra of the two substances were identical.

G. *trans,trans*-II.—The reaction of 0.30 g. (0.0011 mole) of the bromohydrin with 0.60 g. of silver oxide in 30 ml. of hexane was carried out for 24 hr. to give 0.20 g. (94%) of pale yellow oil, $n^{20}\text{D}$ 1.5305, with the odor of the acetylcyclopentane X and which gave a negative Beilstein test for halogen. The infrared spectrum of the product was identical with that in the corresponding reaction of *cis,cis*-II. Treatment with semicarbazide hydrochloride gave 0.23 g. (87%) of semicarbazone, m.p. 169.5–170°. Recrystallization from 67% ethanol gave 0.18 g. (68%) of colorless leaflets, m.p. 171.5–172.5°, which when mixed with the semicarbazone of X prepared from cyclopentene had m.p. 172–172.5.°

Reaction of *trans*-4-Phenylcyclohexene Oxide (*trans*-VI) with Hydrobromic Acid.—When 60 mg. of *trans*-VI in 3 ml. of ether was treated with 0.5 ml. of 48% hydrobromic acid with intermittent shaking at 25°, removal of the ether layer gave, after washing, drying and removal of the ether by distillation under reduced pressure, 64 mg. (73%) of *trans,-trans*-VII, m.p. 85.5–86.5°, mixed m.p. with an authentic sample, 86–87°. The infrared spectra of the two samples were identical.

***cis*-3-Phenylcyclohexanol.**—*m*-Phenylphenol was hydrogenated under conditions similar to those used by Ungnade[21] for the *p*-isomer. The oil which was obtained was dissolved in 100 ml. of hexane and the solution cooled in a Dry Ice–acetone-bath. The fluffy crystals (15 g. from 29 g. of *m*-phenylphenol) were collected by filtration to give a waxy solid which was dissolved in 10 ml. of hot carbon tetrachloride and the solution poured with rapid stirring into 250 ml. of hexane. The crystals which separated amounted to 5.5 g. with m.p. 79.5–80.5°. When recrystallized from 100 ml. of hexane, radiating clusters of transparent needles, m.p. 82–82.5°, were obtained (reported for 3-phenylcyclohexanol,[31] m.p. 79.5–80.5°).

***trans*-3-Phenylcyclohexanol.**—To a suspension of 0.06 g. of lithium aluminum hydride in 10 ml. of ether was added 0.23 g. (0.0013 mole) of *trans*-4-phenylcyclohexene oxide *trans*-VI and after 3 hr. at room temperature with occasional stirring the excess hydride was decomposed with wet ether and then dilute hydrochloric acid was added. Separation of the ether layer followed by washing with water, drying and evaporation of the ether under reduced pressure gave 0.22 g. (95%) of crystals, m.p. 59–61.5°. Comparison of the infrared spectrum with that of the more highly purified product described below (using absorption intensities at 976 and 1124 cm.$^{-1}$) indicated that 87 ± 1% of the product was *trans*-3-phenylcyclohexanol. Two recrystallizations from pentane gave m.p. 64.5–65°.

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.7; H, 9.2. Found: C, 81.7; H, 9.1.

Oxidation of *cis*- and *trans*-3-Phenylcyclohexanol. 3-Phenylcyclohexanone 2,4-Dinitrophenylhydrazone.—The oxidations were carried out by the method of Boyd, Clifford and Probert,[27] the oily 3-phenylcyclohexanone being obtained in 90% yield from the *cis*-alcohol and 80% yield from the *trans*. Preparation of the 2,4-dinitrophenylhydrazone gave, on recrystallization from ethyl acetate, in each case a product with m.p. 172.5–173 (reported[32] m.p. 183–186°). A mixed m.p. of the samples from the *cis*- and *trans*-alcohols showed no depression.

***trans*(?)-1-Acetyl-3-phenylcyclopentane (*trans*(?)-X)** was prepared by the directions of Nenitzescu and Gavat[30] from acetyl chloride, cyclopentene and aluminum chloride. The product was distilled through a 36-cm. Vigreux column and the fraction b.p. 104–106° at 0.4 mm. amounting to 30 g. was redistilled through a spinning band column to give 17 g., b.p. 127–128° at 3 mm. or 124–125° at 2.5 mm., $n^{20}\text{D}$ 1.5305–1.5309. The infrared spectrum showed absorption bands at 1180 and 1365 cm.$^{-1}$ with a ratio of intensities of 0.81.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.9; H, 8.6. Found: C, 83.1; H, 8.7.

The semicarbazone, recrystallized from methanol had m.p. 173–173.5° (reported[30] 170–171°).

***cis*(?)-2-Methyl-4-phenylcyclohexanone (*cis*(?)-XI).**—To 2.3 g. (0.059 mole) of potassium metal in 60 ml. of *t*-butyl alcohol which had been distilled from calcium hydride was added 10 g. (0.058 mole) of 4-phenylcyclohexanone and the mixture stirred for 1 hr. at 25°, heated to 70° to complete solution and cooled to 25° again. Methyl iodide (9.9 g., 0.070 mole) was added over a period of 3 min. and the mixture kept for 1 hr. at 25°. Most of the solvent was removed under reduced pressure, and 150 ml. of water was added, after which extraction with ether followed by drying and removal of the ether by distillation gave 10 g. of pale yellow viscous oil which was distilled through a micro spinning band column to give 2.2 g., b.p. 134–135° at 3.5 mm., $n^{20}\text{D}$ 1.5360; and 0.97 g., b.p. 135° at 3.5 mm., $n^{20}\text{D}$ 1.5352. The residue of 5.6 g. set to a hard yellow glass on cooling to 25°. The analysis of the second fraction is reported here.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.9; H, 8.6. Found: C, 83.1; H, 8.5.

***cis*(?)-2-Methyl-4-phenylcyclohexanone semicarbazone,** prepared from the second fraction above and recrystallized from 75% ethanol, had m.p. 202° dec.

Anal. Calcd. for $C_{14}H_{19}N_3O$: C, 68.5; H, 7.8; N, 17.1. Found: C, 68.6; H, 7.7; N, 17.4.

Oxidation of the trans(?)-Acetylcyclopentane *trans*(?)-X to *trans*(?)-3-Phenylcyclopentanecarboxylic Acid.—To 6.7 g. (0.035 mole) of the *trans*(?)-acetylcyclopentane *trans*(?)-X in 20 ml. of pyridine was added 10 g. of iodine over a period of 10 min. with cooling. The mixture was then heated for 2 hr. on a steam-bath and allowed to stand for 8 hr. at 25°. After filtration of the black crystalline pyridine hydriodide, the black filtrate was treated with 12 g. of sodium hydroxide in 20 ml. of ethanol and 60 ml. of water and the mixture was stirred on the steam-bath for 2 hr. and allowed to stand for 8 hr. at 25°. After stirring with activated charcoal the mixture was filtered and the filtrate acidified with dilute hydrochloric acid and extracted with ether. After drying of the ether layer and distillation of the ether there remained 5.0 g. of dark brown oil. The acid was extracted with 10% aqueous sodium carbonate and acidified and extracted into ether. Anhydrous ammonia passed into the dried ether solution precipitated the unstable ammonium salt[33] which was filtered, washed with ether and redissolved in water. Precipitation of the calcium salt by the addition of calcium chloride solution led, after treatment of a solution in hot water with activated charcoal, acidification and extraction of the liberated acid with ether and evaporation of the ether, to 2.1 g. (31%) of *trans*(?)-3-phenylcyclopentanecarboxylic acid, $n^{20}\text{D}$ 1.5418 (reported[34] $n^{20}\text{D}$ 1.5423).

Conversion of *trans*(?)-3-Phenylcyclopentanecarboxylic Acid to Its *trans*-Amide.—Conditions known not to cause epimerization in other similar cases[35] were employed. To 0.39 g. (0.0020 mole) of *trans*-3-phenylcyclopentanecarboxylic acid was added 2 ml. of purified thionyl chloride[36] after which the mixture was allowed to stand for 8 hr. at 25° and then the thionyl chloride removed under reduced pressure and the residue added to 20 ml. of cold aqueous ammonia with stirring. The amide which separated amounted to 0.34 g. (89%) and had m.p. 145.5–146.5°. Recrystallization from ethylene chloride gave 0.26 g., m.p. 148.5–149° (reported[34] 147–148°).

Oxidation of *cis*(?)-3-Phenylcyclohexanecarboxaldehyde. *cis*(?)-3-Phenylcyclohexanecarboxylic Acid.—A suspension of silver oxide was prepared by the addition of 0.6 g. of sodium hydroxide in 2.5 ml. of water to 1.2 g. of silver nitrate in 2.5 ml. of water and the addition of 2 ml. more of water. *cis*-3-Phenylcyclopentanecarboxaldehyde (0.50 g., 0.0029 mole) obtained from the rearrangement of *trans,trans*-I

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[32] G. F. Woods and I. W. Tucker, This Journal, **70**, 2174 (1948).

[33] W. Borsche and W. Menz, *Ber.*, **41**, 190 (1908).

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[35] C. D. Gutsche, This Journal, **70**, 4150 (1948).

[36] L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed., D. C. Heath and Co., Boston, Mass., 1955, p. 345.

was added dropwise at 0°, with stirring. After stirring at 0° for 5 min., the solution was allowed to warm to room temperature, and the silver salts and silver metal were filtered off. Acidification of the filtrate and extraction with ether gave, after removal of the ether under reduced pressure, 0.49 g. (90%) of pale yellow oil, $n^{20}D$ 1.5412. The infrared spectrum was identical with that of the *trans* isomer described above except in the 1230–1260 cm.$^{-1}$ region where the *cis* compound had two bands of approximately equal intensity at 1232 and 1256 cm.$^{-1}$ while the *trans* isomer had a somewhat stronger band at 1236 cm.$^{-1}$ with a shoulder at 1255 cm.$^{-1}$. This difference appeared in several preparations of each compound. The amide prepared from 0.21 g. (0.0011 mole) of the acid by the method employed for the *trans*-amide was obtained as 0.18 g. (86% yield), m.p. 155.5–157°. Recrystallization from ethylene chloride gave 0.12 g. of *cis*-amide, m.p. 158–158.5°. The m.p. was not changed by further recrystallization. A mixed m.p. with the *trans*-amide was 151.5–154°.

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.2; H, 8.0; N, 7.4. Found: C, 76.2; H, 8.0; N, 7.4.

Conversion of *cis*(?)-and *trans*(?)-3-Phenylcyclopentanecarboxylic Acid to 3,4-Benz-2-ketobicyclo[3.2.1]octane (IX).—A mixture of the cyclopentanecarboxylic acid and polyphosphoric acid was stirred intermittently at room temperature for 3 hr. and then on a steam-bath for 1–1.5 hr. The reaction mixture was then poured into 100 ml. of ice-water and extracted with ether. The ether solution was extracted with 10% sodium carbonate to remove any unreacted acid and, after drying, the solvent was distilled off under reduced pressure. From 1.4 g. (0.0074 mole) of *trans*-carboxylic acid and 16 g. of polyphosphoric acid was obtained 0.99 g. (78%) of IX as a light red oil, $n^{25}D$ 1.5798 (reported[34] 1.577). From 0.52 g. (0.0027 mole) of *cis*-acid and 7.7 g. of polyphosphoric acid was obtained 0.40 g. (85%) of red IX, $n^{25}D$ 1.5791. In each case the infrared spectra had strong carbonyl stretching absorption at 1692 cm.$^{-1}$. The spectrum of the sample from the *cis*-acid differed from that of the *trans* only by a weak band at 1775 cm.$^{-1}$. In each case the 2,4-dinitrophenylhydrazone recrystallized from dioxane had m.p. 250.5–251.5° (reported[34] 248–249°).

URBANA, ILL.

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

Chemistry of Spiropentane. II. The Chlorination of Spiropentane

BY DOUGLAS E. APPLEQUIST, GEORGE F. FANTA AND BERTEL W. HENRIKSON

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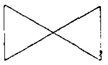
The product mixture obtained by free-radical chlorination of spiropentane has been shown to consist in part of the normal substitution product, chlorospiropentane, but mainly of chlorides which can be accounted for by initial ring-opening attack of a chlorine atom on carbon. The latter products include 1,1-bis-(chloromethyl)-cyclopropane, 4-chloro-2-chloromethyl-1-butene and 1,2,4-trichloro-2-chloromethylbutane.

Although spiropentane(I) has been known for a number of years,[1] no substituted spiropentanes are known except the perdeuterated spiropentane.[2] Since the standard preparation of spiropentane by dehalogenation of pentaerythrityl tetrahalides is not readily extended to the synthesis of spiropentane derivatives, a promising approach to the preparation of such derivatives appeared to be direct free-radical substitution reactions on spiropentane, analogous to the reported successful chlorination[3] and nitration[4] of cyclopropane. This paper reports a study of the free-radical chlorination of spiropentane, a reaction expected to yield chlorospiropentane (II), which was desired for an investigation to be described in a future publication.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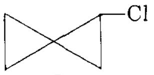
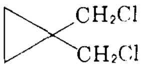
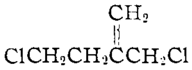


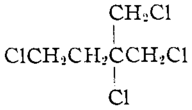
II

Photoinduced chlorination of spiropentane in the gas phase was studied with spiropentane to chlorine mole ratios of 10:1 to 30:1 with provision for removing chlorinated products as they formed. Distillation and gas chromatography of the reaction mixture revealed that there were four major products, which are here assigned the structures II–V.



III


$$\overset{\displaystyle CH_2}{\overset{\|}{ClCH_2CH_2CCH_2Cl}}$$
IV


$$ClCH_2CH_2\underset{\displaystyle Cl}{\overset{\displaystyle CH_2Cl}{C}}CH_2Cl$$
V

The structure of chlorospiropentane (II) was assigned on the basis of its analysis, its reduction to spiropentane with lithium in tetrahydrofuran followed by ethanol (78% yield) and by its n.m.r. and infrared spectra. The n.m.r. spectrum (60 mc.) showed a quartet of nearly equal signals centered at 1.48 p.p.m. from water and spaced 3 cycles apart, which was assigned to the hydrogen α to the chlorine. There was a triplet (areas approximately 1:2:1, with the central signal nearly resolved into two) at 3.38 p.p.m., spaced 6 cycles apart, which was assigned to one of the β-hydrogens; and there was a quartet centered at 3.65 p.p.m., spaced successively 3,2 and 3 cycles apart, which was assigned to the other β-hydrogen. The foregoing signals constitute a typical first-order three-proton spectrum in which all three protons are different.[5] In the present case, the two α-β coupling constants are 3 and 6 c.p.s. and the β-β coupling constant is about 5 c.p.s. The methylenes of the unsubstituted ring were represented by a strong signal at 3.82 p.p.m., with shoulders partially resolved on each side. The quartets for the β-hydrogens were found to be partially superimposed at 40 mc., making interpretation difficult. Spiropentane itself showed a single sharp signal at 4.04 p.p.m. The infrared spectrum of chlorospiropentane showed no C=C absorption, and contained

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[2] H. O. House, R. C. Lord and H. S. Rao, *ibid.*, **21**, 1487 (1956).

[3] J. D. Roberts and P. H. Dirstine, THIS JOURNAL, **67**, 1281 (1945).

[4] H. B. Hass and H. Shechter, *ibid.*, **75**, 1382 (1953).

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