Elimination Reactions of 2-Methylcyclohexyl Derivatives

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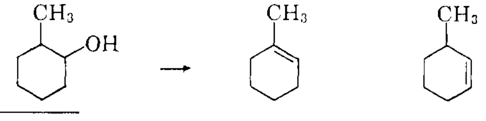
Received January 29, 1962

Elimination reactions of *cis*- and *trans*-2-methylcyclohexanol catalyzed by phosphoric acid and alumina, and of the 2-methylcyclohexyl chlorides and xanthates have been studied. No stereospecificity was observed in the pyrolysis of the 2-methylcyclohexyl *S*-methyl xanthates. The usual *cis* stereochemistry in the Chugaev reaction of 2-alkylcyclohexanols and its absence in this case are probably the result of differences in preferred conformation. Addition of benzoyl peroxide increases the proportion of 1-methylcyclohexene formed from the *trans* ester. The methoxide ion-induced elimination reaction has been used as a proof of configuration of the 2-methylcyclohexyl chlorides.

An investigation of elimination reactions of the nearly symmetrical 3-heptyl and 2,4-dimethyl-3-hexyl derivatives reemphasized the importance of steric factors in a number of such reactions.[2] It is generally agreed that unimolecular ester or tertiary amine oxide pyrolysis proceeds predominately with elimination of a *cis*-β-hydrogen,[3] in contrast to such base induced reactions as dehydrohalogenation and quaternary ammonium or tertiary sulfonium hydroxide pyrolysis, which are *trans* eliminations.[4] Enough exceptions have been noted, particularly in the Chugaev reaction,[5] that the possibility of *trans* elimination cannot be overlooked, particularly when *cis* elimination is difficult.

Several studies of 2-alkylcyclohexyl derivatives have been reported,[6] most often with the menthyl-neomenthyl or 2-phenylcyclohexyl series. It is surprising that so little use has been made of 2-methylcyclohexyl derivatives in studying the stereochemistry of elimination reactions, compared to the other systems. Separation of *cis-trans* isomers is readily accomplished, by crystallization of derivatives or by careful fractional distillation. No evidence of extensive rearrangement was found, unlike some reactions of 2-phenylcyclohexanol. Furthermore, the conformation of *cis*-2-methylcyclohexyl derivatives may be deduced with a greater certainty than that of the more complicated neomenthyl derivatives. In the former series, Saytzeff elimination results in formation of 1-methylcyclohexene, while the Hofmann product is 3-methylcyclohexene.



The reactions of 3-heptyl derivatives seemed to fall into two groups. The first, which gave 43–48% of 2-heptene and 52–57% of 3-heptene included not only the usual *cis* eliminations (dimethylamine oxide, xanthate, and carboxylate esters), but also the alumina-catalyzed dehydration of 3-heptanol. The second, which gave 55–67% of 2-heptene, included the usual *trans* eliminations of 3-chloroheptane and 3-heptyltrimethylammonium hydroxide and dehydrations catalyzed by strong acids. We anticipated that a study of these reactions in an alicyclic system would shed further light on the mechanism of acid- and alumina-catalyzed reactions.

The aluminum oxide-catalyzed dehydrations of the 2-methylcyclohexanols might have been expected to show a preferential *cis* elimination. An equal mixture of 1- and 3-methylcyclohexanes was obtained from the *trans* alcohol, but *cis*-2-methylcyclohexanol gave only 52% of 3-methylcyclohexene. Since it has recently been shown that similar reactions conducted in a stream of ammonia are stereospecific, but that acidic centers in the catalyst affect the product mixture if an inert gas is used,[7] no theoretical significance should be ascribed to this data, but it has been included as an example of results with a readily available commercial catalyst. The probability that rearrangement following elimination occurred similarly limits the utility of the data in the reaction catalyzed by phosphoric acid.

The mechanism of the Chugaev reaction can no longer always be considered a concerted, cyclic *cis* ionic mechanism, since Bordwell[5] has shown that *cis*-2-*p*-tolylsulfonylcyclohexyl *S*-methyl xanthate forms mostly 1-*p*-tolylsulfonylcyclohexene, while Nace[8] has presented evidence for an alternative free radical mechanism. In an attempt to clarify the situation, pyrolyses of *cis*- and *trans*-2-methylcyclohexyl methyl xanthates were carried out in the presence of a free radical inhibitor, then in the presence of a free radical initiator. Although nearly identical olefin mixtures were obtained from the *cis* xanthates, addition of benzoyl peroxide to the *trans* xanthate caused an increase in the relative amount

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(2) D. G. Botteron and G. P. Shulman, *J. Org. Chem.* **27**, 785 (1962).

(3) C. H. De Puy and R. W. King, *Chem. Rev.*, **60**, 431 (1960).

(4) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 467.

(5) Summarized by F. G. Bordwell and P. S. Landis, *J. Am. Chem. Soc.*, **80**, 2450 (1958).

(6) (a) W. Huckel, W. Tappe, and G. Legutke, *Ann.*, **543**, 191 (1940). (b) A. C. Cope and E. M. Acton, *J. Am. Chem. Soc.*, **80**, 355 (1958). (c) N. L. McNiven and J. Read, *J. Chem. Soc.*, 153 (1952). (d) E. L. Eliel, J. W. McCoy, and C. C. Price, *J. Org. Chem.*, **22**, 1533 (1957).

(7) H. Pines and C. N. Pillai, *J. Am. Chem. Soc.*, **82**, 2921 (1960).

(8) H. R. Nace, D. G. Manly, and S. Fuco, *J. Org. Chem.*, **23**, 687 (1958).

TABLE I

ELIMINATION REACTIONS OF 2-METHYLCYCLOHEXYL DERIVATIVES[15]

2-Methylcyclohexyl Derivatives	Quantity Added, G.	Other Material Added	Yield of Olefins, %	Boiling Range	Composition of Olefin Mixture[a] Relative % of 1-	Composition of Olefin Mixture[a] Relative % of 3-	Composition of Olefin Mixture[a] % of unknown
cis-OH	11.4	H_3PO_4	67	100–117	79	21	6.6
cis-OH	11.4	Al_2O_3	75	98–113	48	52	18.0
cis-Cl					79	21	7.8
cis-$OCSSCH_3$	10.2	*p*-$C_6H_5(OH)_2$	20	[c]	49	51	15
cis-$OCSSCH_3$	10.2	BzOOBz	37	[c]	49	51	15
trans-OH	3.8	H_3PO_4	85	98–120	71	29	1.4
trans-OH	3.8	Al_2O_3	35	98–115	50	50	1.4
trans-Cl	13.2	$NaOCH_3$[b]	5	111–120	44	56	29.5
trans-$OCSSCH_3$	10.2	*p*-$C_6H_4(OH)_2$	31	[c]	56	44	1
trans-$OCSSCH_3$	10.2	BzOOBz	7	[c]	67	33	9

[a] 1-Methylcyclohexene, 3-methylcyclohexene, impurities. [b] 60 hr. refluxing. [c] Not distilled. [d] Washed in two portions of sodium plumbite solution, filtered, then dried over calcium chloride and distilled.

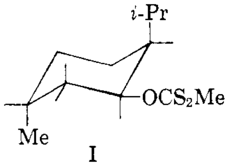
of 1-:3-methylcyclohexene (67:33% compared to 56:44% with hydroquinone added).

This suggests the action of a free radical mechanism, although it is certainly not conclusive. Apparently, the free radical mechanism operates most easily with *cis* geometry, as shown by the appearance of the effect only with the *trans* xanthate.

The equal mixtures of 1- and 3-methylcyclohexene formed from *cis*-2-methylcyclohexyl xanthate cannot be reconciled with a preferential *cis* elimination. We feel that the evidence which led to acceptance of the *cis* mechanism needs re-examination, particularly since an ion pair mechanism has been suggested for this reaction.[9] This type of mechanism allows for *trans* elimination without intermediate formation of the highly strained *trans* olefin. Kinetic data[9,10] support a cyclic mechanism, although the first-order kinetics cited as evidence for unimolecularity does not really prove this. Measurements made on a pure liquid, with volatile products, are necessarily pseudo first order, since the concentration must remain constant at 100% xanthate ester.

The assignment of *cis* geometry has been made mainly on the basis of reactions in the alicyclic series. A study of the conformation of the alicyclic xanthates provides an answer to the problem.

For the neomenthyl system, conformation I, in which two groups are axial, should be a poor second choice relative to conformation II. From the equatorial position, the xanthate thiocarbonyl sulfur can reach either of the equatorial β-hydrogens with equal ease. From the axial position, it can never reach the tertiary hydrogen. This accounts for the 80% of 2-menthene formed in its reactions.[6a] Phenyl or *t*-butyl groups are also bulkier than a xanthate, so they should occupy the equatorial position (III) preferentially, accounting for the 96–100% of 3-phenylcyclohexene[6d] or 100% of 3-*t*-butylcyclohexene[9] formed.



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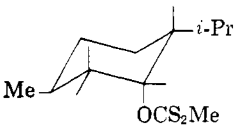

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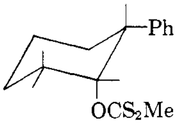
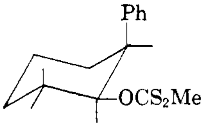
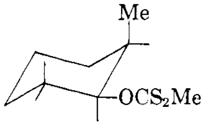


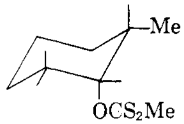
III



IV



V



VI

The situation is reversed in 2-methylcyclohexyl methyl xanthate. With the alkyl group smaller than the xanthate, conformation V should be much more stable. The equatorial xanthate group can reach either of the equatorial β-hydrogens with equal ease, explaining the equal mixture which formed. The formation of 2-methylindene from *cis*-2-methylindanyl xanthate has also been explained in this way.[9]

The *trans* isomers are all capable of assuming conformations with all groups equatorial, so these considerations do not apply. Orientation then follows the Saytzeff rule. It has been found that steric factors predominate when hyperconjugation differences between the isomeric olefins are small.[2] The pyrolysis of sulfoxides involves two competitive unimolecular processes, one of either *cis* or *trans* stereochemistry, and one of *cis* stereochemistry, favored at high and low temperatures, respectively. The low temperature reaction appears to be a concerted cyclic reaction, analogous to those proposed for ester or amine oxide pyrolysis. The high temperature reaction probably proceeds *via* a radical pair, within a solvent cage. Kingsbury[11] and Cram point out that "neither the stereochemistry nor the kinetics taken separately can be used to differentiate between these mechanisms"; *i.e.*, the

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(9) F. G. Bordwell and P. S. Landis, *J. Am. Chem. Soc.*, **80**, 6379 (1958).

(10) G. L. O'Connor and H. R. Nace, *J. Am. Chem. Soc.*, **74**, 5454 (1952); **75**, 2118 (1953).

(11) C. A. Kingsbury and D. J. Cram, *J. Am. Chem. Soc.*, **82**, 1810 (1960).

classical Hurd mechanism and a radical pair mechanism. In light of their work, of the limited scope of the kinetic study of the Chugaev reaction, and of our results, need for a detailed investigation of the kinetics of the Chugaev reaction is indicated. It is certainly possible that the anomalous stereochemistry in 2-methylcyclohexyl xanthate pyrolysis results from spatial relationships particularly conductive to radical pair reaction.

Three factors contribute to the greater stereospecificity observed with carboxylate esters. First, the smaller size of the ring formed in the transition state will promote a true *cis* elimination. Second, the smaller esters, such as acetates, have a smaller steric requirement than the xanthates; hence, are more likely to be forced into an axial position, making attack on the tertiary hydrogen impossible. Finally, and most important, an ion pair mechanism would seem to be less important in carboxylate pyrolysis.

In the course of this work, it was found that some previous work on the preparation and proof of configuration of the 2-methylcyclohexyl chlorides was of dubious value. Mousseron[12] reported the preparation of a mixture containing mostly the *cis* isomer by treatment of *trans*-2-methylcyclohexanol with refluxing hydrochloric acid. The *trans* chloride was reportedly formed preferentially by treatment of this same isomer with phosphorus trichloride. In two reactions of commercial (mostly *trans*) 2-methylcyclohexanol with hydrochloric acid, only *trans*-2-methylcyclohexyl chloride was found. Some *cis* isomer was finally prepared from *cis*-2-methylcyclohexanol by reaction with thionyl chloride in pyridine. The material was obtained in too small a quantity for rigorous purification and accurate determination of physical properties, however. Mousseron's "proof" of configuration involved preparation of the Grignard reagents and carbonation or oxidation. This method had already been reported to be of no value,[13] and has since been proven faulty with closely related halides (including 3-methylcyclohexyl chloride).[14]

The E2 reaction of alkyl halides with a base takes place with elimination of a hydrogen *trans* to the halogen.[4] *cis*-2-Methylcyclohexyl chloride can give either 1-methyl- or 3-methylcyclohexene by *trans* elimination, but by Saytzeff's rule it should give mostly 1-methylcyclohexene. *trans*-2-Methylcyclohexyl chloride can give only 3-methylcyclohexene by *trans* elimination, so that should be the predominate product. The halide presumed to be *cis* gave 79% of 1-methylcyclohexene, in good agreement with the predicted value. The halide presumed to be *trans* did give mainly 3-methylcyclohexene.

The 79% of 1-methylcyclohexene formed from the *cis*-chloride is in remarkably good agreement with the 75% of 3-menthene formed from neomenthyl chloride,[6] considering the differences in the reaction conditions. Far less specificity was observed with 2-methylcyclohexyl chloride than with menthyl chloride (100% of 2-menthene). The reaction was extremely slow, as is expected whenever *trans* elimination to the Saytzeff product is impossible. Since no sign of a higher boiling isomer was found during the distillation of the starting material, presence of *cis* impurity is probably not the cause. It is possible that rearrangement to the more stable isomer occurred during the reaction (seventy-two hours in refluxing 3 M sodium methoxide). It seems probable that inversion *via* a carbanion or carbonium ion preceded elimination, but in the absence of kinetic data or optical activity, the extent of solvolysis could not be ascertained. The present data is adequate for proof of configuration, however.

Experimental

Separation of *cis*- and *trans*-2-Methylcyclohexanol.—A commercial sample of 2-methylcyclohexanol was fractionated on a glass helix-packed, 53-plate Todd distillation apparatus at a reflux ratio of 50:1. Samples of *cis* 2-methylcyclohexanol, b.p. 163.5–164°, n^{20}D 1.4640, and of *trans*-2-methylcyclohexanol, b.p. 165–165.2°, n^{20}D 1.4620, were obtained.[15]

Hydrolysis of *trans*-2-Methylcyclohexyl Hydrogen Phthalate.—A mixture of 16.0 g. of *trans*-2-methylcyclohexyl hydrogen phthalate and 100 ml. of 30% sodium hydroxide solution was refluxed for 1 hr., then cooled. The upper layer was washed three times with an equal volume of water, dried over magnesium sulfate, and distilled, giving 4.0 g. of *trans*-2-methylcyclohexanol, b.p. 160–165°, n^{20}D 1.4620.

Preparation of *cis*-2-Methylcyclohexyl Hydrogen Phthalate.—A 40% yield of this ester was obtained by refluxing 11.4 g. of *cis*-2-methylcyclohexanol and 22 g. of phthalic anhydride for 24 hr. The melting point was 104–106°.[15b]

Preparation of *trans*-2-Methylcyclohexyl Hydrogen Phthalate.—A 20% yield of this ester was obtained by refluxing 85 g. of commercial 2-methylcyclohexanol and 120 g. of phthalic anhydride for 72 hr., then recrystallizing the product. The melting point was 124–125°.[15b]

Preparation of 2-Methylcyclohexyl Methyl Xanthates.—In a three-neck flask fitted with a condenser, sealed stirrer (Teflon gland type), and dropping funnel were placed 150 ml. of dry *p*-xylene and 5.2 g. of sodium; then 22.8 of 2-methylcyclohexanol was added. After addition of 150 ml. of dry ether, 30.5 g. of carbon disulfide was added over a 0.5-hr. period. The material was refluxed for 2 hr., then 57 g. of methyl iodide was added over a 0.5-hr. period. The mixture was refluxed for 12 hr., filtered, distilled to remove material boiling below 80° at 20 mm., then the residue was distilled *cis*-2-Methylcyclohexanol gave 22 g. (54%) of the xanthate, b.p. 110–112° at 5 mm., n^{23}D 1.5490.

Anal. Calcd. for $C_9H_{16}OS_2$: C, 52.9; H, 7.84; S, 31.4. Found: C, 51.6; H, 7.58; S, 32.6.[16]

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[12] M. Mousseron *et al.*, *Bull. soc. chim. France*, (**V**), 13, 244 (1946).

[13] K. von Auwers and F. Dersch, *J. prakt. Chem.*, (II), **124**, 209 (1930).

[14] H. L. Goering and F. H. McCarron, *J. Am. Chem. Soc.*, **80**, 2287 (1958).

[15] Reported values: *cis*-2-methylcyclohexanol, b.p. 165°, n^{20}D 1.4640–1.4649; *trans*-, b.p. 166.5°, n^{20}D 1.4611–1.4616; *cis*-2-methylcyclohexyl hydrogen phthalate, m.p. 102–104°, *trans*-, m.p. 124–125° (a) A. Skita and W. Faust, *Ber.*, **64**, 2878 (1931). (b) L. M. Jackman *et al.*, *J. Chem. Soc.*, 1717 (1949).

[16] Microanalysis by Weiler and Strauss, Oxford, England

trans-2-Methylcyclohexanol gave 21 g. (52%) of the xanthate, b.p. 113–114° at 5 mm., n^{20}D 1.5473.

Anal. Found: C, 53.0; H, 7.00; S, 32.3.

Preparation of *cis*-2-Methylcyclohexyl Chloride.—To a mixture of 11.4 g. of *cis*-2-methylcyclohexanol and 8.0 g. of pyridine, 24.0 g. of thionyl chloride was added dropwise. The mixture was allowed to cool, the upper phase was separated, washed with water, 5% sodium hydroxide, then twice more with water. After drying over calcium chloride, the product was distilled, giving 1.3 g. of *cis*-2-methylcyclohexyl chloride, b.p. 50–52° at 12 mm., n^{20}D 1.4065.[13]

Anal. Calcd. for $C_7H_{13}Cl$: C, 63.3; H, 9.80; Cl, 26.8. Found: C, 64.6; H, 9.80; Cl, 24.1.

Preparation of *trans*-2-Methylcyclohexyl Chloride.—A mixture of 500 ml. of hydrochloric acid, 160 g. of calcium chloride, and 228 g. of 2-methylcyclohexanol was refluxed for 18 hr. The organic phase was washed with water, 5% sodium bicarbonate solution, then with a saturated salt solution, dried over calcium chloride, and distilled, the fraction of boiling range 145–155° being collected. Redistillation on the Todd column at a reflux ratio of 10:1 gave 62 g., b.p. 39–40° at 10 mm., n^{20}D 1.4588,[18] followed by a fraction of b.p. 52–55° at 10 mm., probably 2-methylcyclohexanol. A mixture of 45.6 g. of 2-methylcyclohexanol and 100 ml. of hydrochloric acid was refluxed for 3 hr. The organic phase was washed with water, twice with sulfuric acid, then with water, dried over calcium chloride, and distilled giving *trans*-2-methylcyclohexyl chloride, b.p. 78° at 58 mm., n^{20}D 1.4588.[17]

Preparation of 2-Methylcyclohexylamine.—A solution of 50 g. of hydroxylamine hydrochloride and 80 g. of crystalline sodium acetate in 200 ml. of water was warmed to 45°, 50 g. of 2-methylcyclohexanone was added, the mixture was shaken for 30 min., then left overnight. The oil was separated and dried over magnesium sulfate. After 200 ml. of absolute alcohol had been added, the magnesium sulfate was removed by filtration, then 800 ml. more alcohol was added. The solution was placed in a flask fitted with an Allihn condenser and heated to boiling, then 60 g. of sodium was added so as to maintain the refluxing. When the mixture had cooled, 1 l. of water was added, the mixture was distilled to dryness, then 200 ml. of 30% sodium hydroxide was added to the residue. The oil was separated, dried over sodium hydroxide, and distilled, aniline being used as a chaser. The fraction boiling at 150–160° was redistilled on the Todd column, giving 15 ml., b.p. 148°, n^{20}D 1.4561.[18] It appears that the material is mainly *trans*-2-methylcyclohexylamine.

Preparation of *trans*-2-Methylcyclohexyldimethylamine.—A solution of 11.3 g. of 2-methylcyclohexylamine in 20 ml. of methanol was prepared. Addition of 14.2 g. of methyl iodide caused a vigorous reaction, after which the mixture was refluxed for 10 min. Following addition of 5.4 g. of sodium methoxide, 14.2 g. of methyl iodide was added, then the mixture was refluxed for 30 min. and poured into 100 ml. of water. The oil which separated on addition of 100 ml. of 10% sodium hydroxide was dried over sodium hydroxide, then distilled, giving 6.0 g. (43% yield), b.p. 168–170°, n^{20}D 1.4517.

Anal. Calcd. for $C_9H_{19}N$: C, 76.6; H, 13.4; N. 9.9. Found: C, 77.0; H, 13.4; N, 9.5.

Preparation of 2-Methylcyclohexyltrimethylammonium Iodide.—A solution of 3.0 g. of *trans*-2-methylcyclohexyldimethylamine and 10 g. of methyl iodide in 12 ml. of benzene was refluxed for 20 min. After 10 ml. of anhydrous ether had been added, the precipitate was filtered and dried. The hydroxide was prepared and pyrolyzed.[19]

Elimination Reactions.—The procedures for most of the elimination reactions have been described in an earlier paper.[2]

Dehydrohalogenation of *cis*-2-Methylcyclohexyl Chloride.—A 1.3-g. sample of *cis*-2-methylcyclohexyl chloride was sealed in a tube with a solution of 0.23 g. of sodium in 3.5 ml. of methanol and heated at 100° for 13 hr. The tube was opened, then the mixture was washed with water, dried over calcium chloride, and analyzed.

Decomposition of 2-Methylcyclohexyl Methyl Xanthates.—A 10.2-g. sample of the xanthate ester was placed in a micro-distillation apparatus fitted with a cold finger condenser, then 1.0 g. of either hydroquinone or benzoyl peroxide was added. The material was heated until distillation ceased. The distillate was distilled twice, fractions of b.p. 90–120° being collected.

Gas Chromatographic Analysis.[20]—A reference sample of 1-methylcyclohexene was prepared from cyclohexanone and methylmagnesium iodide. A 3-methylcyclohexene sample was obtained by distillation of the mixture formed by dehydrating 2-methylcyclohexanol over alumina.

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(17) Reported values: *cis*-, b.p. 41–42° at 10 mm., n^{20}D 1.4569; *trans*-, b.p. 39–40°, n^{20}D 1.4586 (ref. 8).

(18) Reported values: *cis*-, b.p. 153.5–154°, n^{20}D 1.4688; *trans*-, b.p. 149.7–150.2°, n^{20}D 1.4650. D. S. Noyce and F. W. Bachelor, *J. Am. Chem. Soc.*, **74**, 4577 (1952).

(19) T. H. Brownlee and W. H. Saunders [*Proc. Chem. Soc.*, 314 (1961)] report that the *trans* isomer forms only 3-methylcyclohexene and the *cis* isomer 95% of 1-methylcyclohexene under these conditions. The amines and ammonium salts therefore contained approximately 24% of *cis* and 76% of *trans* isomers.

(20) Details of analysis are given in ref. 2.