ency of the chlorine-activated compounds to undergo bimolecular elimination is shown by their greater reactivities (second-order rate constants are 300-2400 times as great as the methyl analogs).

Acknowledgments.—The authors are indebted to the Office of Naval Research and to the National Science Foundation for support of this work.

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Isomers for Electrophilic Studies. Preparation of and Structural Assignments to *cis*- and *trans*-4-Methylcyclohexylmercuric Bromides[1,2,3]

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RECEIVED MARCH 21, 1959

cis- and *trans*-4-methylcyclohexylmercuric bromides have been prepared in pure form in order to obtain a pair of stereoisomers suitable for studying electrophilic aliphatic substitution. The configurational assignments were largely based on the observed C–D axial and equatorial infrared absorption frequencies of the 1-deuterated isomers. In connection with these results, it was found that the group containing the mercury atom, as compared to the methyl group, has a relatively small preference for equatorial over axial conformation.

Although considerable attention has been devoted to nucleophilic and homolytic aliphatic substitution, the physical–organic chemistry of electrophilic aliphatic substitution has been largely ignored. This is due to a substantial extent to the difficulty of obtaining stereoisomers of aliphatic compounds which undergo electrophilic substitution. The present paper reviews the compounds which have been used in electrophilic studies and reports the preparation of and structural assignments to a pair of simple aliphatic isomeric mercury compounds, *cis*- and *trans*-4-methylcyclohexylmercuric bromides. Organomercurials have been selected because of their high stability and because they can be readily converted to other organometallic compounds. Geometrical rather than optical isomers were chosen because of the relative ease of establishing the configuration of the compounds.

Until the recent report of the preparation of optically active *sec*-butylmercuric bromide,[5,6] no simple isomeric saturated organometallic compounds were available for electrophilic substitution studies, and the result of studies with these compounds have been only reported in preliminary form.[6] However, studies have been reported using stereochemically complex organomercurials. *cis*- and *trans*-2-methoxycyclohexylmercuric chloride have been used for stereochemical studies.[7–9] The results with these compounds are not definitive since it is possible that the neighboring methoxy group participates in the reactions and influences the stereochemistry. Also, a full analysis of these results is complicated by the conflict between the earlier assignment of structure by X-ray analysis[10] and the assignment from chemical studies.[11] Stereochemical studies have been reported utilizing the diastereomers of 3-bromomercuricamphor[12] and the *l*-methyl ester of α-bromomercuriphenylacetic acid.[13] These compounds are also unsuited for definitive stereochemical studies since they contain permanent asymmetric induction and have groups near the reaction center which contain unshared pairs of electrons.

The preliminary account of a study of electrophilic substitution utilizing simple stereoisomers not of organometallic origin has been reported.[14] In this study, the fate of the 2-phenylbutyl carbanion generated from an optically active source was investigated.

Results and Discussion

A mixture of the isomeric 4-methylcyclohexylmercuric bromides was prepared in 65% yield by treating 4-methylcyclohexylmagnesium bromide with mercuric bromide. A crude separation of the isomers was obtained based on their different solubilities in benzene. The less soluble *trans* isomer was further purified by recrystallizing from benzene yielding pure *trans*-4-methylcyclohexylmercuric bromide with a m.p. 157.7–158.0°. The crude *cis* isomer was purified by chromatography on alumina yielding pure *cis*-4-methylcyclohexylmercuric bromide with a m.p. 130.8–131.2°. To our knowledge, this is the first report of the use of chromatography to purify an organometallic compound.

The 4-methylcyclohexyl bromide (I) was obtained from the Hunsdiecker reaction on *cis*- or *trans*-4-methylcyclohexanecarboxylic acid. This synthetic route was necessary because of the difficulty in converting 4-alkylcyclohexanols to the corresponding bromides without rearrangement.[15]

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[1] Electrophilic Aliphatic Substitution III, Organomercurials, I.

[2] This work has been supported in part by a grant from the Research Corporation.

[3] A preliminary report of these results has been given; F. R. Jensen and L. H. Gale, THIS JOURNAL, **81**, 1261 (1959).

[4] Allied Chemical and Dye Corp. Fellow, 1958–1959.

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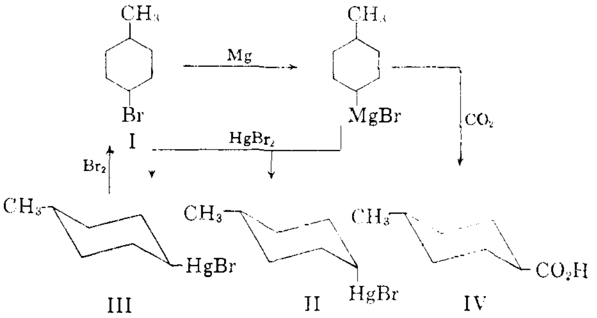
Also it was found that when commercial 4-methylcyclohexyl bromide was used, an appreciable quantity of 3-methylcyclohexylmercuric bromide was isolated, and it was not possible to obtain pure *cis*-4-methylcyclohexylmercuric bromide from the reaction mixture.

The structures of the *cis*- and *trans*-4-methylcyclohexylmercuric bromides were proved by the following sequence of reactions. *trans*-4-Methylcyclohexylmercuric bromide (III) was cleaved by bromine[16] to yield 4-methylcyclohexyl bromide (I).



The alkyl bromide was converted to the corresponding Grignard reagent and approximately one-third was carbonated to yield *trans*-4-methylcyclohexanecarboxylic acid (IV). The remaining two-thirds of the Grignard solution was treated with mercuric bromide and the crude mixture was separated into the *cis*- and *trans*-mercury compounds. Additional structural evidence was obtained by the electrolytic reduction of 4-methylcyclohexanone at a mercury cathode according to the procedure described by Tafel.[17] This process resulted in di-4-methylcyclohexylmercury in low yield which was cleaved by mercuric bromide to give a 50/50 mixture of *cis*- and *trans*-4-methylcyclohexylmercuric bromides.

The tentative assignment of configuration based on the physical properties, relative stabilities and product distribution from the Grignard reaction was confirmed by measuring the C–D stretching frequencies of the corresponding 1-deuterio compounds. Corey and co-workers[18] have previously determined the C–D stretching frequencies for equatorial and axial deuterium atom in cyclohexane systems. The deuterium was incorporated into the cyclohexane molecule by either a base-catalyzed exchange of methyl 4-methylcyclohexanecarboxylate by sodium methoxide in deuteriomethanol or an acid-catalyzed exchange of 4-methylcyclohexanecarboxylic acid by deuteriosulfuric acid in deuterium oxide. In order to increase their solubility for infrared measurements, the *cis*- and *trans*-4-methylcyclohexyl-1-*d*-mercuric bromides were converted to the corresponding alkylmercuric acetates or benzoates by treatment with silver acetate or benzoate.

The infrared spectra of the deuterated *cis*- and *trans*-benzoates and *trans*-acetate and the corresponding non-deuterated compounds were recorded in the C–D stretching region. The infrared spectrum of *trans*-4-methylcyclohexyl-1-*d*-mercuric acetate showed absorptions at 2125 (medium), 2147 (strong) and 2166 (weak) cm.$^{-1}$. Similarly, the spectrum of *trans*-4-methylcyclohexyl-1-*d*-mercuric benzoate showed characteristic absorption at 2127 (weak), 2148 (strong) and 2168 (medium) cm.$^{-1}$. In contrast, the infrared spectrum of *cis*-4-methylcyclohexyl-1-*d*-mercuric benzoate showed a similar triplet displaced to higher frequency absorbing at 2141 (medium). 2166 (strong) and 2191 (shoulder) cm.$^{-1}$. Corey studied three sets of epimers and found that the high frequency absorption band of the isomer with equatorial deuterium occurred at a higher frequency than the high frequency band of the corresponding axial isomer. Hence, the displacement to higher frequency which we recorded in the latter compound is evidence that the deuterium atom is predominately equatorial and therefore the benzoxymercuri group is axial or *cis* to the 4-methyl group.[18a]

The above results indicate that the methyl group is controlling the conformation of each isomer, *i.e.*, that the methyl group relative to a benzoxymercuri group has a greater preference for equatorial over an axial conformation. This seems to indicate that the methyl group is larger than the benzoxymercuri group. A number of groups have a smaller preference for equatorial over axial conformation than might have been expected from their sizes as indicated by their radii.[19] In each of the examples, the bonds to carbon are long. In the present case the radius of the mercury atom[20] is 1.44 Å., but the carbon mercury bond is very long,[21] 2.23 Å. Evidently, the length of the bond and the size of the group are both important in determining the relative configurational preference.

Experimental[22]

4-Methylcyclohexyl Bromide (I).—*p*-Toluic acid was reduced to 4-methylcyclohexanecarboxylic acid by either low pressure hydrogenation according to the procedure described by Keats[23] or high pressure hydrogenation according to the procedure described by Cooke and Macbeth.[24] The acid was converted to 4-methylcyclohexyl bromide by the Hunsdiecker reaction using standard procedures.

Preparation of *cis*- and *trans*-4-Methylcyclohexylmercuric Bromides (II, III) by the Grignard Reagent.—4-Methylcyclohexylmagnesium bromide was prepared by treating 350 g. (1.98 moles) of 4-methylcyclohexyl bromide with 49 g. (2 moles) of magnesium turnings in 1250 ml. of anhydrous ether. To the Grignard solution was added slowly, 723 g. (2 moles) of mercuric bromide. The reactants were stirred for two hours at room temperature and then decomposed with ice and acidified with 50 ml. of 48% HBr. The ether was removed at room temperature by an air stream and the solid material was collected by filtration. The crude prod-

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(16) The cleavage of aklylmercuric halides by bromine is discussed in the next paper of this series; F. R. Jensen and L. H. Gale, THIS JOURNAL, **81**, 148 (1959).

(17) J. Tafel, *Ber.*, **39**, 3628 (1906).

(18) E. J. Corey, M. G. Howell and A. Boston, THIS JOURNAL, **78**, 5036 (1956).

(18a) NOTE ADDED IN PROOF.—The n.m.r. spectra, to be reported later, of the deuterated and undeuterated *cis*- and *trans*-4-methylcyclohexylmercuric bromides provide supplementary proof of the structural assignments.

(19) E. L. Eliel and R. G. Haber, *Chemistry & Industry*, 264 (1958); R. A. Pickering and C. C. Price, THIS JOURNAL, **80**, 4931 (1958).

(20) T. Moeller, "Inorganic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1952, p. 135.

(21) G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, p. 715.

(22) Melting points and boiling points are uncorrected. Analyses are by the Microanalytical Laboratory of the University of California.

(23) G. Keats, *J. Chem. Soc.*, 2003 (1937).

(24) R. G. Cooke and A. Macbeth, *ibid.*, 1245 (1939)

uct was recrystallized from benzene yielding three fractions of crude *trans*-4-methylcyclohexylmercuric bromide totaling 351 g. The mother liquid was reduced to dryness yielding 137 g. of crude *cis*-4-methylcyclohexyl-mercuric bromide. The infrared spectrum of this material indicated that it contained 10–15% of the *trans* isomer. The total yield of product was 488 g. (65%). The *trans*-4-methylcyclohexylmercuric was purified by recrystallization from benzene to give 223 g., m.p. 157.7–158.0°.

Anal. Calcd. for $C_7H_{13}HgBr$: C, 22.26; H, 3.47; Br, 21.16. Found: C, 22.10; H, 3.65; Br, 20.99.

The crude *cis*-4-methylcyclohexylmercuric bromide was purified by chromatography on alumina. A 132-g. sample of crude material was dissolved in 25% hexane–75% carbon tetrachloride and placed on a column containing 6 lb. of alumina, height to diameter ratio of 45.5 cm./8.7 cm. The column was developed using a hexane–ether mixture containing increasing amounts of ether to 15%. Material was removed from the column by adding 2% chloroform to the 85% hexane–15% ether mixture. The 63.1 g. of pure *cis*-4-methylcyclohexylmercuric bromide obtained was further purified by recrystallization from benzene–hexane yielding material with a m.p. 130.8–131.2°. The reported m.p. for 4-methylcyclohexylmercuric bromide (configuration unknown) is 142°.[25]

Anal. Found: C, 22.14; H, 3.34.

Establishing the Structures of *cis*- and *trans*-4-Methylcyclohexylmercuric Bromides.—A 37.2-g. (0.098 mole) sample of pure *trans*-4-methylcyclohexylmercuric bromide (m.p. 160.8–161.1°) was cleaved with bromine in chloroform to yield 12.1 g. (0.068 mole) of 4-methylcyclohexyl bromide, b.p. 57–60° (11 mm.). The bromide was converted to the corresponding Grignard reagent in the usual manner. Approximately one-third of the Grignard reagent was treated with carbon dioxide yielding 0.36 g. (0.0025 mole) of acid which was recrystallized from formic acid–water yielding *trans*-4-methylcyclohexanecarboxylic acid (IV), m.p. 110.4–111.4° (lit.[26] m.p. 112°).

Anal. Calcd. for $C_7H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.37; H, 9.69.

The remaining two-thirds of the Grignard reagent was treated with mercuric bromide yielding 7.6 g. (0.02 mole) of crude 4-methylcyclohexylmercuric bromide. The crude product was recrystallized from absolute alcohol yielding 2.15 g. of *trans*-4-methylcyclohexylmercuric bromide which was recrystallized from dioxane, m.p. 159.1–159.6°.

Anal. Calcd. for $C_7H_{13}HgBr$: C, 22.26; H, 3.47; Br, 21.16. Found: C, 22.40; H, 3.48; Br, 21.50.

The absolute alcohol mother liquid was reduced to dryness yielding 1.14 g. of impure *cis*-4-methylcyclohexylmercuric bromide, m.p. 115.9–116.9° dec. The infrared spectrum of the product indicated that it contained approximately 10% of the *trans*-isomer.

Preparation of *cis*- and *trans*-4-Methylcyclohexylmercuric Bromides by Electrolytic Reduction of 4-Methylcyclohexanone.—In a mercury cathode chamber was placed 350 ml. of solution containing the following components (percentage by volume): 21% sulfuric acid, 30% acetic acid and 6% 4-methylcyclohexanone. In the anode compartment was placed 100 ml. of 20% sulfuric acid. The electrolytic process was carried out with a cell potential of 8 volts (4–5 amp.) for 1.5 hr. at 48°. To the cathode solution was added 1.5 l. of water and the organic later was extracted with ether. The ether extracts were washed with water, dilute sodium bicarbonate and water. The ether was removed and the resulting oil dissolved in 150 ml. of absolute alcohol. A 15-g. sample of mercuric bromide was added to the alcohol solution, causing a white solid to appear which dissolved upon heating and recrystallized when cooled, yielding 2.2 g. of 4-methylcyclohexylmercuric bromide (4%), m.p. 138° dec. The infrared spectrum of this material indicated that it contained approximately 50% *cis*- and 50% *trans*-4-methylcyclohexylmercuric bromide.

Deuteration of 4-Methylcyclohexanecarboxylic Acid by Acid-catalyzed Exchange.—A 343-g. (2.2 moles) sample of methyl 4-methylcyclohexanecarboxylate was hydrolyzed by heating with 10 ml. of D_2SO_4 and 47.6 g. (2.4 moles) of D_2O. The deuteriomethanol formed was removed by distillation. The deuterium exchange was carried out on the resulting acid by introducing a steam of nitrogen saturated with D_2O into the reaction flask, which was heated to 175°. The steam of nitrogen thus introduced fresh D_2O into the reaction vessel where acid-catalyzed exchange occurred and swept out the resulting D_2O–H_2O vapor which was recovered in a Dry Ice trap. In this manner, 90 g. (4.5 moles) of D_2O was introduced into the reaction flask over a period of one week. The crude deuterated acid was purified by distilling at reduced pressure yielding 231 g. of 4-methylcyclohexane-1-*d*-carboxylic acid (73%), b.p. 123.0–124.5° (10.5 mm.), deuterium content 72%.[27]

Deuteration of Methyl 4-Methylcyclohexanecarboxylate by Base-catalyzed Exchange.—A 156-g. (1.0 mole) sample of methyl 4-methylcyclohexanecarboxylate was refluxed successively with three dilute solutions of sodium methoxide in deuteriomethanol, prepared by adding 1.5 g. (0.065 mole) of sodium to 99 g. (3 moles) of deuteriomethanol. After a 3-week period deuteration had occurred to an extent greater than 96%. A mixture of 127 g. (0.814 mole) of methyl 4-methylcyclohexane-1-*d*-carboxylate was refluxed with 33 g. (0.825 mole) of sodium hydroxide dissolved in 1000 ml. of water until solution was complete (16 hr.). The solution was acidified with 40 ml. of concd. hydrochloric acid and the resulting 4-methylcyclohexane-1-*d*-carboxylic acid was isolated in the usual fashion to give 109 g. (94%) of product, deuterium content 46%.[27]

Preparation of Alkylmercuric Benzoates and Acetates.—A typical experiment is described. A 5.0-g. (0.0132 mole) sample of *trans*-4-methylcyclohexylmercuric bromide was stirred with 11.45 g. (0.05 mole) of silver benzoate in 1 liter of methanol for 2.5 days at 25°. The precipitated silver bromide and unreacted silver benzoate were removed by filtration and the volume of methanol was reduced to approximately 100 ml. The resulting solution was filtered and reduced to dryness yielding 4.6 g. of crude *trans*-benzoate (83%). This material was recrystallized once from acetone–water and isopropyl alcohol–water yielding 1.95 g. of pure *trans*-4-methylcyclohexylmercuric benzoate, 99.2–99.8°.

Anal. Calcd. for $C_{14}H_{18}O_2Hg$: C, 40.14; H, 4.33; Hg, 47.89. Found: C, 40.32; H, 4.26; Hg, 47.70.

By a similar procedure the following compounds were prepared: *cis*-4-Methylcyclohexylmercuric benzoate, m.p. 44.4–44.9°.

Anal. Found: C, 40.20; H, 4.32; Hg, 47.65. *trans*-4-Methylcyclohexyl-1-*d*-mercuric benzoate, m.p. 99.4–99.8°.

Anal. Calcd. for $C_{14}H_{17}DO_2Hg$: C, 40.04; H, 4.56; Hg, 47.78. Found: C, 40.12; H, 3.38; Hg, 47.65. *cis*-4-Methylcyclohexyl-1-*d*-mercuric benzoate, m.p. 44.2–44.9°.

Anal. Found: C, 40.48; H, 4.38; Hg, 47.60. *trans*-4-Methylcyclohexyl-1-*d*-mercuric acetate, m.p. 114.4–115.4°.

Anal. Calcd. for $C_9H_{15}DO_2Hg$: C, 30.21; H, 4.78; Hg, 56.06. Found: C, 30.17; H, 4.37; Hg, 56.0.

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[27] We are indebted to Seymour Meyerson of the Standard Oil Co. of Indiana for the mass spectra analyses.