ing negative signs. Values of $\Phi$ extend from +100% for perfect correlation ($\epsilon = 0$) to small or even negative values when there is serious scatter. Values of $\Phi$ from 80 to 100% are designated arbitrarily as "excellent," 50–80% as "good," 20–50% as "fair," and less than 20% as "poor," which is generally in accord with subjective evaluation of the corresponding plots by independent observers.

Figure 1 is a plot of one of the oldest linear free-energy relationships, which is included simply to show how much a $\Phi = 77\%$ correlation scatters. The Brönsted equation implies that the free energy of activation of a base- or acid-catalyzed reaction is a constant fraction of the free energy of ionization of the base or acid. The slope $\beta$ is also a measure of the fraction of completion of the proton transfer at the transition state.

Table V gives data for typical fits, which vary from "poor" to "excellent."

CAMBRIDGE 39, MASSACHUSETTS

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, LOS ANGELES]

# Mechanisms of Reaction of Organomercurials.[1] I. Stereochemistry of Electrophilic Displacement on *cis*-2-Methoxycyclohexylneophylmercury by Radio-mercuric Chloride

BY S. WINSTEIN, T. G. TRAYLOR[2] AND C. S. GARNER

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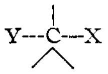
Electrophilic substitution at a saturated carbon atom has been discussed sometimes as analogous to nucleophilic substitution. Possible contrast between the two varieties of substitution, based on electronic and stereoelectronic considerations, is discussed in the present paper. Further, the stereochemistry of electrophilic substitution at a saturated carbon atom has been studied in the case of electrophilic substitution by mercuric chloride on *cis*-2-methoxycyclohexylneophylmercury. The use of radio-mercuric chloride has disclosed the proportions of *cis*-2-methoxycyclohexyl– and neophyl–mercury cleavage. The methoxycyclohexylmercuric chloride derived from the cleavage reaction has been shown, by a sensitive test for the *trans* isomer, to be very pure *cis* material. This result, coupled with the information on the extent of methoxycyclohexyl–mercury bond cleavage in the substitution, shows that substitution on *cis*-2-methoxycyclohexyl proceeds with retention predominating over inversion by a factor of at least 100 to 1. Possible mechanisms for the substitution with retention of configuration are discussed.

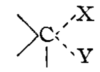
Electrophilic substitution at a saturated carbon atom, much less understood than the nucleophilic variety, has been discussed sometimes as analogous to nucleophilic substitution. Thus, Hughes and Ingold,[3] in their 1935 review of substitution, suggested an $S_E1$–$S_E2$ classification for electrophilic substitution analogous to $S_N1$–$S_N2$ for the nucleophilic case. They suggested a rate sequence, *t*-Bu > *i*-Pr > Et > Me, for $S_E2$, opposite to the one generally prevailing for $S_N2$. Also, at that time, they tentatively visualized, for the stereochemical outcome of electrophilic substitution, inversion of configuration in $S_E2$, as in $S_N2$,[4] and retention of configuration in $S_E1$, as in $S_N1$.[4] Much more recently, Dewar[5] has commented that "cationoid replacements undoubtedly conform to the same general principles as do their anionoid counterparts."

We have been interested in the analogy between electrophilic and nucleophilic substitution at a saturated carbon atom. Just as for nucleophilic substitution, internal or cyclic mechanisms of electrophilic substitution, $S_Ei$, need to be considered. Also, for the spectrum of possible transition states in $S_E2$ or SEi substitution, we must visualize various degrees of importance of bond formation to the carbon atom undergoing substitution.

Considering stereochemical outcome of $S_N2$ substitution, the most stable transition state I is attained by trigonal ($sp^2$) hybridization of orbitals on the central carbon atom, a *p* orbital serving for the partial bonds to the leaving and entering nucleophiles. This arrangement, leading to inverted product, apparently maximizes bonding[6] and minimizes repulsion[7] between electron pairs, of which there are five, in separate bonds. It does not follow that this type of orbital hybridization will be favored also for the transition state in $S_E2$, involving one less pair of electrons in the five full or partial bonds to the central carbon atom. Not only is repulsion between separate electron pairs in a transition state of the type II less serious in electrophilic than in nucleophilic substitution, but, in some cases extra stabilization may be associated with this variety of transition state. In electrophilic substitution on carbon by an electrophilic reagent, E, the transition state may be regarded as electron-deficient, and, in some cases at least, extra stabilization may be derived from bonding between the leaving group X and the incoming group E. This is symbolized with the contribution of structure IIIc to the hybrid transition III, or by the summary symbol IV. At any rate, we ap-



I



II

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(1) Some of the material of this paper was presented at the Organic Reaction Mechanisms Conference, Northwestern University, Evanston, Ill., Aug. 31, 1950.

(2) U. S. Rubber Co. Fellow, 1951–1952.

(3) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 244 (1935).

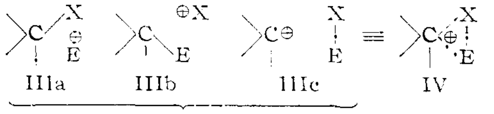
(4) Subsequent work on nucleophilic substitution proved inversion the rule in $S_N2$. However, a number of possible outcomes of nucleophilic substitution by way of cationic intermediates is possible, depending on the stability and ion pair character of the intermediate, nucleophilic character of the solvent, anchimeric effects, etc.

(5) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Oxford University Press, Oxford, 1949, p. 81.

(6) Reference 5, page 64.

(7) E. D. Hughes and C. K. Ingold, *et al.*, *J. Chem. Soc.*, 1252 (1937).

proached electrophilic substitution with the expectation that retention of configuration would be an entirely plausible and possibly general stereochemical outcome of concerted substitution.[8]


IIIa IIIb IIIc IV

Cases of concerted electrophilic substitution at a saturated carbon atom are at least very rare, except with organometallic substances. Many electrophilic substitutions at a saturated carbon atom, such as halogenation or deuterium exchange of ketones or certain decarboxylations, are to be classed as $S_E1$. Also, many attacks of electrophilic reagents on saturated carbon compounds occur on an atom other than carbon and thus lead to nucleophilic substitution on carbon. For example, the powerfully electrophilic carbonium ions tend to attack hydrocarbons or alkyl halides on hydrogen or halogen, respectively.[9] The carboxylic acid silver salt–bromine reaction has been suggested[10] to proceed by an $S_E2$ mechanism with Walden inversion, but the mechanism of this reaction is clearly radical.[11]

A simple way to provide for concerted electrophilic substitution on saturated carbon is to employ an organometallic substance as the substrate. Organomercurials represent some of the most convenient materials for experimental study. Also, with organomercurials there already exists a broad qualitative background and some semiquantitative impression of relative reactivities.[12] This series of papers reports some mechanistic studies with organomercurials, not only in electrophilic substitution but in other reactions.

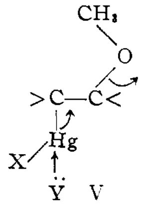
In the present paper we report the results of a study of the stereochemistry of substitution by mercuric chloride on an unsymmetrical dialkylmercury,[13] R–Hg–R′, as in equation 1. The reaction of mercuric chloride with dialkylmercuries is well known,[13] but the only previous cases where

$$R{-}Hg{-}R' + HgCl_2 \longrightarrow RHgCl + ClHgR' \quad (1)$$

the stereochemical result is clear involve divinylmercury compounds.

Bis-2-chlorovinylmercury reacts with mercuric chloride to yield 2-chlorovinylmercuric chloride with retention of configuration.[14] Retention of configuration at a trigonal carbon atom also is observed in other substitution reactions of organomercury or antimony compounds.[15] In fact, retention of configuration at a trigonal carbon atom is common in other conversions[16,17] of vinyl compounds, $>C{=}C\langle^{X}$, to $>C{=}C\langle^{E}$ where X = Br, E = Li; X = Li, E = $CO_2$; X = COOH, E = H, X = Cl, E = H; and X = $C_6H_5CO$, E = H. From stereoelectronic considerations retention of configuration at a trigonal carbon atom seems a perfectly normal result for $S_E1$, $S_E2$ or $S_Ei$ substitution. However, these results have little bearing on the stereoelectronically dissimilar substitution at a saturated carbon atom.

For the R group in R–Hg–R′ we employed *cis*-2-methoxycyclohexyl, derived from 1-chloromercuri-2-methoxycyclohexane (VI), whose configuration recently has been investigated by X-ray diffraction.[18] For the method of incorporation of R with unchanged configuration into a dialkylmercury, the reaction of RHgCl with a Grignard reagent,[13] R′MgCl, was employed. This reaction, representing nucleophilic displacement on mercury of the RHgCl, should preserve configuration of R. The *cis*-2-methoxycyclohexylmercuric chloride (VI) was the more suitable diastereomer for this type of synthesis because of the relative inertness to E2 type elimination reactions, favorable in the case of the *trans* isomer, as symbolized in V.


V

To balance possible sluggishness of electrophilic substitution on cyclohexyl, neophyl was employed for R′ in RHgR′ because of other evidence of relatively slow electrophilic substitution on neophyl.[19,20] To determine how much R–Hg cleavage actually occurred in the reaction of RHgR′ with mercuric chloride (equation 1), mercuric chloride labeled with $Hg^{203}$ was employed in the substitution.

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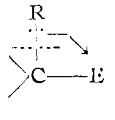
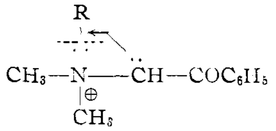
[8] In many rearrangements of the Wagner–Meerwein, Beckmann and Lossen type, electrophilic displacement on the migrating group R by the electrophilic center, in what can be classified as an $S_Ei$ substitution, occurs with retention of configuration. However, these results may not be extrapolated to $S_E2$ substitution, since even an $S_Ni$ analog of the above $S_Ei$ cases, where substitution on R is by a nucleophilic center proceeds with retention [A. Campbell, A. H. J. Houston and J. Kenyon, *J. Chem. Soc.*, **93**, (1947); C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 527; J. H. Brewster and M. W. Kline, Abstracts of 122nd Meeting of American Chemical Society, Atlantic City, N. J., Sept. 14-19, 1952, p. 29M].


$S_Ei$


$S_Ni$

[9] P. D. Bartlett, F. E. Condon and A. Schneider, THIS JOURNAL, **66**, 1531 (1944).

[10] J. Kenyon, C. L. Arcus and A. Campbell, *J. Chem. Soc.*, 1510 (1949).

[11] *E.g.*, C. Berr, Dissertation, U. C. L. A., 1952, and many references quoted therein.

[12] F. C. Whitmore, "Organic Compounds of Mercury," Chemical Catalog Co. (Reinhold Publ. Corp), New York, N. Y., 1921.

[13] M. S. Kharasch and R. Marker, THIS JOURNAL, **48**, 3130 (1926).

[14] A. N. Nesmeyanov, A. E. Borisov and A. N. Guskova, *Bull. Acad. Sci. U.R.S.S. Classe sci. chim.*, 639 (1945); *C. A.*, **40**, 4659 (1946).

[15] A. N. Nesmeyanov, *et al.*, (a) *Bull. acad. sci. U.R.S.S., Classe, sci. chim.*, 239 (1945); (b) *Doklady Akad. Nauk. S.S.S.R.*, **60**, 67 (1948); (c) *Izvest. Akad. Nauk., S.S.S.R. Otdel Khim. Nauk*, 578 (1949).

[16] See L. Crombie, *Quart. Revs.*, **6**, 137 (1952), for a review.

[17] E. Grovenstein, Jr., and D. E. Lee, THIS JOURNAL, **75**, 2639 (1953).

[18] G. F. Wright and A. G. Brook, *Acta Cryst.*, **4**, 50 (1951).

[19] J. Keller, Dissertation, U. C. L. A., 1948.

[20] S. Winstein and T. G. Traylor, THIS JOURNAL, **77**, 3747 (1955).

As is clear from equations 2 and 3, R–Hg cleavage (A) results in incorporation of radiomercury into

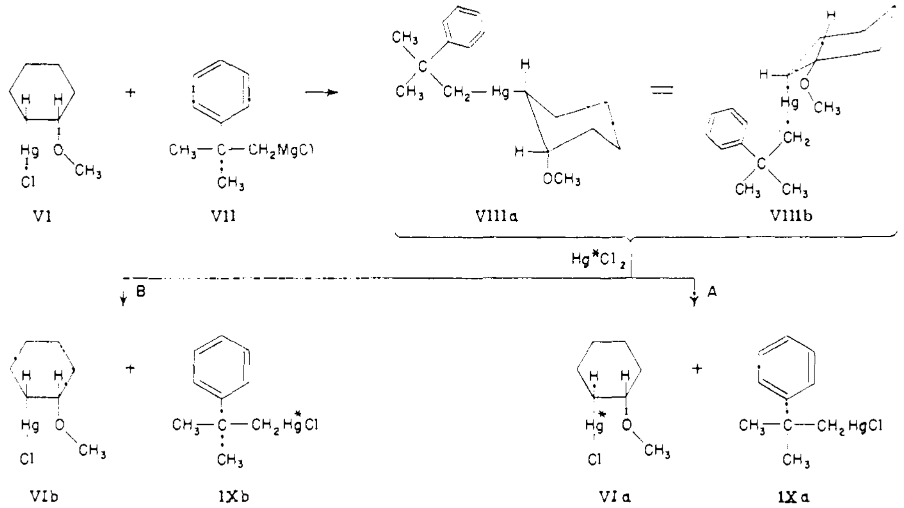
$$\text{R—Hg—R}' + \overset{*}{\text{Hg}}\text{Cl}_2 \xrightarrow{\text{A}} \text{R}\overset{*}{\text{Hg}}\text{Cl} + \text{R}'\text{HgCl} \quad (2)$$

$$\text{R—Hg} + \text{R}'\text{—}\overset{*}{\text{Hg}}\text{Cl}_2 \xrightarrow{\text{B}} \text{RHgCl} + \text{R}'\overset{*}{\text{Hg}}\text{Cl} \quad (3)$$

RHgCl, while R′–Hg cleavage (B) incorporates it into R′HgCl.

## Results

**Cleavage of *cis*-2-Methoxycyclohexylneophylmercury.**—*cis*-2-Methoxycyclohexylneophylmercury (VIII) was prepared in ether solution by reaction of *cis*-2-methoxycyclohexylmercuric chloride (VI) and neophylmagnesium chloride (VII) at −5°. Titration for the Grignard reagent before and after reaction indicated complete disappearance of the Grignard reagent. The mixed dialkylmercury VIII was not isolated as such, but was treated directly with approximately an equimolar quantity of labeled mercuric chloride at −5°. The *cis*-2-methoxycyclohexylmercuric chloride (VIab) crystallized out of the reaction mixture very soon, indicating rapid reaction of the mixed mercurial.



**Isolation and Identification of the Cleavage Products.**—The products of the reaction were separated by crystallization from methanol in which neophylmercuric chloride (IX) is much more soluble than is *cis*-2-methoxycyclohexylmercuric chloride (VI). Recrystallizations gave rise to *cis*-2-methoxycyclohexylmercuric chloride (VI), identified by melting point, mixed melting point with authentic *cis*-2-methoxycyclohexylmercuric chloride, mixed melting point with *trans*-2-methoxycyclohexylmercuric chloride (30° depression), and carbon–hydrogen analysis. The yield of the very pure fractions of *cis*-2-methoxycyclohexylmercuric chloride (VI) was 50%, based on the amount of this compound used initially. The purification of neophylmercuric chloride (IX) was somewhat more difficult because it contained about 0.5 g. of unreacted mercuric chloride. However, a small yield (29%) of the pure product, plus an equal amount of impure product, was obtained by recrystallizing from acetic acid the remainder of the product after separation of *cis*-2-methoxycyclohexylmercuric chloride (VI).

It was possible to place an upper limit on the amount of *trans*-2-methoxycyclohexylmercuric chloride obtained in the cleavage of *cis*-2-methoxycyclohexylneophylmercury (VIII) on the basis of a test depending on the sensitivity of the *trans* isomer to acid. A one-minute period in acetic acid solvent on the steam-bath causes elimination of the elements of HgCl(OCH$_3$) from the *trans* isomer, so that subsequent treatment with excess sodium hydroxide gives yellow mercuric oxide. Controls showed the test would indicate the presence of less than 3% of the *trans* compound in other more resistant mercurials. Tests for the *trans* isomer were performed both on the methoxycyclohexylmercuric chloride part and the neophylmercuric chloride part of the cleavage product.

The residue from evaporation of the filtrate from recrystallization of *cis*-2-methoxycyclohexylmercuric chloride (VI) was shown by the test to contain less than 3% of *trans* isomer. If a small amount of *trans* isomer were present, it would concentrate in the filtrate, and thus the residue would contain essentially all of the *trans* compound present as contaminant in the *cis*-2-methoxycyclohexylmercuric chloride part of the cleavage product. Since the residue represented only *ca.* one-tenth of this part of the cleavage product, less than 0.3% of the *trans* isomer must have been present in the whole part.

When *ca.* one-fifth of the neophylmercuric chloride part of the cleavage product (the residue from recrystallizations) was tested for *trans*-2-methoxycyclohexylmercuric chloride, it also showed less than 3% of this compound present. Therefore, this part of the product contained less than 0.6% of the *trans* compound, and the entire reaction product contained less than 0.3% of *trans*-2-methoxycyclohexylmercuric chloride.

**Tests for Exchange between Mercuric Chloride and Alkylmercuric Chlorides.**—As a control on possible exchange of mercury between mercuric chloride and *cis*-2-methoxycyclohexyl- (VI), neophyl- (IX) and *trans*-2-methoxycyclohexyl- (T) mercuric chlorides, each of the three alkyl mercuric salts was allowed to react for six times the duration of the cleavage experiment with labeled mercuric chloride, and the alkyl mercuric salts were recovered, purified, and counted for radioactivity. The results of the experiments are summarized in Table I.

Although the activity observed for some of the recovered products was close to background, the slight net count indicated was compared with the activity which would result if statistical distribution of the labeled mercury were obtained. This yielded a percentage exchange in each case, tabulated in column 7 as 0.5, 2.0 and 6.0% for VI, T and IX.

TABLE I

TESTS FOR EXCHANGE OF MERCURY BETWEEN MERCURIC CHLORIDE AND ALKYLMERCURIC CHLORIDES

| Compound | Net count,[a] c./m. | Count per 30 ml. soln., c./m. | Wt. solute in 30 ml., g. | Activity per gram solute, c./m./g. | Theor.[b] act. for sample counted, c./m. | % of theoretical activity in sample | % std. devn. in cols. 2 and 3 |
|---|---|---|---|---|---|---|---|
| $HgCl_2$ | 3150 | 4730 | 1.1133 | 4250 | | | 1.8 |
| IX | 21 | 31 | 0.3257 | | 520 | 6.0 | 11.5 |
| VI | 4 | 6 | .8215 | | 1250 | 0.5 | 43 |
| T[c] | 12 | 18 | .9120 | | 904 | 2.0 | 24 |

[a] All samples were counted the same day on the same apparatus, so that no decay or other corrections were necessary. [b] In this column is recorded the activity that would be observed in the sample counted if the activity were statistically distributed between the two compounds. This number is obtained as follows: the activity per gram of mercuric chloride (1 g. used in each experiment) was multiplied by the ratio of the moles of mercurial to the total number of gram atoms of mercury in the experiment, and this product was multiplied by the fraction of the mercurial which was counted. [c] *trans*-2-Methoxycyclohexylmercuric chloride.

TABLE II

RADIOACTIVITY OF PRODUCTS AND STARTING MATERIALS IN THE REACTION OF *cis*-2-METHOXYCYCLOHEXYLNEOPHYLMERCURY WITH MERCURIC CHLORIDE

| Compound | Date | Counter tube number | Net count, c./m. | Count per 30 ml. soln., c./m. | Wt. prod. in 30 ml. soln., g. | Mmoles[a] prod. in 30 ml. soln. | Count per mg.-atom Hg in prod., c./mg.-at./m. | Count per mg.-atom Hg decay cor., c./mg.-at./m. | % Activity based on $HgCl_2$ used | % std. devn. col. 9 |
|---|---|---|---|---|---|---|---|---|---|---|
| Radio-$HgCl_2$ | 12 | 5090[b] | 3470 | 4160 | 0.5743 | 2.115 | 1970 | 1970 | 100 | 1.2 |
| 1st crop of VI | 12 | 5090 | 1195 | 1435 | .7317 | 2.100 | 684 | 684 | 34.7 | 2.0 |
| 2nd crop of VI | 26 | 5157[c] | 399 | 490[d] | .3185 | 0.914 | 537 | 670 | 34.0 | 2.9 |
| 1st crop of IX | 21 | 5090 | 1007 | 1207 | .5012 | 1.357 | 890 | 1029 | 52.3 | 2.2 |
| 2nd crop of IX | 26 | 5157 | 1010 | 1242[d] | .554 | 1.500 | 828 | 1035 | 52.5 | 2.2 |
| Same soln. used in line 4 + 1.0 g. $HgCl_2$ | 26 | 5090 | 952 | 1142 | | Ratio 0.819 | | 1232[e] | | 2.3 |
| Same as above | 26 | 5157 | 932 | 1396 | | | | | | 2.3 |

[a] Since all products contain one mercury atom per molecule, this column is actually the number of mg.-atoms of mercury in the sample of product weighed for counting. [b] 25.00 ml. [c] 20.00 ml. [d] Corrected to correspond to measurements made by tube 5090. [e] This number is taken from column 5, line 6, and decay corrected to compare with column 5, line 4.

Thus, exchange is within experimental error of zero for *cis*-2-methoxycyclohexylmercuric chloride (VI), the most important case, and negligible even with neophylmercuric chloride (IX) if one allows for the long duration of the exchange experiments.

**Radioactivity of the Cleavage Products.**—The radioactivities of the cleavage products are summarized in Table II. For comparison of the activities of the products with that of the original mercuric chloride, all counts were converted to counts per mg.-atom of mercury. These were decay corrected using the 43.5 day half-life. When the corrected activity per mg.-atom of mercury is divided by the activity per mg.-atom of mercury in the mercuric chloride, the result is the fraction of labeled mercury in the product (column 10).

As a check whether the observed activities of the reaction products were affected by impurities, two crops from recrystallization of each product were counted. The activities of successive crops were identical in each case, as summarized in Table II.

## Discussion

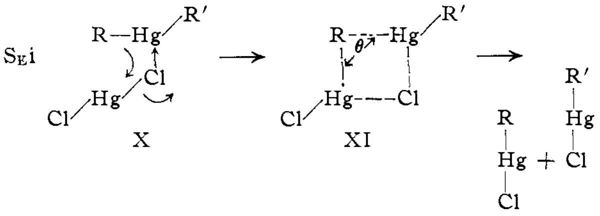
From the data in Table II it is clear that, of the recovered products, the *cis*-2-methoxycyclohexylmercuric chloride (VI) contained 0.35 times and the neophylmercuric chloride (IX) contained 0.52 times the activity per mole contained in the starting mercuric chloride. Since titration of the reaction mixture just before the addition of mercuric chloride showed no Grignard reagent present, and some mercuric chloride was recovered from the cleavage reaction, it is clear that somewhat insufficient neophyl Grignard reagent VII was used in the synthesis of *cis*-2-methoxycyclohexylneophylmercury (VIII). Since there was no excess Grignard reagent, all the neophylmercuric chloride (IX) is derived from the cleavage reaction. Therefore, the activity found in this product is a true measure of the extent of reaction of the *cis*-2-methoxycyclohexylneophylmercury (VIII) by path B with neophyl–mercury bond cleavage (*i.e.*, 52%). Therefore, the percentage of *cis*-2-methoxycyclohexyl-mercury bond cleavage (path A) is 48.

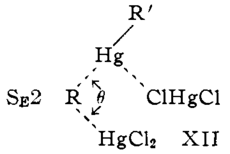
On the basis of the radioactivity measurements, 35% of the 2-methoxycyclohexylmercuric chloride (VI) which was isolated was derived from 2-methoxycyclohexyl–mercury bond cleavage (A). Since less than 3 parts of *trans*-2-methoxycyclohexylmercuric chloride per thousand of the *cis* isomer was observed in the over-all product, *cis*-2-methoxycyclohexyl-mercury bond cleavage (A) is associated with formation of less than 1% of *trans*- and more than 99% of *cis*-2-methoxycyclohexylmercuric chloride (VI).

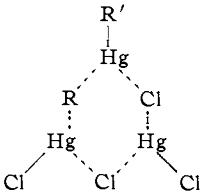
The lack of exchange between mercuric chloride and the *cis*- and *trans*-2-methoxycyclohexylmercuric chlorides and neophylmercuric chloride demonstrates that the introduction of radio-mercury into the organic substances is associated with the cleavage of the dialkylmercury VIII. It makes untenable any explanation of the stereochemical outcome of the cleavage based on prior formation of some or entirely *trans*-2-methoxycyclohexylmercuric chloride which is in turn converted to *cis* isomer by another Walden inversion.

The present work shows that electrophilic displacement by mercuric chloride on *cis*-2-methoxycyclohexyl (A) in the mercurial VIII, proceeds with retention of configuration predominating over inversion by a factor of at least 100. Thus, whatever the mechanism of the reaction, the transition state geometry must be such as to lead to retention.

The importance of nucleophilic attack on the metal atom in reactions of organometallic substances, often commented[21] on, must be taken into account in the case of organomercurials.[19] In the absence of a kinetic study of the present reaction, which could disclose the composition of the transition state, two general style mechanisms are consistent with the present stereochemical results. The most attractive mechanism has one mercuric chloride molecule playing the roles of both the nucleophilic and electrophilic agent. It is a cyclic or 4-center mechanism which can be labeled $S_Ei$, pictured as a reaction of a complex X obtained by coördination of mercuric chloride to the dialkylmercury. This mechanism is similar to that suggested by Johnson[21] for cleavage of a dialkylmercury by hydrogen chloride. Other possible mechanisms are variations of the $S_E2$ type; for example, one involving one mercuric chloride molecule in an electrophilic role and another in a nucleophilic one, as in the transition state XII. The depicted transition states XI and XII for the possible $S_Ei$ and $S_E2$ mechanisms do not specifically indicate still other possible bonding interactions. For example, in XII, the two attacking mercuric chloride molecules may be coördinated through a chlorine atom as in XIII. On this basis one might prefer the $S_Ei$ designation. Also, if one considers reasonable values of the Hg–R–Hg angle, $\theta$, in XI or XII and the known[18,22,23] bonding radius of mercury, it is seen that the Hg–Hg distance can be sufficiently short for some Hg–Hg bonding in the sense of formulas IIIc or IV.

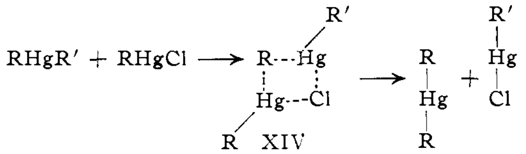


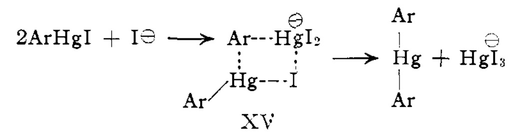




XIII

Another reaction with probably an analogous mechanism is the disproportionation[24] of dialkylmercury compounds by alkylmercuric chloride, RHgCl, a poorer electrophile than mercuric chloride. Still another is the formation of diarylmercury[25] by the action of iodide ion on arylmercuric iodide. Possible transition states are XIV and XV.





The strong preference for retention rather than inversion of configuration in the electrophilic substitution of VIII suggests that retention may be a generally favored result of concerted electrophilic displacements. However, the present results on one electrophilic reagent, mercuric chloride, on a cyclohexyl system, and even then with a $\beta$-alkoxyl group, should not be generalized without data on other reagents and systems.

Since completion of the present investigation, some reports of other pertinent investigations have appeared. Wright[26] treated *trans*-2-methoxycyclohexylmercuric chloride with aqueous alkaline hydrazine. Under these conditions, the mercurial is converted in part, presumably by a free radical path, to a mixture of *cis–cis*, *cis–trans* and *trans–trans* dialkylmercury. Treatment of this mixture with methanolic mercuric acetate and then aqueous sodium chloride gave a mixture of *cis*- and *trans*-2-methoxycyclohexylmercuric chloride.[27] However, isolation of the most stable component of the dialkyl mercury by repeated distillation and treatment of it with methanolic-mercuric acetate and aqueous sodium chloride gave pure *cis*-2-methoxycyclohexylmercuric chloride (VI). Although another assumption was possible, it was assumed that the most stable bis-2-methoxycyclohexylmercury was *cis–cis*, and, therefore, that the reaction with mercuric acetate proceeded with retention of configuration. The present proof that displacement on *cis*-2-methoxycyclohexyl proceeds with retention of configuration, together with the plausible extrapolation that displacement on *trans*-2-methoxycyclohexyl also gives retention, confirms Wright's assignment of configuration.

Some displacements at the asymmetric carbon atom of some optically active mercurials recently have been reported by Nesmeyanov and co-workers.[28] Each pure diastereomeric *l*-menthoxy $\alpha$-phenyl-$\alpha$-bromomercuriacetate (XVI) was reported to react stereospecifically with ammonia in chloroform to yield pure LL- or DD-dialkylmercury XVII with retention of configuration. However, the reaction of XVII with mercuric bromide in boiling acetone was reported to be non-stereospecific, the same approximately equimolar mixture of diastereo-

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[21] *E.g.*, J. Johnson, Chapter 25 in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1943.

[22] *E.g.*, P. W. Allen and L. E. Sutton, *Acta Cryst.*, **3**, 52 (1950).

[23] D. Grdenic, *ibid.*, **5**, 367 (1952).

[24] *E.g.*, G. Calingaert, H. Soroos and V. Hnizda, THIS JOURNAL, **62**, 1107 (1940).

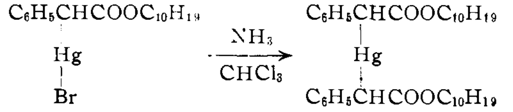
[25] F. C. Whitmore and R. J. Sobatski, *ibid.*, **55**, 1128 (1933).

[26] G. F. Wright, *Can. J. Chem.*, **30**, 268 (1952).

[27] Similar results are obtained by conversion of *trans*-2-methoxycyclohexylmercuric chloride to dialkylmercury with sodium stannite, followed by treatment of the mixed dialkylmercury with ethereal mercuric chloride [T. G. Traylor, Dissertation, U.C.L.A., 1952].

[28] A. N. Nesmeyanov, O. A. Reutov and S. S. Poddubnaya, *Doklady Akad. Nauk S.S.S.R.*, **88**, 479 (1953); *C. A.*, **48**, 2632 (1954).

mers of XVI being derived from each pure XVII. The approximately equimolar nature of the product XVI is equivalent to the occurrence of inversion at the seat of substitution in the reaction of XVII.



$$\underset{\text{XVI}}{\begin{array}{c}C_6H_5CHCOOC_{10}H_{19}\\ |\\ Hg\\ |\\ Br\end{array}} \xrightarrow[CHCl_3]{NH_3} \underset{\text{XVII}}{\begin{array}{c}C_6H_5CHCOOC_{10}H_{19}\\ |\\ Hg\\ |\\ C_6H_5CHCOOC_{10}H_{19}\end{array}}$$

The retention of configuration claimed in the formation of dialkylmercury XVII from alkylmercuric bromide XVI would be in line with the present work. A likely mechanism for the reaction would be akin to the one for the action of iodide ion on arylmercuric iodide to yield diarylmercury (see XV). However, the reported inversion of configuration in the reaction of dialkylmercury XVII with mercuric bromide would need to be either $S_E2$ or $S_E1$. Actually, the presence of both a phenyl and a carboalkoxy group on the asymmetric carbon atom in XVII could seriously affect matters. One effect would be to strongly favor an $S_E1$ mechanism, but other effects are possible. Further investigation of this and other structures would be desirable.

## Experimental Part

All melting points are corrected.

**Measurement of Radioactivity.**—All activity was measured in solution with a dipping Geiger–Mueller tube and an associated scale-of-64 circuit. The tube, holder, and cell were similar to those used and described by Meier.[29] Counting rates were sufficiently low so that coincidence loss corrections were unnecessary. A correction for background (*ca.* 25 c./m.) was applied. Essentially only the $\gamma$-radiation associated with the decay of $Hg^{203}$ was detected, the 0.2 Mev. negatrons being absorbed fully in the counter tube wall.

The solid samples were weighed accurately, dissolved in 30.00 ml. of dimethylformamide (Eastman Kodak white label), and either 20.00 ml. or 25.00 ml. (depending on the counter tube used) of the solution pipetted into the dipping counter cell. This solution was counted as described by Meier.[29] The concentration of inactive mercuric chloride was shown to have little influence on the count of the solution.

**Radiomercury Tracer.**—The 43.5 day $Hg^{203}$ isotope was used as the mercury tracer. It was supplied by the Oak Ridge Laboratory as catalog item number 80B-R processed as mercuric nitrate in 2 formal nitric acid, and reported to be 99.9% radiochemically pure. No further purification was carried out. Half-life measurements gave a value of 41 days, in approximate agreement with 43.5 days reported by Saxon.[30] The mercuric nitrate solution (0.3 ml.), labeled with $Hg,^{203}$ contained about 90 mg. of mercury and 1 millicurie of radioactivity. Twenty-five microliters of this solution was placed in a 250-ml. erlenmeyer flask and evaporated to dryness. A 5-ml. quantity of 12 *N* hydrochloric acid was added, and the solution was again evaporated to near-dryness. Mercuric chloride (5.0 g., J. T. Baker analyzed) and about 100 ml. of water were added and the resulting mixture heated until the mercuric chloride dissolved. The resulting solution was filtered and evaporated to dryness. The resulting solid was dissolved in 200 ml. of ethyl ether, and the filtered solution was evaporated slowly to produce large prisms of mercuric chloride whose radioactivity is recorded in Table II.

***cis*-2-Methoxycyclohexylmercuric Chloride.**—*trans*-2-Methoxycyclohexylmercuric chloride, m.p. 116.0–116.3°, was isomerized to the *cis* compound, m.p. 112.0–112.5°, with benzoyl peroxide as described by Wright and Romeyn.[31] The mixed m.p. of the above compounds was 85–95°.

***cis*-2-Methoxycyclohexylneophylmercury.**—Neophyl Grignard reagent was prepared from neophyl chloride by the usual method using a 50% excess of magnesium and a dry nitrogen atmosphere. (The entire synthesis of *cis*-2-methoxycyclohexylneophylmercury and its subsequent cleavage by mercuric chloride were carried out under dry nitrogen.) Titration of the solution by the method of Gilman[32] indicated the concentration of the Grignard reagent to be 1.16 *M*.

An 8.9-ml. aliquot (0.01 mole) of the Grignard reagent was pipetted (by use of an automatic pipet which was part of the Grignard apparatus designed to exclude air) into a 100-ml. flask containing about 60 ml. of dry ethyl ether. After cooling the resulting solution to −80°, the *cis*-2-methoxycyclohexylmercuric chloride (3.48 g., 0.01 mole) was added quickly, and the mixture was allowed to warm to −5°. It was stirred overnight at this temperature. The magnesium chloride which had precipitated was removed by filtering the solution (at −5°) through a medium porosity sintered glass filter funnel. Titration of an aliquot of the filtrate showed only a trace of basic material.

**Reaction of Labeled Mercuric Chloride with *cis*-2-Methoxycyclohexylneophylmercury.**—To the above filtrate (which was kept at −5°) was added 2.71 g. (0.01 mole) of the labeled mercuric chloride. The resulting mixture was allowed to warm to room temperature. *cis*-2-Methoxycyclohexylmercuric chloride crystallized out, indicating very rapid reaction.

After 24 hours, the mixture was filtered, and the precipitate was washed with water, air-dried and recrystallized from Skellysolve B–chloroform to yield 0.4 g. of *cis*-2-methoxycyclohexylmercuric chloride, m.p. 112.3–113.1°. The filtrate (ether solution) was evaporated to dryness. The colorless solid which was obtained was dissolved in 50 ml. of methanol at 50°, and this solution was allowed to cool until most of the *cis*-2-methoxycyclohexylmercuric chloride crystallized as large prisms and neophylmercuric chloride began to precipitate (very fine needles). This mixture was warmed enough to dissolve the neophylmercuric chloride, and the mother liquor (M) was decanted from the solid. The solid, m.p. 107–110°, mixed m.p. with authentic *cis*-2-methoxycyclohexylmercuric chloride 109°, weighed 1.5 g., the total crude yield being 1.9 g. (55%). The crude product was recrystallized from methanol. The first crop of crystals, m.p. 112.3–114.3°, mixed m.p. with *trans*-2-methoxycyclohexylmercuric chloride 86–94°, weighed 1.2 g.

*Anal.*[33] Calcd. for $C_7H_{13}OHgCl$: C, 24.14; H, 3.76. Found: C, 24.11; H, 3.83.

The crystallization from methanol yielded a 0.4-g. second crop of material, m.p. 111.7–113.3°, and a 0.12-g. third crop, m.p. 111.8–113.7°, for a 1.72-g. (50%) total yield of pure *cis*-2-methoxycyclohexylmercuric chloride. Radioactivity measurements on the first two crops of material are listed in Table II.

The methanolic filtrate was evaporated to dryness to give 0.18 g. of solid which was tested for *trans*-2-methoxycyclohexylmercuric chloride as follows. A small amount was heated in acetic acid on the steam-bath for 1 minute, cooled, and poured into an excess of 6 *N* sodium hydroxide in ice. A white precipitate was obtained. A mixture of *trans*-2-methoxycyclohexylmercuric chloride and neophylmercuric chloride containing 3% of the former, when treated as above, gave a very definite yellow color of mercuric oxide. Water was added to the mother liquor designated M at 40° until it was turbid. Then it was cooled to 0° to produce colorless needles. These were filtered off and air-dried to yield 2.65 g. of material, m.p. 67–74°. This solid contained 0.5 g. of mercuric chloride which was removed by extracting the neophylmercuric chloride into Skellysolve B–chloroform and evaporating to dryness. The crude neophylmercuric chloride was recrystallized from acetic acid–water, four crops being taken. These were washed with water and dried over sodium hydroxide pellets. The first crop weighed 0.56 g., m.p. 77–79° (m.p. of authentic neophylmercuric chloride is 79.5–80.5°), and the second crop weighed 0.554 g., m.p. 74.3–77.3°. Radioactivity measurements on these first two crops totalling 29% yield, are given in Table II.

The filtrate from the 4 crops of neophylmercuric chloride

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(29) D. J. Meier, Dissertation, U. C. L. A., 1951.

(30) D. Saxon, *Phys. Rev.*, **74**, 849 (1948).

(31) G. F. Wright and J. Romeyn, THIS JOURNAL, **69**, 697 (1947).

(32) H. Gilman, *et al.*, *ibid.*, **45**, 156 (1923).

(33) Analysis by Dr. A. Elek, Los Angeles, California.

was evaporated to dryness to leave *ca.* 0.5 g. of solid residue. This gave a negative test for mercuric chloride (or *trans*-2-methoxycyclohexylmercuric chloride) by the procedure described above.

**Tests for Exchange between Mercuric Chloride and Alkylmercuric Chlorides.**—To 1.5 g. (0.0043 mole) of *cis*-2-methoxycyclohexylmercuric chloride in *ca.* 40 ml. of ethyl ether was added 1.0 g. (0.0037 mole) of labeled mercuric chloride. The mixture was heated to dissolve the reactants and left at room temperature for 6 days, after which time it was evaporated to dryness. The solid obtained was treated with 30 ml. of 10% sodium hydroxide solution with stirring for about 30 minutes, to convert the mercuric chloride into insoluble mercuric oxide and the alkylmercuric chloride into the water-soluble hydroxide. After the mercuric oxide was separated by centrifugation, the mother liquor was added to 10 g. of lithium chloride in water and neutralized with 6 *N* acetic acid, precipitating *cis*-2-methoxycyclohexylmercuric chloride. After filtering, washing with water, and air drying at 40° for several hours, this product weighed 1.3 g. Recrystallization from 30 ml. of methanol–acetone (5 to 1) gave 1.0 g. (67%) of large crystals, m.p. 110.8–113.8°, whose radioactivity is shown in Table I.

Labeled mercuric chloride (1.0 g., 0.0037 mole) was allowed to react with *trans*-2-methoxycyclohexylmercuric chloride (3.0 g., 0.0086 mole) and the product was isolated by the method described above for the *cis* compound. (It was necessary to add 25 ml. of acetone to the reaction mixture to dissolve the reactants.) The 2.7 g. of crude *trans*-2-methoxycyclohexylmercuric chloride recovered was recrystallized from 20 ml. of chloroform–Skellysolve B to yield 1.3 g., which was then recrystallized from 15 ml. of 95% ethanol to give 1.05 g. (34%) of colorless crystals, m.p. 115.3–116.8°, whose radioactivity is shown in Table I.

Labeled mercuric chloride (1.0 g., 0.0037 mole) was dissolved in 40–50 ml. of ethyl ether containing 1.3 g. (0.0035 mole) of neophylmercuric chloride and the solution was allowed to stand 6 days at room temperature. This solution was evaporated to dryness and the resulting solid treated with 10% sodium hydroxide. The mercuric chloride was converted to the oxide, but only a very small amount of the neophylmercuric chloride dissolved. The solid mixture was separated, dried, and the neophylmercuric chloride extracted from the mercuric oxide with chloroform. The extract was evaporated to dryness and the resulting solid recrystallized from ethyl acetate–Skellysolve B. (The finely divided mercuric oxide was difficult to separate by filtration and probably accounts for the small residual radioactivity of the product.) The recrystallized neophylmercuric chloride weighed 0.4 g., the radioactivity being shown in Table I.

LOS ANGELES, CALIFORNIA

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA, LOS ANGELES]

# Mechanisms of Reaction of Organomercurials. II. Electrophilic Substitution on Saturated Carbon. Acetolysis of Dialkylmercury Compounds

BY S. WINSTEIN AND T. G. TRAYLOR[1]

RECEIVED FEBRUARY 4, 1955

Acetolysis of dialkylmercuries has been investigated as an example of electrophilic substitution on carbon. Good first-order kinetics have been observed for the conversion of $R_2Hg$ to RH and RHgOAc in the case of the diphenyl, di-*s*-butyl, di-*n*-butyl and dineophyl derivatives. Acetolysis stops cleanly with cleavage of the first alkyl group, cleavage of the second group being extremely slow. With dineophylmercury, addition of sodium acetate does not affect acetolysis rate, but inclusion of perchloric acid introduces a rapid second-order acidic acetolysis mechanism. In the neutral acetolysis, relative rates give the rate sequence, $(C_6H_5)_2Hg > (s\text{-Bu})_2Hg > (n\text{-Bu})_2Hg > (\text{neophyl})_2Hg$, qualitatively similar to the sequence in triiodide ion cleavage of RHgI. Probable mechanisms for neutral and acidic acetolysis of $R_2Hg$ are discussed along with some of the factors determining rate of electrophilic substitution on carbon.

The acid cleavage of alkylmercury compounds is of interest as an example of electrophilic substitution on carbon.[2] In the case of hydrogen chloride cleavage, unsymmetrical diorganomercury compounds have been studied extensively by Kharasch and co-workers[3] and by Whitmore.[4] What we would now call an $S_E1$ mechanism was suggested by Kharasch for this cleavage. However, typical substances clearly do not follow an $S_E1$ mechanism, but one which requires concerted attack on carbon by the proton donor. The rate of cleavage depends on the presence and the nature of the electrophilic proton donor.[5,6]

Our original plan for the study of electrophilic substitution of organomercury compounds by acids was to measure the rates of reaction of acids with alkylmercuric salts. In this way the HgX moiety of RHgX could be kept constant and secondary effects due to changes in X would not be superimposed on the effects of structural changes in R. However, preliminary work showed that alkylmercuric salts reacted too slowly for rate measurement with glacial acetic acid, or with other non-halogen acids in water and acetic acid as solvents.[6] Alkylmercuric bromides reacted readily with hydrogen bromide in acetic acid, but a study of the kinetics of this reaction and the effects of peroxide and hydroquinone proved this reaction to go completely by a radical path.[6] On the other hand, dialkylmercury compounds react at convenient rates with glacial acetic acid. The kinetics of acetolysis of several dialkyl mercury compounds have been investigated, partly preliminary to stereochemical study. The kinetic study is reported in the present paper.

Corwin and Naylor[5] previously have reported an investigation of the kinetics of the reaction of diphenylmercury (I) with dioxane–acetic acid or dioxane–formic acid mixtures. Following the reaction dilatometrically, these authors observed that the reaction is unaffected by peroxides, faster with formic than acetic acid, first order in diphenylmercury (I) within a run, and slightly less than first order between runs. A typical electrophilic aro-

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(1) U. S. Rubber Co. Fellow, 1951-1952.

(2) S. Winstein, T. G. Traylor and C. S. Garner, THIS JOURNAL, **77**, 3741 (1955).

(3) M. S. Kharasch and R. Marker, *ibid.*, **48**, 3130 (1926).

(4) F. C. Whitmore and H. Bernstein, *ibid.*, **60**, 2626 (1938).

(5) *E.g.*, A. H. Corwin and M. A. Naylor, *ibid.*, **69**, 1004 (1947).

(6) (a) J. L. Keller, Dissertation, U.C.L.A., 1948; (b) S. Winstein, Paper at Organic Reaction Mechanisms Conference, Northwestern University, Evanston, Ill., Aug. 31, 1950.