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

Mechanisms of Reaction of Organomercurials. III. Preparation and Substitution Reactions of Bridgehead Mercurials[1]

BY S. WINSTEIN AND T. G. TRAYLOR[2]

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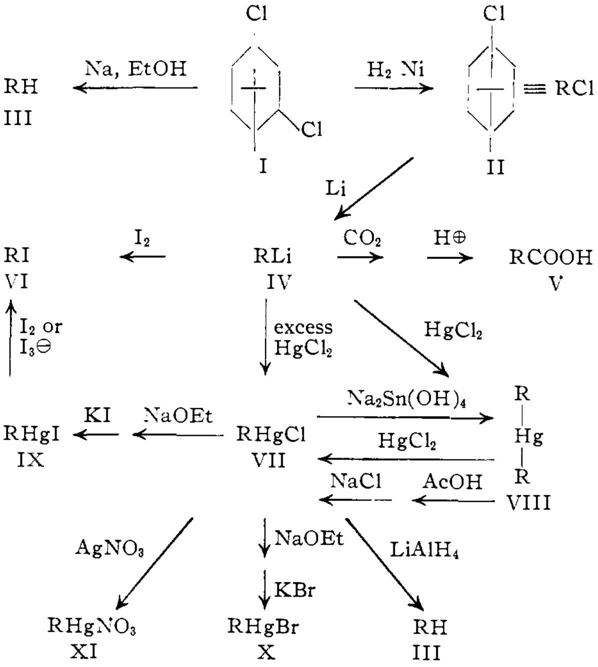
The device of incorporating, as the site of substitution, the bridgehead of a bicyclo[2.2.1]heptane system, illuminating in connection with nucleophilic substitution, has been employed in the study of the behavior of organomercurials. 4-Camphylmercuric chloride, bromide, iodide and nitrate, as well as dicamphylmercury, have been prepared, and substitution reactions of some of these materials have been studied. The prohibitive factor against generation of a cationic center at the bicyclo[2.2.1]heptyl bridgehead, resulting from inefficient use of the 2*s* orbital, is not present in the case of the free radical. Thus, a number of reactions involving bicyclo[2.2.1]heptyl bridgehead radicals are known to proceed well. In the present work, two apparently radical reactions of organomercurials proceeded normally with the 4-camphylmercury derivatives. One reaction involved the conversion of 4-camphylmercuric chloride to dicamphylmercury with sodium stannite solution. The other involved the conversion of 4-camphylmercuric iodide to 4-iodocamphane by iodine in dioxane. This reaction, strikingly oxygen-retarded, proceeded at a rate approximately equal to that for *n*-butylmercuric iodide. In contrast with the inertness of the bicyclo[2.2.1]heptyl bridgehead position to nucleophilic substitution is the relative ease of electrophilic substitution with the 4-camphylmercury derivatives. The investigated electrophilic substitution reactions included the reaction between di-4-camphylmercury and mercuric chloride, neutral first-order and acidic second-order acetolysis of dicamphylmercury, and the second order reaction between 4-camphylmercuric iodide and triiodide ion in slightly aqueous dioxane. All of the electrophilic substitutions of the 4-camphylmercury derivatives necessarily proceed with retention of configuration. The bridgehead derivatives are not especially unreactive, occupying an intermediate position in reactivity between the neophyl and butyl analogs. Thus, there is no indication that the brideghead derivatives are forced to react by a mechanism leading to retention simply because another inherently much more preferable one is excluded by the bridgehead restriction.

The unique situation of the bicyclo[2.2.1]heptyl bridgehead carbon atom completely precludes inversion of configuration and makes extremely difficult the generation of a cationic center in substitution reactions at the bridgehead. For these reasons, bridgehead derivatives have proved illuminating in connection with nucleophilic substitution in the original elegant studies of Bartlett[3] and the more recent ones of Doering.[4,5]

The device of incorporating as the seat of substitution the bridgehead of a bicyclo[2.2.1]heptane system should also be effective in studying electrophilic substitution. In fact, Hughes and Ingold[6] have used the supposed inertness of bridgehead carbon in electrophilic substitution as the basis of a tentative suggestion that S_E2 displacement on saturated carbon normally proceeds with inversion of configuration. These authors judged the bridgehead position to be relatively inert on the basis of available information on liquid phase nitration, a reaction which they, at that time, apparently assumed to be an electrophilic substitution.

In the course of our study of organomercurials[7] several 4-camphylmercury derivatives have been prepared, and they have been subjected, not only to electrophilic substitution reactions, but also to free radical reactions. This work is reported in the present article.

Preparations.—The bridgehead chloride 4-chlorocamphane[4a] (II) was prepared from *dl*-camphor by way of the 2,4-dichlorocamphane[8] (I) very satisfactorily by the method of Doering and Schoenewaldt.[4a] The 4-chlorocamphane (II) was converted to 4-camphyllithium (IV) by a method similar to that described by Doering.[5] When the 4-camphyllithium was treated with excess mercuric chloride, 4-camphylmercuric chloride (VII), a high-melting stable material, was obtained in good yield. When half a mole of mercuric chloride was employed, di-4-camphylmercury (VIII) was obtained, although the yield was not good, perhaps for solubility reasons. The 4-camphylmercuric chloride



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[1] Part of the material of this paper was reported at the Organic Reaction Mechanisms Conference, Northwestern University, Evanston, Ill., August 31, 1950.

[2] U. S. Rubber Company Predoctoral Fellow, 1951–1952.

[3] (a) P. D. Bartlett and L. H. Knox, THIS JOURNAL, **61**, 3184 (1939); (b) P. D. Bartlett and S. G. Cohen, *ibid.*, **62**, 1184 (1940); (c) P. D. Bartlett and E. S. Lewis, *ibid.*, **72**, 1005 (1950).

[4] (a) W. von E. Doering and E. F. Schoenewaldt, *ibid.*, **73**, 2333 (1951); (b) W. von E. Doering, M. Levitz, A. Sayigh, M. Sprecher and W. P. Whelan, Jr., *ibid.*, **75**, 1008 (1953).

[5] (a) W. von E. Doering, private communication; (b) W. von E. Doering, page 35M of Abstracts, 123rd Meeting of the American Chemical Society, Los Angeles, Calif., March 15–19, 1953.

[6] E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 255 (1935).

[7] (a) S. Winstein, T. G. Traylor and C. S. Garner, THIS JOURNAL, **77**, 3741 (1955); (b) S. Winstein and T. G. Traylor, *ibid.*, **77**, 3747 (1955).

[8] (a) H. Meerwein and R. Wortman, *Ann.*, **435**, 190 (1923); (b) J. Houben and E. Pfankuch, *ibid.*, **501**, 219 (1933).

(VII) could be converted conveniently by metathesis to the bromide X, iodide IX and nitrate XI. Alternatively, the bromide X was derived from 4-camphyllithium (IV) and mercuric bromide.

Radical Reactions at the Bridgehead. Reduction of 4-Camphylmercuric Chloride VII with Sodium Stannite.—Although evidence on the mechanism of formation of dialkylmercury from alkylmercuric halide and sodium stannite is very scanty, the indications are that this reaction involves the alkyl free radical.[9] Treatment of 4-camphylmercuric chloride (VII) with aqueous sodium stannite was at first quite unsuccessful for production of di-4-camphylmercury (VIII) but this failure appeared to be due to extreme insolubility of 4-camphylmercuric chloride (VII) in aqueous base. When the suspension of 4-camphylmercuric chloride in sodium stannite solution was stirred for a time with a high speed stirrer, conversion to di-4-camphylmercury (VIII) did take place.

Reaction of 4-Camphylmercuric Iodide (IX) with Iodine.—A thorough study by Keller[10] of the reaction of alkylmercuric iodides with iodine in dioxane showed this reaction to be free radical in nature. The rate of this reaction is very sensitive to light and peroxides, and it is very strongly retarded by oxygen. Only when the reaction mixture was in equilibrium with an atmosphere of air or oxygen was the reaction rate reduced sufficiently to be conveniently measured. Although the rates were somewhat erratic, they were usually reproducible for the first portion of the reaction. The study showed the reaction rate to be roughly second order in iodine and nearly independent of alkylmercuric iodide concentration. Reaction rate was quite insensitive to changes in structure of the alkylmercuric iodide and approximately inversely proportional to oxygen concentration. The observations were consistent with a chain reaction involving attack of iodine atoms on mercury to generate alkyl radicals and reaction of the latter with iodine as in equations 1 and 2.

$$\mathrm{I}\cdot + \mathrm{RHgI} \longrightarrow \mathrm{R}\cdot + \mathrm{HgI_2} \qquad (1)$$

$$\mathrm{R}\cdot + \mathrm{I_2} \longrightarrow \mathrm{RI} + \mathrm{I}\cdot \qquad (2)$$

With butylmercuric iodide,[1,10] the strong oxygen retardation of its reaction with iodine was strikingly demonstrated by the following procedure.[10] A dioxane solution, 0.025 M in iodine and 0.05 M in *n*-butylmercuric iodide, when saturated with air, required *ca.* 9000 seconds for 50% reaction. However, when oxygen was removed by successive degassing of the separate iodine and mercurial solutions in a two-legged flask, and then the solutions were mixed, the iodine was completely consumed in *ca.* 18 seconds. When this procedure was carried out with 0.05 M 4-camphylmercuric iodide (IX) and 0.025 M iodine, the iodine was completely consumed in *ca.* 15 seconds. In air-saturated solution, 4 to 6 hours was required to consume the iodine. Thus, the bridgehead organomercurial IX is analogous to butylmercuric iodide and other mercurials in the clearly radical nature of the reaction with iodine.

Using the technique developed by Keller,[10] several rate runs were made on the radical reaction of iodine with 4-camphylmercuric iodide (IX) in dry, purified, peroxide-free dioxane. These rates were even more erratic than those of Keller. A sample run is illustrated in Table I. However, even the slowest runs at 40° in air-saturated dioxane gave a second-order rate constant of 1.4×10^{-3} sec.$^{-1}$ M^{-1}, approximately equal to the value observed[10] for *n*-butylmercuric iodide, namely, $1.5\text{–}2 \times 10^{-3}$ sec.$^{-1}$ M^{-1}.

TABLE I

REACTION OF 4-CAMPHYLMERCURIC IODIDE (IX) WITH IODINE IN AIR-SATURATED DIOXANE AT 40.0°

0.02407 M RHgI, 0.05022 M I_2

Time, sec.	Thiosulfate, ml.[a]	$[I_2]$, M	$10^4 k_2$,[b] sec.$^{-1}$ M^{-1}
0	5.025	0.04962	
845	4.765	.04705	13.0
1,645	4.690	.04631	8.8
2,805	4.424	.04368	9.8
3,720	4.130	.04078	11.7
4,500	3.780	.03732	14.8
5,145	3.401	.03358	18.7
6,540	2.705	.02671	
10,000	2.697	.02663[c]	
15,000	2.680	.02646[d]	
		Mean	13

[a] Volume of 0.1003 N thiosulfate solution for a 5.0-ml. aliquot. [b] Second-order rate constant defined by the expression, $-\mathrm{d}[I_2]/\mathrm{d}t = k_2[I_2]^2$. [c] 98% completion. [d] 99.3% completion.

The product of the radical reaction of 4-camphylmercuric iodide (IX) with iodine was 4-iodocamphane (VI), isolated in high yield. The isolated material was identical with that prepared by treatment of 4-camphyllithium (IV) with iodine.

Electrophilic Substitution at the Bridgehead. Reaction of 4-Camphylmercuric Iodide (IX) with Triiodide Ion.—An extensive study by Keller[1,10] of the reaction of alkylmercuric iodides with iodine in the presence of iodide ion in aqueous dioxane has revealed an ionic mechanism for the substitution. Excellent second-order rate constants, first order in triiodide ion and first order in the alkylmercuric iodide, were obtained for the reaction of typical organomercuric iodides. In general, under the ionic conditions the radical reaction did not contribute appreciably. However, with neophylmercuric iodide (2-methyl-2-phenyl-1-propylmercuric iodide) the ionic reaction is slow enough that with 0.05 M reactants the radical reaction accounts for an appreciable amount of the total reaction even in oxygen-saturated solutions. This difficulty could be overcome by reducing the iodine concentration and increasing the mercurial concentration. Because the radical reaction is approximately second order in iodine and zero order in alkylmercuric iodide, reducing the iodine concentration and increasing the alkylmercuric iodide concentration, so as to keep the product constant, has the effect of reducing the importance of the radical reaction. By taking the rate in solutions initially 0.01 M in iodine and 0.2 M in neophylmercuric iodide, good second-order constants were obtained.[10]

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[9] (a) T. G. Traylor, Thesis, U. C. L. A., 1952; (b) reference 7a, footnote 27.

[10] J. Keller, Thesis, U. C. L. A., 1948.

In the present work, the rates of reaction of 4-camphylmercuric iodide (IX) with iodine and excess iodide ion have been measured by the same method and under nearly the same conditions as those employed by Keller[10] with neophylmercuric iodide. Because of the slight solubility of 4-camphylmercuric iodide (IX) the solvent in the present work contained 5% water by volume instead of 10% as used by Keller. Also, it was necessary to reduce the lithium iodide concentration to 0.125 *M* in order to maintain a single liquid phase. The kinetic behavior of 4-camphylmercuric iodide (IX) proved to be similar to that of neophylmercuric iodide.

With 0.05 *M* iodine and 0.025 *M* 4-camphylmercuric iodide (IX), second-order rate constants, k_2, calculated on the basis of equation 3, showed definite drifts. Also, the reaction was still about one-fifth as fast in the absence of iodide ion as in

$$\frac{-\mathrm{d[RHgI]}}{\mathrm{d}t} = k_2[\mathrm{RHgI}][\mathrm{I_3}^{\ominus}] \qquad (3)$$

the presence of 0.125 *M* iodide. Apparently, the radical reaction complicates the kinetics of the reaction of triiodide ion with 4-camphylmercuric iodide (IX).

In increasing the ratio of mercurial to iodine to render the radical reaction unimportant, the relatively low solubility of 4-camphylmercuric iodide (IX) in 95% dioxane (*ca.* 0.05 *M*) was a difficulty. This made it necessary to employ initial iodine concentrations below 0.005 *M*, rendering the usual titration methods with visual end-points too inaccurate. The reactions could be followed satisfactorily, however, by an electrometric determination of the end-point in the thiosulfate titration of the iodine.

At the low iodine concentrations, satisfactory second-order behavior was displayed by 4-camphylmercuric iodide (IX) in the reaction with triiodide ion. In Table II is illustrated one of the runs at 0.0036 *M* iodine, and the results of three runs are summarized in Table III. These results show the second-order rate constants insensitive to a two-fold change of iodine concentration and to the change in lithium iodide concentration from 0.125 to 0.05 *M*.

TABLE II

REACTION AT 55.0° OF 0.0336 *M* 4-CAMPHYLMERCURIC IODIDE (IX) WITH 0.00357 *M* IODINE IN 95% DIOXANE, 0.125 *M* IN LITHIUM IODIDE[a]

Time, sec.	Thiosulfate, ml.[b]	$[\mathrm{I_2}]$, 10^3 *M*	[RHgI], 10^2 *M*	$10^3 k_2$, sec.$^{-1}$ M^{-1}
0	11.264	3.500	3.363	
3,720	9.905	3.077	3.321	1.04
7,500	7.921	2.461	3.259	1.42
8,460	7.817	2.429	3.256	1.30
15,630	6.073	1.887	3.202	1.21
20,450	4.998	1.553	3.168	1.22
21,275	4.438	1.379	3.151	1.35
33,590	2.942	0.914	3.104	1.25
57,915	0.908	0.282	3.041	1.39
			Mean	1.27 ± 0.09

[a] Oxygen was bubbled at the rate of 3 ml. per minute through dioxane at 55° and then through the reaction mixture. [b] Volume of 0.001516 *N* sodium thiosulfate per 4.880-ml. aliquot.

TABLE III

SUMMARY OF RATES OF REACTION OF 4-CAMPHYLMERCURIC IODIDE (IX) WITH TRIIODIDE ION IN 95% DIOXANE AT 55.0°

[RHgI], 10^2 *M*	[LiI], 10^2*M*	$[\mathrm{I_2}]$, 10^2 *M*	$10^3 k_2$, sec.$^{-1}$ M^{-1}
3.36	12.5	0.357	1.27 ± 0.09
3.48	12.5	.218	1.5 ± .5
3.89	5.00	.445	1.53 ± .14

As in the case of the reaction under radical conditions, the product of the action of triiodide ion on 4-camphylmercuric iodide (IX), under largely ionic conditions, was 4-iodocamphane (VI), isolated in good yield.

Acetolysis of Di-4-camphylmercury (VIII).—The acetolysis of di-4-camphylmercury (VIII) was studied, as were the several other dialkylmercuries reported in the previous article.[7b] The alkylmercuric acetate was titrated with hydrogen bromide in acetic acid using hydroquinone to decrease end-point drift. This drift was somewhat of a problem, although not as acute as with di-*s*-butylmercury or diphenylmercury.

At 50 and 75°, first-order rate constants of acetolysis of di-4-camphylmercury (VIII) showed no definite drift. The data for one run at 75° are given in Table IV, and several runs are summarized in Table V, which lists also the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ of the reaction. Isolation of the product of acetolysis after 10 reaction half-lives by treatment of an aliquot with excess aqueous lithium chloride gave rise to 4-camphylmercuric chloride (VII).

TABLE IV

ACETOLYSIS OF 0.0271 *M* DI-4-CAMPHYLMERCURY (VIII) AT 75.0°

Time, sec.	HBr, ml.[a]	$[\mathrm{R_2Hg}]$, *M*	$10^5 k$, sec.$^{-1}$
0	0.247	0.02428	
3,900	.530	.02101	3.71
8,100	.790	.01800	3.70
11,915	1.090	.01453	4.31
18,300	1.315	.01193	3.88
23,835	1.500	.00978	3.82
29,460	1.660	.00793	3.80
42,240	1.860	.00562	3.46
52,830	1.988	.00414	3.35
467,940	2.322[b]		
		Mean	3.75 ± 0.20

[a] Volume of 0.05000 *M* hydrogen bromide per 4.321-ml. aliquot. [b] 99% completion; a trace of metallic mercury observed.

TABLE V

RATES OF ACETOLYSIS OF DI-4-CAMPHYLMERCURY (VIII)

Temp., °C.	$[\mathrm{R_2Hg}]$, 10^2 *M*	*k*, sec.$^{-1}$
25.0[a]		5.2×10^{-7}
49.6[b]	2.71	$(5.1 \pm 0.5) \times 10^{-6}$
75.0	2.71	$(3.75 \pm .20) \times 10^{-5}$
75.0	1.06	$(3.7 \pm .4) \times 10^{-5}$
25.9	1.78[c]	$(1.6 \pm .3) \times 10^{-3}$[d]

[a] Extrapolated from the data at the other temperatures. [b] $\Delta H^{\ddagger}$ = 17 kcal./mole; $\Delta S^{\ddagger}$ = −12 e.u. [c] 0.0447 *M* $\mathrm{HClO_4}$. [d] Second-order rate constant; sec.$^{-1}$ M^{-1}.

As with dineophylmercury,[7b] inclusion of perchloric acid in the glacial acetic acid gave a much enhanced rate of solvolysis of the di-4-camphylmercury (VIII). The second-order rate constant observed with 0.0447 *M* perchloric acid at 25.9°, recorded in Table V, was 1.6×10^{-3} sec.$^{-1}$ M^{-1}. Comparison with the first order rate constant extrapolated to 25° (Table V) shows that the second-order rate constant exceeds the first-order one by a factor of *ca.* 3000.

Reaction of Di-4-camphylmercury (VIII) with Mercuric Chloride.—Di-4-camphylmercury (VIII) and mercuric chloride, both very soluble in ether, react readily in this solvent at 25° to give a high yield of 4-camphylmercuric chloride (VII). Although no measurements of rate were carried out, the reaction was obviously not slow, since a large amount of the product had already crystallized out after *ca.* 6 hours.

Reduction of 4-Camphylmercuric Chloride with Lithium Aluminum Hydride.—Alkylmercuric chlorides are reduced to hydrocarbon by lithium aluminum hydride. The mechanism of the reaction is not clear, but there is some indication that the carbanion is an intermediate.[9a] Application of this reaction to the bridgehead mercurial VII gave camphane (III) in relatively low yield, at least partly because of loss due to volatility.

Discussion

Regarding ease of generation of cation, radical and anion centers at the bridgehead position of the bicyclo[2.2.1]heptyl skeleton, the most important consideration appears to be promotion energy associated with inefficient use of the 2*s* orbital in orbital hybridization about the bridgehead carbon atom. Since the change from sp^2 hybridization at an ordinary carbonium ion center to sp^3 corresponds to promotion of one-fourth of a 2*s* electron to 2*p*, Kimball[11] estimates that a planar cation with sp^2 hybridization is more stable than a pyramidal cation with sp^3 hybridization by 24 kcal./mole. Considering the great strain associated with any approach to planarity and thus return of promotion energy, the extreme difficulty of generation of a cationic center at the bicyclo[2.2.1]heptyl bridgehead position[3–5,12] becomes understandable.

In the case of a free radical, the 2*s* orbital is employed equally efficiently in sp^2 or sp^3 hybridization of the bonding orbitals. Thus, the prohibitive factor opposing a bridgehead cationic center is not present in the case of the analogous radical. Some reactions which proceed relatively normally by way of bicyclo[2.2.1]heptyl bridgehead free radicals are: (i) the thermal decomposition of diapocamphoryl peroxide in carbon tetrachloride, which produces considerable apocamphyl chloride[3c,13]; (ii) the peroxide-catalyzed decarbonylation of apocamphane-1-carboxaldehyde[14]; and (iii) the brominative decarboxylation of silver salts of the appropriate carboxylic acids to produce 1-bromoapocamphane,[15] 4-bromocamphane[5] and 1-bromo[2,2,1]bicycloheptane.[5] In the present work, the reactions by way of the 4-camphyl free radical, namely, the conversion of 4-camphylmercuric iodide (IX) to 4-camphyl iodide (VI) with iodine and the conversion of 4-camphylmercuric chloride (VII) to di-4-camphylmercury (VIII) with sodium stannite, proceeded normally.

In the case of a carbanion center, the most efficient use of the 2*s* orbital by the carbanionic carbon atom occurs in sp^3 hybridization. Again, the prohibitive factor opposing the bridgehead cationic center is absent in the case of the anion. The 4-camphyllithium[5,12] preparation, and possibly the lithium aluminum hydride reduction of 4-camphylmercuric chloride VII, illustrate this point.

In contrast with the inertness of the bicyclo[2.2.1]heptyl bridgehead position to nucleophilic substitution[3–5,12] is the relative ease of electrophilic substitution at such a position. For 4-camphyl derivatives, some electrophilic substitution reactions are summarized in Table VI. These include the reactions of 4-camphyllithium with carbon dioxide,[5,12] iodine, mercuric chloride and bromide, and 4-camphylmercuric chloride. These substitution reactions might be classified as SE1 if they are described as reactions of the 4-camphyl anion.[12] However, they may be classified as SEi[16] or SE2 if one wishes to emphasize such features as the covalent character of the R–Li bond, and ion pair attractive forces in the initial camphyllithium and the final lithium salt, for example, lithium iodide. The need to emphasize such features is illustrated by the considerable survival of optical activity observed by Letsinger[17] in the preparation and carbonation of 1-methylheptyllithium in petroleum ether at −70°.

TABLE VI

ELECTROPHILIC SUBSTITUTION REACTIONS OF 4-CAMPHYL DERIVATIVES

Compound	Reagent	Product
RLi	CO_2	RCO_2Li
	I_2	RI
	$HgCl_2$	RHgCl
	RHgCl	RHgR
	$HgBr_2$	RHgBr
RHgCl	$LiAlH_4$	RH
RHgI	I_2, $I^{\ominus}$	RI
R_2Hg	$HgCl_2$	2RHgCl
	HOAc	RH + RHgOAc
	$AcOH_2^{\oplus}ClO_4^{\ominus}$	RH + $RHgClO_4$

Three other electrophilic substitution reactions of 4-camphyl derivatives in Table VI involve the ionic cleavage of 4-camphylmercuric iodide (IX) by triiodide ion, and the conversion of di-4-camphylmercury (VIII) to 4-camphylmercuric chloride (VII) by mercuric chloride and 4-camphylmercuric acetate (and camphane) by acetic acid. On the basis of previous considerations,[1,7,10] these examples of electrophilic substitution are most likely SEi. Likely transition states may be represented by XII, XIII and XIV.

On inclusion of the order of 0.01 *M* perchloric acid in the glacial acetic acid solvent, the first-order neutral acetolysis of di-4-camphylmer-

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(11) Reference 4b, footnote 4.

(12) D. E. Applequist and J. D. Roberts, *Chem. Revs.*, **54**, 1065 (1954).

(13) M. S. Kharasch, F. Engelmann and W. H. Urry, THIS JOURNAL, **65**, 2428 (1943).

(14) W. von E. Doering, M. Farber, M. Sprecher and K. B. Wiberg, *ibid.*, **74**, 3000 (1952).

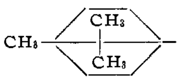
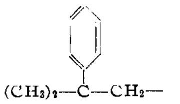
(15) P. Wilder, Jr., and A. Winston, *ibid.*, **75**, 5370 (1953).

(16) D. Curtin and E. E. Harris, *ibid.*, **73**, 2716 (1951).

(17) R. L. Letsinger, *ibid.*, **72**, 4842 (1950).

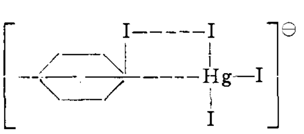
TABLE VII

RELATIVE RATES OF ELECTROPHILIC SUBSTITUTION OF BRIDGEHEAD AND OTHER MERCURIALS

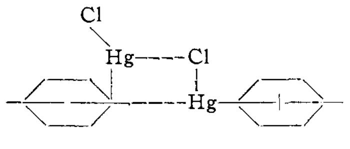
Reaction	R = $CH_3(CH_2)_2CH_2$—		
$R_2Hg + AcOH$; 25°	65	14	1
$R_2Hg + AcOH_2^{\oplus}ClO_4^{\ominus}$; 37°		5^a	1
$RHgI + I_2 + I^{\ominus}$; 90% dioxane,[10] 55°	66	3.1^b	1

[a] This approximate figure at 37° was based on the relative first-order rates at 25° of the 4-camphyl and neophyl derivatives and the k_2/k_1 ratios, 10^4 for neophyl at 50° and 3×10^3 for camphyl at 25°. [b] The second-order rate constant was corrected approximately to 90% dioxane by multiplication by 1.7, the factor which was observed between 90 and 95% dioxane for *n*-butylmercuric iodide by Keller.[10]

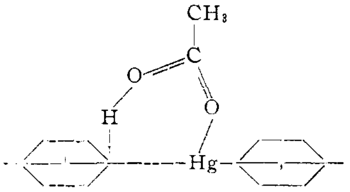
cury (VIII) is supplanted by the acidic second-order solvolysis. This behavior was observed previously with dineophylmercury.[7b] Since the second-order rate constant is *ca.* 3×10^3 times the first-order one, the ratio of second-order to first-order solvolysis of di-4-camphylmercury (VIII) is *ca.* 30 even at 0.01 *M* perchloric acid. For the acidic solvolysis, an SE2 mechanism seems most likely,[7b] the transition state being represented by XV.



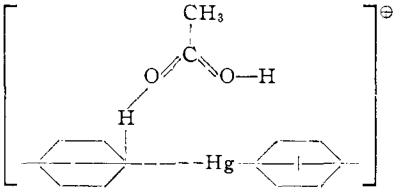
XII



XIII



XIV



XV

All of the electrophilic substitutions of the 4-camphylmercury derivatives necessarily proceed with retention of configuration. One of the substitution reactions, namely, the one involving the action of mercuric chloride on a dialkylmercury, already has been shown to proceed with complete retention of configuration with a substance without the bridgehead restriction, namely, methoxycyclohexylneophylmercury.[7a] For the other substitution reactions, involving the action of triiodide ion on an alkylmercuric iodide and that of acetic or perchloric acid on a dialkylmercury, the bridgehead work shows that they can proceed by mechanisms leading to retention of configuration. Further insight into the nature of these substitution reactions may be gained from the observed relative reactivities of the bridgehead mercurials compared to non-bridgehead derivatives.

As summarized in Table VII, the 4-camphylmercury derivatives occupy an intermediate position, between neophyl and *n*-butyl, with respect to reactivity toward triiodide ion, acetic acid and perchloric acid. Since the bridgehead mercurials are not especially unreactive, there is no indication that the bridgehead derivatives are forced to react by a mechanism leading to retention simply because another inherently much more preferable one is excluded by the bridgehead restriction. This suggests that retention of configuration in electrophilic substitution at a saturated carbon atom may be fairly general. Possibly the most interesting of the electrophilic substitutions in the present work involves the action of perchloric acid on the dialkylmercury. If this substitution is indeed SE2, then it represents an electrophilic substitution with retention of configuration, but without the compulsion toward retention which an SEi mechanism affords.

Experimental Part

All melting points are uncorrected unless otherwise indicated.

4-Chlorocamphane.—2,4-Dichlorocamphane, m.p. 175°, prepared from synthetic camphor[4a,8] in 43% yield, was hydrogenated[4a] in absolute ethanol containing potassium hydroxide using W-4 Raney nickel catalyst[18] under 48 pounds hydrogen pressure. The 4-chlorocamphane, m.p. 180° (reported[4a] 175–176°), was obtained in 52% yield.

4-Camphyllithium.—The solution of this material was prepared in an apparatus designed by Knight[19] for preparation, filtration and delivery of alkyllithium reagents. This apparatus consists of a medium porosity sintered glass funnel (about 100-ml. volume) equipped with joints above for reflux condenser, stirrer, addition funnel and a joint below for attaching the funnel to another reaction flask.

The materials employed were carefully purified. Eastman Kodak Co. white label cyclohexane was run through a three-foot (1.5 inch diameter) column of silica gel and distilled from sodium immediately before use. The 4-chlorocamphane was dried over sodium hydroxide pellets at 1 mm. for 3 hours. The nitrogen employed was passed over copper turnings at 450° and then through Drierite.

After the entire apparatus was dried and flushed with dry nitrogen, 25 ml. of cyclohexane was placed in the sintered glass funnel and held in place by nitrogen pressure. The stirrer was removed and, as nitrogen was passed through the system, 85 inches (9.7 g., 1.4 g. atom) of $^1/_4 \times {}^1/_{32}''$ lithium ribbon from Metalloy Lithium Salts Co. was wiped once to remove the excess protective petroleum jelly and cut in 1 mm. lengths directly into the cyclohexane. The 4-chlorocamphane (17.2 g., 0.1 mole) was dissolved in 50 ml. of cyclohexane in the dropping funnel. After the sintered funnel was heated to reflux the cyclohexane (with the aid of a heating coil around the funnel), one-third of the 4-chlorocamphane solution was added. Reaction started in about 5 minutes. The remainder of the 4-chlorocamphane solution was added with stirring over a 30-minute period, and the mixture was refluxed for an additional 8 hours. Another 100 ml. of cyclohexane was added to aid filtration, and the mixture was forced through the sintered glass with nitrogen pressure, stirring being maintained during filtration. The filtrate was clear and colorless.

4-Camphylmercuric Chloride.—The filtrate described above was dropped directly from the sintered glass funnel

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[18] A. A. Pavlic and H. Adkins, THIS JOURNAL, **68**, 1471 (1946).

[19] J. D. Knight, Thesis, U. C. L. A., 1952.

into a second reaction flask containing 40.7 g. (0.15 mole) of carefully dried mercuric chloride and 25 ml. of cyclohexane. The resulting mixture was stirred rapidly at 50° for about 15 hours, after which time the reaction mixture was cooled to 0° and filtered through a Soxhlet thimble. The solid in the Soxhlet thimble was dried at 40°, washed with hot water by extraction in the Soxhlet extractor for two days, and then dried at 40° for 24 hours. The solid in the thimble was then extracted with acetone until evaporation of the extract gave no more product. The product obtained from the acetone extracts weighed 27 g. (72% yield from the chloride). This was dissolved in hot ethyl acetate, decolorized, and crystallized to give 21.2 g. (57%) of material, m.p. 255–256°, m.p. 258.5–259.0° after two recrystallizations from ethyl acetate.

Anal.[20] Calcd. for $C_{10}H_{17}HgCl$: C, 32.17; H, 4.59. Found: C, 32.33; H, 4.52.

4-Camphanecarboxylic Acid.—An aliquot of the 4-camphyllithium solution, containing 0.01 mole (theoretical), was siphoned into a bubbler tube and treated with dried gaseous carbon dioxide. The carbonation was continued until a drop of the solution gave a neutral aqueous solution. The brown suspension in cyclohexane was extracted with aqueous sodium bicarbonate. This extract was filtered and acidified with dilute sulfuric acid. There was obtained 0.009 mole (90%) of white solid after drying over phosphorus pentoxide, m.p. 197.5–199.5°, m.p. 199–200° after recrystallization from ethanol–water, m.p. reported[5] 200.5–201.5°.

4-Iodocamphane.—An aliquot of 4-camphyllithium solution, containing 0.01 mole, was forced into a solution of 2.54 g. (0.01 mole) of resublimed iodine in 5 ml. of cyclohexane. The iodine was not completely consumed. The solution was taken up in petroleum ether, washed with water, thiosulfate solution and again with two portions of water. It was then dried over potassium carbonate and evaporated to dryness to produce a yellow-orange solid. This solid was recrystallized from methanol to yield 0.68 g. (26%) of material, m.p. 126.9–127.3° (cor.), m.p. 127.8–128.0° (cor.) after another recrystallization from methanol.

Anal. Calcd. for $C_{10}H_{17}I$: C, 45.48; H, 6.50. Found: C, 45.62; H, 6.57.

4-Camphylmercuric Iodide.—To 40 ml. of absolute ethanol containing 0.62 g. (0.027 g. atom) of sodium (as sodium ethylate) was added 5.0 g. (0.0134 mole) or 4-camphylmercuric chloride. The mixture was kept at 50°, with moisture excluded, until the mercurial dissolved. The resulting suspension was cooled to 10°. The sodium chloride which separated was removed by filtering the suspension directly into an aqueous solution of 6.5 g. (0.030 mole) of potassium iodide, and the resulting mixture was acidified with dilute acetic acid. The solid product obtained was filtered, washed with water, air dried, and recrystallized from ethyl acetate. There was obtained 4.0 g. (60%) of fine white needles, m.p. 240.5–241.2°, m.p. 239.9–240.0°, after a second recrystallization.

Anal. Calcd. for $C_{10}H_{17}HgI$: C, 25.84; H, 3.68. Found: C, 25.89; H, 3.76.

4-Camphylmercuric Bromide.—This compound, m.p. 250.6–251.2°, was prepared in the same way as was 4-camphylmercuric iodide. A sample prepared from camphyllithium and mercuric bromide, after several recrystallizations, gave the same melting point.

Anal. Calcd. for $C_{10}H_{17}HgBr$: C, 28.75; H, 4.10. Found: C, 29.28; H, 4.55.

4-Camphylmercuric Nitrate.—4-Camphylmercuric chloride (3 g., 0.008 mole) was added to a solution of 1.6 g. (0.009 mole) of silver nitrate in 200 ml. of absolute ethanol. This suspension was stirred for 18 hours, then evaporated to dryness. The solid residue was extracted with 100 ml. of petroleum ether, and the extract was evaporated to 70 ml. The solution was decolorized, filtered and cooled slowly to produce 1.3 g. (50%) of large colorless crystals, m.p. 138.6–139.1° (cor.). Another run gave a 75% yield.

Anal. Calcd. for $C_{10}H_{17}NO_3Hg$: C, 30.04; H, 4.28. Found: C, 30.77; H, 3.93.

This compound was found to be soluble in water to the extent of 0.001 *M* by evaporating a saturated solution and weighing the product.

Di-4-camphylmercury.—A solution of sodium stannite was prepared by adding 6 *N* sodium hydroxide to a solution of 20 g. (0.089 mole) of stannous chloride dihydrate in 100 ml. of water until the precipitate, which first appeared, just dissolved. This solution was diluted to 500 ml. with water, and 10 g. (0.0268 mole) of 4-camphylmercuric chloride was added. This mixture was stirred in a high-speed stirring apparatus at 6000 r.p.m. for 24 hours. The suspension was filtered, and the solid was placed in a new sodium stannite solution prepared as described above. This mixture was stirred for an additional 12 hours. The final color of the suspension was gray-green. The mixture was extracted with two 125-ml. portions of petroleum ether, and the extract was dried over potassium carbonate and evaporated to dryness. The solid was recrystallized from a mixture of 70 ml. of methanol and 30 ml. of ethyl acetate at −80°. There was obtained 2.5 g. (39%) of material, m.p. 182–186°

A second synthesis was carried out exactly as above, except that more of the petroleum ether was used to extract the product from the reaction mixture. A mixture of 4-camphylmercuric chloride and di-4-camphylmercury was obtained. The 4-camphylmercuric chloride was removed by partially dissolving the mixture in ligroin and cooling to precipitate the 4-camphylmercuric chloride. The mother liquor was evaporated to dryness, and the residue was recrystallized twice from acetone-water to yield material, m.p. 186.5–188.0°.

Anal. Calcd. for $C_{20}H_{34}Hg$: C, 50.56; H, 7.21. Found: C, 50.91; H, 7.48.

A solution of 4-camphyllithium, containing 0.085 mole, was filtered into a round-bottom flask, and 8.1 g. (0.038 mole) of dry mercuric chloride was added slowly with stirring to this solution. All the precautions described in the preparation of 4-camphylmercuric chloride were taken here also. The mixture was refluxed with stirring for 12 hours, cooled and the solid filtered off. The filtrate was evaporated to dryness, and the resulting solid was dissolved in a hot mixture of acetone–methanol. Cooling this solution slowly to 0° produced 1.1 g. of white solid. This solid, after being dried over sodium hydroxide pellets for two days, melted at 181–185°, undepressed by the di-4-camphylmercury described above. Less pure crops of product were obtained from the solution for a total yield of *ca.* 20%, the yield of pure di-4-camphylmercury being *ca.* 10%.

Reduction of 4-Camphylmercuric Chloride with Lithium Aluminum Hydride.—Absolute ether was refluxed for four hours over lithium aluminum hydride and distilled. To 75 ml. of this ether was added 3.7 g. (0.01 mole) of 4-camphylmercuric chloride. The solid partially dissolved. This suspension was added slowly to a stirred suspension of 0.29 g. (0.005 mole) of lithium aluminum hydride in absolute ether. The reaction mixture was held at 0° during the addition. After a few hours, the reaction mixture was allowed to warm to 25° and stirred for an additional 12 hours. Any excess lithium aluminum hydride was decomposed with water, and the ether layer was separated in a separatory funnel, washed three times with water and dried over potassium carbonate. When the ether solution was cooled to −80°, 0.18 g. (5%) of the starting mercurial was precipitated. The ether was evaporated to dryness and the solid obtained was recrystallized from methanol. There was obtained 0.26 g. (19%) of camphane, m.p. 149–151°, mixed m.p. with authentic camphane, 150–154°. At least some camphane was lost during evaporation of the ether.

Following the method of Meerwein and Wortman,[8a] authentic camphane was prepared from 10 g. of 2,4-dichlorocamphane by sodium reduction in ethanol. Crude camphane, m.p. 135–140°, was obtained in 37% yield out of methanol, while two recrystallizations from methanol brought the m.p. to 154–155° (cor.) (reported[8a] 154°).

Reaction of 4-Camphylmercuric Iodide with Iodine.—J. T. Baker resublimed iodine (1.1178 g., 0.00441 mole) was weighed into a volumetric flask and made up to 50 ml. with peroxide-free dioxane. A 5.0-ml. aliquot of this solution (0.000441 mole of iodine) was pipetted into one leg of a two-legged reaction flask. 4-Camphylmercuric iodide (0.3809 g., 0.000823 mole) was weighed into the other leg of the flask and dissolved in 10 ml. of dioxane. The flask was cooled in Dry Ice and pumped at 6 mm. pressure for about an hour, then warmed slowly and filled with oxygen-free nitrogen. A drop of the iodine solution was allowed to run into the mercurial solution. This did not decolorize imme-

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[20] Analyses of organomercurials were performed by Dr. A. Elek of the Elek Microanalytical Laboratories, Los Angeles, Calif.

diately but decolorized slowly as the flask was warmed up after the second pumping. (A similar solution took about 4 to 6 hours to decolorize before pumping and filling with nitrogen.) After four cycles of cooling, pumping, warming and pressuring with nitrogen, the flask was warmed to room temperature and the two solutions mixed rapidly. The resulting solution decolorized in *ca.* 15 seconds. The original concentrations in this experiment were 0.0294 *M* for iodine and 0.0547 *M* for mercurial. Another 5.0-ml. aliquot of the iodine solution was added to the above mixture (to give a slight excess of iodine) and the degassing procedure repeated. After 12 hours, the entire solution was poured into 200 ml. of 0.1 *N* sodium thiosulfate. The white precipitate which separated was filtered on a weighed, sintered glass crucible and dried to constant weight over sodium hydroxide pellets to yield 0.192 g. (88.4%) of 4-iodocamphane, m.p. 128°, mixed m.p. with authentic 4-iodocamphane, 127.8–128.6°.

The method for measuring the rate of this reaction was exactly that described by Keller,[10] except that the titration was carried out in water instead of methanol and starch was used as an indicator.

Reaction of 4-Camphylmercuric Iodide with Iodine and Excess Iodide.—The method of rate measurement in this reaction was similar to that described by Keller.[10] The solvent composition and iodide concentration were changed, and the titration was carried out by draining the aliquot into approximately 40 ml. of water containing a known amount of sodium thiosulfate and back-titrating with iodine, using starch as described by Kolthoff and Sandell.[21]

For the rate measurements at low iodine concentration, the end-point in the thiosulfate titration of the iodine was determined by the electrometric method developed by Foulk and Bawden[22] and modified by Boyer.[23] This titration was not affected by the presence of mercuric iodide, 4-camphylmercuric iodide or dioxane.

The product of the action of iodine and lithium iodide on 4-camphylmercuric iodide was obtained from a reaction solution after 15 half-lives by pouring the solution into excess sodium thiosulfate, and isolating the product in exactly the same way as for the radical reaction. The 4-iodocamphane, m.p. 127.7–128.2°, mixed m.p. with pure 4-iodocamphane, 127.8–128.6°, was obtained in 70% yield.

Reaction of Di-4-camphylmercury with Acetic Acid.—The method of measuring the rate of acetolysis of di-4-camphylmercury both with and without added perchloric acid was identical with that employed for dineophylmercury.[7b] The titration of acetolysis reaction mixtures containing dicamphylmercury with hydrogen bromide in glacial acetic acid gave end-points which were stable for only *ca.* two seconds even in the presence of hydroquinone.

After the 0.0106 *M* dicamphylmercury solution was held for 10 half-lives, 40 ml. was added to a solution of 5 g. of lithium chloride in 10 ml. of water, and the resulting solution was diluted to 125 ml. with water. The white solid was filtered off, dried over sodium hydroxide pellets, and recrystallized from about 5 ml. of an acetone–petroleum ether mixture at −80°. The large crystals obtained (55.4 mg., 37%) melted at 254–255.5°.

Reaction of Di-4-camphylmercury with Mercuric Chloride.—J. T. Baker analyzed mercuric chloride (0.0816 g., 0.000301 mole), dried at 110° for 12 hours, and 0.1432 g. (0.000314 mole) of di-4-camphylmercury were dissolved in 3.1 ml. of ether. After *ca.* 7 hours at room temperature, large crystals were observed. The mixture was allowed to stand for 48 hours and cooled to 0°. The crystals were filtered off and air-dried to yield 0.141 g. of material, m.p. 255–256°, mixed m.p. with authentic 4-camphylmercuric chloride, 254.5–256.5°. An additional 0.053 g., m.p. 255–256°, was obtained by evaporating the filtrate to dryness and recrystallizing the solid from petroleum ether–ethyl acetate. The total yield was 0.197 g. (87%).

Los Angeles 24, California

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[21] I. M. Kolthoff and E. B. Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1943, p. 620.

[22] C. W. Foulk and A. T. Bawden, This Journal, **48**, 2045 (1926).

[23] M. H. Boyer, Thesis, U. C. L. A., 1951.

[Contribution from the William Ramsay and Ralph Forster Laboratories, University College, London]

A Reinvestigation of the Role of Phenylsulfamic Acid in the Formation of Aminobenzenesulfonic Acids

By Gabriello Illuminati[1]

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The tendency of phenylsulfamic acid to rearrange to anilinesulfonic acids has been investigated in connection with a debated problem concerning the mechanism of sulfonation of aniline. The main results we have established can be summarized as follows: (1) Bamberger and Kunz's rearrangement of phenylsulfamic acid to orthanilic acid in cold glacial acetic acid has been disproved with the aid of a large number of experiments under varying conditions. (2) Rearrangement can be performed in dry dioxane at 100° and the product of the reaction was found to consist essentially of sulfanilic acid. (3) Phenylsulfamic acid proved to be a side-product, not an intermediate, in the reaction of β-phenylhydroxylamine with sulfur dioxide leading to orthanilic acid. These results show that phenylsulfamic acid has no tendency to rearrange to orthanilic acid under a variety of experimental conditions and remove the only piece of evidence for Bamberger's postulation that orthanilic acid is an intermediate in the course of sulfonation of aniline.

Bamberger's early theory on the mechanism of sulfonation of aniline with sulfuric acid involves an *ortho*-rearrangement of the supposedly intermediate phenylsulfamic acid, followed by rearrangement of the orthanilic acid thus formed to sulfanilic acid at a higher temperature.[2–5] Evidence for the tendency of phenylsulfamic acid to rearrange to orthanilic acid in cold glacial acetic acid was claimed by Bamberger and Kunz. However, in the course of a discussion on the subject by Hughes and Ingold,[6] from which the present work originated, the reaction appeared never to have been confirmed. Previous reports on the *para*-rearrangement of phenylsulfamic acid have dealt with thermal reactions of the corresponding salts in the solid state.[2,7] Also, the free acid is quite unstable in aqueous acidic media[8] and can be quantitatively cleaved into aniline and sulfuric acid under very mild conditions.[9]

The reaction of β-phenylhydroxylamine with sul-

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[1] On leave from the Department of General Chemistry, University of Rome, Italy.

[2] E. Bamberger and E. Hindermann, *Ber.*, **30**, 654 (1897).

[3] E. Bamberger and J. Kunz, *ibid.*, **30**, 2274 (1897).

[4] C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 247.

[5] E. R. Alexander, This Journal, **69**, 1599 (1947).

[6] E. D. Hughes and C. K. Ingold, *Quart. Revs.*, **6**, 51 (1952); see also C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 628–631.

[7] A. Seyewets and Bloch, *Bull. soc. chim.*, [4] **1**, 320 (1907).

[8] C. D. Hurd and N. Kharasch, This Journal, **69**, 2113 (1947).

[9] W. H. Hunter and M. M. Sprung, *ibid.*, **53**, 1443 (1931).