Electrophilic Substitution at Saturated Carbon in Mercurials. Alkyl Ligands as Mechanistic Probes in the Cleavage of Organometals

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Abstract: Alkyl substituent effects on electrophilic cleavage have been examined in a complete series of dialkylmercury compounds containing methyl, ethyl, isopropyl, and *tert*-butyl ligands. The pseudo-first-order rate constants k for acetolysis [RHgR′ + HOAc → RH + AcOHgR′] show large kinetic isotope effects k_H/k_D in the range 9–11, which are determined by both comparative and competitive methods. The effects of alkyl groups on log k can be classified into two independent categories based on the leaving group HgR′ and the cleaved group R. All the rates of acetolysis are correlated by a single equation: $\log k/k_0 = L + C$, where k_0 and k are the rate constants for cleavage of MeHgMe and R–HgR′, respectively, **L** is the leaving group constant for HgR′, and C is the cleaved group constant for R. The applicability of such a linear free-energy relationship indicates that steric interactions due to the leaving group are unimportant in acetolysis. **L** reflects only an electronic effect and shows a striking relationship with the vertical ionization potentials of RHgR′ determined by He(I) photoelectron spectroscopy. Incremental changes in **L** on proceeding from R′ = Me < Et < *i*-Pr < *t*-Bu become "saturated", in contrast to the additive relationship characteristic of Taft σ^* parameters for the same alkyl substituents. The origin of the saturation pattern for alkyl substituents is traced to a "polarizability" factor, examined by comparing the ionization potentials of various alkyl compounds RX with those of the organometals (RM). The cleaved alkyl group parameter **C** varies in a nonsystematic order R = Me < Et > *i*-Pr > *t*-Bu. C includes contributions from electronic effects which are opposed to steric effects at the reaction site. The latter is negligible in electrophilic cleavages proceeding via a prior electron transfer in which the outer-sphere process is rate limiting. Under these circumstances electronic effects are dominant and the relative rates of cleavage of Me, Et, *i*-Pr, and *t*-Bu groups from organometals follow the "saturation" pattern. These results together with the known stereochemical retention of configuration support the notion of a three-center transition state for protonolysis in which sizable charge is developed on both the cleaved group as well as the leaving group (HgR′). The bearing of this conclusion on electrophilic substitution at saturated carbon is discussed.

Introduction

Organometals RM, as a characteristic, are susceptible to cleavage by electrophiles generally:

$$R\text{-}M + E^+ \rightarrow R\text{-}E + M^+ \qquad (1)$$

Such displacement reactions are basic to our understanding of a wide variety of organic syntheses proceeding via organometallic intermediates. Despite extensive studies,[1,2] however, there is surprisingly limited knowledge concerning the structural factors important in electrophilic displacements at a carbon–metal bond. For example, there is almost no meaningful *quantitative* information regarding even the conceptually simple act involved in the protonolysis of an organometal.

Organomercury compounds are less subject to steric effects than other metals due to the large radius and two-coordination of Hg. Thus, they are ideal models for such studies and have been used extensively.[1,2] However, it is even more important to appreciate that the dialkylmercury compounds are completely substitution stable, in contrast to derivatives such as alkylmercury halides, and there is little ambiguity as to the identity of the species extant in solution. The literature on the protonolysis of mercurials has been critically evaluated by Jensen and Rickborn,[3]

$$R\text{-}Hg\text{-}R' + HY \rightarrow R\text{-}H + R'\text{-}Hg\text{-}Y \qquad (2)$$

and we perceive at least four major points which must be recognized in any mechanistic consideration. They are summarized below.

1. Mechanistic information obtained from extensive studies of protonolysis of unsaturated organomercurials is not directly applicable to the saturated alkyl analogues. Protonolyses of aryl- and vinylmercury compounds proceed via a prior rate-limiting *addition* of a proton to the unsaturated organic moiety.[4-6] No analogous intermediate can be implicated in the protonolysis of alkylmercury compounds. The enhanced rate of cleavage of arylmercurials[3] can thus be attributed to their properties as π donors, in contrast to alkylmercurials which are σ donors.[7]

2. A meaningful study of alkyl substituent effects in proto-demercuration must distinguish between the effect of the group being cleaved (R in eq 2) and that of the leaving group R′Hg. This distinction is generally absent in previous studies of proto-demercuration.[8,9] Thus, both Kharasch[8] and instein[11] in their pioneering studies of unsymmetrical and symmetrical dialkylmercury compounds, respectively, assumed implicitly that the protonolysis was solely dependent on the structure of the group being cleaved. As a result, the relative reactivity of *s*-Bu > *n*-Bu, deduced from a comparison of symmetrical dialkylmercury compounds,[11a] for example, is exactly reversed from that obtained using the unsymmetrical counterparts.[12]

3. Stereochemical configuration is retained at the carbon center undergoing protonolysis. Although competing racemization of the starting material is a complication, a number of experimental studies,[13] including that by Jensen and Gale[14] on *cis*- and *trans*-4-methylcyclohexylmercury, favor protonolysis with retention of stereochemistry.[3]

4. Concrete evidence for nucleophilic participation by the conjugate base during protonolysis is meager and ambiguous.[15,16,17]

The availability of experimental methods for directly examining the protonolysis of simple alkyl groups together with the information regarding the bonding in organomercurials by photoelectron spectroscopy allowed us to study a complete series of symmetrical as well as unsymmetrical dialkylmercury compounds. We feel that the quantitative results of this study have provided interesting insights into the structural factors involved in the protonolysis of alkyl–mercury bonds. Infor-

Table I. Rates of Acetolysis of Dialkylmercurials[a]

RHgR′ R	RHgR′ R′	10^7k, s^{-1}	$10^7k'$, s^{-1}	7 + log k	7 + log k'	IP,[b] eV
Me	Me	3.90	3.90[c]	0.59	0.59	9.33
Me	Et	23.5	14.3	1.37	1.16	8.84
Me	*i*-Pr	85.8	8.45	1.93	0.93	8.47
Me	*t*-Bu	120	*d*	2.08		8.32
Et	Et	81.8	81.8[c]	1.91	1.91	8.45
Et	*i*-Pr	255	47.0	2.41	1.67	8.18
Et	*t*-Bu	378	~3[d]	2.58		8.06
i-Pr	*i*-Pr	154	154[c]	2.19	2.19	8.03
i-Pr	*t*-Bu	224	~10[d]	2.35		7.73
t-Bu	*t*-Bu	*d*	*d*			7.57

[a] Pseudo-first-order rate constants in HOAc solvent at 37.5 °C. [b] First vertical ionization potential by He(I) photoelectron spectroscopy, work done in collaboration with J. Ulman and T. P. Fehlner. [c] Rates for symmetrical mercurials are statistically corrected. [d] Rates for cleavage of *t*-Bu groups were too slow for direct measurement by this procedure.

mation gained from this simplest electrophilic species will provide the mechanistic basis for the consideration of more complex electrophiles in the cleavage of organometals, particularly those involving electron transfer.

Results

All ten combinations of dialkylmercury compounds, RHgR′, encompassing methyl, ethyl, isopropyl, and *tert*-butyl groups, were synthesized in analytically pure form. The acetolysis of these compounds was carried out in glacial acetic acid solution at 37.5 °C. Organomercury compounds, especially *tert*-butyl derivatives, are susceptible to autoxidation.[18] All product and kinetic studies were thus carried out under an argon atmosphere designed to preclude oxygen. The alkyl groups in RHgR′ were chosen to allow continuous analysis of the gaseous hydrocarbon products directly from solution by gas chromatography using the internal standard method. The organomercury products were characterized in solution by their proton NMR spectra.

Products and Stoichiometry. Acetolysis of dialkylmercury compounds liberated 1 equiv of alkane and of alkylmercury acetate according to the following equations:

$$\text{R–Hg–R′} + \text{HOAc} \xrightarrow{k} \text{RH} + \text{R′HgOAc} \quad (3)$$

$$\text{R–Hg–R′} + \text{HOAc} \xrightarrow{k'} \text{R′H} + \text{RHgOAc} \quad (4)$$

in agreement with earlier studies.[3] Under the reaction conditions, the further cleavage of alkylmercury acetate was too slow to interfere with the acetolysis study of dialkylmercury. However, the four *tert*-butylmercurials were the exceptions, owing to the subsequent solvolysis of *tert*-butylmercury acetate which generally afforded discrete amounts of isobutylene, *tert*-butyl acetate, and mercury.[19]

Alkylmercury acetates formed under these conditions can undergo rather slow alkyl exchange with dialkylmercury. For example, isopropyl(methyl)mercury (0.1 M) in acetic acid-d_4 after 42 h at 37.5 °C in a sealed tube showed the presence of less than 5% dimethylmercury by an examination of its characteristic proton NMR spectrum. No exchange was observed in a 4-h period.

$$\text{CH}_3\text{HgOAc} + \text{CH}_3\text{HgPr}^i \rightarrow \text{CH}_3\text{HgCH}_3 + i\text{-PrHgOAc} \quad (5)$$

In an inert solvent such as benzene, neither isopropyl- nor *tert*-butyl(methyl)mercury in 0.1 M solutions showed any signs of Me_2Hg due to symmetrization when heated for more than 50 h at 37.5 °C.

Kinetics. The pseudo-first-order rate constants for acetolysis, k and k', in eq 3 were determined from the rates of liberation of alkanes RH and R′H, respectively. Careful calibration under reaction conditions allowed the amounts of each alkane generated to be monitored continuously during the course of acetolysis. The rates of reaction of diethyl- and diisopropylmercury followed first-order kinetics to at least 3 half-lives. However, the behavior of di-*tert*-butylmercury[20] was quite unusual, showing a very slow initial rate, followed by an accelerated decomposition leading to isobutylene and mercury in addition to isobutane. The apparent autocatalytic nature of the reaction suggests the incursion of a chain process, and this anomalous cleavage is under further investigation.

The presence of salts exerts only a minor effect on the rate of acetolysis of dialkylmercury. For example, the addition of as much as 1.3 equiv of ethylmercury acetate to 0.122 M diethylmercury only caused the pseudo-first-order rate constant to increase by less than 4%. Similarly, the rate of acetolysis of dineophylmercury in the presence and absence of an equimolar amount of sodium acetate was found earlier to differ by no more than the combined experimental errors.[11a]

The rate of protonolysis of dialkylmercury in acetic acid solutions is extremely sensitive to the presence of certain metallic contaminants. Previous studies with organolead compounds have shown that transition metal complexes, particularly those of copper, are highly efficient catalysts for acetolysis of organometals.[21] Catalysis occurs by a prior alkyl transfer to copper in eq 6, followed by the rapid protonolysis (eq 7) of the organocopper intermediate, e.g.,

$$\text{R}_2\text{Hg} + \text{Cu}^{\text{I}}\text{OAc} \rightarrow \text{RHgOAc} + \text{RCu}^{\text{I}} \quad (6)$$

$$\text{RCu} + \text{HOAc} \xrightarrow{\text{fast}} \text{RH} + \text{CuOAc, etc.} \quad (7)$$

Kinetic studies were carried out, therefore, under conditions in which the introduction of adventitious metals was avoided.

Individual pseudo-first-order rate constants k and k' for the protonolysis of each of the alkyl–mercury groups in all of the dialkylmercury compounds were obtained by this procedure and listed in Table I. Accurate determinations of the rate constants for protonolysis of the *tert*-butyl–mercury groups, however, were limited due to their slow rates and interference from the competing solvolysis of *tert*-butylmercury acetate, and these data will not be used in the quantitative treatments.

Examination of the complete series of RHgR′ in Table I allows the effects of alkyl groups in eq 3 to be separated into two classes, namely, (a) the effect due to the leaving group HgR′ and (b) the effect due to the cleaved group R.[22] The results are retabulated accordingly in Chart I to emphasize these two important considerations in the cleavage of organometals.

(a) To examine the effect of the *leaving group* HgR′, three series of compounds, Me-HgR′, Et-HgR′, and *i*-Pr-HgR′ (where R′ = Me, Et, *i*-Pr, and *t*-Bu) were considered, in which the cleaved alkyl group R was common in each series, viz., Me, Et, and *i*-Pr, respectively. The results of Chart I (horizontal rows of numbers) show that the rate of cleavage of a particular alkyl group R is highly dependent on the nature of the leaving group HgR′, and as the leaving group varies, the rate *increases* (logarithmically) in the order:

$$\text{HgMe:HgEt:HgPr}^i\text{:HgBu}^t = 0\text{:}0.76\text{:}1.28\text{:}1.44 \quad (8)$$

The relationship in eq 8 is independent of cleaved group R as shown by the linearity of the curves in Figure 1, in which the acetolysis rates are correlated between pairs of dialkylmercury compounds, i.e., EtHgR′ vs. MeHgR′ (lower curve) as well as EtHgR′ vs. *i*-PrHgR′ (upper curve). The same slopes of the

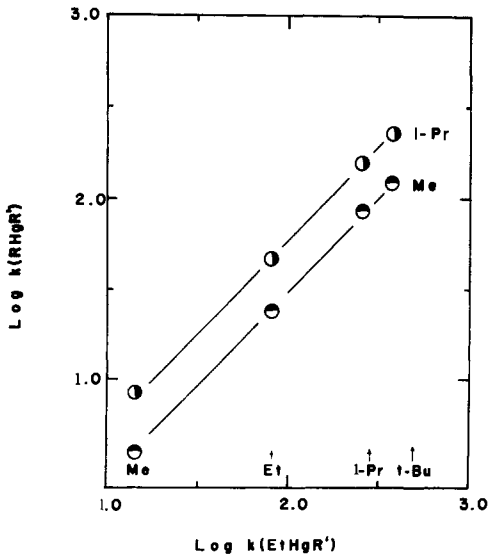


Figure 1. Leaving group effects. Correlation of the rates of liberation of ethane in EtHgR′ with the rates of liberation of methane (◓) and propane (◑) from MeHgR′ and *i*-PrHgR′, respectively, in acetic acid solutions.

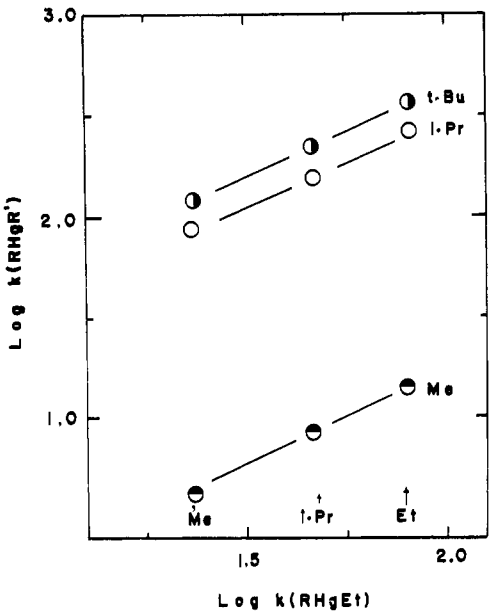


Figure 2. Cleaved group effects. Correlation of the rates of cleavage of RH (methane, propane, and isobutane) in RHgEt with the rates of liberation of the same hydrocarbons from a series of RHgMe (◓), RHgPr^i (○), and RHgBu^t (◑) in acetic acid solutions.

Chart I. Leaving Group and Cleaved Group Effects of Alkyl Ligands in the Protonolysis of Organomercurial.

CLEAVED GROUP \ LEAVING GROUP	HgMe	HgEt	HgPr^i	HgBu^t
Me	0.59	1.37	1.93	2.08
Et	1.16	1.91	2.41	2.58
i-Pr	0.93	1.67	2.19	2.35

lines in the figure also demonstrate that leaving HgR′ group effects in eq 8 are not dependent on whether a methyl or isopropyl group is cleaved.

(b) To examine the effect of the *cleaved alkyl group*, four series of compounds, R-HgMe, R-HgEt, R-HgPr^i, and R-HgBu^t [where R = Me, Et, and *i*-Pr] were considered, in which the leaving group was common in each series, viz., HgMe, HgEt, HgPr^i, and HgBu^t, respectively. The results in Chart I (i.e., vertical columns of numbers) show that when the leaving HgR′ group is the same, the rates of cleavage of Me, Et, and *i*-Pr groups do not increase monotonically. The reactivity of *i*-Pr is actually intermediate between that of Me and Et. However, the relative rates of cleavage of Me, Et, and *i*-Pr groups are largely independent of HgR′ as shown by the three similar slopes in Figure 2 which correlates the rates of acetolysis of the series of R-HgEt with those of R-HgMe, R-HgPr^i, and R-HgBu^t, respectively. The same correlation extends to R-HgPr^i with R-HgBu^t and other combinations.

Deuterium Isotope Effects. The kinetic isotope effect in the protonolysis of dialkylmercury was examined with HOAc and DOAc using two independent methods. First, the rates were measured in pure HOAc as well as in DOAc and k_H/k_D determined from the ratio of the pseudo-first-order rate constants. These values were checked for the series of *i*-PrHgR by a competition method in which the acetolysis was carried out in a known HOAc/DOAc mixture and the deuterium content of the liberated 2-propane-d_i analyzed by mass spectroscopy (GC-MS).

All of the dialkylmercury compounds showed a large kinetic isotope effect in the range between 9–11 (Table II). The values determined by the competition method were approximately 20–30% higher than those obtained from the comparative method, and the differences are in the direction expected for a secondary solvent isotope effect.[23] The kinetic isotope effect in the cleavage of a methyl group in the Me-HgR′ series apparently decreases as the leaving group varies from HgMe, HgEt, HgPr^i to HgBu^t. The accuracy of the data, however, limits a quantitative evaluation of the effect. No other trend in the kinetic isotope effects with structural variation can be discerned from the data. Despite these limitations, the comparative and competitive methods unequivocally demonstrate the presence of large primary isotope effects during acetolysis.

^{199}Hg-^{1}H NMR Coupling Constants of Methyl(alkyl)mercury. The proton NMR spectrum of dimethylmercury shows a singlet (δ 0.29 ppm) and a doublet due to splitting by ^{199}Hg ($I = \frac{1}{2}$, 16.86% natural abundance) with the expected relative intensities.[24] The coupling constants ($J_{^{199}Hg-^1H}$) for the methyl protons in the CH_3-HgR′ series are listed in Table III. Such large couplings are generally conceded to arise almost entirely through a Fermi contact mechanism[25] and should reflect the electron density of the methyl-mercury bond in the ground state. It is interesting to note the linear correlation of log *k* for acetolysis and $J_{^{199}Hg-H}$ in the series of CH_3HgR' (compare data in Tables I and III).

He(I) Photoelectron Spectra of Methyl(alkyl)mercury. The He(I) photoelectron spectrum of dimethylmercury shows principal bands at 9.33 and 14.93 eV, assigned to the lowest ionization potential and mercury $5d^{10}$ ionization potential, respectively.[26] In the CH_3HgR' series, the energy of the first band shifts progressively to lower energies as R′ is varied from Me (9.33), Et (8.84), *i*-Pr (8.47) to *t*-Bu (8.32) as illustrated in Figure 3. These vertical ionization potentials are related to the energetics of electron detachment from the organomercurial in the gas phase and are listed in Table I together with those of other mercurials.

Discussion

The protonolysis of dialkylmercury in acetic acid solutions

Table II. Deuterium Isotope Effects in Acetolysis of Dialkylmercury

R–Hg–R′ R	R	$10^7 k_H$, s^{-1}	$10^7 k_D$,[a] s^{-1}	k_H[b] / k_D	k_H', s^{-1}	k_D'[a], s^{-1}	k_H'[b] / k_D'
Me	Me	3.9	0.45[c]	10.3			
Me	Et	23.5	2.82	9.8	14.3	1.60	10.7
Me	*i*-Pr	85.8	10.4	9.7	8.45	1.01	9.8 (13)
Me	*t*-Bu	120	15.3	9.1	nd		
Et	Et	81.8	9.30[c]	10.5			
Et	*i*-Pr	255	28.0	10.9	47.0	5.42	10.3
Et	*t*-Bu	378	42.2	10.7	nd		(12)
i-Pr	*i*-Pr	154	18.0[c]	10.1 (12)			
i-Pr	*t*-Bu	224	24.2	11.1 (12)	nd		

[a] Observed rate constant in 98 atom % DOAc. [b] Corrected for isotopic composition of the solvent. Values in parentheses are obtained from competitive protonolysis in 5.75 DOAc:HOAc. [c] Statistically corrected for two R groups per molecule. nd = not determined.

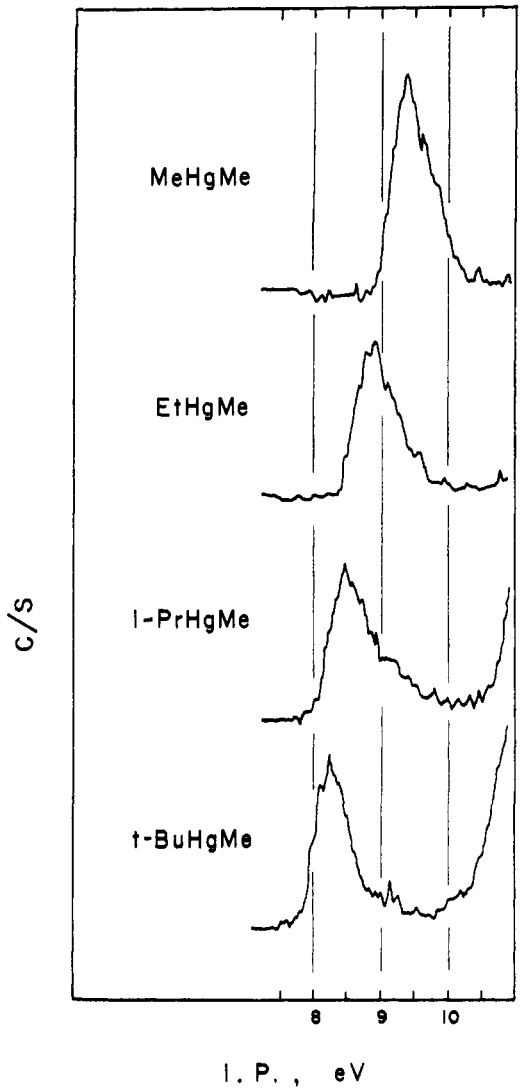


Figure 3. He(I) photoelectron spectra of the first bands in a series of MeHgR′ where R = Me, Et, *i*-Pr, and *t*-Bu. Units in the ordinate are arbitrary.

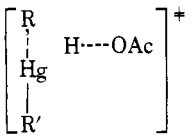
proceeds by a rate-limiting proton transfer. The experimental values of the kinetic isotope effect are close to the theoretical maximum expected for the transfer of deuterium relative to proton in this system.[27,28] The large values of k_H/k_D also suggest a rather linear transition state for proton transfer in which the contribution from the symmetric stretching mode is small.[29] Such a transfer of a proton halfway in the transition state places a considerable positive charge on mercury.

Table III. Proton and Carbon-13 NMR Spectra of Methyl(alkyl)mercury Compounds[d]

CH_3HgR'	δ (CH_3),[a] ppm	$J_{^{199}Hg-^1H}$ CH_3,[b] Hz	δ ^{13}C, ppm	$J_{^{199}Hg-^{13}C}$, Hz
CH_3	0.29	102	105.6	697.6
CH_2CH_3	0.29	93	105.8	590.2
$CH(CH_3)_2$	0.29	88	106.3	513.9
$CH_2CH(CH_3)_2$	0.27	94	[c]	
$C(CH_3)_3$	0.31	85	106.1	468.0

[a] In carbon tetrachloride solution, Me_4Si internal standard. [b] Neat liquids. [c] Not determined. [d] ^{13}C spectra in benzene solution containing 2% $Cr(acac)_3$.

These results together with the retention of configuration during proto-demercuration and recent theoretical studies[30] are consistent with a three-center transition state of the type depicted below in I:



I

The more or less triangular array of carbon, mercury, and the proton in the transition state for protonolysis was originally proposed by Kreevoy and Hansen.[31] Indeed, Olah has recently suggested the involvement of similar three-center transition states as a characteristic of all electrophilic reactions occurring at single bonds to carbon.[32] The extent to which there is nucleophilic assistance during acetolysis of dialkylmercury is not directly indicated by the results on hand and will not be treated explicitly.[15-17]

We wish to focus our attention here on the effects of alkyl groups on the cleavage reaction, which we classify into two categories: namely, leaving group (HgR′) effects and cleaved group (R) effects. The linear relationships and the parallel lines in Figure 1 indicate that steric effects due to the leaving groups are unimportant in acetolysis. The same conclusion pertains to the series in Figure 2, and it helps to limit the mechanistic considerations to the immediate locus of the reaction site.

Leaving Group Effects (HgR′). The effect of leaving groups HgR′ on the cleavage of a particular alkyl-mercury bond was examined in the three series shown in Figure 1. The rates for HgR′ accelerate in the order: R′ = Me < Et < *i*-Pr < *t*-Bu.

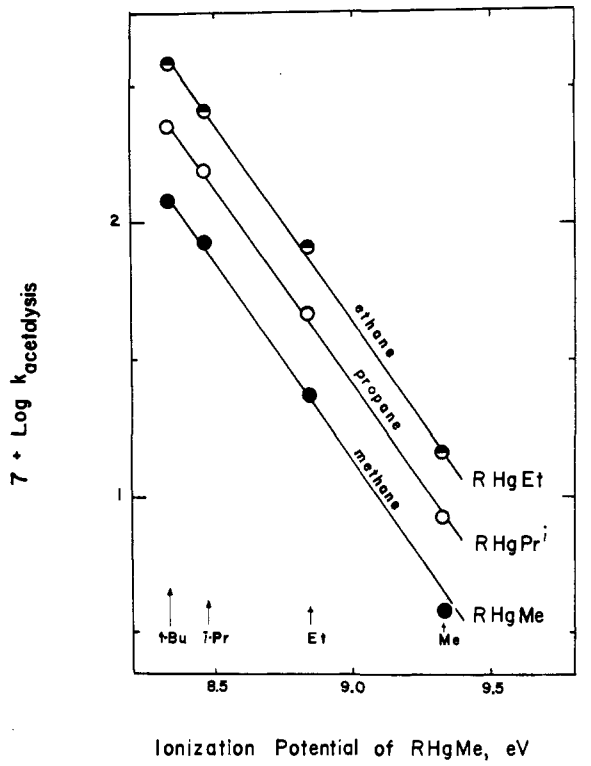


Figure 4. Correlation of the rates of liberation of methane (●), propane (○), and ethane (◒) from a series of MeHgR′, i-PrHgR′, and EtHgR′, respectively, in acetic acid with the vertical ionization potential of the corresponding MeHgR′.

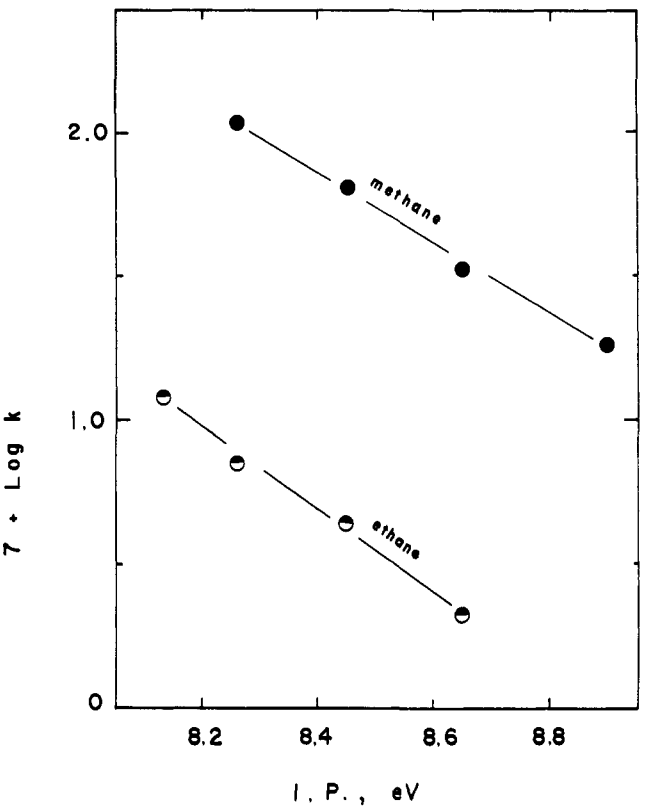


Figure 5. Correlation of the rates of liberation of methane (●) and ethane (◒) from a series of $Me_nEt_{4-n}Pb$ (where n = 0, 1, 2, 3, 4 from left to right) in acetic acid with the vertical ionization potential of the tetraalkyllead compounds.

This reactivity sequence represents the increasing ability of these alkyl groups to accommodate a positive charge when they are attached to the departing cationic mercury (HgR′). Electron release by various alkyl groups in response to a fixed electron demand in the ground state of CH_3HgR' is reflected in the magnitudes of the methyl proton coupling constants [$J_{^{199}Hg\text{-}^1H}$] listed in Table III. More appropriately, electron release by alkyl groups in the transition state for acetolysis may be modeled by the cation radical of dialkylmercury. The latter may be probed independently by measuring the energetics of electron detachment from a homologous series of RHgR′, e.g.,[26,33]

$$CH_3\text{-}Hg\text{-}R' \rightarrow [CH_3\text{-}Hg\text{-}R']^+ + \epsilon \qquad (9)$$

Indeed, Figure 4 shows the linear correlation of log k for acetolysis and the vertical ionization potentials of a series of CH_3HgR'. Since photoelectron ionization is a vertical process, it is electronic in origin and must be largely free of steric factors. The correlation in Figure 4, thus, supports the foregoing conclusion that steric effects of leaving groups are unimportant in acetolysis. The easy access to mercury is also in accord with its relatively large atomic radius and linear configuration in RHgR′.[34]

The correlation between rates of cleavage and ionization potential is not restricted to organomercurials. The same relationship is also obtained in four-coordinate organolead compounds.[35] Figure 5 shows that the rate of acetolysis of the

$$Me_nEt_{4-n}Pb + HOAc \xrightarrow{k_{Me}} CH_4 + Me_{n-1}Et_{4-n}PbOAc \qquad (10a)$$

$$Me_nEt_{4-n}Pb + HOAc \xrightarrow{k_{Et}} CH_3CH_3 + Me_nEt_{3-n}PbOAc \qquad (10b)$$

Me-Pb bond (i.e., log k_{Me}) decreases linearly with the ionization potential of $Me_nEt_{4-n}Pb$ where n = 0, 1, 2, 3, 4 and a parallel relationship is obtained during the concomitant cleavage of the Et-Pb bond (log k_{Et}). Increasing steric factors in the leaving group (i.e., trialkyllead) prevent extension to higher homologues.

Table IV. Leaving Group Parameters in Acetolysis of Dialkylmercury. Comparison with Taft σ^*

Leaving group (HgR′)	L	L′	σ^*
$HgCH_3$	0	0	0
$HgCH_2CH_3$	0.76	0.10	0.10
$HgCH(CH_3)_2$	1.28	0.17	0.19 (0.20)[a]
$HgC(CH_3)_3$	1.44	0.19	0.30

[a] See text.

In the acetolysis of dialkylmercury, the leaving group (HgR′) effects [under conditions of constant cleaved (R) group] can be expressed quantitatively by the linear free-energy relationship:

$$\log (k/k_0) = \mathbf{L} \qquad (11)$$

where k_0 is the rate constant for acetolysis of R-HgR′ in eq 3 when R′ = Me, and k is that for R′ = Et, *i*-Pr, or *t*-Bu. **L** is a leaving group constant which has a characteristic value for each HgR′, and it does not depend on the nature of the cleaved group (R). Normalizations of **L** to **L**(Et) = 0.10 are listed in Table IV as **L′** to allow direct comparison with the Taft σ^* constants.

There is a striking difference between the values of **L′** and σ^*, although both are due to electronic or polar effects. Thus, there is a "saturation" in incremental changes in energy for **L** as each hydrogen in $RHgCH_3$ is sequentially replaced by methyl groups in the series: $RHgCH_3$, $RHgCH_2CH_3$, $RHgCH(CH_3)_2$, and $RHgC(CH_3)_3$.[36] On the other hand, the corresponding changes in σ^* are "additive", increasing linearly

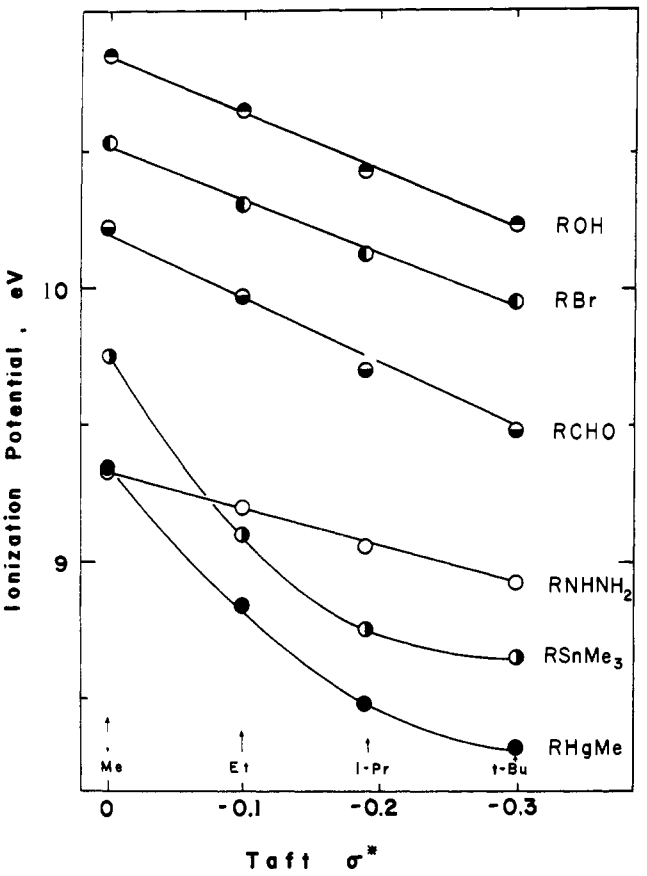


Figure 6. Comparisons of the polar effects of alkyl groups using the Taft σ^* values and those obtained from the ionization potentials. Additivity effects in alcohols (◓), alkyl bromide (◐), aldehydes (◒), and alkyl hydrazines (○) from ref 38. Saturation effects in alkyl(methyl)mercury (●) and alkyl(trimethyl)tin (◑) from ref 39. [Note that linearity of the additivity effects would be further improved in every case by the use of $\sigma^* = -0.20$ for *i*-Pr.]

from CH_3, CH_2CH_3, $(CH_3)_2CH$ to $(CH_3)_3C$.[37] Indeed, Taft has employed the additivity requirement for identifying polar effects.

The difference between energy effects which are *saturated* and those that are *additive* provides the key, we feel, to the understanding of substituent effects in electrophilic cleavages. Figure 6 demonstrates a strong linear correlation between σ^* values and the ionization potentials of a series of alcohols, alkylhydrazines, aldehydes, and alkyl halides represented by the process: $RX \rightarrow R\text{-}X^{+\cdot} + \epsilon$.[38] (Note that linearity would be improved in every case by the use of $\sigma^* = -0.20$ for *i*-Pr.) On the other hand, the ionization potentials of a series of organomercurials CH_3HgR' also plotted against σ^* show a saturation effect equivalent to that in acetolysis. The saturation also obtains for ionization from the same series of Grignard reagents and alkyl-trimethyltin compounds, $(CH_3)_3SnR'$, measured independently.[39] The difference between saturation and additivity effects can be explained by considering the highest occupied molecular orbital (HOMO) in each series. For those compounds containing nonbonding electrons, the ionization proceeds from a HOMO which is largely orthogonal to the orbital involved in the bonding of X to carbon in R-X, and its effect on the electron density in the bond is minimal. In contrast, the ionization process in organometals such as Me_2Hg proceeds from a bonding molecular orbital with a node at mercury.[40] Consequently, the electron density in the bond to carbon is diminished substantially, and the cationic character of the α carbon is accompanied by a decrease in electron repulsion which is not effectively constant as the alkyl group is systematically varied from Me to *t*-Bu.[41] Indeed the validity of this description is shown by values of the ionization potentials of alkyl radicals [i.e., $R\cdot \rightarrow R^+ + \epsilon$], which agree remarkably well with those obtained from SCF-MO calculations.[41a,42] Significantly, the ionization potentials of alkyl radicals[41,42] show the characteristic saturation effect described above, and they also correlate well with log *k* for acetolysis and the ionization potentials of the organomercurials examined in this study.

Table V. Cleaved Group Parameters in Acetolysis of Dialkylmercury

Cleaved alkyl group (R)	C
CH_3	0
CH_3CH_2	0.55
$(CH_3)_2CH$	0.29
$(CH_3)_3C$	−0.9[a]

[a] Approximate value (see text).

It is noteworthy that leaving group (HgR′) effects due to substitution of methyl groups in the β position of the alkyl chain R′ are highly attenuated relative to that accompanying α substitution. For instance, the pseudo-first-order rate constant for methane evolution from MeHgEt is 2.35×10^{-6} s^{-1} and that for $MeHgBu^i$ is 2.39×10^{-6} s^{-1}. Thus leaving group effects are not simply related to the size of the alkyl group (R′).

Cleaved Group Effects (R). The rates of acetolysis of alkyl groups from dialkylmercury decrease in the order: R = Et > *i*-Pr > Me > *t*-Bu in the four series shown in Figure 2. The cleaved alkyl group effects [under conditions in which the leaving group (HgR′) is constant] can be expressed quantitatively by:

$$\log (k'/k_0') = \mathbf{C} \qquad (12)$$

where k_0' is the rate constant for acetolysis of R-HgR′ in eq 3 when R = Me, and k' is that for R = Et or *i*-Pr. **C** is a cleaved alkyl group constant which has a characteristic value for each R, and it does not depend on the leaving group HgR′.

The nonsystematic trend in the values of **C** in Table V suggests that there are at least two opposing effects present in the acetolysis of an alkyl-mercury bond. The *decrease* observed in proceeding from Et, *i*-Pr to *t*-Bu follows from the increase in steric bulk at the site of protonation.[51] On the other hand, the *increase* from Me to Et (and to *i*-Pr) is in accord with electron release from these R groups accompanying protonolysis, as described earlier.

The rates of protonolysis of alkylmercury iodides[31] in *aqueous* perchloric and sulfuric acid follow the order expected from a dominance of steric factors, viz., Me:Et:*i*-Pr:*t*-Bu in the relative order: 123:49:16:1.0. The small kinetic isotope effect (k_H/k_D) measured from the protonolysis of methylmercury iodide [31b]may reflect either a transition state in which the bond to carbon is poorly formed or one in which it is almost complete.[27,29] The latter could account for reactivity pattern, but other uncertainties in this system discourage further discussion.[43]

A similar effect, however, can be observed during the acetolysis of a series of well-behaved methyl-ethyllead compounds [$Me_nEt_{4-n}Pb$, when $n = 0, 1, 2, 3$].[35] If leaving group effects are taken into account, the cleavage of Me-Pb is consistently 8.6 times more facile than Et-Pb cleavage in all three intramolecular competitions as well as in the intermolecular competition using $Me_nEt_{4-n}Pb$ ($n = 1, 2, 3$) and Me_4Pb/Et_4Pb, respectively. It is noteworthy that the Me/Et reactivity in tetraalkyllead is reversed from that in dialkylmercury ($k_{Me}/k_{Et} = 0.30$), although the kinetic isotope effect of 9 in the ac-

Table VI. Experimental and Calculated Rate Constants for Acetolysis of Dialkylmercury

R-Hg-R′		log k_{obsd}	log k_{calcd}	log k'_{obsd}	log k'_{calcd}
Me	Me	0.59	0.59		
Me	Et	0.74	0.76	1.16	1.14
Me	*i*-Pr	1.27	1.28	0.93	0.88
Me	*t*-Bu	1.43	1.44	*a*	
Et	Et	1.91	1.90		
Et	*i*-Pr	2.41	2.42	1.67	1.64
Et	*t*-Bu	2.58	2.58	*a*	
i-Pr	*i*-Pr	2.19	2.16		
i-Pr	*t*-Bu	2.35	2.32	*a*	

[a] Not determined, see text. All rate constants are given as 7 + log k.

etolysis of tetraethyllead[21a] is comparable with that observed with diethylmercury. The difference, we believe, is due to increased steric hindrance in the four-coordinate organolead compounds compared with the more accessible two-coordinate organomercury analogues. The severe steric restrictions imposed on tetraalkyllead compounds is also borne out by the failure to extend the linear free-energy relationships to higher alkyl homologues in protonolysis studies.[35]

Generalized Equation for Protonolysis of Dialkylmercury. The linear free-energy relationships in eq 11 and 12 for leaving group effects and cleaved group effects, respectively, during acetolysis of dialkylmercury suggests that a generalized relationship is possible which correlates all the rates using the empirical parameters in Tables IV and V, i.e.,

$$\log (k/k_0) = \mathbf{L} + \mathbf{C} \qquad (13)$$

where k_0 represents the rate constant for acetolysis of Me_2Hg and k is that for any other RHgR′ in Table I. The validity of eq 13 is shown in Table VI by comparing the experimental rate constants with those calculated from the equation.

Electron Release by the Cleaved Group in Electrophilic Substitution as Measured in Electron Transfer Processes. Saturation Effects in Alkyl Groups. The empirical constant **C** in the generalized eq 13 for acetolysis of dialkylmercury takes into account any steric interactions due to the cleaved group (R) *at the reaction site.* In the absence of such steric effects, the cleaved group effect in electrophilic substitution should be influenced primarily by electron release and thus parallel the leaving group (HgR′) effects we described in eq 11 and Table IV. This situation will obtain during an electrophilic process in which a rate-limiting electron-transfer step precedes the actual bond breaking, e.g.,

$$\text{R-M} + \text{E}^+ \xrightarrow{\text{slow}} \text{R-M}^{+\cdot} + \text{E} \xrightarrow{\text{fast}} \text{R-E} + \text{M}^+ \qquad (14)$$

These conditions will be optimized when the organometal R-M has a relatively low ionization potential and the electrophile E^+ may function (as an oxidant) without the requirement for bond formation.[44d]

Four such processes have recently been demonstrated, viz., the alkylation of tetracyanoethylene with tetraalkyllead compounds, the cleavage of Grignard reagents with di-*tert*-butyl peroxide, as well as the cleavages of tetraalkyllead and of dialkylmercury with hexachloroiridate(IV).[33,44] In each of these examples, Figure 7 shows that the (logarithmic) rate of cleavage is a linear function of the energetics of electron detachment from the organometal as measured by the oxidation or ionization potentials. The excellent linearity in the plots militates against the presence of any important steric factors in electron transfer, as it should be in outer-sphere electron-transfer processes.[45]

Significantly, the relative reactivities of the *cleaved* alkyl groups in electron-transfer cleavages follow a pattern in which incremental changes in energy for R = Me, Et, *i*-Pr, and *t*-Bu

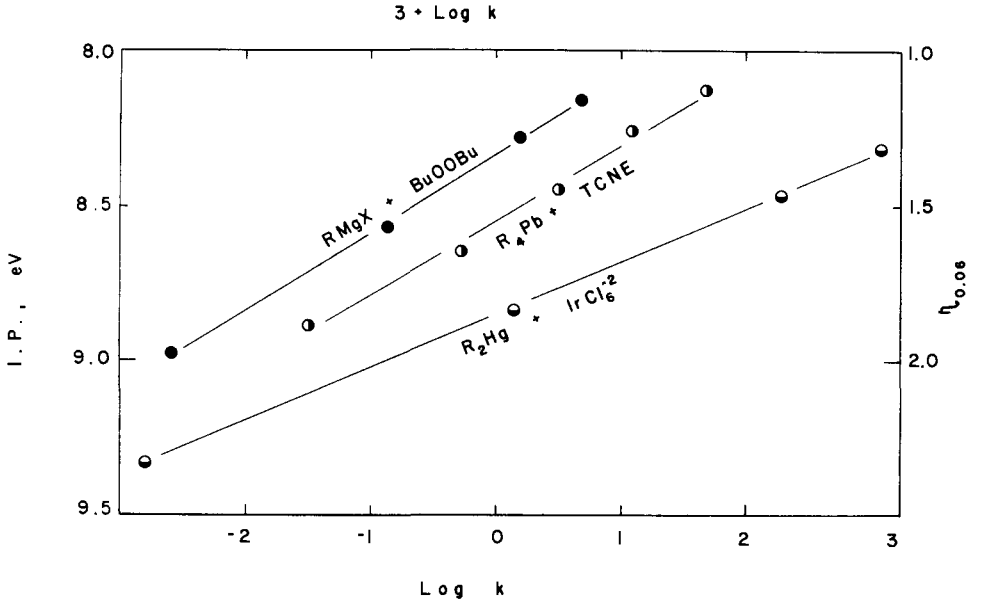


Figure 7. Electron-transfer processes in electrophilic substitutions. Saturation effects followed by alkyl substituents in the cleavage of organometals during the treatment with various electrophiles: scale left and bottom for: (◑) tetraalkyllead with tetracyanoethylene and (◒) dialkylmercury with hexachloroiridate(IV). Scale right (Tafel potential from ref 39b) and top for Grignard reagents and di-*tert*-butyl peroxide (●).

Table VII. Elemental Analysis of Dialkylmercurials

R–Hg–R′		Bp, °C (mmHg)	Elemental analysis[a] C Calcd	C Found	H Calcd	H Found
Me	Et	54/54	14.73	14.94	3.29	3.44
Me	*i*-Pr	56/30	18.57	19.07	3.90	4.00
Me	*t*-Bu	53/20	22.04	22.31	4.44	4.63
Et	*i*-Pr	74/20	22.04	21.83	4.44	4.32
Et	*t*-Bu	39/3.4	25.13	25.30	4.92	4.75
i-Pr	*t*-Bu	46/4.0	27.95	28.58	5.36	6.00
Me	*i*-Bu	50/15	22.04	22.24	4.44	4.62
t-Bu	*t*-Bu	58.5[b]	30.52	30.77	5.76	5.87

[a] Analysis performed by Midwest Microlab, Ltd., Indianapolis. [b] Melting point in sealed capillary (cf. ref 20).

show a "saturation" effect, which is the same as that observed in the *leaving* group effect (HgR′) denoted by **L** in Table IV. Moreover, the same linear correlations in Figure 6 are obtained if the scissa relating to oxidation or ionization potentials is replaced with **L**. Thus the saturation pattern for alkyl groups is independent of whether they are involved as cleaved (R) groups or as leaving (HgR′) groups. It clearly relates to an intrinsic property of the alkyl–mercury bonds and reflects the manner in which an alkyl group responds to the presence of a positive charge on mercury. Indeed, we propose that the saturation pattern for alkyl groups be used as a diagnostic probe for the mechanism of cleavage in organometals.

Electrophilic Substitution at Saturated Carbon. Concluding Remarks. Acetolysis studies on dialkylmercury have demonstrated not only the importance of the cleaved group (R) but also the leaving group (HgR′) in electrophilic substitution. Alkyl groups are excellent probes for measuring these electronic effects quantitatively, and the correlations of the rates with the ionization potentials show that a positive charge is developed on both the leaving group (R) and the cleaved group (HgR′). These facets of the reactivity of dialkylmercurials toward protonic electrophiles may be extended more generally, since it has been long recognized that nucleophilic reactivity is influenced by the "polarizability" of the nucleophile. Thus, the Edwards oxybase equation contains both a term related to the oxidation potential of the nucleophile as well as a term related to its basicity.[46] The molecular orbital analogue of the Edwards equation has been developed by Klopman, in which electrostatic and covalent terms are the counterparts to basicity and polarizability, respectively.[47,48] Organometallic nucleophiles are σ donors and have negligible basicity in the Edwards sense.[7] Thus, we anticipate that the nucleophilic reactivity of organometals, using either the Edwards or Klopman model, should reduce to an equation such as (13), in which electron release by alkyl groups is the important consideration. The latter, in essence, represents a "virtual" ionization of the carbon–metal bond by the electrophile since it can be directly related to the energetics of electron detachment.[40] The three-center transition state represented as I is an adequate model at this juncture. Furthermore, *hard* electrophiles[49] such as Bronsted acids as well as *soft* electrophiles such as tetracyanoethylene, hexachloroiridate(IV), and peroxides evoke the same electron demand from the organometal in the absence of steric factors. This similarity underscores the strong caveat that the oft-cited correlations between activation parameters (e.g., log k) and ionization or oxidation potentials by themselves represent insufficient proof that a reaction proceeds by an electron-transfer mechanism.

Experimental Section

Materials. Acetic acid (Mallinckrodt analytical reagent, 99.7%) was redistilled from 1.5% acetic anhydride under argon immediately prior to use but produced no change in the rate constants determined otherwise. Acetic acid-d_1 was obtained from Diaprep, Inc. and analyzed as 98 atom % D by its proton NMR spectrum. Mercuric bromide and alkyl bromides used in the syntheses were generally analytical reagent grade and used as received. Isobutyl bromide was stirred for two 1-h periods with an equal volume of 2 N nitric acid to hydrolyze any *tert*-butyl bromide impurity. It was then dried over $CaCl_2$ and distilled from CaH_2.

Preparation of Dialkylmercurials. The general procedure of Singh and Reddy[25d] was followed for the preparation of the unsymmetrical mercurials. The alkylmercury bromide of the *more* reactive alkyl group was treated with a 1.5 equiv excess of the Grignard reagent of the less reactive alkyl group. Using this procedure any symmetrical dialkylmercury formed by exchange (generally less than 1%) should be the less reactive species and thus should have minimal effect on the kinetics. The mixture of alkylmercury bromide and Grignard reagent in ether was stirred for 5 min prior to hydrolysis, drying, and distillation.

Most of the alkylmercury bromides used in these preparations were prepared in the usual manner[50] involving treatment of excess mercuric bromide with the corresponding Grignard reagent. A useful alternative, employed when the symmetrical mercurial is available, involves dissolving 1 equiv of mercuric bromide in a minimum amount of tetrahydrofuran (THF). Upon the addition of 1 equiv of dialkylmercury, white crystals of the corresponding alkylmercury bromide immediately precipitated and could be recovered by decantation of the solvent. In all cases, the alkylmercury bromides were purified, generally by recrystallization from ethanol and occasionally by sublimation in high vacuo. Di-*tert*-butylmercury was prepared in THF by the procedure described by Blaukat and Neumann[20] and additionally purified by vacuum sublimation.

The dialkylmercurials were examined by NMR, mass spectroscopy, and elemental analysis. In addition, the mercurials could be examined by gas chromatography using a 6-ft. column consisting of 10% polyethylene glycol 600 and 1% quadrol on 80/100 Chromosorb W. Elemental analyses for the more unusual mercurials are given in Table VII.

Kinetics. Typical Procedure. Into a scrupulously cleaned and dried 25-ml flask was transferred 3.00 ml of HOAc by glass pipet. A Teflon-covered magnetic stirring bar was inserted, and the system was sealed with a gas-tight rubber septum, then flushed with argon. Internal standard gas (1.00 ml) was injected, and the flask equilibrated in a constant temperature oil bath held at 37.5 °C. A 40 μl sample of mercurial was injected by means of a syringe and an electronic timer started. The weight of the mercurial was determined by weighing the syringe. At regular intervals (4 to 15 min depending on the mercurial), the gases in the flask were sampled and analyzed by gas chromatography with flame ionization detection using a 6-ft. column Porapak Q at 120 °C. Yields of gases were calculated using standards carefully calibrated under reaction conditions. Reactions were followed to less than 5% conversion. The pseudo-first-order rate constants obtained in this manner were consistently reproducible to within ±2%.

Solvent Isotope Effects. Kinetic studies were carried out as described above using acetic acid-d_1. The values of k_{obsd} so obtained were corrected for 2 atom % HOAc using the equation: $k_H/k_D = 0.98/(k_{obsd}/k_H - 0.02)$.

Competition Isotope Effects. A stock solution consisting of 85.2% DOAc and 14.8% HOAc was prepared and 5 ml of this mixture was placed in a series of constricted glass tubes equipped with a 14/40 joint. Each tube was degassed three times by a freeze–pump–thaw

cycle on a vacuum line and 100 μl of the mercurial was transferred by bulb-to-bulb distillation. The tubes were sealed and heated at 37.5 °C for 48 h. Thereafter, the tubes were opened individually and the gaseous products were vacuum transferred into another flask using a bath consisting of a frozen heptane slush. The mixture of propane and 2-propane-d_1 so obtained was examined by GC–MS using a column of graphitized carbon black. The gas was led via a Pd/H_2 separator at 260 °C into a Varian CH7 mass spectrometer interfaced with a Varian 620i data collection system. The isotope effect was calculated using the expression: $k_H/k_D = (I_H/I_D)[X/(1-X)]$ where I_D is the total intensity at m/e 45, I_H is the total intensity of m/e 44 corrected for the contribution from 2-propane-d_1, and X is the atom fraction of protium in the acetic acid.

Alkylmercury acetates were isolated by removal of the acetic acid and other volatiles in vacuo. The residue was dissolved in pyridine containing a Me_4Si internal standard and examined by proton NMR spectroscopy. Methylmercury acetate: δ 2.23 (3 H, s, CH_3 acetate), 0.86 (3 H, s, $J_{^{199}Hg-^1H}$ = 225 Hz, CH_3). Ethylmercury acetate: δ 2.17 (3 H, s, CH_3 acetate), 1.76 (2 H, g, J_{H-H} = 7 Hz, $J_{^{199}Hg-^1H}$ = 214 Hz, CH_2), 1.20 (3 H, t, J_{H-H} = 7 Hz, $J_{^{199}Hg-^1H}$ = 296 Hz, CH_3). Isopropylmercury acetate: δ 2.16 (3 H, s, CH_3 acetate), 1.38 (6 H, d, J_{H-H} = 6 Hz, $J_{^{199}Hg-^1H}$ = 279 Hz, CH_3), methine septet largely obscured by the acetate resonance. Alternatively, the formation of alkylmercury acetates could be followed directly by carrying out the reactions in NMR tubes sealed in vacuo using either acetic acid or acetic acid-d_4.

$J_{^{199}Hg-^1H}$ coupling constants were determined on a Varian EM360 NMR spectrometer using the neat mercurials. The ^{13}C NMR spectra were recorded on a Varian XL100 spectrometer.

First vertical ionization potentials were determined by He(I) photoelectron spectroscopy. The spectra were kindly recorded for us by Drs. J. Ulman and T. P. Fehlner.

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(51) Further evidence for a large steric contribution to **C** (and not to **L**) is supplied by preliminary studies on the effect of β-methyl substitution. Thus the value of **L** along the series: Et, *n*-Pr, *i*-Bu, neopentyl remains essentially constant, but **C** drops off sharply. A quantitative study of steric and polar contributions to **C** is in progress.

Dihydrodiols from Anthracene and Phenanthrene

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Abstract: Relative stereochemistry has been assigned to the vicinal dihydrodiols produced from anthracene and phenanthrene by bacterial and mammalian enzymes. The mutant strains, *Beijerinckia* strain B-836 and *Pseudomonas putida* strain 119, which are deficient in dihydrodiol dehydrogenase activity, accumulate (+)-*cis*-1,2-dihydroxy-1,2-dihydroanthracene and (+)-*cis*-3,4-dihydroxy-3,4-dihydrophenanthrene in the culture medium when incubated with anthracene and phenanthrene, respectively. *cis*-1,2-Dihydroxy-1,2-dihydrophenanthrene was also detected as a minor product from phenanthrene. Trans dihydrodiols at the 1,2, 3,4, and 9,10 positions of phenanthrene were synthesized by reduction of *o*-quinones, and the kinetics of their formation by epoxide hydrase from the corresponding arene oxides were determined. The 9,10-oxide proved to be one of the best known substrates for epoxide hydrase. Rates of dehydration and the ratio of phenols produced from the dihydrodiols were highly dependent on both configuration and conformation. Coupling constants for vicinal, trans hydrogens in cyclic systems tend to be much larger than those for the corresponding cis isomers. In contrast to this, *cis*-3,4-dihydroxy-3,4-dihydrophenanthrene was found to have a larger coupling constant ($J_{3,4}$ = 5.5 Hz) than the corresponding trans isomer ($J_{3,4}$ = 2.0 Hz) due to unusual conformational effects for these diols near the hindered bay position of phenanthrene. Coupling constants are reported for cis and trans, non-K-region dihydrodiols in each of the four possible conformations.

Systematic studies of the stereochemistry of the mammalian and bacterial dihydrodiols from anthracene and phenanthrene have not been reported. Relative stereochemistry of vicinal dihydrodiols of biological origin is of interest as it relates to the fundamental mechanisms utilized by living organisms for the metabolism of aromatic hydrocarbons.[2] Dihydrodiols formed during the mammalian metabolism of aromatic hydrocarbons are generally thought to arise by the trans enzymatic hydration of initially formed arene oxides,[3] whereas dihydrodiols formed from aromatic hydrocarbons by bacteria have cis stereochemistry and are produced by the action of dioxygenases which incorporate both oxygen atoms from the same oxygen molecule into the substrate.[4]

Metabolism of phenanthrene to a dihydrodiol can occur at any of three ring positions with destruction of aromaticity in only one of the three aromatic rings. Mammals form dihydrodiols at each of these positions. The preponderant dihydrodiol has been assigned as *trans*-9,10-dihydroxy-9,10-dihydrophenanthrene.[5,6] The trans relative stereochemistry was firmly assigned, since the corresponding cis isomer was known from the action of osmium tetroxide on the parent hydrocarbon.[7] The 1,2-dihydrodiol[6,8,9] has been assumed to be the trans isomer. Very small amounts of another dihydrodiol, assumed to be *trans*-3,4-dihydroxy-3,4-dihydrophenanthrene, have been isolated.[9] These three dihydrodiols are detectable as in vitro metabolites formed when phenanthrene is incubated with hepatic microsomes.[10]

3,4-Dihydroxy-3,4-dihydrophenanthrene was identified as an intermediate in the degradation of phenanthrene by a *Flavobacterium* species,[11] which led to the suggestion that soil pseudomonas oxidize phenanthrene through *trans*-3,4-dihydroxy-3,4-dihydrophenanthrene to 3,4-dihydroxyphenanthrene.[12] However, the authors pointed out that neither of these reactions had been demonstrated enzymatically, nor were definitive assignments of stereochemistry made.

Mammals oxidize anthracene to *trans*-1,2-dihydroxy-1,2-dihydroanthracene.[13] Interestingly, evidence has been presented for the formation of *trans*-9,10-dihydroxy-9,10-dihydroanthracene.[14] Since the carbinol groups are at remote positions of the central aromatic ring, this dihydrodiol may not originate from an arene oxide. A 1,2-dihydrodiol of unknown stereochemistry has been implicated as a metabolite in the degradation of anthracene by a *Flavobacterium* species.[15]

The results described below establish relative stereochemistry of the dihydrodiols formed from anthracene and phenanthrene by mammals and bacteria on the basis of their proton magnetic resonance spectra. A prior study of the cis and trans 1,2-dihydrodiols of naphthalene[2] established the applicability of the Karplus equation[16] to dihydrodiols of polycyclic aromatic hydrocarbons. These four spin systems are particularly suited to conformational analysis due to the angular dependence of the magnitudes of the coupling constants. Although trans isomers generally have much larger coupling constants[17] than the corresponding cis isomers, unequivocal assignments