Theoretical Characterization of the Mechanism of Hg−C Bond Cleavage by Halogenic Acids

Vincenzo Barone,[†] Alessandro Bencini,*,[‡] Federico Totti,[‡] and
Myriam G. Uytterhoeven[‡]

Dipartimento di Chimica, Università Federico II, via Mezzocannone 4, I-80134 Napoli, Italy, and Dipartimento di Chimica, Università degli Studi di Firenze, via Maragliano 75, I-50144 Firenze, Italy

Received October 23, 1995[⊗]

Ab initio calculations at the MP2 level show that the CH_3−Hg bond is broken by halogenic acids by a one-step mechanism, proceeding through a closed transition state in which, however, bond forming and breaking are not completely synchronous. Activation energies closely parallel Hg−C bond strengths and are strongly influenced by the electronegativity of the ligands bound to Hg. For instance, the energy barrier decreases by roughly 50% on going from CH_3HgCl to CH_3HgCH_3. The general agreement between computed and experimental trends gives further support to the reaction mechanism.

Introduction

Mercurials, e.g. methylmercury ion, arylmercurials, and dissolved inorganic salts of mercury(II), are widely dispersed in the biosphere,[1] but they do not appear to have any relevant biological function. On the contrary, the high affinity of organomercurials for thiols and their lipophilic nature make them highly toxic to living organisms and organomercurials have been widely used as antiseptics in surgery applications. The methylmercury ion, $MeHg^+$, is probably the most ubiquitous compound and, owing to its enhanced solubility in water, is a dangerous pollutant agent, which has a strong tendency to accumulate in the food chain.[2] Bacteria respond to the toxicity of the organomercurial compounds by developing two peculiar resistance mechanisms which involve the cleavage of the Hg−C bond and the reduction of the mercuric residues to elemental mercury. The relevant catalysts which perform the above reactions are MerB, organomercurial lyase, and MerA, mercuric ion reductase.[3] The proposed mechanism by which the MerB enzyme carries out the hydrolysis of the Hg−C bond occurs through an S_E2 reaction in which the mercuric ion is coordinated by three sulfurs of three different cysteine residues.

Much attention has been devoted, in the literature, to the study of the protic acid cleavage of dialkyl- and diarylmercury (R_2Hg) and organomercuric halides[4] (RHgX). Reactions of R_2Hg with hydrochloric acid in dimethyl sulfoxide−dioxane solutions have been found to follow a kinetic law of the type $v = k[HCl][R_2Hg]$. The suggested mechanism is a concerted S_E2 one with complete retention of configuration[5,6] in which the reacting species is the undissociated hydrochloric acid. Reactions of organomercuric halides have been more usually performed in aqueous media, in which the halogenic acid is dissociated, and side reactions with solvolysis products have been claimed to occur. Only for the MeHgX derivatives was the solvolysis of Me^+ found to be slow. Some general findings common to all of the reactions are as follows: (a) the acid cleavage of the R_2Hg derivatives is facile while the reaction of the RHgX compounds with the proton is slow; (b) the aryl−mercury bond is broken much more easily than the alkyl−mercury bond. Recently a peculiar complex of methylmercury[7] with the formula $[(np_3)HgMe]^+$ (np_3 = tris(2-(diphenylphosphino)ethyl)amine), in which the Hg atom is coordinated by three P atoms of the triphosphine ligand, showed a marked tendency to hydrolyze even in acetic acid solutions at room temperature, thus suggesting a possible effect of the coordination geometry on the reaction path.

It appeared to us that a theoretical characterization of the thermochemistry and of the kinetics of Hg−C bond cleavage would actually be of importance in order to rationalize the observed reactions and, possibly, to predict new routes to break the bond. To proceed in this direction, one needs a quantum-chemical tool of calculation which can be applied to large chemical systems (which can mimic the protein environment) at reasonable computer expense. In a recent study, we have shown that accurate geometrical structures, thermochemical parameters, and vibrational frequencies can be obtained, for mercury compounds, by coupling Hartree−Fock geometry optimizations with a medium-sized basis set to single-point energy evaluations at the MP2 level, adding f orbitals on Hg as polarization functions.[8] Since the elucidation of the mechanism of cleavage of the Hg−C bond by halogenic acids seems particularly significant and these systems are small enough to allow further tests of the model of calculation, we have applied

---

[†] Università Federico II.

[‡] Università degli Studi di Firenze.

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1996.

(1) Summers, A. O.; Silver, S. *Annu. Rev. Microbiol.* **1978**, *32,* 637.

(2) (a) Nelson, N. *Environ. Res.* **1971**, *4*, 1. (b) Bache, C. A.; Gutenmann, W. H.; Lisk, D. J. *Science* **1971**, *172,* 951.

(3) Moore, M. J.; Distefano, M. D.; Zydowsky, L. D.; Cummings, R. T.; Walsh, W. T. *Acc. Chem. Res.* **1990**, *23,* 301.

(4) Jensen, F. R.; Rickborn, B. *Electrophilic Substitution of Organomercurials*; McGraw-Hill: New York, 1968.

(5) (a) Kreevoy, M. M. *J. Am. Chem. Soc.* **1957**, *79,* 5927. (b) Kreevoy, M. M.; Hansen, R. L. *J. Am. Chem. Soc.* **1961**, *83,* 626.

(6) (a) Dessy, R. E.; Reynolds, G. F.; Kim, J.-Y. *J. Am. Chem. Soc.* **1959**, *81,* 2683. (b) Dessy, R. E.; Kim, J.-Y. *J. Am. Chem. Soc.* **1960**, *82,* 686.

(7) Barbaro, P.; Cecconi, F.; Ghilardi, C. A.; Midollini, S.; Orlandini, A.; Vacca, A. *Inorg. Chem.* **1994**, *33,* 6163.

(8) Barone, V.; Bencini, A.; Totti, F.; Uytterhoeven, M. G. *J. Phys. Chem.* **1995**, *99,* 12743.

0276-7333/96/2315-1465$12.00/0

the procedure developed in ref 8 for thermochemical and geometrical properties to calculate the kinetics of the reaction between dimethylmercury and methylmercury halides and halogenic acids.

Here we wish to report the results obtained for the structures of the transition states of the reactions involving dimethylmercury and methylmercury halides obtained under vacuum. The reaction paths leading to cleavage of the Hg−C bond in methylmercury halogenides will also be shown.

These results should be considered as preliminary steps toward the development of a more general model which should include solvent effects. In the present calculations, therefore, we will consider undissociated halogenic acids, as observed for the cleavage reactions in dioxane-containing media. The influence of the electronegativity of the R′ substituent on the reaction rate is considered for the series of compounds RHgR′ (R′ = Cl, Br, I).

Computational Details

Both semiempirical and *ab initio* calculations have been performed. *Ab initio* molecular orbital calculations were performed by using the GAMESS and GAUSSIAN 94 system of programs.[9,10] Geometries of the energy minima and of the first-order saddle points have been optimized by following the procedure described in ref 8. Semiempirical AM1 calculations[11] have been performed using MOPAC in order to explore the potential surface for locating a reasonable transition-state geometry from which to start *ab initio* saddle point searches. The nature of the transition states (TS) has been confirmed by computing the harmonic frequencies at the Hartree−Fock (HF) level. In all the computations SBK pseudopotentials and a medium-sized valence basis set with one d polarization function on C, P, and halogens have been used.[8] On the C and P atoms a 31G* basis was used, while a more extended 311G* set was applied to the halogens. For Hg a 5111G basis was used for the valence s and p orbitals and a 311G basis was used for the d ones. For H an unscaled 31G basis was applied. Electronic contributions to the reaction, ΔH_r, and activation enthalpies, $\Delta H^{\ddagger}$, have been computed at the MP2 level, adding one f polarization function on Hg. HF geometries have been generally used for transition states, except when explicitly stated in the text. Vibrational contributions have been computed using HF harmonic frequencies.[8]

Intrinsic reaction path (IRP) has been computed for the reaction (1a) in Scheme 1 by following the Gonzales−Schlegel second-order method.[12,13] Tracing of the IRP has required the calculations of about 60 points along the intrinsic reaction coordinate (IRC), each point roughly corresponding to a full geometrical optimization.

Results and Discussion

Transition state structures for the reactions

$$CH_3HgX + HX \rightarrow CH_4 + HgX_2 \qquad (1)$$

$$CH_3HgCH_3 + HX \rightarrow CH_4 + CH_3HgX \qquad (2)$$

where X = Cl, Br, I, have been searched with AM1 calculations by placing the HX molecule in several positions around the substrate in order to explore a wide part of the potential energy surface. Only one geometry has been attained for the transition state independently from the relative position of HX and the substrate at the starting point. The transition-state structure found for the reaction with MeHgX is shown in Figure 1. A very similar result was obtained for the dimethyl derivative, and it is also shown in Figure 1. In Figure 1 the atoms of the halogenic acid are indicated with an asterisk, and this convention will be used in the following for distinguishing the atoms coming from the acid from those of the substrate in the transition state. Using the geometrical arrangements of the reactants shown in Figure 1, we have performed transition-state searches at the HF level by following the method outlined in the previous section. The overall geometry of the transition state does not change, while, of course, new values for bond distances and angles are computed. In Figure 1, we report the relevant geometrical parameters obtained for the transition state of the reaction between MeHgCl and HCl and between Me_2Hg and HCl. The geometrical parameters computed for reactions 1 and 2 are shown in Scheme 1.

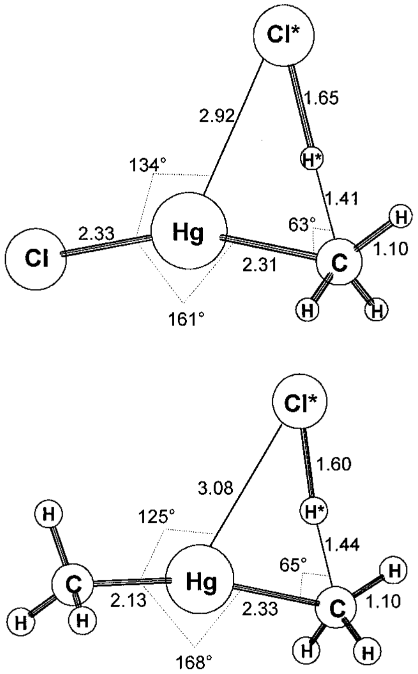


Figure 1. Transition-state structures with the most meaningful geometrical parameters for reactions 1a and 2a with X = Cl. Atoms marked with an asterisk refer to the attacking hydrochloric acid. Bond distances are in Å and bond angles in deg. The geometrical parameters are computed at the HF level.

In order to estimate the effect of neglecting the electron correlation on the actual geometry of the transition state, we have performed a transition-state search including correlation at the MP2 level for reaction 1a. The relevant computed geometrical parameters

---

(9) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comput. Chem.* **1993**, *14*, 1347.

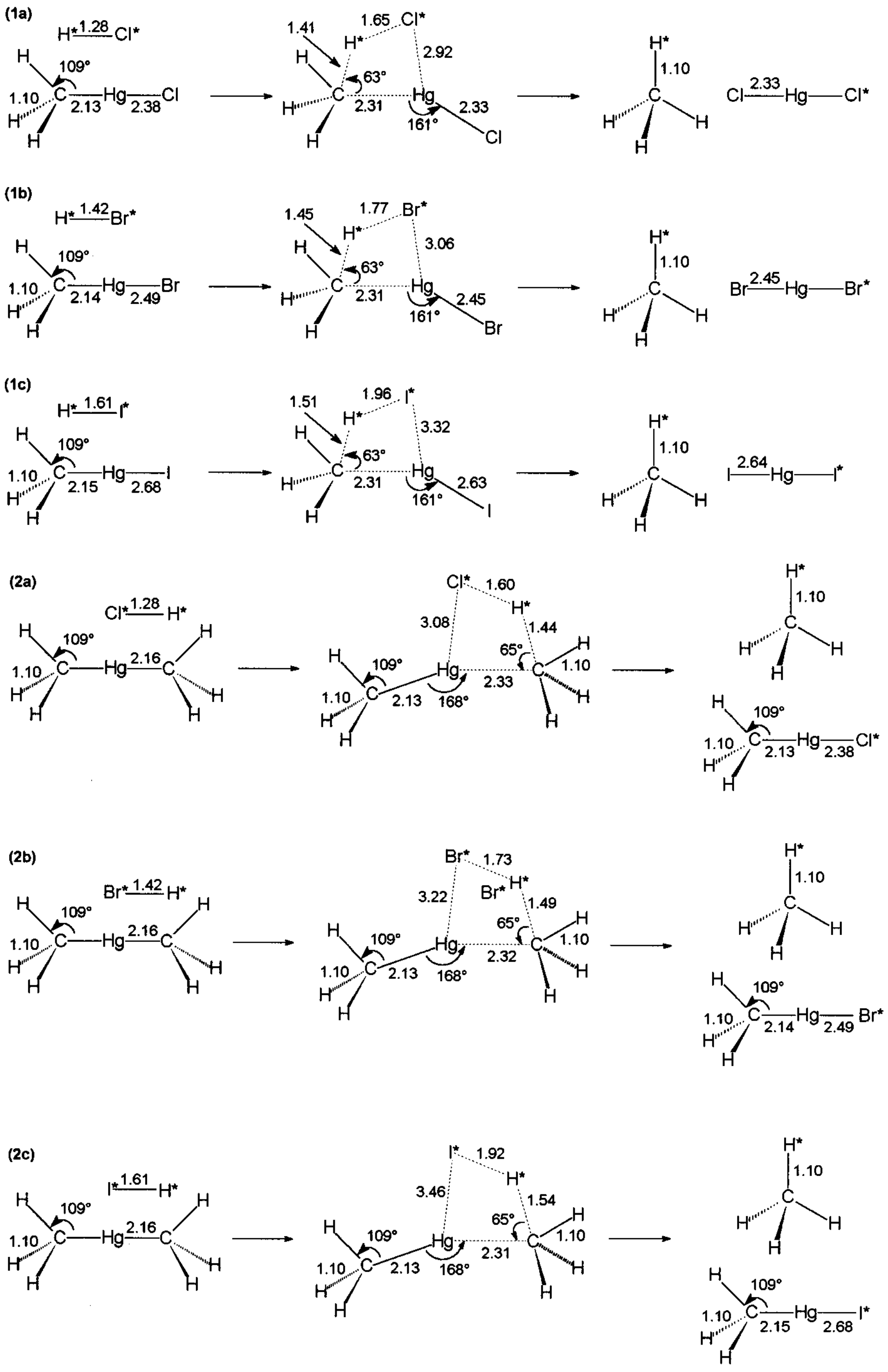
(10) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, B.; Stefanov, B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; DeFrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian 94 (Revision B.2); Gaussian, Inc., Pittsburgh, PA, 1995.

(11) Dewar, M. J. S.; Zoebish, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(12) Gonzales, G.; Schlegel, H. B. *J. Phys. Chem.* **1990**, *94*, 5523.

(13) Gonzales, G.; Schlegel, H. B. *J. Phys. Chem.* **1991**, *95*, 5853.

Scheme 1



are as follows: Hg–C = 2.30 Å, Hg–Cl = 2.72 Å, Hg–Cl* = 2.72 Å, H*–Cl* = 1.66 Å, CHgCl = 156°, HgCH* = 60°. The TS geometry obtained through MP2 calculation matches quite well that obtained at the HF level, the largest deviation of bond distances being 0.2 Å for Hg–Cl*. This can be taken as evidence that electronic correlation, at least at the MP2 level of approximation, does not substantially alter the computed geometries. It has already been found that thermochemical data for Me_2Hg and MeHgX can be accurately reproduced using MP2 energies computed on HF geometries.[8] Furthermore, activation energies computed at the MP2 level using HF and MP2 transition-state structures, in turn, differ by less than 0.3 kcal mol^{-1}. On these grounds, all the other geometrical calculations have been therefore performed at the HF level. Another point which can be questioned concerns the reliability of the MP2 procedure, which is a low-order perturbative approach, in computing correlation contributions to activation energies. This has been checked by the QCISD[T][14] method, which can be veiwed as an infinite-order many-body approach for single and double excitations plus a perturbative estimation of the effect of triple excitations. These calculations performed on the same reaction gave an activation energy larger than the MP2 value by only 0.7 kcal mol^{-1}.

All the computed transition-state structures present a deep similarity: they support the S_E2 mechanism[6] suggested for reactions 1 in which electrophilic attack

---

[14] Raghavachari, K.; Pople, J. A.; Replogle, E. S.; Head-Gordan, M. *J. Phys. Chem.* **1990**, *94*, 5579.

Table 1. Selected Bond Orders and Net Atomic Charges for the Hg−C Bond Cleavage Reactions 1 and 2 Computed for the Reagents, Transition States, and Products

reagents[a]	Hg−C	C	Hg	R′[b]
Me_2Hg	0.952	−0.361	0.294	−0.361
MeHgCl	1.058	−0.316	0.427	−0.404
MeHgBr	1.029	−0.313	0.454	−0.432
MeHgI	1.015	−0.328	0.392	−0.366

transition state	Hg−C	Hg−X	C−H	C	Hg	R′[b]
Me_2Hg−HCl	0.595	0.118	0.313	−0.406	0.372	−0.324
Me_2Hg−HBr	0.618	0.130	0.304	−0.410	0.377	−0.324
Me_2Hg−HI	0.640	0.122	0.244	−0.397	0.360	−0.325
MeHgCl−HCl	0.664	0.230	0.317	−0.402	0.611	−0.364
MeHgBr−Br	0.670	0.216	0.298	−0.395	0.589	−0.335
MeHgI−HI	0.675	0.202	0.240	−0.387	0.492	−0.252

products	Hg−X	C−H	C	Hg	R′[b]
CH_4		0.995	−0.223		
$HgCl_2$	0.903			0.687	−0.344
$HgBr_2$	0.963			0.661	−0.330
HgI_2	0.977			0.524	−0.262

[a] Products for reaction 2. [b] R′ indicates C for Me_2Hg and halogen elsewhere.

Table 2. Computed Reaction (ΔH_r) and Activation Energies ($\Delta H^{\ddagger}$)[a] for the Reaction MeHgR′ + HX → CH_4 + R′HgX (R′ = Halogen, Me; X = Halogen)

	MeHgCl + HCl	MeHgBr + HBr	MeHgI + HI	Me_2Hg + HCl	Me_2Hg + HBr	Me_2Hg + HI
ΔH_r	−23.3	−29.3	−36.7	−36.7	−40.9	−45.4
$\Delta H^{\ddagger}$	34.9	28.7	26.4	20.7	15.9	15.9

[a] Energies are expressed in kcal mol^{-1}. The computational procedure is described in the text.

is carried out by molecular or ion-paired HCl with the subsequent formation of a four-membered ring. The symmetry of the computed transition states was in any case very close to C_s, all the atoms except two hydrogens of each methyl group lying on the symmetry plane. Our computations suggest that bond forming and breaking in the transition state are not completely synchronous. Taking reaction 1a as an example, the inspection of the bond orders for C−H* (0.995 in the products and 0.317 in the transition state) and for Hg−Cl* (0.903 in the products and 0.230 in the transition state) suggests that, at the saddle point, the C−H* bond is more completely formed than the Hg−Cl* one. At the same time the Hg−C bond is broken only to a lower extent (the corresponding bond orders are 1.058 in the reactants and 0.664 in the transition state). The computed bond lengths, shown in Figure 1, conform to the above considerations. The net charges on Hg and C atoms obtained by a Mulliken population analysis increase on passing from the reactant to the transition state. In particular, they are 0.427 and −0.316 in the reactant and 0.611 and −0.402 in the transition state of reaction 1a. The net charge on the Cl atoms goes from −0.404 to −0.364. Similar trends are obtained for all the other halogens.

Since the reaction mechanisms appear to be slightly asynchronous, the transition state can have some biradical character. In this case a single-configuration method could be inappropriate to describe the features of the saddle points. In order to check how significant the biradical character could be, we have performed, for reaction 1a, a multiconfiguration SCF-CI calculation using a wave function with two electrons in two active molecular orbitals, which we have taken to be the HOMO and the LUMO. This wave function originates three singlet states, the one with the [11] occupation giving the biradical character. The results of this calculation are that the ground configuration is a linear combination of the [20], [11], and [02] states with coefficients 0.994, 0.006, and −0.112, respectively. The next excited state, mainly the [11] one, is 444 kcal mol^{-1} higher in energy. This result, combined with the QCISD[T] calculations, shows that our MP2 approach is quite efficient in giving reliable information on the structure and energetics of the reactions.

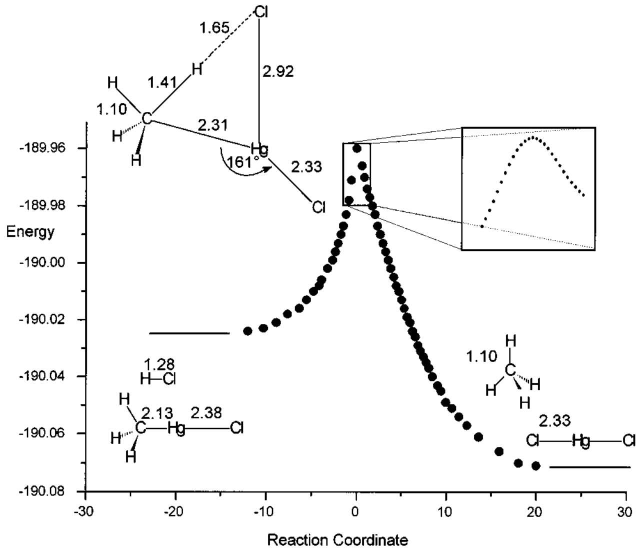


Figure 2. Intrinsic reaction path for reaction 1a. Energies are given in hartrees; units for the reaction coordinate are in $amu^{1/2}$ bohr. Data between −12 and +20 $amu^{1/2}$ bohr have been computed as described in the text. The asymptotic energy values for reagents and products are indicated with horizontal lines. The insert shows the details of the TS zone between −0.7 and +0.7 $amu^{1/2}$ bohr.

Bond orders and net charges for reactions 1 and 2 are collected in Table 1. The transition-state structure of reaction 2 is close to that of reaction 1, the main difference being the computed charge on mercury, which is smaller than that computed for reaction 1. From the results stated above, we can infer that the TS of reactions 1 and 2 should be stabilized when reducing the electronegativity of ligands coordinated to Hg.

Using the computed geometries for the saddle points, we have calculated the activation energies, $\Delta H^{\ddagger}$, for reactions 1 and 2 at the MP2 level. The results of these calculations are collected in Table 2. The computed energy barriers decrease on passing from Cl to Br and I, following the trend outlined above with the electronegativity of the ligands coordinated to mercury, and are also in qualitative agreement with the only available experimental data,[4] which show that the decrease of ability to react is in the order MeHgCl < MeHgBr < MeHgI. The computed activation energies for reactions 2 are consistently much smaller than those computed for reactions 1, again in general agreement with the experimental observations[4] that diaryl and dialkyl derivatives are more reactive than the methylmercuric halides.

In order to look in more detail at the actual path of the Hg−C bond-breaking reaction, we have also performed calculations in order to find the "reaction

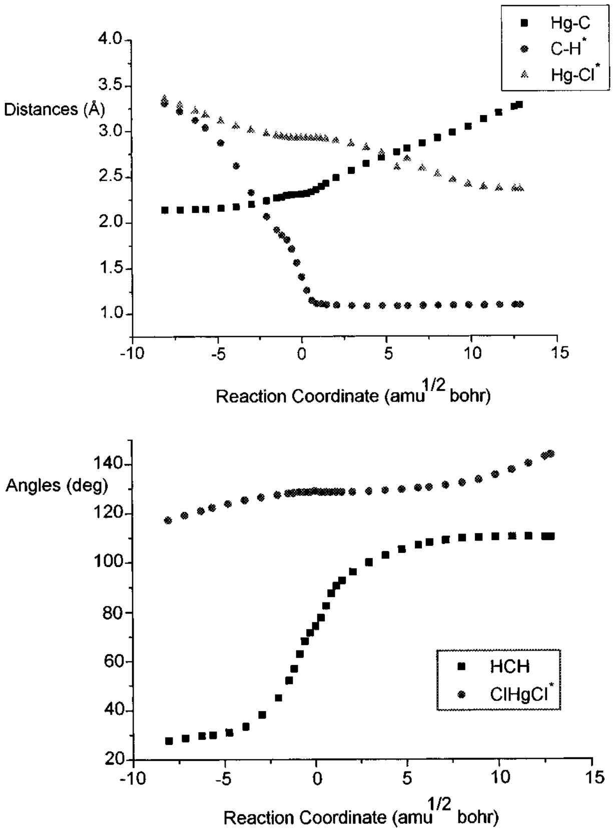


Figure 3. Variation of the most meaningful geometrical parameters for reaction 1a as a function of the intrinsic reaction coordinate.

coordinate" or the "reaction path".[15,16] This was achieved by computing the intrinsic reaction path (IRP), starting at the saddle point. The results of the calculation for reaction 1a are collected in Figure 2. The reaction is confirmed to be a one-step reaction of the S_E2 type. In order to give a chemical meaning to the reaction coordinate, we show in Figure 3 the most significant variations of bond distances and angles as a function of the reaction coordinate. According to the Hammond[17] postulate the path between the transition state and the less stable (higher energy) minimum, corresponding in our case to the reagents HCl + CH_3HgCl, is much shorter than the other half-path leading to the products. Near the energy minima the tangent to the reaction path is, of course, dominated by the relative motion of the two partners which approach each other.[18] The situation is more involved near the TS. In particular, just before the transition state, the path tangent is dominated by C−H* stretching and the first part of the second half-path essentially corresponds to opening the H*−C−H angle toward the equilibrium tetrahedral value of methane. Note that the effective reduced mass for these motions is much lower than the asymptotic values for the relative motion of reactants or products. This explains the very rapid fall-off of the energy in this region when the energy is plotted against mass-weighted coordinates as in Figure 2.

Conclusions

Ab initio calculations at the HF and MP2 level show that the protic acid cleavage of the mercury−carbon bond in the gas phase proceeds through a one-step reaction mechanism involving a four-center transition state in which bond forming and breaking are not completely synchronous. The above mechanism is common to all of the reactions in which R = Me and R′ = Me, halogen. The activation barrier is strongly influenced by the nature of R′ and decreases by roughly 50% on passing from the halogens to the methyl group. The electronegativity of R′ also influences the velocity of the reactions, which are faster when R′ is less electronegative.

These conclusions are in good general agreement with the experimental findings,[4] even if reactions involving organomercuric halides have been more often performed in solvents containing water molecules, in which the attacking electrophile is presumably a solvated proton.

The present results convince us that HF calculations can give important insight into the reaction mechanisms of organomercurials, and efforts will be made to extend the present study by including reactions in aqueous media.

Acknowledgment. We thank our colleagues of the CNR of Firenze, S. Midollini, A. Orlandini, and C. A. Ghilardi, for many helpful discussions. Thanks are also expressed to Prof. A. Vacca, Università di Firenze, for many bibliographical suggestions, and to Prof. P. Fantucci, Università di Milano, for his interest during the work. Finally, we must express our consideration for the help received by M. Fontanelli, Università di Firenze, who takes care of the computer facilities.

OM9508391

---

[15] Fukui, K.; Kato, S.; Fujimoto, H. *J. Am. Chem. Soc.* **1975**, *97*, 1.

[16] Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363.

[17] Hammond, G. S. *J. Am. Chem. Soc.* **1955**, *77*, 334.

[18] Salem, L. *Electrons in Chemical Reactions*; Wiley: New York, 1982.