

A Computer Model for Flexible Hydrocarbon Chain Behavior in the Mass Spectrometer

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Abstract: A flexible chain model is presented to explain long-range interaction in the mass spectra of molecules containing hydrocarbon chains. The model is applicable to any system in which hydrogen abstraction in the molecular ion competes with other fragmentation processes. Quantitative predictions are made, based upon Monte Carlo estimations of hydrocarbon chain conformations. Molecules are modeled in a diamond lattice, and full account is taken of excluded volume. Comparison of the predictions of the model with a wide variety of mass spectral data suggests that three systems in particular, trimellitic anhydride *n*-alkyl esters, *n*-alkoxybenzoic acids, and their corresponding methyl esters, behave upon electron impact in a manner consistent with the model for flexible, randomly oriented hydrocarbon chains.

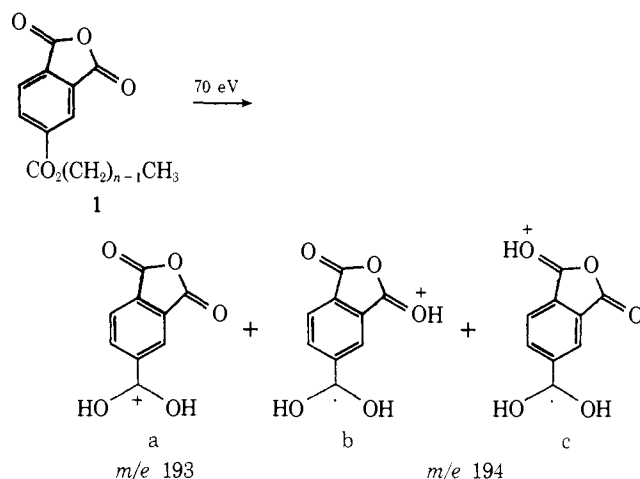
While the mass spectrometry of molecules containing long hydrocarbon chains has received extensive attention in the experimental literature,^{1,2} the extent to which the flexibility of the chain contributes to the observed mass spectra is still an open question. Several authors have invoked coiling of flexible molecules to explain long-range interactions in their mass spectra.³ Coiling might occur in the neutral molecule upon transfer to the gas phase or might occur upon electron impact.⁴ Coiling of hydrocarbon chains in the gas phase has recently been questioned.⁵

Coiling in molecular ions implies that there is an enthalpy sufficient to overcome the entropy requirements of a flexible chain at high internal energies. In ions derived from bifunctional molecules with electron-rich functional groups, charge exchange⁶ is most often invoked as the driving force for coiling of the chain. Rearrangement reactions in these ions are often highly stereoselective,¹ suggesting that the two functional groups efficiently achieve close proximity. When the second functional group is an unactivated hydrocarbon chain, hydrogen transfer reactions occur from random sites along the chain.^{2,4} Interaction with the charge would be much weaker.

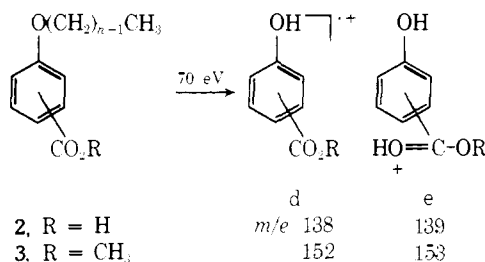
Meyerson and Leitch,⁴ in their recently proposed internal solvation model, invoke coiling of alkyl chains to explain long-range hydrogen transfer reactions in the mass spectrometer. "Such coiling," these authors contend, "very likely occurs in the neutral molecule, although it may be enhanced upon ionization. The role of electron impact may well be chiefly to trigger a sequence of reactions the precise path of which depend upon and thus reflect the preexisting orientation of the molecule."⁴

These authors themselves point out that the experimental results in such systems are compatible with freely flexible chains.⁷ A flexible chain model has not been formulated in any testable way. A rigorously defined model of flexible chain behavior is needed before one can distinguish it from the solvation model. Indeed, a flaw in the internal solvation model is that it does not lead to testable predictions.

We present in this paper a model for the conformational behavior of flexible hydrocarbon chains, applicable to any system which involves intramolecular hydrogen abstraction as the rate-limiting step in a rearrangement process. For example, rearrangement upon electron impact in long-chain esters of trimellitic anhydride (TMA, **1**) leads to ions at both *m/e* 193 and 194.⁸ The latter ion, which has been assigned the structures **b** and **c**,⁸ results from hydrogen abstraction from the chain prior to rearrangement and loss of the chain fragment. The ion ratio *m/e* 194/193 increases with chains length.



Long-chain ethers of *m*- and *p*-hydroxybenzoic acid⁹ and their methyl esters⁹ also give two ions upon electron impact, one of which results from intramolecular hydrogen abstraction preceding fragmentation and loss of the chain. Here ion **d** at *m/e* 138 or 152 is the product of a normal phenyl ether rearrangement. It is formed competitively with ion **e** at *m/e* 139 or 153. The ion ratios *m/e* 139/138 and 153/152 increase with chain length, which we have previously shown is indicative of rate-determining hydrogen abstraction.⁹



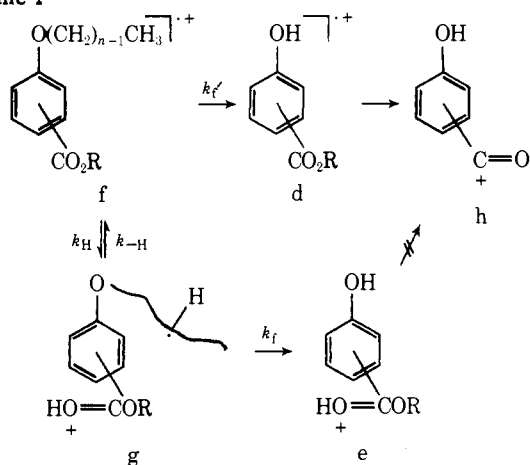
The model for flexible chain behavior contends that changes in ion ratios with changes in chain length are conformational in origin. In the above examples, hydrogen abstraction from the chain leading to ions at *m/e* 194, 153, or 139 is assumed to result from a conformation of the chain which brings one of its methylenes within a reactive distance of an ionized carbonyl oxygen. To generate curves comparable with the reported ion ratio data, one must calculate the probability that a chain of length *n* occupies the reactive volume of the appropriate carbonyls during the lifetime of the molecular ion.

Analytical calculations cannot take account of steric and excluded volume effects;¹⁰ furthermore, calculation by that approach of the distribution functions we seek would require untenable assumptions for the relatively short chains (compared with polyethylene) which we wish to examine. We have turned to a Monte Carlo estimation of chain conformation in which the molecule is weakly embedded in a tetrahedral lattice. Details of the Monte Carlo method for similar molecules have appeared elsewhere,¹¹ including the importance sampling techniques used to bring the calculations into the realm of financial feasibility.

The Chemistry

Rearrangements in the mass spectra of *m*- and *p*-alkoxybenzoic acids and their methyl esters have been studied in some detail.⁹ Ion structures were assigned, and the reaction was interpreted in terms of Scheme I. The rate constants in Scheme I, in accord with the quasi-equilibrium theory (QET) of mass spectrometry,¹² represent the value of k averaged over the internal energy distribution of the molecular ions.

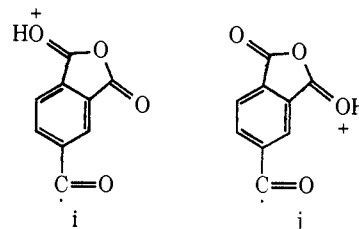
Scheme I



We wish to develop a model which relates the intensity of ions resulting from hydrogen abstraction, here e, to the conformational mobility of the hydrocarbon chain in the molecular ion f. We infer the existence of a number of intermediates g resulting from hydrogen abstraction and focus attention on those pathways which lead to the formation and breakdown of g. If it can be shown that the hydrogen abstraction step, k_H , is rate-determining in the formation of e, then the ion ratio $e/(d + h)$ can be related directly to the probability that the hydrocarbon chains in f will achieve a reactive conformation. Later sections of this paper show how this probability can be calculated for randomly oriented, flexible chains.

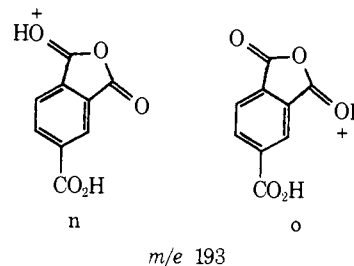
The usefulness of the alkoxybenzoic acids for these studies lies in the simplicity of their mass spectra.⁹ Only one ion, e, results from hydrogen abstraction. The molecular ion is weak, so that there is no complication introduced by uncertainty in the fraction of $[\text{M}]^+$ having the structure f or g. The ion e does not lose ROH to form h; consequently one can account separately for those ions involving, and not involving, hydrogen abstraction at the remote carbonyl. In addition, the ion ratio e/d is not detectably sensitive to changes in electron impact energy. Both d and e have the same appearance potentials.

Trimellitic anhydride esters have more complex mass spectra than the alkoxybenzoic acids.⁸ Two ions, at m/e 194 and 176, derive from hydrogen abstraction. Each may be assigned two structures, a, b,^{8,13} and i, j,^{8c,13} respectively. We do not require a detailed description of reaction path-



ways in order to carry out a conformational analysis of the system. We do require a complete accounting of major ion intensities which involve hydrogen abstraction remote to the point of attachment of the chain.

For **1**, we require, ideally, the chain length dependence of ion intensities at m/e 194, 193, 192, 176, and 175, as well as some structural information about the ions at m/e 149, 148, and 126. Values of the m/e 176 and 175 intensities are available for only a few chain lengths. Good data are available for the ions at m/e 194, 193, and 192; the m/e 192 ion carries almost negligible ion current. We must make a number of assumptions in attempting to quantitate the amount of remote hydrogen abstraction in this system. First, we must assume that the ion intensities at m/e 149, 148, and 126 make unimportant contributions to the chain length dependence of hydrogen abstraction, as inferred from the m/e 194/(193 + 192) ratio. Second, we assume that the m/e 176/175 ratio is similar in magnitude to the m/e 194/193 ratio so that we may safely ignore the former. While there is no theoretical basis for invoking this assumption, both Djerassi^{8c} and Meyerson^{8a} have published data which suggest that this assumption is experimentally, albeit fortuitously, valid at 70 eV. Third, we must assume that ions of the structure n and o make a negligible contribution to the ion intensity at m/e 193. While this assumption appears at

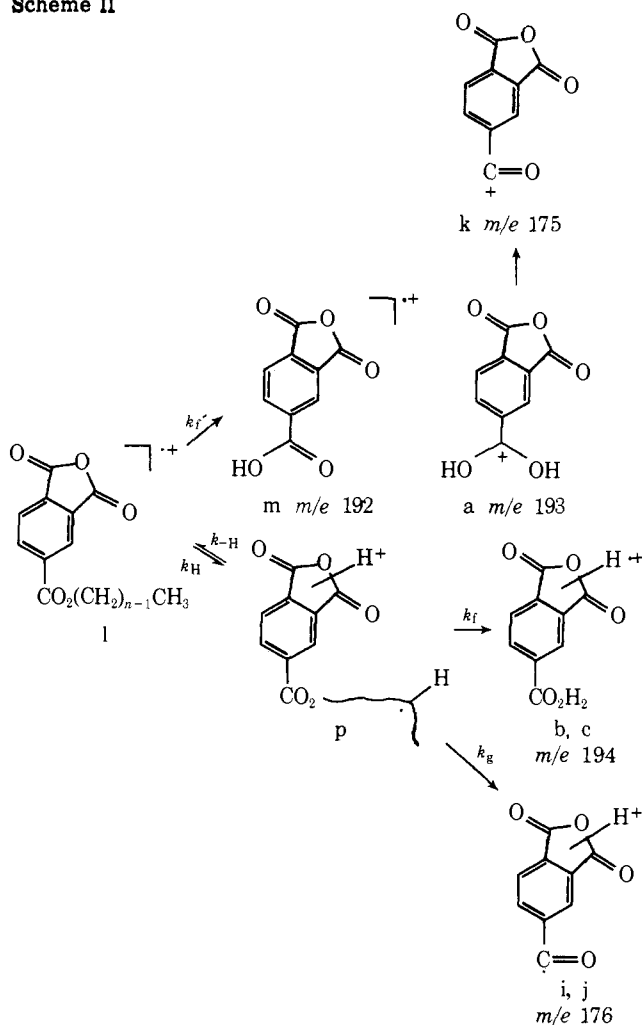


first glance to be precarious,^{8a} we have observed a strong substituent effect on aromatic ester rearrangements.¹⁴ Electron-donating groups give rise to large values of $[\text{ArCO}_2\text{H}]^+ / [\text{ArCO}_2\text{H}_2]^+$, whereas electron-withdrawing substituents give very small values of this ratio. These preliminary experiments and the small intensity of the m/e 192 ion in the mass spectra of **1** suggest that we may safely ignore the contributions of n and o to the ion ratios we examine.¹⁴

We, therefore, take Scheme II as the working model for remote hydrogen abstraction in trimellitic anhydride esters. Our Monte Carlo calculations are not sensitive to the assumptions in Scheme II. The choice of experimental data for proper comparison with the conformational calculations is very sensitive to assumptions made in Scheme II. As more complete data for the trimellitic anhydride esters become available, the assumptions and limitations of Scheme II will have to be modified.

Some of the published experimental data from the mass spectra of trimellitic anhydride esters⁸ have been interpreted in terms of the sites of hydrogen abstraction within the chain. These data may be compared directly (*vide infra*) with similar predictions of our computer calculations.

Scheme II



Kinetic Considerations

Ion intensity ratios, for competing and consecutive unimolecular processes, may be set equal to ratios of rate constants for ions derived from a common precursor. In Scheme I, d, e, and h all derive from f.

We have previously shown that the rate constant k_H , which leads to e, may be considered to be the product of k_{PH} , an intrinsic rate constant for reaction of $[M]^+$ with an unactivated CH_2 group, times the probability P_n that any CH_2 group of the chain will occupy the reactive volume about the carbonyl oxygen.⁹ P_n , in turn, is the sum of the probabilities that each CH_2 group in an n carbon chain will occupy that volume. The factor of 2 accounts for the two hydrogens per methylene group.

$$k_H = 2k_{PH}P_n \quad (1)$$

$$P_n = \sum_i^{n-1} P_{i,n} \quad (2)$$

The reverse reaction, described by k_{-H} , is similarly dependent on chain length. If we call $k_{P(-H)}$ the intrinsic rate constant for the reverse hydrogen transfer, k_{-H} depends on the same encounter probability as does k_H .

$$k_{-H} = k_{P(-H)}P_n \quad (3)$$

$$k_H/k_{-H} = 2k_{PH}/k_{P(-H)} \quad (4)$$

If g and f are in rapid equilibrium, the probability dependence disappears. It follows that if the fragmentation step is rate determining in the formation of e (i.e., if $k_f \ll k_{-H}$),

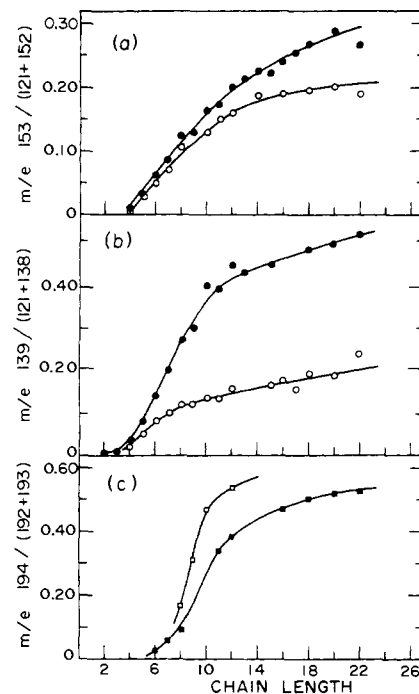


Figure 1. Ion ratio data as a function of chain length for n -alkyl ethers and esters; (a) meta (○) and para (●) alkoxybenzoic acids; (b) meta (○) and para (●) alkoxy O-methyl benzoates (data from ref 9); (c) esters of trimellitic anhydride (data (■) from Meyerson, *et al.*;^{2c} data (□) from Cable and Djerassi^{8c}).

the ion ratio $e/(d + h)$ would be invariant with chain length. This is not the case (Figure 1).

For rate-determining hydrogen abstraction, the ion intensity ratio is described by eq 5. The intensity ratio increases with the increase in the probability that a CH_2 group in the chain will occupy the reactive volume about the carboxylate carbonyl oxygen during the lifetime of the molecular ion. Because the appearance potentials for the ions derived from the processes described by k_H and k'_f are the same, and the ion intensity ratios are insensitive to electron impact energy,⁹ we assume that only the probability term in eq 5 is responsible for the increase in the ion ratio with chain length.

$$\frac{e}{d + h} = \frac{2k_{PH}}{k'_f} \sum_{i=1}^{n-1} P_i \quad (5)$$

Equation 5 is rigorously true as long as hydrogen abstraction is not diffusion controlled. It says nothing about the factors which determine the encounter probability, P_n . These might be chain coiling in the neutral, internal solvation in the ion or the random encounters of a freely flexible chain.

P_n is equal to the ratio of (reactive conformations)/(all conformations) of the hydrocarbon chain. We can rewrite eq 5 as eq 6. It should be emphasized that the measured ion ratio $e/(d + h)$ is proportional to, and not equal to, the reactive fraction of conformations. The proportionality constant Q is unknown. It could conceivably be large, since k_{PH} represents the rate constant for hydrogen abstraction in a system which has an interaction probability of unity.

$$\frac{e}{d + h} = \frac{2k_{PH}P_n}{k'_f} = Q \frac{\text{reactive conformations}}{\text{all conformations}} \quad (6)$$

Using Scheme II, we can apply these considerations to trimellitic anhydride esters, keeping in mind the assumptions made in the previous section. Here eq 7 describes the appropriate ion ratio.

$$m/e \frac{194}{192 + 193} \approx \frac{176 + 194}{175 + 192 + 193} = Q' \frac{\text{reactive conformations}}{\text{all conformations}} \quad (7)$$

We present in this paper Monte Carlo calculations which estimate the ratio of (reactive conformations)/(all conformations) as a function of chain length, for flexible, randomly oriented chains with tetrahedral bond angles. We compare the results of these calculations with published ion ratios and show that the chain length dependence of the ion ratios is entirely consistent with flexible chains, randomly oriented.

The Model

Molecules are modeled in a diamond lattice. Chains are grown stepwise from the ether oxygen in **2** and **3** (and the ester oxygen in **1**) to a length of 30 carbons. Figure 2a shows the model representation for **2** indicating the first three steps in chain growth. C₄ is added as follows. One of the three lattice sites adjacent to C₃ is chosen at random for C₄; the remaining valences on C₃ are filled with hydrogens. This process is repeated for C₅, C₆, The method of Rosenbluth and Rosenbluth¹⁵ is incorporated to diminish the attrition rate in chain growth. Proper use of weighting functions removes the bias introduced by this importance sampling technique.

We define a "hit" as the occupancy of a lattice site next to a reactive oxygen by a methylene hydrogen. We estimate the partition function for both hitting conformations and for all conformations of length *n*. We assume this ratio equals the ratio of (reactive conformations)/(all conformations) for that chain length. In **2** and **3** the carbonyl oxygens are chosen to be the reactive sites. Both syn (O_s) and anti (O_a) rotamers are possible. "Free rotation" about the phenyl-carboxyl bond is modeled by including in the compilation hits at lattice sites adjacent to O_⊥ (see Figure 2). Free rotation about the ether-phenyl bond is modeled by allowing one-third of the chains to take vector 3 as the choice for placing C₁. Hits by methyl groups are not counted, in accord with labeling experiments reported by Djerassi for TMA esters.^{8c}

In the TMA model, Figure 2b, both anhydride carbonyl oxygens are allowed to be reactive. Syn and anti rotamers are modeled by choosing O_s and O_a, respectively, as the starting site for growing hydrocarbon chains. Free rotation about the carboxyl-phenyl bond is modeled by allowing chains to be grown from O_⊥.

Since only even-membered rings are possible on a tetrahedral lattice, it is a straightforward matter to estimate the number of conformations of chains having a hydrogen from a CH₂ group occupy one of the second tier of lattice sites around a reactive oxygen. We call these "outer hits." While, strictly speaking, outer hits refer to a 2.51 Å reactive distance, inner hits imply that the CH₂ group approaches within the O-H bond distance. Outer hits, then, model hydrogen abstraction at 1.6 times that distance.

The lattice nature of the calculations requires that all angles be strictly tetrahedral. This assumption is adequate for the hydrocarbon chain. Benzene rings and the anhydride group in TMA, however, must be modeled as the corresponding cyclohexane chains, in which equatorial, but not axial, hydrogens may be included. Space-filling models indicate that this model is nearly isosteric with the molecule in the case of hydroxybenzoic acid. In trimellitic anhydride, there is some distortion in the modeling of the anhydride in that five-membered rings are not possible on a tetrahedral lattice.

Two other problems are inherent in on-lattice models.

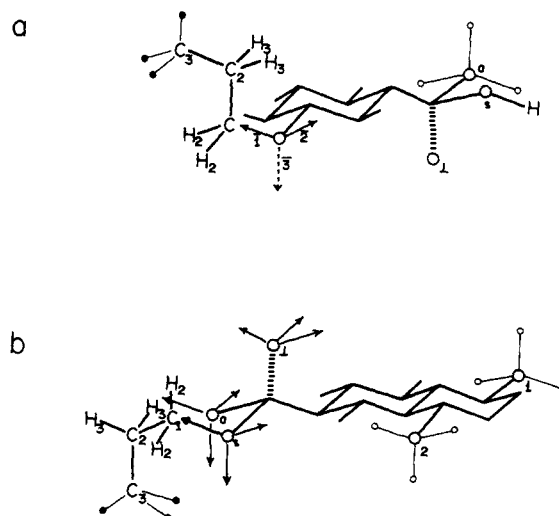
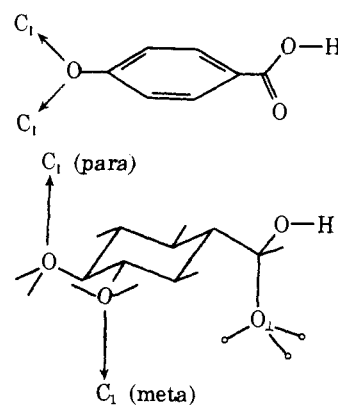


Figure 2. Diamond lattice model representation of (a) *m*-hydroxybenzoic acid O-alkyl ethers and (b) trimellitic anhydride O-alkyl esters. Open circles (O) represent hit sites. Vectors (→) indicate possible initial steps in chain growing. Small closed circles (●) represent possible loci for placing C₄.

Equal bond lengths overestimate the C-H bond distance. Hard-sphere nonbonding potentials underestimate collision radii. While these have an offsetting effect,^{16,17} we have some indication that the model overemphasizes short-range steric effects. Examining outer hits partially alleviates this problem. We prefer, however, to report inner hits and plot these data in the figures.

A more subtle problem may be seen in the drawing below. In the out-of-plane rotamers of aromatic molecules, the first bond vector may point either toward or away from the reactive carbonyl oxygen. Very short chains must react from the former conformation. In the lattice model for free rotation, the first bond vector is directed away from the hit sites in the para ethers and toward the hit sites in the meta ethers. The lattice model may overemphasize the reactivity of short-chains in the meta isomers. Reactive conformations of short-chain para ethers, however, are prevented by this artifact of the tetrahedral lattice model.



Because of the high internal energies in those molecular ions which react to give ions a-e, we neglect the 0.5-kcal/mol differences in energy between gauche and trans rotamers of the chain.

Results and Discussion

Molecular models are often very useful for examining the course and stereochemistry of chemical reactions. For **2**, considering only the planar conformations and assuming the bond angles are rigidly tetrahedral, we can calculate

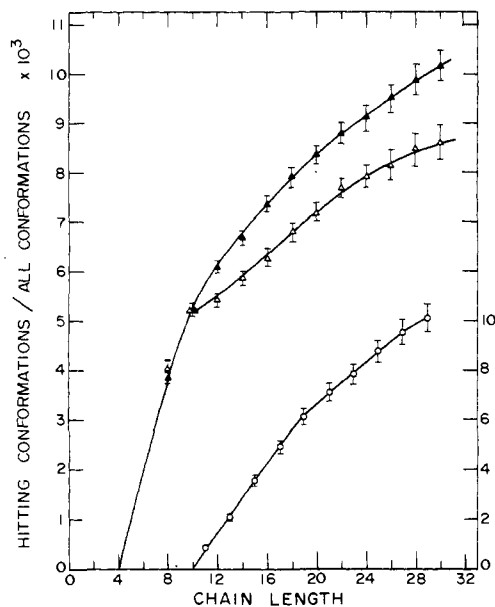


Figure 3. Ratio of estimated hitting conformations vs. all conformations for *m*- and *p*-hydroxybenzoic acid ethers in their planar conformation. Left ordinate, meta acids (\blacktriangle) and the corresponding methyl esters (\triangle). Right ordinate, para acids (\circ). Error bars are one standard deviation.

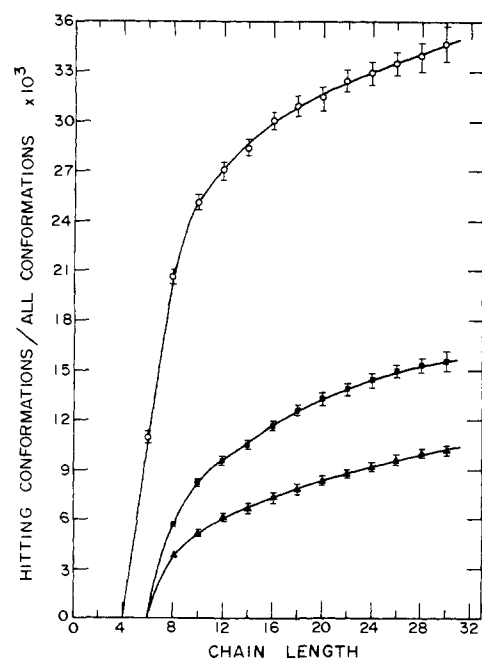


Figure 4. Effect of simulating free rotation on the estimate of hitting conformations vs. all conformations for *m*-hydroxybenzoic acid ethers. Planar conformation (\blacktriangle); simulated free rotation about the carboxyl-phenyl bond (\blacksquare); simulated free rotation about both the ether-phenyl and carboxyl-phenyl bonds (\circ).

that there are 42 million conformations of its 20-carbon chain, of which 220,000 conformations are reactive. For a 30-carbon chain, there are 260 billion discrete conformations of which 2 billion are reactive. Our calculations, in their simplest sense, represent a molecular-model-like sampling technique for estimating reactive and total chain conformations. In terms of thermodynamics, the calculations provide a direct estimate of configurational entropy.

Resonance and Free Rotation. Resonance structures for the molecular ions of **2** and **3** suggested to us that we limit our consideration to those conformations in which the ester

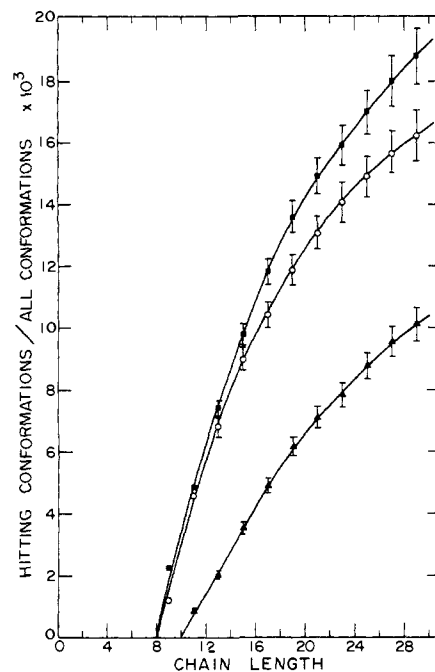
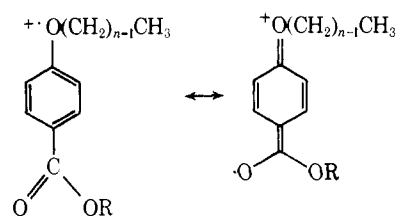


Figure 5. Effect of simulating free rotation on the estimate of hitting conformations vs. all conformations for *p*-hydroxybenzoic acid ethers. Lower curve, planar conformation. Upper curve, simulated free rotation about carboxyl-phenyl bond. Middle curve, simulated free rotation about both the ether-phenyl and carboxyl-phenyl bonds.

and ether functions are coplanar with the aromatic ring. Figure 3 presents the results of calculations (inner hits) for **2** and **3** restricted to the coplanar conformation. While these curves share gross general features with those of the experimental data in Figure 1, there are important differences. In particular, hydrogen abstraction is observed in the mass spectrometer for five-carbon chains. Hitting chains occur for 8- and 11-carbon chains, respectively, for the meta and para isomers.



Figures 4 and 5 indicate the effects of allowing free rotation to be simulated in the calculations. In the meta isomer free rotation about the phenyl-carboxylate bond increases the fraction of chains which hit. As the middle curve in Figure 4 indicates, this effect is more pronounced at the shorter chain lengths. Simulating additional free rotation at the ether-phenyl bond has a marked effect on the ratio of (hitting conformations)/(all conformations). Six-carbon chains now are seen to be reactive (five carbon chains for outer hits). The curve rises steeply and begins to level off when the chain length is 12 to 14 carbons. This curve is quite similar in its general features to the experimental curves in Figure 1.

Introducing the rotamers which simulate free rotation into the calculations for the para-substituted ethers also has a pronounced effect on the ratio of (hitting conformations)/(all conformations). Here nine-carbon chains are reactive, and there is some tendency for the curve to rise less steeply at long chain length. The out-of-plane rotamers do not contribute a short distance pathway for the chain to reach the

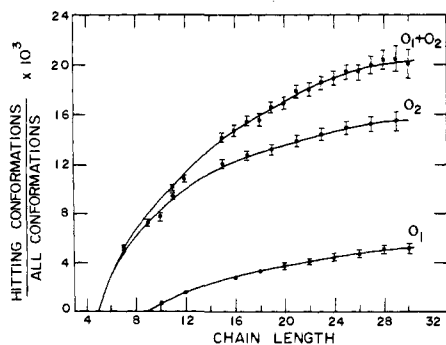


Figure 6. Ratio of estimated hitting conformations vs. all conformations for long-chain esters of trimellitic anhydride. The calculation includes simulation of free rotation about the carboxyl-phenyl bond. O_2 is meta; O_1 , para to the carboxylate. See the text for details.

reactive oxygen, since the appropriate vectors point to opposite sides of the aromatic ring (*vide supra*).

We conclude that the molecular ions of both meta and para isomers of **2** and **3** have ready access to out-of-plane rotational conformations. This is best explained in terms of molecular ion internal energies sufficient to allow free rotation about the carboxyl-phenyl and ether-phenyl bonds. The appearance potentials (AP) for both the m/e 153 and 152 ions have been reported to be 11.5 eV for *p*-**3**-16.⁹ The ionization potential (IP) for both *p*- and *m*-methoxybenzoic acids is 9.06 eV.¹⁸ The AP for m/e 139 is 11.6 eV for *p*-**2**-12.¹⁹ These values suggest a minimum internal energy of 2.4 eV (or 55 kcal/mol) for those molecular ions reacting to form e. In addition, space-filling models for *p*-**2** and **3** show that (CH_2) -4 and (CH_2) -5 of the hydrocarbon chain can reach the carbonyl oxygen only when both the carboxyl group and $O-CH_2$ bonds are twisted nearly perpendicular to the plane of the ring.

The data reported for TMA esters in Figure 6 are those from calculations compiled assuming free rotation about the phenyl-carboxyl bond as described in the previous section.

Flexible Chains. In Figure 7, we compare ion ratio measurements as a function of chain length with the calculated ratios of (hitting conformations)/(all conformations). Figure 7a depicts the *m*-alkoxybenzoic acid data; Figure 7b, the corresponding *p*-alkoxybenzoic acid data. In Figure 7c, comparisons are made for trimellitic anhydride esters. The curves derived from the conformational calculations are those in which free rotation was simulated in the model.

The conformational calculations agree remarkably well with the measured ion ratios for the *m*-alkoxybenzoic acids (Figure 7a). The experimental curve shows that ion e first appears for five-carbon chains. The curve rises steeply, then begins to level off, showing only a modest increase with chain length when the chains are 10–12 carbons long. The theoretical curve has an almost identical shape. The shortest hitting chain has six carbons (five for outer hits). There is a steep rise in the curve, followed by a decrease in slope, which occurs in the region of 9–11-carbon chains.

In the *p*-alkoxybenzoic acids (Figure 7b), the theoretical curve for flexible chains is similar in shape to that of the ion intensity ratios. It is shifted horizontally by four carbons from the experimental curve. This shift is caused by an artifact in modeling out-of-plane rotamers of *p*-alkoxybenzoic acid in a diamond lattice²⁰ (*vide supra*), which prevents short chains on the lattice from achieving a hitting conformation. The initial slope of the experimental curve is steeper than that of the theoretical curve. The decrease in slope, which occurs about carbon 12, is more pronounced in the former. We are inclined, at this point, to consider these dif-

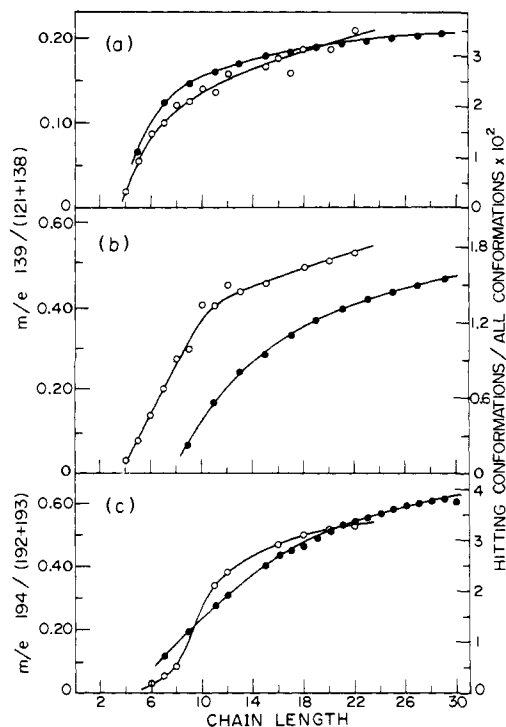


Figure 7. Comparison of the calculated ratio of hitting conformations vs. all conformations (●), with observed ion intensity ratios (○), as a function of chain length; (a) *m*-alkoxybenzoic acids, (b) *p*-alkoxybenzoic acids, (c) trimellitic anhydride esters. In (a) and (b), free rotation about the ether-phenyl and carboxyl-phenyl bonds are simulated in the Monte Carlo calculations. In (c), free rotation about the carboxyl-phenyl bond is simulated in the Monte Carlo calculations. The ion ratio data are taken from Figure 1.

ferences in shape minor and attribute them to the limitations of a model which depends upon a diamond lattice representation.

The trimellitic anhydride esters are compared with the theoretical model in Figure 7c. The curves share some features in common and show some marked differences. The shortest chain to give a measurable amount of b and c is the six-carbon chain. The computer calculations show that seven-carbon chains are reactive when considering inner hits, and that six-carbon chains reach a reactive carbonyl oxygen when we count outer hits. There is a more pronounced rise in the experimental curve for 10- and 11-carbon esters. The data, however, are rather sparse in this region and quantitative inferences are premature.

One assumption in obtaining the uppermost curve in Figure 6 is that O_1 and O_2 contribute equally to the hydrogen abstraction reaction. Since, from Scheme II, $k_H = k_1 P_{n,O1} + k_2 P_{n,O2}$, this is tantamount to assuming that the intrinsic rate constant for hydrogen abstraction in 1 by the carbonyl (O_1) para to the ester group, k_1 , is the same as that, k_2 , by the meta carbonyl (O_2). A substituent effect on this reaction (CO_2R , meta vs. para) would make this assumption a poor one. In fact, if k_1 were three to four times as large as k_2 , the weighted sum of the two lower curves in Figure 6 would generate the experimentally observed curve in Figure 7c.

Within the limitations of the diamond lattice model and the data currently available, we believe that the ion ratio data in Figure 7 are consistent with randomly oriented flexible chains.

Sites of Hydrogen Abstraction. Both Cable and Djerassi,^{8c} and Meyerson, *et al.*,^{8a} have reported data which they have interpreted in terms of sites of hydrogen abstraction within a hydrocarbon chain. The former authors examined

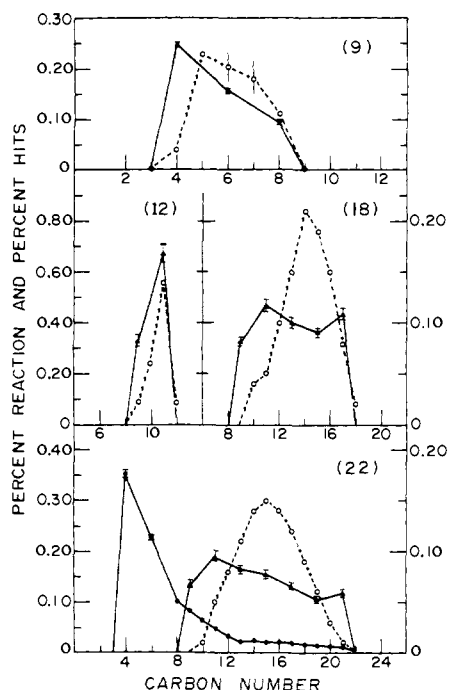


Figure 8. Per cent reaction (dotted lines) and per cent hits (solid lines) as a function of carbon number for *n*-alkyl esters of trimellitic anhydride. (9) 9-carbon ester: ion ratio (O) data from ref 8c; calculated hits (●) assuming both carbonyl oxygens reactive. (12) 12-carbon ester: data (O) from ref 8a, based upon $[M - C_jH_{2j}]^+$ ions (see text); calculated hits (▲) assuming only O_1 is reactive. (18) 18-carbon ester. (22) 22-carbon ester: data (O) from $[M - C_jH_{2j}]^+$ ions (right ordinate); calculated hits assuming both carbonyl oxygens (●) are reactive (left ordinate); that only O_1 (▲) is reactive (right ordinate). Error bars are one standard deviation. The vertical lines in (9) imply uncertainty in the measured values, see text. For 9-, 18-, and 22-carbon chains, the per cent hits at each carbon number is plotted as one-half the calculated value. Since hits occur only at every other carbon atom, this makes the total area under the curve add up to 100%.

specifically deuterium-labeled *n*-nonyl esters of TMA. At 70 eV, ions are observed at *m/e* 175 and 176; the latter one, assigned structures i and j, is attributed to hydrogen abstraction from the chain. At 15 eV, only the *m/e* 176 ion is observed. Consequently, at 15 eV, the *m/e* 177/176 ratio in the deuterated esters, barring isotope effects, is a measure of hydrogen abstraction from specific sites within the chain.

In Figure 8-(9), we plot these data, taking the liberty of proportioning the reported 39% deuterium transfer from $(CH_2)_6$ and $(CH_2)_7$ to favor the former. Our computer program generates similar information, calculating the relative number of conformations which hit at each methylene. These data are also shown in Figure 8-(9). The curves are remarkably similar in shape, considering the limitations of the tetrahedral lattice model. We should point out that at this chain length, hits at O_1 contribute negligibly to the reaction.

Meyerson and his coworkers^{8a} have reported a rather remarkable series of ions in the mass spectra of TMA esters. These $[M - C_jH_{2j}]^+$ ions result from loss of small olefin molecules from the molecular ion. Meyerson invokes the mechanism shown below to account for these ions. Although these ions carry only a tiny fraction of the ion current, they provide an insight into the relative extent of hydrogen abstraction from each carbon in a chain. In Figures 8-(12), 8-(18), and 8-(22), we have plotted these data in terms of per cent hydrogen abstraction from each carbon in 12-, 18-, and 22-carbon chains.

In Figure 8-(22), we plot the per cent hits at each carbon in a 22-carbon chain. If we assume both oxygens are reac-

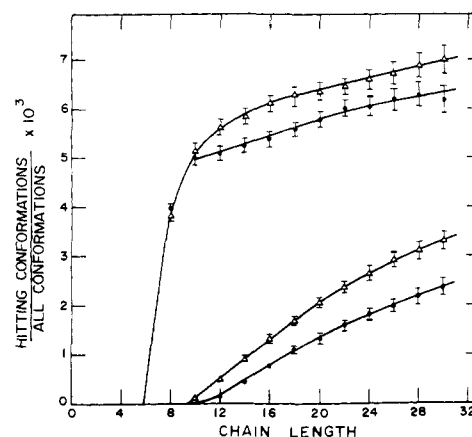
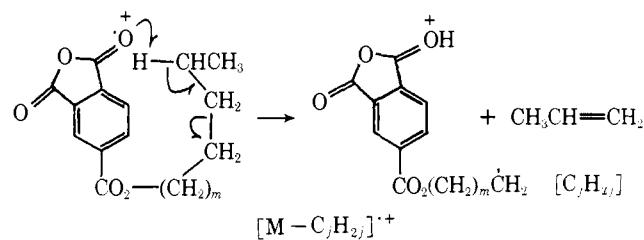


Figure 9. Steric effects in the estimate of hitting conformations vs. all conformations for planar forms of alkoxybenzoic acid (Δ) and alkoxy O-methyl benzoate (\bullet). Lower curves: carbonyl is anti to the ether oxygen. Upper curves: carbonyl is syn to the ether oxygen. See text for details.



tive, hits at the meta oxygen (O_2) dominate, and the calculated distribution of hit sites is skewed dramatically in favor of hits at low carbon number. This curve clearly has little in common with the distribution of hydrogen abstraction sites. Meyerson's data, with a maximum probability of reaction at $(CH_2)_{15}$, suggest that only hydrogen abstraction at the para oxygen (O_1) leads to the $[M - C_jH_{2j}]^+$ ions.

Distributions of hits at the para carbonyl oxygen in 22-carbon esters of TMA are plotted in Figure 8-(22), and for 12- and 18-carbon esters, respectively, in Figures 8-(12) and 8-(18). There are differences in curve shape, yet the distribution of hits contains the same sites within the respective chains. From the results of our calculations, we suggest the possibility that the $[M - C_jH_{2j}]^+$ ions occur only from reaction of the chain with carbonyl oxygen in TMA para to the ester group.

Steric Effects in the Model. The methyl esters **2** have about 15% fewer hitting conformations for the long-chain ethers than do the corresponding acids. The calculations indicate that this is an excluded volume effect.²² The methyl group excludes certain reactive conformations which sterically would be permitted for the acids. We have examined this effect in detail for the planar conformations of *m*-**1** and **2**. Two rotamers contribute to this effect, of which we had expected **4** to be the more important.

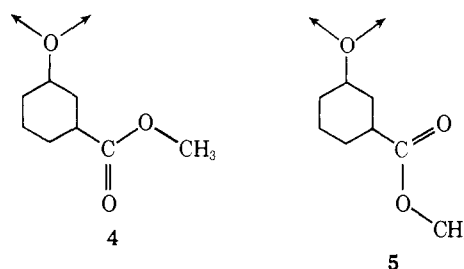


Figure 9 indicates that while **5** contributes a large fraction of the hitting conformations, its contribution to the ex-

cluded volume effect is fairly small. Rotamer 4 in which the methyl is syn to the ether oxygen has a large excluded volume effect. For 30-carbon chains, nearly 25% of all of the reactive conformations in the acid are prevented. The effect on estimated total chain conformations is undetectable.

Cyclization Probability and Entropy. Mass spectra are interpreted in terms of quasi-equilibrium theory which is derived by simplification from the RRKM theory of highly energetic reactions.¹² The working equation in QET is (8),

$$k(E) = \nu[(E - E_a)/E]^S \quad (8)$$

which describes the dependence of the unimolecular rate constant $k(E)$ in terms of the frequency factor ν , the internal energy of the ion E , and the activation energy E_a for the reaction under consideration. S refers to the effective number of degrees of freedom in the molecule and is always found to be less than the total number of degrees of freedom. E_a is usually calculated from $IP - AP$, the difference in electron volts between the ionization potential of the molecule and the appearance potential of the daughter ion under consideration.

Our calculations describe the total reversible cyclization probability for a chain of length n at a reactive atom (here, a remote carbonyl oxygen). The number of reactive conformations is a direct estimate of the configurational entropy for reaction.²³ The ratio (reactive conformations)/(all conformations) is related to the configurational component for the entropy of activation for hydrogen abstraction. The term ν contains activation entropy in eq 8. Our calculations suggest that the increase in extent of hydrogen abstraction at long chain length relates to an increase in ν in eq 8.

Increasing the length of the hydrocarbon chain increases S in eq 1. The magnitude of this effect is not known; however, the fractional increase in S is greatest at short chain length.

Comparison with the Internal Solvation Model. Comparison of the flexible chain model with the internal solvation model is made difficult because the latter is so difficult to assess quantitatively. Meyerson and Leitch⁴ believe that the hydrocarbon chain conformation at the instant of electron impact determines the extent and sites of hydrogen abstraction. Several lines of reasoning are at odds with that contention. Strong metastable peaks for the $[M]^+ \rightarrow 138(152)$ and $[M]^+ \rightarrow 139(153)$ in **2** and **3**⁹ suggest that much of the ion intensity derives from molecular ions which react with $k(E) = 10^6$ to 10^9 sec⁻¹. RRKM considerations suggest that partition of energy into various vibrational modes occurs in 10^{-11} to 10^{-10} sec. The chain has time to flail about.

As an illustrative example, imagine that the end of the chain moves as a particle of molecular weight = 100, at a temperature (250°) equal to the source temperature in the above experiments. Its average velocity may be calculated to be 330 m/sec or 3300 Å/nsec.²⁴ Even without considering the added internal energy upon electron impact, the end of the chain would move ~33 Å relative to the aromatic ring in 10^{-11} sec.

We believe that a model for hydrocarbon chain behavior in the mass spectrometer based upon internal solvation, whether in the neutral before electron impact or in the molecular ion, should show saturation effects. If such a model is correct, at some chain length solvation sites should be saturated. An increase in chain length should then not result in an increase in the appropriate ion ratio. The chain length at which saturation occurs must be consistent with spacial limitations around the reactive functional group. And the enthalpy of solvation must be sufficient to overcome the entropy requirements of the chain at large internal energies.

The agreement between the predictions of the flexible chain model and the mass spectrometric results is probably as good as one might hope, considering the crude nature of the model. The wide variety of experiments which correlate with the predictions of the computer program and the fact that the data in the literature are from several different laboratories suggest that the flexible chain hypothesis is the correct one.

We cannot exclude the possibility that solvation effects in the molecular ion give rise to "sticky" collisions, *i.e.*, that the short-range ion-induced dipole interactions perturb the flexible chains from a truly random distribution of conformations. Such effects can in principle be incorporated into our model. Studies to that end are in progress.

Several kinds of experimental data would provide sensitive tests for the flexible chain model. Ion intensity ratios measured at discrete molecular ion internal energies, either by examining metastable ion ratios or from charge-transfer spectra, would be very useful. Careful measurement of vertical and adiabatic ionization potentials, as a function of chain length, would probe internal solvation, respectively in the neutral and in the molecular ion.

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data in ref 8b, we note that $[\text{ArCO}_2\text{H}]^+ / [\text{ArCO}_2\text{H}_2]^+$ drops from 0.16 in hexyl benzoate to 0.008 in the hexyl ester of TMA; in the respective *n*-hexadecyl esters, the values are 0.083 (benzoate) and 0.004 (TMA). Neglecting *n* and *o* introduces an error of less than 1% to the amount of hydrogen abstraction by the anhydride group inferred from the *m/e* 194/(192 + 193) ion ratio.

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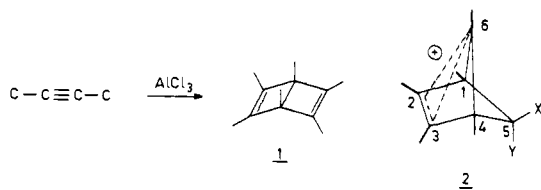
Electrophilic Additions to Hexamethyl(Dewar benzene) and Subsequent Cationic Rearrangements¹

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Abstract: Reactions of hexamethyl(Dewar benzene) (**1**) with HCl , Cl_2 , and Br_2 are reported, as well as the reaction of hexamethyl(Dewar benzene) epoxide (**15**) with HCl . It is shown that **1** is protonated exclusively (or nearly so) on the endo side. The resulting carbonium ion is not observed; it immediately undergoes intramolecular rearrangement. At low temperature bicyclo[2.1.1]hexenyl cations **2a** and **2b** are formed. At higher temperatures these convert to the bicyclo[3.1.0]hexenyl cation **7b**, which in turn gives cyclopentadienyl cation **9**. Finally, **9** is isomerized to the relatively stable hexamethylbenzenium ion **11**. At all stages in this sequence the ions can be trapped providing covalent products. The reactions of **1** with Cl_2 and Br_2 and the reaction of **15** with HCl all give bicyclo[2.1.1]hexenyl cations analogous to **2b**. These can be observed spectrally and in some cases can be trapped. They rearrange to give cyclopentadienyl cations analogous to **9**. These cations then give rise to various reaction products.

In 1966 it was discovered that 2-butyne could be trimerized, thus providing a simple synthetic route to hexamethyl(Dewar benzene) (**1**).² Numerous studies employing **1** have



been reported. In particular a number of electrophilic additions to **1** have been examined; they afford synthetic routes to a large number of strained cyclic compounds and also involve interesting mechanistic problems.^{3,4}

One would predict electrophilic attack upon **1** to occur preferentially on its endo side due to the greater concentration of electron density on the endo face of the molecule.⁵ However, exo attack might well be preferred from steric considerations. In fact hexamethyl(Dewar benzene) reacts with a few electrophilic reagents at the exo side,⁴ so that it must be concluded that the electronic factor does not always determine the direction of attack. Unambiguous examples of endo attack were not presented until just recently^{1a,6} because previous work on this subject dealt with the intermediacy of 1,2,3,4,5,6-hexamethylbicyclo[2.1.1]hexenyl cations (**2**). Various endo- and exo-5-methyl isomers of **2** have been shown to undergo rapid interconversion, thus destroying any information about the orientation of the initial attack.⁷

The reaction of **1** with chlorosulfonyl isocyanate provides

an example of the problems involved in assigning the stereochemistry of the initial attack of an electrophile. From the exo-exo methyl stereochemistry of the bicyclo[3.1.0]hexenyl product, it was concluded that the initial attack occurred from the endo side.⁵ Performing the reaction at -70° , however, yielded a bicyclo[2.1.1]hexenyl product.⁸ This suggests that the reaction at higher temperature to give [3.1.0] structures proceeds *via* [2.1.1] intermediates (a phenomenon that will be discussed in more detail below). Therefore conclusions about the direction of the initial attack cannot be safely made on the basis of the stereochemistry of [3.1.0] products. Such a conclusion would be valid only if it were established that the exo-endo relationship of the [3.1.0] product was unchanged from that of the first-formed [2.1.1] ion.

Discussion

Endo Attack on 1 by Acids. The exo 5-H and endo 5-H ions **2a** and **2b** were previously prepared by reaction of **1** with strong acid ($\text{HF}-\text{BF}_3$, $\text{FHSO}_3-\text{SbF}_5$).⁷ It is also possible to do this using the more weakly acidic system $\text{HCl}-\text{CH}_2\text{Cl}_2$ (1:2 v/v) (Scheme I). At temperatures between -50 and -100° , the pmr spectrum of these ions is the same in either the more strongly acidic solutions or in $\text{HCl}-\text{CH}_2\text{Cl}_2$, a 3:1 equilibrium mixture, respectively, of ions **2a** and **2b**. Quenching of such a mixture in $\text{HCl}-\text{CH}_2\text{Cl}_2$ with sodium methoxide in methanol gives the ethers **3a** and **3b** in a 3:1 ratio. These too are identical with the products obtained on quenching a more strongly acidic solution.^{7d}

The amount of HCl was decreased in a subsequent experiment at -80° to twice that of **1**. Not only the ions **2a** and