

1075, 955 cm^{-1} ; nmr (acetone- d_6) δ 3.08 (d of d, 1 H, $J = 10$, 2 Hz), 3.44 (s, 3 H), 3.70 (d of m, 1 H, $J = 10$ Hz), 3.62 (m, 1 H), 4.47 (m, 1 H), 5.99 (m, 2 H), 7.4 ppm (very broad, 3 H), irradiation of the multiplet at 4.47 ppm caused collapse of the signal at 3.08 ppm to a clean doublet ($J = 10$ Hz); m/e 198 (8), 180 (10), 170 (7), 168 (7),

166 (7), 154 (21), 153 (22), 128 (100), 122 (25), 109 (42), 105 (22), 97 (32), 96 (81), 81 (29), 74 (48), 71 (24), 68 (49), 65 (25), 45 (37), 41 (42), 39 (51).

Anal. Calcd for $\text{C}_9\text{H}_{12}\text{O}_6$: C, 50.00; H, 5.60. Found: C, 49.90; H, 5.68.

Conformational Effects in the Mass Spectra of Long Chain Ethers of *p*- and *m*-Hydroxybenzoic Acid

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Abstract: Long chain ethers of *m*- and *p*-hydroxybenzoic acid, and their methyl esters, show ions in their mass spectra which are due to hydrogen abstraction from the hydrocarbon chain by the remote, ionized carboxy group. These ions appear at m/e 139 and 153, one mass unit greater than those of the intense ions due to phenyl ether rearrangement. The m/e 139/138 and 153/152 ratios increase with chain length. Kinetic arguments support hydrogen abstraction as rate determining, although the possibility of a change in the rate-determining step at low voltage with increase in chain length is discussed. Probability considerations are introduced as a step toward understanding in detail the effects of the conformational mobility of a hydrocarbon chain in mass spectral reactions leading to hydrogen abstraction. These ideas are compared with an internal solvation model recently proposed by Meyerson.

There are many examples in mass spectrometry of interaction, leading to hydrogen transfer, between two functional groups separated by a hydrocarbon chain.¹ Hydrogen transfer is an important process in long range interactions between a functional group and the chain itself,² and the effect of ring size on the hydrogen abstraction reaction has been noted.^{1a, 2d} Hydrogen abstraction can be activated by methyl or phenyl substitution on the chain,³ leading to selective, but not specific, hydrogen abstraction. Chain coiling has been invoked by a number of authors⁴ to explain these phenomena, which require that two groups, apparently separated by a flexible chain, be brought into spatial proximity during the lifetime of the molecular ion.

Meyerson and Leitch⁵ proposed a model for such interactions in their discussion of the mass spectra of ω -phenylalkanols in which they envisaged the chain coiled in the gas phase. Their data are also compatible with a freely flexible chain. Since vapor phase coiling of

hydrocarbon chains has been called into question,⁶ this defines the nature of the problem: to understand the contribution of the conformational requirements of the chains to the interaction of groups separated by a linear hydrocarbon. We omit from our consideration reactions which involve the interaction of two heteroatom-containing functional groups. These are dominated by highly specific interactions to the exclusion of chain length effects.^{1, 7} We devote our attention to the effects of hydrocarbon chain conformation on the hydrogen abstraction reaction. The nonspecificity in abstraction from unactivated hydrocarbon chains⁸ and the enhanced specificity in cases of local chemical activation^{3b, 5} suggest that conformational properties of the chain play an important role in determining the extent and stereochemistry of the hydrogen abstraction process.

An approach to this problem is to gather data in the proper form for comparison with calculations of hydrocarbon conformational statistics.⁹ Such calculations, in principle, would allow one to separate the purely conformational contributions from the van der Waals and ion-induced dipole effects. These, in turn, could then be incorporated into conformational calculations. We have taken this approach, choosing to examine the interaction in the mass spectrometer between a hydrocarbon chain and a remote functional group, which can be presented and interpreted in terms of the reversible cyclization probability of the chain.

(1) (a) J. A. McCloskey and M. J. McClelland, *J. Amer. Chem. Soc.*, **87**, 5090 (1965); (b) R. E. Wolff, M. Greff, and J. A. McCloskey, *Advan. Mass. Spectrom.*, **4**, 193 (1968); (c) R. Brandt and C. Djerassi, *Helv. Chim. Acta*, **51**, 1750 (1968); (d) G. H. Draffan, R. N. Stillwell, and J. A. McCloskey, *Org. Mass. Spectrom.*, **1**, 669 (1968); (e) A. Casper, G. Teller, and R. E. Wolff, *ibid.*, **3**, 1351 (1970); (f) C. Wolff, R. E. Wolff, and J. A. McCloskey, *Tetrahedron Lett.*, 4335 (1966); (g) P. Brown, A. H. Albert, and G. R. Pettit, *J. Amer. Chem. Soc.*, **92**, 3212 (1970).

(2) (a) R. Ryhage and E. Stenhagen, "Mass Spectrometry of Organic Ions," F. W. McLafferty, Ed., Academic Press, New York, N. Y., 1963; (b) L. Dolejš, P. Beran, and J. Hradec, *Org. Mass. Spectrom.*, **1**, 563 (1968); (c) S. Meyerson, I. Puskas, and E. K. Fields, *Chem. Ind. (London)*, 1845 (1968); (d) G. Eadon and C. Djerassi, *J. Amer. Chem. Soc.*, **91**, 2724 (1969).

(3) (a) R. Ryhage and E. Stenhagen, *Ark. Kemi*, **15**, 291 (1959); (b) S. Meyerson and L. C. Leitch, *J. Amer. Chem. Soc.*, **88**, 56 (1966).

(4) (a) R. Ryhage and E. Stenhagen, *J. Lipid Res.*, **1**, 361 (1960); (b) P. Bommer and K. Biemann, *Annu. Rev. Phys. Chem.*, **16**, 492 (1965); (c) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 179.

(5) S. Meyerson and L. C. Leitch, *J. Amer. Chem. Soc.*, **93**, 2244 (1971).

(6) E. F. Meyer and K. S. Stec, *J. Amer. Chem. Soc.*, **93**, 5451 (1971).

(7) E. White, V. S. Tsuboyama, and J. A. McCloskey, *J. Amer. Chem. Soc.*, **93**, 6340 (1971); I. Dzidic and J. A. McCloskey, *ibid.*, **93**, 4955 (1971).

(8) (a) J. Cable and C. Djerassi, *J. Amer. Chem. Soc.*, **93**, 3905 (1971); (b) S. Meyerson, I. Puskas, and E. K. Fields, *ibid.*, **95**, 6056 (1973).

(9) (a) P. J. Flory, "Statistical Mechanics of Chain Molecules," Interscience, New York, N. Y., 1969; (b) M. Lal, *Brit. Polym. J.*, **3**, 240 (1971); (c) M. Sisido, *Macromolecules*, **4**, 737 (1971); (d) R. P. Smith and E. M. Mortensen, *J. Chem. Phys.*, **35**, 714 (1961).

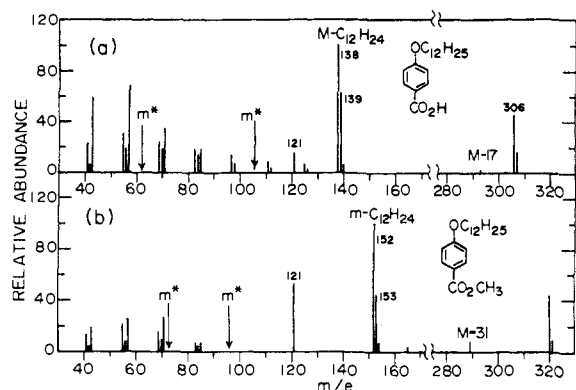
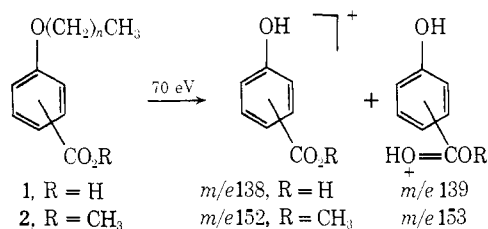


Figure 1. Mass spectra at 70 eV of (a) 4-(*O*-1'-dodecyloxy)benzoic acid; (b) methyl 4-(*O*-1'-dodecyloxy)benzoate. Source temperature was 210–230°.

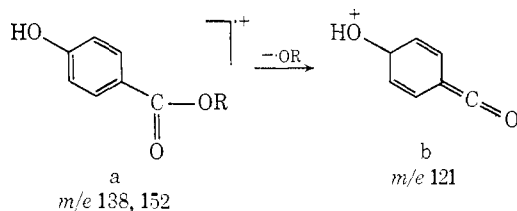
We approach the problem from the point of view of positional isomers, steric effects related to the excluded volume question, and dependence on chain length. Long chain ethers of hydroxybenzoic acid (**1**) and their methyl esters (**2**) were chosen for this study. Both



meta and para isomers are readily available. We also expected the mass spectra of long chain ethers to be simpler and easier to interpret in terms of hydrogen transfer than the mass spectra of long chain esters.

Results

Figure 1 shows the mass spectra of the 12-carbon para ethers of **1** and of **2**. With the exception of the shortest chain ethers of the para-substituted molecules, the ions at m/e 138 and 152 are the most intense in their respective spectra. There are prominent metastable peaks (*vide infra*) for the transitions $M^+ \rightarrow 152$, $152 \rightarrow 121$ for the esters and $M^+ \rightarrow 138$, $138 \rightarrow 121$ for the



acids. Figure 2 indicates the dependence of the intensities of the $[M]^+$ (molecular) and m/e 121 ions on chain length for **1** and **2**. The larger values of m/e 121 in the para-substituted species are most likely due to resonance stabilization of this ion, which is not possible when the substitution is meta.

These ion intensities appear to level off at long chain length. The scatter in $[M]^+$ for long chain derivatives may reflect the sensitivity of these ions to source temperature.¹⁰ In these experiments the source tempera-

(10) Cf. S. Meyerson, T. D. Nevitt, and P. Rylander, *Advan. Mass. Spectrom.*, **2**, 313 (1963); S. Meyerson, *Appl. Spectrosc.*, **22**, 30 (1968).

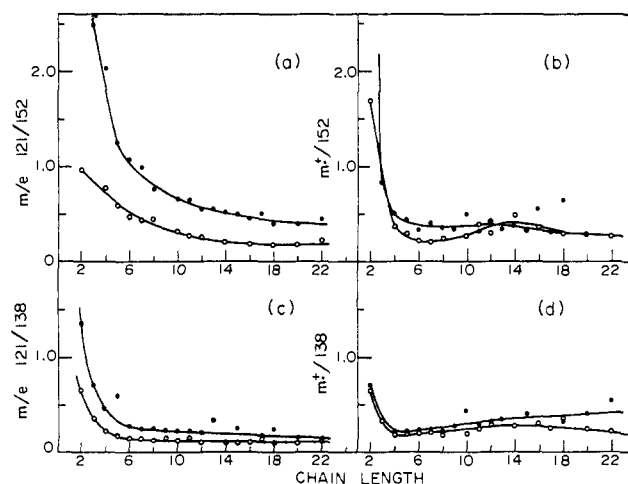


Figure 2. Effect of chain length on ion intensities at 70 eV for meta (O) and para (●) alkoxybenzoic acids (**1**) and methyl esters (**2**): (a) **2**, m/e 121/152; (b) **2**, $[M]^+/152$; (c) **1**, m/e 121/138; (d) **1**, $[M]^+/138$.

ture varied between 210 and 230°. Figure 1a indicates that the $[M + 1]^+$ ions were consistently larger in **1** than would be expected on the basis of ¹³C contribution. This intermolecular protonation is common to mass spectra of carboxylic acids.¹¹

Two- to Four-Carbon Chains. These mass spectra resemble those of other phenyl ethers,^{4c} with intense peaks at m/e 138 or 152 due to rearrangement to the phenol¹² accompanied by loss of the chain. A minor pathway to give the $[M - \cdot OR]^+$ ion is typical of benzoic acid¹³ and methyl benzoates.^{4c} Weak intensities at m/e 93 and 65 are seen here for the sequence



At longer chain length, these ions are too weak to be observed. The ratios of m/e 153/152 and 139/138 are, unexpectedly, slightly larger than those expected from ¹³C contribution. It is not necessary, however, to invoke the second functional group to explain these ions; we examined phenoxyethane and 1-phenoxybutane¹² and found that a previously unreported two-hydrogen rearrangement takes place with chain loss, leading to m/e 95/94 ratios respectively of 0.49 and 1.05% after correction for ¹³C.

5- to 22-Carbon Chains. While qualitatively similar to the mass spectra of the short chain analogs, the mass spectra of the 5- to 22-carbon ethers show more intense hydrocarbon fragment ions at m/e 41, 43, 55, 57, 69, 71, ... New peaks also appear at m/e 139 in **1** and m/e 153 in **2**, and these data are presented in Figure 3. We measured m/e 95/94 in 1-phenoxytetradecane to be 2.0%. These intensities are far greater and must involve the remote functional group. We believe that the m/e 139 and 153 ions arise by hydrogen abstraction from the chain by the carboxy and carboxymethyl functions, prior to fragmentation of the molecu-

(11) F. W. McLafferty, *Anal. Chem.*, **29**, 1782 (1957); **34**, 26 (1962); see also M. H. Wilson and J. A. McCloskey, *J. Amer. Chem. Soc.*, **94**, 3865 (1972).

(12) A. N. H. Yeo and C. Djerassi, *J. Amer. Chem. Soc.*, **94**, 482 (1972); see also F. W. McLafferty and L. J. Schiff, *Org. Mass. Spectrom.*, **2**, 757 (1969).

(13) (a) S. Meyerson and J. L. Corbin, *J. Amer. Chem. Soc.*, **87**, 3045 (1965); (b) F. Benoit, *Org. Mass. Spectrom.*, **7**, 295 (1973).

lar ion. A similar phenomenon has been observed with long chain esters of trimellitic anhydride.^{2c,8}

Small peaks at m/e 154 and 165 are ubiquitous in the spectra of **2**, but analogous ions are not seen in **1**. The m/e 154 peak has about the same intensity, after correction for ^{13}C , as the m/e 95 peak in 1-phenoxytetradecane and may be due to a similar (three-hydrogen) rearrangement. The other ion, at m/e 165, probably arises from C–C bond fission α to the ether oxygen.

Metastable Peaks. Two metastable peaks are found in the spectra of the acids: that at m/e 106.1 results from the reaction m/e 138 \rightarrow 121, the second peak from $[\text{M}]^+ \rightarrow$ 138 or 139. These ions are very weak in the longer chain ethers and cannot be detected when the chain is longer than 12 carbons. Corresponding metastable transitions are found in the methyl esters, **2**: that at m/e 96.3 corresponds to m/e 152 \rightarrow 121, the other to $[\text{M}]^+ \rightarrow$ 152 or 153. At high sensitivity, these metastable peaks can be observed even in the 22-carbon ethers. They are, however, noticeably less intense in the longer chain derivatives.

A defocusing technique¹⁴ was used to examine in detail the shape of the metastable transition at 96.3 leading to the ion at m/e 121 in the butyl and hexadecyl ethers of *p*-carboxymethylphenol. No differences in peak shape could be noted. A shoulder, or at least broadening, would have been expected if the reaction m/e 153 \rightarrow 121 ($m^* = 95.7$) were significant.

Low-Voltage Spectra. Low-voltage spectra were run routinely, usually at a nominal 15 eV electron beam energy. These spectra showed increased molecular and decreased m/e 121 ion intensities. The m/e 139/138 and 153/152 ratios were not significantly changed under these conditions. A few esters were examined in detail for their sensitivity to electron beam energy and source temperature. These data are collected in Table I.

Table I. Effects of Ionizing Voltage and Source Temperature on Ion Intensities

Compd	Mol wt	eV ^a	121 ^b	153 ^b	M ^{+,b}	Source temp, deg
<i>p</i> -2-12 ^c	320	70	54.9 \pm 2.8 ^d	31.2 \pm 0.7	41.7 \pm 1.5	220
	320	15	28.7 ^e	33.2 \pm 1.2	63.5 \pm 1.2	220
<i>p</i> -2-18	404	70	39.6 \pm 1.1	37.9 \pm 0.3	64.5 \pm 1.0	200
	404	15	13.9 \pm 0.5	37.7 \pm 0.3	76.9 \pm 1.0	200
<i>m</i> -2-22	460	70	13.8 \pm 0.4	25.3 \pm 1.0	10.2 \pm 0.1	250
	460	70	14.6 \pm 1.1	29.5 \pm 2.8	26.4 \pm 1.5	200
	460	12	0	33.2 \pm 0.4	97 \pm 3	200

^a Nominal electron beam energy. ^b Per cent of m/e 152 intensity; m/e 153 is corrected for ^{13}C abundance. ^c Number of carbons in the chain. ^d Error limits are average deviations; for 70-eV spectra, four or more scans of m/e 121 and 153 peaks; all other peaks, two to four scans. ^e Single measurement.

The molecular ions are sensitive to source temperature¹⁰ decreasing in intensity, as expected, at the higher temperature; they increase markedly in the low-voltage spectra. The variation in m/e 153/152 is outside of experimental error in only one example, *m*-2-22. The increase in this value both at lower source temperature and beam energy is in accord with Meyerson's observations.^{8b,10} The appearance potentials of the m/e 152

(14) C. W. Tsang and A. G. Harrison, *Org. Mass. Spectrom.*, **3**, 647 (1970); we thank Dr. B. G. Keyes for these experiments.

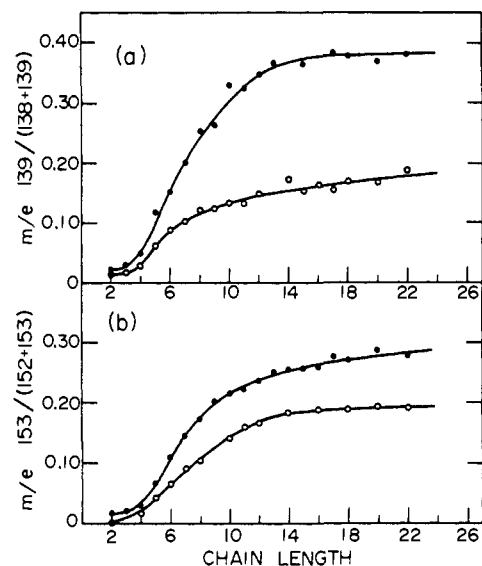


Figure 3. Effect of chain length on ion intensities attributed to hydrogen transfer for meta (○) and para (●) **1** (a) and **2** (b). See text for details.

and 153 ions in *p*-2-16 were estimated to be 11.5 eV by measuring the applied voltage at which these ion intensities, and that of xenon, decreased to 1% of their respective 70-eV values. The dramatic decrease in the m/e 121 ion intensity, disappearing in the 12-eV spectra, reflects a higher activation energy for this fragmentation reaction.¹⁵

Discussion

The mass spectrometric transformations of **1** and **2** will be interpreted in terms of a structure-reactivity correlation. The assumptions in this treatment are those of the quasi-equilibrium theory (QET) of mass spectrometry,¹⁶ namely that all ions are produced by competing and consecutive unimolecular reactions, sharing the molecular ion as a common precursor. Rate constants are taken to refer to those values of the rate constants averaged over the energy distributed in the parent ions at 70 and 15 eV electron beam energy.

Scheme I requires the additional knowledge that the ions at m/e 139 and 153 result from hydrogen abstraction from the chain by the carboxy group. This may be inferred as follows. Increasing the chain length in *m*- and *p*-ethoxybenzoic acid and its methyl esters to three or four carbons affects only ion intensities as shown in Figure 2. These effects are fairly well understood and arise from an increase of the normal modes in the molecular ion.¹⁷ The five and longer chain ethers show new ions at m/e 139 and 153 which must be due to interaction with the remote functional group. Mass considerations make it necessary to invoke abstraction of a hydrogen. The chain is the only source of hydrogen in the molecule.⁸ Hydrogen abstraction must

(15) (a) D. H. Williams and R. G. Cooks, *Chem. Commun.*, 663 (1968); (b) A. N. H. Yeo and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 395 (1971); (c) F. W. McLafferty and D. J. McAdoo, *ibid.*, **91**, 5400 (1969).

(16) A. G. Harrison and C. W. Tsang, "Biochemical Applications of Mass Spectrometry," G. R. Waller, Ed., Wiley, New York, N. Y., 1972, p 135.

(17) (a) F. W. McLafferty and W. T. Pike, *J. Amer. Chem. Soc.*, **89**, 5951, 5953 (1967); (b) F. W. McLafferty, T. Wachs, and W. T. Pike, *Advan. Mass. Spectrom.*, **4**, 153 (1968).

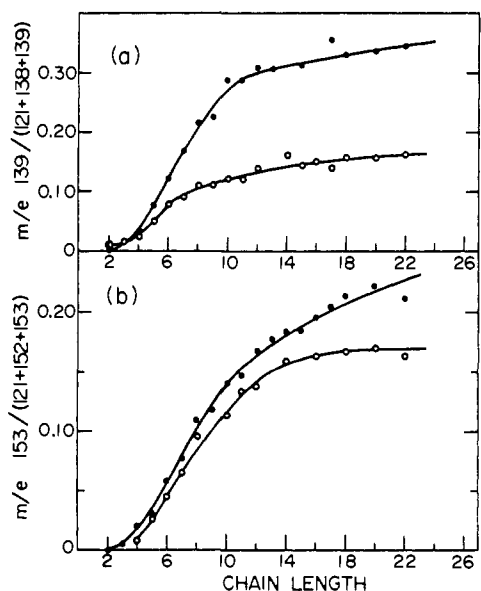
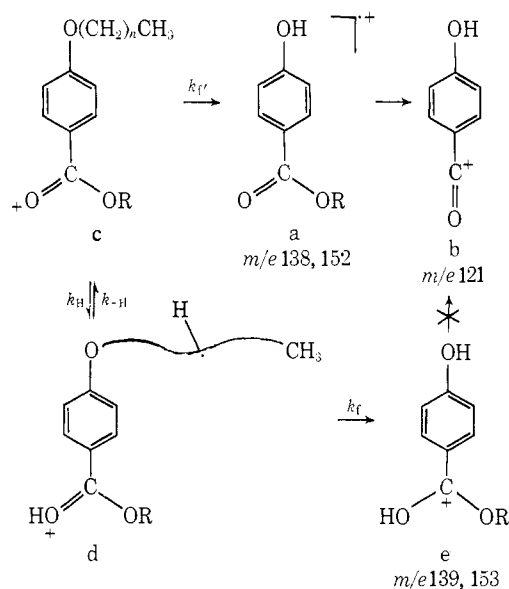


Figure 4. Effect of chain length on the fraction of aromatic-ring-containing ions attributed to hydrogen transfer for meta (O) and para (●) **1** (a) and **2** (b).

Scheme I



occur from many positions along the chain to account for the data in Figures 3 and 4.⁸ Our approach to the question of conformational contribution by the hydrocarbon chain was designed to circumvent the need to know the distribution of abstraction sites in each chain. Scheme I, which is used as the framework for our analysis, depends only on the above assumptions. Ionization gives c with charge most likely distributed at both the ether and ester oxygens. Hydrogen transfer (k_H) to yield d competes with fragmentation (k_f') to yield a. a may lose hydroxy or methoxy to give b. Metastable peak shape analyses (*vide supra*) suggest e may not.

Recent experiments of Yeo and Djerassi¹² support assignment of the structures in Scheme I to the ions at m/e 121, 138, 139, 152, and 153.¹⁸ We would expect

(18) Whether a, b, and e have the corresponding tautomeric dienone structure¹² is not critical for our analysis of the role played by the hydrocarbon chain in these transformations. The concertedness of

that hydrogen migration in the rearrangement $c \rightarrow a$ would not be site specific.¹²

In Figure 3 we have plotted m/e 139/(138 + 139) and m/e 153/(152 + 153) against chain length. These ratios are insensitive to electron beam energy and only moderately sensitive to source temperature (see Table I). At 70 eV, these represent the ratio of ion intensities of e to a expressed in fractional form, where e is produced by hydrogen abstraction from the chain by the carboxy group. Some of the difference between the meta and para ion ratios is due to more favorable conversion $a \rightarrow b$ in the para series of ethers. To accommodate this, we plot m/e 139/(121 + 138 + 139) and m/e 153/(121 + 152 + 153) in Figure 4. These represent the ratio of e to all the fragment ions derived from the aromatic part of c. This has the effect of accentuating the steepness of the curves in the region of five- to ten-carbon-atom chains.

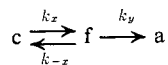
The invariance of m/e 153/152 in the mass spectra of **2** at different electron beam energies is rather surprising. Since the intensity at m/e 121 decreases at low-ionizing voltage and $[M]^+$ increases, Figure 3 should approximate the changes in the extent of hydrogen transfer to the carbonyl group at voltages approaching the appearance potentials for a and e.

None of these plots take account of the fraction of molecular ions which exist as d. When $[M]^+$ carries a sizable fraction of the ion current, that fraction having the structure d should be included in the accounting of ions which have undergone remote hydrogen transfer. This is potentially measurable, given an ion-cyclotron resonance apparatus capable of operating at high temperatures.

The remaining differences in meta and para ion ratios in Figure 4 have several possible explanations. Benoit^{13b} has invoked different energy distributions in meta- and para-substituted benzoic acids to explain differences in ion and metastable peak intensities in two pathways to the $[C_7H_5O]^+$ ion. He was led to this conclusion by the inability of arguments, based on rate enhancement by resonance-stabilized daughter ions, to explain differences in metastable peak intensities between para and meta isomers. He advanced the same suggestion to explain the different $[RC_6H_4CO]^+/[M]^+$ ratios observed by Chin and Harrison for the meta and para isomers of amino- and methoxybenzoic acids.¹⁹ Considering the structural similarities between **1** and **2** and the molecules studied by Benoit and by Harrison, we should expect different energy distributions in the meta and para isomers we examined.

Rate-Determining Step. It is possible to demonstrate that the rate-determining step in the formation of e is the hydrogen abstraction step described by k_H and that the reverse k_{-H} must be relatively unimportant in the chemistry we observe. The argument presumes identical intrinsic reactivity of chemically equivalent

the reactions described by k_t and k_t' also does not affect our arguments. For example, if



$k_t' = k_y k_x / (k_y + k_{-x})$, and the form of eq 1 through 8 is unchanged. We do make the explicit assumption that the processes described by k_t and k_t' are similarly dependent on chain length.

(19) M. S. Chin and A. G. Harrison, *Org. Mass. Spectrom.*, **2**, 1073 (1969).

methylenes. There is abundant evidence in solution that unactivated methylenes react with equal rates in bimolecular hydrogen abstraction reactions.²⁰ Let k_{PH} be the intrinsic rate constant for hydrogen abstraction in c. Then $k_{\text{H}i} = 2k_{\text{PH}}P_i$, where $k_{\text{H}i}$ is the rate constant for hydrogen abstraction from the i th carbon, the factor 2 describes the two hydrogens per methylene group, and P_i is the probability that the i th carbon will occupy the reactive volume during the lifetime of the ion. Since P_i is a dimensionless quantity, k_{PH} has units of a first-order rate constant. It, too, is an intrinsic rate constant for hydrogen abstraction in c from an unactivated CH_2 group along the chain. Note that, in c the hydrogens on (CH_2) -1, and perhaps (CH_2) -2, are activated by their proximity to the ether oxygen. The equations developed here hold because $P_1 = P_2 = 0$.

$$k_{\text{H}} = 2k_{\text{PH}} \sum_{i=1}^n P_i = 2k_{\text{PH}} P_{\text{CH}_2} \quad (1)$$

Equation 1 defines the rate constant for the reaction $c \rightarrow d$ in terms of the sum of the probabilities that each CH_2 would occupy the reactive volume in space. For a chain $n + 1$ carbons long, we must sum $k_{\text{H}i}$ over the n CH_2 groups from which hydrogen abstraction could take place, in accord with Djerassi's observation^{8a} that negligible abstraction occurs from the methyl group. For convenience in later discussion, we also define P_{CH_2} in eq 1.

The reverse rate, described by $k_{-\text{H}}$, is similarly dependent on chain length.

$$k_{-\text{H}i} = k_{\text{P}(-\text{H})} P_i \quad (2)$$

$$k_{-\text{H}} = k_{\text{P}(-\text{H})} \sum_{i=1}^n P_i \quad (3)$$

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

Here $k_{\text{P}(-\text{H})}$ is the intrinsic rate constant for the reverse reaction $d \rightarrow c$.

In order to derive an expression for the relative intensities of a and e, it is necessary to invoke the steady state approximation for c and d, the former being produced at a constant rate under continuous irradiation.²¹ The form of eq 5, and the equations which follow,

$$\frac{e}{a+b} = \frac{k_f}{k_f'} \left[\frac{k_{\text{H}}}{k_{-\text{H}} + k_f} \right] \quad (5)$$

depends only on the assumptions that the molecular ion is a common intermediate to the resulting fragment ions, that those processes which expel neutral fragments

are irreversible, and that the m/e 139 and 153 ions reasonably may be attributed to result from hydrogen abstraction. The conclusions we reach are general for any intramolecular hydrogen abstraction reaction, the extent of which depends upon chain length, and certainly extends beyond the specific details implied in Scheme I.

The fragmentation rate constants k_f and k_f' do not depend upon P_i . We assume they show a similar dependence on chain length. In the limiting case that k_f is rate determining, $k_f \ll k_{-\text{H}}$, eq 6 describes the ion

$$\frac{e}{a+b} = \frac{k_f k_{\text{H}}}{k_f' k_{-\text{H}}} = \frac{k_f K}{k_f'} \quad (k_f \ll k_{-\text{H}}) \quad (6)$$

ratio. It predicts that m/e 139/(138 + 121) and 153/(152 + 121) are constant with chain length. This is clearly not the case.

At the other extreme, if k_{H} is rate determining, $k_{-\text{H}} \ll k_f$, the conditions in eq 7 hold, and the ion ratios

$$\frac{e}{a+b} = \frac{2k_{\text{PH}}}{k_f'} \sum_{i=1}^n P_i \quad (k_f \gg k_{-\text{H}}) \quad (7)$$

should increase with P_{CH_2} . This is what is observed. Although the increment added to $\sum P_i$ as $i \rightarrow n$ becomes progressively smaller, it is not at all clear, in the absence of statistical calculations, whether or not P_{CH_2} approaches a limiting value. This is an important consideration, since one hope in carrying out this work was to be able to relate the curve shapes in Figures 3 and 4 to conformational probabilities. For example, if at small n ($n = 5, 6, 7$) $k_{-\text{H}} \ll k_f$, but at large n ($n \geq 14$) $k_f \ll k_{-\text{H}}$, since $k_{-\text{H}}$ increases with n , the ion intensities would increase until the latter conditions were fulfilled and then level off.

This may in fact explain the curve shapes in Figure 3, which seem to approach a limit around $n = 14-18$. Figure 3 approximates the low-voltage limit of the hydrogen abstraction phenomenon. We know from Table I that k_f' is more sensitive to a decrease in incident electron energy than $k_{\text{H}i}$. If k_f decreases with a decrease in electron beam energy more rapidly than $k_{-\text{H}i}$, a change in rate-determining step may very well explain the data in Figure 3.

The curves in Figure 4, with one exception, have not leveled off for 22-carbon chains. This is particularly evident for the para esters 2. We feel confident in concluding that, at 70 eV, k_{H} is rate determining, even at long chain length.

Conformational Considerations. The simplest explanation for the peak shapes in Figures 3 and 4 is that short chains cannot reach the carboxy groups and longer chains reach increasingly more easily as their length increases. This effect begins to level off at long chain lengths. An explanation in terms of internal solvation,^{4,5} based on the similarity of curve shapes in Figures 3 and 4, would be that the hydrocarbon chain solvates the ionized carboxyphenyl ring. When the chain is sufficiently long, solvation "sites" become saturated, and hydrogen transfer should not increase with chain length. This occurs for only one example in Figure 4.

An explanation based on a mobile, flexible hydrocarbon chain may be drawn in analogy to considerations by Morawetz in his study of the contribution of

(20) (a) N. C. Deno, R. Fishbein, and C. Pierson, *J. Amer. Chem. Soc.*, **92**, 1451 (1970); (b) P. Smith and H. J. den Hertog, *Recl. Trav. Chim. Pays-Bas*, **83**, 891 (1964).

(21) Chin and Harrison¹⁹ have shown that one serious problem in invoking the steady state assumption is that it fails to account for changes in the fraction of molecular ions with insufficient energy to react (these appear as $[\text{M}]^{\cdot-}$). In studies of substituent effects, this problem is particularly severe, since substituents which affect the ionization potential of the molecule seriously affect as well the molecular ion intensity. In our examples, once the chain length exceeds three carbons, the change in $[\text{M}]^{\cdot-}$ with chain length is fairly small (Figure 2) and may be neglected. These ion intensities and those at m/e 121 reflect the change in internal energy with increase in chain length (*i.e.*, increase in internal degrees of freedom in the hydrocarbon chain). These changes also are small for six or more carbons in the chain. We, therefore, consider the problems in the steady state treatment raised by Chin and Harrison to be relatively unimportant in the specific examples presented in this work.

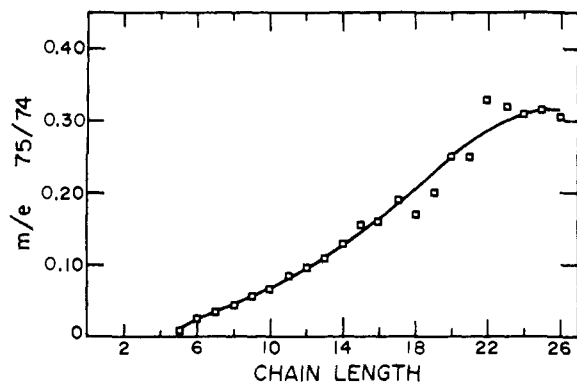


Figure 5. Effect of chain length on ion intensities attributed to hydrogen transfer in the methyl esters of saturated fatty acids. The data are taken from Ryhage and Stenhagen, ref 25.

polymer conformation to reaction.^{22,23} The process $c \rightarrow d$ is a unimolecular reaction and k_H has units of reciprocal seconds. The rate constant k_H can be considered to be the product of a second-order rate constant times the "effective concentration" of the chain in the vicinity of the carbonyl oxygen. If the "bimolecular" reaction is not diffusion controlled, the ratio of the products of unimolecular/"bimolecular" reactions is proportional to P_{CH_2} . This argument is rigorously true even if internal solvation is the dominant energy contributor to the conformations leading to hydrogen transfer, in which case solvation would lead to large values of P_{CH_2} .

Equation 7 may be rewritten as (8). This form of the

$$m/e \frac{153}{121 + 152 + 153} = \frac{2k_{PH}P_{CH_2}}{k_t' + 2k_{PH}P_{CH_2}} \quad (8)$$

data lends itself to Monte Carlo simulation of the conformational phenomena,²⁴ where the right-hand term is proportional to reactive conformations/all chain conformations.

A useful comparison is presented in Figure 5. Here we have plotted data reported by Ryhage and Stenhagen from the mass spectra of fatty acid methyl esters.²⁵ If we ascribe the m/e 75 ion to hydrogen transfer before rearrangement (see Scheme II), we can apply a similar interpretation to the shape of the curve in Figure 5.

Scheme II is consistent with extensive labeling studies recently reported by Dinh-Nguyen,²⁶ who synthesized and reported the mass spectra of 20 different deuterium-substituted methyl octadecanoates. His experiments show that the McLafferty rearrangement to give the m/e 74 ion occurs almost exclusively through γ -hydrogen abstraction and that one hydrogen in the m/e 75 ion derives from C_γ . The other hydrogen derives only from positions further along the chain. One can estimate that 15–20% of the hydrogens in the m/e 75 ion originate at C_5 – C_7 , none derive from the methyl group, and the remainder derive from C_8 – C_{17} . Primary isotope effects of unknown magnitude and the small changes in ion ratios observed make more quantitative inferences

(22) H. Morawetz, "Macromolecules in Solution," Vol. 21, Interscience, New York, N. Y., 1965, p 122 ff.

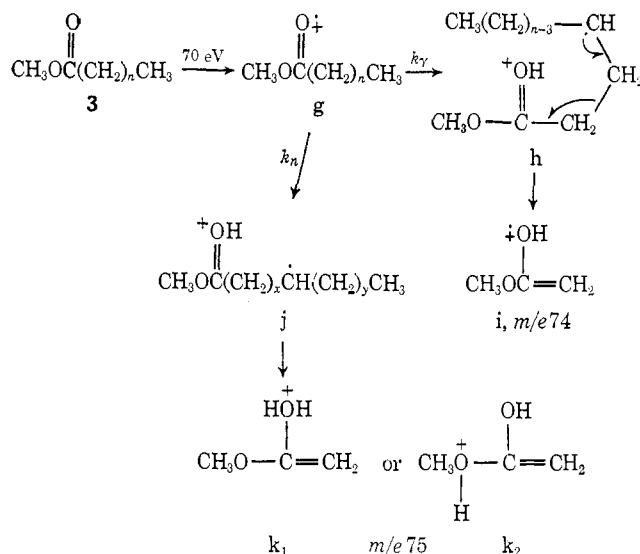
(23) (a) N. Goodman and H. Morawetz, *J. Polymer Sci., Part C*, 31, 177 (1970); (b) *J. Polymer Sci., Part A-2*, 9, 1657 (1971).

(24) We have begun these calculations in collaboration with Professor S. G. Whittington.

(25) R. Ryhage and E. Stenhagen, *Ark. Kemi*, 13, 523 (1959).

(26) N. Dinh-Nguyen, *Arch. Mass Spectral Data*, 2, 101 (1971).

Scheme II



about the internal distribution of hydrogen abstraction sites tenuous.

The structure–reactivity correlation approach is more incisive here and leads to the conclusion that charge solvation cannot be the driving force for hydrogen abstraction, which leads to the data in Figure 5. If we invoke internal solvation, which saturates at long chain length to explain the leveling off of the m/e 75/74 ion ratio, we are faced with a logical contradiction. In m -2, saturation (according to the solvation hypothesis) is achieved when the ion contains 14 CH_2 groups. Since the first four cannot reach, one might argue that 10 CH_2 groups are sufficient to satisfy the solvation requirements of the ionized carboxymethyl group. In **3** at least 20 CH_2 groups are required before the ratio begins to level off. The solvation–saturation explanation could accommodate an observation that more CH_2 groups were able to solvate c than g since the charge is spatially more disperse, but the opposite is found. The reactive volume around the carboxymethyl group is finite, however. It is difficult to imagine 10 CH_2 groups, let alone 20, fitting into that space.

A probability-of-encounter argument can also explain the curve shape in Figure 5. Formation of the ion at m/e 74 should occur with rate-determining hydrogen abstraction (k_γ).²⁷ Similarly, we can argue (*vide supra*) that hydrogen abstraction (k_n) is rate determining in the formation of k . The entropy requirements for formation of i , the normal McLafferty rearrangement ion, can be expressed as a probability of encounter, P_4 , with the proper geometry for reaction. If we assume the same intrinsic rate constant for hydrogen abstraction at each position for carbons five through n , eq 9 follows.

$$m/e \frac{75}{74} = \frac{k_n}{k_\gamma P_4} \sum_{i=5}^n P_i \quad (9)$$

Whether (8) and (9) can account quantitatively for the curve shapes in Figures 3–5 is not obvious. It must await the application of conformational calculations sophisticated enough to accommodate the appropriate intramolecular interactions.

(27) R. B. Fairweather and F. W. McLafferty, *Org. Mass. Spectrom.*, 2, 755 (1969); J. S. Smith and F. W. McLafferty, *ibid.*, 5, 483 (1971).

Experimental Section

Mass spectra were obtained using a CEC 21-490 mass spectrometer with all samples admitted through the solid sample probe. Source temperatures, except as noted, were in the range 210–230°. Probe temperatures varied from 80 to 160° for the esters **2** and to 300° for the longest chain acids. Detailed examination of the metastable peak leading to the ion at m/e 121 was carried out as described by Tsang and Harrison.¹⁴ Peak intensities were measured as the heights of peaks in the photographic traces of the mass spectra. Repetitive scans (at least four for m/e 121, 138, 139, 152, 153) were used to ascertain the average error. Appearance potentials were measured on the MS-902.

Alkoxybenzoic Acid Methyl Esters 2. The original synthetic approach of Cohen and Dudley²⁸ was modified as follows.

Methyl *p*-hydroxybenzoate (0.258 g, 1.7 mmol), 1-bromononane (0.31 g, 1.5 mmol), and sodium methoxide (0.092 g, 1.7 mmol) were placed in a 25-ml erlenmeyer flask. After addition of 1.2 ml of *N,N*-dimethylformamide (DMF), the flask was heated in an oil bath for 30 min with magnetic stirring. When cool, the contents were poured into 50 ml of petroleum ether (bp 30–60°) and 20 ml of water in a 125-ml separatory funnel. An additional 10-ml portion of petroleum ether was used to wash the remaining material in the flask into the separatory funnel. The layers were separated. The organic layer was washed successively with 10% NaOH (2 × 20 ml) and saturated sodium bicarbonate (1 × 20 ml). The solution was then dried over sodium sulfate, concentrated, and recrystallized from methanol. The white crystals weighed 0.25 g, 66%: mp 48°; nmr (CCl₄) δ 0.8–2.0 (m, 19.1 H), 3.84 s + 3.94 t ($J = 7$ Hz, CH₂O + CH₂O, 5.0 H), 6.90 (d, $J = 9$ Hz, 2.0 H), 7.87 (d, $J = 9$ Hz, 2.0 H). The ester was further characterized by hydrolysis (*vide infra*) to the corresponding acid, mp 95° (lit.²⁹ 94°).

Meta ethers were prepared similarly from methyl *m*-hydroxybenzoate. Isolated yields varied from 50 to 75% and were not maximized. The meta ethers of chain length 2–7 and the para ethers of chain length 2–6 were obtained as colorless oils. Molecular distillation of the *p*-butyl ether gave the same mass spectrum as the crude material. Other oils were examined without further purification.

Alkoxybenzoic Acids 1. *p*-Dodecyloxybenzoic acid was obtained from Aldrich. The other acids were obtained by basic hydrolysis of the respective esters by standard methods. The acids were all recrystallized from hot methanol. They have been independently synthesized and characterized by Jones.^{29, 30}

Appendix

The argument that hydrogen abstraction is rate determining in Schemes I and II contained the implicit assumption that hydrogen migration within the chain in *d* (and *h*) does not affect ion intensities. We can ask the question of what effect hydrogen migration³¹ in the hydrocarbon chain will have on the observed ion ratios. This question may be treated as follows.

(28) J. B. Cohen and H. W. Dudley, *J. Chem. Soc., London*, **97**, 1737 (1910).

(29) G. W. Gray and B. Jones, *J. Chem. Soc., London*, 4179 (1953).

(30) B. Jones, *J. Chem. Soc., London*, 430 (1943); 420 (1939); 1834, 1874 (1935).

(31) For leading references to mechanisms of hydrogen scrambling, see W. Carpenter, A. M. Duffield, and C. Djerassi, *J. Amer. Chem. Soc.*, **90**, 160 (1968).

Consider the limiting case in which hydrogen migration from (CH₂)-*i* to (·CH)-*j* is faster than k_{-H} in *d*; the rate of re-formation of *c* from *d*, the species produced

$$k_{-Hj} = k_{P(-H)} \sum_{i=1}^n P_i \quad (10)$$

by initial hydrogen abstraction from carbon *j*, is then given by eq 10. Rapid hydrogen migration in the hydrocarbon chain in *d* implies that collision of any CH₂ with the protonated oxygen can lead to formation of *c*. The return rates from the *n* possible species *d* are therefore identical. This leads to

$$k_{-H} = \sum_{j=1}^n k_{-Hj} = nk_{-Hj} \quad (11)$$

$$k_{-H} = k_{P(-H)} n \sum_{i=1}^n P_i \quad (12)$$

If k_t is rate determining under these conditions, eq 12 and 13 hold, and we should observe a *decrease* in the

$$\frac{k_H}{k_{-H}} = \frac{2k_{PH}}{nk_{P(-H)}} = \frac{1}{n} K \quad (13)$$

$$m/e \frac{153}{152} \alpha \frac{k_t}{n} K \quad (14)$$

m/e 153/152 and 139/138 ratios with an increase in chain length.

For hydrogen scrambling to affect the intensity of ion *e*, k_t must be rate determining. We treated two limiting cases: if hydrogen migration in *d* is very slow, the intensity of *e* is predicted to be invariant with chain length. For very rapid scrambling, its intensity decreases linearly with *n*. It follows qualitatively that if the rate of hydrogen scrambling is of the same order of magnitude as k_{-H} , it must contribute to a decrease in the intensity of *e* with increase in chain length. Since this is counter to our observations, we conclude that hydrogen scrambling cannot affect our conclusion that k_H is rate determining in the pathway leading to *e*. One might still observe hydrogen scrambling in deuterated derivatives of **1** and **2**. It cannot, however, contribute to the intensity ratios we observe, nor can it occur by the pathway described by k_{-H} .

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