Mass Spectrometry in Structural and Stereochemical Problems. CCIII.[1] The Course of a Triple Hydrogen Migration in Esters of Trimellitic Anhydride[2]

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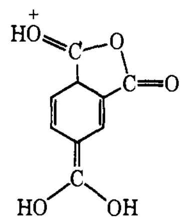
Abstract: The nature of a triple hydrogen migration observed in the electron impact induced fragmentation of *n*-alkyl esters of trimellitic anhydride has been investigated. The origin of the "third" itinerant hydrogen has been defined through deuterium labeling. When the anhydride moiety was replaced by the corresponding imide the triple hydrogen migration was still observed, while replacement by one or two methyl ester groups was not sufficient to maintain the process. The elimination of methanol in the fragmentation of 1,2-dimethyl *n*-alkyl trimellitates is also discussed.

Electron impact induced fragmentations of organic molecules which involve hydrogen migration have been extensively studied and their importance is well recognized. Generally these processes involve the transfer of one hydrogen,[4] but instances involving the transfer of two hydrogens in a unidirectional[5a] or reciprocal[5b] manner are also well documented. A fragmentation process which involves the transfer of three hydrogens has been observed in only two series of compounds,[6,7] one of which will be discussed at length in this paper.

Meyerson and collaborators investigated the electron impact induced fragmentation of *n*-alkyl esters of trimellitic anhydride[7] and showed that *O*-alkyl cleavage is accompanied by the expected transfer of two hydrogens (typical of carboxylic acid esters other than methyl)[5a,8] leading to a peak at *m/e* 193, but that it is also accompanied by a process involving the transfer of three hydrogens (peak at *m/e* 194). They demonstrated that the abundance of the ion of mass 194 was dependent upon the length of the alkyl chain with a minimum requirement of *n*-hexyl before the process was observed. The abundance increases as the alkyl group is extended from *n*-hexyl to *n*-dodecyl, but further extension only slightly affects the abundance of this ion. The corresponding *n*-alkyl benzoates have been studied[7,9] and in these compounds *O*-alkyl cleavage of the ester is accompanied by the usual migration[5a,8] of two hydrogens to give the protonated benzoic acid fragment, but no triple hydrogen migration was encountered.

These results lead to the conclusion that the third hydrogen was being transferred from the alkyl chain to the anhydride moiety and that a sufficiently long alkyl chain was required, since the two groups probably need to come within reasonable proximity for the transfer to take place. Meyerson[7] indicated that the ion of mass 194 might best be represented by a series of resonance structures, typified by a, in which the third hydrogen may be bound to any one of the three anhydride oxygens. However, no labeling of the alkyl chain was carried out to define the origin of the hydrogen pictured as migrating from the alkyl chain to the anhydride although the results presented indicated that it was probably abstracted from the more remote positions of the chain.



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We were interested in further investigating the nature of the triple hydrogen transfer in these compounds. In particular we wished to establish whether the anhydride moiety could be replaced by one or two ester groups and to define the origin of the itinerant hydrogens through deuterium labeling.

In accord with the first objective we prepared methyl decyl terephthalate (I), methyl dodecyl terephthalate (II), methyl decyl isophthalate (III), methyl dodecyl isophthalate (IV), 1,2-dimethyl nonyl trimellitate (V), and 1,2-dimethyl dodecyl trimellitate (VI) and examined their mass spectra. Cleavage of the *O*-alkyl bond of the long chain ester with concurrent transfer of two hydrogens would lead to an ion of mass 181 for compounds I–IV, and to an ion of mass 239 for compounds V and VI, as shown below.

The ion of mass 181 was responsible for the base peak of the spectra of the relevant compounds (see for instance Figure 1), but no fragment of mass 182 was observed. In the spectra of compounds V and VI, the *m/e* 239 peak is of approximately 30% relative intensity (see Figure 2) but no ion of mass 240 was apparent. These observations indicate that the anhydride cannot

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[1] For paper CCII, see M. Sheehan, R. J. Spangler, M. Ikeda, and C. Djerassi, *J. Org. Chem.*, **36**, 1796 (1971).

[2] Financial support by the National Institutes of Health (Grants No. AM 12758 and AM 04257) is gratefully acknowledged.

[3] Postdoctoral Fellow, 1968–1970.

[4] For leading references, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967.

[5] See, for instance, (a) C. Djerassi and C. Fenselau, *J. Amer. Chem. Soc.*, **87**, 5756 (1965); (b) L. Tokes, G. Jones, and C. Djerassi, *ibid.*, **90**, 5465 (1968); G. Eadon and C. Djerassi, *ibid.*, **91**, 2724 (1969).

[6] M. Katoh and C. Djerassi, *ibid.*, **92**, 731 (1970).

[7] S. Meyerson, I. Puskas, and E. K. Fields, *Chem. Ind.* (*London*), 1845 (1968).

[8] A. G. Sharkey, Jr., J. L. Shultz, and R. A. Friedel, *Anal. Chem.*, 31, 87 (1959).

[9] F. W. McLafferty and R. S. Gohlke, *ibid.*, 31, 2076 (1959).

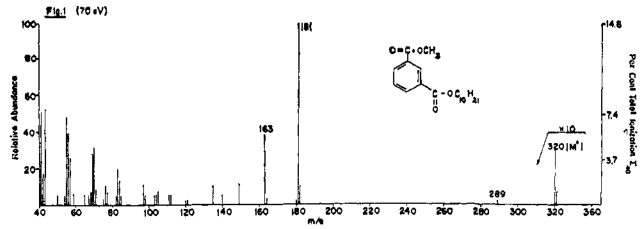


Figure 1. Mass spectrum of methyl decyl isophthalate (III).

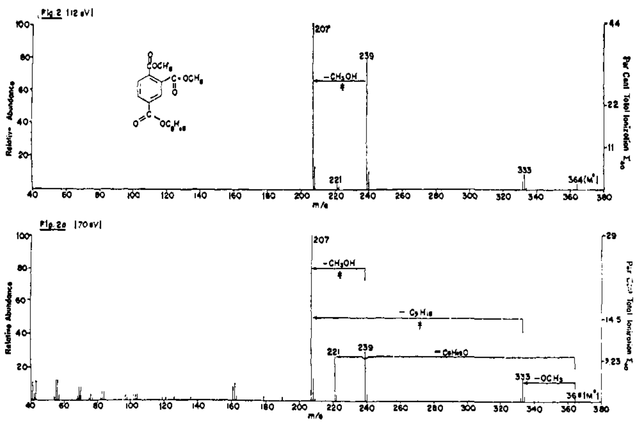
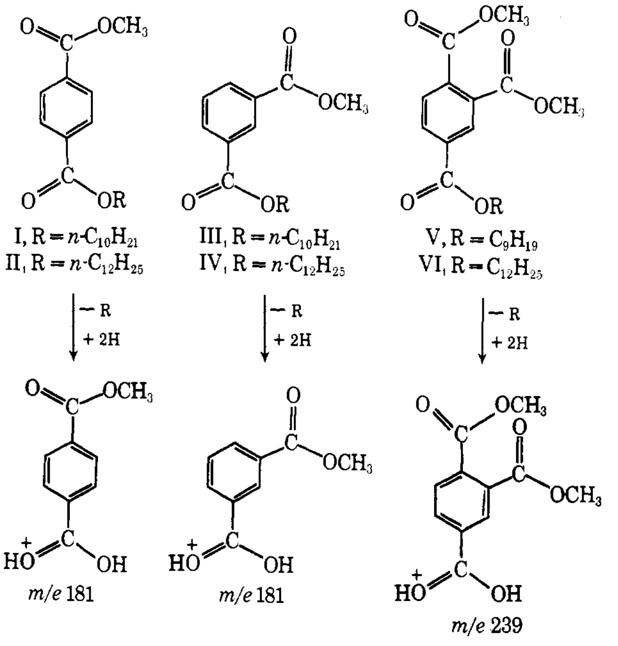


Figure 2. Mass spectrum of 1,2-dimethyl 4-*n*-nonyl trimellitate (V).

be replaced by either one or two ester groups for the transfer of the third hydrogen to be maintained.



I, R = n-$C_{10}H_{21}$
II, R = n-$C_{12}H_{25}$

III, R = n-$C_{10}H_{21}$
IV, R = n-$C_{12}H_{25}$

V, R = C_9H_{19}
VI, R = $C_{12}H_{25}$

$-R$ $+2H$

m/e 181

m/e 181

m/e 239

Conversion of the cyclic anhydride to the corresponding imide is a simple procedure;[10] consequently we included a mass spectrometric study of compounds such as VII.

In these compounds *O*-alkyl cleavage of the ester with transfer of two hydrogens leads to a peak at *m/e* 192 and this ion was associated with the base peak of the spectra in all instances (see Figure 3). Interestingly the abundance of the ion of mass 193 (triple hydrogen

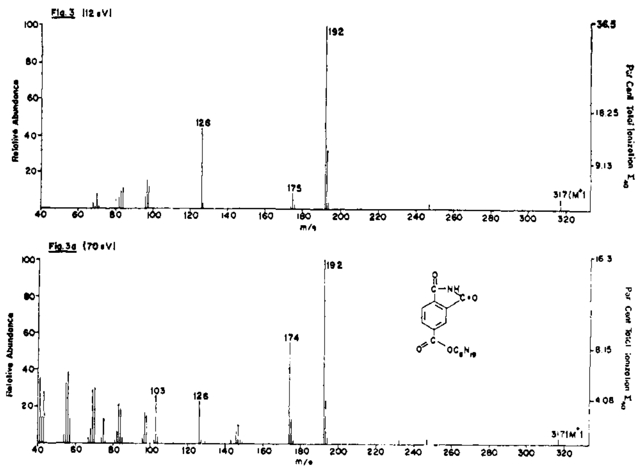
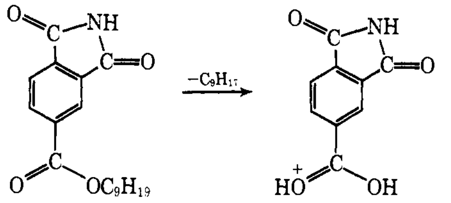


Figure 3. Mass spectrum of 4-nonoxycarbonylphthalimide (VII).

transfer) in these compounds exhibited the same chain length dependence as did the triple hydrogen transfer peak (*m/e* 194) in the spectra[7] of the anhydrides. In all the imides the abundance of the ion of mass 193, expressed as a percentage of the peak group 192–193, was somewhat reduced when compared with the abundance of the ion of mass 194, in relation to the peak group 193–194, in the corresponding anhydrides. Table I shows the relevant data for the series of anhydrides studied and the corresponding imides, with the values recorded being expressed as percentage of the respective peak groups calculated after first correcting the observed values for contribution of natural ^{13}C isotope.

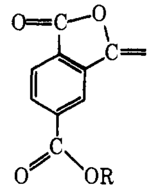
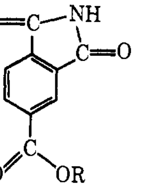


VII

m/e 192

The triple hydrogen transfer proceeds to the extent of 24% of the peak group *m/e* 193–194 when *n*-nonyl trimellitic anhydride is subjected to electron impact (see Figure 4), and we chose to prepare a series of specifically

Table I. The Effect of Alkyl Chain Length upon the Importance of Hydrogen Migrations in the Spectra of *n*-Alkyl Esters of Trimellitic Anhydride and the Corresponding Imides

								
	m/e				*m/e*			
R	193	194	175	176	192	193	174	175
n-C_4H_9	100		100		100		100	
n-C_8H_{17}	86	14	83	17	91	9	93	7
n-C_9H_{19}	76	24	76	24	88	12	88	12
n-$C_{10}H_{21}$	68	32	65	35	84	16	85	15
n-$C_{12}H_{25}$	65	35	66	34	80	20	81	19

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(10) W. A. Noyes and P. K. Porter, "Organic Syntheses," Collect. Vol. I, Wiley, New York, N. Y., 1941, p 457.

deuterated analogs of this compound in an effort to elucidate the origin of the hydrogen being transferred to the anhydride moiety. The labeled compounds listed in Table II were prepared and their spectra examined.

Table II. Percentage of Total Ionization (Σ_{193}^{196} and Σ_{175}^{177}) of the Two Peak Groups, *m/e* 193–196 and *m/e* 175–177, in the Spectra of *n*-Nonyl Trimellitic Anhydride and Deuterated Analogs

Compd	Ionization, eV	*m/e* 193	*m/e* 194	*m/e* 195	*m/e* 196	*m/e* 175	*m/e* 176	*m/e* 177
Unlabeled	70	76	24			76	24	
	15	67	33				100	
3-d$_2$	70	50	45	5		75	25	
	15	38	56	6			100	
4-d$_2$	70	59	35	5		76	23	1
	15	48	41	11			96	4
5-d$_2$	70	59	28	10	3	72	23	5
	15	50	28	16	6		77	23
6,7-d$_4$	70	55	30	12	3		61	39
	15	48	33	15	5		61	39
8,9-d$_4$	70	67	28	5		70	26	4
	15	57	37	6			88	12
9-d$_3$	70	75	25			75	25	
	15	67	33				100	

An explanation of the inclusion of the peak group 174–177 in Tables I and II will follow later in the discussion.

While it is obvious from Table II that labeling the alkyl chain in the positions shown markedly affects in all instances the relative abundances of the ions of mass 193 and 194 with the exception of the terminal position, it is not possible to obtain quantitative data relevant to the transfer of a hydrogen to the anhydride moiety from this peak group because of the following considerations.

Benz and Biemann[11] have demonstrated that the formation of protonated acetic acid from pentyl acetate in the mass spectrometer involves the transfer of one hydrogen which originates exclusively from the 2 and 3 positions of the pentyl group, but that the second hydrogen is abstracted randomly from all positions of the chain. Members of this laboratory[5a] have investigated the *O*-alkyl cleavage and concomitant double hydrogen migration leading to protonated benzoic acid in the mass spectrum of butyl benzoate. While the preponderance of the two hydrogens transferred originated from positions 2 and 3 of the butyl group, the sharp definition of origin observed by Benz and Biemann in pentyl acetate did not appear to operate. This rather nonspecific transfer of hydrogens in the double hydrogen migration is probably applicable to the *O*-alkyl cleavage and back-transfer of two hydrogens leading to the ion of mass 193 in the esters of trimellitic anhydride. This makes analysis of the peak group 193–194 in the deuterium labeling experiments difficult for obvious reasons. It is only possible to conclude that if *m/e* 196 is observed in the spectrum of the labeled compound and provided the compound is not labeled at positions 2 and 3 (the presumed origin of one hydrogen atom) then one of the deuterium atoms must be involved in the migration which is peculiar to the anhydrides or imides.

Examination of the spectra of the series of anhydrides at low ionizing voltage produced some interesting observations with regard to the peak group *m/e* 175–176. All the anhydrides studied display an ion of mass 175 of 60–70% relative abundance when the spectra are determined at 70 eV. In addition there is a peak at *m/e* 176 which shows a similar dependence of intensity upon the length of the alkyl chain, as was observed for the peak at *m/e* 194 (see Table I). At low ionizing voltage (nominal 15 eV) the ion of mass 175 is absent from the spectra, while in instances where the ion of mass 176 is present in the 70-eV spectra, this peak remains at low voltage. In the spectrum of *n*-nonyl trimellitic anhydride (Figure 4) determined at 15 eV this ion was of 16% relative abundance while *m/e* 193 was the base peak.

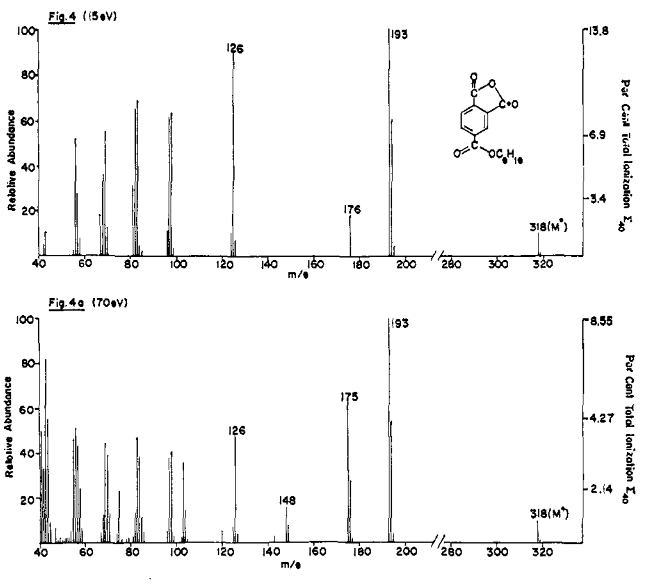
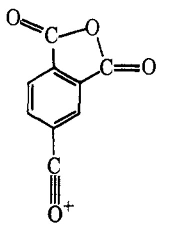
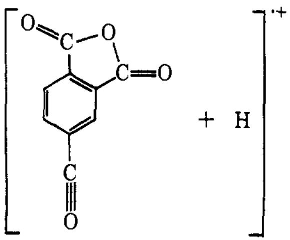


Figure 4. Mass spectrum of 4-*n*-nonyl trimellitic anhydride.

High resolution mass measurements of *m/e* 175 and *m/e* 176 confirm that the two fragments differ by one hydrogen and the elemental compositions are in accord with the following structural representations.



m/e 175



m/e 176

A possible rationalization of the disappearance of the peak at *m/e* 175 but not at *m/e* 176 at low voltage is suggested by information gained by scanning in the metastable mode,[12] which indicated that while the ion of mass 175 may originate either from the parent ion (*via* acyl oxygen cleavage of the long chain ester) or from the ion of mass 193 (*via* loss of water), the ion of mass 176 originates only from the parent ion and not from the ion of mass 194. The occurrence of the loss of water from the ion of mass 193 compared with its absence from the ion of mass 194 is readily rationalized since in the former ion the charge is localized on the protonated carboxylate group while in the latter the charge is spread over the oxygens of the anhydride group.

Comparison of the data obtained for the peak groups 175–176 and 193–194 of several esters of trimellitic an-

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[11] W. Benz and K. Biemann, *J. Amer. Chem. Soc.*, **86**, 2375 (1964).

[12] K. R. Jennings in "Some Newer Physical Methods in Structural Chemistry," R. Bonnett and J. G. Davis, Ed., United Trade Press, London, 1967, p 105.

hydride at 70 eV shown in Table I indicates that the hydrogen which is transferred in the genesis of the charged fragment of mass 176 is involved in a mechanism which has similar character to that operating in the process which transfers the "third" hydrogen to the anhydride moiety in the formation of the ion of mass 194. However, while the interpretation of the data (Table II) gained for the ion of mass 194 in the labeling study is difficult due to the simultaneous involvement of three hydrogens, the process leading to the ion of mass 176 involves the shift of only one hydrogen, ostensibly to the anhydride moiety. Since *m/e* 176 is an isolated peak in the spectra determined at 15 eV (see Figure 4) the interpretation of the results from the deuterium labeling study was based on these spectra.

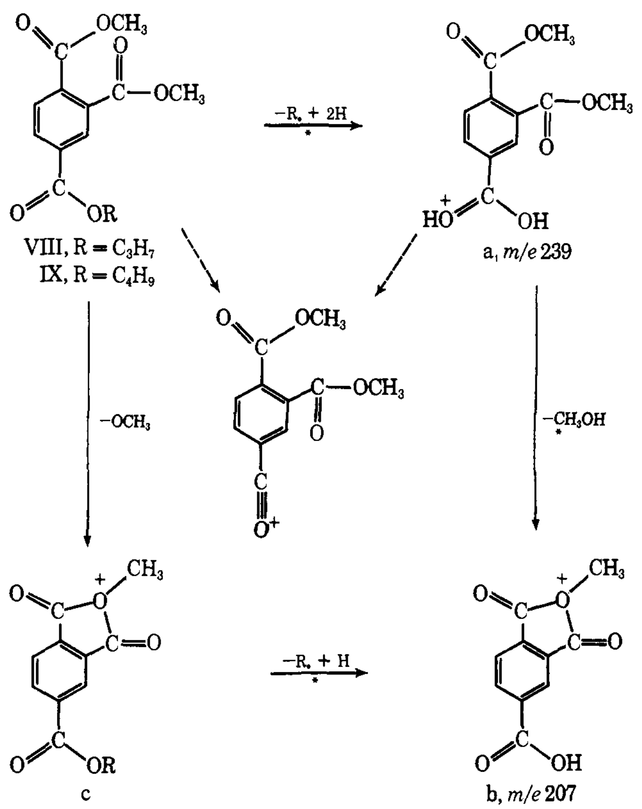
From the shift of the peak at *m/e* 176 to *m/e* 177 given in Table II it is apparent that the hydrogen being transferred in this process may originate from positions 5, 6, 7, and 8 of the alkyl chain. The process does not appear to exhibit high specificity, though it is surprising that the contribution from position 5 is so important. The process, however, does not involve random transfer from every position in the alkyl chain. No transfer from the terminal position of the alkyl chain was observed and this is in accord with the difficulty of removing a hydrogen from a primary position due to the instability of the resultant radical which has been well documented in mass spectrometry.[13]

We conclude that while the anhydride may be replaced by the corresponding imide without precluding the triple hydrogen transfer observed by Meyerson[7] in the *n*-alkyl esters of trimellitic anhydride, replacement by one or two ester functionalities is not sufficient to maintain the process. The deuterium labeling study of *n*-nonyl trimellitic anhydride indicates that the hydrogen being transferred to the anhydride moiety does not arise from a specific site but supports the observation that a minimum chain length of *n*-hexyl is required for the process, since this is the first compound included in this study with C-5 as a secondary position.

Dreiding models indicate that the hydrogen is probably transferred initially to the oxygen atom of the *m*-carbonyl with respect to the ester since it appears difficult for the hydrogens attached to position 5 in the esters to reach either of the other two anhydride oxygens unless the aromatic ring has been opened prior to rearrangement. Once the hydrogen is situated at the *m*-carbonyl group, then further shift may occur to the para position from where the positive charge may resonate to the ester group to trigger either *O*-alkyl cleavage accompanied by back-transfer of two hydrogens to give the ion of mass 194, or *O*-acyl cleavage leading to the ion of mass 176.

The Mass Spectra of *n*-Alkyl Esters of 1,2-Dimethyl Trimellitic Acid. As mentioned we had occasion to prepare esters such as V and VI in the effort to establish the nature of the triple hydrogen migration. In addition we studied the mass spectra of 1,2-dimethyl *n*-propyl trimellitate (VIII) and 1,2-dimethyl *n*-butyl trimellitate (IX). While the ion of mass 239 is a substantial peak in the mass spectra of all these compounds, the ion of mass 207 is the base peak in all instances (see for instance Figure 2). The fragment of mass 239 arises by *O*-alkyl cleavage of the long chain ester with the concurrent transfer of two hydrogens as already discussed. It is interesting that the ion of mass 239 fragments to give the ion of mass 207 (b) with the loss of 32 amu, presumably methanol, in all these spectra, the process being supported by the presence of a metastable peak at *m/e* 179.2. At 70 eV there is an alternate pathway available for the formation of the peak at *m/e* 207 as outlined in Scheme I. This involves the loss of 31 amu (OCH_3) from the parent ion to give the ion c which may further fragment *via* the loss of the alkyl group with back-transfer of one hydrogen to give the ion of mass 207. The fragmentation of ion c to ion b is supported by the presence of the appropriate metastable peak in each instance. However, at 12 eV this metastable peak is no longer observed while that supporting the pathway of ion a to ion b is evident. Since the ion of mass 207 is responsible for the base peak of the spectra at both 70 and 12 eV it follows that the formation of this ion *via* the loss of methanol from the ion of mass 239 constitutes its major genesis. The loss of 31 amu (OCH_3) from the peak at *m/e* 239, which would give rise to an ion of mass 208, was not observed in the spectra of the compounds studied.

Scheme I



As the mass spectrum of 1,2-dimethyltrimellitic acid (X) shows only the loss of 31 amu (OCH_3) from the parent ion, it appears reasonable that one of the hydrogens, which is transferred concurrently with the *O*-alkyl cleavage of the long-chain ester, is involved in the subsequent loss of methanol from the ion of mass 239.

To investigate this proposal the mass spectrum of 1,2-dimethyl 4-*n*-(perdeuterio)propyl trimellitate (XI) was examined. Here ion a appeared at *m/e* 241 in accord with *O*-alkyl cleavage of the propyl ester accompanied by the transfer of two deuterium atoms. This ion then

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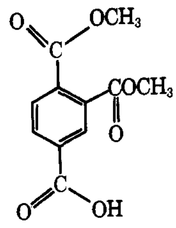
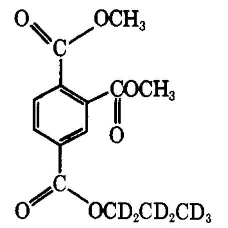
[13] H. Budzikiewicz, C. Fenselau, and C. Djerassi, *Tetrahedron*, 22, 1391 (1966).



X

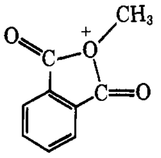


XI

undergoes further fragmentation with the loss of 33 amu (CH_3OD) to give a peak at *m/e* 208, the process being supported by the presence of a metastable peak at *m/e* 179.5. Loss of 32 amu to give a fragment of mass 209 is not observed, and examination of the spectrum of the unlabeled compound indicates that ion a is shifted cleanly from *m/e* 207 to *m/e* 208.

The only other major peak in the spectra of compound V, VI, VIII, and IX occurs at *m/e* 221 (see Figure 2) and probably arises *via* acyl cleavage of the long-chain ester. At 70 eV this fragment is of approximately 50% relative intensity (R. I.), while at 12 eV it is reduced to about 5% R.I. Since both this fragmentation and the formation of *m/e* 207 *via* ion c involve an acyl cleavage, this observation further supports the postulate that *m/e* 239 is the main source of *m/e* 207.

The structure of ion b must be regarded as tentative but there is some circumstantial evidence to support its structure. The mass spectrum of methyl decyl isophthalate (III) shows a peak at *m/e* 181 corresponding to a, but no loss of methanol (to give *m/e* 149). The mass spectrum of methyl decyl terephthalate (I) is similar to that of III and so it appears that the 1,2-dimethyl ester moiety is necessary for the loss of methanol to occur from these molecules following *O*-alkyl cleavage and the back-transfer of the two hydrogens. In addition dimethyl phthalate exhibits *m/e* 163 as the base peak and this may be rationalized in terms of structure d.



d

Since the ion of mass 207 is the most abundant one, and there is little fragmentation leading to ions of lower mass, then it must have a relatively stable structure. The structure indicated for b is in accord with these considerations.

Experimental Section

Melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer Model 700 spectrophotometer. Nuclear magnetic resonance spectra were obtained with a Varian Model T-60 spectrometer. All nmr measurements were made on deuteriochloroform solutions and chemical shifts are reported in parts per million downfield from tetramethylsilane, employed as the internal standard, while coupling constants are reported in cycles per second.

Low resolution mass spectra were obtained by Mr. R. Conover using an Atlas CH-4 spectrometer (source temperature 190–200°), while the high resolution data were obtained by Mr. R. Ross using an A.E.I. MS-9 spectrometer. All compounds for mass spectral analysis were checked for purity by vpc using an F & M Model 402 gas chromatograph. Elemental analyses were done by Mr. E. Meier and Mr. J. Consul of the Stanford microanalytical laboratory.

Methyl Decyl Terephthalate (I). A solution of terephthalic acid monomethyl ester[14] (1.0 g, 5.5 mmol) and thionyl chloride (0.6 g, 6.1 mmol) was heated under reflux for 2 hr; decyl alcohol (0.8 g, 5.0 mmol) was added and the mixture was stirred for 1 hr. The reaction mixture was diluted with water and extracted several times with chloroform. The combined chloroform extract was washed with water and then dried (Na_2SO_4). Thin layer chromatographic examination of the residue after evaporation of the chloroform extract showed the presence of three compounds and purification of the product by preparative tlc confirmed that the least polar component was the desired methyl decyl terephthalate: ir 1720 cm^{-1} (C=O); mass spectrum *m/e* 320 (M^+).

Methyl Dodecyl Terephthalate (II). Treatment of terephthalic acid monomethyl ester with thionyl chloride and dodecyl alcohol in a manner analogous to the preparation of compound I followed by purification by preparative tlc on silica gel gave II in 41% yield: ir 1720 cm^{-1} (C=O); mass spectrum *m/e* 348 (M^+).

Methyl Decyl Isophthalate (III). Treatment of isophthalic acid monomethyl ester[15] with thionyl chloride and the appropriate alcohol in a manner similar to that used in the preparation of compounds I and II gave methyl decyl isophthalate (III) and methyl dodecyl isophthalate (IV): ir 1720 cm^{-1} (C=O); mass spectrum *m/e* 320 (M^+) and *m/e* 348 (M^+), respectively.

1,2-Dimethyl 4-*n*-Nonyl Trimellitate (V). The 1,2-dimethyl 4-*n*-alkyl esters of trimellitic acid were prepared by diazomethane treatment of the appropriate 4-alkyl ester of trimellitic anhydride in methanol as outlined below for compound V.

A solution of diazomethane in ether (prepared from *N*-nitrosomethylurea[16]) was added slowly to a cooled solution of *n*-nonyl trimellitic anhydride in methanol with stirring until a faint yellow coloration persisted. Sufficient glacial acetic acid was added to remove the excess diazomethane and the reaction mixture was poured into water. Examination of the ether extract of the resulting suspension by tlc and vpc indicated essentially complete conversion of the anhydride to the desired 1,2-dimethyl moiety. Preparative vpc on a 3% OV-25 5 ft column gave a pure sample of V: ir (film) 1720 cm^{-1} (C=O); nmr 3.93 (singlet, 6 protons, $2CH_3CO-$), 4.39 (triplet, $J = 7$, 2 protons, $-CH_2CO-$), 7.73 (doublet, $J = 9$, 1 proton, aromatic C-6 H), 81.7 (2 doublets, $J = 9$ and $J = 2$, 1 proton, aromatic C-5 H), 8.40 (doublet, $J = 2$, 1 proton, aromatic C-3 H); mass spectrum *m/e* 364 (M^+).

Anal. Calcd for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 65.83; H, 7.62.

1,2-Dimethyl *n*-Dodecyl Trimellitate (VI). The reaction of diazomethane with *n*-dodecyl trimellitic anhydride in the same manner as outlined for the preparation of V, followed by preparative vpc using a 5 ft glass column packed with 3% OV-25 on Gas Chrom Q, gave a pure sample of VI: ir (film) 1720 cm^{-1} (C=O); mass spectrum *m/e* 406 (M^+).

4-Alkyl Esters of Trimellitic Anhydride. All the analogs of this series of compounds were prepared by use of the appropriate alcohol in the procedure outlined below for the preparation of 4-*n*-nonyl trimellitic anhydride.

Nonyl alcohol (0.65 g, 4.5 mmol) was added to a solution of trimellitic anhydride acid chloride[17] in anhydrous ether (5.0 ml) containing anhydrous K_2CO_3 (1.0 g). The mixture was stirred overnight at room temperature and then poured into water. The aqueous solution was extracted three times with ether and the combined ethereal extracts were washed with water and dried (Na_2SO_4). Evaporation of the ether gave a clear oil which crystallized from acetone–petroleum ether as plates: mp 43–44°; ir 1850, 1780 (anhydride C=O), 1720 cm^{-1} (ester C=O); nmr 4.42 (triplet, $J = 6.5$, 2 protons, $-CH_2CO-$), 8.10 (two doublets, $J = 9$ and $J = 2$, 1 proton, aromatic C-5 H), 8.57 (doublet, $J = 9$, 1 proton, aromatic C-6 H), 8.63 (doublet, $J = 2$, 1 proton, aromatic C-3 H); mass spectrum *m/e* 318 (M^+).

Anal. Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.80; H, 6.95.

The following *n*-alkyl esters of trimellitic anhydride were prepared using this general procedure. The compounds were obtained pure by preparative vpc using a 5 ft 3% SE-30 glass column and the ir and nmr data from these compounds were essentially the

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same as that given for the *n*-nonyl derivative: 4-*n*-butyl trimellitic anhydride;[18] mass spectrum *m/e* 248 (M^+); 4-*n*-octyl trimellitic anhydride, mp 37–38°; mass spectrum *m/e* 304 (M^+).

Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 67.20; H, 6.68; 4-*n*-decyl trimellitic anhydride, mp 51–52°; mass spectrum *m/e* 332 (M^+); 4-*n*-dodecyl trimellitic anhydride, mp 63°; mass spectrum *m/e* 360 (M^+).

4-Nonoxycarbonylphthalimide (VII). The cyclic imide esters were all prepared from the corresponding cyclic anhydride esters by the general procedure outlined below for the *n*-nonyl ester.

A mixture of *n*-nonyl trimellitic anhydride (1.0 g) and concentrated ammonia solution was heated with a propane flame for a period of 5 min.[10] The residue upon sublimation gave the desired compound VII as colorless needles: mp 127°; ir 3440, 3260 (N–H), 1790, 1710 (imide C=O), 1720 cm^{-1} (ester C=O); nmr 4.40 (triplet, J = 6.5, 2 protons, $-CH_2CO-$), 7.98 (two doublets, J = 9 and J = 2, 1 proton, aromatic C-5 H), 8.48 (doublet, J = 9, 1 proton, aromatic C-6 H), 8.54 (doublet, J = 2, 1 proton, aromatic C-3 H); mass spectrum *m/e* 317 (M^+).

Anal. Calcd for $C_{18}H_{23}O_4N$: C, 68.12; H, 7.30. Found: C, 68.13; H, 7.20.

4-Octoxycarbonylphthalimide (VIIa) was prepared as outlined above and was characterized in the following manner: mp 131°; ir 3430, 3260 (N–H), 1790, 1710 (imide C=O), 1720 cm^{-1} (ester C=O); mass spectrum *m/e* 303 (M^+).

Anal. Calcd for $C_{17}H_{21}O_4N$: C, 67.31; H, 6.98. Found: C, 67.1; H, 6.95.

Other analogs prepared by this procedure were 4-decoxycarbonylphthalimide, mp 129°, mass spectrum *m/e* 331 (M^+); 4-dodecoxycarbonylphthalimide, mp 132–133°; mass spectrum *m/e* 359 (M^+).

Specifically Deuterated Nonyl Alcohols. The series of 4-*n*-nonyl trimellitic anhydrides with deuterium located in specific points in the nonyl chain were prepared from the appropriately labeled nonyl alcohol and trimellitic anhydride monoacid chloride as previously described. Many of the reactions were carried out using less than 50 mg of labeled alcohol and in these instances the product was obtained pure by preparative vpc using a 5 ft glass column packed with 3% OV-25 on Gas Chrom Q with the oven temperature at 225°. The methods of preparation of the appropriate nonyl alcohols are outlined below.

Nonanol-*3,3-d*$_2$. Heptanoic acid was reduced to 1,1-dideuterioheptanol employing lithium aluminum deuteride[19] (LAD) in anhydrous ether and the alcohol was converted to 1,1-dideuterioheptyl bromide using triphenylphosphine and bromine.[20] A solution of the bromide in anhydrous ether was added to dry magnesium turnings and the resulting Grignard compound was treated with ethylene oxide at 0°. Work-up by the usual methods gave the desired labeled nonyl alcohol which was purified by preparative vpc using a 5 ft 5% SE-30 column with the oven temperature at 130°.

Nonanol-*4,4-d*$_2$. Hexanoic acid was reduced with LAD to give 1,1-dideuteriohexanol which was converted to 1,1-dideuteriohexyl bromide using triphenylphosphine and bromine. Addition of a solution of the bromide in anhydrous ether to magnesium turnings yielded the desired Grignard compound to which a solution of trimethylene oxide[21] (oxetane) was added at 0°. Work-up by the methods gave the desired nonanol in 35% yield. A pure sample of the alcohol for the reaction with trimellitic anhydride monoacid chloride was obtained by preparative vpc.

Nonanol-*5,5-d*$_2$. Addition of an ethereal solution of valeric anhydride to LAD in ether gave 1-pentanol-*1,1-d*$_2$ which was converted to the corresponding bromide using triphenylphosphine and bromine. Formation of the Grignard compound and addition of ethylene oxide gave 1-heptanol-*3,3-d*$_2$ which was cycled through the same series of reactions to give the desired 1-nonanol-*5,5-d*$_2$. A pure sample was obtained by preparative vpc under the established conditions.

The series of reactions used in the preparation of the above three alcohols is not readily applicable to preparing labeled alcohols with the deuterium located further down the chain because of the number of reactions involved after the introduction of the deuterium atoms and hence the cumbersome nature of the general procedure.

Nonanol-*6,6,7,7-d*$_4$. Sodium borohydride (3.0 g) was added slowly to a stirred mixture of iodine (7.2 g) and tetrahydropyran (5.0 g).[22] The reaction mixture was stirred for 2 hr and then water was added slowly. The aqueous solution was extracted with ether and the combined ethereal extract was washed with water and dried (Na_2SO_4). Evaporation of the ether and examination of the residual oil indicated 5-iodopentan-1-ol was the major product (90%). This compound was converted to the corresponding tetrahydropyranyl ether through treatment with dihydropyran and a catalytic amount of *p*-toluenesulfonic acid.

A solution of butyllithium in hexane (3.8 ml of 2.67 *M* solution, 0.01 mol) was added dropwise to a mixture of 1-butyne and tetrahydrofuran at −78°, and the mixture was allowed to warm slowly to room temperature. A solution of 5-iodopentan-1-ol tetrahydropyranyl ether (2.5 g, 0.0085 mol) in dry hexamethylphosphoramide (1.5 ml) was then added and the mixture was stirred for 1 hr and then diluted with water. Examination of the ethereal extract indicated the desired non-6-yn-1-ol tetrahydropyranyl ether had been formed in high yield; ir 2210 (C≡C) cm^{-1}; mass spectrum *m/e* 223 ($M^+ - 1$).

The acetylenic alcohol was dissolved in acetone (10 ml) containing tris(triphenylphosphine)rhodium chloride[23] (100 mg) and the solution was saturated with deuterium gas prior to the addition of an acetone solution of the acetylenic alcohol. The consumption of deuterium gas was rapid initially, but stirring overnight was necessary for the complete uptake of 2 mol. Removal of the acetone gave a brown residue which was washed with hexane several times. The combined washings were chromatographed on a column of silica gel and elution with hexane gave the desired 1-nonanol-*6,6,7,7-d*$_4$ tetrahydropyranyl ether, the mass spectrum of which indicated that there was no contamination with olefin from partial reduction. Cleavage of the tetrahydropyranyl ether with dilute aqueous HCl gave 1-nonanol-*6,6,7,7-d*$_4$ which was obtained pure by preparative vpc.

1-Nonanol-*8,8,9,9-d*$_4$. Diborane[24] was added slowly to a cooled solution of 7-bromoheptanoic acid[25] in anhydrous ether and the mixture was allowed to warm to room temperature. Addition of water and extraction with ether gave the desired 7-bromoheptanol as the only product. This compound was converted to the tetrahydropyranyl ether in the usual manner and the product reacted with lithium acetylide in the following manner. Lithium acetylide as the ethylenediamine complex[26] (276 mg, 2.8 mmol) was added to dry dimethyl sulfoxide (10 ml) under nitrogen and 7-bromoheptanol tetrahydropyranyl ether (750 mg, 2.7 mmol) in DMSO (2.0 ml) was added. The mixture was stirred for 4 hr at 30° and concentrated HCl (10 ml) was added slowly followed by water (30 ml). The ether extract of the aqueous solution was washed with water (2 × 20 ml) and dried (Na_2SO_4). Vpc analysis of the residual oil after removal of the ether indicated that the desired non-8-yn-1-ol tetrahydropyranyl ether was obtained in higher than 90% yield. Homogeneous catalytic reduction using tris(triphenylphosphine)rhodium chloride and deuterium gas followed by work-up as described above gave 1-nonanol-*8,8,9,9-d*$_4$.

Nonanol-*9,9,9-d*$_3$. Reduction of 16-bromo-9-hexadecenoic acid[21] using LAD in anhydrous ether gave 9-hexadecenol-*1,1-d*$_2$ in good yield. Treatment with *p*-toluenesulfonyl chloride in anhydrous pyridine at 0° overnight yielded the desired tosylate derivative which was reduced with LAD in ether to give 9-hexadecene-*1,1,1-d*$_3$. Oxidation of the deuterated olefin using chromium trioxide and acetic acid followed by reduction of the acidic product with LAH in ether gave a mixture of alcohols. Preparative vpc on a 5 ft 20% SE-30 column gave good separation of the alcohol mixture and allowed purification of nonanol-*9,9,9-d*$_3$ which was the major component of the mixture.

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