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SUBSTITUENT EFFECTS AND REARRANGEMENTS IN THE ELECTRON-IMPACT SPECTRA OF LONG CHAIN ESTERS OF *m*- AND *p*-METHOXYBENZOIC ACID

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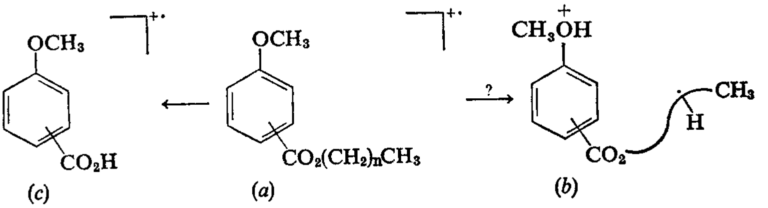
Abstract—The mass spectra of eighteen *n*-alkyl esters of *p*- and *m*-methoxybenzoic acid are examined. Few differences exist in the spectra of the corresponding *para* and *meta* isomers. We describe a new rearrangement, loss of ·OH from the molecular ion, which is observed only in the *para* substituted isomers. Oxygen-18 labeling indicates that the oxygen lost in the $[M - OH]^+$ ion derives from the carbonyl. No indication is found of hydrogen abstraction from the chain by the methoxy group competing with the benzoate ester rearrangement. We find a substituent effect on that rearrangement, with electron-donating groups decreasing the values of $[ArCO_2H_2]^+/[ArCO_2H]^{+\cdot}$ ion ratios. This ratio increases as the ester chain length increases.

THE MASS spectra of bifunctional molecules are interesting because the molecular ion is forced to choose among pathways in which the functional groups react independently and those in which they interact prior to fragmentation. In molecules containing disubstituted aromatic rings one substituent may perturb the partitioning of ions among reactions centered at the other functional group. Such a perturbation is called a substituent effect.[1]

We have been interested in the mass spectra of molecules which, upon electron-impact, are offered a choice of hydrogen abstraction at one functional group from a hydrocarbon chain attached to a second functional group. When hydrogen abstraction competes successfully with other rearrangement processes,[2–4] one can learn a great deal about the conformational behavior of the hydrocarbon chain in the mass spectrometer.[4,5]

We have studied previously the mass spectra of long chain ethers of *m*- and *p*-hydroxymethylbenzoate.[4] In those molecules, hydrogen abstraction by the carboxyl group competes favorably with a phenyl ether rearrangement and gives rise to a new ion in the mass spectrum when the chain is of sufficient length to reach the carboxyl group.[2,3] Since hydrogen abstraction in the mass spectra of ethers is well documented,[6] we sought a system in which hydrogen abstraction by an ether oxygen might occur, but not via 4-, 5- or 6- center transition states. The invert isomers of our previous study[4] appealed to us. Here hydrogen abstraction from the chain by the methoxy group must compete with a benzoate ester rearrangement.[4] In this paper we examine the mass spectra of eighteen *n*-alkyl esters of *p*- and *m*-methoxybenzoic acid.



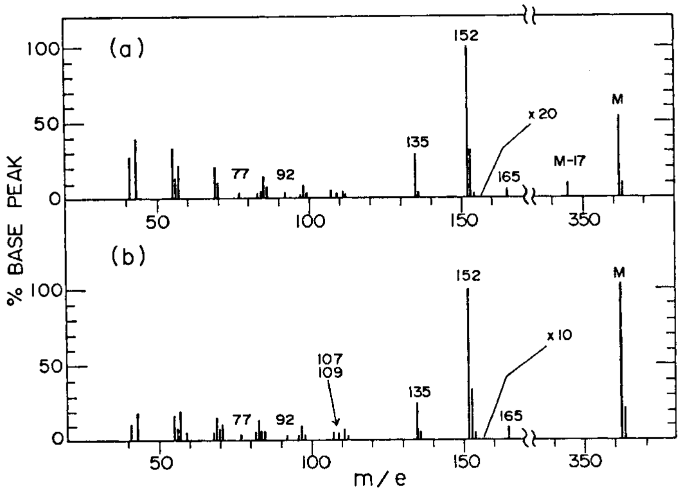


FIG. 1. 70 eV electron-impact spectrum of (a) *p*- and (b) *m*-methoxy-O-pentadecyl-benzoate. Source 200 °C, probe 120 °C.

RESULTS AND DISCUSSION

The 70 eV mass spectra of the pentadecyl esters of *p*- and *m*-methoxybenzoic acid are shown in Fig. 1. The spectra are remarkably similar. The most obvious differences are those of the molecular ion intensities and the presence of a small peak at *m/e* 345 ($[M - 17]^+$) in the *para* isomer. Figure 2 shows the variation in $[M]^{+\cdot}/152$ as a function of chain length. While $[M]^{+\cdot}/152$ is always larger for the *meta* isomers than for the *para* isomers, the scatter and lack of obvious trends makes the molecular ion intensity useless for structure identification.

In some of the low resolution spectra, metastable peaks for $[M]^{+\cdot} \rightarrow 152$ and $[M]^{+\cdot} \rightarrow 153$ transitions are clearly resolved. In most spectra, however, we observe only a broad metastable encompassing both reactions. In one metastable defocusing[8]

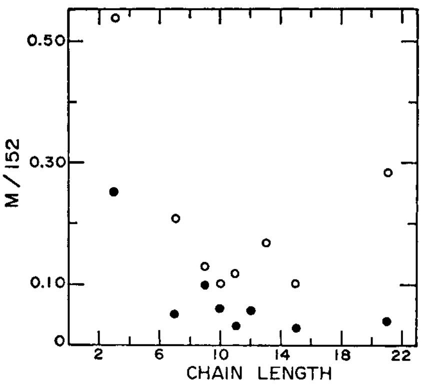


FIG. 2. Comparison of relative molecular ion intensities in *n*-alkyl esters of *meta* (○) and *para* (●) methoxybenzoic acid; as a function of chain length.

TABLE 1. IONS AND THEIR PRECURSORS

Mass	Composition	Fractional mass	Precursor ions
165	$C_9H_9O_3$	0·0552[a] (0·0552)[b]	
153	$C_8H_9O_3$	0·0540[c] (0·0552)	M[d]
152	$C_8H_8O_2$	0·0473 (0·0473)	M[d]
136	$^{13}CC_7H_7O_2$	0·0485 (0·0480)	M, 153[e]
135	$C_8H_7O_2$	0·0447 (0·0446)	M, 152 and/or 153[d,e]
109	C_7H_9O	0·0653 (0·0653)	
107	C_7H_7O	0·0494 (0·0496)	135[d]
92	C_6H_4O	0·0262 (0·0262)	
77	C_6H_5	0·0391 (0·0391)	107[a]
[M − 17]	$C_{11}H_{13}O_2$[a]	177·0915[a] (0·0915)	
[M − 17]	$C_{20}H_{31}O_2$	303·2319 (0·2324)	

[a] *Para* 3.

[b] Calculated exact mass.

[c] *Para*-12, unless otherwise noted.

[d] Appropriate metastable peaks appear in the spectra of all esters.

[e] Measured by metastable defocusing.[8]

experiment (*para*-12)† we determined that m^* for (152 and/or 153) → 135 is 580 times as intense as that for $[M]^{+\cdot} \rightarrow 135$.

Exact mass measurements and precursor ions inferred from metastable ions are collected in Table 1.

All of the *para* esters (except the ethyl ester) show ions at $[M - 17]^+$. In each case, $[M - 17]^+/152 \approx 0{\cdot}5\%$. Exact mass measurements (Table 1) indicate that this ion results from loss of ·OH from the molecular ion. A small ion at $[M - 17]^+$ can be seen in the published mass spectrum of butylbenzoate.[9] We never observed such an ion in the mass spectra of the *meta* isomers, although we could have detected the ion at one tenth of the relative intensity of those in the *para* substituted esters. These ions serve as the distinguishing feature between the *m*-methoxy- and *p*-methoxybenzoate esters.

The reaction sequences depicted in Scheme 1 are consistent with results reported in this study. Asterisks above the arrows indicate that the requisite metastable peaks were observed. Keeping in mind the limitations of such reaction sequences, we use Scheme 1 as a convenient framework for interpreting our observations.

Substituent effects

Long chain esters of *m*- and *p*-methoxybenzoic acid undergo benzoate ester rearrangement[7] upon electron-impact. Both ions of mass $[ArCO_2H]^{+\cdot}$ and $[ArCO_2H_2]^+$ are formed. As in the unsubstituted benzoate esters,[2a] the ratio $[ArCO_2H_2]^+/[ArCO_2H]^{+\cdot}$ increases with increase in chain length. These data are presented in Fig. 3b.

The ratio *m*/*e* 153/152 is sensitive to the location of the methoxy group. This ratio increases linearly for the *meta* substituted esters, attaining a value of 0·37, after correction for ^{13}C natural abundance, for the eicosanyl ester. In the *para* isomers, there appears to be a marked increase in this ratio between 3 and 7 carbon esters, followed

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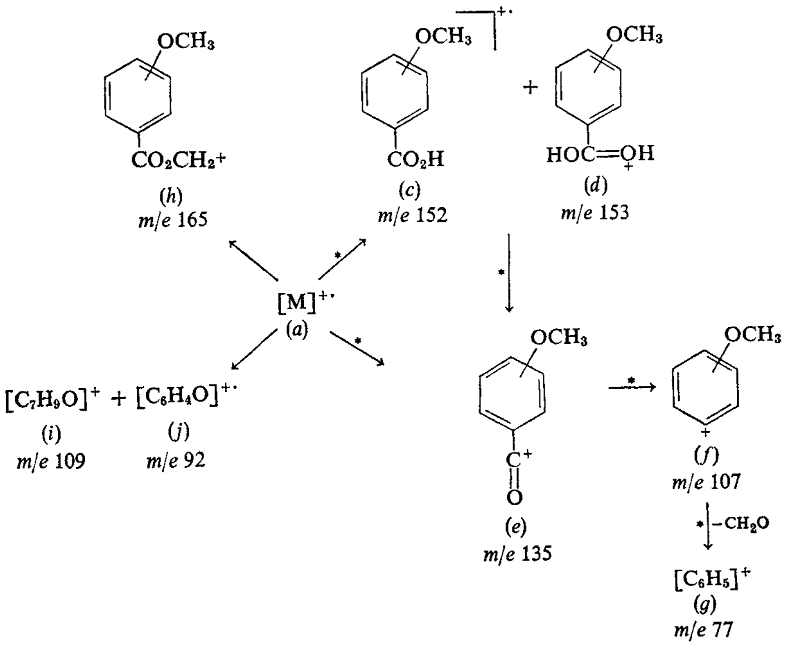
† For convenience, we have abbreviated the names of the long chain esters. *Para*-12 refers to the dodecyl ester of *p*-methoxybenzoic acid.



SCHEME 1

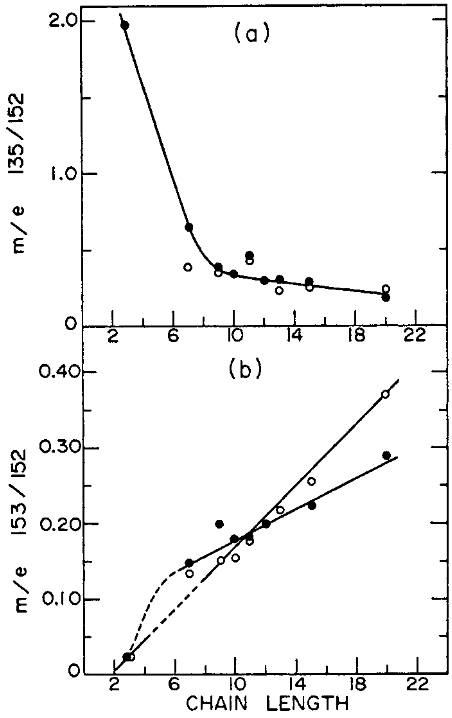


FIG. 3. Chain length dependence of ion ratios in the 70 eV mass spectra of *n*-alkyl esters of *meta* (○) and *para* (●) methoxybenzoic acid.

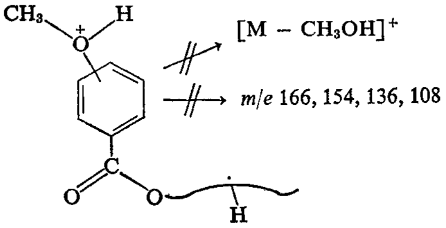
by a more gradual increase in the *m/e* 153/152 ratio. The increase is less pronounced than in the *meta* isomers. A value of 0·29 is attained for the 20 carbon ester.

In the unsubstituted benzoate esters, the ratio $[ArCO_2H_2]^+/[ArCO_2H]^{+\cdot}$ is greater than 1. Values of 5·1, 9·6 and 13·8 were reported by Meyerson, for the 6, 12 and 18 carbon esters of benzoic acid.[2a] In trimellitic anhydride long chain esters, the $[ArCO_2H]^{+\cdot}$ peak at *m/e* 192 is very small and the $[ArCO_2H_2]^+$ peak at *m/e* 193 is the base peak in the mass spectrum.[2,3] These results imply a pronounced substituent effect on the benzoate ester rearrangement, such that electron-donating groups favor formation of the $[ArCO_2H]^{+\cdot}$ ion and electron-withdrawing groups favor formation of $[ArCO_2H_2]^+$.

The *m/e* 135/152 ratio decreases with chain length (Fig. 3a). This is consistent with the concomitant increase in the number of vibrational modes in the molecule.

Hydrogen abstraction by the methoxy group?

The methoxy group, either *meta* or *para*, is not observed to compete by hydrogen abstraction with the benzoate ester rearrangement. We have searched for evidence for hydrogen abstraction by the methoxy group from the chain in the following way. We looked for the appearance of new ions in the mass spectra of molecules with chain lengths sufficient to reach the CH_3O group. In principle, one might observe a new reaction pathway, leading for example to $[M - CH_3OH]^{+\cdot}$.[2,3] Alternatively, one might observe an ion at one higher mass unit than one resulting from a prominent rearrangement of a short chain analog.[2–4] Here we looked in the mass spectra of the long chain esters at the ion ratios *m/e* 166/165, 154/153, 136/135 and 108/107. After correcting the intensities for the presence of heavy isotopes, we found no increase in these ratios of over the corrected ratios in the ethyl and propyl esters. Ion intensity at *m/e* 153 is, of course, equivocal, since it increases with chain length. We have no way of determining the locus of the second hydrogen.



The ion at *m/e* 109 might conceivably arise from hydrogen abstraction by the methoxy group. We have no evidence about the structure of this ion. It does carry very little of the total ion current.

Oxygen-18 labeling

In order to gain insight into the mechanism of loss of OH from the molecular ion of the *para* substituted esters, we prepared *n*-propyl 4-methoxybenzoate, carbonyl ^{18}O(I). Precise ion ratio measurements of the molecular ions using a Vacuumetrics ratiometer indicated 5·51 ± 0·10% ^{18}O enrichment over natural abundance. We observed an ion ratio of 0·086 for *m/e* 179/177, which, if corrected only for natural

^{18}O abundance, would suggest that ^{18}O was retained in the rearrangement (see Table 2). The unlabeled material, however, showed a similar ratio of *m/e* 179/177.

Because the ion current carried by the ion at *m/e* 179 was so small (*c.* 0·02% of the base peak), we felt that it would be useful to resolve the ions contributing to the peak at *m/e* 179. With a resolution of 10 000 on the MS-902, we were able to resolve peaks due to $C_{13}H_{23}$, $C_{10}H_{11}O_3$ and $C_{11}H_{13}O^{18}O$. The ^{18}O-containing peak showed the same intensity relative to the *m/e* 177 peak for both the labeled and unlabeled materials. Using peak heights as a measure of relative ion abundance, we could calculate that, within experimental uncertainty, the $C_{11}H_{13}O^{18}O$ ion was of the intensity expected from natural ^{18}O abundance. Thus, in the rearrangement $[M]^{+\cdot} \rightarrow [M - OH]^+$ at least 90% of the ^{18}O enrichment is lost.

TABLE 2. CARBONYL ^{18}O-ENRICHED *n*-PROPYL *p*-METHOXYBENZOATE

Ions	Measured intensity ratio[a]	Calculated[b]	^{18}O Retained[c]
196/194	0·0679	0·0128	5·51%
195/194	0·1216	0·1223	—
179/177	0·0855	0·0108	7·5[d]
179·0958/177	0·0103[e]	0·0108	0[e]
178/177	0·1272	0·1217	—
154/152	0·0663	0·0095	5·68
137/135	0·0622	0·0074	5·48

Mass	Composition	Fractional mass	Relative intensity
196	$C_{11}H_{14}O_2{}^{18}O$	0·0985 (0·0985)[f]	—
194	$C_{11}H_{14}O_3$	0·0943 (0·0943)	—
154	$C_8H_8O_2{}^{18}O$	0·0516 (0·0516)	—
179	$C_{13}H_{23}$	0·1799 (0·1799)	0·21
179	$C_{11}H_{13}O^{18}O$	0·0958 (0·0959)	0·12
179	$C_{10}H_{11}O_3$	0·0709 (0·0708)	0·67

[a] Measured by peak matching using a Vacuumetrics ratiometer.

[b] Expected natural abundance heavy isotope contribution from ions of lower mass.

[c] Corrected for natural abundance ^{18}O.

[d] Not properly corrected for background ion intensity at *m/e* 179.

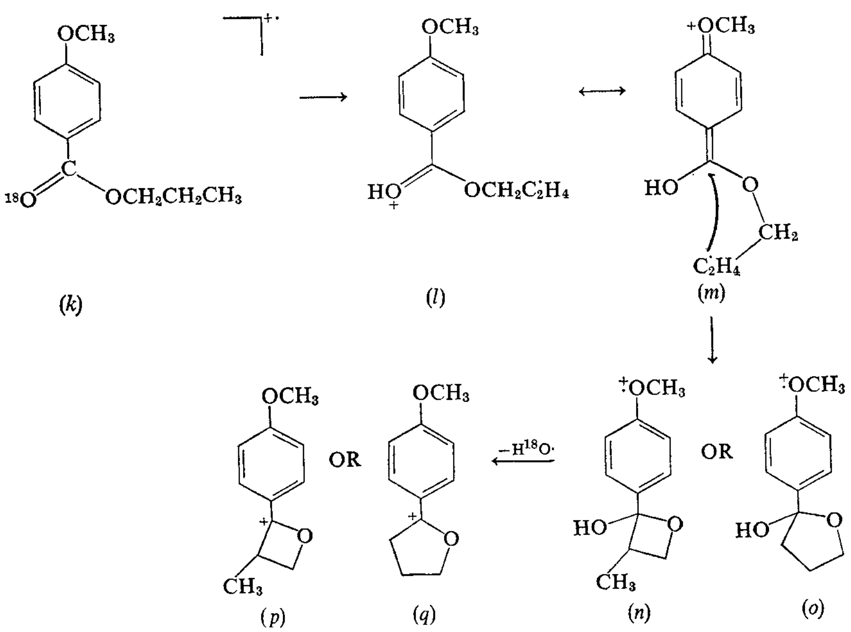
[e] Ion intensity due to $C_{11}H_{13}O^{18}O$, which represents 12·1% of the ion intensity at *m/e* 179. Here 0·0103 = 0·121 × 0·0855.

[f] Calculated.

While we can envision other mechanisms, that depicted in Scheme 2 provides a rationalization for preferential loss of ·OH in the *p*-methoxybenzoate esters.

First, we visualize cyclization of *m* to *n* or *o*. In this way, the odd electron and the charge may be delocalized onto the methoxy group. This delocalization is not possible when the methoxy group is *meta* to the carboxylate. Second, we note that loss of ·OH leads to a more resonance-stablized cation *p*/*q* if the methoxy group is *para* than if it is *meta*. Both factors enhance loss of ·OH from the molecular ion in the *para* isomers. Indeed, one can argue that a *meta* methoxy group can retard both cyclization and loss of ·OH from *n*/*o* by its inductive effect. Deuterium labeling studies are needed to establish the site of the hydrogen lost as ·OH.

The mass spectrum of the ^{18}O labeled analog (I) provides insights into other aspects of the chemistry of these esters upon electron-impact. We note that the intense



Scheme 2

ions at *m*/*e* 152 and 135, common to all of these esters, are here accompanied by enhanced [P + 2] ions at *m*/*e* 154 and 137. The low resolution spectrum run on the CEC-490 mass spectrometer indicates that the carbonyl oxygen is retained in the *m*/*e* 165 ion, but eliminated in the rearrangements to ions at *m*/*e* 107 and 92. These results are in accord with the reactions postulated in Scheme 1.

The magnitude of the *m*/*e* 137/135 ion ratio is surprisingly high. After correction for naturally abundant heavy isotopes, this ion ratio is indistinguishable in magnitude from the ^{18}O contribution to the molecular ion. This suggests that more than 95% of the ion intensity of ion *e* at *m*/*e* 135 in the 70 eV spectrum arises from α-cleavage in the molecular ion. A two-step process via McLafferty rearrangement to ions *c* and *d* would scramble the ^{18}O label. On a slower time scale, in the defocusing experiments (*vide supra*) the latter pathway is preferred by a factor of 580.

EXPERIMENTAL

Mass spectra were recorded on a CEC-490 mass spectrometer with the source kept at 220 °C and the probe temperature adjusted as necessary to maintain suitable sample pressure. The heated inlet system was employed for ethyl and propyl esters. Longer chain esters were introduced into the mass spectrometer via the solid sample probe. Ion intensity ratios were obtained from triplicate scans of the low resolution spectra.

Propyl and ethyl esters were prepared by Fischer esterification of the respective *meta* and *para* anisic acids, and were distilled. Longer chain esters were prepared by treatment of the sodium salt of the acid with the appropriate alkyl bromide in dimethylformamide at 130 °C. The example which follows is typical. Several of these esters have been characterized previously.[10] Major i.r. bands are those of the example below; n.m.r. positions are identical, with only the integration of the methylene envelope increasing as expected with chain length. Melting points of crystalline products (recrys, MeOH) are as follows: *meta*-18, 38 °C; *meta*-20, 42 °C; *para*-15, 40 °C; *para*-18, 42 °C; *para*-20, 48 °C. Mass spectra are reported in the text.

n-Pentadecyl 4-methoxybenzoate. In 1·2 ml of dimethylformamide in a 10 ml round bottom flask were mixed 0·44 g (1·5 mmol) of 1-bromopentadecane and 0·30 g (1·7 mmol) of sodium 4-methoxy benzoate. The flask was immersed for 1 h into an oil bath kept at 130 °C. The contents were stirred magnetically. After cooling to room temperature, the reaction mixture was treated with 50 ml petroleum ether and 20 ml water. These were separated, the organic layer was washed twice with 10 ml portions of aqueous sodium bicarbonate, dried over magnesium sulfate and filtered. The solvent was removed and the clear oil that remained was crystallized from methanol, yielding 0·38 g (70%) of a white crystal, m.p. 40 to 41 °C. I.r. (KBr, cm^{-1}): 1700(C=O), 1600, 1270, 1160. N.m.r. (CCl_4, TMS, δ): 7·90(d, $J = 9$, 2H); 6·80(d, $J = 9$, 2H); 4·21(t, $J = 7$, 2H); 3·86(s, 3H), 0·7 to 2·0(m, *c.* 30H).

n-Propyl 4-methoxybenzoate carbonyl ^{18}O. In a 25 ml round bottom flask containing a magnetic stirring bar, a gas inlet tube and a condenser topped with a drying tube filled with calcium chloride, was placed 0·47 g (3·53 mmol) of 4-methoxybenzonitrite (anisonitrile, Aldrich) in 2·5 ml *n*-propanol. HCl gas, dried by passing it through successive towers of sulfuric acid and calcium chloride, was bubbled through the solution for 5 min. The solution stood at room temperature for 4 h. After this time, the iminoester hydrochloride had precipitated. Labeled water (125 μl, 6·9 mmol, Miles Laboratories, estimated 12% enriched in ^{18}O) was added by syringe. The solution was heated to reflux while more HCl gas was passed through the apparatus. The reflux was continued for 12 h. When cool, 40 ml of hexane was added. The solution was filtered, concentrated and molecularly distilled at 160 °C (bath)/10 mm. Since the i.r. spectrum indicated the presence of anisic acid (2500 to 3500 cm^{-1}), the distilled product was taken up in 40 ml hexane, washed twice with aqueous sodium bicarbonate, dried with calcium chloride, concentrated and distilled. The final yield was 0·43 g of a clear oil, 63%.

I.r.(KBr, cm^{-1}): 2950, 1700(C=O), 1600, 1500, 1270, 1245, 1160, 1090, 770. N.m.r.(CCl_4, TMS, δ): 7·88(d, $J = 9$, 2H); 6·76(d, $J = 9$, 2H) aromatic; 4·16(t, $J = 7$, 2H)CH_2O; 3·77(S, 3H) CH_3O; 1·71(sextuplet, $J = 7$, 2H) CH_2—C; 0·96(t, J=7, 3H) CH_3—C (See text for ^{18}O enrichment).

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