The Mechanism of the Rearrangement of β-Acyloxyalkyl Radicals

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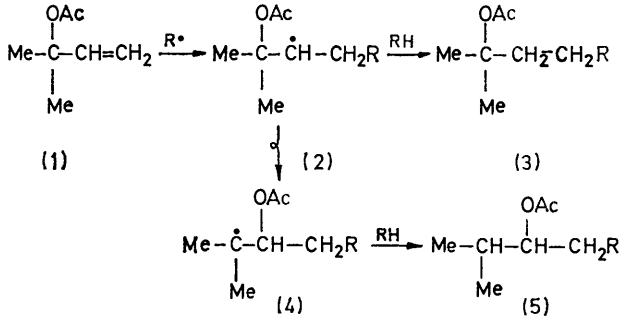
Determination of the distribution of products from decarbonylation of 2-formyl-1,1-dimethylethyl heptanoate (6d) and other esters of 3-hydroxy-3-methylbutanal, and from the reaction of tributylstannane with 2-bromo-1,1-dimethylethyl benzoate (11b), 2-bromo-1-methyl-1-phenylethyl acetate (11c), and similar bromo-esters, has enabled the rates of rearrangement of some β-acyloxyalkyl radicals to be evaluated. The kinetic data together with the results of reactions using ^{18}O labelled substrates indicate that 1,2-acyloxy-transfer proceeds *via* a concerted mechanism involving a five-membered cyclic transition state. The rate of rearrangement of the 2-acetoxy-2-phenylpropyl radical (12c) by 1,2-aryl migration has also been determined.

SUITABLY constituted β-acyloxyalkyl radicals rearrange by 1,2-migration of the acyloxy-group.[1-6] The mechanism of this intramolecular transfer is of especial interest because it appears to have no direct intermolecular analogue although acyloxy-transfer from metal to carbon may occur in some lead tetra-acetate oxidations [7] and copper catalysed free-radical reactions.[8]

The rearrangement of β-acyloxyalkyl radicals was first reported by Surzur and Teissier [1,2] who observed that radical addition of ethyl cyanoacetate (RH) to the acetate (1) of 2-methylbut-3-en-2-ol affords a mixture of the two acetates (3) and (5). As expected according to the suggested mechanism (Scheme 1) the yield of rearranged product (5) varied with the nature of the addend; poor hydrogen-atom donors give proportionately high yields of (5).

Tanner and Law [3] also observed β-acetoxyalkyl radical rearrangement when they studied free-radical initiated decarbonylation of 3-acetoxy-3-methylbutanal (6a) in benzene or chlorobenzene. The products included isobutyl acetate (10a) as well as the expected t-butyl ester (8a). In accord with the suggested pathways (Scheme 2) the yield of the rearranged product (10a) as compared with its unrearranged isomer (8a) increased with decreasing aldehyde concentration.



SCHEME 1

According to the mechanism given in Scheme 2 the ratio of the yields of the products (8a) and (10a) should

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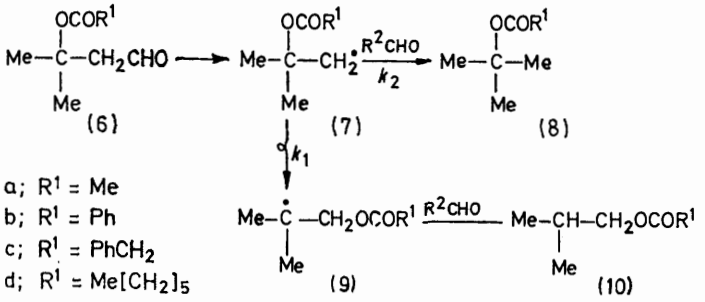
[1] J.-M. Surzur and P. Teissier. *Compt. rend.*, 1967, **264***C*, 1981.
[2] J.-M. Surzur and P. Teissier, *Bull. Soc. chim. France*, 1970, 3060.
[3] D. D. Tanner and F. C. P. Law, *J. Amer. Chem. Soc.*, 1969, **91**, 7535.
[4] S. Julia and R. Lorne, *Compt. rend.*, 1971, **273C**, 174.
[5] A. L. J. Beckwith and P. K. Tindal, *Austral. J. Chem.*, 1971, **24**, 2099.
[6] S. N. Lewis, J. J. Miller, and S. Winstein, *J. Org. Chem.*, 1972, **37**, 1478.
[7] J. K. Kochi, R. A. Sheldon, and S. S. Lande, *Tetrahedron*, 1969, **25**, 1197.
[8] D. J. Rawlinson and G. Sosnovsky, *Synthesis*, 1972, 1 and references cited therein.

be related to the concentration of aldehyde R^2CHO [equation (1)].

$$(8a)\%/(10a)\% = k_2 \cdot [R^2CHO]/k_1 \qquad (1)$$

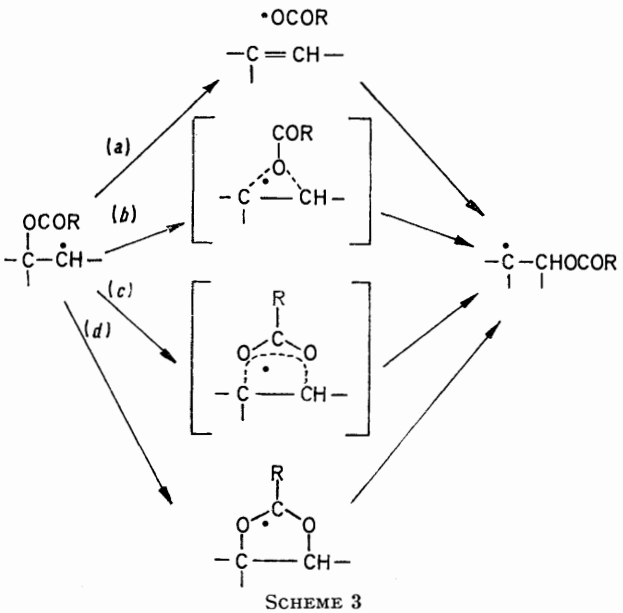
The data of Tanner and Law [3] accord qualitatively with this relationship and allow the estimation of k_1, the rate constant for rearrangement, as approximately



SCHEME 2

3×10^3 s^{-1} at 75°.[5] Consideration of the results reported by Suzur and Teissier leads to a somewhat similar value for k_1.[5]

Four distinct mechanistic pathways (Scheme 3) may be considered for the intramolecular acyloxy-group transfer [*e.g.* (7) ⟶ (9)]. One of them (*a*) involves an



SCHEME 3

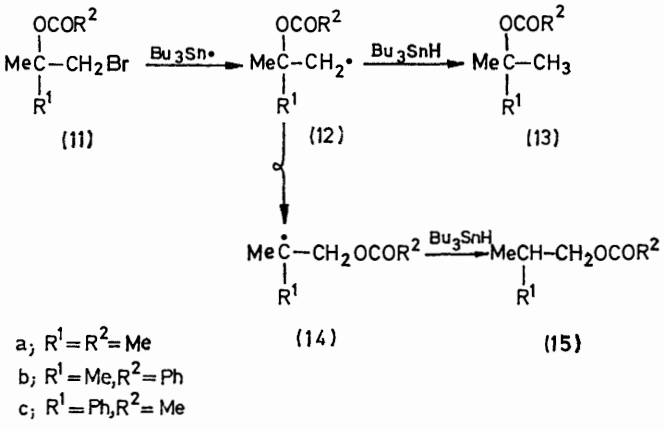
addition–elimination mechanism, two (*b*) and (*c*) envisage concerted bond-breaking and bond-making and proceed through three- and five-membered cyclic transition states respectively, and the last (*d*) involves a two-step mechanism proceeding through an intermediate 1.3-dioxolanyl radical.

None of the existing evidence provides conclusive proof for the validity of any one of these mechanisms. However, the results of e.s.r. experiments have indicated that route (*d*) is unlikely,[5] and a similar conclusion with respect to (*a*) has been reached on the basis of product studies.[3] We sought to distinguish unambiguously between the four mechanisms by the use of kinetic methods and isotopically labelled substrates.

It was considered desirable to use the same systems for both kinetic and labelling studies. To be suitable for our purposes the systems chosen must (i) afford products which could be identified and accurately estimated by g.l.c., (ii) involve steps for which mechanisms and rate constants are known, (iii) afford rearranged products in yields sufficient for isotopic analysis, and (iv) employ starting materials which could be conveniently and specifically labelled with ^{18}O.

Preliminary studies were carried out on systems similar to those investigated by Tanner and Law.[3] Decarbonylation of 3-acetoxy-3-methylbutanal (6a) was not suitable because of the volatility of the products, and therefore exploratory work was focused on the same reaction with higher esters of 3-hydroxy-3-methylbutanal. However, even the heptanoate (6d), which proved to be the best of the compounds investigated, gave poor overall yields of decarbonylated products, and although the kinetic data were acceptable, this system was unsuitable for labelling studies.

Further experiments demonstrated that the reaction of tributylstannane with β-bromoalkyl esters met our needs. The expected reaction pathways [9,10] are shown in Scheme 4.



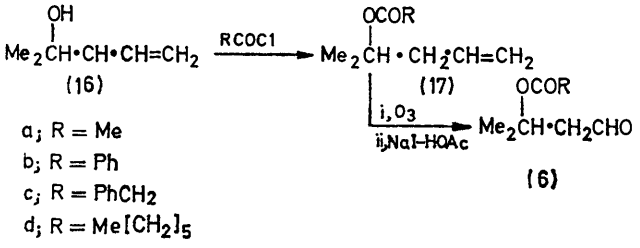
SCHEME 4

[9] H. Kuivila, *Accounts Chem. Res.*, 1968, **1**, 299.
[10] D. J. Carlsson and K. U. Ingold, *J. Amer. Chem. Soc.*, 1968 **90**, 7047.

It was found that suitable starting materials (11b and c) specifically labelled with ^{18}O could be readily synthesized, and when reduced under conditions of low stannane concentration, gave amounts of rearranged products adequate for isotopic analysis.

METHODS AND RESULTS

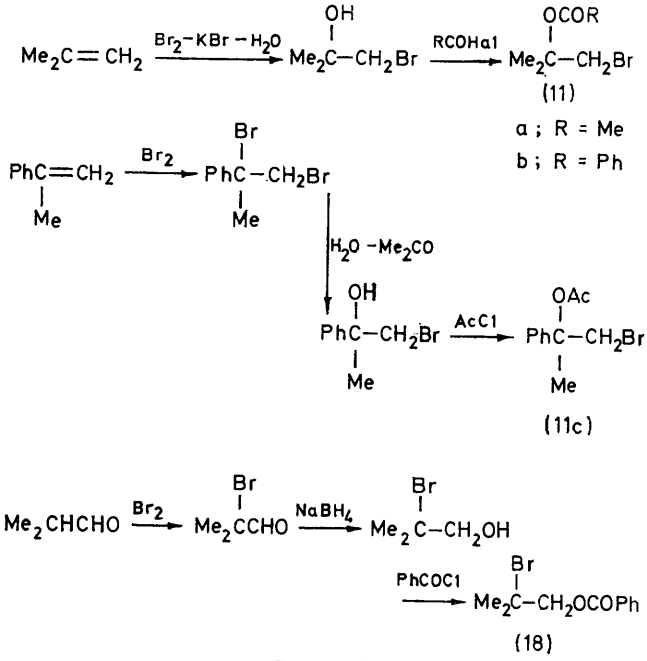
Kinetic Studies.—The benzoate (6b), phenylacetate (6c), and heptanoate (6d) of 3-hydroxy-3-methylbutanal were prepared by ozonolysis of the appropriate unsaturated esters (17b—d). The purification of each of them was made difficult by their propensity to undergo elimination of carboxylic acid to form β-methylcrotonaldehyde. This tendency was most pronounced in the benzoate (6b) which rapidly lost benzoic acid even at room temperature.



Decarbonylation of the aldehydes (6b—d) was achieved by heating degassed benzene solutions of each of them with suitable free-radical initiators in sealed tubes. G.l.c. analysis of the mixtures (Table 1) showed that the yields of decarbonylated products from the benzoate (6b) and the phenylacetate (6c) were too low to be used for kinetic analysis.

The heptanoate (6d) gave somewhat better results. When heated with 0·1 mol. equiv. of benzoyl peroxide it afforded combined yields of isobutyl and t-butyl heptanoate of up to 20%, and a further improvement in yield was effected by using 1 mol. equiv. of initiator. The results, which were used for the determination of rate constants, are recorded in Table 2. Unfortunately, the mean values of aldehyde concentration are subject to significant error since they are based on n.m.r. determination of residual aldehyde; g.l.c. could not be used because the aldehyde decomposed on the column.

The bromo-esters (11a—c) and (18) required as precursors for the generation of β-acyloxyalkyl radicals by reduction with tributylstannane were prepared by the methods outlined in Scheme 5.



SCHEME 5

An exploratory experiment was conducted by heating the bromo-acetate (11a) with tributylstannane and azobisisobutyronitrile (AIBN) in degassed t-butylbenzene as solvent at 70°. Only t-butyl acetate was formed in substantial yield, and the amounts of the isobutyl ester

TABLE 1

Yields of products from decarbonylation of $RCO_2CMe_2CH_2CHO$

R	[Aldehyde] (M)	Solvent	Initiator *	Temp. (°C)	Time (h)	Yields of products (%) RCO_2CMe_3	Yields of products (%) $RCO_2CH_2CHMe_2$
Ph	0·199	PhH	$(PhCO_2)_2$	75	72	0·30	1·17
$PhCH_2$	0·196	PhH	$(PhCO_2)_2$	75	68	3·35	1·34
$PhCH_2$	0·205	PhCl	$(PhCO_2)_2$	100	84	2·30	0·93
$PhCH_2$	0·202	PhH	$PhCO_2OBu^t$	75	72	2·36	0·56
$PhCH_2$	0·206	PhH	AIBN †	75	72	1·80	0·75
$PhCH_2$	0·824	PhH	$(PhCO_2)_2$	75	72	3·88	0·93
$Me[CH_2]_5$	0·0775	PhH	$(PhCO_2)_2$	75	72	5·28	2·16
$Me[CH_2]_5$	0·0775	PhH	$(PhCO_2)_2$	75	192	5·54	2·11
$Me[CH_2]_5$	0·2144	PhH	$(PhCO_2)_2$	75	72	8·87	2·65
$Me[CH_2]_5$	0·7138	PhH	$(PhCO_2)_2$	75	72	17·11	2·34
$Me[CH_2]_5$	0·7138	PhH	$(PhCO_2)_2$	75	192	16·29	1·95

* Initiator concentration = 0·1 × [aldehyde]. † Azobisisobutyronitrile.

TABLE 2

Distribution of products from decarbonylation of $Me[CH_2]_5CO_2CMe_2CH_2CHO$ (6d) in benzene at 75° for 72 h *

[6d] (M) Initial	[6d] (M) Mean	Yields of products (%) (8d)	(10d)	(8d)/(10d)
0·079	0·058	10·3	4·14	2·50
0·162	0·106	16·1	5·00	3·22
0·327	0·186	23·8	5·70	4·18
0·703	0·368	28·1	4·64	6·05

* Benzoyl peroxide was used as initiator; $[(PhCO_2)_2] = [6d]$.

obtained were so small that labelling studies were deemed unlikely to succeed.

When equimolar amounts of tributylstannane and the bromo-benzoate (11b) were heated with AIBN in benzene at 70° for 24 h, six products were detected by g.l.c. Four of them were isolated by preparative g.l.c. and were identified as t-butyl benzoate, isobutyl benzoate, methylallyl benzoate (19), and tributyltin bromide. The two unidentified products were formed in very small amounts, and one of them clearly arose from the initiator. In this and other experiments conducted with different reactant concentrations the material balance was essentially quantitative. A similar experiment with the isomeric bromo-benzoate (18) afforded mainly isobutyl benzoate together with a small amount of t-butyl benzoate and traces of two unidentified compounds. Separate control experiments demonstrated that isobutyl and t-butyl benzoate are stable under the reaction conditions. No conversion of the bromo-benzoate (11b) into its isomer (18) occurred when it was heated in benzene for 64 h with AIBN or with AIBN and tributyltin chloride.

Of the products listed in Table 3, the isobutyl and t-butyl esters are expected on the basis of the pathways shown in

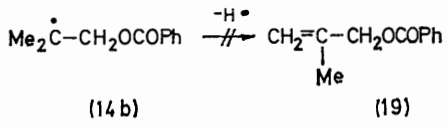
TABLE 3

Product distribution from reaction of β-bromoalkyl benzoates with tributylstannane in benzene at 70° for 24 h *

Compd.	10^2[Bu_3SnH] (M) †	Yields of products ‡ (13b)	(15b)	(19)	(13b)/(15b)
(11b)	0·38	95·6	3·14	1·25	30·4
(11b)	1·18	96·5	2·17	1·34	44·5
(11b)	2·51	96·5	1·79	1·73	53·9
(11b)	2·55	97·2	1·77	1·36	54·9
(11b)	5·52	97·2	1·16	1·72	87·6
(18)	1·12	1·13	98·8		0·0114

* AIBN was used as initiator; [AIBN] *ca.* 2×10^{-3}M. † Mean value. ‡ Mole per 100 mole of total products.

Scheme 4, but the mode of formation of methylallyl benzoate (19) from the bromo-compound (11b) has not been elucidated. The most obvious route, *viz.* hydrogen-atom abstraction from the rearranged radical (14b) appears unlikely because there is no clear relationships between the yields of the allyl ester (19) and isobutyl benzoate.



(14b) (19)

The bromo-acetate (11c) gave mainly cumyl acetate (13c) and 2-phenylpropyl acetate (15c) when heated with tributylstannane and AIBN in degassed benzene (see Table 4). The minor products included two unidentified compounds and 1-methyl-2-phenylethyl acetate (22) the formation of which is ascribed to rearrangement of the radical (12c) by aryl migration. Many similar rearrangements of substituted phenylethyl radicals have been reported.[11]

Labelling Studies.—The bromo-benzoate (11b) and the bromo-acetate (11c) were each prepared in isotopically labelled forms by the routes [12] illustrated. The molecular ion in the mass spectrum of the bromo-benzoate (23) was

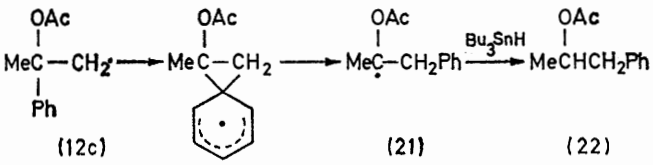
TABLE 4

Product distribution from reaction of 1-bromomethyl-1-phenylethyl acetate (11c) with tributylstannane in benzene at 70° for 74 h *

10^2[Bu_3SnH] (M) †	Yields of products ‡ (13c)	(15c)	(22)	(13c)/(15c)
0·358	38·9	57·2	3·9	0·68
1·15	58·6	38·3	3·1	1·53
2·00	68·5	28·7	2·8	2·39
2·61	78·1	20·4	1·5	3·83
4·15	82·8	17·2		4·84
6·63	88·1	11·9	<1	7·45

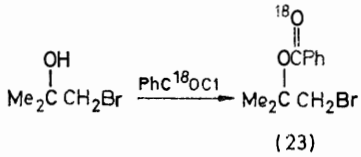
* AIBN was used as initiator; [AIBN] = 2×10^{-3}M. † Mean value. ‡ Mole per 100 mole of total products.

too weak to allow it to be used for the accurate determination of isotopic abundance, but suitable measurements could be made on the $M - Br$, $M - CH_2Br$, and *m/e* 123 ($PhCO_2\overset{+}{H}_2$) ions. The results, which were in close agreement, indicated the ^{18}O content to be 10·18 ± 0·1%.

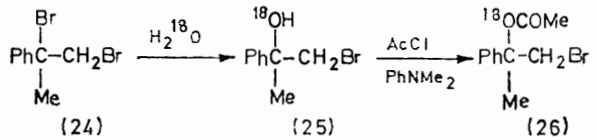


(12c) (21) (22)

Examination of the $M - Br$ and $M - CH_2Br$ peaks in the mass spectrum of the bromo-acetate (26) showed an ^{18}O content of 4·25 ± 1%. The fact that this is considerably lower than the isotopic content (10%) of the $H_2{}^{18}O$ used in the synthesis is thought to be due to the operation of an exchange reaction between water and the acetone used as solvent. It was calculated that complete exchange should give a product containing 4·21% of ^{18}O. Interestingly, the mass spectrum of the bromo-acetate (26) showed the ion $C_9H_{11}O^+$, which results from loss of Br and CH_2CO from the molecular ion, to contain 1·87% of ^{18}O.



(23)



(24) (25) (26)

Apparently the two oxygen atoms of the ester (26) become randomized during, or before, the fragmentation process, possibly by acetoxonium ion formation.[13]

Heating of the isotopically labelled bromo-benzoate (23) with tributylstannane in degassed benzene afforded a mixture of labelled t-butyl, isobutyl, and methylallyl

[11] R. Kh. Friedlina, *Adv. Free Radical Chem.*, 1965, **1**, 211.
[12] L. Ponticorvo and D. Rittenberg, *J. Amer. Chem. Soc.*, 1954, **76**, 1705.
[13] R. H. Shapiro and K. B. Tomer, *Org. Mass Spectrometry*, 1970, **3**, 333.

benzoate. The mixture was separated by preparative g.l.c. into its components, each of which was then reduced with lithium aluminium hydride in ether and the mixture of alcohols so produced subjected to combined g.l.c. and mass spectrometry. The benzyl alcohol formed from t-butyl benzoate was found to have an ^{18}O content of 9·24%; the selective labelling of the starting bromo-benzoate (23) at the acyl oxygen was thus confirmed.

The rearranged product (27) gave, upon reduction, a mixture of isobutyl and benzyl alcohol. The former was found to have an ^{18}O content of 9·76%, but the latter was essentially unlabelled. We conclude that the isobutyl benzoate formed from the bromo-benzoate (23) is specifically labelled at the alkyl oxygen. In similar fashion the methylallyl benzoate formed from the bromo-benzoate (23) was shown to be labelled at its alkyl oxygen.

$$Me_2CHCH_2{}^{18}OCOPh \xrightarrow{LiAlH_4} Me_2CHCH_2{}^{18}OH + PhCH_2OH$$
(27)

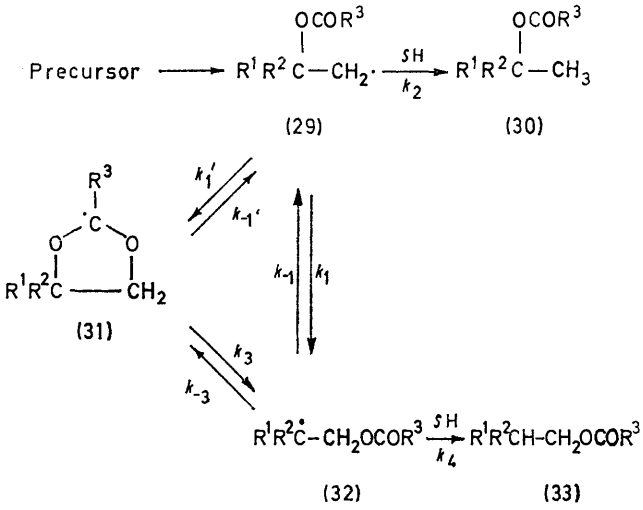
Some experimental difficulties were experienced when similar methods were applied to the product mixture obtained by reduction of the bromo-acetate (26) with tributylstannane. In particular, cumyl acetate decomposed on attempted preparative g.l.c. However, a sample of 2-phenylpropyl acetate (28) was satisfactorily collected. Upon reduction with lithium aluminium hydride it afforded 2-phenylpropanol containing $\leqslant$0·25% of ^{18}O. We conclude that the 2-phenylpropyl acetate (28) formed from the bromo-acetate (26) is specifically labelled at the acyl oxygen atom.

$$PhCHCH_2OC{}^{18}OMe \xrightarrow{LiAlH_4} PhCHCH_2OH + EtOH$$
(28)

DISCUSSION

We shall turn first to a consideration of the results of experiments with isotopically labelled compounds since these allow some of the suggested rearrangement mechanisms to be unambiguously precluded. Of the pathways represented in Scheme 3, that (*a*) involving a dissociation–recombination mechanism should lead from a specifically labelled starting material to a randomly labelled product, unless the recombination within the solvent cage occurs so rapidly that there is no rotation of the carboxylate radical with respect to the olefin, in which case this mechanism becomes essentially identical to one or other of the one-step pathways (*b*) and (*c*). Mechanism (*b*) involving a three-membered cyclic transition state should afford products having the same labelling pattern in the ester group as the starting material. However, the experimental results clearly indicate that the 1,2-acyloxy-shift is accompanied by an inversion in the labelling pattern; the acyl oxygen of the starting material becomes the alkyl oxygen of the rearranged product. Consequently, we conclude that the rearrangement of β-acyloxyalkyl radicals proceeds either by a concerted process (*c*) involving a five-membered cyclic transition state or a two-step route (*d*) *via* an intermediate 1,3-dioxolanyl radical.

The kinetic data give further information concerning the mechanism. Steady-state analysis of the reaction on the basis of a reversible one-step rearrangement process (Scheme 6, $k_1 \gg k_1'$, $k_{-1} \gg k_{-3}$) affords the rate equation (2) in which *S*H represents the hydrogen-atom donor (either aldehyde or tributylstannane in these experiments). A similar approach to the two-step rearrangement mechanism [Scheme 6, the rearrangement proceeding solely *via* (31)] gives the rate equation (3).



SCHEME 6

$$\frac{d[30]}{d[33]} = \frac{k_2[SH]}{k_1} + \frac{k_2 \cdot k_{-1}}{k_4 \cdot k_1} \quad (2)$$

$$\frac{d[30]}{d[33]} = \frac{k_2(k_{-1}' + k_3)[SH]}{k_1' \cdot k_3} + \frac{k_{-1}' \cdot k_2 \cdot k_{-3}}{k_1' \cdot k_3 \cdot k_4} + \frac{k_2 \cdot k_{-3}}{k_1' \cdot k_4} \quad (3)$$

According to either rate equation a plot of the ratio of percentage yields of unrearranged (30) and rearranged (33) products against the mean concentration of hydrogen-atom donor (aldehyde or stannane) should lie on a straight line having a positive intercept on the product axis. Figures 1—3 demonstrate that the data obtained from our experiments and from those of Tanner and Law,[3] * conform to the expected relationship, and thus allow both irreversible rearrangement, which should give a straight-line graph passing through the origin, and more complex mechanisms, which would show a non-linear dependence of product distribution on hydrogen-atom donor concentration, to be discounted. The reversibility of the rearrangement of the benzoyloxyalkyl radical (12b) was confirmed by the formation of t-butyl benzoate from reduction of the bromo-benzoate (18) with tributyl stannane.

Since k_2 at 70° may be reasonably assigned a value of

* The appropriate points in Figure 1 are subject to considerable uncertainty because the results quoted by Tanner and Law do not allow the product distribution to be calculated with precision.

$4{\cdot}6 \times 10^6$ l mol^{-1} s^{-1} for the reactions involving tributylstannane [10]* and $3{\cdot}6 \times 10^4$ l mol^{-1} s^{-1} for decarbonylation [14]† it is possible to obtain values for the rate

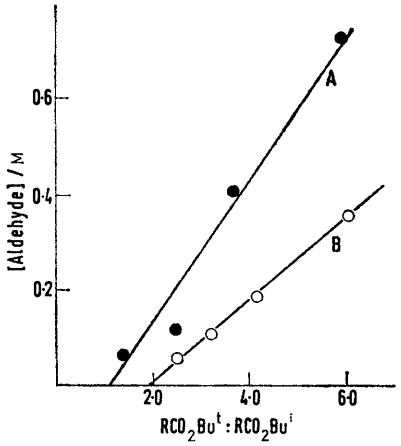


FIGURE 1 Dependence of product ratio on mean aldehyde concentration for free-radical decarbonylation of A, 3-acetoxy-3-methylbutanal (ref. 3); and B, 3-heptanoyloxy-3-butanal

constants of the rearrangement process from the gradients of the straight line graphs in Figures 1—3. Values of k_1, the rate constant for the forward rearrangement by a one-step mechanism, calculated directly from the gradients,‡ are given in Table 5.

The values of k_1', the rate constant for the cyclization reaction in the two-step mechanism, cannot be so readily obtained, for according to rate equation (3) the graph of product distribution against [SH] has, as gradient, a function of k_2, k_1', k_{-1}', and k_3 of which only k_2 is known. Nevertheless, approximate values of k_1'

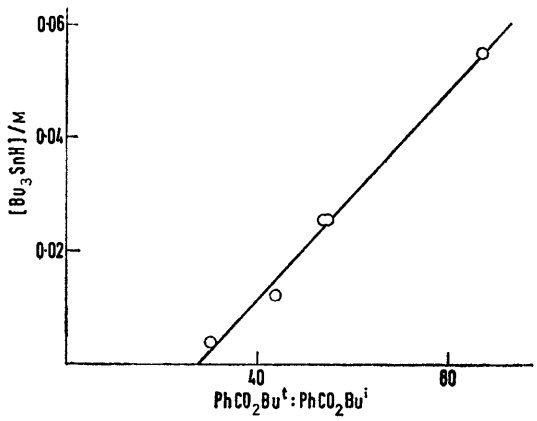


FIGURE 2 Dependence of product ratio on mean stannane concentration for reaction of tributylstannane with 1-bromomethyl-1-methylethyl benzoate (11b)

can be obtained, for it is widely accepted that radical β-scission proceeds in that direction which affords the most stable radical product, and hence it follows that $k_{-1}' < k_3$, since the tertiary radical (32) is expected to be considerably more stable than the primary radical (29). Consequently the value of $k_3 \cdot (k_{-1}' + k_3)^{-1}$ must lie between 0·5 and 1 and is probably very close to 1. The values of k_1' in the two step mechanism are therefore probably only very slightly larger than the values of the function $k_1' \cdot k_3(k_{-1}' + k_3)^{-1}$ given in Table 5.

Values of the rate constants for reverse steps in the rearrangement reaction should, in principle, be obtainable from the values of the intercepts in Figures 1—3. According to the rate equation (2) for the one-step rearrangement mechanism the intercept on the product distribution axis is given by $k_2 \cdot k_{-1}/k_4 \cdot k_1$. Available data indicate that $k_2/k_4 = ca.$ 1 for the decarbonylation reaction [14] and *ca.* 3·5 for reduction of bromo-compounds

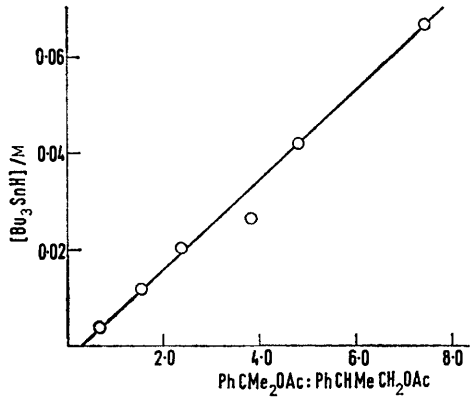


FIGURE 3 Dependence of product ratio on mean stannane concentration for reaction of tributylstannane with 1-bromomethyl-1-phenylethyl acetate (11c)

with tributylstannane.[10] It is expected that $k_{-1}/k_1 < 1$ since the tertiary radical (32) is more stable than the primary (29). The results for the rearrangement of the

TABLE 5

Rate constants for the reaction $MeCR^1(OCOR^2)CH_2^{\bullet} \longrightarrow MeC^{\bullet}R^1CH_2OCOR^2$

Temp. (°C)	R^1	R^2	k_1 or $\frac{k_1 \cdot k_3}{k_{-1}' + k_3}$ / s^{-1}
75	Me	Me	$6{\cdot}2 \times 10^3$
75	Me	$Me[CH_2]_5$	$3{\cdot}6 \times 10^3$
70	Me	Ph	$3{\cdot}9 \times 10^3$
70	Ph	Me	$4{\cdot}1 \times 10^4$

acetoxyalkyl radical (12c) accord with this prediction; k_{-1}/k_1 is calculated to be *ca.* 0·1. However, the value of

* Based on k_2 at 25° = 1×10^6 l mol^{-1} s^{-1} and assuming log A = 11 (see J. W. Wilt, S. N. Massie, and R. B. Dabek, *J. Org. Chem.*, 1970, **35**, 2803).

† Based on Arrhenius parameters for reaction of isobutyl radicals with isovaleraldehyde.

‡ Initial experiments using different samples of tributylstannane and bromobenzoate (11b) gave a straight-line plot having an intercept very similar to that in Figure 2 but with approximately twice the gradient. However, the results reported in Table 3 were reproducible with samples of reagents whose purity was rigorously tested. The cause of the discordance between the results of the first experiments and those obtained later has not yet been identified. Possibly the initial sample of the bromo-benzoate (11b) contained a small proportion of the isomer (18) formed by anti-Markownikov addition during the synthesis.

[14] J. A. Kerr and A. F. Trotman-Dickenson, *Progr. Reaction Kinetics*, 1961, **1**, 107.

k_{-1}/k_1, for rearrangement of the heptanoyloxyalkyl radical (7d), calculated to be *ca.* 1·8, is clearly too large whilst that for the rearrangement of the benzoyloxyalkyl radical (12b) is quite unacceptable, being $\geqslant 1$. Values of rate constants similarly estimated from the intercepts in Figures 1—3 on the basis of rate equation (3) are also clearly in error.

Our failure to obtain reasonable values for k_{-1}/k_1 for two of the reactions studied in detail indicates that there must be a route for the formation of unrearranged esters which is not accounted for in Schemes 2 and 4. Probably, other components of the reaction mixtures, besides aldehyde or stannane are able to act as hydrogen-atom donors. Support for this view, at least in the case of the decarbonylation reaction, was provided by the fact that large amounts of initiator were required, thus indicating that the reaction has a short chain length. Further work intended to identify the nature of possible hydrogen-atom donors in the stannane system is currently in progress.

A better estimate, although still approximate, of the importance of the reverse reaction, is provided by the results of the reduction of 2-bromo-2-methylpropyl benzoate (18) with tributylstannane (see Table 3). In terms of the one-step mechanism the ratio of yields of unrearranged and rearranged products is given by equation (4). Since $k_4/k_2 = 0{\cdot}29$ and the value of k_1 is

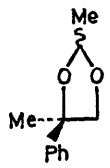
$$\frac{(15b)\%}{(13b)\%} = \frac{k_4[Bu_3SnH]}{k_{-1}} + \frac{k_4 \cdot k_1}{k_2 \cdot k_{-1}} \qquad (4)$$

known (Table 5) the value of the rate constant k_{-1} for the rearrangement of the radical (16c) can be calculated. The value obtained, $1{\cdot}8 \times 10^2$ s^{-1}, indicates that the rearrangement of the primary radical (12b) into its tertiary isomer (14b) is *ca.* 25 times faster than the reverse reaction.

Since both the one-step and the two-step mechanisms for the rearrangement require a linear dependence of product distribution on hydrogen-atom donor concentration, as exhibited by our data, it is not possible to distinguish between them on the basis of the experimentally determined kinetic form. However, the relative magnitudes of the rate constants, as deduced from our results, strongly indicate that the rearrangement proceeds *via* the one-step concerted mechanism. The driving force for the one-step process is the conversion of a primary radical into its more stable tertiary isomer, and we should expect, therefore, that the rate of the reaction would be sensitive to the nature of the substituent at the tertiary centre. This is what is observed; the rate constant, k_1, for the formation of the highly stabilized benzylic tertiary radical (14c) is much greater than those for the formation of the substituted t-butyl radicals (9a, b, and d). Although the substituent in the ester group should have some influence on the stability of the cyclic transition state for the one-step process we expect that such effects should be relatively small. The results show that the benzoyloxyalkyl radical (7b) has a rate constant for rearrangement similar in magnitude to those of the related acyloxyalkyl radicals (7a and d). Quite clearly the aryl substituent in (7b) exerts no special influence.

These results are incompatible with the two-step mechanism according to which the apparent rate constant for rearrangement is $k_1' \cdot k_3(k_{-1}' + k_3)^{-1}$. The dominant factor in this function is k_1', the rate constant for formation of the intermediate 1,3-dioxolanyl radical (31), and consequently the rate of rearrangement by the two-step process should be sensitive to changes in the constitution of the acyl group. On the other hand, the nature of the substituents on the tertiary radical centre should be relatively unimportant since, for the reasons outlined above, the value of $k_3(k_3 + k_{-1}')^{-1}$ should lie within the range 0·5—1. Consequently, it would be predicted on the basis of the two-step mechanism that the rearrangement proceeding from the benzoyloxyalkyl radical (7b) through a phenyl substituted dioxolanyl radical would be more ready than those for acyloxyalkyl radicals; in fact the reverse was observed.

The conclusion that 1,2-acyloxy-migration in β-acyloxyalkyl radicals involves a one-step mechanism proceeding *via* a five-membered cyclic transition state is supported by our inability to detect the two isomeric dioxolans (34) which should be formed by hydrogen-atom transfer from tributylstannane to the cyclic radical (31; R^1 = Ph, R^2 = R^3 = Me) envisaged as an intermediate in the two-step rearrangement of the benzoyloxyalkyl radical (7b). A separate experiment showed a mixture of the isomeric dioxolans (34) to be stable to tributylstannane and tributyltin chloride.

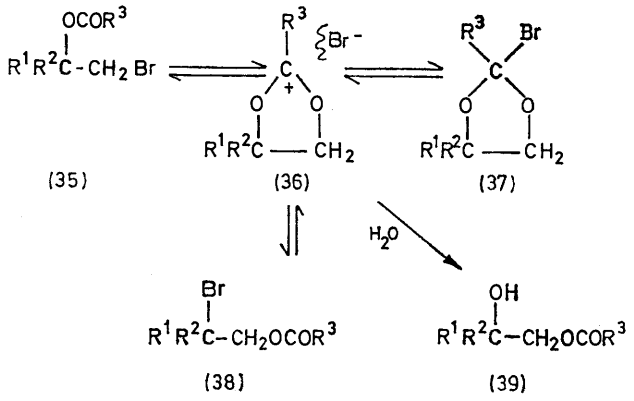


(34)

None of the previously published results discords with the hypothesis of a one-step rearrangement mechanism. Thus an examination of the e.s.r. spectra of β-acyloxyalkyl radicals and substituted 1,3-dioxolanyl radicals generated in a flow system gave results incompatible with the expected behaviour of reactants in a two-step process.[5] Also, it has been observed that the rearrangement of primary radicals to tertiary is much more rapid than the rearrangement of secondary radicals,[3] and that, in steroids, the acyloxy-group is on the same face of the product molecule as it was in the starting material.[4]

The mechanistic conclusions based on the results of both the labelling studies and the kinetic experiments would be invalid if the overall reaction pathways proposed for the reactions involving tributylstannane (Scheme 4) were incorrect. It was necessary, therefore, to consider the possibility that these reactions might involve prior formation of the bromodioxolan (37) or the related acyloxonium ion (36) which could then undergo

reduction by tributylstannane to afford the 1,3-dioxolanyl radical (31). However, the bromodioxolan (37) would be expected to exist in equilibrium with both of the bromo-esters (35) and (38).[15] In fact, when a control experiment was conducted in which the bromo-ester (35; $R^1 = R^2 = Me$, $R^3 = Ph$) was heated with tributyltin chloride in benzene for 24 h, the rearranged bromide (38; $R^1 = R^2 = Me$, $R^3 = Ph$) could not be



detected. Also, when 2 equiv. of silver acetate was added to a benzene solution of tributylstannane and the bromo-ester (11c) the major product (79%) was the hydroxy-acetate (39; $R^1 = R^3 = Me$, $R^2 = Ph$) formation of which is ascribed to the preferential reaction of intermediate acetoxonium ion with adventitious water. Only in one of the reactions recorded was hydroxy-acetate (39; $R^1 = R^3 = Me$, $R^2 = Ph$) detected and then only in negligible amounts. We conclude that the reaction of bromo-esters with tributylstannane does not involve intermediate formation of cyclic acyloxonium ions.

The recognition of a one-step concerted mechanism for the rearrangement of β-acyloxyalkyl radicals raises the questions of why the 2-substituted 1,3-dioxolanyl radical (31) does not lie on the reaction pathway and of the essential difference between such species and the suggested cyclic transition state. No clear answer can yet be given to the first question, but one answer to the second lies in the geometries of the two intermediates. The cyclic transition state would be expected to have the five annular atoms and the 2-substituent in the one plane, whereas e.s.r. studies have conclusively shown that the radical centres in 1,3-dioxolan-2-yl radicals (31) are distinctly pyramidal.[5,16]

Finally, it is noteworthy that the data for the reduction of the bromo-acetate (11c) with tributylstannane (Table 4) allow the rate constant for the aryl migration process (12c) ⟶ (21) to be estimated. A graphical method similar to that employed above for the rearrangement of β-acyloxyalkyl radicals indicates that the rate constant for conversion of the radical (12c) into the rearranged radical (21) is *ca.* 5×10^3 s^{-1} at 70°.

EXPERIMENTAL

^1H N.m.r. spectra were recorded for solutions in deuteriochloroform on a Varian T60 spectrometer. Mass spectra were determined on a Perkin-Elmer–Hitachi RMU-6D spectrometer operating at 70 eV unless stated otherwise, samples being introduced into the source region *via* a heated inlet system operating at 200—220°. Combined g.l.c.–mass spectrometry was achieved using a Perkin-Elmer F11 chromatograph coupled *via* a membrane separator to an A.E.I. MS30 spectrometer or, for the 1-bromomethyl-1-phenylethyl acetate system, a Pye chromatograph (series 104, model 24) coupled *via* a molecular separator to an A.E.I. MS12 spectrometer. M.p.s were taken on a Kofler micro-hotstage and are uncorrected. G.l.c. was conducted on a Perkin-Elmer 881 instrument using the following columns: (*a*) 9 ft × 1/8 in 10% Carbowax 20M glass column; (*b*) 10 ft × 1/8 in 10% Carbowax 20M metal column; (*c*) 7 ft × 1/8 in 10% SE52 column; (*d*) 10 ft × 1/8 in 5% Apiezon M column; and (*e*) 12 ft × 1/8 in 5% FFAP column. All stationary phases were coated on Chromosorb W. Preparative g.l.c. was carried out on an Aerograph Autoprep 705 instrument using either a 12 ft × 1/4 in 20% Carbowax 20M metal column or an 11 ft × 1/4 in 20% Carbowax 20M glass column.

Products were identified by comparison of their retention times with those of authentic samples on at least two columns. Confirmation of the assigned structures was achieved, in some cases, by combined g.l.c.–mass spectrometry and, in others, by comparison of the spectral characteristics of samples isolated by preparative g.l.c. with those of authentic materials. A hydrogen flame ionization detector gave a linear response and the relationship between peak areas of products and standard was determined from synthetic mixtures. Yields (mol %) were generally reproducible to within ±3% but the accuracy was less for products obtained in low yield. For ozonolysis an OREC O3C1 ozonator was employed. Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

Materials.—Benzene (AnalaR) and t-butylbenzene were distilled from sodium wire. [^{18}O]Water was Prochem reagent and contained 10·1% label. Isobutyl benzoate was B.D.H. laboratory reagent. t-Butyl acetate was available. Tri-n-butylstannane, prepared by the method of Kuivila and Beumel,[17] had b.p. 75—76·5° at 0·6 mmHg (lit.,[17] 68—74° at 0·3 mmHg) and was stored under nitrogen until required. Isobutyl acetate was prepared by refluxing isobutyl alcohol (23 ml), acetic acid (30 ml), and concentrated sulphuric acid (1 ml) for 5 h. The solution was poured into water, washed with water and saturated sodium bicarbonate solution, and dried ($MgSO_4$). Distillation gave isobutyl acetate (18·1 g, 62%), b.p. 115—116° (lit.,[18] 118°).

t-Butyl benzoate, prepared by the method of Norris and Rigby,[19] had b.p. 60·5—61° at 0·4 mmHg (lit.,[20] 91·3° at 7·5 mmHg). 2-Methylallyl benzoate was prepared similarly

[15] M. S. Newman and H. C. Chen, *J. Amer. Chem. Soc.*, 1972, **94**, 2149.
[16] A. J. Dobbs, B. C. Gilbert, and R. O. C. Norman, *J. Chem. Soc.* (*A*), 1971, 124.
[17] H. G. Kuivila and O. F. Beumel, *J. Amer. Chem. Soc.*, 1961, **83**, 1246.
[18] J. Heilbron and H. M. Bunbury, 'Dictionary of Organic Compounds,' 3rd edn., Eyre and Spottiswoode, London, 1953.
[19] J. F. Norris and G. W. Rigby, *J. Amer. Chem. Soc.*, 1932, **54**, 2088.
[20] M. L. Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626.

from 2-methylallyl alcohol (10 ml) and benzoyl chloride (10 ml) in pyridine (15 ml). Distillation gave the ester (12·6 g, 61%) as a liquid, b.p. 63—64° at 0·1 mmHg (lit.,[21] 66—67° at 0·12—0·15 mmHg), τ 1·82—2·09 (2H, m, *o*-ArH), 2·43—2·80 (3H, m, *m*- and *p*-ArH), 4·95 and 5·07 (2H, two br s, $=CH_2$), 5·30 (2H, s, CH_2), and 8·17 (3H, s, CH_3).

t-Butyl phenylacetate (49% yield) was obtained by the method of Kenyon *et al.*[22] and had b.p. 114—116° at 17 mmHg (lit.,[22] 108—110° at 15 mmHg), τ 2·72 (5H, s, ArH), 6·50 (2H, s, CH_2), and 8·58 (9H, s, CH_3). Isobutyl phenylacetate was prepared similarly in 83% yield and had b.p. 130—132° at 13 mmHg (lit.,[23] 247° at 760 mmHg), τ 2·70 (5H, s, ArH), 6·12 (2H, d, *J* 6·5 Hz, CH_2O), 6·37 (2H, s, CH_2CO), 8·08 (1H, nonet, $J = J' = 6·5$ Hz, CH), and 9·12 (6H, d, *J'* 6·5 Hz, CH_3). *t-Butyl heptanoate* (7·0 g, 35%) was obtained in the same way from t-butanol (8 g), *NN*-dimethylaniline (14 g), and heptanoyl chloride (12 g) in dry ether (35 ml) as a liquid, b.p. 91—92° at 13 mmHg, τ 7·78br (t, *J* 7 Hz, CH_2CO), 8·57 (s, t-butyl), and 8·07—8·93 (aliphatic envelope) (Found: C, 71·3; H, 11·7. $C_{11}H_{22}O_2$ requires C, 70·9; H, 11·9%). Isobutanol similarly gave isobutyl heptanoate (15·5 g, 78%), b.p. 105—107° at 13 mmHg (lit.,[24] 95—97° at 12 mmHg), τ 6·10 (d, *J* 6 Hz, CH_2O), 7·67br (t, *J'* 7 Hz, CH_2CO), 7·75—9·33 (aliphatic envelope), and 9·06 (d, *J''* 7 Hz, CH_3).

2-Methylpent-4-en-2-ol (16).—Allyl chloride (38 g) in dry ether (150 ml) was added over 1 h to magnesium turnings (15 g) under dry ether (100 ml), and the mixture was then refluxed for 30 min and cooled. Acetone (29 g) in dry ether (150 ml) was then added slowly. After refluxing the solution for 1 h and cooling, the magnesium complex was decomposed by pouring onto a concentrated hydrochloric acid–ice mixture. The ether layer was dried ($MgSO_4$), the solvent removed, and the product distilled to give 2-methylpent-4-en-2-ol (14 g, 28%) as a liquid, b.p. 116—119° (lit.,[25] 118—118·2°).

1,2-Dimethylbut-3-enyl Benzoate (17b).—2-Methylpent-4-en-2-ol (4·5 g), pyridine (7 ml), and benzoyl chloride (9·4 ml) were mixed, with cooling, and left overnight. The mixture was diluted with water, extracted with ether, the extracts washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Distillation of the dark red liquid obtained on removal of the solvent gave the *benzoate* (5·8 g, 63%) as a liquid, b.p. 67—69° at 0·5 mmHg, τ 1·97—2·20 (2H, m, *o*-ArH), 2·50—2·80 (3H, m, *m*- and *p*-ArH), 3·77—4·50 (1H, m, CH=), 4·80br and 5·02br (2H, d, $=CH_2$), 7·34br (2H, d, CH_2), and 8·45 (6H, s, CH_3) (Found: C, 76·2; H, 7·8. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%). The residue from distillation was largely benzoic anhydride.

1,2-Dimethylbut-3-enyl Phenylacetate (17c).—Freshly distilled phenylacetyl chloride (5 g) was added to 2-methylpent-4-en-2-ol (2·8 g) and *NN*-dimethylaniline (5 ml) in dry ether (15 ml) and the mixture was refluxed for 2 h. After cooling, the solution was poured into water, the ether layer separated, washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Evaporation gave a yellow liquid containing some phenylacetic anhydride which was removed by shaking for 10 min with 10% sodium hydroxide solution (25 ml). The ether extract from this mixture, after drying and evaporation of the solvent, gave, on distillation, the *phenylacetate* (2·4 g, 39%) as a liquid, b.p. 78—80° at 0·3 mmHg, τ 2·80 (5H, m, ArH), 3·97—4·67 (1H, m, =CH), 4·93 and 5·15 (2H, two m, $=CH_2$), 6·52 (2H, s, CH_2Ar), 7·55 (2H, d, *J* 7 Hz, CH_2), and 8·60 (6H, s, CH_3) (Found: C, 77·0; H, 8·3. $C_{14}H_{18}O_2$ requires C, 77·2; H, 8·2%).

1,2-Dimethylbut-3-enyl Heptanoate (17d).—The *heptanoate* (12·1 g, 47%) was obtained similarly from 2-methylpent-4-en-2-ol (12 g), *NN*-dimethylaniline (16 g), ether (42 ml), and heptanoyl chloride (14·2 g) as a liquid, b.p. 55—57° at 0·2 mmHg, τ 3·83—4·37 (1H, m, =CH), 4·82br and 5·05br (2H, two s, $=CH_2$), 7·46 (d, *J* 7 Hz, CH_2–C=), 7·79br (t, CH_2CO), 8·58 (s, CH_3), and 7·46—9·35 (21H, aliphatic envelope) (Found: C, 73·7; H, 11·3. $C_{13}H_{24}O_2$ requires C, 73·5; H, 11·4%).

Aldehydes.—The three esters of 2-methylpent-4-en-2-ol were converted to the 3-hydroxy-3-methylbutanal esters by the following general method. Ozone was bubbled through a solution of the olefin ester (0·02 mol) in methanol (50 ml), cooled in an acetone–dry ice, until the solution took on a faint blue colour (*ca.* 40 min). The flask was then flushed with oxygen for 10 min and a solution of sodium iodide (7 g) in methanol (15 ml) and acetic acid (5 ml) added. After warming to room temperature over a period of 1 h, the mixture was concentrated, poured into water, extracted with ether, the extract washed with sodium thiosulphate solution, and dried ($MgSO_4$). Removal of the solvent followed by distillation yielded the pure aldehydes. *2-Formyl-1,1-dimethylethyl benzoate* (6b) (2·1 g, 51%) had b.p. 94—96° at 0·2 mmHg, τ 0·12 (1H, t, *J* 2 Hz, CHO), 1·93—2·17 (2H, m, *o*-ArH), 2·47—2·73 (3H, m, *m*- and *p*-ArH), 7·07 (2H, d, *J* 2 Hz, CH_2), and 8·31 (6H, s, CH_3). The compound eliminates benzoic acid relatively rapidly at room temperature. It proved impossible to obtain a satisfactory microanalysis. *2-Formyl-1,1-dimethylethyl phenylacetate* (6c) (3·0 g, 68%) had b.p. 108—110° at 0·3 mmHg, τ 0·28 (1H, t, *J* 2·4 Hz, CHO), 2·75 (5H, s, ArH), 6·47 (2H, s, CH_2Ar), 7·40 (2H, d, *J* 2·4 Hz, CH_2CHO), and 8·47 (6H, s, CH_3) (Found: C, 70·6; H, 7·3. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3). *2-Formyl-1,1-dimethylethyl heptanoate* (6d) (2·6 g, 61%) had b.p. 88—90° at 0·2 mmHg, τ 0·13 (1H, t, *J* 2·5 Hz, CHO), 7·17 (2H, d, *J* 2·5 Hz, CH_2CHO), 7·78br (2H, t, CH_2CO), 8·45 (s, CH_3), and 8·25—9·20 (19H, aliphatic envelope) (Found: C, 67·1; H, 10·0. $C_{12}H_{22}O_3$ requires C, 67·2; H, 10·3%).

1-Bromo-2-methylpropan-2-ol.—Isobutene was bubbled through water (100 ml) to which was slowly added, with rapid stirring, a solution of bromine (15 ml) and potassium bromide (40 g) in water (750 ml). When addition was complete, the solution was stirred for a further 2 h and the red oily layer of dibromide was then separated. The aqueous solution was extracted three times with ether, the combined extracts washed with sodium thiosulphate solution, and dried ($MgSO_4$). Evaporation of the solvent yielded, on distillation, 1-bromo-2-methylpropan-2-ol (9·5 g, 21%) as a liquid, b.p. 49—50° at 19 mmHg (lit.,[26] 49·5° at 16 mmHg), τ 6·62 (2H, s, CH_2), 6·95 (1H, s, OH removed by D_2O), and 8·67 (6H, s, CH_3).

[21] E. S. Blake, U.S.P. 3,378,578 (*Chem. Abs.*, 1968, **69**, 51,849).
[22] W. G. Kenyon, R. B. Meyer, and C. R. Hauser, *J. Org. Chem.*, 1963, **28**, 3108.
[23] R. C. Maginn, U.S.P. 3,330,860 (*Chem. Abs.*, 1967, **67**, 99,869).
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[25] H. R. Hence, B. B. Allen, and W. B. Leslie, *J. Org. Chem.*, 1942, **7**, 326.
[26] C. M. Suter and H. R. Zook, *J. Amer. Chem. Soc.*, 1944, **66**, 738.

1-*Bromomethyl*-1-*methylethyl Acetate* (11a).—A solution of 1-bromo-2-methylpropan-2-ol (4·5 g), *NN*-dimethylaniline (5·5 g), and acetyl bromide (8 ml) in dry ether (12 ml) was refluxed for 2 h, cooled, and poured into water. The ether layer was washed with dilute sulphuric acid and sodium carbonate solution and dried ($MgSO_4$). Evaporation of the solvent followed by distillation gave the *acetate* (14·6 g, 80%) as a liquid, b.p. 63—64° at 20 mmHg, τ 6·28 (2H, s, CH_2), 8·02 (3H, s, OAc), and 8·47 (6H, s, CH_3), *m/e* 179/181 (*M* − Me, 0·5/0·5%), 135/137 (*M* − AcO, 3/3), 134/136 (*M* − AcOH, 10/10), 101 (*M* − CH_2Br, 29), 59 (*M* − CH_2Br − CH_2CO, 23), 55 ($C_4H_7^+$, 44), and 43 (CH_3CO^+, 100) (Found: C, 39·2; H, 5·8; Br, 43·4. $C_4H_{11}BrO_2$ requires C, 38·9; H, 6·0; Br, 43·2%). When acetyl chloride was employed instead of acetyl bromide the n.m.r. spectrum of the crude bromoacetate showed it to be contaminated with a second component (τ 6·18 and 8·50; ratio *ca.* 1·3). The mass spectrum of the crude product suggested this to be 1-chloromethyl-1-methylethyl acetate, *m/e* 91/93 ($Me_2\overset{+}{C}CH_2Cl$) and 90/92 ($Me_2C{=}\overset{+}{C}HCl$), presumably arising *via* nucleophilic displacement of the bromine by chloride ion possibly with neighbouring acetate group participation.

1-*Bromomethyl*-1-*methylethyl Benzoate* (11b).—Benzoyl chloride (4 ml) was added with cooling to 1-bromo-2-methylpropan-2-ol (2·5 g) in pyridine (2·5 ml). The reactants were left for 18 h at room temperature before being poured into water. The aqueous mixture was then extracted with ether, washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Evaporation of the solvent followed by distillation gave first, benzoyl chloride and second, the *benzoate* (3·7 g, 85%) as a liquid, b.p. 86—87° at 0·2 mmHg, τ 1·92—2·08 (2H, m, *o*-ArH), 2·37—2·65 (3H, m, *m*- and *p*-ArH), 6·17 (2H, s, CH_2), and 8·30 (6H, s, CH_3), *m/e* 177 (*M* − Br, 1%), 134/136 (*M* − $PhCO_2H$, 4/4), 123 ($PhCO_2H_2^+$, 4), 122 ($PhCO_2H$, 4), 105 ($PhCO^+$, 100), 77 ($C_6H_5^+$, 61), 55 ($C_4H_7^+$, 65), 51 ($C_4H_3^+$, 36) (Found: C, 51·8; H, 5·3; Br, 31·8. $C_{11}H_{13}BrO_2$ requires C, 51·4; H, 5·1; Br, 31·1%).

1-*Bromomethyl*-1-*methylethyl* [^{18}O]*Benzoate* (23).—^{18}O-Labelled benzoic acid (17·70% [^{18}O]benzoic acid, 3·11% [$^{18}O_2$]benzoic acid) was prepared by the method of Ponticorvo and Rittenberg.[12] The labelled acid (3·5 g) was added to thionyl chloride (10 ml), left for 2 h, refluxed for 2 h, and distilled, to give [^{18}O]benzoyl chloride (3·4 g, 84%). To this was added 1-bromo-2-methylpropan-2-ol (2·5 g) in pyridine (3 ml) and the mixture was left for 18 h. Work-up as for the unlabelled material yielded the [^{18}O]benzoate (3·8 g, 90%), b.p. 90—91° at 0·4 mmHg. Mass spectrometry at 15 eV showed the ^{18}O content to be 10·15% (based on *M* − Br peak), 10·28% (based on *M* − CH_2Br peak), and 10·10% (based on $PhCO_2H_2^+$); average 10·18%.

2-*Bromo*-2-*methylpropyl Benzoate* (18).—α-Bromoisobutyraldehyde was prepared by a modification of the method of Favorskaya and Shkurgina.[27] Bromine (11 ml) was added, with stirring and cooling during 0·5 h, to isobutyraldehyde (15 g) in ether (125 ml). After standing for a further 45 min, the solution was washed with sodium carbonate solution and dried ($MgSO_4$). An n.m.r. spectrum of the yellow oil (30 g) obtained on evaporation of the ether showed the crude product to be essentially pure α-bromoisobutyraldehyde [τ 0·58 (1H, s, CHO) and 8·22 (6H, s, CH_3)]. This was taken up in ice-cold methanol (100 ml) and sodium borohydride (2·7 g) in weakly alkaline ice–water (35 ml) was added during 20 min with stirring. After a further 2 h the excess of borohydride was decomposed by the addition of dilute hydrochloric acid, the solution poured into water (600 ml), extracted thrice with ether, and the combined extracts dried ($MgSO_4$). Evaporation of the solvent left a pale yellow liquid (23·8 g) which the n.m.r. spectrum showed to be exclusively 2-bromo-2-methylpropan-1-ol, τ 6·52 (2H, s, CH_2), 7·73br (1H, s, OH removed by D_2O), and 8·27 (6H, s, CH_3). To this crude bromohydrin (6 g) in pyridine (6 ml) was added, with cooling, benzoyl chloride (9 ml). After being left overnight the solution was poured into water, extracted with ether, the extract washed successively with dilute hydrochloric acid, sodium carbonate solution, and water, and dried ($MgSO_4$). Evaporation of the solvent left a yellow liquid (14·5 g) which on distillation yielded first a small amount of benzoyl chloride, second, a fraction, b.p. 85—90° at 0·3 mmHg, whose n.m.r. spectrum showed it to be almost pure bromobenzoate, and third, 2-*bromo*-2-*methylpropyl benzoate* (6·1 g, 61%) as a liquid, b.p. 92—95° at 0·3 mmHg, τ 1·77—2·03 (2H, m, *o*-ArH), 2·37—2·62 (3H, m, *m*- and *p*-ArH), 5·58 (2H, s, CH_2), and 8·17 (6H, s, CH_3), *m/e* 256/258 (M^+, 0·16/0·16%), 177 (*M* − Br, 27), 135/137 (*M* − $PhCO_2$, 1/1), 134/136 (*M* − $PhCO_2H$, 1/1), 123 ($PhCO_2H_2^+$, 2), 122 ($PhCO_2H^+$, 2), 105 ($PhCO^+$, 100), 77 ($C_6H_5^+$, 19), 55 ($C_4H_7^+$, 7), and 51 ($C_4H_3^+$, 5) (Found: C, 51·1; H, 5·1; Br, 30·5. $C_{11}H_{13}BrO_2$ requires C, 51·4; H, 5·1; Br, 31·1%).

2-*Phenylpropan*-1-*ol*.—This was prepared by a method similar to that described by Brown and Subba Rao.[28] Boron trifluoride–ether (6 ml) was added, with stirring, to redistilled α-methylstyrene (11·8 g) and sodium borohydride (2·2 g) in diglyme (40 ml) under a nitrogen atmosphere. After stirring for 1 h, water (10 ml) was added, followed by 3M-sodium hydroxide solution (12 ml). 30% Hydrogen peroxide solution (13 ml) was then added at such a rate as to maintain gentle reflux. After cooling, the mixture was poured into ice–water (180 ml), extracted with ether, the extracts washed with water, and dried ($MgSO_4$). Evaporation of the ether and distillation of the residue gave 2-phenylpropan-1-ol (9·6 g, 71%) as a liquid, b.p. 61—62° at 0·35 mmHg (lit.,[28] 110—112° at 15 mmHg).

1-*Phenylpropan*-2-*ol*.—This was obtained by adding a solution of sodium borohydride (2·5 g) in slightly alkaline ice-cold water (30 ml) to benzyl methyl ketone (20 g) in methanol (75 ml) cooled in ice. After 1 h, the excess of borohydride was decomposed by the addition of dilute hydrochloric acid and the solution was poured into water and extracted with ether. The extract was washed with water, dried ($MgSO_4$), the solvent removed, and the residue distilled to give 1-phenylpropan-2-ol (15·5 g, 76%) as a liquid, b.p. 50—51° at 0·3 mmHg (lit.,[29] 103—104° at 14 mmHg).

1-*Methyl*-1-*phenylethyl Acetate*.—To 2-phenylpropan-2-ol (Fluka) (13·6 g) and *NN*-dimethylaniline (15·7 g) in dry ether (55 ml) was cautiously added acetyl chloride (14 ml). The mixture was refluxed for 2·5 h, poured into water and extracted with ether, the extract was washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Removal of the solvent gave a pale yellow oil containing significant quantities of α-methylstyrene (n.m.r.

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spectra). Distillation gave the acetate (7·3 g, 41%) as a liquid, b.p. 54—55° at 0·3 mmHg (lit.,[30] 93—94° at 10 mmHg). τ 2·80br (5H, s, ArH), 8·05 (3H, s, OAc), and 8·28 (6H, s, CH_3). Care had to be taken during the distillation to prevent decomposition of the acetate.

2-Phenylpropan-1-ol and 1-phenylpropan-2-ol were similarly converted into their acetates. 2-Phenylpropyl acetate (78% yield) had b.p. 67—68° at 0·7 mmHg (lit.,[31] 93—95° at 3 mmHg), τ 2·72 (5H, s, ArH), 5·84 (2H, d, J 6·5 Hz, CH_2), 6·92 (1H, sextet $J = J' = 6·5$ Hz, CH), 8·00 (3H, s, OAc), and 8·71 (3H, d, J' 6·5 Hz, CH_3). 1-Benzylethyl acetate (81% yield) had b.p. 59—60° at 0·4 mmHg (lit.,[32] 107—108° at 13 mmHg), τ 2·78 (5H, s, ArH), 4·89 (1H, *ca.* sextet J 6·5, J' 7·3 Hz, CH), 7·17 (2H, *ca.* 2d of d at τ 7·02 and 7·30, J' 7·3, J'' 14·4 Hz, non-equivalent CH_2), 8·04 (3H, s, OAc), and 8·82 (3H, d, J 6·5 Hz, CH_3).

1-*Bromomethyl*-1-*phenethyl Acetate* (11c).—A solution of bromine in dichloromethane was added to redistilled α-methylstyrene (15 g) in dichloromethane (100 ml) until a faint colour persisted. Removal of the solvent gave a pale yellow oil (34 g) which n.m.r. spectroscopy showed to be almost pure 1,2-dibromo-2-phenylpropane [τ 2·35—2·88 (5H, m, ArH), 5·71br (1H, d, J 10 Hz, part of CH_2 AB system), 5·94 (1H, d, J 10 Hz, part of CH_2 AB system), and 7·72br (3H, s, CH_3)]. Water (50 ml) in acetone (250 ml) was added and the mixture was stirred for 48 h at room temperature. The resultant homogeneous solution was concentrated to *ca.* 75 ml, taken up in ether, washed with water, and dried ($MgSO_4$). Removal of the solvent left an almost colourless oil (22 g) consisting largely of 1-bromo-2-phenylpropan-2-ol [τ 2·47—2·93 (5H, m, ArH), 6·37 (2H, s, CH_2), 7·73br (1H, s, OH removed by D_2O), and 8·40 (3H, s, CH_3)] and some minor products which may be 3-bromo-2-phenylpropene and 1-bromo-2-phenylpropene. A mixture of this crude product (7·6 g), *NN*-dimethylaniline (8·4 g), and acetyl chloride (11 ml) were left at room temperature for 16 h, poured into water, and extracted with ether, the extracts were washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Evaporation of the solvent gave a pale red liquid (7·7 g) which, on careful recrystallization from methanol containing a small amount of water, gave 1-bromomethyl-1-phenylethyl acetate (2·5 g, 24% overall yield) as crystals, m.p. 50·5—52° (lit.,[33] 49—50°), n.m.r. spectrum as previously reported.[33]

1-*Bromo*-2-*phenylpropan*-2-[^{18}O]*ol Acetate* (26).—Crude 1,2-dibromo-2-phenylpropane (2·8 g), ^{18}O-labelled water (1 g), and acetone (6 ml) were stirred at room temperature for 48 h, concentrated, and poured into water. The resultant ether extract was dried ($MgSO_4$) and the solvent removed to give crude 1-bromo-2-phenylpropan-2-[^{18}O]ol (2·21 g). To this was added *NN*-dimethylaniline (3·3 g) and acetyl chloride (5 ml). After standing overnight the mixture was worked up as for the unlabelled compound to give the labelled acetate (1·0 g, 33%) as crystals, m.p. 49—51°. Mass spectrometry showed the ^{18}O content to be 4·14% (based on M — Br peak) and 4·36% (based on M — CH_2Br peak), average 4·25% (calculations on the M — Br — CH_2CO peak gave an ^{18}O content of 1·87% implying equilibration of the oxygen atom during fragmentation, possibly *via* an ion with the acetoxonium structure [13]). If complete equilibration of the oxygens in the water and the acetone were to occur incorporation of ^{18}O into the bromo-acetate should be 4·21%.

Attempted Preparation of 1-*Bromomethyl*-1-*phenylethyl Benzoate*.—Benzoyl chloride (8 ml) was added with cooling to crude 1-bromo-2-phenylpropan-2-ol (7·8 g) in pyridine (5·5 ml). After standing overnight, the mixture was diluted with water and extracted with ether, the extract was washed with dilute hydrochloric acid and sodium carbonate solution, and dried ($MgSO_4$). Evaporation of the solvent gave a product whose n.m.r. spectrum suggested the presence of some of the desired bromo-benzoate [τ 7·93 (CH_3) and 6·05 and 6·12 (non-equivalent CH_2)]. However, some unchanged bromohydrin was also present and the major product appeared to be benzoic anhydride. No method could be found to isolate the relatively labile bromo-benzoate in a pure state. Other synthetic routes proved equally futile. The synthesis of 2-phenylpropane-1,2-diol 1-acetate has been described previously.[34]

2,4-*Dimethyl*-4-*phenyldioxolan* (34).—This was prepared by a method similar to that of Read *et al.*[35] 2-Phenylpropane-1,2-diol [34] (5 g), acetaldehyde (1·5 g), and 5 drops of concentrated sulphuric acid were heated on a steam-bath for 6 h, the resultant oil was taken up in ether, washed with dilute sodium carbonate solution, and dried (Na_2SO_4). Evaporation of the ether and distillation of the residue gave an approximately equimolar mixture of the two diastereoisomers of the *dioxolan* (3·5 g, 60·5%) as a liquid, b.p. 104—105° at 10 mmHg, τ 2·70br (5H, s, Ph), 3·05 and 3·25 (1H, 2q, J 5·0 Hz, CH), 5·88—6·37 (2H, 2 overlapping AB systems, CH_2), and 8·45, 8·47, 8·55, and 8·63 (6H, 4s, CH_3) (Found: C, 74·15; H, 7·75. $C_{11}H_{14}O_2$ requires C, 74·15; H, 7·9%).

Radical Reactions.—(a) *Bromo-esters*. A typical reaction was conducted as follows. Accurately weighed samples of the bromo-ester and tri-n-butylstannane (1 equiv.) in a standard flask (5 ml) were made up to the mark with benzene or t-butylbenzene and a small quantity of azobisisobutyronitrile was added. Known weights (*ca.* 1 g) of the solution were placed in ampoules (1 ml), and the samples were degassed, sealed under vacuum, and heated at 70 (±1)° for 24 h. An ampoule was then opened, and its contents and washings were added to a known weight of standard. The mixture was then analysed by g.l.c. For the 1-bromomethyl-1-methylethyl benzoate and acetate systems column *b* was used, and propiophenone was employed as standard in the former case. With the 1-bromomethyl-1-phenylethyl acetate system column *a* had to be used to prevent thermal decomposition of the products and the standard was 2-methylallyl benzoate.

(b) *Aldehyde esters*. A typical reaction was conducted as follows. Accurately weighed amounts of the aldehyde ester and benzoyl peroxide (0·1 or 1 equiv.) in a standard flask (5 ml) were made up to the mark with benzene. Known weights of these solutions (*ca.* 1 g) were placed in ampoules (1 ml) and the samples were degassed, sealed under vacuum, and heated at 75 (±1)° for 72 h. The ampoule contents were then analysed as above using column

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a with standards for benzoates, propiophenone; for phenylacetates, *p*-nitroanisole; and for heptanoates, nitrobenzene.

Isolation and Analysis of Labelled Products.—(*a*) 1-Bromomethyl-1-methylethyl [^{18}O]benzoate (0·800 g) and tri-n-butylstannane (0·972 g) were weighed into a standard flask (100 ml) and made up to the mark with benzene. A small amount of azobisisobutyronitrile was added. The solution was transferred into ampoules (20 ml) which were degassed, sealed, and then heated at 70° for 24 h. The contents of the ampoules were combined, concentrated, and subjected to preparative g.l.c. using the metal column *b*. Four fractions were collected (i) t-butyl benzoate, (ii) isobutyl benzoate, (iii) 2-methylallyl benzoate, and (iv) a tin-containing compound believed to be tri-n-butyltin bromide on the following grounds. Its n.m.r. spectrum was almost identical with that of an authentic sample of tri-n-butyltin chloride; its mass spectrum contained groups of ions of correct isotopic abundance at *m/e* 305—319 ($Bu^n_2SnBr^+$), 283—295 ($Bu^n_3Sn^+$), 249—263 (Bu^nSnBrH^+), 227—239 ($Bu^n_2SnH^+$), 191—205 ($SnBr^+$), and 169—183 ($SnBu^+$). The structures of the three benzoates were confirmed by n.m.r. spectroscopy. A solution of each benzoate in dry ether was added to lithium aluminium hydride and dry ether and refluxed for 20 min. Dilute hydrochloric acid–salt solution was added to decompose the excess of hydride, the ether layer was separated and dried ($MgSO_4$), and the solvent was carefully removed. The resultant products were subjected to g.l.c.–mass spectral analysis to determine the ^{18}O distribution.

(*b*) 1-Bromo-2-phenylpropan-2-[^{18}O]ol acetate (0·594 g) and tri-n-butylstannane (0·683 g) in benzene (100 ml) were heated as above and the products were separated by preparative g.l.c. Of the esters produced only 2-phenylpropyl acetate could be obtained in a pure state; 1-methyl-1-phenylethyl acetate decomposed on the metal surfaces of the injector and collector and resolution was not sufficiently good to enable 1-benzylethyl acetate to be obtained uncontaminated by the tertiary ester. 2-Phenylpropyl acetate was reduced with lithium aluminium hydride as above and the ^{18}O content of the resultant 2-phenylpropan-1-ol determined by introduction of the crude product into the mass spectrometer *via* the heated inlet system, some difficulty being experienced with decomposition of the alcohol on g.l.c.–mass spectrometry using a metal column.

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