# A Study of the Koch Synthesis of Carboxylic Acids

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The Koch carboxylic acid synthesis with formic and sulphuric acids has been applied to oct-1-ene, 2-methylheptan-2-ol, n-pentylcyclopropane, and related cyclopropanes. Mass spectral breakdown shows that oct-1-ene and the cyclopropanes lead mainly to acids of the structural type $Me_2C(R) \cdot CO_2H$ and $MeEtC(R) \cdot CO_2H$. Example of Koch synthesis with transannular cyclisation are described, and data relating to the laboratory use of carbon monoxide in place of formic acid are presented.

IN the Koch synthesis[1] of carboxylic acids ($R^+$ + CO $\longrightarrow RCO^+ \longrightarrow RCO_2H$) the carbonium species $R^+$ may be derived from a protonated alkene or alkanol. The tertiary ion being commonly the most stable, and hydride and alkyl shifts rapid, the Koch reaction leads to mainly tertiary alkanecarboxylic acids. We sought to apply mass spectrometry and $^1H$–$^2H$ exchange to monitor the preferred modes of rearrangement of an n-alkyl chain, by comparing the acid products generated from oct-1-ene (1), with those from 2-methylheptan-2-ol (2), chosen as a direct source of a tertiary carbonium ion.

$$Me[CH_2]_5 \cdot CH=CH_2 \qquad Me[CH_2]_4 \cdot CMe(OH)Me$$

$$(1) \qquad\qquad (2)$$
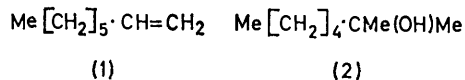
With formic and sulphuric acids oct-1-ene gave in 91% yield an acidic product comprising 8% of a dimer-acid, $C_{16}H_{33} \cdot CO_2H$, and 92% of an acid, $C_8H_{17} \cdot CO_2H$, yielding a methyl ester characterised by sharp n.m.r. signals at $\tau$ 8·88 and 8·82, a terminal $CH_3$ triplet at $\tau$ 9·1 ($J$ 6 Hz), and a broad band at $\tau$ 8·72. The corresponding acid derived from (2) either by Koch synthesis, or *via* the sequence: (2) $\longrightarrow$ bromide $\longrightarrow$ MgBr derivative $\longrightarrow$ carboxylic acid $\longrightarrow$ methyl ester, showed only the $\tau$ 8·82 signal of the $\tau$ 8·88, 8·82 pair in the product from (1).

The origin of this difference in n.m.r. signals was clarified by observation of the McLafferty fragmentation of the methyl esters. The ester derived from oct-1-ene gave a molecular ion of $m/e$ 172, ions of $m/e$ 144 and 130, due to loss of alkene units, and ions of $m/e$ 141 (172 − OMe) and 113 (172 − $CO_2Me$), together with strong McLafferty fragment ions $m/e$ 116 and 102 corresponding to structures (3) and (4). Metastable ion transitions [$m/e$ 65·25 (116 $\longrightarrow$ 87 + 29) and 87·9 (116 $\longrightarrow$ 101 +



(3)          (4)
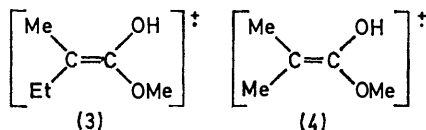
15)] confirmed the presence of Me and Et substituents in the ion (3), and a corresponding metastable ion transition [$m/e$ 74·2 (102 $\longrightarrow$ 87 + 15)] characterised the ion (4).

Thus compounds (5) and (6) represent major constituents in the acid derived from oct-1-ene. The corresponding product from 2-methylheptan-2-ol, on the

other hand, is mainly (6): the methyl ester showed a strong $m/e$ 102 ion, the homologous ion of $m/e$ 116 being weak.



(5)          (6)
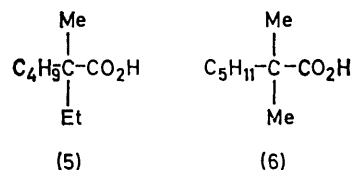
The Koch synthesis carried out in [$^2H_2$]sulphuric acid confirmed these results. The methyl esters of the deuteriated acids gave molecular ions of relative peak heights ($h$) as follows:

(i) from oct-1-ene:

| $m/e$ | 178 | 179 | 180 | 181 | 182 | 183 | 184 | 185 | 186 | 187 | 188 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $^2H$ | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 |
| $h$ | 0·04 | 0·14 | 0·32 | 0·50 | 0·68 | 0·86 | 1·0 | 0·68 | 0·45 | 0·18 | 0·04 |

(ii) from 2-methyl heptan-2-ol:

| $m/e$ | 175 | 176 | 177 | 178 | 179 | 180 | 181 | 182 | 183 | 184 |
|---|---|---|---|---|---|---|---|---|---|---|
| $^2H$ | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| $h$ | 0·10 | 0·10 | 0·48 | 0·57 | 0·95 | 1·0 | 0·76 | 0·57 | 0·29 | 0·19 |

Thus whereas the 2-methylheptyl cation shows some exchange beyond the protons adjacent to the cationic centre, the carbonium ions derived from oct-1-ene permit more extensive rearrangement and exchange.

The rearrangement exemplified by (1) $\longrightarrow$ (5) and (6) appeared to be general for a group of alkenes (*cf.* Table 1), with some indication of increasing proportions
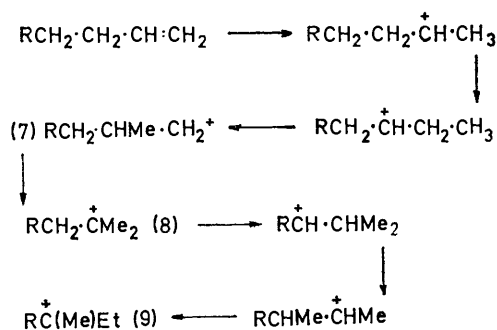
TABLE 1

Intensity of ion $m/e$ 116 relative to ion $m/e$ 102 in the mass spectra of methyl esters derived from Koch synthesis on various alkenes *etc.*

| | | | |
|---|---|---|---|
| Hept-1-ene | 0·6 | Oct-1-ene | 0·82 |
| Dodec-1-ene | 0·99 | Oct-2-ene | 0·87 |
| Octan-2-ol | 0·79 | 2-Methylheptan-2-ol | 0·24 |
| n-Pentylcyclopropane | | 0·87 | |
| n-Hexylcyclopropane | | 0·99 | |
| *cis*-1-Methyl-2-n-pentylcyclopropane | | 1·13 | |

of acids or type (5) with increasing chain length, *i.e.* with reduced solubility of the alkene, and presumably also of the alkyl carbonium intermediate in sulphuric acid.

[1] H. Koch and W. Haaf, *Annalen*, 1958, **618**, 251; 1960, **638**, 122; J. A. Olah, ' Friedel Crafts and Related Reactions,' Wiley-Interscience, New York, vol. 3, 1964, p. 1284; W. Haaf, *Org. Synth.*, 1966, **46**, 72.

Table 1 also includes examples of the application of the Koch synthesis to appropriate cyclopropanes. These were included since a direct sequence for re-arrangement:

$$RCH_2 \cdot CH_2 \cdot CH{:}CH_2 \longrightarrow RCH_2 \cdot CH_2 \cdot \overset{+}{C}H \cdot CH_3$$

$$(7)\ RCH_2 \cdot CHMe \cdot CH_2{}^+ \longleftarrow RCH_2 \cdot \overset{+}{C}H \cdot CH_2 \cdot CH_3$$

$$RCH_2 \cdot \overset{+}{C}Me_2\ (8) \longrightarrow R\overset{+}{C}H \cdot CHMe_2$$

$$R\overset{+}{C}(Me)Et\ (9) \longleftarrow RCHMe \cdot \overset{+}{C}HMe$$

involves the improbable intermediate ion (7), *i.e.* re-arrangement must be considered to occur, at least in part, by 1,3-shifts *via* a protonated cyclopropane.[2]
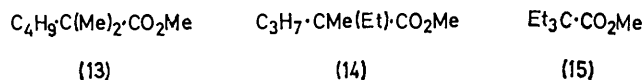
n-Pentyl-, n-hexyl-, and *cis*-1-methyl-2-n-pentyl-cyclo-propane gave the corresponding carboxylic acids in yields of 72, 75, and 81%, respectively, and methyl esters characterised by strong McLafferty fragment ions of $m/e$ 102 and 116, and showing n.m.r. signals at $\tau$ 8·82 and 8·88. The intensity of the $m/e$ 116 ion in the spectrum of the methyl ester obtained from *cis*-1-methyl-2-n-pentylcyclopropane suggests that fission (a) as in (10) is favoured relative to (b), but the general correspondence of the products from alkenes and cyclo-propanes was marked. Moreover, since intermediates such as (11) or (12) must be of closely similar energy it is
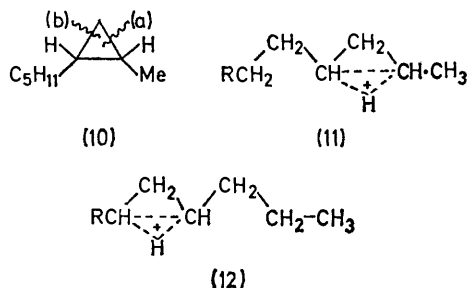


possible to account for exchange of 12 or more protons per molecule by a process in which the protonated cyclopropane ' rolls ' along the alkane chain.

The apparent preference for the formation of the $Me_2\overset{+}{C}R$ and $Me\overset{+}{C}(Et)R'$ ions led us to examine the fate of 3-ethylpentan-3-ol in the Koch reaction. The product methyl ester, $m/e$ 158 ($C_7H_{15} \cdot CO_2Me$), showed the characteristic $\tau$ 8·82 and 8·88 n.m.r. signals already

noted, and an intense fragment ion of $m/e$ 116, with smaller peaks at $m/e$ 102 and 130. This is indicative of the formation of esters (13), (14), and (15), and although the $Et_3C^+$ cation has been observed[3] in solution in $FSO_3H$–$SbF_5$–$SO_2ClF$ it appears to be relatively less stable than the $Me(Et)\overset{+}{C}$ and $Me_2\overset{+}{C}$ ions under our conditions.

$$C_4H_9 \cdot C(Me)_2 \cdot CO_2Me \qquad C_3H_7 \cdot CMe(Et) \cdot CO_2Me \qquad Et_3C \cdot CO_2Me$$
$$(13) \qquad\qquad (14) \qquad\qquad (15)$$

The evident mobility of the carbonium centre in an alkane chain raised the question of the applicability of the Koch synthesis to a difunctional molecule. How-ever, undec-10-enoic acid was found to give in high yield a dicarboxylic acid, dimethyl ester $m/e$ 258 $[C_{10}H_{20}(CO_2Me)_2]$, which showed the characteristic $\tau$ 8·82 and 8·88 n.m.r. singlet signals together with a triplet at $\tau$ 7·65 (2H) and the ester protons at $\tau$ 6·30 (6H). The fragmentation pattern proved consistent with the major components being (16) and (17).
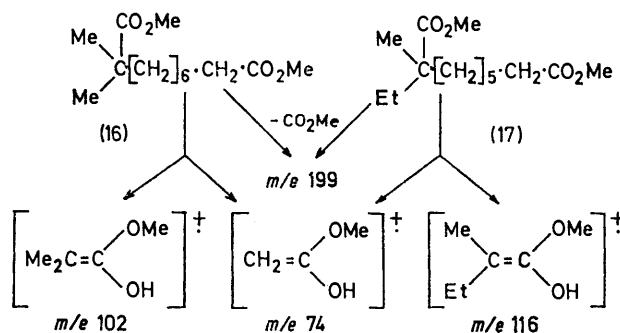


Undec-10-en-1-ol gave an isomeric acid product, methyl ester $m/e$ 258, $\tau$ 8·82 (s) and 8·88 (s), with a broad $\tau$ 8·71 signal, and fragment ions $m/e$ 102 and 116, the ion $m/e$ 74 being absent. This is consistent with rearrangement at each end of the carbon chain.

A suitable difunctional molecule also allows of Koch synthesis coupled with transannular cyclisation. Cyclo-octa-1,5-diene readily gave an acid, methyl ester $m/e$ 168 ($C_8H_{13} \cdot CO_2Me$), which showed a fragmentation pattern consistent with structure (18). The bicyclo[3,3,0]octan-1-yl carbonium ion has been examined[4] by n.m.r. and shown to yield *cis*-bicyclo-octyl derivatives. Compound (18) has recently been synthesised less directly.[5]

Cyclododeca-1,5,9-triene similarly gave an acid, methyl ester $m/e$ 222 ($C_{12}H_{19} \cdot CO_2Me$), most rationally

[2] J. L. Fry and G. J. Karabatsos, ' Carbonium Ions, eds. G. A. Olah and P. von R. Schleyer, Wiley-Interscience, New York, 1970, vol. II, p. 521; D. M. Brouwer, *Rec. Trav. chim.*, 1968, **87**, 1435; 1969, **88**, 9; D. M. Brouwer and J. M. Oelderik, *ibid.*, 1968, **87**, 721; D. M. Brouwer and J. A. Van Dorn, *ibid.*, 1969, **88**, 573.

[3] G. A. Olah and J. Lukas, *J. Amer. Chem. Soc.*, 1967, **89**, 4739.
[4] G. A. Olah, J. M. Bollinger, and D. P. Kelly, *J. Amer. Chem. Soc.*, 1970, **92**, 1432.
[5] M. A. McKervey, H. A. Quinn, and J. J. Rooney, *J. Chem. Soc.* (C), 1971, 2430.

formulated as (19) in agreement with the breakdown pattern.
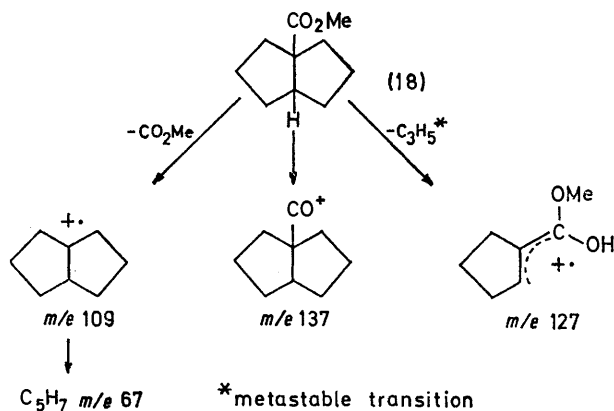


Whilst the formic acid–sulphuric acid procedure gives satisfactory yields, gaseous carbon monoxide may also be employed.[6] We have examined this method on the
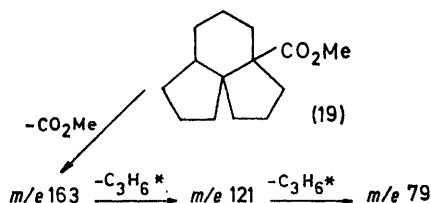


laboratory scale with an apparatus in which the rate of carbon monoxide uptake may be measured. To avoid carbonium ion–alkene condensation we examined first adamantanol in sulphuric acid with tetrahydrothiophen dioxide as diluent, varying the reactant concentrations and temperature. From the results (Table 2) we note

TABLE 2

Initial rate of carbon monoxide uptake for adamantan-1-ol in sulphuric acid–tetrahydrothiophen dioxide (THTD) at 18 °C

(a) $H_2SO_4$ (98%; 55 g); THTD (9 ml)

| Adamantanol | | | | | |
|---|---|---|---|---|---|
| (mol × $10^4$) | 16·5 | 33·0 | 66·0 | 132 | 198 |
| CO (ml h$^{-1}$) | 195 | 260 | 315 | 380 | 385 |

(b) Adamantanol (66 × $10^{-4}$ mol); $H_2SO_4$ (55 g); THTD (9 ml)

| $H_2SO_4$ (%) | 92·8 | 94·5 | 96·2 | 97·1 | 97·5 | 98 |
|---|---|---|---|---|---|---|
| CO(ml h$^{-1}$) | 74 | 124 | 170 | 210 | 240 | 315 |

(c) Adamantanol (66 × $10^{-4}$ mol); $H_2SO_4$ (98%; 55 g); THTD (9 ml)

| $T$/K | 273 | 291 | 313 | 323 | 403·5 |
|---|---|---|---|---|---|
| CO (ml h$^{-1}$) | 127 | 315 | 564 | 825 | 1090 |

that at an adamantanol concentration above *ca.* 0·3M the rate of carbon monoxide supply becomes limiting. The graph of the data in (b) showed a rate rising in-

[6] J. Falbe, 'Synthesen mit Kohlenmonoxyd,' Springer Verlag, Berlin, 1967, p. 120.

creasingly steeply with acid concentration, owing to the two-step generation of the carbonium ion (AdOH $\longrightarrow$ AdO$\overset{+}{H}_2$ $\longrightarrow$ Ad$^+$). The data in (c) gave a good linear plot of $\log_{10}$ rate constant *vs.* $1/T$, leading to an activation energy of 27 kJ mol$^{-1}$.

We then sought to optimise the experimental conditions for use of carbon monoxide with alkenes, using the total gas uptake as an index of the degree of alkene polymerisation. However, this necessitates the use of a two-phase system; alkenes and sulphuric acid are not mutually soluble in any co-solvent.

TABLE 3

$CH_3\cdot[CH_2]_n\cdot CH=CH_2$ (31·4 × $10^{-3}$ mol); $CCl_4$ (15 ml); 93·5% $H_2SO_4$ (55 g); 4 °C

| $n$ | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| CO (ml h$^{-1}$)† | 40 | 770 | 1250 | 600 | 290 | 130 |
| CO (% uptake) | 5 | 50 | 51 | 79 | 81 | 78 |

† Initial rates.

The data in Table 3 indicate the critical importance of solubility and partitioning of the olefin into the acid in determining the degree of olefin polymerisation. However, the data of Table 4 indicate that acid rather

TABLE 4

(a) Hept-1-ene; $CCl_4$ (15 ml); $H_2SO_4$ (93·5%; 55 g); 4 °C

| Heptene (mol × $10^3$) | 11·7 | 15·3 | 16·3 | 31·1 | 31·4 | 38·8 | 57·0 |
|---|---|---|---|---|---|---|---|
| CO (ml h$^{-1}$) † | 450 | 680 | 650 | 1180 | 1230 | 1520 | 1970 |
| CO (% uptake) | 63 | 63 | 62 | 60 | 60 | 60 | 58 |

(b) Heptene (31·4 × $10^{-3}$ mol); $CCl_4$ (15 ml); $H_2SO_4$ (55 g); 4 °C

| $H_2SO_4$ (%) | 93·5 | 95·3 | 96·9 | 98·0 |
|---|---|---|---|---|
| CO (ml h$^{-1}$) † | 1230 | 2800 | 4300 | 5340 |
| CO (% uptake) | 60 | 54 | 45 | 40 |

† Initial rates.

than olefin concentration is the more important variable in determining yield with carbon monoxide supply becoming limiting only at the highest reaction rates.

TABLE 5

Oct-1-ene (31·4 × $10^{-3}$ mol); $H_2SO_4$ (93·5%; 55 g); 4 °C

| $CCl_4$ (ml) | 7·5 | 15 | 20 | 30 | 40 | 50 |
|---|---|---|---|---|---|---|
| CO (ml h$^{-1}$) | 390 | 600 | 550 | 515 | 325 | 325 |
| CO (% uptake) | 25 | 78 | 80 | 83 | 88 | 88 |

Table 5 indicates the influence of the volume of carbon tetrachloride diluent. We infer that an olefin concentration of 0·5M in carbon tetrachloride gives a useful rate of reaction and acceptable yield.

EXPERIMENTAL

*Materials.*—2-Methylheptan-2-ol was obtained from methyl hexanoate and methylmagnesium iodide; b.p. 156°, $\nu_{max.}$ 3360 cm$^{-1}$, $\tau$ 8·90 (6H, s), 9·10 (3H, t, *J* 6 Hz), and 8·70 (8H). 2,2-Dimethylheptanoic acid was prepared from carboxylation of 2-methylheptan-2-ylmagnesium bromide;

methyl ester, b.p. 70° at 15 mmHg, $m/e$ 172. n-Pentyl-cyclopropane had b.p. 128°, $m/e$ 112, 97, 84, 83, 69, and 55, τ 8·7 (8H, m), 9·1 (3H, t, $J$ 6 Hz), and 9·55 (3H, m), $ν_{max.}$ 3100 cm⁻¹. n-Hexylcyclopropane had b.p. 148°, $m/e$ 126, 111, 97, 84, 83, 70, 69, 56, and 55, τ 8·70 (10H, m), 9·11 (3H, t, $J$ 6 Hz), and 9·55 (3H, m), $ν_{max.}$ 3100 cm⁻¹. cis-1-Methyl-2-pentylcyclopropane, b.p. 153°, $m/e$ 126, 111, 97, 83, 70, 69, and 55, τ 8·62 (6H, m), 9·0 (6H, m), 9·29 (3H, m), and 10·32 (1H, m), $ν_{max.}$ 3100 cm⁻¹, was obtained from cis-oct-2-ene.

*Koch Reaction.*—(a) *With formic acid.* Formic acid (0·2 ml) was added to 98% sulphuric acid (33 g) at 15°, followed by the olefin, alkanol, or cyclopropane (0·017 mol), and formic acid (3·1 g) was then added gradually during 1 h with stirring. Experiments in [²H₂]sulphuric acid were conducted similarly (one-third scale).

(b) *With carbon monoxide.* Sulphuric acid in a flask with side arm was equilibrated with carbon monoxide supplied from an Englehard hydrogen control unit. The reactant in carbon tetrachloride was then added (amounts indicated in the discussion) *via* the side arm, and the flask was shaken vigorously. In the control unit gas absorption causes release of further carbon monoxide from a reservoir *via* a solenoid valve which actuates a recorder to give a time–uptake graph.

*Results.*—With formic acid, 2-methylheptan-2-ol gave an acid; methyl ester, b.p. 69° at 15 mmHg, yield 68%, τ 9·1 (3H, t, $J$ 6 Hz), 8·88 (weak), and 8·82 (intense), $m/e$ 172. Under the same conditions oct-1-ene gave an acid; methyl ester, b.p. 87° at 43 mmHg, yield 81%, τ 9·10 (3H, t, $J$ 6 Hz), 8·88 (strong), 8·82 (strong), 8·72 (broad), and 6·30 (3H), $m/e$ 172. n-Pentylcyclopropane [7] gave an acid, methyl ester, b.p. 70—71° at 15 mmHg, yield 72%, τ 6·30 (3H, s), 9·10 (3H, t, $J$ 6 Hz), 8·88 (strong), 8·82 (strong), and 8·72 (broad), $m/e$ 172.

n-Hexylcyclopropane [7] gave an acid; methyl ester, b.p. 95—97° at 15 mmHg, τ 6·30 (3H, s), 9·10 (3H, t, $J$ 6 Hz), 8·88 (strong), 8·82 (strong), and 8·72 (broad), $m/e$ 186, 171, and 155. cis-1-Methyl-2-pentylcyclopropane [7] gave an acid; methyl ester, b.p. 93—94° at 15 mmHg, yield 75%, τ 6·30, 9·10 (3H, t, $J$ 6 Hz), 8·88 (strong), 8·82 (strong), and 8·72 (broad), $m/e$ 186.

The methyl ester from octan-2-ol had b.p. 86—87 at 43 mmHg, yield 82%, τ 9·10 (3H, t, $J$ 6 Hz), 8·88 (strong), 8·82 (strong), 8·72 (broad), and 6·30, $m/e$ 172. 3-Ethyl-pentan-3-ol gave an acid; methyl ester, b.p. 60—62° at 15 mmHg, yield 55%, τ 6·30 (3H, s), 8·82, 8·88, and 8·70, $m/e$ 159 ($M$ + 1), 158, 130, 116, and 102.

Cyclo-octa-1,5-diene (1·8 g) in carbon tetrachloride (10 ml) with formic acid (3·1 g) and 96% sulphuric acid (33·0 g) gave an acid product; methyl ester (18), b.p. 95° at 15 mmHg, yield 33%, $ν_{max.}$ 1730 cm⁻¹, τ 6·35 (3H, s), 7·80 (1H, m), and 8·48 (12H) (Found: C, 85·5; H, 9·65. Calc. for $C_{10}H_{16}O_2$: C, 85·35; H, 9·6%).

Cyclododeca-1,5,9-triene (6·5 g) in carbon tetrachloride (10 ml) with formic acid (3·1 g) and 96% sulphuric acid (33 g) gave an acid; methyl ester (19) (42%), b.p. 132° at 15 mmHg, τ 6·30 (3H) and 8·40 (19H).

Undec-10-enoic acid (3·4 g) in carbon tetrachloride (10 ml) with 96% sulphuric acid (33·0 g) and formic acid (3·1 g) gave a product yielding a dimethyl ester, b.p. 122—124° at 15 mmHg, 58% yield, $ν_{max.}$ 1730 cm⁻¹, τ 6·30 (6H, s), 7·65 (2H, t, $J$ 6 Hz), 8·82 (s) and 8·88 (s), and 8·67 (broad), $m/e$ 258, 199, 116, 102, 101, 83, 74, 109, and 55.

Undec-10-en-1-ol similarly gave a dimethyl ester, b.p. 128—130° at 15 mmHg, 15% yield, $ν_{max.}$ 1735 cm⁻¹, τ 6·35 (6H, s), 8·82 (s) and 8·88 (s), and 8·78 (broad), $m/e$ 213 (272 − $CO_2Me$), 171, 116, 102, and 101.

[7] H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.,* 1959, **81**, 4256.