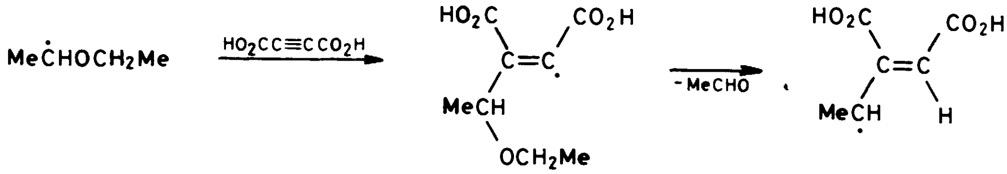
# Electron Spin Resonance Evidence for Rapid Cyclization of Alkenyl Radicals formed by Readily Occurring 1,5- and 1,6-Hydrogen Shifts in Vinyl Radicals

**Bruce C. Gilbert*** and **David J. Parry**
*Department of Chemistry, University of York, Heslington, York YO1 5DD*

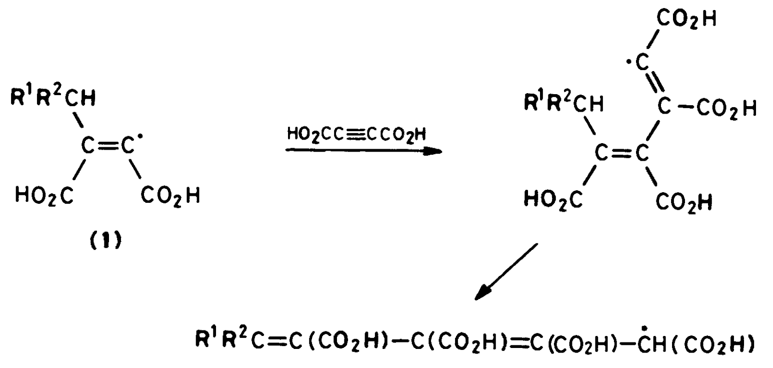
Vinyl radicals have been generated (for *in situ* study by e.s.r. spectroscopy) by the addition of first-formed alkyl radicals to the triple bond in butynedioic acid. It is shown that rearrangements occur readily *via* 1,5- and 1,6-hydrogen shifts (with $k > 10^4\ \mathrm{s^{-1}}$), even from unactivated C–H bonds. Subsequent rapid cyclization of the resulting alkenyl radicals (with $k \geqslant 10^3\ \mathrm{s^{-1}}$) can evidently be assisted by both electronic and steric effects: regioselectivity of ring closure leads to the formation of five-membered rings by reaction in the *exo* mode of hex-5-enyl radicals (formed *via* 1,6-shifts) and, in an unusually rapid reaction, by *endo* closure of the pent-4-enyl radicals (formed *via* 1,5-shifts).

The ready addition of alkyl radicals to alkynes provides a convenient method for the rapid generation of specific vinyl radicals, for some of which readily occurring transformations have been revealed by e.s.r. spectroscopy.[1,2] For example, the addition of $^\bullet$CHMeOEt (generated from reaction of diethyl ether with $^\bullet$OH, from the $\mathrm{Ti^{III}}$–$\mathrm{H_2O_2}$ couple) to butynedioic acid leads to the occurrence of a 1,5-hydrogen shift followed by (or concerted with) fragmentation [reaction (1)].[1] On the other hand, addition of $^\bullet$Me, $^\bullet$Et, or $^\bullet\mathrm{Pr^i}$ (from reaction of $^\bullet$OH with the appropriate sulphoxides) to butynedioic acid ($10^{-2}$ mol dm$^{-3}$) leads to the direct detection of the appropriate vinyl radical (**1**) and, at higher concentrations of alkyne (*ca.* 0.1 mol dm$^{-3}$), the pentadienyl species (**2**) formed by subsequent addition and rearrangement [reaction (2)].

We describe here an investigation of the occurrence of 1,*n*-shifts (*n* = 5 or 6) in which the potential hydrogen-transfer reactions generally lack both the apparently activating effects of the (+*M*) oxygen-substituent [reaction (1)] and the formation of a highly conjugated radical [reaction (2)]. A series of unusually rapid shifts is reported, together with evidence for subsequent cyclization of the intermediate alkenyl radicals, the regioselectivity of which is discussed.



(1)



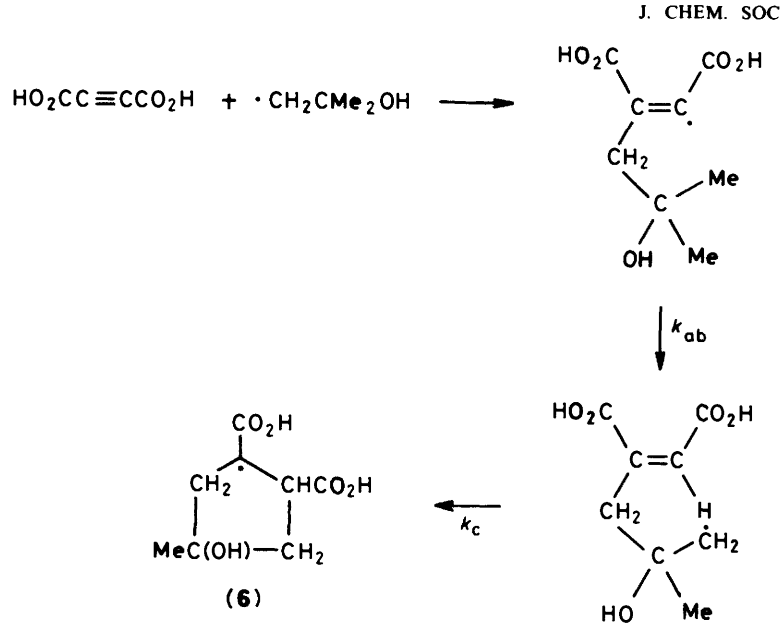
(2)

(**2**)

## Results and Discussion

Experiments were carried out as described previously,[1,2] by the generation of radicals in a continuous-flow system in which three streams containing, respectively, titanium(III), hydrogen peroxide, and the substrates, were mixed *ca.* 50 ms before their passage through the cavity of an e.s.r. spectrometer. Experiments were normally carried out at both pH *ca.* 1 and *ca.* 8 [achieved *via* addition of ammonia, with ethylenediamine-tetra-acetic acid (EDTA) as sequestering agent], with low concentrations of alkyne (to avoid its reaction with $^\bullet$OH) and much higher concentrations of substrate RH (to ensure scavenging of $^\bullet$OH to give radicals $\mathrm{R^\bullet}$, subsequent addition of which to the alkyne was to be studied).

(*a*) *Reactions of Alcohols*.—The reactions of $^\bullet\mathrm{CH_2OH}$, and $^\bullet$CHMeOH, to give radicals of the type (**1**) (at low [alkyne]) and (**2**) (at higher concentrations of alkyne) closely resemble those of $^\bullet$Me and $^\bullet$Et, respectively [reaction (2)], as previously described.[2] On the other hand, completely different behaviour is observed for several radicals with longer carbon chains, and the behaviour of $\mathrm{Bu^tOH}$ (where only a single primary radical is generated) is most clear-cut.



Scheme 1.

In experiments with t-butyl alcohol at pH 1, addition of $HO_2CC{\equiv}CCO_2H$ ($2 \times 10^{-2}$ mol dm$^{-3}$) led to a reduction in the intensity of the signal from $^{\cdot}CH_2CMe_2OH$ (3)* and to the appearance of a signal with *g* 2.0031 and three large doublet splittings (2.55, 3.23, and 3.22 mT) as well as a small triplet splitting (0.04 mT). Traces of other new signals detected could not be unambiguously analysed. In experiments with higher concentrations of alkyne (up to 0.1 mol dm$^{-3}$) no other signals were detected, though signals from (3) were essentially completely removed. At high pH (*ca.* 8), signals from (3) were reduced in intensity as [alkyne] was increased and the same spectrum (with three large proton splittings) was obtained, though its intensity was significantly lower than at low pH.

Related behaviour was also observed at low pH for the two radicals derived from neopentyl alcohol with $^{\cdot}OH$: the e.s.r. spectrum from the dominant species $^{\cdot}CHOHCMe_3$ (4) was removed first when $HO_2CC{\equiv}CCO_2H$ was added (at a concentration of $10^{-3}$ mol dm$^{-3}$), to be replaced by a spectrum with two large splittings (see Table 1), and the subsequent decrease (with [alkyne] $2 \times 10^{-2}$ mol dm$^{-3}$) in the concentrations of the minor radical $^{\cdot}CH_2CMe_2CH_2OH$ (5) was accompanied by the appearance of a correspondingly weak signal with parameters similar to that obtained from $^{\cdot}CH_2CMe_2OH$; other weaker resonances were also observed. At higher pH secondary radicals of this type could not be clearly characterized and the initial radicals appeared to be relatively unaffected by the presence of alkyne (*ca.* 0.1 mol dm$^{-3}$).

The large hyperfine splittings in the secondary radicals detected at low pH are evidently associated with β-protons, and interpretation of their magnitudes in terms of the expected angular dependence ($B\cos^2\theta$) for $a$(β-H) indicates that the radical centre must be incorporated in a relatively small ring:[4] in particular, a five-membered ring is suggested by comparison with splittings reported for a variety of cyclopentane-derived species[5–7] [for example, cyclopentyl itself has (at 100 K) $a$(2 H) 4.33, $a$(2 H) 2.37 mT]. The second part of this paper provides more detailed structural evidence to support this interpretation.

We propose that the addition of the first-formed alkyl radicals (3)—(5) to butynedioic acid leads to the formation of intermediate vinyl radicals which undergo rapid 1,5-shifts and subsequent *endo* cyclization to radicals (6)—(8), respectively [see *e.g.* Scheme 1 for the formation of (6) from $^{\cdot}CH_2CMe_2OH$]. It should be noted that the *g* values of the secondary radicals are characteristic of carboxy-conjugated radicals, that the number and magnitude of the β-splittings are entirely are expected and, in addition, that the resolvable γ-proton hyperfine splittings observable in some cases are in accord with the proposed structure [see (6), for example]. If this mechanistic and structural interpretation is correct (see later) then several features are particularly worthy of note. The first is the rapidity of the 1,5-abstraction from an unactivated C–H bond.† This presumably reflects the hybridization of the unpaired electron [*cf.* the greater bond strength[8] (by *ca.* 40 kJ mol$^{-1}$) of C($sp^2$)–H than C($sp^3$)–H and the consequent exothermicity of the reaction] as well as the number of suitably placed hydrogen atoms. The presence of the geminal β-substituents in (3)—(5) might also be expected to be a contributory factor in assisting hydrogen transfer (*cf.* the Thorpe–Ingold effect[9]). The second is the unexpected ease of cyclization and its *endo* regioselectivity,[10,11] a process which again may be encouraged by β-disubstitution (for pent-4-enyl itself, it has been suggested[12] that the rate constant for *exo* cyclization, the mode of attack expected, is less than 1.0 s$^{-1}$ at 60 °C). It seems likely that the lower signal intensity detected for (6) at high pH (compared with pH 1) and the failure to detect (7) and (8) under these conditions reflect one (or more) of several factors, including a lower rate of addition to the dicarboxylate dianion, a decrease in the reactivity of the vinyl radical (possibly as a result of delocalization or change in hybridization) and a reduction in the rate of cyclization.

When propan-1-ol is oxidized with $^{\cdot}OH$, the e.s.r. spectra detected characterize the predominance of $^{\cdot}CHEtOH$ (9), together with weaker signals from $^{\cdot}CHMeCH_2OH$ and $^{\cdot}CH_2CH_2CH_2OH$. In the presence of relatively low concentr-

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* Data on first-formed radicals have been previously reported (see *e.g.* ref. 3) and will not be repeated here.

† We estimate from the failure to trap intermediate vinyl and alkyl radicals at pH *ca.* 1 with more alkyne (even up to *ca.* 0.1 mol dm$^{-3}$) that $k_{ab}$ and $k_c$ are $> 10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$ (the rate constants for reaction of both vinyl and alkyl radicals with butynedioic acid at pH *ca.* 1.0 are[2] *ca.* $10^6$ dm$^3$ mol$^{-1}$ s$^{-1}$).

**Table 1.** E.s.r. parameters of cyclic radicals derived *via* addition of radicals to butynedioic acid[a]

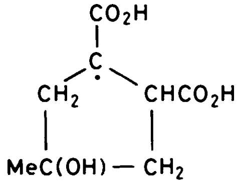
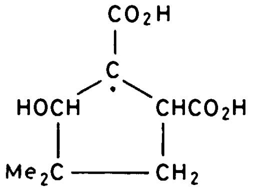
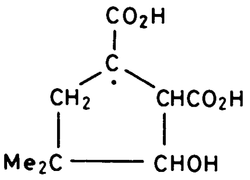
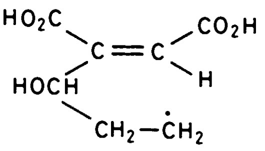
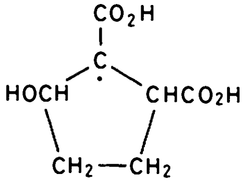
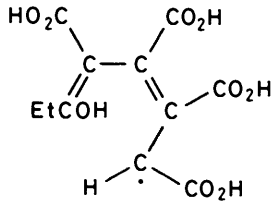
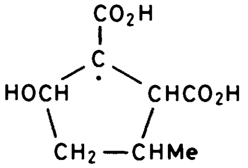
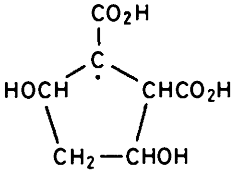
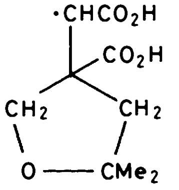
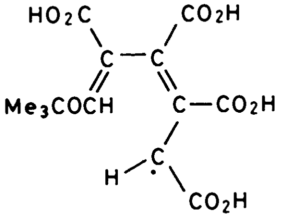
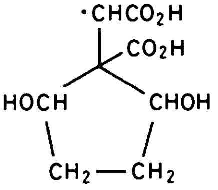
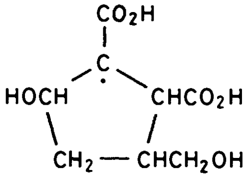
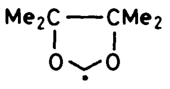
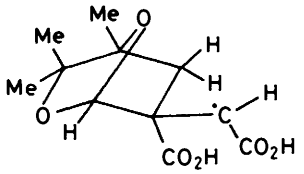
| Substrate | Radical | Radical detected | Hyperfine splitting (mT)[b] | | | $g^c$ |
|---|---|---|---|---|---|---|
| | | | $a(\alpha$-H) | $a(\beta$-H) | $a$(other) | |
| Bu$^t$OH | $\cdot CH_2CMe_2OH$<br>(3) | <br>**(6)** | | 3.23<br>3.22<br>2.55 | 0.04(2) | 2.0031 |
| Neopentyl alcohol | $\cdot CH(OH)CMe_3$<br>(4) | <br>**(7)** | | 3.49<br>3.35 | | 2.0031 |
| | $\cdot CH_2CMe_2CH_2OH$<br>(5) | <br>**(8)** | | 3.75<br>3.15<br>2.50 | 0.05 | 2.0032 |
| Propan-1-ol | $\cdot CHEtOH$<br>(9) | <br>**(10)** | 2.20(2) | 2.52<br>2.63 | 0.09 | 2.0026 |
| | | <br>**(11)** | | 2.32<br>3.13 | | 2.0030 |
| | | <br>**(13)** | 1.14 | | | 2.0033 |
| Butan-1-ol | $\cdot CHPrOH$<br>(14) | <br>**(15)** | | 3.54<br>3.35 | | 2.0031 |

**Table 1** (*continued*)

| Substrate | Radical(s) | Radical detected | Hyperfine splitting (mT)[b] $a$(α-H) | $a$(β-H) | $a$(other) | $g$[c] |
|---|---|---|---|---|---|---|
| Propane-1,3-diol | $^{\bullet}CH(OH)CH_2CH_2OH$<br>**(16)** | <br>**(17)** | | 3.51<br>2.71 | | 2.0033 |
| Methyl t-butyl ether | $^{\bullet}CH_2OCMe_3$<br>**(18)** | <br>**(21)** | 2.04 | | 0.10(2) | 2.0031 |
| | | <br>**(22)** | 0.98 | | 0.29 | 2.0032 |
| Butane-1,4-diol | $^{\bullet}CH(OH)CH_2CH_2CH_2OH$<br>**(23)** | <br>**(24)** | 2.05 | | | 2.0031 |
| | | <br>**(25)** | | 4.32<br>2.28 | | 2.0031 |
| 4,4,5,5-Tetramethyl--1,3-dioxolane | <br>**(26)** | <br>**(27)** | 2.02 | | 0.10(3) | 2.0032 |

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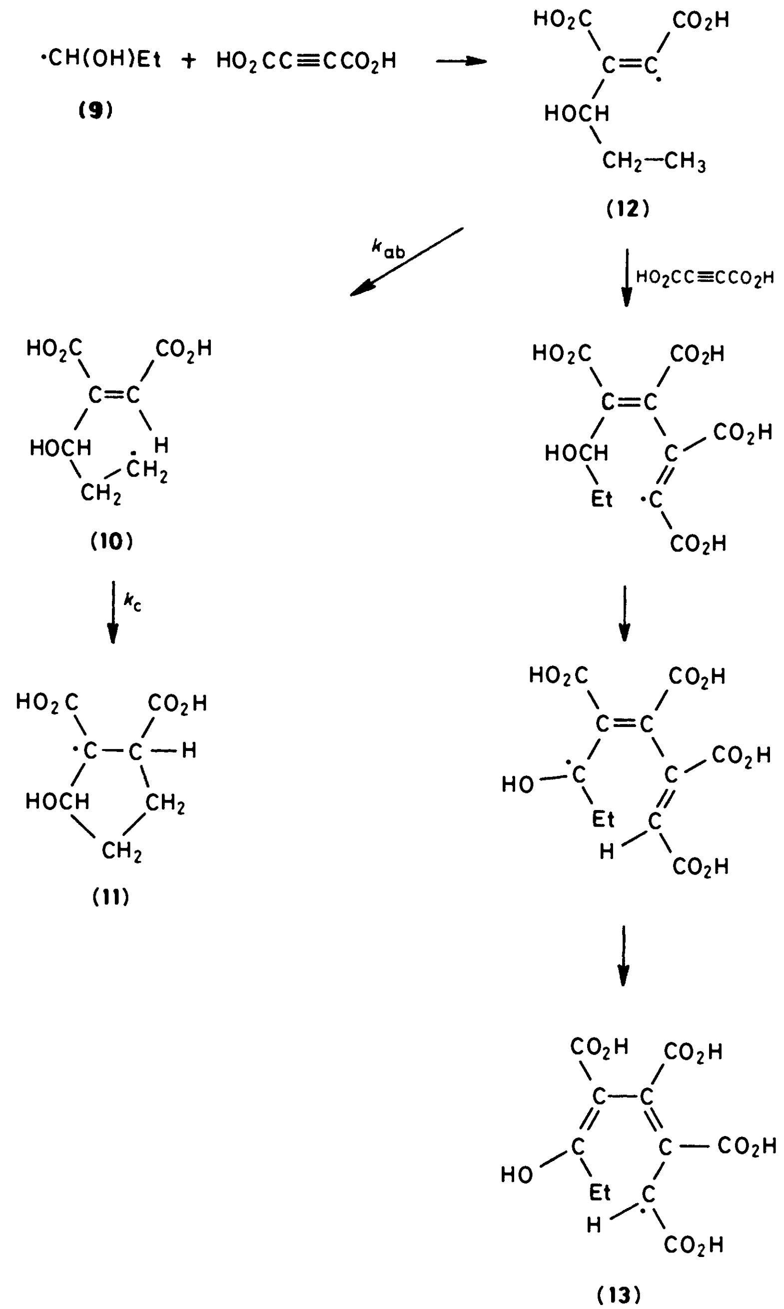
[a] At pH *ca.* 1: related species also detected at high pH (*ca.* 8) are referred to in the text. [b] ±0.01 mT; number of protons in parentheses (one unless indicated). [c] ±0.0001.



Scheme 2.

ations of butynedioic acid (6 × $10^{-3}$ mol $dm^{-3}$) signals from (**9**) were reduced in intensity (although the signals from the other two radicals remained essentially unchanged): this is consistent with the faster attack of radicals with $+M$ substituents at the radical centre. Two new signals, in particular, were detected, in approximately equal concentrations (see Figure 1). The first of these has a splitting pattern which comprises two equivalent α-protons (*a* 2.20 mT), two splittings of 2.52 and 2.63 mT attributed to non-equivalent β-protons (and typical of chiral radicals in which the β-carbon is attached to an asymmetric γ-carbon[13]) and a single small γ-proton splitting (0.09 mT): the *g* value is typical of a non-conjugated alkyl radical, and the structure $^{\bullet}CH_2CH_2CH(OH)C(CO_2H)=CHCO_2H$ (**10**) is proposed (see Scheme 2). {To support this assignment we generated the radical $^{\bullet}CH_2CH_2CH(NH_3^+)CO_2^-$ by reaction of $^{\bullet}OH$ with methionine *S*-oxide:[14] under conditions of high resolution the non-equivalence of the β-protons is revealed, and the spectrum [*a*(two α-H) 2.22, *a*(β-H) 2.48 and 2.53, *a*(γ-H) 0.05 mT, *g* 2.0026] shows a remarkable similarity to that attributed to (**10**)} The second extra radical is typified by two large β-proton splittings (as already described) and a *g* value characteristic of a carboxy-conjugated radical: it is assigned the cyclic structure (**11**) by analogy with the structural assignments for radicals from t-butyl alcohol, neopentyl alcohol, and some cyclopentane derivatives (see later). As [alkyne] was increased, the two signals first grew, as might be expected if both are derived from the first-formed vinyl radical (**12**) (the rate of formation of which would thus be increased) but then diminished (with $[HO_2CC{\equiv}CCO_2H] > 2 \times 10^{-2}$ mol $dm^{-3}$) as a further radical, attributed structure (**13**), was detected [with

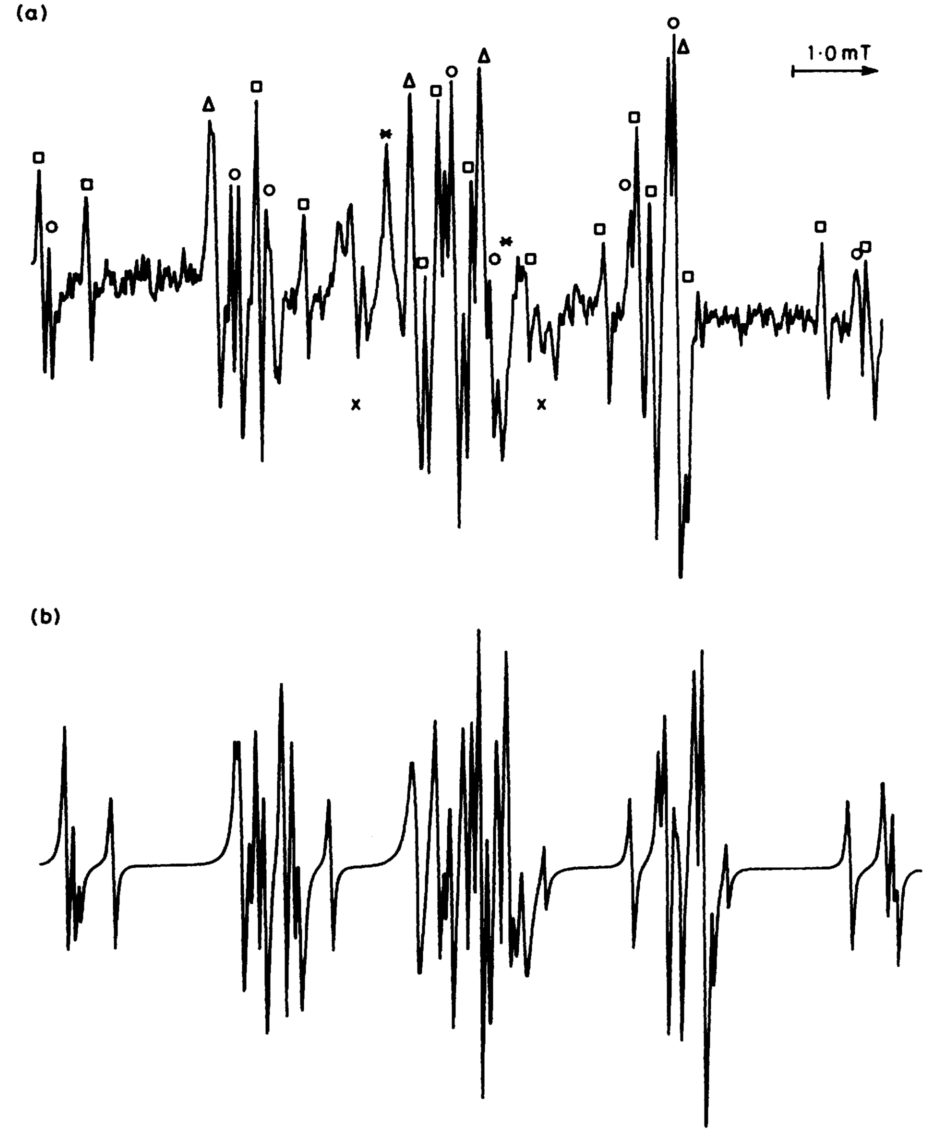


**Figure 1.** (a) E.s.r. spectra of (**10**) (○), (**11**) (△), and (**13**) (✱) (all derived from $\cdot$CHEtOH) as well as of unchanged $\cdot$CHMeCH$_2$OH (□), obtained from reaction of $\cdot$OH with propan-1-ol (0.2 mol dm$^{-3}$) in the presence of butynedioic acid (0.02 mol dm$^{-3}$) at pH *ca.* 1; resonances marked × are unassigned. (b) Simulated spectrum

*a*(1 H) 1.14 mT, *g* 2.0033]: the latter has parameters closely similar to those previously obtained from $\cdot$CH$_2$OH and $\cdot$CHMeOH and *two* molecules of alkyne. The mechanism of reaction outlined in Scheme 2 is proposed.*

From the concentration of alkyne at which (**13**) appears in significant proportions, we estimate that the 1,5-shift has $k_{ab}$ *ca.* $10^4$ s$^{-1}$: the observation of (**10**) and (**11**) in similar concentrations then implies that the rate of cyclization in this case is *ca.* $10^3$ s$^{-1}$.† In experiments with propanol at higher pH, signals from $\cdot$CH(OH)Et were readily removed when butynedioic acid was added: although strong signals from (**10**) (presumably in ionized form) were detected, the cyclized radical (**11**) was present in much lower concentration than at low pH. This indicates that the ionized vinyl radical akin to (**12**) also possesses the latter's high reactivity towards 1,5-hydrogen abstraction, but that cyclization onto the carbon–carbon double bond is retarded by the carboxylate substituents.

Reaction of butan-1-ol with $\cdot$OH at low pH leads to a complex mixture of all four radicals which can be obtained by hydrogen-atom abstraction, with $\cdot$CHPrOH (**14**) present in highest concentration though not dominant. When butynedioic acid was also present (at *ca.* $10^{-2}$ mol dm$^{-3}$) an even more complex overall spectrum resulted in which it was clear that the concentration of (**14**) had been reduced and that a cyclized radical [attributed the structure (**15**)] had been formed (*cf.* propan-1-ol); a signal from an intermediate akin to (**11**), if formed, may well have been masked by the other signals present. No extra information could be derived by experiments at high pH.

With propane-1,3-diol the radical $\cdot$CH(OH)CH$_2$CH$_2$OH (**16**) (dominant in the spectrum) was replaced by a spectrum dominated by a strong signal assigned to (**17**) in the presence of alkyne ($2 \times 10^{-3}$ mol dm$^{-3}$) at pH *ca.* 1. The magnitude of the signal and the failure to trap intermediate radicals with a greater

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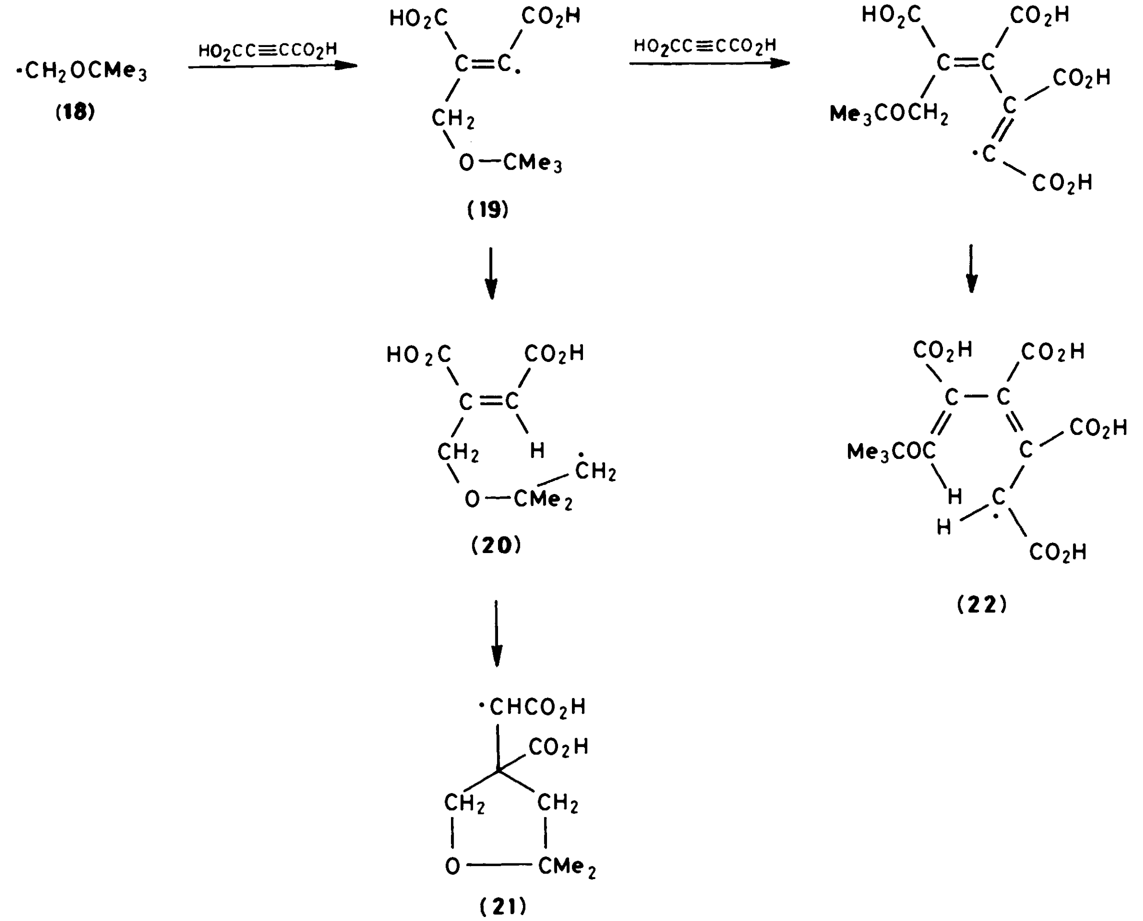
* The e.s.r. spectrum does not allow enol and keto tautomers of (**13**) to be distinguished.

† This follows from a steady-state calculation for (**11**): $k_c[(\mathbf{10})] \simeq 2k_t[(\mathbf{11})]^2$, with $[(\mathbf{10})] \simeq 2[(\mathbf{11})] \simeq 1 \times 10^{-6}$ mol dm$^{-3}$, and $2k_t$ taken[15] as $2 \times 10^9$ dm$^3$ mol$^{-1}$ s$^{-1}$.



Scheme 3.

concentration of alkyne suggests that there is a particularly effective route to the cyclized radical, and it seems likely that both internal hydrogen abstraction and cyclization are assisted by the polar effect of the $+M$ group on the γ-carbon atom in the first-formed radical.

Methyl t-butyl ether was studied in an attempt to ascertain whether rapid 1,6-shifts (and subsequent cyclization) could similarly be characterized. The replacement of the signal from $^{\bullet}CH_2OBu^t$ (**18**) by a strong signal with $a$(α-H) and $g$ value typical of a carboxy-conjugated radical is interpreted in terms of the conversion of (**18**) *via* (**19**) and a subsequent 1,6-shift to give (**20**), and hence (**21**) (Scheme 3); at high concentrations of butynedioic acid (*ca.* 0.1 mol dm$^{-3}$) (**18**) also reacted to give a signal [with $a$(1 H) 0.98, 0.29 mT, $g$ 2.0032], attributed to (**22**), as with small alkyl radicals. This indicates that the rate of internal 1,6-hydrogen abstraction in (**19**) is *ca.* $10^5$ s$^{-1}$ (somewhat less than for some of the 1,5-shifts previously mentioned, as might be expected): in this case the evident preference for *exo* rather than *endo* cyclization apparently reflects stereoelectronic control of addition *via* optimum overlap between the orbital of the unpaired electron and the π*-orbital of the double bond (in accordance with Beckwith's rules[10,11,16]). No evidence for rapid addition and subsequent shifts at high pH was obtained.

Similar behaviour was observed for the radical $^{\bullet}CH(OH)CH_2CH_2CH_2OH$ (**23**) from butane-1,4-diol, in which the observation of signals assigned to radicals (**24**) (dominant in the spectrum) and (**25**) (present as a minor component) is attributed to the occurrence of competing modes of abstraction (1,6- and 1,5-) and cyclization (*endo* and *exo*), respectively (see Scheme 4): though a 1,5-shift might normally be preferred to a 1,6-shift the latter is evidently encouraged in this case by the presence of the adjacent oxygen atom. With the radical (**26**) from 4,4,5,5-tetramethyl-1,3-dioxolane (chosen so as to give a vinyl radical with no route to 1,5-hydrogen abstraction and fragmentation), a similar 1,6-shift and cyclization is suggested by the observation of a spectrum with parameters which characterize structure (**27**).

Experiments were also carried out by generating a variety of first-formed radicals (including $^{\bullet}CHEtOH$ and $^{\bullet}CH_2CMe_2OH$) in the presence of propynoic acid and butyne-1,4-diol. Although $^{\bullet}OH$ itself adds readily to these alkynes (see *e.g.* ref. 1), only weak and complex signals were detected with other first-formed radicals, and no reaction scheme akin to those of butynedioic acid could be characterized.

(*b*) *Oxidation of Some Model Compounds.*—In an attempt to provide evidence for the foregoing structural assignments, we studied the oxidation with $^{\bullet}OH$ of both cyclopentane-*r*-1,*c*-2,*c*-3,*c*-4-tetracarboxylic acid (**28**) and a commercial sample of tetrahydrofuran-2,3,4,5-tetracarboxylic acid (**29**).*

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* The $^1$H n.m.r. spectrum of this compound shows an AA′XX′ pattern,[17] which was satisfactorily simulated with parameters H-2,-5 δ 5.03; H-3,-4 δ 3.85, $J_{2,3}$ 5.5, $J_{2,4}$ −0.7, $J_{2,5}$ *ca.* 0, and $J_{3,4}$ 7.8 Hz. While this information does not provide unambiguous stereochemical assignment it is consistent with a *trans* geometry for the protons on C-2 and C-3 and *cis* geometry for those on C-3 and C-4 (*i.e.* αββα) (see *e.g.* ref. 18), a conclusion which is reinforced by the e.s.r. results.

**Table 2.** E.s.r. spectra of radicals derived by oxidation of cyclopentane-*r*-1,*c*-2,*c*-3,*c*-4-tetracarboxylic acid (**28**) and tetrahydrofuran-2,3,4,5-tetracarboxylic acid (**29**)[a]

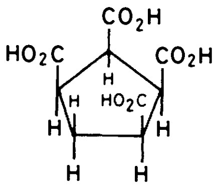
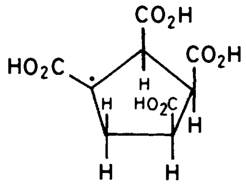
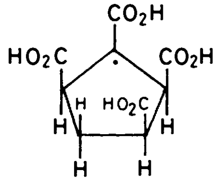
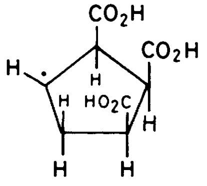
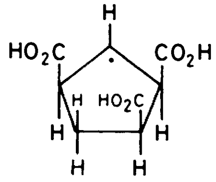
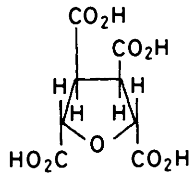
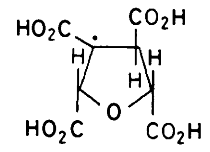
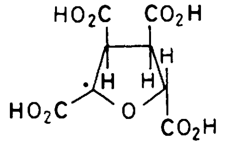
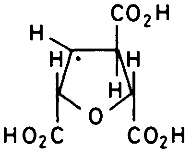
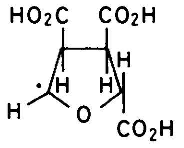
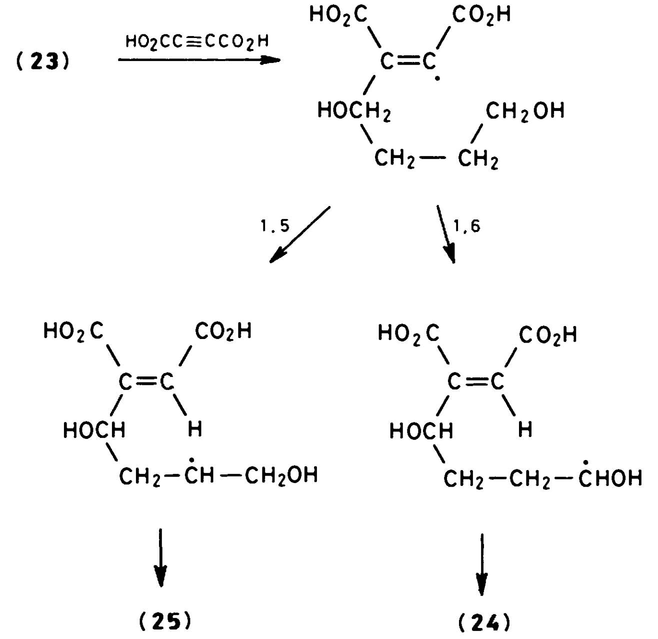
| Substrate | Reacting radical | Radicals detected | pH | Hyperfine splittings (mT)[b] | | | *g*[c] |
|---|---|---|---|---|---|---|---|
| | | | | *a*(α-H) | *a*(β-H) | *a*(γ-H) | |
|  (**28**) | ·OH |  (**30**) | 0—2 | | 4.10<br>3.39<br>2.34 | | 2.0031 |
| | | | 8—10 | | 4.27<br>3.50<br>1.86 | 0.06(2) | 2.0031 |
| | |  (**31**) | 0—2 | | 3.20<br>1.95 | | 2.0031 |
| | | | 8—10 | | 3.29<br>1.82 | 0.04(3) | 2.0031 |
| | $SO_4^{-\cdot}$ | (**30**), (**31**) | | | | | |
| | |  (**32**) | 8 | 2.10 | 4.35<br>4.25<br>2.60 | 0.05(2) | 2.0026 |
| | |  (**33**) | 8 | 2.15 | 4.35<br>2.92 | 0.03(3) | 2.0026 |
|  (**29**) | ·OH |  (**34**) | 0—2 | | 3.48<br>2.38 | | 2.0031 |
| | | | 8—10 | | 3.52<br>3.21 | 0.04 | 2.0029 |
| | |  (**35a**) | 0—2 | | 1.52 | 0.38 | 2.0038 |
| | | | 8—10 | | 1.30 | 0.36<br>0.04 | 2.0035 |

**Table 2** (*continued*)

| Substrate | Reacting radical | Radicals detected | pH | Hyperfine splittings (mT)[b] | | | $\bar{g}$[c] |
|---|---|---|---|---|---|---|---|
| | | | | $a$(α-H) | $a$(β-H) | $a$(γ-H) | |
| **(29)** (*continued*) | ·OH | **(35b)** | 0—2 | | 3.00 | 0.02(2) | 2.0038 |
| | | **(34)**,**(35a)**,**(35b)** | 8—10 | | 2.95 | 0.15<br>0.08 | 2.0035 |
| | $SO_4^{-\cdot}$ |  **(36)** | 8 | 2.10 | 4.06<br>3.92 | 0.05 | 2.0025 |
| | |  **(37)** | 8 | 1.31 | 3.01 | 0.12<br>0.08 | 2.0030 |

[a] For details of stereochemistry, see text. [b] ±0.01; number of protons in parentheses (one unless indicated). [c] ±0.0001.



**Scheme 4.**

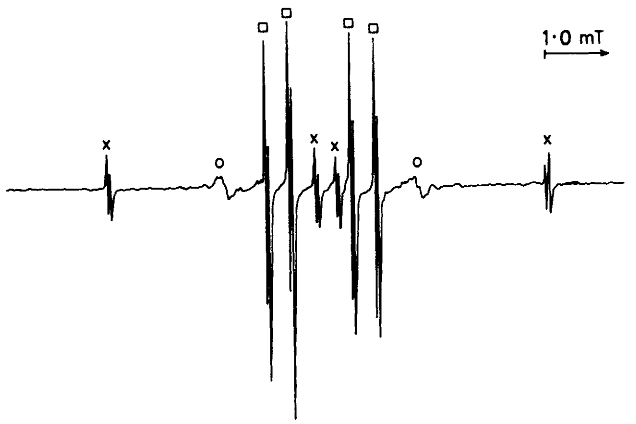
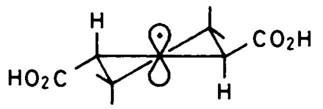


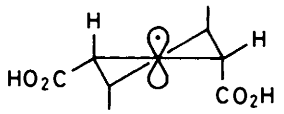
**Figure 2.** E.s.r. spectra of radicals **(34)** ( × ), **(35a)** (□), and **(35b)** (○) obtained from reaction of **(29)** with ·OH at pH 8

Reaction of **(28)** at pH 1 led to the detection in approximately equal concentrations of two carboxy-conjugated radicals **(30)** and **(31)** (see Table 2), assigned on the basis of the $g$ values and the number of β-proton splittings; signals were sharper and somewhat stronger at high pH (*cf.* Figure 2), evidently on account of the loss of unresolved hydroxy-proton splittings and a reduced rate of bimolecular decay (which reflects the high overall negative charge[15]). Oxidation of **(28)** with $SO_4^{-\cdot}$ under similar conditions at pH 8 gave **(30)** and **(31)** as well as two decarboxylated radicals **(32)** and **(33)**, which are identified on the basis of the $g$ values, the α-proton splittings, and the number of β-proton splittings.

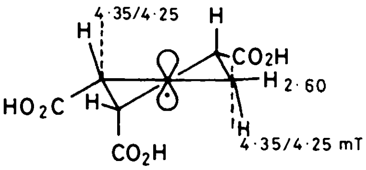
Reaction of **(29)** at low pH led to the detection of three signals. Of these, the $g$ value of 2.0031 and the associated β-splittings enable the (minor) carboxy-conjugated radical **(34)** to be characterized: the other two have $g$ values which typify radicals which are both oxygen- and carboxy-conjugated and the signals are attributed (see later) to the (conformational) isomers **(35a)** and **(35b)**: one has a large γ-proton splitting. The analogous radicals have extended lifetimes, sharper lines, but similar splittings at high pH (see Table 2 and Figure 2). Reaction with $SO_4^{-\cdot}$ also enabled the decarboxylated radicals **(36)** and **(37)** to be identified. Under all conditions preference for



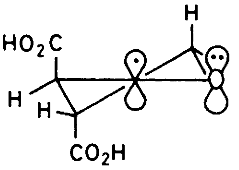
**(38)**



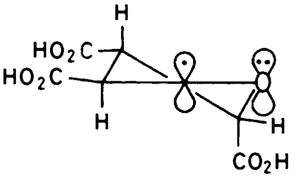
**(39)**



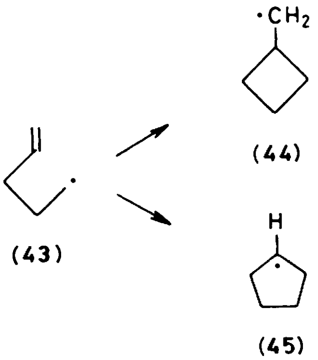
**(40)**



**(41)**



**(42)**



**(43)** **(44)** **(45)**

attack at the C–H bond adjacent to the oxygen atom in the ring is observed.

(i) *Conformational analysis.* For each of those radicals with three β-hydrogen splittings, *i.e.* **(32)** and **(30)**, two of the splittings are considerably greater than the third: the magnitudes are greater for **(32)** [with $a$(β-H) 4.35, 4.25, and 2.60 mT] than for **(30)**, which is consistent with a small extent of delocalization of the unpaired electron away from the radical centre and onto the carboxylate group[19] [contrast values of $a$(β-H) for $^{\bullet}CHMe_2$ and $^{\bullet}CMe_2CO_2H$ of 2.47 and 2.16 mT respectively (refs. 20 and 21)]. Where there are two β-proton splittings, we can contrast those derived from **(28)**, in which there is one large and one significantly smaller splitting [*i.e.* 3.20 and 1.95 mT for the conjugated radical **(31)**, 4.35 and 2.92 mT for the unconjugated species **(33)**] with the radicals from **(29)**, for which two large proton splittings are detected [see *e.g.* 4.06 and 3.92 mT for the unconjugated species **(36)**: the somewhat lower values for **(34)** presumably reflect conjugation onto the carbonyl group].

The difference in behaviour must reflect the *cis*-relationship between the β-protons in the radicals from **(28)** and the *trans*-geometry of the β-protons in those from **(29)**. These results (both the differences and the observation of β-proton splittings greater than 4 mT) clearly indicate that the rings are not planar (in which case no differences would have been observed); they can however be interpreted on the basis of a half-chair conformation with two pseudo-axial protons in radicals **(34)** and **(36)** derived from **(29)** [see *e.g.* **(38)**] and one axial and one equatorial β-proton in radicals **(31)** and **(33)** from **(28)** [see *e.g.* **(39)**]. Where there are three β-proton splittings [see *e.g.* **(32)**] their magnitudes suggest that there are two axial protons and one equatorial proton, consistent with a conformation [see **(40)**] in which the single substituent adjacent to the radical centre prefers a pseudo-equatorial orientation (as might be expected, since this maximizes the number of such substituents).

This interpretation also allows us to understand the existence of two isomers of the radical **(35)**, which differ in the magnitudes of their β-proton splittings. In **(35a)** the relatively low β-proton splitting (1.52 mT at pH 1) typifies a pseudo-equatorial orientation for the appropriate hydrogen atom, whereas in the conformational isomer **(35b)** this is much larger (3.00 mT), evidently on account of the increased hyperconjugative interaction with the axial β-proton. Our assignment of conformations **(41)** and **(42)** respectively is also consistent with the occurrence of a large γ-proton interaction (0.38 mT) in the former, in which the *axial* γ-proton would be expected to interact much more effectively with the spin density in the $p(\pi)$ orbital on oxygen than the equatorial γ-proton in the latter.[22] It also follows that, unlike most radicals in cyclopentane rings, conformational interconversion between **(35a)** and **(35b)** is slow on the e.s.r. timescale (see *e.g.* ref. 5); we attribute this to the steric influence of four adjacent carboxy groups.

A more detailed conformational analysis can be achieved if it is assumed that the β-proton interaction is effectively given by $\rho_{\alpha}B\cos^2\theta$, where $\rho_{\alpha}$ is the spin density on the radical centre, B is a constant and θ is the dihedral angle between the orbital of the unpaired electron and the β-C–H bond.[4] Taking ρB as 4.74 mT for the unconjugated radicals and as 4.32 mT for the carboxy-conjugated species (4.34 mT for the ionized analogues),* we can calculate values of θ in individual radicals.

For the unconjugated cyclopentane-derived species **(32)** the β-splittings of 4.35, 4.25, and 2.60 mT correspond to calculated torsion angles of 20, 22, and 43.5° respectively. These values are consistent with two pseudo-axial and a pseudo-equatorial proton in a twist-chair or half-chair conformation [see **(40)**] (with a degree of twist of *ca.* 10° away from a planar conformation: *cf.* a variety of related radicals,[5] including cyclopentyl itself[7]). It is encouraging to find that the sum of the proton splittings for a pair of methylene protons (*ca.* 7.0 mT) is close to that expected for a half-chair (contrast *ca.* 5.0 mT for an envelope) and that the sum of the two appropriate torsion angles [43.5 + 20 (or 22)] is *ca.* 60° (which would be expected since the torsion angle between the two C–H bonds should be *ca.* 120°). For the corresponding carboxy-conjugated radical, the β-splittings 4.10, 3.39, and 2.34 mT give torsion angles of 13, 28 and 43°, respectively. The greater difference between the two pseudo-axial protons (which cannot be separately assigned) presumably reflects a distortion in the ring skeleton away from a twist or half-chair (presumably on account of interaction between α- and β-carboxy groups). This appears to be greatest in the ionized analogue, in which the angles are 8, 26, and 49°, respectively (we presume that the values of 8 and 49° correspond to the pair of methylene hydrogens: *cf.* calculated values of 10 and 50° for a half-chair): repulsion between carboxylate groups may well be implicated.

For the *cis*-disubstituted radicals **(33)** (unconjugated) and **(31)** the pairs of torsion angles are calculated as 20 and 40°, and 31 and 48°, respectively (in each case corresponding to pseudo-

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* Derived from the values of 2.47 mT for $a$(β-H) in[20] $^{\bullet}CHMe_2$ and 2.16 mT for[21] $a$(β-H) in $^{\bullet}CMe_2CO_2H$ (*cf.* also 2.17 mT for[23] $^{\bullet}CMe_2CO_2^-$), for which the average value of $\cos^2\theta$ in each case is 0.5.

axial and pseudo-equatorial β-protons, respectively). The angles calculated for the former resemble closely those for the analogous unsubstituted radical (**32**). For the radical (**31**) the values correspond closely to those for (**30**) as long as in the latter the splitting of 3.39 mT (3.50 mT at high pH) is associated with the methine-proton coupling (as already suggested).

In contrast, as expected for the *trans*-β-protons in the tetrahydrofuran-derived species (**36**), the calculated torsion angles are similar and characteristic of pseudo-axial protons (25 and 27°). The corresponding values for (**34**) are 25 and 31° (for the carboxylate anion) and 26 and 42° (at low pH). The values for (**36**) and (**34**) (pH 8) indicate a smaller degree of twist from planarity than for the cyclopentane-derived species, evidently because of the incorporation of the oxygen into the ring [the low splitting for the protonated form of (**34**) appears anomalous]. The extent of twist (*ca.* 5°) in these furanose radicals may also be compared with the geometry of the parent compound (**29**): the n.m.r. parameters suggest that (on average) the tetrahydrofuran ring assumes a half-chair conformation with torsion angles between the *cis*-protons (H-3 and H-4) and the *trans*-protons (H-2 and H-3) of $<20°$ and $>160°$, respectively.[18]

(ii) *The geometry of the* (*cyclic*) *radicals from alkynes*. The e.s.r. parameters for the substituted cyclopentane- and tetrahydrofuran-derived radicals reported here lend considerable support to our assignment to cyclic species of signals detected in the reaction of butynedioic acid with $^{\bullet}CH_2CMe_2OH$ (**3**), $^{\bullet}CH_2CMe_2CH_2OH$ (**5**), and related radicals. For example, the general pattern and magnitude of the β-proton splittings detected from (**3**) and (**5**) [3.23, 3.25, and 2.55 mT; 3.75, 3.15, and 2.50 mT, respectively] show a very close resemblance to those of the corresponding carboxy-conjugated radical (**30**) (4.10, 3.39, 2.34 at low pH) [*cf.* also the pattern for (**32**)].

For those reactions in which radicals with two β-proton splittings are obtained, the parameters for (**7**) and (**15**) (3.49 and 3.35, 3.54, and 3.35 mT, respectively) suggest that ring closure leads mainly to radicals in which the substituents at C-2 and C-5 (OH and $CO_2H$) are *trans* to each other [*cf.* (**36**)]. This is probably also true for (**17**) (3.51 and 2.71 mT), though for (**11**) the splittings of 3.13 and 2.32 suggest the generation of a radical with *cis*-geometry, which is clearly appropriate for (**25**) [with $a$(β-H) 4.32 and 2.28 mT]. A more complete mechanistic and conformational analysis should involve detailed assignment of all structures (including minor species) and consideration of the possible influence of other substituents around the ring (*e.g.* in affecting ring geometry and the ease of interconversion of different conformations): this is not justified on the basis of available evidence. However, it may be significant first that the preferred addition to give the *trans* product [for (**7**), (**11**), and (**15**)] maximizes the torsion angle between the $^{\bullet}C(1)-CO_2H$ and $C(2)-OH$ bonds (which would be almost eclipsed for the *cis*-addition); secondly, these *trans*-isomers possess two (pseudo) equatorial substituents at C-2 and C-5, which is likely to be the most stable configuration (a preference possibly reflected in the transition state for formation).

## Conclusions

We have demonstrated that vinyl radicals generated by addition of some simple alkyl radicals (*e.g.* $^{\bullet}CHOHEt$, $^{\bullet}CH_2CMe_2OH$) to butynedioic acid undergo rapid 1,5-shifts, with $k > 10^4\ s^{-1}$; evidence has been obtained for steric and electronic assistance (*e.g.* as indicated by the behaviour of radicals from t-butyl alcohol and propane-1,3-diol, respectively). 1,6-Shifts (with $k$ *ca.* $10^5\ s^{-1}$) are also evidently similarly encouraged, as indicated by the reaction of vinyl radicals from $^{\bullet}CH_2OCMe_3$ and $^{\bullet}CH(OH)CH_2CH_2OH$. The ease of 1,5- and 1,6-hydrogen abstraction is believed to reflect the reactivity bestowed upon the initial vinyl radicals by the $sp^2$ hybridization of the unpaired electron (and it is also suggested that the necessary *cis*-geometry is achieved *via* rapid *cis–trans* isomerization).

Although in only one case [that of $^{\bullet}CH(OH)Et$] could the intermediate alkyl radical be detected, the presence of such radicals has been inferred by the detection of cyclized radicals (correct structural assignment of which is supported by the generation of radicals from model substrates). For pent-4-enyl-type radicals the ring closure is remarkable both for its rapidity ($>10^5\ s^{-1}$ in some cases) and its *endo*-regioselectivity. Thus it has been noted that the pent-4-enyl radical (**43**) might be expected to resemble hex-5-enyl and cyclize faster in the *exo*-mode [*via* kinetic (stereoelectronic) control in a transition state in which the orbital of the unpaired electron attacks from directly above the π* orbital] despite the expected lower stability of the *exo*-isomer (**44**).[12] A direct test of this hypothesis was not possible: whereas the radical (**43**) is directly detectable in steady-state experiments at 210 K (in cyclopropane),[24] attempts to generate it at room temperature and aqueous solution by the reaction of $CO_2^{-\bullet}$ with pent-4-enyl bromide (see *e.g.* ref. 25) failed to yield signals due to any of the radicals (**43**)—(**45**). Nevertheless we believe, with Beckwith and Ingold,[12] that any such cyclization is slow.

The apparent preference for *endo*-cyclization of the pent-4-enyl radicals described here [and the acceleration compared with (**43**)] is believed to reflect the stabilization thereby available in the delocalization of the unpaired electron onto the carboxy substituent: although no reliable thermochemical estimation appears to be available, e.s.r. measurements[26] indicate there to be a barrier of *ca.* 40 kJ mol$^{-1}$ to rotation about the $^{\bullet}C-C$ bond in radicals of the type $^{\bullet}CH_2-C(O)OR$. Although this stabilization would also be available for the *exo*-adduct, this would be expected to be outweighed by the strain involved in the formation of the smaller ring, as well as steric effects from addition at the disubstituted end of the double bond. The cyclization is not apparently readily reversible (since stereochemical integrity is preserved in the analogous radicals generated from cyclic substrates) so that we conclude that the crucial effect of the carboxy groups operates by lowering the energy of the transition state for *endo*-addition. It is perhaps significant that in related instances of ring closure (*e.g.* of[27] 4-phenylpent-4-enyl) such stabilization is also available.

Finally, for the *exo*-ring closure of the substituted hex-5-enyl radicals generated here, the ease of reaction is evidently associated with the ready achievement of a transition state in which the orbital of the unpaired electron can overlap with the π*-orbital of the double bond (in accordance with Beckwith's rules).[16] Though steric effects at the disubstituted carbon might be expected to provide a certain degree of inhibition, this may be more than offset by the incipient stabilization available *via* delocalization.

## Experimental

E.s.r. spectra were recorded with a Varian E-104 spectrometer equipped with an *X*-band klystron and 100 KHz modulation. Splitting constants were measured to within ±0.01 mT and *g* factors to within ±0.0001 by comparison with an aqueous solution of Fremy's salt [$a$(N) 1.309 mT,[28] $g$ 2.0055 (ref. 29)]. Relative radical concentrations were determined by spectrum simulation using a program supplied by Dr. M. F. Chiu. N.m.r. spectra were recorded with JEOL FX90Q ($^1H$ 90 MHz) and Bruker WP80 ($^1H$ 80 MHz) spectrometers and spectral simulation was achieved with the latter.

For the rapid-flow experiments, a mixing chamber was employed which allowed simultaneous mixing of three reagent streams *ca.* 50 ms before passage through the cavity of the e.s.r. spectrometer. The flow was maintained using a Watson-Marlowe 502 peristaltic pump positioned on the inlet tubing.

For experiments with $^{\bullet}OH$, the solutions used were as follows: stream (i) contained titanium(III) chloride (0.008 mol $\mathrm{dm}^{-3}$), stream (ii) contained hydrogen peroxide (0.024 mol $\mathrm{dm}^{-3}$), and the third stream contained the substrate (at a concentration up to 0.5 mol $\mathrm{dm}^{-3}$) together with butynedioic acid (up to 0.1 mol $\mathrm{dm}^{-3}$). For experiments at pH 1, concentrated sulphuric acid was added to stream (i); for basic conditions, EDTA (3 g $\mathrm{dm}^{-3}$) was added to stream (i) together with sufficient $NH_3$ to give the desired pH. In experiments with $SO_4^{-\bullet}$ at pH 8, stream (i) contained titanium(III) chloride (0.016 mol $\mathrm{dm}^{-3}$), EDTA (6 g $\mathrm{dm}^{-3}$), and ammonia, and stream (ii) contained sodium peroxydisulphate (0.025 mol $\mathrm{dm}^{-3}$). pH Measurements were made using a Pye-Unicam PW9410 pH meter with the electrode inserted into the effluent stream. All solutions were deoxygenated both before and during use by purging with oxygen-free nitrogen.

The chemicals employed were all commercial samples (tetrahydrofuran-2,3,4,5-tetracarboxylic acid was obtained from Aldrich Chemical Company Ltd.) and used as supplied.

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