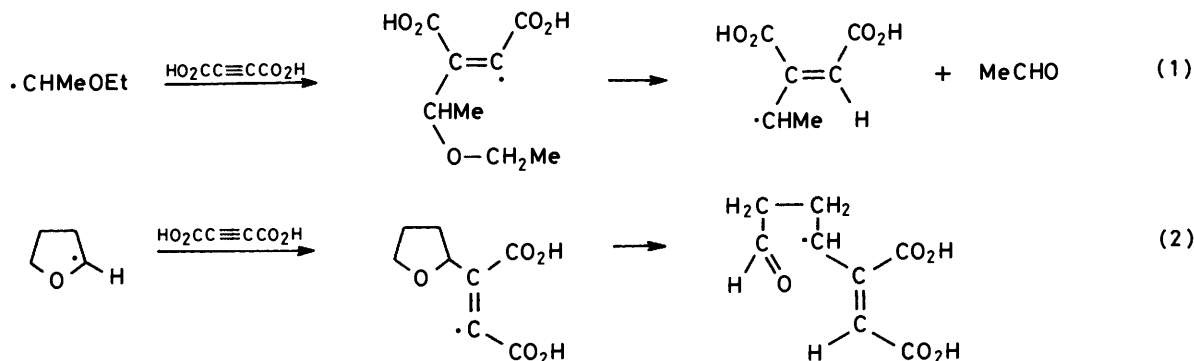# Fragmentation, Ring-opening, and Addition Reactions of Oxygen-conjugated Alkenyl Radicals derived by Rapid 1,5-Hydrogen Shifts in Vinyl Radicals. An Electron Spin Resonance and Kinetic Investigation

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The addition of ether-derived oxygen-conjugated radicals $\cdot CR^1R^2OCHR^1R^2$ to alkynes $R^3C\equiv CR^4$ leads to vinyl radicals, most of which undergo a rapid 1,5-shift ($k > 10^5$ s^{-1}) to give radicals $\cdot CR^1R^2OCR^1R^2CR^3=CHR^4$. The reactions of the latter species, as revealed by e.s.r. spectroscopy, include fragmentation (to give $R^1R^2C=O$ and $\cdot CR^1R^2CR^3=CHR^4$), ring-opening (e.g. for radicals from tetrahydrofuran and dioxane and their derivatives), and trapping via reaction with a further molecule of alkyne. A kinetic analysis is presented and results are interpreted in terms of the electronic and steric effects of substituents in the intermediates.

Examples of the diverse reactivity of vinyl radicals have been revealed by e.s.r. experiments involving the addition of first-formed radicals to alkynes. Thus a number of 1,4- and 1,5-hydrogen shifts have been shown to occur for vinyl radicals derived from thiols [1] and 1,6-shifts compete with 1,5-shifts (both leading to subsequent cyclization) in species derived from a variety of aliphatic carbon-centred radicals.[2] A particularly unusual sequence of reactions appears to occur for certain α-alkoxy-substituted radicals:[3] for example, $\cdot CHMeOEt$ (from diethyl ether) adds readily to butynedioic acid to give an intermediate vinyl radical which reacts rapidly via a 1,5-hydrogen shift, either concerted with or followed by fragmentation [as shown in reaction (1)]. The tetrahydrofuran-2-yl radical also reacts under similar conditions to give a resonance-stabilized allyl radical, presumably via an analogous ring-opening reaction mechanism [reaction (2)].
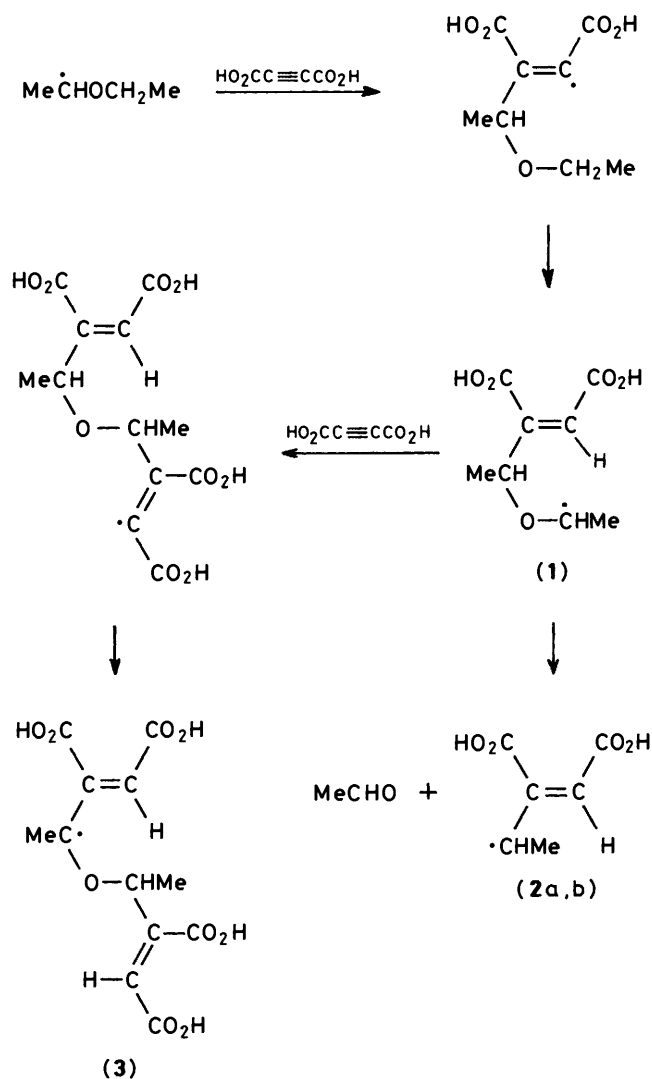
passage through the spectrometer cavity. Experiments were normally carried out at both pH ca. 1 and ca. 8, with a large excess of the added ether (RH) over the alkyne, so as to ensure scavenging of the hydroxyl radical (from Ti^{III}–H_2O_2) to give R·, the subsequent addition of which to the alkyne was to be studied.

(a) Reaction of Acyclic Ethers.—When butynedioic acid (2×10^{-3} mol dm^{-3})† was added in experiments involving an excess of diethyl ether at pH ca. 1, the e.s.r. signal from the major ether-derived radical $\cdot CHMeOEt$ was completely removed, that from $\cdot CH_2CH_2OEt$ being essentially unaffected. The removal of $\cdot CHMeOEt$ [consistent with the more rapid addition to the alkyne of radicals possessing an activating ($+M$) α-oxygen substituent] was accompanied by the appearance of a new spectrum with a(4 H) 1.25, a(1 H) 1.33 mT and g 2.0028 (cf. ref.

$$\cdot CHMeOEt \xrightarrow{HO_2CC\equiv CCO_2H} \quad \text{(1)}$$

$$\xrightarrow{HO_2CC\equiv CCO_2H} \quad \text{(2)}$$

In the investigation reported here we set out to determine the role of electronic and steric factors in governing the ease of abstraction, fragmentation, and ring-opening typified by reactions (1) and (2), and, in particular, to establish whether or not these processes involve discrete intermediate radicals formed via 1,5-shifts [e.g. (1) in Scheme 1].

Results and Discussion

An e.s.r. spectrometer was employed in conjunction with a continuous flow system in which three streams, containing titanium(III) (8×10^{-3} mol dm^{-3}), hydrogen peroxide (3×10^{-2} mol dm^{-3}), and the substrates were mixed ca. 40 ms before

3) as well as that from a minor radical with closely similar parameters: these are attributed to geometrical isomers of the allylic radical (2) (with restricted rotation about the C–C–C backbone: individual assignments cannot be unambiguously made). There was no evidence for the presence of pentadienyl species which would be formed by the addition of an initially formed vinyl radical to a second molecule of alkyne, as observed [4] for certain alkyl radicals (e.g. $\cdot Me$, $\cdot CH_2OH$): since the rate constant for such addition is ca. 10^6 dm^3 mol^{-1} s^{-1}, then the 1,5-shift (see Scheme 1) must occur with $k > 10^4$ s^{-1}.‡

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† Concentrations quoted are those after mixing.

‡ Here and elsewhere in this and related papers [1–4] we have represented the α-carboxyvinyl radicals with a conventional vinyl radical σ-structure: it has not been established unambiguously for radicals of this type whether the unpaired electron occupies an sp^2- or p-type orbital on the radical centre (see the detailed discussion in ref. 4).

MeĊHOCH$_2$Me $\xrightarrow{\text{HO}_2\text{CC}\equiv\text{CCO}_2\text{H}}$

HO$_2$C, CO$_2$H
C=C.
MeCH
O—CH$_2$Me

HO$_2$C, CO$_2$H
C=C
MeCH, H
O — CHMe
C—CO$_2$H
·C
CO$_2$H

$\xleftarrow{\text{HO}_2\text{CC}\equiv\text{CCO}_2\text{H}}$

HO$_2$C, CO$_2$H
C=C
MeCH, H
O—ĊHMe

(1)

HO$_2$C, CO$_2$H
C=C
MeĊ·, H
O—CHMe
C—CO$_2$H
H—C
CO$_2$H

(3)

MeCHO +

HO$_2$C, CO$_2$H
C=C
·CHMe, H

(2a,b)

Scheme 1.

On increasing [HO$_2$CC≡CCO$_2$H] to *ca.* 2 × 10^{-2} mol dm^{-3} the signals from the isomeric allyl radicals decreased in intensity and a new spectrum appeared: this, evidently also from an allylic species, shows splittings from four protons (1.19 mT), together with a smaller longer-range splitting (0.08 mT), and *g* 2.0033 (see Figure 1). At high pH, analogous behaviour was observed, though the splittings from the appropriate ionized radicals were slightly different from their protonated counterparts and the spectra obtained were sharper and more intense (presumably on account of the loss of unresolved hydroxy proton splittings and a reduced rate of bimolecular decay).

We propose that the new allylic species [which compared with (2) has one less α-proton splitting and an extra γ-proton splitting] is (3) (and its ionized counterpart at high pH), formed *via* attack of the intermediate radical (1) on a second molecule of alkyne, followed by a second rapid 1,5-hydrogen shift analogous to that involved in the formation of (1) (see Scheme 1). As with the formation of (1) the second 1,5-shift implied by this mechanism is probably assisted by the presence of the incipient α-oxygen substituent, as well as the producton of a delocalized allylic radical. Further evidence to support our structural assignment and mechanistic interpretation is given below. Reaction of ·CHMeOEt with propynoic acid gave only signals from the allyl radical (4) (see Table 1) formed *via* addition (to the unsubstituted end of the triple bond), 1,5-shift, and

fragmentation (rather than further addition) and similarly ·CMe$_2$OCHMe$_2$ (from di-isopropyl ether) gave only signals derived *via* addition, rearrangement, and fragmentation [(5) from butynedioic acid, (6) from propynoic acid]. These results suggest that *fragmentation* of the intermediate [*cf.* (1)], rather than addition to a second molecule of alkyne, is favoured by increasing alkylation at the radical centre.

This conclusion is supported by results for the radical ·CH$_2$OMe (from dimethyl ether). At relatively low concentrations of butynedioic acid (*ca.* 2 × 10^{-3} mol dm^{-3}) the reduction in [·CH$_2$OMe] was matched by the appearance of signals with similar parameters which appear to characterize the intermediate (7), detected presumably on account of an even slower rate of fragmentation than for (1) (Scheme 1). When the concentration of butynedioic acid was increased to *ca.* 10^{-2} mol dm^{-3} at high pH, signals from a second new radical appeared while those from (7) and ·CH$_2$OMe decreased in intensity. The observation of allylic splittings [*a*(2 H) 1.22 mT, together with *a*(2 H) 0.10 mT] and *g* 2.0031 (see Figure 2), characteristic of oxygen conjugation, as well as its appearance at higher [alkyne], support its assignment to radical (8) (formed by a mechanism analogous to that in Scheme 1). At low pH, similar behaviour was observed, with, in addition, a further radical detected at high alkyne concentrations with two large splittings (2.68, 3.38 mT) which appear to typify β-protons in an cyclic species (probably with a five-membered ring[2]). While unambiguous analysis for this species is not possible we suggest that cyclization of (8) or its immediate precursor may be involved. With propynoic acid at low pH radical (9) was detected, but no further signals at this or at high pH could be reliably assigned.

(b) *Reaction of Alicyclic Ethers with Two Oxygen Atoms.*— Signals from the two radicals derived by reaction of ·OH with dimethoxymethane, ·CH(OMe)$_2$, and ·CH$_2$OCH$_2$OMe, were removed on addition of butynedioic acid (2 × 10^{-3} mol dm^{-3}), to be replaced by spectra attributed to the allylic species (10) and (11), respectively (see Table 1). The mechanism for their formation is believed to involve addition, 1,5-shift, and fragmentation, as outlined for ·CHMeOEt in Scheme 1. A further allylic radical detected at high concentrations of alkyne (2 × 10^{-2} mol dm^{-3}) is attributed to (12), formed *via* interception of the intermediate ·CH(OMe)OCH$_2$C(CO$_2$H)=CHCO$_2$H by further addition to HO$_2$CC≡CCO$_2$H and a second 1,5-shift [*i.e.* by analogy with the formation of (3) in Scheme 1].

Particularly complex spectra were obtained from 1,2-dimethoxyethane and ·OH in the presence of butynedioic acid (*ca.* 2 × 10^{-3} mol dm^{-3}). The appearance at high pH of a signal similar to that of ·CH(OMe)CH$_2$OMe but with only *two* γ-proton splittings is attributed to the formation of (13) formed by reaction of ·CH$_2$OCH$_2$CH$_2$OMe and subsequent 1,5 hydrogen shift (see Scheme 2); detection of (11), most clearly identified at low pH, is in keeping with the subsequent fragmentation of (13) under acidic conditions. The other first formed radical, ·CH(OMe)CH$_2$OMe, is believed to be the precursor of a radical with two large β-proton splittings (3.00, 2.84 mT) which is assigned a cyclic structure (15). If this interpretation is correct then the reaction sequence to give (15) presumably again reflects a preference for 1,5-hydrogen shift (especially when assisted by the +*M* effect of a neighbouring oxygen atom: *cf.* Scheme 1) followed by rapid *endo* cyclization facilitated by polar effects (+*M* on the radical centre, −*M* on the alkyne) in the transition state. This is not an unexpected pathway in view of the relative reluctance of radical (7) to fragment and the ease of cyclization of radicals lacking the α-oxygen substituent.

Of the radicals detected from 2-methoxyethanol, ·CH$_2$OCH$_2$-CH$_2$OH and ·CH(OMe)CH$_2$OH behaved in a related manner: the former gave (16), from addition and 1,5-shift, and sub-
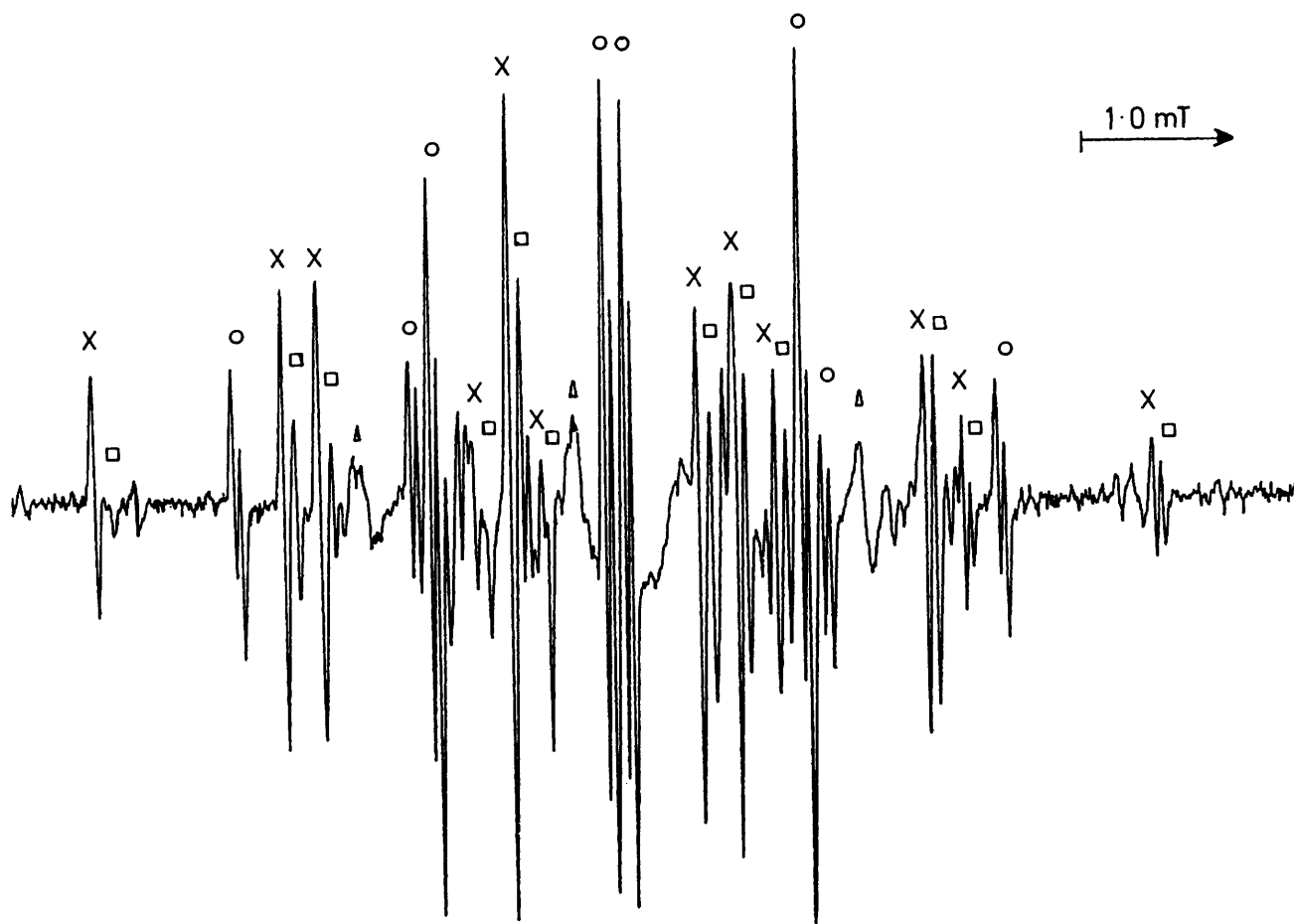
Figure 1. E.s.r. spectra of the radicals (2a) (X), (2b) (□), and (3) (○) formed in the reaction between ˙CHMeOEt and $HO_2CC\equiv CCO_2H$ at pH 8. Signals marked (△) arise from reaction of ˙OH with edta
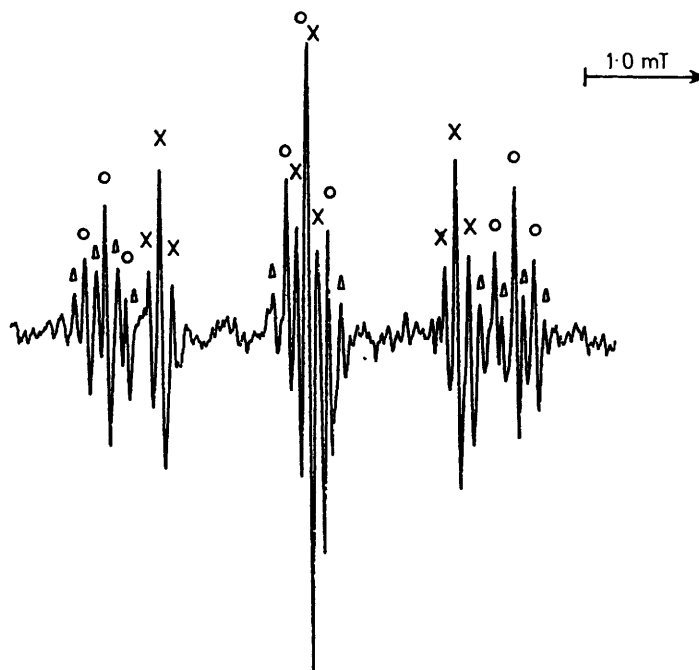
Figure 2. E.s.r. spectra of (7) (○) and (8) (X) derived from reaction of ˙CH$_2$OMe (△) with $HO_2CC\equiv CCO_2H$ at pH 8

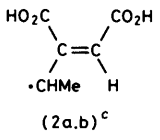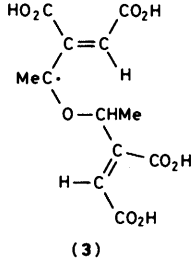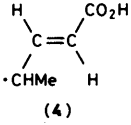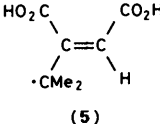**Table 1.** E.s.r. parameters of radicals detected *via* addition of acyclic ether-derived radicals to alkynes
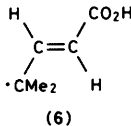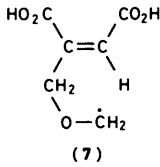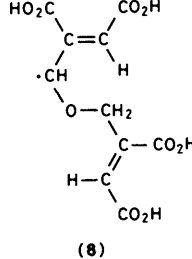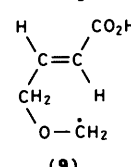
Substrate	Radical	Alkyne[a]	Radicals detected	pH	Hyperfine splittings (mT)[b]			g[c]
					a(α-H)	a(β-H)	a(other)	
Diethyl ether	•CHMeOEt	B	HO₂C–C(=C)(CO₂H), •CHMe H — **(2a.b)**[c]	0—2	1.33, 1.25	1.25(3)		2.0028
				8—10	1.29(2)	1.52(3)		2.0028
				0—2	1.50, 1.17	1.17(3)		2.0027
				8—10	1.25(2)	1.48(3)		2.0027
		B	HO₂C–C(=C)(CO₂H), MeC•–O–CHMe–C(CO₂H)=CH–CO₂H — **(3)**	0—2	1.19	1.19(3)	0.08	2.0033
				8—10	1.17	1.30(3)	0.05	2.0033
		P	H–C(=C)(CO₂H), •CHMe H — **(4)**	0—2	1.26, 1.21	1.51(3)	0.30	2.0029
Di-isopropyl ether	•CMe₂OCHMe₂	B	HO₂C–C(=C)(CO₂H), •CMe₂ H — **(5)**	0—2	1.22	1.37(3), 1.10(3)		2.0029
				8—10	1.19	1.42(3), 1.15(3)		2.0029
		P	H–C(=C)(CO₂H), •CMe₂ H — **(6)**	0—2	1.14	1.36(3), 1.18(3)	0.28	2.0029
Dimethyl ether	•CH₂OMe	B	HO₂C–C(=C)(CO₂H), CH₂ H, O–ĊH₂ — **(7)**	0—2	1.70(2)		0.16(2)	2.0031
				8—10	1.69(2)		0.16(2)	2.0031
		B	HO₂C–C(=C)(CO₂H), •CH–O–CH₂–C(–CO₂H)=CH–CO₂H — **(8)**	0—2	1.25, 1.19		0.06(2)	2.0031
				8—10	1.22(2)		0.10(2)	2.0031
			Unassigned[d]	0—2		2.68, 3.38	0.25	2.0031
		P	H–C(=C)(CO₂H), CH₂ H, O–ĊH₂ — **(9)**	0—2	1.70(2)		0.17(2)	2.0031

Table 1 (*continued*)
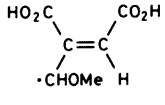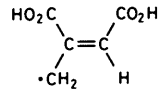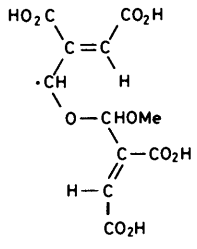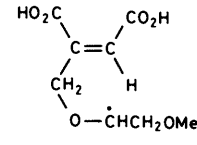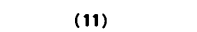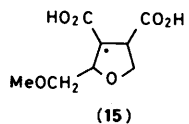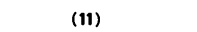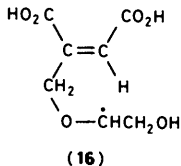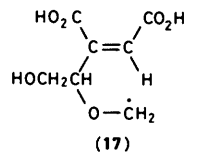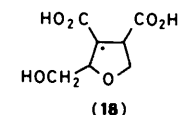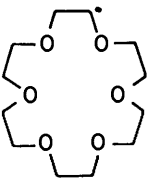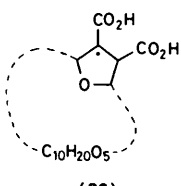
Substrate	Radical	Alkyne[a]	Radicals detected	pH	a(α-H)	a(β-H)	a(other)	g[c]
Dimethoxy-methane	·CH(OMe)₂	B	(10) HO₂C–C=C–CO₂H, ·CHOMe, H	1—2	1.25, 1.00		0.13(3)	2.0031
				8—10	1.27, 1.05		0.12(3)	2.0031
	·CH₂OCH₂OMe	B	(11) HO₂C–C=C–CO₂H, ·CH₂, H	1—2	1.46, 1.25, 1.23			2.0028
				8—10	1.41, 1.33, 1.26			2.0031
			(12) HO₂C–C=C–CO₂H, ·CH, O—CHOMe, C—CO₂H, H—C, CO₂H	1—2	2.15[e]		0.12	2.0031
				8—10	2.34[e]		0.12	2.0032
1,2-Dimethoxy-ethane	·CH₂OCH₂CH₂OMe	B	(13) HO₂C–C=C–CO₂H, CH₂, H, O—·CHCH₂OMe	8—10	1.77	0.88(2)	0.17(2)	2.0031
			(11)	1—2				
	·CH(OMe)CH₂OMe	B	(15) HO₂C–CO₂H ring, MeOCH₂, O	0—2		3.00, 2.84		2.0031
2-Methoxy-ethanol	·CH₂OCH₂CH₂OH	B	(11)	1—2				
			(16) HO₂C–C=C–CO₂H, CH₂, H, O—·CHCH₂OH	8—10	1.77	0.88(2)	0.09(2)	2.0031
	·CH(OMe)CH₂OH		(17) HO₂C–C=C–CO₂H, HOCH₂CH, H, O—·CH₂	8—10	1.23(2)		0.06	2.0031
			(18) HO₂C–CO₂H ring, HOCH₂, O	0—2		5.62[f]		2.0031

Table 1 (*continued*)

Substrate	Radical	Alkyne[a]	Radicals detected	pH	Hyperfine splittings (mT)[b]			g[c]
					a(α-H)	a(β-H)	a(other)	
18-crown-6	(19)		(20)	0—4		3.45(2)		2.0031

[a] B = Butynedioic acid; P = propynoic acid. [b] ±0.01 mT: number of protons in parentheses (one unless indicated). [c] ±0.0001. [d] See text. [e] Sum of two α-proton splittings (individual values not assigned). [f] Sum of two β-proton splittings: see text.

Scheme 2.
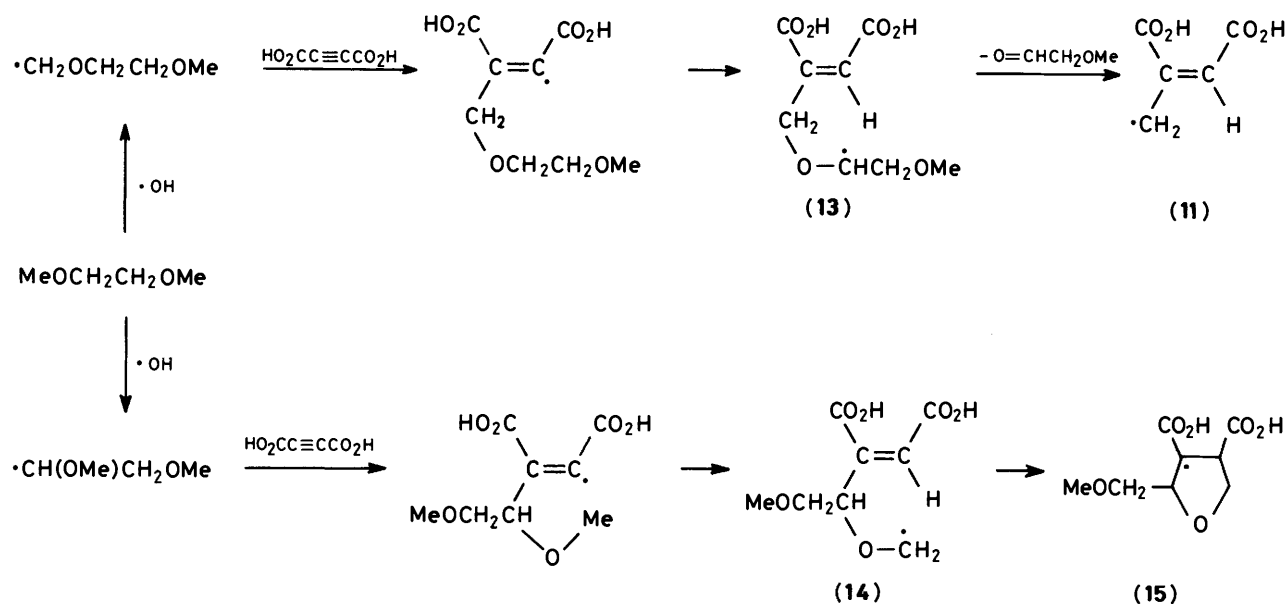
sequently (11), *via* fragmentation, while, for the latter, addition and 1,5-shift, to give (17), is also followed by *endo*-cyclization at low pH. [Conditions were arranged such that addition of 'CH(OMe)CH$_2$OH to butynedioic acid was competitive with its acid-catalysed rearrangement[5] to 'CH$_2$CH(OH)OMe, which was also detected.]

The cyclic ether 18-crown-6 was also chosen as substrate since its reaction with 'OH leads to the formation of a single (α,β-dioxygen-substituted) radical (19), with a(2 H) 0.88, a(2 H) 0.19, a(1 H) 1.74 mT, g 2.0031. At pH <2, this was shown to undergo acid-catalysed fragmentation and hydration to give a species assigned the structure 'CH$_2$CH(OH)OR [R = CH$_2$CH$_2$(O-CH$_2$CH$_2$)$_4$OH], with a(2 H) 2.25, a(1 H) 1.88 mT, g 2.0026. In the presence of butynedioic acid, reaction of (19) led to the detection of a cyclized radical assigned the structure (20) (and evidently formed *via* addition, 1,5-shift, and cyclization).

Comparison of results for ethers containing one or two oxygens suggests that, following addition and 1,5-shift, the fragmentation of the resulting α-alkoxy-substituted intermediate 'CR^{1}R^{2}OCR^{1}R^{2}C(CO$_2$H)=CHCO$_2$H is assisted by alkyl substitution [Pr$^i_2$O > Et$_2$O > Me$_2$O], presumably reflecting increased stabilities of the resultant allyl radicals and carbonyl moieties, but retarded by a β-oxygen substituent [*cf.* radicals

(13) and (16)]. Additional α-oxygen substituents, either in the intermediate radical or resulting allyl radical, appear to accelerate fragmentation, as judged by the behaviour of radicals from dimethoxymethane.

(c) *Addition of Cyclic Ether-derived Radicals.*—At pH 1, reaction of tetrahydrofuran-2-yl with butynedioic acid (10^{-3} mol dm^{-3}) gives (22), presumably *via* addition followed by 1,5-shift to give (21) and subsequent rapid ring-opening (see Table 2 and Scheme 3). In experiments at high pH and with higher concentrations of alkyne (up to *ca.* 2 × 10^{-2} mol dm^{-3}) signals from (22) were found to be largely replaced by those of two new allylic species, the major one of which is characterized by one less α-coupling than (22), two larger β-proton couplings, and a γ-proton splitting pattern dominated by a doublet (0.13 mT). These parameters, and those of the minor species, are attributed (as with the analogous observations for Et$_2$O) to isomers of radical (23) formed by interception of (21) by the alkyne and subsequent 1,5-shift; the β-proton splittings are, as expected on account of allylic delocalization, lower than for non-conjugated five-membered cyclic radicals, and the larger γ-proton splittings are typical of γ-CH protons adjacent to oxygen in tetrahydro-furan-2-yl radicals. Detection of the isomeric radicals only at

Table 2. E.s.r. parameters of radicals detected following addition of cyclic ether-derived radicals to butynedioic acid and propynoic acid[a]
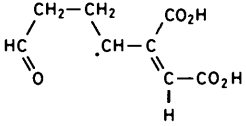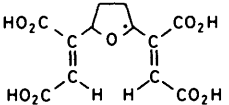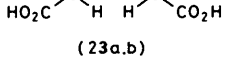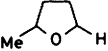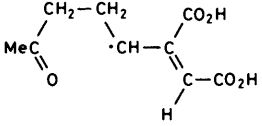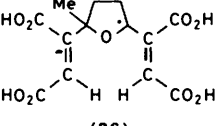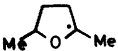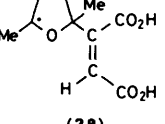
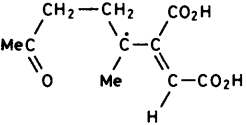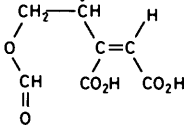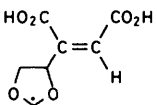| Substrate	Radical	Radical formed	pH	Hyperfine splittings (mT)[b]			g^c
				$a(\alpha\text{-H})$	$a(\beta\text{-H})$	a(other)	
Tetrahydrofuran	(structure)	(22)	0—10	1.28, 1.20	1.20(2)	0.08(2)	2.0030
		(23a,b)	8—10	1.18	1.59, 1.50	0.13, 0.04(2)	2.0035
			8—10	1.18	1.30, 1.06	0.20, 0.04(2)	2.0036
2-Methyltetra-hydrofuran	(24)	(25)	0—2	1.31, 1.29	1.17(2)		2.0030
		(26)	8—10	1.18	1.94, 1.19	0.10, 0.04	2.0036
2,5-Dimethyltetra-hydrofuran	(27)	(28)	0—2		1.18(3), 1.98, 0.88		2.0032
		(29)	0—2	1.25	1.39(3), 0.72(2)		2.0031
1,3-Dioxolane	(30)	(31)	0—2	1.17(2)	1.34(2)	0.09	2.0027
			8—10	1.15(2)	1.28(2)	0.12	2.0027
		(32)	0—2	0.93		0.10(2), 0.20	2.0031
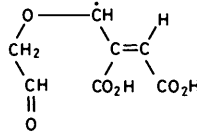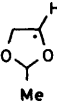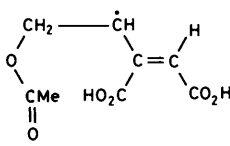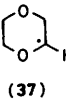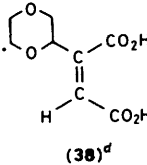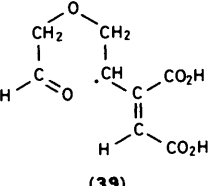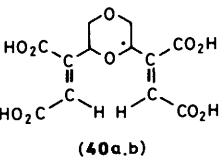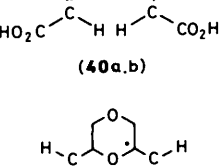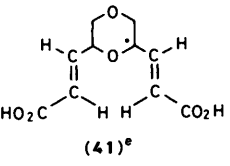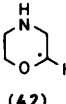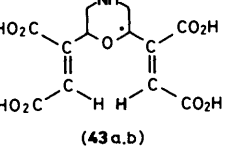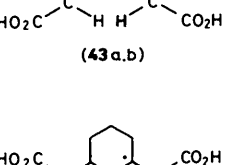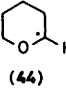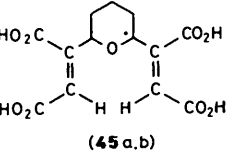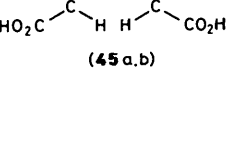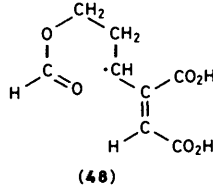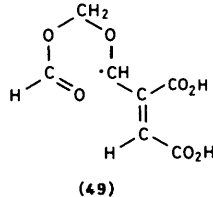
Table 2 (*continued*)

Substrate	Radical	Radical formed	pH	a(α-H)	a(β-H)	a(other)	g^c
	(33)	(34)	8—10	1.15(2)		0.07(2)	2.0034
2-Methyl-1,3-dioxolane	(35)	(36)	0—2	1.21(2)	1.21(2)		2.0032
1,4-Dioxane	(37)	(38)^d	0—2	1.72	4.55($\beta_1 + \beta_2$)		2.0031
		(39)	0—2	1.33, 1.24	1.33(2)		2.0031
		(40a,b)	0—2	{ 1.23	1.46, 1.30	0.17	2.0034
				1.17	1.34, 1.15	0.26	2.0035
			8—10	{ 1.18	1.34, 1.26	0.14	2.0034
				1.00	1.35, 1.00	0.22	2.0035
		(41)^e	0—2	1.19	1.49, 1.16	0.18, 0.15	2.0033
Morpholine	(42)	(43a,b)	0—2	1.24	1.35, 1.04	0.20, 0.21(N)	2.0034
			0—2	Spectral width 4.28			2.0032
Tetrahydropyran	(44)	(45a,b)	{ 0—2	1.07	1.35, 0.97	0.32	2.0035
			8—10	1.13	1.28, 0.91	0.20	2.0035
			{ 0—2	1.18	1.42, 1.22	0.22	2.0034
			8—10	1.17	1.64, 1.03	0.14	2.0034

Hyperfine splittings (mT)^b

Table 2 (*continued*)

Substrate	Radical	Radical formed	pH	Hyperfine splittings (mT)[b]			g^c
				$a(\alpha\text{-H})$	$a(\beta\text{-H})$	$a(\text{other})$	
1,3-Dioxane	(46)	(48)	0—2	1.33, 1.29	1.16(2)		2.0029
			8—10	1.36, 1.30	1.29(2)		2.0029
1,3,5-Trioxane	(47)	(49)	0—2	1.31, 1.12		0.05(2)	2.0032
			8—10	1.37, 1.26		0.04(2)	2.0032
		(50)[e]	0—2	1.21(2)		0.23, 0.05(2)	2.0032

[a] Reaction with butynedioic acid except where indicated otherwise. For conditions, see text. [b] ±0.01 mT. Number of protons in parenthesis (one unless otherwise indicated). [c] ±0.0001. [d] Approximate values. [e] Reaction with propynoic acid.

high pH is presumably a consequence of the high negative charge and longer lifetime.

2-Methyltetrahydrofuran behaved similarly. Thus signals from (24), dominant in the spectrum from ·OH and this substrate, were replaced following addition of butynedioic acid by those from (25) at low pH, and (26) at high pH. With 2,5-dimethyltetrahydrofuran the spectrum from (27) was replaced at pH 1 by that from two new radicals: one of these appears to be the ring-opened allylic radical (29), the other being assigned to its precursor (28). No further information was obtained at high pH [we note that if addition of (29) to alkyne were to occur, a subsequent 1,5-shift from a position activated by oxygen would now be impossible].

Reaction of (30), from 1,3-dioxolane, gave (31), as previously noted,[3] together with signals which were identified as those from the precursor (32): it was also possible to identify the acyclic radical (34), presumably formed by addition of (33) to $HO_2CC{\equiv}CCO_2H$, followed by 1,5-hydrogen shift and ring-opening. With 2-methyl-1,3-dioxolane, the spectrum of (36) replaced that of (35). For none of the dioxolane-derived radicals was an intermediate radical trapped with a second molecule of alkyne (unlike tetrahydrofuran-derived radicals). This presumably reflects a faster rate of ring-opening for the radical with two ring-oxygen atoms.

The detection of an allyl radical in the reaction between ·OH and 1,4-dioxane in the presence of butynedioic acid has been tentatively interpreted in terms of a 1,3-shift in the initially formed vinyl radical.[3] In view both of the lack of further evidence to support this interpretation (as far as we are aware, no examples of 1,3-shifts in solution have been established) and of the contrast with the reactions of tetrahydrofuran-derived analogues, we re-examined this reaction, particularly as a function of alkyne concentration. As [$HO_2CC{\equiv}CCO_2H$] was
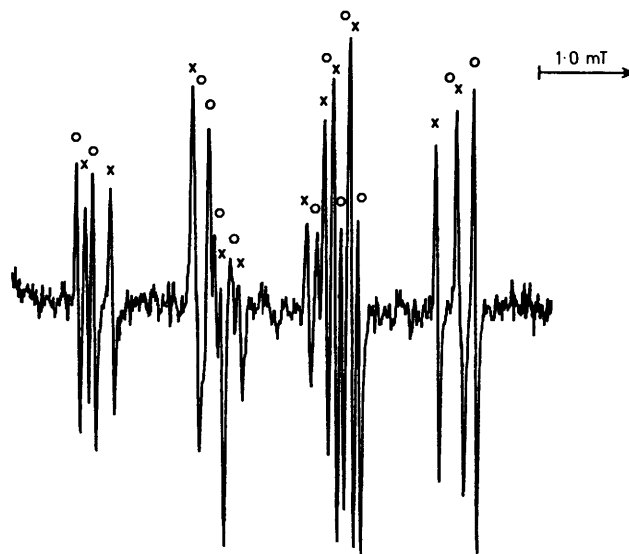
Figure 3. E.s.r. spectra of (40a) (○) and (40b) (X) formed by reaction of 1,4-dioxanyl (37) with $HO_2CC{\equiv}CCO_2H$ (2 × 10⁻² mol dm⁻³) at pH 1

gradually increased to *ca.* 2 × 10⁻³ mol dm⁻³ in experiments at pH *ca.* 1 a reduction in (37) was accompanied by the appearance of two spectra. One, clearly identified in the wings of the spectrum, has parameters and overall width closely similar to that of (37) itself, and is assigned to (38) (individual β-proton splittings could not be assigned); the second has allyl-type parameters bearing a close resemblance to those for the ring-
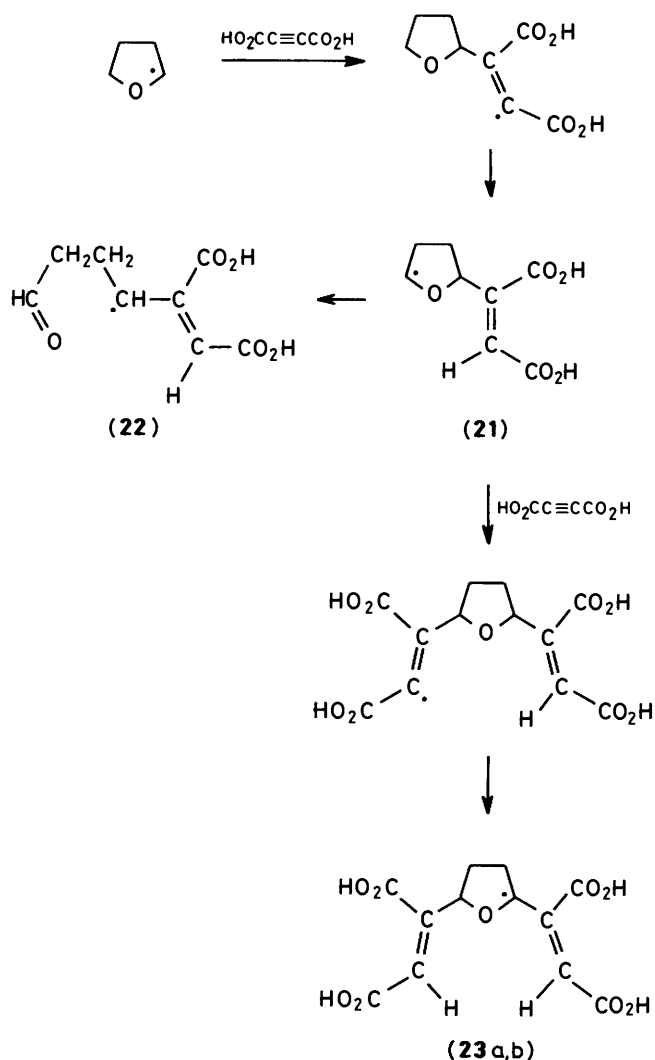
Scheme 3.

Scheme 4.

opened species (22), derived from tetrahydrofuran, and is assigned structure (39). Addition of (37) to butynedioic acid is evidently followed by 1,5-shift [to give (38)] and subsequent, relatively slow, ring-opening, so that both (38) and (39) are detected together (*i.e.* with a rate constant for ring-opening of *ca.* 10^3 s^{-1}). When [$HO_2CC\equiv CCO_2H$] was further increased, the signals from (37)—(39) were completely replaced (for [alkyne] 2×10^{-2} mol dm^{-3}) by signals from two (isomeric) radicals with closely similar splittings (and as noted previously; see Figure 3). The reassignment to (40a, b) is indicated not only by analogy to that for (23), from THF, and (3), from diethyl ether, and by the magnitude of the α, β, and γ-proton splittings but also by the evidence for involvement in their formation of *two* molecules of alkyne. A reaction mechanism analogous to Scheme 3 is proposed to account for these observations [but with slower ring opening of (38) compared with (21), for which the increased rate may reflect greater strain in the five-membered ring]. A kinetic analysis of this reaction sequence (Scheme 4) is described below.

In experiments with (37) at high pH, particularly intense signals of the ionized counterparts of (40a and b) were obtained, though analogues of (38) and (39) were not seen; (37) also reacted with propynoic acid to give signals assigned to the analogous species (41) (though signal intensities were much lower with this substrate). Similar behaviour was noted for the
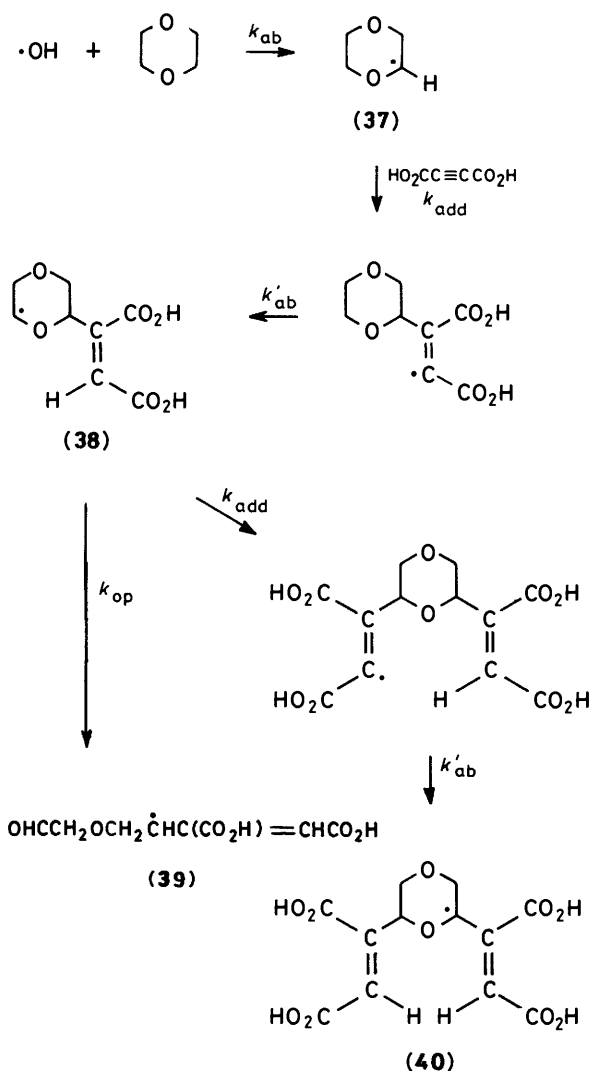
oxygen-conjugated radicals from morpholine [radical (42) gave isomers (43a and b)] and tetrahydropyran [(44) gave (45a and b)] which indicates that reaction is independent of the γ-substituent in the six-membered ring.

In contrast, the radicals (46) and (47) from 1,3-dioxane and 1,3,5-trioxane gave ring-opened radicals (48) and (49), respectively [the latter substrate also gave signals assigned to (50) from reaction with propynoic acid]. The failure to trap radicals prior to ring-opening, even at high [alkyne], is attributed to their faster fragmentation rates, which may reflect both the extra conjugation to oxygen in either or both the allyl radical and carbonyl moiety.

Reaction of oxetane with ·OH led to the detection of only the oxygen-conjugated radical (51). Introduction of butynedioic acid (*ca.* 2×10^{-3} mol dm^{-3}) at both pH *ca.* 1 and 8 led to detection in its place of the vinyl radical (52), with $a(2H)$ 0.05 mT, g 2.0029 [see reaction (3)]: there was no evidence that this radical can undergo a 1,3-, 1,4-, or 1,5-shift, presumably on account of the unfavourable geometry involved. However, increasing [alkyne] to 2×10^{-2} mol dm^{-3} at low pH led to the removal of signals from (52) and their replacement by those attributed to the pentadienyl species (53), with $a(\alpha$-H) 1.11, $a(2$ H) 0.10 mT, g 2.0032 (*cf.* ref. 4), formed *via* addition to a second molecule of alkyne and subsequent shift (the addition is expected to be significantly retarded at high pH).
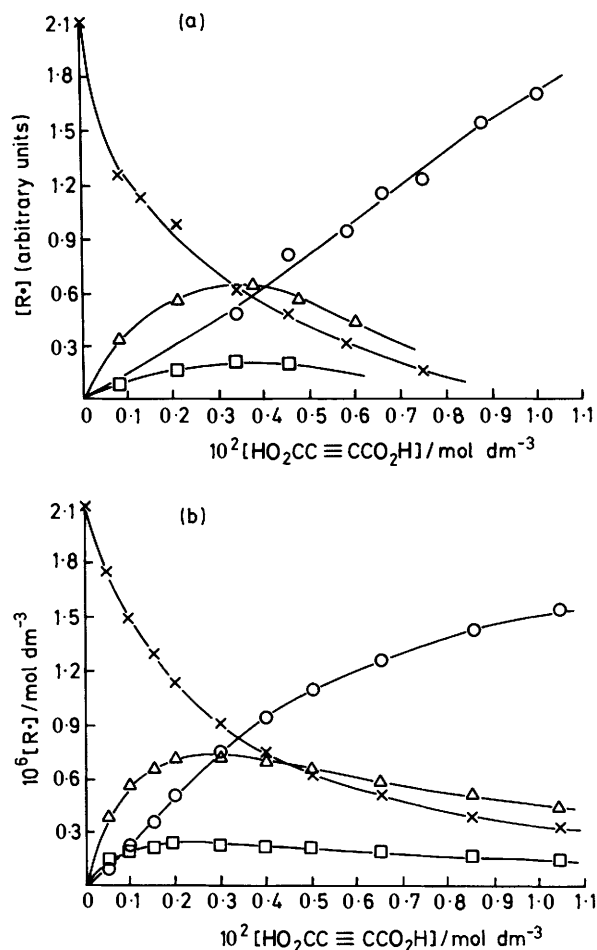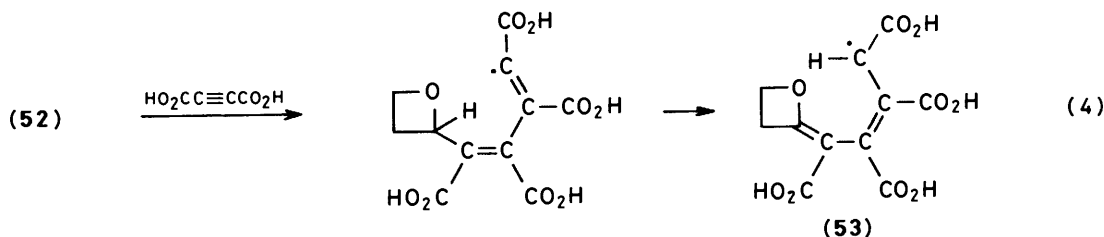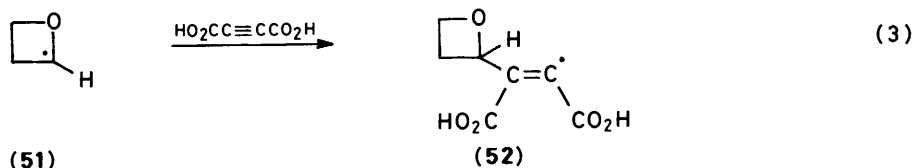
(3)

(51)   (52)

(52)   (4)

(53)

Figure 4. Experimental (a) and simulated (b) variation of [(37)] (X)], [(38)] (△), [(39)] (□)] and [(40)] (○) with butynedioic acid concentration in the reaction between 'OH, 1,4-dioxane, and HO₂CC≡C-CO₂H (pH ca. 1, mixing time 0.040 s: for the conditions, concentrations and rate constants, see text)

(d) *Kinetic Analysis.*—In order to provide further support for our mechanistic and structural interpretation we have determined the changes in absolute radical concentrations detected for the 1,4-dioxane reaction as a function of the concentration of alkyne; the observed values (see Figure 4a) have then been compared with those calculated on the basis of the mechanism shown in Scheme 4, using a kinetic simulation program (as employed previously).[1]

First the decrease in the original intensity of the 1,4-dioxanyl radical (37) was monitored for a series of low concentrations of $HO_2CC\equiv CCO_2H$ (up to 5 × 10⁻³ mol dm⁻³), conditions under which the bimolecular decay of (37) simply competes with its addition to alkyne. This behaviour was successfully simulated using k_{ab} [for the formation of (37) from 'OH] 2 × 10⁹ dm³ mol⁻¹ s⁻¹,[6] $2k_t$ for (37) 2 × 10⁹ dm³ mol⁻¹ s⁻¹,[7] $k(Ti^{III} + H_2O_2)$ 2 × 10³ dm³ mol⁻¹ s⁻¹,[8] a typical time after mixing of 0.040 s, and an optimum value of the rate of addition k_{add} 5 × 10⁶ dm³ mol⁻¹ s⁻¹. This is somewhat faster than the rate constant for simple alkyl radicals (ca. 10⁶ dm³ mol⁻¹ s⁻¹) which presumably reflects the effect of the electron-releasing ($+M$) oxygen substituent in accelerating addition to an alkyne with electron-withdrawing substituents.

Since the intermediate (38), detected at low [alkyne], has a similar structure to (37) around the radical centre, we assumed that its addition to $HOCC\equiv CCO_2H$ also has k 5 × 10⁶ dm³ mol⁻¹ s⁻¹. This value, together with those employed above, was next used in the simulation program with higher values of [alkyne] in an attempt to reproduce the observed behaviour, namely the competition between ring-opening of (37), to give (39), and addition, to give (40) (after 1,5-shift). Optimum agreement between observed and simulated behaviour (see Figures 4a and b) was obtained for k_{op} 1 × 10³ s⁻¹, with values of k_{ab} (for the 1,5-shifts) greater than a lower limit of ca. 10⁵ s⁻¹ (as concluded earlier on the basis of the lack of detection of pentadienyl species: for values of k_{ab} greater than this there was, as expected, no significant effect on the calculated concentrations of radicals). We also note that the lower limit of 10⁵ s⁻¹ for the rate constant for the 1,5-shift confirms the accelerating effect of the incipient α-oxygen substituent (cf. a value of ca. 10⁴ s⁻¹ for related radicals lacking this substituent) which may reflect either or both the electron-delocalizing effect of oxygen in the product radical or its polar ($+M$) effect on a transition state involving a relatively electrophilic vinyl radical.

The overall agreement between observed and simulated behaviour (Figure 4) supports the structural and mechanistic assignments presented earlier (Scheme 4).

(e) *Conclusions.*—Our results establish that oxygen-conjugated radicals add particularly rapidly to the alkyne butynedioic acid (k ca. 5 × 10⁶ dm³ mol⁻¹ s⁻¹) and that in most cases the resulting vinyl radical undergoes rapid 1,5-hydrogen transfer (k > 10⁵ s⁻¹). In both reactions oxygen appears to exert a rate-enhancing electronic effect. Inspection of models suggests that geometric factors are also important: whereas for the radicals from 1,4-dioxane and tetrahydrofuran the closest distance of approach for the vinyl-radical centre and the appropriate hydrogen is ca. 0.15 nm (with the alkene substituent axial or pseudoaxial respectively) the distance is much greater for

potential 1,6- or 1,4-shifts (*ca.* 0.25—3 nm); further, for the oxetanyl adduct, which fails to undergo even a 1,5-shift, the closest distance of approach for this reaction is 0.34 nm.

Whilst it has not been possible to achieve a *detailed* kinetic analysis of behaviour of the various related radicals $\cdot CR^1R^2OCR^1R^2C(CO_2H)=CH(CO_2H)$ generated in this way, we conclude that, for the cyclic analogue derived from 1,4-dioxanyl, ring-opening to give an allyl radical, with k 1×10^3 s^{-1}, is in competiton with further addition (5×10^6 dm^3 mol^{-1} s^{-1}). For tetrahydrofuran-2-yl, ring-opening is somewhat faster, presumably on account of strain in the ring, so that the intermediate is not detected and there is a requirement for higher [alkyne] to characterize addition. For the acyclic series, the formation of a discrete intermediate from the vinyl radical is followed by competition between addition (as above) and a related fragmentation process. Compared with the adduct from $\cdot CH_2OMe$, which, like those from 1,4-dioxane, has a fragmentation rate of *ca.* 10^3 s^{-1}, the rates of scission for the adducts from Et$_2$O and Pr$^i_2$O are considerably enhanced by alkylation.

Experimental

E.s.r. spectra were recorded on a Varian E-104 spectrometer equipped with X-band klystron and 100 kHz modulation. Hyperfine splitting 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,[9] g 2.0055[10]]. Relative radical concentrations were determined by spectrum simulation using a program supplied by Dr M. F. Chiu and modified for use on a BBC Microcomputer; absolute radical concentrations were determined by comparison with spectra obtained from standard solutions of vanadyl sulphate, *via* double integration with a Datalab DL 4000 microcomputer.

A mixing chamber was employed which allowed the simultaneous mixing of three reagent streams *ca.* 40 ms before passage through the cavity of the spectrometer: the flow was maintained using a Watson–Marlowe 502 peristatic pump positioned on the inlet tubing. The solutions used were as follows: stream (i) contained titanium(III) chloride (0.008 mol dm^{-3}), stream (ii) contained hydrogen peroxide (0.030 mol dm^{-3}), and the third stream contained the substrate (at a concentration of *ca.* 0.5 mol dm^{-3}) and butynedioic acid (up to 0.1 mol dm^{-3}) or propynoic acid. For experiments at pH *ca.* 1, concentrated sulphuric acid was added to stream (i); for basic conditions, edta (as its sodium salt; 3 g dm^{-3}) was added to stream (i) together with sufficient NH$_3$ (d 0.880) to give the desired pH. 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.

All chemicals employed were commercial samples used as supplied: butynedioic acid was obtained and used as its dipotassium salt.

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