EPR and computational studies of the formation and β-scission of cyclic and acyclic dialkoxyalkyl radicals

Alistair J. Fielding, Paola Franchi, Brian P. Roberts* and Teika M. Smits

Christopher Ingold Laboratories, Department of Chemistry, University College London, 20 Gordon Street, London, UK WC1H 0AJ

EPR spectroscopy and density functional theory have been applied to study the formation and subsequent β-scission of a series of dialkoxyalkyl radicals. Abstraction of hydrogen by photochemically-generated *tert*-butoxyl radicals from acyclic acetals $R^1O(R^2O)CHR^3$, and from cyclic analogues derived from diols, takes place mainly from the acetal carbon atom to give radicals of the type $R^1(R^2O)\dot{C}R^3$ and relative rates of abstraction have been determined in competition experiments. When R^3 = phenyl or vinyl, the activating influence of these substituents on hydrogen-atom abstraction is smaller than might be expected, probably because delocalisation of the unpaired electron on to the unsaturated group comes at the expense of planarisation at C_a, in opposition to the natural pyramidalising tendency of the two α-alkoxy groups. Absolute rate constants and Arrhenius activation parameters for β-scission of $R^1O(R^2O)\dot{C}R^3$ have been determined by a steady-state EPR method and the results can be understood in terms of angle-strain and stereoelectronic effects. β-Scission of selected cyclic dialkoxyalkyl radicals that carry a phenyl or vinyl substituent at the radical centre has been investigated using density functional theory at the UB3LYP/6-31G(d,p) level. Computed activation parameters are in good agreement with the experimental results, where comparison is possible. Both experiment and theory indicate that benzylic 2-phenyl-1,3-dioxan-2-yl radicals undergo β-scission more readily than the corresponding allylic 2-vinyl-1,3-dioxan-2-yl radicals.

Ongoing research in our laboratory is concerned with the application of polarity-reversal catalysis[1] (PRC) by thiols to mediate the radical-chain deoxygenation of alcohols, diols and related compounds.[2–4] For example, in the presence of an initiator and a thiol catalyst, an acetal **1** formally derived from two alcohols R^1OH and R^2OH (or from the diol HOR^1R^2OH) can undergo a radical-chain redox reaction that affords a reduced product R^1H and an ester of R^2OH, as shown in eqn. (1). In the case of
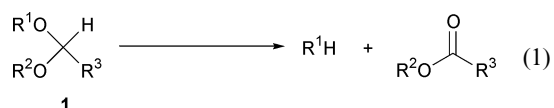
a cyclic acetal derived from a diol, the two product functional groups are joined, such that the overall reaction represents a redox rearrangement process.

The propagation stage of the chain mechanism is shown in Scheme 1 and abstraction of hydrogen from the acetal by the thiyl radical (step a) and β-scission of dialkoxyalkyl radical **2** (step b) are key elementary processes that must both be rapid
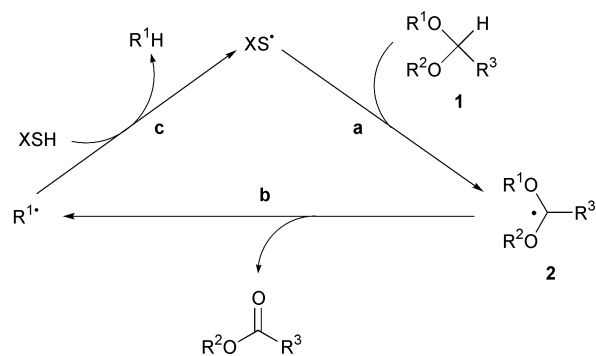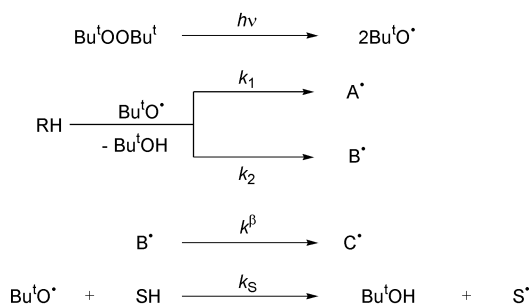
Scheme 1

if the overall reaction is to be effective; step c is uniformly fast for abstraction of hydrogen from thiols by simple alkyl radicals. In general, in order to plan successful radical-chain reactions it is necessary to understand the factors that are important in determining the rates of the elementary steps involved. In the present paper we report an EPR spectroscopic study of hydrogen-atom abstraction by *tert*-butoxyl radicals from acyclic and cyclic acetals to form the corresponding dialkoxyalkyl radicals. Although *tert*-butoxyl radicals abstract hydrogen much more rapidly from CH groups than do thiyl radicals, both species are electrophilic and their reactivity patterns should be qualitatively similar. We have also used EPR spectroscopy to determine the absolute rates of β-scission for selected dialkoxyalkyl radicals (Scheme 1, step b) and have carried out density functional calculations to compute the activation barriers for selected examples of these cleavage processes.

Results and discussion

Reaction kinetics

Relative rate constants were determined using well-established kinetic EPR methods,[5–7] in which transient radical intermediates are generated continuously and their steady-state concentrations are monitored directly. Di-*tert*-butyl peroxide (DTBP) was subjected to photolysis with high-intensity UV light in the presence of an acetal hydrogen-atom donor RH and, if appropriate, a reference hydrogen donor SH to permit the determination of the relative reactivity of RH. The relevant reactions are generalised in Scheme 2, where hydrogen abstraction from RH is shown as taking place at two sites to give radicals $A^{\bullet}$ and $B^{\bullet}$, respectively, and the radical $B^{\bullet}$ is transformed (by β-scission) into the radical $C^{\bullet}$. It is assumed that all the radicals present in detectable concentrations are removed at the diffusion-controlled rate by self- and cross-reactions with other such radicals with rate constants $2k_t$ and k_x, respectively, which are

Bu^{t}OOBu^t $\xrightarrow{h\nu}$ 2Bu^{t}O$^\bullet$

RH $\xrightarrow[\text{- Bu}^t\text{OH}]{\text{Bu}^t\text{O}^\bullet}$ $\left\{\begin{array}{l} \xrightarrow{k_1} \text{A}^\bullet \\ \xrightarrow{k_2} \text{B}^\bullet \end{array}\right.$

B$^\bullet$ $\xrightarrow{k^\beta}$ C$^\bullet$

Bu^{t}O$^\bullet$ + SH $\xrightarrow{k_S}$ Bu^{t}OH + S$^\bullet$

Scheme 2

independent of the nature of the radicals involved; it is further assumed that $2k_t = k_x$.[5-7] Under these conditions, eqns. (2) and (3) apply to the steady-state radical concentrations determined by EPR spectroscopy.

$$(k_1/k_2) = [\text{A}^\bullet]/([\text{B}^\bullet] + [\text{C}^\bullet]) \qquad (2)$$

$$(k_1/k_S) = ([\text{A}^\bullet]/[\text{S}^\bullet]) \times ([\text{SH}]/[\text{RH}]) \qquad (3)$$

In the absence of SH, the rate constant for β-scission of B$^\bullet$ can be determined relative to $2k_t$ using eqn. (4).[8,9] The value of

$$(k^\beta/2k_t) = ([\text{C}^\bullet]/[\text{B}^\bullet]) \times ([\text{A}^\bullet] + [\text{B}^\bullet] + [\text{C}^\bullet]) \qquad (4)$$

$2k_t$ for all the transient radicals is taken as equal to the corresponding value for the *tert*-butyl radical in the same solvent at the same temperature, obtained from the reliable measurements reported by Schuh and Fischer.[10] For *tert*-butylbenzene and fluorobenzene solvents, experimental values of $2k_t(\text{Bu}^{t\bullet})$ are not available and the published data for heptane solvent were scaled using solvent viscosities[11] according to eqn. (5).[10] The Arrhenius relationship for $2k_t$ obtained in this way by Walton[12] for *tert*-butylbenzene solvent is given in eqn. (6), where $\theta =$

$$2k_t(\text{Bu}^{t\bullet})_{\text{solvent}} = 2k_t(\text{Bu}^{t\bullet})_{\text{heptane}} \times (\eta_{\text{heptane}}/\eta_{\text{solvent}}) \qquad (5)$$

$$\log_{10} [2k_t(\text{PhBu}^t)/\text{M}^{-1}\,\text{s}^{-1}] = 12.17 - 14.64/\theta \qquad (6)$$

$2.303RT$ kJ mol^{-1}. The corresponding relationship for fluorobenzene, obtained by us in the same manner, is given in eqn. (7). Schuh and Fischer[10] have reported experimental values for $2k_t(\text{Bu}^{t\bullet})$ in 3-methylpentan-3-ol (3MP) and their results in the temperature range 330–370 K, appropriate for this work, conform to the Arrhenius relationship shown in eqn. (8).

$$\log_{10} [2k_t(\text{PhF})/\text{M}^{-1}\,\text{s}^{-1}] = 11.59 - 10.17/\theta \qquad (7)$$

$$\log_{10} [2k_t(\text{3MP})/\text{M}^{-1}\,\text{s}^{-1}] = 12.81 - 18.41/\theta \qquad (8)$$

Hydrogen-atom abstraction from acetals

Relative molar rate constants for abstraction of hydrogen from cyclic and acyclic acetals by *tert*-butoxyl radicals were determined by competition experiments at 229 K in fluorobenzene solvent. One of the two competing acetals was always either 1,3-dioxolane or 2-methyl-1,3-dioxolane, chosen to avoid line overlap with the radical(s) derived from the second acetal. Stock mixtures of the two compounds were made up by weight and aliquots were mixed with DTBP (15–20% v/v) and diluted with fluorobenzene; the total acetal concentration was *ca.* 1.5 M. The sample was cooled in an ice bath, to avoid evaporative loss, in a standard Suprasil quartz EPR tube and de-oxygenated by bubbling a fine stream of argon through the liquid. EPR spectra were monitored during continuous UV irradiation of samples positioned in the variable-temperature insert of the spectrometer; relative radical concentrations were determined

by double integration of appropriate lines and confirmed by computer simulation of the spectra. Relative rates of hydrogen-atom abstraction from the acetals **3**–**12** to give the radicals **13**–**25** were investigated and the results are summarised in Table 1. The radicals **26**–**36** were also generated in this work, either by hydrogen abstraction from the parent acetals or by β-scission of the dialkoxyalkyl radicals derived from them; the EPR parameters of all radicals are collected in Table 2.

The temperature-dependence of the rate constant k_3 for hydrogen-atom abstraction from 2-methyl-1,3-dioxolane **8** by *tert*-butoxyl radicals has been measured by Malatesta and Scaiano[13] using the laser-flash photolysis method and the Arrhenius relationship obtained is given in eqn. (9). Our EPR

$$\log_{10} (k_3/\text{M}^{-1}\,\text{s}^{-1}) = (8.63 \pm 0.26) - (8.74 \pm 1.34)/\theta \quad (9)$$

results show that abstraction of hydrogen from **8** takes place effectively exclusively from C(2) and so the value of k_3 at 229 K (4.34×10^6 M^{-1} s^{-1}) obtained from eqn. (9) can be used to put our relative rate data on to an absolute basis; these results are included in Table 1.

Abstraction of hydrogen from **3**–**5** takes place competitively from the acetal CH and *O*-methyl groups and the relative reactivities of **3** and **4** are essentially as expected on statistical grounds (entries 1 and 2). The methyl group attached to the acetal carbon atom in **5** (entry 3) exerts a significant activating effect on abstraction of the remaining tertiary hydrogen atom. The effect of the phenyl group at the acetal carbon atom in **6** (entry 4) is even more activating towards abstraction of the tertiary hydrogen and it was not possible to measure the much lower reactivity of the *O*-methyl groups. Cyclic and acyclic dialkoxyalkyl radicals, in which hydrogen or an alkyl group is attached to the trivalent carbon atom, are strongly pyramidal at this centre.[14,15] However, if an α-phenyl group is present then the radical centre is believed to be effectively planar.[16] Such planarity allows full benzylic delocalisation of the unpaired electron on to the phenyl group (as indicated by the ring-proton hyperfine splittings), but this comes at the expense of frustrating the inherent pyramidalising effect of the two α-oxygen substituents. Thus, the activating effect of the phenyl group in **6** is not as large as might be expected by comparison with molecules in which the product radical centre is naturally close to planar.

The high reactivity of the hydrogen atom attached to the acetal carbon C(2) in 1,3-dioxolane **7** (entry 5) is probably mainly a consequence of stereoelectronic effects.[13] Thus, the C(2)–H bonds subtend a relatively small and fixed dihedral angle with the lone pairs on the adjacent oxygen atoms and the transition state is effectively stabilised by charge transfer (polar effects) of the type [RO$^-$ H$^\bullet$ $^+$CH(OR)$_2$].[13,17] The activating effect of the 2-methyl group in **8** (entry 6) is similar to that found for the acyclic analogue **5** in comparison with **3**.

The relatively low reactivities of the C(2)–H groups in the benzylidene acetals **9** and **10** (entries 7 and 8), compared with that in 2-methyl-1,3-dioxolane **8**, is surprising at first sight, in view of the fact that the phenyl group in **6** is more activating than the 2-methyl group in acetal **5**. However, the radical centres in the cyclic benzylic radicals **22** and **23** are both planar[16] (see Table 2 and the computational section), which introduces angle strain into the 5- and 6-membered rings when hydrogen is abstracted from C(2) in their protic parents **9** and **10**. In contrast, the OCO angle in the acyclic analogue **19** derived from **6** is free to open to *ca.* 120°.

2-Vinyl-1,3-dioxolane **11** (entry 9) is intermediate in reactivity between the 2-phenyl analogue **9** and the 2-methyl analogue **8**. 2-Vinyl-1,3-dioxane **12** (entry 10) is similarly more reactive than 2-phenyl-1,3-dioxane **10** but, nevertheless, the 2-vinyl groups in **11** and **12** are still less activating than might be expected. The radical centres in the derived allylic radicals **24** and **25** must be near-planar (as judged from their EPR spectra) and presumably the reason for the relatively low reactivities of

Table 1 Relative and absolute rate constants for hydrogen abstraction from acetals by *tert*-butoxyl radicals in fluorobenzene at 229 K [a]

Entry	Acetal	Site of reaction	k(relative)	k(absolute)[b]/M^{-1} s^{-1}
1	(MeO)$_2$CH$_2$ **3**	CH_2	(1)	5.2×10^4
		CH_3O	1.0	5.2×10^4
2	Bu^{t}O(MeO)CH$_2$ **4**	CH_2	1.5	7.8×10^4
		CH_3O	0.6	3.1×10^4
3	(MeO)$_2$CHMe **5**	CHMe	3.4	1.8×10^5
		CH_3O	1.6	8.4×10^4
4	(MeO)$_2$CHPh **6**	CHPh	6.5	3.4×10^5
5	1,3-Dioxolane **7**	C(2)H_2	37	1.9×10^6
6	2-Methyl-1,3-dioxolane **8**	C(2)HMe	83	(4.3×10^6)
7	2-Phenyl-1,3-dioxolane **9**	C(2)HPh	40	2.1×10^6
8	2-Phenyl-1,3-dioxane **10**	C(2)HPh	48	2.5×10^6
9	2-Vinyl-1,3-dioxolane **11**	C(2)HVin	69	3.6×10^6
10	2-Vinyl-1,3-dioxane **12**	C(2)HVin	92	4.8×10^6

[a] Rate constants are *not* statistically corrected on the basis of the number of equivalent abstractable hydrogen atoms. [b] Obtained by taking the rate constant for abstraction from 2-methyl-1,3-dioxolane to be 4.34×10^6 M^{-1} s^{-1} at 229 K.

Table 2 EPR parameters for dialkoxyalkyl radicals and for the radicals produced by their β-scission

| Radical[a]	Solvent	T/K	Hyperfine splittings/G[b]
13	PhF	223	12.9 (1 H$_\alpha$), 0.81 (6 H$_\gamma$)
14	PhF	223	18.3 (2 H$_\alpha$), 0.78 (2 H$_\gamma$)
15	PhF	213	11.3 (1 H$_\alpha$), 0.91 (3 H$_\gamma$)
16	PhF	213	18.0 (2 H$_\alpha$), 0.87 (2 H$_\gamma$)
17	PhF	223	14.1 (3 H$_\beta$), 0.68 (6 H$_\gamma$)
18	PhF	223	17.8 (2 H$_\alpha$), 0.30 (1 H$_\gamma$)
19	PhF	223	6.15 (1 H$_p$), 5.04 (2 H$_o$), 1.60 (2 H$_m$), 0.23 (6 H$_\gamma$)
20	PhF	223	22.1 (1 H$_\alpha$), 1.46 (4 H$_\gamma$)
21	PhF	223	13.2 (3 H$_\beta$), 1.19 (4 H$_\gamma$)
22	PhF	223	6.88 (1 H$_p$), 5.25 (2 H$_o$), 1.64 (2 H$_m$), 0.96 (4 H$_\gamma$)
23	PhF	260	6.40 (1 H$_p$), 4.90 (2 H$_o$), 1.52 (2 H$_m$), 0.76 (4 H$_\gamma$)
24	PhF	200	15.06 (1 H), 14.32 (1 H), 2.26 (1 H), 1.20 (2 H), 0.84 (2 H)
25	PhF	229	13.97 (1 H), 13.36 (1 H), 2.70 (1 H), 0.68 (2 H), 0.56 (2 H)
26[c]	c-C$_3$H$_6$	233	21.3 (1 H$_\alpha$)
27[b]	PhH	353	21.8 (6 H$_\beta$), 0.7 (6 H$_\gamma$), 2.2 (CHO)
28	PhBu^t	203	6.93 (1 H$_p$), 5.32 (2 H$_o$), 1.68 (2 H$_m$), 1.16 (2 H$_\gamma$)
29	PhBu^t	388	23.3 (6 H$_\beta$), 15.9 (2 H$_\beta$)
30	PhBu^t	229	6.14 (1 H$_p$), 4.96 (2 H$_o$), 1.55 (2 H$_m$), 1.15 (2 H$_\gamma$)
31	PhBu^t	340	23.3 (6 H$_\beta$), 17.3 (2 H$_\beta$)
32[d]	PhBu^t	230	5.99 (1 H$_p$), 5.15 (2 H$_o$), 1.61 (2 H$_m$), 1.04 (2 H$_\gamma$)
33	PhBu^t	320	33.0 (4 H$_\beta$), 19.1 (2 H$_\beta$)
34[e]	PhBu^t	229	14.94 (1 H), 14.15 (1 H), 2.27 (1 H), 1.26 (2 H)
35[f]	PhBu^t	229	14.14 (1 H), 13.50 (1 H), 2.64 (1 H), 1.03 (2 H)
36	PhBu^t	229	6.47 (1 H$_p$), 5.25 (2 H$_o$), 1.70 (2 H$_m$)

[a] The g-values of all dialkoxyalkyl radicals are 2.0031 ± 0.0002; those of the alkyl radicals formed by β-scission are all 2.0028 ± 0.0001. [b] Generally ±0.05 G, except where the lines were relatively broad. However, simulations of the spectra of allylic and benzylic radicals were often very sensitive to the exact relationships between the coupling constants. [c] Ref. 20. [d] Relatively broad lines. [e] *syn*- and *anti*-Isomers were detectable; the coupling constants for the major (65%) isomer are given. The minor isomer (35%) showed 14.99 (1 H), 14.01 (1 H), 2.28 (1 H) and 0.91 (2 H). [f] The EPR spectra of the *syn*- and *anti*-isomers, assuming that both are present, could not be resolved within the line-width.

the allylic CH groups in **11** and **12** is analogous to that given for the low reactivity of the benzylic CH groups in the 2-phenyl derivatives. The low reactivities of **11** and **12** towards hydrogen-atom abstraction at C(2) are consonant with the relatively small amount of isomerisation of these acetals to the corresponding enol ethers observed under radical-chain conditions.[18] Both

results can be seen as a consequence of the strain developed in the rings when C(2) becomes a planar, sp^2-hybridised centre.

β-Scission of dialkoxyalkyl radicals

The β-scission processes shown in eqns. (10)–(15) were considered. Samples usually consisted of the acetal (*ca.* 15% v/v)
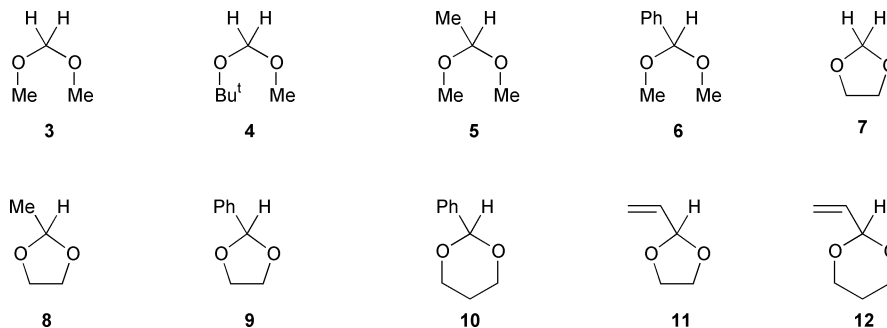
and DTBP (*ca.* 20% v/v) in fluorobenzene, *tert*-butylbenzene or 3-methylpentan-3-ol as solvent and absolute radical concentrations were determined by comparison with the signal obtained from a standard solution of 2,2,6,6-tetramethylpiperidine-*N*-oxyl (TEMPO) in fluorobenzene. Values of k^β over a range of temperatures, for which EPR spectra of both the parent radical and its β-scission product were detectable, were obtained using eqn. (4) in conjunction with the appropriate value of $2k_t$ derived from eqns. (6)–(8). The Arrhenius plots are shown in Figs. 1–6 and the linear regression lines correspond to
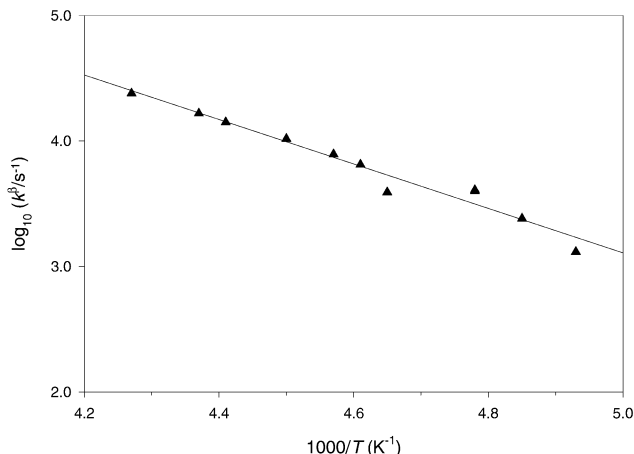
Fig. 1 Arrhenius plot for the β-scission of the *tert*-butoxy(methoxy)-methyl radical **15** in fluorobenzene

Fig. 2 Arrhenius plot for the β-scission of the 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl radical **26** in *tert*-butylbenzene

the activation parameters given in Table 3. For the dialkoxyalkyl radicals **15**, **28**, **30** and **32**, in which the alkoxy substituents differ, only cleavage of the tertiary carbon–oxygen bond was observed. For the dioxolanyl and dioxanyl radicals **20**–**25** without substituents on the alkoxy carbon atoms, β-scission was not detectable by EPR spectroscopy below *ca.* 390 K.
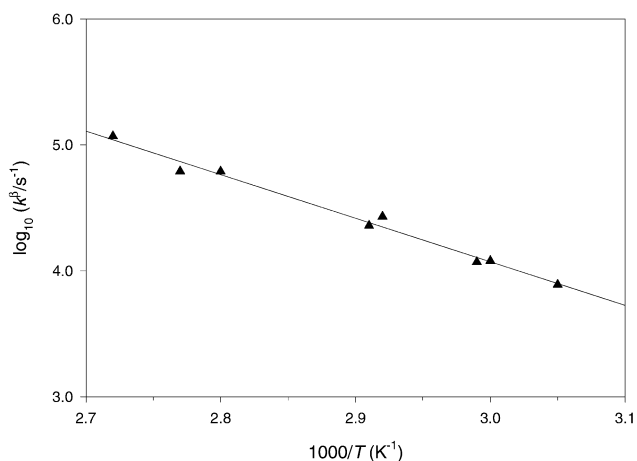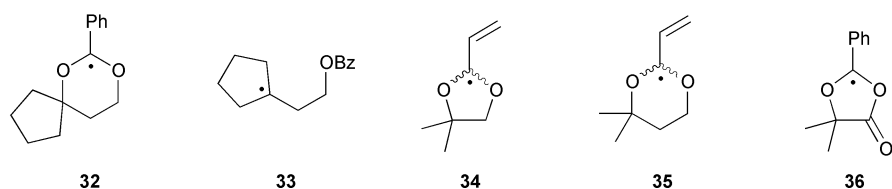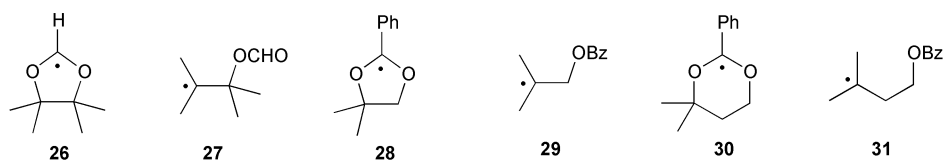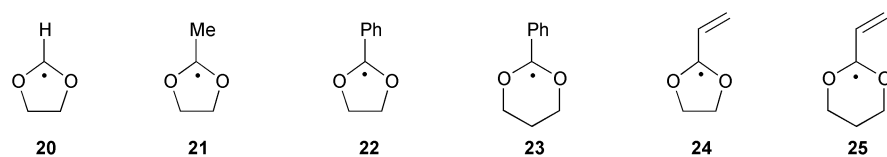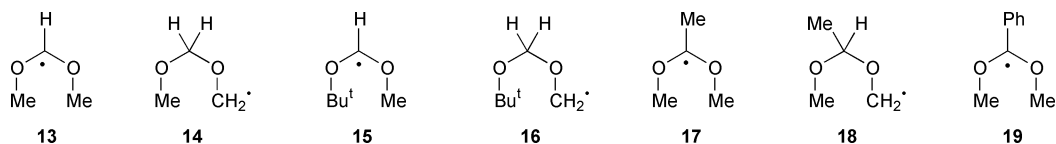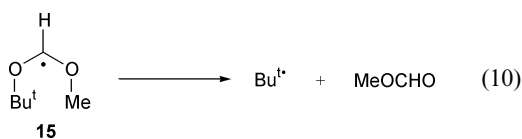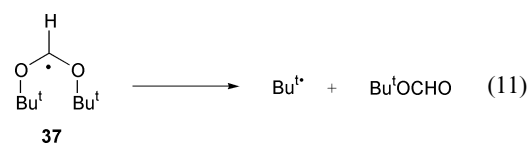

$$\text{(10)}$$

In this context, it is important not to focus solely on the nature of the radical centre in the product and caution must be exercised when qualitatively assessing the enthalpy changes associated with alternative modes of homolytic cleavage.[3,4] For example, while **31** contains a stabilised tertiary alkyl radical centre, it is also a primary alkyl benzoate. The alternative mode of β-scission of **30** would give $\text{BzOCMe}_2\text{CH}_2\text{CH}_2{}^\bullet$ and, although this species contains a less stabilised primary radical centre, it is also a tertiary alkyl benzoate. Since, provided steric crowding is unimportant, branched molecules are generally more stable than their straight-chain isomers,[11,19] the relative stabilities of the ester moieties will act to offset the relative stabilities of the alkyl radical moieties and tend to make the enthalpies of reaction for the two modes of cleavage for **30** more similar than would be anticipated by consideration of the radical centres alone. At the UB3LYP/6-31G(d,p) level (see
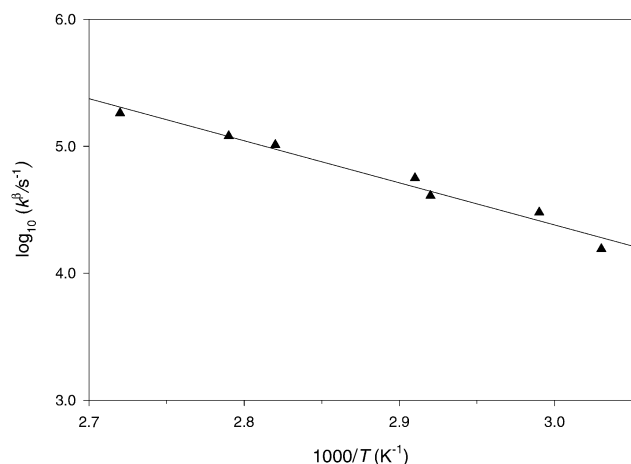

$$\text{(11)}$$

Fig. 3 Arrhenius plot for the β-scission of the 4,4,5,5-tetramethyl-1,3-dioxolan-2-yl radical **26** in 3-methylpentan-3-ol

Fig. 6 Arrhenius plot for the β-scission of the 2-phenyl-4,4-dimethyl-1,3-dioxan-2-yl radical **30** in *tert*-butylbenzene
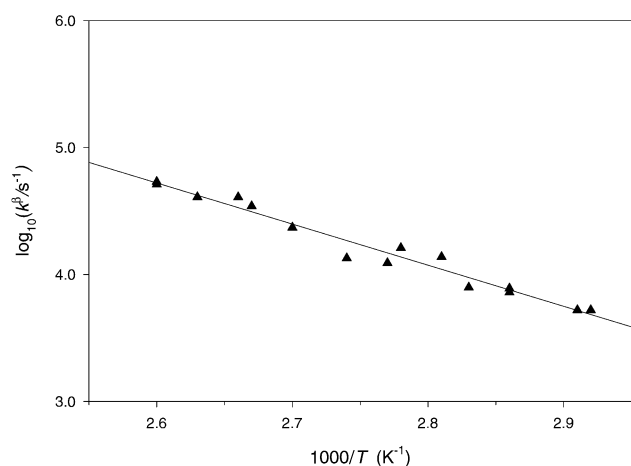

Fig. 4 Arrhenius plot for the β-scission of the 2-phenyl-4,4-dimethyl-1,3-dioxolan-2-yl radical **28** in *tert*-butylbenzene
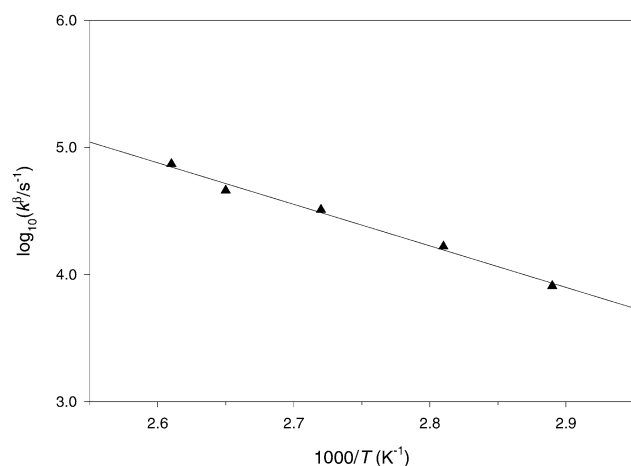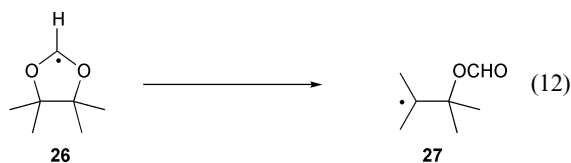

Fig. 5 Arrhenius plot for the β-scission of the 2-phenyl-4,4-dimethyl-1,3-dioxolan-2-yl radical **28** in 3-methylpentan-3-ol

computational section), the enthalpy of formation of the tertiary alkyl radical **31** is calculated to be lower than that of the primary radical $BzOCMe_2CH_2CH_2{}^{\bullet}$, but by only 14.7 kJ mol^{-1}, less than might be expected in view of the difference in
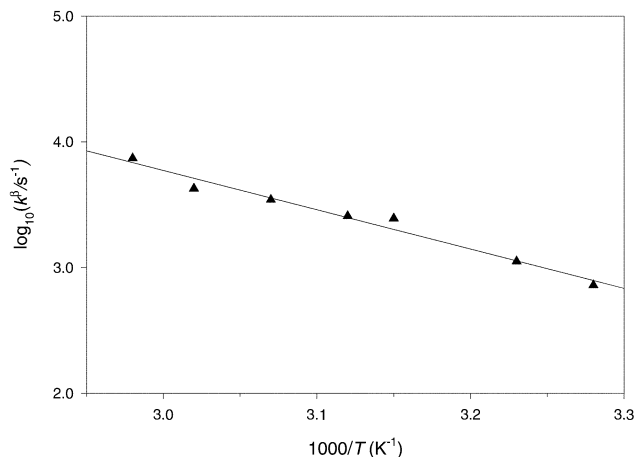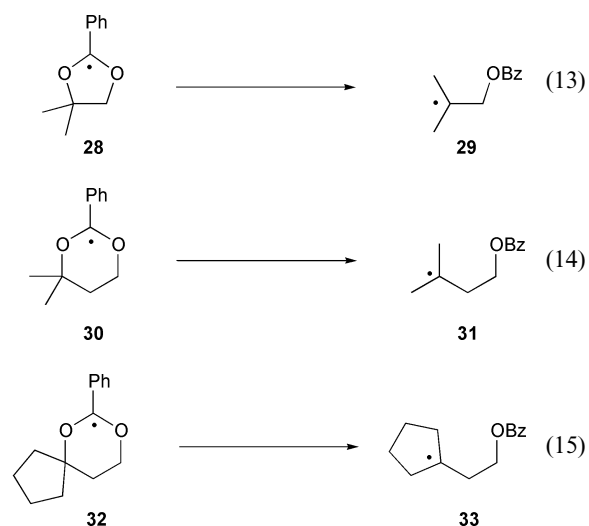

enthalpies of formation[11] of the *tert*-butyl and the *n*-butyl radicals (29.1 kJ mol^{-1}). To illustrate the point further using experimental data,[11] although the *tert*-butyl radical is more stable than the *n*-butyl radical by 29.1 kJ mol^{-1}, the C–Cl bond dissociation enthalpies for Bu^{t}–Cl and Bu^{n}–Cl are almost the same at 355 and 357 kJ mol^{-1}, respectively, because *tert*-butyl chloride is more stable than *n*-butyl chloride by 27.8 kJ mol^{-1}. The difference in stability of Bu^{t}–X and Bu^{n}–X decreases as X becomes less electronegative[11,19c] but, even with a methyl substituent attached to carbon, the Bu^{t}–Me and Bu^{n}–Me bond strengths (366 and 374 kJ mol^{-1}, respectively) differ by only 8 kJ mol^{-1}. Thus, the increased stability of the branched molecules compared to their straight-chain counterparts[11,19] acts in opposition to the increased stability of the *tert*-butyl radical relative to the *n*-butyl radical to render the C–X bonds relatively similar in strength.

β-Scission of the *tert*-butoxy(methoxy)methyl radical **15** [eqn. (10)] to give the *tert*-butyl radical (entry 1) is very rapid above room temperature, in accord with our demonstration that tertiary alcohols can be successfully deoxygenated *via* thiol-catalysed radical-chain decomposition of their methoxymethyl ethers.[2] The activation parameters for the β-scission of **15** are very similar to those obtained previously[20] for the corresponding cleavage of the di-*tert*-butoxymethyl radical **37** [eqn. (11), entry 2], when the latter are recalculated using revised values for $\log_{10}(2A_t)$ and E_t applicable to cyclopropane as solvent (see Table 3) and consistent with the values used in the present work.

Our quantitative kinetic data for the ring opening of the dioxolanyl radical **26** [eqn. (12), entry 3] support the previous qualitative conclusion[20] that this cyclic radical undergoes β-scission much less readily than analogous acyclic dialkoxyalkyl
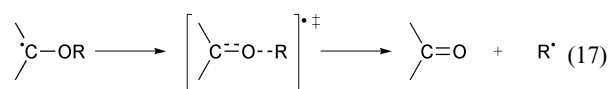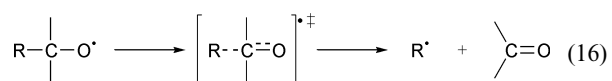
Table 3 Arrhenius parameters for β-scission of dialkoxyalkyl radicals

Entry	Dialkoxyalkyl radical	Product radical	Solvent	$\log_{10}(A^\beta/\text{s}^{-1})^a$	$E_a^\beta/\text{kJ mol}^{-1\,b}$	$k^\beta(298\text{ K})/\text{s}^{-1}$
1	**15**	Bu$^{t\bullet}$	PhF	12.0	33.8	1.2×10^6
2	**37**^{c}	Bu$^{t\bullet}$	c-C$_3$H$_6$	12.2^{c,d}	36.4^{c,d}	6.7×10^5
3	**26**	**27**	PhBu^t	14.5	66.1	8.3×10^2
4	**26**	**27**	3MP	14.3	63.4	1.6×10^3
5	**28**	**29**	PhBu^t	13.1^e	62.0^e	$1.7 \times 10^{2\,e}$
6	**28**	**29**	3MP	13.4	62.4	2.9×10^2
7	**30**	**31**	PhBu^t	13.2	59.8	5.3×10^2

^{a} Estimated error ±0.3. ^{b} Estimated error ±1.0 kJ mol^{-1}. ^{c} Values of $\log_{10}(A^\beta/2A_t)$ and $(E^\beta - E_t)$ taken from ref. 20. ^{d} Taking $\log_{10}(2k_t/\text{M}^{-1}\text{ s}^{-1}) = 11.19 - 4.19/\theta$ in cyclopropane solvent, calculated from viscosity data as described in the text. ^{e} $\log_{10}(k^\beta/\text{M}^{-1}\text{ s}^{-1}) = 13.0 - 66.9/\theta$ ($k^\beta = 19$ M^{-1} s^{-1} at 298 K) is recommended in ref. 22a.

radicals such as **15** and **37**. The transition states for this type of β-scission process appear to be product-like (see computational section) and the rate difference can be attributed in part to the angle strain that develops at C(2) in the transition structure for β-scission of the cyclic radical, as a result of planarisation at this centre. Stereoelectronic factors probably also play a part, because the need to achieve maximum overlap between the O–CMe$_2$ bond undergoing cleavage and the orbital of the unpaired electron is frustrated by the constraints imposed by the cyclic nature of the transition state.

β-Scission of alkoxyl radicals [eqn. (16)] is facilitated by polar solvents, particularly by hydrogen-bond donor solvents, that stabilise the transition state more than the ground state.[21] β-Scission of an alkoxyalkyl radical [eqn. (17)] is a closely

$$R-\overset{|}{\underset{|}{C}}-O^\bullet \longrightarrow \left[R\cdots\overset{|}{C}{=}O\right]^{\bullet\ddagger} \longrightarrow R^\bullet + \overset{}{\underset{}{>}}C{=}O \quad (16)$$

$$\overset{}{\underset{}{>}}C-OR \longrightarrow \left[\overset{}{\underset{}{>}}C{=}O\cdots R\right]^{\bullet\ddagger} \longrightarrow \overset{}{\underset{}{>}}C{=}O + R^\bullet \quad (17)$$

related process and so the ring opening of **26** to give the β-formyloxyalkyl radical **27** was also studied in 3-methylpentan-3-ol as solvent (entry 4). Although the rate of β-scission was greater in the alcohol solvent, the increase was relatively small.

The β-scission of the 2-phenyl-1,3-dioxolanyl radical **28** in *tert*-butylbenzene solvent [eqn. (13), entry 5] has been studied previously by Ingold and co-workers.[22] Our results indicate that ring opening of **28** to give the β-benzoyloxyalkyl radical **29** is rather more rapid than reported previously and the difference is attributable mainly to a lower activation energy determined in the present work. β-Scission of the benzylic radical **28** is only about 6 times slower at 298 K than opening of the unsubstituted analogue **26**, which would be expected to cleave twice as fast as **28** simply on statistical grounds. The geometry at C(2) is planar in **28**, as it is at this carbon atom in the product ester radical **29**, while in **26** C(2) is strongly pyramidal and this centre has to become planar in the product formate. Thus, there is less structural reorganisation on going to the transition structure for cleavage of **28**, compared with the situation for **26**, and this will act to offset the loss of benzylic stabilisation that accompanies β-scission. The effect of the substituent at C(2) on the stability of the emerging C=O bond in the transition state is probably also important in determining the activation energy for β-scission. As was found for β-scission of **26**, there is only a modest increase in the rate of ring opening of **28** on moving from *tert*-butylbenzene to 3-methylpentan-3-ol as solvent (entry 6).

β-Scission of **30** [eqn. (14), entry 7], the six-membered-ring analogue of **28**, takes place more readily than cleavage of the latter. The ring opening of **30** to give **31** is calculated to be more exothermic by 5 kJ mol^{-1} than corresponding β-scission of **28** (see computational section) and, since the transition states are

product-like, this is probably the most important factor controlling the relative rates. The observed rate difference may also be partly stereoelectronic in origin, because the presence of the larger ring permits better overlap of the β-O–CMe$_2$ bond with the orbital of the unpaired electron on moving to the transition state.

β-Scission of the spirocyclic radical **32** to give **33** [eqn. (15)] was included in this study because we have found evidence from end-product analysis that constraining the bond angles at the emerging radical centre can have a major effect on the rate of ring opening of bicyclic carbohydrate-derived 2-phenyl-1,3-dioxan-2-yl radicals.[4] Unfortunately, because of the relatively broad (and therefore weak) EPR signal from the benzylic radical **32** it was not possible to obtain accurate kinetic data. However, the temperature at which the concentration of **32** is approximately equal to that of **33** is *ca.* 20 K lower than that (*ca.* 312 K) at which [**30**] = [**31**], implying that the spirocyclic **32** undergoes β-scission *more rapidly* than its 4,4-dimethyl analogue **30**.†

No EPR spectroscopic evidence was found for β-scission of the benzylic radical **36** and its spectrum was still readily detectable at 400 K in *tert*-butylbenzene. Although other effects may also be operative, the slow β-scission of **36** seems likely to be mainly stereoelectronic in origin, in that the ring system will be quite rigidly planar thus preventing overlap of the β-O–CMe$_2$ bond with the SOMO. Likewise, no EPR evidence was found for β-scission of the allylic radicals 2-vinyl-4,4-dimethyl-1,3-dioxolan-2-yl **34** or 2-vinyl-4,4-dimethyl-1,3-dioxan-2-yl **35** and their spectra were still readily observable at 400 K, some 50 K above the highest temperature at which **30**, the 2-phenyl analogue of **35**, could be detected. This implies that **34** and **35** undergo β-scission more slowly than the 2-phenylated derivatives. However, we note that ring opening of **34** and **35** would yield radicals that contain acrylate ester functions and it would be difficult in any case to obtain quantitative kinetic data for cleavage of such allylic radicals, because of the ease of alkyl radical addition to acrylates.

Density functional calculations

To aid interpretation of the experimental results, a number of calculations were carried out at the UB3LYP/6-31G(d,p) level of density functional theory, using the GAUSSIAN 98 package of programs.[23] Ground-state radicals and transition structures were fully optimised with respect to all geometrical variables with no symmetry constraints. The set of normal harmonic frequencies was computed for each structure, first in order to confirm it as a local minimum or a transition state and then to obtain the zero-point vibrational energy (ZPVE), third-law entropy and thermal contribution to the enthalpy at 298 K.

† When B$^\bullet$ and C$^\bullet$ are the only radicals present in significant concentrations and [B$^\bullet$] = [C$^\bullet$], eqn. (4) reduces to $(k^\beta/2k_t) = 2$[B$^\bullet$]. Since radical concentrations will be approximately the same in the two experiments, it follows that the value of k^β for **30** at 312 K is approximately equal to the value of k^β for **32** at 292 K.

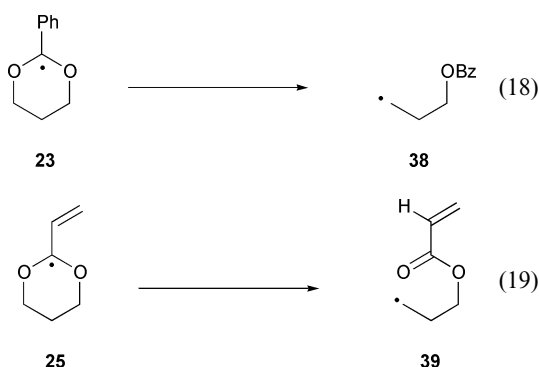**Table 4** Results of density functional molecular orbital calculations at the UB3LYP/6-31G(d,p) level[a]

Radical	Electronic energy/hartree	Number of imag. freqs. (cm⁻¹)	r(C–O)[b]/Å	r(C=O)[c]/Å	ZPVE[d,e]/kJ mol⁻¹	H(298 K)[e]/hartree	S(298 K)[e]/J mol⁻¹ K⁻¹
28	−577.425324	0	1.433	1.368	567.6	−577.196291	452.4
TS 40	−577.399773	1 (−729.5)	1.894	1.276	560.2	−577.173400	457.4
29	−577.434344	0		1.218	562.0	−577.205958	507.0
30	−616.738966	0	1.462	1.362	644.2	−616.479889	467.9
TS 41[f]	−616.714120	1 (−536.7)	1.953	1.264	636.1	−616.457826	477.9
31	−616.749305	0		1.217	637.5	−616.491079	527.0
32	−694.156809	0	1.467	1.360	741.2	−693.859921	496.5
TS 42	−694.134808	1 (−549.5)	1.940	1.267	734.1	−693.840648	494.5
23[g]	−498.779591	0	1.437	1.365	422.1	−498.608834	416.0
TS 43	−498.750911	1 (−842.7)	1.921	1.265	414.1	−498.583331	420.3
25	−384.439491	0	1.437[h]	1.365[i]	372.2	−384.289209	361.1
TS 44	−384.403444	1 (−658.8)	1.955	1.262	362.5	−384.256671	366.8
TS 45	−384.402531	1 (−686.4)	1.949	1.261	362.1	−384.255841	367.7

[a] 1 hartree = 2625.5 kJ mol⁻¹. [b] Length of the C–O single bond that will undergo cleavage or is undergoing cleavage in the transition state. [c] Length of the C–O single bond that will become a C=O double bond in the product, or the length of the developing carbonyl C=O bond in the transition state or length of the C=O bond in the product radical. [d] Negative vibrational frequencies are ignored in the calculation of ZPVE. [e] Low frequency normal modes are treated as vibrations, rather than rotations. Any errors caused by this approximation are expected to be small. [f] See Fig. 7. [g] Effective C_s symmetry. [h] Both non-equivalent bonds are the same length. [i] Length of the *cis*-C–O bond is 1.364 Å, that of the *trans*-C–O bond is 1.366 Å.

In addition to selected examples of the β-scission processes studied experimentally, the prototypical reactions shown in eqns. (18) and (19) were examined computationally. The reac-

tions investigated proceed *via* the transition structures **40–45** and the results are presented in Table 4. The ring-opening β-scission of the unsubstituted 1,3-dioxolan-2-yl radical **20**, along with similar cleavage of its 2-methyl derivative **21** and of the 2-trifluoromethyl analogue, have been examined theoretically by Zipse[24] as part of a study of the 1,2-acyloxy rearrangement that takes place for β-acyloxyalkyl radicals.
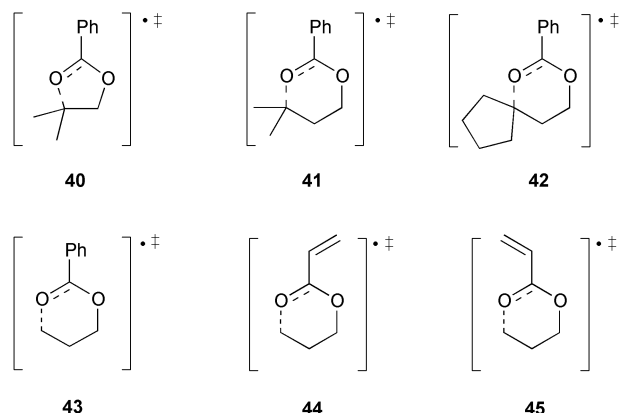
Calculated activation parameters and rate constants were obtained using eqns. (20) and (21),[25] in which k_B is Boltzmann's constant and e is the base of natural logarithms; the transmission constant in classical transition state theory is taken to be unity and the temperature is 298 K throughout. The computed activation parameters and rate constants are given in Table 5.

$$A^\beta = (k_B Te/h)\exp(\Delta S^\ddagger/R) \tag{20}$$

$$E_a^\beta = \Delta H^\ddagger + RT \tag{21}$$

In agreement with the conclusions based on their EPR spectra, the parent benzylic or allylic 1,3-dioxolanyl and 1,3-dioxanyl radicals are all predicted to be effectively planar at C(2) (angle sums ≥ 358°): the configuration at C(2) in all the transition states **40–45** is also planar (angle sum > 359.5°). The configuration at the emerging alkyl radical centres in the transition structures are all strongly flattened (angle sums 352.6 ± 0.4°) in comparison with those centres in the starting radicals. The developing C=O bond is relatively short (1.263–1.276 Å) and the rupturing C–O bond is relatively long (1.894–1.953 Å), structural features which suggest that the transition states should be regarded as 'product-like'. The computed lengths of the C=O bonds in the product radicals **29** and **31** are 1.218 and 1.217 Å, respectively. The developing C=O bond is shorter and the C–O bond undergoing cleavage is longer in the 6-membered transition structure **41**, as compared with the 5-membered analogue **40**. Within the series of 6-membered transition states, the developing C=O bond distance varies very little, while the length of the rupturing C–O bond increases with increasing methylation of the new radical centre. The computed structure of **41** is shown in Fig. 7 and this typifies the stereochemical and geometrical features of all the transition states.
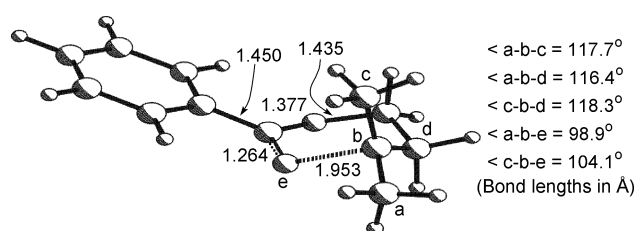

Fig. 7 UB3LYP/6-31G(d,p)-optimised structure of the transition state **41**

Ring-opening of **28** to give **29** is computed to be appreciably exothermic ($\Delta H = -25.4$ kJ mol⁻¹) and, as expected, the associated entropy change is large and positive ($\Delta S = +54.6$ J mol⁻¹ K⁻¹). Ring opening of **30**, the 6-membered-ring analogue of **28**, to give **31** is more favourable ($\Delta H = -29.4$ kJ mol⁻¹, $\Delta S = +59.1$ J mol⁻¹ K⁻¹). The reverse of these ring openings, namely 6-*endo*-cyclisation of the benzoyloxyalkyl radicals **29** and **31**, is thus predicted to be relatively unfavourable (*e.g.* $\Delta H^\ddagger = +87.3$ kJ mol⁻¹, $\Delta S^\ddagger = +69.1$ J mol⁻¹ K⁻¹ for the cyclisation of **31** to give **30**).

Table 5 Calculated activation parameters for β-scission of cyclic dialkoxyalkyl radicals in the gas phase at 298 K

Reaction	$\Delta H^{\ddagger}(298\ \mathrm{K})/\mathrm{kJ\ mol^{-1}}$	$\Delta S^{\ddagger}(298\ \mathrm{K})/\mathrm{J\ mol^{-1}\ K^{-1}}$	$E_a^{\beta\,a}/\mathrm{kJ\ mol^{-1}}$	$\log_{10}(A^{\beta}/\mathrm{s^{-1}})^a$	$k^{\beta}_{\mathrm{calc}}/\mathrm{s^{-1}}$ at 298 K^a
28 ⟶ 29	60.1	+5.0	62.6 (62.0)	13.5 (13.1)	3.3×10^2 (1.7×10^2)
30 ⟶ 31	57.9	+10.0	60.4 (59.8)	13.8 (13.2)	1.5×10^3 (5.3×10^2)
32 ⟶ 33	50.6	−2.0	53.1	13.1	6.6×10^3
23 ⟶ 38	74.2	+4.3	76.7	13.5^b	1.0
25 ⟶ 39^c	85.4	+5.7	87.9	13.6	1.3×10^{-2}

^{a} Experimental values determined in *tert*-butylbenzene are given in parentheses. ^{b} The statistical factor of 2, because there are two equivalent β-C–O bonds, has not been included. ^{c} *Via* transition state **44** to give the s-*trans*-acrylate ester.

The computed activation entropies for ring opening are small, corresponding to Arrhenius pre-exponential factors in the region of $10^{13.4}\ \mathrm{s^{-1}}$. For the two benzylic radicals for which experimental data are available, the agreement with the computed activation parameters is gratifying and gives credence to both sets of values.

The spirocyclic 1,3-dioxan-2-yl radical **32** is computed to undergo β-scission to give the tertiary radical **33** more rapidly than its non-spirocyclic analogue **30** cleaves to give **31**, in accord with the experimental results. The allylic 1,3-dioxan-2-yl radical **25** is predicted to undergo β-scission significantly less readily than its benzylic analogue **23**, consistent with the experimental observation that 4,4-dimethylated derivatives of these two prototypes (**30** and **35**, respectively) show the same trend. β-Scission of **25** is predicted to take place preferentially *via* the *anti*-transition state **44** to give the *trans*-acrylate radical **39**; the activation energy *via* the *syn*-transition state **45** is calculated to be greater by 2.2 kJ mol⁻¹.

Conclusion

EPR spectroscopic studies, complemented by density functional calculations, can provide a basis for understanding the rates of the elementary reactions involved in the deoxygenation of alcohols and diols by way of their acyclic and cyclic acetal derivatives. For the β-scission processes studied by both experiment and theory, agreement between the two approaches is good. The results obtained from this work should facilitate development of a more complete understanding of the unexpected regioselectivity that has been observed for the β-scission of certain bicyclic 1,3-dioxan-2-yl radicals during the radical-chain redox ring opening of carbohydrate-derived benzylidene acetals.[4]

Experimental

EPR spectra were recorded during continuous UV irradiation of samples positioned in a standard variable temperature insert in the microwave cavity of a Varian E-109 or a Bruker ESP-300 spectrometer operating at 9.1–9.4 GHz.[26] The light source was a 500 W mercury discharge lamp (Osram HBO 500 W/2) and the optical system has been described previously.[26a] The temperature of the sample during photolysis was determined, using the method described previously,[26] by measurement of the value of $a(\mathrm{H}_{\beta})$ for the isobutyl radical. The heating effect at full light intensity was *ca.* 7 K.

Relative radical concentrations were determined by double integration of appropriate lines in each spectrum and confirmed by computer simulation of the composite spectrum; care was taken to avoid selective saturation of the spectra. Computer simulations were obtained using a modified version of ESRSPEC2,[27] extended to handle composite spectra from up to four radicals with different centres, second-order shifts for coupling to single nuclei with $I > \frac{1}{2}$, and lineshapes continuously variable between 100% Gaussian and 100% Lorentzian. The experimental methods for determination of relative rate constants using the steady-state EPR method have been described in detail previously.[26,28] Absolute radical concentrations were determined by comparison with the EPR signal obtained from a standard solution of 2,2,4,4-tetramethyl-piperidine-*N*-oxyl (TEMPO, Aldrich) in fluorobenzene, using the signal from a piece of synthetic ruby fixed to the inside wall of the microwave cavity as a sensitivity reference.

NMR spectra were recorded for samples in CDCl₃ using a Bruker ADVANCE 500 instrument (500 MHz for ¹H, 125.7 MHz for ¹³C). Chemical shifts are reported relative to Me₄Si, *J* values are quoted in Hz and the use of [multiplet] indicates an apparent multiplet associated with an averaged coupling constant.

Materials

Di-*tert*-butyl peroxide (98%, Aldrich) was washed repeatedly with 5% w/v aqueous sodium iodide containing 2% w/v sulfuric acid, until no more iodine was liberated. It was then washed successively with water, saturated aqueous sodium hydrogen carbonate, and saturated brine, before being dried (MgSO₄), passed down a column of basic alumina (activity 1) and finally distilled (bp 46–47 °C/76 Torr); it was stored under argon at 4 °C. Fluorobenzene and *tert*-butylbenzene were distilled from calcium hydride and stored under argon; 3-methylpentan-3-ol was distilled from sodium and stored similarly.

The acetals **3**, **5–9**, and **11** were commercial products (Aldrich) and were used as received.

tert-Butyl methoxymethyl ether[29] was prepared by the reaction of chloromethyl methyl ether with potassium *tert*-butoxide in dimethyl formamide at 0 °C; bp 100–101 °C at atmospheric pressure. 2-Phenyl-1,3-dioxane **10**,[30] 2-phenyl-4,4-dimethyl-1,3-dioxolane[31] and 2-phenyl-5,5-dimethyl-1,3-dioxolan-4-one[32] were prepared from benzaldehyde and the corresponding diol or hydroxy acid in the presence of toluene-*p*-sulfonic acid catalyst and with azeotropic removal of water, as described in the literature. 2-Vinyl-1,3-dioxane[33] and 2-vinyl-4,4-dimethyl-1,3-dioxolane[34] were prepared in a similar fashion from acrolein and the appropriate diol, using pyridinium toluene-*p*-sulfonate as catalyst. 4,4,5,5-Tetramethyl-1,3-dioxolane[35] was prepared from pinacol and paraformaldehyde using syrupy phosphoric acid as catalyst. The 1,3-dioxanes that have not been reported previously are described below; they were prepared from benz-aldehyde or acrolein and the appropriate 1,3-diol in refluxing benzene, in the presence of pyridinium toluene-*p*-sulfonate as catalyst, by azeotropic removal of water using a Dean and Stark separator.[30]

2-Phenyl-4,4-dimethyl-1,3-dioxane. Bp 75–78 °C/0.1 mmHg. δ_{H} 1.33 (3H, s, CH₃), 1.40 (1H, d[t], *J* 13.4 and 2.0, H^eq-5), 1.43 (3H, s, CH₃), 2.01 (1H, ddd, *J* 13.4, 10.4 and 8.0, H^ax-5), 4.07 (2H, m, H-6), 5.71 (1H, s, PhC*H*), 7.28–7.36 (3H, m, aromatic-H), 7.47–7.49 (2H, m, aromatic-H); δ_{C} 21.5, 31.7, 35.8, 63.5, 72.1, 95.2, 126.1, 128.1, 128.5, 139.2. (Found: C, 74.9; H, 8.7. C₁₂H₁₆O₂ requires C, 75.0; H, 8.4%.)

2-Phenyl-4,4-spiropentyl-1,3-dioxane. This was prepared from 1-(2-hydroxyethyl)cyclopentanol;[36] bp 69–70 °C/0.4 mmHg. δ_{H} 1.42 (1H, d[t], *J* 13.3 and 1.9, H^eq-5), 1.57–1.97 (7H, m, CH₂),

2.19 (2H, m, CH$_2$), 4.01 (1H, ddd, J 13.0, 11.5 and 2.4, H^{ax}-6), 4.15 (1H, ddd, J 11.5, 5.3 and 1.5, H^{eq}-6), 5.64 (1H, s, PhCH), 7.33 (3H, m, aromatic-H), 7.50 (2H, m, aromatic-H); δ_C 23.0, 24.4, 32.9, 34.9, 41.6, 64.9, 84.0, 96.3, 126.0, 128.1, 128.5, 139.3. (Found: C, 76.7; H, 8.3. C$_{14}$H$_{18}$O$_2$ requires C, 77.0; H, 8.3%).

2-Vinyl-4,4-dimethyl-1,3-dioxane. Bp 56 °C/12 mmHg. δ_H 1.25 (3H, s, CH$_3$), 1.29 (1H, d[t], J 13.3 and 1.9, H^{eq}-5), 1.31 (3H, s, CH$_3$), 1.87 (1H, ddd, J 13.3, 12.8 and 5.8, H^{ax}-5), 3.89 (1H, ddd, J 13.0, 11.7 and 2.4, H^{ax}-6), 3.95 (1H, ddd, J 11.7, 5.8 and 1.4, H^{eq}-6), 5.13 (1H, d, J 4.8, vinylCH), 5.22 (1H, dd, J 10.6 and 1.2, vinyl-H), 5.40 (1H, dd, J 17.4 and 1.2, vinyl-H), 5.79 (1H, ddd, J 17.4, 10.6 and 4.8, vinyl-H); δ_C 21.4, 31.6, 35.7, 62.9, 71.7, 94.4, 118.2, 135.5. (Found: C, 67.8; H, 9.9. C$_8$H$_{14}$O$_2$ requires C, 67.6; H, 9.9%).

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