Application of EPR spectroscopy to the determination of the rates of reaction and selectivity of attack of the *tert*-butoxyl radical on esters: the interplay of electronic, polar, steric and stereoelectronic factors

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Rate constants have been determined by steady-state EPR spectroscopy experiments for hydrogen-atom abstraction by $\mathrm{Bu^tO^{\bullet}}$ from a variety of esters. The values, which range over two orders of magnitude (5×10^3–5×10^5 $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$ at *ca.* 300 K) are significantly lower than those for related ketones and ethers and reflect, at least in part, the importance of the appropriate C–H bond dissociation energies and the stabilization of carbonyl-conjugated radicals. The relative lack of reactivity of C–H bonds in unsubstituted five-membered rings is believed to reflect ring-strain in the derived radicals; possible stereoelectronic effects are discussed.

Introduction

There is considerable contemporary interest in the factors that govern the selectivity of radical reactions and, especially, in the ways in which understanding of these can lead to enhanced control of radical reactions (*e.g.* for subsequent use in synthetic pathways[1]). In a particularly detailed analysis, Roberts and Steel have summarized[2] an extensive set of kinetic results for hydrogen-abstraction reactions (including some for oxygen-centred radicals) and shown how an improved correlation between activation energies and reaction enthalpies (the Evans–Polanyi relationship) can be obtained by making quantitative allowance for a variety of factors, including the stabilization and geometry of the intermediate radicals, as well as the polar nature of the transition state (or the attacking species). In his review, Beckwith[3] has drawn attention to the importance of other factors, most notably stereoelectronic effects, in the cyclization of alkenyl and related radicals; *e.g.* the regioselective cyclization of the hex-5-enyl radical yields the less stable cyclopentylmethyl radical in preference to the more stable cyclohexyl radical, under stereoelectronic control.[3]

The principal aim of the research described here was to determine the factors which govern the reactivity of esters towards oxygen-centred radicals. These substrates were chosen since examples are increasingly used as constituents of base oils employed in lubricant technology[4] (*e.g.* long-chain diesters and pentaerythritol esters), especially as it is believed that their behaviour and performance will reflect, in part, the way in which they react with alkoxyl and peroxyl radicals formed in autoxidation processes. A comprehensive kinetic and spectroscopic study has not been previously reported (*e.g.* no data on esters appear in ref. 2), though liquid-phase reactions of certain acyclic esters with $\mathrm{Bu^tO^{\bullet}}$ have been reported,[5] in which restricted rotation about the $\mathrm{^{\bullet}C{-}C(O)}$ bond is revealed by EPR spectroscopy (see also ref. 6). Studies of fatty acid esters,[7] as well as extensive gas-phase studies of the radical reactivity of $\mathrm{^{\bullet}OH}$ with esters have been undertaken:[8,9] in the latter, Wallington *et al.* suggest the possible coordination of the $\mathrm{^{\bullet}OH}$ radical to the carbonyl group prior to hydrogen abstraction *via* a six-membered ring, to explain the increased reactivity of C–H bonds β to the carbonyl group. These limited studies are in contrast to the comprehensive studies reported of the reactions of $\mathrm{Bu^tO^{\bullet}}$ with, for example, ethers, including approaches involving laser flash-photolysis–EPR spectroscopy[10,11] and spin-trapping techniques:[12–14] in the latter, for example, Busfield and co-workers have concluded that an oxygen atom α to C–H strongly enhances the abstraction rate, whereas a β-oxygen retards abstraction; the reactivity at the position γ to oxygen is slightly enhanced. They also concluded that the rate of abstraction from a tertiary C–H occurs at approximately the same rate as for a secondary C–H, both of which are faster than for primary C–H bonds.[12] Also note that Roberts and co-workers have studied the reactions of several esters and ketones with the *tert*-butoxyl radical in the presence of a series of amine–borane complexes which act as polarity reversal catalysts and give carbonyl conjugated radicals (detected by EPR spectroscopy) in reactions which exhibit the characteristics of nucleophilic radical attack (*via* intermediate amine–boryl radicals).[6,15,16]

This paper describes the results of an investigation by kinetic-EPR spectroscopy of the direct reaction of the electrophilic radical $\mathrm{Bu^tO^{\bullet}}$ with a range of esters at room temperature, in which the overall rates of reaction and selectivity of attack have been determined. The results demonstrate the importance of C–H bond strength in determining the position of attack (rather than the influence of polar effects); with selected cyclic compounds ring-strain and stereoelectronic effects also appear to play a significant role.

Results and discussion

Approach employed

In situ photolysis of solutions of esters in di-*tert*-butyl peroxide were carried out in the cavity of an EPR spectrometer at *ca.* 300 K. Photolysis with both the filtered and unfiltered radiation from 1 kW mercury–xenon compact arc lamps generally gave rise to spectra with good signal-to-noise ratios, assignable to radicals derived by hydrogen abstraction from the esters employed (see Table 1 for parameters). A variety of concentration ratios, as well as the use of co-solvents, were explored; optimum conditions for radical generation and detection were typically found to be with the di-*tert*-butyl peroxide present in considerable excess (approximately twice as much peroxide as ester, by volume, was usually used). When the presence of a solvent was necessary, either to promote miscibility and/or to reduce polarity (to permit a 3 mm id

Table 1 EPR parameters and rate constants of formation of a variety of radicals obtained by reaction between $Bu^tO^{\bullet}$ and esters

Substrate	Radicals	Hyperfine splittings[a]/ mT[a]	g[b]	Selectivity (%)[c]	Rate constant per hydrogen/ $dm^3\ mol^{-1}\ s^{-1}$[d]	Overall rate constant/dm^3 $mol^{-1}\ s^{-1}$[d]
$MeC(O)OMe$	$^{\bullet}CH_2C(O)OMe$	$a(2H) = 2.14$ $a(3H) = 0.14$	2.0034	30	1.8×10^3	5.4×10^3
	$^{\bullet}CH_2OC(O)Me$	$a(2H) = 2.04$ $a(3H) = 0.13$	2.0027	70	4.1×10^3	1.3×10^4
$Bu^tC(O)OMe$	$^{\bullet}CH_2Me_2CC(O)OMe$	$a(2H) = 2.21$ $a(6H) = 0.03$	2.0026	40	9.3×10^2	8.4×10^3
	$^{\bullet}CH_2OC(O)Bu^t$	$a(2H) = 2.04$	2.0027	60	4.1×10^3	1.3×10^4
$MeC(O)OBu^t$	$^{\bullet}CH_2C(O)OBu^t$	$a(2H) = 2.14$	2.0035	29	1.8×10^3	5.4×10^3
	$^{\bullet}CH_2Me_2COC(O)Me$	$a(2H) = 2.21$ $a(6H) = 0.12$	2.0025	71	1.5×10^3	1.3×10^4
$MeC(O)OEt$	$^{\bullet}CHMeOC(O)Me$	$a(1H) = 1.93$ $a(3H) = 2.39$ $a(3H) = 0.13$	2.0028	100	2.7×10^4	5.4×10^4
$EtC(O)OMe$	$^{\bullet}CHMeC(O)OMe$	$a(1H) = 2.07$ $a(3H) = 2.49$ $a(3H) = 0.15$	2.0033	100	6.0×10^4	1.2×10^5
$Bu^tC(O)OCH_2Bu^t$	$^{\bullet}CH^tBuOC(O)Bu^t$	$a(1H) = 1.83$	2.0027	45	3.4×10^3	6.8×10^3
	$^{\bullet}CH_2CMe_2–$	$a(2H) = 2.22$ $a(6H) = 0.03$	2.0026	55	9.3×10^2	8.4×10^3
$EtC(O)OPr$	$^{\bullet}CHMeC(O)OPr$	$a(1H) = 2.08$ $a(3H) = 2.51$ $a(2H) = 0.15$	2.0033	53	7.0×10^4	1.4×10^5
	$^{\bullet}CHEtOC(O)Et$	$a(1H) = 1.92$ $a(2H) = 2.30$ $a(2H) = 0.18$	2.0027	20	2.7×10^4	5.4×10^4
	$^{\bullet}CHMeCH_2OC(O)Et$	$a(1H) = 2.19$ $a(2H) = 1.88$ $a(3H) = 2.54$	2.0026	27	3.65×10^4	7.3×10^4
$MeC(O)OCHMe_2$	$^{\bullet}CH_2C(O)OCHMe_2$	$a(2H) = 2.13$ $a(1H) = 0.10$	2.0033	14	1.8×10^3	5.4×10^3
	$^{\bullet}CMe_2OC(O)Me$	$a(6H) = 2.26$ $a(3H) = 0.05$	2.0029	29	1.1×10^4	1.1×10^4
	$^{\bullet}CH_2CHMeOC(O)Me$	$a(2H) = 2.21$ $a(1H) = 2.31$	2.0025	57	3.6×10^3	2.1×10^4
$Me_2CHC(O)OMe$	$^{\bullet}CMe_2C(O)OMe$	$a(6H) = 2.16$ $a(3H) = 0.13$	2.0032	100	2.5×10^5	2.5×10^5
$PrC(O)OCH_2Bu^t$	$^{\bullet}CHMeCH_2C(O)OCH_2Bu^t$	$a(1H) = 2.27$ $a(2H) = 2.32$ $a(3H) = 2.50$	2.0026	27	2.8×10^4	5.6×10^4
	$^{\bullet}CHEtC(O)OCH_2Bu^t$	$a(1H) = 2.03$ $a(2H) = 2.31$ $a(2H) = 0.15$	2.0030	63	6.5×10^4	1.3×10^5
	$^{\bullet}CHBu^tOC(O)Pr$	$a(1H) = 2.04$ $a(2H) = 0.15$	2.0028	10	1.0×10^4	2.1×10^4

[a] ±0.02. [b] ±0.0001. [c] Average of several measurements ±15%. [d] Estimated error ±30%.

cylindrical cell to be tuned), benzene was generally used; under the conditions employed no detectable signals due to benzene were found in the EPR spectra. We also carried out some more detailed investigations of the variation of relative radical concentrations as a function of solvent composition (benzene : ester, in the range 2:1–200:1 v/v, with a typical constant peroxide concentration of 0.7 mol dm^{-3}); for a small number of substrates, studies were undertaken as a function of temperature.

Our approach involved both double integration of the signals and spectrum simulation to provide an estimate of the relative steady-state concentrations and hence reactivities of different positions. It was assumed that all the radicals detected have the same termination rate constant ($2k_t$), so that differences in $[R^{\bullet}]_{obs}$ directly reflect the concentrations of substrates and the relative rates of attack;[2,17–19] absolute rates of reaction were obtained in direct competition experiments in the presence of α-methyl-γ-butyrolactone for which the rate constant for hydrogen abstraction of the tertiary hydrogen by the $Bu^tO^{\bullet}$ radical was found to be $5.0 \times 10^5\ dm^3\ mol^{-1}\ s^{-1}$ at *ca.* 300 K, by a competition reaction with the more reactive tetrahydrofuran. This substrate, rather than tetrahydrofuran, was chosen as an internal standard since comparable concentrations of the two substrates could be used. In all cases the analysis was carried out on spectra which were recorded shortly after the commencement of photolysis (up to 12 min), as minor signals from secondary radicals could be observed in some samples after a longer period of continuous photolysis (see ref. 6). (These are believed to be due to hydrogen abstraction from the products of dimerization of substrate-derived radicals.)

Selected examples of the results for acyclic esters: identification of the main trends in behaviour

Figs. 1 and 2 illustrate the typical quality of the spectra obtained, with good signal-to-noise ratio and resolution, together with selected examples of the results of spectrum simulation (with optimized fit to spectrum parameters, linewidths and relative concentrations). The results are collected together in Table 1; spectral assignment is based on results for some of the radicals, or their analogues, reported elsewhere.[20] In a few cases involving molecules with only primary hydrogens, low concentrations of the methyl radical were observed (presumably from decomposition of $Bu^tO^{\bullet}$).

The following discussion describes highlights of the key findings, presented largely in order of increasing complexity of the substrate. For the simplest substrate, methyl ethanoate (

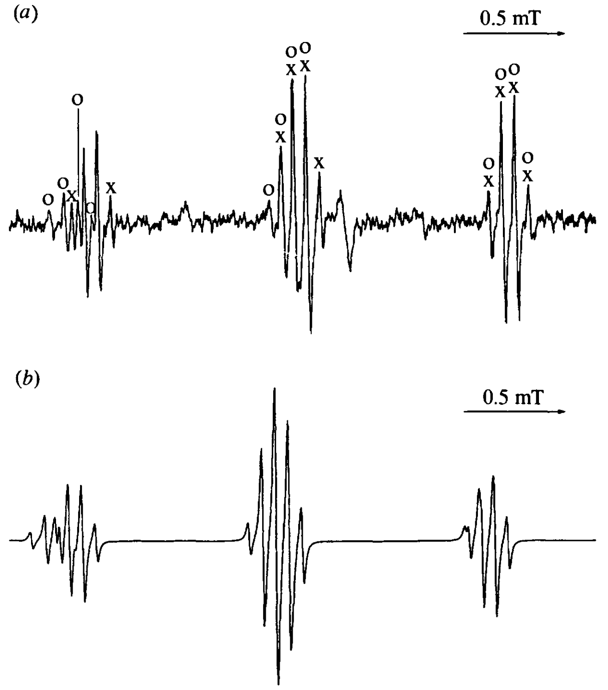


Fig. 1 EPR spectra (and simulation) of radicals produced by the reaction of MeC(O)OMe with $Bu^tO^•$ (from *in situ* photolysis of Bu^tOOBu^t) at *ca.* 300 K, showing signals from $^•CH_2C(O)OMe$ (o) and $^•CH_2OC(O)Me$ (x) together with traces of $CH_3^•$. The additional peak in the spectra arises from the quartz sample cell.

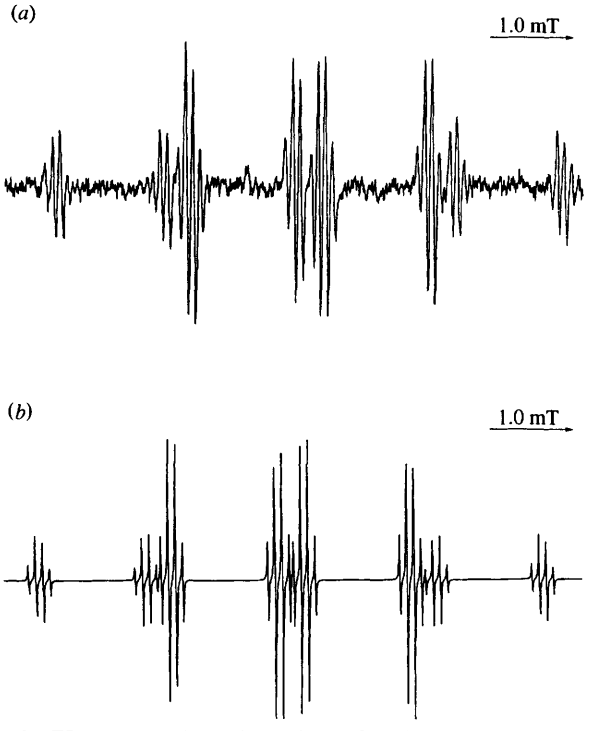
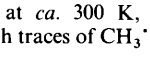


Fig. 2 EPR spectra (and simulation) of radicals produced by the reaction of MeC(O)OEt with $Bu^tO^•$ (from *in situ* photolysis of Bu^tOOBu^t) at *ca.* 300 K, showing signals from $^•CHMeOC(O)Me$ together with traces of $CH_3^•$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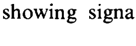
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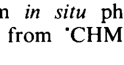
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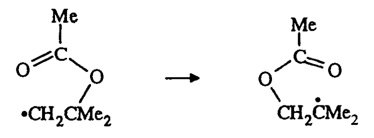
Fig. 1), the observation of radicals **1** (minor) and **2** (major) suggests that polar effects may be important (since $Bu^tO^•$ is an electrophilic radical) and also that the extra (expected) stability of radical **1** is outweighed by this factor. Lung-min and Fischer[5] have observed restricted rotation about the $^•C–C(O)$ bond in ester-derived radicals; the observed barrier of 47 kJ mol^{-1} for $^•CHMeC(O)OEt$ gives a delocalization energy of 40 kJ mol^{-1}. The stabilization energy in **2** has not to our knowledge been measured, but the high value of $a(\alpha\text{-}H)$ and especially the low *g*-value indicate that the extent of delocalization of the unpaired electron is not substantial.

Few C–H bond dissociation energies in esters have been measured; however bond dissociation energies, E_d for $H–CH_2CO_2Me$ and $H–CH_2OC(O)Ph$ are 406[21] and 419[22] kJ mol^{-1}, respectively, compared with a value of 421[23] kJ mol^{-1} for $H–CH_2CH_3$. We note that the relatively high values for esters may be due in part to the $-$I effect of the $–CO_2–$ moiety (which offsets some of the expected stabilization from adjacent C=O and O groups), as observed, for example, for fluorine-containing hydrocarbons ($CH_3CF_2–H$, E_d = 416 kJ mol^{-1}; $CF_3CH_2–H$, E_d = 446 kJ mol^{-1} [23]). Consideration of the important canonical structure **3** for the parent compound also suggests that polar effects might be diminished here and that delocalization in **1** and **2** might be expected to be less important than for ketones or ethers and alcohols {*e.g.* differences in pK_a values between esters and ketones, [*e.g.* $CH_3C(O)CH_3$, pK_a 20; $CH_3C(O)OCH_2CH_3$, pK_a 25[24]] confirm that the electron-withdrawing effect of the carbonyl group in the ketone is much greater than that in the ester}.

The relative reactivity observed for the non-conjugated C–H bonds in $MeC(O)OBu^t$ and $Bu^tC(O)OMe$ (see Table 1) strongly reinforces the conclusions that the (primary) methyl groups attached to the carbonyl group and oxygen atom are not significantly activated to attack by $Bu^tO^•$ (*i.e.* that polar and delocalization effects are clearly not of great importance). Several other features are worthy of special note. First, the detection of $^•CH_2CMe_2OC(O)Me$ (**4**) from $MeC(O)OBu^t$, and not the rearranged species[25,26] $^•CMe_2CH_2OC(O)Me$ (**5**) over the temperature range explored (243–363 K, see also ref. 25) is in contrast to the detection of **5** when **4** is generated in aqueous solution;[27] this reinforces the conclusion[25,28] that a cyclic, polar transition state may be involved in the 1,2-shift [reaction (1); *k* for reaction (1) is *ca.* 10^3 s^{-1} in water at 293 K[28]]. However at higher temperatures the signal from **4** is steadily replaced by that from $^•CH_2C(O)OBu^t$ (**6**), such that by 373 K there are no remaining signals from the precursor. This strongly suggests the occurrence of a rapid 1,5-hydrogen shift, [reaction (2)]; intermolecular hydrogen-atom transfer was discounted on the basis of experiments involving the variation of substrate concentration, since no significant variation of relative radical concentrations was observed. Reaction (2) would be expected to be slightly exothermic, given the resulting stabilization of **6**, and encouraged by the nucleophilic character of **4**, due to the first-formed species being a non-conjugated, carbon-centred radical (*cf.* the rate constant for attack of $Me^•$ on the C–H bonds in, for example, ethanoic acid $k = 3 \times 10^3$ dm^3 mol^{-1} s^{-1} at 293 K[29]). From studies of the relative concentrations of **4** and **6** we estimate *k* to be *ca.* 2.3×10^3 s^{-1} at *ca.* 300 K again making the assumption that the termination rates of all the ester-derived radicals are approximately the same.[18,19] Finally the detection of $^•CH_2CMe_2C(O)OMe$ from $Bu^tC(O)OMe$ is in contrast to our finding[30] that $^•CH_2CMe_2C(O)Me$ (**7**) [when generated from the reaction of $^•OH$ and $Bu^tC(O)Me$, in aqueous solution, in a continuous-flow EPR experiment] gives rise to signals from the radical $^•CMe_2CH_2C(O)Me$ (**8**), as expected on the basis of the 1,2-acyl shift proposed for the corresponding radical derived from di-*tert*-butyl ketone for which *k* is 1.7×10^5 dm^3 mol^{-1} s^{-1} at 298 K[31] [reaction (3)]. The failure of $^•CH_2CMe_2C(O)OMe$ to undergo ready rearrangement analogous to reaction (3) (*k* must be < *ca.* 10^3 s^{-1} for the precursor to be solely detected) may reflect the reduction in positive character of the carbonyl carbon in the ester-derived radical compared with the analogous ketone-derived radical.



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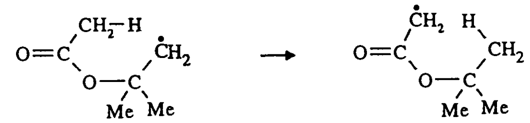

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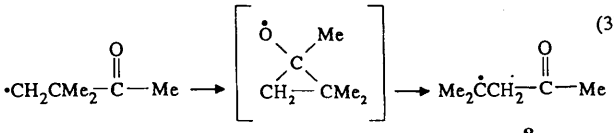


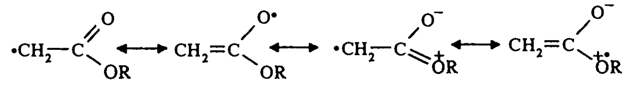
7 8 (3)

The compounds MeC(O)OEt (see Fig. 2), and EtC(O)OMe both gave spectra dominated by the (conjugated) secondary radicals, $^{\bullet}CHMeOC(O)Me$ and $^{\bullet}CHMeC(O)OMe$. This strongly suggests that it is the bond dissociation energy that largely governs the site of attack and that stabilization by conjugation to the carbonyl and oxygen in the transition state is of minor importance. Where two methylene groups adjacent to the carbonyl and ether oxygen are present, attack at the former is clearly dominant [*cf.* the results for EtC(O)OPr, for which the major radical detected is $^{\bullet}CHMeC(O)OPr$]. We note that the bond dissociation energy for H–CHMeC(O)OMe is reported to be 397 kJ mol^{-1},[32] although no values have been reported for H–CHROC(O)R′.

These conclusions are reinforced by the observations of spectra from esters with non-conjugated methylene groups, *e.g.* EtC(O)OPr gives signals from $^{\bullet}CHMeCH_2OC(O)Et$ which are more prominent than those from $^{\bullet}CHEtOC(O)Et$ [though less than $^{\bullet}CHMeC(O)OPr$], and $PrC(O)OCH_2Bu^t$ gives a significant concentration of $^{\bullet}CHMeCH_2C(O)OCH_2Bu^t$ as well as $^{\bullet}CHEtC(O)OCH_2Bu^t$ (predominant) and $^{\bullet}CHBu^tOC(O)Pr$. It is notable that in this case there are no detectable signals from attack at the Bu^t group. This is in contrast to the reaction with $Bu^tC(O)OCH_2Bu^t$ in which significant concentrations of both $^{\bullet}CH_2CMe_2C(O)OCH_2Bu^t$ and $^{\bullet}CH_2CMe_2CH_2OC(O)Bu^t$ are observed (with very similar, overlapping spectra), suggesting that the secondary C–H bond (conjugated with O) is relatively ineffective in competition with the primary alkyl groups (see later).

The spectra for $Me_2CHC(O)OMe$ are dominated by $^{\bullet}CMe_2C(O)OMe$, as expected if the bond dissociation energy of the tertiary C–H bond is crucial. For $MeC(O)OCHMe_2$ however, the spectra observed consist of a number of radicals, the most prominent of which results from removal of a primary hydrogen to give $^{\bullet}CH_2CHMeOC(O)Me$. This again suggests that attack at the tertiary site in the alkyl chain is significantly slower than when C–H is adjacent to C=O (*i.e.* as observed for the corresponding methylene groups).

Table 1 summarizes the appropriate rate constants for hydrogen abstraction at a given position (overall and expressed on a per-hydrogen basis), obtained by competitive experiments involving mixtures of the esters with the internal standard α-methyl-γ-butyrolactone. The rate constants obtained, ranging from *ca.* 5.4×10^3 dm^3 mol^{-1} s^{-1} for the unactivated primary CH_3 group to *ca.* 2.5×10^5 dm^3 mol^{-1} s^{-1} for the activated methylene group adjacent to a carbonyl group, are noticeably lower than those of comparable acyclic ketones and ethers under similar circumstances [*e.g.* $k \approx 2.8 \times 10^6$ dm^3 mol^{-1} s^{-1} (determined by double integration of the signals followed by spectral simulation), for attack at the methylene group in Et_2CO and $k = 3.9 \times 10^6$ dm^3 mol^{-1} s^{-1} at 300 K for Et_2O[33]]. We believe that this emphasizes the influence of bond dissociation energies rather than polar effects [values of E_d for the methylene-group hydrogens in EtC(O)Me[34] and Et_2O[35] are 386 and 383 kJ mol^{-1}, respectively, compared with 397 kJ mol^{-1} for the methylene group in EtC(O)OMe[32]]. The preference for formation of $^{\bullet}C$–C(O)– and the observation of a significant stabilization energy for these radicals (perhaps surprising in view of the relative acidities of esters and ketones) is nevertheless consistent with the occurrence of one-electron delocalization in $^{\bullet}C$–C(O)– probably involving a significant contribution of the resonance structure **9**.



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The particularly low rate constant of the reaction of the tertiary C–H bond adjacent to oxygen (1.1×10^4 dm^3 mol^{-1} s^{-1}) contrasts with that of the corresponding secondary hydrogen atoms in methyleneoxy groups (typically 2.7×10^4 dm^3 mol^{-1} s^{-1} per hydrogen) and the corresponding tertiary C–H adjacent to the carbonyl group in $Me_2CHC(O)OMe$ (2.5×10^5 dm^3 mol^{-1} s^{-1}) which suggests that steric or stereoelectronic effects may also be important. To explore this possibility MOPAC calculations were performed for both $Me_2CHC(O)OMe$ and $MeC(O)OCHMe_2$ (see *e.g.* Fig. 3); these indicate that in the preferred conformation for Me_2CHC-(O)OMe the tertiary C–H bond which is abstracted is more or less confined to the –C–C(O)–O–C– plane with the hydrogen in an *anti* (periplanar) configuration with respect to the carbonyl group. Whereas this conformation will minimise any polar retardation by C–H/C=O overlap, it would fail to provide the evident enthalpic stabilization (delocalization) in the transition state by conjugation between the developing radical centre and the C=O bond. The rapidity of C–H abstraction is hence surprising and we presume that the barrier to rotation may be low; it may also be relevant that the preferred conformation is such that the tertiary C–H points away from the remainder of the molecule so that attack of $Bu^tO^{\bullet}$ is unhindered. In the case of $MeC(O)OCHMe_2$ the tertiary C–H bond is predicted to sit at an angle of 40° to the –C(O)–O–C– plane in a *syn* conformation with the carbonyl group (presumably due in part to repulsion between the carbonyl oxygen and the methyl groups on the alkyl chain). The low rate constant for abstraction of the tertiary C–H presumably now reflects the fact that this C–H is not positioned to benefit from any stereoelectronic enhancement predicted for C–H bonds eclipsed with p(π) electrons on oxygen,[36,37] and may be further hindered by steric repulsion[6] to the approach of $Bu^tO^{\bullet}$ by the carbonyl group.

We conclude that the order of reactivity is primary H–C–C(O)– < primary H–C–O– < tertiary H–C–O– < secondary H–C–O– < secondary H–C–C(O)– < tertiary H–C–C(O)–; this pattern is due mainly to the differences in bond dissociation energies and possibly a steric/stereoelectronic effect (see later). It should be noted that there is no apparent evidence for interactions of the type previously suggested by Wallington *et al.* (see ref. 9).

Reactions of $Bu^tO^{\bullet}$ with some cyclic esters (lactones)

Table 2 contains details of the EPR spectra obtained by reaction of the *tert*-butoxyl radical with a series of lactones. Some of the radicals have been previously reported (see *e.g.* refs. 3 and 38), though several structural features are worthy of special note. For example, the low α-H splitting for **10** (see Fig. 4) of 1.56 mT is a clear indication of a degree of non-planarity at the radical centre (*cf.* the more marked extent of bending in

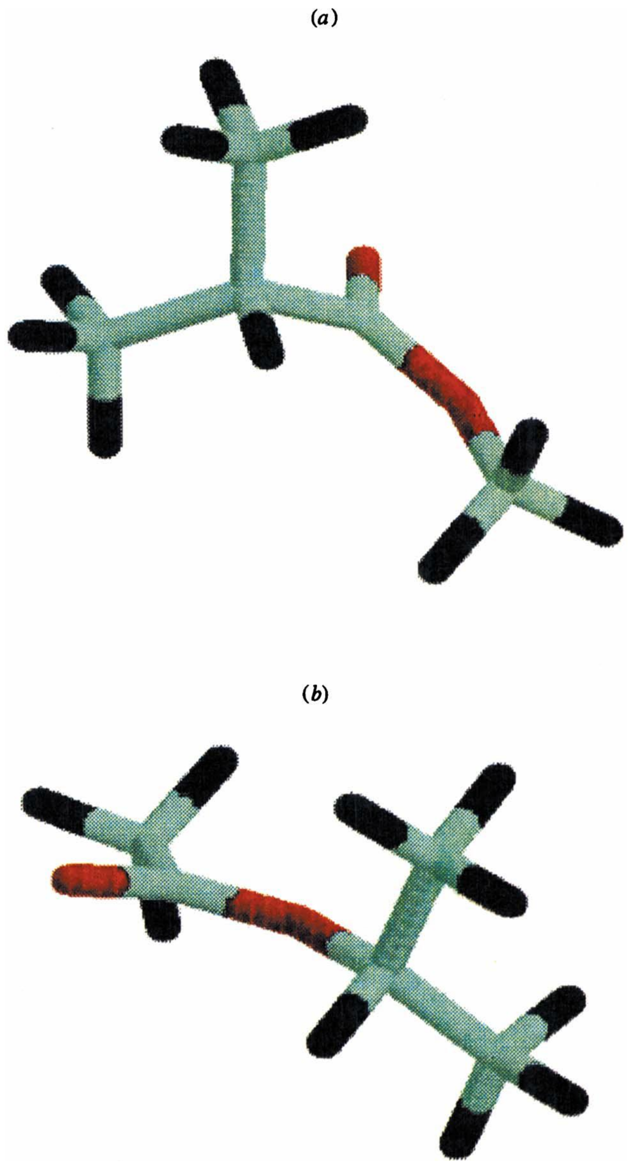


Fig. 3 (*a*) AM1 UHF minimum energy configuration of $Me_2CHC(O)OMe$ showing the tertiary C–H bond more or less confined to the –C–C(O)–O–C– plane; (*b*) AM1 UHF minimum energy configuration of $MeC(O)OCHMe_2$ showing the tertiary C–H bond at an angle of *ca.* 40° to the –C(O)–O–C– plane

the corresponding α-THF radical[38] for which α-H is 1.20 mT). This presumably reflects the existence of a +M effect of the neighbouring oxygen atom (*cf.* alcohol- and ether-derived radicals) encouraged by the good overlap expected in a planar (almost-rigid) ring. The β-H splitting [a(2H) = 3.12 mT] is typical of a five-membered ring with some degree of flexibility; as this value is larger than the α-THF-derived radical it suggests a greater amount of spin density on the carbon. Of further interest is the very large β-H coupling in **11** [a(2 H) = 4.06 mT] which is even larger than that observed for the corresponding 2-oxocyclopentyl radical [a(2H) = 3.62 mT].[38] This is typical of a rigid, planar species with additional distortion at the β-methylene group. The angles which these C–H bonds subtend to the orbital containing the unpaired electron can be calculated by employing a $B \cos^2 \theta$ relationship [using a value of a(β-H) of 2.49 mT for $^\bullet CHMeC(O)OMe$ gives a B value of 4.98 mT, assuming free rotation about the $^\bullet CH–Me$]; this leads to the prediction of dihedral angles of *ca.* 25° between the orbital of the unpaired electron and the β C–H bonds, clearly indicative of a very strained ring.

The value for the α-H splitting of 1.92 mT for **12** suggests a planar radical centre; the value of 2.77 mT for the β C–H is characteristic of some degree of chair character, as expected of six- rather than five-membered rings.[38] Radical **13** also has a planar radical centre but the larger β-H splitting value of 3.50 mT is reminiscent of a locked and planar ring with little distortion (see ref. 38).

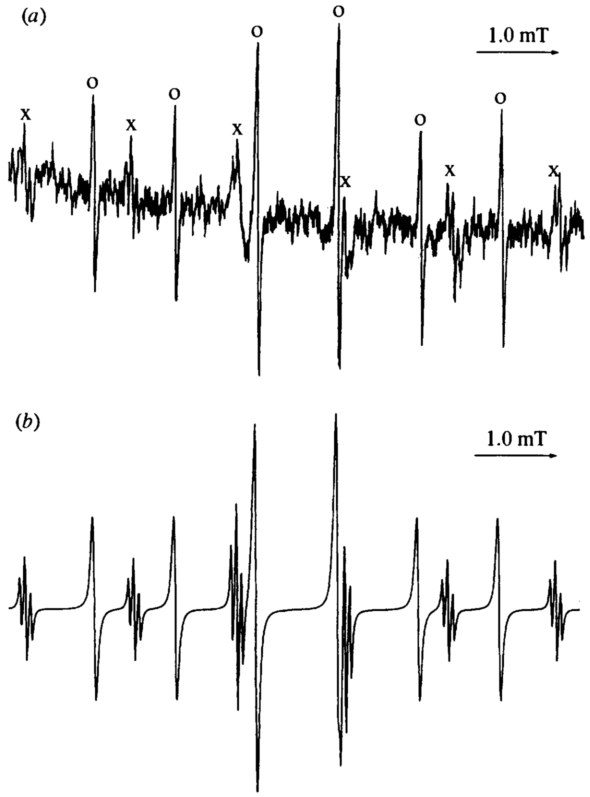
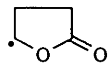
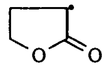
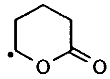
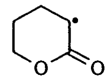


Fig. 4 EPR spectra (and simulation) of radicals produced by the reaction of γ-butyrolactone with $Bu^tO^\bullet$ (from *in situ* photolysis of Bu^tOOBu^t) at *ca.* 300 K, showing signals from **10** (o) and **11** (x): the central parts of the signal from **11** are broadened due to ring inversion


10


11


12


13

For the parent five-membered ring (γ-butyrolactone) attack next to the oxygen atom in **10** is favoured, as noted by Beckwith,[3] although our spectra also reveal the presence of the acyl-conjugated radical **11**.[6,39] However, when a methyl group is introduced adjacent to either function, attack to give solely the appropriate tertiary radical is observed (in apparent contrast to the interpretation of spectra presented[40] recently by Beckwith and Zavitsas); this finding strongly supports the claim that the bond dissociation energy is of major importance.† In contrast, for the unsubstituted six-membered analogue (δ-valerolactone) attack next to the carbonyl function is clearly favoured. Further, the rates of attack are greater for the six-membered ring than the five-membered analogue; compared with acyclic examples, the methylene group adjacent to the carbonyl in the former is activated, whereas the five-membered methylene position is deactivated.

In order to gain further information concerning the reasons for selectivity, studies of the relative reactivity of C–H bonds in

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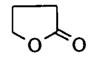
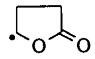
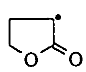
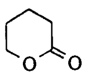
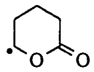
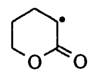
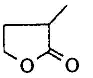
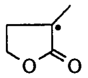
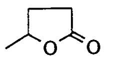
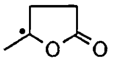
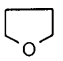
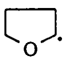
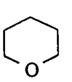
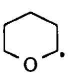
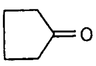
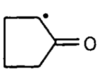
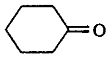
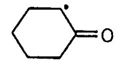
† A recent paper by Beckwith and Zavitsas claims[40] that in the case of α-methyl-γ-butyrolactone, the only radical observed is at the secondary position adjacent to the oxygen; this appears to be a result of misassignment in the text.

Table 2 EPR parameters and rate constants of formation of a variety of radicals obtained by reaction of $\mathrm{Bu^tO^\bullet}$ with lactones and some related compounds

Substrate	Radical		Hyperfine splittings[a]/mT[a]	g[b]	Selectivity (%)[c]	Rate constant per hydrogen/ $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$[d]	Overall rate constant/ $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$[d]
		**10**	a(1H) = 1.56 a(2H) = 3.12	2.0026	71	3.15 × 10^4	6.3 × 10^4
		**11**	a(1H) = 2.03 a(2H) = 4.06 a(2H) = 0.10	2.0033	29	1.25 × 10^4	2.5 × 10^4
		**12**	a(1H) = 1.92 a(2H) = 2.77	2.0027	36	4.2 × 10^4	8.4 × 10^4
		**13**	a(1H) = 1.97 a(2H) = 3.50 a(2H) = 0.06	2.0033	64	7.5 × 10^4	1.5 × 10^5
		**14**	a(3H) = 2.15 a(2H) = 3.65 a(2H) = 0.06	2.0031	100	5.0 × 10^5	5.0 × 10^5
		**15**	a(3H) = 2.09 a(2H) = 2.87	2.0026	100	1.3 × 10^5	1.3 × 10^5
			a(1H) = 1.20 a(2H) = 2.83 a(2H) = 0.17 a(2H) = 0.08	2.0032 (ref. 42)	100	2.1 × 10^6 (ref. 10)	8.3 × 10^6 (ref. 10)
			a(1H) = 1.58 a(2H) = 2.50 a(2H) = 0.07	2.0029 (ref. 43)	100	6.8 × 10^5 (ref. 36)	2.7 × 10^6 (ref. 36)
			a(1H) = 1.84 a(2H) = 3.62 a(2H) = 0.25	2.0045	100	5.0 × 10^5	2.0 × 10^6
			a(1H) = 1.79 a(2H) = 3.28	2.0045	100	3.0 × 10^5 (ref. 44)	1.2 × 10^6 (ref. 44)

[a] ±0.02. [b] ±0.0001. [c] Average of several measurements ±15%. [d] Estimated error ±30%.

the appropriate cyclic ketones were undertaken (see Table 2, which also contains details of the reactions of the corresponding ethers[10,36]). For both ketones and ethers the five-membered ring is of greater reactivity than the six-membered ring; this may be due in part, to a greater release in ring strain when the radical is formed though, as has been pointed out previously, reaction with the ethereal C–H bond is particularly rapid, due to a stereoelectronic effect[36,37] which reflects the stabilization gained by conjugation between the oxygen lone-pair and the unpaired electron. The rate of attack is found to be significantly less for carbonyl compounds, evidently due to electron-deficiency at the position adjacent to the C=O group; the radical once formed is however, stabilized by delocalization into the carbonyl π-orbitals, as noted earlier.

The rate constants for the reaction of the cyclic esters with $\mathrm{Bu^tO^\bullet}$ are considerably lower than those of the corresponding cyclic ethers and ketones [2.5 × 10^4–5.0 × 10^5 $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$ compared with (1.2–8.3) × 10^6 $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$; see Table 2], but of the same magnitude as the acyclic esters (5.4 × 10^3–2.5 × 10^5 $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$). The most notable feature is the general lack of reactivity of the C–H bonds in the unsubstituted five-membered ester ring; this is in contrast to the cyclic ether and ketones in which the five-membered rings are more reactive than the six-membered rings, although in all cases the substituents dominate the abstraction pattern observed. We suggest that this may be explained by the remarkably high ring-strain observed on radical formation, particularly in **10**, which results in a rigid planar ring arrangement (see above).

On the other hand, the relatively high reactivity of the α-CH bonds in the corresponding methyl-substituted lactones, to give **14** and **15** is notable. The value of 1.3 × 10^5 $\mathrm{dm^3\ mol^{-1}\ s^{-1}}$ for **15** is considerably higher than that of the acyclic analogue, $\mathrm{^\bullet CMe_2OC(O)Me}$. This implies the presence of a stereoelectronic effect which is favourable for the abstraction of C–H to give **15** *via* overlap in the transition state of a pseudo-axial hydrogen (see **16**). For **14** the particularly notable acceleration compared

16

with **11** [5.0×10^5 *versus* 2.5×10^4 $dm^3\ mol^{-1}\ s^{-1}$; note also the value of 2.5×10^5 $dm^3\ mol^{-1}\ s^{-1}$ for $^{\bullet}CMe_2C(O)OMe$] is presumably a result of a low bond dissociation energy with good (enthalpic) delocalization in the transition state, favoured by stereoelectronic effects (see also **16**).

Experimental

EPR spectra were recorded on a Bruker ESP300 spectrometer equipped with an X-band microwave bridge and 100 kHz modulation. The unfiltered radiation from an Hanovia 977B-1 1 kW mercury–xenon compact arc (at York) and the filtered radiation from a mercury–xenon 1 kW Oriel lamp (at Shell), were used to photolyse the samples in a standard variable temperature insert; the temperature in the cavity during irradiation was measured to be 300 ± 3 K using an external thermocouple, no differences were observed between spectra run at Shell and York using the different light systems. Hyperfine splittings and g-values were determined directly from the spectrometer's field scan, this having been calibrated with the signal from the methyl radical [$a(H) = 2.28$ and $g = 2.0026$[41]]. Relative rate constants were determined by double integration of the signal and/or computer simulation, to give the relative steady-state concentrations and hence by comparison with the known rate constant for abstraction of the α-secondary hydrogen in tetrahydrofuran absolute rate constants were determined. Absolute radical concentrations were determined by comparison with the double integration of the spectra of a solution of known concentration (2.6×10^{-4} mol dm^{-3}), of the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical (supplied by Aldrich at 95% purity) in toluene. All chemicals employed, other than $Bu^tC(O)OCH_2Bu^t$ and $PrC(O)OCH_2Bu^t$ which were prepared by Mr E. Nagatomi, were commercial samples and were used as supplied.

The minimum energy configurations were calculated using a Silicon Graphics Indigo 2 workstation incorporating Cerius 2 software as supplied by Molecular Simulations Incorporated. The radical simulation program was originally written by Dr M. F. Chiu and modified by Dr A. C. Whitwood to run on a Viglen 4SX25 PC.

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