Reactions of *tert*-Butoxyl Radicals with Acyclic Ethers Studied by the Radical Trapping Technique

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1,1,3,3-Tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl has been used as a radical trap to investigate the pattern of hydrogen abstraction reactions occurring in a range of acyclic ethers by *tert*-butoxyl radicals. The results confirm the high degree of selectivity for abstraction at C atoms adjacent to ethereal O. The presence of two α ethereal O atoms is less effective in enhancing abstraction than one. This is possibly due to a stereoelectronic effect whereby the 1,3-oxygen orbital interactions reduce the ability of either oxygen to interact effectively with the developing radical centre. Whereas the presence of an α-oxygen enhances the rate of hydrogen abstraction, the presence of a β-oxygen retards the rate of hydrogen abstraction. Abstraction at a methine C atom adjacent to ethereal O occurs at about the same rate or a little faster than at a methylene C atom, whereas abstraction at methyl groups is much slower. A temperature study of the abstraction from methyl and methylene sites in dimethoxymethane shows that the difference in abstraction rates at these sites is predominantly an entropy effect. A lower entropy of activation due to the loss of the internal rotational mode of the methyl group in the formation of the transition state is the probable reason. Ethers appear to be less reactive than alcohols in hydrogen abstraction reactions.

The rates of radical abstraction reactions and hence the selectivities for abstraction reactions on substrates containing a range of possible reaction sites are not easy to rationalise. The primary factors governing rate constants are of course the energy E_a, and entropy, $\Delta S^{\ddagger}$ of activation. The difficulty of calculating or even estimating values of $\Delta S^{\ddagger}$ has led to widespread acceptance of the assumption that entropy factors are negligible compared with energy factors. In fact, although a large number of experimentally determined frequency factors for abstraction reactions by polyatomic radicals lie in the expected range of 10^8–10^{10} dm^3 mol^{-1} s^{-1}, a number of unexpected and unexplained values well outside this have been observed.[1,2] In general however the results indicate that the assumption is reasonable for large differences in rates of abstraction but in cases of small differences, say with rate ratios < 100, entropy factors may make a significant contribution. The difficulty of estimating $\Delta S^{\ddagger}$ arises from the lack of knowledge of the transition state. In the formation of the transition state in a bimolecular process, three translational and three rotational motional modes are lost (for polyatomic radicals) and five vibrational modes are formed whilst the sixth mode becomes the reaction coordinate. Four of the new vibrational modes will be low energy bending motions associated mainly with the new bonds involved in transition state formation and the fifth will be an internal rotation. All are likely to make a small contribution to the entropy of the transition state at normal temperatures. Although the information required for calculation is not generally available, entropy factors should always be borne in mind when energy-based arguments prove inadequate. It should also be noted that the majority of experimentally determined frequency factors available refer to gas phase abstraction reactions. There are added complications for $\Delta S^{\ddagger}$ predictions relating to reactions in solution, particularly if the solvents are polar. An entropy factor, which is more easily accounted for, occurs in substrates containing a number of identical reaction sites, n. It is normally allowed for, as in this work, by dividing the observed relative rate constant k_{obs} by n, *i.e.*, $k_{obs} = nk_H$. Values of E_a are equally difficult to calculate, but the fact that there is often a correlation between reaction exothermicity and a favourable reaction has led to the general opinion that E_a is linked to ΔH. The Evans–Polanyi equation:[3] $E_a = \alpha\Delta H + B$, a specialised form of this relationship, has been shown to have only restricted application to series of reactions having very similar features.[3] It is important to recognise that E_a may bear no relationship to ΔH, *e.g.*, when the transition state occurs early along the reaction coordinate, in which case, E_a is strongly influenced by the nature of the reaction site and is little influenced by aspects of the product species.

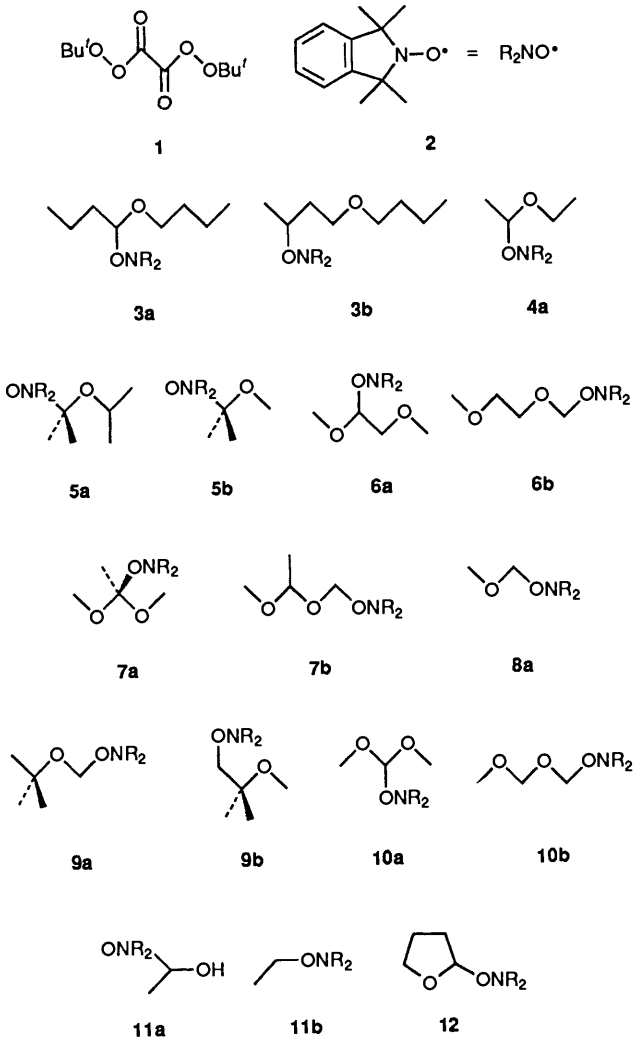
In the case of H abstraction reactions from ethers, the subject of this paper, previous authors have observed favourable reaction at the C atom adjacent to ethereal oxygen.[4–8] This is said to be due to conjugative delocalisation between the non-bonding orbitals of the O atom and the C radical. Thus the increased exothermicity in radical formation reduces E_a relative to that of competing processes. Since the extent of conjugative delocalisation is a function of the dihedral angle between the interacting orbitals, being maximum at 0° and minimum at 90°, the rates of these reactions are also said to be under stereoelectronic control.[3,9,10] This may be an important factor in substrates with restricted motional freedom, *e.g.* cyclic ethers, but it can only be a minor factor for acyclic ethers in which free rotation allows easy conformer interchange. The previous work on the reaction of *tert*-butoxyl radicals with ethers has involved (*a*) photolysis followed by EPR analysis[5] at −60 °C and (*b*) an indirect method in which the influence of the ether abstraction reaction at 25 °C on the build-up of diphenylhydroxymethyl radicals following laser flash photolysis was monitored.[4] The latter method gave no indication of the site of abstraction and the former is critically dependent on EPR assignments and presumably spectral simulations.

In this paper we report the results of the reaction of *tert*-butoxyl radicals, produced by the thermal decomposition of di-*tert*-butyl diperoxyoxalate **1** at 60 °C, with each of a range of acyclic ethers and one alcohol (**3**–**11**) (Table 1) in the presence of 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl **2**, a radical scavenger which is known to combine with C-centred radicals at near diffusion controlled rates.[11] Thus the primary abstraction products are efficiently trapped. Separation, identification and quantification of the trapped products enables the pattern of abstraction reactions by *tert*-butoxyl radicals for each ether to be determined.

Table 1 Relative reactivity towards H-abstraction[a]

	Substrate	Rel. reactivity[b]
	Cyclohexane	1.0
11	CH_3CHHOH	28.8
3	$CH_3(CH_2)_3OCHH(CH_2)_2CH_3$	12.6
4	$CH_3CH_2OCHHCH_3$	8.0
5	$(CH_3)_2CHOCH(CH_3)_2$	8.0
7	$CH_3CH(OCH_3)_2$	5.6
6	$CH_3OCHHCH_2OCH_3$	4.1
10	$CH_3OCHHOCH_3$	2.8
6	$CH_3OCH_2CH_2OCHH_2$	2.2
9	$(CH_3)_3COCHH_2$	2.2
8	CH_3OCHH_2	1.5
3	$CH_3(CH_2)_3O(CH_2)_2CHHCH_3$	1.4
7	$CH_3OCH(CH_3)OCHH_2$	0.8
10	$CH_3OCH_2OCHH_2$	0.7
9	$CH_3OC(CH_3)_2CHH_2$	0.2

[a] *H* indicates the hydrogen abstracted. [b] Per equivalent hydrogen.



The use of internal standards in each experiment has enabled the results for separate ethers to be referred to a common standard. The determination of rate constant ratios from product ratios requires that the substrate ether and the reference ether are both present in excess of the initiator.

Results and Discussion

The structures of products isolated and characterised are shown as **3a–11b**. Rate constants at 60 °C (25 °C for dimethyl ether) for abstraction by *tert*-butoxyl radicals from acyclic ethers **3–10** and ethanol **11** relative to the rate constant for abstraction from tetrahydrofuran (THF) are given in Table 2, where they are compared with literature values. There is reasonable agreement only with the values for diethyl ether, determined by the flash photolysis method and for dimethoxymethane determined by the EPR method. It is unlikely that the discrepancies can be completely explained by the different temperatures or additives (solvents) used, although the data necessary for a precise comparison are not available.

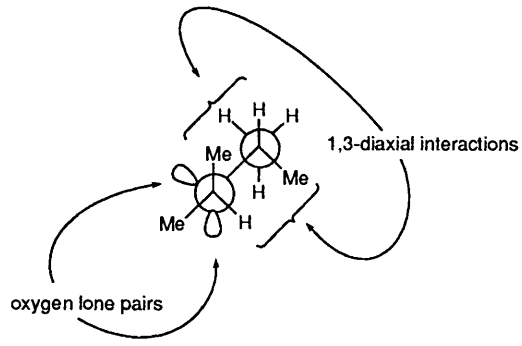


Fig. 1

In order to examine the molecular features influencing the reactivity at individual H atoms, values of the rate constants per equivalent H atom in the substrate relative to the rate constant per single H atom in cyclohexane are listed in Table 3 in decreasing order, along with the proximity of chemical groups. Values for THF and cyclohexane, which were used as internal standards in the series, are included although discussion of abstraction from cyclic substrates by *tert*-butoxyl radicals is presented in the accompanying paper. For ease of comparison, structure and relative reactivities towards hydrogen abstraction by *tert*-butoxyl radicals are also displayed in Table 1.

A number of generalisations can be made as follows. (*i*) Oxygen α to C–H strongly enhances abstraction. (*ii*) Oxygen β to C–H retards abstraction (*cf.* **3**, **4** and **6**). (*iii*) Oxygen γ to C–H slightly enhances abstraction. (*cf.* **3**). (*iv*) Two oxygens α to C–H are less effective in the enhancement of abstraction than one (*cf.* **5** and **7**; **4** and **10**). (*v*) Abstraction at CH is at about the same rate as at CH_2 (*cf.* **4** and **5**) or a little faster (*cf.* **7** and **10**). (*vi*) Abstraction at CH_3 is slower than at CH_2 or CH. (*vii*) A hydroxy group α to C–H very strongly enhances abstraction.

Generalisation (*i*) has been well documented previously.[4–8] The presence of an adjacent ether-oxygen atom enhances the ease of abstraction at a C–H group owing to the donation of electron density from the oxygen lone pair into the antibonding orbital of the C–H bond. There is thus a conformational requirement for α-oxygen enhancement of C–H abstraction. This is illustrated in the low rate of abstraction from **5**. A stable conformation for **5** where the oxygen lone pairs have the correct alignment for interaction with the antibonding orbital of the methine C–H bonds is shown in Fig. 1. It is clear that attack by the bulky *tert*-butoxyl radical will be hindered by the proximity of the neighbouring methyl groups. Thus, the reduced rate of abstraction in **5** (which would be expected to be higher than in **4**) is due largely to steric factors. However, it is also possible that in order to minimise non-bonded interactions, **5** adopts a conformation in which the oxygen lone pair can no longer interact as effectively with the antibonding orbital of the C–H bond. A similar argument has been used by Malatesta and Scaiano.[4]

Rate retardation at the β position is almost certainly due to polar effects. The *tert*-butoxyl radical is known to have some electrophilic character[1,2] which will discourage reaction at the β site due to the electron attracting effect of the ethereal O. This effect is apparently too small to compete with the conjugative

Table 2 Rate constants for H abstraction by *tert*-butoxyl radicals from acyclic ethers at 60 °C relative to that from tetrahydrofuran

Substrate	Product	k/k_{THF}	Lit. values of k/k_{THF} Ref. 4[a]	Ref. 5[b]	$k^c/10^6$ dm^3 mol^{-1} s^{-1}
3	**3a**	0.655			5.5
	3b	0.071			0.6
4	**4a**	0.419	0.47	0.16	3.5
5	**5a**	0.207	0.14		1.7
6	**6a**	0.214			1.8
	6b	0.170			1.4
7	**7a**	0.073	0.27		0.6
	7b	0.065			0.5
8	**8a**	0.116[d]			
9	**9a**	0.086			0.7
	9b	0.025			0.2
10	**10a**	0.094	0.10	0.13	0.8
	10b	0.075		0.08	0.6
11	**11a**	0.75		0.14	6.2

[a] 25 °C. [b] −60 °C. [c] Based on the value for cyclopentane calculated from data in ref. 23, *i.e.* k(60 °C) = 1.3 × 10^6 dm^3 mol^{-1} s^{-1}. [d] 25 °C.

Table 3 Relative rate constants for H abstraction by *tert*-butoxyl radicals from reaction sites in acyclic ethers compared with the proximity of chemical groups

Substrate (S)	Group abstracted	Product[a]	$k_H(S)/k_H(Cy)$[b]	α Groups	β Groups
11	CH_2	**11a**	28.8	OH, CH_3	
THF	CH_2(cyclic)	*c*	19.2	O, CH_2	CH_2, CH_2
3	CH_2	**3a**	12.6	O, CH_2	CH_2, CH_2
4	CH_2	**4a**	8.0	O, CH_3	CH_2
5	CH	**5a**	8.0	O, CH_3, CH_3	CH
7	CH	**7a**	5.6	O, O, CH_3	CH_3, CH_3
6	CH_2	**6a**	4.1	O, CH_2	O, CH_3
10	CH_2	**10a**	2.8	O, O	CH_3, CH_3
9	CH_3	**9a**	2.2	O	C
6	CH_3	**6b**	2.2	O	CH_2
8	CH_3	**8a**	1.5	O	CH_3
3[c]	CH_2	**3b**	1.4	CH_3, CH_2	CH_2
Cy[b]	CH_2(cyclic)	*d*	1.0	CH_2, CH_2	CH_2, CH_2
7	CH_3	**7b**	0.8	O	CH
10[c]	CH_3	**10b**	0.7	O	CH_2
9	CH_3	**9b**	0.2	C	O, CH_3 (×2)

[a] No abstraction products [*i.e.* $k_H(S)/k_H(Cy)$ < 0.2] were observed at the β CH_2 and δ CH_3 positions in **3** or at the β CH_3 position in **4**, **5**, **7** and **11**. [b] Cy = cyclohexane, $k_H(S)$ = rate constant per individual equivalent H atom in S. [c] γ Group is oxygen. [d] (1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxy)cyclohexane.

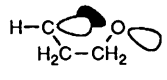


Fig. 2

stabilisation effect of the O lone pair at the α sites and is too weak to influence attack at the γ site in **3** where some abstraction is observed. Similar patterns of abstraction have been observed in butan-1-ol.[13,14] It is interesting to note that the β-(retardation) effect observed here is opposite to the β-effect found by Barton *et al.*[15] An explanation for this dichotomy will be presented elsewhere.

The small rate enhancement for H abstraction γ to oxygen may be due to donation of electron density from a p-type[7] oxygen lone pair into the antibonding orbital of the γ C–H bond. It is clear from a study of molecular models that an orbital interaction of this type is conformationally possible for a γ C–H, but difficult for a β C–H antibonding orbital. Such an orbital overlap (Fig. 2) is much weaker than for the corresponding overlap between the oxygen lone pair and the antibonding orbital of an α C–H bond.

It is more difficult to explain why two α O atoms are less effective in enhancing abstraction than a single α O atom [generalisation (*iv*)]. Thermochemical measurements[16] have established that a pair of acyclic ethereal O atoms in the 1,3 positions stabilizes the molecule to the extent of 17 kJ mol^{-1} relative to a methylene chain in which the two O atoms are isolated from each other. With the same reference structure, two O atoms in the 1,4 positions are shown to destabilize the molecule by 10 kJ mol^{-1}. It is highly probable that this medium range interaction between O atoms in the 1,3 positions reduces the conjugation potential of the O non-bonding orbitals for assisting radical formation at the methine group in **7**. One might anticipate that O atoms 1,4 to each other would cause enhancement of the conjugation potential in the α position. It is interesting to observe that apart from **9**, the largest extent of abstraction to occur from a methyl group in the whole series was with **6** which contains O atoms 1,4 to each other. Note that the methylene group in the other α position in **6** is also β to the second O atom, *i.e.* a mixture of activation and deactivation presumably operates.

Substrates **10** and **6** have also been studied by Beckwith and Brumby.[17] These authors found that for **10**, a methylene hydrogen was 2.4 times as reactive as a methyl hydrogen towards hydrogen abstraction at −35 °C. This compares with a figure of 4.0 found here (Table 3) and a figure of 5.0 (at −60 °C)

Table 4 Temperature effect on rate constants for abstraction by *tert*-butoxyl radicals from dimethoxymethane

T/°C	Reaction time	Product ratio[a]	$k_H(1)/k_H(2)$[b]
0	2 weeks	0.708	0.236
30	18 h	0.745	0.248
60	70 min	0.744	0.248
100	30 min	0.774	0.258

[a] (Product **10b**)/(product **10a**). [b] k_H is rate constant per equivalent H atom in the substrate. $k_H(1)$ and $k_H(2)$ refer to the rate constants for eqns. (1) and (2) respectively.

reported by Malatesta and Ingold.[5] Similarly for **6**, Beckwith and Brumby found that the relative reactivity of methylene:methyl was 1.33:1 at −43 °C and 1.97:1 at −111 °C. Our figure (Table 3) was 1.86:1. As mentioned earlier, the reason for these discrepancies is not yet clear. We are confident in the reproducibility of our data and suggest that the experimental error is about ± 5%.

Malatesta and Scaiano[4] also found that the presence of two α O atoms did not enhance abstraction rates over those in the presence of one O atom in acyclic ethers, *e.g.* for di- and trimethoxymethane, k_H/k_H (THF) have values of 0.20 and 0.24 respectively compared with a value of 0.47 for diethyl ether. However, enhancement was observed for the five membered cyclic ethers showing that different rules apply with restricted conformations.

The order of reactivity at C atoms adjacent to a single O atom according to extent of substitution is approximately CH > CH_2 ≫ CH_3 although it must be remembered that a minor effect is being considered here in the presence of the major effect of ethereal O proximity. *tert*-Butoxyl radicals have previously been observed to attack with medium selectivity due partly to their bulky nature and partly to their electrophilic character. For example, in abstraction reactions from alkanes, *tert*-butoxyl falls between F and CH_3 in terms of discrimination between primary, secondary and tertiary reaction sites in the alkane.[3] The bulky nature of *tert*-butoxyl radicals is apparent in the reduced reactivity of the C–H α to oxygen in diisopropyl ether **5** as discussed earlier. Thus whereas CH is generally more reactive than CH_2 (*cf.* **7** and **10**), the reactivity of CH in **5** was approximately equal to the reactivity of CH_2 in diethyl ether **4**.

The low degree of reactivity at a methyl group may be due primarily to the loss of the methyl internal rotational mode of motion in the formation of the transition state. This will have the effect of lowering $\Delta S^{\ddagger}$ relative to the value for abstraction at methylene and methine sites and, in the absence of significant energy of activation effects, will lead to a reduced rate constant. The relative rates of abstraction at the methylene and methyl sites in dimethoxymethane were studied over a 100 °C temperature range. The results are shown in Table 4. A very small increase in k_1/k_2 with temperature is observed where the subscripts refer to eqns. (1) and (2) below. An Arrhenius

$$(CH_3)_3CO^{\bullet} + CH_3OCH_2OCH_3 \longrightarrow (CH_3)_3COH + CH_3OCH_2OCH_2^{\bullet} \quad (1)$$

$$(CH_3)_3CO^{\bullet} + CH_3OCH_2OCH_3 \longrightarrow (CH_3)_3COH + CH_3O\dot{C}HOCH_3 \quad (2)$$

treatment of the data leads to the values: $E_a(1) - E_a(2) = 0.7 \pm 0.6$ kJ mol^{-1}; $\Delta S^{\ddagger}(1) - \Delta S^{\ddagger}(2) = -9.3 \pm 2.0$ J K^{-1} mol^{-1}. The error values are based on our estimated precision of ± 5% in the rate constant ratios.

Thus, in this example the difference between k_1 and k_2 is mainly due to the difference in the entropies of activation for the respective processes and a major contributing factor is the loss of the internal rotational mode of motion of the methyl group in the formation of the transition state in reaction (1). The corresponding loss of entropy in the formation of the transition state in reaction (2) involves vibrational motion and is consequently a significantly lower value. Benson has suggested that the entropy contribution of a freely rotating methyl group[18] is 24 J K^{-1} mol^{-1}. In the absence of E_a effects, this is equivalent to a maximum value of 18 for k_1/k_2. However, there are of course, many compensating contributions which lower this value.

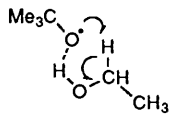


Fig. 3

Abstraction at the α C atom of ethanol **11** was virtually exclusive and occurred at a higher rate than any observed for the ethers. Previous work on propan-1-ol and butan-1-ol[13,14] has shown that predominant abstraction occurs at the α C atom and that almost negligible abstraction occurs at the terminal methyl group. Malatesta and Scaiano[4] also found a fairly high abstraction rate for *tert*-butoxyl attack on propan-2-ol. Assuming exclusive abstraction at the α C atom their data give: k_H (propan-2-ol)/k_H(cyclohexane) = 16.9. The most likely explanation is that the presence of the H atom, which is more electropositive than carbon, enhances the ability of the non-bonding electron pairs of the O atom to stabilize an unpaired electron on the α C atom in free radical formation. However, solvation of the transition state by the alcohol may also be a contributing factor (Fig. 3). This might account for the higher reactivity of ethanol (28.8) compared with propan-2-ol (16.9). Propan-2-ol is less polar than ethanol and more sterically hindered.

Experimental

Substrates.—The acyclic ethers **3**–**7**, **9** and **10**, were each refluxed over $LiAlH_4$, and then fractionally distilled. Compound **8** was used as supplied. Ethanol **11**, absolute grade, was fractionally distilled under argon. THF was dried over KOH before fractional distillation. Cyclohexane, AR grade, was fractionally distilled before use. All substrates were stored over molecular sieves, 3 Å.

Di-*tert*-butyl diperoxyoxalate* **1** was prepared by the method of Bartlett *et al.*[19] from oxalyl chloride and *tert*-butyl hydroperoxide. Radical trap **2** was prepared as previously described.[20]

Radical Trapping Experiment. General Procedure.—Reaction mixtures (5 cm^3) consisted of substrate and internal standard in 1:1 molar ratio as solvent, initiator and radical trap, 0.086 and 0.186 mol dm^{-3} respectively. Following degassing by successive freeze–thaw cycles on a high vacuum line, reaction mixtures were maintained at 60 °C (± 1 °C) for 68 min (10 half-lives), except for ether **8** which was left overnight at 25 °C, and for ether **10** which was allowed to react for 2 weeks at 0 °C, overnight at 30 °C and 30 min at 100 °C in separate experiments, additional to that at 60 °C. Quantitative analysis was achieved by direct injection of each mixture into a reversed phase HPLC instrument. Acetonitrile–water or methanol–water mixtures were used as eluent and 270 nm was the wavelength for detection. For preparative scale experiments initiator and trap content was scaled up by a factor of 6 and

* **CAUTION**: explosion hazard.

Table 5 Influence of trap concentration on product ratios. Substrate is 1 : 1 molar mixture of THF and cyclohexane[a]

THF/trap[b]	A/B[c]
4	6.44
16	6.36
23	6.41
64	6.42
100	6.46
550	6.38

[a] Initiator concentration constant. [b] Molar ratio. [c] Ratio of peak areas in HPLC chromatograph of products. A = product from THF abstraction; B = product from cyclohexane abstraction.

volatile material was removed prior to preparative scale HPLC. For the analytical experiments internal standards were used as appropriate, *i.e.* cyclohexane for substrates **5–8**, THF for **4** and **9–11** and diethyl ether for **3**.

Product Analysis.—Peak areas from HPLC chromatograms were converted directly into % molar yields of products. Alkoxyamine compounds containing one mol equiv. of the radical trapping moiety and no other UV chromophoric groups have been shown to have almost identical molar extinction coefficients at 270 nm.[21]

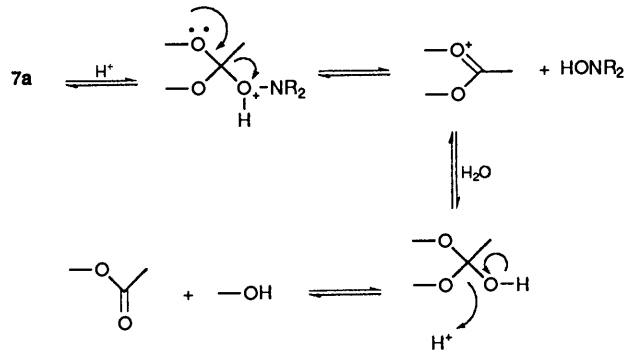
The HPLC-separated products were identified by NMR techniques as described previously.[22] ^{1}H and ^{13}C NMR spectra (proton-noise decoupled; off-resonance decoupled) were recorded on a Bruker WM-250 spectrometer (at 250.12 and 62.80 MHz) using deuteriated chloroform as solvent and tetramethylsilane as internal standard.

Trap Concentration Effects.—A check on the effect of trap concentration on product ratios was carried out on 1 : 1 molar mixtures of THF and cyclohexane. The results, Table 5, show that in the range 9×10^{-4} to 1.25×10^{-1} of trap to substrate molar ratio there is negligible variation of the product ratio. The relative reactivity of THF *vs.* cyclohexane was taken as 6.41, the average value found.

Solvent Effects.—Although we have ignored solvent effects in deriving the rate constants presented in Table 2, some small but significant solvent effects were observed. For example, when hydrogen abstraction ratios for dimethoxymethane were determined with THF as internal standard, the ratio of the two products **10a** : **10b** was 1.25. When the experiment was repeated using cyclohexane as internal standard, the ratio of **10a** : **10b** was 1.34 (both at 60 °C). These two experiments gave rate constants for the corresponding hydrogen abstraction processes of (*a*) 0.78×10^{-6} dm^3 mol^{-1} s^{-1} (formation of **10a** in THF), (*b*) 0.60×10^{-6} dm^3 mol^{-1} s^{-1} (formation of **10a** in cyclohexane), (*c*) 0.62×10^{-6} dm^3 mol^{-1} s^{-1} (formation of **10b** in THF) and (*d*) 0.45×10^{-6} dm^3 mol^{-1} s^{-1} (formation of **10b** in cyclohexane). A more detailed study of solvent effects will be presented elsewhere.

Stability of Products.—The majority of trapped products were stable under reaction and HPLC analytical conditions. The unstable ones were as follows.

(*i*) The adduct **7** formed by abstraction at the methine group of **7** and trapping, was sufficiently stable in HPLC eluent for reproducible quantitative analysis to be obtained. However rapid decomposition occurred in either $CDCl_3$ or dimethyl sulfoxide resulting in a ^{13}C NMR spectrum of, at best, an impure product. GC was used to show that the decomposition products contained methyl acetate and methanol, thus adding further evidence in favour of the structure suggested by NMR. The decomposition mechanism is shown in Scheme 1.

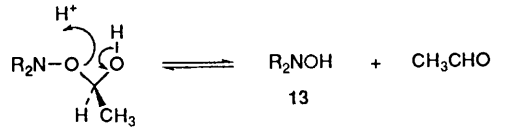


Scheme 1

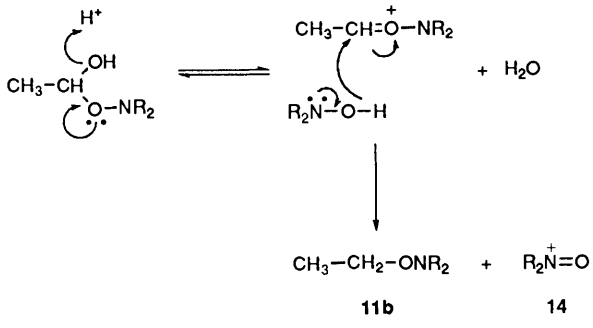
(*ii*) The adduct **5a** formed by abstraction at the methine group of **5** and trapping, slowly decomposed in the presence of methanol by acetal exchange to form **5b**. Reproducible quantitative results were obtained as long as analyses were performed rapidly. Both the adduct and the decomposition product were characterised by ^{13}C NMR.

(*iii*) The adduct **11a**, an unstable hemiacetal formed by abstraction at the methylene group of **11** and trapping, decomposed to give acetaldehyde and **11b**. The reactivity of ethanol *vs.* THF was determined as follows. A known amount of di-*tert*-butyl diperoxyoxalate **1** was decomposed in neat ethanol in the presence of the aminoxyl **2**. The yield of acetaldehyde (83% based on **1**) was calculated by GC comparison with ethanol samples containing known amounts of acetaldehyde. The yield of **11b** was thus assumed to be $\leqslant$17%. When the same reaction was carried out in an equimolar mixture of THF and ethanol, the ratio of product **11b** to the product of α-abstraction from THF **12** was 0.128 : 1.0 respectively (by HPLC). Using the figure of 17% for the yield of **11b** gives a ratio of **11a** (the precursor of acetaldehyde and of **11b** see below) to **12** of 0.75 : 1.0.

The acetaldehyde presumably arises by a simple hydrolysis of the hemiacetal (Scheme 2). The formation of **11b** however,



Scheme 2



Scheme 3

requires a reduction. A possible mechanism is suggested in Scheme 3. The product **14** would be expected rapidly to oxidise the hydroxylamine **13** (see Scheme 2) reforming the aminoxyl **2**. Schemes 2 and 3 suggest that a substantial amount of **2** should be recovered. This was confirmed by HPLC. Product **11b** was characterised unambiguously by ^{13}C and ^{1}H NMR. Unfortunately there was insufficient material for a microanalysis and it failed to give a parent ion in the mass spectrum.

New Compounds.—New alkoxyamine products were characterised by the spectroscopic data listed below. *J* Values are given in Hz, ring CH_3 refers to methyl substituents as isoindole.

Butyl 1-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*butyl ether* **3a**. (Found: MH^+, 320.257. $C_{20}H_{34}NO_2$ requires MH^+, 320.259. $\delta_C(CDCl_3)$ 13.7 ($CH_3CH_2CH_2CH_2$), 14.0 [$CH_3CH_2CH_2CH(ONR_2)$], 18.1 ($CH_3CH_2CH_2CH_2$), 19.1 [$CH_3CH_2CH_2CH(ONR_2)$], 25.2, 28.9 and 30.0 (4 × ring CH_3), 32.1 ($CH_3CH_2CH_2CH_2$), 36.0 [$OHC(ONR_2)CH_2$], 67.5 and 67.8 (C-1, C-3), 68.9 ($CH_3CH_2CH_2CH_2O$), 108.0 [$OHC(ONR_2)$], 121.3 and 121.6 (C-4, C-7), 127.2 (C-5, C-6), 145.1 and 145.6 (C-3a, C-7a); $\delta_H(CDCl_3)$ 0.9–1.8 (m, 26 H, 4 × CH_2, 2 × CH_3, 4 × ring CH_3), 3.6 (dt, 1 H, $^2J_{gem}$ 9.3, ^3J 6.9, $CH_3CH_2CH_2HCHO$), 3.9 (dt, 1 H, $^2J_{gem}$ 9.3, ^3J 6.9, $CH_3CH_2CH_2HCHCHO$), 4.86 [t, 1 H, ^3J 5.6, $OHC(ONR_2)$], 7.1 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

Butyl 3-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*butyl ether* **3b**. (Found: MH^+, 320.259. $C_{20}H_{34}NO_2$ requires MH^+, 320.259); $\delta_C(CDCl_3)$ 13.8 ($CH_3CH_2CH_2$), 19.3 ($CH_3CH_2CH_2$), 26.0 (CH_3CH), 26.8 [$CH_3CH(ONR_2)CH_2$], 31.8 ($CH_3CH_2CH_2$), 67.8 (C-1, C-3), 70.7 (CH_2OCH_2), 77.1 [$CH_3CH(ONR_2)$], 121.5 (C-4, C-7), 127.3 (C-5, C-6), 145.7 (C-3a, C-7a); $\delta_H(CDCl_3)$ 0.9 (t, 3 H, *J* 7.2, CH_3CH_2), 1.2–1.7 (m, 20 H, 8 × aliphatic H, 4 × ring CH_3), 3.44 and 3.41 (2 × t, 4 H, ^3J 6.2, ^3J 6.5, CH_2OCH_2), 3.9 [M, 2 H, $CH(ONR_2)$, $OCH_2HCHCHONR_2$], 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

Ethyl 1-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*ethyl ether* **4a**. (Found: MH^+, 264.195. $C_{16}H_{26}NO_2$ requires MH^+, 264.196); $\delta_C(CDCl_3)$ 15.3 (CH_3CH_2O), 19.6 [$CH_3CH(ONR_2)$], 25.4 (br s, 2 × ring CH_3), 29.2 (br s, 1 × ring CH_3), 29.9 (s, 1 × ring CH_3), 63.1 (CH_3CH_2O), 68.5 (br s, C-1, C-3), 104.9 [$CH_3CH(ONR_2)O$], 121.6 (C-4, C-7), 127.3 (C-5, C-6), 143.9 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.2–1.6 (m, 18 H, 4 × ring CH_3, 2 × CH_3), 3.6 (dq, 1 H, $^2J_{gem}$ 9.3, ^3J 7.0, CH_3HCHO), 3.9 (dq, 1 H, $^2J_{gem}$ 9.3, ^3J 7.0, CH_3HCHO), 5.0 [br q, 1 H, ^3J 5.5, $CH_3CH(O)ONR_2$], 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

Prop-2-*yl* 2-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*prop*-2-*yl ether* **5a**. $\delta_C(CDCl_3)$ 24.2 [$CH(CH_3)_2$], 24.5 [$C(CH_3)_2ONR_2$], 25.3 and 28.9 (4 × ring CH_3), 63.8 [$(CH_3)_2CHO$], 67.0 (C-1, C-3), 104.3 [$OC(CH_3)_2O$], 121.1 (C-4, C-7), 126.6 (C-5, C-6), 145.1 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.35 [d, 6 H, ^3J 6.5 $(CH_3)_2CH$], 1.45 (s, 6 H, 2 × ring CH_3), 1.60 and 1.61 (2 × 6 H, 4 × CH_3), 4.3 [sept, 1 H, *J* 6.5, $(CH_3)_2CH$], 7.2 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

Methyl 2-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*prop*-2-*yl ether* **5b**. $\delta_C(CDCl_3)$ 24.4 [$OCH(CH_3)_2$], 25.2, 25.2 and 29.3 (4 × ring CH_3), 49.6 (OCH_3), 67.4 (C-1, C-3), 104.0 [$OC(CH_3)_2O$], 121.5 (C-4, C-7), 127.1 (C-5, C-6), 145.5 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.3–1.6 (v br s, 18 H, 2 × CH_3, 4 × ring CH_3), 3.40 (s, 3 H, OCH_3), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

1,2-*Dimethoxy*-1-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*ethane* **6a**. (Found: MH^+, 280.192. $C_{16}H_{26}NO_3$ requires MH^+, 280.191); $\delta_C(CDCl_3)$ 25.0 and 24.7 (2 × ring CH_3), 29.4 and 28.6 (2 × ring CH_3), 56.0 (CH_3OCH_2), 58.9 (CH_3OCH), 67.1 and 67.7 (C-1, C-3), 72.0 [$OCH_2CHO(ONR_2)$], 106.9 [$OCH(ONR_2)$], 121.1 and 121.3 (C-4, C-7), 127.0 (C-5, C-6), 144.6 and 144.9 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.6 and 1.55 (2 × 3 H, 2 × ring CH_3), 1.4 (br s, 6 H, 2 × ring CH_3), 3.5 and 3.6 (2 × s, 2 × 3 H, 2 × CH_3O), 3.5 [dd, 1 H, ^2J 10.5, ^3J 5.6, $OHCHCH(O)ONR_2$], 3.6 [dd, 1 H, ^2J 10.5, ^3J 5.3, $OHCHCH(O)ONR_2$], 5.0 (dd, 1 H, ^3J 5.3, ^3J 5.6, $OCHONR_2$), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

2-*Methoxy*-1-[(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*methoxy*]*ethane* **6b**. (Found: MH^+, 280.189. $C_{16}H_{26}NO_3$ requires MH^+, 280.191); $\delta_C(CDCl_3)$ 25.1 (v br s, 2 × ring CH_3), 29.1 (v br s, 2 × ring CH_3), 58.9 (CH_3OCH_2), 67.3 (C-1, C-3), 68.1 ($CH_3OCH_2CH_2$), 71.8 ($OCH_2CH_2OCH_2$), 101.1 (OCH_2O), 121.5 (C-4, C-7), 127.2 (C-5, C-6), 144.9 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.4 (br s, 6 H, 2 × ring CH_3), 1.5 (br s, 6 H, 2 × ring CH_3), 3.4 (s, 3 H, CH_3O), 3.7 (m, 2 H, OCH_2CH_2O), 3.9 (m, 2 H, OCH_2CH_2O), 5.1 (s, 2 H, OHCHO), 7.1 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

1,1-*Dimethoxy*-1-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*ethane* **7a**. $\delta_C(CDCl_3)$ (partially decomposed) 22.8 and 26.8 (2 × br s, 4 × ring CH_3), 23.2 (O_3CCH_3), 62.8 and 64.4 (OCH_3), 118.9 and 119.4 [br s, $O_3C(CH_3)$], 124.6 (br s), 127.0 (br s, C-5, C-6), 142.6 (C-3a, C-7a), 167.0 [$OC(O)CH_3$].

1-*Methoxy*-1-[(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*methoxy*]*ethane* **7b**. (Found: MH^+, 280.188. $C_{16}H_{26}NO_3$ requires MH^+, 280.191); $\delta_C(CDCl_3)$ 19.8 [$OCH(O)CH_3$], 25.1 (v br s, 2 × ring CH_3), 29.2 (v br s, 2 × ring CH_3), 52.1 (CH_3O), 67.3 (C-1, C-3), 96.7 [$OC(CH_3)HO$], 99.3 (R_2NOCH_2O), 121.6 (C-4, C-7), 127.3 (C-5, C-6), 145.0 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.4 (br s, 6 H, 2 × ring CH_3), 1.5 (d, 3 H, ^3J 5.3, $CHCH_3$), 1.5 (br s, 6 H, 2 × ring CH_3), 3.4 (s, 3 H, OCH_3), 5.02 (q, ^3J 5.3, $CHCH_3$), 5.1 (d, 1 H, ^2J 7.3, ONR_2HCHO), 5.2 (d, 1 H, ^2J 7.3, ONR_2HCHO), 7.1 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

Methyl (1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*methyl ether* **8a**. (Found: M^+, 235.157. $C_{14}H_{21}NO_2$ requires M^+, 235.157); $\delta_C(CDCl_3)$ 25.2 and 29.1 (4 × ring CH_3), 56.3 (OCH_3), 67.3 (C-1, C-3), 102.2 [$(CH_3O)CH_2ONR_2$], 121.7 (C-4, C-7), 127.3 (C-5, C-6), 145.1 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.37 (br s, 6 H, 2 × ring CH_3), 1.47 (br s, 6 H, 2 × ring CH_3), 3.49 (s, 3 H, OCH_3) 4.89 (s, 2 H, CH_2ONR_2), 7.10 (m, 2 H, 4-H, 7-H), 7.21 (m, 2 H, 5-H, 6-H).

tert-*Butyl* (1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*methyl ether* **9a**. (Found M^+, 277.204. $C_{17}H_{27}NO_2$ requires M^+, 277.204); $\delta_C(CDCl_3)$ 25.1 and 28.1 (4 × ring CH_3), 28.6 [$(CH_3)_3C$], 67.1 (C-1, C-3), 74.1 [$(CH_3)_3COCH_2$], 95.2 (OCH_2ONR_2), 121.6 (C-4, C-7), 127.2 (C-5, C-6), 145.3 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.21 (s, 9 H, 3 × CH_3), 1.25 (br s, 6 H, 2 × ring CH_3), 1.44 (br s, 6 H, 2 × ring CH_3), 4.98 (s, 2 H, OCH_2ONR_2), 7.14 (m, 2 H, 4-H, 7-H), 7.21 (m, 2 H, 5-H, 6-H).

2-*Methyl*-1-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*prop*-2-*yl ether* **9b**. (Found: M^+, 277.203. $C_{17}H_{27}NO_2$ requires M^+, 277.204); very poor signal : noise due to the small amount of sample, however peaks observed at $\delta_C(CDCl_3)$ 23.2 [$(CH_3)_2C(OCH_3)$], 121.6 (C-4, C-7) and 127.5 (C-5, C-6); $\delta_H(CDCl_3)$ 1.26 (s, 6 H, 2 × CH_3), 1.44 (br s, 6 H, 2 × ring CH_3), 1.56 (br s, 6 H, 2 × ring CH_3), 3.31 (s, 2 H, OCH_2), 3.47 [s, 3 H, $(CH_3)_2COCH_3$], 7.09 (m, 2 H, 4-H, 7-H), 7.22 (m, 2 H, 5-H, 6-H).

Dimethoxy(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*methane* **10a**. (Found: M^+, 265.169. $C_{15}H_{23}NO_3$ requires M^+, 265.168); $\delta_C(CDCl_3)$ 25.1 and 29.1 (4 × ring CH_3), 52.0 [$(CH_3O)_2C$], 67.8 (C-1, C-3), 120.1 [$(CH_3O)_2HCONR_2$], 121.5 (C-4, C-7), 127.5 (C-5, C-6), 144.5 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.40 (br s, 6 H, 2 × ring CH_3), 1.51 (br s, 6 H, 2 × ring CH_3), 3.47 (s, 6 H, 2 × OCH_3), 5.32 [s, 1 H, $(CH_3O)_2CHONR_2$], 7.11 (m, 2 H, 4-H, 7-H), 7.24 (m, 2 H, 5-H, 6-H).

Methoxy(1,1,3,3-*tetramethyl*-1,2-*dihydro*-1H-*isoindol*-2-*yloxy*)*methoxymethane* **10b**. (Found: M^+, 265.169. $C_{15}H_{23}NO_3$ requires M^+, 265.168); $\delta_C(CDCl_3)$ 25.0 and 29.0 (4 × ring CH_3), 55.6 (OCH_3), 67.5 (C-1, C-3), 94.4 (CH_3OCH_2O), 97.0 ($CH_2OCH_2ONR_2$), 121.6 (C-4, C-7), 127.4 (C-5, C-6), 145.0 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.36 (br s, 6 H, 2 × ring CH_3), 1.50 (br s, 6 H, 2 × ring CH_3), 3.40 (s, 3 H, OCH_3), 4.85 (s, 2 H, $CH_3OCH_2OCH_2$), 5.05 (s, 2 H, $CH_3OCH_2OCH_2ONR_2$), 7.10 (m, 2 H, 4-H, 7-H), 7.20 (m, 2 H, 5-H, 6-H).

2-*Ethoxy*-1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindole* **11b**. $\delta_C(CDCl_3)$ 14.1 (CH_3CH_2), 25.1 and 28.1 (4 × ring CH_3), 64.4 (CH_2O) 66.2 (C-1, C-3), 121.5 (C-4, C-7), 127.7 (C-5, C-6), 144.0

(C-3a, C-7a); $\delta_H(CDCl_3)$ 1.3 (t, 3 H, ^3J 7.1, CH_3CH_2), 1.4 (s, 6 H, 2 × ring CH_3), 1.5 (s, 6 H, 2 × ring CH_3), 4.3 (q, 2 H, ^3J 7.1, CH_3CH_2), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

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References

1 E. Whittle, *MTP Int. Rev. Sci.: Chem. Kinet.*, 1972, vol. 9, p. 70.
2 J. A. Kerr, *Comprehensive Chemical Kinetics*, eds. C. H. Bamford and C. F. H. Tipper, 1976, vol. 18, p. 58.
3 D. C. Nonhebel, J. M. Tedder and J. C. Walton, *Radicals*, Cambridge University Press, London, 1979.
4 V. Malatesta and J. C. Scaiano, *J. Org. Chem.*, 1982, **47**, 1455.
5 V. Malatesta and K. U. Ingold, *J. Am. Chem. Soc.*, 1981, **103**, 609.
6 D. Griller, J. A. Howard, P. R. Marriott and J. C. Scaiano, *J. Am. Chem. Soc.*, 1981, **103**, 619.
7 A. L. J. Beckwith and C. J. Easton, *J. Am. Chem. Soc.*, 1981, **103**, 615.
8 W. K. Busfield, I. D. Jenkins, S. H. Thang, E. Rizzardo and D. H. Solomon, *J. Chem. Soc., Perkin Trans. 1*, 1988, 485.
9 A. L. J. Beckwith, *Tetrahedron*, 1981, **37**, 3073.
10 P. Deslongchamps, *Tetrahedron*, 1975, **31**, 2463.
11 A. L. J. Beckwith, V. W. Bowry and G. Moad, *J. Org. Chem.*, 1988, **53**, 1632; A. L. J. Beckwith, V. W. Bowry and K. U. Ingold, *J. Am. Chem. Soc.*, 1992, **114**, 4983; V. W. Bowry and K. U. Ingold, *J. Am. Chem. Soc.*, 1992, **114**, 4992.
12 See, S. Bottle, W. K. Busfield, I. D. Jenkins, B. W. Skelton, A. H. White, E. Rizzardo and D. H. Solomon, *J. Chem. Soc., Perkin Trans. 2*, 1991, 1001 and references contained therein.
13 R. D. Grant, P. G. Griffiths, G. Moad, E. Rizzardo and D. H. Solomon, *Aust. J. Chem.*, 1983, **36**, 2447.
14 B. Giese, *Radicals in Organic Synthesis*, Pergamon Press, Oxford, 1986, p. 229.
15 D. H. R. Barton, W. Hartwig and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1982, 447.
16 M. Mannson, *J. Chem. Thermodyn.*, 1969, **1**, 141.
17 A. L. J. Beckwith and S. Brumby, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1801.
18 S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, 2nd edn., 1976.
19 P. D. Bartlett, E. P. Benzing and R. E. Pincock, *J. Am. Chem. Soc.*, 1960, **82**, 1762.
20 P. G. Griffiths, G. Moad, E. Rizzardo and D. H. Solomon, *Aust. J. Chem.*, 1982, **36**, 397.
21 E. Rizzardo, A. K. Serelis and D. H. Solomon, *Aust. J. Chem.*, 1982, **35**, 2013.
22 W. K. Busfield, I. D. Jenkins, S. H. Thang, E. Rizzardo and D. H. Solomon, *Aust. J. Chem.*, 1985, **38**, 689.
23 S. K. Wong, *J. Am. Chem. Soc.*, 1979, **101**, 1235.

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