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

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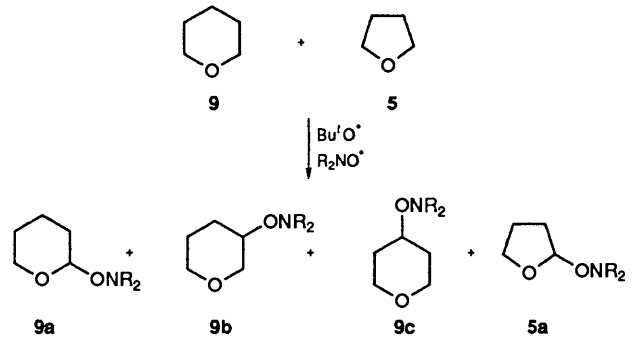
The pattern and relative rate of abstraction reactions of *tert*-butoxyl radicals with fourteen cyclic alkanes and cyclic ethers have been investigated by the aminoxyl radical trapping technique. Oxygen α to C–H strongly enhances abstraction, but β to C–H generally retards abstraction. The rate of abstraction of hydrogens α to oxygen in cyclic ethers was found to decrease with ring size in the order 5 > 7 ⩾ 6 > 4. The results are discussed in terms of ring size, abstraction position relative to ethereal oxygen atoms in the ring and aliphatic substitution. Factors such as polarity, torsional strain, hybridisation of the oxygen (whether sp^2 or sp^3) and the anomeric effect are considered.

In this paper we describe an investigation into the course of H abstraction reactions by *tert*-butoxyl radicals in a series of cyclic ethers and cyclic hydrocarbons using the radical trapping technique. Corresponding abstraction reactions of some of the cyclic ethers have been investigated previously but the techniques used either could not distinguish the site of the abstraction reaction[1] or were only semi-quantitative.[2] The technique used in this work relies on the high efficiency[3] of 1,1,3,3-tetramethyl-2,3-dihydro-1*H*-isoindol-2-yloxyl **2** in trapping C-centred radicals and the stability of the trapped products. The products are separated by HPLC and identified by NMR spectroscopy. Thus the pattern of reactivity on substrates with multiple available reaction sites can be established. It is not easy to determine absolute values of rate constants by this method; however, by the addition of internal standards, the results for different substrates have been related to a common base. For example, the relative rate constants for abstraction from the ring positions in tetrahydropyran **9** were obtained in relation to that for abstraction at the 2 position in tetrahydrofuran **5** by carrying out an experiment on a 1:1 molar mixture of **9** and **5** and comparing the yield of products (Scheme 1).

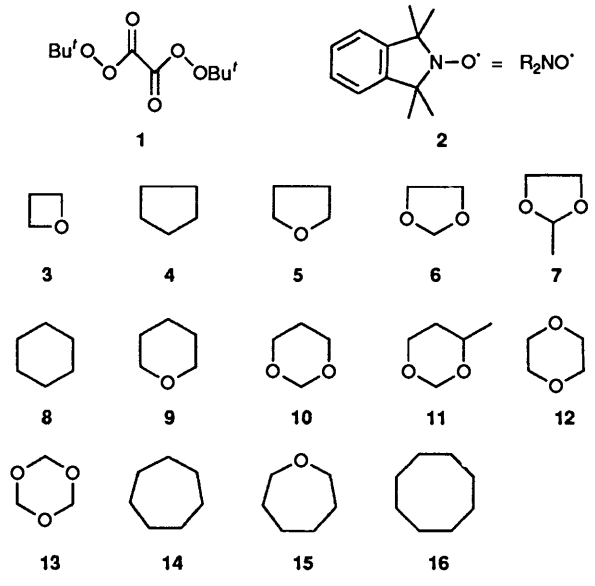


Scheme 1

The ratio of the molar yield of products is then equal to the ratio of rate constants for their formation as long as the substrates are present in large excess in the experiment. The relative rate constants have been converted into absolute rate constants by utilizing the results of a similar experiment with a 1:1 mixture of **5** and cyclopentane **4** and the literature value[4] for the rate constant of the reaction of *tert*-butoxyl radicals with **4** at the same temperature. One problem with this method is that since large concentrations of substrate are necessary for the analyses, the solvent for each system is different. We have assumed the results to be independent of solvent on the basis that most hydrogen-atom transfer to alkoxyl radical reactions are not strongly influenced by the nature of the solvent.[5]

Results and Discussion

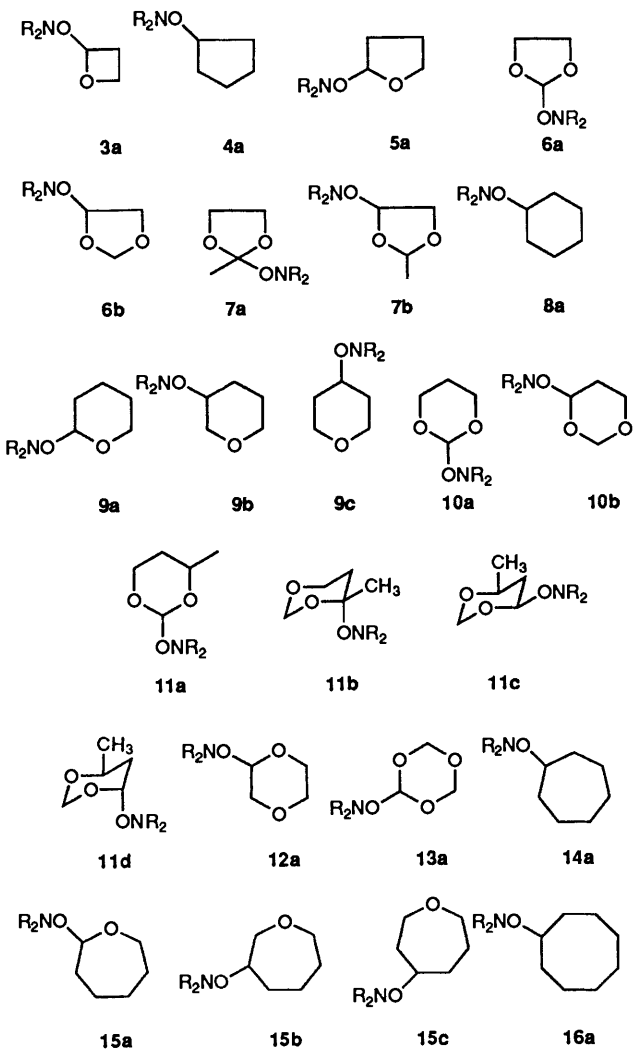
The structures of the products isolated and characterised from the reactions of **3–16** with *tert*-butoxyl radicals in the presence



Initiator, trap and substrates

of radical trap **2** are shown as **3a–16a**. Structure **11a** is only tentative, the product was too unstable in solution for a satisfactory NMR spectrum to be obtained. The structure suggested is that most likely with the knowledge of the other characterised products from substrate **11**. The two stereoisomers of **7b** were isolated in the ratio 1:3. It was, however, not possible to determine from the NMR spectra which was which.

The rate constants for H abstraction by *tert*-butoxyl radicals from the cyclic ethers and hydrocarbons relative to that from tetrahydrofuran **5**, all at 60 °C are listed according to ring size in Table 1. Corresponding rate constant ratios from the literature are also given for comparison. Although these related to lower temperatures *i.e.* 27 °C[1] and −60 °C,[2] rate constant ratios are not expected to change markedly over a small temperature range. There is reasonable agreement with the results of Malatesta and Scaiano,[1] who used a flash photolysis technique to measure the competition of radical formation in the substrate



Products

with the formation of diphenylhydroxymethyl radicals. The method gave no indication of the site of abstraction. Agreement with the results of Malatesta and Ingold[2] is on the other hand very poor, particularly for 1,3-dioxolane **6**, tetrahydropyran **9** and 1,3,5-trioxane **13**. The discrepancies may, of course, be due to a temperature effect. These authors used an EPR technique to measure radical concentrations produced by photolysis of the substrate. This technique did identify the site of abstraction. Although our technique gives reliable data for *relative* reactivities both within a substrate and between substrates, it has not allowed a direct evaluation of absolute rate constants. The values listed in Table 1 are based on literature data given for abstraction by *tert*-butoxyl radicals from cyclopentane.[4]

Rate constants per equivalent H atom in the cyclic hydrocarbons and ethers at 60 °C relative to that in cyclohexane **8**, are given in Table 2 in descending numerical order and are compared with the proximity of O atoms in the ethers. For this purpose H atoms on each single C atom in all the cyclic systems have been taken as equivalent. Discussion on this point is presented later. It is immediately apparent from Table 2 that, as with acyclic ethers,[6] the presence of an ethereal O atom adjacent to an abstraction site strongly enhances the rate of abstraction relative to that in cyclic hydrocarbons. This effect has been observed previously[1,2,7] and is generally understood to be due to a kind of generalised anomeric effect[8] with donation of electron density from the oxygen lone pair into the antibonding (σ^*_{C-H}) orbital of the C–H bond (Fig. 1).

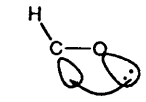


Fig. 1

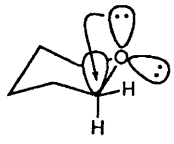


Fig. 2

It is clear from Fig. 1 that the degree of lowering of the energy of activation, E_a will be strongly dependent on (*i*) the dihedral angle between the C–H bond and the lone pair orbital (being a maximum when the dihedral angle is 180° and a minimum when it is 90°) and (*ii*) the hybridisation of the oxygen atom (all other things being equal, electrons in a p-type orbital would be expected to be more effective than electrons in a sp^3- or sp^2-type orbital, the latter have more s-character and are therefore closer to the nucleus). There is evidence to suggest that in ethers the two lone pairs of electrons on the oxygen atom have different energies[9] so that the oxygen is considered to be sp^2 hybridised with one lone pair in a p-type orbital and the other in an sp^2-type orbital. We believe that the present data on relative reactivities of cyclic ethers towards hydrogen abstraction are best interpreted if it is assumed that the oxygen lone pairs can be either p-like or sp^3-like depending on the conformational and steric requirements of the ring system, *i.e.* the system will adopt that hybridisation which results in maximum orbital interaction (and hence maximum electron delocalisation) of the type shown in Fig. 1.

In the series of cyclic monoethers **3**, **5**, **9** and **15**, the influence of ring size on the abstraction rate α to oxygen is: $5 > 7 \gg 6 > 4$. As five- and seven-membered rings exhibit greater torsional strain (due to non-bonded interactions) than six-membered rings, it is tempting to attribute the higher reactivity of five- and seven-membered rings to a reduction in torsional strain associated with the hydrogen abstraction process. This is probably the major factor with seven-membered rings. Thus, cycloheptane **14** is twice as reactive as cyclohexane **8**, while oxepane **15** is (similarly) twice as reactive as tetrahydropyran **9** in hydrogen abstraction reactions with *tert*-butoxyl radicals (Table 2). However, a reduction in torsional strain appears insufficient to explain the higher reactivity of the five-membered ring compound, tetrahydrofuran **5**. In this case, $k_{THF}/k_{THP} = 2.3$ whereas cyclopentane was only 1.2 times as reactive as cyclohexane. This marked difference suggests that an oxygen atom in a five-membered ring is exerting a stronger activating effect on the hydrogen abstraction reaction than an oxygen in a six- or seven-membered ring. From a careful study of molecular models, it is clear that with tetrahydropyran, effective orbital overlap of the type shown in Fig. 1 occurs between an axial hydrogen † and an sp^3-type lone pair orbital on oxygen (Fig. 2). Use of a p-type orbital gives less effective overlap.[10] However, the converse is true with a five-membered ring. Thus, in tetrahydrofuran, assuming an ^2E (envelope) conformation, a p-type lone pair orbital on oxygen gives more effective overlap with the neighbouring σ^*_{C-H}, orbital (Fig. 3) than does an sp^3 type lone pair orbital. It is suggested therefore, that the higher reactivity of the five-membered ring compound tetrahydrofuran, *versus* the six-membered ring (tetrahydro-

† Beckwith and Easton[7a] have conclusively shown that abstraction by *tert*-butoxyl radicals at the axial position in conformationally 'locked' six-membered cyclic ethers, occurs much faster than at the equatorial position.

Table 1 Rate constants for H abstraction by *tert*-butoxyl radicals from cyclic hydrocarbons and ethers relative to that from tetrahydrofuran at 60 °C

Substrate (ring size)	Product	k/k_{THF}	Lit. values of k/k_{THF} Ref. 1	Ref. 2	$k^a/10^6$ dm^3 mol^{-1} s^{-1}
3 (4)	**3a**	0.39	0.48		3.4
4 (5)	**4a**	0.15			1.3
5 (5)	**5a**	1.00	1.00	1.00	8.7
6 (5)	**6a**	0.69	0.93	4.4	6.0
	6b	0.23		0.32	2.0
7 (5)	**7a**	1.43	1.50	1.3	12.4
	7b	0.17[b]		0.19	1.5
8 (6)	**8a**	0.16			1.4
9 (6)	**9a**	0.44	0.33	0.06	3.8
	9b	0.03			0.2
	9c	0.03			0.3
10 (6)	**10a**	0.24			2.0
	10b	0.20			1.8
11 (6)	**11a**[c]	0.22		0.14	1.9
	11b	0.21			1.8
	11c	0.03			0.3
	11d	0.10			0.8
12 (6)	**12a**	0.14	0.18	0.09	1.2
13 (6)	**13a**	0.29	0.24	0.90	2.5
14 (7)	**14a**	0.36			3.1
15 (7)	**15a**	0.90	0.54		7.8
	15b	0.10			1.1
	15c	0.12			0.9
16 (8)	**16a**	0.36			3.1

[a] Based on the value for cyclopentane calculated from data in ref. 4, *i.e.* k (60 °C) = 1.3 × 10^6 dm^3 mol^{-1} s^{-1}. [b] A mixture of 2 stereoisomers in the ratio of 2.7 : 1.0 (separate identity not determined). [c] Tentative structure.

Table 2 Relative rate constants for H abstraction by *tert*-butoxyl radicals from cyclic ethers and hydrocarbons compared with ring size and proximity of chemical groups

Substrate	Product	$k_H(S)/k_H(Cy)$[a]	Ring size	Lone pair proximity
7	**7a**	114	5	α α
6	**6a**	27	5	α α
5	**5a**	20	5	α
15	**15a**	18	7	α
11	**11b**	16	6	α γ
10	**10a**	9.3	6	α α
9	**9a**	8.7	6	α
11	**11a**[b]	8.7	6	α α
3	**3a**	7.7	4	α γ
11	**11c** + **11d**	5.0	6	α γ
6	**6b**	4.5	5	α β
10	**10b**	4.0	6	α γ
13	**13a**	3.7	6	α α
7	**7b**	3.4	5	α β
15	**15c**	2.5	7	γ
15	**15b**	2.0	7	β
14	**14a**	2.0	7	—
16	**16a**	1.8	8	—
12	**12a**	1.4	6	α β
9	**9c**	1.4	6	γ
4	**4a**	1.2	5	—
8	**8a**	1.0	6	—
9	**9b**	0.6	6	β

[a] All ring positions have been assumed equivalent for the calculation of $k_H(S)$, the rate constant per equivalent H atom in substrate S. Cy = cyclohexane. [b] Tentative structure.

pyran) is due not only to the reduction in torsional strain associated with the hydrogen abstraction process, but also to a change in the hybridisation of the ring oxygen from sp^3-like in tetrahydropyran to sp^2-like in tetrahydrofuran. The same reactivity order would of course be predicted by assuming a p-type orbital on oxygen in both ring systems, with more effective overlap in the case of the five-membered ring. This was

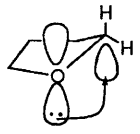


Fig. 3

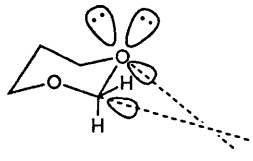


Fig. 4

suggested by Malatesta and Ingold,[2] although they concluded that relief of strain was the main factor responsible for the higher reactivity of five-membered ring systems.

Some support for a change in hybridisation from sp^2-like in five-membered rings to sp^3-like in six-membered rings comes from an examination of 1,3-dioxygen systems. Here we find that, in contrast to the acyclic ethers,[6] the introduction of a second oxygen atom α to an abstractable hydrogen atom results in an enhanced abstraction rate in both five (36%) and six (6%) membered rings compared with the corresponding mono ethers (see Table 1).

Considering 1,3-dioxane first, if the oxygens are sp^2-like, there is very little overlap possible between the oxygen lone pairs (σ or π) and the neighbouring σ^*_{C-O}, orbital (Fig. 4). Moreover, there would be a severe repulsion between the p-type lone pairs, as they point towards each other. If on the other hand the oxygens are sp^3-like, effective overlap between an 'equatorial' lone pair and the adjacent σ^*_{C-O}, orbital is possible (Fig. 5), leaving the 'axial' lone pair orbital free to overlap with an adjacent σ^*_{C-H}, orbital (of an axial hydrogen).

Turning now to 1,3-dioxolane, it is clear from a study of models that irrespective of whether the oxygens are sp^2-like, or sp^3-like, overlap between a lone pair orbital and the adjacent σ^*_{C-H} orbital is much less effective than in the case of the

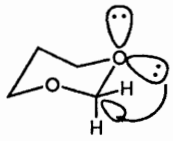


Fig. 5

corresponding six-membered ring. As discussed in the preceding paper,[6] strong backbonding from the oxygen lone pair orbitals into adjacent σ^*_{C-O} orbitals should weaken the lone pair–σ^*_{C-H} interaction. Thus, the reactivity towards hydrogen abstraction in 1,3-dioxygen systems will depend on the effectiveness of the lone pair–σ^*_{C-H} interaction, which in turn will be moderated by the oxygen–oxygen interaction. A weak oxygen–oxygen interaction, as predicted for 1,3-dioxolane, should result in an increase in reactivity towards hydrogen abstraction compared with the corresponding monoether (THF) as there are two oxygen atoms that can interact with the respective σ^*_{C-H} orbital. This is consistent with the 36% enhancement observed. The stronger oxygen–oxygen interaction predicted for 1,3-dioxane is consistent with the much weaker enhancement (6%) observed for the six-membered ring. Evidence in support of our suggestion that there is less effective oxygen–oxygen interaction (analogous to the anomeric effect) in five-membered rings than in six-membered rings is provided by X-ray structural data for representative 1,3-dioxolane **17** and 1,3-dioxane **18** derivatives.

17 R = *p*-$CH_3C_6H_4CO$ **18** R = $CH(p\text{-}OCH_3C_6H_4)_2$

Overlap between the lone pair orbitals on one oxygen and the adjacent σ^*_{C-O} orbital should result in bond-shortening. This appears to be the case with **17** where the 'anomeric' carbon–oxygen bond lengths are both 1.40 Å while the 'non-anomeric' carbon–oxygen bond lengths are 1.43 Å.[11] Conversely, in the five-membered ring derivative **18**, the 'anomeric' carbon–oxygen bond lengths (1.42 and 1.43 Å) are approximately the same as the 'non-anomeric' carbon–oxygen bond lengths (1.43 and 1.42 Å respectively).[12]

One apparently anomalous result is the reduced reactivity of 1,3,5-trioxane **13** towards hydrogen abstraction. Based on the previous arguments, the reactivities of 1,3,5-trioxane and of 1,3-dioxane might have been expected to be comparable, at least for the hydrogen atoms α to two oxygen atoms. Such hydrogen atoms exhibit a much reduced reactivity in 1,3,5-trioxane, reacting at less than half the rate of those in 1,3-dioxane. A recent X-ray structure of 1,3,5-trioxane[13] (co-crystallised with a zinc porphyrin complex) shows that the C–O bond lengths (1.40–1.41 Å) are comparable to the analogous C–O bond lengths in 1,3-dioxane, suggesting that the lone pair–σ^*_{C-O} interactions are similar in both systems. The reduced reactivity of 1,3,5-trioxane may be due to an electronegativity effect. Thus, whereas each methylene group of the trioxane is subjected to electron withdrawal by two flanking oxygen atoms, the analogous methylene of the dioxane will experience a slightly reduced electron withdrawal due to the moderating influence of the (electron donating) trimethylene chain. Electron withdrawal would be expected to result in a reduced rate of hydrogen abstraction by the (electrophilic) *tert*-butoxyl radical. Further evidence for the deactivating influence of electronegative groups comes from the 'β-effect'. It was found with acyclic ethers[6] that the presence of a β-oxygen retards the rate of hydrogen abstraction. This has also been found to be true with four-, five- and six-membered ring ethers. Thus, in oxetane **3**, THF **5** and

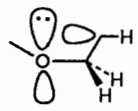
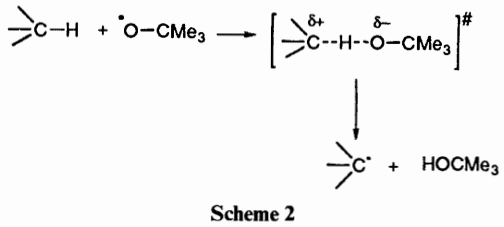


Fig. 6

the 1,3-dioxanes **10** and **11**, no β-hydrogen abstraction product was observed, while in tetrahydropyran **9**, the reactivity of the β-hydrogen was substantially less than that of a cyclohexane hydrogen. Similarly, the reduced reactivity of 4-H in 1,3-dioxolane **6** compared with tetrahydrofuran and of the hydrogens in 1,4-dioxane **12** compared with tetrahydropyran, can be attributed to the deactivating influence of the β-oxygen. It should be mentioned that, in contrast to our observations, the β abstraction product from **5** by *tert*-butoxyl radicals was observed by Grant *et al.*[14] at a rate of one third that of the α abstraction product. The result is in doubt however since the product could not be separated from the α abstraction product by HPLC; it was identified and quantified by ^{1}H NMR analysis of the mixture. We have tested the possibility of co-elution of two products in the THF system by allowing the reaction mixture to stand for 16 h at ambient temperature in 2 mol dm^{-3} hydrochloric acid, conditions which are normally sufficient completely to hydrolyse products containing acetal groups. Other trapped products are normally stable in these conditions. This treatment resulted in the complete disappearance of the product peak which was present prior to hydrolysis. This indicates the absence in detectable quantities of non-acetal type products. In addition both ^{1}H and ^{13}C NMR analysis fully supported the product being the α abstraction product alone (see Experimental section). The only exception to this 'β-effect' deactivation was with the seven-membered ring oxepane **15**, where the rate of hydrogen abstraction at the β-position was comparable to that at the γ-position and to the reactivity of a C–H bond in cycloheptane **14**. From a study of models, and assuming the oxygen is sp^2-like, it is clear that even though the oxygen p-orbital and the β-CH σ* orbital are approximately at right angles, these orbitals point towards each other, so that interaction between the p-type lone pair and the σ^*_{C-H} is possible (Fig. 6). Such an interaction (which is analogous to α-enhancement) is not possible with four-, five-and six-membered rings. The slightly higher reactivity of the γ-position in **15** compared with **14** is consistent with the small activating effect of γ-oxygen, observed with acyclic ethers.[6]

We attribute the β-effect to inductive withdrawal by the electronegative oxygen atom. This inductive effect will destabilise the (slightly polar) transition state for hydrogen abstraction by *tert*-butoxyl radicals (Scheme 2). The importance



Scheme 2

of polarity in hydrogen abstraction reactions has been discussed.[5,15,16] Although the inductive effect will be even stronger for oxygen in the α-position, this effect will be opposed by the generally more important resonance interaction involving back-donation from a lone pair orbital on the oxygen, as discussed above. It should be noted that the β-effect reported by Barton *et al.*[17] was activating not deactivating. Activation was attributed to radical stabilisation by β-oxygen.

The least reactive cyclic monoether studied was oxetane **3**.

The reactivity of this compound towards abstraction of the α hydrogens was slightly less than that of tetrahydropyran. From a study of molecular models, an sp^3-hybridised oxygen atom gives very poor lone pair–σ^*_{C-H} interaction. An sp^2-hybridised oxygen gives a better interaction and interestingly, the reactivity of oxetane is comparable to that of the acyclic 'analogue' diethyl ether,[6] suggesting that for four-membered rings, conformational factors have little or no effect on the reactivity towards hydrogen abstraction. This is in contrast to the case with five-, six- and seven-membered rings. Thus, using dibutyl ether[6] as an acyclic 'analogue' for tetrahydrofuran, tetrahydropyran and oxepane, the conformational effect of a five-membered ring results in a large (50%) increase in reactivity, a six-membered ring results in a decrease (30%) in reactivity and a seven-membered ring results in an increase (40%) in reactivity.

The most reactive system studied was the methyl-substituted dioxolane **7** where abstraction at the methine position was four times faster than at the corresponding methylene position in the unsubstituted dioxolane **6**. A similar fourfold increase in reactivity was observed with the methyl-substituted dioxane **11** compared with the unsubstituted compound **10**. This rate increase is significantly higher than that observed in similar acyclic ether pairs,[6] *e.g.* diethyl ether and diisopropyl ether exhibited the same reactivity. We attribute this increased reactivity in the cyclic systems to a conformational effect whereby the methyl substituent adopts an equatorial orientation (or a pseudo-equatorial position in the case of the five-membered ring) thus forcing the methine hydrogen into the (more reactive) axial position.* Bond-energy effects are probably also important here.

Abstraction rates at the substituted methyl groups in **7** and **11** were too low for products to be observed. This was also found to be the case for abstraction at methyl groups in most acyclic ethers[6] when the methyl group was not adjacent to ethereal O atoms. The lower rate of abstraction at a methyl group may be due to an entropy effect. In the formation of the transition state for abstraction at a methyl group, the loss of entropy due to internal rotation of the methyl group increases the free energy barrier to formation of the transition state. A recent study of the effect of temperature on relative rate constants for abstraction at methylene and methyl positions in an acyclic ether suggests that entropy is by far the main contributing factor.[6]

Even in the absence of the influence of ethereal oxygen, abstraction reactions occur much faster in seven- or eight-membered than in the five- or six-membered cyclic hydrocarbons. Wagner and Walling[18] observed that abstraction of cyclopentane **4** and cyclohexane **8** by *tert*-butoxyl radicals occurred at similar rates in agreement with our observations but there have been no comparable investigations of abstraction from cycloheptane **14** and cyclooctane **16**. We observe the rates for **14** and **16** to be very similar to each other and to be about twice the rate for **4** and **8** on a per equivalent H basis (see Table 2). As discussed earlier, this rate increase is due mainly to release of torsional strain in the transition state for hydrogen abstraction.

Conclusions

The rate of abstraction of hydrogens α to oxygen in cyclic ethers by *tert*-butoxyl radicals was found to decrease with ring size in the order 5 > 7 ≫ 6 > 4. Oxygen α to C–H strongly enhances abstraction but β to C–H generally retards abstraction. In the case of five-membered rings two oxygens α to C–H are much more effective in the enhancement of abstraction than one, but in the case of six-membered rings the enhancement is marginal. The results can best be interpreted in terms of the various ring systems imposing different conformational constraints on the interaction between a lone pair orbital on the oxygen atom and the adjacent antibonding orbital of the respective C–H bond. It is suggested that the hybridisation of the oxygen may be sp^2-like or sp^3-like depending upon the conformational and steric requirements of the ring system.

Experimental

Substrates.—The cyclic ethers and hydrocarbons **4**, **5**, **7**–**12** and **14**–**16** were dried over anhydrous $MgSO_4$, 3 Å molecular sieves, Na wire (substrate **7** and **11**) or KOH (substrate **5** only) and fractionally distilled before use. Ethers **3** and **6** were stored over 3 Å molecular sieves; no impurities could be detected by GC. Ether **13** was obtained from Aldrich and recrystallized from hexane (m.p. 58 °C).

Di-*tert*-butyl diperoxyoxalate† **1** was prepared by the method of Bartlett[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 as the solvent in 1:1 or 5:1 (substrate **7** only) molar ratio, containing initiator (0.008 mol dm^{-3}) and radical trap (0.018 mol dm^{-3}). 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). For analytical purposes, the reaction mixtures were directly analysed by reversed phase HPLC using acetonitrile–water or methanol–water mixtures as eluent and 270 nm wavelength for detection. For preparative scale experiments initiator/trap content was scaled up by a factor of 6 and the internal standard was omitted. 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**, **7** and **11**–**13**; THF for **3**, **4**, **6**, **8**–**10** and **14**–**16**. In a typical experiment, **2** (17.0 mg, 0.089 mmol) and **1** (10.0 mg, 0.043 mmol) were dissolved in a mixture of cyclohexane (3.09 cm^3, 28 mmol) and 1,3-dioxolane (2.0 cm^3, 28 mmol) and the mixture treated as above.

Product Analysis.—Peak areas from HPLC chromatograms were converted directly into % molar yields of products. Alkoxyamine compounds containing one mole equiv. of the radical trapping moiety and no other UV chromatophoric groups have been shown[21] to have almost identical molar extinction coefficients at 270 nm. One product **7a** was insoluble in HPLC solvents. It was precipitated, dried and the yield determined by weighing.

The HPLC-separated products were identified by NMR techniques as described previously.[22,23] The quaternary carbons of the isoindoline moiety (C-1, C-3, C-3a, C-7a) were generally weak and not always observed. One product decomposed before NMR data could be collected. The structure assigned **11a**, is the most likely on the basis of the structures determined for the other products from substrate **11**. The products **3a** derived from oxetane and **7a** from methyl dioxolane **7** were also rather unstable and failed to give satisfactory elemental analyses or high resolution mass spectral data on successive attempts at purification (**3a** did not give a parent ion by CI or EI).

^1H and ^{13}C NMR spectra (proton-noise decoupled; off-resonance decoupled) were recorded on a Brüker WM-250

* Beckwith and Easton[7a] have conclusively shown that abstraction by *tert*-butoxyl radicals at the axial position in conformationally 'locked' six-membered cyclic ethers, occurs much faster than at the equatorial position.

† **CAUTION**: explosion hazard.

spectrometer (at 250.12 and 62.80 MHz). Mass spectra were recorded on a Kratos MS-25 spectrometer or on a Vg micromass instrument (CSIRO, Melbourne). Microanalyses were carried out by the Australian microanalytical Service, AMDEL, Melbourne.

Trap Concentration Effects.—Previous work has shown that product ratios are independent of the trap concentration as long as it is in excess (twice the initiator concentration).[6]

New Compounds.—Most of the alkoxyamine products (except **11a**, see above) were stable under the reaction and HPLC analytical conditions. New products were characterised by the spectroscopic data listed below. *J* values are given in Hz; ring CH_3 refers to methyl substituents on isoindole.

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*oxetane* **3a**. $\delta_C(CDCl_3)$ 25.5 (v br s, 2 × ring CH_3), 28.9 (v br s, 2 × rings CH_3), 29.04 (CH_2CH_2CHON), 63.2 (OCH_2CH_2), 67.0 (C-1, C-3), 109.8 (OCHON), 121.5 and 121.4 (C-4, C-7), 127.4 and 127.2 (C-5, C-6), 144.73 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.42 (v br s, 12-H, 4 × CH_3), 2.8 (m, 2 H, CH_2CH_2CHON), 4.38 (m, 2 H, OCH_2CH_2), 5.7 (t, 1 H, ^3J 5.4, OCHON), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 5-H, 6-H).

(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yl*)*oxycyclopentane* **4a** (Found: M, 259.1939. $C_{17}H_{25}NO$ requires *M*, 259.1936); $\delta_C(CDCl_3)$ 23.4 ($CH_2CH_2CH_2CH_2$), 25.1 (br s, 2 × ring CH_3), 30.2 (br s, 2 × ring CH_3), 32.1 ($CH_2CH_2CH_2CH_2$), 67.3 (C-1, C-3), 86.2 [$CH_2CH(ONR_2)CH_2$], 121.6 (C-4, C-7), 127.1 (C-5, C-6), 145.5 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.3 (s, 6 H, 2 × ring CH_3), 1.5 (s, 6-H, 2 × ring CH_3), 1.5–1.9 (8-H, m, 4 × CH_2), 4.4 [1 H, m, $CH(ONR_2)$], 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxolane* **6a** (Found: MH^+, 264.158. $C_{15}H_{21}NO_3H$ requires MH^+, 264.159), $\delta_C(CDCl_3)$ 25.2 (br s, 2 × ring CH_3), 29.05 (br s, 2 × ring CH_3), 63.8 (OCH_2CH_2O), 67.3 (C-1, C-3), 120.3 [OCH(O)ONR_2], 121.5 (C-4, C-7), 127.2 (C-5, C-6), 144.7 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.4 (s, 6-H, 2 × ring CH_3), 1.5 (s, 6-H, 2 × ring CH_3), 3.9–4.0 (m, 2 H, OHCHHCHO),* 4.1–4.2 (m, 2 H, OHCHHCHO),* 6.1 [s, 1 H, $OCH(ONR_2)O$], 7.1 (m, 2 H, 4-H, 5-H), 7.2 (m, 2 H, 5-H, 6-H).

4-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxolane* **6b** (Found: MH^+, 264.160. $C_{15}H_{21}NO_3H$ requires MH^+, 264.159); $\delta_C(CDCl_3)$ 25.4 (v br s, 2 × ring CH_3), 29.1 (v br s, 2 × ring CH_3), 67.5 (C-1, C-3), 68.9 [$OCH_2CH(ONR_2)$], 106.0 ($OCHONR_2$), 94.0 (OCH_2O), 121.7 (C-4, C-7), 127.4 (C-5, C-6), 145.1 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.4 (br d, 9 H, 3 × ring CH_3), 1.5 (br s, 3 H, 1 × ring CH_3), 3.8 (dd, 1 H, ^2J 9.2, $^3J_{cis}$ 3.1, HCHCHONR_2), 4.0 (dd, 1 H, ^2J 9.2, $^3J_{trans}$ 5.2, HCHHCONR_2), 4.96 (s, 1 H, OHCHO), 5.07 (s, 1 H, OHCHO), 5.5 [dd, 1 H, $^3J_{trans}$ 5.2, $^3J_{cis}$ 3.1, $OCH(ONR_2)CH_2O$], 7.0 (m, 2-H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

2-*Methyl*-2-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxolane* **7a** (Found: MH^+, 278. $C_{16}H_{23}NO_3$ requires MH^+, 277); $\delta_C(CDCl_3)$ 22.8 (CCH_3) 25.5 and 29.1 (4 × ring CH_3) 65.4 (OCH_2CH_2O), 68.1 (C-1, C-3), 121.6 (C-4, C-7), 122.8 [$OC(CH_3)(ONR_2)O$], 127.1 (C-5, C-6), 145.3 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.27 (s, 6 H, 2 × ring CH_3), 1.46 (s, 6 H, 2 × ring Me), 1.53 (s, 3 H, O_3CCH_3), 3.78–3.92 (m, 2 H, OHCHHCHO)† 4.14–4.27 (m, 2 H, OHCHHCHO)† 7.03 (m, 2 H, 4-H, 7-H), 7.15 (m, 2 H, 5-H, 6-H).

2-*Methyl*-4-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxolane* **7b**. (Obtained as a mixture of stereoisomers in the ratio of 1:2.7.) Isomer 1 (minor isomer) (Found: M, 277.167. $C_{16}H_{23}NO_3$ requires *M*, 277.168); $\delta_C(CDCl_3)$ 20.92 ($OCHCH_3O$), 25.66, 27.87, 29.87 and 29.52 (4 × ring CH_3), 70.72 (CH_2O), 103.91 [$OCH(CH_3)O$], 105.71 [$HC(ONR_2)O$], 121.56 (C-4, C-7), 128.00 (C-5, C-6); $\delta_H(CDCl_3)$ 1.33, 1.39, 1.49 and 1.64 (4 × s, 12 H, 4 × ring CH_3), 1.53 (d, 3-H, ^3J 4.9, $CHCH_3$), 3.95 (dd, 1 H, ^2J 9.4, $^3J_{trans}$ 4.8, OHCHHC), 4.18 (dd, 1 H, ^2J 9.4, $^3J_{cis}$ 1.3, OHCHHC), 5.26 [q, 1 H, ^3J 4.9, $OCH(CH_3)O$], 5.68 [m, 1 H, $CH(ONR_2)$], 7.10 (m, 2 H, 4-H, 7-H), 7.23 (m, 2 H, 5-H, 6-H).

Isomer 2 (major isomer) (Found: M, 277.168. $C_{16}H_{23}NO_3$ requires *M*, 277.168); $\delta_C(CDCl_3)$ 19.19 [$OCH(CH_3)O$], 25.75, 28.19 and 29.58 (4 × ring CH_3), 69.67 (CH_2O), 100.64 [$OCH(CH_3)O$], 105.88 [$HC(ONR_2)O$], 121.67 (C-4, C-7), 127.95 (C-5, C-6); $\delta_H(CDCl_3)$ 1.35, 1.39, 1.37 and 1.71 (4 × br s, 12 H, 4 × ring CH_3), 1.43 (d, 3 H, ^3J 4.9, $CHCH_3$), 3.80 (dd, 1 H, ^2J 9.5, ^3J 3.4, OHCHHC), 4.28 (dd, 1 H, ^3J 5.5, ^2J 9.5, OHCHHC), 5.26 [q, 1 H, ^3J 4.9, $OCH(CH_3)O$], 5.99 [m, 1 H, $CH(ONR_2)$], 7.10 (m, 2 H, 4-H, 7-H), 7.26 (m, 2 H, 5-H, 6-H).

(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*cyclohexane* **8a**. $\delta_H(CDCl_3)$ 1–2.2 (m, 22 H, aliphatic H), 3.4 (m, 1 H, $CHONR_2$), 7.0–7.2 (m, 2 H, 4-H, 7-H), 7.2–7.3 (m, 2 H, 5-H, 6-H). Identical to an authentic sample.[15]

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*tetrahydro*-2H-*pyran* **9a** (Found: MH^+, 276.196. $C_{17}H_{25}NO_2H^+$ requires MH^+, 276.196); $\delta_C(CDCl_3)$ 25.2 and 29.3 (v br s, ring CH_3), 20.4 (CH_2CH_2CHO), 25.4 (CH_2CH_2O), 29.9 (CH_2CHO), 63.3 (CH_2O), 67.3 (C-1, C-3), 104.9 (CH_2CHON), 121.6 (C-4, C-7), 127.2 (C-5, C-6); $\delta_H(CDCl_3)$ 1.25–2.0 (m, 18 H, CH_3 and CH_2), 3.6 (m, 1 H, CHO), 4.1 [(m, 1 H, CHO), 5.0 (dd, 1 H, ^3J 2.6, ^3J 4.8, OCHO (these coupling constants are consistent with an axial isoindole moiety)], 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

3-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*tetrahydro*-2H-*pyran* **9b** (Found: MH^+, 276.198. $C_{17}H_{25}NO_2H^+$ requires MH^+, 276.196); $\delta_C(CDCl_3)$ 24.0 (OCH_2CH_2), 25.2, 29.7 and 30.5 (4 × ring CH_3), 29.1 [$CH_2CH(ONR_2)$], 68.0 (CH_2CH_2O), 70.6 (OCH_2CH), 76.2 ($CHONR_2$), 121.6 (C-4, C-7), 127.3 (C-5, C-6), 144.7 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.34 (d, 6 H, 2 × ring CH_3), 1.5 (d, 6 H, 2 × ring CH_3), 1.8 (m, 2 H, $CH_2CH_2CH_2O$), 2.1 (m, 2 H, CH_2CH_2O), 3.5 (m, 2 H, CH_2O), 3.7 (m, 1 H, ^2J 11.1, OHCHCHON), 3.8 (v br s, 1 H, CHON), 4.0 (ddd, 1 H, ^2J 11.1, ^3J 3.5, ^3J 1.4, OHCHCHON), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

4-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*tetrahydro*-2H-*pyran* **9c** (Found: MH^+, 276.197. $C_{17}H_{25}NO_2H^+$ requires MH^+, 276.196); $\delta_C(Me_2SO)$ 25.3 (2 × ring CH_3), 30.3 (2 × ring CH_3), 32.4 (2 × CH_2CHON), 65.1 (2 × OCH_2), 66.9 (C-1, C-3), 77.5 (CHON), 121.5 (C-4, C-7), 127.2 (C-5, C-6), 144.7 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.33 (br s, 6 H, 2 × CH_3), 1.49 (br s, 6 H, 2 × CH_3), 1.64 (m, 2 H, CH_2CH_2CHON), 2.49 (m, 2 H, CH_2CH_2CHON), 3.44 (ddd, 2 H, ^2J 11.7, ^3J 10.2, ^3J 2.6, OCH_2, axial H), 3.95 (br m, 1 H, CHON), 3.97 (dt, 2 H, ^2J 11.7, ^3J 4.2, OCH_2, equatorial H), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxane* **10a** and 4-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxane* **10b**. These two compounds were inseparable by HPLC using various solvent mixtures of MeOH–H_2O and MeCN–H_2O. They were analysed as a mixture (Found: MH^+, 278.1765. $C_{16}H_{23}NO_3H$ requires MH^+, 278.176); $\delta_C(CDCl_3)$ 23.9 ($OCH_2CH_2CH_2$, **a**), 24.4 (br s, 4 × ring CH_3), 28.2 (br s, 4 × ring CH_3), 29.6 (OCH_2CH_2CHON, **b**), 62.0 ($OCH_2CH_2CH_2O$, **a**), 63.4 (OCH_2CH_2, **b**), 66.7 (C-1, C-3), 88.6 (OCH_2O, **b**), 102.3 (CHON, **b**), 115.9 (CHON, **a**), 120.7 (C-4, C-7), 126.5 (C-5, C-6), 143.9 (C-3a, C-7a); $\delta_H(CDCl_3)$ 1.48 (d, 24 H, 8 × ring CH_3), 1.5–1.9 (m, 3 H), 2.04–2.15 (m, 1 H, OCH_2HCHCH_2, **a**, OCH_2CH_2, **b**), 3.9 (m, 3 H), 4.1 (m, 1 H), 4.3 [m, 2 H, OCH_2CH_2O, **a**,

* A 7 peak multiplet is observed as a result of an A_2B_2 system where second order effects are experienced.

† The same pattern as observed for these protons in 1,3-dioxolane.

$OC(ONR_2)HCH_2CH_2O$, **b**], 4.8 (d, 1 H, $^2J_{eq}$ 6.3, OHC*H*O, **b**), 5.1 [dd, 1 H, $^3J_{eq}$ 3.3, ^3J 5.4, $OCH(ONR_2)CH_2$, **b**], 5.2 (d, 1 H, $^2J_{ax}$ 6.3, O*H*CHO, **b**), 5.6 (s, 1 H, C*H*ONR$_2$, **a**), 7.1 (m, 4 H, 4-H, 7-H), 7.3 (m, 4 H, 5-H, 6-H).

4-*Methyl*-4-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxane* **11b** (Found: M, 291.183. $C_{17}H_{25}NO_3$ requires *M*, 291.183); δ_C($CDCl_3$) 24.61 [OC(*C*H$_3$)], 24.87, 25.70, 28.71 and 29.27 (4 × ring CH$_3$), 36.27 (OCH_2CH_2), 63.18 (OCH_2CH_2), 66.97 and 67.40 (C-1, C-3), 88.01 (OCH_2O), 100.29 [O*C*(CH$_3$)(ONR$_2$)], 121.26 and 121.47 (C-4, C-7), 126.99 and 127.18 (C-5, C-6), 144.32 and 145.41 (C-3a, C-7a); δ_H($CDCl_3$) 1.34 [s, 3 H, C(ONR$_2$)C*H*$_3$], 1.41, 1.44, 1.52 and 1.53 (4 × s, 12 H, 4 × ring CH$_3$), 1.89 (ddd, 1 H, ^2J 13.4, $^3J_{ax/eq}$ 2.89, $^3J_{eq/eq}$ 2.89, $OCH_2H_bCH_a$), 2.03–2.19 (m, 1 H, OCH_2-H_bCH_a), 3.88–3.97 (m, 1 H, $OH_bCH_aCH_2$), 4.08 (ddd, 1 H, ^2J 11.25, $J_{ax/ax}$ 11.25, $J_{ax/eq}$ 3.1, $OH_bCH_aCH_2$), 4.87 (d, 1 H, ^2J 6.0, OH_aCH_bO), 5.38 (d, 1 H, ^2J 6.0, OH_aCH_bO), 7.11 (m, 2 H, 4-H, 7-H), 7.24 (m, 2 H, 5-H, 6-H).

cis-4-*Methyl*-6-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxane* **11c** (Found: C, 70.1; H, 8.6; N, 4.6. $C_{17}H_{25}NO_3$ requires C, 70.1, H, 8.7, N, 4.8%); δ_C($CDCl_3$) 21.32 (CH*C*H$_3$), 25.78 and 28.75 (4 × ring CH$_3$), 37.72 [*C*H$_2$-CH(CH$_3$)], 71.82 [CH$_2$*C*H(CH$_3$)], 90.68 (OH*C*HO), 104.4 [OH*C*(ONR$_2$)], 121.56 (C-4, C-7), 127.96 (C-5, C-6); δ_H-($CDCl_3$) 1.28 (d, 3 H, ^3J 6.20, CHC*H*$_3$), 1.35, 1.37, 1.48 and 1.55 (4 × s, 4 × ring CH$_3$), 1.5 [m, 1 H, HCH_{ax}HC(CH$_3$)], 1.89 [br dt, 1 H, ^2J 12.8, $^3J_{eq/ax}$ 2.0–2.5, HCH_{eq}CH(CH$_3$)], 3.75 [ddq, 1 H, ^3J 6.2, $^3J_{ax/ax}$ 11.2, $^3J_{eq/eq}$ 2.5, C*H*(CH$_3$)], 4.73 (d, 1 H, ^2J 6.8, O*H*CHO), 4.97 [br dd, 1 H, $^3J_{ax/ax}$ 10.0, $^3J_{ax/eq}$ 2–2.2, O*H*C(ONR$_2$)], 5.12 (d, 1 H, ^2J 6.8, OHC*H*O), 7.08 (m, 2 H, 4-H, 7-H), 7.21 (m, 2 H, 5-H, 6-H).

trans-4-*Methyl*-6-(1,1,3,3-*tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3-*dioxane* **11d** (Found: M, 291.183. $C_{17}H_{25}NO_3$ requires *M*, 291.183); δ_C($CDCl_3$) 21.5 (CH*C*H$_3$), 25.3 and 29.1 (4 × ring CH$_3$), 37.29 [OCH(CH$_3$)*C*H$_2$], 67.6 (C-1, C-3), 68.45 [OH*C*(CH$_3$)], 87.01 (OH*C*HO), 101.24 [OH*C*(ONR$_2$)], 121.56 (C-4, C-7), 127.37 (C-5, C-6), 145.3 (C-3a, C-7a); δ_H($CDCl_3$) 1.22 [d, 3 H, ^3J 6.2, HC(*C*H$_3$)], 1.45 (br s, 12 H, 4 × ring CH$_3$), 1.82–1.95 [m, 2 H, *H*C*H*CH(CH$_3$)], 4.04 [m, 1 H, H_{ax}C(CH$_3$)], 4.91 (d, 1 H, ^2J 6.0, O*H*CHO), 5.33 [dd, 1 H, $^3J_{eq/ax}$ 1.4, $J_{eq/eq}$ 3.6, O*H*C(ONR$_2$)], 5.36 (d, 1 H, ^2J 6.0, OHC*H*O), 7.09 (m, 2 H, 4-H, 7-H), 7.23 (m, 2 H, 5-H, 6-H).

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,4-*dioxane* **12a** (Found: C, 68.9; H, 8.5; N, 4.9%; MH$^+$, 278.175. $C_{16}H_{23}NO_3$ requires C, 69.2; H, 8.35; N, 5.04%; *M*H$^+$, 278.175); δ_C($CDCl_3$) 25.4 (br s, 2 × ring CH$_3$), 29.7 (br s, 2 × ring CH$_3$), 62.6 ($OCH_2CH_2OCH_2$), 66.1 (OCH_2CH_2-OCH_2), 67.2 ($OCH_2CH_2OCH_2$), 101.6 (O*C*HON), 121.5 (C-4, C-7), 127.3 (C-5, C-6); δ_H($CDCl_3$) 1.43 (s, 6 H, 2 × ring CH$_3$), 1.57 (s, 6 H, 2 × ring CH$_3$), 3.7 (m, 3 H, OCH_2HCHO), 3.85 [dd, 1 H, ^3J 2.7, $^2J_{gem}$ 11.5, OHC*H*CH(ONR$_2$)], 4.2 (m, 1 H, OHC*H*CH$_2$), 3.7 [dd, 1 H, ^3J 4.5, $^2J_{gem}$ 11.5, OHC*H*CH-(ONR$_2$)], 4.9 (dd, 1 H, $^3J_{cis}$ 2.7, $^3J_{trans}$ 4.5 CH$_2$C*H*ON), 7.1 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-1,3,5-*trioxane* **13a** (Found: MH$^+$, 280.155. $C_{15}H_{21}NO_4H^+$ requires *M*H$^+$, 280.155); δ_C($CDCl_3$) 25.2 (v br s, 2 × ring CH$_3$), 29.1 (v br s, 2 × ring CH$_3$), 67.8 (C-1, C-3), 89.9 (OCH_2O), 116.2 [OCH(O)ON], 121.6 (C-4, C-7), 127.5 (C-5, C-6), 144.4 (C-3a, C-7a); δ_H($CDCl_3$) 1.43 and 1.51 (2 × 6 H, 4 × ring CH$_3$), 5.1 (d, 2 H, ^2J 6.3, O*H*CHO*H*CHO), 5.4 (d, 2 H, ^2J 6.3, OHC*H*OHC*H*O), 5.8 [s, 1 H, OCHO(O)], 7.1 (m, 2 H, 4-H, 7-H), 7.3 (m, 2 H, 5-H, 6-H).

(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*cyclo*-*heptane* **14a** (Found: M, 287.224. $C_{19}H_{29}NO$ requires *M*, 287.224); δ_C($CDCl_3$) 23.0 ($CH_2CH_2CH_2CH_2CH_2CH_2$), 25.3 (s, 2 × ring CH$_3$), 28.9 ($CH_2CH_2CH_2CH_2CH_2CH_2$), 30.4 (s, 2 × ring CH$_3$), 33.4 ($CH_2CH_2CH_2CH_2CH_2CH_2$), 67.4 (C-1, C-3), 83.9 [m, *C*H(ONR$_2$)], 121.6 (C-4, C-7), 127.1 (C-5, C-6), 145.6 (C-3a, C-7a).

2-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*oxepane* **15a** (Found: C, 74.7; H, 9.4; N, 4.8%; MH$^+$, 290.212. $C_{18}H_{27}NO_2$ requires C, 74.7; H, 9.6; N, 4.8%; *M*H$^+$, 290.212); δ_C($CDCl_3$) 22.9 (t, *C*H$_2$CH$_2$CH$_2$CHON), 25.3 (br s, 2 × ring CH$_3$), 29.5 (t, OCH$_2$*C*H$_2$), 29.6 (br s, 2 × ring CH$_3$), 30.8 (t,*C*H$_2$CH$_2$OCHON), 32.9 [t, *C*H$_2$CHO(ONR$_2$)], 62.0 (t, *C*H$_2$OCHON), 66.8 and 67.8 (C-1, C-3), 107.7 (d, OCHON), 121.7 (C-4, C-7), 127.2 (C-5, C-6), 145.1 and 145.3 (C-3a, C-7a); δ_H($CDCl_3$) 1.3–1.9 (m, 19 H, 2 × CH$_2$, CH, 4 × ring CH$_3$), 2.2 (m, 1 H, CH), 3.7 (dtd, 1 H, *J* 1.3, ^3J 3.5 Hz, ^2J 12.5, O*H*CHCH$_2$), 3.9 (ddd, 1 H, ^2J 12.5, ^3J 10.1, ^3J 2.5, OHC*H*CH$_2$), 5.1 (dd, 1 H, ^3J 9.7, ^3J 5.6, OCHO), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

3-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*oxepane* **15b** (Found: MH$^+$, 290.210. $C_{18}H_{27}NO_2H^+$ requires *M*H$^+$, 290.212); δ_C($CDCl_3$) 21.3 (*C*H$_2$CH$_2$CH$_2$O) 25.3 (br s, 2 × ring CH$_3$), 30.5 (s, 2 × ring CH$_3$), 31.1 (CH$_2$*C*H$_2$CHON), 32.1 (*C*H$_2$CH$_2$CH$_2$O), 67.6 (C-1, C-3), 72.4 (CH$_2$CH$_2$*C*H$_2$O), 73.5 (O*C*H$_2$CHON), 83.4 (*C*HONR$_2$), 121.6 (C-4, C-7), 127.3 (C-5, C-6), 145.4 (C-3a, C-7a); δ_H($CDCl_3$), 1.3–2.2 (m, 18 H, 4 × ring CH$_3$, C*H*$_2$CHONR$_2$, C*H*$_2$C*H*$_2$CHONR$_2$), 3.5–4.1 (m, 5 H, 2 × CH$_2$O, C*H*ONR$_2$), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

4-(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)-*oxepane* **15c** (Found: MH$^+$, 290.212. $C_{18}H_{27}NO_2H^+$ requires *M*H$^+$, 290.212); δ_C($CDCl_3$) 24.9 (t, *C*H$_2$CH$_2$CHON) 25.3 (br s, 2 × ring CH$_3$), 30.5 (br s, 2 × ring CH$_3$), 31.3 (CH$_2$*C*H$_2$C-H$_2$O), 36.2 (*C*H$_2$CH$_2$CH$_2$O) 65.2 (CH$_2$CH$_2$*C*H$_2$O), 67.6 (C-1, C-3), 70.1 (O*C*H$_2$CH$_2$CHON), 81.9 (*C*HON), 121.6 (C-4, C-7), 127.3 (C-5, C-6), 145.4 (C-3a, C-7a); δ_H($CDCl_3$) 1.3 (br s, 6 H, 2 × ring CH$_3$), 1.48 and 1.51 (2 × 3 H, 2 × ring CH$_3$), 1.5–2.1 (m, 4 H, C*H*$_2$C*H*$_2$CH$_2$CHONR$_2$), 2.1–2.3 (m, 2 H, C*H*$_2$C-HONR$_2$), 3.5–3.9 (m, 4 H, 2 × CH$_2$O), 4.0–4.1 (m, 1 H, CHON), 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

Note the assignments for **15b** and **15c** are tentative and may be reversed. As **15b** and **15c** were formed in comparable amounts, reversing the assignments does not dramatically change the relative reactivities given in Table 1.

(1,1,3,3-*Tetramethyl*-2,3-*dihydro*-1H-*isoindol*-2-*yloxy*)*cyclo*-*octane* **16a** (Found: M, 301.241. $C_{20}H_{31}NO$ requires *M*, 301.241); δ_C($CDCl_3$) 23.2 ($CH_2CH_2CH_2CH_2CH_2CH_2CH_2$), 25.3 (br s, 2 × ring CH$_3$), 25.5 ($CH_2CH_2CH_2CH_2CH_2$-CH_2CH_2), 27.6 ($CH_2CH_2CH_2CH_2CH_2CH_2CH_2$), 30.4 (br s, 2 × ring CH$_3$), 30.7 [$CH_2CH(ONR_2)CH_2$], 67.5 (C-1, C-3), 83.5 [*C*H(ONR$_2$)], 121.6 (C-4, C-7), 127.1 (C-5, C-6), 145.7 (C-3a, C-7a); δ_H($CDCl_3$) 1.3 (s, 6 H, 2 × ring CH$_3$), 1.5 (s, 6 H, 2 × ring CH$_3$), 1.5–1.6 (m, 8 H, aliphatic H), 1.7–1.9 (m, 4 H, aliphatic H), 1.9–2.1 (m, 2 H, aliphatic H), 3.9–4.0 [m, 1 H, C*H*(ONR$_2$)], 7.1 (m, 2 H, 4-H, 7-H), 7.2 (m, 2 H, 5-H, 6-H).

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