Base-catalysed ring openings of 1,2-diphenylcycloalkanols having five-, six-, seven- and eight-membered rings

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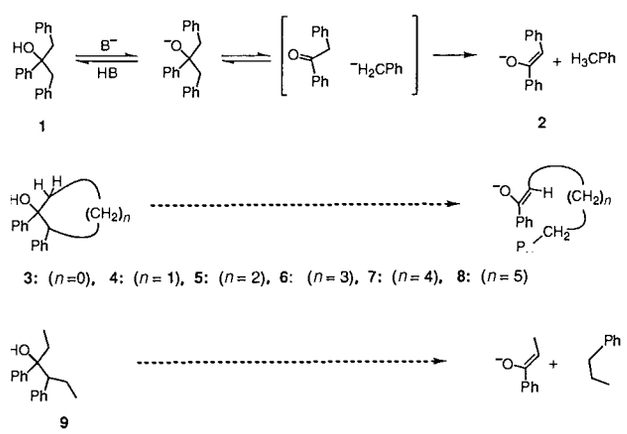
***trans*-Isomers of 1,2-diphenylcyclopentanol, 5, 1,2-diphenylcyclohexanol, 6, 1,2-diphenylcycloheptanol, 7, and 1,2-diphenylcyclooctanol, 8, have been prepared as have their acyclic analogues, *threo*- and *erythro*-3,4-diphenylhexan-3-ol, 9. All structural assignments are confirmed by X-ray crystal structure determinations and experimentally determined structures are compared with the results of empirical force field calculations which also yield strain energies for each of the compounds. With alkali metal dimsyl–dimethyl sulfoxide or 1,3-diaminopropane with its potassium salt as base, the cycloalkanols are isomerised to enolates of corresponding 1,*n*-diphenylalkan-1-ones, and the acyclic alkanols cleaved to propylbenzene and the enolate of propiophenone. The products are consistent with a polar mechanism involving collapse of alkoxide to expel a benzylic carbanion, followed by one or more proton transfers to yield the observed products. Rates increase in the order, 6 < 5 ≪ 7 < 9 < 8, with a spread in reactivities of *ca.* 10^6. Logarithms of relative rates correlate poorly with estimates of strain release in the reactions. Correlations are improved by incorporation of estimates of entropy changes associated with ring opening or cleavage, but remain poor. The fate of isotopic labels in the reactions of 2,*n*,*n*-trideuterio-1,2-diphenylcycloalkanols. [$^2H_3$]-5, [$^2H_3$]-7 and [$^2H_3$]-8, shows that protonation of the benzylic carbanion is by solvent DMSO for the cyclooctanol, [$^2H_3$]-8, and that competing intramolecular proton transfer occurs in the cycloheptanol, [$^2H_3$]-7, and cyclopentanol, [$^2H_3$]-5. Kinetic isotope effects associated with the labelling patterns are consistent with a change in rate-limiting step from the initial carbon–carbon bond cleavage in the case of 8, to rate-limiting proton transfer in the case of 5.**

Introduction

Since tertiary alkoxides are adducts of strongly basic carbanions and ketones, studies of their decomposition by C–C bond homolysis or heterolysis provide an alternative aspect on the mechanisms of these synthetically and biologically important reactions. We have made a detailed study of decompositions of the alkoxide of 1,2,3-triphenylpropan-2-ol, **1**. Rate and product data for the reaction in dimethyl sulfoxide (DMSO) solution are consistent with a collapse of this alkoxide by expulsion of benzyl anion. The products are toluene, shown to incorporate a proton from solvent DMSO, and the enolate of 1,2-diphenylethanone,[1] **2**, formed by deprotonation of the ketone, presumably by dimsyl anion, as shown in Scheme 1. Light and heavy



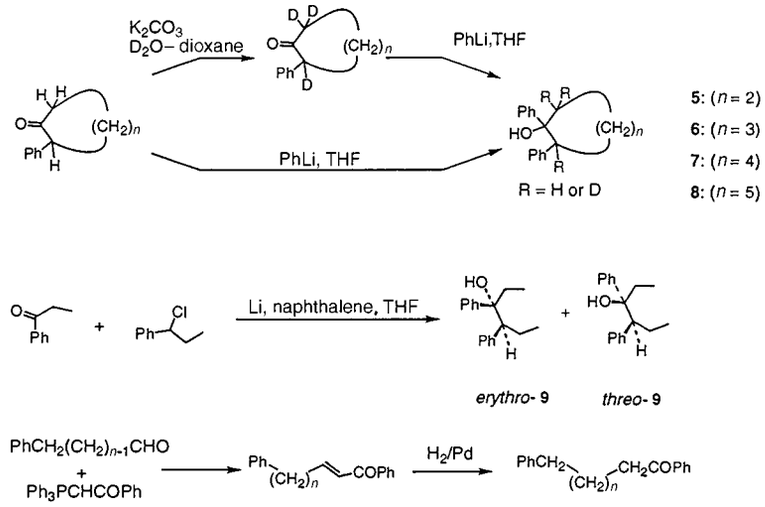
Scheme 1 Decompositions of alkoxides of linear and cyclic 1,2-diphenylalkanols

atom kinetic isotope effects are consistent with the carbon–carbon bond cleavage occurring in an initial rate-limiting step, so that this is formally an E1 elimination of toluene[2] as shown in Scheme 1. An interest in the relationships between structure and reactivity in these carbanion forming reactions has led us to examine the reactions of the 1,2-diphenylcycloalkanols, where the analogous reaction would, according to Stirling's classification,[3] be nucleophile eliminative ring fissions of the class *exo* O=C: Cn, yielding enolates of the isomeric linear ketones. Variation of reactivity in intramolecular reactions with ring size is more often studied in reactions involving ring formation,[4] and these alkoxide fragmentations afford a rare chance to examine relative reactivities in ring-openings of other than small rings which have been studied already (*trans*-**3** and *cis*-**3** by Jencks and Thiblin,[5] and *trans*-**4** and *cis*-**4** by Forward *et al.*[6]). Both the cyclopropanols and cyclobutanols are sufficiently reactive for ring-openings to be observable in aqueous base, albeit at elevated temperatures in the cyclobutanol case, and in this protic medium the products observed are ketones rather than their enolates. Again, the available evidence was consistent with rate-limiting formation of a benzylic carbanion. Hoffmann and Cram,[7] however, have shown that with sodium dimsyl in DMSO solution, equilibration of (−)-(1*R*;2*R*)-*cis*-1,2-dimethyl-2-phenylcyclopentanol and (−)(1*S*;2*R*)-*trans*-1,2-dimethyl-2-phenylcyclopentanol occurs many times faster than formation of acyclic material, indicating that carbanion formation is not rate-limiting in this case.

In this study we compare reactions of the homologous series comprising 1,2-diphenylcyclopentanol, **5**, 1,2-diphenylcyclohexanol, **6**, 1,2-diphenylcycloheptanol, **7** and 1,2-diphenylcyclooctanol, **8**. We also describe the behaviour of their close acyclic analogues, *threo*- and *erythro*-3,4-diphenylhexanol, **9**.

Preparation and structures

The normal and medium ring cycloalkanols were prepared by the reaction schemes which involved addition of phenyllithium to the corresponding 2-phenylcycloalkanone. In all cases, the addition yielded a major product alcohol, on steric grounds expected to be the *trans*-isomer of the 1,2-diphenylcycloalkanol. ^{1}H NMR spectroscopic evidence was always consistent



Scheme 2 Preparations of 1,2-diphenylcycloalkanols, their linear isomers (n = 2–5) and 3,4-diphenylhexan-3-ols (THF = tetrahydrofuran)

with this stereochemical assignment, but was hardly conclusive[8] even in the cyclohexanol case, of necessity being based almost entirely on the couplings to methine hydrogen. Fortunately, all the isolated alcohols were nicely crystalline, and their structures, discussed below, were confirmed as *trans*-1,2-diphenylcycloalkanols by X-ray crystallography. The isotopically labelled compounds, [2,5,5-$^2H_2$]-**5**, [2,6,6-$^2H_3$]-**6**, [2,7,7-$^2H_3$]-**7** and [2,8,8-$^2H_3$]-**8**, were available by exchange with basic D_2O at the ketone stage, and authentic samples of the expected product ketones were also prepared as shown. Coupling of propiophenone and 1-phenylpropyllithium yielded both isomers of 3,4-diphenylhexan-3-ol, one of which crystallised and was shown by X-ray crystallography to be the *erythro*-isomer.

Crystallographic studies were undertaken, in the first instance, to secure the structural assignments made in the course of the preparative chemistry, but we comment briefly on the features of each structure.

The asymmetric unit in the crystal structure of 1,2-diphenylcyclopentanol contains two non-equivalent molecules linked by a hydrogen bond [intermolecular d(O · · · O) = 2.961 Å]. Molecular conformations differ only in minor detail and we show only one of the molecules in the unit (see Fig. 1). The five-membered ring adopts a distorted envelope conformation, with a C1C3–C4C5 torsion angle of only −8.1°, so that these four atoms are within 0.06 Å of their mean plane. The fifth ring atom, C2, lies 0.63 Å out of this plane and forms the point of the 'flap' of the envelope. The phenyls are attached at C1 and C2, such that C1-phenyl has a near perfect *gauche* relationship to the hydroxy and phenyl at C2. One of the cyclopentanols shows a notably long bond (1.562 Å) between phenylated ring carbons. Dihedral angles from the C2 methine hydrogen to hydrogens of the adjacent methylene are 48 and 169°, consistent with the doublets of doublets (J 7.5 and 11.5 Hz) observed in the solution ^{1}H NMR spectrum of this compound.

The crystal structure of 1,2-diphenylcyclohexanol is disordered, with the hydroxy having an occupancy of 62.2% on C1 and 37.8% on C2 by occupancy refinement. Intermolecular hydrogen bonding occurs from a hydroxy group in one molecule either to the hydroxy or a phenyl group of a second. Nevertheless, the structure is clearly established as that of *trans*-1,2-diphenylcyclohexanol, with the chair cyclohexane ring carrying two equatorial phenyls and an axial hydroxy group. Dihedral angles between the C2-methine hydrogen and adjacent methylenes are 179 and 62°, consistent with the observed couplings of J 13.0 and 3.5 Hz.

As with the cyclopentanol, the crystal structure of 1,2-diphenylcycloheptanol has an asymmetric unit containing two non-equivalent molecules, but these are not linked by a hydrogen bond. Rather, asymmetric units are hydrogen bonded together [intermolecular d(O · · · O) = 2.912 Å]. The molecular conformations differ only in minor details and again we depict only one of the molecules in the unit (see Fig. 1). The cycloheptanol ring adopts a distorted chair conformation with the atoms C2, C3, C6 and C7 lying within 0.08 Å of their mean plane. Atoms C4 and C5 lie 1.18 and 0.94 Å below this plane, and the point atom, C1, carrying the axial hydroxy group, lies 0.567 Å above it. The *trans*-phenyl groups occupy 'equatorial' positions on the ring. Dihedral angles from the C2 methine to hydrogens at adjacent methylene are 12 and 99°, and observed coupling constants are J 11.5 and 2.0 Hz in the solution ^{1}H NMR spectrum.

The crystal structure of 1,2-diphenylcyclooctanol contains centrosymmetric hydrogen-bonded dimers [d(O · · · O) = 2.935 Å]. In the molecule, the eight-membered ring adopts a near ideal boat–chair conformation with (ignoring the substitution) a plane of pseudo-symmetry running through C1 and C5. This places the 'in' hydrogens at C3 and C7 in van der Waals contact [d(H7A · · · H3A) = 1.96 Å]. The hydroxy group then occupies the 'axial' position at the point of the chair, and the phenyl substituents equatorial on this chair portion. Dihedral angles to the methine hydrogen at C2 are 25 and 83°, and these are consistent with the observation of a doublet (J 7.7) as the signal from this hydrogen in the solution ^{1}H NMR spectrum. The C1–C2 bond linking the phenylated carbons is long (1.566 Å).

Disorder was again present in the structure of 3,4-diphenylhexan-3-ol, and OH sites at hydroxys and the hydrogen at the adjacent central carbon were given occupancies of 0.5 to fit the requirements of space group No. 14 in which the molecule has a centre of symmetry. Two molecules form a hydrogen-bonded dimer and the crystal lattice is stabilised by hydrogen bonding interactions to an adjacent asymmetric unit. Despite the disorder, the *erythro* relationship is clearly established, and within the molecules the pairs of phenyl groups and of ethyl groups are fully staggered.

In favourable cases, structures of series of reactive molecules determined in this way have shown unusual bond lengths or angles interpretable as distortions along a reaction coordinate.[9] In the expected reactions, the C1–C2 bonds are to be cleaved and the alcohol residue at C1 is transformed to a carbonyl. Structural modifications along the ring-opening reaction coordinate might therefore be lengthened C1–C2 bonds, shortened C1–O bonds, and angular distortions indicating sp^3 to sp^2 rehybridisation at C1. We have examined bond lengths and angles at these atoms (Table 1), and can find no link between any of the geometric parameters, or between any parameter set and ring size. Neither, as will be seen later, is there any relationship between reactivity of alkoxides and the parameters.

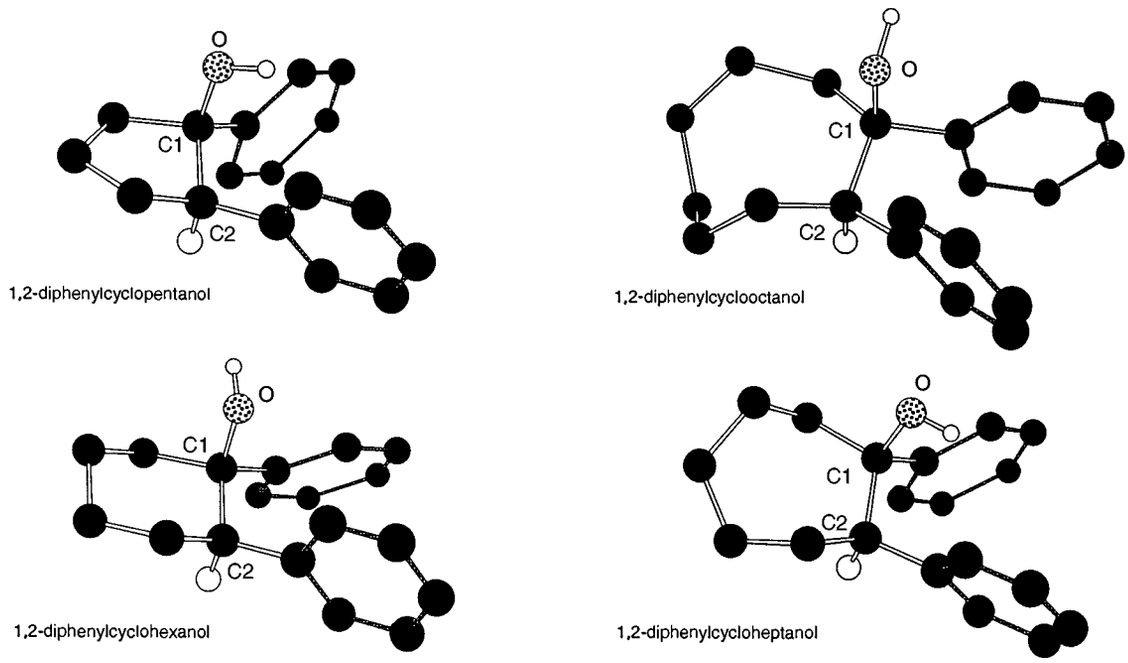


Fig. 1 X-Ray crystal structures of 1,2-diphenylcycloalkanols

Table 1 Some angles and distance at bonds at reacting atoms in the X-ray crystal structures of the tertiary-alcohols

Molecule	r(C1–C2)/Å	r(C1–O)/Å	φ(Ph–C1–C2–Ph)/°	θ(O–C1–Ph)/°
erythro-3,4-Diphenylhexanol	1.563	1.54	180	322.9
Cyclopentanol(mol A)	1.545(9)	1.421(6)	66.7	111.4
Cyclopentanol(mol B)	1.562(9)	1.422(7)	66.7	107.7
Cyclohexanol	1.555(3)	1.451	55.8	110.0
Cycloheptanol(mol A)	1.563(4)	1.442(4)	62.8	110.1
Cycloheptanol (mol B)	1.559(4)	1.431(4)	55.2	110.0
Cyclooctanol	1.566(3)	1.440(2)	53.5	110.5

Molecular mechanics calculations, using the MM3 empirical forcefield[10] as implemented in MACROMODEL 4.5[11] (MM3*), were carried out on all the *trans*-1,2-diphenylcycloalkanols using full conformational searches, which found global minimum energy conformations corresponding closely to those in the crystal structures. Table 2 summarises the results of the EFF calculations on the cycloalkanols, and on both *threo*- and *erythro*-3,4-diphenylhexan-3-ol. The bracketed values in the first column are steric energy differences between the global minimum and the next lowest conformation of each alkanol. These differences range from 8.22 kcal mol^{-1} (1 cal = 4.184 J) for the cyclohexanol (where the second conformation is a twist boat conformation) to 5.54 kcal mol^{-1} for the cyclopentanol (where the second conformation corresponds to a pseudo-rotation which places the hydroxylated carbon at the point of the flap of an envelope). The calculations thus suggest that the *trans*-1,2-diphenyl groups are effective conformational locking groups for the cycloalkanols. Even for the cyclopentanol, the population of the second conformation will be less than 0.01% at normal temperatures. For the acyclics, in the *threo*-isomer the three conformations by rotation about the C3–C4 bond are within 0.1 kcal mol^{-1} of each other; in the *erythro* isomer, the conformation with fully staggered phenyl and ethyl groups is favoured over all others, but only by 1.07 kcal mol^{-1}.

These calculations provide a basis for comparing the strain released in the expected ring openings. Strain in organic molecules is an enthalpy measured by comparing their heats of formation with those estimated for a 'strain free' model constructed using bond or group increments based on thermochemical data of an agreed set of 'strain free' molecules.[12] Heats of formation can be obtained from EFF calculations, provided that there are appropriate group or bond energy increments to add to the steric energies. Heats of isomerisation would therefore be obtained by taking the difference in steric energies of the cyclic and linear isomers, added to a correction involving increments for those groups involved in the bonding changes in the ring opening, which is constant in the series of molecules examined in this work. Differences in steric energies alone then should accurately reflect differences in heats of isomerisation for the series. The products of isomerisation may be regarded as the 1,5-, 1,6-, 1,7- or 1,8-diphenylalkanones, or their enols, and Table 2 also contains steric energies obtained for these products in their fully extended conformation. The second and third columns present steric energy differences between ground state conformation of the alcohols and ketone or *Z*-enol isomers. In both cases, these increase in the order: cyclohexanol ≈ acyclics < cycloheptanol < cyclopentanol < cyclooctanol < cyclobutanol, and this is the expected reactivity ordering in reactions in which strain relief is dominant in transition state formation. For the ketones, differences range from 4.22 kcal mol^{-1} for the cyclohexanol, to 18.69 kcal mol^{-1} for the cyclooctanol, with a difference in strain release of 14.47 kcal mol^{-1}. There are good qualitative indications that steric effects are important in alkoxide decompositions,[13,14] and correlations between strain relief, calculated by empirical forcefield methods, and reactivity in fragmentation of sets of sterically congested acyclic lithium tertiary-alkoxides in hexamethylphosphoric triamide (HMPA) have been described by Lomas and Dubois.[15] If steric energy release were fully expressed in the same way in the 1,2-diphenylcycloalkanols, then the reactivity range would be very large with cyclooctanol expected to be *ca.* 10^{10} more reactive than the cyclohexanol.

Table 2 Steric energies for tertiary alcohols and their acyclic isomers from MM3* empirical forcefield calculations[a]

Compounds	E_{steric}/kcal mol^{-1}	ΔE_s(*Z*-enol)/kcal mol^{-1}	ΔE_s (ketone)/kcal mol^{-1}
trans-1.2-Diphenylcyclobutanol	43.06 (3.73)	28.16	25.70
1,4-Diphenylbutan-1-one	17.36		
(*Z*)-1,4-Diphenylbut-1-en-1-ol	14.90		
trans-1,2-Diphenylcyclopentanol	32.86 (5.54)	19.06	13.80
1,5-Diphenylpentan-1-one	19.06		
(*Z*)-1,5-Diphenylpent-1-en-1-ol	13.80		
trans-1,2-Diphenylcyclohexanol	24.85 (8.22)	8.83	4.22
1,6-Diphenylhexan-1-one	20.62		
(*Z*)-1,6-Diphenylhex-1-en-1-ol	16.01		
trans-1,2-Diphenylcycloheptanol	34.49 (6.66)	17.41	13.02
1,7-Diphenylheptan-1-one	21.47		
(*Z*)-1,7-Diphenylhept-1-en-1-ol	16.68		
trans-1,2-Diphenylcyclooctanol	41.49 (6.53)	23.45	18.69
1,8-Diphenyloctan-1-one	22.80		
(*Z*)-1,8-Diphenyloct-1-en-1-ol	18.04		
threo-3,4-Diphenylhexanol	26.36 (0.02)	10.35	7.46
erythro-3,4-Diphenylhexanol	24.46 (1.07)	8.45	5.56
1-Phenylpropan-1-one	11.88		
(*Z*)-1-Phenylprop-1-en-1-ol	8.99		
1-Phenylpropane	7.02		

[a] 1 cal = 4.184 J.

Reactivity studies

These normal and medium ring cycloalkanols were stable to the aqueous basic conditions which induce ring openings in the cyclobutanols and cyclopropanols. Reactions were therefore examined in more strongly basic media used earlier in studies of cleavages of 1,2,3-triphenylpropanols. Initially, each alcohol was treated separately with excess dimsylsodium in DMSO solution at 40 °C, completely converting the alcohol to its alkoxide.[16] Attempts to monitor formation of ketone enolate UV-spectrophotometrically were not successful, and sampling methods were therefore adopted. Aliquots of the reaction mixture were periodically withdrawn, quenched with dilute aqueous acid, and then analysed by GLC. These studies established that the anticipated isomerisations to the linear ketones, identified by GC–MS comparison with the authentic samples, occurred under these conditions. Provided oxygen was rigorously excluded, these ketones were the sole products of reaction after dilute aqueous acidic quench. If oxygen was not excluded, then a variety of products arising from oxidation of the ketone enolate were formed.

Disappearances of the alcohol for the relatively fast reactions of **7**, **8** and **9** showed good first order behaviour over at least three half-lives. For the cyclohexanols, reaction was very slow and it was only practical to observe them to *ca.* 20% conversion which required nearly 72 h at 50 °C with dimsyl potassium in DMSO. The disappearance of the cyclohexanol was fitted to a first-order decay. For the cyclopentanol reactions which showed rates between those of the cyclohexanol and the faster reacting group, first order behaviour was also obtained, but small additional peaks (always <3% of the *trans*-1,2-diphenylcyclopentanol), with retention times close to those of *trans*-1,2-diphenyl-cyclopentanol, were observed in the GLC of the reaction mixtures early in the course of the reaction monitoring. These peaks showed identical MS fragmentations patterns to the *trans*-1,2-diphenylcyclopentanol, and we assign them to small amounts of transiently formed *cis*-1,2-diphenylcyclopentanol, which is indicated by molecular mechanics calculation to be 1.7 kcal mol^{-1} less stable than the *trans* isomer. For the six-, seven- and eight-membered ring 1,2-diphenylcycloalkanols, *cis*-isomers are calculated to be >4 kcal mol^{-1} more strained than the *trans*-isomers.

These experiments established approximate relative reactivities with the cyclooctanol being more than 10^5 times more reactive than the cyclohexanol. Construction of a more accurate scale of alkoxide reactivities is complicated by ion-pair formation of alkali metal alkoxides in DMSO,[17] and the large differences in reactivity of 'free' and 'paired' alkoxides in their fragmentation or ring openings. The reaction scheme given by eqns. (1)–(3), with ion pairing constants (K_{ass}) in DMSO

$$RO^- + M^+ \overset{K_{ass}}{\rightleftharpoons} RO^-M^+ \quad (1)$$

$$RO^- \xrightarrow{k_{free}} P \quad (2)$$

$$RO^-M^+ \xrightarrow{k_{ip}} P \quad (3)$$

ranging from 10 (for M = K) to 10^4 (for M = Li), and $k_{free} \gg k_{ip}$, has been shown to describe the behaviour of the alkoxides of 1,2,3-triphenylpropan-2-ol, and is expected to apply here also. Under these circumstances, the reaction velocity is given by eqn. (4) where $c = [RO^-] + [RO^-M^+]$. Pseudo-first-order rate

$$v = [k_{free}/(K_{ass}[M^+])]c \quad (4)$$

constants ($k_{obs} = k_{free}/K_{ass}[M^+]$) for product formation thus depend on both metal ion concentration and K_{ass}. For this series of structurally similar alkoxides, we assume that association constants for ion-pair formation with a particular metal are not strongly structure dependent. For reactions of two or more alcohols in the same metal dimsyl solution, the nature of the metal ion and metal ion concentrations are identical, and experimentally determined relative rates then reflect relative magnitudes of k_{free} for the alkoxides involved. This approach allows use of the ion-pairing constants with different metals to adjust experimental reactivities to conveniently observable values, and the rate data are collected in Table 3. Thus, for the more reactive alcohols (the acyclics, cyclooctanol and cycloheptanol) use of dimsyllithium solution gave rates which were convenient for sampling and analysis. Reactions were conducted at two different temperatures, and relative reactivities at 18 and 35 °C are the same. The cyclooctanol–cycloheptanol pair were also examined in 1,3-diaminopropane (DAP) with its potassium salt as base (DAP–KAPA),[18] and the constancy of the cyclooctanol–cycloheptanol rate ratio in two different solvent–base systems provides some support for this approach to the construction of a scale of reactivities. For the less reactive alcohols (cyclohexanol and cyclopentanol), dimsylpotassium was used, but even so higher temperatures were necessary to permit the cyclohexanol fragmentation to be observed. Overlap between the extremes of reactivity was made by simultaneous

Table 3 Rate data for base induced isomerisations of 1,2-diphenylcycloalkanols and for cleavage of 3,4-diphenylhexan-3-ols

Substrate sets	Solvent/base	T/ °C	k_{obs}/s^{-1}	Rate ratio
Cyclooctanol	KAPA–DAP	30	1.13 (±0.07) × 10^{-3}	k_8/k_7 = 115
Cycloheptanol			9.81 (±0.40) × 10^{-6}	
Cyclooctanol	KAPA–DAP	50	1.29 (±0.03) × 10^{-2}	k_8/k_7 = 104
Cycloheptanol			1.24 (±0.11) × 10^{-4}	
Cyclopentanol	K dimsyl–DMSO	30	6.16 (±0.48) × 10^{-6}	k_7/k_5 = 807
Cycloheptanol			4.97 (±0.17) × 10^{-3}	
Cyclopentanol	K dimsyl–DMSO	40	7.34 (±0.48) × 10^{-6}	k_7/k_5 = 754
Cycloheptanol			5.54 (±0.17) × 10^{-3}	
Cyclopentanol	K dimsyl–DMSO	50	2.65 (±0.10) × 10^{-5}	k_5/k_6 = 25.5
Cycloheptanol			1.04 (±0.05) × 10^{-6}	
Cyclopentanol	K dimsyl–DMSO	50	2.38 (±0.13) × 10^{-5}	k_5/k_6 = 14.3
Cycloheptanol			1.66 (±0.25) × 10^{-6}	
erythro-Hexanol	Li dimsyl–DMSO	18	3.05 (±0.21) × 10^{-6}	k_{th}/k_{er} = 3.77
threo-Hexanol			1.15 (±0.17) × 10^{-5}	
Cyclooctanol			4.09 (±0.44) × 10^{-5}	k_8/k_{th} = 3.55
Cycloheptanol			3.97 (±0.52) × 10^{-7}	k_8/k_7 = 113
erythro-Hexanol	Li dimsyl–DMSO	35	3.54 (±0.24) × 10^{-5}	k_{th}/k_{er} = 3.13
threo-Hexanol			1.11 (±0.17) × 10^{-4}	
Cyclooctanol			3.58 (±0.66) × 10^{-4}	k_8/k_{th} = 3.22
Cycloheptanol			3.17 (±0.11) × 10^{-6}	k_8/k_7 = 103

reaction of cyclopentanol and cycloheptanol, and for this pair, the reactivity difference was largest.

Attempts to place the reactivity for the ring opening of 1,2-diphenylcyclobutanol on the same scale by using a paired reaction with 1,2-diphenylcyclooctanol with dimsyllithium as base were not successful. At the lowest possible temperature (*ca.* 18 °C), ring opening of the cyclobutanol was complete before the first sample could be extracted and quenched (*ca.* 30 s). We can only estimate that the cyclobutanol is >100 times more reactive than the cyclooctanol.

The combined rate measurements permit the construction of a ladder of reactivities for this set of compounds, contained in Table 4, and scaled relative to that of *erythro*-3,4-diphenylhexan-3-ol. The span of reactivities is greater than 10^6, and for the cycloalkanols, rates increase with increasing steric energy of the cycloalkanol. However, as shown in Fig. 2(*a*), values of log k_{rel} correlate poorly with ΔE_{steric} for isomerisation of cycloalkanols to the acyclic ketones. For the ketone steric energy data, the best straight line is given by log k_{rel} = $0.397\Delta E_{steric} - 7.154$ ($r^2 = 0.724$). Use of steric energy differences for isomerisations to the enols does not improve the correlation. Notably, the acyclic hexanols are >10^5 times more reactive than the cyclohexanol, despite showing similar release of steric energy on cleavage of benzylic bonds.

Such behaviour is not entirely unexpected since these steric energy differences take no account of the entropy changes accompanying ring-opening or fragmentation. Release of the constraints on rotation about single bonds in ring-openings has been estimated[19] to contribute an entropy increase of *ca.* 4 cal K^{-1} mol^{-1} for each single bond lying between the reaction atoms. At 300 K, this would reduce free energies of isomerisation by 4.8, 6.0, 7.2 and 8.4 kcal mol^{-1} respectively for five-, six-, seven- and eight-membered rings. In the cleavage of the linear models, an entropy change associated with the three additional translational and rotational degrees of freedom in the production of two molecules from one, must be taken into account. For standard states of 1 M in solute, at 25 °C, this has been estimated to be as much as 50 cal K^{-1} mol^{-1}, or 15 kcal mol^{-1} in the free energy of the cleavage reaction at 300 K. Addition of these entropic corrections to the estimates of enthalpic strain release produces a crude measure of the relative free energy change (ΔG_{rel}) in the isomerisations or cleavages, and these estimates are also included in Table 4. Fig. 2(*b*) shows a plot of log k_{rel} against these values for ΔG_{rel} for ketone formations, and it is clear that inclusion of the entropic factors moves all points, including those from the linear models, closer to a single correlation line (log k_{rel} = $0.411\Delta G_{rel} - 9.543$ with $r^2 = 0.801$). Even so, the fit is not a particularly good one, and can be improved by using a smaller contribution for entropy increase (*ca.* 2.5 cal K^{-1} mol^{-1}) for each single bond lying between the reacting atoms, suggesting that free rotation about these bonds is not achieved in the transition states. Dispersion may arise also from variation in transition structure with differing extents of carbon–carbon bond cleavage for each ring size, or a change in rate-determining step within the series of compounds from carbon–carbon bond cleavage to rate-limiting proton transfer, and indeed, observations of *trans–cis* isomerism accompanying the ring opening of the cyclopentanol are consistent with rate-limiting proton transfer in this case. Variation of product labelling patterns in ring openings of the deuteriated cycloalkanols, [$^2H_3$]-**5**, [$^2H_3$]-**6**, [$^2H_3$]-**7** and [$^2H_3$]-**8** supports such mechanistic differences.

For the 3,4-diphenylhexanols (whose reactivity is very close to that found in earlier work for 1,2,3-triphenylpropanol[1]) the rate ratio $k_{threo}/k_{erythro}$ should reflect differences in steric energy release, with little contribution from differential entropy change. The molecular mechanics calculations show that the *threo* compound is 1.9 kcal mol^{-1} more strained than its *erythro* isomer, and full expression of this difference would give $k_{threo}/k_{erythro}$ *ca.* 24, while the experimental value is *ca.* 3.5, suggesting that strain release is far from complete in the rate-limiting step which, our earlier studies[2] on closely related 1,2,3-triphenylpropanol suggest is carbon–carbon bond cleavage to yield the ketone–benzylic carbanion complex.

Labelling studies and kinetic isotope effects

For ring-openings of triply deuteriated 1,2-diphenylcycloalkanols in [$^1H_6$]DMSO, the possible product labelling patterns are shown in Scheme 3. Ring opening, and protonation of the benzylic carbanion by DMSO (pK_a = 33), should yield, after quench, doubly deuteriated ketone. Ring-opening and intramolecular transfer of a relatively acidic (pK_a *ca.* 25) C^2-deuteron[16] to the benzylic carbon should, after quenching of the enolate, yield triply deuteriated ketone. Because exchange at the enolizeable positions is not fully controlled under the quench conditions, the isolated ketones were treated with aqueous potassium carbonate, conditions known to exchange hydrogens at these positions, but not the benzylic positions. Ring cleavages involving external and internal proton transfers would thus yield, finally, [$^2H_1$]- and [$^2H_2$]-ketones, respectively, with the deuterium incorporated at the benzylic positions. Interpretation of the product labelling patterns, however, is complicated

Table 4 Relative reactivities in ring opening reactions of diphenylcycloalkanols or fragmentations of 3,4-diphenylhexanols, steric energy release for ketone formation, and estimated relative free energy changes for isomerisations

Diphenylalkanol	k_{rel}	log k_{rel}	ΔE_{steric} /kcal mol^{-1}	ΔG_{rel} at 300 K/kcal mol^{-1}
Cyclohexanol	7.1×10^{-6}	−5.15	4.22	10.22
erythro-Hexan-3-ol	1.0	0.00	5.56	20.56
threo-Hexan-3-ol	3.5	0.54	7.46	22.46
Cycloheptanol	1.1×10^{-1}	−0.96	13.02	20.22
Cyclopentanol	1.4×10^{-4}	−3.85	13.80	18.60
Cyclooctanol	1.2×10^{1}	1.07	18.69	27.09

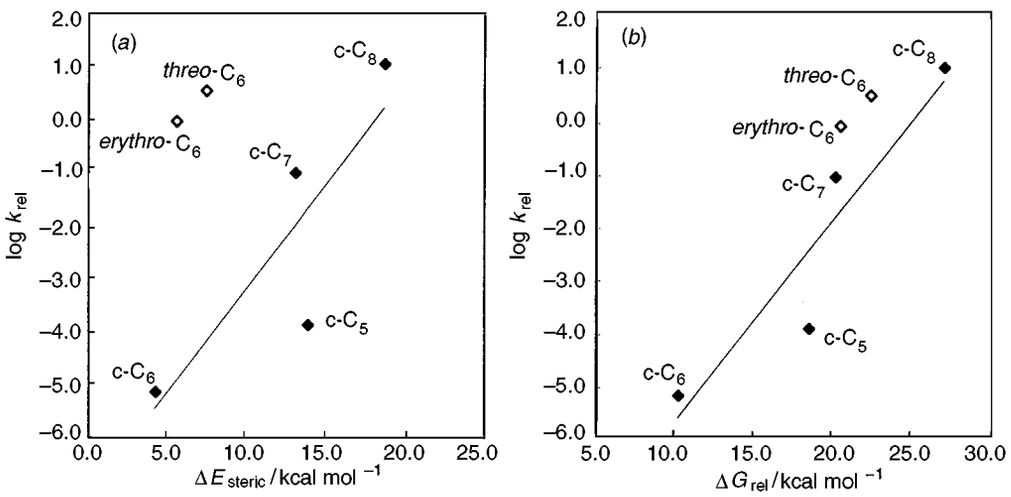
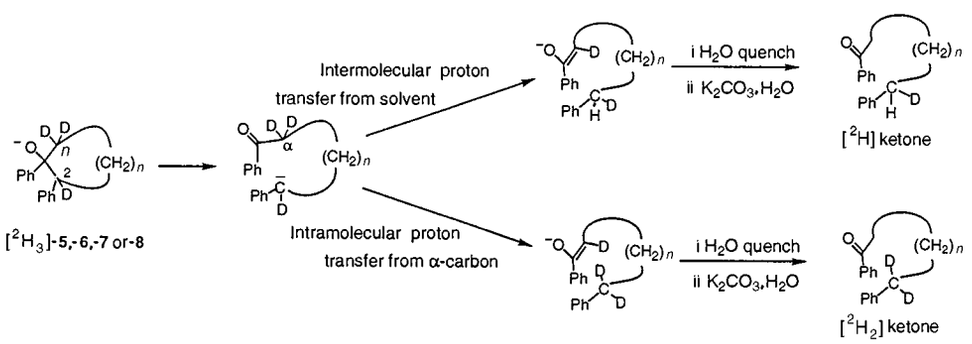


Fig. 2 Plots of log k_{rel} against steric energy release in ketone formation (*a*), or against steric energy release with entropic corrections (*b*). Lines are best straight lines for the cycloalkanol data only. In (*a*), log $k_{rel} = 0.397\Delta E_s - 7.154$ ($r^2 = 0.724$); in (*b*) log $k_{rel} = 0.378\Delta G_{rel} - 9.422$ ($r^2 = 0.872$).



Reactant	Ketone label incorporation	Kinetic isotope effect
[$^2H_3$] **5** ; ($n = 2$)	[^2H]:[$^2H_2$] = 65:35	k_{H_3}/k_{D_3} = 2.47(±0.07)
[$^2H_3$] **6** ; ($n = 3$)	no experiment	no experiment
[$^2H_3$] **7** ; ($n = 4$)	[^2H]:[$^2H_2$] = 42:58	k_{H_3}/k_{D_3} = 1.37(±0.07)
[$^2H_3$] **8** ; ($n = 5$)	[^2H]:[$^2H_2$] = 95:5	k_{H_3}/k_{D_3} = 1.43(±0.08)

Scheme 3 Fate of isotopic labels in reactions of [$^2H_3$]-1,2-diphenylcyclopentanol, [$^2H_3$]-1,2-diphenylcycloheptanol and [$^2H_3$]-1,2-diphenylcyclooctanol, and associated kinetic hydrogen isotope effects

by a superimposed exchange of deuterium at benzylic positions with DMSO in these strongly basic solutions. These could occur either in the cycloalkanol,[20] or more probably in the product, to reduce deuterium incorporations at benzylic positions, so that measured incorporations will always represent lower limits for those from the competing proton transfers which follow the ring-opening. Rates of exchange at benzylic positions have been measured for toluene, ethylbenzene and cumene[21] with 0.56 M KOBu^t in DMSO at 30 °C, and half-lives for exchange are 43 min, 3 h and 30 h respectively. It is likely therefore, that reactions of the cyclooctanol using dimsylsodium and cycloheptanol using dimsylpotassium, which are complete in less than 10 min at $T < 30$ °C, are fast enough for the contribution of solvent exchange at the benzylic position to be small, and comparable with the uncertainties in the measurement of the incorporations (± *ca.* 3%). For the cyclopentanols, which require *ca.* 2 h at 50 °C even with dimsylpotassium, the contribution is expected to be significant, and for the very slowly reacting cyclohexanol, uncertainties arising from benzylic exchange completely undermine the usefulness of an experiment with this alcohol.

The results of experiments with [$^2H_3$]-**5**, [$^2H_3$]-**7** and [$^2H_3$]-**8** are shown in Scheme 3. Deuterium incorporations are from measurements of parent ion peak ratios in the EI mass spectra of the ketones. These fragment to yield benzyl cations (*ca.* 30%) and analysis of peak ratios at $m/z = 91$, 92 and 93 confirmed that the residual deuterium was incorporated at the benzylic positions.

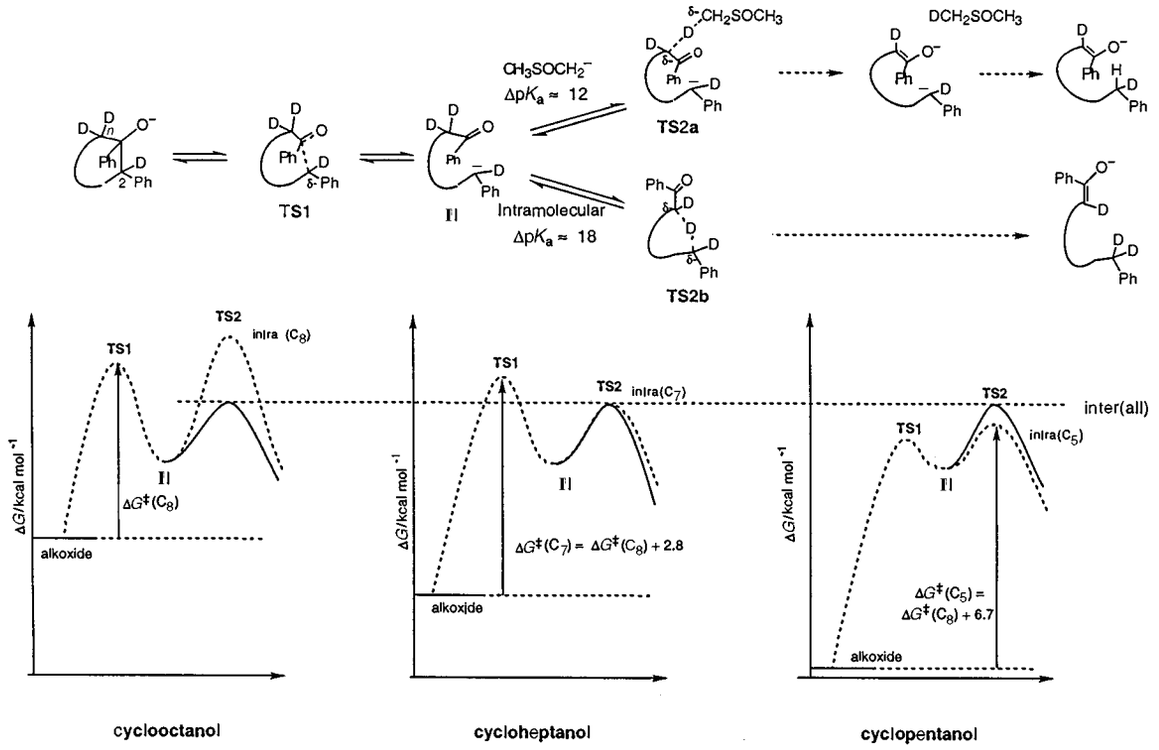


Fig. 3 Mechanisms and reaction profiles for ring opening reactions

The results are consistent with the polar mechanism but the deuterium incorporations show a clear distinction between the cyclooctanol ring opening and those of the cyclopentanol and cycloheptanol. Formation of >95% of 8-deuterio-1,8-diphenyloctanone indicates protonation of the intermediate carbanion by DMSO, despite the availability of a more acidic intramolecular proton source. The same situation was found[1] in the cleavage of the acyclic 1,2,3-triphenylpropanol, **1**, also in DMSO. Less surprisingly perhaps, ring openings of the small ring 1,2-diphenylcycloalkanols, **3**[5] and **4**,[6] in deuteriated aqueous medium also yielded products in which the intermediate benzylic carbanions were protonated by solvent. For the cycloheptanol, and cyclopentanol, the isolation of 57 and 35% of [$^2H_2$]ketones, respectively, indicates important amounts of deuteron transfer from the ketone α-carbons (C*n* to C2), presumably intramolecularly, and in view of the solvent exchange discussed above, that process in the cyclopentanol is probably the major reaction pathway.

The kinetic isotope effects (kie values) associated with the labelling were measured by monitoring the time course of the composition of a mixture of labelled and unlabelled cycloalkanols reacting in the same DMSO–dimsyl solution. The composition changes are related[22] to the kie by the relationship in eqn. (5), where x_{H_0} and x_{D_0} are the mole fractions of

$$\text{kie} = \frac{\ln[a(x_H/x_{H_0})]}{\ln[a(x_D/x_{D_0})]} \qquad (5)$$

unlabelled ($^2H_0$) and labelled ($^2H_3$) alcohol at initial time, and x_H and x_D are the mole fractions of unlabelled and labelled alcohol at time when a is the fraction of unreacted alcohol. The results of kie measurements are also collected in Scheme 3. Average values of 2.47, 1.37 and 1.43 are obtained for cyclopentanol, cycloheptanol and cyclooctanol, respectively. Uncertainties quoted are the standard deviations of a number of measurements taken throughout the reactions. Base catalysed exchange at the benzylic sites in the cycloalkanols will mean that the true kie values should be always greater than those obtained from the relationship using experimentally determined label incorporations, but the consistency of the data (see Experimental section) suggests that this is not a major source of error, even in the cyclopentanol reaction.

We again discuss these effects within the framework of initial carbon–carbon cleavage to yield a transient benzylic carbanion, followed by proton transfers to yield the enolate of the acyclic ketone. In the event that the initial carbon–carbon bond cleavage is rate limiting (TS1 in Fig. 3), then the major contribution to the observed rate ratio should be a secondary α-deuterium isotope effect associated with the hydron at the benzylic position. Labels at the methylene position seem too remote from the reaction site for their bonds to be strongly perturbed. At the benzylic position, the carbon atom would be undergoing an sp^3 to sp^2 rehybridisation, and, theoretically, values up to 1.4 per D could be attributed to such secondary isotope effects.[23] Values of between 1.2 and 1.3 per D have been observed in other reactions where benzylic[2] or allylic[24] carbanions have been formed. These large secondary isotope effects are associated with bending frequencies at allylic anionic (and presumably also at benzylic) centres which are substantially lower even than those at an ordinary olefinic C–H bond.[25] The values reported in Scheme 3 for the cyclooctanol and cycloheptanol are at the extreme end of the range of plausible values for secondary effects. Those for the cyclopentanol are clearly outside that range, and must contain a contribution from an isotope effect on one of three possible subsequent proton transfer steps.

If a proton is transferred from DMSO to the benzylic carbanion (not shown in Fig. 3), any isotope effect on that step would be associated with the α-deuterium at that site and rehybridisation of the carbon from sp^2 to sp^3. This is expected to be small and inverse. Because of the exothermicity of the proton transfers, it is unlikely that any subsequent proton transfers to yield the final product could be rate limiting, and the overall kinetic isotope effect for rate-limiting protonation of the benzylic carbanion by DMSO should be a combination of the secondary α-deuterium effect on carbanion formation, and the inverse secondary effect on its protonation yielding an effect rather smaller than that found in any of the reactions studied. The experimental data thus suggest that this pathway is not followed for any of the ring openings.

In the second of these, a hydron may be abstracted by dimsyl anion from the methylene adjacent to the carbonyl, yielding a dianion (*via* TS2a in Fig. 3). This is also carbon-to-carbon proton transfer, expected to be strongly exoergic on the basis of the relative pK_a values[16] of DMSO and acetophenone. In such a proton transfer, primary kinetic effects are expected to be much reduced from their Westheimer maximum of *ca.* 7.[26] Because of the labelling pattern, there will be a secondary α-deuterium effect from rehybridisation of the methylene carbon. Again, since this proton transfer is so strongly exoergic, it is extremely unlikely that a second exoergic proton transfer required to complete the reaction could be rate limiting.

The final possibility is that there may be an intramolecular transfer of hydron from the methylene to the benzylic anion (*via* TS2b in Fig. 3) to yield the product enolate directly. This is also a carbon-to-carbon proton transfer, which should be even more exoergic than the second possibility. Again, there will be secondary effects associated with rehybridisation at proton donating and proton accepting sites. Since these effectively exchange their hybridisations, it can be expected that the net secondary contributions will be small.

If either of these proton transfers were rate limiting, then the overall rate ratio should be the product of the secondary α-deuterium effect on the formation of the benzylic carbanion, and the contribution on transfer of the hydron at the methylene adjacent to the carbonyl to either dimsyl or benzylic carbanion. For the cyclooctanol reaction, product labelling patterns permit only the proton transfer *via* TS2a, but the observed rate ratio (kie = 1.43) suggests that its contribution is not large, and we suggest that carbanion formation is rate limiting, a situation resembling that proposed for cleavage of the acyclic compound 1,2,3-triphenylpropanol.[2] For the cycloheptanol reaction, the product labelling experiments permit reaction pathways by both TS2a and TS2b, but again, the size of the kie suggests that the carbanion formation is rate limiting. For the cyclopentanol reaction the observed ratio is large enough to reflect an equilibrium secondary effect (*ca.* 1.3) on a reversible ring opening (TS1) and rate-limiting proton transfers *via* both TS2a and TS2b with kie values of *ca.* 1.9, which would not be unreasonable for these strongly exoergic proton transfers.[27]

Conclusion

The behaviour of these alkoxides has illustrated almost all the possible complexities that can arise in structure–reactivity relationships, even when compounds with closely similar reacting groups are compared. Qualitative free energy profiles of the cyclooctanol, cycloheptanol and cyclopentanol ring openings, consistent with the available data are also presented in Fig. 3. In constructing them, we have assumed that the intermediate carbanions, I1, are of similar energy and that barriers to intermolecular proton transfer, *via* TS2b (solid line), are not strongly dependent on ring size. The intramolecular proton transfers, however, occur through cyclic arrays of the same size (on an atom for atom basis) as those for ring closures, and barriers for both are expected to vary in response to the entropic and enthalpic factors discussed earlier, but not with exactly the same sensitivity. Barriers to ring closure decreasing with ring size eventually result in reversible ring opening; and barriers to intramolecular proton transfer decreasing with ring size yield increasing amounts of the intramolecular proton transfer products.

Experimental

GLC was carried out on a Carlo Erba 4130 chromatograph fitted with a capillary column (5 m × 0.22 mm) with a 0.25 μ OV-1 cross-bonded stationary phase and hydrogen at 1 cm^3 min^{-1} as carrier gas. Merck precoated silica plates (0.25 mm Kieselgel 60 F_{254}) were used for analytical TLC. Kieselgel H and a range of solvents, all distilled before use, were used in column chromatography. Light petroleum refers to the fraction of bp 40–60 °C. IR spectra were recorded on a Perkin-Elmer 1710-FT spectrometer, routinely on thin films on NaCl plates. UV spectra were recorded on a Shimadzu UV-260 spectrometer on solutions in 95% aqueous ethanol. Routine ^{1}H NMR spectra were run on a Bruker AC 300E spectrometer operating at 300 MHz or a Gemini running at 200 MHz. ^{13}C NMR spectra were run on the Bruker AC 300E spectrometer at 75 MHz. Chemical shifts are reported in ppm (δ) relative to internal $SiMe_4$. *J* values are in Hz. Signal splittings are reported as: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublet (dd), doublet of doublet of doublet (ddd), triplet of doublet (td) and multiplet (m). Routine mass spectra were run on a Fisons VG Trio 2000 spectrometer using electron impact ionisation at 70 eV or chemical ionisation with ammonia as the reagent gas. Negative Cl mass spectra were run on a Kratos Concept LS1; the GC–MS were run on a Perkin-Elmer Sigma 3 GLC in conjunction with the Kratos MS 25 mass spectrometer. Deuterium incorporations were calculated by solving the equations given by Biemann,[28] using a computer program written in BASIC for the BBC Micro. Melting points were determined on a Kofler hot stage microscope and are uncorrected. All microanalyses were carried out at the University of Manchester Microanalytical Laboratories under the direction of Mr M. Hart. X-Ray crystal structures were determined by Mr R. Beddoes at the X-ray crystallographic service at the University of Manchester.

2-Phenyl-2,*n*,*n*-trideuteriocycloalkanones

These were prepared by potassium carbonate catalysed exchange of 2-phenylcycloalkanones with D_2O in dioxane following a published procedure.[6] For [$^2H_3$]-**5**, mass spectrometric analysis (positive Cl) gave incorporation: $^2H_2$ 10.6 ± 0.1%, $^2H_3$ 89.1 ± 0.1%; for [$^2H_3$]-**6** $^2H_2$ 10.1 ± 0.1%, $^2H_3$ 89.6 ± 0.1%; [$^2H_3$]-**7**: $^2H_1$ 1.2 ± 0.1%, $^2H_2$ 6.6 ± 0.1% and $^2H_3$ 92.2 ± 0.1%; and [$^2H_3$]-**8**: $^2H_1$ 0.6 ± 0.1%, $^2H_2$ 10.6 ± 0.1%, $^2H_3$ 88.5 ± 0.1%.

trans-1,2-Diphenylcyclopentanol, 5, and 1,2-diphenyl-2,5,5-trideuteriocyclopentanol, [$^2H_3$]

2-Phenylcyclopentanone (3.55 g, 22 mmol) in 30 ml of dry diethyl ether was added slowly to phenyllithium (30 ml of 0.8 M solution in diethyl ether) and allowed to react for 2 h. The mixture was then poured into 60 ml of cold 1 M HCl solution before separation of the ether layer and further extraction and drying ($MgSO_4$). Evaporation yielded an oil which was chromatographed on silica (light petroleum–diethyl ether solvent gradient). The alcohol crystallised from the main fraction and recrystallisation from light petroleum gave white crystals; mp 48–49 °C (Found: C, 85.7; H, 7.62. Calc. for $C_{17}H_{18}O$: C, 85.67; H, 7.61%); ν_{max}/cm^{-1} (KBr) 3557, 1602, 1495, 1447, 1332, 1284, 1163 and 1018; δ_H(200 MHz; $CDCl_3$) 1.62 (1H, s, OH), 1.88–2.55 (6H, m), 3.52 (1H, dd, J_{cis} 11.5 and J_{trans} 7.5), 7 (2H, m) and 7.14–7.4 (8H, M); δ_C(75 MHz; $CDCl_3$) 22.74, 29.76, 43.25, 57.74, 83.94, 125.1, 126.46, 126.98, 128.03, 128.22, 128.85, 138.11 and 146.5; *m/z* (EI) 238 (M^+, 41), 220 ([M − H_2O]$^+$, 16), 133 (56), 120 (95), 105 (100), 91 (31) and 77 (37); (CI, NH_3) 266 ([M + 2NH_4]$^+$, 2), 256 ([M + NH_4]$^+$, 25), 238 (M^+ or [M − H_2O + NH_4]$^+$, 100), 221 ([M − OH]$^+$ or [M − H_2O + H]$^+$, 87), 105 (7) and 91 (2).

Reaction of 2-phenyl-2,5,5-trideuteriocyclopentanone similarly yielded *trans*-1,2-diphenyl-2,5,5-trideuteriocyclopentanol (60%); mp 48–49 °C (Found: C, 84.78; H, 7.62. Calc. for $C_{17}H_{15}D_3O$: C, 84.6; H, 7.51%). Mass spectrometric analysis (positive CI) gave incorporation: $^2H_1$ 4.6 ± 0.1%, $^2H_2$ 26.5 ± 0.1% and $^2H_3$ 68.8 ± 0.1%.

trans-1,2-Diphenylcyclohexanol, 6 and *trans*-1,2-diphenyl-2,6,6-trideuteriocyclohexanol, [$^2H_3$]-6

These compounds were prepared by the literature methods[29]

and had spectroscopic properties in full agreement with reported data. The crystals had mp 66–67 °C (lit., 64–65 or 67–69 °C) (Found: C, 85.4; H, 7.9. Calc. for $C_{18}H_{20}O$: C, 85.67; H, 7.98%).

Reaction of 2-phenyl-2,6,6-trideuteriocyclohexanone (1.8 g, 7 mmol) with phenylithium (0.8 g, 10 mmol) as described above yielded *trans*-1,2-diphenyl-2,6,6-trideuteriocyclohexanol: mp (hexane) 65–67 °C (Found: C, 84.72; H, 8. Calc. for $C_{18}H_{17}D_3O$: C, 84.65; H, 7.89%). Mass spectroscopy (positive CI) indicated the following deuterium incorporation: $^2H_1$ 1.2 ± 0.1%, $^2H_2$ 6.3 ± 0.1% and $^2H_3$ 92.4 ± 0.1%.

trans-1,2-Diphenylcycloheptanol, 7, and 1,2-diphenyl-2,7,7-trideuteriocycloheptanol, [$^2H_3$]-7

Reaction of 2-phenylcycloheptanone (2.4 g, 12.6 mmol) with phenyllithium (20 ml of a 0.8 molar solution, 16 mmol in THF) at −15 °C yielded, after bulb-to-bulb distillation and chromatography on silica (gradients of light petroleum–diethyl ether), the alcohol (3.3 g, 91%) which was crystallised from light petroleum (40–60), mp 57 °C (Found: C, 85.88; H, 8.73. Calc. for $C_{19}H_{22}O$: C, 85.67; H, 8.32%); ν_{max}/cm^{-1} (NaCl) 3562, 3027, 2928, 1601, 1493, 1297, 1070, 1050, 923; δ_H(200 MHz; $CDCl_3$) 1.55–2.27 (10H, m), 2.36 (1H, m), 3.24 (1H, dd, *J* 11.5 and 2), 6.82 (2H, m) and 7–7.35 (8H, m, ArH); δ_C(75 MHz; $CDCl_3$) 21.19, 28.19, 28.26, 29.51, 42.51, 57.1, 77.8, 124.59, 126.11, 126.14, 127.72, 127.77, 129.1, 143.23 and 149.75; *m/z* (EI) 266 (M^+, 18.3), 248 ([M − H_2O]$^+$, 7.66), 144 (74), 133 (67), 120 (76), 105 (100) and 91 (28); (CI, NH_3) 284 ([M + NH_4]$^+$, 6.7), 266 (M^+, 7), 249 ([M − OH]$^+$, 100).

Similar treatment of 2-phenyl-2,7,7-trideuteriocycloheptanone yielded [$^2H_3$]-**7**; mp 57 °C (Found: C, 84.79; H, 8.36. Calc. for $C_{19}H_{19}D_3O$: C, 84.7; H, 8.23%). Mass spectrometric analysis (positive CI) gave incorporation: ^2H, 1.2 ± 0.1%, $^2H_2$ 6.6 ± 0.1% and $^2H_3$ 92.2 ± 0.1%).

trans-1,2-Diphenylcyclooctanol, 8

A solution of 2-phenylcyclooctanone (0.8 g, 4 mmol) in 20 ml of dry diethyl ether was added dropwise to a stirred phenyllithium solution (25 ml of a 0.8 M solution in diethyl ether). The mixture was allowed to stir and reflux overnight before quenching with saturated aqueous ammonium chloride. Extraction with diethyl ether, drying ($MgSO_4$) and evaporation yielded an oil, containing about 40% of unreacted ketone. The oil was heated under reflux for 2 h with Girard reagent 'T' (1.0 g in 9 ml of ethanol and 1 g of acetic acid) and the alcohol was then isolated by adding the mixture to water, neutralising with sodium carbonate and extracting with diethyl ether. Evaporation of the extracts and recrystallisation from light petroleum gave white crystals, 0.5 g (45%), mp 73–74 °C (lit.,[30] mp 73.5–74.5 °C) (Found: C, 85.8; H, 8.7. Calc. for $C_{20}H_{24}O$: C, 85.6; H, 8.6%); ν_{max}/cm^{-1} (NaCl) 3563, 3058, 2921, 2852, 1492, 1447, 1325, 1035 and 758 and 701; δ_H(200 MHz, $CDCl_3$) 1.5–2.1 (11H, m), 2.28 (1H, t, *J* 8.5, methylene), 2.58 (1H, m, methylene), 3.47 (1H, d, *J* 7.7, methine) and 6.9–7.37 (10H, m, ArH); δ_C(75 MHz, $CDCl_3$) 22.4, 24.9, 26.9, 30.26, 30.69, 38.4, 52.2, 78.2, 125.2, 125.8, 126.1, 127.67, 127.75, 129.5, 145 and 147.6; *m/z* (EI) 280 (M^+, 5), 262 ([M − H_2O]$^+$, 17.6), 158 (89), 133 (87), 120 (100), 105 (86) and 91; (CI, NH_3) 298 ([M + NH_4]$^+$, 7.6), 280 (M^+, 10), 263 ([M − OH]$^+$, 100).

Reaction of 2-phenyl-2,8,8-trideuteriocyclooctanone (0.82 g, 4 mmol) similarly yielded 0.5 g (50%) of pure alcohol, mp 73–74 °C (Found: C, 85; H, 8.4. Calc. for $C_{20}H_{21}D_3O$: C, 84.75; H, 8.48%). Mass spectrometric analysis (positive CI) gave incorporation: $^2H_1$ 0.9 ± 0.1%, $^2H_2$ 10.6 ± 0.1%, $^2H_3$ 87.3 ± 0.1%.

erythro- and *threo*-3,4-Diphenylhexan-3-ol, *erythro*- and *threo*-9

A mixture of propiophenone (4.02 g, 30 mmol) and 1-chloro-1-phenylpropane (5.56 g, 36 mmol) was added slowly to a solution of lithium naphthalenide (from lithium, 0.59 g and naphthalene, 10.88 g, in THF, 50 ml) maintaining 25 > *T* > 27 °C. Excess of lithium–naphthalene was then destroyed by the addition of a little methanol, before dilution with water, extraction with diethyl ether and drying (Na_2SO_4). Solvent evaporation and bulb-to-bulb distillation (95–105 °C, 0.2 mmHg) gave 7.5 g of a colourless oil, which GLC analysis showed to be 1:1 mixture of isomers. The isomers were separated by chromatography on silica (elution with 20% diethyl ether in light petroleum) to give the *threo*-isomer (28%) as a colourless oil, and the *erythro*-isomer (28%) as colourless crystals. The *erythro*-isomer was then recrystallised from light petroleum and its structure determined by X-ray crystallography.

For *threo*-3,4-diphenylhexan-3-ol; ν_{max}/cm^{-1} (NaCl) 3476, 3027, 2968, 1494, 1378 and 968; δ_H(200 MHz, $CDCl_3$) 7.1–7.4 (8H, m), 6.95 (2H, m), 2.85 (1H, dd, *J* 12 and 3.7), 1.73–2.15 (4H, m), 1.6 (1H, s) and 0.6–0.8 (6H, m); *m/z* (EI) 237 ([M − OH]$^+$, 90), 236 ([M − H_2O]$^+$, 26), 207 (29), 167 (36), 135 (100), 91 (23) and 57 (50); *m/z* (positive CI, NH_3) 272 ([M + NH_4]$^+$, 6), 255 ([M + 1]$^+$, 5), 254 (M^+, 25), 238 (28), 237 ([M − OH]$^+$, 100), 135 (8).

For *erythro*-3,4-diphenylhexan-3-ol: mp 61.5–63.5 °C; ν_{max}/cm^{-1} (NaCl) 3583, 3025, 2969, 1446, 1375 and 895; δ_H(200 MHz, $CDCl_3$) 7.23–7.49 (10H, m), 2.83 (1H, dd, *J* 12 and 3.4), 1.65–1.92 (2H, m), 1.63 (1H, s, OH), 1.25–1.47 (2H, m), 0.45–0.65 (6H, m); *m/z* (EI) 237 ([M − OH]$^+$, 84), 236 ([M − H_2O]$^+$, 41), 225 (35), 223 (23), 207 (54), 165 (47), 135 (100), 91 (22); *m/z* (positive CI, NH_3) 272 ([M + NH_4]$^+$, 5.5), 255 ([M + 1]$^+$, 5), 254 (M^+, 23), 237 ([M − OH]$^+$, 100) (Found: C, 84.75; H, 8.67. $C_{18}H_{22}O$ requires: C, 84.99; H, 8.72).

1,5-Diphenylpentan-1-one and 1,5-diphenylpentane

Low pressure hydrogenation of cinnamylideneacetophenone over 10% Pd/C yielded the ketone with properties in accord with literature data.[31]

Prolonged exposure to the hydrogenation conditions yielded a hydrocarbon: bp 100–105 °C (0.2 mmHg), and identified as 1,5-diphenylpentane; ν_{max}/cm^{-1} (NaCl) 3084, 2930, 2855, 1604, 1495, 1089, 906; δ_H($CDCl_3$) 7.15–7.38 (10H, m), 2.65 (4H, t, *J* 7.5), 1.7 (4H, quintet, *J* 7.5), 1.45 (2H, m); *m/z* (EI) 224 (M^+, 30), 133 (16), 117 ([Ph $(CH_2)_3$]$^+$, 6), 92 ([$PhCH_3$]$^+$, 100), 77 (9); *m/z* (positive CI, NH_3) 242 ([M + NH_4]$^+$, 100), 240 (4), 224 (M^+, 2.8), 108 (11), 91 (14).

4-Phenylbutyraldehyde, 5-phenylvaleraldehyde and 6-phenylhexanal

These were prepared from commercially available phenylalkanols by DMSO–oxalyl chloride oxidation.[32]

4-Phenylbutyraldehyde (95%), bp 70–75 °C (0.3 mmHg); ν_{max}/cm^{-1} (NaCl film) 3027, 2938, 1723, 1603, 1497, 1454, 749 and 700; δ_H(200 MHz, $CDCl_3$) 1.98 (2H, quintet, *J* 8), 2.47 (2H, dt, *J* 8 and 1.5), 2.65 (2H, t, *J* 8), 7.12–7.4 (5H, m) and 9.77 (1H, t, *J* 1.5); *m/z* (EI) 148 (M^+, 18), 105 ([$PhCH_2CH_2$]$^+$, 14), 104 ([$PhCH{=}CH_2$]$^+$, 100), 91 ([$PhCH_2$]$^+$, 73) and 78 (8); *m/z* (positive CI, NH_3) 166 ([M + NH_4]$^+$, 100), 148 (M^+, 20), 104 (100) and 91 (48).

5-Phenylvaleraldehyde (94%), colourless liquid, bp 75–80 °C (0.4 mmHg); ν_{max}/cm^{-1} (NaCl) 3027, 2936, 1724, 1497, 700 and 666; δ_H(200 MHz, $CDCl_3$) 9.77 (1H, t, *J* 1.5), 7.1–7.4 (5H, m), 2.65 (2H, m), 2.4 (2H, m) and 1.6–1.7 (4H, m); *m/z* (EI) 162 (M^+, 6), 160 ([M − 2]$^+$, 4), 104 (41) and 91 (100); *m/z* (positive CI, NH_3) 180 ([M + NH_4]$^+$, 100), 162 (M^+, 4), 160 ([M − 2]$^+$, 4) and 91 (7).

6-Phenylhexanal (95%), colourless oil, bp 80–85 °C (0.4 mmHg); ν_{max}/cm^{-1} (NaCl) 3062, 2934, 1724, 1604, 1497, 1454, 1030, 748 and 666; δ_H(200 MHz, $CDCl_3$) 9.9 (1H, t, *J* 1.5), 7.12–7.37 (5H, m), 2.65 (2H, t, *J* 7.5), 2.37 (2H, t, *J* 7.5), 1.57–1.70 (4H, m) and 1.34–1.50 (2H, m); *m/z* (EI) 176 (M^+, 16), 174 ([M − 2]$^+$, 5), 130 (60), 105 (21), 92 (32) and 91 (100); *m/z* (positive CI, NH_3) 194 ([M + NH_4]$^+$, 100), 176 (M^+, 18), 130 (20) and 91 (21).

1,6-Diphenylhex-2-en-1-one, 1,7-diphenylhept-2-en-1-one and 1,8-diphenyloct-2-en-1-one

These were prepared by reaction of the aldehydes with benzoyl methylene(triphenyl)phosphine[33] in refluxing toluene. Addition of light petroleum precipitated remaining Wittig reagent and triphenylphosphine oxide which were filtered and discarded. Remaining impurities of Wittig reagent and triphenylphosphine oxide were removed using a short column of alumina. Evaporation of solvent and bulb-to-bulb distillation yielded the ketones as colourless oils.

1,6-Diphenylhex-2-en-1-one (93%) had bp 100–105 °C (0.3 mmHg); ν_{max}/cm^{-1} (NaCl) 3026, 2929, 1670, 1449, 1339, 1244 and 748; δ_H(200 MHz, $CDCl_3$) 7.92 (2H, d, *J* 6.5), 7.4–7.6 (4H, m), 7.1–7.35 (6H, m), 2.7 (2H, t, *J* 7.5), 2.37 (2H, q, *J* 7.5), 1.88 (2H, quin, *J* 7.5); *m/z* (EI) 251 ($[M + 1]^+$, 5), 146 (38), 130 (48), 115 (42), 105 (96), 104 (57), 91 (100) and 77 (62); *m/z* (positive CI, NH_3) 268 ($[M + NH_4]^+$, 50), 251 ($[M + 1]^+$, 100), 146 (6.5), 130 (8), 105 (8), 104 (6.5), 91 (5) and 78 (8).

1,7-Diphenylhept-2-en-1-one (87%) had bp 130 °C (0.5 mmHg); ν_{max}/cm^{-1} (NaCl) 3026, 2932, 1671, 1496, 1449, 1283, 1223, 1128 and 748; δ_H($CDCl_3$) 7.95 (2H, m), 7.4–7.7 (3H, m), 7.05–7.38 (7H, m), 2.48–2.73 (4H, m) and 1.48–1.85 (4H, m); *m/z* (EI) 264 (M^+, 4.5), 144 (19), 117 (14), 105 (100), 91 (85) and 77 (59); *m/z* (positive CI, NH_3) 298 (22), 282 ($[M + NH_4]^+$, 28), 265 ($[M + 1]^+$, 100), 180 (27), 166 (22), 149 (20), 105 (29) and 91 (15).

1,8-Diphenyloct-2-en-1-one (80%) had bp 125–130 °C (0.4 mmHg); ν_{max}/cm^{-1} (NaCl) 3026, 2932, 1671, 1449, 1283 and 696; δ_H(200 MHz, $CDCl_3$) 7.95 (2H, m, ArH), 7.42–7.66 (3H, m, ArH), 7.1–7.35 (7H, m), 2.52–2.75 (4H, m), 1.53–1.80 (4H, m) and 1.35–1.52 (2H, m); *m/z* (EI) 278 (M^+, 2), 117 (13), 105 (75), 91 (100) and 77 (28); *m/z* (positive CI, NH_3) 296 ($[M + NH_4]^+$, 14), 295 (15), 279 ($[M + 1]^+$, 100), 277 (20), 157 (16), 105 (80) and 91 (38).

1,6-Diphenylhexan-1-one, 1,7-diphenylheptan-1-one, and 1,8-diphenyloctan-1-one

These were prepared by low pressure hydrogenation of the 1,*n*-diphenylalk-2-en-1-ones over 10% Pt/C in ethyl acetate solution. After uptake of one equivalent of hydrogen, the catalyst was separated by filtration through Celite, the filtrate was concentrated and chromatographed on silica (elution with 20% diethyl ether–light petroleum to give the ketones.

1,6-Diphenylhexan-1-one: bp 125–130 °C (0.3 mmHg); ν_{max}/cm^{-1} (NaCl) 3085, 2932, 1686, 1598, 1496, 1216 and 749; δ_H(200 MHz, $CDCl_3$) 7.98 (2H, d, *J* 7.5), 7.42–7.62 (3H, m), 7.13–7.35 (5H, m), 2.97 (2H, t, *J* 7), 2.65 (2H, t, *J* 8), 1.6–1.9 (4H, m) and 1.36–1.54 (2H, m); *m/z* (EI) 253 ($[M + 1]^+$, 17), 252 (M^+, 12), 133 (44), 130 (94), 120 (91), 105 (100) and 91 (37); *m/z* (negative CI, NH_3) 252 (M, 18), 251 ($[M - 1]^-$, 100), 121 (3), 119, (2), 91 (1.2) and 87 (3).

1,7-Diphenylheptan-1-one: bp 140 °C (0.3 mmHg); ν_{max}/cm^{-1} (NaCl) 3026, 2931, 1686, 1598, 1496, 1211 and 749; δ_H(200 MHz, $CDCl_3$) 7.96 (2H, d, *J* 7.5, ArH), 7.52 (3H, m, ArH), 7.13–7.38 (5H, m, ArH), 2.97 (2H, t, *J* 8), 2.64 (2H, t, *J* 7.5), 1.58–1.88 (4H, m) and 1.3–1.55 (4H, m); *m/z* (EI) 267 ($[M + 1]^+$, 14), 266 (M^+, 15), 144 (66), 133 (42), 120 (91), 105 (100), 91 (32); *m/z* (positive CI, NH_3) 267 ($[M + 1]^+$, 100), 120 (24) and 105 (38); *m/z* (negative CI, BuONO) 265 ($[M - 1]^-$, 100), 263 (3.5) and 177 (1.5).

1,8-Diphenyloctan-1-one: bp 150 °C (0.3 mmHg), mp 46–47 °C; ν_{max}/cm^{-1} (NaCl) 3026, 2921, 1449, 1367, 1073 and 909; δ_H(200 MHz, $CDCl_3$) 7.97 (2H, d, *J* 7.5), 7.42–7.62 (3H, m), 7.13–7.35 (5H, m), 2.97 (2H, t, *J* 7.5), 2.6 (2H, t, *J* 7.5), 1.55–1.85 (4H, m), 1.28–1.48 (6H, m); *m/z* (EI) 281 ($[M + 1]^+$, 10), 280 (M^+, 4), 158 (80), 133 (48), 120 (97), 105 (100), 91 (43); *m/z* (negative CI, BuONO) 280 (M^+, 20), 279 ($[M - 1]^-$, 100).

Rate measurements

DMSO and 1,3-diaminopropane were purified, and solutions of their anions were prepared by the method of Arnett *et al.*,[18] stored under argon on a gas line, and transferred gas tight by syringe. The reaction vessel was a cylindrical glass flask fitted with a thermostatically controlled water jacket, and linked directly to a high vacuum manifold. About 15 mg of each alcohol together with 10 mg of 1,5-diphenylpentane or dibenzyl ether (internal standards) were weighed accurately and placed in the reaction vessel. A small crystal of triphenylmethane was also added. The apparatus was evacuated, and the vacuum then released to argon. Dry DMSO or 1,3-diaminopropane (5 ml) was injected. After *ca.* 30 min, a solution of metal dimsyl or metal diaminopropanamide (0.2 ml of 0.2 M) was injected as quickly as possible into the stirring alcohol solution using a gas tight 5 ml syringe to initiate reaction. Portions of the reacting mixture (0.2 ml) were syringed out at appropriate time intervals, quenched in 1 ml of cold 0.2 M HCl solution, and organic material was extracted into 1 ml of distilled light petroleum 40–60 for analysis by GLC. Ratios of the substrate peak areas to internal standard peak area (Y) and reaction time (X) were fitted to an equation of the form: $Y = A_1 \exp [A_2(-X)]$ where A_1 = initial value of Y, and A_2 = rate constant using a non-linear least square fitting process (PASSAGE f.00). The values of A_1 and A_2 were allowed to vary in obtaining the best fit, and values of A_1 thus obtained agreed with measured values within experimental uncertainty in all cases.

Isotopic labelling studies

The apparatus and the conditions were those used for rate measurements. About 50 mg of deuteriated alcohol was placed in the apparatus and dissolved in DMSO or DAP as before. A control sample was syringed out and quenched with 2 ml of HCl (2% solution) before initiation of reaction by addition of base. Further samples were then taken after two and ten half-lives and quenched, and extracted and dried as before. Ketonic product was isolated by bulb-to-bulb distillation, dissolved in 20 ml of dry dioxane, then refluxed with a solution of potassium carbonate (0.5 g) in distilled water (10 ml). Diethyl ether extraction as before yielded samples for analysis by GC–MS to measure content deuterium and site of the residual deuterium.

Kinetic isotope effect measurements

The apparatus was the same as for rate measurements described above, and a *ca.* 1:1 mixture of deuteriated and non-deuteriated 1,2-diphenylcycloalkanols (50 mg) was placed in the reaction vessel, together with the internal reference. Three to five samples (1 ml each) were syringed out at time intervals from the beginning of the reaction until the third half-life, quenched in 3 ml of cold 0.2 M HCl solution, organic materials extracted with diethyl ether (5 ml), and washed with 3% aqueous NaCl (3 ml) and dried ($MgSO_4$). The samples, together with a control sample taken before addition of the base, were analysed by capillary GLC using a 5 m × 0.22 mm OV1 column. Analysis of deuterium content of the remaining substrates was performed by GC–MS using positive CI mass spectral data. More than ten scans were normally taken for each sample at relatively high and consistent ion current for the *m/z* region of interest. Kinetic isotope effects were calculated using relationships described in the main text. For the cyclooctanol, [$^2H_3$]-**8**, reacting in dimsylsodium at 20 °C values of k_{H_3}/k_{D_3} obtained were 1.42 (α = 0.380), 1.49 (α = 0.260), 1.50 (α = 0.125), 1.46 (α = 0.037) and 1.30 (α = 0.022); for the cycloheptanol, [$^2H_3$]-**7**, reacting in dimsylsodium at 40 °C, values were 1.34 (α = 0.54), 1.44 (α = 0.158), 1.32 (α = 0.003); for the cyclopentanol, [$^2H_3$]-**5**, reacting in dimsylpotassium at 50 °C, values were 2.41 (α = 0.478), 2.50 (α = 0.240) and 2.50 (α = 0.009).

X-Ray structure determinations

Details of crystal data and of the measurements and solution are in Tables 5 and 6. Measurements were made on a Rigaku

Table 5 Crystal data for *trans*-1,2-diphenylcycloalkanols, and *erythro*-3,4-diphenylhexan-3-ol

Parameter	Cyclopentanol, **5**	Cyclohexanol, **6**	Cycloheptanol, **7**	Cyclooctanol, **8**	Hexanol, **9**
Empirical formula	$C_{17}H_{18}O$	$C_{18}H_{20}O$	$C_{19}H_{22}O$	$C_{20}H_{24}O$	$C_9H_{11}O_{0.5}$
Formula mass	238.33	252.36	266.38	280.41	127.19
Crystal colour and habit	Colourless, acicular	Colourless tabular	Colourless prisms	Colourless prismatic	Colourless prismatic
Crystal dimensions/mm	0.5 × 0.12 × 0.50	0.07 × 0.25 × 0.25	0.4 × 0.45 × 0.50	0.30 × 0.60 × 0.60	0.23 × 0.25 × 0.30
Crystal system	monoclinic	monoclinic	triclinic	monoclinic	monoclinic
Number of reflections for unit cell determination (2θ range)	25 (29.3 − 36.6°)	25 (1.26 + 0.3 tan θ)	25 (29.3 − 34.9°)	25 (29.3 − 34.9°)	24 (76.9 − 79.8°)
ω-Scan peak width half height	0.03	0.29	0.25	0.22	0.22
Lattice parameters					
a/Å	9.184(2)	13.563(2)	11.779(3)	8.124(2)	8.0343(8)
b/Å	20.528(6)	5.932(2)	11.984(6)	21.632(4)	8.9286(4)
c/Å	7.856(3)	18.380(3)	11.393(1)	9.906(3)	11.0351(6)
α/°			95.60(4)		
β/°	114.65(2)	107.28(2)	106.71(2)	111.32(2)	106.983(6)
γ/°			93.89(3)		
V/Å^3	1346(2)	15411.9(6)	1525(1)	1622(1)	761.67(9)
Space group	*Pc* (No. 7)	$P2_1/n$ (No. 14)	$P\bar{1}$ (No. 2)	$P2_1/c$ (No. 14)	$P2_1/c$ (No. 14)
Z	4	4	4	4	4
D_c/g cm^{-3}	1.176	1.187	1.160	1.148	1.109
F_{000}	512	544	576	608	276
μ/cm^{-1}	5.16 (Cu-Kα)	5.16 (Cu-Kα)	5.00 (Cu-Kα)	4.91 (Cu-Kα)	4.78 (Cu-Kα)

Table 6 Intensity measurements, solution and refinement of crystal structures of *trans*-1,2-diphenylcycloalkanols, and *erythro*-3,4-diphenylhexan-3-ol

Parameter	Cyclopentanol, **5**	Cyclohexanol, **6**	Cycloheptanol, **7**	Cyclooctanol, **8**	Hexanol, **9**
Scan width/°	(1.31 + 0.30 tan θ)	(1.26 + 0.30 tan θ)	(1.31 + 0.30 tan θ)	(1.57 + 0.30 tan θ)	(1.47 + 0.30 tan θ)
Scan rate/° min^{-1}	16.0 (in ω), 2 rescans	8 (in ω), 3 rescans	32.0 (in ω), 2 rescans	32.0 (in ω), 2 rescans	32.0 (in ω), 2 rescans
Number of reflections					
Total	2242	2445	4799	2691	1305
Unique	2233 (R_{int} = 0.032)	2346 (R_{int} = 0.108)	4541 (R_{int} = 0.077)	2491 (R_{int} = 0.081)	
Ranges of					
h	−10 to 9	0 to 21	−5 to −13	0 to 9	0 to 9
k	−23 to 0	0 to 34	−13 to 13	0 to 24	0 to 10
l	0 to 8	0 to 10	−12 to 12	−11 to 10	−12 to 11
Corrections					
Trans. factors	0.69−1.13	0.78−1.00	0.81−1.07	0.93−1.13	0.69−1.33
Decay	0.50%	8.50%	3.6%	3.38%	1.67%
p-Factor	0.03	0.03	0.03	0.02	0.03
No. observations [$I > 3.00\sigma(I)$]	1556	1564	3346	2859	1004
No. variables	323	182	361	334	91
Reflection/parameter	4.82	8.59	19.27	8.56	11.03
Residuals R, R_w	0.052, 0.060	0.055, 0.070	0.070, 0.089	0.064, 0.078	0.076, 0.119
Goodness of fit indicator	1.91	2.58	3.18	3.34	4.67
Max shift in final cycle	<0.05	<0.05	<0.04	<0.01	<0.01
Max/min peaks in final difference map/e Å^{-3}	0.22 and 0.16	0.20 and −0.15	0.73 and −0.22	0.49 and −0.19	0.28 and −0.16

AFC5R X-ray diffractometer with graphite-monochromated Cu-Kα (λ 1.541 78 Å) radiation. Attenuators were Zr foil (factors 3.6, 12.2, 44.0). The data were collected at a temperature of 20 ± 1 °C using the $\omega/2\theta$ scanning technique to a maximum 2θ value of 120.1°. ω Scans of several intense reflections, made prior to data collection, had an average width at half-height of 0.22° with a take-off angle of 6°. The weak reflections [$I < 10\sigma(I)$] were rescanned and the counts were accumulated to assure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 0.5 mm and the crystal to detector distance was 400 mm utilising a continuously evacuated beam tunnel to reduce absorption by air. The intensities of three representative reflections were measured after every 150 reflections, and a linear correction factor was applied to the data to compensate small observed decays. Empirical absorption corrections, using the program DIFABS,[34] were applied resulting in the tabulated transmission factors. Data were corrected for Lorentz-polarisation effects and absorption, and the structure was solved by direct methods.[35] Hydrogen atoms were placed in calculated positions (C−H = 0.95 Å) or located in difference Fourier transforms. The refinement was by full-matrix least-squares minimisation of $w(F_o - F_c)^2$, with $w = 4F_o^2/\sigma^2(F_o)^2$. Non-hydrogen atoms were refined anisotropically; hydrogen atoms were assigned isotropic thermal parameters 20% greater than the equivalent B value of the atom to which they were bonded. Atomic scattering factors were calculated according to Cromer and Waber.[36] Anomalous dispersion effects were included in F_c.[37] All calculations were carried out on a VAXstation 3520 with the TEXSAN package.[38] Molecular diagrams were obtained with ORTEP[39] or with PLUTO.[40] In the final cycle of full-matrix least-squares refinement, the weighting scheme was based on counting statistics and included a factor (p) to downweight the intense reflections. Plots of $\Sigma w(|F_o| - |F_c|)^2$ *versus* $|F_o|$, reflection order in data

collection, sin θ/λ, and various classes of indices showed no unusual trends. Crystal data and further details of the measurements and solution are tabulated.

Fractional coordinates, bond lengths and angles, torsion angles for non-hydrogen atoms and other relevant structural and experimental details have been deposited at the Cambridge Crystallographic Data Centre.†

Empirical forcefield calculations

The molecular modelling package was MACROMODEL 4.5,[11] running on a Silicon Graphics 4D 240 GTX work station. The MM3* forcefield of Allinger *et al.*[10] was used for calculations with no modification of parameters.

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† For details of the CCDC deposition scheme see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 2*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 188/72.

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