Rapid Intramolecular 1,4-Hydride Transfers in Rigid Boat-conformation 4-Hydroxycyclohexanones

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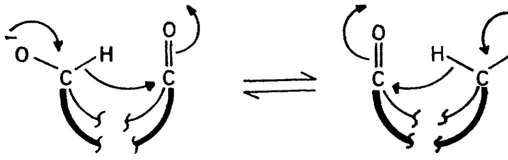
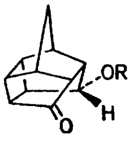
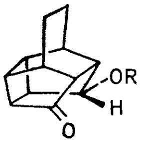
Summary The ketols (**1a**)—(**3a**), have been prepared and barriers for degenerate rearrangement, by intramolecular hydride transfer, in the derived sodium alkoxides, (**1b**)—(**3b**) have been determined from their temperature dependent ^{13}C n.m.r. spectra.

Barriers for intramolecular hydride transfer from an alkoxide group to a carbonyl carbon atom (Figure) appear to parallel those for hydride transfer in carbocations. Shifts occur readily when the reacting carbon termini are 1,5- in seven-, eight-, or larger-membered rings,[1] reflecting, presumably, the small energies required for these rings to adopt favourable conformations. When the termini are 1,4-with respect to six-membered rings, shifts have only been observed in molecules in which the usually preferred chair conformation is destabilized by other structural features.[2]



Figure


(1)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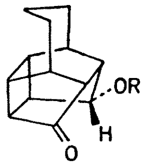
(3)

a; R = H
b; R = Na

The ketols (**1a**)—(**3a**) all contain 4-hydroxycyclohexanones held in rigid boat conformations by cage structures. Cookson[3] has pointed out that increasing the length of the methylene bridge in this series forces the reacting centres together, and this can be seen in the structure of the ketols (Table), calculated by an empirical force field (EFF) method.[4] Increasing interaction of the alcohol and carbonyl groups is also reflected in the changes in the contribution from the C · · C and C · · H non-bonded repulsions to the steric energy. We have examined the effect of these quite subtle changes on the rates of hydride transfer.

Compounds (**1a**)—(**3a**) were prepared from the diene–*p*-benzoquinone Diels–Alder adducts[5] (Scheme). The required *exo*-configuration at the hydroxy group was achieved by Dibal reduction of the ene-diones[6] prior to sensitized photocyclisation and semi-oxidation. The salts were generated by treatment of $(CD_3)_2SO$ solutions of the ketols with 1 equiv. of CD_3SOCD_2Na,[7] and were examined by ^{13}C n.m.r. spectroscopy. Hydride transfers in these salts would be degenerate, leading to exchange of five carbon sites in (**1b**), and six in both (**2b**) and (**3b**).†

Table. Details of the calculated structures of the ketols (**1a**)—(**3a**)

	Angles/°			Distances/Å		$E_{\text{non-bond}}$/kcal mol^{-1}	
Structure	O(1)–C(1)–H	O(2)–C(2)–H	C(1)–H–C(2)	C(1) · · C(2)	H · · C(2)	C(1) · · C(2)	H ·C · (2)
(**1a**)	101·8	99·84	82·9	2·613	2·510	0·66	0·87
(**2a**)	98·1	97·13	84·4	2·555	2·416	0·91	1·38
(**3a**)	102·1	93·89	82·5	2·516	2·410	1·12	1·44

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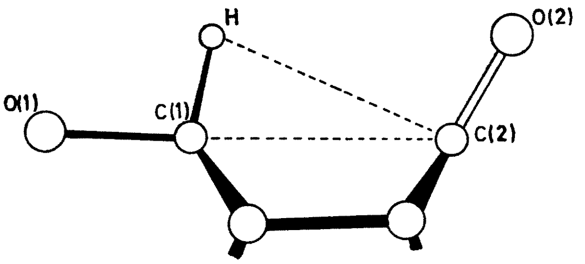
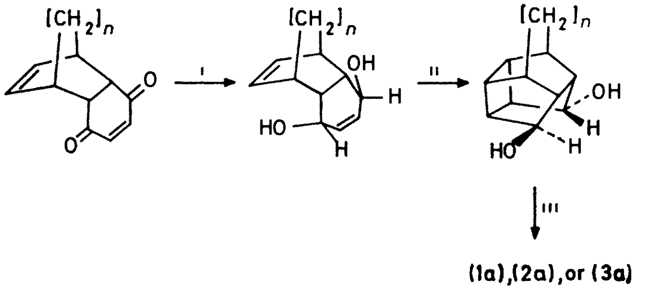
† The ketols (**1a**)—(**3a**) were all sharp-melting crystalline solids with the expected analytical and spectral properties.



The spectrum (20·1 MHz) of (**2b**) shows peaks at δ 19·0 and 17·7 which are triplets in the off-resonance decoupled spectrum and are securely assigned to methylene bridge carbons These signals coalesce at 373 ± 3 °C, giving $\Delta G^{\ddagger}_{373}$ 19·0 ± 0·3 kcal mol^{-1} for the exchange[8] Similarly, methylene signals at δ 29 3 and 31·0 in the spectrum of (**3b**) coalesce at 345 ± 3 °C, giving $\Delta G^{\ddagger}_{345}$ 17·3 ± 0 2 kcal mol^{-1}, and a third methylene signal at δ 24·9, assigned to the central non-exchanging methylene group, remains sharp Other temperature dependent changes occur at lower field in these spectra, but, since coalescing pairs overlap and are partially obscured by solvent, coalescence temperatures are difficult to obtain The changes are reversible, provided the samples are not heated at over 95 °C‡ for prolonged periods, and the ketols were recovered unchanged§ in over 80% yield from the solutions after quenching with water



SCHEME $n = 1$, 2, or 3 Reagents i Bu^i_2AlH–toluene, ii, *h*ν, acetone, iii, CrO_3–acetone

We therefore associate the barriers for exchange with the degenerate hydride transfer

The spectrum of (**1b**) showed no coalescences below 100 °C, but, from the small line broadening,¶ (<0·5 Hz) it was possible to set a lower limit of $\Delta G^{\ddagger}_{373} \geqslant 21{\cdot}7$ kcal mol^{-1} We can estimate, therefore, that (**3b**) rearranges $10^{0\,7}$ times faster than (**2b**) which in turn, rearranges at least 10^2 times faster than (**1b**) The barriers for 1,4-hydride transfers in both (**2b**) and (**3b**), are less than that found for a 1,5-shift across an eight-membered ring in the sodium salt of *exo*-7-hydroxybicyclo[3 3.1]nonan-3-one[1] These results demonstrate a sensitivity of the rearrangements to exact molecular geometry, consistent with the large negative activation volumes found in intermolecular transfers[9] The increasing non-bonded interactions between the functional groups in the series (**1**)—(**3**) could be viewed as arising from progress towards the transition state, and, since most progress has been made in the ground state of (**3**), the remaining energy required to reach the transition state is least

Since the shifts involve formal expulsion of hydride from alkoxide and addition of hydride to carbonyl, the potential energy hypersurface for the rearrangement should be related to that for the interaction of hydride with an isolated carbonyl group In principle then, the variation of barrier with ground state molecular geometry could be used to map the hydride + carbonyl reaction pathway[10] In practice, this would require accurate molecular structures for the salts since these could differ in important respects from the calculated alcohol structures Simple application of the force field method does not allow adequately for crucial ground state distortions along the reaction coordinate[11] The salts (**1b**)—(**3b**) crystallize well from the Me_2SO solutions and we hope to describe their crystal structures at a later date

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‡ After 18 h at 100 °C there was partial quenching of the alkoxide presumably caused by Me_2SO decomposition products

§ Mass spectral analysis showed no deuterium incorporation

¶ $k = \pi(w - w_0)$ in the slow exchange limit Widths in the absence of exchange were taken from the non exchanging central methylene signal

[1] R S Henry, F G Riddell W Parker, and C I F Watt, *J C S Perkin II*, 1976 1549, and references therein

[2] E W Warnhoff, *Canad J Chem* , 1977, **55**, 1635, I Watt, *Tetrahedron Letters*, 1978, 4175

[3] R C Cookson, E Crundwell, R R Hill, and J Hudec, *J Chem Soc* , 1964, 3062 For a recent investigation of transannular reactions in this series see P Singh, *J Org Chem* , 1979, **44**, 842

[4] For the EFF calculations we have used Allinger's 1971 force field N L Allinger, M T Tribble, M A Miller, and D H Wertz, *J Amer Chem Soc* , 1971, **93**, 1637

[5] For cyclopentadiene and cyclohexadiene adducts see O Diels, J H Blom and W Koll *Annalen* 1925 **443** 247 and O Diels and K Alder, *Chem Ber* , 1929 **62**, 2337 The cycloaddition of cycloheptadiene required boron trifluoride etherate catalysis

[6] K E Wilson, R T Seidner, and S Masamune, *Chem Comm* , 1970, 213

[7] E J Corey and M Chakovsky, *J Amer Chem Soc* 1965, **87**, 1345

[8] $\Delta G^{\ddagger}(T_c) = RT_c[22\ 96 + \ln(T_c/\delta\nu)]$, J A Pople H J Bernstein and W G Schneider 'High Resolution N M R Spectroscopy,' McGraw-Hill, New York, 1959, ch 10 The quoted errors in T_c reflect the high signal to noise ratio in these spectra Solutions of greater than 0 8 M concentration could not be prepared, owing to the low solubility of the salts

[9] K R Brower and D H Hughes, *J Amer Chem Soc* , 1978, **100**, 7591

[10] H B Burgi, J D Dunitz, J M Lehn and G Wipff *Tetrahedron*, 1974, **30**, 1563

[11] H B Burgi, J D Dunitz, and E Shefter, *J Amer Chem Soc* , 1973, **95**, 5065, H B Burgi, *Angew Chem Internat Edn* , 1975, **14**, 460, P Murray-Rust, H B Burgi, and J D Dunitz, *J Amer Chem Soc* , 1975, **97**, 921