Barriers to Intramolecular Hydride Transfers in Some Polycyclic Hydroxyketones

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The hydroxyketones (1) and (2) have been prepared from the Diels–Alder adducts of p-benzoquinone with cyclopentadiene and cyclohexa-1,3-diene. The boron trifluoride-ether catalysed reaction of cyclohepta-1,3-diene with p-benzoquinone gave good yields of the Diels–Alder adduct which was converted into hydroxyketone (3). Experiments with cyclohexanol and adamant-2-ol established characteristic $^{13}$C n.m.r. chemical shifts associated with deprotonation of alcohols by dimethyl sodium in dimethyl sulphoxide. Solutions of the sodium salts of (1)-(3) were prepared and dynamic $^{13}$C n.m.r. spectroscopy gave barriers for their degenerate rearrangement of >21.7 (100 °C), 19.0 (100 °C), and 17.3 (72 °C) kcal mol$^{-1}$, respectively. The relationship between variation of barrier and molecular geometry is discussed with the aid of empirical force field calculations.

The literature contains a number of examples of rearrangement of compounds containing both carbonyl and primary or secondary alcohol groups in which these functionalities are apparently interchanged on treatment with acid or base.$^{1,10}$ Enediol or enediolate intermediates have been implicated in the rearrangement of α-hydroxyketones (acyloins)$^{11}$ but, with more widely separated groups, the available evidence is consistent with intramolecular transfer of hydride from the alcohol to carbonyl carbon. Indeed the base-induced process may be regarded as an intramolecular variant of the familiar Meerwein–Ponndorf–Verley–Oppenauer redox couple$^{12}$ (see Figure 1). In most cases, an alternative mechanism involving homoenolization$^{13}$ to a 1,2-diol and subsequent reketonization is excluded by the observation that the alcohol methine hydrogen does not exchange with solvent or other proton source.

Examples of 1,4-, 1,5-, and 1,6-hydride transfers$^{10}$ of this type have been described. Generally, the reactions occur under mild conditions, giving high isolated yields of the rearranged products. In this respect, at least, these rearrangements differ from hydride transfer in carbocationic species, where the long-range shifts must compete with 1,2-hydride shifts and Wagner–Meerwein rearrangements.$^{14}$ In as much as carbonyl may be regarded as a stabilized carbocation, these reactions offer an attractively clean reacting system in which to examine the steric requirements for hydride migration.

We note also that the base-induced process combines both extremes of the reaction path for interaction of hydride with carbonyl carbon.$^{15}$ In contrast to the vast body of experimental data (dynamic and static)$^{16}$ which has been accumulated for other nucleophiles, hydride, the simplest nucleophile, has been investigated only by computational methods.$^{17}$ The obstacle to experimental investigation lies in the placement of hydride, or potential hydride, in a well defined stereochemical relationship to the accepting carbonyl. This rearrangement overcomes the obstacle, and the variation of the barrier for hydride transfer with molecular geometry could, in principle, afford an experimental mapping of the hydride pathway. Such an investigation would require incorporation of the carbonyl and alkoxide groups into a variety of stereochemical relationships, accurate determination of molecular geometry, and measurement of barriers for the hydride transfer, in each case.

![Figure 1](https://example.com/fig1.png) Homoenolization and hydride-transfer mechanisms for base-catalysed rearrangement of 1,α-hydroxyketones
In only two of the examples cited are kinetic measurements available. Lansbury and Saeva have reported rates for the t-butoxide induced isomerization of 1-chloro-7-hydroxypleiadene-12(7H)-one (see Figure 2) in dimethyl sulphoxide solution. This hydroxyketone however, exists as its internal hemiacetal, and since the hemiacetal hydroxy-group is more acidic than a simple secondary alcohol,19 it is possible that the rates are those of interconversion of the isomeric hemiacetal salts rather than the hydroxyketones.

Henry et al.,5 have determined a barrier of 19.4 kcal mol \(^{-1}\) for the degenerate rearrangement of the sodium salt of exo-7-hydroxybicyclo[3.3.1]nonan-3-one, also in dimethyl sulphoxide. In contrast with the pleiadene derivative, the structural features of this substrate preclude internal hemiacetal formation, and the measured barrier can be associated with the hydride transfer process. The crystal structures of exo-7-hydroxybicyclo[3.3.1]nonan-3-one and its derived methyl ether have recently been reported.20

In this paper we describe the preparation and rearrangement, by intramolecular hydride transfer, of the homologous hydroxyketones (1)–(3).21 In these substrates the reacting sites have been incorporated into rigid cage structures. Reacting conformations should be well defined, and the structures also exclude the possibility of internal hemiacetal formation as well as other unwelcome complications such as elimination of water, enolate formation, or retro-aldol cleavage under the strongly basic conditions necessary for alkoxide formation. Following the example of Henry et al.,8 we have chosen to examine degenerate rearrangements. In the long term, the resulting symmetrical reaction coordinate should allow some simplifying assumptions in the interpretation of the expected structure-reactivity relationships. Our unsystematic numbering of the structures (1)–(3) emphasises the symmetry of the process: primed and unprimed sites should exchange, and starred sites should be unaffected by hydride transfer.

RESULTS

Synthesis of the Hydroxyketones.—The main features of the preparation of hydroxyketone (1) are shown in the Scheme. The sequence starts from (4; \(n = 1\)), the Diels–Alder adduct of cyclopentadiene and \(p\)-benzoquinone.22 Cookson et al.23 have described the photocyclization of this adduct to the cage diene, (5; \(n = 1\)), and have also described the sodium borohydride reduction of (5; \(n = 1\)) to a hydroxyketone (6), which differs from (1) only in stereochemistry at the alcohol function at C-3'. The stereochemistry of the alcohol in (6) is well established since its spectroscopic properties show that, in CDCl\(_3\) solution at least, it exists in equilibrium with its internal hemiacetal.24 The course of the borohydride reduction can be rationalised in terms of delivery of hydride from the less hindered outside face of the cage diene. Introduction of hydride into the more congested position in (3) is the main point of synthetic interest, and, to achieve this we have reversed the manipulative sequence of closure and reduction.

Masamune et al.25 have described the reduction of the adduct, (4; \(n = 1\)), to a dienediol with di-isobutylaluminium hydride. The \(^{13}\)C n.m.r. spectrum of this diol shows only six lines, confirming that it has a plane of symmetry through C-6*. The spectroscopic data do not indicate clearly whether the symmetrical diol has bis-endo- or bis-exo-hydroxy-groups, but the indicated structure (7; \(n = 1\)), would be expected on the basis of delivery of hydride from the less hindered exo-face of the enedione function, and the following transformations confirm this.

Acetone-sensitized photoclosure of (7; \(n = 1\)) yielded a cage diol (8; \(n = 1\)), isomeric with the product of lithium aluminium hydride reduction of the cage diene (5; \(n = 1\)).26 The symmetry of (8; \(n = 1\)) was evident from its \(^{13}\)C n.m.r. spectrum which again showed only six lines. Careful oxidation of this diol with Jones reagent gave a hydroxyketone (1) not identical (i.r., n.m.r., and m.s. comparison) with Cookson’s hydroxyketone (6) and showing no evidence of internal hemiacetal formation. That (1) and (6) differ only in stereochemistry at the alcohol group was demonstrated by their oxidation to the same dione (5; \(n = 1\)).

The \(^1\)H n.m.r. spectrum of (1) shows a two-proton AB pattern, centred at \(\delta\ 1.78\), arising from the \(6^*\)-methylene, and a sharp one-proton singlet (\(J_{\text{HH}}\ ca.\ 3.0\ Hz\) at \(\delta\ 4.08\)

![Figure 2](image-url)
associated with the alcohol methine hydrogen. The narrowness of this signal is consistent with the torsional angles (ca. 80° from Dreiding models) to hydrogens at the adjacent C-2' and -4' positions. The epimer, the dihedral angles are 40–45° (again from Dreiding models) and larger couplings are expected. The remainder of the proton spectra of (1) and (6), while consistent with the structures, is not well resolved (at 300 MHz) and, since

![Diagram](image)

Scheme Reagents: i, hv; ii, Bu₃AlH; iii, NaBH₄; iv, hv, sensitized; v, CrO₃ H⁺

the alcohol methine hydrogen does not participate in any W-type arrangements with other hydrogens, so that long-range couplings are not expected. In contrast, the proton spectrum of (6) shows distinct triplets at δ 4.0 (J 4.1 Hz) and 4.55 (J 6.0 Hz) arising from the alcohol and ethereal methine hydrogens in the two tautomeric forms. In this determination of the barriers by dynamic n.m.r. methods requires well resolved spectra, we have examined the ¹³C n.m.r. spectrum of (1).

The spectrum of (1) shows the expected eleven lines (see Table 1). Those at δ 219.1 and 74.5 p.p.m. can be reliably assigned to carbonyl (C-3) and alcohol (C-3') carbons
respectively on the basis of their chemical shifts. For the remainder of the signals, arising from the hydrocarbon part of the cage, such assignment is not possible. Additivity relationships are not applicable in this strained situation, and comparisons with spectra of symmetrical diene \((5; n = 1)\), and diol \((7; n = 1)\), have not proved helpful. However, with off-resonance decoupling, all the high-field signals are doublets except for that at \(37.5\) p.p.m., which is a clear triplet and can therefore be assigned to the methylene \((C-6^\#)\). Acetylation of \((1)\) induces the expected downfield shift in the \(C-3^\#\) signal and upfield shifts of 2.7 and 2.4 p.p.m., in the signals at \(54.1\) and \(44.4\) p.p.m., respectively. All other hydrocarbon signals move by less than 0.5 p.p.m. The two signals strongly shielded by acetylation can be assigned to carbons adjacent to the \(n\)-catalyzed, with properties in agreement with those reported by Barborak. This adduct requires careful manipulation as it forms a stable hydrate on exposure to aqueous acid or on chromatography on silica. The spectral properties of the hydrate are consistent with the indicated structure \((9)\), but we have not attempted to determine the stereochemistry of the oxygen bridge. As with \((1)\) and \((2)\) the sequence of reduction, photolysis, and semi-oxidation gave a hydroxyketone \((3)\), with spectral and analytical properties consistent with the structure, and oxidation of \((3)\) gave the same cage diene \((5; n = 2)\), as that formed on photocyclization \((2)\) of the original adduct \((4; n = 3)\).

The \(^{13}C\) n.m.r. spectra of \((2)\) and \((3)\) are fully resolved and the data for \((2)\) and \((3)\) and their acetates are included in Table 1. Again, chemical shifts can be assigned to carbonyl and alcohol carbon signals, and multiplicity allow identification of the methylene derived signals, \(C-6^*\) and \(-7^*\) in \((3)\). Acetylation-induced shifts allow assignment of the signals arising from carbons \((C-2^*\) and \(-4^*\) or \(-C^*\) and \(-2^*\)) adjacent to the alcohol.

In all the hydroxyketones \((1)-(3)\) the signals for \(C-1, -1', -2, -4, -5, -6', -7, -9\) and \(-10\) are fully resolved and \(C-1, -1', -2, -4, -5, -6', -7, -9\) and \(-10\) are not firmly assigned. Since the structures of \((1)-(3)\) are supported by chemical correlations, and do not depend crucially on these assignments, no further detailed experiments have been undertaken to establish assignments. However, the degenerate hydride-transfer exchanges live sites in \((1)\) and \((2)\) and \((3)\), and dynamic n.m.r. experiments on the salts were expected to aid in the assignments besides providing barriers for the rearrangements.

**Preparation of Alkoxides and Kinetic Experiments.**—As our interest in these rearrangements centres on the barrier for the hydride transfer in the alkoxides, we have chosen to use dimethyl sulphoxide as solvent and dimethyl sodium \(^{23}\) as base. The reported \(pK_a\) values for \(pK_a\) of secondary alcohols \((pK_a 27-29)\) in dimethyl sulphoxide \((pK_a ca. 33)\) are such that it should be possible to generate the salts quantitatively by treatment of solutions of the alcohols with stoichiometric amounts of the base. The measured barriers would then have no contribution arising from pre-hydride-transfer prototropic equilibrium.

To our knowledge, \(^{13}C\) n.m.r. spectra of alkoxide salts have not been studied before, and, since the spectra of \((1)-(3)\) are not fully assigned, we have examined the effects of ionization on chemical shifts in two simple alcohols for which assignments are available.

Comparison of the \(^{13}C\) n.m.r. spectra of cyclohexanol in deuteriochloroform and in \([\text{D}_2]\)DMSO \(^{24}\) showed that there are only small chemical shift changes associated with the change of solvent. \([\text{D}_2]\)DMSO solutions were then pre-

<table>
<thead>
<tr>
<th>Substrate (solvent)</th>
<th>C-3</th>
<th>C-3'</th>
<th>C-2' + -4'</th>
<th>C-1, -1', -2, -4, -5, and -6'</th>
<th>C-6 - 6' - 7'</th>
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<tbody>
<tr>
<td>((1)-\text{H(DCl)})</td>
<td>219.1</td>
<td>74.5</td>
<td>54.1; 44.4</td>
<td>51.0; 46.5; 43.5; 42.7; 41.9; 36.6</td>
<td>37.5</td>
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<tr>
<td>((2)-\text{H(DCl)})</td>
<td>216.7</td>
<td>77.4</td>
<td>51.4; 42.0</td>
<td>51.1; 47.0; 43.4; 42.8; 42.0; 36.6</td>
<td>37.6</td>
</tr>
<tr>
<td>((1)-\text{H(DMSO)})</td>
<td>217.7</td>
<td>73.0</td>
<td>53.6; 43.9</td>
<td>50.4; 46.2; 42.9; 42.5; 41.2; 35.9</td>
<td>36.9</td>
</tr>
<tr>
<td>((2)-\text{Na}(\text{DMSO}))</td>
<td>219.5</td>
<td>77.3</td>
<td>58.4; 48.1</td>
<td>50.8; 46.3; 43.2; 42.5; 41.5; 35.8</td>
<td>36.7</td>
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<tr>
<td>((3)-\text{Na}(\text{DMSO}))</td>
<td>218.6</td>
<td>74.8</td>
<td>48.0; 43.3</td>
<td>47.7; 45.0; 37.4; 32.7; 32.1; 31.6</td>
<td>32.2</td>
</tr>
<tr>
<td>((4)-\text{Ac(CDCl)})</td>
<td>215.8</td>
<td>77.0</td>
<td>43.2; 42.7</td>
<td>47.5; 45.1; 37.4; 32.8; 32.3; 31.7</td>
<td>31.6</td>
</tr>
<tr>
<td>((5)-\text{Ac(CDCl)})</td>
<td>216.7</td>
<td>73.0</td>
<td>44.9; 44.5</td>
<td>47.1; 44.3; 36.9; 32.0; 31.5; 31.1</td>
<td>31.6</td>
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<tr>
<td>((6)-\text{Na}(\text{DMSO}))</td>
<td>219.1</td>
<td>78.6</td>
<td>49.7; 49.5</td>
<td>48.5; 44.8; 37.3; 32.7; 31.8; 31.6</td>
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<td>((7)-\text{Na}(\text{DMSO}))</td>
<td>217.3</td>
<td>74.2</td>
<td>46.7; 41.5</td>
<td>50.0; 44.2; 40.7; 38.7; 38.5; 36.2</td>
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<tr>
<td>((8)-\text{Na}(\text{DMSO}))</td>
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<td>76.4</td>
<td>41.1; 39.3</td>
<td>49.6; 44.1; 40.2; 39.0; 38.6; 36.2</td>
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<td>72.7</td>
<td>46.5; 40.7</td>
<td>49.6; 43.5; 40.1; 38.1; 37.8; 35.3</td>
<td>35.3</td>
</tr>
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<td>78.4</td>
<td>50.7; 45.4</td>
<td>50.7; 44.0; 40.9; 39.6; 37.9; 35.3</td>
<td>35.3</td>
</tr>
</tbody>
</table>

* Acetates had also signals at \(170.0\) and \(21.1\) p.p.m. from \(\text{CH}_2\text{CO}\) residue.

\(^*\) Numbering is that shown in structures \((1)-(3)\).
pared containing 0.3, 0.7, 1.0, 1.3, 9 and 1.7 mol equiv. of [2H₄]dimesyl sodium. The solutions containing less than the full equivalent of base were not stable, becoming turbid in <2 h at room temperature. The ¹³C n.m.r. spectra of these solutions showed lines attributable to cyclohexanol itself and cyclohexene. We speculate that the instability of these solutions is caused by base-induced elimination of water from the un-ionized cyclohexanol. Solutions containing one or more equivalents of base were stable for at least four days at room temperature, and comparison of the spectra in presence and absence of base gave the shifts shown in Figure 3 for addition of one equivalent of base. Importantly, the chemical shifts do not change further in the solutions with 1.3 and 1.7 equivalents of base, providing strong experimental support for complete ionization with one equivalent.

With adamantant-2-ol and cyclohexanol in [2H₄]DMSO and, in parentheses, shifts on addition of one equivalent of [2H₄]dimesyl sodium

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With adamantant-2-ol small changes in chemical shift were again found when the solvent was changed from CDCl₃ to [2H₄]DMSO. Solutions containing less than one equivalent of base were stable; not surprisingly elimination of water to the anti-Bredt olefin does not occur. As with the cyclohexanol solutions, the base-induced chemical-shift changes are complete after addition of one equivalent of base, and are also shown in Figure 3. With less than the full equivalent of base, the fractional changes in chemical shifts were nicely proportional to the amount of added base.

In both alcohols, the largest shifts are in the β-carbon signals, with those in the adamantanol being rather less, presumably because of branching at these carbons and their different steric environment.

Solutions of the sodium salt of (1) were prepared by addition of one equivalent of [2H₄]dimesyl sodium to a solution of (1) in [2H₂]DMSO. The ¹³C n.m.r. data of the resulting solution are included in Table 1 and comparison of the spectra in presence and absence of base shows that only three signals have been shifted appreciably. The alcohol carbon (C-3') signal shifts downfield by 4.3 p.p.m. on addition of base and those earlier assigned to the adjacent β-carbons (C-2' and -4') at 2 7.0 3.6 and 43.9 p.p.m. also move downfield by 4.8 and 4.2 p.p.m., respectively. The shift in the C-3' signal is almost exactly that found in the control experiments with cyclohexanol and adamantanol, and, while there is no reason to expect the ionization shifts to be independent of substrate, this similarity encourages the belief that the solutions contain high concentrations of the salt. Since excess of dimesyl sodium would be expected to react at the ketone as a nucleophile to give a β-hydroxy-sulphoxide, it is not possible to check that the observed shifts correspond to full conversion of (1) into its salt by addition of excess of base.

The ¹⁴C n.m.r. spectra of this salt were not spectacularly temperature dependent in the range 25–90 °C, but close inspection revealed small variation in the apparent signal intensities. In this substrate C-6' lies on the symmetry plane of the degenerate rearrangement and its signal will not be broadened by the exchange. It can therefore serve as an internal reference against which to measure all other signals arising from exchanging sites. At the higher temperatures, all signals are reduced in apparent height compared with the C-6' line, and this behaviour can be reconciled with a relatively slow exchange of the expected type. We can estimate that a line broadening of ca. 0.5 Hz in the exchanging signals would give the observed effects at 100 °C. With this estimate, using the expression for broadening in the slow exchange limit, we can only set an upper limit for the exchange rate of 1.7 s⁻¹ and a corresponding lower limit to the barrier of 21.7 kcal mol⁻¹ at 100 °C.

Some high-temperature spectra showed evidence of quenching of the salt, presumably by DMSO decomposition products, during the time required to collect the spectral data. Lines which had the highest ionization induced shifts, those associated with C-3', -2', and -4', were broadened, with squared shapes, and much reduced in height relative to other signals. The central positions of the envelopes of these signals were also shifted upfield by ca. 1 p.p.m. from their positions in a freshly prepared salt solution. When the spectrum of the heated sample was run at 85 °C, all signals were again sharp, but the positions of the C-3', -2', and -4' lines were now shifted upfield by 1.6 p.p.m. compared with those in a fresh sample, consistent with rapid proton transfer between alkoxide and alcohol in a 60 : 40 mixture of the hydroxyketone and its salt.

Solutions of the sodium salts of (2) and (3) were prepared as described above for (1), and the spectral data at 35 °C are shown in Table 1. Downfield shifts are again apparent in signals associated with C-3', -2', and -4', consistent with high conversions of (2) and (3) into their salts. The spectra were nicely temperature dependent, in a manner consistent with the expected degenerate rearrangement by intramolecular hydride transfer.

In the case of (2) the clearest indication comes from the signals securely assigned (on the basis of their multiplicities) to the exchanging C-6 and -6' pair. These signals are well clear of all others and are not obscured by the solvent. Their behaviour is shown in Figure 4. The observed coalescence at 100 ± 3 °C allows calculation of a barrier ΔG° of 19.0 ± 0.3 kcal mol⁻¹ and a rate of 59 s⁻¹ for the exchange at that temperature. The behaviour of the remainder of the spectrum, while consistent with the exchange, is less susceptible to quantitative analysis as coalescing pairs overlap and are partially masked by solvent signals. In principle, multiple coalescences should allow determination of ΔG° at different temperatures leading to enthalpies and entropies of activation. In practice, the coalescence temperatures cannot be found to the required high accuracy, and we confine ourselves to presenting the data from the C-6 and -6' coalescence. The 6° spread in our estimate of this coalescence temperature allows for difficulties in localizing the coalescence in these spectra which have a relatively high noise-to-signal ratio.

In the temperature range 30–90 °C, the temperature-induced spectral changes were reversible. Spectra obtained in the 95 and 100 °C experiments showed none of the 'squaring' of the C-2', -3', and -4' signals associated with quenching of the salt during the n.m.r. experiment. How-
ever, the spectrum of the sample re-run at room temperature, did show small upfield shifts in these signals. The shift of 0.7 p.p.m. in the C-3' signal is associated with ca. 12% quenching of the salt.

It is evident that slow quenching occurs at temperatures above 90 °C. With partially quenched samples the spec-

trum is that of a mixture of hydroxyketone and its salt, rapidly interconverting by proton transfer, and the measured barrier is associated with exchange in the total population of protonated and deprotonated substrate. If, as seems reasonable, the hydride transfer occurs only in the salt, it is possible to find the barrier for its rearrangement by applying a correction for the quenching to the experimentally determined barrier. Since the quenching is small, the error arising from uncertainty in the coalescence temperature is much larger than the correction, and we have not applied it in the quoted results.

In (3), the methylene carbon (C-6, C-6', and C-7*) signals are also clear of solvent and the rest of the spectrum. C-6 and -6' are an exchanging pair, while C-7* is on the symmetry plane of the reaction, and, as expected, two of the three signals broaden and coalesce as the temperature is raised, while the third remains sharp (see Figure 4). The separation of the lines and coalescence temperature of 72 ± 3 °C gives a barrier of 17.3 ± 0 3 kcal mol⁻¹ and a rate of 75 s⁻¹ for the exchange at this temperature.⁴⁰ As with (2), coalescences in the remainder of the spectrum overlapped, and were obscured by solvent signals. It was possible nevertheless, to identify the signal at δ 50.7 p.p.m. as arising from a second coalesced exchanging pair (Tc < 35 °C) and those at δ 44.0 and 45.4 p.p.m. as arising from a third (Tc ca. 60 °C). With the rearrangement of (3) being faster than (2), the determination of barrier does not require temperatures above 80 °C, and problems associated with quenching of the salt correspondingly were less. The shift in the C-3' signal was consistent with <3% quenching.

The parent hydroxyketones (2) and (3) were recovered in high yield from the n.m.r. solutions by quenching with water and extraction. Mass spectral examination of the recovered material showed that there was no deuterium incorporation from the [2H₆]DMSO during salt formation or rearrangement. The absence of deuterium incorporation firmly excludes the homoenolization mechanism,¹³ and we associate the measured barriers with the depicted intramolecular hydride transfer.

**DISCUSSION**

The finding that the barriers vary in the order (1) > (2) > (3) was not unexpected. In comparing the u.v. spectra of the diones (5; n = 1 and 2), Cookson noted an enhanced interaction between the carbonyl groups in (5; n = 2),²³ and pointed out that extending the methylene bridge compresses the functionality at C-3 and -3' in the lower ring. The effect is well shown qualitatively by molecular models; the methylene bridge acts as a lever on C-1' and -1, controlling their separation and torsional angles to adjacent bridgehead sites at C-2, -2', -5, and -5'. C-2 and -2' are held apart by a relatively incompressible carbon–carbon single bond, and act as pivots, transmitting the conformational changes to the lower ring.⁴² Since Cookson's work, other investigators have commented on the relative ease of bridging across C-3 and -3' in a variety of derivatives, but our results appear to be the first quantitative measure of the change of reactivity in this series.

Any discussion of the detailed relationship between structure and reactivity in the hydride transfer must start from accurate molecular structures of the hydroxyketones or of the salts themselves. Experimentally determined geometries are not yet available and we have therefore calculated geometries for (1)—(3), using Allinger's 1971 force field.⁴⁴ Although this early force field is known to over-estimate non-bonded interactions to hydrogen,⁴⁵ it is expected to reproduce trends well in this closely related series and also allows comparison of the steric interactions across the reacting centres. The measured barriers are those in the salts, and we must emphasize that their structures could differ in important detail from those calculated for the hydroxyketones. For example, a recent ab initio comparison of methanol and sodium methoxide⁴⁶ shows that conversion of the alcohol into its salt weakens and lengthens the alcohol C–H bond while shortening and strengthening the C–O bond. Besides changes associated with conversion of the alcohol into its salt, the interacting alkoxide and carbonyl fragments may suffer distortions along the reaction co-ordinate⁴⁷ in a manner not reproduced by the empirical force field calculation. Indeed, comparison of experimental and calculated structures might afford one method of finding such motion along the reaction co-ordinate.
Details of the calculated structures and some interactions at the reaction sites are shown in Table 2. In all cases the hydride migrates 1,4- across a six-membered ring held in a boat conformation by the cage structure. The diagram is a projection on the plane of C-3,-3', and the migrating hydrogen. The alcoholic oxygen in (3) is 0.10Å out of this plane; all other oxygens are <0.05Å from the plane.

Table 2 shows clearly that the changes in the series are greater between (1) and (2) than between (2) and (3). Notably, the non-bonded C-⋯H distance is only 0.01Å less in (3) than in (2) and the non-bonded repulsion term is only 0.06 kcal mol⁻¹ greater. In contrast, the non-bonded distances and repulsion terms in (1) and (2) differ by 0.09Å and 0.51 kcal mol⁻¹, respectively. Since the C-⋯H non-bonded repulsion is lost as the reaction goes to the transition state, these changes are in qualitative accord with the experimental finding that the barrier in (1) is at least 2.7 kcal mol⁻¹ greater than in (2) which is, in turn, only 1.7 kcal mol⁻¹, greater than in (3). A second notable feature of the calculated structures is the constancy of the angular relationships, both at migrating hydrogen and at the carbon termini. The variation of barrier therefore does not afford any information about preferred angular relationships in the hydride transfer. Indeed, it is apparent that significantly different angles can only be found in rings larger than six, and experiments with hydroxyketones in constrained seven- and eight-membered rings are in progress.

In making these correlations with substrate structure we have assumed that there is no specific interaction between the sodium ion and any one of the substrates. Recent conductivity measurements on solutions of alkali metal alkoxides in DMSO⁴⁸ have shown that they are highly associated (for Na⁺ + BuO⁻ = NaOBu, Kass ca. 10⁶). The counterion therefore cannot be ignored, but our experiments shed no light on this aspect of the rearrangement. It is instructive, however, to compare the intramolecular hydride transfer with the more familiar intermolecular process. The currently accepted mechanism for the intermolecular reaction postulates a six-centre cyclic transition state with simultaneous transfer of metal and hydrogen from the alkoxide to the carbonyl partner. Traditionally, Ap⁺ is the mediating counterion, but alkali metals also promote the transfer ⁵⁰ and the most effective of them is Li⁺. It can hardly be coincidence that Al³⁺ and Li⁺ have comparable small ionic radii (0.50 and 0.60Å, respectively ⁵¹) and bind most strongly. With intermolecular reaction, there are no strong steric constraints on the distance between the oxygen atoms in the reaction partners. The calculated structures, however, show intramolecular oxygen-oxygen distances of between 4.62 and 4.80Å, and, even with the larger sodium ion (ionic radius 0.95Å), co-ordination to both oxygens ⁵² of the same molecule would require molecular distortions, with concomitant increase in energy. It is possible that the intramolecular transfer of hydride occurs with intermolecular transfer of sodium in a dimeric species (see Figure 5).

![Figure 5](image)

**Figure 5.** Possible dimeric arrangement of the alkoxides. The O-Na distance is scaled to a typical 2.4Å found in many Na⁺ complexes ⁴⁴.

Structures of this type are attractive since hydrogen-bonded dimers have been found in the crystal structure of exo-7-hydroxybicyclo[3.3.1]nonan-3-one.⁵⁰ Provided that the equilibrium constant for dimer formation is high, no concentration dependence of the barrier would be expected except at very low substrate concentration. Limitations imposed by the combination of low salt solubility and the low sensitivity of the ¹³C n.m.r. method have restricted us to concentrations in the range 0.33—0.55M, and we have observed no concen-
tration dependence. Experiments to explore this possibility are in progress.

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 457G spectrophotometer. Routine 1H n.m.r. spectra were determined at 90 MHz on a Perkin-Elmer R32 or at 300 MHz on a Varian SC 300 spectrometer. 13C n.m.r. spectra were recorded on a Bruker WP 80 spectrometer at 20.1 MHz. Mass spectra were determined on an AEI MS 9 instrument. Analytical g.l.c. used a 1.7 m x 2 mm glass column with 3% Dexsil 410 on Supelcoport 100—120 as stationary phase at 230° with nitrogen at an inlet pressure of 20 lb in−2 as carrier gas. Silica gel GF254 was used for analytical t.l.c. and PF254 for preparative t.l.c. Light petroleum refers to the fraction boiling between 40 and 60°C. A locally adapted version of the program STRAIN was used for the e.f.f. calculations, on a CDC 7600 computer at U.M.R.C.C.

Tricyclo[6.2.1.01,6]undeca-4,9-diene-3,6-dione (4; n = 1).—This compound was prepared by Diels–Alder reaction of cyclopentadiene and p-benzoquinone according to published methods.22

Tricyclo[6.2.2.01,6]undeca-4,9-diene-3,6-dione (4; n = 2).—This compound was prepared by Diels–Alder reaction of cyclohexadiene and p-benzoquinone according to published methods.22

Tricyclo[6.3.2.01,6]trideca-4,12-diene-3,6-dione (4; n = 3).—Freshly sublimed p-benzoquinone (6.0 g) and methylene chloride (100 ml) were placed in a flask equipped for nitrogen atmosphere and magnetic stirring. Freshly distilled boron trifluoride–ether (3 ml) was added to the stirred, cooled (−20°C) solution followed by cycloheptadiene (5.3 g),39 dropwise over 15 min. When addition of the diene was complete, the mixture was stirred for a further 15 min at −20°C under nitrogen before removal of the cooling bath, and stirring for a further 30 min. The mixture, now dark brown, was poured into ice-cold potassium hydroxide solution (100 ml, 30%) and stirred vigorously for 10 min. The flask was rinsed with ether (100 ml) which was added to the basic mixture. After filtration through Celite, the organic layer was separated, dried (K2CO3), and evaporated to yield a yellow-brown, crystalline mass. Recrystallization from ether–light petroleum gave yellow plates (8.57 g), m.p. 81–82°C (lit. 82°), υmax(CCl4) 3450, 2930, 1640, and 1630 cm−1; δH (CDCl3) 1.65 (6 H, m), 3.05 (2 H, m), 3.22 (2 H, s), 6.02 (dd, J 5.0, 3.5 Hz), and 6.68 (2 H, s); δC (CDCl3) 23.04, 29.33, 37.02, 50.99, 132.94, 141.65, and 200.34 p.p.m. (Found: C, 75.4; H, 9.0. C13H10O2 requires C, 75.7; H, 8.7%).

J.C.S. Perkin II

Exo-exo-Pentacyclo[5.4.0.01,6,0.03,0,09.13]undecane-8,11-diol (8; n = 1).—A solution of the diene-diol (7; n = 1) in freshly distilled acetone (1.28 g in 600 ml) was placed in the well of a standard photocolorimeter apparatus. Dry nitrogen was bubbled through the solution for 30 min before irradiating through quartz with a medium-pressure mercury lamp. After 2 h, the solution was transferred to a round-bottom flask and solvent removed under reduced pressure to leave a light yellow solid (1.44 g). Recrystallization from acetone gave chunky crystals (0.69 g), m.p. 221–223°C (Nujol) 3 280, 1 060, 970 cm−1; δH ([1H]pyrrole) 1.60 (2 H, m), 2.42 (2 H, m), 2.72 (4 H, m), 3.0 (2 H, m), 4.46 (2 H, s, W3 Hz), and 5.6 (2 H, s, removed by D2O), δC ([1H]- DMSO) 33.5, 41.2, 41.7, 45.1, 48.4, and 70.0 p.p.m. m/e 66 (100%), 95 (80), 160 (23), and 178 (15). (Found: C, 74.4; H, 8.2%; C13H10O2 requires C, 74.2; H, 7.9%; C13H10O2 requires C, 74.2; H, 7.9%).

Exo-exo-Pentacyclo[6.4.0.01,6,10,09,13]dodecane-9,12-diol (8; n = 2).—This diol was prepared by irradiation of a solution of (7; n = 2) in acetone (1.17 g in 600 ml) as described above for (7; n = 1). Evaporation of solvent and recrystallization from acetone gave crystals (0.60 g), m.p. 209–210°C, υmax(Nujol) 3 220, 1 010, and 953 cm−1, δH ([1H]pyrrole) 1.75 (4 H, m), 2.2–3.1 (8 H, unresolved),
Pentacyclo[5.4.0.0^2,6,12,16]tridecan-10,13-dione (5; n = 3).—Authentic samples of these cage
diones were prepared by literature procedures by irradiation
of ethyl acetate solutions of the Diels–Alder adducts (4; n = 1–3).21,22

_**Jones Oxidation of (1)–(3) and (6).**—Jones reagent (0.27 g per ml of CrO3) was added in portions to a stirred, cooled (0 °C) solution of the hydroxyketone in acetone (5 ml) until the orange color persisted for 10 min. Excess of reagent
was then destroyed by addition of a few drops of propan-2-ol before decanting the solution from the chromium salts. The acetone solution was diluted with ether (50 ml), washed with aqueous sodium hydrogen carbonate solution and dried (Na₂SO₄), before evaporation of solvent and sublimation of the residue (100 °C at 10 mmHg). G.I.C. and m.s. comparison with authentic samples showed that oxidation of (1) and (6) gave (5; n = 1), (2) gave (5; n = 2), and (3) gave (5; n = 3).

Acetylation of (1)–(3).—The hydroxyketones (1)–(3) were converted into the corresponding acetates by the conventional procedure (acetic anhydride-pyridine). The acetates were obtained as oils, δ₃ (see Table 1).

endo-11-Hydroxypentacyclo[5.4.0.0^2,6,12,16]tridecan-8-one (6).—This compound was prepared by sodium borohydride reduction of the dione (5; n = 1), according to the method of Cookson 23 (one molar proportion of reductant), δ₃ (300 MHz; CDCl₃) 1.42 and 1.48 (1 H, 2d, J 12 Hz), 1.82 (1 H, t, J 12 Hz), 2.3–3.0 (8 H, m), 3.17 (0.5 H, s, removed on addition of D₂O), 5.0 (0.5 H, t, J 4.1 Hz), 4.55 (0.5 H, t, J 6.0 Hz), and 4.75 (0.5 H, s, removed on addition of D₂O), δ₅ (CDCl₃) 36.9, 38.4, 40.6, 41.6, 41.9, 42.1, 43.1, 43.3, 43.5, 44.6, 44.8, 45.2, 45.9, 49.9, 54.3, 54.9, 56.1, 72.1, 81.7, 119.4, and 219.8 p.p.m.

_N.m.r. Spectroscopy of Sodium Alkoxides._—(a) _Sample preparation._ Ampoules of [H₄]DMSO were opened under nitrogen immediately before use. Solutions of [H₄]dimethylsulfoxide sodium in [H₄]DMSO (0.7–1.5 m) were prepared 22 under nitrogen and standardised (a) by titration against formanilide using triphenylmethane as indicator 24 and (b) by quenching of a portion with water and titration of the resulting solution against acetic acid (phenolphthalein). Only if (a) and (b) were identical within experimental error (±5%) was one equivalent of the [H₄]dimethylsulfoxide solution added under nitrogen to a stirred solution of the alcohol (0.15–0.25 mmol) in sufficient [H₄]DMSO to give a final volume of 0.45 ml. The resulting clear, virtually colourless solution was transferred under nitrogen pressure via a double-ended needle 55 to a 5 mm o.d. n.m.r. tube which was then sealed. The sodium alkoxides were too insoluble in [H₄]DMSO for the preparation of more concentrated solutions.

(b) _Kinetic measurements._ ¹³C _N.m.r._ spectra were recorded at 20.1 MHz on a Bruker WP-80 Fourier transform spectrometer. Chemical shifts were referenced to internal [H₄]DMSO (δ 39.6 p.p.m. relative to tetramethylsilane) and the solvent also provided the internal deuterium field-frequency lock.

The acquisition parameters for routine chemical shift determination resulted in a digital resolution of only 1.471 Hz, but in a typical kinetic experiment, 8K memory points over a spectral width of 1 800 Hz, gave an acquisition time of 2.269 s and improved the digital resolution to 0.441 Hz. The accumulation of ca. 30 000 scans with broad-band pro-
ton decoupling, using a pulse width of 3 μs (flip angle of 50°–60°), and the introduction of 1.0 Hz exponential line-broadening on transformation reduced the noise to an acceptable level in the kinetic spectra.

Temperatures were regulated with a Bruker B VT1000 temperature unit and were stable to ±0.3 °C. Coalescence temperatures determined on duplicate samples were identical within experimental error.

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