Equilibration of Alkene Regioisomers in *trans*- and *cis*-Octalins[1,†]

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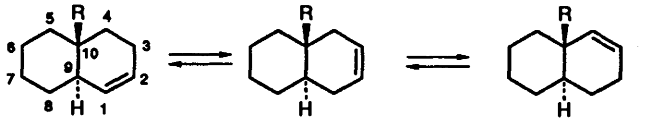
As models for studying the energetics of double-bond regiochemistry in the octalin system, the enol acetates of *trans*- and *cis*-2-decalone (**1**, **4**), *trans*- and *cis*-10-methyl-2-decalone (**7**, **10**) and *trans*- and *cis*-9-methyl-2-decalone (**13**, **16**) have been synthesised. Acid-catalysed equilibrations of double-bond position were conducted in acetic anhydride at *ca.* 60, 100 and 140 °C and assessed by integration of the vinyl-proton NMR signals, which were unambiguously assigned to each enol acetate either by the observed splitting pattern or synthesis. Values of ΔH and ΔS (Δ^2:Δ^1) are derived and compared with experimental and theoretical literature values. Values of ΔH for the enol acetates of **1** and **4** are −0.69 and 0.0 kcal mol^{-1}, respectively, and addition of an angular methyl decreases the relative stability (ΔH) of the Δ^1 isomer, by 1.25–2.25 kcal mol^{-1} for the *trans* skeleton and by 1.0–1.4 kcal mol^{-1} for the *cis* skeleton. For a given angular substituent, changing *cis* stereochemistry to *trans* also decreases the relative Δ^1-stability, by 0.7 kcal mol^{-1} when R = H and 0.95–1.55 kcal mol^{-1} when R = Me. Values of ΔS are all small, between +0.1 and −3.2 cal mol^{-1} K^{-1}. Trends in the data and features of the ^{1}H NMR spectra related to conformation are discussed, and an approach is suggested for calculating approximate ΔH, ΔS and ΔG values for Δ^1-9-methyl- *vs.* Δ^1-10-methyloctalin in the *trans* and *cis* series.

Several problems in our laboratory have interested us in the energy relationships among stereoepimers and alkene regioisomers in the decalin ring system. We have already presented a study of benzoctalones bearing on this question, using the benzo substituents to fix the alkene positions and the carbonyl groups to facilitate equilibration of ring-juncture stereochemistry.[2]

The present work instead sets ring-juncture stereochemistry and examines the relative energies of the various double-bond isomers (Scheme 1). This question finds a practical application in the well known tendency of 3-oxosteroids with AB *trans*- and *cis*-fusions to undergo certain α-substitutions predominantly—sometimes exclusively—at the 2- and 4-positions, respectively.[3] Although some such reactions may be complicated by kinetically controlled processes, this selectivity has been explained in terms of the relative thermodynamic stabilities of Δ^2 and Δ^3 steroid enol species.



Scheme 1

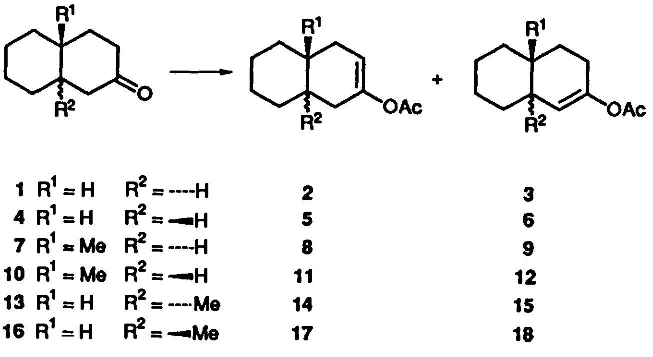
Several studies have examined this matter theoretically[4] and in steroids,[5] but few experimental data exist for the simplest models, like octalins and methyloctalins.[6] In the unsubstituted octalins, acquisition of useful experimental data is hampered by the heavy predominance at equilibrium of the double-bond isomers that directly involve the ring juncture and therefore have no *trans*–*cis* epimerism. A thermodynamic study of octalin isomers over a temperature range of 200 °C, found 72–92% tetrasubstituted isomer and 6–21% trisubstituted isomer, but the total amounts of *trans* isomers were never more than 7.5% and the *cis* isomers were either undetectable or immeasurable.[6a,c]

An approach by way of isomerism in stable enol derivatives of 2-decalones was suggested by older equilibrium data for enol acetates and enamines of *trans*-2-decalone (**1**),[7–10] *cis*-2-decalone (**4**)[7,11] and *trans*-10-methyl-2-decalone (**7**),[10] although some of these data were quite inexact.[10,11] Recently Huffman and Balke[12] have reported a careful study of isomerism in the enol trimethylsilyl ethers of a series of decalone steroid models, providing ΔG data for **1**, **4**, **7**, **10** and several new *cis*-10-methyl-2-decalones that are locked in the 'steroidal' AB-ring conformation.

In all the above data, ΔH, as opposed to ΔG, values, usable for evaluating steric strains and assessing molecular modelling programs, are available for only one Δ^2/Δ^1 isomer pair, the unsubstituted *trans*-octalins.[6c] We determined to carry out a series of variable-temperature equilibrations on 2-decalone enol species, to allow the accurate calculation of ΔH and ΔS.

Results and Discussion

After trials with enamines and enol ethers, we settled upon enol acetates as our experimental system. They are easily produced in high yield, and can be made by non-thermodynamic processes and subsequently equilibrated in a separate step. In addition they are distillable and not excessively labile toward water, heat or oxygen, and the isomer mixtures offer several possible methods of analysis. The ketones we used (Scheme 2) were *trans*- and *cis*-2-decalone (**1**, **4**), *trans*- and *cis*-10-methyl-2-decalone (**7**, **10**) and *trans*- and *cis*-9-methyl-2-decalone (**13**, **16**). All were racemic materials, produced and refined to purities of 98% or greater by standard methods (see the Experimental



Scheme 2

[†] IUPAC-recommended name: octahydronaphthalenes.

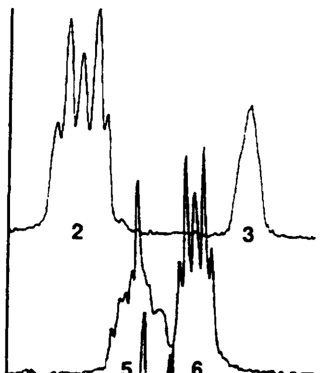
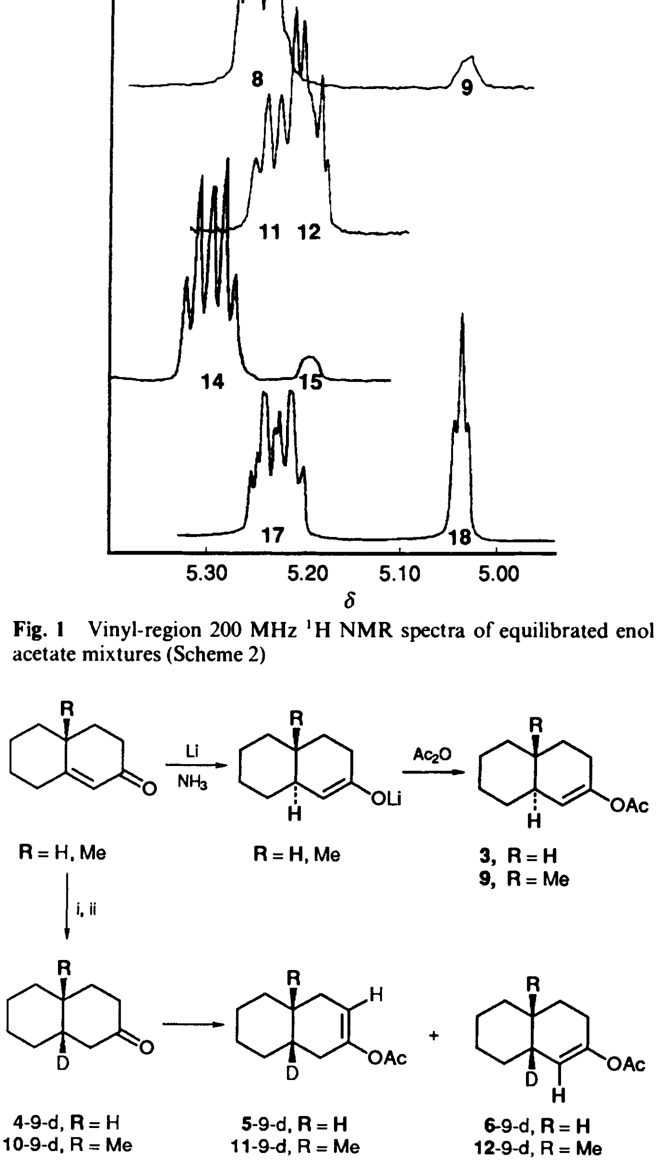


Fig. 1 Vinyl-region 200 MHz ^{1}H NMR spectra of equilibrated enol acetate mixtures (Scheme 2)



Scheme 3 *Reagents*: i, D_2–Pd/C; ii, NaOMe–MeOH

section). Enol acetates were produced by acid-catalysed exchange with isopropenyl acetate. This generally provided non-equilibrium mixtures, which were isolated, purified by distillation, and separately equilibrated by acid catalysis in acetic anhydride solution at approximately 60, 100 and 140 °C. The equilibrated, neutralised and redistilled mixtures were analysed quantitatively by ^{1}H NMR spectroscopy (see the Experimental section), employing the vinyl absorptions in the region δ 5.0–5.35. GC ratios, where obtainable, were found to agree with these NMR area ratios to within 1%.

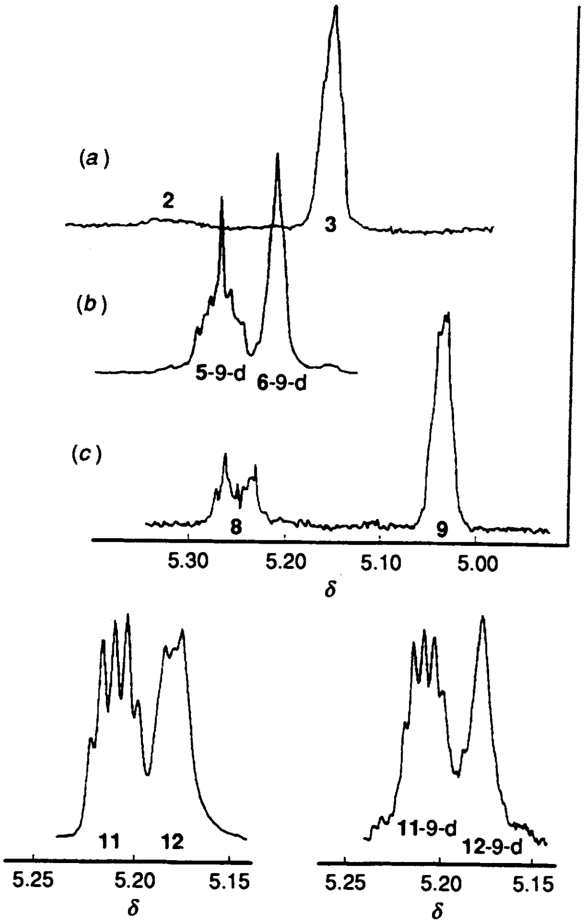


Fig. 2 (top) Vinyl-region 200 MHz ^{1}H NMR spectra of enol acetate mixtures obtained (*a*), (*c*) by direct acetylation of enolates from Li–NH, reduction of octalones and (*b*) from decalone **4**-9-d (Scheme 3); (bottom) vinyl-region 400 MHz ^{1}H NMR spectra of enol acetate mixtures derived, respectively, from **10** and **10**-9-d (Schemes 2, 3)

Only for the derivatives of the 9-methyl-2-decalones (**13**, **16**) was it unambiguously evident from the splitting patterns of the vinyl absorptions (**14**, **15**; **17**, **18**), which regioisomer was which, owing to the removal of all ^3J coupling in the Δ^1 isomers (Fig. 1). In the other cases (**1**, **4**, **7**, **10**), despite previous assumptions in the literature, we wished to obtain proof as to which of the vinyl absorptions we were using for quantitation belonged to each regioisomer. This was done as shown in Scheme 3.

The *trans*-2-decalones **1** and **7** were synthesised by lithium–ammonia reduction of the corresponding α,β-unsaturated ketones.[13] Direct acetylative trapping of the lithium enolates generated by the reductions[14] gave the Δ^1 enol acetates **3** and **9** in predominances far from the equilibrium ratios (Fig. 2). The *cis*-2-decalones **4** and **10** could be produced from the same unsaturated ketones by catalytic hydrogenation.[15] With D_2, catalytic reduction led to β-deuterio ketones the enol acetates of which clearly differentiated the Δ^2 from the Δ^1 isomer by diminution of the vinyl-proton splitting in the latter (Figs. 1 and 2).

As may be seen, the vinyl absorption for a given Δ^2 compound invariably appears downfield relative to that for the corresponding Δ^1 isomer. In the 200 MHz NMR spectra, the individual absorptions due to Δ^2 and Δ^1 derivatives are adequately separated for quantitation in every instance except that of *cis*-10-methyl-2-decalone (**10**⟶**11**, **12**), where the ratio data were supplied by spectra at 400 MHz (Fig. 2) and by quantitation of the angular methyl peaks.

The vinyl-hydrogen splitting patterns contain information on

Table 1 Data derived from equilibration of 2-decalone enol acetates

Ketone	$\%\Delta^2:\%\Delta^1(T/°C)$[a]			$\Delta S°$/ cal mol^{-1} K^{-1}	$\Delta H°$/ kcal mol^{-1}	ΔH_{calc}/ kcal mol^{-1}	ΔG_{298}/ kcal mol^{-1}	ΔG_{lit}/ kcal mol^{-1}[h]
1	75:25 (60)	73:27 (100)[c]	71:29 (140)	0.11[d]	−0.69[e]	−0.68[b]	−0.73	−0.56
4	45:55(61)	45:55 (100)[c]	45:55 (140)	−0.40[f]	0.0	0.78[g]	0.12	0.26
7	95:5 (58)	91:9 (102)	89:11 (138)	−3.08	−2.94	−1.65[b]	−2.02	−1.53
10	62 : 38 (58)	56:44 (102)	52:48 (138)	−3.21	−1.39		−0.42	−0.09
13	94.5:5.5 (62)	93:7 (100)	91:9 (142)	−0.05	−1.93		−1.91	
16	65:35 (69)	63:37 (94)	59:41 (142)	−1.66	−0.99		−0.50	

[a] Equilibrium percentages considered accurate to ±2%. [b] Ref. 12: experimental ΔG values for enol Me_3Si-ethers; MM2 calculations (ΔH values) for unsubstituted octalins. [c] Ratios of 72:28 (**1**) and 40:60 (**4**) found (GC) at 100 °C in ref. 7. [d] For the unsubstituted *trans*-octalins, ΔS values of −1.37 and −1.38 cal mol^{-1} K^{-1}, respectively, are derivable from experimental data in ref. 6(*c*) and have been 'calculated'.[4d] [e] For the unsubstituted *trans*-octalins a ΔH value of −0.65 kcal mol^{-1} was found experimentally in ref. 6(*c*). [f] For the unsubstituted *cis*-octalins, a ΔS value of −1.34 has been calculated.[4d] [g] Ref. 4(*d*).

preferred conformations. For all the *trans*-fused enol acetates, derived from **1**, **7** and **13**, models suggest relatively little conformational flexibility, particularly for the Δ^1 derivatives. For these Δ^1 compounds, the models show that the dihedral angle determining the vinyl-H ^3J couplings should be close to 90°, with the value for J therefore near a minimum, and that the ^4J dihedral angles should be about 60°. Theory suggests ^3J values near 2.5 and ^4J values near 1.5 Hz for hydrocarbons lacking electronegative substituents.[16] Experimentally, however, no individual splittings are discernible in these peaks for the Δ^1 compounds. Those in **3** and **9** are narrow ($w_{\frac{1}{2}} \simeq 4.85$ and 4.4 Hz), fully consistent with the presence of three small and similar but not identical J values. However the failure of this pattern to change appreciably when ^3J coupling is absent, in **15** ($w_{\frac{1}{2}} \simeq 4.3$ Hz), shows that this ^3J coupling must actually be appreciably smaller than the above 'minimum' of 2.5 Hz. This is consistent with the known effect of electronegative substituents on vicinal coupling constants.[16] The generally triangular aspect of these peaks seems most consistent with principal splitting into an approximate triplet, and smaller doublet splitting, presumably due to coupling with the protons on, respectively, C3 and C9.

Each *trans*-fused Δ^2 derivative produces a generally similar vinyl-H pattern that approximates an overlapping doublet-of-triplets (with that for **8** rather distorted and overlapping less) but each differs from the others in the particular J values. It is noteworthy that, of the four potential couplings to allylic protons, only three are reliably observed. Since theoretically, in the absence of electronegative substituents, only the four-bond coupling constants can fall to zero and only ^3J can reach absolute values greater than *ca.* 2.5–3 Hz, these patterns are most consistent with major ^3J splitting by a single proton (J = 4.6–5.5 Hz), and further doublet-of-doublet or triplet splitting due to one ^3J and one ^4J coupling ($J \simeq 2$ Hz), while the remaining ^4J coupling is—or averages to—an extremely small value, near zero.*

The vinyl-H patterns for the pairs **2**/**3** and **14**/**15** are broadly similar, indicating essentially analogous conformations. However the differences in δ and J values for the other *trans* pair, **8**/**9**, suggest a change of conformation associated with the 10-methyl group. The more complex NMR patterns of the *cis*-fused series reflect their greater conformational mobility.

The results of the equilibrations are shown in Table 1. The data, collected over a range of *ca.* 80 °C, provide values for $\Delta H°$ and $\Delta S°$ which allow extrapolation of $\Delta G°$ to other temperatures. The values found for $\Delta S°$ are all small, as expected, and offer no obvious patterns. Table 1 also gives our values of ΔG_{298} and comparisons with experimental ΔG_{298} values published by Huffman and Balke[12] for the enol trimethylsilyl ethers of **1**, **4**, **7** and **10** and with some published calculated values for $\Delta H°$.

Two trends are evident in our ΔH data for the Δ^2/Δ^1 isomer ratio. The first trend is that, for any given angular substituent, a change from *cis* to *trans* stereochemistry decreases the relative stability of the Δ^1 isomer, by 0.7 kcal mol^{-1} when R = H and by 0.95–1.55 kcal mol^{-1} when R = Me, with the greater effect when the ring juncture farther from the carbonyl is methylated. The second trend observed is that addition of an angular methyl at either ring juncture to either the *trans* or the *cis* skeleton also consistently disfavours the Δ^1 isomer. The effect is greater when the ring juncture remote from the ketone carbonyl is methylated (1.4–2.25 kcal mol^{-1}) *vs.* when methyl is added to the one nearer the carbonyl (1.0–1.25 kcal mol^{-1}). The Δ^1-decrement is 1.25–2.25 kcal mol^{-1} in the *trans* and 1.0–1.4 kcal mol^{-1} in the *cis* compounds, depending on which ring-juncture position is involved. The greatest Δ^2-preferences are found when the angular methyl and *trans* stereochemistry appear together, in compounds **7** and **13**.

A perturbation like the introduction of a methyl group may 'begin' conceptually as a local non-bonded steric interaction, but actually will be distributed throughout the molecule as torsional and angular as well as steric strain in whichever way minimises the total energy. In general, the more flexible the system, the less localised the strain and the more difficult it will be to pinpoint its locale and type.[12] The specific unfavourable interactions introduced into **2**/**3** and **5**/**6** along with the methyl group are certainly not obvious, but seem easiest to understand in the case of **14** *vs.* **15**.

Our compounds do not allow equilibration of **9** with **15**, hence differences in ΔG, ΔH and ΔS for this pair cannot be obtained directly. However, the carbon and hybridisation framework are identical for **8** and **14**, which differ only in transposition of their vinyl substituents. These both project outward in the plane of the molecule and appear to have so little steric interaction with any part of the molecule other than the allylic hydrogens that it seems a reasonable approximation that **8** and **14** should be isoenergetic, *i.e.*, that $\Delta G_{14\ 8}$ (and $\Delta H_{14\ 8}$ and $\Delta S_{14\ 8}$) = 0. Compounds **9** and **15** can then be considered in equilibrium with each other through the intermediacy of the species '**8**=**14**,' and for the imaginary equilibrium $\mathbf{9} \rightleftharpoons \mathbf{15}$, values of $\Delta H_{15\ 9}$, *e.g.*, may be obtained directly from the tabulated $\Delta H_{9\ 8}$ and $\Delta H_{15\ 14}$ values.

The values of $\Delta H_{15\ 9}$ and $\Delta S_{15\ 9}$ obtained in this way are −1.0 kcal mol^{-1} and −3.0 cal mol^{-1} K^{-1}; axial methyl interaction with a C4-hydrogen in compound **15** appears to be the principal

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* In vinyl–allylic coupling, the theoretical curve for dependence of ^4J on dihedral angle has both positive and negative portions, passing through zero at *ca.* 180° and 35°.[16a] Because time-averaging of coupling constants through conformational flexing depends on the non-absolute values of J, ^4J may become zero by the averaging of conformations having positive and negative J values.

ΔH culprit. If the above assumptions are valid, the prediction is that equilibration of *trans*-Δ^1-9-methyloctalin and *trans*-Δ^1-10-methyloctalin would favour the former below 60 °C but the latter above 60 °C.

Application of these assumptions to the enol acetates derived from **10** and **16** is probably more uncertain because of the greater flexibility of the *cis*-junctured system, which may permit more interaction of the vinyl substituent with nearby groups. However, with the assumption that ΔG, ΔH and ΔS all = 0 for **11** *vs.* **17**, the resulting imaginary equilibrium **12** $\rightleftharpoons$ **18** yields a value for $\Delta H_{18/12}$ of -0.40 kcal mol^{-1} and for $\Delta S_{18/12}$ of -1.55 cal mol^{-1} K^{-1}, favouring **12**, *i.e.*, *cis*-Δ^1-10-methyloctalin, at any temperature above -15 °C.

One justification for the above treatment is that actual experimental data would be quite difficult to obtain and these assumptions lead to ΔH, ΔS and ΔG values not many steps removed from experiment. Nevertheless, they clearly should be taken with a grain of salt. One caution concerning the assumption that **8** and **14** are isoenergetic is that their vinyl-H NMR patterns are, as noted above, not identical (Fig. 1), suggesting conformations which differ because of some difference in energy. However skeptically one views values derived by this data treatment, they may be no worse than ones obtained from some molecular mechanics calculations, judging from the relatively poor agreement with experimental data in Table 1 (except for the equilibrium **2** $\rightleftharpoons$ **3**, the experimental data of which may well have been used in devising the modelling programs).[4d]

Experimental

M.p.s and b.p.s are uncorrected. GC analyses were carried out on a Perkin-Elmer 8500 or Bendix 2300 instrument with He carrier gas. In the former case, a 12 m × 22 mm (ID) glass column coated with a 0.25 µm film of BP1 silicone was used with a flame-ionisation detector; in the latter case a 6 ft × 0.125 in stainless-steel column packed with 10% 20M Carbowax (polyethylene glycol) on 80–100 mesh Anakrom Q support was used isothermally (150 °C) with a thermal-conductivity detector and a gas flow of 20 cm^3 min^{-1}. IR spectra were determined with a Perkin-Elmer 1330 spectrometer on neat samples in the case of liquids and Nujol mulls for solids. NMR spectra were determined, with $CDCl_3$ as the solvent, at 200 MHz on an IBM (Bruker) WP 200-SY or, if specified as 400 MHz, on a Varian VXR-400S instrument. Only significant absorption or resonance signals are presented for IR and NMR spectra. Mass spectra were determined in the electron-impact mode at 70 eV on a Finnigan MAT INCOS-50 instrument, employing a Hewlett-Packard 5890 GC with a 30 m × 0.25 mm (ID) glass column coated with a 0.25 µm film of DB5 silicone; peaks below *m*/*z* 50 are not reported. Microanalyses were performed through the kindness of Dr. Franz Scheidl at Hoffmann-La Roche Inc.

Preparation, Equilibration and Analysis of Enol Acetates.—In a typical procedure, ketone (7.9 mmol) was heated with isopropenyl acetate (6.00 cm^3, 54.5 mmol) and toluene-*p*-sulfonic acid (10 mg) at 100 °C. Acetone was distilled off continuously and heating was stopped when acetone evolution ceased. The excess of isopropenyl acetate (b.p. 94 °C) was removed by rotary evaporation, the mixture was neutralised and the residue was distilled under vacuum to yield 80% of mixed enol acetates. Samples of enol acetate mixtures (1–4 g) in Ac_2O (4–14 cm^3) were heated in the presence of toluene-*p*-sulfonic acid (10–40 mg), and the isomer ratio was monitored at 1 day intervals until it was constant for two consecutive readings. The times required for this were 1, 2 and 7 days, at 140, 100 and 60 °C, respectively. For analysis, equilibrated mixtures were quenched with cold aqueous $NaHCO_3$ and extracted with hexane. The dried extracts were concentrated under vacuum and the residue was distilled. Regioisomer ratios were determined by integrating vinyl-proton peak areas in the ^1H NMR spectra, using at least two independent equilibrations at each temperature, which were found to agree to within 2%. T_1 relaxation times found for the C3 proton in **2** (4.102 s) and the C1 proton in **3** (4.117 s) differed by less than 0.4%, and the **2**/**3** area ratio did not change when relaxation delays were lengthened systematically from 0 to 160 s. NMR ratios were also compared with GC ratios for **2**/**3**, **5**/**6**, **11**/**12** and **17**/**18** and found to agree within 1%; **8**/**9** and **14**/**15** were not resolved by GC.

trans-2-*Decalone* (**1**).—This was prepared from Δ^1-2-octalone[17] by a reported[18,19] $Li-NH_3$ procedure in 79% yield, was purified by conversion to the semicarbazone, m.p. 193–195 °C (lit., 192–192.5,[18] 192–193[20] °C). Recrystallisation from MeOH, regeneration with pyruvic acid in refluxing HOAc,[21] and distillation at 45 °C and 0.2–0.3 mm (lit., 118.5–120 °C at 25 mmHg;[19] 127–128 °C at 28 mmHg[22]) yielded **1** of purity >98% (GC); ν_{max}/cm^{-1} 1720.

Enol acetates **2** and **3** were prepared from **1** in 80% yield as a mixture by the general procedure, b.p. 54–58 °C at 0.06–0.09 mmHg (lit., 68–69 °C at 0.2 mmHg;[7] 110–112 °C at 15 mmHg[23]); ν_{max}/cm^{-1} 1758, 1680; δ_H 5.32 (dt, *J* 5.3, 2 Hz), 5.15 (br s) and 2.1 (3 H, s); *m*/*z* for **2**, 194 (M$^+$, 22%), 152 (100) and 70 (100); for **3** 194 (M$^+$, 11) and 152 (100).

2-*Acetoxy*-trans-Δ^1-*octalin* (**3**).—Δ^1-2-Octalone[17] (5.0 g, 33 mmol) was reduced by the previously employed $Li-NH_3$ procedure; the excess of Li was destroyed by addition of lithium benzoate, and NH_3 was allowed to evaporate and removed under vacuum at 0 °C. Dry Et_2O (100 cm^3) was added and then Ac_2O (5.1 g, 50 mmol) was added with stirring over 15 min at -20 °C. The mixture was stirred an additional 15 min at -20 °C and 1.0 mol dm^{-3} aqueous $NaHCO_3$ (100 cm^3) was added. The usual extraction and concentration procedure led to **3** (5.2 g, 81%), b.p. 74–78 °C at 0.5 mmHg; ν_{max}/cm^{-1} 1758 and 1680; δ_H 5.15 (1 H, br s) and 2.1 (3 H, s); *m*/*z* 194 (M$^+$, 13%) and 152 (100).

cis-2-*Decalone* (**4**).—A commercial (Aldrich) mixture of decahydro-2-naphthols, cooled to -20 °C overnight in hexane and filtered, yielded 45% '*cis–cis*' isomer after recrystallisation, m.p. 104–105.5 °C (lit., 104–105,[24] 105–106[25] °C); ν_{max}/cm^{-1} 3260, 1055 and 1030; δ_H 3.61 (septet) and 1.13–1.79 (complex); *m*/*z* 154 (M$^+$, 2%) and 94 (100). This alcohol was oxidised with Jones reagent to give a 91% distilled yield of **4** of purity >99% (GC), b.p. 67–68 °C at 1.1 mmHg (lit.,[26] 74–76 °C at 2 mmHg); ν_{max}/cm^{-1} 1705; δ_H 2.33 (4 H, complex), 1.97–2.05 (2 H, complex) and 1.32–1.94 (10 H, complex); *m*/*z* 152 (M$^+$, 60%) and 55 (100).

Enol Acetates **5** and **6** were prepared from **4** in 85% yield as a mixture by the general procedure, b.p. 84–88 °C at 0.4–0.5 mmHg (lit., 67 °C at 0.2 mmHg;[7] 81–86 °C at 0.7 mmHg[11]); ν_{max}/cm^{-1} 1750 and 1665; δ_H 5.27 (m), 5.21 (dt, *J* 3.6, 1.4 Hz) and 2.1 (3 H, s); *m*/*z* for **5**, 194 (M$^+$, 11%) and 109 (100); for **6**, 194 (M$^+$, 15) and 152 (100).

cis-2-*Decalone*-9-d (**4-9-d**).—Δ^1-2-Octalone[17] (5.3 g, 35 mmol) was dissolved in EtOH (30 cm^3), acidified with HCl[15,22] (3 mol dm^{-3}; 2.7 cm^3) and stirred with 10% Pd–C (530 mg) under 1 atm of D_2 for 10 h. The filtrate was concentrated, dissolved in Et_2O, neutralised, reconcentrated and treated at 25 °C with 1% MeONa–MeOH (25 cm^3) for 4 h. Reconcentration, neutralisation and distillation gave **4-9-d** (3.8 g, 70%), b.p. 70–74 °C at 0.8–1.0 mmHg; ν_{max}/cm^{-1} 1705; *m/z* 153 (M$^+$, 85%) and 55 (100).

Enol acetates **5-9-d** and **6-9-d** were prepared from **4-9-d** in 86% yield as a mixture by the general procedure, b.p. 58–61 °C at 0.1 mmHg; ν_{max}/cm^{-1} 1754 and 1682; δ_H 5.27 (m), 5.20 (br s) and 2.1 (3 H, s); *m/z* for **5-9-d**, 195 (M$^+$, 8%) and 153 (100); for **6-9-d**, 195 (M$^+$, 7%) and 153 (100).

10-*Methyl*-trans-2-*decalone* (**7**).—This was prepared from 10-methyl-Δ^1-2-octalone[27] by the previously employed Li–NH$_3$ procedure in 75% yield, and purified by conversion into the semicarbazone, m.p. 202–203 °C (lit.,[28] 202–203 °C). Recrystallisation from MeOH, regeneration with pyruvic acid in refluxing HOAc, and distillation at 63–65 °C and 0.3 mmHg (lit.,[29] 60 °C at 0.1 mmHg) yielded **7** of purity >98% (GC); ν_{max}/cm^{-1} 1705; δ_H 1.04 (3 H, s); *m/z* 166 (M$^+$, 61%).

Enol acetates **8** and **9** were prepared from **7** in 84% yield as a mixture by the general procedure, b.p. 92–100 °C at 0.7 mmHg; ν_{max}/cm^{-1} 1765, 1690 and 833; δ_H 5.23 (m), 5.03 (br s), 2.09 (3 H, s) and 0.88 (3 H, s); *m/z* (**8** and **9** not resolved) 208 (M$^+$, 22%) and 166 (100).

2-*Acetoxy*-10-*methyl*-trans-Δ^1-*octalin* (**9**).—10-Methyl-Δ^1-2-octalone[27] (5.00 g, 30.5 mmol) was reduced by the previously employed Li–NH$_3$ procedure; the excess of Li was destroyed by addition of lithium benzoate, and NH$_3$ was allowed to evaporate and removed under vacuum at 0 °C. Dry Et$_2$O (100 cm^3) was added at −20 °C and then Ac$_2$O (3.40 g, 33.3 mmol) was added with stirring over 15 min at −20 °C. The mixture was stirred an additional 15 min at −20 °C and aqueous NaHCO$_3$ (1.0 mol dm^{-3}; 100 cm^3) was added. The usual extraction and concentration procedure, followed by distillation at 92–98 °C (0.7 mmHg), led to **9** (4.8 g, 75%); ν_{max}/cm^{-1} 1765, 1690 and 833; δ_H 5.23 (m), 5.03 (br s), 2.09 (3 H, s) and 0.88 (3 H, s); the areas of the vinyl peaks indicated an **8**/**9** ratio of *ca.* 4:9.

10-*Methyl*-cis-2-*decalone* (**10**).—This was prepared by hydrogenation of 10-methyl-Δ^1-2-octalone[27] (9.0 g, 55 mmol) in a mixture of EtOH (45 cm^3) and HCl[15,22] (3 mol dm^{-3}; 4.5 cm^3) over 10% Pd–C catalyst (810 mg) at 1 atm. The usual work-up gave a crude, low-melting solid, which led to **10** (4.0 g, 44%) of purity >99% (GC), m.p. 49–50 °C (hexane) (lit., 46,[30] 47,[26,31] 47–47.6,[32] 46–48,[28] °C); ν_{max}/cm^{-1} 1720; δ_H 1.19 (3 H, s); *m/z* 166 (M$^+$, 49%).

Enol acetates **11** and **12** were prepared from **10** in 75% yield as a mixture by the general procedure, b.p. 72–74 °C at 0.3 mmHg; ν_{max}/cm^{-1} 1754 and 1688; δ_H(400 MHz) 5.22 (dt, *J* 5.5, 2.5 Hz), 5.18 (complex), 2.10 (3 H, s), 0.99 (s) and 0.97 (s); *m/z* for **11**, 208 (M$^+$, 13%) and 96 (100); for **12**, 208 (M$^+$, 13) and 96 (100).

10-*Methyl*-cis-2-*decalone*-9-d (**10-9-d**).—This was prepared in 40% yield from 10-methyl-Δ^1-2-octalone[27] as described previously for **4-9-d**, m.p. 48–50 °C (hexane); ν_{max}/cm^{-1} 1718; δ_H 1.18 (3 H, s); *m/z* 167 (M$^+$, 36%) and 96 (100).

Enol acetates **11-9-d** and **12-9-d** were prepared from **10-9-d** in 63% yield as a mixture by the general procedure, b.p. 62–63 °C at 0.1 mmHg; ν_{max}/cm^{-1} 1763 and 1696; δ_H(400 MHz) 5.21 (dt, *J* 5.6, 2.8), 5.17 (br s), 2.10 (3 H, s), 0.99 (s) and 0.96 (s); *m/z* for **11-9-d**, 209 (M$^+$, 14%) and 96 (100); for **12-9-d**, 209 (M$^+$, 7) and 97 (100).

3,3-(*Ethylenedithio*)-10-*methyl*-trans-2-*decalone* (**21**).—For the carbonyl transposition,[33] compound **7** was first converted into the corresponding 3-hydroxymethylene derivative[29,34] in 72% yield, m.p. 73–75 °C (lit.,[29] 75.5–76 °C); ν_{max}/cm^{-1} 1633 and 1580; δ_H 14.44 (1 H, d, *J* 3.4), 8.54 (1 H, d, *J* 2.9), 2.26 (1 H, dd, *J* 19.0, 5.65), 1.08–2.09 (12 H, complex) and 0.82 (3 H, s). This material (2.00 g, 10.2 mmol), along with ethylene bis(toluene-*p*-sulfonate)[35] (4.20 g, 10.3 mmol) and KOAc (5.0 g, 51 mmol), was heated at reflux in MeOH (60 cm^3) for 4–5 h. Concentration, dilution with ice–water and filtration of the precipitate gave crude **21** (2.5 g, 96%), m.p. 105–106 °C, leading to material of m.p. 123–125 °C (EtOAc–cyclohexane 1:1); ν_{max}/cm^{-1} 1712; δ_H 3.27 (4 H, m), 2.8 (1 H, dd, *J* 14.3, 15.1), 2.23 (3 H, m), 1.02–1.75 (9 H, complex) and 1.16 (3 H, s) (Found: C, 60.75; H, 7.8. $C_{13}H_{20}OS_2$ requires C, 60.89; H, 7.86%).

3,3-(*Ethylenedithio*)-2-*hydroxy*-10-*methyl*-trans-*decalin* (**22**).—A solution of **21** (2.4 g, 9.4 mmol) in dry Et$_2$O (60 cm^3) was added with stirring under N$_2$ to a mixture of a THF solution of LiAlH$_4$ (1 mol dm^{-3}; 10 cm^3, 10 mmol) and dry Et$_2$O (60 cm^3). After 15 h of stirring at room temperature, the usual aqueous-extractive work-up produced crude **22** (2.3 g, 94%), m.p. 92–95 °C, leading to off-white material of m.p. 101–102 °C (EtOAc); ν_{max}/cm^{-1} 3475; δ_H(400 MHz) 3.67 (1 H, ddd, *J* 12, 8.2, 4.3), 3.28–3.43 (3 H, m), 3.18 (1 H, m), 2.38 (1 H, d, *J* 8.2), 2.17 (1 H, d, *J* 14.47), 1.97 (1 H, d, *J* 14.47), 0.95–1.74 (11 H, complex) and 0.97 (3 H, s) (Found: C, 60.5; H, 8.65. $C_{13}H_{22}OS_2$ requires C, 60.41; H, 8.58%).

2-*Acetoxy*-3,3-(*ethylenedithio*)-10-*methyl*-trans-*decalin* (**23**).—A mixture of **22** (2.30 g, 8.75 mmol), NaOAc (1.70 g, 20.7 mmol) and Ac$_2$O (25 cm^3) was refluxed for 5–6 h, cooled and concentrated under vacuum. The usual isolation procedure yielded **23** (2.6 g, 99%), m.p. 102–110 °C, leading to material of m.p. 120–122 °C (EtOAc); ν_{max}/cm^{-1} 1735; δ_H(400 MHz) 4.92 (1 H, dd, *J* 9, 6), 3.42 (1 H, m), 3.17–3.34 (3 H, m), 2.15 (1 H, d, *J* 14.08), 2.08 (3 H, s), 2.08 (1 H, d, *J* 14.08), 0.95–1.74 (11 H, complex) and 1.01 (3 H, s) (Found: C, 60.05; H, 8.1. $C_{15}H_{24}O_2S_2$ requires C, 59.96; H, 8.05%).

3-*Acetoxy*-9-*methyl*-trans-2-*decalone* (**24**).—A mixture of **23** (2.60 g, 8.67 mmol), HgCl$_2$ (4.50 g, 16.6 mmol), CdCO$_3$ (2.75 g, 16.0 mmol) and H$_2$O (4.1 cm^3) in MeCN (70 cm^3) was stirred at 50 °C for 7 h. Filtration of the cooled mixture and the usual isolation from the filtrate provided **24** (1.9 g, 99%), m.p. 148–150 °C (lit.,[33] 137–148 °C); ν_{max}/cm^{-1} 1753 and 1615; δ_H 5.20 (1 H, dd, *J* 11.46, 7.3), 2.15 (3 H, s) and 0.81 (3 H, s); *m/z* 224 (M$^+$, 1%).

9-*Methyl*-trans-2-*decalone* (**13**).—To complete the carbonyl transposition,[33] a solution of **24** (2.6 g, 1.16 mmol) in dry Et$_2$O (150 cm^3) was added over 10 min to a solution of Ca (6.10 g, 152 mmol) in NH$_3$ (600 cm^3). The crude product, isolated by the usual procedure, was dissolved in acetone (100 cm^3) and oxidised with Jones' reagent, to afford crude **13** (1.8 g). Distillation at 87–88 °C and 1.2 mmHg (lit.,[33] 70 °C at 0.05 mmHg) gave **13** (1.65 g, 86%) of purity ⩾99% (GC); ν_{max}/cm^{-1} 1725; δ_H 2.34 (2 H, m), 2.15 (1 H, d, *J* 13.5), 2.09 (1 H, dd, *J* 13.6, 1.4), 1.15–1.60 (11 H, complex) and 0.79 (3 H, s); *m/z* 166 (M$^+$, 71%).

Enol acetates **14** and **15** were prepared from **13** in 88% yield as a mixture by the general procedure, b.p. 86–90 °C at 1.5 mmHg; ν_{max}/cm^{-1} 1762 and 1695; δ_H 5.29 (dt, *J* 5.1, 2.4), 5.19 (br s), 2.09 (3 H, s) and 0.89 (3 H, s); *m/z* (**14** and **15** not resolved) 208 (M$^+$, 24%) and 166 (100).

9-*Methyl*-cis-2-*decalone* (**16**).—Based on the procedure of Birch and Robinson,[36a] a solution of **19** (12.00 g, 80 mmol) in dry Et$_2$O (50 cm^3) was added under He at ice-bath temperature to a solution prepared from Mg (3.00 g, 120 mmol), MeI (19.5 g, 140 mmol) and dry Et$_2$O (150 cm^3), to which CuBr (200 mg, 1.4 mmol) had been added. The usual work-up provided crude **16** (11 g), which was purified by conversion into the semicarbazone, m.p. 208–209 °C (lit., 210–212,[37] 212–213[36a] °C). Recrystallisation from MeOH, regeneration with pyruvic acid in refluxing HOAc, and distillation at 69–71 °C and 0.4 mmHg (lit.,[37] 122–123 °C at 14 mmHg) yielded **16** (6.5 g, 49%) of purity >98% (GC); ν_{max}/cm^{-1} 1715; δ_H 0.96 (3 H, s); *m*/*z* 166 (M^+, 51%).

Enol acetates **17** and **18** were prepared from **16** in 84% yield as a mixture by the general procedure, b.p. 80–85 °C at 0.4 mmHg; ν_{max}/cm^{-1} 1765 and 1697; δ_H 5.23 (dt, *J* 5.4, 1.3 Hz), 5.04 (t, *J* 1.4), 2.10 (s), 2.09 (s), 1.06 (s) and 0.97 (s); *m*/*z* for **17**, 208 (M^+, 6%) and 151 (100); for **18**, 208 (M^+, 8%) and 151 (100).

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