Studies of Reaction Pathways by *X*-Ray Crystallography: a Spectroscopic, Crystallographic, and Theoretical (*ab initio*) Investigation of 6-Oxobicyclo[2.2.1]heptane-*endo*-2-carboxylic Acid

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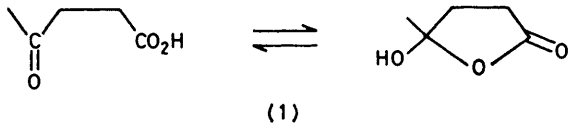
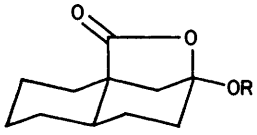
I.r. and n.m.r. spectroscopic evidence shows that the title compound (a norbornane derivative) exists, in solution, as a mixture of ' open ' (γ-keto-acid) and ' closed ' (hydroxylactone) forms separated by a low energy barrier. The structural differences between the norbornane and analogous *cis*- and *trans*-decalin keto-acids are discussed in terms of trajectory differences for ring closure: the results of calculations are presented in support of this.

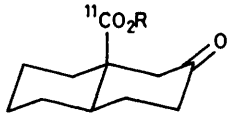
In a previous paper,[1] an attempt was made to use crystal structure, *X*-ray diffraction analysis to obtain information about the reaction pathway for the interconversion of a γ-keto-acid and a γ-hydroxylactone (1). In that study, crystal structure determination for four



(1)



(2) a; R = H
b; R = Me



(3) a; R = H
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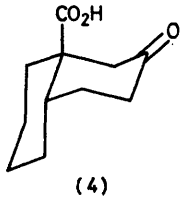
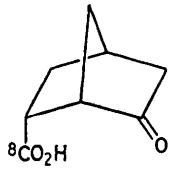
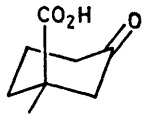


(4)

model compounds, two (2a and b) on the ' closed ' (hydroxylactone) side of the equilibrium and two (3b) and (4) on the ' open ' (keto-acid) side, together with i.r., and ^1H and ^{13}C n.m.r. spectroscopy, allowed several conclusions to be drawn about geometric and energetic features of the reaction path: (i) keto-acid (3a) cyclises *via* nucleophilic attack of the acid carbonyl oxygen on the ketone group, with simultaneous proton transfers; (ii) as this attack proceeds, the acid carbonyl group leaves its minimum energy conformation (roughly eclipsed with a C_α–C_β bond) and moves into a more optimal position for ring closure; (iii) during this closure, the ketone group undergoes pyramidalisation; (iv) towards the end of the closure reaction, and in the early stages of the reverse opening, there is coupling between antisymmetric C–O bond stretching and C–C–O bond angle variation at the reaction centre (the geminally dioxo-substituted, sp^3 carbon atom), lone-pair-σ^* (C–O) electronic interactions being important in this connection, and (v) during reaction, an approximately tetrahedral angle is maintained between the incoming nucleophile and the ketonic carbonyl group. In the work presented here we have tried to explore further the importance of trajectory of closure in isomerisation (1) through the synthesis and study of the norbornane γ-keto-acid (5) which must necessarily have a disposition of functional groups very different from that in the analogous decalins (3a) and (4). The results of a crystal structure analysis and spectroscopic investigation of (5) are presented below along with *ab initio*, molecular orbital calculations on (5) and (6)



(5)



(6)

(which is the crucial structural fragment in the decalin acids), and the molecular structures of (4) and (5) are compared with those of other γ-keto-acids and -esters retrieved from the Cambridge Crystallographic database.

RESULTS AND DISCUSSION

Spectroscopic Evidence.—The i.r., and ^1H and ^{13}C n.m.r., spectra of the norbornane keto-acid (5) show that its behaviour in solution resembles that of the analogous *trans*-decalin acid (3a) in that it exists, at room temperature, as a mixture of open and closed forms. The i.r. spectrum (in CCl_4) displays carbonyl absorptions at 1 790 (γ-lactone), 1 760 (ketonic carbonyl), and 1 710 cm^{-1} (free acid?), the relative intensities of which give a very approximate estimate of the [open] : [closed] concentration ratio as 10 : 1.

The ^1H n.m.r. spectrum of (3a)[1] is unusually broad.

Addition of D_2O broadens the signals further, H_2O has no effect, and a trace of HCl sharpens the signals. From these observations, it seems that the reaction rate is on the rapid-exchange side of the coalescence region, and that the rate-limiting step of the isomerisation involves proton transfer. The spectrum of (5) is not unduly broad, addition of D_2O has little effect, but addition of a proton acid causes slight line-broadening. These observations are consistent with the isomerisation rate being on the slow-exchange side of the coalescence region with proton transfer still involved in the rate-limiting step. In agreement with this conclusion, no significant change in the spectrum was observed on cooling of the solution to 163 K.

TABLE 1

Temperature dependence of the intensities [a] (in arbitrary units) for the C(8) signals in open and closed (5)

Open	20	95	30	30	40	20	20
Closed	3	22	7	9	12	8	10
Equilibrium constant K	6.67	4.41	4.32	3.33	3.29	2.50	2.00
T/K	254	250	244	233	228	208	193

[a] Intensity measurements are judged to be reproducible to ±5%.

The ^{13}C n.m.r. spectrum of (5) shows only seven absorptions at 300 K; cooling of the CD_2Cl_2 solution, however, leads to signal broadening, and at 190 K the presence of 16 signals (some still broad) indicates the coexistence of open and closed isomers. As the solution is warmed from 190 K, signals coalesce; for the signals corresponding to C(8), coalescence is complete at 258 K. Measurement of the relative intensities of the signals for C(8) in the open and closed forms as a function of temperature below 258 K (Table 1) and application of the Van't Hoff isochore (a plot of ln$K$ *versus* $1/T$ gives a straight line with slope −815.57, correlation coefficient 0.94) allows the estimation of thermodynamic parameters for the closed ⇌ open equilibrium: $\Delta H°$ 6 800(700) * J mol^{-1}, $\Delta S°$ 40 (4) J K^{-1} mol^{-1}, $\Delta G°_{298}$ −5 200(500) J mol^{-1}. [This treatment assumes that the nuclear Overhauser enhancement experienced by the C(8) nuclei in the two isomers is the same and that the resonances are not saturated.]

TABLE 2

Temperature dependence of the intensities [a] (in arbitrary units) for the C(11) signals in open and closed (3a)

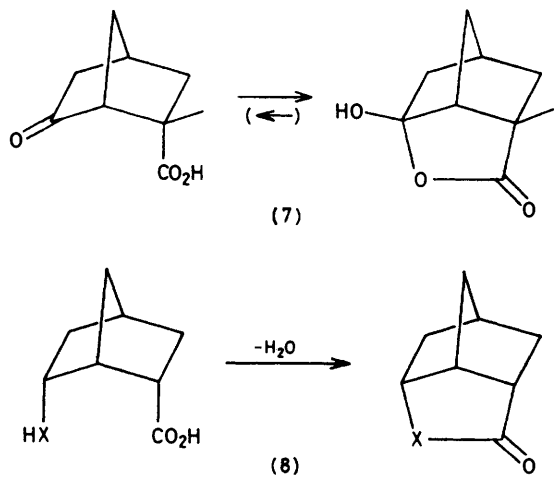
Open	40	20	20	20
Closed	30	8	7	6
K	1.33	2.50	2.86	3.33
T/K	210	218	223	228

[a] Reproducibility as in Table 1.

The *trans*-decalin acid (3a) similarly shows 22 ^{13}C resonances below *ca.* 235 K, corresponding to a mixture of open and closed isomers. The variation in intensities of the C(11) signals with temperature change (Table 2) again furnishes an estimate of thermodynamic parameters for the closed ⇌ open equilibrium: $\Delta H°$ 20 300(2 000) J mol^{-1}, $\Delta S°$ 100(10) J K^{-1} mol^{-1}, $\Delta G°_{298}$ −94 00(900) J mol^{-1}. Although these numbers are necessarily approximate, the differences between (3a) and (5) are marked. In both compounds, the entropy change on ring closure is unfavourable (as expected) whereas the enthalpy change is favourable.

However, the enthalpy of closure of the decalin acid is about three times that of the norbornane acid. This arises because of the greater degree of substitution at the carbon α to the carboxy-group in the former and the consequentially greater relief of steric strain on closure. It is worthwhile noting, in this connection, that alkylation α to the carboxy-group encourages closure in laevulinic acids,[2] and that the α-methylnorbornane acid (7) exists essentially completely in the hydroxylactone form in solution.[3] Furthermore, molecular mechanics calculations [4] suggest that little extra strain is introduced into the norbornane system by closure of the system shown in (8).

The entropy of opening is significantly larger for the decalin hydroxylactone than for the analogous norbornane. This may in part reflect the presence of a greater



number of rotational isomers of similar energy in the decalin keto-acid than in the norbornane keto-acid. More light is shed on this problem by the results of the *ab initio* calculations presented later.

The values of $\Delta G°_{298}$ found from the n.m.r. studies agree well with those predicted from i.r. spectroscopy.

Full line-shape analysis of the temperature dependence of the resonances due to C(8) in (5) and C(11) in (3a) affords estimates of activation parameters for ring closure of E_a *ca.* 28(6) kJ mol^{-1} for (3a) [1] and 29(6) kJ mol^{-1} for (5), *i.e.* the same within experimental error.

* Estimated errors are shown in parentheses.

Such measurements are rarely precise in natural-abundance ^{13}C n.m.r. spectroscopy: in this case the imprecision is compounded by the extreme sensitivity of the line shapes to traces of proton acids in the n.m.r. solutions, as expected for a process in which proton transfer is involved in the rate-limiting step. Few strong conclusions can therefore be drawn from these kinetics studies. The differences in enthalpy and entropy of activation for the two systems will presumably resemble the equilibrium thermodynamic parameters (these would suggest faster closure for the norbornane system) but superimposed upon these are *inter alia* the effects of the different approach geometries of the nucleophile to the carbonyl group in the two cases. The crystallographic results presented in the next section provide information on this latter point and a clue to the slower than expected closure in the norbornane keto-acid.

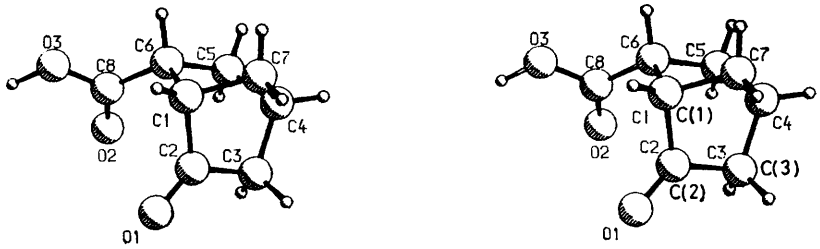


FIGURE 1 Stereoscopic picture of a molecule of (5) drawn with PLUTO 78 (Cambridge Crystallographic Data Centre, Cambridge)

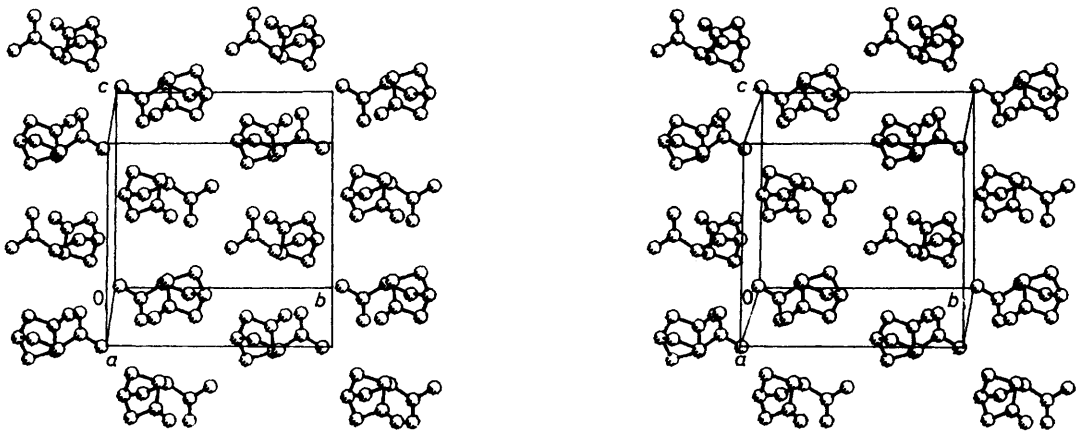


FIGURE 2 Stereoscopic picture of part of the crystal structure of (5) drawn with PLUTO 78

Crystallographic Evidence.—The results of a crystal structure analysis * of the norbornane keto-acid (5) are shown in Figure 1 (molecular structure), Figure 2 (crystal structure), and Table 3 (molecular geometry). Atom positions are listed in Table 4. Structure factors and components of vibration tensors are listed in Supplementary Publication No. SUP 23266 (15 pp.).†

If the crystal structures of (3a) and (5) reflected their solution thermodynamic stabilities then both substances would crystallise in the open, keto-acid forms. It might be argued, on the other hand, that the open forms are favoured solely because of rotational entropy and that this should be discounted in the solid state: on this basis, (3a) and (5) should crystallise as the thermochemically (ΔH) favoured hydroxylactone isomers. In practice, the situation is less clear cut: whereas the decalin keto-acid (3a) crystallises as a hydroxylactone, the analogous norbornane (5) exists as a keto-acid in the solid state. Additionally, the *cis*-decalin keto-acid (4), which exists in solution essentially exclusively in the open form (there is an additional entropy term in favour of this since the *cis*-decalin system can undergo ring inversion), crystallises also in the open form. It is, perhaps, naive to expect the crystal structures to reflect solution thermodynamics (or thermochemistry) for such finely balanced equilibria. Comparatively small changes in, for example, the pattern of hydrogen bonding between solution and solid state would be sufficient to tip the balance from one form to the other.

Although both *cis*-decalin (4) and norbornane (5) keto-acids crystallise in the open forms, there are important and significant differences in their structures. Whereas in the decalin the acid group is rotated through 9° from

* The data for this analysis were collected by R. W. H. S. at Lancaster.

† For details of Supplementary Publications see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 2*, 1981, Index Issue.

TABLE 3

Molecular geometry for (5). Estimated standard deviations are 0.005—0.008 Å for bond lengths and 0.3—0.5° for bond angles not involving hydrogen atoms. Some additional values are C–H and O–H 0.90—1.04 Å; angles involving hydrogen 105—121°

Bond lengths (Å)	
C(1)–C(2)	1.517
C(2)–C(3)	1.529
C(4)–C(5)	1.523
C(6)–C(8)	1.494
C(1)–C(6)	1.560
C(2)–O(1)	1.192
C(4)–C(7)	1.532
C(8)–O(2)	1.226
C(1)–C(7)	1.524
C(3)–C(4)	1.535
C(5)–C(6)	1.547
C(8)–O(3)	1.306
Bond angles (°)	
C(2)–C(1)–C(6)	106.7
C(1)–C(2)–C(3)	105.4
C(2)–C(3)–C(4)	102.3
C(5)–C(4)–C(7)	102.2
C(1)–C(6)–C(8)	112.9
C(6)–C(8)–O(2)	123.9
C(2)–C(1)–C(7)	101.2
C(1)–C(2)–O(1)	128.3
C(3)–C(4)–C(5)	107.9
C(4)–C(5)–C(6)	103.7
C(5)–C(6)–C(8)	115.4
C(6)–C(8)–O(3)	113.7
C(6)–C(1)–C(7)	100.1
C(3)–C(2)–O(1)	126.3
C(3)–C(4)–C(7)	100.7
C(1)–C(6)–C(5)	103.0
C(1)–C(7)–C(4)	95.4
O(2)–C(8)–O(3)	122.4
Torsion angles (°)	
C(6)–C(1)–C(2)–C(3)	72.5
C(7)–C(1)–C(2)–C(3)	−31.7
C(2)–C(1)–C(6)–C(5)	−68.0
C(7)–C(1)–C(6)–C(5)	37.1
C(2)–C(1)–C(7)–C(4)	53.6
C(1)–C(2)–C(3)–C(4)	−3.5
C(2)–C(3)–C(4)–C(5)	−69.4
C(3)–C(4)–C(5)–C(6)	73.3
C(3)–C(4)–C(7)–C(1)	−56.1
C(4)–C(5)–C(6)–C(1)	−2.8
C(1)–C(6)–C(8)–O(2)	−96.0
C(5)–C(6)–C(8)–O(2)	22.1
C(6)–C(1)–C(2)–O(1)	−108.3
C(7)–C(1)–C(2)–O(1)	147.4
C(2)–C(1)–C(6)–C(8)	57.2
C(7)–C(1)–C(6)–C(8)	162.2
C(6)–C(1)–C(7)–C(4)	−55.8
O(1)–C(2)–C(3)–C(4)	177.4
C(2)–C(3)–C(4)–C(7)	37.2
C(7)–C(4)–C(5)–C(6)	−32.4
C(5)–C(4)–C(7)–C(1)	55.0
C(4)–C(5)–C(6)–C(8)	−126.3
C(1)–C(6)–C(8)–O(3)	81.2
C(5)–C(6)–C(8)–O(3)	−160.7

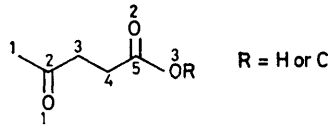
a generally favoured position where it can eclipse a C_α–C_β bond to one allowing non-bonded interaction with the ketone group (with concomitant pyramidalisation at this group), the carboxy-group in the norbornane acid is displaced by *ca.* 20° from C_α–C_β bond eclipsing but with no evidence for any nucleophile–ketone interaction: this position presumably represents a compromise between energetically favourable C_α–C_β bond eclipsing and unfavourable interactions with *endo*-hydrogen atoms. The hydrogen-bonding patterns in crystals of (4) and (5) are also quite different. In the decalin, the hydroxy hydrogen of one molecule is bonded to the ketone oxygen of a neighbour which, as we have proposed elsewhere,[1] may mimic the pattern of proton transfer occurring in solution; the norbornane simply forms hydrogen-bonded dimers in common with the majority of other carboxylic acids. In other words, whereas it can be argued that (4) shows, in its geometry, displacement along the reaction pathway for ring closure, (5) does not.

TABLE 4

Atomic co-ordinates for (5) ($\times 10^4$ for C and O and $\times 10^3$ for hydrogen atoms)

	x/a	*y/b*	*z/c*
C(1)	8 877(5)	2 674(3)	2 918(3)
C(2)	9 682(5)	2 790(3)	1 858(3)
C(3)	8 685(6)	3 918(3)	1 097(3)
C(4)	7 247(6)	4 308(3)	1 745(3)
C(5)	5 138(5)	3 527(3)	1 184(3)
C(6)	6 199(5)	2 413(3)	2 014(3)
C(7)	8 816(5)	3 906(3)	3 301(3)
C(8)	5 636(5)	1 380(3)	1 103(3)
O(1)	10 863(4)	2 156(2)	1 657(3)
O(2)	5 041(4)	1 399(2)	−0 167(2)
O(3)	5 933(4)	0 438(2)	1 802(2)
H(1)	973(6)	216(3)	361(4)
H(31)	774(8)	373(4)	005(5)
H(32)	996(7)	−059(4)	367(4)
H(4)	687(6)	513(3)	164(4)
H(51)	446(7)	340(4)	017(4)
H(52)	400(7)	379(3)	141(4)
H(6)	562(7)	232(4)	272(4)
H(71)	812(7)	394(4)	385(4)
H(72)	1 034(7)	422(3)	374(4)
H(8)	558(7)	−029(4)	118(4)

Detailed analysis of the geometries of the two systems shows that the minimum possible approach distance =O · · · C=O in the *cis*-decalin is 2.87 Å with an approach angle at the carbonyl group of 107°, *i.e.* close to the values of 2.91 Å and 102° observed in the crystal, whereas in the norbornane the closest approach is 2.66 Å at an angle of 78° (the values found in the crystal are 3.18 Å and 93°). When the angle of approach in the norbornane is close to tetrahedral (the preferred angle, according to Dunitz[5]) the internuclear separation is 4.0 Å. Thus, the norbornane can never adopt a conformation where both approach distance and angle favour an attractive interaction between carboxy and ketone groups, whereas this is readily possible in the *cis*-decalin. The crystal structures reflect these differences as may also the kinetics of ring closure alluded to above.



(9)

A search of the Cambridge Crystallographic database for molecules containing the structural fragment (9) yielded 11 compounds whose structures were derived from diffractometer data and were not disordered. The pyramidalisation at the ketone group for each compound was estimated by calculation of Δd, the deviation of the

carbon atom C(2) from the ketonic plane defined by C(1)O(1)C(3) (Figure 3). Two non-bonded interatomic distances r_1 and r_2 between the carboxy oxygens and the ketonic carbonyl carbon were calculated in each case

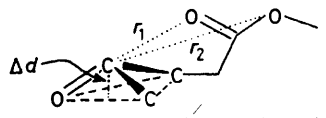


FIGURE 3 Definitions of Δd and $r_{1,2}$ (see text)

and the shorter distance was taken to indicate which of the oxygen atoms (if any) was acting as an incipient nucleophile. A plot of Δd *versus* separation (Figure 4) gives a fairly good straight line (correlation coefficient 0.728) on which keto-acids (4) and (5) fall closely.

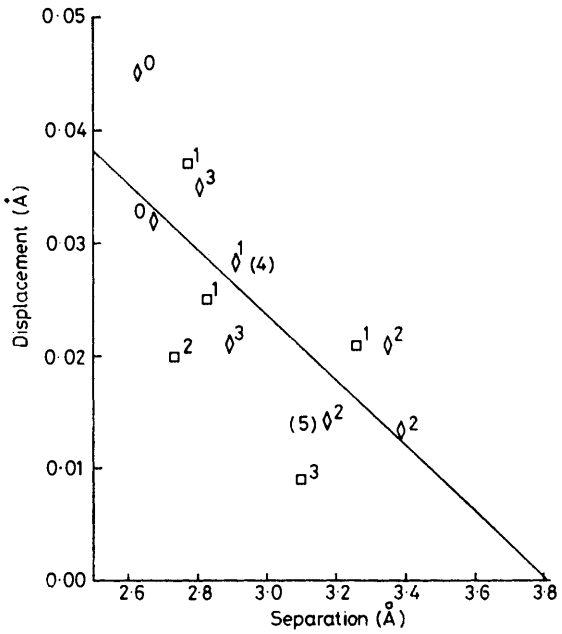


FIGURE 4 Plot of displacement *versus* separation for acids ◇ and esters □. Numerical superscripts key the average standard deviations of C–C bonds in individual structures following the Cambridge Data Centre convention: 0 ≡ unspecified; 1 ≡ 0.001—0.005; 2 ≡ 0.006—0.010; 3 ≡ 0.011—0.030 Å

Theoretical Calculations. In order to explore further the dependence of non-bonded attractive interactions on geometry implied by the crystallographic and spectroscopic work, *ab initio* calculations were performed (with the Gaussian 70 [6] package) on the norbornane keto-acid (5) crystal geometry and on the methylcyclohexane keto-acid (6) as a model for the *cis*-decalin keto-acid (4) [the limit of 70 atomic orbitals in the Gaussian 70 programs does not permit calculations on (4)]. In each case, the total molecular energy was calculated at 10° intervals of the torsional angle (defined in Figures 5 and 6), *i.e.* as a function of the disposition of the carboxy group with respect to the remainder of the molecule, with additional calculations interpolated around the extrema. A minimal STO-3G basis set was used generally, since test calculations with an extended (and, in

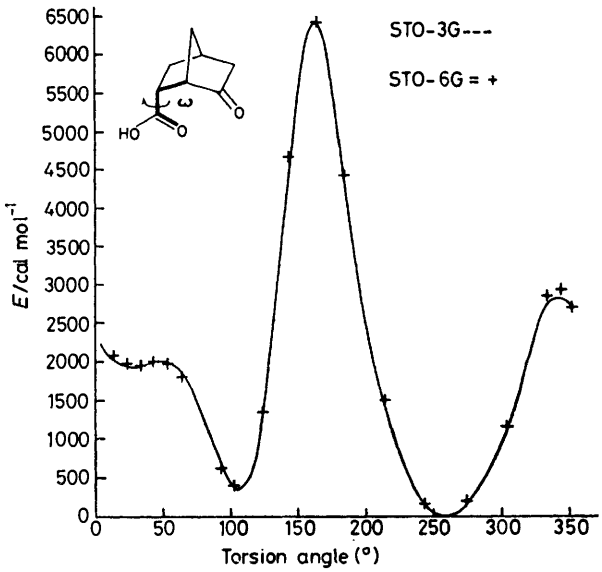


FIGURE 5 Dependence of total energy on torsion angle for (5); 1 Hartree = 627.505 06 kcal mol^{-1}

terms of computer time, much more costly) STO-6G basis set showed no significant changes. The variation in energy with ω, relative to the minimum energy conformation set to zero energy, is plotted in Figures 5 for (5) and 6 for (6).*

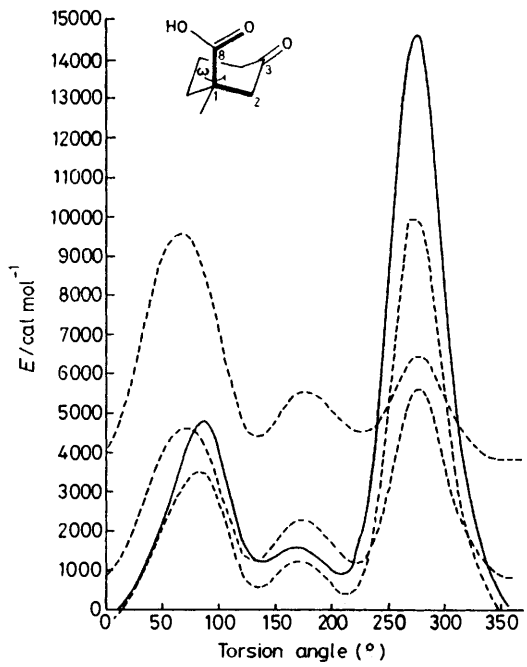


FIGURE 6 Dependence of total energy on torsion angle for methyl cyclohexane keto-acid (6) as a model for the *cis*-decalin keto-acid (4)

* Torsional angles from crystallographic data are presented in Table 3 in the range −180 to +180° whereas, for clarity, those used in the *ab initio* calculations are presented in the range 0 to 360°: the two systems are simply related by $-\omega = 360 - \omega$. The usual sign convention is used throughout, *i.e.* the angle 1–2–3–4 is positive when the sense of rotation from 1 to 4 is clockwise as viewed along the 2–3 bond.

In the norbornane case (Figure 5), there are two minima, one at the geometry found in the crystal, and one where the carboxy-group is rotated through 150°, *i.e.* the carbonyl group of the carboxy-function is as close to eclipsing or being antiperiplanar to a C_α–C_β bond as hindrance with *endo*-hydrogen atoms will allow: these conformations are shown diagrammatically in Figure 7.

FIGURE 7 Diagrammatic representations of minimum energy conformations for (5)

As expected, the global minimum energy conformation is that with approximate eclipsing of carbonyl and C_α–C_β bonds (ω 260°), being *ca.* 800 cal mol^{-1} more stable than when ω = 110°. This energy difference agrees well with the figure of *ca.* 1 kcal mol^{-1} predicted on the basis of i.r. work on similar systems.[7] There is no evidence of attractive interactions between carboxy and ketone functions.

Calculations on the *cis*-decalin model (6) predict three minima, the lowest of which, at ω 7°, has a structure gratifyingly close to that (ω 9.1°) found in the crystal for (4); the remaining minima (ω 140 and 215°) (Figure 8)

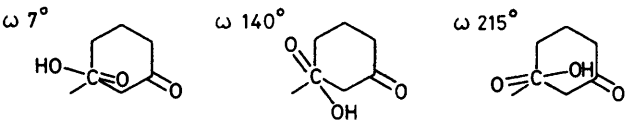


FIGURE 8 Diagrammatic representations of minimum energy conformations for (6)

correspond to structures in which the hydroxy-group may interact with the ketone carbonyl system. The existence of two minima separated by a small energy barrier for this interaction may well be an artefact. Presumably, lone-pair direction is important in such interactions (it has been noted,[8] for example, that a nitrogen nucleophile approaches a carbonyl group along a trajectory collinear with the three-fold axis through nitrogen): in the calculations described here, no attempt was made to adjust the lone-pair directions on the hydroxy oxygen as ω was changed. Most importantly, for present purposes, is the support that these calculations give to the presence of attractive electrophile–nucleophile interactions in the *cis*-decalin analogue (6).

The calculated energy barriers to rotation in (5) and (6) are too large, this being because the calculations are based on unrelaxed geometries. It is reasonable to suppose, in practice, that as the carboxy-group rotates through 360° the molecule will, at any instant, adjust bond and torsional angles slightly to minimise, insofar as possible, compression between adjacent groups. We have explored this possibility (fairly crudely) in the case of (6) by relaxing the 1,3-diaxial interaction between the CO_2H group and the axial hydrogen atom through reduction of the torsional angle Φ C(8)C(1)C(2)C(3) (Figure 6) by 2, 6, and 10°, respectively. The dramatic changes in predicted barrier magnitudes (though not, significantly, in the positions of minima) are shown, by dashed curves, in Figure 6. The large increase in total energy, for all values of ω, when Φ = 280.6° presumably indicates an excessive relaxation.

Conclusions.—The spectroscopic results show that keto-acid (5) behaves, in solution, in a similar fashion to the *trans*-decalin analogue (3a) and has a low energy barrier to isomerisation with the hydroxylactone form. Crystal structure determination reveals marked differences, however, between (5) and both *cis*-(4) and *trans*-decalin keto-acids which arise because the molecular geometry does not permit an attractive interaction between the functional groups in (5). This is supported by the results of molecular orbital calculations, which agree closely with experimental observations. Comparison of the structures of (4) and (5) with those of γ-keto-acids and -esters taken from the literature indicates that they show signs of movement along the reaction co-ordinate for ring closure commensurate with the separation of the functional groups.

EXPERIMENTAL

Synthesis.—Reaction of cyclopentadiene with acrylic acid,[9] iodolactonisation of the product,[10] and base treatment of the iodolactone gave keto-acid (5), m.p. 102—103 °C (lit.,[11] 103—104 °C). Crystals were obtained by slow evaporation of a solution in cyclohexane–ethyl acetate.

Spectroscopy.—I.r. spectra were measured on Perkin-Elmer 257 and 521 spectrometers. ^{1}H N.m.r. spectra were recorded on a Perkin-Elmer R34 spectrometer (220 MHz) and ^{13}C spectra on a Varian XL-100 spectrometer (25.15 MHz). Solutions in $CDCl_3$ or CD_2Cl_2 (dried over molecular sieves and passed through an alumina column prior to use) were *ca.* 1M in substrate for ^{13}C n.m.r. spectroscopy.

Crystallography.—$C_8H_{10}O_3$, M = 154.05. Monoclinic, a = 6.703(7), b = 11.836(12), c = 10.918(7) Å, β = 121.6 (2)°, Z = 4, D_c = 1.39 g cm^{-3}, space group $P2_1/c$.

Intensities of 1 446 reflexions [1 298 with $I \geqslant 3\sigma(I)$] were recorded on a Stoe STADI-2 diffractometer with graphite-monochromatised Mo-K_α radiation. The structure was solved by direct methods (MULTAN 78 [12]) and refined by full-matrix, least squares procedures (*X*-Ray '72 [13]) with unit weights. At an intermediate stage in the refinement, all hydrogen atom positions were located from a difference-Fourier map. Final refinement cycles included anisotropic vibration parameters for non-hydrogen, isotropic parameters for hydrogen atoms and separate refinement of inter-layer scale factors: an extinction correction was not required. The final R factor was 0.063. Analysis of vibrational ellipsoids for non-hydrogen atoms in terms of rigid-body motion [14] gave poor agreement between observed and calculated tensor components [$\langle\sigma^2(U_{ij})\rangle^{1/2}$ = 0.0043 Å^2], large discrepancies occurring for the atoms of the carboxy-group suggesting libration with respect to the norbornane ring system. A final difference synthesis revealed no significant electron density maxima.

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