identified unambiguously. The disorder in the α-cyclopentyl-4-carboxypropiophenone structure makes it difficult to establish H-atom positions, and the closest γ-H···O distances of 3·46 and 3·10 Å in the two conformers (Table 3) are rather long for abstraction. The cyclohexyl and cyclooctyl compounds have more typical H···O distances of 2·73 and 2·59 Å, respectively, with τ angles of 65 and 50°, and Δ angles of 73 and 79° (Table 3).

As for all the acetophenones previously studied, the amounts of cyclization products for the cycloalkylpropiophenones are relatively insensitive to reaction medium (Table 3), again indicating that the photoreactions are controlled mainly by intramolecular factors. There is a similar, although not so marked tendency for increase in cyclization with increasing cycloalkyl ring size. Despite the large changes in molecular conformation there is little difference between the cyclization-to-cleavage ratios for the aceto- and propiophenones (Table 3). The only significant change is an increase in cyclization for the cyclopentylpropiophenone, in accord with the behaviour noted previously in related systems. The cyclohexyl- and cyclooctylacetophenones give mainly cyclization products anyway, so it is perhaps not surprising that α-methyl substitution does not increase the amount of cyclization further. The radical *p*-orbital angles for the cycloalkylpropiophenones are in fact more favourable for cleavage than are those in the acetophenones (Table 3). The photochemical data are insufficiently well established for comment to be made on ratios of the various possible cyclobutanol photoproducts, although the geometry of the cyclooctylpropiophenone molecule suggests that *trans*-fused ring products will again predominate for the larger cycloalkyl rings.

We thank Professor J. R. Scheffer, Dr N. Omkaram and Mr B. Harkness for collaborative photochemical studies, the Natural Sciences and Engineering Research Council of Canada for financial support, and the University of British Columbia Computing Centre for assistance.

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Structure of an Asymmetrically Substituted Tetrahydro-1,4-naphthoquinone and Conformational Energy Surfaces

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(*Received* 28 *December* 1987; *accepted* 26 *April* 1988)

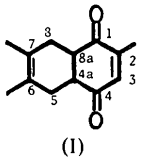
Abstract

The crystal structure of an asymmetrically substituted tetrahydro-1,4-naphthoquinone has been determined, and the structural results have been used to study the conformational inversion pathways. 2,6,7-Trimethyl-4aβ,5,8,8aβ-tetrahydro-1,4-naphthoquinone, $C_{13}H_{16}O_2$, $M_r = 204{\cdot}27$, monoclinic, $P2_1/n$, $a = 19{\cdot}191\ (11)$, $b = 5{\cdot}278\ (2)$, $c = 22{\cdot}330\ (15)$ Å, $\beta = 90{\cdot}70\ (3)°$, $V = 2261{\cdot}6\ (2{\cdot}2)$ Å^3, $Z = 8$ [two molecules, (I*a*) and (I*b*), per asymmetric unit], $D_x = 1{\cdot}199$ g cm^{-3}, Mo $K\alpha_1$, $\lambda = 0{\cdot}70930$ Å, $\mu = 0{\cdot}74$ cm^{-1}, $F(000) = 880$, $T = 295$ K, $R = 0{\cdot}095$ for 1463 observed reflections. The two crystallographically independent molecules have different conformations, each molecule being twisted such that the bridgehead H atoms are staggered, with a torsion angle of −52° for molecule (I*a*), 51° for (I*b*). Bond lengths and angles are close to normal values. Molecular-energy calculations are used to determine the energies of the two observed molecular conformers of tetrahydronaphthoquinone and of hypothetical higher-energy conformations, and thus to map the conformational energy surface. The two conformers are interconvertible (in solution) *via* higher-energy conformations, with an energy barrier of about 33 kJ mol^{-1}.

0108-7681/88/050538-07$03.00

Introduction

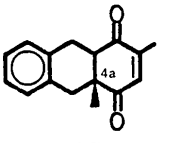
The present crystallographic study of compound (I) was undertaken as part of a study of the photochemistry of asymmetrically substituted 1,4-naphthoquinone systems (Ariel, Evans, Hwang, Jay, Scheffer, Trotter & Wong, 1985; Ariel & Trotter, 1987).



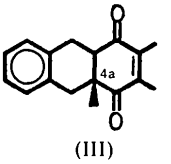
(I)

The tetrahydronaphthoquinone ring system can exist as two low-energy conformers, *A* and *B* (Fig. 1); both have fused six-membered rings with half-chair conformations, and are folded and twisted about the C(4a)–C(8a) bond. For consistency with previous studies of naphthoquinols (Trotter, 1983), conformer *A* is here defined as that with a C(5) H atom in a position suitable for abstraction by the ene-dione C=C bond, and *B* with an abstractable C(8) H atom. *A* and *B* conformers can be interconverted by ring 'flipping' involving single-bond rotation, *via* a higher-energy conformation, such as *C*, with eclipsed 4a/8a bridgehead substituents (Fig. 1).

All the tetrahydronaphthoquinones studied previously (Phillips & Trotter, 1977) are symmetrically substituted, so that conformers *A* and *B* are exactly equivalent (but enantiomorphic; however, all the materials studied are racemates, so that both enantiomers are present). Recently the crystal structures of the tetrahydronaphthoquinone analogues (II) and (III) have been determined (Ariel & Trotter, 1987); these molecules are asymmetric because of the C(4a)–Me substituent. For (II), only conformer *B* is found in the solid state* (Fig. 1), with the C(4a)–Me substituent in a pseudo-axial site on the half-chair cyclohexenedione ring; for (III), only conformer *A* is present in the crystal, with a pseudo-equatorial C(4a)–Me substituent on the cyclohexenedione ring. A qualitative study of the molecular structures of (II) and (III) suggests that conformation *B* is slightly more stable for these molecules, since conformation *A* exhibits unfavourable 1–3 diaxial steric interactions between the cyclohexenedione pseudo-equatorial C(4a)–Me group (which is pseudo-axial on the central ring) and the pseudo-axial H atom on C(8) of the central ring. This was confirmed by molecular-mechanics calculations, using the *MMP*2 computer program (Allinger & Flanagan, 1983), which determined the energy differences between the *A* and *B* conformations of both compounds. Although the energy differences are small, they are in accord with conformation *B* being slightly more stable than *A*, by 0·4 and 1·2 kJ mol^{-1} for (II) and (III), respectively (Ariel & Trotter, 1987).



(II)



(III)

We report here the crystal structure of compound (I), and utilize the structural data to determine the energies of conformational inversion in these systems.

Experimental

Crystal size 0·2 × 0·3 × 0·5 mm, m.p. 366–367 K, Enraf–Nonius CAD-4 diffractometer, graphite-monochromatized Mo $K\alpha$ radiation; lattice parameters from settings of 19 reflections with $6 \le \theta \le 16°$; 4590 reflections measured with $\theta \le 25°$, $h = -22$ to 22, $k = 0$–6, $l = 0$–26; ω–(2/3)θ scan, ω-scan width $(1{\cdot}00 + 0{\cdot}35\tan\theta)°$, extended 25% on each side for background measurement, horizontal aperture $(1{\cdot}0 + \tan\theta)$ mm, vertical aperture 4 mm; Lp correction. Three standard reflections (128, 523, 901) were monitored every hour of exposure time for random intensity fluctuations, and every 150 reflections for orientation control; intensity decay during data collection of 17%, although corrected, limited the accuracy of the data set. Structure was solved by direct methods using *SHELX*76 (Sheldrick, 1976) and refined by full-matrix least squares minimizing $\sum w(|F_o| - |F_c|)^2$. Except for the ethylenic H atom (located in a difference synthesis), all H atoms were placed in calculated positions; methyl H atoms were then refined as rigid groups possessing a local C_3 symmetry; temperature factors of all H atoms were refined isotropically. 327 parameters refined consisting of 114 positional parameters, 180 anisotropic temperature factors, 32 isotropic temperature factors, and a scale factor. No corrections for absorption. Five intense low-order reflections omitted

* In Ariel & Trotter (1987), the conformation of compound (II) was arbitrarily named *A*, and that of (III) *B*; these labels are here interchanged, for consistency with the present paper and with previous descriptions of the tetrahydronaphthoquinols (Trotter, 1983).

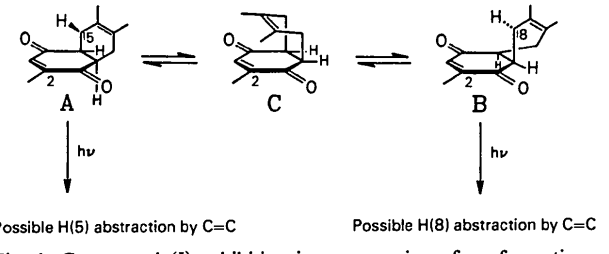


Fig. 1. Compound (I) exhibiting interconversion of conformations *A* and *B* *via* conformer *C*.

Table 1. *Atom coordinates* ($\times 10^4$) *and equivalent isotropic temperature factors* ($Å^2 \times 10^3$)

$$U_{eq} = \tfrac{1}{3}\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j .$$

	Molecule (I*a*)				Molecule (I*b*)			
	x	y	z	U_{eq}	x	y	z	U_{eq}
O(1)	9605 (2)	−15646 (9)	−2896 (2)	79	8008 (2)	301 (10)	278 (2)	89
O(4)	9680 (2)	−7777 (10)	−1426 (2)	97	7591 (2)	−7519 (9)	−1165 (2)	76
C(1)	9574 (4)	−13560 (15)	−2644 (3)	61	7900 (4)	−1434 (13)	−75 (3)	61
C(2)	8952 (4)	−12740 (15)	−2319 (3)	63	8502 (4)	−2840 (15)	−320 (3)	65
C(21)	8281 (4)	−14201 (16)	−2439 (4)	77	9237 (4)	−2080 (19)	−130 (5)	99
C(3)	9006 (4)	−10820 (15)	−1927 (3)	68	8387 (4)	−4817 (15)	−700 (3)	64
C(4)	9671 (4)	−9512 (15)	−1799 (3)	72	7696 (4)	−5505 (15)	−912 (3)	61
C(4a)	10328 (4)	−10357 (13)	−2085 (3)	56	7120 (4)	−3515 (13)	−846 (3)	57
C(5)	10668 (3)	−12318 (14)	−1648 (3)	64	6387 (4)	−4537 (14)	−975 (3)	65
C(6)	11245 (3)	−13844 (12)	−1937 (3)	61	6069 (3)	−5923 (13)	−455 (3)	57
C(61)	11717 (5)	−15207 (19)	−1480 (3)	93	5432 (4)	−7516 (19)	−627 (4)	82
C(7)	11318 (3)	−14053 (12)	−2525 (3)	59	6333 (3)	−5829 (12)	96 (3)	50
C(71)	11882 (4)	−15580 (16)	−2822 (4)	81	6061 (5)	−7381 (18)	613 (3)	82
C(8)	10834 (3)	−12712 (14)	−2962 (3)	65	6967 (4)	−4266 (14)	255 (3)	60
C(8a)	10173 (3)	−11620 (12)	−2691 (3)	56	7182 (3)	−2325 (14)	−217 (3)	56

from final refinement because of suspected extinction errors. Convergence at $R = 0{\cdot}095$, $wR = 0{\cdot}065$ for 1463 observed reflections for which $F \geq 3\sigma(F)$, where $\sigma^2(I) = S + 2B + [0{\cdot}04(S-B)]^2$, S = scan count, B = time-averaged background count. $R = 0{\cdot}192$, $wR = 0{\cdot}078$ for all data, $w = 1/\sigma^2(F)$, $(\Delta/\sigma)_{max} = 0{\cdot}4$, highest $\Delta\rho$ peak in final difference synthesis ($0{\cdot}34$ e $Å^{-3}$) is located near C(21). Atomic scattering factors from Cromer & Mann (1968) and Stewart, Davidson & Simpson (1965). The high final value of R is a result of the poor quality of the crystal available.

Discussion

Final atomic coordinates for (I) are in Table 1, and bond distances, bond angles and selected torsion angles in Table 2.*

Crystals of (I) contain two molecules, (I*a*) and (I*b*), in the asymmetric unit, each molecule having the usual twisted conformation (Phillips & Trotter, 1977). The most important and interesting feature of the structure is that the two independent molecules have *different* low-energy conformations, conformation *A* for molecule (I*a*) and *B* for (I*b*) (Fig. 2). The degrees of 'twist' are shown by the torsion angles C(5)–C(4a)–C(8a)–C(1), 70 (1)° for (I*a*), and C(4)–C(4a)–C(8a)–C(8), −70 (1)° for (I*b*); the corresponding values of the H–C(4a)–C(8a)–H torsion angles (calculated H-atom positions) are −52 and 51°. Molecules (I*a*) and (I*b*) can be interconverted (in solution media) by rotation about the C(4a)–C(8a) bond. A ^{13}C NMR study of compound (I) suggests a rapid equilibrium between two conformers in solution, with splitting of peaks in the solid state indicating the presence of the two conformers (Northcote, 1985). The ring systems in the two molecules are enantiomeric and, because of the presence of the C(2)–Me substituent, the two molecules are diastereomers (which are interconvertible in solution); the material is racemic, so that both enantiomers of both diastereomers are present in the crystal. Molecules (I*a*) and (I*b*) are related in the crystal approximately by reflection in a plane at $x = 0{\cdot}87$, plus translation, $y = 0{\cdot}80$, $z = 0{\cdot}17$ [except for methyl group C(21)] (Fig. 3). Bond lengths and angles in molecules (I*a*) and (I*b*) (Table 2) are generally close to normal values. There is some apparent asymmetry in both molecules with bonds C(4)–C(4a) in molecule (I*a*) and C(1)–C(8a) in molecule (I*b*), which are both equatorial with respect to the cyclohexene ring, shorter [at 1·489 (11) and 1·486 (10) Å, respectively] than the same bonds in the other molecule, which are axial [1·533 (11) and 1·545 (10) Å, respectively]; there are also related differences in bond angles at C(4a) and C(8a), *e.g.* C(4)–C(4a)–C(5) = 106·3 (5) and 113·7 (6)°, C(1)–C(8a)–C(8) = 113·5 (6) and 108·7 (5)°, in (I*a*) and (I*b*), respectively. Such asymmetry has not been observed previously in tetrahydronaphthoquinone systems (Phillips & Trotter, 1977) and while it may possibly result from the asymmetry in C(2)/C(3) substitution, it may also be an artifact resulting from the rather poor-quality diffraction data.

Three principal reaction pathways are found in photolysis of tetrahydronaphthoquinones; the relevant structural data for possible pathways for compound (I) are:

(1) (2+2) intermolecular cycloaddition in the solid state. The C(2)=C(3) bonds of molecules (I*a*) (x, $1+y$, z) and (I*b*) (x, y, z) are almost antiparallel, and separated by 3·9 Å [C(2)(I*a*)···C(3)(I*b*) = 3·94 (1) Å, C(3)(I*a*)···C(2)(I*b*) = 3·87 (1) Å] (Fig. 4), an ideal arrangement for photoaddition to give a dimeric product (Trotter, 1983).

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and bond distances and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44993 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å), *bond angles* (°) *and selected torsion angles* (°)

	Molecule (I*a*)	Molecule (I*b*)
C(1)–O(1)	1·237 (9)	1·225 (9)
C(1)–C(2)	1·469 (10)	1·483 (11)
C(2)–C(21)	1·521 (11)	1·521 (11)
C(2)–C(3)	1·343 (11)	1·361 (11)
C(3)–C(4)	1·475 (12)	1·450 (12)
C(4)–O(4)	1·238 (9)	1·220 (9)
C(4)–C(4a)	1·489 (11)	1·533 (11)
C(4a)–C(5)	1·560 (9)	1·531 (10)
C(5)–C(6)	1·519 (10)	1·508 (10)
C(6)–C(61)	1·536 (11)	1·528 (11)
C(6)–C(7)	1·325 (10)	1·327 (10)
C(7)–C(71)	1·511 (10)	1·513 (10)
C(7)–C(8)	1·514 (9)	1·508 (10)
C(8)–C(8a)	1·524 (9)	1·532 (9)
C(1)–C(8a)	1·545 (10)	1·486 (10)
C(4a)–C(8a)	1·534 (9)	1·541 (9)
C(2)–C(1)–O(1)	122·1 (7)	119·0 (7)
C(8a)–C(1)–O(1)	121·2 (6)	121·5 (7)
C(8a)–C(1)–C(2)	116·6 (6)	119·2 (6)
C(21)–C(2)–C(1)	117·1 (6)	119·3 (7)
C(3)–C(2)–C(1)	119·2 (7)	119·5 (7)
C(3)–C(2)–C(21)	123·8 (7)	121·2 (7)
C(4)–C(3)–C(2)	122·7 (7)	122·4 (7)
C(3)–C(4)–O(4)	118·8 (7)	121·0 (7)
C(4a)–C(4)–O(4)	120·4 (7)	121·8 (7)
C(4a)–C(4)–C(3)	120·7 (7)	117·1 (6)
C(5)–C(4a)–C(4)	106·3 (5)	113·7 (6)
C(8a)–C(4a)–C(4)	110·6 (6)	108·6 (5)
C(8a)–C(4a)–C(5)	109·8 (5)	112·1 (5)
C(6)–C(5)–C(4a)	112·7 (5)	113·9 (5)
C(61)–C(6)–C(5)	113·1 (6)	113·8 (6)
C(7)–C(6)–C(5)	123·5 (6)	122·9 (6)
C(7)–C(6)–C(61)	123·4 (6)	123·3 (6)
C(71)–C(7)–C(6)	124·3 (6)	123·7 (6)
C(8)–C(7)–C(6)	121·8 (6)	122·5 (6)
C(8)–C(7)–C(71)	113·8 (6)	113·7 (6)
C(8a)–C(8)–C(7)	115·3 (5)	115·3 (5)
C(8)–C(8a)–C(1)	113·5 (6)	108·7 (5)
C(4a)–C(8a)–C(1)	111·4 (5)	112·6 (5)
C(8)–C(8a)–C(4a)	111·2 (5)	109·7 (6)
O(1)–C(1)–C(2)–C(3)	162*	178
C(8a)–C(1)–C(2)–C(3)	−21	4
O(1)–C(1)–C(8a)–C(4a)	−137	153
O(1)–C(1)–C(8a)–C(8)	−11	−85
C(2)–C(1)–C(8a)–C(4a)	46	−33
C(2)–C(1)–C(8a)–C(8)	172	89
C(1)–C(2)–C(3)–C(4)	−1	5
C(2)–C(3)–C(4)–O(4)	−179	−167
C(2)–C(3)–C(4)–C(4a)	−3	17
O(4)–C(4)–C(4a)–C(5)	85	15
O(4)–C(4)–C(4a)–C(8a)	−156	140
C(3)–C(4)–C(4a)–C(5)	−91	−170
C(3)–C(4)–C(4a)–C(8a)	28	−44
C(4)–C(4a)–C(5)–C(6)	166	82
C(8a)–C(4a)–C(5)–C(6)	46	−42
C(4)–C(4a)–C(8a)–C(1)	−47	51
C(4)–C(4a)–C(8a)–C(8)	−175	−70
C(5)–C(4a)–C(8a)–C(1)	70	177
C(5)–C(4a)–C(8a)–C(8)	−58	56
C(4a)–C(5)–C(6)–C(7)	−19	13
C(5)–C(6)–C(7)–C(8)	2	2
C(6)–C(7)–C(8)–C(8a)	−13	14
C(7)–C(8)–C(8a)–C(1)	−85	−165
C(7)–C(8)–C(8a)–C(4a)	42	−42

* Standard deviations for all torsion angles equal 1°.

(2) β-H abstraction from C(8) of (I*a*) [or C(5) of (I*b*)] by carbonyl O(1) [or O(4)] atom. The parameters for molecules (I*a*) and (I*b*) are favourable for such a process, with H···O = 2·44, 2·46 Å, τ (angle subtended by the O···Hβ vector and its projection on the plane of the carbonyl group) = 7, 5°, and C=O···H = 85, 85° (ideal values are < 2·7 Å, 0 and 90°, respectively). The next step in the reaction involves C(1)···C(6) [or C(4)···C(7)] bonding, with 3·56 (1) and 3·48 (1) Å distances which are of the order of the van der Waals separations.

(3) γ-H abstraction of H(51) of (I*a*) [or H(82) of (I*b*)] by enone C(2) [or C(3)] atom, followed by C(3)···C(5) [or C(2)···C(8)] bonding. The relevant Hγ···C distances of 3·16 and 3·03 Å are rather long for abstraction, but the τ and Δ (C=C···H) angles and C···C distances are quite favourable [43, 46°; 71, 74°; 3·35 (1), 3·33 (1) Å].

Photolysis of (I) in solution (Scheffer, Jennings & Louwerens, 1976) results in β-H abstraction by the two non-equivalent O atoms in the molecule to form biradical intermediates, yielding five products that were isolated and identified. Three of the products were considered to have resulted from the abstraction of an

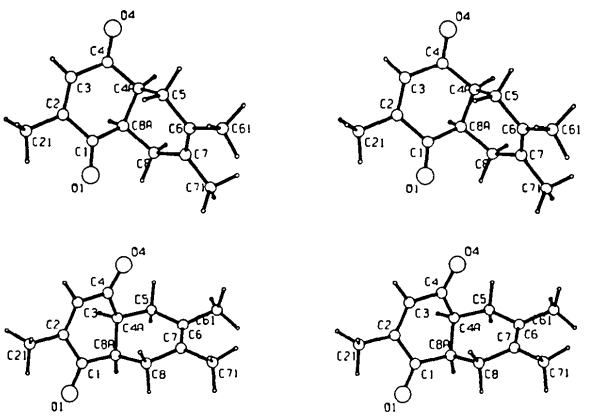


Fig. 2. Stereoviews of compound (I) with crystallographic atom labelling. Top – molecule (I*a*), exhibiting conformation *A*. Bottom – molecule (I*b*), exhibiting conformation *B*.

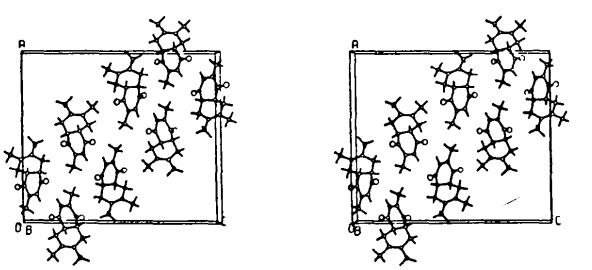


Fig. 3. Stereoview of the packing arrangement of compound (I). Origin lower left, *a* axis vertical, *c* axis horizontal, *b* axis into plane of paper.

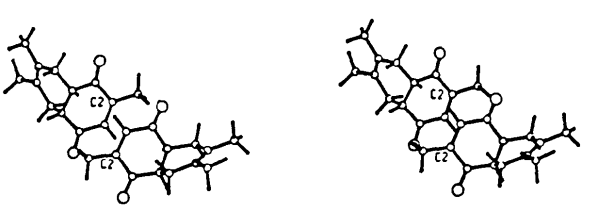


Fig. 4. Stereoview of molecules (I*a*) and (I*b*) aligned for (2 + 2) photodimerization.

H atom from C(5) by O(4), the remaining two from the abstraction of an H atom from C(8) by O(1). The ratio of photoproducts obtained *via* these two routes (2:1) shows preference for the C(5)—H abstraction, since some extra stability is afforded to the allyl radical in the enedione ring by the C(2) methyl group. Two of the products involve C(1)—C(6) and C(4)—C(7) bond formation, for which no major conformational changes are needed. The other products require conformational inversion to allow C(3)—C(6), C(3)—C(8) and C(2)—C(5) bonding. There is some evidence that the C(1)—C(6) and C(4)—C(7) compounds may be the sole initial products, with the other products resulting from subsequent rearrangements of these initial products.

The solid-state photolysis is much slower than solution photolysis; this could be an intrinsic property of the solid-state reaction caused by the molecular rigidity associated with the crystal lattice or could be caused by the greater concentration of chromophores in the solid as compared with solution (Northcote, 1985). The solid-state photoproducts are similar to those found in solution, indicating that β-H abstraction by an O atom is again the favoured route. The C(1)—C(6) and C(4)—C(7) bonded molecules are the topochemically allowed photoproducts, but the occurrence of the other products indicates either loss of topochemical control, or subsequent rearrangement processes.

The absence in solution and in the solid state of photoproducts derived from γ-H abstraction by enone C may be a result of the rather long H$\gamma\cdots$C distances; in addition, this route has been observed previously only for 2,3-dimethyl-substituted molecules.

The solid-state photolysis gives a very small amount of dimeric product (Northcote, 1985). However, the presence of a dimer peak and a $(2M-18)$ peak in the mass spectrum indicates that it may be an alcoholic dimer, rather than a (2+2)-cycloaddition dimer. This suggests a possible intermolecular H-atom abstraction and subsequent dimerization, a reaction not previously reported in solid-state organic photochemistry. There is an intermolecular H$\cdots$O contact of 2·54 Å between an H atom of a C(21) Me group and O(4), although the τ angle of 80° is not favourable for abstraction, and a C(21)$\cdots$C(4) distance of 3·68 Å. The absence of a (2+2) dimer may result from intermolecular steric compression between neighbouring C(21) methyl groups during a dimerization reaction (Ariel, Askari, Evans, Hwang, Jay, Scheffer, Trotter, Walsh & Wong, 1987).

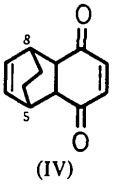
Conformational energies

The observation of two different molecular conformations, *A* and *B*, for the two molecules (I*a*) and (I*b*) of compound (I) afforded the opportunity of making a detailed study of the energy changes involved in their interconversion.

A qualitative examination of the molecular structure of (I) suggests that conformations *A* and *B* have equal energies, since the asymmetry introduced by the methyl group on C(2) is too far from the ring junction to exert any significant steric influence. A more-quantitative estimate of the energies was obtained from molecular-mechanics calculations, using the *MMP*2 program, which indicated equal conformational energies for the two conformers.

The molecular volumes of conformers *A* and *B* were calculated, to evaluate if there is any size difference between them. The van der Waals radii used were 1·75 Å for C, 1·40 Å for O, and 1·17 Å for H atoms. It was found that both conformers occupy the same molecular volume of 196 Å^3. These two conformers are thus of equal conformational energy and molecular volume. The reason for compound (I) exhibiting conformational dimorphism might be to achieve better crystal packing (Fig. 3), although it is difficult to pinpoint any specific packing benefits of this particular arrangement.

The complete conformational-energy surface was now examined. To simplify the procedure, the analysis was performed for the parent compound, 4aβ,5,8,8aβ-tetrahydro-1,4-naphthoquinone; for this symmetrical compound, conformers *A* and *B* are enantiomers with identical energies, and detailed molecular-geometry parameters are available (Phillips & Trotter, 1977). Reliable molecular parameters can also be obtained for the possible high-energy conformation *C* (Fig. 1), based on the structure of compound (IV), in which the ethano bridge locks the molecule into a conformation with eclipsed ring-junction H atoms, and parallel C=C bonds separated by 3·53 Å (Greenhough & Trotter, 1980). The ene-1,4-dione ring of (IV) is close to planar, and the other six-membered rings have boat conformations. Conformation *C* was generated from (IV) by replacing the ethano group with two H atoms (Fig. 5). Two other high-energy conformations, *C'* and *C''* (Fig. 5), were generated from *C*; *C'* was obtained by reflecting the C(5)—C(6)—C(7)—C(8) portion of *C* in the C(5)—C(4a)—C(8a)—C(8) plane; and *C''* by 55° rotation of the C(6)—C(7) region around C(5)$\cdots$C(8), followed by minor adjustments of bond lengths and angles.



(IV)

The conformational energies of each of *A*–*C''* were calculated using the *MMP*2 program. The energy-minimization procedure of *MMP*2 can result in large changes in total steric energy as a result of fairly minor

changes in bond lengths and angles (including those involving H atoms) to fit the idealized parameters of *MMP*2. The conformational energy was therefore taken as the total steric energy, less the energy of bond compression and stretching, but including angle-bending energy which is of importance in conformation *C''*, where the planar cyclohexene ring is considerably strained. Conformations *A* and *B* are preserved in the energy-minimization process, which confirms that these are the most stable conformers. Conformations *C* and *C'* have approximately equal energies, but energy minimization results in major changes in conformation, with the final energy-minimized conformations being either *A* or *B*. The higher-energy conformation *C''* also results in *A* or *B* on energy minimization, *via* pathways which merge with those of the *C*, *C'*→*A*, *B* routes.

The intermediate points in these energy minimizations allow mapping of the complete conformational-energy surface. This surface is shown in Fig. 6, as a function of the ring-junction torsion angle (which changes from −60 to +60° in converting *A* to *B*) and of the total displacement of C(6) and C(7) from a mean plane through C(5)–C(4a)–C(8a)–C(8). The detailed contours in Fig. 6 are somewhat speculative, but are based on the calculated values of the energies for the conformations shown on the figure. The minimum-energy pathways for interconversion of conformers *A* and *B* are *via* the higher-energy conformations *C* or *C'* (Figs. 5 and 6), both pathways involving calculated energy barriers of about 33 kJ mol^{-1}; this probably corresponds most closely to the enthalpy barrier. Previous temperature-dependent ^{13}C NMR measurements for 4a,8a-dimethyl-substituted compounds have indicated free-energy-barrier, $\Delta G^{\ddagger}$, values for the conformational inversions of about 37 kJ mol^{-1} (Ariel, Scheffer, Trotter & Wong, 1983); the calculated energy barriers therefore appear to be of the correct order of magnitude, and give some confidence that the calculated conformational-energy surface shown in Fig. 6 has some validity.

We thank Professor J. R. Scheffer and Mr P. T. Northcote for their collaborative studies on the solid-

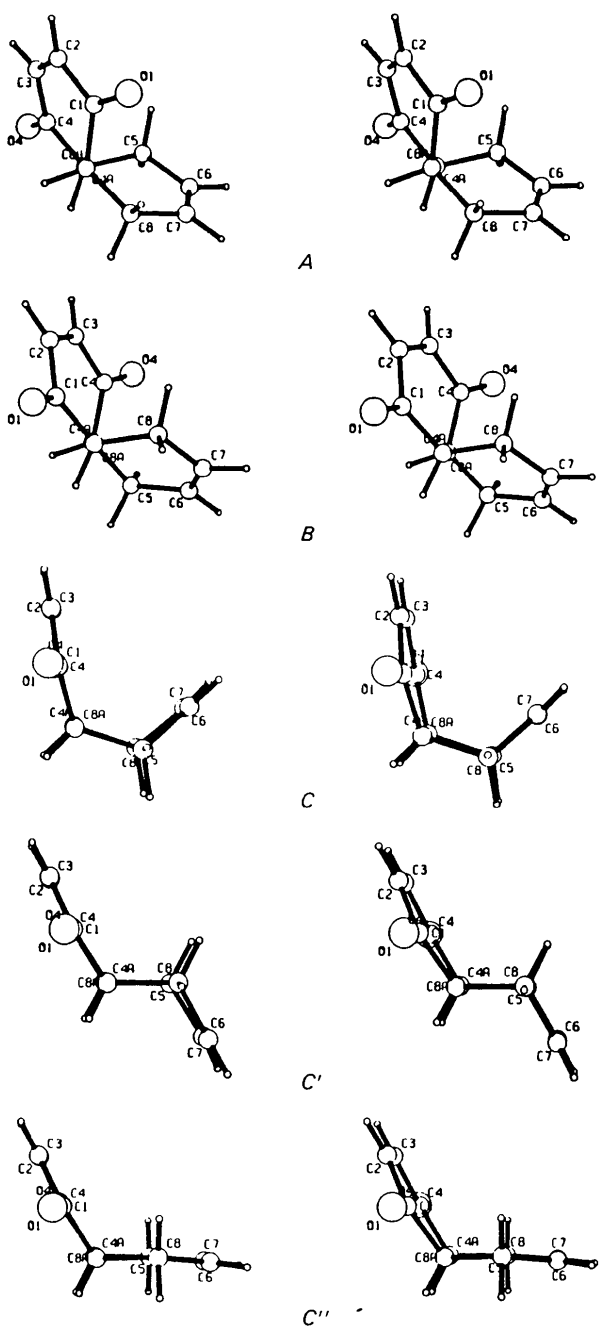


Fig. 5. Stereoviews of five conformations of tetrahydro-1,4-naphthoquinone.

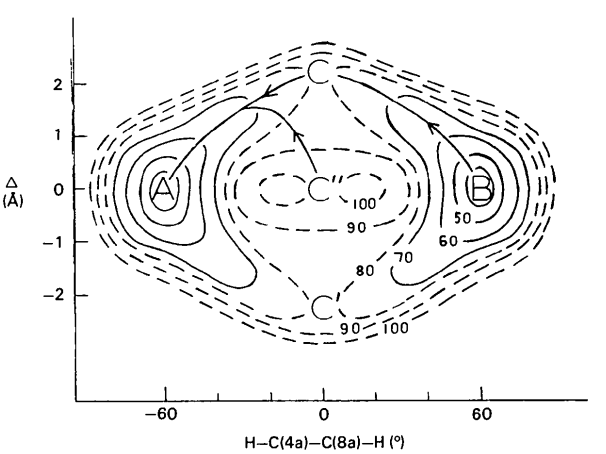


Fig. 6. Conformational energy surface for tetrahydro-1,4-naphthoquinone. Energies in kJ mol^{-1}; Δ = sum of displacements of C(6) and C(7) from C(5)–C(4a)–C(8a)–C(8) mean plane. Energies (see text) were calculated at conformations *A* (46 kJ mol^{-1}), *B* (46), *C* (79), *C'* (79), *C''* (96), at various points in the region between *C''* and *A*, and on the minimization pathways. The least-energy paths from *B* to *A* (*via C*) and from *C''* to *A* are shown.

state photochemistry, the Natural Sciences and Engineering Research Council of Canada for financial support, and the University of British Columbia Computing Centre for assistance.

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Book Review

Works intended for notice in this column should be sent direct to the Book-Review Editor (R. O. Gould, Department of Chemistry, University of Edinburgh, West Mains Road, Edinburgh EH9 3JJ, Scotland). As far as practicable books will be reviewed in a country different from that of publication.

Acta Cryst. (1988). B**44**, 544

Protein structure and design. Edited by DALE L. OXENDER. **(UCLA symposia on molecular and cellular biology, New series,** Volume 69.) Pp. x + 576. Alan R. Liss, New York, 1987. Price US $110.

In a brief essay on protein crystallography and its new revolution, Dodson surveyed the impact that the technique is having on modern biochemistry [*Trends Biochem. Sci.* (1986), **11**, 309]. Not only is the technique itself developing rapidly through advances in synchrotron X-ray sources, supercomputers, interactive graphics and, less directly, site-directed mutagenesis, but also it is being applied to an ever-widening range of exciting biological problems. The insight afforded from a detailed knowledge of molecular architecture has long been appreciated by crystallographers, and it is refreshing to see this appreciation flooding into the field of biology. This book is the proceedings of a Du Pont–UCLA conference, and it provides ample evidence of the impact protein crystallography is having on biology and, in particular, protein engineering. Further, the significant company participation shows that there is considerable commercial interest in the subject. However, it must be said that this is not a book from which to learn directly of specific techniques, rather it is in the results obtained from nine topical areas that the reader is immersed. Also, the results are not obtained from X-ray diffraction alone, although that could be said to have provided the basis of much of what is described.

The first section has eight papers on the structure and interactions of DNA-binding proteins: those involved in processing, or controlling the processing, of DNA. The next section on protein structural analysis comprises 11 papers including X-ray determinations, solution studies by nuclear magnetic resonance and circular dichroism and modelling studies based on existing coordinates. Energy considerations and molecular dynamics, the third section, provide a basis for studying binding of ligands to proteins, whilst the seven papers on enzyme catalysis include some beautiful examples of how site-directed mutagenesis (SDM) can help elucidate enzyme mechanisms. That a given polypeptide chain folds up to produce a unique tertiary structure has generated much speculation as to the nature of the pathway by which this occurs. Protein folding forms the fifth section in which SDM is shown to be a powerful tool for studying the problem and the seventh part is concerned with peptide and protein design: how the 'rules' so far extracted from analyses of protein structure can be put into practice. This section also includes a discussion of the strategies best suited to maximizing the production of a protein once the gene has been cloned. The previous section deals with mutagenesis of the cloned gene. Section 8 is short and deals with the interactions between antibody and antigen. The final part has two papers on viruses. The first links back to the previous section by considering the surface peptides of the poliovirus which are responsible for the host immune response and so may help in vaccine development. The second, all too brief, abstract refers to a crystallographic *tour de force*, the structures of several icosahedral viruses, their assembly and function.

The book is well produced from camera-ready typescript, though one or two of the stereo diagrams have been reproduced on too small a scale. There is a fairly full, if somewhat idiosyncratic, subject index but no author index. The reviewer found the book contained much of value but, as with many conference proceedings, was left with the feeling that it was aimed primarily at the participants.

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