

Conformation of (–)-membrenone-C

Rebecca A. Sampson, Michael V. Perkins and Max R. Taylor*

School of Chemistry, Physics and Earth Sciences,
The Flinders University of South Australia, GPO
Box 2100, Adelaide, SA 5001, AustraliaCorrespondence e-mail:
max.taylor@flinders.edu.au

Key indicators

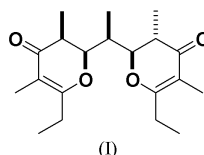
Single-crystal X-ray study
 $T = 123\text{ K}$
Mean $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$
 R factor = 0.040
 wR factor = 0.079
Data-to-parameter ratio = 10.0For details of how these key indicators were
automatically derived from the article, see
<http://journals.iucr.org/e>.

The conformation of (–)-membrenone-C, (2*S*,2'*R*,3*S*,3'*S*)-(1*S*)-2,2'-ethane-1,1-diylbis(6-ethyl-3,5-dimethyl-2,3-dihydro-4*H*-pyran-4-one), $\text{C}_{20}\text{H}_{30}\text{O}_4$, in the solid state is found to be the same as that predicted in solution by ^1H NMR spectroscopy and nOe (nuclear Overhauser effect) correlations.

Received 21 October 2003
Accepted 28 October 2003
Online 8 November 2003

Comment

Membrenone-C was first isolated as a natural product, along with membrenone-A and membrenone-B, from a Mediterranean mollusc *Pleurobranchus membranaceus* by Ciavatta *et al.* (1993). Subsequent synthesis of (–)-membrenone-A and (–)-membrenone-B by Sampson & Perkins (2002) indicated an apparent error in the sign of the optical rotation reported for natural membrenone-C in the original isolation paper (Ciavatta *et al.*, 1993). It was thus concluded by Sampson & Perkins (2002) that the structure of natural membrenone-C is enantiomeric to that reported here for (–)-membrenone-C. Both (+)- and (–)-membrenone-C have since been synthesized by Marshall & Ellis (2003) and their stereochemical results are consistent with ours (Perkins & Sampson, 2001; Sampson & Perkins, 2002).



The crystal structure of (–)-membrenone-C, (I), reveals that the two dihydropyran-4-one rings each have pseudo-equatorial and axial substituents at their two tetrahedral centres (Fig. 1). For the (2*S*,3*S*)-dihydropyran ring, both the methyl substituent and the larger alkyl group are in pseudo-equatorial positions. The (2'*R*,3'*S*)-dihydropyran ring, however, has the large alkyl group in a pseudo-equatorial orientation but the methyl group is in a pseudo-axial position. The conformation about the central C1–C2 and C1–C2' bonds is shown to be such that the A 1,3 strain is minimized. The 1,3-*syn* pentane interactions present all involve at least one H atom and are thus expected to be small. All other possible staggered conformations about the C1–C2 and C1–C2' bonds lead to 1,3-*syn* pentane interactions of large (non-H) groups. The interplanar angle between the dihydropyran rings is approximately 62°. The above conformation is the same as that determined in solution by ^1H NMR spectroscopy and nOe (nuclear Overhauser effect) correlations (Perkins & Sampson, 2001; Sampson, 2001). The observed coupling H3–H2 of $J = 13.8\text{ Hz}$ is consistent with a dihedral angle close to

180°, as expected for pseudo-diaxial H atoms (pseudo-diequatorial alkyl groups). Similarly, the observed coupling H3'–H2' of $J = 2.1$ Hz is consistent with a dihedral angle close to 60°, as expected for a pseudo-axial to equatorial coupling (pseudo-axial methyl and pseudo-equatorial alkyl group). The couplings H1–H2, $J = 3.0$ Hz and H1–H2', $J = 10.2$ Hz are consistent with HC–CH dihedral angles of $\sim 60^\circ$ and $\sim 180^\circ$, respectively. Corresponding values from the crystal structure are listed in Table 1. Further evidence for this conformation in solution comes from the strong nOe correlation between H3' and H2, showing that these two protons are close in space ($H3' \cdots H2 = 2.240$ Å in the crystal). Other nOe correlations consistent with this conformation were observed. This conformation is also predicted, by molecular modelling studies, to be the low energy conformer in solution (Sampson, 2001).

Experimental

The (–)-membrenone-C used in this study was obtained *via* a short enantiocontrolled synthesis (Perkins & Sampson, 2001) and crystallized from ether.

Crystal data

$C_{20}H_{30}O_4$	Mo $K\alpha$ radiation
$M_r = 334.46$	Cell parameters from 3123 reflections
Orthorhombic, $P2_12_12_1$	$\theta = 2.6\text{--}25.1^\circ$
$a = 9.836$ (3) Å	$\mu = 0.08$ mm $^{-1}$
$b = 13.065$ (4) Å	$T = 123$ (2) K
$c = 14.391$ (4) Å	Needle, colourless
$V = 1849.3$ (10) Å 3	$0.75 \times 0.12 \times 0.11$ mm
$Z = 4$	
$D_x = 1.201$ Mg m $^{-3}$	

Data collection

Bruker P4/SMART CCD area-detector diffractometer	1648 reflections with $F^2 > 2\sigma(F^2)$
ω scans	$R_{\text{int}} = 0.07$
Absorption correction: none	$\theta_{\text{max}} = 27.7^\circ$
12757 measured reflections	$h = -12 \rightarrow 12$
2294 independent reflections	$k = -16 \rightarrow 17$
	$l = -18 \rightarrow 6$

Refinement

Refinement on F^2	H-atom parameters not refined
$R[F^2 > 2\sigma(F^2)] = 0.040$	$w = 1/[\sigma^2(F_o^2) + (0.02F_o^2)^2]^{1/2}$
$wR(F^2) = 0.079$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.20$	$\Delta\rho_{\text{max}} = 0.26$ e Å $^{-3}$
2177 reflections	$\Delta\rho_{\text{min}} = -0.33$ e Å $^{-3}$
217 parameters	

Table 1

Selected torsion angles (°).

H2–C2–C3–H3	177	H2'–C2'–C3'–H3'	–52
H2–C2–C1–H1	–58	H2'–C2'–C1–H1	178

All reflections with $F^2 > 0$ were included in the least-squares refinement. Friedel pairs (1725 pairs) were averaged owing to the lack of significant anomalous scattering. H atom peaks were observed in a difference map but these atoms were placed at calculated positions ($C-H = 0.946\text{--}0.968$ Å). Their coordinates were not refined but were recalculated several times during the refinement.

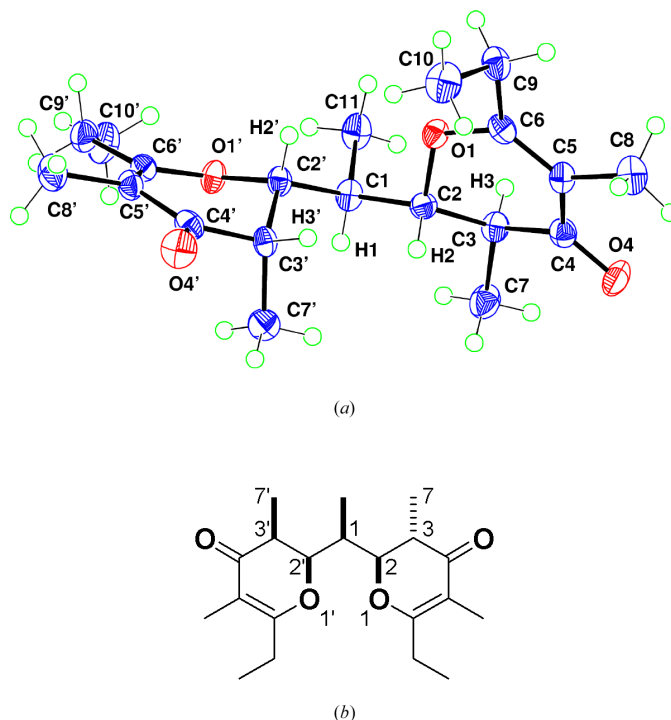


Figure 1

(a) The molecular structure of (–)-membrenone-C, showing the atomic labelling and displacement ellipsoids for non-H atoms at the 50% probability level. H atoms are spheres of arbitrary radius. Only those H atoms referred to in the text are labelled. (b) A structural diagram of (–)-membrenone-C, showing the chiral centers.

Data collection: SMART (Bruker, 1999); cell refinement: SMART; data reduction: SAINT (Bruker, 1999) and Xtal3.7 ADDREF and SORTRF (Hall *et al.*, 2000); program(s) used to solve structure: SIR97 (Altomare *et al.*, 1999); program(s) used to refine structure: Xtal3.7 CRYLSQ; molecular graphics: Xtal3.7; software used to prepare material for publication: Xtal3.7 BONDLA and CIFIO.

We thank Dr Jan Wikaira of the University of Canterbury, Christchurch, New Zealand, for collecting the data, and the Australian Research Council for financial support.

References

- Altomare, A., Burla, M. C., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
- Bruker (1999). SMART and SAINT. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
- Ciavatta, M. L., Trivellone, E., Villani, G. & Cimino, G. (1993). *Tetrahedron Lett.* **34**, 6791–6794.
- Hall, S. R., du Boulay, D. J. & Olthof-Hazekamp, R. (2000). Editors. *Xtal3.7 System*. University of Western Australia, Perth: Lamb.
- Marshall, J. A. & Ellis, K. C. (2003). *Org. Lett.* **5**, 1729–1732.
- Perkins, M. V. & Sampson, R. A. (2001). *Org. Lett.* **3**, 123–126.
- Sampson, R. A. (2001). PhD thesis, The Flinders University of South Australia, Adelaide, Australia.
- Sampson, R. A. & Perkins, M. V. (2002). *Org. Lett.* **4**, 1655–1658.