Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

rac-(*R*)-2-[(2*R*,5*R*)-5-Methyltetrahydrofuran-2-yl]propanoic acid

François Loiseau,[a] Reinhard Neier[a] and Helen Stoeckli-Evans[b]*

[a]Institut de Chimie, Université de Neuchâtel, Rue Emile Argand 11, CH-2009 Neuchâtel, Switzerland, and [b]Institut de Microtechnique, Université de Neuchâtel, Rue Emile Argand 11, CH-2009 Neuchâtel, Switzerland

Correspondence e-mail: francois.loiseau@unine.ch

Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.003 Å
R factor = 0.060
wR factor = 0.186
Data-to-parameter ratio = 22.4

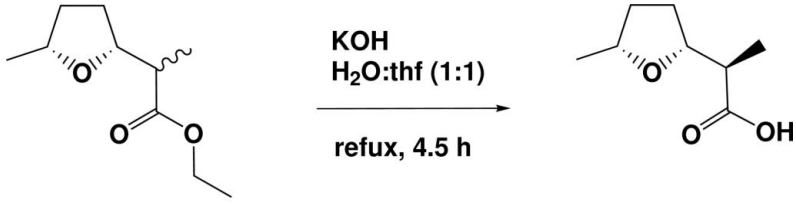
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 12 July 2006
Accepted 12 July 2006

In the crystal structure of the title compound, $C_8H_{14}O_3$, the 2,5-tetrahydrofuran ring junction is *cis*. The relative configuration of position 2 in the propanoic acid group was found to be the same as that in positions 2 and 5 in the tetrahydrofuran ring. In the crystal structure, symmetry-related molecules are linked by O—H···O hydrogen bonds to form centrosymmetric dimers.

Comment

Disubstituted *cis*-2,5-tetrahydrofuran (2,5-thf) ring junctions are important because they form a part of natural antibiotics. Typical examples are the members of the nactin family, which show antibiotic properties against a wide range of gram-positive bacteria, mycobacteria and fungi (Corbaz *et al.*, 1955; Meyers *et al.*, 1965; Bennett *et al.*, 1962), and insecticidal properties (Oishi *et al.*, 1970). The ionophore nonactin, the lowest homologue of this family, is used in analytical chemistry as an ammonia sensor (Bühlmann *et al.*, 1998), while tetranactin has shown immuno-suppressive properties equal to cyclosporine (Tanouchi & Shichi, 1988). During our investigations of complexity in bioactive molecules, we were interested in the synthesis of models of nonactic acid, such as the title compound, (Rac-II). Nonactic acid is the main biosynthetic precursor of the nactin macrotetrolides. To determine the configuration of the centre in the position alpha to the carbonyl of the diastereoisomerically pure ethylester (Rac-I), which is an oil, the title compound, (Rac-II), was prepared by saponification of (Rac-I).



Rac-I Rac-II

The molecular structure of (Rac-II) is illustrated in Fig. 1, and selected bond distances and angles are given in Table 1. The bond distances and angles are similar to those in an analogous compound, {1-[5-(2-azidopentyl)tetrahydro2-furyl]-ethyl}carboxylic acid (Bernsmann *et al.*, 2002). It can be seen in Fig. 1 that the 2,5-ring junctions (C1 and C4) in the thf unit of (Rac-II) are *cis*, while the relative configuration of the H atom at C6 is *anti* with respect to the H atom at C1. The thf ring has a half-chair conformation twisted on bond O1—C1 [the Cremer & Pople (1975) puckering parameters are q_2 =

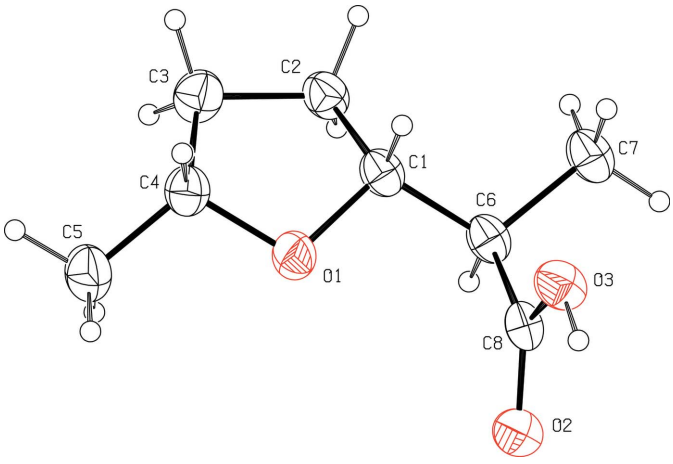


Figure 1
The molecular structure of (Rac-II), showing the crystallographic atom-numbering scheme and with displacement ellipsoids drawn at the 30% probability level.

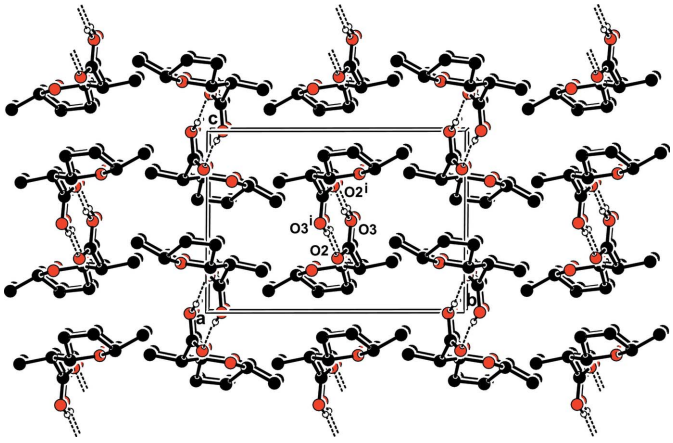


Figure 2
The crystal packing of (Rac-II), viewed down the *a* axis. O—H···O hydrogen bonds are shown as dashed lines. H atoms not involved in hydrogen bonding have been omitted for clarity. [Symmetry code: (i) $2-x, 1-y, 1-z$.]

0.370 (2) Å and $\varphi(2) = 15.8\ (4)^\circ$]. This is different from the situation in the analogous compound mentioned above, in which the thf ring has an envelope conformation.

In the crystal structure of (Rac-II), symmetry-related molecules are linked by O—H···O hydrogen bonds to form centrosymmetric dimers, typical for carboxylic acids (see Table 2 and Fig. 2 for details).

Experimental

Compound (Rac-II) was prepared by the saponification of (Rac-I) following the method described by Kirby & Amyes (1988). The synthesis of the ethyl ester, *viz*. (Rac-I), will be described elsewhere (Loiseau, 2006). In a two-necked 250 ml flask fitted with a reflux condenser, (Rac-I) (0.6 g, 3.2 mmol) in tetrahydrofuran (35 ml) was stirred magnetically. KOH (595 mg, 10.6 mmol) dissolved in water (35 ml) was then added slowly at room temperature. The mixture was heated to reflux for 4.5 h. After cooling to room temperature, the tetrahydrofuran was removed by evaporation *in vacuo* and then 32% HCl (1.44 ml, 12.8 mmol) was added dropwise. The product was extracted with 4 × 30 ml of diethyl ether and the organic layers were washed with 40 ml of brine. The organic layers were then combined and dried over $MgSO_4$. After filtration, the diethyl ether was removed by evaporation *in vacuo*. The colourless oil obtained was dried *in vacuo* (0.06 mm Hg) to afford the desired acid, (Rac-II), and stored at 277 K (yield 0.51 g, 3.2 mmol, 100%). After several days, colourless rod-shaped crystals suitable for X-ray analysis were obtained.

Crystal data

$C_8H_{14}O_3$
$M_r = 158.19$
Monoclinic, $P2_1/n$
$a = 8.7400\ (17)$ Å
$b = 11.870\ (3)$ Å
$c = 9.2749\ (16)$ Å
$\beta = 117.022\ (13)^\circ$
$V = 857.2\ (3)$ Å^3
$Z = 4$
$D_x = 1.226$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.09$ mm^{-1}
$T = 173\ (2)$ K
Rod, colourless
0.50 × 0.23 × 0.22 mm

Data collection

Stoe IPDS-2 diffractometer
φ and ω scans
Absorption correction: none
10718 measured reflections
2312 independent reflections
1392 reflections with $I > 2\sigma(I)$
$R_{int} = 0.117$
$\theta_{max} = 29.3^\circ$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.061$
$wR(F^2) = 0.186$
$S = 1.03$
2312 reflections
103 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1002P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C1	1.430 (2)	C2—C3	1.520 (3)
O1—C4	1.438 (2)	C3—C4	1.528 (3)
O2—C8	1.253 (2)	C4—C5	1.492 (3)
O3—C8	1.277 (2)	C6—C8	1.508 (3)
C1—C6	1.514 (3)	C6—C7	1.536 (3)
C1—C2	1.512 (3)		
C1—O1—C4	106.04 (15)	C5—C4—C3	115.95 (19)
O1—C1—C6	108.16 (16)	C8—C6—C1	109.90 (15)
O1—C1—C2	104.31 (15)	C8—C6—C7	109.65 (16)
C6—C1—C2	115.54 (16)	C1—C6—C7	111.29 (17)
C1—C2—C3	103.44 (16)	O2—C8—O3	123.42 (18)
C2—C3—C4	105.39 (17)	O2—C8—C6	119.73 (17)
O1—C4—C5	108.59 (18)	O3—C8—C6	116.84 (18)
O1—C4—C3	104.75 (15)		

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O2^{i}	0.84	1.80	2.630 (2)	170

Symmetry code: (i) $-x+2, -y+1, -z+1$.

All H atoms could be located in difference Fourier maps. However, as the crystal was not of the best quality ($R_{int} = 0.117$), they were included in calculated positons and treated as riding atoms: O—H = 0.84 Å with $U_{iso}(H) = 1.5U_{eq}(O)$, and C—H = 0.98–1.00 Å with $U_{iso}(H) = 1.5$ or $1.2U_{eq}(C)$.

Data collection: *X-AREA* (Stoe, 2005); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL97*.

Financial support from the Swiss National Science Foundation is gratefully acknowledged.

References

Bennett, R. E., Brindle, C. A., Giuffre, N. A., Jackson, P. W., Kowald, J., Pansy, F. E., Perlman, D. & Trejo, W. H. (1962). *Antimicrob. Agents Chemother.* **1961**, 169–172.

Bernsmann, H., Wang, Y., Fröhlich, R. & Metz, P. (2002). *Tetrahedron*, **58**, 4451–4457.

Bühlmann, P., Pretsch, E. & Bakker, E. (1998). *Chem. Rev.* **98**, 1593–1687.

Corbaz, R., Ettinger, L., Gaumann, E., Keller-Schlierlein, W., Kradolfer, F., Kyburz, E., Neipp, L., Prelog, V. & Zahner, H. (1955). *Helv. Chim. Acta*, **38**, 1445–1448.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Kirby, A. J. & Amyes, T. L. (1988). *J. Am. Chem. Soc.* **110**, 6505–6514.

Loiseau, F. (2006). PhD thesis, Université de Neuchâtel, Switzerland.

Meyers, E., Pansy, F. E., Perlmann, D., Smith, D. A. & Weisenborn, F. L. (1965). *J. Abtibiot.* **18**, 128–129.

Oishi, H., Sugawa, T., Okutomi, T., Suzuki, K. & Hayashi, T. (1970). *J. Antibiot.* **23**, 105–106.

Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

Spek, A. L. (2003). *J. Appl. Cryst.* **36**, 7–13.

Stoe (2005). *X-AREA* (Version 1.26) and *X-RED32* (Version 1.26). Stoe & Cie GmbH, Darmstadt, Germany.

Tanouchi, Y. & Shichi, H. (1988). *Immunology*, **63**, 471–475.