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

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In the crystal structure of the title compound, C₉H₁₄O₃, 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 tetraactin has shown immuno-suppressive properties equal to cyclosporine (Tanouchi & Shiigi, 1988). During our investigations of complexity in bioactive molecules, we were interested in the synthesis of models of nonactinic acid, such as the title compound, (Rac-II). Nonactinic 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).

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 O1C1 0.370 (2) Å and ϕ(2) = 15.8 (4). 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).
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 MgSO₄. 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, the colourless rod-shaped crystals suitable for X-ray analysis were obtained.

**Crystal data**

\[ \text{C₄H₈O₃} \]

\[ M_r = 158.19 \]

Monoclinic, \( P2_1/n \)

\( a = 8.7400 \) Å

\( b = 11.870 \) Å

\( c = 9.2749 \) Å

\( \beta = 117.022 \) (Å²)

\( V = 857.2 \) Å³

**Data collection**

Stoe IPDS-2 diffractometer

\( \psi \) and \( \omega \) 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 \( F^2 \)

\( R[F^2 > 2\sigma(F^2)] = 0.061 \)

\( wR(F^2) = 0.138 \)

\[ S = 1.03 \]

2312 reflections

103 parameters

H-atom parameters constrained

\[ w = 1/\sigma^2(F^2) \]

where \( P = (F^2 + 2F^2)^3 \)

\( \Delta \rho_{min} = 0.21 \) e Å⁻³

\( \Delta \rho_{max} = -0.28 \) e Å⁻³

**Table 1**

<table>
<thead>
<tr>
<th>( \text{O1} )</th>
<th>( \text{C1} )</th>
<th>( \text{C2} )</th>
<th>( \text{C3} )</th>
<th>( \text{C4} )</th>
<th>( \text{C5} )</th>
<th>( \text{C6} )</th>
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<td>104.41 (15)</td>
<td>104.41 (15)</td>
<td>104.40 (15)</td>
</tr>
</tbody>
</table>

**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%
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.

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References


