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rac-(*Z*)-Ethyl 2-bromo-2-[(3*R*,5*R*)-3-bromo-5-methyltetrahydrofuran-2-ylidene]acetate

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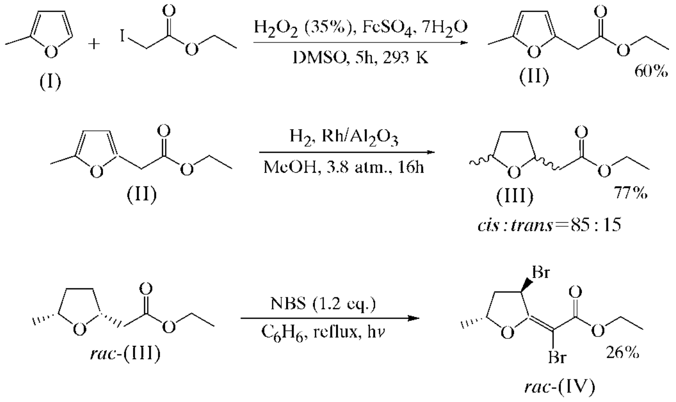
In the title compound, $C_9H_{12}Br_2O_3$, a (tetrahydrofuran-2-ylidene)acetate, the double bond has the *Z* form. In the tetrahydrofuran group, the relative configuration of the Br atom in the 3-position and the methyl group in the 5-position is *anti*. The compound crystallizes with two independent molecules per asymmetric unit and, in the crystal structure, the individual molecules are linked to their symmetry-equivalent molecules by C—H···O hydrogen bonds, so forming centrosymmetric hydrogen-bonded dimers.

Comment

For the synthesis of bioactive molecules, reduced derivatives of substituted furans have been studied intensively as synthetic building blocks. α-(Tetrahydrofuran-2-ylidene)-acetates have been synthesized using widely different strategies (Bryson, 1973). They are the most common intermediates in many of the reported syntheses of nonactic acid (Ferraz & Payret-Arrua, 1998), which is the degradation product of the ionophore nonactin (Keller-Schierlein & Gerlach, 1968). Nonactin, the lowest homologue of the nactin family, is used in analytical chemistry as an ammonia sensor (Bühlmann *et al.*, 1998) and has shown antibiotic and insecticidal properties (Meyers *et al.*, 1965; Oishi *et al.*, 1970). In the context of our research programme on the preparation of nonactin derivatives that are more hydrophobic (Loiseau, 2006), we decided to study the functionalization of models of nonactic acid, for example, compound (III) (see scheme). Hydrophobic nonactin derivatives should have a longer lifetime in the semi-permeable membrane of ammonia sensors (Pretsch *et al.*, 1988). The lifespan of these electrodes is limited owing to the loss of nonactin into the aqueous solution. The synthetic strategy to prepare racemic (III) involves two steps. Firstly, compound (II) was synthesized by the radical coupling (Baciocchi *et al.*, 1992) of 2-methylfuran, (I), with ethyl iodoacetate. The furan ring was then hydrogenated (Schmidt & Werner, 1986) to give racemic (III).



One of our approaches to modify compound (III) was based on the introduction of a Br atom as a functional group. Bromine can be replaced using well known reactions, such as radical or nucleophilic substitution reactions, Grignard reactions, or Reformatsky enolate chemistry. We needed to develop a method to introduce selectively the Br atom in the α-position of the ester function. On bromination (Schultz *et al.*, 1983) of (III), however, the unexpected polybrominated racemic compound (IV) was isolated. We report here the structure of this totally new, highly functionalized (tetrahydrofuran-2-ylidene)acetate.

The molecular structures of the two independent molecules (*A* and *B*) of (IV) are illustrated in Fig. 1. Selected bond distances and angles for molecule *A* are given in Table 1. It can

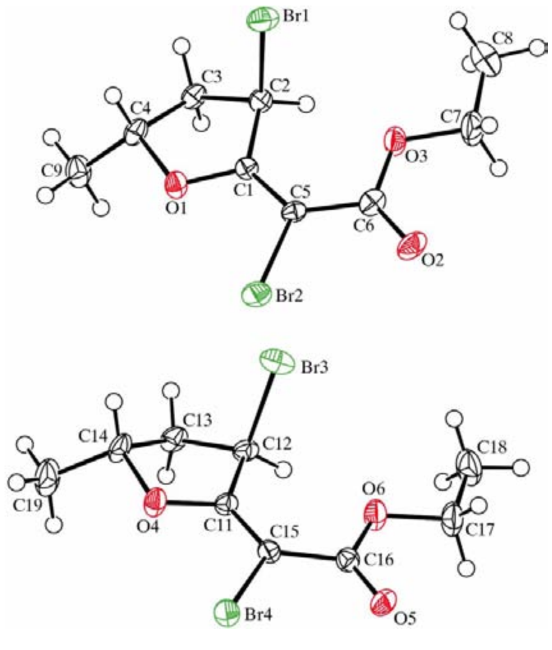


Figure 1
The molecular structure of the two independent molecules (*A* above and *B* below) of the racemic compound (IV), showing the crystallographic atom-numbering scheme and displacement ellipsoids drawn at the 50% probability level.

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be seen that the relative configuration of the Br atom in the 3-position (C2) and the methyl group in the 5-position (C4) of the tetrahydrofuran (THF) group is *anti*. The THF ring in each molecule has an envelope conformation, with atom C3 as the flap atom in molecule *A* and atom C13 as the flap atom in molecule *B*. The Cremer & Pople (1975) puckering parameters are $Q(2) = 0.318$ (4) Å and $\varphi(2) = 106.6$ (7)° for molecule *A*, and $Q(2) = 0.339$ (4) Å and $\varphi(2) = 107.4$ (7)° for molecule *B*. The two molecules differ only in the orientation of the ethoxycarbonyl group with respect to the plane through the bromotetrahydrofuranylidene group. The relevant torsion angles about the C5—C6 (molecule *A*) and C15—C16 bonds (molecule *B*) are given in Table 1, and it can be seen that the difference is of the order of *ca* 4°.

In the crystal structure of (IV), the individual molecules (*A* and *B*) are linked to their symmetry-equivalent molecules by C—H$\cdots$O hydrogen bonds, so forming centrosymmetric hydrogen-bonded dimers (details are given in Table 2). There are also two short Br$\cdots$Br contacts (Table 1). A search of the Cambridge Structural Database (CSD; Version 1.8, last update May 2006; Allen, 2002) indicates that such short intermolecular Br$\cdots$Br distances are not unusual. These centrosymmetric dimers are further linked by a Br$\cdots$O interaction (see Table 1 and Fig. 2 for details). This interaction is also associated with the C13—H13*A*$\cdots$O5$^{\rm iv}$ interaction, leading to a Br$\cdots$O$\cdots$H13*A* angle of *ca* 139°. A search of the CSD indicates that O$\cdots$Br interactions involving carbonyl O atoms are not uncommon; more than 600 such interactions in the range 2.80–3.37 Å have been observed previously.

The two Br atoms introduced are vinylic [the average bond distance is 1.894 (2) Å] and allylic [the average bond distance is 1.974 (2) Å]. Effectively, only arylic, vinylic and allylic halogen atoms can prevent α-elimination and can therefore be involved in modern palladium-catalyzed organometallic couplings such as the Heck or Suzuki reactions. It is highly probable that (IV) was the synthetic result of three radical eliminations followed by an elimination of HBr. The X-ray diffraction analysis of (IV) has proven the possible synthetic mechanism of formation, where the Br atom in the 3-position of the THF ring is inserted on the less hindered face, *i.e. anti* with respect to the methyl group in the 5-position of the THF ring.

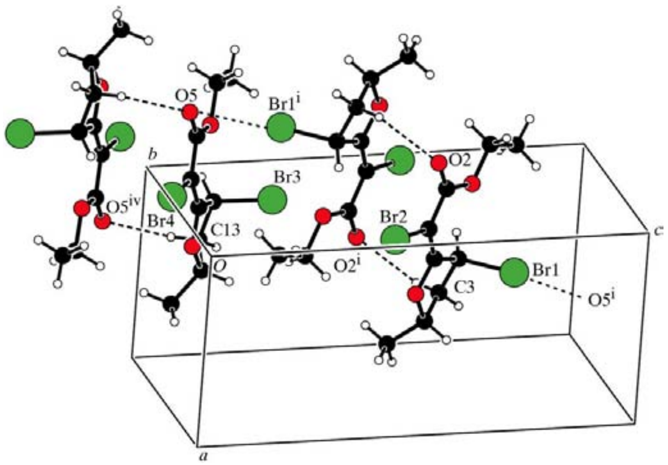

Figure 2
A segment of the crystal packing of compound (IV), viewed down the *a* axis. The Br$\cdots$O interactions and C—H$\cdots$O hydrogen bonds are shown as dashed lines [symmetry codes: (i) $-x, -y + 1, -z + 1$; (iv) $-x, -y + 2, -z$].

A search of the CSD reveals only three structures containing the tetrahydrofuran-2-ylideneacetate group (Brussani *et al.*, 1986; Scheffler *et al.*, 2002; Bellur *et al.*, 2005), none of which are substituted in the α-position of the ester function. To the best of our knowledge, this is also the first crystal structure analysis of a tetrahydrofuran-2-ylidene compound in which a halogen substituent is present on the THF ring.

Experimental

Compound (II), namely ethyl 2-(5-methylfuran-2-yl)acetate, was prepared by stirring freshly distilled 2-methylfuran (100 g, 1218 mmol), ethyl iodoacetate (7.66 ml, 64.1 mmol) and $FeSO_4\cdot7H_2O$ (8.20 g, 29.5 mmol) in dimethyl sulfoxide (DMSO, 550 ml) in a three-necked 1 l flask. H_2O_2 (35% in water–brine, 10.4 ml, 121.8 mmol) was then added dropwise at 288–303 K and the temperature was maintained with a water bath. After 5 h, brine (550 ml) was added portionwise. The product was extracted four times with diethyl ether (200 ml). The combined organic layers were washed with brine (500 ml) and then dried over $MgSO_4$. Filtration and evaporation *in vacuo* afforded 12.7 g of a brown oil. This oil was purified by chromatography on a silica-gel column using *n*-hexane/AcOEt (95:5) to afford the desired product, (II), as a yellow oil (6.40 g, 38 mmol, yield 60%). Compound (III), namely racemic ethyl 2-(5-methyltetrahydrofuran-2-yl)acetate, was prepared by placing compound (II) (400 mg, 2.38 mmol) and 5% rhodium over alumina (50 mg, 0.024 mmol) in MeOH (15 ml) under 3.8 atm pressure of hydrogen in a Parr apparatus (1 atm = 101 325 Pa). After 16 h, the mixture was filtered on a Celite/silica 2:1 mixture. Evaporation *in vacuo* afforded compound (III) (316 mg, 1.83 mmol, 77%). According to NMR and GC analyses, the *cis*/*trans* ratio was 85:15. Compound (IV) was prepared by magnetically stirring compound (III) (0.5 g, 2.9 mmol) in dried benzene (15 ml) in a three-necked 25 ml flask fitted with a reflux condenser and under an atmosphere of argon. *N*-Bromosuccinimide (NBS; 1.86 g, 10.5 mmol) was added slowly and the mixture was refluxed for 2 h under the illumination of a 200 W lamp. The mixture was cooled to 283 K and the solid obtained was filtered off. Benzene was removed by evaporation *in vacuo*. The oil obtained was purified by chromatography on a silica-gel column using *n*-hexane/AcOEt (9:1) as eluant, giving finally the brominated product (IV) as a yellow oil (yield 250 mg, 0.7 mmol, 26%). As the oil contained a small amount of impurities, *ca* 100 mg were recrystallized from hexane. Colourless crystals suitable for X-ray diffraction were obtained.

Crystal data

$C_9H_{12}Br_2O_3$
$M_r = 328.01$
Triclinic, $P\overline{1}$
$a = 9.0779$ (8) Å
$b = 9.1402$ (9) Å
$c = 15.3942$ (13) Å
$\alpha = 85.740$ (7)°
$\beta = 82.209$ (7)°
$\gamma = 64.386$ (7)°

$V = 1140.98$ (18) Å^3
$Z = 4$
$D_x = 1.909$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 7.09$ mm^{-1}
$T = 173$ (2) K
Block, colourless
0.30 × 0.23 × 0.20 mm

Data collection

Stoe IPDS-II diffractometer
φ and ω scans
Absorption correction: multi-scan (*MULABS* in *PLATON*; Spek, 2003)
$T_{\min} = 0.126$, $T_{\max} = 0.245$

17073 measured reflections
6151 independent reflections
4464 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.060$
$\theta_{\max} = 29.2°$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.088$
$S = 0.90$
6151 reflections
257 parameters

H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0485P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.83$ e Å^{-3}
$\Delta\rho_{\min} = -1.19$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

Br1—C2	1.973 (3)	O3—C6	1.333 (5)
Br2—C5	1.896 (3)	C1—C2	1.505 (5)
O1—C1	1.346 (4)	C1—C5	1.354 (6)
O2—C6	1.217 (5)	C5—C6	1.471 (5)
Br1···O5$^{\rm i}$	3.220 (3)	Br4···Br4$^{\rm iii}$	3.6128 (7)
Br2···Br3$^{\rm ii}$	3.5681 (7)		
C2—C1—C5	129.4 (3)	Br2—C5—C1	117.7 (3)
O1—C1—C5	120.2 (3)	Br2—C5—C6	114.9 (3)
O1—C1—C2	110.4 (3)	C1—C5—C6	127.4 (3)
Br1—C2—C1	108.0 (2)	O2—C6—O3	124.0 (4)
Br1—C2—C3	110.5 (3)	O3—C6—C5	112.4 (3)
C1—C2—C3	101.8 (3)	O2—C6—C5	123.7 (4)
Br2—C5—C6—O2	−4.4 (5)	Br4—C15—C16—O5	−0.5 (4)
Br2—C5—C6—O3	175.9 (2)	Br4—C15—C16—O6	179.4 (2)

Symmetry codes: (i) $-x, -y+1, -z+1$; (ii) $x, y-1, z$; (iii) $-x, -y+1, -z$.

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

D—H···A	D—H	H···A	D···A	D—H···A
C3—H3A···O2$^{\rm i}$	0.99	2.59	3.321 (5)	131
C13—H13A···O5$^{\rm iv}$	0.99	2.57	3.353 (5)	136

Symmetry codes: (i) $-x, -y+1, -z+1$; (iv) $-x, -y+2, -z$.

The H atoms could all be located from difference Fourier maps. They were included in calculated positions and treated as riding atoms, with C—H distances of 0.98–1.00 Å and $U_{\rm iso}$(H) values of 1.2 or 1.5 times $U_{\rm eq}$(C).

Data collection: *X-AREA* (Stoe & Cie, 2005); cell refinement: *X-AREA*; data reduction: *X-RED32* (Stoe & Cie, 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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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GA3026). Services for accessing these data are described at the back of the journal.

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