

## Anhydrous sodium naproxen

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## Key indicators

Single-crystal X-ray study

$T = 298\text{ K}$

Mean  $\sigma(\text{C}-\text{C}) = 0.004\text{ \AA}$

$R$  factor = 0.049

$wR$  factor = 0.131

Data-to-parameter ratio = 12.3

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

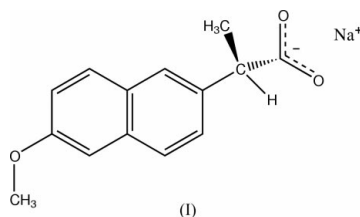
The title compound, anhydrous sodium (*S*)-(–)-6-methoxy- $\alpha$ -methyl-2-naphthaleneacetate,  $[\text{Na}(\text{C}_{14}\text{H}_{13}\text{O}_3)]$ , has two independent molecules in the asymmetric unit, with structures closely related to that of the monohydrate. The most significant differences between the two molecules are in the O–C–C torsion angles,  $-10.4(3)$  and  $-37.7(3)^\circ$ , of the side-chain carboxylate groups.

## Comment

Different polymorphs and pseudopolymorphs of pharmaceutical compounds may be generated during processing steps such as crystallization, lyophilization, wet granulation, and aqueous film-coating or spray-drying, and through storage in humid environments (Khankari & Grant, 1995). The pseudopolymorphs differ in properties such as melting points, crystal shape and dissolution kinetics.

Naproxen is an anti-inflammatory non-steroidal drug. The sodium salt has much higher solubility in water than does its free-acid form, which enhances the applicability of the sodium salt as a pharmaceutical compound. The structure of naproxen (Ravikumar *et al.*, 1985) has been determined previously and the structure of the monohydrated sodium salt (Kim *et al.*, 1990) is also known. However, the structure of the anhydrous form of the sodium salt has not previously been determined. The present work was undertaken to determine the structure of anhydrous sodium naproxen.

The asymmetric unit of anhydrous sodium naproxen, (I), contains two independent anions, denoted *A* and *B*, and two cations (Fig. 1). There are significant differences between the O1a–C12a–C11a–C13a torsion angle [ $-10.4(3)^\circ$ ] of molecule *A* and the O1b–C12b–C11b–C13b torsion angle [ $-37.7(3)^\circ$ ] of molecule *B*. The difference in the torsion angles seems to be due to interactions between the carboxy O atoms and the  $\text{Na}^+$  ions.

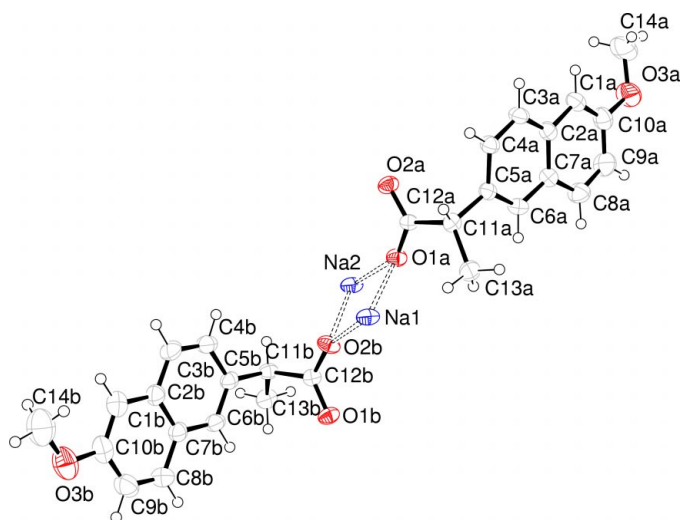


The methoxy group in each molecule is essentially coplanar with the naphthyl ring system, thus bringing about an enlargement of the C1a–C10a–O3a and C1b–C10b–O3b angles and a narrowing of the C9a–C10a–O3a and C9b–C10b–O3b angles (Table 1). A similar effect was reported previously

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**Figure 1**  
A perspective drawing of the two independent anions, *A* and *B*, and two cations of (I) (50% probability ellipsoids).

and was attributed to some degree of conjugation between the O atom in the methoxy group and the adjacent benzene ring, giving rise additionally to some shortening of the C—O bond (Domiano *et al.*, 1979).

The molecular geometry in the anhydrous material was compared with that in the monohydrate. The bond lengths and bond angles of the methoxy group for the corresponding atoms are very similar to one another. However, the torsion angle [ $-4.1^\circ$ ] for the methoxy group in the monohydrate is slightly smaller than those found in the anhydrous material [ $C1a-C10a-O3a-C14a = -7.4(5)^\circ$  in molecule *A* and  $C1b-C10b-O3b-C14b = -5.2(5)^\circ$  in molecule *B*].

Both the anhydrous and the monohydrated salts crystallize in space group  $P2_1$ . However, the monohydrate has only one ion pair in the asymmetric unit, whereas the anhydrous material has two anions and two cations. The removal of water leads to a slight change in packing and cell volumes. To compare the cell volumes, the volume of the monohydrate was doubled, since  $Z' = 2$  for the anhydrous material. The unit-cell volume of the anhydrous material is smaller than the doubled unit-cell volume of the monohydrate by 11.33%. The change in packing and cell volumes is presumably driven by changes in sodium coordination as the water is removed.

In the anhydrous material, the  $Na^+$  ion is four-coordinate (Table 1). It has four nonequivalent Na—O bonds that involve the carboxy groups of four different naproxen anions. However, in the monohydrate, the  $Na^+$  ion has five Na—O interactions, involving four carboxy O atoms in three naproxen anions and an O atom from a water molecule.

## Experimental

Sodium naproxen was supplied by Albemarle Corp. It was used without further purification in obtaining the crystals studied. Single crystals of anhydrous sodium naproxen were prepared by slow evaporation of a saturated solution in methanol at room temperature.

The crystals were washed with cyclohexane to inhibit powder generation on the surface of the crystals.

## Crystal data

$[Na(C_{14}H_{13}O_3)]$   
 $M_r = 252.23$   
 Monoclinic,  $P2_1$   
 $a = 9.969(3) \text{ \AA}$   
 $b = 5.9346(16) \text{ \AA}$   
 $c = 20.823(6) \text{ \AA}$   
 $\beta = 102.025(5)^\circ$   
 $V = 1204.9(6) \text{ \AA}^3$   
 $Z = 4$

$D_x = 1.390 \text{ Mg m}^{-3}$   
 Mo  $K\alpha$  radiation  
 Cell parameters from 881 reflections  
 $\theta = 2.5\text{--}27.4^\circ$   
 $\mu = 0.13 \text{ mm}^{-1}$   
 $T = 298(2) \text{ K}$   
 Prism, colorless  
 $0.71 \times 0.61 \times 0.34 \text{ mm}$

## Data collection

Bruker SMART 1000 diffractometer  
 $\omega$  scans  
 Absorption correction: multi-scan (Blessing, 1995)  
 $T_{\min} = 0.915$ ,  $T_{\max} = 0.958$   
 6886 measured reflections

4036 independent reflections  
 3269 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.035$   
 $\theta_{\max} = 26.8^\circ$   
 $h = -11 \rightarrow 12$   
 $k = -6 \rightarrow 7$   
 $l = -26 \rightarrow 24$

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.050$   
 $wR(F^2) = 0.131$   
 $S = 1.01$   
 4036 reflections  
 329 parameters

H-atom parameters constrained  
 $w = 1/[\sigma^2(F_o^2) + (0.0807P)^2]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\max} = 0.004$   
 $\Delta\rho_{\max} = 0.32 \text{ e \AA}^{-3}$   
 $\Delta\rho_{\min} = -0.35 \text{ e \AA}^{-3}$

**Table 1**

Selected geometric parameters ( $\text{\AA}$ ,  $^\circ$ ).

Na1—O1b <sup>i</sup>	2.259(2)	Na2—O2a <sup>iii</sup>	2.276(2)
Na1—O2b	2.270(2)	Na2—O2a <sup>iv</sup>	2.291(2)
Na1—O1b <sup>ii</sup>	2.290(2)	Na2—O1a	2.328(2)
Na1—O1a	2.394(2)	Na2—O2b	2.341(2)
O3b—C10b—C1b	125.0(4)	C1a—C10a—O3a	125.3(3)
O3b—C10b—C9b	114.9(3)	O3a—C10a—C9a	114.4(3)

Symmetry codes: (i)  $-x, \frac{1}{2} + y, -z$ ; (ii)  $x, 1 + y, z$ ; (iii)  $-1 - x, y - \frac{1}{2}, -z$ ; (iv)  $x, y - 1, z$ .

Ideal H-atom coordinates were calculated, with C—H distances fixed at 0.96  $\text{\AA}$ .  $U_{\text{iso}}(\text{H})$  values were set at  $1.2U_{\text{eq}}(\text{C})$  [ $1.5U_{\text{eq}}(\text{C})$  for methyl H atoms]. The absolute structure could not be determined from the data.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 1998; program(s) used to solve structure: *SHELXTL* (Bruker, 1998); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *SHELXTL*.

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