Petcher, T. J. & Weber, H.-P. (1976). *J. Chem. Soc. Perkin Trans. 2*, pp. 1415–1420.
Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures*. University of Göttingen, Germany.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Stoe & Cie (1987*a*). *DIF4. Diffractometer Control Program*. Version 6.2. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1987*b*). *EMPIR. Empirical Absorption Correction Program*. Version 6.2. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1987*c*). *REDU4. Data Reduction Program*. Version 6.2. Stoe & Cie, Darmstadt, Germany.

Acta Cryst. (1996). C**52**, 393–395

Absolute Configuration of (*R*)-1-Phenylethylammonium (*S*)-2-(6-Methoxy-2-naphthyl)propionate

LÉON DUPONT,[a]* BERNARD PIROTTE,[b] PASCAL DE TULLIO[b] AND JACQUES DELARGE[b]

[a]*Unité de Cristallographie, Institut de Physique B5, Université de Liège au Sart Tilman, B-4000 Liège, Belgium, and* [b]*Laboratoire de Chimie Pharmaceutique, Institut de Pharmacie F1, Université de Liège, Rue Fusch, 5, B-4000 Liège, Belgium. E-mail: u210406@vm1.ulg.ac.be*

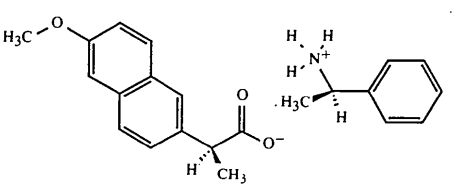
(*Received 19 June 1995; accepted 29 August 1995*)

Abstract

The title salt, $C_8H_{12}N^+.C_{14}H_{13}O_3^-$, results from the reaction of known (*R*)-1-phenylethylamine with naproxen, an inhibitor of the cyclo-oxygenase responsible for the biosynthesis of prostaglandins. Naproxen exhibits anti-inflammatory, analgesic and antipyretic activity in man. The crystal structure determination confirms the absolute *S* geometry of the chiral C atom of naproxen previously reported. There are three intermolecular hydrogen bonds between the NH_3^+ and COO^- groups.

Comment

Naproxen, (*S*)-2-(6-methoxy-2-naphthyl)propionic acid, is a non-steroidal anti-inflammatory agent (Goodman & Gilman, 1980) and an optically pure carboxylic acid advantageously used in the resolution of racemic mixtures of aliphatic amines. Moreover, the determination of the crystal structure of the ammonium salt obtained from the reaction of the resolved amine with naproxen allows the identification of the absolute geometry of the chiral C atom in the pure enantiomeric amine. We report here the structure of the title salt, (I).



(I)

The distances and angles in the naproxen ion in the title compound are similar to those found in naproxen itself, $C_{14}H_{14}O_3$, (II) (Ravikumar, Rajan, Pattabhi & Gabe, 1985). The methoxy group is nearly coplanar with the naphthalene moiety in both crystal structures. However, the orientations of the naphthalene moiety with respect to the —CH(CH_3)—COOH group are quite different, as shown by the torsion angles C9—C8—C13—C15 [152.5 (3) in (I), −70.5 (8)° in (II)] and C9—C8—C13—C14 [−82.2 (4) in (I), 48.9 (9)° in (II)]. The torsion angles around the C13—C15 bond differ to a lesser extent [C8—C13—C15—O17 −83.4 (3) in (I), −90.3 (8)° in (II); C14—C13—C15—O17 151.8 (3) in (I), 149.4 (7)° in (II)]. The determination of the structure of the title salt confirms the absolute *S* configuration of the chiral atom C13 of naproxen reported by Riegel, Maddox & Harrison (1974). The crystal packing is characterized by three N—H···O intermolecular hydrogen bonds, detailed in Table 3.

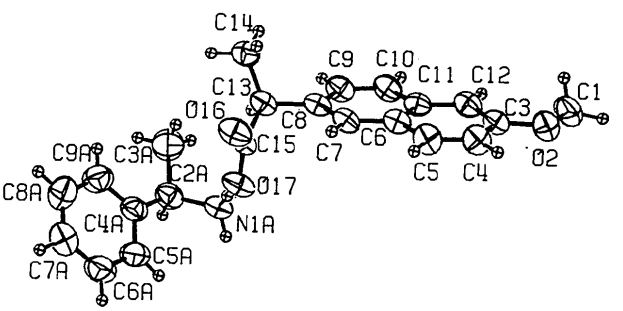


Fig. 1. The molecular structure of the title salt with the atom-labelling scheme. Displacement ellipsoids are shown at the 50% probability level for non-H atoms; H atoms are drawn as small circles of arbitrary radii.

Experimental

(*R*)-(+)-1-Phenylethylamine and naproxen were obtained from Aldrich Chemie (Belgium). The salt was prepared at the Laboratory of Medicinal Chemistry of Liège.

Crystal data

$C_8H_{12}N^+.C_{14}H_{13}O_3^-$
M_r = 351.43
Cu $K\alpha$ radiation
λ = 1.5418 Å

Monoclinic
$P2_1$
a = 11.6395 (9) Å
b = 5.9814 (6) Å
c = 13.6907 (9) Å
β = 94.462 (14)°
V = 950.26 (14) Å^3
Z = 2
D_x = 1.228 Mg m^{-3}

Cell parameters from 25 reflections
θ = 24.60–31.04°
μ = 0.648 mm^{-1}
T = 293 (2) K
Plate
0.53 × 0.27 × 0.19 mm
Colourless

Data collection

Stoe Siemens AED four-circle diffractometer
ω-scans
Absorption correction: ψ scan (*EMPIR*; Stoe & Cie, 1987*b*)
T_{min} = 0.802, T_{max} = 0.994
1529 measured reflections
1459 independent reflections

1081 observed reflections [$I > 2\sigma(I)$]
R_{int} = 0.0213
θ_{max} = 57.53°
$h = -12 \rightarrow 12$
$k = 0 \rightarrow 6$
$l = 0 \rightarrow 14$
2 standard reflections
frequency: 60 min
intensity decay: 5.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.0376
$wR(F^2)$ = 0.0946
S = 0.944
1459 reflections
248 parameters
H atoms were included as riding atoms
$w = 1/[\sigma^2(F_o^2) + (0.0716P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.132 e Å^{-3}
$\Delta\rho_{min}$ = −0.160 e Å^{-3}

Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.0072 (12)
Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)
Absolute configuration: Flack (1983) parameter = −0.03 (43)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$U_{eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	U_{eq}
C1	0.2588 (3)	0.1978 (9)	0.0700 (3)	0.0778 (12)
O2	0.2929 (2)	−0.0092 (5)	0.1165 (2)	0.0713 (8)
C3	0.4096 (3)	−0.0490 (6)	0.1332 (2)	0.0575 (9)
C4	0.4339 (3)	−0.2512 (7)	0.1832 (3)	0.0643 (10)
C5	0.5459 (3)	−0.3115 (7)	0.2056 (2)	0.0625 (9)
C6	0.6376 (3)	−0.1745 (6)	0.1804 (2)	0.0522 (9)
C7	0.7553 (3)	−0.2312 (6)	0.2040 (2)	0.0526 (9)
C8	0.8433 (3)	−0.0951 (6)	0.1815 (2)	0.0485 (9)
C9	0.8153 (3)	0.1052 (6)	0.1323 (2)	0.0588 (10)
C10	0.7037 (3)	0.1660 (7)	0.1067 (2)	0.0612 (10)
C11	0.6116 (3)	0.0272 (6)	0.1308 (2)	0.0506 (8)
C12	0.4939 (3)	0.0879 (7)	0.1065 (2)	0.0579 (9)
C13	0.9697 (3)	−0.1572 (6)	0.2054 (2)	0.0513 (9)
C14	1.0206 (3)	−0.2635 (8)	0.1174 (2)	0.0704 (11)
C15	0.9846 (3)	−0.3063 (7)	0.2961 (2)	0.0518 (8)
O16	0.9853 (2)	−0.5095 (5)	0.2847 (2)	0.0669 (7)
O17	0.9909 (2)	−0.2085 (4)	0.3788 (2)	0.0642 (7)
N1A	1.0769 (2)	0.2014 (6)	0.4281 (2)	0.0545 (7)
C2A	1.2053 (3)	0.2147 (7)	0.4285 (2)	0.0616 (10)
C3A	1.2368 (4)	0.2625 (11)	0.3243 (3)	0.099 (2)
C4A	1.2610 (3)	0.0069 (7)	0.4747 (2)	0.0582 (9)
C5A	1.2307 (3)	−0.0687 (8)	0.5656 (2)	0.0726 (12)
C6A	1.2834 (4)	−0.2488 (8)	0.6119 (3)	0.0789 (13)
C7A	1.3686 (3)	−0.3585 (8)	0.5703 (3)	0.0767 (12)
C8A	1.4005 (3)	−0.2930 (9)	0.4798 (3)	0.0818 (12)
C9A	1.3458 (3)	−0.1121 (8)	0.4334 (3)	0.0751 (12)

Table 2. *Selected geometric parameters (Å, °)*

C1—O2	1.434 (6)	C15—O16	1.226 (5)
O2—C3	1.380 (4)	C15—O17	1.270 (4)
C8—C13	1.528 (5)	N1A—C2A	1.497 (4)
C13—C14	1.522 (5)	C2A—C4A	1.517 (6)
C13—C15	1.528 (5)	C2A—C3A	1.527 (5)
C3—O2—C1	117.2 (3)	C14—C13—C15	111.9 (3)
C12—C3—O2	125.3 (3)	C8—C13—C15	111.3 (3)
C12—C3—C4	122.0 (3)	O16—C15—O17	124.7 (3)
O2—C3—C4	112.8 (3)	O16—C15—C13	118.4 (3)
C7—C8—C9	117.9 (3)	O17—C15—C13	116.8 (3)
C7—C8—C13	122.3 (3)	N1A—C2A—C4A	110.6 (3)
C9—C8—C13	119.7 (3)	N1A—C2A—C3A	108.6 (3)
C14—C13—C8	111.0 (2)	C4A—C2A—C3A	114.6 (4)
C1—O2—C3—C12	−2.1 (5)	C8—C13—C15—O16	93.9 (4)
C13—C8—C9—C10	178.2 (3)	C14—C13—C15—O17	151.8 (3)
C7—C8—C13—C14	96.1 (4)	C8—C13—C15—O17	−83.4 (3)
C9—C8—C13—C14	−82.2 (4)	N1A—C2A—C4A—C9A	132.4 (4)
C7—C8—C13—C15	−29.3 (4)	C3A—C2A—C4A—C9A	9.2 (5)
C9—C8—C13—C15	152.5 (3)	N1A—C2A—C4A—C5A	−50.4 (4)
C14—C13—C15—O16	−30.9 (4)	C2A—C4A—C5A—C6A	−176.5 (4)

Table 3. *Hydrogen-bonding geometry (Å, °)*

D—H···A	D—H	H···A	D···A	D—H···A
N1A—H1AA···O17	0.92 (4)	1.81	2.714 (4)	168
N1A—H1AB···O17^i	0.84 (3)	2.03	2.869 (4)	170
N1A—H1AC···O16^{ii}	1.03 (4)	1.76	2.767 (4)	164

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

Data collection: *DIF*4 (Stoe & Cie, 1987*a*). Cell refinement: *DIF*4. Data reduction: *REDU*4 (Stoe & Cie, 1987*c*). Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

The authors thank M. M. Vermeire for his helpful assistance in the diffractometry measurements and the Belgian FNRS (Fonds National de la Recherche Scientifique) for financial support.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: PA1198). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Goodman, M. & Gilman, A. (1980). Editors. *The Pharmacological Basis of Therapeutics*, 6th ed. New York: Macmillan.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Ravikumar, K., Rajan, S. S., Pattabhi, V. & Gabe, E. J. (1985). *Acta Cryst.* C**41**, 280–282.
Riegel, J., Maddox, L. & Harrison, I. T. (1974). *J. Med. Chem.* **17**, 377–378.
Sheldrick, G. M. (1990). *SHELXS*86. *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1993). *SHELXL*93. *Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Stoe & Cie (1987*a*) *DIF*4. *Diffractometer Control Program*. Version 6.2. Stoe & Cie, Darmstadt, Germany.

Stoe & Cie (1987*b*) *EMPIR. Empirical Absorption Correction Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1987*c*) *REDU4. Data Reduction Program.* Version 6.2. Stoe & Cie, Darmstadt, Germany.

Acta Cryst. (1996). C**52**, 395–397

An Orange Form of Coumarin 314

TERUYUKI HONDA,[a] ISAO FUJII,[a] NORIAKI HIRAYAMA,[a]* NORIHITO AOYAMA[b] AND AKIRA MIIKE[b]

[a]*Department of Biological Science and Technology, Tokai University, 317 Nishino, Numazu, Shizuoka 410-03, Japan, and* [b]*Research Laboratories, Kyowa Medex Co. Ltd, 600-1 Minami-Ishiki, Nagaizumi-cho, Sunto-gun, Shizuoka 411, Japan*

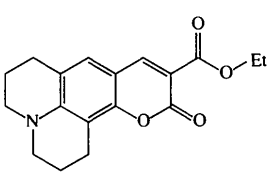
(*Received 24 July 1995; accepted 4 September 1995*)

Abstract

A new form of the title compound, ethyl 2,3,6,7-tetrahydro-11-oxo-1*H*,5*H*,11*H*-[1]benzopyrano[6,7,8-*ij*]-quinolizine-10-carboxylate, $C_{18}H_{19}NO_4$, was recrystallized from ethanol and is orange in colour. The coumarin moiety is planar and the conformation of the ethoxycarbonyl group is different from that of the yellow form. One of the piperidine rings is disordered and the N atom is in a planar configuration. The crystal packing is governed by van der Waals interactions.

Comment

The title compound, (I) (Eastman Kodak Co., Rochester, NY, USA), is used as an efficient laser dye. Derivatives with a structurally rigid amino group, such as the title compound, have been reported to show a high quantum yield of fluorescence in polar solvent (Reynolds & Drexhage, 1975). In order to understand the correlation between their structure and laser efficiency, crystal structure analyses of these derivatives are indispensable. The crystal structure of the yellow form of the title compound, recrystallized from a mixture of chloroform and ethanol, has been reported recently (Yip *et al.*, 1995). We have obtained a second polymorph, the orange form, from an ethanol solution and undertaken the X-ray analysis which is presented here.



(I)

An *ORTEP*II drawing (Johnson, 1976) of the title compound together with the atomic numbering scheme is shown in Fig. 1. The coumarin moiety is almost planar, with a mean deviation from the least-squares plane of 0.010 (2) Å; atom O2 deviates significantly from the least-squares plane [0.029 (2) Å]. One of the piperazine rings (C6—C7—N18—C17—C16—C15) is disordered at the C16 atom. Two positions of the atom were located and refined with occupancies for C16*A* and C16*B* of 0.75 and 0.25, respectively. Both rings adopt sofa conformations. The ring containing atom C16*B* adopts a more flattened conformation. The torsion angles in the major and minor rings are in the ranges −52.1 (3) to 48.1 (3)° and −31.3 (9) to 29 (1)°, respectively. The conformation of the ring in the yellow form is between a sofa and a half chair. The second piperidine ring (C7—C8—C21—C20—C19—N18) also takes a sofa conformation, as in the yellow form. The conformation of the ethoxycarbonyl group is remarkably different from that in the yellow form, the carbonyl O atom being *cis* with respect to the C2 atom in the yellow form but *trans* in the orange form. The group is planar and makes a dihedral angle of 4.4 (2)° with the plane of the coumarin moiety, which is significantly smaller than the value of 12.29 (7)° found in the yellow form.

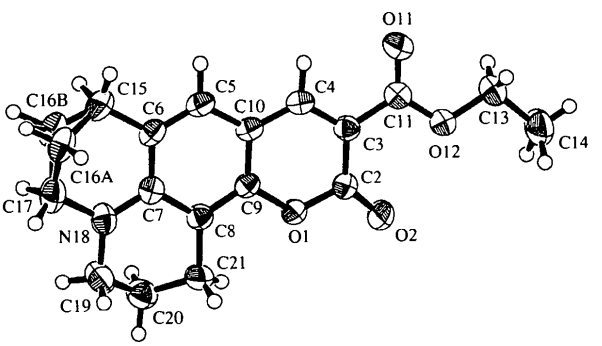


Fig. 1. *ORTEP*II drawing (Johnson, 1976) representing heavy atoms as 50% probability ellipsoids and H atoms as circles of arbitrary size.

The C2—C3 and O11—C11 bonds are significantly longer and the C20—C21 and N18—C7 bonds significantly shorter than the corresponding values in the yellow form (Yip *et al.*, 1995). The sum of the bond angles around the N18 atom is 360.0 (2)° and indicates that the N18 atom adopts a completely planar configuration, as in the yellow form. The exocyclic bond angles around the carbonyl group are highly asymmetric, just as in the yellow form. The bond angles around the C11 atom are significantly different from the corresponding values in the yellow form, the O11—C11—C3 angle being remarkably smaller. The molecules are packed together in the crystal according to van der Waals interactions.