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The Molecular Structure of (+)-6-Methoxy-α-methyl-2-naphthaleneacetic Acid Determined by X-Ray Method

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Abstract ☐ The molecular structure of (+)-6-Methoxy-α-methyl-2-naphthaleneacetic acid(Naproxen), $C_{14}H_{14}O_3$, was determined by X-Ray diffraction technique. Naproxen crystallized in $P2_1$ with two molecules in the unit cell of dimensions $a=7.855$, $b=5.783$, $c=13.347$Å and $\beta=93.9°$. The structure was solved with the SHELX program system. The present R-value is 0.099. The molecules are connected by the intermolecular OH···O hydrogen bonds.

Keywords ☐ Naproxen, Anti-inflammatory agent, Torison angle, Dihedral angle between planes, Intermolecular hydrogen bonds.

Like other non-steroidal anti-inflammatory agents, (+)-6-methoxy-α-methyl-2-naphthaleneacetic acid(Naproxen) is also believed to act through the inhibition of prostaglandin biosynthesis.[1-2]

The investigation of the molecular structures of related compounds and elucidation of the relationship between the molecular conformations and their physiological functions are of interest.

This paper presents briefly the molecular structure of Naproxen and discussion of some structural similarities between related compounds.

EXPERIMENTAL METHODS

The molecular structure of Naproxen was determined by x-ray diffraction methods. This compound was recrystallized from ethanol solution as colorless, transparent prism. The space group was determined from Weissenberg photographs and the lattice constants were obtained from measurement on a computer-controlled four-circle diffractometer with CuK_α radiations.

The density was measured by the flotation method on a mixture of benzene and carbon tetrachloride. The crystal data are listed in Table I.

Three dimensional intensity data were collected on a computer-controlled four-circle diffractometer (Rigaku Denki Co.Ltd.) with Ni-filtered CuK_α radiation.

403 reflections ($h_{max}=7$, $k_{max}=5$, $l_{max}=12$ and $\sin\theta/\lambda<0.50$Å^{-1}) were recorded by the ω-2θ scan technique. (scan speed=8°/min)

The structure was solved by the *SHELX* system.[3]

All the calculations were carried out on a VAX-11/780 at the Seoul National University Computer Centre. The refinement ot structure is now in pregress.

Table I: Crystal data.

(+)-6-Methoxy-α-methyl-2-naphthaleneacetic acid	
Molecular formula: $C_{14}H_{14}O_3$	M.W. 230.26
Colorless transparent prism,	Monoclinic
$a=7.855(4)$Å	$b=5.783(4)$Å
$c=13.349(32)$Å	$\beta=93.9(2)°$
Volume of unit cell	604.98Å^3
$D_{obs}=1.26$g/cm^3	$D_{cal}=1.264$g/cm^3
$Z=2$	space group; $P2_1$

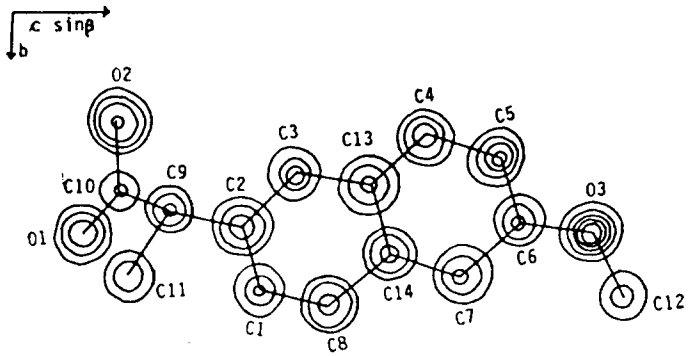

Fig. 1: Fourier map of Naproxen.

RESULTS AND DISCUSSION

Fig. 1. shows the Fourier map at the stage of R-value 0.099.

The bond lengths and angles are reasonable values compared with those of other compounds such as alclofenac[4], ibuprofen[5], flurbiprofen[6], 4-cyclohexyl-1-naphthalene propionic acid (ACNP)[7], (+)-(2R,αS)-2-isopropyl-α-methyl-5-indanacetic acid[8].

The torsion angle, C(2)-C(9)-C(10)-O(2), is -87.9°. The corresponding values of 2-substituted propionic acid derivatives are 89.3° for ibuprofen, 77.3° for flurbiprofen, 114.7° for ACNP and molecule A; -102.2°, molecule B; 109.7° for (+)-(2R,αS)-2-isopropyl-α-methyl-5-indanacetic acid.

The naphthalene ring is planar and the dihedral angle between this plane and that passing through C(10)-O(1)-O(2) is 72.3°.

The Naproxen molecules are connected by intermolecular OH(2)···O(1) hydrogen bonds between the two oxygen atoms of the carboxyl group as shown in Fig. 2.

Further details of the structure will be published elsewhere in the near future.

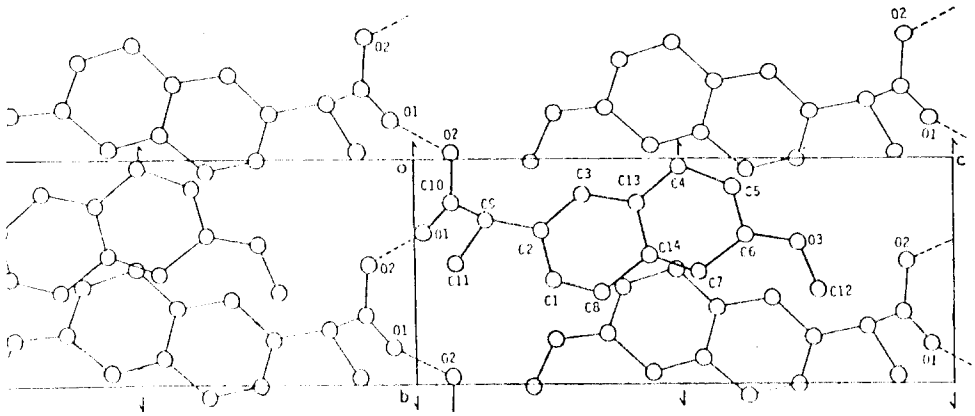

Fig. 2: Hydrogen bondings around original molecule.

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