Structure of a Chiral Cyclopentanone Precursor in Neocarzinostatin Synthetic Studies, C20H21NO3S.H2O

The Harvard community has made this article openly available. Please share how this access benefits you. Your story matters.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Schaefer, William P., Elaine Y. Kuo, Philip M. Harrington, and Andrew G. Myers. 1991. Structure of a chiral cyclopentanone precursor in neocarzinostatin synthetic studies, C20H21NO3S.H2O. Acta Crystallographica Section C: Crystal Structure Communications C47(12): 2578-2580</th>
</tr>
</thead>
<tbody>
<tr>
<td>Published Version</td>
<td><a href="http://dx.doi.org/10.1107/S0108270191005449">http://dx.doi.org/10.1107/S0108270191005449</a></td>
</tr>
<tr>
<td>Citable link</td>
<td><a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:3190376">http://nrs.harvard.edu/urn-3:HUL.InstRepos:3190376</a></td>
</tr>
<tr>
<td>Terms of Use</td>
<td>This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA">http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA</a></td>
</tr>
</tbody>
</table>
Final parameters are given in Table 1* for isomers (I) and (II).

Discussion. The two stereoisomers whose structures are described here show good similarities in bond distances and regular structures with no significant departures from expected bond lengths or angles. The disorder at C12 in isomer (I) makes comparisons in that region meaningless, but for the rest of the molecule these statements hold true (Table 2). The nine-membered ring has a certain amount of flexibility, but the two conformations, while differing at C1, are otherwise nearly equivalent. The carbonyl bond in both isomers exhibits normal van der Waals contacts across the ring: Si to the center of (C10, O3) is 3.56 Å in isomer (I) and 3.62 Å in isomer (II). We expected 3.55–3.65 Å based on data taken from Pauling (1960). The shortest (relatively speaking) contact we observed is Si–C10 = 3.39 Å in isomer (I); this is still approximately a van der Waals distance (radii for Si = 1.95, C = 1.50 Å).

In both structures the ketone O atom O3 has some contacts with H atoms on the benzene ring. In isomer (I) O3⋯H3 = 2.59 Å and in isomer (II) O3⋯H4 = 2.71 Å. These are not short enough to be considered as hydrogen bonds, but may indicate a small interaction between molecules in the crystal. Fig. 1 shows the numbering schemes for isomers (I) and (II). Figs. 2 and 3 show the packing of the isomers (I) and (II).

We thank the National Science Foundation, the David and Lucile Packard Foundation, and the Caltech Consortium in Chemistry and Chemical Engineering (members: E. I. duPont de Nemours & Co., Inc., Eastman Kodak Company, and Minnesota Mining and Manufacturing Company) for financial support.

References


Structure of a Chiral Cyclopentanone Precursor in Neocarzinostatin Synthetic Studies, C_{20}H_{21}NO_{3}S.H_{2}O

BY WILLIAM P. SCHAEFER, ELAINE Y. KUO, PHILIP M. HARRINGTON AND ANDREW G. MYERS

The Beckman Institute and Division of Chemistry and Chemical Engineering,*
California Institute of Technology, Pasadena, California 91125, USA

(Received 26 October 1990; accepted 3 May 1991)

Abstract. (1E,2S,3R)-2-[(4R,5R)-4,5-Dimethyl-1,3-dioxolan-2-yl]-3-(2-naphthylthio)cyclopentanone oxime, \(M_r = 373.47\), orthorhombic, \(P2_12_12_1\), \(a = 5.374\) (13), \(b = 18.135\) (3), \(c = 20.487\) (5) Å, \(V = 1997\) (5) Å\(^3\), \(Z = 4\), \(D_x = 1.24\) g cm\(^{-3}\), Mo \(K\alpha\), \(\lambda = 0.71073\) Å, \(\mu = 1.87\) cm\(^{-1}\), \(F(000) = 792\), room temperature, crystal volume \(2.7 \times 10^{-4}\) mm\(^3\), final \(R = 0.127\) for 971 reflections with \(F^2 > 0\) out of 1131 data, \(R = 0.065\) for 467 reflections with \(F^2 > 3\sigma(F^2)\). Despite the small crystal size (all larger crystals were twinned), a structural solution of adequate precision was obtained. Bond distances and angles in the molecule are normal; the water molecules are hydrogen bonded in a chain along the \(a\) axis and each
accepts a hydrogen bond from the oxime group and
donates a weak hydrogen bond to O3 in the dioxo-
lane group.

**Introduction.** The enantiomerically pure cyclopenta-
none derivative (1), a key intermediate in studies
directed towards the synthesis of the antitumor anti-
biotic neocarzinostatin chromophore, was obtained
by selective crystallization from a hexane solution
containing equal parts of (1) and its diastereomer (2)
(Myers, Harrington & Kuo, 1991). It was necessary
to determine unambiguously the relative stereo-
chemistry of (1) for these studies. Although we were
unable to obtain suitable crystals of (1), the anti
oxime derivative (3) provided small crystals, one of
which was usable for our purposes.

![Chemical structures](image)

**Experimental.** Needle-like crystal with diamond
cross-section 0.19 mm long, with perpendicular dia-
mond diagonals of 0.04 and 0.07 mm (total weight
~0.3 μg); many other larger crystals shown to be
twins. CAD-4 diffractometer; 25 reflections used in
the range 12 < 2θ < 24° for unit-cell dimensions; no
absorption correction (μmax = 0.04); (sinθ/λ)max =
0.48 Å⁻¹; data collected for h = 0 to 5, k = 0 to 17, l
= 0 to 19; two standard reflections (034, 004) showed
no variations greater than those expected from
counting statistics; 1164 reflections measured, 1131
unique (only the standards were duplicated); all
reflections used in solution and refinement of struc-
ture; structure solved by MULTAN (Main, Fiske,
Hull, Lessinger, Germain, Declercq & Woolfson,
1980), which gave positions of sulfur and five carbon
atoms; remainder found by successive structure-
factor Fourier cycles; refinement on F²; hydrogen
atoms placed by calculation (C—H = 0.95 Å) with
staggered geometry (oxime-hydrogen atom left out);
final cycles included coordinates and anisotropic dis-
placement parameters for the sulfur, oxime-oxygen,
methyl-carbon and water-oxygen atoms, coordinates
and isotropic thermal parameters for the remaining
oxygen and carbon atoms and a scale factor; abso-
lute configuration from the dioxolane moiety; a
secondary extinction parameter went negative so it
was not used. For 971 reflections with Fo² > 0, R =
0.127, wR = 0.021; for 467 reflections with Fo² >
3σ(Fo²), R = 0.065, wR = 0.010; S = 1.27 for 1131
reflections and 131 parameters; variances of the
reflections based on counting statistics plus an addi-
tional term 0.02F²; weights taken as 1/σ²(Fo²); maxi-
mum shift/e.s.d. in final cycle 0.01; maximum and
minimum heights in final difference map +0.52,
−0.49 e Å⁻³; atomic scattering factors taken from
Cromer & Waber (1974), dispersion correction from
Cromer (1974); programs used were those of the
CRYM crystallographic computing system
(Duchamp, 1964), MULTAN (Main et al., 1980) and
ORTEP (Johnson, 1976). Much effort was expended
trying to grow larger crystals but no better material
could be produced. As the data are weak the results,
while unequivocal, are not highly precise and the R
index is larger than is usual.

**Discussion.** Table 1 lists the final refined parameters
and Table 2 gives selected distances and angles.*
Figs. 1 and 2 show the molecule and how it packs in
the cell.

The two sulfur–carbon distances are quite unequal
[S—CN2, 1.744 (15) Å and S—C3, 1.826 (15) Å] but
are in the same order as expected [1.819 Å for
S—CHC₂, 1.773 Å for S—C(aromatic)] (Allen,
The bonds in the naphthalene group average
1.39 (4) Å (the precision is not high enough to distin-
guish the various types of naphthalene bonds) and
the other C—C distances are acceptably close to
expected values. The water molecule is hydrogen
bonded to O(N), the oxime oxygen atom [O—O—O,
2.68 (2) Å] and to O3, in the dioxolane group [O—O,
2.97 (2) Å]. There are weak water–water interactions
along the a axis, with O4—O4 distances of 3.36 (2) Å.
If these are considered hydrogen bonds, then there is
a chain of water molecules along a, with each water
molecule donating a hydrogen bond to another
water molecule and to O3, and accepting one from
O(N) and another water molecule. The geometry
about one water molecule is roughly tetrahedral,
with O—O—O angles ranging from 68 to 144°; the
average difference from 109.5° of the six angles
involved is 26°.

* Figures showing the numbering system and lists of anisotropic
displacement parameters, complete distances and angles, structure
factors and assigned H-atom parameters have been deposited with
the British Library Document Supply Centre as Supplementary
Publication No. SUP 54229 (12 pp.). Copies may be obtained
through The Technical Editor, International Union of Crystallog-
raphy, 5 Abbey Square, Chester CH1 2HU, England.
Table 1. Final atomic coordinates ($\times 10^4$) and $U_{eq}$ values ($\AA^2 \times 10^4$) for C$_{20}$H$_{23}$NO$_4$S

<table>
<thead>
<tr>
<th>S</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>B$<em>{eq}$/U$</em>{eq}$/$\AA^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CN1</td>
<td>1720</td>
<td>1599</td>
<td>2025</td>
<td>711 (13)</td>
</tr>
<tr>
<td>CN2</td>
<td>1583</td>
<td>2533</td>
<td>1502</td>
<td>4.0 (4)</td>
</tr>
<tr>
<td>CN3</td>
<td>1356</td>
<td>1748</td>
<td>1155</td>
<td>4.1 (4)</td>
</tr>
<tr>
<td>CN4</td>
<td>-2396</td>
<td>2204</td>
<td>763</td>
<td>6.5 (5)</td>
</tr>
<tr>
<td>CN5</td>
<td>-2224</td>
<td>3533</td>
<td>332</td>
<td>6.7 (5)</td>
</tr>
<tr>
<td>CN6</td>
<td>1086</td>
<td>4117</td>
<td>318</td>
<td>7.6 (6)</td>
</tr>
<tr>
<td>CN7</td>
<td>1058</td>
<td>4335</td>
<td>664</td>
<td>6.0 (5)</td>
</tr>
<tr>
<td>CN8</td>
<td>2084</td>
<td>3787</td>
<td>1059</td>
<td>5.5 (4)</td>
</tr>
<tr>
<td>CN9</td>
<td>849</td>
<td>3090</td>
<td>1103</td>
<td>4.9 (4)</td>
</tr>
<tr>
<td>CN10</td>
<td>1271</td>
<td>2969</td>
<td>728</td>
<td>5.0 (4)</td>
</tr>
<tr>
<td>N</td>
<td>407</td>
<td>1793</td>
<td>4002</td>
<td>4.8 (3)</td>
</tr>
<tr>
<td>O(N)</td>
<td>260</td>
<td>1258</td>
<td>4460</td>
<td>714 (33)</td>
</tr>
<tr>
<td>C1</td>
<td>2957</td>
<td>2045</td>
<td>3044</td>
<td>4.3 (4)</td>
</tr>
<tr>
<td>C2</td>
<td>4133</td>
<td>1493</td>
<td>2553</td>
<td>4.6 (4)</td>
</tr>
<tr>
<td>C4</td>
<td>5059</td>
<td>857</td>
<td>2993</td>
<td>6.5 (5)</td>
</tr>
<tr>
<td>C5</td>
<td>3241</td>
<td>704</td>
<td>3559</td>
<td>5.4 (4)</td>
</tr>
<tr>
<td>C6</td>
<td>5057</td>
<td>2533</td>
<td>3267</td>
<td>5.5 (4)</td>
</tr>
<tr>
<td>O1</td>
<td>4138</td>
<td>3096</td>
<td>3704</td>
<td>6.1 (3)</td>
</tr>
<tr>
<td>O3</td>
<td>5990</td>
<td>2956</td>
<td>2114</td>
<td>6.1 (3)</td>
</tr>
<tr>
<td>C7</td>
<td>5829</td>
<td>3726</td>
<td>3632</td>
<td>6.7 (5)</td>
</tr>
<tr>
<td>C8</td>
<td>4521</td>
<td>4393</td>
<td>3911</td>
<td>1483 (90)</td>
</tr>
<tr>
<td>C9</td>
<td>6251</td>
<td>3710</td>
<td>2908</td>
<td>5.3 (4)</td>
</tr>
<tr>
<td>C10</td>
<td>8704</td>
<td>4006</td>
<td>2682</td>
<td>1100 (70)</td>
</tr>
<tr>
<td>O4</td>
<td>1056</td>
<td>3046</td>
<td>4055</td>
<td>1268 (48)</td>
</tr>
</tbody>
</table>

$U_{eq} = \sum a^i a^j U_{ij}$

Table 2. Distances ($\AA$) and angles ($^\circ$) not involving H atoms for C$_{20}$H$_{23}$NO$_4$S

<table>
<thead>
<tr>
<th>S-CN2</th>
<th>1-744 (15)</th>
<th>C4-C5</th>
<th>1-52 (2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-C3</td>
<td>1-862 (15)</td>
<td>C6-C0</td>
<td>1-42 (2)</td>
</tr>
<tr>
<td>CN1-CN2</td>
<td>1-39 (2)</td>
<td>C0-C1</td>
<td>1-42 (2)</td>
</tr>
<tr>
<td>CN1-CN9</td>
<td>1-41 (2)</td>
<td>C1-C7</td>
<td>1-42 (2)</td>
</tr>
<tr>
<td>CN2-CN3</td>
<td>1-46 (2)</td>
<td>C7-C9</td>
<td>1-42 (2)</td>
</tr>
<tr>
<td>CN3-CN4</td>
<td>1-36 (2)</td>
<td>C9-C0</td>
<td>1-42 (2)</td>
</tr>
<tr>
<td>CN4-CN10</td>
<td>1-37 (2)</td>
<td>C10-C2</td>
<td>1-53 (2)</td>
</tr>
<tr>
<td>CN5-CN6</td>
<td>1-32 (3)</td>
<td>C2-C10</td>
<td>1-53 (2)</td>
</tr>
<tr>
<td>CN5-CN10</td>
<td>1-40 (2)</td>
<td>C10-C2</td>
<td>1-53 (2)</td>
</tr>
<tr>
<td>CN6-CN7</td>
<td>1-38 (3)</td>
<td>C1-C3</td>
<td>1-53 (2)</td>
</tr>
<tr>
<td>CN7-CN8</td>
<td>1-40 (2)</td>
<td>C3-N(O)</td>
<td>1-396 (16)</td>
</tr>
<tr>
<td>CN8-CN9</td>
<td>1-43 (2)</td>
<td>C2-C3</td>
<td>1-55 (2)</td>
</tr>
<tr>
<td>CN9-CN10</td>
<td>1-39 (2)</td>
<td>C2-C6</td>
<td>1-54 (2)</td>
</tr>
<tr>
<td>C1-N</td>
<td>1-265 (19)</td>
<td>C3-C4</td>
<td>1-55 (2)</td>
</tr>
</tbody>
</table>

Fig. 1. An ORTEP drawing of the molecule with 50% thermal ellipsoids. Hydrogen atoms were given small arbitrary $B$ values.

Fig. 2. An ORTEP projection of four molecules with a unit cell outlined. Atoms are shown as 60% thermal ellipsoids; hydrogen atoms are not shown. Two extra water-molecule oxygen atoms are shown (top center) to illustrate the chain of water molecules along z. Hydrogen bonding is indicated by thin bonds.

References


