Structure of Methyl 6-Oxo-2aα,3,4,5,5aα,6,7,8,8aα,8bα-decahydro-2*H*-naphtho[1,8-*bc*]-furan-8bα-carboxylate

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Abstract. $C_{13}H_{18}O_4$, monoclinic, $P2_1/c$, $a = 8.039$ (2), $b = 14.275$ (4), $c = 11.730$ (3) Å, $\beta = 118.04$ (2)°, $Z = 4$, $D_x = 1.33$, $D_m = 1.35$ (2) Mg m^{-3}. The structure, which was refined to $R = 0.053$ with 1765 observations, reveals the stereochemistry at the furan–naphthone ring juncture and thus the stereospecificity of the catalytic hydrogenation which produced it.

Introduction. The African army worm after consuming a portion of a leaf from the ajuga plant, *Ajuga remota* (Labiatae), stops further feeding and eventually dies of malnutrition (Kubo, Lee, Balogh-Nair, Nakanishi & Chapya, 1976). A compound ajugarin I, (I), has been isolated from this plant and has been shown to have the observed anti-feeding activity (Hosazawa, Kato & Munakata, 1974).

(I)   (II)   (III)
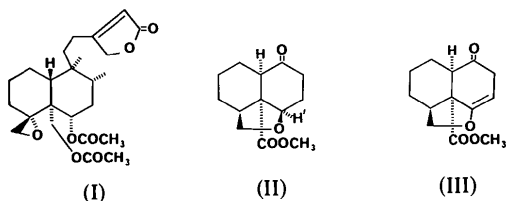
Creating a *de novo* synthesis of this natural product requires that the sterochemistry of several intermediates along the proposed synthetic route be determined. The title compound, (II), whose synthesis will be described in detail elsewhere (Goldsmith & Thottathil, 1982), is prepared by the platinum-catalyzed hydrogenation of compound (III). It was necessary to know if the hydrogen shown as H' was *cis* or *trans* to the methyl ester. If the ester group and H' in compound (II) were *cis*, then the cyclic ether would more likely undergo ring opening by nucleophilic attack by acetate ion and thus lead to the required intermediate in the ajugarin I synthesis.

Colorless crystals of (II) were grown from an ether–hexane solution. Several crystals were mounted on quartz fibers with epoxy cement with their long axis parallel to the fiber. Preliminary characterization of the

crystals using precession photographs showed systematic absences in the *h*0*l* and 0*k*0 reflections which were consistent with the space group $P2_1/c$. Intensity data was collected using a Syntex $P2_1$ four-circle diffractometer. Monochromatic Mo $K\alpha$ radiation $(2\theta_{max} = 12.2°)$ was used for determining the lattice parameters, establishing the orientation matrix and collecting the intensity data. Initially 15 diffraction peaks were machine-centered, and used in an unconstrained least-squares refinement of the lattice parameters and orientation matrix. A total of 2115 unique reflections with $\sin \theta/\lambda < 0.59$ Å^{-1} were collected using the $2\theta/\theta$ scan technique. A scan width of 2° was sufficient to collect all of the peak intensity. A variable scan rate ranging from 4.88 to 29.3° min^{-1} was used. Stationary background measurements were made at the beginning and at the end of each scan for a total time equal to the scan time. No significant fluctuations were observed in the intensities of three reference reflections monitored every 100 reflections. The data were corrected for background, Lorentz, and polarization factors. No absorption correction was applied.

The structure was solved by direct methods and refined by full-matrix least squares using the *SHELX* 76 (Sheldrick, 1976) program. After anisotropic refinement of the non-H atoms, the H atoms were each located in an electron density difference synthesis and included in the refinement with isotropic thermal parameters. Using the 1765 reflections with $I > 2\sigma(I)$ refinement converged to $R = 0.053$, $R_w = 0.063$ $\{R_w = \sum w^{1/2}(|F_o| - |F_c|)/\sum w^{1/2}|F_o|$, and $w = 1.2216/[\sigma(F_o)^2 + 0.002615F_o^2]$ (Grant, Killean & Lawrence, 1969)}.[†] The final electron density difference map showed no peaks exceeding 0.32 e Å^{-3}.

Discussion. The observed bond distances and selected bond angles are presented in Fig. 1. The final refined positional parameters are listed in Table 1 and a stereo

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† Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36982 (7 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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ORTEP drawing (Johnson, 1965) is shown in Fig. 2. For the naphthofuran the average C—C bond distance for the decalin system is 1·524 Å. This value is in close agreement with the average C—C bond distance observed in a similar ring system: 1·527 Å in the structure of methyl 5α-acetoxymethyl-4β-methoxy-1-oxo-1,2,3,4,4aβ,5,6,7,8,8aα-decahydronaphthalene-4aβ-carboxylate (Rubin, Epstein & Brooks, 1983). The molecular configuration shown in Fig. 2 shows the H on C(7) to be *cis* to the ester function on C(6). The

Table 1. *Final atomic positional parameters and isotropic temperature factors with e.s.d.'s in parentheses*

$$B_{eq} = \tfrac{4}{3} \sum_i B_{ii}.$$

|	x	y	z	B_{eq}/B (Å²)
C(1)	0·0284 (3)	0·1929 (2)	0·3857 (2)	3·04 (5)
C(2)	0·1757 (4)	0·1241 (2)	0·4762 (2)	3·80 (5)
C(3)	0·2216 (4)	0·0486 (2)	0·4045 (3)	4·66 (7)
C(4)	0·2904 (4)	0·0916 (2)	0·3157 (3)	4·78 (7)
C(5)	0·1552 (3)	0·1636 (2)	0·2238 (2)	3·50 (5)
C(6)	0·0811 (3)	0·2367 (1)	0·2858 (2)	2·77 (4)
C(7)	−0·0943 (3)	0·2751 (2)	0·1653 (2)	3·42 (5)
C(8)	−0·2516 (4)	0·3038 (2)	0·1946 (3)	4·23 (6)
C(9)	−0·3241 (2)	0·2198 (2)	0·2366 (3)	4·57 (7)
C(10)	−0·1709 (2)	0·1550 (2)	0·3268 (2)	3·59 (5)
C(11)	−0·0269 (4)	0·1244 (2)	0·1166 (2)	4·33 (6)
C(12)	0·2150 (2)	0·3182 (2)	0·3507 (2)	3·36 (5)
C(13)	0·4526 (4)	0·4156 (2)	0·3516 (3)	4·73 (8)
O(3)	0·2156 (4)	0·3651 (2)	0·4352 (3)	9·47 (8)
O(4)	0·3306 (2)	0·3346 (1)	0·3035 (2)	4·58 (4)
O(2)	−0·2075 (3)	0·0804 (1)	0·3567 (2)	5·51 (5)
O(1)	−0·1579 (2)	0·2012 (1)	0·0724 (2)	4·50 (4)
H(11)	0·0207 (28)	0·2419 (15)	0·4331 (21)	3·27 (23)
H(21)	0·1307 (37)	0·0972 (17)	0·5343 (27)	4·35 (30)
H(22)	0·2858 (44)	0·1614 (24)	0·5307 (31)	5·70 (42)
H(31)	0·3131 (37)	0·0065 (20)	0·4637 (25)	4·50 (32)
H(32)	0·1058 (37)	0·0115 (18)	0·3548 (24)	4·03 (30)
H(41)	0·3064 (38)	0·0445 (22)	0·2638 (28)	5·13 (37)
H(42)	0·4118 (42)	0·1231 (19)	0·3668 (27)	4·82 (34)
H(51)	0·2140 (34)	0·1947 (17)	0·1837 (24)	3·56 (28)
H(71)	−0·0526 (38)	0·3320 (20)	0·1311 (29)	4·60 (34)
H(81)	−0·2015 (41)	0·3573 (23)	0·2630 (31)	5·75 (40)
H(82)	−0·3436 (37)	0·3342 (18)	0·1248 (27)	4·00 (30)
H(91)	−0·4140 (47)	0·1826 (21)	0·1607 (35)	6·43 (43)
H(92)	−0·3971 (46)	0·2386 (24)	0·2766 (31)	6·89 (44)
H(111)	−0·0830 (35)	0·0727 (19)	0·1440 (25)	4·31 (32)
H(112)	−0·0080 (40)	0·1007 (21)	0·0454 (30)	5·26 (37)
H(131)	0·5342 (60)	0·4093 (27)	0·4452 (45)	7·91 (54)
H(132)	0·3987 (45)	0·4662 (25)	0·3556 (33)	8·05 (50)
H(133)	0·5520 (81)	0·4092 (36)	0·3331 (57)	12·40 (98)
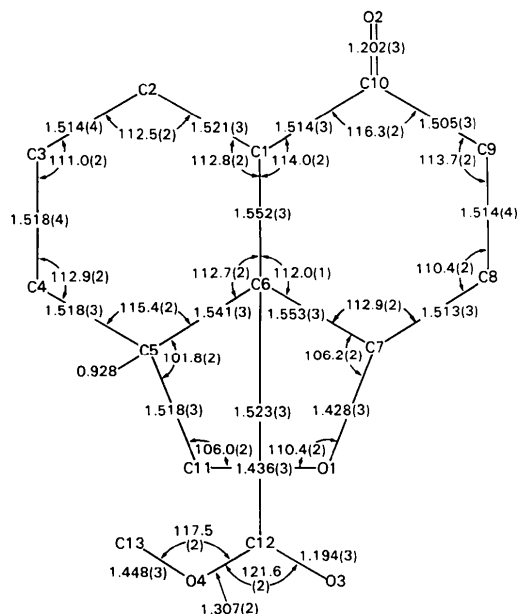
Fig. 1. Bond lengths (Å) and selected bond angles (°). The estimated errors in the least significant digits are shown parenthetically. The numbering shown is that used in Table 1.
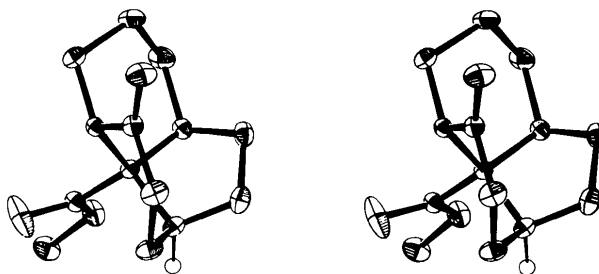

Fig. 2. An *ORTEP* stereodrawing of the title compound. The thermal ellipsoids are drawn at the 33% probability level.

torsion angles for the three rings are presented in Table 2. Examination of the six-membered ring containing C(7) shows it to be in the highly strained twisted-boat conformation while the C(1)–C(6) ring is in the more stable chair conformation.

Table 2. *Ring torsion angles* (°)

E.s.d.'s are 0·5°.

Cyclohexane ring		Ketone ring		Furan ring	
C(1)–C(2)–C(3)–C(4)	−57·7	C(1)–C(6)–C(7)–C(8)	−27·1	C(6)–C(7)–O(1)–C(11)	6·9
C(2)–C(3)–C(4)–C(5)	53·9	C(6)–C(7)–C(8)–C(9)	63·4	C(7)–O(1)–C(11)–C(5)	17·2
C(3)–C(4)–C(5)–C(6)	47·2	C(7)–C(8)–C(9)–C(10)	−41·5	O(1)–C(11)–C(5)–C(6)	−33·8
C(4)–C(5)–C(6)–C(1)	42·2	C(8)–C(9)–C(10)–C(1)	13·6	C(11)–C(5)–C(6)–C(7)	−36·4
C(5)–C(6)–C(1)–C(2)	−44·7	C(9)–C(10)–C(1)–C(6)	−49·5	C(5)–C(6)–C(7)–O(1)	−27·4
C(6)–C(1)–C(2)–C(3)	−53·5	C(10)–C(1)–C(6)–C(7)	−27·2		

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Structure of *N*-[1-(2-Hydroxy-2-phenylethyl)-4-piperidyl]-*N*-phenylpropanamide Hydrochloride (R4333*), an Analgesic of the Fentanyl Family

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Abstract. $C_{22}H_{28}N_2O_2 \cdot HCl$, $P2_1/c$, $a = 12\cdot104\,(5)$, $b = 11\cdot560\,(5)$, $c = 15\cdot013\,(5)$ Å, $\beta = 101\cdot14\,(5)°$, $M_r = 388\cdot9$, $D_m = 1\cdot25\,(1)$, $D_x = 1\cdot25\,(2)$ Mg m^{-3}, $Z = 4$, $T = 293$ K, $R = 0\cdot06$ for 2538 reflexions. The conformation is similar to that found for other compounds of the fentanyl family. Packing is governed by van der Waals interactions; the chloride ion does not contribute to the formation of intermolecular H bonds.

Introduction. The crystal structure determination of the title compound (I) is part of a more general study of conformations for narcotic analgesics, particularly those of the fentanyl family. Some of these compounds are very potent analgesics (Van Daele, De Bruyn, Boey, Sanezuk, Agten & Janssen, 1976); in particular R4333 was revealed as being more than 150 times more active than meperidine (Janssen & Van Der Eycken, 1968). Crystals have been obtained from a chloroform/ethanol mixture slowly evaporated. The space group was determined by photographs. Final cell dimensions and intensities were measured on a Nonius CAD-4 four-circle computer-controlled diffractometer.

(I)
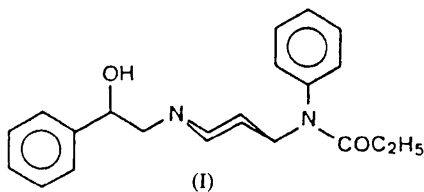
* Janssen Pharmaceutica internal code number.
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Table 1. *Instrumental settings for the data collection*

Source Cu *Kā* $\lambda = 1\cdot54178$ Å
Graphite monochromator
Scan ω–2θ
$\Delta 2\theta = 0\cdot80 + 0\cdot30$ tg θ (°)
Aperture $= 2\cdot5 + 0\cdot5$ tg θ (mm)
Confidence level: $2\cdot5\,\sigma$, where $\sigma^2 = S = B + (0\cdot03S)^2$, S being the scan and B the background count
$2 \le \theta \le 70°$
Total number of independent reflexions 3921
Total observed reflexions 2538

The instrumental settings are listed in Table 1. No corrections were applied for absorption.

The structure was solved with *MULTAN* 78 (Main, Woolfson, Lessinger, Germain & Declercq, 1978). All non-H atoms were located on the most probable *E* map computed with the 208 largest $\langle E \rangle$. Refinement was performed (Sheldrick, 1976) by Fourier maps and full-matrix anisotropic least squares for non-H atoms. Their final coordinates are listed in Table 2. H-atom coordinates were calculated but not refined. The final $R = \sum ||F_o| - |F_c||/\sum |F_o| = 0\cdot06$ for the observed reflexions.‡

‡ Lists of structure factors, anisotropic thermal parameters and H atom coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36976 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.