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7,8-Didehydro-4,5-epoxy-17-methylmorphinan-6-yl naphthalene-1-carboxylate

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Key indicators

Single-crystal X-ray study
T = 123 K
Mean σ(C–C) = 0.003 Å
R factor = 0.036
wR factor = 0.082
Data-to-parameter ratio = 9.7

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

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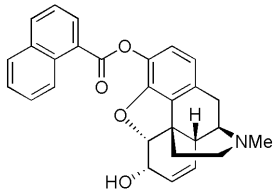
The crystal structure of morphine 3-(1-naphthoate), (or 7,8-didehydro-4,5-epoxy-17-methylmorphinan-6-yl naphthalene-1-carboxylate), $C_{28}H_{25}NO_4$, was determined at 123 K. An intramolecular hydrogen bond exists between the secondary alcohol and the naphthoate group. Within the crystal structure, there is no significant π–π stacking, but there are significant intermolecular C—H$\cdots\pi$ interactions.

Comment

As part of our work investigating protecting group methodology of opiate compounds and their properties, we have studied the use of the 1-naphthoate group. We have recently reported the preparation, properties and crystal structure of morphine di-(1-naphthoate) (Gathergood *et al.*, 2003). We describe herein the crystal structure of morphine 3-(1-naphthoate), (I), and unambiguously assign the position of the naphthoate group.



(I)

There are several examples of morphine-based opiates reacting at the phenol position with acid chlorides to give the mono-ester product (Mignat *et al.*, 1996; Otter *et al.*, 2001; Preechagoon *et al.*, 1998; Sy *et al.*, 1986). Despite the steric bulk of the 1-naphthoyl group, we expected reaction at the phenol (see above); however, we were keen to unambiguously assign the product by X-ray crystallography. The results (Fig. 1) show definitively that the phenolic alcohol reacted to give the title compound, morphine 3-(1-naphthoate).

Present in (I) is an intramolecular hydrogen bond between the secondary alcohol group and the carbonyl O atom of the naphthoate group. There are also extensive intermolecular C—H$\cdots\pi$ interactions (Table 2). Hydrogen bonding to the N atom of the opiate backbone is not observed.

Experimental

Morphine 3-(1-naphthoate), (I), was prepared from (−)-morphine by addition of 1-naphthoyl chloride in pyridine and stirring at room temperature for 48 h. Pyridine was removed by rotary evaporation and the residue dissolved in dichloromethane and washed with 5% sodium bicarbonate solution, then brine. The organic phase was dried over magnesium sulfate, filtered and the solvents removed by rotary evaporation. The crude product was purified by column chromatography. Needle-like crystals of morphine 3-(1-naphthoate) were grown by slow evaporation of a methanol solution.

Crystal data

$C_{28}H_{25}NO_4$	D_x = 1.325 Mg m^{-3}
M_r = 439.49	Mo $K\alpha$ radiation
Monoclinic, $P2_1$	Cell parameters from 14 873 reflections
a = 12.7421 (2) Å	θ = 2.8–28.3°
b = 7.1908 (1) Å	μ = 0.09 mm^{-1}
c = 12.9536 (3) Å	T = 123 (2) K
β = 111.900 (1)°	Acicular, colourless
V = 1101.23 (4) Å^3	0.24 × 0.20 × 0.12 mm
Z = 2	

Data collection

Nonius KappaCCD diffractometer	R_{int} = 0.044
Thick-slice φ and ω scans	θ_{max} = 28.3°
14 873 measured reflections	$h = -16 \rightarrow 16$
2909 independent reflections	$k = -9 \rightarrow 9$
2423 reflections with $I > 2\sigma(I)$	$l = -17 \rightarrow 17$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0416P)^2 + 0.1452P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.036	$(\Delta/\sigma)_{max}$ = 0.002
$wR(F^2)$ = 0.082	$\Delta\rho_{max}$ = 0.19 e Å^{-3}
S = 1.04	$\Delta\rho_{min}$ = −0.20 e Å^{-3}
2909 reflections	
300 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

C1—O1	1.372 (2)	C9—O2	1.426 (2)
C1—C2	1.376 (3)	C9—C10	1.501 (3)
C2—O3	1.406 (2)	C10—C11	1.324 (3)
C7—C12	1.540 (3)	C11—C12	1.504 (3)
C7—C8	1.546 (3)	C18—O4	1.208 (2)
C8—O1	1.480 (2)	C18—O3	1.367 (2)
C8—C9	1.545 (3)	C18—C19	1.491 (3)
O1—C1—C2	127.39 (16)	C10—C11—C12	120.73 (19)
C1—C2—O3	122.05 (16)	C11—C12—C7	108.97 (17)
C12—C7—C8	116.34 (15)	O4—C18—O3	123.25 (16)
O1—C8—C9	108.95 (16)	O4—C18—C19	126.59 (17)
O1—C8—C7	105.49 (13)	O3—C18—C19	110.15 (15)
C9—C8—C7	113.94 (15)	C20—C19—C18	117.65 (19)
O2—C9—C10	113.09 (17)	C28—C19—C18	121.31 (17)
O2—C9—C8	111.10 (15)	C1—O1—C8	106.24 (13)
C10—C9—C8	113.60 (15)	C18—O3—C2	117.36 (14)
C11—C10—C9	121.94 (19)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···O4	0.84	2.23	3.067 (2)	171
C3—H3···$Cg1^{i}$	0.95	2.70	3.577 (2)	154
C16—H16b···$Cg1^{ii}$	0.99	3.14	4.004 (2)	146
C14—H14a···$Cg2^{iii}$	0.99	3.24	4.068 (2)	143
C25—H25···$Cg3^{iv}$	0.95	2.84	3.643 (3)	143

Symmetry codes: (i) $-x, \frac{1}{2}+y, -z$; (ii) $x, y-1, z$; (iii) $-x, y-\frac{1}{2}, -z$; (iv) $1-x, \frac{1}{2}+y, 1-z$. Cg1–3 are the centroids of rings C1–C6, C19–C23/C28 and C23–C28, respectively.

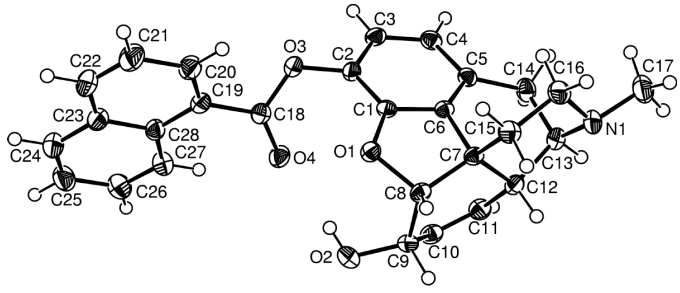


Figure 1
ORTEP-3 (Farrugia, 1997) view of (I). Displacement ellipsoids are drawn at the 50% probability level.

H atoms were placed in calculated positions, with C—H distances of 0.95, 0.98, 0.99 and 1.00 Å for aromatic, methyl, methylene and methine H atoms, respectively. They were included in the refinement in a riding-model approximation, with U_{iso} = 1.2U_{eq} (1.5U_{eq} for methyl H atoms) of the carrier atom. In the absence of significant anomalous dispersion effects, Friedel pairs were merged. The absolute configuration was assigned by reference to (−)-morphine.

Data collection: *COLLECT* (Nonius, 1997–2002); cell refinement: *HKL SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *HKL DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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