Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-Methoxy-*N*-[2-(3-thienyl)-1,2,3,4-tetrahydro-1-naphthyl]acetamide

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Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.006 Å
R factor = 0.059
wR factor = 0.158
Data-to-parameter ratio = 16.8

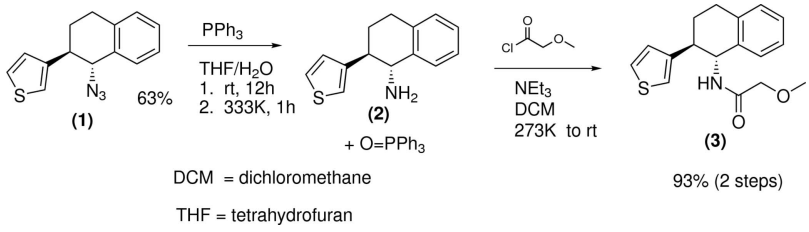
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 23 December 2005
Accepted 10 January 2006

The asymmetric unit of the title compound, $C_{17}H_{19}NO_2S$, contains two independent molecules with different conformations. Both molecules are linked by intermolecular N—H···O hydrogen bonds [N···O = 3.033 (4) and 2.969 (4) Å] to form two types of one-dimensional chains running in the *b* direction.

Comment

Tetralins (tetrahydronaphthalenes) can be considered as privileged structures, as they are present in a variety of important bioactive compounds, such as the antidepressant sertraline and the anticancer agent podophyllotoxin. One useful method for the synthesis of these scaffolds involves the metal-catalyzed ring-opening reaction of heterobicyclic alkenes (for a review, see Lautens *et al.*, 2003). Earlier, we reported that Rh^I catalysts can promote the highly enantioselective ring-opening of oxabicyclic alkenes with boronic acids (Lautens *et al.*, 2002). Recently, we have utilized this method to synthesize several tetralin scaffolds for drug discovery efforts with our industrial collaborators (Dockendorff, 2006). During the course of this project, the title amide, (3), was synthesized from azide (1), and we report its X-ray crystal structure here.



The two independent molecules, *A* and *B*, in the asymmetric unit of (3) are shown in Figs. 1 and 2, respectively. Table 1 lists the pertinent torsion angles, which describe the differences in the conformations between the two molecules. The dihedral angles between the mean planes of the thiophene and benzene rings are 81.4 (2) and 44.9 (2)° for molecules *A* and *B*, respectively.

The conformational analysis of the cyclohexene ring (C5/C6/C7/C12–C14) in each molecule (Duax *et al.*, 1976) shows that the conformation is a half-chair, with a local pseudo-twofold axis running through the midpoints of the C5*A*—C14*A* (C5*B*—C14*B*) and C7*A*—C12*A* (C7*B*—C12*B*) bonds.

In the crystal structure of (3), two independent one-dimensional *C*4 chains (Bernstein *et al.*, 1995) running along the *b* direction are formed *via* intermolecular N—H···O hydrogen bonds (Table 2 and Fig. 2). Chains of both types of

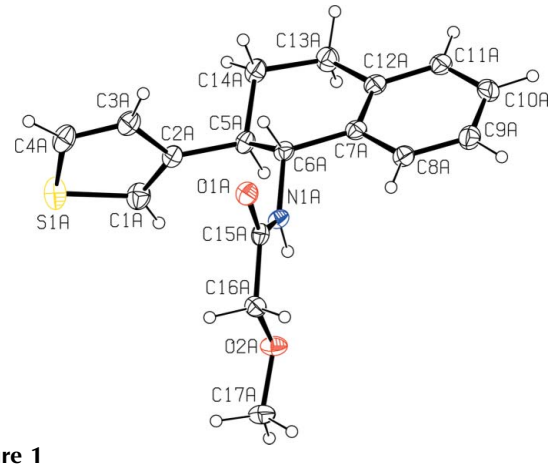


Figure 1
A view of molecule *A* of (3), showing 30% probability displacement ellipsoids (arbitrary spheres for the H atoms).

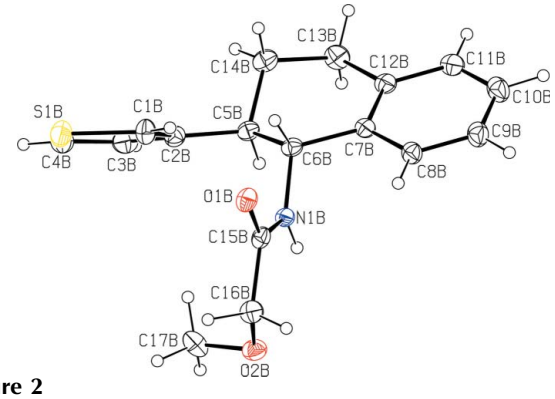


Figure 2
A view of molecule *B* of (3), showing 30% probability displacement ellipsoids (arbitrary spheres for the H atoms).

molecule are, in turn, linked together into a two-dimensional framework *via* weak intermolecular C—H···O hydrogen bonds (Table 2).

Experimental

Azide (1) (253 mg, 0.991 mmol) and PPh_3 (520 mg, 1.98 mmol) were added to a 50 ml round-bottomed flask with a stirrer bar. The flask was sealed and flushed with nitrogen before tetrahydrofuran (THF; 9 ml) and water (deionized, 0.9 ml) were added. The reaction mixture was stirred for 12 h, after which time analysis by thin-layer chromatography (TLC) [50% dichloromethane (DCM)/hexanes] showed no azide remaining. The reaction mixture was then heated in an oil bath at 333 K for 2 h to hydrolyze all the phosphoimine intermediate. The reaction mixture was then evaporated and dried under high vacuum to remove most of the water. The resulting crude amine, (2), was dissolved in DCM, dried over $MgSO_4$, filtered and transferred to a flame-dried 25 ml round-bottomed flask with a stirrer bar and further DCM (5 ml). The flask was sealed and flushed with N_2 and then cooled in an ice bath, before NEt_3 (275 µl, 1.98 mmol) and methoxyacetyl chloride (136 µl, 1.49 mmol) were added dropwise *via* a syringe. The reaction mixture was removed from the ice bath and stirred for 4 h, after which time TLC analysis (5% MeOH/DCM) showed no amine remaining. The reaction mixture was diluted with saturated aqueous NH_4Cl and DCM in a 60 ml separating funnel, separated and the aqueous layer re-extracted twice with DCM. The

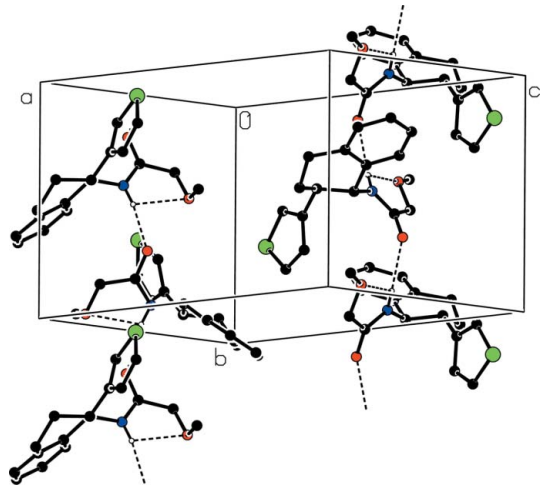


Figure 3
A partial packing plot of (3), showing hydrogen bonds as dashed lines. H atoms not involved in hydrogen bonding have been omitted.

combined organics were dried over $MgSO_4$, filtered and evaporated down to a pale-yellow oil. The crude product was purified by flash chromatography (2.5 × 15.2 cm SiO_2, crude product loaded as solution in DCM, eluted with 0–70% EtOAc/hexanes) (yield 93%). X-ray quality crystals of (3) were obtained by dissolving the compound in a minimum volume of boiling EtOH and then cooling to room temperature in a sealed 1-dram vial, before storing in a freezer at 258 K for 20 h. Spectroscopic analysis: ^{1}H NMR (300 MHz, $CDCl_3$, δ, p.p.m.): 7.31–7.23 (2H, *m*), 7.22–7.16 (2H, *m*), 7.12 (1H, *m*), 7.02 (1H, *d*, *J* = 4.1 Hz), 6.67 (1H, *br d*, *J* = 9.4 Hz), 5.46 (1H, *dd*, *J* = 9.1 Hz), 3.92 (1H, *d*, *J* = 15.2 Hz), 3.78 (1H, *d*, *J* = 15.2 Hz), 3.29 (3H, *s*), 3.13 (1H, *ddd*, *J* = 9.7, 9.7 and 3.2 Hz), 3.03–2.77 (2H, *m*), 2.25–1.99 (2H, *m*).

Crystal data

$C_{17}H_{19}NO_2S$
M_r = 301.39
Monoclinic, $P2_1$
a = 10.5344 (3) Å
b = 9.7241 (4) Å
c = 15.1999 (6) Å
β = 99.594 (2)°
V = 1535.2 (1) Å^3
Z = 4
D_x = 1.304 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 12544 reflections
θ = 2.6–27.5°
μ = 0.22 mm^{-1}
T = 150 (1) K
Needle, colourless
0.20 × 0.08 × 0.05 mm

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer
φ scans, and ω scans with κ offsets
Absorption correction: multi-scan (*SORTAV*; Blessing, 1995)
T_{min} = 0.619, T_{max} = 0.993
12544 measured reflections
6434 independent reflections
4012 reflections with $I > 2\sigma(I)$
R_{int} = 0.076
θ_{max} = 27.5°
h = −13 → 13
k = −12 → 11
l = −18 → 19

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.059
$wR(F^2)$ = 0.158
S = 1.01
6434 reflections
382 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0723P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.32 e Å^{-3}
Extinction correction: *SHELXTL*/*PC* (Sheldrick, 2001)
Extinction coefficient: 0.012 (2)
Absolute structure: Flack (1983), with 2710 Friedel pairs
Flack parameter: −0.07 (9)

Table 1
Selected torsion angles (°).

C6*A*—C5*A*—C2*A*—C1*A*	−130.6 (4)	C15*A*—C16*A*—O2*A*—C17*A*	−172.1 (3)
C6*B*—C5*B*—C2*B*—C1*B*	23.4 (5)	C15*B*—C16*B*—O2*B*—C17*B*	−75.7 (4)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*NA*···O2*A*	0.88	2.19	2.613 (4)	109
N1*B*—H1*NB*···O2*B*	0.88	2.35	2.741 (4)	107
N1*A*—H1*NA*···O1*A*^{i}	0.88	2.28	3.033 (4)	144
N1*B*—H1*NB*···O1*B*^{ii}	0.88	2.10	2.969 (4)	168
C1*B*—H1*B*···O2*B*^{iii}	0.95	2.54	3.386 (5)	148
C3*A*—H3*AA*···O2*A*^{iv}	0.95	2.52	3.441 (5)	164
C4*B*—H4*B*···O1*A*^{v}	0.95	2.49	3.419 (5)	165
C10*A*—H10*A*···O1*B*^{vi}	0.95	2.55	3.276 (5)	134

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

H atoms were placed in calculated positions, with C—H distances in the range 0.95–1.00 Å and an N—H distance of 0.88 Å. They were included in the refinement in the riding-model approximation, with $U_{iso}(H) = 1.2U_{eq}(C)$, or $1.5U_{eq}(C)$ for methyl H atoms.

Data collection: *COLLECT* (Nonius, 2002); cell refinement: *DENZO-SMN* (Otwinowski & Minor, 1997); data reduction: *DENZO-SMN*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXTL*/*PC* (Sheldrick, 2001); molecular graphics: *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXTL*/*PC*.

The authors acknowledge NSERC, the University of Toronto, AstraZeneca Inc. and the W. C. Sumner foundation for funding.

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