Cosier, J. & Glazer, A. M. (1986). *J. Appl. Cryst*, **19**, 105–107.
Sheldrick, G. M. (1990). *Acta Cryst.* A**46**, 467–473.
Sheldrick, G. M. (1992). *SHELXTL/PC*. Version 4.3. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures*. University of Göttingen, Germany.
Stoe & Cie (1990*a*). *DIF4. Diffractometer Control Program*. Version 7.09/DOS. Stoe & Cie, Darmstadt, Germany.
Stoe & Cie (1990*b*). *REDU4. Data Reduction Program*. Version 7.03/DOS. Stoe & Cie, Darmstadt, Germany.

Acta Cryst. (1996). C**52**, 197–199

N-Hexyl-*N*-phenyl-5-ethylthioindole-2-carboxamide

Sandra Ianelli,[a] Mario Nardelli,[a]* Daniele Belletti,[a] Brigitte Jamart-Grégoire,[b] Catherine Caubère[b] and Paul Caubère[b]

[a]*Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica, Università degli Studi di Parma, Centro di Studio per la Strutturistica Diffrattometrica del CNR, Viale delle Scienze 78, I-43100 Parma, Italy, and* [b]*Laboratoire de Chimie Organique I, UA CNRS No. 457, Université de Nancy I, BP 239, 54506 Vandoeuvre-Les-Nancy CEDEX, France*

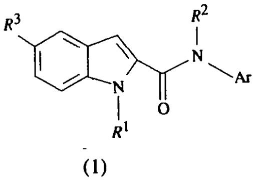
(*Received 4 January 1995; accepted 6 June 1995*)

Abstract

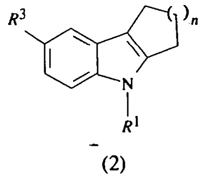
Knowledge of the position of the ethylthio group in the title compound, $C_{23}H_{28}N_2OS$, allows generalization of the behaviour of two families of indoles undergoing alkylthiolation reactions. The ^1H NMR spectrum of this compound is in agreement with that recently observed for other 1-carboxamide indole derivatives. The structure and conformation of the molecule is discussed and compared with that of the analogous compound *N*-methyl-*N*-phenyl-2-(5-methoxyindole)carboxamide.

Comment

A research program aimed at the synthesis of 5-hydroxyindole-2-carboxamides (1) (R^3 = OH) led us to study the demethylation of the corresponding methyl ethers (1) (R^3 = OMe) with $AlCl_3$/EtSH.



(1)



(2)

During previous investigations carried out with polycyclic indoles (2) (R^3 = OMe), a new reaction was discovered leading to the replacement of the methoxy group with an ethylthio substituent to give compound (2) (R^3 = EtS) (Caubère, Caubère, Renard, Bizot-Espiart & Jamart-Gregoire, 1994). Demethylation performed with (1) (R^3 = OMe) showed that the presence of the carboxamide group dramatically increased the reactivity of the substrates towards $AlCl_3$/EtSH.

The position of the ethylthio group could not be determined from the usual spectroscopic data. Moreover, taking into account the difference in reactivity observed between (1) and (2), it was not possible to conclude that the alkylthiolation observed with the two families of indoles was identical. Fortunately, compound (1) [R^3 = OMe, R^1 = H, R^2 = *n*-hexyl, Ar = Ph] gave single crystals suitable for X-ray diffraction, allowing us to conclude that the replacement of the OMe substituent of (1) took place analogously to the reaction observed with (2).

Fig. 1 shows an *ORTEP* (Johnson, 1965) drawing of the title molecule and Table 2 presents selected geometrical parameters which compare well with those recently found for the analogous *N*-methyl-*N*-phenyl-2-(5-methoxyindole)carboxamide (Ianelli, Nardelli, Belletti, Jamart-Grégoire, Caubère & Caubère, 1995). Bond distances and angles involving the disordered hexyl chain (see *Experimental*) have no chemical significance and have been omitted.

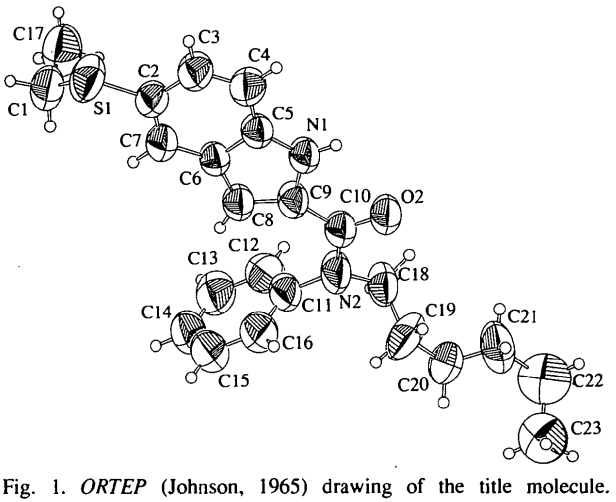


Fig. 1. *ORTEP* (Johnson, 1965) drawing of the title molecule. Ellipsoids are at the 50% probability level and only one of the two disorder components of the hexyl chain is shown.

An important aspect connected with the comparison of the two compounds is that the ^1H NMR spectrum of compound (1) shows a resonance at 5.1 p.p.m. indicating an aromatic H atom strongly shielded by the phenyl ring, as observed for the methoxy derivative. Other relevant observations are: (i) steric hindrance prevents coplanarity of atom C1 with the indole benzene ring, as indicated by the value of 147.6 (4)° for the C1—S1—C2—C3 torsion angle; (ii) the junctions of the ethylthio and carboxamide substituents with the central indole core are asymmetric, the asymmetry being larger for carboxamide, as indicated by the angles S1—C2—C3 117.2 (4) and S1—C2—C7 123.4 (4)°, and N1—C9—C10 114.4 (4) and C8—C9—C10 137.3 (4)°; (iii) the C9—C10 bond is synperiplanar to N2—C11 in both compounds, but the torsion angle is larger for the methoxy derivative, the values of C9—C10—N2—C11 being 1.8 (8) and 13.1 (3)° for the two compounds; and (iv) the orientation of the phenyl substituent in the title compound, defined by the torsion angles C10—N2—C11—C12 [91.4 (7)°] and C10—N2—C11—C16 [−89.9 (7)°], is different from that found in the methoxy derivative, for which these torsion angles have values of −117.2 (2) and 65.1 (3)°, respectively.

The packing contact of major relevance is a hydrogen bond of the N—H···O type involving the indole N atom and the amide O atom of an adjacent molecule [N1···O2^{i} 2.820 (5), H···O2^{i} 2.02 Å, N1—H···O2^{i} 154°; symmetry code: (i) $1-x$, $-y$, $1-z$].

Experimental

Crystals of the title compound were obtained from CH_2Cl_2 solution.

Crystal data

$C_{23}H_{28}N_2OS$
$M_r = 380.55$
Monoclinic
$P2_1/c$
$a = 13.184\ (2)$ Å
$b = 9.077\ (2)$ Å
$c = 17.750\ (4)$ Å
$\beta = 91.98\ (1)°$
$V = 2122.9\ (7)$ Å^3
$Z = 4$
$D_x = 1.191$ Mg m^{-3}

Cu $K\alpha$ radiation
$\lambda = 1.54178$ Å
Cell parameters from 30 reflections
$\theta = 20.27–37.74°$
$\mu = 1.452$ mm^{-1}
$T = 293\ (2)$ K
Prism
0.43 × 0.35 × 0.28 mm
Colourless

Data collection

Siemens AED diffractometer
$\theta/2\theta$ scans
Absorption correction: none
4087 measured reflections
3963 independent reflections
1315 observed reflections [$I > 2\sigma(I)$]
$R_{\rm int} = 0.0296$

$\theta_{\rm max} = 70.06°$
$h = -15 \rightarrow 16$
$k = -3 \rightarrow 11$
$l = -6 \rightarrow 21$
1 standard reflection monitored every 50 reflections
intensity decay: none

Refinement

Refinement on F^2
$R(F) = 0.0636$
$wR(F^2) = 0.1629$
$S = 1.258$
3945 reflections

Extinction correction: *SHELXL*93 (Sheldrick, 1993)
Extinction coefficient: 0.012 (1)

300 parameters
H atoms riding
$w = 1/[\sigma^2(F_o^2) + (0.1110P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.234$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.236$ e Å^{-3}

Atomic scattering factors from *International Tables for Crystallography* (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters (Å^2)*

$$U_{\rm eq} = (1/3)\Sigma_i\Sigma_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	$U_{\rm eq}$
S1	−0.00515 (10)	0.2280 (2)	0.28703 (9)	0.1172 (7)
O2	0.5293 (2)	−0.1755 (4)	0.4635 (2)	0.1036 (11)
N1	0.3719 (2)	−0.0047 (4)	0.4273 (2)	0.0784 (10)
N2	0.5021 (3)	−0.3382 (5)	0.3698 (3)	0.130 (2)
C1	−0.0022 (4)	0.1905 (7)	0.1898 (3)	0.116 (2)
C17	0.0782 (5)	0.2759 (8)	0.1493 (3)	0.141 (2)
C2	0.1113 (3)	0.1634 (5)	0.3252 (3)	0.0845 (13)
C3	0.1538 (4)	0.2399 (5)	0.3876 (3)	0.0946 (14)
C4	0.2410 (4)	0.1939 (5)	0.4257 (3)	0.0939 (15)
C5	0.2873 (3)	0.0670 (5)	0.4001 (2)	0.0741 (12)
C6	0.2487 (3)	−0.0099 (5)	0.3369 (2)	0.0712 (11)
C7	0.1582 (3)	0.0392 (5)	0.3004 (3)	0.0804 (13)
C8	0.3134 (3)	−0.1337 (5)	0.3277 (2)	0.0782 (12)
C9	0.3874 (3)	−0.1293 (5)	0.3839 (2)	0.0761 (12)
C10	0.4771 (3)	−0.2149 (5)	0.4068 (3)	0.0886 (14)
C11	0.4461 (4)	−0.3930 (6)	0.3048 (4)	0.098 (2)
C12	0.4714 (4)	−0.3528 (6)	0.2340 (4)	0.110 (2)
C13	0.4150 (5)	−0.4069 (7)	0.1723 (4)	0.114 (2)
C14	0.3350 (5)	−0.5005 (7)	0.1839 (4)	0.114 (2)
C15	0.3117 (4)	−0.5407 (6)	0.2542 (4)	0.116 (2)
C16	0.3681 (5)	−0.4889 (6)	0.3158 (3)	0.108 (2)
C18†	0.6145 (9)	−0.3830 (13)	0.3710 (7)	0.096 (4)
C19†	0.6173 (14)	−0.5176 (17)	0.4173 (10)	0.132 (5)
C20†	0.7157 (14)	−0.6005 (22)	0.4150 (17)	0.183 (7)
C21†	0.7884 (13)	−0.5617 (24)	0.4651 (13)	0.187 (7)
C22†	0.8858 (14)	−0.6557 (28)	0.4780 (14)	0.145 (7)
C23†	0.8615 (26)	−0.8114 (29)	0.4942 (22)	0.144 (8)
C24†	0.5635 (10)	−0.4510 (16)	0.4177 (9)	0.118 (5)
C25†	0.6616 (12)	−0.4502 (29)	0.3832 (14)	0.174 (7)
C26†	0.7436 (18)	−0.5494 (23)	0.4243 (22)	0.204 (9)
C27†	0.7578 (15)	−0.6827 (26)	0.4652 (14)	0.202 (8)
C28†	0.8689 (17)	−0.699 (3)	0.4906 (15)	0.184 (9)
C29†	0.886 (3)	−0.855 (4)	0.4751 (27)	0.167 (9)

† Partial occupancy.

Table 2. *Selected geometric parameters (Å, °)*

S1—C2	1.758 (4)	C5—C6	1.402 (5)
S1—C1	1.761 (6)	C6—C7	1.410 (5)
O2—C10	1.252 (5)	C6—C8	1.424 (5)
N1—C5	1.365 (5)	C8—C9	1.373 (5)
N1—C9	1.388 (5)	C9—C10	1.461 (6)
N2—C10	1.344 (6)	C11—C12	1.361 (7)
N2—C11	1.438 (6)	C11—C16	1.366 (7)
C1—C17	1.514 (7)	C12—C13	1.392 (7)
C2—C7	1.366 (6)	C13—C14	1.375 (8)
C2—C3	1.406 (6)	C14—C15	1.346 (8)
C3—C4	1.379 (6)	C15—C16	1.383 (7)
C4—C5	1.387 (6)		
C2—S1—C1	105.4 (2)	C9—C8—C6	107.9 (4)
C5—N1—C9	109.1 (3)	C8—C9—N1	108.2 (4)
C10—N2—C11	123.6 (4)	C8—C9—C10	137.3 (4)
C17—C1—S1	114.0 (4)	N1—C9—C10	114.4 (4)
C3—C2—S1	117.2 (4)	O2—C10—N2	119.6 (4)
C7—C2—S1	123.4 (4)	O2—C10—C9	119.2 (4)
C7—C2—C3	119.3 (4)	N2—C10—C9	121.1 (4)
C4—C3—C2	122.7 (4)	C12—C11—N2	120.8 (6)
C3—C4—C5	117.3 (4)	C12—C11—C16	120.9 (5)
N1—C5—C4	130.0 (4)	C16—C11—N2	118.3 (7)

N1—C5—C6	108.4 (4)	C11—C12—C13	119.4 (6)
C4—C5—C6	121.6 (4)	C14—C13—C12	119.4 (6)
C5—C6—C7	119.2 (4)	C15—C14—C13	120.5 (6)
C5—C6—C8	106.4 (4)	C14—C15—C16	120.4 (6)
C7—C6—C8	134.2 (4)	C11—C16—C15	119.4 (6)
C2—C7—C6	119.8 (4)		
C2—S1—C1—C17	−65.2 (5)	C10—N2—C11—C12	91.4 (7)
C1—S1—C2—C3	147.6 (4)	C10—N2—C11—C16	−89.9 (7)
C1—S1—C2—C7	−36.6 (5)	N1—C9—C10—O2	2.9 (6)
C11—N2—C10—C9	1.8 (8)	C8—C9—C10—N2	−3.2 (9)

The integrated intensities were obtained by a modified version (Belletti, Ugozzoli, Cantoni & Pasquinelli, 1979) of the Lehmann & Larsen (1974) peak-profile analysis procedure. All the H atoms were placed in calculated positions, riding on their attached C atoms, with atomic displacement coefficients 1.5 times the U_{eq} of the attached atom. The amide N atom shows a rather high anisotropy ratio, indicating disorder which propagates to the attached *n*-hexyl chain, as frequently happens for long hydrocarbon chains. A satisfactory model was obtained assuming this chain was disordered over two overlapping positions having site-occupation factors of 0.515 (12) (C18–C23) and 0.485 (12) (C24–C29). This disorder caused the refinement to be rather cumbersome, but did not significantly influence the results concerning the geometry of the rest of the molecule (see Table 2).

Data collection: local programs. Cell refinement: *LQPARM* (Nardelli & Mangia, 1984). Data reduction: local programs. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP* (Johnson, 1965). Software used to prepare material for publication: *PARST* (Nardelli, 1983) and *PARSTCIF* (Nardelli, 1991).

Financial support from the European Community Commission under contract No. SC1000657 is gratefully acknowledged.

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: CF1000). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Belletti, D., Ugozzoli, F., Cantoni, A. & Pasquinelli, G. (1979). *Gestione on Line di Diffrattometro a Cristallo Singolo Siemens AED con Sistema General Automation Jumbo* 220. Internal Report 1-3/79. Centro di Studio per la Strutturistica Diffrattometrica del CNR, Parma, Italy.

Caubère, C., Caubère, P., Renard, P., Bizot-Espiart, J. G. & Jamart-Gregoire, B. (1994). *Synth. Commun.* pp. 1799–1807.

Ianelli, S., Nardelli, M., Belletti, D., Jamart-Grégoire, B., Caubère, C. & Caubère, P. (1995). *Acta Cryst.* C**51**, 1341–1345.

Johnson, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

Lehmann, M. S. & Larsen, F. K. (1974). *Acta Cryst.* A**30**, 580–589.

Nardelli, M. (1983). *Comput. Chem.* **7**, 95–98.

Nardelli, M. (1991). *PARSTCIF. Program for Creating a CIF from the Output of PARST.* University of Parma, Italy.

Nardelli, M. & Mangia, A. (1984). *Ann. Chim. (Rome)*, **74**, 163–174.

Sheldrick, G. M. (1985). *SHELXS86. Program for the Solution of Crystal Structures.* University of Göttingen, Germany.

Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.

Acta Cryst. (1996). C**52**, 199–201

(*S*)-3-(1,1-Dimethyloxycarbonylamino)-1-phenylmethyloxypiperidine-2,6-dione,[†] $C_{17}H_{22}N_2O_5$

Alain Tomas,[a] Pascale Lemoine,[a] Bernard Viossat,[a] Sylvie Robin,[b] Jiarong Zhu[b] and Hervé Galons[b]

[a]*Laboratoire de Physique, Faculté des Sciences Pharmaceutiques et Biologiques de Paris V, 4 Avenue de l'Observatoire, 75270 Paris CEDEX 06, France, and* [b]*Laboratoire de Chimie Organique 2, Faculté des Sciences Pharmaceutiques et Biologiques de Paris V, 4 Avenue de l'Observatoire, 75270 Paris CEDEX 06, France*

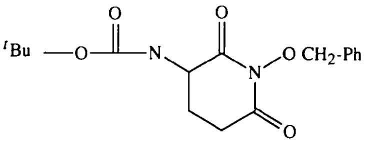
(*Received 25 January 1995; accepted 3 July 1995*)

Abstract

The two molecules in the asymmetric unit differ in the orientation of the glutarimide ring. The glutarimide moiety adopts an envelope conformation in molecule *A* and a twisted conformation in molecule *B*. The other features are similar.

Comment

We have studied the preparation of biologically active compounds containing hydroxamate groups. The attempted condensation of the α-phenyl ester of BOC-glutamic acid with benzyloxyamine failed to provide the expected acyclic product but led to the cyclic derivative whose structure we now present.



(I)

The asymmetric unit consists of two independent molecules, *A* and *B*, whose structures differ essentially in the conformation of the glutarimide moiety. The glutarimide ring assumes an envelope conformation in molecule *A*. Atom C4 deviates by 0.70 (1) Å from the least-squares plane *P1* defined by N1, C2, C3, C5, C6, which has a maximum deviation of −0.013 (9) Å for C2 and C6. The O2, C2, N1, C6, O6 atoms define the least-squares plane *P2*; O1 deviates by +0.16 (2) Å from this plane. Such an envelope-like conformation has been observed in the crystal structures of *N*-(α-glutarimido)-4-bromophthalimide and of glutarimide (Petersen, 1969, 1971). C17 lies in the carbamate plane

---

[†] Alternative name: (*S*)-*tert*-butyl 2,6-dioxo-1-benzyloxypiperidine-3-carbamate.

Acta Crystallographica Section C
ISSN 0108-2701 ©1996