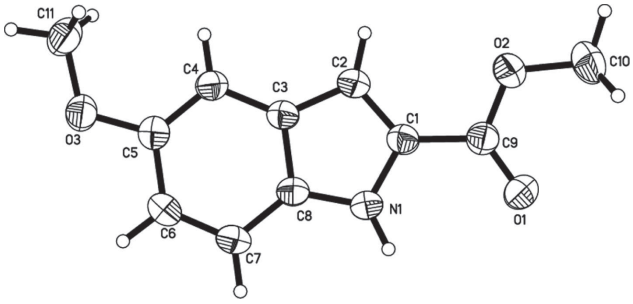
Open Access

Mohamed I. Attia, Hazem A. Ghabbour* and Hoong-Kun Fun

Crystal structure of methyl 5-methoxy 1*H*-indole-2-carboxylate, $C_{11}H_{11}NO_3$



DOI 10.1515/ncrs-2015-0162
Received November 25, 2015; accepted January 14, 2016; available online February 13, 2016

Abstract

$C_{11}H_{11}NO_3$, monoclinic, $P2_1/n$ (no. 14), $a = 7.8956(6)$ Å, $b = 5.8304(4)$ Å, $c = 22.0407(16)$ Å, $\beta = 91.919(3)°$, $V = 1014.06(13)$ Å^3, $Z = 4$, $R(F) = 0.045$, $wR(F^2) = 0.125$, $T = 100$ K.

CCDC no.: 1052719

The crystal structure is shown in the figure. Tables 1–3 contain details of the measurement method and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Yellow, block, size 0.247×0.268×0.410 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	0.99 cm^{-1}
Diffractometer, scan mode:	Bruker APEX-II D8 venture, φ and ω scans
$2\theta_{max}$:	55.98°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	9399, 2407
$N(param)_{refined}$:	143
Programs:	SHELX [9]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	Site	*x*	*y*	*z*	U_{iso}
H(1)	4*e*	0.493(2)	0.997(3)	0.4334(9)	0.067(5)
H(2)	4*e*	0.2783	0.4333	0.3646	0.058
H(4)	4*e*	0.3770	0.5179	0.2388	0.054
H(6)	4*e*	0.6422	1.1114	0.2244	0.059
H(7)	4*e*	0.6152	1.1930	0.3269	0.058
H(10A)	4*e*	0.2808	0.4280	0.5771	0.102
H(10B)	4*e*	0.1628	0.2299	0.5485	0.102
H(10C)	4*e*	0.0881	0.4824	0.5573	0.102
H(11A)	4*e*	0.5479	0.4489	0.1537	0.095
H(11B)	4*e*	0.5184	0.5815	0.0907	0.095
H(11C)	4*e*	0.3665	0.5577	0.1365	0.095

Source of material

A suspension of 5-methoxy-1*H*-indole-2-carboxylic acid (2 g, 0.01 mol) in absolute methanol (30 mL) and a few drops of concentrated sulfuric acid was heated to reflux for 4 h. The reaction mixture was allowed to cool to room temperature and the precipitated solid was filtered off to give 2.1 g (96%) of methyl 5-methoxy 1*H*-indole-2-carboxylate as yellow crystals m.p. 450–451 K [1]. Single crystals of the title compound were obtained *via* slow evaporation of methanolic solution.

Discussion

The pineal hormone melatonin (*N*-acetyl-5-methoxy-tryptamine, MLT) is primarily synthesized and released by the pineal gland in a circadian rhythm, with elevated peripheral blood levels at night. MLT appears to have sleep-inducing properties in addition to the other effects reported in the literature like anti-inflammatory, pain modulatory, antitumor and antioxidant properties [2–5]. MLT exerts its effects *via* manipulation of two G-protein-coupled receptors, namely MT_1 and MT_2 receptors as well as a low-affinity putative MLT binding site called MT_3 [6, 7]. The title compound is the starting material of a number of melatoninergic

***Corresponding author: Hazem A. Ghabbour,** Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia, e-mail: ghabbourh@yahoo.com; and Department of Medicinal Chemistry, Faculty of Pharmacy, Mansoura University, Mansoura 35516, Egypt
Mohamed I. Attia: Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia; and Medicinal and Pharmaceutical Chemistry Department, Pharmaceutical and Drug Industries
Hoong-Kun Fun: Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia; and X-ray Crystallography Unit, School of Physics, Universiti Sains Malaysia, 11800 Penang, Malaysia

Table 3: Atomic displacement parameters (Å^2).

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(1)	4*e*	0.3386(2)	0.7911(2)	0.52344(5)	0.0837(9)	0.0780(9)	0.0492(7)	−0.0277(7)	0.0068(6)	−0.0117(6)
O(2)	4*e*	0.2416(2)	0.4563(2)	0.48726(5)	0.0785(8)	0.0548(7)	0.0535(7)	−0.0138(6)	0.0164(5)	0.0012(5)
O(3)	4*e*	0.5395(1)	0.7856(2)	0.16189(5)	0.0583(6)	0.0568(7)	0.0465(6)	0.0026(5)	0.0083(4)	0.0002(5)
N(1)	4*e*	0.4484(2)	0.9017(2)	0.40557(6)	0.0482(6)	0.0447(7)	0.0449(7)	−0.0090(5)	−0.0016(5)	−0.0038(5)
C(1)	4*e*	0.3620(2)	0.7040(2)	0.41916(6)	0.0431(7)	0.0444(7)	0.0472(8)	−0.0053(6)	0.0008(5)	0.0000(6)
C(2)	4*e*	0.3358(2)	0.5762(3)	0.36759(7)	0.0512(7)	0.0433(8)	0.0502(8)	−0.0111(6)	0.0043(6)	−0.0027(6)
C(3)	4*e*	0.4106(2)	0.6973(2)	0.31937(6)	0.0413(6)	0.0399(7)	0.0471(7)	−0.0040(5)	0.0008(5)	−0.0014(6)
C(4)	4*e*	0.4255(2)	0.6517(2)	0.25680(6)	0.0467(7)	0.0422(7)	0.0474(8)	−0.0041(6)	0.0020(6)	−0.0042(6)
C(5)	4*e*	0.5121(2)	0.8064(2)	0.22290(6)	0.0401(6)	0.0465(7)	0.0449(7)	0.0054(5)	0.0013(5)	0.0013(6)
C(6)	4*e*	0.5829(2)	1.0077(3)	0.24923(7)	0.0470(7)	0.0452(8)	0.0559(9)	−0.0045(6)	0.0046(6)	0.0078(6)
C(7)	4*e*	0.5681(2)	1.0570(2)	0.30969(7)	0.0484(7)	0.0410(7)	0.0564(9)	−0.0093(6)	−0.0001(6)	−0.0005(6)
C(8)	4*e*	0.4813(2)	0.8997(2)	0.34489(6)	0.0391(6)	0.0400(7)	0.0463(7)	−0.0029(5)	−0.0015(5)	−0.0019(6)
C(9)	4*e*	0.3151(2)	0.6599(3)	0.48138(7)	0.0433(7)	0.0513(8)	0.0472(8)	−0.0031(6)	0.0009(5)	−0.0007(7)
C(10)	4*e*	0.1891(2)	0.3941(3)	0.54741(8)	0.072(1)	0.072(1)	0.061(1)	−0.0025(9)	0.0191(8)	0.0154(9)
C(11)	4*e*	0.4892(2)	0.5774(3)	0.13351(8)	0.077(1)	0.062(1)	0.0512(9)	0.0072(8)	0.0072(8)	−0.0090(8)

ligands [8] and can serve as a starting synthon for other new compounds able to modulate melatonin receptors. The asymmetric unit of the title structure contains one complete molecule in which the indole moiety is nearly planar. The stability of the molecules in the crystal structure is ensured by one intermolecular hydrogen bond, of which O1 works as hydrogen bond acceptor and N1 works as hydrogen bond donor. The distance of the interactions between N1—H1$\cdots$O1 is 2.03(1) Å and the angle is 160°.

Acknowledgements: The authors would like to extend their sincere appreciation to the Deanship of Scientific Research at King Saud University for its funding of this research through the Research Group Project No. RGP-VPP-196.

References

1. Coowar, D.; Bouissac, J.; Hanbali, M.; Paschaki, M.; Mohier, E.; Luu, B.: Effects of indole fatty alcohols on the differentiation of neural stem cell derived neurospheres. J. Med. Chem. **47** (2004) 6270–6282.
2. Genovese, T.; Mazzon, E.; Muia, C.; Bramanti, P.; De Sarro, A.; Cuzzocrea, S.: Attenuation in the evolution of experimental spinal cord trauma by treatment with melatonin. J. Pineal Res. **38** (2005) 198–208.
3. Peres, M. F. P.: Melatonin, the pineal gland and their implications for headache disorders. Cephalalgia **25** (2005) 403–411.
4. Witt-Enderby, P. A.; Radio, N. M.; Doctor, J. S.; Davis, V. L.: Therapeutic treatments potentially mediated by melatonin receptors: potential clinical uses in the prevention of osteoporosis, cancer and as an adjuvant therapy. J. Pineal Res. **41** (2006) 297–305.
5. Sofic, E.; Rimpapa, Z.; Kundurovic, Z.; Sapcanin, A.; Tahirovic, I.; Rustembegovic, A.; Cao, G. J.: Antioxidant capacity of the neurohormone melatonin. Neural Transm. **112** (2005) 349–358.
6. Csernus, V.; Mess, B.: Biorhythms and pineal gland. Neuroendocrinol. Lett. **24** (2003) 404–411.
7. Nosjean O.; Ferro M.; Coge F.; Beauverger P.; Henlin J.-M.; Lefoulon F.; Fauchere J.-L.; Delagrange P.; Canet E.; Boutin J. A.: Identification of the melatonin binding site MT_3 as the quinone reductase 2. J. Biol. Chem. **275** (2000) 31311–31317.
8. Attia, M. I.; Witt-Enderby, P. A.; Julius, J.: Synthesis and pharmacological evaluation of pentacyclic 6a,7-dihydrodiindole and 2,3-dihydrodiindole derivatives as novel melatoninergic ligands. Bioorg. Med. Chem. **16** (2008) 7654–7661.
9. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112—122.