Open Access

Ahmed M. El-Agrody, Abd El-Galil E. Amr*, Nermien M. Sabry, Mohamed A. Al-Omar and Hazem A. Ghabbour

Crystal structure of 3-amino-9-methoxy-1-phenyl-1*H*-benzo[*f*]chromene-2-carbonitrile, C₂₁H₁₆N₂O₂

DOI 10.1515/ncrs-2016-0128

Received April 19, 2016; accepted August 2, 2016; available online August 18, 2016

***Corresponding author: Abd El-Galil E. Amr**, Pharmaceutical Chemistry Department, College of Pharmacy, Drug Exploration and Development Chair (DEDC), King Saud University, Riyadh 11451, Saudi Arabia; and Applied Organic Chemistry Department, National Research Centre, Dokki, Giza 12622, Egypt, e-mail: aamr@ksu.edu.sa

Ahmed M. El-Agrody: Chemistry Department, Faculty of Science, Al-Azhar University, 11884 Nasr City, Cairo, Egypt

Nermien M. Sabry: Applied Organic Chemistry Department, National Research Center, Dokki 12622, Cairo, Egypt; and Chemistry Department, Girls College of Education, King Khalid University, Abha, Saudi Arabia

Mohamed A. Al-Omar: Pharmaceutical Chemistry Department, College of Pharmacy, Drug Exploration and Development Chair (DEDC), King Saud University; and Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia

Hazem A. Ghabbour: Department of Pharmaceutical Chemistry, College of Pharmacy, King Saud University, P.O. Box 2457, Riyadh 11451, Saudi Arabia; and Department of Medicinal Chemistry, Faculty of Pharmacy, University of Mansoura, Mansoura 35516, Egypt

Abstract

C₂₁H₁₆N₂O₂, monoclinic, *P*2₁/*n* (no. 14), *a* = 13.4768(7) Å, *b* = 6.9225(3) Å, *c* = 18.2840(8) Å, β = 107.601(2)°, *V* = 1625.92(13) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0593, *wR*_{ref}(*F*²) = 0.1529, *T* = 100 K.

CCDC no.: 1474776

The asymmetric unit of the title crystal structure is shown in the figure. Tables 1 and 2 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:	Colourless blocks
Wavelength:	Size 0.38 × 0.26 × 0.17 mm
μ:	Mo <i>K</i> α radiation (0.71073 Å)
Diffractometer, scan mode:	0.9 cm ^{−1}
2θ _{max} , completeness:	Broker APEX-II, φ and ω
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	54°, >99%
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	20809, 3545, 0.082
<i>N</i> (<i>param</i>) _{refined} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 2057
Programs:	235
	SHELX [20], Bruker programs [21]

Source of material

A mixture of 7-methoxy-2-naphthol (0.01 mol), malononitrile (0.01 mol), benzaldehyde (0.01 mol), ethanol (30 mL) and piperidine (0.5 mL) was heated under reflux for 1 h. After complete precipitation occurred the solid product was collected by filtration, washed by methanol and recrystallized from ethanol to give the title compound as colourless crystals; yield 89%; M.p.: 528–529 K.

Experimental details

Carbon-bound hydrogen atoms were placed in calculated positions and were included in the refinement in the riding model approximation. The H atoms of the methyl groups were allowed to rotate with a fixed angle around the C–C bond to best fit the experimental electron density.

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	U _{iso} [*] /U _{eq}
O1	0.59082(13)	0.8745(2)	0.82067(9)	0.0455(4)
O2	0.57781(14)	0.1833(2)	0.52137(9)	0.0534(5)
N1	0.57577(19)	0.8190(4)	0.93596(13)	0.0532(6)
N2	0.5218(2)	0.3050(4)	0.94082(13)	0.0724(8)
C1	0.61127(16)	0.8104(3)	0.75389(12)	0.0359(5)
C2	0.66193(17)	0.9495(3)	0.72213(12)	0.0420(6)
H2A	0.6782	1.0732	0.7451	0.050*
C3	0.68721(18)	0.9030(3)	0.65776(13)	0.0419(6)
H3A	0.7221	0.9953	0.6359	0.050*
C4	0.66262(16)	0.7201(3)	0.62279(11)	0.0357(5)
C5	0.68903(18)	0.6689(4)	0.55621(12)	0.0439(6)
H5A	0.7260	0.7591	0.5351	0.053*
C6	0.66320(19)	0.4947(4)	0.52143(13)	0.0452(6)
H6A	0.6812	0.4643	0.4764	0.054*
C7	0.60963(18)	0.3606(3)	0.55281(12)	0.0393(6)
C8	0.58386(17)	0.4031(3)	0.61805(12)	0.0375(5)
H8A	0.5483	0.3093	0.6387	0.045*
C9	0.60900(16)	0.5824(3)	0.65500(11)	0.0326(5)
C10	0.58411(16)	0.6312(3)	0.72383(11)	0.0327(5)
C11	0.53168(17)	0.4876(3)	0.76307(11)	0.0354(5)
H11A	0.5679	0.3606	0.7655	0.043*
C12	0.54723(17)	0.5550(3)	0.84513(12)	0.0365(5)
C13	0.57007(17)	0.7403(3)	0.86761(12)	0.0379(5)
C14	0.5326(2)	0.4192(4)	0.89841(13)	0.0475(6)
C15	0.41735(18)	0.4575(4)	0.71922(12)	0.0421(6)
C16	0.3489(2)	0.6117(5)	0.70379(14)	0.0568(7)
H16A	0.3736	0.7369	0.7215	0.068*
C17	0.2453(2)	0.5870(7)	0.66315(17)	0.0847(11)
H17A	0.1995	0.6948	0.6528	0.102*
C18	0.2084(3)	0.4068(9)	0.6378(2)	0.1089(18)
H18A	0.1372	0.3896	0.6095	0.131*
C19	0.2745(3)	0.2521(8)	0.6532(2)	0.1045(16)
H19A	0.2487	0.1272	0.6358	0.125*
C20	0.3789(2)	0.2758(5)	0.69413(16)	0.0676(9)
H20A	0.4240	0.1671	0.7049	0.081*
C21	0.6061(2)	0.1246(4)	0.45597(13)	0.0565(7)
H21A	0.5792	−0.0055	0.4406	0.085*
H21B	0.6821	0.1239	0.4685	0.085*
H21C	0.5766	0.2148	0.4137	0.085*
H2N1	0.550(2)	0.756(4)	0.9687(15)	0.054(8)*
H1N1	0.590(3)	0.935(5)	0.9423(18)	0.084(12)*

Discussion

Chromene and benzochromene derivatives have attracted considerable interest owing to their biological and pharmaceutical activities such as antibacterial [1–3], antifungal [4–6], vascular-disrupting [7], antioxidant [8, 9], anticancer [10–13], estrogenic anticoagulant and antispasmodic [14], antileishmanial [15], antiproliferative and apoptosis inducing [16–19].

In the title structure the asymmetric unit contains one independent molecule. All bond lengths and angles

are in the expected ranges. The phenyl ring (C16–C20) is perpendicular to the plane of the rest of the molecule (84°). The molecules are connected in the crystal structure via two symmetry related strong classical intermolecular hydrogen bonds, N1–H2N1···N2ⁱ (H···A distance = 2.20(3) Å; N–H···N angle = 162(3)°; symmetry code: (i) −x + 1, −y + 1, −z + 2).

Acknowledgements: The project was financially supported by King Saud University, Vice Deanship of Research Chairs.

References

- Kidwai, M.; Poddar, R.; Bhardwaj, S.; Singh, S.; Mehta, L. P.: Aqua mediated synthesis of 2-amino-6-benzothiazol-2-ylsulfanyl-chromenes and its *in vitro* study, explanation of the structure–activity relationships (SARs) as antibacterial agent. *Eur. J. Med. Chem.* **45** (2010) 5031–5038.
- Qian-Zhu, L.; Xiao-Yan, N.; Jie, L.: Novel coumarin and 4*H*-chromene derivatives containing 4,5-dihydropyrazole moiety: synthesis and antibacterial activity. *Lett. Drug. Des. Discov.* **8** (2010) 558–561.
- Xin-Hua, L.; Jin-Xin, L.; Lin-Shan, B.; Guo-Lin, L.; Chu-Xiou, P.: Novel dihydropyrazole derivatives linked with 4*H*-chromene: microwave-promoted synthesis and antibacterial activity. *Lett. Drug. Des. Discov.* **7** (2010) 487–490.
- Thomas, N.; Zachariah, S. M.: Pharmacological activities of chromene derivatives: an overview. *Asian J. Pharm. Clin. Res.* **6** (2013) 11–15.
- Agarwal, S. K.; Verma, S.; Singh, S. S.; Tripathi, A. K.; Khan, Z. K.; Kumar, S.: Antifeedant and antifungal activity of chromene compounds isolated from *Blepharispermum subsessile*. *J. Ethnopharm.* **71** (2000) 231–234.
- Abrunhosa, L.; Costa, M.; Areias, F.; Venâncio, A.; Proenca, F.: Antifungal activity of a novel chromene dimer. *J. Ind. Microbiol. Biotechnol.* **34** (2007) 787–792.
- Kasibhatla, S.; Gourdeau, H.; Meerovitch, K.; Drewe, J.; Reddy, S.; Qiu, L.; Zhang, H.; Bergeron, F.; Bouffard, D.; Yang, Q.; Herich, J.; Lamothe, S.; Cai, S. X.; Tseng, B.: Discovery and mechanism of action of a novel series of apoptosis inducers with potential vascular targeting activity. *Mol. Cancer Ther.* **3** (2004) 1365–1373.
- Singh, O. M.; Devi, N. S.; Thokchom, D. S.; Sharma, G. J.: Novel 3-alkanoyl/aroyl/heteroaroyl-2*H*-chromene-2-thiones: synthesis and evaluation of their antioxidant activities. *Eur. J. Med. Chem.* **45** (2010) 2250–2257.
- Vukovic, N.; Sukdolak, S.; Solujic, S.; Niciforovic, N.: Substituted imino and amino derivatives of 4-hydroxycoumarins as novel antioxidant, antibacterial and antifungal agents: synthesis and *in vitro* assessments. *Food Chem.* **120** (2010) 1011–1018.
- El-Agrody, A. M.; Fouda, A. M.; Khattab, E. S. A. E. H.: Synthesis, antitumor activity of 2-amino-4*H*-benzo[*h*]chromene derivatives, and structure–activity relationships of the 3- and 4-positions. *Med. Chem. Res.* **22** (2013) 6105–6120.
- El-Agrody, A. M.; Khattab, E. S. A. E. H.; Fouda, A. M.: Synthesis, structure-activity relationship (SAR) studies on some 4-Aryl-4*H*chromenes and relationship between

- lipophilicity and antitumor activity. *Lett. Drug. Des. Discov.* **11** (2014) 1167–1176.
12. Sabry, N. M.; Mohamed, H. M.; Khattab, E. S. A. E. H.; Motlaq, S. S.; El-Agrody, A. M.: Synthesis of 4*H*-chromene, coumarin, 12*H*-chromeno[2,3-*d*]pyrimidine derivatives and some of their antimicrobial and cytotoxicity activities. *Eur. J. Med. Chem.* **46** (2011) 765–772.
 13. Mahmoodi, M.; Aliabadi, A.; Emami, S.; Safavi, M.; Rajabalian, S.; Mohagheghi, M. A.; Khoshzaban, A.; Samzadeh-Kermani, A.; Lamei, N.; Shafiee, A.; Foroumadi, A.: Synthesis and in-vitro cytotoxicity of poly-functionalized 4-(2-Arylthiazol-4-yl)-4*H*-chromenes. *Arch. Pharm. Chem.* **343** (2010) 411–416.
 14. Jain, N.; Xu, J.; Kanojia, R. M.; Du, F.; Guo, J.-Z.; Pacia, E.; Lai, M.-T.; Musto, A.; Allan, G.; Reuman, M.; Li, X.; Hahn, D.; Cousineau, M.; Sean Peng, S.; Ritchie, D.; Russell, R.; Lundeen, S.; Sui, Z.: Identification and structure-activity relationships of chromene-derived selective estrogen receptor modulators for treatment of postmenopausal symptoms. *J. Med. Chem.* **52** (2009) 7544–7569.
 15. Tanaka, J. C. A.; Da Silva, C. C.; Ferreira, I. C. P.; Machado, G. M. C.; Leon, L. L.; De Oliveira, A. J. B.: Antileishmanial activity of indole alkaloids from *Aspidosperma ramiflorum*. *Phytomedicine* **14** (2007) 377–380.
 16. Zhang, D.; Ma, Y.; Liu, Y.; Liu, Z.-P.: Synthesis of sulfonylhydrazone- and acylhydrazone-substituted 8-ethoxy-3-nitro-2*H*-chromenes as potent antiproliferative and apoptosis inducing agents. *Arch. Pharm. Chem.* **347** (2014) 576–588.
 17. Szulawska-Mroczek, A.; Szumilak, M.; Szczesio, M.; Olczak, A.; Nazarski, R. B.; Lewgowd, W.; Czyz, M.; Stanczak, A.: Synthesis and biological evaluation of new bischromone derivatives with antiproliferative activity. *Arch. Pharm. Chem.* **346** (2013) 34–43.
 18. Xiao, G.-Q.; Liang, B.-X.; Chen, S.-H.; Ou, T.-M.; Bu, X.-Z.; Yan, M.: 3-Nitro-2*H*-chromenes as a new class of inhibitors against thioredoxin reductase and proliferation of cancer cells. *Arch. Pharm. Chem.* **345** (2012) 767–770.
 19. Magedov, I. V.; Manpadi, M.; Evdokimov, N. M.; Elias, E. M.; Rozhkova, E.; Ogasawara, M. A.; Bettale, J. D.; Przheval'skii, N. M.; Rogelj, S.; Kornienko, A.: Antiproliferative and apoptosis inducing properties of pyrano[3,2-*c*]pyridones accessible by a one-step multicomponent synthesis. *Bioorg. Med. Chem. Lett.* **17** (2007) 3872–3876.
 20. Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr.* **A64** (2008) 112–122.
 21. Bruker. APEX2, SAINT and SADABS. Bruker AXS Inc., Madison, WI, USA, 2009.