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Crystal structure of 6-iodo-3-phenyl-2-propylquinazolin-4(3*H*)-one, C₁₇H₁₅IN₂O

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.54 × 0.15 × 0.09 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	2.07 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	35.0°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	24639, 6425, 0.071
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3747
$N(\text{param})_{\text{refined}}$:	191
Programs:	SHELX [1], Bruker [2]

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
I1	0.374876(13)	1.19557(10)	0.372485(19)	0.04893(8)
O1	0.58205(13)	0.5644(5)	0.7401(2)	0.0401(6)
N1	0.51639(15)	0.3658(6)	0.7769(2)	0.0359(6)
N2	0.38303(18)	0.3940(8)	0.6580(3)	0.0535(9)
C1	0.52114(18)	0.5234(6)	0.7140(3)	0.0317(7)
C2	0.44832(17)	0.6385(6)	0.6189(3)	0.0346(8)
C3	0.44657(19)	0.8162(7)	0.5550(3)	0.0350(7)
H3A	0.4918	0.8614	0.5713	0.042*
C4	0.3780(2)	0.9243(7)	0.4681(3)	0.0378(8)
C5	0.3118(2)	0.8615(9)	0.4446(3)	0.0508(10)
H5A	0.2652	0.9410	0.3853	0.061*
C6	0.31347(17)	0.6860(15)	0.5064(3)	0.0534(9)
H6A	0.2677	0.6425	0.4888	0.064*
C7	0.38268(19)	0.5683(8)	0.5963(3)	0.0418(9)
C8	0.4469(2)	0.3008(9)	0.7435(3)	0.0474(10)
C9	0.4506(3)	0.1084(10)	0.8145(4)	0.0660(15)
H9A	0.4776	−0.0343	0.8187	0.079*
H9B	0.4813	0.1712	0.8925	0.079*
C10	0.3769(3)	0.0302(11)	0.7732(4)	0.0723(15)
H10A	0.3449	−0.0273	0.6941	0.087*
H10B	0.3507	0.1694	0.7732	0.087*
C11	0.3853(3)	−0.1702(12)	0.8453(5)	0.0800(17)
H11A	0.3347	−0.2318	0.8099	0.120*
H11B	0.4107	−0.1072	0.9208	0.120*
H11C	0.4159	−0.3013	0.8520	0.120*
C12	0.5876(2)	0.2786(6)	0.8826(3)	0.0334(7)
C13	0.6222(3)	0.0754(7)	0.8862(4)	0.0513(10)
H13A	0.5998	−0.0130	0.8192	0.062*
C14	0.6910(3)	0.0013(9)	0.9907(6)	0.0736(18)
H14A	0.7157	−0.1400	0.9952	0.088*

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Abstract

C₁₇H₁₅IN₂O, monoclinic, *C*2 (no. 5), $a = 23.6958(12)$ Å, $b = 5.5334(2)$ Å, $c = 15.9712(9)$ Å, $\beta = 132.329(3)^\circ$, $V = 1548.16(13)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.046$, $wR_{\text{ref}}(F^2) = 0.093$, $T = 296(2)$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
C15	0.7228(3)	0.1294(11)	1.0855(5)	0.073(2)
H15A	0.7695	0.0761	1.1561	0.088*
C16	0.6893(3)	0.3323(12)	1.0819(4)	0.0666(13)
H16A	0.7125	0.4214	1.1491	0.080*
C17	0.6204(2)	0.4089(8)	0.9789(3)	0.0463(9)
H17A	0.5963	0.5508	0.9752	0.056*

Source of material

A mixture of 6-iodo-2-propyl-4*H*-benzo[*d*][1,3]oxazin-4-one (3 mmol, 945 mg) and aniline (3.25 mmol, 303 mg) in 15 mL dry pyridine was heated under reflux for 16 h. The reaction mixture was cooled, the solvent was removed under reduced pressure, and the residue obtained was stirred with ice containing 10% hydrochloric acid. The solid obtained was filtered, washed with water, dried and recrystallized from ethanol.

Experimental details

The structure was solved by direct methods. All non-H atoms were refined with anisotropic displacement parameters. H-atoms were refined using the SHELXL [1] riding model using the appropriate AFIX commands. The Flack parameter was refined to $-0.03(3)$.

Comment

Epilepsy is one of the most common neurological problems in the world upsetting 1% of the population [3]. Methaqualone is one of the most important anticonvulsant drugs containing the quinazoline pharmacophore [4].

New derivative of methaqualone was prepared and evaluated for their anticonvulsant activity in mice. The results of this study demonstrated that 3-substituted-4(3*H*)-quinazolinone derivatives control a good anticonvulsant activity [4, 6–9].

In our laboratory, research efforts have concentrated on synthesizing quinazoline derivatives with substituted moieties having high lipophilic properties in the hope of developing effective and safe compounds [4–18]. Herein, we report the crystal structure of 6-iodo-3-phenyl-2-propylquinazolin-4(3*H*)-one as a methaqualone analogue.

The asymmetric unit of the title compound contains one independent molecule. Geometric parameters are in the expected range [19]. The quinazolin-4(3*H*)-one ring (N1/C1-C7/N2/C8) makes a nearly perpendicular dihedral angle of 88.81° with the phenyl ring (C12–C17). The molecules pack *via* non-classical intermolecular hydrogen bonds C13–H13A⋯O1ⁱ and C15–H15A⋯O1ⁱⁱ. Symmetry codes: (i) $x, y - 1, z$, (ii) $1.5 - x, -1/2 + y, 2 - z$ [D⋯A distances of

3.370(6) and 3.453(6) Å, respectively; D–H⋯A angle of 144.1 and 137.0°, respectively].

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References

- Sheldrick, G. M.: SHELXT—integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
- Bruker: APEX S. SADABS and SHELXT. Bruker-AXS, Madison, WI, USA (2014).
- Stefan, H.; Feuerstein, T.: Novel anticonvulsant drugs. *Pharmacol. Ther.* **113** (2007) 165–183.
- El-Azab, A. S.; Abdel-Hamde, S. G.; Sayed-Ahmed, M. M.; Hassan, G. S.; El-Hadiyah, T. M.; Al-Shabanah, O. A.; Al-Deeb, O. A.; El-Subbagh, H. I.: Novel 4(3*H*)-quinazolinone analogs: synthesis and anticonvulsant activity. *Med. Chem. Res.* **22** (2013) 2815–2827.
- El-Azab, A. S.; Al-Dhfyan, A.; Abdel-Aziz, A. A.; Abou-Zeid, L. A.; Alkahtani, H. M.; Al-Obaid, A. M.; Al-Gendy, M. A.: Synthesis, anticancer and apoptosis-inducing activities of quinazolinone-isatin conjugates: epidermal growth factor receptor-tyrosine kinase assay and molecular docking studies. *J. Enzyme Inhib. Med. Chem.* **32** (2017) 935–944.
- El-Azab, A. S.; Abdel-Aziz, A. A.; Ghabbour, H. A.; Al-Gendy, M. A.: Synthesis, *in vitro* antitumor activity, and molecular docking study of novel 2-substituted mercapto-3-(3,4,5-trimethoxybenzyl)-4(3*H*)-quinazolinone analogues. *J. Enzyme Inhib. Med. Chem.* **32** (2017) 1229–1239.
- Alanazi, A. M.; Abdel-Aziz, A. A.; Shawer, T. Z.; Ayyad, R. R.; Al-Obaid, A. M.; Al-Agamy, M. H.; Maarouf, A. R.; El-Azab, A. S.: Synthesis, antitumor and antimicrobial activity of some new 6-methyl-3-phenyl-4(3*H*)-quinazolinone analogues: *in silico* studies. *J. Enzyme Inhib. Med. Chem.* **31** (2016) 721–735.
- Abdel-Aziz, A. A.; Abou-Zeid, L. A.; ElTahir, K. E. H.; Ayyad, R. R.; El-Sayed, M. A.; El-Azab, A. S.: Synthesis, anti-inflammatory, analgesic, COX-1/2 inhibitory activities and molecular docking studies of substituted 2-mercapto-4(3*H*)-quinazolinones. *Eur. J. Med. Chem.* **121** (2016) 410–421.
- Mohamed, M. A.; Ayyad, R. R.; Shawer, T. Z.; Abdel-Aziz, A. A.; El-Azab, A. S.: Synthesis and antitumor evaluation of trimethoxyanilides based on 4(3*H*)-quinazolinone scaffolds. *Eur. J. Med. Chem.* **112** (2016) 106–113.
- El-Sayed, M. A.; El-Husseiny, W. M.; Abdel-Aziz, N. I.; El-Azab, A. S.; Abuelizz, H. A.; Abdel-Aziz, A. A.: Synthesis and biological evaluation of 2-styrylquinolines as antitumor agents and EGFR kinase inhibitors: molecular docking study. *J. Enzyme Inhib. Med. Chem.* **33** (2018) 199–209.
- Alanazi, A. M.; Alaa, A.-M.; Al-Suwaidan, I. A.; Abdel-Hamde, S. G.; Shawer, T. Z.; El-Azab, A. S.: Design, synthesis and biological evaluation of some novel substituted quinazolines as antitumor agents. *Eur. J. Med. Chem.* **79** (2014) 446–454.

12. Alanazi, A. M.; Al-Suwaidan, I. A.; Alaa, A.-M.; Mohamed, M. A.; El_Morsy, A. M.; El-Azab, A. S.: Design, synthesis and biological evaluation of some novel substituted 2-mercapto-3-phenethylquinazolines as antitumor agents. *Med. Chem. Res.* **22** (2013) 5566–5577.
13. El-Azab, A. S.; ElTahir, K. E.: Design and synthesis of novel 7-aminoquinazoline derivatives: antitumor and anticonvulsant activities. *Bioorg. Med. Chem. Lett.* **22** (2012) 1879–1885.
14. Grever, M. R.; Schepartz, S. A.; Chabner, B. A.: The National Cancer Institute: cancer drug discovery and development program. In: *Seminars in oncology*, Volume 19 (Ed. Fojo, A. T.), p. 622–638. WB Saunders Co Independence Square West Curtis Center, STE 300, Philadelphia, PA 19106-3399 (1992).
15. Alaa, A.-M.; Abou-Zeid, L. A.; ElTahir, K. E. H.; Mohamed, M. A.; El-Enin, M. A. A.; El-Azab, A. S.: Design, synthesis of 2,3-disubstitued 4 (3*H*)-quinazolinone derivatives as anti-inflammatory and analgesic agents: COX-1/2 inhibitory activities and molecular docking studies. *Bioorg. Med. Chem.* **24** (2016) 3818–3828.
16. Al-Suwaidan, I. A.; Abdel-Aziz, A. A.-M.; Shawer, T. Z.; Ayyad, R. R.; Alanazi, A. M.; El-Morsy, A. M.; Mohamed, M. A.; Abdel-Aziz, N. I.; El-Sayed, M. A.-A.; El-Azab, A. S.: Synthesis, antitumor activity and molecular docking study of some novel 3-benzyl-4 (3*H*) quinazolinone analogues. *J. Enzyme Inhib. Med. Chem.* **31** (2016) 78–89.
17. Al-Suwaidan, I. A.; Alanazi, A. M.; Alaa, A.-M.; Mohamed, M. A.; El-Azab, A. S.: Design, synthesis and biological evaluation of 2-mercapto-3-phenethylquinazoline bearing anilide fragments as potential antitumor agents: molecular docking study. *Bioorg. Med. Chem. Lett.* **23** (2013) 3935–3941.
18. El-Azab, A. S.; Abdel-Aziz, A. A.; Bua, S.; Nocentini, A.; El-Gendy, M. A.; Mohamed, M. A.; Shawer, T. Z.; AlSaif, N. A.; Supuran, C. T.: Synthesis of benzensulfonamides linked to quinazoline scaffolds as novel carbonic anhydrase inhibitors. *Bioorg. Chem.* **87** (2019) 78–90.
19. Yu, M. J.; McCowan, J. R.; Mason, N. R.; Deeter, J. B.; Mendelsohn, L. G.: Synthesis and x-ray crystallographic analysis of quinazolinone cholecystokinin/gastrin receptor ligands. *J. Med. Chem.* **35** (1992) 2534–2542.