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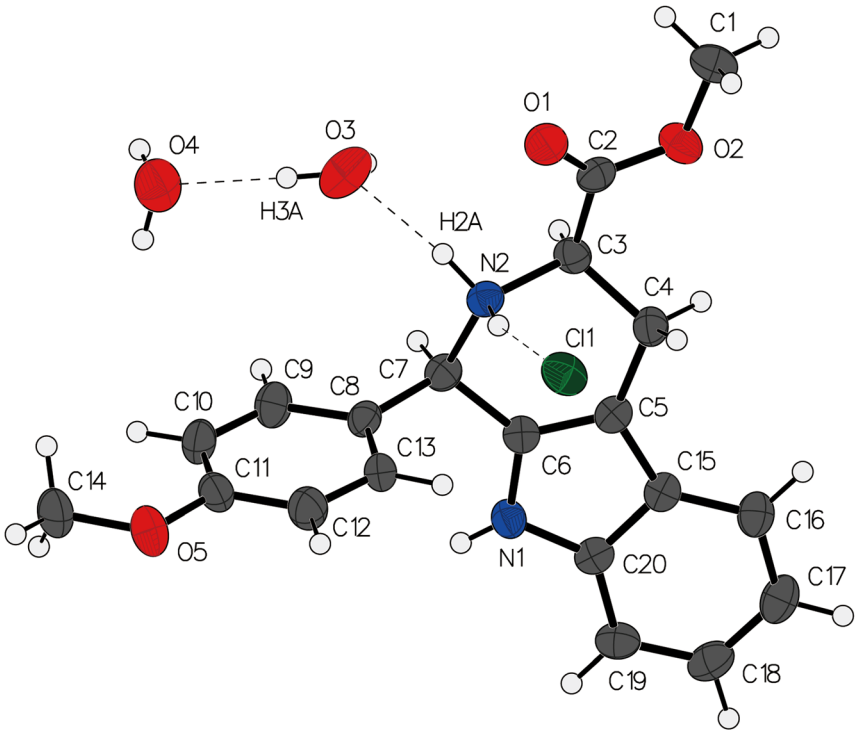
Crystal structure of 3-(methoxycarbonyl)-1-(4-methoxyphenyl)-2,3,4,9- tetrahydro-1*H*-pyrido [3,4-*b*]indol-2-ium chloride hydrate, $C_{40}H_{48}Cl_2N_4O_9$



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Abstract

$C_{40}H_{48}Cl_2N_4O_9$, monoclinic, *C*2 (no. 5), a = 13.434(2) Å, b = 7.2089(11) Å, c = 20.691(3) Å, β = 95.931(4)°, V = 1993.0(5) Å^3, Z = 2, $R_{gt}(F)$ = 0.0478, $wR_{ref}(F^2)$ = 0.1091, T = 173 K.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.19 × 0.15 × 0.12 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.22 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	27.5°, >99 %
N $(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	8183, 4444, 0.034
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 3624
$N(param)_{refined}$:	265
Programs:	Bruker [1], SHELX [2, 3], Olex2 [4]

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.8650 (3)	0.4984 (6)	0.15598 (19)	0.0387 (9)
H1A	0.886449	0.542666	0.114847	0.058*
H1B	0.877907	0.364900	0.160272	0.058*
H1C	0.902342	0.564067	0.192212	0.058*
C2	0.7213 (3)	0.5209 (5)	0.21375 (17)	0.0301 (8)
C3	0.6111 (2)	0.5675 (6)	0.20534 (15)	0.0288 (7)
H3	0.604186	0.704552	0.198981	0.035*
C4	0.5537 (2)	0.4711 (5)	0.14694 (16)	0.0311 (8)
H4A	0.569809	0.530713	0.106200	0.037*
H4B	0.573856	0.339111	0.145804	0.037*
C5	0.4434 (3)	0.4844 (5)	0.15213 (16)	0.0280 (7)
C6	0.4039 (2)	0.5295 (5)	0.20799 (15)	0.0266 (8)
C7	0.4616 (2)	0.5822 (6)	0.27136 (15)	0.0286 (7)
H7	0.461642	0.720505	0.275251	0.034*
C8	0.4246 (2)	0.5009 (5)	0.33159 (15)	0.0278 (8)
C9	0.4082 (3)	0.6138 (6)	0.38395 (18)	0.0379 (9)
H9	0.415802	0.744248	0.380184	0.046*
C10	0.3810 (3)	0.5399 (6)	0.44181 (18)	0.0415 (10)
H10	0.369527	0.619400	0.476909	0.050*
C11	0.3708 (3)	0.3511 (6)	0.44769 (17)	0.0361 (9)
C12	0.3857 (3)	0.2348 (6)	0.39526 (19)	0.0388 (9)
H12	0.378455	0.104267	0.399099	0.047*
C13	0.4111 (3)	0.3114 (5)	0.33787 (17)	0.0326 (8)
H13	0.419411	0.232466	0.302051	0.039*
C14	0.3344 (4)	0.3728 (9)	0.55796 (18)	0.0598 (14)
H14A	0.273599	0.448083	0.550423	0.090*
H14B	0.392647	0.454308	0.566603	0.090*
H14C	0.329423	0.291382	0.595422	0.090*
C15	0.3604 (3)	0.4517 (5)	0.10363 (16)	0.0279 (8)
C16	0.3523 (3)	0.3941 (5)	0.03896 (16)	0.0354 (9)
H16	0.410478	0.373430	0.017519	0.043*
C17	0.2581 (3)	0.3675 (6)	0.00656 (18)	0.0412 (10)
H17	0.251640	0.325293	−0.037163	0.049*
C18	0.1720 (3)	0.4021 (6)	0.03748 (18)	0.0400 (10)
H18	0.108213	0.385056	0.013873	0.048*
C19	0.1773 (3)	0.4602 (5)	0.10112 (17)	0.0334 (8)
H19	0.118612	0.483805	0.121771	0.040*
C20	0.2731 (3)	0.4831 (5)	0.13415 (16)	0.0281 (8)
Cl1	0.59735 (7)	0.08162 (14)	0.26183 (5)	0.0398 (3)
N1	0.3018 (2)	0.5304 (4)	0.19803 (14)	0.0303 (7)
H1	0.263 (2)	0.562 (5)	0.2229 (15)	0.019 (9)*
N2	0.5687 (2)	0.5173 (4)	0.26732 (13)	0.0283 (7)
H2A	0.608439	0.567074	0.301208	0.034*
H2B	0.570778	0.391801	0.271935	0.034*
O1	0.76796 (19)	0.4776 (5)	0.26421 (12)	0.0469 (7)
O2	0.75906 (18)	0.5329 (4)	0.15690 (12)	0.0377 (7)
O3	0.6492 (3)	0.7667 (4)	0.35930 (15)	0.0537 (9)
H3A	0.632534	0.799750	0.396134	0.080*
H3B	0.638099	0.855110	0.332354	0.080*
O4[a]	0.5890 (5)	0.9115 (9)	0.4713 (3)	0.0529 (15)
H4C[a]	0.600931	1.027111	0.474550	0.079*
H4D[a]	0.525843	0.903092	0.471240	0.079*
O5	0.3454 (2)	0.2634 (5)	0.50206 (13)	0.0528 (8)

[a]Occupancy: 0.5.

1 Source of materials

To a solution of D-tryptophan methyl ester hydrochloride (2.55 g, 10 mmol) in methanol (30 mL) was added 4-methoxybenzaldehyde (1.63 g, 12 mmol). The mixture was refluxed for 3 h, until the TLC indicated the reaction was completed. The solvent was evaporated to dryness, yielding the crude product that was then purified to obtain a single crystal of high quality. For crystal growth, the crude product was dissolved in a minimal amount of hot ethanol and slowly cooled to room temperature.

2 Experimental details

Hydrogen atoms were assigned isotropic displacement factors: U_{iso}(H) = 1.2 times U_{eq}(C). All hydrogen atoms were refined as being bonded to their respective parent atoms.

3 Comment

Tryptophan plays a crucial role in protein functionality as a constituent of both proteins and non-ribosomal peptides. The hydrophobic and electrostatic characteristics of the indole group are of paramount importance [5]. Tryptophan and its derivatives exhibit biological activity and serve as significant building blocks in drug development, with numerous crystal structures having been reported [6–10]. In this study, we have synthesized and reported the detailed single-crystal structure of a new tryptophan derivative.

The crystal structure, depicted in the figure, reveals that the carbon and nitrogen atoms within the indole group are almost coplanar. The phenyl ring in the benzylmethoxy moiety is nearly orthogonal to the indole plane, with a dihedral angle of 82.1°. The bond lengths, bond angles, and dihedral angles in the molecular structure fall within reasonable ranges [11–14].

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Bruker. *SAINT*, *APEX2 and SADABs*; Bruker AXS Inc.: Madison, WI, USA, 2012.
2. Sheldrick G. M. *SHELXTL* – integrated space-group and crystal-structure determination. *Acta Crystallogr.* 2015, *A71*, 3–8.
3. Sheldrick G. M. Crystal structure refinement with SHELXTL. *Acta Crystallogr.* 2015, *C71*, 3–8.
4. Dolomanov O. V., Bourhis L. J., Gildea R. J., Howard J. A. K., Puschmann H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* 2009, *42*, 339–341.
5. Blaser G., Sanderson J. M., Batsanov A. S., Howard J. A. K. The facile synthesis of a series of tryptophan derivatives. *Tetrahedron Lett*. 2008, *49*, 2795–2798.
6. Chauhan J., Luthra T., Gundla R., Ferraro A., Holzgrabe U., Sen S. A diversity oriented synthesis of natural product inspired molecular libraries. *Org. Biomol. Chem.* 2017, *15*, 9108–9120.
7. Geetha D. V., Harsha K. B., Rangappa K. S., Sridhar M. A., Kant R., Anthal S. Crystal structure and Hirshfeld surface analysis of (6bR,14bR,15R,15aR)-ethyl 5-bromo-14b-phenyl-1,6b,8,9,14,14b,15,15a-octahydrochromeno [3′,4′:2,3] indolizino [8,7-b] indole-15-carboxylate. *Chem. Data Collect* 2017, *7–8*, 93–101.
8. Shimpi M. R., Alhayali A., Cavanagh K. L., Rodríguez-Hornedo N., Velaga S. P. Tadalafil-malonic acid cocrystal: physicochemical characterization, pH-solubility, and supersaturation studies. *Cryst. Growth Des.* 2018, *18*, 4378–4387.
9. Samundeeswari S., Chougala B., Holiyachi M., Shastri L., Kulkarni M., Dodamani S., Jalalpur S., Joshi S., Dixit S., Sunagar V., Hunnur R. Design and synthesis of novel phenyl-1, 4-beta-carboline-hybrid molecules as potential anticancer agents. *Eur. J. Med. Chem.* 2017, *128*, 123–139.
10. Nagaraju V., Purnachander D., Goutham K., Suresh S., Sridhar B., Karunakar G. V. Synthesis of tetracyclic tetrahydro-β-carbolines by acid-promoted one-pot sequential formation of C–C and C–N bonds. *Asian J. Org. Chem.* 2016, *5*, 1378–1387.
11. Dhiman S., Mishra U. K., Ramasastry S. S. V. One-pot trimetallic relay catalysis: a unified approach for the synthesis of β-carbolines and other [c]-fused pyridines. *Angew. Chem. Int. Ed.* 2016, *55*, 7737–7741.
12. Wu Q.-F., Zheng C., Zhuo C.-X., You S.-L. Highly efficient synthesis and stereoselective migration reactions of chiral five-membered aza-spiroindolenines: scope and mechanistic understanding. *Chem. Sci.* 2016, *7*, 4453–4459.
13. Li-Hua W., Xi-Shi T. The crystal structure of 2-(2-(2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-2-ium-1-yl)phenoxy)acetate, $C_{19}H_{18}N_2O_3$. *Z. Kristallogr. N. Cryst. Struct.* 2020, *235*, 1275–1276.
14. Zhang J., Gu M., Bai X. The crystal structure of (1*S*,3*R*)-1-(4-isopropylphenyl)-3-(methoxycarbonyl)-2,3,4,9-tetrahydro-1*H*-pyrido [3,4-*b*]indol-2-iumchloride monohydrate, $C_{22}H_{27}ClN_2O_3$. *Z. Kristallogr. N. Cryst. Struct.* 2022, *237*, 619–621.