Crystal structure of 1-carbamoyl-3-cyano-β-carboline, $C_{13}H_8N_4O$

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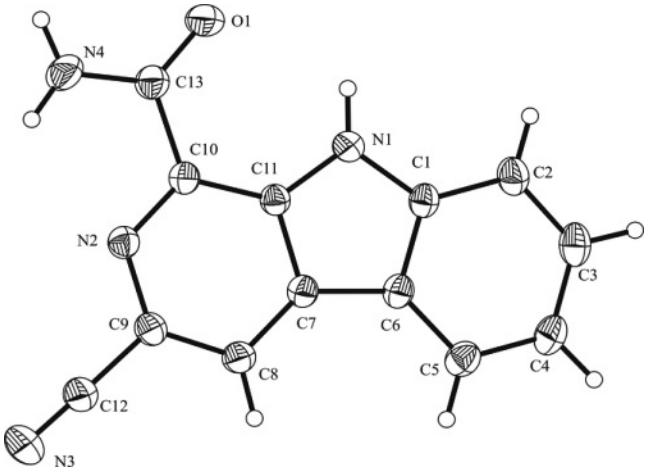

Abstract

$C_{13}H_8N_4O$, monoclinic, $P2_1/c$ (no. 14), a = 9.748(2) Å, b = 14.661(3) Å, c = 7.364(2) Å, β = 93.22(3)°, V = 1050.8 Å^3, Z = 4, $R_{gt}(F)$ = 0.0485, $wR_{ref}(F^2)$ = 0.1500, T = 293 K.

Table 1. Data collection and handling.

Crystal:	colourless prisms, size 0.10×0.10×0.30 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.01 cm^{-1}
Diffractometer, scan mode:	Nonius CAD4, $\omega/2\theta$
$2\theta_{max}$:	50.8°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4084, 1934
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 1360
$N(param)_{refined}$:	163
Programs:	ORTEP-3 [8], XCAD [9], SHELX [10]

Source of material

γ-Tryptophan was chosen as the starting material for this study, converted to 1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid according to the Pictet-Spengler [1] reaction in good yield. Treatment with an excess of thionyl chloride in anhydrous EtOH at reflux for 6 h and dehydrogenation with $KMnO_4$ in dimethylformamide (DMF) at room temperature for 24 h gave ethyl β-carboline-3-carboxylate as a white solid. The intermediate product was reduced with $LiAlH_4$ and then oxidized by MnO_2 to obtain the 3-formyl-β-carboline. Then the reaction with iodine and ammonia solution gave 3-cyano-β-carboline. Subsequently, we treated 3-cyano-β-carboline with $FeSO_4$ and H_2O_2 in formamide under mild conditions via the Minisci reaction [2-3], giving the expected title compound 1-carbamoyl-3-cyano-β-carboline.

Experimental details

At first, all H atoms were located from the difference Fourier maps, and then were treated as riding [benzene C–H = 0.93 Å and methyl C–H = 0.97 Å; U_{iso}(H) = 1.2 times U_{eq}; amine N–H = 0.86 Å; U_{iso}(H) = 1.5 times U_{eq}].

Discussion

The β-carboline moiety in many natural products is a key pharmacophore exhibiting potent biological activities such as the anticancer activity against colon and lung cancers, and as the biological control agent for receptor research on bio-enzyme inhibitors [4-6]. So it is urgent and significant to synthesize a large number of novel series of β-carboline derivatives with various substituents at 1-, 3-, and 6-positions. Herein, we report a novel crystal structure of 1-carbamoyl-3-cyano-β-carboline which should be useful for the further structure-activity relationships determination in drug design. In the crystal structure of the title compound, the carbamoyl group at 1-position are nearly coplanar with the carboline ring, indicating by the torsion angle of N2–C10–C18–N14 being 179.3(2)°. This rigid planar structure was further stablilized by the intramolecular H-bonding interaction between N1–H1B and O1. The cyano group is expectedly in a linear geometry to the C9 atom. The N3 atom is a H-bond acceptor in the intermolecular hydrogen bond N4–H4B···N3 (–1–x, $\frac{1}{2}$+y, $\frac{1}{2}$–z). The carboline ring is stacking with the adjacent one at in face-to-face mode along c axis direction, evidenced by the interplanar distance of 3.497(2) Å. Besides this $\pi\cdots\pi$ interaction, the intermolecular H-bond between N1–H1B and O1(–x, 1–y, –z) joins the formation of three-dimensional hydrogen-bonding network.

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(1B)	4*e*	0.0762	0.4070	0.0630	0.048
H(4B)	4*e*	–0.3724	0.4793	0.2282	0.070
H(4C)	4*e*	–0.3874	0.3784	0.2417	0.070
H(2B)	4*e*	0.3431	0.3778	–0.0284	0.055
H(3A)	4*e*	0.4955	0.2616	–0.0807	0.060
H(4A)	4*e*	0.4333	0.1109	–0.0550	0.061
H(5A)	4*e*	0.2168	0.0719	0.0274	0.055
H(8A)	4*e*	–0.0648	0.0746	0.1405	0.048

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Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	4*e*	0.0764(2)	0.3484(1)	0.0669(2)	0.036(1)	0.0358(9)	0.048(1)	–0.0012(7)	0.0057(8)	0.0017(7)
C(1)	4*e*	0.1866(2)	0.2932(1)	0.0303(3)	0.032(1)	0.045(1)	0.034(1)	0.0018(8)	0.0035(8)	0.0030(9)
N(4)	4*e*	–0.3385(2)	0.4254(1)	0.2189(3)	0.049(1)	0.049(1)	0.079(1)	0.0121(9)	0.024(1)	0.005(1)
N(2)	4*e*	–0.2541(2)	0.2534(1)	0.1968(2)	0.0352(9)	0.0396(9)	0.041(1)	0.0001(7)	0.0039(7)	0.0013(7)
O(1)	4*e*	–0.1324(2)	0.4771(1)	0.1337(3)	0.055(1)	0.0385(9)	0.103(2)	–0.0006(7)	0.024(1)	0.0028(9)
C(2)	4*e*	0.3173(2)	0.3170(2)	–0.0176(3)	0.036(1)	0.056(1)	0.045(1)	–0.003(1)	0.0061(9)	0.007(1)
C(3)	4*e*	0.4071(2)	0.2474(2)	–0.0483(3)	0.035(1)	0.074(2)	0.043(1)	–0.000(1)	0.0095(9)	0.004(1)
N(3)	4*e*	–0.4025(2)	0.0496(1)	0.2667(3)	0.055(1)	0.059(1)	0.084(2)	–0.017(1)	0.014(1)	0.007(1)
C(4)	4*e*	0.3700(2)	0.1564(2)	–0.0324(3)	0.039(1)	0.061(1)	0.053(1)	0.011(1)	0.010(1)	0.000(1)
C(5)	4*e*	0.2413(2)	0.1328(2)	0.0162(3)	0.045(1)	0.047(1)	0.046(1)	0.007(1)	0.009(1)	0.001(1)
C(6)	4*e*	0.1478(2)	0.2019(1)	0.0486(3)	0.034(1)	0.045(1)	0.032(1)	0.0027(9)	0.0050(8)	0.0023(9)
C(7)	4*e*	0.0076(2)	0.2026(1)	0.1019(3)	0.034(1)	0.040(1)	0.032(1)	0.0010(8)	0.0040(8)	0.0021(8)
C(8)	4*e*	–0.0868(2)	0.1363(1)	0.1431(3)	0.041(1)	0.038(1)	0.043(1)	0.0008(9)	0.0049(9)	0.0003(9)
C(9)	4*e*	–0.2156(2)	0.1657(1)	0.1884(3)	0.037(1)	0.042(1)	0.037(1)	–0.0034(9)	0.0042(8)	0.0014(9)
C(10)	4*e*	–0.1644(2)	0.3179(1)	0.1587(3)	0.034(1)	0.040(1)	0.034(1)	0.0005(8)	0.0018(8)	0.0003(8)
C(11)	4*e*	–0.0316(2)	0.2952(1)	0.1103(3)	0.032(1)	0.037(1)	0.033(1)	–0.0007(8)	0.0021(8)	0.0016(8)
C(12)	4*e*	–0.3195(2)	0.1001(1)	0.2322(3)	0.043(1)	0.045(1)	0.050(1)	–0.002(1)	0.007(1)	0.000(1)
C(13)	4*e*	–0.2103(2)	0.4149(1)	0.1691(3)	0.042(1)	0.043(1)	0.047(1)	0.002(1)	0.009(1)	0.001(1)

References

1. Whaley, W. M.; Govindachari, T. R.: The Pictet-Spengler synthesis of tetrahydroisoquiolines and related compounds. Org. React. **6** (1951) 151-190.
2. Minisci, F.; Galli, R.; Cecere, M.; Malatesta, V.; Caronna, T.: Nucleophilic character of alkyl radicals: New syntheses by alkyl radicals generated in redox processes. Tetrahedron Lett. **54** (1968) 5609-5612.
3. Minisci, F.; Gardini, G. P.: A new selectibe type of aromatic substitution: Homolytic amidation. Tetrahedron Lett. **1** (1970) 15-16.
4. Molina, P.; Fresneda, P. M.; Zafra, G. S.; Almendros, P.: Iminophosphorane-mediated syntheses of the fascaplysin alkaloid of marine origin and nitramarine. Tetrahedron Lett. **35** (1994) 8851-8854.
5. Schlecker, W.; Huth, A.; Ottow, E.; Mulzer, J.: Regioselective metalation of 9-methoxymethyl-β-carboline-3-carboxamides with amidomagnesium chlorides. Synthesis (1995) 1225-1227.
6. Dodd, H. R.; Ovannes, C.; Robert, G.; Potier, P.: Hybrid molecules: Growth inhibition of leishmania donovani promastigotes by thiosemicarbazones of 3-carboxy-beta-carbolines. J. Med. Chem. **54** (1989) 1272-1276.
7. Enraf-nonius: CAD-4 Software. Version 5. Enraf-nonius, Delft, The Netherlands. (1989).
8. Farrugia, L. J.: WinGX and ORTEP for Windows: an update. J. Appl. Crystallogr. **45** (2012) 849-854.
9. Harms, K.; Wocadlo, S.: XCAD4. University of Marburg, Germany 1995.
10. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112-122.