Synthesis, crystal structure and biological activity of β-carboline based selective CDK4-cyclin D1 inhibitors.

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Electronic Supplementary Data

Colour Figures

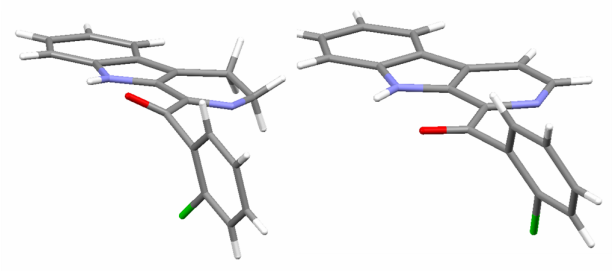


Fig 2. MERCURY capped sticks representation of the minimal asymmetric unit in the crystalline structure for compound 3d (left) and 4d (right).

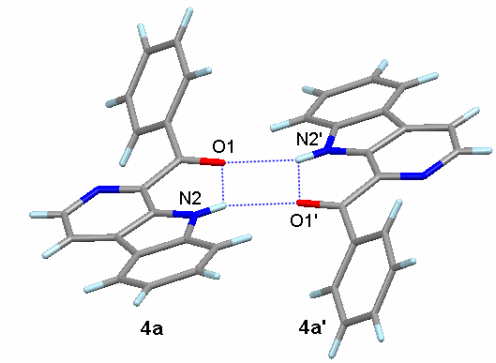
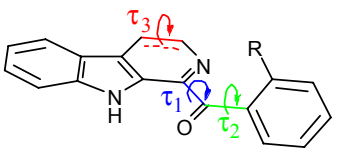


Fig. 3. MERCURY capped sticks representation of the cyclic symmetric dimer formed by two molecules of **4a** (symmetry codes x,y,z and -x+1,-y,-z)**.** Intramolecular (N2H1···O1, N2′H2′···O1) and intermolecular (N2H···O1′, N2′H′···O1) Hydrogen bonds shown as dashed blue lines.

Table 1. Geometrical data discussed in the text.



3b dihydro R = F
3d dihydro R = Br
4a dehydro R = H
4b dehydro R = F
4c dehydro R = Cl
4d dehydro R = Br

Structure	Monomers d(N2..O1) (Å)	∠N2HO1 (°)	τ_1 (°)	τ_2 (°)	τ_3 (°)	d(N1..R) (Å)	Dimers d(N2'..O1) (Å)	∠N2HO1 (°)	[c]di (Å)
[b]**4a**	2.744	117.2	2.13	50.05	--	2.603	2.945	154.9	0.616
	2.767	115.7	11.78	-49.70	--	2.567	2.944	154.2	0.616
4b	2.889	113.4	-12.54	-63.18	--	3.099	3.056	144.4	1.095
4c	2.808	113.9	-5.70	-70.49	--	3.262	2.996	145.6	0.275
4d	2.813	114.2	-4.11	-68.10	--	3.351	3.013	145.0	0.000
3b	2.837	120.5	19.90	50.34	-45.53	2.939	---	---	---
3d	2.935	116.6	-24.94	-58.96	-17.30	3.361	3.088	153.8	0.770

[a] Data measured using the program Mercury. [b]Two different conformers are presented in the asymmetric unit cell for compound **4a**.[c] Perpendicular distance between the parallel planes containing the β-carboline (type **4** compounds) or indolyl (type **3**) moieties of the molecules involved in the double hydrogen bonding.

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Crystal structure determinations‡

Single crystals of compounds **3b**/**d** and **4a-d** suitable for X-ray diffractometry were obtained by dissolving crystals of the corresponding pure compound in the minimum quantity of cold EtOH in an open vial that was then placed in a larger container with a little H_2O in its bottom; the container was closed, and after a few days in a cool, dark place free from vibrations afforded the desired single crystals. These were mounted in inert oil and transferred to the cold gas stream of the diffractometer.

Crystal data 3b: $C_{18}H_{13}FN_2O$, M = 292.30, monoclinic, a = 11.686(3) Å, b = 7.3469(16) Å, c = 16.098(4) Å, U = 1362.3(5) Å^3, T = 150(2) K, space group P2(1)/n, Z = 4, μ (Mo-Kα) = 0.099 mm^{-1}, 9489 reflections measured, 2402 unique (R_{int} = 0.0667) wich were used in all calculations. The final *wR(F2)* was 0.937 (all data).

Crystal data 3d: $C_{18}H_{13}BrN_2O$, M = 353.21, monoclinic, a = 23.342(4) Å, b = 7.5017 (14) Å, c = 17.360(3) Å, U = 2961.3(9) Å^3, T = 150(2) K, space group C2/c, Z = 8, μ (Mo-Kα) = 2.779 mm^{-1}, 10329 reflections measured, 2606 unique (R_{int} = 0.0481) wich were used in all calculations. The final *wR(F2)* was 0.964 (all data).

Crystal data 4a: $C_{18}H_{11}N_2O$, M = 272.30, triclinic, a = 6.2230(18) Å, b = 13.841(4) Å, c = 15.692(5) Å, U = 1312.3(7) Å^3, T = 150(2) K, space group P-1, Z = 4, μ (Mo-Kα) = 0.087 mm^{-1}, 9574 reflections measured, 4594 unique (R_{int} = 0.0501) wich were used in all calculations. The final *wR(F2)* was 1.003 (all data).

Crystal data 4b: $C_{18}H_{11}FN_2O$, M = 290.29, monoclinic, a = 8.6767(12) Å, b = 7.7705(11) Å, c = 19.715(3) Å, U = 1329.0(3) Å^3, T = 150(2) K, space group P2(1)/c, Z = 4, μ (Mo-Kα) = 1.101 mm^{-1}, 9282 reflections measured, 2343 unique (R_{int} = 0.0845) wich were used in all calculations. The final *wR(F2)* was 1.020 (all data).

Crystal data 4c: $C_{18}H_{11}ClN_2O$, M = 306.74, orthorhombic, a = 7.605(2) Å, b = 14.272(4) Å, c = 26.587(7) Å, U =2885.6(13) Å^3, T = 150(2) K, space group Pbca, Z = 8, μ (Mo-Kα) = 0.267 mm^{-1}, 19314 reflections measured, 2525 unique (R_{int} = 0.2061) wich were used in all calculations. The final *wR(F2)* was 1.029 (all data).

Crystal data 4d: $C_{18}H_{11}BrN_2O$, M = 351.20, orthorhombic, a = 7.5911(12) Å, b = 14.524(2) Å, c = 26.489(4) Å, U = 2920.5(8) Å^3, T = 150(2) K, space group Pbca, Z = 8, μ (Mo-Kα) = 2.818 mm^{-1}, 19679 reflections measured, 2559 unique (R_{int} = 0.0930) wich were used in all calculations. The final *wR(F2)* was 0.868 (all data).

Notes and references

‡ CCDC621742-CCDC621747 contain, respectively, the supplementary crystallographic data for compounds **3b**/**d** and **4a-d** described in this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.