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Single crystal X-ray structure of 3-amino-5-(4-chlorophenyl)pyridazine-4-carbonitrile

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The title compound 3-amino-5-(4-chlorophenyl)pyridazine-4-carbonitrile was prepared by a one-pot three-component reaction of malononitrile with corresponding arylglyoxal in the presence of hydrazine hydrate at room temperature in water and ethanol. Its structure was also confirmed by its IR, ^{1}H, ^{13}C-NMR, Mass spectral data and elemental analysis. The compound was crystallized in the monoclinic system, space group $P2_1/c$, a = 3.817(3) Å, b = 13.533(10) Å, c = 19.607(15) Å, β = 93.401(10)°, Z=4, R1 = 0.0906 and wR2 = 0.1422. The crystal structure of the compound also shows a weak intermolecular interaction between N1 atom of one molecule and N3 atom of the other molecule.

1. Introduction

In recent years, a great deal of current interest is focused on development of novel multicomponent reactions,[1] due to the simplicity of a one-pot procedure, the possible structural variation, the accessible complexity of the molecules, straightforward reaction design, and the environmental friendliness.

Among one-pot synthetic methods, multicomponent reactions, leading to nitrogen-containing heterocyclic compounds have been indispensable structural unit for both organic chemists and biochemists because of their biological and pharmaceutical properties. The pyridazine fragment is an important pharmacophore and is known to exhibit promising biological properties such as analgesics,[2] insecticidals,[3] fungicidals,[4,5] cardiotonics[6] and bacteriocides.[7] Hence, the synthesis of pyridazine derivatives has been studied for many years.[8-14]

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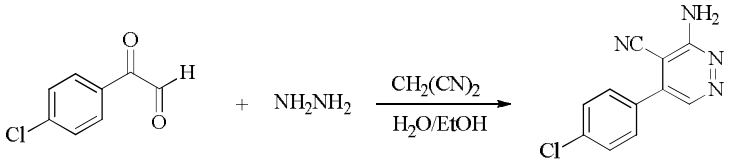
In continuation of recent reports on synthesis of pyridazine derivatives,[15-23] we would like to report the single crystal X-ray structure of 3-amino-5-(4-chlorophenyl)pyridazine-4-carbonitrile prepared by a one-pot three-component reaction of malononitrile with corresponding arylglyoxal in the presence of hydrazine hydrate at room temperature.[23]

2. Results and Discussion

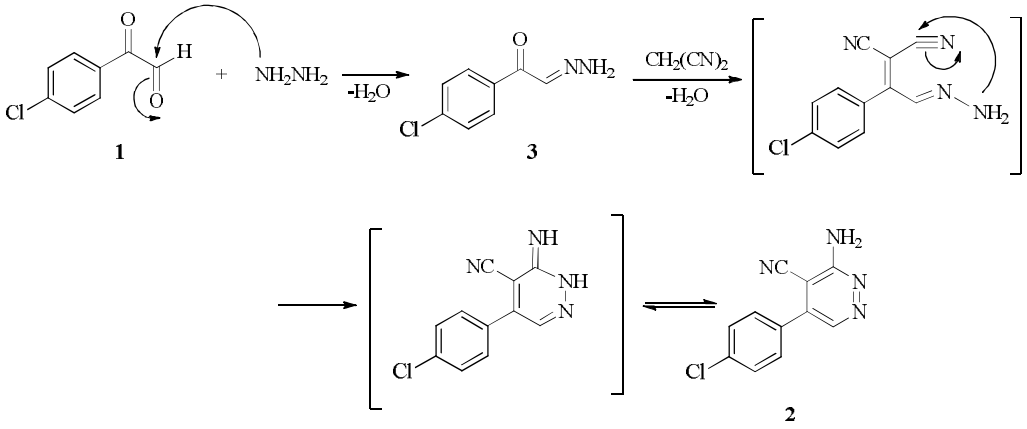
The arylglyoxal **1** was prepared from 4-chloroacetophenone[24] and used in the synthesis of the compound **2**, as shown in **Scheme 1**. To confirm this, the preparation of **2** was carried out in two stages, with the isolation of the hydrazone **3**, which was then reacted with malononitrile, leading to the formation of the product **2**. The spectral data of **2** prepared by the two stages method was identical with that produced in the one pot sequence.



1 **2**

Scheme 1

The proposed mechanism of the formation of **2** is shown in **Scheme 2**.



1 **3** **2**

Scheme 2

Crystal structure determination of 2

The crystal structure of **2** is shown in Fig. 1. Single-crystals of compound **2** were used for data collection on a Bruker Smart Apex diffractometer using SMART software.[25] Suitable crystals were selected and mounted on a glass fiber using epoxy-based glue. The data sets were collected at room temperature for sample employing a scan of 0.3° in ω with an exposure time of 20 s/frame. The cell refinement and data reduction were carried out with SAINT,[26] the program SADABS was used for the absorption correction.[26] The structure was solved by direct methods using SHELXS-97,[27] and difference Fourier syntheses. Full-matrix least-squares refinement against $|F^2|$ was carried out using the SHELXTL-PLUS,[27] suit of programs. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed geometrically and held in the riding mode during the final refinement. The crystallographic data for structure **2** were deposited to the Cambridge Crystallographic Data Center (entry no. CCDC-948077) and are available free of charge upon request to CCDC, 12 Union Road, Cambridge, UK (Fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk).

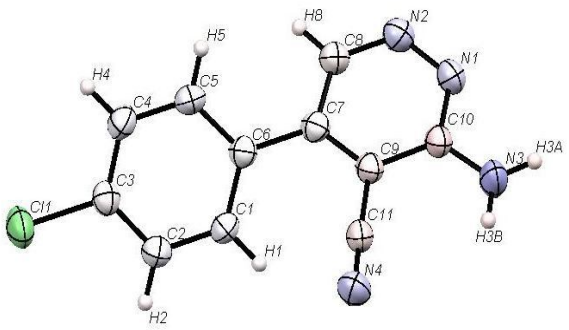


Fig 1. Crystal structure of **2**

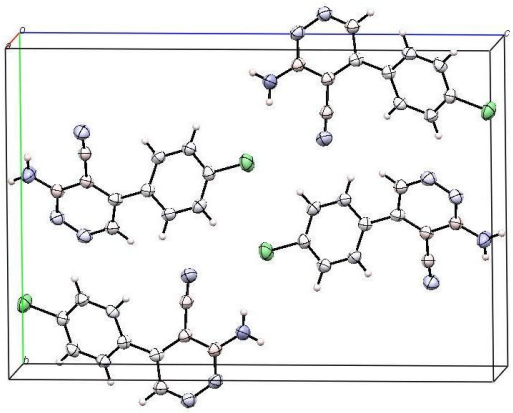


Fig 2. Crystal packing of **2**

Description of the crystal structure of 2

The crystal structure of **2**($C_{11}H_7ClN_4$) and its crystal structure packing are shown in Figs. 1 and 2, respectively. The selected crystallographic data and experimental details for **2** are given in **Table 1**, while selected bond lengths and angles for this compound are shown in **Table 2**. The hydrogen bonds geometry are shown in **Table 3**. The crystal structure of **2** also shows a weak intermolecular interaction between N1 atom of one molecule and N3 atom of the other molecule. The benzene and pyridazine rings moieties are not in the same plane together. The torsion angles of C1-C6-C7-C9, C7-C9-C11-N4 equal to -43.4° and -132°, respectively. The angles of N3-C10-N1, N4-C11-C9 and N2-N1-C10 are equal to 116.4, 176.2 and 120.08° respectively. Bond lengths of N1-N2 and N3-C10 are equal to 1.336 and 1.333 respectively. The torsion angles of N1-N2-C8-C7, C11-C9-C10-N3 are equal to -1.1°, and 2.6° respectively.

Table 1. Crystal Data and Experimental Details for **2**.

Empirical formula	$C_{11}H_7ClN_4$	Scan type	ω
Formula weight	230.66	θ range, deg	1.83-28.36
Crystal size, mm^3	0.50×0.07×0.03	Index range	-5≤h≤5, -18≤k≤18,-26≤l≤26
Crystal color	colorless	Measured reflections	11911
Crystal system	monoclinic	Independent reflections	2489
Space group	$P2_1/c$	Observed refl. I ≥ 2σ(I)	1610
Z	4	Completeness to θ = 28.36◦	98.9
V, $A^{\circ 3}$	1011.0(13)	Refinement on	F^2
D (calc), $g.cm^{-3}$	1.515	Data, restraints, parameters	2489, 0, 145
a , A°	3.817(3)	R ($Fo^2 > 2\sigma(Fo^2)$)	*R1 = 0.0529, wR2 = 0.1273*
b, A°	13.533(10)	R (all data)	*R1 = 0.0906, wR2 = 0.1422*
c, A°	19.607(15)	Goodness-of-fit = S	1.070
β, deg	93.401(10)	Weighting parameter a/b	0.0622/0.2374
μ, mm^{-1}	0.351	Δρ (max; min), $e.A^{\circ -3}$	0.326; -0.360
F(000), e	472	CCDC	948077

Table 2. Selected Bond Lengths and Angles (Å, °) of **2**.

Bond	*d*	Angle	ω
Cl(1)-C(3)	1.740(3)	N(2)-N(1)-C(10)	120.08(19)
N(1)-N(2)	1.336(3)	C(8)-N(2)-N(1)	120.2(2)
N(1)-C(10)	1.345(3)	C(10)-N(3)-H(3A)	120.0
N(2)-C(8)	1.317(3)	H(3A)-N(3)-H(3B)	120.0
N(3)-C(10)	1.333(3)	C(1)-C(6)-C(5)	118.2(2)
N(3)-H(3A)	0.8600	C(2)-C(1)-C(6)	121.2(2)
N(3)-H(3B)	0.8600	C(3)-C(4)-C(5)	119.1(2)
N(4)-C(11)	1.143(3)	C(6)-C(1)-H(1)	119.4
C(1)-C(2)	1.382(3)	C(3)-C(2)-C(1)	118.8(2)
C(1)-C(6)	1.395(3)	C(3)-C(2)-H(2)	120.6
C(1)-H(1)	0.9300	C(4)-C(3)-C(2)	121.4(2)
C(2)-C(3)	1.381(3)	C(2)-C(3)-Cl(1)	119.55(19)
C(2)-H(2)	0.9300	C(3)-C(4)-H(4)	120.5
C(3)-C(4)	1.380(4)	C(4)-C(5)-H(5)	119.4
C(4)-C(5)	1.377(3)	C(5)-C(6)-C(7)	120.9(2)
C(4)-H(4)	0.9300	C(9)-C(7)-C(8)	115.1(2)
C(5)-C(6)	1.393(3)	C(9)-C(7)-C(6)	123.7(2)
C(5)-H(5)	0.9300	N(2)-C(8)-C(7)	124.4(2)
C(6)-C(7)	1.472(3)	N(2)-C(8)-H(8)	117.8
C(7)-C(9)	1.380(3)	C(7)-C(9)-C(10)	119.2(2)
C(7)-C(8)	1.412(3)	C(7)-C(9)-C(11)	122.8(2)
C(8)-H(8)	0.9300	C(10)-C(9)-C(11)	118.1(2)
C(9)-C(10)	1.423(3)	N(3)-C(10)-N(1)	116.4(2)
C(9)-C(11)	1.435(3)	N(3)-C(10)-C(9)	122.7(2)
		N(1)-C(10)-C(9)	120.9(2)
		N(4)-C(11)-C(9)	176.2(3)

Table 3. Hydrogen bond geometry in **2** (Å, º).

D—H···A	*d*(D—H)	*d*(H···A)	*d*(D···A)	D—H···A
N(3)-H(3A)...N(1)	0.86	2.15	3.002(3)	172.8
N(3)-H(3B)...Cl(1)	0.86	2.76	3.594(3)	162.9

Symmetry codes: (i) *-x+1, -y+1, -z* (ii) *x, -y+1/2, z-1/2*

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Experimental

Materials and Instruments

^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM-300 spectrometer at 300 and 75 MHz, respectively. The spectra were measured in $CDCl_3$ using TMS as the internal standard. Melting point was determined on a digital melting point apparatus (Electrothermal) and remains uncorrected.

Infrared spectra was determined on a Thermo Nicolet (Nexus 670) FT-IR spectrometer, using KBr disks. Microanalyses were performed on a Leco Analyzer 932.

3-Amino-5-(4-chlorophenyl)pyridazine-4-carbonitrile (2)

A mixture of 4-chloroacetophenone (1 mmol) and hydrazine hydrate (4 mmol) in water and ethanol (1:1) (3 mL) was stirred at room temperature for 30 min. Then malononitrile (1 mmol) was added to the reaction mixture and was stirred for a further 30 min at room temperature. The product was then collected as a white precipitate, washed with hot water, and purified by recrystallization from ethanol to give the title compound as white solid (Yield: 87%), mp 290 ºC (dec.). FT-IR ν_{max} 3450, 3300, 3091, 2220, 1646, 1594, 1560, 1496, 1475, 1096, 829 cm^{-1}; ^{1}H-NMR δ (ppm) 8.75 (s, 1H, Ar), 7.73 (d, J = 8.4 Hz, 2H, Ar), 7.66 (d, J = 8.4 Hz, 2H, Ar), 7.43 (bs, 2H, exchanged by D_2O addition, NH_2); ^{13}C-NMR δ (ppm) 159.30, 141.71, 141.07, 139.99, 132.33, 131.04, 129.60, 114.80, 96.60; Mass spectrum m/z (%): 232 (M+2, 34), 230 (M^+, 100), 202 (20), 174 (12), 140 (20), 136 (34), 101 (40), 75 (43), 66 (23), 51 (23). Anal. Calc. for $C_{11}H_7ClN_4$: C, 57.28; H, 3.06; N, 24.29. Found: C, 57.31; H, 3.01; N, 24.33.

References

1. Toure B. B., and Hall D. G. (2009) Natural product synthesis using multicomponent reaction strategies. *Chem. Rev.,* 109, 4439-4486.
2. Rohet F., Rubat C., Coudert P., and Couquelet J. (1997) Synthesis and analgesic effects of 3-substituted 4,6-diarylpyridazine derivatives of the arylpiperazine class. *Bioorg. Med. Chem.,* 5, 655-659.
3. Deeb A., Mourad E., and Elenany D. (2009) Pyridazine Derivatives and Related Compounds, Part 221: Synthesis, Reactions, and Insecticidal Activity of 3-Amino-5,6-diaryl-1*H*-pyrazolo[3,4-*c*]pyridazines. *Phosphorus, Sulfur, and Silicon and the Related Elements.,* 185, 222-231.
4. Foks H., Wisterowicz K., Miszke A., Brozewicz K., Wisniewska K., and Dabrowska-Szponar M. (2009) Synthesis, Fungicidal and Antibacterial Activity of New Pyridazine Derivatives. *Heterocycles.*, 78, 961-976.
5. Lamberth C., Trah S., Wendeborn S., Dumeunier R., Courbot M., Godwin J., and Schneiter P. (2012) Synthesis and fungicidal activity of tubulin polymerisation promoters. Part 2: Pyridazines. *Bioorg. Med. Chem.,* 20, 2803–2810.
6. Smolyar N. N., Yutilov Yu. M., and Gres′ko, S. V. (2009) Synthesis of 4-amino-6-(hetaryl)pyridazin-3-ones as analogs of pyridazine-based cardiotonic agents. *Pharm. Chem. J.*, 43, 87-88.
7. Ungureanu M., Mangalagiu I., Grosu G., and Petrovanu M. (1997) Antimicrobial activity of new pyridazine derivatives. *Ann. Pharm. Fr.,* 55, 69-72.
8. Amer A. M., El-Mobayed M., Ateya A. M., and Muhdi T. S. (2002) On Condensation Reactions of Aceanthrene Quinone: Novel Heterocycles. *Monatsh. Chem.,* 133, 79-88.
9. Gomaa M. Abdel-Motaal. (2003) An efficient and facile synthesis of substituted cinnoline and benzo[*h*]cinnoline. *Tetrahedron Lett*., 44, 3493-3496.
10. Al-Mousawi S. M., Moustafa M. S., Meier H., Kolshorn H., and Elnagdi M. H. (2009) Polyfunctional Nitriles in Organic Syntheses: A Novel Route to Aminopyrroles, Pyridazines and Pyrazolo[3,4-*c*]pyridazines. *Molecules,* 14, 798-806.
11. Abdelrazek F. M., Fadda A. A., and Elsayed A. N. (2011) Novel Synthesis of Some New Pyridazine and Pyridazino[4,5-*d*]pyridazine Derivatives. *Synth. Com.,* 41, 1119-1126.
12. Eicher T., and Hauptmann S. (2003) *The Chemistry of Heterocycles*, 2nd Ed, Wiely-VCH Veriag GmbH, 392.
13. Tisler M., and Stanovnik R. (1968) Pyridazines. *Adv. Heterocycl. Chem.,* 9, 211-320.

14. Schmidt P., and Druey J. (1954) Heilmittelchemische Studien in der heterocyclischen Reihe. 5. Mitteilung. Pyridazine II. Eine neue Pyridazinsynthese. *Helv. Chim. Acta.,* 37, 134-140.
15. Khalafy J., Rimaz M., Ezzati M., and Prager R. H. (2012) A Green One-Pot Protocol for Regioselective Synthesis of New Substituted 7,8-Dihydrocinnoline-5(6*H*)-ones, *Bull. Korean Chem. Soc.*, 33, 2890-2896.
16. Khalafy J., Rimaz M., Panahi L., and Rabiei H. (2011). A regiospecific one-pot, three component synthesis of 4-aryl-6,8-dimethylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones as new potential monoamine oxidase inhibitors. *Bull. Korean Chem. Soc.,* 32, 2428-2432.
17. Rimaz M., and Khalafy J. (2010) Novel one-pot, three component synthesis of alkyl 6-aryl-3-methylpyridazine-4-carboxylates in water. *Arkivoc*, ii, 110-117.
18. Rimaz M., Khalafy J., and Najafi Moghadam P. (2010) A regioselective one-pot, three component synthesis of 6-aryl-4-cyano-3(2*H*)-pyridazinones in water. *Aust. J. Chem.,* 63, 1396-1401.
19. Rimaz M., Noroozi Pesyan N., and Khalafy J. (2010) Tautomerism and isotopic multiplets in the ^{13}C-NMR spectra of partially deuterated 3-arylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones and their sulfur analogs-evidence for elucidation of the structure backbone and tautomeric forms. *Magn. Reson. Chem.,* 48, 276-285.
20. Rimaz M., Khalafy J., Noroozi Pesyan N., and Prager R. H. (2010) A simple one-pot, three component synthesis of 3-arylpyrimido[4,5-*c*]pyridazine-5,7(6*H*,8*H*)-diones and their sulfur analogues as potential monoamine oxidase inhibitors. *Aust. J. Chem*., 63, 507-510.
21. Khalafy J., Rimaz M., and Ezzati M. (2012) Regioselective one-pot, three component synthesis of ethyl 6-aryl-3-propylpyridazine-4-carboxylates in water, *Curr. Chem. Lett.,* 1, 115-122.
22. Khalafy J., Parsa Habashi B., Poursattar Marjani A., and Najafi Moghadam P. (2012) The synthesis of 2-arylquinoxaline derivatives. *Curr. Chem. Lett.,* 1, 139-46.
23. Khalafy J., Rimaz M., Farajzadeh S., and Ezzati M. (2013) A simple three-component synthesis of 3-amino-5-arylpyridazine-4-carbonitriles. *S. Afri. J. Chem.,* 66*,* 179-182.
24. Riley H. A., and Gray A. R. (1943) *Organic Syntheses*, Collect. Vol. II, p. 509 (Wiley & Sons: New York, NY).
25. Bruker, SMART. Bruker AXS Inc., Madison, Wisconsin, USA 2002.
26. Bruker SAINT & SADABS. Bruker AXS Inc., Madison, Wisconsin, USA, 2008.
27. Sheldrick G. M. (2008) A short history of SHELX, *Acta Crystallographica*., A64, 112-122.