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Scientific paper

Synthesis, Spectroscopic Characterization, Crystal Structures and Antibacterial Activity of Benzohydrazones Derived from 4-Pyridinecarboxaldehyde with Various Benzohydrazides

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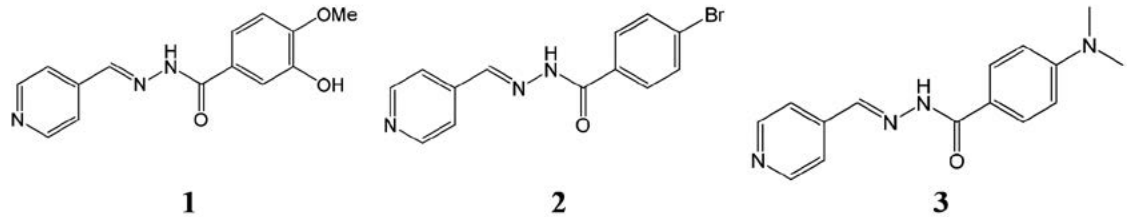
Abstract

Reaction of 4-pyridinecarboxaldehyde with 3-hydroxy-4-methoxybenzohydrazide, 4-bromobenzohydrazide and 4-dimethylaminobenzohydrazide, respectively in methanol afforded three new benzohydrazones. They are 3-hydroxy-4-methoxy-*N*'-(pyridin-4-ylmethylene)benzohydrazide (**1**), 4-bromo-*N*'-(pyridin-4-ylmethylene)benzohydrazide (**2**), and 4-(dimethylamino)-*N*'-(pyridin-4-ylmethylene)benzohydrazide (**3**). The compounds have been characterized by elemental analysis, ^{1}H and ^{13}C NMR and IR spectroscopy, as well as single crystal X-ray diffraction. The antibacterial activities of the compounds against *E. coli, P. aeruginosa, B. subtilis, and S. aureus* were investigated and gave interesting results.

Keywords: Benzohydrazones; 4-pyridinecarboxaldehyde; synthesis; crystal structure; antibacterial activity.

1. Introduction

Hydrazones are a class of compounds containing –C(O)–NH–N=CH– groups, which can be facile synthesized from the condensation reactions of aldehydes with hydrazides. The compounds have wide application in biological fields like antibacterial,[1] antifungal,[2] antitumor,[3] anti-inflammatory,[4] and cytotoxic.[5] It was reported that the compounds containing halide groups on the aromatic rings usually show improved biological activities especially the antibacterial and antifungal activities.[6] Rai and co-workers reported a series of fluoro, chloro, bromo, and iodo-substituted compounds, and found that they have significant antimicrobial activities.[7] In addition, nicotinohydrazide has remarkable antituberculotic activity. As a continuation of work on the exploration of novel antibacterial drugs, in the present paper, three new benzohydrazones, 3-hydroxy-4-methoxy-*N*'-(pyridin-4-ylmethylene) benzohydrazide (**1**), 4-bromo-*N*'-(pyridin-4-ylmethylene) benzohydrazide (**2**), and 4-(dimethylamino)-*N*'-(pyridin-4-ylmethylene)benzohydrazide (**3**) were prepared and evaluated for their antibacterial activities.



Scheme 1. The benzohydrazones

2. Experimental

2. 1. Materials and Measurements

Commercially available 4-pyridinecarboxaldehyde, 3-hydroxy-4-methoxybenzohydrazide, 4-bromobenzohydrazide and 4-dimethylaminobenzohydrazide were purchased from Sigma-Aldrich and used without further purification. Other solvents and reagents were made in China and used as received. C, H and N elemental analyses were performed with a Perkin-Elmer elemental analyzer. Infrared spectra were recorded on a Nicolet AVATAR 360 spectrometer as KBr pellets in the 4000–400 cm^{-1} region. ^1H NMR spectra were recorded on a Bruker 500 MHz instrument. Single crystal X-ray diffraction was carried out on a Bruker D8 VENTURE PHOTON diffractometer equipped with MoK_α radiation.

2. 2. Synthesis of the Compounds

The three compounds were synthesized according to the same method as described. 4-Pyridinecarboxaldehyde (1.0 mmol, 11 mg) dissolved in methanol (20 mL) was added to the methanolic solution (20 mL) of 3-hydroxy-4-methoxybenzohydrazide (1.0 mmol, 18 mg), 4-bromobenzohydrazide or 4-dimethylaminobenzohydrazide aroylhydrazine, and were stirred at room temperature for 30 min to give clear solution. X-ray quality single crystals were formed by slow evaporation of the solution in air for a few days.

2. 2. 1. 3-Hydroxy-4-methoxy-*N*'-(pyridin-4-ylmethylene)benzohydrazide (1)

Colorless crystals. Yield: 76%. Anal. calcd. for $C_{29}H_{32}N_6O_8$: C, 58.78; H, 5.44; N, 14.18; found C, 58.63; H, 5.55; N, 14.06%. Characteristic IR data (cm^{-1}): 3484 (w), 3409 (w), 3205 (w), 1657 (s), 1604 (s), 1560 (m), 1510 (s), 1445 (w), 1361 (w), 1289 (s), 1221 (m), 1141 (m), 1069 (m), 1018 (w), 947 (w), 853 (m), 752 (w), 532 (m). ^1H NMR (500 MHz, d_6-DMSO): δ: 11.87 (s, 1H, NH), 9.76 (s, 1H, OH), 8.65 (s, 2H, PyH), 8.43 (s, 1H, CH=N), 7.65 (s, 2H, PyH), 7.50 (s, 1H, ArH), 7.47 (d, 1H, ArH), 6.90 (d, 1H, ArH), 3.85 (s, 3H, CH_3). ^{13}C NMR (126 MHz, d_6-DMSO): δ: 162.91, 150.38, 150.19, 147.29, 144.36, 141.64, 123.72, 121.56, 120.85, 114.96, 111.79, 55.73.

2. 2. 2. 4-Bromo-*N*'-(pyridin-4-ylmethylene) benzohydrazide (2)

Colorless crystals. Yield: 82%. 1-173 °C. Anal. calcd. for $C_{15}H_{18}N_4O_2$: C, 62.92; H, 6.34; N, 19.57; found C, 63.11; H, 6.26; N, 19.43%. Characteristic IR data (cm^{-1}): 3188 (w), 1645 (s), 1602 (s), 1517 (s), 1353 (w), 1281 (s), 1196 (m), 1128 (m), 1065 (w), 938 (w), 820 (w), 756 (w), 672 (w), 506 (w). ^1H NMR (500 MHz, d_6-DMSO): δ: 11.93 (s, 1H, NH), 8.65 (s, 2H, PyH), 8.45 (s, 1H, CH=N), 7.72 (s, 2H, PyH), 7.81 (d, 2H, ArH), 7.72 (d, 2H, ArH). ^{13}C NMR (126 MHz, d_6-DMSO): δ: 162.83, 150.17, 146.85, 144.22, 132.33, 131.53, 128.76, 125.83, 120.12.

2. 2. 3. 4-(Dimethylamino)-*N*'-(pyridin-4-ylmethylene)benzohydrazide (3)

Colorless crystals. Yield: 73%. Anal. calcd. for $C_{13}H_{10}BrN_3O$: C, 51.34; H, 3.31; N, 13.82; found C, 51.19; H, 3.22; N, 13.75%. Characteristic IR data (cm^{-1}): 3396 (w), 3243 (w), 1650 (s), 1603 (s), 1590 (w), 1539 (s), 1466 (m), 1436 (w), 1342 (w), 1280 (m), 1141 (m), 1073 (w), 1062 (w), 1011 (w), 957 (w), 915 (m), 851 (w), 780 (w), 745 (w), 658 (w), 618 (w), 526 (w). ^1H NMR (500 MHz, d_6-DMSO): δ: 12.16 (s, 1H, NH), 8.65 (s, 2H, PyH), 8.45 (s, 1H, CH=N), 7.88 (d, 2H, PyH), 7.76 (d, 2H, ArH), 7.67 (d, 2H, ArH), 3.13 (s, 6H, CH_3). ^{13}C NMR (126 MHz, d_6-DMSO): δ: 162.43, 153.73, 150.23, 145.65, 141.33, 132.08, 131.52, 129.76, 120.95, 42.7.

2. 3. Single Crystal X-ray Crystallography

Diffraction intensities for the compounds were collected at 298(2) K using a Bruker D8 VENTURE PHOTON diffractometer with MoK_α radiation (λ = 0.71073 Å). The collected data were reduced using the SAINT program,[8] and multi-scan absorption corrections were performed using the SADABS program.[9] The structures were solved by direct method, and refined against F^2 by full-matrix least-squares method using the SHELXTL.[10] All of the non-hydrogen atoms were refined anisotropically. The water and amino hydrogen atoms were located from difference Fourier maps and refined isotropically, with O–H, H···H and N–H distances restrained to 0.85(1), 1.37(2) and 0.90(1) Å, respectively. All other hydrogen atoms were placed in idealized positions and constrained to ride on their parent atoms. The crystallographic data for the complexes are summarized in Table 1.

3. Results and Discussion

3. 1. Chemistry

The benzohydrazones were prepared by the condensation reaction of equimolar quantities of 4-pyridinecarboxaldehyde with 3-hydroxy-4-methoxybenzohydrazide, 4-bromobenzohydrazide and 4-dimethylaminobenzohydrazide, respectively, in methanol. The compounds have been characterized by elemental analysis, IR, ^1H and ^{13}C NMR spectra. Structures of the compounds were further confirmed by single crystal X-ray diffraction.

The three compounds were crystallized as well-shaped single crystals. They are soluble in MeOH, EtOH, MeCN, $CHCl_3$, DMF and DMSO. The characteristic intense bands in the range 1645–1657 cm^{-1} are generated by the ν(C=O) vibrations, whereas the bands in the range 1602–1604 cm^{-1} are assigned to the ν(C=N) vibrations.[11]

Table 1. Crystallographic data and refinement parameters for the compounds

	1·0.5MeOH·0.5H_2O	**2**·H_2O	**3**
Chemical formula	$C_{29}H_{32}N_6O_8$	$C_{15}H_{18}N_4O_2$	$C_{13}H_{10}BrN_3O$
Mr	592.60	286.33	304.15
Crystal color, habit	Colorless, block	Colorless, block	Colorless, block
Crystal system	Monoclinic	Orthorhombic	Orthorhombic
Space group	$P2_1/n$	$P2_12_12_1$	*Pbca*
Unit cell parameters			
a (Å)	12.2635(15)	7.2634(5)	10.183(2)
b (Å)	12.3785(15)	11.7864(9)	7.949(1)
c (Å)	19.569(2)	17.1102(12)	30.863(2)
β (°)	97.977(1)		
V (Å^3)	2942.0(6)	1464.8(2)	2498.3(5)
Z	4	4	8
D_{calc} (g cm^{-3})	1.338	1.298	1.617
μ (mm^{-1})	0.099	0.089	3.281
F(000)	1248	608	1216
Collected data	17255	10810	13785
Number of unique data	5469	3625	2330
Number of observed data [$I > 2\sigma(I)$]	4119	2839	1759
Number of parameters	406	201	167
Number of restraints	5	4	1
R_1, wR_2 [$I > 2\sigma(I)$]	0.0415, 0.1028	0.0423, 0.0902	0.0355, 0.0758
R_1, wR_2 (all data)	0.0586, 0.1165	0.0611, 0.1015	0.0563, 0.0840
Goodness of fit on F^2	1.013	1.035	1.019

In the spectrum of **1**, there are broad absorptions centered at 3484 and 3409 cm^{-1}, which can be attributed to the hydrogen-bonded phenol and hydroxyl groups. The sharp and weak bands in the range 3188–3243 cm^{-1} are assigned to the *ν*(N–H) vibrations. The C, H, N analyses were in accordance with the chemical formulae proposed by the single crystal X-ray crystallography.

3. 2. Crystal Structure Description

The molecular structures of compounds **1**–**3** are shown in Figures 1–3, respectively. Selected bond lengths are listed in Table 2. The asymmetric unit of compound **1** contains two benzohydrazone molecules, one methanol molecule and one water molecule. The asymmetric unit of compound **2** contains one benzohydrazone molecule and one water molecule. There is only one benzohydrazone molecule in compound **3**. The benzohydrazone molecules of the compounds adopt *E* configuration with respect to the methylidene units. The distances (1.270–1.273 Å) of the methylidene bonds in the compounds are comparable to each other, which confirm them as typical double bonds. The shorter distances of the C–N bonds and the longer distances of the C=O bonds for the –C(O)–NH– units than usual, suggest the presence of conjugation effects in the molecules. All the bond lengths in the three compounds are within normal values.[12] The dihedral angles between the benzene ring and the pyridine ring in the benzohydrazone molecules are 17.3(2) and 22.8(2)° for **1**, 44.8(2)° for **2**, and 19.1(3)° for **3**.

In the crystal structure of compound **1**, the benzohydrazone molecules are linked by water molecules through O–H···O hydrogen bonds to form a dimer. The dimers are further linked through O–H···N hydrogen bonds to form chains. The methanol molecules are linked to the benzohydrazone molecules through O–H···N and O–H···O hydrogen bonds (Table 3, Figure 4). In the crystal structure of compound **2**, the benzohydrazone molecules are linked by water molecules through O–H···O, O–H···N, N–H···O and C–H···O hydrogen bonds to form a three-dimensional network (Figure 5). In the crystal structure of compound **3**, the benzohydrazone molecules are linked through N–H···O hydrogen bonds to form chains (Figure 6).

Table 2. Selected bond distances (Å) for the compounds

	1 · 0.5MeOH·0.5H_2O		
N1–C6	1.273(2)	N1–N2	1.3683(17)
N2–C7	1.358(2)	N4–C20	1.270(2)
N4–N5	1.3727(17)	N5–C21	1.356(2)
O1–C7	1.2236(19)	O4–C21	1.2242(19)
	2 · H_2O		
N1–C6	1.270(3)	N1–N2	1.379(2)
N2–C7	1.366(3)	O1–C7	1.226(3)
	3		
N1–C7	1.359(3)	N1–N2	1.376(3)
N2–C8	1.272(3)	O1–C7	1.229(3)

Table 3. Hydrogen bond distances (Å) and bond angles (°) for the compounds

D–H···*A*	*d*(*D*–H), Å	*d*(H···*A*), Å	*d*(*D*···*A*), Å	Angle (*D*–H···*A*),°
1·0.5MeOH·0.5H_2O				
O2–H2B···N6^{i}	0.82	1.96	2.727(2)	156(3)
O5–H5B···N3^{ii}	0.82	1.91	2.687(2)	157(3)
O8–H8···O4^{iii}	0.82	2.27	2.985(2)	146(3)
O8–H8···N4^{iii}	0.82	2.38	3.079(2)	144(3)
N2–H2···O7	0.90(1)	1.95(1)	2.846(2)	171(2)
N5–H5···O8	0.90(1)	1.96(1)	2.839(2)	167(2)
O7–H7A···O1^{iv}	0.85(1)	2.01(1)	2.823(2)	158(2)
O7–H7A···N1^{iv}	0.85(1)	2.66(2)	3.282(2)	131(2)
O7–H7B···O5	0.85(1)	1.98(1)	2.826(2)	170(2)
C28–H28A···O3^{v}	0.96	2.58(2)	3.371(3)	140(3)
2·H_2O				
N2–H2···O2^{vi}	0.90(1)	1.98(2)	2.844(2)	159(3)
O2–H2A···N3^{vii}	0.85(1)	2.02(1)	2.848(3)	164(3)
O2–H2B···O1	0.85(1)	2.05(2)	2.854(2)	159(3)
O2–H2B···N1	0.85(1)	2.53(2)	3.146(3)	131(2)
C6–H6···O2^{vi}	0.93	2.59(2)	3.226(3)	126(3)
C9–H9···O2^{vi}	0.93	2.52(2)	3.427(3)	166(3)
3				
N1–H1···O1^{viii}	0.90(1)	1.98(1)	2.877(3)	174(4)

Symmetry codes: i) 2 – *x*, – *y*, 1 – *z*; ii) – *x*, – *y*, – *z*; iii) ½ – *x*, ½ + *y*, ½ – *z*; iv) 3/2 – *x*, ½ + *y*, ½ – *z*; (v) –3/2 + *x*, ½ – *y*, –½ + *z*; vi) 1 – *x*, ½ + *y*, ½ – *z*; vii) –½ + *x*, ½ – *y*, 1 – *z*; viii) ½ – *x*, ½ + *y*, *z*.

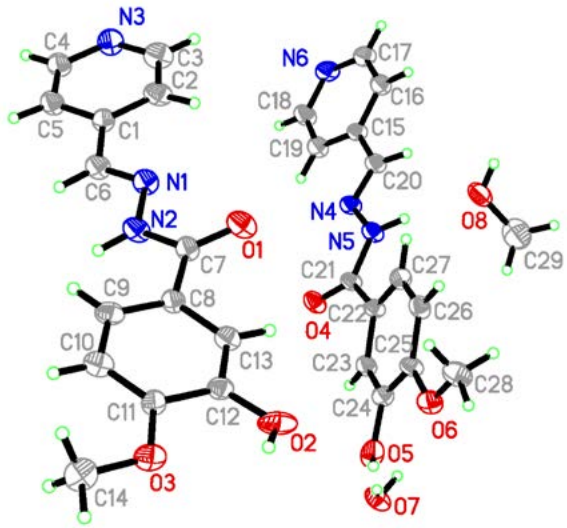


Figure 1. ORTEP plot of the crystal structure of **1**. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level.

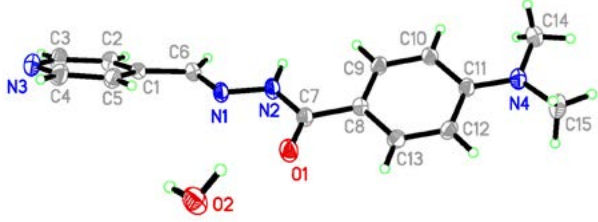


Figure 2. ORTEP plot of the crystal structure of **2**. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level.

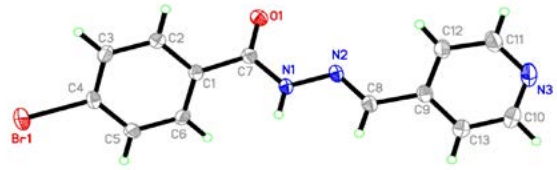


Figure 3. ORTEP plot of the crystal structure of **3**. Displacement ellipsoids of non-hydrogen atoms are drawn at the 30% probability level.

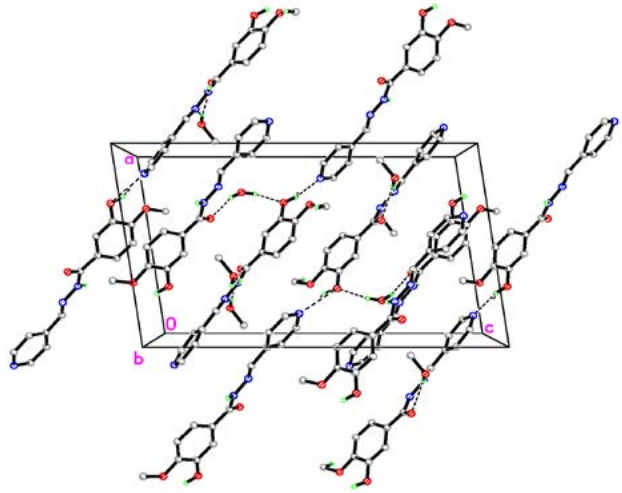


Figure 4. Molecular packing diagram of **1**. Viewed along the *b* axis. Hydrogen atoms not related to hydrogen bonding are omitted. Hydrogen bonds are shown as dashed lines.

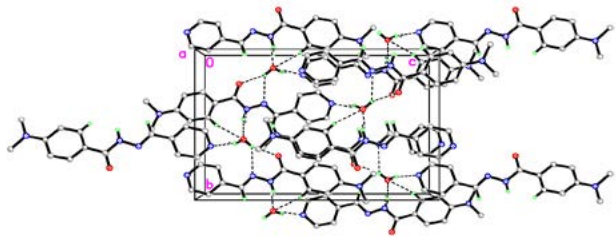


Figure 5. Molecular packing diagram of **2**. Viewed along the *a* axis. Hydrogen atoms not related to hydrogen bonding are omitted. Hydrogen bonds are shown as dashed lines.

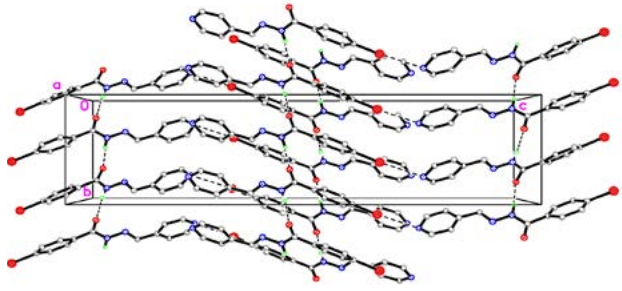


Figure 6. Molecular packing diagram of **3**. Viewed along the *a* axis. Hydrogen atoms not related to hydrogen bonding are omitted. Hydrogen bonds are shown as dashed lines.

3. 3. Antibacterial Activity

The antibacterial assay was performed according to the literature method.[13] Penicillin G was used as a standard drug. DMSO was used as solvent and the solutions were further diluted by distilled water. The DMSO at the tested concentration has no activity on the bacteria. The zone of inhibition for the 5000 μg mL^{-1} test solutions on the four bacteria *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi* and *Staphylococcus aureus* is given in Table 4. The MIC values are given in Table 5. The results indicated that the compounds have from weak to strong activities against the four bacteria. Compound **1** has medium activity on *E. coli* and *P. aeruginosa*, and weak activity on *B. subtilis* and *S. aureus*. Compound **2** has strong activity on *E. coli* and *P. aeruginosa*, and medium activity on *B. subtilis* and *S. aureus*. Compound **3** has medium activity on *E. coli* and *P. aeruginosa*, strong activity on *B. subtilis*, and weak activity on *S. aureus*. Among the compounds, compound **2** has the most activity on *E. coli* and *P. aeruginosa* with MIC values of 3.13 μg mL^{-1}, which is even comparable to Penicillin G. The four compounds have better activities against *E. coli*, *B. subtilis* and *S. aureus* than the pyrroles bearing thiazole moiety.[14] Compounds **2** and **3** have stronger activity against *E. coli*, weak activity against *B. subtilis*, and similar activity against *S. aureus* when compared with the fluoro-substituted aroylhydrazones.[15]

After careful comparison we noticed that the Br substituent group in compound **2** might contribute to the activity on *E. coli* and *P. aeruginosa*, and the NMe_2 group in compound **3** may contribute to the activity on *B. subtilis*.

Table 4 Antibacterial screening results

Compound	Zone of inhibition (mm)			
	E. coli	*P. aeruginosa*	*B. subtilis*	*S. aureus*
1	17 ± 1.9	14 ± 1.7	5.3 ± 1.4	7.2 ± 1.6
2	25 ± 2.8	23 ± 2.5	18 ± 2.6	15 ± 1.7
3	21 ± 2.3	18 ± 2.0	22 ± 2.5	11 ± 1.4
Penicillin G	30 ± 2.8	26 ± 3.1	30 ± 3.2	24 ± 2.9

Table 5 Antibacterial activities as MIC values (μg mL^{-1})

Compound	*E. coli*	*P. aeruginosa*	*B. subtilis*	*S. aureus*
1	12.5	12.5	25	25
2	3.13	3.13	6.25	6.25
3	6.25	6.25	3.13	12.5
Penicillin G	3.13	6.25	1.56	6.25

4. Conclusions

In summary, three new benzohydrazone compounds were prepared and structurally characterized. The antibacterial activities against the bacteria *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. aureus* were evaluated. Among the compounds, 4-bromo-*N'*-(pyridin-4-ylmethylene)benzohydrazide has strong activity on *E. coli* and *P. aeruginosa*, and 4-(dimethylamino)-*N'*-(pyridin-4-ylmethylene)benzohydrazide has strong activity on *B. subtilis*, with MIC values of 3.13 μg mL^{-1}. The compounds could be useful as templates for future development through modification to explore more effective antibacterial agents.

Supplementary Material

CCDC–2246870 (**1**), 2246872 (**2**), and 2246873 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdc.cam.ac.uk/const/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk.

5. References

1. (a) S. Verma, S. Lal, R. Narang, K. Sudhakar, *ChemMedChem* **2023**, **DOI:**10.1002/cmdc.202200571
   (b) M. A. Shah, A. Uddin, M. R. Shah, I. Ali, R. Ullah, P A. Hannan, H. Hussain, *Molecules* **2022**, *27*, 6770;
   (c) M. Nabizadeh, M. R. Naimi-Jamal, M. Rohani, P. Azerang, A. Tahghighi, *Lett. Appl. Microbiol.* **2022**, *75*, 667–679 **DOI:**10.1111/lam.13692 **DOI:**10.3390/molecules27196770
   (d) G.-X. He, L.-W. Xue, *Acta Chim. Slov.* **2021**, *68*, 567–574 **DOI:**10.17344/acsi.2020.6333
   (e) K. Pyta, A. Janas, M. Szukowska, P. Pecyna, M. Jaworska, M. Gajecka, F. Bartl, P. Przybylski, *Eur. J. Med. Chem.* **2019**, *167*, 96–104 **DOI:**10.1016/j.ejmech.2019.02.009
   (f) I. Shabeeb, L. Al-Essa, M. Shtaiwi, E. Al-Shalabi, E. Younes, R. Okasha, M. Abu Sini, *Lett. Org. Chem.* **2019**, *16*, 430–436. **DOI:**10.2174/1570178616666181227122326
2. (a) M. Aydin, A. Ozturk, T. Duran, U. O. Ozmen, E. Sumlu, E. B. Ayan, E. N. Korucu, *J. Mycologie Medicale* **2023**, *33*, 101327 **DOI:**10.1016/j.mycmed.2022.101327
   (b) I. R. Silva, T. Kronenberger, E. C. L. Gomes, I. C. Cesar, R. B. Oliveira, V. G. Maltarollo, *Eur. J. Pharm. Sci.* **2021**, *156*, 105575 **DOI:**10.1016/j.ejps.2020.105575
   (c) I. A. Khodja, H. Boulebd, C. Bensouici, A. Belfaitah, *J. Mol. Struct.* **2020**, *1218*, 128527 **DOI:**10.1016/j.molstruc.2020.128527
   (d) A. E. Dascalu, A. Ghinet, E. Lipka, C. Furman, B. Rigo, A. Fayeulle, M. Billamboz, *Bioorg. Med. Chem. Lett.* **2020**, *30*, 127220 **DOI:**10.1016/j.bmcl.2020.127220
   (e) N. R. Appna, R. K. Nagiri, R. B. Korupolu, S. Kanugala, G. K. Chityal, G. Thipparapu, N. Banda, *Med. Chem. Res.* **2019**, *28*, 1509–1528 **DOI:**10.1007/s00044-019-02390-w
   (f) A. Erguc, M. D. Altintop, O. Atli, B. Sever, G. Iscan, G. Gormus, A. Ozdemir, *Lett. Drug Des. Discov.* **2018**, *15*, 193–202; **DOI:**10.2174/1570180814666171003145227
   (g) N. J. P. Subhashini, P. Janaki, B. Bhadraiah, *Russ. J. Gen.*

Chem. **2017**, *87*, 2021–2026.
DOI:10.1134/S1070363217090183
3. (a) M. S. A. Abdelrahman, F. M. Omar, A. A. Saleh, M. A. Elghamry, *J. Mol. Struct.* **2022**, *1251*, 131947
DOI:10.1016/j.molstruc.2021.131947
(b) B. Ay, O. Sahin, B. S. Demir, Y. Saygideger, J. M. Lopez-de-Luzuriaga, G. Mahmoudi, D. A. Safin, *New J. Chem.* **2020**, *44*, 9064–9072 **DOI:**10.1039/D0NJ00921K
(c) E. M. Gungor, M. D. Altintop, B. Sever, G. A. Ciftci, *Lett. Drug Des. Discov.* **2020**, *17*, 1380–1392
DOI:10.2174/1570180817999200618163507
(d) H. M. A. Abumelha, *J. Heterocycl. Chem.* **2018**, *55*, 1738–1745 **DOI:**10.1002/jhet.3211
(e) H. F. He, X. Y. Wang, L. Q. Shi, W. Y. Yin, Z. W. Yang, H. W. He, Y. Liang, *Bioorg. Med. Chem. Lett.* **2016**, *26*, 3263–3270.
DOI:10.1016/j.bmcl.2016.05.059
4. (a) M. A. M. B. Medeiros, M. G. E. Silva, J. D. Barbosa, E. M. de Lavor, T. F. Ribeiro, C. A. F. Macedo, L. A. M. D. Duarte-Filho, T. A. Feitosa, J. D. Silva, H. H. Fokoue, C. R. M. Araujo, A. D. Gonsalves, L. A. D. Ribeiro, J. R. G. D. Almeida, *Plos One* **2021**, *16*, e0258094 **DOI:**10.1371/journal.pone.0258094
(b) M. X. Song, B. Liu, S. W. Yu, S. H. He, Y. Q. Liang, S. F. Li, Q. Y. Chen, X. Q. Deng, *Lett. Drug. Des. Discov.* **2020**, *17*, 502–511 **DOI:**10.2174/1570180816666190731113441
(c) U. Debnath, S. Mukherjee, N. Joardar, S. P. S. Babu, K. Jana, A. K. Misra, *Eur. J. Pharm. Sci.* **2019**, *134*, 102–115
DOI:10.1016/j.ejps.2019.04.016
(d) U. Kendur, G. H. Chimmalagi, S. M. Patil, K. B. Gudasi, C. S. Frampton, C. V. Mangannavar, I. S. Muchchandi, *J. Mol. Struct.* **2018**, *1153*, 299–310
DOI:10.1016/j.molstruc.2017.10.022
(e) V. Gorantla, R. Gundla, S. S. Jadav, S. R. Anugu, J. Chimakurthy, S. K. Nidasanametla, R. Korupolu, *New J. Chem.* **2017**, *41*, 13516–13532 **DOI:**10.1039/C7NJ03332J
(f) M. A. Abdelgawad, M. B. Labib, M. Abdel-Latif, *Bioorg. Chem.* **2017**, *74*, 212–220. **DOI:**10.1016/j.bioorg.2017.08.014
5. (a) E. Aydin, A. M. Senturk, H. B. Kucuk, M. Guzel, *Molecules* **2022**, *27*, 7309
(b) M. A. Shah, A. Uddin, M. R. Shah, I. Ali, R. Ullah, P. A. Hannan, H. Hussain, *Molecules* **2022**, *27*, 6770
DOI:10.3390/molecules27196770
(c) F. Beygi, A. Mostoufi, A. Mojaddami, *Chem. Biodivers.* **2022**, *19*, e202100754 **DOI:**10.1002/cbdv.202100754
(d) Z. Ozdemir, N. Basak-Turkmen, I. Ayhan, O. Ciftci, M. Uysal, *Pharm. Chem. J.* **2019**, *52*, 923–929
DOI:10.1007/s11094-019-01927-y
(e) J. C. Coa, W. Castrillon, W. Cardona, M. Carda, V. Ospina, J. A. Munoz, I. D. Velez, S. M. Robledo, *Eur. J. Med. Chem.* **2015**, *101*, 746–753. **DOI:**10.1016/j.ejmech.2015.07.018
6. (a) L. C. Felton, J. H. Brewer, *Science* **1947**, *105*, 409–410
DOI:10.1126/science.105.2729.409
(b) M. Gopalakrishnan, J. Thanusu, V. Kanagarajan, R. Govindaraju, *J. Enzym. Inhib. Med. Chem.* **2009**, *24*, 52–58
DOI:10.1080/14756360801906632
(c) L. Shi, H.-M. Ge, S.-H. Tan, H.-Q. Li, Y.-C. Song, H.-L. Zhu, R.-X. Tan, *Eur. J. Med. Chem.* **2007**, *42*, 558–564
DOI:10.1016/j.ejmech.2006.11.010
(d) M. Zhang, D.-M. Xian, H.-H. Li, J.-C. Zhang, Z.-L. You, *Aust. J. Chem.* **2012**, *65*, 343–350. **DOI:**10.1071/CH11424
7. (a) N. P. Rai, V. K. Narayanaswamy, T. Govender, B. K. Manuprasad, S. Shashikanth, P. N. Arunachalam, *Eur. J. Med. Chem.* **2010**, *45*, 2677–2682 **DOI:**10.1016/j.ejmech.2010.02.021
(b) N. P. Rai, V. K. Narayanaswamy, S. Shashikanth, P. N. Arunachalam, *Eur. J. Med. Chem.* **2009**, *44*, 4522–4527.
8. Bruker, SMART and SAINT, Bruker AXS Inc., Madison, Wisconsin, USA, **2012**.
9. G. M. Sheldrick, SADABS Program for Empirical Absorption Correction of Area Detector, University of Göttingen, Germany, **1996**.
10. G. M. Sheldrick, *Acta Crystallogr.* **2008**, *A64*, 112–122.
DOI:10.1107/S0108767307043930
11. W. J. Geary, *Coord. Chem. Rev.* **1971**, *7*, 81–122.
DOI:10.1016/S0010-8545(00)80009-0
12. (a) M. Kuriakose, M. R. P. Kurup, E. Suresh, *Spectrochim. Acta A* **2007**, *66*, 353–358 **DOI:**10.1016/j.saa.2006.03.003
(b) L.-W. Xue, S.-T. Li, Y.-J. Han, X.-Q. Luo, *Acta Chim. Slov.* **2022**, *69*, 385–392 **DOI:**10.17344/acsi.2021.7252
(c) G.-X. He, L.-W. Xue, *Acta Chim. Slov.* **2021**, *68*, 567–574.
DOI:10.17344/acsi.2020.6333
13. (a) Y. M. Chumakov, B. Y. Antosyak, V. I. Tsapkov, N. M. Samus, *J. Struct. Chem.* **2001**, *42*, 335–339
DOI:10.1023/A:1010587923496
(b) Y.-J. Han, X.-Y. Guo, L.-W. Xue, *Acta Chim. Slov.* **2022**, *69*, 928–936 **DOI:**10.17344/acsi.2022.7817
(c) H.-Y. Zhu, *Acta Chim. Slov.* **2021**, *68*, 65–71.
DOI:10.17344/acsi2020.6138
14. M. A. Salem, S. Y. Abbas, M. A. M. Sh. El-Sharief, M. H. Helal, M. A. Gouda, M. A. Assiri, T. E. Ali, *Acta Chim. Slov.* **2021**, *68*, 990–996. **DOI:**10.17344/acsi.2021.6980
15. F.-M. Wang, L.-J. Li, G.-W. Zang, T.-T. Deng, Z.-L. You, *Acta Chim. Slov.* **2021**, *68*, 541–547. **DOI:**10.17344/acsi.2020.6051

Povzetek

Reakcija 4-piridinkarboksaldehida s 3-hidroksi-4-metoksibenzohidrazidom, 4-bromobenzohidrazidom in 4-dimetilaminobenzohidrazidom v metanolu je dala tri nove benzohidrazone. To so 3-hidroksi-4-metoksi-*N*'-(piridin-4-ilmetilen) benzohidrazid (**1**), 4-bromo-*N*'-(piridin-4-ilmetilen)benzohidrazid (**2**) in 4-(dimetilamino)-*N*'-(piridin-4-ilmetilen) benzohidrazid (**3**). Spojine smo okarakterizirali z elementno analizo, ^{1}H in ^{13}C NMR in IR spektroskopijo ter monokristalno rentgensko difrakcijo. Preučevali smo antibakterijske aktivnosti spojin proti *E. coli*, *P. aeruginosa*, *B. subtilis* in *S. aureus* ter dobili zanimive rezultate.