Molbank **2014**, M826; doi:10.3390/M826

OPEN ACCESS

molbank

ISSN 1422-8599

www.mdpi.com/journal/molbank

Short Note

4-[5-(2-Methoxyphenyl)-1,3,4-oxadiazol-2-yl]benzohydrazide

Muhammad Taha [1,2,*], Nor Hadiani Ismail [1,2], Syahrul Imran [1,2] and Khalid M. Khan [3]

[1] Atta-ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA, Puncak Alam Campus, Puncak Alam 42300, Malaysia

[2] Faculty of Applied Science, Universiti Teknologi MARA, Shah Alam 40450, Selangor D. E. Malaysia

[3] H.E.J. Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi 75270, Pakistan

* Author to whom correspondence should be addressed; E-Mail: taha_hej@yahoo.com or muhamm9000@puncakalam.uitm.edu.my; Tel.: +60-332-584-761; Fax: +60-332-584-770.

Received: 9 April 2014 / Accepted: 23 May 2014 / Published: 30 May 2014

Abstract: 4-(5-(2-Methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzohydrazide (**5**) was synthesized by three steps. The synthesis started with 2-methoxybenzohydrazide to form hydrazone (**3**) which was then cyclized to oxadiazole (**4**) and finally, treatment of oxadiazole (**4**) with hydrazine hydrate afforded the final product (**5**).

Keywords: 2-methoxybenzohydrazide; oxadiazole; hydrazone

Introduction

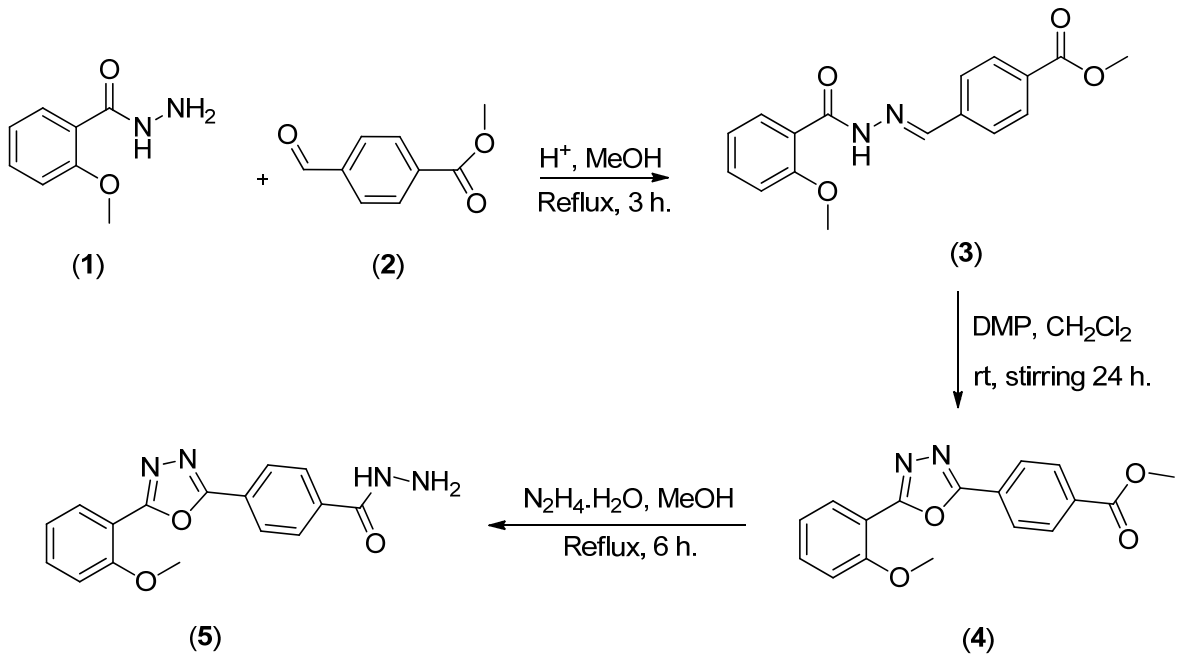
Benzohydrazides have been reported to possess various biological activities such as antileishmanial [1], antioxidant [2] or antibacterial effects [3]. Benzohydrazides are easily converted into hydrazones by treating with aldehyde or ketone [4]. Benzohydrazones are applicable in mass spectrometry as alternate UV-LDI matrices for the analysis of peptides with significantly low background signals [5]. Recent studies on benzohydrazones also showed that they are potent antileishmanial [6] antioxidant [7,8] antidiabetic [9,10] antibacterial [3] and antifungal [11] agents. Benzohydrazones can be converted into oxadiazole by using cerium ammonium nitrate (CAN) [12], bis(trifluoroacetoxy)iodobenzene [13] or Dess–Martin reagent (DMP) [14]. Literature search showed that oxadiazole carrying a benzoyl hydrazine moiety has not been reported. Therefore, 4-(5-(2-methoxyphenyl)-1,3,4-oxadiazol-2-

yl)benzohydrazide (**5**), a new oxadiazole containing a benzoyl hydrazine unit, was obtained as shown in Scheme 1. The product was prepared with satisfactory yield and fully characterized by spectroscopy.

Results and Discussion

We have synthesized (*E*)-methyl 4-((2-(2-methoxybenzoyl)hydrazinylidene)methyl)benzoate (**3**) by condensing 2-methoxybenzohydrazide (**1**) with methyl 4-formylbenzoate (**2**) [6]. Compound **3** was then cyclized to form methyl 4-(5-(2-methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzoate (**4**) by using DMP [13]. Finally oxadiazole **4** was refluxed with hydrazine hydrate for 6 hours to give 4-(5-(2-methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzohydrazide (**5**) in high yield (Scheme 1).

Scheme 1. Synthesis of 4-(5-(2-methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzohydrazide.



(**1**) (**2**) (**3**) (**4**) (**5**)

Experimental

4-(5-(2-Methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzohydrazide

4-(5-(2-Methoxyphenyl)-1,3,4-oxadiazol-2-yl)benzohydrazide (**5**) was synthesized by mixing compound **4** (0.620 g, 2 mmol) with 2 mL hydrazine hydrate and 10 mL methanol. The mixture was refluxed for 6 h. Excess hydrazine hydrate and solvent were evaporated to afford pure product **5** (94%, yield 0.58 g). M.p. above 250 °C; ^{1}H-NMR (500 MHz, DMSO-d_6): 10.01 (s, 1H, NH), δ 8.14 (d, 2H, $J_{2',3'}$ = $J_{6',5'}$ = 8.5 Hz, H-2'/H-6'), 8.02 (d, 2H, $J_{3',2'}$ = $J_{5',6'}$ = 8.5 Hz, H-3'/H-5'), 7.97 (dd, 1H, $J_{3,4}$ = 6.0, $J_{3,5}$ = 2.0 Hz, H-3), 7.64 (ddd, 1H, $J_{4,3}$ = 7.5, $J_{4,5}$ = 6.5, $J_{4,6}$ = 2.0 Hz, H-4), 7.29 (d, 1H, $J_{6,5}$ = 8.5, H-6), 7.16 (t, 1H, $J_{5(6,4)}$ = 8.5, H-5), 4.58 (s, 2H, NH_2), 3.93 (s, 3H, O-CH_3); ^{13}C-NMR (125 MHz, DMSO-d_6): δ 165.41, 163.79, 163.59, 158.02, 136.50, 134.22, 130.70, 130.70, 128.48, 128.48, 127.05, 125.98, 121.28, 113.22, 112.45, 56.55; Anal. Calcd for $C_{16}H_{14}N_4O_3$, C, 61.93; H, 4.55; N, 18.06; Found C, 61.95; H, 4.56; N, 18.04; EI MS *m/z* 310.

Acknowledgments

Authors would like to acknowledge Research Management Institute of UiTM for the financial support under CIFI Scheme 600-RMI/DANA 5/3/CIFI (141/2013).

Author Contributions

Muhammad Taha designed the experiment and synthesized the compound. Syahrul Imran analyzed the compound using NMR. Nor Hadiani Ismail and Khalid Muhammad Khan write the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

References and Notes

1. Alptuzun, V.; Cakiroglu, G.; Limoncu, M.E.; Erac, B.; Hosgor-Limoncu, M.; Erciyas, E. Synthesis and antileishmanial activity of novel pyridinium-hydrazone derivatives. *J. Enzyme Inhib. Med. Chem.* **2013**, *28*, 960–967.
2. Li, T.R.; Yang, Z.Y.; Wang, B.D. Synthesis, characterization and antioxidant activity of naringenin Schiff base and its Cu(II), Ni(II), Zn(II) complexes. *Chem. Pharm. Bull.* **2007**, *55*, 26–28.
3. Khattab, S.N. Synthesis and Biological Activity of Novel Amino Acid-(N'-Benzoyl) Hydrazide and Amino Acid-(N'-Nicotinoyl) Hydrazide Derivatives. *Molecules* **2005**, *10*, 1218–1228.
4. Khan, K.M.; Jamil, W.; Ambreen, N.; Taha, M.; Perveen, S.; Morales, G.A. An Expeditious Synthetic Approach towards the Synthesis of Bis-Schiff Bases (Aldazines) Using Ultrasound. *Ultrason. Sonochem.* **2014**, *21*, 1200–1205.
5. Musharraf, S.G.; Bibi, A.; Shahid, N.; Najam-ul-Haq, M.; Khan, M.; Taha, M.; Mughal, U.R.; Khan, K.M. Acylhydrazide and Isatin Schiff Bases as Alternate UV-Laser Desorption Ionization (LDI) Matrices for Low Molecular Weight (LMW) Peptides Analysis. *Am. J. Anal. Chem.* **2012**, *3*, 779–789.
6. Taha, M.; Baharudin, M.S.; Ismail, N.H.; Khan, K.M.; Jaafar, F.M.; Samreen; Siddiqui, S.; Choudhary, M.I. Synthesis of 2-methoxybenzoylhydrazone and evaluation of their antileishmanial activity. *Bioorg. Med. Chem. Lett.* **2013**, *23*, 3463–3466.
7. Taha, M.; Ismail, N.H.; Jamil, W.; Yousuf, S.; Jaafar, F.M.; Ali, M.I.; Kashif, S.M.; Hussain, E. Synthesis, Evaluation of Antioxidant Activity and Crystal Structure of 2,4-Dimethylbenzoylhydrazones. *Molecules* **2013**, *18*, 10912–10929.
8. Khan, K.M.; Shah, Z.; Ahmad, V.U.; Khan, M.; Taha, M.; Ali, S.; Perveen, S.; Choudhary, M.I.; Voelter, W. 2,4,6-Trichlorophenylhydrazine Schiff Bases as DPPH Radical and Super Oxide Anion Scavengers. *Med. Chem.* **2012**, *8*, 452–461.
9. Taha, M.; Naz, H.; Rasheed, S.; Ismail, N.H.; Rahman, A.A.; Yousuf, S.; Choudhary, M.I. Synthesis of 4-Methoxybenzoylhydrazones and Evaluation of Their Antiglycation Activity. *Molecules* **2014**, *19*, 1286–1301.

10. Khan, K.M.; Taha, M.; Rahim, F.; Fakhri, M.I.; Jamil, W.; Khan, M.; Rasheed, S.; Karim, A.; Perveen, S.; Choudhary, M.I. Acylhydrazide Schiff Bases: Synthesis and Antiglycation Activity. *J. Chem. Soc*. *Pak.* **2013**, *35*, 929–937.
11. Sundriyal, S.; Sharma, R.K.; Jain, R. Current advances in antifungal targets and drug development. *Curr. Med. Chem.* **2006**, *13*, 1321–1335.
12. Dabiri, M.; Salehi, P.; Baghbanzadeha, M.; Bahramnejada, M. A facile procedure for the one-pot synthesis of unsymmetrical 2,5-disubstituted 1,3,4-oxadiazoles. *Tetrahedron Lett*. **2006**, *47*, 6983–6986.
13. Shang, Z.; Reiner, J.; Chang, J.; Zhao, K. Oxidative cyclization of aldazines with bis(trifluoroacetoxy)iodobenzene. *Tetrahedron Lett.* **2005**, *46*, 2701–2704.
14. Cristian, D.; Paraschivescu, C.C.; Dumitru, I.; Matache, M.; Baciu, I.; Rută L.L. Convenient preparation of unsymmetrical 2,5-disubstituted 1,3,4-oxadiazoles promoted by Dess–Martin reagent. *Tetrahedron Lett.* **2009**, *50*, 1886–1888.