molbank

MDPI

Short Note

N-[4-(1-Methyl-1*H*-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine

Dhafer S. Zinad [1,*], Dunya L. AL-Duhaidahaw [2], Ahmed Al-Amiery [3,*] and Abdul Amir H. Kadhum [4]

1 Applied Science Department, University of Technology, Baghdad 10001, Iraq
2 Pharmaceutical Chemistry Department, College of Pharmacy, University of Kufa, AL-Najaf 31001, Iraq; dunyal.mohammed@uokufa.edu.iq
3 Energy and Renewable Energies Technology Center, University of Technology, Baghdad 10001, Iraq
4 Department of Chemical & Process Engineering, Faculty of Engineering & Built Environment, Universiti Kebangsaan Malaysia, Bangi, Selangor 43600, Malaysia; amir8@ukm.edu.my
* Correspondence: dhafer.utech.78@gmail.com (D.S.Z.); dr.ahmed1975@gmail.com (A.A.-A.); Tel.: +964-770-171-9279 (D.S.Z.); +96-477-0067-1115 (A.A.-A.)

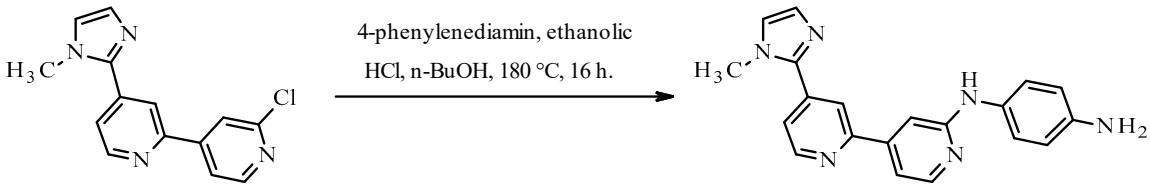
Received: 29 October 2018; Accepted: 12 November 2018; Published: 16 November 2018

Abstract: *N*-[4-(1-Methyl-1*H*-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine was synthesized with a good yield by the reaction of 2′-chloro-4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridine with 4-phenylenediamine. The functionalization of the pyridine was accomplished by a nucleophilic aromatic substitution (SNAr) reaction that afforded the target compound. The synthesized compound was characterized by chemical analysis, which includes nuclear magnetic resonance (NMR) (^{1}H-NMR and ^{13}C-NMR), Thin Layer Chromatography-Mass Spectrometry (TLC-MS), high-performance liquid chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), and elemental analysis.

Keywords: 4-phenylenediamine; fluorescent; butanol; bipyridine; imidazole

1. Introduction

Imidazoles are an important and essential class of heterocyclic compounds and include many substances of both biological and chemical interest. In literature, research and applications of imidazole-based compounds have been rapidly developed and they involve a variety of broad potential applications as medicinal drugs, agrochemicals, human-made materials, artificial acceptors, supramolecular ligands, biomimetic catalysts, and so on [1–3]. Medicinal properties of imidazole-containing compounds comprise a broad spectrum of pharmacological activities, including anticancer, antimicrobial, antibacterial, antifungal, antioxidant, and anti-Parkinson activities [4–6]. Insertion of heterocyclic molecules, such as pyrazole and pyridine moieties in an imidazole, remains of great interest due to the broad applications of such heterocycles in the pharmaceutical and agrochemical industry [7]. In continuation of previous studies [8–19], a new imidazole–bipyridine derivative was synthesized for the first time, accomplished by a nucleophilic aromatic substitution (SNAr) reaction (Scheme 1).



2'-chloro-4-(1-methyl-1 *H*-imidazol-2-yl)-2,4'-bipyridine

N-[4-(1-methyl-1 *H*-imidazol-2-yl)-2,4'-bipyridin-2'-yl]benzene-1,4-diamine

Scheme 1. Synthesis of *N*-[4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine.

2. Results and Discussion

A one-pot, efficient and straightforward synthesis of the new imidazole-bipyridine derivative named *N*-[4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine was achieved in this paper with a good yield, based on a nucleophilic aromatic substitution reaction of 2′-chloro-4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridine with 4-phenylenediamine. The desired compound was characterized by chemical analysis methods, which include nuclear magnetic resonance (NMR), Liquid chromatography-mass spectrometry (LC-MS), high-performance liquid chromatography (HPLC), Gas Chromatography-Mass Spectrometry (GC-MS), and elemental analysis. The purity of the target compound was also examined by HPLC technique.

3. Materials and Methods

All chemicals were purchased from commercial sources unless otherwise specified and were used without further purification. Thin-layer chromatography (TLC) reaction controls were performed for all reactions using fluorescent silica gel 60 F254 plates (Merck, Darmstadt, Germany) and visualized under natural light and UV illumination at 254 and 366 nm. The purity of the target compound was confirmed to be >95%, as determined by reversed-phase high- performance liquid chromatography (HPLC).

Nuclear magnetic resonance (NMR) data were obtained on a Bruker ARX NMR spectrometer (Bruker BioSpin AG, Faellanden, Switzerland) at 250 MHz, on a Bruker AVANCE III HD NMR spectrometer (Bruker BioSpin AG) at 300 MHz at ambient temperature. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS). NMR Spectra are calibrated against the (residual proton) peak of the deuterated solvent used. A mass spectrum was recorded on an Advion expression S electrospray ionization mass spectrometer (ESI-MS) (Shimadzu Corporation, Kyoto, Japan) with TLC interface.

Synthesis of N-[4-(1-Methyl-1H-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine

A mixture of 2′-chloro-4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridine (0.075 g, 0.277 mmol), 4-phenylenediamin (0.045 g, 0.415 mmol) and a 1.25 M solution of HCl in EtOH (226 µL, 0.277 mmol) in *n*-butanol (5 mL) as solvent was stirred and heated in a pressure vial at 180 °C for 16 h. The solvent was evaporated at reduced pressure and the residue was purified by flash column chromatography (SiO_2, CH_2Cl_2/EtOH 95:05) to yield the title compound (0.055 g, 58%) as a yellow oil. ^{1}H-NMR (300.13 MHz, DMSO-d_6) δ = 3.92 (s, 3H), 4.63 (br s, 2H), 6.40 (s, 1H), 6.59 (s, 1H), 7.12 (s, 1H), 7.24–7.32 (m, 2H), 7.43 (d, *J* = 11.8 Hz, 2H), 7.77 (d, *J* = 3.6 Hz, 1H), 8.13–8.24 (m, 2H), 8.62 (s, 1H), 8.77 ppm (d, *J* = 5.1 Hz, 1H). ^{13}C-NMR (75.47 MHz, DMSO-d_6) δ = 35.3, 106.5, 110.6, 114.8, 116.1, 119.1, 122.1, 122.2, 125.9, 129.0, 131.1, 139.1, 139.3, 144.1, 146.7, 148.8, 150.6, 155.2, 158.1, 158.4 ppm; ESI-MS *m/z:* $[M + H]^+$ calcd. for $C_{20}H_{19}N_6$: 343.2, found: 343.3; HPLC retention time (t_R) = 1.265 min (96.9%). Anal. calcd. for $C_{20}H_{18}N_6$: C, 70.16; H, 5.30; N, 24.54. Found: C, 70.46; H, 5.56; N, 24.60.

4. Conclusions

We could demonstrate the synthesis of *N*-[4-(1-methyl-1*H*-imidazol-2-yl)-2,4′-bipyridin-2′-yl]benzene-1,4-diamine through a nucleophilic aromatic substitution (SNAr) reaction and we characterized the title compound by physicochemical and spectral methods.

Supplementary Materials: The following are available online, Figure S1: HPLC, Figure S2: MS, Figure S3: ^{13}C-NMR, Figure S4: DEPT, Figure S5: ^{1}H-NMR.

Author Contributions: D.Z. methodology, D.A.; characterization; A.H. and A.A. writing of the manuscript.

Funding: This research was funded by University of Technology grant number 2017-9-1.

Acknowledgments: The authors acknowledge support of the Institute of Pharmaceutical Sciences at the University of Tübingen, Germany, for providing laboratory and other basic facilities for carrying out experimental work.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Forte, B.; Malgesini, B.; Piutti, C.; Quartieri, F.; Scolaro, A.; Papeo, G. A submarine journey: The pyrroleimidazole alkaloids. *Mar. Drugs* **2009**, *7*, 705–753. [CrossRef] [PubMed]
2. Jiang, H.Y.; Zhou, C.H.; Luo, K.; Chen, H.; Lan, J.B.; Xie, R.G. Chiral imidazole metalloenzyme models: Synthesis and enantioselective hydrolysis for α-amino acid esters. *J. Mol. Catal. A Chem.* **2006**, *260*, 288–294. [CrossRef]
3. Jin, Z. Muscarine, imidazole, oxazole, and thiazole alkaloids. *Nat. Prod. Rep.* **2011**, *28*, 1143–1191. [CrossRef] [PubMed]
4. Rani, N.; Sharma, A.; Gupta, G.K.; Singh, R. Imidazoles as potential antifungal agents: A review. *Mini Rev. Med. Chem.* **2013**, *13*, 1626–1655. [CrossRef] [PubMed]
5. Emami, S.; Foroumadi, A.; Falahati, M.; Lotfali, E.; Rajabalian, S.; Ebrahimi, S.; Farahyar, S.; Shafiee, A. 2-Hydroxyphenacyl azoles and related azolium derivatives as antifungal agents. *Bioorg. Med. Chem. Lett.* **2007**, *18*, 141–146. [CrossRef] [PubMed]
6. Pandey, J.; Tiwari, V.K.; Verma, S.S.; Chaturvedi, V.; Bhatnagar, S.; Sinha, S.; Gaikwad, A.N.; Tripathi, R.P. Synthesis and antitubercular screening of imidazole derivatives. *Eur. J. Med. Chem.* **2009**, *44*, 3350–3355. [CrossRef] [PubMed]
7. Isloor, A.M.; Kalluraya, B.; Shetty, P. Regioselective reaction: synthesis, characterization and pharmacological studies of some new Mannich bases derived from 1,2,4-triazoles. *Eur. J. Med. Chem.* **2009**, *44*, 3784–3787. [CrossRef] [PubMed]
8. Kadhum, A.A.H.; Mohamad, A.B.; Al-Amiery, A.A.; Takriff, M.S. Antimicrobial and antioxidant activities of new metal complexes derived from 3-aminocoumarin. *Molecules* **2011**, *16*, 6969–6984. [CrossRef] [PubMed]
9. Al-Amiery, A.A.; Musa, A.Y.; Kadhum, A.H.; Mohamad, A.B. The use of umbelliferone in the synthesis of new heterocyclic compounds. *Molecules* **2011**, *16*, 6833–6843. [CrossRef] [PubMed]
10. Kadhum, A.A.H.; Al-Amiery, A.A.; Musa, A.Y.; Mohamad, A.B. The Antioxidant Activity of New Coumarin Derivatives. *Int. J. Mol. Sci.* **2011**, *12*, 5747–5761. [CrossRef] [PubMed]
11. Al-Amiery, A.A.; Kadhum, A.A.H.; Mohamad, A.A. Antifungal Activities of New Coumarins. *Molecules* **2012**, *17*, 5713–5723. [CrossRef] [PubMed]
12. Al-Majedy, Y.K.; Al-Duhaidahawi, D.L.; Al-Azawi, K.F.; Al-Amiery, A.A.; Kadhum, A.A.H.; Mohamad, A.B. Coumarins as Potential Antioxidant Agents Complemented with Suggested Mechanisms and Approved by Molecular Modeling Studies. *Molecules* **2016**, *21*, 135. [CrossRef] [PubMed]
13. Al-Amiery, A.A.; Al-Majedy, Y.K.; Kadhum, A.A.H.; Mohamad, A.B. New Coumarin Derivative as an Eco-Friendly Inhibitor of Corrosion of Mild Steel in Acid Medium. *Molecules* **2015**, *20*, 366–383. [CrossRef] [PubMed]
14. Al-Majedy, Y.K.; Kadhum, A.A.H.; Al-Amiery, A.A.; Mohamad, A.B. Synthesis and Characterization of Some New 4-Hydroxy-coumarin Derivatives. *Molecules* **2014**, *19*, 11791–11799. [CrossRef] [PubMed]
15. Kadhum, A.A.H.; Mohamad, A.B.; Hammed, L.A.; Al-Amiery, A.A.; San, N.H.; Musa, A.Y. Inhibition of Mild Steel Corrosion in Hydrochloric Acid Solution by New Coumarin. *Materials* **2014**, *7*, 4335–4348. [CrossRef] [PubMed]

16. Al-Amiery, A.A.; Kadhum, A.A.H.; Kadihum, A.; Mohamad, A.B.; How, C.K.; Junaedi, S. Inhibition of Mild Steel Corrosion in Sulfuric Acid Solution by New Schiff Base. *Materials* **2014**, *7*, 787–804. [CrossRef] [PubMed]
17. Al-Amiery, A.A.; Kadhum, A.A.H.; Alobaidy, A.H.M.; Mohamad, A.B.; Hoon, P.S. Novel Corrosion Inhibitor for Mild Steel in HCl. *Materials* **2014**, *7*, 662–672. [CrossRef] [PubMed]
18. Al-Amiery, A.A.; Kadhum, A.A.H.; Mohamad, A.B.; Musa, A.Y.; Li, C.J. Electrochemical Study on Newly Synthesized Chlorocurcumin as an Inhibitor for Mild Steel Corrosion in Hydrochloric Acid. *Materials* **2013**, *6*, 5466–5477. [CrossRef] [PubMed]
19. Al-Amiery, A.A.; Kadhum, A.A.H.; Mohamad, A.B.; Junaedi, S. A Novel Hydrazinecarbothioamide as a Potential Corrosion Inhibitor for Mild Steel in HCl. *Materials* **2013**, *6*, 1420–1431. [CrossRef] [PubMed]