Short Note

1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine

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Abstract: 1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine compound has been successfully synthesized by reacting *p*-Toluic hydrazide and glycine via polyphosphoric acid condensation route. The course of the reaction was found to be high yielding and the title compound was spectroscopically characterized by FT-IR, DSC, $^{13}C/^{1}H$-NMR and Mass spectrometric techniques.

Keywords: FTIR; Heterocyclic amines; NMR; Oxadiazole; Polyphosphoric acid

PACS:

1. Introduction

Among the preeminent heterocyclic compounds, oxadiazole structures has been demonstrated as good electron-transporting (ET) materials and prominent hole-blockers (HB) used in organic optoelectronic devices [1–3]. 1,3,4-Oxadiazoles are the most widely studied classes of ET materials due to their electron deficiency, high photoluminescence quantum yield, good thermal, and chemical stabilities [4–6]. The better performances of the device can be addressed by using oxadiazole as ET layer in organic light emitting diodes (OLEDs) and organic solar cells by effectively reducing the operation voltages [7–9].

The first reported small organic molecule as ET layer in organic light-emitting diodes (OLEDs) is 2-*tert*-butylphenyl-5-biphenyl-1,3,4-oxadiazole (PBD) [10]. Subsequently, the preferences of using oxadiazole motifs in polymeric and hyper-branched dendrimeric structures extensively improved the photoluminescence and electroluminescence characteristics for their utilization in green OLED devices [11–14]. Since, oxadiazole diamine molecules with ether links are designed to develop flexible aromatic polyimides [15, 16], post polymer modification of specific carboxylic acid pendant polymers are easily performed by oxadiazole amines by mild reaction conditions, effectively tune the dielectric properties of resulting polymers for specialized applications [17, 18]. In recent past, a series of 1,3,4-oxadiazole derivatives were tested for their optical nonlinearity. To tune the electronic properties and study the origin of the nonlinearity in the molecules, various aromatic donors and acceptor functional groups were inserted to oxadiazoles. Literature explicitly indicated that 1,3,4-oxadiazole rings have been explored in electroluminescent and light emitting devices because of their good electron withdrawing effect [19]. Keeping this in view, chromophores made of oxadiazole moiety were successfully designed and employed in easily processable polymers and studied nonlinear optical (NLO) responses [20, 21].

1,3,4-Oxadiazole derivatives are not only familiar in materials science but also exhibited there extensive performances in medicinal chemistry as a potent pharmaceutical scaffold. The improved biological activity and less toxicity of the oxadiazole moiety has attracted a wide attention of the medicinal chemists for the development of novel drugs [22]. Since, the heterocyclic azo compounds are well known for their medicinal importance as anti-inflammatory, antibacterial and antidiabetics [R], several alkyl and aryl azo derivatives of 1,3,4-oxadiazoles are developed and screened for their antimicrobial, anticancer and *in vitro* antioxidant properties [23].

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A number of synthetic routes have been reported for the synthesis of 1,3,4-Oxadaizole derivatives, most commonly used synthetic route includes reactions of acid hydrazides with acid carboxylic acids and direct cyclization of diacylhydrazines using a variety of dehydrating agents such as phosphorous oxychloride, thionyl chloride, phosphorous pentaoxide, triflic anhydride etc., [24, 25]. However, polyphosphoric acid mediated condensation route is more prominent and convenient path with high purity [26]. The present paper describes the synthesis of 1,3,4-Oxadiazole compound with amine functionality by polyphosphoric acid condensation route, and the title compound can be exploited easily to other functional clusters, or inserted to various functional polymers for pharmacological and technological applications.

2. Experimental Section

2.1. Materials

p-Toluic hydrazide ≥99%, Glycine ≥99%, Polyphosphoric acid (115% H_3PO_4 basis) and Sodium bicarbonate were procured from Sigma Aldrich, Seoul, South Korea. All the other chemicals and solvents were of AR grade and used without any further purification. Double distilled water was used throughout the study.

2.2. Instrumentaion

NMR spectra were recorded on an Agilent Technologies 400-MR DD2 spectrometer. ^{1}H and ^{13}C NMR spectra were referenced to external $SiMe_4$ (tetramethylsilane) using the residual protio solvent peaks as internal standards [with a 5 mm dual broad-band probe, 5 mm dual inverse broad-band probe, 1.7 mm triple resonance (^{1}H-^{13}C) probe]. LCMS measurement was performed on Liquid chromatography system with mass spectrometry detection (Q-TOF) – Agilent ACCURATE MASS 6530 Q TOF LC/MS. The elemental analysis was carried on a VARIO EL III Elemental analyzer (Elementar Analysensysteme GmbH, Hanau, Germany) and the results for C, H, and N were within 0.5% of the theoretical values. FTIR analysis was carried out on Nicolet 6700 (ATR) in the scanning range 4000-500 cm^{-1}. The resolution was 4 cm^{-1} with 64 scans and the measurement was done with Germanium crystal.

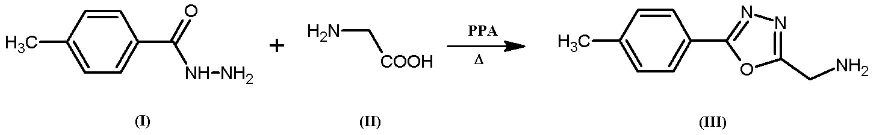
2.3. Synthesis of 1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine

Synthesis was performed using oven-dried glasswares under an atmosphere of nitrogen. The pulverized mixture of 1g (6.65 mmol) of *p*-Toluic hydrazide (**I**) and 0.499g (6.65 mmol) of glycine (**II**) in 20g of polyphosphoric acid was gradually heated to 120 °C for 2h with stirring (Scheme 1). Further, the heating was raised to 160 °C for 12h to accomplish the cyclization reaction, resulting in the formation of the title compound (**III**). The reaction mixture was cooled to 80 °C and poured slowly on crushed ice (500g) with agitation. The obtained grey solids were separated by filtration and suspended in 1M sodium bicarbonate solution for 1h and filtered again. The title compound was washed with distilled water until the pH of the filtrate is neutral. The product was vacuum dried at 60°C for 12h and recrystallized using ethyl alcohol. The desired product was achieved as grey solids (1.1g) in 87% of yield and it was confirmed by FTIR, DSC, ^{1}H, ^{13}C-NMR, and LCMS analyses.

Grey Solid; m.p. 174.63 °C (DSC); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 8.00 (d, 2H, J = 8.0 Hz), 7.42 (d, 2H), J = 8.0 Hz, 4.05 (s, 2H), 2.39 (s, 3H), ^{13}C-NMR (100 MHz, DMSO-d_6): (ppm) 164.32, 161.98, 142.59, 130.40, 127.05, 121.11, 50.24, 21.59. Anal. calcd. for $C_{10}H_{11}N_3O$ (189.213): C, 63.48; H, 5.86; N, 22.21. Found: C, 63.29; H, 5.78; N, 21.98. LCMS (ESI): m/z = 190.066 (Found), 189.213 (Expected for [M + H]$^+$), FTIR (Ge Crystal): 3435, 3375 cm^{-1} (-NH Stretch, Primary amine); 3065 cm^{-1} (C-H, Aromatic); 1625 cm^{-1} (C=N, Oxadiazole); 1520 cm^{-1} (C=C, Aromatic); 1315 cm^{-1} (CH_2); 1190 cm^{-1} (C-N); 1025 cm^{-1} (C-O-C, Oxadiazole); 755 cm^{-1} (N-H wag).

3. Results and Discussion

The use of polyphosphoric acid (PPA) as a reagent for the condensation of glycine and *p*-Toluic hydrazide has been reported (Scheme 1). The target compound is grey solid, insoluble in water, non-polar solvents such as *n*-hexane and completely soluble in tetrahydrofuran, dimethylformamide, methanol, ethanol, isopropanol and dimethyl sulfoxide.



Scheme 1. Synthesis of 1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine

The ^{1}H and ^{13}C NMR spectral data of the title compound is in good agreement with the proposed structure. From ^{1}H NMR spectra (Figure 1), the peaks at 8.00 δ and 7.42 δ corresponds to aromatic protons. The methyl and methylene proton signals has appeared at 2.39 δ and 4.05 δ respectively. ^{13}C NMR spectra contributes eight carbon signals (Figure 2). The signals at 164.32 and 161.98 δ value corresponds to oxadiazole ring carbons. The signal for aromatic carbon attached to the oxadiazole ring and methyl group has appeared at 121.11 δ and 142.59 δ respectively. The aliphatic carbon attached to the oxadiazole moiety has appeared at 50.24 δ. The δ values at 130.40 and 127.05 corresponds aromatic carbons of the benzene ring. The δ value at 21.59 ascribed to carbon of methyl functionality.

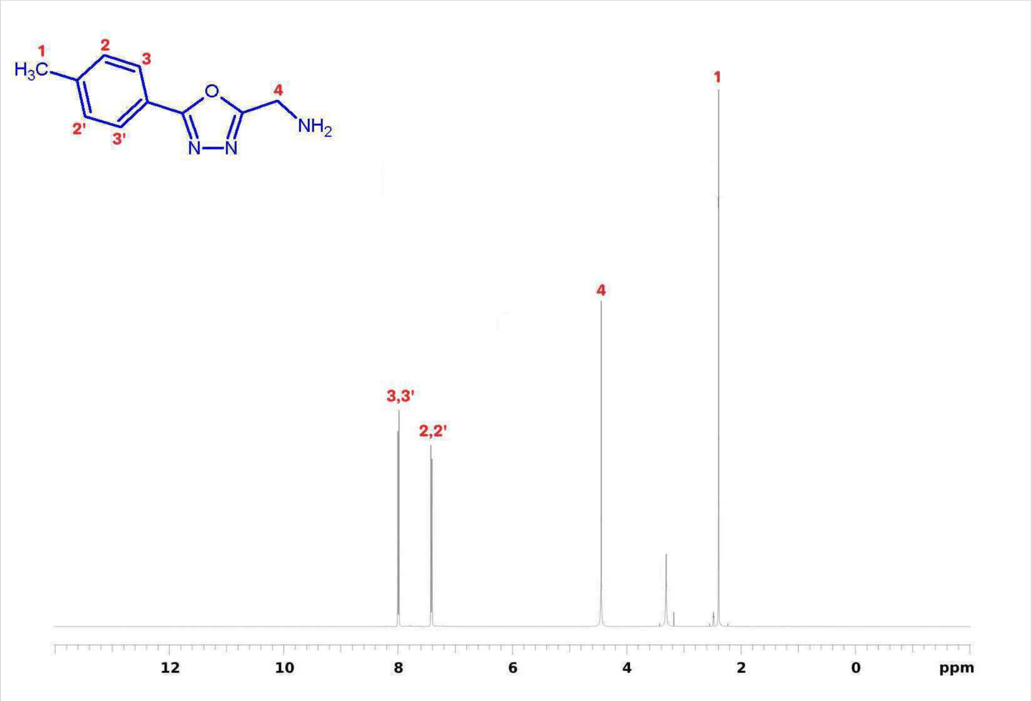


Figure 1. ^{1}H-NMR spectra of 1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine

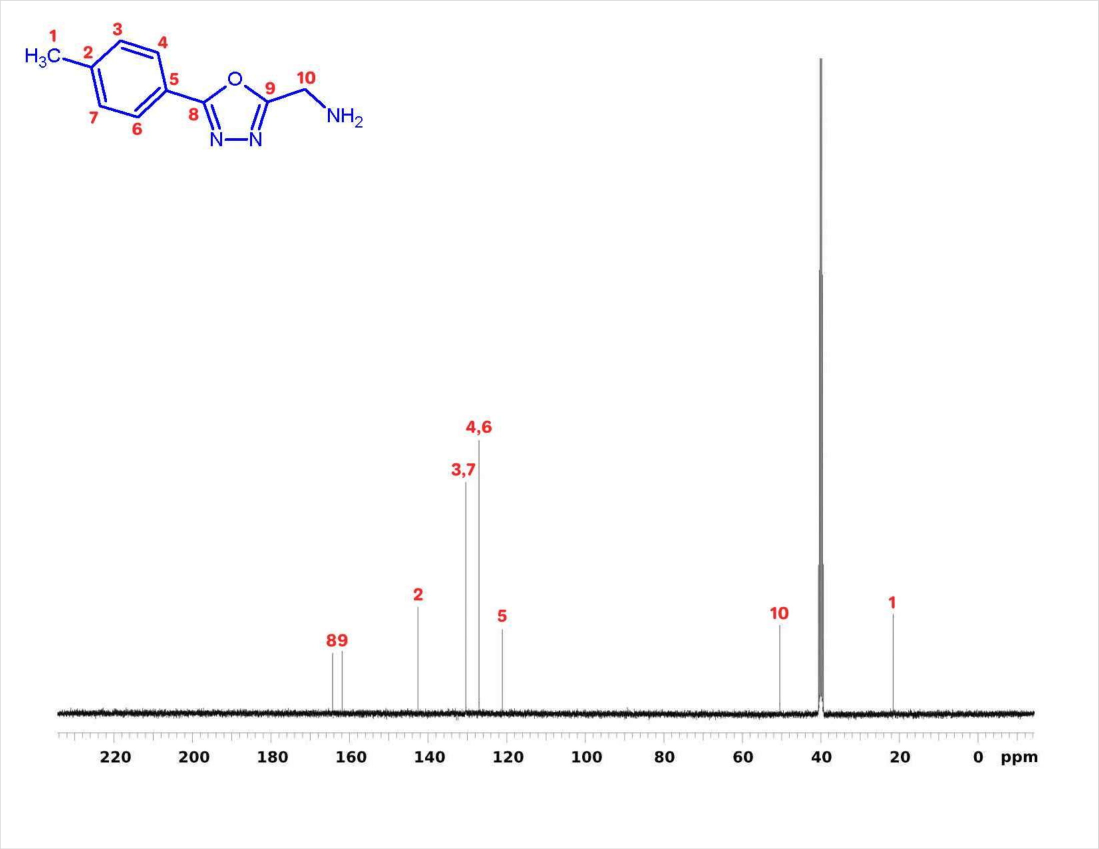


Figure 2. ^{13}C NMR spectrum of 1-[5-(4-methylphenyl)-1,3,4-oxadiazol-2-yl]methanamine

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Author Contributions: G.S., designed the synthesis, carryout the experiments for the title compound synthesis and wrote the article. E.-J.S., helped in the analysis of the compound. S.-Y.K., supervised the research. All the authors have read and approved the final manuscript.

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

References

1. Liu, C.; Zhao, P.; Huang, W. New oxadiazole derivatives as promising electron transport materials: synthesis and characterization of thermal, optical and electrochemical properties. *Central European Journal of Chemistry*, **2007**, 5(1), 303–315, DOI: 10.2478/s11532-006-0052-y
2. Kaippamangalath, N.; Gopalakrishnapanicker, U. Synthesis and evaluation of properties of poly(p-phenylenevinylene) based 1,3,4-oxadiazole systems for optoelectronics and nonlinear optical applications. *Polym Int*, **2016**, 65, 1221–1231, DOI: 10.1002/pi.5183
3. Chandrakantha, B.; Isloor, A.M.; Philip, R.; Mohesh, M.; Shetty, P.; Vijesh, A.M. Synthesis and nonlinear optical characterization of new 1,3,4-oxadiazoles. *Bull. Mater. Sci.*, **2011**, 34(4), 887–891, DOI: 10.1007/s12034-011-0210-5

4. Ichikawa, M.; Kawaguchi, T.; Kobayashi, K.; Miki, T.; Furukawa, K.; Koyama, T.; Taniguchi, Y. Bipyridyl oxadiazoles as efficient and durable electron-transporting and hole-blocking molecular materials. *J. Mater. Chem.*, **2006**, 16, 221–225, DOI: 10.1039/B510720B
5. Carli, S.; Baena, J.P.C.; Marianetti, G.; Marchetti, N.; Lessi, M.; Abate, A.; Caramori, S.; Grätzel, M.; Bellina, F.; Bignozzi, C.A.; Hagfeldt, A. A New 1,3,4-Oxadiazole-Based Hole-Transport Material for Efficient $CH_3NH_3PbBr_3$ Perovskite Solar Cells. *ChemSusChem*, **2016**, 9, 657–661, DOI: 10.1002/cssc.201501665
6. Chidirala, S.; Ulla, H.; Valaboju, A.; Kiran, M.R.; Mohanty, M.E.; Satyanarayan, M.N.; Umesh, G,; Bhanuprakash, K.; Rao, V.J. Pyrene–Oxadiazoles for Organic Light-Emitting Diodes: Triplet to Singlet Energy Transfer and Role of Hole-Injection/Hole-Blocking Materials. *J. Org. Chem.*, **2016**, 81(2), 603–614, DOI: 10.1021/acs.joc.5b02423
7. Kim, J.H.; Lee, H. Enhancement of efficiency in luminescent polymer by incorporation of conjugated 1,3,4-oxadiazole side chains as hole-blocker/electron-transporter. *Synthetic Metals*, **2004**, 143(1), 13–19, DOI: 10.1016/j.synthmet.2003.09.023
8. Xu, X.; Li, Z.; Bi, Z.; Yu, T.; Ma, W.; Feng, K.; Li, Y.; Peng, Q. Highly Efficient Nonfullerene Polymer Solar Cells Enabled by a Copper(I) Coordination Strategy Employing an 1,3,4-Oxadiazole-Containing Wide-Bandgap Copolymer Donor. *Adv. Mater.*, **2018**, 30, 1800737, DOI: 10.1002/adma.201800737
9. Mehmood, U.; Hussein, I.A.; Daud, M. New 1,3,4-Oxadiazole Based Photosensitizers for Dye Sensitized Solar Cells (DSSCs). *International Journal of Photoenergy*, **2015**, 2015, Article ID 637652, 8 pages, DOI: 10.1155/2015/637652
10. Lü, Z.; Deng, Z.; Zheng, J.; Xu, D.; Chen, Z.; Zhou, E.; Wang, Y. Organic light-emitting diodes with 2-(4-biphenylyl)-5(4-tert-butyl-phenyl)-1,3,4-oxadiazole layer inserted between hole-injecting and hole-transporting layers. *Vacuum*, **2010**, 84, 1287–1290, DOI: 10.1016/j.vacuum.2010.02.004
11. Ma, D.; Lupton, J.M.; Samuel, D.W.; Lo, S.C.; Burn, P.L. Bright electroluminescence from a conjugated dendrimer. *Applied Physics Letters*, **2002**, 81(12), 2285, DOI: 10.1063/1.1507826
12. Paun, A.; Hadade, N.D.; Paraschivescu, C.C.; Matache, M. 1,3,4-Oxadiazoles as luminescent materials for organic light emitting diodes via cross-coupling reactions. *J. Mater. Chem. C*, **2016**, 4, 8596–8610, DOI: 10.1039/C6TC03003C
13. Kim, S.J.; Zhang, Y.; Zuniga, C.; Barlow, S.; Marder, S.R.; Kippelen, B. Efficient green OLED devices with an emissive layer comprised of phosphor-doped carbazole/bis-oxadiazole side-chain polymer blends. *Organic Electronics*, **2011**, 12(3), 492–496, DOI: 10.1016/j.orgel.2010.12.006
14. Ichikava, M.; Shimizu, C.; Koyama, T.; Taniguchi, Y. Improvement of photovoltaic performances of organic thin-film solar cells by fast electron mobility oxadiazole as an exciton blocking layer material. *Phys Stat Sol.*, **2008**, 205(5), 1222–1225, DOI: 10.1002/pssa.200723290
15. Mansoori, Y.; Ghanbari, M. Novel polyimides obtained from a new aromatic diamine (BAPO) containing pyridine and 1,3,4-oxadiazole moieties for removal of Co(II) and Ni(II) ions. *Polym. Adv. Technol.*, **2015**, 26, 658–664, DOI: 10.1002/pat.3500
16. Mercer, F.W.; McKenzie, M.T.; Dielectric and thermal characterization of fluorinated polyimides containing heterocyclic moieties. *High Performance Polymers*, **1993**, 5(2), 97–106, DOI: 10.1088/0954-0083/5/2/002
17. Ganesh, S.D.; Pai, V.K.; Kariduraganavar, M.Y.; Jayanna, M.B. Functional Aromatic Poly(1,3,4-Oxadiazole-Ether)s with Benzimidazole Pendants: Synthesis, Thermal and Dielectric Studies. *International Scholarly Research Notices*, **2014**, 2014, Article ID 790702, 8 pages, DOI: 10.1155/2014/790702
18. Ganesh, S.D.; Pai, V.K.; Kariduraganavar, M.Y.; Jayanna, M.B. Thermal and Dielectric Behavior Studies of Poly(Arylene Ether Sulfone)s with Sulfonated and Phosphonated Pendants. *Journal of Materials*, **2016**, 2016, Article ID 7271959, 10 pages, DOI: 10.1155/2016/7271959
19. Bruma, M.; Hamciuc, E.; Schulz, B.; Kopnick, T.; Kaminorz, Y.; Robison, J. Synthesis and study of new polyamides with side oxadiazole rings. *Journal of Applied Polymer Science*, **2003**, 87, 714–721, DOI: 10.1002/app.11367
20. Tasaganva, R.G.; Tambe, S.M.; Kariduraganavar, M.Y. Synthesis and characterization of thermally stable second-order nonlinear optical side-chain polyurethanes containing nitro-substituted oxadiazole and thiazole chromophores. *Journal of Molecular Structure*, **2011**, 1000(1-3), 10–23, DOI: 10.1016/j.molstruc.2011.04.032

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21. Tasaganva, R.G.; Doddamani, R.V.; Inamdar, S.R.; Kariduraganavar, M.Y. Synthesis of thermally stable new polyurethanes containing nitro-substituted 1,3,4-oxadiazole chromophores for second order nonlinear optical applications. *Optik*, **2015**, 126(24), 4991–5000, DOI: 10.1016/j.ijleo.2015.09.132
22. Sun, J.; Makawana, J.A.; Zhu, H.L. 1,3,4-Oxadiazole Derivatives as Potential Biological Agents. *Mini-Reviews in Medicinal Chemistry*, **2013**, 13(12), 1725–1743, DOI: 10.2174/13895575113139990071
23. Shridhar, A.H.; Keshavayya, J.; Peethambar, S.K.; Hoskeri, H.J. Synthesis and biological activities of Bis alkyl 1,3,4-oxadiazole incorporated azo dye derivatives. *Arabian Journal of Chemistry*, **2016**, 9(2), S1643–S1648, DOI: 10.1016/j.arabjc.2012.04.018
24. Kadi, A.A.; El-Brollosy, N.R.; Al-Deeb, O.A.; Habib, E.E.; Ibrahim, T.M.; El-Emam, A.A. Synthesis, antimicrobial, and anti-inflammatory activities of novel 2-(1-adamantyl)-5-substituted-1,3,4-oxadiazoles and 2-(1-adamantylamino)-5-substituted-1,3,4-thiadiazoles. *European Journal of Medicinal Chemistry*, **2007**, 42(2), 235–242, DOI: 10.1016/j.ejmech.2006.10.003
25. Mickevičius, V.; Vaickelioniene, R.; Sapijanskaite, B. Synthesis of substituted 1,3,4-oxadiazole derivatives. *Chemistry of Heterocyclic Compounds*, **2009**, 45(2), 215–218, DOI: 10.1007/s10593-009-0252-4
26. Gomes, D.; Borges, C.P.; Pinto, J.C. Study of the synthesis of poly(4,4′-diphenylether-1,3,4-oxadiazole) in solutions of poly(phosphoric acid). *Polymer*, **2001**, 42(3), 851–865, DOI: 10.1016/S0032-3861(00)00458-4