

SYNTHESIS, CHARACTERIZATION OF SOME MANNICH BASE NEW 1, 3, 4- OXADIAZOLE-2-THIONE DERIVATIVES

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ABSTRACT

Two new oxadiazole compounds 3,3'-[methylin-bis(1,4-phenylene-iminomethylene)]-bis-(5-phenyl-1,3,4-oxadiazol)-2,3(H)-thione and 5-phenyl3-[4-(5-phenyl-1,3,4-oxadiazole-3yl)methyl]amino}phenyl]amino]methyl1,3,4-oxadiazolidine-2-thione thiooxamethane have been synthesized. The reaction was done in pH= 7 and in presences of amin molecules by Mannich reaction. The structures of the compounds were characterized by FT-IR, ¹³C NMR and ¹H NMR techniques.

KEYWORDS

1,3,4 oxadiazole, Mannich reaction, Thiol, Synthesis, Characterization.

INTRODUCTION

1,3-Oxadiazoles are five membered heterocycles containing one oxygen and two nitrogen atoms at position and 4 position respectively. Oxadiazoles are susceptible to nucleophilic attack as because it readily undergoes ring cleavage with aqueous acid or base hence both carbon positions are substituted (2,5 disubstituted).

1,3,4-Oxadiazoles are an important class of heterocyclic compounds with broad spectrum of biological activities. Substituted 1,3,4-oxadiazoles have revealed antibacterial [1], antimycobacterial [2], antifungal [3], anti-inflammatory [4], analgesic [5], anticonvulsant [6] and anticancer [7] properties.

It was reported that 1,3,4-oxadiazole derivatives, suitably substituted at the 2 and 5 positions, exhibited considerable antibacterial and antifungal activity[5-8]. Mannich reaction provides important tools for the synthesis of novel compounds [8] that find application as antimicrobial, cardio tonics antineoplastic, analgesics, antibiotic and anticancer drugs [9-12].

In recent years, the application of 1,3,4-oxadiazoles consisting of five membered heterocyclic have been described [13].

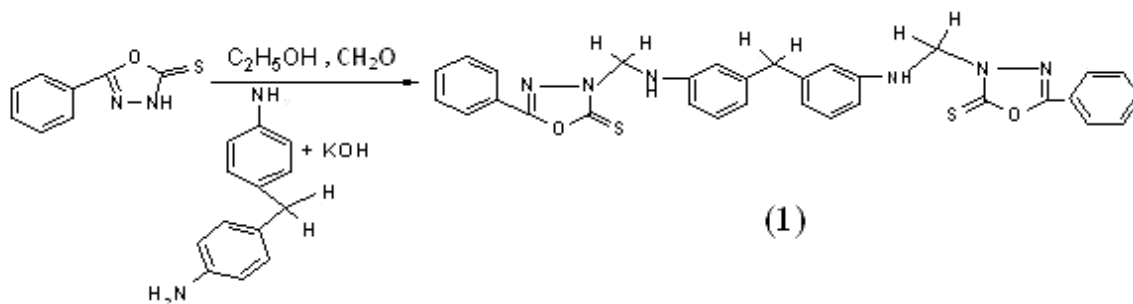
Keeping the above facts in view, we considered it of interest to synthesis some new 3,3'-[methylin-bis(1,4-phenylene-iminomethylene)]bis(5-phenyl-1,3,4-oxadiazol)-2,3(H)-thione (1) and 5-phenyl3-[4-(5-phenyl-1,3,4-oxadiazole-3yl) methyl]amino}phenyl]amino]methyl1,3,4-oxadiazolidine-2-thione thiooxamethane (2). This work describes the synthesis and characterization 1,3,4-oxadiazole derivatives.

EXPERIMENTAL

General Procedures: Chemicals were purchased from Fluka and Aldrich. Melting points were determined in open capillaries with electrical melting point apparatus and are uncorrected. IR spectra were recorded in Perkin Elmer FT-IR Spectrophotometer using KBr disc technique. ^1H , ^{13}C were carried out on a Bruker AVANCE DRX 500 spectrometer at 500, 125 using in DMSO- d_6 with tetramethylsilane as an internal standard. All the new compounds gave satisfactory analytical results.

Synthesis 3,3'-[methylin-bis(1,4-phenylene-iminomethylene)]-bis-(5-phenyl-1,3,4-oxadiazol)-2,3(H)-thione (1)

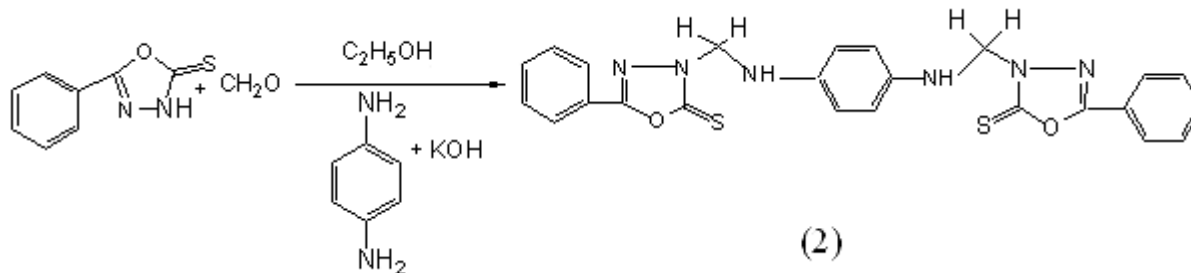
A mixture of thione (0.017 mole, 3 g), formaldehyde (0.017 mole, 1.3 ml), and 4,4-diamino, diphenyl methane (0.00085 mole, 0.17 g) was stirred in ethanol. The resulting thioether solution was removed by vacuum evaporation, and the products collected by filtration, washed with water, dried and recrystallised from a suitable solvent. mp 178-182 °C. ^1H NMR (DMSO- d_6 , 500 MHz) δ 6.76-7.87 (m, 10H), 5.42-5.43 (d, 2H), 3.12-3.62 (s, 1H); ^{13}C NMR (DMSO- d_6 , 125 MHz) δ 176.42 (C=S), 159.66 (N-C-O), 59.23 (CH₂). IR (KBr) ν_{max} 3360 (N-H), 2911 (C-H), 1613 (C=N), 1602 (C=S), 1425 (CH₂). *Anal.* C 62.74%, H 4.71%, N 15.09%, Calcd for C₂₉H₂₆N₆S₂O₂, C 62.80%, H 4.69%, N 15.15%.



Synthesis 5-phenyl 3-[4-(5-phenyl-1,3,4 oxadiazolidine-3yl)methyl]amino}phenyl]amino]methyl 1,3,4-oxadiazolidine-2-thione thiooxamethane (2)

A mixture of thione (0.0017 mole, 0.3 g), formaldehyde (0.0017 mole, 1.3 ml), and 1,4-phenyldiamin (0.008 mole, 0.9 g) was stirred in ethanol. The resulting thioether solution was removed by vacuum evaporation, and the products collected by filtration, washed with water, dried and recrystallised from a suitable solvent. mp 206-210 °C. ^1H NMR (DMSO- d_6 , 500 MHz) δ 5.41 (2H, d), 6.74 (2H, s), 7.55-7.60 (1H, m), 7.83 (1H, s); ^{13}C NMR (DMSO- d_6 , 125 MHz) δ

176.4 (C=S), 155.2 (N-C-O), 59.4 (CH₂). IR (KBr) ν_{\max} 3370 (N-H), 2917 (C-H), 1633 (C=N), 1591 (C=S), 1435 (CH₂). *Anal.* C 56.76%, H 4.28%, N 18.12%, Calcd for C₂₂H₂₀N₆S₂O₂, C 56.88%, H 4.30%, N 18.09%.



RESULTS AND DISCUSSION

The 3,3'-[methylin-bis(1,4-phenylene-iminomethylene)]bis(5-phenyl-1,3,4-oxadiazol)-2,3(H)-thione (1) and 5-phenyl-3-[4-(5-phenyl-1,3,4-oxadiazole-3-yl)methyl]amino}phenyl)amino]methyl-1,3,4-oxadiazolidine-2-thione thiooxamethane (2) were prepared in good yield and are stable in air and light (Scheme 1). The compounds were characterized by several techniques using elemental analysis (C, H, N), IR and NMR spectra. The FT-IR spectra and the high resolution ¹H and ¹³C NMR spectra of 3,3'-[methylin-bis(1,4-phenylene-iminomethylene)]bis(5-phenyl-1,3,4-oxadiazol)-2,3(H)-thione (1) and 5-phenyl-3-[4-(5-phenyl-1,3,4-oxadiazole-3-yl)methyl]amino}phenyl)amino]methyl-1,3,4-oxadiazolidine-2-thione thiooxamethane (2) have been recorded and analyzed. In the IR spectra (Fig. 2) the prominent peaks around 3360 and 3370 cm⁻¹ are attributed to ν (N-H), 1613 and 1633 cm⁻¹ owing to the ν (C=N), respectively (1) and (2). In the FT-IR spectra the C=S vibrations assigned in the region 1602, 1591 cm⁻¹ for the compounds (1) and (2) respectively.

In the ¹H NMR spectra all the protons seen occurred in the expected chemical shift and integral values. In the ¹H NMR spectra recorded in DMSO-d₆, the NH protons of (1) and (2) are at 5.43 and 5.41 ppm. The other protons have chemical shifts as expected. The ¹³C NMR spectra of (1) and (2) in DMSO-d₆ show C=S signals at 176.4-176.4 ppm and N-C-O signals at 159.6-155.2 ppm and CH₂ signals at 59.2-59.4 ppm.

REFERENCES

- [1] B.S. Holla, R. Gonsalves, S. Shenoy, *Eur. J. Med. Chem.* 35, 267 (2000).
- [2] F. Macaev, G. Rusu, S. Pogrebnoi, A. Gudima, E. Stingaci, L. Vlad, N. Shvets, F. Kandemirli, A. Dimoglo, R. Reynolds, *Bioorg. Med. Chem.* 13, 4842 (2005).
- [3] X.J. Zou, L.H. Lai, G.Y. Jin, Z.X. Zhang, *J. Agric. Food Chem.* 50, 3757 (2002).
- [4] E. Palaska, G. Sahin, P. Kelicen, N.T. Durlu, G. Altinok, *Il Farmaco.* 57, 101 (2002).
- [5] M. Amir, K. Shikha, *Eur. J. Med. Chem.* 39, 535 (2004).
- [6] A. Zarghi, A. Sayyed, M. Tabatabai, A. Faizi, P. Ahadian, V. Navabi, A. Zanganeh Shafiee, *Bioorg. Med. Chem. Lett.* 15, 1863 (2005).

- [7] J.J. Bhat, B.R. Shah, H.P. Shah, P.B. Trivedi, N.K. Undavia, N.C. Desai, *Indian J. Chem.* 33B, 189 (1994).
- [8] M. Tramontini, L. Angiolini, *Tetrahedron* 46, 1791 (1990).
- [9] H. Schönenberger, T. Bastug, L. Bindl, A. Adam, D. Adam, A. Petter, W. Zwez, *Pharm. Acta Helv.* 44, 691 (1969).
- [10] K. von Thiele, U. Schimassek, A. Schlichtegroll, *Arzneimittel Forschung* 16, 1064 (1966).
- [11] B.S. Holla, B. Veerendra, M.K. Shivananda, B. Poojary, *Eur. J. Med. Chem.* 42, 759 (2003).
- [12] W. Malinka, P. Swiatek, B. Filipek, J. Sapa, A. Jerierska, A. Koll, *Il Farmaco* 60, 961 (2005).
- [13] P. Rajakumar, S. Raja, *Tetrahedron Letters* 50, 223 (2009).

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