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AN EFFICIENT SYNTHESIS OF 2-(3-ARYL-1,2,4-OXADIAZOL-5-YL)-N-PHENYLACETAMIDE DERIVATIVES

Srivani K.[1,2], Thirupathaiah T.[1], Laxminarayana E.[2] and Thirumala Chary M.[1,*]
[1]Jawaharlal Nehru Technological University, Kukatpally, Hyderabad, (Telangana) India
[2]S. R. Engineering College(Autonomous), Ananthsagar, Hasanparthy,
Warangal, (Telangana) India
[3]Sreenidhi Institute of Science and Technology (Autonomous) Yamnampet,
Ghatkesar, Hyderabad (Telangana) India
*E-mail: mtcharya@yahoo.com

ABSTRACT
A simple and efficient method was developed to synthesis 2-(3-aryl-1,2,4-oxadiazol-5-yl)-N-phenylacetamide derivatives using acid chlorides from 3-(hydroxyimino)3-amino-N-phenylpropanamide. All the synthesized compounds were characterized by NMR and mass analyses.
Keywords: 1,2,4-oxadiazole, phenylpropanamide, phenylacetamide, hydroxyimine

INTRODUCTION

Oxadiazole nucleus shows a variety of helpful biological effects. 1,3,4-Oxadiazole and 3-arylpropionic acid nucleus are significant because of their adaptable biological actions. In particular, compounds having the 1,3,4-oxadiazole moiety are known to have exclusive anti-inflammatory and antioedema activities[1-3]. Another way, substituted oxadiazole derivatives have also been found to have other attractive behavior such as analgesic[2,3], antimicrobial[4], antitubercular[5], anticonvulsant[6] and anti-hepatitis B viral activities[7]. Non-steroidal anti-inflammatory drugs NSAIDs form a category of therapeutic agents that are most widely used because of their anti-inflammatory, analgesic and antipyretic effects. The widespread adverse effects of NSAIDs are the occurrence of gastrointestinal side effects like gastric upset, irritation and ulceration[8]. 3-(4-Bromobenzoyl)propionic acid is an example of the well known arylpropionic acid class of non steroidal anti-inflammatory agents. Arylpropionic acids are successful anti-inflammatory agents and some of them are available commercially; yet, they are connected with gastrointestinal side effects[9,10]. Reviews suggest that direct tissue contact of these agents plays a significant role in the making of side effects[11] and the reported literature confirms that gastrointestinal side effects of aroylpropionic acids are due to the presence of a free carboxylic group in the parent drug[10].

EXPERIMENTAL

Thin layer chromatography was run on silica gel-G and visualization was done using UV light or iodine. IR spectra were recorded by Perkin-Elmer 1000 instrument in KBr pellets. ^{1}H –NMR spectra were recorded in $CDCl_3$ or DMSO-D6 solvent using trimethylsilane as the internal standard by the 400MHz spectrometer. By Jeol-JMS D-300 spectrometer, mass spectra were recorded. Starting materials which were used in this chapter were obtained from commercial sources and used as such.

RESULTS AND DISCUSSION

N-phenyl-2-thiocyanatoacetamide **(1)** reacts with hydrazine hydrate to offered 3-(hydroxyimino)3-amino-N-phenylpropanamide **(2)** which on further reaction with acid chlorides gave title compounds. All these compounds were characterized by spectral analysis.

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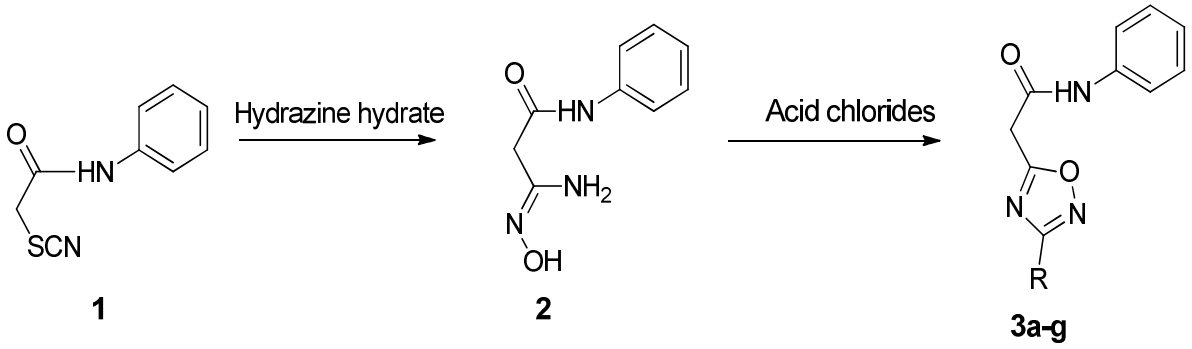

R= phenyl, 4-chlorophenyl, 3-chlorophenyl, 4-fluorophenyl, 3-fluorophenyl, 4-methoxyphenyl, 3-methoxyphenyl

Scheme-1

3-(hydroxyimino)3-amino-N-phenylpropanamide (2)
To a solution of hydrazinehydrate (0.02 mol) in 1,4-dioxane (20 mL), N-phenyl-2-thiocyanatoacetamide **(1)** (0.02 mol) was added. The reaction mixture was stirred at room temperature for 1 hr then poured onto a beaker containing an ice/water mixture. The solid product formed was collected by filtration and dried.
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.80 (brs, 1H), 7.62 (d, 2H), 7.40 (brs, 3H), 7.21 (m, 1H), 7.17 (m, 2H), 2.88 (d, 2H); MS: m/z, 194 (M^++H).

General procedure for synthesis of 2-(3-aryl-1,2,4-oxadiazol-5-yl)-N-phenylacetamide (3a-g)
To a solution of the acid chloride (0.02 mole) in glacial acetic acid (30 ml), 3-(hydroxyimino)3-amino-N-phenylpropanamide **(2)** (0.02 mole) was added. The reaction mixture was stirred at room temperature overnight, water was added and the precipitate obtained was filtered off dried and crystallizes from ethanol.

(3a): 2-(3-(4-chlorophenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.82 (brs, 1H), 8.02 (d, 2H, J=8.2Hz), 7.42(d, 2H, J=8.2Hz), 7.28(m, 3H); MS: m/z, 314 (M^++H).

(3b): 2-(3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.80 (brs, 1H), 8.11 (d, 2H, J=8.2Hz), 7.42 (d, 2H, J=8.2Hz), 7.28 (m, 3H); MS: m/z, 314 (M^++H).

(3c): 2-(3-(4-fluororophenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide
^{1}H NMR ((DMSO-d_6, 400MHz); = δ 8.80 (brs, 1H), 8.11 (m, 2H), 7.48 (m, 2H), 7.31 (m, 3H); MS: m/z, 298 (M^++H).

(3d): 2-(3-(3-fluororophenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.88 (brs, 1H), 8.12 (m, 2H), 7.47 (m, 2H), 7.30 (m, 3H); MS: m/z, 298 (M^++H).

(3e): N-phenyl-2-(3-phenyl-1,2,4-oxadiazol-5-yl)acetamide
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.85 (brs, 1H), 8.06 (d, 2H), 7.41 (m, 3H), 7.31 (m, 3H); MS: m/z, 280 (M^++H).
(3f): 2-(3-(3-methoxyphenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide
^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.76 (brs, 1H), 8.05(d, 2H), 7.38(m, 2H), 7.29 (m, 3H), 3.82 (S, 3H); MS: m/z, 310 (M^++H).

(3g): 2-(3-(2-methoxyphenyl)-1,2,4-oxadiazol-5-yl)-N-phenylacetamide

^{1}H NMR (DMSO-d_6, 400MHz); = δ 8.75 (brs, 1H), 8.04(d, 2H), 7.37(m, 2H), 7.28 (m, 3H), 3.81 (S, 3H); MS: m/z, 310 (M^++H).

REFERENCES

1. F. A. Omar, N. M. Mahfouz and M. A. Rahman, *Eur. J. Med. Chem*., **31**, 819, (1996).
2. B. Narayana, K. K. Vijayaraj, B. V. Ashlatha and N. S. Kumari *Arch. Pharm*. (Weinheim), **338**, 373, (2005).
3. M. Amir and S. Kumar, *Acta Pharm*., **57**, 31, (2007).
4. S. L. Gaonkar, K. M. Rai and B. Prabhuswamy, *Eur. J. Med. Chem*., **41**, 841, (2006).
5. M. A. Ali and M. S. Yar, O *Bioorg. Med. Chem. Lett.,* **17**, 3314, (2007).
6. A. Zarghi, S. A. Tabatabai, M. Faizi, A. Ahadian, P. Navabi, V. Zanganeh and A. Shafiee, *Bioorg. Med. Chem. Lett*., **15**, 1863, (2005).
7. T. M. Tan, Y. Chen, K. H. Kong, J. Bai, Y. Li, S. G. Lim, T. H. Ang and Y. Lam, *Antiviral Res.,* **71**, 7, (2006).
8. F. L. Lanza, *Am. J. Gastroenterol*., **93**, 2037, (1998).
9. F. Buttgereit, G. Burmester and L. S. Simon, *Am. J. Med*., **110**, 135, (2001).
10. K. A. Metwally, S. H. Yaseen, E. M. Lashine, H. M. El-Fayomi and M. E. El-Sadek, Eur. *J. Med. Chem*., **42**, 152, (2007).

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