



Short Communication

Synthesis of some Novel 1,3,4-Oxadiazole derivatives

Rashidi N.A¹ and Berad B.N²

Post Graduate Department of Chemistry, Shri Shivaji Science College Amravati, (M.S) INDIA
Department of Chemistry, RTM Nagpur University, Nagpur PINCode-440033, (M.S) INDIA

Available online at: www.isca.in

Received 18th July 2012, revised 31st December 2012, accepted 23rd January 2013

Abstract

A series of *N*-(4-chlorophenyl) amino-5-aryl-1,3,4-oxadiazole (IVa-f) have been synthesized by the condensation of acid hydrazides (Ia-f) and 4-(chlorophenyl) isocyanodichloride (II). Six different aromatic acid hydrazides were obtained by the esterification of aromatic acid followed by treatment with hydrazine hydrate. The compound (II) was prepared by the exhaustive chlorination of *p*-chloro isothiocyanate. Structures of all the newly synthesized compounds were confirmed by physical characterization and IR and NMR and Mass spectral analysis.

Keywords: 1,3,4-oxadiazole, acid hydrazides, 4-(chlorophenyl) isocyanodichlorides.

Introduction

Oxadiazole, a heterocyclic nucleus has attracted a wide attention of the chemist in search for the new therapeutic molecules. Literature survey reveals that out of various isomers particularly 1,3,4-oxadiazole derivatives exhibit wide range of biological activities. Also various route for the synthesis of 1,3,4-oxadiazole have been reported¹⁻⁷. Acid hydrazides⁸⁻¹¹ have been in general use as the starting materials in some 1,3,4-oxadiazole. In view of these observations, in the present study we have used acid hydrazide as one of the starting material. These acid hydrazides on condensation with highly reactive intermediate 4-chlorophenyl isocyanodichloride resulted in the formation of some new derivatives of 1,3,4-oxadiazole.

Research Methodology

Melting point was determined by Thieles tube method using liquid paraffin and was uncorrected. The purity of compounds was established by thin layer chromatography (TLC). Precoated silica gel aluminium plates were used for TLC (E. Merck). Iodine was used to develop the TLC plates. Infrared (IR) spectra were recorded on a Shimadzu (Japan) 8400 S FT-IR spectrophotometer model using nujol and potassium bromide pellets (ν^{\max} in cm^{-1}). ¹HNMR spectra were recorded on Bruker multinuclear FT NMR spectrometer model AV-400, 400 MHz using deuterated dimethylsulfoxide-containing tetramethylsilane (Me₄Si) as internal standard (chemical shifts in δ ppm). The Mass spectrum was recorded on TOF MS ES+ Mass spectrometer. Aromatic acid hydrazides and 4-chloro isothiocyanate¹² and 4-chloro isocyanodichloride¹³ were prepared by following the reported methods.

Synthesis of 2-(4-chlorophenyl) amino-5-(4-nitrophenyl)-1,3,4-oxadiazole (IVa):

The 4-nitro benzohydrazide (Ia) was refluxed with *N*-(4-chlorophenyl) isocyanodichloride (II) in boiling chloroform for 3.0 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixture and distilling off chloroform afforded sticky mass, which on washing with petroleum ether several times gave solid. It was found to be acidic to litmus and on titrimetric analysis identified as monohydrochlorides of *N*-(4-chlorophenyl)-5-(4-nitrophenyl)-1,3,4-oxadiazole-2-amine hydrochloride (IIIa). It was crystallized from ethanol, m.p 134^oC. This on basification with dilute ammonium hydroxide solution afforded free bases (IV) crystallized from aqueous ethanol (70%), m.p 184^oC. The product was soluble in organic solvent but insoluble in water.

On extending the above reaction to other acid hydrazides (Ia-f), the related 1,3,4-oxadiazoles were isolated in good yield.

(IVa): **IR spectra**¹⁴⁻¹⁵: (KBr) cm^{-1} : 3330 (N-H), 3242(N-H), 3179, 3109, 3050 (Ar-H), 1648 (N-N), 1597 (C=N), 1334 (C-N), 1095 (C-O-C), 716 (C-Cl);

¹H-NMR (DMSO-d₆) ppm: 4.5 (1H,s, N-H), 7.1 (2H, d, Ar-H), 7.2 (2H, d, Ar-H, ortho to Cl), 8.02 (2H, d, Ar-H), 8.03 (2H,d, Ar-H, ortho to NO₂)

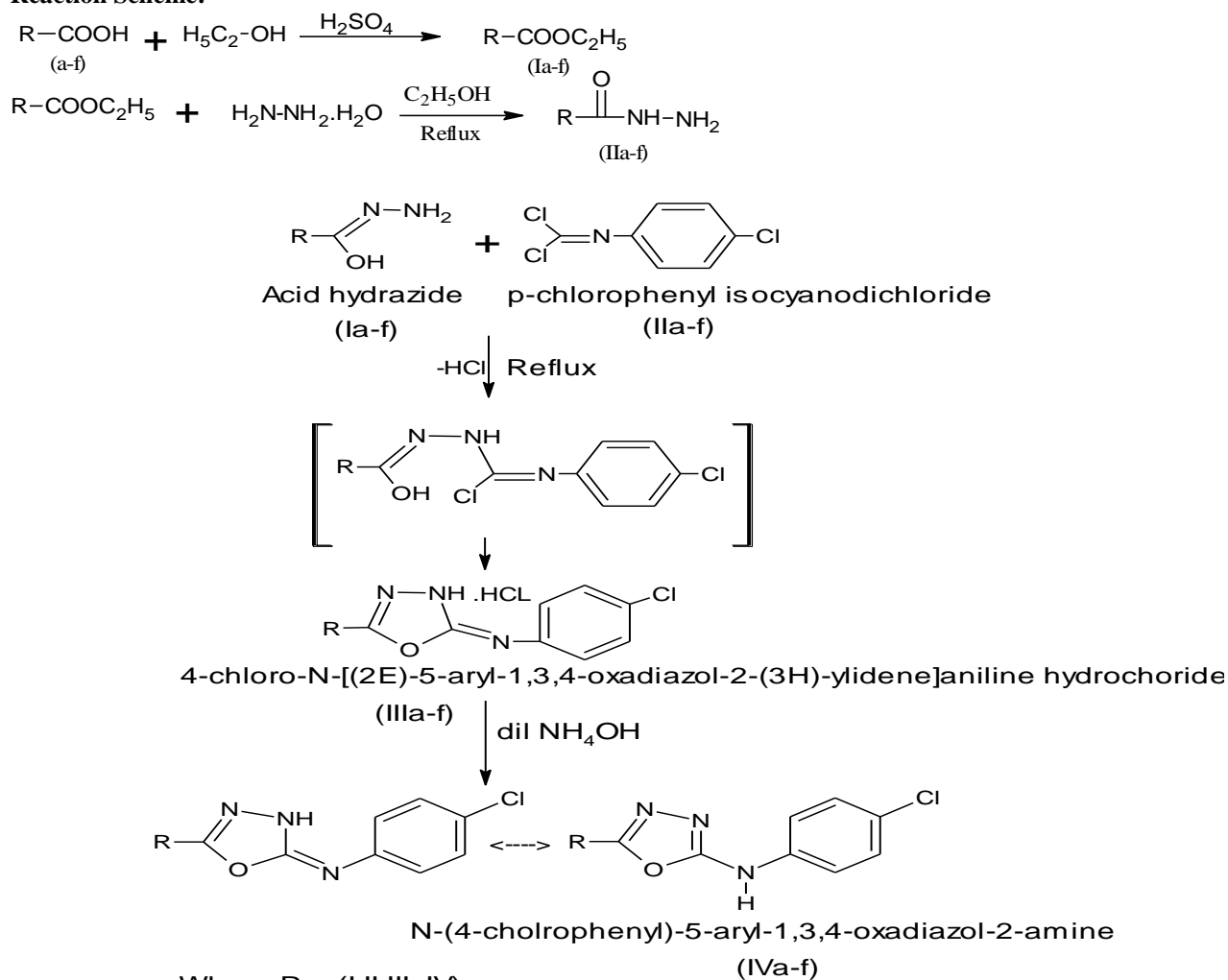
Mass (m/z) :318 (M⁺+2), 280,207,190,170,154,126,111

Synthesis of 2-(4-chlorophenyl) amino-5-aryl-1,3,4-oxadiazole (IV):

Table-1
Reagents: Aromatic acid hydrazide (I) and 4-chlorophenyl isocyanodichloride (II)

Acid Hydrazide (I)	2-(4-chlorophenyl) amino-5-aryl-1,3,4-oxadiazole hydrochloride (III)	Yield %	M.P	Eq.wt Found (Calcd)	2-(4-chlorophenyl) amino-5-4-aryl-1,3,4-oxadiazole (IV) (free base)	M.P °C
4-nitro bezohydrazide (Ia)-5(4-nitrophenyl)-1,3,4-oxadiazole hydrochloride (IIIa)	89	134	350.8 (353.1)-5(4-nitrophenyl)-1,3,4-oxadiazole (IVa)	184
Isonicotinic acid hydrazide (Ib)-5(4-pyridinyl)-1,3,4-oxadiazole hydrochloride (IIIb)	82	162	304.5 (309.1)-5(4-pyridinyl)-1,3,4-oxadiazole (IVb)	174
Phenyl acetic acid hydrazide (Ic)-5-benzyl-1,3,4-oxadiazole hydrochloride(IIIc)	78	154	318.9 (322.2)-5-benzyl-1,3,4-oxadiazole (IVc)	163
Benzohydrazide (Id)-5-phenyl-1,3,4-oxadiazole hydrochloride(IIIId)	74	118	303.6 (308.1)-5-phenyl-1,3,4-oxadiazole (IVd)	132
2-hydroxy benzohydrazide (Ie)-5(2-hydroxyphenyl)-1,3,4-oxadiazole hydrochloride(IIIe)	80	166	323.2 (324.2)-5(2-hydroxyphenyl)-1,3,4-oxadiazole (IVe)	178
2-chlorobenzo hydrazide (If)-5(2-chlorophenyl)-1,3,4-oxadiazole hydrochloride(IIIIf)	70	125	439.6 (342.6)-5(2-chlorophenyl)-1,3,4-oxadiazole (IVf)	151

Reaction Scheme:



Where R = (I,II,III, IV)

a = p-NO₂C₆H₄-, b = -C₅H₄N c = -CH₂C₆H₅,

d = -C₆H₅, e = O-OHC₆H₄-, f = O-CIC₆H₄-

Scheme 1.1 : Synthesis of 1,3,4oxadiazole derivative

Results and Discussion

The synthetic route is outlined in Scheme. The condensation of 4-nitro benzohydrazide (Ia) with 4-chlorophenyl isocyanodichloride in chloroform was carried out for 3 hr. The evolution of hydrogen chloride gas was observed and tested with moist blue litmus paper. Cooling the reaction mixture and distilling off the solvent afforded a sticky mass, which on washing with petroleum ether followed by addition of a little ethanol gave a light yellow solid. It was crystallized from aqueous ethanol (70%), m.p 134 °C. It was acidic to litmus. On determination of equivalent weight it was found to be mono hydrochloride (IIIa). On basification with ammonium hydroxide, afforded a free base (IVa) crystallized from aqueous ethanol, m.p 184°C. The doublet signals at 7.1, 7.2, 8.02, 8.03δ ppm are due to two para substituted benzene ring and a singlet at 4.5 δ ppm in the 1H NMR spectrum of (IVa) was assigned to N-H protons. The mass spectrum exhibited the (M⁺+2) peak at m/z 318 and other fragment ion peak at 280,207,190,170,154,126,111 which confirmed its molecular weight and possible fragments.

On the basis of spectral data IR and 1H NMR and above facts the compound (IVa) has been assigned the structure as 2-(4-chlorophenyl) amino-5-(4-nitrophenyl)-1,3,4-oxadiazole (IVa).

The other compounds (IVb-f) were prepared by extending the above reaction to other acid hydrazides (Ib-f) and the related 1,3,4-oxadiazoles (IVb-f) were isolated in good yield (Table-1).

Conclusion

Oxadiazole moiety and its various derivatives studied frequently in the past time and found potent in various pharmacological and pathological conditions. In the article the attempt to synthesize some new oxadiazole derivatives were successfully carried out. The structures of all the synthesized compounds were confirmed on the basis of IR, ¹H NMR, and mass spectral data These synthesized compounds are expected to possess biological activities.

Acknowledgement

The Authors are thankful to the Principal, Shri Shivaji Science college, Amravati and Shri Mungsaji Maharaj Mv. Darwha for providing the lab facilities and constant encouragement. The

Authors are also thankful to the Director, RSIC, Punjab University, and Chandigarh for providing elemental analysis and IR, PMR, Mass Spectral data.

References

1. Hiremath S.P. and Goudar N.N., *Ind. J. Chem.*, **21B**, 321-324 (1982)
2. Dutta M.M., Goswami B.N. and Katakya J.C., *J. Ind. Chem. Soc*, **LXIV** 195-978 (1987)
3. Parekh O., Sharma V. and Batra H., *Ind. J. Chem.*, **37**, 797-800 (1998)
4. Farah M., Pilotti A., *Drug Discovery Today*, **11(3-4)**, 165-174 (2006)
5. Waston B., Tierney J. and Lidstrom P., *Drug Discovery Today*, **6**, 373-380 (2002)
6. Kidwai M., Kumar P. and Goel Y., *Ind. J. Chem.*, **36B**, 175-179 (1997)
7. Khan K.M., Rani M. and Haider S.M., *Lett. Org. Chem.*, **1**, 151 (2004)
8. Vogel. A.I, Tatchell. A.R, Furnis B.S. and Hannaford A.J, P.W.G. Smith Vogel's Text Book of Practical Organic Chemistry, 5th Ed. Singapore: Pearson Education, 699 (2004)
9. Sudeep K. Mandal et al.; *International Journal of Pharma Sciences and Research (IJPSR)*, **1(11)**, 465-472 (2010)
10. Zamani K., et al., Synthesis of Some New Substituted 1,2,4-Triazole and 1,3,4-Thiadiazole and Their Derivatives *Turk J Chem.*, **27**, 119-125 ((2003)
11. Ilango K., Valentina P., Umarani N. and Kumar T., *Indian J Chem.*, **2009**, **1(1)**, 72-78.
12. A I. Vogel., A Text Book of Practical Organic Chemistry, Including Qualitative Analysis, Longmans, **IIIrd** Ed, (1958)
13. Dyson G.M. and Harington, *J. Chem. Soc.*, 191 (1940)
14. Kalsi P.S., 'Spectroscopy of Organic Compounds', New Age International (P) Ltd., Vth edition (2004)
15. Kemp W., 'Organic Spectroscopy', Palgrave, IIIth edition (2002)