Asian Journal of Chemistry; Vol. 23, No. 10 (2011), 4563-4565

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Microwave Assisted Synthesis and Characterization of Azomethines of Aryl Oxazole

V. NIRAIMATHI*, A. JERAD SURESH and T. LATHA

Department of Pharmaceutical Chemistry, College of Pharmacy, Madras Medical College, Chennai-600 003, India

*Corresponding author: E-mail: vnm_anr@yahoo.co.in

(*Received*: 21 December 2010; *Accepted*: 27 June 2011) AJC-10099

2-Chloro N-phenyl acetamide (**3**) generated by condensation of aniline with chloroacetylchloride in alkali reacts with urea to form phenyl oxazole diamine (**5**) which on heating under reflux with various aromatic aldehydes forms azomethines of aryl oxazoles (**7a-e**).

Key Words: Microwave assisted, Heterocyclic compound, Aryl oxazoles, Azomethines, NMR spectroscopy.

INTRODUCTION

Oxazoles are considered as important class of heterocyclic compounds which are found to be structural subunits of various biologically active natural products and are valuable synthetic precursors in designing new pharmacophore; several derivatives of which have been found to possess diversified type of biological activities including antibacterial[1], antifungal[2], antitubercular[3], antihyperglycemic[4], antiinflammatory[5,6], antiproliferative[7] and antihypertensive activity. The biological importance of oxazoles and azomethines prompted the synthesis of azomethines of aryl oxazoles. The use of microwave assisted reaction has become an important tool for the chemists to get products which are more pure, time- saving and friendly with simple operational procedures.

EXPERIMENTAL

Melting points were taken in open capillary tube and are presented uncorrected. IR spectra was recorded in Perkin-Elmer spectrum one/IR spectrometer using KBr disc method. The ^{1}H NMR were recorded in Bruker Avance III 500 NMR spectrometer. Chemical shifts values are reported as values in ppm relative to TMS (δ = 0) as internal standard. The mass spectra were recorded on Joel GC mate II mass spectrometer. In the present work, azomethines of aryl oxazoles have been synthesized by condensation of compound (**3**) with urea (**4**), the resultant product (**5**) is condensed with various aromaric aldehydes. The synthesis consists of 3 steps, which are as follows:

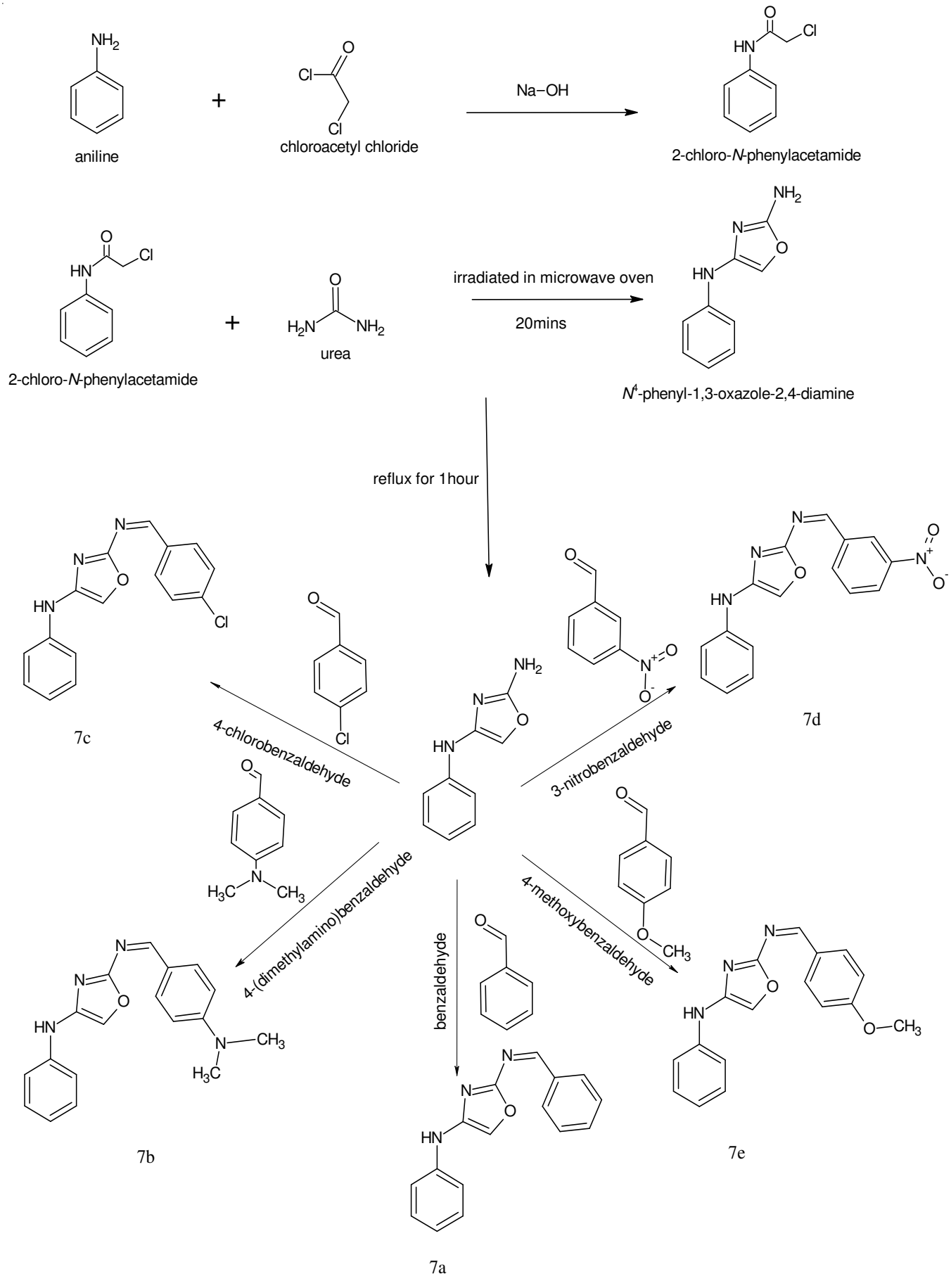
Step-1: Preparation of 2-chloro-N-phenyl acetamide[8] (3): To a mixture of aniline (0.01 mol) and 3 % of sodium hydroxide, (0.02 mol) of chloroacetylchloride was added in one portion with cooling and vigorous stirring. The stirring was continued for *ca.* 1 h until the excess chloroacetylchloride had been decomposed. The crystals separated were filtered and recrystallized from ethanol.

Step-2: Preparation of N-phenyl, 1-3 oxazole-2-4-diamine (5): Equimolar quantity of 2-chloro-N-phenyl acetamide (**3**) and of urea (pulverized condition) was well mixed with the aid of alcohol to ensure homogeneity and subjected to microwave irradiation at power (40 W) for 20 min, with intermittent stirring at the gap of 3 min. To avoid charring alcohol is added periodically. On cooling, the resultant irradiated N-phenyl, 1-3 oxazole-2-4-diamine (**5**) separates out in the form of white needle like crystals which was once again recrystallized from ethanol.

Step-3: Preparation of azomethines of aryl oxazole derivatives (7a-e): Equimolar quantity of N-phenyl, 1-3-oxazole-2-4-diamine (**5**) and aromatic aldehydes in ethanol was taken and acidified with glacial acetic acid to pH (4.5-5.0), were refluxed on a water bath for 1 h. The various aromatic aldehydes used are benzaldehyde, dimethylamino benzaldehyde, *p*-chlorobenzaldehyde, *m*-nitroanisaldehyde and *p*-anisaldehyde. The reaction mixture was poured into ice. The solid product was filtered and recrystallized from ethanol. The physical characteristics of the synthesized azomethines of aryl oxazoles are given in Table-1. The spectral data[9,10] of the synthesized compounds **7a-e** are given below;

7a: IR (KBr, ν_{max}, cm^{-1}): -C=C (str.) 1602, -NH (str.) 3436, Ar-C-H (str.) 3144, C=N (str.) 1671, C-O-C (str.). ^{1}H NMR (δ ppm) 4.1 (s, NH), 7.12-7.15 (m, Ar-H), 7.32-7.36 (m, -N=CH), 7.57-7.59 (d, hetero Ar-H). Mass m/z M$^+$ peak-263.

7b: IR (KBr, ν_{max}, cm^{-1}): -C=C (str.) 1536, -NH (str.) 3435, A-C-H (str.) 3144, -C=N (str.) 1661, -CH_3 (str.) 2902, C-O-C


aniline
chloroacetyl chloride
Na–OH
2-chloro-*N*-phenylacetamide
urea
irradiated in microwave oven
20mins
*N*⁴-phenyl-1,3-oxazole-2,4-diamine
reflux for 1hour
4-chlorobenzaldehyde
3-nitrobenzaldehyde
4-(dimethylamino)benzaldehyde
benzaldehyde
4-methoxybenzaldehyde
7a
7b
7c
7d
7e

Scheme-I

TABLE -1
PHYSICAL DATA OF AZOMETHINES OF ARYL OXAZOLES

Compd.	Colour	m.p. (ºC)	Yield (%)	m.f.	m.w.
7a	White	125-135	61.25	$C_{16}H_{13}N_3O$	263.39
7b	Yellow	53- 54	65.28	$C_{18}H_{18}N_4O$	305.85
7c	White	78-80	50.38	$C_{16}H_{12}N_3OCl$	297.28
7d	Light brown	64-84	60.00	$C_{16}H_{12}N_4O_3$	308.09
7e	White	120-123	54.54	$C_{17}H_{15}N_3O_2$	293.12

(str.) 1252. ^{1}H NMR (δ ppm) 4.1 (s, NH), 7.14 (m, Ar-H), 7.32-7.36 (m, -N=CH), 7.74 (d, hetero Ar-H), 3.1 (s CH_3-H). Mass m/z M^+ - 1 peak-305.

7c: IR (KBr, ν_{max}, cm^{-1}): -C=C (str.) 1557, -NH (str.) 3430, Ar -C-H (str.) 3144, -C=N (str.) 1672, C-Cl (str.) 750, C-O-C (str.) 1252. ^{1}H NMR (δ ppm) 4.1 (s, NH), 7.14 (m, Ar-H), 7.33-7.36 (m, -N=CH), 7.57-7.59 (d, hetero Ar-H). Mass m/z M^+ peak-297.

7d: IR (KBr, ν_{max}, cm^{-1}): -C=C (str.) 1536, -NH (str.) 3435, Ar-C-H (str.) 3145, -C=N (str.) 1670, -CH_3 (str. *trans* isomer) 1673, C-O-C (str.) 1252. ^{1}H NMR (δ ppm) 4.1 (s, NH), 7.13-7.16 (m, Ar-H), 7.57-7.63 (m, -N=CH), 7.83-7.89 (d, hetero Ar-H). Mass m/z M^+ peak-308.

7e: IR (KBr, ν_{max}, cm^{-1}): -C=C (str.) 1557,-NH (str.) 3435, Ar-C-H (str.) 3144, -C=N (str.) 1672, -C-O-CH_3 (str.) 2902. ^{1}H NMR (δ ppm) 4.1 (s, NH), 7.13-7.16 (m, Ar-H), 7.32-7.35 (m, -N=CH), 7.59 (d, hetero Ar-H. Mass m/z M^+ peak-293.

RESULTS AND DISCUSSION

In this work, 5 simple azomethines of aryl oxazoles were synthesized using readily available and simple starting materials to give good to moderate yield. Purification of the synthesized compounds were done by recrystallisation technique. The recrystallized product was identified by TLC and characterised by IR, ^{1}H NMR and mass spectroscopy. Like other oxazole derivatives, these compounds are quite stable and anticipated to possess good biological activity which will be the further scope of study.

ACKNOWLEDGEMENTS

The authors are grateful to SAIF for recording IR, ^{1}H NMR and mass spectra and Department of Pharmaceutical Chemistry, College of Pharmacy, Madras Medical College, Chennai for providing the necessary research facilities.

REFERENCES

1. C. George, N. Martin and R. Ray, *J. Med. Chem*., **16**, 1402 (1973).
2. C.-K. Ryu, R.-Y. Lee, N.Y. Kim, Y.H. Kim and A.L. Song, *Bioorg. Med. Chem. Lett*., **19**, 5924 (2009).
3. C.G. Anna, I.M.B. Helena, G.F. Scott, E.B. Clifton and R.C. Erent, *Terahedron Lett*., **46**, 7355 (2003).
4. A. Kumar, P. Ahmad, R.A. Maurya, A.B. Singh and A.K. Srivastara, *Eur. J. Med. Chem*., **44**, 109 (2009).
5. C. George and J.F. Michael, *J. Med. Chem.*, **14**, 1075 (1971).
6. H. Hashimoto, K. Maeda, K. Ozawa, J.-I. Haruta and K. Wakitani, *Biorg. Med. Chem. Lett*., **12**, 65 (2003).
7. X.-H. Liu, P.-C. Lv, J.-Y. Xue, B.-A. Song and H.L. Zhu, *Eur. J. Med. Chem.*, **44**, 3930 (2009).
8. H. Kalo, K. Tanaka and M. Ohta, *Bull. Chem. Soc. (Japan)*, **39**, 1248 (1966).
9. R.M. Silverstein and F.X. Webster, Spectrometric Identification of Organic Compounds, vol. **6**, p. 15 (1998).
10. B.S. Furniss, A.J. Hannaford, P.W.G. Smith and A. Rtatchell, Vogels Textbook of Practical Organic Chemistry, Vol. 5, pp. 1413-1441 (2008).