Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Chemica Sinica, 2015, 6(5):86-89

Pelagia Research Library

ISSN: 0976-8505
CODEN (USA) CSHIA5

Catalyst-free and facile green synthesis of some novel oxazepine derivatives

Purnima Verma, Sarita Gupta and V. S. Yadav*

Department of Chemistry, Lucknow University, Lucknow, India

ABSTRACT

The present research work involves the synthesis of some new oxazepine derivatives from o-aminophenol as starting material. All these compounds were characterized by elemental analysis and spectroscopy.

Key words: Schiff bases, oxazepine, substituted aromatic aldehydes, biological activity

---

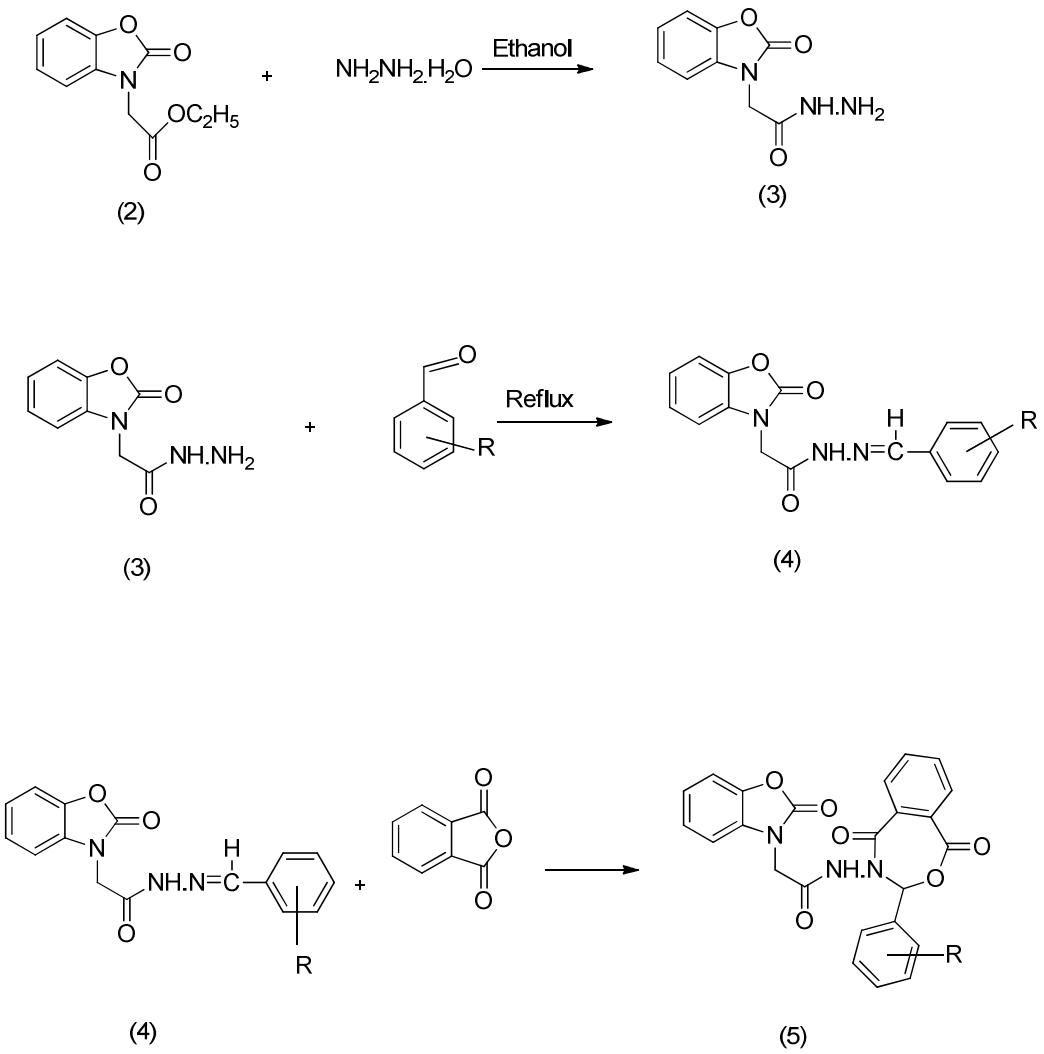
INTRODUCTION

The chemistry of heterocyclic compounds has been an interesting field of study for a long time due to its vast applications in various fields such as medicinal , agricultural , pharmaceutical as potent and selective drugs[1]. In addition , some urea and thiourea derivatives are known to be associated with wide range of biological activities such as analgesic , antitumor , anti HIV and antimicrobial properties[2]. These oxazepines were synthesized by the cycloaddition reaction between Schiff bases and Phthalic anhydride, which were characterized by C H N analysis and advanced spectral techniques. One striking structural feature inherent to heterocyclic's, which continue to be exploited is their ability to manifest substituent around a core scaffold i:e

Benzoxazole[3]. 1,3– oxazipenes are prepared by condensation of Schiff bases with anhydride to give corresponding cycloaddition products. According to the above mentioned facts, we decided to synthesize new 1, 3- oxazipenes derivatives which are expected to have some important biological activities.

In the present study, a series of new heterocyclic moieties have been synthesized and describes the path used for the preparation of target compounds[4]. These Schiff bases were characterized by elemental analysis, FT-IR & 1H NMR spectroscopy. Such compounds were evaluated for anticonvulsant properties against seizures induced by maximal electroshock (MES), and chemically induced seizures in mice [5]. Microwave assisted organic reaction enhancement is now days a well established technique for the synthesis of various heterocyclic compounds through cycloaddition reaction, especially in the case when high temperature are required. These syntheses can be carried out safely in microwave reactor with remarkable rate enhancement due to the super heating effect [6]. A pericyclic reaction is a concerted process based on principal of conservation of molecular orbital symmetry between the reaction components during the reaction proceeding which is leading to a cyclic transition state corresponds with arrangement of participating orbitals [7].

Benzo oxazole-2(3H) - one **1** when treated with ethyl acetoacetate gave the corresponding acetate 2 . Hydrazinolysis of **2** with hydrazine hydrate furnished 2-[2-oxobenzoxazole-3(2H)-yl]acetohydrzine **3**. Refluxing of **3** with appropriate aldehyde yielded acetohydrazide derivatives **4** .Cyclization of **4** with Phthalic anhydride afforded [1,3] oxazepine derivatives **5**. The structures of all the new compounds were confirmed by elemental analysis and spectral data.



(2) (3) (3) (4) (4) (5)

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and are uncorrected. All of the solvents used were of analytical grade or were purified according to standard procedure. Chemicals & solvents were of analytical grade (supplied by either Merck or Fluka, Aldrich). The ^{1}H NMR was recorded on Bruker advanced–II NMR-300 MHz instruments using $CDCl_3$/DMSO-d6 as solvent and tetramethylsilane as internal standard, chemical shifts were expressed as δ values (ppm). FT.IR spectra were recorded using Fourier transform infrared SHIMADZU FT.IR-8400S infrared spectrophotometer by KBr disc.

General Procedure

Benzoxazol-2(3H)-one 1. A dry flask charged with o-aminophenol (1 mmol) and urea (2 mmol) was placed in microwave synthesis system and irradiated at 400 w for 15 min. While the temperature was set to 140^0 C. After the reaction was completed, the flask was cooled to room temperature and the solid was dissolved in 5% solution of sodium hydroxide . After acidification with concentrated HCl, the desired product was obtained[8].Yield 78%, m.p 134^{0}C.

Ethyl 2 – (2-oxobenzo oxazole -3(2H)-yl)acetate 2. Compound **1**(1mmol) was refluxed with equivalent amount of sodium in absolute ethanol for 2 hrs. Then ethyl acetoacetate (1mmol) was added and mixture was refluxed for additional 5 hrs. After concentrating the reaction mixture at 40^{0}C under reduced pressure, a semi solid mass appeared .This was recrystallized from ethanol to get the desired compound as a solid. Yield 72%, m.p 210^{0}C.

2-(2-oxobenzo oxazole-3(2H)-yl) acetohydrazide 3. A solution of **2** (1mmol) in ethanol was refluxed with hydrazine hydrate (1mmol) for 4 hrs. After concentrating the reaction mixture, a white solid mass appeared. This was recrystallized from ethanol to get desired product as solid. Yield 65%, m.p 250^{0}C.

N'-benzylidene-2-(2-oxobenzo oxazol-3-(2H)-yl)acetohydrazide 4. A mixture of **3** and appropriate aromatic aldehyde in equal amount was refluxed in ETOH for 3 hrs. The excess of solvent was removed under reduced pressure , the ppt formed after cooling was collected by filtration and recrystallized from ETOH to get the desired product[9] .Yield 60% , m.p 284^{0}C.

N-(1-5-dioxo-3-phenyl benzo [1,3]oxazepine-4-yl)-2-(2-oxobenzo oxazol-3(2H)-yl)acetamide 5. A mixture of **4** (1mmol) and Phthalic anhydride (1mmol) were ground with a mortor, mixed, dried and subjected to the MW irradiation for some min. After completion of the reaction mixture was cooled to room temperature and the solid obtained was recrystallized twice from absolute EtOH[10]. Yield 65%, m.p 230^{0}C.

The Schiff's base derivatives **5(a-f)** were confirmed by spectroscopic data and physical method.

Table I – Characterization of compound 5a-f

Compd	R	Mol. Formula	m.p °C	Yield %	Found% (calcd)					
					C		H		N	
5a	2-Chloro	$C_{24}H_{16}N_3O_6Cl$	234	82.2	60.35	(60.37)	3.37	(3.35)	8.83	(8.80)
5b	mesitaldehyde	$C_{27}H_{23}N_3O_6$	232	81.0	66.75	(66.80)	4.78	(94.74)	8.63	(8.66)
5c	2-Chloro5-Nitro	$C_{24}H_{15}N_4O_8Cl$	238	84.7	55.12	(55.11)	2.89	(2.87)	10.69	(10.71)
5d	4-Bromo	$C_{24}H_{16}N_3O_6Br$	226	82.6	55.19	(56.25)	3.09	(3.12)	8.14	(8.20)
5e	2-Nitro	$C_{24}H_{16}N_4O_8$	230	81.4	59.00	(59.01)	3.30	(3.27)	11.50	(11.47)
5f	Furfuraldehyde	$C_{22}H_{15}N_3O_7$	236	83.6	60.94	(60.96)	3.42	(3.46)	9.35	(9.39)

Comp.5a IR (KBr): υ max 1771 (Lactone C=O), 1712 and 1669(C=O ester and amide), 3034 to 2926 (C-H, aromatic),1597-1502(C=C, aromatic), 1301 and 1255(O-C-O and -N-C),1170 (C-O). 1HNMR (300 MHz, DMSO-d6): δ 5.10(s, 2H, CH_2), 6.80-7.20(m, 12H, Ar-H), 11.49(s, 1H, NH), 7.69(O-CH-N) EI-MS: m/Z= 477.5(M+)

Comp.5b IR (KBr): υ max 1777 (Lactone C=O), 1714 and 1651(C=O ester and amide), 3032 to 2920(C-H, aromatic), 1594-1500 (C=C, aromatic), 1HNMR(300 MHz, DMSO-d6): δ 5.4(s, 2H, CH_2), 6.84-7.22 (m, 10H, Ar-H), 11.45(s, 1H, NH), 7.60 (O-CH-N) EI-MS: m/Z= 485(M+)

Comp.5c IR (KBr): υ max 1773 (Lactone C=O), 1709 and 1659(C=O ester and amide), 3034 to 2928(C-H, aromatic), 1598-1511(C=C, aromatic), 1HNMR (300 MHz, DMSO-d6): δ 5.2(s, 2H, CH_2), 6.80-7.02 (m,11H, Ar-H), 11.42 (s, 1H, NH), 7.62 (O-CH-N), EI-MS: m/Z= 522(M+)

Comp.5d IR (KBr): υ max 1772 (Lactone C=O), 1712 and 1657(C=O ester and amide), 3030 to 2926(C-H, aromatic), 1594-1508(C=C, aromatic), 1HNMR (300 MHz, DMSO-d6): δ 5.16(s, 2H, CH_2), 6.74-6.96(m, 12H, Ar-H), 11.43(s, 1H, NH), 7.65 (O-CH-N) EI-MS: m/Z= 512(M+)

Comp.5e IR (KBr): υ max 1770 (Lactone C=O), 1711 and 1653(C=O ester and amide), 3033 to 2920(C-H, aromatic) , 1597-1510 (C=C, aromatic), 1HNMR (300 MHz, DMSO-d6): δ 5.6(s, 2H, CH_2), 6.28-7.20 (m, 12H, Ar-H), 11.59 (s, 1H, NH), 7.69 (O-CH-N) EI-MS: m/Z= 488 (M+)

Comp.5f IR (KBr): υ max 1775 (Lactone C=O), 1715 and 1654(C=O ester and amide), 3032 to 2926(C-H, aromatic), 1590-1512 (C=C, aromatic), 1HNMR (300 MHz, DMSO-d6): δ 5.61(s, 2H, CH_2), 6.47-6.69 (m,11H, Ar-H), 11.42(s, 1H, NH), 7.63 (O-CH-N) EI-MS: m/Z= 433 (M+)

RESULTS AND DISCUSSION

TLC were performed on pre coated sheets with 0.25 mm layer of silica gel of Merk company. The spot was developed with iodine . Melting Points (m.p) were determined by capillary method and are uncorrected. The structure of synthesized compound were confirmed by IR spectral analysis. IR of these compounds showed the appearance of stretching band at1490 -1685 cm^{-1} attributed to the imine C=N group. The Schiff bases are known to react smoothly with acid halides and anhydride to give corresponding cycloaddition products.

It is impressive to note that the absorption band at (1740-1780) cm^{-1} and at (1800-1850) cm^{-1} in the IR spectra of pure Phthalic anhydride have disappeared after the complete formation of 7-membered ring of (1,3) oxazepine. The objective of this work is to synthesize some new seven-membered heterocyclic compounds by using a pericyclic reaction between new imines with cyclic anhydrides.

CONCLUSION

All the six new oxazepines were synthesized by the cycloaddition reaction between appropriate Schiff bases and Phthalic anhydride. Hence there is ample scope in taking up this oxazepine derivatives for further studies as bioactive agents.

Acknowledgement
One of the Authors, Purnima Verma (RGNF) is thankful to UGC, New Delhi for financial assistance to carry out this research work at the Chemistry Department of Lucknow University, Lucknow.

REFERENCES

[1]Thalla N, Rao. D , Ozgen B , Raja N. Chamarathi , *Der Chemica Sinica* , **2012** , 3(4), 808-816
[2]Gulkok Y, Bicer T , Onurdag , Selda O , Sahin F M , Dogruer D S, *Turk J. Chem* , **2012** , 36 , 279-291.
[3]Srikanth.L, Naik U, Jadhav R , Raghunandan N and Rao V J , *International Journal of Pharma and Bio Science* , **2010 ,**4(1) ,
[4]Kodari K K, Chourasia O P, *Heteroletters .org*, **2013** , 3(1) , 49-56
[5]Pandey S and srivastava R S *Pharmacologyonline* , **2009** , 2 , 1048-1074
[6]Hameed A, *Journal of Al-Nahrain university* , **2012** , 15(4) , 47-59
[7]Haiwal R T , *journal of Karbala university* , **2011**, 9(3) , 265-283
[8]Goken E , Serder U, Maria N T , Luis L, L , Antonio E, Erden B ,*Bioorganic and Medicinal Chemistry* , **2010** ,18 6367-6376
[9]Cacic M , Trkovnik M , Cacic H F, *Molecules*, **2006** , 11, 134- 147
[10] Al-Jibory A M, Kareem A ,Al Samarriie A T, *Diyala Journal For Pure Science* , **2013** , 9(1) , 112-119