Volume-3, Issue-7, July-2014 • ISSN No 2277 - 8160

Research Paper | Medical Science

PTSA Catalysed Expeditious Synthesis and Antimicrobial Activities of Dihydro-3, 5-Diphenylisoxazole Derivatives

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ABSTRACT

There is increasing interest in the utility of environmentally benign reagents and particularly solvent-free conditions under microwave irradiation. Chalcone are associated with wide range of biological activities. Chalcone can be modified by the reaction of the substituted benzaldehyde with acetophenone and 10% NaOH under microwave irradiation in domestic oven. This method of synthesis is of great importance and in recent years organic reaction in the absence of solvent has been attracting the synthetic organic chemists because of their simplicity and synthetic value. Organic synthesis without using solvent keeps the environment pollution free by making no use of hazardous solvent like dioxin or strongly acidic and tedious work-up method. This paper describe the use of PTSA as a catalyst in the synthesis of 4,5-dihydro-3,5-diphenylisoxazole derivatives from chalcone and hydroxyl amines hydrochloride under solvent-free condition. The reaction time, yield and 1HNMR spectra are summarized

KEYWORDS : Diphenylisoxazole derivatives , chalcone , hydroxylamines hydrochloride, p-tolunesulphonic acid , solvent-free & microwave energy.

The conventional method available for the title compound is not satisfactory because it requires long reaction times, use of expensive and hazardous solvents and yield are only moderates. Therefore, we have devised a simple and useful method for synthesis of title compound under mild and environmentally safer reaction conditions. Due to its operational simplicity, generality and efficacy this method is expected to have wider applicability in organic synthesis.

With increasing global environmental concerns application of eco-friendly and mineral supported reagents[1], solvent-free reactions[2] and microwave irradiation techniques has increased dramatically in recent years since by doing so use of expensive and hazardous organic solvents and reagents can be avoided significantly.

Microbial infections often produce pain and inflammation. A systematic investigation of this class of heterocycle revealed that isoxazole containing pharmaco-active agents play important role in medicinal chemistry. The reactive intermediate chalcones[3,4] involved in their synthesis also exhibit wide range of biological activities. It has been reported that isoxazolines possess analgesic, anti-inflammatory[5,6] and anti -microbial[7,8]activities. In view of their application, the synthesis of isoxazole continues to be interesting to many synthetic organic chemists[9].

In continuation of our work on heterocycles[10], an attempt has been made for the synthesis of novel 4,5-dihydro-3,5-diphenylisoxazole using chalcone and PTSA as a catalyst.Chalcone can be obtained by the reaction of the substituted benzaldehyde with acetophenone and 10% NaOH under microwave irradiation. This method is of great importance because of their simplicity and synthetic value.[11,12]

The present paper describe the use of PTSA as a catalyst in the synthesis of isoxazole from chalcone under microwave irradiation gives selectively the corresponding isoxazole in enhance yield and short reaction time. The reaction time, yield, and ^{1}HNMR spectra are summarized below. The synthetic sequence leading to the formation of 4,5-dihydro-3,5-diphenylisoxazole derivatives is depicted in Scheme [1].

Experimental section

Melting points were determined in open capillaries and were uncorrected. The progress of the reaction was monitored by TLC. The solvent system used for TLC was a 8:2 mixture of chloroform: methanol. An unmodified domestic household microwave oven (Kenstar OM-34 ECR) operating at 2450 MHz was used at a power output of 300 W for all experiments. IR spectra were recorded in KBr as a Perkin-Elmer BX series FT-IR spectrophotometer..^{1}HNMR ($CDCl_3$) spectra were recorded on Bruker AMX 500 MHz and AC 200 MHz spectrometer using TMS as internal reference. Mass spectra were recorded on a Shimadzu-GCMS 50508. All the solvents used were of analytical grade. The yield and melting point are given in below.

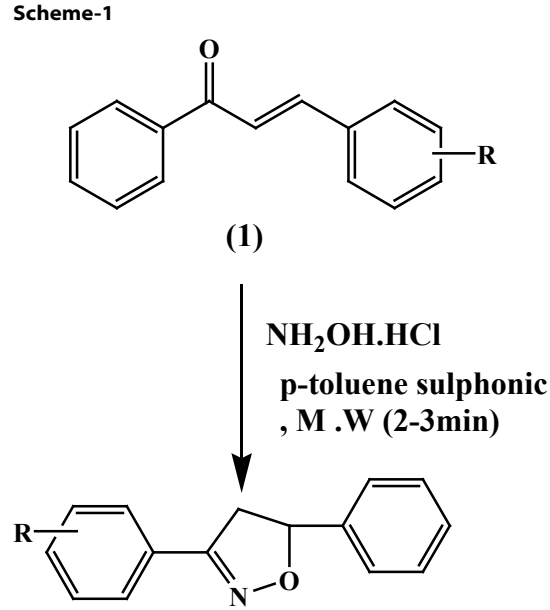
General Procedure :

Thermal synthesis of 4,5-dihydro-3,5-diphenylisoxazole derivatives 2(a-f) :

The chalcone 1 (0.001 mol) and hydroxylamine hydrochloride (0.001 mol) was first dissolved in ethanol . Then reaction mixture was refluxed on water bath at the specified time. The completion of reaction was checked by TLC and after completion of reaction. The reaction-mixture was allowed to attain room temperature, then reaction-mixture was poured on crushed ice. The solid separated was filtered and dried then recrysatallized from Benzene to obtained 2(a-f).

Microwave assisted synthesis of 4,5-dihydro-3,5-diphenylisoxazole derivatives 2(a-f) :A mixture of chalcone 1 (0.001 mol), hydroxylamine hydrochloride (0.001 mol) and p-toluene sulphonic acid (PTSA) as a catalyst in a catalytic amount taken in a beaker and was irradiated in microwave oven at 150 watt for the specified period (2-3 min) given below .The completion of reaction was checked by TLC and after completion of reaction. The reaction-mixture was allowed to attain room temperature, and then reaction-mixture was poured on crushed ice. The solid separated was filtered and dried then recrysatallized from Benzene to obtained 2(a-f).

Scheme-1



Compound	R	MWI (sec)	Thermal (hour)
2a	H	60	4
2b	2-Cl	80	3
2c	4-OCH_3	70	5
2d	4-NO_2	60	4
2e	4-$N(CH_3)_2$	90	5
2f	3-OH,4-OCH_3	90	3

3,5-Diphenyl-4,5-dihydro-isoxazole (2a) :
Yield 76 % (MWI), 46% (Thermal); m.p. 237 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.22(d,2H,-CH_2-), 4.5(t,1H,-CH-)7.1-7.6 (m,10H,Ar-H);EIMS m/z, 237 (M^+). Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27; O, 7.17.

3-(2-Chloro-phenyl)-5-phenyl-4,5-dihydro-isoxazole (2b) :
Yield 86 % (MWI), 47% (Thermal); m.p. 155 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.22(d,2H,-CH_2-), 4.5(t,1H,-CH-),7.2-7.4(m,9H,Ar-H) ;EIMS m/z, 257 (M^+). Anal. Calcd for $C_{15}H_{12}ClNO$: C, 69.91; H, 4.69; Cl, 13.76; N, 5.43; O, 6.21.

3-(2-Methoxy-phenyl)-5-phenyl-4,5-dihydro-isoxazole (2c) :
Yield 80 % (MWI), 50% (Thermal); m.p. 220 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.22(d,2H,-CH_2-), 4.5(t,1H,-CH-),3.78 (s,3H,Ar-OCH_3)6.8-7.2(m,9H,Ar-H) ;EIMS m/z, 253 (M^+). Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.87; H, 5.97; N, 5.53; O, 12.63.

3-(2-Nitro-phenyl)-5-phenyl-4,5-dihydro-isoxazole (2d) :
Yield 79 % (MWI), 52% (Thermal); m.p. 260 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.32(d,2H,-CH_2-), 4.4(t,1H,-CH-),7.1-8.6 (m,9H,Ar-H) ;EIMS m/z, 268 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44; O, 17.89.

Dimethyl-[2-(5-phenyl-4,5-dihydro-isoxazol-3-yl)-phenyl]-amine (2e) :
Yield 82% (MWI), 57% (Thermal); m.p. 168 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.30(d,2H,-CH_2-), 4.20(t,1H,-CH-), 2.8(s,6H,Ar-N,$N(CH_3)_2$ 6.6-.4(m,9H,Ar-H);EIMS m/z, 268 (M^+). Anal. Calcd for $C_{17}H_{18}N_2O$ C, 76.66; H, 6.81; N, 10.52; O, 6.01.

5-Methoxy-2-(5-phenyl-4,5-dihydro-isoxazol-3-yl)-phenol (2d) :
Yield 84% (MWI), 62% (Thermal); m.p. 168 ^{0}C; ^{1}H NMR (400 MHz,DMSO-d6), 3.33(d,2H,-CH_2-), 4.5(t,1H,-CH-),3.9(s,3H,Ar-OCH_3) 5.0(S,1H,Ar-OH)6.6-7.0(m,8H,Ar-H) ;EIMS m/z, 269 (M^+). Anal. Calcd for $C_{17}H_{18}N_2O$: C, 71.36; H, 5.61; N, 5.20; O, 17.82

Antimicrobial Screening
All the compound screened for antibacterial activity against Bacillus subtilis, staphylococcus aureus, Escherichia coli and pseudomonas auroginosa at 50 and 100 g/ml concentration using disc diffusion method. The test solutions were prepared in DMF.

Acknowledgement
The authors would like to express their gratitude and thanks to Department of Chemistry ,DIT , School of Engineering (Part of AMITY Education Group) Greater Noida for necessary facilities to carry out this research work and RSIC, CDRI Lucknow for spectral analysis.

REFERENCES

1.Clark JH, Cullen SR,Barlon SJ &Basteck TW, J Chem. Soc. Perkin Trans,2,1994,1117. | 2. (a) Deloude Land Laszlo P ,J Org.Chem.,61,1996,6360. | (b) Verma RS & DahiyaR ,Synlett,1997,857. | 3. dimmock Jonuthan R & Manavathu Eliaks,Chem.Abstr.132,2000,107880 n. | 4. Abdel-Rahman TM, Bull Chem Farm, 1998,Chem.Abstr.,132,2000,93276 B. | 5. Rani, P., Srivastava, V.K. and Kumar, A. 2003. Isoxazolinyl Derivatives of Anthranilic Acid as Anti-Inflammatory Agents.Ind. J. Chem. 42B, 1729-1733. | 6. Habeeb, G.A., Rao, P.N.P. and Kanus, E.E. 2001. Design and Synthesis of 4,5-Diphnyl-4-isoxazoline: Novel Inhibitors of Cyclooxygenase-2 with Analgesic and Anti-inflammatory Activity. J. Med. Chem. 44, 2921-2927. | 7. Goda, F.E., Maarouf, A.R, and EL-Bendary, E.R. 2003. "Synthesis and Antimicrobial Evaluation of New Isoxazole and PyrazoleDerivaties."S. Pharm. Journal. 11, 111-117. | 8. Diadone, G., Raffa, D., Maggio, B., Plescia, F., Curuli, VMC., Mangano, N.G. and Caruso, A. 2007. Synthesis and Pharmacological Activities of Novel-3-(Isoxazol-3-yl)-Quinazolin-4(3H)-one.Archive Pharmazie. 340A, 163-164. | 9. (a) Penning TD,Talley JJ, Bertenshaw SR,Cartar JS, Collins PW ,Doctor S,Graneto MJ, Lee LF, Malecha JW,Miyashiro JM ,rogers RS, Rogier DJ, Yu SS, Anderson GD, burton EG,CogburnJN,Gregory SA, Koboldt CM, Perkins WE .Seinbert K , Veenhuizen AW , Zhang YY & Isakson PC, J.Med.Chem. 40,1997,1347. | (b) ZhihuaS,GuanJ,Michael FP ,Kathy M,Michael WP, William MV,MonicaS,MicheleS,Dave RM & Dennis C, Bio Org.Med.Chem.Lett, 10,2000,601. | 10. Elgemeie GH &Metwally NH,J.chem Res (S) ,6,1999,384. | 11. R.Perrin, R. Lamartine,M.Perrin and A.Thozet , in organic solid state Chemistry, G.R. Desiraju ,Ed.Elsevier Amsterdam,1987,217. | 12. N.B.singh , R.J. singh and N.P. Singh,Tetrahedron,50,1994,6441. |