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Microwave Assisted Synthesis of Some New 1,5-benzodiazepines from Chalcones

Archana P Shetye[1*], Pawar MG[2]

[1]Priyadarshini Indira Gandhi College of Engineering, Nagpur, India
[2]Yeshwant Mahavidyalaya, Nanded, India

ABSTRACT

Some new 1,5-benzodiazepines were synthesized by using 2-amino aniline and α, β-unsaturated ketones such as chalcones by conventional as well as microwave method. The microwave method is eco-friendly, non-hazardous, completes in short time, and gives better yield.

Keywords: 1,5-benzodiazepines, 2-amino aniline, Chalcone, Microwave

INTRODUCTION

Chalcone derivatives are found to be useful in synthesis of various heterocyclic compounds such as flavonones, flavones, flavnols, benzodiazepines, etc. Benzodiazepines are found to possess wide biological activities. Benzodiazepines, the most widely prescribed psycholtropic drugs, are often used in patients with depressive disorders. The antidepressant efficiency of benzodiazepines [1] which are GABA receptor agonist is proved to be consistent with the GABA theory of depression. The clinical use of benzodiazepines as antianxiety agent and their therapeutic use were reported [2]. There has been long standing debit regarding whether benzodiazepines possess analgesic properties [3] that may have different effects on mood and alertness. The clinical treats suggest a potential role for treatment with benzodiazepines for acute muscle spam, concomitant chronic pain, anxiety and neuropathic pain. Benzodiazepines also have commercial use in photographs [4] and as anti-inflammatory agents [5]. Various 1,5-benzodiazepines derivatives have been reported to possess cancero static activity [6]. A series of eleven new 9H-bis[1,2,4]triazolo [4,3-9:3',4'-d]1,5-benzodiazepine were synthesized and tested *in vitro* in order to evaluate their cytotoxic and anti-HIV-I properties [7]. Different substituted benzodiazepines act as anticonvulsant agents [8]. 1,5-benzodiazepines derivatives are very important and useful compounds in organic and pharmaceutical chemistry. Synthesis of benzodiazepines has been intensely studied and numerous procedures found. In this work, we report the synthesis of 1,5-benzodiazepine by the reaction of chalcone and 2-amino aniline by conventional as well as microwave irradiation method. This microwave method gives smooth reaction condition, short reaction time (2-3 min), no side products are formed and easy product isolation take place.

MATERIALS AND METHODS

Experimental

All melting points were determined in open capillary and are uncorrected. The IR spectra were recorded on Perkin-Elmer 157 spectrometer. ^{1}H NMR was recorded on Aveanue-300 and Brucker WM 400 FT MHz instrument using TMS as an internal standard. The reactions were monitored on TLC and the spots were located in iodine chamber.

General procedure for synthesis of 2(2′-hydroxy-4′-methyl-5′-chloro phenyl)-4-(2′hydroxy phenyl) 1,5-benzodiazepines by conventional method

A mixture of 1-(2′-hydroxy-4′-methyl-5′-chloro phenyl) 3-(4′-chloro phenyl)-2-propen-1-one (0.01 mol) and 2-amino aniline (0.012 mol) and piperidine in ethanol (15 ml) were refluxed on boiling water bath for 15-35 min. Half of the solvent was evaporated and solution cooled to room temperature. The separated solid was filtered, washed with water and crystallized from ethanol. M.P. and analytical data given in Table 1.

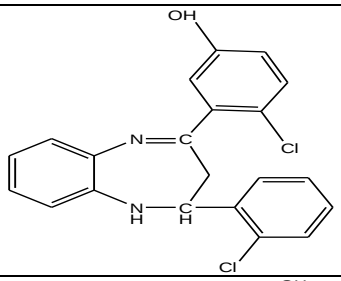
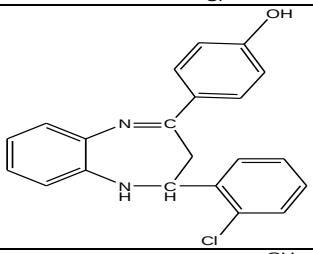
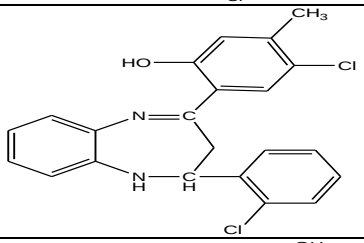
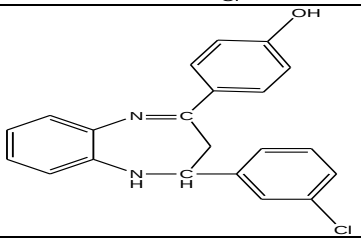
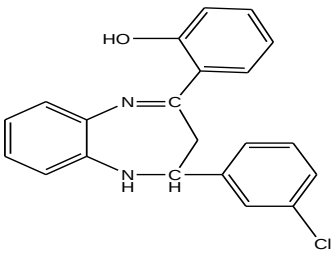
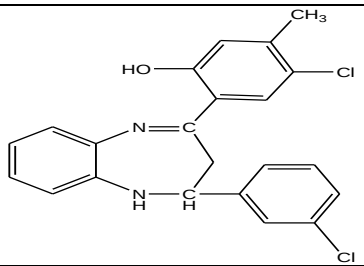
General procedure for synthesis of 2(2′-hydroxy-4′-methyl-5′-chloro phenyl)-4-(2′hydroxy phenyl) 1,5-benzodiazepines by microwave method

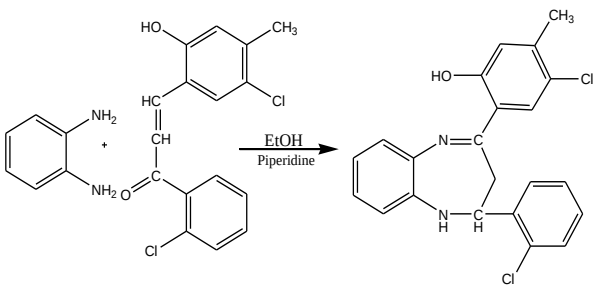
A mixture of 1-(2′-hydroxy-4′-methyl-5′-chloro phenyl) 3-(4′-chloro phenyl)-2-propen-1-one (0.01 mol) and 2-amino aniline (0.012 mol) and piperidine in ethanol (15 ml) were taken in a beaker capped with watch glass and placed in microwave oven and irradiated for 2 min. (1+1 min) with an interval of 4-5 min. The reaction mixture cool to room temperature and treated with cold water. Solid separated out which was washed with cold water, dried and crystallized from ethanol. M.P. and mixed M.P. with sample prepared by conventional method was undepressed (Scheme 1).

Spectral data of 2(2'-hydroxy-4'-methyl-5'-chloro phenyl)-4-(2'hydroxy phenyl) 1,5-benzodiazepines

IR ν_{max} cm^{-1}: 3342 (OH), 3348 (NH), 1620 (C=N), 3047 (Ar-H), 1591, 1494 (C=C Aromatic), 3062 (=CH).
^{1}HNMR: δ 3.12 (dd, 1H, HA), 3.83 (dd, 1H, HB), 4.71 (dd, 1H, HX), 7.1 (s, 1H, NH), 7.8-8.7 (m, 10H, Ar-H), 12 (s, 1H, OH).

Table 1: M.P. and analytical data

S. No.	Structure	M.P. (°C)	Appearance	% Yield	Elemental Analysis Found (Required)
1		138	Yellow	58	20.12 (18.97)
2		182	Pale yellow	60	10.76 (10.49)
3		138	Yellow	55	19.27 (18.51)
4		76	Yellow	50	10.76 (10.49)
5		76	Yellow	60	10.52 (10.92)
6		137	Yellow	55	18.27 (18.73)



Scheme 1: Synthesis of 1,5-benzodiazepines

RESULTS AND DISCUSSION

We have synthesized some new substituted 1,5-benzodiazepines by using α, β-unsaturated ketones such as chalcones and 2-amino aniline by using ethyl alcohol and piperidine as solvent. All 1,5-bezodiazepines were synthesized by conventional as well as microwave irradiation method. In conventional method, chalcones and 2-amino aniline dissolved in piperidine in ethanol and the reaction mixture was refluxed in boiling water bath for 35 min. On cooling, solid separated out which was filtered, washed with water and crystallized from ethanol. In microwave irradiation method, the same reactants and solvent were taken in a beaker capped with watch glass and irradiated for 2 min with interval of 4 to 5 min. The structure of all synthesized compounds was confirmed by halogen analysis and spectra.

CONCLUSION

Newly synthesized 1,5-benzodiazepines were prepared by conventional as well as microwave irradiation method. Microwave assisted synthesis gave same products in short time, less solvent use and excellent yield. Hence under the framework of green chemistry, we have followed an environmentally benign synthesis of 1,5-benzodiazepines.

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