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Journal of Chemical and Pharmaceutical Research, 2013, 5(5):37-40

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

One pot Solvent-free synthesis of 1,5-benzodiazepine derivatives

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ABSTRACT

Zinc oxide has been used for the synthesis of 1,5-benzodiazepines from o-phenylenediamine and ketones. This method is simple, effective and environmentally friendly and gives better yields.

Keywords: 1,5-benzodiazepines, Zinc oxide, solvent free condition

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INTRODUCTION

Benzodiazepines are biologically active compounds with anti-inflammatory [1], antianxiety, anticonvulsant, and hypnotic activity [2,3]. Due to its wide biological utility, the syntheses of these types of compounds have gained much importance in last few years. Benzadiazepines have been synthesized by the condensation of *o*-phenylenediamines with α,β-unsaturated Diffpounds, β-haloketones or ketones. is conrs have been used for this type of condensation which majorly includes like lead nitrate [4], L-proline [5], BF_3-etherate [6], polyphosphoric acid [7], $NaBH_4$ [8], SiO_2 [9], $MgO/POCl_3$ [10], acetic acid under microwave conditions [11] and in ionic liquids [12]. Many of these processes suffer from one or more limitations, such as long reaction times, occurrence of several side reactions, drastic reaction conditions, low yields, and tedious work-up procedure. Therefore, the search continues for a better catalyst for the synthesis of 1,5-benzadiazepines in terms of mild reaction conditions, operational simplicity, economic viability and selectivity.

We are herewith reporting simple, efficient and practical method for the synthesis of 1,5-benzodiazepines using ZnO catalyst.

Initially, we studied the catalytic properties of Zinc Oxide for the synthesis of 1,5-benzodiazepines (3a-3h)) using *o*-phenylenediamine (1) and the ketone (2) substrates (Scheme –1) and varying the mol % of Zinc Oxide (Table 1). Among the results obtained, use of 20 mol % gave better yield (94%) for synthesis of 3a.

We investigated the reaction of number of ketones with *o*-phenylenediamine to get the corresponding 1,5-benzodiazepines (Table 2). All synthesized derivatives were characterized using mass and ^{1}H NMR.

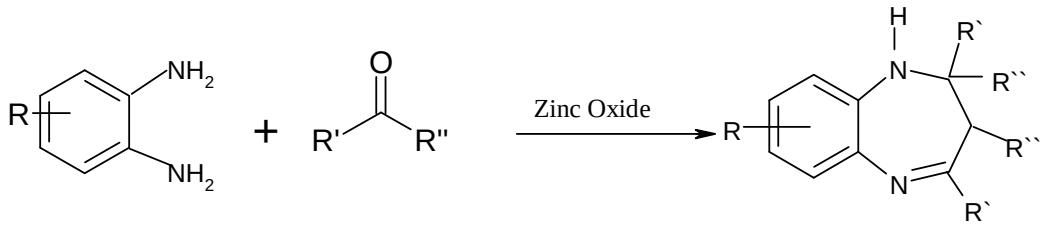
In conclusion, we have developed an efficient and simple alternative for the preparation of substituted 1,5-benzodiazepines *via* solvent-free condensation of *o*-phenylenediamine and the ketone using zinc oxide catalyst.

General procedure for preparation of 1,5-benzodiazepines:
A mixture of *o*-phenylenediamine (1mmol), ketone (2mmol) and Zinc oxide (0.1mmol) was stirred at 80°C untill completion of the reaction (as indicated by TLC). Then the reaction mixture was poured in water.The solid was filtered and dried. The crude compound was purified by silica gel column chromatography.

Spectral data of compound 3a: yellow solid, mp 137-139°C ^{1}HNMR ($CDCl_3$): 1.29 (S, 6H), 2.22 (S, 2H), 2.33 (S, 3H), 3.08 (br S, 1H, NH), 6.69-7.26 (M, 4H arom); MS: 189 (M-H), 190,

All the synthesized compounds were characterized using mass, and ^{1}H NMR. Also the melting points of synthesized compounds were compared with the corresponding reported melting points in literature [8,14,15].

Scheme 1

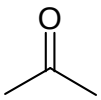
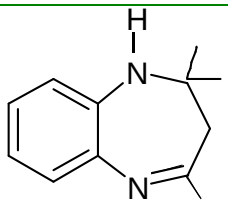
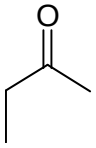
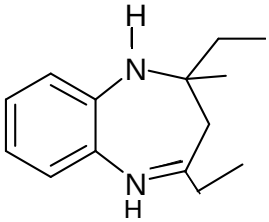
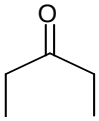
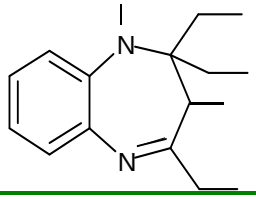


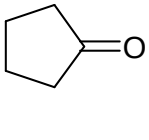
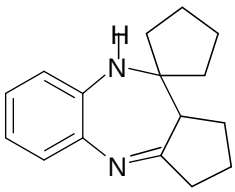
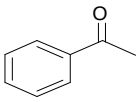
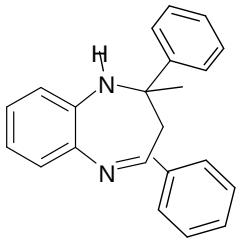
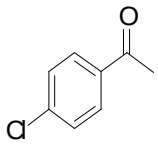
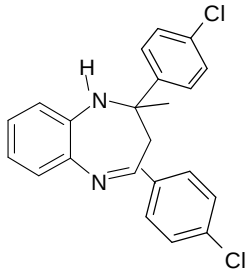
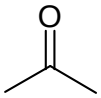
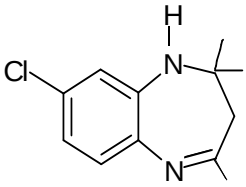
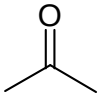
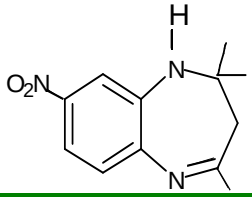
1 **2** **3a-3i**

Table 1. Optimization of reaction conditions and the concentration of ZnO for the synthesis of 3a:

Mol % of ZnO	Reaction time (min)	Yield %
5	120	85
10	120	90
15	100	90
20	100	94

Table 2. Zinc Oxide Catalyzed synthesis of 2,3-dihydro-1 H -1,5-benzodiazepines

	Ketone	Product	Time	M.P.^{oC} Found	M.P.^{oC} Reported [Ref]	Yield %
3a			100	137-139	136-138 [14]	94
3b			110	198-140	137-139 [15]	93
3c			100	144-145	143-144 [08]	94

3d			100	135-136	137-138 [14]	93
3e			110	155-156	150-152 [15]	93
3f			100	162-163	160-161 [08]	93
3g			100	91-92	90-92 [15]	94
3h			100	110-111	111-112 [15]	93

REFERENCES

[1] J. R. De Baun, F. M. Pallos and D. R. Baker, US Patent 3, 978, 227, **1976**; *Chem. Abstr*. 1977, 86, 5498d.
[2] (a) H. Schultz, Benzodiazepines (Springer: Heidelberg, **1982**);
[3] (b) R.K. Smiley, Comprehensive Organic Chemistry; (Pergamon: Oxford, **1979**)
[4] (c) Landquist, J.K. Comprehensive Heterocyclic Chemistry (Pergamon: Oxford, **1984**); Vol. 1,166, 170.
[5] L. O. Randall, B. Kappel, Benzodiazepines; S.Garattini, E.Mussini, (Raven Press: New York, **1973**).
[6] R. Kumar, P. Chaudhary, S. Nimesh, A. K. Verma and R.Chandra Green chemistry 8 (**2006**) 519.
[7] *V. Sivamurugan, K. Deepa, M. Palanichamy and V. Murugesan, Synthetic Commun. 34 (***2004***) 3833.*
[8] J. A. Herbert and L. H. Suschitzky, *J. Chem. Soc., Perkin Trans.* 1 (**1974**) 2657.
[9] H. R. Morales, A. Bulbarela, and R.Contreras, *Heterocycles*, 24(**1986**)135.
[10] D. I. Jung, T. W. Choi, Y. Y. Kim, I. S. Kim, Y. M. Park, Y. G.Lee, and D. H. Jung, *Synth. Commun.* 29 (1999) 1941.
[11] M. S. Balakrishna and B. Kaboudin, *Tetrahedron Lett.*, 42 (**2001**)1127.
[12] M. Curini, F. Epifano, M. C. Marcotullio and O. Rosati, *Tetrahedron Lett.*42(**2001**) 3193.

[13] P. Minothora, S. S. Julia, and A. T. Constantinos, *Tetrahedron Lett.* 43 (**2002**) 1755.
[14] D. V. Jarikote, S. A. Siddiqui, R. Rajagopal, D. Thomas, R. J. Lahotiands and K. V. Srinivasan, *Tetrahedron Lett.* 44(**2003**) 1835.
[15] R. Lenarsic, M. Kocevar, S. Polanc, *J. Org. Chem.* 64 (**1999**) 2558.
[16] J. S. Yadav, B.V. S. Reddy, S. Praveen Kumar, K. Nagaiah, *Synthesis (***2005**) 480.
[17] J. S.Yadav, B. V. S. Reddy, S. Praveen Kumar, K. Nagaiah and P.S Saiprasad, *Synthesis* (**2004**) 901.
[18] A. Hegedu, Z. Hell and A. Potor, *Catalysis Letters* 105(**2005**) 229