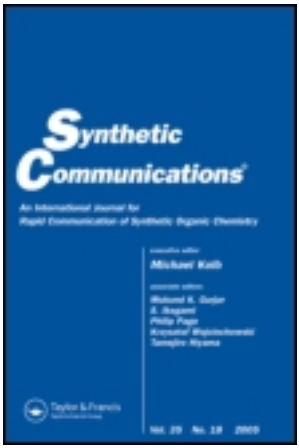


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

[(L)Proline]$_2$Zn Catalysed Synthesis of 1,5-Benzodiazepine Derivatives Under Solvent-Free Condition

V. Sivamurugan [a], K. Deepa [a], M. Palanichamy [a] & V. Murugesan [a]
[a] Department of Chemistry, Anna University, Chennai, 600 025, India
Published online: 10 Jan 2011.

SYNTHETIC COMMUNICATIONS®
Vol. 34, No. 21, pp. 3833–3846, 2004

[(L)Proline]$_2$Zn Catalysed Synthesis of 1,5-Benzodiazepine Derivatives Under Solvent-Free Condition

V. Sivamurugan, K. Deepa, M. Palanichamy, and V. Murugesan*

Department of Chemistry, Anna University, Chennai, India

ABSTRACT

This communication demonstrates that a novel Lewis acid complex, Zn[(L)proline]$_2$, catalysed one pot synthesis of 1,5-benzodiazepine derivatives under solvent-free conditions. The efficiency of the catalyst has been examined by conventional method and microwave irradiation technique. 1,5-Benzodiazepine is obtained in moderate to good yield (up to 93%) in all the reactions within a shorter reaction time under microwave irradiation. The recycling ability of the catalyst has also been evaluated. The catalyst is reusable up to five times without appreciable loss of its catalytic activity.

Key Words: 1,5-Benzodiazepine; Lewis acid; Multi component reaction; One-pot condensation; Solvent-free; Zn-proline.

*Correspondence: V. Murugesan, Department of Chemistry, Anna University, Chennai 600 025, India; Fax: +91-44-22200660; E-mail: v_murugu@hotmail.com.

DOI: 10.1081/SCC-200034752 0039-7911 (Print); 1532-2432 (Online)

INTRODUCTION

Benzodiazepines are pharmacologically active compounds finding application as antiinflammatory,[1] antianxiety, anticonvulsant, and hypnotic agents.[2,3] The synthesis of 1,5-benzodiazepines is associated with a condensation of *o*-phenylene diamine with aryl/alkyl ketone or α, β-unsaturated carbonyl compounds,[4] or β-haloketones[5] in the presence of conventional acid catalyst, Lewis acid catalysts like BF_3-etherate,[6] $NaBH_4$,[7]and polyphosphoric acid.[8] Furthermore, the synthesis of 1,5-benzodiazepine derivatives catalysed by $MgO/POCl_3$,[9] $Yb(OTf)_3$,[10] ionic liquid,[11] and sulfated zirconia[12] has been reported recently.

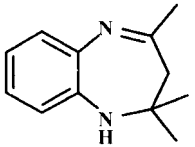
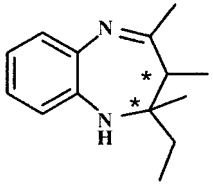
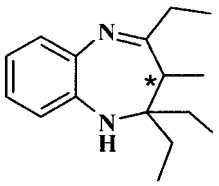
In recent years, organic synthesis under solvent-free conditions is of great interest in view of a flowering environmental awareness.[13a,b] Among the solvent-free techniques, microwave accelerated organic synthesis is an effective route proposed during the last decade due to drastic reduction of reaction time, minimize cumbersome workup, and improved yields.[14a,b] After a few initial attempts with Al_2O_3/P_2O_5[15] or AcOH,[16] we investigated the possibility of Zn[(L)proline]$_2$, a recyclable and inexpensive Lewis acid complex, in the synthesis of 1,5-benzodiazepine derivatives under solvent-free conditions assisted with microwave irradiation.

Symmetrical and asymmetrical alkyl ketones, alicyclic ketones, and substituted aryl ketones have been used for the synthesis of 1,5-benzodiazepine derivatives employing Zn[(L)proline]$_2$ complex. However, aryl-1,2-diamine is the unchanged substrate in all the reactions. In all the reactions 5 mmol of *o*-phenylene diamine have been condensed with 11 mmol of ketone in the presence of 0.2 mmol of the catalyst. In order to evaluate the catalytic activity of the catalyst, the reactions were carried out by conventional heating and microwave irradiation. The progress of the reactions was monitored by TLC analysis. After completion of reaction, the reaction mixture was diluted with 100 mL of CH_2Cl_2 and the product was separated by simple filtration. The excess solvent was removed by evaporation and purified through column chromatography, and the product was obtained with acceptable purity.

The catalyst is soluble in water, sparingly soluble in methanol, ethanol, and THF, and insoluble in dichloromethane and other nonpolar solvents. Thus, the solubility nature of the catalyst can facilitate the separation of products from the catalyst. The used catalyst can be recycled and used for the next reaction without any further purification.

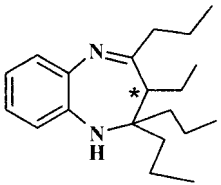
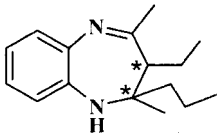
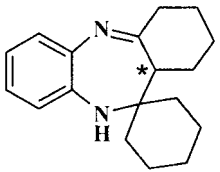
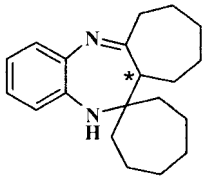
From Table 1, it is observed that microwave-irradiated reactions have afforded good yield within shorter reaction time than conventional method.

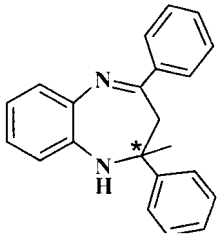
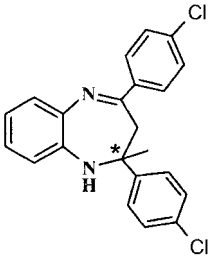
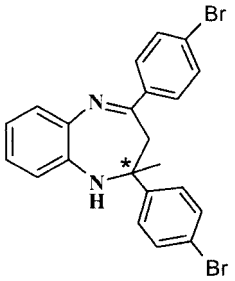
Table 1. Synthesis of 1,5-benzodiazepine derivatives.

			Conventional		Microwave irradiation	
Entry	Ketone	Product[a]	Time[b] (hr)	Yield[c] (%)	Time[b] (min)	Yield[c] (%)
a	Acetone		2	88	2	93
b	2-Butanone		2	85	3	90
c	3-Pentanone		2	80	3	92

(*continued*)

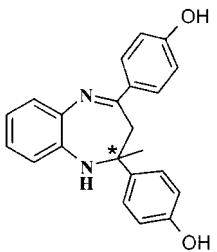
Table 1. Continued.

Entry	Ketone	Product[a]	Conventional		Microwave irradiation	
			Time[b] (hr)	Yield[c] (%)	Time[b] (min)	Yield[c] (%)
d*	4-Heptanone		2.5	80	3	89
e	Methyl-n-propyl ketone		1.5	85	2	93
f	Cyclohexanone		2.5	83	4	90
g	Cycloheptanone		3	80	4	85

h	Acetophenone		2	85	3	90
i*	p-Chloro acetophenone		1.5	88	2	92
j*	p-Bromo acetophenone		1.5	85	2	90

(*continued*)

Table 1. Continued.

Entry	Ketone	Product[a]	Conventional		Microwave irradiation	
			Time[b] (hr)	Yield[c] (%)	Time[b] (min)	Yield[c] (%)
k*	4-Hydroxy acetophenone		2.5	80	3	92

[a]The products were confirmed by elemental analysis, UV-Visible, FTIR, ^{1}H NMR, and MS spectral analysis and compared with reported literature.
[b]The reaction time monitored by TLC technique.
[c]Isolated yield after column chromatography (silica gel 100–200 mesh size; eluent: n-hexane : ethyl acetate 80 : 20).
*New compounds.

For all the reactions, 325 w (≈50% of MW power), which is 50% less than the literature reported values, has been used to obtain moderate to good yield.[16] This demonstrates clearly that $[(L)proline]_2Zn$ complex effectively catalyses 1,5-benzodiazepine synthesis.

The catalytic efficiency has been evaluated from the recycling ability of the catalyst. The reaction of *o*-phenylene diamine with acetone in the presence of 0.2 mmol of the catalyst has been taken as a model reaction for recycling studies. The reaction has been carried out by conventional heating and microwave irradiation. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with CH_2Cl_2 (5×20 mL) until complete removal of organic components. The catalyst was dried in vacuum for 2 hr at 60°C and used for the next cycle. Thus, the same catalyst was reused for six cycles. It is found that the catalyst does not lose its activity up to five cycles. The reduction of yield in the sixth cycle is due to the decomposition of the metal complex. The reaction time and yield of the product for different cycles are listed in Table 2.

The present investigation revealed that $Zn[(L)proline]_2$ complex is found to be a viable catalyst for the synthesis of 1,5-benzodiazepine derivatives. This catalyst can be used for a wide range of ketones. $Zn[(L)proline]_2$ complex assisted microwave-irradiated reactions afford moderate to good yield. This complex exhibits good catalytic activity even in low MW power (≈325 w) and can be used up to five cycles without appreciable loss of catalytic activity.

Table 2. The catalyst recycling studies.[a]

Catalyst recycle	Conventional		Microwave irradiation	
	Time (hr)[b]	Yield (%)[c]	Time (min)[b]	Yield (%)[c]
I	2	90	3	92
II	2	90	3	90
III	2	85	3	90
IV	2	83	3	88
V	2	80	3	85
VI	2	75	3	76

[a]Model reaction: *o*-phenylene diamine with acetone in the presence of 0.2 mmol of catalyst.
[b]Reaction progress monitored by TLC analysis.
[c]Isolated yield.

EXPERIMENTAL

Materials and Methods

All the materials used in this study were of pure quality and purchased from E-merck (Germany). The melting point of the products was determined on Raga hot stage apparatus and were uncorrected. The UV-visible spectra of the products were recorded in a Shimadzu (model: UV-1601) UV-Visible spectrophotometer. The FTIR spectra of the products were recorded on a Nicolet 360 FTIR using KBr pellet technique. ^{1}H NMR spectra were recorded on a JEOL GSX-400 spectrometer at ambient temperature using TMS as internal standard and $CDCl_3$ as solvent. The data were recorded as chemical shift in ppm from the internal standard. The elemental analysis of the derivatives was carried out in a Heraeus CHNO rapid analyzer. The mass spectra of all the products were recorded on a Finnigan Mat 8230MS spectrometer.

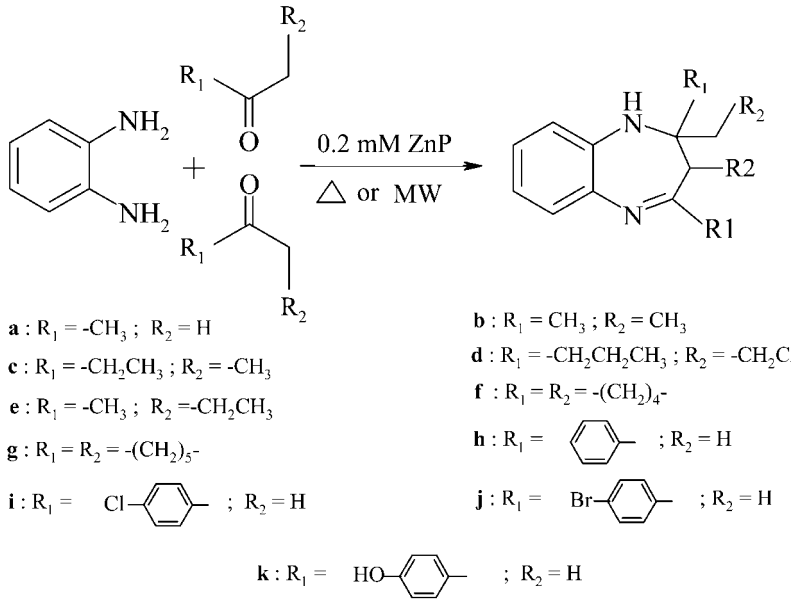
Synthesis of Bis[(L)Prolinato-N, O]Zn Complex

Twenty mmol of (L)proline was dissolved in 50 mL absolute ethanol containing 20 mmol potassium hydroxide and stirred well for 15 min. In order to maintain the metal to ligand ratio 1 : 2, 10 mmol of $Zn(NO_3)_2 \cdot 6H_2O$ was dissolved in a small quantity of double distilled water and this solution was added in drops to the solution of (L)proline. The contents were vigorously stirred at room temperature for 6 hr. Zn[(L)proline]$_2$ complex was obtained as a white solid. It was filtered and dried at 70°C in vacuum for 6 hr. Yield: 94%. FT IR (ν cm^{-1}): 3206, 2995, 1605, 1516, 1403, 1239, 825, and 533. Elemental composition ($C_{10}H_{16}N_2O_4Zn$). Calc: C, 40.91; H, 5.49; N, 9.54; O, 21.80%. Found: C, 40.74; H, 5.60; N, 9.30; O, 21.70%.

Synthesis of 1,5-Benzodiazepine Derivatives

Conventional Method

A mixture of 5 mmol of *o*-phenylene diamine and 11 mmol of acetone was thoroughly mixed with 0.2 mmol of the catalyst and adsorbed on alumina (neutral). The alumina supported mixture was taken in a 15 mL clean stainless steel autoclave and thermostated at 100°C for 2 hr. After completion of the reaction the mixture was diluted with CH_2Cl_2 and the product was separated



Scheme 1.

by simple filtration. The alumina-supported catalyst was washed thoroughly until complete removal of the product. The catalyst was dried in vacuum at 70°C for 6 hr and reused for the next reaction without any further purification. The excess solvent from the product was removed by rotary evaporator. The product was purified by column chromatography (*n*-hexane to ethyl acetate ratio = 80 : 20) and recrystallized from ethanol. The product was obtained as a yellow crystalline solid. The same procedure was followed for other reactions (Sch. 1). The reaction time and yield for all the reactions are presented in Table 1.

Microwave Irradiation

A mixture of 5 mmol of *o*-phenylene diamine and 11 mmol of ethyl methyl ketone was thoroughly mixed with 0.2 mmol of catalyst and adsorbed on alumina (neutral). The alumina-supported mixture was taken in an open Erlenmeyer flask (100 mL) and irradiated using a household microwave oven (model: IFB 17PM 1S) with a power range of 325 w and a pulse of 15 seconds. The progress of the reaction was monitored by TLC (silica gel

precoated plate; *n*-hexane to ethyl acetate ratio = 75 : 25). After completion of the reaction, the mixture was diluted with CH_2Cl_2 and the product was separated by column chromatography (*n*-hexane to ethyl acetate ratio = 80 : 20) and recrystallized from ethanol. The same procedure was adopted for all the reactions (Sch. 1). The reaction time and yield are presented in Table 1.

Spectral Characterization of the Products (a–k)

2,2,4-Trimethyl-2,3-dihydro-1*H*-1,5-benzodiazepine (a). Yellow solid. M.p.: 137–139°C (from ethanol/hexane = 9 : 1). UV-Visible (λ_{max}, nm): 458, 313, 260. FTIR spectrum (KBr, cm^{-1}): 3350 (N-Hstr), 2980 (alkyl C-Hstr), 1625 (C=Nstr), 1520(aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 7–7.25 (m, 4H, Ar-H), 3.5 (br, s, 1H, N-H), 3 (s, 2H, N=C–CH_2), 2.5 (m, 3H, N=C–CH_3), 1.50–1.75 (s, 6H, $2CH_3$). $C_{12}H_{16}N_2$ (188.13) Calcd.: C, 76.56; H, 8.57; N, 14.88. Found: C, 76.25; H, 8.40; N, 14.5. MS: m/z $M^+ = 188$.

2-Ethyl-2,3,4-trimethyl-2,3-dihydro-1*H*-1,5-benzodiazepine (b). Yellow solid. M.p.: 139–141°C (from ethanol/hexane = 9 : 1). UV-Visible (λ_{max}, nm): 486, 458, 304, 263. FTIR spectrum (KBr, cm^{-1}): 3340 (N-Hstr), 2975 (alkyl C-Hstr), 1635 (C=Nstr), 1530 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 7–7.25 (m, 4H, Ar-H), 3.75 (br, s, 1H, N-H), 2.85 (q, 1H, N=C–$\underline{CH}$–CH_3), 2.5 (s, 3H, N=C–CH_3), 1.75 (d, 3H, N=C–CH-$\underline{CH_3}$), 1.50 (s, 3H, N–C–CH_3), 1.25 (q, 2H, $\underline{CH_2}$–CH_3), 0.98 (t, 3H, CH_2–$\underline{CH_3}$)·$C_{14}H_{20}N_2$ (216.33) Calcd.: C, 77.73; H, 9.32; N, 12.95. Found: C, 77.50; H, 9.50; N, 12.75. MS: m/z $M^+ = 216$.

2,2,4-Triethyl-3-methyl-2,3-dihydro-1*H*-1,5-benzodiazepine (c). Yellow solid. M.p.: 145°C (from ethanol). UV-Visible (λ_{max}, nm): 354, 304, 279, 260. FTIR spectrum (KBr, cm^{-1}): 3330 (N-Hstr), 2980 (alkyl C-Hstr), 1640 (C=Nstr), 1535 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.9–7.25 (m, 4H, Ar-H), 3.8 (br, s, 1H, N-H), 2.85 (q, 1H, N=C–$\underline{CH}$–CH_3), 2 (d, 3H, N=C–CH–$\underline{CH_3}$), 1.6–1.3 (m, 6H, $\underline{CH_2}$–CH_3), 1.2-0.95 (m, 9H, CH_2–$\underline{CH_3}$). $C_{16}H_{24}N_2$ (244.38) Calcd.: C, 78.64; H, 9.90; N, 11.46. Found: C, 78.50; H, 10.10; N, 11.35. MS: m/z $M^+ = 244$.

3-Ethyl-2,2,4-tri-*n*-propyl-2,3-dihydro-1*H*-1,5-benzodiazepine (d). Yellow solid. M.p.: 146–148°C (from ethanol). UV-Visible (λ_{max}, nm): 355, 304, 260. FTIR spectrum (KBr, cm^{-1}): 3335 (N-Hstr), 2980 (alkyl C-Hstr), 1635 (C=Nstr), 1530 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.8–7.2 (m, 4H, Ar-H), 4.2 (br, s, 1H, N-H), 2.4 (t, 1H,

N=C–CH–CH_2CH_3), 1.6–1.4 (m, 8H, CH_2–CH_2), 1.25–0.85(m, 18H, CH_2–CH_2–CH_3). $C_{20}H_{32}N_2$ (300.49) Calcd.: C, 79.94; H, 10.73; N, 9.32. Found: C, 79.75; H, 10.65; N, 9.40. MS: m/z $M^+ = 300$.

3-Ethyl-2,4-dimethyl-2-*n*-propyl–2,3-dihydro-1*H*-1,5-benzodiazepine (e). Yellow solid. M.p.: 143°C (from ethanol/hexane). UV-Visible (λ_{max}, nm): 458, 305, 255. FTIR spectrum (KBr, cm^{-1}): 3360 (N-Hstr), 2980 (alkyl C-Hstr), 1630 (C=Nstr), 1525 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 7–7.25 (m, 4H, Ar-H), 3.9 (br, s, 1H, N-H), 2.4 (t, 1H, N=C–CH–CH_2CH_3), 2.2 (S, 3H, N-C-CH_3) 1.85 (s, 3H, N=C–CH_3), 1.50–1.75 (m, 2H, CH_2CH_3), 1.3–0.8 (m, 10H, CH_2–CH_2CH_3). $C_{16}H_{24}N_2$ (244.38) Calcd.: C, 78.64; H, 9.90; N, 11.46. Found: C, 78.55; H, 9.75; N, 11.55. MS: m/z $M^+ = 244$.

Spirocyclohexan-2,3,4,10,11,11a-hexahydro-1*H*-dibenzo[*b,e*][1,4]diazepine (f). Yellow solid. M.p.: 137°C (from ethanol/hexane). UV-Visible (λ_{max}, nm): 458, 304, 275, 261. FTIR spectrum (KBr, cm^{-1}): 3350 (N-Hstr), 2980 (alkyl C-Hstr), 1625 (C=Nstr), 1520 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 7–7.3 (m, 4H, Ar-H), 3.8 (br, s, 1H, N-H), 2.85–3.15 (m, 3H, N=C–CH and N=C–CH_2), 1.96–2.75 (m, 8 × CH_2, 16H). $C_{18}H_{24}N_2$ (268.41) Calcd.: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.45; H, 8.95; N, 10.35. MS: m/z $M^+ = 268$.

Spirocycloheptan-6,7,8,9,10,10a,11,12-octahydrobenzo[*b*]cyclo hepta [*e*][1,4]diazepine (g). Dark yellow solid. M.p.: 135°C (from ethanol/hexane). UV-Visible (λ_{max}, nm): 489, 440, 299, 260. FTIR spectrum (KBr, cm^{-1}): 3350 (N-Hstr), 2980 (alkyl C-Hstr), 1625 (C=Nstr), 1520 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 7–7.3 (m, 4H, Ar-H), 3.8 (br, s, 1H, N-H), 2.9–3.2 (m, 3H, N=C–CH and N=C–CH_2), 1.5–2.75 (m, 10 × CH_2, 20H). $C_{20}H_{28}N_2$ (296.46) Calcd.: C, 81.03; H, 9.52; N, 9.45. Found: C, 81.25; H, 9.45; N, 9.40. MS: m/z $M^+ = 296$.

2-Methyl-2,4-diphenyl-2,3-dihydro-1*H*-1,5-benzodiazepine (h). Dark yellow solid. M.p.: 150–152°C (from ethanol). UV-Visible (λ_{max}, nm): 485, 300, 265. FTIR spectrum (KBr, cm^{-1}): 3325 (N-Hstr), 3010 (aromatic C-H str), 2975 (alkyl C-Hstr), 1630 (C=Nstr), 1535(aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.8-7.55 (m, 14H, Ar-H), 4.1 (br, s, 1H, N-H), 3.1 (s, 2H, N=C-CH_2), 1.75 (s, 3H, CH_3). $C_{22}H_{20}N_2$ (312.42) Calcd.: C, 84.58; H, 6.45; N, 8.97. Found: C, 84.45; H, 6.53; N, 8.75. MS: m/z $M^+ = 312$.

2-Methyl-2,4-di(4-chlorophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (i). Dark yellow solid. M.p.: 160–163°C (from ethanol). UV-Visible (λ_{max}, nm): 475, 310, 260. FTIR spectrum (KBr, cm^{-1}): 3330 (N-Hstr), 3010 (aromatic C-Hstr), 2950 (alkyl C-H str), 1625 (C=Nstr), 1520 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.85–7.45 (m, 12H, Ar-H),

4 (br, s, 1H, N-H), 2.95 (s, 2H, N=C–CH_2), 1.65 (s, 3H, CH_3). $C_{22}H_{18}N_2Cl_2$ (381.31) Calcd.: C, 69.30; H, 4.76; N, 8.97. Found: C, 69.10; H, 4.55; N, 8.85. MS: m/z $M^+ = 381$.

2-Methyl-2,4-di(4-bromophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (j). Dark yellow solid. M.p.: 171°C (from ethanol/hexane). UV-Visible (λ_{max}, nm): 480, 299, 260. FTIR spectrum (KBr, cm^{-1}): 3335 (N-Hstr), 3015 (aromatic C-Hstr), 2960 (alkyl C-H str), 1635 (C=Nstr), 1515 (aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.8–7.40 (m, 12H, Ar-H), 4.2 (br, s, 1H, N-H), 3.2 (s, 2H, N=C–CH_2), 1.65 (s, 3H, CH_3). $C_{22}H_{18}N_2Br_2$ (470.21) Calcd.: C, 56.20; H, 3.86; N, 5.96. Found: C, 56.25; H, 3.75; N, 5.80. MS: m/z $M^+ = 470$.

2-Methyl-2,4-di(4-hydroxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (k). Yellow solid. M.p.: 137–139°C (from ethanol/hexane). UV-Visible (λ_{max}, nm): 490, 312, 276, 246. FTIR spectrum (KBr, cm^{-1}): 3340 (N-Hstr), 3010 (aromatic C-Hstr), 2970 (alkyl C-H str), 1635 (C=Nstr), 1515(aromatic C=C). ^{1}HNMR spectrum ($CDCl_3$, 400 MHz): 6.95–7.50 (m, 12H, Ar-H), 3.9 (br, s, 1H, N-H), 2.9 (s, 2H, N=C-CH_2), 1.60 (s, 3H, CH_3). $C_{22}H_{20}N_2O_2$ (344.42) Calcd.: C, 76.72; H, 5.85; N, 9.29. Found: C, 76.65; H, 5.70; N, 9.40. MS: m/z $M^+ = 344$.

ACKNOWLEDGMENT

The authors are grateful to University Grants Commission (UGC), New Delhi for financial support in the form of a major sponsored project. One of the authors (V. Sivamurugan) thanks the Council of Scientific and Industrial Research (CSIR), New Delhi for the award of senior research fellow.

REFERENCES

1. De Baun, J.R.; Pallos, F.M.; Baker, D.R. 5-Furoyl-2,2,4-trimethyl-2,5-dihydro-1H-1,5-benzodiazepine as an anti-inflammatory agent. US Patent 3, 978, 227, 1976; Chem. Abstr. **1977**, *86*, 5498d.
2. (a) Schultz, H. *Benzodiazepines*; Springer: Heidelberg, 1982; (b) Smailey, R.K. *Comprehensive Organic Chemistry*; Barton, D., Ollis, W.D., Eds.; Pergamon: Oxford, 1979; Vol. 4, 600; (c) Landquist, J.K. *Comprehensive Heterocyclic Chemistry*; Katritzky, A.R., Rees, C.W., Eds.; Pergamon: Oxford, 1984; Vol. 1, 166, 170.

3. Randall, L.O.; Kappel, B. *Benzodiazepines*; Garattini, S., Mussini, E., Randall, L.O., Eds.; Raven Press: New York, 1973; 27.
4. Stahlofen, P.; Ried, W. Heterocyclic seven-membered ring systems. V. Reaction of *o*-phenylene diamine with α,β-unsaturated carbonyl compounds. Chem. Ber. **1957**, *90*, 815–824.
5. Ried, W.; Torinus, E. Heterocyclic seven-membered ring systems. X. Synthesis of condensed 5-, 7-, & 8-membered heterocycles with 2-nitrogen atoms. Chem. Ber. **1959**, *92*, 2902–2916.
6. Herbert, J.A.L.; Suschitzky, H.J. Syntheses of heterocycles compounds. Part XXIX. Substituted 2,3-dihydro-1*H*-1,5-benzodiazepines. J. Chem. Soc., Perkin Trans. 1 **1974**, 2657–2661.
7. Morales, H.R.; Bulbarela, A.; Contreras, R. New synthesis of dihydro and heterohydro-1,5-benzodiazepines by reductive condensation of *o*-phenylene diamine and ketones in the presence of sodium borohydride. Heterocycles **1986**, *24*, 135–139.
8. Jung, D.I.; Choi, T.W.; Kim, Y.Y.; Kim, I.S.; Park, Y.M.; Lee, Y.G.; Jung, D.H. Synthesis of 1,5-benzodiazepine derivatives. Synth. Commun. **1999**, *29*, 1941–1951.
9. Balakrishna, M.S.; Kaboudin, B. A simple and new method for the synthesis of 1,5-benzodiazepine derivatives on a solid surface. Tetrahedran Lett. **2001**, *42*, 1127–1129.
10. Curini, M.; Epifano, F.; Marcotullio, M.C.; Rosati, O. Ytterbium triflate promoted synthesis of 1,5-benzodiazepine derivatives. Tetrahedran Lett. **2001**, *42*, 3193–3195.
11. Jarikote, D.V.; Siddiqui, S.A.; Rajagopal, R.; Thomas, D.; Lahoti, R.J.; Srinivasan, K.V. Room temperature ionic liquid promoted synthesis of 1,5-benzodiazepine derivatives under ambient conditions. Tetrahedran Lett. **2003**, *44*, 1835–1838.
12. Reddy, B.M.; Sreekanth, P.M. An efficient synthesis of 1,5-benzodiazepine derivatives catalysed by a solid superacid sulfated zirconia. Tetrahedran Lett. **2003**, *44*, 4447–4449.
13. (a) Tanaka, K.; Toda, F. Solvent-free organic synthesis. Chem. Rev. **2000**, *100*, 1025–1074; (b) Gareth, W.W.C.; Colin, L.R.; Janet, L.S. Recent advances in solvent less organic reactions towards benign synthesis with remarkable versatility. Chem. Commun. **2001**, 2159–2169.
14. (a) Varma, R.S. Solvent-free organic syntheses using supported reagents and microwave irradiation. Green Chemistry **1999**, 43–55; (b) Lidstrom, P.; Tierny, J.; Wathey, B.; Westman, J. Microwave assisted organic synthesis-a review. Tetrahedran **2001**, *57*, 9225–9283.

15. Kaboudin, B.; Navace, B. Alumina/phosphorous pentaoxide (APP) as an efficient reagent for the synthesis of 1,5-benzodiazepines under microwave irradiation. Heterocycles **2001**, *55*, 1443–1446.
16. Minothora, P.; Julia, S.S.; Constatinos, A.T. An efficient method for the synthesis of 1,5-benzodiazepine derivatives under microwave irradiation without solvent. Tetrahedran Lett. **2002**, *43*, 1755–1758.

Received in India June 14, 2004