Green Chemistry

RSC Publishing

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Green Chem.*, 2013, **15**, 1849

Received 28th March 2013,
Accepted 1st May 2013

DOI: 10.1039/c3gc40592c

www.rsc.org/greenchem

Synergistic catalysis by an aerogel supported ionic liquid phase (ASILP) in the synthesis of 1,5-benzodiazepines

Rajanikant Kurane, Jagannath Jadhav, Sharanabasappa Khanapure, Rajashri Salunkhe and Gajanan Rashinkar*

An ionic liquid film of [Bmim]Cl containing an organometallic catalyst (Cp_2ZrCl_2) has been anchored on the porous matrix of an aerogel by adsorption interactions. The synthesized aerogel supported ionic liquid phase catalyst was successfully employed in the synthesis of medicinally relevant 1,5-benzodiazepines.

The unique properties of ionic liquids (ILs) such as negligible vapour pressure, high thermal stability, good electrical conductivity and the ability to dissolve a variety of organic and inorganic compounds, have attracted extensive interest as an alternative reaction media to conventional organic solvents.[1] A unique attribute of ILs is their modularity, which allows the tuning of their physical–chemical properties by alterations in the cation–anion combinations, making them process compatible.[2] However, despite their well recognized advantages, a series of drawbacks such as their high cost as compared to organic solvents, poor biodegradability and (eco)toxicological properties still exist.[3] Contemporary studies have revealed that some of the ILs are even more toxic for aquatic organisms than the classical organic solvents that they are aiming to replace.[4] The recognition of these inherent limitations of ILs has led to the new concept of supported ionic liquid phase (SILP) catalysis, involving the immobilization of ILs onto the surface of a porous high area support material.[5] The strategy provides an elegant approach to circumvent the drawbacks associated with ILs. This novel class of advanced materials dramatically reduces the amount of ILs used, retaining their properties. Other advantages of SILP catalysts are the ease of the purification process after the reaction, as well as facilitating significant advances in selectivity, recycling reproducibility, and activity. The SILP catalysts are prepared by depositing ILs on the surface of a high area support material either by covalent bonding or adsorption interactions. The most common supports used for synthesis of SILP catalysts are silica or polymer based materials.[6] In addition, carbon nanotubes,[7] active carbon cloth,[8] chitosan,[9] magnetic nanoparticles[10] *etc.*, have also been sporadically employed as supports. To expand the catalytic properties of SILPs, it is highly desirable to search for new support materials for their synthesis. The scrutiny of a suitable support is often governed by the process conditions at which a SILP catalyst has to operate. Nevertheless, one of the key features of a support material is to exhibit a large specific surface area onto which the IL can be deposited with a very high dispersion. In this regard, we sought to explore the compatibility of silica aerogels,[11] which are a class of extremely low density (0.004–0.500 g cm^{-3}) materials characterized by an open cross-linked silica network with particles usually <10 nm and pore sizes usually <50 nm in diameter, as a support material for the synthesis of SILP catalysts. We envisioned that their high porosity (80–99.8%), large inner surface area (500–1200 m^2 g^{-1}) and amorphous nature are extremely suitable to serve as a robust support material for the synthesis of SILPs.

1,5-Benzodiazepines are arguably one of the most important classes of azaheterocycles that are extensively used as anticonvulsant, antianxiety, antitumor, psychosis, hypnotic, antipyretic and anti-inflammatory agents.[12] They are key intermediates in the synthesis of triazoles, as well as oxadiazoles.[13] Moreover, many of their derivatives are used as dyes for acrylic fibres.[14] The widespread utility of 1,5-benzodiazepines has stimulated the development of numerous methodologies for their synthesis. The condensation reaction between *o*-phenylene diamine (OPD) with α,β-unsaturated carbonyl compounds, β-haloketones, β-aminoketones or ketones has been extensively used for their synthesis. Although a large number of catalytic systems have been developed for the synthesis of 1,5-benzodiazepines using the aforementioned routes,[15] there is a still scope for improvement especially towards developing an efficient protocol using a highly robust catalyst.

In continuation of research related to SILP catalysts,[16] we report herein the synthesis of 1,5-benzodiazepines from OPD and ketones using an aerogel supported ionic liquid phase (ASILP) catalyst.

Department of Chemistry, Shivaji University, Kolhapur, 416004 M.S., India. E-mail: gsr_chem@unishivaji.ac.in; Fax: +91 231 2692333; Tel: +91 231 260 9169

Initially, silica aerogel was prepared from tetraethoxysilane by a two-step, acid–base catalyzed sol–gel process, followed by the supercritical drying following the literature procedure.[11] Next, we focused our attention on the synthesis of the ASILP. As a representative catalyst for the preparation of the ASILP catalyst, bis(cyclopentadienyl)zirconium dichloride (Cp_2ZrCl_2) was chosen since it had been extensively employed as a catalyst in organic synthesis on account of its Lewis acidic character.[17] In a typical procedure for the preparation of the ASILP catalyst, a mixture of powdered aerogel, ionic liquid (1-butyl-3-methylimidazolium chloride, [Bmim]Cl) and catalyst (Cp_2ZrCl_2) was stirred in ethanol at ambient temperature for 24 h. The removal of the solvent under vacuum afforded the desired ASILP in the form of a fine powder that was used for further studies without any further treatment.

The confinement of [Bmim]Cl and Cp_2ZrCl_2 in the aerogel matrix was confirmed by FTIR spectroscopy. The FTIR spectrum of ASILP displayed characteristic vibrational bands of the Cp rings at 3114, 1455, 1380, 1165, 1085, 791 cm^{-1} and intense stretching vibrations at 2970, 2865 (aliphatic C–H stretch), 1515 (in-plane C–C and C–N stretching vibrations of imidazolium ring), 1455 (C–H bending vibration of CH_3). The amount of Cp_2ZrCl_2 in the ASILP catalyst was quantified by using energy dispersive X-ray (EDX) analysis. The analysis indicated 17% of Zr (Fig. 1).

X-ray diffraction (XRD) was performed to determine the nature of the ASILP catalyst. The powder XRD pattern of the ASILP catalyst was obtained from Bragg's law, $n\lambda = 2d \sin \theta$, using CuKα radiation and is displayed in Fig. 2. The XRD pattern reveals that the ASILP is non-crystalline or amorphous in nature as it shows a characteristic broad peak in the 2θ region between 20° to 30° and large background contribution. This implies that the loading of the ionic liquid layer containing the organometallic catalyst on the aerogel does not induce the crystallinity as the amorphous nature of aerogel was replicated in the ASILP.

The size and morphology of the ASILP catalyst was studied by field emission scanning electron microscopy (FESEM). A typical FESEM image of the ASILP is presented in Fig. 3. The FESEM image shows that ASILP particles are spherical in shape.

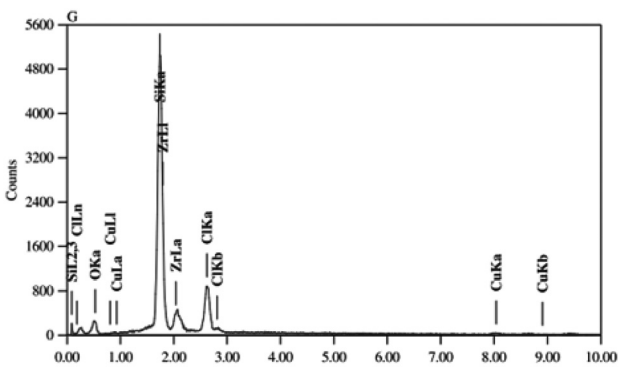


Fig. 1 EDX spectrum of the ASILP catalyst.

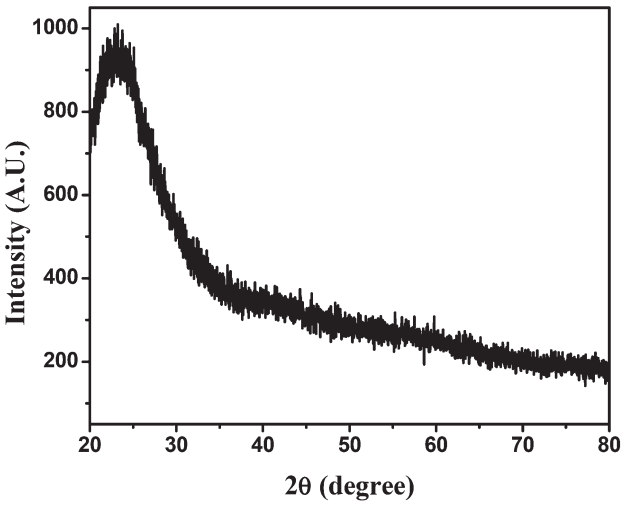


Fig. 2 XRD pattern of the ASILP catalyst.

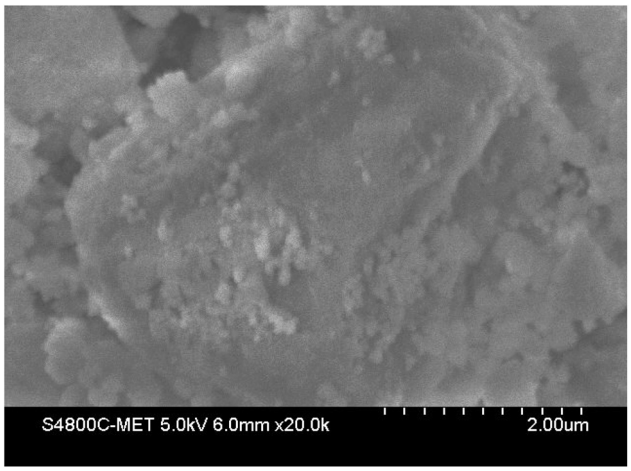


Fig. 3 FESEM image of the ASILP catalyst.

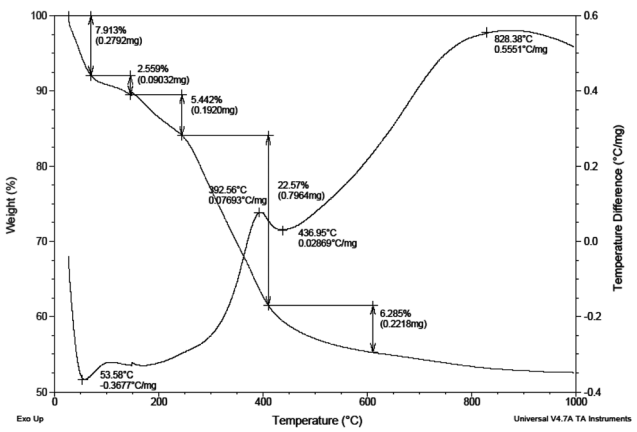
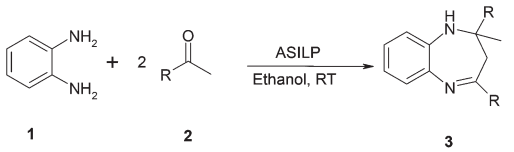


Fig. 4 TGA profile of the ASILP catalyst.

The thermal stability profile of the ASILP catalyst was studied using TGA-DSC analysis in the temperature range of 25–1000 °C. The TGA-DSC profile is shown in Fig. 4. The

initial weight loss of 10.5% may be attributed to the loss of physisorbed water. Further weight loss of 5% might be due to the elimination of water of crystallization or any water associated with the ionic liquid through hydrogen bonding. The steep weight loss of 28.8% is plausibly due to collective loss of [Bmim]Cl, as well as Cp_2ZrCl_2. The individual TGA profiles of [Bmim]Cl and Cp_2ZrCl_2 show their major weight losses around 237 °C and 277 °C, respectively. Thus, our observations are in good agreement with the individual TGA profiles of [Bmim]Cl and Cp_2ZrCl_2 reported in the literature.[18,19] This suggests that there is no significant change in the stabilities of [Bmim]Cl and Cp_2ZrCl_2 after anchoring on a support. Finally, the large residual weight of around 54% retained in the thermogram of the ASILP catalyst corresponds to the formation of non-volatile oxide materials, mainly SiO_2 from the aerogel and ZrO_2 from Cp_2ZrCl_2.

Our next task was to evaluate the catalytic activity of the ASILP catalyst. Initially, to optimize the reaction conditions, OPD (1 mmol) and acetophenone (2 mmol) were chosen as model substrates for the synthesis of 1,5-benzodiazepines in the presence of a catalytic amount of ASILP catalyst in ethanol at ambient temperature. Ethanol was chosen as a solvent since it is acknowledged as a green solvent as it is produced from agricultural feed stocks. We investigated the amount of ASILP required to catalyze the transformation. Using 50 mg of the ASILP catalyst afforded 52% of product after 25 h (Table 1, entry 1). Increasing the quantity to 100 mg substantially improved the yield to 84% in 9 h (Table 1, entry 2). However, further increase in the catalyst quantity did not improve the yield of the product (Table 1, entries 3, 4). Thus, 100 mg of the ASILP catalyst was selected as the optimal catalyst loading for further studies. The generality of the protocol was evaluated by the reactions of several diversified ketones with OPD under the optimized reaction conditions (Scheme 1). It was interesting to observe that aromatic (Table 2, entries a–h), cyclic (Table 2, entry i), as well as aliphatic ketones (Table 2, entries j, k), reacted efficiently affording the corresponding 1,5-benzodiazepines in excellent yields (Table 2). It is worth mentioning that there was no influence of the electronic nature of the substituents on the aryl ring on the yield of products, as acetophenones with electronic donating as well as electron withdrawing groups resulted in the formation of products in nearly quantitative yields. The identity of all the products was ascertained on the basis of ^{1}H NMR, ^{13}C NMR, FTIR spectroscopy and mass spectrometry. The spectroscopic data are consistent with the proposed structures and are in harmony with the literature values.[20]



1 2 3

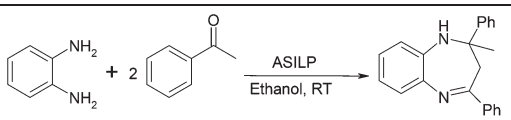
Scheme 1 ASILP catalyzed synthesis of 1,5-benzodiazepines.

It is worth noting that in control experiments where Cp_2ZrCl_2, [Bmim]Cl and aerogel were used as the only catalyst, all the reactions were incomplete and less than 60% yields were obtained (Table 1, entries 5–9). These results suggest that aerogel particles in combination with Cp_2ZrCl_2 and [Bmim]Cl exhibit synergistic catalysis. The enhanced reactivity for the synthesis of 1,5-benzodiazepines in the presence of the ASILP catalyst may be attributed to the Lewis acidic character of Cp_2ZrCl_2 and Brønsted acidity of the ring hydrogens of the imidazolium cation that plays the crucial role of activating the carbonyl group.[21] In the proposed mechanism (Scheme 2), Cp_2ZrCl_2 coordinates with aryl aldehyde causing the electrophilic activation of the carbonyl moiety, which triggers the nucleophilic attack of OPD to generate the intermediate imine–enamine (**I**), which undergoes a 1,3-hydrogen shift to form the isomeric diimine (**II**). Further rearrangement of **II** furnishes the anticipated 1,5-benzodiazepine.

The leaching of the IL film containing the catalyst was studied by ICP-AES. Only a small amount of Cp_2ZrCl_2 (<3.6%) was detected leaching into the solvent, indicating that most of the IL along with the catalyst remain immobilized on the support. The minute leaching observed is presumably caused by a small portion of IL residing on the outer surface of the aerogel particles. This indicates that the aerogel confined IL-containing catalyst is significantly embedded in the porous network of the aerogel, thus making the ASILP catalyst leaching resistant for good retrieval and reusability. Using the same amount of Cp_2ZrCl_2 as that leached out, the model reaction could not be initiated even after prolonged reaction time (24 h). This suggests that the leached species is, obviously, not participating in the catalytic process.

The reusability and reproducibility of the catalyst was investigated on the model reaction. An important feature of the ASILP catalyst was its easy and reliable separation from the reaction mixture. The built-in heterogeneous nature of the ASILP catalyst allowed its facile recovery by simple filtration,

Table 1 Optimization of the reaction conditions in the synthesis of 1,5-benzodiazepines[a]



1 2 a 3 a

Entry	Catalyst	Amount of catalyst (g)	Time (h)	Yield[b] (%)
1	ASILP	0.050	25	52
2	ASILP	0.100	9	84
3	ASILP	0.200	9	86
4	ASILP	0.300	8	87
5	Aerogel	0.100	24	10
6	Cp_2ZrCl_2	0.029 (10 mol%)	24	48
7	Cp_2ZrCl_2	0.058 (20 mol%)	24	51
8	Cp_2ZrCl_2	0.087 (30 mol%)	24	55
9	[Bmim]Cl	1	24	58

[a] All products were characterized by IR, ^{1}H and ^{13}C NMR, and mass spectrometry. [b] Isolated yields after chromatography.

Table 2 Reactions of OPD with ketones in the presence of ASILP catalyst[a,b]

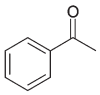
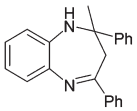
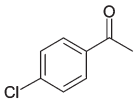
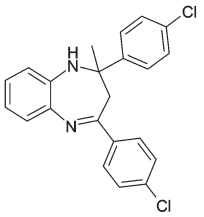
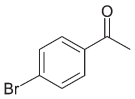
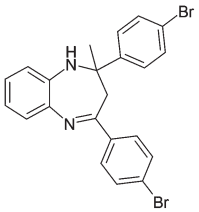
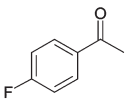
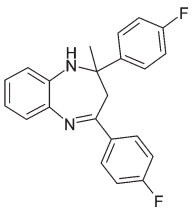
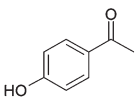
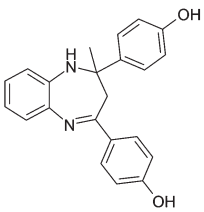
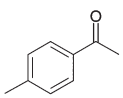
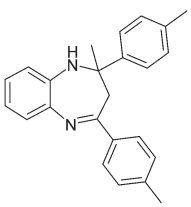
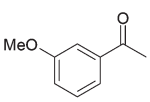
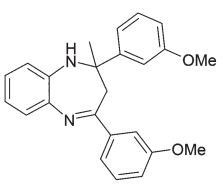
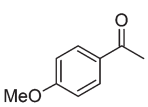
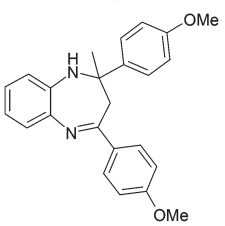
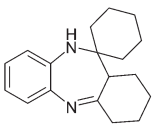
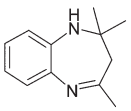
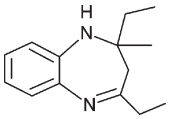
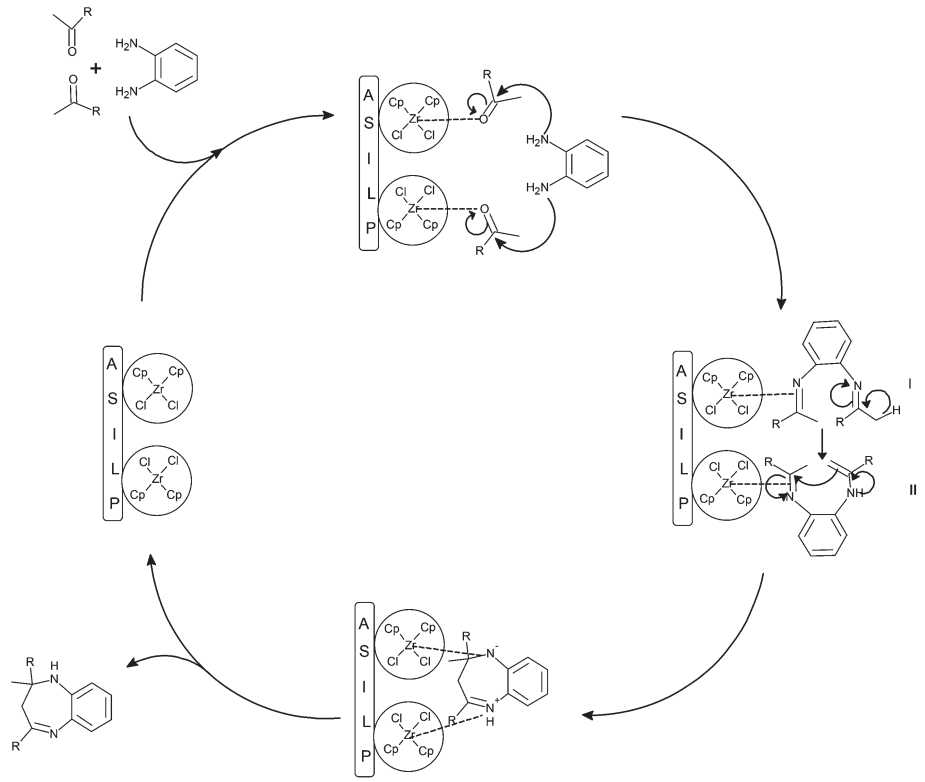
Entry	Ketone **2**	Product **3**	Time (h)	Yield[c] (%)	Melting point (°C)[d]
a			8	84	150 (151–152)[20a]
b			8	86	145 (144–146)[20a]
c			8	80	147–148 (148–150)[20a]
d			7	90	106 (106–107)[20a]
e			10	72	136 (137)[20c]
f			9	78	142 (142–144)[20b]
g			9	80	122 (123–124)[20d]
h			9	79	121 (118–120)[20a]

Table 2 *(Contd.)*

Entry	Ketone **2**	Product **3**	Time (h)	Yield[c] (%)	Melting point (°C)[d]
i			9	70	136 (133–134)[20b]
j			9	75	145 (146–148)[20d]
k			9	72	136 (139–140)[20b]

[a] General reaction conditions: OPD (1 mmol), ketone (2 mmol) and ASILP catalyst (100 mg) in ethanol at RT. [b] All products were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy as well as by mass spectrometry. [c] Isolated yields after chromatography. [d] Literature value in parenthesis.



Scheme 2 Probable mechanism for synthesis of 1,5-benzodiazepines using ASILP catalyst.

thus providing an opportunity for recycling experiments. In the reusability studies, the catalyst was separated from the reaction mass by filtration and reused for further catalytic reactions. The ASILP catalyst showed poor recycling performance as there was a significant loss in the product yield with the extended reaction time during each consecutive run. The decrease in catalytic performance was rationalized on the basis of accumulation of reactant and product molecules that might occupy the catalyst sites. Therefore, we attempted reusability studies after reactivation at each cycle. The reactivation involved vacuum treatment of the ASILP catalyst so as to remove the adsorbed reactant and product moieties on the surface. The reactivation resulted in improved catalytic performance, as the corresponding yields started at 84% and reached 72% at the fourth run without extended reaction time (Fig. 5). The decline in the yields of the products even after reactivation is probably due to agglomeration of the support particles into larger crystallites, which limits the diffusion of reacting molecules to the active catalytic site.

The heterogeneity of the ASILP catalyst was assessed for the model reaction between OPD and acetophenone. After 50% conversion was achieved (GC), the reaction mixture was split,

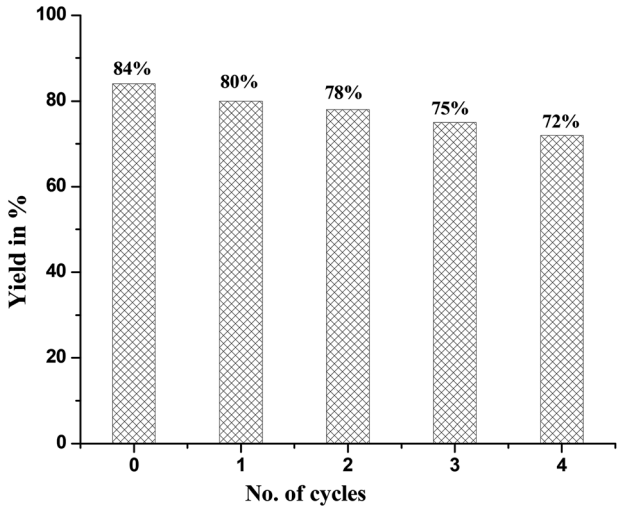


Fig. 5 Reusability of ASILP catalyst in the synthesis of 1,5-benzodiazepine.

with one half separated (by filtration) into a separate reaction flask. The reaction mixture containing the ASILP catalyst proceeded to completion, whereas the filtered portion did not show any increase in the amount of product beyond 50% even after prolonged reaction time.

In conclusion, we have portrayed a facile synthesis of 1,5-benzodiazepines by the condensation of ketones with *o*-phenylene diamine using a novel aerogel supported ionic liquid phase catalyst and environmentally benign solvent. The simple procedure combined with the ease of recovery and reuse of the catalyst make this method economic and a waste-free chemical process for the synthesis of bioactive 1,5-benzodiazepines.

Experimental

General

Melting points were determined in an open capillary and are uncorrected. All reactions were carried out under air atmosphere in dried glassware. Infrared spectra were measured with a Perkin-Elmer one FTIR spectrophotometer. The samples were examined as KBr discs ~5% w/w. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Brucker AC spectrometer (300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR), using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) are expressed in parts per million (ppm) values with tetramethylsilane (TMS) as the internal reference and coupling constants are expressed in hertz (Hz). Mass spectra were recorded on a Shimadzu QP2010 GCMS. The thermal gravimetric analysis (TGA) curves were obtained using the instrument TA SDT Q600 in the presence of static air at a linear heating rate of 10 °C min^{-1} from 25 °C to 1000 °C. FESEM was performed using a HITACHI S-4800 and XRD was taken using a Brucker D2 Phaser. Elemental analyses were performed on a EURO EA3000 vectro model. All the chemicals were obtained from local suppliers and were used as received.

Preparation of ASILP catalyst

A mixture of [Bmim]Cl (2 g, 11.43 mmol), Cp_2ZrCl_2 (1 g, 3.42 mmol) and silica aerogel (5 g) in ethanol (50 mL) was stirred at ambient temperature. After 24 h, the solvent was removed under vacuum to get the desired ASILP catalyst.

General procedure for the synthesis of 1,5-benzodiazepine using the ASILP catalyst

A mixture of OPD (1.0 mmol) and ketone (2.0 mmol) was stirred at ambient temperature in the presence of 100 mg of ASILP catalyst in ethanol (5 mL) for an appropriate time as indicated in Table 2. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered and ethanol was evaporated on a water bath to yield the desired compound. The crude product was purified by column chromatography over silica gel using petroleum ether–ethyl acetate (4 : 1 v/v) as an eluent.

Spectral data of the representative compounds

2-Methyl-2,4-diphenyl-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry a). Yellow solid, mp 150 °C (lit., 151–152 °C);[20a] IR (KBr, thin film): ν = 3310, 2900, 1630, 1425, 1295 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, 4H), 7.26 (m, 8H), 7.05 (m, 2H), 3.50 (bs, 1H, NH), 3.14 (d, J = 13.2 Hz, 1H), 2.98 (d, J = 13.2 Hz, 1H), 1.78 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 129.6, 128.7, 128.3, 127.9, 127.1, 127.0, 126.2, 125.4, 121.7, 121.2, 73.5, 42.9, 29.8; MS (EI): m/z 312 [M]$^+$.

2-Methyl-2,4-di(4-chloro phenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry b). Yellow solid, mp 145 °C (lit., 144–146 °C);[20a] IR (KBr, thin film): ν = 3334, 3053, 1924, 1610, 1550, 1470, 1245, 1092, 829, 802 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (m, 4H), 7.25 (m, 5H), 7.06 (m, 2H), 6.79 (m, 1H), 3.37 (bs, 1H, NH), 3.05 (d, J = 13.2 Hz, 1H), 2.88 (d, J = 13.2 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 165.3, 145.8, 140.6, 137.6, 137.4, 136.2, 133.2, 128.4, 128.3, 128.2, 126.9, 126.5, 122.1, 121.4, 73.4, 42.8, 29.8; MS (EI): m/z 380 [M]$^+$.

2-Methyl-2,4-di(4-bromophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry c). Pale yellow solid, mp 147–148 °C (lit., 148–150 °C);[20a] IR (KBr, thin film): ν = 3317, 3035, 2980, 1620, 1350 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (m, 4H), 7.27 (s, 5H), 7.07 (m, 2H), 6.83 (m, 1H), 3.54 (bs, 1H, NH), 3.09 (d, J = 13.2 Hz, 1H), 2.87 (d, J = 13.2 Hz, 1H), 1.76 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 137.8, 131.4, 131.4, 128.9, 128.6, 127.3, 122.0, 121.5, 121.3, 73.7, 43.1, 29.9; MS (EI): m/z 455 [M]$^+$.

2-Methyl-2,4-di(4-fluorophenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry d). Yellow solid, mp 106 °C (lit., 106–107 °C);[20a] IR (KBr, thin film): ν = 3360, 3015, 2942, 1615, 1520, 1270 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.57 (m, 4H), 7.29 (d, 1H), 7.10 (m, 2H), 6.92 (m, 5H), 3.43 (bs, 1H, NH), 3.1 (d, J = 13.2 Hz, 1H), 2.91 (d, J = 13.2 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 166.5, 165.6, 163.5, 162.3, 160.2, 143.1, 139.9, 137.7, 135.5, 129.1, 129.0, 128.4, 127.4, 127.30, 126.5, 122.0, 121.5, 115.1, 114.9, 114.8, 73.7, 43.2, 29.9; MS (EI): m/z 348 [M]$^+$.

2-Methyl-2,4-di(4-methylphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry f). Yellow solid, mp 142 °C (lit., 142–144°C);[20b] IR (KBr, thin film): ν = 3350, 3015, 2960, 1650, 1520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.60 (d, J = 8.1 Hz, 2H), 7.51 (d, J = 7.8 Hz, 2H), 7.28 (s, 1H), 7.13 (m, 6H) 6.85 (m, 1H), 3.55 (bs, 1H, NH), 3.1 (d, J = 13.2 Hz, 1H), 3.0 (d, J = 13.2 Hz, 1H), 2.37 (s, 3H), 2.33 (s, 3H), 1.76 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 167.6, 144.9, 140.2, 138.3, 136.7, 129.01, 128.9, 128.5, 127.3, 126.3, 125.2, 121.6, 121.5, 73.4, 42.9, 29.9, 29.7, 21.3, 20.9; MS (EI): m/z 340 $[M]^+$.

2-Methyl-2,4-di(3-methoxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry g). Pale yellow solid, mp 122 °C (lit., 123–124 °C);[20d] IR (KBr, thin film): ν = 3340, 3060, 2940, 1640, 1290 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (d, 1H), 7.26 (m, 3H), 7.18 (m, 3H), 7.09 (m, 2H), 6.86 (m, 2H), 6.74 (d, 1H), 3.78 (s, 3H), 3.70 (s, 3H), 3.54 (bs, 1H, NH), 3.14 (d, J = 13.2 Hz, 1H), 2.97 (d, J = 13.2 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 159.57, 159.47, 149.34, 138.06, 129.40, 128.96, 128.57, 126.50, 121.78, 121.50, 119.90, 117.73, 116.69, 112.54, 111.70, 111.58, 73.87, 55.32, 55.24, 43.16, 29.85; MS (EI): m/z 372 $[M]^+$.

2-Methyl-2,4-di(4-methoxyphenyl)-2,3-dihydro-1*H*-1,5-benzodiazepine (Table 2, entry h). Yellow solid, mp 121 °C (lit., 118–120 °C);[20a] IR (KBr, thin film): ν = 3350, 3020, 2935, 1601, 1270 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.67 (d, J = 8.7 Hz, 2H), 7.53 (d, 2H), 7.28 (s, 1H), 7.09 (m, 2H), 6.83 (m, 5H), 3.83 (s, 3H), 3.78 (s, 3H), 3.5 (bs, 1H, NH), 3.11 (d, J = 13.2 Hz, 1H), 2.95 (d, J = 13.2 Hz, 1H), 1.76 (s, 3H); ^{13}C NMR (75 Hz, $CDCl_3$): δ 158.6, 139.9, 138.1, 129.0, 128.2, 126.6, 126.1, 121.9, 121.6, 113.5, 113.4, 73.5, 55.3, 42.9, 29.8; MS (EI): m/z 372 $[M]^+$.

Acknowledgements

The authors GSR, RSS and RMK thank UGC, New Delhi for financial assistance [F. No. 40-96/2011 (SR)] and for the research fellowship.

References

1 (*a*) J. D. Holbrey and K. R. Seddon, *J. Chem. Soc., Dalton Trans.*, 1999, 2133; (*b*) T. Welton, *Chem. Rev.*, 1999, **99**, 2071; (*c*) M. J. Earle, P. B. McCormac and K. R. Seddon, *Green Chem.*, 1999, **1**, 23; (*d*) H. Olivier-Bourbigou, L. Magna and D. Morvan, *Appl. Catal., A*, 2010, **373**, 1; (*e*) J. P. Hallett and T. Welton, *Chem. Rev.*, 2011, **111**, 3508; (*f*) P. Wasserchеid, in *Organic Synthesis Highlights V*, ed. H.-G. Schmalz and T. Wirth, Wiley-VCH, Weinheim, 2003, p. 105.

2 P. Wasserscheid, *Angew. Chem., Int. Ed.*, 2000, **39**, 3772.

3 (*a*) M. T. Garcia, N. Gathergood and P. J. Scammells, *Green Chem.*, 2005, **7**, 9; (*b*) K. M. Docherty and C. F. Kulpa, *Green Chem.*, 2005, **7**, 185; (*c*) C. Pretti, C. Chiappe, D. Pieraccini, M. Gregori, F. Abramo, G. Monni and L. Intorre, *Green Chem.*, 2006, **8**, 238.

4 S. Zhu, R. Chen, Y. Wu, Q. Chen, X. Zhang and Z. Yu, *Chem. Biochem. Eng. Q.*, 2009, **23**, 207.

5 (*a*) A. Riisager, R. Fehrmann, M. Haumann and P. Wasserscheid, *Top. Catal.*, 2006, **40**, 91; (*b*) C. Van Doorslaer, J. Wahlen, P. Mertens, K. Binnemans and D. De Vos, *Dalton Trans.*, 2010, **39**, 8377; (*c*) C. P. Mehnert, *Chem.–Eur. J.*, 2005, **11**, 50.

6 (*a*) H. Li, P. S. Bhadury, B. Song and S. Yang, *RSC Adv.*, 2012, **2**, 12525; (*b*) M. I. Burguete, H. Erythropel, E. Garcia-Verdugo, S. V. Luis and V. Sans, *Green Chem.*, 2008, **10**, 401; (*c*) M. A. Gelesky, S. S. X. Chiaro, F. A. Pavan, J. H. Z. dos Santos and J. Dupont, *Dalton Trans.*, 2007, 5549; (*d*) G. Rashinkar and R. Salunkhe, *J. Mol. Catal. A: Chem.*, 2010, **316**, 146; (*e*) V. Sans, N. Karbass, M. I. Burguete, V. Compan, E. Garcia-Verdugo, S. V. Luis and M. Pawlak, *Chem.–Eur. J.*, 2011, **17**, 1894; (*f*) D. A. Kotadia and S. S. Joshi, *J. Mol. Catal. A: Chem.*, 2012, **353–354**, 44.

7 L. Rodríguez-Pérez, E. Teuma, A. Falqui, M. Gómez and P. Serp, *Chem. Commun.*, 2008, 4201.

8 J. Mikkola, P. Virtanen, H. Karhu, T. Salmia and D. Y. Murzin, *Green Chem.*, 2006, **8**, 197.

9 N. Clousier, R. Moucel, P. Naik, P.-J. Madec, A. C. Gaumont and I. Dez, *C. R. Chim.*, 2011, **14**, 680.

10 Y. Qiao, H. Li, L. Hua, L. Orzechowski, K. Yan, B. Feng, Z. Pan, N. Theyssen, W. Leitner and Z. Hou, *ChemPlusChem*, 2012, **77**, 1128.

11 V. G. Parale, D. B. Mahadik, M. S. Kavale, A. V. Rao, P. B. Wagh and S. C. Gupta, *Soft Nanosci. Lett.*, 2011, **1**, 97.

12 (*a*) H. Schutz, *Benzodiazepine*, Springer, Heidelberg, 1982; (*b*) J. K. Landquist, in *Compressive Heterocyclic Chemistry*, ed. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 1, p. 166; (*c*) R. I. Fryer, Bicyclic diazepines, in *Comprehensive Heterocyclic Chemistry*, ed. E. C. Taylor, Wiley, New York, 1991, ch. II, vol. 50; (*d*) C. O. Randall and B. Kappel, in *Benzodiazepines*, ed. S. Garattini, E. Musini and L. O. Randall, Raven Press, New York, 1973, p. 27.

13 (*a*) M. C. Aversa, A. Ferlazzo, P. Gionnetto and F. H. Kohnke, *Synthesis*, 1986, 230; (*b*) M. Essaber, A. Hasnaoui, A. Benharref and J. P. Lavergne, *Synth. Commun.*, 1998, **28**, 4097; (*c*) A. M. EI. Sayed, H. Abdel-Ghany and A. M. EI. Saghier, *Synth. Commun.*, 1999, **29**, 3561; (*d*) A. Chimirri, S. Grasso, R. Ottano, G. Romeo and M. J. Zappala, *J. Heterocycl. Chem.*, 1990, **27**, 371.

14 R. C. Harris and J. M. Straley, *U. S. pat.*, 1, 537, 757, 1968; *Chem. Abstr.*, 1970, **73**, 100054W.

15 (*a*) J. S. Yadav, B. V. S. Reddy, B. Eshwaraiah and K. Anuradha, *Green Chem.*, 2002, **4**, 592; (*b*) D. V. Jarikote, S. A. Siddiqui, R. Rajagopal, T. Daniel, R. J. Lahoti and K. V. Srinivasan, *Tetrahedron Lett.*, 2003, **44**, 1835; (*c*) P. M. Sreekanth and B. M. Reddy, *Tetrahedron Lett.*, 2003, **44**, 4447; (*d*) R. A. Gibbs and S. K. De, *Tetrahedron Lett.*, 2005, **46**, 1811; (*e*) R. Varala, R. Enugala, S. Nuvula and S. R. Adapa, *Synlett*, 2006, 1009; (*f*) M. Pozarentzi, J. Stephanidou-Stephanatou, C. A. Tsoleridis, C. Zika and V. Demopoulos, *Tetrahedron*, 2009, **65**, 7741; (*g*) M. Munoz, G. Sathicq, G. Romanelli, S. Hernandez, C. I. Cabello,

I. L. Botto and M. Capron, *J. Porous Mater.*, 2013, **20**, 65; (*h*) C. S. Radatz, R. B. Silva, G. Perin, E. J. Lenardao, R. G. Jacob and D. Alves, *Tetrahedron Lett.*, 2011, **52**, 4132.

16 (*a*) V. Gaikwad, R. Kurane, J. Jadhav, R. Salunkhe and G. Rashinkar, *Appl. Catal., A*, 2013, **451**, 243; (*b*) J. Jadhav, V. Gaikwad, R. Kurane, R. Salunkhe and G. Rashinkar, *Tetrahedron*, 2013, **69**, 2920.

17 Y. Nishihara, D. Saito, K. Tanemura, S. Noyori and K. Takagi, *Org. Lett.*, 2009, **11**, 3546.

18 D. Bianchini, I. S. Butler, M. M. Barsan, W. Martens, R. L. Frost, G. B. Galland and J. H. Z. dos Santos, *Spectrochim. Acta, Part A*, 2008, **71**, 45.

19 K. Y. Lee, C. S. Kim, H. Kim, M. Cheong, D. K. Mukherjee and K.-D. Jung, *Bull. KoreanChem. Soc.*, 2010, **31**, 1937.

20 (*a*) J. Qian, Y. Liu, J. Cui and Z. Xu, *J. Org. Chem.*, 2012, **77**, 4484; (*b*) Z. Shi, Y. Liu and Z. Xu, *J. Zhejiang Univ. Sci. B.*, 2010, **11**, 102; (*c*) V. Sivamurugan, K. Deepa, M. Palanichamy and V. Murugesan, *Synth. Commun.*, 2004, **34**, 3833; (*d*) A. Hegedues, *Catal. Lett.*, 2005, **105**, 229.

21 (*a*) R. Qiu, X. Xu, Y. Li, G. Zhang, L. Shao, D. An and S. Yin, *Chem. Commun.*, 2009, 1679; (*b*) A. R. Gholap, K. Venkatesan, T. Daniel, R. J. Lahoti and K. V. Srinivasan, *Green Chem.*, 2003, **5**, 693; (*c*) R. Kumar, P. Chaudhary, S. Nimesh, A. Verma and R. Chandra, *Green Chem.*, 2006, **8**, 519.

