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Journal of Molecular Catalysis A: Chemical 256 (2006) 99–105
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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Silica supported fluoroboric acid as a novel, efficient and reusable catalyst for the synthesis of 1,5-benzodiazepines under solvent-free conditions

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Received 13 March 2006; received in revised form 6 April 2006; accepted 8 April 2006
Available online 16 June 2006

Abstract

An efficient synthesis of 1,5-benzodiazepines from *o*-phenylenediamine and ketones under solvent-free conditions in the presence of a catalytic amount of HBF_4–SiO_2 is discussed. Cyclic and acyclic ketones reacted smoothly to furnish high yield of the products with selectivity in short reaction time.

Keywords: Benzodiazepines; *o*-Phenylenediamine; Ketones; HBF_4–SiO_2; Solvent free

Benzodiazepines are interesting and very important compounds because of their pharmacological properties [1,2]. Most of the members of this family have wide applications in medicinal chemistry such as anti-inflammatory [3], anticonvulsant, antianxiety, sedative, antidepressive and hypnotic agents [4]. Although benzodiazepines were introduced very earlier, research in this area is still very active and is directed towards the synthesis of compounds with enhanced pharmacological activity. In addition, 1,5 benzodiazepines are valuable synthons used for the preparation of other fused ring compounds such as triazolo [5], oxadiazolo [6], oxazino [7] or furano-benzodiazepines [8]. Benzodiazepine derivatives also found commercial use as dyes for acrylic fibers in photography [9].

Despite their wide range of pharmacological activities, industrial and synthetic applications, the synthesis of 1,5-benzodiazepines have received little attention and few methods for their preparations are reported in the literature. These include condensation reaction of *o*-phenylenediamines with α–β unsaturated carbonyl compounds [10], β-haloketones [11] or ketones in presence of BF_3–OEt_2 [12], $NaBH_4$ [13], polyphosphoric acid or SiO_2 [14], MgO and $POCl_3$ [15], Yb-$(OTf)_3$ [16], Al_2O_3/P_2O_5 under MW[17], AcOH under MW [18] and ionic liquid [19].

Unfortunately many of these processes suffer from one or other limitations such as drastic reaction conditions, expensive reagents, low to moderate yields, tedious work-up procedures, relatively long reaction times and co-occurrence of several side reactions. Moreover, the main disadvantage of most of the existing methods is that the catalysts are destroyed in work-up procedure and could not be recovered or reused. Therefore the search continues for a better catalyst for the synthesis of 1,5-benzodiazepines in terms of operational simplicity, reusability, economic viability and greater selectivity.

Interest in exploring the usefulness and wide range of applications of benzodiazepines, a catalyst choice is important which is easily available and less costly, less toxic and operable under environmentally friendly conditions, fulfilling the philosophy of green chemistry. Therefore the leading contender for environmentally acceptable alternative is the use of supported reagents which have good thermal and mechanical stabilities, can be easily handled and are less toxic, non-corrosive, free flowing powders, inexpensive and easily separated from the reaction mixture through filtration. Thus the solvent-less protocol with supported reagents provides an excellent tool for achieving an environmentally friendly and economic organic synthesis. Using supported reagent, we report for the first time a facile method

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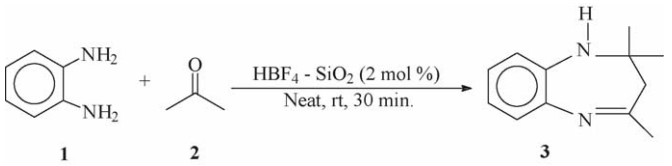
doi:10.1016/j.molcata.2006.04.024



Scheme 1.

for the synthesis of 1,5-benzodiazepines by the condensation of *o*-phenylenediamine with ketones in presence of a catalytic amount of HBF_4–SiO_2 [20] under solvent-free conditions at room temperature (Scheme 1).

Initially a systematic study was carried out for evaluation of HBF_4–SiO_2 as a catalyst for the reaction of *o*-phenylendiamine with acetone under various conditions (Table 1). The reaction was very slow with low yield in the absence of catalyst (Table 1, entry 1), while the reaction was very slow giving poor yields of the product with silica as a catalyst at 25 °C (Table 1, entries 2–3). Moreover, in presence of stoichiometric amount of HBF_4 as a catalyst, we obtained low yields of the corresponding product (Table 1, entries 4–5). Next, we optimised the quantity of the catalyst (HBF_4–SiO_2) at room temperature under solvent-free conditions (Table 1, entries 6–11) and it was observed that the use of just 2 mol% is sufficient to produce an excellent yield of the product (Table 1, entry 9) where as more than 2 mol% of the catalyst did not improve the results (Table 1, entries 10–11). Inferior results were obtained in the presence of solvents (Table 1, entries 12–15).

In all cases, neat reactions were carried out at room temperature by taking a 1:2.2 mol ratio of *o*-phenylenediamine and the ketone in the presence of 2 mol% of HBF_4–SiO_2 to give the desired products in excellent yields. It is noteworthy that in unsymmetrical ketone such as 2-butanone, the ring closure occurs selectively only from one side of the carbon skeleton yielding a single product this indicates the selectivity of present method as compared to the reported ones [15]. This study was further extended to acyclic and cyclic ketones which react without any significant difference to give the corresponding 1,5-benzodiazepines in good yields. Several pharmacologically relevant 1,5-benzodiazepines were prepared by using this procedure. To establish the generality of this protocol, various *o*-phenylenediamines are reacted with a wide range of ketones and the results are presented in Table 2.

Table 1
Reaction of *o*-phenylenediamine with acetone under various conditions

Entry	Solvent	Catalyst (mol%)	Time min (h)	Yield (%)
1	Neat	–	(10)	10
2	Neat	SiO_2 (50 mg)	35	42
3	Neat	SiO_2 (100 mg)	50	62
4	Neat	HBF_4 (1 equiv.)	35	60
5	Neat	HBF_4 (2 equiv.)	50	74
6	Neat	HBF_4–SiO_2 (0.5)	10	65
7	Neat	HBF_4–SiO_2 (1.0)	20	80
8	Neat	HBF_4–SiO_2 (1.5)	25	85
9	Neat	HBF_4–SiO_2 (2.0)	30	96
10	Neat	HBF_4–SiO_2 (2.5)	30	94
11	Neat	HBF_4–SiO_2 (3.5)	35	94
12	CH_2Cl_2	HBF_4–SiO_2 (2)	50	70
13	THF	HBF_4–SiO_2 (2)	55	65
14	CH_3CN	HBF_4–SiO_2 (2)	45	75
15	$CHCl_3$	HBF_4–SiO_2 (2)	45	70

The scope and generality of this process is illustrated by comparing the results obtained using HBF_4–SiO_2 with previous and recently reported methods (Table 3). This indicates the superiority of present protocol in terms of catalyst loading and reaction time. Moreover, the triflet [21] and indium halides [22] as catalysts are expensive and economic point of view less useful for industrial applications. In addition, in case of molecular iodine [23] catalyzed synthesis of 1,5-benzodiazepine derivatives, recycling of the catalyst is not possible. However present catalyst could be recycled and reused at least four times without any appreciable loss of activity.

In conclusion, we report a novel, mild and highly efficient protocol for the synthesis of 1,5-benzodiazepines under solvent-free conditions. The use of inexpensive and easily available catalyst, experimental simplicity, simple work-up procedure, high yields with selectivity, recovery and reusability of the catalyst, relatively short reaction time and potentially useful for industrial applications are the attractive features of this method.

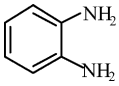
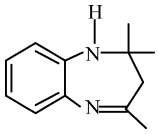
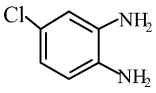
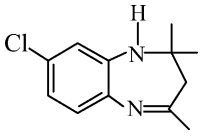
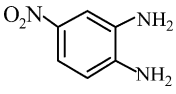
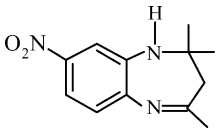
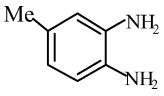
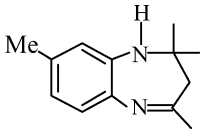
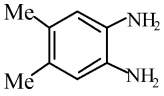
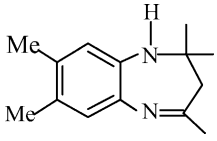
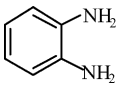
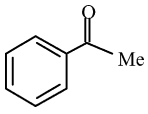
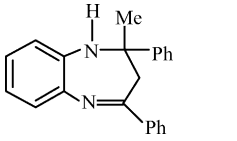
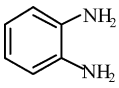
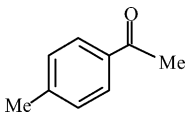
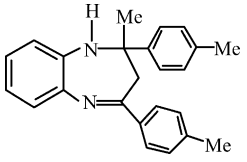
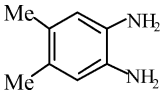
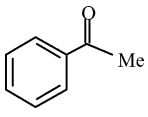
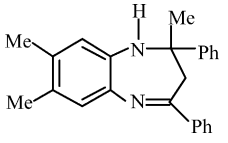
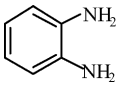
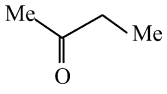
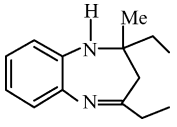
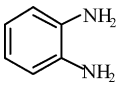
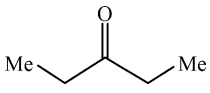
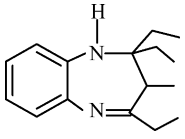
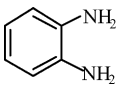
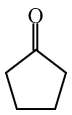
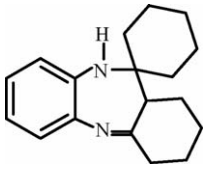
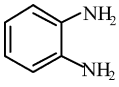
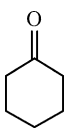
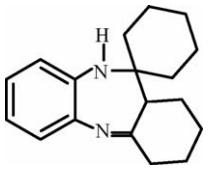
1. Experimental

The ^1H NMR spectra were recorded in $CDCl_3$ on 200 MHz using TMS as internal standard. IR spectra were recorded on Bomen MB 104 IR spectrometer. Mps are uncorrected. Column Chromatography was performed using Silica gel (100–200 mesh). Chemical shifts are given in ppm with respect to internal TMS, and *J* values are quoted in Hz. Mass spectra were recorded at 70 eV. A typical experimental procedure. For the synthesis of 2,2,4-Trimethyl-2,3-dihydro-1*H*-1,5-benzodiazepine: A mixture of o-phenylenediamine (2.5 mmol) and acetone (6 mmol) was stirred at room temperature in the presence of 100 mg (2 mol%) HBF_4–SiO_2 catalyst. After completion of the reaction (TLC), the reaction mixture was diluted with ethyl acetate (10 ml) and filtered. The catalyst was washed with ethyl acetate (3× 5 ml). The organic layer was dried over anhydrous sodium sulphate and concentrated in vacuum. If required, purified by column chromatography (silica gel, Merck 60–120 mesh, petroleum ether: ethyl acetate 9:1) to afford pure product in 96% yield and structure was confirmed by IR, ^1H NMR and Mass. The recovered catalyst was activated by heating at 80 °C for 2 h under vacuum and reused for four times in the case of model reaction of *o*-phenylenediamine and acetone resulting in excellent yield of the corresponding product in 92, 90, 85 and 80% in short reaction time 30, 30, 35 and 40 min, respectively.

*1.1. 2,2,4-Trimethyl-2,3-dihydro-1H-1,5-benzodiazepine (**3a**)*

Yellow solid crystals; mp 138 °C; IR (KBr) (cm^{-1}): 3340, 1650, 1600; ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.35$ (s, 6H), 2.20 (s, 2H), 2.35 (s, 3H), 2.95 (br s, 1H), 6.65–.3 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 29.7, 30.4, 45.0, 67.8, 121.6, 122.0, 125.4, 126.7, 137.8, 140.6, 171.8$. EIMS: *m/z* (% relative inten-

Table 2
HBF_4–SiO_2 catalyzed synthesis of 1,5-benzodiazepine derivatives

Entry	Substrate	Ketone	Product	Time (min)	Yield (%)
a				30	96
b				30	90
c				35	83
d				35	94
e				35	90
f				30	93
g				30	86
h				35	84
i				30	90
j				30	89
k				30	94
l				30	91

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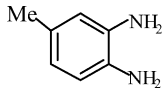
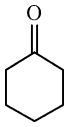
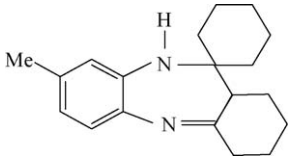
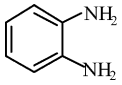
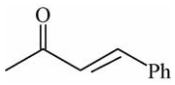
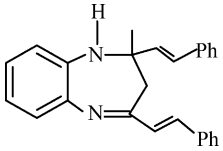
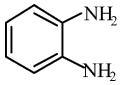
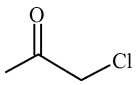
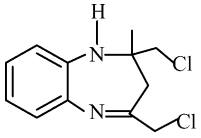
Entry	Substrate	Ketone	Product	Time (min)	Yield (%)
m				35	87
n				35	70
o				35	85

sity) = 188 (M^+, 100), 173 (52), 132 (15), 104 (15), 77 (32), 65 (20); Anal. Calcd. for $C_{12}H_{16}N_2$: C, 76.55; H, 8.56; N, 14.87. Found: C, 76.65; H, 8.70; N, 14.68.

*1.2. 2,2,4-Trimethyl-2,3-dihydro-8-chloro-1H-1,5-benzodiazepine (**3b**)*

Yellow solid; mp 92–94 °C; IR (KBr) (cm^{-1}): 3283, 1649, 1597; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.27 (s, 6H), 2.23 (s, 2H), 2.26 (s, 3H), 5.58 (s, 1H), 6.86(s, 1H), 6.98 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.2, 29.8, 30.0, 44.9, 67.0, 120.4, 120.8, 125.9, 127.8, 129.8, 139.1, 172.5; EIMS: *m/z* (% relative intensity) = 222 (M^+, 10), 207 (24), 167 (38), 142 (100), 114 (20), 80 (25), 41 (30); Anal. Calcd. for $C_{12}H_{15}N_2Cl$: C, 64.71; H, 6.78; N, 12.91; Cl, 15.68. Found: C, 64.80; H, 6.65; N, 12.85; Cl, 15.64.

*1.3. 2,2,4-Trimethyl-2,3-dihydro-8-nitro-1H-1,5-benzodiazepine (**3c**)*

Yellow solid; mp 114–115 °C; IR (KBr) (cm^{-1}): 3280, 1645, 1600; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.90 (s, 6H), 2.95 (s, 3H), 3.20 (s, 2H), 7.18 (s, 1H), 8.0–8.15 (m, 1H), 8.75–8.80 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.9, 30.0, 30.2, 45.6, 60.8, 118.3, 121.2, 126.2, 132.4, 137.9, 145.2, 170.7; EIMS: *m/z* (% relative intensity) = 233 (M^+, 30), 218 (100), 177 (48), 172 (48), 131 (30), 90 (40), 63 (45); Anal. Calcd. for $C_{12}H_{15}N_3O_2$: C, 61.78; H, 6.48; N, 18.01. Found: C, 61.90; H, 6.58; N, 18.20.

*1.4. 2,2,4-Trimethyl-2,3-dihydro-8-methyl-1H-1,5-benzodiazepine (**3d**)*

Yellow solid; mp 128–129 °C; IR (KBr) (cm^{-1}): 3325, 1665, 1600; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30 (s, 6H), 2.19 (s, 2H), 2.23 (s, 3H), 2.80 (s, 3H), 6.68 (s, 1H), 6.70–6.80 (m, 1H), 7.05–7.10 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.9, 29.6, 30.4, 30.8, 45.8, 67.0, 122.6, 126.6, 127.0, 131.8, 136.7, 138.1, 174.3; EIMS: *m/z* (% relative intensity) = 202 (M^+, 40), 187 (100), 146 (70), 77 (15), 41 (20); Anal. Calcd. for $C_{13}H_{18}N_2$: C, 77.18; H, 8.96; N, 13.84. Found: C, 77.25; H, 8.82; N, 13.72.

*1.5. 2,2,4-Trimethyl-2,3-dihydro-7,8-dimethyl-1H-1,5-benzodiazepine (**3e**)*

Yellow solid; mp 113–114 °C; IR (KBr) (cm^{-1}): 3290, 1635, 1597; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.35 (s, 6H), 2.19 (s, 3H), 2.20 (s, 3H), 2.22 (s, 2H), 2.34 (s, 3H), 2.80 (br s, 1H), 6.39 (s, 1H), 6.52 (s, 1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.9, 19.1, 29.8, 30.3, 30.4, 45.3, 67.7, 122.8, 127.8, 129.9, 133.6, 135.5, 138.4, 171.3; EIMS: *m/z* (% relative intensity) = 216 (M^+, 20), 201 (60), 161 (30), 145 (15), 97 (17), 71 (50), 43 (100); Anal. Calcd. for $C_{14}H_{20}N_2$: C, 77.73; H, 9.31; N, 12.94. Found: C, 77.85; H, 9.40; N, 12.82.

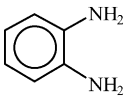
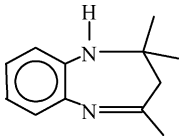
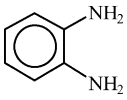
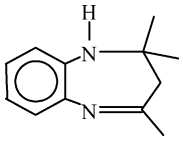
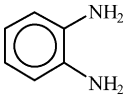
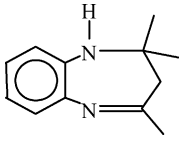
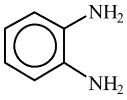
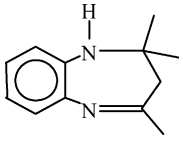
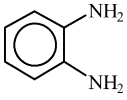
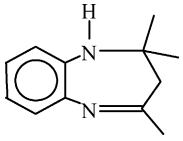
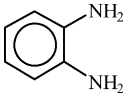
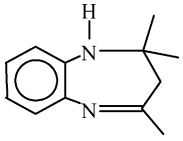
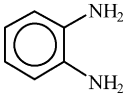
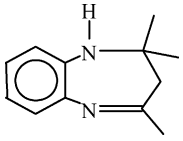
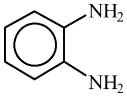
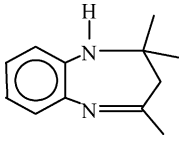
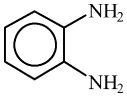
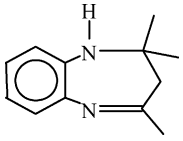
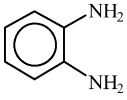
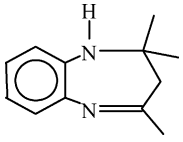
*1.6. 2-Methyl-2,4-diphenyl-2,3-dihydro-1H-1,5-benzodiazepine (**3f**)*

Yellow crystalline solid; mp 152–154 °C; IR (KBr) (cm^{-1}): 3325, 1635, 1598; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.80 (s, 3H), 2.95 (d, 1H, J = 12.8 Hz), 3.15 (d, 1H, J = 12.8 Hz), 3.45 (br s, 1H), 6.65–7.0 (m, 3H), 7.15–7.35 (m, 7H), 7.55–7.65 (m, 4H). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 29.7, 42.9, 73.3, 121.2, 121.4, 125.2, 126.1, 126.8, 126.9, 127.8, 128.1, 128.5, 129.5, 137.9, 139.5, 139.9, 147.4, 167.3; EIMS: *m/z* (% relative intensity) = 312 (M^+, 10), 295 (100), 235 (25), 194 (30), 103 (20), 77 (60), 40 (80); Anal. Calcd. for $C_{22}H_{20}N_2$: C, 84.58; H, 6.45; N, 8.96. Found: C, 84.70; H, 6.54; N, 8.74.

*1.7. 2-Methyl-2,4-ditoluyl-2,3-dihydro-1H-1,5-benzodiazepine (**3g**)*

Yellow solid; mp 141–143 °C; IR (KBr) (cm^{-1}): 3270, 1644, 1602; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.11 (s, 9H), 3.05 (d, 1H, J = 13.6 Hz), 3.17 (d, 1H, J = 13.6 Hz), 3.60 (br s, 1H),

Table 3
Comparison of the catalyst loading with the reported literature methods

Entry	Substrate	Ketone	Catalyst (mol%)	Product	Time, h (min)	Yield (%)
1			BF_3–OEt_2 [12] (10)		0.5–2	91
2			$NaBH_4$ [13] (100) Stoichiometry		24	50
3			$MgO/POCl_3$ [15] (100) Stoichiometry		0.5	90
4			$Yb(OTF)_2$ [16] (5)		4	96
5			[bbim]Br [19] (50)		(50 min)	93
6			$Sc(OTF)_3$ [21] (5)		3	90
7			I [23] (10)		(5 min)	95
8			$lnCl_3$ [22] (20)		5	91
9			$lnBr_3$ [22] (10)		1.5	95
10			HBF_4–SiO_2 (2)		(30 min)	96

7.12–7.61 (m, 11H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.3, 24.4, 28.4, 29.0, 46.4, 52.5, 114.7, 122.2, 126.2, 127.1, 128.6, 132.7, 133.1, 133.6, 135.5, 136.1, 164.9; EIMS: *m/z* (% relative intensity) = 312 (M^+, 10), 295 (100), 235 (25), 194 (30), 103 (20), 77 (60), 40 (80); Anal. Calcd. for $C_{24}H_{24}N_2$: C, 84.66; H, 7.10; N, 8.22. Found: C, 84.78; H, 7.22; N, 8.28.

*1.8. 2-Methyl-2,4-diphenyl-2,3-dihydro-7,8-dimethyl-1H-1,5-benzodiazepine (**3h**)*

Yellow solid; mp 115–116 °C; IR (KBr) (cm^{-1}): 3285, 1635, 1609; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.70 (s, 3H), 2.25 (s, 6H), 2.90 (d, 1H, J = 12.8 Hz), 3.10 (d, 1H, J = 12.8 Hz), 3.45 (br s,

1H), 6.60 (s, 1H), 7.15 (s, 1H), 7.18–7.30 (m, 6H), 7.50–7.60 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.6, 19.3, 29.7, 43.2, 73.0, 122.3, 125.4, 126.8, 126.9, 127.8, 128.2, 129.3, 129.4, 129.6, 134.8, 135.7, 137.6, 139.7, 147.8, 166.8; EIMS: *m/z* (% relative intensity) = 340 (M^+), 195, 103, 77, 65; Anal. Calcd. for $C_{24}H_{24}N_2$: C, 84.66; H, 7.10; N, 8.22. Found: C, 84.78; H, 7.25; N, 8.35.

*1.9. 2,4-Diethyl-2-methyl-2,3-dihydro-1H-1,5-benzodiazepine (**3i**)*

Yellow solid; mp 137–139 °C; IR (KBr) (cm^{-1}): 3329, 1637, 1605; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.99 (t, 3H, J = 6.9 Hz), 1.25 (t, 3H, J = 7.0 Hz), 1.70 (q, 2H, J = 6.9 Hz), 2.15 (m, 2H), 2.35 (s, 3H), 2.69 (q, 2H, J = 7Hz), 3.25 (br s, 1H), 6.78–7.35 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 8.7, 10.8, 26.9, 35.5, 35.7, 42.1, 70.5, 121.8, 125.4, 126.2, 127.0, 137.9, 140.8, 175.6; EIMS: *m/z* (% relative intensity) = 216 (M^+, 15), 141 (5), 108 (100), 80 (38), 40 (75); Anal. Calcd. for $C_{14}H_{20}N_2$: C, 77.33; H, 9.31; N, 12.94. Found: C, 77.45; H, 9.40; N, 12.82.

*1.10. 2,2,4-Triethyl-3-methyl-2,3-dihydro-1H-1,5-benzodiazepine (**3j**)*

Colorless solid; mp 144–145 °C; IR (KBr) (cm^{-1}): 3320, 1638, 1596; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.75–1.05 (m, 10H), 1.20–1.38 (m, 4H), 1.50–1.65 (m, 2H), 2.40–2.60 (m, 2H), 2.87 (q, 1H, J = 6.9Hz), 3.75 (br s, 1H), 6.57 (d, 1H, J = 8.0 Hz), 6.65 (t, 1H, J = 8.0 Hz), 6.90 (t, 1H, J = 8.0 Hz), 7.38 (d, 1H, J = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 7.5, 7.9, 11.5, 12.3, 28.0, 28.4, 35.6, 46.2, 68.6, 117.5, 118.0, 126.6, 132.8, 139.0, 142.4, 173.8; EIMS: *m/z* (% relative intensity) = 244 (M^+, 30), 229 (25), 215 (100); Anal. Calcd. for $C_{16}H_{24}N_2$: C, 78.63; H, 9.89; N, 11.46. Found: C, 78.74; H, 9.76; N, 11.28.

*1.11. 10-Spirocyclopentane-1,2,3,9,10,10a-hexahydrobenzo[b]cyclopenta[e][1,4]-diazepine (**3k**)*

Yellow solid; mp 138–140 °C; IR (KBr) (cm^{-1}): 3338, 1659, 1600; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.30–1.90 (m, 12H), 2.30–2.60 (m, 3H), 4.50 (br s, 1H), 6.70–7.39 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 23.4, 24.1, 24.3, 28.7, 33.4, 38.5, 39.2, 54.4, 67.3, 118.6, 119.3, 126.9, 132.1, 139.2, 143.4, 178.0; EIMS: *m/z* = 240 (M^+); Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.96; H, 8.39; N, 11.66. Found: C, 79.64; H, 8.22; N, 11.45.

*1.12. 10-Spirocyclohexane-2,3,4,10,11,11a-hexahydro-1H-dibenzo[b,e][1,4]-diazepine (**3l**)*

Yellow solid; mp 137–138 °C; IR (KBr) (cm^{-1}): 3290, 1640, 1600; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.23–1.85 (m, 16H), 2.30–2.70 (m, 3H), 4.50 (br s, 1H), 6.65–7.35 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.6, 21.7, 23.2, 24.5, 25.3, 33.2, 34.4, 39.3, 40.5, 52.4, 63.1, 121.3, 121.5, 126.3, 129.6, 138.1, 142.6, 178.9; EIMS: *m/z* = 268 (M^+); Anal. Calcd. for $C_{18}H_{24}N_2$: C, 80.55; H, 9.01; N, 10.44. Found: C, 80.26; H, 9.54; N, 10.31.

*1.13. 11-Spirocyclohexane-2,3,4,10,11,11a-hexahydro-8-methyl-1H-dibenzo[b,e][1,4]-diazepine (**3m**)*

Yellow liquid; IR (Neat) (cm^{-1}): 3305, 1660, 1597; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.20–1.80 (m, 16H), 2.25 (s, 3H), 2.30–2.70 (m, 3H), 4.50 (br s, 1H), 6.40 (s, 1H), 6.70 (d, 1H, J = 8.1 Hz), 7.20 (d, 1H, J = 8.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 20.2, 20.8, 23.6, 26.5, 27.5, 33.2, 34.8, 43.9, 47.6, 113.4, 123.6, 127.5, 128.6, 132.8, 134.1, 164.8; EIMS: *m/z* (% relative intensity) = 282 (M^+, 15), 199 (30), 142 (20), 98 (10), 71 (35), 43 (100); Anal. Calcd. for $C_{19}H_{26}N_2$: C, 80.80; H, 9.27; N, 9.91. Found: C, 80.68; H, 9.40; N, 9.78.

*1.14. 2,4-Diethylene-1-phenyl-2-methyl-2,3-dihydro-1H-1,5-benzodiazepine (**3n**)*

Yellow solid; mp 120–122 °C; IR (KBr) (cm^{-1}): 3320, 1650, 1599; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.38 (s, 3H), 2.28 (s, 2H), 3.46 (br s, 1H), 4.97 (d, 1H, J = 16.2 Hz), 5.48 (d, 2H, J = 16.2 Hz), 5.70 (d, 1H, J = 16.2 Hz), 6.80–7.10 (m, 4H), 7.25 (m, 10H); EIMS: *m/z* = 364 (M^+). Anal. Calcd. for $C_{26}H_{24}N_2$: C, 85.65; H, 6.63; N, 7.71. Found: C, 85.78; H, 6.52; N, 7.84.

*1.15. 2,4-Dichloromethyl-2-methyl-2,3-dihydro-1H-1,5-benzodiazepine (**3o**)*

Yellow solid; mp 130–132 °C; IR (KBr) (cm^{-1}): 3283, 1649, 1597; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.35 (s, 3H), 2.25 (s, 2H), 2.35 (s, 4H), 3.45 (br s, 1H), 6.8–7.05 (m, 4H); EIMS: *m/z* = 257 (M^+); Anal. Calcd. for $C_{12}H_{14}N_2Cl_2$: C, 56.04; H, 5.48; N, 10.89; Cl, 27.57. Found: C, 56.18; H, 5.62; N, 10.70; Cl, 27.68.

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