Room-Temperature Multicomponent Synthesis of 3,4-Dihydroquinoxalin-2-amine Derivatives Using Highly Ordered 3D Nanoporous Aluminosilicate Catalyst

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Abstract: Here we demonstrate on the synthesis of multifunctional 3,4-dihydroquinoxalin-2-amine derivatives through a three-component condensation of substituted *o*-phenylenediamines (OPDA), diverse ketones, and various isocyanides in the presence of AlKIT-5 catalyst which was found to be highly active and selective, affording excellent yields (85–98%) in ethanol at room temperature (2–4 h).

Key words: three-component condensation, *o*-phenylenediamines, ketones, isocyanides, AlKIT-5, 3,4-dihydroquinoxalin-2-amine derivatives

Multicomponent reactions[1] have been receiving much attention in recent years because of their wide range of applications in the industries dealing with the synthesis of fine chemicals and drugs. Multicomponent reactions offer significant benefits like saving energy, time, money, and raw materials over conventional linear-step syntheses. In addition, multicomponent reactions help to avoid the usage of expensive, toxic, and hazardous solvents as the multistep synthesis involves various steps which produce considerable amount of wastes due to isolation and separation of the products after each step which makes these reactions eco- and energy-friendly. Among the various multicomponent reactions, the synthesis of isocyanide-based heterocycles[2,3] is particularly attractive which exhibit a wide range of biological activities. Moreover, they have been extensively used in the pharmaceutical industry.[4–6] Among these isocyanide-based derivatives, quinoxalinone and its derivatives are very interesting nitrogen-containing heterocylic compounds and have been widely used in dyes, pharmaceuticals, and electrical/photochemical materials. They also exhibit a wide variety of biological activities, including, antibacterial, antidiabetic,[7] and antiviral.[8]

Consequently, several synthesis strategies have been followed for the preparation of quinoxaline derivatives.[9–12] One of the most important methods being the simple condensation of an aryl 1,2-diamine with a 1,2-dicarbonyl compound in refluxing ethanol or acetic acid which offers high yield. Iodine and iodoxybenzoic acid have also been used as catalysts for the synthesis of quinoxaline derivatives. Among the quinoxaline derivatives, dihydroquinoxalines are quite attractive as they possess biological activity mainly as inhibitors of cholesteryl ester transfer proteins. However, the reports on the synthesis of these compounds are quite limited. Recently, Shaabani et al. reported the preparation of 3,4-dihydroquinoxaline-2-amine through a simple three-component condensation reaction of *o*-phenylenediamines, diverse carbonyl compounds, and isocyanides in the presence of a catalytic amount of *p*-toluenesulfonic acid (PTSA).[11] Unfortunately, PTSA is a homogenous catalyst and cannot be recyclable which makes the process costly.

Recently, in organic synthesis, the use of heterogeneous catalysts[13,14] especially nanoporous materials[15–22] which can offer high specific surface area, large pore volume, and uniform pore diameter has received considerable importance because of their ease of handling, recoverability, enhanced reaction rates, greater selectivity, and simple workup. Among the various heterogeneous nanoporous silica catalysts, nanoporous catalysts with 3D structures are more advantageous than the catalysts with 1D nanoporous structures. We have recently demonstrated the synthesis of AlKIT-5 material, which is highly acidic and possesses a 3D mesostructure with *Fm*3*m* symmetry and large cage-type pores.[15] In continuation of our earlier work[16–22] on the synthesis of various organic fine chemicals, we have used AlKIT-5 as an efficient acidic catalyst instead of PTSA for the synthesis of 3,4-dihydroquinoxalin-2-amine derivatives. To the best of our knowledge, there has been no report available on the synthesis of 3,4-dihydroquinoxalin-2-amine derivatives using nanoporous materials as catalysts until now. Here, we demonstrate a simple, convenient, and efficient method for the synthesis[23] of 3,4-dihydroquinoxalin-2-amine derivatives under ethanol solvent using AlKIT-5 catalyst through one-pot condensation reaction of substituted *o*-phenylenediamines, diverse ketones, and various isocyanides.

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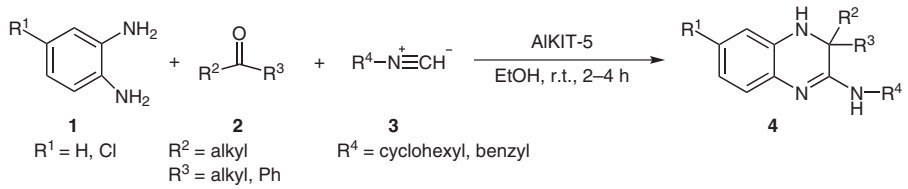


Scheme 1 Synthesis of 3,4-dihydroquinoxalin-2-amine derivatives using AlKIT-5 catalyst at r.t.

Initially to optimize the reaction conditions, *o*-phenylenediamine **1** (108 mg, 1 mmol), butanone **2** (72 mg, 1 mmol), and cyclohexyl isocyanide **3** (109.7 mg, 1 mmol) were employed for the synthesis of novel 3,4-dihydroquinoxalin-2-amine derivative **4a** (Table 3, entry 1) using AlKIT-5 catalyst with different Al contents in ethanol at room temperature (Scheme 1).

The reaction was also carried out in the absence of AlKIT-5 catalyst. Unfortunately, no product was formed under such conditions. However, as expected, a significant difference in the activity of the catalyst was observed upon increasing the Al content in the sample. The catalyst with a high Al content registers a high activity with a high product yield. A similar result was also obtained in our previous work on various acid-catalyzed transformations using AlKIT-5 as the catalyst.[16–22] Interestingly, the activity of the catalyst increased with increasing the amount of the catalyst in the reaction mixture which is mainly due to the availability of more number of active adsorption sites in the reaction mixture. The yield of the final product increased from 70 to 94% with increasing the catalyst weight from 50 to 200 mg. The effect of the amount of AlKIT-5 catalyst on the synthesis of dihydroquinoxalines is presented in the Table 1. Among the catalyst studied, the AlKIT-5 with n_{Si}/n_{Al} ratio of 10 was found to be highly active which is mainly due to its high acidity and large surface area. The catalyst afforded the yield of product **4a** almost 94% within three hours reaction time.

Table 1 Effect of the Weight on the Catalytic Activity of the AlKIT-5 Catalysts and Comparison with Other Catalysts for the Synthesis of Novel 3,4-Dihydroquinoxalin-2-amine Derivatives[a]

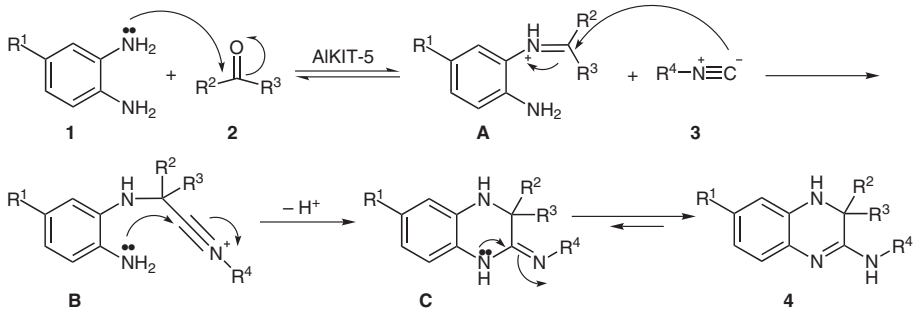
Entry	Catalyst	Weight of catalyst (mg)	Dp_{ads}, BJH (nm)	Acidity (mmol/g)	Yield (%)
1	AlKIT-5 (10)	50	6.0	0.50	70
2	AlKIT-5 (10)	100	6.0	0.50	94
3	AlKIT-5 (10)	150	6.0	0.50	94
4	AlKIT-5 (10)	200	6.0	0.50	94
5	AlKIT-5 (28)	150	5.6	0.32	84
6	AlKIT-5 (44)	150	5.2	0.14	75
7	Amberlyst	100	–	–	92
8	Montmorillonite	100	–	–	85

[a] Reaction conditions: substrate: *o*-phenylenediamine, butanone, and cyclohexyl isocyanide; reaction time: 3 h, reaction temperature: r.t., solvent: EtOH, Dp: pore diameter.

We surmise that AlKIT-5 catalyst acts as a Brønsted acid catalyst and the possible mechanism for the formation of 3,4-dihydroquinoxalin-2-amine derivatives **4**, as proposed by Shaabani et al. is shown in Scheme 2.[11] During the reaction, firstly the intermediate **A** is formed in the pore channel of the AlKIT-5 by the reaction with the diamine **1** and the ketone which are adsorbed on the Brønsted acid sites of the catalyst. The intermediate **A** was converted into another intermediate **B** with the help of the nucleophilic attack of isocyanide **3**, which was further converted into intermediate **C** through an intramolecular nucleophilic attack of NH_2 group to the activated nitrile moiety. Finally, the intermediate undergoes the imine–enamine tautomerization to yield the final product **4**. It is

Table 2 The Effect of Solvent on the Synthesis of 3,4-Dihydroquinoxalin-2-amine Derivatives

Entry	Solvent	Yield (%)
1	CH_2Cl_2	78
2	THF	80
3	MeCN	84
4	EtOH	94



Scheme 2 Proposed mechanism for the synthesis of 3,4-dihydroquinoxalin-2-amine derivatives **4** using diamines **1**, ketones **2**, and isocyanides **3**

amazing to note that all the reaction processes are taken place inside the nanochannels of AlKIT-5 where pores with large cages are available. These results reveal that AlKIT-5 is the best catalyst to synthesize dihydroquinoxalines via a multicomponent reaction pathway.

The effect of solvents was also investigated for this synthesis. Among the various solvents like dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), acetonitrile (MeCN), and ethanol (EtOH) studied, ethanol was found to be the excellent solvent for this transformation, and the results are shown in Table 2 (using substrates as shown in Table 3, entry 1).

Table 3 Synthesis of 3,4-Dihydroquinoxalin-2-amine Derivatives **4** Using Diamines **1**, ketones **2**, and Isocyanides **3**

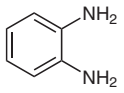
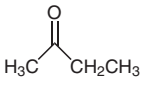
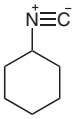
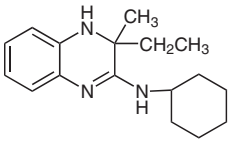
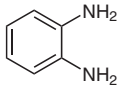
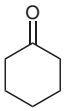
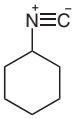
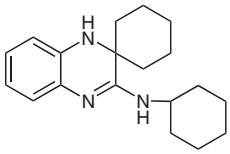
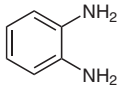
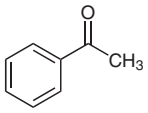
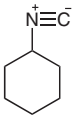
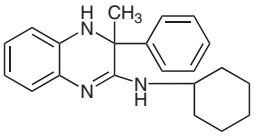
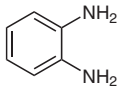
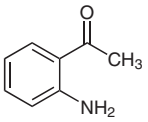
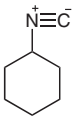
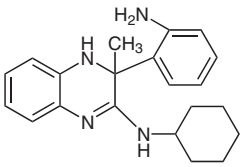
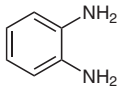
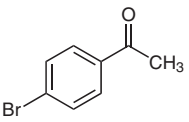
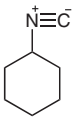
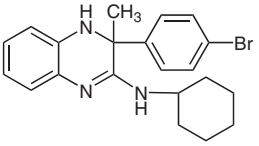
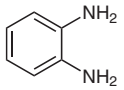
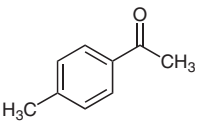
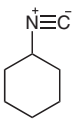
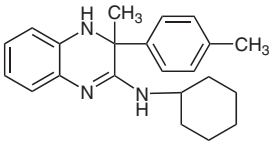
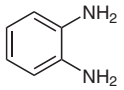
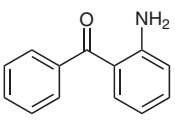
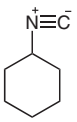
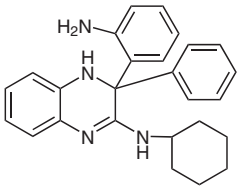
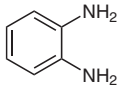
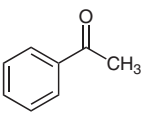
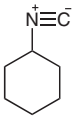
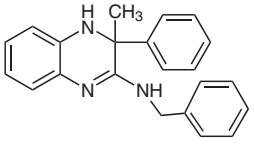
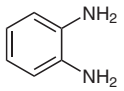
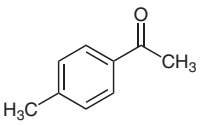
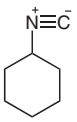
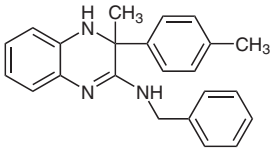
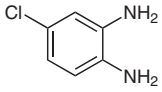
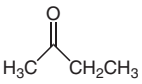
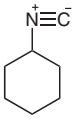
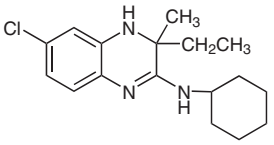
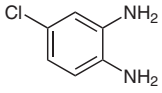
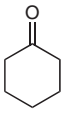
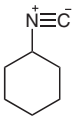
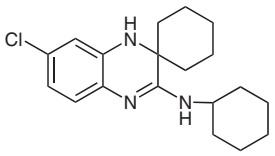
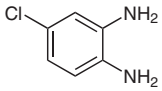
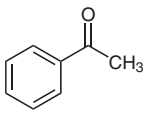
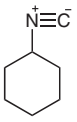
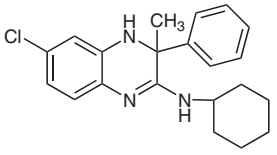
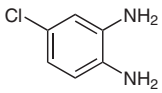
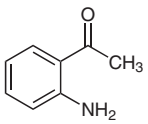
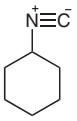
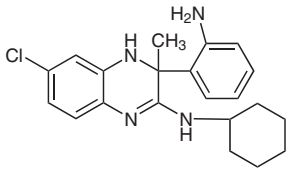
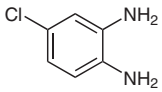
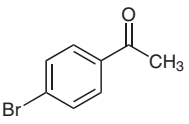
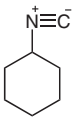
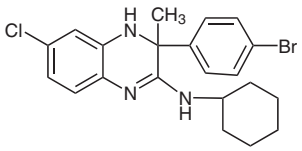
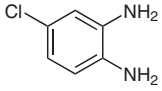
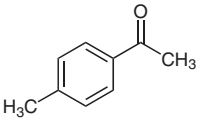
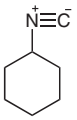
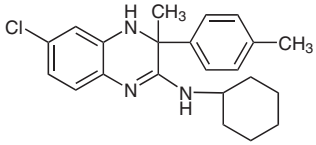
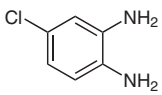
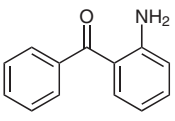
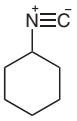
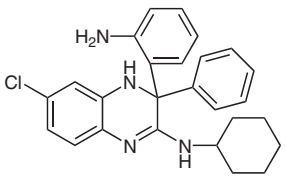
Entry	Diamine **1**	Ketone **2**	Isocyanide **3**	Product **4**[a]	Time (h)	Yield (%)[b]
1				 **4a**	3	94
2				 **4b**	3	91
3				 **4c**	3	93
4				 **4d**	3	90
5				 **4e**	4	90
6				 **4f**	2	98
7				 **4g**	3	92
8				 **4h**	3	91

Table 3 Synthesis of 3,4-Dihydroquinoxalin-2-amine Derivatives **4** Using Diamines **1**, ketones **2**, and Isocyanides **3** (continued)

Entry	Diamine **1**	Ketone **2**	Isocyanide **3**	Product **4**[a]	Time (h)	Yield (%)[b]
9				 **4i**	3	92
10				 **4j**	3	90
11				 **4k**	3	88
12				 **4l**	3	91
13				 **4m**	3	88
14				 **4n**	4	85
15				 **4o**	3	92
16				 **4p**	3	87

[a] The products were characterized by ^{1}H NMR and IR spectroscopy, and mass spectrometry.
[b] Yield refers to pure products after crystallization.

The reaction was also carried out with various substituted *o*-phenylenediamines **1**, ketones **2**, and isocyanides **3** using AlKIT-5 catalyst at room temperature for two to four hours (Table 3). Several structurally diverse isocyanides **3**

including cyclohexyl- and benzyl-substituted ones were used to get the products **4** in excellent yields. It was found that the catalyst also worked well with other substituted aryl and cyclic diamines and afforded good yields. All synthesized products (**4a**–**p**) were stable and characterized by using IR, ^{1}H NMR, and MALDI-mass spectral analysis.[23] In addition, elemental analysis and melting point measurements were carried out in order to confirm the purity of the products.

The reactions were very clean and no other side products were observed. Diamines and chloro-substituted diamines **1**, aliphatic, aromatic, and cyclic ketones **2** and cyclohexyl and benzyl isocyanides **3** gave satisfactory results (Table 3, entries 1–16). As shown in Table 3, the catalyst also gave good yield when aliphatic ketones were used (Table 3, entries 1 and 10). Furthermore, cyclic ketones were then introduced to prepare structurally interesting spirocyclic compounds (Table 3, entries 2 and 11). Chloro-substituted diamines and various electrophilic and nucleophilic substituted aromatic ketones were used to synthesize multifunctionalized 3,4-dihydroquinoxalin-2-amine derivatives. In addition, benzophenone also underwent smooth conversion to afford the corresponding product with reasonable yields (Table 3, entries 7 and 16). Particularly, the detection and isolation of these compounds are very easy, since the colors of the compounds were yellow and brown. It has been also found that the presence of the electron-donating methyl group (Table 3, entries 6, 9, and 15) in the ketone significantly enhances the rate of the reaction and afforded a high yield. The recyclability of the catalyst was also checked to prove the heterogeneous nature and its repeated use. We found that the catalyst showed 90%, 88%, and 85% of yields (Table 3, entry 1) in 2nd, 3rd, and 4th cycles, respectively.

In summary, we have synthesized novel polysubstituted 3,4-dihydroquinoxalin-2-amine derivatives using various aromatic diamines, carbonyl compounds, and diverse isocyanides in the presence of AlKIT-5 catalyst. The catalyst was very active and afforded high yield in a short reaction time and worked well for the synthesis of derivatives of 3,4-dihydroquinoxalin -2-amine using substituted ketones and the diamines. The catalyst can also be recyclable and truly heterogeneous. These excellent structural features of the AlKIT-5 catalyst make this process simple and clean which promote its use in various acid-catalyzed multicomponent reactions and create a platform for the development of various pharmaceutical products.

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(23) **Experimental Procedure**

All chemicals and solvents were obtained from Aldrich and used without further purification. The ^{1}H NMR spectra of samples were recorded on a JEOL 300-MHz NMR spectrometer using TMS as an internal standard in DMSO-d_6. Mass spectra were recorded on a MALDI-MS. FT-IR spectra of all the final products were recorded on a Perkin Elmer 100 instrument by averaging 50 scans with a resolution of 2 cm^{-1} measuring in absorbance mode by using the KBr self-supported pellet technique. The melting points of the novel products were determined by using melting point apparatus.

Typical Procedure for the Synthesis of 3,4-Dihydroquinoxalin-2-amine Derivatives

To a solution of diamine (1 mmol), ketone (1 mmol), and isocyanide (1 mmol) in EtOH (3 mL) was added AlKIT-5 (100 mg). The resulting mixture was stirred for 2–4 h at r.t. After completion of the reaction, as indicated by TLC (EtOAc–*n*-hexane, 2:1). The catalyst was filtered off, and the product in filtrate was precipitated by addition of cold H_2O (10 mL). The residue was crystallized from EtOH to give **4a**–**p** as crystals. All products were characterized by spectral (IR, NMR and MS) data and also by the melting points of the samples. The spectral data of all novel compounds are given below.

Compound **4a**: white solid; mp 218–220 °C. IR (KBr): ν_{max} = 3293, 2935, 2861, 1642, 1619, 1508, 1455, 1211, 1178, 750, 681 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.88 (t, *J* = 3.0 Hz, 3 H, CH_2CH_3), 1.35 (q, *J* = 2.8 Hz, 2 H, CH_2), 1.49 (s, 3 H, CH_3), 1.11–2.34 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 3.99 (br s, 1 H, CHNH), 6.31–6.41 (br s, 1 H, NH), 6.70–6.74 (br s, 1 H, NH), 6.78–7.65 (m, 4 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 271. Anal. Calcd for $C_{17}H_{25}N_3$: C, 75.23; H,9.28; N,15.48. Found: C, 75.20; H, 9.24; N, 15.45.

Compound **4b**: off white solid; mp 230–232 °C. IR (KBr): ν_{max} = 3351, 2935, 2851, 1622, 1541, 1508, 1448, 1314, 1190, 738, 685 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.98–1.95 (m, 20 H, 2 × 5 CH_2 of cyclohexyl), 3.86 (br s, 1 H, CHNH), 6.69 (br s, 1 H, NH), 6.77 (br s, 1 H, NH), 7.02–7.46 (m, 4 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 297. Anal. Calcd for $C_{19}H_{27}N_3$: C, 76.72; H, 9.15; N, 14.13. Found: C, 76.69; H, 9.10, N, 14.10.

Compound **4c**: pale yellow solid; mp 305–307 °C. IR (KBr): ν_{max} = 3300, 3252, 2938, 2863, 1649, 1621, 1512, 1462, 1213, 1179, 752, 683 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.06–2.33 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.89 (s, 3 H, CH_3), 4.05 (br s, 1 H, CHNH), 6.64–6.71 (br s, 1 H, NH), 6.95–6.99 (br s, 1 H, NH), 7.09–7.67 (m, 9 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 319. Anal. Calcd for $C_{21}H_{25}N_3$: C, 78.96; H, 7.89; N, 13.15. Found: C, 78.93; H, 7.86; N, 13.10.

Compound **4d**: pale yellow solid; mp 240 °C. IR (KBr): ν_{max} = 3249, 2925, 2864, 1647, 1620, 1508, 1397, 1451, 1187, 752, 679 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.01–2.28 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.39 (s, 3 H, CH_3), 3.90 (br s, 1 H, CHNH), 6.52 (br s, 1 H, NH), 6.74 (br s, 1 H, NH), 6.77–7.51 (m, 8 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 334. Anal. Calcd for $C_{21}H_{26}N_4$: C, 75.41; H, 7.84; N, 16.75. Found: C, 75.37; H, 7.80; N, 16.70.

Compound **4e**: white solid; mp 262 °C. IR (KBr): ν_{max} = 3253, 2937, 2864, 1642, 1620, 1509, 1455, 1202, 1190, 753, 680 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.00–2.29 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.39 (s, 3 H, CH_3), 3.97 (br s, 1 H, CHNH), 6.53 (br s, 1 H, NH), 6.77 (br s, 1 H, NH), 6.79–7.51 (m, 8 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 398. Anal. Calcd for $C_{21}H_{24}BrN_3$: C, 63.32; H, 6.07; N, 10.55. Found: C, 63.28; H, 6.01; N, 10.50.

Compound **4f**: white solid; mp 202 °C. IR (KBr): ν_{max} = 3249, 2937, 2858, 1644, 1622, 1508, 1452, 1397, 1204, 1184, 754, 680 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.05–2.31 (m, 10 H, 2 × 5 CH_2 of cyclohexyl) 1.37 (s, 3 H, CH_3), 1.38–1.50 (s, 3 H, CH_3 of tolyl), 3.89 (br s, 1 H, CHNH), 6.33–6.41 (br s, 1 H, NH), 6.69–6.73 (br s, 1 H, NH), 6.73–7.57 (m, 8 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 333. Anal. Calcd for $C_{22}H_{27}N_3$: C, 79.24; H, 8.16; N, 12.60. Found: C, 79.20; H, 8.12; N, 12.56.

Compound **4g**: white solid; mp 250–252 °C. IR (KBr): ν_{max} = 3252, 2925, 2880, 1648, 1622, 1508, 1451, 1209, 1188, 753, 679 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.10–2.29 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 3.90 (br s, 1 H, CHNH), 6.50–6.58 (br s, 1 H, NH), 6.74–6.77 (br s, 1 H, NH), 6.78–7.56 (m, 13 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 396. Anal. Calcd for $C_{26}H_{28}N_4$: C, 78.75; H, 7.12; N, 14.13. Found: C, 78.70, H, 7.09; N, 14.10.

Compound **4h**: off white solid; mp 160–162 °C. IR (KBr): ν_{max} = 3276, 2947, 2780, 1656, 1624, 1490, 1455, 1211, 1192, 815, 682 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.92 (s, 3 H, CH_3), 2.32 (s, 2 H, CH_2 of benzyl), 4.03 (br s, 1 H, NH), 4.93 (br s, 1 H, NH), 6.97–7.83 (m, 14 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 327. Anal. Calcd for $C_{22}H_{21}N_3$: C, 80.70; H, 6.46; N, 12.38. Found: C, 80.66, H, 6.40, N, 12. 80.

Compound **4i**: pale yellow solid; mp 140–142 °C. IR (KBr): ν_{max} = 3250, 2996, 2850, 1654, 1624, 1489, 1450, 1190, 1160, 815, 680 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.17 (s, 3 H, CH_3), 2.34 (s, 3 H, CH_3 of tolyl), 3.56–3.61 (m, 2 H, CH_2 of benzyl), 4.03 (br s, 1 H, NH), 4.90 (br s, 1 H, NH), 7.12–7.79 (m, 13 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 342. Anal. Calcd for $C_{23}H_{23}N_3$: C, 80.90; H, 6.79; N, 12.31. Found: C, 80.86; H, 6.70; N, 12.28.

Compound **4j**: light grey solid; mp 190–192 °C. IR (KBr): ν_{max} = 3261, 2933, 2860, 1640, 1620, 1502, 1455, 1200, 1191, 815, 682 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.87 (t, *J* = 3.0 Hz, 3 H, CH_2CH_3), 1.22 (q, *J* = 2.8 Hz, 2 H, CH_2), 1.50 (s, 3 H, CH_3), 1.30–2.33 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 3.93–4.04 (br s, 1 H, CHNH), 6.45–6.56 (br s, 1 H, NH), 6.72–6.84 (br s, 1 H, NH), 6.89–7.65 (m, 3 H, Ar-H) ppm. MALDI-MS: *m/z* [M$^+$] = 305. Anal. Calcd for $C_{17}H_{24}ClN_3$: C, 66.76; H, 7.91; N, 13.74. Found: C, 66.71; H, 7.88, N, 13.70.[11]

Compound **4k**: brown solid; mp 148–150 °C. IR (KBr): ν_{max} = 3338, 2929, 2890, 1636, 1619, 1500, 1450, 1198, 1186, 815, 684 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.81–2.32 (m, 20 H, 2 × 5 CH_2 of cyclohexyl), 3.86 (br s, 1 H, CHNH), 6.69–6.76 (br s, 1 H, NH), 6.76–6.85 (br s, 1 H, NH), 7.01–7.52 (m, 3 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 331. Anal. Calcd for $C_{19}H_{26}ClN_3$: C, 68.76; H, 7.90; N,12.66. Found: C, 68.69; H, 7.87; N, 12.64.[11]

Compound **4l**: pale pink solid; mp 245–247 °C. IR (KBr): ν_{max} = 3259, 2938, 2859, 1644, 1619, 1501, 1456, 1212, 1182, 816, 680 cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.04–2.28 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.40 (s, 3 H, CH_3), 3.92–4.19 (br s, 1 H, CHNH), 6.70–6.88 (br s, 1 H, NH), 6.88–7.07 (br s, 1 H, NH), 7.08–7.88 (m, 8 H, ArH) ppm. MALDI-MS: *m/z* [M$^+$] = 353. Anal. Calcd for $C_{21}H_{24}ClN_3$: C, 71.27; H, 6.84; N, 11.87. Found: C, 71.23; H, 6.80; N, 11.80.[11]

Compound **4m**: pale pink solid; mp 258–260 °C. IR (KBr): ν_{max} = 3273, 2923, 2851, 1646, 1625, 1513, 1458, 1401,

1207, 1188, 810, 680 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 1.04–2.28 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.40 (s, 3 H, CH_3), 3.83–3.94 (br s, 1 H, CHNH), 6.69–6.74 (br s, 1 H, NH), 6.75–6.78 (br s, 1 H, NH), 6.78–7.50 (m, 7 H, ArH) ppm. MALDI-MS: *m/z* [M^+] = 369. Anal. Calcd for $C_{21}H_{25}ClN_4$: C, 68.37; H, 6.83; N, 15.19. Found: C, 68.31; H, 6.80; N, 15.12.[11]

Compound **4n**: violet solid; mp 218–220 °C. IR (KBr): ν_{max} = 3270, 2938, 2864, 1648, 1620, 1503, 1456, 1205, 1185, 815, 680 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 1.02–2.27 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.37 (s, 3 H, CH_3), 4.01 (br s, 1 H, CHNH), 6.68–6.74 (br s, 1 H, NH), 6.75–6.81 (br s, 1 H, NH), 6.89–7.57 (m, 7 H, ArH) ppm. MALDI-MS: *m/z* [M^+] = 432. Anal. Calcd for $C_{21}H_{23}BrClN_3$: C, 58.28; H, 5.36; N, 9.71. Found: C, 58.22; H, 5.28; N, 9.65.[11]

Compound **4o**: brown solid; mp 235–237 °C. IR (KBr): ν_{max} = 3272, 2924, 2853, 1647, 1612, 1513, 1457, 1208, 1188, 810, 680 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ = 0.98–2.20 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 1.37 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3 of tolyl), 4.00 (br s, 1 H, CHNH), 6.58–6.74 (br s, 1 H, NH), 6.74–6.77 (br s, 1 H, NH), 6.77–7.49 (m, 7 H, Ar) ppm. MALDI-MS: *m/z* [M^+] = 367. Anal. Calcd for $C_{22}H_{26}ClN_3$: C, 71.82; H, 7.12; N, 11.42. Found: C, 71.78; H, 7.08; N, 11.36.[11]

Compound **4p**: pale brown solid; mp 258–260 °C. IR (KBr): ν_{max} = 3275, 2925, 2864, 1639, 1629, 1501, 1458, 1401, 1200, 1186, 810, 679 cm^{-1}. ^1H NMR (DMSO-d_6): δ = 1.14–2.29 (m, 10 H, 2 × 5 CH_2 of cyclohexyl), 3.87 (br s, 1 H, CHNH), 6.71–6.74 (br s, 1 H, NH), 6.75–6.78 (br s, 1 H, NH), 6.79–7.52 (m, 12 H, ArH) ppm. MALDI-MS: *m/z* = 430. Anal. Calcd for $C_{26}H_{27}ClN_4$: C, 72.46; H, 6.31; N, 13.00. Found: C, 72.40, H, 6.29, N, 13.05.[11]