# A facile and efficient one-pot synthesis of polysubstituted benzenes in guanidinium ionic liquids†

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A facile and efficient synthesis of polysubstituted benzenes has been developed *via* sequential Michael addition, Knoevenagel condensation and nucleophilic cyclization reactions of readily available chalcones with active methylene compounds in guanidinium ionic liquids.



## Introduction

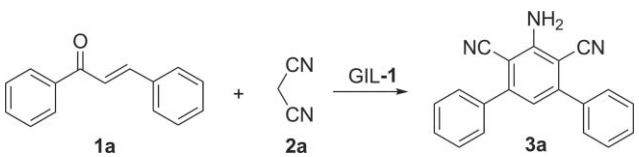
Polysubstituted benzenes represent an important class of organic compounds with numerous applications in organic synthetic chemistry, natural product chemistry, medicinal chemistry, and material chemistry as well.[1] So far, there are many approaches available for the synthesis of polysubstituted benzenes, either by the modification of the given arenes *via* electrophilic or nucleophilic substitutions,[2] coupling reactions catalyzed by transition metals,[3] and metalation-functionalization reactions,[4] or by the construction of the aromatic skeleton from acyclic precursors. For the latter, a series of benzannulation reactions including the [3+2+1] Dötz reaction of Fischer carbene complexes,[5] Danheiser alkyne–cyclobutenone [4+2] cyclization,[6] [4+2] cycloaddition of metalacyclopentadienes with alkynes,[7] transition-metal-catalyzed [2+2+2] and [4+2] cycloaddition,[8] [3+3] cyclocondensation of bielectrophiles and binucleophiles,[9] 1,6-electrocyclization reaction,[10] and [5+1] benzannulation of α-alkenoyl ketene-*S*,*S*-acetals and nitroalkane[11] have been developed. Some of these methodologies have been applied in the synthesis of natural products and met with considerable success, as the formation of regioisomeric mixtures can be avoided in most cases.[12] Each of these approaches represents an important advance toward the objective of a general method for the synthesis of polysubstituted benzenes; however, to match the increasing scientific and practical demands, it is still of continued interest and great importance to explore novel and efficient synthetic approaches.

On the other hand, ionic liquids have attracted extensive interest due to their non-volatility, non-flammability, excellent chemical and thermal stability, high polarity and reusability.[13,14] Over the past few years, a variety of catalytic reactions have been successfully conducted with ionic liquids as solvents or catalysts. Many interesting results have been obtained, which have demonstrated the advantages of using ionic liquids as alternatives for organic solvents. As a new generation of diverse ionic liquids, a wide range of guanidinium ionic liquids (GILs) has been synthesized and used in many organic reactions, such as the Henry reaction and aldol reactions.[15] In our recent work, we achieved Knoeveagel condensation and Michael addition reactions in GILs.[16] For a Heck reaction, we found GILs could act as a solvent, as a strong base to facilitate β-hydride elimination, and as a ligand to stabilize activated Pd species.[17]

In continuation with our research interests regarding the development of the synthetic utility of GILs, we envisaged to explore Michael addition reactions of malononitrile and chalcones in GILs. By this research, we developed a facile and efficient protocol for the synthesis of polysubstituted benzenes from chalcones and active methylene compounds in GILs under mild reaction conditions. Herein, we wish to report our primary experimental results and the mechanisms involved.

## Results and discussion

According to our previous work, a series of GILs were prepared from guanidines and inorganic or organic acids with varied chemical structures as shown in Table 1.[16] With a series of GILs in hand, we selected GIL-**1** as the reaction medium to investigate the Michael addition of malononitrile to chalcones. Thus, the reaction of chalcone **1a** with malononitrile **2a** (1.5 equiv.) was initially performed in GIL-**1** at room temperature under stirring. As indicated by TLC, several products were formed after the starting material **1a** was consumed. When the reaction was conducted at 60 °C, a main product was obtained, which was characterized as a substituted benzene **3a**[18] on the basis of its spectral and analytical data (Scheme 1).




**Scheme 1** Reaction of chalcone **1a** and malononitrile **2a**.

The reaction conditions, including reaction media, *i.e.* GILs, reaction temperature and the feed ratio of malononitrile **2a** and chalcone **1a**, were then investigated. A series of reactions of **1a** with **2a** were conducted in GIL-**1**, which revealed that the optimal results could be obtained when the reaction of **1a** with 2.0 equivalents of **2a** was carried out at room temperature for

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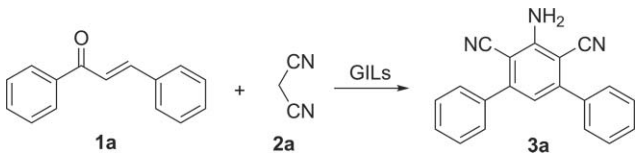
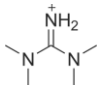
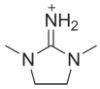
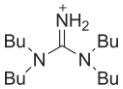
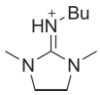
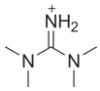
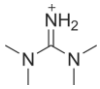
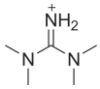
**Table 1** Reactions of chalcone **1a** with malononitrile **2a** in different GILs




| Entry | GIL | Anion | Cation | Viscosity/mPa s[a] | pH[b] | $T$/°C | Time/h | Yield (%)[c] |
|---|---|---|---|---|---|---|---|---|
| 1 | GIL-**1** | $CH_3CH(OH)COO^-$ |  | 163 | 12.38 | 60 | 4.0 | 89 |
| 2 | GIL-**2** | $CH_3CH(OH)COO^-$ |  | 345 | 12.23 | 60 | 10.0 | 35 |
| 3 | GIL-**3** | $CH_3CH(OH)COO^-$ |  | 308 | 11.20 | 60 | 10.0 | 19 |
| 4 | GIL-**4** | $CH_3CH(OH)COO^-$ |  | 142 | 6.20 | 60 | 10.0 | 55 |
| 5 | GIL-**5** | $CF_3COO^-$ |  | 149 | 5.08 | 60 | 10.0 | 0[d] |
| 6 | GIL-**6** | $PF_6^-$ |  | 263 | 1.46 | 60 | 10.0 | 0[e] |
| 7 | GIL-**7** | $CH_3COO^-$ |  | 206 | 8.13 | 95 | 10.0 | 43[f] |

[a] For entries 1–6, measured at 60 °C; for entry 7, measured at 95 °C. [b] Measured with 0.1 M aqueous solution of GIL. [c] Isolated yield for **3a**. [d] Only the Michael adduct was formed. [e] No reaction. [f] Melting point 86 °C.

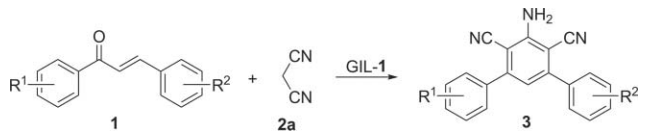
1.5 h, then 60 °C for 2.5 h, whereby the yield of **3a** reached 89% (Table 1, entry 1). The reactions of **1a** with **2a** in varied GILs were examined. It was observed that the reactions of **1a** with **2a** proceeded slowly in GIL-**2**–**4**, with low to moderate yields of **3a** even after prolonged reaction time (Table 1, entries 2–4); whereas in GIL-**5**, only the corresponding Michael adduct was formed (Table 1, entry 5), and in GIL-**6** no reaction occurred (Table 1, entry 6). Since GIL-**7** is solid at 60 °C, the reaction of **1a** with **2a** in GIL-**7** was performed at a higher temperature at which GIL-**7** could act as the reaction medium. In this case, **3a** could be obtained but with low yield (Table 1, entry 7).

The above results suggested that the chemical structures of GILs, including both the anion and cation parts, played a crucial role in the cyclization reaction.[19] Indeed, a significant hurdle in the widespread application of ionic liquids is the effect that they have on reaction outcomes. When a reaction is carried out in an ionic liquid, differences in the rates and selectivities of the process are often observed when compared to the corresponding reaction in a molecular solvent or a different ionic liquid.[20] At this stage there are limited reports detailing the origins of such changes, which is in marked contrast to the extensive understanding of the effect on reaction outcome upon changing from one molecular solvent to another.[21] In the present work, from the data listed in Table 1, it seems that the GILs with low viscosity and strong basicity would facilitate the cyclization reaction of **1a** with **2a**.

Having established the optimal conditions for the cyclization, we intended to determine its scope and limitations with respect to the chalcones with varied substituents. Thus, a range of reactions of chalcones **1b–i** with malononitrile **2a** were carried out in GIL-**1** under the optimized conditions as described in Table 1, entry 1. The reactions of **1b–h** with **2a** proceeded smoothly to afford the corresponding substituted benzenes **3b–h**[22] in good yields (Table 2, entries 2–8). In the case of chalcone **1i** with very a strong electron-withdrawing group, *i.e.* $NO_2$, the reaction proceeded slowly to give the corresponding benzene **3i** with poor yield (Table 2, entry 9). Nevertheless, the efficiency of the cyclization proved to be suitable for most chalcones **1** bearing electron-donating (Table 2, entries 1–3, 5) and electron-withdrawing aryl groups (Table 2, entries 4, 6–8).

**Table 2** Synthesis of polysubstituted benzenes **3**[a,30]



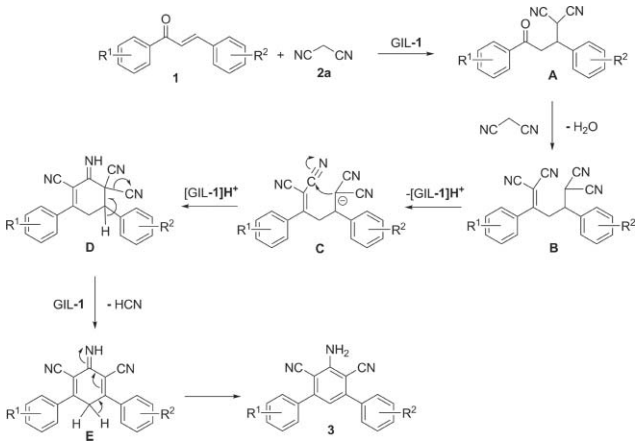

| Entry | Substrate 1 | $R^1$ | $R^2$ | Time/h[b] | 3 | Yield (%)[c] |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | H | 4.0 | **3a** | 89 |
| 2 | **1b** | H | 4-$CH_3$ | 4.0 | **3b** | 76 |
| 3 | **1c** | H | 2-$CH_3O$ | 4.0 | **3c** | 85 |
| 4 | **1d** | H | 4-Cl | 3.5 | **3d** | 81 |
| 5 | **1e** | H | 3,4-($OCH_2O$) | 4.5 | **3e** | 84 |
| 6 | **1f** | 4-Cl | H | 4.0 | **3f** | 79 |
| 7 | **1g** | 4-Cl | 4-$CH_3O$ | 4.0 | **3g** | 83 |
| 8 | **1h** | 4-Cl | 4-Cl | 3.5 | **3h** | 86 |
| 9 | **1i** | H | 4-$NO_2$ | 5.0 | **3i** | 32 |
| 10[d] | **1a** | H | H | 4.0 | **3a** | 85 |
| 11[e] | **1a** | H | H | 4.0 | **3a** | 82 |
| 12[f] | **1a** | H | H | 4.0 | **3a** | 73 |
| 13[g] | **1a** | H | H | 4.0 | **3a** | 69 |

[a] Reagents and conditions: **1** (2.0 mmol), **2a** (4.0 mmol), GIL-**1** (5.0 mL), r.t. 1.5 h, then 60 °C 2.0–3.5 h. [b] Total reaction time. [c] Isolated yield. [d] Reuse of GIL-**1** from entry 1. [e] Reuse of GIL-**1** from entry 10. [f] Reuse of GIL-**1** from entry 11. [g] Reuse of GIL-**1** from entry 12.

Clearly, GIL-**1** plays dual roles as a solvent and a catalyst in the cyclization reactions of **1** and **2a** to polysubstituted benzenes of type **3**. In the present work, it was found that the organic compounds could be easily extracted from the reaction mixture by diethyl ether, which prompted us to investigate the reusability of GIL-**1**. Thus, the reactions of **1a** and **2a** were carried out with the used GIL-**1** following the similar fashion as described above (Table 2, entries 10–13). It was observed that GIL-**1** could attain good catalytic activity even when it was used for the fifth time. The results demonstrated that GIL-**1** could be reused, at least for several times, after removal of the organic products by extraction with diethyl ether.

Actually, *m*-triphenyls[23] are useful intermediates and act as building blocks for cyclophanes[24] to create a large molecular cavity[25] and host–guest complexes.[26] In addition, some *m*-triphenyls have been reported showing important optical properties.[27] So far, there are many approaches available for the synthesis of *m*-terphenyls;[18,22,28] however, most of these methods suffer from several drawbacks, such as multi-step reactions, long reaction time, lower product yields, harsh refluxing conditions, or excess of volatile organic solvents. We herein provided an alternative one-pot synthesis of polysubstituted *m*-triphenyls of type **3** under mild reaction conditions.

To gain insight into the mechanism of the cyclization, a separate experiment was conducted. The reaction of **1b** with malononitrile **2a** (1.0 equiv.) was performed in GIL-**1** at room temperature, and the Michael adduct (**A-b**, see ESI†) was obtained in high yield. On the basis of the experimental results combined together with reports from the literature,[18,22] a mechanism for this cyclization is proposed, as depicted in Scheme 2. Initially, Michael addition of malononitrile **2a** to the chalcone **1** leads to the formation of adduct **A**,[16b] which undergoes a Knoevenagel condensation with another molecule of **2a** to afford intermediate **B**. In the presence of basic GIL-**1**,

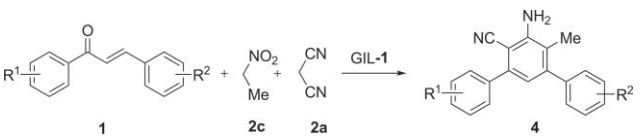



**Scheme 2** Plausible mechanism of the cyclization reaction of chalcones **1** and malononitrile **2a**.

deprotonation of **B** and subsequent intramolecular cycloaddition take place to generate intermediate **D**, which undergoes an elimination of hydrogen cyanide and aromatization to give a substituted *m*-triphenyl **3**.

The cyclocondensation of chalcone **1** with malononitrile **2a** involves a two-component, three-molecule reaction process. With the aim of expanding the scope of this protocol, we performed the reaction of chalcone **1a** with ethyl-2-cyanoacetate **2b** and then malononitrile **2a** under the identical reaction conditions. Unfortunately, the reaction produced a complex mixture. When **1a** and nitroethane **2c** (1.0 equiv.) were subjected to GIL-**1** at room temperature for 3.0 h, followed by the addition of **2a** (1.0 equiv.) at 60 °C, the reaction proceeded smoothly to furnish a product, which was characterized as a substituted *m*-triphenyl **4a** (Table 3, entry 1).

**Table 3** Synthesis of polysubstituted benzenes **4**[a,31]

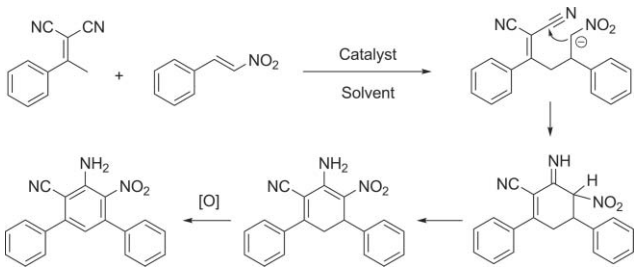



| Entry | Substrate 1 | $R^1$ | $R^2$ | Time[b]/h | 4 | Yield[c](%) |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | H | 6.5 | **4a** | 82 |
| 2 | **1b** | H | 4-$CH_3$ | 6.0 | **4b** | 77 |
| 3 | **1c** | H | 2-$CH_3O$ | 7.0 | **4c** | 72 |
| 4 | **1d** | H | 4-Cl | 5.5 | **4d** | 80 |
| 5 | **1e** | H | 3,4-($OCH_2O$) | 7.0 | **4e** | 79 |
| 6 | **1f** | 4-Cl | H | 6.0 | **4f** | 69 |
| 7 | **1g** | 4-Cl | 4-$CH_3O$ | 7.5 | **4g** | 82 |
| 8 | **1h** | 4-Cl | 4-Cl | 6.5 | **4h** | 83 |
| 9 | **1i** | H | 4-$NO_2$ | 8.0 | **4i** | 0[d] |
| 10[e] | **1a** | H | H | 6.5 | **4a** | 79 |
| 11[f] | **1a** | H | H | 6.5 | **4a** | 73 |
| 12[g] | **1a** | H | H | 6.5 | **4a** | 70 |
| 13[h] | **1a** | H | H | 6.5 | **4a** | 66 |

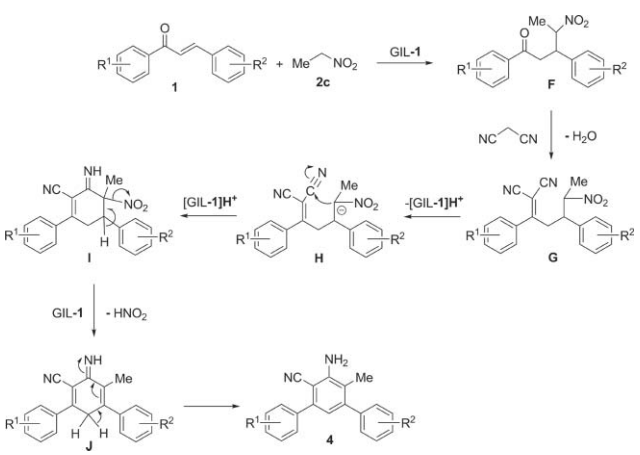
[a] Reagents and conditions: (i) **1** (2.0 mmol), **2c** (2.0 mmol), GIL-**1** (5.0 mL), r.t. 2.5–3.5 h; (ii) **2a** (2.0 mmol), 60 °C, 3.0–4.0 h. [b] Total reaction time. [c] Isolated yield. [d] Complex mixture was formed. [e] Reuse of GIL-**1** from entry 1. [f] Reuse of GIL-**1** from entry 10. [g] Reuse of GIL-**1** from entry 11. [h] Reuse of GIL-**1** from entry 12.

Encouraged by this result, a range of reactions among chalcones **1**, nitroethane **2c** and malononitrile **2a** were carried out in GIL-**1** under the conditions as described in Table 3, entry 1. The reactions of chalcones **1b–h** with nitroethane **2c** and malononitrile **2a** proceeded smoothly to afford the corresponding substituted benzenes **4b–h** in moderate to good yields (Table 3, entries 2–8). In the case of **1i**, however, substituted benzene **4i** was not obtained (Table 3, entry 9). The reusability of GIL-**1** was also studied, and the results revealed that GIL-**1** could maintain good catalytic activity for five runs (Table 3, entries 10–13). The efficiency of the cyclization has been demonstrated for chalcones **1a–1h** bearing electro-neutral, electron-rich, or electron-deficient aryl groups. It should be mentioned that when chalcone **1a**, nitromethane **2d** or nitropropane **2e**, and malononitrile **2a** were subjected to GIL-**1** under the identical conditions, only a complex mixture was obtained. Nevertheless, we provided a novel one-pot synthesis of polysubstituted benzenes of type **4**.

Recently, Xue *et al.* and Su *et al.* achieved the synthesis of polysubstituted *m*-triphenyls by one-pot reaction of vinyl malononitriles with nitroolefins, in which an oxidation reaction was involved as described in Scheme 3.[29] In contrast with their work, we obtained the polysubstituted benzene **4** without the nitro substituent group, which indicated that a different mechanism might be involved in the cyclization process. Moreover, we performed the reaction of **1b** with nitroethane **2c** (1.0 equiv.) in GIL-**1** at room temperature, and obtained Michael adducts (isomers **F-b**, **F-b′**, see ESI†). According to our experimental results, a mechanism for the cyclization reaction of chalcone **1** with nitroethane **2c** and malononitrile **2a** is proposed, as depicted in Scheme 4. Similar to the cyclization reaction of chalcone **1** and malonitrile **2a** (see Scheme 2), the reaction commences from the Michael addition of nitroethane **2c** to chalcone **1**. Subsequently, Knoeveangel condensation of the adduct **F** with malononitrile **2a** occurs to give intermediate **G**, which undergoes an intramolecular cycloaddition to afford intermediate **I**. In the presence of basic GIL-**1**, elimination of nitrous acid ($HNO_2$), rather than oxidation by air, and an aromatization of **J** furnishes the polysubstituted *m*-triphenyl of type **4**. Most possibly, in the case of nitromethane **2d**, both elimination of $HNO_2$ and an oxidation take place, and hence lead to the formation of a complex mixture.




**Scheme 3** Synthesis of *m*-triphenyls *via* reaction of vinyl malononitriles and nitroolefins.[29]




**Scheme 4** A proposed mechanism for the formation of **4**.

## Conclusions

In summary, a facile and efficient one-pot synthesis of polysubstituted *m*-triphenyl of type **3** and **4** has been developed *via* sequential Michael addition, Knoevenagel condensation and nucleophilic cyclization reactions of readily available chalcones **1** with active methylene compounds malononitrile **2a**, and nitroethane **2c**/malononitrile **2a**, respectively, in guanidinium ionic liquid, GIL-**1**. Valuable features of this protocol including simple procedure, mild conditions, good yields, and reusable solvent, *i.e.* GILs, make it an efficient and promising synthetic strategy to build benzene skeletons.

## Acknowledgements

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30 **Typical procedure for the Synthesis of polysubstituted benzenes 3 (3c as an example)**: To a solution of chalcone **1c** (2.0 mmol) in GIL-**1** (5 mL) was added malononitrile **2a** (4.0 mmol) in one portion, and stirred at room temperature for 1.5 h. After the substrate **1c** was consumed (monitored by TLC), the resulting mixture was heated to 60 °C, stirred for 2.5 h, then cooled to room temperature and extracted with diethyl ether (3 × 20 mL). The combined organic phases were concentrated *in vacuo*, and purified by flash chromatography (silica gel, petroleum ether: ethyl acetate = 15 : 1, v : v) to give **3c** as a white solid (85%).**Selected data for 3c**: White solid; mp 168-169 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 3.87 (s, 3H), 5.29 (s, 2H), 6.86 (s, 1H), 7.03-7.08 (m, 2H), 7.28 (m, 1H), 7.43 (d, $J$ = 8.0 Hz, 1H), 7.46-7.49 (m, 3H), 7.58-7.60 (m, 2H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ = 55.4, 93.5, 96.3, 111.7, 115.7, 116.0, 119.3, 120.6, 126.4, 128.5, 128.6, 129.3, 130.2, 130.9, 137.4, 147.6, 149.5, 153.3, 156.0; Anal. Calcd for $C_{21}H_{15}N_3O$: C, 77.52; H, 4.65; N, 12.91; Found: C, 77.38; H, 4.61; N, 12.83.
**3i**: Yellow solid; mp 239-241 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 5.45 (s, 2H), 6.90 (s, 1H), 7.52-7.55 (m, 3H), 7.57 (d, $J$ = 8.0 Hz, 2H), 7.76 (d, $J$ = 8.8 Hz, 2H), 8.37 (d, $J$ = 8.8 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO) $\delta$ = 93.9, 95.1, 115.6, 115.7, 118.4, 123.6, 127.9, 128.5, 128.7, 129.5, 130.2, 137.2, 143.7, 147.5, 150.1, 154.0; Anal. Calcd for $C_{20}H_{12}N_4O_2$: C, 70.58; H, 3.55; N, 16.46; Found: C, 70.79; H, 3.60; N, 16.53.
31 **Typical procedure for the synthesis of polysubstituted benzenes 4 (4a as an example)**: To a solution of chalcone **1a** (2.0 mmol) in GIL-**1** (5 mL) was added nitroethane **2c** (2.0 mmol) in one portion and stirred at room temperature for 3.0 h. After the substrate **1a** was consumed (monitored by TLC), malononitrile **2a** (2.0 mmol) was added. The resulting mixture was heated to 60 °C, stirred for 3.5 h, then cooled to room temperature and extracted with diethyl ether (3 × 20 mL). The combined organic phases were concentrated *in vacuo*, and purified by flash chromatography (silica gel, petroleum ether : ethyl acetate = 15 : 1, v : v) to give **4a** as a white solid (82%).**Selected data for 4**:
**4a**: white solid: mp 202-204 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 2.11 (s, 3H), 4.62 (s, 2H), 6.77 (s, 1H), 7.29-7.32 (m, 2H), 7.38-7.45 (m, 6H), 7.57 (d, $J$ = 6.6 Hz, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 94.1, 118.0, 118.5, 120.9, 127.6, 128.3, 128.31, 128.5, 128.6, 128.9, 138.8, 140.9, 142.5, 147.0, 149.3; IR (KBr, cm$^{-1}$) 818, 1092, 1494, 1545, 1589, 1641, 2208, 3382; Anal. Calcd for $C_{20}H_{16}N_2$: C 84.48; H 5.67; N 9.85; Found: C 84.55; H 5.78; N 9.81.
**4b**: white solid: mp 185-187 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 2.11 (s, 3H), 2.41 (s, 3H), 4.59 (s, 2H), 6.76 (s, 1H), 7.19-7.23 (m, 4H), 7.39-7.46 (m, 3H), 7.55-7.57 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 21.2, 93.9, 118.0, 118.6, 120.9, 128.3, 128.5, 128.6, 128.8, 128.9, 137.4, 137.9, 138.9, 142.5, 147.0, 149.3. IR (KBr, cm$^{-1}$) 826, 966, 1018, 1269, 1548, 1637, 1676. Anal. Calcd for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08; N, 9.39; Found: C, 84.39; H, 6.13; N, 9.42.
**4c**: white solid: mp 171-173 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 1.98 (s, 3H), 3.79 (s, 3H), 4.56 (s, 2H), 6.74 (s, 1H), 7.00-7.04 (m, 2H), 7.16 (d, $J$ = 8.0 Hz, 1H), 7.36-7.43 (m, 4H), 7.58 (d, $J$ = 8.0 Hz, 2H). $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ = 14.3, 55.4, 94.3, 110.7, 118.1, 120.2, 120.6, 121.3, 128.2, 128.5, 128.6, 129.3, 129.7, 130.6, 138.9, 142.3, 143.7, 148.7, 156.3. Anal. Calcd for $C_{21}H_{18}N_2O$: C, 80.23; H, 5.77; N, 8.91; Found: C, 80.11; H, 5.67; N, 8.82.
**4d**: white solid: mp 190-191 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 2.09 (s, 3H), 4.62 (s, 2H), 6.72 (s, 1H), 7.23-7.25 (m, 2H), 7.40-7.45 (m, 5H), 7.54-7.57 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 94.4, 117.8, 118.4, 120.6, 128.4, 128.5, 128.6, 130.3, 133.7, 138.6, 139.3, 142.7, 145.7, 149.3. IR (KBr, cm$^{-1}$) 695, 1037, 1233, 1250, 1438, 1501, 1641, 2208, 3388. Anal. Calcd for $C_{20}H_{15}ClN_2$: C, 75.35; H, 4.74; N, 8.79; Found: C, 75.44; H, 4.65; N, 8.81.
**4e**: white solid: mp 167-168 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 2.11 (s, 3H), 4.60 (s, 2H), 6.00 (s, 2H), 6.73-6.78 (m, 3H), 6.86 (d, $J$ = 7.2 Hz, 1H), 7.39-7.46 (m, 3H), 7.55 (d, $J$ = 6.6 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 94.0, 101.2, 108.2, 109.5, 118.0, 118.6, 120.9, 122.4, 128.3, 128.51, 128.55, 134.7, 138.8, 142.5, 146.6, 147.1, 147.5, 149.3. IR (KBr, cm$^{-1}$) 695, 1037, 1233, 1250, 1438, 1501, 1641, 2208, 3388. Anal. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53; Found: C, 77.13; H, 4.82; N, 8.72.
**4f**: white solid: mp 211-212 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 2.11 (s, 3H), 4.63 (s, 2H), 6.72 (s, 1H), 7.28-7.30 (d, $J$ = 6.9 Hz, 2H), 7.38-7.43 (m, 5H), 7.46-7.52 (m, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 93.9, 117.8, 119.0, 120.7, 127.7, 128.3, 128.8, 128.9, 129.9, 134.5, 137.2, 140.7, 141.2, 147.1, 149.4. IR

(KBr, $cm^{-1}$) 826, 966, 1018, 1269, 1548, 1637, 1676. Anal. Calcd for $C_{20}H_{15}ClN_2$: C, 75.35; H, 4.74; N, 8.79; Found: C, 75.17; H, 4.86; N, 8.73.

**4g**: white solid: mp 203-204 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ = 2.12 (s, 3H), 3.86 (s, 3H), 4.60 (s, 2H), 6.71 (s, 1H), 6.97 (d, $J$ = 8.0 Hz, 2H), 7.23 (d, $J$ = 8.0 Hz, 2H), 7.42 (d, $J$ = 8.0 Hz, 2H), 7.50 (d, $J$ = 8.0 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.4, 55.3, 113.7, 117.8, 119.0, 120.8, 128.7, 129.9, 130.1, 133.0, 134.4, 137.3, 141.1, 146.8, 149.4, 159.2. IR (KBr, $cm^{-1}$) 826, 966, 1018, 1269, 1548, 1637, 1676. Anal. Calcd for $C_{21}H_{17}ClN_2O$: C, 72.31; H, 4.91; N, 8.03; Found: C, 72.52; H, 4.81; N, 8.17.

**4h**: white solid: mp 209-211 °C; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ = 2.08 (s, 3H), 4.64 (s, 2H), 6.67 (s, 1H), 7.22 (d, $J$ = 8.1 Hz, 2H), 7.40-7.43 (m, 4H), 7.48 (d, $J$ = 8.1 Hz, 2H). $^{13}$C NMR (75 MHz, $CDCl_3$) $\delta$ = 14.3, 94.1, 117.6, 118.8, 120.3, 128.5, 128.8, 129.8, 130.2, 133.8, 134.6, 137.0, 139.0, 141.4, 145.8, 149.4. IR (KBr, $cm^{-1}$) 818, 1092, 1466, 1496, 1640, 2208, 3381. Anal. Calcd for $C_{20}H_{14}Cl_2N_2$: C, 68.00; H, 3.99; N, 7.93; Found: C, 67.68; H, 4.12; N, 7.79.



 