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

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Received 14th October 2009, Accepted 19th February 2010 First published as an Advance Article on the web 23rd March 2010 DOI: 10.1039/b921390b

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 nitroalkane¹¹ 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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[†] Electronic supplementary information (ESI) available: Copies of NMR spectra for the new compounds. See DOI: 10.1039/b921390b

			•	CN GILs	NC NH ₂			
Entry	GIL	Anion	Cation	Za ~ Viscosity/mPa s ^a	3a pH [*]	<i>∽</i> <i>T/</i> °C	Time/h	Yield (%) ^c
1	GIL-1	OH CH₃CHCOO	N	163	12.38	60	4.0	89
2	GIL-2	он сн₃снсоо		345	12.23	60	10.0	35
3	GIL-3	OH CH₃CHCOO	Bu Bu Bu Bu Bu Bu	308	11.20	60	10.0	19
4	GIL-4	он сн₃снсоо	HN ^{+, Bu} N N N	142	6.20	60	10.0	55
5	GIL-5	CF ₃ COO	N	149	5.08	60	10.0	0^d
6	GIL- 6	PF_6^-	N N N N N N N N N N	263	1.46	60	10.0	0 ^e
7	GIL-7	CH ₃ COO	NH2 N N	206	8.13	95	10.0	43 ^f

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

^{*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. ^{*c*} 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.* NO₂, 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 2Synthesis of polysubstituted benzenes $3^{a,30}$



^{*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. ^{*c*} 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*-triphenyls²³ are useful intermediates and act as building blocks for cyclophanes²⁴ to create a large molecular cavity²⁵ 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,¹⁶⁶ 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 malonitrile 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 $4^{a,31}$

R ¹	0	, C-t	$R^2 + \langle NO_2 \rangle + \langle N$	GIL-1	NC	Me R ²
	1 Sub	etrata	2C 2a			4
Entry	1		R ²	_ Time ^b /h	4	Yield ^c (%)
1	1a	Н	Η	6.5	4a	82
2	1b	Н	$4-CH_3$	6.0	4b	77
3	1c	Н	2-CH ₃ O	7.0	4c	72
4	1d	Н	4-C1	5.5	4d	80
5	1e	Н	3,4-(OCH ₂ O)	7.0	4e	79
6	1f	4-Cl	Н	6.0	4f	69
7	1g	4-Cl	4-CH ₃ O	7.5	4g	82
8	1h	4-Cl	4-C1	6.5	4h	83
9	1i	Н	$4-NO_2$	8.0	4i	0^d
10^{e}	1a	Н	Н	6.5	4a	79
11^{f}	1a	Н	Н	6.5	4a	73
12 ^g	1a	Н	Н	6.5	4a	70
13 ^h	1a	Н	Н	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. ^{*c*} Reuse of GIL-1 from entry 10. ^{*s*} Reuse of GIL-1 from entry 10. ^{*s*} 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



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



Scheme 4 A proposed mechanism for the formation of 4.

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 (HNO₂), 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 HNO₂ and an oxidation take place, and hence lead to the formation of a complex mixture.

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

Financial support of this research by the National Natural Science Foundation of China (20572013 and 20872136) is greatly acknowledged.

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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 $(3 \times 20 \text{ mL})$. 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; ¹H NMR (400 MHz, CDCl₃) $\delta = 3.87$ (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); ¹³C 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 C21H15N3O: 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; ¹H NMR (400 MHz, CDCl₃) δ = 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); ¹³C NMR (100 MHz, DMSO) δ = 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 C₂₀H₂N₄O₂: 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; ¹H NMR (300 MHz, CDCl₃) δ = 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); ¹³C NMR (75 MHz, CDCl₃) δ = 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 C₂₀H₁₆N₂: 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; ¹H NMR (400 MHz, CDCl₃) δ = 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). ¹³C NMR (75 MHz, CDCl₃) δ = 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 C₂₁H₁₈N₂: 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; ¹H NMR (400 MHz, CDCl₃) δ =

4c: white solid: mp 171-173 °C; ¹H NMR (400 MHz, CDCl₃) δ = 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). ¹³C NMR (100 MHz, CDCl₃) δ = 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 C₂₁H₁₈N₂O: 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; ¹H NMR (300 MHz, CDCl₃) δ = 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). ¹³C NMR (75 MHz, CDCl₃) δ = 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 C₂₀H₁₅ClN₂: 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; ¹H NMR (300 MHz, CDCl₃) δ = 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). ¹³C NMR (75 MHz, CDCl₃) δ = 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 C₂₁H₁₆N₂O₂: 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; ¹H NMR (300 MHz, CDCl₃) $\delta = 2.11$ (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). ¹³C NMR (75 MHz, CDCl₃) $\delta = 14.4$, 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 C₂₀H₁₅ClN₂: 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; ¹H NMR (400 MHz, CDCl₃) δ = 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). ¹³C NMR (75 MHz, CDCl₃) $\delta = 14.4$, 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 C₂₁H₁₇ClN₂O: 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; ¹H NMR (300 MHz, CDCl₃) δ = 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). ¹³C NMR (75 MHz, CDCl₃) $\delta = 14.3, 94.1, 117.6, 118.8, 120.3, 128.5, 128.8, 129.8, 130.2, 133.8,$ 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.