Tetrahedron Letters 54 (2013) 5974–5978

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Catalyst free, regioselective one-pot three-component synthesis of thiazol-2-imine derivatives in ionic liquid

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ARTICLE INFO

Article history:
Received 17 June 2013
Revised 12 August 2013
Accepted 17 August 2013
Available online 27 August 2013

Keywords:
Amine
Phenyl isothiocyanate
β-Nitroacrylate
Thiazol-2-imines
Regioselectivity and ionic liquid

ABSTRACT

A one-pot three-component approach for the synthesis of thiazol-2-imines has been described by the reaction of amine, phenyl isothiocyanate and β-nitroacrylate in [Hbim]BF_4 ionic liquid. The method is applicable for aromatic, benzylic, aliphatic and cyclic amines. Reusable reaction media, regioselectivity, mild reaction condition, catalyst free and high yield of products are the salient features of this protocol.

Thiazole moiety is found as a core unit in various pharmaceuticals as well in agrochemicals such as acrecides, insecticides and plant growth regulators.[1] Particularly, 2-iminothiazoline has been shown to possess different biological activities[2] such as anti-inflammatory, analgesic and kinase (CDK1, CDK5 and GSK3) inhibition,[3] antifungal,[4] melanin-reducing activity (skin whitening agent)[5] and as platelet GPIIb/IIIa receptor antagonists.[6] Recently, Pifithrin (Pft-α) having 2-iminothiazoline skeleton has been projected as a possible lead for the treatment of major neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Stroke and cancer therapy (Fig. 1).[7]

There are various methods for the synthesis of iminothiazolines. Hantzsch condensation reaction was the first method reported for the synthesis of 2-aminothiazole moiety using α-haloketone and thiourea as starting materials.[8] Subsequently other alternative methods have been reported including copper-catalysed N-phenylation of 2-aminobenzothiazole derivatives,[9] condensation of thiazol-2(3*H*)-imines with 4-chloro and 4-isothiocyanato acridines,[3] cycloaddition of 5-imino-1,2,4-thiazolidin-3-ones with both electrophilic and nucleophilic unsaturated compounds such as enamines and ester enolates.[10] Another method is based on the ring expansion of 1-aryl methyl-2-(thiocyanatomethyl) aziridine with an acyl chloride in the presence of $TiCl_4$.[11] In addition to this the synthesis of thiazol-2-imines was also accomplished by the reaction of substituted amines with isothiocyanates.[12] Some of the methods for the synthesis of thiazol-2-imines comprise the use of *N*,*N*′-dialkylthiourea and in situ generated α-bromoketones in one-pot protocol, which is limited to symmetrical thioureas and a few selected ketones.[13] Recently, the three component reaction of phenacyl bromide or 2-chloro-1,3-dicarbonyl compound, amine and phenyl isothiocynate has been reported to give thiazol-2-imines.[14] Murru et al.[15] reported the one-pot reaction of enolisable ketones and disubstituted thioureas in presence of 1,10-(ethane-1,2-diyl) dipyridinium bistribromide (EDPBT) as a brominating agent to give thiazol-2-imines. Though the reported methods are satisfactory for the synthesis of thiazol-2-imines, some drawbacks like harsh reaction condition, low yield, prolonged reaction time and use of polar, volatile and hazardous organic solvents have been encountered. In addition to this some of the methods are limited to

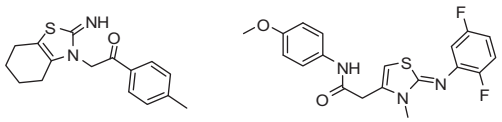

Figure 1. Representative examples of biologically active thiazol-2-imine derivatives.

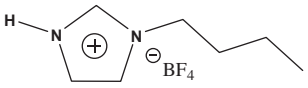

Figure 2. Chemical structure of 1-*n*-butylimidazolium tetrafluoroborate [Hbim]BF_4 ionic liquid.

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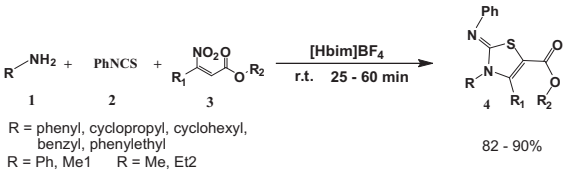
0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.08.056



Scheme 1. Three component synthesis of substituted thiazol-2-imines under catalyst-free condition by using $[Hbim]BF_4$ as a reaction medium.

Table 1
Screening of reaction media[a]

Entry	Reaction media	Time (min)	Yield[b] (%)
1	$[Hbim]BF_4$	55	90
2	$[Hbim]BF_4$	120	90
3	$[bmim]BF_4$	120	75
4	$[bmim]PF_6$	120	72
5	$[emim]BF_4$	120	65

[a] Reaction condition: aniline **1a** (1 mmol), phenyl isothiocyanate **2** (1 mmol) and β-nitroacrylates ((Z)-ethyl 3-nitrobut-2-enoate) **3a** (1 mmol) in 5 mL ionic liquid.
[b] Isolated yield.

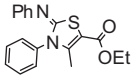
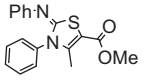
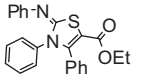
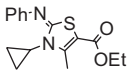
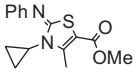
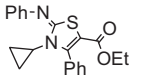
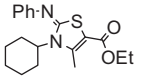
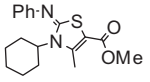
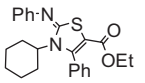
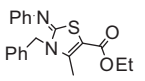
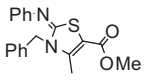
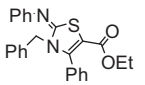
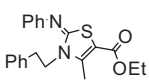
symmetrical thio urea and selected ketones and lack regioselectivity. In this regard it is desirable to develop efficient one pot method for the regioselective formation of thiazol-2-imines under mild reaction conditions.

Multicomponent reactions (MCRs) have recently emerged as valuable tools in pharmaceutical chemistry because of their wide range of applications such as atom economy, simplicity and time-saving features. MCRs are convergent reactions, producing an extremely high increase of molecular complexity in just one step.[16,17] Due to these significant useful attributes of MCRs, they have attracted more and more attention from the medicinal chemistry community.

The use of ionic liquids as a recyclable and environmentally benign medium has been attracting considerable attention for chemical transformations including non-catalytic reactions. The main advantage of ionic liquids is to reduce or eliminate the use of hazardous and toxic solvents.[18] In this context, ionic liquids have emerged as environmentally friendly substitutes for volatile organic compounds.[19]

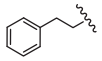
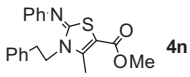
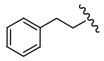
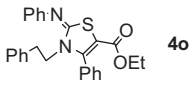
Due to prominent biological activity of thiazol-2-imines and as a part of our ongoing interest in the application of ionic liquids[20]

Table 2
Synthesis of substituted thiazol-2-imines[a] in $[Hbim]BF_4$

Entry	R	R^1	R^2	Product	Time (min)	Yield[b] (%)
1		CH_3	Et	 **4a**	55	90
2		CH_3	Me	 **4b**	55	89
3		ph	Et	 **4c**	25	89
4		CH_3	Et	 **4d**	55	87
5		CH_3	Me	 **4e**	55	86
6		ph	Et	 **4f**	25	86
7		CH_3	Et	 **4g**	60	84
8		CH_3	Me	 **4h**	60	84
9		ph	Et	 **4i**	30	82
10		CH_3	Et	 **4j**	57	84
11		CH_3	Me	 **4k**	57	84
12		ph	Et	 **4l**	27	82
13		CH_3	Et	 **4m**	55	88

(*continued on next page*)

Table 2 (*continued*)

Entry	R	R^1	R^2	Product	Time (min)	Yield[b] (%)
14		CH_3	Me	 **4n**	55	88
15		ph	Et	 **4o**	25	86

[a] All products exhibited physical and spectral (NMR, mass and IR) properties in accordance with the assigned structure.
[b] Isolated yield.

for the synthesis of biologically active molecules, we herein report a catalyst free one-pot three component protocol of amine, phenyl isothiocyanate and β-nitroacrylates to give thiazol-2-imines by using ionic liquid 1-*n*-butylimidazolium tetrafluoroborate [Hbim]BF_4 (Fig. 2) as a reusable reaction medium. (Scheme 1). To the best of our knowledge there is no report of a catalyst-free three component synthesis of thiazol-2-imines by using β-nitroacrylates as one of the starting materials.

β-Nitroacrylates are an emerging class of electron-poor alkenes, having two electron-withdrawing groups in α- and β-positions, since they can be employed as Michael acceptors with indoles,[21] β-dicarbonyl derivatives,[22] and amines.[23] β-Nitroacrylates are less readily available compared to 2-chloro-1,3-dicarbonyl compounds. However, β-nitroacrylates and their derivatives display a significantly higher reactivity and efficiency towards *N*,*N*′-disubsituted thiourea compared to the 2-chloro-1,3-dicarbonyl compounds. The functionalized β-nitroacrylates are easily prepared by nitroaldol reaction followed by dehydration of nitroalkane and ethyl glyoxalate.[24] Therefore, β-nitroacrylates are one of the versatile intermediates which have replaced highly toxic and lachrymatory 2-chloro-1,3-dicarbonyl compounds to prepare a variety of heterocycles.[25]

Accordingly, we first attempted the reaction of aniline **1a** (1 mmol), phenyl isothiocyanate **2** (1 mmol) and β-nitroacrylate, ((Z)-ethyl 3-nitrobut-2-enoate) **3a** (1 mmol) in 5 mL ionic liquid [Hbim]BF_4 (Scheme 1).[27] After completion of reaction (55 min), the desired product **4a** was obtained in 90% yield, which was confirmed by analysing spectral data (Table 2, entry 1). We have not observed the formation of any isomeric thiazol-2-imine.

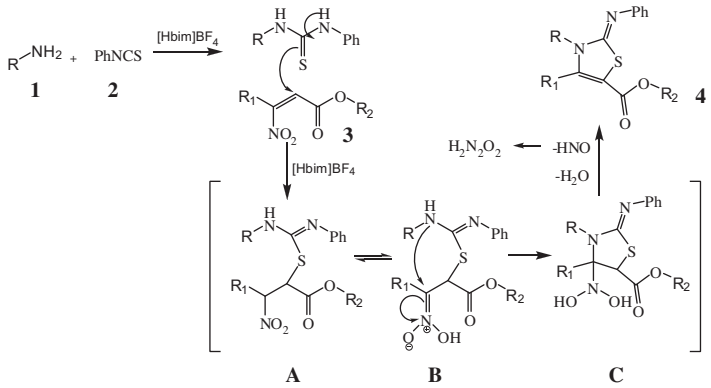
Encouraged by this result, we turned our focus on various imidazole based ionic liquids such as 1-*n*-butylimidazolium tetrafluoroborate [Hbim]BF_4, 1-butyl-3-methylimidazolium tetrafluoroborate [bmim]BF_4, 1-butyl-3-methyl imidazolium hexafluoro phosphate [bmim]PF_6 and 1-ethyl-3-methylimidazolium tetrafluoroborate [emim]BF_4 to study the model reaction in a specific aspect. We noticed that the reaction proceeded smoothly in ionic liquid [Hbim]BF_4 without using additional catalyst and gave high yields of products within a shorter reaction time at rt. The results evaluating the merits of various ionic liquids are presented in Table 1.

Various amines like aryl, benzylic, cyclic and aliphatic underwent smooth reaction under standard conditions to furnish thiazol-2-imines in high yields. The reaction of anilines was very rapid and led to high yields of the expected products (Table 2, entries 1, 2 and 3). However other substituted amines reacted comparatively slowly to give the corresponding products. For example the reaction of benzylamine and phenylethylamine proceeded smoothly under standard reaction conditions to produce the expected products in good to excellent yields (Table 2, entries 10–15). It is worthy to mention that cyclopropylamine and cyclohexylamine underwent condensation under same reaction conditions to furnish corresponding products in good yields (Table 2, entries 4–9).

The plausible mechanism of thiazol-2-imines is proposed based on one of the literature reports.[26] Initially amine reacts with phenyl isothiocyanate to form *N*,*N*′-disubsituted thiourea which on Michael addition to β-nitroacrylate forms Michael adduct **A**, then **A** tautomerizes into the reactive species **B** (*aci*-nitro tautomer), which is promptly attacked by the nitrogen atom, with the formation of the five membered ring **C**. Finally, elimination of water and nitroxyl molecules, lead to the formation of the target thiazole-2-imines **4**.

Further we investigate the reusability aspect of [Hbim]BF_4 in detail for the product **4a** (Table 2, entry 1). After completion of the reaction, the product was isolated from [Hbim]BF_4 by simply extracting with ether. Then the residual ionic liquid was dried under vacuum and reused for three cycles. It was noticed that the yield of the product gradually decreased from first to third cycle (90%, 87% and 84%), respectively. Hence, our protocol can avoid the use of organic solvents and metallic reagents significantly (Scheme 2).

In summary, we have demonstrated a catalyst free one-pot three component synthesis of thiazole-2-imines in an environmentally benign manner. Moreover this protocol is operationally simple and can afford the products in high yield. This procedure is



Scheme 2. Plausible mechanistic pathway for the formation of substituted thiazole-2-imines in the presence of [Hbim]BF_4.

suitable for a variety of amines as well as β-nitroacrylates. Our method describes the use of β-nitroacrylates for the first time in a one-pot three component reaction for the synthesis of thiazole-2-imine derivatives as single isomeric products. Usage of ionic liquid [Hbim]BF_4 makes this procedure very mild, rapid and efficient. The present protocol is also amenable for the synthesis of new novel compounds which were not prepared earlier (Table 2, entries 3–15). We believe that the present protocol may be an attractive alternative over the earlier methods.

Acknowledgements

The author G.S.K. thanks CSIR for the award of a fellowship and S.P.R. thanks Dr. A. Kamal, Outstanding scientist and Head of the MCP Division, for his support and encouragement.

The authors thank CSIR, New Delhi for financial support as part of XII Five Year plan programme under title ORIGIN (CSC-0108).

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24. For the preparation of β-nitroacrylates, see: (a) Shin, C.; Yonezawa, Y.; Narukawa, H.; Nanjo, K.; Yoshimura, J. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3595; (b) Ballini, R.; Fiorini, D.; Palmieri, A. *Tetrahedron Lett.* **2004**, *45*, 7027.
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27. *General procedure:* A mixture of amine (1 mmol), phenyl isothiocyanate (1 mmol) in 5 mL ionic liquid [Hbim]BF_4 was stirred for 5 min at room temperature then the β-nitroacrylate (1 mmol) was added and the mixture was stirred at rt for a stipulated time (see Table 2). The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was extracted with ether (3 × 15 mL). The combined organic layers were washed with brine solution, and dried over Na_2SO_4. Na_2SO_4 was filtered off and the solvent was removed under vacuum. The residue obtained was then purified by silica gel column chromatography (100–200 mesh) using ethyl acetate/hexane as eluent to get corresponding products. All the obtained products were characterized by ^{1}H NMR, ^{13}C NMR, Mass and IR spectral data.[29]
28. Spectral data of compounds:
Compound 4a: White solid; Mp 149–151 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, *J* = 7.19 Hz, 3H), 2.23 (s, 3H), 4.23 (q, *J* = 7.19 Hz, 2H), 6.92 (d, *J* = 7.19 Hz, 2H), 7.02 (t, *J* = 7.19 Hz, 1H), 7.28 (t, *J* = 7.19 Hz, 2H) 7.35 (d, *J* = 7.19 Hz, 2H), 7.48 (d, *J* = 7.19 Hz, 1H), 7.55 (t, *J* = 7.19 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.5, 14.1, 60.7, 100.5, 121.1, 123.5, 128.8, 129.1, 129.3, 129.7, 136.5, 146.8, 151.0, 158.3, 162.0 ppm; IR (KBr): ν = 697, 1092, 1225, 1256, 1296, 1380, 1488, 1581, 1693 cm^{-1}; MS-ESI: *m*/*z* = 339 $[M+1]^+$.
Compound 4b: White solid; Mp 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (3H, s), 3.76 (3H, s), 6.92 (d, *J* = 7.29 Hz, 2H), 7.02 (t, *J* = 7.29 Hz, 1H), 7.27 (t, *J* = 7.29 Hz, 2H), 7.36 (d, *J* = 7.29 Hz, 2H), 7.49 (t, *J* = 7.29 Hz, 1H), 7.55 (t, *J* = 7.29 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 11.6, 60.7, 100.4, 121.1, 123.5, 128.6, 129.1, 129.2, 129.7, 136.4, 146.8, 151.1, 158.3, 162.2 ppm; IR (KBr) ν = 698, 766, 1089, 1222, 1257, 1303, 1579, 1614, 1705 cm^{-1}; MS-ESI: *m*/*z* = 325 $[M+1]^+$.
Compound 4c: Yellow solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.07 (t, *J* = 7.19 Hz, 3H), 4.05 (q, *J* = 7.19 Hz, 2H), 6.98 (d, *J* = 8.22 Hz, 2H), 7.05 (t, *J* = 7.19 Hz, 1H), 7.14–7.35 (m, 12H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3, 60.1, 102.4, 120.4, 123.0, 127.0, 127.6, 128.2, 128.4, 128.6, 128.8, 129.2, 129.3, 136.0, 147.1, 150.3, 157.1, 160.2 ppm; IR (KBr): ν = 698, 708, 761, 1075, 1143, 1319, 1489, 1581, 1615, 1673 cm^{-1}; MS-ESI: *m*/*z* = 401 $[M+1]^+$.
Compound 4d: Orange viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): 0.99 (s, 2H), 1.17 (d, *J* = 7.17 Hz, 2H), 1.21 (t, *J* = 7.17 Hz, 3H), 2.61 (s, 3H), 2.76–2.82 (m, 1H), 4.15 (q, *J* = 7.17 Hz, 2H), 6.97 (d, *J* = 7.17 Hz, 2H), 7.03 (t, *J* = 7.17 Hz, 1H), 7.30 (t, *J* = 7.17, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.7, 13.9, 15.2, 28.6, 60.6, 101.8, 121.2, 123.6, 127.9, 149.2, 151.3, 158.4, 160.8 ppm; IR (KBr) ν = 698, 771, 1085, 1301, 1579, 1617, 1698 cm^{-1}; MS-ESI: *m*/*z* = 303 $[M+1]^+$.
Compound 4e: Yellow solid; Mp 80–82 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.04 (s, 2H), 1.23 (d, *J* = 6.05 Hz, 2H), 2.66 (s, 3H), 2.81–2.87 (m, 1H), 3.72 (s, 3H), 6.99 (d, *J* = 7.78 Hz, 2H), 7.07 (t, *J* = 7.78 Hz, 1H), 7.33 (t, *J* = 7.78 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.2, 14.1, 26.8, 51.5, 99.3, 121.2, 123.5, 129.5, 149.0, 151.3, 158.3, 162.2 ppm; IR (KBr): ν = 697, 773, 1087, 1304, 1583, 1615, 1700 cm^{-1}; MS-ESI: *m*/*z* = 289 $[M+1]^+$.
Compound 4f: Yellow solid; Mp 122–124 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.66 (s, 2H), 0.77 (d, *J* = 6.86 Hz, 2H), 2.76–2.81 (m, 1H), 4.04 (q, *J* = 6.86 Hz, 2H), 7.05–7.13 (m, 3H), 7.34–7.49 (m, 7H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 9.6, 15.1, 28.4, 60.4, 101.5, 120.5, 123.1, 128.0, 129.8, 131.3, 149.4, 151.1, 156.2, 156.5, 156.8, 161.0 ppm; IR (KBr): ν = 699, 767, 1073, 1151, 1313, 1369, 1581, 1608, 1670 cm^{-1}; MS-ESI: *m*/*z* = 365 $[M+1]^+$.
Compound 4g: Pale yellow solid; mp 120–122 °C; ^{1}HNMR (300 MHz, $CDCl_3$): δ 1.25 (t, *J* = 7.65 Hz, 3H), 1.30–1.94 (m, 10H), 2.61 (s, 3H), 2.8 (m, 1H), 4.18 (q, *J* = 7.65 Hz, 2H), 6.99 (d, *J* = 7.65 Hz, 2H), 7.05 (t, *J* = 7.65 Hz, 1H), 7.33 (t, *J* = 7.65 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 14.2, 24.9, 26.4, 28.8, 67.8, 60.4, 97.3, 121.1, 123.2, 129.5, 134.9, 147.4, 151.3, 162.2 ppm; IR (KBr): ν = 699, 775, 1101, 1207, 1293, 1587, 1620, 1701 cm^{-1}; MS-ESI: *m*/*z* = 345 $[M+1]^+$.
Compound 4h: Yellow solid; mp 119–121 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.11–1.97 (m, 10H), 2.62 (s, 3H), 2.8 (m, 1H), 3.71 (s, 3H), 6.99 (d, *J* = 8.30 Hz, 2H), 7.05 (t, *J* = 7.55 Hz, 1H), 7.33 (t, *J* = 8.30 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.6, 24.9, 26.3, 28.7, 51.4, 58.1, 98.9, 120.9, 123.1, 151.1, 156.5, 162.3 ppm; IR (KBr): ν = 698, 771, 1090, 1205, 1291, 1585, 1612, 1695 cm^{-1}; MS-ESI: *m*/*z* = 331 $[M+1]^+$.
Compound 4i: Yellow solid; mp 140–142 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.02 (t, *J* = 7.55 Hz, 3H), 1.41–1.80 (m, 10H), 2.8 (m, 1H), 3.98 (q, *J* = 7.55 Hz, 2H), 7.06 (t, *J* = 7.55 Hz, 3H), 7.27–7.32 (m, 2H), 7.37 (t, *J* = 7.55 Hz, 2H), 7.47–7.53 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0, 24.8, 26.0, 28.6, 59.6, 60.4, 101.5, 121.0, 123.3, 128.4, 128.8, 129.6, 131.4, 149.1, 151.4, 156.0, 156.3, 160.9 ppm; IR (KBr): ν = 696, 762, 1068, 1199, 1290, 1579, 1612, 1713 cm^{-1}; MS-ESI: *m*/*z* = 407 $[M+1]^+$.
Compound 4j: Orange viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, *J* = 7.08 Hz, 3H), 2.49 (s, 3H), 4.20 (q, *J* = 7.08, 2H), 5.25 (s, 2H), 7.01–7.10 (m, 3H), 7.24–7.38 (m, 7H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): 13.3, 14.4, 47.2, 60.6, 99.7, 121.4, 123.6, 126.7, 127.7, 128.8, 129.5, 136.3, 147.0, 150.6, 157.5, 162.1 ppm; IR (KBr): ν = 697, 750, 1092, 1206, 1262, 1401, 1581, 1617, 1696 cm^{-1}; MS-ESI: *m*/*z* = 353 $[M+1]^+$.
Compound 4k: Yellow solid; Mp 82-84 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.49 (s, 3H), 3.74 (s, 3H), 6.26 (s, 2H), 7.02–7.11 (m, 3H), 7.25–7.38 (m, 7H) ppm; ^{13}C

NMR (75 MHz, $CDCl_3$): δ 13.2, 47.2, 51.7, 99.4, 121.1, 123.5, 126.5, 127.6, 128.8, 129.4, 136.0, 147.1, 150.4, 157.4, 162.3 ppm; IR (KBr): ν = 701, 752, 1099, 1202, 1267, 1402, 1589, 1621, 1701 cm^{-1}; MS-ESI: m/z = 339 $[M+1]^+$.

Compound 4l: Yellow solid; mp 104–106 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.04 (t, J = 6.92 Hz, 3H), 4.03 (q, J = 6.92 Hz, 2H), 4.99 (s, 2H), 7.01–7.05 (m, 2H), 7.10(d, J = 8.65 Hz, 3H), 7.15(d, J = 7.78 Hz, 2H), 7.21–7.25(m, 3H), 7.38(t, J = 7.78 Hz, 4H), 7.44(d, J = 7.78 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.8, 48.2, 60.6, 102.2, 121.2, 123.5, 127.1, 127.2, 128.1, 129.3, 129.5, 129.6, 129.9, 136.5, 148.1, 150.5, 157.1, 160.8 ppm; IR (KBr): ν = 696, 756, 1078, 1124, 1206, 1278, 1390, 1486, 1582, 1611, 1708 cm^{-1}; MS-ESI: m/z = 415 $[M+1]^+$.

Compound 4m: Yellow solid; mp 83–85 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.26 (t, J = 7.16 Hz, 3H), 2.28 (s, 3H), 3.10 (t, J = 6.79 Hz, 2H), 4.12–4.22 (m, 4H), 7.07 (d, J = 7.16 Hz, 3H), 7.21 (d, J = 7.16 Hz, 2H), 7.26(s, 1H), 7.31 (t, J = 7.16 Hz, 2H), 7.37 (t, J = 7.16 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.7, 14.3, 33.9, 46.1, 60.6, 99.3, 121.3, 123.5, 126.9, 128.7, 129.0, 129.5, 138.2, 148.9, 150.9, 156.8, 162.1 ppm; IR (KBr): ν = 697, 750, 1095, 1179, 1216, 1279, 1403, 1566, 1698 cm^{-1}; MS-ESI: m/z = 367 $[M+1]^+$.

Compound 4n: Yellow solid; mp 103–105 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 2.25 (s, 3H), 3.10 (t, J = 6.79 Hz, 2H), 3.71 (s, 3H), 4.15 (t, J = 6.79 Hz, 2H), 7.06 (d, J = 8.30, 3H), 7.18–7.40 (m, 7H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.6, 33.8, 46.2, 51.6, 88.8, 121.3, 123.6, 126.9, 128.7, 128.9, 129.5, 138.2, 147.2, 150.8, 156.7, 162.4 ppm; IR (KBr): ν = 698, 774, 1102, 1215, 1272, 1401, 1587, 1619, 1704 cm^{-1}; MS-ESI: m/z = 353 $[M+1]^+$.

Compound 4o: Light green solid; mp 86–88 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 1.03 (t, J = 6.79 Hz, 3H), 2.98 (t, J = 6.79 Hz, 2H), 3.88 (t, J = 6.79 Hz, 2H), 4.00 (q, J = 6.79 Hz, 2H), 6.95 (d, J = 7.55 Hz, 2H), 7.05 (d, J = 7.55 Hz, 2H), 7.13 (d, J = 6.79 Hz, 3H), 7.23 (t, J = 6.79 Hz, 3H), 7.35–7.55 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 33.6, 46.8, 60.3, 101.8, 121.23, 123.6, 126.5, 127.3, 128.3, 128.5, 128.9, 129.1, 129.5, 130.2, 138.0, 150.7, 156.5, 160.9 ppm; IR (KBr): ν = 700, 772, 1122, 1214, 1289, 1389, 1589, 1608, 1708 cm^{-1}; MS-ESI: m/z = 429 $[M+1]^+$.