One-Pot Van Leusen Synthesis of 4,5-Disubstituted Oxazoles in Ionic Liquids

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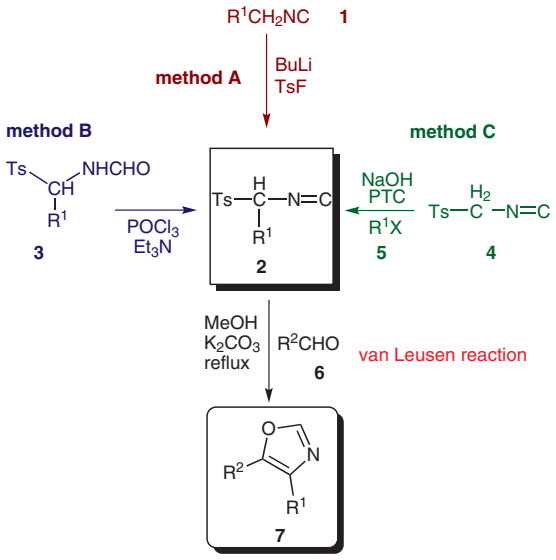
Abstract: An efficient and mild protocol for the preparation of 4,5-disubstituted oxazoles through an improved one-pot van Leusen oxazole synthesis in ionic liquids is described. The oxazole products were prepared from tosylmethyl isocyanide (TosMIC), aliphatic halides and various aldehydes in high yields. The recovered ionic liquids could be reused as solvent for six runs without significant loss of yields.

Key words: ionic liquids, van Leusen oxazole synthesis, tosylmethyl isocyanide, halides, aldehydes

Oxazole ring, as a fundamental construction unit, exists in a large number of pharmacological compounds.[1] Therefore, many strategies for the synthesis of oxazoles have been developed,[2] but only a few approaches are available for the preparation of 4,5-disubstituted oxazoles **7**.[3] Among these protocols, a rather convenient and attractive way is the cyclocondensation between aldehydes **6** and monosubstituted tosylmethyl isocyanide **2** developed by van Leusen et al.[3i,j] However, the bottleneck of this procedure lies with the preparation of precursors **2**.

Today, ionic liquids have shown their significant role in controlling reactions as solvents or catalysts.[4] They have been recognized as an alternative green reaction media because of their unique chemical and physical properties, including nonvolatility, high polarity, thermal stability, nonflammability, controlled miscibility and recyclability. We have recently shown that van Leusen pyrrole synthesis could be efficiently carried out from tosylmethyl isocyanide (TosMIC; **4**) and nitroolefins in ionic liquids.[5] Subsequently, we further extended our studies to explore the novel uses of ionic liquids in van Leusen oxazole-forming reaction.

As shown in Scheme 1, monosubstituted TosMIC precursors **2** could be prepared by three methods. The drawbacks of method A[6] are the toxicity and instability of alkyl isocyanides **1**. Method B[7] is suitable for both aryl- and alkyl-substituted TosMIC, but the synthesis of isocyanides precursors **3** is expensive, and the yield of **2** is moderate. Method C,[8] although it is unsuitable for the halide **5** when R^1 = Ar or *t*-Bu, and the total yields of **7** were moderate (32–78%)[3i,j] with occasional formation of a disubstituted side products, works well with primary alkyl halides, and the basic reaction conditions are similar to those required for the formation of **7** as final products in next step. Therefore, by combining Method C and the van Leusen oxazole reaction, we studied the one-pot synthesis of **7**, in which two steps were involved, from TosMIC **4**, aliphatic halides **5** and aldehydes **6** in ionic liquids.



Scheme 1

In this study, 1-bromobutane (**5a**) was used to optimize the reaction conditions for the preparation of precursors **2**, and the results are summarized in Table 1. Both the base used and the temperature employed had considerable effects on the reaction, but the anion of ionic liquids had nearly no influence. In the presence of a strong base such as NaOH and KOH, the reactions in [bmim]Br were much faster (entries 1 and 7) than those with a weaker base such as K_2CO_3 (entry 8). However, the reactions with strong bases always led to the decreased yields of **2a** due to the formation of disubstituted product **8a** and the decomposition of TosMIC. On the other hand, no products were detected with Na_2CO_3 (entry 19). The reactions in [bmim]Br (1-butyl-3-methylimidazolium bromide), [bmim][BF_4] (1-butyl-3-methylimidazolium fluoroborate) and [bmim]-[PF_6] (1-butyl-3-methylimidazolium hexafluorophosphate) gave almost same results (entries 8, 17 and 18). In these reactions, the target compound **2a** could be obtained in high yields without any formation of disubstituted byproduct. Methanol, a traditional solvent for van Leusen oxazole synthesis, was tested, and the results indicated that no substituted products were found (entries 3 and 10).

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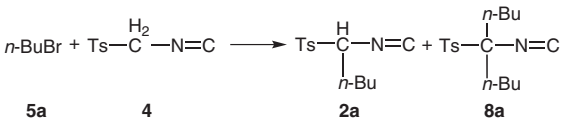
Table 1 Optimization of Monosubstitution Reaction Conditions[a]



Entry	Base	Solvent	Temp (°C)	Time (h)[b]	Yield (%)[c] of **2a**	Yield (%)[c] of **8a**
1	NaOH	[bmim]Br	r.t.	4	50	20
2	NaOH	[bmim]Br–H_2O[d]	r.t.	4	33	15
3	NaOH	MeOH	r.t.	4	0	0
4	NaOH	[bmim]Br–MeOH[d]	r.t.	4	25	15
5	NaOH	THF	r.t.	10	20	30
6	NaOH	MeCN	r.t.	10	30	25
7	KOH	[bmim]Br	r.t	4	42	27
8	K_2CO_3	[bmim]Br	r.t	12	95	0
9	K_2CO_3	[bmim]Br–H_2O[d]	r.t	10	75	0
10	K_2CO_3	MeOH	r.t	6	0	0
11	K_2CO_3	[bmim]Br–MeOH[d]	r.t	6	35	10
12[e]	K_2CO_3	THF	r.t.	24	trace	0
13[e]	K_2CO_3	MeCN	r.t.	24	trace	0
14	K_2CO_3	[bmim]Br	0	12	95	0
15	K_2CO_3	[bmim]Br	40	6	90	0
16	K_2CO_3	[bmim]Br	60	4	75	5
17	K_2CO_3	[bmim][BF_4]	r.t	10	95	0
18	K_2CO_3	[bmim][PF_6]	r.t	10	94	0
19[e]	Na_2CO_3	[bmim]Br	r.t	24	0	0

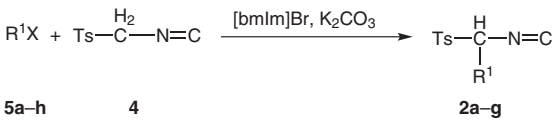
[a] Reaction conditions: **5a** (1.5 mmol), base (2 mmol), TosMIC **4** (1 mmol), solvent (2.5 mL).
[b] Monitored by TLC (PE–EtOAc, 5:1).
[c] Isolated yields, product was identified by ^{1}H NMR and ^{13}C NMR.
[d] Ratio of volume (2:1).
[e] About 70% of TosMIC was recovered.

Absolutely anhydrous condition was not necessary for the reaction, but the addition of water or methanol to the reaction resulted in a lower yield of **2a** with the formation of **8a** (entries 2, 4, 9 and 11). Other solvents, such as THF and acetonitrile were also tested. However, both **2a** and **8a** were obtained in the presence of NaOH (entries 5 and 6), but no reaction product was found with K_2CO_3 (entries 12 and 13). Because of the instability of TosMIC, higher temperatures (entries 15 and 16) were not suitable for the reaction. So the conditions in entry 6 were chosen for next investigations.

In order to evaluate the scope of this reaction sequence, a series of products **2a**–**g**, serving as cyclocondensation precursors for the van Leusen oxazole synthesis, was prepared on the basis of the success of the monosubstitution model system. From the results listed in Table 2, all monoalkyl products were obtained in excellent yields from TosMIC and primary aliphatic halides including allyl bromide (entry 7) and benzyl halides (entries 5 and 6). Secondary alkyl halide also gave monosubstituted TosMIC in good yield (entry 8). For tertiary alkyl halides, this method failed due to the steric hindrance. Furthermore, aryl halides could not give any desired products.

Subsequent studies were then focused on the one-pot synthesis of 4,5-disubstituted oxazoles. After a brief optimization, the generality of the present synthetic method was extended to different aliphatic halides and aldehydes. The results are listed in Table 3. Treatment of different aldehydes with monosubstituted TosMIC formed in situ afforded the corresponding 4,5-disubstituted oxazoles **7** in high yields. Aliphatic aldehydes (entries 13, 14, 17 and 19) had only slightly lower yields than the reactions using

Table 2 Preparation of Monosubstituted TosMIC from Aliphatic Halides and TosMIC in [bmim]Br[a,9]



5a–h 4 2a–g

Entry	R^1X	Temp (°C)	Time[b] (h)	Product	Yield (%)[c]
1	BuBr (**5a**)	r.t.	12	**2a**	95
2	MeI (**5b**)	0	4	**2b**	96
3	EtBr (**5c**)	r.t.	10	**2c**	96
4	$Me(CH_2)_7Br$ (**5d**)	r.t.	12	**2d**	90
5	BnBr (**5e**)	r.t	6	**2e**	90
6	BnCl (**5f**)	r.t.	10	**2e**	95
7	CH_2=$CHCH_2Br$ (**5g**)	r.t.	10	**2f**	94
8[d]	*i*-PrBr (**5h**)	r.t.	24	**2g**	80

[a] Reaction conditions: **5a**–**h** (1.5 mmol), K_2CO_3 (2 mmol), TosMIC **4** (1 mmol), [bmim]Br (2.5 mL).
[b] Monitored by TLC (PE–EtOAc, 5:1).
[c] Isolated yields, product was identified by ^{1}H NMR and ^{13}C NMR.
[d] Amount of **5h** used: 2 mmol.

aromatic and heterocyclic aldehydes as substrates (entries 1–12, 15, 16 and 18). Aromatic aldehydes with electron-withdrawing group displayed higher reactivity (entries 4 and 9). On the other hand, steric effects of either *ortho* substituents on aryl ring (entry 6) or secondary alkyl halide (entry 20) decreased the yields.

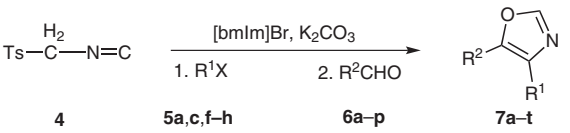
The recyclability of ionic liquid for the one-pot van Leusen oxazole synthesis was investigated on a relatively larger scale (15 mL; Table 4). After completion of the first run, the reaction mixture was poured into equal volume of water and extracted with diethyl ether. Evaporation of water layer under reduced pressure gave the recovered ionic liquid, which could be used in the next run. The recovered ionic liquid could be reused for several times with slight decrease of reaction yields in each run.

Table 4 Recycling of Ionic Liquid Solvent

Entry	Run	Yield (%)[a]
1	1[b]	85
2	2[c]	82
3	3[c]	78
4	4[c,d]	75
5	5[c]	70
6	6[c]	64

[a] Isolated yields; product was identified by GC–MS.
[b] Reaction conditions: K_2CO_3 (15 mmol), **5a** (7.5 mmol), TosMIC (5 mmol), [bmim]Br (15 mL), **6a** (6 mmol).
[c] Reaction conditions: K_2CO_3 (7.5 mmol), **5a** (7.5 mmol), TosMIC (5 mmol), recycled [bmim]Br (about 15ml), **6a** (6 mmol).
[d] Another 2 mL of fresh [bmim]Br was added.

Table 3 One-Pot Preparation of 4,5-Disubstituted Oxazoles **7** from Aliphatic Halides, TosMIC and Aldehydes in [bmim]Br[a,b,10,11]



4 5a,c,f–h 6a–p 7a–t

Entry	R^1	R^2	Product	Yield (%)[c]
1	*n*-Bu (**5a**)	Ph (**6a**)	**7a**	85
2	*n*-Bu (**5a**)	4-$MeOC_6H_4$ (**6b**)	**7b**	80
3	*n*-Bu (**5a**)	4-MeC_6H_4 (**6c**)	**7c**	82
4	*n*-Bu (**5a**)	4-FC_6H_4 (**6d**)	**7d**	90
5	*n*-Bu (**5a**)	4-BrC_6H_4 (**6e**)	**7e**	85
6	*n*-Bu (**5a**)	2-ClC_6H_4 (**6f**)	**7f**	78
7	*n*-Bu (**5a**)	3-ClC_6H_4 (**6g**)	**7g**	82
8	*n*-Bu (**5a**)	4-ClC_6H_4 (**6h**)	**7h**	86
9	*n*-Bu (**5a**)	4-$O_2NC_6H_4$ (**6i**)	**7i**	88
10	*n*-Bu (**5a**)	1-naphthyl (**6j**)	**7j**	81
11	*n*-Bu (**5a**)	styryl (**6k**)	**7k**	82
12	*n*-Bu (**5a**)	1-furyl (**6l**)	**7l**	90
13[d]	*n*-Bu (**5a**)	*i*-Bu (**6m**)	**7m**	78
14[d]	*n*-Bu (**5a**)	*c*-Hex (**6n**)	**7n**	75
15	Et (**5c**)	Ph (**6a**)	**7o**	87
16	Bn (**5f**)	Ph (**6a**)	**7p**	85
17[d]	Bn (**5f**)	*n*-Pr (**6o**)	**7q**	80
18	allyl (**5g**)	Ph (**6a**)	**7r**	87
19[d]	allyl (**5g**)	*n*-Hex (**6p**)	**7s**	80
20[e]	*i*-Pr (**5h**)	Ph (**6a**)	**7t**	75

[a] Reaction conditions: K_2CO_3 (3 mmol), aliphatic halides **5** (1.5 mmol), TosMIC (**4**; 1 mmol), [bmim]Br (2.5 mL), after **4** was consumed, aldehyde **6** (1.2 mmol) was added. After about another 10 h the reaction was complete.
[b] Monitored by TLC (PE–EtOAc, 5:1).
[c] Isolated yields; product was identified by ^{1}H NMR, ^{13}C NMR and GC–MS.
[d] Aliphatic aldehyde **6** (2 mmol).
[e] Amount of **5h** used: 2 mmol.

In conclusion, we have demonstrated that the synthesis of 4,5-disubstituted oxazoles could be achieved in one pot from TosMIC, aliphatic halides and aldehydes. The improved van Leusen oxazole synthesis offers marked improvements with regard to its operational simplicity, mild conditions, general applicability, high isolated yields of products, and recyclable green solvent. Although it was not suitable for tertiary alkyl or aryl halides, it provides a

practical alternative procedure better than the existing methods.[3]

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

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(9) **Representative Preparation of Monosubstituted TosMIC**: 1-Bromobutane (**5a**; 0.206 g, 1.5 mmol) was added to the mixture of TosMIC (**4**; 0.195 g, 1 mmol), K_2CO_3 (0.414 g, 3 mmol) and [bmim]Br (2.5 mL). After vigorous stirring for 12 h at r.t., the mixture was poured into H_2O (10 mL), and was extracted with Et_2O (3 × 10 mL). The combined organics were washed with H_2O and brine. The organic phase was dried over Na_2SO_4, and concentrated in vacuum. The crude product was purified by chromatography on silica gel (PE–EtOAc, 4:1) to provide pure compound **2a** (95%).

(10) **Representative Preparation of 4,5-Disubstituted Oxazoles**: 1-Bromobutane (**5a**; 0.206 g, 1.5 mmol) was added to the mixture of TosMIC (**4**; 0.195 g, 1 mmol), K_2CO_3 (0.414 g, 3 mmol) and [bmim]Br (2.5 mL). After vigorous stirring 12 h at r.t., **4** was consumed, and benzaldehyde (**6a**; 0.127 g, 1.2 mmol) was added. After about 10 h of stirring, the mixture was poured into H_2O (10 mL), and was extracted with Et_2O (3 × 10 mL). The combined organics were washed with H_2O and brine. The organic phase was dried over Na_2SO_4, and concentrated in vacuum. The crude product was purified by chromatography on silica gel (PE–EtOAc, 10:1) to provide pure compound **7a** (85%).

(11) **Spectroscopic Data for Products:**
Compound **2a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91–0.95 (t, *J* = 14.4 Hz, 3 H), 1.33–1.49 (m, 3 H), 1.56–1.65 (m, 1 H), 1.79–1.88 (m, 1 H), 2.15–2.21 (m, 1 H), 2.48 (s, 3 H), 4.43–4.46 (m, 1 H), 7.41–7.44 (d, *J* = 8.0 Hz, 2 H), 7.85–7.87 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 21.8, 21.8, 27.4, 28.2, 73.0, 130.1, 130.2, 131.2, 146.6, 164.9.
Compound **2b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.74–1.75 (d, *J* = 6.8 Hz, 3 H), 2.50 (s, 3 H), 4.60–4.65 (m, 1 H), 7.44–7.46 (d, *J* = 8.0 Hz, 2 H), 7.87–7.89 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.5, 21.8, 68.3, 130.2, 130.7, 146.7, 164.6.
Compound **2c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.19 (t, *J* = 15.2 Hz, 3 H), 1.84–1.92 (m, 1 H), 2.23–2.29 (m, 1 H), 2.49 (s, 3 H), 4.38–4.42 (m, 1 H), 7.42–7.44 (d, *J* = 8.0 Hz, 2 H), 7.86–7.88 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.9, 21.8, 22.5, 74.2, 130.0, 130.2, 131.3, 146.6, 164.9.
Compound **2d**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86–0.90 (t, *J* = 13.6 Hz, 3 H), 1.27–1.37 (m, 10 H), 1.40–1.48 (m, 1 H), 1.58–1.65 (m, 1 H), 1.78–1.88 (m, 1 H), 2.14–2.22 (m, 1 H), 2.49 (s, 3 H), 4.43–4.47 (m, 1 H), 7.42–7.44 (d, *J* = 8.0 Hz, 2 H), 7.86–7.88 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.0, 22.8, 25.6, 28.6, 28.8, 29.2, 29.3, 31.9, 73.2, 130.3, 130.3, 131.4, 146.7, 165.1.
Compound **2e**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 (s, 3 H), 2.96–3.02 (m, 1 H), 3.58–3.62 (m, 1 H), 4.58–4.61 (m, 1 H), 7.26–7.27 (m, 2 H), 7.29–7.37 (m, 3 H), 7.43–7.45 (d, *J* = 8.0 Hz, 2 H), 7.90–7.92 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 34.8, 74.2, 128.1, 129.1, 129.3, 130.2, 130.2, 131.2, 133.3, 146.8, 166.0.
Compound **2f**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.49 (s, 3 H), 2.53–2.61 (m, 1 H), 2.95 (s, 1 H), 4.47–4.51 (m, 1 H), 5.28–5.33 (m, 2 H), 5.73–5.83 (m, 1 H), 7.43–7.45 (d, *J* = 8.0 Hz, 2 H), 7.87–7.89 (d, *J* = 8.4 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 21.8, 29.7, 33.1, 72.3, 121.3, 121.4, 129.3, 130.2, 131.1, 146.7, 165.5.
Compound **2g**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16–1.18 (d, *J* = 6.8 Hz, 3 H), 1.21–1.22 (d, *J* = 6.4 Hz, 3 H), 2.48 (s, 3 H), 2.70–2.77 (m, 1 H), 4.33–4.34 (d, *J* = 3.6 Hz, 1 H), 7.41–7.43 (d, *J* = 8.0 Hz, 2 H), 7.86–7.88 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9, 20.8, 27.9, 30.9, 78.0, 129.6, 130.2, 133.0, 146.4, 165.5.
Compound **7a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–0.97 (t, *J* = 14.8 Hz, 3 H), 1.38–1.48 (m, 2 H), 1.69–1.77 (m, 2 H), 2.75–2.79 (t, *J* = 15.6 Hz, 2 H), 7.31–7.35 (t, *J* = 14.8 Hz, 1 H), 7.42–7.46 (t, *J* = 15.2 Hz, 2 H), 7.59–7.61 (d, *J* = 8.8 Hz, 2 H), 7.83 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ =

13.9, 22.5, 26.7, 30.8, 125.6, 127.8, 128.7, 129.0, 135.8, 145.3, 149.1. GC–MS (ES): *m*/*z* = 201 $[M]^+$.

Compound **7b**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92–0.96 (m, 3 H), 1.37–1.46 (m, 2 H), 1.68–1.75 (m, 2 H), 2.71–2.75 (t, *J* = 15.2 Hz, 2 H), 3.84 (s, 3 H), 6.96–6.98 (m, 2 H), 7.51–7.53 (m, 2 H), 7.80 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 26.6, 30.9, 55.3, 114.3, 121.7, 130.1, 130.1, 134.4, 145.4, 148.7, 159.3. GC–MS (ES): *m*/*z* = 231 $[M]^+$.

Compound **7c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92–0.96 (t, *J* = 14.8 Hz, 3 H), 1.37–1.47 (m, 2 H), 1.68–1.76 (m, 2 H), 2.38 (s, 3 H), 2.73–2.77 (t, *J* = 15.2 Hz, 2 H), 7.23–7.25 (d, *J* = 8.0 Hz, 2 H), 7.48–7.50 (d, *J* = 8.0 Hz, 2 H), 7.81 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 21.2, 22.5, 26.7, 30.9, 125.7, 126.2, 129.5, 135.2, 137.8, 145.5, 148.9. GC–MS (ES): *m*/*z* = 215 $[M]^+$.

Compound **7d**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92–0.96 (t, *J* = 14.8 Hz, 3 H), 1.36–1.46 (m, 2 H), 1.67–1.75 (m, 2 H), 2.71–2.74 (t, *J* = 15.2 Hz, 2 H), 7.10–7.16 (m, 2 H), 7.53–7.58 (m, 2 H), 7.81 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 26.6, 30.8, 115.8, 116.0, 125.2, 125.2, 127.5, 135.5, 135.5, 144.6, 149.1, 161.0, 163.5. GC–MS (ES): *m*/*z* = 219 $[M]^+$.

Compound **7e**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–0.96 (t, *J* = 14.8 Hz, 3 H), 1.39–1.44 (m, 2 H), 1.68–1.74 (m, 2 H), 2.72–2.76 (t, *J* = 5.6 Hz, 2 H), 7.45–7.47 (d, *J* = 8.8 Hz, 2 H), 7.56–7.58 (d, *J* = 8.4 Hz, 2 H), 7.84 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 26.7, 30.7, 121.8, 127.1, 127.9, 128.1, 132.0, 136.4, 144.4, 149.3. GC–MS (ES): *m*/*z* = 279 $[M]^+$.

Compound **7f**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85–0.89 (t, *J* = 14.4 Hz, 3 H), 1.29–1.35 (m, 2 H), 1.61–1.67 (m, 2 H), 2.51–2.55 (t, *J* = 15.2 Hz, 2 H), 7.33–7.39 (m, 3 H), 7.49–7.51 (m, 1 H), 7.91 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 22.3, 25.7, 30.6, 126.7, 127.9, 130.2, 130.5, 131.8, 134.2, 137.9, 143.4, 150.2. GC–MS (ES): *m*/*z* = 235 $[M]^+$.

Compound **7g**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94–0.97 (t, *J* = 14.8 Hz, 3 H), 1.38–1.47 (m, 2 H), 1.69–1.77 (m, 2 H), 2.75–2.78 (t, *J* = 15.2 Hz, 2 H), 7.29–7.31 (m, 1 H), 7.35–7.39 (t, *J* = 15.6 Hz, 1 H), 7.46–7.49 (m, 1 H), 7.59–7.60 (t, *J* = 3.6 Hz, 1 H), 7.84 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.4, 22.5, 26.7, 30.7, 123.6, 125.6, 127.8, 130.0, 130.6, 134.8, 136.9, 144.1, 149.4. GC–MS (ES): *m*/*z* = 235 $[M]^+$.

Compound **7h**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–0.96 (t, *J* = 14.8 Hz, 3 H), 1.39–1.45 (m, 2 H), 1.68–1.76 (m, 2 H), 2.72–2.76 (t, *J* = 15.2 Hz, 2 H), 7.39–7.42 (m, 2 H), 7.51–7.53 (m, 2 H), 7.83 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 26.7, 30.7, 126.8, 127.4, 129.0, 129.4, 129.4, 133.7, 136.3, 144.4, 149.2. GC–MS (ES): *m*/*z* = 235 $[M]^+$.

Compound **7i**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95–0.99 (t, *J* = 14.8 Hz, 3 H), 1.42–1.48 (m, 2 H), 1.72–1.78 (m, 2 H), 2.82–2.86 (t, *J* = 15.6 Hz, 2 H), 7.77–7.79 (m, 2 H), 7.93 (s, 1 H), 8.30–8.32 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.5, 27.1, 30.6, 124.3, 125.7, 128.1, 129.8, 134.9, 139.6, 143.5, 146.7, 150.3. GC–MS (ES): *m*/*z* = 246 $[M]^+$.

Compound **7j**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82–0.86 (t, *J* = 14.8 Hz, 3 H), 1.26–1.35 (m, 2 H), 1.63–1.71 (m, 2 H), 2.55–2.59 (t, *J* = 15.6 Hz, 2 H), 7.50–7.56 (m, 4 H), 7.83–7.85 (m, 1 H), 7.89–7.95 (m, 2 H), 8.00 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 22.4, 25.9, 31.0, 125.1, 125.5, 126.0, 126.3, 126.7, 128.4, 128.5, 129.8, 131.9, 133.8, 137.8, 145.2, 150.2. GC–MS (ES): *m*/*z* = 251 $[M]^+$.

Compound **7k**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93–0.97 (t, *J* = 14.8 Hz, 3 H), 1.34–1.43 (m, 2 H), 1.63–1.71 (m, 2 H), 2.60–2.63 (t, *J* = 4.8 Hz, 2 H), 6.85–6.89 (d, *J* = 16.4 Hz, 1 H), 6.99–7.03 (d, *J* = 16.4 Hz, 1 H), 7.26–7.29 (t, *J* = 12.0 Hz, 1 H), 7.34–7.38 (t, *J* = 15.2 Hz, 2 H), 7.47–7.49 (d, *J* = 7.6 Hz, 2 H), 7.77 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 13.9, 22.3, 31.0, 31.1, 112.5, 112.5, 126.4, 128.0, 128.0, 128.3, 128.4, 128.8, 128.8, 136.7, 136.7, 137.7, 145.1, 149.4, 149.4. GC–MS (ES): *m*/*z* = 227 $[M]^+$.

Compound **7l**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–0.94 (t, *J* = 14.4 Hz, 3 H), 1.33–1.43 (m, 2 H), 1.64–1.71 (m, 2 H), 2.75–2.79 (t, *J* = 15.2 Hz, 2 H), 6.47–6.48 (m, 1 H), 6.54–6.54 (d, *J* = 3.2 Hz, 1 H), 7.47 (s, 1 H), 7.76 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 22.3, 25.8, 30.8, 107.1, 111.3, 136.0, 138.6, 142.4, 149.0. GC–MS (ES): *m*/*z* = 191 $[M]^+$.

Compound **7m**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87–0.93 (m, 9 H), 1.28–1.34 (m, 2 H), 1.53–1.59 (m, 2 H), 1.88–1.95 (m, 1 H), 2.37–2.43 (m, 4 H), 7.65 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.3, 22.4, 25.3, 28.1, 31.2, 33.5, 135.0, 146.5, 148.9. GC–MS (ES): *m*/*z* = 181 $[M]^+$.

Compound **7n**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89–0.92 (t, *J* = 14.4 Hz, 3 H), 1.26–1.35 (m, 6 H), 1.50–1.59 (m, 4 H), 1.70–1.83 (m, 4 H), 2.42–2.49 (m, 2 H), 2.60–2.66 (m, 1 H), 7.64 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 22.3, 25.3, 25.8, 26.3, 31.5, 31.7, 34.8, 132.7, 148.5, 151.1. GC–MS (ES): *m*/*z* = 207 $[M]^+$.

Compound **7o**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31–1.35 (t, *J* = 15.2 Hz, 3 H), 2.78–2.84 (m, 2 H), 7.32–7.35 (t, *J* = 14.8 Hz, 1 H), 7.41–7.46 (m, 2 H), 7.59–7.61 (d, *J* = 7.6 Hz, 2 H), 7.84 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 20.3, 125.7, 127.9, 128.8, 128.9, 136.9, 145.1, 149.2. GC–MS (ES): *m*/*z* = 173 $[M]^+$.

Compound **7p**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.15 (s, 2 H), 7.19–7.28 (m, 4 H), 7.30–7.35 (m, 2 H), 7.40–7.43 (m, 2 H), 7.59–7.62 (m, 2 H), 7.87 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.9, 125.9, 126.5, 128.3, 125.5, 128.5, 128.6, 128.9, 133.9, 138.6, 146.6, 149.5. GC–MS (ES): *m*/*z* = 235 $[M]^+$.

Compound **7q**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89–0.92 (t, *J* = 14.8 Hz, 3 H), 1.58–1.67 (m, 2 H), 2.55–2.59 (t, *J* = 14.8 Hz, 2 H), 3.82 (s, 1 H), 7.11–7.22 (m, 4 H), 7.24–7.30 (m, 1 H), 7.70 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.6, 21.6, 26.5, 32.1, 126.3, 128.5, 128.6, 133.2, 139.3, 148.0, 149.1. GC–MS (ES): *m*/*z* = 235 $[M]^+$.

Compound **7r**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.53–3.54 (d, *J* = 6.0 Hz, 2 H), 5.12–5.14 (m, 1 H), 5.17 (s, 1 H), 6.00–6.10 (m, 1 H), 7.30–7.34 (t, *J* = 14.4 Hz, 1 H), 7.40–7.44 (t, *J* = 15.2 Hz, 2 H), 7.58–7.60 (d, *J* = 8.0 Hz, 2 H), 7.84 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.4, 116.6, 125.8, 128.2, 128.6, 128.8, 133.1, 134.4, 146.2, 149.4. GC–MS (ES): *m*/*z* = 185 $[M]^+$.

Compound **7s**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.85–0.88 (t, *J* = 13.6 Hz, 3 H), 1.27 (s, 6 H), 1.55–1.60 (m, 2 H), 2.57–2.61 (t, *J* = 14.8 Hz, 2 H), 3.21–3.23 (d, *J* = 6.4 Hz, 2 H), 5.05–5.11 (m, 2 H), 5.87–5.96 (m, 1 H), 7.69 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.0, 22.5, 24.4, 28.1, 28.7, 30.2, 31.4, 116.0, 131.9, 135.2, 147.9, 148.9. GC–MS (ES): *m*/*z* = 193 $[M]^+$.

Compound **7t**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32–1.34 (t, *J* = 6.8 Hz, 6 H), 3.23–3.30 (m, 1 H), 7.32–7.36 (t, *J* = 15.2 Hz, 1 H), 7.43–7.46 (t, *J* = 15.2 Hz, 2 H), 7.57–7.60 (t, *J* = 8.4 Hz, 2 H) 7.84 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0, 25.7, 126.1, 128.0, 128.8, 129.0, 140.9, 144.2, 149.4. GC–MS (ES): *m*/*z* = 187 $[M]^+$.

Compound **8a**: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90–0.94 (t, *J* = 14.8 Hz, 6 H), 1.29–1.36 (m, 4 H), 1.38–1.46 (m, 2 H), 1.49–1.55 (m, 2 H), 1.88–2.05 (m, 4 H), 2.48 (s, 3 H), 7.40–7.42 (d, *J* = 8.0 Hz, 2 H), 7.85–7.87 (d, *J* = 8.4 Hz, 2 H).