One-Pot Regioselective Synthesis of 3-Benzylthiazolo[3,2-*a*]indoles by Sequential Sonogashira Coupling Followed by Triethylamine-Induced Cyclization

K. C. Majumdar,*[1] Sanjay Nath

Department of Chemistry, University of Kalyani, Kalyani 741235, W. B., India
Fax +91(33)25828282; E-mail: kcm_ku@yahoo.co.in

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Abstract: A number of 2-(prop-2-ynylthio)-1*H*-indoles have been utilized for the synthesis of 3-benzylthiazolo[3,2-*a*]indoles by Sonogashira acetylide-coupling followed by triethylamine-induced regioselective cyclization in a one-pot operation. The cyclization is dependent on the nature of the substituents on the phenyl ring of the substrates.

Key words: Sonogashira coupling, palladium catalyst, base-promoted cyclization, aryl iodide, thiazoloindole

Thiazoles are useful heterocycles and building blocks and a prominent structural moiety of compounds relevant to treatment of cancer, bacterial, fungal, and viral infections,[2] and are known to exhibit pharmacological activities.[3] Because of their wide range of important biological activities, they serve as attractive targets to the synthetic organic chemists. Thiazoles fused to different heterocyclic compounds are of importance not only as medicinal agents but also as organic functional materials such as fluorescent dyes.[4] Several of such heterocycle-fused thiazole derivatives have been prepared by Sonogashira cross-coupling methodology.[5]

Moreover, indole nucleus is a prominent structural subunit present in numerous natural products and synthetic compounds with vital medicinal value.[6] The assembly of functionalized indole and condensed indole derivatives has captured the attention of synthetic chemists for decades due to their pharmacological activities. Furo[3,2-*b*]indoles show analgestic and anti-inflammatory activity.[7] Thienoindole derivatives are potentially biologically active.[8] Several condensed indole derivatives including thiazoloindole derivatives can act as $5HT_4$ receptor antagonists.[9] Considering the potent bioactivities of compounds possessing a thiazoloindole core, the development of a new strategy to synthesize efficiently thiazolo[3,2-*a*]indole derivatives has attracted our attention. Additional interest is derived from our long-standing efforts in the synthesis of indole annulated heterocyclic compounds.[10]

Palladium/copper-catalyzed cross-coupling reaction of terminal acetylene with sp^2-C halides, that is, Sonogashira coupling[11] provides a useful method for synthesizing conjugated acetylenic compounds, which are important class of molecules. Heterocyclization could be effected from these conjugated acetylenic compounds either by transition-metal-mediated,[12] or by base-mediated,[13] or by iodocyclization.[14] We have recently reported the synthesis of various heterocyclic systems via Sonogashira cross coupling followed by copper(I) iodide[15] or gold-catalyzed[16] cyclization. We undertook a study for the synthesis of thiazolo[3,2-*a*]indole derivatives, a structural core worthy of evaluation for biological properties by combining Sonogashira acetylide coupling followed by triethylamine-induced annulation reaction in a one-pot operation. The results are reported here.

Although a method[9] is available for the synthesis of thiazolo[3,2-*a*]indole, a literature survey showed no reference concerning the use of a Pd/Cu-catalyzed preparation of this system.

The required precursors 2-(prop-2-ynylthio)-1*H*-indoles **1a–e** were synthesized according to the published procedure.[10c] When Sonogashira coupling reaction were performed on 2-(prop-2-ynylthio)-1*H*-indoles **1a–e** with aryl iodide **2a** in the presence of bis(triphenylphosphine)palladium(II) chloride as catalyst, cuprous iodide as co-catalyst, and base triethylamine in anhydrous *N*,*N*-dimethylformamide at room temperature for three hours, a single compound was obtained as detected by TLC. The new compound was identified from its spectral data as the expected Sonogashira coupling product **3a**. The compound **3a** was heated at 90 °C under basic condition for four hours to yield the desired 3-(4-acetylbenzyl)thiazolo[3,2-*a*]indole (**4a**) in 82% yield (Scheme 1). The product **4a** was identified from its spectral data. The ^{1}H NMR spectrum exhibits one singlet for two protons at $\delta = 4.49$, which correspond to benzylic protons. It also reveals one singlet at $\delta = 5.97$ and another one singlet at $\delta = 6.57$, which correspond to the protons of thiazole and pyrrole ring, respectively. The ^{13}C NMR spectrum and HRMS analysis also support the proposed structure. It is relevant to mention here that the substrate **1a** at 90 °C readily undergoes thio-Claisen rearrangement to give the product **5**.[17] On the basis of this the substrate **3a** when heated at 90 °C is also expected to provide compounds **6** and/or **7**. Notably we did not obtain any **6** or **7** at all.

To optimize the cycloisomerization reaction a series of experiments were performed on the compound **3a** under different conditions where sequential changes were made to the base, solvent, and temperature (Table 1). It was

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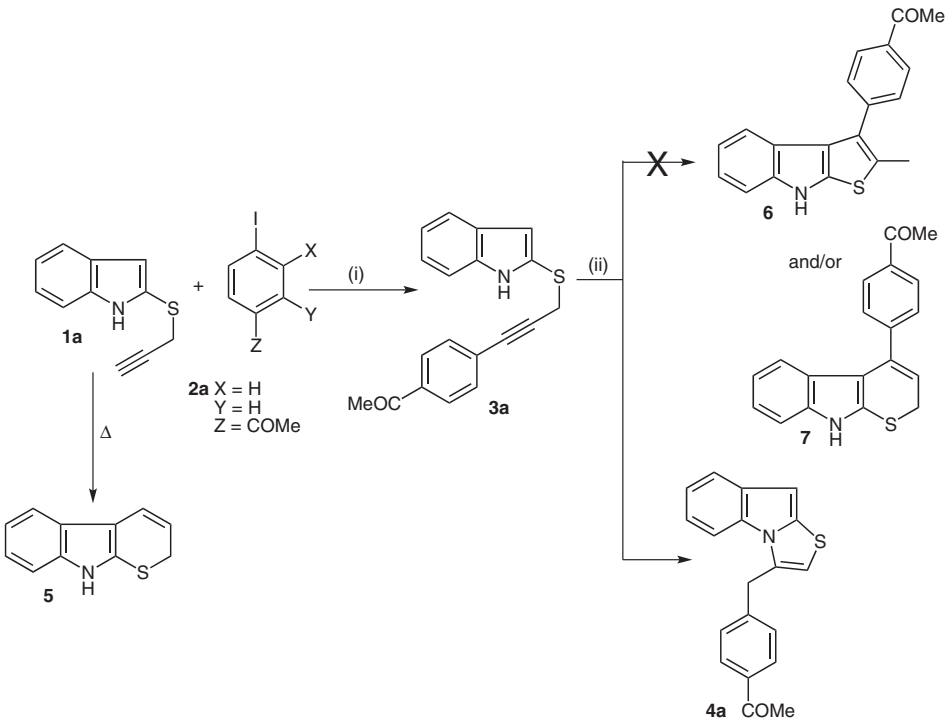


Scheme 1 *Reagents and conditions*: (i) $Pd(PPh_3)_2Cl_2$ (3 mol%), CuI (3 mol%), Et_3N, DMF, r.t., 3 h (ii) Et_3N, DMF, 90 °C, 4 h.

found that using triethylamine as a base in *N*,*N*-dimethylformamide at 90 °C for four hours (Table 1, entry 2) is suitable for running the reaction to afford the product **4a** in 82% yield. Use of triethylamine in acetonitrile was found to be effective, but yield of the cyclized product was low (35%). Changing the base to potassium acetate or potassium carbonate in *N*,*N*-dimethylformamide or acetonitrile was found to be ineffective and the product formation did not occur at all. Use of potassium *tert*-butoxide was effective but the yield of the product is low (15%). Temperature plays an important role in the reaction. When the reaction is performed at 60 °C, it did not proceed at all. However, with increasing the temperature the reaction proceeds slowly and it is optimum when the temperature reaches to 90 °C. Further increase in temperature decreases the yield of the product due to decomposition of the cyclized product. The optimization experiments are summarized in Table 1.

The reaction involves two-steps, a Sonogashira cross coupling followed by base-induced cyclization. However, the reaction can be conducted in a one-pot operation. The one-pot reaction was achieved by Sonogashira coupling reaction of the compound **1a** with aryl iodide **2a** at room temperature for three hours to give **3a** using the same catalytic combination as mentioned before followed by heating the reaction mixture at 90 °C for four hours to afford the desired cyclic product **4a** in 80% yield (Table 2, entry 2). Other products **4b** and **4d–l** were prepared similarly. Our attempts to achieve the same results by performing the two steps of the same reaction in one pot at 90 °C resulted in the formation of an inseparable complex mixture of products.

Substituents on the phenyl ring of the substrate **3** play a vital role in this cycloisomerization reaction. It was found that the presence of electron-withdrawing groups such as COMe, NO_2, CO_2Et on the phenyl ring of the substrate **3** is essential for successful cycloisomerization. Aryl iodides without electron-withdrawing substituents undergo Sonogashira coupling readily but triethylamine-induced cyclization does not occur even after long heating at elevated temperature. The absence of at least one electron-withdrawing substituents on the phenyl ring of the substrate **3** inhibits the triethylamine-induced cyclization

Table 1 Optimization of Base-Induced Cycloisomerization Reaction of **3a**

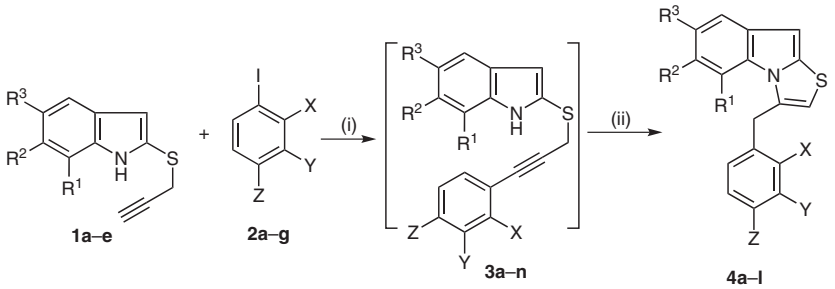
Entry	Solvent	Base	Temp (°C)	Yield (%)
1	DMF	Et_3N	60	n.r.[a]
2	DMF	Et_3N	90	82
3	MeCN	Et_3N	90	35
4	MeCN	K_2CO_3	90	n.r.[a]
5	DMF	K_2CO_3	90	n.r.[a]
6	DMF	KOAc	90	n.r.[a]
7	MeCN	KOAc	90	n.r.[a]
8	DMF	*t*-BuOK	90	20
9	MeCN	*t*-BuOK	90	15
10	DMF	Et_3N	>120	dec.[b]

[a] No reaction.
[b] Decomposition.

(Table 2, entries 14, 15). However, for the substrate 4-iodonitrobenzene (**2c**) (Table 2, entries 5, 6) and 3-chloro-4-iodonitrobenzene (**2e**) (Table 2, entries 12, 13), both Sonogashira coupling as well as cyclization occur at room temperature in one-step to give the products **4d**,**e** and **4k**,**l**, respectively. Intermediate Sonogashira coupling products are not isolable in these cases. These results are summarized in Table 2. The products **4g–l** are unstable and found to decompose at room temperature while recording their NMR spectra.

It is found that the cycloisomerization process does not require any metal catalysis and that triethylamine used as cosolvent as well as base was the sole reagent involved in the heteroannulation reaction. Moreover, the presence of an electron-withdrawing group such as COMe, NO_2, CO_2Et on the aryl iodide is essential for the cycloisomerization. For aryl iodides with chloro substitution (Table 2, entry 14) or without substitution (Table 2, entry 15) cyclization does not occur. Further, for 4-nitro- (Table 2, entries 5, 6) and 2-chloro-4-nitro-substituted (Table 2, entries 12, 13) aryl iodides cyclization occur at room temperature. In the light of these observations, a plausible rationalization for the formation of the products **4** may be outlined[18] (Scheme 2). Abstraction of the NH proton of the indole moiety by triethylamine may generate the anion **8**. The latter may then undergo regioselective anionic 5-*exo*-trig cyclization to form anionic thiazolo intermediate **9**, which upon capture of a proton may furnish **10**. Subsequent [1,3] proton shift in the presence of triethylamine may furnish the desired 3-benzylthiazolo[3,2-*a*]indole **4**. The presence of an electron-withdrawing group on the phenyl ring stabilizes the anionic intermediate **9** and, therefore, cyclization may occur smoothly. For 4-nitroaryl iodide (**2c**) and 2-chloro-4-nitroaryl iodide (**2e**), the intermediate **9** derives more stability due to the presence

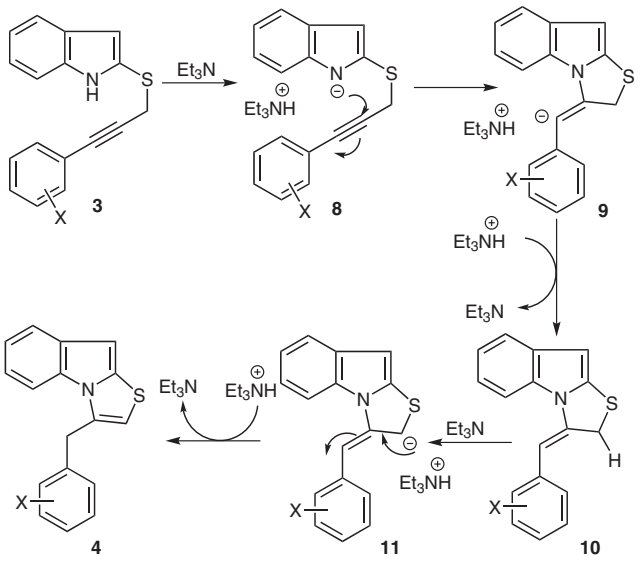
Table 2 Summarized Results of the Heteroannulation Reaction[a]



Entry	Substrates	R^1	R^2	R^3	X	Y	Z	Product/Yield (%)	Product/Yield (%)
1	**1a/2a**	H	H	H	H	H	COMe	**3a**, 80	**4a**, 82
2	**1a/2a**	H	H	H	H	H	COMe	–[b]	**4a**, 80
3	**1b/2a**	Me	H	H	H	H	COMe	–[b]	**4b**, 78
4	**1a/2b**	H	H	H	H	H	CO_2Et	**3c**, 85	**4c**, 82
5	**1a/2c**	H	H	H	H	H	NO_2	–[c]	**4d**, 85
6	**1b/2c**	Me	H	H	H	H	NO_2	–[c]	**4e**, 75
7	**1a/2d**	H	H	H	H	NO_2	H	–[b]	**4f**, 80
8	**1c/2d**	H	H	Me	H	NO_2	H	–[b]	**4g**, 60[d]
9	**1d/2d**	Me	Me	H	H	NO_2	H	–[b]	**4h**, 65[d]
10	**1e/2d**	Me	Cl	H	H	NO_2	H	–[b]	**4i**, 70[d]
11	**1e/2b**	Me	Cl	H	H	H	CO_2Et	–[b]	**4j**, 80[d]
12	**1a/2e**	H	H	H	Cl	H	NO_2	–[c]	**4k**, 75[d]
13	**1b/2e**	Me	H	H	Cl	H	NO_2	–[c]	**4l**, 73[d]
14	**1a/2f**	H	H	H	H	H	Cl	**3m**, 73	n.r.[e]
15	**1a/2g**	H	H	H	H	H	H	**3n**, 75	n.r.[e]

[a] Reaction conditions: (i) $Pd(PPh_3)_2Cl_2$ (3 mol%), CuI (3 mol%), Et_3N, DMF, r.t., 3 h; (ii) Et_3N, DMF, 90 °C, 4 h.
[b] Product was not isolated, one-pot reaction was performed.
[c] Product could not be isolated, cyclization occurs at r.t.
[d] Products were isolated in pure form by column chromatography, but decomposes at r.t. while recording the NMR spectra.
[e] No reaction.

of nitro group at para position, which exerts more electron-withdrawing effect. Therefore, the cycloisomerization is facile and occurs smoothly at room temperature.



Scheme 2 Plausible mechanism for the triethylamine-induced cycloisomerization reaction

In conclusion, we have developed an efficient and extremely useful method for the regioselective synthesis of 3-benzylthiazolo[3,2-*a*]indole from 2-(prop-2-ynylthio)-1*H*-indole via in situ sequential Sonogashira acetylide-coupling followed by triethylamine-induced heteroannulation reaction. The cycloisomerization reaction does not require any transition metal catalyst. The method is simple and straightforward and provides an easy access to the thiazoloindole derivatives.

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a PerkinElmer L 120-000A spectrometer (cm^{-1}) on KBr disks. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 and Bruker DPX-300 spectrometers in $CDCl_3$ with TMS as internal standard. Silica gel (60–120 mesh and 230–400 mesh, Spectrochem, India) were used for chromatographic separation. Silica gel G and silica gel GF-254 (Spectrochem, India) were used for TLC. Petroleum ether (PE) refers to the fraction boiling between 60–80 °C. Indole-2-yl prop-2-ynyl sulfide (**1a**) was prepared according to the published procedure.[10c]

Sonogashira Coupling Reaction; 1-{4-[3-(1*H*-indol-2-ylsulfanyl)prop-1-ynyl]phenyl}ethan-1-one (3a); Typical Procedure

A mixture of 4-iodoacetophenone (**2a**; 197 mg, 0.80 mmol), $Pd(PPh_3)_2Cl_2$ (10.08 mg, 0.0144 mmol), CuI (2.7 mg, 0.0144 mmol), and Et_3N (1.0 mL, 12.2 mmol) in anhyd DMF (5 mL) was stirred at r.t. under N_2 atmosphere. Indol-2-yl prop-2-ynyl sulfide (**1a**; 150 mg, 0.80 mmol) was then added and the mixture was stirred at r.t. for 3 h. After completion of the reaction as monitored by TLC, H_2O (10 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 15 mL) and the combined organic layers were washed successively with H_2O (3 × 15 mL) and brine (20 mL), and dried (Na_2SO_4). Evaporation of the solvent furnished a crude mass, which was purified by column chromatography over silica gel. Elution of the column with EtOAc–PE (8:92) afforded the product **3a** as a viscous liquid; yield: 195 mg (80%).

IR (KBr): 1673, 2215, 3338 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.58 (s, 3 H, $COCH_3$), 3.75 (s, 2 H, SCH_2), 6.81 (s, 1 H, ArH), 7.12 (t, *J* = 7.6 Hz, 1 H, ArH), 7.22–7.28 (m, 1 H, ArH), 7.32 (d, *J* = 8.0 Hz, 1 H, ArH), 7.40 (d, *J* = 7.2 Hz, 2 H, ArH), 7.59 (d, *J* = 7.6 Hz, 1 H, ArH), 7.87 (d, *J* = 7.2 Hz, 2 H, ArH), 8.39 (br s, 1 H, NH).

MS: *m*/*z* for $C_{19}H_{15}NOS$ = 306 [M^+ + H].

3c

Yield: 228 mg (85%); colorless solid; mp 105 °C.

IR (KBr): 1702, 2218, 3350 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 3.74 (s, 2 H, SCH_2), 4.37 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 6.81 (d, *J* = 1.6 Hz, 1 H, ArH), 7.12 (t, *J* = 7.6 Hz, 1 H, ArH), 7.23 (dq, *J* = 6.8, 0.8 Hz, 1 H, ArH), 7.32 (d, *J* = 8.0 Hz, 1 H, ArH), 7.38 (d, *J* = 8.0 Hz, 2 H, ArH), 7.59 (d, *J* = 8.0 Hz, 1 H, ArH), 7.96 (d, *J* = 8.4 Hz, 2 H, ArH), 8.37 (br s, 1 H, NH).

MS: *m*/*z* for $C_{20}H_{17}NO_2S$ = 336 [M^+ + H].

3m

Yield: 174 mg (73%); colorless solid; mp 95 °C.

IR (KBr): 2219, 3348 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 2 H, SCH_2), 6.80 (d, *J* = 1.6 Hz, 1 H, ArH), 7.12 (t, *J* = 8.0 Hz, 1 H, ArH), 7.22 (t, *J* = 7.2 Hz, 1 H, ArH), 7.26–7.28 (m, 3 H, ArH), 7.33 (d, *J* = 8.0 Hz, 2 H, ArH), 7.60 (d, *J* = 8.0 Hz, 1 H, ArH), 8.32 (br s, 1 H, NH).

MS: *m*/*z* for $C_{17}H_{12}ClNS$ = 298 [M^+ + H].

3n

Yield: 158 mg (75%); viscous liquid.

IR (neat): 2220, 3353 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.72 (s, 2 H, SCH_2), 6.80 (s, 1 H, ArH), 7.12 (t, *J* = 7.2 Hz, 1 H, ArH), 7.20–7.24 (m, 1 H, ArH), 7.26 (br s, 5 H, ArH), 7.32 (d, *J* = 8.4 Hz, 1 H, ArH), 7.59 (d, *J* = 8.0 Hz, 1 H, ArH), 8.31 (br , 1 H, NH).

MS: *m*/*z* for $C_{17}H_{13}NS$ = 264 [M^+ + H].

3-(4-Acetylbenzyl)thiazolo[3,2-*a*]indole (4a); Typical Procedure 1

Compound **3a** (100 mg, 0.32 mmol) was dissolved in DMF (5 mL) and Et_3N (2 mL, 14.3 mmol) was added. The reaction mixture was heated at 90 °C for 4 h. After completion of the reaction, H_2O (5 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were washed with H_2O (3 × 15 mL) followed by brine (15 mL), and dried (Na_2SO_4). Evaporation of the solvent furnished a crude mass, which was purified by column chromatography over silica gel. Elution of the column with EtOAc–PE (5:95) afforded the product **4a**.

One-Pot Preparation of 3-(4-Acetylbenzyl)thiazolo[3,2-*a*]indole (4a); Typical Procedure 2

A mixture of 4-iodoacetophenone (**2a**; 197 mg, 0.80 mmol), $Pd(PPh_3)_2Cl_2$ (10.08 mg, 0.0144 mmol), CuI (2.7 mg, 0.0144 mmol), and Et_3N (1.0 mL, 12.2 mmol) in anhyd DMF (5 mL) was stirred at r.t. under N_2 atmosphere. Indol-2-yl prop-2-ynyl sulfide (**1a**; 150 mg, 0.80 mmol) was then added to the mixture and the mixture was stirred at r.t. for 3 h. After completion of the reaction as monitored by TLC, the reaction mixture was heated at 90 °C for 4 h. H_2O (10 mL) was added to the mixture and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed successively with H_2O (3 × 15 mL) and brine (20 mL), and dried

(Na_2SO_4). Evaporation of CH_2Cl_2 furnished a crude mass, which was purified by column chromatography over silica gel. Elution of the column with EtOAc–PE (5:95) afforded the product **4a** as a colorless solid; yield: 82 mg (82%); mp 110 °C.

IR (KBr): 1672 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.62 (s, 3 H, $COCH_3$), 4.49 (s, 2 H, $ArCH_2$), 5.97 (s, 1 H, =CH), 6.57 (s, 1 H, ArH), 7.03 (t, *J* = 8.0 Hz, 1 H, ArH), 7.18 (t, *J* = 7.6 Hz, 1 H, ArH), 7.41 (d, *J* = 8.0 Hz, 2 H, ArH), 7.61 (dd, *J* = 8.0, 2.8 Hz, 2 H, ArH), 7.95 (d, *J* = 8.0 Hz, 2 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 26.6, 34.9, 91.6, 106.3, 111.2, 119.1, 119.8, 121.1, 129.0, 129.1, 129.9, 133.2, 133.5, 136.2, 138.8, 141.5, 197.6.

HRMS: *m*/*z* calcd for $C_{19}H_{15}NOS$ + Na: 328.0772 $[M + Na]^+$; found: 328.0775 $[M + Na]^+$.

4b

Yield: 200 mg (78%); colorless solid; mp 145 °C.

IR (KBr): 1678 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, $ArCH_3$), 2.58 (s, 3 H, $COCH_3$), 4.48 (s, 2 H, $ArCH_2$), 5.97 (s, 1 H, =CH), 6.57 (s, 1 H, ArH), 6.95–7.00 (m, 2 H, ArH), 7.40 (d, *J* = 8.0 Hz, 2 H, ArH), 7.46 (d, *J* = 8.0 Hz, 1 H, ArH), 7.94 (d, *J* = 7.6 Hz, 2 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 19.0, 26.7, 34.9, 90.1, 106.3, 108.8, 119.2, 121.2, 129.1, 129.5, 133.1, 133.6, 136.2, 138.3, 141.6, 197.7.

HRMS: *m*/*z* calcd for $C_{20}H_{17}NOS$ + Na: 342.0929 $[M + Na]^+$; found: 342.0921 $[M + Na]^+$.

4c

Yield: 88 mg (82%); colorless solid; mp 95 °C.

IR (KBr): 1712 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3), 4.37 (q, *J* = 7.2 Hz, 2 H, CH_2CH_3), 4.48 (s, 2 H, $ArCH_2$), 5.94 (s, 1 H, =CH), 6.56 (s, 1 H, ArH), 7.03 (t, *J* = 7.6 Hz, 1 H, ArH), 7.18 (t, *J* = 7.2 Hz, 1 H, ArH), 7.38 (d, *J* = 8.0 Hz, 2 H, ArH), 7.62 (d, *J* = 8.4 Hz, 2 H, ArH), 8.04 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 14.4, 35.0, 61.1, 91.5, 106.2, 111.2, 119.1, 119.7, 121.1, 128.9, 129.6, 129.9, 130.2, 133.2, 133.7, 138.8, 141.1, 166.3.

HRMS: *m*/*z* calcd for $C_{20}H_{17}NO_2S$ + Na: 358.0878 $[M + Na]^+$; found: 358.0876 $[M + Na]^+$.

4d

Yield: 210 mg (85%); yellow solid; mp 155 °C.

IR (KBr): 1519 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.54 (s, 2 H, $ArCH_2$), 6.02 (s, 1 H, =CH), 6.58 (s, 1 H, ArH), 7.03 (t, *J* = 7.6 Hz, 1 H, ArH), 7.19 (t, *J* = 7.6 Hz, 1 H, ArH), 7.48 (d, *J* = 8.4 Hz, 2 H, ArH), 7.54 (d, *J* = 8.4 Hz, 1 H, ArH), 7.63 (d, *J* = 8.0 Hz, 1 H, ArH), 8.21 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 34.7, 91.8, 106.8, 110.9, 119.2, 119.9, 121.3, 124.2, 129.6, 129.7, 132.6, 133.2, 138.7, 143.6, 147.3.

HRMS: *m*/*z* calcd for $C_{17}H_{12}N_2O_2S$: 331.0517 $[M + Na]^+$; found: 331.0523 $[M + Na]^+$.

4e

Yield: 193 mg (75%); yellow solid; mp 135 °C.

IR (KBr): 1519 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, $ArCH_3$), 4.54 (s, 2 H, $ArCH_2$), 6.04 (s, 1 H, =CH), 6.59 (s, 1 H, ArH), 6.97 (quint, *J* = 6.8 Hz, 2 H, ArH), 7.38 (d, *J* = 8.0 Hz, 1 H, ArH), 7.47 (d, *J* = 8.4 Hz, 2 H, ArH), 8.21 (d, *J* = 8.4 Hz, 2 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 19.0, 34.7, 90.3, 106.8, 108.6, 119.4, 121.3, 124.2, 129.2, 129.4, 129.6, 132.6, 133.1, 138.1, 143.7, 147.3.

HRMS: *m*/*z* calcd for $C_{18}H_{14}N_2O_2S$: 345.0674 $[M + Na]^+$; found: 345.0676 $[M + Na]^+$.

4f

Yield: 197 mg (80%); greenish yellow solid; mp 170 °C.

IR (KBr): 1528 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.55 (s, 2 H, $ArCH_2$), 5.98 (s, 1 H, =CH), 6.58 (s, 1 H, ArH), 7.05 (t, *J* = 7.6 Hz, 1 H, ArH), 7.19 (t, *J* = 7.6 Hz, 1 H, ArH), 7.54 (t, *J* = 8.0 Hz, 1 H, ArH), 7.62 (t, *J* = 8.0 Hz, 3 H, ArH), 8.18 (d, *J* = 8.0 Hz, 1 H, ArH), 8.23 (s, 1 H, ArH).

^{13}C NMR (400 MHz, $CDCl_3$): δ = 34.6, 91.8, 106.8, 111.0, 119.2, 119.9, 121.2, 122.6, 123.9, 129.8, 130.0, 133.0, 133.2, 134.9, 138.1, 138.8, 148.7.

MS: *m*/*z* for $C_{17}H_{12}N_2O_2S$ = 309 $[M^+ + H]$.

4g

Yield: 154 mg (60%); viscous gum.

IR (KBr): 1525 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.56 (s, 3 H, $ArCH_3$), 4.54 (s, 2 H, $ArCH_2$), 5.99 (s, 1 H, =CH), 6.58 (s, 1 H, ArH), 7.01 (d, *J* = 6.4 Hz, 1 H, ArH), 7.45 (d, *J* = 8.0 Hz, 1 H, ArH), 7.52–7.54 (m, 1 H, ArH), 7.63 (d, *J* = 8.2 Hz, 2 H, ArH), 8.17 (d, *J* = 8.0 Hz, 1 H, ArH), 8.23 (s, 1 H, ArH).

4h

Yield: 175 mg (65%); viscous gum.

IR (KBr): 1528 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, $ArCH_3$), 2.56 (s, 3 H, $ArCH_3$), 4.54 (s, 2 H, $ArCH_2$), 5.99 (s, 1 H, =CH), 6.58 (s, 1 H, ArH), 7.01 (d, *J* = 6.8 Hz, 1 H, ArH), 7.45 (d, *J* = 8.0 Hz, 1 H, ArH), 7.65 (d, *J* = 8.4 Hz, 2 H, ArH), 8.19–8.21 (m, 1 H, ArH), 8.23 (s, 1 H, ArH).

4i

Yield: 200 mg (70%); viscous gum.

IR (KBr): 1525 cm^{-1}.

^1H NMR (400 MHz $CDCl_3$): δ = 2.78 (s, 3 H, $ArCH_3$), 4.52 (s, 2 H, $ArCH_2$), 5.76 (s, 1 H, =CH), 6.59 (s, 1 H, ArH), 6.86 (d, *J* = 7.6 Hz, 1 H, ArH), 7.47 (s, 1 H, ArH), 7.56 (d, *J* = 6.0 Hz, 2 H, ArH), 8.19–8.21 (m, 2 H, ArH).

4j

Yield: 245 mg (80%); viscous gum.

IR (KBr): 1716 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.0 Hz, 3 H, CH_2CH_3), 2.77 (s, 3 H, $ArCH_3$), 4.39 (q, *J* = 7.1 Hz, 2 H, CH_2CH_3), 4.47 (s, 2 H, $ArCH_2$), 5.78 (s, 1 H, =CH), 6.57 (s, 1 H, ArH), 6.88 (d, *J* = 1.6 Hz, 1 H, ArH), 7.29–7.31 (m, 2 H, ArH), 7.45 (d, *J* = 2.4 Hz, 1 H, ArH), 8.02–8.05 (m, 2 H, ArH).

4k

Yield: 206 mg (75%); viscous gum.

IR (KBr): 1520 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.60 (s, 2 H, ArCH_2), 6.09 (s, 1 H, =CH), 6.60 (s, 1 H, ArH), 7.03 (t, *J* = 8.0 Hz, 1 H, ArH), 7.19 (t, *J* = 8.0 Hz, 1 H, ArH), 7.30 (d, *J* = 8.4 Hz, 1 H, ArH), 7.40 (d, *J* = 8.0 Hz, 1 H, ArH), 7.63 (d, *J* = 2.4 Hz, 1 H, ArH), 8.02 (dd, *J* = 6.4, 2.0 Hz, 1 H, ArH), 8.38 (d, *J* = 2.4 Hz, 1 H, ArH).

4l

Yield: 208 mg (73%); viscous gum.

IR (KBr): 1520 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.52 (s, 3 H, ArCH_3), 4.59 (s, 2 H, ArCH_2), 6.10 (s, 1 H, =CH), 6.60 (s, 1 H, ArH), 6.95 (t, *J* = 8.0 Hz, 1 H, ArH), 7.00 (d, *J* = 7.2 Hz, 1 H, ArH), 7.23 (d, *J* = 8.4 Hz, 2 H, ArH), 8.00 (dd, *J* = 8.0, 2.0 Hz, 1 H, ArH), 8.37 (d, *J* = 2.0 Hz, 1 H, ArH).

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