Green Synthesis of Benzopyran-Annulated Thiopyrano[2,3-*b*]thiochromen-5(4*H*)-ones by Domino Knoevenagel–Hetero-Diels–Alder Reaction

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Abstract: Benzopyran-annulated thiopyrano[2,3-*b*]thiochromen-5(4*H*)-ones have been synthesized by the domino Knoevenagel–hetero-Diels–Alder (DKHDA) reaction of 4-hydroxydithiocoumarin with O-allylated salicylaldehyde and O-propargylated salicylaldehyde in aqueous medium. The reaction requires only a single step operation and is highly regio- and stereoselective providing potentially bioactive polycyclic heterocycles in high yields.

Key words: aqueous medium, domino Knoevenagel–hetero-Diels–Alder reaction, stereoselective, regioselective, 4-hydroxydithiocoumarin

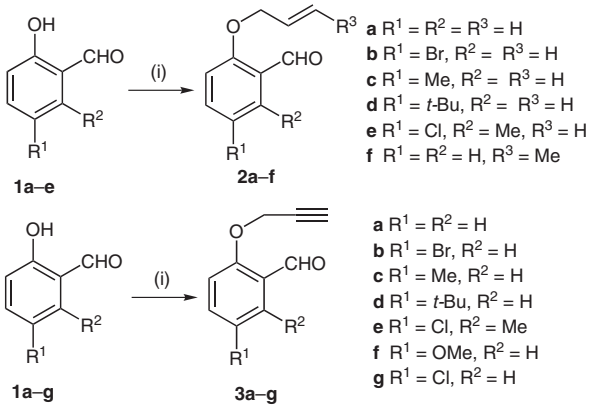
Recently, there is a flurry of activities in the development of newer synthetic methods for the construction of complex molecules from simple substrates following the principle of 'green chemistry'.[1] The main principles of green chemistry are avoidance of toxic reagents, reduction of waste, and responsible utilization of resources.[2] Recently, the development of solvent-free syntheses[3] or replacement of toxic or hazardous solvents with environmentally benign solvents[4] is one of the main areas of green chemistry. In modern organic chemistry water,[5] ionic liquid,[6] fluorous,[7] supercritical media,[8] and polyethylene glycol[9] have been used as alternative reaction solvents. The use of water as an environmentally benign and economically favorable alternative of organic solvents has developed a highly active field of research in synthetic chemistry and catalysis.[10] Water is environment friendly, nontoxic, nonflammable, and ubiquitous in nature.[5a,b,11] A number of reactions including Diels–Alder reaction have been carried out in aqueous media.

Hetero-Diels–Alder reaction is one of the most important synthetic tools for the construction of heterocycles as well as natural products. A number of heterocyclic compounds have been prepared by domino Knoevenagel–hetero-Diels–Alder (DKHDA) reaction.[12] Tietze and co-workers have extensively utilized this reaction for the synthesis of tetracyclic compounds containing a pyran ring using unsaturated aromatic and aliphatic aldehydes with several 1,3-dicarbonyl compounds.[13] There are several reports on the intramolecular DKHDA reaction with alkenes and alkynes.[14] The methodology is useful for the construction of annulated [6,6]-fused pyranobenzopyran or thiopyranobenzopyran derivatives.[13,14] Recently, we have synthesized indole- and thiochromen-annulated [6,6]-fused thiopyranobenzopyran derivatives using DKHDA reaction,[14a,f,g] which are difficult to prepare by usual radical cyclization and Claisen rearrangement.[15]

Thieno[2,3-*b*]benzopyran-4-one skeleton has been used as an intermediate for the synthesis of a series of antipsychotic drugs.[16] Similarly, pharmacophores containing a chromone moiety show biological activity and many of them also have useful medicinal applications.[17] There are reports on the synthesis of thieno[2,3-*b*]thiochromen-4-one[18] and thiochromone-annulated [6,5]-fused benzofurothiopyran derivatives.[19] But no such reports of thiochromone-annulated [6,6]-fused benzopyranothiopyran derivatives are known, except our preliminary report.[14g]

In continuation of our interest in the synthesis of annulated [6,6]-fused thiopyranobenzopyran derivatives[14a,f,g] and in order to explore the utility of this methodology we became interested to synthesize thiochromone-annulated [6,6]-fused thiopyranobenzopyran derivatives using 4-hydroxydithiocoumarin and O-allylated/crotylated salicylaldehydes in environmentally benign water medium. The results are reported here.

The required precursors **2a–f** were prepared in high yields by refluxing various substituted salicylaldehydes **1a–e** with allyl bromide or crotyl bromide in the presence of anhydrous potassium carbonate and a catalytic amount of NaI in anhydrous acetone at room temperature.[20] Other precursors **3a–g** were prepared in high yields and purity by the reaction of substituted salicylaldehydes **1a–g** and propargyl bromide in the presence of anhydrous potassi-



Scheme 1 *Reagents and conditions*: (i) allyl/crotyl bromide, anhyd K_2CO_3, anhyd acetone, NaI, reflux, (ii) propargyl bromide, anhyd K_2CO_3, DMF, r.t.

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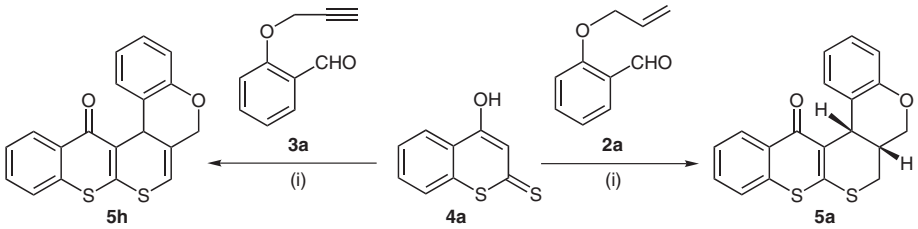


Scheme 2 *Reagents and conditions*: (i) reflux in H_2O.

um carbonate in anhydrous DMF at room temperature[21] (Scheme 1).

The *O*-allylsalicylaldehyde (**2a**) was used first as a model substrate in order to study the DKHDA reactions of 4-hydroxydithiocoumarin (**4a**) with *O*-allyl/crotylsalicylaldehydes **2a**–**f** and *O*-propargylsalicylaldehydes **3a**–**g**.[14g]

According to the published procedure,[14a] the hetero-Diels–Alder reaction of **4a** and **2a** was carried out in refluxing acetic acid and triethylamine and the final product **5a** was obtained in 85% yield after 4 hours. Very recently, we have reported the DKHDA reaction of the alkynes in water medium.[14f,g] Therefore, it was decided to try this reaction on alkenes in water medium. Accordingly, the reaction of **4a** and **2a** in refluxing water instead of acetic acid and triethylamine was carried out for 4 hours and to our delight the product **5a** was obtained in 84% yield. Similarly, the DKHDA reactions of 4-hydroxydithiocoumarin (**4a**) with O-propargylated salicylaldehydes **3a**–**g** were carried out[14g] in aqueous medium under refluxing condition (Scheme 2).

In the case of the DKHDA reaction of 4-hydroxydithiocoumarin (**4a**) with O-propargylated salicylaldehydes **3a**–**g**, the optimized condition was standardized through a series of experiments, where the influences of Lewis acid, base, and solvents were examined in the reaction (Table 1). Table 1, entry 3 reveals that increasing the amount of catalyst decreases the yield of the product. The reason may be due to the coordination of soft sulfur atom[22] with the d^{10} copper ions, which prevents the hetero-Diels–Alder reaction and thereby decreasing the yield of the product. Highest yield of the final product was obtained when the reaction was carried out in refluxing aqueous medium in the absence of any catalyst.

The reaction is highly regio- and stereoselective. The reaction of 4-hydroxydithiocoumarin (**4a**) with *O*-allylsalicylaldehyde (**2a**) give only the *cis*-annulated [6,6]-fused thiopyrano benzopyran derivative **5a**. The structure and stereochemistry of the product **5a** was determined by spectral analysis and single crystal X-ray diffraction[23] (Figure 1).

To extend the utility of this methodology, DKHDA reaction was carried out for other O-allylated/crotylated and O-propargylated salicylaldehydes **2b**–**f** and **3b**–**g** with 4-hydroxydithiocoumarins **4a**,**b** (Table 2). The structures of the products obtained by the reaction of 4-hydroxydithiocoumarin (**4a**) with O-propargylated salicylaldehydes **3a**–**g** were determined from their elemental analyses and spectroscopic data. The characteristic peaks for **5h**–**n** in the ^{1}H NMR spectra appear as AB quartets for the OCH_2 protons between δ = 4.62 and 4.94 followed closely by singlets for the SCH= protons at δ = 5.99–6.57. The corresponding carbon signal for the OCH_2, SCH=, and C=O groups of compound **5h** in the ^{13}C NMR spectra appear at δ = 69.7, 109.4, 177.1, respectively.

Table 1 Influence of Catalyst, Solvent, and Base on the DKHDA Reaction of **4a** with **3a**[a]

Entry	Lewis acid (mol%)	Solvent	Base	Yield (%)
1	–	H_2O	–	80
2	CuI (20)	H_2O	–	58
3	CuI (30)	H_2O	–	49
4	CuI (20)	H_2O	Et_3N	65
5	CuI (20)	MeOH	Et_3N	35
6	CuI (20)	MeCN	Et_3N	32
7	CuI (20)	1,4-dioxane	Et_3N	29
8	CuI (20)	toluene	Et_3N	45
9	CuI (20)	H_2O	$(NH_4)_2HPO_4$	60
10	CuI (20)	MeOH	$(NH_4)_2HPO_4$	34
11	CuI (20)	MeCN	$(NH_4)_2HPO_4$	28
12	CuI (20)	1,4-dioxane	$(NH_4)_2HPO_4$	23

[a] All reactions were carried out for 4 h.

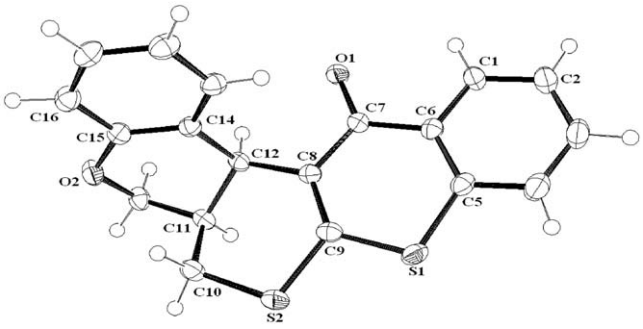
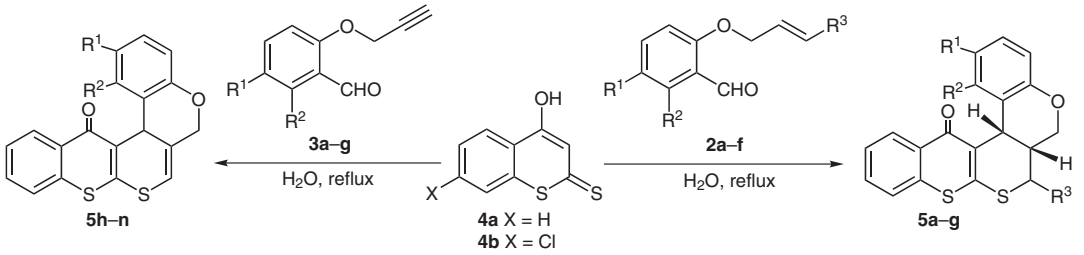


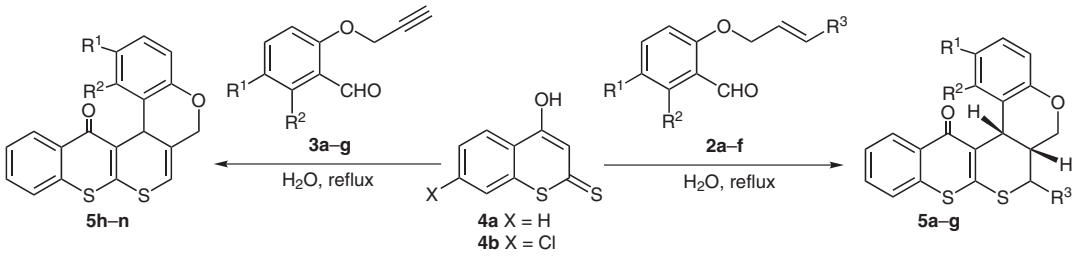
Figure 1 Single crystal X-ray structure of compound **5a**

Table 2 DKHDA Reaction of **4a**,**b** with **2a–f** and **3a–g** in Aqueous Medium[a]



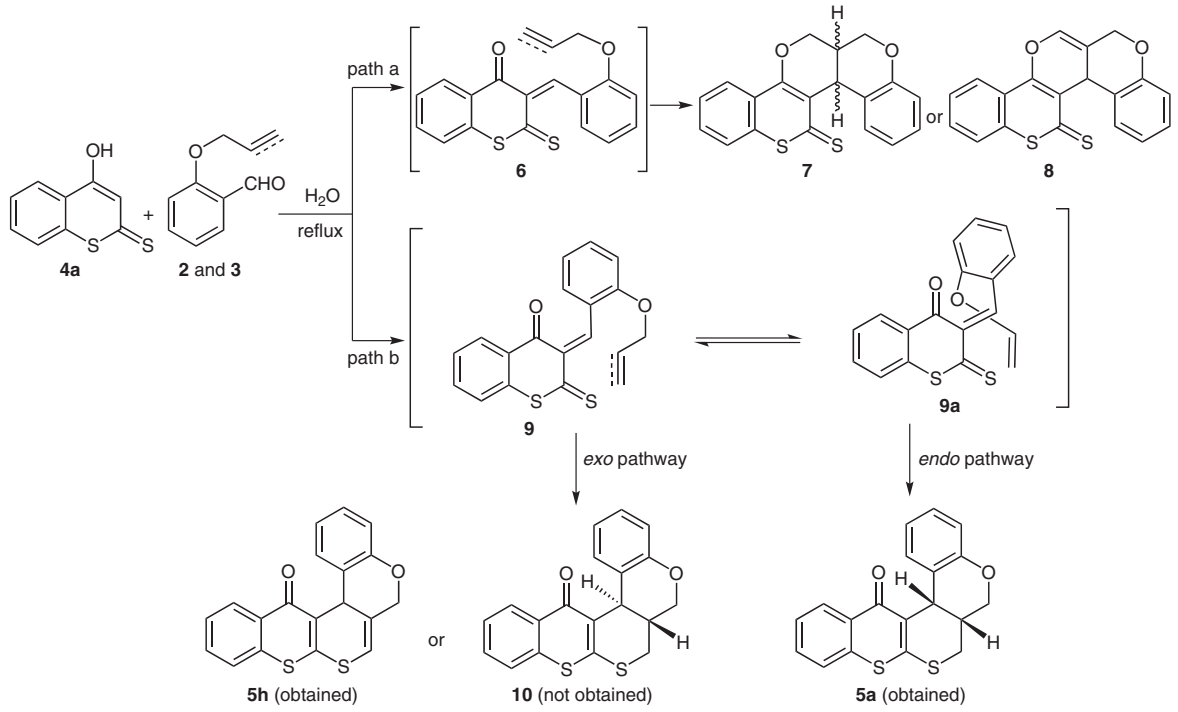
Entry	4	Aromatic aldehyde	Product	Yield (%)[b]
1	**4a**	**2a**	**5a**	84
2	**4a**	**2b**	**5b**	82
3	**4a**	**2c**	**5c**	74
4	**4a**	**2d**	**5d**	73
5	**4a**	**2e**	**5e**	65
6	**4a**	**2f**	**5f**	70
7	**4b**	**2c**	**5g**	72

Table 2 DKHDA Reaction of **4a**,**b** with **2a–f** and **3a–g** in Aqueous Medium[a] (continued)



Entry	4	Aromatic aldehyde	Product	Yield (%)[b]
8	**4a**	**3a**	**5h**	80
9	**4a**	**3b**	**5i**	79
10	**4a**	**3c**	**5j**	75
11	**4a**	**3d**	**5k**	72
12	**4a**	**3e**	**5l**	69
13	**4a**	**3f**	**5m**	76
14	**4a**	**3g**	**5n**	77

[a] All reactions were carried out in refluxing aqueous medium for 4 h.
[b] Isolated yields.



Scheme 3 Probable mechanism of DKHDA reaction

It is notable that the DKHDA reaction of 4-hydroxydithiocoumarins **4** with O-allylated/crotylated salicylaldehydes **2a–f** occurs in the absence of any base (Et_3N) or catalyst (EDDA) and reaction with unactivated alkynes **3a–g** occurs without the help of a Lewis acid/catalyst. The reason may perhaps be explained by considering the presence of soft sulfur atom in the diene moiety of the substrates. The sulfur atom may offer itself a reactive center and is more polarizable compared to other heteroatoms. Moreover, there are empty d-orbitals at the sulfur atom having a matching symmetry with that of the π-orbitals of the acetylene moiety for interaction.[14f]

The stereochemistry of the final product and the mechanism of the reaction are depicted in Scheme 3. Initially, Knoevenagel condensation between 4-hydroxydithiocoumarin (**4a**) and O-allylated **2** or O-propargylated salicylaldehyde **3** occurs to give the heterodiene intermediate. There is a possibility for the formation of two heterodiene intermediates (intermediates **6** and **9**) giving two products, angularly-fused product **7** (when O-allylated salicylaldehyde is used) or **8** (when O-propargylated salicylaldehyde is used) or linearly fused **5a** or **10** (when O-allylated salicylaldehyde is used) and **5h** (when O-propargylated salicylaldehyde is used). But only linearly fused products **5a** and **5h** were isolated, which show that the reactions proceed via path 'b'. This selectivity may be attributed to the presence of the sulfur atom. High polarizability and softness of sulfur atom make the HOMO-LUMO energy gap smaller when thiocarbonyl group of thioester acts as a heterodiene than that of the carbonyl group of α,β-unsaturated ketone system and thus the reaction follows via path 'b' to afford the linearly fused products. In the case of the DKHDA reaction with O-allylated salicylaldehydes, the stereochemistry of the final products depends on the *exo*- and *endo*-orientation of the dienophiles in the transition states. The intermediate **9** may undergo rotation around the single bond to assume the structure **9a**, which may then undergo cyclization via *endo*-selectivity of the hetero Diels–Alder reaction to give the product **5a**. The reaction does not proceed via *exo*-pathway to give the product **10** perhaps due to the sp^2-geminal effect of 1,3-allylic strain.[24]

In conclusion, we have developed a mild, efficient, regio- and stereoselective protocol for the synthesis of benzopyran-annulated thiopyranothiochromen-5(4*H*)-ones by domino Knoevenagel–hetero-Diels–Alder reaction of 4-hydroxydithiocoumarin with alkenes and alkynes. This protocol conforms to several green chemistry principles. Green aspects of this reaction include: (i) water is used as a reaction medium, which is benign, safe, and easily available, avoiding the use of conventional volatile organic solvents; (ii) the reaction is highly atom economic – only water is the by-product; (iii) no additive or base is required; and (iv) the reaction occurs in a single-step operation.

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Perkin–Elmer L 120-000A spectrometer on KBr disks. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300, Bruker DPX-400, or Bruker DPX-500 spectrometer in $CDCl_3$ with TMS as internal standard. CHN values were recorded on 2400 series II CHN Perkin–Elmer analyzer. Mass spectra and HRMS were recorded on a QTOF Micro YA 263 instrument at the Indian Association for the Cultivation of Science, Kolkata. Silica gel [(60–120, 230–400 mesh), Rankem, India] was used for chromatographic separation. Silica gel G [CDH,

(India)] was used for TLC. Petroleum ether (PE) used refers to the fraction boiling between 60–80 °C.

Compounds 5a–n; General Procedure

A mixture of 4-hydroxydithiocoumarin **4a**,**b** (0.26 mmol) and *O*-allylsalicylaldehyde **2a**–**f** (0.26 mmol) or *O*-propargylsalicylaldehyde **3a**–**g** (0.26 mmol) was refluxed in H_2O (7 mL) for 4 h. After completion of the reaction as monitored by TLC, the reaction mixture was cooled and diluted with H_2O (25 mL). The mixture was extracted with EtOAc (3 × 25 mL). The combined organic extracts were washed with brine (2 × 20 mL) and dried (Na_2SO_4). The resulting crude product obtained after removal of the solvent was purified by column chromatography over silica gel (60–120 mesh) using PE–EtOAc mixture as eluent to give compounds **5a**–**n** (Table 2).

5a

Yield: 84%; colorless solid; mp 210–212 °C.

IR (KBr): 1221, 1514, 1600, 2931 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.42–2.45 (m, 1 H), 2.94 (ddd, *J* = 1.2, 4.0, 12.0 Hz, 1 H), 3.35 (t, *J* = 12.0 Hz, 1 H), 4.34 (dd, *J* = 1.6, 11.2 Hz, 1 H), 4.59 (dd, *J* = 2.0, 11.2 Hz, 1 H), 5.15 (d, *J* = 3.6 Hz, 1 H), 6.68 (d, *J* = 7.6 Hz, 1 H), 6.73–6.79 (m, 2 H), 7.06 (t, *J* = 7.6 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.53 (t, *J* = 8.0 Hz, 1 H), 7.56–7.59 (m, 1 H), 8.57 (dd, *J* = 1.2, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.8, 29.9, 33.1, 69.8, 116.3, 121.1, 121.9, 124.8, 127.4, 127.9, 128.0, 129.2, 129.7, 130.0, 131.4, 136.1, 150.5, 152.6, 177.1.

HRMS: *m*/*z* calcd for $C_{19}H_{14}O_2S_2$ $[M + H]^+$: 339.0508; found: 339.0547.

5b

Yield: 82%; colorless solid; mp 213–215 °C.

IR (KBr): 1224, 1518, 1603, 2923 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.40–2.44 (m, 1 H), 2.94 (ddd, *J* = 1.5, 4.1, 12.3 Hz, 1 H), 3.28 (t, *J* = 12.2 Hz, 1 H), 4.33 (dd, *J* = 1.8, 11.3 Hz, 1 H), 4.56 (dd, *J* = 2.1, 11.3 Hz, 1 H), 5.11 (d, *J* = 3.3 Hz, 1 H), 6.66 (d, *J* = 8.5 Hz, 1 H), 6.76 (s, 1 H), 7.17 (dd, *J* = 1.8, 8.5 Hz, 1 H), 7.48 (d, *J* = 8.1 Hz, 1 H), 7.54 (t, *J* = 7.1 Hz, 1 H), 7.59 (dd, *J* = 1.3, 8.2 Hz, 1 H), 8.57 (dd, *J* = 1.3, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.8, 29.7, 33.1, 69.8, 113.2, 118.2, 124.1, 124.8, 127.2, 127.6, 129.7, 129.9, 130.9, 131.5, 131.7, 136.1, 151.1, 151.9, 176.9.

MS: *m*/*z* = 416, 418 (M^+).

Anal. Calcd for $C_{19}H_{13}BrO_2S_2$: C, 54.68; H, 3.14. Found: C, 54.89; H, 3.10.

5c

Yield: 74%; colorless solid; mp 153–155 °C.

IR (KBr): 1243, 1518, 1608, 2923 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 3 H), 2.59–2.66 (m, 1 H), 2.88–2.98 (m, 2 H), 4.10 (dd, *J* = 9.6, 11.6 Hz, 1 H), 4.29 (d, *J* = 11.2 Hz, 1 H), 4.40 (dd, *J* = 5.6, 9.6 Hz, 1 H), 6.28 (s, 1 H), 6.75 (d, *J* = 8.0 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 7.50 (d, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 7.6 Hz, 1 H), 7.62 (t, *J* = 8.0 Hz, 1 H), 8.41 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 29.2, 39.7, 41.7, 71.3, 116.6, 124.7, 125.7, 126.5, 126.6, 127.7, 128.1, 129.2, 129.3, 131.4, 131.7, 135.9, 149.1, 152.5, 178.6.

MS: *m*/*z* = 352 (M^+).

Anal. Calcd for $C_{20}H_{16}O_2S_2$: C, 68.15; H, 4.58. Found: C, 68.01; H, 4.65.

5d

Yield: 73%; colorless solid; mp 175–177 °C.

IR (KBr): 1225, 1506, 1598, 2926 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 9 H), 2.40–2.42 (m, 1 H), 2.93 (dd, *J* = 2.6, 12.3 Hz, 1 H), 3.36 (t, *J* = 12.2 Hz, 1 H), 4.31 (dd, *J* = 1.8, 11.2 Hz, 1 H), 4.54 (dd, *J* = 1.8, 11.2 Hz, 1 H), 5.14 (d, *J* = 3.7 Hz, 1 H), 6.70 (d, *J* = 8.2 Hz, 2 H), 7.08 (dd, *J* = 1.7, 8.5 Hz, 1 H), 7.46 (d, *J* = 7.9 Hz, 1 H), 7.52 (t, *J* = 7.9 Hz, 1 H), 7.57–7.60 (m, 1 H), 8.58 (d, *J* = 7.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.9, 30.1, 31.3 (3 C), 33.2, 34.0, 69.7, 115.7, 121.0, 124.8, 124.9, 125.9, 127.4, 128.2, 129.5, 130.1, 131.3, 136.0, 143.5, 150.1, 150.2, 177.3.

MS: *m*/*z* = 394 (M^+).

Anal. Calcd for $C_{23}H_{22}O_2S_2$: C, 70.02; H, 5.62. Found: C, 70.21; H, 5.57.

5e

Yield: 65%; colorless solid; mp 174–176 °C.

IR (KBr): 1256, 1494, 1611, 2922 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.95 (s, 3 H), 2.84–2.89 (m, 1 H), 2.91 (d, *J* = 5.2 Hz, 1 H), 3.16 (dd, *J* = 8.8, 12.0 Hz, 1 H), 4.15 (dd, *J* = 4.0, 15.2 Hz, 1 H), 4.21 (dd, *J* = 2.0, 11.2 Hz, 1 H), 5.11 (d, *J* = 5.6 Hz, 1 H), 6.66 (d, *J* = 9.2 Hz, 1 H), 7.11 (d, *J* = 8.8 Hz, 1 H), 7.48 (d, *J* = 8.0 Hz, 1 H), 7.53 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.60 (dt, *J* = 1.2, 7.6 Hz, 1 H), 8.46 (dd, *J* = 1.2, 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2, 33.5, 35.9, 38.1, 69.2, 115.1, 124.4, 125.2, 127.1, 127.7, 127.9, 129.6, 131.2, 131.5, 134.9, 135.6, 136.6, 150.7, 155.4, 177.5.

MS: *m*/*z* = 386 (M^+).

Anal. Calcd for $C_{20}H_{15}ClO_2S_2$: C, 62.08; H, 3.91. Found: C, 62.23; H, 3.83.

5f

Yield: 70%; colorless solid; mp 190–192 °C.

IR (KBr): 1215, 1511, 1598, 2925 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.50 (d, *J* = 6.4 Hz, 3 H), 2.06 (d, *J* = 10.4 Hz, 1 H), 3.67 (dd, *J* = 6.4, 10.5 Hz, 1 H), 4.47 (d, *J* = 11.4 Hz, 1 H), 4.56 (d, *J* = 11.4 Hz, 1 H), 5.20 (s, 1H), 6.68 (d, *J* = 7.4 Hz, 1 H), 6.73 (d, *J* = 7.3 Hz, 1 H), 6.76 (d, *J* = 8.6 Hz, 1 H), 7.07 (t, *J* = 7.6 Hz, 1 H), 7.46 (d, *J* = 7.8 Hz, 1 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 8.57 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.9, 29.7, 35.6, 37.0, 66.8, 116.1, 121.1, 122.3, 124.9, 127.4, 127.8, 127.9, 129.0, 129.6, 130.7, 131.3, 136.2, 151.3, 153.2, 177.0.

MS: *m*/*z* = 352 (M^+).

Anal. Calcd for $C_{20}H_{16}O_2S_2$: C, 68.15; H, 4.58. Found: C, 68.39; H, 4.61.

5g

Yield: 72%; colorless solid; mp 204–206 °C.

IR (KBr): 1239, 1494, 1627, 2919 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.11 (s, 3 H), 2.59–2.62 (m, 1 H), 2.92–2.98 (m, 2 H), 4.11 (t, *J* = 10.5 Hz, 1 H), 4.26 (d, *J* = 11.2 Hz, 1 H), 4.40 (dd, *J* = 5.2, 9.2 Hz, 1 H), 6.23 (s, 1 H), 6.75 (d, *J* = 8.0 Hz, 1 H), 6.89 (d, *J* = 7.6 Hz, 1 H), 7.48 (d, *J* = 8.4 Hz, 2 H), 8.34 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2, 33.5, 35.9, 38.0, 69.2, 115.1, 124.4, 125.2, 127.1, 127.7, 127.9, 129.5, 131.2, 131.5, 134.9, 135.6, 136.6, 150.7, 155.3, 177.5.

MS: *m*/*z* = 386 (M^+).

Anal. Calcd for $C_{20}H_{15}ClO_2S_2$: C, 62.08; H, 3.91. Found: C, 62.25; H, 3.85.

5h
Yield: 80%; colorless solid; mp 212–214 °C (Lit.[14g] mp 212–214 °C).

The spectral data were in accordance with the reported values.

5i
Yield: 79%; colorless solid; mp 238–240 °C.

IR (KBr): 741, 1158, 1614, 2921 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 4.65 (d, *J* = 11.8 Hz, 1 H), 4.93 (d, *J* = 11.7 Hz, 1 H), 5.42 (s, 1 H), 6.08 (s, 1 H), 6.57 (s, 1 H), 6.71 (d, *J* = 8.6 Hz, 1 H), 7.18 (dd, *J* = 2.3, 8.6 Hz, 1 H), 7.52–7.58 (m, 2 H), 7.63 (t, *J* = 7.8 Hz, 1 H), 8.52 (d, *J* = 8.1 Hz, 1 H).

MS: *m*/*z* = 413, 415 (M^+).

Anal. Calcd for $C_{19}H_{11}BrO_2S_2$: C, 54.95; H, 2.67. Found: C, 54.79; H, 2.76.

5j
Yield: 75%; colorless solid; mp 208–210 °C.

IR (KBr): 744, 1158, 1608, 2923 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.13 (s, 3 H), 4.63 (d, *J* = 11.8 Hz, 1 H), 4.92 (d, *J* = 11.8 Hz, 1 H), 5.41 (s, 1 H), 6.00 (s, 1 H), 6.28 (s, 1 H), 6.73 (d, *J* = 8.2 Hz, 1 H), 6.87 (d, *J* = 7.9 Hz, 1 H), 7.52–7.57 (m, 2 H), 7.63 (t, *J* = 8.0 Hz, 1 H), 8.52 (dd, *J* = 1.3, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz): δ = 20.8, 35.8, 72.8, 108.9, 116.8, 121.7, 125.1, 125.2, 127.2, 127.8, 128.2, 129.7, 130.1, 130.6, 131.0, 131.7, 135.8, 146.1, 151.9, 176.9.

MS: *m*/*z* = 350 (M^+).

Anal. Calcd for $C_{20}H_{14}O_2S_2$: C, 68.54; H, 4.03. Found: C, 68.29; H, 4.14.

5k
Yield: 72%; colorless solid; mp 206–208 °C.

IR (KBr): 742, 1157, 1600, 2924 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.11 (s, 9 H), 4.63 (d, *J* = 11.8 Hz, 1 H), 4.90 (d, *J* = 11.6 Hz, 1 H), 5.46 (s, 1 H), 6.03 (s, 1 H), 6.50 (d, *J* = 1.1 Hz, 1 H), 6.76 (d, *J* = 8.5 Hz, 1 H), 7.09 (dd, *J* = 2.0, 8.4 Hz, 1 H), 7.52–7.56 (m, 2 H), 7.64 (m, 1 H), 8.51 (dd, *J* = 1.1, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.3 (3 C), 34.0, 36.0, 72.6, 109.1, 116.3, 121.7, 122.0, 124.5, 125.1, 125.7, 127.8, 129.3, 130.5, 130.8, 131.7, 135.6, 143.2, 145.7, 151.8, 177.3.

MS: *m*/*z* = 392 (M^+).

Anal. Calcd for $C_{23}H_{20}O_2S_2$: C, 70.38; H, 5.14. Found: C, 70.51; H, 5.08.

5l
Yield: 69%; colorless solid; mp 168–170 °C.

IR (KBr): 736, 1155, 1614, 2920 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 3.69 (s, 1 H), 4.68 (d, *J* = 13.8 Hz, 1 H), 4.84 (d, *J* = 13.8 Hz, 1 H), 6.57 (s, 1 H), 6.91 (d, *J* = 8.6 Hz, 1 H), 7.29 (d, *J* = 8.6 Hz, 1 H), 7.44 (t, *J* = 8.0 Hz, 1 H), 7.49 (d, *J* = 7.4 Hz, 1 H), 7.55 (t, *J* = 8.1 Hz, 1 H), 8.18 (dd, *J* = 0.8, 8.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.8, 35.8, 72.7, 108.9, 116.8, 121.7, 125.1, 125.2, 127.2, 127.8, 128.2, 129.7, 130.1, 130.6, 131.0, 131.7, 135.8, 146.1, 151.9, 176.9.

MS: *m*/*z* = 384 (M^+).

Anal. Calcd for $C_{20}H_{13}ClO_2S_2$: C, 62.41; H, 3.40. Found: C, 62.56; H, 3.37.

5m
Yield: 76%; colorless solid; mp 182–184 °C.

IR (KBr): 743, 1160, 1601, 2932 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.61 (s, 3 H), 4.62 (d, *J* = 12.0 Hz, 1 H), 4.91 (d, *J* = 11.6 Hz, 1 H), 5.41 (s, 1 H), 5.99 (s, 1 H), 6.09 (d, *J* = 2.8 Hz, 1 H), 6.62 (dd, *J* = 2.8, 8.8 Hz, 1 H), 6.78 (d, *J* = 8.8 Hz, 1 H), 7.50–7.55 (m, 2 H), 7.62 (t, *J* = 7.2 Hz, 1 H), 8.49 (d, *J* = 7.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 35.9, 55.6, 72.8, 108.9, 111.4, 111.8, 117.3, 121.3, 125.1, 127.8, 129.0, 129.6, 130.6, 130.9, 131.7, 135.6, 146.3, 148.1, 153.7, 176.9.

MS: *m*/*z* = 366 (M^+).

Anal. Calcd for $C_{20}H_{14}O_3S_2$: C, 65.55; H, 3.85. Found: C, 65.76; H, 3.81.

5n
Yield: 77%; colorless solid; mp 224–226 °C.

IR (KBr): 738, 1158, 1603, 2925 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.65 (d, *J* = 11.6 Hz, 1 H), 4.93 (d, *J* = 11.6 Hz, 1 H), 5.41 (s, 1 H), 6.08 (s, 1 H), 6.44 (s, 1 H), 6.76 (d, *J* = 8.4 Hz, 1 H), 7.04 (d, *J* = 8.0 Hz, 1 H), 7.52–7.79 (m, 3 H), 8.52 (d, *J* = 8.0 Hz, 1 H).

MS: *m*/*z* = 370 (M^+).

Anal. Calcd for $C_{19}H_{11}ClO_2S_2$: C, 61.53; H, 2.99. Found: C, 61.34; H, 2.92.

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