Synthesis of 3-(γ,δ-Disubstituted)allylidene-2-Oxindoles from Isatins by Wittig Reaction with Morita–Baylis–Hillman Bromides

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Various 3-(γ,δ-disubstituted)allylidene-2-oxindoles were synthesized by the Wittig reaction between isatins and the phosphorous ylide derived *in situ* from the Morita–Baylis–Hillman bromides. The 3-allylidene-2-oxindole could be used as an efficient synthetic precursor of 1-thiacarbazole derivatives. During the conversion of 2-oxindole moiety to 2-thiooxindole by Lawesson's reagent, 1-thiacarbazole derivative was obtained in good yield.

Keywords: 3-Allylidene-2-oxindoles, Wittig reaction, Morita–Baylis–Hillman bromides, Isatins

Introduction

The 3-alkylidene-2-oxindole ring system represents a key substructure found in many biologically important compounds.[1] In this line, further functionalizations of the 3-alkylidene moiety including an extension of the conjugation with C=C double bond have received much attention.[2–4] Takemoto *et al.* have reported the synthesis of 3-(β,δ-disubstituted)allylidene-2-oxindoles via a palladium-catalyzed Heck/Heck domino reaction of alkynamide precursor, as shown in Scheme 1 (Eq. 1).[2a] Pontikis *et al.* also reported the synthesis of 3-(β,-δ-disubstituted)allylidene-2-oxindoles via a palladium-catalyzed Heck/Suzuki–Miyaura domino reaction of alkynamide and styrylboronic acid.[2b,c] Recently, we have reported the *N,N*-dimethylaminomethylenation of 3-alkylidene-2-oxindoles with *N,N*-dimethylformamide dimethylacetal (DMF-DMA) to make 3-(β,δ-disubstituted)allylidene-2-oxindoles, as shown in Scheme 1 (Eq. 2).[3a]

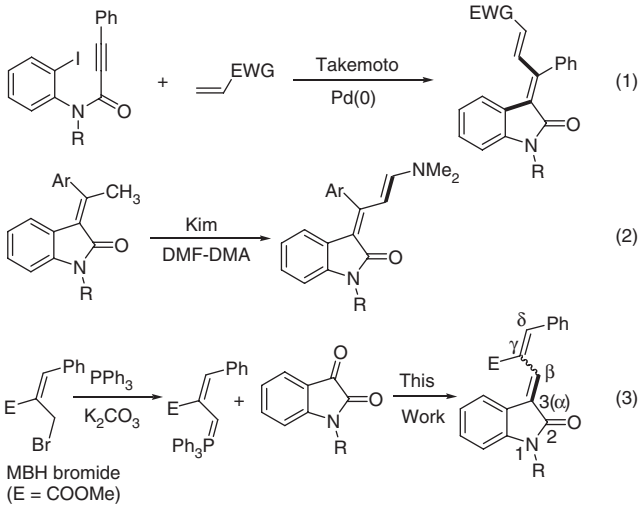
Results and Discussion

The phosphorous ylides derived from Morita–Baylis–Hillman (MBH) bromides have been used for the synthesis of functionalized 1,3-dienes, which are used in many reactions such as Diels–Alder reaction or 6π-electrocyclization.[5,6] In these contexts, we envisaged that the Wittig reaction of isatin with phosphorous ylide derived from the MBH bromide could provide 3-(γ,δ-disubstituted)allylidene-2-oxindoles, as shown in Scheme 1 (Eq. 3). To the best of our knowledge, no report has been published for the synthesis of 3-allylidene-2-oxindoles using the Wittig reaction.[7]

Thus, two representative MBH bromides **1a**-*Z* and **1b**-*E* were prepared stereoselectively according to the reported method.[6] The reaction of MBH bromide **1a**-*Z* and triphenylphosphine in CH_3CN afforded the corresponding phosphonium bromide at room temperature within 4 h. Isatin (**2a**) and K_2CO_3 were added to the reaction mixture, and the Wittig reaction was completed within 3 h at room temperature. The desired 3-allylidene-2-oxindoles **3a**-*EE* (51%) and **3a**-*ZE* (41%) were isolated, as shown in Table 1 (entry 1). The reactions with 5-chloroisatin (**2b**), 5-methoxyisatin (**2c**), 5-nitroisatin (**2d**), *N*-methylisatin (**2e**), and *N*-acetylisatin (**2f**) afforded the corresponding products **3b–f** (entries 2–6) in good to moderate yields (76–94%). The *EE*-isomers were formed as the major products in all cases. As an example, the stereochemistry of **3e**-*EE* was unequivocally confirmed by its X-ray crystal structure (Figure 1).[8]

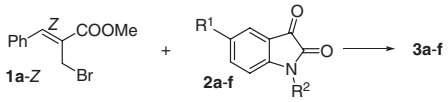
It is interesting to note that the two ortho-protons of δ-phenyl group of **3a**-*EE* appeared at downfield (δ = 7.48–7.54 ppm) as compared to the remaining three meta/para protons (δ = 7.32–7.37 ppm), while the corresponding five aromatic protons of **3a**-*ZE* appeared together as an apparent singlet at δ = 7.41 ppm. The downfield shift of two ortho-protons of the δ-phenyl group of **3a**-*EE* might be due to the anisotropic effect of the carbonyl group of 2-oxindole moiety (see Figure 1).[1c] Similarly, the ortho-protons of the δ-phenyl group of *EE*-isomers of **3b–f** appeared at downfield (δ = 7.44–7.63 ppm) compared to the remaining three meta/para protons (δ = 7.30–7.44 ppm).

As a next entry, the reaction of nitrile-containing MBH bromide **1b**-*E*[6] was examined, as shown in Scheme 2. The reaction provided **3g**-*EZ* in good yield (74%), and the structure of **3g**-*EZ* was unequivocally confirmed by its X-ray crystal structure (Figure 2).[9] The formation of the other isomer was observed on thin-layer chromatography (TLC) at the right position in trace amounts; however, the isolation failed because of the presence of some impurity near the spot. The proton H-4 of the isatin moiety appeared at downfield (δ = 8.13 ppm) as a result of the anisotropy of the nitrile group.[10] The two ortho-protons of the phenyl moiety at the δ-position of **3g**-*EZ* appeared downfield (δ = 7.94–7.99 ppm) compared to the three meta/para-protons (δ = 7.50–7.55 ppm) because of the same anisotropy of the nitrile group. Similarly, the reaction of **1b**-*E* and *N*-methyl-5-chloroisatin (**2g**) showed a similar

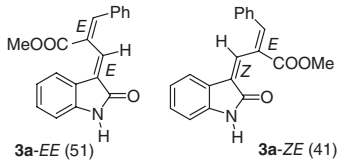
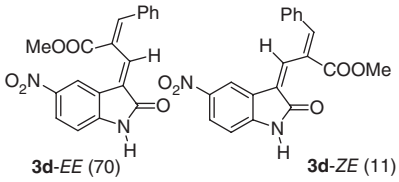
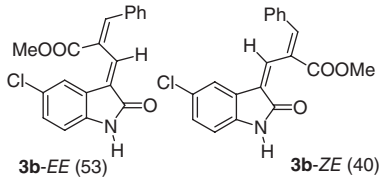
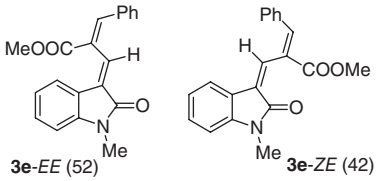
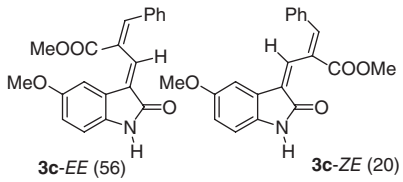
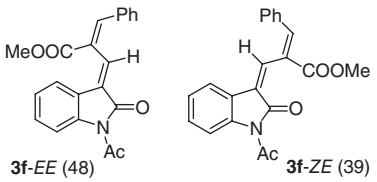


Scheme 1. Synthesis of 3-allylidene-2-oxindoles.

Table 1. Synthesis of 3-allylidene-2-oxindoles **3a–f**.[a]



2a: R^1 = H, R^2 = H; **2b**: R^1 = Cl, R^2 = H
2c: R^1 = OMe, R^2 = H; **2d**: R^1 = NO_2, R^2 = H
2e: R^1 = H, R^2 = Me; **2f**: R^1 = H, R^2 = COMe

Entry	2	Product (%)	Entry	2	Product (%)
1	**2a**	 **3a**-*EE* (51) **3a**-*ZE* (41)	4	**2d**	 **3d**-*EE* (70) **3d**-*ZE* (11)
2	**2b**	 **3b**-*EE* (53) **3b**-*ZE* (40)	5	**2e**	 **3e**-*EE* (52) **3e**-*ZE* (42)
3[b]	**2c**	 **3c**-*EE* (56) **3c**-*ZE* (20)	6	**2f**	 **3f**-*EE* (48) **3f**-*ZE* (39)

[a] Conditions: (i) MBH bromide **1a** (1.2 equiv), PPh_3 (1.2 equiv), CH_3CN, room temperature, 4 h, and (ii) isatin **2a–f** (1.0 equiv), K_2CO_3 (2.0 equiv), room temperature, 3 h.
[b] Reaction time for step (ii) was 5 h.

result to afford **3h**-*EZ* in good yield (76%). Also, the corresponding H-4 proton (δ = 8.16 ppm) and the two ortho-protons of the phenyl moiety at the δ-position appeared downfield (δ = 7.95–8.00 ppm).

In order to extend the conjugation of double bonds, we examined the Wittig reaction of *N*-methylisatin (**2e**) with *in situ* generated ylide from the MBH bromide **1c**-*ZE*,[6] as shown in Scheme 3. Compound **3i**-*EEE* was obtained in good yield

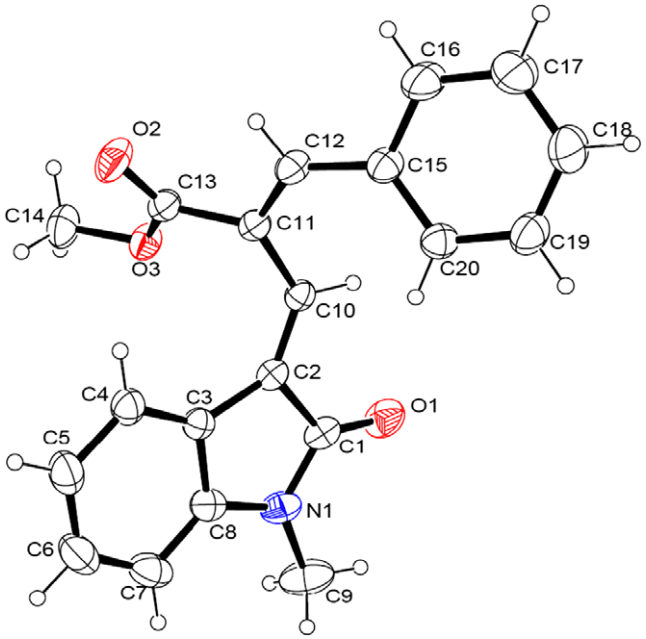


Figure 1. ORTEP drawing of **3e**-*EE*.

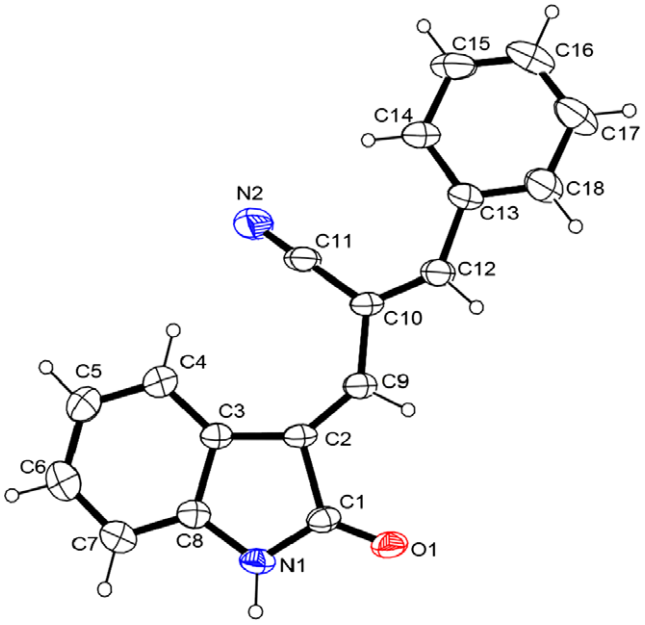
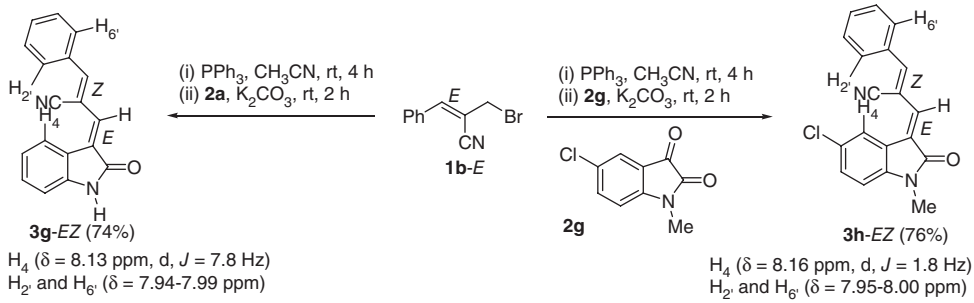


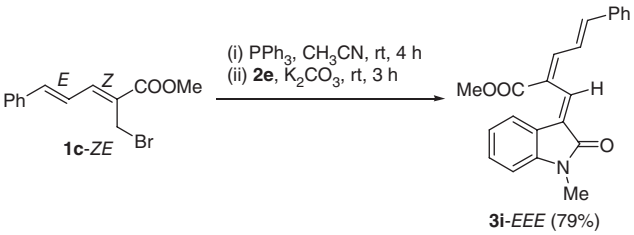
Figure 2. ORTEP drawing of **3g**-*EZ*.



Scheme 2. Synthesis of 3g and 3h.

(79%). The formation of the minor *ZEE*-isomer was observed on TLC at the right position in trace amounts; however, we failed to isolate the compound in appreciable amount.

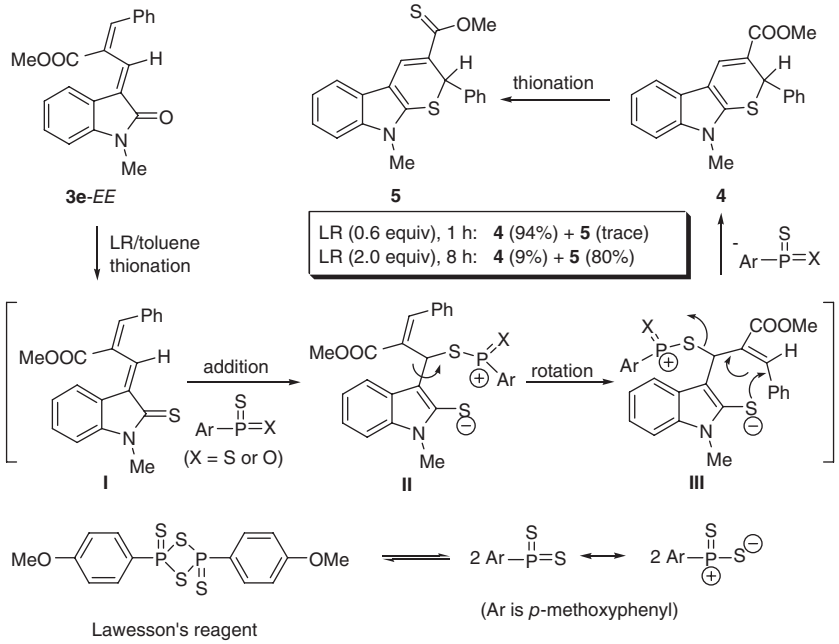
As one of the synthetic applications of prepared compounds, the reaction of **3e**-*EE* and Lawesson's reagent (LR)[11] was examined, as shown in Scheme 4. The reaction of **3e**-*EE* and LR (0.6 equiv) in toluene at 100 °C in a short time (1 h) afforded 1-thiacarbazole derivative[12] **4** in good yield (94%). In the reaction, the formation of a trace amount of side product was observed. The compound was identified as a thionoester derivative **5**.[11] Actually, compound **5** was formed as a major product (80%) by using an excess amount of LR (2.0 equiv) for 8 h. The 1-thiacarbazole **4** could be produced via the sequential thionation of oxindole moiety to thiooxindole **I** and (*p*-MeOPh)PS(=*X*)-catalyzed Michael-type cyclization process involving the intermediates **II** and **III**.[13] The formations of **4** and **5** were not observed at lower temperatures (room temperature to 70 °C); however, double-bond isomerization of **3e**-*EE* to **3e**-*ZE* was observed to some extent presumably by $ArPS_2$.



Scheme 3. Synthesis of 3 i.

Conclusion

In summary, various 3-(γ,δ-disubstituted)allylidene-2-oxindoles have been synthesized by the Wittig reaction between isatins and the phosphorous ylide derived *in situ* from the MBH bromides. Further studies on the biological activity and chemical transformations of prepared compounds are under progress and the results will be released in due course.



Scheme 4. The reaction of 3e and Lawesson's reagent.

Experimental Section

Typical Procedure for the Synthesis of 3a. A mixture of MBH bromide **1a**-*Z* (306 mg, 1.2 mmol) and PPh_3 (315 mg, 1.2 mmol) in CH_3CN (3.0 mL) was stirred at room temperature for 4 h. The corresponding phosphonium salt, monitored by TLC, was formed quantitatively. To the reaction mixture, isatin (**2a**, 147 mg, 1.0 mmol) and K_2CO_3 (276 mg, 2.0 mmol) were added, and the reaction mixture was stirred at room temperature for 3 h. After the usual aqueous extractive work-up and column chromatographic purification process (hexanes/EtOAc, 2:1), compounds **3a**-*EE* (156 mg, 51%) and **3a**-*ZE* (125 mg, 41%) were obtained as yellow solids. Other compounds were synthesized similarly, and the spectroscopic data of **3a–i** (see Supporting Information) are as follows:

Compound 3a-*EE*: 51%; yellow solid, mp 162–164 °C; IR (KBr) 3200, 1709, 1614, 1465, 1255, 1205 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.76 (s, 3H), 6.84–6.92 (m, 2H), 7.14 (d, J = 7.8 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 7.32–7.37 (m, 3H), 7.48–7.54 (m, 2H), 7.59 (d, J = 1.8 Hz, 1H), 7.98 (d, J = 1.8 Hz, 1H), 8.78 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.61, 110.04, 121.91, 122.15, 124.12, 126.10, 128.74, 129.88, 129.97, 130.33, 130.72, 130.90, 134.24, 141.39, 144.29, 166.99, 169.43; ESIMS *m/z* 306 $[M + H]^+$. Anal. calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59; found: C, 74.96; H, 5.07; N, 4.34.

Compound 3a-*ZE*: 41%; yellow solid, mp 158–160 °C; IR (KBr) 3287, 1717, 1615, 1269, 1258, 1203 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.81 (s, 3H), 6.91 (d, J = 7.8 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 1.8 Hz, 1H), 7.26 (t, J = 7.8 Hz, 1H), 7.41 (s, 5H), 7.47 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 1.8 Hz, 1H), 8.52 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.28, 110.04, 120.60, 121.99, 123.29, 128.53, 128.59, 128.80, 129.79, 129.85, 130.68, 130.81, 135.00, 140.86, 142.86, 167.68, 168.15; ESIMS *m/z* 306 $[M + H]^+$. Anal. calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59; found: C, 74.71; H, 4.82; N, 4.41.

Compound 3b-*EE*: 53%; yellow solid, mp 208–210 °C; IR (KBr) 3173, 1709, 1613, 1453, 1265 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.82 (s, 3H), 6.77 (d, J = 8.1 Hz, 1H), 7.06 (d, J = 1.8 Hz, 1H), 7.14 (dd, J = 8.1 and 1.8 Hz, 1H), 7.31–7.38 (m, 3H), 7.45–7.52 (m, 2H), 7.63 (d, J = 1.5 Hz, 1H), 8.01 (d, J = 1.5 Hz, 1H), 8.48 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.73, 110.76, 123.13, 124.46, 125.65, 127.46, 128.81, 129.53, 129.61, 130.52, 130.54, 131.55, 134.16, 139.66, 145.03, 166.50, 168.92; ESIMS *m/z* 340 $[M + H]^+$, 342 $[M + H + 2]^+$. Anal. calcd for $C_{19}H_{14}ClNO_3$: C, 67.16; H, 4.15; N, 4.12; found: C, 67.02; H, 4.37; N, 4.04.

Compound 3b-*ZE*: 40%; yellow solid, mp 162–164 °C; IR (KBr) 3261, 1722, 1615, 1472, 1259 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.80 (s, 3H), 6.83 (d, J = 8.1 Hz, 1H), 7.22 (dd, J = 8.1 and 2.1 Hz, 1H), 7.23 (d, J = 2.1 Hz, 1H), 7.37–7.45 (m, 6H), 7.83 (d, J = 1.8 Hz, 1H), 8.43 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.32, 110.99, 120.81, 124.72, 127.56, 128.42, 128.71, 129.47, 129.81, 130.07, 130.80, 134.82, 139.13, 143.67, 167.39, 167.73, one carbon was overlapped; ESIMS *m/z* 340 $[M + H]^+$, 342 $[M + H + 2]^+$.

Compound 3c-*EE*: 56%; yellow solid, mp 166–168 °C; IR (KBr) 3230, 1708, 1483, 1259, 1203 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.67 (s, 3H), 3.79 (s, 3H), 6.73 (d, J = 8.1 Hz, 1H), 6.74 (s, 1H), 6.79 (d, J = 8.1 Hz, 1H), 7.30–7.38 (m, 3H), 7.49–7.57 (m, 2H), 7.60 (d, J = 1.8 Hz, 1H), 7.97 (d, J = 1.8 Hz, 1H), 9.09 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.63, 55.70, 110.22, 110.49, 115.63, 122.57, 125.98, 128.75, 130.12, 130.38, 130.65, 131.32, 134.19, 135.34, 144.13, 155.27, 166.98, 169.76; ESIMS *m/z* 336 $[M + H]^+$.

Anal. calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18; found: C, 71.48; H, 5.35; N, 4.17.

Compound 3c-*ZE*: 20%; yellow solid, mp 178–180 °C; IR (KBr) 3271, 1718, 1487, 1260, 1202 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.79 (s, 3H), 3.80 (s, 3H), 6.81 (apparent d, *J* = 1.5 Hz, 2H), 7.03 (dd, *J* = 1.5 and 1.2 Hz, 1H), 7.19 (d, *J* = 1.8 Hz, 1H), 7.41 (s, 5H), 7.79 (d, *J* = 1.8 Hz, 1H), 8.57 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.28, 55.92, 106.88, 110.56, 115.30, 124.14, 128.60, 128.63, 128.75, 129.80, 130.81, 131.21, 134.83, 134.99, 142.86, 155.45, 167.69, 168.38; ESIMS *m/z* 336 $[M + H]^+$.

Compound 3d-*EE*: 70%; yellow solid, mp 246–248 °C; IR (KBr) 3177, 1714, 1615, 1517, 1333, 1252, 1202 cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz) δ 3.77 (s, 3H), 7.00 (d, *J* = 8.7 Hz, 1H), 7.32–7.44 (m, 3H), 7.45–7.63 (m, 3H), 7.75 (s, 1H), 8.07 (s, 1H), 8.13 (d, *J* = 8.7 Hz, 1H), 11.35 (br s, 1H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 52.73, 109.98, 118.90, 121.18, 125.53, 126.61, 128.29, 128.78, 130.43, 130.72, 131.88, 133.93, 141.63, 144.70, 148.35, 165.85, 168.20; ESIMS *m/z* 351 $[M + H]^+$. Anal. calcd for $C_{19}H_{14}N_2O_5$: C, 65.14; H, 4.03; N, 8.00; found: C, 65.35; H, 4.20; N, 7.81.

Compound 3d-*ZE*: 11%; yellow solid, mp 172–174 °C; IR (KBr) 3271, 1724, 1621, 1523, 1338, 1260 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.81 (s, 3H), 7.04 (d, *J* = 8.7 Hz, 1H), 7.37–7.50 (m, 6H), 7.91 (d, *J* = 2.1 Hz, 1H), 8.22 (dd, *J* = 8.4 and 2.1 Hz, 1H), 8.34 (d, *J* = 2.1 Hz, 1H), 9.23 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.44, 109.88, 116.36, 123.68, 126.07, 127.91, 128.75, 128.87, 130.52, 130.84, 132.29, 134.52, 143.24, 144.95, 145.65, 167.16, 168.11; ESIMS *m/z* 351 $[M + H]^+$.

Compound 3e-*EE*: 52%; yellow solid, mp 112–114 °C; IR (KBr) 3056, 2950, 1711, 1610, 1469, 1254 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.27 (s, 3H), 3.75 (s, 3H), 6.79 (d, *J* = 7.5 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 7.15 (d, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.5 Hz, 1H), 7.30–7.37 (m, 3H), 7.48–7.54 (m, 2H), 7.60 (d, *J* = 1.5 Hz, 1H), 7.95 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.09, 52.56, 108.01, 121.31, 122.11, 123.76, 126.18, 128.72, 129.67, 129.77, 130.26, 130.52, 130.73, 134.26, 144.00, 144.06, 167.03, 167.58; ESIMS *m/z* 320 $[M + H]^+$. Anal. calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39; found: C, 75.19; H, 5.43; N, 4.22.

Compound 3e-*ZE*: 42%; yellow solid, mp 118–120 °C; IR (KBr) 3056, 2948, 1705, 1610, 1470, 1257 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.23 (s, 3H), 3.83 (s, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 1.8 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.39 (s, 5H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.84, 52.27, 108.08, 120.21, 121.93, 122.51, 128.11, 128.52, 128.94, 129.64, 129.73, 130.37, 130.75, 135.03, 142.29, 143.45, 166.21, 167.60; ESIMS *m/z* 320 $[M + H]^+$. Anal. calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39; found: C, 75.41; H, 5.50; N, 4.47.

Compound 3f-*EE*: 48%; yellow solid, mp 142–144 °C; IR (KBr) 2950, 1743, 1714, 1602, 1459, 1371, 1302 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.77 (s, 3H), 3.74 (s, 3H), 7.08 (t, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.32–7.43 (m, 3H), 7.44–7.55 (m, 2H), 7.64 (s, 1H), 8.01 (s, 1H), 8.28 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.80, 52.65, 116.58, 122.06, 123.33, 124.82, 125.75, 128.82, 129.29, 130.26, 130.58, 130.71, 131.20, 134.12, 140.12, 144.97, 166.57, 167.76, 170.75; ESIMS *m/z* 348 $[M + H]^+$. Anal. calcd for $C_{21}H_{17}NO_4$: C, 72.61; H, 4.93; N, 4.03; found: C, 72.87; H, 5.20; N, 3.94.

Compound 3f-*ZE*: 39%; yellow solid, mp 156–158 °C; IR (KBr) 1733, 1713, 1465, 1373, 1282, 1163 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.70 (s, 3H), 3.83 (s, 3H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 2.1 Hz, 1H), 7.36–7.45 (m, 6H), 7.55 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 2.1 Hz, 1H), 8.30 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.74, 52.38, 116.88, 119.79, 123.17, 124.92, 128.40, 128.71, 129.07, 129.95, 130.12, 130.29, 130.85, 134.81, 139.58, 143.70, 166.57, 167.29, 170.82; ESIMS *m/z* 348 $[M + H]^+$.

Compound 3g-*EZ*: 74%; yellow solid, mp 190–192 °C; IR (KBr) 3149, 2220, 1707, 1605, 1464, 1325, 1201 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 6.90 (d, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.8 Hz, 1H), 7.35 (s, 1H), 7.50–7.55 (m, 3H), 7.65 (s, 1H), 7.94–7.99 (m, 2H), 8.08 (br s, 1H), 8.13 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 106.03, 110.12, 117.24, 120.69, 122.44, 126.79, 128.17, 129.26, 130.20, 130.64, 131.75, 132.27, 132.84, 141.84, 153.01, 169.24; ESIMS *m/z* 273 $[M + H]^+$. Anal. calcd for $C_{18}H_{12}N_2O$: C, 79.39; H, 4.44; N, 10.29; found: C, 79.43; H, 4.29; N, 10.12.

Compound 3h-*EZ*: 76%; red solid, mp 196–198 °C; IR (KBr) 2213, 1707, 1607, 1484, 1370, 1111 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.27 (s, 3H), 6.77 (d, *J* = 8.1 Hz, 1H), 7.31 (dd, *J* = 8.1 and 1.8 Hz, 1H), 7.42 (d, *J* = 0.9 Hz, 1H), 7.48–7.56 (m, 3H), 7.64 (d, *J* = 0.9 Hz, 1H), 7.95–8.00 (m, 2H), 8.16 (d, *J* = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.45, 105.73, 109.05, 117.22, 121.32, 126.76, 126.95, 127.69, 129.30, 130.07, 130.30, 132.52, 132.71, 133.05, 143.16, 153.91, 167.72; ESIMS *m/z* 321 $[M + H]^+$, 323 $[M + H + 2]^+$. Anal. calcd for $C_{19}H_{13}ClN_2O$: C, 71.14; H, 4.08; N, 8.73; found: C, 71.40; H, 4.23; N, 8.71.

Compound 3i-*EEE*: 79%; yellow solid, mp 122–124 °C; IR (KBr) 2950, 1712, 1609, 1469, 1375, 1275, 1235 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.31 (s, 3H), 3.81 (s, 3H), 6.79 (dd, *J* = 15.3 and 11.7 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 6.87 (t, *J* = 7.8 Hz, 1H), 7.11 (d, *J* = 15.3 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.26 (s, 5H), 7.61 (s, 1H), 7.69 (d, *J* = 11.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.15, 52.34, 107.94, 120.75, 122.15, 124.55, 124.67, 125.81, 127.51, 128.74, 129.29, 129.55, 129.56, 129.73, 135.85, 142.93, 143.71, 144.26, 166.74, 167.79 ; ESIMS *m/z* 346 $[M + H]^+$. Anal. calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06; found: C, 76.42; H, 5.71; N, 3.93.

Synthesis of 1-Thiacarbazole Derivatives 4 and 5. Compounds **4** and **5** were prepared from **3e**-*EE* and LR in toluene (100 °C), and the spectroscopic data are as follows:

Compound 4: yellow solid, mp 166–168 °C; IR (KBr) 1692, 1598, 1485, 1228 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz)

δ 3.61 (s, 3H), 3.79 (s, 3H), 5.51 (s, 1H), 7.16–7.25 (m, 6H), 7.31–7.38 (m, 2H), 7.63–7.71 (m, 1H), 8.25 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.79, 43.13, 51.89, 109.09, 110.08, 111.75, 117.04, 121.30, 121.89, 126.38, 126.77, 127.84, 128.52, 132.23, 136.45, 138.53, 141.48, 167.15; ESIMS *m/z* 336 $[M+H]^+$. Anal. calcd for $C_{20}H_{17}NO_2S$: C, 71.62; H, 5.11; N, 4.18; found: C, 71.55; H, 5.32; N, 4.06.

Compound 5: orange solid, mp 171–173 °C; IR (KBr) 1582, 1557, 1482, 1263, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.60 (s, 3H), 4.18 (s, 3H), 6.17 (s, 1H), 7.15–7.25 (m, 6H), 7.33–7.39 (m, 2H), 7.67–7.74 (m, 1H), 8.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.94, 45.39, 58.53, 109.23, 111.33, 117.29, 120.54, 121.57, 122.29, 126.83, 126.95, 127.64, 128.36, 129.38, 138.88, 138.99, 141.23, 208.43; ESIMS *m/z* 352 $[M+H]^+$. Anal. calcd for $C_{20}H_{17}NOS_2$: C, 68.34; H, 4.88; N, 3.99; found: C, 68.60; H, 4.81; N, 3.87.

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Supporting Information. Additional supporting information is available in the online version of this article.

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9. Crystal data of compound **3g**-*EZ*: solvent of crystal growth (EtOH); empirical formula $C_{18}H_{12}N_2O$, Fw = 272.3, crystal dimensions 0.20 × 0.11 × 0.09 mm^3, Orthorhombic, space group $P2_12_12_1$, a = 4.4968(13) Å, b = 12.156(4) Å, c = 25.162(8) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 1375.4(7) $Å^3$, Z = 4, D_{calcd} = 1.315 mg/m^3, F_{000} = 568, MoKα (λ = 0.71073 Å), R_1 = 0.0544, wR_2 = 0.1156, GOF = 1.029 ($I > 2\sigma(I)$). The X-ray data have been deposited in CCDC with number 1013826.
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