Received: 11 July 2019 | Revised: 5 October 2019 | Accepted: 13 October 2019

DOI: 10.1002/jccs.201900278

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

ARTICLE

Synthesis of selenium-containing biindolyls and their Diels–Alder reaction toward the synthesis of heteroannulated [*a*]- and [*c*]-carbazoles

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Funding information
the Ministry of Science of Taiwan, Grant/Award Number: MOST 105-2113-M-032-001

Abstract

We reported the first syntheses of 2- and 3-(2-(benzo[*b*]selenophen-2-yl)-indoles and their Diels–Alder reactions to furnish six unique annulated benzoselenphene carbazoles. This facile route can be used to synthesize selenium-containing biindolyl derivatives that possessed potential pharmaceutical activities.

KEYWORDS

biindolyl, carbazole, Castro–Stephens indole synthesis, Diels–Alder reaction, Glaser coupling, selenium

1 | INTRODUCTION

K252a, staurosporine, and arcyriaflavin are classified as the indolocarbazole family of natural products[1] (Figure 1). They all exhibited inhibitors of protein kinase C, as well as cytotoxicity of cancer cell lines.[1,2] These three representative molecules all possessed a biindolyl skeleton.[3] Therefore, biindolyl was used as a key intermediate in the synthesis of indolocarbazole derivatives.[4] On the other hand, the synthesis of 2,3′-indolo[3,2,-*b*]indole3a[5] to obtain arcyriaflavin derivatives[6] also attracted attention.

Elemental selenium is a trace nutrient in the prevention of human diseases and is associated with the similar role of vitamin E.[7] Selenium is very essential to our daily life; however, lower or the higher levels of selenium content in foods are correlated to humans' health. There are some selenium-containing enzymes in humans; therefore, people with a selenium deficiency have Keshan and Kashin–Beck diseases.7b The development of selenium-containing agents to mimic selenoenzymes properties has attracted considerable concern.[8] Besides, benzo[*b*]selenophene derivatives, as well as its analogues benzo[*b*]thiophenes, were widely applied in optoelectronic devices.[9] As a consequence, selenium-containing molecules were not only used as anticancer agents but also applied in material chemistry.

Due to the importance of selenium, we tried to replace one of the nitrogen atoms of biindolyl with a selenium element to synthesize 2- and 3-(2-(benzo[*b*]selenophen-2-yl)-indoles (Figure 2) and applied them in the synthesis of indolocarbazole derivatives through the Diels–Alder reaction.[6,10]

2 | RESULTS AND DISCUSSION

In order to synthesize 2- and 3-(benzo[*b*]seleophen-2-yl)-indoles (via *infra*), we needed to prepare two compounds, **5** and **6** (Scheme 1). Although compounds **5** and **6** were commercially available, their list prices were costly. The facile route was to use compounds **1** and **2,** respectively, coupled with tirmethylsilylacetylene (TMSA),[11] followed by the removal of silane by tetrabutylammonium fluoride (TBAF) to furnish compounds **5** and **6** with high yields in two steps. It is worth noting that compound **6** should be handled with care owing to its volatility.

Compounds **5** and **6** underwent 4-(dimethylamino) pyridine (DMAP)-catalyzed Glaser heterocoupling of

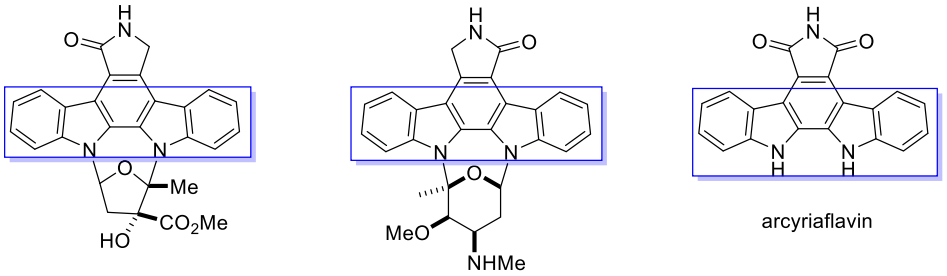


FIGURE 1 Bioactive molecules with symmetrical biindolyl (2,2′-biindole) framework (marked in blue color)

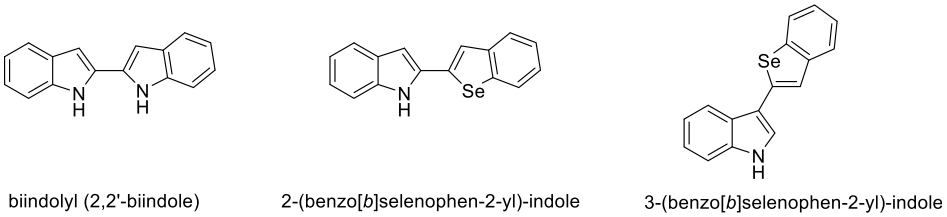
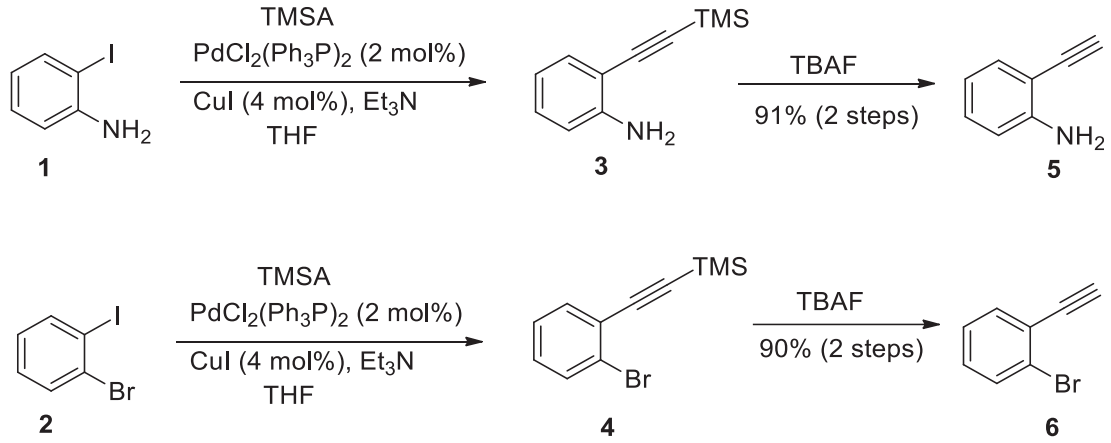


FIGURE 2 Frameworks of biindolyl and its 2- and 3-(2-benzo[*b*] selenophen-2-yl)-indole derivatives



SCHEME 1 Synthesis of **5** and **6**

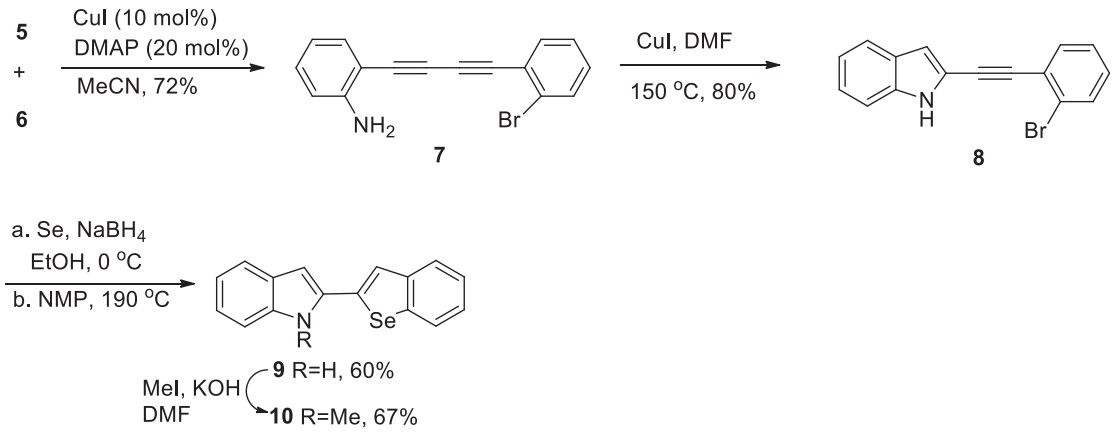
terminal alkynes[12] to furnish **7**. However, it required the slow addition of five equivalents of compound **5** into a solution to obtain the optimized yield (Scheme 2 and in supporting information). Fortunately, the side product of the above-mentioned reaction was mainly the homo coupling of **5**, which can be used for further synthesis of biindolyl. Compound **7** was conducted by Glaser method[13] to afford C-2 indole derivative **8**. In this course of cyclization to synthesize 2-benzo[*b*]selenophene-indole **9**, the key step is to replace the C-Br bond of **8** with a C-Se bond. There are some standard preparations to achieve this goal, such as metal–halogen exchange (*tert*-BuLi/Se),[11] Cu cat,[14] and Cu cat/additive.[15] We selected the in situ reduction of selenium powder by $NaBH_4$ in EtOH[16] mixing with **8,** followed by subsequent cyclization to afford **9,** which was methylated to furnish **10**. Both steps gave satisfactory yields.

On the other hand, the synthesis of 3-(benzo[*b*] selenophen-2-yl)-indoles used a strategy similar to Scheme 2. Indole (**11**) was iodinated and protected by Boc_2O to furnish **12,** which was not stable, and was immediately coupled with **6** to afford **13** (Scheme 3). The selenium was introduced, followed by intramolecular cyclization, and deprotected the Boc group in one step to provide **14,** which was methylated to afford **15**.

Compound **9** was conducted using the Diels–Alder reaction with different dienophiles, diphenylacetylene (**16),** and diethyl acetylenedicarboxylate (**17**) in different reaction conditions10a (Scheme 4). The expected cyclic adduct **18** was not obtained, but **19 was obtained** in a low yield. On the contrary, compound **10** underwent Diels–Alder reaction with both dienophiles to afford **20** and **21** but suffered low yields.

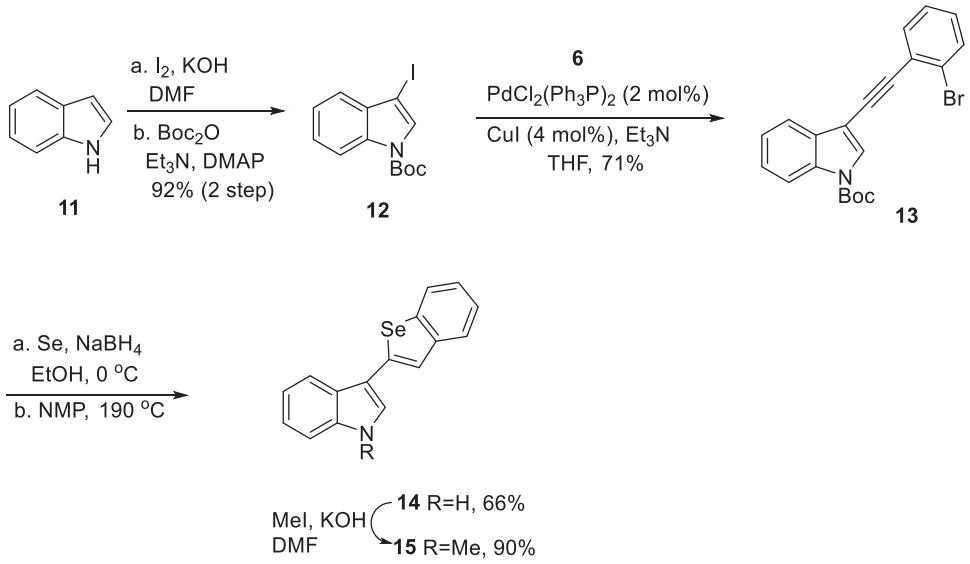
Condition a: $Pd(OAc)_2$, TBAB, PivOH,K_2CO_3, DMF, O_2, 150°C for reacting with **16**; condition b: xylene, 185°C for. reacting with **17**. *Yield given in parenthesis is reported as yield of recovery of starting material.

Compound **14** underwent the same process as compound **9** in reactions with **16** and **17** (Scheme 5). Again,



SCHEME 2 Synthesis of 2-(benzo[*b*]selenophen-2-yl)-indole derivatives **9** and **10**

SCHEME 3 Synthesis of 3-(benzo[*b*]selenophen-2-yl)-indole derivatives **14** and **15**



compound **14** was inactive with **16** but was active **17** to afford the expected **23** with a satisfactory yield. Compound **15** in reaction with **16** and **17** afforded **24** and **25** in low to moderate yields.

Condition a: $Pd(OAc)_2$, TBAB, PivOH, K_2CO_3, DMF, O_2, 150°C for reacting with **16**; *condition b*: xylene, 185°C for reacting with **17**.

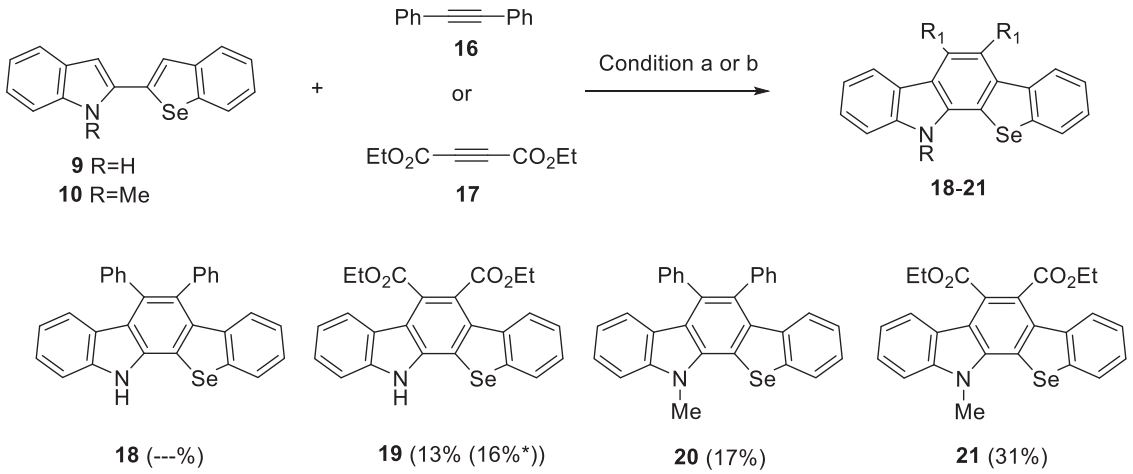
It has been reported that the electron-donating, electron-withdrawing, or bulky substituents of alkynes did not have much influence on the yields of the synthesis of carbazoles by Diels–Alder reaction;10a however, the ester group (CO_2Et) rather than phenyl group furnished better results in both Schemes 4 and 5.

3 | EXPERIMENTAL

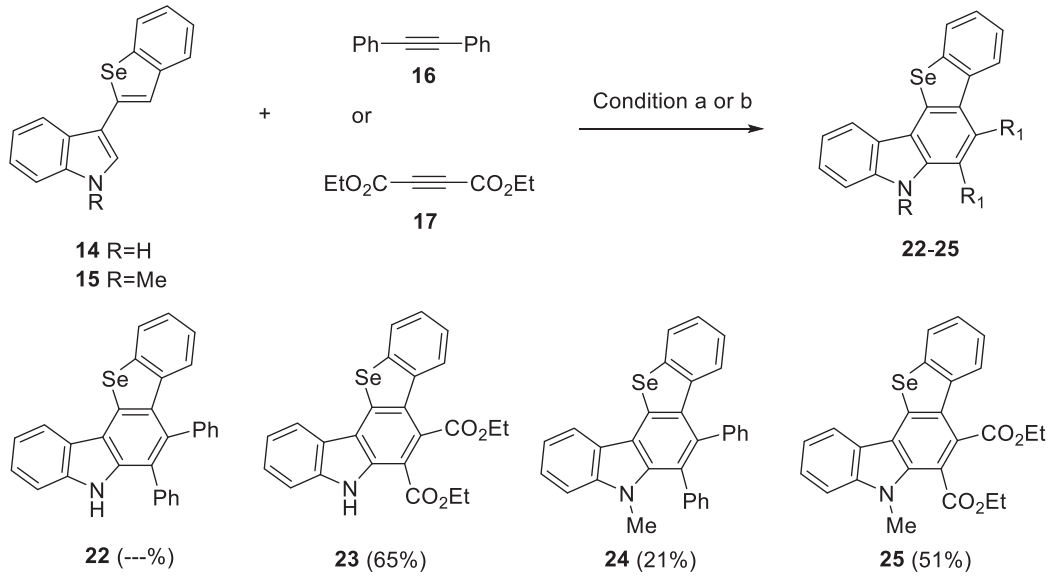
All chemicals were commercially available and used without further purification. The ^1H and ^{13}C NMR spectra were recorded on a Bruker 600 MHz instrument. The chemical shifts were reported in part per million (ppm) and referenced the residual of solvents: $CDCl_3$ (7.26 ppm for ^1H; 77.0 ppm for ^{13}C) and $(CD_3)_2CO$ (2.04 ppm for ^1H; 206.5 ppm for ^{13}C). The melting points were determined on a Fargo MP-2D apparatus and not corrected. High resolution mass (HRMS) were measured on TMS-700.

3.1 | 2-Ethynylaniline (5)

A mixture of $PdCl_2(PPh_3)_2$ (0.064 g, 0.091 mmol) and CuI (0.034 g, 0.182 mmol) in a flask was vacuumed and then introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this flask was sequentially added tetrahydrofuran (THF) (10 ml), Et_3N (10 ml), and 2-iodoaniline (1.0 g, 4.56 mmol). This mixture was stirred for 10 min, followed by addition of TMSA (0.67 g, 6.84 mmol), and then stirred for 12 hr. The resulting mixture was filtrated, and the solvents were removed under reduced pressure and diluted with EtOAc and H_2O. The organic layer was dried



SCHEME 4 The Diels–Alder reaction of 2-benzoselenophen-2-yl-indoles (**9** and **10**) with dienophiles **16** and **17**



SCHEME 5 The Diels–Alder reaction of 3-benzoselenophen-2-yl-indoles (**14** and **15**) with dienophiles **16** and **17**

($MgSO_4$), filtrated, and concentrated to afford **3**. Compound **3** was dissolved in THF (20 ml) and TBAF (4.5 ml, 4.5 mmol) was added and then stirred for 30 min at room temperature. The resulting mixture was concentrated and diluted with CH_2Cl_2 and H_2O. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:10) to afford **5** (0.480 g, 4.104 mmol) as a red-brown liquid in 91% yield (two step). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.32 (d, J = 6.0 Hz, 1H), 7.14 (t, J = 7.8 Hz, 1H), 6.69 (d, J = 7.8 Hz, 1H), 6.67 (d, J = 7.8 Hz, 1H), 3.38 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.5, 132.6, 130.1, 117.8, 114.3, 106.6, 82.4, 80.6. HRMS (EI) calculated for C_8H_8N $[M + H]^+$ 118.0657. Found: 118.0659.

3.2 | 1-Bromo-2-ethynylbenzene (6)

A mixture of $PdCl_2(PPh_3)_2$ (0.027 g, 0.038 mmol) and CuI (0.015 g, 0.077 mmol) in a flask was vacuumed and then introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this flask was sequentially added THF (10 ml), Et_3N (10 ml), and 2-iodoaniline (0.55 g, 1.944 mmol). This mixture was stirred for 10 min, followed by addition of TMSA (0.286 g, 2.916 mmol), and then stirred for 12 hr. The resulting mixture was filtrated, and the solvents were removed under reduced pressure and diluted with EtOAc and H_2O. The organic layer was dried ($MgSO_4$), filtrated, and concentrated to afford **4**. Compound **4** was dissolved in THF (10 ml) and TBAF (2.0 ml, 2.0 mmol) was added and then stirred for 30 min

at room temperature. The resulting mixture was concentrated and diluted with CH_2Cl_2 and H_2O. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was purified by flash column chromatography (230–400 mesh SiO_2, pentane) to afford **6** as a clear liquid in 90% (two step). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.1, 1.2 Hz, 1H), 7.53 (dd, J = 7.7, 1.7 Hz, 1H), 7.26 (td, J = 7.7, 1.1 Hz, 1H), 7.19 (td, J = 7.7, 1.7 Hz, 1H), 3.39 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 134.0, 132.4, 129.9, 130.0, 125.5, 124.2, 81.8, 81.7. LRMS (EI) for C_8H_5Br $[M]^+$ 181.03. Found: 181.0.

3.3 | 2-([2-Bromophenyl]Buta-1,3-diyn-1-yl)aniline (7)

Compound **6** (0.10 g, 0.55 mmol) and CuI (0.010 g, 0.055 mmol) were dissolved in MeCN (3.0 ml), followed by slow addition of compound **5** (0.32 g, 2.76 mmol) in MeCN (5 ml) over 15 min. under air. The mixture was stirred for 12 hr at ambient temperature. The solvent was concentrated, and the resulting mixture was purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:30–1:4) to afford **7** (0.117 g, 0.396 mmol) in a yield of 72%. Mp = 88–90°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.60 (d, J = 8.1 Hz, 1H), 7.55 (d, J = 7.7, 1.1 Hz, 1H), 7.36 (d, J = 7.7 Hz, 1H), 7.28 (t, J = 7.6 Hz, 1H), 7.21 (td, J = 7.9, 1.4 Hz, 1H), 7.17 (td, J = 7.9, 1.4 Hz, 1H), 6.71–6.67 (m, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.5, 134.4, 133.2, 132.6, 130.9, 130.1, 127.1, 126.1, 124.3, 118.1, 114.5, 106.0, 80.8, 80.2, 78.9, 78.1. HRMS (FAB) calculated for $C_{16}H_{11}BrN$ $[M + H]^+$ 296.0069. Found: 296.0076.

3.4 | 2-([2-Bromophenyl]ethynyl)-1*H*-indole (8)

To a sure-sealed tube, **7** (0.62 g, 2.09 mmol) and CuI (0.80 g, 4.19 mmol) were added in DMF (18 ml). This mixture was heated at 150°C for 3 hr. The solvent was concentrated and diluted with EtOAc/H_2O. The organic layer was dried ($MgSO_4$), concentrated, and purified with flash column chromatography (230–400 mesh, EtOAc: Hexane = 1:30–1:10) to afford **8** (0.495 g, 1.672 mmol) as a yellow solid in 80% yield. Mp = 115–118°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.63 (t, J = 7.1, 0.7 Hz, 2H), 7.57 (dd, J = 7.6, 1.3 Hz, 1H), 7.36 (d, J = 8.2 Hz, 1H), 7.31 (td, J = 7.6, 1.0 Hz, 1H), 7.26 (td, J = 7.6, 1.0 Hz, 1H), 7.20 (td, J = 8.0, 1.6 Hz, 1H), 7.14 (td, J = 7.9, 0.7 Hz, 1H), 6.90 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.3, 133.1, 132.5, 129.6, 127.8, 127.1, 125.3, 124.9, 123.8, 121.0, 120.6, 118.3, 110.8, 109.4, 91.1, 86.3. HRMS (FAB) calculated for $C_{16}H_{11}BrN$ $[M + H]^+$ 296.0069. Found: 296.0075.

3.5 | 2-(Benzo[*b*]selenophen-2-yl)-1*H*-indole (9)

A mixture of selenium powder (0.053 g, 0.675 mmol) and $NaBH_4$ (0.025 g, 0.675 mmol) in a flask was equipped with a Dean-Stark trap. The system was vacuumed and introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this system was added EtOH (4 ml), and the mixture was stirred for 1 hr in an ice bath. Compound **8** (0.10 g, 0.337 mmol) in NMP (8 ml) was added and heated at 190°C for 12 hr, and EtOH was distilled during the reaction course. The resulting black mixture was diluted with saturated NH_4Cl (100 ml), filtrated by suction, and washed with small amount of toluene. The filtrate was extracted with toluene and washed with brine thrice. The organic layer was dried ($MgSO_4$), filtrated, and concentrated. The resulting mixture was purified by flash column chromatography (230–400 mesh SiO_2, EtOAc: Hexane = 1:20–1:4) to afford **9** (0.060 g, 0.202 mmol) as a light-brown solid with a 60% yield. Mp = 275–277°C. ^{1}H NMR (600 MHz, $(CD_3)_2CO$) δ 7.97 (d, J = 8.0 Hz, 1H), 7.90 (s, 1H), 7.79 (d, J = 7.9 Hz, 1H), 7.55 (d, J = 7.9 Hz, 1H), 7.42 (d, J = 8.1 Hz), 7.36 (t, J = 7.5 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 7.02 (t, J = 7.6 Hz, 1H), 6.77 (s, 1H). ^{13}C NMR (150 MHz, $(CD_3)_2CO$) δ 144.1, 144.1, 138.8, 138.7, 138.6, 138.5, 135.0, 134.8, 129.8, 129.8, 126.3, 126.1, 125.9, 125.5, 123.4, 123.3, 121.2, 120.7, 112.1, 112.1, 102.9, 102.9. HRMS (EI) calculated for $C_{16}H_{11}NSe$ $[M]^+$ 297.0057. Found: 297.0058.

3.6 | 2-(Benzo[*b*]selenophen-2-yl)-1-methyl-1*H*-indole (10)

A solution of **9** (0.050 g, 0.16 mmol) and KOH (0.047 g, 0.84 mmol) in DMF was stirred for 10 min., followed by addition of MeI (0.47 g, 0.33 mmol). This mixture was stirred for 3 hr at room temperature. The resulting mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), concentrated, and purified with flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:10) to afford **10** (0.033 g, 0.1072 mmol) as a yellow solid in 67% yield. Mp = 170–173-°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.56 (s, 1H), 7.41–7.38 (m, 2H), 7.36–7.27 (m, 2H), 7.15 (t, J = 7.3 Hz, 1H), 6.76 (s, 1H), 3.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.6, 141.8, 138.8, 136.8, 135.5, 127.7, 126.5, 125.2, 125.0, 124.8, 122.5, 120.7, 120.2, 119.1, 109.6,

104.2, 31.3. HRMS (EI) calculated for $C_{17}H_{13}NSe$ $[M]^+$ 311.0213. Found: 311.0211.

3.7 | *tert*-butyl 3-iodo-1*H*-indole-1-carboxylate (12)

A solution of indole (1.0 g, 8.53 mmol) in DMF (30 ml) was added to KOH (1.20 g, 21.34 mmol) and stirred for 10 min. at room temperature. To this solution was added I_2 (2.16 g, 8.53 mmol) and stirred for 1 hr at room temperature. The mixture was diluted with Na_2SO_3 (saturated) (80 ml) and extracted with EtOAc. The organic layer was dried ($MgSO_4$) and concentrated. The crude product was dissolved in CH_2Cl_2 (40 ml), followed by the addition of Et_3N (3.6 ml, 25.60 mmol), DMAP (0.104 g, 0.85 mmol), and Boc_2O (2.235 g, 10.24 mmol). This mixture was stirred for 1 hr and diluted with CH_2Cl_2 and H_2O. The organic layer was dried ($MgSO_4$) and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:10) to afford **12** as a clear liquid (2.692 g, 7.847 mmol) with a 92% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 6.6 Hz, 1H), 7.74 (s, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.38 (t, J = 7.6 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 1.68 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 148.7, 134.8, 132.1, 130.1, 125.3, 123.3, 121.5, 115.0, 84.3, 65.4, 28.1 (3×). LRMS calculated for $C_{13}H_{14}INO_2$ $[M]^+$ 343.16. Found: 343.0.

3.8 | *tert*-butyl 3-([2-bromophenyl] ethynyl)-1*H*-indole-1-carboxylate (13)

A mixture of $PdCl_2(Ph_3P)_2$ (0.015 g, 0.022 mmol)and CuI (0.008 g, 0.044 mmol) in a flask was vacuumed and then introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this flask was sequentially added THF (4 ml), Et_3N (4 ml), and **12** and was stirred for 10 min at room temperature. To this mixture was added **6** (0.13 ml, 1.10 mmol) portion wise and stirred for 12 hr. The resulting mixture was filtrated by suction, concentrated, and diluted with EtOAC and H_2O. The organic layer was dried ($MgSO_4$) and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:30–1:10) to afford **13** (0.309 g, mmol) as an orange-yellow liquid with a 71% yield. ^1H NMR (600 MHz, $CDCl_3$) δ 8.18 (d, J = 7.8 Hz, 1H), 7.90 (s, 1H), 7.87 (d, J = 7.8 Hz, 1H), 7.64 (dd, J = 8.0, 1.0 Hz, 1H), 7.60 (dd, J = 7.7, 1.6 Hz 1H), 7.40 (t, J = 8.0 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 7.31 (td, J = 7.6, 1.0 Hz, 1H), 7.18 (td, J = 7.8, 1.7 Hz, 1H), 1.70 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 149.0, 134.7, 133.1, 132.4, 130.5, 129.2, 129.0, 127.0, 125.6, 125.3, 125.2, 123.4, 120.4, 115.2, 103.2, 91.4, 86.2, 84.4, 28.1 (3x). HRMS (EI) calculated for $C_{21}H_{18}BrNO_2$ $[M]^+$ 395.0521. Found: 395.0521.

3.9 | 3-(Benzo[*b*]selenophen-2-yl)-1*H*-indole (14)

To a round-bottomed flask was added selenium powder (0.20 g, 2.52 mmol) and $NaBH_4$ (0.10 g, 2.52 mmol) and set up with a Dean-Stark trap. The system was vacuumed and introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this system was added EtOH (5 ml), and the mixture was stirred for 1 hr in an ice bath. Compound **13** (0.50 g, 1.26 mmol) in NMP (10 ml) was added and heated at 190°C for 12 hr, and EtOH was distilled during the reaction course. The resulting black mixture was diluted with saturated NH_4Cl (100 ml), filtrated by suction, and washed with a small amount of toluene. The filtrate was extracted with toluene and washed with brine thrice. The organic layer was dried ($MgSO_4$), filtrated, and concentrated. Purification by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:20–1:10) afforded **14** (0.246 g, 0.8316 mmol) as a light yellow solid with a 66% yield. Mp = 178–180°C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.08 (d, J = 7.3 Hz, 1H), 7.87 (d, J = 7.9 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.69 (s, 1H), 7.47 (s, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.37 (t, J = 7.1 Hz, 1H), 7.31–7.27 (m, 2H), 7.23 (t, J = 7.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.3, 140.3, 139.8, 136.6, 125.3, 125.2, 124.7, 124.6, 123.8, 123.3, 123.0, 122.1, 120.9, 120.0, 114.2, 111.5. HRMS (ESI) calculated for $C_{16}H_{12}NSe$ $[M + H]^+$ 298.0129. Found: 298.0135.

3.10 | 3-(Benzo[b]selenophen-2-yl)-1-methyl-1*H*-indole (15)

A solution of **14** (0.050 g, 0.16 mmol) and KOH (0.047 g, 0.84 mmol) in DMF was stirred for 10 min, followed by addition of MeI (0.47 g, 0.33 mmol). This mixture was stirred for 3 hr at room temperature. The resulting mixture was diluted with H_2O and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$), concentrated, and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:10) to afford **15** (0.0446 g, 0.144 mmol) as a red solid with a 90% yield. Mp = 132–134°C. ^1H NMR (600 MHz, $CDCl_3$) δ 8.06 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.65 (s, 1H), 7.37–7.31 (m, 4H), 7.27 (t, J = 7.8 Hz, 1H), 7.21 (t, J = 7.8 Hz, 1H), 3.84 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.5, 140.4, 137.5, 128.0, 125.8, 125.2, 124.7, 124.5, 123.6, 122.5, 121.4, 120.5, 120.1, 112.5, 109.7, 33.0. HRMS (EI) calculated for $C_{17}H_{13}NSe$ $[M]^+$ 311.0213. Found: 311.0213.

3.11 | Diethyl 12*H*-benzo[4,5]selenopheno[2,3-*a*]carbazole-5,6-dicarboxylate (19)

Compounds **9** (0.030 g, 0.1013 mmol) and **17** (0.069 g, 0.4054 mmol) were dissolved in xylene (2 ml) and heated at 185°C for 24 hr in a sealed tube. At the end of reaction time, the mixture was concentrated and purified by flash column chromatography (230–400 mesh SiO_2, Hexane:CH_2Cl_2 = 1:2–0:1) to afford **19** (0.0061 g, 0.0131 mmol) as a brown solid with a 13% yield (16% based on recovery of 0.0060 g of **9**). Mp = 207–210°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.07 (d, J = 7.8 Hz, 1H), 8.21 (d, J = 8.2 Hz, 1H), 8.07 (t, J = 8.2 Hz, 1H), 7.94 (d, J = 7.7 Hz, 1H), 7.53 (dd, J = 7.4, 0.6 Hz, 1H), 7.49 (d, J = 6.2 Hz, 1H), 7.46 (td, J = 8.2, 1.3 Hz, 1H), 7.41 (td, J = 7.9, 1.3 Hz, 1H), 7.28 (dd, J = 8.2, 1.0 Hz, 1H), 4.61 (q, J = 7.2 Hz, 2H), 4.58 (q, J = 7.2 Hz, 2H), 4.25 (s, 3H), 1.51 (t, J = 7.2 Hz, 3H), 1.46 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.3, 168.1, 140.3, 139.0, 137.4, 137.3, 132.1, 126.9, 126.8, 125.5, 125.4, 125.3, 124.7, 124.0, 123.3, 123.1, 122.4, 120.8, 117.1, 11.2, 62.0 (2x), 14.2, 14.0. HRMS (ESI) calculated for $C_{24}H_{18}NO_4Se$ $[M\text{-}H]^+$ 464.0401. Found: 464.0402.

3.12 | 12-Methyl-5,6-diphenyl-12*H*-benzo[4,5]selenopheno[2,3-*a*]carbazole (20)

Compound **10** (0.030 g, 0.096 mmol), compound **16** (0.0260 g, 0.145 mmol), $Pd(OAc)_2$ (0.0020 g, 0.009 mmol), TBAB (0.016 g, 0.048 mmol), PivOH (0.010 g, 0.096 mmol), and K_2CO_3 (0.0040 g, 0.029 mmol) were added to a Schlenk flask and vacuumed and then introduced to a nitrogen atmosphere. This procedure was repeated thrice. To this mixture was added DMF (3 ml) and heated at 100°C for 12 hr under an oxygen atmosphere. The mixture was concentrated and diluted with EtOAc and H_2O. The organic layer was dried ($MgSO_4$) and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:20–1:10) to afford **20** (0.0079 g, 0.0163 mmol) as a white solid with a 17% yield. Mp = 251–253°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 8.4 Hz, 1H), 7.40 (t, J = 7.8 Hz, 1H), 7.30–7.21 (m, 11H), 7.00 (t, J = 7.8 Hz, 1H), 6.91 (t, J = 7.2 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 6.61 (d, J = 7.8 Hz, 1H), 4.32 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.8, 140.2, 139.6, 139.2, 139.1, 137.5, 134.9, 134.7, 131.4, 131.1, 130.3, 128.1, 127.9, 127.0, 126.8, 126.7, 125.5, 125.4, 125.2, 124.3, 123.0, 122.4, 119.4, 119.3, 108.5, 30.7. HRMS (EI) calculated for $C_{31}H_{21}NSe$ $[M]^+$ 487.0839. Found: 487.0838.

3.13 | Diethyl 12-methyl-12*H*-benzo[4,5]selenopheno[2,3-*a*]carbazole-5,6-dicarboxylate (21)

Compounds **10** (0.0140 g, 0.045 mmol) and **17** (0.030 g, 0.18 mmol) were dissolved in xylene (3 ml) and heated at 185°C for 24 hr in a sealed tube. At the end of reaction time, the mixture was concentrated and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc: Hexane =1:10–1:4) to afford **21** as a white solid (0.007 g, 0.014 mmol) with a 31% yield. Mp = 198–200°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.8 Hz, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.54 (t, J = 7.8 Hz, 1H), 7.49–7.41 (m, 3H), 7.28 (t, J = 7.8 Hz, 1H), 4.60 (q, J = 7.2 Hz, 2H), 4.56 (q, J = 7.2 Hz, 2H), 4.25 (s, 3H), 1.48 (t, J = 7.2 Hz, 3H), 1.44 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.4, 168.3, 142.1, 139.2, 139.0, 136.7, 132.5, 126.7 (2×), 125.5, 125.4, 125.1, 124.5, 123.4, 122.8, 122.1, 121.3, 120.3, 116.4, 109.1, 62.0, 61.9, 30.8, 14.1, 14.0. HRMS (EI) calculated for $C_{25}H_{21}NO_4Se$ $[M]^+$ 479.0636. Found: 479.0635.

3.14 | Diethyl 5*H*-benzo[4,5]selenopheno[3,2-*c*]carbazole-6,7-dicarboxylate (23)

Compounds **14** (0.050 g, 0.168 mmol) and **17** (0.0860 g, 0.507 mmol) were dissolved in xylene (3 ml) and heated at 185°C for 12 hr in a sealed tube. At the end of reaction time, the mixture was concentrated and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane =1:10–1:4) to afford **23** as an orange-red solid (0.050 g, 0.109 mmol) with a 65% yield. Mp = 179–181°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.09 (d, J = 7.8 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 7.1 Hz, 1H), 7.47 (t, J = 7.1 Hz, 1H), 7.41 (t, J = 7.5 Hz, 2H), 4.67 (q, J = 7.2 Hz, 2H), 4.56 (q, J = 7.1 Hz, 2H), 1.53 (t, J = 7.2 Hz, 3H), 1.48 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 166.5, 139.8, 139.7, 138.7, 137.1, 136.3, 129.9, 126.7, 126.6, 126.2, 126.1, 125.4, 124.1, 121.9, 121.3, 121.1, 120.7, 111.3, 107.5, 62.1, 61.9, 14.4, 14.0. HRMS (FAB) calculated For $C_{24}H_{19}NO_4NaSe$ $[M + Na]^+$ 488.0377. Found: 488.0377.

3.15 | 5-Methyl-6,7-diphenyl-5*H*-benzo[4,5]selenopheno[3,2-*c*]carbazole (24)

Compound **15** (0.030 g, 0.096 mmol), compound **16** (0.0260 g, 0.145 mmol), $Pd(OAc)_2$ (0.0020 g, 0.009 mmol), TBAB (0.0160 g, 0.048 mmol), PivOH (0.010 g, 0.096 mmol), and K_2CO_3 (0.0040 g, 0.029 mmol) were added to a Schlenk flask and vacuumed and then introduced to a nitrogen

atmosphere. This procedure was repeated thrice. To this mixture was added DMF (3 ml) and heated at 100°C for 12 hr under an oxygen atmosphere. The mixture was concentrated and diluted with EtOAc and H_2O. The organic layer was dried ($MgSO_4$) and purified by flash column chromatography (230–400 mesh SiO_2, EtOAc:Hexane = 1:10–1:4) to afford **24** (0.0098 g, 0.02016 mmol) as a white solid with a 21% yield. Mp = 253–255°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 7.42 (dd, J = 17.3, 8.8 Hz, 2H), 7.28–7.17 (m, 11H), 6.98 (t, J = 8.1 Hz, 1H), 6.48 (d, J = 8.3 Hz, 1H), 3.22 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 142.3, 140.1, 139.1, 139.0, 138.0, 137.9, 137.1, 132.5, 132.0 (2×), 130.6 (2×), 128.6, 128.1 (2×), 127.3, 126.9, 126.8, 125.9, 125.8, 125.7, 124.7, 124.3, 124.0, 122.4, 121.0, 119.9, 119.1, 109.0, 32.0. HRMS (ESI) calculated for $C_{31}H_{22}NSe$ $[M + H]^+$ 488.0912. Found: 488.0917.

3.16 | Diethyl 5-methyl-5*H*-benzo[4,5]selenopheno[3,2-*c*]carbazole-6,7-dicarboxylate (25)

Compounds **15** (0.030 g, 0.168 mmol) and **17** (0.0638 g, 0.387 mmol) were dissolved in xylene (1 ml) and heated at 185°C for 12 hr in a sealed tube. At the end of reaction time, the mixture was concentrated and purified by flash column chromatography (230–400 mesh SiO_2, Hexane:CH_2Cl_2 = 2:1–1:2) to afford **25** (0.0236 g, 0.0492 mmol) as an orange solid with a 51% yield. Mp = 196–198°C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.14 (d, J = 7.6 Hz, 1H), 8.00 (d, J = 8.0 Hz, 2H), 7.63 (td, J = 8.1, 0.8 Hz, 1H), 7.54 (d, J = 8.2 Hz, 1H), 7.47–7.44 (m, 2H), 7.40 (td, J = 7.3, 1.1 Hz, 1H), 4.60 (q, J = 7.2 Hz, 2H), 4.53 (q, J = 7.2 Hz, 2H), 1.49 (t, J = 7.2 Hz, 3H), 1.47 (t, J = 7.2 Hz, 3H). ^{13}NMR (150 MHz, $CDCl_3$) δ 169.1, 167.6, 142.6, 138.9, 136.4, 135.2, 127.7, 126.8, 126.1, 126.0, 125.2, 124.3, 121.8, 121.6, 121.4, 120.6, 113.7, 109.4, 62.2, 62.1, 32.3, 14.2, 14.0. HRMS (ESI) calculated for $C_{25}H_{21}NNaO_4NaSe$ $[M + Na]^+$ 502.0533. Found: 502.0536.

4 | CONCLUSIONS

Due to the importance of elemental selenium in pharmacological activity and material chemistry, this is the first synthesis of selenium-containing benzo[*b*]selenophenylindoles (**9**, **10**, **14** and **15**), which was used to evaluate their Diels–Alder reactions. In comparison with the results in Schemes 4 and 5, we concluded that 3-benzoselenophen-2-yl-indoles (**14** and **15**) were more suitable dienes in Diels–Alder reactions. We believe that the resulting target molecules (**19**–**21** and **23**–**25**) are valuable, and their biological activities will be evaluated in the near future.

ACKNOWLEDGMENTS

We gratefully acknowledge the Ministry of Science (MOST 105-2113-M-032-001) for supporting this work. We thank the National Taiwan Normal University for LRMS and HRMS measurements.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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How to cite this article: Wang R-Y, Kao W-T, Shih T-L. Synthesis of selenium-containing biindolyls and their Diels–Alder reaction toward the synthesis of heteroannulated [*a*]- and [*c*]-carbazoles. *J Chin Chem Soc*. 2019;1–9. https://doi.org/10.1002/jccs.201900278