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Iodine-Mediated Cascade Cyclization of Enediynes to Iodinated Benzo[*a*]carbazoles

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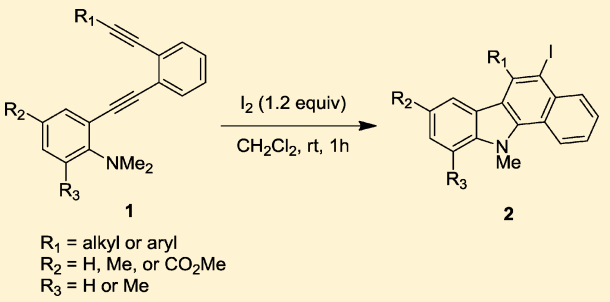
Supporting Information

ABSTRACT: Treatment of *N*,*N*-dimethyl 2-[2-(2-ethynylphenyl)-ethynyl]anilines (**1**) with 1.2 equiv of iodine in CH_2Cl_2 gave benzo[*a*]carbazoles (**2**) in good yields. Mechanistic studies showed this reaction must go through the haloindole (**3**) followed by iodonium ion catalyzed atom-transfer cyclization reaction to give the benzo[*a*]carbazoles.

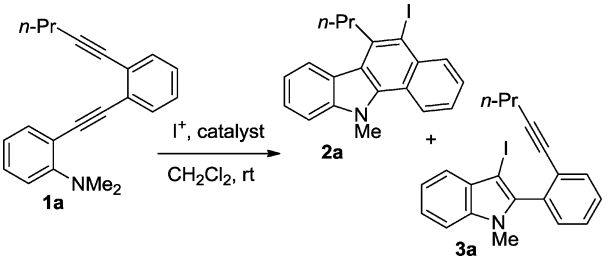


Carbazole and its derivatives have attracted much attention as synthetic targets due to their diverse biological[1] and unique optical properties.[2] Although many synthetic methods have been developed to construct these heterocycles,[3] the cascade cyclization of enediynes or aryldiynes provided another efficient method to synthesize functionalized carbazoles.[4]

In our recent report,[4d] we found that treatment of *N*,*N*-dimethyl 2-[2-(2-alkynylphenyl)ethynyl]anilines (**1**) with 10 mol % of palladium chloride and 2 equiv of cupric chloride in refluxing THF gave chlorinated benzo[*a*]carbazoles in good yields. The bromo analogues can be prepared in a similar manner except using cupric bromide followed by 10 mol % of palladium acetate. When we attempted to prepare the iodo analogues by treatment of *N*,*N*-dimethyl-2-[2-(2-pentynylphenyl)ethynyl]aniline (**1a**) with 2 equiv of iodine (I_2) in dichloromethane for 1 h at room temperature,the iodinated carbazole **2a** was obtained directly in 96% yield (Table 1, entry 1). This result encouraged us to continue the investigation of the iodine mediated cascade cyclization[5] of enediynes.

To optimize the reaction conditions, the amount of iodine was reduced to 1.2 equiv to give carbazole **2a** in a competitive yield (Table 1, entry 2). An indole adduct **3a** was obtained in 90% yield when iodine was replaced by NIS (*N*-iodosuccinimide) (Table 1, entry 3). However, 5 mol % of $Pd(OAc)_2$ was introduced into the reaction mixture of **1a** and NIS, and the reaction mixture was stirred for 20 h to give carbazole **2a** in 89% yield (Table 1, entry 4). Similar results were observed using Ipy_2BF_4 (bis(pyridine)iodonium tetrafluoroborate) as the iodinating agent (Table 1, entries 5 and 6). A gold catalyst, Ph_3PAuCl, was also employed in this study. Thus, treatment of **1a** with 2 equiv of NIS in the presence of 3 mol % of Ph_3PAuCl for 20 h at room temperature gave **2a** in 90% yield (Table 1, entry 7).

Table 1. Optimization of Cascade Iodocyclization of 1a



entry	I^+ (equiv)	catalyst (mol %)	time (h)	products/yield (%)
1	I_2 (2)		1	**2a**/96
2	I_2 (1.2)		1	**2a**/95
3	NIS (2)		20	**3a**/90
4	NIS (2)	$Pd(OAc)_2$ (5)	20	**2a**/89
5	Ipy_2BF_4 (2)		24	**3a**/86
6	Ipy_2BF_4 (2)	$Pd(OAc)_2$ (5)	20	**2a**/80
7	NIS (2)	Ph_3PAuCl (3)	20	**2a**/88

With the metal-free synthetic method to iodinated carbazoles in hand, we then extended this cascade cyclization reaction to other substituted *N*,*N*-dimethyl-2-[2-(2-alkynylphenyl)-ethynyl]anilines (**1b**–**l**).[6] The results are summarized in Table 2. Under the optimized reaction conditions, compounds bearing either alkyl or aryl substituents on the terminal alkynes gave the iodinated benzo[*a*]carbarzoles in good to excellent yields except for compound **1c** (Table 2, entry 2). The failure

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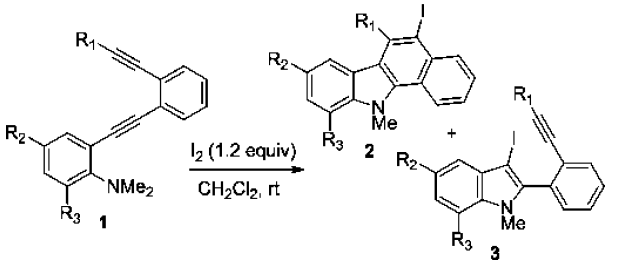
Table 2. Cascade Cyclization to Benzo[*a*]carbazoles



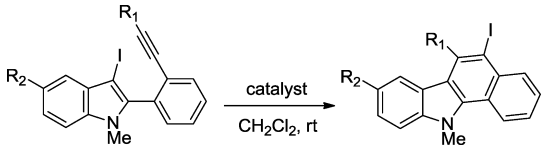
entry	compds	time (h)	products/yield[a] (%)
1	**1b**, R_1 = *i*-Bu, R_2 = R_3 = H	2	**2b**/90
2	**1c**, R_1 = *t*-Bu, R_2 = R_3 = H	2	**3c**/82
3	**1d**, R_1 = 4-$CH_3OC_6H_4$, R_2 = R_3 = H	0.5	**2d**/90
4	**1e**, R_1 = 4-$CH_3C_6H_4$, R_2 = R_3 = H	0.5	**2e**/95
5	**1f**, R_1 = 3-$CH_3C_6H_4$, R_2 = R_3 = H	0.5	**2f**/85
6	**1g**, R_1 = 2-$CH_3C_6H_4$, R_2 = R_3 = H	0.5	**2g**/85
7	**1h**, R_1 = C_6H_5, R_2 = R_3 = H	0.5	**2h**/90
8	**1i**, R_1 = 4-ClC_6H_4, R_2 = R_3 = H	0.5	**2i**/70
9	**1j**, R_1 = 4-BrC_6H_4, R_2 = R_3 = H	0.5	**2j**/54
10	**1k**, R_1 = 4-$CF_3C_6H_4$, R_2 = R_3 = H	0.5	**2k**/93
11	**1l**, R_1 = 4-$NO_2C_6H_4$, R_2 = R_3 = H	0.5	**2l**/95
12	**1m**, R_1 = *n*-Pr, R_2 = R_3 = Me	2	**2m**/79
13	**1n**, R_1 = Ph, R_2 = R_3 = Me	1	**2n**/84
14	**1o**, R_1 = *n*-Pr, R_2 = CO_2Me, R_3 = H	48	**3o**/87
15	**1o**, R_1 = *n*-Pr, R_2 = CO_2Me, R_3 = H	48	**2o**/67[b]
16	**1p**, R_1 = Ph, R_2 = CO_2Me, R_3 = H	48	**3p**/88
17	**1p**, R_1 = Ph, R_2 = CO_2Me, R_3 = H	48	**2p**/75[b]
18	**1q**, R_1 = 4-$CF_3C_6H_4$, R_2 = CO_2Me, R_3 = H	48	**3q**/94
19	**1q**, R_1 = 4-$CF_3C_6H_4$, R_2 = CO_2Me, R_3 = H	48	**2q**/77[b]

[a]Isolated yields. [b]Under refluxing THF.

to obtain the carbazole adduct with **1c** must be because of the steric effect of the bulky *tert*-butyl substituent to prevent the second cyclization step. Compounds **1m**–**q** were prepared in the same manner as **1a**–**l** and subjected to the cyclization reactions under the optimized reaction conditions. Compounds **1m** and **1n** bearing electron-donating groups at the aniline ring proceed smoothly at room temperature to give the carbazole adducts **2m** and **2n** in yields of 79% and 84%, respectively. When an aniline ring bearing an electron-withdrawing group, such as compounds **1o**–**q**, was used the major products obtained were only the indole adducts **3o**–**q** after 48 h of stirring at room temperature, and the yields were 87–94%. However, when the reactions of **1o**–**q** with 1.2 equiv of iodine were carried out in refluxing THF for 48 h, the carbazole adducts **2o**–**q** were obtained in 67%, 75%, and 77% yields, respectively.

To gain insight into the reaction mechanism of this iodine-mediated tandem cyclization reaction, we took the iodinated indole **3a** and treated it with a catalytic amount (5 mol %) of iodine in CH_2Cl_2 at room temperature for 2 h, and the iodinated carbazole **2a** was obtained in 90% yield (Table 3, entry 1). Palladium acetate was also found to be efficient for the catalysis of the atom-transfer dienyne cyclization reaction. The gold catalyst, Ph_3PAuCl, is less efficient for catalyzing the cyclization than iodine and palladium (Table 3, entry 3). Interestingly, mixing 5 mol % of NIS with 3 mol % of Ph_3PAuCl can accelerate the rate of the cyclization reaction

Table 3. Study of the Conversion of Indole to Carbazole



entry	compds	catalyst (mol %)	time (h)	products/yield (%)
1	**3a**, R_1 = *n*-Pr, R_2 = H	I_2 (5)	2	**2a**/90
2	**3a**, R_1 = *n*-Pr, R_2 = H	$Pd(OAc)_2$ (5)	4	**2a**/86
3	**3a**, R_1 = *n*-Pr, R_2 = H	Ph_3PAuCl (3)	168	**2a**/80
4	**3a**, R_1 = *n*-Pr, R_2 = H	Ph_3PAuCl (3)/ NIS (5)	20	**2a**/82
5	**3a**, R_1 = *n*-Pr, R_2 = H	ICl (5)	60	**2a**/85
6	**3a**, R_1 = *n*-Pr, R_2 = H	Ph_3PAuCl_3 (3)	72	**2a**/60
7	**3a**, R_1 = *n*-Pr, R_2 = H	$AuCl_3$ (3)	2	**2a**/68
8	**3o**, R_1 = *n*-Pr, R_2 = CO_2Me	I_2 (5)	48	**2o**/82[a]
9	**3p**, R_1 = Ph, R_2 = CO_2Me	I_2 (5)	48	**2p**/85[a]
10	**3c**, R_1 = *t*-Bu, R_2 = H	I_2 (5)	72	–[a,b]
11	**3c**, R_1 = *t*-Bu, R_2 = H	$Pd(OAc)_2$ (5)	72	–[a,b]

[a]Under refluxing THF. [b]Starting material was recovered.

(Table 3, entry 4). Using ICl as the catalyst, the reaction required a longer reaction time (60 h) to give **2a** in 85% yield (Table 3, entry 5). When we mixed a 2:1 mixture of ICl and Ph_3PAuCl, a solid of Ph_3PAuCl_3 was obtained. Supposedly, the byproduct of this reaction is iodine, so the reaction in entry 4 is truly the iodine-catalyzed reaction. This can explain why the reaction rate was increased when ICl was mixed with Ph_3PAuCl. A control experiment was carried out by using the freshly prepared Ph_3PAuCl_3 as the catalyst, and the reaction required 72 h to go to completion and give the product **2a** in 60% yield (Table 3, entry 6). Gold trichloride ($AuCl_3$) was found to be as efficient as iodine and $Pd(OAc)_2$ to catalyze the iodo transfer cyclization reaction (Table 3, entry 7). It was found that conversion of indoles **3o** and **3p**, both bearing an electron-withdrawing group at the 5-position, to carbazoles **2o** and **2p** required higher temperature and longer reaction time. Thus, treatment of **3o** and **3p** with 5 mol % of iodine in refluxing THF for 48 h gave carbazoles **2o** and **2p** in 82% and 85%, respectively (Table 3, entries 8 and 9). Indole **3a** bearing a bulky *tert*-butyl group at the terminus alkyne was found to resist formation of the carbazole using either iodine or palladium acetate as the catalyst even in refluxing THF for 72 h (Table 3, entries 10 and 11).

On the basis of the experimental results, a proposed reaction mechanism is outlined in Scheme 1. Initially, iodine or *N*-iodosuccinimide can promote the cyclization of **1** to form the iodoindole **3**. The excess of iodine can further coordinate to the triple bond to promote the second cyclization to give the intermediate **4**. The iodide could attack the iodonium ion at the indole ring to give the carbazole **2** and regenerate iodine to continue the catalytic cycle. As in our previous report,[4d] palladium acetate could also coordinate to the triple bond followed by intramolecular Wacker-type cyclization to give **5**. The released acetate would then come back to kick out the iodonium ion to form the palladated carbazole **6**. Finally, iodination of **6** with iodoacetate[7] would give the iodinated carbazole **2** and regenerate $Pd(OAc)_2$. A similar reaction pathway can be rationalized by using $AuCl_3$ as the catalyst.

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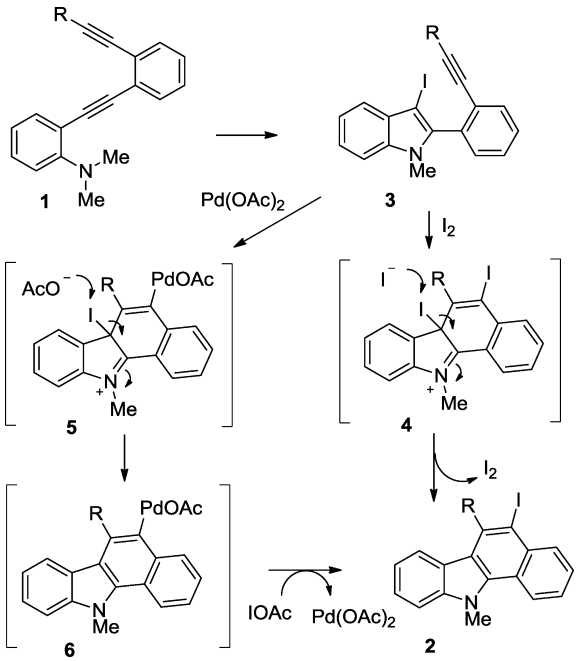
Scheme 1



In conclusion, we have developed an efficient synthetic method to iodinated benzo[*a*]carbazoles by the reaction of *N*,*N*-dimethyl 2-[2-(2-alkynylphenyl)ethynyl]anilines with slightly more than 1 equiv of iodine or with NIS in the presence of a catalytic amount of $Pd(OAc)_2$ or Ph_3PAuCl. We also demonstrated that iodonium ion as well as palladium(II) and gold catalysts can catalyze the iodo atom transfer cyclization reaction of 1-iododienynes to give the iodinated carbocycles. The application of this methodology to the synthesis of pharmaceutical or material interest molecules is under investigation.[4]

EXPERIMENTAL SECTION

General Procedure for the Preparation of Compounds 1m–q. The reaction mixture of aryl halide (0.1 mmol) and terminal alkyne (0.15 mmol) in the presence of $Pd(PPh_3)_4$ (0.05 equiv), CuI (0.1 equiv), and *n*-$BuNH_2$ (1.0 equiv) in ether (5.0 mL) was stirred at room temperature for 4–12 h. The saturated aqueous solutions of NH_4Cl and $NaHCO_3$ were then added subsequently into the reaction mixture and extracted with EtOAc. The combined organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by column chromatography to give the products.

General Procedure for Iodination of Compound 1 to Compounds 2 and 3. The mixture of compound **1** (0.1 mmol) in the presence of I_2 (0.12 mmol) in CH_2Cl_2 (3 mL) was stirred at room temperature for 0.5–2 h. The saturated aqueous solution of $Na_2S_2O_3$ was then added into the reaction mixture and extracted with EtOAc. The organic extracts were dried over anhydrous $MgSO_{4(s)}$. After filtration and removal of solvent, the residue was purified by column chromatography to give the products.

Preparation of Ph_3PAuCl_3. The mixture of Ph_3PAuCl (100 mg, 0.2 mmol) with ICl (65 mg, 0.4 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 30 min. The saturated aqueous solution of $Na_2S_2O_3$ was then added into the reaction mixture and extracted with CH_2Cl_2. The organic extracts were dried over anhydrous $MgSO_{4(s)}$. After removal of CH_2Cl_2, Ph_3PAuCl_3 was obtained in 102 mg (90%) as a white solid: mp 184–187 °C (lit.[8] mp 179–181 °C).

***N*,*N*,2,4-Tetramethyl-6-((2-(pent-1-ynyl)phenyl)ethynyl)-benzenamine (1m):** yield 77 mg, 92%; brown oil; R_f = 0.33 (80:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, J = 7.2 Hz, 3H), 1.66 (x, J = 7.2 Hz, 2H), 2.25 (s, 3H), 2.28 (s, 3H), 2.45 (t, J = 7.2 Hz, 2H), 2.96 (s, 6H), 6.98 (s, 1H), 7.17 (s, 1H), 7.22–7.26 (m, 2H), 7.42–7.45 (m, 1H), 7.49–7.52 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 18.5, 20.5, 21.7, 22.2, 43.2, 79.8, 92.3, 92.6, 94.5, 120.5, 126.0, 126.1, 127.2, 131.5, 132.1, 132.2, 132.9, 133.6, 136.7, 150.6; MS (70 eV) m/z 315.3 (8) [M^+], 273.3 (24), 272.3 (100), 257.4 (30); HRMS (ESI-TOF) calcd for $C_{23}H_{25}N$, 315.1987, found 315.1987.

***N*,*N*,2,4-Tetramethyl-6-((2-(phenylethynyl)phenyl)ethynyl)-aniline (1n):** yield 80 mg, 86%; brown oil: R_f = 0.58 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.11 (s, 3H), 2.27 (s, 3H), 2.93 (s, 6H), 6.99 (s, 1H), 7.21 (s, 1H), 7.30–7.35 (m, 5H), 7.56–7.59 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 20.4, 43.3, 88.5, 92.4, 93.2, 93.3, 120.4, 123.3, 125.3, 126.4, 127.7, 128.0, 128.3, 128.4, 131.5, 131.7, 132.0, 132.3, 133.0, 133.6, 136.7, 150.6; MS (70 eV) m/z 349 (49) [M^+], 272 (100); HRMS (ESI-TOF) calcd for $C_{26}H_{23}N$ 349.1830, found 349.1828.

Methyl 4-(dimethylamino)-3-((2-(pent-1-ynyl)phenyl)-ethynyl)benzoate (1o): yield 82 mg, 95%; brown oil; R_f = 0.38 (10:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, J = 7.2 Hz, 3H), 1.68 (x, J = 7.2 Hz, 2H), 2.48 (t, J = 6.8 Hz, 2H), 3.17 (s, 6H), 3.87 (s, 3H), 6.81 (d, J = 8.8 Hz, 1H), 7.22–7.25 (m, 2H), 7.42–7.49 (m, 2H), 7.86 (dd, J = 8.8, 2.4 Hz, 1H), 8.18 (d, J = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 21.6, 22.2, 42.8, 51.7, 79.6, 92.0, 93.8, 94.6, 111.7, 115.1, 120.1, 125.8, 126.1, 127.2, 127.7, 130.7, 131.3, 132.0, 137.2, 156.9, 166.5; MS (70 eV) m/z 345.1 (25) [M^+], 344.3 (22), 302.3 (100), 256.3 (23); HRMS (ESI-TOF) calcd for $C_{23}H_{23}NO_2$ 345.1729, found 345.1729.

Methyl 4-(dimethylamino)-3-((2-(phenylethynyl)phenyl)-ethynyl)benzoate (1p): yield 83 mg, 88%; brown oil; R_f = 0.55 (5:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.10 (s, 6H), 3.85 (s, 3H), 6.81 (d, J = 8.8 Hz, 1H), 7.29–7.35 (m, 5H), 7.54–7.60 (m, 4H), 7.88 (dd, J = 8.4, 2.0 Hz, 1H), 8.24 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7, 51.7, 88.3, 92.7, 93.3, 93.5, 111.3, 115.1, 120.0, 123.2, 125.1, 126.0, 127.8, 127.9, 128.3, 128.3, 130.9, 131.5, 131.7, 131.9, 137.1, 156.9, 166.4; MS (70 eV) m/z (%): 379 (47) [M^+], 378 (65), 302 (100); HRMS (ESI-TOF) calcd for $C_{26}H_{21}NO_2$ 379.1572, found 379.1570.

Methyl 4-(dimethylamino)-3-((2-((4-(trifluoromethyl)-phenyl)ethynyl)phenyl)ethynyl)benzoate (1q): yield 77 mg, 69%; brown solid; R_f = 0.58 (5:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 (s, 6H), 3.84 (s, 3H), 6.82 (d, J = 8.8 Hz, 1H), 7.30–7.37 (m, 2H), 7.55–7.61 (m, 4H), 7.69 (d, J = 8.0 Hz, 2H), 7.89 (dd, J = 8.8, 2.4 Hz, 1H), 8.22 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.8, 51.7, 90.7, 91.8, 93.1, 93.3, 111.3, 115.2, 120.2, 124.5, 125.2, 125.2, 125.3, 125.3, 126.3, 127.9, 128.6, 131.0, 131.5, 132.0, 132.1, 137.2, 156.9, 166.4; mp 100–102 °C; MS (70 eV) m/z 447 (38) [M^+], 446 (54), 302 (74), 57 (100); HRMS (ESI-TOF) calcd for $C_{27}H_{20}F_3NO_2$ 447.1446, found 447.1447.

5-Iodo-11-methyl-6-propyl-11*H*-benzo[*a*]carbazole (2a): yield 39 mg, 95%; colorless solid; R_f = 0.33 (50:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (t, J = 7.6 Hz, 3H), 1.88 (x, J = 9.2 Hz, 2H), 3.62–3.66 (m, 2H), 4.36 (s, 3H), 7.35–7.39 (m, 1H), 7.52–7.62 (m, 4H), 8.15 (d, J = 8.0 Hz, 1H), 8.58–8.64 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 22.0, 34.6, 42.7, 97.5, 109.3, 118.1, 120.1, 122.0, 122.2, 122.3, 122.4, 124.7, 124.9, 126.3, 133.5, 134.5, 141.1, 141.1; mp 138–140 °C; MS (70 eV) m/z 399.1 (68) [M^+], 257.3 (40), 245.3 (44), 244.3 (100); HRMS (ESI-TOF) calcd for $C_{20}H_{18}IN$ 399.0484, found 399.0483; IR (KBr, cm^{-1}) 3051, 2962, 1604, 1510.

5-Iodo-6-isobutyl-11-methyl-11*H*-benzo[*a*]carbazole (2b): yield 37 mg, 90%; colorless solid; R_f = 0.76 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09 (d, J = 5.6 Hz, 6H), 2.38 (h, J = 6.8 Hz, 1H), 3.52–3.68 (b, 2H), 4.22 (s, 3H), 7.29–7.33 (m, 1H), 7.45–7.58 (m, 4H), 8.11 (d, J = 8.4 Hz, 1H), 8.52 (d, J = 8.8 Hz, 1H), 8.59 (dd, J = 8.4, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 29.1, 34.5, 47.8, 99.1, 109.2, 118.3, 119.8, 121.9, 122.2, 122.4, 122.6, 124.5, 124.8, 126.3, 133.5, 135.0, 136.4, 140.3, 141.0; mp 154–157 °C; MS (70 eV) m/z 413 (100) [M^+], 244 (82), 243 (29); HRMS (ESI-TOF) calcd for $C_{21}H_{20}IN$ 413.0640, found 413.0643. IR (KBr, cm^{-1}) 3046, 2959, 2869, 1608, 1507.

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5-Iodo-6-(4-methoxyphenyl)-11-methyl-11*H*-benzo[*a*]carbazole (2d): yield 42 mg, 90%; colorless solid; R_f = 0.22 (20:1 Hex/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 3H), 4.44 (s, 3H), 6.58 (d, J = 7.8 Hz, 1H), 6.99 (t, J = 7.5 Hz, 1H), 7.14 (d, J = 8.7 Hz, 2H), 7.29 (d, J = 8.7 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.67−7.64 (m, 2H), 8.64−8.61 (m, 1H), 8.77−8.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5, 55.3, 108.8, 114.1, 114.2, 119.3, 119.7, 122.1, 122.4, 122.6, 122.7, 124.9, 125.7, 126.5, 130.5, 133.2, 134.0, 134.9, 138.1, 140.9, 141.9, 159.3; mp 158−160 °C; MS (70 eV) m/z 463 (100) [M$^+$], 335 (15), 292 (19); HRMS (ESI-TOF) calcd for $C_{24}H_{18}INO$ 463.0433, found 463.0431; IR (KBr, cm^{-1}) 3052, 2936, 1609, 1506, 1263.

5-Iodo-11-methyl-6-*p*-tolyl-11*H*-benzo[*a*]carbazole (2e): yield 43 mg, 95%; colorless solid; R_f = 0.36 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.56 (s, 3H), 4.41 (s, 3H), 6.51 (d, J = 8.4 Hz, 1H), 6.97 (td, J = 8.0, 1.2 Hz, 1H), 7.24−7.26 (m, 2H), 7.38−7.43 (m, 3H), 7.50 (d, J = 8.8 Hz, 1H), 7.62−7.66 (m, 2H), 8.60−8.62 (m, 1H), 8.70−8.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 34.5, 96.5, 108.8, 119.1, 119.7, 122.1, 122.4, 122.5, 122.6, 124.9, 125.6, 126.5, 129.1, 129.5, 133.2, 134.8, 135.9, 137.7, 140.9, 142.2, 142.6; mp 170−172 °C; MS (70 eV) m/z 447 (100) [M$^+$], 319 (20), 305 (18); HRMS (ESI-TOF) calcd for $C_{24}H_{18}IN$ 447.0484, found 447.0482; IR (KBr, cm^{-1}) 3053, 2925, 1608, 1507.

5-Iodo-11-methyl-6-*m*-tolyl-11*H*-benzo[*a*]carbazole (2f): yield 38 mg, 85%; colorless solid; R_f = 0.36 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (s, 3H), 4.42 (s, 3H), 6.47 (d, J = 8.0 Hz, 1H), 6.96 (td, J = 8.0, 0.8 Hz, 1H), 7.18 (d, J = 8.4 Hz, 1H), 7.19 (s, 1H), 7.38−7.42 (m, 2H), 7.50 (t, J = 7.2 Hz, 2H), 7.64−7.66 (m, 2H), 8.61−8.63 (m, 1H), 8.72−8.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 34.5, 96.0, 108.8, 119.0, 119.7, 122.1, 122.4, 122.5, 122.6, 124.9, 125.7, 126.3, 126.5, 128.7, 128.7, 129.9, 133.2, 134.8, 135.9, 138.4, 141.0, 142.3, 145.3; mp 144−146 °C; MS (70 eV) m/z 447 (100) [M$^+$], 305 (12); HRMS (ESI-TOF) calcd for $C_{24}H_{18}IN$ 447.0484, found 447.0484. IR (KBr, cm^{-1}) 3048, 2926, 1606, 1514.

5-Iodo-11-methyl-6-*o*-tolyl-11*H*-benzo[*a*]carbazole (2g): yield 38 mg, 85%; colorless solid; R_f = 0.34 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 4.45 (s, 3H), 6.40 (dd, J = 8.0, 0.8 Hz, 1H), 6.96 (td, J = 8.0, 0.8 Hz, 1H), 7.22 (d, J = 7.2 Hz, 1H), 7.39−7.46 (m, 3H), 7.51 (t, J = 7.6 Hz, 2H), 7.66−7.68 (m, 2H), 8.61−8.63 (m, 1H), 8.75−8.77 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 34.5, 96.1, 108.8, 118.6, 120.0, 121.5, 122.5, 122.6, 122.6, 124.9, 125.7, 126.5, 126.5, 128.4, 129.3, 130.3, 133.3, 134.6, 136.1, 136.1, 140.9, 141.7, 144.6; mp 156−158 °C; MS (70 eV) m/z 447 (100) [M$^+$], 320 (29), 305 (50); HRMS (ESI-TOF) calcd for $C_{24}H_{18}IN$ 447.0484, found 447.0487. IR (KBr, cm^{-1}) 3053, 2925, 1607, 1508.

5-Iodo-11-methyl-6-phenyl-11*H*-benzo[*a*]carbazole (2h): yield 39 mg, 90%; colorless solid; R_f = 0.30 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (s, 3H), 6.44 (dd, J = 8.0, 1.2 Hz, 1H), 6.95 (td, J = 8.0, 1.2 Hz, 1H), 7.37−7.42 (m, 3H), 7.52 (d, J = 8.4 Hz, 1H), 7.60−7.67 (m, 5H), 8.61−8.64 (m, 1H), 8.73−8.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5, 96.1, 108.9, 119.0, 119.7, 122.0, 122.4, 122.6, 122.6, 124.9, 125.7, 126.6, 128.1, 128.8, 129.4, 133.2, 134.9, 136.0, 141.0, 142.2, 145.5; mp 60−63 °C; MS (70 eV) m/z 433 (100) [M$^+$], 307 (32), 291 (31), 149 (39), 61 (31); HRMS (ESI-TOF) calcd for $C_{23}H_{16}IN$ 433.0327, found 433.0327. IR (KBr, cm^{-1}) 3053, 2927, 1605, 1507.

6-(4-Chlorophenyl)-5-iodo-11-methyl-11*H*-benzo[*a*]carbazole (2i): yield 33 mg, 70%; colorless solid; R_f = 0.30 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (s, 3H), 6.54 (dd, J = 8.0, 1.2 Hz, 1H), 7.01 (td, J = 8.0, 1.2 Hz, 1H), 7.31−7.34 (m, 2H), 7.43 (td, J = 8.0, 1.2 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.58−7.62 (m, 2H), 7.65−7.70 (m, 2H), 8.60−8.62 (m, 1H), 8.74−8.76 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5, 96.1, 109.0, 118.7, 119.9, 121.8, 122.3, 122.5, 122.7, 125.1, 126.0, 126.7, 129.2, 130.9, 133.1, 134.0, 134.9, 136.1, 140.8, 141.0, 143.8; mp 177−180 °C; MS (70 eV) m/z 469 (35) [M + 2], 467 (100) [M$^+$], 109 (28), 93 (28); HRMS (ESI-TOF) calcd for $C_{23}H_{15}ClIN$ 466.9938, found 466.9935. IR (KBr, cm^{-1}) 3054, 2927, 1606, 1491.

6-(4-Bromophenyl)-5-iodo-11-methyl-11*H*-benzo[*a*]carbazole (2j): yield 25 mg, 54%; colorless solid; R_f = 0.29 (20:1 Hex/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.43 (s, 3H), 6.55 (d, J = 8.1 Hz, 1H), 7.01 (t, J = 7.2 Hz, 1H), 7.27−7.24 (m, 2H), 7.43 (td, J = 6.9, 0.9 Hz, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.67−7.63 (m, 2H), 7.76−7.67 (m, 2H), 8.61−8.58 (m, 1H), 8,78−8.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5, 96.0, 109.0, 118.5, 119.9, 121.8, 122.2, 122.2, 122.4, 122.6, 125.1, 125.9, 126.7, 131.2, 132.1, 133.1, 134.8, 136.0, 140.8, 140.9, 144.3; mp 188−190 °C; MS (70 eV) m/z 469 (35) [M + 2], 467 (100) [M$^+$], 109 (28), 93 (28); HRMS (ESI-TOF) calcd for $C_{23}H_{15}BrIN$ 510.9433, found 510.9435; IR (KBr, cm^{-1}) 3057, 2927, 1607, 1489.

5-Iodo-11-methyl-6-(4-(trifluoromethyl)phenyl)-11*H*-benzo[*a*]carbazole (2k): yield 47 mg, 93%; colorless solid; R_f = 0.32 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (s, 3H), 6.39 (d, J = 8.0 Hz, 1H), 6.97 (td, J = 8.0, 0.8 Hz, 1H), 7.42 (td, J = 8.0, 0.8 Hz, 1H), 7.48−7.53 (m, 3H), 7.64−7.70 (m, 2H), 7.87 (dd, J = 8.0, 0.8 Hz, 2H), 8.58−8.61 (m, 1H), 8.71−8.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.5, 95.4, 109.1, 118.4, 119.9, 121.5, 122.1, 122.5, 122.7, 125.1, 125.8, 125.9, 125.9, 125.9, 126.1, 126.8, 130.0, 133.0, 134.8, 136.1, 140.5, 140.9, 148.9; mp 172−174 °C; MS (70 eV) m/z 501 (100) [M$^+$], 373 (23); HRMS (ESI-TOF) calcd for $C_{24}H_{15}F_3IN$ 501.0201, found 501.0200; IR (KBr, cm^{-1}) 3052, 2929, 1616, 1508.

5-Iodo-11-methyl-6-(4-nitrophenyl)-11*H*-benzo[*a*]carbazole (2l): yield 46 mg, 95%; pale yellow solid; R_f = 0.12 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.46 (s, 3H), 6.41 (d, J = 8.0 Hz, 1H), 6.99 (td, J = 7.2, 1.2 Hz, 1H), 7.44 (td, J = 6.8, 1.2 Hz, 1H), 7.55−7.60 (m, 3H), 7.68−7.74 (m, 2H), 8.48−8.52 (m, 2H), 8.59−8.61 (m, 1H), 8.76−8.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.6, 94.8, 109.2. 118.0, 120.0, 121.3, 121.8, 122.5, 122.8, 124.3, 125.3, 126.4, 127.0, 130.9, 132.9, 134.8, 136.2, 139.7, 141.0, 147.7, 151.9; mp 218−220 °C; MS (70 eV) m/z (%): 487 (100) [M$^+$], 290 (17); HRMS (ESI-TOF) calcd for $C_{23}H_{15}IN_2O_2$ 478.0178, found 478.0179; IR (KBr, cm^{-1}) 3054, 2927, 1601, 1523, 1348.

5-Iodo-8,10,11-trimethyl-6-propyl-11*H*-benzo[*a*]carbazole (2m): yield 41 mg, 79%; brown solid; R_f = 0.52 (20:1 Hex/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3H), 1.84 (x, J = 7.5 Hz, 2H), 2.53 (s, 3H), 2.84 (s, 3H), 3.62−3.56 (m, 2H), 4.30 (s, 3H), 7.08 (s, 1H), 7.60−7.51 (m, 2H), 7.74 (s, 1H), 8.35 (dd, J = 7.2, 2.1 Hz, 1H), 8.53 (dd, J = 7.5, 1.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 20.6, 21.7, 22.0, 39.0, 42.5, 97.9, 119.0, 120.0, 121.4, 121.7, 123.2, 124.4, 124.6, 126.2, 129.5, 129.9, 133.6, 134.4, 140.1, 140.8, 141.5; mp 98−100 °C; MS (70 eV) m/z 427 (100) [M$^+$], 308 (51), 281 (92), 272 (60); HRMS (ESI-TOF) calcd for $C_{22}H_{22}IN$ 427.0797, found 427.0795; IR (KBr, cm^{-1}): 3051, 2957, 2926, 2870, 1604, 1469.

5-Iodo-8,10,11-trimethyl-6-phenyl-11*H*-benzo[*a*]carbazole (2n): yield 39 mg, 84%; pale yellow solid; R_f = 0.55 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.15 (s, 3H), 2.83 (s, 3H), 4.43 (s, 3H), 6.00 (s, 1H), 6.95 (s, 1H), 7.34−7.37 (m, 2H), 7.57−7.67 (m, 5H), 8.49−8.53 (m, 1H), 8.56−8.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 21.2, 38.7, 96.4, 119.8, 120.9, 122.4, 123.2, 124.5, 125.4, 126.5, 127.9, 128.2, 128.3, 128.5, 128.7, 129.4, 129.5, 129.5, 129.7, 131.5, 133.2, 134.7, 136.9, 145.5; mp 110−112 °C; MS (70 eV) m/z 461 (41) [M$^+$], 335 (55), 149 (82), 61 (100); HRMS (ESI-TOF) calcd for $C_{25}H_{20}IN$ 461.0640, found 461.0639; IR (KBr, cm^{-1}) 3053, 2926, 2855, 1604, 1462.

Methyl 5-iodo-11-methyl-6-propyl-11*H*-benzo[*a*]carbazole-8-carboxylate (2o): yield 31 mg, 67%; colorless solid; R_f = 0.43 (5:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J = 7.2 Hz, 3H), 1.80−1.90 (m, 2H), 3.59−3.63 (m, 2H), 4.00 (s, 3H), 4.33 (s, 3H), 7.52 (d, J = 8.8, 1H), 7.54−7.63 (m, 2H), 8.19 (dd, J = 8.8, 1.6 Hz, 1H), 8.55−8.58 (m, 2H), 8.87 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 21.8, 34.8, 42.7, 52.0, 98.5, 108.8, 118.2, 121.8, 121.8, 122.2, 124.9, 125.3, 126.0, 126.7, 133.7, 134.7, 137.1, 140.9, 143.4, 167.8; mp 188−190 °C; MS (70 eV) m/z 457 (100) [M$^+$], 302 (53); HRMS (ESI-TOF) calcd for $C_{22}H_{20}INO_2$ 457.0539, found 457.0541; IR (KBr, cm^{-1}) 3052, 2955, 1710, 1610, 1429.

Methyl 5-iodo-11-methyl-6-phenyl-11*H*-benzo[*a*]carbazole-8-carboxylate (2p): yield 37 mg, 75%; colorless solid; R_f = 0.40 (5:1

Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (s, 3H), 4.45 (s, 3H), 7.14 (d, J = 1.6 Hz, 1H), 7.37−7.40 (m, 2H), 7.49 (d, J = 8.8 Hz, 1H), 7.64−7.70 (m, 5H), 8.08 (dd, J = 8.8, 2.0 Hz, 1H), 8.62−8.66 (m, 1H), 8.71−8.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.7, 51.7, 97.0, 108.5, 119.4, 121.6, 122.2, 122.2, 122.5, 124.9, 126.1, 127.0, 128.2, 129.1, 129.1, 133.5, 135.0, 136.7, 142.1, 143.3, 144.9, 167.5; mp 186−188 °C; MS (70 eV) m/z 491 (100) [M$^+$], 304 (21); HRMS (ESI-TOF) calcd for $C_{25}H_{18}INO_2$ 491.0382, found 491.0381; IR (KBr, cm^{-1}): 3054, 2926, 1710, 1611, 1429.

Methyl 5-iodo-11-methyl-6-(4-(trifluoromethyl)phenyl)-11*H*-benzo[*a*]carbazole-8-carboxylate (2q): yield 43 mg, 77%; colorless solid; R_f = 0.30 (5:1 Hex/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 3H), 4.41 (s, 3H), 6.92 (s, 1H), 7.48 (d, J = 8.4 Hz, 3H), 7.77−7.67 (m, 2H), 7.91 (d, J = 8.1 Hz, 2H), 8.10 (dd, J = 8.7, 1.8 Hz, 1H), 8.63−8.60 (m, 1H), 8.72−8.68 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 34.8, 51.6, 96.0, 108.8, 118.9, 121.6, 121.8, 122.3, 122.7, 124.0, 126.1, 126.1, 126.1, 126.5, 126.6, 127.2, 129.9, 133.3, 135.0, 136.8, 140.5, 143.3, 148.3, 167.3; mp 218−220 °C; MS (70 eV) m/z 559 (100) [M$^+$], 57 (85); HRMS (ESI-TOF) calcd for $C_{26}H_{17}F_3INO_2$ 559.0256, found 559.0255; IR (KBr, cm^{-1}) 3053, 2952, 1711, 1612, 1430.

2-(2-(3,3-Dimethylbut-1-ynyl)phenyl)-3-iodo-1-methyl-1*H*-indole (3c): yield 34 mg, 82%; pale orange oil; R_f = 0.78 (20:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 9H), 3.62 (s, 3H), 7.19−7.31 (m, 3H), 7.38−7.43 (m, 3H), 7.48−7.54 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.7, 30.5, 31.6, 58.9, 77.1, 102.5, 109.4, 120.2, 121.1, 122.5, 125.7, 127.3, 128.9, 130.1, 131.5, 131.6, 134.7, 137.3, 141.4; MS (70 eV) m/z (%): 413 (58) [M$^+$], 286 (100), 271 (30), 256 (47); HRMS (ESI-TOF) calcd for $C_{21}H_{20}IN$ 413.0640, found 413.0641.

Methyl 3-iodo-1-methyl-2-(2-(pent-1-ynyl)phenyl)-1*H*-indole-5-carboxylate (3o): yield 40 mg, 87%; pale yellow oil; R_f = 0.60 (5:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.57 (t, J = 7.6 Hz, 3H), 1.15−1.29 (m, 2H), 2.11 (t, J = 6.8 Hz, 2H), 3.65 (s, 3H), 3.97 (s, 3H), 7.32 (d, J = 8.8 Hz, 1H), 7.36−7.46 (m, 3H), 7.55−7.58 (m, 1H), 8.00 (dd, J = 8.4, 1.6 Hz, 1H), 8.25 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.9, 21.2, 21.7, 31.9, 51.9, 60.7, 78.6, 94.5, 109.3, 122.4, 123.9, 124.1, 125.6, 127.5, 129.2, 129.8, 131.6, 132.2, 133.7, 139.9, 142.9, 167.9; MS (70 eV) m/z 457 (22) [M$^+$], 302 (43), 105 (90), 57 (100); HRMS (ESI-TOF) calcd for $C_{22}H_{20}INO_2$ 457.0539, found 457.0538.

Methyl 3-iodo-1-methyl-2-(2-(phenylethynyl)phenyl)-1*H*-indole-5-carboxylate (3p): yield 43 mg, 88%; pale yellow oil; R_f = 0.50 (5:1 Hex/EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.70 (s, 3H), 3.98 (s, 3H), 7.05−7.00 (m, 2H), 7.20−7.13 (m, 3H), 7.36 (dd, J = 8.6, 0.6 Hz, 1H), 7.54−7.46 (m, 3H), 7.72−7.69 (m, 1H), 8.06−8.01 (m, 1H), 8.30−8.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.0, 51.9, 61.2, 87.4, 93.3, 109.5, 122.5, 122.6, 124.2, 124.3, 124.8, 128.2, 128.4, 129.4, 129.9, 131.4, 131.7, 132.1, 133.8, 140.0, 142.5, 167.9; MS (70 eV) m/z 491 (9) [M$^+$], 364 (100), 305 (87); HRMS (ESI-TOF) calcd for $C_{25}H_{18}INO_2$ 491.0382, found 491.0382.

Methyl 3-iodo-1-methyl-2-(2-((4-(trifluoromethyl)phenyl)-ethynyl)phenyl)-1*H*-indole-5-carboxylate (3q): yield 53 mg, 94%; colorless oil; R_f = 0.68 (4:1 Hex/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.99 (s, 3H), 7.01 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.4 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.47−7.56 (m, 3H), 7.71−7.74 (m, 1H), 8.04 (dd, J = 8.4, 1.6 Hz, 1H), 8.30 (d, J = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 32.0, 52.0, 61.4, 89.7, 91.8, 109.5, 122.8, 124.1, 124.3, 124.4, 125.1, 125.1, 125.2, 125.2, 125.3, 126.3, 128.9, 129.5, 129.9, 131.6, 131.8, 132.3, 134.1, 139.9, 142.2, 167.9; MS (70 eV) m/z 559 (34) [M$^+$], 432 (100), 373 (96); HRMS (ESI-TOF) calcd for $C_{26}H_{17}F_3INO_2$ 559.0256, found 559.0259.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and full spectral data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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