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SYNTHESIS OF INDOLO[1,2-*a*]INDOLE DERIVATIVES BY CATIONIC AU(I)-CATALYZED *EXO*-SELECTIVE CYCLOISOMERIZATION AND THEIR PHOTOPHYSICAL PROPERTIES

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Dedicated to Professor Toru Fukuyama on the occasion of his 70th birthday

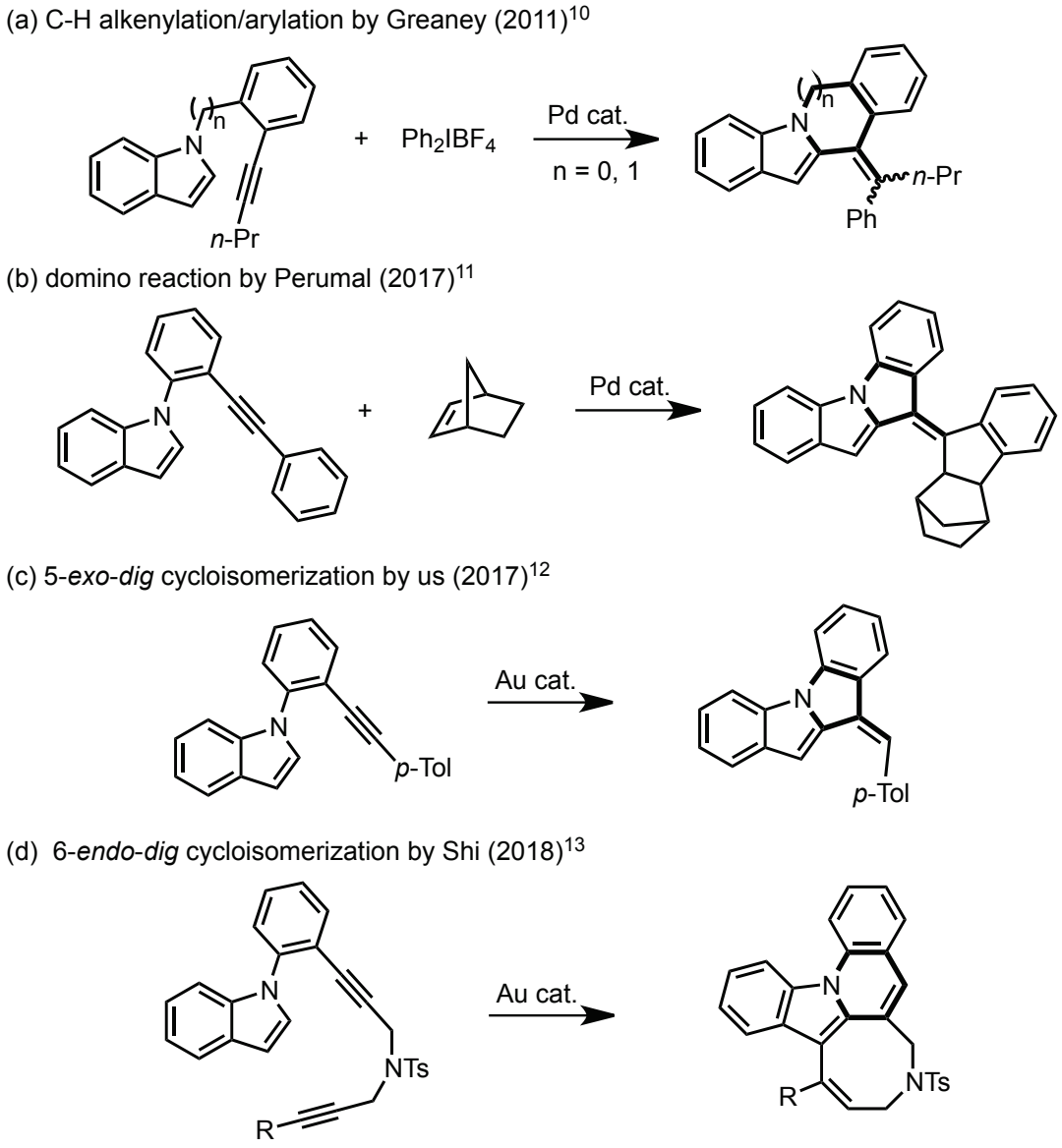
Abstract – Cationic Au(I)-catalyzed intramolecular cycloisomerization of *N*-(2-alkynylphenyl)indoles proceeded efficiently in *exo*-selective manner, and (*Z*)-10-(arylidene)indolo[1,2-*a*]indole derivatives were obtained in moderate to high yields. Their photophysical properties were also measured.

Numerous natural products and biologically active molecules are comprised of nitrogen-containing heterocycles and a variety of well-established methods for their syntheses are available in the literature. Development of new approaches to their syntheses, employing efficient and economical routes, is still an area of active research. In particular, indole skeleton is contained in many active pharmaceutical ingredients[1]: for example, indolo[1,2-*a*]indole and their reduced and oxidized forms occur widely among natural products.[2] The nitrogen-containing tetracyclic structure is also employed for chromogenic and fluorogenic indicators, exhibiting a solvatochromic effect and strong fluorescence in a variety of materials.[3,4]

Against this background, various approaches to the synthesis of indolo[1,2-*a*]indole derivatives have been reported. [3+2] Annulation of methyl indole-2-carboxylates with arynes is a facile method of the preparation of substituted indolo[1,2-*a*]indolones.[5] Regarding a catalytic protocol, Cu-catalyzed intramolecular *N*-arylation of 2-(2-bromobenzyl)indole is a pioneering example,[6] and various Cu-catalyzed reactions were reported in recent years.[7] Pd-Catalyzed reactions were also used for the

construction of indolo[1,2-*a*]indole skeleton[8]: intramolecular dehydrogenative coupling of indole C3-H bond with iminyl hydrogen is a successful example.[9]

We here disclose a facile synthesis of various 10-(arylidene)indolo[1,2-*a*]indole derivatives via Au(I)-catalyzed intramolecular 5-*exo*-*dig* cycloisomerization. Greaney showed the synthesis of 10-(arylidene)indolo[1,2-*a*]indole (n = 0) as an entry of Pd-catalyzed tandem C-H alkenylation and arylation (Scheme 1a).[10] Perumal also demonstrated it in a Pd-catalyzed domino reaction including the activation of indole C2-H bond (Scheme 1b).[11] In contrast, we reported the synthesis of 10-(benzylidene)indolo[1,2-*a*]indole as a preliminary result in the research of Au(I)-catalyzed cycloisomerization of *N*-(2-alkynylphenyl)indoles (Scheme 1c).[12] After our publication, Shi reported an

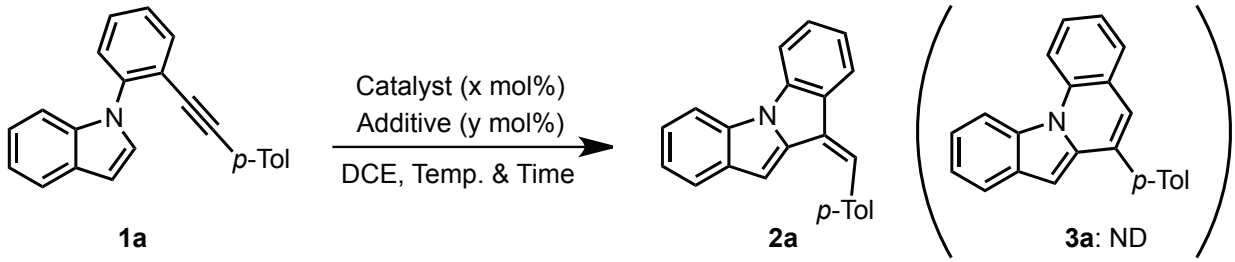


Scheme 1. Intramolecular catalytic reactions of *N*-(2-alkynylphenyl)indoles

elegant synthesis of eight-membered-ring-fused indolo[1,2-*a*]quinoline via Au(I)-catalyzed 6-*endo-dig* cycloisomerization of *N*-(2-alkynylphenyl)indoles (Scheme 1d).[13]

We conducted the screening of reaction conditions for the intramolecular cycloisomerization of *N*-(2-(*p*-tolylethynyl)phenyl)indole (**1a**) in 1,2-dichloroethane (DCE) (Table 1). The cationic Au(I) catalyst prepared from AuCl(PPh_3) and AgOTf realized the moderate yield of 5-*exo-dig* product **2a**[12] without the formation of 6-*endo-dig* product **3a**[14] (Entry 1). At lower temperature, the yields were decreased along with recovery of substrate (Entries 2 and 3). Cationic Pt(II) and Pd(II) counterparts gave **2a**, albeit in lower yields (Entries 4 and 5). AgOTf itself and even trifluoromethanesulfonic acid also promoted the cycloisomerization, but the reaction was messy and the yields were very low (Entries 6 and 7). When the cationic Au(I) catalysts with electron-deficient phosphine ligands were used, the reaction proceeded even at room temperature, but the substrate was not consumed completely and the yield of **2a** was comparable or low at the elevated reaction temperature (Entries 8 and 9). We determined entry 1 as the best conditions and examined the substrate scope.

Table 1. Screening of reaction conditions

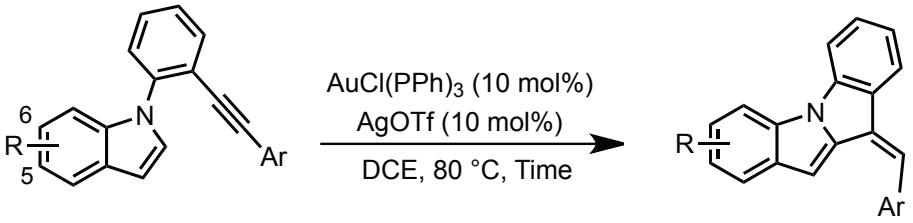


1a **2a** **3a**: ND

Entry	Catalyst (x mol%)	Additive (y mol%)	Temp. and Time	Yield (%) of **2a**
1	$AuCl(PPh_3)$ (10)	AgOTf (10)	80 °C, 24 h	58
2	$AuCl(PPh_3)$ (10)	AgOTf (10)	60 °C, 24 h	33
3	$AuCl(PPh_3)$ (10)	AgOTf (10)	rt, 24 h	21
4	$PtCl_2(PPh_3)_2$ (10)	AgOTf (20)	rt, 1 h, then 60 °C, 24 h	45
5	$PdCl_2(PPh_3)_2$ (10)	AgOTf (20)	60 °C, 24 h	18
6	AgOTf (10)	none	80 °C, 3 h	22
7	TfOH (30)	none	rt, 1 h, then 60 °C, 1 h	19
8	$AuCl[P(4\text{-}CF_3C_6H_4)_3]$ (10)	AgOTf (10)	rt, 5 h, then 80 °C, 24 h	56
9	$AuCl[P(C_6F_5)_3]$ (10)	AgOTf (10)	rt, 1 h, then 80 °C, 2 h	29

We subjected various *N*-(2-(arylethynyl)phenyl)indoles **1b-1e** possessing various substituents at the *para*-position of the arene moiety to the optimum reaction conditions (Table 2, Entries 1-4). Compared with the parent phenyl, electron-rich anisyl group realized the best yield of 76% (Entries 1 and 2). While electron-deficient aryl groups were also tolerated, the yield was decreased (Entries 3 and 4). Regarding the substituent on the indole ring, we examined the reaction of 5- and 6-substituted indoles and obtained the corresponding tetracyclic products (Entries 5-7). In each entry, 5-*exo-dig*- and *Z*-selective cycloisomerization proceeded, and 6-*endo-dig*-cycloadducts were not detected.[15]

Table 2. Substrate scope of Au(I)-catalyzed 5-*exo-dig* cycloisomerization



1 **2**

Entry	R	Ar	Time (h)	Yield (%)
1	H	Ph (**1b**)	24	71 (**2b**)
2	H	4-$MeOC_6H_4$ (**1c**)	6	76 (**2c**)
3	H	4-FC_6H_4 (**1d**)	6	55 (**2d**)
4	H	4-$CF_3C_6H_4$ (**1e**)	24	50 (**2e**)
5	5-MeO	4-$MeOC_6H_4$ (**1f**)	6	67 (**2f**)
6	6-Me	4-$MeOC_6H_4$ (**1g**)	6	61 (**2g**)
7	6-F	4-$MeOC_6H_4$ (**1h**)	6	60 (**2h**)

While the obtained compounds have distinct fluorescence emission, we evaluated their photophysical properties by UV-Vis and fluorescence spectroscopy (Table 3). They emit fluorescence from 400 to 600 nm in the visible range. Regarding the effects of the *p*-substituent on aryl group, an electron-withdrawing trifluoromethylphenyl group (**2e**: $\lambda_{max(em)}$ = 511 nm) shows a redshift compared to the parent phenyl group (**2b**: $\lambda_{max(em)}$ = 492 nm) whereas electron donating 4-tolyl (**2a**: $\lambda_{max(em)}$ = 487 nm) and 4-anisyl group (**2c**: $\lambda_{max(em)}$ = 484 nm) induce a slight blueshift (Entries 1-3 and 5). Comparison of the fluorescence maxima of **2c** with those of **2f**-**2h** implies that the 5-position on the indolo[1,2-*a*]indole skeleton is more sensitive than the 6-position (Entries 3, 6-8). Electron-withdrawing fluoro group at 6-position shows fluorescence at 478 nm whereas electron-donating methyl group shows fluorescence at 491 nm (Entries 7 and 8). Meanwhile, the effects of the substituents to absorption spectra are smaller than those to the fluorescence

spectra (e.g. the largest maximum absorption wavelengths ($\lambda_{max(abs)}$) of **2** are similar around 395-404 nm. Electron-donating group on the skeleton shows higher absorbance than electron-withdrawing group (Entries 6-8). Indolo[1,2-*a*]indole derivative with a tetrasubstituted alkene moiety (Scheme 1b) show emission at 590 nm,[11] whereas almost all our compounds show emissions below 500 nm except **2e**. This is probably due to inefficient conjugation of the aryl group with indolo[1,2-*a*]indole skeleton. As for the fluorescence quantum yield, there was little effect of substituents on both of aryl and indole rings: moderate quantum yields were achieved except for compound **2b**.

Table 3. Photophysical properties of compounds **2a**-**2h**

Entry	Comp.	$\lambda_{max(abs)}$ (nm) [ε (x10^3 cm^{-1})]^{a,b}	$\lambda_{max(em)}$ (nm)^{a,b,c}	$\Phi^{a,b,c}$
1	**2a**	255 (1.2), 280 (1.6), 401 (0.3)	487	0.67
2	**2b**	280 (2.5), 399 (0.3)	492	0.23
3	**2c**	238 (1.4), 282 (1.9), 398 (0.3)	484	0.64
4	**2d**	245 (1.8), 280 (2.2), 400 (0.4)	490.5	0.60
5	**2e**	242 (2.1), 282 (2.0), 395 (0.4)	511	0.42
6	**2f**	234 (2.6), 283 (3.8), 401 (0.7)	487	0.49
7	**2g**	253 (2.6), 281 (4.1), 404 (0.8)	491	0.66
8	**2h**	251 (1.6), 277 (2.3), 397 (0.5)	478	0.67

(a) Measured in CH_2Cl_2. (b) **2a** 1.9x10^{-6} M; **2b** 1.7x10^{-6} M; **2c** 3.0x10^{-6} M; **2d** 1.5x10^{-6} M; **2e** 1.6x10^{-6} M; **2f** 1.9x10^{-6} M; **2g** 2.4x10^{-6} M; **2h** 3.3x10^{-6} M. (c) Excitation wavelength: **2a** 280 nm; **2b** 280 nm; **2c** 282 nm; **2d** 280 nm; **2e** 282 nm; **2f** 283 nm; **2g** 281 nm; **2h** 277 nm.

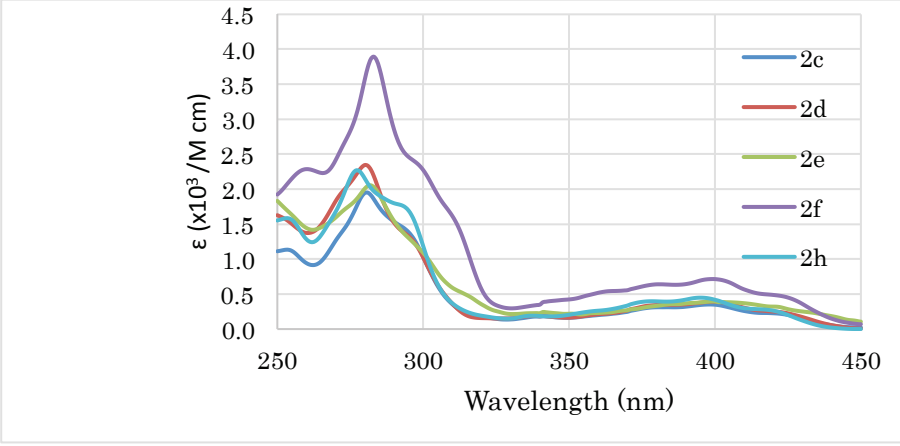


Figure 1. Selected UV-Vis spectra

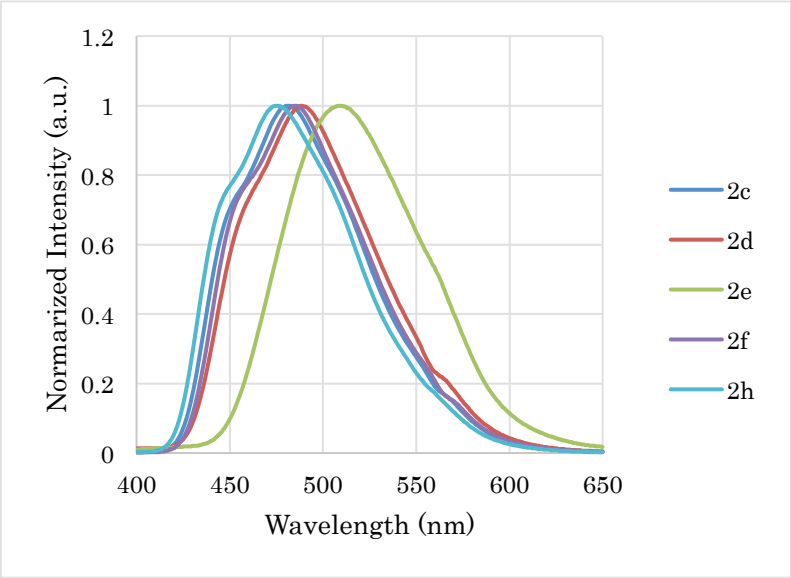


Figure 2. Selected fluorescence spectra

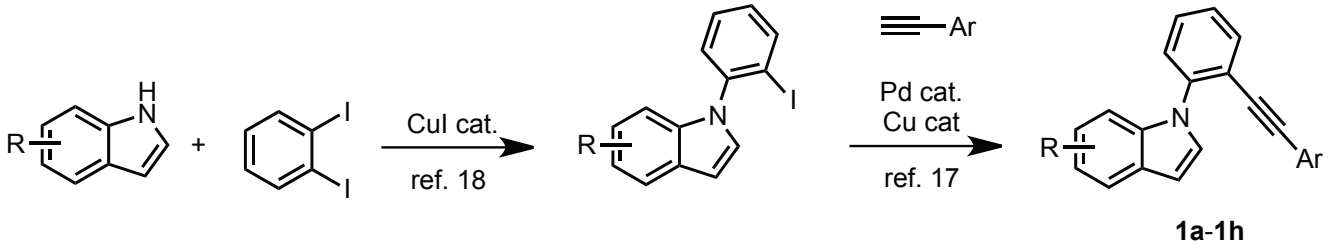
In summary, we have developed a new protocol for the synthesis of indolo[1,2-*a*]indole skeleton via Au(I)-catalyzed 5-*exo*-*dig*-selective cycloisomerization. Various (*Z*)-10-(arylidene)indolo[1,2-*a*]indole derivatives were obtained in moderate to good yields. They emitted fluorescence from 400 nm to 600 nm in the visible range of blue to green and moderate absolute quantum yields were achieved.

EXPERIMENTAL

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with JEOL ECX-500 (500 MHz) spectrometer. Chemical shift values for protons are reported in parts per million (δ) relative to internal standard TMS (0.0 ppm). ^{13}C NMR spectra were obtained by JEOL ECX-500 (125 MHz) spectrometers and referenced to the internal solvent signals (central peak is 77.0 ppm in $CDCl_3$). ^{19}F NMR spectra were obtained by JEOL ECX-500 (470 MHz) spectrometers and referenced to the fluorine resonance of external standard: trifluoroacetic acid (-76.5 ppm). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, m = multiplet, dd = doublet of doublets), coupling constant in hertz (Hz), and area integration. High-resolution mass spectra (HRMS) were measured with an electrospray ionization (ESI)-orbitrap mass spectrometer or a direct analysis in real time (DART)-orbitrap mass spectrometer.[16] UV-Vis spectra were measured on a JASCO V-630 photometer. Fluorescence spectra were taken on a JASCO FP-8200 spectrofluorometer and quantum yields were determined with an integrating sphere (diameter 10 cm). Absolute PL quantum yield was measured by Hamamatsu Photonics C9920-02 spectrometer. Preparative thin-layer chromatography (PTLC) was performed with silica gel-precoated glass plates (Merck 60 GF254) prepared in our laboratory. All reagents were weighed and handled in air and backfilled under argon at room temperature. All reactions were performed under an argon atmosphere. Unless otherwise noted, organic compounds and solvents were purchased from Tokyo

Kasei Co., Aldrich Inc., and other commercial suppliers and were used without further purification. Compounds **1**[17] is known and its ^{1}H and ^{13}C NMR spectra were accorded with those in literature.

Starting Materials. *N*-(2-Alkynylphenyl)indoles were prepared from the corresponding indoles and 1,2-diiodobenzene in two steps: Cu-catalyzed *N*-arylation of indole with 1,2-diiodobenzene gave *N*-(2-iodophenyl)indole.[18] Subsequent Sonogashira coupling afforded substrate **1a-1h**.[17]



1a-1h

Typical experimental procedure for Au(I)-catalyzed cycloisomerization. $AuCl(PPh_3)$ (0.0050 mmol), AgOTf (0.0050 mmol), and *N*-(2-alkynylphenyl)indole derivatives **1a-1h** (0.050 mmol) were placed in a Schlenk tube under an argon atmosphere in globe box, which was then evacuated and backfilled with argon (×3). To the reaction vessel was added anhydrous DCE (0.50 mL), then the solution was stirred at 80 °C (bath temperature). The reaction mixture was cooled to room temperature, and the solution was passed through cotton filtration. After removal of solvent, the crude products were purified by PTLC to give **2a-2h**.

1-(2-(Phenylethynyl)phenyl)-1*H*-indole (1b): it was isolated by PTLC (hexane only). The title compound was obtained as yellow viscous oil (78.1 mg, 85%). ^{1}H NMR δ 7.71 (dd, J = 7.3, 1.8 Hz, 2H), 7.53-7.47 (m, 3H), 7.42-7.36 (m, 2H), 7.26-7.15 (m, 5H), 7.08 (dd, J = 7.6, 1.8, Hz, 2H), 6.71 (d, J = 3.2 Hz, 1H); ^{13}C NMR δ 140.9, 136.7, 133.5, 131.6, 129.3, 129.0, 128.6, 128.3, 127.3, 127.2, 122.9, 122.2, 121.0, 120.3, 111.2, 103.0, 94.7, 86.4 (two pairs of peaks at the aromatic region are overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{16}N$ ($[M+H]^+$) 294.1277, found 294.1277.

1-(2-((4-Methoxyphenyl)ethynyl)phenyl)-1*H*-indole (1c): it was isolated by PTLC (hexane/EtOAc = 99/1). The title compound was obtained as brown viscous oil (93.2 mg, 92%). ^{1}H NMR δ 7.72-7.67 (m, 2H), 7.51-7.36 (m, 5H), 7.22-7.15 (m, 2H), 7.02 (d, J = 8.7 Hz, 2H), 6.75-6.67 (m, 3H), 3.67 (s, 3H); ^{13}C NMR δ 159.9, 140.7, 136.7, 133.2, 133.0, 129.3, 128.8, 127.3, 127.1, 122.1, 121.4, 120.9, 120.3, 114.9, 114.0, 111.3, 102.9, 94.9, 85.2, 55.4 (a pair of peaks at the aromatic region is overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{18}NO$ ($[M+H]^+$) 324.1383, found 324.1383.

1-(2-((4-Fluorophenyl)ethynyl)phenyl)-1*H*-indole (1d): it was isolated by PTLC (hexane/EtOAc = 99/1). The title compound was obtained as brown viscous oil (82.9 mg, 85%). ^{1}H NMR δ 7.69 (d, J = 8.7 Hz, 2H), 7.50-7.34 (m, 5H), 7.19-7.17 (m, 2H), 7.01-7.00 (m, 2H), 6.91-6.87 (m, 2H), 6.70-6.68 (m, 1H); ^{13}C NMR δ 163.9 (d, J = 249.4 Hz), 140.9, 136.7, 133.5, 133.3, 133.2, 129.2, 128.9 (d, J = 12.9 Hz), 127.4 (d, J = 16.8 Hz), 122.2, 121.0, 120.9, 120.2, 118.9, 118.8, 115.7 (d, J = 22.0 Hz), 111.2, 103.0, 93.7,

86.1; ^{19}F NMR δ -110.4; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{15}FN$ ($[M+H]^+$) 312.1183, found 312.1183.

1-(2-((4-Trifluoromethyl)phenyl)ethynyl)phenyl-1*H*-indole (1e): it was isolated by PTLC (hexane/EtOAc = 99/1). The title compound was obtained as brown viscous oil (78.1 mg, 69%). ^{1}H NMR δ 7.71 (d, *J* = 7.8 Hz, 2H), 7.58-7.44 (m, 6H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.20-7.16 (m, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.72 (d, *J* = 2.6 Hz, 1H); ^{13}C NMR δ 141.3, 136.6, 133.5, 131.6, 129.9, 129.0, 128.9, 127.4, 127.2, 125.3 (q, *J* = 4.1 Hz), 125.0, 122.2, 121.0, 120.3, 111.2, 103.1, 93.1, 88.6 (three pairs of peaks at the aromatic region are overlapped); ^{19}F NMR δ -62.8; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{15}F_3N$ ($[M+H]^+$) 362.1150, found 362.1151.

5-Methoxy-1-(2-((4-methoxyphenyl)ethynyl)phenyl)-1*H*-indole (1f): it was isolated by PTLC (hexane/EtOAc = 95/5). The title compound was obtained as yellow viscous oil (66.8 mg, 66%). ^{1}H NMR δ 7.68 (d, *J* = 7.3 Hz, 1H), 7.58-7.41 (m, 3H), 7.38-7.34 (m, 1H), 7.28 (d, *J* = 9.2 Hz, 1H), 7.18 (s, 1H), 7.08 (d, *J* = 2.3 Hz, 2H), 6.87 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.76 (d, *J* = 8.7 Hz, 2H), 6.63-6.61 (m, 1H), 3.89 (s, 3H), 3.71 (s, 3H); ^{13}C NMR δ 161.3 (d, *J* = 237.5 Hz), 159.9, 140.2, 136.8 (d, *J* = 12.2 Hz), 133.3, 133.0, 128.9 (d, *J* = 3.8 Hz), 127.7, 126.9, 125.3, 121.6 (d, *J* = 10.0 Hz), 121.4, 114.8, 114.0, 109.1 (d, *J* = 24.4 Hz), 108.8, 102.9, 97.9 (d, *J* = 26.8 Hz), 95.1, 84.8, 55.3; ^{19}F NMR δ -120.8; HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{19}NNaO_2$ ($[M+Na]^+$) 376.1308, found 376.1308.

1-(2-((4-Methoxyphenyl)ethynyl)phenyl)-6-methyl-1*H*-indole (1g): it was isolated by PTLC (hexane/EtOAc = 99/1). The title compound was obtained as brown viscous oil (71.3 mg, 70%). ^{1}H NMR δ 7.69 (d, *J* = 7.3 Hz, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.52-7.37 (m, 4H), 7.18-7.16 (m, 1H), 7.07-7.01 (m, 3H), 6.75 (d, *J* = 8.7 Hz, 2H), 6.66-6.64 (m, 1H), 3.77 (s, 3H), 2.43 (s, 3H); ^{13}C NMR δ 159.9, 140.7, 137.0, 133.3, 133.0, 131.9, 128.8, 127.2, 127.1, 126.8, 122.0, 121.3, 120.6, 115.1, 113.9, 111.2, 102.7, 94.8, 85.2, 55.4, 21.9 (a pair of peaks at the aromatic region is overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{19}NNaO$ ($[M+Na]^+$) 360.1358, found 360.1359.

6-Fluoro-1-(2-((4-methoxyphenyl)ethynyl)phenyl)-1*H*-indole (1h): it was isolated by PTLC (hexane/EtOAc = 95/5). The title compound was obtained as yellow viscous oil (81.0 mg, 80%). ^{1}H NMR δ 7.68 (d, *J* = 7.8 Hz, 1H), 7.62-7.58 (m, 1H), 7.46-7.40 (m, 4H), 7.01 (d, *J* = 9.2 Hz, 3H), 6.95-6.90 (m, 1H), 6.74 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 2.8 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR δ 161.3 (d, *J* = 237.5 Hz), 159.9, 140.2, 136.8 (d, *J* = 12.2 Hz), 133.3, 133.0, 128.9 (d, *J* = 3.8 Hz), 127.7, 126.9, 125.3, 121.6 (d, *J* = 10.0 Hz), 121.4, 114.8, 114.0, 109.1 (d, *J* = 24.4 Hz), 108.8, 102.9, 97.9 (d, *J* = 26.8 Hz), 95.1, 84.8, 55.3; ^{19}F NMR δ -120.8; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}FNO$ ($[M+H]^+$) 342.1285, found 342.1289.

(*Z*)-10-(4-Methylbenzylidene)indolo[1,2-*a*]indole (2): it was isolated by PTLC (hexane/CH_2Cl_2 = 10/1). The title compound was obtained as yellow solid (18.0 mg, 58%). The *Z* stereochemistry was determined

by the correlation between the singlet proton of the C2 position of the indole ring and aromatic protons of tolyl group in the NOESY spectrum; mp 134-135 °C; ^{1}H NMR δ 8.57 (d, *J* = 8.2 Hz, 1H), 8.48 (d, *J* = 8.2 Hz, 1H), 7.80 (d, *J* = 7.4 Hz, 1H), 7.55-7.66 (m, 4H), 7.27-7.43 (m, 5H), 7.07 (s, 1H), 6.85 (s, 1H), 2.44 (s, 3H); ^{13}C NMR δ 138.2, 136.8, 136.2, 136.0, 133.5, 133.1, 130.3, 129.5, 129.0, 128.5, 128.4, 124.8, 123.0, 122.7, 122.0, 122.0, 121.4, 115.4, 114.4, 97.9, 21.5; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{18}N$ ($[M+H]^+$) 308.1434, found 308.1431.

(*Z*)-10-Benzylidene-10*H*-indolo[1,2-*a*]indole (2b): it was isolated by PTLC (hexane/CH_2Cl_2 = 9/1). The title compound was obtained as a yellow solid (20.8 mg, 71%); mp 100-102 °C; ^{1}H NMR δ 8.62 (d, *J* = 8.2 Hz, 1H), 8.52 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.75-7.71 (m, 2H), 7.69-7.67 (m, 1H), 7.64-7.60 (m, 1H), 7.55-7.30 (m, 6H), 7.12 (s, 1H), 6.87 (s, 1H); ^{13}C NMR δ 138.9, 136.7, 136.3, 133.6, 133.1, 129.1, 128.8, 128.6, 128.5, 128.4, 124.8, 123.1, 123.0, 122.1, 122.0, 121.5, 120.8, 115.5, 114.5, 97.9 (a pair of peaks at the aromatic region is overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{16}N$ ($[M+H]^+$) 294.1280, found 294.1277.

(*Z*)-10-(4-Methoxybenzylidene)-10*H*-indolo[1,2-*a*]indole (2c): it was isolated by PTLC (hexane/CH_2Cl_2 = 9/1). The title compound was obtained as a yellow solid (24.5 mg, 76%); mp 120-122 °C; ^{1}H NMR δ 8.61 (d, *J* = 8.7 Hz, 1H), 8.51 (d, *J* = 8.7 Hz, 1H), 7.83 (d, *J* = 6.9 Hz, 1H), 7.68-7.66 (m, 3H), 7.62-7.58 (m, 1H), 7.45-7.31 (m, 3H), 7.08-7.04 (m, 3H), 6.87 (s, 1H), 3.90 (s, 3H); ^{13}C NMR δ 159.8, 136.9, 136.1, 133.5, 132.7, 131.3, 130.3, 129.7, 128.9, 128.3, 124.8, 123.0, 122.5, 121.9, 115.3, 114.4, 114.1, 97.8, 55.5 (two pairs of peaks at the aromatic region are overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}NNaO$ ($[M+Na]^+$) 346.1203, found 346.1202.

(*Z*)-10-(4-Fluorobenzylidene)-10*H*-indolo[1,2-*a*]indole (2d): it was isolated by PTLC (hexane/CH_2Cl_2 = 9/1). The title compound was obtained as yellow solid (17.0 mg, 55%); mp 106-108 °C; ^{1}H NMR δ 8.61 (d, *J* = 8.7 Hz, 1H), 8.51 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.71-7.68 (m, 3H), 7.64-7.60 (m, 1H), 7.46-7.32 (m, 3H), 7.23-7.17 (m, 2H), 7.07 (s, 1H), 6.81 (s, 1H); ^{13}C NMR δ 164.1 (d, *J* = 247.3 Hz), 136.6, 136.3, 134.9, 134.8, 133.5, 132.0, 130.7, 130.4 (d, *J* = 8.4 Hz), 128.7, 125.6, 123.1, 123.0, 122.2 (d, *J* = 8.9 Hz), 121.4, 120.9, 115.8, 115.6 (d, *J* = 21.8 Hz), 114.4, 97.8; ^{19}F NMR δ -113.4; HRMS (ESI, positive): *m/z* calcd. for $C_{22}H_{14}FN$ ($[M]^+$) 311.1105, found 311.1105.

(*Z*)-10-(4-(Trifluoromethyl)benzylidene)-10*H*-indolo[1,2-*a*]indole (2e): it was isolated by PTLC (hexane/CH_2Cl_2 = 9/1). The title compound was obtained as a yellow solid (18.1 mg, 50%); mp 125-127 °C; ^{1}H NMR δ 8.63 (d, *J* = 8.7 Hz, 1H), 8.52 (d, *J* = 8.7 Hz, 1H), 7.87-7.78 (m, 5H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.67-7.63 (m, 1H), 7.48-7.34 (m, 3H), 7.14 (s, 1H), 6.82 (s, 1H); ^{13}C NMR δ 136.4, 133.5, 131.7, 130.8, 129.3, 129.1, 129.0, 125.8 (q, *J* = 4.1 Hz), 125.1, 124.4, 123.6, 123.2, 122.2, 121.4, 121.2, 121.0, 115.5, 114.5, 111.2, 103.2, 97.7; ^{19}F NMR δ -62.4; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{15}F_3N$ ($[M+H]^+$) 362.1149, found 362.1151.

(*Z*)-3-Methoxy-10-(4-methoxybenzylidene)-10*H*-indolo[1,2-*a*]indole (2f): it was isolated by PTLC (hexane/CH_2Cl_2 = 7/3). The title compound was obtained as a yellow solid (23.7 mg, 67%); mp 162-164 °C; ^{1}H NMR δ 8.53 (d, *J* = 8.7 Hz, 1H), 8.39 (d, *J* = 9.2 Hz, 1H), 7.69-7.65 (m, 3H), 7.61-7.56 (m, 1H), 7.33-7.29 (m, 1H), 7.25-7.20 (m, 1H), 7.08-7.03 (m, 4H), 6.79 (s, 1H), 3.91 (s, 6H); ^{13}C NMR δ 159.7, 155.3, 137.2, 135.9, 132.4, 131.3, 129.7, 128.9, 128.7, 128.3, 124.6, 122.8, 122.3, 115.3, 114.9, 114.1, 112.2, 101.9, 97.4, 55.7, 55.5 (a pair of peaks at the aromatic region is overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{20}NO_2$ ($[M+H]^+$) 354.1490, found 354.1489.

(*Z*)-10-(4-Methoxybenzylidene)-2-methyl-10*H*-indolo[1,2-*a*]indole (2g): it was isolated by PTLC (hexane/CH_2Cl_2 = 7/3). The title compound was obtained as a yellow solid (20.6 mg, 61%); mp 182-184 °C; ^{1}H NMR δ 8.59 (d, *J* = 8.2 Hz, 1H), 8.30 (s, 1H), 7.71-7.65 (m, 4H), 7.61-7.75 (m, 1H), 7.33-7.30 (m, 1H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.06-7.03 (m, 3H), 6.81 (s, 1H), 3.90 (s, 3H), 2.66 (s, 3H); ^{13}C NMR δ 159.7, 136.5, 136.2, 133.9, 132.8, 131.9, 131.4, 129.7, 128.8, 128.1, 124.9, 123.8, 122.9, 121.9, 120.9, 115.4, 114.4, 114.1, 97.7, 55.5, 22.6 (a pair of peaks at the aromatic region is overlapped); HRMS (ESI, positive): *m/z* calcd. for $C_{24}H_{20}NO$ ($[M+H]^+$) 338.1541, found 338.1539.

(*Z*)-2-Fluoro-10-(4-methoxybenzylidene)-10*H*-indolo[1,2-*a*]indole (2h): it was isolated by PTLC (hexane/CH_2Cl_2 = 9/1). The title compound was obtained as a yellow solid (20.5 mg, 60%); mp 157-159 °C; ^{1}H NMR δ 8.42 (d, *J* = 8.2 Hz, 1H), 8.19 (d, *J* = 8.7 Hz, 1H), 7.74-7.71 (m, 1H), 7.68-7.57 (m, 4H), 7.35-7.32 (m, 1H), 7.18-7.13 (m, 1H), 7.06-7.04 (m, 3H), 6.82 (s, 1H), 3.90 (s, 3H); ^{13}C NMR δ 161.0, 160.6 (d, *J* = 237.9 Hz), 159.8, 137.4 (d, *J* = 3.6 Hz), 135.8, 132.9 (d, *J* = 15.3 Hz), 131.1, 129.7, 128.9, 128.3, 126.8, 124.9, 123.4, 122.2, 121.9 (d, *J* = 10.1 Hz), 114.9, 114.2, 110.9 (d, *J* = 24.7 Hz), 101.3 (d, *J* = 28.3 Hz), 97.7, 55.5; ^{19}F NMR δ -119.1; HRMS (ESI, positive): *m/z* calcd. for $C_{23}H_{17}FNO$ ($[M+H]^+$) 342.1292, found 342.1289.

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