Synthesis of 2,3-Disubstituted Indole Using Palladium(II)-Catalyzed Cyclization with Alkenylation Reaction

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The reaction of ethyl 2-ethynylphenylcarbamate derivative with alkenes in the presence of a palladium(II) catalyst, copper dichloride and tetrabutylammonium fluoride (TBAF) produced 2-substituted 3-ethenylindoles during refluxing. The intramolecular cyclization reaction of ethyl 2-ethynylphenylcarbamates, which have an ethenyl part in the ethynyl group, was also used to produce carbazole derivatives.

Key words palladium-catalyzed cyclization; indole; carbazole; tetrabutylammonium fluoride

Heterocyclic compounds, especially indoles, widely occur in natural products and have unique biological activities.[1)] Many synthetic methods for producing the indole structure have been reported.[2)] The cyclization of the 2-ethynylanilines is one of the most useful methods for the synthesis of multi-substituted indoles, because 2-ethynylanilines can be easily prepared from 2-haloanilines with terminal acetylenes by the Sonogashira reaction,[3)] and many synthetic methods of the 2-haloanilines have been reported. For example, the preparation for 2-haloanilines is easily achieved by the *ortho*-lithiation of *N*-protected anilines with alkyllithium.[4)] In our previous paper, we reported the tetrabutylammonium fluoride (TBAF)-promoted cyclization of 2-alkynylanilines to prepare the 2-substituted indoles.[5)] The method under mild conditions is useful for the synthesis of substituted indoles except for the 3-substituted indoles. On the other hand, we reported the palladium(II) catalyzed cyclization of 2-ethynylanilines in the presence of alkenes to give the 2,3-disubstituted indoles *via* the Heck reaction of the indolylpalladium intermediate with alkenes (Chart 1).[6)] However, this cyclization has the following limitations; 1) the alkenes must have an electron-withdrawing group, and 2) the mesyl group as a protecting group for the primary amino groups of anilines is required for the cyclization.

Moreover, we reported that the palladium-catalyzed cross-coupling reaction of *N*-(2-iodophenyl)methanesulfonamide with terminal alkynes produced the 2-substituted indoles instead of the corresponding 2-ethynylanilnes.[7)] In short, the Sonogashira reaction of *N*-(2-alkynylphenyl)methanesulfonamides with terminal acetylenes under the general conditions produces the corresponding indoles instead of 2-ethynylanilines, and only the *N*-(2-alkynylphenyl)methanesulfonamides are available for the palladium-cyclization reaction with the alkenylation reaction under the previously reported conditions.[6)] These facts show the limitation of the synthetic route for 2-ethynylanilines as a starting material for the palladium catalyzed cyclization with alkenylation reaction.

Based on the background described above, we now report the cyclization reaction of ethyl 2-alkynylphenylcarbamates in the presence of alkenes using a palladium(II) catalyst and TBAF to produce 2,3-disubstituted indoles.

The reaction conditions for the cyclization reaction of alkynylanilines (**1**) to form 2,3-disubutituted indoles (**2**) were examined using ethyl 2-phenylethynylphenylcarbamate and methyl acrylate as shown in Table 1. The amount of TBAF influenced the yields of the cyclization. A stoichiometric amount of TBAF was required (runs 1, 2), but the cyclization reaction under dry conditions using anhydrous $CuCl_2$ instead of $CuCl_2 \cdot H_2O$ in dry tetrahydrofuran (THF) occurred with only a low yield (run 8). Differences in the reaction solvent did not significantly influence the yields (runs 4—7). For the cyclization reaction, $Cu(OAc)_2$, 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), and pyridine 1-oxide did not work at all as a re-oxidant (runs 9—11). As a result, the reaction using TBAF (1.2 eq), palladium dichloride and $CuCl_2 \cdot H_2O$ as a re-oxidant in THF at refluxing temperature gave **2a** in 64% yield (run 5). The cyclization of **1a** with ethyl acrylate under the previous conditions ($PdCl_2$, $CuCl_2$, K_2CO_3 and NaOAc in acetonitrile at 50 °C) proceeded in only 34% yield.[6)]

Under the same reaction conditions, the cyclization of various 2-ethynylanilines with alkenes was investigated. As shown in Table 2, the synthesis of 2-aryl- (*e.g.*, run 2) and 2-alkyl-3-alkenylindoles (run 6) could be achieved in 42—68% using the corresponding alkenes and 2-ethynylanilines, which were prepared by the Sonogashira reaction of the 2-iodoanilines with the terminal alkynes. The cyclization reaction in the presence of alkenes having either an electron-withdrawing (runs 1, 2, 6—11) or electron-donating group (runs 3, 4) occurred. The synthesis of the 2,3-disubstituted indoles with a functional group like cyano (run 8), chloro (runs 7, 9), or methoxy group (run 5) in benzene can be achieved under the same conditions using the corresponding ethynylanilines

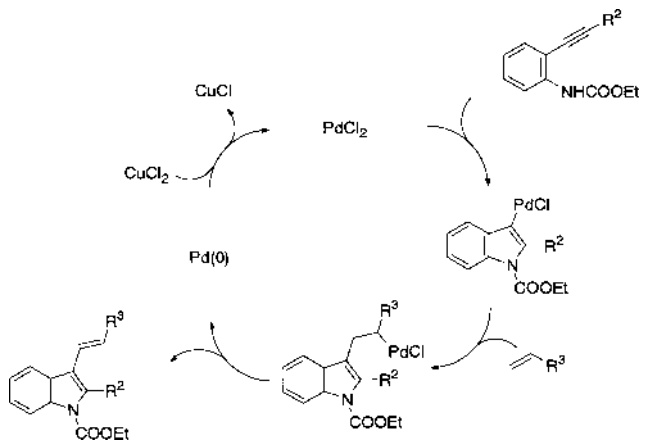

Chart 1

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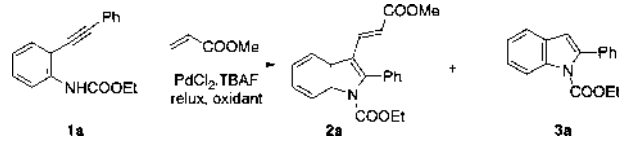
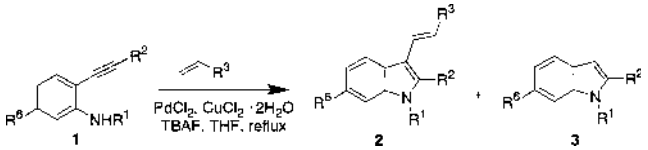
Table 1. The Cyclization Reaction in Presence of Methyl Acrylate under Verious Conditions



1a 2a 3a

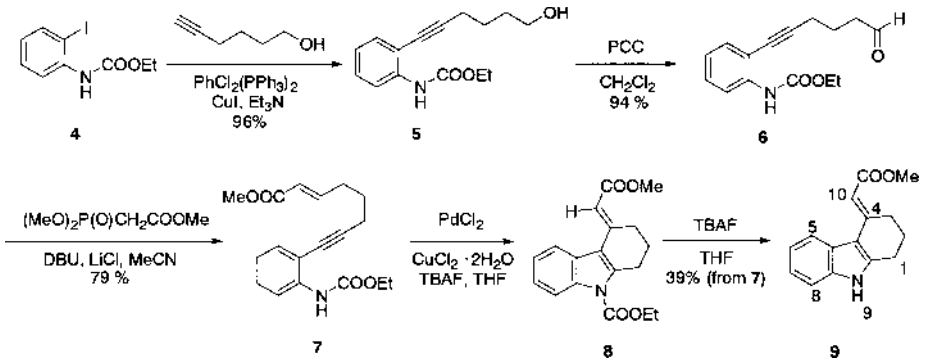
Run	TBAF	COOMe	Solvent	Oxidant	Time (h)	**2a**	**3a**
1	1.0	1.0	THF	$CuCl_2 \cdot 2H_2O$	18	52	0
2	0.25	1.0	THF	$CuCl_2 \cdot 2H_2O$	2	22	42
3	1.5	1.5	THF	$CuCl_2 \cdot 2H_2O$	17	63	11
4	1.2	1.5	THF	$CuCl_2 \cdot 2H_2O$	4	64	17
5	1.2	1.5	MeCN	$CuCl_2 \cdot 2H_2O$	2	60	19
6	1.2	1.5	THF–H_2O	$CuCl_2 \cdot 2H_2O$	20	52	9
7	1.2	1.5	MeCN–H_2O	$CuCl_2 \cdot 2H_2O$	47	54	15
8	1.2	1.5	Dry THF	$CuCl_2$	24	17	0
9	1.2	1.5	THF	$Cu(OAc)_2$	24	0	0
10	1.2	1.5	THF	DDQ	24	0	0
11	1.2	1.5	THF	pyridine 1-oxide	24	0	0

Table 2. The Cyclizaiton Reaction of Various 2-Ethynylanilines in Presence of Alkenes



1 2 3

Run		R^1	R^2	R^3	R^6	Time (h)	**2**	**3**
1	**a**	COOEt	Ph	COOMe	H	4	64	17
2	**b**	Boc	Ph	COOMe	H	4	57	19
3	**c**	Ms	Bu	COOMe	H	1	58	39
4	**d**	COOEt	Ph	Bu	H	3	68	0
5	**e**	COOEt	Ph	Bu	MeO	8	42	0
6	**f**	COOEt	Bu	COOMe	H	6	42	34
7	**g**	COOEt	Ph	COOMe	Cl	6	66	0
8	**h**	COOEt	Ph	COOMe	CN	22	66	0
9	**i**	COOEt	Ph	CN	Cl	4.5	31	0
10	**j**	COOEt	Ph	Ac	H	16	51	9
11	**k**	COOEt	^{t}Bu	Ac	H	25	22	16



4 5 6 7 8 9

Chart 2

with the functional groups as the starting materials.

When the reaction of the 2-ethynylaniline derivative with an internal alkene occurs, it can construct another carbocycle. We first tried the cyclization of methyl 8-[2-(ethoxycarbonylamino)phenyl]oct-2-en-7-ynoate (**7**). According to Grissom's synthetic method,[8] **7** was prepared from ethyl 2-iodophenylcarbamate in 71% overall yield *via* three steps, *i.e.*, the Sonogashira reaction, the oxidation with pyridinium chlorochromate, and the Horner–Emmons reaction with trimethyl phosphonoacetate as shown in Chart 2. The cyclization reaction of **7** proceeded, but it gave a mixture of the corresponding carbazole (**8**) and unknown compound, which could not be completely separated by column chromatography. In order to confirm the structure of **8**, we tried the deprotection of the *N*-ethoxycarbonyl group with sodium methoxide in THF to get methyl 2-(1,2,3,4-trihydrocarbazol-

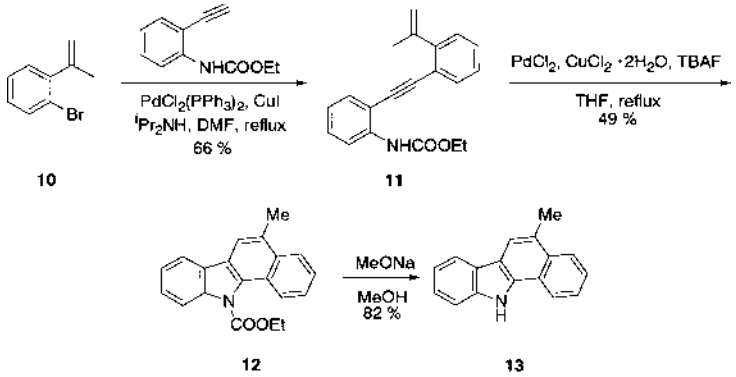


Chart 3

4-ylidene)acetate (**9**) in 39% yield (2 steps). Compound **9** had an *E*-configuration in the double bond, which was determined from the nuclear Overhauser effect spectroscopy (NOESY) spectrum. The H-10 (δ 6.40) proton of **9** has a NOESY correlation to the H-5 (δ 7.90—7.93) proton.

We investigated the intramolecular reaction of ethyl 2-[2-(2-propenyl)phenylalkynyl]phenylcarbamate (**11**) which was also easily prepared by the Sonogashira reaction of 1-bromo-2-(2-propenyl)benzene with a terminal acetylene. We proposed that the alkene moiety in **11** connects to the benzene ring which is an electron withdrawing group, and the carbon-carbon bond formation occurred on the terminal carbon atom of the alkene to give 3-methyl-9-ethoxycarbonylbenzo[*a*]carbazole (**12**).

The results of this study show that the palladium(II)-catalyzed cyclization reaction of the ethynylphenylcarbamates with TBAF in the presence of not only alkenes with electron-withdrawing groups, but also alkenes such as hexene, gave the corresponding 2,3-disubstituted indoles, and the intramolecular cyclization also gave the corresponding carbazoles, although some problems still remain with respect to the cyclization reaction yields.

Experimental

General All melting points and boiling points are uncorrected. IR spectra were taken on a JASCO IR-810 and Shimadzu FT-IR 8400 spectrophotometer. ^{1}H-NMR spectra were recorded on Varian Gemini 200 (300 MHz) spectrometers. Chemical shifts are expressed in δ (ppm) values with tetramethylsilane (TMS) as the internal reference, and coupling constants are expresses in herts (Hz). Mass spectra (MS) and high resolution mass spectra were recorded on JMS-DX303 and JMS-AX500 instruments. Column chromatography was carried out with silica gel [Silica gel 60 N (Kanto chemical)]

General Procedure A mixture of 2-ethynyl anilines (1 mmol), alkenes (1.5 mmol), $PdCl_2$ (5 mol%), $CuCl_2 \cdot 2H_2O$, 1 M TBAF–THF solution (1.2 ml) and THF (20 ml) was refluxed. Water was added to the mixture and the mixture was extracted with AcOEt. The residue obtained from the extract was purified by silica gel column chromatography. The product was purified by distillation or recrystallization.

Methyl (*E*)-3-(1-Ethoxycarbonyl-2-phenylindol-3-yl)propenoate (**2a**): Colorless prisms from hexane–acetone; mp 115—116 °C. IR (KBr) cm^{-1}: 1732, 1699. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, t, J=7.1 Hz), 3.75 (3H, s), 4.16 (2H, q, J=7.1 Hz), 6.57 (1H, d, J=16.5 Hz), 7.31—7.48 (7H, m), 7.55 (1H, d, J=16.2 Hz), 7.93 (1H, d, J=7.4 Hz), 8.29 (1H, d, J=7.4 Hz). MS *m/z* 349 (M$^+$). *Anal.* Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48; N, 4.01. Found: C, 72.23; H, 5.55; N, 3.97.

1-Ethoxycarbonyl-2-phenylindole (**3a**)[5]: Colorless viscous oil. IR (neat) cm^{-1}: 1736. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (3H, t, J=7.1 Hz), 4.24 (2H, q, J=7.1 Hz), 6.60 (1H, s), 7.24—7.46 (7H, m), 7.56 (1H, d, J=7.3 Hz), 8.20 (1H, d, J=8.2 Hz). MS *m/z* 265 (M$^+$).

Methyl (*E*)-3-(1-*tert*-Butoxycarbonyl-2-phenylindol-3-yl)propenoate (**2b**): Colorless viscous oil. IR (KBr) cm^{-1}: 1734, 1632. ^{1}H-NMR ($CDCl_3$) δ: 1.23 (9H, s), 3.75 (3H, s), 6.54 (2H, d, J=16.2 Hz), 7.33—7.49 (7H, m), 7.54 (1H, d, J=16.2 Hz), 7.92 (1H, d, J=7.1 Hz), 8.31 (1H, d, J=7.1 Hz). High resolution (HR)-MS *m/z*: 377.1627 (Calcd for $C_{23}H_{23}NO_4$: 377.1622).

1-*tert*-Butoxycarbonyl-2-phenylindole (**3b**): Colorless scales from hexane–Et_2O; mp 76—77 °C (lit.[10] 76—77 °C). IR (KBr) cm^{-1}: 1720. ^{1}H-NMR ($CDCl_3$) δ: 1.30 (9H, s), 6.65 (1H, s), 7.23—7.42 (7H, m), 7.54 (1H, d, J=8.2 Hz), 8.22 (1H, d, J=8.2 Hz). MS *m/z* 293 (M$^+$).

Methyl (*E*)-3-(1-Methylesulfonyl-2-butylindol-3-yl)propenoate (**3c**): Colorless needles form hexane–Et_2O; mp 128—129 °C. IR (KBr) cm^{-1}: 1710, 1377. ^{1}H-NMR ($CDCl_3$) δ: 0.96 (3H, t, J=7.4 Hz), 1.41—1.48 (2H, m), 1.65—1.72 (2H, m), 3.09 (3H, s), 3.15 (2H, t, J=7.4 Hz), 3.85 (3H, s), 6.58 (1H, d, J=16.0 Hz), 7.34—7.40 (2H, m), 7.84—7.87 (1H, m), 7.89 (1H, d, J=16.0 Hz), 8.06—8.10 (1H, m). HR-MS *m/z*: 335.1197 (Calcd for $C_{17}H_{21}NO_4S$: 335.1191). *Anal.* Calcd for $C_{17}H_{21}NO_4S \cdot 1/4H_2O$: C, 60.07; H, 6.37; N, 4.12; S, 9.43. Found: C, 60.10; H, 6.29; N, 4.13; S, 9.61.

1-Methylesulfonyl-2-phenylindole (**3c**): Colorless needles from hexane–Et_2O; mp 115—116 °C (lit.[5] 116—117 °C). IR (KBr) cm^{-1}: 1370. ^{1}H-NMR ($CDCl_3$) δ: 2.74 (3H, s), 6.73 (1H, s), 7.35—7.45 (5H, m), 7.56—7.63 (3H, m), 8.15 (1H, d, J=7.1 Hz). MS *m/z*: 271 (M$^+$).

1-Ethyoxycarbonyl-2-phenyl-3-[(1*E*)-hexenyl]indole (**2d**): Colorless viscous oil; IR (neat) cm^{-1}: 1729. ^{1}H-NMR ($CDCl_3$) δ: 0.89 (3H, t, J=6.3 Hz), 0.98 (3H, t, J=7.1 Hz), 1.29—1.41 (4H, m), 2.14 (2H, q, J=6.3 Hz), 4.15 (2H, q, J=7.1 Hz), 6.17 (1H, d, J=17.0 Hz), 6.27 (1H, dt, J=17.0, 6.3 Hz), 7.29—7.43 (7H, m), 7.88 (1H, d, J=8.2 Hz), 8.26 (1H, d, J=8.2 Hz). HR-MS *m/z*: 347.1901 (Calcd for $C_{23}H_{25}NO_2$: 347.1886).

1-Ethoxycarbonyl-2-phenyl-3-[(1*E*)-hexenyl]-6-methoxyindole (**2e**): Colorless viscous oil. IR (neat) cm^{-1}: 1730. ^{1}H-NMR ($CDCl_3$) δ: 0.94 (6H, m), 1.37 (4H, m), 2.14 (2H, q, J=6.9 Hz), 3.91 (3H, s), 4.12 (2H, q, J=7.1 Hz), 6.15 (1H, d, J=16.2 Hz), 6.26 (1H, dt, J=16.2, 6.5 Hz), 6.95 (1H, dd, J=8.8, 2.5 Hz), 7.30—7.44 (5H, m), 7.75 (1H, d, J=8.8 Hz), 7.87 (1H, d, J=2.5 Hz). HR-MS *m/z*: 377.1968 (Calcd for $C_{24}H_{27}NO_3$: 377.1990).

Methyl (*E*)-3-(1-Ethoxycarbonyl-2-butylindol-3-yl)propenoate (**2f**): Colorless viscous oil. IR (neat) cm^{-1}: 1736, 1628. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, t, 7.4), 1.39—1.65 (7H, m), 3.20 (2H, t, 7.4), 3.84 (3H, s), 4.56 (2H, q, 7.1), 6.57 (1H, d, 16.0), 7.30—7.34 (2H, m), 7.82—7.85 (1H, m), 7.93 (1H, d, 16.0), 8.14—8.17 (1H, m). HR-MS *m/z*: 329.1642 (Calcd for $C_{19}H_{23}NO_4$: 329.1627).

1-Ethoxycarbonyl-2-butylindole (**3f**): White solid. bp 180—190 °C/3 mmHg, mp 35 °C (lit.[5] 35 °C). IR (KBr) cm^{-1}: 1730. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, t, J=7.4 Hz), 1.49—1.51 (5H, m), 1.64—1.74 (2H, m), 3.01 (2H, t, J=6.8 Hz), 4.52 (2H, q, J=7.4 Hz), 6.37 (1H, s), 7.17—7.24 (2H, m), 7.44 (1H, d, J=5.9 Hz), 8.11 (1H, d, J=8.2 Hz). MS *m/z* 245 (M$^+$).

Methyl (*E*)-3-(1-Ethoxycarbonyl-2-phenyl-6-chloroindol-3-yl)propenoate (**2g**): Colorless needles from acetone–hexane. mp 172—173 °C. IR (KBr) cm^{-1}: 1745, 1722, 1634. ^{1}H-NMR ($CDCl_3$) δ: 0.94 (3H, t, J=7.2 Hz), 3.75 (3H, s), 4.18 (2H, q, J=7.2 Hz), 6.48 (1H, d, J=16.2 Hz), 7.32—7.48 (6H, m), 7.50 (1H, d, J=16.2 Hz), 7.82 (1H, d, J=8.7 Hz), 8.32 (1H, d, J=1.8 Hz). HR-MS *m/z*: 383.0912 (Calcd for $C_{21}H_{18}ClNO_4$: 383.0923). *Anal.* Calcd for $C_{21}H_{18}ClNO_4$: C, 65.71; H, 4.73; N, 3.65. Found: C, 65.79; H, 4.84; N, 3.58.

Methyl (*E*)-3-(1-Ethoxycarbonyl-2-phenyl-6-cyanoindol-3-yl)propenoate (**2h**): Colorless needles from acetone–hexane. mp 237—239 °C. IR (KBr) cm^{-1}: 2222, 1753, 1722, 1637. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, J=7.1 Hz), 3.76 (3H, s), 4.21 (2H, q, J=7.1 Hz), 6.47 (1H, d, J=16.5 Hz), 7.33—7.53 (6H, m), 7.64 (1H, d, J=8.5 Hz), 7.98 (1H, d, J=8.5 Hz), 8.65 (1H, s). HR-

MS *m/z*: 374.1257 (Calcd for $C_{22}H_{18}N_2O_4$: 374.1265). *Anal.* Calcd for $C_{22}H_{18}N_2O_4 \cdot 1/4H_2O$: C, 69.74; H, 4.92; N, 7.39. Found: C, 70.00; H, 5.03; N, 7.31.

(*E*)-3-(1-Ethoxycarbonyl-2-phenyl-6-chloroindol-3-yl)propenitrile (**2i**): Pale yellow viscous oil. IR (neat) cm^{-1}: 2216, 1742. ^{1}H-NMR ($CDCl_3$) δ: 0.98 (3H, t, J=7.1 Hz), 4.16 (2H, q, J=7.1 Hz), 5.84 (1H, d, J=16.8 Hz), 7.15 (1H, d, J=16.8 Hz), 7.30—7.52 (6H, m), 7.67 (1H, d, J=8.5 Hz), 8.34 (1H, s). HR-MS *m/z*: 350.0833 (Calcd for $C_{20}H_{15}ClN_2O_2$: 350.0822).

1-Ethoxycarbonyl-2-phenyl-3-[3-oxo-(1*E*)-butenyl]indole (**2j**): Pale yellow viscous oil. IR (neat) cm^{-1}: 1740, 1688, 1660. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (3H, t, J=7.1 Hz) 2.33 (3H, s), 4.19 (2H, q, J=7.1 Hz), 6.85 (1H, d, J=16.5 Hz), 7.33—7.51 (8H, m), 7.95 (1H, d, J=7.8 Hz), 8.29 (1H, d, J=7.9 Hz). HR-MS *m/z*: 333.1380 (Calcd for $C_{21}H_{19}NO_3$: 333.1364).

1-Ethoxycarbonyl-2-*tert*-butyl-3-[3-oxo-(1*E*)-butenyl]indole (**2k**): Colorelss viscous oil. IR ($CHCl_3$) cm^{-1}: 1743, 1685, 1599. ^{1}H-NMR ($CDCl_3$) δ: 1.48 (3H, t, J=7.2 Hz), 1.58 (9H, s), 2.41 (3H, s), 4.50 (2H, q, J=7.2 Hz), 6.69 (1H, d, J=16.2 Hz), 7.20—7.33 (2H, m), 7.68—7.74 (2H, m), 8.00 (1H, d, J=16.2 Hz). HR-MS *m/z*: 313.1702 (Calcd for $C_{19}H_{23}NO_3$: 313.1678).

1-Ehoxycarbonyl-2-*tert*-butylindole (**3k**): Pale yellow viscous oil. IR (KBr) cm^{-1}: 1740. ^{1}H-NMR ($CDCl_3$) δ: 1.51 (9H, s), 1.52 (3H, t, J= 7.2 Hz), 4.53 (2H, q, J=7.2 Hz), 6.51 (1H, s), 7.17 (1H, t, J=7.1 Hz), 7.20 (1H, t, J=7.1 Hz), 7.45 (1H, d, J=7.1 Hz), 7.92 (1H, d, J=7.1 Hz). HR-MS *m/z*: 245.1394 (Calcd for $C_{15}H_{19}NO_2$: 245.3169).

6-[(2-Ethoxycarbonylamino)phenyl]hex-5-yn-1-ol (5) A mixture of ethyl 2-iodophenylcarbamate (522 mg, 1.80 mmol), 5-hexynyl-1-ol (212 mg, 2.16 mmol), $PdCl_2(PPh_3)_2$ (63 mg, 0.90 mmol), CuI (35 mg, 1.80 mmol), and Et_3N (20 ml) was stirred at room temperature for 3 h. Water (50 ml) was added to the mixture and extracted with AcOEt (30 ml×3). The AcOEt layer was washed with water (50 ml×2). The residue obtained from the AcOEt extract was purified by silica gel column chromatography using AcOEt–hexane (1 : 10) as an eluent. The product was purified by distillation. Pale yellow liquid (451 mg, 96%). bp 180—190 °C (45 mmHg). IR ($CHCl_3$) cm^{-1}: 3400, 1740. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, t, J=6.0 Hz), 1.67—1.77 (5H, m), 2.56 (2H, t, J=6.6 Hz), 3.72—3.75 (2H, m), 4.25 (2H, q, J=7.1 Hz), 6.95 (2H, t, J=7.7 Hz), 7.27—7.34 (2H, m), 8.10 (1H, d, J=8.2 Hz). HR-MS *m/z*: 261.1327 (Calcd for $C_{15}H_{19}NO_3$: 261.1364).

6-[(2-Ethoxycarbonylamino)phenyl]hex-5-ynal (6) Pyridinium chlorochromate (6.0 g, 28 mmol) was added to a mixture of **5** (4.0 g, 14 mmol), Celite® (1.0 g), and CH_2Cl_2 (50 ml). After stirring for 2 h at room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved to $CHCl_3$. The solution was filtered through Celite® pad and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as an eluent. The product was purified by distillation. Pale yellow liquid (3.4 g, 94%), bp 130—145 °C (45 mmHg). IR ($CHCl_3$) cm^{-1}: 3400, 1730, 1720. ^{1}H-NMR ($CDCl_3$) δ: 1.32 (3H, t, J=7.3 Hz), 2.00 (2H, quintet, J=6.9 Hz), 2.58 (2H, t, J=6.9 Hz), 2.68 (2H, t, J=7.1 Hz), 4.24 (2H, q, J=7.1 Hz), 6.97 (1H, d, J=8.7 Hz), 7.26—7.35 (2H, m), 8.10 (1H, d, J=8.5 Hz), 9.58 (1H, s). HR-MS *m/z*: 259.1195 (Calcd for $C_{15}H_{17}NO_3$: 259.1207).

Methyl (*E*)-8-[2-(Ethoxycarbonylamino)phenyl]oct-2-en-7-ynoate (7) 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) (2.65 g, 17.4 mmol) in dry MeCN (30 ml) was added to a mixture of trimethyl phosphonoacetate (3.17 g, 17.4 mmol), LiCl (983 mg, 23.2 mmol), and dry MeCN (30 ml) under Ar atmosphere. After stirring for 30 min at room temperature, **6** (566 mg, 2.3 mmol) in MeCN (10 ml) was added to the mixture. The mixture was stirred at room temperature for 1 h and concentrated under reduced pressure. Water (100 ml) was added to the residue and extracted with $CHCl_3$ (100 ml×3). The residue obtained from the $CHCl_3$ extract was purified by silica gel column chromatography using AcOEt–hexane (1 : 3) as an eluent. The product was purified by distillation. Colorless liquid (2.9 g, 79%), bp 162—180 °C (45 mmHg). IR ($CHCl_3$) cm^{-1}: 3400, 1730, 1210. ^{1}H-NMR ($CDCl_3$) δ: 1.33 (3H, t, J=7.1 Hz), 1.81 (2H, quintet, J=7.4 Hz), 2.40 (2H, q, J=6.0 Hz), 2.54 (2H, t, J=7.1 Hz), 3.73 (3H, s), 4.25 (2H, q, J=7.1 Hz), 5.90 (1H, d, J=18.9 Hz), 6.93—7.04 (2H, m), 7.25—7.35 (3H, m), 8.12 (1H, d, J=8.5 Hz). HR-MS *m/z*: 315.1452 (Calcd for $C_{18}H_{21}NO_4$: 315.1469).

Methyl (*E*)-2-(1,2,3,4-Trihydrocarbazol-4-ylidene)acetate (9) After **7** (510 mg, 1.62 mmol) was dropped into a mixture of $PdCl_2$ (57 mg, 0.34 mmol), $CuCl_2 \cdot 2H_2O$ (552 mg, 3.24 mmol), 1 M TABF in THF (1.90 ml, 1.90 mmol), and THF (30 ml) at refluxing temperature during 30 min, the resultant mixture was refluxed for 1 h. The mixture was filtrated and THF was removed under reduced pressure. Water (50 ml) was added to the residue and the mixture was extracted with AcOEt (30 ml×3). The AcOEt layer was washed with brine (50 ml×2). One molar TBAF in THF (1.80 ml, 1.80 mmol) and THF (30 ml) were added to the residue obtained from the AcOEt extract. After the mixture had been refluxed for 5 h, the mixture was concentrated under reduced pressure. The residue was dissolved with AcOEt (50 ml) and the AcOEt solution was washed with brine (50 ml×2). The residue obtained from the AcOEt extract purified by silica gel column chromatography using AcOEt–hexane (1 : 15) as an eluent. The product was purified by recrystallization from acetone–hexane. Colorless prisms (152 mg, 39%), mp 176—178 °C. IR (nujol) cm^{-1}: 3277, 1682. ^{1}H-NMR ($CDCl_3$) δ: 2.03 (2H, quintet, 6.3), 2.87 (2H, t, 6.3), 3.26—3.30 (2H, m), 3.75 (3H, s), 6.40 (1H, s), 7.20—7.23 (2H, m), 7.32—7.35 (1H, m), 7.90—7.94 (1H, m), 8.25 (1H, br). HR-MS *m/z*: 241.1120 (Calcd for $C_{15}H_{15}NO_2$: 241.1102). *Anal.* Calcd for $C_{15}H_{15}NO_2 \cdot 1/8H_2O$: C, 74.02; H, 6.25; N, 5.53. Found: C, 73.98; H, 6.31; N, 5.75.

Ethyl 2-(2-(2-Propenylphenyl)ethynyl)phenylcarbamete (11) After ethyl 2-ethynylphenylcarbamate (421 mg, 2.23 mmol) in *N*,*N*-dimethylformamide (DMF) (5 ml) was dropped into a mixture of 1-bromo-2-(2-propenyl)benzene (364 mg, 1.86 mmol), $PdCl_2(PPh_3)_2$ (65 mg, 0.93 mmol), CuI (18 mg, 0.93 mmol), diisopropylamine (3 ml), and DMF (5 ml) at refluxing temperature during 1 h, the resultant mixture was refluxed for 2 h. Water (50 ml) was added to the mixture and extracted with Et_2O (50 ml×3). The ethereal layer was washed with brine (50 ml×3). The residue obtained from the ethereal extract purified by silica gel column chromatography using AcOEt–hexane (1 : 20) as an eluent. Colorless viscous oil (377 mg, 67%). IR ($CHCl_3$) cm^{-1}: 1740. ^{1}H-NMR ($CDCl_3$) δ: 1.36 (3H, t, J=7.1 Hz), 2.21 (3H, s), 4.29 (2H, q, J=7.1 Hz), 5.23 (1H, s), 5.40 (1H, s), 7.00 (1H, dt, J=1.1, 7.4 Hz), 7.24—7.35 (4H, m), 7.45 (1H, d, J=6.9 Hz), 7.55—7.57 (2H, m), 8.21 (1H, d, J=8.5 Hz). HR-MS *m/z*: 305.1394 (Calcd for $C_{20}H_{19}NO_2$: 305.1415).

5-Methyl-11-ethoxycarbonylbenzo[*a*]carbazole (12) According to the synthetic procedure for **8**, **12** was obtained from the reaction using **11** (71 mg, 0.23 mmol). Colorless viscous oil (35 mg, 49%). IR ($CHCl_3$) cm^{-1}: 1732. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, t, J=7.1 Hz), 2.81 (3H. s), 4.59 (2H, q, J=7.1 Hz), 7.39 (1H, t, J=8.0 Hz), 7.47 (1H, t, J=8.0 Hz), 7.54—7.57 (2H, m), 7.88 (1H, s), 7.99 (1H, d, J=7.4 Hz), 8.09—8.13 (1H, m), 8.21 (1H, d, J=7.4 Hz), 8.27—8.31 (1H, m). HR-MS *m/z*: 303.1284 (Calcd for $C_{20}H_{17}NO_2$: 303.1260).

5-Methylbenzo[*a*]carbazole (13) A mixture of **14** (100 mg, 0.33 mmol), 3 N KOH (0.17 ml), and methanol (5 ml) was refluxed for 1 h. The methanol was removed under reduced pressure. Water (100 ml) was added to the residue and extracted with $CHCl_3$ (50 ml×3). The residue obtained from the $CHCl_3$ extract was purified by silica gel column chromatography using AcOEt–hexane (1 : 20) as an eluent. The product was purified by recrystallization from acetone–hexane. Colorless prisms (62 mg, 82%). mp 183—185 °C. IR (KBr) cm^{-1}: 3412. ^{1}H-NMR ($CDCl_3$) δ: 2.81 (3H, s), 7.26—7.31 (1H, m), 7.39—7.45 (1H, m), 7.55—7.62 (3H, m), 7.98 (1H, s), 8.09—8.15 (3H, m), 8.72 (1H, bs). ^{13}C ($CDCl_3$) δ: 19.4, 110.6, 117.6, 119.2, 119.4, 119.5, 120.5, 120.9, 123.8, 124.3, 124.7, 124.9, 125.2, 125.6, 131.3, 133.6, 138.1. MS *m/z*: 231 (M^+). *Anal.* Calcd for $C_{17}H_{13}N$: C, 88.28; H, 5.67; N, 6.06. Found: C, 88.37; H, 5.94; N, 5.97.

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