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A General Synthesis of Indole-3-carboxylic Esters by Palladium-Catalyzed Direct Oxidative Carbonylation of 2-Alkynylaniline Derivatives

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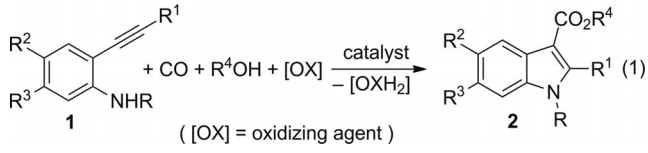
A general synthesis of indole-3-carboxylic esters by direct Pd-catalyzed oxidative carbonylation of readily available 2-alkynylaniline derivatives is reported. In particular, 2-alkynylanilines bearing an internal triple bond and a secondary amino group (**1**) were directly converted into indole-3-carboxylic esters **2** in fair to good yields (50–84 %) when let to react with CO, O_2, and an alcohol in the presence of the PdI_2/KI catalytic system, under relatively mild conditions [100 °C and 20 atm (at 25 °C) of a 4:1 mixture CO/air]. On the other hand, under similar conditions, but in the presence of $HC(OMe)_3$, 2-alkynylanilines bearing an internal triple bond and a primary amino group (**7**) afforded 1-(dimethoxymethyl)indole-3-carboxylic esters **9** through the intermediate formation of *N*-(dimethoxymethyl)-2-alkynylaniline derivatives **II**. Compounds **9** could be conveniently converted into *N*-unsubstituted indole-3-carboxylic esters **10** by a simple acidic treatment carried out in $MeOH/H_2O$ at 80 °C.

Introduction

Indole-3-carboxylic esters are a very important class of heterocyclic compounds. A variety of molecules incorporating this heterocyclic motif has in fact shown a wide range of biological activities,[1–10] including anticancer,[1] antiviral,[2] antibacterial,[3] antiinflammatory,[4] 5-HT4 antagonist,[5] inhibitor of 5-lipoxygenase,[6] serotonin receptor antagonist,[7] modulator of nicotinic receptors,[8] and S1P receptor antagonist[9] activities, among others.[10] Moreover, these compounds have proved to be valuable synthetic intermediates for the preparation of different indole derivatives.[11] Indole-3-carboxylic esters have been so far obtained by various synthetic approaches. More specifically, compounds belonging to the sub-class of 5-oxyindole-3-carboxylic ester have been prepared by a classical method, involving the reaction between benzoquinone and β-aminocrotonic esters (Nenitzescu reaction).[12] More recently, several novel approaches have been developed, mainly based on cyclization reactions and transition-metal catalysis, which include the intramolecular Pd-catalyzed condensation of halophenylenamino esters,[13] the DMAP-promoted reaction between suitably substituted arylhydroxylamines and methyl propiolate,[14] the Pd^0-catalyzed intramolecular α-arylation of β-(2-iodoanilino) esters,[15] the Cu^I-catalyzed intramolecular amination of (2-bromophenyl)acetates,[16] and the Pd^0-catalyzed reductive cyclization of 2-(2-nitrophenyl)acrylates,[17] among others.[18] Metallation of the indole ring at C-3 followed by the reaction with an alkyl chloroformate has also been reported.[19]

An attractive alternative method for the synthesis of indole-3-carboxylic esters **2** would consist in the direct oxidative carbonylation of 2-alkynylanilines **1**, according to Equation (1). The possibility to obtain some particular indole-3-carboxylic esters by oxidative carbonylation of simple or *N*-(methylsulfonyl)-substituted 2-alkynylanilines has been briefly mentioned in the literature (30–76%, 4 examples).[20] The general applicability of this method, however, was not demonstrated; moreover, an excess of a metallic reoxidant ($CuCl_2$, 3 equiv. with respect to the substrate) and of two different bases (2 equiv. of AcONa and 2 equiv. of K_2CO_3) was needed for the reaction to occur, with a maximum turnover number of ca. 11 mol of product per mol of palladium. Therefore, the development of a more efficient, selective and general method for the direct synthesis of **2** by oxidative carbonylation of **1** is still highly desirable. In this work, we report such a method, which is based on the use of the



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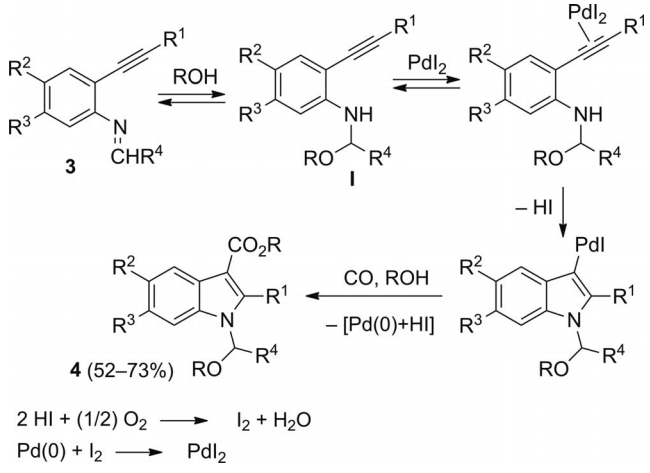
PdI_2/KI system as the catalyst,[21] in the presence of only oxygen as the oxidizing agent; see Equation (1), catalyst: PdI_2/KI, [OX] = (1/2)O_2, [OXH_2] = H_2O.

Results and Discussion

We have recently reported an innovative approach to 1-(alkoxyarylmethyl)indole-3-carboxylic esters **4**, based on an unprecedented multicomponent cascade reaction, involving ROH addition to the imino group of 2-alkynylaniline imines **3** to give [(alkoxymethyl)(2-alkynylaryl)]amines **I** as intermediates, followed by the PdI_2-catalyzed reaction of the latter with CO, ROH, and O_2 to give the final products



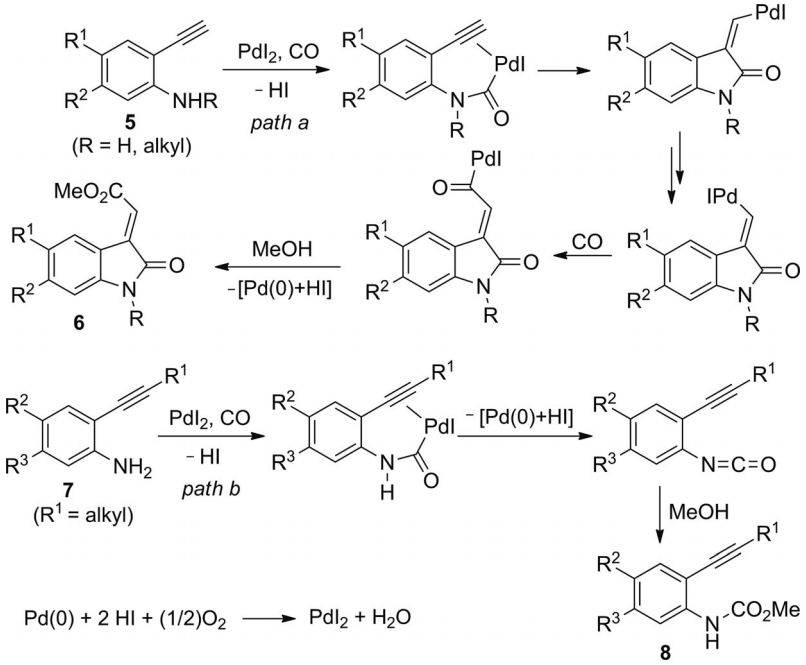
Scheme 1. Multicomponent cascade reaction leading to 1-(alkoxyarylmethyl)indole-3-carboxylic esters **4** from 2-alkynylaniline imines **3** through the intermediate formation of [(alkoxymethyl)(2-alkynylaryl)]amines **I**.[22]

(Scheme 1; anionic iodide ligands are omitted for clarity).[22] Reactions were carried out at 80 °C in a 3:1 $HC(OMe)_3$/MeOH mixture as the solvent, in the presence of 2 mol-% of PdI_2 in conjunction with an excess of KI (KI/PdI_2 molar ratio 10:1), and under a total pressure of 40 atm of a 4:1 mixture CO/air.

The reactivity showed by [(alkoxymethyl)(2-alkynylaryl)]-amines **I** in this process was completely different from that we previously observed in the case of 2-ethynylanilines bearing a terminal triple bond and a primary or secondary amino group (**5**) which, under analogous conditions, selectively led to dihydroindol-2-one derivatives **6** through a cyclocarbonylation–alkoxycarbonylation process, (Scheme 2, path *a*),[23] and from that observed in the case of 2-alkynylanilines bearing an internal triple bond and a primary amino group (**7**), which led to the formation of acyclic carbamates **8** through the intermediate formation of isocyanates (Scheme 2, path *b*).[23,24]

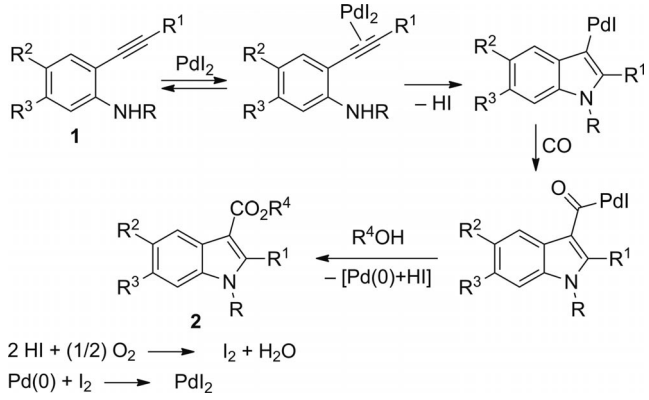
In fact, in the case of **I** (Scheme 1), formation of an isocyanate cannot occur, since the amino group in **I** is secondary, while the cyclocarbonylation-alkoxycarbonylation mechanism is hindered by the fact that an internal triple bond does not insert into a palladium-carbamoyl bond for steric reasons.[25] Therefore, an alternative mechanism takes place, involving 5-*endo*-*dig* intramolecular nucleophilic attack of nitrogen to the triple bond coordinated to Pd^{II}, followed by alkoxycarbonylation, to give **2**, HI and Pd^0. The latter is then reoxidated to PdI_2 according to the mechanism we demonstrated several years ago,[26] involving oxidation of HI by O_2 to give I_2, followed by oxidative addition of the latter to Pd^0 to regenerate PdI_2 (Scheme 1).

These results and considerations prompted us to study in detail the reactivity of *N*-substituted 2-alkynylanilines **1**,



Scheme 2. Formation of dihydroindol-2-one derivatives **6** and (2-alkynylphenyl)carbamates **8** through PdI_2/KI-catalyzed oxidative carbonylation of 2-alkynylaniline derivatives **5** and **7**, respectively.[23,24]

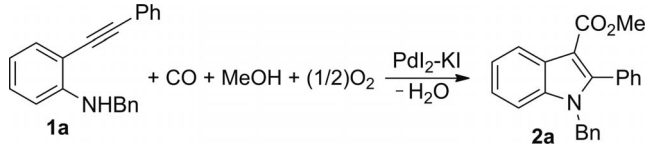
bearing a secondary amino group and an internal triple bond, under PdI_2-catalyzed oxidative carbonylation conditions, in order to develop a general and convenient synthesis of indole-3-carboxylic esters **2**, according to Scheme 3.



Scheme 3. Mechanistic hypothesis for the formation of indole-3-carboxylic esters **2** by PdI_2-catalyzed oxidative carbonylation of *N*-substituted 2-alkynylanilines **1**, bearing a secondary amino group and an internal triple bond.

N-Benzyl-2-(phenylethynyl)aniline (**1a**) was used as a model substrate for assessing the reactivity of secondary 2-alkynylanilines **1** under PdI_2-catalyzed oxidative carbonylation conditions. Carbonylation of **1a** was initially carried out in MeOH at 80 °C and under 20 atm (at 25 °C) of a 4:1 mixture of CO/air, in the presence of 2 mol-% of PdI_2 and 20 mol-% of KI, with a substrate concentration of 0.2 mmol per mL of solvent. After 3 h, conversion of **1a** was ca. 90%, with formation of methyl 1-benzyl-2-phenyl-1*H*-indole-3-carboxylate (**2a**) in 64% GLC (Table 1, entry 1).

Table 1. Reactions of *N*-benzyl-2-(phenylethynyl)aniline (**1a**) with CO, O_2 and MeOH in the presence of PdI_2/KI catalytic system.[a]

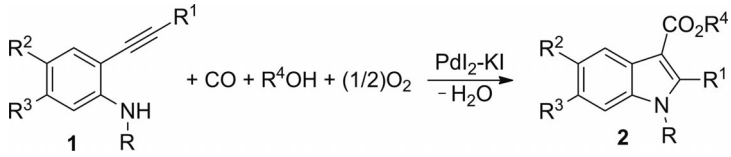


Entry	KI/PdI_2 molar ratio	*T* [°C]	Conc. of **1a**[b]	*t* [h]	Conv. of **1a** [%][c]	Yield of **2a** [%][d]
1	10	80	0.2	3	90	64
2[e]	10	80	0.2	3	79	56
3	5	80	0.2	3	93	61
4	50	80	0.2	3	38	16
5	10	80	0.5	3	95	15
6	10	80	0.1	3	87	72
7	10	80	0.05	3	83	75
8	10	100	0.2	1	100	72
9[f]	10	100	0.2	1	100	66

[a] Unless otherwise noted, all reactions were carried out under 20 atm (at 25 °C) of a 4:1 mixture of CO/air in the presence of 2 mol-% of PdI_2. [b] Mmol of starting **1a** per mL of solvent. [c] Determined by GLC. [d] GLC yield based on starting **1a**. The formation of unidentified heavy products (chromatographically immobile materials) accounted for the difference between the substrate conversion and the product yield. [e] The reaction was carried out under 40 atm (at 25 °C) of a 4:1 mixture CO/air. [f] The reaction was carried out with 1 mol-% of PdI_2.

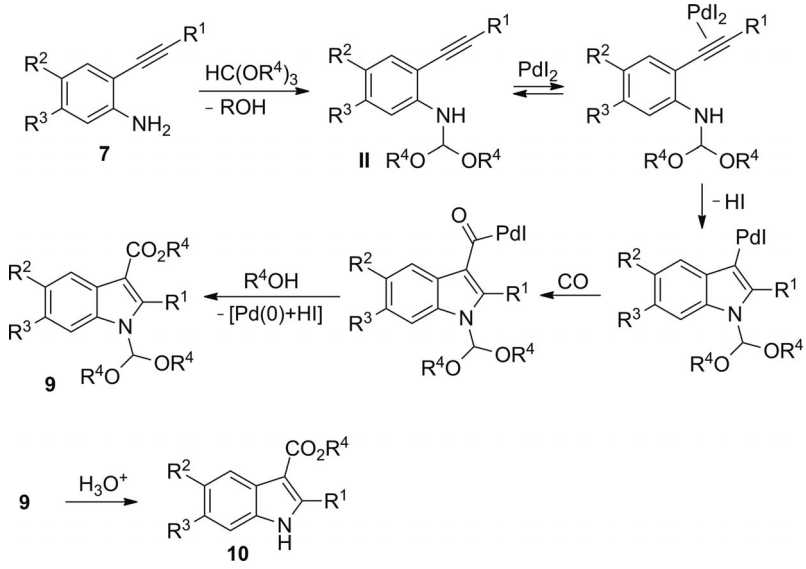
This very promising initial result confirmed the validity of our work hypothesis (Scheme 3). We then carried out a systematic study on the influence of the reaction parameters on product yield; the results obtained by varying pressure, KI/PdI_2 molar ratio, temperature, **1a** concentration, and **1a**/Pd molar ratio are reported in Table 1, entries 2–9. As can be seen from Table 1, the optimal reaction conditions in

Table 2. Synthesis of *N*-substituted indole-3-carboxylic esters **2** by PdI_2/KI-catalyzed oxidative carbonylation of *N*-substituted 2-alkynylanilines **1**.[a]



Entry	**1**	R	R^1	R^2	R^3	R^4	Time [h]	**2**	Yield of **2** [%][b]
1	**1a**	Bn	Ph	H	H	Me	1.5	**2a**	72 (76)
2	**1b**	Bn	*p*-Br-C_6H_4	H	H	Me	2	**2b**	74
3	**1c**	Bn	*p*-Me-C_6H_4	H	H	Me	1	**2c**	81
4	**1d**	Bn	Bu	H	H	Me	2	**2d**	74
5	**1e**	Bn	Ph	Cl	H	Me	3	**2e**	69
6	**1f**	Bn	Ph	Me	H	Me	1	**2f**	77
7[c]	**1g**	Bn	Ph	H	CF_3	Me	3	**2g**	73
8	**1h**	Bn	Ph	H	Me	Me	3	**2h**	78
9	**1i**	Bu	Ph	H	H	Me	3	**2i**	72
10	**1j**	*i*Bu	Bu	H	H	Me	5	**2j**	50
11	**1c**	Bn	*p*-Me-C_6H_4	H	H	Et	2	**2c′**	84
12	**1f**	Bn	Ph	Me	H	Et	3	**2f′**	73

[a] Unless otherwise noted, all reactions were carried out in ROH (substrate concentration: 0.05 mmol of **1** per mL of ROH) at 100 °C under 20 atm (at 25 °C) of a 4:1 mixture of CO/air in the presence of 2 mol-% of PdI_2 and 20 mol-% of KI. [b] Isolated yield (GLC yield) based on starting **1**. [c] The reaction was carried out with a substrate concentration of 0.2 mmol of **1g** per mL of MeOH.



Scheme 4. Formation of 1-(dialkoxymethyl)indole-3-carboxylic esters **9** from primary 2-alkynylanilines **7** in the presence of $HC(OR^4)_3$, and hydrolysis of **9** to give *N*-unsubstituted indole-3-carboxylic esters **10**.

terms of product yield corresponded to a substrate concentration of 0.05 mmol of **1a** per mL of MeOH at 100 °C and under 20 atm total pressure, in the presence of 2 mol-% of PdI_2 in conjunction with 20 mol-% of KI. Under these conditions, **2a** was obtained, after 1.5 h reaction time, in 76% GLC yield (72% isolated, Table 2, entry 1).

The reaction was then successfully extended to several differently substituted 2-alkynylaniniles bearing a secondary amino group **1b**–**j**, as shown by the results reported in Table 2, entries 2–10. As can be seen, fair to high yields (50–81%) of the corresponding *N*-substituted indole-3-carboxylic esters **2b**–**j** could be obtained by varying the substituent on the triple bond as well as on nitrogen and on the aromatic ring. In particular, electron-withdrawing as well as electron-releasing groups on the aromatic ring could be tolerated, and both benzyl and simple alkyl groups (including bulky substituents, such as isobutyl, entry 10) could be present on nitrogen. In the case of particularly deactivated substrates, such as **1g** ($R^3 = CF_3$), better results were observed working with a higher substrate concentration (Table 2, entry 7). The reaction could also be carried out using a higher alcohol, such as EtOH, as the reactant and solvent, as shown in Table 2, entries 11 and 12.

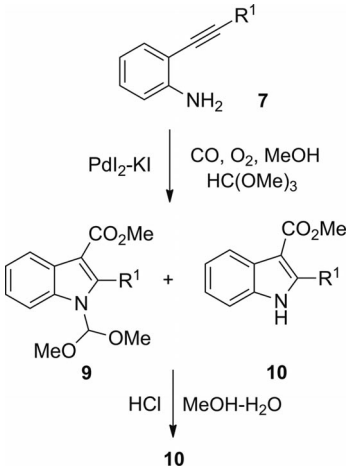
As we have seen above, *N*-unsubstituted indole-3-carboxylic esters could not be obtained by direct PdI_2/KI-catalyzed oxidative carbonylation of primary 2-alkynylanilines **7**, since acyclic carbamates **8** were formed instead (Scheme 2, path *b*). We have, however, explored the possibility to obtain *N*-unsubstituted indole-3-carboxylic esters in an indirect way, by transforming in situ the primary amino group of **7** into a secondary group using an easily removable substituent. We accordingly tested the reactivity of **7** under oxidative carbonylation conditions and in the presence of $HC(OR)_3$, in order to obtain the selective formation of 1-(dialkoxymethyl)indole-3-carboxylic esters **9** through the intermediate formation of acetal derivatives **II** (Scheme 4). *N*-unsubstitued indole-3-carboxylic esters **10** would then be easily produced by removal of the acetal group of **9** under acidic conditions (Scheme 4).

Thus, 2-(phenylethynyl)aniline **7a** (R^1 = Ph, $R^2 = R^3$ = H) was allowed to react under the conditions already optimized for *N*-substituted 2-alkynylanilines **1** [100 °C and 20 atm (at 25 °C) of a 4:1 mixture CO/air, in the presence of 2 mol-% of PdI_2 and 20 mol-% of KI, **7a** concentration = 0.05 mmol of **7a** per mL of solvent], but in a 2:1 $HC(OMe)_3$/MeOH mixture as the solvent (R^4 = Me). After 3 h, methyl 1-(dimethoxymethyl)-2-phenyl-1*H*-indole-3-carboxylate (**9a**) and methyl 2-phenyl-1*H*-indole-3-carboxylate (**10a**) were indeed obtained in 46% and 2% isolated yields, respectively (Table 3, entry 1). According to the synthetic hypothesis shown in Scheme 4, selective formation of the *N*-unsubstituted indole **10a** (48% isolated yield) was attained after treatment of the carbonylation crude with aqueous HCl (Table 3, entry 1). A higher overall isolated yield of **10a** (55%) could be obtained by carrying out the carbonylation step in the presence of a larger amount of catalyst (5 mol-%, Table 3, entry 2). The validity of this 2-step protocol was then assessed with other substrates **7b**–**d**, bearing different aryl or alkyl substituents on the triple bond (R^1 = 3-thienyl, *p*-Br-C_6H_4, butyl), which were successfully converted into the corresponding indole-3-carboxylic esters **10b**–**d** in moderate to fair overall yields (45–63%, Table 3, entries 3–5).

Conclusions

In conclusion, we have found that a variety of 2-alkynylanilines bearing an internal triple bond and a secondary amino group (**1**) can be conveniently converted into *N*-substituted indole-3-carboxylic esters **2** in fair to high yields (50–84%) in one step by PdI_2/KI-catalyzed oxidative 5-

Table 3. Synthesis of *N*-unsubstituted indole-3-carboxylic esters **10** by PdI_2/KI-catalyzed oxidative carbonylation of primary 2-alkynylanilines **7** followed by acidic treatment.[a,b]



Entry	7	R^1	Yield of **9** [%][c]	Yield of **10** [%][c]	Overall yield of **10** [%][d]
1[e]	**7a**	Ph	46	2	48
2	**7a**	Ph	52	4	55
3	**7b**	3-thienyl	59	5	63
4	**7c**	*p*-Br-C_6H_4	58	0	56
5	**7d**	Bu	30	16	45

[a] Unless otherwise noted, all carbonylation reactions were carried out at 100 °C for 3 h under 20 atm (at 25 °C) of a 4:1 mixture of CO/air, in a 2:1 (v/v) $HC(OMe)_3$/MeOH mixture as the solvent (0.05 mmol of starting **7** per mL of solvent, 1–2 mmol scale based on **7**), in the presence of 5 mol-% of PdI_2 and with a KI/PdI_2 molar ratio of 10:1. [b] The acidic treatment was carried out on the crude products deriving from the carbonylation reaction, by dilution with MeOH, water and concd. HCl followed by heating of the resulting mixture at 80 °C for 15 h (see the Exp. Section for details). [c] Isolated yield based on starting **7**, referred to the oxidative carbonylation step. [d] Overall isolated yield based on starting **7**, referred to the oxidative carbonylation step followed by the acidic treatment. [e] The carbonylation reaction was carried out in the presence of 2 mol-% of PdI_2 and 20 mol-% of KI.

endo-dig heterocyclization-alkoxycarbonylation, carried out using only oxygen as the oxidant. This reactivity is complementary to that we previously observed in the case of 2-ethynylanilines bearing a terminal triple bond and a primary or secondary amino group (**5**) which, under analogous conditions, selectively led to dihydroindol-2-one derivatives **6**,[23] and to that observed in the case of 2-alkynylanilines bearing an internal triple bond and a primary amino group (**7**), which led to the formation of acyclic carbamates **8**.[23,24]

We have also found that an indirect way to obtain *N*-unsubstituted indol-3-carboxylic esters **10** from **7** may consist in a simple 2-step procedure, involving oxidative carbonylation of **7** carried out in the presence of trimethyl orthoformate [which in situ converts the primary amino group of **7** into a secondary *N*-(dimethoxymethyl)amino group], to give 1-(dialkoxymethyl)indole-3-carboxylic esters **9**, followed by acidic treatment of the reaction crude to achieve nitrogen deprotection.

Experimental Section

General: Melting points were taken on a Reichert Thermovar apparatus. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$ solutions with a Bruker DPX Avance 300 or 500 spectrometer operating at 300 MHz and 75 MHz, or 500 MHz and 126 MHz, respectively, with Me_4Si as internal standard. ^{19}F NMR spectra were recorded at 25 °C in $CDCl_3$ solutions with a Bruker DPX Avance 500 spectrometer at 471 MHz with CF_2Br_2 as internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. IR spectra were taken with a JASCO FT-IR 4200 spectrometer. Mass spectra were obtained using a Shimadzu QP-2010 GC–MS apparatus at 70 eV ionization voltage or an ABSciex API 2000 mass spectrometer equipped with a turbo ion spray ionization source in the positive mode [ion spray voltage (IS) 4500 V; curtain gas 10 psi; temperature 25 °C; ion source gas (1) 20 psi; declustering and focusing potentials 50 and 400 V, respectively]. Microanalyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. All reactions were analyzed by TLC on silica gel 60 F_{254} (Merck) or on neutral alumina (Merck) and by GLC using a Shimadzu GC-2010 gas chromatograph and capillary columns with polymethylsilicone + 5% phenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh) or neutral alumina 90 (Merck, 70–230 mesh). Evaporation refers to the removal of solvent under reduced pressure.

Preparation of Substrates: *N*-Substituted 2-alkynylanilines **1a–j** were prepared by reductive amination of the corresponding primary 2-alkynylanilines [prepared in their turn by Sonogashira coupling between the appropriate 2-haloaniline and 1-alkynes, as we previously described[22] and as described below for 4-methyl-2-(phenylethynyl)aniline]. All other materials were commercially available and were used without further purification.

Preparation of 4-Methyl-2-(phenylethynyl)aniline: To a stirred solution of 2-iodo-4-methylaniline[27] (1.6 g, 6.9 mmol) in DMF (1 mL) and Et_2NH (1 mL) were added under nitrogen phenylacetylene (0.91 g, 8.9 mmol), $Pd(PPh_3)_4$ (40 mg, 0.034 mmol) and CuI (13 mg, 0.068 mmol). The reaction mixture was stirred overnight under nitrogen at room temperature, and then 0.1 N HCl (30 mL) and Et_2O (30 mL) were added. The organic layer was separated, the aqueous layer was extracted with diethyl ether (2× 30 mL), and the combined organic phases were dried with Na_2SO_4. After filtration and evaporation of the solvent, the product was purified by column chromatography on silica gel using 9:1 hexane/AcOEt as eluent, to give 4-methyl-2-(phenylethynyl)aniline as a yellow solid (m.p. 129–131 °C, ref.[28] 129–130 °C), whose spectroscopic data agreed with those reported in the literature[28,29] (yield: 1.01 g, 71% based on starting 2-iodo-4-methylaniline).

General Procedure for the Preparation of *N*-Substituted 2-Alkynylaniline 1a–j: To a stirred solution of the 2-alkynylaniline derivative (9.61 mmol) [2-(phenylethynyl)aniline: 1.86 g; 2-(4-bromophenylethynyl)aniline: 2.62 g; 2-(*p*-tolylethynyl)aniline: 1.99 g; 2-(hex-1-ynyl)aniline: 1.66 g; 4-chloro-2-(phenylethynyl)aniline: 2.19 g; 4-methyl-2-(phenylethynyl)aniline: 1.99 g; 5-(trifluoromethyl)-2-(phenylethynyl)aniline: 2.51 g; 5-methyl-2-(phenylethynyl)aniline: 1.99 g] in anhydrous MeOH (37 mL) were added under nitrogen the aldehyde (11.5 mmol) (benzaldehyde: 1.22 g; butyraldehyde: 0.83 g; isobutyraldehyde: 0.83 g), anhydrous $ZnCl_2$ (1.57 g, 11.5 mmol) and $NaBH_3CN$ (0.72 g, 11.5 mmol). The reaction mixture was refluxed under nitrogen for 2 h. After cooling, the reaction mixture was diluted with 1 M aqueous NaOH (12 mL), concentrated by rotary evaporation and then extracted with Et_2O (3× 20 mL). The combined organic phases were dried with Na_2SO_4. After filtration

and evaporation of the solvent, the products were purified by column chromatography on silica gel using 9:1 hexane/AcOEt as the eluent.

***N*-Benzyl-2-(phenylethynyl)aniline (1a):** Yield: 1.99 g, starting from 1.86 g of 2-(phenylethynyl)aniline (73%). Colorless solid, m.p. 56–57 °C. IR (KBr): $\tilde{\nu}$ = 3410 (m), 2208 (w), 1581 (m), 1575 (m), 1510 (s), 1430 (m), 1384 (m), 1326 (m), 1265 (m), 1162 (w), 1024 (w), 749 (s), 692 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.44 (m, 2 H, aromatic), 7.43–7.24 (m, 9 H, 8 H aromatic + 3-H), 7.19–7.10 (m, 1 H, 5-H), 6.66 (td, J = 7.5, 1.0 Hz, 1 H, 4-H), 6.57 (distorted d, br., J = 8.5, 0.8 Hz, 1 H, 6-H), 5.13 (br. s, 1 H, NH), 4.42 (d, J = 4.9 Hz, 2 H, CH_2Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.7, 139.2, 132.2, 131.4, 130.0, 128.7, 128.37, 128.18, 127.2, 127.1, 123.3, 116.7, 110.0, 107.6, 95.3, 86.1, 47.7 ppm. GC–MS: *m*/*z* (%) = 283 (20) [M^+], 207 (17), 206 (100), 204 (11), 178 (7), 165 (12), 128 (4), 91 (22), 65 (9). $C_{21}H_{17}N$ (283.37): C 89.01, H 6.05, N 4.94; found C 89.01, H 6.07, N 4.92.

***N*-Benzyl-2-(4-bromophenylethynyl)aniline (1b):** Yield: 2.60 g, starting from 2.62 g of 2-(4-bromophenylethynyl)aniline (75%). Yellow solid, m.p. 67–68 °C. IR (KBr): $\tilde{\nu}$ = 3409 (m), 2210 (w), 1600 (m), 1571 (m), 1511 (s), 1384 (m), 1327 (m), 1266 (m), 1163 (w), 1067 (w), 1008 (m), 827 (m), 750 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.43 (m, 2 H, aromatic), 7.42–7.27 (m, 8 H, 7 H aromatic + 3-H), 7.21–7.13 (m, 1 H, 5-H), 6.67 (td, J = 7.7, 0.8 Hz, 1 H, 4-H), 6.58 (br. d, J = 8.5 Hz, 1 H, 6-H), 5.08 (br. s, 1 H, NH), 4.46 (d, J = 5.3 Hz, 2 H, CH_2Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.8, 139.0, 132.8, 132.2, 131.6, 130.3, 128.7, 127.3, 127.0, 122.4, 122.2, 116.7, 110.0, 107.2, 94.2, 87.2, 47.7 ppm. GC–MS: *m*/*z* (%) = 363 (27) [M + 2]$^+$, 361 (27) [M^+], 286 (95), 284 (100), 206 (55), 204 (30), 191 (18), 190 (17), 176 (9), 164 (20), 163 (18), 91 (57), 65 (17). $C_{21}H_{16}BrN$ (362.26): C 69.62, H 4.45, Br 22.06, N 3.87; found C 69.54, H 4.46, Br 22.12, N 3.88.

***N*-Benzyl-2-(*p*-tolylethynyl)aniline (1c):** Yield: 2.07 g, starting from 1.99 g of 2-(2-*p*-tolylethynyl)aniline (72%). Colorless solid, m.p. 73–75 °C. IR (KBr): $\tilde{\nu}$ = 3410 (m), 2207 (vw), 1600 (m), 1572 (m), 1512 (s), 1448 (m), 1384 (w), 1362 (m), 1326 (m), 1266 (m), 1180 (w), 1163 (w), 1061 (w), 1017 (w), 989 (w), 930 (w), 818 (s), 749 (s), 728 (s), 695 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 8 H, 7 H aromatic + 3-H), 7.15–7.06 (m, 3 H, 2 H aromatic + 5-H), 6.63 (td, J = 7.7, 0.8 Hz, 1 H, 4-H), 6.54 (d, J = 8.1 Hz, 1 H, 6-H), 5.13 (t, br., J = 4.8 Hz, 1 H, NH), 4.39 (d, J = 4.8 Hz, 2 H, CH_2Ph), 2.31 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.6, 139.1, 138.3, 132.0, 131.3, 129.8, 129.1, 128.6, 127.1, 127.0, 120.2, 116.6, 109.9, 107.8, 95.4, 85.3, 47.6, 21.4 ppm. GC–MS: *m*/*z* (%) = 297 (29) [M^+], 296 (18), 221 (19), 220 (100), 206 (24), 204 (13), 191 (6), 179 (8), 178 (12), 165 (2), 152 (3), 128 (4), 115 (2), 91 (13). $C_{22}H_{19}N$ (297.39): C 88.85, H 6.44, N 4.71; found C 88.84, H 6.46, N 4.70.

***N*-Benzyl-2-(hex-1-ynyl)aniline (1d):** Yield: 1.74 g, starting from 1.66 g of 2-(hex-1-ynyl)aniline (69%). Yellow oil. IR (film): $\tilde{\nu}$ = 3400 (m, br.), 2930 (m), 2860 (m), 2221 (vw), 1600 (m), 1577 (m), 1508 (s), 1458 (m), 1323 (m), 1282 (s), 1161 (w), 1028 (w), 745 (s), 698 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.18 (m, 6 H, 5 H aromatic + 3-H), 7.09–7.02 (m, 1 H, 5-H), 6.58 (td, J = 7.5, 1.2 Hz, 1 H, 4-H), 6.50 (br. d, J = 8.1 Hz, 1 H, 6-H), 4.99 (br. s, 1 H, NH), 4.33 (br. s, 2 H, CH_2Ph), 2.41 (t, J = 6.9 Hz, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 1.59–1.33 (m, 4 H, CH_2CH_2CH$_3$), 0.86 (t, J = 7.3 Hz, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.6, 139.2, 131.9, 129.0, 128.6, 127.2, 127.1, 116.4, 109.6, 108.6, 96.2, 77.1, 47.8, 30.9, 22.0, 19.3, 13.6 ppm. GC–MS: *m*/*z* (%) = 263 (100) [M^+], 234 (7), 220 (21), 218 (18), 206 (87), 186 (88), 172 (4), 156 (6), 144 (12), 143 (15), 130 (21), 115 (19), 103 (7), 91 (81), 77 (12), 65 (21). $C_{19}H_{21}N$ (263.38): C 86.65, H 8.04, N 5.32; found C 86.64, H 8.06, N 5.30.

***N*-Benzyl-4-chloro-2-(phenylethynyl)aniline (1e):** Yield: 2.07 g, starting from 2.19 g of 4-chloro-2-(phenylethynyl)aniline (68%). Yellow solid, m.p. 83–86 °C. IR (KBr): $\tilde{\nu}$ = 3398 (m), 2205 (vw), 1591 (w), 1566 (w), 1488 (s), 1468 (m), 1412 (m), 1384 (m), 1321 (m), 1262 (m), 1150 (w), 1121 (w), 1067 (w), 879 (m), 803 (m), 754 (s), 689 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.44 (m, 2 H, aromatic), 7.37–7.25 (m, 9 H, 8 H aromatic + 3-H), 7.08 (dd, J = 8.9, 2.4 Hz, 1 H, 5-H), 6.47 (d, J = 8.9 Hz, 1 H, 6-H), 5.12 (t, br., J = 5.7 Hz, 1 H, NH), 4.43 (d, J = 5.7 Hz, 2 H, CH_2Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.3, 138.7, 131.5, 131.4, 129.8, 128.8, 128.5, 128.4, 127.4, 127.0, 122.8, 121.0, 111.1, 109.0, 96.2, 84.7, 47.8 ppm. GC–MS: *m*/*z* (%) = 319 (9) [M + 2]$^+$, 317 (26) [M^+], 316 (11), 242 (32), 240 (100), 204 (10), 191 (10), 190 (8), 176 (5), 164 (9), 163 (9), 91 (34), 65 (11). $C_{21}H_{16}ClN$ (317.81): C 79.36, H 5.07, Cl 11.16, N 4.41; found C 79.40, H 5.06, Cl 11.14, N 4.40.

***N*-Benzyl-4-methyl-2-(phenylethynyl)aniline (1f):** Yield: 2.21 g, starting from 1.99 g of 4-methyl-2-(phenylethynyl)aniline (77%). Yellow solid, m.p. 36–37 °C. IR (KBr): $\tilde{\nu}$ = 3483 (m), 2196 (w), 1614 (w), 1511 (s), 1489 (w), 1451 (w), 1401 (m), 1384 (m), 1317 (m), 1273 (w), 1157 (w), 1068 (w), 1024 (w), 792 (m), 731 (m), 685 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.44 (m, 2 H, aromatic), 7.40–7.19 (m, 9 H, 8 H aromatic + 3-H), 6.96 (dd, J = 8.5, 1.8 Hz, 1 H, 5-H), 6.48 (d, J = 8.5 Hz, 1 H, 6-H), 4.99 (t, br., J = 5.7 Hz, 1 H, NH), 4.42 (d, J = 5.7 Hz, 2 H, CH_2Ph), 2.21 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.6, 139.4, 132.4, 131.4, 130.7, 128.6, 128.4, 128.1, 127.1, 127.0, 125.7, 123.3, 110.1, 107.5, 95.0, 86.2, 47.9, 20.2 ppm. GC–MS: *m*/*z* (%) = 297 (28) [M^+], 296 (12), 221 (19), 220 (100), 204 (11), 191 (10), 178 (15), 152 (5), 91 (34), 65 (11). $C_{22}H_{19}N$ (297.39): C 88.85, H 6.44, N 4.71; found C 88.82, H 6.46, N 4.72.

***N*-Benzyl-2-(phenylethynyl)-5-(trifluoromethyl)aniline (1g):** Yield: 2.75 g, starting from 2.51 g of 5-(trifluoromethyl)-2-(phenylethynyl)aniline (82%). Colorless solid, m.p. 54–56 °C. IR (KBr): $\tilde{\nu}$ = 3436 (m), 2204 (vw), 1612 (m), 1577 (m), 1521 (w), 1434 (m), 1335 (s), 1274 (m), 1163 (s), 1120 (s), 1081 (w), 1021 (w), 913 (w), 850 (w), 814 (m), 755 (m), 689 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.42 (m, 2 H, aromatic), 7.40–7.25 (m, 9 H, 8 H aromatic + 3-H), 6.90 (br. d, J = 8.1 Hz, 1 H, 4-H), 6.80 (br. s, 1 H, 6-H), 5.24 (t, br., J = 5.7 Hz, 1 H, NH), 4.45 (d, J = 5.7 Hz, 2 H, CH_2Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.7, 138.3, 132.3, 131.60 (q, J = 32.0 Hz), 131.56, 128.9, 128.7, 128.5, 127.6, 127.2, 124.2 (q, J = 272.6 Hz), 122.6, 113.1 (q, J = 4.0 Hz), 111.0, 106.2 (q, J = 4.0 Hz), 97.1, 84.7, 47.7 ppm. ^{19}F NMR (471 MHz, $CDCl_3$): δ = –63.0 (s, 3 F, CF_3) ppm. GC–MS: *m*/*z* (%) = 351 (19) [M^+], 275 (19), 274 (100), 233 (8), 204 (7), 190 (7), 163 (4), 91 (76), 65 (24). $C_{22}H_{16}F_3N$ (351.36): C 75.20, H 4.59, F 16.22, N 3.99; found C 75.16, H 4.57, F 16.27, N 4.00.

***N*-Benzyl-5-methyl-2-(phenylethynyl)aniline (1h):** Yield: 1.75 g, starting from 1.99 g of 5-methyl-2-(phenylethynyl)aniline (61%). Yellow solid, m.p. 101–102 °C. IR (KBr): $\tilde{\nu}$ = 3308 (m, br.), 2230 (w), 1664 (m), 1537 (m), 1490 (w), 1385 (w), 1315 (m), 1280 (m), 1258 (m), 1158 (m), 1112 (m), 1009 (m), 856 (w), 756 (m), 692 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.42 (m, 2 H, aromatic), 7.41–7.23 (m, 9 H, 8 H aromatic + 3-H), 6.49 (dd, J = 7.7, 0.8 Hz, 1 H, 4-H), 6.41 (br. s, 1 H, 6-H), 5.05 (br. s, 1 H, NH), 4.42 (br. s, 2 H, CH_2Ph), 2.40 (s, 3 H, Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.7, 140.3, 139.2, 131.9, 131.3, 128.7, 128.3, 127.9, 127.2, 127.1, 123.5, 117.7, 110.6, 104.8, 94.7, 86.2, 47.7, 22.1 ppm. GC–MS: *m*/*z* (%) = 297 (100) [M^+], 220 (6), 206 (28), 191 (5), 179 (19), 178 (12), 152 (2), 128 (2), 115 (1), 102 (2), 91 (70), 77 (9),

65(9). $C_{22}H_{19}N$ (297.39): C 88.85, H 6.44, N 4.71; found C 88.80, H 6.47, N 4.73.

***N*-Butyl-2-(phenylethynyl)aniline (1i):** Yield: 1.20 g, starting from 1.86 g of 2-(phenylethynyl)aniline (50%). Yellow oil. IR (film): $\tilde{\nu}$ = 3410 (m), 2206 (vw), 1596 (m), 1575 (m), 1511 (m), 1456 (m), 1324 (w), 1283 (w), 1216 (m), 1162 (w), 756 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.47–7.40 (m, 2 H, aromatic), 7.33–7.21 (m, 4 H, 3 H aromatic + 3-H), 7.15–7.09 (m, 1 H, 4-H), 6.58–6.50 (m, 2 H, 5-H + 6-H), 4.56 (br. s, 1 H, NH), 3.15–3.07 (m, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 1.62–1.54 (m, 2 H, CH_2CH$_2$CH$_3$), 1.44–1.34 (m, 2 H, CH_2CH$_3$), 0.89 (t, J = 7.4 Hz, 3 H, Me) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.0, 131.1, 130.4, 129.0, 127.4, 127.1, 122.4, 115.0, 108.5, 106.2, 94.0, 85.1, 42.2, 30.5, 19.2, 12.9 ppm. GC–MS: *m*/*z* (%) = 249 (34) [M$^+$], 220 (6), 207 (17), 206 (100), 204 (19), 179 (16), 178 (21), 165 (6), 152 (4), 128 (8), 102 (4), 77 (5). $C_{18}H_{19}N$ (249.35): C 86.70, H 7.68, N 5.62; found C 86.68, H 7.70, N 5.62.

2-(Hex-1-ynyl)-*N*-isobutylaniline (1j): Yield: 1.32 g, starting from 1.66 g of 2-(hex-1-ynyl)aniline (60%). Yellow oil. IR (film): $\tilde{\nu}$ = 3418 (m), 2212 (vw), 1642 (m), 1602 (m), 1509 (m), 1458 (m), 1323 (m), 1162 (w), 742 (s) cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.22 (dd, J = 7.2, 1.6 Hz, 1 H, 3-H), 7.16–7.07 (m, 1 H, 4-H), 6.63–6.45 (m, 2 H, 5-H + 6-H), 4.66 (br. s, 1 H, NH), 2.96 (br. d, J = 6.5 Hz, 2 H, CH_2CHMe$_2$), 2.46 (t, J = 6.9 Hz, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 1.91 (nonuplet, J = 6.5 Hz, 1 H, CH$_2$CHMe$_2$), 1.66–1.40 (m, 4 H, CH_2CH_2CH$_3$), 0.99 (d, J = 6.5 Hz, 6 H, CH_3CHCH_3), 0.94 (t, J = 7.0 Hz, 3 H, CH_2CH$_3$) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ = 149.0, 131.8, 129.0, 115.8, 109.3, 108.3, 95.9, 77.2, 51.3, 31.1, 28.1, 22.0, 20.4, 19.3, 13.6 ppm. GC–MS: *m*/*z* (%) = 229 (66) [M$^+$], 200 (3), 187 (26), 186 (45), 172 (35), 156 (12), 144 (100), 131 (69), 130 (22), 115 (21), 103 (11), 89 (7), 77 (11). $C_{16}H_{23}N$ (229.36): C 83.79, H 10.11, N 6.11; found C 83.78, H 10.10, N 6.12.

Synthesis of *N*-Substituted Indole-3-carboxylic Esters 2a–f, 2c′, 2f′, 2h–j (Table 2, entries 1–6, 8–12): A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (6.0 mg, 1.67×10^{-2} mmol), KI (27.7 mg, 0.17 mmol), anhydrous ROH (R = Me or Et, 16.7 mL) and 0.83 mmol of *N*-substituted-2-alkynylaniline [*N*-benzyl-2-(phenylethynyl)aniline (**1a**): 235 mg; *N*-benzyl-2-(4-bromophenylethynyl)aniline (**1b**): 300 mg; *N*-benzyl-2-(*p*-tolylethynyl)aniline (**1c**): 246 mg; *N*-benzyl-2-(hex-1-ynyl)aniline (**1d**): 218 mg; *N*-benzyl-4-chloro-2-(phenylethynyl)aniline (**1e**): 264 mg; *N*-benzyl-4-methyl-2-(phenylethynyl)aniline (**1f**): 246 mg; *N*-benzyl-5-methyl-2-(phenylethynyl)aniline (**1h**): 246 mg; *N*-butyl-2-(phenylethynyl)aniline (**1i**): 207 mg; *N*-isobutyl-2-(hex-1-ynyl)aniline (**1j**): 190 mg]. The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for the time required (see Table 3), the autoclave was cooled, degassed and opened. The solvent was evaporated, and the products were purified by column chromatography on silica gel using 95:5 to 9:1 hexane/AcOEt as eluent.

Methyl 1-Benzyl-2-phenyl-1*H*-indole-3-carboxylate (2a): Yield: 205 mg, starting from 235 mg of **1a** (72%) (Table 2, entry 1). Colorless solid, m.p. 126–127 °C. IR (KBr): $\tilde{\nu}$ = 1697 (s), 1539 (m), 1497 (m), 1437 (m), 1410 (m), 1351 (w), 1284 (m), 1238 (m), 1188 (m), 1151 (s), 1119 (w), 1086 (m), 1029 (w), 927 (w), 822 (m), 727 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.27 (dt, J = 7.8, 1.1 Hz, 1 H, 4-H), 7.45–7.18 (m, 11 H, aromatic), 6.93–6.87 (m, 2 H, aromatic), 5.18 (s, 2 H, CH_2Ph), 3.76 (s, 3 H, CO$_2$Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 147.1, 136.9, 136.3, 131.2, 130.2, 129.1, 128.7, 128.1, 127.4, 126.7, 126.0, 123.1, 122.2, 122.0, 110.8, 105.6, 50.8, 47.6 ppm. GC–MS: *m*/*z* (%) = 341 (90) [M$^+$], 310 (24), 282 (6), 280 (5), 235 (5), 219 (3), 204 (7), 190 (8), 179 (7), 165 (3), 131 (2), 91 (100), 65 (14). $C_{23}H_{19}NO_2$ (341.40): C 80.92, H 5.61, N 4.10; found C 80.83, H 5.62, N 4.09.

Methyl 1-Benzyl-2-(4-bromophenyl)-1*H*-indole-3-carboxylate (2b): Yield: 258 mg, starting from 300 mg of **1b** (74%) (Table 2, entry 2). Colorless solid, m.p. 125–127 °C. IR (KBr): $\tilde{\nu}$ = 1709 (s), 1633 (m), 1481 (w), 1454 (w), 1384 (m), 1229 (m), 1148 (s), 1120 (w), 1072 (w), 1011 (w), 741 (m), 698 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.28–8.23 (m, 1 H, 4-H), 7.56–7.50 (m, 2 H, aromatic), 7.35–7.17 (m, 8 H, aromatic), 6.92–6.86 (m, 2 H, aromatic), 5.18 (s, 2 H, CH_2Ph), 3.79 (s, 3 H, CO$_2$Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4, 145.6, 136.7, 136.5, 131.8, 131.4, 130.1, 128.8, 127.6, 126.6, 125.9, 123.7, 123.4, 122.4, 122.1, 110.7, 105.9, 50.9, 47.6 ppm. GC–MS: *m*/*z* (%) = 421 (40) [M + 2]$^+$, 419 (38) [M$^+$], 390 (5), 388 (5), 340 (3), 280 (4), 249 (8), 190 (10), 178 (7), 163 (4), 91 (100), 65 (12). $C_{23}H_{18}BrNO_2$ (420.30): C 65.73, H 4.32, Br 19.01, N 3.33; found C 65.75, H 4.32, Br 19.05, N 3.34.

Methyl 1-Benzyl-2-*p*-tolyl-1*H*-indole-3-carboxylate (2c): Yield: 240 mg, starting from 246 mg of **1c** (81%) (Table 2, entry 3). Colorless solid, m.p. 90–92 °C. IR (KBr): $\tilde{\nu}$ = 1706 (s), 1496 (m), 1461 (m), 1429 (m), 1384 (m), 1350 (m), 1283 (m), 1230 (m), 1185 (w), 1147 (s), 1118 (m), 1017 (w), 829 (m), 754 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.28–8.22 (m, 1 H, 4-H), 7.32–7.15 (m, 10 H, aromatic), 6.93–6.87 (m, 2 H, aromatic), 5.17 (s, 2 H, CH_2Ph), 3.77 (s, 3 H, CO$_2$Me), 2.38 (s, 3 H, CH_3C$_6$H$_4$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 147.4, 138.9, 136.9, 136.2, 130.0, 128.8, 128.7, 128.1, 127.4, 126.7, 125.9, 122.9, 122.2, 122.0, 110.8, 105.4, 50.7, 47.5, 21.4 ppm. GC–MS: *m*/*z* (%) = 355 (100) [M$^+$], 324 (29), 297 (6), 294 (3), 264 (6), 249 (13), 218 (6), 204 (11), 193 (9), 177 (4), 165 (3), 139 (3), 91 (75), 65 (9). $C_{24}H_{21}NO_2$ (355.43): C 81.10, H 5.96, N 3.94; found C 81.15, H 5.94, N 3.95.

Ethyl 1-Benzyl-2-*p*-tolyl-1*H*-indole-3-carboxylate (2c′): Yield: 257 mg, starting from 246 mg of **1c** (84%) (Table 2, entry 11). Colorless solid, m.p. 92–93 °C. IR (KBr): $\tilde{\nu}$ = 1695 (s), 1535 (m), 1496 (w), 1465 (m), 1417 (m), 1353 (m), 1291 (m), 1236 (m), 1157 (m), 1116 (m), 1030 (w), 789 (w), 752 (s), 696 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.32–8.25 (m, 1 H, 4-H), 7.31–7.13 (m, 10 H, aromatic), 6.93–6.86 (m, 2 H, aromatic), 5.16 (s, 2 H, CH_2Ph), 4.24 (q, J = 7.3 Hz, 2 H, CO$_2$CH_2CH$_3$), 2.37 (s, 3 H, CH_3C$_6$H$_4$), 1.22 (t, J = 7.3 Hz, 3 H, CO$_2$CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1, 147.2, 138.9, 137.0, 136.3, 130.1, 128.72, 128.65, 128.3, 127.4, 126.9, 126.0, 122.9, 122.1, 122.0, 110.7, 105.7, 59.4, 47.5, 21.4, 14.3 ppm. GC–MS: *m*/*z* (%) = 369 (70) [M$^+$], 324 (18), 297 (29), 278 (2), 262 (2), 250 (5), 233 (3), 218 (5), 204 (9), 190 (4), 179 (9), 165 (2), 115 (2), 91 (100), 65 (10). $C_{25}H_{23}NO_2$ (369.46): C 81.27, H 6.27, N 3.79; found C 81.20, H 6.25, N 3.80.

Methyl 1-Benzyl-2-butyl-1*H*-indole-3-carboxylate (2d): Yield: 197 mg, starting from 218 mg of **1d** (74%) (Table 2, entry 4). Yellow solid, m.p. 72–74 °C. IR (KBr): $\tilde{\nu}$ = 1691 (s), 1469 (m), 1416 (s), 1358 (m), 1298 (w), 1235 (m), 1174 (s), 1116 (m), 1078 (m), 1039 (m), 824 (m), 789 (m), 730 (m), 658 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.18 (br. d, J = 8.1 Hz, 1 H, 4-H), 7.27–7.08 (m, 6 H, aromatic), 6.97–6.89 (m, 2 H, aromatic), 5.31 (s, 2 H, CH_2Ph), 3.92 (s, 3 H, CO$_2$Me), 3.18–3.07 (m, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 1.59–1.32 (m, 4 H, CH_2CH_2CH$_3$), 0.88 (t, J = 7.1 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 149.9, 136.6, 136.3, 128.8, 127.6, 126.7, 125.8, 122.3, 121.9, 121.6, 109.9, 103.9, 50.7, 46.5, 31.6, 25.5, 22.8, 13.8 ppm. GC–MS: *m*/*z* (%) = 321 (51) [M$^+$], 280 (12), 279 (58), 246 (15), 221 (9), 220 (45), 218 (19), 188 (4), 170 (4), 156 (4), 129 (5), 115 (4), 91 (100). $C_{21}H_{23}NO_2$ (321.41): C 78.47, H 7.21, N 4.36; found C 78.42, H 7.20, N 4.37.

Methyl 1-Benzyl-5-chloro-2-phenyl-1*H*-indole-3-carboxylate (2e): Yield: 216 mg, starting from 264 mg of **1e** (69%) (Table 2, entry 5). Colorless solid, m.p. 170–171 °C. IR (KBr): $\tilde{\nu}$ = 1689 (s), 1538 (w), 1482 (m), 1457 (m), 1384 (m), 1224 (m), 1158 (m), 1128 (w), 1065 (m), 1027 (w), 888 (m), 803 (w), 736 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (br. d, J = 2.0 Hz, 1 H, 4-H), 7.47–7.38 (m, 3 H, aromatic), 7.37–7.31 (m, 2 H, aromatic), 7.27–7.20 (m, 3 H, aromatic), 7.17 (distorted dd, J = 8.5, 2.0 Hz, 1 H, 6-H), 7.11 (distorted d, J = 8.5 Hz, 1 H, 7-H), 6.91–6.85 (m, 2 H, aromatic), 5.17 (s, 2 H, CH_2Ph), 3.77 (s, 3 H, CO_2Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.1, 148.2, 136.5, 134.8, 130.8, 130.1, 129.3, 128.8, 128.2, 127.8, 127.7, 126.0, 123.5, 121.7, 111.9, 105.4, 50.9, 47.8 ppm. GC–MS: m/z (%) = 377 (21) $[M + 2]^+$, 375 (59) $[M^+]$, 344 (10), 284 (2), 269 (4), 253 (2), 213 (3), 190 (8), 178 (3), 91 (100), 65 (11). $C_{23}H_{18}ClNO_2$ (375.85): C 73.50, H 4.83, N 3.73; found C 73.59, H 4.84, N 3.72.

Methyl 1-Benzyl-5-methyl-2-phenyl-1*H*-indole-3-carboxylate (2f): Yield: 228 mg, starting from 246 mg of **1f** (77%) (Table 2, entry 6). Colorless solid, m.p. 132–134 °C. IR (KBr): $\tilde{\nu}$ = 2923 (m), 1685 (s), 1462 (m), 1405 (s), 1384 (w), 1243 (w), 1149 (m), 788 (m), 722 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (br. s, 1 H, 4-H), 7.46–7.30 (m, 5 H, aromatic), 7.25–7.16 (m, 3 H, aromatic), 7.09 (distorted d, J = 8.1 Hz, 1 H, 7-H), 7.03 (distorted dd, J = 8.1, 1.0 Hz, 1 H, 6-H), 6.93–6.84 (m, 2 H, aromatic), 5.13 (s, 2 H, CH_2Ph), 3.75 (s, 3 H, CO_2Me), 2.49 (s, 3 H, Me at C-5) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 147.0, 137.0, 134.7, 131.7, 131.4, 130.1, 129.0, 128.7, 128.0, 127.4, 127.0, 126.0, 124.6, 121.7, 110.4, 105.1, 50.7, 47.5, 21.6 ppm. GC–MS: m/z (%) = 355 (76) $[M^+]$, 324 (19), 296 (6), 264 (5), 249 (9), 232 (7), 218 (4), 204 (6), 193 (8), 176 (3), 91 (100), 65 (13). $C_{24}H_{21}NO_2$ (355.43): C 81.10, H 5.96, N 3.94; found C 81.17, H 5.94, N 3.94.

Ethyl 1-Benzyl-5-methyl-2-phenyl-1*H*-indole-3-carboxylate (2f′): Yield: 225 mg, starting from 246 mg of **1f** (73%) (Table 2, entry 12). Colorless solid, m.p. 109–111 °C. IR (KBr): $\tilde{\nu}$ = 1694 (s), 1536 (w), 1483 (m), 1456 (m), 1402 (m), 1347 (w), 1313 (w), 1166 (m), 1081 (m), 998 (m), 934 (w), 783 (m), 745 (m), 706 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 1 H, 4-H), 7.44–7.30 (m, 5 H, aromatic), 7.25–7.18 (m, 3 H, aromatic), 7.10 (distorted d, J = 8.4 Hz, 1 H, 7-H), 7.04 (distorted dd, J = 8.4, 1.5 Hz, 1 H, 6-H), 6.93–6.87 (m, 2 H, aromatic), 5.16 (s, 2 H, CH_2Ph), 4.20 (q, J = 7.2 Hz, 2 H, $CO_2CH_2CH_3$), 2.50 (s, 3 H, Me at C-5), 1.16 (t, J = 7.2 Hz, 3 H, $CO_2CH_2CH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.2, 146.8, 137.1, 134.8, 131.7, 130.3, 128.8, 128.7, 127.9, 127.4, 127.3, 126.0, 124.6, 121.7, 110.4, 105.5, 59.3, 47.6, 21.6, 14.1 ppm. GC–MS: m/z (%) = 369 (100) $[M^+]$, 341 (4), 324 (23), 297 (23), 250 (3), 232 (4), 204 (4), 179 (4), 91 (56). $C_{25}H_{23}NO_2$ (369.46): C 81.27, H 6.27, N 3.79; found C 81.42, H 6.25, N 3.78.

Methyl 1-Benzyl-6-methyl-2-phenyl-1*H*-indole-3-carboxylate (2h): Yield: 231 mg, starting from 246 mg of **1h** (78%) (Table 2, entry 8). Yellow solid, m.p. 99–101 °C. IR (KBr): $\tilde{\nu}$ = 1702 (s), 1535 (w), 1495 (w), 1437 (m), 1401 (m), 1275 (w), 1239 (w), 1188 (m), 1129 (s), 1082 (m), 810 (m), 775 (w), 701 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.13 (br. d, J = 8.5 Hz, 1 H, 4-H), 7.43–7.29 (m, 5 H, aromatic), 7.26–7.18 (m, 3 H, aromatic), 7.13 (dd, J = 8.5, 0.8 Hz, 1 H, 5-H), 7.02 (d, J = 0.8 Hz, 1 H, 7-H), 6.93–6.86 (m, 2 H, aromatic), 5.15 (s, 2 H, CH_2Ph), 3.75 (s, 3 H, CO_2Me), 2.42 (s, 3 H, Me at C-6) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 146.6, 137.1, 136.8, 133.0, 131.4, 130.2, 128.9, 128.7, 128.0, 127.4, 124.6, 124.0, 121.7, 110.6, 105.5, 50.7, 47.4, 21.8 ppm. GC–MS: m/z (%) = 355 (95) $[M^+]$, 324 (20), 296 (7), 264 (5), 249 (9), 232 (6), 218 (5), 204 (6), 193 (8), 178 (4), 165 (2), 138 (1), 118 (2), 91 (100), 65 (10). $C_{24}H_{21}NO_2$ (355.43): C 81.10, H 5.96, N 3.94; found C 81.14, H 5.97, N 3.93.

Methyl 1-Butyl-2-phenyl-1*H*-indole-3-carboxylate (2i): Yield: 183 mg, starting from 207 mg of **1i** (72%) (Table 2, entry 9). Yellow solid, m.p. 69–71 °C IR (KBr): $\tilde{\nu}$ = 1705 (s), 1652 (m), 1543 (w), 1409 (m), 1384 (m), 1264 (w), 1222 (w), 1161 (m), 1108 (m), 1021 (w), 768 (m), 704 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.28–8.20 (m, 1 H, 4-H), 7.53–7.45 (m, 3 H, aromatic), 7.44–7.35 (m, 3 H, aromatic), 7.35–7.26 (m, 2 H, aromatic), 4.00–3.91 (m, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 3.74 (s, 3 H, CO_2Me), 1.70–1.55 (m, 2 H, CH_2CH$_2$CH$_3$), 1.24–1.10 (m, 2 H, CH_2CH$_3$), 0.77 (t, J = 7.3 Hz, 3 H, CH$_2$CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.6, 146.8, 135.9, 131.7, 130.1, 128.9, 128.1, 126.7, 122.7, 122.0, 121.9, 110.2, 50.7, 43.7, 31.8, 19.9, 13.5 ppm. GC–MS: m/z (%) = 307 (5) $[M^+]$, 281 (16), 258 (16), 251 (64), 236 (15), 220 (79), 207 (43), 193 (42), 191 (37), 176 (16), 165 (38), 135 (27), 117 (28), 115(30), 105 (24), 91 (43), 83 (19), 77 (38), 73 (54), 69 (41). $C_{20}H_{21}NO_2$ (307.39): C 78.15, H 6.89, N 4.56; found C 78.20, H 6.88, N 4.57.

Methyl 2-Butyl-1-isobutyl-1*H*-indole-3-carboxylate (2j): Yield: 119 mg, starting from 190 mg of **1j** (50%) (Table 2, entry 10). Yellow oil. IR (film): $\tilde{\nu}$ = 2960 (m), 1688 (s), 1533 (m), 1463 (m), 1440 (m), 1420 (w), 1216 (m), 1158 (w), 1114 (m), 1024 (w), 757 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.17–8.09 (m, 1 H, 4-H), 7.32–7.12 (m, 3 H, aromatic), 3.91 (s, 3 H, CO_2Me), 3.90 (d, J = 6.9 Hz, 2 H, CH_2CHMe$_2$), 3.25–3.09 (m, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 2.21 (nonuplet, 1 H, CH$_2$CHMe$_2$), 1.68–1.35 (m, 4 H, CH_2CH_2CH$_3$), 0.97 (t, J = 7.3 Hz, 3 H, CH$_2$CH_3), 0.91 (d, J = 6.9 Hz, 6 H, CH$_3$CHCH$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3, 150.0, 136.2, 126.8, 121.8, 121.6, 110.1, 103.3, 50.6, 50.5, 31.9, 29.3, 25.6, 22.9, 20.3, 13.8 ppm. GC–MS: m/z (%) = 287 (100) $[M^+]$, 156 (29), 245 (79), 244 (43), 230 (45), 212 (35), 202 (62), 190 (18), 189 (91), 184 (26), 172 (15), 170 (24), 158 (18), 144 (13), 130 (24), 115 (16). $C_{18}H_{25}NO_2$ (287.40): C 75.22, H 8.77, N 4.87; found C 75.18, H 8.75, N 4.86.

Synthesis of Methyl 1-Benzyl-2-phenyl-6-(trifluoromethyl)-1*H*-indole-3-carboxylate (2g) (Table 2, entry 7): A 35 mL stainless steel autoclave was charged in the presence of air with PdI_2 (6.0 mg, 1.67×10^{-2} mmol), KI (27.7 mg, 0.17 mmol), anhydrous MeOH (4.2 mL) and *N*-benzyl-5-(trifluoromethyl)-2-(phenylethynyl)aniline **1g** (292 mg; 0.83 mmol). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for 3 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and the product **2g** was purified by column chromatography on silica gel using 95:5 hexane/AcOEt. Yield: 247 mg, starting from 292 mg of **1g** (73%) (Table 3, entry 7). Colorless solid, m.p. 121–122 °C. IR (KBr): $\tilde{\nu}$ = 1701 (s), 1533 (w), 1480 (w), 1436 (m), 1410 (m), 1339 (m), 1308 (m), 1278 (w), 1223 (m), 1151 (s), 1116 (m), 1061 (m), 871 (m), 832 (m), 702 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.36 (br. d, J = 8.1 Hz, 1 H, 4-H), 7.57–7.49 (m, 2 H, aromatic), 7.48–7.38 (m, 3 H, aromatic), 7.37–7.29 (m, 2 H, aromatic), 7.27–7.19 (m, 3 H, aromatic), 6.92–6.83 (m, 2 H, aromatic), 5.23 (s, 2 H, CH_2Ph), 3.76 (s, 3 H, CO_2Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.0, 149.3, 130.6, 130.0, 129.5, 129.2, 128.9, 128.7, 128.5, 128.2, 127.8, 125.9, 125 6 (q, J = 32.1 Hz), 124.8 (q, J = 271.7 Hz), 122.7, 118.9 (q, J = 3.3 Hz), 108.2 (q, J = 4.5 Hz), 106.1, 51.0, 47.8 ppm. ^{19}F NMR (471 MHz, $CDCl_3$): δ = –60.8 (s, 3 F, CF_3) ppm. GC–MS: m/z (%) = 409 $[M^+]$ (40), 378 (6), 348 (2), 318 (2), 303 (5), 272 (2), 190 (3), 91 (100), 65 (12). $C_{24}H_{18}F_3NO_2$ (409.40): C 70.41, H 4.43, N 3.42; found C 70.48, H 4.41, N 3.43.

Synthesis of 1-(Dimethoxymethyl)indole-3-carboxylic Esters 9a–d (Table 3, entries 2–5): A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (24.9 mg, $6.91 \times$

10^{-2} mmol), KI (114.8 mg, 0.69 mmol), $HC(OMe)_3$ (18.4 mL), anhydrous MeOH (9.2 mL), and the 2-alkynylaniline (1.38 mmol) {2-(phenylethynyl)aniline (**7a**): 267 mg; 2-(thiophen-3-ylethynyl)aniline (**7b**): 275 mg; 2-[2-(4-bromophenyl)ethynyl]aniline (**7c**): 375 mg; 2-(hex-1-ynyl)aniline (**7d**): 239 mg}. The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for 3 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products were purified by column chromatography on neutral alumina using 98:2 hexane/acetone (for **9a**, **9b**, **9d**) or pure hexane (for **9c**) as eluent.

Methyl 1-(Dimethoxymethyl)-2-phenyl-1*H*-indole-3-carboxylate (9a): Yield: 235 mg, starting from 267 mg of **7a** (52%) (Table 3, entry 2). Yellow solid, m.p. 48–50 °C. IR (KBr): $\tilde{\nu}$ = 2986 (m), 1674 (s), 1490 (m), 1447 (m), 1394 (s), 1265 (m), 1164 (m), 1080 (m), 1052 (m), 763 (m), 692 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.24–8.18 (m, 1 H, 4-H), 7.94–7.87 (m, 1 H, 7-H), 7.54–7.40 (m, 5 H, aromatic), 7.34–7.24 (m, 2 H, aromatic), 5.58 [s, 1 H, C*H*$(OMe)_2$], 3.73 (s, 3 H, CO_2Me), 3.25 (s, 6 H, C*H*$_3$OCHOC*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.4, 145.5, 133.8, 131.1, 130.3, 129.3, 128.2, 126.8, 123.4, 122.7, 121.7, 113.9, 106.5, 105.5, 54.4, 50.9 ppm. GC–MS (direct injection): *m*/*z* = 325 (19) [M^+], 294 (6), 265 (16), 251 (7), 234 (6), 220 (12), 190 (5), 165 (6), 121 (2), 89 (2), 75 (100). $C_{19}H_{19}NO_4$ (325.36): C 70.14, H 5.89, N 4.31; found C 70.20, H 5.91, N 4.30.

Methyl 1-(Dimethoxymethyl)-2-(thiophen-3-yl)-1*H*-indole-3-carboxylate (9b): Yield: 270 mg, starting from 275 mg of **7b** (59%) (Table 3, entry 3). Yellow solid, m.p. 86–89 °C. IR (KBr): $\tilde{\nu}$ = 1710 (s), 1463 (m), 1401 (m), 1311 (w), 1265 (m), 1214 (m), 1146 (m), 1107 (m), 1071 (m), 993 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.22–8.14 (m, 1 H, 4-H), 7.94–7.86 (m, 1 H, 7-H), 7.50–7.44 (m, 2 H, aromatic), 7.33–7.24 (m, 2 H, aromatic), 7.21 (dd, *J* = 4.4, 1.6 Hz, 1 H, 4-H on thienyl ring), 5.67 [s, 1 H, C*H*$(OMe)_2$], 3.78 (s, 3 H, CO_2Me), 3.28 (s, 6 H, C*H*$_3$OCHOC*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3, 140.2, 134.3, 130.7, 129.6, 127.0, 125.4, 123.5, 122.7, 121.8, 114.0, 107.4, 105.9, 54.3, 50.8 ppm. MS (ESI+, direct infusion): *m*/*z* (%) = 354 $[M + Na]^+$, 332 $[M + H]^+$. $C_{17}H_{17}NO_4S$ (331.39): C 61.61, H 5.17, N 4.23, S 9.68; found C 61.69, H 5.18, N 4.21, S 9.71.

Methyl 2-(4-Bromophenyl)-1-(dimethoxymethyl)-1*H*-indole-3-carboxylate (9c): Yield: 325 mg, starting from 375 mg of **7c** (58%) (Table 3, entry 4). Colorless solid, m.p. 94–96 °C. IR (KBr): $\tilde{\nu}$ = 1694 (s), 1456 (m), 1402 (m), 1347 (w), 1313 (w), 1218 (m), 1190 (m), 1166 (m), 1127 (m), 1081 (m), 998 (m), 871 (m), 783 (m), 743 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.23–8.15 (m, 1 H, 4-H), 7.94–7.86 (m, 1 H, 7-H), 7.69–7.61 (m, 2 H, aromatic), 7.38–7.27 (m, 4 H, aromatic), 5.57 [s, 1 H, C*H*$(OMe)_2$], 3.77 (s, 3 H, CO_2Me), 3.27 (s, 6 H, C*H*$_3$OCHOC*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3, 143.9, 134.2, 132.9, 132.0, 131.5, 126.7, 123.8, 123.7, 122.8, 121.8, 114.0, 107.0, 105.6, 54.4, 50.9 ppm. MS (ESI+, direct infusion): *m*/*z* (%) = 428 $[M + 2 + Na]^+$, 426 $[M + Na]^+$. $C_{19}H_{18}BrNO_4$ (404.25): C 56.45, H 4.49, Br 19.77, N 3.46; found C 56.51, H 4.47, Br 19.83, N 3.45.

Methyl 2-Butyl-1-(dimethoxymethyl)-1*H*-indole-3-carboxylate (9d): Yield: 125 mg, starting from 239 mg of **7d** (30%) (Table 3, entry 5). Yellow oil. IR (film): $\tilde{\nu}$ = 2956 (m), 2932 (m), 1680 (s), 1472 (s), 1333 (w), 1208 (m), 1117 (m), 1099 (m), 1075 (m), 750 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.07–7.99 (m, 1 H, 4-H), 7.73–7.65 (m, 1 H, 7-H), 7.20–7.10 (m, 2 H, 5-H + 6-H), 6.02 [s, 1 H, C*H*$(OMe)_2$], 3.86 (s, 3 H, CO_2Me), 3.34 (s, 6 H, C*H*$_3$OCHOC*H*$_3$), 3.25–3.17 (m, 2 H, C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.65–1.50 (m, 2 H, CH$_2$C*H*$_2$CH$_3$), 1.50–1.36 (m, 2 H, C*H*$_2$CH$_3$), 0.91 (t, *J* = 7.3 Hz, 3 H, CH$_2$C*H*$_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 148.8, 134.4, 126.8, 122.6, 122.2, 121.4, 112.7, 105.4, 104.7, 54.5, 50.8, 32.1, 25.4, 22.9, 13.9 ppm. MS (ESI+, direct infusion): *m*/*z* (%) = 328 $[M + Na]^+$. $C_{17}H_{23}NO_4$ (305.37): C 66.86, H 7.59, N 4.59; found C 66.91, H 7.57, N 4.60.

Synthesis of Indole-3-carboxylic Esters 10a–d (Table 3, entries 2–5): A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (24.9 mg, 6.91×10^{-2} mmol), KI (114.8 mg, 0.69 mmol), $HC(OMe)_3$ (18.4 mL), anhydrous MeOH (9.2 mL), and the 2-alkynylaniline (1.38 mmol) {2-(phenylethynyl)aniline (**7a**): 267 mg; 2-(thiophen-3-ylethynyl)aniline (**7b**): 275 mg; 2-[2-(4-bromophenyl)ethynyl]aniline (**7c**): 375 mg; 2-(hex-1-ynyl)aniline (**7d**): 239 mg}. The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (16 atm) and air (up to 20 atm). After being stirred at 100 °C for 3 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and the crude products were diluted with MeOH (2.4 mL), water (2.0 mL) and concd HCl (37% w/w, 0.2 mL) in this order. The mixture was heated at 80 °C with stirring for 15 h in a Schlenk flask. After cooling, Et_2O (5 mL) was added to the mixture and phases were separated. The aqueous layer was extracted with Et_2O (3 × 5 mL), and the combined organic phases were dried with Na_2SO_4. After filtration and evaporation of the solvent, the products were purified by column chromatography on silica gel using hexane/AcOEt 9:1 as eluent.

Methyl 2-Phenyl-1*H*-indole-3-carboxylate (10a):[30] Yield: 190 mg, starting from 267 mg of **7a** (55%) (Table 3, entry 2). Colorless solid, m.p. 153–154 °C, ref.[20] 150–151 °C. IR (KBr): $\tilde{\nu}$ = 3302 (m, br.), 1692 (s), 1496 (w), 1468 (m), 1416 (m), 1235 (m), 1174 (m), 1039 (m), 752 (m), 730 (m), 698 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.56 (br. s, 1 H, NH), 8.25–8.17 (m, 1 H, 4-H), 7.69–7.60 (m, 2 H, aromatic), 7.48–7.34 (m, 4 H, aromatic), 7.32–7.21 (m, 2 H, aromatic), 3.83 (s, 3 H, CO_2Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8, 144.6, 135.1, 132.0, 129.5, 129.3, 128.2, 127.5, 123.3, 122.2, 122.1, 111.0, 104.5, 50.9 ppm. GC–MS: *m*/*z* (%) = 251 (92) [M^+], 221 (19), 220 (100), 193 (15), 191 (17), 190 (13), 165 (38), 139 (5), 126 (5), 96 (15), 82 (5). $C_{16}H_{13}NO_2$ (251.28): C 76.48, H 5.21, N 5.57; found C 76.40, H 5.21, N 5.58.

Methyl 2-(Thiophen-3-yl)-1*H*-indole-3-carboxylate (10b): Yield: 224 mg, starting from 275 mg of **7b** (63%) (Table 3, entry 3). Colorless solid, m.p. 91–92 °C. IR (KBr): $\tilde{\nu}$ = 3446 (m br.), 1709 (s), 1569 (w), 1437 (m), 1384 (w), 1366 (w), 1267 (m), 1213 (m), 1189 (m), 1145 (m), 1108 (s), 1070 (s), 993 (m), 785 (m), 756 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.93 (br. s, 1 H, NH), 8.21–8.13 (m, 1 H, 4-H), 7.78 (dd, *J* = 2.8, 1.2 Hz, 1 H, 2-H on thienyl ring), 7.45 (distorted dd, *J* = 5.2, 1.2 Hz, 1 H, 5-H), 7.33–7.18 (m, 4 H, aromatic), 3.87 (s, 3 H, CO_2Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 139.5, 135.1, 132.2, 128.5, 127.6, 126.3, 125.4, 123.3, 122.2, 122.1, 111.0, 104.3, 51.0 ppm. GC–MS: *m*/*z* (%) = 257 (53) [M^+], 227 (13), 226 (67), 207 (14), 199 (10), 193 (9), 171 (9), 154 (9), 135 (12), 118 (7), 105 (6), 91 (13), 73 (19), 69 (10). $C_{14}H_{11}NO_2S$ (257.31): C 65.35, H 4.31, N 5.44, S 12.44; found C 65.32, H 4.31, N 5.42, S 12.48.

Methyl 2-(4-Bromophenyl)-1*H*-indole-3-carboxylate (10c): Yield: 256 mg, starting from 375 mg of **7c** (56%) (Table 3, entry 4). Colorless solid, m.p. 169–172 °C. IR (KBr): $\tilde{\nu}$ = 3299 (m br.), 1683 (s), 1492 (m), 1426 (m), 1389 (w), 1336 (w), 1279 (m), 1213 (m), 1127 (m), 1067 (m), 1043 (m), 1011 (m), 829 (m), 786 (m), 753 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.89 (br. s, 1 H, NH), 8.22–8.12 (m, 1 H, 4-H), 7.49–7.40 (m, 4 H, aromatic), 7.35–7.23 (m, 3 H, aromatic), 3.81 (s, 3 H, CO_2Me) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 143.2, 135.3, 131.3, 131.0, 130.8, 127.4, 123.6, 123.5,

122.3, 122.2, 111.2, 104.8, 51.0 ppm. GC–MS: *m/z* (%) = 331 (98) $[M + 2]^+$, 329 (100) $[M^+]$, 300 (74), 298 (76), 271 (9), 235 (12), 219 (44), 191 (19), 190 (31), 164 (13), 163 (13), 125 (14), 96 (17). $C_{16}H_{12}BrNO_2$ (330.18): C 58.20, H 3.66, Br 24.20, N 4.24; found C 58.28, H 3.65, Br 24.27, N 4.23.

Methyl 2-Butyl-1*H*-indole-3-carboxylate (10d): Yield: 145 mg, starting from 239 mg of **7d** (45%) (Table 3, entry 5). Colorless solid, m.p. 67–69 °C, ref.[20] 67–68 °C. IR (KBr): $\tilde{\nu}$ = 3287 (m br.), 1664 (s), 1581 (w), 1457 (m), 1384 (w), 1327 (w), 1209 (m), 1118 (m), 1074 (m), 787 (m), 743 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 8.92 (br. s, 1 H, NH), 8.18–8.08 (m, 1 H, 4-H), 7.34–7.14 (m, 3 H, aromatic), 3.93 (s, 3 H, CO_2Me), 3.17–3.09 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.74–1.62 (m, 2 H, $CH_2CH_2CH_3$), 1.44–1.29 (m, 2 H, CH_2CH_3), 0.89 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 149.0, 134.6, 127.2, 122.3, 121.7, 121.3, 110.8, 103.9, 50.8, 31.4, 27.7, 22.6, 13.8 ppm. GC–MS: *m/z* (%) = 231 (77) $[M^+]$, 200 (26), 189 (100), 188 (52), 170 (46), 158 (27), 157 (18), 156 (58), 143 (15), 130 (89), 129 (36), 128 (46), 115 (17), 102 (19), 89 (10), 77 (11). $C_{14}H_{17}NO_2$ (231.29): C 72.70, H 7.41, N 6.06; found C 72.76, H 7.39, N 6.05.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra for all products.

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