# Facile Access to 2-Arylindolines and 2-Arylindoles by Microwave-Assisted Tandem Radical Cyclization

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Dedicated to Prof. Reinhard W. Hoffmann on the occasion of his 75th birthday

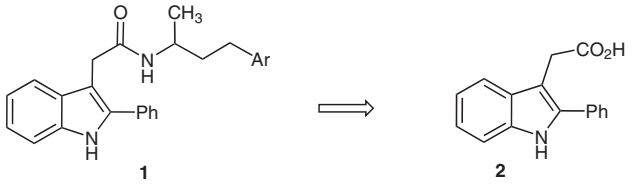
**Abstract:** A new route providing access to 2-arylindoles has been developed. The synthesis consists of a tin-mediated tandem radical cyclization of appropriate precursors to form 2,3-disubstituted dihydroindoles, which in turn are oxidized to yield the corresponding 2-arylindoles. The reactions proceed smoothly under microwave irradiation, furnishing the desired products in good yields.

**Key words:** indoles, cyclizations, heterocycles, radical reactions, dehydrogenations, microwave irradiation

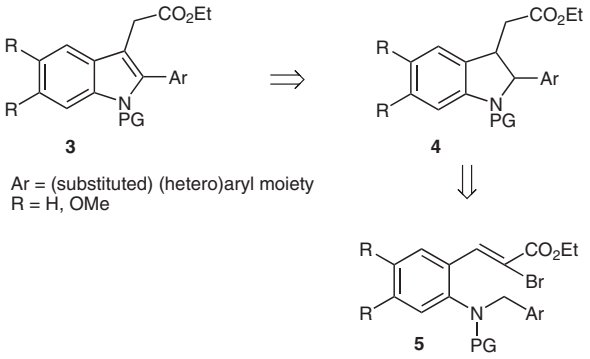
The indole moiety is a privileged scaffold in medicinal chemistry, being present in a wide range of biologically active natural and artificial compounds.[1] Recently, a novel class of highly selective ERα ligands (SERAMs) such as **1** derived from the 2-(2-phenyl-1*H*-indol-3-yl)acetic acid moiety **2** as a crucial building block was disclosed, with this key intermediate having potential utilization as a lead structure towards the treatment of breast cancer (Scheme 1).[2]

To date, several elegant methods for assembling 2-arylindol-3-ylacetic acids have been established. These strategies consist of transition-metal-assisted intermolecular annulation and concomitant derivatization,[3] cyclization of imidoyl radicals[4] in combination with arylations,[5] twofold elimination protocols of vinyl sulfones,[6] base-catalyzed cyclization exploiting umpolung of imines,[7] or the Fischer indolization approach.[8]

We report here a different approach that allows the direct synthesis of 2-(2-arylindol-3-yl)acetic acid derivatives **3** as well as their corresponding indoline derivatives **4** from 3-(2-aminophenyl)acrylates **5** by tandem radical cyclization involving 1,6-hydrogen transfer followed by 5-*exo* ring closure (Scheme 2), a synthetic method that was pioneered by Parsons et al. for the synthesis of mitomycins.[9]



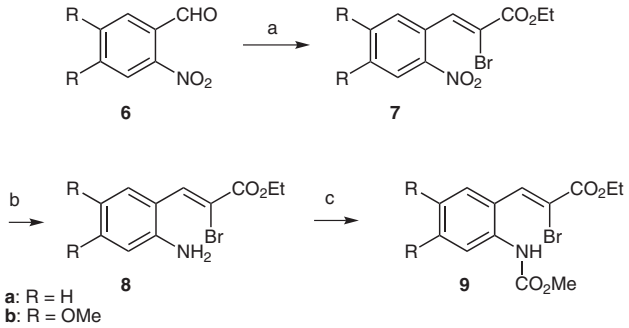

**Scheme 1**




**Scheme 2**

Anilines **8** were readily synthesized in high yields from commercially available 2-nitrobenzaldehydes **6**, which formed acrylates **7** by a Horner–Wadsworth–Emmons reaction with triethyl α-bromophosphonoacetate generated in situ (Scheme 3). Subsequent reduction of the thus formed acrylates **7** with iron powder under acidic conditions following a literature procedure[4,9] gave anilines **8** (Scheme 3).

The direct monobenzylation of **8** by reaction with benzyl bromide failed: a complex mixture of unchanged starting material, and dibenzylated product along with the desired monobenzylated product was observed. To circumvent this lack of selectivity, the introduction of an appropriate protecting group was first necessary. For this, aniline **8**




**Scheme 3** *Reagents and conditions*: (a) NaH (1.4 equiv), triethyl α-bromophosphonoacetate (1.3 equiv), THF, 0 °C, 5.5 h [95% (**7a**), 75% (**7b**)]; (b) Fe (3.5 equiv), EtOH/HCl, reflux, 2 h [86% (**8a**), 56% (**8b**)]; (c) $ClCO_2Me$ (1.4 equiv), py (3 equiv), DMF, 40 °C, 4 h [91% (**9a**), 85% (**9b**)].

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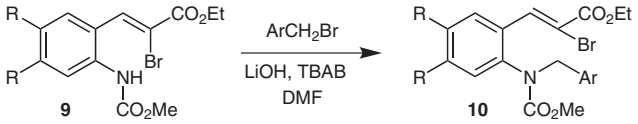
**Table 1** Preparation of Precursors **10a–h** for Radical Cyclization[a]

| Entry | Product **10** | R | Ar | Yield (%) |
|---|---|---|---|---|
| 1 | **10a** | H | Ph | 91 |
| 2 | **10b** | H | 3-$ClC_6H_4$ | 88 |
| 3 | **10c** | H | 4-$O_2NC_6H_4$ | 93 |
| 4 | **10d** | H | PMP | 89 |
| 5 | **10e** | H | 3-$MeOC_6H_4$ | 90 |
| 6 | **10f** | H | Naph | 72 |
| 7 | **10g** | H | 2-furyl | 76 |
| 8 | **10h** | OMe | Ph | 88 |

[a] Reagents and conditions: LiOH (1.5 equiv), TBAB (0.1 equiv), $ArCH_2Br$ (2 equiv), DMF, 40 °C, 4 h.

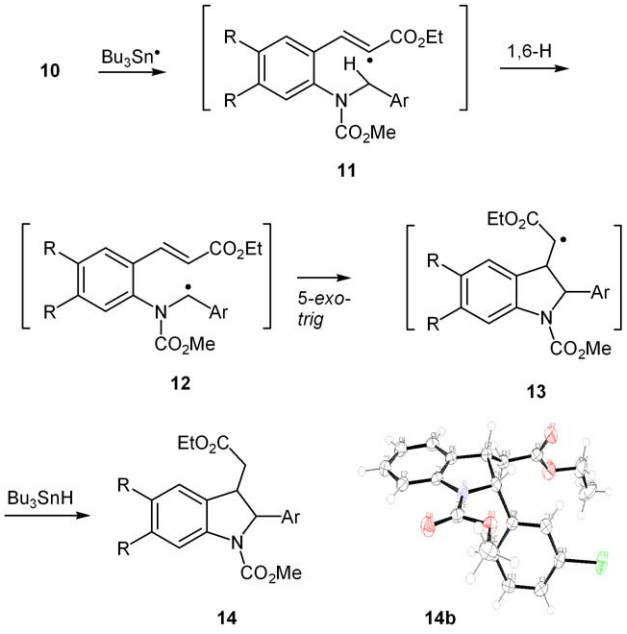



**Scheme 4**

was initially *N*-Boc-protected; however, the successive benzylation produced only small amounts of desired product, presumably due to the steric effects of the space-demanding protecting group. Therefore, the methoxycarbonyl group (Moc) was introduced by reaction of **8** with methyl chloroformate to give **9** in very good yield [91% (**9a**), 85% (**9b**)] (Scheme 3).

After careful optimization of the reaction conditions, the thus-protected anilines **9** could be successfully alkylated with a broad variety of benzyl bromides under phase-transfer conditions using lithium hydroxide/tetrabutylammonium bromide in *N*,*N*-dimethylformamide (Scheme 4, Table 1). Weaker bases such as potassium carbonate or triethylamine proved to be less effective, while the utilization of stronger bases like sodium hydride was avoided due to the danger of possible elimination of hydrogen bromide from the bromoacrylate. This was already observed in part when the reaction temperature was increased to above 45 °C when lithium hydroxide was used as base, but, on the other hand, decreasing the reaction temperature to room temperature led to significantly reduced yields even if the reaction time was extended to 24 hours.

Compounds **10a–d** were submitted to radical cyclization mediated by tributyltin hydride (Scheme 5), which was carried out initially under refluxing toluene conditions, with a low concentration of tributyltin hydride in the reaction mixture maintained by the addition of this reagent via a syringe pump over two hours; for this, a protocol that has proved successful for a related tandem radical cyclization to dihydrobenzofurans was followed.[10] The reaction furnished 2,3-disubstituted indolines **14a**,**b**,**d** in yields of 62–76% (Table 2, entries 1,3,6), but no cyclization occurred with substrate **10c** (entry 5). In the latter case, be-




**Scheme 5**

sides starting material, small amounts of products containing a reduced nitro group could be detected in the crude reaction mixture. Performing the cyclization under microwave heating in an open vessel resulted in some shortening of the reaction time (3.5 h instead of 5 h for complete consumption of starting material), but, more importantly, yields were significantly improved to 76–89% (Table 2, entries 2,4,7). Consequently, these conditions were also applied for the cyclization of **10e–h** to give the corresponding indolines **14e–h** in 25–73% yield (Table 2, entries 8–11).

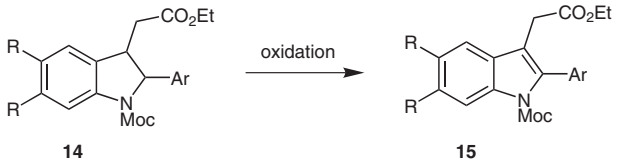
The *cis*/*trans* ratios of indolines **14** (Scheme 5, Table 2) were determined by $^1$H NMR spectroscopy, with the final assignments accomplished by NOESY experiments. Diastereomers of **14a–e** could be separated by crystallization of the product mixture, and the *cis*-diastereomer of **14b** could be additionally characterized by X-ray crystallography (Scheme 5).[11] The *cis*-diastereomers of **14** are kinetically favored (Table 2),[12] and thus formed predominantly (*cis*/*trans* ca. 2:1) in the course of the reaction, with the exception being naphthyl derivative **14f**, which was obtained in a reversed *cis*/*trans* diastereoselectivity (1:3), albeit in low yields of 25% along with reduced but uncyclized starting material (Table 2, entry 9). This may be a consequence of a relatively long lifetime of the uncyclized radical intermediate **12f** (cf. Scheme 5) stabilized by the adjacent naphthyl group, leading to a preferred formation of the sterically less hindered, but thermodynamically favored *trans*-diastereomer.

The transformation of indolines **14** into the desired 2-arylindoles **15** (Scheme 6) was investigated with several dehydrogenation reagents[13] (Table 3), of which 2,3-dichloro-5,6-dicyano-1,4-benzoquinone proved to be most effective, with respect to yields as well as ease of workup and purification of the products (Table 3, entries

**Table 2** Radical Cyclization of **10a–h** to 2,3-Substituted Indolines **14a–h**

| Entry | Conditions[a] | Indoline **14** | R | Ar | Yield (%) | Ratio *cis*/*trans* |
|---|---|---|---|---|---|---|
| 1 | A | **14a** | H | Ph | 71 | 66:34 |
| 2 | B | **14a** | H | Ph | 86 | 66:36 |
| 3 | A | **14b** | H | 3-$ClC_6H_4$ | 62 | 67:33 |
| 4 | B | **14b** | H | 3-$ClC_6H_4$ | 76 | 64:36 |
| 5 | A | **14c** | H | 4-$O_2NC_6H_4$ | –[b] | – |
| 6 | A | **14d** | H | PMP | 76 | 63:37 |
| 7 | B | **14d** | H | PMP | 89 | 60:40 |
| 8 | B | **14e** | H | 3-$MeOC_6H_4$ | 73 | 60:40 |
| 9 | B | **14f** | H | Naph | 25 | 25:75 |
| 10 | B | **14g** | H | 2-furyl | 68 | 67:33 |
| 11 | B | **14h** | OMe | Ph | 64 | 59:41 |

[a] Reagents and conditions: $Bu_3SnH$ (1.4 equiv), AIBN (2 × 0.25 equiv), toluene; Method A: reflux, 5 h; Method B: open vessel, 100–105 °C, microwave (2.45 GHz), 3.5 h.
[b] No cyclized product was obtained, only partially reduced acyclic products were observed.




**14** **15**

**Scheme 6**

1, 2, and 6). Treatment of **14a** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in benzene at 50 °C for two days provided the desired indole **15a** in 48% yield along with unchanged, exclusively *trans*-configured starting material **14a** (25%) (Table 3, entry 1). Because of the obvious lower reactivity of the *trans*-diastereomer towards aromatization, the reaction temperature was increased by changing the solvent to toluene. The reaction was carried out at reflux temperature for five days until no starting material could be detected by TLC, and **15a** was isolated in 63% yield (Table 3, entry 2). Further improvements were possible by carrying out this transformation under microwave heating in a sealed vessel at 120 °C, resulting again in slightly improved yields, but, moreover, the reaction time could be shortened to four hours (Table 3, entry 6). Under the same conditions, indolines **14b**,**d–h** were also subjected to dehydrogenation, and, with the exception of furyl derivative **14g**, smoothly yielded the corresponding indoles **15b–e**,**g** (Scheme 6, Table 4).

In conclusion, a facile method for the synthesis of the (2-arylindol-3-yl)acetic acid moiety, representing a potential lead structure for the development of drugs against breast cancer, could be developed.

**Table 3** Conditions for the Dehydrogenation of Indoline **14a** to Indole **15a**

| Entry | Reaction conditions | Yield (%) |
|---|---|---|
| 1 | DDQ (2 equiv), benzene, 50 °C, 2 d | 48 |
| 2 | DDQ (2 equiv), toluene, reflux, 5 d | 63 |
| 3 | $Mn_2O$ (10 equiv), benzene, reflux, 2 d | 11 |
| 4 | NBS (1.5 equiv), $CCl_4$, reflux, 12 h | 53 |
| 5 | CAN (2 equiv), MeCN–$H_2O$, 70 °C, 3 h | 32 |
| 6 | DDQ (2 equiv), toluene, sealed vessel, 120 °C, MW, 4 h | 66 |

**Table 4** Microwave-Induced, 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone-Promoted Aromatization of Indolines **14** to Indoles **15**[a]

| Entry | Starting material **14**[a] | Product **15** | R | Ar | Yield (%) |
|---|---|---|---|---|---|
| 1 | **14a** | **15a** | H | Ph | 66 |
| 2 | **14b** | **15b** | H | 3-$ClC_6H_4$ | 60 |
| 3 | **14d** | **15c** | H | PMP | 61 |
| 4 | **14e** | **15d** | H | 3-$MeOC_6H_4$ | 60 |
| 5 | **14f** | **15e** | H | Naph | 55 |
| 6 | **14g** | **15f** | H | 2-furyl | –[b] |
| 7 | **14h** | **15g** | OMe | Ph | 69 |

[a] Reagents and conditions: DDQ (2 equiv), toluene, sealed vessel, 120 °C, MW, 4 h.
[b] Decomposition, only small amounts of product **15f**.

All nonaqueous reactions were carried out in oven-dried glassware under $N_2$. Toluene and benzene were distilled from Na. THF was distilled from Na/benzophenone ketyl under $N_2$. All other reagents were commercially available and were used without further purification. Preparative flash chromatography was performed on Silica Gel 60 (Merk Geduran 60, 0.063–0.200 mm). $^1H$ and $^{13}C$ NMR spectra were recorded on Bruker Avance 300, 400, and 600 instruments; $CDCl_3$ or DMSO-$d_6$ was used as solvent. IR spectra were recorded on an FT IR spectrometer (Excalibur Series FT3000MX), melting points were recorded on a Büchi-SMP-20 apparatus and are uncorrected, HRMS was performed on Varian MAT 311A, Finnigan MAT95, and Thermoquest Finnigan TSQ 7000 spectrometers, and elemental analysis was carried out on a Vario EL III or Mikro-Rapid CHN (Heraeus) instrument. Microwave-assisted reactions were performed in a CEM Focused Microwave Synthesis System, Discover. Reactions were monitored by TLC on Merck 60 $F_{254}$ silica gel TLC plates. Spots were visualized by UV light at 254 and 356 nm. All solvents used for column chromatography were distilled.

**2-Bromo-3-(2-nitrophenyl)acrylates 7; General Procedure**

A 60% suspension of NaH in fuel oil (3.7 g, 92.6 mmol, 1.40 equiv) was added to THF (50 mL) at 0 °C under $N_2$. $(EtO)_2P(O)CH_2CO_2Et$ (18.08 g, 86.1 mmol, 1.30 equiv) dissolved in THF (30 mL) was added dropwise over 15 min, and stirring of the resulting mixture continued for 45 min. $Br_2$ (14.29 g, 89.4 mmol, 1.35 equiv) was add-

ed dropwise over 15 min, and stirring of the reaction mixture continued for 30 min at 0 °C. A 60% suspension of NaH in fuel oil (3.7 g, 92.6 mmol, 1.40 equiv) was added over 20 min, and stirring continued for 1 h at 0 °C. 2-Nitrobenzaldehyde **6** (66.17 mmol, 1.0 equiv) dissolved in THF (20 mL) was added and the reaction mixture was slowly warmed to r.t. and stirred for 5.5 h. Sat. aq $NH_4Cl$ (15 mL) was added and the mixture was extracted with $Et_2O$ (3 × 50 mL). The combined organic phases were washed with brine (30 mL), dried ($Na_2SO_4$), filtered, and concentrated. The crude product was recrystallized from *i*-PrOH (25 mL) to give pale yellow crystals of **7**.

**Ethyl (*Z*)-2-Bromo-3-(2-nitrophenyl)acrylate (7a)**
Yield: 18.9 g (95%); mp 61–62 °C; $R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 621, 691, 751, 868, 1038, 1245, 1276, 1340, 1470, 1570, 1602, 1622, 1719, 2936, 2995, 3062 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 4.38 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 7.56–7.62 (m, 1 H, CH), 7.64 (d, *J* = 7.2 Hz, 1 H, CH), 7.73 (dd, *J* = 1.2, 7.4 Hz, 1 H, CH), 8.21 (dd, *J* = 1.2, 8.2 Hz, 1 H, CH), 8.49 (s, 1 H, CH).

$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 63.1 ($CH_2$), 117.4 (C), 124.9 (CH), 129.9 (CH), 131.0 (C), 131.2 (CH), 133.6 (CH), 139.1 (CH), 147.0 (C), 162.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 301.1 (2) $[M]^+$, 220.1 (17) $[M - Br]^+$, 29.3 (100) $[C_2H_5]^+$.

**Ethyl (*Z*)-2-Bromo-3-(4,5-dimethoxy-2-nitrophenyl)acrylate (7b)**
Yield: 17.9 g (75%); mp 137–138 °C; $R_f$ = 0.3 (hexanes–EtOAc, 5:1).

IR (KBr): 613, 749, 787, 868, 985, 1045, 1219, 1282, 1329, 1513, 1725, 2854, 2945, 2993, 3078 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.40 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.98 (s, 6 H, $CH_3$), 4.39 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 7.18 (s, 1 H, CH), 7.75 (s, 1 H, CH), 8.49 (s, 1 H, CH).

$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 56.5 ($CH_3$), 56.7 ($CH_3$), 63.0 ($CH_2$), 107.6 (CH), 112.3 (CH), 116.4 (C), 125.1 (C), 139.7 (C), 149.4 (C), 153.1 (C), 162.5 (C).

Anal. Calcd for $C_{13}H_{14}BrNO_6$: C, 43.35; H, 3.92; N, 3.89. Found: C, 43.70; H, 4.14; N, 3.89.

**3-(2-Aminophenyl)-2-bromoacrylates 8; General Procedure**
3-(2-Nitrophenyl)acrylate **7** (25.5 mmol, 1.0 equiv) was dissolved under reflux in EtOH (70 mL). Then Fe powder (5 g, 89.4 mmol, 3.5 equiv) and 37% aq HCl (19.5 mL) were added portionwise over 1.3 h under reflux, and the mixture was refluxed for an additional 30 min. The mixture was concentrated on a rotary evaporator to 35 mL, and $CH_2Cl_2$ (60 mL) was added. Sat. aq $NaHCO_3$ (40 mL) was added to adjust the pH of the aqueous layer to 8, and the aqueous layer was then extracted with $CH_2Cl_2$ (3 × 60 mL). The combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated. The crude mixture was purified by chromatography (silica gel, hexanes–EtOAc, 5:1); this gave **8**.

**Ethyl (*Z*)-3-(2-Aminophenyl)-2-bromoacrylate (8a)**
Yield: 5.93 g (86%); mp 43 °C; $R_f$ = 0.3 (hexanes–EtOAc, 3:1).

IR (KBr): 490, 588, 751, 822, 888, 1037, 1157, 1194, 1245, 1278, 1366, 1454, 1489, 1590, 1641, 1687, 2903, 2986, 3063, 3345, 3416 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.39 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.70 (s, 2 H, $NH_2$), 4.35 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 6.75 (dd, *J* = 0.9, 8.1 Hz, 1 H, CH), 6.83 (dt, *J* = 0.9, 7.5 Hz, 1 H, CH), 7.21 (dt, *J* = 0.9, 7.5 Hz, 1 H, CH), 7.63 (dd, *J* = 0.9, 7.5 Hz, 1 H, CH), 8.16 (s, 1 H, CH).

$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 13.2 ($CH_3$), 61.8 ($CH_2$), 114.6 (C), 115.0 (CH), 117.2 (CH), 118.8 (C), 128.3 (CH), 129.9 (CH), 136.4 (CH), 143.9 (C), 162.2 (C).

MS (EI, 70 eV): *m*/*z* (%) = 270.9 (18) $[M^+]$, 269.0 (16) $[M]^+$, 226.0 (24) $[M - OCH_2CH_3]^+$, 223.9 (26) $[M - OCH_2CH_3]^+$, 144.0 (100) $[M - OCH_2CH_3,Br]^+$.

**Ethyl (*Z*)-3-(2-Amino-4,5-dimethoxyphenyl)-2-bromoacrylate (8b)**
Yield: 4.71 g (56%); mp 219 °C; $R_f$ = 0.3 (hexanes–EtOAc, 3:1).

IR (KBr): 567, 602, 756, 841, 911, 1003, 1155, 1244, 1400, 1447, 1508, 1623, 1655, 2789, 2897, 2976, 3136 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.67–3.80 (s, 2 H, $NH_2$), 3.83 (s, 3 H, $OCH_3$), 3.92 (s, 3 H, $OCH_3$), 3.95 (s, 3 H, $OCH_3$), 4.36 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 6.29 (s, 1 H, CH), 7.49 (s, 1 H, CH), 8.19 (s, 1 H, CH).

$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 14.3 ($CH_3$), 55.8 ($CH_3$), 56.4 ($CH_3$), 62.6 ($CH_2$), 100.3 (CH), 111.0 (C), 111.8 (C), 112.1 (CH), 114.1 (C), 114.7 (CH), 152.1 (C), 163.6 (C).

MS (EI, 70 eV): *m*/*z* (%) = 329.0 (10) $[M]^+$, 284.0 (100) $[M - OCH_2CH_3]^+$, 270.0 (46) $[M - OCH_2CH_3, CH_3]^+$.

**2-Bromo-3-{2-[(methoxycarbonyl)amino]phenyl}acrylates 9; General Procedure**
To a soln of **8** (14.81 mmol, 1.0 equiv) in DMF (15 mL) was added pyridine (3.51 g, 44.42 mmol, 3 equiv) and $ClCO_2Me$ (1.96 g, 20.73 mmol, 1.4 equiv). The mixture was heated to 40 °C for 4 h, subsequently diluted with EtOAc (35 mL) and sat. aq $NH_4Cl$ (10 mL), and extracted with EtOAc (3 × 20 mL). The combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated. The crude mixture was purified by chromatography (silica gel, hexanes–EtOAc, 3:1); this gave pale yellow solid **9**.

**Ethyl (*Z*)-2-Bromo-3-{2-[(methoxycarbonyl)amino]phenyl}acrylate (9a)**
Yield: 4.4 g (91%); mp 72–73 °C; $R_f$ = 0.2 (hexanes–EtOAc, 5:1).

IR (KBr): 488, 575, 612, 706, 757, 833, 860, 908, 945, 1037, 1069, 1109, 1190, 1248, 1273, 1364, 1450, 1537, 1581, 1616, 1702, 2943, 2986, 3030, 3301 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.38 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 4.15 (s, 4 H, $CH_2$), 4.39 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 6.23 (s, 1 H, NH), 7.01 (d, *J* = 8.0 Hz, 1 H, CH), 7.16 (dt, *J* = 7.6, 0.9 Hz, 1 H, CH), 7.39 (dt, *J* = 7.8, 1.3 Hz, 1 H, CH), 7.56 (d, *J* = 7.7 Hz, 1 H, CH), 7.85 (d, *J* = 7.7 Hz, 1 H, CH), 8.15 (s, 1 H, CH).

$^{13}C$ NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 52.6 ($CH_3$), 63.1 ($CH_2$), 118.4 (C), 121.9 (CH), 123.9 (CH), 125.7 (C), 129.0 (CH), 130.3 (CH), 135.5 (C), 137.5 (CH), 154.1 (C), 162.6 (C).

MS (CI): *m*/*z* (%) = 347.1 (100) $[MNH_4]^+$, 345.0 (98) $[M + NH_4]^+$, 330.1 (8) $[M + H]^+$, 328.1 (8) $[M + H]^+$, 267.2 (9), 248.2 (12), 202.3 (37) $[M - OCH_2CH_3,Br]^+$

**Ethyl (*Z*)-2-Bromo-3-{4,5-dimethoxy-2-[(methoxycarbonyl)amino]phenyl}acrylate (9b)**
Yield: 4.9 g (85%); mp 141 °C; $R_f$ = 0.3 (hexanes–EtOAc, 3:1).

IR (KBr): 510, 574, 653, 751, 854, 993, 1035, 1123, 1210, 1234, 1339, 1510, 1590, 1695, 2836, 2955, 3275 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.72 (s, 3 H, $CH_3$), 3.89 (s, 3 H, $CH_3$), 3.91 (s, 3 H, $CH_3$), 4.38 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 6.42 (s, 1 H, NH), 7.41 (s, 2 H, CH), 8.15 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 52.6 ($CH_3$), 56.0 ($CH_3$), 56.2 ($CH_3$), 62.9 ($CH_2$), 111.2 (CH), 115.3 (C), 130.4 (C), 136.3 (CH), 150.7 (C), 154.5 (C), 163.0 (C).

Anal. Calcd for $C_{15}H_{18}BrNO_6$: C, 46.41; H, 4.67; N, 3.61. Found: C, 46.68; H, 4.91; N, 3.50.

### 3-{2-[(Arylmethyl)(methoxycarbonyl)amino]phenyl}-2-bromoacrylates 10; General Procedure

LiOH (1.5 mmol, 1.5 equiv) was added portionwise over 30 min to a soln of **9** (1.0 mmol, 1.0 equiv), TBAB (0.1 mmol, 0.1 equiv), and $ArCH_2Br$ (2.0 mmol, 2.0 equiv) in DMF (3 mL) at 40 °C. The mixture was stirred at this temperature for a further 3.5 h, after which the reaction mixture was diluted with EtOAc (10 mL), washed with sat. aq $NH_4Cl$ (10 mL), and extracted with EtOAc (3 × 15 mL). The combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated. The crude mixture was purified by chromatography (silica gel, hexanes–EtOAc); this gave **10**.

### Ethyl (*Z*)-3-{2-[Benzyl(methoxycarbonyl)amino]phenyl}-2-bromoacrylate (10a)

Colorless oil; yield: 91%; $R_f$ = 0.3 (hexanes–EtOAc, 9:1).

IR (KBr): 455, 631, 701, 764, 984, 1040, 1103, 1138, 1191, 1254, 1290, 1380, 1446, 1484, 1618, 1713, 2954, 2984, 3031 cm$^{-1}$.

$^1$H NMR (300 MHz, DMSO-$d_6$, 343 K): δ = 1.29 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.58 (s, 3 H, $CH_3$), 4.26 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 4.76 (s, 2 H, $CH_2$), 7.13–7.17 (m, 2 H, CH), 7.22–7.27 (m, 4 H, CH), 7.36 (dt, *J* = 7.6, 1.5 Hz, 1 H, CH), 7.44 (dt, *J* = 7.6, 1.5 Hz, 1 H, CH), 7.74 (s, 1 H, CH), 7.76 (dd, *J* = 7.6, 1.3 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, DMSO-$d_6$, 343 K): δ = 13.5 ($CH_3$), 52.3 ($CH_3$), 53.6 ($CH_2$), 62.0 ($CH_2$), 115.0 (C), 126.6 (CH), 127.1 (CH), 127.7 (CH), 127.9 (CH), 128.0 (CH), 128.8 (CH), 130.2 (CH), 132.1 (C), 136.6 (C), 137.4 (CH), 140.3 (C), 154.8 (C), 161.6 (C).

MS (EI, 70 eV): *m*/*z* (%) = 417.0 (2) [M$^+$], 338.1 (8) [M – Br]$^+$, 91.1 (100) [$C_7H_7$]$^+$.

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}BrNO_4$: 417.0576; found: 417.0567.

### Indolines 14 by Radical Cyclization of 2-Bromo-3-phenylacrylates 10; General Procedure

A mixture of *n*-$Bu_3SnH$ (185 μL, 0.7 mmol, 1.4 equiv) and AIBN (22 mg, 0.13 mmol, 0.25 equiv) in toluene (10 mL) was added via a syringe pump over 3 h to a refluxing (microwave irradiation at 100–105 °C under open-vessel conditions) soln of **10** (0.5 mmol, 1.0 equiv) and AIBN (22 mg, 0.13 mmol, 0.25 equiv) in toluene (10 mL). The solvent was evaporated and the residue was dissolved in $Et_2O$ (100 mL). DBU (2.7 equiv, 1.35 mmol) was added to the soln, which was titrated with 0.1 M $I_2$ in $Et_2O$ and filtered through silica gel.[14] The crude product was purified by chromatography (silica gel, hexanes–EtOAc); this gave **14** as white solids.

### Methyl 3-(2-Ethoxy-2-oxoethyl)-2-phenylindoline-1-carboxylate (14a)

$R_f$ = 0.3 (hexanes–EtOAc, 5:1).

IR (KBr): 456, 700, 754, 849, 934, 1022, 1057, 1171, 1193, 1275, 1312, 1385, 1443, 1484, 1602, 1713, 2955, 2982, 3030 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14a**) = 1.20 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.02 (dd, *J* = 10.2, 17.4 Hz, 1 H, $CH_2$), 2.63 (dd, *J* = 17.4, 5.00 Hz, 1 H, $CH_2$), 3.68 (s, 3 H, $CH_3$), 4.09 (dq, *J* = 7.2, 0.9 Hz, 2 H, $CH_2$), 4.28 (dt, *J* = 10.0, 5.0 Hz, 1 H, CH), 5.63 (d, *J* = 10.0 Hz, 1 H, CH), 6.98–7.09 (m, 4 H, CH), 7.16–7.33 (m, 4 H, CH), 7.87 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14a**) = 1.27 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.67 (dd, *J* = 8.2, 6.2 Hz, 2 H, $CH_2$), 3.55 (ddd, *J* = 8.2, 6.2 Hz, 1.4 Hz, 1 H, CH), 3.75 (s, 3 H, $CH_3$), 4.20 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.22 (d, *J* = 1.4 Hz, 1 H, CH), 6.98–7.10 (m, 1 H, CH), 7.12–7.22 (m, 1 H, CH), 7.24–7.39 (m, 6 H, CH), 7.98 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14a**) = 14.2 ($CH_3$), 34.2 ($CH_2$), 41.0 (CH), 52.7 ($CH_3$), 60.7 ($CH_2$), 66.4 (CH), 114.6 (CH), 123.1 (CH), 123.4 (CH), 126.9 (CH), 127.9 (CH), 128.4 (CH), 128.4 (CH), 132.0 (C), 138.3 (C), 153.5 (C), 172.2 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14a**) = 13.2 ($CH_3$), 40.1 ($CH_2$), 46.4 (CH), 51.7 ($CH_3$), 59.8 ($CH_2$), 67.1 (CH), 114.0 (CH), 122.3 (CH), 123.8 (CH), 124.2 (CH), 126.4 (CH), 127.6 (CH), 128.5 (C), 131.0 (C), 141.3 (C), 152.7 (C), 170.5 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{21}NO_4$: 339.1471; found: 339.1471.

Anal. Calcd for $C_{20}H_{21}NO_4$: C, 70.78; H, 6.24; N, 4.13. Found: C, 70.59; H, 6.45; N, 4.02.

### Methyl 2-(3-Chlorophenyl)-3-(2-ethoxy-2-oxoethyl)indoline-1-carboxylate (14b)

$R_f$ = 0.3 (hexanes–EtOAc, 5:1).

IR (KBr): 480, 509, 575, 631, 706, 752, 791, 849, 888, 934, 1024, 1056, 1080, 1138, 1180, 1254, 1271, 1308, 1335, 1381, 1442, 1483, 1575, 1597, 1717, 2957 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14b**) = 1.22 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.00 (dd, *J* = 10.6, 17.5 Hz, 1 H, $CH_2$), 2.68 (dd, *J* = 17.4, 4.2 Hz, 1 H, $CH_2$), 3.70 (s, 3 H, $CH_3$), 4.12 (dq, *J* = 7.2, 2.4 Hz, 2 H, $CH_2$), 4.30 (dt, *J* = 9.7, 4.2 Hz, 1 H, CH), 5.61 (d, *J* = 9.7 Hz, 1 H, CH), 6.87 (d, *J* = 7.4 Hz, 1 H, CH), 7.01–7.32 (m, 6 H, CH) 7.89 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14b**) = 1.27 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.67 (dd, *J* = 2.0, 7.4 Hz, 2 H, $CH_2$), 3.52 (ddd, *J* = 8.4, 7.4 Hz, 1.4 Hz, 1 H, CH), 3.70 (s, 3 H, $CH_3$), 4.20 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.19 (d, *J* = 1.4 Hz, 1 H, CH), 7.01–7.32 (m, 7 H, CH), 7.89 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14b**) = 14.2 ($CH_3$), 34.2 ($CH_2$), 41.0 (CH), 52.8 ($CH_3$), 60.9 ($CH_2$), 65.8 (CH), 114.7 (CH), 123.3 (CH), 123.5 (CH), 124.9 (CH), 127.3 (CH), 128.2 (CH), 128.4 (CH), 128.6 (CH), 129.8 (CH), 134.3 (C), 140.4 (CH), 153.4 (C), 172.1 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14b**) = 14.2 ($CH_3$), 41.1 ($CH_2$), 46.5 (CH), 52.8 ($CH_3$), 60.9 ($CH_2$), 67.7 (CH), 115.1 (CH), 123.6 (CH), 125.6 (CH), 127.3 (CH), 127.7 (CH), 128.2 (CH), 128.6 (C), 128.8 (CH), 130.0 (CH), 131.0 (C), 140.5 (C), 153.4 (C), 171.4 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}ClNO_4$: 373.1081; found: 373.1080.

Anal. Calcd for $C_{20}H_{20}ClNO_4$: C, 64.26; H, 5.39; N, 3.75. Found: C, 64.51; H, 5.62; N, 3.67.

### Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)indoline-1-carboxylate (14d)

$R_f$ = 0.3 (hexanes–EtOAc, 5:1).

IR (KBr): 640, 743, 818, 839, 880, 927, 1028, 1055, 1107, 1137, 1173, 1254, 1304, 1383, 1440, 1485, 1516, 1609, 1717, 2851, 2952, 2982 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14d**) = 1.21 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.06 (dd, *J* = 10.1, 17.4 Hz, 1 H, $CH_2$), 2.64 (dd, *J* = 17.4, 5.0 Hz, 1 H, $CH_2$), 3.69 (s, 3 H, $CH_3$), 3.75 (s, 3 H, $CH_3$) 4.10 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 4.22 (ddd, *J* = 10.1, 9.6 Hz, 5.1 Hz, 1 H, CH), 5.59 (d, *J* = 9.6 Hz, 1 H, CH), 6.73 (d, *J* = 8.8 Hz, 2 H, CH), 6.91 (d, *J* = 8.8 Hz, 2 H, CH), 7.00–7.04 (m, 2 H, CH), 7.25–7.30 (m, 1 H, CH), 7.85 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14d**) = 1.26 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.65 (dd, *J* = 1.7, 6.2 Hz, 2 H, $CH_2$), 3.53 (ddd, *J* = 8.3, 6.2

Hz, 1.7 Hz, 1 H, CH), 3.76 (s, 3 H, $CH_3$), 4.19 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.16 (d, *J* = 1.7 Hz, 1 H, CH), 6.79 (d, *J* = 8.8 Hz, 2 H, CH), 6.98–7.17 (m, 2 H, CH), 7.12 (d, *J* = 8.8 Hz, 2 H, CH), 7.25–7.30 (m, 6 H, CH), 7.85 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14d**) = 14.2 ($CH_3$), 34.1 ($CH_2$), 41.1 (CH), 52.7 ($CH_3$), 55.2 ($CH_3$), 60.7 ($CH_2$), 66.0 (CH), 113.7 (CH), 114.6 (CH), 123.1 (CH), 123.4 (CH), 128.1 (CH), 128.3 (CH), 130.4 (C), 132.1 (C), 153.5 (C), 159.1 (C), 172.3 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14d**) = 14.2 ($CH_3$), 41.1 ($CH_2$), 46.8 (CH), 52.6 ($CH_3$), 55.2 ($CH_3$), 60.8 ($CH_2$), 67.8 (CH), 114.0 (CH), 115.0 (CH), 123.3 (CH), 124.8 (CH), 126.56 (CH), 128.6 (CH), 130.4 (C), 134.6 (C), 153.9 (C), 158.9 (C), 171.6 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{23}NO_5$: 369.1576; found: 369.1580.

Anal. Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 67.88; H, 6.48; N, 3.61.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(3-methoxyphenyl)indoline-1-carboxylate (14e)**

$R_f$ = 0.3 (hexanes–EtOAc, 5:1).

IR (KBr): 745, 820, 840, 879, 931, 1026, 1056, 1112, 1140, 1172, 1258, 1300, 1384, 1440, 1486, 1515, 1607, 1716, 2849, 2953, 2980 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14e**) = 1.21 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.07 (dd, *J* = 10.1, 17.3 Hz, 1 H, $CH_2$), 2.67 (dd, *J* = 17.3, 5.00 Hz, 1 H, $CH_2$), 3.71 (s, 6 H, $CH_3$), 4.11 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 4.19–4.31 (m, 1 H, CH), 5.63 (d, *J* = 9.6 Hz, 1 H, CH), 6.61 (s, 1 H, CH), 6.74–6.82 (m, 2 H, CH), 6.98–7.10 (m, 2 H, CH), 7.12–7.19 (m, 1 H, CH), 7.25–7.29 (m, 1 H, CH), 7.92 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14e**) = 1.25 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.67 (dd, *J* = 1.7, 6.3 Hz, 2 H, $CH_2$), 3.55 (m, 1 H, CH), 3.77 (s, 6 H, $CH_3$), 4.18 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.15 (d, *J* = 1.7 Hz, 1 H, CH), 6.62 (s, 1 H, CH), 6.73–6.83 (m, 2 H, CH), 6.99–7.09 (m, 2 H, CH), 7.11–7.16 (m, 1 H, CH), 7.23–7.28 (m, 1 H, CH), 7.92 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14e**) = 13.2 ($CH_3$), 33.0 ($CH_2$), 39.9 (CH), 51.6 ($CH_3$), 54.0 ($CH_3$), 59.6 ($CH_2$), 65.3 (CH), 111.3 (CH), 111.7 (CH), 118.2 (CH), 122.1 (CH), 122.3 (CH), 127.3 (CH), 128.6 (CH), 130.9 (C), 138.9 (C), 152.4 (C), 158.4 (C), 171.2 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14e**) = 13.0 ($CH_3$), 40.0 ($CH_2$), 45.7 (CH), 51.6 ($CH_3$), 54.0 ($CH_3$), 59.7 ($CH_2$), 66.9 (CH), 110.3 (CH), 112.0 (CH), 113.9 (CH), 116.4 (CH), 122.4 (CH), 123.7 (CH), 127.5 (CH), 129.9 (CH), 130.9 (C), 152.7 (C), 158.7 (C), 170.4 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{23}NO_5$: 369.1576; found: 369.1580.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(2-naphthyl)indoline-1-carboxylate (14f)**

$R_f$ = 0.3 (hexanes–EtOAc, 9:1).

IR (KBr): 476, 553, 608, 665, 752, 822, 858, 960, 1030, 1057, 1137, 1184, 1269, 1310, 1381, 1442, 1483, 1699, 710, 2955, 2981 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14f**) = 1.27 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.04 (dd, *J* = 10.0, 18.6 Hz, 1 H, $CH_2$), 2.65 (dd, *J* = 5.5, 18.6 Hz, 1 H, $CH_2$), 3.70 (s, 3 H, $CH_3$), 4.09–4.19 (m, 2 H, $CH_2$), 4.38 (dt, *J* = 5.5, 9.7 Hz, 1 H, CH), 5.83 (d, *J* = 9.7 Hz, 1 H, CH), 6.95–8.12 (m, 11 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14f**) = 1.28 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.74 (dd, *J* = 6.0, 7.3 Hz, 2 H, $CH_2$), 3.60–3.70 (m, 1 H, CH), 3.70 (s, 3 H, $CH_3$), 4.22 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.40 (d, *J* = 1.6 Hz, 1 H, CH), 7.04 (dt, *J* = 0.9, 7.5 Hz, 1 H, CH), 7.16 (d, *J* = 7.5 Hz, 1 H, CH), 7.31–7.46 (m, 4 H, CH), 7.60 (s, 1 H, CH), 7.72–8.12 (m, 4 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14f**) = 14.0 ($CH_3$), 34.4 ($CH_2$), 41.1 (CH), 52.9 ($CH_3$), 60.7 ($CH_2$), 65.6 (CH), 114.7 (CH), 123.2 (CH), 124.25 (CH), 124.5 (CH), 126.0 (CH), 126.4 (CH), 126.9 (CH), 127.9 (CH), 128.3 (CH), 128.5 (CH), 132.0 (C), 133.0 (CH), 134.0 (C), 140.0 (C), 153.6 (C), 172.3 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14f**) = 14.3 ($CH_3$), 41.2 ($CH_2$), 46.7 (CH), 52.9 ($CH_3$), 60.9 ($CH_2$), 68.3 (CH), 115.1 (CH), 123.4 (CH), 123.8 (CH), 124.8 (CH), 125.8 (CH), 126.1(CH), 127.7 (CH), 128.0 (CH), 128.5 (CH), 128.7 (CH), 129.9 (CH), 132.9 (CH), 133.25 (CH), 134.0 (C), 139.7 (C), 153.9 (C), 171.5 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{23}NO_4$: 389.1627; found: 389.1626.

Anal. Calcd for $C_{24}H_{23}NO_4$: C, 74.02; H, 5.95; N, 3.60. Found: C, 73.95; H, 6.22; N, 3.58.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(2-furyl)indoline-1-carboxylate (14g)**

$R_f$ = 0.4 (hexanes–EtOAc, 3:1).

IR (KBr): 734, 914, 1024, 1060, 1150, 1179, 1269, 1331, 1385, 1444, 1601, 1714, 2989 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14g**) = 1.26 (t, *J* = 6.6 Hz, 3 H, $CH_3$), 2.13 (dd, *J* = 10.2, 17.5 Hz, 1 H, $CH_2$), 2.76 (dd, *J* = 17.4, 5.00 Hz, 1 H, $CH_2$), 3.75 (s, 3 H, $CH_3$), 4.17 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 4.19–4.25 (m, 1 H, CH), 5.73 (d, *J* = 9.3 Hz, 1 H, CH), 6.08 (s, 1 H, CH), 6.24 (dd, *J* = 1.8, 3.3 Hz, 1 H, CH), 7.02–7.05 (m, 1 H, CH), 7.23–7.29 (m, 3 H, CH), 7.83 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14g**) = 1.24 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.65 (d, *J* = 7.1 Hz, 2 H, $CH_2$), 3.71–3.79 (m, 1 H, CH), 3.80 (s, 3 H, $CH_3$), 4.15 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 5.30 (d, *J* = 1.5 Hz, 1 H, CH), 6.14 (s, 1 H, CH), 6.26 (dd, *J* = 1.9, 3.3 Hz, 1 H, CH), 7.01–7.02 (m, 1 H, CH), 7.17–7.28 (m, 3 H, CH), 7.82 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14g**) = 14.2 ($CH_3$), 33.8 ($CH_2$), 39.4 (CH), 52.7 ($CH_3$), 60.5 (CH), 60.8 ($CH_2$), 108.9 (C), 110.2 (CH), 114.9 (CH), 123.1 (C), 123.1 (CH), 128.2 (CH), 142.1 (CH), 151.7 (C), 153.7 (C), 172.1 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14g**) = 14.2 ($CH_3$), 40.5 ($CH_2$), 46.8 (CH), 52.7 ($CH_3$), 60.8 ($CH_2$), 62.1 (CH), 108.2 (C), 110.1 (CH), 115.3 (CH), 121.4 (C), 123.3 (CH), 124.5 (CH), 128.5 (CH), 142.0 (CH), 151.7 (C), 153.2 (C), 171.2 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{19}NO_5$: 329.1263; found: 329.1262.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-5,6-dimethoxy-2-phenylindoline-1-carboxylate (14h)**

$R_f$ = 0.3 (hexanes–EtOAc, 2:1).

IR (KBr): 458, 492, 598, 702, 731, 760, 846, 1027, 1118, 1186, 1219, 1282, 1394, 1448, 1501, 1702, 2954 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ (*cis*-**14h**) = 1.09 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 1.90 (dd, *J* = 10.1, 17.3 Hz, 1 H, $CH_2$), 2.48 (dd, *J* = 17.4, 5.00 Hz, 1 H, $CH_2$), 3.52 (s, 3 H, $CH_3$), 3.73 (s, 3 H, $CH_3$), 3.84 (s, 3 H, $CH_3$), 3.98 (q, *J* = 7.1 Hz, 2 H, $CH_2$), 4.10–4.18 (m, 1 H, CH), 5.51 (d, *J* = 9.5 Hz, 1 H, CH), 6.54 (s, 1 H, CH), 6.90–6.91 (m, 1 H, CH), 7.07–7.16 (m, 4 H, CH), 7.61 (s, 1 H, CH).

$^1$H NMR (300 MHz, $CDCl_3$): δ (*trans*-**14h**) = 1.16 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 2.58 (dd, *J* = 7.3, 3.0 Hz, 2 H, $CH_2$), 3.35–3.40 (m, 1 H, CH), 3.56 (s, 3 H, $CH_3$), 3.70 (s, 3 H, $CH_3$), 3.84 (s, 3 H, $CH_3$), 4.09 (q, *J* = 7.2 Hz, 2 H, $CH_2$), 5.11 (s, 1 H, CH), 6.62 (s, 1 H, CH), 6.91–6.93 (m, 1 H, CH), 7.08–7.07 (m, 4 H, CH), 7.62 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*cis*-**14h**) = 14.1 ($CH_3$), 34.4 ($CH_2$), 40.8 (CH), 46.9 ($CH_3$), 56.4 ($CH_3$), 56.1 ($CH_3$), 60.5 ($CH_2$),

66.6 (CH), 99.4 (CH), 107.4 (CH), 125.1 (CH), 127.8 (CH), 128.3 (CH), 128.5 (CH), 128.7 (CH), 138.3 (C), 145.2 (C), 148.9 (C), 153.4 (C), 171.5 (C).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ (*trans*-**14h**) = 14.2 ($CH_3$), 41.1 ($CH_2$), 46.8 ($CH_3$), 46.9 (CH), 56.3 ($CH_3$), 56.1 ($CH_3$), 60.7 ($CH_2$), 68.4 (CH), 99.7 (CH), 108.2 (CH), 125.2 (CH), 126.8 (CH), 127.4 (CH), 128.3 (CH), 128.6 (CH), 142.4 (C), 145.4 (C), 149.2 (C), 153.6 (C), 172.1 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{20}NO_6$: 399.1682; found: 399.1677.

**Indoles 15 by Dehydrogenation of Indolines 14; General Procedure**

A soln of indoline **14** (0.3 mmol, 1.0 equiv) and DDQ (0.6 mmol, 2.0 equiv) in toluene (7 mL) was placed in a sealed vessel in a microwave and irradiated at 120 °C for 4 h. After completion of the reaction, the solvent was removed and the residue was washed with sat. aq $NaHCO_3$ (5 mL) and extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic phases were dried ($Na_2SO_4$), filtered, and concentrated. The crude product was purified by chromatography (silica gel, hexanes–EtOAc); this gave indoles **15** as oils.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-phenyl-1*H*-indole-1-carboxylate (15a)**

$R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 642, 701, 752, 822, 940, 1028, 1076, 1154, 1230, 1330, 1360, 1441, 1605, 1732, 1896, 2854, 2929, 2956, 2981, 3055 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.54 (s, 2 H, $CH_2$), 3.76 (s, 3 H, $CH_3$), 4.14 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 7.29–7.39 (m, 2 H, CH), 7.40–7.47 (m, 5 H, CH), 7.59 (d, *J* = 7.9 Hz, 1 H, CH), 8.19 (d, *J* = 7.9 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 30.9 ($CH_2$), 53.4 ($CH_3$), 61.0 ($CH_2$), 114.5 (CH), 115.6 (CH), 123.3 (CH), 124.9 (CH), 127.9 (CH), 128.2 (CH), 129.6 (C), 129.9 (CH), 132.7 (C), 136.0 (C), 137.8 (C), 152.2 (C), 171.2 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{19}NO_4$: 337.1314; found: 337.1310.

**Methyl 2-(3-Chlorophenyl)-3-(2-ethoxy-2-oxoethyl)-1*H*-indole-1-carboxylate (15b)**

$R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 758, 871, 1025, 1072, 1096, 1171, 1225, 1267, 1328, 1441, 1566, 1599, 1733, 2956, 2982 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.53 (s, 2 H, $CH_2$), 3.79 (s, 3 H, $CH_3$), 4.15 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 7.28–7.45 (m, 6 H, CH), 7.61 (d, *J* = 8.0 Hz, 1 H, CH), 8.18 (d, *J* = 8.0 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 30.8 ($CH_2$), 53.5 ($CH_3$), 61.1 ($CH_2$), 115.1 (C), 115.6 (CH), 119.3 (CH), 123.4 (CH), 125.3 (CH), 128.2 (CH), 128.3 (CH), 129.1 (CH), 129.4 (C), 129.9 (CH), 133.8 (C), 134.5 (C), 136.0 (C), 136.1 (C), 152.0 (C), 170.9 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{18}ClNO_4$: 371.0924; found: 371.0925.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(4-methoxyphenyl)-1*H*-indole-1-carboxylate (15c)**

$R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 756,837, 1030, 1076, 1177, 1246, 1329, 1358, 1452, 1510, 1611, 1734, 2838, 2935, 2956 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.53 (s, 2 H, $CH_2$), 3.78 (s, 3 H, $CH_3$), 3.87 (s, 3 H, $CH_3$), 4.14 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 6.97 (d, *J* = 8.8 Hz, 2 H, CH), 7.27–7.39 (m, 4 H, CH), 7.56–7.59 (m, 1 H, CH), 8.16 (d, *J* = 8.2 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 30.9 ($CH_2$), 53.4 ($CH_3$), 55.3 ($CH_3$), 60.0 ($CH_2$), 113.3 (CH), 114.3 (C), 115.6 (CH), 119.0 (CH), 123.2 (CH), 124.8 (CH), 124.9 (C), 129.6 (C), 131.1 (CH), 135.9 (C), 137.7 (C), 152.2 (C), 159.4 (C), 171.3 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{21}NO_5$: 367.1420; found: 367.1417.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(3-methoxyphenyl)-1*H*-indole-1-carboxylate (15d)**

$R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 699, 755, 785, 1021, 1090, 1145, 1222, 1326, 1356, 1439, 1595, 1730, 2960 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.55 (s, 2 H, $CH_2$), 3.77 (s, 3 H, $CH_3$), 3.84 (s, 3 H, $CH_3$), 4.14 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 6.94–7.00 (m, 3 H, CH), 7.30–7.39 (m, 3 H, CH), 7.59 (d, *J* = 8.2 Hz, 1 H, CH), 8.17 (d, *J* = 8.2 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 13.2 ($CH_3$), 29.9 ($CH_2$), 52.4 ($CH_3$), 54.2 ($CH_3$), 59.9 ($CH_2$), 112.8 (CH), 113.4 (C), 114.3 (CH), 114.5 (CH), 118.1 (CH), 121.3 (CH), 122.2 (CH), 123.9 (CH), 127.7 (CH), 128.5 (C), 132.9 (C), 135.0 (C), 136.5 (C), 151.0 (C), 158.1 (C), 170.1 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{21}NO_5$: 367.1420; found: 367.1418.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-2-(2-naphthyl)-1*H*-indole-1-carboxylate (15e)**

$R_f$ = 0.4 (hexanes–EtOAc, 5:1).

IR (KBr): 733, 819, 862, 910, 1025, 1072, 1150, 1227, 1321, 1358, 1440, 1734, 2932, 2990, 3055 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.58 (s, 2 H, $CH_2$), 3.72 (s, 3 H, $CH_3$), 4.15 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 7.31–7.44 (m, 2 H, CH), 7.47 (dd, *J* = 1.7, 8.5 Hz, 1 H, CH), 7.51–7.57 (m, 2 H, CH), 7.63 (d, *J* = 7.7 Hz, 1 H, CH), 7.87–7.93 (m, 3 H, CH), 7.95 (s, 1 H, CH), 8.22 (d, *J* = 8.3 Hz, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 31.0 ($CH_2$), 53.4 ($CH_3$), 61.0 ($CH_2$), 114.9 (C), 115.6 (CH), 119.2 (CH), 123.3 (CH), 125.1 (CH), 126.3 (CH), 126.5 (CH), 127.1 (CH), 127.8 (CH), 127.9 (CH), 128.3 (CH), 128.7 (CH), 129.7 (C), 130.2 (C), 133.0 (C), 136.1 (C), 137.7 (C), 152.3 (C), 171.2 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{21}NO_4$: 387.1471; found: 387.1471.

**Methyl 3-(2-Ethoxy-2-oxoethyl)-5,6-dimethoxy-2-phenyl-1*H*-indole-1-carboxylate (15g)**

$R_f$ = 0.4 (hexanes–EtOAc, 2:1).

IR (KBr): 702, 754, 849, 1030, 1080, 1167, 1205, 1312, 1364, 1442, 1485, 1514, 1603, 1707, 1725, 2841, 2956 cm$^{-1}$.

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.1 Hz, 3 H, $CH_3$), 3.44 (s, 2 H, $CH_2$), 3.69 (s, 3 H, $CH_3$), 3.98 (s, 3 H, $CH_3$), 3.99 (s, 3 H, $CH_3$), 4.13 (q, *J* = 7.1 Hz, 2 H, $CH_3$), 7.01 (s, 1 H, CH), 7.29–7.46 (m, 5 H, CH), 7.88 (s, 1 H, CH).

$^{13}$C NMR (75.5 MHz, $CDCl_3$): δ = 14.2 ($CH_3$), 31.1 ($CH_2$), 53.2 ($CH_3$), 56.2 ($CH_3$), 56.3 ($CH_3$), 61.0 ($CH_2$), 99.5 (CH), 100.8 (CH), 114.2 (C), 122.3 (C), 127.8 (CH), 128.4 (CH), 128.2 (CH), 129.9 (CH), 130.4 (C), 133.0 (C), 136.1 (C), 146.8 (C), 148.2 (C), 152.3 (C), 171.2 (C).

HRMS–FAB: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{23}NO_6$: 397.1525; found: 397.1523.

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