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Brönsted Acid-Catalyzed One-Pot Synthesis of Indoles from *o*-Aminobenzyl Alcohols and Furans

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Abstract

Brönsted acid-catalyzed one-pot synthesis of indoles from *o*-aminobenzyl alcohols and furans has been developed. This method operates via the in situ formation of aminobenzylfuran, followed by its recyclization into the indole core. The method proved to be efficient for substrates possessing different functional groups, including -OMe, -CO₂Cy, and -Br. The resulting indoles can easily be transformed into diverse scaffolds, including 2,3- and 1,2-fused indoles, and indole possessing an α,β -unsaturated ketone moiety at the C-2 position.

1. Introduction

Low resonance energy of furan ring¹ allows for its facile recyclization reactions into different carbo-² and heterocycles.³ Of particular interest, is recyclization reaction of furan into indole, since valuable indole⁴ fragments can be obtained from readily available starting materials.⁵ Hence, a few reports document an intramolecular Pd-catalyzed arylation recyclization of furan-containing aryl- or hetaryl halides **A** into indoles **B** (Scheme 1-1).^{3f,3g} Recently, one of us developed a Brönsted acid-mediated process for recyclization of furan derivatives **4** into indoles **3** (Scheme 1-2a).⁶ This method needs preparation of furylmethyl aniline **4**, which is accomplished by condensation of benzyl alcohol **1** with furan **2**. The recyclization step requires the use of overstoichiometric amounts of HCl/AcOH, which substantially limits the scope of this method. We thought that the development of more environmentally benign and general catalytic method for recyclization of furan, which would exhibit wider substrate scope and potentially would allow for a one-pot synthesis of indoles **3** directly from **1** and **2** is justified. Herein, we wish to report general and efficient Brönsted acid-catalyzed synthesis of indoles from *o*-aminobenzyl alcohols and furans, which features a one-pot protocol, wider substrate scope, and higher functional group tolerance than the previously published two-step procedure (Scheme 1-2b).

2. Results and Discussion

Optimization of the One-Pot Synthesis of Indole **3** from *o*-Aminobenzyl Alcohol **1a**

Recognizing that both steps of the sequence depicted in Scheme 1-2a proceed under electrophilic conditions, we hypothesized that finding conditions for formation of indole **3**

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Supporting Information availability statement ¹H and ¹³C NMR spectra for compounds **1a-1o**, **3aa-3ar**, **4as**, **3ba-3oa**, **4ae**, **4ao**, **10**, and **5-9**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

directly from aminobenzyl alcohol **1** and 2-methylfuran **2** is feasible. To this end, different Lewis acid catalysts were first screened for the one-pot recyclization of **1a** and **2a** into **3aa** (Table 1). Thus, employment of FeCl₃ resulted in efficient formation of intermediate **4aa** with only traces of target indole **3aa** produced (entry 1). Employment of copper, indium, and silver triflates was more efficient for the second step leading to better ratios of **3aa/4aa** (entries 2–4). Use of Sc(OTf)₃ resulted in nearly complete conversion of starting materials into indole **3aa** (entry 5). In order to verify whether Sc(OTf)₃ is the true catalyst in this recyclization reaction, or if it is catalyzed by the Brønsted acid⁷ (TfOH) produced by a hydrolysis of Sc(OTf)₃ during the first dehydrocondensation step, the following test experiments were performed. First, addition of activated molecular sieves, which scavenged the forming water and thus suppressed the hydrolysis of Sc(OTf)₃, resulted in much more sluggish recyclization reaction, producing intermediate **4aa** as a major product (entry 6). Moreover, addition of 30 mol% of a proton scavenger 2,4,6-tritertbutylpyrimidine (TTBP)⁸ had a similar inhibition effect on the second step of the reaction (entry 7). Finally, addition of both water- and a proton scavengers completely shut down the recyclization step, thus producing furylmethyl aniline **4aa** as a single reaction product (entry 8). These results unambiguously demonstrate that TfOH is the true catalyst of the recyclization step (**4aa**→**3aa**). Consequently, we examined several other Brønsted acids in the recyclization reaction of **1a** and **2a** into **3aa**. It was found that employment of HNTf₂, HCl, and CF₃CO₂H produced only intermediate **4aa** in low to moderate yields (entries 9–12). Use of H₂SO₄ and TsOH gave mixtures of indole **3aa** and furyl aniline derivative **4aa** (entries 13, 14). Remarkably, in the presence of MsOH and TfOH indole **3aa** was produced in 87% and 95% yields, respectively (entries 15, 16). The following optimization with TfOH as the catalyst (entries 17–19) revealed optimal conditions for this Brønsted acid-catalyzed transformation (entry 18), which allowed for a facile and complete conversion of **1a** and **2a** into indole **3aa**.

Scope of Furans in the One-Pot Synthesis of Indoles

With the optimized conditions in hand, we explored the generality of this one-pot recyclization reaction. First, the scope of recyclization reaction of aminoalcohol **1a** with different furans **2** was examined (Table 2). Thus, 2-alkyl- and 2-cycloalkylfurans **2a–d** were smoothly converted into the corresponding indoles **3ab–3ad** in good to excellent yields (entries 1–5). We also showed that recyclization reaction could be easily scaled up to a gram-scale synthesis of indole **3aa** (entry 2). Different 2-arylfurans **2e–m**, possessing MeO-, Br-, F-, and CF₃- groups were also efficiently transformed into indoles **3ae–3am** (entries 6–14). Remarkably, it was found that sterically bulky 2-arylfurans **2g–2i** are also competent reactants in this reaction providing the corresponding indoles **3ag–3ai** in good yields (entries 8–10). Furans **2n** and **2o**, possessing an ester group in a side chain, recyclized uneventfully producing indoles **3an** and **3ao** in 61% and 68% yield, respectively (entry 15–16). Likewise, 2,3-disubstituted furans, such as 2,3-dimethylfuran **2p** and 4,5,6,7-tetrahydrobenzofuran **2q**, produced the corresponding indoles **3ap** and **3aq** in high yields (entries 17–18). Benzofuran **2r** also underwent recyclization to produce benzylphenolindole derivative **3ar** in moderate yield (entry 19). However, when C-4 substituted menthofuran **2s** was used, no recyclization product **3as** was formed (entry 20). Noteworthy, not only these catalytic one-pot conditions are more convenient experimentally, but they also exhibit wider substrate scope. Thus, attempts on recyclization of intermediate **4ae** under previously developed conditions (HCl-EtOH)⁶ in 12 hours produced no detectable amounts of indole **3ae**. Moreover, recyclization of furylmethyl aniline **4ao** using HCl-EtOH produced transesterified indole **3an**.⁹

Scope of α -Aminobenzyl Alcohols in the One-Pot Synthesis of Indoles

Next, the scope of the reaction with regard to the R¹ substituent at the α -position of aminobenzyl alcohol **1** was examined (Table 3, entries 1–8). It was found that alkyl-

substituted benzyl alcohols, such as methyl-, *iso*-propyl-, *tert*-butyl-, and cyclohexyl-, can be easily transformed into indoles **3ba–3ea** in good to excellent yields (entries 1–4). Likewise, aryl-containing aminoalcohols, possessing F-, Me-, and MeO- groups efficiently cyclized into indoles **3fa–3ha** (entries 5–7). Recyclization of 2-thienyl-substituted benzyl alcohol **1i** produced the corresponding indole **3ia** in 41% yield (entry 8).

Next, aminoalcohols possessing different substituents at the aniline ring were tested in this recyclization reaction (Table 3, entries 9–14). Thus, reaction of 4,5-difluoro- and 4,5-dimethoxybenzyl alcohols **1j** and **1k** led to the formation of indoles **3ja** and **3ka** in good yields (entries 9–10). 5-Trifluoromethylbenzyl alcohol **1l** and 4-bromobenzyl alcohol **1m** provided indoles **3la** and **3ma** in good yields, as well (entries 11–12). It is worth mentioning that 6-methyl aminoalcohol **1n** was not efficient in this reaction (entry 13), whereas recyclization of 6-chloro aminoalcohol **1o** provided *N*-detosylated indole **3oa** in reasonable yield (entry 14).

Further Modifications of the Obtained Indoles

After establishing the scope of this one-pot recyclization reaction, we then performed several transformations that highlight the utility of the synthesized indoles. Thus, the formed indole **3ae**, upon reduction of its carbonyl group into alcohol group and subsequent Friedel-Crafts-type cyclization, was smoothly converted into tetracyclic indole core **5** (Scheme 2).¹⁰ Removal of the tosyl group with sodium naphthalenide,¹¹ produced *N*-H indole **6**, which upon oxidation with DDQ, furnished α,β -unsaturated ketone **7**. Alternatively, upon reaction with excess Mg in methanol,¹² the tosyl group in indole **3aa** was efficiently removed with simultaneous reduction of the carbonyl group to produce alcohol **8**. The latter, upon mesylation and subsequent intramolecular *N*-alkylation,¹³ was easily converted into dihydropyrroloindole **9**, an important motif found in a number of drug candidates and natural products.¹⁴

3. Conclusion

In summary, we developed an efficient one-pot Brønsted acid-catalyzed method for synthesis of indoles from *o*-aminobenzyl alcohols and furans. This method features initial formation of aminobenzylfuran, followed by its recyclization into indole possessing ethyl ketone moiety. This method proved to have wider substrate scope and higher functional group tolerance than the previously reported two-step procedure. The formed indoles can be further transformed into valuable 2,3- and 1,2-fused indoles, and into indoles possessing an α,β -unsaturated ketone moiety.

4. Experimental Section

General Information

Column chromatography was carried out employing Silicycle Silica-P flash silica gel (40–63 μm). Precoated silica gel plates F-254 were used for thin-layer analytical chromatography (TLC). Chemical shifts for ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were reported in parts per million (ppm, δ). HRMS analyses were performed on either Micromass 70-VSE mass spectrometer by using electron ionization (EI) technique with Spector analyzer or by using electrospray ionization (ESI) with time-of-flight (TOF) analyzer. Anhydrous solvents purchased from suppliers were additionally purified on solvent purification system and/or stored over calcium hydride/molecular sieves. 2-Aryl/alkylfurans, if not commercially available, were synthesized from 2-bromofuran.¹⁵

Synthesis of Starting Materials

2-(*N*-tosylamino)benzaldehyde **ab1** was prepared as described.¹⁶

To a solution of 2-aminobenzyl alcohol (6.2 g, 50.0 mmol) and pyridine (1.2 equiv, 4.8 mL, 60.0 mmol) in CHCl_3 (165 mL), TsCl (0.98 equiv, 9.3 g, 49.0 mmol) in CHCl_3 (50 mL) was added dropwise at room temperature. The reaction mixture was stirred for 3 h and then quenched with water (50 mL). The organic phase was separated, washed with water, dried over Na_2SO_4 , and concentrated to give the 2-(*N*-tosylamino)benzyl alcohol (13.5 g, 48.6 mmol, 97%), which was used directly in the next step.

To a stirred suspension of PCC (1.5 equiv, 15.7 g, 72.9 mmol) in CH_2Cl_2 (240 mL), a solution of the 2-(*N*-tosylamino)benzyl alcohol in CH_2Cl_2 (360 mL) was added dropwise at room temperature. The mixture was stirred for 3 h. The liquid was decanted from the solid, and the remaining solid was washed several times with Et_2O (3×100 mL). The combined organic fractions were passed through a short pad of silica gel. The silica gel was additionally washed with CH_2Cl_2 (3×100 mL) and the combined organic solutions were evaporated to give the crude product. The product was recrystallized from $\text{CHCl}_3/\text{EtOH}$ (1/5, 100 mL) to yield aldehyde **ab1** as a white-yellow solid (11.2 g, 40.8 mmol, 84%), which was used directly in the synthesis of alcohols **1**.

General procedure for the synthesis of 2-(*N*-tosylamino)-4,5-difluorobenzaldehyde **ab2**, 2-(*N*-tosylamino)-4-trifluoromethylbenzaldehyde **ab3**, 2-(*N*-tosylamino)-5-bromobenzaldehyde **ab4**, and 2-(*N*-tosylamino)-3-chlorobenzaldehyde **ab5**.¹⁷

To a solution of a proper 2-aminobenzoic acid (5 mmol) and Na_2CO_3 (2.5 equiv) in distilled water (0.4 M) heated to 60 °C, TsCl (1.25 equiv) was added during the course of 15 min. The mixture was then heated to 85 °C and stirred at this temperature for 3 h. The hot mixture was then cooled down and mixed with ice. HCl (6 N) was added dropwise to the resulted mixture until slightly acidic pH (*caution: CO₂ evolution!*). The resulted white suspension was extracted with EtOAc (3×10 mL), and combined organic solutions were additionally washed with HCl (1 N), dried over Na_2SO_4 , and evaporated to give the 2-(*N*-tosylamino)benzoic acid. The crude product was used directly in the next step.

Under a nitrogen atmosphere, to an ice-cooled stirred suspension of LiAlH_4 (2.0 equiv) in THF (0.2M), a solution of 2-(*N*-tosylamino)benzoic acid in minimum amount of THF was added dropwise. The reaction mixture was allowed to warm up to room temperature and stirred for 3 h. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 2:1), the reaction mixture was cooled down (ice bath) and saturated aqueous NH_4Cl (2.0 mL) was added dropwise (*caution: H₂ evolution!*). The resulting sluggish mixture was filtered through Celite® and concentrated. The crude product was used directly in the next step.

The resulted alcohol was oxidized to aldehyde using PCC as described earlier. The obtained aldehydes **ab2–ab5** were used directly in the synthesis of alcohols **1**.

General procedure for the synthesis of 2-(*N*-tosylamino)-4,5-dimethoxybenzaldehyde **ab6** and 2-(*N*-tosylamino)-3-methylbenzaldehyde **ab7**.¹⁸

A solution of a proper 2-aminobenzoic acid (5 mmol), methanol (10 mL), and concentrated H_2SO_4 (2 mL) was heated under reflux for 24 h. The reaction mixture was cooled down, concentrated, poured into ice, neutralized with solid Na_2CO_3 (*caution: CO₂ evolution!*), and extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with water, saturated aqueous NaHCO_3 , dried over Na_2SO_4 , and concentrated to provide a crude methyl 2-aminobenzoate, which was used directly in the next step.

To a solution of crude methyl 2-aminobenzoate and pyridine (3 equiv) in CH_2Cl_2 (10 mL), a solution of TsCl (0.98 equiv) in CH_2Cl_2 (5 mL) was added dropwise at room temperature. The reaction mixture was stirred for 3 h and then quenched with water (10 mL). The organic layer was separated, washed with water, dried over Na_2SO_4 , and concentrated. The crude product was used directly in the next step.

Reduction of methyl ester with LiAlH_4 and subsequent oxidation of the resulted alcohol to aldehyde with PCC was done as described earlier. The obtained aldehydes **ab6–ab7** were used directly in the synthesis of alcohols **1**.

General procedure for the synthesis of 2-(*N*-tosylamino)benzyl alcohols **1** from 2-(*N*-tosylamino)benzaldehydes **ab**.

An oven dried, argon flushed 25 mL flask was loaded with 2-(*N*-tosylamino)benzaldehyde **ab** (1.0 mmol) and THF (8.0 mL, 0.125 M). The flask was cooled to -78°C and a solution of $\text{R}^2\text{Li}/\text{R}^2\text{MgCl}(\text{Br})$ (2.2 mmol, 2.2 equiv) was added dropwise. The resulting mixture was allowed to warm up to 0°C , and saturated NH_4Cl (5 mL) was added. The organic layer was separated and the water layer was washed with ethyl acetate (2×5 mL). The combined organic solutions were dried over Na_2SO_4 and the solvents were evaporated. The resulted crude product was purified by recrystallization from $^i\text{PrOH}$ to give pure alcohol **1** as a white solid.

N-(2-(hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1a**) was obtained from aldehyde **ab1** and PhLi , 332 mg (94%), $R_f = 0.09$ (hexanes/ $\text{EtOAc} = 4/1$). The spectral data matched that of the previously synthesized material. ^1H NMR (500 MHz, CDCl_3) δ 8.00 (s, 1H), 7.48–7.46 (m, 3H), 7.32–7.30 (m, 3H), 7.23 (t, $J = 7.3$ Hz, 1H), 7.17–7.14 (m, 4H), 7.02 (t, $J = 7.7$ Hz, 1H), 6.92 (d, $J = 7.3$ Hz, 1H), 5.67 (s, 1H), 2.69 (broad s, 1H), 2.36 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.6, 141.0, 136.6, 135.8, 133.1, 129.5, 129.0 (2C), 128.6, 127.9, 127.2, 126.3, 124.6, 122.1, 74.7, 21.5. HRMS (EI+) calcd. for $\text{C}_{20}\text{H}_{19}\text{NO}_3\text{S}$ $[\text{M}]^+$: 353.1086, measured: 353.1087.

N-(2-(1-hydroxyethyl)phenyl)-4-methylbenzenesulfonamide (**1b**) was obtained from aldehyde **ab1** and MeLi , 255 mg (88%), $R_f = 0.18$ (hexanes/ $\text{EtOAc} = 4/1$). The spectral data matched that of the previously synthesized material. ^1H NMR (500 MHz, CDCl_3) δ 8.51

(broad s, 1H), 7.68–7.67 (m, 2H), 7.41 (d, $J = 8.1$ Hz, 1H), 7.22–7.20 (m, 2H), 7.17 (dt, $J = 7.3, 1.7$ Hz, 1H), 7.09–7.02 (m, 2H), 4.84 (q, $J = 6.6$ Hz, 1H), 2.68 (broad s, 1H), 2.36 (s, 3H), 1.34 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.7, 136.9, 135.7, 134.0, 129.6, 128.5, 127.1, 127.0, 124.6, 121.8, 69.8, 22.8, 21.5. HRMS (EI+) calcd. for $\text{C}_{15}\text{H}_{17}\text{NO}_3\text{S}$ $[\text{M}]^+$: 291.0929, measured: 291.0935.

N-(2-(1-hydroxy-2-methylpropyl)phenyl)-4-methylbenzenesulfonamide (**1c**) was obtained from aldehyde **ab1** and $^i\text{PrMgCl}$, 213 mg (67%), $R_f = 0.21$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.48 (broad s, 1H), 7.67–7.66 (m, 2H), 7.48 (d, $J = 7.5$ Hz, 1H), 7.21–7.15 (m, 3H), 7.00–6.95 (m, 2H), 4.23 (d, $J = 9.0$ Hz, 1H), 2.70 (broad s, 1H), 2.36 (s, 3H), 1.66 (m, 1H), 1.00 (d, $J = 6.6$ Hz, 3H), 0.43 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.7, 136.8, 135.8, 132.0, 129.5, 129.2, 128.3, 127.1, 123.9, 121.3, 81.3, 33.4, 21.5, 19.4, 19.2. HRMS (EI+) calcd. for $\text{C}_{17}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}]^+$: 319.1242, measured: 319.1245.

N-(2-(1-hydroxy-2,2-dimethylpropyl)phenyl)-4-methylbenzenesulfonamide (**1d**) was obtained from aldehyde **ab1** and $^t\text{BuMgCl}$, 209 mg (63%), $R_f = 0.23$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.86 (broad s, 1H), 7.76–7.74 (m, 2H), 7.38 (d, $J = 8.3$ Hz, 1H), 7.24–7.23 (m, 2H), 7.14 (m, 1H), 6.99–6.93 (m, 2H), 4.51 (s, 1H), 2.53 (broad s, 1H), 2.38 (s, 3H), 0.98 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.6, 137.1, 136.6, 130.5, 129.6, 128.4, 128.1, 127.3, 122.6, 119.4, 84.0, 37.3, 26.3, 21.5. HRMS (EI+) calcd. for $\text{C}_{18}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 333.1399, measured: 333.1404.

N-(2-(cyclohexyl(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (**1e**) was obtained from aldehyde **ab1** and CyMgBr , 305 mg (85%), $R_f = 0.20$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.62 (broad s, 1H), 7.70–7.69 (m, 2H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.23–7.17 (m, 3H), 7.00–6.97 (dt, $J = 7.5, 1.1$ Hz, 1H), 6.92 (dd, $J = 7.7, 1.5$ Hz, 1H), 4.29 (d, $J = 9.0$ Hz, 1H), 2.65 (broad s, 1H), 2.37 (s, 3H), 2.05 (m, 1H), 1.73 (m, 1H), 1.58 (m, 1H), 1.48 (m, 1H), 1.30 (m, 1H), 1.14–1.01 (m, 2H), 0.95–0.89 (m, 2H), 0.79 (m, 1H), 0.67 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.7, 137.0, 135.9, 131.2, 129.6, 129.3, 128.3, 127.1, 123.6, 120.9, 80.7, 42.5, 29.6, 29.5, 26.1, 25.6, 25.4, 21.5. HRMS (EI+) calcd. for $\text{C}_{20}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}]^+$: 359.1555, measured: 333.1558.

N-(2-((4-fluorophenyl)(hydroxy)methyl)phenyl)-4-methylbenzenesulfonamide (**1f**) was obtained from aldehyde **ab1** and $4\text{-FC}_6\text{H}_4\text{MgBr}$, 248 mg (67%), $R_f = 0.13$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.06 (broad s, 1H), 7.47 (d, $J = 7.9$ Hz, 1H), 7.44–7.43 (m, 2H), 7.21 (dt, $J = 8.1, 1.5$ Hz, 1H), 7.13–7.12 (m, 2H), 7.10–7.08 (m, 2H), 7.02 (dt, $J = 7.5, 0.7$ Hz, 1H), 6.94–6.90 (m, 3H), 5.72 (s, 1H), 3.10 (broad s, 1H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 163.2 (d, $J_{\text{C-F}} = 246.0$ Hz), 143.7, 136.9 (d, $J_{\text{C-F}} = 2.8$ Hz), 136.4, 135.7, 133.0, 129.5, 129.1 (d, $J_{\text{C-F}} = 3.7$ Hz), 127.9 (d, $J_{\text{C-F}} = 8.3$ Hz), 127.0, 124.7, 122.1, 115.3 (d, $J_{\text{C-F}} = 22.2$ Hz), 74.1, 21.5. HRMS (EI+) calcd. for $\text{C}_{20}\text{H}_{18}\text{NO}_3\text{SF}$ $[\text{M}]^+$: 371.0991, measured: 371.0986.

N-(2-(hydroxy(p-tolyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1g**) was obtained from aldehyde **ab1** and $4\text{-MeC}_6\text{H}_4\text{MgBr}$, 256 mg (70%), $R_f = 0.12$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.08 (broad s, 1H), 7.49–7.47 (m, 3H), 7.22 (m, 1H), 7.15–7.10 (m, 4H), 7.04–7.00 (m, 3H), 6.93 (d, $J = 7.7$ Hz, 1H), 5.62 (d, $J = 3.1$ Hz, 1H), 2.81 (d, $J = 3.5$ Hz, 1H), 2.39 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.5, 138.0, 137.5, 136.5, 135.8, 133.1, 129.4, 129.3, 128.9, 128.8, 127.1, 126.2, 124.5, 121.9, 74.5, 21.5, 21.1. HRMS (EI+) calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}]^+$: 367.1242, measured: 367.1240.

N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1h**) was obtained from aldehyde **ab1** and $4\text{-MeOC}_6\text{H}_4\text{MgBr}$, 321 mg (84%), $R_f = 0.06$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.19 (broad s, 1H), 7.47–7.45 (m, 3H), 7.19

(m, 1H), 7.13–7.11 (m, 2H), 7.05–6.99 (m, 3H), 6.91 (d, $J = 7.7$ Hz, 1H), 6.80–6.78 (m, 2H), 5.59 (broad s, 1H), 3.79 (s, 3H), 3.11 (m, 1H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 159.1, 143.5, 136.5, 135.7, 133.2, 129.4, 128.9, 128.7, 127.6, 127.1, 124.4, 121.8, 113.9, 74.3, 55.2, 21.4. HRMS (EI+) calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_4\text{S}$ $[\text{M}]^+$: 383.1191, measured: 383.1194.

N-(2-(hydroxy(thiophen-2-yl)methyl)phenyl)-4-methylbenzenesulfonamide (**1i**) was obtained from aldehyde **ab1** and thiophen-2-yl lithium (prepared by mixing 2-bromothiophene with 1.1 equiv of *n*-BuLi in THF at -78°C), 341 mg (95%), $R_f = 0.15$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.10 (broad s, 1H), 7.49–7.48 (m, 2H), 7.45 (d, $J = 8.1$ Hz, 1H), 7.26–7.21 (m, 2H), 7.15–7.13 (m, 2H), 7.10–7.03 (m, 2H), 6.87 (dd, $J = 5.1, 3.5$ Hz, 1H), 6.59 (m, 1H), 5.93 (m, 1H), 3.41 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, acetone- d_6) δ 148.7, 144.9, 138.3, 137.4, 134.7, 130.8, 129.9 (2C), 128.4, 126.4, 125.6, 125.3, 121.9, 72.6, 21.8. HRMS (EI+) calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_3\text{S}_2$ $[\text{M}]^+$: 359.0650, measured: 359.0648.

N-(4,5-difluoro-2-(hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1j**) was obtained from aldehyde **ab2** and PhLi, 303 mg (78%), $R_f = 0.19$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 7.46–7.45 (m, 2H), 7.30–7.26 (m, 4H), 7.18–7.16 (m, 2H), 7.09–7.08 (m, 2H), 6.66 (dd, $J = 10.8, 8.6$ Hz, 1H), 5.53 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 149.5 (dd, $J_{\text{C-F}} = 249.7, 13.9$ Hz), 147.1 (dd, $J_{\text{C-F}} = 247.8, 12.9$ Hz), 144.3, 140.4, 135.8, 131.8 ($J_{\text{C-F}} = 6.5$ Hz), 131.0, 129.8, 128.8, 128.2, 127.1, 126.3, 117.6 ($J_{\text{C-F}} = 19.4$ Hz), 112.2 ($J_{\text{C-F}} = 21.3$ Hz), 73.2, 21.5. HRMS (EI+) calcd. for $\text{C}_{20}\text{H}_{17}\text{NO}_3\text{SF}_2$ $[\text{M}]^+$: 389.0897, measured: 389.0895.

N-(4,5-dimethoxy-2-(hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1k**) was obtained from aldehyde **ab6** and PhLi, 313 mg (76%), $R_f = 0.10$ (hexanes/EtOAc = 2/1). ^1H NMR (500 MHz, CDCl_3) δ 7.53–7.51 (m, 2H), 7.31–7.27 (m, 4H), 7.21–7.19 (m, 2H), 7.15–7.13 (m, 2H), 6.83 (s, 1H), 6.45 (s, 1H), 5.62 (d, $J = 3.3$ Hz, 1H), 3.75 (s, 3H), 3.68 (s, 3H), 2.73 (broad s, 1H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 148.7, 146.8, 143.8, 141.6, 136.3, 129.6, 128.7, 128.5, 127.7, 127.4, 126.3, 111.5, 108.6, 73.0, 55.9, 21.5. HRMS (EI+) calcd. for $\text{C}_{22}\text{H}_{23}\text{NO}_5\text{S}$ $[\text{M}]^+$: 413.1297, measured: 413.1294.

N-(2-(hydroxy(phenyl)methyl)-5-(trifluoromethyl)phenyl)-4-methylbenzenesulfonamide (**1l**) was obtained from aldehyde **ab3** and PhLi, 341 mg (81%), $R_f = 0.16$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.34 (broad s, 1H), 7.72 (s, 1H), 7.45–7.44 (m, 2H), 7.33–7.31 (m, 3H), 7.26–7.24 (d, $J = 8.1$ Hz, 1H), 7.18–7.14 (m, 4H), 7.07 (d, $J = 8.1$ Hz, 1H), 5.77 (s, 1H), 3.18 (s, 1H), 2.38 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 144.2, 140.3, 136.4, 136.0, 135.7, 131.1 (q, $J_{\text{C-F}} = 32.4$ Hz), 129.7, 129.5, 128.8, 128.2, 127.2, 126.2, 123.5 (q, $J_{\text{C-F}} = 272.8$ Hz), 120.8, 118.0, 74.5, 21.5. HRMS (EI+) calcd. for $\text{C}_{21}\text{H}_{18}\text{NO}_3\text{SF}_3$ $[\text{M}]^+$: 421.0960, measured: 421.0940.

N-(4-bromo-2-(hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1m**) was obtained from aldehyde **ab4** and PhLi, 401 mg (93%), $R_f = 0.12$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.02 (broad s, 1H), 7.45–7.43 (m, 2H), 7.33–7.32 (m, 5H), 7.16–7.14 (m, 4H), 7.07 (d, $J = 1.8$ Hz, 1H), 5.61 (s, 1H), 2.96 (broad s, 1H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 143.9, 140.2, 136.1, 135.1, 134.6, 131.8, 131.7, 129.7, 128.8, 128.2, 127.1, 126.3, 123.5, 117.7, 74.2, 21.5. HRMS (ES+) calcd. for $\text{C}_{20}\text{H}_{18}\text{NO}_3\text{SBrNa}$ $[\text{M} + \text{Na}]^+$: 454.0088, measured: 454.0090.

N-(2-(hydroxy(phenyl)methyl)-6-methylphenyl)-4-methylbenzenesulfonamide (**1n**) was obtained from aldehyde **ab7** and PhLi, 235 mg (64%), $R_f = 0.08$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 7.63–7.61 (m, 2H), 7.33–7.27 (m, 5H), 7.21–7.19 (m, 2H), 7.11–

7.07 (m, 2H), 6.94 (d, $J = 9.0$ Hz, 1H), 6.73 (s, 1H), 5.96 (s, 1H), 3.11 (broad s, 1H), 2.45 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 144.1, 142.8, 142.5, 137.1, 137.0, 132.0, 130.7, 129.8, 128.3, 128.0, 127.3, 127.2, 127.1, 126.5, 71.3, 21.6, 18.4. HRMS (EI+) calcd. for $\text{C}_{21}\text{H}_{21}\text{NO}_3\text{S}$ $[\text{M}]^+$: 367.1242, measured: 367.1241.

N-(2-chloro-6-(hydroxy(phenyl)methyl)phenyl)-4-methylbenzenesulfonamide (**1o**) was obtained from aldehyde **ab5** and PhLi, 232 mg (60%), $R_f = 0.10$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 7.55–7.54 (m, 2H), 7.37–7.35 (m, 2H), 7.32–7.21 (m, 6H), 7.14–7.13 (m, 2H), 6.67 (broad s, 1H), 6.61 (s, 1H), 3.78 (broad s, 1H), 2.42 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 146.4, 144.5, 142.9, 135.6, 132.0, 130.2, 129.6, 129.2, 129.0, 128.6, 128.1, 127.6, 127.0, 126.1, 70.2, 21.6. HRMS (EI+) calcd. for $\text{C}_{20}\text{H}_{18}\text{NO}_3\text{SCl}$ $[\text{M}]^+$: 387.0696, measured: 387.0697.

One-Pot Synthesis of Indoles from *o*-Aminobenzyl Alcohols

Optimization of the One-Pot Synthesis of Indoles from *o*-Aminobenzyl Alcohols (Table 1)

—In a 1 mL Wheaton microreactor vial, equipped with a Teflon pressure cap, a mixture of *o*-aminobenzyl alcohol **1a** (0.1 mmol, 35.3 mg), 2-methylfuran **2a** (0.2 mmol, 2 equiv, 18 μL), catalyst, and DCE (0.4 mL, 0.25M) was stirred at 80°C. The progress of the reaction was monitored by TLC (eluent hexanes:EtOAc = 4:1). After completion, the reaction mixture was filtered through Celite®, the solvent was evaporated and crude product was analyzed by ^1H NMR.

General procedure for one-pot synthesis of indoles from

aminobenzylalcohols and furans—In a 3 mL Wheaton microreactor vial, to a stirred suspension of aminobenzylalcohol **1** (0.4 mmol) and furan **2** (0.6 mmol, 1.5 equiv) in DCE (1.3 mL, 0.3M), triflic acid (0.04 mmol, 10 mol%, 3.6 μL) was added. The microreactor was capped with a Teflon pressure cap and placed into pre-heated (80°C) aluminum block. The resulted solution was stirred for 1–2 h at this temperature. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 4:1), microreactor, containing product **3**, was cooled down and the reaction mixture was diluted with 1.5 mL of hexanes. The product was purified using flash silica gel column chromatography.

N-tosyl-2-(3-oxobutyl)-3-phenylindole (3aa): 150 mg (90%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.42$ (hexanes/EtOAc = 4/1). The spectral data matched that of the previously synthesized material. ^1H NMR (500 MHz, CDCl_3) δ 8.26 (d, $J = 8.4$ Hz, 1H), 7.65 (d, $J = 8.1$ Hz, 2H), 7.46–7.43 (m, 2H), 7.39–7.28 (m, 5H), 7.23–7.18 (m, 3H), 3.35 (t, $J = 7.7$ Hz, 2H), 2.94 (t, $J = 7.7$ Hz, 2H), 2.34 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 207.3, 144.9, 136.7, 136.3, 135.5, 132.6, 130.6, 129.9, 129.8, 128.7, 127.7, 126.4, 124.7, 124.4, 123.9, 119.5, 115.2, 44.7, 29.8, 21.6, 21.3. HRMS (EI+) calcd. for $\text{C}_{25}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 417.1399, measured: 417.1388.

N-tosyl-2-(3-oxoheptyl)-3-phenylindole (3ab): 174 mg (95%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.42$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, $J = 8.0$ Hz, 1H), 7.65 (d, $J = 8.4$ Hz, 2H), 7.45–7.42 (m, 2H), 7.39–7.29 (m, 4H), 7.26–7.22 (m, 2H), 7.19 (d, $J = 8.4$ Hz, 2H), 3.22 (t, $J = 7.7$ Hz, 2H), 2.89 (t, $J = 7.7$ Hz, 2H), 2.37 (t, $J = 7.3$ Hz, 2H), 2.32 (s, 3H), 1.58–1.52 (m, 2H), 1.34–1.26 (m, 2H), 0.90 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 209.7, 144.9, 136.6, 136.5, 135.5, 132.7, 130.5, 129.8 (2C), 128.7, 127.6, 126.4, 124.7, 124.3, 123.9, 119.5, 115.2, 43.7, 42.4, 26.0, 22.3, 21.6, 21.3, 13.9. HRMS (EI+) calcd. for $\text{C}_{28}\text{H}_{29}\text{NO}_3\text{S}$ $[\text{M}]^+$: 459.1868, measured: 459.1867.

N-tosyl-2-(3-oxo-3-cyclopentylpropyl)-3-phenylindole (3ac): 175 mg (93%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.36$ (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz,

CDCl_3) δ 8.27 (d, $J = 9.1$ Hz, 1H), 7.65 (d, $J = 8.1$ Hz, 2H), 7.45–7.42 (m, 2H), 7.38–7.28 (m, 5H), 7.24–7.22 (m, 1H), 7.19 (d, $J = 8.1$ Hz, 2H), 3.24 (t, $J = 7.7$ Hz, 2H), 2.96 (t, $J = 7.7$ Hz, 2H), 2.85 (pent, $J = 8.4$ Hz, 1H), 2.34 (s, 3H), 1.84–1.70 (m, 4H), 1.68–1.54 (m, 4H). ^{13}C NMR (125 MHz, CDCl_3) δ 211.6, 144.8, 136.7, 136.7, 135.7, 132.8, 130.6, 129.8, 129.8, 128.7, 127.6, 126.4, 124.6, 124.2, 123.8, 119.5, 115.2, 51.3, 42.8, 28.8, 26.0, 21.5, 21.4. HRMS (EI+) calcd. for $\text{C}_{29}\text{H}_{29}\text{NO}_3\text{S}$ $[\text{M}]^+$: 471.1868, measured: 471.1877.

N-tosyl-2-(3-oxo-3-cyclohexylpropyl)-3-phenylindole (3ad): 146 mg (75%), yellow oil, eluent: hexanes/EtOAc = 9/1; $R_f = 0.41$. ^1H NMR (500 MHz, CDCl_3) δ 8.27 (d, $J = 8.4$ Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.45–7.42 (m, 2H), 7.38–7.27 (m, 5H), 7.26–7.21 (m, 1H), 7.19 (d, $J = 8.0$ Hz, 2H), 3.21 (t, $J = 7.7$ Hz, 2H), 2.94 (t, $J = 7.7$ Hz, 2H), 2.34 (s, 3H), 1.85–1.75 (m, 4H), 1.66–1.64 (m, 1H), 1.34–1.17 (m, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 212.5, 144.8, 136.8, 136.7, 135.6, 132.7, 130.6, 129.8, 129.7, 128.6, 127.6, 126.4, 124.6, 124.2, 123.8, 119.4, 115.2, 50.7, 41.7, 28.5, 25.9, 25.7, 21.5, 21.3. HRMS (ES+) calcd. for $\text{C}_{30}\text{H}_{32}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$: 486.2103, measured 486.2081.

N-tosyl-2-(3-phenyl-3-oxopropyl)-3-phenylindole (3ae): 166 mg (87%), yellow oil, eluent: hexanes/EtOAc = 9/1; $R_f = 0.38$. ^1H NMR (400 MHz, CDCl_3) δ 8.30 (d, $J = 9.7$ Hz, 1H), 7.95–7.93 (m, 2H), 7.68 (d, $J = 8.4$ Hz, 2H), 7.56–7.53 (m, 1H), 7.45–7.42 (m, 4H), 7.38–7.31 (m, 5H), 7.25–7.19 (m, 3H), 3.49–3.42 (m, 4H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 198.6, 144.9, 136.8, 136.6, 136.5, 135.6, 133.0, 132.7, 130.6, 129.9, 129.8, 128.7, 128.5, 128.1, 127.7, 126.4, 124.7, 124.5, 123.9, 119.5, 115.2, 40.1, 21.8, 21.5. HRMS (ES+) calcd. for $\text{C}_{30}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$: 480.1633, measured: 480.1638.

N-tosyl-2-[3-(2-methoxyphenyl)-3-oxopropyl]-3-phenylindole (3af): 173 mg (85%), colorless oil, eluent: hexanes/EtOAc = 5/1; $R_f = 0.24$. ^1H NMR (500 MHz, CDCl_3) δ 8.30 (d, $J = 8.4$ Hz, 1H), 7.74–7.72 (m, 1H), 7.68 (d, $J = 8.0$ Hz, 2H), 7.44–7.42 (m, 3H), 7.36–7.32 (m, 5H), 7.24–7.22 (m, 1H), 7.19 (d, $J = 8.0$ Hz, 2H), 7.01–6.92 (m, 2H), 3.84 (s, 3H), 3.49 (t, $J = 7.1$ Hz, 2H), 3.41 (t, $J = 7.1$ Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 200.4, 158.8, 144.7, 137.2, 136.7, 135.8, 133.4, 132.9, 130.7, 130.4, 129.9 (2C), 129.7 (2C), 128.7 (2C), 127.8, 127.5, 126.4 (2C), 124.5, 124.1, 123.8, 120.5, 119.4, 115.2, 111.5, 55.5, 45.0, 21.8, 21.5. HRMS (EI+) calcd. for $\text{C}_{31}\text{H}_{27}\text{NO}_4\text{S}$ $[\text{M}]^+$: 509.1661, measured: 509.1663.

N-tosyl-2-[3-(2-trifluoromethylphenyl)-3-oxopropyl]-3-phenylindole (3ag): 122 mg (56%), colorless oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.26$. ^1H NMR (500 MHz, CDCl_3) δ 8.27 (d, $J = 8.4$ Hz, 1H), 7.71–7.69 (m, 1H), 7.67 (d, $J = 8.4$ Hz, 2H), 7.61–7.58 (m, 1H), 7.56–7.50 (m, 2H), 7.47–7.44 (m, 2H), 7.41–7.29 (m, 5H), 7.24–7.20 (m, 3H), 3.43–3.36 (m, 4H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.7, 144.9, 139.9, 136.7, 135.8, 135.6, 132.5, 131.8, 130.5, 130.0, 129.9, 129.7, 128.7, 127.8, 127.1, 126.9 (q, $J_{\text{C-F}} = 32.4$ Hz), 126.6 (q, $J_{\text{C-F}} = 4.4$ Hz), 126.4, 124.8, 124.6, 123.9, 123.6 (q, $J_{\text{C-F}} = 272.5$ Hz), 119.6, 115.1, 44.4, 21.6, 21.4. HRMS (EI+) calcd. for $\text{C}_{31}\text{H}_{24}\text{NO}_3\text{SF}_3$ $[\text{M}]^+$: 547.1429, measured: 547.1435.

N-tosyl-2-[3-(naphthyl-1)-3-oxopropyl]-3-phenylindole (3ah): 112 mg (53%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.28$. ^1H NMR (500 MHz, CDCl_3) δ 8.60 (d, $J = 8.4$ Hz, 1H), 8.29 (d, $J = 8.8$ Hz, 1H), 7.97 (d, $J = 8.4$ Hz, 1H), 7.90–7.86 (m, 2H), 7.69 (d, $J = 8.0$ Hz, 2H), 7.59–7.51 (m, 2H), 7.48–7.43 (m, 3H), 7.40–7.32 (m, 5H), 7.25–7.22 (m, 1H), 7.20 (d, $J = 8.0$ Hz, 2H), 3.53–3.49 (m, 4H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.8, 144.9, 136.8, 136.5, 135.7, 135.5, 133.9, 133.2, 132.9, 132.7, 132.6, 130.5, 130.1, 129.8, 128.8, 128.4, 127.8, 127.7, 126.4, 126.3, 125.8, 124.7, 124.5, 124.4, 123.9, 119.5, 115.2,

43.3, 22.1, 21.5. HRMS (ES+) calcd. for $C_{34}H_{27}NO_3S$ $[M+H]^+$: 530.1790, measured: 530.1791.

N-tosyl-2-[3-(2,4,6-tri-iso-propylphenyl)-3-oxopropyl]-3-phenylindole (3ai): 116 mg (48%), colorless oil, eluent: hexanes/EtOAc = 9/1; R_f = 0.33. 1H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J = 8.4 Hz, 1H), 7.71 (d, J = 8.4 Hz, 2H), 7.48–7.39 (m, 3H), 7.34–7.31 (m, 4H), 7.23–7.20 (m, 3H), 6.98 (s, 2H), 3.45 (t, J = 7.5 Hz, 2H), 3.25 (t, J = 7.5 Hz, 2H), 2.88 (sept, J = 6.6 Hz, 1H), 2.60 (sept, J = 6.6 Hz, 2H), 2.36 (s, 3H), 1.25 (d, J = 6.6 Hz, 6H), 1.20 (d, J = 6.6 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 149.4, 144.8, 143.6, 137.5, 136.6, 136.3, 135.8, 132.9, 130.5, 129.9, 129.8, 128.7, 127.7, 126.4, 124.6, 124.4, 123.8, 121.0, 119.4, 115.1, 47.7, 34.3, 30.9, 24.5, 24.0, 21.6, 21.1. HRMS (EI+) calcd. for $C_{39}H_{43}NO_3S$ $[M]^+$: 605.2964, measured: 605.2958.

N-tosyl-2-[3-(4-trifluoromethylphenyl)-3-oxopropyl]-3-phenylindole (3aj): 131 mg (60%), colorless oil; eluent: hexanes/EtOAc = 9/1; R_f = 0.23. 1H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.45–7.42 (m, 2H), 7.39–7.30 (m, 5H), 7.25–7.22 (m, 1H), 7.20 (d, J = 8.4 Hz, 2H), 3.51–3.43 (m, 4H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 145.0, 139.2, 136.8, 136.0, 135.5, 134.3 (q, J_{C-F} = 32.4 Hz), 132.6, 130.5, 129.9, 129.8, 128.8, 128.4, 127.8, 126.4, 125.6 (q, J_{C-F} = 3.0 Hz), 124.9, 124.8, 124.0, 123.7 (q, J_{C-F} = 272.7 Hz), 119.6, 115.2, 40.4, 21.8, 21.5. HRMS (EI+) calcd. for $C_{31}H_{24}NO_3SF_3$ $[M]^+$: 547.1429, measured: 547.1437.

N-tosyl-2-[3-(4-fluorophenyl)-3-oxopropyl]-3-phenylindole (3ak): 165 mg (83%), light blue oil; eluent: hexanes/EtOAc = 7/1; R_f = 0.31. 1H NMR (500 MHz, $CDCl_3$) δ 8.30 (d, J = 8.8 Hz, 1H), 7.98–7.95 (m, 2H), 7.67 (d, J = 7.7 Hz, 2H), 7.45–7.42 (m, 2H), 7.38–7.31 (m, 5H), 7.25–7.19 (m, 3H), 7.11–7.08 (m, 2H), 3.44 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 165.7 (d, J_{C-F} = 255 Hz), 144.9, 136.8, 136.4, 135.6, 133.1, 132.6, 130.7 (d, J_{C-F} = 9.25 Hz), 130.5, 129.9, 129.8, 128.8, 127.7, 126.4, 124.6, 124.4 (d, J_{C-F} = 105 Hz), 119.6, 115.7, 115.5, 115.2, 40.0, 21.8, 21.5. HRMS (EI+) calcd. for $C_{30}H_{24}NO_3SF$ $[M]^+$: 497.1461, measured: 497.1455.

N-tosyl-2-[3-(4-bromophenyl)-3-oxopropyl]-3-phenylindole (3al): 156 mg (70%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0.28. 1H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.8 Hz, 2H), 7.45–7.45 (m, 2H), 7.39–7.30 (m, 5H), 7.25–7.19 (m, 3H), 3.43 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 144.9, 136.8, 136.2, 135.5, 135.3, 132.6, 131.8, 130.5, 129.9, 129.8, 129.6, 128.8, 128.2, 127.7, 126.4, 124.8, 124.7, 123.9, 119.6, 115.2, 40.0, 21.8, 21.5. HRMS (ES+) calcd. for $C_{30}H_{24}NO_3SBr$ $[M+H]^+$: 558.0739, measured: 558.0742.

N-tosyl-2-[3-(4-methoxyphenyl)-3-oxopropyl]-3-phenylindole (3am): 114 mg (56%), colorless oil, eluent: hexanes/EtOAc = 4/1; R_f = 0.33. 1H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 9.1 Hz, 1H), 7.92 (d, J = 8.4 Hz, 2H), 7.68–7.66 (m, 2H), 7.44–7.41 (m, 2H), 7.37–7.29 (m, 5H), 7.24–7.21 (m, 1H), 7.19 (d, J = 8.4 Hz, 2H), 6.91–6.89 (m, 2H), 3.86 (s, 3H), 3.41 (s, 4H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.2, 163.4, 144.8, 136.8, 132.7, 130.6, 130.3, 129.9, 129.5, 128.9, 128.7, 128.0, 127.6, 126.4, 125.9, 124.7, 124.3, 123.9, 119.5, 115.2, 113.6, 55.4, 39.8, 21.9, 21.5. HRMS (ES+) calcd. for $C_{31}H_{28}NO_4S$ $[M+H]^+$: 510.1739, measured: 510.1741.

N-tosyl-2-[3-oxo-5-(etoxycarbonyl)pentyl]-3-phenylindole (3an): 123 mg (61%), yellow oil, eluent: hexanes/EtOAc = 5/1; R_f = 0.20. 1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 9.7

Hz, 1H), 7.64 (d, $J = 8.4$ Hz, 2H), 7.45–7.42 (m, 2H), 7.38–7.27 (m, 5H), 7.23–7.18 (m, 3H), 4.12 (q, $J = 7.0$ Hz, 2H), 3.26 (t, $J = 7.7$ Hz, 2H), 2.96 (t, $J = 7.7$ Hz, 2H), 2.73 (t, $J = 6.6$ Hz, 2H), 2.58 (t, $J = 6.6$ Hz, 2H), 2.34 (s, 3H), 1.24 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 207.3, 172.6, 144.8, 136.7, 136.3, 135.6, 132.6, 130.5, 129.8, 129.7, 128.7, 127.7, 126.3, 124.7, 124.4, 123.9, 119.5, 115.2, 60.6, 43.7, 36.9, 28.0, 21.5, 21.5, 14.2. HRMS (EI+) calcd. for $\text{C}_{29}\text{H}_{29}\text{NO}_5\text{S}$ $[\text{M}]^+$: 503.1766, measured: 503.1759.

N-tosyl-2-[3-oxo-5-(cyclohexyloxycarbonyl)pentyl]-3-phenylindole (3ao): 189 mg (68%), colorless oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.21$. ^1H NMR (400 MHz, CDCl_3) δ 8.26 (d, $J = 8.0$ Hz, 1H), 7.65–7.63 (m, 2H), 7.45–7.42 (m, 2H), 7.39–7.36 (m, 1H), 7.34–7.26 (m, 4H), 7.23–7.17 (m, 3H), 4.74 (sept, $J = 4.2$ Hz, 1H), 3.28–3.24 (m, 2H), 2.98–2.94 (m, 2H), 2.73 (t, $J = 6.7$ Hz, 2H), 2.56 (t, $J = 6.6$ Hz, 2H), 2.33 (s, 3H), 1.83–1.80 (m, 2H), 1.73–1.68 (m, 2H), 1.55–1.50 (m, 1H), 1.44–1.22 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 207.3, 172.1, 144.9, 136.7, 136.3, 135.6, 132.6, 130.5, 129.8, 129.8, 128.7, 127.7, 126.4, 124.7, 124.4, 123.9, 119.5, 115.2, 72.9, 43.7, 37.1, 31.5, 28.4, 25.3, 23.7, 21.6, 21.3. HRMS (EI+) calcd. for $\text{C}_{30}\text{H}_{35}\text{NO}_5\text{S}$ $[\text{M}]^+$: 557.2236, measured: 557.2243.

N-tosyl-2-(2-methyl-3-oxobutyl)-3-phenylindole (3ap): 150 mg (87%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.31$. ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, $J = 8.0$ Hz, 1H), 7.61 (d, $J = 8.0$ Hz, 2H), 7.45–7.42 (m, 2H), 7.39–7.27 (m, 5H), 7.23–7.20 (m, 1H), 7.18 (d, $J = 8.0$ Hz, 2H), 3.47 (dd, $J = 14.4, 4.4$ Hz, 1H), 3.32–3.25 (m, 1H), 2.97 (dd, $J = 14.4, 9.5$ Hz, 1H), 2.33 (s, 3H), 2.13 (s, 3H), 0.82 (d, $J = 7.3$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 211.8, 144.8, 137.0, 135.3, 135.1, 132.7, 130.8, 130.2, 129.7, 128.7, 127.7, 126.8, 126.3, 124.8, 124.1, 119.6, 115.5, 47.5, 29.4, 28.5, 21.5, 15.4. HRMS (EI+) calcd. for $\text{C}_{26}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}]^+$: 431.1555, measured: 431.1559.

N-tosyl-2-[(2-oxocyclohexyl)methyl]-3-phenylindole (3aq): 128 mg (70%), yellow oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.16$. ^1H NMR (500 MHz, CDCl_3) δ 8.26 (d, $J = 8.7$ Hz, 1H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.44–7.40 (m, 2H), 7.35–7.26 (m, 3H), 7.25–7.16 (m, 5H), 3.65 (dd, $J = 14.6, 3.5$ Hz, 1H), 3.08–3.00 (m, 1H), 2.89 (dd, $J = 14.6, 9.9$ Hz, 1H), 2.33 (s, 3H), 2.34–2.31 (m, 2H), 2.05–1.99 (m, 1H), 1.81–1.76 (m, 1H), 1.68–1.65 (m, 1H), 1.59–1.48 (m, 2H), 0.90–0.83 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 212.0, 144.8, 137.0, 135.6, 135.2, 133.0, 130.8, 130.2, 129.7, 128.6, 127.6, 126.6, 126.4, 124.6, 124.0, 119.4, 115.5, 51.2, 42.0, 32.7, 27.8, 26.7, 25.1, 21.5. HRMS (EI+) calcd. for $\text{C}_{28}\text{H}_{27}\text{NO}_3\text{S}$ $[\text{M}]^+$: 457.1712, measured: 457.1716.

N-tosyl-2-(2-hydroxyphenylmethyl)-3-phenylindole (3ar): 82 mg (45%), colorless oil, eluent: hexanes/EtOAc = 7/1; $R_f = 0.39$. ^1H NMR (500 MHz, CDCl_3) δ 8.19 (d, $J = 8.4$ Hz, 1H), 7.46–7.33 (m, 9H), 7.27–7.25 (m, 1H), 7.08–7.03 (m, 3H), 6.80–6.65 (m, 3H), 5.53 (s, 1H), 4.45 (s, 2H), 2.31 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.0, 144.6, 136.7, 135.6, 134.7, 132.7, 130.2, 129.8, 129.6, 129.6, 126.4, 128.8, 127.7, 127.4, 126.5, 126.1, 124.8, 123.7, 120.9, 119.7, 116.2, 115.1, 26.0, 21.5. HRMS (EI+) calcd. for $\text{C}_{28}\text{H}_{23}\text{NO}_3\text{S}$ $[\text{M}]^+$: 453.1399, measured: 453.1407.

2-N-Tosylaminophenyl(phenyl)(menthofuryl-2)methane (4as): 184 mg (95%), colorless oil, eluent: hexanes/EtOAc = 9/1; $R_f = 0.39$. ^1H NMR (500 MHz, CDCl_3) δ 7.58 (d, $J = 8.1$ Hz, 2H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.27–7.25 (m, 1H), 7.24–7.20 (m, 3H), 7.06 (dd, $J = 8.1, 7.0$ Hz, 1H), 6.81–6.78 (m, 3H), 6.43 (d, $J = 7.0$ Hz, 1H), 4.88 (d, $J = 4.0$ Hz, 1H), 2.60–2.52 (m, 1H), 2.43 (s, 3H), 2.37–2.27 (m, 2H), 2.13–2.05 (m, 1H), 1.91–1.79 (m, 2H), 2.66 (d, $J = 4.0$ Hz, 3H), 1.38–1.26 (m, 2H), 1.05 (d, $J = 7.0$ Hz, 3H), 1.01–0.84 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 150.0, 145.4, 143.8, 140.1, 137.0, 135.4, 135.3, 134.4, 129.7,

128.7, 128.6, 127.7, 127.1, 126.9, 126.0, 124.9, 124.8, 118.2, 116.5, 44.7, 31.4, 31.2, 29.6, 21.5, 20.1, 7.9. HRMS (EI+) calcd. for $C_{30}H_{31}NO_3S$ $[M]^+$: 485.2025, measured: 485.2015.

N-tosyl-2-(3-oxobutyl)-3-methylindole (3ba): 125 mg (88%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,31. 1H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, J = 8.4 Hz, 1H), 7.57–7.56 (m, 2H), 7.37 (d, J = 7.7 Hz, 1H), 7.31–7.23 (m, 2H), 7.15–7.14 (m, 2H), 3.23–3.20 (m, 2H), 2.94–2.91 (m, 2H), 2.31 (s, 3H), 2.17 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 144.5, 136.6, 135.6, 135.4, 131.4, 129.7, 126.2, 124.3, 123.5, 118.5, 117.6, 115.0, 43.9, 29.9, 21.5, 20.7, 8.9. HRMS (ES+) calcd for $C_{20}H_{22}NO_3S$ $[M+H]^+$: 356.1320, measured: 356.1323.

N-tosyl-2-(3-oxobutyl)-3-isopropylindole (3ca): 117 mg (76%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,35. 1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 7.7 Hz, 1H), 7.55–7.53 (m, 2H), 7.26 (m, 1H), 7.21 (m, 1H), 7.16–7.14 (m, 2H), 3.24–3.20 (m, 2H), 3.14 (sept, J = 7.0 Hz, 1H), 2.90–2.87 (m, 2H), 2.32 (s, 3H), 2.18 (s, 3H), 1.32 (d, J = 7.2 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.7, 144.5, 137.2, 135.7, 134.2, 129.7, 129.2, 127.3, 126.2, 123.8, 123.0, 120.2, 115.4, 44.6, 30.0, 25.9, 22.1, 21.5, 20.8. HRMS (ES+) calcd for $C_{22}H_{26}NO_3S$ $[M+H]^+$: 384.1633, measured: 384.1636.

N-tosyl-2-(3-oxobutyl)-3-tertbutylindole (3da): 100 mg (63%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,33 (hexanes/EtOAc = 4/1). 1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 8.4 Hz, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.49–7.48 (m, 2H), 7.24 (m, 1H), 7.19 (m, 1H), 7.15–7.14 (m, 2H), 3.45–3.42 (m, 2H), 2.91 (broad s, 2H), 2.32 (s, 3H), 2.19 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.6, 144.5, 137.7, 135.7, 135.0, 130.3, 129.6, 129.0, 126.1, 123.7, 122.9, 122.3, 115.8, 45.4, 34.0, 31.6, 29.9, 21.6, 21.5. HRMS (ES+) calcd for $C_{23}H_{28}NO_3S$ $[M+H]^+$: 398.1790, measured: 398.1797.

N-tosyl-2-(3-oxobutyl)-3-cyclohexylindole (3ea): 141 mg (83%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,36 (hexanes/EtOAc = 4/1). 1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 7.7 Hz, 1H), 7.54–7.52 (m, 2H), 7.24 (t, J = 8.3 Hz, 1H), 7.19 (t, J = 7.9 Hz, 1H), 7.15–7.13 (m, 2H), 3.25–3.22 (m, 2H), 2.90–2.87 (m, 2H), 2.72 (m, 1H), 2.31 (s, 3H), 2.18 (s, 3H), 1.90–1.77 (m, 5H), 1.61–1.59 (m, 2H), 1.42–1.26 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.8, 144.5, 137.2, 135.7, 124.6, 129.7, 126.6, 126.2, 123.8, 123.0, 120.5, 115.3, 44.7, 36.7, 32.0, 30.0, 26.9, 26.1, 21.5, 20.8. HRMS (ES+) calcd for $C_{25}H_{30}NO_3S$ $[M+H]^+$: 424.1946, measured: 424.1944.

N-tosyl-2-(3-oxobutyl)-3-(4-fluorophenyl)indole (3fa): 126 mg (72%), yellow oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,23 (hexanes/EtOAc = 4/1). 1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 1H), 7.65–7.64 (m, 2H), 7.33 (t, J = 8.3 Hz, 1H), 7.28–7.22 (m, 4H), 7.20–7.19 (m, 2H), 7.14 (d, J = 8.6 Hz, 2H), 3.24–3.20 (m, 2H), 2.95–2.91 (m, 2H), 2.34 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.1, 162.3 (d, J_{C-F} = 247.8 Hz), 145.0, 136.6, 136.5, 135.5, 131.5 (d, J_{C-F} = 7.4 Hz), 130.5, 129.9, 128.6 (d, J_{C-F} = 2.8 Hz), 126.4, 124.4 (d, J_{C-F} = 105.4 Hz), 123.4, 119.3, 115.9, 115.7, 115.2, 44.6, 29.7, 21.6, 21.2. HRMS (ES+) calcd for $C_{25}H_{23}FNO_3S$ $[M+H]^+$: 436.1383, measured: 436.1376.

N-tosyl-2-(3-oxobutyl)-3-(4-methylphenyl)indole (3ga): 103 mg (60%), yellow oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,25 (hexanes/EtOAc = 4/1). 1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 9.0 Hz, 1H), 7.65–7.64 (m, 2H), 7.33–7.31 (m, 2H), 7.28–7.26 (m, 2H), 7.23 (m, 1H), 7.20–7.18 (m, 4H), 3.24–3.20 (m, 2H), 2.95–2.91 (m, 2H), 2.42 (s, 3H), 2.34 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.3, 144.8, 137.4, 136.6, 136.1, 135.5, 130.6, 129.8, 129.6, 129.5, 129.4, 126.3, 124.6, 124.4, 123.8, 119.5, 115.1, 44.7, 29.7, 21.5, 21.3, 21.2. HRMS (EI+) calcd for $C_{26}H_{25}NO_3S$ $[M]^+$: 431.1555, measured: 431.1561.

N-tosyl-2-(3-oxobutyl)-3-(4-methoxyphenyl)indole (3ha): 127 mg (71%), yellow oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,19 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, J = 8.8 Hz, 1H), 7.65–7.63 (m, 2H), 7.33–7.30 (m, 2H), 7.21–7.17 (m, 5H), 6.99–6.97 (m, 2H), 3.85 (s, 3H), 3.26–3.23 (m, 2H), 2.95–2.92 (m, 2H), 2.33 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 207.3, 159.1, 144.8, 136.6, 136.0, 135.5, 130.9, 130.8, 129.8, 126.3, 124.7, 124.6, 124.1, 123.8, 119.4, 115.1, 114.2, 55.2, 44.6, 29.7, 21.5, 21.3. HRMS (EI+) calcd for $\text{C}_{26}\text{H}_{25}\text{NO}_4$ + 25 4S [M] : 447.1504, measured: 447.1509.

N-tosyl-2-(3-oxobutyl)-3-(thiophen-2-yl)indole (3ia): 69 mg (41%), yellow oil, eluent: hexanes/EtOAc = 7/1; R_f = 0,22 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, J = 8.4 Hz, 1H), 7.67–7.65 (m, 2H), 7.54 (d, J = 7.7 Hz, 1H), 7.39 (dd, J = 5.3, 0.7 Hz, 1H), 7.34 (m, 1H), 7.26 (m, 1H), 7.21–7.20 (m, 2H), 7.14 (m, 1H), 7.05 (dd, J = 3.5, 0.7 Hz, 1H), 3.36–3.33 (m, 2H), 3.00–2.97 (m, 2H), 2.34 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 207.1, 145.1, 137.6, 136.3, 135.6, 133.1, 130.1, 129.9, 127.5, 127.4, 126.4, 126.0, 124.9, 124.0, 119.6, 116.8, 115.0, 44.7, 29.8, 21.6, 21.4. HRMS (ES+) calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_3\text{S}_2$ [M+H]⁺: 424.1041, measured: 424.1042.

N-tosyl-2-(3-oxobutyl)-3-phenyl-5,6-difluoroindole (3ja): 143 mg (79%), colorless solid, eluent: hexanes/EtOAc = 7/1; R_f = 0,27 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.12 (dd, J = 11.4, 7.0 Hz, 1H), 7.64–7.62 (m, 2H), 7.46–7.43 (m, 2H), 7.38 (m, 1H), 7.25–7.22 (m, 4H), 7.12 (dd, J = 9.9, 7.9 Hz, 1H), 3.21–3.18 (m, 2H), 2.93–2.90 (m, 2H), 2.37 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 206.9, 148.8 (ddd, $J_{\text{C-F}}$ = 244.1, 19.4, 14.8 Hz), 145.4, 137.6 (d, $J_{\text{C-F}}$ = 4.6 Hz), 135.1, 131.9, 131.6, 131.6, 130.0, 129.5, 128.9, 128.0, 126.3, 123.8, 107.6 (d, $J_{\text{C-F}}$ = 19.4 Hz), 104.5 (d, $J_{\text{C-F}}$ = 24.0 Hz), 44.5, 29.7, 21.6, 21.3. HRMS (ES+) calcd for $\text{C}_{25}\text{H}_{22}\text{NO}_3\text{SF}_2$ [M+H]⁺ : 454.1288, measured: 454.1291.

N-tosyl-2-(3-oxobutyl)-3-phenyl-5,6-dimethoxyindole (3ka): 114 mg (60%), yellow solid, eluent: hexanes/EtOAc = 3/1; R_f = 0,19. The spectral data matched that of the previously synthesized material. ^1H NMR (500 MHz, CDCl_3) δ 8.85 (s, 1H), 7.59–7.57 (m, 2H), 7.46–7.43 (m, 2H), 7.37 (m, 1H), 7.26–7.25 (m, 2H), 7.19–7.17 (m, 2H), 6.72 (s, 1H), 4.00 (s, 3H), 3.79 (s, 3H), 3.19–3.16 (m, 2H), 2.93–2.90 (m, 2H), 2.33 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 207.3, 147.8, 147.4, 144.7, 135.3, 134.8, 132.8, 130.7, 129.7, 129.6, 128.7, 127.6, 126.1, 124.7, 123.5, 100.8, 99.3, 56.4, 56.0, 44.7, 29.7, 21.5, 21.4. HRMS (ES+) calcd for $\text{C}_{27}\text{H}_{28}\text{NO}_5\text{S}$ [M+H]⁺: 478.1688, measured: 478.1679.

N-tosyl-2-(3-oxobutyl)-3-phenyl-6-trifluoromethylindole (3la): 122 mg (63%), colorless solid, eluent: hexanes/EtOAc = 7/1; R_f = 0,24 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.57 (d, J = 0.7 Hz, 1H), 7.67–7.65 (m, 2H), 7.48–7.45 (m, 3H), 7.42–7.38 (m, 2H), 7.28–7.23 (m, 4H), 3.28–3.25 (m, 2H), 2.95–2.92 (m, 2H), 2.36 (s, 3H), 2.14 (d, J = 1.3 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 206.8, 145.4, 139.1, 135.8, 135.2, 132.9, 131.9, 130.0, 129.7, 128.9, 128.0, 126.7 (q, $J_{\text{C-F}}$ = 31.4 Hz), 126.4, 124.6 (q, $J_{\text{C-F}}$ = 271.9 Hz), 123.9, 120.6 (d, $J_{\text{C-F}}$ = 2.8 Hz), 119.8, 112.5 (d, $J_{\text{C-F}}$ = 3.7 Hz), 44.4, 29.7, 21.5, 21.2. HRMS (ES+) calcd for $\text{C}_{26}\text{H}_{23}\text{NO}_3\text{SF}_3$ [M+H]⁺: 486.1351, measured: 486.1350.

N-tosyl-2-(3-oxobutyl)-3-phenyl-5-bromoindole (3ma): 121 mg (61%), yellowish solid, eluent: hexanes/EtOAc = 7/1; R_f = 0,21 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 8.13 (d, J = 8.6 Hz, 1H), 7.63–7.62 (m, 2H), 7.46–7.38 (m, 5H), 7.26–7.21 (m, 4H), 3.24–3.20 (m, 2H), 2.94–2.91 (m, 2H), 2.35 (s, 3H), 2.13 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 206.9, 145.2, 137.7, 135.3, 135.2, 132.3, 131.9, 129.9, 129.7, 128.9, 128.0, 127.5, 126.3, 123.6, 122.2, 117.5, 116.6, 44.5, 29.7, 21.6, 21.2. HRMS (ES+) calcd for $\text{C}_{25}\text{H}_{23}\text{BrNO}_3\text{S}$ [M+H]⁺: 496.0582, measured: 496.0583.

2-(3-oxobutyl)-3-phenyl-7-chloroindole (3aa): 68 mg (58%), colorless solid, eluent: hexanes/EtOAc = 7/1; R_f = 0.23 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3) δ 9.05 (broad s, 1H), 7.52–7.44 (m, 5H), 7.37 (m, 1H), 7.19 (d, J = 7.5 Hz, 1H), 7.04 (t, J = 7.7 Hz, 1H), 3.14–3.12 (m, 2H), 2.92–2.89 (m, 2H), 2.22 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3) δ 209.5, 135.8, 134.8, 132.4, 129.6, 129.0, 128.6, 126.3, 121.1, 120.5, 117.5, 116.2, 115.5, 43.8, 30.0, 19.6. HRMS (EI+) calcd for $\text{C}_{18}\text{H}_{16}\text{ClNO}$ $[\text{M}]^+$: 297.0920, measured: 297.0923.

Procedure for a gram-scale synthesis of indole 3aa from aminobenzylalcohol 1a and furan 2a—In a 25 mL pressure tube, to a stirred suspension of aminobenzylalcohol **1a** (4.0 mmol, 1.41 g) and furan **2a** (6.0 mmol, 1.5 equiv, 537.0 μL) in DCE (13.3 mL, 0.3M), triflic acid (0.4 mmol, 10 mol%, 36.0 μL) was added. The tube was capped with a Teflon pressure cap and placed into pre-heated (80°C) oil bath. The resulted solution was stirred for 2 h at this temperature. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 4:1), the pressure tube, containing product **3aa**, was cooled down and the solvent was evaporated. The product was purified using silica gel column chromatography (eluent hexanes:EtOAc = 7:1) to yield indole **3aa** (1.38 g, 83%) as a yellow oil, crystallizing upon staying.

General Procedure for the Synthesis of Furylmethyl Aniline Derivatives 4.⁶

A mixture of alcohol **1a** (0.5 mmol), *p*-TsOH (4.3 mg, 5 mol%), and furan (0.6 mmol, 1.2 equiv) in benzene (5 mL) was refluxed with azeotropic removal of water for 30 min (TLC monitoring, eluent: hexanes:EtOAc = 4:1). After completion, the reaction flask was cooled down and the product was purified using flash silica gel column chromatography.

N-Tosyl-(2-(phenyl(5-phenylfuran-2-yl)methyl))aniline (4ae)—179 mg (75%), yellowish solid, eluent: hexanes/EtOAc = 7/1; R_f = 0.16. ^1H NMR (400 MHz, CDCl_3) δ 7.61–7.58 (m, 2H), 7.57–7.54 (m, 2H), 7.47 (dd, J = 8.0, 1.2 Hz, 1H), 7.38–7.34 (m, 2H), 7.30–7.23 (m, 7H), 7.13 (dt, J = 7.7, 1.3 Hz, 1H), 6.94–6.92 (m, 2H), 7.86 (dd, J = 7.8, 1.2 Hz, 1H), 6.54 (d, J = 3.3 Hz, 1H), 6.28 (s, 1H), 5.80 (dd, J = 3.4, 0.8 Hz, 1H), 5.05 (s, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 153.4, 143.9, 139.5, 136.8, 125.6, 134.1, 130.6, 129.8, 129.6, 129.0, 128.7, 128.6, 128.0, 127.5, 127.4, 127.1, 126.6, 125.9, 123.6, 111.3, 105.6, 46.1, 21.5. HRMS (EI+) calcd. for $\text{C}_{30}\text{H}_{25}\text{NO}_3\text{S}$ $[\text{M}]^+$: 479.1555, measured: 479.1546.

Cyclohexyl 3-(5-((2-N-tosylaminophenyl)(phenyl)methyl)furan-2-yl)propanoate (4ao)—189 mg (68%), colorless oil, eluent: hexanes/EtOAc = 7/1; R_f = 0.19. ^1H NMR (400 MHz, CDCl_3) δ 7.58–7.56 (m, 2H), 7.45 (dd, J = 8.0, 1.0 Hz, 1H), 7.27–7.21 (m, 6H), 7.10 (dt, J = 7.7, 1.2 Hz, 1H), 6.80–6.78 (m, 2H), 7.73 (dd, J = 7.8, 1.3 Hz, 1H), 6.28 (s, 1H), 5.90 (d, J = 3.1 Hz, 1H), 5.59 (d, J = 3.1 Hz, 1H), 4.91 (s, 1H), 4.75 (sept, J = 4.2 Hz, 1H), 2.91–2.87 (m, 2H), 2.59–2.56 (m, 2H), 2.43 (s, 3H), 1.82–1.79 (m, 2H), 1.73–1.69 (m, 2H), 1.56–1.51 (m, 1H), 1.42–1.22 (m, 5H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.8, 154.4, 152.8, 143.8, 139.6, 136.9, 135.6, 134.1, 129.8, 129.5, 128.8, 128.7, 127.9, 127.3, 127.1, 126.5, 125.7, 109.8, 105.9, 72.8, 45.9, 33.0, 31.6, 25.3, 23.7, 21.5. HRMS (EI+) calcd. for $\text{C}_{33}\text{H}_{35}\text{NO}_5\text{S}$ $[\text{M}]^+$: 557.2236, measured: 557.2231.

General Procedure for Recyclization Reaction of 4 into Indole 3.⁶

A solution of compound **4** (0.2 mmol) in 2 mL of HCl-EtOH (1.25M) was stirred under reflux for 12h, after what the solvent was evaporated, and the product was purified using flash silica gel column chromatography.

(1) **4ae**→**3ae**: 94% of **4ae** was recovered.

- (2) **4ao**→**3ao**: Conversion of **4ao** (>95%). Compound **3an** was isolated instead of **3ao** as a result of transesterification reaction.

Formation of Tetrahydrobenzo[3,4]cyclohepta[1,2-b]indole **5** from Indole **3ae**

Reduction of ketone (3ae**→**10**)**—To an ice-cooled stirred suspension of LiAlH₄ (0.5 mmol, 0.5 equiv, 18.0 mg) in THF (5.0 mL), a solution of indole **3ae** (1.0 mmol, 417.0 mg) in THF (2.0 mL) was added. The reaction mixture was allowed to warm up to room temperature and stirred for 30 min. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 4:1), reaction mixture was cooled down (ice bath) and aqueous sat. NH₄Cl (1.0 mL) was added dropwise (*caution: H₂ evolution!*). The resulting sluggish mixture was filtered through Celite® and concentrated. The alcohol **10** was purified using flash silica gel column chromatography. 406 mg (97%), yellow-brown solid, eluent: hexanes/EtOAc = 3/1; R_f = 0.13. ¹H NMR (500 MHz, CDCl₃): δ ppm 8.27 (d, *J* = 8.4 Hz, 1H), 7.62–7.61 (m, 2H), 7.46–7.43 (m, 2H), 7.39 (s, 1H), 7.36–7.29 (m, 8H), 7.26–7.21 (m, 2H), 7.19–7.17 (m, 2H), 4.69 (m, 1H), 3.23–3.17 (m, 1H), 3.11–3.05 (m, 1H), 2.34 (s, 3H), 2.28–2.19 (m, 2H), 2.07 (broad s, 1H). ¹³C NMR (125 MHz, CDCl₃): δ ppm 144.7, 144.0, 137.3, 136.7, 135.7, 132.9, 130.5, 129.7, 128.7, 128.3, 127.5, 127.3, 126.2, 125.8, 124.5, 124.0, 124.0, 123.8, 119.4, 115.2, 73.6, 40.1, 23.2, 21.5. HRMS (EI⁺) calcd. for C₃₀H₂₇NO₃S [M]⁺: 481.1712, measured: 481.1712.

Cyclization (10**→**5**)**—In a 3 mL Wheaton vial, to a stirred solution of alcohol **10** (0.2 mmol, 96.2 mg) in DCM (1.0 mL), a solution of BF₃·Et₂O (0.2 mmol, 1.0 equiv, 24.7 μL) was added. The reaction mixture was stirred at room temperature for 12 h. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 4:1) the resulting mixture was diluted with hexanes (1.0 mL). The cyclized product **5** was purified using flash silica gel column chromatography. 56 mg (61%), colorless solid, eluent: hexanes/EtOAc = 25/1; R_f = 0.45 (hexanes/EtOAc = 4/1). ¹H NMR (500 MHz, CDCl₃): δ ppm 8.35 (d, *J* = 8.5 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.69–7.67 (m, 2H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 6.1 Hz, 1H), 7.35–7.30 (m, 4H), 7.27–7.26 (m, 1H), 7.18–7.14 (m, 5H), 6.88 (d, *J* = 7.9 Hz, 1H), 3.92–3.88 (m, 1H), 3.74–3.69 (m, 1H), 2.77–2.67 (m, 2H), 2.53–2.46 (m, 1H), 2.30 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ ppm 144.8, 143.5, 132.1, 137.9, 137.1, 136.1, 133.1, 129.8, 129.1, 128.6, 128.3, 128.2, 128.1, 126.9, 126.5, 126.3, 126.0, 124.2, 123.8, 121.3, 119.1, 115.2, 46.5, 39.1, 23.7, 21.5. HRMS (EI⁺) calcd. for C₃₀H₂₅NO₂S [M]⁺: 463.1606, measured: 463.1599.

Formation of α,β -Unsaturated Ketone **7** from Indole **3aa**

Tosyl- group deprotection (3aa**→**6**)**—In a 25 mL round-bottom argon flushed flask, equipped with a stirring bar and septum, to a dry-ice cooled solution of indole **3aa** (1 mmol, 417 mg) in DME (10 mL), a solution of sodium naphthalenide in DME (1.0–1.1 equiv) was added dropwise (addition of sodium naphthalenide continues until the dark green color of its solution stops disappearing. It is important not to add excess of sodium naphthalenide!). The resulting yellow-green solution was allowed to warm up to room temperature (turned yellow) and the solvent was evaporated. The mixture, containing product **6** and naphthalene was purified using flash silica gel column chromatography. 189 mg (72%), colorless solid, eluent: hexanes/EtOAc = 7/1; R_f = 0,18 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3): δ ppm 8.81 (broad s, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.49–7.47 (m, 4H), 7.38–7.33 (m, 2H), 7.20 (t, J = 7.2 Hz, 1H), 7.12 (t, J = 7.3 Hz, 1H), 3.13–3.10 (m, 2H), 2.91–2.88 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ ppm 210.0, 135.3, 135.0 (2C), 129.7, 128.5, 127.5, 126.0, 121.8, 119.8, 118.9, 114.4, 110.7, 44.1, 30.1, 19.5. HRMS (EI+) calcd. for $\text{C}_{18}\text{H}_{17}\text{ON}$ $[M]^+$: 263.1310, measured: 263.1313.

Oxidation (6**→**7**)**—In a 3 mL Wheaton vial, to a stirred solution of ketone **6** (0.2 mmol, 52.6 mg) in DCE (2.0 mL), DDQ (0.24 mmol, 1.2 equiv, 54.5 mg) was added. The reaction mixture was stirred at room temperature for 2 h. After completion of the reaction (determined by TLC, eluent hexanes:EtOAc = 4:1) the resulting mixture was diluted with hexanes (2.0 mL). The product **7** was purified using flash silica gel column chromatography. 43 mg (83%), deep yellow solid, eluent: hexanes/EtOAc = 7/1; R_f = 0,15 (hexanes/EtOAc = 4/1). ^1H NMR (500 MHz, CDCl_3): δ ppm 8.81 (broad s, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 16.3 Hz, 1H), 7.55–7.53 (m, 4H), 7.47–7.43 (m, 2H), 7.35 (t, J = 7.3 Hz, 1H), 7.17 (t, J = 7.2 Hz, 1H), 7.61 (d, J = 16.3 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ ppm 198.6, 137.6, 133.5, 132.8, 130.2, 129.8, 128.8, 127.7, 127.3, 125.6, 125.1, 124.8, 120.9, 120.7, 111.5, 26.8. HRMS (EI+) calcd. for $\text{C}_{18}\text{H}_{15}\text{ON}$ $[M]^+$: 261.1154, measured: 261.1157.

Formation of Dihydropyrroloindole **9** from Indole **3aa**

Tosyl- group deprotection/reduction of carbonyl group (3aa**→**8**)**—To a 25 mL round-bottom argon flushed flask, indole **3aa** (1 mmol, 417 mg), Mg (15 mmol, 15 equiv, 360 mg), and methanol (15 mL) were added. The flask was sonicated in the ultrasound bath until the start of the dihydrogen evolution from magnesium surface, and then reaction mixture was stirred at room temperature until all magnesium reacted (1–2 h). The resulting mixture was filtered through Celite® and concentrated. The alcohol **8** was purified using flash silica gel column chromatography. 230 mg (87%), yellow oil, eluent: hexanes/EtOAc = 4/1; R_f = 0,08. ^1H NMR (500 MHz, CDCl_3): δ ppm 8.67 (broad s, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.56–7.49 (m, 4H), 7.37–7.34 (m, 2H), 7.22 (t, J = 7.0 Hz, 1H), 7.16 (d, J = 7.9 Hz, 1H), 3.86 (m, 1H), 3.05–2.96 (m, 2H), 1.88–1.78 (m, 3H), 1.22 (d, J = 5.7 Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ ppm 135.6, 135.5, 135.3, 129.6, 128.6, 127.8, 126.0, 121.6, 119.8, 118.9, 114.4, 110.6, 67.6, 38.6, 23.8, 22.6. HRMS (EI+) calcd. for $\text{C}_{18}\text{H}_{19}\text{ON}$ $[M]^+$: 265.1467, measured: 265.1468.

Cyclization (8→9)—In a 10 mL round-bottom flask, to a solution of alcohol **8** (0.2 mmol, 53.0 mg), triethylamine (0.3 mmol, 1.5 equiv, 42.5 μ L), and DMAP (0.02 mmol, 0.1 equiv, 2.4 mg) in DCM (1.0 mL), MsCl (0.24 mmol, 1.2 equiv, 19.0 μ L) was added. The reaction mixture was stirred at room temperature for 2 h and then filtered through Celite® and concentrated. The crude product was dissolved in 0.2 mL of DMF and added to an ice-cooled suspension of NaH (0.24 mmol, 1.2 equiv, 5.8 mg) in DMF (0.8 mL). The resulting mixture was allowed to warm up to room temperature and stirred for 2 h. After, the reaction mixture was poured into water (10.0 mL) and the product **9** was extracted with diethyl ether (3×5 mL). The combined organic fractions were washed with brine, dried over Na₂SO₄, and concentrated. The crude dihydropyrroloindole **9** was purified using flash silica gel column chromatography. 39 mg (79%), colorless oil, eluent: hexanes/EtOAc = 25/1; *R*_f = 0.50 (hexanes/EtOAc = 4/1). ¹H NMR (500 MHz, CDCl₃): δ ppm 7.94 (d, *J* = 7.2 Hz, 1H), 7.68–7.67 (m, 2H), 7.50–7.47 (t, *J* = 7.5 Hz, 2H), 7.40 (d, *J* = 6.1 Hz, 1H), 7.26 (m, 1H), 7.23–7.17 (m, 2H), 4.66 (m, 1H), 3.27 (m, 1H), 3.16 (m, 1H), 2.83 (m, 1H), 2.29 (m, 1H), 1.61 (d, *J* = 6.4 Hz, 3H). ¹³C NMR (125 MHz, CDCl₃): δ ppm 141.7, 136.2, 132.3, 130.8, 128.6, 127.4, 124.9, 120.6, 119.5, 109.6, 107.5, 52.6, 36.0, 23.7, 20.3. HRMS (EI+) calcd. for C₁₈H₁₇N [M]⁺: 247.1361, measured: 247.1365.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

- (1). For a review, see: Balaban AT, Oniciu DC, Katritzky AR. Chem. Rev. 2004; 104:2777. [PubMed: 15137807]
- (2). For recent examples on synthesis of aromatic compounds via furan recyclization reactions, see: Hashmi ASK, Frost TM, Bats JW. J. Am. Chem. Soc. 2000; 122:11553. Hashmi ASK, Weyrauch JP, Rudolph M, Kurpejovic E. Angew. Chem., Int. Ed. 2004; 43:6545. Liu L, Gao Y, Che C, Wu N, Wang DZ, Li C-C, Yang Z. Chem. Commun. 2009:662. Chen Y, Lu Y, Li G, Liu Y. Org. Lett. 2009; 11:3838. [PubMed: 19673487]. Chen Y, Li G, Liu Y. Adv. Synth. Catal. 2011; 353:392. Chen Y, Liu Y. J. Org. Chem. 2011; 76:5274. [PubMed: 21599033]. Petronijevic FR, Wipf P. J. Am. Chem. Soc. 2011; 133:7704. [PubMed: 21517102]. Zubkov FI, Airiyan IK, Ershova JD, Galeev TR, Zaytsev VP, Nikitina EV, Varlamov AV. RSC Advances. 2012; 2:4103. Huguet N, Lebœuf D, Echavarren AM. Chem. Eur. J. 2013; 19:6581. [PubMed: 23559498]
- (3). For recent examples on heterocycles synthesis via furan recyclization reactions, see: Harris JM, Padwa A. J. Org. Chem. 2003; 68:4371. [PubMed: 12762739]. Kelly AR, Kerrigan MH, Walsh PJ. J. Am. Chem. Soc. 2008; 130:4097. [PubMed: 18314989]. Bi J, Aggarwal VK. Chem. Commun. 2008:120. Zhou X, Wu W, Liu X, Lee C-S. Org. Lett. 2008; 10:5525. [PubMed: 19053740]. Frutos MR, Alvarez E, Mar Diaz-Requejo M, Perez PJ. J. Am. Chem. Soc. 2010; 132:4600. [PubMed: 20230037]. El Kaïm L, Grimaud L, Wagschal S. Chem. Commun. 2011:1887. Yin B, Cai C, Zeng G, Zhang R, Li X, Jiang H. Org. Lett. 2012; 14:1098. [PubMed: 22316069]. Uchuskin MG, Pilipenko AS, Serdyuk OV, Trushkov IV, Butin AV. Org. Biomol. Chem. 2012; 10:7262. [PubMed: 22814312]. Trushkov IV, Nevolina TA, Shcherbinin VA, Sorotskaya LN, Butin AV. Tetrahedron Lett. 2013; 54:3974. Parr BT, Green SA, Davies HML. J. Am. Chem. Soc. 2013; 135:4716. [PubMed: 23477809]. Zhang S-Y, Tu Y-Q, Cao X-P. Chem. Eur. J. 2013; 19:5246. [PubMed: 23495122]
- (4). For reviews on synthesis and application of indoles, see: Sundberg RJ. Indoles. 1996 Academic Press London. Joule JA, Thomas EJ. Indole and its Derivatives. Science of Synthesis, Houben-

- Weyl Methods of Molecular Transformations. 2000; Vol. 10(Chapter 10-13)George Thieme VerlagStuttgart, Germany. Maes BUW. Gribble GW. Top. Heterocycl. Chem. Heterocyclic Scaffolds II: Reactions and Applications of Indoles. 2010; Vol. 26Springer-VerlagBerlin, Heidelberg. Shiri M. Chem. Rev. 2012; 112:3508. [PubMed: 22390139] . Shiri M, Zolfigol MA, Kruger HG, Tanbakouchian Z. Chem. Rev. 2010; 110:2250. [PubMed: 20041637]
- (5). For reviews on furan synthesis, see: Gallezot P. Chem. Soc. Rev. 2012; 41:1538. [PubMed: 21909591] . van Putten R-J, van der Waal JC, de Jong E, Rasrendra CB, Heeres HJ, de Vries JG. Chem. Rev. 2013; 113:1499. [PubMed: 23394139] . Gulevich AV, Dudnik AS, Chernyak N, Gevorgyan V. Chem. Rev. 2013; 113:3084. [PubMed: 23305185]
- (6). Butin AV, Smirnov SK, Stroganova TA, Bender W, Krapivin GD. Tetrahedron. 2007; 63:474.
- (7). For discussion on Bronsted acid catalysis in metal-catalyzed reactions, see for example: Rhee JU, Krische MJ. Org. Lett. 2005; 7:2493. [PubMed: 15932231] . Li Z, Zhang J, Brouwer C, Yang C-G, Reich NW, He C. Org. Lett. 2006; 8:4175. [PubMed: 16956180] . Rosenfeld DC, Shekhar S, Takemiya A, Utsunomiya M, Hartwig JF. Org. Lett. 2006; 8:4179. [PubMed: 16956181] . Hashmi ASK. Catal. Today. 2007; 122:211.
- (8). For employment of TTBP as proton scavenger, see for example: Crich D, Vinogradova O. J. Org. Chem. 2006; 71:8473. [PubMed: 17064022] . Dudnik AS, Sromek AW, Rubina M, Kim JT, Kel'in AV, Gevorgyan V. J. Am. Chem. Soc. 2008; 130:1440. [PubMed: 18173272]
- (9). See, Experimental Section for details
- (10). For transition metal-catalyzed synthesis of 2,3-fused indoles, see: Sun K, Liu S, Bec PM, Driver TG. Angew. Chem., Int. Ed. 2011; 50:1702.. Maity S, Zheng N. Angew. Chem., Int. Ed. 2012; 51:9562.
- (11). McIntosh JM, Matassa LC. J. Org. Chem. 1988; 53:4452.
- (12). Fleming I, Frackenhohl J, Ila H. J. Chem. Soc., Perkin Trans. 1998; 1:1229.
- (13). Schrader TO, Johnson BR, Lopez L, Kasem M, Gharbaoui T, Sengupta D, Buzard D, Basmadjian C, Jones RM. Org. Lett. 2012; 14:6306. [PubMed: 23210718]
- (14). For importance of dihydropyrroloindoles, see: Ding Z, Yoshikai N. Angew. Chem., Int. Ed. 2013; 52:8574. and references cited therein.
- (15). Haner J, Jack K, Nagireddy JR, Raheem M-A, Durham R, Tam W. Synthesis. 2011:731.
- (16). Hechavarría Fonseca M, Eibler E, Zabel M, König B. Tetrahedron: Asymmetry. 2003; 14:1989.
- (17). Fan C, Vederas JC. Org. Biomol. Chem. 2012; 10:5815. [PubMed: 22371097]
- (18). Poloukhine A, Rassadin V, Kuzmin A, Popik VV. J. Org. Chem. 2010; 75:5953. [PubMed: 20684502]
- (19). Gao W-C, Jiang S, Wang R-L, Zhang C. Chem. Commun. 2013:4890.

1. Pd-Catalyzed Recyclization of Furans into Indoles

2. Brønsted Acid-Assisted Recyclization of Furans into Indoles

Scheme 1.
Methods for Recyclization of Furans into Indoles

Scheme 2.
Further Modifications of the Obtained Indoles

Table 1Optimization of the One-Pot Synthesis of Indole 3 from *o*-Aminobenzyl Alcohol **1a**^a

entry	catalyst	time, h	yield 3 (4), % ^b
1	10% FeCl ₃	12	<5 (91)
2	10% Cu(OTf) ₂	16	53 (38)
3	10% In(OTf) ₃	2	87 (10)
4	10% AgOTf	1	80 (13)
5	10% Sc(OTf) ₃	12	92 (<1)
6 ^c	10% Sc(OTf) ₃	24	29 (61)
7 ^d	10% Sc(OTf) ₃	24	22 (70)
8 ^{c,d}	10% Sc(OTf) ₃	24	-- (94)
9	10% HNTf ₂	12	-- (68)
10 ^e	10% HCl	12	-- (38)
11 ^e	100% HCl	12	-- (21)
12	10% CF ₃ COOH	12	-- (58)
13	10% H ₂ SO ₄	12	39 (50)
14	10% TsOH	12	41 (48)
15	10% MsOH	4	87 (0)
16	10% TfOH	1	95 (0)
17	5% TfOH	4	91 (0)
18^f	10% TfOH	1	94 (0)
19 ^g	10% TfOH	1	73 (0)

^a Reaction conditions: *o*-Aminobenzyl alcohol **1a** (0.2 mmol), 2-methylfuran **2a** (2 equiv, 0.4 mmol, 35.8 μ L), and catalyst were stirred in DCE (0.7 mL, 0.3 M) at 80°C. The progress of the reaction was monitored by TLC.

^b NMR Yield.

^c In the presense of 50 mg molecular sieves 4Å.

^d In the presence of 30 mol% 2,4,6-tritertbutylpyrimidine.

^e 4M HCl in dioxane was used.

^f 1.5 equiv of 2-methylfuran was used.

^g 1.2 equiv of 2-methylfuran was used.

Table 2

Scope of Furans in the One-Pot Synthesis of Indoles from *o*-Aminobenzyl Alcohol^a

entry	furan	product	3, yield
1	2a : R = Me	3aa : R = Me	90%
2 ^b	2a : R = Me	3aa : R = Me	83%
3	2b : R = <i>n</i> -Bu	3ab : R = <i>n</i> -Bu	95%
4	2c : R = Cpent	3ac : R = Cpent	93%
5	2d : R = Cy	3ad : R = Cy	75%
6 ^c	2e : R = H	3ae : R = H	87%
7	2f : R = 2-OMe	3af : R = 2-OMe	85%
8	2g : R = 2-CF ₃	3ag : R = 2-CF ₃	56%
9	2h : R = 2,3-benzo	3ah : R = 2,3-benzo	53%
10	2i : R = 2,4,6-tr ⁱ Pr	3ai : R = 2,4,6-tr ⁱ Pr	48%
11	2j : R = 4-CF ₃	3aj : R = 4-CF ₃	60%
25	2k : R = 4-F	3ak : R = 4-F	83%
13	2l : R = 4-Br	3al : R = 4-Br	70%
14	2m : R = 4-OMe	3am : R = 4-OMe	56%
15	2n : R = Et	3an : R = Et	61%
16	2n : R = Et	3ao : R = Cy	68%

entry	furan	product	3, yield
17	2p	3ap	87%
18	2q	3aq	70%
19	2r	3ar	45%
20	2s	3as	0% ^d

^aReaction conditions: *o*-Aminobenzyl alcohol **1a** (0.5 mmol), furan **2** (1.5 equiv, 0.75 mmol), and TfOH (10 mol%, 4.5 μ L) were stirred in DCE (1.6 mL, 0.3 M) at 80°C. The progress of the reaction was monitored by TLC.

^bReaction was performed on 4.0 mmol scale in a pressure tube.

^cReaction mixture (entries 6–14) was heated at 110°C for 2h.

^dFurylmethyl aniline intermediate **4ar** was isolated in 95% yield.

Table 3

Variation of Substituents at α -Position and at Aniline Phenyl Ring of *o*-Aminobenzyl Alcohols^a

entry	aminoalcohol	product	3, yield ^b
1	1b : R ¹ = Me	3ba : R ¹ = Me	88%
2	1c : R ¹ = <i>i</i> Pr	3ca : R ¹ = <i>i</i> Pr	76%
3	1d : R ¹ = <i>t</i> Bu	3da : R ¹ = <i>t</i> Bu	63%
4	1e : R ¹ = Cy	3ea : R ¹ = Cy	83%
5	1f : R ¹ = 4-FC ₆ H ₄ -	3fa : R ¹ = 4-FC ₆ H ₄ -	72%
6	1g : R ¹ = 4-MeC ₆ H ₄ -	3ga : R ¹ = 4-MeC ₆ H ₄ -	60%
7	1h : R ¹ = 4-MeOC ₆ H ₄ -	3ha : R ¹ = 4-MeOC ₆ H ₄ -	71%
8	1i : R ¹ = 2-thienyl	3ia : R ¹ = 2-thienyl	41%
9	1j : R ² = R ³ = F	3ja : R ² = R ³ = F	79%
10	1k : R ² = R ³ = OMe	3ka : R ² = R ³ = OMe	60%
11	1l : R ² = H, R ³ = CF ₃	3la : R ² = H, R ³ = CF ₃	63%
12	1m : R ² = Br, R ³ = H	3ma : R ² = Br, R ³ = H	61%
13	1n : R ⁴ = Me	3na : R ⁴ = Me, G = Ts	traces
14	1o : R ⁴ = Cl	3oa : R ⁴ = Cl, G = H	58%

^aReaction conditions: *o*-Aminobenzyl alcohol **1** (0.5 mmol), 2-methylfuran **2a** (1.5 equiv, 0.75 mmol, 67.1 μ L), and TfOH (10 mol%, 4.5 μ L) were stirred in DCE (1.6 mL, 0.3 M) at 80°C. The progress of the reaction was monitored by TLC.