Substituent Diversity-Directed Synthesis of Indole Derivatives

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Received November 29, 2008

This paper reports a versatile, good-yielding, solution-phase method that is a substituent diversity-directed synthesis of 1*H*-indoles (**6**−**13**, **17**−**20**) and 1-hydroxyindoles (**14**, **15**) starting from commercially available 1,5-difluoro-2,4-dinitrobenzene. The synthetic products possessed the maximum six diversity points.

Introduction

Indoles are probably the most important privileged structures for drug discovery, with a broad range of biological activities.[1,2] Aside from the endogeneous biologically active substances tryptophan, 5-hydrotryptophan, melatonin, and brassinin, many drugs in clinical use, such as nonsteroidal anti-inflammatory indomethacin, antiemetic ondansetron, and antimigraine sumatriptan (Figure 1), are indole based. In the past decade, many other biologically active indole derivatives, such as HIV-1 nonnucleoside reverse transcriptase inhibitor,[3] 5-HT receptor agonists or antagonists,[4] peroxisome proliferator-activated receptor (PPAR) agonists,[5] protein tyrosine kinase inhibitors,[6] benzodiazepine receptor (BzR) ligands,[7] human cytosolic phospholipase A2α inhibitor,[8] and blood coagulation factor Xa inhibitor[9] have also been presented. In addition, 1-hydroxyindoles also show a range of biological activities, including anticancer activity, α2-blocking, osteoporosis therapeutic activity, antifungal activity, melatonin receptor agonist activity, inhibition of blood platelet aggregation,[10] etc. With these significant observations, it is very attractive to develop practical and efficient methods of generating diverse indoles and 1-hydroxyindoles.

Starting from 1,5-difluoro-2,4-dinitrobenzene (DFDNB), we have developed a "scaffold-directed" method to construct various benzofused chemical libraries,[11] including 2-hydroxyquinoxaline,[12] benzimidazole,[13] imidazoquinoxalinol,[14] indolin-2-one,[15] benzo[1,4]oxazin-3-one,[16] benzo[1,4] thiazin-3-one,[17] 1,5-benzothiazepin-4-one,[18] 1,5-benzodiazepin-2-one,[19] and their benzofused tricycles.[20] To continue these efforts, we report herein a solution-phase method for synthesis of 1*H*-indoles (**6**−**13**, **17**−**20**) and 1-hydroxyindoles (**14**, **15**) with a maximum of six substituent diversity points (Figure 2). In contrast to current methods, this strategy permitted us to introduce a great molecular diversity at the 1,2,3,5,6-position. A large number of structurally diverse indole derivatives for drug development projects can be rapidly synthesized in good purity and high yield using this method.

Results and Discussion

The synthetic route to the key intermediates **4** and **5** is depicted in Scheme 1. The quantitative primary substitution of DFDNB (**1**) by either N- or O-nucleophiles to give **2** was performed as previously reported.[11] Displacement of the remaining fluorine atom by anions of various β-keto esters introduced the second diversity point to give **3** in high yield. The two reactions went smoothly at room temperature, and no side reactions were observed. To reduce quantitatively the *m*-dinitrogroups in **3** and produce 1*H*-indole **4** and 1-hydroxyindole **5**, we systematically investigated various reductive methods[12,21] including H_2−Pd/C at 1 atm, $SnCl_2.2H_2O$/HCl, Sn/HCl, Fe/HCl, Zn/HOAc, Fe/HOAc $HCOOCH_4$−Pd/C. As expected, intermediate **4** could be obtained in 75−80% yield by reduction with $HCOONH_4$−Pd/C in THF/EtOH (v/v = 1:1) at 65 °C. However 1-hydroxyindoles **5** were obtained in 90−95% yield by reduction with stannous chloride in the presence of hydrochloric acid (38%) in ethanol (Scheme 1). Other techniques mainly produced a mixture of **4** and **5** because the intermediate **5** is an incompletely reduced product. This is deduced from the strong driving force of pyrrole ring formation that enables the cyclization to finish before complete reduction of the dinitro group by $SnCl_2.2H_2O$/HCl. However, the $HCOOCH_4$−Pd/C method guaranteed that reduction was faster than cyclization. Typical intermediates **4** (Table 1) and **5** (Table 4) were synthesized and fully characterized by mp, HRMS, ^{1}H NMR, and ^{13}C NMR.

Derivatives of 1*H*-Indole 4. The 6-amino group of intermediate **4** was further derivatized by acylation, sulfonation, and reductive alkylation according to our previous methods,[16] producing amides, ureas, thioureas, sulfonamides, and secondary amines, respectively (compounds **6**−**10**, Scheme 2). Typical compounds were synthesized and fully characterized by mp, HRMS, ^{1}H NMR, and ^{13}C NMR (Table 1).

To diversify the N1-position of the 1*H*-indole, N1-acylation, N1-sulfonylation, and N1-alkylation were successfully performed to produce **11** (Scheme 3). The N1-

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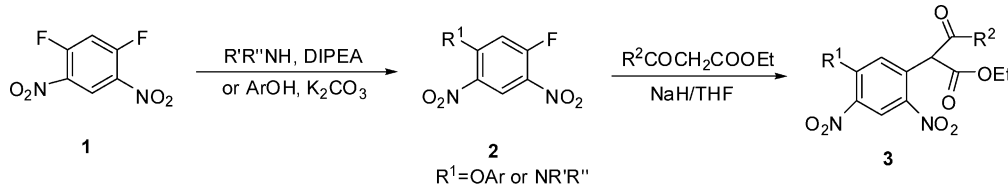
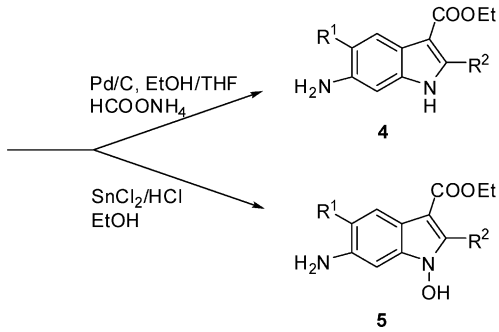
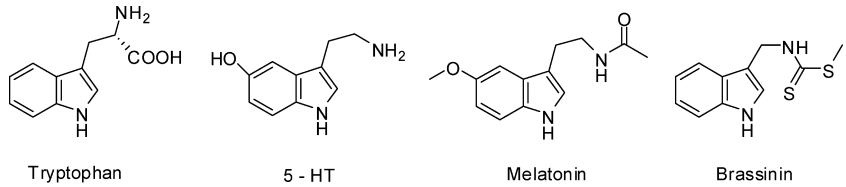
10.1021/cc800198p CCC: $40.75
Published on Web 05/26/2009

Scheme 1. Synthesis of the Essential Intermediates **4** and **5** from DFDNB







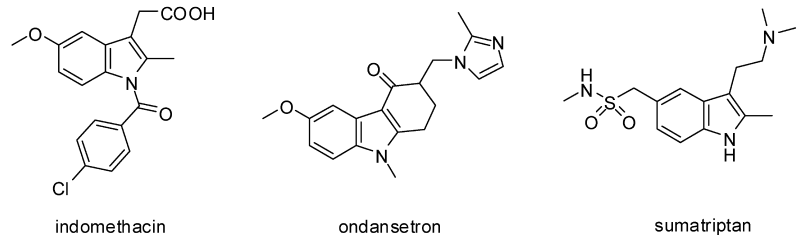


Figure 1. Endogeneous substances and marketed drugs with indole substructures.

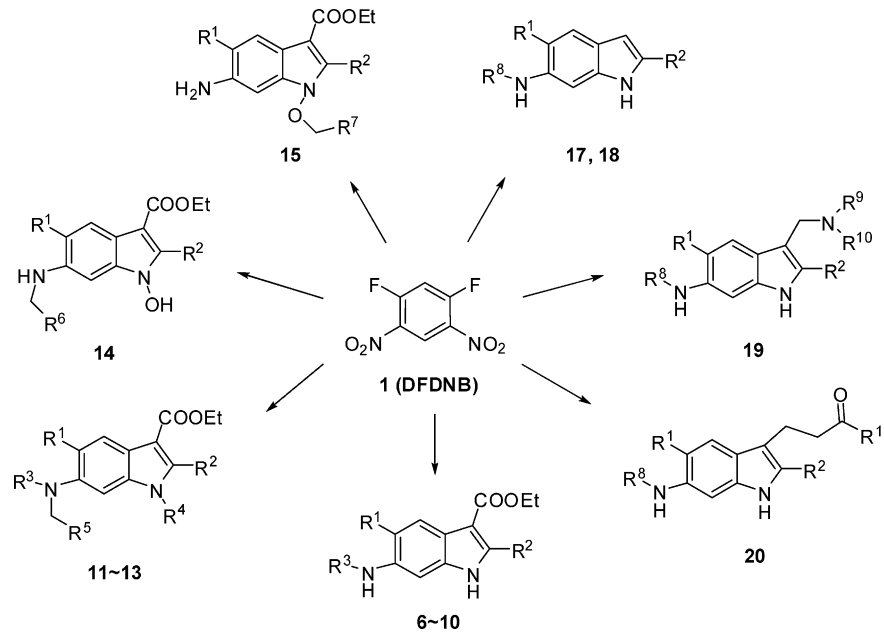
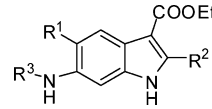


Figure 2. 1*H*-indoles and 1-hydroxyindoles prepared from DFDNB.

acylation and N1-sulfonylation were performed smoothly with 50−60% yields by treatment of **6** and **7** with corresponding acyl chloride and sulfonyl chloride, respectively, in the presence of KOH in EtOH at room temperature.[22]

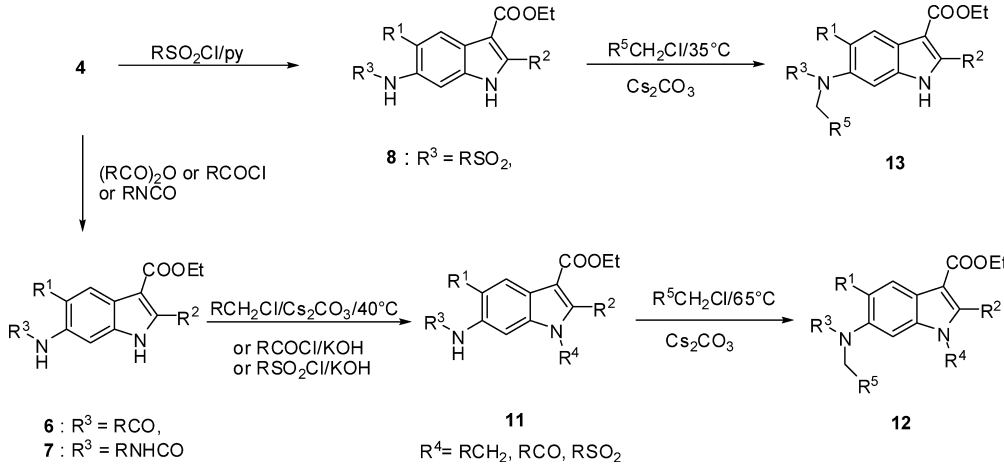
Table 1. Representative 1*H*-Indoles **4** and **6**−**10**



Entry	R^1	R^2	R^3	mp (°C)	Yield (%)	HRMS $(M + H)^+$	
						Calcd	found
4a		CH_3	H	138–140	75.8	288.1712	288.1713
4b			H	178–180	79.6	401.1865	401.1866
4c		CH_3	H	158–160	77.5	330.2182	330.2174
6a		CH_3		145–146	62.4	414.2005	414.2015
6b				169–170	69.8	410.2080	410.2082
6c		CH_3		238–239	60.1	418.2131	418.2128
6d		CH_3		166–168	68.4	330.1818	330.1824
6e		CH_3		171–172	70.5	382.1767	382.1761
6f		CH_3		161–163	69.7	342.1818	342.1815
6g				158–160	70.0	497.1688	497.1687
6h				226–228	71.6	477.1581	477.1562
6i				170–172	65.3	530.2080	530.2073
7a		CH_3		106–108	56.1	521.2376	521.2327
7b		CH_3		140–142	67.0	425.1989	425.1986
7c				169–170	60.6	542.3019	542.3016
8a		CH_3		123–125	53.0	488.2219	488.2224
8b		CH_3		145–147	58.4	380.1644	380.1638
8c				162–164	62.2	521.2110	521.2097
8d				158–160	66.9	493.1797	493.1786
9a		CH_3		109–110	68.6	521.2198	521.2366
10a		CH_3		148–149	61.4	452.2549	452.2549
10b				220–221	71.4	485.2804	485.2808

Scheme 2. Derivatization of **4** at the 6-Aromatic Amino Group to Produce **6**−**10**

Scheme 3. Synthetic Route from **4** to Substituted 1*H*-Indoles **11**, **12**, and **13**



However, the N1-alkylation was successful using various halohydrocarbons only in the presence of Cs_2CO_3 in anhydrous acetone at 40 °C (Scheme 3). Other inorganic bases, including NaH and K_2CO_3, were also investigated. The former gave N1, 6-*N*-dialkylate products, and the latter was unable to alkylate either of the N1, 6-N positions. Typical compounds of structure **11** (Table 2) were synthesized and fully characterized by mp, HRMS, ^{1}H NMR, and ^{13}C NMR.

In contrast with intermediates **6** and **7**, intermediate **8** from sulfonylation of **4** was instead benzylated at the 6-N position to generate **13** rather than **11** when reacted with benzyl chloride in the presence of Cs_2CO_3 (Scheme 3). This result was accounted for the strong electron-withdrawing effect of the sulfone group increasing the proton acidity of the *6*-N proton of the indole compared with the N1 proton. Typical compounds of structure **13** were synthesized and fully characterized by mp, HRMS (Table 3), ^{1}H NMR, and ^{13}C NMR.

As anticipated, benzylation of **6** or **7** resulted in simultaneous benzylation of N1 and 6-N when the reaction temperature was raised to 65 °C in the presence of Cs_2CO_3. This fact encouraged us to introduce different substituent groups at the 6-N position of the indole by using different benzyl chlorides and controlling the reaction temperature (Scheme 3). Sample products **12** are shown in Table 3.

Derivatives of 1-Hydroxyindole 5. Derivatives of 1-hydroxyindoles were produced smoothly by reductive alkylation of the free amino group at the 6-position and benzylation of the 1-hydroxy group of **5**.[23] Intermediate **5** reacted with aldehydes in the presence of $NaBH(OAc)_3$ to generate the corresponding compounds **14** in good yield (about 85%). This reductive alkylation was fast at room temperature and completed within 30 min. It is noteworthy that some of the compounds of structure **14** were unstable under the conditions used for purification and storage. Furthermore, treatment of **5** with benzyl chlorides and K_2CO_3 in anhydrous methanol at 40 °C afforded **15** in 70−80% yield (Scheme 4, Table 4).

Derivatives of the C3-Position of 1*H*-Indole. Derivatives of the C3-position are important for the presentation of biological activity because all endogenetic substances and marketed drugs with indole-based structures were modified at the C3-position (Figure 1). Therefore, the 3-carboxyl group of **4** was removed under reflux condition in the presence of concentrated HCl in EtOH to obtain key intermediate **16** (Scheme 5).[24]

Before Mannich reaction and Michael addition at the C3 position, the 6-position amine group of **16** was acylated, sulfonylated, and reductively alkylated to produce compounds **17** and **18** as described above (Table 5). The 6-NH_2 group of **16** was more chemically reactive than that of **4** because of the elimination of the electron-withdrawing carboxyl ester group at the C3 position.

The Mannich reaction was carried out smoothly at the C3 position of **18**, using formaldehyde and secondary amines in glacial acetic acid at room temperature, to afford **19** in 65−80% yield (Scheme 5).[25] Compound **20**, expected from the Michael addition reaction, was obtained in 30% yield when **18** reacted with vinyl ketone in glacial acetic acid/acetic anhydride (v/v = 3:1) at 120 °C according to a literature method.[26] An acetylation byproduct was observed by LC-MS analysis. A minor modification of the reaction procedure was made by abandoning acetyl anhydrides, so that the yield was increased to 80% (Scheme 5). Because of the abundance of commercially available secondary amines and vinyl ketones, these two mild reactions at the C3 position of the indole scaffold enable us to synthesize a large number of compounds. To demonstrate the advantage over other methods, 11 typical compounds of **19** (Table 6) and **20** (Table 7) were synthesized and fully characterized by mp, HRMS, ^{1}H NMR, and ^{13}C NMR.

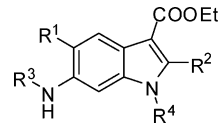
Conclusions

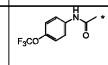
In summary, we have reported a versatile, good-yielding, solution-phase method of synthesis 1*H*-indoles and 1-hydroxyindoles with a maximum of six diversity points starting from commercially available 1,5-difluoro-2,4-dinitrobenzene. All of the reactions described herein are highly effective under mild conditions. Additionally, the new synthetic strategy holds great promise of being developed into a parallel synthetic method to a large number of structurally diverse indole derivatives for drug development projects.

Experimental Section

All chemical reagents were purchased from Alfa Aesar Co. Ltd. and Acros Organics (Geel, Belgium) and used

Table 2. Representative Substituted 1*H*-Indoles **11**

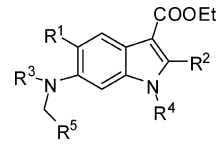


Entry	R^1	R^2	R^3	R^4	mp (°C)	Yield (%)	HRMS $(M + H)^+$	
							Calcd	found
11a					192–193	48.6	594.2604	594.2606
11b					197–198	50.7	592.2811	592.2803
11c					150–151	61.0	558.2393	558.2380
11d					168–170	60.3	601.1661	601.1661
11e		CH_3			146–147	39.3	689.2354	689.2360
11f		CH_3			171–172	59.2	457.2240	457.2238
11g		CH_3			135–137	60.0	428.2185	428.2184
11h		CH_3			155–157	58.8	466.1897	466,1895
11i		CH_3			126–128	63.8	500.2161	500.2155
11j					155–157	49.1	632.3488	632.3491
11k					151–153	50.1	628.3387	628.3387
11l					184–185	53.3	666.3099	666.3101
11m					136–137	54.5	700.3362	700.3369
11n		CH_3			152–154	52.9	508.2600	508.2600
11o		CH_3			145–146	44.3	582.1983	582.1986
11p					117–118	41.9	568.1918	568.1918
11q					185–186	38.3	532.2248	532.2241

without further purification. Tetrahydrofuran (THF) was redistilled from sodium before used. Acetone was dried by anhydrous K_2CO_3. Melting points are uncorrected and measured with the Yanoco micromelting point apparatus. Automatic HPLC-MS analysis was performed on a ThermoFinnigan LCQ-Advantage mass spectrometer equipped with an Agilent pump, an Agilent detector, an Agilent liquid handler, and a fluent splitter. The employed column was a Kromasil C18 column (4.6 μm, 4.6 mm $\times$ 50 mm) from DIKMA for analysis. The eluent was a mixture of acetonitrile and water containing 0.05% HCOOH with a linear gradient from 5:95 (v/v) acetonitrile/H_2O to 95:5 (v/v) acetonitrile/H_2O within five minutes at a 1 mL/min for analysis. The UV detection was carried out at UV wavelength of 254 nm. Five percent of the eluent was split into the MS system. Mass spectra were recorded in either positive or negative ion mode using electrospray ionization (ESI). High-resolution LC-MS was carried out by Agilent LC/MSD TOF using a column of Agilent ZORBAX SB-C18 (rapid resolution, 3.5 μm, 2.1 $\times$ 30 mm) at a flow of 0.40 mL/min. The solvent is methanol/water = 75:25 (v/v) containing 5 mmol/L ammonium formate. The ion source is electrospray ionization (ESI) too. All NMR experiments were carried out on a Varian Mercury 300 or 400 or 500 MHz NMR spectrometer using DMSO-d_6 as the solvent. Chemical shifts were reported in ppm (δ) relative to the solvent signal, and coupling constant (J) value reported in Hz. Parallel synthesis was carried out on an H + P Labortechnik GmbH parallel synthesizer. Flash column chromatography was performed with silica gel 60 (200−300 mesh) from Qindao Haiyang Chemical Factory.

General Procedure for the Synthesis of Intermediate 2. Method 1. A solution of 1.0 equiv of secondary amine in 25 mL of THF was added dropwise to a magnetically stirred solution of 1.0 equiv (typically 5.0 mmol) of 1,5-difluoro-

Table 3. Representative Substituted 1*H*-Indoles **12** and **13**



Entry	R^1	R^2	R^3	R^4	R^5	mp (°C)	Yield (%)	HRMS (M + H)$^+$ Calcd	found
12a		CH_3				135–136	52.1	581.2319	581.2320
12b						161–162	50.0	682.2473	682.2462
13a		CH_3		H		121–123	29.8	495.2066	495.2067
13b				H		161–163	42.3	636.2532	636.2549
13c				H		105–107	36.8	661.1775	661.1774

Scheme 4. Synthetic Route from **5** to Substituted 1*H*-Indoles **14** and **15**

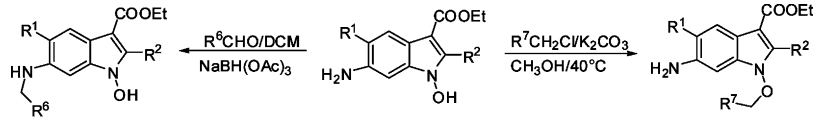
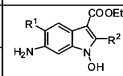
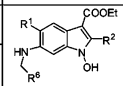
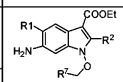


Table 4. Representative Substituted 1-Hydroxyindoles **5**, **14**, and **15**

Entry	Core structure	R^1	R^2	R^6/R^7	mp (°C) or appearance	Yield (%)	HRMS (M + H)$^+$ Calcd	found
5a			CH_3		137–139	91.8	304.1661	304.1667
5b			CH_3		177–179	95.0	346.2131	346.2125
14a			CH_3		Yellow oil	77.1	436.2600	436.2617
14b			CH_3		Yellow oil	78.8	430.3070	430.3073
15a			CH_3		Light-yellow oil	68.8	428.1741	428.1759
15b			CH_3		Yellow oil	63.3	462.2005	462.2015
15c			CH_3		Colorless oil	75.1	436.2600	436.2616
15d			CH_3		Yellow oil	69.2	514.2109	514.2108
15e			CH_3		Yellow oil	74.1	504.1821	504.1826

2,4-dinitrobenzene **1** and 1.0 equiv of *N*,*N*-diisopropylethylamine (DIPEA) in 50 mL of THF. The reaction mixture was stirred continuously for an additional 1 h at room temperature. After the solvent was evaporated in vacuo, water was added to precipitate **2**. The desired intermediate **2** was then collected by filtration, washed thoroughly with water, and used directly for the next reaction. Typically, 1-(5-fluoro-2, 4-dinitrophenyl) pyrrolidine **2** was obtained as a yellow powder in 98% yield, with an HPLC purity >95%.

Method 2. One equivalent of phenol and 2.0 equiv of anhydrous K_2CO_3 were added to a magnetically stirred solution of 1.0 equiv (typically 5.0 mmol) of 1,5-difluoro-2,4-dinitrobenzene **1** in 20 mL of acetone. The reaction mixture was shaken mechanically at room temperature for more than 5 h until the disappearance of **2** was complete, as monitored by HPLC. Undissolved excess K_2CO_3 was removed by filtration. The solvent was evaporated in vacuo. The obtained residue was used directly for the next reaction. Typically, 1-fluoro-2,4-dinitro-5-phenoxybenzene **2** was obtained as yellow powder in 98% yield, with an HPLC purity >95%.

General Procedure for the Synthesis of Intermediate 3. Various solutions of 12 mmol of β-keto esters in 30 mL of THF were added dropwise to the slurry of 12 mmol of sodium hydride in 30 mL of THF. After completion of the addition, the reaction mixture was stirred continuously at room temperature until the solution turned clear. Compound **2** (10 mmol) was then added, and the reaction mixture was

Scheme 5. Synthetic Route from **4** to Substituted 1*H*-Indoles **16**−**20**

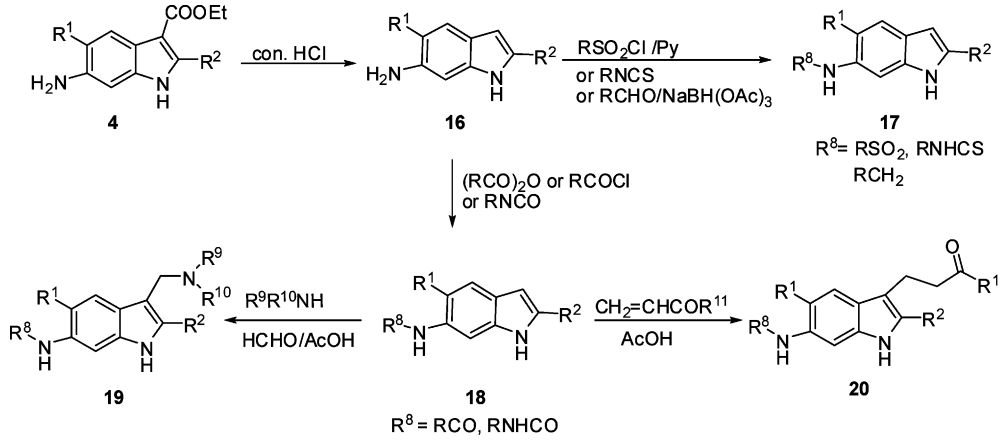
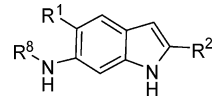
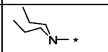
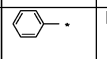
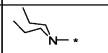
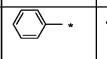
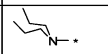
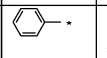
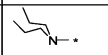
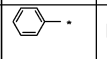
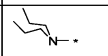
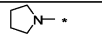
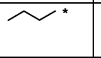
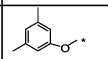
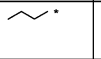
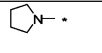
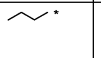
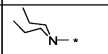
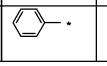


Table 5. Analytical Data for Representative Substituted 1*H*-Indoles **16**−**18**

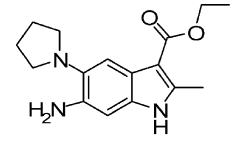


Entry	R^1	R^2	R^8	mp (°C)	Yield (%)	HRMS $(M + H)^+$	
						Calcd	found
16			H	123–125	75.6	308.2127	308.2129
17a				154–155	66.5	442.2495	442.2488
17b				145–146	51.4	462.2215	462.2211
17c				110–111	64.2	461.2175	461.2174
18a		CH_3		123–125	66.6	288.2076	288.2074
18b				185–187	62.7	286.1919	286.1916
18c				158–160	60.6	337.1916	337.1906
18d				166–168	58.5	447.2008	447.2008
18e				143–145	61.2	362.2232	362.2231

stirred strongly at room temperature. The reaction was monitored by fast LC-MS analysis until the intermediate **2** had completely disappeared. After the solvent was evaporated, water was added. The solution was carefully neutralized using 2.0 mol/L HCl and then extracted twice using ethyl acetate (100 mL × 2). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo to give crude **3**, which was used directly in the next reaction. A typical product, such as ethyl 2-(5-(dipropylamino)-2,4-dinitrophenyl)-3-oxobutanoateethyl ester **3**, was obtained as red oil in 92% yield, with an HPLC purity >95%. HRMS (ESI): for $C_{18}H_{26}N_3O_7$, $(M + H^+)$ calcd 396.1771; found 396.1775.

General Procedure for the Synthesis of Intermediate 4. A three-necked 250 mL round-bottomed flask fitted with a condenser was charged with a solution of 5.0 mmol of **3** in 50 mL of EtOH/THF (v/v = 1:1) and $HCOONH_4$ (50 mmol). Two grams of 10% Pd/C was added quickly and carefully at 65 °C, and the reaction mixture was stirred for 30 min. The catalyst and excess $HCOONH_4$ were removed by filtration. The filtrate was concentrated in vacuo and extracted with EtOAc (100 mL × 3). The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography using ethyl acetate/petroleum ether as eluent to give **4** in 75−80% yield, with an HPLC purity of >99%.

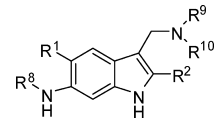
Ethyl 6-Amino-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (4a).



compound **4a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.313 (t, 3H, J = 7.2 Hz), 1.854 (br, 4H), 2.531 (s, 3H), 2.930 (br, 4H), 4.198 (q, 2H, J = 7.2 Hz), 4.537 (s, 2H), 6.623 (s, 1H), 7.468 (s, 1H), 11.136 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.608,

Table 6. Representative Substituted 1*H*-Indoles **19**



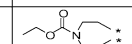
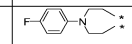
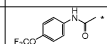
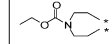
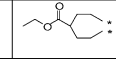
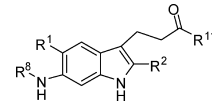
Entry	R^1	R^2	R^8	R^9/R^{10}	mp (°C)	Yield (%)	HRMS $(M + H)^+$	
							Calcd	found
19a		CH_3			132–133	51.9	387.2760	387.2755
19b		CH_3			165–166	48.6	458.3131	458.3140
19c		CH_3			147–148	44.0	480.3139	480.3139
19d		CH_3			200–202	52.6	345.2654	345.2643
19e		CH_3			136–138	50.6	400.3076	400.3043
19f		CH_3			145–147	47.3	371.2811	371.2796
19g					142–144	38.0	504.2586	504.2577
19h					162–164	45.8	456.2975	456.2796
19i					157–159	47.0	398.2920	398.2920
19j					155–157	48.3	412.3076	412.3067
19k					160–161	49.5	455.3022	455.3024

Table 7. Representative Substituted 1*H*-Indoles **20**



Entry	R^1	R^2	R^8	R^{11}	mp (°C)	Yield (%)	HRMS $(M + H)^+$	
							Calcd	found
20a		CH_3			98–100	51.9	372.2651	372.2643
20b					166–168	50.2	370.2495	370.2499
20c					165–167	46.7	421.2491	421.2493

14.459, 23.442, 50.890, 58.274, 95.658, 102.295, 109.455, 118.266, 132.062, 133.210, 139.081, 141.030, 165.270.

Ethyl 6-Amino-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (4b).

compound **4b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.095 (t, 3H, J = 5.4 Hz), 2.208 (s, 6H), 4.085 (q, 2H, J = 5.4 Hz), 4.777 (brs, 2H), 6.537 (s, 2H), 6.668 (s, 1H), 6.841 (s, 1H), 7.409−7.468 (m, 4H), 7.645 (d, 2H, J = 5.4 Hz), 11.606 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.013, 20.944, 58.670, 96.401, 102.669, 112.208, 114.145, 118.629, 123.619, 127.670, 128.317, 129.672, 132.178, 133.797, 137.642, 138.808, 139.736, 142.336, 158.279, 164.457.

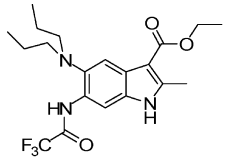
Ethyl 6-Amino-5-(cyclohexyl(methyl)amino)-2-methyl-1*H*-indole-3-carboXylate (4c).

compound **4c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.105−1.217 (m, 4H), 1.303 (t, 3H, J = 7.2 Hz), 1.400−1.533 (m, 2H), 1.670−1.768 (m, 4H), 2.524 (s, 3H), 2.551 (s, 3H), 2.673−2.709 (m, 1H), 4.188 (q, 2H, J = 7.2 Hz), 4.637 (brs, 2H), 6.612 (s, 1H), 7.499 (s, 1H), 11.319 (s, 1H).

General Procedure for the Derivatization of 4 at the 6-Aromatic Amino Group. Method 1. Pyridine (0.3 mmol) and 0.3 mmol of anhydride, acyl chloride, or sulfonyl chloride were added to a solution of 0.10 mmol of **4** in 5 mL of dry DCM, and the reaction mixture was stirred at 45 °C. Chemical conversion was monitored by LC-MS analysis. After the reaction was completed, the solvent was evaporated in vacuo. The final products, **6** or **8**, were characterized after purification by silica gel column chromatography.

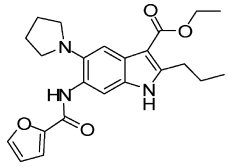
Ethyl 5-(Dipropylamino)-2-methyl-6-(2,2,2-trifluoroacetamido)-1*H*-Indole-3-carboxylate (6a).



compound **6a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.810 (t, 6H, J = 7.5 Hz), 1.272−1.3593 (m, 7H), 2.623 (s, 3H), 2.847 (t, 4H, J = 7.5 Hz), 4.254 (q, 2H, J = 7.2 Hz), 7.899 (s, 1H), 8.206 (s, 1H), 10.374 (s, 1H), 11.900 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 11.367, 13.786, 14.350, 57.883, 58.852, 101.626, 102.870, 114.277, 115.015, 117.145, 124.682, 127.872, 131.836, 136.047, 145.443, 153.025, 164.749.

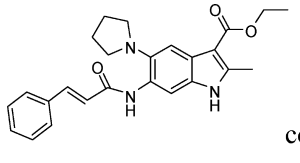
Ethyl 6-(Furan-2-carboxamido)-2-propyl-5-(pyrrolidin-1-yl)-1H-indole-3-carboxylate (6b).



compound **6b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.906 (t, 3H, J = 7.2 Hz), 1.340 (t, 3H, J = 7.2 Hz), 1.682 (m, 2H), 1.965 (br, 4H), 3.014 (m, 6H), 4.245 (q, 2H, J = 7.2 Hz), 6.707 (dd, 1H, J = 1.8 Hz, J = 3.3 Hz), 7.256 (d, 1H, J = 3.3 Hz), 7.779 (s, 1H), 7.942 (d, 1H, J = 1.8 Hz), 8.174 (s, 1H), 9.619 (s, 1H), 11.684 (s, 1H).

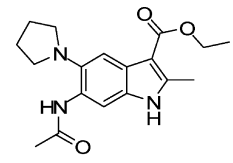
Ethyl 6-Cinnamamido-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (6c).



compound **6c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.342 (t, 3H, J = 7.2 Hz), 1.945 (br, 4H), 2.608 (s, 3H), 3.026 (br, 4H), 4.245 (q, 2H, J = 7.2 Hz), 7.167 (d, 1H, J = 15.6 Hz), 7.385−7.465 (m, 3H), 7.560 (d, 1H, J = 15.6 Hz), 7.650−7.673 (m, 3H), 8.100 (s, 1H), 9.228 (s, 1H), 11.636 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.784, 14.425, 24.140, 51.942, 58.591, 102.452, 104.893, 109.203, 123.405, 123.617, 127.245, 127.790, 128.854. 129.537, 130.498, 134.942, 137.173, 139.634, 144.207, 163.328, 165.037.

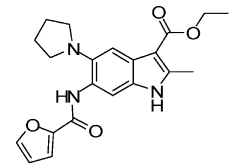
Ethyl 6-Acetamido-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (6d).



compound **6d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.331 (t, 3H, J = 7.2 Hz), 1.909 (br, 4H), 2.090 (s, 3H), 2.590 (s, 3H), 3.023 (br, 4H), 4.231 (q, 2H, J = 7.2 Hz), 7.599 (s, 1H), 7.819 (s, 1H), 8.983 (s, 1H), 11.547 (s, 1H).

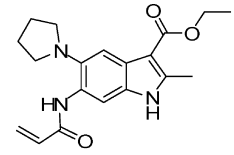
Ethyl 6-(Furan-2-carboxamido)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (6e).



compound **6e**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.341 (t, 3H, J = 6.9 Hz), 1.954 (br, 4H), 2.610 (s, 3H), 3.034 (m, 4H), 4.250 (q, 2H, J = 6.9 Hz), 6.706 (br, 1H), 7.256 (d, 1H, J = 2.2 Hz), 7.759 (s, 1H), 7.941 (br, 1H), 8.158 (s, 1H), 9.613 (s, 1H), 11.704 (s, 1H).

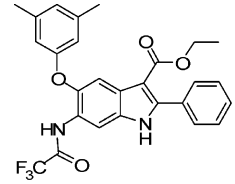
Ethyl 6-Acrylamido-2-methyl-5-(pyrrolidin-1-yl)-1H-indole-3-carboxylate (6f).



compound **6f**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.336 (t, 3H, J = 7.2 Hz), 1.908 (br, 4H), 2.600 (s, 3H), 3.018 (br, 4H), 4.238 (q, 2H, J = 7.2 Hz), 5.700 (dd, 1H, J = 10.2 Hz, J = 1.8 Hz), 6.217 (dd, 1H, J = 16.8 Hz, J = 1.8 Hz), 6.651 (dd, 1H, J = 10.2 Hz, J = 16.8 Hz), 7.625 (s, 1H), 7910 (s, 1H), 9.247 (s, 1H), 11.606 (s, 1H).

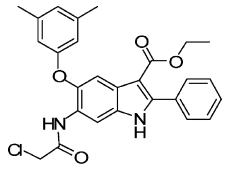
Ethyl 5-(3,5-Dimethylphenoxy)-2-phenyl-6-(2,2,2-trifluoroacetamido)-1*H*-indole-3-carboxylate (6g).



compound **6g**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.074 (t, 3H, J = 7.2 Hz), 2.216 (s, 6H), 4.097 (q, 2H, J = 7.2 Hz), 6.585 (s, 2H), 6.742 (s, 1H), 7.480−7.503 (m, 3H), 7.605 (s, 1H),7.628 (s, 1H), 7.684 (dd, 2H, J = 2.1 Hz, J = 5.4 Hz), 10.902, 12.260 (s, 1H).

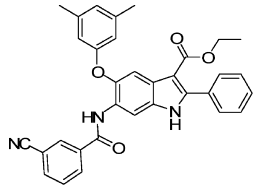
Ethyl 6-(2-Chloroacetamido)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (6h).



compound **6h**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.046 (t, 3H, J = 7.2 Hz), 2.242 (s, 6H), 4.065 (q, 2H, J = 7.2 Hz), 4.371 (s, 2H), 6.656 (s, 2H), 6.781 (s, 1H), 7.461−7.508 (m, 4H), 7.650−7.682 (m, 2H), 8.296 (s, 1H), 9.727, (s, 1H), 12.101 (s, 1H).

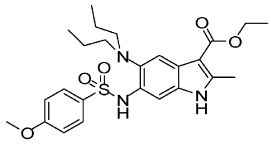
Ethyl 6-(3-Cyanobenzamido)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (6i).



compound **6i**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.110 (t, 3H, J = 7.2 Hz), 2.183 (s, 6H), 4.123 (q, 2H, J = 7.2 Hz), 6.586 (s, 2H), 6.684 (s, 1H), 7.477−7.508 (m, 3H), 7.645−7.716 (m, 4H), 7.918 (s, 1H), 7.989−8.072 (m, 3H), 9.995, (s, 1H), 12.193 (s, 1H).

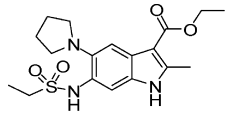
Ethyl 5-(Dipropylamino)-6-(4-methoxyphenylsulfonamido)-2-methyl-1*H*-indole-3-carboxylate (8a).



compound **8a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.686 (t, 6H, J = 7.2 Hz), 1.037−1.160 (m, 4H), 1.294 (t, 3H, J = 7.2 Hz), 2.502−2.547 (m, 4H), 2.589 (s, 3H), 3.741 (s, 3H), 4.215 (q, 2H, J = 7.2 Hz), 7.021 (d, 2H, J = 7.5 Hz), 7.537 (s, 1H), 7.675 (d, 2H, J = 7.5 Hz), 7.687 (s, 1H), 8.494 (s, 1H), 11.743 (s, 1H).

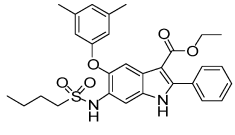
Ethyl 6-(Ethylsulfonamido)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (8b).



compound **8b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.225 (t, 3H, J = 6.9 Hz), 1.335 (t, 3H, J = 7.2 Hz), 1.934−1.976 (m, 4H), 2.609 (s, 3H), 2.960−3.135 (m, 4H), 3.340 (m, 2H), 4.247 (q, 2H, J = 7.2 Hz), 7.325 (s, 1H), 7.702 (s, 1H), 8.421 (s, 1H), 11.675 (s, 1H).

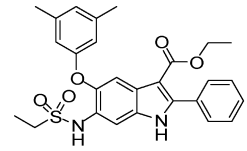
Ethyl 6-(Butylsulfonamido)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (8c).



compound **8c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.762 (t, 3H, J = 7.2 Hz), 1.038 (t, 3H, J = 7.2 Hz), 1.243 (m, 2H), 1.610 (m, 2H), 2.240 (s, 6H), 2.957 (t, 2H, J = 7.8 Hz), 4.065 (q, 2H, J = 7.2 Hz), 6.644 (s, 2H), 6.769 (s, 1H), 7.465−7.536 (m, 5H), 7.650−7.682 (m, 2H), 9.227, (s, 1H), 12.119 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d$_6$): δ 13.360, 13.749, 20.775, 20.875, 25.128, 51.370, 58.919, 102.688, 109.287, 110.454, 115.775, 124.380, 124.594, 125.391, 127.798, 128.950, 129.739, 131.505, 131.616, 139.050, 145.496, 145.771, 157.263, 164.045.

Ethyl 5-(3,5-Dimethylphenoxy)-6-(ethylsulfonamido)-2-phenyl-1*H*-indole-3-carboxylate (8d).

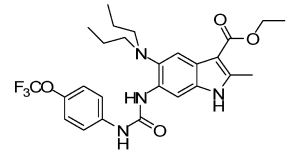


compound **8d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.028 (t, 3H, J = 6.9 Hz), 1.187 (t, 3H, J = 7.2 Hz), 2.249 (s, 6H), 3.029 (t, 2H, J = 7.2 Hz), 4.055 (q, 2H, J = 6.9 Hz), 6.660 (s, 2H), 6.783 (s, 1H), 7.470−7.527 (m, 5H), 7.650−7.664 (m, 2H), 9.217, (s, 1H), 12.106 (s, 1H).

Method 2. The corresponding acylating reagent (isocyanate or isothiocyanate, 0.12 mmol) was added to a solution of 0.10 mmol of **4** in 5 mL of anhydrous THF. The reaction mixture was stirred using an H + P Labortechnik GmbH parallel synthesizer at 45 °C. Chemical conversion was monitored by LC-MS analysis. After the reaction was completed, the solvent was then evaporated under vacuum to obtain the crude product **7** or **9**. The final products were characterized after chromatographic purification on silica gel. The yields ranged from 70% to 90%.

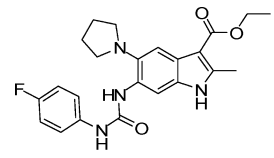
Ethyl 5-(Dipropylamino)-2-methyl-6-(3-(4-(trifluoromethoxy)phenyl)ureido)-1*H*-indole-3-carboxylate (7a).



compound **7a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.763 (t, 6H, J = 5.4 Hz), 1.277−1.334 (m, 4H), 1.346 (t, 3H, J = 7.2 Hz), 2.596 (s, 3H), 2.855 (t, 4H, J = 7.5 Hz), 4.239 (q, 2H, J = 7.2 Hz), 7.274 (d, 2H, J = 8.1 Hz), 7.598 (d, 2H, J = 8.1 Hz), 7.744 (s, 1H), 8.204 (s, 1H), 8.679 (s, 1H), 9.725 (s, 1H), 11.587 (s, 1H).

Ethyl 6-(3-(4-Fluorophenyl)Ureido)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (7b).

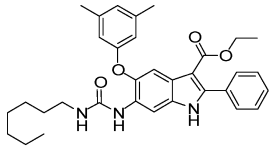


compound **7b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.334 (t, 3H, J = 7.2 Hz), 1.957 (br, 4H), 2.592 (s, 3H), 2.988 (br, 4H), 4.235 (q, 2H, J = 7.2 Hz), 7.114 (t, 2H, J = 8.7 Hz), 7.487 (t, 2H, J

= 8.7 Hz, *J* = 8.7 Hz), 7.694 (s, 1H), 8.080 (s, 1H), 8.157 (s, 1H), 9.454 (s, 1H), 11.533 (s, 1H).

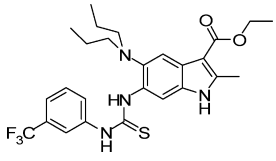
Ethyl 5-(3,5-Dimethylphenoxy)-6-(3-heptylureido)-2-phenyl-1*H*-indole-3-carboxylate (7c).



compound **7c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.848 (t, 3H, *J* = 6.9 Hz), 1.047 (t, 3H, *J* = 7.2 Hz), 1.248 (br, 8H), 1.393 (m, 2H), 2. 236 (s, 6H), 3.066 (q, 2H, *J* = 6.0 Hz), 4.085 (q, 2H, *J* = 7.2 Hz), 6.613 (s, 2H), 6.752 (s, 1H), 6.867 (t, 1H, *J* = 5.4 Hz), 7.409−7.496 (m, 4H), 7.645 (dd, 2H, *J* = 5.7 Hz, *J* = 2.1 Hz), 8.018 (s, 1H), 8.380 (s, 1H), 11.904 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 13.841, 13.898, 20.878, 22.027, 26.306, 26.375, 28.412, 29.590, 30.025, 31.227, 101.368, 102.577, 110.347, 115.508, 121.134, 124.464, 127.706, 128.584, 128.755, 129.739, 131.871, 132.333, 139.042, 141.434, 143.894, 155.185, 157.805, 164.274.

Ethyl 5-(Dipropylamino)-2-methyl-6-(3-(3-(trifluoromethyl)phenyl)thioureido)-1*H*-indole-3-carboxylate (9a).

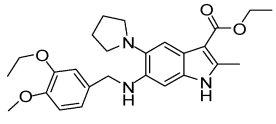


compound **9a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.736 (t, 6H, *J* = 7.2 Hz), 1.230−1.308 (m, 4H), 1.332 (t, 3H, *J* = 7.2 Hz), 2.602 (s, 3H), 2.776 (t, 4H, *J* = 7.5 Hz), 4.242 (q, 2H, *J* = 7.2 Hz), 7.523 (d, 1H, *J* = 7.8 Hz), 7.609 (t, 1H, *J* = 7.8 Hz), 7.726 (s, 1H), 7.789 (d, 1H, *J* = 7.8 Hz), 8.526 (s, 1H), 9.557 (s, 1H), 10.457 (s, 1H), 11.765 (s, 1H).

Method 3 (Reductive Alkylation). A solution of **4** (0.1 mmol) in 5 mL of anhydrous DCM was added to aldehydes (0.1 mmol), glacial acetic acid (100 μL) and $NaBH(OAc)_3$ (0.2 mmol) respectively. The reaction mixture was stirred using an H + P Labortechnik GmbH parallel synthesizer at 45 °C. Chemical conversion was monitored by LC-MS analysis. After the reaction was completed, the solution was evaporated in vacuo to dryness. The crude residue was dissolved in 15 mL of DCM and then washed with saturated $NaHCO_3$ (2 × 10 mL) and brine (2 × 10 mL). After the DCM layer was completely dried over anhydrous Na_2SO_4, the filtrate was concentrated in vacuo to obtain the crude product. The final product **10** was characterized after chromatographic purification on silica gel. The yields ranged from 80% to 90%.

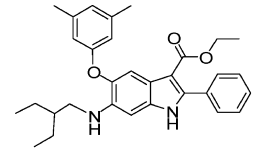
Ethyl 6-(3-Ethoxy-4-methoxybenzylamino)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (10a).



compound **10a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.286 (t, 3H, *J* = 7.2 Hz), 1.311 (t, 3H, *J* = 7.2 Hz), 1.878−1.989 (m, 4H), 2.505 (s, 3H), 2.977 (br, 4H), 3.713 (s, 3H), 3.946 (q, 2H, *J* = 7.2 Hz), 4.200 (q, 2H, *J* = 7.2 Hz), 4.250 (d, 2H, *J* = 5.7 Hz), 5.343 (t, 1H, *J* = 5.7 Hz), 6.317 (s, 1H), 6.857 (br, 2H), 6.988 (s, 1H), 7.551 (s, 1H), 11.150 (s, 1H).

Ethyl 5-(3,5-Dimethylphenoxy)-6-(2-ethylbutylamino)-2-phenyl-1*H*-indole-3-carboxylate (10b).

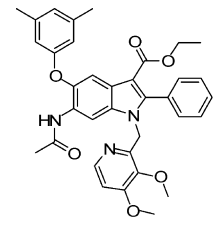


compound **10b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.820 (t, 6H, *J* = 7.2 Hz), 1.096 (t, 3H, *J* = 7.2 Hz), 1.200−1.296 (m, 4H), 1.498−1.559 (m, 1H), 2.203 (s, 6H), 2.987 (t, 2H, *J* = 6.0 Hz), 4.085 (q, 2H, *J* = 7.2 Hz), 4.712 (t, 1H, *J* = 6.0 Hz), 6.546 (s, 2H), 6.627 (s, 1H), 6.686 (s, 1H), 7.379−7.482 (m, 4H), 7.640 (m, 2H), 11.660 (s, 1H).

General Procedure for the Synthesis of 11. Method 1. A mixture of compound **6** or **7** (0.2 mmol), benzyl chloride (0.2 mmol), and Cs_2CO_3 (0.4 mmol) was stirred at 40 °C in dry acetone. The reaction mixture was monitored by LC-MS analysis. After the reaction was completed, the solid was filtered, and the filtrate was collected and evaporated to dryness. The final product **11** was obtained as white or light-yellow solid and characterized after chromatographic purification on silica gel. The yields ranged from 70 to 90%.

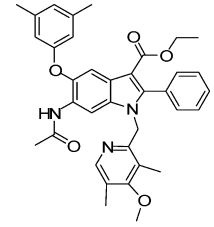
Ethyl 6-Acetamido-1-((3,4-dimethoxypyridin-2-yl)-methyl)-5-(3,5-dimet hylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (11a).



compound **11a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.897 (t, 3H, *J* = 7.2 Hz), 1.979 (s, 3H), 2.236 (s, 6H), 3.625 (s, 3H), 3.855 (s, 3H), 3.940 (q, 2H, *J* = 7.2 Hz), 5.221 (s, 2H), 6.627 (s, 2H), 6.759 (s, 1H), 7.020 (d, 1H, *J* = 6.0 Hz), 7.356−7.403 (m, 5H), 7.536 (s, 1H), 8.020 (d, 1H, *J* = 6.0 Hz), 8.029 (s, 1H), 9.337 (s, 1H).

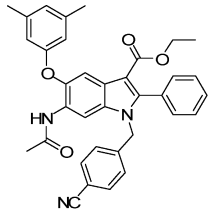
Ethyl 6-Acetamido-5-(3,5-dimethylphenoxy)-1-((4-methoxy-3,5-dimeth ylpyridin-2-yl)methyl)-2-phenyl-1*H*-indole-3-carboxylate (11b).



compound **11b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.899 (t, 3H, J = 7.2 Hz), 1.983 (s, 3H), 2.087 (s, 3H), 2.134 (s, 3H), 2.238 (s, 6H), 3.685 (s, 3H), 3.855 (s, 3H), 3.940 (q, 2H, J = 7.2 Hz), 5.176 (s, 2H), 6.634 (s, 2H), 6.759 (s, 1H), 7.326−7.413 (m, 5H), 7.530 (s, 1H), 8.004 (s, 1H), 8.023 (s, 1H), 9.336 (s, 1H).

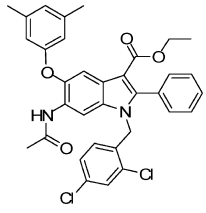
Ethyl 6-Acetamido-1-(4-cyanobenzyl)-5-(3,5-dimethylphenoxy)-2-phen yl-1*H*-indole-3-carboxylate (11c).



compound **11c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.893 (t, 3H, J = 7.2 Hz), 1.977 (s, 3H), 2.244 (s, 6H), 3.945 (q, 2H, J = 7.2 Hz), 5.300 (s, 2H), 6.653 (s, 2H), 6.782 (s, 1H), 7.058 (d, 2H, J = 8.1 Hz), 7.339−7.451 (m, 5H), 7.560 (s, 1H), 7.718 (d, 1H, J = 8.1 Hz), 8.072 (s, 1H), 9.418 (s, 1H).

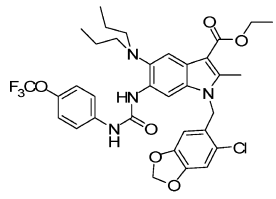
Ethyl 6-Acetamido-1-(2,4-dichlorobenzyl)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (11d).



compound **11d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.894 (t, 3H, J = 7.2 Hz), 2.001 (s, 3H), 2.251 (s, 6H), 3.947 (q, 2H, J = 7.2 Hz), 5.209 (s, 2H), 6.460 (d, 1H, J = 8.4 Hz), 6.665 (s, 2H), 6.789 (s, 1H), 7.261−7.439 (m, 6H), 7.572 (s, 1H), 7.613 (d, 1H, J = 1.8 Hz), 8.072 (s, 1H), 9.433 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 13.563, 20.886, 23.709, 44.593, 58.868, 104.881, 105.067, 109.872, 116.309, 122.432, 124.884, 126.738, 127.925, 128.383, 128.861, 129.046, 129.936, 130.472, 131.770, 132.705, 133.233, 139.101, 144.714, 146.605, 157.163, 163.583, 168.660.

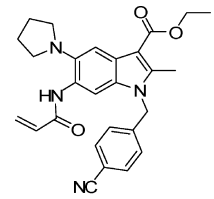
Ethyl 1-((6-Chlorobenzo[*d*][1,3]dioxol-5-yl)methyl)-5-(dipropylamino)-2-methyl-6-(3-(4-(trifluoromethoxy)phenyl)ureido)-1*H*-indole-3-carboxylate (11e).



compound **11e**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.790 (t, 6H, J = 7.5 Hz), 1.292−1.317 (m, 4H), 1.366 (t, 3H, J = 6.9 Hz), 2.619 (s, 3H), 2.875 (t, 4H, J = 7.5 Hz), 4.286 (q, 2H, J = 6.9 Hz), 5.316 (brs, 2H), 5.747 (s, 1H), 5.988 (s, 2H), 7.209 (s, 1H), 7.255 (d, 2H, J = 8.1 Hz), 7.555 (d, 2H, J = 8.1 Hz), 7.870 (s, 1H), 8.145 (s, 1H), 8.704 (s, 1H), 9.738 (s, 1H).

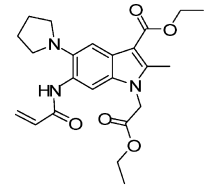
Ethyl 6-Acrylamido-1-(4-cyanobenzyl)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11f).



compound **11f**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.361 (t, 3H, J = 7.2 Hz), 1.901 (br, 4H), 2.621 (s, 3H), 3.046 (br, 4H), 4.277 (q, 2H, J = 7.2 Hz), 5.545 (s, 2H), 5.678 (dd, 1H, J = 10.2 Hz, J = 1.8 Hz), 6.174 (dd, 1H, J = 16.8 Hz, J = 1.8 Hz), 6.603 (dd, 1H, J = 10.2 Hz, J = 16.8 Hz), 7.124 (d, 2H, J = 8.1 Hz), 7.686 (s, 1H), 7.784 (d, 2H, J = 8.1 Hz), 7.835 (s, 1H), 9.308 (s, 1H).

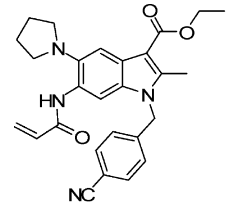
Ethyl 6-Acrylamido-1-(2-ethoxy-2-oxoethyl)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11g).



compound **11g**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.186 (t, 3H, J = 7.2 Hz), 1.357 (t, 3H, J = 7.2 Hz), 1.902 (br, 4H), 2.608 (s, 3H), 3.0516 (br, 4H), 4.156 (q, 2H, J = 7.2 Hz), 4.272 (q, 2H, J = 7.2 Hz), 5.082 (s, 2H), 5.707 (dd, 1H, J = 10.2 Hz, J = 1.8 Hz), 6.219 (dd, 1H, J = 16.8 Hz, J = 1.8 Hz), 6.637 (dd, 1H, J = 10.2 Hz, J = 16.8 Hz), 7.641 (s, 1H), 7.816 (s, 1H), 9.345 (s, 1H).

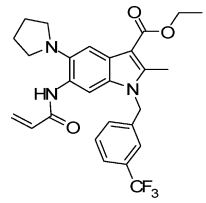
Ethyl 6-Acrylamido-1-(4-chlorobenzyl)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11h).



compound **11h**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.358 (t, 3H, J = 7.2 Hz), 1.901 (br, 4H), 2.637 (s, 3H), 3.051 (br, 4H), 4.271 (q, 2H, J = 7.2 Hz), 5.420 (s, 2H), 5.680 (dd, 1H, J = 10.2 Hz, J = 1.8 Hz), 6.182 (dd, 1H, J = 16.8 Hz, J = 1.8 Hz), 6.612 (dd, 1H, J = 10.2 Hz, J = 16.8 Hz), 6.994 (d, 2H, J = 8.4 Hz), 7.369 (d, 2H, J = 8.4 Hz), 7.680 (s, 1H), 7.870 (s, 1H), 9.302 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.709, 14.364, 24.247, 45.164, 51.351, 58.877, 103.081, 105.637, 108.654, 123.411, 126.070, 126.345, 127.882, 128.717, 131.147, 131.856, 132.287, 136.121, 138.936, 144.749, 163.092, 164.094.

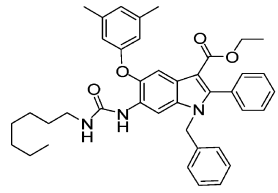
Ethyl 6-Acrylamido-2-methyl-5-(pyrrolidin-1-yl)-1-(3-(trifluoromethyl)benzyl)-1*H*-indole-3-carboxylate (11i).



compound **11i**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.363 (t, 3H, J = 7.2 Hz), 1.901 (br, 4H), 2.637 (s, 3H), 3.063 (br, 4H), 4.274 (q, 2H, J = 7.2 Hz), 5.553 (s, 2H), 5.678 (dd, 1H, J = 11.1 Hz, J = 1.2 Hz), 6.178 (dd, 1H, J = 15.6 Hz, J = 1.2 Hz), 6.603 (dd, 1H, J = 11.1 Hz, J = 15.6 Hz), 7.090 (d, 1H, J = 8.1 Hz), 7.492−7.553 (m, 2H), 7.625 (d, 1H, J = 8.1 Hz), 7.682 (s, 1H), 7.863 (s, 1H), 9.316 (s, 1H).

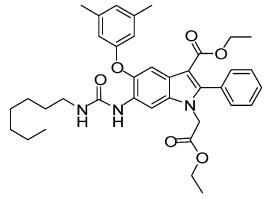
Ethyl 1-Benzyl-5-(3,5-dimethylphenoxy)-6-(3-heptylureido)-2-phenyl-1*H*-indole-3-carboxylate (11j).



compound **11j**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.836 (t, 3H, J = 6.9 Hz), 0.890 (t, 3H, J = 7.2 Hz), 1.227 (br, 8H), 1.355 (m, 2H), 2. 244 (s, 6H), 3.009 (q, 2H, J = 6.6 Hz), 3.932 (q, 2H, J = 7.2 Hz), 5.169 (s, 2H), 6.643 (s, 2H), 6.776 (s, 1H), 6.842−6.891 (m, 3H), 7.195−7.277 (m, 3H), 7.334−7.444 (m, 5H), 7.487 (s, 1H), 8.085 (s, 1H), 8.335 (s, 1H).

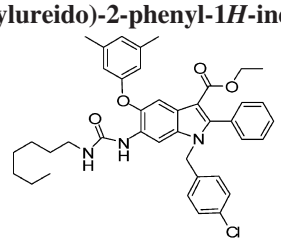
Ethyl 5-(3,5-Dimethylphenoxy)-1-(2-ethoxy-2-oxoethyl)-6-(3-heptylureido)-2-phenyl-1*H*-indole-3-carboxylate (11k).



compound **11k**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.869 (m, 6H), 1.127 (t, 3H, J = 7.2 Hz), 1.247 (br, 8H), 1.393 (m, 2H), 2.246 (s, 6H), 3.050 (q, 2H, J = 6.0 Hz), 3.935 (q, 2H, J = 7.2 Hz), 4.085 (q, 2H, J = 7.2 Hz), 4.718 (s, 2H), 6.639 (s, 2H), 6.773 (s, 1H), 6.892 (t, 1H, J = 5.4 Hz), 7.333 (dd, 2H, J = 5.4 Hz, J = 2.1 Hz), 7.457∼7.491 (m, 4H), 8.117 (s, 1H), 8.342 (s, 1H).

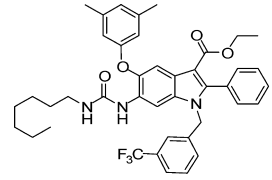
Ethyl 1-(4-Chlorobenzyl)-5-(3,5-dimethylphenoxy)-6-(3-heptylureido)-2-phenyl-1*H*-indole-3-carboxylate (11l).



compound **11l**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.836 (t, 3H, J = 6.9 Hz), 0.888 (t, 3H, J = 7.2 Hz), 1.229 (br, 8H), 1.357 (m, 2H), 2. 247 (s, 6H), 3.011 (q, 2H, J = 6.6 Hz), 3.931 (q, 2H, J = 7.2 Hz), 5.156 (s, 2H), 6.644 (s, 2H), 6.779 (s, 1H), 6.849−6.90 (m, 3H), 7.288−7.358 (m, 4H), 7.381−7.445 (m, 3H), 7.489 (s, 1H), 8.098 (s, 1H), 8.304 (s, 1H).

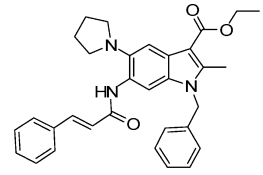
Ethyl 5-(3,5-Dimethylphenoxy)-6-(3-heptylureido)-2-phenyl-1-(3-(trifluoromethyl)benzyl)-1*H*-indole-3-carboxylate (11m).



compound **11m**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.832 (t, 3H, J = 6.9 Hz), 0.886 (t, 3H, J = 7.2 Hz), 1.226 (br, 8H), 1.358 (br, 2H), 2.245 (s, 6H), 3.011 (q, 2H, J = 6.6 Hz), 3.932 (q, 2H, J = 7.2 Hz), 5.283 (s, 2H), 6.644 (s, 2H), 6.780 (s, 1H), 6.863 (t, 1H, J = 5.4 Hz), 7.103 (d, 1H, J = 7.5 Hz), 7.236 (s, 1H), 7.308−7.478 (m, 6H), 7.495 (s, 1H), 7.576 (d, 1H, J = 7.5 Hz), 8.105 (s, 1H), 8.371 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.589, 13.875, 20.867, 22.000, 26.302, 26.348, 28.374, 28.435, 29.545, 30.021, 31.204, 31.246, 46.564, 58.728, 100.251, 104.824, 109.966, 110.122, 115.882, 118.518, 119.864, 124.804, 126.795, 127.882, 128.881, 129.205, 130.140, 130.773, 132.325, 132.589, 139.168, 142.254, 142.689, 145.580, 155.047, 157.397, 163.710.

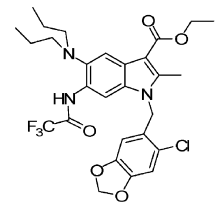
Ethyl 1-Benzyl-6-cinnamamido-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11n).



compound **11n**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.365 (t, 3H, J = 7.2 Hz), 1.938 (br, 4H), 2.666 (s, 3H), 3.075 (br, 4H), 4.280 (q, 2H, J = 7.2 Hz), 5.425 (s, 2H), 7.022 (d, 2H, J = 6.9 Hz), 7.119 (d, 1H, J = 15.6 Hz), 7.242−7.446 (m, 6H), 7.520 (d, 1H, J = 15.6 Hz), 7.624 (d, 2H, J = 6.6 Hz), 7.732 (s, 1H), 8.082 (s, 1H), 9.269 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 11.792, 14.395, 24.244, 45.870, 51.680, 58.885, 102.993, 104.731, 109.129, 122.839, 123.075, 126.062, 127.205, 127.319, 127.768, 128.763, 128.878, 129.571, 131.522, 134.900, 137.030, 138.311, 139.764, 144.815, 163.453, 164.971.

Ethyl 1-((6-Chlorobenzo[*d*][1,3]dioxol-5-yl)methyl)-5-(dipropylamino)-2-methyl-6-(2,2,2-trifluoroacetamido)-1*H*-indole-3-carboxylate (11o).

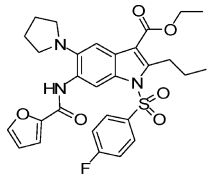


compound **11o**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.810 (t, 6H, J = 7.5 Hz), 1.292−1.390 (m, 7H), 2.675 (s, 3H), 2.858 (t, 4H, J = 7.2 Hz), 4.299 (q, 2H, J = 7.2 Hz), 5.396 (s, 2H), 5.863 (s, 1H), 5.993 (s, 2H), 7.201 (s, 1H), 7.997 (s, 1H), 8.065 (s, 1H), 10.372 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.343, 11.682, 14.287, 20.207, 44.031, 57.439, 59.201, 101.288, 102.181, 103.707, 106.117, 109.958, 115.470, 123.049, 124.014, 126.783, 128.240, 132.680, 137.398, 146.221, 147.117, 147.537, 153.243, 164.568.

Method 2. KOH pellets (0.30 mmol) were added to a solution of **6** (0.24 mmol) in ethanol (5 mL) at room temperature, and the mixture was stirred until complete dissolution had occurred. The ethanol was completely removed under vacuum, and acetone (5 mL) was added, followed by sulfonyl chloride (0.3 mmol). A precipitate was filtered off, and the solution was concentrated in vacuo. The final product **11p** was obtained in 60% yield and characterized after chromatographic purification on silica gel.

Ethyl 1-(4-Fluorophenylsulfonyl)-6-(furan-2-carboxamido)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11p).

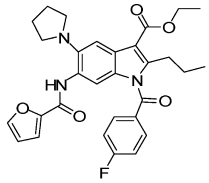


compound **11p**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.969 (t, 3H, J = 7.2 Hz), 1.347 (t, 3H, J = 7.2 Hz), 1.635−1.709 (m, 2H), 1.892 (br, 4H), 3.117 (br, 4H), 3.357−3.407 (m, 2H), 4.305 (q, 2H, J = 7.2 Hz), 6.714 (dd, 1H, J = 1.8 Hz, J = 3.3 Hz), 7.341 (d, 1H, J = 3.3 Hz), 7.428−7.486 (m, 2H), 7.603 (s, 1H), 7.947−7.993 (m, 3H), 8.522 (s, 1H), 9.673 (s, 1H).

Method 3. KOH pellets (0.30 mmol) were added to a solution of **6** (0.24 mmol) in ethanol (5 mL) at room temperature, and the mixture was stirred until complete dissolution had occurred. The ethanol was completely removed in vacuo, and 1 g of anhydrous Na_2SO_4 was added, followed by acetone (5 mL) and acetyl chloride (0.3 mmol). The mixture was stirred for 30 min. The solid was filtered off, and the solution was concentrated in vacuo to give the crude product. The final product **11q** was obtained in 55% yield and characterized after chromatographic purification on silica gel.

Ethyl 1-(4-Fluorobenzoyl)-6-(furan-2-carboxamido)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (11q).

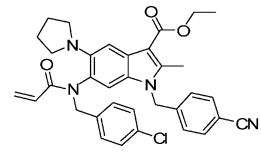


compound **11q**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.833 (t, 3H, J = 7.2 Hz), 1.388 (t, 3H, J = 7.2 Hz), 1.532−1.604 (m, 2H), 1.928 (br, 4H), 3.074−3.155 (m, 6H), 4.349 (q, 2H, J = 7.2 Hz), 6.657 (dd, 1H, J = 1.8 Hz, J = 3.3 Hz), 7.256 (d, 1H, J = 3.3 Hz), 7.417−7.475 (m, 2H), 7.537(s, 1H), 7.797−7.861 (m, 3H), 7.896 (s, 1H), 9.498 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.666, 14.169, 22.931, 24.197, 27.817, 51.832, 59.827, 107.002, 108.627, 110.115, 112.361, 114.593, 116.610, 116.610, 123.278, 127.428, 129.766, 131.196, 133.256, 133.332, 138.775, 145.740, 147.449, 148.845, 155.375, 164.209, 164.694, 166.715, 168.249.

General Procedure for the Synthesis of 12. A mixture of compound **11** (0.2 mmol), benzyl chloride (0.4 mmol), and Cs_2CO_3 (0.4 mmol) was refluxed in anhydrous acetone. The reaction mixture was monitored by LC-MS analysis. After the reaction was completed, the solid was filtered, and the filtrate was collected and evaporated to dryness. The final product **12** was obtained as a white powder and was characterized after chromatographic purification on silica gel. The yields ranged from 80 to 90%.

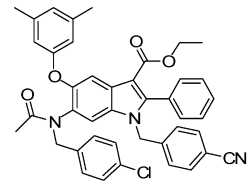
Ethyl 6-(*N*-(4-chlorobenzyl)acrylamido)-1-(4-cyanobenzyl)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (12a).



compound **12a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.357 (t, 3H, J = 7.2 Hz), 1.836−1.976 (m, 4H), 2.580 (s, 3H), 2.980 (br, 2H), 3.257 (br, 2H), 4.114 (d, 1H, J = 14.4 Hz), 4.268 (q, 2H, J = 7.2 Hz), 5.336−5.481 (m, 3H), 5.521−5.563 (m, 1H), 6.164−6.216 (m, 2H), 6.758 (s, 1H), 6.915 (d, 2H, J = 8.1 Hz), 6.989 (d, 2H, J = 8.7 Hz), 7.087 (d, 2H, J = 8.7 Hz), 7.607 (s, 1H), 7.708 (d, 2H, J = 8.1 Hz).

Ethyl 6-(*N*-(4-chlorobenzyl)acetamido)-1-(4-cyanobenzyl)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (12b).

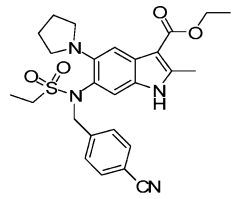


compound **12b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.870 (t, 3H, J = 7.2 Hz), 1.807 (s, 3H), 2.249 (s, 6H), 3.929 (q, 2H, J = 7.2 Hz), 4.480 (d, 1H, J = 14.4 Hz), 5.013 (d, 1H, J = 14.4 Hz), 5.178 (d, 1H, J = 17.4 Hz), 5.427 (d, 1H, J = 17.4 Hz), 6.553 (s, 2H), 6.810 (s, 1H), 6.896 (d, 2H, J = 8.4 Hz), 7.051 (d, 2H, J = 8.1 Hz), 7.145 (d, 2H, J = 8.1 Hz), 7.303−7.323 (m, 2H), 7.383−7.452 (m, 4H), 7.538 (s, 1H), 7.679 (d, 1H, J = 8.4 Hz).

General Procedure for the Synthesis of 13. 0.20 mmol of benzyl chloride and 0.2 mmol of Cs_2CO_3 were added to a solution of 0.20 mmol **8** in 5 mL of dry acetone at 35 °C. The reaction mixture was monitored by LC-MS analysis. After the reaction was completed, the solid was filtered, and the filtrate was collected and evaporated to dryness. The final product **13** was obtained as light-yellow solid and was characterized after chromatographic purification on silica gel. The yields ranged from 50% to 70%.

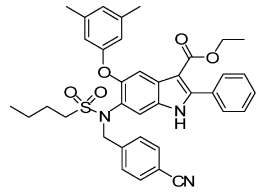
Ethyl 6-(*N*-(4-Cyanobenzyl)ethylsulfonamido)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (13a).



compound **13a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.308 (t, 3H, J = 7.5 Hz), 1.319 (t, 3H, J = 7.2 Hz), 1.862 (br, 4H), 2.570 (s, 3H), 3.131 (br, 4H), 3.353 (q, 2H, J = 7.5 Hz), 4.223 (q, 2H, J = 7.2 Hz), 4.854 (brs, 2H), 6.946 (s, 1H), 7.344 (d, 2H, J = 8.1 Hz), 7.540 (s, 1H), 7.710 (d, 2H, J = 8.1 Hz), 11.513 (s, 1H).

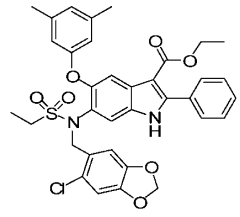
Ethyl 6-(*N*-(4-Cyanobenzyl)butylsulfonamido)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (13b).



compound **13b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.750 (t, 3H, J = 7.2 Hz), 0.959 (t, 3H, J = 7.2 Hz), 1.243−1.365 (m, 2H), 1.685−1.787 (m, 2H), 2.270 (s, 6H), 3.247 (t, 2H, J = 7.2 Hz), 4.002 (q, 2H, J = 7.2 Hz), 4.917 (s, 2H), 6.708 (s, 2H), 6.849 (s, 1H), 7.178 (s, 1H), 7.419(s, 1H), 7.437−7.459 (m, 3H), 7.500 (d, 2H, J = 8.4 Hz), 7.588−7.620 (m, 2H), 7.770 (d, 2H, J = 8.4 Hz), 12. 099 (s, 1H).

Ethyl 6-(*N*-((6-Chlorobenzo[*d*][1,3]dioxol-5-yl)methyl)-ethylsulfonamido)-5-(3,5-dimethylphenoxy)-2-phenyl-1*H*-indole-3-carboxylate (13c).

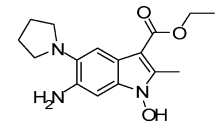


compound **13c**

^{1}H NMR (300 MHz, DMSO-d$_6$): δ 0.967 (t, 3H, J = 6.9 Hz), 1.319 (t, 3H, J = 7.2 Hz), 2.279 (s, 6H), 3.279 (t, 2H, J = 7.2 Hz), 4.011 (q, 2H, J = 6.9 Hz), 4.914 (s, 2H), 6.043 (s, 2H), 6.744 (s, 2H), 6.866 (s, 1H), 6.954 (s, 1H), 7.118 (s, 1H), 7.229 (s, 1H), 7.395(s, 1H), 7.448−7.479 (m, 3H), 7.614−7.647 (m, 2H), 12.091 (s, 1H).

General Procedure for the Synthesis of Intermediate 5. A solution of **3** (3 mmol) in 30 mL of ethanol was added $SnCl_2 \cdot 2H_2O$ (18 mmol) and 12 M HCl (2 mL). The mixture reacted for 2 h under reflux before being poured slowly and carefully into a cold 30%(w/v) NaOH solution (60 mL). The resulting mixture was extracted with DCM (30 mL × 3). The organic layers were combined and concentrated under reduced pressure. The residue was dried completely over anhydrous Na_2SO_4 and purified by silica gel column chromatography using dichloromethane/methanol as the eluent to give **5** in 90−95% yield.

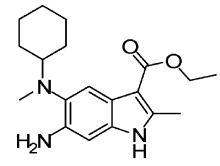
Ethyl 6-Amino-1-hydroxy-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (5a).



compound **5a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.344 (t, 3H, J = 7.2 Hz), 1.862 (br, 4H), 2.534 (s, 3H), 2.944 (br, 4H), 4.207 (q, 2H, J = 7.2 Hz), 4.695 (br, 2H), 6.675 (s, 1H), 7.509 (s, 1H), 11.136 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 10.477, 14.478, 23.482, 50.886, 58.485, 92.820, 97.250, 109.451, 113.597, 130.492, 133.933, 138.116, 139.620, 165.085.

Ethyl 6-Amino-5-(cyclohexyl(methyl)amino)-2-methyl-1*H*-indole-3-carboxylate (5b).

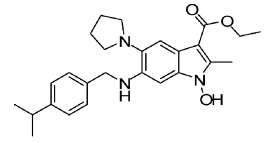


compound **5b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.112−1.188 (m, 4H), 1.316 (t, 3H, J = 7.2 Hz), 1.400−1.543 (m, 2H), 1.678−1.774 (m, 4H), 2.554 (s, 3H), 2.564 (s, 3H), 2.655−2.726 (m, 1H), 4.204 (q, 2H, J = 7.2 Hz), 4.788 (br, 2H), 6.647 (s, 1H), 7.555 (s, 1H), 11.119 (s, 1H).

General Procedure for the Synthesis of 14 and 15. The procedure for the synthesis of **14** was similar to that for **10** except that a lower temperature was used and the final product was obtained as yellow oil. For the synthesis of **15**, a mixture of compound **5** (0.2 mmol), benzyl chloride (0.4 mmol), and K_2CO_3 (0.4 mmol) was stirred at 40 °C in anhydrous methanol and was monitored by LC-MS analysis. After the reaction was completed, the solid was filtered off, and the filtrate was collected and evaporated to dryness. The final product **15** was obtained as yellow oil and characterized after chromatographic purification on silica gel.

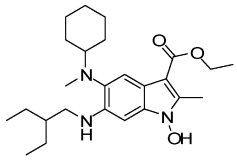
Ethyl 1-Hydroxy-6-(4-isopropylbenzylamino)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (14a).



compound **14a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.157 (s, 3H), 1.181(s, 3H), 1.318 (t, 3H, J = 7.2 Hz), 1.894 (br, 4H), 2.515 (s, 3H), 2.828 (m, 1H), 2.993 (br, 4H), 4.205 (q, 2H, J = 7.2 Hz), 4.314 (d, 2H, J = 6.0 Hz), 5.488 (d, 1H, J = 6.0 Hz), 6.369 (s, 1H), 7.181 (d, 2H, J = 7.8 Hz), 7.278 (d, 2H, J = 7.8 Hz), 7.598 (s, 1H), 11.150 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 10.404, 14.432, 23.587, 23.892, 46.930, 51.523, 58.4685, 88.903, 97.203, 110.034, 112.689, 126.238, 126.802, 130.723, 133.912, 137.726, 137.833, 140.213, 146.576, 164.976.

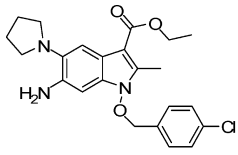
Ethyl 5-(Cyclohexyl(methyl)amino)-6-(2-ethylbutylamino)-1-hydroxy-2-methyl-1*H*-indole-3-carboxylate (14b).



compound **14b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.892 (s, 6H), 1.070−1.130 (m, 4H), 1.319 (t, 3H, J = 7.2 Hz), 1.368−1.440 (m, 4H), 1.527−1.5870 (m, 2H), 1.678−1.710 (m, 4H), 2.554 (s, 3H), 2.566 (s, 6H), 2.611−2.681 (m, 1H), 2.988 (t, 2H, J = 5.4 Hz), 4.210 (q, 2H, J = 7.2 Hz), 4.970 (t, 1H, J = 5.4 Hz), 6.426 (s, 1H), 7.596 (s, 1H), 11.224 (s, 1H).

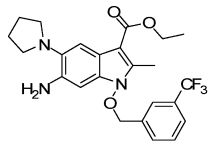
Ethyl 6-Amino-1-(4-chlorobenzyloxy)-2-methyl-5-(pyrrolidin-1-yl)-1*H*-indole-3-carboxylate (15a).



compound **15a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.321 (t, 3H, J = 7.2 Hz), 1.873 (br, 4H), 2.472 (s, 3H), 2.958 (br, 4H), 4.220 (q, 2H, J = 7.2 Hz), 4.778 (brs, 2H), 5.176 (s, 2H), 6.803 (s, 1H), 7.532−7.545 (m, 5H).

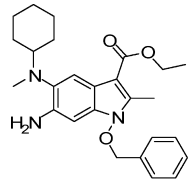
Ethyl 6-Amino-2-methyl-5-(pyrrolidin-1-yl)-1-(3-(trifluoromethyl)benzyloxy)-1*H*-indole-3-carboxylate (15b).



compound **15b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.320 (t, 3H, J = 7.2 Hz), 1.875 (br, 4H), 2.479 (s, 3H), 2.961 (br, 4H), 4.223 (q, 2H, J = 7.2 Hz), 4.777 (brs, 2H), 5,292 (s, 2H), 6.818 (s, 1H), 7.554 (s, 1H), 7.682−7.868 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 10.248, 14.390, 23.446, 50.771, 58.728, 77.739, 92.622, 98.546, 109.798, 113.540, 125.929, 126.230, 126.261, 128.332, 129.816, 133.866, 134.320, 135.297, 137.559, 140.202, 164.801.

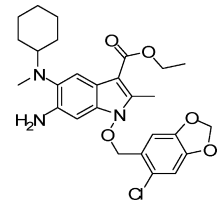
Ethyl 6-Amino-1-(benzyloxy)-5-(cyclohexyl(methyl)amino)-2-methyl-1*H*-indole-3-carboxylate (15c).



compound **15c**

^{1}H NMR (300 MHz, DMSO-d$_6$): δ 1.124−1.222 (m, 4H), 1.317 (t, 3H, J = 7.2 Hz), 1.500−1.550 (m, 2H), 1.693−1.792 (m, 4H), 2.496 (s, 3H), 2.580 (s, 3H), 2.7101−2.750 (m, 1H), 2.988 (t, 2H, J = 5.4 Hz), 4.220 (q, 2H, J = 7.2 Hz), 4.871 (brs, 2H), 5.173 (s, 2H), 6.813 (s, 1H), 7.449−7.471 (m, 3H), 7.517−7.604 (m, 2H), 7.604 (s, 1H).

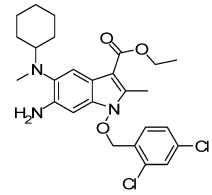
Ethyl 6-Amino-1-((6-chlorobenzo[*d*][1,3]dioxol-5-yl)-methoxy)-5-(cyclohexyl(methyl)amino)-2-methyl-1*H*-indole-3-carboxylate (15d).



compound **15d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.107−1.258 (m, 4H), 1.319 (t, 3H, J = 7.2 Hz), 1.500−1.547 (m, 2H), 1.687−1.977 (m, 4H), 2.544 (s, 3H), 2.572 (s, 3H), 2.670−2.706 (m, 1H), 2.988 (t, 2H, J = 5.4 Hz), 4.222 (q, 2H, J = 7.2 Hz), 4.889 (brs, 2H), 5.148 (s, 2H), 6.111 (s, 2H), 6.813 (s, 1H), 7.228 (s, 2H), 7.592 (s, 1H).

Ethyl 6-Amino-5-(cyclohexyl(methyl)amino)-1-(3,5-dichlorobenzyloxy)-2-methyl-1*H*-indole-3-carboxylate (15e).

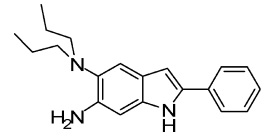


compound **15e**

^{1}H NMR (300 MHz, DMSO-d_6): δ 1.056−1.199 (m, 4H), 1.296 (t, 3H, J = 7.2 Hz), 1.450−1.527 (m, 2H), 1.667−1.763 (m, 4H), 2.480 (s, 3H), 2.552 (s, 3H), 2.670−2.683 (m, 1H), 4.200 (q, 2H, J = 7.2 Hz), 4.873 (brs, 2H), 5.250 (s, 2H), 6.769 (s, 1H), 7.507 (dd, 1H, J = 8.1 Hz, J = 2.1 Hz), 7.574 (s, 1H), 7.621 (d, 1H, J = 8.1 Hz), 7.768 (d, 1H, J = 2.1 Hz).

General Procedure for the Synthesis of Intermediate 16. Fifty equivalents of 12 mol/L hydrochloric acid was added to a solution of 5 mmol of **4** in 30 mL of ethanol. The mixture was refluxed until **4** had completely disappeared, as monitored by fast LC-MS analysis. The solvent was then evaporated in vacuo, and the residue was stirred vigorously and adjusted to pH 8−9 by adding aqueous 30% (w/v) NaOH with cooling (5 °C). The mixture was extracted twice with 100 mL of ethyl acetate. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo to give crude **16**, which was used directly in the next reaction. For a typical product, such as 2-phenyl-*N*5,*N*5-dipropyl-1*H*-indole-5,6-diamine (**16**), a pale powder was obtained and characterized after chromatographic purification on silica gel, with an HPLC purity of >99%.

2-Phenyl-*N*5,*N*5-dipropyl-1*H*-indole-5,6-diamine (16).



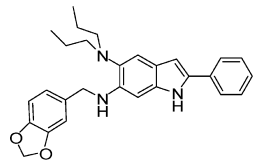
compound **16**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.810 (t, 6H, J = 7.5 Hz), 1.304−1.401 (m, 4H), 2.794 (t, 4H, J = 7.5 Hz), 4.753 (brs, 2H), 6.623 (d, 1H, J = 1.8 Hz), 6.653 (s, 1H), 7.116 (s, 1H), 7.181 (t, 1H, J = 7.5 Hz), 7.368 (t, 2H, J = 7.5 Hz), 7.721 (d, 2H, J = 7.5 Hz), 10.822 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.713, 20.078, 56.441, 94.707,

98.700, 113.449, 120.569, 123.990, 126.042, 128.688, 132.594, 132.949, 134.461, 135.804, 141.540.

General Procedure for the Derivatization of 16 into 17 and 18 at the 6-Amino Group. The procedure for derivatization of **16** at the 6-amino group was similar to that for **6**−**10**. A shorter reaction time or lower reaction temperature was necessary to obtain the anticipated derivatives of **17** and **18**.

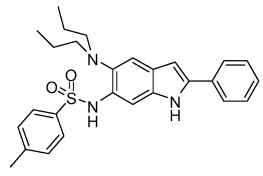
***N*6-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-2-phenyl-*N*5,*N*5-dipropyl-1*H*-indole-5,6-diamine (17a).**



compound **17a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.805 (t, 6H, J = 7.5 Hz), 1.334−1.405 (m, 4H), 2.814 (t, 4H, J = 7.5 Hz), 4.27 (d, 2H, J = 6.0 Hz), 5.694 (t, 1H, J = 6.0 Hz), 5.959 (s, 2H), 6.348 (s, 1H), 6.636 (s, 1H), 6.825−6.894 (m, 3H), 7.142∼7.191 (m, 2H), 7.351 (t, 2H, J = 7.2 Hz), 7.684 (d, 2H, J = 7.2 Hz), 10.893 (s, 1H).

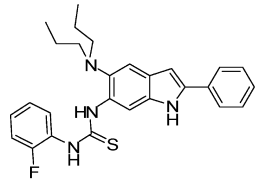
***N*-(5-(Dipropylamino)-2-phenyl-1*H*-indol-6-yl)-4-methylbenzenesulfonamide (17b).**



compound **17b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.695 (t, 6H, J = 7.2 Hz), 1.045−1.162 (m, 4H), 2.286 (s, 3H), 2.596 (t, 4H, J = 7.2 Hz), 6.751 (s, 1H), 7.283−7.359 (m, 4H), 7.434 (t, 2H, J = 7.2 Hz), 7.591 (s, 1H), 7.679 (d, 2H, J = 7.5 Hz), 7.775 (d, 2H, J = 7.5 Hz), 8.595 (s, 1H), 11.468, (s, 1H).

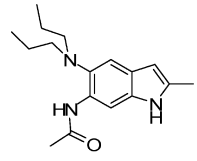
1-(5-(Dipropylamino)-2-phenyl-1*H*-indol-6-yl)-3-(2-fluorophenyl)thiourea (17c).



compound **17c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.703 (t, 6H, J = 7.2 Hz), 1.129−1.203 (m, 4H), 2.684 (t, 4H, J = 7.5 Hz), 6.793 (s, 1H), 7.270−7.450 (m, 7H), 7.541 (t, 1H, J = 7.5 Hz), 7.812 (d, 2H, J = 7.5 Hz), 8.866 (s, 1H), 9.644 (s, 1H), 9.966 (s, 1H), 11.496, (s, 1H).

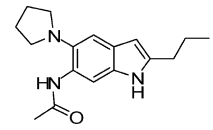
***N*-(5-(Dipropylamino)-2-methyl-1*H*-indol-6-yl)acetamide (18a).**



compound **18a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.813 (t, 6H, J = 7.5 Hz), 1.256−1.329 (m, 4H), 2.085 (s, 3H), 2.313 (s, 3H), 2.787 (t, 4H, J = 7.2 Hz), 5.978 (t, 1H, J = 1.2 Hz), 7.266 (s, 1H), 8.228 (s, 1H), 9.091 (s, 1H), 10.718 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 11.668, 13.393, 20.284, 24.519, 58.083, 98.865, 100.041, 112.907, 124.256, 130.010, 132.749, 133.429, 135.153, 166.883.

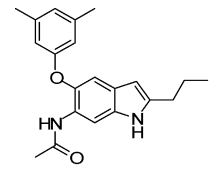
***N*-(2-Propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)acetamide (18b).**



compound **18b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.908 (t, 3H, J = 7.5 Hz), 1.589−1.688 (m, 2H), 1.865−1.978 (m, 4H), 2.077 (s, 3H), 2.615 (t, 2H, J = 7.5 Hz), 2.941−2.979 (m, 4H), 5.974 (d, 1H, J = 1.2 Hz), 7.110 (s, 1H), 7.817 (s, 1H), 8.895 (s, 1H), 10.650 (s, 1H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 13.678, 22.108, 24.043, 24.117, 29.765, 52.145, 97.956, 104.548, 108.075, 124.808, 126.296, 131.981, 135.017, 139.927, 167.665.

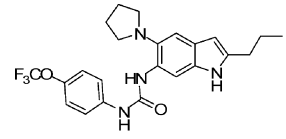
***N*-(5-(3,5-Dimethylphenoxy)-2-propyl-1*H*-indol-6-yl)acetamide (18c).**



compound **18c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.925 (t, 3H, J = 7.5 Hz), 1.631−1.705 (m, 2H), 1.965 (s, 3H), 2.185 (s, 6H), 2.636 (t, 2H, J = 7.5 Hz), 6.020 (s, 1H), 6.498 (s, 2H), 6.654 (s, 1H), 6.935 (s, 1H), 7.895 (s, 1H), 9.110 (s, 1H), 10.844 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 13.744, 20.925, 22.054, 23.649, 29.770, 98.263, 105.675, 109.481, 114.777, 123.706, 124.233, 124.874, 132.482, 138.694, 141.075, 141.129, 158.628, 168.228.

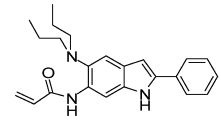
1-(2-Propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (18d).



compound **18d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.913 (t, 3H, J = 7.5 Hz), 1.618−1.692 (m, 2H), 1.935 (br, 4H), 2.617 (t, 2H, J = 7.2 Hz), 2.952 (br, 4H), 5.967 (s, 1H), 7.197 (s, 1H), 7.271 (d, 2H, J = 8.4 Hz), 7.584 (d, 2H, J = 8.4 Hz), 8.000 (s, 1H), 8.191 (s, 1H), 9.587 (s, 1H), 10.595 (s, 1H).

***N*-(5-(Dipropylamino)-2-phenyl-1*H*-indol-6-yl)acrylamide (18e).**

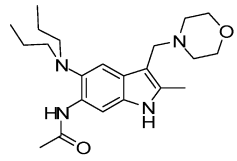


compound **18e**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.810 (t, 6H, J = 7.2 Hz), 1.267−1.389 (m, 4H), 2.842 (t, 4H, J = 7.2 Hz), 6.623 (d, 1H, J = 1.8 Hz), 5.756 (dd, 1H, J = 10.5 Hz, J = 1.5 Hz), 6.226 (dd, 1H, J = 16.8 Hz, J = 1.5 Hz), 6.534 (dd, 1H, J = 10.5 Hz, J = 16.8 Hz), 6.796 (s, 1H), 7.276 (t, 1H, J = 7.5 Hz), 7.406−7.456 (m, 3H), 7.798 (d, 2H, J = 7.5 Hz), 8.507 (s, 1H), 9.430 (s, 1H), 11.462 (s, 1H).

General Procedure for the Synthesis of 19 (Mannich Reaction). The appropriate secondary amine (0.21 mmol) was dissolved in acetic acid (4 mL), and 37% aqueous formaldehyde (0.24 mmol) was added. The reaction mixture was stirred for five minutes. Intermediate **18** (0.2 mmol) was added, and the resulting mixture was stirred at room temperature and monitored by LC-MS analysis. After the reaction was completed, the reaction mixture was basified using saturated $NaHCO_3$ solution and extracted twice using dichloromethane. The combined extracts were washed with brine (20 mL) and dried over $MgSO_4$. The organic layer was concentrated under reduced pressure. The crude product **19** was purified by silica gel column chromatography using dichloromethane/methanol as eluent.

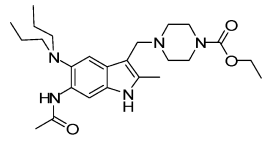
***N*-(5-(Dipropylamino)-2-methyl-3-(morpholinomethyl)-1*H*-indol-6-yl)acetamide (19a).**



compound **19a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.816 (t, 6H, J = 7.5 Hz), 1.2582−1.351 (m, 4H), 2.085 (s, 3H), 2.286 (s, 3H), 2.330 (br, 4H), 2.805 (t, 4H, J = 7.2 Hz), 3.509 (br, 4H), 7.414 (s, 1H), 8.186 (s, 1H), 9.062 (s, 1H), 10.659 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.480, 11.678, 20.200, 24.494, 52.316, 52.972, 57.931, 66.376, 100.033, 105.999, 112.171, 124.529, 129.945, 132.310, 132.508, 133.386, 166.898.

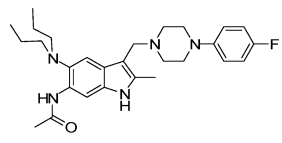
Ethyl 4-((6-Acetamido-5-(dipropylamino)-2-methyl-1*H*-indol-3-yl)methyl)piperazine-1-carboxylate (19b).



compound **19b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.813 (t, 6H, J = 7.5 Hz), 1.137 (t, 3H, J = 7.2 Hz), 1.249−1.347 (m, 4H), 2.085 (s, 3H), 2.279 (s, 3H), 2.310 (br, 4H), 2.810 (t, 4H, J = 7.5 Hz), 3.292 (br, 4H), 3.526 (br, 2H), 3.992 (t, 4H, J = 7.2 Hz), 7.395 (s, 1H), 8.187 (s, 1H), 9.063 (s, 1H), 10.672 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.472, 11.667, 14.512, 20.192, 24.487, 43.513, 51.824, 52.026, 57.908, 60.563, 100.037, 106.018, 112.140, 124.540, 129.945, 132.287, 132.550, 132.481, 154.483, 166.898.

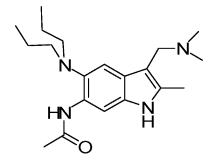
***N*-(5-(Dipropylamino)-3-((4-(4-fluorophenyl)piperazin-1-yl)methyl)-2-methyl-1*H*-indol-6-yl) acetamide (19c).**



compound **19c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.805 (t, 6H, J = 7.5 Hz), 1.253−1.372 (m, 4H), 2.086 (s, 3H), 2.310 (s, 3H), 2.797 (t, 4H, J = 7.2 Hz), 3.292 (br, 4H), 3.008 (br, 4H), 3.571 (br, 2H), 6.868−6.914 (m, 2H), 7.008 (t, 2H, J = 9.0 Hz), 7.449 (s, 1H), 8.201 (s, 1H), 9.065 (s, 1H), 10.671 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 11.514, 11.678, 20.192, 20.491, 49.169, 51.961, 52,293, 57.912, 100.049, 112.289, 115.088, 115.260, 116.980, 124.502, 129.968, 132.344, 133.283, 147.941, 166. 981.

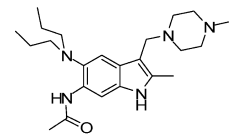
***N*-(3-((Dimethylamino)Methyl)-5-(dipropylamino)-2-methyl-1*H*-indol-6-yl)acetamide (19d).**



compound **19d**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.817 (t, 6H, J = 7.2 Hz), 1.273−1.345 (m, 4H), 2.087 (s, 3H), 2.234 (s, 6H), 2.308 (s, 3H), 2.807 (t, 4H, J = 7.2 Hz), 3.589 (br, 2H), 7.377 (s, 1H), 8.212 (s, 1H), 9.092 (s, 1H), 10.787 (s, 1H).

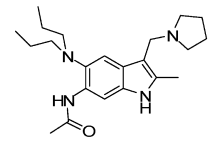
***N*-(5-(Dipropylamino)-2-methyl-3-((4-methylpiperazin-1-yl)methyl)-1*H*-indol-6-yl)acetamide (19e).**



compound **19e**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.815 (t, 6H, J = 7.5 Hz), 1.252−1.372 (m, 4H), 2.083 (s, 3H), 2.142 (s, 3H), 2.279 (s, 3H), 2.280−2.484 (m, 6H), 2.801 (t, 4H, J = 7.2 Hz), 3.327 (br, 2H), 3.538 (br, 2H), 7.419 (s, 1H), 8.180 (s, 1H), 9.059 (s, 1H), 10.678 (s, 1H).

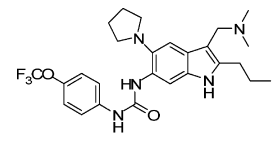
***N*-(5-(Dipropylamino)-2-methyl-3-(pyrrolidin-1-ylmethyl)-1*H*-indol-6-yl)acetamide (19f).**



compound **19f**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.813 (t, 6H, J = 7.2 Hz), 1.271−1.3449 (m, 4H), 1.710 (br, 4H), 2.086 (s, 3H), 2.323 (s, 3H), 2.645 (br, 4H), 2.808 (t, 4H, J = 7.2 Hz), 3.830 (br, 2H), 7.441 (s, 1H), 8.202 (s, 1H), 9.083 (s, 1H), 10.804 (s, 1H).

1-(3-((Dimethylamino)methyl)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)-3-(4-(trifluoromethoxy)phenyl)urea (19g).

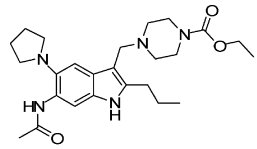


compound **19g**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.893 (t, 3H, J = 7.2 Hz), 1.634−1.708 (m, 2H), 1.965 (br, 4H), 2.706 (s, 6H), 2.751 (t, 2H, J = 7.5 Hz), 3.020 (br, 4H), 7.272 (d, 2H, J =

8.7 Hz), 7.516 (s, 1H), 7.605 (d, 2H, J = 8.7 Hz), 8.063 (s, 1H), 8.299 (s, 1H), 9.837 (s, 1H), 11.056 (s, 1H).

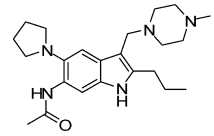
Ethyl-4-((6-acetamido-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-3-yl)methyl)piperazine-1-carboxylate (19h).



compound **19h**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.873 (t, 3H, J = 7.2 Hz), 1.149 (t, 3H, J = 7.2 Hz), 1.585−1.660 (m, 2H), 1.894 (br, 4H), 2.077 (s, 3H), 2.310 (br, 4H), 2.629 (t, 2H, J = 7.5 Hz), 2.974 (br, 4H), 3.314 (br, 4H), 3.506 (br, 2H), 4.003 (t, 3H, J = 7.2 Hz), 7.258 (s, 1H), 7.777 (s, 1H), 8. 901 (s, 1H), 10.557 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.675, 14.552, 22.555, 24.026, 24.088, 27.611, 43.058, 52.027, 52.188, 60.586, 104.564, 105.912, 107.222, 125.152, 126.384, 131.156, 134.910, 137.939, 154.521, 167.654, 167.704.

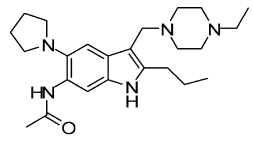
***N*-(3-((4-Methylpiperazin-1-yl)methyl)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)acetamide (19i).**



compound **19i**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.874 (t, 3H, J = 7.2 Hz), 1.588−1.662 (m, 2H), 1.891 (br, 4H), 2.079 (s, 3H), 2.188 (s, 3H), 2.409 (br, 6H), 2.638 (t, 2H, J = 7.2 Hz), 2.974 (br, 4H), 3.342 (br, 2H), 3.550 (br, 2H), 7.263 (s, 1H), 7.781 (s, 1H), 8. 905 (s, 1H), 10.583 (s, 1H).

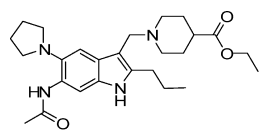
***N*-(3-((4-Ethylpiperazin-1-yl)methyl)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)acetamide (19j).**



compound **19j**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.874 (t, 3H, J = 7.2 Hz), 0.968 (t, 3H, J = 7.2 Hz), 1.588−1.687 (m, 2H), 1.898 (br, 4H), 2.079 (s, 3H), 2.345 (br, 8H), 2.660 (t, 2H, J = 7.2 Hz), 2.978 (br, 4H), 3.319 (br, 2H), 3.516 (br, 2H), 7.263 (s, 1H), 7.781 (s, 1H), 8. 903 (s, 1H), 10.559 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 11.688, 13.675, 22.530, 24.045, 24.092, 27.628, 51.440, 52.221, 104.525, 105.889, 107.309, 125.164, 126.400, 131.156, 134.912, 138.056, 167.704.

Ethyl 1-((6-Acetamido-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-3-yl)methyl)piperidine-4-carboxylate (19k).

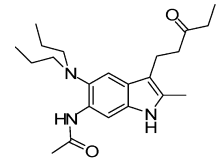


compound **19k**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.870 (t, 3H, J = 7.2 Hz), 1.148 (t, 3H, J = 7.2 Hz), 1.471−1.505 (m, 2H), 1.557−1.682 (m, 2H), 1.728−1.764 (m, 2H), 1.896 (br, 4H), 2.078 (s, 3H), 2.256 (m, 1H), 2.625 (t, 2H, J = 7.2 Hz), 2.758 (br, 2H), 2.970 (br, 4H), 3.318 (br, 2H), 3.466 (br, 2H), 4.030 (t, 2H, J = 7.2 Hz), 7.251 (s, 1H), 7.777 (s, 1H), 8. 900 (s, 1H), 10.528 (s, 1H).

General Procedure for the Synthesis of 20 (Michael Addition Reaction). Commercial ethyl vinyl ketone (0.6 mmol) was added to a solution of 0.20 mmol intermediate **18** in 5 mL of glacial acetic acid. The reaction mixture was heated at 100 °C, and the initial yellow solution turned dark brown. After the reaction was completed, the reaction mixture was basified using 2 N NaOH and extracted twice using DCM. The combined extracts were washed with brine (20 mL) and dried over anhydrous $MgSO_4$. The DCM extracts were concentrated in vacuo to give crude product **20**, which was purified by silica gel column chromatography using dichloromethane/methanol as eluent. The yield was about 80%.

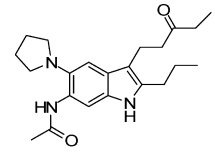
***N*-(5-(Dipropylamino)-2-methyl-3-(3-oxopentyl)-1*H*-indol-6-yl)acetamide (20a).**



compound **20a**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.832 (m, 9H), 1.268−1.341 (m, 4H), 2.079 (s, 3H), 2.238 (s, 3H), 2.348 (q, 2H, J = 7.2 Hz), 2.615 (t, 2H, J = 7.2 Hz), 2.764 (t, 2H, J = 7.2 Hz), 2.811 (t, 4H, J = 7.2 Hz), 7.235 (s, 1H), 8.179 (s, 1H), 9.091 (s, 1H), 10.508 (s, 1H).

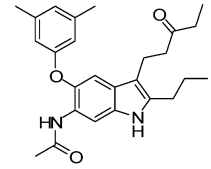
***N*-(3-(3-Oxopentyl)-2-propyl-5-(pyrrolidin-1-yl)-1*H*-indol-6-yl)acetamide (20b).**



compound **20b**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.845−0.903 (m, 6H), 1.555−1.653 (m, 2H), 1.899 (br, 4H), 2.076 (s, 3H), 2.374 (q, 2H, J = 7.2 Hz), 2.554−2.627 (m, 4H), 2.766 (t, 2H, J = 7.2 Hz), 2.981 (br, 4H), 7.084 (s, 1H), 7.790 (s, 1H), 8. 901 (s, 1H), 10.392 (s, 1H).

***N*-(5-(3,5-Dimethylphenoxy)-3-(3-oxopentyl)-2-propyl-1*H*-indol-6-yl)acetamide (20c).**



compound **20c**

^{1}H NMR (300 MHz, DMSO-d_6): δ 0.815 (t, 3H, J = 7.2 Hz), 0.905 (t, 3H, J = 7.5 Hz), 1.582−1.658 (m, 2H), 1.929 (s, 3H), 2.180 (s, 6H), 2.316 (q, 2H, J = 7.2 Hz), 2.534−2.627 (m, 4H), 2.710 (t, 2H, J = 6.6 Hz), 6.481 (s, 2H), 6.634 (s, 1H), 6.976 (s, 1H), 7.824 (s, 1H), 9.100 (s,

1H), 10.721 (s, 1H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 7.471, 13.776, 18.109, 20.905, 22.587, 23.556, 27.493, 28.942, 35.206, 42.738, 105.896, 108.616, 109.104, 114.230, 115.676, 123.408, 124.380, 131.383, 136.918, 138.566, 140.374, 158.804, 168.157, 210.641.

Acknowledgment. We are grateful to Dr Tian-ming Yang for his discussion and kind suggestions concerning the chemistry in this paper. This research was supported financially by the National Natural Science Foundation of China (No. 90713045).

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