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5-Hydroxyindoles by Intramolecular Alkynol–Furan Diels–Alder Cycloaddition

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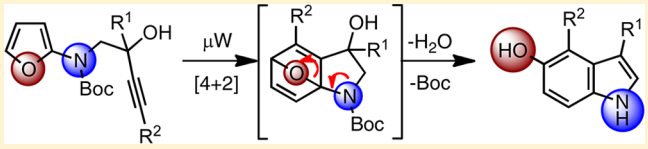
Supporting Information

ABSTRACT: A convergent approach provides a convenient access to synthetically and biologically useful 3,4-disubstituted 5-hydroxyindoles. The one-pot procedure uses microwave heating to initiate an intramolecular [4 + 2]-cycloaddition of an alkynol segment onto a furan followed by a fragmentation, aromatization, and *N*-Boc deprotection cascade. Yields range from 15 to 74%, with aromatic substituents providing better conversions. 4-Trimethylsilylated analogues undergo a 1,3-silatropic rearrangement to give the *O*-TMS ethers.



INTRODUCTION

Second only to pyridines, indoles are among the most common aromatic scaffolds present in bioactive molecules.[1] The 5-hydroxyindole moiety alone currently has >15000 substructure hits from >140000 literature references in SciFinder. In addition to their prominence in the neurotransmitter serotonin and its many analogues, 5-hydroxyindoles are found in a vast array of pharmacologically active agents and natural products (Figure 1). Furthermore, the hydroxy group can be readily converted to derivatives that allow scaffold extensions, cross-coupling or nucleophilic addition reactions of the indole nucleus.[2]

The Nenitzescu reaction is frequently used for the construction of 5-hydroxyindoles.[3] Alternative protocols include the coumarin–indole transformation[4] and the Pd-catalyzed coupling of 2-iodoanilines with alkynes (Scheme 1).[5] All of these protocols start with a functionalized 6-membered ring, and add the pyrrole moiety in a linear sequence. We have recently reported an alternative strategy for a convergent indole synthesis that uses an intramolecular Diels–Alder furan (IMDAF) cycloaddition to assemble both benzene and pyrrole moieties simultaneously.[6,7] We are now reporting an extension of this procedure to the direct preparation of 5-hydroxyindoles.

In our previous reaction sequence,[6] the 1,2-addition of lithiated **1** to enone **2** provided the allylic alcohol **3** (Scheme 2). Microwave heating of **3** led to the tricyclic IMDAF product **4** and subsequently through sequential elimination of 2 equiv of water via **5** and **6** to indoles **7**. We reasoned that the use of an alkynone in place of the enone would give us the opportunity to branch out from this reaction pathway, eliminate the bridging oxygen atom in **4** to give **8**, aromatize the intermediate at an earlier stage to give phenol **9**, and finally only eliminate a single molecule of water and, concomitantly, the *N*-protective group[8] to yield 5-hydroxyindole **10**.

RESULTS AND DISCUSSION

The hypothesis that an alkynyl intermediate **3** would lead to the formation of 5-hydroxyindole **10** was readily tested. Furanylstannane **13** was prepared from iodide **11**[9] and *N*-Boc-2-aminofuran **12**[10] in the presence of NaH (Scheme 3). Stannane **13** underwent a rapid transmetalation (5 min) to **1** with *n*-BuLi at −78 °C, and after the addition of 1 equiv of 1,3-diphenylprop-2-yn-1-one **14a**, the tertiary alcohol **15a** was isolated in 57% yield. Microwave heating to 220 °C for 1 h effected the desired IMDAF process and aromatization to give 5-hydroxyindole **16a** in 74% yield after chromatographic purification of the reaction mixture on SiO_2. The Boc group was cleaved off under the thermal conditions.[8] Interestingly, the ethoxycarbonyl protective group[7c] on nitrogen led to lower yields, possibly due to an *N*→*O* acyl shift in intermediate **3**.

In order to further investigate the scope of this new process, we converted commercially available carbonyl compounds into ynones **14b–e** according to literature protocols.[11,12] The lithium reagent derived from stannane **13** was then added to these ynones to give the corresponding alkynols **15b–e** in unoptimized 44–52% yield. As shown in Table 1, microwave irradiation of **15b–e** in *o*-dichlorobenzene for 1 h produced the expected 5-hydroxyindoles **16b–e** in moderate (36%) to good (63%) yields.

The reaction tolerated both aromatic and heteroaromatic groups (i.e., phenyl, **16a**, and thiophene, **16b**) as well as branched and cyclic aliphatic substituents (i.e., *n*-hexyl, **16c**, phenethyl, **16d**, and *c*-hexyl, **16e**) at the R^1 position. We explored fewer variations of the R^2 groups, but as the *n*-butyl derivative **16e** demonstrated, aliphatic groups appear to be acceptable substituents at R^2. The lowest yield, 36%, was

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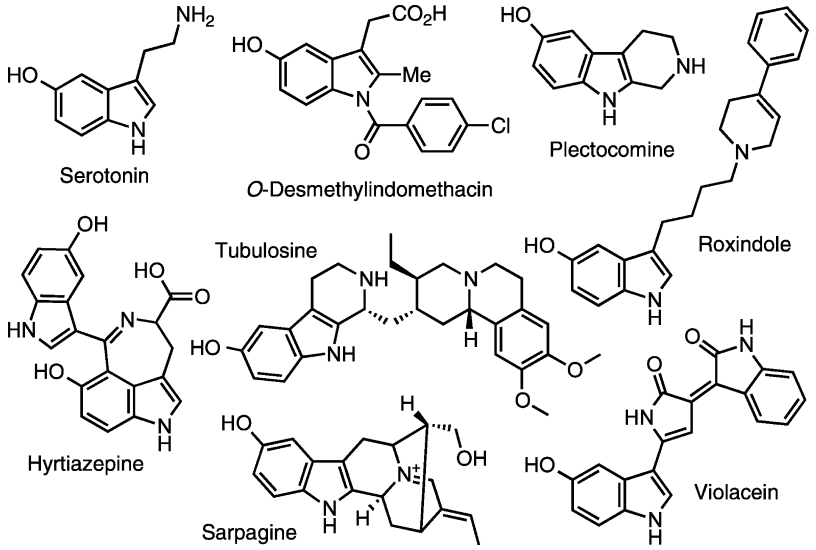
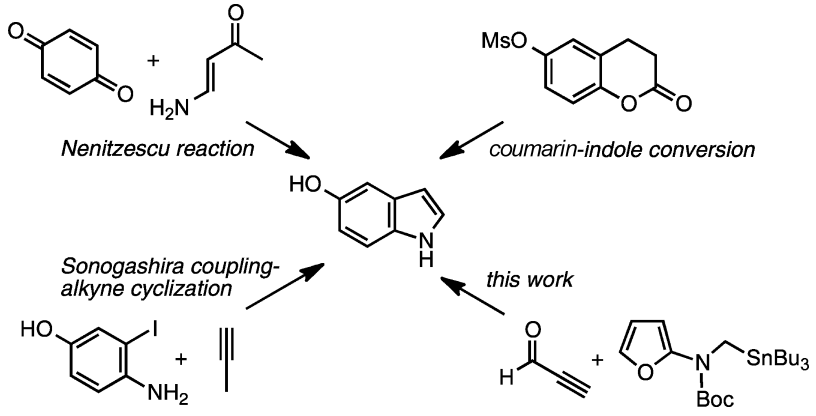


Figure 1. Representative biologically active 5-hydroxyindoles.

Scheme 1. Methods for Formation of 5-Hydroxyindoles



obtained with R^1 and R^2 both being aliphatic residues, which could indicate that either indole stabilization through conjugative substituents at R^1 and R^2 or the presence of sterically bulky groups such as phenyl rings promotes product formation. Therefore, we tested silylated alkynes derived from silyl ketones as substrates that provide steric shielding in the absence of π-electron resonance effects.

When the four trimethylsilyl (TMS) alkynols **15f–i**[13] were subjected to the microwave-mediated cycloaddition conditions at 180 °C, the cycloaddition occurred smoothly and provided indole products in good yields (Scheme 4 and Table 2). However, rather than the expected 4-trimethylsilyl derivatives **16′f–i**, a mixture of 5-(trimethylsilyloxy)indoles **17f–i** and the corresponding 5-hydroxyindoles **16f–i** was isolated. Presumably, the TMS-ethers result from a 1,3-silatropic C to O rearrangement,[14] induced by the thermal conditions and rendered quantitative by the strong O–Si bond. In order to generate a homogeneous product fraction, the crude reaction mixtures were treated with 2% HCl in MeOH to desilylate **17f–i** and cleanly afford the 5-hydroxyindole products **16f–i**.[15]

As a further test of this methodology, the reaction sequence was extended to aldehyde substrates, and the secondary alkynols **15j–q** were prepared[16] in unoptimized 20–57% yields by addition of lithiated **13** to ynals **14j–q** (Scheme 5). As expected, the microwave conditions promoted cycloadditions to ultimately afford the 4-substituted 5-hydroxyindoles **16j–q**. Similar to our previous observations, aromatic substrates gave better isolated yields compared to the alkyl-substituted alkynols (Table 3).

Indoles with 4-aryl residues **16j–n** were isolated in 42–64% yield, and no obvious trend for electron-withdrawing or -donating substituents was observed. The two alkyl-chain containing products **16o** and **16p** were formed in low (15–20%) yields, and the 3-chloropropyl analogue **16p** partially cyclized and produced an additional 7% of the corresponding pyran **18**. The cyclized ether[17] could also be obtained in 53% yield by treatment of isolated **16p** with NaH in THF. Finally, the cyclohexene derivative **15q** led to the introduction of a 4-alkene group in **16q**, but the yield (23%) was similarly low as observed for aliphatic substrates. Nonetheless, this methodology allows for the rapid introduction of a diverse range of substituents at carbons 3 and 4 of the 5-hydroxyindole scaffold.

■ CONCLUSION

The use of alkynones and alkynals as starting materials extends our microwave-assisted IMDAF-aromatization cascade reaction to the direct formation of synthetically and biologically valuable 5-hydroxyindoles. The requisite substituted alkynes are readily available, and the methodology represents an unusual convergent formation of both the benzene and the pyrrole

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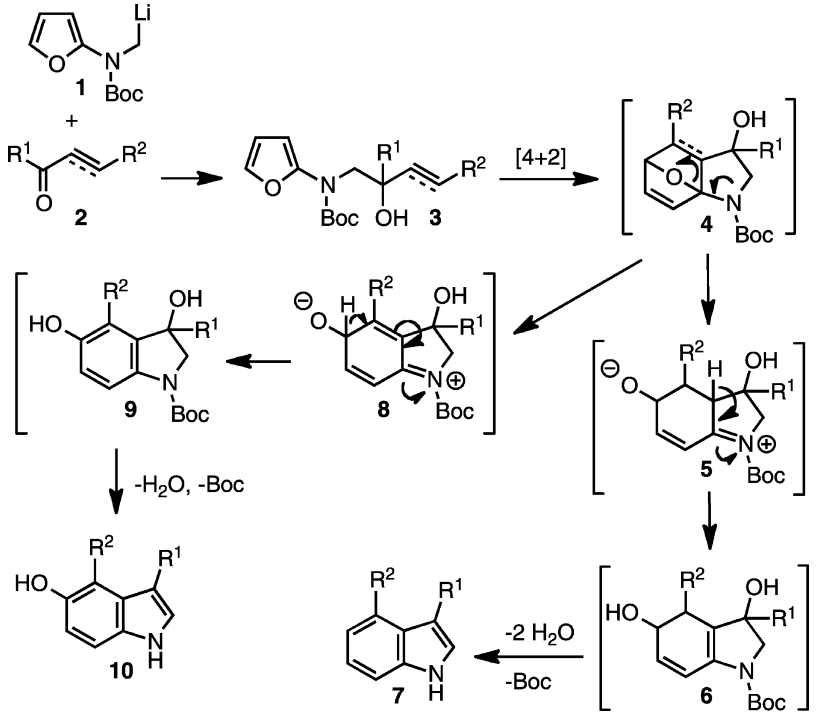
Scheme 2. Proposed Reaction Pathways for Indole and 5-Hydroxyindole Formation by Intramolecular Diels–Alder Reaction with Furans



Scheme 3. Formation of Propargyl Alcohol and Thermal Cycloaddition Reaction

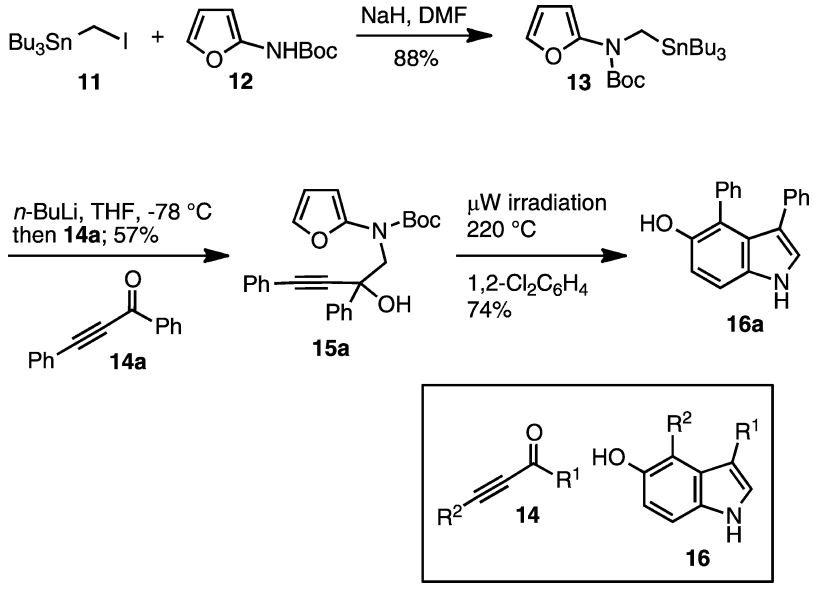


Table 1. Synthesis of 5-Hydroxyindoles 16b–e from Tertiary Alkynols 15b–e

entry	15	% yield[a]	R^1	R^2	16	% yield[b]
1	**b**	52	2-thiophene-yl	Ph	**b**	61
2	**c**	44	*n*-hexyl	Ph	**c**	58
3	**d**	47	CH_2CH_2Ph	Ph	**d**	63
4	**e**	49	*c*-hexyl	*n*-butyl	**e**	36

[a]Yields of isolated alkynols **15**. [b]Yields of isolated indoles **16**.

subunits of the indole ring system. Yields range from 15 to 74%, and the efficiency of the conversion benefits from aromatic substituents that can stabilize the charged and/or reactive intermediates **4**, **8**, and **9** in the cascade indole formation process. We also observed an interesting 1,3-silatropic rearrangement of the putative 4-silylated intermediates **16′**. Overall, due to the straightforward access to ynones and ynals, the convergent nature of the retrosynthetic disconnection, and the convenient thermal reaction conditions, this new reaction provides a significant alternative to other common methods for 5-hydroxyindole construction, especially for projects where a diverse range of 3- and 4-substitutions is desired.

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Scheme 4. Formation of 3-Substituted 5-Hydroxyindoles from Silylated Alkynones

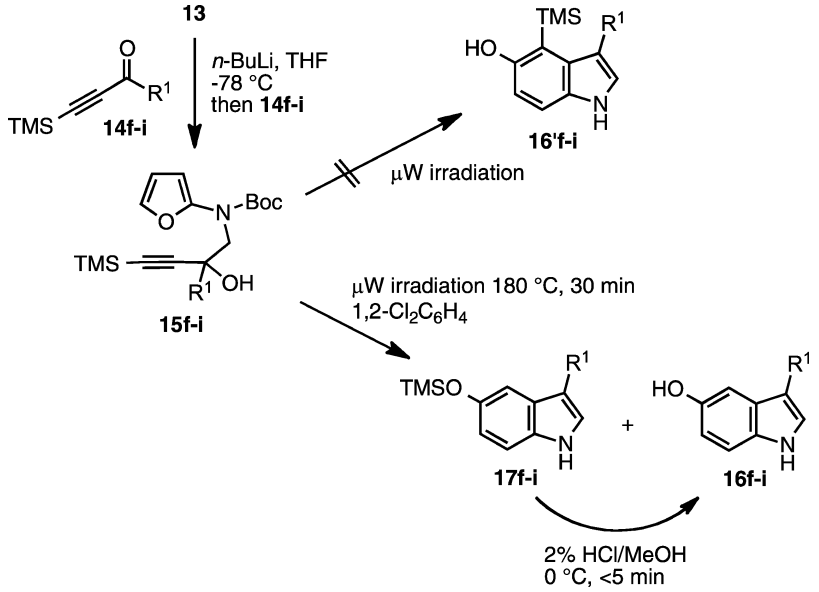


Table 2. Synthesis of 5-Hydroxyindoles 16f–i from Tertiary Alkynols 15f–i

entry	15	% yield[a]	R^1	16	% yield[b]
1	f	58	Ph	f	63
2	g	60	2-naphthyl	g	60
3	h	58	2-benzofuryl	h	63
4	i	52	*c*-propyl	i	47

[a]Yields of isolated alkynols **15**. [b]Yields of isolated indoles **16**.

Table 3. Synthesis of 5-Hydroxy Indoles 16j–q from Secondary Alkynols 15j–q

entry	15	% yield[a]	R^2	16	% yield[b]
1	j	43	Ph	j	48
2	k	57	3-OMePh	k	42
3	l	52	4-MePh	l	47
4	m	26	4-CF_3Ph	m	64
5	n	20	4-F-Ph	n	44
6	o	54	$(CH_2)_2CH(CH_3)_2$	o	15
7	p	52	$(CH_2)_3Cl$	p	20[c]
8	q	38	1-cyclohexene	q	23

[a]Yields of isolated alkynols **15**. [b]Yields of isolated indoles **16**. [c]The pyran-containing indole product **18**[17] was also isolated in 7% yield (see the Supporting Information).

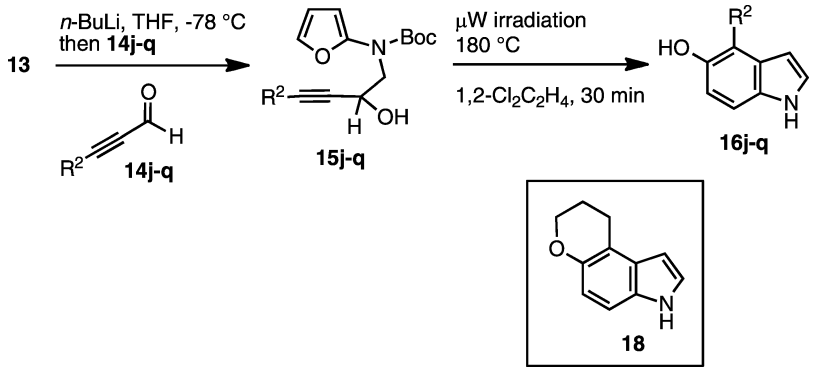
EXPERIMENTAL SECTION

General Information. Microwave reactions were performed at 200–250 W using a Biotage Initiator. Ketones **14a** and **14b** are commercially available and were used without further purification. Ketones **14c**,[11,18] **14d**,[11,19] **14e**,[12,20] **14f**,[21,22] **14g**,[21,23] **14h**,[21] and **14i**,[21,24] and aldehydes **14j**,[25] **14k**,[11,26] **14l**,[11,27] **14m**,[11,28] **14n**,[11,29] **14o**,[25] **14p**,[25,30] and **14q**[25,31] were prepared according to literature procedures.

*1-(Benzofuran-2-yl)-3-(trimethylsilyl)prop-2-yn-1-one (**14h**).* According to a literature protocol,[21] **14h** was obtained as a yellow oil (2.50 g, 84%): IR (neat) 2963, 2158, 1630, 1548 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.94 (s, 1 H), 7.88 (d, J = 7.6 Hz, 1 H), 7.66 (d, J = 8.5 Hz, 1 H), 7.60 (ddd, J = 1.2, 7.0, 7.0 Hz, 1 H), 7.40 (ddd, J = 0.9, 8.0, 8.0 Hz, 1 H), 0.34 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 165.9, 157.3, 154.0, 130.3, 127.9, 125.3, 124.9, 118.9, 113.2, 101.1, 99.7, −0.78; HRMS (TOF APCI+) m/z calcd for $C_{14}H_{15}O_2Si$ (M + H) 243.0841, found 243.0865.

General Protocol A. *tert-Butyl Furan-2-yl(2-hydroxy-2,4-diphenylbut-3-ynyl)carbamate (**15a**).* A flame-dried 25-mL round-bottom flask was charged with a solution of furanylstannane **13** (0.608 g, 1.25 mmol) in dry THF (4 mL). The solution was cooled to −78 °C and treated with BuLi (1.0 mL, 1.6 M in hexanes) using a syringe pump over 10 min. The reaction mixture was then treated with alkyne **14a** (0.253 g, 1.23 mmol) in THF (4 mL) via syringe pump over 10 min. After 1 h, the orange solution was diluted with satd NH_4Cl, extracted

Scheme 5. Formation of 4-Substituted 5-Hydroxyindoles from Alkynals



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with EtOAc, washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (ISCO-Companion, 0−100% EtOAc/hexanes, 25 min gradient) to give alcohol **15a** (0.29 g, 0.72 mmol, 57%) as a yellow oil: IR (neat) 3395, 2982, 1713, 1681 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.73 (d, J = 7.2 Hz, 2 H), 7.44−7.28 (m, 8 H), 7.24 (dd, J = 1.0, 2.2 Hz, 1 H), 6.32 (dd, J = 2.4, 3.2 Hz, 1 H), 6.02 (br s, 1 H), 5.39 (br s, 1 H), 4.16−4.04 (m, 2 H), 4.07 (d, J = 14.2 Hz, 1 H), 1.29 (s, 9 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 150.0, 144.2, 138.9, 132.6, 129.4, 129.3, 128.8, 128.5, 127.1, 123.8, 111.7, 91.9, 86.4, 81.7, 73.8, 60.8, 28.2; HRMS (TOF ES+) m/z calcd for $C_{25}H_{25}NO_4Na$ (M + Na) 426.1681, found 426.1698.

*tert-Butyl Furan-2-yl(2-hydroxy-4-phenyl-2-(thiophen-2-yl)but-3-ynyl)carbamate (**15b**).* According to general protocol A, **15b** was obtained as a yellow oil (0.350 g, 52%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3384, 2982, 2918, 1713, 1681 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.46−7.37 (m, 6 H), 7.27−7.25 (m, 2 H), 7.01 (dd, J = 3.6, 4.4 Hz, 1 H), 6.34 (dd, J = 2.4, 3.2 Hz, 1 H), 6.08 (br s, 1 H), 5.78 (br s, 1 H), 4.20 (s, 2 H), 1.35 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.8, 149.1, 138.9, 132.6, 132.4, 129.5, 129.3, 127.5, 126.1, 125.7, 123.5, 111.8, 91.2, 86.0, 81.8, 60.8, 28.2; HRMS (TOF ES+) m/z calcd for $C_{23}H_{23}NO_4SNa$ (M + Na) 432.1245, found 432.1281.

*tert-Butyl Furan-2-yl(2-hydroxy-2-(phenylethynyl)octyl)carbamate (**15c**).* According to general protocol A, **15c** was obtained as a yellow oil (0.225 g, 44%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3422, 2956, 2931, 2855, 1718, 1686, 1591 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.34−7.32 (m, 5 H), 7.27 (br s, 1 H), 6.35 (s, 1 H), 6.14 (s, 1 H), 4.53 (br s, 1 H), 3.91 (s, 2 H), 1.72−1.51 (m, 4 H), 1.39 (s, 9 H), 1.29 (br s, 6 H), 0.87 (t, J = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 150.2, 139.0, 132.5, 129.2, 129.1, 124.1, 111.8, 102.9, 92.2, 85.4, 81.8, 72.1, 58.5, 40.8, 32.6, 28.3, 24.9, 23.3, 14.4; HRMS (TOF ES+) m/z calcd for $C_{25}H_{33}NO_4Na$ (M + Na) 434.2307, found 434.2281.

*tert-Butyl Furan-2-yl(2-hydroxy-2-phenethyl-4-phenylbut-3-ynyl)carbamate (**15d**).* According to general protocol A, **15d** was obtained as a yellow oil (0.310 g, 47%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3409, 3054, 2976, 2928, 1712, 1591 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.43−7.16 (m, 11 H), 6.37 (dd, J = 2.0, 3.2 Hz, 1 H), 6.17 (dd, J = 0.8, 3.2 Hz, 1 H), 4.78 (br s, 1 H), 4.01 (s, 2 H), 3.00−2.85 (m, 2 H), 2.06−1.99 (m, 2 H), 1.40 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 150.2, 143.3, 139.1, 132.6, 129.3, 129.23, 129.20, 126.6, 124.0, 111.8, 103.0, 91.8, 85.8, 81.8, 71.8, 58.3, 42.9, 31.4, 28.3; HRMS (TOF ES+) m/z calcd for $C_{27}H_{29}NO_4Na$ (M + Na) 454.1994, found 454.2024.

*tert-Butyl 2-Cyclohexyl-2-hydroxyoct-3-ynyl(furan-2-yl)carbamate (**15e**).* According to general protocol A, **15e** was obtained as a yellow oil (0.438 g, 49%, SiO_2, EtOAc/hexanes, 1:9): IR (neat) 3422, 3285, 2931, 2855, 1694, 1590 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.31 (dd, J = 0.8, 1.6 Hz, 1 H), 6.39 (dd, J = 2.4, 3.2 Hz, 1 H), 6.13 (dd, J = 0.8, 3.2 Hz, 1 H), 4.15 (br s, 1 H), 3.89 (d, J = 14.4 Hz, 1 H), 3.79 (d, J = 14.4 Hz, 1 H), 2.16 (app t, J = 6.8 Hz, 2 H), 2.03−2.01 (m, 1 H), 1.75−1.63 (m, 4 H), 1.49−1.44 (m, 13 H), 1.22−1.13 (m, 6 H), 0.91 (t, J = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 150.3, 139.0, 111.9, 111.7, 102.8, 86.3, 81.8, 81.7, 74.7, 57.1, 46.4, 31.7, 28.8, 28.4, 28.3, 27.5, 27.3, 27.1, 27.0, 22.6, 18.9, 13.9; HRMS (EI) m/z calcd for $C_{23}H_{35}NO_4Na$ (M + Na) 412.2464, found 412.2472.

*tert-Butyl Furan-2-yl(2-hydroxy-2-phenyl-4-(trimethylsilyl)but-3-ynyl)carbamate (**15f**).* According to general protocol A, **15f** was obtained as a yellow oil (0.335 g, 58%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3390, 2956, 2918, 1713, 1681 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.66 (d, J = 7.2 Hz, 2 H), 7.34 (dd, J = 6.8, 7.2 Hz, 2 H), 7.29−7.26 (m, 2 H), 6.34 (s, 1 H), 5.96 (br s, 1 H), 5.34 (br s, 1 H), 4.00 (s, 2 H), 1.30 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.8, 143.8, 138.7, 128.6, 128.4, 127.1, 111.7, 108.2, 102.7, 90.3, 81.7, 73.5, 60.8, 28.2, 0.09; HRMS (TOF ES+) m/z calcd for $C_{22}H_{29}NO_4SiNa$ (M + Na) 422.1764, found 422.1778.

*tert-Butyl Furan-2-yl(2-hydroxy-2-(naphthalen-2-yl)-4-(trimethylsilyl)but-3-ynyl)carbamate (**15g**).* According to general protocol A, **15g** was obtained as a yellow oil (0.413 g, 60%, SiO_2, EtOAc/hexanes, 1:9): IR (neat) 3395, 2956, 2140, 1718, 1681 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, J = 1.5 Hz, 1 H), 7.90−7.83 (m, 3 H), 7.72 (dd, J = 1.8, 8.7 Hz, 1 H), 7.52−7.49 (m, 2 H), 7.13 (br s, 1 H), 6.26 (br s, 1 H), 5.78 (br s, 1 H), 4.09 (s, 2 H), 1.41 (s, 9 H), 0.22 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 148.9, 140.4, 137.8, 133.1, 133.0, 128.2, 127.5, 127.4, 126.03, 125.99, 125.0, 124.6, 110.8, 107.3, 101.9, 89.8, 80.8, 72.7, 59.6, 27.2, −0.74; HRMS (TOF ES+) m/z calcd for $C_{26}H_{31}NO_4SiNa$ (M + Na) 472.1920, found 472.1915.

*tert-Butyl 2-(Benzofuran-2-yl)-2-hydroxy-4-(trimethylsilyl)but-3-ynyl(furan-2-yl)carbamate (**15h**).* According to general protocol A, **15h** was obtained as a yellow oil (0.151 g, 58%, SiO_2, ISCO-Companion, 0−100% EtOAc/hexanes, 15 min gradient): IR (neat) 3377, 2969, 1718, 1681 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 7.59 (d, J = 7.6 Hz, 1 H), 7.44 (d, J = 8.0 Hz, 1 H), 7.28 (ddd, J = 1.2, 7.2, 7.2 Hz, 1 H), 7.26−7.21 (m, 1 H), 7.16 (dd, J = 0.8, 1.6 Hz, 1 H), 6.89 (d, J = 0.8 Hz, 1 H), 6.22 (br s, 1 H), 5.94 (br s, 1 H), 5.64 (br s, 1 H), 4.25 (s, 2 H), 1.27 (s, 9 H), 0.17 (s, 9 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 158.0, 156.0, 149.3, 138.7, 129.0, 125.1, 123.6, 122.0, 112.0, 111.5, 105.3, 105.2, 103.0, 90.8, 81.7, 69.6, 57.4, 28.1, −0.06; HRMS (TOF ES+) m/z calcd for $C_{24}H_{29}NO_5SiNa$ (M + Na) 462.1713, found 462.1749.

*tert-Butyl 2-Cyclopropyl-2-hydroxy-4-(trimethylsilyl)but-3-ynyl-(furan-2-yl)carbamate (**15i**).* According to general protocol A, **15i** was obtained as a yellow oil (0.139 g, 52%, SiO_2, ISCO-Companion, 0−100% EtOAc/hexanes, 15 min gradient): IR (neat) 3427, 2974, 1718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, J = 1.2, 2.0 Hz 1 H), 6.33 (dd, J = 2.4, 3.6 Hz, 1 H), 6.06 (br s, 1 H), 3.96 (br s, 2 H), 1.45 (s, 9 H), 1.15−1.08 (m, 1 H), 0.71−0.66 (m, 1 H), 0.49−0.45 (m, 3 H), 0.12 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.1, 148.9, 137.9, 110.9, 103.6, 101.7, 89.8, 82.2, 73.4, 59.0, 28.1, 18.2, 1.58, 1.35, −0.14; HRMS (TOF ES+) m/z calcd for $C_{19}H_{29}NO_4SiNa$ (M + Na) 386.1764, found 386.1757.

*tert-Butyl Furan-2-yl(2-hydroxy-4-phenylbut-3-ynyl)carbamate (**15j**).* According to general protocol A, **15j** was obtained as a yellow oil (0.210 g, 43%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3422, 2974, 2931, 1705, 1625 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.44−7.42 (m, 2 H), 7.32−7.26 (m, 3 H), 7.22 (s, 1 H), 6.37 (s, 1 H), 6.11 (br s, 1 H), 4.86−4.83 (m, 1 H), 4.00 (dd, J = 8.0, 14.4 Hz, 1 H), 3.88 (dd, J = 3.6, 14.4 Hz, 1 H), 1.47 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 138.3, 134.8, 131.7, 128.4, 128.2, 122.3, 111.0, 101.8, 87.3, 82.1, 62.3, 54.8, 28.0; HRMS (EI) m/z calcd for $C_{19}H_{21}NO_4Na$ (M + Na) 350.13968, found 350.1361.

*tert-Butyl Furan-2-yl(2-hydroxy-4-(3-methoxyphenyl)but-3-ynyl)-carbamate (**15k**).* According to general protocol A, **15k** was obtained as a yellow oil (0.250 g, 57%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3459, 2982, 1712, 1599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22 (app t, J = 8.4 Hz, 2 H), 7.02 (d, J = 7.6 Hz, 1 H), 6.96 (s, 1 H), 6.89 (dd, J = 2.4, 8.4 Hz, 1 H), 6.37 (app t, J = 2.8 Hz, 1 H), 6.11 (br s, 1 H), 4.84 (dd, J = 4.0, 7.6 Hz, 1 H), 4.00 (dd, J = 8.0, 14.4 Hz, 1 H), 3.88 (dd, J = 4.0, 14.4 Hz, 1 H), 3.80 (s, 3 H), 1.47 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 160.5, 149.8, 139.2, 130.4, 124.8, 117.3, 115.7, 111.8, 89.8, 85.4, 81.6, 61.5, 55.7, 55.0, 28.3; HRMS (TOF ES+) m/z calcd for $C_{20}H_{23}NO_5Na$ (M + Na) 380.1474, found 380.1477.

*tert-Butyl Furan-2-yl(2-hydroxy-4-(p-tolyl)but-3-yn-1-yl)-carbamate (**15l**).* According to general protocol A, **15l** was obtained as a yellow oil (0.144 g, 52%, SiO_2, EtOAc/hexanes, 1:15): ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0 Hz, 2 H), 7.19 (dd, J = 0.8, 2.0 Hz, 1 H), 7.10 (d, J = 7.6 Hz, 2 H), 6.34 (dd, J = 2.0, 3.2 Hz, 1 H), 6.08 (br s, 1 H), 4.83−4.78 (m, 1 H), 3.97 (dd, J = 8.0, 14.4 Hz, 1 H), 3.85 (dd, J = 4.0, 14.4 Hz, 1 H), 2.34 (s, 3 H), 1.61 (br s, 1 H), 1.45 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.0, 148.2, 138.4, 138.2, 131.6, 128.9, 119.3, 110.9, 101.8, 86.9, 85.8, 81.9, 62.0, 54.7, 28.0, 21.3; HRMS (TOF ES+) m/z calcd for $C_{20}H_{23}NO_4Na$ (M + Na) 364.1525, found 364.1494.

*tert-Butyl Furan-2-yl(2-hydroxy-4-(4-(trifluoromethyl)phenyl)but-3-yn-1-yl)carbamate (**15m**).* According to general protocol A, **15m** was obtained as a yellow oil (0.067 g, 26%, SiO_2, EtOAc/hexanes, 1:15): ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 8.5 Hz, 2 H), 7.49 (d, J = 8.5 Hz, 2 H), 7.18 (dd, J = 1.0, 2.0 Hz, 1 H), 6.34 (dd, J = 2.0,

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3.0 Hz, 1 H), 6.07 (br s, 1 H), 4.84 (dd, J = 4.0, 8.0 Hz, 1 H), 3.98 (dd, J = 8.0, 14.5 Hz, 1 H), 3.89 (dd, J = 4.0, 14.5 Hz, 1 H), 1.44 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 138.4, 132.0, 130.2 (q, J = 32.5 Hz), 126.2, 125.2 (q, J = 3.8 Hz), 123.8 (d, J = 270.5 Hz), 111.1, 101.8, 90.1, 84.4, 82.2, 62.2, 60.4, 54.6, 28.1; HRMS (TOF ES+) m/z calcd for $C_{20}H_{21}F_3NO_4$ (M + H) 396.1423, found 396.1404.

*tert-Butyl (4-(4-Fluorophenyl)-2-hydroxybut-3-yn-1-yl)(furan-2-yl)carbamate (**15n**).* According to general protocol A, **15n** was obtained as a yellow oil (0.042 g, 20%, SiO_2, EtOAc/hexanes, 1:15): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.36 (m, 2 H), 7.19 (dd, J = 0.8, 2.0 Hz, 1 H), 7.02−6.96 (m, 2 H), 6.34 (dd, J = 2.0, 4.0 Hz, 1 H), 6.07 (br s, 1 H), 4.80 (dd, J = 4.0, 8.0 Hz, 1 H), 3.97 (dd, J = 8.0, 14.4 Hz, 1 H), 3.86 (dd, J = 4.0, 14.4 Hz, 1 H), 3.25−3.21 (m, 1 H), 1.45 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6 (d, J = 248.8 Hz), 148.2, 138.4, 133.7 (d, J = 8.8 Hz), 118.4, 115.5 (d, J = 21.2 Hz), 111.0, 101.8, 87.1, 84.8, 82.2, 62.3, 54.8, 28.1; HRMS (TOF ES+) m/z calcd for $C_{19}H_{20}FNO_4Na$ (M + Na) 368.1274, found 368.1258.

*tert-Butyl Furan-2-yl(2-hydroxy-7-methyloct-3-ynyl)carbamate (**15o**).* According to general protocol A, **15o** was obtained as a yellow oil (0.073 g, 54%, SiO_2, ISCO-Companion, 0−100% EtOAc/hexanes, 20 min gradient): IR (neat) 3429, 2933, 2881, 1714 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.29 (d, J = 1.2 Hz, 1 H), 6.38 (dd, J = 2.0, 3.2 Hz, 1 H), 6.10 (d, J = 2.8 Hz, 1 H), 4.50−4.41 (m, 2 H), 3.68 (d, J = 6.4 Hz, 2 H), 2.19 (ddd, J = 2.0, 7.2, 7.2 Hz, 2 H), 1.67 (sept, J = 6.8 Hz, 1 H), 1.42 (s, 9 H), 1.36 (d, J = 7.2 Hz, 1 H), 1.33 (d, J = 7.2 Hz, 1 H), 0.87 (d, J = 6.4 Hz, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.9, 139.1, 111.8, 102.6, 85.9, 81.4, 80.7, 61.2, 55.5, 38.4, 28.3, 27.8, 22.5, 17.2; HRMS (TOF ES+) m/z calcd for $C_{18}H_{27}NO_4Na$ (M + Na) 344.1838, found 344.1830.

*tert-Butyl 7-Chloro-2-hydroxyhept-3-ynyl(furan-2-yl)carbamate (**15p**).* According to general protocol A, **15p** was obtained as a yellow oil (0.089 g, 52%, SiO_2, ISCO-Companion, 0−100% EtOAc/hexanes, 15 min gradient): IR (neat) 3440, 2969, 1705, 1617 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (s, 1 H), 6.35 (app t, J = 2.4 Hz, 1 H), 6.05 (br s, 1 H), 4.58−4.55 (m, 1 H), 3.84 (dd, J = 8.4, 14.4 Hz, 1 H), 3.73 (dd, J = 4.4, 14.4 Hz, 1 H), 3.62 (t, J = 6.4 Hz, 2 H), 2.38 (ddd, J = 2.0, 6.8, 6.8 Hz, 2 H), 1.94 (ddd, J = 6.8, 6.8, 13.2 Hz, 2 H), 1.45 (s, 9 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 149.8, 111.8, 84.2, 81.7, 81.5, 61.1, 55.3, 44.5, 32.3, 28.3, 16.6; HRMS (TOF ES+) m/z calcd for $C_{16}H_{22}ClNO_4Na$ (M + Na) 350.1135, found 350.1100.

*tert-Butyl 4-Cyclohexenyl-2-hydroxybut-3-ynyl(furan-2-yl)-carbamate (**15q**).* According to general protocol A, **15q** was obtained as a yellow oil (0.313 g, 38%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3435, 2982, 1705, 1612 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (dd, J = 0.8, 2.0 Hz, 1 H), 6.32 (dd, J = 2.4, 3.2 Hz, 1 H), 6.08−6.05 (m, 2 H), 4.69−4.65 (m, 1 H), 3.87 (dd, J = 8.0, 14.4 Hz, 1 H), 3.73 (dd, J = 8.0, 14.4 Hz, 1 H), 2.07−2.04 (m, 4 H), 1.62−1.52 (m, 4 H), 1.43 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 138.3, 135.6, 119.9, 110.9, 101.7, 84.6, 81.9, 62.1, 54.8, 28.9, 28.0, 25.5, 22.1, 21.4; HRMS (TOF ES+) m/z calcd for $C_{19}H_{25}NO_4Na$ (M + Na) 354.1681, found 354.1674.

General Protocol B. *3,4-Diphenyl-1H-indol-5-ol (**16a**).* A solution of alcohol **15a** (0.087 g, 0.21 mmol) in o-DCB (2.1 mL) was subjected to microwave irradiation at 220 °C for 60 min. The crude solution was purified by chromatography on SiO_2 (0−20%, EtOAc/hexanes) to give indole **16a** (0.046 g, 74%) as a light brown solid: mp 184−185 °C; IR (neat) 3504, 3403, 3054, 1599 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.32 (br s, 1 H), 7.37 (d, J = 8.8 H, 1 H), 7.28 (d, J = 2.8 Hz, 1 H), 7.12−7.10 (m, 2 H), 7.08 (s, 1 H), 7.03−6.99 (m, 3 H), 6.96−6.82 (m, 6 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 148.0, 137.2, 132.9, 131.5, 129.5, 127.7, 127.4, 126.5, 125.6, 125.3, 124.9, 119.5, 119.0, 112.9, 112.0; HRMS (TOF APCI+) m/z calcd for $C_{20}H_{16}NO$ 286.1232 (M + H), found 286.1226.

*4-Phenyl-3-(thiophene-2-yl)-1H-indol-5-ol (**16b**).* According to general protocol B, **16b** was obtained as a brown solid (0.057 g, 61%, SiO_2, EtOAc/hexanes, 1:6): mp 166−167 °C; IR (neat) 3528, 3390, 3067, 1574 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 10.42 (br s, 1 H), 7.37 (d, J = 8.8 Hz, 1 H), 7.36 (s, 1 H), 7.19−7.16 (m, 2 H), 7.13−7.09 (m, 4 H), 7.01 (dd, J = 1.2, 5.2 Hz, 1 H), 6.95 (d, J = 8.8 Hz, 1 H), 6.55 (dd, J = 3.6, 5.2 Hz, 1 H), 6.04 (dd, J = 1.2, 3.6 Hz, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 148.5, 138.7, 137.3, 132.9, 131.5, 128.0, 127.2, 127.1, 126.9, 126.6, 125.8, 123.7, 120.0, 113.4, 112.4, 111.0; HRMS (TOF ES+) m/z calcd for $C_{18}H_{13}NOSK$ (M + K) 330.0355, found 330.0370.

*3-Hexyl-4-phenyl-1H-indol-5-ol (**16c**).* According to general protocol B, **16c** was obtained as a brown oil (0.054 g, 58%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3535, 3472, 3403, 1725, 1591 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 9.76 (br s, 1 H), 7.44−7.32 (m, 5 H), 7.21 (d, J = 8.4 Hz, 1 H), 6.99 (d, J = 2.4 Hz, 1 H), 6.80 (d, J = 8.0 Hz, 2 H), 2.09−2.03 (m, 2 H), 1.21−1.01 (m, 6 H), 0.97−0.89 (m, 2 H), 0.81 (t, J = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 146.4, 137.4, 131.8, 130.7, 127.1, 126.2, 125.6, 123.0, 118.8, 115.8, 111.0, 110.6, 31.1, 30.8, 26.2, 22.0, 13.1; HRMS (TOF ES+) m/z calcd for $C_{20}H_{24}NO$ (M + H) 294.1858, found 294.1841.

*3-Phenethyl-4-phenyl-1H-indol-5-ol (**16d**).* According to general protocol B, **16d** was obtained as a brown solid (0.063 g, 63%, SiO_2, EtOAc/hexanes, 1:6): mp 102−103 °C; IR (neat) 3528, 3409, 3067, 3054, 1559 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 9.87 (br s, 1 H), 7.49−7.40 (m, 5 H), 7.27 (d, J = 8.4 Hz, 1 H), 7.18−7.14 (m, 2 H), 7.10−7.06 (m, 2 H), 6.92 (s, 1 H), 6.87 (d, J = 8.4 Hz, 1 H), 6.83−6.81 (m, 2 H), 2.49−2.37 (m, 4 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 147.6, 143.1, 138.6, 132.9, 131.8, 128.8, 128.5, 128.4, 127.4, 126.4, 125.9, 124.7, 119.7, 116.0, 112.1, 111.7, 38.6; HRMS (EI) m/z calcd for $C_{22}H_{19}NO$ (M^+) 313.1467, found 313.1464.

*4-Butyl-3-cyclohexyl-1H-indol-5-ol (**16e**).* According to general protocol B, **16e** was obtained as a brown oil (0.050 g, 36%, SiO_2, 0−10%, EtOAc/hexanes): IR (neat) 3395, 1681 cm^{-1}; ^{1}H NMR (400 MHz, acetone-d_6) δ 9.64 (br s, 1 H), 7.26 (s, 1 H), 7.02 (d, J = 2.4 Hz, 1 H), 7.00 (d, J = 8.4 Hz, 1 H), 6.69 (d, J = 8.4 Hz, 1 H), 3.00−2.87 (m, 4 H), 2.07−2.04 (m, 3 H), 1.87−1.76 (m, 3 H), 1.64−1.58 (m, 2 H), 1.54−1.43 (m, 7 H), 1.00 (t, J = 6.8 Hz, 3 H); ^{13}C NMR δ 148.1, 132.8, 126.1, 123.1, 121.5, 119.7, 112.0, 109.5, 36.9, 36.7, 34.0, 29.0, 27.9, 27.0, 26.7, 23.7, 14.3; HRMS (EI) m/z calcd for $C_{18}H_{25}NO$ (M^+) 271.1936, found 271.1928.

General Protocol C. *3-Phenyl-1H-indol-5-ol (**16f**).*[15] A solution of alcohol **15f** (0.057 g, 0.14 mmol) in o-DCB (1.0 mL) was subjected to microwave irradiation at 180 °C for 30 min. The reaction mixture was cooled to 0 °C and treated with dry methanolic HCl (2%, 0.2 mL). After 5 min, the solution was concentrated, and the crude residue was purified by chromatography on SiO_2 (ISCO-Rf, 0−100%, EtOAc/hexanes; 12 min gradient) to give indole **16f** (0.019 g, 63%) as a light brown oil: IR (neat) 3385, 1687 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.26 (br s, 1 H), 7.76 (s, 1 H), 7.67 (dd, J = 1.2, 8.4 Hz, 2 H), 7.55 (d, J = 2.7 Hz, 1 H), 7.42 (app t, J = 7.8 Hz, 2 H), 7.38 (d, J = 2.4 Hz, 1 H), 7.32 (d, J = 8.7 Hz, 1 H), 7.25−7.19 (m, 1 H), 6.79 (dd, J = 2.4, 8.7 Hz, 1 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 152.2, 137.2, 132.7, 129.2, 127.2, 126.9, 125.7, 123.9, 116.8, 112.8, 112.5, 103.9; HRMS (TOF ES+) m/z calcd for $C_{14}H_{12}NO$ (M + H) 210.0919, found 210.0925.

*3-(Naphthalen-2-yl)-1H-indol-5-ol (**16g**).* According to general protocol C, **16g** was obtained as a brown oil (0.028 g, 60%, SiO_2, flash system, 0−100%, EtOAc/hexanes; 15 min gradient): IR (neat) 3390, 1699 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.27 (br s, 1 H), 8.12 (s, 1 H), 7.88 (d, J = 8.7 Hz, 2 H), 7.84−7.79 (m, 2 H), 7.72 (s, 1 H), 7.64 (d, J = 2.7 Hz, 1 H), 7.47−7.44 (m, 2 H), 7.41−7.35 (m, 2 H), 7.30 (d, J = 8.7 Hz, 1 H), 6.77 (dd, J = 2.4, 8.7 Hz, 1 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 152.4, 134.9, 134.8, 132.8, 132.4, 128.7, 128.2, 127.1, 126.7, 126.6, 125.5, 124.7, 124.4, 116.6, 112.9, 112.6, 104.2; HRMS (TOF ES+) m/z calcd for $C_{18}H_{13}NO$ (M^+) 259.0997, found 259.0970.

*3-(Benzofuran-2-yl)-1H-indol-5-ol (**16h**).* According to general protocol C, **16h** was obtained as a light orange solid (0.022 g, 63%, SiO_2, ISCO-Rf, 0−100%, EtOAc/hexanes; 15 min gradient): mp 169−172 °C; IR (neat) 3364, 3295, 1629 cm^{-1}; ^{1}H NMR (300 MHz, acetone-d_6) δ 10.55 (br s, 1 H), 7.94 (s, 1 H), 7.88 (d, J = 3.0 Hz, 1 H), 7.62−7.53 (m, 1 H), 7.52−7.50 (m, 2 H), 7.38 (d, J = 8.7 Hz, 1 H), 7.25−7.21 (m, 2 H), 6.95 (d, J = 1.0 Hz, 1 H), 6.86 (dd, J = 2.4, 8.7 Hz, 1 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 154.6, 154.3, 152.8, 132.3, 130.7, 126.0, 125.1, 123.4, 123.3, 120.5, 113.1, 110.8, 107.2,

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104.7, 98.6; HRMS (TOF ES+) m/z calcd for $C_{16}H_{11}NO_2$ (M^+) 249.0790, found 249.0783.

*3-Cyclopropyl-1H-indol-5-ol (**16i**).* According to general protocol C, **16i** was obtained as a light yellow oil (0.018 g, 47%, SiO_2, flash system, 0−100%, EtOAc/hexanes; 15 min gradient): IR (neat) 3435, 3364, 1581 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.56 (br s, 1 H), 7.50 (s, 1 H), 7.10 (d, J = 8.4 Hz, 1 H), 7.00 (d, J = 2.4 Hz, 1 H), 6.89 (d, J = 1.6 Hz, 1 H), 6.63 (dd, J = 2.0, 8.4 Hz, 1 H), 1.83−1.76 (m, 1 H), 0.78−0.74 (m, 2 H), 0.52−0.50 (m, 2 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 151.1, 132.3, 129.7, 122.2, 117.6, 112.2, 112.0, 103.4, 6.6, 6.0; HRMS (TOF ES+) m/z calcd for $C_{11}H_{12}NO$ (M + H) 174.0919, found 174.0913.

General Protocol D. *4-Phenyl-1H-indol-5-ol (**16j**).* A solution of alcohol **15j** (0.052 g, 0.16 mmol) in 1,2-dichloroethane (1.0 mL) was subjected to microwave irradiation at 180 °C for 30 min. The crude solution was concentrated and purified by chromatography on SiO_2 (flash system, 0−100% EtOAc/hexanes, 15 min gradient) to give **16j** as a light brown oil (0.016 g, 48%): IR (neat) 3535, 3409, 3045, 2918, 1580 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.95 (br s, 1 H), 7.48 (d, J = 7.6 Hz, 2 H), 7.31 (app t, J = 7.6 Hz, 2 H), 7.20−7.15 (m, 2 H), 7.13−7.11 (m, 2 H), 6.73 (d, J = 8.8 Hz, 1 H), 6.14 (br s, 1 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 145.9, 135.6, 130.9, 129.9, 129.3, 127.8, 127.7, 125.1, 117.8, 111.9, 111.3, 101.6; HRMS (TOF APCI+) m/z calcd for $C_{14}H_{12}NO$ (M + H) 210.0919, found 210.0895.

*4-(3-Methoxyphenyl)-1H-indol-5-ol (**16k**).* According to general protocol D, **16k** was obtained as a light brown oil (0.015 g, 42%, SiO_2, flash system, 0−100%, EtOAc/hexanes; 15 min gradient): IR (neat) 3528, 3403, 2924, 1712, 1580 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 10.11 (br s, 1 H), 7.37 (t, J = 8.4 Hz, 1 H), 7.30−7.26 (m, 3 H), 7.20−7.18 (m, 2 H), 6.90 (dd, J = 2.4, 8.0 Hz, 1 H), 6.87 (d, J = 8.8 Hz, 1 H), 6.30 (app t, J = 2.4 Hz, 1 H), 3.85 (s, 3 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 160.5, 147.7, 140.1, 132.3, 129.8, 129.4, 126.3, 123.6, 118.8, 116.8, 113.2, 112.9, 112.0, 101.6, 55.5; HRMS (TOF ES+) m/z calcd for $C_{15}H_{13}NO_2$ (M^+) 239.0946, found 239.0940.

*4-(p-Tolyl)-1H-indol-5-ol (**16l**).* According to general protocol D, **16l** was obtained as a light brown solid (0.011 g, 47%, SiO_2, EtOAc/hexanes, 1:8): mp 112−114 °C; IR (neat) 3523, 3409, 3021, 2917 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (br s, 1 H), 7.47 (d, J = 8.5 Hz, 2 H), 7.35 (d, J = 8.0 Hz, 2 H), 7.27 (dd, J = 0.5, 8.5 Hz, 1 H), 7.17 (app t, J = 3.0 Hz, 1 H), 6.94 (d, J = 9.0 Hz, 1 H), 6.32 (ddd, J = 1.0, 2.0, 3.0 Hz, 1 H), 5.00 (br s, 1 H), 2.45 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.0, 137.4, 132.5, 130.9, 130.0, 129.8, 127.9, 125.0, 117.8, 111.9, 111.1, 101.7, 21.3; HRMS (TOF ES+) m/z calcd for $C_{15}H_{14}NO$ (M + H) 224.1075, found 224.1074.

*4-(4-(Trifluoromethyl)phenyl)-1H-indol-5-ol (**16m**).* According to general protocol D, **16m** was obtained as a light brown solid (0.013 g, 64%, SiO_2, EtOAc/hexanes, 1:8): mp 140−142 °C; IR (neat) 3491, 2922 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (br s, 1 H), 7.79 (d, J = 8.0 Hz, 2 H), 7.73 (d, J = 8.0 Hz, 2 H), 7.32 (dd, J = 0.5, 8.5 Hz, 1 H), 7.21 (app t, J = 3.0 Hz, 1 H), 6.92 (d, J = 9.0 Hz, 1 H), 6.31 (ddd, J = 1.0, 2.5, 3.0 Hz, 1 H), 4.76 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 139.9, 131.0, 130.4, 129.5 (q, J = 32.2 Hz), 127.7, 126.0 (q, J = 3.6 Hz), 125.5, 124.2 (q, J = 270.1 Hz), 116.7, 112.3, 112.0, 101.4; HRMS (TOF ES+) m/z calcd for $C_{15}H_{11}NOF_3$ (M + H) 278.0793, found 278.0794.

*4-(4-Fluorophenyl)-1H-indol-5-ol (**16n**).* According to general protocol D, **16n** was obtained as a brown solid (0.006 g, 44%, SiO_2, EtOAc/hexanes, 1:8): mp 145−148 °C; IR (neat) 3491, 3409, 2919 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (br s, 1 H), 7.57−7.53 (m, 2 H), 7.29 (dd, J = 1.0, 9.0 Hz, 1 H), 7.25−7.21 (m, 2 H), 7.18 (app t, J = 3.0 Hz, 1 H), 6.93 (d, J = 8.5 Hz, 1 H), 6.28 (ddd, J = 1.0, 2.0, 3.0 Hz, 1 H), 4.80 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.3 (d, J = 245.0 Hz), 146.0, 131.8 (d, J = 7.5 Hz), 131.5 (d, J = 2.5 Hz), 130.9, 128.0, 125.2, 116.9, 116.2 (d, J = 24.2 Hz), 112.1, 111.4, 101.5; HRMS (TOF ES+) m/z calcd for $C_{14}H_{11}NOF$ (M + H) 228.0825, found 228.0827.

*4-Isopentyl-1H-indol-5-ol (**16o**).* According to general protocol D, **16o** was obtained as a brown oil (0.005 g, 15%, SiO_2, ISCO-Rf, 0−100%, EtOAc/hexanes; 15 min gradient): IR (neat) 3405, 2974, 1686 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.92 (br s, 1 H), 7.31 (s, 1 H), 7.23 (app t, J = 2.0 Hz, 1 H), 7.07 (d, J = 8.4 Hz, 1 H), 6.73 (d, J = 8.4 Hz, 1 H), 6.41 (br s, 1 H), 2.90 (t, J = 8.0 Hz, 2 H), 1.77 (sept, J = 6.8 Hz, 1 H), 1.59−1.53 (m, 2 H), 0.99 (d, J = 6.4 Hz, 6 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.0, 132.0, 129.7, 125.3, 118.9, 112.5, 109.5, 100.3, 39.7, 28.9, 25.5, 22.9; HRMS (TOF ES−) m/z calcd for $C_{13}H_{16}NO$ (M-H) 202.1232, found 202.1229.

*4-(3-Chloropropyl)-1H-indol-5-ol (**16p**).* According to general protocol D, **16p** was obtained as a brown oil (0.007 g, 20%, SiO_2, flash system, 0−100%, EtOAc/hexanes; 15 min gradient): IR (neat) 3409, 2934, 1705 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.99 (br s, 1 H), 7.50 (s, 1 H), 7.26 (app t, J = 2.8 Hz, 1 H), 7.12 (d, J = 8.4 Hz, 1 H), 6.75 (d, J = 8.4 Hz, 1 H), 6.47 (app s, 1 H), 3.66 (t, J = 6.8 Hz, 2 H), 3.04 (t, J = 7.6 Hz, 2 H), 2.15 (pent, J = 7.2 Hz, 2 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.3, 131.9, 129.9, 125.6, 116.9, 112.4, 110.1, 100.2, 45.7, 33.7, 24.9; HRMS (TOF ES+) m/z calcd for $C_{11}H_{13}NOCl$ (M + H) 210.0686, found 210.0657.

*4-Cyclohexenyl-1H-indol-5-ol (**16q**).* According to general protocol B, **16q** was obtained as a brown oil (0.021 g, 23%, SiO_2, EtOAc/hexanes, 1:6): IR (neat) 3403, 2931, 1705, 1612 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.94 (br s, 1 H), 7.19 (t, J = 2.8 Hz, 1 H), 7.12 (dd, J = 0.8, 8.8 Hz, 1 H), 6.84 (s, 1 H), 6.70 (d, J = 8.8 Hz, 1 H), 6.30−6.29 (m, 1 H), 5.76−5.76 (m, 1 H), 2.41−2.37 (m, 2 H), 2.24−2.20 (m, 2 H), 1.82−1.78 (m, 4 H); ^{13}C NMR (100 MHz, acetone-d_6) δ 147.1, 135.9, 132.1, 128.9, 127.6, 125.6, 121.3, 112.6, 110.9, 101.5, 26.3, 23.9, 23.2; HRMS (TOF ES+) m/z calcd for $C_{14}H_{15}NO$ (M^+) 213.1154, found 213.1171.

*3,7,8,9-Tetrahydropyrano[3,2-e]indole (**18**).*[17] A solution of phenol **16p** (0.023 g, 0.11 mmol) in THF (1.5 mL) was treated with NaH (0.008 g, 0.20 mmol, 60% dispersion) followed by TBAI (0.045 g, 0.19 mmol) at room temperature. After 30 min, the solution was diluted with brine and extracted with diethyl ether. The organic layers were dried (Na_2SO_4), filtered, and concentrated. The crude residue was purified by chromatography on SiO_2 (ISCO-Rf, 0−100% EtOAc/hexanes, 15 min gradient) to give pyran **18** (0.010 g, 53%) as a light yellow semisolid: IR (neat) 3428, 2934, 1493 cm^{-1}; ^1H NMR (400 MHz, acetone-d_6) δ 9.91 (br s, 1 H), 7.11 (app t, J = 2.8 Hz, 1 H), 6.99 (d, J = 8.8 Hz, 1 H), 6.43 (d, J = 8.8 Hz, 1 H), 6.21 (br s, 1 H), 3.99 (t, J = 5.2 Hz, 2 H), 2.76 (t, J = 6.8 Hz, 2 H), 2.72−2.68 (m, 2 H); ^{13}C NMR (75 MHz, acetone-d_6) δ 148.9, 131.4, 128.7, 125.3, 112.9, 112.2, 110.4, 99.7, 66.4, 23.1, 22.5; HRMS (TOF ES+) m/z calcd for $C_{11}H_{12}NO$ (M + H) 174.0919, found 174.0895.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^1H NMR spectra for **14e,i,k−q** and copies of ^1H NMR and ^{13}C NMR spectra for all other compounds, except the commercial compounds **14a** and **14b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to the memory of Professor Robert E. Ireland.

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