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Study of the Addition of Grignard Reagents to 2-Aryl-3*H*-indol-3-ones[1]

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Grignard reagents are added to the carbonyl group of 2-aryl-3*H*-indol-3-ones to generate 3-alkyl-(or phenyl)-2-aryl-3*H*-indol-3-ols, which are in turn rearranged to yield 2-alkyl(or phenyl)-2-aryl-1,2-dihydro-3*H*-indol-3-ones.

Indol-3-ones having a quaternary center at the 2 position are potentially useful intermediates in the synthesis of alkaloids and pharmaceutical agents. 2,2-Diaryl-1,2-dihydro-3*H*-indol-3-ones were originally prepared by Lednicer and Emmert using the base-induced rearrangement of 2,3-diaryl-3*H*-indol-3-ols, which were obtained from 4*H*-3,1-benzoxazines.[2] The thermally induced rearrangement of a 2-aryl-3-methyl-3*H*-indol-3-ol to 2-aryl-2-methyl-1,2-dihydro-3*H*-indol-3-one has also been observed.[3] This type of rearrangement is well-known when the migrating group is tethered to the indoline nucleus, and it can be induced thermally, under acidic conditions, or under basic conditions.[4] It has been elegantly employed as a key step in the synthesis of natural products such as austamide, brevianamide, and aristotelone.[5] The driving force for this type of rearrangement is the gain in the resonance stabilization of the vinylogous amide present in the rearrangement product relative to the lack of such stabilization in the tertiary alcohol and imine present in the starting material.

Indol-3-ones having a quaternary center at the 2 position have also been prepared by the addition of dialkyl malonate anion to 2-phenyl-3*H*-indol-3-one.[6] Marchetti and co-workers have studied the addition of Grignard reagents to 2-phenyl-3*H*-indol-3-one (**1**).[7] They observed that simple alkyl Grignard reagents appeared to add primarily to the carbonyl group to yield tertiary alcohols (**2**) often accompanied by a small amount of 2-alkyl-2-phenyl-1,2-dihydro-3*H*-indol-3-ones (**3**), while addition of benzyl and *tert*-butyl Grignard reagents to the same compound appeared to yield directly the 2-benzyl-(or *tert*-butyl)-2-phenyl-1,2-dihydro-3*H*-indol-3-ones (**3d** or **3h**) as the exclusive or preponderant product (Scheme 1 and the data in the parentheses of Table 1). To account for this divergence in products formed, Marchetti and co-workers proposed a single electron-transfer mechanism (Scheme 2) to account for what they believed to be the direct formation of 2-alkyl-2-phenyl-1,2-dihydro-3*H*-indol-3-ones (**3**). When benzyl and *tert*-butyl Grignard reagents were added to **1**, they proposed that the single electron-transfer mechanism was the predominant pathway.[7]

SCHEME 1

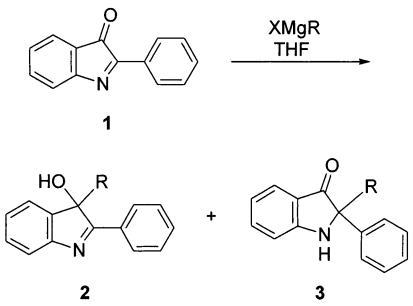

TABLE 1. Yields[a] of 2 and 3 from Reaction in Scheme 1

	RMgX		yield[a] (%)	
entry	R	X	**2**	**3**
a	Me	Br	87 (59)	1.1 (6)
b	Et	Br	81 (51)	2 (8)
c	*i*-Pr	Cl	73 (25)	8.7 (12)
d	*t*-Bu	Cl	67 (14)	15 (55)
e	vinyl	Br	92	0
f	allyl	Br	78	5.8
g	Ph	Br	91 (92)	0 (0)
h	Bn	Cl	73 (0)	22 (93)

[a] Results of Marchetti et al.[7] are in the parentheses.

(1) Presented in preliminary form: Liu, Y.; McWhorter, W. W., Jr. *Abstracts of Papers*, 224th National Meeting of the American Chemical Society, Boston, MA, Aug 17−22, 2002; American Chemical Society: Washington, DC, 2002; ORGN 698.

(2) Lednicer, D.; Emmert, D. E. *J. Heterocycl. Chem.* **1970**, 575−581.

(3) Robinson, B.; Uppal Zubair, M. *Pak. J. Sci. Ind. Res.* **1976**, *19*, 214−214.

(4) (a) Witkop, B *J. Am. Chem. Soc.* **1950**, *72*, 614−620. (b) Patrick, J. B.; Witkop, B. *J. Am. Chem. Soc.* **1950**, *72*, 633−634. (c) Witkop, B.; Patrick, J. B. *J. Am. Chem. Soc.* **1951**, *73*, 1558−1564. (d) Witkop, B.; Patrick, J. B. *J. Am. Chem. Soc.* **1951**, *73*, 2188−2195.

(5) For examples, see: (a) Hutchison, A. J.; Kishi, Y. *Tetrahedron Lett.* **1978**, 539−542. (b) Hutchison, A. J.; Kishi, Y. *J. Am. Chem. Soc.* **1979**, *101*, 6786−6788. (c) Williams, R. M.; Glinka, T.; Kwast, E.; Coffman, H.; Stille, J. K. *J. Am. Chem. Soc.* **1990**, *112*, 808−821. (d) Stoermer, D.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 564−568.

(6) (a) Adam, J.-M.; Winkler, T. *Helv. Chim. Acta* **1984**, *67*, 2186−2191. (b) Ling, K.-Q. *Chin. J. Chem.* **1996**, *14*, 265−270. (c) Tommasi, G.; Bruni, P.; Greci, L.; Sgarabotto, P.; Right, L. *J. Chem. Soc., Perkin Trans. 1* **1999**, 681−686

(7) Berti, C.; Greci, L.; Marchetti, L. *J. Chem. Soc., Perkin Trans. 2* **1979**, 233−236.

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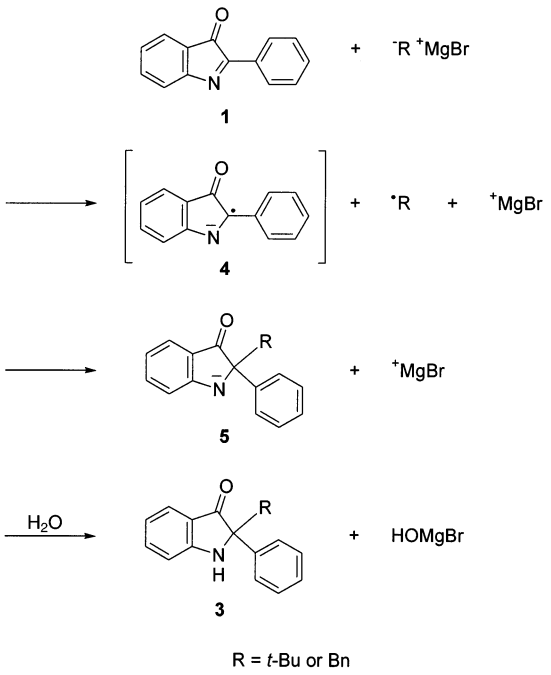
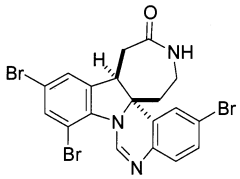
SCHEME 2



When planning to carry out a total synthesis of hinckdentine A (**6**), we initially sought to apply the observations of Marchetti and co-workers to the direct construction of the quaternary center of the hinckdentine A structure.[8] We felt that if Marchetti and co-workers[7]



were correct, an allyl Grignard reagent would behave similarly to benzyl and *tert*-butyl Grignard reagents and add to the imine rather than the carbonyl group of the indol-3-one. The major product obtained from the addition of allylmagnesium bromide to 2-(2-bromophenyl)-3*H*-indol-3-one (**7**) was somewhat unstable and was found to rearrange with time to a ketone, the minor product of the initial reaction (Scheme 3 and Table 2, R = allyl). We found that this rearrangement could be induced to occur very cleanly by treating the initial adduct under acidic condition (HCOOH/toluene). We identified the rearrangement product as 2-allyl-2-(2-bromophenyl)-1,2-dihydro-3*H*-indol-3-one (**9f**) and found the initial adduct to be 3-allyl-2-(2-bromophenyl)-3*H*-indol-3-ol (**8f**). This result appeared to be inconsistent with the reaction mechanism proposed by Marchetti and co-workers.[7]

It could be argued that the presence of the bromine atom might cause the 2-aryl substituent to rotate too far out of the plane of the 3*H*-indol-3-one ring, thus making the radical anion intermediate **4** proposed by Marchetti and co-workers[7] less stable. Lower stability of the postulated radical anion intermediate could favor addition of the Grignard reagent to the carbonyl group as we observed. Therefore, we decided to examine the addition of allylmagnesium bromide to 2-phenyl-3*H*-indol-3-one (**1**) (Scheme 1, R = allyl). In this case, we again observed the addition of allylmagnesium bromide to the carbonyl group to yield 3-allyl-2-phenyl-3*H*-indol-3-ol (**2f**), which could be rearranged under acidic conditions (HCO_2H/toluene) to 2-allyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (**3f**).

(8) Liu, Y.; McWhorter, W. W. Synthesis of 8-Desbromohinckdentine A. *J. Am. Chem. Soc.* **2003**, *125*, in press.

SCHEME 3

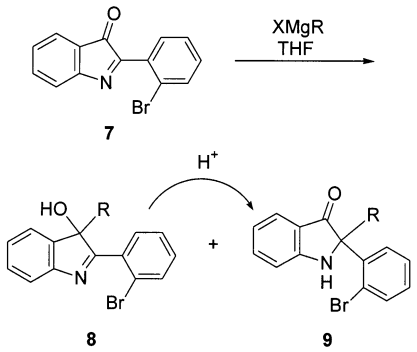


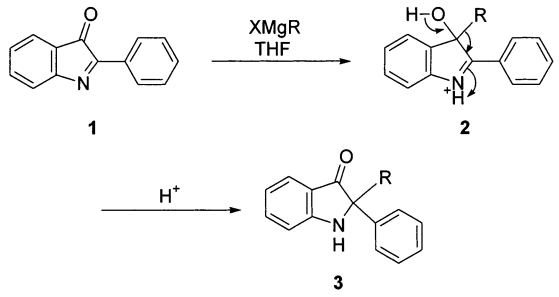
TABLE 2. Yields of 8 and 9 from Reaction in Scheme 3

	RMgX		yield (%)	
entry	R	X	**8**	**9**
a	Me	Br	92	0
b	Et	Br	90	1
c	*i*-Pr	Cl	83	5
d	*t*-Bu	Cl	59	6.2
e	vinyl	Br	93	0
f	allyl	Br	89	2.9
g	Ph	Br	96	0
h	Bn	Cl	90	5.2

As a result, we began a systematic reexamination of the results reported by Marchetti and co-workers.[7] In each case, we observed the formation of 3-alkyl(or phenyl)-2-phenyl-3*H*-indol-3-ols (**2**) as the major or exclusive product when a Grignard reagent was added to 2-phenyl-3*H*-indol-3-one (**1**) (Scheme 1 and Table 1). Further, we found that each of these compounds could be rearranged to the corresponding 2-alkyl(or phenyl)-2-phenyl-1,2-dihydro-3*H*-indol-3-ones (**3**) (the minor products of the first reaction, except in the cases of the vinyl and phenyl Grignard reagents) under acidic conditions. We also found that the acid-induced rearrangements were particularly fast in the case of the *tert*-butyl (**2d)** and benzyl (**2h**) derivatives. In fact, in these cases, significant (15−22%) rearrangement apparently took place during the Grignard addition reactions or during the workup of these reactions. We believe that addition of the Grignard reagent always takes place at the carbonyl group and that in some cases the minor products, 2-alkyl-2-phenyl-1,2-dihydro-3*H*-indol-3-ones (**3**), arise by rearrangement of the resulting tertiary alcohol (**2**) during the course of the reaction or the workup of the reaction (Scheme 4).

Thus, it is possible that acidic or basic[2] conditions arising either during the reactions or during the workup caused Marchetti and co-workers[7] to miss the formation of 3-benzyl-2-phenyl-3*H*-indol-3-ol (**2h**) and to greatly underestimate the extent to which 3-*tert*-butyl-2-phenyl-3*H*-indol-3-ol (**2d**) is formed. We have worked up the

SCHEME 4



R = Me, Et, *i*-Pr, *t*-Bu, vinyl, allyl, Ph, or Bn; X = Cl or Br.

SCHEME 5

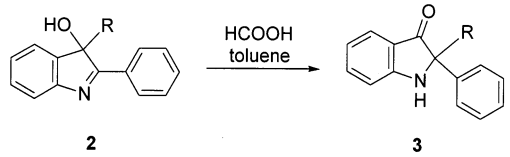


TABLE 3. Yield of Rearrangement of 2 into 3

entry	R	yield (%) of **3**
a[a]	Me	30
b	Et	84
c	*i*-Pr	89
d[b]	*t*-Bu	65
e	vinyl	88
f	allyl	89
g	Ph	88
h	Bn	88

[a] At reflux for 2 h. [b] In chloroform and at room temperature for 17 h.

formation of **2d** and **2h** according to the published experimental procedures of Marchetti and co-workers.[7] In so doing, we obtained a higher percentage of rearrangement products **3d** and **3h**, but we did not observe exclusive formation of **3h** or as high a percentage of **3d** as previously reported.[7] Since Marchetti and co-workers[7] published only a general experimental procedure, it is likely that an unpublished detail of their experimental procedure accounts for this difference. Apparently, they did not realize that **2** can be rearranged to **3** and consequently proposed the mechanism shown in Scheme 2, which we believe is superseded by the data presented herein.

After investigating a variety of conditions, we found that the rearrangement of **2** into **3** occurred most efficiently upon refluxing a solution of **2** in toluene in the presence of formic acid for 30 min (Scheme 5), except in the case of **2d** to **3d** (R = *t*-Bu) where the rearrangement was best carried out with formic acid in chloroform at room temperature for 17 h. The results of the rearrangement reaction are presented in Table 3.

We have also explored the addition of Grignard reagents to 2-(2-bromophenyl)-3*H*-indol-3-one (**7**). The reactions were also carried out in THF at room temperature (Scheme 3) and results similar to those shown in Table 1 were observed (Table 2). The rearrangement reactions of **8** were also explored (Scheme 6), and the results are presented in Table 4. Like the rearrangement of **2d** to **3d**, the rearrangement of **8d** to **9d** was carried out in a solution of formic acid in chloroform at room temperature.

SCHEME 6

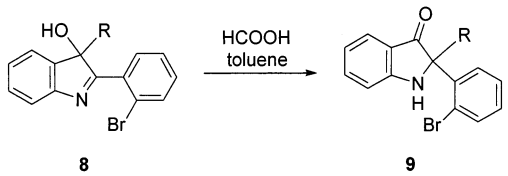


TABLE 4. Yield of Rearrangement of 8 into 9

entry	R	yield (%) of **9**
a[a]	Me	51
b	Et	88
c	*i*-Pr	65
d[b]	*t*-Bu	76
e	vinyl	90
f	allyl	96
g	Ph	96
h	Bn	96

[a] At reflux for 2 h. [b] In chloroform and at room temperature for 17 h.

In conclusion, we have studied the addition of Grignard reagents to 2-phenyl-3*H*-indol-3-one and 2-(2-bromophenyl)-3*H*-indol-3-one. The additions of the Grignard reagents take place at the carbonyl group, and the resulting tertiary alcohols are rearranged to the 2-alkyl(or phenyl)-2-aryl-1,2-dihydro-3*H*-indol-3-ones under acidic conditions. Our results and literature reports show that the rearrangement of **2** to **3** often takes place with great facility under acidic or basic conditions or that it may be thermally induced. It may be that the apparent addition of malonate anion to the imine of indol-3-ones[6] is in fact an addition to the carbonyl group followed by a base-mediated rearrangement to the observed products. Thus, we believe that nucleophiles add to the carbonyl group of indol-3-ones and that the resulting adducts rearrange or can easily be caused to rearrange to 2,2-disubstituted-1,2-dihydro-3*H*-indol-3-ones.

Experimental Section

General. Proton magnetic resonance spectra were recorded on a 400 MHz spectrometer and are reported in ppm on the δ scale (J values are given in Hz). Infrared spectra (IR) and high-resolution mass spectra (HRMS) were determined by the Analytical Chemistry Department of Pharmacia. Anhydrous THF was distilled prior to use from sodium metal/benzophenone. Brine refers to a saturated aqueous sodium chloride solution. Solvent removal was accomplished by a rotary evaporator operating at house vacuum (40−50 Torr). Column chromatography was performed with silica gel 60 (230-400 mesh ASTM).

2-Phenyl-3-vinyl-3*H*-indol-3-ol (2e). Indolone **1** (207.2 mg, 1 mmol) was dissolved in dry THF (80 mL). Under protection of nitrogen and at room temperature, a solution of vinylmagnesium bromide in THF (1.0 M, 1.1 mL, 1.1 mmol) was added dropwise and slowly. After stirring for 2 h, the reaction mixture was concentrated under reduced pressure at 25−28 °C to a small volume, diluted with EtOAc (100 mL), and washed with 10% NH_4Cl solution (30 mL). The aqueous wash was extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were washed with brine (20 mL) and dried over Na_2SO_4 for 50 min. Evaporation of solvent and then chromatography with a mixture of hexane and EtOAc afforded **2e** (217 mg, 92%): ^{1}H NMR ($CDCl_3$) 2.55 (br s, 1H, OH), 5.35 (dd, J = 10.6 and 1.0, 1H, =CH_2), 5.73 (dd, J = 17.1 and 1.0, 1H, =CH_2), 5.90 (dd, J = 17.1 and 10.6, 1H, =CH), 7.26 (ddd, J = 7.4, 7.3 and 1.0, 1H, ArH), 7.38−7.51 (5H, ArH), 7.61 (d, J =

7.6, 1H, ArH), 8.31 (dd, J = 8.3 and 1.5, 2H, ArH); HRMS calcd for $C_{16}H_{14}NO$ (MH^+) 236.1075, found 236.1069.

3-Methyl-2-phenyl-3*H*-indol-3-ol (2a): yield 87%; ^{1}H NMR ($CDCl_3$) 1.73 (s, 3H, CH_3), 2.40 (br s, 1H, OH), 7.26 (ddd, J = 7.4, 7.1 and 1.0, 1H, ArH), 7.40 (ddd, J = 7.6, 7.5 and 1.2, 1H, ArH), 7.48-7.54 (4H, ArH), 7.59 (d, J = 7.7, 1H, ArH), 8.37 (dd, J = 8.3 and 1.8, 2H, ArH); HRMS $C_{15}H_{14}NO$ (MH^+) calcd 224.1075, found 224.1070.

3-Ethyl-2-phenyl-3*H*-indol-3-ol (2b): yield 81%; ^{1}H NMR ($CDCl_3$) 0.51 (t, J = 7.5, 3H, CH_2CH_3), 1.83 (s, 1H, OH), 2.16 (dq, J = 13.3 and 7.5, 1H, CH_2Me), 2.30 (dq, J = 13.3 and 7.5, 1H, CH_2Me), 7.27−7.56 (6H, ArH), 7.61 (d, J = 7.5, 1H, ArH), 8.38 (dd, J = 8.1 and 1.7, 2H, ArH); HRMS $C_{16}H_{16}NO$ (MH^+) calcd 238.1232, found 238.1237.

2-Phenyl-3-*iso*-propyl-3*H*-indol-3-ol (2c): yield 73%; ^{1}H NMR ($CDCl_3$) 0.37 (d, J = 6.8, 3H, $CHCH_3$), 1.33 (d, J = 6.8, 3H, $CHCH_3$), 1.55 (br s, 1H, OH), 2.51 (septet, J = 6.8, 1H, $CHMe_2$), 7.26 (ddd, J = 7.9, 7.5 and 0.8, 1H, ArH), 7.41 (dd, J = 7.5 and 7.4, 1H, ArH), 7.47−7.54 (4H, ArH), 7.59 (d, J = 7.7, 1H, ArH), 8.39 (dd, J = 6.8 and 1.2, 2H, ArH); HRMS $C_{17}H_{18}NO$ (MH^+) calcd 252.1388, found 252.1397.

3-*tert*-Butyl-2-phenyl-3*H*-indol-3-ol (2d): yield 67%; ^{1}H NMR ($CDCl_3$) 0.93 (s, 9H, $C(CH_3)_3$), 2.43 (br s, 1H, OH), 7.22 (ddd, J = 7.6, 7.5 and 1.0, 1H, ArH), 7.38 (dd, J = 7.5 and 7.3, 1H, ArH), 7.41−7.48 (4H, ArH), 7.55 (d, J = 7.5, 1H, ArH), 8.16 (dd, J = 6.8 and 1.2, 2H, ArH); HRMS $C_{18}H_{20}NO$ (MH^+) calcd 266.1545, found 266.1545.

3-Allyl-2-phenyl-3*H*-indol-3-ol (2f): yield 78%; ^{1}H NMR ($CDCl_3$) 2.50 (br s, 1H, OH), 2.73 (dd, J = 13.7 and 7.7, 1H, CH_2), 3.03 (dd, J = 13.7 and 6.8, 1H, CH_2), 4.83 (dd, J = 17.0 and 1.4, 1H, $=CH_2$), 4.92 (dd, J = 10.2 and 1.4, 1H, $=CH_2$), 5.37 (dddd, J = 17.0, 10.2, 7.7 and 6.8, 1H, =CH), 7.27 (ddd, J = 7.6, 7.5 and 1.0, 1H, ArH), 7.41 (dd, J = 7.7 and 7.4, 1H, ArH), 7.46 (d, J = 7.5, 1H, ArH), 7.48−7.54 (3H, ArH), 7.58 (d, J = 7.7, 1H, ArH), 8.37 (dd, J = 8.3 and 1.8 Hz, 2H, ArH); HRMS $C_{17}H_{16}NO$ (MH^+) calcd 250.1232, found 250.1223.

2,3-Diphenyl-3*H*-indol-3-ol (2g): yield 91%; ^{1}H NMR ($CDCl_3$) 2.72 (s, 1H, OH), 7.17−7.44 (11H, ArH), 7.67 (d, J = 7.7, 1H, ArH), 8.09 (dd, J = 8.3 and 1.4, 2H, ArH); HRMS $C_{20}H_{16}NO$ (MH^+) calcd 286.1232, found 286.1241.

3-Benzyl-2-phenyl-3*H*-indol-3-ol (2h): yield 73%; ^{1}H NMR ($CDCl_3$) 2.52 (s, 1H, OH), 3.11 (d, J = 13.3, 1H, $PhCH_2$), 3.60 (d, J = 13.3, 1H, $PhCH_2$), 6.77 (d, J = 7.1, 2H, ArH), 7.04−7.20 (5H, ArH), 7.35 (ddd, J = 7.7, 7.5 and 1.3, 1H, ArH), 7.46 (d, J = 7.5, 1H, ArH), 7.52−7.57 (3H, ArH), 8.09 (dd, J = 8.3 and 1.9, 2H, ArH); HRMS $C_{21}H_{18}NO$ (MH^+) calcd 300.1388, found 300.1395.

2-(2-Bromophenyl)-3-methyl-3*H*-indol-3-ol (8a): yield 92%; ^{1}H NMR ($CDCl_3$) 1.59 (s, 3H, CH_3), 2.32 (br s, 1H, OH), 7.32−7.37 (2H, ArH), 7.42−7.47 (2H, ArH), 7.50 (ddd, J = 7.3, 1.5 and 0.6, 1H, ArH), 7.63−7.66 (2H, ArH), 7.74 (dd, J = 8.0 and 1.2, 1H, ArH); HRMS $C_{15}H_{13}BrNO$ (MH^+) calcd 302.0181, found 302.0177.

2-(2-Bromophenyl)-3-ethyl-3*H*-indol-3-ol (8b): yield 90%; ^{1}H NMR ($CDCl_3$) 0.79 (t, J = 7.5, 3H, CH_2CH_3), 1.88 (dq, J = 13.7 and 7.5, 1H, CH_2Me), 2.07 (dq, J = 13.7 and 7.5, 1H, CH_2Me), 2.40 (br s, 1H, OH), 7.32-7.36 (2H, ArH), 7.41−7.48 (3H, ArH), 7.66 (d, J = 7.7, 1H, ArH), 7.75 (dd, J = 8.1 and 1.0, 1H, ArH), 7.82 (dd, J = 7.7 and 1.7, 1H, ArH); HRMS $C_{16}H_{15}BrNO$ (MH^+) calcd 316.0337, found 316.0339.

2-(2-Bromophenyl)-3-*iso*-propyl-3*H*-indol-3-ol (8c): yield 83%; ^{1}H NMR ($CDCl_3$) 0.62 (d, J = 6.8, 3H, $CHCH_3$), 1.22 (d, J = 6.8, 3H, $CHCH_3$), 2.25 (septet, J = 6.8, 1H, $CHMe_2$), 2.48 (br s, 1H, OH), 7.28−7.35 (2H, ArH), 7.40−7.50 (3H, ArH), 7.67 (d, J = 7.5, 1H, ArH), 7.76 (dd, J = 8.1 and 0.8, 1H, ArH), 8.00 (dd, J = 7.8 and 1.6, 1H, ArH); HRMS $C_{17}H_{17}BrNO$ (MH^+) calcd 330.0494, found 330.0498.

2-(2-Bromophenyl)-3-*tert*-butyl-3*H*-indol-3-ol (8d): yield 59%; ^{1}H NMR ($CDCl_3$) 0.98 (s, 9H, $C(CH_3)_3$), 2.42 (s, 1H, OH), 7.25−7.30 (2H, ArH), 7.37 (ddd, J = 7.7, 7.5 and 1.2, 1H, ArH), 7.42 (ddd, J = 7.7, 7.5 and 1.2, 1H, ArH), 7.49 (d, J = 7.3, 1H, ArH), 7.64 (d, J = 7.7, 1H, ArH), 7.74 (dd, J = 8.1 and 1.3, 1H, ArH), 8.11 (dd, J = 7.8 and 1.3, 1H, ArH); HRMS $C_{18}H_{19}BrNO$ (MH^+) calcd 344.0650, found 344.0651.

2-(2-Bromophenyl)-3-vinyl-3*H*-indol-3-ol (8e): yield 93%; ^{1}H NMR ($CDCl_3$) 2.53 (s, 1H, OH), 5.34 (dd, J = 10.6 and 1.0, 1H, $=CH_2$), 5.54 (dd, J = 17.1 and 1.0, 1H, $=CH_2$), 5.82 (dd, J = 17.1 and 10.6, 1H, =CH), 7.30−7.41 (4H, ArH), 7.46 (ddd, J = 7.7, 7.5 and 1.5, 1H, ArH), 7.64 (dd, J = 7.7 and 1.7, 1H, ArH), 7.67 (d, J = 7.7, 1H, ArH), 7.72 (dd, J = 8.0 and 1.1, 1H, ArH); HRMS $C_{16}H_{13}BrNO$ (MH^+) calcd 314.0181, found 314.0184.

3-Allyl-2-(2-bromophenyl)-3*H*-indol-3-ol (8f): yield 89%; ^{1}H NMR ($CDCl_3$) 2.53 (s, 1H, OH), 2.53 (dd, J = 14.0 and 7.9, 1H, CH_2), 2.75 (dd, J = 14.0 and 6.8, 1H, CH_2), 5.09 (dd, J = 17.0 and 1.5, 1H, $=CH_2$), 5.14 (dd, J = 10.2 and 1.5, 1H, $=CH_2$), 5.67 (dddd, J = 17.0, 10.2, 7.9 and 6.8, 1H, =CH), 7.30−7.36 (2H, ArH), 7.41−7.47 (3H, ArH), 7.66 (d, J = 7.7, 1H, ArH), 7.74 (dd, J = 8.0 and 1.1, 1H, ArH), 7.78 (dd, J = 7.7 and 1.7, 1H, ArH); HRMS $C_{17}H_{15}BrNO$ (MH^+) calcd 328.0337, found 328.0329.

2-(2-Bromophenyl)-3-phenyl-3*H*-indol-3-ol (8g): yield 96%; ^{1}H NMR ($CDCl_3$) 2.78 (br s, 1H, OH), 6.99 (dd, J = 7.6 and 1.4, 1H, ArH), 7.17 (ddd, J = 7.6, 7.5 and 1.2, 1H, ArH), 7.20−7.35 (9H, ArH), 7.49 (m, 1H, ArH), 7.64 (dd, J = 8.0 and 1.0, 1H, ArH), 7.74 (d, J = 7.7, 1H, ArH); HRMS $C_{20}H_{15}BrNO$ (MH^+) calcd 364.0337, found 364.0333.

3-Benzyl-2-(2-bromophenyl)-3*H*-indol-3-ol (8h): yield 90%; ^{1}H NMR ($CDCl_3$) 2.47 (br s, 1H, OH), 2.81 (d, J = 13.7, 1H, $PhCH_2$), 3.28 (d, J = 13.7, 1H, $PhCH_2$), 6.65 (d, J = 6.9, 1H, ArH), 7.07−7.09 (2H, ArH), 7.15 (ddd, J = 7.6, 7.5 and 0.9, 1H, ArH), 7.26−7.47 (7H, ArH), 7.65 (d, J = 7.7, 1H, ArH), 7.77 (dd, J = 8.1 and 1.0, 1H, ArH), 7.91 (dd, J = 7.7 and 1.7, 1H, ArH); HRMS $C_{21}H_{17}BrNO$ (MH^+) calcd 378.0494, found 378.0483.

2-Phenyl-2-vinyl-1,2-dihydro-3*H*-indol-3-one (3e). Indolol **2e** (141.1 mg, 0.6 mmol) was dissolved in toluene (20 mL), and 88% aqueous formic acid (5 mL) was added. After stirring and refluxing for 30 min, the reaction mixture was cooled to room temperature and carefully poured into saturated Na_2CO_3 solution (100 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of solvent and chromatography with a mixture of hexane and EtOAc afforded **3e** (124.2 mg, 88%). IR 3348 (N−H), 3088, 3057, 3030, 1726, 1690, 1676, 1620, 1586, 1494, 1410, 1003, 980, 928, 894, 751, 730, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$) 5.00 (br s, 1H, NH), 5.33 (dd, J = 10.4 and 0.8, 1H, $=CH_2$), 5.50 (dd, J = 17.1 and 0.8, 1H, $=CH_2$), 6.33 (dd, J = 17.1 and 10.4, 1H, =CH), 6.89 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 6.98 (d, J = 8.1, 1H, ArH), 7.29−7.39 (3H, ArH), 7.49−7.54 (3H, ArH), 7.64 (d, J = 7.9, 1.3 and 0.8, 1H, ArH); HRMS calcd for $C_{16}H_{14}NO$ (MH^+) 236.1075, found 236.1069.

2-Methyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (3a): yield 30% (at reflux for 2 h); IR (selected) 3370 (N-H), 1660 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) 1.60 (s, 3H, CH_3), 5.97 (br s, 1H, NH), 6.87 (ddd, J = 7.8, 7.2 and 0.6, 1H, ArH), 6.97 (d, J = 8.3, 1H, ArH), 7.27−7.38 (3H, ArH), 7.50−7.54 (3H, ArH), 7.63 (ddd, J = 7.9, 1.3 and 0.8, 1H, ArH); HRMS $C_{15}H_{14}NO$ (MH^+) calcd 224.1075, found 224.1081.

2-Ethyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (3b): yield 84%; IR (selected) 3369 (N−H), 1666 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.89 (t, J = 7.5, 3H, CH_2CH_3), 2.19 (q, J = 7.5, 2H, CH_2CH_3), 5.03 (br s, 1H, NH), 6.84 (ddd, J = 7.9, 7.0 and 0.8, 1H, ArH), 6.99 (d, J = 8.3, 1H, ArH), 7.26−7.38 (3H, ArH), 7.50 (ddd, J = 8.2, 7.2 and 1.3, 1H, ArH), 7.56−7.60 (3H, ArH); HRMS $C_{16}H_{16}NO$ (MH^+) calcd 238.1232, found 238.1234.

2-Phenyl-2-*iso*-propyl-1,2-dihydro-3*H*-indol-3-one (3c): yield 89%; IR (selected) 3338 (N−H), 1678 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) 0.84 (d, J = 6.6, 3H, CH_3), 0.87 (d, J = 6.6, 3H, CH_3), 2.85 (septet, J = 6.6, 1H, $CHMe_2$), 5.10 (br, 1H, NH), 6.80 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 7.01 (d, J = 8.3, 1H, ArH), 7.25−7.37 (3H, ArH), 7.48 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.55 (ddd, J = 7.9, 1.2 and 0.8, 1H, ArH), 7.62 (dd,

J = 7.9 and 1.3, 2H, ArH); HRMS $C_{17}H_{18}NO$ (MH^+) calcd 252.1388, found 252.1380.

2-Allyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (3f): yield 89%; IR (selected) 3339 (N−H), 1677 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 2.66 (dd, J = 13.9 and 8.5, 1H, CH_2), 3.08 (dd, J = 13.9 and 5.8, 1H, CH_2), 5.05 (br s, 1H, NH), 5.10 (dd, J = 10.2 and 2.4, 1H, ═CH_2), 5.19 (dd, J = 17.1 and 2.4, 1H, ═CH_2), 5.37 (dddd, J = 17.1, 10.2, 8.5 and 5.8, 1H, ═CH), 6.86 (ddd, J = 7.9, 7.1 and 0.8, 1H, ArH), 6.99 (d, J = 8.1, 1H, ArH), 7.28−7.39 (3H, ArH), 7.51 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.59 (ddd, J = 7.9, 1.2 and 0.6, 1H, ArH), 7.64 (dd, J = 8.3 and 1.4, 2H, ArH); HRMS $C_{17}H_{16}NO$ (MH^+) calcd 250.1232, found 250.1228.

2,2-Diphenyl-1,2-dihydro-3*H*-indol-3-one (3g): yield 88%; IR (selected) 3351 (N−H), 1676 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 5.20 (s, 1H, NH), 6.90 (ddd, J = 7.9, 7.1 and 0.8, 1H, ArH), 6.96 (d, J = 8.1, 1H, ArH), 7.31−7.37 (6H, ArH), 7.41−7.44 (4H, ArH), 7.52 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.68 (d, J = 7.5, 1H, ArH); HRMS $C_{20}H_{16}NO$ (MH^+) calcd 286.1232, found 286.1231.

2-Benzyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (3h): yield 88%; IR (selected) 3327 (N−H), 1675 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 3.25 (d, J = 13.7, 1H, $PhCH_2$), 3.54 (d, J = 13.7, 1H, $PhCH_2$), 4.97 (br s, 1H, NH), 6.79 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 6.87 (d, J = 8.3, 1H, ArH), 6.95−6.98 (2H, ArH), 7.15−7.18 (3H, ArH), 7.30−7.39 (3H, ArH), 7.43 (ddd, J = 8.3, 7.0 and 1.2, 1H, ArH), 7.56 (ddd, J = 7.9, 1.2 and 0.6, 1H, ArH), 7.66 (dd, J = 8.9 and 1.4, 2H, ArH); HRMS $C_{21}H_{18}NO$ (MH^+) calcd 300.1388, found 300.1396.

2-(2-Bromophenyl)-2-methyl-1,2-dihydro-3*H*-indol-3-one (9a): yield 51% (at reflux for 2 h); IR (selected) 3306 (N−H), 1688 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 1.82 (s, 3H, CH_3), 5.42 (br s, 1H, NH), 6.87-6.91 (2H, ArH), 7.19 (ddd, J = 7.7, 7.5 and 1.7, 1H, ArH), 7.34 (ddd, J = 7.9, 7.5 and 1.2, 1H, ArH), 7.51 (ddd, J = 8.1, 7.3 and 1.5, 1H, ArH), 7.62 (dd, J = 7.9 and 1.5, 1H, ArH), 7.63 (dd, J = 7.9 and 1.7, 1H, ArH), 7.73 (ddd, J = 7.9, 1.5 and 0.6, 1H, ArH); HRMS $C_{15}H_{13}BrNO$ (MH^+) calcd 302.0181, found 302.0186.

2-(2-Bromophenyl)-2-ethyl-1,2-dihydro-3*H*-indol-3-one (9b): yield 88%; IR (selected) 3303 (N−H), 1685 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.84 (t, J = 7.5, 3H, CH_2CH_3), 2.22 (dq, J = 13.9 and 7.5, 1H, CH_2Me), 2.52 (dq, J = 13.9 and 7.5, 1H, CH_2Me), 6.01 (br s, 1H, NH), 6.82 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 6.89 (d, J = 8.3, 1H, ArH), 7.15 (ddd, J = 7.9, 7.3 and 1.7, 1H, ArH), 7.29 (ddd, J = 7.5, 7.3 and 1.3, 1H, ArH), 7.47 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.62−7.66 (2H, ArH), 7.68 (ddd, J = 7.9, 1.3 and 0.8, 1H, ArH); HRMS $C_{16}H_{15}BrNO$ (MH^+) calcd 316.0337, found 316.0333.

2-(2-Bromophenyl)-2-*iso*-propyl-1,2-dihydro-3*H*-indol-3-one (9c): yield 65%; IR (selected) 3395 (N−H), 1680 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 0.92 (d, J = 6.8, 6H, CH_3), 2.85 (septet, J = 6.8, 1H, $CHMe_2$), 6.29 (br s, 1H, NH), 6.78 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 6.87 (d, J = 8.3, 1H, ArH), 7.13 (ddd, J = 7.9, 7.3 and 1.7, 1H, ArH), 7.30 (ddd, J = 8.7, 7.3 and 1.5, 1H, ArH), 7.45 (ddd, J = 8.3, 6.9 and 1.3, 1H, ArH), 7.62−7.64 (2H, ArH), 7.83 (dd, J = 8.0 and 1.8, 1H, ArH); HRMS $C_{17}H_{17}BrNO$ (MH^+) calcd 330.0494, found 330.0497.

2-(2-Bromophenyl)-2-vinyl-1,2-dihydro-3*H*-indol-3-one (9e): yield 90%; IR (selected) 3284 (N−H), 1672 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 5.35 (d, J = 10.2, 1H, ═CH_2), 5.49 (d, J = 17.2, 1H, ═CH_2), 5.52 (br s, 1H, NH), 6.33 (dd, J = 17.1 and 10.4, 1H, ═CH), 6.89 (dd, J = 7.7 and 7.3, 1H, ArH), 6.93 (d, J = 8.3, 1H, ArH), 7.21 (ddd, J = 7.8, 7.6 and 1.6, 1H, ArH), 7.34 (ddd, J = 7.7, 7.5 and 1.2, 1H, ArH), 7.50 (ddd, J = 8.3, 7.2 and 1.1, 1H, ArH), 7.59 (dd, J = 8.0 and 1.6, 1H, ArH), 7.63 (dd, J = 7.9 and 1.0, 1H, ArH), 7.70 (d, J = 7.7, 1H, ArH); HRMS $C_{16}H_{13}BrNO$ (MH^+) calcd 314.0181, found 314.0170.

2-Allyl-2-(2-bromophenyl)-1,2-dihydro-3*H*-indol-3-one (9f): yield 96%; IR (selected) 3345 (N−H), 1680 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 2.90 (dd, J = 14.0 and 7.1, 1H, CH_2), 3.30 (dd, J = 14.0 and 7.3, 1H, CH_2), 5.03 (d, J = 10.0, 1H, ═CH_2), 5.18 (dd, J = 17.0 and 1.3 , 1H, ═CH_2), 5.37 (dddd, J = 17.0, 10.0, 7.3 and 7.1, 1H, ═CH), 5.95 (br s, 1H, NH), 6.84 (dd, J = 7.7 and 7.3, 1H, ArH), 6.88 (d, J = 8.3, 1H, ArH), 7.17 (ddd, J = 7.8, 7.5 and 1.5, 1H, ArH), 7.31 (ddd, J = 7.9, 7.3 and 1.2, 1H, ArH), 7.47 (ddd, J = 8.3, 7.0 and 1.3, 1H, ArH), 7.64−7.69 (3H, ArH); HRMS $C_{17}H_{15}BrNO$ (MH^+) calcd 328.0337, found 328.0340.

2-(2-Bromophenyl)-2-phenyl-1,2-dihydro-3*H*-indol-3-one (9g): yield 96%; IR (selected) 3336 (N−H), 1689 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 6.33 (s, 1H, NH), 6.87 (dd, J = 7.7 and 7.3, 1H, ArH), 6.99 (d, J = 8.3, 1H, ArH), 7.21−7.38 (7H, ArH), 7.53 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.63−7.68 (3H, ArH); HRMS $C_{20}H_{15}BrNO$ (MH^+) calcd 364.0337, found 364.0327.

2-Benyl-2-(2-bromophenyl)-1,2-dihydro-3*H*-indol-3-one (9h): yield 96%; IR (selected) 3346 (N−H), 1690 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 3.46 (d, J = 13.5, 1H, $PhCH_2$), 3.84 (d, J = 13.5, 1H, $PhCH_2$), 6.21 (br s, 1H, NH), 6.65−6.68 (2H, ArH), 7.07−7.36 (8H, ArH), 7.53 (dd, J = 8.4 and 1.0, 1H, ArH), 7.70 (dd, J = 8.0 and 1.4, 1H, ArH), 7.77 (dd, J = 7.9 and 1.7, 1H, ArH); HRMS $C_{21}H_{17}BrNO$ (MH^+) calcd 378.0494, found 378.0483.

2-*tert*-Butyl-2-phenyl-1,2-dihydro-3*H*-indol-3-one (3d). Indolol **2d** (106.1 mg, 0.4 mmol) was dissolved in chloroform (32 mL), and 88% aqueous formic acid (100 μL) was added. After stirring for 17 h at room temperature, the reaction mixture was concentrated under reduced pressure to a small volume, diluted with EtOAc (40 mL), and washed with 2 M Na_2CO_3 solution (20 mL). The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic solution was washed with brine (10 mL) and dried over Na_2SO_4. Evaporation of solvent and chromatography with 16:1 hexane/EtOAc afforded **3d** (69 mg, 65%): IR 3329 (N−H), 3056, 2976, 1658, 1619, 1496, 1467, 1447, 1330, 1300, 1097, 893, 746, 716 cm^{-1}; ^1H NMR ($CDCl_3$) 1.03 (s, 9H, $C(CH_3)_3$), 5.40 (br s, 1H, NH), 6.77 (ddd, J = 7.7, 7.0 and 0.6, 1H, ArH), 6.91 (d, J = 8.3, 1H, ArH), 7.26−7.36 (3H, ArH), 7.43 (ddd, J = 8.2, 7.1 and 1.3, 1H, ArH), 7.58 (ddd, J = 7.7, 1.2 and 0.8, 1H, ArH), 7.76 (dd, J = 7.5 and 1.5, 2H, ArH); HRMS $C_{18}H_{20}NO$ (MH^+) calcd 266.1545, found 266.1547.

2-(2-Bromophenyl)-2-*tert*-butyl-1,2-dihydro-3*H*-indol-3-one (9d): yield 76%; IR (selected) 3434 (N−H), 1684 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$) 1.08 (s, 9H, $C(CH_3)_3$), 6.73 (ddd, J = 7.8, 7.1 and 0.7, 1H, ArH), 6.92 (d, J = 8.3, 1H, ArH), 7.07 (s, 1H, NH), 7.11 (ddd, J = 8.0, 7.2 and 1.7, 1H, ArH), 7.30 (ddd, J = 8.1, 7.3 and 1.7, 1H, ArH), 7.43 (ddd, J = 8.3, 7.1 and 1.2, 1H, ArH), 7.55−7.60 (2H, ArH), 8.42 (dd, J = 8.3 and 1.7, 1H, ArH); HRMS calcd for $C_{18}H_{19}BrNO$ (MH^+) 344.0650, found 344.0672.

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Supporting Information Available: ^1H NMR spectra of **2a**−**h**, **3a**−**h**, **8a**−**h**, **9a**−**h**. This material is available free of charge via the Internet at http://pubs.acs.org.

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