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Iodine-Induced Regioselective C−C and C−N Bonds Formation of *N*-Protected Indoles

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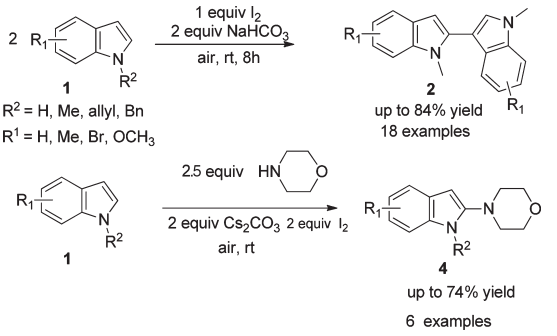

A mild, metal-free, and environmently benign iodine-promoted regioselective C−C and C−N bonds formation of *N*-protected indole derivatives giving 2,3′-biindoles **2** and 4-(1*H*-indol-2-yl)morpholines **4** is successfully demonstrated. Various bioactive 2,3′-biindoles and 4-(1*H*-indol-2-yl)morpholines, bearing electron-rich to moderately electron-poor substituents, can be prepared in moderate to good yields.

Since the first preparation of indole by Baeyer in 1866,[1] its chemistry has been extensively investigated as a consequence of its prevalence in the structures of many biologically active natural products, including some useful drugs.[1,2] For instance, biologically active natural products, such as the Gliocladins A and B,[3] Mollenine A,[4] Asperazine,[5] and a great number of dimeric diketopiperazine alkaloids,[6] are all based on the structure having an indole core (Figure 1). Thus, the

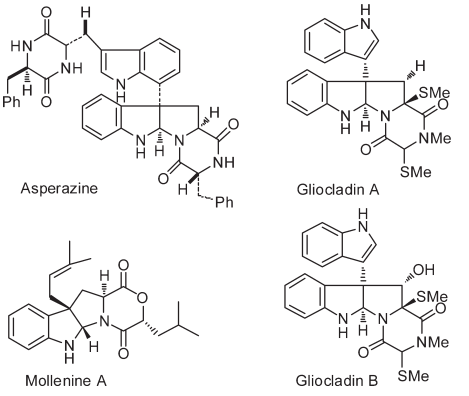

FIGURE 1. Natural products of indole alkaloids.

direct functionalization of the indoles has attracted great attention in recent years. However, the direct formation of C−C and C−N bonds of indole derivatives is particularly challenging because of the poor control of both the chemo- and regioselectivities. Synthesis of 2,3′-biindolyl[7a−d] and 4-(1*H*-indol-2-yl)morpholine scaffolds,[7e] which are useful structural units that are frequently found in pharmaceuticals and functional materials, look quite attractive. Both chemical and enzymatic synthetic methods have been reported for the construction of biindolyls.[8] Recently, a few publications have been reported by employing transition metal-catalyzed cross coupling reaction and direct functionalization of the indole derivatives to afford biindolyls.[9] For instance, Zhang and co-workers first reported the oxidative cross dimerization of *N*-protected indole derivatives to give 2,3′-linked products (Scheme 1a).[10] Shi and co-workers reported oxidative dimerization of *N*-protected and free indole derivatives affording 3,3′-biindoles via Pd-catalyzed direct C−H transformations (Scheme 1b).[11]Most of these procedures require

(1) (a) Baeyer, A. *Justus Liebigs Ann. Chem.* **1866**, *140*, 295. For historical overviews of indole chemistry, see: (b) Julian, P. L.; Meyer, E. W.; Printy, H. C. in *Heterocyclic Compounds*; Elderfield, R. C, Ed.; Wiley: New York, 1952; Vol. 3, pp 1−274. (c) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, 1970. (d) Sundberg, R. J. *Indoles*; Academic Press:, London, UK, 1996.

(2) Brancale, A.; Silvestri, R. *Med. Res. Rev.* **2007**, *27*, 209.

(3) Usami, Y.; Yamaguchi, J.; Numata, A . *Heterocycles.* **2004**, *63*, 1123.

(4) Wang, H.-J.; Gloer, J. B.; Wicklow, D. T.; Dowd, P. F. *J. Nat. Prod.* **1998**, *61*, 804.

(5) Varoglu, M.; Corbett, T. H.; Valeriote, F. A.; Crews, P. *J. Org. Chem.* **1997**, *62*, 7078.

(6) (a) Springer, J. P.; Buchi, G.; Kobbe, B.; Demain, A. L.; Clardy, J. *Tetrahedron Lett.* **1977**, *18*, 2403. (b) Barrow, C. J.; Cai, P.; Snyder, J. K.; Sedlock, D. M.; Sun, H. H.; Cooper, R. *J. Org. Chem.* **1993**, *58*, 6016. (c) Greiner, D.; Bonaldi, T.; Eskeland, R.; Roemer, E.; Imhof, A. *Nat. Chem. Biol.* **2005**, *1*, 143. (d) Zhang, Y.-X.; Chen, Y.; Guo, X.-N.; Zhang, X.-W.; Zhao, W.-M.; Zhong, L.; Zhou, J.; Xi, Y.; Lin, L.-P.; Ding, J. *Anti-Cancer Drugs* **2005**, *16*, 515.

(7) (a) Koulouri, S.; Malamidou-Xenikaki, E.; Spyroudis, S. *Tetrahedron* **2005**, *61*, 10894. (b) Talaz, O.; Saracoglu, N. *Tetrahedron* **2010**, *66*, 1902. (c) Tsuchimoto, T.; Matsubayashi, H.; Kaneko, M.; Nagase, Y.; Shirakawa, E. *J. Am. Chem. Soc.* **2008**, *130* (47), 15823. (d) Gómez-Lor, B.; Echavarren, A. M. *Org. Lett.* **2004**, *6*, 2993. (e) Velezheva, V. S.; Ryabova, S. Yu.; Mel'man, A. I.; Pol'shakov, V. I. *Khim. Geterotsikl. Soedin.* **1992**, 49.

(8) (a) Duong, H. A.; Chua, S.; Huleatt, P. B.; Chai, C. L. L. *J. Org. Chem.* **2008**, *73*, 9177. (b) Skelton, B. W.; White, A. H. *Tetrahedron Lett.* **2009**, *50*, 2501. *J. Org. Chem.* **2007**, *72*, 9225. (c) Panzella, L.; Pezzella, A.; Napolitano, A.; d'Ischia, M. *Org. Lett.* **2007**, *9*, 1411. (d) Cornella, J.; Lu, P.; Larrosa, I. *Org. Lett.* **2009**, *11*, 5506.

(9) (a) Dyker, G.; Hildebrandt, D.; Liu, J.-H.; Merz, K. *Angew. Chem., Int. Ed.* **2003**, *42*, 4399. (b) Tsuchimoto, T.; Matsubayashi, H.; Kaneko, M.; Nagase, Y.; Miyamura, T.; Shirakawa, E. *J. Am. Chem. Soc.* **2008**, *130*, 15823. (c) Kraus, G. A; Guo, H.-T. *Org. Lett.* **2008**, *10*, 3061. (d) Lin, C. I.; Selvi, S.; Fang, J.-M.; Chou, P.-T.; Lai, C.-H.; Cheng, Y.-M. *J. Org. Chem.* **2007**, *72*, 3537. (e) Kraus, G. A.; Guo, H.-T *J. Org. Chem.* **2009**, *74*, 5337.

(10) Liang, Z.; Zhao, J.; Zhang, Y. *J. Org. Chem.* **2010**, *75*, 170.

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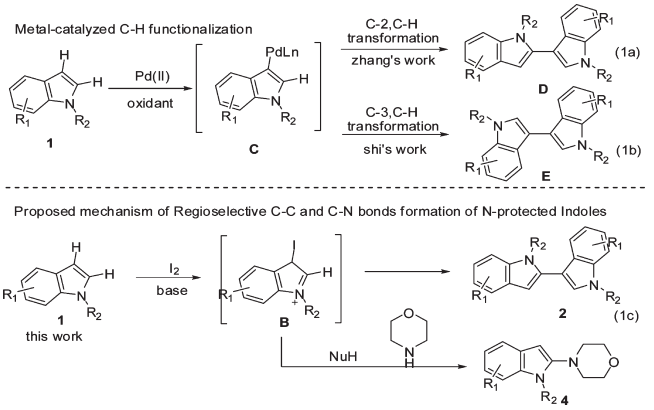
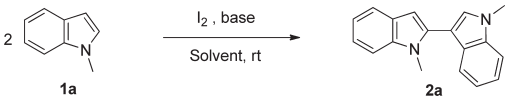
SCHEME 1. Design of Iodine-Mediated Tandem Reaction



expensive metal catalysts and high loading of metal oxidants and more attention has been payed to the direct C−C bond formation of indoles. However, examples of the direct functionalization of indoles with selective C−N bond formation are rarely reported. Therefore, a new and effective practical reaction system, involving mild, environmently benign, atom economic, and metal-free conditions, for the regioselective construction of C−C and C−N bonds of *N*-protected indole derivatives is still of high demand in modern organic synthesis.

In recent years, the electrophile-promoted tandem reactions have proven to be an effective method for the synthesis of heterocyclic compounds.[12] We and others have reported that the electrophilic cyclization[13] can be a very powerful tool for the preparation of a wide variety of interesting heterocyclic compounds, due to the efficient, mild, and clean reactions. Thus, electrophile-promoted tandem reactions continue to be an area of active research in the field of synthetic chemistry. In this communication, we report the first successful example of iodine-induced regioselective C−C and C−N bonds formation of *N*-protected indole derivatives affording 2,3′-biindoles **2** and 4-(1*H*-indol-2-yl)morpholines **4** (Scheme 1c), in which the key step is the attack of indoles or morpholine on 3-iodo-3*H*-indol-1-iums **B** triggered by iodonium at room temperature.

TABLE 1. Optimization of the Dimerization [a]



entry	I_2 (equiv)	additive (equiv)	solvent	time (h)	yield (%)[b]
1	1.0	$(CH_3)_3COK$	DCE	8	56
2	1.0	KOH	DCE	10	41
3	1.0	Na_2CO_3	DCE	12	–[c]
4	1.0	K_2CO_3	DCE	8	60
5	1.0	NaOAc	DCE	12	–[c]
6	1.0	$NaHCO_3$	DCE	8	83
7	1.0	$N(C_2H_5)_3$	DCE	12	–[c]
8	1.0	$NaHCO_3$	CH_2Cl_2	8	50
9	1.0	$NaHCO_3$	toluene	8	63
10	1.0	$NaHCO_3$	THF	12	–[c]
11	1.0	$NaHCO_3$	CH_3CN	12	–[c]
12	1.0	$NaHCO_3$	dioxane	12	–[c]
13	1.0	$NaHCO_3$	DMF	12	–[c]
14	1.0	$NaHCO_3$	NMP	12	–[c]
15	2.0	$NaHCO_3$	DCE	8	74
16	1.5	$NaHCO_3$	DCE	8	73
17	0.75	$NaHCO_3$	DCE	8	77
18	0.5	$NaHCO_3$	DCE	8	28
19	0	$NaHCO_3$	DCE	8	0

[a]Conditions: 0.5 mmol **1a** with 1-equiv of I_2 in 1,2-dichloroethane (DCE) (2.0 mL) at room temperature. [b]Isolated yield. [c]Mixture.

Initially, we started by using 0.5 mmol of *N*-methylindole **1a**, 1.0 equiv of I_2, and 2.0 equiv of $(CH_3)_3COK$ in 1,2-dichloroethane (DCE) at room temperature; to our delight, the desired product 1,1′-dimethyl-1*H*,1′*H*-2,3′-biindole **2a** was isolated in 56% yield after 8 h (Table 1, entry 1). To improve the reaction efficiency, the effect of bases was then investigated (entries 2−7). It was found that the weak base $NaHCO_3$ gave the best result and an 83% yield was obtained after 8 h (entry 6), whereas other bases, such as KOH, Na_2CO_3, NaOAc, and $N(C_2H_5)_3$, were less effective or ineffective. With an attempt to optimize the yield of the product, we further studied the influence of different reaction media (entries 10−14). From the results obtained, it can be seen that the use of CH_2Cl_2 and toluene gave an almost identical result, albeit with a lower yield (entries 8 and 9). THF, CH_3CN, 1,4-dioxane, DMF, and NMP proved to be less effective. Furthermore, the iodine loading was also investigated in this reaction, and the yield is good with anywhere from 0.75 to 2 equiv of I_2, but at 0.5 equiv it drops significantly (entries 15−18). We also carried out this reaction in the absence of I_2 but no expected product was observed (entry 19). With a series of detailed investigations mentioned above, the reaction conditions were eventually optimized as (entry 6) follows: 0.5 mmol of 1, 1.0 equiv of I_2, 2.0 equiv of $NaHCO_3$ as the base, DCE (2.0 mL) as solvent at room temperature.

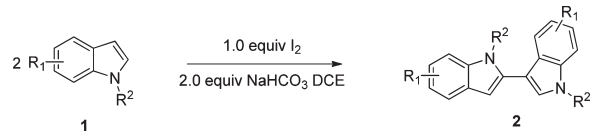
With the optimized conditions in hand, various representative *N*-protected indole derivatives **1a**−**q** were then subjected to the optimized conditions, as depicted in Table 2. Thus, a tandem carbon−carbon bond formation of *N*-protected indoles **1a**−**q** proceeded smoothly to provide corresponding 2,3′-biindoles in moderate to good yields, except **1f** and **1 h**. The molecular structure of the representative product

(11) Li, Y.; Wang, W.-H.; Yang, S.-D.; Li, B.-J.; Feng, C.; Shi, Z.-J. *Chem. Commun.* **2010**, *46*, 4553.

(12) For early studies on electrophilic cyclization reaction, see: (a) Ren, X.-F.; Turos, E. *Tetrahedron Lett.* **1993**, *34*, 1575. (b) Kitamura, T.; Takachi, T.; Kawasato, H.; Taniguchi, H. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1969. (c) Kitamura, T.; Kobayashi, S.; Taniguchi, H.; Hori, K. *J. Am. Chem. Soc.* **1991**, *113*, 6240. (d) Ten Hoedt, R. W. M.; Van Koten, G.; Noltes, J. G. *Synth. Commun.* **1977**, *7*, 61. (e) Sonoda, T.; Kawakami, M.; Ikeda, T.; Kobayashi, S.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1976**, 612. For selected examples, see: (f) Hessian, K. O.; Flynn, B. L. *Org. Lett.* **2003**, *5*, 4377. (g) Barluenga, J.; Vazque-Villa, H.; Ballesteros, A.; Gonzalez, J. M. *J. Am. Chem. Soc.* **2003**, *125*, 9028. (h) Yue, D.; Della Ca, N.; Larock, R. C. *Org. Lett.* **2004**, *6*, 1581. (i) Sniady, A.; Wheeler, K. A.; Dembinski, R. *Org. Lett.* **2005**, *7*, 1769. (j) Zhang, X.; Larock, R. C. *J. Am. Chem. Soc.* **2005**, *127*, 12230. (k) Tang, B.-X.; Tang, D.-J.; Tang, S.; Yu, Q.-F.; Zhang, Y.-H.; Liang, Y.; Zhong, P.; Li, J.-H. *Org. Lett.* **2008**, *10*, 1063. (l) Mohapatra, D. K.; Das, P. P.; Pattanayak, M. R.; Yadav, J. S. *Chem.—Eur. J.* **2010**, *16*, 2072. (m) Huo, Z.; Gridnev, I. D.; Yamamoto, Y. *J. Org. Chem.*, **2010**, *75*, 1266 and reference cited therein.

(13) (a) Bi, H.-P.; Guo, L.-N.; Duan, X.-H.; Gou, F.-R.; Huang, S.-H.; Liu, X.-Y.; Liang, Y.-M. *Org. Lett.* **2007**, *9*, 397. (b) Xie, Y.-X.; Liu, X.-Y.; Wu, L.-Y.; Han, Y.; Zhao, L.-B.; Fan, M.-J.; Liang, Y.-M. *Eur. J. Org. Chem.* **2008**, 1013. (c) Wen, S.-G.; Liu, W.-M.; Liang, Y.-M. *J. Org. Chem.* **2008**, *73*, 4342. (d) Xie, Y.-X.; Yan, Z.-Y.; Qian, B.; Deng, W.-Y.; Wu, L.-Y.; Liu, X.-Y.; Liang, Y.-M. *Chem. Commun.* **2009**, 5451. (e) Xie, Y.-X.; Yan, Z.-Y.; Wang, D.-Z.; Wu, L.-Y.; Qian, B.; Liu, X.-Y.; Liang, Y.-M. *Eur. J. Org. Chem.* **2009**, 2283. (f) Ji, K.-G.; Zhu, H.-T.; Yang, F.; Shu, X.-Z.; Zhao, S.-C.; Shaukat, A.; Liu, X.-Y.; Liang, Y.-M. *Chem.—Eur. J.* **2010**, *16*, 1615. (g) Ji, K.-G.; Zhu, H.-T.; Yang, F.; Shaukat, A.; Xia, X.-F.; Yang, Y.-F.; Liu, X.-Y.; Liang, Y.-M. *J. Org. Chem.* **2010**, *75*, 5670.

TABLE 2. Iodine-Induced Regioselective C−C Bond Formation of *N*-Protected Indoles toward 2-(1*H*-indol-3-yl)-1*H*-indole 2[a]



1 2

Entry	Indole	R^1	R^2	Products **2**	Yield(%)[b]
1	**1a**	H	Me	**2a**	80
2	**1b**	4- Me	Me	**2b**	77
3	**1c**	5-Me	Me	**2c**	58
4	**1d**	5-OCH_3	Me	**2d**	84
5	**1e**	7- Me	Me	**2e**	62
6	**1f**	5-Br	Me	**2f**	45
7	**1g**	6-$COOCH_3$	Me	**2g**	trace[c]
8	**1h**		Me	**2h**	NR
9	**1i**	H	Bn	**2i**	83
10	**1j**	4- Me	Bn	**2j**	62
11	**1k**	5-Me	Bn	**2k**	70
12	**1l**	5-OCH_3	Bn	**2l**	63
13	**1m**	7- Me	Bn	**2m**	59
14	**1n**	4- Me	Allyl	**2n**	68
15	**1o**	5-Me	Allyl	**2o**	61
16	**1p**	5-OCH_3	Allyl	**2p**	60
17	**1q**			**2q**	NR

[a]Conditions: 0.5 mmol **1a** with 0.5 mmol of I_2, 1.0 mmol of $NaHCO_3$ in 1,2-dichloroethane (DCE, 2.0 mL) at room temperature. [b]Isolated yield. [c]Only a trace amount of **2g** was observed after 24 h.

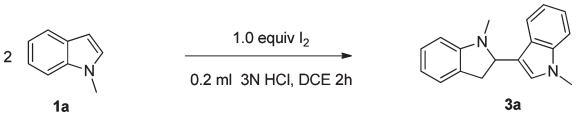
2a was determined by X-ray crystallography. The reaction can tolerate a variety of functional groups at the 4, 5, and 7 positions of *N*-protected indoles. Electron-rich groups showed better results than electron-withdrawing groups in this dimerization (**1d** vs **1f**). Substrate **1g** with an electron-withdrawing R^1 group only gave a trace amount of desired product **2g** (entry 7). When **1h** was subjected to the optimized conditions, no desired product was obtained (entry 8).To explore more the scope of this reaction, different *N*-protected R^2 groups were also investigated (entries 9−18). It was found that under the optimized conditions, the substrates **1i**−**q** were transferred into 2,3′-biindoles **2i**−**q** in moderate to good yield (entries 9−16). Unfortunately, substrates like **1q** gave no reaction (entry 17).

Furthermore, we also investigated the dimerization of 0.5 mmol of **1a**, 1.0 equiv of I_2, and 2.0 equiv of HCl; fortunately, 1,1′-dimethyl-2′,3′-dihydro-1*H*,1′*H*-2,3′-biindole **3a** was obtained in 76% yield (Scheme 2). The molecular structure of the representative product **3a** was determined by X-ray crystallography. In 1996, Anna Berlin and co-workers reported the same result, which is an acid-catalyzed reaction of *N*-protected indole toward 3-(2-indolinyl)indole through Smith's mechanism.[14]

As we know, the regioselective C−N bond formation of *N*-protected indoles is very important in modern organic synthesis, especially for the synthesis of alkaloids. So, we investigated the reaction of a wide range of *N*-protected indole derivatives with morpholine in the presence of iodine.

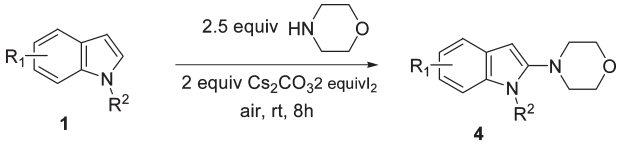
(14) Berlin, A.; Canavesi, A *Tetrahedron* **1996**, *52*, 7947.

SCHEME 2. Synthesis 1,1′-Dimethyl-2′,3′-dihydro-1*H*,1′*H*-2,3′-biindole 3a from *N*-Protected Indole 1a



1a 3a

TABLE 3. Iodine-Induced Regioselective C−N Bond Formation of N-Protected Indoles toward 4-(1*H*-Indol-2-yl)morpholines 4[a]



1 4

entry	indole	R^1	R^2	products**4**	yield[b] (%)
1	**1a**	H	Me	**4a**	74
2	**1b**	4- Me	Me	**4b**	60
3	**1c**	5- Me	Me	**4c**	50
4	**1e**	7- Me	Me	**4e**	55
5	**1p**	5-OCH_3	Allyl	**4p**	54
6	**1j**	4- Me	Bn	**4j**	70

[a]Conditions: 0.5 mmol **1a**, 1.25 mmol of morpholine with 1.0 mmol of I_2, 1.0 mmol of $NaHCO_3$ in acetonitrile (2.0 mL) at room temperature. [b]The molecular structure of the representative product **4a** was determined by X-ray crystallography.

To our surprise, various 4-(1*H*-indol-2-yl)morpholines **4** were obtained in good to excellent yield, as depicted in Table 3.

In summary, we have developed an efficient method for the regioselective C−C and C−N bonds formation of *N*-protected indole derivatives to prepare 2,3′-biindoles **2** and 4-(1*H*-indol-2-yl)morpholines **4** by iodine in moderate to good yield. Further functionalization of indoles and other heterocycles are the future goals of our research group.

Experimental Section

General Procedure for the Synthesis of 2-(1*H*-indol-3-yl)-1*H*-indole Derivatives 2. A mixture of indole derivative (0.5 mmol), $NaHCO_3$ (84 mg, 1 mmol), I_2 (254 mg, 1 mmol), and 1,2-dichloroethane (2 mL) was stirred at room temperature for 8 h. The reaction mixture was quenched with a saturated solution of $Na_2S_2O_3$ (5 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic phases were washed with brine (45 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography, using a mixture of petrolium ether and ethyl acetate (15:1) as eluent, to afford the corresponding products **2a** as a white solid (83% yield): mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.71 (d, J = 8.0 Hz,1H), 7.64 (d, J = 7.6 Hz, 1H), 7.12−7.41 (m, 7H), 6.62 (s, 1H), 3.89 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 138.0, 137.0, 135.1, 128.4, 127.7, 122.4, 121.0, 120.4, 120.2, 120.1, 119.6, 109.6, 109.4, 107.4, 101.4, 33.0, 31.0; IR (neat, cm^{-1}) 2925, 2854, 1462, 740.

General Procedure for the Synthesis of 1,1′-Dimethyl-2′,3′-dihydro-1*H*,1′*H*-2,3′-biindole 3a. A mixture of 1-methyl-1*H*-indole (0.5 mmol), HCl (3 N, 0.2 mL), I_2 (254 mg, 1 mmol), and dichloroethane (2 mL) was stirred at room temperature for 2 h. The reaction mixture was quenched with a saturated solution of $Na_2S_2O_3$ (5 mL) and extracted with ethyl acetate (3 × 25 mL). The combined organic phases were washed with brine (45 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography, using a mixture of petroleum ether and ethyl acetate (15:1) as

eluent, to afford the corresponding products **3a** as a white solid (76% yield): mp 112−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.73 (d, J = 7.6 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H), 7.26−7.30 (m, 1H), 7.10−7.21 (m, 4H), 6.76 (t, J = 7.2 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 4.66 (dd, J = 11.2 Hz, 8.8 Hz, 1H), 3.82 (s, 3H), 3.35 (dd, J = 8.8 Hz, 15.6 Hz, 1H), 3.24 (dd, J = 11.2 Hz, 15.6 Hz, 1H), 2.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 153.4, 137.5, 129.2, 127.5, 127.3, 126.8, 124.0, 121.8, 120.1, 119.0, 117.7, 115.2, 109.3, 107.1, 64.7, 37.9, 34.1, 32.7; IR (neat, cm^{-1}) 2925, 1462, 748; HRMS (M + H) calcd for $C_{18}H_{18}N_2$ (MP) 263.1543, found 263.1545.

General Procedure for the Synthesis of 4-(1*H*-indol-2-yl)morpholines 4. A mixture of indole derivative (0.5 mmol), morpholine (128 mg, 1.25 mmol), Cs_2CO_3 (325 mg, 1 mmol), I_2 (254 mg, 1 mmol), and acetonitrile (2 mL) was stirred at room temperature for 8 h. The reaction mixture was quenched with a saturated solution of $Na_2S_2O_3$ (5 mL) and extracted with ethyl acetate (3×25 mL). The combined organic phases were washed with brine (45 mL), dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by flash column chromatography, using a mixture of petroleum ether and ethyl acetate (10:1) as eluent, to afford the corresponding products **4a** as a white solid (74% yield): ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.47 (d, J = 7.6 Hz, 1H), 7.20−7.05 (m, 3H), 5.91 (s, 1H), 3.84 (t, J = 4.8 Hz, 4H), 3.57 (s, 3H), 2.97 (t, J = 4.8 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$, TMS) δ 149.9, 135.2, 127.4, 120.3, 119.5, 119.3, 108.6, 86.9, 66.8, 52.7, 28.9; IR (neat, cm^{-1}) 2838, 1547, 1114, 741; HRMS (M+H) calcd for $C_{13}H_{16}ON_2$ (MP) 217.1335, found 217.1338.

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Supporting Information Available: The detailed experimental procedure and copies of ^{1}H NMR and ^{13}C NMR spectra of all compounds and X-ray data of **2a**, **3a**, and **4a** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.