Further Investigations into the Regioselectivity of 6,7-Indole Aryne Cycloadditions with 2-Substituted Furans: Remarkable Contrasteric Preference Depends on Pyrrole and Benzene Ring Substitution

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This paper is warmly dedicated to Professor Scott Denmark on the occasion of his 60th birthday.

Abstract: A series of related 6,7-dibromoindole compounds were prepared to study the effects of pyrrole and benzene ring substitution patterns on the regioselectivity of 6,7-indole aryne cycloadditions with 2-*tert*-butylfuran. The arynes were generated by our metal–halogen exchange/elimination protocol. The results of this investigation reveal that substitution at the 3-position on the indole ring in particular results in remarkable regiocontrol that favored the contrasteric products. Aromatic conjugation at this site significantly enhanced this effect. However, the presence of most 4- or 5-substituents generally resulted in markedly reduced selectivity. Exceptions in this latter series included the 4-ethyl and 4-iodo cases both of which also gave predominantly contrasteric products even in the absence of a beneficial C-3 substituent.

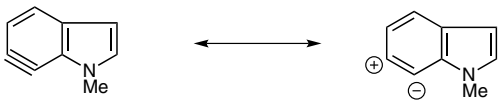
Key words: alkaloids, arynes, cycloaddition, indoles, regioselectivity

Arynes are becoming a main theme and an increasingly common and versatile functional group in organic synthesis.[1] The Buszek laboratories pioneered the discovery, development, and application of indole arynes (indolynes),[2] benzofuran arynes (benzofuranynes),[3] and benzothiophene arynes (benzothiophenynes)[4] which we began reporting in 2007. Since that time we designed the first general route to all of these arynes associated with the benzene side of the aromatic nucleus via facile and selective metal–halogen exchange and elimination of their corresponding *o*-dibromo systems.[2a]

The practical value of this powerful new methodology is already evident. One application in particular, namely cycloadditions with 6,7-indole arynes, became a key strategy in the total synthesis of several important 6,7-benzannulated indole alkaloid natural products, including the trikentrins and the herbindoles,[2b,d,f] and represented the first use of this tactic in natural products total synthesis. Additional efforts that combined 6,7-indole aryne cycloadditions with various cross-coupling reactions in 4,6,7-tribromoindoles culminated in the first benzannulated polycyclic indole libraries.[5] The value of the indole aryne chemistry was further validated by numerous subsequent contributions from the Garg[6] and Lautens[7] laboratories.

During the course of these investigations we found a remarkable preference in the 6,7-indole aryne cycloadditions with 2-substituted furans for the more sterically crowded or contrasteric regioisomer **2** (Table 1). By contrast no regiochemical preference was observed for the other two indole arynes, namely, the 4,5- and 5,6-indole arynes. An *ab initio* computational study by Buszek and Cramer using DFT methods revealed that the 6,7-indole aryne can be viewed appropriately as a highly polarized bond in the manner shown (Scheme 1), with the nucleophilic center at C-7, and as such, cycloadditions at this site impart substantial asynchronous electrophilic substitution character in the initial bond forming step in the cycloaddition process.[2e] The calculations predicted, *inter alia*, that a similar trend would be observed in the corresponding benzofuran and benzothiophene aryne systems, and that prediction has now been confirmed experimentally.[3,4]

The original regiochemical preference with 6,7-indole arynes was made with *N*-methyl-6,7-dibromo-3-phenylindole (**1**), which exhibited a remarkable 49:1 preference for the contrasteric isomer. The decision to use a 3-phenyl substituent in these studies was fortuitous since it was subsequently found that in cases in which a 3-substituent is absent, there is sharply diminished regiocontrol. These curious and surprising results prompted us to embark on an empirical study to identify the type and position of various substituents on the pyrrole and benzene sides of the indole nucleus responsible for regiocontrol in 6,7-indole aryne cycloadditions. The results are now presented herewith.



4 5

Scheme 1

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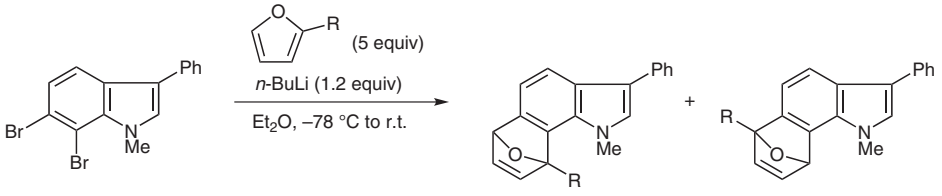
Table 1 Regioselective 3-Phenyl-6,7-indole Aryne Cycloadditions with 2-Substituted Furans[a]



1 2 3

Entry	R	2	3	Yield (%)
1	Me	4	1	89
2	Et	5.3	1	90
3	*i*-Pr	15.7	1	88
4	*t*-Bu	49	1	91
4	Ph	>99	<1	92
5	SO_2Ph	<1	>99	83

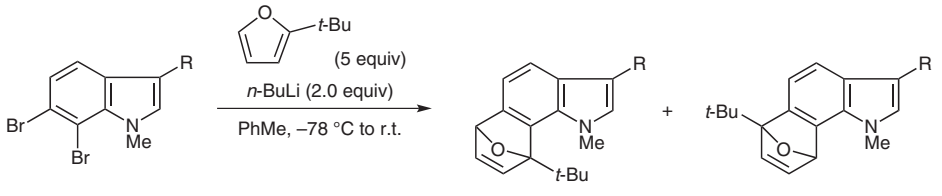
[a] Reference 2e.

We first examined the effect of substituted phenyl and other groups at the C-3 position. The corresponding indole aryne precursors were prepared as described previously, using the Fischer,[2a] the Bartoli,[8] or the Leimgruber–Batcho[9] indole synthetic routes. The arynes were generated via metal–halogen exchange with a slight excess of *n*-BuLi in either diethyl ether or toluene at –78 °C in the presence of excess 2-*tert*-butylfuran.[10] The indole aryne is then formed upon warming to about –35 °C. The reaction mixture was quenched after reaching room temperature. The results are shown in Table 2.

It can be seen that the more electron-rich 4-methoxyphenyl group gave within the limits of our analysis and detection exclusively (>99:1) the contrasteric product **7** (R = 4-$MeOC_6H_4$, Table 2, entry 2). None of the other regioisomer **8** could be detected by NMR analysis. This is a significant increase over a simple phenyl group. On the other hand, the less electron-rich 4-fluorophenyl case (entry 3) exhibited somewhat lower regiocontrol (15.7:1) versus the phenyl example (49:1). The effect of these or other substituents at the *ortho* and *meta* positions were not included in this study. However, there appears from just these limited examples a definitive trend by which increasingly electron-rich aryl groups at C-3 gave the greatest degree of regiocontrol.

The issue of aromatic conjugation at the C-3 position was next examined. Here a benzyl group at that site (entry 4) gave a substantially reduced 10:1 ratio of products com-

Table 2 Regioselective 3-Substituted 6,7-Indole Aryne Cycloadditions with 2-*tert*-Butylfuran

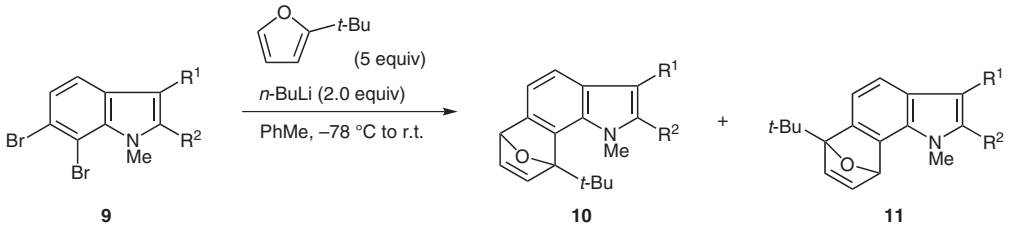


6 7 8

Entry	R	7	8	Yield (%)
1[a]	Ph	49	1	91
2	4-$MeOC_6H_4$	>99	<1	76
3	4-FC_6H_4	15.7	1	59
4	CH_2Ph	10	1	58
5	Et	6.1	1	64
6	H	3.0	1	60

[a] Reference 2e.

Table 3 Regioselective 2-Phenyl- and 2,3-Diphenyl-6,7-indole Aryne Cycloadditions with 2-*tert*-Butylfuran



9 **10** **11**

Entry	R^1	R^2	**10**	**11**	Yield (%)
1[a]	Ph	H	49	1	91
2	H	Ph	9.1	1	61
3	Ph	Ph	6.7	1	62
4[b]	H	H	3.0	1	60

[a] Reference 2e.
[b] Table 2, entry 6.

pared to phenyl, indicating that conjugation appears to favor the contrasteric product to a significant degree. However, the incorporation of just a simple alkyl group, for example, ethyl (entry 5), still gave a reasonable, albeit further diminished, degree of regiocontrol (6.1:1). It is apparent from these examples that any substitution at the indole C-3 position benefits the regiochemistry in 2-substituted furan cycloadditions. Apparently the overall electron density at this site, either by conjugative or inductive effects, is the key for imparting regioselectivity. This point is further supported by entry 6 in which no substitution at C-3 results in the smallest proportion of the contrasteric isomer, or just 3.0:1.

The effect of phenyl substitution at the other pyrrole position, namely C-2, was next examined (Table 3). In this case (Table 3, entry 2) it was found that the regioselectivity favoring **10** was more than 5 times lower (9.1:1) than having the same substituent at C-3, and was in fact similar to having a nonconjugated substituent at C-3. Interestingly, incorporating conjugated phenyl group at both C-2 and C-3 (entry 3) further diminished the selectivity (6.7:1).

This observation might be rationalized by reasonably assuming that steric hindrance between the two phenyl groups at the adjacent positions on the pyrrole prevented effective conjugation at C-3 and thus reduced any beneficial effect of conjugation at that position. Furthermore, it is likely that the electronic contribution by the C-2 phenyl is primarily if not exclusively inductive since planarity with the pyrrole is almost certainly precluded. However, even in this case, the overall effect on regiocontrol was again better than having no substitution at both sites.

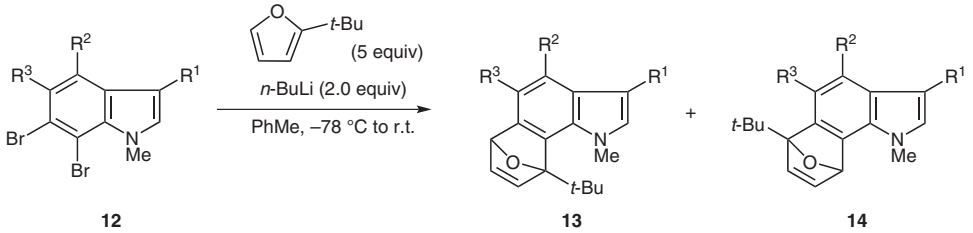
With a reasonable understanding of the electronic contributions to regiocontrol from the C-2 and C-3 sites, we turned our attention to studying substituent effects on the benzene side of the indole ring. Our previous synthetic work with the trikentrin natural products gave us ready access to 4,6,7- and 5,6,7-tribromoindoles.[2b,f] We found that in both of these cases metal–halogen exchange occurs exclusively at the C-7 position, as confirmed by low temperature quenching with water.[2f] Thus, it was possible to generate the 6,7-indole aryne without untoward reaction at the remaining C-4 or C-5 bromine. Accordingly, these examples were chosen to investigate the effects of bromine substitution at C-4 and C-5, with and without electronic contributions from a C-3 phenyl group (Table 4).

From this data, it can be seen that having a bromine substituent at C-4 (entry 1) gave about the same ratio of cycloaddition products **13**:**14** as when no other substituent is present (cf. Table 2, entry 6), or about 3.4:1 and 3.0:1, respectively. The reaction again favored the contrasteric product. The presence of a phenyl group at C-3 only slightly mitigated this effect (entry 2), and gave the regioisomer **13** in a modestly improved 4.6:1 distribution. However, a much more dramatic effect was seen at the C-5 position with the bromine now adjacent to the electrophilic site of the indole aryne (entry 3). In this case, virtually no selectivity was observed (1.4:1), and even the presence of aromatic conjugation at C-3 (entry 4) had no impact, with the same ratio of isomers again observed.

The synthetic challenges associated with the introduction of a wide variety of substituents at the C-5 position on the indole ring are not trivial,[11] so the foregoing examples are necessarily limited to bromine for now. However, placing various groups at C-4, while still a difficult task, is at least synthetically tractable. Thus, a final set of cases to glean some further insight into the factors controlling 6,7-indole aryne regiochemistry from the benzene side of the nucleus was examined (Table 5).

An expanded set of halogens was prepared to gauge the impact of electronegative substituents at C-4. The 4-fluoro example (entry 1) gave the contrasteric isomer **16** in only a 2.3:1 ratio, compared to 3.4:1 with bromine. The much less electronegative iodine (entry 3), however, resulted in a substantially improved 15.7:1 distribution even

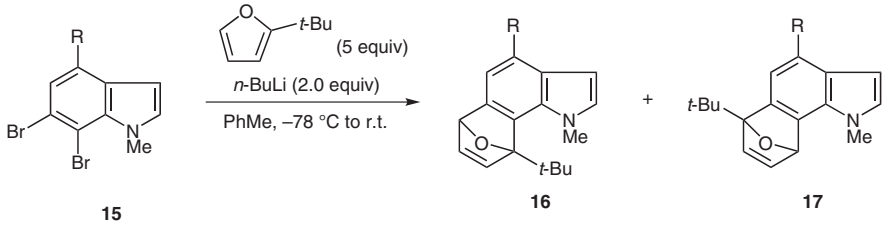
Table 4 Regioselective 4-Bromo-, 5-Bromo-, 3-Phenyl-4-bromo-, and 3-Phenyl-5-bromo-6,7-indole Aryne Cycloadditions with 2-*tert*-Butylfuran



Entry	R^1	R^2	R^3	**13**	**14**	Yield (%)
1[a]	H	Br	H	3.4	1	76
2	Ph	Br	H	4.6	1	76
3[b]	H	H	Br	1.4	1	68
4	Ph	H	Br	1.4	1	62

[a] Reference 5a.
[b] Reference 2f.

Table 5 Regioselective 4-Substituted 6,7-Indole Aryne Cycloadditions with 2-*tert*-Butylfuran

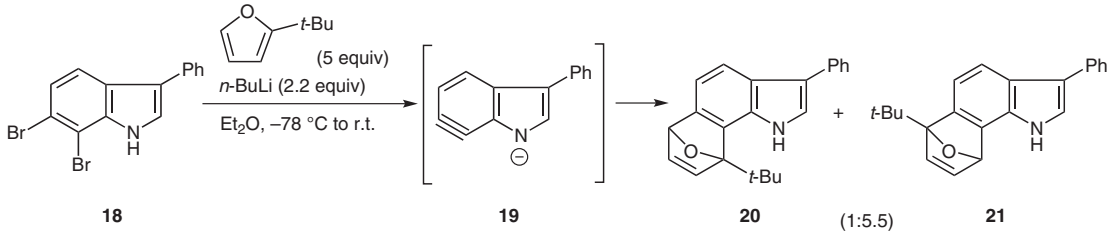


Entry	R	**16**	**17**	Yield (%)
1	F	2.3	1	71
2[a]	Br	3.4	1	76
3	I	15.7	1	65
4[b]	Et	11.5	1	63

[a] Table 4, entry 1; reference 5a.
[b] Reference 2b.

without a C-3 phenyl group. Surprisingly, the presumably more inductively electron-rich ethyl alkyl group was less effective in determining the isomeric outcome (entry 4) and gave the products **16** and **17** in a reduced but still respectable 11.5 distribution. Apparently there is a subtle but still poorly understood interplay between conjugative and inductive effects at least with the halogens that render iodine especially effective in controlling regiochemistry absent even the presence of substituents at C-3.

A further investigation to determine the effect of having various protecting groups on the indole nitrogen on the course of the 6,7-indole aryne cycloaddition is also underway. However, we previously noted that *N*-sulfonyl groups apparently preclude any metal–halogen exchange



Scheme 2

and consequently aryne formation by this method. Curiously, when no protecting group is used, the observed regiochemistry is reversed, favoring the opposite regioisomer to some degree (Scheme 2).

In summary, it has been demonstrated that having a substituent at either position of the pyrrole ring of the indole nucleus substantially enhances the regiochemistry in 6,7-indole aryne cycloadditions with 2-*tert*-butylfuran and greatly favors the contrasteric product. However, substitution on the benzene side of the aromatic system results in most cases in a significant diminution of regiocontrol. Except in the notable examples of iodine and alkyl group substitution at C-4, having an additional group at the C-3 site generally does not mitigate the effect of benzene substitution.

The results from the previous 6,7-dehydrobenzofuran cycloaddition studies[3] in which a high degree of regiocontrol is seen favoring the corresponding contrasteric product (e.g., 11.5:1 for 2-*tert*-butylfuran; >99:1 for 2-phenylfuran), even without having substitution anywhere else on its aromatic nucleus, suggests that the indole system has unique electronic properties that are highly sensitive to aromatic substitution patterns. The origin of these differences is currently being investigated both computationally and experimentally by this laboratory and will be reported in due course.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were performed in $CDCl_3$ unless otherwise noted with reference to residual solvent at δ = 7.26 and 77.0, respectively. Melting points when reported are uncorrected. Unless otherwise noted all commercially available starting materials were used as received. Alkyllithiums were titrated against butan-2-ol in anhyd THF with 1,10-phenanthroline as an indicator prior to use. THF was distilled from sodium and benzophenone under N_2 prior to use. Toluene was distilled from CaH_2 under N_2 prior to use. Temperatures of –78 °C were obtained through the use of a dry ice/acetone cold bath. All reactions were carried out under an inert atmosphere unless otherwise noted.

_N_-Methyl-6,7-dibromo-3-phenylindole (1) and Its Benzannulated Cycloaddducts 2 and 3

The preparation of the aryne precursor *N*-methyl-6,7-dibromo-3-phenylindole (**1**) and the methods for its aryne generation via metal–halogen exchange have been reported.[2a] The physical and spectral data for the cycloadducts **2** and **3** have likewise appeared previously.[2e]

3-Substituted 6,7-Dibromoindoles; 6,7-Dibromo-3-ethyl-1*H*-indole; Typical Procedure

The 3-substituted 6,7-dibromoindoles were generally prepared via the Fischer indole route. In a tube was added 2,3-dibromophenylhydrazine (500 mg 1.88 mmol). This was dissolved in EtOH (20 mL). To the stirred solution was added butyraldehyde (0.20 mL, 2.26 mmol, 1.20 equiv). The tube was sealed and the mixture was heated to 100 °C for 3 h, then cooled to r.t. and the contents were concentrated under reduced pressure. The residue was diluted with *tert*-butyl methyl ether (TBME, 25 mL) and the organic layer was washed with aq $NaHCO_3$ (10 mL), H_2O (10 mL), and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified via flash column chromatography on silica gel using 20% TBME in hexanes as eluent to give 6,7-dibromo-3-ethyl-1*H*-indole as a yellow oil; yield: 273 mg (48%).

^{1}H NMR: δ = 8.04 (br s, 1 H), 7.34 (d, *J* = 7.9 Hz, 1 H), 7.22 (d, *J* = 7.9 Hz, 1 H), 7.09 (s, 1 H), 2.68 (q, *J* = 8.2 Hz, 2 H), 1.25 (t, *J* = 8.2 Hz, 3 H).

^{13}C NMR: δ = 136.16, 126.92, 123.84, 121.57, 120.36, 119.02, 117.15, 106.98, 18.36, 14.35.

HRMS (EI): *m*/*z* calcd for $C_{10}H_9Br_2N$: 300.9101; found: 300.9111.

6,7-Dibromo-3-(4-methoxyphenyl)-1*H*-indole

Obtained as above from the reaction between 2,3-dibromophenylhydrazine and 2-(4-methoxyphenyl)acetaldehyde; yield: 65 mg (62%); yellow oil.

^{1}H NMR: δ = 8.08 (br s, 1 H), 7.79 (s, 1 H), 7.61 (dd, *J* = 2.0, 6.8 Hz, 2 H), 7.53 (dd, *J* = 2.5, 7.2 Hz, 1 H), 7.12 (m, 1 H), 6.92 (dd, *J* = 2.0, 6.8 Hz, 2 H), 3.84 (s, 3 H).

^{13}C NMR: δ = 158.41, 136.34, 128.74, 128.62, 126.94, 124.78, 122.73, 122.04, 119.88, 117.56, 114.32, 113.89, 55.34.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}Br_2NO$: 378.9207; found: 378.9205.

6,7-Dibromo-3-(4-fluorophenyl)-1*H*-indole

Obtained as above from the reaction between 2,3-dibromophenylhydrazine and 4-fluorophenylacetaldehyde as an orange oil; yield: 263 mg (38%).

^{1}H NMR: δ = 8.46 (br s, 1 H), 7.65 (dd, *J* = 0.7, 8.4 Hz, 1 H), 7.55 (dd, *J* = 5.5, 8.9 Hz, 2 H), 7.41 (d, *J* = 8.4 Hz, 1 H), 7.36 (d, *J* = 2.7 Hz, 1 H), 7.16 (app t, *J* = 8.9 Hz, 2 H).

^{13}C NMR: δ = 162.98, 160.53, 130.49 (d, *J* = 3.7 Hz), 129.07 (d, *J* = 8.1 Hz), 125.41, 125.10, 122.43, 119.71, 119.01, 117.87, 115.91 (d, *J* = 22.1 Hz), 107.52.

HRMS (EI): *m*/*z* calcd for $C_{14}H_8FBr_2N$: 366.9007; found: 366.9000.

3-Benzyl-6,7-dibromo-1*H*-indole

Obtained as above from the reaction between 2,3-dibromophenylhydrazine and 2-phenylpropionaldehyde as a brown oil; yield: 281 mg (40%).

^{1}H NMR: δ = 8.12 (br s, 1 H), 7.32–7.20 (m, 7 H), 6.94 (s, 1 H), 4.06 (s, 2 H).

^{13}C NMR: δ = 140.37, 136.21, 128.48, 128.40, 127.06, 126.08, 124.13, 123.39, 119.34, 117.33, 117.23, 107.07, 31.43.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}Br_2N$: 362.9258; found: 362.9261.

6,7-Dibromo-1*H*-indole

Prepared via the Bartoli indole synthesis as follows: In a 250 mL flame-dried round-bottom flask under argon was dissolved 1,2-dibromo-3-nitrobenzene (489 mg, 1.74 mmol) in THF (20 mL) and the solution cooled to –40 °C. To this stirred solution was added in one portion vinylmagnesium bromide (10.4 mL, 1 M, 10.4 equiv). The reaction mixture was stirred at –40 °C for 1 h, then quenched with aq NH_4Cl (100 mL) and the flask warmed to r.t. The mixture was extracted with Et_2O (3 × 50 mL) and the combined organic layers washed with H_2O (1 × 50 mL) and brine (1 × 25 mL), then dried ($MgSO_4$). The solution was filtered and concentrated under reduced pressure. The residue was purified via flash chromatography on silica gel using 10% EtOAc in hexanes to afford a white solid; mp 93.6–94.3 °C; yield: 230 mg (47%).

^{1}H NMR: δ = 8.36 (br s, 1 H), 7.45 (d, *J* = 8.3 Hz, 1 H), 7.34 (d, *J* = 8.3 Hz, 1 H), 7.24 (app t, *J* = 2.8 Hz, 1 H), 6.62 (dd, *J* = 2.0, 3.2 Hz, 1 H).

^{13}C NMR: δ = 135.78, 127.43, 125.26, 124.64, 120.78, 117.27, 107.07, 104.14.

HRMS (EI): *m*/*z* calcd for $C_8H_5Br_2N$: 272.8789; found: 272.8790.

N-Methylated Indoles; 6,7-Dibromo-3-(4-methoxyphenyl)-1-methyl-1*H*-indole (6; R = 4-MeOC$_6$H$_4$); Typical Procedure

In a 50 mL flame-dried round-bottomed flask under argon was added 6,7-dibromo-3-(4-methoxyphenyl)-1*H*-indole (300 mg, 0.79 mmol). This was dissolved in anhyd THF (20 mL) and to this solution was added dry NaH (38 mg, 1.56 mmol, 2.0 equiv). The solution was stirred at r.t. for 30 min, and then MeI (0.10 mL, 1.56 mmol, 2.0 equiv) was added via syringe. The resulting solution was stirred for 1 h, and then quenched by dropwise addition of aq NH_4Cl (25 mL). The aqueous mixture was extracted with Et_2O (3 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified via flash column chromatography on silica gel using 20% TBME in hexanes as eluent to give 6,7-dibromo-3-(4-methoxyphenyl)-1-methyl-1*H*-indole as a yellow oil; yield: 268 mg (86%).

^{1}H NMR: δ = 7.60 (d, *J* = 8.6 Hz, 1 H), 7.45 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.6 Hz, 1 H), 7.05 (s, 1 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 4.19 (s, 3 H), 3.86 (s, 3 H).

^{13}C NMR: δ = 158.34, 130.05, 129.68, 128.82, 128.09, 126.67, 124.81, 119.88, 119.82, 116.40, 114.28, 106.79, 55.32, 37.77.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{13}Br_2NO$: 392.9364; found: 392.9366.

6,7-Dibromo-3-(4-fluorophenyl)-1-methyl-1*H*-indole (6; R = 4-FC$_6$H$_4$)

Obtained as above from 6,7-dibromo-3-(4-fluorophenyl)-1*H*-indole as a colorless oil; yield: 42 mg (92%).

^{1}H NMR: δ = 7.56 (d, *J* = 8.6 Hz, 1 H), 7.49 (m, 2 H), 7.38 (d, *J* = 8.6 Hz, 1 H), 7.14 (app t, *J* = 8.6 Hz, 2 H), 7.09 (s, 1 H), 4.21 (s, 3 H).

^{13}C NMR: δ = 162.85, 160.41, 134.98, 130.02 (d, *J* = 3.7 Hz), 129.14 (d, *J* = 8.1 Hz), 128.24, 127.85, 125.05, 120.01, 119.63, 115.71 (d, *J* = 21.4 Hz), 106.92, 37.85.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}FBr_2N$: 380.9164; found: 380.9169.

6,7-Dibromo-1-methyl-3-benzyl-1*H*-indole (6; R = CH$_2$Ph)

Obtained as above as an orange solid; yield: 394 mg (98%); mp 78–81 °C.

^{1}H NMR: δ = 7.35–7.24 (m, 7 H), 6.67 (s, 1 H), 4.03 (s, 2 H), 4.00 (s, 3 H).

^{13}C NMR: δ = 140.37, 134.59, 130.77, 129.26, 128.40, 128.27, 125.95, 123.87, 119.33, 119.14, 113.85, 106.38, 37.15, 30.94.

HRMS (EI): *m*/*z* calcd for $C_{16}H_{13}Br_2N$: 376.9415; found: 376.9418.

6,7-Dibromo-3-ethyl-1-methyl-1*H*-indole (6; R = Et)

Obtained as above from 6,7-dibromo-3-ethyl-1*H*-indole as a yellow oil; yield: 343 mg (82%).

^{1}H NMR: δ = 7.35 (d, *J* = 8.2 Hz, 1 H), 7.31 (d, *J* = 8.2 Hz, 1 H), 6.76 (s, 1 H), 4.09 (s, 3 H), 2.71 (q, *J* = 7.4 Hz, 2 H), 1.31 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR: δ = 134.63, 129.41, 129.19, 123.65, 119.24, 118.97, 116.98, 106.38, 37.21, 17.77, 14.30.

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}Br_2N$: 314.9258; found: 314.9264.

6,7-Dibromo-1-methyl-1*H*-indole (6; R = H)

Obtained as above from 6,7-dibromo-1*H*-indole as a yellow oil; yield: 173 mg (72%).

^{1}H NMR: δ = 7.38 (d, *J* = 8.4 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 1 H), 6.98 (d, *J* = 3.2 Hz, 1 H), 6.40 (d, *J* = 3.2 Hz, 1 H), 4.15 (s, 3 H).

^{13}C NMR: δ = 134.43, 132.54, 130.14, 124.58, 121.03, 119.37, 106.57, 101.18, 37.73.

HRMS (EI): *m*/*z* calcd for $C_9H_7Br_2N$: 286.8945; found: 286.8950.

Indole Aryne Generation from *o*-Dibromoindoles and Trapping with 2-Substituted Furans; 9-(*tert*-Butyl)-3-ethyl-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (7) (Table 2, Entry 5); Typical Procedure

A flame-dried 50 mL round-bottomed flask was charged with anhyd toluene (20 mL), 6,7-dibromo-3-ethyl-1-methyl-1*H*-indole (109 mg, 0.35 mmol), and 2-*tert*-butylfuran (0.25 mL, 1.75 mmol, 5 equiv) under an atmosphere of argon, and the resulting mixture was cooled to –78 °C. To this cold solution was added *n*-BuLi (16 μL, 2.6 M, 0.42 mmol, 1.2 equiv) in toluene dropwise, and the solution was stirred at –78 °C for 30 min. The cold bath was removed and the solution was allowed to warm slowly to r.t. over 1 h. The reaction was quenched with aq NH_4Cl (25 mL) and the aqueous layer was extracted with Et_2O (3 × 25 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using 20% TBME in hexanes as eluent; yield: 53 mg (55%); yellow oil. All purified products were obtained as solids, or clear to slightly colored oils or foams (Table 2).

^{1}H NMR: δ = 7.30 (d, *J* = 7.4 Hz, 1 H), 7.19 (m, 2 H), 7.10 (d, *J* = 5.5 Hz, 1 H), 6.75 (s, 1 H), 5.79 (d, *J* = 1.5 Hz, 1 H), 3.94 (s, 3 H), 2.78 (q, *J* = 7.8 Hz, 2 H), 1.53 (s, 9 H), 1.38 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR: δ = 147.83, 145.80, 142.62, 134.66, 133.93, 130.75, 129.74, 118.16, 115.55, 112.66, 104.41, 81.83, 39.41, 33.33, 29.43, 18.14, 13.94.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{23}NO$: 281.1781; found: 281.1788.

6-(*tert*-Butyl)-3-ethyl-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (8) (Table 2, Entry 5)

Yield: 9 mg (9%); yellow oil.

^{1}H NMR: δ = 7.29 (d, *J* = 7.9 Hz, 1 H), 7.18 (d, *J* = 7.9 Hz, 1 H), 7.08 (m, 2 H), 6.71 (s, 1 H), 6.21 (d, *J* = 1.6 Hz, 1 H), 3.84 (s, 3 H), 2.71 (q, *J* = 7.5 Hz, 2 H), 1.34 (s, 9 H), 1.28 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR: δ = 144.53, 144.31, 143.67, 134.28, 131.94, 127.67, 126.91, 117.49, 114.45, 113.84, 100.02, 79.82, 34.55, 32.58, 26.81, 18.30, 14.50.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{23}NO$: 281.1781; found: 281.1786.

9-(*tert*-Butyl)-3-(4-methoxyphenyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (7) (Table 2, Entry 2)

Yield: 34 mg (76%); off-white solid; mp 133–135 °C.

^{1}H NMR: δ = 7.50–7.47 (m, 4 H), 7.15 (dd, *J* = 2.2, 5.5 Hz, 2 H), 7.05 (d, *J* = 5.5 Hz, 1 H), 7.00 (m, 1 H), 6.97 (d, *J* = 2.2 Hz, 1 H), 5.72 (d, *J* = 1.8 Hz, 1 H), 4.00 (s, 3 H), 3.86 (s, 3 H), 1.47 (s, 9 H).

^{13}C NMR: δ = 158.11, 148.32, 146.01, 142.62, 134.61, 134.32, 130.41, 129.31, 129.10, 127.57, 117.58, 116.64, 114.08, 113.52, 104.66, 81.84, 55.31, 39.71, 33.39, 29.46.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{25}NO$: 359.1887; found: 359.1880.

9-(*tert*-Butyl)-3-(4-fluorophenyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (7) (Table 2, Entry 3)

Yield: 21 mg (42%); pale yellow oil.

^{1}H NMR: δ = 7.53–7.47 (m, 3 H), 7.19–7.11 (m, 4 H), 7.07 (d, *J* = 5.6 Hz, 1 H), 7.00 (s, 1 H), 5.75 (d, *J* = 1.8 Hz, 1 H), 4.01 (s, 3 H), 1.48 (s, 9 H).

^{13}C NMR: δ = 162.73, 160.30, 148.58, 146.04, 142.59, 134.56 (d, *J* = 5.9 Hz), 131.08 (d, *J* = 3.7 Hz), 130.74, 129.42 (d, *J* = 8.1 Hz), 129.044, 116.98, 116.43, 115.48 (d, *J* = 21.4 Hz), 113.72, 104.71, 81.83, 39.73, 33.39, 29.47.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}FNO$: 347.1687; found: 347.1680.

6-(*tert*-Butyl)-3-(4-fluorophenyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (8) (Table 2, Entry 3)

Yield: 3 mg (3%); green oil.

^{1}H NMR: δ = 8.04 (d, *J* = 8.2 Hz, 1 H), 7.82 (d, *J* = 8.2 Hz, 1 H), 7.56 (m, 3 H), 7.32 (m, 1 H), 7.22-7.14 (m, 3 H), 6.42 (d, *J* = 9.4 Hz, 1 H), 3.89 (s, 3 H), 1.35 (s, 9 H).

^{13}C NMR: δ = 162.54, 149.22, 145.10, 142.11, 136.63, 136.50, 131.11, 130.32, 127.65, 126.64, 126.30, 117.88, 117.86, 116.10, 104.89, 80.71, 37.02, 37.11, 26.67.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}FNO$: 347.1687; found: 347.1685.

3-Benzyl-9-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (7) (Table 2, Entry 4)
Yield: 48 mg (53%); pink oil.

^{1}H NMR: δ = 7.28 (m, 5 H), 7.17 (d, *J* = 7.4 Hz, 1 H), 7.12 (dd, *J* = 1.9, 5.9 Hz, 1 H), 7.07 (d, *J* = 7.4 Hz, 1 H), 7.01 (d, *J* = 5.9 Hz, 1 H), 6.54 (s, 1 H), 5.69 (d, *J* = 2.0 Hz, 1 H), 4.01 (s, 2 H), 3.86 (s, 3 H), 1.43 (s, 9 H).

^{13}C NMR: δ = 148.07, 145.92, 142.56, 140.67, 134.62, 133.95, 131.53, 130.72, 128.70, 128.30, 125.88, 115.92, 115.39, 112.83, 104.49, 81.89, 39.49, 33.34, 31.45, 29.44.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{25}NO$: 343.1938; found: 343.1944.

3-Benzyl-6-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (8) (Table 2, Entry 4)
Yield: 5 mg (6%); pink oil.

^{1}H NMR: δ = 7.26 (m, 5 H), 7.09 (m, 4 H), 6.56 (s, 1 H), 6.20 (d, *J* = 1.6 Hz, 1 H), 4.02 (s, 2 H), 3.83 (s, 3 H), 1.32 (s, 9 H).

^{13}C NMR: δ = 144.54, 144.27, 143.85, 141.13, 134.28, 132.01, 128.68, 128.41, 128.30, 127.60, 125.81, 114.65, 114.52, 114.15, 99.97, 79.86, 34.68, 32.55, 31.58, 26.79.

HRMS (EI): *m*/*z* calcd for $C_{24}H_{25}NO$: 343.1938; found: 343.1937.

9-(*tert*-Butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (7) (Table 2, Entry 6)
Yield: 39 mg (45%); yellow oil.

^{1}H NMR: δ = 7.28 (d, *J* = 2.9 Hz, 1 H), 7.15 (dd, *J* = 1.8, 5.6 Hz, 1 H), 7.11 (d, *J* = 7.3 Hz, 1 H), 7.04 (d, *J* = 5.6 Hz, 1 H), 6.91 (d, *J* = 3.1 Hz, 1 H), 6.48 (d, *J* = 3.1 Hz, 1 H), 5.71 (d, *J* = 1.5 Hz, 1 H), 3.97 (s, 3 H), 1.46 (s, 9 H).

^{13}C NMR (CD_3CN): δ = 149.54, 147.00, 143.74, 135.41, 134.99, 134.34, 118.44, 118.38, 114.18, 105.59, 103.16, 82.65, 40.24, 34.17, 29.80.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{19}NO$: 253.1468; found: 253.1466.

6-(*tert*-Butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (8) (Table 2, Entry 6)
Yield: 14 mg (16%); yellow oil.

^{1}H NMR: δ = 7.31 (d, *J* = 7.9 Hz, 1 H), 7.21 (d, *J* = 7.9 Hz, 1 H), 7.09 (d, *J* = 5.6 Hz, 1 H), 7.07 (dd, *J* = 1.8, 5.6 Hz, 1 H), 6.93 (d, *J* = 3.2 Hz, 1 H), 6.39 (d, *J* = 3.2 Hz, 1 H), 6.22 (d, *J* = 1.8 Hz, 1 H), 3.90 (s, 3 H), 1.34 (s, 9 H).

^{13}C NMR: δ = 144.53, 144.41, 143.80, 134.40, 131.52, 130.42, 128.11, 116.30, 114.65, 101.17, 100.05, 79.89, 34.92, 32.56, 26.79.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{19}NO$: 253.1468; found: 253.1470.

6,7-Dibromo-2-phenylindole and 6,7-Dibromo-2,3-diphenylindole via Fischer Indole Synthesis; 6,7-Dibromo-2-phenyl-1*H*-indole; Typical Procedure
In a 50 mL round-bottomed flask under argon was added 2,3-dibromophenylhydrazine (500 mg, 1.88 mmol). This was dissolved in EtOH (5 mL). To this were added acetophenone (0.22 mL, 1.88 mmol, 1.0 equiv) and a few drops of glacial AcOH. The reaction mixture was heated to reflux for 2 h, then cooled to r.t. and concentrated under reduced pressure to obtain the hydrazone intermediate. The hydrazone was added to polyphosphoric acid (5 g) and heated to 120 °C for 2 h. The reaction mixture was then cooled to r.t. and poured over ice. The aqueous mixture was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were neutralized with aq 2 M NaOH, and washed with H_2O (20 mL) and brine (20 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel using 20% TBME in hexanes as eluent to give 6,7-dibromo-2-phenyl-1*H*-indole as a yellow foam; yield: 271 mg (41%).

^{1}H NMR: δ = 8.47 (br s, 1 H), 7.71 (d, *J* = 9.7 Hz, 1 H), 7.51–7.34 (m, 6 H), 6.87 (s, 1 H).

^{13}C NMR: δ = 139.13, 136.58, 131.33, 129.14, 128.72, 128.40, 125.33, 125.05, 120.59, 117.29, 106.88, 101.03.

HRMS (EI): *m*/*z* calcd for $C_{14}H_9Br_2N$: 348.9102; found: 348.9106.

6,7-Dibromo-2,3-diphenyl-1*H*-indole
Obtained as above from the reaction of 2,3-dibromophenylhydrazine and deoxybenzoin as a light yellow foam; yield: 312 mg (39%).

^{1}H NMR: δ = 8.46 (br s, 1 H), 7.45 (m, 4 H), 7.38–7.29 (m, 8 H).

^{13}C NMR: δ = 137.88, 135.98, 133.85, 132.86, 130.46, 129.34, 128.75, 128.58, 128.30, 127.23, 126.04, 125.29, 121.70, 121.15, 116.52, 111.33.

HRMS (EI): *m*/*z* calcd for $C_{20}H_{13}Br_2N$: 424.9415; found: 424.9406.

6,7-Dibromo-1-methyl-3-phenyl-1*H*-indole (9; R^1 = Ph, R^2 = H)
For preparation, see reference 2e.

6,7-Dibromo-1-methyl-2-phenyl-1*H*-indole (9; R^1 = H, R^2 = Ph)
Obtained as above by methylation of 6,7-dibromo-2-phenyl-1*H*-indole as yellow foam; yield: 327 mg (79%).

^{1}H NMR: δ = 7.41–7.20 (m, 7 H), 6.42 (s, 1 H), 3.93 (s, 3 H).

^{13}C NMR: δ = 144.69, 136.69, 132.05, 129.75, 129.59, 128.56, 128.38, 125.20, 120.56, 119.65, 107.00, 102.62, 35.49.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{11}Br_2N$: 362.9258; found: 362.9266.

6,7-Dibromo-1-methyl-2,3-diphenyl-1*H*-indole (9; R^1 = R^2 = Ph)
Obtained as above by methylation of from 6,7-dibromo-2,3-diphenyl-1*H*-indole as light yellow foam; yield: 323 mg (78%).

^{1}H NMR: δ = 7.52 (d, *J* = 8.6 Hz, 1 H), 7.49 (d, *J* = 8.6 Hz, 1 H), 7.37 (m, 4 H), 7.29–7.24 (m, 4 H), 7.19 (m, 3 H), 4.01 (s, 3 H).

^{13}C NMR: δ = 140.72, 135.78, 133.93, 131.19, 131.16, 129.91, 128.45, 128.43, 128.41, 128.25, 126.09, 125.28, 120.15, 119.65, 115.82, 106.95, 35.24.

HRMS (EI): *m*/*z* calcd for $C_{21}H_{15}Br_2N$: 438.9572; found: 438.9568.

9-(*tert*-Butyl)-1-methyl-2-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (10) (Table 3, Entry 2)
Yield: 37 mg (55%); pale yellow foam.

^{1}H NMR: δ = 7.56–7.08 (m, 9 H), 6.62 (s, 1 H), 5.71 (d, *J* = 1.6 Hz, 3 H), 3.56 (s, 3 H), 1.45 (s, 9 H).

^{13}C NMR: δ = 147.97, 147.46, 146.19, 142.01, 139.72, 135.66, 132.61, 130.96, 128.80, 128.55, 127.91, 117.12, 114.33, 104.68, 103.79, 81.45, 39.55, 33.97, 29.14.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{23}NO$: 329.1781; found: 329.1788.

6-(*tert*-Butyl)-1-methyl-2-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (11) (Table 3, Entry 2)
Yield: 4 mg (6%); pale yellow foam.

^{1}H NMR: δ = 8.09–7.22 (m, 9 H), 6.49 (s, 1 H), 6.31 (d, *J* = 0.8 Hz, 1 H), 3.84 (s, 3 H), 1.36 (s, 9 H).

^{13}C NMR: δ = 147.87, 144.54, 144.32, 142.94, 136.13, 128.79, 128.75, 128.45, 127.44, 125.63, 121.34, 115.92, 115.13, 102.09, 100.40, 80.07, 39.13, 33.10, 32.14, 39.55.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{23}NO$: 329.1781; found: 329.1789.

9-(*tert*-Butyl)-1-methyl-2,3-diphenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (10) (Table 3, Entry 3)
Yield: 54 mg (53%); yellow foam.

^{1}H NMR: δ = 7.33–7.27 (m, 11 H), 7.15 (m, 2 H), 7.07 (d, *J* = 5.5 Hz, 1 H), 5.71 (d, *J* = 1.6, 1 H), 3.53 (s, 3 H), 1.46 (s, 9 H).

^{13}C NMR: δ = 148.43, 146.22, 142.95, 142.18, 138.24, 135.69, 135.07, 131.80, 130.94, 130.74, 130.02, 128.29, 128.21, 127.80, 125.98, 117.78, 116.29, 114.28, 104.03, 81.46, 39.25, 34.04, 29.28.

HRMS (EI): *m*/*z* calcd for $C_{29}H_{27}NO$: 405.2094; found: 405.2099.

6-(*tert*-Butyl)-1-methyl-2,3-diphenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (11) (Table 3, Entry 3)
Yield: 9 mg (9%); yellow foam.

^{1}H NMR: δ = 7.31 (m, 2 H), 7.23–7.17 (m, 10 H), 7.09 (m, 2 H), 6.32 (d, *J* = 0.9 Hz, 1 H), 3.77 (s, 3 H), 1.37 (s, 9 H).

^{13}C NMR: δ = 144.70, 146.56, 142.32, 139.02, 135.14, 134.67, 132.36, 131.54, 131.10, 129.84, 128.38, 128.11, 126.51, 125.56, 117.84, 115.29, 115.15, 100.33, 100.06, 80.25, 32.83, 32.56, 29.66.

HRMS (EI): *m*/*z* calcd for $C_{29}H_{27}NO$: 405.2094; found: 405.2090.

5,6,7-Tribromoindoles via Leimgruber–Batcho Indole Synthesis
These compounds were prepared according to references 2f and 5a.

5,6,7-Tribromo-1*H*-indole
For preparation, see reference 2f.

4,6,7-Tribromo-1-methyl-1*H*-indole (12; $R^1 = R^3 = H$; $R^2 = Br$)
For preparation see, reference 5a.

4,6,7-Tribromo-1-methyl-3-phenyl-1*H*-indole (12; $R^1 = Ph$, $R^2 = Br$; $R^3 = H$)
Yield: 132 mg (84%); yellow oil.

^{1}H NMR: δ = 7.54 (s, 1 H), 7.41–7.26 (m, 5 H), 6.99 (s, 1 H), 4.2 (s, 3 H).

^{13}C NMR: δ = 134.75, 133.69, 133.06, 131.45, 130.03, 128.41, 127.22, 126.97, 119.46, 118.12, 114.01, 106.26, 38.22.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}Br_3N$: 440.8363; found: 440.8370.

5,6,7-Tribromo-1-methyl-1*H*-indole (12; $R^1 = R^2 = H$, $R^3 = Br$)
Yield: 338 mg (82%); white solid; mp 147–149 °C.

^{1}H NMR: δ = 7.87 (s, 1 H), 7.04 (d, *J* = 3.1 Hz, 1 H), 6.65 (d, *J* = 3.1 Hz, 1 H), 3.76 (s, 3 H).

^{13}C NMR: δ = 136.21, 131.70, 126.61, 123.98, 120.85, 120.63, 109.77, 99.13, 35.70.

HRMS (EI): *m*/*z* calcd for $C_9H_6Br_3N$: 364.8050; found: 364.8051.

5,6,7-Tribromo-1-methyl-3-phenyl-1*H*-indole (12; $R^1 = Ph$, $R^2 = H$, $R^3 = Br$)
Yield: 334 mg (81%); yellow solid; mp 144–146 °C.

^{1}H NMR: δ = 8.06 (s, 1 H), 7.55–7.26 (m, 5 H), 7.13 (s, 1 H), 4.15 (s, 1 H).

^{13}C NMR: δ = 134.13, 133.55, 131.24, 128.92, 128.62, 127.61, 126.62, 123.12, 121.57, 116.11, 115.79, 107.88, 37.84.

HRMS (EI): *m*/*z* calcd for $C_{15}H_{10}Br_3N$: 440.8363; found: 440.8365.

4-Bromo-9-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (13) (Table 4, Entry 1)
Yield: 37 mg (59%); yellow oil.

^{1}H NMR: δ = 7.27 (s, 1 H), 7.10 (dd, *J* = 1.8, 5.5 Hz, 1 H), 7.01 (d, *J* = 5.5 Hz, 1 H), 6.96 (d, *J* = 3.5 Hz, 1 H), 6.54 (d, *J* = 3.5 Hz, 1 H), 5.66 (d, *J* = 1.8 Hz, 1 H), 3.96 (s, 3 H), 1.42 (s, 9 H).

^{13}C NMR: δ = 149.63, 145.81, 142.66, 133.84, 133.42, 130.60, 116.63, 111.13, 104.99, 104.69, 103.02, 81.57, 39.80, 33.26, 29.38.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}BrNO$: 331.0572; found: 331.0575.

4-Bromo-6-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (14) (Table 4, Entry 1)
Yield: 11 mg (17%); yellow oil.

^{1}H NMR: δ = 7.46 (s, 1 H), 7.07 (m, 2 H), 6.95 (d, *J* = 3.1 Hz, 1 H), 6.42 (d, *J* = 3.1 Hz, 1 H), 6.18 (m, 1 H), 3.98 (s, 3 H), 1.30 (s, 9 H).

^{13}C NMR: δ = 145.60, 144.61, 144.23, 134.17, 131.00, 128.17, 122.95, 117.93, 109.88, 101.66, 100.07, 79.77, 35.14, 29.72, 26.73.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}BrNO$: 331.0572; found: 331.0577.

4-Bromo-9-(*tert*-butyl)-1-methyl-3-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (13) (Table 4, Entry 2)
Yield: 46 mg (62%); off-white solid; mp 154–156 °C.

^{1}H NMR: δ = 7.40 (m, 3 H), 7.35(m, 3 H), 7.30 (s, 1 H), 7.12 (dd, *J* = 1.8, 2.3 Hz, 1 H), 7.05 (d, *J* = 5.5 Hz, 1 H), 5.67 (d, *J* = 1.8 Hz, 1 H), 3.96 (s, 3 H), 1.45 (s, 9 H).

^{13}C NMR: δ = 149.47, 145.78, 142.54, 135.46, 135.05, 134.22, 133.76, 131.41, 127.05, 126.62, 126.46, 119.06, 118.69, 110.77, 104.94, 81.32, 39.71, 33.60, 29.52.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}BrNO$: 407.0886; found: 407.0890.

4-Bromo-6-(*tert*-butyl)-1-methyl-3-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (14) (Table 4, Entry 2)
Yield: 10 mg (14%); off-white solid; mp 185–187 °C.

^{1}H NMR: δ = 7.49 (s, 1 H), 7.40 (m, 2 H), 7.35 (m, 3 H), 7.09 (m, 2 H), 6.94 (s, 1 H), 6.24 (d, *J* = 1.8 Hz, 1 H), 3.92 (s, 3 H), 1.33 (s, 9 H).

^{13}C NMR: δ = 145.71, 144.66, 144.16, 134.71, 134.42, 132.34, 131.39, 131.09, 127.12, 126.52, 124.03, 119.96, 118.22, 109.74, 100.05, 79.99, 35.13, 32.52, 26.72.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}BrNO$: 407.0886; found: 407.0889.

5-Bromo-9-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (13) (Table 4, Entry 3)
Yield: 34 mg (39%); yellow oil.

^{1}H NMR: δ = 7.36 (s, 1 H), 7.19 (dd, *J* = 1.8, 5.5 Hz, 1 H), 7.04 (d, *J* = 5.5 Hz, 1 H), 6.91 (d, *J* = 3.3 Hz, 1 H), 6.39 (d, *J* = 3.3 Hz, 1 H), 5.91 (d, *J* = 1.9 Hz, 1 H), 3.94 (s, 3 H), 1.43 (s, 9 H).

^{13}C NMR: δ = 147.09, 145.69, 142.95, 139.86, 136.93, 134.28, 133.31, 120.37, 107.27, 105.91, 102.05, 82.44, 39.77, 33.43, 29.41.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}BrNO$: 331.0572; found: 331.0580.

5-Bromo-6-(*tert*-butyl)-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (14) (Table 4, Entry 3)
Yield: 25 mg (29%); brown oil.

^{1}H NMR: δ = 7.43 (s, 1 H), 7.04 (m, 2 H), 6.94 (d, *J* = 3.1, 1 H), 6.31 (d, *J* = 3.3 Hz, 1 H), 6.24 (d, *J* = 1.6 Hz, 1 H), 3.88 (s, 3 H), 1.46 (s, 9 H).

^{13}C NMR: δ = 144.38, 144.15, 143.61, 137.69, 132.50, 130.82, 130.59, 122.26, 106.96, 103.28, 100.11, 79.15, 35.23, 32.65, 29.81.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}BrNO$: 331.0572; found: 331.0579.

5-Bromo-9-(*tert*-butyl)-1-methyl-3-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (13) (Table 4, Entry 4)
Yield: 24 mg (36%); yellow oil.

^{1}H NMR: δ = 7.62 (s, 1 H), 7.50 (m, 2 H), 7.42 (m, 2 H), 7.29 (m, 1 H), 7.18 (dd, *J* = 1.8, 5.5 Hz, 1 H), 7.06 (d, *J* = 5.5 Hz, 1 H), 7.01 (s, 1 H), 5.93 (d, *J* = 1.8 Hz, 1 H), 3.99 (s, 3 H), δ 1.45 (s, 9 H).

^{13}C NMR: δ = 145.34, 144.67, 138.60, 136.02, 135.95, 133.47, 128.50, 128.30, 127.07, 126.30, 123.65, 118.85, 117.01, 114.27, 100.76, 79.70, 39.37, 36.75, 26.67.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}BrNO$: 407.0886; found: 407.0895.

5-Bromo-6-(*tert*-butyl)-1-methyl-3-phenyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (14) (Table 4, Entry 4)
Yield: 17 mg (26%); brown oil.

^{1}H NMR: δ = 7.66 (s, 1 H), 7.48 (m, 2 H), 7.35 (m, 2 H), 7.21 (m, 1 H), 7.04 (s, 1 H), 6.99 (m, 2 H), 6.21 (d, *J* = 1.8 Hz, 1 H), 3.86 (s, 3 H), 1.48 (s, 9 H).

^{13}C NMR: δ = 146.88, 145.43, 136.78, 136.73, 134.62, 133.90, 128.50, 128.12, 127.10, 126.94, 126.30, 118.78, 116.33, 100.41, 100.34, 80.11, 37.85, 37.07, 26.82.

HRMS (EI): *m*/*z* calcd for $C_{23}H_{22}BrNO$: 407.0886; found: 407.0890.

4- Substituted 6,7-Dibromoindoles via Bartoli Indole Synthesis; 6,7-Dibromo-4-fluoro-1*H*-indole; Typical Procedure
In a 250 mL flame-dried round-bottomed flask under argon was dissolved 1,2-dibromo-5-fluoro-3-nitrobenzene (0.50 g, 3.35 mmol) in THF (20 mL) and cooled to –40 °C. To this stirred solution was added a solution of vinylmagnesium bromide in THF (1 M, 11.7 mmol) at –40 °C. The reaction mixture was stirred at –40 °C for 1 h, then quenched with aq NH_4Cl (100 mL), and allowed to warm to r.t. The mixture was extracted with Et_2O (3 × 50 mL), the combined organic layers washed with H_2O (1 × 50 mL), brine (25 mL), and dried ($MgSO_4$). The solution was filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography on silica gel using 10% EtOAc in hexanes to give 6,7-dibromo-4-fluoro-1*H*-indole as an off-white solid; yield: 150 mg (31%); mp 84–86 °C.

^{1}H NMR: δ = 8.46 (br s, 1 H), 7.23 (m, 1 H), 7.10 (d, *J* = 9.4 Hz, 1 H), 6.71 (dd, *J* = 2.1, 3.3 Hz, 1 H).

^{13}C NMR: δ = 156.26, 153.75, 125.05, 116.91 (d, *J* = 24.0 Hz), 116.38 (d, *J* = 9.6 Hz), 110.32 (d, *J* = 24.2 Hz), 102.12, 100.58.

HRMS (EI): *m*/*z* calcd for $C_8H_4FBr_2N$: 290.8694; found: 290.8690.

4,6,7-Tribromo-1*H*-indole
For preparation, see reference 5a.

6,7-Dibromo-4-iodo-1*H*-indole
Yield: 330 mg (33%); purple solid; mp 91–93 °C.

^{1}H NMR: δ = 8.50 (br s, 1 H), 7.55 (s, 1 H), 7.30 (dd, *J* = 2.5, 3.3 Hz, 1 H), 6.66 (dd, *J* = 2.3, 3.3 Hz, 1 H).

^{13}C NMR: δ = 135.36, 128.69, 126.69, 125.76, 117.16, 114.08, 106.46, 104.70.

HRMS (EI): *m*/*z* calcd for $C_8H_4IBr_2N$: 398.7755; found: 398.7766.

6,7-Dibromo-4-ethyl-1*H*-indole
For preparation, see reference 2b.

6,7-Dibromo-4-fluoro-1-methyl-1*H*-indole (15; R = F)
Yield: 102 mg (77%); brown solid; mp 69–71 °C.

^{1}H NMR: δ = 7.07 (d, *J* = 9.0 Hz, 1 H), 6.95 (d, *J* = 3.1 Hz, 1 H), 6.51 (d, *J* = 3.1 Hz, 1 H), 4.15 (s, 1 H).

^{13}C NMR: δ = 156.03, 153.54, 132.30, 119.43 (d, *J* = 24.9 Hz), 118.17 (d, *J* = 11.9 Hz), 110.10 (d, *J* = 22.5 Hz), 101.73, 97.37, 37.59.

HRMS (EI): *m*/*z* calcd for $C_9H_6FBr_2N$: 304.8851; found: 304.8852.

4,6,7-Tribromo-1-methyl-1*H*-indole (15; R = H)
For preparation, see reference 5a.

6,7-Dibromo-4-iodo-1-methyl-1*H*-indole (15; R = I)
Yield: 100 mg (79%); purple oil.

^{1}H NMR: δ = 7.51 (s, 1 H), 7.03 (d, *J* = 3.3 Hz, 1 H), 6.48 (d, *J* = 3.3 Hz, 1 H), 4.15 (s, 1 H).

^{13}C NMR: δ = 134.07, 133.00, 130.56, 126.68, 119.11, 114.33, 106.10, 101.94, 37.98.

HRMS (EI): *m*/*z* calcd for $C_9H_6IBr_2N$: 412.7912; found: 412.7915.

6,7-Dibromo-4-ethyl-1-methyl-1*H*-indole (15; R = Et)
Yield: 140 mg (89%); yellow oil.

^{1}H NMR: δ = 7.21 (s, 1 H), 6.96 (d, *J* = 3.1 Hz, 1 H), 6.44 (d, *J* = 3.1 Hz, 1 H), 4.14 (s, 1 H), 2.83 (q, *J* = 7.6 Hz, 2 H), 1.31 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR: δ = 136.85, 132.05, 131.79, 129.37, 123.10, 119.44, 103.81, 99.39, 37.71, 25.51, 14.35.

HRMS (EI): *m*/*z* calcd for $C_8H_4FBr_2N$: 314.9258; found: 314.9260.

9-(*tert*-Butyl)-4-fluoro-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (16) (Table 5, Entry 1)
Yield: 39 mg (49%); yellow oil.

^{1}H NMR: δ = 7.12 (dd, *J* = 1.7, 1.7 Hz, 1 H), 7.03 (d, *J* = 5.5 Hz, 1 H), 6.84 (d, *J* = 3.5 Hz, 1 H), 6.82 (d, *J* = 8.0 Hz, 1 H), 6.52 (d, *J* = 3.3 Hz, 1 H), 5.65 (d, *J* = 1.7 Hz, 1 H), 3.96 (s, 3 H), 1.43 (s, 9 H).

^{13}C NMR: δ = 154.55, 152.10, 149.95 (d, *J* = 7.3 Hz), 145.66, 143.17, 132.36, 129.73, 104.62, 100.38, 99.85 (d, *J* = 21.2 Hz), 98.15, 81.86, 39.61, 33.20, 29.39.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}FNO$: 271.1373; found: 271.1380.

6-(*tert*-Butyl)-4-fluoro-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (17) (Table 5, Entry 1)
Yield: 17 mg (22%); pale yellow solid; mp 118–120 °C.

^{1}H NMR: δ = 7.08 (d, *J* = 1.2 Hz, 1 H), 7.03 (d, *J* = 0.6 Hz, 1 H), 7.01 (d, *J* = 0.6 Hz, 1 H), 6.89 (d, *J* = 3.1 Hz, 1 H), 6.44 (d, *J* = 3.1 Hz, 1 H), 6.19 (d, *J* = 0.8 Hz, 1 H), 3.88 (s, 3 H), 1.31 (s, 9 H).

^{13}C NMR: δ = 154.17, 151.73, 145.55 (d, *J* = 7.4 Hz), 145.04, 144.18, 133.26, 130.02, 115.80 (d, *J* = 23.4 Hz), 101.60 (d, *J* = 22.7 Hz), 100.31 (d, *J* = 27.1 Hz), 97.35, 79.82, 34.99, 32.50, 26.67.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}FNO$: 271.1373; found: 271.1372.

9-(*tert*-Butyl)-4-iodo-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (16) (Table 5, Entry 3)
Yield: 50 mg (61%); purple solid; mp 99–101 °C.

^{1}H NMR: δ = 7.28 (s, 1 H), 7.11 (dd, *J* = 1.8, 5.5 Hz, 1 H), 7.01 (d, *J* = 5.5 Hz, 1 H), 6.96 (d, *J* = 3.3 Hz, 1 H), 6.54 (d, *J* = 3.3 Hz, 1 H), 5.66 (d, *J* = 1.8 Hz, 1 H), 3.96 (s, 3 H), 1.42 (s, 9 H).

^{13}C NMR: δ = 149.61, 145.80, 142.65, 133.89, 133.83, 133.42, 130.58, 116.61, 111.12, 104.68, 102.99, 81.55, 39.80, 33.25, 29.73.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}INO$: 379.0434; found: 379.0444.

6-(*tert*-Butyl)-4-iodo-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (17) (Table 5, Entry 3)
Yield: 9 mg (4%); purple solid; mp 136–138 °C.

^{1}H NMR: δ = 7.46 (s, 1 H), 7.07 (m, 2 H), 6.99 (d, *J* = 3.3 Hz, 1 H), 6.42 (d, *J* = 3.3 Hz, 1 H), 6.18 (m, 1 H), 3.88 (s, 3 H), 1.32 (s, 9 H).

^{13}C NMR: δ = 145.58, 144.61, 144.21, 134.15, 131.46, 131.01, 128.15, 118.82, 117.91, 109.87, 101.65, 79.76, 35.13, 29.69, 26.72.

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}INO$: 379.0434; found: 379.0450.

9-(*tert*-Butyl)-4-ethyl-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (16) (Table 5, Entry 4)
Yield: 50 mg (58%); yellow oil.

^{1}H NMR: δ = 7.15 (dd, *J* = 1.8, 1.8 Hz, 1 H), 7.05 (d, *J* = 5.7 Hz, 1 H), 7.02 (s, 1 H), 6.92 (d, *J* = 3.5 Hz, 1 H), 6.53 (d, *J* = 3.3 Hz, 1 H),

5.71 (d, *J* = 1.8 Hz, 1 H), 3.97 (s, 3 H), 2.89 (q, *J* = 7.6 Hz, 2 H), 1.47 (s, 9 H), 1.34 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR: δ = 148.39, 145.76, 142.84, 133.67, 133.23, 132.17, 131.35, 129.41, 112.45, 104.54, 100.65, 81.96, 39.64, 33.27, 29.40, 25.67, 14.51.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{23}NO$: 281.1781; found: 281.1787.

6-(*tert*-Butyl)-4-ethyl-1-methyl-6,9-dihydro-1*H*-6,9-epoxybenzo[*g*]indole (17) (Table 5, Entry 4)
Yield: 4 mg (5%); dark yellow oil.

^{1}H NMR: δ = 7.14 (s, 1 H), 7.07 (m, 2 H), 6.92 (d, *J* = 3.3 Hz, 1 H), 6.41 (d, *J* = 3.3 Hz, 1 H), 6.20 (d, *J* = 1.6 Hz, 1 H), 3.88 (s, 3 H), 2.86 (q, *J* = 7.6 Hz, 2 H), 1.34 (s, 9 H), 1.29 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR: δ = 144.79, 144.26, 132.35, 132.02, 131.39, 129.63, 113.88, 105.00, 100.10, 99.60, 89.10, 79.90, 34.96, 32.58, 29.69, 26.69, 15.19.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{23}NO$: 281.1781; found: 281.1783.

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