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SYNTHESIS OF 2- AND 3-INDOLYLPYRROLES *VIA* 1,3-DIPOLAR CYCLOADDITIONS OF MÜNCHNONES AND NITROALKENES [†]

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Abstract – A series of 2- and 3-indolylpyrroles were generated *via* 1,3-dipolar cycloadditions between (2-nitrovinyl)indoles and symmetrical and unsymmetrical 1,3-oxazolium-5-olates (münchnones).

INTRODUCTION

Methods for the synthesis of biheteroaryl compounds are of great importance due to the broad applicability and privileged nature¹ of these structures, which include natural products,² pharmaceuticals,³ and materials such as polymers⁴ and dyes.⁵ Naturally occurring biheteroaryl structures exist as unfused² or fused systems, examples of which are shown in **Figure 1**.²

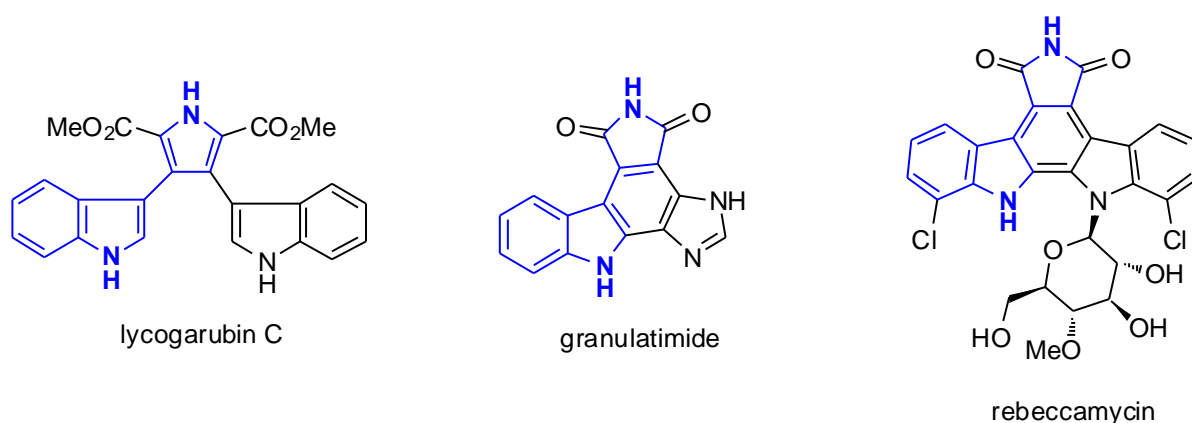
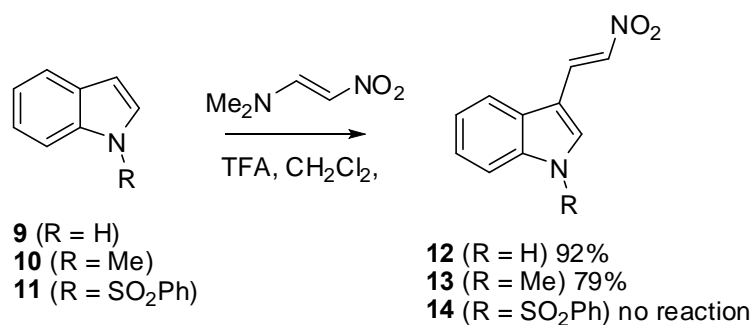


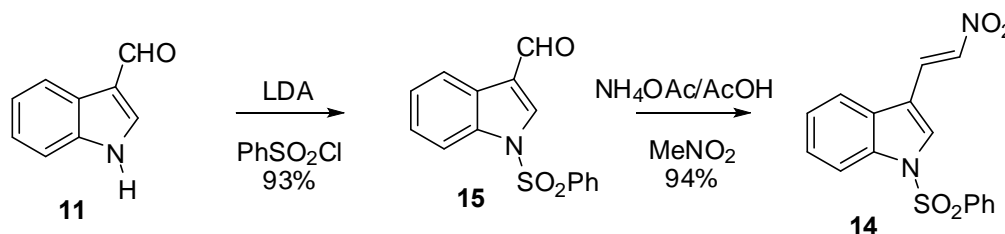
Figure 1. Indolylpyrrole-based Natural Products

[†] Dedicated to Professor Albert Eschenmoser in celebration of his 85th birthday and his many outstanding contributions to synthetic organic chemistry.



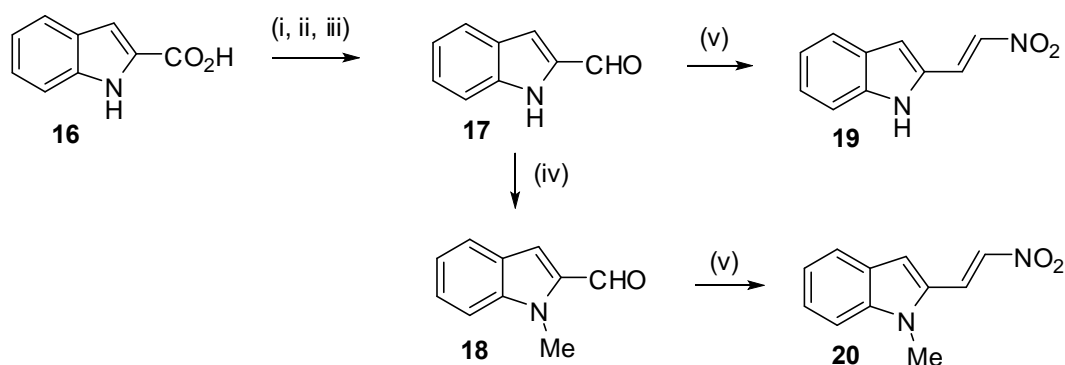
Scheme 2. Synthesis of 3-(2-nitrovinyl)indoles

Compound **14** was instead prepared by *N*-protection of indole-3-carboxaldehyde¹² followed by condensation with nitromethane in a standard Henry reaction¹³ (**Scheme 3**).



Scheme 3. Synthesis of 3-(2-nitrovinyl)-1-(phenylsulfonyl)indole

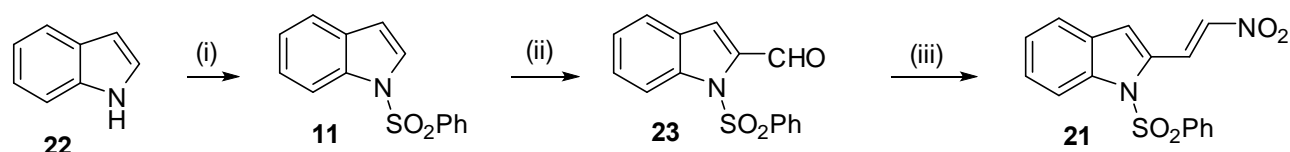
The unprotected and methyl-protected 2-(2-nitrovinyl)indoles were generated in four and five steps, respectively, from commercially available indole-2-carboxylic acid through a sequence of esterification,¹⁴ reduction,¹⁵ oxidation,¹⁵ protection¹⁶ (for the *N*-methyl derivative), and condensation with nitromethane¹⁷ (**Scheme 4**). Attempted generation of **20** from **19** with methyl iodide or dimethyl sulfate did not yield an appreciable amount of the desired product.



(i) H₂SO₄, MeOH; (ii) DIBAL-H, THF; (iii) MnO₂, MeCN, 94% over three steps; (iv) Aliquat 336, dimethyl sulfate, 50% aq. NaOH, CH₂Cl₂, 98%; (v) a) 50% aq. NaOH, MeNO₂, MeOH, b) 20% aq. HCl (**19**, 87%; **20**, 84%)

Scheme 4. Synthesis of 2-(2-nitrovinyl)indoles from indole-2-carboxylic acid

Instead, 1-(phenylsulfonyl)indole derivative **21** was generated (**Scheme 5**) from indole *via* *N*-protection,¹⁸ C2-lithiation (quenching with DMF),¹⁹ and condensation with nitromethane.¹⁷

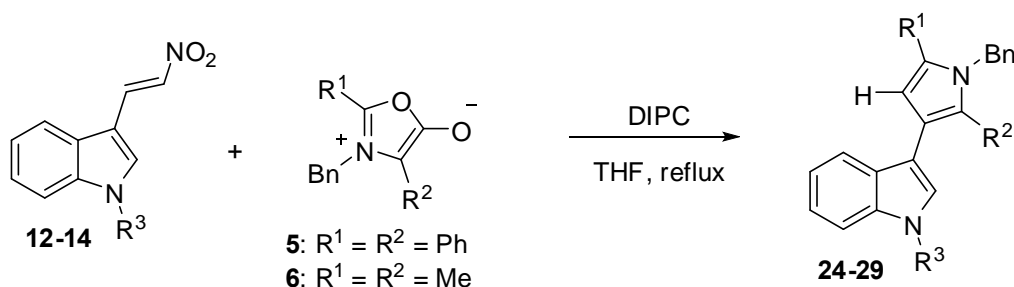


(i) PhSO_2Cl , NaOH , $n\text{-Bu}_4\text{NHSO}_4$, CH_2Cl_2 , 97%; (ii) a) $n\text{-BuLi}$, THF, b) DMF, 69%; (iii) a) 50% aq. NaOH , MeNO_2 , MeOH , b) 20% aq. HCl , 87%

Scheme 5. Synthesis of 2-(2-nitrovinyl)-1-(phenylsulfonyl)indole

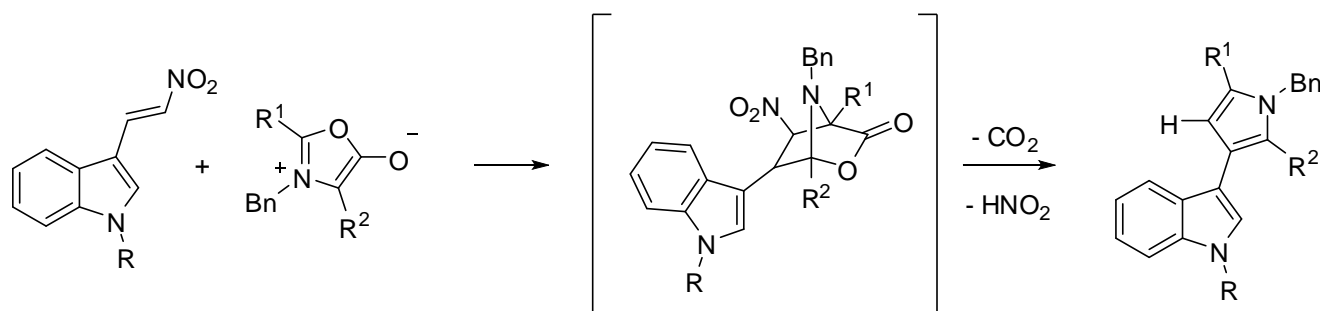
With the nitroalkenes in hand, their reactivity with münchnones **5-8** was investigated. Gratifyingly, 3-(2-nitrovinyl)indoles **12-14** reacted smoothly with symmetrical münchnones **5** and **6** to give the corresponding pyrrole products **24-29** in good yields (**Table 1**). It is proposed that the 1,3-dipolar cycloadditions proceed through a bicyclic adduct which expels carbon dioxide and eliminates nitrous acid to give the substituted *N*-benzyl-3-indolylpyrroles (**Scheme 6**).⁹ The protecting group on the indole (or lack thereof) seemingly had no effect on the reaction.

Table 1. Reaction of 3-Nitroalkenes with Symmetrical Münchnones.



Indole	Münchnone	R ³	Product	Yield ^a
12	5	H	24	78%
13	5	Me	25	62%
14	5	SO_2Ph	26	81%
12	6	H	27	84%
13	6	Me	28	75%
14	6	SO_2Ph	29	68%

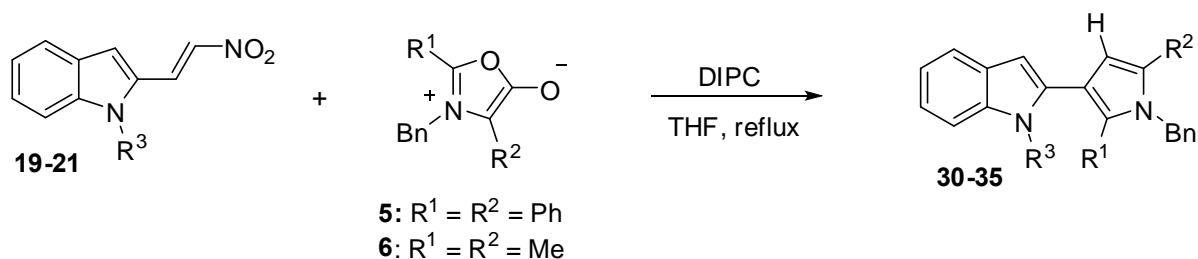
^aYield refers to isolated products after column chromatography.



Scheme 6. Proposed Course of 1,3-Dipolar Cycloadditions

In a similar manner, 2-(2-nitrovinyl)indoles **19-21** were allowed to react with symmetrical münchnones **5** and **6**. The corresponding 3-pyrrolo-2-ylindoles were obtained in high yield and again, the various protecting groups on the starting indoles had no effect on the outcome of the reaction (**Table 2**).

Table 2. Reaction of 2-Nitroalkenes with Symmetrical Münchnones.



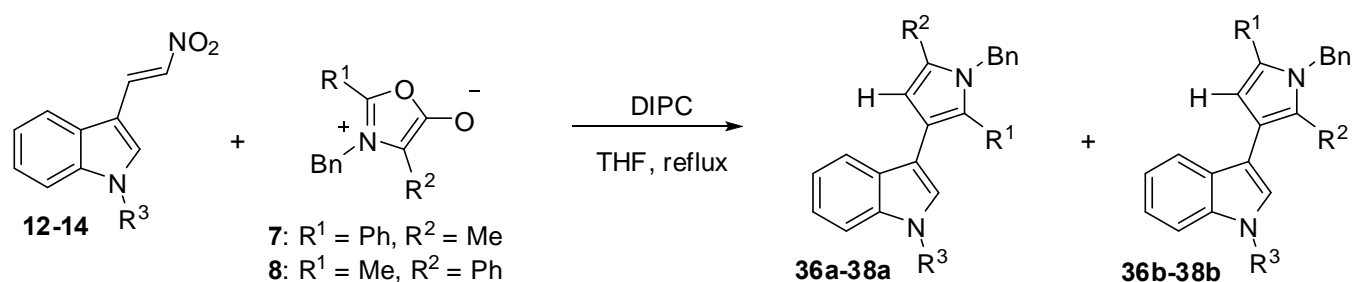
Indole	Münchnone	R ³	Product	Yield ^a
19	5	H	30	92%
20	5	Me	31	90%
21	5	SO ₂ Ph	32	94%
19	6	H	33	92%
20	6	Me	34	70%
21	6	SO ₂ Ph	35	86%

^aYield refers to isolated products after column chromatography.

With the success of münchnones **5** and **6**, we turned our attention to unsymmetrical münchnones **7** and **8** and tested them under the same reaction conditions. The reaction of münchnone **7** with 3-(2-nitrovinyl)indoles **12-14** gave the expected pyrrole products in moderate to good yield with reasonably good regioselectivity (**Table 3**). The protecting group on the indole nitrogen did appear to

alter the reaction; phenylsulfonyl derivative **14** was optimal and yielded the major product in an 88:12 ratio and in 71% overall yield. However, münchnone **8** gave substantially different results (Table 3). In each case, **8** was both less reactive (lower yielding) and less regioselective. Phenylsulfonyl derivative **14** still provided the highest yielding reaction (65%) but was completely nonselective, giving essentially a 1:1 mixture of isomers.

Table 3. 3-Nitroalkenes with Unsymmetrical Münchnones

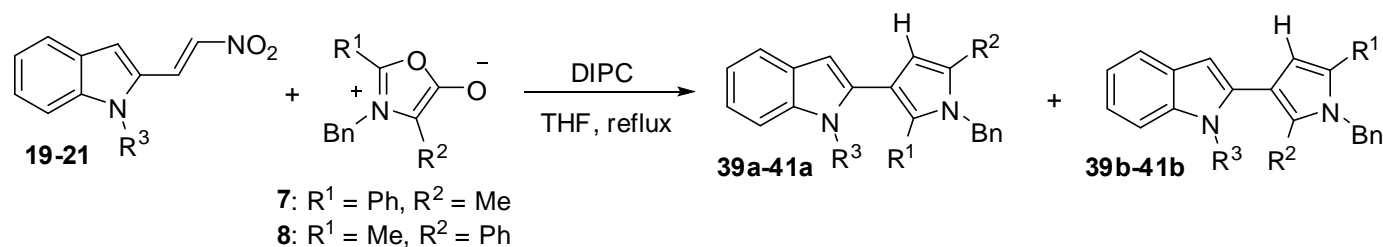


Indole	Münchnone	R ³	Products	Ratio (a:b) ^a	Yield ^b
12	7	H	36a : 36b	77 : 23	51%
13	7	Me	37a : 37b	74 : 26	86%
14	7	SO ₂ Ph	38a : 38b	88 : 12	71%
12	8	H	36a : 36b	37 : 63	20%
13	8	Me	37a : 37b	44 : 56	39%
14	8	SO ₂ Ph	38a : 38b	49 : 51	65%

^aRegiochemistry was determined by NOE interactions of the pyrrole ring proton with either the methyl or phenyl group of the pyrrole.

^bYield refers to isolated products after column chromatography.

Once again, 2-(2-nitrovinyl)indoles **19-21** proved more reactive than their isomeric counterparts. The reactions with münchnone **7** proceeded in good to excellent yield with good regioselectivity (Table 4). While phenylsulfonyl indole **21** gave the best yield, it also showed the lowest selectivity of the group. Methyl-protected indole **20** exhibited a 9:1 selectivity with a 76% yield. As expected, münchnone **8** was less reactive in all cases; however, the selectivity was reasonably good in each case. Most surprisingly, *N*-methylindole **20** afforded the opposite major product than what was expected based on the other results in this study. The reason for this change is unknown and currently under investigation. As has mostly been the case, *N*-phenylsulfonylindole **21** gave optimal results with a ratio of 91:9 in 78% yield.

Table 4. 2-Nitroalkenes with Unsymmetrical Münchnones

Indole	Münchnone	R ³	Products	Ratio (a:b) ^a	Yield ^b
19	7	H	39a : 39b	87 : 13	89%
20	7	Me	40a : 40b	90 : 10	76%
21	7	SO ₂ Ph	41a : 41b	79 : 21	95%
19	8	H	39a : 39b	26 : 74	62%
20	8	Me	40a : 40b	70 : 30	45%
21	8	SO ₂ Ph	41a : 41b	9 : 91	78%

^aRegiochemistry was determined by NOE interactions of the pyrrole ring proton with either the methyl or phenyl group of the pyrrole.

^bYield refers to isolated products after column chromatography.

In summary, we report a reaction protocol that allows access to a variety of substituted 2- and 3-indolyl pyrroles in moderate to high yields. In the case of unsymmetrical münchnones, the regioselectivity varies substantially from being completely nonselective to where the major products are obtained in a 9:1 ratio. Extensions of this methodology to other heterocyclic systems as well as mechanistic and computational studies designed to rationalize both the reactivity and regioselectivity are currently underway and will be reported in due course.

EXPERIMENTAL

General: ¹H NMR (300 MHz), ¹³C NMR (75 MHz), and NOE experiments were performed on a Varian Unity spectrometer. Chemical shifts are reported in ppm with the solvent signal used as an internal reference (CDCl₃, 7.26 ppm). Coupling constants are reported in Hz and peak splittings are listed as broad singlet (br s), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), or multiplet (m). Tetrahydrofuran (THF) was obtained by distillation from sodium benzophenone ketyl immediately prior to use. All other commercial reagents were used as received.

3-(2-Nitrovinyl)-1*H*-indole¹¹ (12): A round bottom flask was charged with 1-(dimethylamino)-2-nitroethylene (1.06 g, 9.1 mmol, 1.2 eq.) and CH₂Cl₂ (25 mL). The flask was cooled

to 0 °C. Trifluoroacetic acid (2.02 g, 17.7 mmol, 2.3 eq.) was added slowly, followed by a solution of indole (2.00 g, 7.6 mmol, 1.0 eq.) in CH₂Cl₂ (15 mL). The resulting solution was stirred at 0 °C for 65 min then poured into ice water (100 mL) and the layers separated. The aqueous layer was extracted with CH₂Cl₂ (2 x 60 mL) and the combined organic extracts were washed with saturated aqueous NaHCO₃ (1 x 60 mL), brine (1 x 60 mL), dried over Na₂SO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **12** as a light brown solid (1.32 g, 92%). ¹H NMR (CDCl₃) δ 8.74 (br s, 1H), 8.30 (d, 1H, J = 13.4 Hz), 7.83-7.78 (m, 2H), 7.68 (d, 1H, J = 2.9 Hz), 7.50-7.46 (m, 1H), 7.39-7.32 (m, 2H).

1-Methyl-3-(2-nitrovinyl)-1H-indole¹¹ (**13**): A round bottom flask was charged with 1-(dimethylamino)-2-nitroethylene (2.12 g, 18.2 mmol, 1.2 eq.) and CH₂Cl₂ (50 mL). The flask was cooled to 0 °C. Trifluoroacetic acid (4.04 g, 35.4 mmol, 2.3 eq.) was added slowly, followed by a solution of 1-methylindole (2.00 g, 15.2 mmol, 1.0 eq.) in CH₂Cl₂ (30 mL). The resulting solution was stirred at 0 °C for 45 min then poured into ice water (150 mL) and the layers separated. The aqueous layer was extracted with CH₂Cl₂ (2 x 100 mL) and the combined organic extracts were washed with saturated aqueous NaHCO₃ (1 x 100 mL), brine (1 x 100 mL), dried over Na₂SO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **13** as an orange solid (2.43 g, 79%). ¹H NMR (CDCl₃) δ 8.25 (d, 1H, J = 13.4 Hz), 7.78-7.73 (m, 2H), 7.52 (s, 1H), 7.42-7.31 (m, 3H), 3.87 (s, 3H).

3-(2-Nitrovinyl)-1-(phenylsulfonyl)-1H-indole²⁰ (**14**): A round bottom flask was charged with ammonium acetate (2.14 g, 27.8 mmol, 2.4 eq.), nitromethane (4.87 g, 79.8 mmol, 6.9 eq.), and acetic acid (25 mL). 1-(phenylsulfonyl)indole-3-carboxaldehyde (3.30 g, 11.6 mmol, 1 eq.) was added and the mixture was heated to 100 °C for 6 h, cooled to room temperature, and stirred overnight. The reaction mixture was poured into distilled water (100 mL) and 2M NaOH was added with stirring until the pH = 7. The aqueous solution was extracted with EtOAc (4 x 50 mL); the combined organic extracts were washed with brine (1 x 50 mL), dried over Na₂SO₄, and concentrated *in vacuo*. The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **14** as a tan solid (3.58 g, 94%). ¹H NMR (CDCl₃) δ 8.15 (s, 1H), 8.05-7.94 (m, 2H), 7.77-7.37 (m, 9H).

Representative procedure for the synthesis of 19-21: A round bottom flask was charged with indole-2-carboxaldehyde (1.0 g, 6.89 mmol, 1.0 eq.), nitromethane (1.5 g, 24.6 mmol, 3.6 eq), and methanol (25 mL). The flask was cooled to 0 °C (ice bath) and 50% aqueous sodium hydroxide (7.5 mL) was added slowly dropwise with vigorous stirring. After 90 min, an ice-water mixture (25 mL) was

added. The resulting mixture was poured slowly into ice cold 20% aqueous HCl (150 mL) under stirring. After 5 min, the crude **19** which precipitated was collected by vacuum filtration over sintered glass and dried in air.

2-(2-Nitrovinyl)-1H-indole¹⁷ (19): The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **19** as a light brown solid (1.13 g, 87%). ¹H NMR (CDCl₃) δ 8.31 (br s, 1H), 8.05 (d, 1H, J = 13.4 Hz), 7.66 (d, 1H, J = 8.1 Hz), 7.50 (d, 1H, J = 13.7 Hz), 7.42-7.32 (m, 2H), 7.20-7.15 (m, 1H), 7.07 (s, 1H).

1-Methyl-2-(2-nitrovinyl)-1H-indole²¹ (20): The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **20** as an orange solid (1.17 g, 84%). ¹H NMR (CDCl₃) δ 8.17 (d, 1H, J = 13.4 Hz), 7.71-7.63 (m, 2H), 7.35 (d, 2H, J = 5.6 Hz), 7.19-7.13 (m, 1H), 7.10 (s, 1H), 3.88 (s, 3H).

2-(2-Nitrovinyl)-1-(phenylsulfonyl)-1H-indole (21): The crude product was purified by flash chromatography over silica gel (30% EtOAc in hexanes) to give **21** as a yellow solid (0.91 g, 87%). ¹H NMR (CDCl₃) δ 8.81 (d, 1H, J = 13.4 Hz), 8.26 (d, 1H, J = 8.6 Hz), 7.76 (d, 1H, J = 9.5 Hz), 7.59-7.26 (m, 8H), 7.11 (s, 1H); HRMS (ESI⁺) m/z calculated for C₁₆H₁₃N₂O₄S (MH⁺) 329.0596, found 329.0602.

Representative procedure for the reaction of nitroalkenes and münchnones (24-41): A round bottom flask was charged with the 3-(2-nitrovinyl)indole (94 mg, 0.50 mmol, 1 eq.), münchnone precursor **1** (518 mg, 1.5 mmol, 3 eq.) and THF (20 mL). DIPC (233 μL, 1.5 mmol, 3 eq.) was added and the mixture was heated to reflux under nitrogen for 18-24 h. Once TLC indicated complete consumption of the nitroalkene, the mixture was cooled to room temperature and concentrated *in vacuo*. The residue was purified directly by flash chromatography over silica gel (1:3 CH₂Cl₂:hexanes) to yield pure **24**.

3-(1-Benzyl-2,5-diphenyl-1H-pyrrol-3-yl)-1H-indole (24): White solid, 78% yield; ¹H NMR (CDCl₃) δ 7.87 (d, 2H, J = 7.1 Hz), 7.52-7.11 (m, 16H), 6.81 (s, 1H), 6.76 (d, 2H, J = 7.6 Hz), 6.70 (s, 1H), 5.20 (s, 2H); ¹³C NMR (CDCl₃) δ 139.7, 136.2, 135.7, 133.9, 133.8, 132.3, 132.1, 131.6, 131.1, 129.3, 129.1, 129.0, 128.9, 128.7, 128.5, 128.5, 128.0, 127.6, 127.2, 127.0, 126.3, 122.0, 120.6, 119.7, 117.0, 112.2, 111.2, 110.4, 48.8; HRMS (ESI⁺) m/z calculated for C₃₁H₂₅N₂ (MH⁺) 425.2018, found 425.2026.

3-(1-Benzyl-2,5-diphenyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (25): White solid, 62% yield; ¹H NMR (CDCl₃) δ 7.79 (d, 1H, J = 7.8 Hz), 7.48 (d, 2H, J = 6.8 Hz), 7.38-7.06 (m, 15H), 6.75-6.72 (m, 3H), 6.57

(s, 1H), 5.18 (s, 2H), 3.64 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.7, 137.0, 135.6, 134.0, 133.8, 132.1, 131.5, 129.3, 128.6, 128.4, 128.4, 127.7, 127.5, 127.2, 126.9, 126.7, 126.3, 121.5, 120.8, 119.1, 110.7, 110.5, 109.2, 74.0, 48.8, 32.9; HRMS (ESI^+) m/z calculated for $\text{C}_{32}\text{H}_{27}\text{N}_2$ (MH^+) 439.2174, found 439.2172.

3-(1-Benzyl-2,5-diphenyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (26): Light orange solid, 81% yield; ^1H NMR (CDCl_3) δ 8.05 (d, 1H, $J = 8.3$ Hz), 7.78 (d, 1H, $J = 7.8$ Hz), 7.67 (d, 2H, $J = 7.8$ Hz), 7.52-7.17 (m, 18H), 7.13 (s, 1H), 6.77-6.74 (m, 3H), 5.22 (s, 2H), ^{13}C NMR (CDCl_3) δ 139.3, 138.3, 136.0, 135.4, 133.7, 133.5, 132.9, 131.4, 131.2, 129.4, 129.3, 128.8, 128.7, 128.6, 127.9, 127.4, 127.2, 124.8, 123.5, 123.0, 121.3, 118.9, 114.5, 113.9, 110.1, 48.9; HRMS (ESI^+) m/z calculated for $\text{C}_{37}\text{H}_{29}\text{N}_2\text{O}_2\text{S}$ (MH^+) 565.1950, found 565.1942.

3-(1-Benzyl-2,5-dimethyl-1H-pyrrol-3-yl)-1H-indole (27): Light yellow solid, 84% yield; ^1H NMR (CDCl_3) δ 8.07 (br s, 1H), 7.80 (d, 1H, $J = 7.8$ Hz), 7.41-7.14 (m, 7H), 7.00 (d, 2H, $J = 7.6$ Hz), 6.23 (s, 1H), 5.13 (s, 2H), 2.26 (s, 6H); ^{13}C NMR (CDCl_3) δ 138.9, 136.4, 129.0, 127.7, 127.3, 126.0, 122.1, 121.6, 120.7, 119.6, 113.5, 113.3, 111.2, 107.6, 47.3, 12.6, 11.4; HRMS (ESI^+) m/z calculated for $\text{C}_{21}\text{H}_{21}\text{N}_2$ (MH^+) 301.1705, found 301.1703.

3-(1-Benzyl-2,5-dimethyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (28): Yellow solid, 75% yield; ^1H NMR (CDCl_3) δ 7.82 (d, 1H, $J = 7.8$ Hz), 7.39-7.26 (m, 5H), 7.18 (t, 1H, $J = 6.8$ Hz), 7.15-7.01 (m, 3H), 6.24 (s, 1H), 5.15 (s, 2H), 3.84 (s, 3H), 2.28 (s, 6H); ^{13}C NMR (CDCl_3) δ 138.9, 137.1, 129.0, 128.1, 127.6, 127.3, 126.4, 126.0, 124.5, 121.7, 120.9, 119.1, 113.4, 112.0, 109.3, 107.6, 47.3, 33.0, 12.6, 11.5; HRMS (ESI^+) m/z calculated for $\text{C}_{22}\text{H}_{23}\text{N}_2$ (MH^+) 315.1861, found 315.1856.

3-(1-Benzyl-2,5-dimethyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (29): Orange solid, 68% yield; ^1H NMR (CDCl_3) δ 8.09 (d, 2H, $J = 8.3$ Hz), 7.96-7.90 (m, 3H), 7.74 (d, 2H, $J = 7.8$ Hz), 7.54-7.25 (m, 6H), 6.98 (d, 2H, $J = 8.0$ Hz), 6.19 (s, 1H), 5.12 (s, 2H), 2.23 (s, 6H); ^{13}C NMR (CDCl_3) δ 138.4, 138.3, 135.6, 133.9, 131.6, 129.4, 129.1, 128.4, 127.7, 127.0, 125.9, 125.4, 123.5, 122.2, 121.4, 120.0, 113.9, 111.0, 107.1, 47.3, 12.6, 11.4; HRMS (ESI^+) m/z calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2\text{O}_2\text{S}$ (MH^+) 441.1637, found 441.1631.

2-(1-Benzyl-2,5-diphenyl-1H-pyrrol-3-yl)-1H-indole (30): White solid, 92% yield; ^1H NMR (CDCl_3) δ 7.73 (br s, 1H), 7.56-7.36 (m, 11H), 7.20-7.07 (m, 6H), 6.77-6.75 (m, 3H), 6.47 (s, 1H), 5.12 (s, 2H); ^{13}C NMR (CDCl_3) δ 139.1, 136.3, 136.0, 134.7, 133.3, 132.9, 131.9, 131.6, 129.4, 129.3, 129.1, 129.0, 128.8, 128.6, 127.8, 127.2, 126.2, 121.2, 120.0, 119.9, 115.6, 110.5, 108.3, 98.7, 48.7; HRMS (ESI^+) m/z

calculated for $C_{31}H_{25}N_2$ (MH^+) 425.2018, found 425.2018.

2-(1-Benzyl-2,5-diphenyl-1*H*-pyrrol-3-yl)-1-methyl-1*H*-indole (31): Pale yellow solid, 90% yield; 1H NMR ($CDCl_3$) δ 7.53-7.03 (m, 17H), 6.72 (d, 2H, $J = 7.8$ Hz), 6.49 (s, 1H), 6.34 (s, 1H), 5.23 (s, 2H), 3.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 139.2, 132.0, 130.7, 130.0, 129.4, 129.0, 128.7, 128.6, 128.5, 128.4, 127.7, 127.6, 127.1, 126.2, 120.7, 120.1, 119.4, 112.1, 109.4, 101.7, 49.1, 30.9; HRMS (ESI^+) m/z calculated for $C_{32}H_{27}N_2$ (MH^+) 439.2174, found 439.2176.

2-(1-Benzyl-2,5-diphenyl-1*H*-pyrrol-3-yl)-1-(phenylsulfonyl)-1*H*-indole (32): White solid, 94% yield; 1H NMR ($CDCl_3$) δ 8.32 (d, 1H, $J = 8.3$ Hz), 7.62 (d, 2H, $J = 9.5$ Hz), 7.51-7.11 (m, 17H), 6.95 (dd, 2H, $J = 1.5, 8.1$ Hz), 6.75-6.72 (m, 2H), 6.51 (s, 1H), 6.25 (s, 1H), 5.20 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 139.6, 139.1, 137.9, 136.8, 136.3, 135.2, 133.5, 133.4, 132.2, 130.9, 130.4, 129.4, 129.0, 128.7, 128.5, 128.2, 127.7, 127.5, 127.2, 126.4, 124.2, 123.8, 120.5, 116.0, 114.1, 113.9, 113.0, 49.1; HRMS (ESI^+) m/z calculated for $C_{37}H_{29}N_2O_2S$ (MH^+) 565.1950, found 565.1945.

2-(1-Benzyl-2,5-dimethyl-1*H*-pyrrol-3-yl)-1*H*-indole (33): White solid, 92% yield; 1H NMR ($CDCl_3$) δ 8.11 (br s, 1H), 7.64 (d, 1H, $J = 6.6$ Hz), 7.40-7.30 (m, 4H), 7.20-7.14 (m, 2H), 7.00 (d, 2H, $J = 7.6$ Hz), 6.49 (s, 1H), 6.19 (s, 1H), 5.12 (s, 2H), 2.41 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.2, 136.0, 135.7, 130.0, 129.1, 128.7, 127.5, 126.1, 125.9, 121.0, 119.9, 119.9, 112.7, 110.5, 105.1, 98.5, 47.2, 25.7, 12.6, 11.7; HRMS (ESI^+) m/z calculated for $C_{21}H_{21}N_2$ (MH^+) 301.1705, found 301.1706.

2-(1-Benzyl-2,5-dimethyl-1*H*-pyrrol-3-yl)-1-methyl-1*H*-indole (34): Pale yellow solid, 70% yield; 1H NMR ($CDCl_3$) δ 7.66 (d, 1H, $J = 7.8$ Hz), 7.42-7.15 (m, 6H), 7.03 (d, 2H, $J = 7.3$ Hz), 6.45 (s, 1H), 6.10 (s, 1H), 5.15 (s, 2H), 3.78 (s, 3H), 2.28 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.4, 137.8, 129.1, 128.6, 128.1, 127.7, 127.5, 125.9, 120.8, 120.0, 119.5, 111.6, 109.4, 108.0, 101.0, 47.4, 31.0, 12.6, 11.3; HRMS (ESI^+) m/z calculated for $C_{22}H_{23}N_2$ (MH^+) 315.1861, found 315.1864.

2-(1-Benzyl-2,5-dimethyl-1*H*-pyrrol-3-yl)-1-(phenylsulfonyl)-1*H*-indole (35): Light orange solid, 86% yield; 1H NMR ($CDCl_3$) δ 8.39 (d, 1H, $J = 8.3$), 7.50-7.07 (m, 13H), 6.40 (s, 1H), 6.09 (s, 1H), 5.08 (s, 2H), 2.26 (s, 3H), 1.92 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 138.8, 138.4, 138.1, 138.0, 133.4, 130.9, 129.1, 128.7, 127.5, 127.1, 127.0, 126.1, 124.1, 124.1, 120.3, 116.5, 112.4, 111.1, 110.1, 47.4, 12.6, 11.1; HRMS (ESI^+) m/z calculated for $C_{27}H_{25}N_2O_2S$ (MH^+) 441.1637, found 441.1641.

3-(1-Benzyl-5-methyl-2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indole (36a): White solid, 51% (obtained as the

major isomer – 77:23 ratio of **36a:36b**); ^1H NMR (CDCl_3) δ 7.80 (d, 1H, $J = 7.6$ Hz), 7.45-7.08 (m, 11H), 7.00 (d, 2H, $J = 7.1$ Hz), 6.69 (d, 1H, $J = 2.4$ Hz), 6.49 (s, 1H), 5.09 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.4, 136.2, 133.9, 131.4, 129.1, 129.0, 128.9, 128.7, 128.5, 127.3, 127.1, 126.0, 122.3, 121.9, 121.9, 120.7, 119.6, 115.3, 112.6, 111.2, 108.4, 47.9, 12.8; HRMS (EI^+) m/z calculated for $\text{C}_{26}\text{H}_{22}\text{N}_2$ (M^+) 362.17830, found 362.17707.

3-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1H-indole (36b): Clear oil, 20% (obtained as the major isomer – 63:37 ratio of **36b:36a**); ^1H NMR (CDCl_3) δ 8.09 (s, 1H), 7.85 (d, 1H, $J = 7.8$), 7.43-7.06 (m, 14H), 6.62 (s, 1H), 5.26 (s, 2H), 2.26 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.3, 136.4, 134.4, 129.0, 128.9, 128.9, 128.7, 127.3, 127.3, 127.0, 126.0, 122.3, 121.9, 121.8, 120.7, 119.8, 115.1, 113.0, 111.3, 109.7, 48.3, 11.7; HRMS (EI^+) m/z calculated for $\text{C}_{26}\text{H}_{22}\text{N}_2$ (M^+) 362.17830, found 362.17743.

3-(1-Benzyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (37a): Orange solid, 86% (obtained as the major isomer – 74:26 ratio of **37a:37b**); ^1H NMR (CDCl_3) δ 7.73 (d, 1H, $J = 8.1$ Hz), 7.41-7.18 (m, 9H), 7.09 (t, 2H, $J = 6.8$ Hz), 7.00 (d, 2H, $J = 7.6$), 6.59 (s, 1H), 6.45 (s, 1H), 5.08 (s, 2H), 3.65 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.5, 137.0, 134.0, 131.3, 129.0, 128.9, 128.5, 127.3, 127.1, 126.6, 126.0, 121.4, 120.9, 119.0, 115.4, 111.2, 109.2, 108.5, 47.9, 32.8, 12.8; HRMS (ESI^+) m/z calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2$ (MH^+) 377.2018, found 377.2021.

3-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (37b): Orange oil, 39% (obtained as the major isomer – 56:44 ratio of **37b:37a**); ^1H NMR (CDCl_3) δ 7.91 (d, 1H, $J = 7.8$ Hz), 7.50-7.12 (m, 14H), 6.67 (s, 1H), 5.31 (s, 2H), 3.87 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.4, 137.1, 134.3, 131.4, 129.2, 128.9, 128.7, 127.2, 126.9, 126.5, 126.0, 121.8, 120.8, 119.3, 115.3, 111.1, 109.8, 109.4, 48.3, 33.0, 11.7; HRMS (ESI^+) m/z calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2$ (MH^+) 377.2018, found 377.2021.

3-(1-Benzyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (38a): Pale orange solid, 71% (obtained as the major isomer – 88:12 ratio of **38a:38b**); ^1H NMR (CDCl_3) δ 8.02 (d, 1H, $J = 8.3$ Hz), 7.67 (d, 2H, $J = 7.8$ Hz), 7.50-7.19 (m, 13H), 7.08 (s, 1H), 6.96 (d, 2H, $J = 7.1$ Hz), 6.39 (s, 1H), 5.07 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.9, 138.3, 135.4, 133.7, 133.1, 131.7, 131.2, 129.7, 129.3, 129.1, 129.0, 128.7, 127.9, 127.3, 127.0, 126.0, 124.7, 123.6, 122.8, 121.3, 119.4, 113.8, 112.8, 108.2, 48.0, 12.8; HRMS (ESI^+) m/z calculated for $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ (MH^+) 503.1793, found 503.1789.

3-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (38b): Orange solid, 65% (obtained as the major isomer – 51:49 ratio of **38b:38a**); ^1H NMR (CDCl_3) δ 8.10 (d, 2H, $J = 8.3$

Hz), 7.94 (d, 2H, $J = 7.6$ Hz), 7.77 (d, 2H, $J = 7.6$ Hz), 7.66 (d, 2H, $J = 7.6$ Hz), 7.54-7.18 (m, 10H), 7.04 (d, 2H, $J = 7.1$ Hz), 6.55 (s, 1H), 5.24 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.9, 138.3, 135.4, 133.6, 133.0, 131.4, 131.3, 129.7, 129.3, 129.1, 129.0, 128.7, 127.9, 127.3, 127.0, 125.9, 124.6, 123.4, 122.5, 121.3, 119.4, 113.8, 112.7, 108.2, 48.0, 11.7; HRMS (ESI^+) m/z calculated for $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ (MH^+) 503.1793, found 503.1795.

2-(1-Benzyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-1H-indole (39a): Off-white solid, 89% (obtained as the major isomer – 87:13 ratio of **39a:39b**); ^1H NMR (CDCl_3) δ 7.68 (br s, 1H), 7.53-7.25 (m, 8H), 7.15-7.03 (m, 3H), 6.94 (d, 2H, $J = 7.1$ Hz), 6.43 (s, 1H), 6.40 (d, 1H, $J = 1.7$ Hz), 4.98 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.8, 135.9, 135.1, 133.1, 131.6, 130.2, 130.1, 129.2, 129.1, 129.0, 128.9, 128.8, 127.4, 125.9, 125.9, 120.9, 119.8, 119.7, 114.0, 110.4, 106.4, 98.3, 47.7, 12.7; HRMS (ESI^+) m/z calculated for $\text{C}_{26}\text{H}_{23}\text{N}_2$ (MH^+) 363.1861, found 363.1862.

2-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1H-indole (39b): Off-white solid, 62% (obtained as the major isomer – 74:26 ratio of **39b:39a**); ^1H NMR (CDCl_3) δ 8.16 (br s, 1H), 7.64 (d, 2H, $J = 7.1$ Hz), 7.38-7.02 (m, 12H), 6.54-6.52 (m, 2H), 5.23 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.7, 136.1, 135.1, 133.3, 131.6, 129.9, 129.2, 129.1, 129.0, 128.9, 128.8, 127.6, 127.5, 125.9, 125.9, 121.3, 120.1, 119.8, 114.3, 110.6, 107.1, 99.0, 48.2, 11.9; HRMS (ESI^+) m/z calculated for $\text{C}_{26}\text{H}_{23}\text{N}_2$ (MH^+) 363.1861, found 363.1859.

2-(1-Benzyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (40a): Yellow solid, 76% (obtained as the major isomer – 90:10 ratio of **40a:40b**); ^1H NMR (CDCl_3) δ 7.55 (d, 1H, $J = 7.8$ Hz), 7.39-6.99 (m, 13H), 6.34 (s, 1H), 6.23 (s, 1H), 5.15 (s, 2H), 3.40 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.0, 137.6, 132.9, 130.5, 129.8, 129.1, 129.1, 128.8, 128.6, 128.6, 127.5, 127.4, 125.9, 120.6, 120.0, 119.3, 113.5, 110.1, 109.4, 101.5, 48.1, 30.8, 12.8; HRMS (ESI^+) m/z calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2$ (MH^+) 377.2018, found 377.2019.

2-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1-methyl-1H-indole (40b): Yellow oil, 45% (obtained as the minor isomer – 30:70 ratio of **40b:40a**); ^1H NMR (CDCl_3) δ 7.66 (d, 1H, $J = 7.6$ Hz), 7.40-7.00 (m, 13H), 6.49 (s, 1H), 6.44 (s, 1H), 5.26 (s, 2H), 3.80 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.9, 137.6, 132.8, 130.5, 129.8, 129.1, 129.0, 128.8, 128.7, 128.6, 127.5, 127.4, 125.9, 120.9, 120.1, 119.6, 113.4, 110.1, 109.5, 101.3, 48.4, 31.0, 11.5; HRMS (ESI^+) m/z calculated for $\text{C}_{27}\text{H}_{25}\text{N}_2$ (MH^+) 377.2018, found 377.2018.

2-(1-Benzyl-5-methyl-2-phenyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (41a): Tan solid, 95% (obtained as the major isomer – 79:21 ratio of **41a:41b**); ^1H NMR (CDCl_3) δ 8.26 (d, 1H, $J = 8.5$ Hz), 7.63-7.12 (m, 13H), 7.02-6.97 (m, 5H), 6.28 (s, 1H), 6.23 (s, 1H), 5.09 (s, 2H), 2.24 (s, 3H); ^{13}C NMR (CDCl_3) δ 139.6, 138.9, 137.8, 137.5, 134.2, 133.5, 132.5, 130.8, 129.1, 129.0, 129.0, 128.9, 128.8, 128.8, 128.3, 127.4, 127.2, 127.1, 124.1, 123.8, 120.5, 116.0, 113.0, 111.7, 48.1, 12.8; HRMS (ESI^+) m/z calculated for $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ (MH^+) 503.1793, found 503.1801.

2-(1-Benzyl-2-methyl-5-phenyl-1H-pyrrol-3-yl)-1-(phenylsulfonyl)-1H-indole (41b): Tan solid, 78% (obtained as the major isomer – 91:9 ratio of **41b:41a**); ^1H NMR (CDCl_3) δ 8.40 (d, 1H, $J = 8.1$ Hz), 7.53-7.10 (m, 18H), 6.49 (s, 1H), 6.39 (s, 1H), 5.22 (s, 2H), 1.97 (s, 3H); ^{13}C NMR (CDCl_3) δ 138.8, 138.8, 138.1, 137.4, 133.5, 131.5, 130.8, 129.1, 129.1, 128.9, 128.9, 128.7, 128.7, 128.3, 127.5, 127.3, 127.1, 126.1, 124.3, 124.1, 120.4, 116.5, 112.6, 112.2, 48.3, 11.5; HRMS (ESI^+) m/z calculated for $\text{C}_{32}\text{H}_{27}\text{N}_2\text{O}_2\text{S}$ (MH^+) 503.1793, found 503.1797.

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