ethyl acetate/5% acetic acid/60% hexane as eluant provided 2.39 g (84%) of colorless lunularic acid: mp 194–195 °C dec (lit.[9] mp 195–196 °C); ^{1}H NMR (DMSO-d_6) δ 2.64–2.73 (m, 2 H, CH_2CH_2), 2.79–3.08 (m, 2 H, CH_2CH_2) 6.62–6.77 (m, 4 H, ArH), 6.98 (t, J = 8 Hz, 2 H, ArH), 7.16 (t, J = 8 Hz, 1 H, ArH); ^{13}C NMR (CD_3OD) δ 38.7, 39.7, 113.7, 115.1, 116.1 (2 C), 120.9, 123.3, 130.3 (2 C) 134.4, 146.0 156.4, 162.7 174.3; IR (KBr) 3461, 3012, 2939, 2850, 1606, 1514, 1466, 1293, 1246, 1170, 1147, 902, 825, 773 cm^{-1}; MS (70 eV) m/e (rel intensity) 258 (12), 107 (100), 105 (5), 77 (12). Anal. Calcd for $C_{15}H_{14}O_2$: C, 69.76; H, 5.46. Found: C, 69.59; H, 5.50.

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Regiocontrolled Nucleophilic Addition to Selectively Activated *p*-Quinone Diimines: Alternative Preparation of a Key Intermediate Employed in the Preparation of the CC-1065 Left-Hand Subunit

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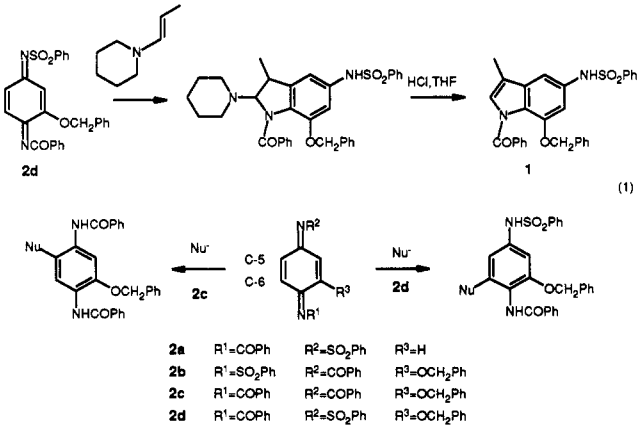
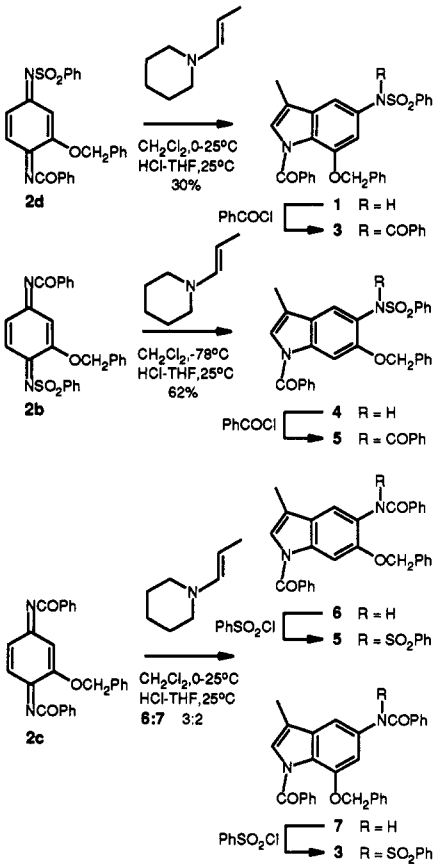
In the course of studies on the total synthesis of (+)-CC-1065 and structurally related agents[2] we have detailed the use of a regiospecific nucleophilic addition to a selectively activated *p*-quinone diimine in the preparation of indole **1**. In these studies, base-catalyzed nucleophilic addition to N^1,N^4-dibenzoyl-*p*-benzoquinone diimine **2c** proceeded predictably with selective C-5 substitution, *and* the inherent regioselectivity of this nucleophilic addition was reversed by the introduction of the N^4-phenylsulfonyl imide of *p*-quinone diimine **2d**. Thus, the selective electrophilic activation of C-6 by the N^4-phenylsulfonyl imide of **2d** proved sufficient to override the inherent preference for C-5 nucleophilic addition observed with the *p*-quinone diimine **2c**, eq 1. Herein we detail a full study of the



regiocontrol available to base-catalyzed, acid-catalyzed, and

Scheme I



Lewis acid-catalyzed nucleophilic additions to selectively activated *p*-quinone diimines and describe its application to the preparation of substituted indoles.[3,4] The reversal of the regioselectivity of nucleophilic addition to *p*-quinone diimine **2c** for reactions under control of Lewis acid activation permitted an alternative and improved preparation of N^1,N^5-dibenzoyl-5-amino-7-(benzyloxy)-3-methylindole, a key intermediate employed in the synthesis of the left-hand subunit of CC-1065.[2]

Enamine Additions to 2b–d. The nucleophilic addition of 1-piperidino-1-propene to **2c** followed by acid-catalyzed aromatization proceeded to provide a mixture of **6** and **7** in which the predominant product **6** (**6**:**7**, 3:2) was derived from nucleophilic addition to C-5 albiet in modest conversion, Scheme I. This preference for C-5 nucleophilic addition was enhanced in **2b** with the N^1-phenylsulfonyl selective activation of C-5 addition and its treatment with 1-piperidino-1-propene followed by acid-catalyzed aromatization provided **4** exclusively in good yield (62–71%). Thus, the complementary N^1-phenylsulfonyl activation in **2b** was found to further enhance the *p*-quinone diimine rate and regioselectivity of C-5 nucleophilic addition. In addition, as previously detailed,[2] the inherent preference for C-5 nucleophilic addition was reversed in **2d** with the overriding N^4-phenylsulfonyl activation of C-6 addition. Treatment of **2d** with 1-piperidino-1-propene followed by acid-catalyzed aromatization provided **1**. Thus, the noncomplementary N^4-

(1) National Institutes of Health research career development award recipient, 1983–1988 (Grant CA01134). Alfred P. Sloan research fellow, 1985–1989.

(2) Boger, D. L.; Coleman, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 1321. Boger, D. L.; Coleman, R. S. *J. Am. Chem. Soc.* **1988**, *110*, 4796.

(3) Adams, R.; Reifschneider, W. *Bull. Chim. Soc. Fr.* **1958**, 23.

(4) For recent efforts with *p*-quinone diimines, see: Mukaiyama, T.; Sagawa, Y.; Kobayashi, S. *Chem. Lett.* **1987**, 2169. Ohnuma, T.; Sekine, Y.; Ban, Y. *Tetrahedron Lett.* **1979**, *20*, 2533. Rajappa, S.; Shenoy, S. J. *Tetrahedron* **1986**, *42*, 5739. Rajappa, S.; Sreenivasan, R.; Rane, A. V. *Tetrahedron Lett.* **1983**, *24*, 3155. Holmes, T. J., Jr.; Lawton, R. G. *J. Org. Chem.* **1983**, *48*, 3146.

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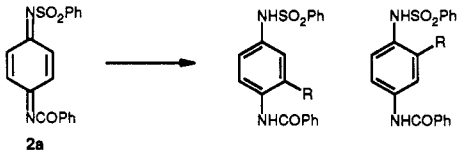
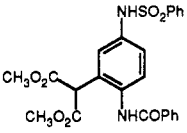
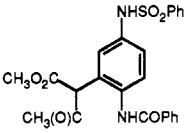
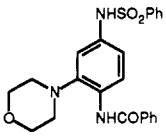
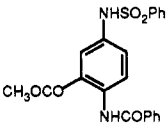
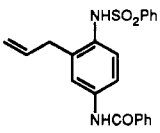
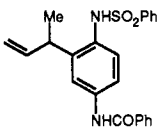
Table I. Nucleophilic Additions to 2a



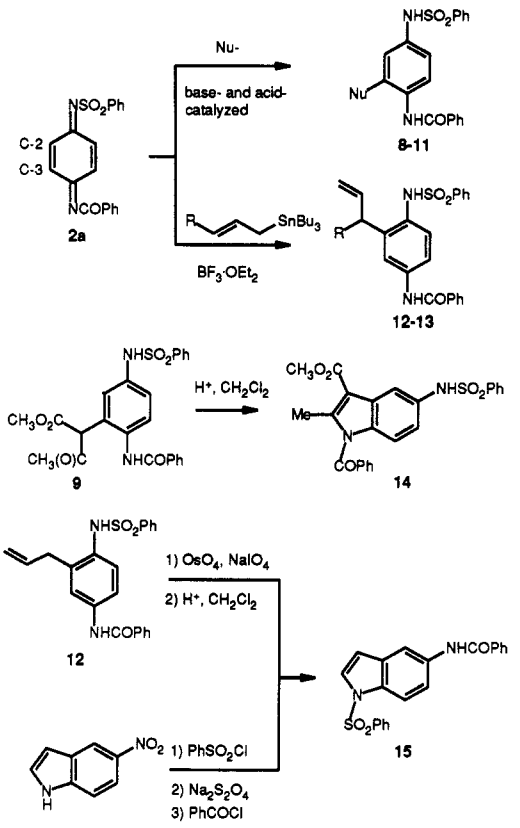
2a

entry	nucleophile	conditions: solvent, temp, time	products	yield, %
1	CH_3O_2C, CO_2CH_3	MeONa (0.2 equiv) THF, 0°C, 6 h		8 81
2	$CH_3(O)C$, CO_2CH_3	MeONa (0.2 equiv) THF, -35°C, 12 h		9 80
3		Et_2O, -20°C, 12 h		10 60
4	CH_3COOH	H_2SO_4 (0.1 equiv) CH_3CO_2H, 25°C, 15 h		11 50
		BF_3·OEt_2 (0.1 equiv) CH_3CO_2H, 25°C, 8 h		57
5	Bu_3Sn	BF_3·OEt_2 (0.25 equiv) CH_2Cl_2, -20°C, 24 h		12 67
6	Bu_3Sn	BF_3·OEt_2 (0.25 equiv) CH_2Cl_2, -78°C, 12 h -20°C, 12 h		13 54

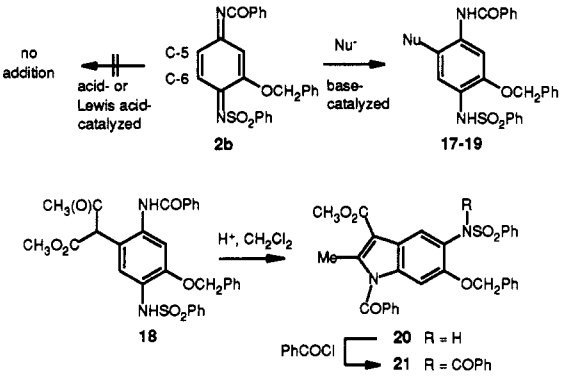
phenylsulfonyl activation of C-6 addition proved sufficient to control the regioselectivity of nucleophilic addition. The structure of the addition products **1**, **4**, **6–7** were deduced initially through spectroscopic techniques and confirmed through the unambiguous correlations with the authentic indole **1**[2] as detailed in Scheme I.

Nucleophilic Additions to N^4-Benzoyl-N^1-(phenylsulfonyl)-*p*-benzoquinone Diimine (2a). The results of a study of the base-catalyzed nucleophilic addition of soft nucleophiles (dimethyl malonate, methyl acetoacetate, morpholine) and the acid-catalyzed nucleophilic addition of a weak nucleophile (acetic acid) to **2a** are summarized in Table I and Scheme II. In each instance, the base-catalyzed *or* acid-catalyzed nucleophilic addition to **2a** was found to proceed with selective C-3 addition (≥20:1) under the control of the selective activation of the N^1-phenylsulfonyl imide and proceeded with greater facility than that observed with the symmetrical and less activated parent N^1,N^4-dibenzoyl-*p*-benzoquinone diimine.[2,3] The addition of acetic acid to **2a** proceeded slowly in the absence of additional catalyst, was accelerated by the addition of catalytic sulfuric acid (0.1 equiv), and proceeded most rapidly and cleanly in the presence of catalytic boron trifluoride etherate (0.1 equiv). In marked contrast, the Lewis acid catalyzed (0.25 equiv of BF_3·OEt_2) addition of allyltri-*n*-butylstannane and 2-butenyltri-*n*-

Scheme II



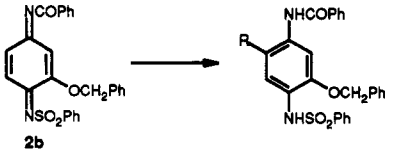
Scheme III



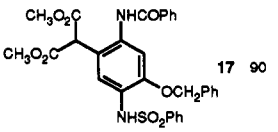
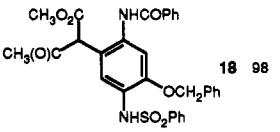
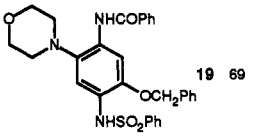
butylstannane proceeded with clean C-2 addition to **2a** under the control of the selective Lewis acid activation of the more basic N^4-benzoyl imide, Table I, entries 5–6.[5] Thus, the inherent preference for C-3 nucleophilic addition to the selectively activated *p*-quinone diimine **2a** (**2a** → **8–10**) may be reversed for nucleophilic additions that proceed under conditions that require Lewis acid activation (**2a** → **12–13**). The structure of the addition products **8–13** were deduced through spectroscopic techniques (**8–10**),[6]

(5) Attempts to promote the nucleophilic addition of allyltri-*n*-butylstannane or allyltrimethylsilane to **2a** under thermal (110 °C, toluene) or pressure-promoted conditions (6.2–12 kbar, CH_2Cl_2, 25 °C) provided reduced *p*-quinone diimine.

Table II. Nucleophilic Additions to 2b



2b

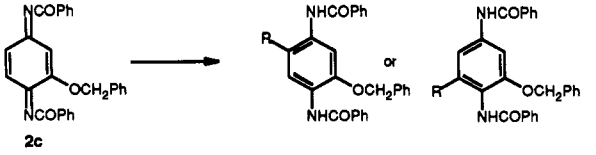
entry	nucleophile	conditions: solvent, temp, time	products	yield, %
1	CH_3O_2C CO_2CH_3	MeONa (0.2 equiv) THF, -78°C, 12 h 0°C, 1 h	 **17**	90
2	$CH_3(O)C$ CO_2CH_3	MeONa (0.2 equiv) THF, -20°C, 1 h	 **18**	98
3		THF, -78°C, 2 h	 **19**	69
4	CH_3COOH	THF, 25°C, 72 h	no reaction	
		CH_2Cl_2, 25°C, BF_3·OEt_2	reduced **2b**	
		CH_3CO_2Na, THF, 25°C	reduced **2b**	
		CH_3CO_2Na, DMF, 25°C	no reaction	

correlation and comparison with authentic material (11), and in the case of **12** and **13** confirmed upon subsequent conversion of **12** to the authentic indole **15**, Scheme II.

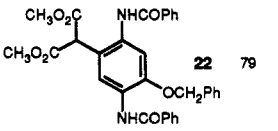
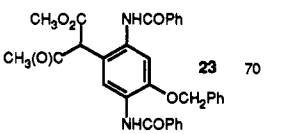
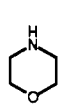
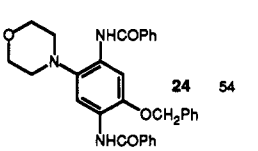
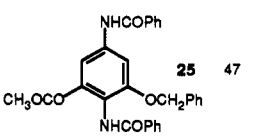
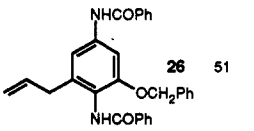
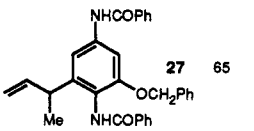
Nucleophilic Additions to N^4-Benzoyl-N^1-(phenylsulfonyl)-2-(benzyloxy)-*p*-benzoquinone Diimine (2b). The results of the study of the base-catalyzed, acid-catalyzed, and Lewis acid catalyzed nucleophilic addition to **2b** are summarized in Table II and Scheme III. The selective N^1-phenylsulfonyl activation of C-5 toward nucleophilic addition coupled with the complementary C-2 benzyloxy electronic deactivation of C-3/C-6 toward nucleophilic addition proved sufficient to provide exclusive base-catalyzed C-5 nucleophilic addition products. As might be anticipated, the base-catalyzed nucleophilic additions to **2b** proceeded with greater facility than **2c** but with less facility than **2a** (intrinsic electrophilic reactivity: **2a** > **2b** > **2c**). The acid-catalyzed nucleophilic addition of acetic acid (CH_3CO_2H, 25 °C) and the Lewis acid catalyzed nucleophilic addition of allyltri-*n*-butylstannane with **2b** failed to provide discernable addition products[7] and presumably reflect the overall electronic deactivation of the system toward productive protonation or Lewis acid coordination. The structure of the addition products **17**–**19** were initially assigned based on spectroscopic evidence,[6] and the structure of **18** was correlated through indoles **20**/**21** with the nucleophilic addition products derived from *p*-quinone diimines **2c**–**d**, Scheme III.

Nucleophilic Additions to N^1,N^4-Dibenzoyl-2-(benzyloxy)-*p*-benzoquinone Diimine (2c). The results of the study of the base-catalyzed, acid-catalyzed, and Lewis acid catalyzed nucleophilic additions to the unsymmetrical but equivalently activated *p*-quinone diimine **2c**[2,3] are summarized in Table III and Scheme IV. The base-catalyzed nucleophilic addition to **2c** provided predominantly (Table III, entries 1 and 2, ≥6:1) or exclusively (Table III, entry 3) the C-5 nucleophilic addition products resulting from electronic deactivation of C-6 nucleophilic addition and the steric and electronic deactivation of C-3 nucleophilic addition attributable to the C-2 benzyloxy substituent (vinylogous acyl imidate). In contrast, the acid-catalyzed nucleophilic addition of acetic acid to **2c** proceeds with exclusive C-6 addition and presumably may be attributed to preferential N^4-benzoyl imide protonation due to its selective nucleophilic activation by the C-2 benzyloxy substituent.[8a] Similarly, the Lewis acid catalyzed (BF_3·OEt_2) nucleophilic addition of allyltri-*n*-butylstannane and 2-butenyltri-*n*-butylstannane to **2c** provided clean C-6 nucleophilic addition, presumably reflecting the preferential Lewis acid coordination of boron trifluoride etherate to the N^4-benzoyl imide.[8b] Thus, the C-2 benzyloxy substituent in the symmetrically activated *p*-quinone diimine serves to deactivate base-catalyzed C-6

Table III. Nucleophilic Additions to 2c



2c

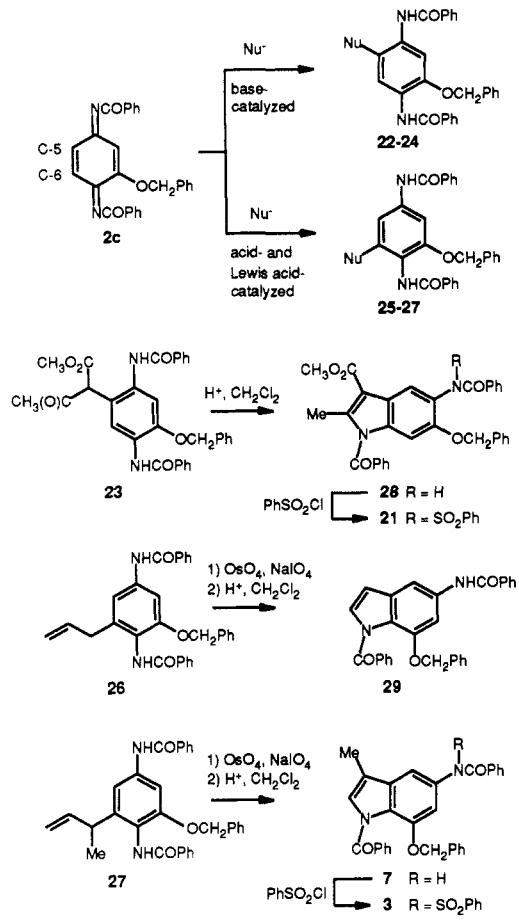
entry	nucleophile	conditions: solvent, temp, time	products	yield, %
1	CH_3O_2C CO_2CH_3	MeONa (0.2 equiv) THF, -10°C, 1 h	 **22**	79
2	$CH_3(O)C$ CO_2CH_3	MeONa (0.2 equiv) THF, -78°C, 4 h 0°C, 8 h	 **23**	70
3		DMF, 25°C, 10 h	 **24**	54
4	CH_3COOH	CH_3CO_2H, 25°C, 48 h	 **25**	47
5	Bu_3Sn	BF_3·OEt_2 (0.5 equiv) CH_2Cl_2, 25°C, 24 h	 **26**	51
6	Bu_3Sn	BF_3·OEt_2 (1.0 equiv) CH_2Cl_2, -78°C, 12 h	 **27**	65

(6) Supplementary material: in addition to characteristic chemical shifts, the assignments were established with the observation of a characteristic meta coupling (J = 0.5–1.5 Hz) and the absence of a para H–H coupling (J = 0 Hz).

(7) Under forcing conditions, reduction of the *p*-quinone diimine **2b** was observed.

(8) (a) Interestingly, the Lewis acid catalyzed (BF_3·OEt_2) addition of acetic acid (CH_3CO_2H, CH_2Cl_2, -45 °C, 24 h) to **2c** provided a mixture of products derived from C-5, C-6, *and* C-3 addition. (b) Lewis acid catalyzed addition of allyltrimethylsilane to **2c** failed to provide addition products in comparable conversions.

Scheme IV

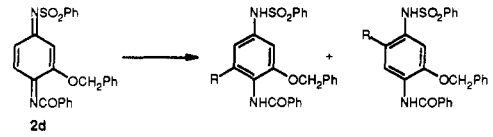


nucleophilic addition, activate acid-catalyzed C-6 nucleophilic addition, and through selective complexation with boron trifluoride etherate may facilitate Lewis acid catalyzed C-6 nucleophilic addition. The structural assignments of the addition products **22–27** were deduced through spectroscopic techniques (**22–25**)[6] and in the case of **23** and **27** were unambiguously established through correlation with the authentic indoles **20**/**21** and **7**/**1**, respectively, Scheme IV.[9] Thus, the addition of 2-butenyltri-*n*-butylstannane to **2c** that proceeds with selective Lewis acid activation toward C-6 nucleophilic addition provided **27** and provided an alternative, improved preparation of the suitably protected indole **7** for use in the synthesis of the left-hand subunit of CC-1065.[2] This predictable and selective Lewis acid activation of **2c** toward C-6 addition for reactions requiring Lewis acid catalysis *overrides* the inherent nature of **2c** to undergo base-catalyzed C-5 nucleophilic addition.

Nucleophilic Additions to N^1-Benzoyl-N^4-(phenylsulfonyl)-2-(benzyloxy)-*p*-benzoquinone Diimine (2d). The results of the study of the nucleophilic additions to *p*-quinone diimine **2d**[2] are summarized in Table IV and Scheme V. As detailed in prior studies,[2] the selective activation of C-6 nucleophilic addition attributable to the N^4-phenylsulfonyl imide proved sufficient to override the intrinsic C-2 benzyloxy deactivation of C-6 addition. Thus,

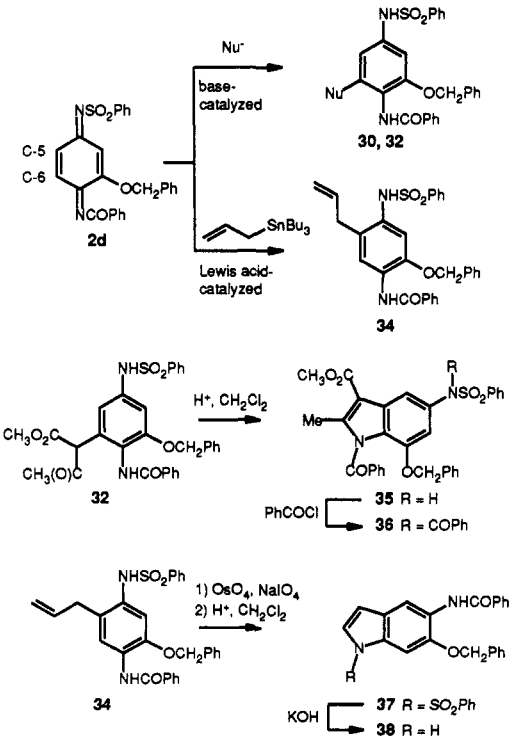
(9) Minor C-5 addition of dimethyl malonate, methyl acetoacetate, allyl- and 2-butenyltri-*n*-butylstannane was observed with **2c**: C-6:C-5 addition = 16:1, 10:1, 10:1, and 12:1 respectively. The minor adduct of **2c** with allyltri-*n*-butylstannane was correlated with the C-5 addition product of allyltri-*n*-butylstannane with **2d** (cf. **38**) and the minor C-5 adduct of the reaction of **2c** with 2-butenyltri-*n*-butylstannane was correlated with **5**.

Table IV. Nucleophilic Additions to 2d



entry	nucleophile	conditions: solvent, temp, time	products (yield, %)
1	CH_3O_2C CO_2CH_3	MeONa (0.2 equiv) CH_2Cl_2, -78°C, 12 h 25°C, 3 h	**30** (65 %) **31** (15 %)
2	$CH_3(O)C$ CO_2CH_3	MeONa (0.2 equiv) CH_2Cl_2, -50°C, 18 h	**32** (71 %) **33** (10 %)
3		DMF, 25°C, 48 h THF, 25°C, 48 h CH_2Cl_2, 25°C, 48 h	no reaction
4	CH_3COOH	CH_3CO_2Na, DMF, 25°C CH_3CO_2H, 25°C, 48 h CH_3CO_2H, $BF_3{\cdot}OEt_2$, CH_2Cl_2	no reaction
5	Bu_3Sn	$BF_3{\cdot}OEt_2$ (0.5 equiv) CH_2Cl_2, 25°C, 4 h	**34** (61 %)

Scheme V



the base-catalyzed nucleophilic addition of soft nucleophiles and enamines[2] to **2d** was found to proceed with selective C-6 substitution. In contrast to the *p*-quinone diimines **2a–c**, the noncomplementary N^4-phenylsulfonyl and C-2 benzyloxy substitution of the *p*-quinone diimine proved sufficient to prevent the observation of nucleophilic addition of morpholine to **2d**. In addition, the acid-catalyzed addition of acetic acid failed to provide an addition product. The Lewis acid catalyzed addition of allyltri-*n*-

butylstannane to **2d** provided **34** derived from C-5 nucleophilic addition and presumably reflects the selective Lewis acid coordination to the N^1-benzoyl imide potentially further facilitated by the proximal C-2 benzyloxy substituent. The structural assignments[6] of the addition products **30–33** were determined by correlation of **32** (through **36**) with **20** and **28** (through **21**), which indicated that **36** and **21** were isomeric with one another. The confirmed structural assignment of **34**[6] rested with its conversion to indole **37**, which upon mild base treatment underwent selective removal of the phenylsulfonyl (versus benzoyl) group.[9]

Thus, in addition to the regiocontrol available for base-catalyzed nucleophilic additions through use of selectively activated *p*-quinone diimines,[2,4] the use of selective Lewis acid activation of unsymmetrical (**2c**) or selectively activated (**2a–b,d**) *p*-quinone diimines for nucleophilic additions Lewis acid catalysis offers an alternative and potentially complementary approach to regiocontrol. The potential of the latter proved useful in the development of an alternative and improved preparation of **7**, a suitably protected indole for use in the preparation of the left-hand subunit of CC-1065.

Experimental Section[10]

N^5-(Phenylsulfonyl)-5-amino-1-benzoyl-7-(benzyloxy)-3-methylindole (1):[2] white, crystalline solid; mp 184–185 °C (EtOAc–hexane, white needles); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.8–7.2 (m, 15 H, ArH), 7.12 (d, 1 H, J = 1.2 Hz, C2-H), 6.77 (d, 1 H, J = 1.8 Hz, C6-H), 6.70 (br s, 1 H, NH), 6.60 (d, 1 H, J = 1.8 Hz, C4-H), 4.87 (s, 2 H, PhCH_2O), 2.14 (d, 3 H, J = 1.2 Hz, ArCH_3); IR (KBr) ν_{max} 3285, 1699, 1616, 1600, 1580, 1499, 1448, 1356, 1340, 1276, 1240, 1157, 1147, 1089, 1002, 835, 755, 720, 687, 668 cm^{-1}; EIMS m/e (relative intensity) 496 (M^+, 2), 355 (6), 249 (1), 169 (3), 141 (1), 125 (1), 105 (base), 91 (48), 77 (40); CIMS (isobutane) m/e 497 (M^+ + H); EIHRMS, m/e 496.1452 ($C_{29}H_{24}N_2O_4S$ requires 496.1457).

N^4-Benzoyl-N^1-(phenylsulfonyl)-*p*-benzoquinone Diimine (2a). A solution of 4-nitroaniline[11] (10 g, 72 mmol, 1.0 equiv) in 240 mL of dry tetrahydrofuran was treated with potassium carbonate (20 g, 145 mmol, 2.0 equiv) and benzoyl chloride (11 g, 76 mmol, 1.05 equiv), and the reaction mixture was stirred for 12 h at 25 °C. The reaction mixture was poured onto 200 mL of 10% aqueous hydrochloric acid and filtered. The collected yellow solid was washed with water (200 mL) and hexane (200 mL) to afford *N*-benzoyl-4-nitroaniline (15.6 g, 89%) as a crystalline solid: mp 199–200 °C (EtOAc–hexane, white needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.27 (d, 2 H, J = 8.9 Hz, C2-H and C6-H, PhCO), 8.06 (s, 1 H, NH), 7.91–7.51 (7 H, ArH); IR (melt) ν_{max} 3854, 3650, 1734, 1718, 1700, 1684, 1654, 1560, 1540, 1508, 1458 cm^{-1}.

A solution of *N*-benzoyl-4-nitroaniline (10 g, 40 mmol, 1.0 equiv) in 200 mL of ethyl acetate was treated with 10% palladium on carbon (2 g, 20% wt equiv), and the reaction mixture was shaken under an atmosphere of hydrogen (50 psi) for 2 h at 25 °C. The reaction mixture was filtered through a layer of Celite, and the filtrate was concentrated in vacuo to afford pure N^1-benzoyl-1,4-diaminobenzene (8.8 g, 99%) as a bright yellow, crystalline solid: mp 125–126 °C (EtOAc–hexane, yellow needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.84 (d, 2 H, J = 7.1 Hz, C2-H and C6-H, PhCO), 7.72 (s, 1 H, NH), 7.55–7.38 (m, 5 H, ArH), 6.69 (d, 2 H, J = 8.6 Hz, C2-H and C6-H), 3.89 (br s, 2 H, NH_2); IR (melt) ν_{max} 3401, 3326, 1644, 1578, 1518, 1448, 1420, 1320, 926, 822, 794, 716 cm^{-1}.

A solution of N^1-benzoyl-1,4-diaminobenzene (7.2 g, 34 mmol, 1.0 equiv) in 120 mL of dry tetrahydrofuran was treated with pyridine (8.4 mL, 100 mmol, 3.0 equiv) and benzenesulfonyl chloride (5.2 mL, 40 mmol, 1.2 equiv) at 25 °C, and the reaction mixture was warmed at reflux for 8 h. The cooled reaction mixture was poured onto 250 mL of 10% aqueous hydrochloric acid, and the mixture was extracted with ethyl acetate (250 mL). The organic extract was washed with water (3 × 100 mL) and saturated aqueous sodium chloride (1 × 100 mL) and dried ($MgSO_4$), and the solvent was removed in vacuo to afford N^4-benzoyl-N^1-(phenylsulfonyl)-1,4-diaminobenzene (10.6 g, 84%) as a white, crystalline solid: mp 219–220 °C (EtOAc–hexane, white plates); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.14 (d, 2 H, J = 5.9 Hz), 7.87 (d, 2 H, J = 7.1 Hz, C2-H and C6-H, PhCO), 7.71 (d, 2 H, J = 6.9 Hz, C2-H and C6-H, $PhSO_2$), 7.61–7.45 (m, 6 H, ArH), 7.03 (d, 2 H, J = 8.7 Hz); IR (melt) ν_{max} 3324, 3272, 1654, 1602, 1534, 1448, 1332, 1166, 1092, 908, 806, 756, 732, 688, 648 cm^{-1}.

A solution of N^4-benzoyl-N^1-(phenylsulfonyl)-1,4-diaminobenzene (10 g, 28 mmol, 1.0 equiv) in 120 mL of dry chloroform was treated with lead tetraacetate (13 g, 28 mmol, 1.0 equiv) at 25 °C under nitrogen, and the reaction mixture was stirred for 12 h at 25 °C. The reaction mixture was filtered through a layer of Celite, and the filtrate was concentrated to afford a brown oil. Trituration with hexane and ether provided **2a** (7.8 g, 79%) as a yellow, crystalline solid: mp 96–97 °C (EtOAc–hexane, yellow needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.06 (d, 1 H, J = 10.5 Hz, C5-H), 8.00 (d, 2 H, J = 7.4 Hz, C2-H and C6-H, PhCO), 7.89 (d, 2 H, J = 7.3 Hz, C2-H and C6-H, $PhSO_2$), 7.65–7.47 (m, 6 H, ArH), 7.04 (d, 1 H, J = 10.4 Hz, C6-H), 6.99 (d, 1 H, J = 9.6 Hz, C3-H), 6.83 (d, 1 H, J = 9.6 Hz, C2-H); IR (melt) ν_{max} 3066, 1674, 1592, 1530, 1448, 1382, 1314, 1244, 1156, 1090, 1056, 1022, 860, 748, 730, 716, 692, 620 cm^{-1}; EIMS m/e (relative intensity) 352 (M^+ + 2, 21), 350 (8), 247 (5), 223 (11), 105 (base), 91 (55), 77 (52); CIMS (isobutane) m/e 353 (M^+ + 3); EIHRMS m/e 352.1286 ($C_{19}H_{16}N_2O_3S$ + 2H requires 252.1289).

Anal. Calcd for $C_{19}H_{16}N_2O_3S$: C, 65.02; H, 4.08; N, 8.00. Found: C, 64.62; H, 3.82; N, 7.83.

N^4-Benzoyl-N^1-(phenylsulfonyl)-2-(benzyloxy)-*p*-benzoquinone Diimine (2b). A solution of 2-amino-5-nitrophenol[11] (7.7 g, 50 mmol, 1.0 equiv) in 75 mL of dry dioxane was treated with di-*tert*-butyl dicarbonate (12 mL, 52 mmol, 1.05 equiv), and the reaction mixture was stirred for 12 h at 25 °C. The reaction mixture was concentrated, poured onto 100 mL of water, and extracted with ethyl acetate (100 mL). The organic extract was washed with water (3 × 100 mL) and saturated aqueous sodium chloride (1 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo to afford *N*-(*tert*-butyloxycarbonyl)-2-amino-5-nitrophenol (11.5 g, 92%) as a yellow, crystalline solid: mp >250 °C (EtOAc–hexane, yellow needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, 1 H, J = 2.5 Hz, C6-H), 7.98 (dd, 1 H, J = 9.0, 2.5 Hz, C4-H), 6.74 (d, 1 H, J = 9.0 Hz, C3-H), 3.62 (br s, 1 H, NH_2), 1.57 (s, 9 H, CH_3); IR (KBr) ν_{max} 3460, 3224, 1756, 1634, 1598, 1490, 1400, 1376, 1286, 1210, 1152, 1088, 870, 812, 780, 642 cm^{-1}.

A solution of *N*-(*tert*-butyloxycarbonyl)-2-amino-5-nitrophenol (6.35 g, 25 mmol, 1.0 equiv) in 100 mL of dry acetone was treated with potassium carbonate (5.0 g, 37 mmol, 1.5 equiv), benzyl bromide (3.3 mL, 27.5 mmol, 1.1 equiv), and a catalytic amount of tetra-*n*-butylammonium iodide (1.8 g, 5.0 mmol, 0.2 equiv), and the reaction mixture was warmed at reflux for 20 h. The cooled reaction mixture was poured onto 200 mL of water and filtered, and the collected solid was washed with water (200 mL) and hexane (200 mL) to afford *N*-(*tert*-butyloxycarbonyl)-*O*-benzyl-2-amino-5-nitrophenol (7.3 g, 85%) as a yellow crystalline solid: mp 177–178 °C (EtOAc–hexane, yellow needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.01 (d, 1 H, J = 2.4 Hz, C6-H), 7.81 (dd, 1 H, J = 9.0, 2.4 Hz, C4-H), 7.51 (m, 5 H, ArH), 6.70 (d, 1 H, J = 8.9 Hz, C3-H), 5.06 (s, 2 H, PhCH_2O), 1.58 (s, 9 H, CH_3); IR (KBr) ν_{max} 3430, 1665, 1621, 1595, 1541, 1500, 1418, 1393, 1349, 1258, 1220, 1130, 1081, 1021, 905, 870, 830, 708 cm^{-1}.

A solution of *N*-(*tert*-butyloxycarbonyl)-*O*-benzyl-2-amino-5-nitrophenol (7.2 g, 20 mmol, 1.0 equiv) and sodium dithionite (17.4 g, 100 mmol, 5.0 equiv) in 100 mL of tetrahydrofuran–water (2:1) was warmed at reflux under nitrogen for 24 h. The reaction mixture was cooled to room temperature, and solid potassium carbonate was added until the mixture was basic (pH = 9–10). The mixture was diluted with water (80 mL) and extracted with ethyl acetate (100 mL). The organic extract was washed with water (3 × 80 mL) and saturated aqueous sodium chloride (1 × 50 mL), dried ($MgSO_4$), filtered through Celite, and concentrated in vacuo. Flash chromatography (10 × 20 cm SiO_2, 20–50% EtOAc–hexane gradient elution) afforded N^2-(*tert*-butyloxy-

(10) *p*-Quinone diimines **2c**[3] and **2d**[2] were prepared according to reported procedures.

(11) Commercially available from Aldrich Chemical Co.

carbonyl)-O-benzyl-2,5-diaminophenol (4.3 g, 69%) as a yellow semisolid: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.81 (dd, 2 H, J = 8.9, 2.5 Hz, C4-H), 7.42 (m, 5 H, ArH), 6.89 (s, 1 H, NH), 6.36 (d, 1 H, J = 9.0 Hz, C3-H), 6.30 (d, 1 H, J = 1.8 Hz, C6-H), 5.08 (s, 2 H, PhCH_2O), 4.02 (br s, 2 H, NH_2), 1.56 (s, 9 H, CH_3); IR (neat) ν_{max} 3434, 3350, 3036, 1657, 1625, 1601, 1570, 1530, 1481, 1440, 1300, 1257, 1230, 1179, 1026, 838, 735 cm^{-1}.

A solution of N^2-(*tert*-butyloxycarbonyl)-O-benzyl-2,5-diaminophenol (3.26 g, 10.0 mmol, 1.0 equiv) in 50 mL of dry tetrahydrofuran was treated with potassium carbonate (2.1 g, 15 mmol, 1.5 equiv) and benzoyl chloride (1.5 mL, 12 mmol, 1.2 equiv), and the reaction mixture was stirred for 10 min at 25 °C. The reaction mixture was poured onto 30 mL of 10% aqueous hydrochloric acid. The solid was collected by filtration and washed with water (100 mL) and hexane (100 mL) to afford N^5-benzoyl-N^2-(*tert*-butyloxycarbonyl)-O-benzyl-2,5-diaminophenol (3.9 g, 90%) as a white, crystalline solid: mp 168–169 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.09 (d, J = 8.6 Hz, C3-H), 7.85 (d, 2 H, J = 6.9 Hz, C2-H and C6-H, PhCO), 7.55–7.36 (m, ArH), 7.02 (d, 1 H, J = 1.3 Hz, C6-H), 6.83 (dd, 1 H, J = 8.7, 1.3 Hz, C4-H), 5.16 (s, 2 H, PhCH_2O), 1.52 (s, 9 H, CH_3); IR (melt) ν_{max} 3430, 3310, 2978, 1728, 1648, 1610, 1522, 1482, 1420, 1368, 1244, 1156, 1050, 1026, 822, 742, 696 cm^{-1}.

A solution of N^5-benzoyl-N^2-(*tert*-butyloxycarbonyl)-O-benzyl-2,5-diaminophenol (3.6 g, 8.6 mmol, 1.0 equiv) in 10 mL of dry dichloromethane was treated with 35 mL of a 0.25 M solution of trifluoroacetic acid in dichloromethane (1:1), and the reaction mixture was stirred for 30 min at 25 °C. The mixture was poured onto 20 mL of saturated aqueous sodium bicarbonate and was extracted with ethyl acetate and diethyl ether (50 mL each). The combined organic extract was washed with water (3 × 30 mL) and saturated aqueous sodium chloride (1 × 30 mL), dried ($MgSO_4$), and concentrated in vacuo to afford N^5-benzoyl-O-benzyl-2,5-diaminophenol (2.4 g, 88%) as a yellow, crystalline solid: mp 139–140 °C (EtOAc–hexane, yellow needles, decomposition); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.90 (s, 1 H, NH), 7.86 (d, 2 H, J = 6.7 Hz, C2-H and C6-H, PhCO), 7.55–7.34 (m, 9 H, ArH), 6.86 (dd, 1 H, J = 8.2, 2.0 Hz, C4-H), 6.71 (d, 1 H, J = 8.3 Hz, C3-H), 5.20 (s, 2 H, PhCH_2O), 3.65 (br s, 2 H, NH_2); IR (KBr) ν_{max} 3460, 3376, 3260, 1642, 1602, 1580, 1516, 1454, 1430, 1382, 1348, 1286, 1264, 1214, 1176, 1140, 1016, 840, 808, 760, 748, 702, 626 cm^{-1}.

A solution of N^5-benzoyl-O-benzyl-2,5-diaminophenol (6.90 g, 21.8 mmol, 1.0 equiv) in 100 mL of dry tetrahydrofuran was treated with pyridine (8.7 mL, 109 mmol, 5.0 equiv) and benzenesulfonyl chloride (3.35 mL, 26.2 mmol, 1.2 equiv), and the reaction mixture was warmed at reflux for 20 h. The cooled reaction mixture was poured onto 200 mL of 10% aqueous hydrochloric acid and was extracted with dichloromethane (200 mL). The organic extract was washed with water (3 × 100 mL) and saturated aqueous sodium chloride (1 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo. Recrystallization from CH_2Cl_2–hexane (1:1, 200 mL) afforded pure N^5-benzoyl-N^2-(phenylsulfonyl)-O-benzyl-2,5-diaminophenol (7.9 g, 79%) as a white, crystalline solid: mp 206–207 °C (EtOAc–hexane, white needles, decomposition); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.19 (s, 1 H, NH), 9.47 (s, 1 H, NH), 7.88 (d, 2 H, J = 7.2 Hz, C2-H and C6-H, PhCO), 7.62 (d, 2 H, J = 7.5 Hz, C2-H and C6-H, $PhSO_2$), 7.6 (d, 1 H, J = 8.1 Hz, C3-H), 7.55 (dd, J = 8.1, 2.4 Hz, C4-H), 7.58–7.17 (m, 14 H, ArH), 4.79 (s, 2 H, PhCH_2O); IR (KBr) ν_{max} 3388, 3178, 1662, 1606, 1538, 1510, 1448, 1416, 1338, 1286, 1166, 1126, 1092, 1026, 916, 846, 804, 732, 712, 686, 624 cm^{-1}.

A slurry of N^5-benzoyl-N^2-(phenylsulfonyl)-O-benzyl-2,5-diaminophenol (1.58 g, 3.3 mmol, 1.0 equiv) in 30 mL of dry chloroform was treated with lead tetraacetate (1.5 g, 3.3 mmol, 1.0 equiv) under nitrogen at 25 °C, and the reaction mixture was stirred for 6 h at 25 °C. The reaction mixture was filtered through Celite (chloroform wash), and the filtrate was concentrated in vacuo. Recrystallization (EtOAc–hexane, 1:1) afforded pure **2b** (1.4 g, 93%) as a bright yellow, crystalline solid: mp 169–170 °C (EtOAc–hexane, yellow needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.08 (d, 2 H, J = 7.4 Hz, C2-H and C6-H, PhCO), 8.0 (d, J = 10.1 Hz, C3-H), 7.92 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, $PhSO_2$), 7.67–7.48 (m, 14 H, ArH), 7.00 (dd, 1 H, J = 10.1, 1.1 Hz, C4-H), 6.16 (d, J = 1.0 Hz, C6-H), 5.01 (s, 2 H, PhCH_2O); IR (melt) ν_{max} 3650, 1654, 1576, 1448, 1314, 1240, 1210, 1126, 1056, 848, 730 cm^{-1}; EIMS m/e (relative intensity) 458 (M^+ + 2H, 6), 317 (7), 105 (base), 91 (82), 77 (44); CIMS (isobutane) m/e 459 (M^+ + 3H); EIHRMS 458.2218 ($C_{26}H_{20}N_2O_4S$ + 2H requires 458.2224).

Anal. Calcd for $C_{26}H_{20}N_2O_4S$: C, 68.40; H, 4.42; N, 6.14; S, 7.02. Found: C, 68.09; H, 4.49; N, 6.07; S, 6.78.

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-7-(benzyloxy)-3-methylindole (3). A solution of **1** (100 mg, 0.20 mmol, 1.0 equiv) in 1 mL of dry tetrahydrofuran was treated with potassium carbonate (139 mg, 1.0 mmol, 5.0 equiv) and benzoyl chloride (26 μL, 0.22 mmol, 1.1 equiv), and the reaction mixture was stirred for 12 h at 25 °C. The reaction mixture was poured onto 5 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 5 mL) and saturated aqueous sodium chloride (1 × 5 mL) and dried ($MgSO_4$), and the solvent was removed in vacuo. Flash chromatography (1 × 15 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded **3** (117 mg, 97%) as a white crystalline solid: mp 225 °C (decomposition, EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.98 (d, 2 H, J = 7.7 Hz, C2-H and C6-H, PhCO), 7.70 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, $PhSO_2$), 7.68–7.08 (m, 17 H, ArH), 6.87 (d, 1 H, J = 0.8 Hz, C2-H), 6.60 (s, 1 H, C4-H), 4.89 (s, 2 H, PhCH_2O), 2.17 (s, 3 H, CH_3); IR (KBr) ν_{max} 3450, 1702, 1578, 1478, 1448, 1422, 1364, 1336, 1272, 1086, 1024, 870, 724, 696, 670, 634 cm^{-1}; EIMS m/e (relative intensity) 600 (M^+, 4), 368 (2), 105 (base), 91 (20), 77 (23); CIMS (isobutane) m/e 601 (M^+ + H); EIHRMS m/e 600.1478 ($C_{36}H_{28}N_2O_5S$ requires 600.1474).

N^5-(Phenylsulfonyl)-5-amino-1-benzoyl-6-(benzyloxy)-3-methylindole (4). A solution of **2b** (200 mg, 0.44 mmol, 1.0 equiv) in 2.5 mL of dry methylene chloride was cooled to −78 °C under nitrogen, and 1-piperidino-1-propene (67 μL, 0.48 mmol, 1.1 equiv) was added in one portion. The reaction mixture was stirred for 1 h at −78 °C. The reaction mixture was warmed to room temperature, the solvent was removed in vacuo, and the residue was dissolved in 3 mL of tetrahydrofuran. The solution was treated with 2 mL of 10% aqueous hydrochloric acid, and the reaction mixture was stirred for 24 h at 25 °C. The reaction mixture was poured onto 10 mL of saturated aqueous sodium bicarbonate and was extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 5 mL) and saturated aqueous sodium chloride (1 × 5 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (2 × 15 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded **4** (135 mg, 62–71%) as a white, crystalline solid: mp 144–145 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.03 (s, 1 H, NH), 7.78 (s, 1 H, C7-H), 7.71–7.18 (m, 15 H, ArH), 7.16 (d, 1 H, J = 1.9 Hz, C2-H), 6.95 (d, 1 H, J = 1.2 Hz, C4-H), 4.87 (s, 2 H, PhCH_2O), 2.24 (s, 3 H, CH_3); IR (KBr) ν_{max} 3222, 1678, 1578, 1476, 1460, 1428, 1394, 1372, 1340, 1286, 1210, 1168, 1092, 1038, 918, 854, 790, 758, 734, 690, 654 cm^{-1}; EIMS m/e (relative intensity) 496 (M^+, 5), 355 (14), 105 (base), 91 (72), 77 (39); CIMS (isobutane) m/e 497 (M^+ + H); EIHRMS m/e 496.1455 ($C_{29}H_{24}N_2O_4S$ requires 496.1457).

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-6-(benzyloxy)-3-methylindole (5). A solution of **4** (30 mg, 0.06 mmol, 1.0 equiv) in 0.5 mL of dry tetrahydrofuran was treated with potassium carbonate (25 mg, 0.18 mmol, 3.0 equiv) and benzoyl chloride (8 μL, 0.066 mmol, 1.1 equiv) and was stirred for 24 h at 25 °C. The reaction mixture was poured onto 2 mL of 5% aqueous hydrochloric acid and was extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL) and dried ($MgSO_4$), and the solvent was removed in vacuo. Flash chromatography (1 × 10 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded **5** (23 mg, 64%) as a white, crystalline solid: mp 255 °C (decomposition, EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.04 (s, 1 H, C4-H), 8.00 (d, 2 H, ArH), 7.79 (s, 1 H, C7-H), 7.7–7.04 (m, 15 H, ArH), 6.98 (s, 1 H, C2-H), 6.93 (m, 3 H, ArH), 4.73 (s, 2 H, PhCH_2O), 2.28 (s, 3 H, CH_3); IR (KBr) ν_{max} 3772, 3450, 1710, 1690, 1600, 1530, 1450, 1392, 1360, 1284, 1266, 1210, 1182, 1084, 1024, 858, 732, 696, 626 cm^{-1}; EIMS m/e (relative intensity) 600 (M^+, 1), 459 (2), 105 (base), 91 (14), 77 (37); CIMS (isobutane) m/e 601 (M^+ + H); EIHRMS m/e 600.1462 ($C_{36}H_{28}N_2O_5S$ requires 600.1460).

N^5,1-Dibenzoyl-5-amino-6-(benzyloxy)-3-methylindole (6) and N^5,1-Dibenzoyl-5-amino-7-(benzyloxy)-3-methylindole (7). A solution of **2c** (300 mg, 0.71 mmol, 1.0 equiv) in 10 mL

of dry methylene chloride was cooled to 0 °C under nitrogen and 1-piperidino-1-propene (0.11 mL, 0.79 mmol, 1.1 equiv) was added in one portion. The reaction mixture was allowed to warm to 25 °C and was stirred for 8 h at 25 °C. The solvent was removed in vacuo, and the residue was dissolved in 5 mL of tetrahydrofuran. The solution was treated with 2 mL of 10% aqueous hydrochloric acid, and the reaction mixture was stirred for 24 h at 25 °C. The reaction mixture was poured onto 10 mL of saturated aqueous sodium bicarbonate and was extracted with ethyl acetate (30 mL). The organic extract was washed with water (5 × 20 mL) and saturated sodium chloride (1 × 20 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (3 × 20 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded **6** and **7** in a ratio of 3:2 (32.5 mg and 20.0 mg).

For **6**: mp 215–216 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.86 (s, 1 H, NH), 8.78 (s, 1 H, C4-H), 8.27 (s, 1 H, C7-H), 7.88–7.4 (m, 15, ArH), 6.96 (d, 1 H, J = 1.3 Hz, C2-H), 5.28 (s, 2 H, PhCH_2O), 2.68 (s, 3 H, CH_3); IR (KBr) ν_{max} 3440, 2918, 1672, 1606, 1528, 1492, 1472, 1398, 1328, 1282, 1232, 1202, 1108, 1040, 918, 852, 724, 702, 666 cm^{-1}; EIMS m/e (relative intensity) 460 (M^+, 2), 369 (2), 105 (base), 91 (10), 77 (31); CIMS (isobutane) m/e 461 (M^+ + H); EIHRMS m/e 460.1783 ($C_{30}H_{24}N_2O_3$ requires 460.1786).

For **7**: mp 223–224 °C (EtOAc–hexane, white needles): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.91 (s, 1 H, C6-H), 7.90 (d, 2 H, J = 7.0 Hz, C2-H and C6-H, PhCO), 7.88 (s, 1 H, NH), 7.70 (d, 2 H, J = 7.7 Hz, C2-H and C6-H, PhCO), 7.54–7.47 (m, 5 H, ArH), 7.36–7.25 (m, 9 H, ArH), 7.24 (s, 1 H, C4-H), 7.22 (s, 1 H, C2-H), 4.96 (s, 2 H, PhCH_2O), 2.26 (s, 3 H, CH_3); IR (KBr) ν_{max} 3752, 3424, 2926, 1696, 1642, 1560, 1482, 1386, 1338, 1300, 1236, 1170, 1094, 710 cm^{-1}; EIMS m/e (relative intensity) 460 (M^+, 18), 105 (base), 91 (12), 77 (24); CIMS (isobutane) m/e 461 (M^+ + H); EIHRMS m/e 460.1780 ($C_{30}H_{24}N_2O_3$ requires 460.1786).

Anal. Calcd for $C_{30}H_{24}N_2O_3$: C, 74.84; H, 5.25; N, 6.18. Found: C, 74.94; H, 5.12; N, 6.30.

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-6-(benzyloxy)-3-methylindole (5) from 6. A solution of **6** (29 mg, 0.064 mmol, 1.0 equiv) in 0.5 mL of dry tetrahydrofuran was added to a slurry of potassium hydride (5.1 mg, 0.13 mmol, 2.0 equiv) in dry tetrahydrofuran (1 mL) under nitrogen, and the mixture was stirred for 0.5 h at 25 °C. The reaction mixture was treated with benzenesulfonyl chloride (10 μL, 0.077 mmol, 1.2 equiv) and was stirred for 6 h at 25 °C. The reaction mixture was poured onto 2 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL) and dried ($MgSO_4$), and the solvent was removed in vacuo. Flash chromatography (1 × 10 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded **5** (28 mg, 73%) as a white, crystalline solid identical with the sample of **5** prepared from **4**.

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-7-(benzyloxy)-3-methylindole (3) from 7. A solution of **7** (93 mg, 0.2 mmol, 1.0 equiv) in 2.0 mL of dry tetrahydrofuran was added to a slurry of potassium hydride (24 mg, 0.6 mmol, 3.0 equiv) in dry tetrahydrofuran (1 mL) under nitrogen, and the reaction mixture was stirred for 0.5 h at 25 °C. The reaction mixture was treated with benzenesulfonyl chloride (52 μL, 0.4 mmol, 2.0 equiv) and was stirred for 12 h at 50 °C. The reaction mixture was poured onto 5 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 5 mL) and saturated aqueous sodium chloride (1 × 5 mL) and dried ($MgSO_4$), and the solvent was removed in vacuo. Flash chromatography (2 × 12 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded **3** (101 mg, 84%) as a white, crystalline solid identical in all respects with authentic **3** prepared from **1**.

N^4-Benzoyl-N^1-(phenylsulfonyl)-1,4-diamino-3-(1,1-bis(methoxycarbonyl)methyl)benzene (8). A solution of **2a** (100 mg, 0.28 mmol, 1.0 equiv) in 1.0 mL of dry tetrahydrofuran at 0 °C was treated with dimethyl malonate (39 μL, 0.29 mmol, 1.05 equiv) and catalytic solid sodium methoxide (3.0 mg, 0.06 mmol, 0.2 equiv), and the reaction mixture was stirred for 6 h at 0 °C. The reaction mixture was made acidic with the addition of saturated aqueous ammonium chloride (1 mL) and extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 20 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded pure **8** (111 mg, 81%) as a white, crystalline solid: mp 138–139 °C (CH_2Cl_2–EtOAc, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.67 (s, 1 H, NH), 7.96 (d, 2 H, J = 7.0 Hz, C2-H and C6-H, PhCO), 7.78 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, $PhSO_2$), 7.69 (d, 1 H, J = 8.6 Hz, C5-H), 7.56–7.42 (m, 6 H, ArH), 7.17 (d, 1 H, J = 2.5 Hz, C2-H), 7.07 (s, 1 H, NH), 6.87 (dd, 1 H, J = 8.4, 2.4 Hz, C6-H), 4.63 (s, 1 H, CH), 3.68 (s, 6 H, OCH_3); IR (KBr) ν_{max} 3147, 1744, 1723, 1662, 1579, 1529, 1436, 1404, 1337, 1308, 1250, 1200, 1169, 1091, 962, 760, 715 cm^{-1}; EIMS m/e (relative intensity) 482 (M^+, 9), 219 (25), 105 (base), 77 (40); CIMS (isobutane) m/e 483 (M^+ + H); EIHRMS m/e 482.1149 ($C_{24}H_{22}N_2O_7S$ requires 482.1148).

Anal. Calcd for $C_{24}H_{22}N_2O_7S$: C, 55.84; H, 4.50; N, 5.35; S, 6.64. Found: C, 55.82; H, 4.49; N, 5.49; S, 6.46.

N^4-Benzoyl-N^1-(phenylsulfonyl)-1,4-diamino-3-(1-(methoxycarbonyl)-2-oxopropyl)benzene (9). A solution of **2a** (100 mg, 0.28 mmol, 1.0 equiv) in 1.0 mL of dry tetrahydrofuran at −35 °C was treated with methyl acetoacetate (31 μL, 0.28 mmol, 1.0 equiv) and catalytic solid sodium methoxide (3 mg, 0.06 mmol, 0.2 equiv), and the reaction mixture was stirred for 12 h at −35 °C. The reaction mixture was allowed to warm to room temperature, made acidic with the addition of saturated aqueous ammonium chloride (1 mL), and extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 15 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded pure **9** (106 mg, 80%) as a white, crystalline solid: mp 158–159 °C (CH_2Cl_2, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 13.11 (s, 1 H, NH), 9.77 (s, 1 H, NH), 8.32 (d, 1 H, J = 8.5 Hz, C5-H), 7.94 (d, 2 H, J = 7.0 Hz, C2-H and C6-H, PhCO), 7.84 (d, 2 H, J = 8.0 Hz, C2-H and C6-H, $PhSO_2$), 7.81–7.48 (m, 6 H, ArH), 7.28 (d, 1 H, J = 2.4 Hz, C2-H), 7.05 (dd, J = 8.7, 2.1 Hz, C6-H), 4.65 (s, 1 H, CH), 3.85 (s, 3 H, CO_2CH_3), 3.71 (s, 3 H, $COCH_3$); IR (KBr) ν_{max} 3259, 1734, 1653, 1613, 1519, 1446, 1398, 1326, 1245, 1159, 1092, 1026, 917, 825, 720, 689 cm^{-1}; EIMS m/e 434 ($M^+ - CH_3OH$), 105 (base); CIMS m/e 435 ($M^+ + H - CH_3OH$); EIHRMS m/e 466.1210 ($C_{24}H_{22}N_2O_6S$ requires 466.1199).

Anal. Calcd for $C_{24}H_{22}N_2O_6S$: C, 61.79; H, 4.75; N, 6.00; S, 6.87. Found: C, 61.96; H, 4.75; N, 5.77; S, 7.03.

N^4-Benzoyl-N^1-(phenylsulfonyl)-1,4-diamino-3-morpholylbenzene (10). A solution of morpholine (35 μL, 0.34 mmol, 1.2 equiv) in 1 mL of dry diethyl ether at −20 °C was treated with **2a** (100 mg, 0.28 mmol, 1.0 equiv), and the reaction mixture was stirred for 12 h at −20 °C. The reaction mixture was made acidic with the addition of saturated aqueous ammonium chloride (1 mL) and extracted with dichloromethane (3 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 20 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded pure **10** (76 mg, 60%) as a white, crystalline solid: mp 203–204 °C (decomposition, CH_2Cl_2–EtOAc, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.32 (s, 1 H, NH), 8.39 (d, 1 H, J = 8.7 Hz, C5-H), 7.80 (d, 2 H, J = 7.1 Hz, C2-H and C6-H, PhCO), 7.73 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, $PhSO_2$), 7.58–7.44 (m, 6 H, ArH), 7.07 (d, 1 H, J = 1.7 Hz, C2-H), 6.77 (dd, 1 H, J = 8.7, 1.5 Hz, C6-H), 6.50 (s, 1 H, NH), 3.88 (t, 4 H, J = 3.8 Hz, NCH_2CH_2O), 2.86 (t, 4 H, J = 3.9 Hz, NCH_2CH_2O); IR (KBr) ν_{max} 3227, 2854, 1665, 1603, 1522, 1450, 1318, 1243, 1160, 1117, 1091, 983, 910, 720, 708, 689, 656 cm^{-1}; EIMS m/e (relative intensity) 437 (M^+, 2), 105 (52), 77 (34), 74 (31), 59 (60), 45 (base); CIMS (isobutane) m/e 438 (M^+ + H); EIHRMS m/e 437.1415 ($C_{23}H_{23}N_3O_4S$ requires 437.1409).

Anal. Calcd for $C_{23}H_{23}N_3O_4S$: C, 63.13; H, 5.31; N, 9.60; S, 7.33. Found: C, 63.10; H, 5.63; N, 9.22; S, 7.55.

N^4-Benzoyl-N^1-(phenylsulfonyl)-3-acetoxy-1,4-diaminobenzene (11). A solution of **2a** (100 mg, 0.28 mmol, 1.0 equiv) in 0.5 mL of acetic acid at 25 °C was treated with a catalytic amount of sulfuric acid (3.0 μL, 0.06 mmol, 0.2 equiv), and the reaction mixture was stirred for 15 h at 25 °C. The reaction mixture was made basic with the addition of saturated aqueous sodium bicarbonate (2.0 mL) and extracted with ethyl acetate (3 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 15 cm

SiO_2, 20–30% EtOAc–hexane gradient elution) afforded pure **11** (60 mg, 50%) as a white, crystalline solid: mp 135–135.5 °C (CH_2Cl_2–EtOAc, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.13 (d, 1 H, J = 8.8 Hz, C5-H), 7.88 (s, 1 H, NH), 7.84 (d, 2 H, J = 7.2 Hz, C2-H and C6-H, PhCO), 7.80 (d, 2 H, J = 7.5 Hz, C2-H and C6-H, $PhSO_2$) 7.62–7.45 (m, 6 H, ArH), 7.18 (d, 1 H, J = 1.9 Hz, C2-H), 6.83 (dd, 1 H, J = 9.0, 1.8 Hz, C6-H), 6.64 (s, 1 H, NH), 2.37 (s, 3 H, $OCOCH_3$); IR (KBr) ν_{max} 3186, 1750, 1653, 1533, 1472, 1373, 1331, 1216, 1158, 1092, 923, 714, 689 cm^{-1}; EIMS m/e (relative intensity) 410 (M^+, 1), 123 (30), 105 (base), 71 (40), 51 (13); CIMS (isobutane) m/e 411 (M^+ + H); EIHRMS m/e 410.0935 ($C_{21}H_{18}N_2O_5S$ requires 410.0937).

N^2-Benzoyl-N^5-(phenylsulfonyl)-2,5-diaminophenol from 11. A solution of **11** (74 mg, 0.18 mmol, 1.0 equiv) in 0.5 mL of dry methanol at 25 °C was treated with 1 mL of 10% hydrochloric acid in methanol, and the reaction mixture was stirred for 3 h at 25 °C. The reaction mixture was neutralized with the addition of saturated aqueous sodium bicarbonate (2 mL) and extracted with ethyl acetate (3 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Recrystallization (EtOAc–CH_2Cl_2, 1:1) afforded pure phenol (59 mg, 89%) as a white, crystalline solid: mp 224–225 °C (decomposition, EtOAc–hexane, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.90 (d, 2 H, J = 7.3 Hz, C2-H and C6-H, PhCO), 7.77 (d, 2 H, J = 7.4 Hz, C2-H and C6-H, $PhSO_2$), 7.62 (d, 1 H, J = 8.7 Hz, C3-H), 7.59–7.46 (m, 6 H, ArH), 6.83 (d, 1 H, J = 2.2 Hz, C6-H), 6.54 (dd, J = 8.6, 2.3 Hz, C4-H); IR (KBr) ν_{max} 3242, 1636, 1576, 1540, 1448, 1402, 1326, 1152, 1090, 978, 908, 860, 734 cm^{-1}; EIMS m/e (relative intensity) 320 (M^+, 12), 209 (2), 123 (30), 105 (base), 77 (40); CIMS (isobutane) m/e 321 (M^+ + H); EIHRMS m/e 320.1679 ($C_{14}H_{12}N_2O_5S$ requires 320.1671).

N^2-Benzoyl-N^5-(phenylsulfonyl)-2,5-diaminophenol from 2d. A solution of **2d** (100 mg, 0.22 mmol, 1.0 equiv) in 2.0 mL of dry tetrahydrofuran at 25 °C was treated with 10% palladium on carbon (10.0 mg, 10% wt equiv). The reaction mixture was stirred under hydrogen (1 atm) for 1 h at 25 °C. The reaction mixture was filtered through a layer of Celite, and the filtrate was concentrated in vacuo to afford pure phenol (75 mg, 93%), identical with that prepared from **11**.[12]

N^4-Benzoyl-N^1-(phenylsulfonyl)-1,4-diamino-2-[3-(1-propenyl)]benzene (12). A solution of **2a** (100 mg, 0.28 mmol, 1.0 equiv) in 1.0 mL of dry dichloromethane at −20 °C was treated with boron trifluoride etherate (9.0 μL, 0.07 mmol, 0.25 equiv). The mixture was stirred for 30 min and treated with 2-propenyltri-*n*-butylstannane (97.5 μL, 0.31 mmol, 1.1 equiv). The reaction mixture was stirred for 24 h at −20 °C before the solvent was removed in vacuo. Acetonitrile was added to the crude product, and the mixture was filtered. The filtrate was washed with *n*-hexane (3 × 5 mL), and the acetonitrile extract was concentrated in vacuo to afford crude **12**. Flash chromatography (1 × 15 cm SiO_2, 10–40% EtOAc–hexane gradient elution) afforded pure **12** (75 mg, 67%) as a white, crystalline solid: mp 179–179.5 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.86 (d, 2 H, J = 7.0 Hz, C2-H and C6-H, PhCO), 7.79 (s, 1 H, NH), 7.67 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, $PhSO_2$), 7.61–7.41 (m, 9 H, ArH), 6.45 (s, 1 H, NH), 5.87–5.71 (m, 1 H, C*H*=CH_2), 5.13 (dd, 1 H, J = 10.0, 1.1 Hz, CH=C*H*H), 4.97 (dd, 1 H, J = 18.3, 1.3 Hz, CH=CH*H*), 3.00 (d, 2 H, J = 6.0 Hz, CH_2CH=CH_2); IR (KBr) ν_{max} 3356, 3138, 1668, 1606, 1534, 1500, 1448, 1394, 1324, 1158, 1094, 914, 764, 710, 690 cm^{-1}; EIMS m/e (relative intensity) 392 (8), 251 (31), 105 (base), 77 (47); CIMS (isobutane) m/e 393 (M^+ + H); EIHRMS m/e 392.1194 ($C_{22}H_{20}N_2O_3S$ requires 392.1194).

Anal. Calcd for $C_{22}H_{20}N_2O_3S$: C, 67.32; H, 5.15; N, 7.14; S, 8.17. Found: C, 67.64; H, 5.36; N, 6.97; S, 7.96.

N^4-Benzoyl-N^1-(phenylsulfonyl)-1,4-diamino-2-[3-(3-methyl-1-propenyl)]benzene (13). Table I, entry 6, following the procedure for the preparation of **12**, **2a** (100 mg, 0.28 mmol, 1.0 equiv) was treated with boron trifluoride etherate (9 μL, 0.07 mmol, 0.25 equiv) and 2-butenyltri-*n*-butylstannane (185 μL, 0.57 mmol, 2.0 equiv) to provide **13** (63 mg, 54%): mp 172–173 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.97 (s, 1 H, N*H*), 7.85 (d, 2 H, J = 7.4 Hz, C2-H and C6-H PhCO), 7.70 (d, 2 H, J = 7.5 Hz, C2-H and C6-H $PhSO_2$), 7.58–7.35 (m, 12 H, ArH), 7.28 (d, 1 H, J = 8.6 Hz, C6-H), 6.56 (s, 1 H, NH), 5.76–5.65 (m, 1 H, C*H*=CH_2), 5.02 (d, 1 H, J = 17.3 Hz, CH=CH*H*), 4.91 (d, 1 H, J = 10.2 Hz, CH=CH*H*), 3.22 (m, 1 H, C*H*CH=CH_2), 1.11 (d, 3 H, J = 7.0 Hz, CH_3); IR (KBr) ν_{max} 3854, 3752, 3676, 3650, 3424, 3278, 2924, 1646, 1578, 1534, 1496, 1448, 1394, 1332, 1166, 1092, 920, 842, 716, 690 cm^{-1}; EIMS m/e (relative intensity) 406 (11), 265 (33), 144 (15), 105 (base), 77 (54); CIMS (isobutane) m/e 407 (M^+ + H); EIHRMS m/e 406.1350 ($C_{23}H_{22}N_2O_3S$ requires 406.1351).

N^5-(Phenylsulfonyl)-5-amino-1-benzoyl-2-methylindole-3-carboxylic Acid Methyl Ester (14). A solution of **9** (50 mg, 0.12 mmol, 1.0 equiv) in 0.5 mL of dry dichloromethane was treated with a solution of sulfuric acid in dichloromethane (20%, 0.5 mL, 3.0 mmol, 15 equiv), and the reaction mixture was stirred for 12 h at 25 °C. The reaction mixture was made basic with the addition of saturated aqueous sodium bicarbonate (2 mL) and extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 15 cm, SiO_2, 10–40% EtOAc–hexane gradient elution) afforded pure **14** (37 mg, 69%) as a white, crystalline solid: mp 162–163 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.79 (d, 2 H, J = 7.5 Hz, C2-H and C6-H, PhCO), 7.77 (d, 2 H, J = 6.0 Hz, C2-H and C6-H, $PhSO_2$), 7.73 (d, 1 H, J = 1.0 Hz, C4-H), 7.71–7.45 (m, 6 H, ArH), 7.00 (d, 1 H, J = 8.8 Hz, C7-H), 6.94 (dd, 1 H, J = 8.9, 1.0 Hz, C6-H), 6.5 (s, 1 H, NH), 3.96 (s, 3 H, CO_2CH_3), 2.70 (s, 3 H, CH_3); IR (KBr) ν_{max} 3257, 1701, 1559, 1464, 1348, 1312, 1214, 1161, 1121, 1092, 924, 723, 689 cm^{-1}; EIMS m/e (relative intensity) 448 (M^+, 1), 105 (base), 77 (39); CIMS (isobutane) m/e 449 (M^+ + 1); EIHRMS m/e 448.1096 ($C_{24}N_{20}N_2O_5S$ requires 448.1093).

N^5-Benzoyl-5-amino-1-(phenylsulfonyl)indole (15). A solution of **12** (48 mg, 0.12 mmol, 1.0 equiv) in 1 mL of acetone–water (3:1) was treated with sodium periodate (78 mg, 0.36 mmol, 3.0 equiv) and osmium tetraoxide (0.13 mg, 0.52 μmol, 0.005 equiv). The reaction mixture was stirred for 2 h at 25 °C before being quenched with the addition of saturated aqueous sodium thiosulfate and extracted with ethyl acetate (3 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. The crude product in dichloromethane (2 mL) was treated with a solution of sulfuric acid in dichloromethane (5%, 1.3 mL, 1.2 mmol, 10.0 equiv), and the reaction mixture was stirred for 8 h at 25 °C. The reaction mixture was made basic with the addition of saturated aqueous sodium bicarbonate (2 mL) and extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 15 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded pure **15** (27 mg, 60%) as a white, crystalline solid: mp 182–183 °C (EtOAc–hexane, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.01 (d, 1 H, J = 1.5 Hz, C4-H), 7.98 (d, 1 H, J = 8.8 Hz, C7-H), 7.87–7.85 (m, 5 H, PhCO), 7.56–7.41 (m, 6 H, $PhSO_2$ and one ArH), 7.37 (dd, 1 H, J = 8.8, 1.8 Hz, C6-H), 7.32 (d, 1 H, J = 3.1 Hz, C2-H), 6.65 (d, 1 H, J = 3.0 Hz, C3-H); IR (KBr) ν_{max} 3442, 2926, 1648, 1594, 1548, 1466, 1370, 1280, 1224, 1180, 1160, 1130, 810, 762, 728, 696, 644 cm^{-1}; EIMS m/e (relative intensity) 376 (M^+, 51), 149 (50), 105 (base), 85 (18), 83 (14), 77 (56), 72 (38), 69 (23), 57 (69), 55 (32), 51 (10); CIMS (isobutane) m/e 377 (M^+ + H); EIHRMS m/e 376.0885 ($C_{21}H_{16}N_2O_3S$ requires 376.0882).

An authentic sample of **15** was prepared from 5-nitroindole.[11] A solution of 5-nitroindole (100 mg, 0.62 mmol, 1.0 equiv) in 1 mL of dry tetrahydrofuran at 25 °C was treated with potassium *tert*-butoxide (76 mg, 0.68 mmol, 1.1 equiv). After 30 min the mixture was treated with benzenesulfonyl chloride (54 μL, 0.74 mmol, 1.2 equiv), and the reaction mixture was stirred for 2 h at 25 °C. The reaction mixture was poured onto 5 mL of 10% aqueous hydrochloric acid and extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 5 mL) and saturated aqueous sodium chloride (1 × 5 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 20 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded 5-

(12) Similarly, hydrogenolysis of **2b** provided N^5-benzoyl-N^2-(phenylsulfonyl)-2,5-diaminophenol which proved distinct from the phenol prepared from **11**.

nitro-1-(phenylsulfonyl)indole (140 mg, 75%) as a white, crystalline solid: mp 188–189 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.72 (d, 2 H, J = 7.7 Hz, C2-H and C6-H, $PhSO_2$), 7.58 (d, 1 H, J = 8.7 Hz, C7-H), 7.43–7.28 (m, 4 H, ArH), 6.76 (d, 1 H, J = 1.6 Hz, C4-H), 6.70 (dd, 1 H, J = 8.7, 1.6 Hz, C6-H), 6.58 (d, 1 H, J = 3.5 Hz, C3-H); IR (KBr) ν_{max} 3450, 2820, 1650, 1602, 1547, 1460, 1371, 1285, 1220, 1171, 1150, 1132, 810, 765, 730, 691, 650 cm^{-1}.

A solution of 5-nitro-1-(phenylsulfonyl)indole (110 mg, 0.41 mmol, 1.0 equiv) in 2 mL of dry tetrahydrofuran was treated with palladium on carbon (11 mg, 10% wt equiv), and the reaction mixture was stirred under hydrogen (1 atm) for 2 h at 25 °C. The reaction mixture was filtered through a layer of Celite, and the filtrate was concentrated in vacuo to afford 5-amino-1-(phenylsulfonyl)indole (96 mg, 100%) as a white, crystalline solid: mp 230–231 °C (decomposition, EtOAc–hexane, white needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.81 (d, 2 H, C2-H and C6-H, $PhSO_2$), 7.79 (d, 1 H, J = 8.8 Hz, C7-H), 7.53–7.38 (m, 4 H, ArH), 6.77 (d, 1 H, J = 1.5 Hz, C4-H), 6.72 (dd, 1 H, J = 8.7, 1.5 Hz, C6-H), 6.48 (d, 1 H, J = 3.6 Hz, C3-H); IR (KBr) ν_{max} 3460, 3430, 2970, 1649, 1590, 1568, 1450, 1295, 1244, 1162, 826, 770, 732, 698, 640 cm^{-1}.

A solution of 5-amino-1-(phenylsulfonyl)indole (53 mg, 0.2 mmol, 1.0 equiv) in 1 mL of dry tetrahydrofuran was treated with potassium carbonate (40 mg, 0.3 mmol, 1.5 equiv) and benzoyl chloride (23 μL, 0.2 mmol, 1.0 equiv), and the mixture was stirred for 6 h at 25 °C. The reaction mixture was poured onto 3 mL of 10% aqueous hydrochloric acid and extracted with ethyl acetate (3 mL). The organic extract was washed with water (3 × 3 mL) and saturated aqueous sodium chloride (1 × 3 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 12 cm SiO_2, 10–30% EtOAc–hexane) afforded pure **15** (62 mg, 85%) as a white, crystalline solid, identical with **15** derived from **12**.[13]

N^5-Benzoyl-5-amino-3-methyl-1-(phenylsulfonyl)indole (16). Scheme II, following the procedure for the preparation of **15**, **13** (41 mg, 0.1 mmol, 1.0 equiv) was treated with sodium periodate (64 mg, 0.3 mmol, 3.0 equiv) and osmium tetraoxide (0.13 mg, 0.5 μmol, 0.005 equiv). The crude product was treated with sulfuric acid in dichloromethane (10%, 1 mL, 1.0 mmol, 10 equiv) to provide **16** (26 mg, 65%): mp 200–201 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.97 (d, 2 H, J = 8.4 Hz, C2-H and C6-H, PhCO), 7.95 (s, 1 H, C4-H), 7.86 (d, J = 9.3 Hz, C6-H), 7.84 (m, 4 H, ArH), 7.56–7.39 (m, 6 H, ArH), 7.37 (d, 1 H, J = 9.3 Hz, C7-H), 7.30 (s, 1 H, C2-H), 2.33 (s, 3 H, CH_3); IR (KBr) ν_{max} 3424, 3296, 2924, 1648, 1578, 1544, 1474, 1446, 1366, 1282, 1174, 1122, 1094, 932, 812, 778, 734, 690, 632, 604 cm^{-1}; EIMS m/e (relative intensity) 390 (13), 105 (base), 77 (41); CIMS (isobutane) m/e 391 (M^+ + H); CIHRMS m/e 391.1823 ($C_{22}H_{18}N_2O_3S$ + H requires 391.1822).

N^5-Benzoyl-O-benzyl-N^2-(phenylsulfonyl)-2,5-diamino-4-(1,1-bis(methoxycarbonyl)methyl)phenol (17). Table II, entry 1, following the procedure for the preparation of **8**, **2b** (100 mg, 0.22 mmol, 1.0 equiv) was treated with dimethyl malonate (26 μL, 0.23 mmol, 1.05 equiv) and sodium methoxide (2.4 mg, 0.044 mmol, 0.2 equiv) to provide **17** (116 mg, 90%): mp 209–210.5 °C (EtOAc–hexane, white needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.92 (s, 1 H, NH), 7.98 (d, 2 H, J = 8.3 Hz, C2-H and C6-H, PhCO), 7.73 (s, 1 H, C6-H), 7.72 (d, 2 H, J = 7.4 Hz, C2-H and C6-H, $PhSO_2$), 7.59–7.17 (m, 11 H, ArH), 6.90 (s, 1 H, C3-H), 4.89 (s, 2 H, $PhCH_2O$), 4.72 (s, 1 H, CH), 3.75 (s, 6 H, CO_2CH_3); IR (KBr) ν_{max} 3434, 3204, 2950, 1744, 1710, 1675, 1618, 1520, 1478, 1446, 1436, 1416, 1340, 1260, 1202, 1164, 1140, 1092, 1018, 930, 836, 802, 756, 692 cm^{-1}; EIMS, m/e (relative intensity) 588 (M^+, 1), 105 (78), 91 (base), 77 (55), 65 (22), 57 (14), 51 (25), 50 (11); CIMS (isobutane) m/e 589 (M^+ + H); EIHRMS m/e 588.1560 ($C_{31}H_{28}N_2O_8S$ requires 588.1566).

Anal. Calcd for $C_{31}H_{28}N_2O_8S$: C, 60.44; H, 4.45; N, 4.68; S, 6.12. Found: C, 60.39; H, 4.44; N, 4.68; S, 6.11.

N^5-Benzoyl-O-benzyl-N^2-(phenylsulfonyl)-2,5-diamino-4-(1-(methoxycarbonyl)-2-oxopropyl)phenol (18). Table II, entry 2, following the procedure for the preparation of **9**, **2b** (100 mg, 0.22 mmol, 1.0 equiv) was treated with methyl acetoacetate (24 μL, 0.22 mmol, 1.0 equiv) and sodium methoxide (2.4 mg, 0.044 mmol, 0.2 equiv) to provide **18** (123 mg, 98%): mp 125–126 °C (EtOAc–H_2O, white needles); ^{1}H NMR (CDCl, 300 MHz), 13.23 (s, 1 H, NH), 9.95 (s, 1 H, NH), 8.23 (s, 1 H, C6-H), 7.93–7.17 (m, 15 H, ArH), 6.94 (s, 1 H, C3-H), 4.91 (s, 2 H, $PhCH_2O$), 4.66 (s, 1 H, CH), 3.72 (s, 3 H, CO_2CH_3), 2.03 (s, 3 H, $COCH_3$); IR (KBr) ν_{max} 3854, 3676, 3412, 1734, 1654, 1618, 1520, 1474, 1446, 1406, 1338, 1254, 1166, 1090, 1026, 916, 726, 692 cm^{-1}; EIMS m/e 540 (M^+ – CH_3OH), 105 (base); CIMS (isobutane) m/e 541 (M^+ + H – CH_3OH); EIHRMS m/e 572.1445 ($C_{31}H_{28}N_2O_7S$ requires 572.1443).

N^5-Benzoyl-O-benzyl-N^2-(phenylsulfonyl)-2,5-diamino-4-morpholylphenol (19). Table II, entry 3, following the procedure for the preparation of **10**, a solution of morpholine (27 μL, 0.26 mmol, 1.2 equiv) in diethyl ether was treated with **2b** (100 mg, 0.22 mmol, 1.0 equiv) to provide **19** (84 mg, 69%): mp 223–224 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.64 (s, 1 H, NH), 8.29 (s, 1 H, C6-H), 7.90 (d, 2 H, J = 7.0 Hz, C2-H and C6-H, PhCO), 7.65 (d, 2 H, J = 7.8 Hz, C2-H and C6-H, $PhSO_2$), 7.59–7.17 (m, 11 H, ArH), 6.87 (s, 1 H, C3-H), 4.86 (s, 2 H, $PhCH_2O$), 3.92 (s, 4 H, OCH_2CH_2N), 2.92 (s, 4 H, OCH_2CH_2N); IR (KBr) ν_{max} 3442, 2838, 2356, 1670, 1600, 1522, 1476, 1438, 1398, 1334, 1250, 1168, 1116, 1092, 1010, 924, 734, 692 cm^{-1}; EIMS m/e (relative intensity) 543 (M^+, 3), 452 (47), 105 (base), 91 (67), 77 (29); CIMS (isobutane) m/e 544 (M^+ + H); EIHRMS m/e 543.1833 ($C_{30}H_{29}N_3O_5S$ requires 543.1818).

N^5-(Phenylsulfonyl)-5-amino-1-benzoyl-6-(benzyloxy)-2-methylindole-3-carboxylic Acid Methyl Ester (20). Scheme III, following the procedure for the preparation of **14**, **18** (100 mg, 0.17 mmol, 1.0 equiv) was treated with sulfuric acid in dichloromethane (20%, 30 μL, 0.17 mmol, 1.0 equiv) to provide **20** (85 mg, 88%): mp 150–151 °C (EtOAc–hexane, white plates); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.24 (s, 1 H, NH), 7.72–7.00 (m, 15 H, ArH), 6.95 (s, 1 H, C7-H), 6.68 (s, 1 H, C4-H), 4.58 (s, 2 H, $PhCH_2O$), 3.97 (s, 3 H, CO_2CH_3), 2.56 (s, 3 H, CH_3); IR (KBr) ν_{max} 3434, 1696, 1560, 1484, 1448, 1404, 1348, 1298, 1204, 1172, 1120, 914, 808, 726, 690 cm^{-1}; EIMS m/e (relative intensity) 554 (M^+, 20), 413 (11), 105 (base), 91 (26), 77 (22); CIMS (isobutane) m/e 555 (M^+ + H); EIHRMS m/e 554.1509 ($C_{31}H_{26}N_2O_6S$ requires 554.1511).

Anal. Calcd for $C_{31}H_{26}N_2O_6S$: C, 67.12; H, 4.73; N, 5.05; S, 5.78. Found: C, 66.78; H, 4.85; N, 5.00; S, 5.92.

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-6-(benzyloxy)-2-methylindole-3-carboxylic Acid Methyl Ester (21) from 20. A solution of **20** (21 mg, 0.037 mmol, 1.0 equiv) in 0.5 mL of dry tetrahydrofuran was added to a slurry of potassium hydride (6.0 mg, 0.15 mmol, 4.0 equiv) in dry tetrahydrofuran (1.0 mL), and the mixture was stirred for 0.5 h at 25 °C under nitrogen. The reaction mixture was treated with benzoyl chloride (9.0 μL, 0.074 mmol, 2.0 equiv) and was stirred for 6 h at 25 °C. The reaction mixture was poured onto 2 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL), dried ($MgSO_4$), and concentrated in vacuo to afford **21** as white, crystalline solid (21 mg, 87%).

21 from 28. A solution of **28** (21 mg, 0.04 mmol, 1.0 equiv) in 0.5 mL of dry tetrahydrofuran was added to a slurry of potassium hydride (6.4 mg, 0.16 mmol, 4.0 equiv) in dry tetrahydrofuran (1.0 mL), and the mixture was stirred for 0.5 h at 25 °C under nitrogen. The reaction mixture was treated with benzenesulfonyl chloride (8.0 μL, 0.06 mmol, 1.5 equiv) and was stirred for 12 h at 25 °C. The reaction mixture was poured onto 2 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (1 × 10 cm SiO_2, 10–30% EtOAc–hexane gradient elution) afforded **21** (19 mg, 71%) as a white, crystalline solid: mp 159–160 °C (EtOAc–hexane, white needles); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.29 (s, 1 H, C7-H), 8.03 (d, 2 H, J = 7.6 Hz, C2-H and C6-H, PhCO), 7.68–6.81 (m, 18 H, ArH), 6.78 (s, 1 H, C4-H), 4.49 (s, 2 H, $PhCH_2O$), 4.01 (s, 3 H, CH_3O), 2.53 (s, 3 H, CH_3); IR (melt) ν_{max} 2926, 1702, 1600, 1560, 1480, 1448, 1364, 1344, 1318, 1264, 1176, 1120, 1086, 1026, 930, 844, 780, 732, 698, 662 cm^{-1}; EIMS,

(13) Similarly, sequential treatment of 5-nitroindole with (1) benzoyl chloride, (2) H_2/Pd–C, (3) phenylsulfonyl chloride provided N^5-(phenylsulfonyl)-1-benzoyl-5-aminoindole, distinct from indole **15** derived from **12**.

m/e (relative intensity) 658 (M^+, 1), 517 (2), 105 (base), 91 (18), 77 (36); CIMS (isobutane), *m/e* 659 ($M^+ + H$); EIHRMS, *m/e* 658.2145 ($C_{38}H_{30}N_2O_7S$ requires 658.2147).

***O*-Benzyl-N^2,N^5-dibenzoyl-2,5-diamino-4-(1,1-bis(methoxycarbonyl)methyl)phenol (22).** Table III, entry 1, following the procedure for the preparation of **8**, **2c** (100 mg, 0.24 mmol, 1.0 equiv) was treated with dimethyl malonate (27 μL, 0.24 mmol, 1.05 equiv) and sodium methoxide (2.6 mg, 0.048 mmol, 0.2 equiv) to provide **22** (104 mg, 79%): mp 186–187 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.98 (s, 1 H, NH), 8.64 (s, 1 H, NH), 8.60 (s, 1 H, C6-H), 8.00 (d, 2 H, *J* = 7.9 Hz, C2-H and C6-H, PhCO), 7.85 (s, 1 H, C3-H), 7.79 (d, 2 H, *J* = 9.2 Hz, C2-H and C6-H, PhCO), 7.53–7.39 (m, 11 H, ArH), 5.23 (s, 2 H, PhCH_2O), 4.75 (s, 1 H, CH), 3.70 (s, 6 H, CO_2CH_3); IR (melt) ν_{max} 3854, 3802, 3736, 3676, 3650, 3630, 3334, 2952, 2360, 1742, 1670, 1610, 1578, 1540, 1508, 1478, 1458, 1420, 1254, 1200, 1154, 1084, 1028, 798 cm^{-1}; EIMS *m/e* (relative intensity) 552 (M^+, 10), 149 (21), 105 (base), 91 (19), 77 (19), 57 (13); CIMS (isobutane) *m/e* 553 ($M^+ + H$); EIHRMS *m/e* 552.1893 ($C_{32}H_{28}N_2O_7$ requires 552.1897).

***O*-Benzyl-N^2,N^5-dibenzoyl-2,5-diamino-4-(1-(methoxycarbonyl)-2-oxopropyl)phenol (23).** Table III, entry 2, following the procedure for the preparation of **9**, **2c** (100 mg, 0.24 mmol, 1.0 equiv) was treated with methyl acetoacetate (26 μL, 0.24 mmol, 1.0 equiv) and sodium methoxide (2.6 mg, 0.048 mmol, 0.2 equiv) to provide **23** (89 mg, 70%): mp 155.5–157 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz), δ 13.26 (s, 1 H, NH), 10.00 (s, 1 H, NH), 8.67 (s, 1 H, C6-H), 8.42 (s, 1 H, C3-H), 7.97–7.39 (m, 15 H, ArH), 5.28 (s, 2 H, PhCH_2O), 4.71 (s, 1 H, CH), 3.83 (s, 3 H, CO_2CH_3); IR (KBr) ν_{max} 3424, 1734, 1707, 1668, 1605, 1580, 1539, 1501, 1480, 1422, 1341, 1250, 1152, 1074, 1027, 895, 797, 734, 695 cm^{-1}; EIMS *m/e* (relative intensity) 536 (M^+, 1), 105 (base), 77 (21); CIMS (isobutane) *m/e* 537 ($M^+ + H$); EIHRMS *m/e* 536.1942 ($C_{32}H_{28}N_2O_6$ requires 536.1947).

Anal. Calcd for $C_{32}H_{28}N_2O_6$: C, 71.63; H, 5.26; N, 5.22. Found: C, 71.96; H, 5.28; N, 5.39.

***O*-Benzyl-N^2,N^5-dibenzoyl-2,5-diamino-4-morpholylphenol (24).** Table III, entry 3, following the procedure for the preparation of **10**, **2c** (50 mg, 0.12 mmol, 1.0 equiv) was treated with morpholine (13 μL, 0.13 mmol, 1.1 equiv) to provide **24** (34 mg, 54%): mp 205–206 °C (EtOAc–hexane, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.78 (br s, 1 H, NH), 8.67 (s, 1 H, C6-H), 7.98 (s, 1 H, C3-H), 7.88 (s, 1 H, NH), 7.81 (d, 2 H, *J* = 7.3 Hz, C2-H and C6-H, PhCO), 7.53–7.38 (m, 13 H, ArH), 5.25 (s, 2 H, PhCH_2O), 3.95 (br s, 4 H, OCH_2CH_2N), 3.04 (br s, 4 H, OCH_2CH_2N); IR (melt) ν_{max} 3854, 3822, 3736, 3676, 3650, 2848, 2360, 1718, 1700, 1654, 1560, 1540, 1420, 1242, 1184, 1112, 884 cm^{-1}; EIMS *m/e* (relative intensity) 507 (M^+, 1), 106 (base), 91 (10), 77 (28); CIMS (isobutane) *m/e* 508 ($M^+ + H$); EIHRMS *m/e* 507.2148 ($C_{31}H_{29}N_3O_4$ requires 507.2158).

***O*-Benzyl-N^2,N^5-dibenzoyl-3-acetoxy-2,5-diaminophenol (25).** Table III, entry 4, following the procedure for the preparation of **11**, a solution of **2c** (200 mg, 0.47 mmol, 1.0 equiv) in acetic acid provided **25** (107 mg, 47%): mp 209–210 °C (CH_2Cl_2–hexane, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.71 (s, 1 H, NH), 7.92 (d, 2 H, *J* = 7.0 Hz, C2-H and C6-H, PhCO), 7.82 (d, 2 H, *J* = 7.2 Hz, C2-H and C6-H, PhCO), 7.54 (d, 1 H, *J* = 2.0 Hz, C6-H, irradiation at 7.12 ppm causes collapse to s), 7.52–7.23 (m, 11 H, ArH), 7.12 (d, 1 H, *J* = 1.9 Hz, C4-H, irradiation at 7.54 ppm causes collapse to s), 5.01 (s, 2 H, PhCH_2O), 2.06 (s, 3 H, $COCH_3$); IR (melt) ν_{max} 3854, 3280, 3062, 2924, 1760, 1646, 1606, 1580, 1540, 1518, 1480, 1458, 1420, 1370, 1314, 1274, 1206, 1170, 1094, 1074, 1028, 886, 842, 796 cm^{-1}; EIMS *m/e* (relative intensity) 480 (M^+, 2), 105 (base), 91 (74), 77 (53), 65 (10); CIMS (isobutane) *m/e* 481 ($M^+ + H$); EIHRMS *m/e* 480.1692 ($C_{29}H_{24}N_2O_5$ requires 480.1685).

***O*-Benzyl-N^2,N^5-dibenzoyl-2,5-diamino-3-[3-(1-propenyl)]phenol (26).** Table III, entry 5, following the procedure for the preparation of **12**, **2c** (100 mg, 0.24 mmol, 1.0 equiv) was treated with boron trifluoride etherate (15 μL, 0.11 mmol, 0.5 equiv) and 2-propenyltri-*n*-butylstannane (81 μL, 0.26 mmol, 1.1 equiv) to provide **26** (56 mg, 51%): mp 176–177 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.64 (1 H, NH), 7.85–7.21 (m, 18 H, ArH), 6.87 (d, 1 H, *J* = 1.5 Hz, C4-H), 5.93–5.84 (m, 1 H, C*H*=CH_2), 5.04 (d, 1 H, *J* = 8.1 Hz, CH=C*H*H), 4.96 (d, 1 H, *J* = 15.2 Hz, CH=CH*H*), 4.92 (s, 2 H, PhCH_2O), 3.43 (d, 2 H, *J* = 6.5 Hz, CH_2CH=CH_2); IR (KBr) ν_{max} 3270, 3062, 2924, 1734, 1642, 1602, 1578, 1542, 1514, 1482, 1458, 1420, 1384, 1316, 1274, 1176, 1114, 1074, 1028, 998, 912, 838, 798 cm^{-1}; EIMS *m/e* (relative intensity) 462 (M^+, 6), 105 (base), 91 (24), 77 (24); CIMS (isobutane) *m/e* 463 ($M^+ + H$); EIHRMS *m/e* 462.1949 ($C_{30}H_{26}N_2O_3$ requires 462.1943).[9]

***O*-Benzyl-N^2,N^5-dibenzoyl-2,5-diamino-3-[3-(3-methyl-1-propenyl)]phenol (27).** Table III, entry 6, following the procedure for the preparation of **12**, **2c** (200 mg, 0.476 mmol, 1.0 equiv) was treated with boron trifluoride etherate (58.0 μL, 0.476 mmol, 1.0 equiv) and 2-butenyltri-*n*-butylstannane (307 μL, 0.95 mmol, 2.0 equiv) to provide **27** (142 mg, 65%): mp 164–165 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.12 (s, 1 H, NH), 7.86 (m, 4 H, C2-H and C6-H, PhCO), 7.69 (d, 1 H, *J* = 1.8 Hz, C6-H), 7.55–7.23 (m, 12 H, ArH), 6.93 (d, 1 H, *J* = 1.9 Hz, C4-H), 6.1–5.94 (m, 1 H, C*H*=CH_2), 5.03 (s, 2 H, PhCH_2O), 5.04 (dd, 1 H, *J* = 15.8, 1.1 Hz, CH=C*H*H), 5.02 (dd, 1 H, *J* = 9.2, 1.3 Hz, CH=CH*H*), 3.76 (m, 1 H, C*H*CH=CH_2), 1.35 (d, 3 H, *J* = 6.9 Hz, CH_3); IR (KBr) ν_{max} 3856, 3442, 3060, 2968, 2360, 1648, 1602, 1580, 1518, 1418, 1304, 1174, 1028, 912, 846, 798, 696, 650 cm^{-1}; EIMS *m/e* (relative intensity) 476 (M^+, 5), 105 (99), 77 (82); CIMS (isobutane) *m/e* 477 ($M^+ + H$); EIHRMS *m/e* 476.2113 ($C_{31}H_{28}N_2O_3$ requires 476.2112).[9]

N^5,1-Dibenzoyl-5-amino-7-(benzyloxy)-3-methylindole (7) from 27. Scheme IV, following the procedure for the preparation of **15**, **27** (96 mg, 0.20 mmol, 1.0 equiv) was treated with sodium periodate (135 mg, 0.63 mmol, 3.0 equiv) and osmium tetraoxide (0.3 mg, 1.0 μmol, 0.005 equiv). The crude product was treated with sulfuric acid in dichloromethane (10%, 1.5 mL, 10 equiv) to provide **7** (47 mg, 50%), identical in all respects with **7** prepared by the addition of 1-piperidino-1-propene to **2c**.[9]

N^5,1-Dibenzoyl-5-amino-6-(benzyloxy)-2-methylindole-3-carboxylic Acid Methyl Ester (28). Scheme IV, following the procedure for the preparation of **14**, **23** (28 mg, 0.05 mmol, 1.0 equiv) was treated with sulfuric acid in dichloromethane (20%, 0.75 mL, 15.0 equiv) to provide **28** (21 mg, 75%): mp 159–159.5 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.20 (s, 1 H, NH), 8.66 (s, 1 H, C4-H), 7.85–7.33 (m, 15 H, ArH), 6.95 (s, 1 H, C7-H), 4.96 (s, 2 H, PhCH_2O), 4.02 (s, 3 H, CO_2CH_3), 2.61 (s, 3 H, CH_3); IR (KBr) ν_{max} 3442, 2924, 1706, 1664, 1600, 1534, 1492, 1464, 1378, 1352, 1312, 1258, 1198, 1126, 894, 730, 702 cm^{-1}; EIMS *m/e* (relative intensity) 518 (M^+, 6), 105 (base), 77 (26), 57 (11); CIMS (isobutane) *m/e* 519 ($M^+ + H$); EIHRMS *m/e* 518.1845 ($C_{32}H_{26}N_2O_5$ requires 518.1842).

N^5,1-Dibenzoyl-5-amino-7-(benzyloxy)indole (29). Scheme IV, following the procedure for the preparation of **15**, **26** (50 mg, 0.11 mmol, 1.0 equiv) was treated with sodium periodate (69 mg, 0.32 mmol, 3.0 equiv) and osmium tetraoxide (0.13 mg, 0.5 μmol, 0.005 equiv). The crude product was treated with sulfuric acid in dichloromethane (5%, 1.0 mL, 8.0 equiv) to provide **29** (34 mg, 70%): mp 197–198 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.90 (d, 2 H, *J* = 7.5 Hz, C2-H and C6-H, PhCO), 7.88 (s, 1 H, C6-H), 7.67 (d, 2 H, *J* = 7.9 Hz, C2-H and C6-H, PhCO), 7.54–7.48 (m, 4 H, ArH), 7.46 (d, 1 H, *J* = 3.5 Hz, C2-H), 7.36 (s, 1 H, C4-H), 7.33–7.20 (m, 6 H, ArH), 6.62 (d, 1 H, *J* = 3.5 Hz, C3-H), 4.95 (s, 2 H, PhCH_2O); IR (melt) ν_{max} 3904, 3854, 3838, 3712, 3690, 3650, 3064, 2924, 2852, 1734, 1700, 1684, 1652, 1618, 1596, 1540, 1508, 1474, 1420, 1330, 1182, 1028, 914, 878, 696, 664 cm^{-1}; EIMS *m/e* (relative intensity) 446 (M^+, 5), 105 (base), 91 (23), 77 (41); CIMS (isobutane) *m/e* 447 ($M^+ + H$); EIHRMS *m/e* 446.1630 ($C_{29}H_{22}N_2O_3$ requires 446.1630).

N^2-Benzoyl-*O*-benzyl-N^5-(phenylsulfonyl)-2,5-diamino-3-(1,1-bis(methoxycarbonyl)methyl)phenol (30). Table IV, entry 1, following the procedure for the preparation of **8**, **2d** (100 mg, 0.22 mmol, 1.0 equiv) was treated with dimethyl malonate (26 μL, 0.23 mmol, 1.05 equiv) and sodium methoxide (2.4 mg, 0.044 mmol, 0.2 equiv) to provide **30** (84 mg, 65%) and **31** (19 mg, 15%). For **30**: mp 175–176 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.30 (s, 1 H, NH), 7.89 (d, 2 H, *J* = 7.2 Hz, C2-H and C6-H PhCO), 7.73 (d, 2 H, *J* = 7.5 Hz, C2-H and C6-H $PhSO_2$), 7.55–7.28 (m, 11 H, ArH), 6.80 (d, 1 H, *J* = 2.0 Hz, C6-H), 6.67 (d, 1 H, *J* = 2.1 Hz, C4-H), 4.88 (s, 2 H, PhCH_2O), 4.72 (s, 1 H, CH), 3.80 (s, 6 H, OCH_3); IR (KBr) ν_{max} 3388, 3140, 1738, 1722, 1650, 1606, 1578, 1522, 1434, 1404, 1332, 1156, 1098, 1018, 988, 908, 850, 756, 736, 718, 690, 670 cm^{-1}; EIMS *m/e* 570 ($M^+ - H_2O$), 105 (base); CIMS (isobutane) *m/e*

589 (M^+ + H); EIHRMS m/e 588.1566 ($C_{31}H_{28}N_2O_8S$ requires 588.1566).

Anal. Calcd for $C_{31}H_{28}N_2O_8S$: C, 71.31; H, 5.57; N, 5.24. Found: C, 71.32; H, 5.56; N, 5.24.

For **31**: mp 198–199 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.57 (s, 1 H, C3-H), 7.49 (s, 1 H, NH), 8.13 (s, 1 H, NH), 7.77 (d, 2 H, J = 7.3 Hz, C2-H and C6-H, $PhSO_2$), 7.55–7.35 (m, 13 H, ArH), 7.00 (s, 1 H, C6-H), 5.01 (s, 2 H, $PhCH_2O$), 4.66 (s, 1 H, CH), 3.71 (s, 6 H, OCH_3); IR (melt) ν_{max} 3854, 3752, 2924, 1736, 1654, 1614, 1534, 1478, 1448, 1436, 1332, 1166, 1090, 1024 cm^{-1}.

N^2-Benzoyl-*O*-benzyl-N^5-(phenylsulfonyl)-2,5-diamino-3-(1-(methoxycarbonyl)-2-oxopropyl)phenol (32). Table IV, entry 2, following the procedure for the preparation of **9**, **2d** (100 mg, 0.22 mmol, 1.0 equiv) was treated with methyl acetoacetate (24 μL, 0.22 mmol, 1.0 equiv) and sodium methoxide (2.4 mg, 0.044 mmol, 0.2 equiv) to provide **32** (90 mg, 72%) and **33** (12 mg, 10%). For **32**: mp 180–181 °C (CH_2Cl_2, white needles); ^1H NMR (DMSO-d_6, 300 MHz) δ 10.46 (s, 1 H, NH), 9.60 (s, 1 H, NH), 7.88 (d, 2 H, J = 7.1 Hz, C2-H and C6-H, PhCO), 7.69 (d, 2 H, J = 7.1 Hz, C2-H and C6-H, $PhSO_2$), 7.68–7.36 (m, 11 H, ArH), 6.89 (d, 1 H, J = 2.0 Hz, C6-H), 6.65 (d, 1 H, J = 2.0 Hz, C4-H), 5.00 (s, 2 H, $PhCH_2O$), 4.90 (s, 1 H, CH), 3.57 (s, 3 H, OCH_3), 1.91 (s, 3 H, $COCH_3$); IR (KBr) ν_{max} 3171, 1735, 1712, 1648, 1606, 1580, 1518, 1399, 1332, 1265, 1156, 1093, 1045, 905, 753, 718 cm^{-1}; EIMS m/e 540 ($M^+ - CH_3OH$), 105 (base); CIMS m/e 541 (M^+ + H – CH_3OH); EIHRMS m/e 572.1438 ($C_{31}H_{28}N_2O_7S$ requires 527.1439).

For **33**: mp 202–203 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 13.04 (s, 1 H, NH), 8.55 (s, 1 H, NH), 8.19 (s, 1 H, C3-H), 7.78 (d, 2 H, J = 8.3 Hz, C2-H and C6-H, $PhSO_2$), 7.58–7.34 (m, 13 H, ArH), 6.49 (s, 1 H, C6-H), 5.27 (s, 2 H, $PhCH_2O$), 4.21 (s, 1 H, CH), 3.53 (s, 3 H, OCH_3), 1.71 (s, 3 H, $COCH_3$); IR (KBr) ν_{max} 3170, 1714, 1710, 1654, 1524, 1605, 1570, 1340, 1250, 1160, 910, 753, 715 cm^{-1}.

N^2-Benzoyl-*O*-benzyl-N^5-(phenylsulfonyl)-4-[3-(1-propenyl)]-2,5-diaminophenol (34). Table IV, entry 5, following the procedure for the preparation of **12**, **2d** (100 mg, 0.22 mmol, 1.0 equiv) was treated with boron trifluoride etherate (13 μL, 0.11 mmol, 0.5 equiv) and 2-propenyltri-*n*-butylstannane (75 μL, 0.24 mmol, 1.1 equiv) to provide **34** (67 mg, 61%): mp 177–178 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.59 (s, 1 H, NH), 8.30 (s, 1 H, C3-H), 7.79 (d, 2 H, J = 7.2 Hz, C2-H and C6-H, PhCO), 7.59 (d, 2 H, J = 7.4 Hz, C2-H and C6-H, $PhSO_2$), 7.58–7.38 (m, 11 H, ArH), 7.27 (s, 1 H, C6-H), 6.51 (s, 1 H, NH), 5.7–5.65 (m, 1 H, $CH{=}CH_2$), 5.20 (s, 2 H, $PhCH_2O$), 5.09 (dd, 1 H, J = 10.0, 0.9 Hz, CH=CHH), 4.92 (dd, 1 H, J = 17.2, 1.1 Hz, CH=CHH), 2.81 (d, 2 H, J = 7.1 Hz, $CH_2CH{=}CH_2$); IR (KBr) ν_{max} 3424, 3256, 1660, 1590, 1534, 1502, 1482, 1448, 1438, 1330, 1256, 1164, 1126, 1090, 1028, 914, 758, 732 cm^{-1}; EIMS m/e (relative intensity) 498 (M^+, 2), 105 (99), 91 (base), 77 (71), 65 (12), 51 (13); CIMS (isobutane) m/e 499 (M^+ + H); EIHRMS m/e 498.1619 ($C_{29}H_{26}N_2O_4S$ requires 498.1613).

Anal. Calcd for $C_{29}H_{26}N_2O_4S$: C, 69.36; H, 5.26; N, 5.62; S, 6.61. Found C: 69.33; H, 5.36; N, 5.55; S, 6.56.

N^5-(Phenylsulfonyl)-5-amino-1-benzoyl-7-(benzyloxy)-2-methylindole-3-carboxylic Acid Methyl Ester (35). Scheme V, following the procedure for the preparation of **14**, **32** (51 mg, 0.09 mmol, 1.0 equiv) was treated with sulfuric acid in dichloromethane (20%, 0.2 mL, 10 equiv) to provide **35** (35 mg, 71%): mp 109–110 °C (ether–hexane, white plates); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.68–7.20 (m, 15 H, ArH), 6.90 (d, 1 H, J = 1.6 Hz, C6-H), 6.68 (d, 1 H, J = 1.3 Hz, C4-H), 6.44 (s, 1 H, NH), 4.72 (s, 2 H, $PhCH_2O$), 3.87 (s, 3 H, CO_2CH_3), 2.69 (s, 3 H, CH_3); IR (KBr) ν_{max} 3240, 2924, 1716, 1648, 1600, 1576, 1520, 1410, 1399, 1325, 1260, 1122, 1090, 1042, 908, 740, 720, 560 cm^{-1}; EIMS m/e (relative intensity) 554 (M^+, 3), 149 (41), 105 (base), 91 (25), 77 (25), 57 (20); CIMS (isobutane) m/e 555 (M^+, H); EIHRMS m/e 554.1508 ($C_{31}H_{26}N_2O_6S$ requires 554.1512).

N^5,1-Dibenzoyl-N^5-(phenylsulfonyl)-5-amino-7-(benzyloxy)-2-methylindole-3-carboxylic Acid Methyl Ester (36). A solution of **35** (13 mg, 0.02 mmol, 1.0 equiv) in 0.5 mL of dry tetrahydrofuran was added to a slurry of potassium hydride (2 mg, 0.05 mmol, 2.5 equiv) in 0.5 mL of dry tetrahydrofuran under nitrogen, and the mixture was stirred for 0.5 h at 25 °C. The reaction mixture was treated with benzoyl chloride (6 μL, 0.05 mmol, 2.5 equiv) and was stirred for 6 h at 25 °C. The reaction mixture was poured onto 1 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (2 mL). The organic extract was washed with water (3 × 2 mL) and saturated aqueous sodium chloride (1 × 2 mL), dried ($MgSO_4$), and the solvent was removed in vacuo. Flash chromatography (1 × 10 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded pure **36** (12.3 mg, 81%) as a white, crystalline solid: mp >250 °C (EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.15 (d, 2 H, J = 7.5 Hz, C2-H and C6-H, PhCO), 7.82 (d, 2 H, J = 7.2 Hz, C2-H and C6-H, PhCO), 7.69 (d, 2 H, J = 7.5 Hz, C2-H and C6-H, $PhSO_2$), 7.66–7.15 (m, 15 H, ArH), 7.00 (d, 1 H, J = 1.6 Hz, C6-H), 6.72 (d, 1 H, J = 1.1 Hz, C4-H), 5.07 (s, 2 H, $PhCH_2O$), 3.72 (s, 3 H, CO_2CH_3), 1.26 (s, 3 H, CH_3); IR (melt) ν_{max} 3854, 1734, 1700, 1654, 1560, 1542, 1508, 1174 cm^{-1}; EIMS m/e (relative intensity) 658 (M^+, 3), 517 (5), 481 (2), 105 (base), 91 (27), 77 (42); CIMS (isobutane) m/e 659 (M^+ + H); EIHRMS m/e 658.2158 ($C_{38}H_{30}N_2O_7S$ requires 658.2158).

N^5-Benzoyl-5-amino-1-(phenylsulfonyl)-6-(benzyloxy)-indole (37). Scheme V, following the procedure for the preparation of **15**, **34** (152 mg, 0.30 mmol, 1.0 equiv) was treated with sodium periodate (196 mg, 0.9 mmol, 3.0 equiv) and osmium tetraoxide (0.4 mg, 1.5 μmol, 0.005 equiv). The crude product was treated with sulfuric acid in dichloromethane (10%, 2 mL, 10 equiv) to provide **37** (89 mg, 62%): mp 193–193.5 °C (decomposition, EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.70 (s, 1 H, NH), 7.84 (d, 2 H, J = 7.8 Hz, C2-H and C6-H, PhCO), 7.68 (s, 1 H, C4-H), 7.63 (d, 2 H, J = 8.3 Hz, C2-H and C6-H, $PhSO_2$), 7.55–7.45 (m, 11 H, ArH), 7.35 (d, 1 H, J = 3.2 Hz, C2-H), 7.27 (s, 1 H, C7-H), 6.63 (d, 1 H, J = 3.5 Hz, C3-H), 5.32 (s, 2 H, $PhCH_2O$); IR (KBr) ν_{max} 3444, 1672, 1592, 1534, 1492, 1464, 1370, 1332, 1260, 1216, 1174, 1158, 1120, 1094, 1018, 826, 762, 726, 700, 684, 612 cm^{-1}; EIMS m/e (relative intensity) 482 (M^+, 21), 391 (20), 105 (base), 91 (28), 77 (27); CIMS (isobutane) m/e 483 (M^+ + H); EIHRMS m/e 482.1301 ($C_{28}H_{22}N_2O_4S$ requires 482.1300).

N^5-Benzoyl-5-amino-6-(benzyloxy)indole (38). A solution of **37** (60 mg, 0.12 mmol, 1.0 equiv) in 1 mL of methanol was treated with 1 mL of 1 N aqueous potassium hydroxide, and the reaction mixture was warmed at reflux (80 °C) for 2 h. The cooled reaction mixture was poured onto 2 mL of 10% aqueous hydrochloric acid and was extracted with ethyl acetate (5 mL). The organic extract was washed with water (3 × 5 mL) and saturated aqueous sodium chloride (5 mL), dried ($MgSO_4$), and concentrated in vacuo. Chromatography (1 × 10 cm SiO_2, 10–20% EtOAc–hexane gradient elution) afforded **38** (37 mg, 87%) as a white, crystalline solid: mp 187–188 °C (decomposition, EtOAc–hexane, white needles); ^1H NMR ($CDCl_3$, 300 MHz) δ 8.81 (s, 1 H, C4-H), 8.70 (s, 1 H, NH), 8.07 (s, 1 H, NH), 7.83 (d, 2 H, J = 7.1 Hz, C2-H and C6-H PhCO), 7.51–7.36 (m, 8 H, ArH), 7.12 (d, 1 H, J = 2.4 Hz, C2-H), 7.00 (s, 1 H, C7-H), 6.54 (d, 1 H, J = 2.1 Hz, C3-H); IR (melt) ν_{max} 3288, 1734, 1718, 1700, 1684, 1654, 1578, 1560, 1540, 1508, 1486, 1458, 1270, 1150 cm^{-1}; EIMS m/e (relative intensity) 342 (M^+, 2), 105 (base), 91 (29), 77 (28); CIMS (isobutane) m/e 343 (M^+ + H); EIHRMS m/e 342.2718 ($C_{22}H_{18}N_2O_2$ requires 342.2718).

Indole **38** proved distinct from the potassium hydroxide hydrolysis (CH_3OH, 80 °C, 2 h) product of indole **29** (major addition product with **2c**, 51%) and identical with the potassium hydroxide hydrolysis (CH_3OH, 80 °C, 2 h) product of the minor isomer (4%) derived from allyltri-*n*-butylstannane addition to **2c**.[9]

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Registry No. **1**, 112764-63-3; **2a**, 124400-30-2; **2b**, 124400-37-9; **2c**, 114996-60-0; **2d**, 112764-62-2; **3**, 124400-38-0; **4**, 124400-39-1; **5**, 124400-40-4; **6**, 124400-41-5; **7**, 124418-02-6; **8**, 124400-42-6; **9**, 124400-43-7; **10**, 124400-44-8; **11**, 124400-45-9; **12**, 124400-47-1; **13**, 124400-48-2; **14**, 124400-49-3; **15**, 124400-50-6; **16**, 124400-53-9; **17**, 124400-54-0; **18**, 124400-55-1; **19**, 124400-56-2; **20**, 124400-57-3; **21**, 124400-58-4; **22**, 124400-60-8; **23**, 124400-61-9; **24**, 124400-62-0; **25**, 124400-63-1; **26**, 124400-64-2; **27**, 124400-65-3; **28**, 124400-59-5; **29**, 124417-92-1; **30**, 124400-66-4; **31**, 124400-67-5; **32**, 124400-68-6;

33, 124400-69-7; 34, 124400-70-0; 35, 124400-71-1; 36, 124400-72-2; 37, 124400-73-3; 38, 124400-74-4; CC-1065, 69866-21-3; 4-nitroaniline, 100-01-6; *N*-benzoyl-4-nitroaniline, 3393-96-2; N^1-benzoyl-1,4-diaminobenzene, 17625-83-1; N^4-benzoyl-N^1-(phenylsulfonyl)-1,4-diaminobenzene, 124400-29-9; 2-amino-5-nitrophenol, 121-88-0; *N*-(*tert*-butyloxycarbonyl)-2-amino-5-nitrophenol, 124400-31-3; *N*-(*tert*-butyloxycarbonyl)-*O*-benzyl-2-amino-5-nitrophenol, 124400-32-4; N^2-(*tert*-butyoxycarbonyl)-*O*-benzyl-2,5-diaminophenol, 124400-33-5; N^5-benzoyl-N^2-(*tert*-butyloxycarbonyl)-*O*-benzyl-2,5-diaminophenol, 124400-34-6; N^5-benzoyl-*O*-benzyl-2,5-diaminophenol, 124400-35-7; N^5-benzoyl-N^2-(phenylsulfonyl)-*O*-benzyl-2,5-diaminophenol, 124400-36-8; 1-piperidino-1-propene, 7182-09-4; dimethyl malonate, 108-59-8; methyl acetoacetate, 105-45-3; N^2-benzoyl-N^5-(phenylsulfonyl)-2,5-diaminophenol, 124400-46-0; 2-propenyl-tri-*n*-butylstannane, 24850-33-7; 2-butenyl-tri-*n*-butylstannane, 31197-41-8; 5-nitroindole, 6146-52-7; 5-nitro-1-(phenylsulfonyl)indole, 124400-51-7; 5-amino-1-(phenylsulfonyl)indole, 124400-52-8; N^5-benzoyl-N^2-(phenylsulfonyl)-2,5-diaminophenol, 124400-75-5; N^5-(phenylsulfonyl)-1-benzoyl-5-aminoindole, 124400-76-6.

Supplementary Material Available: Tabular compilation of the ^{1}H NMR spectra of **1–38** (3 pages). Ordering information is given on any current masthead page.

Synthesis of Rigid, Heterocyclic Dipeptide Analogues[1]

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The preparation of rigid analogues of peptides can be a valuable technique for gaining information about the active conformation of biological ligands and/or for enhancing the proteolytic stability and bioavailability of such systems. In the course of our studies directed toward the design of novel inhibitors of human renin,[2] the aspartic proteinase responsible for initiation of the renin–angiotensin system, we desired a rigid, heterocyclic mimic of an N-terminal phenylalanine containing dipeptide. The analogue that we chose to pursue (**2**) can be conceptually derived from a Phe-Xaa dipeptide **1** by a series of rigidifying events (Figure 1): (a) fixing the dihedral angle between the α and β carbons of phenylalanine;[3] (b) blocking rotation of the side-chain phenyl group;[4] and (c) fixing the directionality of the amide carbonyl group with respect to the indole ring and prohibiting C–N amide-bond rotation.[5] Attachment of **2** to any of a variety of transition-state

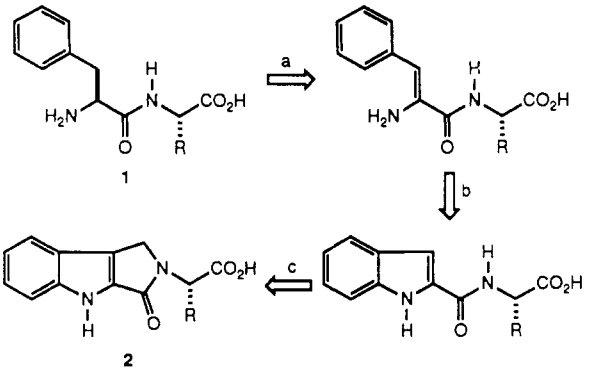

Figure 1. Rigidification of Phe-Xaa dipeptides.

Table I. Synthesis of Heterocyclic Dipeptide Analogues 5a–e

product	R^3	yield,[a] %
5a	(*S*)-4-imidazolylmethyl	31
5b	(*RS*)-4-thiazolylmethyl	61
5c	(*RS*)-3-pyrazolylmethyl	47
5d	(*S*)-$(CH_3)_2CHCH_2$	67
5e	H	16

[a] Overall yield based on **3a**.

analogues[6] designed to occupy the P_1/P_1' subsites of renin was expected to produce a series of potent inhibitors.

Our synthetic approach to **2** is outlined in Scheme I. Benzyl indole-2-carboxylate was subjected to Vilsmeier formylation[7] to give aldehyde **3a** (80%). Reductive amination of **3a** with L-histidine methyl ester dihydrochloride led to **4a** (R = imidazolylmethyl) in 91% yield. Lactam formation[8] was achieved by catalytic hydrogenolysis of **4a** and cyclization using *N*-ethyl-*N*'-[2-(dimethylamino)-ethyl]carbodiimide hydrochloride (EDC) and 4-(dimethylamino)pyridine (DMAP), to give tricyclic ester **5a**. Overall yields for the preparation of **5a–e** from **3a** using a variety of α-amino esters are given in Table I. Hydrolysis of **5a–e** gave the desired tricyclic peptide analogues **2a–e**.[9]

The coupling of **2b–e** to the amino group of a previously described amino glycol transition-state analogue[10] proceeded uneventfully, to give renin inhibitors **6b–e** (Scheme II). Substantial racemization was observed, however, in the coupling of **2a**.[11] This could be avoided through use of an additional protection/deprotection sequence[12] whereby the lithium salt of **2a**, formed in the hydrolysis of **5a**, was treated in the same pot with excess of di-*tert*-butyl dicarbonate. The resulting Boc-protected acid **2f** (R = Boc-imidazolylmethyl) was coupled via its mixed

(1) Presented in part at the 11th American Peptide Symposium, San Diego, CA, July 1989.

(2) (a) Kempf, D. J.; de Lara, E.; Stein, H. H.; Cohen, J.; Plattner, J. J. *J. Med. Chem.* **1987**, *30*, 1978. (b) Kempf, D. J.; de Lara, E.; Stein, H. H.; Cohen, J.; Egan, D. A.; Plattner, J. J. *J. Med. Chem.* In press.

(3) We have previously reported renin inhibitors that contain (*Z*)-dehydrophenylalanine: Plattner, J. J.; Marcotte, P. A.; Kleinert, H. D.; Stein, H. H.; Greer, J.; Bolis, G.; Fung, A. K. L.; Bopp, B. A.; Luly, J. R.; Sham, H. L.; Kempf, D. J.; Rosenberg, S. H.; Dellaria, J. F.; De, B.; Merits, I.; Perun, T. J. *J. Med. Chem.* **1988**, *31*, 2277.

(4) A series of renin inhibitors containing indole-2-carboxylic acid as a phenylalanine replacement has been disclosed: Buhlmayer, P.; Rasetti, V.; Fuhrer, W.; Stanton, J. L.; Goschke, R. U.S. Patent 4,727,060, Feb 23, 1988.

(5) Lactam-containing Phe-Xaa analogues based on cyclizing from the amine nitrogen to the α-carbon of phenylalanine have been reported: (a) Thaisrivongs, S.; Pals, D. T.; Turner, S. R.; Kroll, L. T. *J. Med. Chem.* **1988**, *31*, 1369. (b) Zydowsky, T. M.; Dellaria, J. F.; Nellans, H. N. *J. Org. Chem.* **1988**, *53*, 5607.

(6) For an excellent review, see: Greenlee, W. J. *Pharm. Res.* **1987**, *4*, 364.

(7) Shabica, A. C.; Howe, E. E.; Ziegler, J. B.; Tishler, M. *J. Am. Chem. Soc.* **1946**, *68*, 1156.

(8) Lactam formation by thermolysis of acyclic esters, which has been used in less rigid cases (ref 5b), was unsuccessful in the case of **4** due to decomposition via an alkylidene-3*H*-indole intermediate.

(9) A conceptually more efficient approach to racemic **5** via alkylation of **5e** failed due to decomposition, again via an alkylidene-3*H*-indole. The corresponding indole-*N*-Boc derivative of **5e** underwent competitive proton removal from both the α-carbon and the 1-position of the tricyclic nucleus.

(10) Luly, J. R.; BaMung, N.; Soderquist, J.; Fung, A. K. L.; Stein, H. H.; Kleinert, H. D.; Marcotte, P. A.; Egan, D. A.; Bopp, B. A.; Merits, I.; Bolis, G.; Greer, J.; Perun, T. J.; Plattner, J. J. *J. Med. Chem.* **1988**, *31*, 2264.

(11) We would not have detected racemization of **2b** or **2c** since the starting materials were racemic; however, leucine analogue **2d** did not racemize under the hydrolysis and coupling conditions.

(12) Rosenberg, S. Unpublished results.

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