HETEROCYCLES, Vol. 84, No. 2, 2012, pp. 1345 - 1353. ©2012 The Japan Institute of Heterocyclic Chemistry
Received, 3rd July, 2011, Accepted, 22nd August, 2011, Published online, 24th August, 2011
DOI: 10.3987/COM-11-S(P)76

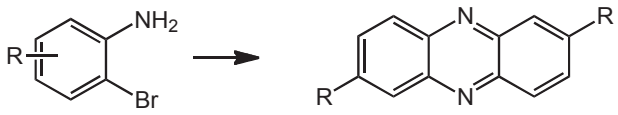
SYNTHESIS OF SUBSTITUTED PHENAZINES *VIA* PALLADIUM-CATALYZED ARYL LIGATION[1]

Jeffrey D. Winkler,* Barry M. Twenter, and Thomas Gendrineau

Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104, USA; winkler@sas.upenn.edu

Abstract – A method for the "ligation" of two aromatic rings has been achieved *via* synthesis of functionalized phenazines by double Buchwald-Hartwig amination of a variety of substituted bromoanilines, followed by *in situ* oxidation.

The ligation of aromatic rings represents an important tool for the synthesis of molecules of increasing complexity,[2] with important applications in the synthesis of natural and unnatural products. We describe here the implementation of such a strategy for the preparation of substituted phenazines,[3] leading to the synthesis of disubstituted heterocycles that cannot be otherwise prepared with comparable levels of efficiency (Figure 1).

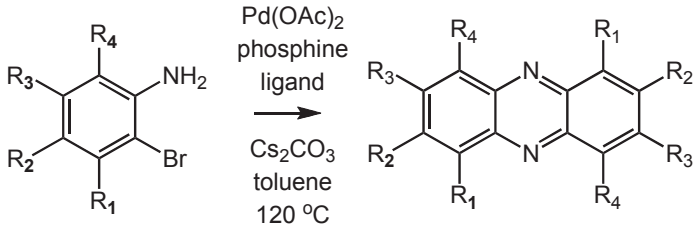


1 **2**

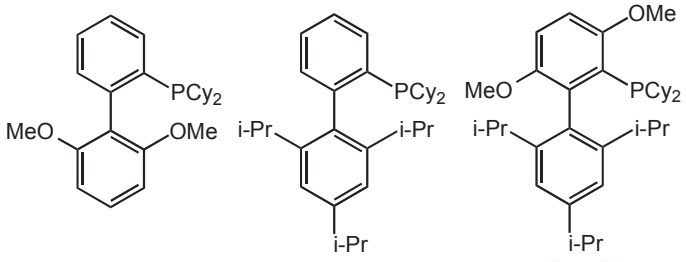
Figure 1. Regiochemistry of Synthesis of Disubstituted Phenazines

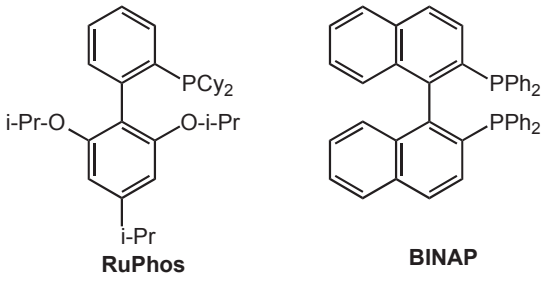
Previous efforts by Beifuss[4] and Senanayake[5] have suggested that such a process should be possible, although with only single examples in unoptimized yields, both of which employ the highly pyrophoric ligand tri-*t*-butyl phosphine.[6] We report herein the optimization of this process and its implementation as a method of choice for the synthesis of unsymmetrically disubstituted phenazines. We further describe the application of this reaction sequence to the aryl ligation of two molecules of tryptophan to generate the previously unreported heterocyclic ring system 1,7-dihydrodipyrrolo-[2,3-*b*:2',3'-*i*]phenazine, a highly fluorescent pentacyclic ring system.

Table 1. The Effect of Phosphine Ligand on Phenazine Yield



Entry	R_1	R_2	R_3	R_4	Phosphine ligand (Yield)
3	H	H	H	H	SPhos (95%) XPhos (95%)
4	Me	H	H	H	BrettPhos (92%) XPhos (59%)
5	H	H	H	Me	RuPhos (92%) BrettPhos (71%)
6	H	*t*-Bu	H	H	XPhos (55%) SPhos (54%)
7	H	CF_3	H	H	XPhos (80%) RuPhos (56%)
8	OMe	H	H	H	RuPhos (72%) BINAP (56%)
9	H	AcN(Me)-	H	H	XPhos (43%) SPhos (41%)





We report herein that a series of bromoanilines that are substituted with either electron-donating or electron-withdrawing groups can be regioselectively converted to the corresponding disubstitutedphenazines in good yields using BINAP or other crystalline phosphine ligands in lieu of tri-*t*-butyl phosphine (Table 1). Using the Buchwald C-N Ligand Kit available from Strem Chemicals, a series of phosphines were surveyed, and the two ligands that afforded the highest yields are presented in the Table for each substrate, illustrating the absence of a single optimal phosphine ligand in this reaction. Similar results were observed with the 2-chloroaniline (64% yield) although the corresponding triflates resulted only in oxygen to nitrogen triflate migration in lieu of the desired coupling reaction. The last entry in Table 1 is particularly notable as, even though the observed yield is moderate, none of the desired phenazine product was observed with BINAP.[7]

We next examined the reaction of more complex aminoaromatics derived from amino acid precursors, as outlined in Figure 2. Aryl ligation of tryptophan using this strategy could lead to the previously undescribed dihydrodipyrrolophenazine ring system shown in **13**. Toward that end, dimerization of **10**,[8] leads to the formation of the corresponding phenazine in 51% yield. However, all attempts to convert **11** to the ring-opened product under the reaction conditions described by Hino and coworkers[7] led to none of the desired product **13**. Direct dimerization of the N-Boc tryptophan **12** produced the desired ring system **15** in 49% yield. The UV spectrum of **13** was notable for a λ_{max} of 406 nm, and the fluorescence spectrum of **13** featured a λ_{em} of 538 nm, with a Stokes' shift of 132 nm.

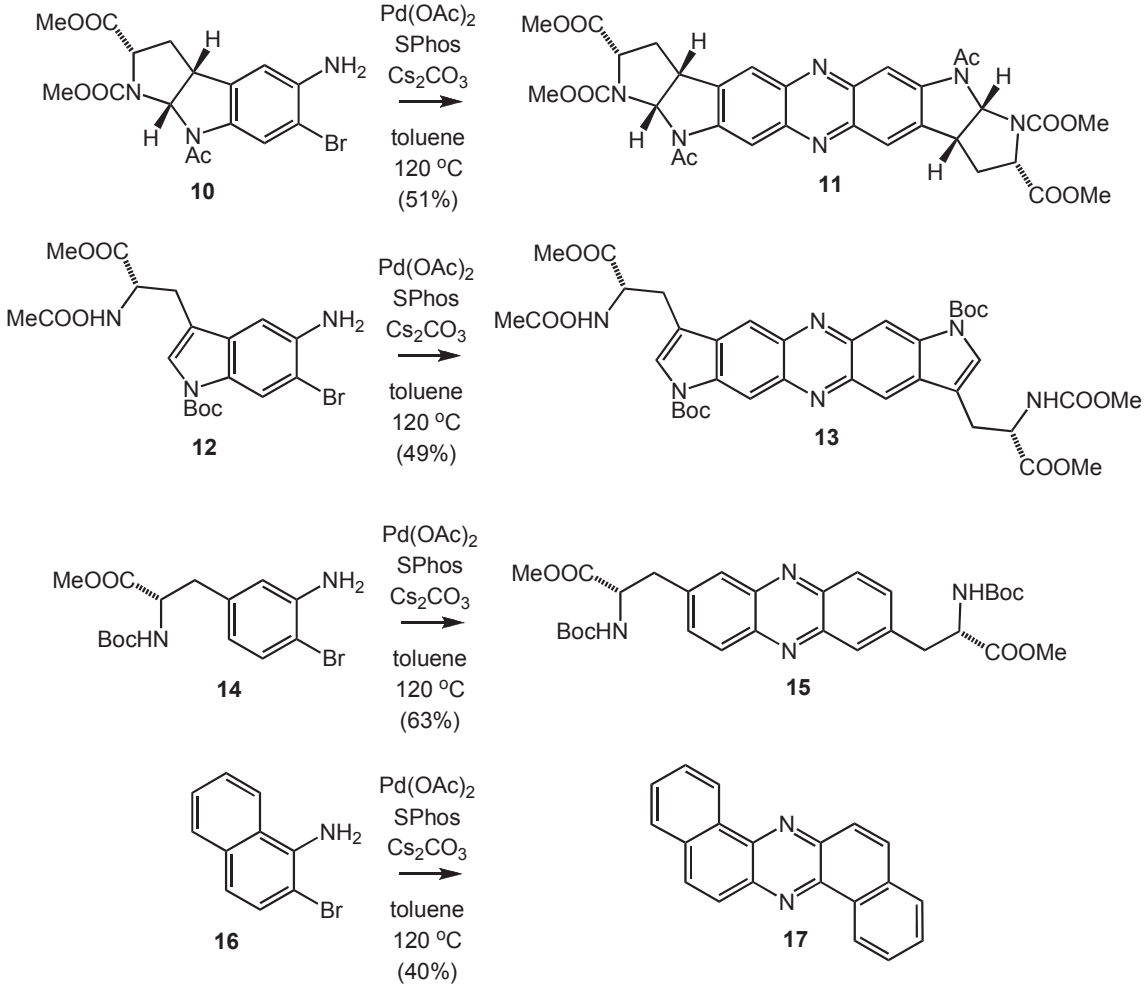


Figure 2. Synthesis of Complex Phenazines

The analogous reaction of the phenylalanine-derived substrate **14** afforded the corresponding phenazine **15** in 63% yield. A further example of the regiochemical control that is possible with this phenazine construction strategy is the formation of **17**, albeit in 40% yield, from **16**, without formation of the corresponding dibenzo[a,j]phenazine, a result that would not be possible using the more classical approaches to the synthesis of substituted phenazines.[9]

Finally, we demonstrate that this strategy is not limited to dimerization. By judicious choice of substituents on the aniline ring, i.e., by exploiting the decreased reactivity of anilines substituted with electron-withdrawing groups, we have demonstrated that the reaction of **18** with 2-bromoaniline leads to the formation of **19** in 65% yield. The application of this methodology to the synthesis of diverse substituted phenazines is currently underway in our laboratory and our results will be reported in due course.

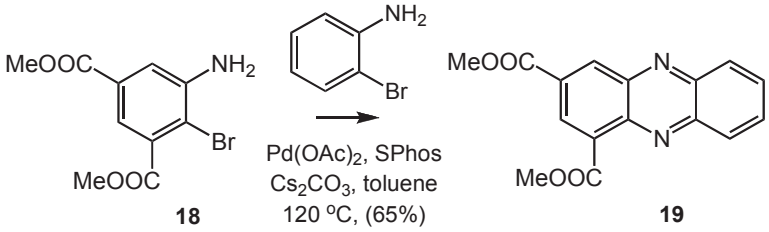


Figure 3. Synthesis of an Unsymmetrical Phenazine

EXPERIMENTAL

General Methods: Solvents used for extraction and purification were certified ACS grade from Fisher. Unless otherwise indicated, all reactions were run under an inert atmosphere of Argon. Anhydrous toluene was obtained *via* distillation from sodium metal. Fisher HPLC grade dichloromethane, chloroform, and methanol were used without further purification as reaction solvents. Commercial reagents were used as received. Deuterated solvents were obtained from Cambridge Isotope labs. Merck pre-coated silica gel plates (250 μm, 60 F254) were used for analytical TLC. Spots were visualized using 254 nm ultraviolet light, with either ceric ammonium molybdate or phosphomolybdic acid stains as visualizing agents. Chromatographic purifications were performed on Sorbent Technologies silica gel (particle size 32-63 microns). ^{1}H and ^{13}C NMR spectra were recorded at 500 MHz, 360 MHz and 125 MHz, 90 MHz respectively, in $CDCl_3$ or $(CD_3)_2SO$ on a Bruker AM-500, DRX-500, or DRX-360 spectrometer. Chemical shifts are reported relative to internal chloroform (δ 7.27 for ^{1}H, δ 77.23 for ^{13}C) or dimethyl sulfoxide (δ 2.50 for ^{1}H, δ 39.53 for ^{13}C). Infrared spectra were recorded on a NaCl plate using a Perkin-Elmer 1600 series Fourier transform spectrometer. Optical rotation measurements were recorded using a Jasco P2000 polarimeter. High resolution mass spectra were obtained on an Autospec high resolution double-focusing electrospray ionization/chemical ionization spectrometer with either DEC 11/73 or OPUS software data system.

General Procedure for Phenazines in Table 1

To a solution of bromide (1 equiv) in toluene (0.1 M) was added Cs_2CO_3 (2.0 equiv), phosphine ligand (0.08 equiv), and $Pd(OAc)_2$ (0.05 equiv) at room temperature. The reaction mixture was allowed to stir

and warm to 120 °C for 4-24 h. Once the reaction appeared to be complete by consumption of the bromide by TLC analysis, the mixture was allowed to cool to room temperature, diluted with $CHCl_3$, and filtered through celite. The solution was concentrated, loaded on silica gel, and purified by silica gel chromatography.

Phenazine (entry 3)

Reaction of 2-bromoaniline according to the general procedure with purification by flash chromatography (10:1 hexanes:EtOAc to 1:1 hexanes:EtOAc) provided phenazine **3** as a yellow solid (95% yield): mp 170 °C. R_f 0.25 (10:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.27 (dd, *J* = 6.7, 3.4 Hz, 4H), 7.86 (dd, *J* = 6.7, 3.4 Hz, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 143.8, 130.7, 129.9. FTIR (thin film) 3739, 3053, 2928, 2857, 1625, 1513, 1462, 1358, 1249, 1181, 1146, 1110, 1007, 953, 895, 819, 752, 743, 600 cm^{-1}. HRMS (ES) Calcd for $C_{12}H_8N_2$: 181.0766 ($M+H^+$), found 181.0735 ($M+H^+$).

1,6-Dimethylphenazine (entries 4 and 5)

Reaction of 2-bromo-3-methylaniline or 2-bromo-6-methylaniline according to the general procedure with purification by flash chromatography (100:1 hexanes:EtOAc to 10:1 hexanes:EtOAc) provided phenazine **4/5** as a yellow solid (92% yield): mp 220 °C. R_f 0.37 (10:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.15 (d, *J* = 8.7 Hz, 2H), 7.72 (dd, *J* = 8.7, 6.7 Hz, 2H), 7.66 (d, *J* = 6.7 Hz, 2H), 2.95 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 143.0, 142.9, 137.8, 130.2, 129.7, 128.1, 18.0. FTIR (thin film) 2921, 1725, 1455, 1370, 1270, 1121, 850, 791, 743 cm^{-1}. HRMS (ES) Calcd for $C_{14}H_{12}N_2$: 209.1079 ($M+H^+$), found 209.1070 ($M+H^+$).

2,7-Di-*tert*-butylphenazine (entry 6)

Reaction of 2-bromo-4-*tert*-butylaniline according to the general procedure with purification by flash chromatography (20:1 hexanes:EtOAc to 10:1 hexanes:EtOAc) provided phenazine **6** as a yellow solid (55% yield): mp 210 °C. R_f 0.35 (10:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.14-8.18 (m, 4H), 7.94 (dd, *J* = 9.1, 2.1 Hz, 2H), 1.50 (s, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 153.5, 143.5, 142.5, 130.3, 128.9, 124.2, 35.7, 31.0. FTIR (thin film) 2957, 2870, 1627, 1467, 1418, 1363, 1259, 1135, 935, 876, 821, 737, 626 cm^{-1}. HRMS (ES) Calcd for $C_{20}H_{24}N_2$: 293.2018 ($M+H^+$), found 293.2011 ($M+H^+$).

2,7-Bis(trifluoromethyl)phenazine (7)

Reaction of 2-bromo-4-(trifluoromethyl)aniline according to the general procedure with purification by flash chromatography (20:1 hexanes:EtOAc to 10:1 hexanes:EtOAc) provided phenazine **7** as a yellow solid (80% yield): mp 115 °C. R_f 0.50 (10:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.63 (s, 2H), 8.41 (d, *J* = 9.1 Hz, 2H), 8.04 (dd, *J* = 9.1, 2.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 144.7,

143.3, 131.8, 128.4, 126.7, 124.7, 122.5. FTIR (thin film) 2925, 1426, 1334, 1266, 1205, 1165, 1135, 1053, 896, 836 cm^{-1}. HRMS (ES) Calcd for $C_{14}H_6F_6N_2$: 316.0435 (M^-), found 316.0444 (M^-).

2,7-Dimethoxyphenazine (8)

Reaction of 2-bromo-5-methoxyaniline according to the general procedure with purification by flash chromatography (5:1 hexanes:EtOAc to 1:1 hexanes:EtOAc) provided phenazine **8** as a yellow solid (72% yield): mp 242 °C. R_f 0.25 (3:1 hexanes:EtOAc). ^1H NMR ($CDCl_3$, 500 MHz): δ = 8.03 (d, *J* = 9.4 Hz, 2H), 7.50 (dd, *J* = 9.4, 2.7 Hz, 2H), 7.40 (d, *J* = 2.7 Hz, 2H), 4.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 160.4, 143.6, 140.6, 130.1, 126.2, 105.1, 56.0. FTIR (thin film) 2920, 1624, 1481, 1428, 1294, 1218, 1112, 1009, 839, 808 cm^{-1}. HRMS (ES) Calcd for $C_{14}H_{12}N_2O_2$: 241.0977 ($M+H^+$), found 241.0973 ($M+H^+$).

***N*,*N*'-(Phenazine-2,7-diyl)bis(N-methylacetamide) (entry 9)**

To a solution of *N*-(4-aminophenyl)-*N*-methylacetamide (136 mg, 0.83 mmol) in $CHCl_3$ (8.3 mL) was added NBS (147 mg, 0.83 mmol) portion wise over 15 min. The reaction was allowed to stir and warm to room temperature over 30 min and then quenched with water (10 mL). The mixture was diluted and extracted with CH_2Cl_2 (3 x 10mL), the combined organic extracts were washed with sat aq $Na_2S_2O_3$ (10 mL), brine (10 mL), and dried over sodium sulfate. The mixture was dried *in vacuo*, loaded onto silica gel, and purified by flash chromatography (3:1 hexanes:acetone to 1:1 hexanes:acetone) to provide bromoaniline 22 as a brown solid (77% yield): mp 120 °C. R_f 0.45 (1:1 hexanes:acetone). ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.26 (d, *J* = 2.3 Hz, 1H), 6.93 (dd, *J* = 8.4, 2.3 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 4.24 (s, 2H), 3.19 (s, 3H), 1.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.2, 144.0, 135.9, 131.3, 127.4, 116.0, 108.9, 37.5, 22.5. FTIR (thin film) 3455, 3336, 1636, 1505, 1423, 1382, 1310, 1144, 1034, 977, 934, 822 cm^{-1}. HRMS (ES) Calcd for $C_9H_{11}BrN_2O$: 240.09976 ($M-H^-$), found 240.9962 ($M-H^-$).

Reaction of *N*-(4-amino-3-bromophenyl)-*N*-methylacetamide according to the general procedure with purification by flash chromatography (20:1 CH_2Cl_2:MeOH to 10:1 CH_2Cl_2:MeOH) provided phenazine **9** as an orange solid (43% yield): mp 240 °C. R_f 0.15 (1:1 hexanes:acetone). ^1H NMR ($CDCl_3$, 500 MHz, 50 °C): δ = 8.27 (d, *J* = 9.2 Hz, 1H), 8.05 (d, *J* = 1.9 Hz, 1H), 7.75 (dd, *J* = 9.2, 1.9 Hz, 1H), 3.48 (s, 3H), 2.11 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz, 50 °C): δ = 170.4, 146.5, 143.9, 142.8, 131.2, 131.1, 125.9, 37.5, 22.9. FTIR (thin film) 2922, 1667, 1479, 1424, 1376, 1340, 1120, 1072, 984, 830 cm^{-1}. HRMS (ES) Calcd for $C_{18}H_{18}N_4O_2$: 323.1508 ($M+H^+$), found 323.1497 ($M+H^+$).

(2S,3aR,7aR,9S,10aR,14aR)-Tetramethyl 7,14-diacetyl-3,3a,7,7a,10,10a,14,14a-octahydropyrrolo-[3',2':4,5]pyrrolo[2,3-*b*]pyrrolo[3',2':4,5]pyrrolo[2,3-*i*]phenazine-1,2,8,9(2*H*,9*H*)-tetracarboxylate (11)

Reaction of bromoaniline **10** according to the general procedure with purification by flash chromatography (20:1 CH_2Cl_2:MeOH to 10:1 CH_2Cl_2:MeOH) provided phenazine **11** as an orange film (51% yield): R_f 0.16 (1:1 hexanes:acetone). ^{1}H NMR ($CDCl_3$, 500 MHz, 50 °C): δ = 8.58 (s, 2H), 7.87 (d, *J* = 1.5 Hz, 2H), 6.46 (d, *J* = 6.4 Hz, 2H), 4.70 (d, *J* = 8.1 Hz, 2H), 4.25 (t, *J* = 6.9 Hz, 2H), 3.76 (s, 6H), 2.96 (s, 6H), 2.70-2.85 (m, 4H), 2.67 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz, 50 °C): δ = 171.1, 170.7, 155.2, 143.8, 143.6, 141.6, 139.7, 124.1, 114.6, 79.1, 60.0, 53.3, 52.0, 45.3, 34.4, 24.1. FTIR (thin film) 3730, 3394, 2292, 1714, 1443, 1391, 1178, 1121. $[\alpha]_D^{25}$ = 191.00 (c = 0.30, $CHCl_3$). HRMS (ES) Calcd for $C_{32}H_{32}N_6O_{10}$: 661.2258 ($M+H^+$), found 661.2272 ($M+H^+$).

Di-tert-butyl 3,9-bis((S)-3-methoxy-2-((methoxycarbonyl)amino)-3-oxopropyl)dipyrrolo[2,3-*b*:2',3'-*i*]-phenazine-1,7-dicarboxylate (13)

To a solution of **12** (51 mg, 0.11 mmol) in toluene (1.1 mL) was added Cs_2CO_3 (72 mg, 0.22 mmol), and RuPhos palladacycle (4 mg, 0.005 mmol) at room temperature. The reaction mixture was heated to 120 °C for 18 h at which point an additional equiv of RuPhos palladacycle (4 mg, 0.005 mmol) was added and reaction continued to stir at 120 °C four more hours. The reaction mixture was cooled to room temperature, diluted with CH_2Cl_2 (20 mL), filtered through celite, dried *in vacuo*, loaded onto silica gel, and purified by flash chromatography (3:1 benzene:EtOAc to 1:1 benzene:EtOAc) to provide phenazine (**13**) as an orange solid (49% yield): mp 180 °C. R_f 0.26 (1:1 hexanes:acetone). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.91 (bs, 2H), 8.36 (s, 2H), 7.71 (s, 2H), 5.48 (d, *J* = 7.3 Hz, 2H), 4.81-4.88 (m, 2H), 3.77 (s, 6H), 3.71 (s, 6H), 3.30-3.48 (m, 4H), 1.78 (s, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.9, 156.3, 149.2, 141.2, 139.7, 137.7, 136.3, 130.4, 116.9, 114.8, 112.7, 84.4, 53.6, 52.6, 52.4, 28.2, 27.9. FTIR (thin film) 3310, 2954, 1726, 1536, 1425, 1374, 1329, 1254, 1153, 1067, 855 cm^{-1}. $[\alpha]_D^{25}$ = 20.7 (c = 0.33, $CDCl_3$). HRMS (ES) Calcd for $C_{38}H_{44}N_6O_{12}$: 799.2915 ($M+Na^+$), found 799.2934 ($M+Na^+$).

(2S,2'S)-Dimethyl 3,3'-(phenazine-2,7-diyl)bis(2-((tert-butoxycarbonyl)amino)propanoate) (15)

Reaction of bromoaniline **14** according to the general procedure with purification by flash chromatography (3:1 hexanes:acetone to 2:1 hexanes:acetone) provided phenazine **15** as a brown film (63% yield): R_f 0.28 (2:1 hexanes:acetone). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.16 (d, *J* = 8.9 Hz, 2H), 7.99 (s, 2H), 7.65 (d, *J* = 8.9 Hz, 2H), 5.14 (d, *J* = 7.9 Hz, 2H), 4.71-4.83 (m, 2H), 3.75 (s, 6H), 3.25-3.48 (m, 4H), 1.39 (s, 18H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 171.9, 155.0, 143.1, 142.7, 139.1, 132.4, 129.5, 129.2, 80.1, 54.0, 52.4, 38.8, 28.1. FTIR (thin film) 2927, 1712, 1510, 1364, 1165, 1057 cm^{-1}. $[\alpha]_D^{25}$ = 11.6 (c = 1.25, $CHCl_3$). HRMS (ES) Calcd for $C_{30}H_{38}N_4O_8$: 605.2587 ($M+Na^+$), found 605.2595 ($M+Na^+$).

Dibenzo[a,h]phenazine (17)

Reaction of bromoaniline **16** according to the general procedure with purification by flash chromatography (25:1 hexanes:EtOAc to 10:1 hexanes:EtOAc) provided phenazine **17** as a yellow solid (40% yield): mp 280 °C. R_f 0.43 (10:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.49 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 9.2 Hz, 1H), 8.11 (d, *J* = 9.2 Hz, 1H), 8.00 (d, *J* = 6.9 Hz, 1H), 7.79-7.89 (m, 2H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 142.1, 141.9, 133.5, 132.4, 131.4, 129.5, 128.4, 127.9, 127.7, 125.3. . FTIR (thin film) 2919, 2851, 1727, 1458, 1382, 1341, 1258, 1115, 827, 741. HRMS (ES) Calcd for $C_{20}H_{12}N_2$: 281.1079 ($M+H^+$), found 281.1080 ($M+H^+$).

Dimethyl phenazine-1,3-dicarboxylate (19)

Reaction of ortho bromo aniline **18** according to the general procedure with purification by flash chromatography (10:1 hexanes:EtOAc to 1:1 hexanes:EtOAc) provided phenazine **19** as a yellow solid (65% yield): mp 144 °C. R_f 0.17 (5:1 hexanes:EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.11 (d, *J* = 1.9 Hz, 1H), 8.77 (d, *J* = 1.9 Hz, 1H), 8.34 (m, 1H), 8.27 (m, 1H), 7.87-7.95 (m, 2H), 4.13 (s, 3H), 4.06 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 166.7, 165.6, 144.7, 144.2, 142.4, 142.3, 136.4, 132.4, 132.2, 131.9, 131.0, 130.7, 130.6, 130.1, 53.1, 53.0. FTIR (thin film) 1725, 1600, 1520, 1435, 1329, 1244, 1099, 1030, 755. HRMS (ES) Calcd for $C_{16}H_{12}N_2O_4$: 297.0875 ($M+H^+$), found 297.0873 ($M+H^+$).

ACKNOWLEDGEMENTS

We grateful acknowledge the invaluable assistance of Professor E. James Petersson (University of Pennsylvania) in obtaining and interpreting the fluorescence data. We also thank Professor Ivan Dmochowski (University of Pennsylvania) for helpful discussions regarding the fluorescence properties of the phenazines, and the donors of the Petroleum Research Fund, administered by the American Chemical Society (ND-48955) for the generous support of this research.

REFERENCES AND NOTES

1. We warmly dedicate this manuscript to our friend and colleague Professor Albert Padwa, in grateful acknowledgement of his lifetime of creative accomplishments in organic chemistry.
2. For an excellent discussion of increasing molecular complexity, see E. J. Corey and X.-M. Cheng, 'The Logic of Chemical Synthesis,' Wiley, New York, 1995.
3. For an excellent recent review, see U. Beifuss and M. Tietze, *Top. Curr. Chem.,* 2005, **244**, 77.
4. Reference 3, p. 109.
5. M. Shen, G. Li, B. Lu, A. Hossain, F. Roschangar, V. Farina, and C. Senanayake, *Org. Lett.*, 2004, **6**, 4129.

6. For conceptually related examples, see a) M. Tietze, A. Iglesias, E. Merisor, J. Conrad, I. Klaiber, and U. Beifuss, *Org. Lett.,* 2005, **7**, 1549; b) T. Emoto, N. Kubosaki, Y. Yamagiwa, and T. Kamikawa, *Tetrahedron Lett.,* 2000, **41**, 355.
7. All compounds were characterized by full spectroscopic (NMR, IR, high resolution MS) data. Yields refer to spectroscopically and chromatographically homogeneous (>95%) materials.
8. Prepared from the known amino compound (M. Taniguchi, A. Gonsho, M. Nakagawa, and T. Hino, *Chem. Pharm. Bull.,* 1983, **31**, 1856) by 1) Boc protection; 2) bromination; and 3) Boc deprotection. For an excellent review on the chemistry of hexahydropyrroloindoles, see D. Crich and A. Banerjee, *Acc. Chem. Res.,* 2007, **40**, 151.
9. For a discussion of the regiochemistry of phenazine formation, see Y. Kosugi, K. Itoho, H. Okazaki, and T. Yanai, *J. Org. Chem.,* 1995, **60**, 5690.