Functionalized (Benzotriazol-1-yl)methanes as 1,1-Dipole Synthon Equivalents in Diverse Annulations to Aromatic and Heteroaromatic Rings

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The title compounds **1a**−**e** readily undergo deprotonation and subsequent reactions with the appropriate electrophiles to form intermediates of types **4** and **7** which, upon treatment with Lewis acids, cyclize to afford fused aromatics **5** and **8**. Tetrahydronaphthalene **11a**, 1,2,3,4-tetrahydrochromanes (**11b**−**d**, **13**), indanes (**16**, **18**), 9,10-dihydrophenanthrenes (**21a**−**c**, **25**), and tetrahydro-[1,2-*a*]indoles (**28**, **30**) with phenyl, substituted phenyl, and thienyl substituents were prepared in this manner.

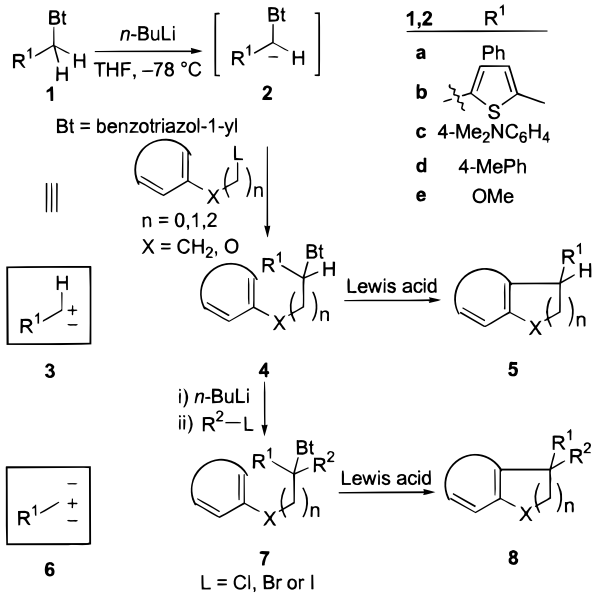
Introduction

Aromatic annulations which form carbocyclic derivatives possessing latent functionality are of considerable utility due to their potential applications in the elaboration of natural products.[1] However, the types of latent groups which have been introduced into molecules during these annulations are still quite limited. Earlier work from our laboratory revealed 1-phenylthiomethylbenzotriazole to be a valuable annulating reagent for the synthesis of phenylthio-substituted carbocyclic compounds.[2] We have also demonstrated that a wide range of functionalized (benzotriazol-1-yl)methanes (Scheme 1) are excellent reagents for insertion of carbon into aldehydes and ketones, due to the ease with which the corresponding carbanions can be generated, together with the facile removal of the benzotriazolyl group to form carbocations.[3] In that work, a wide variety of functionality could be introduced, attached to the carbon atom inserted. We now report that these same functionalized (benzotriazol-1-yl)methane reagents act as 1,1-dipole synthon equivalents (**3** and **6** in Scheme 1) in the annulation of aromatic rings; this enables the synthesis of fused carbocyclic compounds possessing various latent functionality.

Results and Discussion

Benzotriazole derivatives **1a**−**e** were prepared according to previously reported procedures (Scheme 1).[3c,4] Treatment of **1a**−**e** with *n*-butyllithium in THF at −78 °C produced anions **2a**−**e** which, as discussed in detail below, reacted with a series of aromatic ring-substituted

Scheme 1



alkyl halides to afford the corresponding alkylated products **4** (Scheme 1). Importantly, benzotriazole derivatives **4** can be lithiated and alkylated regiospecifically α to the benzotriazolyl group to give compounds **7** (Scheme 1). Compounds **4** and **7**, upon treatment with a Lewis acid, afforded the corresponding annulated aromatic rings **5** and **8**, respectively (Scheme 1). The liberated benzotriazole was easily removed by extraction with dilute aqueous sodium hydroxide.

Compounds **10a**−**d** and **12** were prepared in excellent yields starting from the corresponding 1-(3-bromopropyl)-benzene (**9a**) and 1-(2-bromoethoxy)benzene (**9b**). Subsequently, **10a,b** and **12** were converted into tetrahydronaphthalene **11a** and tetrahydrochromanes **11b**−**d** and **13** in moderate to good yields by six-membered ring annulations (Scheme 2).

These cyclizations were accomplished with $ZnBr_2$ as the Lewis acid in equimolar (**10b,d** and **12**) or double-molar (**10a,d**) amounts (Table 1). In the absence of Lewis acid, even with extended heating, no cyclization was observed. The temperature required for the cyclization

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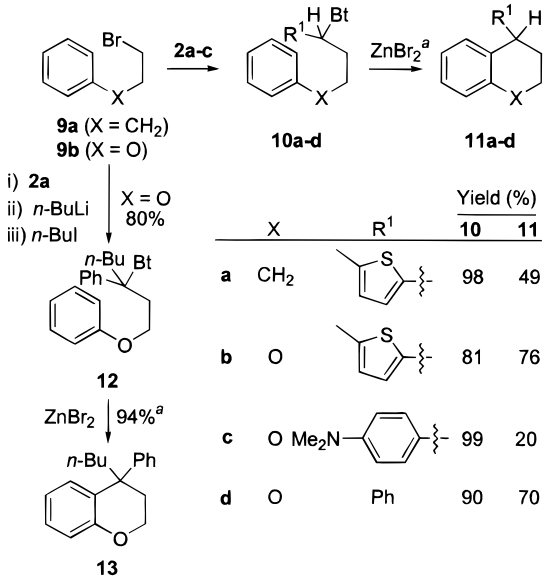
Table 1. Reaction Conditions for the Synthesis of Annulated Compounds

compd	Lewis acid (equiv)	reaction time (h)	temperature (°C)	solvent	yield (%)
11a	$ZnBr_2$ (2.0)	24	62	chloroform	49
11b	$ZnBr_2$ (1.0)	12	120	1,2-diclorobenzene	76
11c	$ZnBr_2$ (2.0)	29	40	methylene chloride	20
11d	$ZnBr_2$ (1.0)	24	170	1,2-dichlorobenzene	70
13	$ZnBr_2$ (1.0)	5	115	1,2-dichlorobenzene	94
16	$ZnBr_2$ (1.8)	12 (24)[a]	130 (160)[a]	1,2-dichlorobenzene	49
18	$ZnBr_2$ (2.0)	12 (24)[a]	140 (160)[a]	1,2-dichlorobenzene	61
21a	$ZnBr_2$ (2.0)	22	25	1,2-dichlorobenzene	95
21b	$AlCl_3$ (1.0)	72	120	methylene chloride	85
21c	$ZnBr_2$ (2.0)	24	130	1,2-dichlorobenzene	61
23	$ZnBr_2$ (2.0)	5	62	chloroform	81
25	$ZnBr_2$ (2.0)	0.5	105	1,2-dichlorobenzene	97
28	$ZnBr_2$ (1.3)	1	150	1,2-dichlorobenzene	30
30	$ZnBr_2$ (1.0)	12	120	1,2-dichlorobenzene	97

[a] The reaction mixture was heated in two stages for the time and at the temperature indicated.

Scheme 2[a]

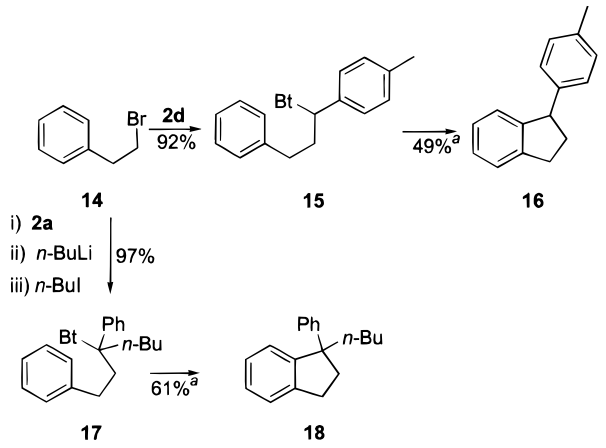


[a] The reaction conditions for the cyclization are shown in Table 1.

is dependent upon the nature of the cation stabilizing group R^1 and the electron density in the aromatic ring. Thus, a more electron-rich R^1 group in **10b** causes a faster and milder cyclization than that of **10d** (Table 1) due to a better stabilization of the developing carbocation. A more electron-rich aromatic ring in **10b** induces faster and cleaner cyclization than in the case of **10a** (Table 1) due to enhanced nucleophilicity of the aromatic ring. Even milder reaction conditions were sufficient in the case of **12** due to the generation of a tertiary carbocation by the departure of benzotriazole. However, compound **10c** undergoes cyclization in low yield, while elimination of benzotriazole and formation of the corresponding alkene is the main process observed experimentally.

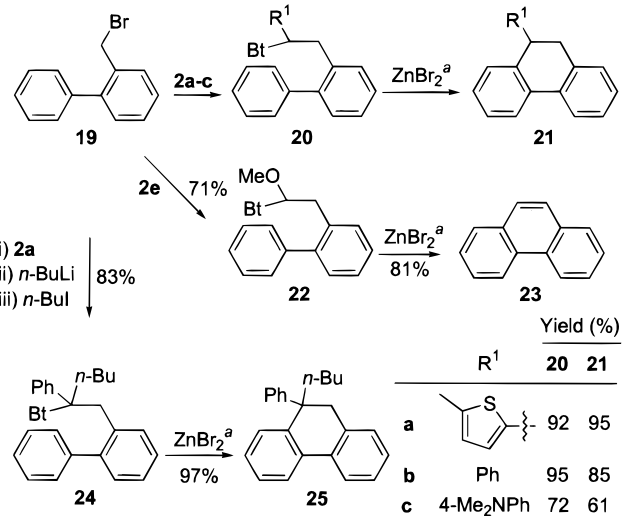
2-Phenylethyl bromide (**14**) reacted cleanly with anions **2d** and **2a** to give **15** and **17**, cyclization precursors for a facile approach to 1-monosubstituted and 1,1-disubstituted indanes **16** and **18**, respectively (Scheme 3). Significant formation of alkenes was observed during five-membered ring annulations. The cyclization of compound **15** was accomplished at high temperature with 1.8 equiv of $ZnBr_2$ (Table 1) to give compound **16** in 49% isolated yield. ^{1}H NMR and GC−MS spectra of the crude product indicated the presence of a mixture of cis and trans

Scheme 3[a]



[a] The reaction conditions for the cyclization are shown in Table 1.

Scheme 4[a]



[a] The reaction conditions for the cyclization are shown in Table 1.

β-substituted styrenes which were generated by the elimination of benzotriazole from compound **15**.

9-Monosubstituted **21a**−**c** and 9,9-disubstituted 9,10-dihydrophenanthrene **25** were prepared in excellent yields starting from 2-(bromomethyl)biphenyl (**19**) by a six-membered ring annulation of biphenyl (Scheme 4). Intermediates **20a**−**b**, **22**, and **24** were prepared by the reaction of **2a**−**c,e** with **19** in excellent yields. Compound

24 was obtained in 83% overall yield from **19** by in situ preparation of **20b** followed by lithiation and alkylation (Scheme 4).

The temperatures required for cyclization of **20a**−**c**, **22**, and **19** were lower than that for the corresponding benzene annulation due to the lower activation entropy necessary in order to reach the transition state. In general, the better the stabilization of the carbocation, the lower the temperature needed and the faster the reaction. Thus, **20a** cyclizes faster than **20b** while **24** cyclizes faster than **20b** (Table 1 and Scheme 4). Interestingly, **22** afforded phenanthrene **23** as the only isolated product, probably by the elimination of methanol from the corresponding 9,10-dihydrophenanthrene (Scheme 4).

Due to the pharmacological importance of mitomycins,[5,6] the search for new drugs by the syntheses of mitomycin skeletons and mitomycin-like 1,2,3,4-tetrahydropyrido[1,2-*a*]indoles has attracted much attention. Existing methods for the construction of the 1,2,3,4-tetrahydropyrido[1,2-*a*]indole skeleton include (i) intramolecular radical cyclizations,[7−9] (ii) a Dieckmann/ring expansion,[10] and (iii) our recent approach via 1-(1*H*-2-indolylmethyl)-1*H*-benzotriazole.[11] We found that the benzotriazole-mediated annulation method discussed above can be further extended to provide a facile alternative route to 1-monosubstituted and 1,1-disubstituted 1,2,3,4-tetrahydropyrido[1,2-*a*]indoles.

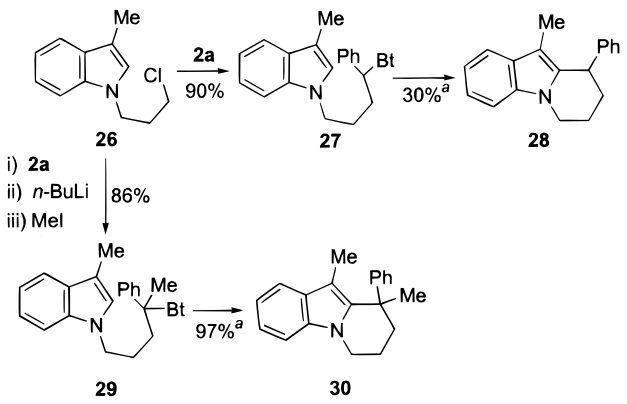
9-Mono- **28** and 9,9-disubstituted 10-methyl-6,7,8,9-tetrahydropyrido[1,2-*a*]indoles **30** were obtained starting from 1-(3-chloropropyl)-3-methyl-1*H*-indole **26** in excellent yields by the six-membered ring annulation of indole. Compound **26** was synthesized from 3-methylindole and 1-bromo-3-chloropropane using a published method for the N-alkylation of indoles.[12] The precursors **27** and **29** were obtained in excellent yields by nucleophilic displacement of chlorine in **26** by **2a** and by in situ alkylation of **27,** respectively (Scheme 5).

Annulation of the indole was accomplished by $ZnBr_2$ in 1,2-dichlorobenzene. Interestingly, the annulation occurs exclusively at the 2-position of indole; no annulation product at the 7-position was observed. The cyclization of **29** to **30** proceeded smoothly and in excellent yield (Table 1). The higher temperature required to cyclize **27** accounts for the moderate yield of **28** isolated.

Conclusion

In conclusion, versatile and general five- and six-membered ring annulations to the benzene, biphenyl, and indole ring systems were developed. These new annulations are the result of the ability of (benzotriazol-1-yl)-methanes to act as 1,1-dipole synthon equivalents. By making use of this new annulation, a series of tetrahydronaphthalenes, tetrahydrochromanes, indanes, 9,10-dihydrophenantrene, and tetrahydropyrido[1,2-*a*]indoles have been synthesized in moderate to excellent yields.

Scheme 5[a]



[a] The reaction conditions for the cyclization are shown in Table 1.

Experimental Section

General Methods. Melting points were determined with a MEL-TEMP capillary melting point apparatus equipped with a Fluke 51 digital thermometer. NMR spectra were taken in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (300 MHz) or solvent as the internal standard for ^{13}C (75 MHz). THF was distilled from sodium/benzophenone under nitrogen immediately prior to use. All reactions with air-sensitive compounds were carried out under an argon atmosphere. Column chromatography was conducted with silica gel (230−400 mesh) or neutral alumina (60−325 mesh), Brockman activity I. Column chromatographic separations were performed, unless otherwise stated, with hexanes and 0.0, 0.5, 1.0, 2.5, 5.0, 7.5, and 10.0% v/v diethyl ether gradient and a flow rate of 20−30 mL/min. 1-Benzyl-1*H*-benzotriazole (**1a**),[3c] 1-(5-methyl-2-thienyl)-1*H*-benzotriazole (**1b**),[3c] 1-(4-*N*,*N*-dimethylaminobenzyl)-1*H*-benzotriazole (**1c**),[4a] and 1-(4-methylbenzyl)-1*H*-benzotriazole (**1d**)[4b] were prepared according to previously reported procedures.

General Procedure for the Synthesis of Intermediates 10a−d, 12, 15, 17, 20a−c, 22, 24, 27, and 29. To a solution of the appropriate **1** (1 mmol) in THF (10 mL) at −78 °C was added *n*-BuLi in hexanes (1.6 M, 1.1 mmol). After 10 min, a solution of the appropriate alkyl halide **9a,b**, **14, 19**, or **21** (1 mmol) dissolved in THF (5 mL) was added. The mixture was stirred at −78 °C for 3 h and then allowed to warm to rt overnight. For the synthesis of **12**, **17**, **24**, and **29**, the mixture was cooled to −78 °C and *n*-BuLi in hexanes (1.6 M, 1 mmol) was added. After 5 min, *n*-butyl iodide (in the case of **12**, **17**, and **24**) or methyl iodide (in the case of **29**) (1 mmol) was added. After 3 h at −78 °C, the mixture was allowed to warm to rt overnight. The solvent was evaporated under reduced pressure, and the residue was treated with water (10 mL) and ethyl ether (10 mL). The aqueous layer was extracted with diethyl ether (3 × 5 mL), and the combined organic layer was dried ($MgSO_4$). The crude product was purified accordingly.

1-[1-(5-Methyl-2-thienyl)-4-phenylbutyl]-1*H*-benzotriazole (10a): recrystallized from hexanes/ethyl acetate, 1:30, light yellow powder; mp 99.2−100.3 °C; ^1H NMR δ 1.47−1.71 (m, 2H), 2.34 (s, 3H), 2.45−2.74 (m, 4H), 6.07 (dd, J = 6.3 and 9.0 Hz, 1H), 6.53 (d, J = 2.4 Hz, 1H), 6.80 (d, J = 3.3 Hz, 1H), 7.06−7.42 (m, 8H), 8.03 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 15.1, 27.9, 34.4, 34.9, 59.2, 109.9, 119.9, 123.7, 124.6, 125.6, 125.8, 127.0, 128.1, 128.2, 132.0, 139.2, 140.3, 141.2, 146.2. Anal. Calcd for $C_{21}H_{21}N_3S$: C, 72.59; H, 6.09; N, 12.09. Found: C, 72.29; H, 6.43; N, 12.09.

1-[3-Phenoxy-1-(5-methylthiophen-2-yl)propyl]-1*H*-benzotriazole (10b): separated by gradient column chromatog-

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raphy on silica gel, light yellow oil; ^{1}H NMR δ 2.38 (s, 3H), 2.95−3.02 (m, 1H), 3.13−3.19 (m, 1H), 3.82−3.89 (m, 1H), 3.96−4.03 (m, 1H), 6.42 (t, J = 7.5 Hz, 1H), 6.56 (d, J = 2.6 Hz, 1H), 6.80 (d, J = 8.0 Hz, 2H), 6.89−6.93 (m, 2H), 7.22 (t, J = 7.6 Hz, 2H), 7.31 (t, J = 7.1 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.50 (d, J = 8.3 Hz, 1H), 8.04 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 15.2, 35.3, 55.6, 63.7, 109.8, 114.5, 120.0, 121.0, 123.9, 124.8, 126.1, 127.2, 129.4, 132.5, 138.8, 140.7, 146.1, 158.3. Anal. Calcd for $C_{20}H_{19}N_3OS$: C, 68.74; H, 5.48; N, 12.02. Found: C, 68.81; H, 5.54; N, 12.39.

***N*-{4-[1-(1*H*-Benzotriazol-1-yl)-3-phenoxypropyl]-phenyl}-*N*,*N*-dimethylamine (10c)**: white microcrystals; mp 106.1−107.2 °C (hexanes/ethyl acetate, 10:1); ^{1}H NMR δ 2.89 (s, 6H), 2.89−2.97 (m, 1H, overlapped), 3.18−3.27 (m, 1H), 3.96 (t, J = 5.6 Hz, 2H), 6.08 (t, J = 7.2 Hz, 1H), 6.63 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.4 Hz, 2H), 6.91 (t, J = 7.2 Hz, 1H), 7.21−7.36 (m, 5H), 7.42 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 34.8, 40.3, 59.6, 64.0, 110.0, 112.3, 114.5, 119.7, 120.8, 123.7, 125.9, 126.9, 127.8, 129.4, 132.9, 146.1, 150.3, 158.5. Anal. Calcd for $C_{23}H_{24}N_4O$: C, 74.17; H, 6.49; N, 15.04. Found: C, 74.23; H, 6.35; N, 15.11.

1-(3-Phenoxy-1-phenylpropyl)-1*H*-benzotriazole (10d): separated by gradient column chromatography on silica gel, light yellow oil; ^{1}H NMR δ 2.91−2.96 (m, 1H), 3.26−3.30 (m, 1H), 3.94−3.99 (m, 2H), 6.16 (dd, J = 6.6 and 8.7 Hz, 1H), 6.83 (d, J = 8.7 Hz, 2H), 6.92 (t, J = 7.2 Hz, 1H), 7.21−7.41 (m, 10H), 8.04 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 35.0, 59.8, 63.9, 109.7, 114.5, 119.9, 121.0, 123.9, 126.8, 127.2, 128.4, 128.9, 129.4, 133.1, 138.8, 146.1, 158.4. Anal. Calcd for $C_{21}H_{19}N_3O$: C, 76.57; H, 5.81; N, 12.76. Found: C, 76.61; H, 6.10; N, 13.10.

1-(1-Butyl-3-phenoxy-1-phenylpropyl)-1*H*-benzotriazole (12): separated by gradient column chromatography on alumina, white solid; mp 105.7−107.7 °C; ^{1}H NMR δ 0.79 (t, J = 6.9 Hz, 3H), 0.70−0.90 (m, 1H, overlapped), 1.12−1.39 (m, 3H), 2.63−2.83 (m, 2H), 3.08−3.26 (m, 2H), 3.54−3.62 (dd, J = 6.9 and 16.5 Hz, 1H), 3.97−4.05 (m, 1H), 6.66 (t, J = 8.3 Hz, 3H), 6.88 (t, J = 7.4 Hz, 1H), 7.10−7.37 (m, 9H), 8.06 (d, J = 8.7 Hz, 1H); ^{13}C NMR δ 13.8, 22.7, 25.4, 36.2, 37.5, 63.2, 69.4, 112.1, 114.2, 120.0, 120.7, 123.6, 126.3, 126.5, 128.0, 128.8, 129.3, 132.1, 142.1, 146.9, 158.3. Anal. Calcd for $C_{25}H_{27}N_3O$: C, 77.89; H, 7.06; N, 10.90. Found: C, 78.17; H, 7.37; N, 11.21.

1-[1-(4-Methylphenyl)-3-phenylpropyl]-1*H*-benzotriazole (15): separated by column chromatography on silica gel with hexanes/ethyl acetate, 4:1, colorless oil; ^{1}H NMR δ 2.29 (s, 3H), 2.58−2.82 (m, 3H), 3.11−3.24 (m, 1H), 5.72 (dd, J = 6.0 and 9.6 Hz, 1H), 7.11 (d, J = 8.9 Hz, 2H), 7.18−7.39 (m, 10H), 8.07 (d, J = 7.8 Hz, 1H); ^{13}C NMR δ 21.0, 32.4, 36.2, 62.3, 109.8, 119.9, 123.8, 126.2, 126.7, 127.0, 128.5, 129.5, 132.8, 136.1, 138.0, 140.4, 146.2. Anal. Calcd for $C_{22}H_{21}N_3$: C, 80.70; H, 6.48; N, 12.84. Found: C, 80.50; H, 6.47; N, 13.04.

3-(1,3-Diphenylheptyl)-1*H*-benzotriazole (17): separated by column chromatography on silica gel with hexanes/ethyl acetate, 4:1, yellow oil; ^{1}H NMR δ 0.82 (t, J = 7.6 Hz, 3H), 0.80−0.84 (m, 1H, overlapped), 1.18−1.32 (m, 3H), 1.98−2.08 (m, 1H), 2.52−2.69 (m, 2H), 2.79−3.02 (m, 3H), 6.69 (d, J = 8.3 Hz, 1H), 7.02 (d, J = 7.4 Hz, 2H), 7.08−7.34 (m, 10H), 8.08 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ 13.8, 22.7, 25.3, 29.8 36.9, 38.9, 70.2, 112.1, 119.9, 123.5, 125.9, 126.3, 127.8, 128.2, 128.3, 128.6, 132.2, 141.1, 142.4, 146.8. Anal. Calcd for $C_{25}H_{27}N_3$: C, 81.26; H, 7.38; N, 11.37. Found: C, 81.03; H, 7.57; N, 11.16.

2-[2-(1*H*-Benzotriazol-1-yl)-2-(5-methyl-2-thienyl)ethyl]biphenyl (20a): white needles, mp 107.8−108.5 °C (hexanes/ethyl acetate, 1:15); ^{1}H NMR δ 2.32 (s, 3H), 3.89−3.96 (m, 2H), 5.88 (dd, J = 6.6 and 8.8 Hz, 1H), 6.44 (d, J = 3.4 Hz, 1H), 6.49 (d, J = 2.6 Hz, 1H), 7.00−7.06 (m, 3H), 7.12−7.17 (m, 2H), 7.24−7.29 (m, 4H), 7.38−7.43 (m, 3H), 7.96 (d, J = 7.5 Hz, 1H); ^{13}C NMR δ 15.1, 39.8, 59.2, 109.5, 119.8, 123.6, 124.6, 125.5, 126.9, 127.0, 127.2, 127.4, 128.5, 129.0, 130.1, 130.4, 132.4, 133.8, 138.9, 140.3, 141.2, 142.0, 145.9. Anal. Calcd for $C_{25}H_{21}N_3S$: C, 75.92; H, 5.35; N, 10.62. Found: C, 75.77; H, 5.38; N, 10.65.

2-[2-(1*H*-Benzotriazol-1-yl)-2-phenylethyl]biphenyl (20b): separated by gradient column chromatography on silica gel, colorless oil; ^{1}H NMR δ 3.86 (dd, J = 6.3 and 14.4 Hz, 1H), 4.09 (dd, J = 9.3 and 14.1 Hz, 1H), 5.61 (dd, J = 6.0 and 9.3 Hz, 1H), 6.89−7.49 (m, 17H), 7.96 (d, J = 6.6 Hz, 1H); ^{13}C NMR δ 39.8, 63.8, 109.8, 120.2, 124.1, 126.9, 127.3, 127.3, 127.7, 127.8, 128.4, 129.0, 129.5, 130.5, 131.2, 133.4, 134.7, 139.3, 141.8, 142.5, 146.2. Anal. Calcd for $C_{26}H_{21}N_3$: C, 83.17; H, 5.64; N, 11.19. Found: C, 83.34; H, 5.50; N, 10.80.

2-[2-(1*H*-Benzotriazol-1-yl)-2-(4-*N*,*N*-dimethylaminophenyl)ethyl]biphenyl (20c): recrystallized from ethyl ether, gray powder, mp 145.0−146.1 °C; ^{1}H NMR δ 2.84 (s, 6H), 3.83 (dd, J = 6.0 and 14.2 Hz, 1H), 4.05 (dd, J = 9.6 and 13.5 Hz, 1H), 5.59 (t, J = 8.8 Hz, 1H), 6.51 (d, J = 8.2 Hz, 2H), 6.88 (d, J = 8.2 Hz, 2H), 7.00−7.54 (m, 12H), 7.94 (d, J = 7.1 Hz, 1H); ^{13}C NMR δ 39.2, 40.3, 63.1, 109.6, 112.1, 119.6, 123.4, 126.4, 126.6, 126.7, 127.1, 127.3, 127.4, 128.4, 129.1, 130.0, 130.7, 132.8, 134.7, 141.5, 142.0, 145.8, 150.1. Anal. Calcd for $C_{28}H_{26}N_4$: C, 80.34; H, 6.27; N, 13.39. Found: C, 80.12; H, 6.51; N, 13.49.

2-[2-(1*H*-Benzotriazol-1-yl)-2-methoxyethyl]biphenyl (22): oil separated by gradient column chromatography on silica gel, light yellow; ^{1}H NMR δ 3.09 (s, 3H), 3.43 (dd, J = 6.9 and 14.1 Hz, 1H), 3.63 (dd, J = 6.6 and 14.1 Hz, 1H), 5.94 (t, J = 6.9 Hz, 1H), 7.15−7.34 (m, 12H), 7.99−8.02 (m, 1H); ^{13}C NMR δ 38.0, 56.6, 92.2, 110.8, 119.9, 124.0, 127.0, 127.1, 127.3, 127.5, 128.2, 129.1, 130.0, 130.2, 131.3, 132.5, 141.0, 142.6, 146.5. Anal. Calcd for $C_{21}H_{19}N_3O$: C, 76.57; H, 5.81; N, 12.76. Found: C, 76.37; H, 5.79; N, 12.57.

2-[2-(1*H*-Benzotriazol-1-yl)-2-*n*-butyl-2-phenylethyl]biphenyl (24): separated by gradient column chromatography on alumina, colorless solid, mp 66.3−69.0 °C; ^{1}H NMR δ −0.01−0.04 (m, 1H), 0.55 (t, J = 7.1 Hz, 3H), 0.55−0.67 (m, 1H, overlapped), 0.89−1.04 (m, 2H), 2.12−2.32 (m, 2H), 4.20 (d, J = 13.5 Hz, 1H), 4.38 (d, J = 13.8 Hz, 1H), 6.09 (d, J = 7.7 Hz, 1H), 6.55 (d, J = 8.2 Hz, 1H), 6.86 (d, J = 7.3 Hz, 2H), 6.87−6.91 (m, 1H, overlapped), 7.04−7.38 (m, 12H), 8.06 (d, J = 8.2 Hz, 1H); ^{13}C NMR δ 13.5, 22.5, 25.2, 36.6, 38.5, 71.4, 112.3, 119.7, 123.3, 126.1, 126.3, 126.5, 126.6, 126.7, 127.5, 128.1, 128.2, 129.4, 130.5, 131.0, 132.3, 132.5, 141.5, 142.0, 143.5, 146.6. Anal. Calcd for $C_{30}H_{29}N_3O$: C, 83.49; H, 6.77; N, 9.74. Found: C, 83.29; H, 6.97; N, 9.66.

1-[4-(3-Methyl-1*H*-indol-1-yl)-1-phenylbutyl]-1*H*-benzotriazole (27): separated by gradient column chromatography on silica gel, light yellow microcrystals, mp 120.9−122.2 °C; ^{1}H NMR δ 1.70−1.75 (m, 2H), 2.25 (s, 3H), 2.31−2.40 (m, 1H), 2.72−2.79 (m, 1H), 3.96 (t, J = 6.8 Hz, 2H), 5.36 (dd, J = 6.3 and 8.9 Hz, 1H), 6.69 (s, 1H), 7.00−7.24 (m, 11H), 7.54 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 8.7 Hz, 1H);^{13}C NMR δ 9.8, 27.2, 32.7, 45.7, 63.2, 109.3, 109.9, 110.6, 118.9, 119.3, 120.0, 121.8, 124.1, 125.5, 126.9, 127.3, 128.5, 129.0, 133.0, 136.4, 139.1, 146.3. Anal. Calcd for $C_{25}H_{24}N_4$: C, 78.92; H, 6.36; N, 14.73. Found: C, 78.85; H, 6.53; N, 14.49.

1-[1-Methyl-4-(3-methyl-1*H*-indol-1-yl)-1-phenylbutyl]-1*H*-benzotriazole (29): separated by gradient column chromatography, light yellow oil; ^{1}H NMR δ 1.35−1.41 (m, 1H), 1.71−1.77 (m, 1H), 1.94 (s, 3H), 2.16 (s, 3H), 2.41−2.51 (m, 1H), 2.56−2.66 (m, 1H), 3.80−3.89 (m, 2H), 6.46 (d, J = 8.5 Hz, 1H), 6.56 (s, 1H), 6.91−7.03 (m, 6H), 7.06−7.16 (m, 4H), 7.42 (d, J = 8.7 Hz, 1H), 7.93 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 9.5, 24.7, 26.7, 37.9, 45.6, 67.2, 108.9, 110.2, 111.9, 118.4, 118.9, 119.8, 121.3, 123.5, 124.9, 125.6, 126.5, 127.8, 128.6, 128.7, 132.0, 136.1, 142.9, 146.8. Anal. Calcd for $C_{26}H_{26}N_4$: C, 79.16; H, 6.64; N, 14.20. Found: C, 79.22; H, 6.94; N, 14.24.

General Procedure for the Synthesis of Compounds 11a−d, 13, 16, 18, 21a−c, 23, 25, 28, and 30. To a solution of the appropriate **10**, **12**, **15**, **17**, **20**, **22**, **24**, **27**, or **29** (1 mmol) in the appropriate solvent (Table 1) (50 mL) was added the appropriate Lewis acid (for the type and amount see Table 1). The mixture was stirred at the temperature indicated (Table 1) until the intermediates were consumed (indicated in Table 1). The solvent was removed under reduced pressure, and the residue was treated with dichloromethane (10 mL) and sodium hydroxide aqueous solution (2 M, 25 mL). The aqueous layer was extracted with dichloromethane (3 × 15 mL) and dried ($MgSO_4$). The crude product was purified accordingly.

1-(5-Methylthiophen-2-yl)-1,2,3,4-tetrahydronaphthalene (11a): separated by column chromatography on silica

gel with hexanes as solvent, colorless oil; ^{1}H NMR δ 1.67−1.71 (m, 1H), 1.81−1.92 (m, 2H), 2.03−2.08 (m, 1H), 2.33 (s, 3H), 2.71−2.78 (m, 2H), 4.21 (t, J = 5.9 Hz, 1H), 6.38 (d, J = 2.7 Hz, 1H), 6.45 (m, 1H), 6.98−7.05 (m, 4H); ^{13}C NMR δ 15.3, 20.4, 29.4, 33.1, 40.5, 124.3, 124.8, 125.5, 126.2, 129.0, 130.0, 136.8, 137.8, 138.7, 148.7. Anal. Calcd for $C_{15}H_{16}S$: C, 78.90; H, 7.06. Found: C, 78.57; H, 7.07.

4-(5-Methylthiophen-2-yl)chromane (11b): separated by column chromatography on alumina with hexanes as solvent, light yellow oil; ^{1}H NMR δ 2.08−2.18 (m, 1H), 2.25−2.40 (m, 1H), 2.42 (s, 3H), 4.20 (t, J = 4.8 Hz, 2H), 4.32 (t, J = 5.4 Hz, 1H), 6.51 (d, J = 3.3 Hz, 1H), 6.55 (s, 1H), 6.81−6.85 (m, 2H), 7.05 (d, J = 7.2 Hz, 1H), 7.13 (t, J = 8.4 Hz, 1H); ^{13}C NMR δ 15.3, 31.7, 36.1, 63.4, 116.9, 120.2, 124.0, 124.5, 125.4, 128.1, 130.5, 138.5, 146.9, 154.5. Anal. Calcd for $C_{14}H_{14}NOS$: C, 73.01; H, 6.13. Found: C, 72.74; H, 6.22.

***N*,*N*-Dimethyl-4-(3,4-dihydro-2*H*-4-chromenyl)-aniline (11c)**: separated by column chromatography on silica gel with hexanes as solvent, light yellow microcrystals; mp 50.8−51.1 °C; ^{1}H NMR δ 1.94−2.10 (m, 1H), 2.13−2.27 (m, 1H), 2.86 (s, 6H), 4.02 (t, J = 6.3 Hz, 1H), 4.10−4.13 (m, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.67−6.82 (m, 3H), 6.93 (d, J = 8.4 Hz, 2H), 7.04 (t, J = 8.8 Hz, 1H); ^{13}C NMR δ 31.8, 40.1, 40.7, 64.0, 112.6, 116.6, 120.2, 127.2, 127.5, 129.2, 130.7, 133.5, 149.3, 155.1. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.93; H, 7.88; N, 5.22.

4-Phenylchromane (11d): separated by column chromatography on alumina with hexanes as solvent, light yellow oil (lit.[13] mp 44 °C); ^{1}H NMR δ 2.02−2.13 (m, 1H), 2.24−2.32 (m, 1H), 4.10−4.18 (m, 3H), 6.75−6.88 (m, 3H), 7.09−7.31 (m, 6H); ^{13}C NMR δ 31.6, 41.0, 63.8, 116.7, 120.3, 124.5, 126.4, 127.8, 128.4, 128.6, 130.6, 145.6, 155.1. Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.79; H, 6.91.

4-(*n*-Butyl)-4-phenylchromane (13): separated by column chromatography on silica gel with hexanes as solvent, colorless oil; ^{1}H NMR δ 0.87 (t, J = 7.2 Hz, 3H), 1.05−1.20 (m, 1H), 1.20−1.40 (m, 3H), 2.02−2.17 (m, 3H), 2.32−2.41 (m, 1H), 3.83 (dt, J = 2.1 and 11.1 Hz, 1H), 4.14 (dt, J = 3.8 and 7.8 Hz, 1H), 6.85−6.92 (m, 2H), 7.07−7.19 (m, 5H), 7.23−7.28 (m, 2H); ^{13}C NMR δ 14.0, 23.4, 26.9, 34.9, 40.6, 43.3, 62.8, 117.1, 120.0, 126.0, 126.5, 127.5, 127.6, 128.1, 129.4, 149.8, 155.4. Anal. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.32. Found: C, 85.78; H, 8.41.

1-(4-Methylphenyl)indane (16): separated by column chromatography on silica gel with hexanes/ethyl acetate, 4:1, colorless oil; ^{1}H NMR δ 1.96−2.09 (m, 1H), 2.32 (s, 3H), 2.49−2.59 (m, 1H), 2.86−3.07 (m, 2H), 4.28 (t, J = 8.3 Hz, 1H), 6.94 (d, J = 7.1 Hz, 1H), 7.00−7.24 (m, 6H), 7.26 (d, J = 7.1 Hz, 1H); ^{13}C NMR δ 21.0, 31.8, 36.6, 51.2, 124.3, 124.9, 126.3, 126.4, 128.0, 129.1, 135.7, 142.4, 144.2, 147.0. Anal. Calcd for $C_{16}H_{16}$: C, 92.25; H, 7.76. Found: C, 92.05; H, 8.07.

1-*n*-Butyl-1-phenylindane (18): separated by column chromatography on silica gel with hexanes/ethyl acetate, 200:1, colorless oil; ^{1}H NMR δ 0.86 (t, J = 7.1 Hz, 3H), 1.14−1.36 (m, 4H), 1.94−2.15 (m, 2H), 2.21−2.30 (m, 1H), 2.36−2.45 (m, 1H), 2.82−2.91 (m, 2H), 7.14−7.26 (m, 9H); ^{13}C NMR δ 14.0, 23.4, 27.3, 30.6, 39.9, 40.7, 56.1, 124.6, 125.1, 125.6, 126.0, 126.5, 126.8, 128.0, 144.1, 147.9, 149.1. Anal. Calcd for $C_{19}H_{22}$: C, 91.13; H, 8.87. Found: C, 91.11; H, 9.24.

9-(5-Methyl-2-thienyl)-9,10-dihydrophenanthrene (21a): separated by column chromatography on silica gel with hexanes as solvent, light yellow oil; ^{1}H NMR δ 2.30 (s, 3H), 3.14 (dd, J = 7.2 and 15.0 Hz, 1H), 3.24 (dd, J = 5.4 and 15.0 Hz, 1H), 4.33 (dd, J = 5.4 and 7.2 Hz, 1H), 6.43 (s, 2H), 7.13−7.31 (m, 6H), 7.73 (t, J = 7.8 Hz, 2H); ^{13}C NMR δ 15.2, 37.1, 40.1, 123.5, 123.8, 124.3, 124.7, 127.2, 127.5, 127.6, 128.1, 128.7, 133.7, 134.0, 135.1, 138.0, 139.3, 144.4. Anal. Calcd for $C_{19}H_{16}S$: C, 82.56; H, 5.83. Found: C, 82.87; H, 6.10.

9-Phenyl-9,10-dihydrophenanthrene (21b): separated by column chromatography on silica gel with hexanes as solvent, white solid, mp 72.4−74.4 °C (lit.[14] mp 84 °C); ^{1}H NMR δ 3.15−3.21 (m, 2H), 4.19 (t, J = 7.6 Hz, 1H), 6.93 (d, J = 7.5 Hz, 1H), 7.09−7.35 (m, 10H), 7.79 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 8.1 Hz, 1H); ^{13}C NMR δ 37.1, 44.8, 123.6, 123.8, 126.5, 127.1, 127.2, 127.6, 128.3, 128.4, 134.4, 134.5, 135.8, 139.8, 143.4. Anal. Calcd for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.47; H, 6.57.

9-(4-*N*,*N*-Dimethylaminophenyl)-9,10-dihydrophenanthrene (21c): separated by column chromatography on silica gel with hexanes/ethyl acetate, 100:1, colorless oil; ^{1}H NMR δ 2.88 (s, 6H), 3.09−3.22 (m, 2H), 4.08 (dd, J = 5.8 and 9.1 Hz, 1H), 6.66 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 7.7 Hz, 1H), 7.04 (d, J = 8.2 Hz, 2H), 7.13−7.21 (m, 3H), 7.28 (t, J = 7.6 Hz, 2H), 7.78 (t, J = 7.4 Hz, 2H); ^{13}C NMR δ 37.1, 40.6, 43.8, 112.7, 123.5, 123.6, 126.9, 127.0, 127.5, 128.3, 128.4, 129.0, 131.2, 134.4, 136.3, 140.7, 149.3. Anal. Calcd for $C_{22}H_{21}N$: C, 88.24; H, 7.08; N, 4.68. Found: C, 88.13; H, 7.41; N, 4.72.

Phenanthrene (23): separated by column chromatography on silica gel with hexanes as solvent; white microcrystals, mp 99.1−100.5 °C (lit.[15] mp 101 °C); ^{1}H NMR δ 7.56−7.67 (m, 4H), 7.73 (s, 2H), 7.88 (d, J = 7.5 Hz, 2H), 8.68 (d, J = 8.4 Hz, 2H); ^{13}C NMR δ 123.1, 127.0, 127.3, 129.0, 130.7, 132.5.

9-*n*-Butyl-9-phenyl-9,10-dihydrophenathrene (25): separated by column chromatography on alumina with hexanes as solvent, colorless oil; ^{1}H NMR δ 0.83 (t, J = 7.1 Hz, 3H), 1.13−1.46 (m, 4H), 1.94−2.00 (m, 2H), 3.04 (d, J = 15.4 Hz, 1H), 3.43 (d, J = 15.4 Hz, 1H), 7.07−7.34 (m, 11H), 7.67 (d, J = 7.1 Hz, 1H), 7.79 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 14.0, 23.3, 27.3, 38.5, 40.9, 46.3, 123.4, 124.3, 125.7, 126.8, 127.2, 127.5, 127.8, 128.4, 134.1, 134.4, 135.7, 142.9, 146.4. Anal. Calcd for $C_{24}H_{24}$: C, 92.26; H, 7.74. Found: C, 92.16; H, 7.89.

10-Methyl-9-phenyl-6,7,8,9-tetrahydropyrido[1,2-*a*]indole (28): separated by column chromatography on alumina with hexanes/ethyl acetate, 200:1 as solvent, white microcrystals that turn yellow on standing in the light, mp 93.7−95.7 °C; ^{1}H NMR δ 1.91 (s, 3H), 1.80−1.95 (m, 1H, overlapped), 1.95−2.07 (m, 1H), 2.18−2.23 (m, 1H), 2.16−2.26 (m, 1H), 3.90−3.99 (m, 1H), 4.16−4.23 (m, 1H), 4.43 (t, J = 5.0 Hz, 1H), 7.06−7.32 (m, 8H), 7.53 (d, J = 7.4 Hz, 1H); ^{13}C NMR δ 8.4, 19.7, 31.0, 39.2, 42.3, 106.5, 108.6, 118.0, 119.0, 120.5, 126.1, 128.0, 128.2, 128.7, 134.0, 135.8, 144.5. Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.04; H, 7.57; N, 5.32.

9,10-Dimethyl-9-phenyl-6,7,8,9-tetrahydropyrido[1,2-*a*]indole (30): separated by column chromatography on alumina with hexanes as solvent, white microcrystals, mp 88.1−89.7 °C; ^{1}H NMR δ 1.84 (s, 3H), 1.91 (s, 3H), 1.87−2.10 (m, 4H, overlapped), 4.08 (t, J = 5.6 Hz, 2H), 7.09−7.30 (m, 8H), 7.51 (d, J = 7.6 Hz, 1H); ^{13}C NMR δ 9.9, 20.1, 27.4, 40.8, 41.2, 42.5, 106.2, 108.6, 117.9, 119.0, 120.6, 125.9, 126.6, 128.1, 128.9, 135.2, 138.7, 148.6. Anal. Calcd for $C_{20}H_{21}N$: C, 87.22; H, 7.69; N, 5.09. Found: C, 86.85; H, 7.94; N, 5.09.

Preparation of 1-(3-chloropropyl)-3-methyl-1*H*-indole (26). A mixture of 3-methylindole (2.66 g, 17 mmol), sodium hydroxide aqueous solution (10%, 10 mL, 30 mmol), 1-bromo-3-chloropropane (1.98 g, 15 mmol), and tetrabutylammonium phosphate (0.17 g, 0.5 mmol) in benzene (10 mL) was heated at reflux for 3 h. The aqueous layer was extracted with benzene (10 mL), and the combined organic layer was washed with hydrochloric acid aqueous solution (10%, 10 mL) and water (10 mL) and then dried (Na_2SO_4). After the solvent was evaporated under reduced pressure, the residue was subjected to column chromatography on silica gel with hexanes (4 drops of pyridine were added for each 200 mL of hexanes to prevent the decomposition of the product). The product was obtained as a colorless oil (2.61 g, 87%) (lit.[8] oil); ^{1}H NMR δ 2.10 (qv, J = 6.2 Hz, 2H), 2.29 (s, 3H), 3.33 (t, J = 6.0 Hz, 2H), 4.14 (t, J = 6.3 Hz, 2H), 6.80 (s, 1H), 7.08 (t, J = 7.4 Hz, 1H), 7.17 (t, J = 7.7 Hz, 1H), 7.25 (d, J = 8.2 Hz, 1H), 7.54 (d, J = 7.7 Hz, 1H); ^{13}C NMR δ 9.5, 32.7, 41.9, 42.4, 109.0, 110.5, 118.7, 119.0, 121.5, 125.5, 128.8, 136.2.

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