Intramolecular Aromatic Nucleophilic Substitution of the Benzimidazole-Activated Nitro Group

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Supporting Information

Table of Contents

1. Experimental Procedures	S-2
1.1. General Methods	S-2
1.2. Synthesis of 2-Aryl-1<i>H</i>-benzimidazoles	S-2
1.3. Epoxide-Ring Opening with 2-Aryl-1<i>H</i>-benzimidazoles.....	S-8
1.4. Synthesis of Diols (20) and (24).....	S-16
1.5. Intramolecular S_NAr Reactions with Monoalcohols	S-22
1.6. Intramolecular S_NAr Reactions with Diols	S-32
1.7. Intermolecular S_NAr Reactions	S-38
2. Selected CSP HPLC Profiles	S-42
3. X-Ray Single-Crystal Data for Benzimidazole (9)	S-48
4. Copies of ¹H and ¹³NMR Spectra	S-67

1. Experimental Procedures

1.1. General Methods

All reactions were performed under anhydrous conditions and an inert atmosphere of argon or nitrogen in the oven-dried glassware with magnetic stirring. Yields refer to chromatographically and spectroscopically (^1H NMR) homogenous materials, unless otherwise indicated. Reagents were used as obtained from commercial sources, or purified according to the guidelines of Perrin and Armarego.¹ Evaporation in vacuo refers to the removal of volatiles on a Büchi rotory evaporator attached to an in-house vacuum system (~20 mm Hg). Flash chromatography was carried out using Merck Kiesegel 60 F₂₅₄ (230-400 mesh) silica gel following the method of Still *et al.*² Only distilled solvents were used as eluents. Thin-layer chromatography (TLC) was performed on Merck DC-Alufolien plates pre-coated with silica gel 60 F₂₅₄, that were visualized either by quenching of ultraviolet fluorescence, or by charring with 5% w/v phosphomolybdic acid in 95% EtOH, 10% w/v ammonium molybdate in 1M H₂SO₄, or 10% KMnO₄ in 1M H₂SO₄. Observed retention factors (R_f) are quoted to the nearest 0.05. All reaction solvents were distilled before use, and stored over activated 4 Å molecular sieves, unless otherwise indicated. Anhydrous CH₂Cl₂ was obtained by refluxing over CaH₂. Anhydrous THF was obtained by distillation, immediately before use, from sodium/benzophenone ketyl under an inert atmosphere of nitrogen. Anhydrous DMF was obtained by distillation under reduced pressure from CaH₂, and stored over 4Å molecular sieves. Petroleum ether refers to the fraction of light petroleum boiling between 40 and 60 °C. High-resolution mass spectrometry (HRMS) measurements are valid to ± 5 ppm. Melting points (mp) are quoted to the nearest 0.5 °C. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA.

1.2. Synthesis of 2-Aryl-1*H*-benzimidazoles

Each of the previously unreported 2-aryl-1*H*-benzimidazoles used in these studies was prepared from an appropriate benzoic acid and 1,2-diaminobenzene derivative. Thus, the benzoic acid was converted to the corresponding acyl chloride by treatment with oxalyl chloride in CH₂Cl₂ in the presence of a catalytic amount of DMF. The crude acyl chloride was used directly to acylate the 1,2-diaminobenzene derivative in CH₂Cl₂ in the presence of Et₃N. The crude *N*-

¹ Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; Pergamon Press: New York, 1988.

² Still, W. C.; Hahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

monoacyl product was subsequently subjected to dehydrocyclization in boiling glacial AcOH in the presence of AcONa to give, after chromatographic purification, the required benzimidazole in high overall yield (>80% in each case). In regards to analytical characterization of these benzimidazoles, it should be mentioned that, due to NH-tautomerism, it was frequently difficult to obtain good quality ^{13}C NMR spectra for these compounds.

4-Methyl-2-(2-nitrophenyl)-1*H*-benzimidazole (**37**)

To a suspension of 2-nitrobenzoic acid **36** (30.0 g, 180 mmol) in CH_2Cl_2 (200 mL) was added $(\text{COCl})_2$ (20 mL, 0.23 mol), followed by two drops of DMF. The resulting mixture was stirred at rt for 17 h, and evaporated in vacuo to give a clear oil. The crude acyl chloride was dissolved in CH_2Cl_2 (100 mL), and added dropwise over 1 h into an ice-cooled solution of 2,3-diaminotoluene³ **35** (21.3 g, 175 mmol) and Et_3N (33 mL, 0.23 mol) in CH_2Cl_2 (1.5 L). After an additional 3 h at 0 °C • rt, the volatiles were removed in vacuo, and the residue was refluxed in glacial AcOH (40 mL) in the presence of AcONa (14.7 g, 175 mmol) for 19 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K_2CO_3 during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo. Purification by flash chromatography (silica gel, CH_2Cl_2 • $\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 6/1) gave the title compound **37** (40.3 g, 91%) as a yellow solid: R_f = 0.55 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp 167.0-167.5 °C ($\text{EtOAc}/\text{petroleum ether}$); ^1H NMR (250 MHz, d_6 - Me_2CO) 2.56 (s, 3H), 7.05 (d, J = 7.0 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.42 (br d, J = 6.5 Hz, 1H), 7.67 (dt, J = 7.5, 2.0 Hz, 1H), 7.73 (dt, J = 7.5, 1.5 Hz, 1H), 7.90 (~dd, J = 7.5, 2.0 Hz, 1H), 7.95 (~dd, J = 7.5, 2.0 Hz, 1H), and 12.2 (br s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_6 -DMSO) 16.48, 17.00, 109.1, 116.6, 121.6, 122.0, 123.0, 123.5, 124.3, 124.7, 124.8, 128.8, 130.7, 131.2, 131.3, 132.5, 132.7, 134.3, 134.5, 143.2, 143.4, 146.7, 147.3, 148.9, and 149.0;⁴ IR (CHCl_3) ν_{max} 1533, 1449, and 1349 cm^{-1} ; MS (ESI) m/z (rel intensity) 254 (100%, MH^+) and 208 (20); HRMS calcd for $\text{C}_{14}\text{H}_{12}\text{N}_3\text{O}_2$ (MH^+) 254.0929,

³ Vanelle, P.; Liegeois, C. T.; Meuche, J.; Maldonado, J.; Crozet, M. P. *Heterocycles* **1997**, *45*, 955-962.

⁴ Most peaks doubled due to the NH-tautomerism.

found 254.0925; Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.50; H, 4.37; N, 16.61.

2-(3-Chloro-2-nitrophenyl)-4-methyl-1H-benzimidazole (39)

To a suspension of 3-chloro-2-nitrobenzoic acid **38** (5.00 g, 24.8 mmol) in CH_2Cl_2 (20 mL) was added $(COCl)_2$ (2.8 mL, 32 mmol), followed by a drop of DMF. After 1 h, the resulting clear solution was evaporated in vacuo to give a white solid. The crude acyl chloride was dissolved in CH_2Cl_2 (50 mL), and added dropwise over 30 min to a solution of 2,3-diaminotoluene³ **35** (2.94 g, 24.1 mmol) and Et_3N (4.5 mL, 32 mmol) in CH_2Cl_2 (250 mL) at 0 °C. After an additional 2 h at 0 °C • rt, the volatiles were removed in vacuo to give a yellow solid. The solid was dissolved in glacial AcOH (50 mL), AcONa (2.03 g, 24.8 mmol) was added, and the mixture was refluxed for 13 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K_2CO_3 during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried ($MgSO_4$), and evaporated in vacuo. Purification by flash chromatography (silica gel, CH_2Cl_2 • $CH_2Cl_2/EtOAc$, 10/1) gave the title compound **39** (6.23 g, 91%) as a light yellow solid: R_f = 0.70 ($CH_2Cl_2/EtOAc$, 9/1); mp 201.5-202.5 °C (Me_2CO); 1H NMR (250 MHz, d_6 - Me_2CO) 2.55 (s, 3H), 7.06 (d, J = 7.0 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.42 (d, J = 7.5 Hz, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.77 (dd, J = 8.0, 2.0 Hz, 1H), 8.07 (dd, J = 7.0, 2.0 Hz, 1H), and 12.0 (br s, 1H); IR (KBr) ν_{max} 1542, 1441, and 1373 cm^{-1} ; MS (ESI) m/z (rel intensity) 288 (100%, MH^+) and 242 (35); HRMS calcd for $C_{14}H_{11}ClN_3O_2$ (MH^+) 288.0540, found 288.0522; Anal. Calcd for $C_{14}H_{10}ClN_3O_2$: C, 58.45; H, 3.50; Cl, 12.32; N, 14.61. Found: C, 58.40; H, 3.44; Cl, 12.43; N, 14.48.

4-Methyl-2-(3-methyl-2-nitrophenyl)-1H-benzimidazole (41)

To a suspension of 3-methyl-2-nitrobenzoic acid **40** (5.00 g, 27.6 mmol) in CH₂Cl₂ (20 mL) was added (COCl)₂ (2.9 mL, 39 mmol), followed by a drop of DMF. After 3 h, the resulting clear solution was evaporated in vacuo to give a white solid. The crude acyl chloride was dissolved in CH₂Cl₂ (50 mL), and added dropwise over 30 min to a solution of 2,3-diaminotoluene³ **35** (3.01 g, 24.6 mmol) and Et₃N (4.6 mL, 33 mmol) in CH₂Cl₂ (300 mL) at 0 °C. After an additional 4 h at 0 °C • rt, the volatiles were removed in vacuo to give a yellow solid. The solid was dissolved in glacial AcOH (50 mL), AcONa (2.26 g, 27.6 mmol) was added, and the mixture was refluxed for 17 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K₂CO₃ during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a crude product as an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ • CH₂Cl₂/EtOAc, 30/1) gave the title compound **41** (5.85 g, 89%) as a white solid: R_f = 0.45 (EtOAc/petroleum ether, 1/1); mp 186.0–187.5 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, *d*₆-DMSO) 2.34 (s, 3H), 2.54 (s, 3H), 7.04 (d, *J* = 7.0 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.42 (br s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), and 7.94 (br s, 1H); IR (CHCl₃) ν_{max} 1537 and 1370 cm⁻¹; MS (ESI) *m/z* (rel intensity) 290 (70%, MNa⁺), 268 (100), and 222 (45); HRMS calcd for C₁₅H₁₃N₃NaO₂ (MNa⁺) 290.0905, found 290.0890; Anal. Calcd for C₁₅H₁₃N₃O₂: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.27; H, 4.86; N, 15.73.

2-(2-Fluorophenyl)-4-methyl-1*H*-benzimidazole (**43**)

To a suspension of 2-fluorobenzoic acid **42** (5.00 g, 35.7 mmol) in CH₂Cl₂ (20 mL) was added (COCl)₂ (4.1 mL, 46 mmol), followed by a drop of DMF. The resulting mixture was stirred at rt for 16 h, and evaporated in vacuo to give a yellow oil. The crude acyl chloride was dissolved in CH₂Cl₂ (50 mL), and added dropwise over 1 h to a solution of 2,3-diaminotoluene³ **35** (4.22 g, 34.6 mmol) and Et₃N (6.3 mL, 45 mmol) in CH₂Cl₂ (250 mL) at 0 °C. After an additional 2 h at 0 °C • rt, the volatiles were removed in vacuo, and the residue was refluxed in glacial AcOH (50 mL) in the presence of AcONa (2.93 g, 35.7 mmol) for 8 h. The reaction

mixture was cooled to rt, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K₂CO₃ during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give an orange foam. Purification by flash chromatography (silica gel, CH₂Cl₂ • CH₂Cl₂/EtOAc, 20/1) gave the title compound **43** (6.80 g, 87%) as a white solid: *R*_f = 0.45 (EtOAc/petroleum ether, 3/1); mp 161.0-161.5 °C (EtOAc/petroleum ether); ¹H NMR (250 MHz, CDCl₃) 2.54 (s, 3H), 6.97 (d, *J* = 7.0 Hz, 1H), 7.03-7.17 (m, 2H), 7.19 (d, *J* = 7.5 Hz, 1H), 7.22-7.46 (m, 2H), 8.40 (dt, *J* = 8.0, 2.0 Hz, 1H), and 9.78 (br s, 1H); IR (CHCl₃) *v*_{max} 1466 cm⁻¹; MS (ESI) *m/z* (rel intensity) 227 (100%, MH⁺); HRMS calcd for C₁₄H₁₂FN₂ (MH⁺) 227.0984, found 227.0987; Anal. Calcd for C₁₄H₁₁FN₂: C, 74.32; H, 4.90; N, 12.38. Found: C, 74.06; H, 4.88; N, 12.36.

2-(2-Chlorophenyl)-4-methyl-1H-benzimidazole (**45**)

To a suspension of 2-chlorobenzoic acid **44** (5.00 g, 31.9 mmol) in CH₂Cl₂ (30 mL) was added (COCl)₂ (3.6 mL, 42 mmol), followed by a drop of DMF. The resulting mixture was stirred at rt for 90 min, and evaporated in vacuo to give a clear oil. The crude acyl chloride was dissolved in CH₂Cl₂ (50 mL), and added dropwise over 40 min to a solution of 2,3-diaminotoluene³ **35** (3.78 g, 30.9 mmol) and Et₃N (5.8 mL, 42 mmol) in CH₂Cl₂ (250 mL) at 0 °C. After an additional 3 h at 0 °C • rt, the volatiles were removed in vacuo to give a pale brown oil. The residue was refluxed in glacial AcOH (50 mL) in the presence of AcONa (2.62 g, 31.9 mmol) for 15 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K₂CO₃ during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a yellow foam. Purification by flash chromatography (silica gel, petroleum ether • petroleum ether/EtOAc, 3/1) gave the title compound **45** (6.80 g, 88%) as a white foam: *R*_f = 0.35 (petroleum ether/EtOAc, 3/1); ¹H NMR (250 MHz, CDCl₃) 2.54 (s, 3H), 6.98 (~d, *J* = 7.0 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.19-7.26 (m, 2H), 7.29-7.38 (m, 2H), 8.11-8.15 (m, 1H), and 9.70 (br s, 1H); IR (CHCl₃) *v*_{max} 1449, 1396, and 1045 cm⁻¹; MS

(ESI) m/z (rel intensity) 265 (30%, MNa^+) and 243(100); HRMS calcd for $\text{C}_{14}\text{H}_{11}\text{ClN}_2\text{Na}$ (MNa^+) 265.0508, found 265.0510.

2-(2-Methoxyphenyl)-1H-benzimidazole (48)

To a solution of 2-methoxybenzoic acid **47** (5.00 g, 32.9 mmol) in CH_2Cl_2 (30 mL) was added $(\text{COCl})_2$ (3.7 mL, 43 mmol), followed by a drop of DMF. After 16 h at rt, the resulting clear solution was evaporated in vacuo to give a pale yellow oil. The crude acyl chloride was dissolved in CH_2Cl_2 (50 mL), and added dropwise over 30 min to an ice-cooled solution of 1,2-diaminobenzene **46** (3.89 g, 31.9 mmol) and Et_3N (6.0 mL, 43 mmol) in CH_2Cl_2 (250 mL). After an additional 3 h at 0 °C • rt, the volatiles were removed in vacuo to give a brown solid. The solid was dissolved in glacial AcOH (50 mL), AcONa (2.7 g, 33 mmol) was added, and the mixture was refluxed for 19 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K_2CO_3 during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a crude product as a yellow solid. Purification by flash chromatography (silica gel, CH_2Cl_2 • $\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 8/1) gave the title compound **48** (7.10 g, 93%) as a white solid: R_f = 0.60 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp 179.5-180.5 °C (EtOAc /petroleum ether) (Lit.⁵ 181 °C); ^1H NMR (250 MHz, CDCl_3) 3.95 (s, 3H), 6.49 (d, J = 8.5 Hz, 1H), 7.03 (dt, J = 7.5, 1.0 Hz, 1H), 7.12-7.20 (m, 2H), 7.30 (ddd, J = 8.5, 7.5, 2.0 Hz, 1H), 7.54 (br s, 2H), 8.49 (dd, J = 8.0, 2.0 Hz, 1H), and 10.6 (br s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (63 MHz, CDCl_3) 55.92, 111.5, 117.9, 121.7, 122.5, 130.2, 131.2, 149.9, and 156.8; IR (CHCl_3) ν_{max} 1472, 1441, 1279, and 1240 cm^{-1} ; MS (ESI) m/z (rel intensity) 225 (100%, MH^+); HRMS calcd for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}$ (MH^+) 225.1028, found 225.1020.

⁵ Nardi, D.; Tajana, A.; Rossi, S. *J. Het. Chem.* **1973**, *10*, 815-819.

2-(3-Chloro-2-nitrophenyl)-1*H*-benzimidazole (**49**)

To a suspension of 3-chloro-2-nitrobenzoic acid **38** (5.00 g, 24.8 mmol) in CH₂Cl₂ (20 mL) was added (COCl)₂ (2.8 mL, 32 mmol), followed by a drop of DMF. After 1 h, the resulting clear solution was evaporated in vacuo to give a white solid. The crude acyl chloride was dissolved in CH₂Cl₂ (50 mL), and added dropwise over 1 h to a solution of 1,2-diaminobenzene **46** (2.60 g, 24.1 mmol) and Et₃N (4.5 mL, 32 mmol) in CH₂Cl₂ (250 mL) at 0 °C. After an additional 2 h at 0 °C → rt, the volatiles were removed in vacuo to give a pale yellow solid. The solid was dissolved in glacial AcOH (50 mL), AcONa (2.03 g, 24.8 mmol) was added, and the mixture was refluxed for 19 h. The reaction mixture was cooled to rt, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The biphasic mixture was cooled in an ice bath, and neutralized with solid K₂CO₃ during vigorous stirring. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a crude product as a creamy solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 2/1) gave the title compound **49** (5.78 g, 88%) as an off-white solid: *R*_f = 0.70 (EtOAc); mp > 260 °C (Me₂CO); ¹H NMR (400 MHz, *d*₆-DMSO) δ 7.22-7.30 (m, 2H), 7.58-7.67 (m, 2H), 7.81 (t, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 8.13 (d, *J* = 7.5 Hz, 1H), and 13.3 (br s, 1H); IR (KBr) ν_{max} 1541, 1450, 1440, 1415, and 1376 cm⁻¹; MS (ESI) *m/z* (rel intensity) 274 (100%, MH⁺); HRMS calcd for C₁₃H₉ClN₃O₂ (MH⁺) 274.0383, found 274.0372; Anal. Calcd for C₁₃H₈ClN₃O₂: C, 57.05; H, 2.95; Cl, 12.95; N, 15.35. Found: C, 56.85; H, 2.86; Cl, 13.13; N, 15.27.

1.3. Epoxide-Ring Opening with 2-Aryl-1*H*-benzimidazoles

The free NH group of 2-aryl-1*H*-benzimidazoles, and in particular 2-(2-nitrophenyl)-1*H*-benzimidazoles, is poorly nucleophilic, so its reaction with epoxides is not very facile. The Cu(OTf)₂-catalyzed reaction used in these studies to prepare the desired alcohols does not usually go to completion. With a few notable exceptions, the levels of conversions are usually low (<50%). In general, 4-substituted 2-aryl-1*H*-benzimidazoles are far better substrates than their unsubstituted counterparts. It presumably stems from a significantly reduced ability, due to steric

reasons, to form Cu(II) complexes by the substrates (and the products derived from them) that are heavily substituted in the vicinity of the benzimidazole nitrogen. For the unsubstituted benzimidazoles, in turn, the catalytic cycle ceases to operate relatively quickly, as an active Cu(II) species gets converted into various unreactive complexes. On a few occasions, we attempted to use stoichiometric amounts of Cu(OTf)₂, but it did not lead to improved yields of the alcohols. As far as epoxide substrates are concerned, it was found that only terminal epoxides are reactive enough, with the 2-monosubstituted derivatives being significantly better substrates than the 2,2-disubstituted ones.

1-[4-Methyl-2-(2-nitrophenyl)benzimidazol-1-yl]propan-2-ol (4**)**

To a solution of benzimidazole **37** (1.27 g, 5.00 mmol) in MeCN (8 mL) were added propylene oxide (2.9 g, 50 mmol) and Cu(OTf)₂ (362 mg, 1.00 mmol). After 22 h at 40 °C, the reaction mixture was cooled to rt and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30 min. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 4/1) gave the recovered starting material **37** (670 mg, 53%) and the title compound **4** (499 mg, 32%) as a pale yellow solid. Alcohol **4**: *R_f* = 0.55 (EtOAc); mp 171.0-172.0 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 1.13 (d, *J* = 6.0 Hz, 3H), 2.66 (s, 4H), 3.95 (dd, *J* = 14.5, 8.5 Hz, 1H), 4.03 (dd, *J* = 14.5, 3.5 Hz, 1H), 4.10-4.20 (m, 1H), 7.15 (d, *J* = 6.5 Hz, 1H), 7.23-7.34 (m, 2H), 7.64 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.68 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.73 (dt, *J* = 7.5, 1.0 Hz, 1H), and 8.16 (dd, *J* = 8.0, 1.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 16.65, 20.63, 52.03, 65.98, 107.8, 123.0, 123.2, 124.9, 126.3, 130.1, 130.9, 132.9, 133.2, 134.6, 142.2, 148.6, and 149.0; IR (CHCl₃) *v*_{max} 1534, 1458, 1397, and 1348 cm⁻¹; MS (ESI) *m/z* (rel intensity) 312 (100%, MH⁺); HRMS calcd for C₁₇H₁₈N₃O₃ (MH⁺) 312.1348, found 312.1328; Anal. Calcd for C₁₇H₁₇N₃O₃: C, 65.58; H, 5.50; N, 13.50. Found: C, 65.49; H, 5.45; N, 13.39.

1-[4-Methyl-2-(2-nitrophenyl)benzimidazol-1-yl]hexan-2-ol (**6**)

To a solution of benzimidazole **37** (1.27 g, 5.00 mmol) in MeCN (8 mL) were added 1,2-epoxyhexane (1.5 g, 15 mmol) and Cu(OTf)₂ (362 mg, 1.00 mmol). After 20 h at reflux, the reaction mixture was cooled to rt and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30 min. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 4/1) gave the recovered starting material **37** (329 mg, 26%) and the title compound **6** (754 mg, 43%) as a yellow solid. Alcohol **6**: R_f = 0.65 (EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 0.87 (t, *J* = 6.5 Hz, 3H), 1.15-1.49 (m, 6H), 2.66 (s, 3H), 3.87-3.96 (m, 2H), 4.07 (dd, *J* = 18.0, 7.0 Hz, 1H), 7.15 (d, *J* = 6.5 Hz, 1H), 7.23-7.33 (m, 2H), 7.60-7.73 (m, 3H), and 8.15 (d, *J* = 7.5 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 14.32, 17.16, 22.89, 27.89, 34.81, 51.49, 70.38, 108.3, 123.5, 123.7, 125.3, 126.7, 130.5, 131.4, 133.5, 133.7, 135.1, 142.6, 149.2, and 149.4; IR (CHCl₃) ν_{max} 2960, 1535, 1458, 1397, 1348, and 1242 cm⁻¹; MS (ESI) *m/z* (rel intensity) 354 (100%, MH⁺) and 254 (15); HRMS calcd for C₂₀H₂₄N₃O₃ (MH⁺) 354.1817, found 354.1830.

3,3-Dimethyl-1-[2-(2-nitrophenyl)benzimidazol-1-yl]butan-2-ol (**8**)

To a suspension of benzimidazole **50**⁶ (2.39 g, 10.0 mmol) in MeCN (40 mL) were added 3,3-dimethyl-1,2-epoxybutane (5.0 g, 50 mmol) and Cu(OTf)₂ (724 mg, 2.00 mmol). After 17 h at reflux, the reaction mixture was cooled to rt and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30 min. The phases were

⁶ Zaika, L. L.; Joullié, M. M. *J. Het. Chem.* **1966**, 3, 289-298.

separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown foam. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 4/1) gave the title compound **8** (603 mg, 18%) as a white solid: *R_f* = 0.70 (EtOAc); mp 191.5-193.0 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 0.90 (s, 9H), 2.58 (br s, 1H), 3.61 (d, *J* = 10.0 Hz, 1H), 3.96 (dd, *J* = 14.5, 10.0 Hz, 1H), 4.24 (d, *J* = 14.5 Hz, 1H), 7.32 (t, *J* = 6.5 Hz, 1H), 7.36 (t, *J* = 7.0 Hz, 1H), 7.62-7.74 (m, 4H), and 8.15 (d, *J* = 8.0 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 25.86, 34.72, 47.56, 77.97, 110.9, 120.5, 122.9, 123.6, 125.1, 126.6, 131.3, 133.4, 133.5, 135.5, 143.4, 149.5, and 150.1; IR (CHCl₃) *v*_{max} 2965, 1534, 1458, 1404, and 1349 cm⁻¹; MS (ESI) *m/z* (rel intensity) 340 (100%, MH⁺) and 240 (10); HRMS calcd for C₁₉H₂₁N₃NaO₃ (MNa⁺) 362.1481, found 362.1473; Anal. Calcd for C₁₉H₂₁N₃O₃: C, 67.24; H, 6.24; N, 12.38. Found: C, 67.14; H, 6.25; N, 12.31.

3,3-Dimethyl-1-[4-methyl-2-(2-nitrophenyl)benzimidazol-1-yl]butan-2-ol (**10**)

To a solution of benzimidazole **37** (2.00 g, 7.91 mmol) and 3,3-dimethyl-1,2-epoxybutane (3.95 g, 39.5 mmol) in MeCN (40 mL) was added Cu(OTf)₂ (573 mg, 1.58 mmol). The reaction mixture was refluxed for 24 h, cooled to rt, and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30 min. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 2/1) gave the recovered starting material **37** (780 mg, 39%) and the title compound **10** (1.39 g, 50%) as a pale yellow solid. Alcohol **10**: *R_f* = 0.70 (EtOAc); mp 203.5-204.5 °C (EtOAc/petroleum ether); ¹H NMR (250 MHz, CDCl₃) δ 0.83 (s, 9H), 2.01 (d, *J* = 4.0 Hz, 1H), 2.61 (s, 3H), 3.56 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.87 (dd, *J* = 14.5, 10.0 Hz, 1H), 4.18 (d, *J* = 14.5 Hz, 1H), 7.07 (d, *J* = 7.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.57-7.72 (m, 3H), and 8.10 (~dd, *J* = 8.0, 1.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 16.69, 25.41, 34.22, 47.17, 77.60, 107.8, 122.9, 123.1,

124.8, 126.5, 130.2, 130.8, 133.0, 133.1, 134.7, 142.4, 148.8, and 149.2; IR (CHCl₃) ν_{max} 2964, 1534, 1458, 1398, and 1348 cm⁻¹; MS (ESI) m/z (rel intensity) 354 (100%, MH⁺) and 254 (10); HRMS calcd for C₂₀H₂₃N₃NaO₃ (MNa⁺) 376.1637, found 376.1644; Anal. Calcd for C₂₀H₂₃N₃O₃: C, 67.97; H, 6.56; N, 11.89. Found: C, 67.97; H, 6.61; N, 11.91.

2-Methyl-1-[4-methyl-2-(2-nitrophenyl)benzimidazol-1-yl]propan-2-ol (14**)**

To a solution of benzimidazole **37** (1.27 g, 5.0 mmol) and 1,2-epoxy-2-methylpropane (1.8 g, 25 mmol) in MeCN (8 mL) was added Cu(OTf)₂ (362 mg, 1.00 mmol) to give a dark-brown suspension. The reaction mixture was refluxed for 24 h, cooled to rt, and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 1 h. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ $\rightarrow$ CH₂Cl₂/EtOAc, 10/1; re-purification: silica gel, CH₂Cl₂/EtOAc, 2/1) gave the recovered starting material **37** (1.08 g, 85%) and the title compound **14** (197 mg, 12%) as a pale yellow solid: R_f = 0.55 (EtOAc); ¹H NMR (400 MHz, CDCl₃) δ 1.12 (s, 6H), 1.98 (s, 1H), 2.64 (s, 3H), 4.08 (s, 2H), 7.09 (d, J = 7.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.31 (d, J = 9.0 Hz, 1H), 7.61 (dd, J = 7.5, 1.0 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.64 (dt, J = 8.0, 1.5 Hz, 1H), 7.72 (dt, J = 7.5, 1.5 Hz, 1H), and 8.12 (dd, J = 8.0, 1.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 16.67, 27.69, 55.07, 71.99, 108.7, 122.9, 123.2, 125.0, 127.1, 130.2, 130.7, 132.8, 133.1, 135.7, 142.3, 148.8, and 149.1; IR (CHCl₃) ν_{max} 1533, 1456, and 1348 cm⁻¹; MS (ESI) m/z (rel intensity) 326 (100%, MH⁺), 308 (20), and 254 (70); HRMS calcd for C₁₈H₁₉N₃NaO₃ (MNa⁺) 348.1324, found 348.1318.

1-[2-(3-Chloro-2-nitrophenyl)-4-methylbenzimidazol-1-yl]-3,3-dimethylbutan-2-ol (16)

To a solution of benzimidazole **39** (2.00 g, 7.04 mmol) and 3,3-dimethyl-1,2-epoxybutane (3.5 g, 35 mmol) in MeCN (50 mL) was added Cu(OTf)₂ (510 mg, 1.41 mmol). The reaction mixture was refluxed for 22 h, cooled to rt, and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30 min. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → EtOAc) gave the recovered starting material **39** (1.31 g, 66%) and the title compound **16** (554 mg, 20%) as a white solid. Alcohol **16**: R_f = 0.70 (CH₂Cl₂/EtOAc, 2/1); mp 235.5-237.0 °C (EtOAc); ¹H NMR (250 MHz, CDCl₃) δ 0.94 (s, 9H), 1.97 (d, *J* = 4.5 Hz, 1H), 2.63 (s, 3H), 3.65 (ddd, *J* = 10.0, 4.5, 1.5 Hz, 1H), 4.05 (dd, *J* = 14.5, 10.0 Hz, 1H), 4.33 (dd, *J* = 14.5, 1.5 Hz, 1H), 7.05-7.28 (m, 3H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), and 7.69 (d, *J* = 7.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, *d*₆-DMSO) δ 16.14, 25.48, 34.41, 46.76, 75.40, 109.1, 122.3, 123.0, 124.6, 125.5, 129.0, 131.3, 131.8, 132.0, 134.9, 141.9, 146.3, and 148.8; IR (CHCl₃) ν_{max} 2965, 1546, 1457, and 1365 cm⁻¹; MS (ESI) *m/z* (rel intensity) 388 (100%, MH⁺) and 288 (10); HRMS calcd for C₂₀H₂₂ClN₃NaO₃ (MNa⁺) 410.1247, found 410.1234.

3,3-Dimethyl-1-[4-methyl-2-(3-methyl-2-nitrophenyl)benzimidazol-1-yl]butan-2-ol (18)

To a solution of benzimidazole **41** (2.00 g, 7.5 mmol) in MeCN (15 mL) were added 3,3-dimethyl-1,2-epoxybutane (3.0 g, 30 mmol) and Cu(OTf)₂ (543 mg, 1.5 mmol) to give a dark-brown solution. After 19 h at reflux, the reaction mixture was cooled to rt and evaporated in vacuo. The residue was partitioned between CH₂Cl₂ and satd NaHCO₃, and stirred at rt for 30

min. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a brown foam. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 4/1) gave the recovered starting material **41** (247 mg, 12%) and the title compound **18** (1.08 g, 39%) as a white solid. Alcohol **18**: $R_f = 0.55$ ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp 216.0-217.5 °C ($\text{EtOAc}/\text{petroleum ether}$); ^1H NMR (400 MHz, d_6 -DMSO) δ 0.86 (s, 9H), 2.40 (s, 3H), 2.51 (s, 3H), 3.59 (dd, $J = 10.5, 5.5$ Hz, 1H), 3.95 (dd, $J = 14.0, 10.5$ Hz, 1H), 4.27 (d, $J = 14.0$ Hz, 1H), 5.12 (d, $J = 5.5$ Hz, 1H), 7.06 (d, $J = 7.0$ Hz, 1H), 7.21 (t, $J = 7.5$ Hz, 1H), 7.44 (d, $J = 8.0$ Hz, 1H), 7.69 (dd, $J = 8.0, 1.0$ Hz, 1H), 7.71 (t, $J = 7.5$ Hz, 1H), and 7.99 (dd, $J = 7.0, 1.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_6 -DMSO) δ 16.18, 17.28, 25.47, 34.37, 46.73, 75.61, 109.1, 122.0, 122.5, 124.0, 128.7, 130.1, 130.4 (2 $\times$ C), 133.0, 134.9, 141.9, 147.9, and 150.8; IR (CHCl_3) ν_{max} 2964, 1535, 1457, and 1365 cm^{-1} ; MS (ESI) m/z (rel intensity) 390 (75%, MNa^+), 368 (100), and 268 (5); HRMS calcd for $\text{C}_{21}\text{H}_{25}\text{N}_3\text{NaO}_3$ (MNa^+) 390.1794, found 390.1805; Anal. Calcd for $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_3$: C, 68.64; H, 6.86; N, 11.44. Found: C, 68.64; H, 6.86; N, 11.30.

1-[2-(2-Fluorophenyl)-4-methylbenzimidazol-1-yl]-3,3-dimethylbutan-2-ol (28**)**

To a solution of benzimidazole **43** (2.00 g, 8.85 mmol) and 3,3-dimethyl-1,2-epoxybutane (4.4 g, 44 mmol) in MeCN (50 mL) was added $\text{Cu}(\text{OTf})_2$ (641 mg, 1.77 mmol). The reaction mixture was refluxed for 16 h, cooled to rt, and evaporated in vacuo. The residue was partitioned between CH_2Cl_2 and satd NaHCO_3 , and stirred at rt for 30 min. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{EtOAc}$) gave the recovered starting material **43** (1.40 g, 70%) and the title compound **28** (298 mg, 10%) as a white solid. Alcohol **28**: $R_f = 0.70$ ($\text{EtOAc}/\text{CH}_2\text{Cl}_2$, 1/1); mp 178.5-179.0 °C ($\text{EtOAc}/\text{petroleum ether}$); ^1H NMR (400 MHz, CDCl_3) δ 0.89 (s, 9H), 1.76 (s, 1H), 2.74 (s, 3H), 3.49 (d, $J = 10.0$ Hz, 1H), 4.06 (dd, $J = 14.5, 10.0$ Hz, 1H), 4.31 (d, $J = 14.5$ Hz, 1H), 7.15 (d, $J = 7.0$ Hz, 1H), 7.19-7.33 (m, 3H), 7.37 (d, $J = 8.0$ Hz,

1H), 7.52 (dd, $J = 13.0, 7.0$ Hz, 1H), and 7.67 (t, $J = 7.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 16.76, 25.29, 34.23, [46.6 (d, $J = 3.0$ Hz)?], 78.31, 108.0, 115.8 (d, $J = 21.5$ Hz), 119.2 (d, $J = 14.5$ Hz), 122.7, 122.9, 124.5 (d, $J = 3.5$ Hz), 130.1, 131.9 (d, $J = 8.0$ Hz), 132.7 (d, $J = 2.0$ Hz), 135.1, 142.3, 148.3, and 160.0 (d, $J = 249$ Hz); IR (CHCl_3) ν_{max} 2964, 1642, 1459, and 1391 cm^{-1} ; MS (ESI) m/z (rel intensity) 327 (100%, MH^+) and 227 (10); HRMS calcd for $\text{C}_{20}\text{H}_{23}\text{FN}_2\text{NaO}$ (MNa^+) 349.1692, found 349.1698; Anal. Calcd for $\text{C}_{20}\text{H}_{23}\text{FN}_2\text{O}$: C, 73.59; H, 7.10; N, 8.58. Found: C, 73.50; H, 7.31; N, 8.64.

1-[2-(2-Chlorophenyl)-4-methylbenzimidazol-1-yl]propan-2-ol (29)

To a solution of benzimidazole **45** (3.00 g, 12.3 mmol) in MeCN (15 mL) were added propylene oxide (3.6 g, 62 mmol) and $\text{Cu}(\text{OTf})_2$ (891 mg, 2.46 mmol) to give a brown suspension. After 20 h at 65 °C, the reaction mixture was cooled to rt and evaporated in vacuo. The residue was partitioned between CH_2Cl_2 and satd NaHCO_3 , and stirred at rt for 40 min. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a light brown foam. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{EtOAc}$) gave the title compound **29** (851 mg, 23%) as a white solid: $R_f = 0.35$ ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp 164.0-165.0 °C (EtOAc /petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 1.02 (d, $J = 6.0$ Hz, 3H), 2.49 (br s, 1H), 2.70 (s, 3H), 3.99 (d, $J = 6.0$ Hz, 2H), 4.06 (heptet, $J = 6.0, 6.0$ Hz, 1H), 7.13 (d, $J = 7.5$ Hz, 1H), 7.24 (t, $J = 7.0$ Hz, 1H), 7.30 (d, $J = 8.0$ Hz, 1H), 7.36 (dt, $J = 7.5, 1.0$ Hz, 1H), 7.44 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.50 (dd, $J = 8.0, 1.0$ Hz, 1H), and 7.53 (dd, $J = 7.5, 1.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 16.76, 20.78, 51.63, 66.20, 108.0, 122.9 (2 $\times$ C), 126.9, 129.6, 130.1, 130.2, 131.2, 132.7, 134.2, 134.6, 142.1, and 150.4; IR (CHCl_3) ν_{max} 1607, 1453, 1391, 1335, and 1241 cm^{-1} ; MS (ESI) m/z (rel intensity) 323 (35%, MNa^+), 301 (100), and 243 (45); HRMS calcd for $\text{C}_{17}\text{H}_{18}\text{ClN}_2\text{O}$ (MNa^+) 301.1107, found 301.1112; Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{ClN}_2\text{O}$: C, 67.88; H, 5.70; Cl, 11.79; N, 9.31. Found: C, 68.02; H, 5.65; Cl, 11.98; N, 9.30.

1.4. Synthesis of Diols (20) and (24)

The diols used in these studies were prepared by the Sharpless asymmetric dihydroxylation reaction (AD) of appropriate *N*-allyl substituted 2-aryl-1*H*-benzimidazoles with commercially available AD-mix- α [containing the (DHQ)₂PHAL ligand]. ¹H NMR analysis of the corresponding Mosher esters revealed that the resulting diols were, in each case, virtually racemic. Presumably, the benzimidazole substrates can act as ligands for osmium and, thus, interfere with the, otherwise highly enantioselective, catalytic cycle.

1-Allyl-2-(2-nitrophenyl)-1*H*-benzimidazole (**51**)

To an ice-cooled suspension of benzimidazole **50**⁶ (3.35 g, 14.0 mmol) in THF (40 mL) was added NaH (60% w/w, 616 mg, 15.4 mmol) portionwise over 5 min. After 10 min at 0 °C, the resulting red solution was treated with allyl bromide (1.6 mL, 18 mmol), and stirred at 0 °C → rt for 16 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a yellow oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 2/1) gave the title compound **51** (3.80 g, 97%) as a pale yellow solid: *R*_f = 0.55 (CH₂Cl₂/EtOAc, 3/1); mp 81.5-83.0 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 4.64 (s, 2H), 5.07 (~d, *J* = 17.0 Hz, 1H), 5.21 (d, *J* = 10.5 Hz, 1H), 5.84-5.94 (m, 1H), 7.28-7.47 (m, 3H), 7.62 (d, *J* = 7.0 Hz, 1H), 7.65-7.88 (m, 3H), and 8.19 (d, *J* = 8.0 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 46.98, 110.4, 117.9, 120.0, 122.4, 123.1, 124.7, 125.9, 131.0, 131.6, 132.5, 133.1, 134.8, 143.0, 148.7, and 149.3; IR (CHCl₃) ν_{max} 1535, 1459, 1401, and 1348 cm⁻¹; MS (ESI) *m/z* (rel intensity) 280 (100%, MH⁺); HRMS calcd for C₁₆H₁₄N₃O₂ (MH⁺) 280.1086, found 280.1092; Anal. Calcd for C₁₆H₁₃N₃O₂: C, 68.81; H, 4.69; N, 15.05. Found: C, 68.74; H, 4.71; N, 15.13.

3-[2-(2-Nitrophenyl)benzimidazol-1-yl]propane-1,2-diol (**20**)

A solution of AD-mix- β (6.2 g) in t BuOH (25 mL) and H_2O (25 mL) was stirred at rt for 1 h. The mixture was cooled in an ice bath, and benzimidazole **51** (1.15 g, 4.12 mmol) was added. After 13 h at $0\text{ }^{\circ}\text{C} \rightarrow \text{rt}$, Na_2SO_3 (4.5 g, 36 mmol) was added, and the reaction mixture was stirred at rt for 1 h. The resulting gray solution was diluted with CH_2Cl_2 and H_2O , and stirred for 5 min. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried ($MgSO_4$), and evaporated in vacuo to give a yellow solid. Purification by flash chromatography (silica gel, EtOAc/ Me_2CO , 10/1) gave the title compound **20** (950 mg, 74%) as a yellow solid: $R_f = 0.15$ (EtOAc); mp $181.5\text{--}183.0\text{ }^{\circ}\text{C}$ (EtOAc); $[\alpha]_D = -0.5$ (c 0.61 in MeOH); 1H NMR (400 MHz, d_6 -DMSO) δ 3.27–3.40 (m, 2H), 3.84–3.90 (m, 1H), 3.96 (dd, $J = 14.5, 8.5$ Hz, 1H), 4.29 (dd, $J = 14.5, 3.0$ Hz, 1H), 4.76 (t, $J = 5.5$ Hz, 1H), 5.11 (d, $J = 5.0$ Hz, 1H), 7.26 (~t, $J = 7.0$ Hz, 1H), 7.33 (dt, $J = 7.0, 1.0$ Hz, 1H), 7.66 (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 1H), 7.83 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.90 (dt, $J = 7.5, 1.0$ Hz, 1H), 7.97 (dd, $J = 7.5, 1.5$ Hz, 1H), and 8.21 (dd, $J = 8.0, 1.0$ Hz, 1H); $^{13}C\{^1H\}$ NMR (63 MHz, d_6 -DMSO) δ 47.78, 63.47, 70.03, 111.5, 119.1, 121.9, 122.5, 124.5, 125.4, 131.2, 133.0, 133.3, 135.4, 142.6, 149.1, and 149.5; IR (KBr) ν_{max} 3073, 1523, 1464, 1446, 1417, and 1349 cm^{-1} ; MS (ESI) m/z (rel intensity) 314 (100%, MH^+); HRMS calcd for $C_{16}H_{16}N_3O_4$ (MH^+) 314.1141, found 314.1146; Anal. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 13.41. Found: C, 61.46; H, 4.84; N, 13.50.

(2*R*,2'*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropionic acid 2-[2-(2-nitrophenyl)benzimidazol-1-yl]-1-(3,3,3-trifluoro-2-methoxy-2-phenylpropionyloxymethyl)ethyl ester (**52**)

To an ice-cooled solution of diol **20** (20.0 mg, 64 μ mol) in CH_2Cl_2 (2 mL) were added (*R*)-MTPA (59.8 mg, 0.26 mmol), DMAP (33 mg, 0.27 mmol), and DCC (158 mg, 0.77 mmol). The reaction mixture was stirred at 0 $^\circ\text{C}$ $\rightarrow$ rt for 40 h, and the resulting white suspension filtered through a plug of cotton. The filtrate was diluted with EtOAc, and washed successively with satd NaHCO_3 , water, and brine. The organic layer was dried (MgSO_4), and evaporated in vacuo to give a pale yellow oil. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 10/1) gave the title compound **52** (44 mg, 92%) as a pale yellow oil: R_f = 0.25 (petroleum ether/EtOAc, 2/1); ^1H NMR (400 MHz, CDCl_3) δ 2.92 (s, 3H), 3.23 (s, 6H), 3.29 (s, 3H), 4.05-4.21 (m, 6H), 4.57 (dd, J = 13.0, 3.0 Hz, 1H), 4.75 (dd, J = 12.5, 2.5 Hz, 1H), 5.49-5.59 (m, 2H), 6.95-7.34 (m, 28H), 7.50-7.77 (m, 6H), and 8.02-8.13 (m, 2H); IR (CHCl_3) ν_{max} 1758 and 1534 cm^{-1} ; MS (ESI) m/z (rel intensity) 768 (90%, MNa^+) and 746 (100); HRMS calcd for $\text{C}_{36}\text{H}_{29}\text{F}_6\text{N}_3\text{NaO}_8$ (MNa^+) 768.1757, found 768.1743.

**1-Allyl-2-(3-chloro-2-nitrophenyl)-4-methylbenzimidazole (53) and
1-allyl-2-(3-chloro-2-nitrophenyl)-7-methylbenzimidazole (54)**

To a yellow solution of benzimidazole **39** (3.00 g, 10.5 mmol) in THF (25 mL) was added NaH (60% w/w, 462 mg, 11.6 mmol) portionwise at 0 $^\circ\text{C}$. After 15 min at rt, the resulting deep-orange solution was treated with allyl bromide (1.2 mL, 13.6 mmol), and stirred at rt for 18 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a yellow solid. Repetitive purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 20/1) gave the title compound **53** (2.39 g, 70%) as a pale yellow solid, and the title compound **54** (618 mg, 18%) as a yellow solid.⁷ Benzimidazole **53**: R_f = 0.55 (EtOAc/petroleum ether, 1/1); mp 124.5-125.5 $^\circ\text{C}$ (EtOAc/petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 2.68 (s, 3H), 4.72-4.73 (m, 2H), 5.05 (d, J = 17.0 Hz, 1H), 5.27 (d, J = 10.0 Hz,

⁷ As the product distribution in *N*-alkylations of unsymmetrical 2-aryl-1*H*-benzimidazoles (e.g., **39**) is usually strongly biased towards a sterically less hindered of the two possible isomers, the major product **53** was assigned the structure as depicted, with the allyl substituent attached to the sterically more accessible benzimidazole nitrogen.

1H), 5.95 (ddt, $J = 17.0, 10.0, 3.5$ Hz, 1H), 7.13 (d, $J = 6.0$ Hz, 1H), 7.21-7.28 (m, 2H), 7.52-7.58 (m, 2H), and 7.67 (~d, $J = 7.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 16.51, 47.10, 108.0, 117.8, 123.2, 123.7, 125.9, 126.5, 129.4, 130.7 ($2 \times \text{C}$), 131.8, 132.1, 134.7, 142.4, 145.8, and 149.5; IR (CHCl_3) ν_{max} 1546, 1455, and 1364 cm^{-1} ; MS (ESI) m/z (rel intensity) 350 (100%, MNa^+) and 328 (50); HRMS calcd for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{NaO}_2$ (MNa^+) 350.0672, found 350.0670; Anal. Calcd for $\text{C}_{13}\text{H}_{14}\text{ClN}_3\text{O}_2$: C, 62.30; H, 4.31; Cl, 10.82; N, 12.82. Found: C, 62.46; H, 4.29; Cl, 10.99; N, 12.86. Benzimidazole **54**: $R_f = 0.50$ (EtOAc/petroleum ether, 1/1); mp 144.0-145.0 °C (EtOAc/petroleum ether); ^1H NMR (400 MHz, CDCl_3) δ 2.64 (s, 3H), 4.75 (~dd, $J = 17.0, 2.0$ Hz, 1H), 4.84-4.86 (m, 2H), 5.22 (~dd, $J = 10.5, 1.5$ Hz, 1H), 5.98 (ddt, $J = 17.0, 10.5, 4.0$ Hz, 1H), 7.03 (d, $J = 7.5$ Hz, 1H), 7.16 (t, $J = 7.5$ Hz, 1H), 7.47-7.52 (m, 2H), and 7.60-7.66 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 17.96, 47.82, 116.7, 118.6, 121.5, 122.9, 125.9, 126.3, 129.3, 130.7, 132.2, 133.7, 134.2, 143.4, 147.4, and 149.5 (one C atom obscured); IR (CHCl_3) ν_{max} 1545, 1454, 1394, and 1363 cm^{-1} ; MS (ESI) m/z (rel intensity) 350 (100%, MNa^+) and 328 (65); HRMS calcd for $\text{C}_{17}\text{H}_{15}\text{ClN}_3\text{O}_2$ (MH^+) 328.0853, found 328.0859; Anal. Calcd for $\text{C}_{17}\text{H}_{14}\text{ClN}_3\text{O}_2$: C, 62.30; H, 4.31; Cl, 10.82; N, 12.82. Found: C, 62.52; H, 4.30; Cl, 10.89; N, 12.90.

3-[2-(3-Chloro-2-nitrophenyl)-4-methyl-benzimidazol-1-yl]propane-1,2-diol (**24**)

A solution of AD-mix- β (5.5 g) in t BuOH (24 mL) and H_2O (24 mL) was stirred at rt for 45 min. The mixture was cooled to 0 °C, and benzimidazole **53** (1.07 g, 3.28 mmol) was added. After 70 h at 0 °C $\rightarrow$ rt, Na_2SO_3 (4.0 g, 32 mmol) was added, and the reaction mixture was stirred at rt for 1 h. The resulting gray suspension was diluted with CH_2Cl_2 and H_2O , and stirred for 5 min. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a white foam. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{EtOAc}$) gave the recovered starting material **53** (116 mg, 11%) and the title compound **24** (1.01 g, 85%) as a yellow solid: $R_f = 0.50$ (EtOAc); mp 165.5-166.5 °C (EtOAc/petroleum ether); ^1H NMR (400

MHz, d_6 -DMSO) δ 2.50 (s, 3H), 3.29-3.41 (m, 2H), 3.82-3.94 (m, 1H), 4.04 (dd, J = 14.5, 9.0 Hz, 1H), 4.35 (dd, J = 14.5, 3.0 Hz, 1H), 4.76 (t, J = 5.5 Hz, 1H), 5.14 (d, J = 5.0 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.82 (t, J = 8.0 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), and 8.11 (d, J = 7.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_6 -DMSO) δ 16.12, 47.85, 63.47, 69.82, 109.1, 122.4, 123.0, 124.6, 125.5, 129.0, 131.0, 132.0 (2 $\times$ C), 135.0, 141.8, 146.2, and 148.7; IR (KBr) ν_{max} 1539, 1459, 1439, and 1364 cm^{-1} ; MS (ESI) m/z (rel intensity) 384 (85%, MNa^+) and 362 (100); HRMS calcd for $\text{C}_{17}\text{H}_{16}\text{ClN}_3\text{NaO}_4$ (MNa^+) 384.0727, found 384.0744; Anal. Calcd for $\text{C}_{17}\text{H}_{16}\text{ClN}_3\text{O}_4$: C, 56.44; H, 4.46; Cl, 9.80; N, 11.61. Found: C, 56.58; H, 4.41; Cl, 9.79; N, 11.65.

(2*R*,2'*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropionic acid 2-[2-(3-chloro-2-nitrophenyl)-4-methylbenzoimidazol-1-yl]-1-(3,3,3-trifluoro-2-methoxy-2-phenylpropionyloxymethyl)-ethyl ester (55**)**

To an ice-cooled solution of diol **24** (15.0 mg, 42 μmol) in CH_2Cl_2 (3 mL) were added (*R*)-MTPA (69 mg, 0.30 mmol), DMAP (38 mg, 0.31 mmol), and DCC (182 mg, 0.88 mmol). The reaction mixture was stirred at 0 $^\circ\text{C}$ $\rightarrow$ rt for 48 h, and the resulting white suspension filtered through a plug of cotton. The filtrate was diluted with EtOAc, and washed successively with satd NaHCO_3 , water, and brine. The organic layer was dried (MgSO_4), and evaporated in vacuo to give a pale yellow oil. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 10/1) gave the title compound **55** (29 mg, 88%) as a clear oil: R_f = 0.25 (petroleum ether/EtOAc, 3/1); ^1H NMR (400 MHz, CDCl_3) δ 2.55 (s, 3H), 2.57 (s, 3H), 2.91 (s, 3H), 3.28 (s, 6H), 3.31 (s, 3H), 4.08-4.27 (m, 6H), 4.57 (dd, J = 13.0, 3.0 Hz, 1H), 4.75 (dd, J = 13.0, 3.0 Hz, 1H), 5.56-5.62 (m, 2H), 7.02-7.39 (m, 30H), and 7.52-7.59 (m, 2H); IR (CHCl_3) ν_{max} 1759, 1545, 1453, 1269, and 1231 cm^{-1} ; MS (ESI) m/z (rel intensity) 816 (90%, MNa^+) and 794 (100); HRMS calcd for $\text{C}_{37}\text{H}_{30}\text{ClF}_6\text{N}_3\text{NaO}_8$ (MNa^+) 816.1523, found 816.1529.

1-Allyl-2-(3-chloro-2-nitrophenyl)-1*H*-benzimidazole (**56**)

To a suspension of benzimidazole **49** (2.00 g, 7.3 mmol) in THF (25 mL) was added NaH (60% w/w, 321 mg, 8.0 mmol) portionwise at 0 °C. After 15 min at rt, the resulting red-brown solution was treated with allyl bromide (821 μ L, 8 mmol), and stirred at rt for 20 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a yellow solid. Purification by flash chromatography (silica gel, CH₂Cl₂ $\rightarrow$ CH₂Cl₂/EtOAc, 20/1) gave the title compound **56** (2.24 g, 98%) as a white solid: *R*_f = 0.45 (EtOAc/petroleum ether, 1/1); mp 148.5-149.5 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 4.69-4.71 (m, 2H), 5.01 (d, *J* = 17.0 Hz, 1H), 5.23 (d, *J* = 10.5 Hz, 1H), 5.92 (ddt, *J* = 17.0, 10.5, 5.0 Hz, 1H), 7.24-7.37 (m, 3H), 7.48 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.64 (dd, *J* = 8.0, 1.5 Hz, 1H), and 7.75-7.79 (m, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 47.04, 110.6, 117.9, 120.6, 122.9, 123.7, 125.6, 126.5, 129.2, 130.8, 131.7, 132.2, 135.1, 142.9, 146.7, and 149.4; IR (CHCl₃) ν_{max} 1546, 1458, 1441, 1393, and 1363 cm⁻¹; MS (ESI) *m/z* (rel intensity) 314 (100%, MH⁺); HRMS calcd for C₁₆H₁₃ClN₃O₂ (MH⁺) 314.0696, found 314.0709; Anal. Calcd for C₁₆H₁₂ClN₃O₂: C, 61.25; H, 3.86; Cl, 11.30; N, 13.39. Found: C, 61.31; H, 3.89; Cl, 11.38; N, 13.35.

3-[2-(3-Chloro-2-nitrophenyl)benzimidazol-1-yl]propane-1,2-diol (**57**)

A solution of AD-mix- β (7.2 g) in ^tBuOH (29 mL) and H₂O (29 mL) was stirred at rt for 1 h. The reaction mixture was cooled in an ice bath, and benzimidazole **56** (1.50 g, 4.78 mmol) was added. After 45 h at 0 °C $\rightarrow$ rt, Na₂SO₃ (5.0 g, 40 mmol) was added, and the reaction mixture was stirred at rt for 1 h. The resulting gray suspension was diluted with CH₂Cl₂ and

H₂O, and stirred for 5 min. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, EtOAc → EtOAc/MeOH, 50/1) gave the recovered starting material **56** (869 mg, 58%) and the title compound **57** (527 mg, 32%). Diol **57**: a white solid: *R*_f = 0.20 (EtOAc); mp 187.5-189.0 °C (EtOAc); [*α*]_D = +0.8 (*c* 0.62 in MeOH); ¹H NMR (400 MHz, *d*₆-DMSO) δ 3.29-3.42 (m, 2H), 3.86-3.95 (m, 1H), 4.09 (dd, *J* = 14.5, 9.0 Hz, 1H), 4.39 (dd, *J* = 14.5, 3.0 Hz, 1H), 4.79 (t, *J* = 5.5 Hz, 1H), 5.18 (d, *J* = 5.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.34 (t, *J* = 7.0 Hz, 1H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.82 (t, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), and 8.14 (d, *J* = 8.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, *d*₆-DMSO) δ 47.78, 63.49, 69.88, 111.7, 119.5, 122.3, 123.1, 124.7, 125.2, 131.0, 132.0, 132.1, 135.5, 142.4, 147.0, and 148.7; IR (KBr) *ν*_{max} 3061, 1528, 1462, 1401, and 1358 cm⁻¹; MS (ESI) *m/z* (rel intensity) 348 (100%, MH⁺); HRMS calcd for C₁₆H₁₅ClN₃O₄ (MH⁺) 348.0751, found 348.0764; Anal. Calcd for C₁₆H₁₄ClN₃O₄: C, 55.26; H, 4.06; Cl, 10.19; N, 12.08. Found: C, 55.28; H, 4.09; Cl, 10.44; N, 12.01.

1.5. Intramolecular S_NAr Reactions with Monoalcohols

(*S*)-(+)-6-*tert*-Butyl-11-[1,3]dioxolan-2-yl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (3)

Method 1 (attempted etherification with 1,8-dibromooctane):

To a solution of alcohol (+)-**1**⁸ (98% ee, 188 mg, 0.46 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 20 mg, 0.5 mmol), and the reaction mixture was stirred at rt for 50 min. 1,8-dibromooctane (42 μL, 0.23 mmol) was added, and the mixture was stirred at rt for 21 h. The reaction mixture was quenched with water, and diluted with EtOAc. The organic phase

⁸ Alcohols **1** and **12** were prepared as part of our studies on the synthesis of optically pure, strapped cyclic bis(benzimidazole) ligands. Results of these studies will be reported in due course.

was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound (+)-**3** (159 mg, 95%) as a white solid. CSP HPLC analysis (Figure S1) revealed it to be of 98% optical purity.

Method 2:

To a solution of alcohol (+)-**1**⁸ (98% ee, 337 mg, 0.82 mmol) in anhydrous DMF (3 mL) was added NaH (60% w/w, 36 mg, 0.9 mmol). After 15 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound (+)-**3** (246 mg, 83%) as a white solid: mp 150.0-152.0 °C (EtOAc/petroleum ether); [α]_D = +147 (*c* 0.90 in CHCl₃).

6,11-Dimethyl-6,7-dihydro-5-oxa-7a,12-diaza-dibenzo[*a,e*]azulene (**5**)

To a solution of alcohol **4** (142 mg, 0.46 mmol) in anhydrous DMF (1 mL) was added NaH (60% w/w, 20 mg, 0.50 mmol). After 14 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **5** (94 mg, 78%) as a white solid: *R*_f = 0.35 (petroleum ether/EtOAc, 9/1); ¹H NMR (250 MHz, CDCl₃) δ 1.44 (d, *J* = 6.5 Hz, 3H), 2.65 (s, 3H), 4.05 (dd, *J* = 14.0, 8.5 Hz, 1H), 4.22 (dd, *J* = 14.0, 2.0 Hz, 1H), 4.43 (ddq, *J* = 8.5, 6.5, 2.0 Hz, 1H), 6.94-7.14 (m, 5H), 7.24 (ddd, *J* = 8.0, 7.5, 2.0 Hz, 1H), and 8.59 (dd, *J* = 8.0, 2.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 19.07, 21.80, 53.85, 78.41, 108.8, 122.4, 123.6, 125.0, 125.3, 125.6, 132.3, 133.5, 133.7, 138.3, 144.6, 151.9, and 158.1; IR (CHCl₃) ν_{max} 1607, 1576, 1473, 1449, 1385, and 1233 cm⁻¹; MS (ESI) *m/z* (rel intensity) 265 (100%, MH⁺); HRMS calcd for C₁₇H₁₆N₂NaO (MNa⁺) 287.1160, found 287.1186.

6-Butyl-11-methyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulene (7)

To a solution of alcohol **6** (664 mg, 1.88 mmol) in anhydrous DMF (62 mL) was added NaH (60% w/w, 83 mg, 2.1 mmol) to give a black solution. After 17 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **7** (432 mg, 75%) as a white solid: *R*_f = 0.45 (petroleum ether/EtOAc, 9/1); ¹H NMR (250 MHz, CDCl₃) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.20-1.91 (m, 6H), 2.67 (s, 3H), 4.03 (dd, *J* = 14.0, 9.0 Hz, 1H), 4.22 (dd, *J* = 14.0, 2.0 Hz, 1H), 6.95-7.14 (m, 5H), 7.24 (ddd, *J* = 8.0, 7.0, 2.0 Hz, 1H), and 8.63 (dd, *J* = 8.0, 2.0 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 14.47, 17.15, 22.92, 28.17, 33.50, 51.21, 80.16, 107.0, 120.7, 121.4, 123.0, 123.3, 123.6, 130.3, 131.5, 131.8, 136.5, 142.7, 149.8, and 156.6; IR (CHCl₃) *v*_{max} 1605, 1576, 1427, 1447, 1376, and 1321 cm⁻¹; MS (ESI) *m/z* (rel intensity) 307 (100%, MH⁺); HRMS calcd for C₂₀H₂₃N₂O (MH⁺) 307.1810, found 307.1798.

6-*tert*-Butyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulene (9)

To a solution of alcohol **8** (100 mg, 0.29 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 12.8 mg, 0.32 mmol) to give a dark-green solution. After 11 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a yellow solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **9** (74 mg, 86%) as a white solid: *R*_f = 0.65 (CH₂Cl₂/EtOAc, 9/1); mp 149.0-150.0 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 1.09 (s, 9H), 3.83 (dd, *J* = 9.5, 1.0 Hz, 1H), 4.19 (dd, *J* = 13.5, 9.5 Hz, 1H), 4.49 (dd, *J* = 13.5, 1.0 Hz, 1H), 7.01 (~d, *J* = 8.0 Hz, 1H),

7.09 (dt, $J = 8.0, 0.5$ Hz, 1H), 7.13-7.29 (m, 4H), 7.74 (dd, $J = 6.5, 2.0$ Hz, 1H), and 8.62 (dd, $J = 8.0, 1.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 26.13, 34.94, 47.54, 86.96, 109.1, 119.5, 119.7, 120.4, 122.6, 122.7, 123.0, 131.3 (2 $\times$ C), 136.5, 142.8, 150.1, and 157.4; IR (KBr) ν_{max} 1611, 1578, 1477, 1441, 1388, 1328, 1308, and 1228 cm^{-1} ; MS (ESI) m/z (rel intensity) 293 (100%, MH^+); HRMS calcd for $\text{C}_{19}\text{H}_{21}\text{N}_2\text{O}$ (MH^+) 293.1654, found 293.1640; Anal. Calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}$: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.70; H, 6.97; N, 9.62.

Single crystals of compound **9** suitable for X-ray analysis were grown by slow evaporation of its CH_2Cl_2 -EtOAc solution (see: Chapter 3, for data).

6-*tert*-Butyl-11-methyl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (11)

To a solution of alcohol **10** (100 mg, 0.28 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 12.5 mg, 0.31 mmol) to give a dark-brown solution. After 13 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO_4), and evaporated in vacuo to give a yellow oil. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 5/1) gave the title compound **11** (83 mg, 96%) as a clear oil that solidified on standing: $R_f = 0.55$ (petroleum ether/EtOAc, 9/1); ^1H NMR (400 MHz, CDCl_3) δ 1.07 (s, 9H), 2.65 (s, 3H), 3.79 (dd, $J = 9.5, 1.0$ Hz, 1H), 4.15 (dd, $J = 13.5, 9.5$ Hz, 1H), 4.45 (dd, $J = 13.5, 1.0$ Hz, 1H), 6.96-7.12 (m, 5H), 7.24 (dt, $J = 7.5, 1.5$ Hz, 1H), and 8.67 (dd, $J = 8.0, 1.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 17.10, 26.58, 35.37, 47.97, 87.53, 107.0, 120.3, 120.8, 123.0, 123.4 (2 $\times$ C), 130.4, 131.5, 131.9, 136.7, 142.7, 149.7, and 157.6; IR (CHCl_3) ν_{max} 2965, 1603, 1576, 1475, 1446, 1373, and 1273 cm^{-1} ; MS (ESI) m/z (rel intensity) 307 (100%, MH^+); HRMS calcd for $\text{C}_{20}\text{H}_{23}\text{N}_2\text{O}$ (MH^+) 307.1810, found 307.1817.

Ethyl 6-*tert*-butyl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene-11-carboxylate (**13**)

To a solution of alcohol **12**⁸ (100 mg, 0.24 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 10.8 mg, 0.27 mmol). After 20 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a clear oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 4/1) gave the title compound **13** (79 mg, 89%) as a clear oil that solidified on standing: *R*_f = 0.55 (petroleum ether/EtOAc, 3/1); ¹H NMR (250 MHz, CDCl₃) δ 1.20 (s, 9H), 1.54 (t, *J* = 7.0 Hz, 3H), 3.91 (~d, *J* = 9.5 Hz, 1H), 4.32 (dd, *J* = 13.5, 9.5 Hz, 1H), 4.56 (q, *J* = 7.0 Hz, 2H), 4.61 (d, *J* = 13.5 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 1H), 7.22 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.28-7.44 (m, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), and 8.89 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 14.92, 26.56, 35.37, 48.29, 61.41, 87.18, 114.0, 119.6, 120.6, 121.7, 122.1, 123.5, 126.0, 132.2, 132.5, 138.3, 142.4, 152.1, 158.0, and 166.7; IR (CHCl₃) ν_{max} 2966, 1708, 1608, 1476, 1427, 1299, and 1256 cm⁻¹; MS (ESI) *m/z* (rel intensity) 365 (100%, MH⁺), 337 (35), and 319 (20); HRMS calcd for C₂₂H₂₄N₂NaO₃ (MNa⁺) 387.1685, found 387.1692.

6-*tert*-Butyl-11-[1,3]dioxolan-2-yl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (**3**)

To a solution of alcohol **1**⁸ (200 mg, 0.49 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 21.6 mg, 0.54 mmol). After 19 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **3** (161 mg, 92%) as a white solid: *R*_f = 0.35 (petroleum ether/EtOAc, 3/1); mp 200.0-201.0 °C

(EtOAc/petroleum ether); ^1H NMR (250 MHz, CDCl_3) δ 1.13 (s, 9H), 3.84 (dd, $J = 9.0, 1.0$ Hz, 1H), 4.05-4.32 (m, 5H), 4.52 (dd, $J = 13.5, 1.0$ Hz, 1H), 6.65 (s, 1H), 7.04 (dd, $J = 8.0, 1.0$ Hz, 1H), 7.12 (dt, $J = 8.0, 1.0$ Hz, 1H), 7.19-7.35 (m, 3H), 7.46 (dd, $J = 6.5, 1.5$ Hz, 1H), and 8.75 (dd, $J = 8.0, 1.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (63 MHz, CDCl_3) δ 26.57, 35.35, 48.01, 66.07 and 66.11 (rotamers?), 87.44, 101.3, 110.4, 120.0, 120.2, 120.7, 122.8, 123.3, 129.1, 131.7, 132.4, 137.4, 141.7, 150.8, and 157.7; IR (CHCl_3) ν_{max} 2965, 1610, 1576, 1475, 1437, and 1076 cm^{-1} ; MS (ESI) m/z (rel intensity) 365 (100%, MH^+) and 321 (15); HRMS calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}_3$ (MH^+) 365.1865, found 365.1870; Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{N}_2\text{O}_3$: C, 72.50; H, 6.64; N, 7.69. Found: C, 72.34; H, 6.68; N, 7.61. The cyclic ether **3** was optically resolved by CSP HPLC (Figure S1).

6,6,11-Trimethyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulene (15)

To a solution of alcohol **14** (100 mg, 0.31 mmol) in anhydrous DMF (1 mL) was added NaH (95% w/w, 8.6 mg, 0.34 mmol) to give a brown solution. After 2 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO_4), and evaporated in vacuo to give a pale brown oil. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 8/1) gave the title compound **15** (58 mg, 68%) as a clear oil: $R_f = 0.40$ (petroleum ether/EtOAc, 3/1); ^1H NMR (400 MHz, CDCl_3) δ 1.48 (s, 6H), 2.79 (s, 3H), 4.05 (s, 2H), 7.09-7.32 (m, 5H), 7.45 (~t, $J = 8.0$ Hz, 1H), and 8.20 (d, $J = 7.5$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (63 MHz, CDCl_3) δ 17.31, 25.64, 52.12, 84.76, 106.5, 123.1 ($2 \times \text{C}^?$), 124.1, 124.2, 124.6, 130.6, 130.8, 131.9, 135.9, 143.0, 151.8, and 153.7; IR (CHCl_3) ν_{max} 1610, 1469, 1455, and 1386 cm^{-1} ; MS (ESI) m/z (rel intensity) 301 (90%, MNa^+) and 279 (100); HRMS calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{O}$ (MH^+) 279.1497, found 279.1494.

6-*tert*-Butyl-4-chloro-11-methyl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (17)

To a solution of alcohol **16** (100 mg, 0.26 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 11.5 mg, 0.29 mmol). After 23 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a white foam. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **17** (70 mg, 80%) as a white solid: *R*_f = 0.55 (petroleum ether/EtOAc, 9/1); mp 191.0-192.0 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 1.24 (s, 9H), 2.74 (s, 3H), 3.98 (d, *J* = 8.5 Hz, 1H), 4.26 (dd, *J* = 14.0, 8.5 Hz, 1H), 4.57 (d, *J* = 14.0 Hz, 1H), 7.05-7.25 (m, 4H), 7.45 (dd, *J* = 7.5, 1.5 Hz, 1H), and 8.68 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 16.90, 26.62, 35.25, 47.15, 88.78, 106.8, 121.2, 123.1 (2 × C), 123.3, 126.0, 130.3, 130.4, 131.9, 136.3, 142.5, 148.8, and 152.3; IR (CHCl₃) ν_{max} 2965, 1468, 1422, and 1369 cm⁻¹; MS (ESI) *m/z* (rel intensity) 341 (100%, MH⁺); HRMS calcd for C₂₀H₂₂ClN₂O (MH⁺) 341.1420, found 341.1407; Anal. Calcd for C₂₀H₂₁ClN₂O: C, 70.48; H, 6.21; Cl, 10.40; N, 8.22. Found: C, 70.43; H, 6.18; Cl, 10.53; N, 8.26.

6-*tert*-Butyl-4,11-dimethyl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (19)

To a solution of alcohol **18** (200 mg, 0.54 mmol) in anhydrous DMF (2 mL) was added NaH (95% w/w, 15.1 mg, 0.6 mmol) to give a deep-violet solution. After 22 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 10/1) gave the title compound **19** (13 mg, 7%) as a white solid: *R*_f = 0.55 (petroleum ether/EtOAc, 9/1); ¹H NMR (400 MHz,

CDCl₃) δ 1.18 (s, 9H), 2.37 (s, 3H), 2.73 (s, 3H), 3.92 (d, J = 7.5 Hz, 1H), 4.22 (dd, J = 14.0, 7.5 Hz, 1H), 4.55 (d, J = 14.0 Hz, 1H), 7.03-7.22 (m, 5H), and 8.55 (d, J = 8.0 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 16.73, 17.36, 26.44, 34.92, 46.64, 87.49, 106.3, 118.4, 122.2, 122.4, 122.9, 129.3, 129.5, 129.9, 132.6, 135.8, 142.2, 150.1, and 154.5; IR (CHCl₃) ν_{max} 2965, 1601, 1475, and 1417 cm⁻¹; MS (ESI) m/z (rel intensity) 321 (100%, MH⁺); HRMS calcd for C₂₁H₂₄N₂NaO (MNa⁺) 343.1786, found 343.1772.

6-*tert*-Butyl-11-methyl-6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulene (11)

To a solution of alcohol **28** (100 mg, 0.31 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 13.5 mg, 0.34 mmol). After 5 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 5/1) gave the title compound **11** (87 mg, 93%) identical (TLC, ¹H NMR) with the product of the nitro-group displacement from alcohol **10** (vide supra).

Attempted Replacement of the Chloro Group in Alcohol (29)

To a solution of alcohol **29** (136 mg, 0.45 mmol) in anhydrous DMF (2 mL) was added NaH (95% w/w, 12.6 mg, 0.50 mmol). After 24 h at rt, the reaction mixture was quenched with water, neutralized with 5% HCl, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo. ¹H NMR analysis of the crude product indicated the presence of the starting material **29**, only. Purification by flash chromatography (silica gel, CH₂Cl₂ → EtOAc) gave the recovered starting material **29** (107 mg, 79%).

(*E/Z*)-2-(4-Methyl-1-propenyl-1*H*-benzimidazol-2-yl)phenol (30**)**

Method 1:

To a solution of alcohol **29** (107 mg, 0.36 mmol) in anhydrous DMF (1 mL) was added NaH (95% w/w, 9.9 mg, 0.4 mmol). After 24 h at 90 °C, the reaction mixture was quenched with water, neutralized with 5% HCl, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a pale brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → EtOAc) gave the title compound **30** (37 mg, 39%, *E/Z* = ~2:1), cyclic ether **5** (~3 mg, ~3%), and recovered starting material **29** (45 mg, 42%). Phenol **30**: a white solid, MS (ESI) *m/z* (rel intensity) 287 (60%, MNa⁺) and 265 (100); HRMS calcd for C₁₇H₁₆N₂NaO (MNa⁺) 287.1160, found 287.1158.

Method 2:

To a solution of the cyclic ether **5** (54 mg, 0.20 mmol) in anhydrous DMF (1 mL) was added NaH (95% w/w, 5.7 mg, 0.2 mmol). After 18 h at 90 °C, the reaction mixture was quenched with water, neutralized with 5% HCl, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → EtOAc) gave the title compound **30** (46 mg, 85%, *E/Z* = ~2:1) as a white solid.

Method 3:

To a solution of alcohol **4** (100 mg, 0.32 mmol) in anhydrous DMF (1 mL) was added NaH (95% w/w, 17.9 mg, 0.7 mmol). After 1 h at rt, followed by 23 h at 90 °C, the reaction mixture was quenched with water, neutralized with 5% HCl, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a brown oil. Purification by flash chromatography (silica gel, CH₂Cl₂) gave the title compound **30** (60 mg, 71%, *E/Z* = ~2.2:1) as a white solid. The two isomeric products were separated by repeated purification by flash chromatography (silica gel, petroleum ether/CH₂Cl₂, 1/1). Phenol (*Z*)-**30**: a white solid: *R_f* = 0.60 (petroleum ether/CH₂Cl₂, 1/1); ¹H NMR (400 MHz, CDCl₃) δ 1.58 (dd, *J* = 7.0, 2.0 Hz, 3H), 2.67 (s, 3H), 6.15 (dq, *J* = 8.0, 7.0 Hz, 1H), 6.83 (dq, *J* = 8.0, 2.0 Hz, 1H), 6.87 (~dt, *J* = 7.5, 1.0 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 7.11 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.12 (~dd, *J* = 7.5, 1.0 Hz, 1H), 7.21 (t, *J* = 8.0 Hz, 1H), 7.32 (ddd, *J* = 8.5, 7.5, 1.5 Hz, 1H), 8.08 (dd, *J* = 8.5, 1.5 Hz, 1H), and 13.7 (br s, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 12.92, 16.54, 108.2, 113.4, 117.9, 118.3, 123.6, 124.6, 126.8, 128.9, 129.3, 131.5, 134.0, 139.4, 149.9, and 159.5 (one C atom obscured); IR (CHCl₃) ν_{max} 1623, 1583, 1484, 1375, 1363, 1271, and 1255 cm⁻¹; MS (ESI) *m/z* (rel intensity) 265 (100%, MH⁺) and 225 (90); HRMS calcd for C₁₇H₁₇N₂O (MH⁺) 265.1341, found 265.1330. Phenol (*E*)-**30**: a white solid: *R_f* = 0.55 (petroleum ether/CH₂Cl₂, 1/1); ¹H NMR (400 MHz, CDCl₃) δ 2.04 (dd, *J* = 7.0, 1.5 Hz, 3H), 2.66 (s, 3H), 6.19 (dq, *J* = 14.0, 7.0 Hz, 1H), 6.80 (~dd, *J* = 14.0, 1.5 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 7.09-7.16 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.34 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), and 13.4 (br s, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 15.36, 16.50, 108.1, 113.3, 117.9, 118.3, 123.5, 123.6, 125.1, 127.3, 127.5, 128.8, 131.4, 134.5, 139.7, 149.7, and 159.3; IR (CHCl₃) ν_{max} 1624, 1584, 1485, 1385, 1373, 1270, and 1256 cm⁻¹; MS (ESI) *m/z* (rel intensity) 265 (100%, MH⁺) and 225 (60); HRMS calcd for C₁₇H₁₇N₂O (MNH⁺) 265.1341, found 265.1323.

1.6. Intramolecular S_NAr Reactions with Diols

(6,7-Dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulen-6-yl)methanol (**22**)

To a solution of diol **20** (1.00 g, 3.19 mmol) in anhydrous DMF (10 mL) was added NaH (60% w/w, 281 mg, 7.0 mmol) to give a dark-brown solution. After 100 min at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 1/1) gave the title compound **22** (818 mg, 96%) as a white solid: *R_f* = 0.65 (EtOAc); mp 142.0-143.5 °C (EtOAc/petroleum ether); [α]_D = -0.7 (*c* 0.88 in CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 3.45 (br s, 1H), 3.98 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.04 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.35 (dd, *J* = 13.0, 8.5 Hz, 1H), 4.39-4.44 (m, 1H), 4.55 (dd, *J* = 13.0, 0.5 Hz, 1H), 7.05 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.20 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.28-7.37 (m, 4H), 7.84-7.86 (m, 1H), and 8.60 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 47.37, 63.15, 80.17, 109.2, 119.3, 119.5, 121.0, 122.9, 123.0, 123.5, 131.2, 131.5, 136.1, 142.5, 150.1, and 155.7; IR (CHCl₃) ν_{max} 2963, 1611, 1576, 1476, 1445, 1387, and 1324 cm⁻¹; MS (ESI) *m/z* (rel intensity) 267 (100%, MH⁺); HRMS calcd for C₁₆H₁₅N₂O₂ (MH⁺) 267.1133, found 267.1122; Anal. Calcd for C₁₆H₁₄N₂O₂: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.00; H, 5.19; N, 10.55. Alcohol **22** was optically resolved by CSP HPLC (Figure S2).

(6,7-Dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulen-6-yl)methanol (**22**) and 6,7-dihydro-5-oxa-7*a*,12-diazadibenzo[*a,e*]azulen-6-ylmethyl acetate (**58**)

To a solution of diol **20** (1.00 g, 3.19 mmol) in anhydrous DMF (10 mL) was added NaH (60% w/w, 281 mg, 7.0 mmol) to give a dark-brown solution. After 2 h at rt, the reaction mixture was diluted with EtOAc, and washed repeatedly with water. The organic layer was dried (MgSO₄), and evaporated in vacuo to give an off-white oil. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 1/1) gave the title compound **58** (301 mg, 31%) as a white semi-solid, and alcohol **22** (588 mg, 69%) as a white solid. Ester **58**: *R*_f = 0.75 (CH₂Cl₂/EtOAc, 2/1); ¹H NMR (250 MHz, CDCl₃) δ 1.97 (s, 3H), 4.12 (dd, *J* = 14.0, 8.5 Hz, 1H), 4.20 (dd, *J* = 11.0, 5.0 Hz, 1H), 4.29 (dd, *J* = 14.0, 2.0 Hz, 1H), 4.35 (dd, *J* = 11.5, 5.0 Hz, 1H), 4.41 (dddd, *J* = 8.5, 5.0, 5.0, 2.0 Hz, 1H), 6.95 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.05 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.10-7.26 (m, 4H), 7.65-7.69 (m, 1H), and 8.44 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 20.57, 47.23, 63.76, 77.42, 108.9, 119.5 (2 × C), 121.0, 122.7, 122.8, 123.6, 131.0, 131.4, 135.9, 142.4, 149.8, 155.3, and 170.3; IR (CHCl₃) *v*_{max} 1744, 1475, and 1445 cm⁻¹; MS (ESI) *m/z* (rel intensity) 309 (100%, MH⁺); HRMS calcd for C₁₈H₁₆N₂NaO₃ (MNa⁺) 331.1059, found 331.1064. Acetate **58** was optically resolved by CSP HPLC (Figure S5).

(6,7-Dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulen-6-yl)methanol (22**)**

To a solution of ester **58** (128 mg, 0.42 mmol) in THF (4 mL) was added 1M LiOH (1.3 mL, 1.3 mmol). The reaction mixture was stirred at rt for 17 h, and partitioned between CH₂Cl₂ and water. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo to give a white solid. Purification by flash chromatography (silica gel, CH₂Cl₂/EtOAc, 1/1) gave the title compound **22** (104 mg, 95%), identical (TLC, ¹H NMR) with the product obtained from the cyclization of diol **20**.

6,7-Dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulen-6-ylmethyl toluene-4-sulfonate (59**)**

To an ice-cooled solution of alcohol **22** (266 mg, 1.00 mmol) in anhydrous pyridine (1 mL) was added TsCl (238 mg, 1.25 mmol). After 14 h at 0 °C → rt, the reaction mixture was partitioned between CH₂Cl₂ and water, and neutralized with 1M HCl. The phases were separated and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄) and evaporated in vacuo to give a white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 2/1) gave the title compound **59** (397 mg, 95%) as a white solid: *R*_f = 0.25 (petroleum ether/EtOAc, 2/1); mp 165.5-166.5 °C (EtOAc/petroleum ether); ¹H NMR (400 MHz, CDCl₃) δ 2.46 (s, 3H), 4.27 (dd, *J* = 10.5, 6.0 Hz, 1H), 4.31 (dd, *J* = 14.0, 8.0 Hz, 1H), 4.41 (dd, *J* = 10.5, 5.0 Hz, 1H), 4.47 (dd, *J* = 14.0, 2.0 Hz, 1H), 4.61 (dddd, *J* = 8.0, 6.0, 5.0, 2.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.21 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.28-7.38 (m, 6H), 7.80-7.82 (m, 1H), 7.81 (d, *J* = 8.0 Hz, 2H), and 8.52 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 21.62, 46.43, 68.33, 77.20, 109.0, 119.7 (2 × C), 121.2, 122.8, 123.0, 123.9, 127.9, 130.0, 131.1, 131.5, 132.2, 135.9, 142.7, 145.4, 149.9, and 154.6; IR (CHCl₃) *v*_{max} 1611, 1599, 1577, 1475, 1446, 1371, and 1191 cm⁻¹; MS (ESI) *m/z* (rel intensity) 421 (100%, MH⁺); HRMS calcd for C₂₃H₂₀N₂NaO₄S (MNa⁺) 443.1041, found 443.1046; Anal. Calcd for C₂₃H₂₀N₂O₄S: C, 65.70; H, 4.79; N, 6.66; S, 7.63. Found: C, 65.71; H, 4.79; N, 6.65; S, 7.55.

6-Methyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulene (23**)**

To an ice-cooled solution of tosylate **59** (100 mg, 0.24 mmol) in THF (2 mL) was added LiAlH₄ (76 mg, 2.0 mmol). After 1.5 h at 0 °C → rt, the reaction mixture was re-cooled in an ice bath, and quenched by a slow addition of water (80 μL), 15% NaOH (240 μL), and water (240 μL). The resulting thick suspension was diluted with CH₂Cl₂, and filtered through a thin pad of

Celite[®]. The filtrate was evaporated in vacuo to give a clear oil. Purification by flash chromatography (silica gel, petroleum ether/EtOAc, 2/1) gave the title compound **23** (47 mg, 79%) as a white solid: R_f = 0.25 (petroleum ether/EtOAc, 2/1); ^1H NMR (250 MHz, CDCl_3) 1.46 (d, J = 6.5 Hz, 3H), 4.09 (dd, J = 14.0, 8.5 Hz, 1H), 4.27 (dd, J = 14.0, 2.0 Hz, 1H), 4.43 (ddq, J = 8.5, 6.5, 2.0 Hz, 1H), 6.96 (dd, J = 8.0, 1.0 Hz, 1H), 7.06 (dt, J = 8.0, 1.5 Hz, 1H), 7.12-7.26 (m, 4H), 7.69-7.73 (m, 1H), and 8.53 (dd, J = 8.0, 1.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (63 MHz, CDCl_3) δ 19.39, 51.52, 75.84, 109.0, 119.5, 119.6, 121.2, 122.7 (2 $\times$ C?), 123.1, 131.2, 131.3, 136.2, 142.7, 150.3, and 155.9; IR (CHCl_3) ν_{max} 1609, 1576, 1476, 1449, 1385, 1325, and 1227 cm^{-1} ; MS (ESI) m/z (rel intensity) 251 (100%, MH^+); HRMS calcd for $\text{C}_{16}\text{H}_{15}\text{N}_2\text{O}$ (MH^+) 251.1184, found 251.1192.

(4-Chloro-11-methyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulen-6-yl)methanol (25)
and cyclic ether (26)

To a solution of diol **24** (642 mg, 1.78 mmol) in anhydrous DMF (4 mL) was added NaH (95% w/w, 95 mg, 3.9 mmol) to give a yellow solution. After 1 h at rt, the reaction mixture was quenched with water, and diluted with CH_2Cl_2 . The organic phase was washed repeatedly with water, dried (MgSO_4), and evaporated in vacuo to give a white solid. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 1/1) gave the title compounds **25** (389 mg, 70%) and **26** (45 mg, 8%) as white solids. Benzimidazole **25**: R_f = 0.70 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp 186.5-188.0 $^\circ\text{C}$ (EtOAc /petroleum ether); ^1H NMR (400 MHz, d_6 -DMSO) δ 2.61 (s, 3H), 3.78⁹ (ddd, J = 11.5, 6.0, 5.5 Hz, 1H), 3.88⁹ (ddd, J = 11.5, 5.5, 5.0 Hz, 1H), 4.44 (dd, J = 14.5, 8.0 Hz, 1H), 4.56 (dddd, J = 8.0, 6.0, 5.0, 2.0 Hz, 1H), 4.69 (dd, J = 14.5, 2.0 Hz, 1H), 5.23 [t, J = 5.5 Hz, 1H (D_2O exchangeable)], 7.19 (d, J = 8.0 Hz, 1H), 7.20 (t, J = 8.0 Hz, 1H), 7.23 (t, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 1H), 7.61 (dd, J = 8.0, 1.5 Hz, 1H), and 8.44 (dd, J = 8.0, 1.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_6 -DMSO) δ 16.33, 46.68, 61.52, 82.11, 107.7, 122.3, 122.6, 122.7, 123.7, 125.5, 128.7, 129.5, 131.3, 135.9, 141.5, 148.0, and 151.0; IR (KBr) ν_{max}

⁹ In the presence of D_2O , the splitting pattern for the signals at 3.78 and 3.88 ppm changed from 'ddd' to 'dd'.

1472, 1459, and 1246 cm^{-1} ; MS (ESI) m/z (rel intensity) 337 (30%, MNa^+) and 315 (100); HRMS calcd for $\text{C}_{17}\text{H}_{16}\text{ClN}_2\text{O}_2$ (MH^+) 315.0900, found 315.0903; Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}_2$: C, 64.87; H, 4.80; Cl, 11.26; N, 8.90. Found: C, 64.90; H, 4.83; Cl, 11.22; N, 8.84. Benzimidazole **26**: R_f = 0.60 ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1); mp >260 °C (EtOAc /petroleum ether); ^1H NMR (400 MHz, d_6 -DMSO) δ 2.58 (s, 3H), 3.98-4.04 (m, 2H), 4.23 (d, J = 3.5 Hz, 1H), 4.29 and 4.30 (ABq, J = 14.5 Hz, 2H), 5.49 [(d, J = 4.0 Hz, 1H (D_2O exchangeable)], 7.06 (d, J = 7.4 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.30 (t, J = 8.0 Hz, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.71 (dd, J = 7.5, 1.5 Hz, 1H), and 7.72 (dd, J = 8.0, 1.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_6 -DMSO) δ 16.35, 47.36, 65.56, 75.70, 108.3, 122.0, 122.5, 124.2, 124.7, 126.3, 128.6, 130.9, 132.1, 136.2, 141.8, 149.5, and 153.5; IR (KBr) ν_{max} 1597, 1471, 1454, 1432, 1397, 1265, 1068, and 994 cm^{-1} ; MS (ESI) m/z (rel intensity) 337 (45%, MNa^+) and 315 (100); HRMS calcd for $\text{C}_{17}\text{H}_{16}\text{ClN}_2\text{O}_2$ (MH^+) 315.0900, found 315.0890; Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{ClN}_2\text{O}_2$: C, 64.87; H, 4.80; Cl, 11.26; N, 8.90. Found: C, 64.44; H, 4.82; Cl, 11.32; N, 8.80. Alcohols **25** and **26** were optically resolved by CSP HPLC (Figures S3 and S4, respectively).

4-Chloro-11-methyl-6,7-dihydro-5-oxa-7a,12-diazadibenzo[*a,e*]azulen-6-ylmethyl toluene-4-sulfonate (**60**)

To an ice-cooled suspension of alcohol **25** (314 mg, 1.00 mmol) in anhydrous pyridine (2 mL) was added TsCl (238 mg, 1.25 mmol). After 17 h at 0 °C $\rightarrow$ rt, the reaction mixture was partitioned between CH_2Cl_2 and water, and neutralized with 1M HCl. The phases were separated and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4) and evaporated in vacuo to give a white solid. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 5/1) gave the title compound **60** (441 mg, 94%) as a white solid: R_f = 0.50 (petroleum ether/ EtOAc , 2/1); mp 168.0-169.0 °C (EtOAc /petroleum ether); ^1H NMR (250 MHz, CDCl_3) δ 2.32 (s, 3H), 2.58 (s, 3H), 4.12-4.36 (m, 4H), 4.52-4.60 (m, 1H), 6.97-7.14 (m, 4H), 7.22 (d, J = 8.0 Hz, 1H), 7.31 (dd, J = 8.0, 1.5 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), and 8.25 (dd, J = 8.0, 1.5 Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (63 MHz,

CDCl₃) δ 17.05, 22.09, 46.41, 68.60, 79.05, 107.1, 123.6, 123.7, 123.8, 125.0, 127.1, 128.5, 130.1, 130.5, 130.7, 132.1, 132.6, 136.1, 142.6, 145.9, 148.8, and 150.6; IR (CHCl₃) ν_{max} 1469, 1450, 1432, 1373, 1228, and 1190 cm⁻¹; MS (ESI) m/z (rel intensity) 491 (60%, MNa⁺) and 469 (100); HRMS calcd for C₂₄H₂₁ClN₂NaO₄S (MNa⁺) 391.0808, found 391.0803; Anal. Calcd for C₂₄H₂₁ClN₂O₄S: C, 61.47; H, 4.51; Cl, 7.56; N, 5.97; S, 6.84. Found: C, 61.61; H, 4.49; Cl, 7.69; N, 5.93; S, 6.78.

8-(1-Chlorovinyl)-1,6,9-trimethyl-5,6-dihydro-7-oxa-4b,10-diazabenz[a]azulene (27)

To an ice-cooled solution of tosylate **60** (100 mg, 0.21 mmol) in THF (2 mL) was added LiAlH₄ (40 mg, 1.1 mmol). After 3 h at 0 °C → rt, the reaction mixture was re-cooled to 0 °C, and quenched by a slow addition of water (40 μ L), 15% NaOH (120 μ L), and water (40 μ L). The resulting thick suspension was diluted with CH₂Cl₂, and filtered through a thin pad of Celite[®]. The filtrate was evaporated in vacuo to give a clear oil. Purification by flash chromatography (silica gel, petroleum ether/CH₂Cl₂, 1/1) gave the title compound **27** (59 mg, 93%) as a white solid: ¹H NMR (400 MHz, CDCl₃) 1.67 (dt, J = 6.5, 1.5 Hz, 3H), 2.75 (s, 3H), 4.25 (ddt, J = 14.0, 8.5, 1.5 Hz, 1H), 4.38 (~d, J = 14.0 Hz, 1H), 4.66 (m, 1H), 7.11-7.28 (m, 4H), 7.48 (~dd, J = 8.0, 1.5 Hz, 1H), and 8.55 (dd, J = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 16.61, 19.36, 51.12, 77.61, 106.5, 122.8, 123.0, 123.1, 123.7, 126.5, 129.7, 130.1, 131.4, 135.8, 142.0, 148.6, and 151.4; IR (CHCl₃) ν_{max} 1470, 1452, 1431, 1422, and 1385 cm⁻¹; MS (ESI) m/z (rel intensity) 321 (55%, MNa⁺) and 299 (100); HRMS calcd for C₁₇H₁₆ClN₂O (MH⁺) 299.0951, found 299.0930.

(4-Chloro-6,7-dihydro-5-oxa-7a,12-diazadibenzo[a,e]azulen-6-yl)methanol (61)

To a solution of diol **57** (100 mg, 0.29 mmol) in anhydrous DMF (2 mL) was added NaH (60% w/w, 25.3 mg, 0.63 mmol). After 21 h at rt, the reaction mixture was quenched with water, and diluted with EtOAc. The organic phase was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give an off-white solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 1/1) gave the title compound **61** (70 mg, 81%) as a white solid: *R_f* = 0.75 (EtOAc); ¹H NMR (400 MHz, *d*₆-DMSO) δ 3.83 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.92 (dd, *J* = 11.0, 5.0 Hz, 1H), 4.52 (dd, *J* = 14.5, 8.5 Hz, 1H), 4.64 (dddd, *J* = 8.5, 5.5, 5.0, 2.0 Hz, 1H), 4.77 (dd, *J* = 14.5, 2.0 Hz, 1H), 5.27 (br s, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.33 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.37 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.63-7.69 (m, 2H), 7.77 (~d, *J* = 7.0 Hz, 1H), and 8.46 (dd, *J* = 8.0, 1.5 Hz, 1H); ¹³C{¹H} NMR (101 MHz, *d*₆-DMSO) δ 46.63, 61.53, 82.10, 110.4, 119.1, 122.1, 122.5, 122.8, 123.7, 125.6, 129.5, 131.5, 136.2, 142.1, 148.9, and 151.2; IR (KBr) *v*_{max} 1474, 1455, 1427, 1259, 1247, 1099, and 1058 cm⁻¹; MS (ESI) *m/z* (rel intensity) 301 (100%, MH⁺); HRMS calcd for C₁₆H₁₄ClN₂O₂ (MH⁺) 301.0744, found 301.0728. Alcohol **61** was optically resolved by CSP HPLC (Figure S6).

1.7. Intermolecular S_NAr Reactions

1-Methyl-2-(2-nitrophenyl)-1*H*-benzimidazole (**31**)

To an ice-cooled suspension of benzimidazole **50**⁶ (2.00 g, 8.37 mmol) in THF (15 mL) was added NaH (60% w/w, 368 mg, 9.2 mmol) portionwise over 5 min. After 10 min at 0 °C, the resulting red solution was treated with MeI (1.3 mL, 21 mmol), and stirred at 0 °C → rt for 16 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH₂Cl₂ and water. The phases were separated, and the extraction was completed with additional portions of CH₂Cl₂. The combined organic extracts were dried (MgSO₄), and evaporated in vacuo. Purification by flash chromatography (silica gel, EtOAc/petroleum ether, 1/1) gave the title compound **31** (1.52 g, 72%) as a yellow solid: *R_f* = 0.60 (EtOAc); mp 132.5-133.5 °C (EtOAc/petroleum ether) (Lit.¹⁰ 135-137 °C); ¹H NMR (400 MHz, CDCl₃) δ 3.60 (s, 3H), 7.32

¹⁰ Hawkins, D.; Lindley, J. M.; McRobbie, I. M.; Meth-Cohn, O. *J. Chem. Soc., Perkin Trans. 1*, **1980**, 2387-2391.

(dt, $J = 7.5, 1.5$ Hz, 1H), 7.36 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.41 (dd, $J = 7.0, 1.5$ Hz, 1H), 7.64 (dd, $J = 8.0, 1.5$ Hz, 1H), 7.68 (dt, $J = 8.0, 1.5$ Hz, 1H), 7.75 (dt, $J = 7.5, 1.0$ Hz, 1H), 7.81 (dd, $J = 7.0, 1.5$ Hz, 1H), and 8.18 (dd, $J = 8.0, 1.0$ Hz, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 30.39, 109.5, 119.8, 122.3, 123.0, 124.6, 125.8, 130.9, 132.6, 133.4, 135.5, 142.7, 148.5, and 149.6; IR (CHCl_3) ν_{max} 1534, 1462, 1438, 1394, and 1348 cm^{-1} ; MS (ESI) m/z (rel intensity) 254 (100%, MH^+) and 207 (25); HRMS calcd for $\text{C}_{14}\text{H}_{12}\text{N}_3\text{O}_2$ (MH^+) 254.0909, found 254.0906; Anal. Calcd for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.69; H, 4.40; N, 16.72.

**2-(2-Methoxyphenyl)-1-methyl-1H-benzimidazole (32) and
2-(2-methoxyphenyl)-1,3-dimethyl-3H-benzimidazol-1-ium iodide (62)**

To a solution of benzimidazole **48** (1.00 g, 4.20 mmol) in THF (20 mL) was added NaH (60% w/w, 185 mg, 4.6 mmol) portionwise at 0 °C. After 15 min at rt, the resulting red solution was treated with MeI (314 μL , 5.0 mmol), and stirred at rt for 18 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo to give a white solid. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 20/1) gave the title compound **32** (600 mg, 57%) as a clear oil that solidified on standing: $R_f = 0.65$ (EtOAc); ^1H NMR (400 MHz, CDCl_3) δ 3.61 (s, 3H), 3.76 (s, 3H), 6.99 (d, $J = 8.5$ Hz, 1H), 7.07 (dt, $J = 7.5, 0.5$ Hz, 1H), 7.22-7.30 (m, 2H), 7.32-7.38 (m, 1H), 7.46 (dt, $J = 8.5, 1.5$ Hz, 1H), 7.56 (dd, $J = 7.5, 1.5$ Hz, 1H), and 7.77-7.82 (m, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, CDCl_3) δ 31.28, 55.97, 109.9, 111.5, 120.1, 120.2, 121.4, 122.3, 122.8, 132.0, 132.8, 136.5, 143.6, 152.6, and 158.0; IR (CHCl_3) ν_{max} 1609, 1477, 1463, 1439, 1388, and 1254 cm^{-1} ; MS (ESI) m/z (rel intensity) 239 (100%, MH^+); HRMS calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}$ (MH^+) 239.1184, found 239.1161.

When an analogous reaction was performed with an excess of MeI (2.5 equiv.), only a small amount (~10%) of benzimidazole **32** was isolated. Instead, the benzimidazolium salt **62** was obtained as the major product (77%). Salt **62**: a white solid: mp >260 °C (EtOAc); ^1H NMR (250 MHz, d_4 -MeOH) δ 3.81 (s, 6H), 3.84 (s, 3H), 7.23 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.33 (d, $J = 8.5$

Hz, 1H), 7.60-7.69 (m, 3H), 7.75 (ddd, $J = 8.5, 7.5, 1.5$ Hz, 1H), and 7.86-7.92 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (101 MHz, d_4 -MeOH) δ 33.32, 56.98, 110.4, 113.8, 114.2, 122.7, 128.2, 133.1, 133.5, 136.9, 150.2, and 159.6; IR (KBr) ν_{max} 1603, 1582, 1516, 1487, 1470, 1446, 1435, and 1259 cm^{-1} ; MS (ESI) m/z (rel intensity) 253 (100%, M^+H^+), 237 (80), and 221 (7); HRMS calcd for $\text{C}_{16}\text{H}_{17}\text{N}_2\text{O}$ (M^+H^+) 253.1341, found 253.1325.

2-(2-Methoxyphenyl)-1-methyl-1H-benzimidazole (32)

To a solution of benzimidazole **31** (100 mg, 0.40 mmol) in anhydrous DMF (2 mL) was added MeONa (213 mg, 3.95 mmol). After 20 h at 100 °C, the reaction mixture was cooled to rt, and partitioned between EtOAc and water. The organic layer was washed repeatedly with water, dried (MgSO_4), and evaporated in vacuo to give a yellow solid. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 3/1) gave an inseparable ~1.9:1 mixture (87 mg) of the starting material **31** and the title compound **32** as a yellow oil. When an analogous reaction was carried out at rt for 25 h, it gave a ~3.3:1 mixture (97 mg) of the starting material **31** and the title compound **32**.

1-Methyl-2-(4-nitrophenyl)-1H-benzimidazole (33)

To a suspension of benzimidazole **63**¹¹ (2.00 g, 8.37 mmol) in THF (15 mL) was added NaH (60% w/w, 368 mg, 9.2 mmol) portionwise at 0 °C. After 15 min at rt, the resulting red solution was treated with MeI (1.3 mL, 21 mmol), and stirred at rt for 19 h. The reaction mixture was quenched with water, evaporated in vacuo, and partitioned between CH_2Cl_2 and water. The phases were separated, and the extraction was completed with additional portions of CH_2Cl_2 . The combined organic extracts were dried (MgSO_4), and evaporated in vacuo. Purification by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2 \rightarrow \text{CH}_2\text{Cl}_2/\text{EtOAc}$, 20/1) gave the title compound **33** (1.47 g, 69%) as a yellow solid: $R_f = 0.75$ ($\text{EtOAc}/\text{CH}_2\text{Cl}_2$, 1/1); mp 208.0-209.0 °C (EtOAc /petroleum

¹¹ Prabhakar Reddy, V.; Prasunamba, P. L.; Reddy, P. S. N.; Ratnam, C. V. *Ind. J. Chem. Sect. B* **1983**, 22, 917-918.

ether) (Lit.¹² 211-213 °C); ¹H NMR (400 MHz, CDCl₃) δ 3.91 (s, 3H), 7.34 (dt, *J* = 7.0, 1.0 Hz, 1H), 7.37 (~t, *J* = 7.0 Hz, 1H), 7.42 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.83 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 2H), and 8.37 (d, *J* = 8.5 Hz, 2H); ¹³C{¹H} NMR (101 MHz, CDCl₃) δ 31.92, 109.9, 120.3, 123.1, 123.8, 123.9, 130.3, 136.3, 136.7, 142.8, 148.4, and 151.0; IR (CHCl₃) *v*_{max} 1604, 1527, and 1350 cm⁻¹; MS (ESI) *m/z* (rel intensity) 254 (100%, MH⁺) and 208 (20); HRMS calcd for C₁₄H₁₂N₃O₂ (MH⁺) 254.0929, found 254.0936; Anal. Calcd for C₁₄H₁₁N₃O₂: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.49; H, 4.41; N, 16.66.

2-(4-Methoxyphenyl)-1-methyl-1*H*-benzimidazole (34)

To a suspension of benzimidazole **33** (100 mg, 0.40 mmol) in anhydrous DMF (2 mL) was added MeONa (213 mg, 3.95 mmol). After 18 h at 100 °C, the reaction mixture was cooled to rt, and partitioned between EtOAc and water. The organic layer was washed repeatedly with water, dried (MgSO₄), and evaporated in vacuo to give a yellow solid. Purification by flash chromatography (silica gel, CH₂Cl₂ → CH₂Cl₂/EtOAc, 20/1) gave the recovered starting material **33** (42 mg, 42%), and the title compound **34** (53 mg, 56%) as a white solid. When an analogous reaction was carried out at rt for 24 h, it gave the recovered starting material **33** (73 mg, 73%) and the title compound **34** (23 mg, 24%). Benzimidazole **34**: *R*_f = 0.25 (EtOAc/petroleum ether, 1/1); ¹H NMR (400 MHz, CDCl₃) δ 3.84 (s, 3H), 3.89 (s, 3H), 7.06 (~dt, *J* = 9.0, 2.5 Hz, 2H), 7.28-7.39 (m, 3H), 7.73 (~dt, *J* = 9.0, 2.5 Hz, 2H), and 7.82-7.86 (m, 1H); ¹³C{¹H} NMR (63 MHz, CDCl₃) δ 31.58, 55.28, 109.4, 114.0, 119.4, 122.2, 122.3, 122.4, 130.7, 136.4, 142.7, 153.6, and 160.7; IR (CHCl₃) *v*_{max} 1614, 1485, 1462, 1436, 1384, 1253, and 1176 cm⁻¹; MS (ESI) *m/z* (rel intensity) 239 (100%, MH⁺); HRMS calcd for C₁₅H₁₅N₂O (MH⁺) 239.1184, found 239.1171.

¹² El'tsov, A. V.; Muravich-Aleksandr, Kh. L. *J. Org. Chem. USSR* (Engl.) **1965**, 1321-1327.

2. Selected CSP HPLC Profiles

Figure S1. Optical resolution of the cyclic ether **3** by CSP HPLC (Chiralcel OD column, 4.6 mm $\times$ 25 cm; 2-propanol/hexanes, 10/90; 1 mL min⁻¹; 40 °C; 254 nm). Top: the racemate; bottom: an enantiomerically enriched sample (ee = 98.0%) obtained by the intermolecular nitro-group displacement in alcohol (+)-**1** (ee = 98.0%).

Figure S2. Optical resolution of alcohol **22** by CSP HPLC (Chiralcel OD column, 4.6 mm × 25 cm; 2-propanol/hexanes, 15/85; 1 mL min⁻¹; 40 °C; 254 nm).

Figure S3. Optical resolution of alcohol **25** by CSP HPLC (Chiralcel OD column, 4.6 mm × 25 cm; 2-propanol/hexanes, 15/85; 1 mL min⁻¹; 40 °C; 230 nm).

Figure S4. Optical resolution of alcohol **26** by CSP HPLC (Chiralcel OD column, 4.6 mm × 25 cm; 2-propanol/hexanes, 8/92; 1 mL min⁻¹; 40 °C; 230 nm).

Figure S5. Optical resolution of acetate **58** by CSP HPLC (Chiralcel OD column, 4.6 mm × 25 cm; 2-propanol/hexanes, 5/95; 1 mL min⁻¹; 40 °C; 254 nm).

Figure S6. Optical resolution of alcohol **61** by CSP HPLC (Chiralcel OD column, 4.6 mm × 25 cm; 2-propanol/hexanes, 5/95; 1 mL min⁻¹; 40 °C; 254 nm).

3. X-Ray Single-Crystal Data for Benzimidazole (9)

The data collection crystal was a colorless, rectangular chunk. Examination of the diffraction pattern on a Nonius Kappa CCD diffractometer indicated a monoclinic crystal system. All work was done at 200 K using an Oxford Cryosystems Cryostream Cooler. The data collection strategy was set up to measure a quadrant of reciprocal space with a redundancy factor of 4, meaning that 90% of the reflections were measured at least 4 times. A combination of phi and omega scans with a frame width of 1.0° was used. Data integration was done with Denzo,¹³ and scaling and merging of the data was done with Scalepack.¹³ Merging the data and averaging the symmetry equivalent reflections resulted in an R(int) value of 0.043. The teXsan package indicated the space group to be $P2_1/n$, based on the systematic absences.¹⁴

The structure was solved by the direct methods in SHELXS-97.¹⁵ There are two molecules in the asymmetric unit and these are labeled as A and B. Full-matrix least-squares refinements based on F^2 were performed in SHELXL-93.¹⁶

For each methyl group, the hydrogen atoms were added at calculated positions using a riding model with $U(H) = 1.5 \times U_{eq}$ (bonded C atom). The torsion angle, which defines the orientation of the methyl group about the C-C bond, was refined. The other hydrogen atoms were included in the model at calculated positions using a riding model with $U(H) = 1.2 \times U_{eq}$ (attached atom). The final refinement cycle was based on all 7009 intensities and 403 variables and resulted in agreement factors of $R_1(F) = 0.071$ and $wR_2(F^2) = 0.099$. For the subset of data with $I > 2\sigma(I)$, the $R_1(F)$ value is 0.040 for 4857 reflections. The final difference electron density map contains maximum and minimum peak heights of 0.20 and -0.17 $e/\text{\AA}^3$. Neutral atom scattering factors were used and include terms for anomalous dispersion.¹⁷

¹³ DENZO: Otwinowski, Z.; Minor, W. in *Methods in Enzymology*; Carter Jr. C. W.; Sweet, R. M., Eds.; Academic Press, 1997, vol 276, pp 307-326.

¹⁴ teXsan: Crystal Structure Analysis Package, version 1.7-2, 1995; Molecular Structure Corporation, The Woodlands, TX.

¹⁵ SHELXS-97: Sheldrick, G. M. Universität Göttingen, Germany, 1997.

¹⁶ SHELXL-93: Sheldrick, G. M. Universität Göttingen, Germany, 1993.

¹⁷ *International Tables for Crystallography, Volume C*. Kluwer Academic Publishers: Dordrecht, 1992.

Table S1. Crystal Data Collection and Refinement Parameters for Benzimidazole (9).

Empirical formula	C ₁₉ H ₂₀ N ₂ O
Formula weight	292.37
Temperature	200(2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	<i>P</i> 2 ₁ / <i>n</i>
Unit cell dimensions	<i>a</i> = 13.088(1) Å <i>b</i> = 10.022(1) Å <i>c</i> = 24.198(3) Å β = 105.15(1)°
Volume	3063.7(6) Å ³
<i>Z</i>	8
Density (calculated)	1.268 Mg/m ³
Absorption coefficient	0.079 mm ⁻¹
F(000)	1248
Crystal size	0.15 × 0.23 × 0.38 mm
Theta range for data collection	2.21 to 27.50°
Index ranges	-16 ≤ <i>h</i> ≤ 17, -13 ≤ <i>k</i> ≤ 12, -31 ≤ <i>l</i> ≤ 31
Reflections collected	57018
Independent reflections	7009 [<i>R</i> (int) = 0.043]
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data / restraints / parameters	7009 / 0 / 403
Goodness-of-fit on <i>F</i> ²	1.034
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0400, <i>wR</i> ₂ = 0.0883
<i>R</i> indices (all data)	<i>R</i> ₁ = 0.0708, <i>wR</i> ₂ = 0.0991
Largest diff. peak and hole	0.203 and -0.172 e/Å ³

Figure S7. ORTEP drawing (50% probability thermal ellipsoids) of the molecular structure of benzimidazole **9**.

Figure S8. Packing diagram of benzimidazole **9**.

Table S2. Atomic Coordinates [(x, y, z), $\times 10^4$] and Equivalent Isotropic Displacement U(eq) Parameters ($\text{\AA}^2 \times 10^3$) for Benzimidazole (9).

	x	y	z	U(eq) ¹⁸
O(1A)	3033(1)	7327(1)	1437(1)	34(1)
N(1A)	2878(1)	7427(1)	2629(1)	31(1)
N(2A)	4367(1)	8258(1)	3215(1)	36(1)
C(1A)	2804(1)	7217(1)	3185(1)	31(1)
C(2A)	2010(1)	6667(1)	3401(1)	37(1)
C(3A)	2178(1)	6683(1)	3989(1)	41(1)
C(4A)	3104(1)	7206(1)	4349(1)	42(1)
C(5A)	3893(1)	7727(1)	4134(1)	41(1)
C(6A)	3734(1)	7744(1)	3540(1)	34(1)
C(7A)	3838(1)	8061(1)	2677(1)	31(1)
C(8A)	4285(1)	8497(1)	2206(1)	31(1)
C(9A)	5183(1)	9320(1)	2351(1)	37(1)
C(10A)	5701(1)	9707(1)	1948(1)	42(1)
C(11A)	5351(1)	9255(1)	1390(1)	42(1)
C(12A)	4463(1)	8461(1)	1235(1)	37(1)
C(13A)	3921(1)	8107(1)	1633(1)	31(1)
C(14A)	2102(1)	7783(1)	1596(1)	31(1)
C(15A)	2046(1)	7022(1)	2125(1)	35(1)
C(16A)	1136(1)	7624(1)	1076(1)	35(1)
C(17A)	189(1)	8306(2)	1217(1)	54(1)
C(18A)	1373(1)	8337(2)	564(1)	49(1)
C(19A)	888(1)	6161(1)	929(1)	41(1)
O(1B)	6688(1)	3706(1)	1469(1)	41(1)
N(1B)	4651(1)	3868(1)	547(1)	31(1)
N(2B)	4516(1)	2270(1)	-118(1)	38(1)
C(1B)	3726(1)	4120(1)	130(1)	33(1)

¹⁸ U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

C(2B)	2971(1)	5117(1)	82(1)	40(1)
C(3B)	2128(1)	5076(2)	-399(1)	47(1)
C(4B)	2044(1)	4082(2)	-814(1)	49(1)
C(5B)	2793(1)	3094(2)	-763(1)	45(1)
C(6B)	3653(1)	3113(1)	-277(1)	36(1)
C(7B)	5101(1)	2748(1)	374(1)	31(1)
C(8B)	6141(1)	2173(1)	654(1)	32(1)
C(9B)	6465(1)	1074(1)	378(1)	39(1)
C(10B)	7473(1)	570(1)	550(1)	47(1)
C(11B)	8212(1)	1156(1)	1002(1)	47(1)
C(12B)	7909(1)	2196(1)	1295(1)	40(1)
C(13B)	6875(1)	2677(1)	1134(1)	33(1)
C(14B)	5653(1)	3863(1)	1557(1)	31(1)
C(15B)	4980(1)	4659(1)	1069(1)	38(1)
C(16B)	5817(1)	4520(1)	2150(1)	33(1)
C(17B)	4742(1)	4759(1)	2276(1)	42(1)
C(18B)	6464(1)	3562(1)	2602(1)	44(1)
C(19B)	6406(1)	5847(1)	2172(1)	41(1)

Table S3. Bond Lengths [$\text{\AA}$] and Angles [$^\circ$] for Benzimidazole (9).

O(1A)-C(13A)	1.378(1)
O(1A)-C(14A)	1.444(1)
N(1A)-C(7A)	1.386(2)
N(1A)-C(1A)	1.390(2)
N(1A)-C(15A)	1.464(2)
N(2A)-C(7A)	1.321(2)
N(2A)-C(6A)	1.382(2)
C(1A)-C(2A)	1.393(2)
C(1A)-C(6A)	1.397(2)
C(2A)-C(3A)	1.383(2)
C(2A)-H(2A)	0.95
C(3A)-C(4A)	1.397(2)
C(3A)-H(3A)	0.95
C(4A)-C(5A)	1.376(2)
C(4A)-H(4A)	0.95
C(5A)-C(6A)	1.396(2)
C(5A)-H(5A)	0.95
C(7A)-C(8A)	1.477(2)
C(8A)-C(13A)	1.398(2)
C(8A)-C(9A)	1.403(2)
C(9A)-C(10A)	1.381(2)
C(9A)-H(9A)	0.95
C(10A)-C(11A)	1.384(2)
C(10A)-H(10A)	0.95
C(11A)-C(12A)	1.377(2)
C(11A)-H(11A)	0.95
C(12A)-C(13A)	1.384(2)
C(12A)-H(12A)	0.95
C(14A)-C(15A)	1.508(2)

C(14A)-C(16A)	1.542(2)
C(14A)-H(14A)	1.00
C(15A)-H(15A)	0.99
C(15A)-H(15B)	0.99
C(16A)-C(19A)	1.525(2)
C(16A)-C(17A)	1.529(2)
C(16A)-C(18A)	1.531(2)
C(17A)-H(17A)	0.98
C(17A)-H(17B)	0.98
C(17A)-H(17C)	0.98
C(18A)-H(18A)	0.98
C(18A)-H(18B)	0.98
C(18A)-H(18C)	0.98
C(19A)-H(19A)	0.98
C(19A)-H(19B)	0.98
C(19A)-H(19C)	0.98
O(1B)-C(13B)	1.373(1)
O(1B)-C(14B)	1.433(1)
N(1B)-C(7B)	1.381(2)
N(1B)-C(1B)	1.381(2)
N(1B)-C(15B)	1.459(2)
N(2B)-C(7B)	1.324(2)
N(2B)-C(6B)	1.382(2)
C(1B)-C(2B)	1.388(2)
C(1B)-C(6B)	1.396(2)
C(2B)-C(3B)	1.379(2)
C(2B)-H(2B)	0.95
C(3B)-C(4B)	1.398(2)
C(3B)-H(3B)	0.95
C(4B)-C(5B)	1.375(2)
C(4B)-H(4B)	0.95

C(5B)-C(6B)	1.399(2)
C(5B)-H(5B)	0.95
C(7B)-C(8B)	1.471(2)
C(8B)-C(13B)	1.394(2)
C(8B)-C(9B)	1.410(2)
C(9B)-C(10B)	1.371(2)
C(9B)-H(9B)	0.95
C(10B)-C(11B)	1.387(2)
C(10B)-H(10B)	0.95
C(11B)-C(12B)	1.375(2)
C(11B)-H(11B)	0.95
C(12B)-C(13B)	1.393(2)
C(12B)-H(12B)	0.95
C(14B)-C(15B)	1.505(2)
C(14B)-C(16B)	1.542(2)
C(14B)-H(14B)	1.00
C(15B)-H(15C)	0.99
C(15B)-H(15D)	0.99
C(16B)-C(19B)	1.532(2)
C(16B)-C(17B)	1.534(2)
C(16B)-C(18B)	1.534(2)
C(17B)-H(17D)	0.98
C(17B)-H(17E)	0.98
C(17B)-H(17F)	0.98
C(18B)-H(18D)	0.98
C(18B)-H(18E)	0.98
C(18B)-H(18F)	0.98
C(19B)-H(19D)	0.98
C(19B)-H(19E)	0.98
C(19B)-H(19F)	0.98

C(13A)-O(1A)-C(14A)	115.06(9)
C(7A)-N(1A)-C(1A)	106.30(9)
C(7A)-N(1A)-C(15A)	131.07(10)
C(1A)-N(1A)-C(15A)	122.63(10)
C(7A)-N(2A)-C(6A)	105.60(10)
N(1A)-C(1A)-C(2A)	132.02(11)
N(1A)-C(1A)-C(6A)	105.55(10)
C(2A)-C(1A)-C(6A)	122.39(11)
C(3A)-C(2A)-C(1A)	116.55(12)
C(3A)-C(2A)-H(2A)	121.7
C(1A)-C(2A)-H(2A)	121.7
C(2A)-C(3A)-C(4A)	121.67(12)
C(2A)-C(3A)-H(3A)	119.2
C(4A)-C(3A)-H(3A)	119.2
C(5A)-C(4A)-C(3A)	121.45(12)
C(5A)-C(4A)-H(4A)	119.3
C(3A)-C(4A)-H(4A)	119.3
C(4A)-C(5A)-C(6A)	117.97(13)
C(4A)-C(5A)-H(5A)	121.0
C(6A)-C(5A)-H(5A)	121.0
N(2A)-C(6A)-C(5A)	129.75(12)
N(2A)-C(6A)-C(1A)	110.26(11)
C(5A)-C(6A)-C(1A)	119.97(12)
N(2A)-C(7A)-N(1A)	112.30(10)
N(2A)-C(7A)-C(8A)	120.41(11)
N(1A)-C(7A)-C(8A)	127.29(11)
C(13A)-C(8A)-C(9A)	117.33(11)
C(13A)-C(8A)-C(7A)	125.49(11)
C(9A)-C(8A)-C(7A)	117.10(11)
C(10A)-C(9A)-C(8A)	121.44(12)
C(10A)-C(9A)-H(9A)	119.3

C(8A)-C(9A)-H(9A)	119.3
C(9A)-C(10A)-C(11A)	119.92(13)
C(9A)-C(10A)-H(10A)	120.0
C(11A)-C(10A)-H(10A)	120.0
C(12A)-C(11A)-C(10A)	119.71(12)
C(12A)-C(11A)-H(11A)	120.1
C(10A)-C(11A)-H(11A)	120.1
C(11A)-C(12A)-C(13A)	120.53(12)
C(11A)-C(12A)-H(12A)	119.7
C(13A)-C(12A)-H(12A)	119.7
O(1A)-C(13A)-C(12A)	116.47(11)
O(1A)-C(13A)-C(8A)	122.54(10)
C(12A)-C(13A)-C(8A)	120.96(11)
O(1A)-C(14A)-C(15A)	107.36(10)
O(1A)-C(14A)-C(16A)	108.60(9)
C(15A)-C(14A)-C(16A)	115.38(10)
O(1A)-C(14A)-H(14A)	108.4
C(15A)-C(14A)-H(14A)	108.4
C(16A)-C(14A)-H(14A)	108.4
N(1A)-C(15A)-C(14A)	112.05(10)
N(1A)-C(15A)-H(15A)	109.2
C(14A)-C(15A)-H(15A)	109.2
N(1A)-C(15A)-H(15B)	109.2
C(14A)-C(15A)-H(15B)	109.2
H(15A)-C(15A)-H(15B)	107.9
C(19A)-C(16A)-C(17A)	110.34(11)
C(19A)-C(16A)-C(18A)	109.55(11)
C(17A)-C(16A)-C(18A)	108.61(12)
C(19A)-C(16A)-C(14A)	111.66(10)
C(17A)-C(16A)-C(14A)	108.17(10)
C(18A)-C(16A)-C(14A)	108.43(10)

C(16A)-C(17A)-H(17A)	109.5
C(16A)-C(17A)-H(17B)	109.5
H(17A)-C(17A)-H(17B)	109.5
C(16A)-C(17A)-H(17C)	109.5
H(17A)-C(17A)-H(17C)	109.5
H(17B)-C(17A)-H(17C)	109.5
C(16A)-C(18A)-H(18A)	109.5
C(16A)-C(18A)-H(18B)	109.5
H(18A)-C(18A)-H(18B)	109.5
C(16A)-C(18A)-H(18C)	109.5
H(18A)-C(18A)-H(18C)	109.5
H(18B)-C(18A)-H(18C)	109.5
C(16A)-C(19A)-H(19A)	109.5
C(16A)-C(19A)-H(19B)	109.5
H(19A)-C(19A)-H(19B)	109.5
C(16A)-C(19A)-H(19C)	109.5
H(19A)-C(19A)-H(19C)	109.5
H(19B)-C(19A)-H(19C)	109.5
C(13B)-O(1B)-C(14B)	119.43(9)
C(7B)-N(1B)-C(1B)	106.82(10)
C(7B)-N(1B)-C(15B)	130.67(10)
C(1B)-N(1B)-C(15B)	122.43(10)
C(7B)-N(2B)-C(6B)	105.52(10)
N(1B)-C(1B)-C(2B)	131.49(12)
N(1B)-C(1B)-C(6B)	105.52(11)
C(2B)-C(1B)-C(6B)	122.98(12)
C(3B)-C(2B)-C(1B)	116.41(13)
C(3B)-C(2B)-H(2B)	121.8
C(1B)-C(2B)-H(2B)	121.8
C(2B)-C(3B)-C(4B)	121.48(13)
C(2B)-C(3B)-H(3B)	119.3

C(4B)-C(3B)-H(3B)	119.3
C(5B)-C(4B)-C(3B)	121.82(13)
C(5B)-C(4B)-H(4B)	119.1
C(3B)-C(4B)-H(4B)	119.1
C(4B)-C(5B)-C(6B)	117.69(13)
C(4B)-C(5B)-H(5B)	121.2
C(6B)-C(5B)-H(5B)	121.2
N(2B)-C(6B)-C(1B)	110.16(11)
N(2B)-C(6B)-C(5B)	130.22(12)
C(1B)-C(6B)-C(5B)	119.61(13)
N(2B)-C(7B)-N(1B)	111.97(11)
N(2B)-C(7B)-C(8B)	121.37(11)
N(1B)-C(7B)-C(8B)	126.47(11)
C(13B)-C(8B)-C(9B)	116.77(12)
C(13B)-C(8B)-C(7B)	126.57(11)
C(9B)-C(8B)-C(7B)	116.38(11)
C(10B)-C(9B)-C(8B)	121.97(13)
C(10B)-C(9B)-H(9B)	119.0
C(8B)-C(9B)-H(9B)	119.0
C(9B)-C(10B)-C(11B)	119.98(13)
C(9B)-C(10B)-H(10B)	120.0
C(11B)-C(10B)-H(10B)	120.0
C(12B)-C(11B)-C(10B)	119.42(13)
C(12B)-C(11B)-H(11B)	120.3
C(10B)-C(11B)-H(11B)	120.3
C(11B)-C(12B)-C(13B)	120.61(13)
C(11B)-C(12B)-H(12B)	119.7
C(13B)-C(12B)-H(12B)	119.7
O(1B)-C(13B)-C(12B)	113.95(11)
O(1B)-C(13B)-C(8B)	125.01(11)
C(12B)-C(13B)-C(8B)	120.96(12)

O(1B)-C(14B)-C(15B)	108.88(10)
O(1B)-C(14B)-C(16B)	106.19(9)
C(15B)-C(14B)-C(16B)	114.47(10)
O(1B)-C(14B)-H(14B)	109.1
C(15B)-C(14B)-H(14B)	109.1
C(16B)-C(14B)-H(14B)	109.1
N(1B)-C(15B)-C(14B)	111.79(10)
N(1B)-C(15B)-H(15C)	109.3
C(14B)-C(15B)-H(15C)	109.3
N(1B)-C(15B)-H(15D)	109.3
C(14B)-C(15B)-H(15D)	109.3
H(15C)-C(15B)-H(15D)	107.9
C(19B)-C(16B)-C(17B)	109.69(11)
C(19B)-C(16B)-C(18B)	109.86(11)
C(17B)-C(16B)-C(18B)	108.68(11)
C(19B)-C(16B)-C(14B)	110.44(10)
C(17B)-C(16B)-C(14B)	109.90(10)
C(18B)-C(16B)-C(14B)	108.24(10)
C(16B)-C(17B)-H(17D)	109.5
C(16B)-C(17B)-H(17E)	109.5
H(17D)-C(17B)-H(17E)	109.5
C(16B)-C(17B)-H(17F)	109.5
H(17D)-C(17B)-H(17F)	109.5
H(17E)-C(17B)-H(17F)	109.5
C(16B)-C(18B)-H(18D)	109.5
C(16B)-C(18B)-H(18E)	109.5
H(18D)-C(18B)-H(18E)	109.5
C(16B)-C(18B)-H(18F)	109.5
H(18D)-C(18B)-H(18F)	109.5
H(18E)-C(18B)-H(18F)	109.5
C(16B)-C(19B)-H(19D)	109.5

C(16B)-C(19B)-H(19E)	109.5
H(19D)-C(19B)-H(19E)	109.5
C(16B)-C(19B)-H(19F)	109.5
H(19D)-C(19B)-H(19F)	109.5
H(19E)-C(19B)-H(19F)	109.5

Table S4. Anisotropic Displacement Parameters ($\text{\AA}^2 \times 10^3$) for Benzimidazole (9).¹⁹

	U11	U22	U33	U23	U13	U12
O(1A)	30(1)	35(1)	37(1)	-5(1)	10(1)	0(1)
N(1A)	30(1)	33(1)	30(1)	-1(1)	8(1)	0(1)
N(2A)	35(1)	39(1)	33(1)	0(1)	6(1)	-2(1)
C(1A)	35(1)	28(1)	31(1)	0(1)	10(1)	4(1)
C(2A)	37(1)	33(1)	42(1)	0(1)	13(1)	-1(1)
C(3A)	49(1)	36(1)	43(1)	5(1)	22(1)	3(1)
C(4A)	57(1)	38(1)	33(1)	2(1)	15(1)	4(1)
C(5A)	46(1)	40(1)	33(1)	0(1)	6(1)	0(1)
C(6A)	36(1)	31(1)	34(1)	1(1)	9(1)	2(1)
C(7A)	29(1)	28(1)	34(1)	0(1)	7(1)	2(1)
C(8A)	28(1)	29(1)	36(1)	2(1)	9(1)	4(1)
C(9A)	33(1)	35(1)	41(1)	2(1)	7(1)	0(1)
C(10A)	33(1)	37(1)	56(1)	7(1)	13(1)	-2(1)
C(11A)	39(1)	44(1)	47(1)	13(1)	21(1)	4(1)
C(12A)	37(1)	39(1)	37(1)	5(1)	13(1)	5(1)
C(13A)	28(1)	27(1)	37(1)	2(1)	9(1)	3(1)
C(14A)	29(1)	29(1)	35(1)	-4(1)	9(1)	2(1)
C(15A)	30(1)	39(1)	35(1)	-3(1)	7(1)	-3(1)
C(16A)	32(1)	35(1)	35(1)	-4(1)	4(1)	1(1)
C(17A)	36(1)	60(1)	57(1)	-16(1)	-2(1)	11(1)
C(18A)	52(1)	46(1)	39(1)	6(1)	-3(1)	-8(1)
C(19A)	40(1)	40(1)	42(1)	-7(1)	10(1)	-6(1)
O(1B)	34(1)	44(1)	47(1)	-14(1)	15(1)	-4(1)
N(1B)	33(1)	32(1)	30(1)	0(1)	9(1)	-1(1)
N(2B)	39(1)	43(1)	33(1)	-6(1)	11(1)	-5(1)
C(1B)	31(1)	38(1)	32(1)	5(1)	11(1)	-5(1)
C(2B)	39(1)	41(1)	43(1)	6(1)	13(1)	0(1)

¹⁹ The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U11 + \dots + 2 h k a^* b^* U12]$.

C(3B)	38(1)	52(1)	50(1)	15(1)	11(1)	1(1)
C(4B)	37(1)	66(1)	40(1)	11(1)	5(1)	-9(1)
C(5B)	42(1)	56(1)	37(1)	-2(1)	9(1)	-12(1)
C(6B)	33(1)	43(1)	33(1)	1(1)	12(1)	-7(1)
C(7B)	35(1)	32(1)	30(1)	-1(1)	14(1)	-5(1)
C(8B)	39(1)	30(1)	32(1)	3(1)	16(1)	-1(1)
C(9B)	51(1)	34(1)	35(1)	0(1)	18(1)	2(1)
C(10B)	62(1)	37(1)	48(1)	5(1)	27(1)	15(1)
C(11B)	49(1)	49(1)	46(1)	11(1)	17(1)	17(1)
C(12B)	40(1)	42(1)	38(1)	7(1)	10(1)	5(1)
C(13B)	38(1)	30(1)	34(1)	3(1)	16(1)	-1(1)
C(14B)	31(1)	29(1)	33(1)	-1(1)	11(1)	-2(1)
C(15B)	48(1)	32(1)	32(1)	-3(1)	9(1)	1(1)
C(16B)	40(1)	30(1)	29(1)	-2(1)	8(1)	1(1)
C(17B)	52(1)	41(1)	37(1)	0(1)	18(1)	4(1)
C(18B)	54(1)	41(1)	35(1)	2(1)	7(1)	6(1)
C(19B)	49(1)	36(1)	36(1)	-6(1)	6(1)	-4(1)

Table S5. Calculated Hydrogen Coordinates [(x, y, z), $\times 10^4$] and Isotropic Displacement Parameters U(eq) ($\text{\AA}^2 \times 10^3$) for Benzimidazole (9).

	x	y	z	U(eq)
H(2A)	1384(1)	6300(1)	3156(1)	44
H(3A)	1650(1)	6328(1)	4153(1)	49
H(4A)	3190(1)	7203(1)	4751(1)	50
H(5A)	4528(1)	8065(1)	4381(1)	49
H(9A)	5440(1)	9617(1)	2735(1)	44
H(10A)	6296(1)	10284(1)	2053(1)	50
H(11A)	5722(1)	9490(1)	1115(1)	50
H(12A)	4220(1)	8155(1)	851(1)	44
H(14A)	2193(1)	8752(1)	1696(1)	37
H(15A)	1346(1)	7174(1)	2199(1)	42
H(15B)	2114(1)	6055(1)	2058(1)	42
H(17A)	6(5)	7831(6)	1532(3)	81
H(17B)	-416(3)	8293(9)	878(1)	81
H(17C)	372(3)	9232(3)	1331(4)	81
H(18A)	1959(5)	7886(6)	459(3)	73
H(18B)	1569(7)	9266(3)	666(2)	73
H(18C)	742(3)	8316(9)	239(1)	73
H(19A)	667(6)	5727(2)	1241(2)	61
H(19B)	1522(2)	5716(2)	874(4)	61
H(19C)	317(5)	6098(1)	575(2)	61
H(2B)	3031(1)	5790(1)	365(1)	48
H(3B)	1592(1)	5738(2)	-450(1)	56
H(4B)	1454(1)	4089(2)	-1141(1)	59
H(5B)	2728(1)	2422(2)	-1046(1)	54
H(9B)	5971(1)	672(1)	64(1)	46
H(10B)	7664(1)	-182(1)	360(1)	56
H(11B)	8922(1)	843(1)	1108(1)	56

H(12B)	8409(1)	2588(1)	1609(1)	48
H(14B)	5328(1)	2962(1)	1564(1)	37
H(15C)	4344(1)	4987(1)	1176(1)	45
H(15D)	5385(1)	5445(1)	997(1)	45
H(17D)	4342(3)	5423(6)	2008(2)	63
H(17E)	4854(1)	5086(8)	2669(1)	63
H(17F)	4344(3)	3920(2)	2232(4)	63
H(18D)	6587(6)	3969(4)	2982(1)	66
H(18E)	7145(3)	3380(7)	2520(2)	66
H(18F)	6074(3)	2724(4)	2594(3)	66
H(19D)	5966(3)	6478(3)	1903(3)	62
H(19E)	7072(3)	5700(2)	2068(4)	62
H(19F)	6558(6)	6214(4)	2561(1)	62