Development of a Friedel-Crafts Triflation

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Supporting Information

General information: Unless otherwise noted, starting materials and analytical grade solvents were obtained from commercial suppliers and used without further purification. Benzene and acetonitrile were distilled from CaH_2 prior to use. Dichloromethane (DCM) was dried by passing it through a column of activated basic alumina.^[1] Tetrahydrofuran (THF) was freshly distilled from sodium using benzophenone as an indicator. Nitromethane was distilled from calcium hydride. Triflic Anhydride was received from Aldrich, distilled from P_2O_5 , and stored under nitrogen. HMPT was distilled from calcium hydride and stored over molsieves 4A under nitrogen. Both reaction mixtures and chromatography fractions were analyzed on Merck silica gel 60 F254 TLC plates. Flash column chromatography was carried out with ICN SiliTech 32-63 D 60 Å silica gel. FT-IR spectra were obtained as thin films on NaCl plates with an ATI Mattson Gemini spectrometer.

Proton and carbon NMR spectra (^1H -NMR and ^{13}C -NMR) were recorded on a Bruker AVQ-400 and AV-500 spectrometer and calibrated to the residual solvent peak. Unless otherwise noted, spectra were recorded at room temperature (294.9 K). Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublet, and were assigned for ^{13}C -NMR spectra based on DEPT90 and DEPT135 experimental data. The prefix b stands for broad signals.

Low resolution mass spectra were recorded using a VG ZAB (FAB) and VGProSpec (EI) mass spectrometer. (NBA = 3-Nitrobenzyl alcohol, LiCl = lithium chloride). Vinylogous esters **20a** and **20b** and indole **21b** were prepared by methods reported in the literature.^[2,3] All other reactions were conducted with oven-dried glassware using standard Schlenk-technique.^[4]

General procedures for the formation of vinylogous esters **22a-f**

Scheme 1. Synthesis of vinylogous esters **22a-f**.

Procedure A:

Vinylogous ester **20** (1 eq) was dissolved in dry THF (100 ml/8 mmol **20**), the solution was cooled to -78°C , and a 1 M solution of LHMDs (1.2 eq) in THF was added dropwise by letting the drops run down the cooled glass wall of the flask. After complete addition, the mixture was stirred at -78°C for 20 minutes, then for an additional 20 minutes after completely removing the cooling bath. The solution was then re-cooled to -78°C and a solution of **21** (2 eq) in THF (20 ml/ 8mmol **21**) was added quickly under vigorous stirring. After complete addition, the mixture was quickly warmed to -20°C and stirred at this temperature until TLC monitoring showed complete conversion (20 minutes to 2 hours). The reaction was quenched by the addition of water (1 ml/10 ml THF), and the mixture was poured over brine (1 ml/ml THF) with concomitant addition of dichloromethane (1 ml/ml THF). The layers were separated, and the aqueous layer was extracted again with the same amount of dichloromethane. The combined organic layers

were dried over Na₂SO₄, concentrated, and purified by column chromatography.

Procedure B:

To a stirred solution of diisopropylamine (1.02 eq) in THF (2 ml/mmol **20**) was added a 2.5 M solution of *n*-BuLi (1.02 eq) in hexane dropwise at 0°C. The mixture was stirred at 0°C for 10 minutes and then cooled to -78°C. Neat vinylogous ester **20** (1.00 eq) was added dropwise via syringe pump (4 min/mmol **20**) while stirring vigorously. After complete addition, the mixture was stirred for an additional 20 minutes followed by a rapid addition of HMPT (0.4 ml/mmol **20**). The mixture was stirred for an additional 10 minutes, and halide **21** (3 eq) was added quickly at -78°C (neat or as a saturated solution in THF), immediately warmed to -20°C, and stirred at this temperature until TLC monitoring showed complete conversion (20 minutes to 1 hour). The reaction was quenched at -20°C by the addition of water (1ml/10 ml THF), and the mixture was poured on water (5 ml/ml THF). Dichloromethane was added (1ml/ml THF), the layers were separated and the aqueous layer extracted 2 times with the same amount of dichloromethane. The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated, and purified by column chromatography.

6-(3,5-Dimethoxy-benzyl)-3-isobutoxy-cyclohex-2-enone (22a):

Vinylogous ester **20b** (4.30 g, 25.6 mmol) was alkylated with 3,5-dimethoxybenzyl bromide **21a** (10.0 g, 43.3 mmol) using Procedure A to yield **22a** (5.86 g, 18.4 mmol, 72%); ¹H NMR (CDCl₃, 400.2 MHz): δ = 6.29 (d, *J*_{H,H} = 2.2 Hz, 2H), 6.25 (t, *J*_{H,H} = 2.2 Hz, 1 H), 5.30 (s, 1H), 3.70 (s, 6H), 3.54 (m, 2H), 3.32-3.19 (m, 1H), 2.44-2.24 (m, 4H), 1.96 (h, *J*_{H,H} = 6.8 Hz, 1H), 1.92-1.83 (m, 1H), 1.63-1.47 (m, 1H), 0.91 (d, *J*_{H,H} = 6.7 Hz, 3H), 0.90(6) (d, *J*_{H,H} = 6.7 Hz, 3H); ¹³C NMR (CDCl₃, 100.6 MHz): δ = 200.1 (s), 177.2 (s), 160.7 (s, 2C), 142.6 (s), 107.1 (d, 2C), 102.1 (d), 97.9 (d), 74.7 (t), 55.1 (q, 2C), 46.9 (d), 36.0 (t), 28.1 (t), 27.7 (d), 25.5 (t), 19.0 (q, 2C); IR (film): ν[cm⁻¹] = 2957, 2940, 2874, 2838, 1652, 1607, 1461, 1428, 1383,

1366, 1308, 1366, 1308, 1295, 1239, 1193, 1152; MS (FAB+, NBA): m/z (%): 319 (100)[$M+H^+$], 263 (25); HRMS (FAB+): $C_{19}H_{27}O_4$: calcd 319.1909, found 319.1905.

3-Isobutoxy-6-[2-(1-methyl-1H-indol-3-yl)-ethyl]-cyclohex-2-enone (22b): Vinylogous ester **20b** (200 mg, 1.19 mmol) was alkylated with indole **21b** (618 mg, 2.59 mmol) using Procedure B to yield **22b** (130 mg, 0.400 mmol, 34%); 1H NMR ($CDCl_3$, 400.2 MHz): δ = 7.69 (d, $J_{H,H}$ = 7.8 Hz, 1H), 7.34-7.22 (m, 2H), 7.16 (m, 1H), 6.92 (s, 1H), 5.38 (s, 1H), 3.74 (s, 3H), 3.62 (dd, $J_{H,H}$ = 1.8, 6.5 Hz, 2H), 3.00-2.80 (m, 2H), 2.53-2.44 (m, 2H), 2.42-2.40 (m, 2H), 2.25-2.13 (m, 1H), 2.07 (h, $J_{H,H}$ = 6.6 Hz, 1H), 1.91-1.74 (m, 2H), 1.02 (d, $J_{H,H}$ = 6.7 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 201.6 (s), 176.9 (s), 137.1 (s), 128.0 (s), 126.3 (d), 121.4 (d), 119.1 (d), 118.6 (d), 114.7 (s), 109.2 (d), 102.3 (d), 74.7 (t), 44.7 (d), 32.6 (t), 30.3 (t), 28.0 (t), 27.8 (d), 26.5 (t), 22.5 (t), 19.2 (q, 2C); IR (film): $\nu[cm^{-1}]$ = 3054, 2957, 2932, 2874, 1652, 1606, 1556, 1471, 1425, 1404, 1382, 1368, 1324, 1240, 1220, 1193, 1177; MS (FAB+, NBA): m/z (%): 326 (100)[$M+H^+$], 325 (74), 168 (68), 157 (56), 144 (54); HRMS (FAB+): $C_{21}H_{27}NO_2$: calcd. 325.2042, found 325.2035.

5-(3,5-Dimethoxybenzyl)-3-isobutoxy-cyclopent-2-enone (22c): Vinylogous ester **20a** (341 mg, 2.21 mmol) was alkylated with 3,5-dimethoxybenzylbromide **21a** (869 mg, 3.76 mmol) using Procedure A to yield **22c** (478 mg, 1.57 mmol, 71%); 1H NMR ($CDCl_3$, 400.2 MHz): δ = 6.35 (d, $J_{H,H}$ = 2.2 Hz, 2H), 6.31 (m, 1H), 5.24 (s, 1H), 3.76 (s, 6H), 3.71 (dd, $J_{H,H}$ = 1.3, 6.6 Hz, 2H), 3.22 (dd, $J_{H,H}$ = 4.0, 13.9 Hz, 1H), 2.81-2.73 (m,

1H), 2.61 (ddd, $J_{\text{H,H}} = 0.9, 7.2, 17.8$ Hz, 1H), 2.48 (dd, $J_{\text{H,H}} = 10.7, 13.8$ Hz, 1H), 2.37 (ddd, $J_{\text{H,H}} = 0.8, 2.8, 17.7$ Hz, 1H), 2.04 (h, $J_{\text{H,H}} = 6.7$ Hz, 1H), 0.91 (d, $J_{\text{H,H}} = 6.8$ Hz, 6H); ^{13}C NMR (CDCl_3 , 100.6 MHz): $\delta = 207.0$ (s), 189.4 (s), 160.9 (s, 2C), 142.1 (s), 107.2 (d, 2C), 103.7 (d), 98.3 (d), 78.0 (t), 55.3 (q, 2C), 46.6 (d), 37.5 (t), 34.3 (t), 27.9 (d), 19.0 (q, 2C); IR (film): $\nu[\text{cm}^{-1}] = 2960, 2937, 2876, 2838, 1692, 1594, 1464, 1429, 1381, 1351, 1290, 1235, 1205, 1153, 1066$; MS (FAB+, NBA): m/z (%): 305 (100) $[\text{M}+\text{H}^+]$, 304 (34) $[\text{M}]$, 249 (77); HRMS (FAB+): $\text{C}_{18}\text{H}_{25}\text{O}_4$: calcd. 305.1753, found 305.1753.

22d

6-Benzyl-3-isobutoxy-cyclohex-2-enone (22d): Vinylogous ester **20b** (439 mg, 2.61 mmol) was alkylated with benzyl bromide **21c** (760 mg, 4.44 mmol) using Procedure A to yield **22d** (338 mg, 1.38 mmol, 53%); ^1H NMR (CDCl_3 , 400.2 MHz): $\delta = 7.26\text{--}7.32$ (m, 2H), 7.17–7.24 (m, 3H), 5.37 (s, 1H), 3.60 (m, 2H), 3.40 (dd, $J_{\text{H,H}} = 3.1, 13.3$ Hz, 1H), 2.31–2.56 (m, 4H), 2.02 (sept, $J_{\text{H,H}} = 6.7$ Hz, 1H), 1.91 (m, 1H), 1.56–1.68 (m, 1H), 0.98 (d, $J_{\text{H,H}} = 6.7$ Hz, 6H); ^{13}C NMR (CDCl_3 , 100.6 MHz): $\delta = 200.4$ (s), 177.3 (s), 140.3 (s), 129.2 (d, 2C), 128.4 (d, 2C), 126.1 (d), 102.3 (d), 74.8 (t), 47.1 (d), 35.7 (t), 28.2 (t), 27.8 (d), 25.6 (t), 19.1 (q, 2C); IR (film): $\nu[\text{cm}^{-1}] = 3062, 3026, 2959, 2934, 2874, 1652, 1608, 1495, 1240, 1194, 1178, 992$; MS (FAB+, NBA): m/z (%): 319 (100) $[\text{M}+\text{H}^+]$, 263 (25); HRMS (FAB+): $\text{C}_{17}\text{H}_{23}\text{O}_2$: calcd. 259.1700, found 259.1694.

22e

3-Isobutoxy-6-(3-methoxy-benzyl)-cyclohex-2-enone (22e): Vinylogous ester **20b** (842 mg, 5.01 mmol) was alkylated with 3-methoxybenzyl bromide **21d** (3.02 g, 5.10 mmol) using Procedure B to yield **22e** (1.36 g,

4.71 mmol, 94%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.18 (m, 1H), 6.79-6.70 (m, 3H), 5.34 (s, 1H), 3.77 (s, 3H), 3.57 (d, $J_{\text{H,H}}$ = 1.3, 6.5 Hz, 2H), 3.34 (d, $J_{\text{H,H}}$ = 10.1 Hz, 1H), 2.53-2.27 (m, 4H), 2.00 (h, $J_{\text{H,H}}$ = 6.6 Hz, 1H), 1.94-1.85 (m, 1H), 1.65-1.53 (m, 1H), 0.95 (d, $J_{\text{H,H}}$ = 6.8 Hz, 6H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 200.4 (s), 177.4 (s), 159.7 (s), 142.0 (s), 129.4 (d), 121.7 (d), 114.9 (d), 111.4 (d), 102.3 (d), 74.9 (t), 55.2 (q), 47.1 (d), 35.8 (t), 28.2 (t), 27.8 (d), 25.6 (t), 19.2 (q, 2C); IR (film): $\nu[\text{cm}^{-1}]$ = 2959, 2874, 2853, 1658, 1607, 1488, 1470, 1455, 1435, 1404, 1368, 1314, 1290, 1258, 1241, 1220, 1194, 1154, 1093; MS (FAB+, NBA): m/z (%): 289 (100)[$\text{M}+\text{H}^+$], 233 (48); HRMS (FAB+): $\text{C}_{18}\text{H}_{25}\text{O}_3$: calcd. 289.1804, found 289.1804.

22f

6-(2-Iodo-3-methoxy-benzyl)-3-isobutoxy-cyclohex-2-enone (22f):

Vinylogous ester **20b** (100 mg, 0.595 mmol) was alkylated with 2-iodo-3-methoxybenzyl bromide **21e** (328 mg, 1.01 mmol) using Procedure B to yield **22f** (149 mg, 0.357 mmol, 60%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.15 (t, $J_{\text{H,H}}$ = 7.9 Hz, 1H), 6.78 (dd, $J_{\text{H,H}}$ = 1.0, 7.6 Hz, 1H), 6.62 (dd, $J_{\text{H,H}}$ = 0.9, 8.2 Hz, 1H), 5.32 (s, 1H), 3.82 (s, 3H), 3.61-3.49 (m, 3H), 2.68-2.53 (m, 2H), 2.37-2.30 (m, 2H), 1.97 (h, $J_{\text{H,H}}$ = 6.9 Hz, 1H), 1.87-1.82 (m, 1H), 1.72-1.59 (m, 1H), 0.92 (d, $J_{\text{H,H}}$ = 6.8 Hz, 3H), 0.91 (d, $J_{\text{H,H}}$ = 6.8 Hz, 3H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.7 (s), 177.1 (s), 158.1 (s), 145.0 (s), 128.7 (d), 123.2 (d), 108.6 (d), 102.2 (d), 93.2 (s), 74.7 (t), 56.5 (q), 45.6 (d), 40.5 (d), 28.6 (t), 27.7 (d), 25.9 (t), 19.1 (q, 2C); IR (film): $\nu[\text{cm}^{-1}]$ = 3069, 3003, 2959, 2873, 2836, 1652, 1607, 1566, 1464, 1425, 1404, 1384, 1368, 1293, 1242, 1194, 1074, 1034; MS (FAB+, NBA): m/z (%): 415 (100)[$\text{M}+\text{H}^+$], 359 (15), 287 (20), 232 (19); HRMS (FAB+): $\text{C}_{18}\text{H}_{24}\text{O}_3\text{I}$: calcd. 415.0770, found 415.0771.

General procedure for the formation of enones 3 and 8b-i:

A solution of the Grignard reagent (1.1 eq) in THF (3M for MeMgCl , 1 M for PhMgBr , 1M for (vinyl) MgBr) was added dropwise to a solution of enone **22** in THF (10 ml/mmol **22**) at 0°C . The mixture was stirred for 45

minutes at this temperature, before a 1N aqueous HCl-solution (1 ml/ml THF) was added. The mixture was slowly warmed to room temperature and stirred overnight. The mixture was then poured on brine (1 ml/10 ml THF), dichloromethane was added (1 ml/ml THF), the layers were separated, and the aqueous layer was extracted 2 times with the same amount of dichloromethane. The combined organic layers were dried over Na₂SO₄, concentrated, and purified by column chromatography.

3

4-(3,5-Dimethoxy-benzyl)-3-methyl-cyclohex-2-enone (3): Treatment of vinylogous ester **22a** (773 mg, 2.43 mmol) with a 3M solution of MeMgCl (1.62 ml, 4.86 mmol) and concomitant acid hydrolysis using the general procedure described above afforded enone **3** (411 mg, 1.58 mmol, 65%); ¹H NMR (CDCl₃, 400.2 MHz): δ = 6.34 (s, 3H), 5.88 (s, 1H), 3.79 (s, 6H), 3.05-2.91 (m, 1H), 2.59-2.38 (m, 3H), 2.26 (dt, *J*_{H,H} = 17.4, 5.1 Hz, 1H), 2.00 (d, *J*_{H,H} = 1.2 Hz, 3H), 1.98-1.87 (m, 1H), 1.84-1.71 (m, 1H); ¹³C NMR (CDCl₃, 100.6 MHz): δ = 199.1 (s), 164.9 (s), 160.8 (s, 2C), 141.9 (s), 126.9 (d), 106.9 (d, 2C), 97.9 (d), 55.2 (q, 2C), 41.1 (d), 37.6 (t), 33.3 (t), 26.0 (t), 23.1 (q); IR (film): ν[cm⁻¹] = 2998, 2942, 2868, 2838, 1667, 1596, 1462, 1431, 1378, 1348, 1314, 1295, 1251, 1205, 1152, 1068; MS (FAB+, NBA): *m/z* (%): 261 (100)[M+H⁺], 260 (43), 203 (19), 152 (44), 151 (62); HRMS (FAB+): C₁₆H₂₀O₃: calcd. 260.1412, found 260.1413.

8a

4-(3,5-Dimethoxy-benzyl)-cyclohex-2-enone (8a): To a stirred solution of vinylogous ester **22a** (200 mg, 0.63 mmol) in 10 mL Et₂O at 0°C was added dropwise a solution of Dibal-H (0.94 mL of a 1.0M solution in hexane). The mixture was stirred at 0°C for an additional 30 min. The reaction was then

quenched by the dropwise addition of 0.250 mL of a saturated aqueous solution of NH_4Cl . The resulting mixture was allowed to gradually warm to room temperature and stirred at room temperature for 1 hour. To this mixture was added 0.100 mg of MgSO_4 , and the mixture was stirred for an additional hour. The crude mixture was filtered over celite, concentrated, and re-dissolved in 70.0 mL of dry Et_2O . To this solution was added 0.350 mL of H_2O and $\text{TsOH}\cdot\text{H}_2\text{O}$ (0.127 g, 0.668 mmol), and the mixture was stirred for one hour at room temperature. The reaction was quenched by the addition of 30.0 mL of a saturated aqueous NH_4Cl solution. The phases were separated, and the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined organic extracts were dried over MgSO_4 and the crude oil purified by flash column chromatography. (46 mg, 0.186 mmol, 30%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 6.83 (d, $J_{\text{H,H}}$ = 10.1 Hz, 1H), 6.33 (s, 3H), 5.96 (dt, $J_{\text{H,H}}$ = 10.1, 1.4 Hz, 1H), 3.77 (s, 6H), 2.75-2.59 (m, 3H), 2.48 (dt, $J_{\text{H,H}}$ = 16.9, 4.8, 1H), 2.32 (ddd, $J_{\text{H,H}}$ = 16.8, 12.4, 4.9, 1H), 2.10-2.00 (m, 1H), 1.76-1.63 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.7 (s), 160.9 (s, 2C), 153.8 (d), 141.3 (s), 129.2 (d), 107.1 (d, 2C), 98.1 (d), 55.2 (q, 2C), 41.1 (t), 37.7 (d), 36.8 (t), 28.7 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 2999, 2942, 2859, 2838, 1676, 1596, 1462, 1430, 1389, 1349, 1314, 1295, 1250, 1206, 1152, 1068; MS (FAB+, NBA, LiCl): m/z (%): 253 (100)[$\text{M}+\text{Li}^+$], 160 (47); HRMS (FAB+): $\text{C}_{15}\text{H}_{18}\text{O}_3\text{Li}$: calcd. 253.1416, found 253.1419.

8b

4-(3,5-Dimethoxybenzyl)-3-phenylcyclohex-2-enone (8b): Treatment of vinylogous ester **22a** (1.00 g, 3.14 mmol) with a 1M solution of PhMgBr (6.20 mL, 6.20 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8b** (749 mg, 2.33 mmol, 74%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.61-7.51 (m, 2H), 7.49-7.39 (m, 3H), 6.31 (s, 4H), 3.77 (s, 6H), 3.34-3.20 (m, 1H), 2.79 (dd, $J_{\text{H,H}}$ = 13.8, 3.8 Hz, 1H), 2.68-2.50 (m, 2H), 2.40 (dt, $J_{\text{H,H}}$ = 17.4, 4.2 Hz, 1H), 2.19-1.94 (m, 2H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.6 (s), 163.8 (s), 161.0 (s, 2C), 142.2 (s), 138.3 (s), 130.2 (d), 129.1 (d, 2C), 126.8 (d, 2C), 126.0 (d), 107.2 (d, 2C),

97.9 (d), 55.4 (q, 2C), 38.3 (d), 37.9 (t), 32.9 (t), 25.0 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3055, 2997, 2942, 2866, 2837, 1666, 1595, 1460, 1429, 1349, 1330, 1313, 1295, 1253, 1204, 1151, 1067; MS (FAB+, NBA): m/z (%): 323 (100)[$\text{M}+\text{H}^+$], 265 (30), 151 (67); HRMS (FAB+): $\text{C}_{21}\text{H}_{23}\text{O}_3$: calcd. 323.1647, found 323.1640.

3-Methyl-4-(1-methyl-1H-indol-3-ylmethyl)-cyclohex-2-enone (8c):

Treatment of vinylogous ester **22b** (100 mg, 0.307 mmol) with a 3M solution of MeMgCl (0.135 ml, 0.405 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8c** (60 mg, 0.22 mmol, 73%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.61 (d, $J_{\text{H,H}}$ = 7.9 Hz, 1H), 7.33 (d, $J_{\text{H,H}}$ = 8.2 Hz, 1H), 7.26 (dt, $J_{\text{H,H}}$ = 1.1, 6.9 Hz, 1H), 7.14 (dt, $J_{\text{H,H}}$ = 1.1, 7.0 Hz, 1H), 6.89 (s, 1H), 5.87 (s, 1H), 3.77 (s, 3H), 2.98 (m, 1H), 2.80 (m, 1H), 2.52 (m, 1H), 2.40-2.30 (m, 2H), 2.21-2.01 (m, 3H), 1.95 (s, 3H), 1.85 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.4 (s), 166.2 (s), 137.0 (s), 127.6 (s), 126.6 (d), 126.0 (d), 121.6 (d), 118.8 (d, 2C), 114.0 (s), 109.2 (d), 39.0 (d), 33.7 (t), 32.5 (d), 31.2 (t), 25.9 (t), 23.3 (t), 22.9 (q); IR (film): $\nu[\text{cm}^{-1}]$ = 2933, 2926, 2880, 2863, 2856, 1667, 1636, 1428, 1437, 13770, 1325, 1249; MS (FAB+, NBA): m/z (%): 274 (100) [$\text{M}+\text{Li}^+$], 267 (48), 212 (40), 160 (92); HRMS (FAB+): $\text{C}_{18}\text{H}_{21}\text{NOLi}$: calcd. 274.1783, found 274.1784.

4-(3,5-Dimethoxy-benzyl)-3-phenyl-cyclopent-2-enone (8d): Treatment of vinylogous ester **22c** (168 mg, 0.553 mmol) with a 1M solution of PhMgBr

(1.10 ml, 1.10 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8d** (102 mg, 0.331 mmol, 60%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.66-7.63 (m, 2H), 7.50-7.49 (m, 3H), 6.45 (s, 1H), 6.32 (s, 1H), 6.27 (s, 2H), 3.88 (bs, 1H), 3.79 (s, 6H), 3.12 (dd, $J_{\text{H,H}}$ = 14.0, 3.2 Hz, 1H), 2.64 (dd, $J_{\text{H,H}}$ = 18.8, 6.8 Hz, 1H), 2.43 (s, 1H), 2.38 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 207.9 (s), 177.8 (s), 160.8 (s, 2C), 141.3 (s), 133.5 (s), 130.9 (d), 129.1 (d), 129.0 (d, 2C), 127.2 (d, 2C), 107.0 (d, 2C), 98.2 (d), 55.2 (q, 2C), 41.6 (d), 41.5 (t), 40.5 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3000, 2935, 2838, 1688, 1595, 1572, 1493, 1463, 1429, 1312, 1294, 1267, 1204, 1152, 1066; MS (FAB+, NBA): m/z (%): 308 (52)[M^+], 151 (100), 128 (37); HRMS (FAB+): $\text{C}_{20}\text{H}_{20}\text{O}_3$: calcd. 308.1413, found 308.1407.

4-(3,5-Dimethoxybenzyl)-3-vinylcyclohex-2-enone (8e): Treatment of vinylogous ester **22a** (480 mg, 1.51 mmol) with a 1M solution of (vinyl)MgBr (3.02 ml, 3.02 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8e** (246 mg, 0.906 mmol, 60%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 6.45 (dd, $J_{\text{H,H}}$ = 10.8, 17.6 Hz, 1H), 6.36 (s, 3H), 5.96 (s, 1H), 5.85 (s, 1H), 5.81 (s, 1H), 5.55 (d, $J_{\text{H,H}}$ = 10.8 Hz, 1H), 3.80 (s, 6H), 3.01-2.89 (m, 2H), 2.65-2.53 (m, 2H), 2.38 (dt, $J_{\text{H,H}}$ = 3.5, 17.8 Hz, 1H), 1.98-1.91 (m, 2H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 200.0 (s), 161.2 (s, 2C), 160.3 (s), 142.3 (s), 137.0 (d), 127.9 (d), 121.1 (t), 107.2 (d, 2C), 98.1 (d), 55.5 (q, 2C), 37.9 (t), 35.2 (d), 33.0 (t), 24.8 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 2960, 1937, 2876, 2838, 1692, 1594, 1464, 1429, 1381, 1351, 1290, 1235, 1205, 1153, 1066; MS (FAB+, NBA, LiCl): m/z (%): 279 (88)[$\text{M}+\text{Li}^+$], 273 (31), 152 (57), 151 (100); HRMS (FAB+): $\text{C}_{17}\text{H}_{20}\text{O}_3$: calcd. 272.1415, found 272.1414.

8f

4-Benzyl-3-methyl-cyclohex-2-enone (8f): Treatment of vinylogous ester **22d** (180 mg, 0.698 mmol) with a 3M solution of MeMgCl (0.255 ml, 0.767 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8f** (56 mg, 0.28 mmol, 40%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.35-7.13 (m, 5H), 5.87 (s, 1 H), 3.02 (dd, $J_{\text{H,H}}$ = 12.6, 3.5 Hz, 1H), 2.56-2.37 (m, 3H), 2.23 (dt, $J_{\text{H,H}}$ = 17.3, 5.1 Hz, 1H), 1.98 (s, 3H), 1.97-1.81 (m, 1H), 1.78-1.66 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.2 (s), 165.1 (s), 139.7 (s), 128.9 (d, 2C), 128.6 (d, 2C), 127.1 (d), 126.5 (d), 41.5 (d), 37.4 (t), 33.4 (t), 26.0 (t), 23.3 (q); IR (film): $\nu[\text{cm}^{-1}]$ = 3084, 3061, 3026, 3942, 1667, 1626, 1453, 1378, 1329, 1250, 1199; MS (FAB+, NBA): m/z (%): 201(100)[$\text{M}+\text{H}^+$]; HRMS (FAB+): $\text{C}_{14}\text{H}_{17}\text{O}^+$: calcd 201.1279, found 201.1274.

8g

4-(3-Methoxy-benzyl)-3-methyl-cyclohex-2-enone (8g): Treatment of vinylogous ester **22e** (866 mg, 3.01 mmol) with a 3M solution of MeMgCl (1.10 ml, 3.30 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8g** (578 mg, 2.51 mmol, 84%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.20 (t, $J_{\text{H,H}}$ = 7.9 Hz, 1H), 6.80-6.66 (m, 3H), 5.84 (s, 1H), 3.76 (s, 3H), 2.98 (m, 1H), 2.58-2.34 (m, 3H), 2.21 (dt, $J_{\text{H,H}}$ = 17.4, 5.3 Hz, 1H), 1.97 (s, 3H), 1.93-1.82 (m, 1H), 1.77-1.66 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.1 (s), 165.1 (s), 159.8 (s), 141.3 (s), 129.6 (d), 126.9 (d), 121.2 (d), 114.8 (d), 111.4 (d), 55.2 (q), 41.3 (d), 37.4 (t), 33.4 (t), 26.0 (t), 23.2 (q); IR (film): $\nu[\text{cm}^{-1}]$ = 3053, 3000, 2942, 2836, 1668, 1600, 1584, 1489, 1455, 1437, 1379, 1346, 1316, 1291, 1259, 1200, 1153, 1083; MS (FAB+, NBA, LiCl): m/z (%): 467 (20) [$2\text{M}+\text{Li}^+$], 237 (100) [$\text{M}+\text{Li}^+$], 231 (85) [$\text{M}+\text{H}^+$]; HRMS (FAB+): $\text{C}_{15}\text{H}_{19}\text{O}_2$: calcd. 231.1385, found 231.1387.

8h

4-(2-Iodo-3-methoxy-benzyl)-3-methyl-cyclohex-2-enone (8h): Treatment of vinylogous ester **22f** (1.24 g, 298 mmol) with a 3M solution of MeMgCl (1.57 ml, 4.71 mmol) and concomitant acid hydrolysis using the general procedure described above afforded **8h** (765 mg, 2.15 mmol, 72%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.22 (t, $J_{\text{H,H}}$ = 8.0 Hz, 1H), 6.80 (dd, $J_{\text{H,H}}$ = 17.4, 1.1 Hz, 1H), 6.68 (dd, $J_{\text{H,H}}$ = 8.2, 0.9 Hz, 1H), 5.87 (s, 1H), 3.86 (s, 3H), 3.20 (m, 1H), 2.81-2.67 (m, 2H), 2.60-2.48 (m, 1H), 2.27 (dt, $J_{\text{H,H}}$ = 17.4, 5.1 Hz, 1H), 2.06 (d, $J_{\text{H,H}}$ = 1.1 Hz, 3H), 1.92-1.79 (m, 1H), 1.78-1.68 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 199.1 (s), 165.2 (s), 158.3 (s), 143.8 (s), 129.0 (d), 127.1 (d), 123.2 (d), 109.0 (d), 92.8 (d), 56.5 (q), 42.0 (t), 39.1 (d), 33.6 (t), 25.6 (t), 23.2 (q); IR (film): $\nu[\text{cm}^{-1}]$ = 3004, 2941, 2866, 2837, 1667, 1624, 1586, 1566, 1465, 1427, 1378, 1346, 1332, 1317, 1293, 1264, 1200, 1185, 1146, 1071; MS (FAB+, NBA): m/z (%): 719(20) [$2\text{M}+\text{Li}^+$], 363(100) [$\text{M}+\text{Li}^+$], 357(100) [$\text{M}+\text{H}^+$], 247 (34); HRMS (FAB+): $\text{C}_{15}\text{H}_{18}\text{O}_2\text{I}$: calcd 357.0352, found 357.0358.

Procedure for the Optimization of the Friedel-Crafts Triflation

Triflic anhydride (26.0 mg, 92.2 μmol , 15.5 μl) was dissolved in 0.5 ml solvent, and a solution of enone **3** (16.0 mg, 61.5 μmol) and base (65.3 μmol) in 0.5 ml solvent was added dropwise at room temperature to the stirred solution. After complete addition, the mixture was stirred for an additional 20 minutes. The solvent was then removed in vacuo, and the residue was dissolved in DCM. A few drops of triethylamine were added, and the mixture was concentrated again and dried under high vacuum. 1,4-Dimethoxybenzene was added, the mixture was redissolved in DCM, homogenized, and concentrated again in vacuo. The mixture was then checked by ^1H -NMR in a CDCl_3 solution.

General Procedure for Intramolecular Friedel-Crafts Triflations

Triflic anhydride (1.50 eq) was dissolved in nitromethane (4 ml/ 0.1 mmol enone) at 0°C and a solution of **3** or **8** (1.00 eq) and DTBP (1.01 eq) in nitromethane (4 ml/ 0.1 mmol enone) was added dropwise to the vigorously stirred solution. After TLC monitoring showed complete conversion of **3** or **8** (5–25 minutes) a concentrated NaHCO₃ solution (1 ml/ml nitromethane) was added while stirring vigorously. The mixture stirred at 0°C for an additional 60 minutes and was then poured over dichloromethane (5 ml/ml nitromethane). The layers were separated and the aqueous layer extracted again with the same amount of dichloromethane. The combined organic layers were washed with brine (1 ml/10 ml DCM), dried over Na₂SO₄, concentrated, and purified by column chromatography. The best results were obtained when the crude mixture was transferred onto the column expediently following removal of all volatiles.

7

Trifluoro-methanesulfonic acid 5,7-dimethoxy-4a-methyl-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (7): Triflic anhydride promoted cyclization using enone **3** (45 mg, 0.17 mmol) using the general procedure described above afforded **7** (47 mg, 0.12 mmol, 70%) ; ¹H NMR (CDCl₃, 400.2 MHz): δ = 6.33 (s, 1H), 6.28 (d, *J*_{H,H} = 1.7 Hz, 1H), 6.18 (s, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.02 (dd, *J*_{H,H} = 7.8, 15.9 Hz, 1H), 2.60 (dd, *J*_{H,H} = 5.4, 10.5 Hz, 1H), 2.35 (m, 2H), 2.22 (m, 1H), 1.96-1.88 (m, 1H), 1.79-1.70 (m, 1H), 1.40 (s 3H); ¹³C NMR (CDCl₃, 100.6 MHz): δ = 161.0 (s), 157.4 (s), 147.9 (s), 143.8 (s), 127.0 (s), 124.8 (d), 118.8 (s, *q*, *J*_{C,F} = 320.2 Hz), 101.6 (d), 97.4 (d), 55.7 (q), 55.3 (q), 48.7 (s), 44.5 (d), 36.2 (t), 26.3 (d), 25.7 (t), 25.4 (t); IR (film): ν[cm⁻¹] = 2957, 2864, 2840, 1596, 1578, 1488, 1465, 1416, 1360, 1334, 1309, 1288, 1247, 1210, 1144, 1093, 1028; MS (FAB+, NBA): *m/z* (%): 393 (82)[M+H⁺], 392 (94), 377 (100), 259 (32); HRMS (FAB+): C₁₇H₁₉O₅F₃S: calcd. 392.0905, found 392.0908.

9a

Trifluoro-methanesulfonic acid 5,7-dimethoxy-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (9a): Triflic anhydride promoted cyclization using enone **8a** (111 mg, 0.452 mmol) using the general procedure described above afforded **9a** (73 mg, 0.19 mmol, 43%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 6.37 (d, $J_{\text{H,H}}$ = 1.8 Hz, 1H), 6.28 (d, $J_{\text{H,H}}$ = 2.0 Hz, 1H), 6.18-6.14 (m, 1H), 3.93-3.87 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.97-2.87 (m, 1H), 2.75-2.62 (m, 2H), 2.47-2.30 (m, 2H), 1.98-1.87 (m, 1H), 1.87-1.74 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 160.9 (s), 156.9 (s), 148.6 (s), 1144.6 (s), 122.7 (s), 119.7 (d), 118.5 (s, q , $J_{\text{C,F}}$ = 320.3 Hz), 101.3 (d), 96.7 (d), 55.5 (q), 55.1 (q), 42.2 (d), 36.4 (d), 36.3 (t), 25.3 (t), 25.1 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3001, 2938, 2840, 1686, 1599, 1491, 466, 1456, 1416, 1364, 1336, 1313, 1289, 1246, 1209, 1143, 1114, 1081, 1049, 1032; MS (FAB+, NBA): m/z (%): 379 (72)[$\text{M}+\text{H}^+$], 378 (69) [M^+], 245 (100); HRMS (FAB+): $\text{C}_{16}\text{H}_{16}\text{O}_5\text{F}_3\text{S}$ [$\text{M}-\text{H}^+$]: calcd. 377.0670, found 377.0664.

9b

Trifluoro-methanesulfonic acid 5,7-dimethoxy-4a-phenyl-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (9b): Triflic anhydride promoted cyclization using enone **8b** (50 mg, 0.16 mmol) using the general procedure described above afforded **9b** (51 mg, 0.11 mmol, 72%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.25 (m, 3H), 7.10 (dt, $J_{\text{H,H}}$ = 7.0, 1.6 Hz, 2H), 6.46 (d, $J_{\text{H,H}}$ = 2.1 Hz, 1H), 6.35 (d, $J_{\text{H,H}}$ = 2.1 Hz, 1H), 6.29 (s, 1H), 3.85 (s, 3H), 3.61 (s, 3H), 2.96 (dd, $J_{\text{H,H}}$ = 7.9, 15.5 Hz, 1H), 2.66 (dd, $J_{\text{H,H}}$ = 6.1, 15.5, 1H), 2.51 (m, 3H), 1.93 (m, 1H), 1.79 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 161.4(s), 157.3 (s), 148.9 (s), 145.8 (s), 145.3 (s), 128.1 (d, 2C), 126.6 (d, 2C), 126.2 (d), 124.6 (s), 122.7 (d), 118.5 (s, q , $J_{\text{C,F}}$ = 318.9 Hz), 101.3 (d), 97.4 (d), 56.9 (s), 55.4 (q), 55.0 (q), 47.7 (d), 35.6 (t), 25.3(t), 24.4 (t); IR

(film): $\nu[\text{cm}^{-1}] = 3058, 3002, 2938, 2840, 1684, 1597, 1455, 1416, 1336, 1210, 1144, 1051, 881, 860$; MS (FAB+, NBA): m/z (%): 454 (100)[M^+], 377 (26), 321 (39); HRMS (FAB+): $\text{C}_{22}\text{H}_{21}\text{O}_5\text{F}_3\text{S}$: calcd. 454.1062, found 454.1072.

Trifluoro-methanesulfonic acid 11,11b-dimethyl-4,4a,5,6,11,11b-hexahydro-3H-benzo[a]carbazol-2-yl ester (9c): Triflic anhydride promoted cyclization using enone **8c** (60 mg, 0.22 mmol) using the general procedure described above afforded **9c** (56 mg, 0.14 mmol, 63%); ^1H NMR (CDCl_3 , 400.2 MHz): $\delta = 7.53$ (d, $J_{\text{H,H}} = 7.8$ Hz, 1H), 7.33 (d, $J_{\text{H,H}} = 8.3$ Hz, 1H), 7.26 (m, 1H), 7.15 (dt, $J_{\text{H,H}} = 1.0, 7.0$ Hz, 1H), 6.27 (s, 1H), 3.85 (s, 3H), 2.84-2.77 (m, 2H), 2.51 (m, 1H), 2.39 (m, 1H), 2.19-2.08 (1H), 2.04-1.84 (m, 4H), 1.62 (s, 3H); ^{13}C NMR (CDCl_3 , 100.6 MHz): $\delta = 149.7$ (s), 138.3 (s), 137.6 (s), 126.4 (s), 123.9 (d), 121.5 (d), 119.0 (d), 118.5 (s, q , $J_{\text{C,F}} = 320.4$ Hz), 118.3 (d), 108.7 (d), 108.2 (s), 40.9 (d), 37.9 (s), 32.0 (q), 28.5 (q), 26.6 (t), 24.9 (t), 24.3 (t), 18.4 (t); IR (film): $\nu[\text{cm}^{-1}] = 3054, 2933, 1684, 1470, 1417, 1368, 1311, 1244, 1211, 1142, 1105, 1063, 1076, 1044, 1020$; MS (FAB+, NBA): m/z (%): 399 (100)[M]; HRMS (FAB+): $\text{C}_{19}\text{H}_{20}\text{NO}_3\text{F}_3\text{S}$: calcd. 399.1116, found 399.1122.

Trifluoro-methanesulfonic acid 4,6-dimethoxy-3a-phenyl-1,3a,8,8a-tetrahydro-cyclopenta[a]inden-2-yl ester (9d): Triflic anhydride promoted cyclization using enone **8d** (65 mg, 0.21 mmol) using the general procedure described above afforded **9d** (45 mg, 0.10 mmol 48%); ^1H NMR (CD_2Cl_2 , 400.2 MHz): $\delta = 7.48$ (d, $J_{\text{H,H}} = 7.3$ Hz, 2H), 7.36 (t, $J_{\text{H,H}} = 7.8$ Hz, 2H), 7.29 (m, 1H), 6.88 (s, 1H), 6.32 (d, $J_{\text{H,H}} = 2.2$ Hz, 1H), 6.22 (d, $J_{\text{H,H}} = 2.1$ Hz, 1H), 3.83 (s, 3H), 3.73 (s, 3H), 3.65 (t, $J_{\text{H,H}} = 5.1$ Hz, 1H), 3.25 (dd, $J_{\text{H,H}} = 4.9, 17.5$ Hz, 1H), 2.84-2.68 (m, 3H); ^{13}C NMR (CD_2Cl_2 , 100.6 MHz): $\delta =$

160.2 (s), 155.9 (s), 142.1 (s), 136.3 (s), 133.1 (s), 130.3 (d), 128.6 (d, 2C), 128.4 (d), 126.0 (d, 2C), 119.0 (s), 118.3 (s, q , $J_{C,F}$ = 319.6 Hz), 106.4 (d), 102.3 (s), 96.5 (d), 55.2 (q), 55.1 (q), 47.7 (t), 39.1 (d), 31.8 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 2943, 2838, 1605, 1581, 1570, 1405, 1338, 1312, 1288, 1245, 1204, 1146, 1093, 1061, 1032, 1007; MS (FAB+, NBA): m/z (%): 440 (72)[M], 291 (34), 265 (100); HRMS (FAB+): $\text{C}_{21}\text{H}_{19}\text{O}_5\text{F}_3\text{S}$: calcd. 440.0905, found 440.0907.

9e

Trifluoro-methanesulfonic acid 7,9-dimethoxy-4,4a,5,10-tetrahydro-3H-dibenzo[*a,d*]cyclohepten-2-yl ester (9e): Triflic anhydride promoted cyclization using enone **8e** (28 mg, 0.10 mmol) using the general procedure described above afforded **9e** (32 mg, 0.080 mmol, 77%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 6.35 (d, $J_{\text{H,H}}$ = 4.1 Hz, 2H), 6.00 (s, 1H), 5.77 (d, $J_{\text{H,H}}$ = 7.8 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.74 (dd, $J_{\text{H,H}}$ = 8.5, 17.6 Hz, 1H), 3.35 (d, $J_{\text{H,H}}$ = 17.6 Hz, 1H), 3.16 (t, $J_{\text{H,H}}$ = 12.5 Hz, 1H), 2.66 (d, $J_{\text{H,H}}$ = 13.1 Hz, 1H), 2.61 (m, 1H), 2.42-2.26 (m, 2H), 1.95 (bm, 1H), 1.82-1.62 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 159.1 (s), 156.8 (s), 147.9 (s), 142.7 (s), 135.8 (s), 129.4 (d), 124.0 (d), 120.5 (s), 118.7 (s, q , $J_{C,F}$ = 320.2 Hz), 105.5 (d), 96.6 (d), 55.9 (q), 55.5 (q), 39.7 (t), 37.9 (d), 31.2 (t), 28.7 (t), 23.1 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 2940, 2839, 1607, 1494, 1456, 1417, 1314, 1247, 1206, 1144, 1098, 1048; MS (FAB+, NBA): m/z (%): 405 (22)[M+H], 403 (17)[M-H], 271 (100); HRMS (FAB+): $\text{C}_{18}\text{H}_{18}\text{O}_5\text{F}_3\text{S}$ [M-H]: calcd. 403.0827, found 403.0828.

Conditions employing resubjection to triflic acid

Treatment of enone **8f** (45 mg, 0.23 mmol) with triflic anhydride following general procedure for intramolecular cyclizations outlined above produced, after chromatography, an inseparable mixture of dienes **10a** and **b** (63 mg, 0.19 mmol, 84%, 1.2 **10a**: 1 **10b**). The mixture was dissolved in 5 ml dry dichloromethane and treated with triflic acid (0.038 mmol) at 0°C. After 15 minutes the mixture was quenched by the addition of triethylamine (0.1 ml), concentrated *in vacuo*, and purified by column chromatography to afford a 14:1 mixture of **10b**:**10a** (55mg, 0.17mmol, 88%). The spectral data below correspond to **10b**. ¹H NMR (CDCl₃, 400.2 MHz): δ = 7.27-7.34 (m, 2H), 7.13-7.26 (m, 3H), 5.86 (s, 1H), 3.47 (s, 2H), 2.39-2.51 (m, 2H), 2.25-2.36 (m, 2H), 1.89 (s, 3H); ¹³C NMR (CDCl₃, 100.6 MHz): δ = 147.0 (s), 139.4 (s), 130.6 (s), 128.5 (d, 2C), 128.4 (d, 2C), 126.3 (d), 123.4 (s), 119.8 (s), 118.5 (s, *q*, *J*_{C,F} = 320.1 Hz), 38.2 (t), 28.8 (t), 26.2 (t), 17.8 (q); IR (film): ν[cm⁻¹] = 3028, 2936, 1677, 1494, 1436, 1419, 1249, 1211, 1141, 1054, 887, 844; MS (FAB+, NBA): *m/z* (%): 332 (100)[M], 255 (10), 199 (30), 157 (40); HRMS (FAB+): C₁₅H₁₅O₃F₃S: calcd. 332.0694, found 332.0690.

Reaction of **8g** (100 mg, 0.43 mmol) with triflic anhydride following general procedure for intramolecular cyclizations outlined above produced, after chromatography, an inseparable mixture of **12a** and **b** and the dienes **11a** and **b** (87 mg, 0.24 mmol, 55% yield). The mixture was dissolved in 5 ml dry dichloromethane and treated with triflic acid (0.043 mmol) at 0°C. After 15 minutes the mixture was quenched by the addition of triethylamine (0.1

ml), concentrated *in vacuo*, and purified by column chromatography to afford **12a** (7 mg, 0.02 mmol, 8%) and **12b** (55 mg, 0.15 mmol, 63 %).

12a

Trifluoro-methanesulfonic acid 5-methoxy-4a-methyl-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (12a): ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.15 (t, $J_{\text{H,H}}$ = 7.9 Hz, 1H), 6.80 (d, $J_{\text{H,H}}$ = 7.4 Hz, 1H), 6.69 (d, $J_{\text{H,H}}$ = 8.0 Hz, 1H), 6.24 (s, 1H), 3.82 (s, 3H), 3.08 (dd, $J_{\text{H,H}}$ = 15.8, 7.6 Hz, 1H), 2.63 (dd, $J_{\text{H,H}}$ = 15.8, 4.8 Hz, 1H), 2.43-2.28 (m, 2H), 2.22 (m, 1H), 1.98-1.86 (m, 1H), 1.74 (m, 1H), 1.42 (s, 3H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 156.6 (s), 148.0 (s), 142.8 (s), 134.3 (s), 128.6 (d), 124.4 (d), 118.6 (s, q , $J_{\text{C,F}}$ = 320.5 Hz), 117.7 (d), 108.9 (d), 55.1 (q), 49.1 (s), 44.1 (d), 35.7 (t), 25.9 (q), 25.6 (t), 25.4 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 2959, 2931, 2851, 1601, 1589, 1479, 1465, 1458, 1441, 1421, 1414, 1374, 1264, 1248, 1209, 1142, 1083; MS (FAB+, NBA): m/z (%): 362 (47)[$\text{M}+\text{H}^+$], 347 (100), 307 (38); HRMS (FAB+): $\text{C}_{16}\text{H}_{17}\text{O}_4\text{F}_3\text{S}$: calcd. 362.0800, found 362.0805.

12b

Trifluoro-methanesulfonic acid 7-methoxy-4a-methyl-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (12b): ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.04 (m, 1H), 6.79-6.73 (m, 2H), 5.72 (s, 1H), 3.79 (s, 3H), 2.95 (dd, $J_{\text{H,H}}$ = 7.8, 15.8 Hz, 1H), 2.72 (dd, $J_{\text{H,H}}$ = 8.3, 15.8 Hz, 1H), 2.51-2.31 (m, 3H), 2.06-1.95 (m, 1H), 1.90-1.78 (m, 1H), 1.40 (s, 3H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 159.3 (s), 147.5 (s), 142.8 (s), 140.2 (s), 124.8 (d), 123.1 (d), 119.0 (s, q , $J_{\text{C,F}}$ = 320.2 Hz), 112.6 (d), 110.6 (d), 55.3 (q), 47.5 (s), 44.4 (d), 34.4 (t), 26.7 (d), 24.7 (t), 23.6 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3002, 2956, 2931, 2864, 2837, 1684, 1608, 1587, 1489, 1467, 1444, 1417, 1376, 1363, 1319,

1291, 1263, 1246, 1210, 1141, 1117, 1107, 1084, 1069, 1027; MS (FAB+, NBA, LiCl): m/z (%): 362 (100)[$M+H^+$], 347 (89); HRMS (FAB+): $C_{16}H_{17}O_4F_3S$: calcd. 362.0780, found 362.0794.

14

Trifluoro-methanesulfonic acid 8-iodo-7-methoxy-4a-methyl-2,4a,9,9a-tetrahydro-1H-fluoren-3-yl ester (14): Reaction of **8h** (100 mg, 0.28 mmol) with triflic anhydride following general procedure for intramolecular cyclizations described above produced, after chromatography, an inseparable mixture of the dienes **13a** and **13b** (84 mg, 0.17 mmol, 61% yield). The mixture was dissolved in 5 ml dry dichloromethane and treated with triflic acid (0.043 mmol) at 0°C. After 15 minutes the mixture was quenched by the addition of triethylamine (0.1 ml), concentrated *in vacuo* and purified by column chromatography to afford **14** (48 mg, 0.10 mmol, 59 %). 1H NMR ($CDCl_3$, 400.2 MHz): δ = 7.05 (d, $J_{H,H}$ = 8.2 Hz, 1H), 6.66 (d, $J_{H,H}$ = 8.2 Hz, 1H), 5.70 (s, 1H), 3.87 (s, 3H), 2.99 (dd, $J_{H,H}$ = 7.8, 16.6 Hz, 1H), 2.70 (dd, $J_{H,H}$ = 7.3, 16.5 Hz, 1H), 2.52-2.28 (m, 3H), 2.06-1.95 (m, 1H), 1.92-1.79 (m, 1H), 1.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 157.5 (s), 147.9 (s), 147.7 (s), 141.0 (s), 124.5 (d), 122.8 (d), 118.6 (s, q , $J_{C,F}$ = 319.8 Hz), 109.5 (d), 86.1 (s), 56.6 (q), 49.2 (s), 44.4 (d), 43.1 (t), 27.0 (q), 24.6 (t), 23.6 (t); IR (film): $\nu[cm^{-1}]$ = 2959, 2934, 2864, 2839, 1688, 1680, 1599, 1566, 1467, 1413, 1363, 1310, 1264, 1247, 1211, 1142, 1098, 1055, 1028; MS (FAB+, NBA, LiCl): m/z (%): 488 (93)[M], 473 (100); HRMS (FAB+): $C_{16}H_{16}O_4F_3SI$: calcd 487.9766, found 487.9780.

General Procedure for Intermolecular Friedel-Crafts Triflation

Arene (3 eq), enone (1 eq) and DTBP (1.2 eq) were dissolved in dry acetonitrile (5 ml/mmol enone), and the solution was cooled to 0°C. Neat triflic anhydride (1.1 eq) was added dropwise under vigorous stirring. After complete addition, the reaction mixture was stirred for an additional 10 minutes before a concentrated $NaHCO_3$ solution (0.4 ml/ml acetonitrile) was added. The mixture was stirred at 0°C for 1 hour and slowly warmed to room temperature over 30 minutes. After stirring an additional 15 minutes at room

temperature, the mixture was poured over dichloromethane (5 ml/ml MeCN), the layers were separated, and the aqueous layer was extracted again with the same amount of dichloromethane. The combined organic layers were washed with brine (1 ml/ml MeCN), dried over Na₂SO₄, concentrated, and purified by column chromatography. The best results were obtained when the crude mixture was transferred without delay directly after removal of all volatiles onto the column.

15a

Trifluoro-methanesulfonic acid 3-(2-methoxy-phenyl)-cyclohex-1-enyl ester (15a). The Friedel-Crafts triflation of 2-cyclohexen-1-one (44 mg, 0.46 mmol) with anisole (0.10 mL, 0.90 mmol) was performed using the general procedure outlined above to afford **15a** (42 mg, 0.12 mmol, 29%); ¹H NMR (CDCl₃, 400.2 MHz): δ = 7.23 (dt, *J*_{H,H} = 8.1, 1.7 Hz, 1H), 7.11 (dd, *J*_{H,H} = 7.5, 1.56 Hz, 1H), 6.94 (dt, *J*_{H,H} = 7.5, 0.8 Hz, 1H), 6.87 (d, *J*_{H,H} = 8.3, 1H), 5.79 (m, 1H), 4.04 (m, 1H), 3.84 (s, 3H), 2.50-2.32 (m, 2H), 2.03-1.93 (m, 1H), 1.91-1.70 (m, 2H), 1.58-1.47 (m, 1H); ¹³C NMR (CDCl₃, 100.6 MHz): δ = 156.5 (s), 150.2 (s), 131.6 (s), 128.2 (d), 127.7 (d), 121.7 (d), 120.5 (d), 118.5 (s, *q*, *J*_{C,F} = 319.9 Hz), 110.2 (d), 55.2 (q), 34.2 (d), 28.5 (t), 27.6 (t), 21.0 (t); IR (film): ν[cm⁻¹] = 3067, 3005, 2944, 2865, 2840, 1686, 1600, 1587, 1493, 1464, 1416, 1363, 1340, 1290, 1243, 1210, 1142, 2942, 2864, 2839, 1685, 1611, 1584, 1513, 1416, 1302, 1244, 1211, 1179, 1142; MS (FAB+, NBA): *m/z* (%): 336 (73)[M⁺], 335 (52), 229 (68), 203 (100); HRMS (FAB+): C₁₄H₁₅O₃F₄S: calcd. 336.0643, found 336.0642.

15b

Trifluoro-methanesulfonic acid 3-(4-methoxy-phenyl)-cyclohex-1-enyl ester (15b): The Friedel-Crafts triflation of 2-cyclohexen-1-one (44 mg,

0.45 mmol) with anisole (0.10 mL, 0.90 mmol) was performed using the general procedure outlined above to afford **15b** (57 mg, 0.17 mmol, 37%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.11 (d, $J_{\text{H,H}}$ = 8.8 Hz, 2H), 6.87 (d, $J_{\text{H,H}}$ = 8.7 Hz, 2H), 5.82 (m, 1H), 3.80 (s, 3H), 3.57 (m, 1H), 2.50-2.32 (m, 2H), 2.03-1.95 (m, 1H), 1.95-1.85 (m, 1H), 1.82-1.70 (m, 1H), 1.54-1.46 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 158.6 (s), 150.4 (s), 136.1 (s), 128.7 (d, 2C), 122.0 (d), 118.8 (s, q , $J_{\text{C,F}}$ = 322.2 Hz), 114.2 (d, 2C), 55.5 (q), 40.7 (d), 31.6 (t), 27.8 (t), 21.3 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3002, 2942, 2864, 2839, 1685, 1611, 1584, 1513, 1416, 1302, 1244, 1211, 1179, 1143, 1067, 1029; MS (FAB+, NBA): m/z (%): 336 (95)[M^+], 335 (62), 229 (60), 203 (100); HRMS (FAB+): $\text{C}_{14}\text{H}_{15}\text{O}_3\text{F}_4\text{S}^+$: calcd. 336.0643, found 336.0644.

16

Trifluoro-methanesulfonic acid 3-(2,4-dimethoxy-phenyl)-cyclohex-1-enyl ester (16): The Friedel-Crafts triflation of 2-cyclohexen-1-one (148 mg, 1.54 mmol) with 1,3-dimethoxybenzene (0.60 mL, 4.6 mmol) was performed using the general procedure outlined above to afford **16** (254 mg, 0.693 mmol, 45%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.03 (d, $J_{\text{H,H}}$ = 9.1 Hz, 1H), 6.51-6.48 (m, 2H), 5.79 (m, 1H), 3.97 (m, 1H), 3.83 (s, 3H), 3.83 (q, 3H), 2.53-2.29 (m, 2H), 2.04-1.68 (m, 3H), 1.60-1.46 (m, 1H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 159.7 (s), 157.6 (s), 150.1 (s), 128.7 (d), 124.2 (s), 122.1 (d), 118.5 (s, q , $J_{\text{C,F}}$ = 319.8 Hz), 103.9 (d), 98.7 (d), 55.4 (q), 55.3 (q), 33.9 (d), 28.8 (t), 27.8 (t), 21.0 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3002, 2944, 2864, 1613, 1588, 1207, 1141, 1026, 900, 840; MS (FAB+, NBA): m/z (%): 366 (100)[M^+], 233 (57); HRMS (FAB+): $\text{C}_{15}\text{H}_{17}\text{O}_5\text{F}_3\text{S}^+$: calcd. 366.0749, found 366.0745.

17

Trifluoro-methanesulfonic acid 3-(1-methyl-1*H*-indol-3-yl)-cyclohex-1-enyl ester (17): The Friedel-Crafts triflation of 2-cyclohexen-1-one (100 mg, 1.04 mmol) with *N*-methylindole (410 mg, 3.13 mmol) was performed using the general procedure outlined above to afford **17** (250 mg, 0.694 mmol, 67%); ^1H NMR (CDCl_3 , 400.2 MHz): δ = 7.63 (d, $J_{\text{H,H}}$ = 7.9 Hz, 1H), 7.35 (d, $J_{\text{H,H}}$ = 8.2 Hz, 1H), 7.28 (t, $J_{\text{H,H}}$ = 7.4 Hz, 1H), 7.16 (t, $J_{\text{H,H}}$ = 7.4 Hz, 1H), 6.84 (s, 1H), 5.99 (bs, 1H), 3.99 (bs, 1H), 3.79 (s, 3H), 2.46 (bs, 2H), 2.10-1.99 (m, 1H), 1.96-1.76 (m, 3H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 149.9 (s), 137.2 (s), 126.7 (d), 126.4 (s), 121.8 (d), 121.7 (d), 118.9 (d), 118.8 (d), 118.5 (s, q , $J_{\text{C,F}}$ = 320.2 Hz), 116.6 (s), 109.4 (d), 32.7 (q), 32.1 (d), 28.8 (t), 27.7 (t), 20.4 (t); IR (film): $\nu[\text{cm}^{-1}]$ = 3056, 3028, 2943, 2864, 1684, 1615, 1549, 1472, 1417, 1375, 1362, 1329, 1302, 1243, 1210, 1143, 1070, 1029, 1011; MS (FAB+, NBA): m/z (%): 359 (100)[M], 226 (47); HRMS (FAB+): $\text{C}_{16}\text{H}_{16}\text{NO}_3\text{F}_3\text{S}$: calcd. 359.0803, found 359.0801.

18

Trifluoro-methanesulfonic acid 3-(5-methyl-furan-2-yl)-cyclohex-1-enyl ester (18): The Friedel-Crafts triflation of 2-cyclohexen-1-one (100 mg, 1.04 mmol) with sylvan (256 mg, 3.12 mmol) was performed using the general procedure outlined above to afford **18** (164 mg, 0.529 mmol, 51%); ^1H NMR (CD_2Cl_2 , 400.2 MHz): δ = 5.92-5.84 (m, 3H), 3.65 (s, 1H), 2.36 (m, 2H), 2.24 (s, 3H), 1.97-1.81 (m, 2H), 1.81-1.68 (m, 2H); ^{13}C NMR (CDCl_3 , 100.6 MHz): δ = 154.0 (s), 151.2 (s), 150.7 (s), 118.9 (d), 118.6 (s, q , $J_{\text{C,F}}$ = 320.2 Hz), 106.2 (d), 105.8 (d), 34.5 (d), 27.4 (t), 26.7 (t), 20.3 (t), 13.1 (q); IR (film): $\nu[\text{cm}^{-1}]$ = 2951, 2868, 1689, 1614, 1565, 1418, 1362,

1244, 1210, 1143, 1070, 1035; MS (EI+): m/z (%): 310 (36)[M], 177 (95), 55 (100); HRMS (FAB+): $C_{12}H_{13}O_4F_3S$: calcd. 310.0486, found 310.0482.

19

Trifluoro-methanesulfonic acid 3-methyl-3-(5-methyl-furan-2-yl)-cyclohex-1-enyl ester (19): The Friedel-Crafts triflation of 3-methyl-2-cyclohexen-1-one (110 mg, 1.00 mmol) with sylvan (256 mg, 3.12 mmol) was performed using the general procedure outlined above to afford **19** (94 mg, 0.29 mmol, 29%); 1H NMR (CD_2Cl_2 , 400.2 MHz): δ = 5.90-5.84 (m, 2H), 5.76 (s, 1H), 2.37-2.31 (m, 2H), 2.25 (s, 3H), 1.97 (ddd, $J_{H,H}$ = 3.2, 6.8, 13.3 Hz, 1H), 1.85-1.68 (m, 2H), 1.54 (m, 1H), 1.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ = 157.7 (s), 151.6 (s), 150.6 (s), 124.6 (d), 119.0 (s, q , $J_{C,F}$ = 320.4 Hz), 106.3 (d), 106.1 (d), 38.4 (s), 34.5 (t), 27.9 (t), 27.1 (q), 19.9 (t), 13.7 (q); IR (film): $\nu[cm^{-1}]$ = 2948, 2872, 1688, 1610, 1557, 1455, 1418, 1362, 1248, 1210, 1143, 1115, 1097, 1066, 1022; MS (FAB+, NBA): m/z (%): 324 (28)[M], 309 (84), 176 (100), 148 (37); HRMS (FAB+): $C_{13}H_{15}O_4F_3S$: calcd. 324.0643, found 324.0649.

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