Intramolecular [4+2] Cycloadditions of Iminoacetonitriles. A New Class of Azadienophiles for Hetero Diels-Alder Reactions

Supporting Information

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General Procedures. All reactions were performed in flame-dried glassware under a positive pressure of argon or nitrogen. Reaction mixtures (with the exception of sealed-tube reactions) were stirred magnetically unless otherwise indicated. Air- and moisture-sensitive liquids and solutions were transferred by syringe or cannula and were introduced into reaction vessels through rubber septa. Reaction product solutions and chromatography fractions were concentrated by using a Bchi rotary evaporator at ca. 20 mmHg and then at ca. 0.1 mmHg (vacuum pump) unless otherwise indicated. Column chromatography was performed on Silicycle silica gel 60 (230-400 mesh).

Materials. Commercial grade reagents and solvents were used without further purification except as indicated below. Tetrahydrofuran was distilled from sodium benzophenone ketyl or dianion, or purified by pressure filtration through activated alumina. Toluene was distilled from calcium hydride or purified by pressure filtration through activated alumina. *N,N*-Diisopropylethylamine was distilled under argon from calcium hydride. Trifluoromethanesulfonic anhydride was distilled under argon from phosphorus pentoxide.

Instrumentation. Melting points were determined with a Fischer-Johns melting point apparatus and are uncorrected. ¹H NMR spectra were measured with a Inova 500 (500 MHz)

spectrometer using CDCl₃ as solvent. ¹³C NMR spectra were measured with Mercury-300 (75 MHz) and Inova 500 (125 MHz) spectrometers using CDCl₃ as solvent. ¹H NMR chemical shifts are expressed in parts per million (δ) downfield from tetramethylsilane; ¹³C NMR chemical shifts are expressed in parts per million (δ) relative to CDCl₃. Infrared spectra were obtained using a Perkin Elmer 1320 grating spectrophotometer and a Perkin Elmer 2000 FT-IR. Elemental analyses were performed by Complete Analysis Laboratories, Inc. of Parsippany, NJ.

***N*-(Cyanomethyl)trifluoromethanesulfonamide.** A 100-mL, three-necked, round-bottomed flask equipped with a rubber septum, glass stopper, and argon inlet adapter was charged with NCCH₂NH₃Cl (3.00 g, 32.4 mmol) and 50 mL of CH₂Cl₂ and diisopropylethylamine (12.4 mL, 9.22 g, 71.3 mmol) was then added in one portion. The pale yellow solution was next cooled at -78 °C while trifluoromethanesulfonic anhydride (5.7 mL, 9.6 g, 34 mmol) was added by syringe over 6 min. The resulting red-brown solution was stirred at -78 °C for 1 h. Aq 1N HCl solution (30 mL) was then added, and the reaction mixture was allowed to warm to room temperature. The aqueous layer was separated and extracted with three 30-mL portions of CH₂Cl₂, and the combined organic layers were dried over MgSO₄, filtered, and concentrated to give 16.5 g of a brown solid. This material was deposited onto 16 g of silica gel and purified on 55 g of silica gel (elution with 25% EtOAc-hexanes) to afford 3.66 g (60%) of the triflamide as a pale yellow oil: IR (film) 3315, 3001, 2966, 2911, 2721, 2274, 1423, 1382, 1198, 1145, 1091, 996, 910 and 841 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.86 (br s, 1 H) and 4.25 (s, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 119.4 (q, *J* = 320 Hz), 114.5, and 31.9; HRMS [*M*-H]⁻ calcd for C₃H₂F₃N₂O₂S: 186.9784, found: 186.9782.

Representative Procedure for the Synthesis of Triflamides via Mitsunobu Reaction.

***N*-(Cyanomethyl)-*N*-(7-(tert-butyldimethylsiloxymethyl)-(*E*)-5,7-**

octadienyl)trifluoromethanesulfonamide (10). A 50-mL, two-necked, round-bottomed flask equipped with a rubber septum and an argon inlet adapter was charged with triphenylphosphine (1.05 g, 4.02 mmol), a solution of HN(Tf)CH₂CN (0.662 g, 3.52 mmol) in 10 mL of THF, and a solution of alcohol **5** (0.906 g, 3.35 mmol) in 10 mL of toluene. DEAD (0.63 mL, 0.70 g, 4.0 mmol) was added dropwise via syringe over 5 min, and the resulting mixture was stirred at rt for 2 h and then concentrated to give 4.44 g of a white solid. This material was deposited onto 9.0 g of silica gel and purified on 60 g of silica gel (gradient elution with 5-20% EtOAc-hexanes) to provide 1.40 g (94%) of **10** as a colorless oil: IR (film) 2940, 2910, 2880, 2840, 1725, 1600, 1445, 1385, 1245, 1225, 1220, 1035, 1005, 960, 893, 835, and 765 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.10 (d, *J* = 15.9 Hz, 1 H), 5.62 (dt, *J* = 15.9, 7.2 Hz, 1 H), 5.22 (d, *J* = 1.2 Hz, 1 H), 5.02 (br s, 1 H), 4.35 (br s, 2 H), 4.31 (s, 2 H), 3.54 (br m, 2 H), 2.16 (app q, *J* = 7.1 Hz, 2 H), 1.71 (quin, *J* = 7.6 Hz, 2 H), 1.48 (quin, *J* = 7.4 Hz, 2 H), 0.93 (s, 9 H), and 0.09 (s, 6 H); ¹³C NMR (125 MHz, CDCl₃) δ 144.6, 131.1, 128.4, 119.8 (q, *J* = 322 Hz), 113.4, 113.3, 63.2, 49.3, 35.8, 32.4, 26.8, 26.1, 25.7, 18.6, and -5.2; HRMS [M+H]⁺ calcd for C₁₈H₃₂F₃N₂O₃SSi: 441.1850, found: 441.1862.

N-(Cyanomethyl)-N-((*E*)-5,7-octadienyl)trifluoromethanesulfonamide (6). IR (film) 3078, 2983, 2935, 2856, 1745, 1598, 1390, 1200, 1135, 1097, 1030, 1000, 947, and 900 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.31 (ddd, *J* = 17.1, 10.4, 10.4 Hz, 1 H), 6.08 (dd, *J* = 15.3, 10.4 Hz, 1 H), 5.66 (dt, *J* = 15.0, 7.0 Hz, 1 H), 5.13 (d, *J* = 17.1 Hz, 1 H), 5.00 (d, *J* = 9.8 Hz, 1 H), 4.31 (br s, 2 H), 3.53 (br s, 2 H), 2.16 (app q, *J* = 7.0 Hz, 2 H), 1.71 (quint, *J* = 7.6 Hz, 2 H), and 1.48 (quint, *J* = 7.4 Hz, 2 H); ¹³C NMR (125 MHz, CDCl₃) δ 137.0, 133.6, 132.3, 119.8 (q, *J* = 322 Hz), 115.8, 113.3, 49.3, 35.8, 31.8, 26.8, and 25.6; HRMS [M+Na]⁺ calcd for C₁₁H₁₅F₃N₂NaO₂S: 319.0698, found: 319.0689.

N-(Cyanomethyl)-N-(2-[[4-methylphenyl)sulfonyl]((E),(E)-2,4-hexadienyl)amino]ethyl)trifluoromethanesulfonamide (7). IR (film) 3010, 2960, 2912, 2838, 1646, 1580, 1485, 1433, 1390, 1335, 1220, 1190, 1148, 1082, 1038, 985, and 918 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.70 (d, $J = 8.2$ Hz, 2 H), 7.35 (d, $J = 8.2$ Hz, 2 H), 6.10 (dd, $J = 15.0, 10.4$ Hz, 1 H), 5.96 (ddd, $J = 15.0, 10.4, 1.5$ Hz, 1 H), 5.71 (dq, $J = 15.0, 6.7$ Hz, 1 H), 5.25 (dt, $J = 15.0, 7.3$ Hz, 1 H), 4.55 (br s, 2 H), 3.81 (d, $J = 7.3$ Hz, 2 H), 3.67 (br, 2 H), 3.33 (br s, 2 H), 2.45 (s, 3 H), and 1.74 (d, $J = 6.7$ Hz, 3 H) ^{13}C NMR (125 MHz, CDCl_3) δ 144.3, 136.6, 135.4, 132.2, 130.2, 130.0, 127.5, 122.7, 119.8 (q, $J = 322$ Hz), 113.6, 51.5, 48.0, 45.1, 37.1, 21.7, and 18.3; HRMS $[\text{M}+\text{Na}]^+$: calcd for $\text{C}_{18}\text{H}_{22}\text{F}_3\text{N}_3\text{NaO}_4\text{S}_2$: 488.0896, found: 488.0903.

N-(Cyanomethyl)-N-[2-[2-((E)-1,3-butadienyl)phenyl]ethyl]trifluoromethanesulfonamide (8). Mp 85.5-86 $^\circ\text{C}$; IR (CH_2Cl_2) 3054, 2987, 1600, 1422, 1398, 1231, 1200, 1142, 1104, 1067, 1005, and 896 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.55 (dd, $J = 7.6, 1.2$ Hz, 1 H), 7.29 (ddd, $J = 7.6, 7.6, 1.5$ Hz, 1 H), 7.24 (ddd, $J = 7.3, 7.3, 1.5$ Hz, 1 H), 7.19 (dd, $J = 7.5, 1.4$ Hz, 1 H), 6.80 (d, $J = 15.6$ Hz, 1 H), 6.74 (dd, $J = 15.6, 9.8$ Hz, 1 H), 6.56 (ddd, $J = 16.8, 9.9, 9.9$ Hz, 1 H), 5.39 (d, $J = 16.8$ Hz, 1 H), 5.24 (d, $J = 10.1$ Hz, 1 H) 3.4-4.4 (br m, 4 H), and 3.13 (t, $J = 7.7$ Hz, 2 H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.1, 136.5, 133.7, 133.2, 130.5, 128.7, 128.4, 128.2, 126.5, 119.8 (q, $J = 323$ Hz), 119.1, 113.4, 50.2, 36.9, and 33.0; HRMS $[\text{M}+\text{Na}]^+$: calcd for $\text{C}_{15}\text{H}_{15}\text{F}_3\text{N}_2\text{NaO}_2\text{S}$: 367.0699, found: 367.0689.

N-(Cyanomethyl)-N-(7-(*t*-butyldimethylsiloxy)-(E)-5,7-octadienyl)trifluoromethanesulfonamide (9). Mp 63.5-64.5 $^\circ\text{C}$; IR (film) 3040, 2980, 2850, 1585, 1412, 1390, 1250, 1220, 1192, 1138, and 1014 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.89-5.98 (m, 2 H), 4.32 (br, 2 H), 4.25 (s, 1 H), 4.24 (s, 1 H), 3.55 (br, 2 H), 2.18 (app q, $J = 6.8$ Hz,

2 H), 1.72 (quint, $J = 7.6$ Hz, 2 H), 1.49 (quint, $J = 7.5$ Hz, 2 H), 0.98 (s, 9 H), and 0.18 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 154.9, 130.0, 129.3, 119.8 (q, $J = 322$ Hz), 113.2, 94.8, 49.2, 35.8, 31.4, 26.9, 26.0, 25.7, 18.5, and -4.4; HRMS $[\text{M}+\text{H}]^+$: calcd for $\text{C}_{17}\text{H}_{30}\text{F}_3\text{N}_2\text{O}_3\text{SSi}$: 427.1693, found: 427.1694.

Representative Procedure for the Synthesis of Iminoacetonitriles. 7-(*tert*-Butyldimethylsiloxymethyl)-(*E*)-5,7-octadienyliminoacetonitrile (15). A 25-mL, one-necked, round-bottomed flask equipped with a reflux condenser fitted with an argon inlet adapter was charged with Cs_2CO_3 (4.41 g, 13.5 mmol) and 10 mL of THF. A solution of triflamide **10** in 6 mL of THF was added, and the reaction mixture was heated at 55 $^\circ\text{C}$ for 3 h. The resulting mixture was allowed to cool to room temperature and then diluted with 30 mL of Et_2O and 30 mL of H_2O . The aqueous layer was separated and extracted with two 30-mL portions of Et_2O , and the combined organic layers were washed with 30 mL of saturated NaCl solution, dried over MgSO_4 , filtered, and concentrated to give 1.06 g of a yellow oil. Column chromatography on 22 g of Et_3N -deactivated silica gel (elution with 1% Et_3N -10% EtOAc -hexanes) provided 0.940 g (90%) of **15** (80:20 mixture of *E* and *Z* imine isomers by ^1H NMR analysis) as a pale yellow oil: IR (film) 3020, 2950, 2930, 2890, 2850, 1625, 1470, 1398, 1370, 1340, 1262, 1110, 1015, and 975 cm^{-1} ; *E* isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.38 (t, $J = 1.5$ Hz, 1 H), 6.08 (d, $J = 15.9$ Hz, 1 H), 5.63 (dt, $J = 16.2, 7.0$ Hz, 1 H), 5.20 (d, $J = 1.8$ Hz, 1 H), 5.00 (s, 1 H), 4.31 (s, 2 H), 3.66 (dt, $J = 1.5, 6.9$ Hz, 2 H), 2.13 (q, $J = 7.3$ Hz, 2 H), 1.71 (app quin, $J = 7.3$ Hz, 2 H), 1.45 (app quin, $J = 7.3$ Hz, 2 H), 0.93 (s, 9 H), and 0.09 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.7, 135.9, 130.5, 129.1, 114.6, 112.8, 63.1, 63.0, 32.7, 29.5, 26.8, 26.0, 18.5, and -5.2. *Z* isomer: ^1H NMR (500 MHz, CDCl_3) δ 7.39 (t, $J = 2.1$ Hz, 1 H), 6.10 (d, $J = 15.9$ Hz, 1 H), 5.64 (dt, $J = 16.2, 7.0$ Hz, 1 H), 5.20 (d, $J = 1.8$ Hz, 1 H), 5.00 (s, 1 H), 4.31 (s, 2 H), 3.84 (dt, $J =$

2.1, 6.9 Hz, 2 H), 2.13 (q, $J = 7.3$ Hz, 2 H), 1.76 (app quin, $J = 7.3$ Hz, 2 H), 1.49 (app quin, $J = 7.6$ Hz, 2 H), 0.93 (s, 9 H), and 0.09 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.7, 131.5, 130.4, 129.1, 112.9, 109.5, 63.1, 59.7, 32.8, 29.5, 26.9, 26.0, 18.5, and -5.2.

(*E*)-5,7-Octadienyliminoacetonitrile (11). IR (film) 3086, 3037, 3008, 2937, 2859, 2235, 1803, 1651, 1623, 1603, 1455, 1440, 1331, 1190, 1158, 1005, 953, 900, and 734 cm^{-1} ; E isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.38 (t, $J = 1.5$ Hz, 1 H), 6.31 (ddd, $J = 17.4, 10.1, 10.1$ Hz, 1 H), 6.04-6.10 (m, 1 H), 5.68 (dt, $J = 15.3, 6.7$ Hz, 1 H), 5.11 (d, $J = 16.5$ Hz, 1 H), 4.99 (d, $J = 10.2$ Hz, 1 H), 3.66 (dt, $J = 6.9, 1.4$ Hz, 2 H), 2.13 (q, $J = 7.6$ Hz, 2 H), 1.69-1.78 (m, 2 H), 1.42-1.52 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3): δ 136.9, 135.7, 134.2, 131.4, 115.1, 114.3, 62.7, 31.9, 29.2, and 26.4; For Z isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.39 (t, $J = 2.1$ Hz, 1 H), 6.32 (ddd, $J = 17.4, 10.1, 10.1$ Hz, 1 H), 6.04-6.10 (m, 1 H), 5.69 (dt, $J = 15.3, 6.7$ Hz, 1 H), 5.11 (d, $J = 16.5$ Hz, 1 H), 4.99 (d, $J = 10.2$ Hz, 1 H), 3.85 (dt, $J = 6.9, 2.1$ Hz, 2 H), 2.15 (q, $J = 7.6$ Hz, 2 H), 1.69-1.78 (m, 2 H), and 1.42-1.52 (m, 2 H); ^{13}C NMR (125 MHz, CDCl_3): δ 137.0, 134.3, 131.4, 131.3, 115.0, 109.2, 59.4, 31.9, 29.2, and 26.4.

(2-[[4-methylphenyl)sulfonyl]](*E*),(*E*)-2,4-hexadienyl]amino]ethyl)iminoacetonitrile (12). IR (film) 3020, 2980, 2920, 2860, 1650, 1610, 1590, 1485, 1435, 1330, 1148, and 1080 cm^{-1} ; For E isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.69 (d, $J = 8.2$ Hz, 2 H), 7.34 (t, $J = 1.8$ Hz, 1 H), 7.33 (d, $J = 8.5$ Hz, 2 H), 6.04 (dd, $J = 15.3, 10.7$ Hz, 1 H), 5.94-6.00 (m, 1 H), 5.64-5.73 (m, 1 H), 5.26 (dt, $J = 15.0, 7.0$ Hz, 1 H), 3.86 (dt, $J = 6.4, 1.5$ Hz, 2 H), 3.79 (d, $J = 7.0$ Hz, 2 H), 3.39 (t, $J = 6.2$ Hz, 2 H), 2.44 (s, 3 H), and 1.74 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ 143.9, 138.0, 135.4, 133.1, 131.5, 130.3, 130.0, 127.4, 124.1, 114.4, 62.6, 51.9, 46.9, 21.7, and 18.3; For Z isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.71 (d, $J = 8.2$ Hz, 2 H), 7.35 (t, $J = 2.4$ Hz, 1 H), 7.32 (d, $J = 8.5$ Hz, 2 H), 6.06 (dd, $J = 15.3, 10.7$ Hz, 1 H), 5.94-6.00 (m, 1 H),

5.64-5.73 (m, 1 H), 5.29 (dt, $J = 15.0, 7.0$ Hz, 1 H), 3.95 (dt, $J = 6.4, 2.4$ Hz, 2 H), 3.79 (d, $J = 7.0$ Hz, 2 H), 3.49 (t, $J = 6.4$ Hz, 2 H), 2.44 (s, 3 H), and 1.74 (d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3): δ 143.7, 136.4, 135.4, 132.5, 131.3, 130.3, 130.0, 127.4, 124.1, 109.4, 58.5, 51.0, 46.4, 21.7, and 18.3.

(2-[2-((*E*)-1,3-butadienyl)phenyl]ethyl)iminoacetonitrile (13). IR (film) 3078, 3058, 3020, 2955, 2855, 1620, 1595, 1477, 1445, 1355, 1330, 1160, 1095, 1060, and 995 cm^{-1} ; For *E* isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.52 (dd, $J = 7.5, 1.4$ Hz, 1 H), 7.15-7.25 (m, 2 H), 7.12 (t, $J = 1.5$ Hz, 1 H), 7.09 (dd, $J = 7.5, 1.7$ Hz, 1 H), 6.69-6.86 (m, 2 H), 6.54 (ddd, $J = 16.8, 10.0, 10.0$ Hz, 1 H), 5.36 (dd, $J = 16.8, 1.2$ Hz, 1 H), 5.21 (dd, $J = 10.1, 1.5$ Hz, 1 H), 3.84 (dt, $J = 7.2, 1.2$ Hz, 2 H), and 3.09 (t, $J = 7.2$ Hz, 2 H); ^{13}C NMR (125 MHz, CDCl_3): δ 137.8, 137.1, 136.7, 136.2, 132.6, 131.1, 130.1, 128.5, 128.0, 126.7, 119.0, 115.0, 64.3, and 34.2; For *Z* isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.53 (dd, $J = 7.5, 1.4$ Hz, 1 H), 7.34 (t, $J = 2.0$ Hz, 1 H), 7.15-7.25 (m, 2 H), 7.09 (dd, $J = 7.5, 1.7$ Hz, 1 H), 6.69-6.86 (m, 2 H), 6.56 (ddd, $J = 16.8, 10.0, 10.0$ Hz, 1 H), 5.35 (dd, $J = 16.8, 1.2$ Hz, 1 H), 5.20 (dd, $J = 10.1, 1.5$ Hz, 1 H), 4.04 (dt, $J = 7.3, 2.1$ Hz, 2 H), and 3.09 (t, $J = 7.2$ Hz, 2 H); ^{13}C NMR (125 MHz, CDCl_3): δ 138.0, 136.9, 136.3, 132.7, 132.6, 131.1, 130.2, 128.5, 127.9, 126.7, 118.8, 100.1, 61.0, and 34.2.

7-(*tert*-Butyldimethylsiloxy)-(*E*)-5,7-octadienyliminoacetonitrile (14). IR (film): 2935, 2895, 2855, 1650, 1620, 1590, 1462, 1365, 1325, 1260, 1028, 970, and 835 cm^{-1} ; For *E* isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.37 (t, $J = 1.5$ Hz, 1 H), 5.94-5.99 (m, 1 H), 5.88 (d, $J = 15.3$ Hz, 1 H), 4.23 (s, 1 H), 4.21 (s, 1 H), 3.65 (dt, $J = 6.9, 1.4$ Hz, 2 H), 2.11-2.18 (m, 2 H), 1.68-1.76 (m, 2 H), 1.42-1.51 (m, 2 H), 0.97 (s, 9 H), and 0.17 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3): δ 155.0, 135.9, 130.8, 128.7, 114.6, 94.4, 63.0, 31.7, 29.5, 26.7, 26.6, 18.4, and -4.5; For *Z* isomer: ^1H NMR (500 MHz, CDCl_3): δ 7.38 (t, $J = 2.1$ Hz, 1 H), 5.94-5.99 (m, 1 H), 5.89 (d, J

= 15.2 Hz, 1 H), 4.23 (s, 1 H), 4.21 (s, 1 H), 3.84 (dt, J = 6.9, 2.1 Hz, 2 H), 2.11-2.18 (m, 2 H), 1.68-1.76 (m, 2 H), 1.42-1.51 (m, 2 H), 0.97 (s, 9 H), and 0.17 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3): δ 155.1, 131.5, 130.9, 128.6, 109.5, 94.3, 59.7, 31.7, 29.6, 26.8, 26.0, 18.4, and -4.5.

3-(*tert*-Butyldimethylsiloxymethyl)-*cis*-3,4-didehydro-1-cyanoquinolizidine (20). A threaded Pyrex tube (ca. 100 mL capacity) equipped with a rubber septum and a nitrogen inlet needle was charged with imine **15** (0.938 g, 3.06 mmol), 4-methyl-2,6-di-*tert*-butylphenol (2.02 g, 9.18 mmol), and 61 mL of toluene. The solution was degassed by three freeze-pump-thaw cycles and then sealed with a threaded Teflon cap. The reaction mixture was heated in a 120 °C oil bath for 14 h and then allowed to cool to rt. Concentration gave 4.32 g of a brown oil which was deposited onto 7.5 g of silica gel and purified by column chromatography on 55 g of silica gel (gradient elution with 1% Et_3N -5-10% EtOAc -hexanes) to yield 0.819 g (87%) of **20** as a pale yellow oil: IR (film) 2934, 2856, 2807, 2767, 2222, 1471, 1462, 1388, 1360, 1326, 1289, 1256, 1229, 1194, 1156, 1129, 1067, 1026, 1006, 939, 838, 777, 738, and 667 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.47 (s, 1 H), 4.06 (s, 2 H), 3.85 (d, J = 6.4 Hz, 1 H), 2.84 (dd, J = 11.6, 1.6 Hz, 1 H), 2.76 (dd, J = 11.0, 2.0 Hz, 1 H), 2.64-2.70 (m, 1 H), 2.51 (dt, J = 3.1, 11.6 Hz, 1 H), 2.24 (d, J = 17.1 Hz, 1 H), 1.70-1.84 (m, 3 H), 1.63 (app tq, J = 4.1, 12.2 Hz, 1 H), 1.42 (app tq, J = 4.0, 12.8 Hz, 1 H), 1.30 (app dq, J = 3.4, 11.6 Hz, 1 H), 0.93 (s, 9 H), and 0.09 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 131.9, 124.2, 117.0, 65.9, 56.6, 54.0, 52.3, 32.0, 29.8, 26.0, 25.9, 24.7, 18.5, and -5.1; Anal. Calcd for $\text{C}_{17}\text{H}_{30}\text{N}_2\text{OSi}$: C, 66.61; H, 9.87; N, 9.14. Found: C, 66.43; H, 10.05; N, 9.28.

***cis*-3,4-Didehydro-1-cyanoquinolizidine (16).** Cycloaddition in this case was carried out at 120 °C for 18 h in toluene. IR (film) 3035, 2936, 2855, 2807, 2221, 1442, 1396, 1332, 1287, 1237, 1205, 1181, 1128, 1106, 1082, 1021, 849, 796 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3)

δ 5.63-5.67 (m, 1 H), 5.54 (d, J = 10.1 Hz, 1 H), 3.79 (d, J = 6.1 Hz, 1 H), 2.86 (br d, J = 11.6 Hz, 1 H), 2.70-2.77 (m, 2 H), 2.51 (dt, J = 3.1, 11.4 Hz, 1 H), 2.29 (m, 1 H), 1.79-1.85 (m, 1 H), 1.59-1.77 (m, 3 H), and 1.26-1.46 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 130.5, 120.4, 116.9, 56.7, 54.0, 51.9, 31.7, 29.5, 25.7, and 24.5; Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{N}_2$: C, 74.03; H, 8.70; N, 17.27. Found: C, 74.12; H, 8.74; N, 17.29.

***cis*-7-Methyl-2(toluene-4-sulfonyl)-1,3,4,6,7,9a-hexahydro-6-cyano-2H-pyrido[1,2-*a*]pyrazine (17).** Cycloaddition in this case was carried out at reflux for 18 h in acetonitrile. Mp 152-153 $^{\circ}\text{C}$; IR (CH_2Cl_2) 3054, 2986, 2305, 1598, 1451, 1422, 1345, 1273, 1257, 1168, 1132, 1025, 896, and 765 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.66 (d, J = 8.2 Hz, 2 H), 7.34 (d, J = 8.5 Hz, 2 H), 5.72 (ddd, J = 10.0, 5.0, 2.5 Hz, 1 H), 5.43 (d, J = 10.1 Hz, 1 H), 3.74-3.78 (m, 2 H), 3.44 (s, 1 H), 3.14 (dt, J = 11.0, 2.1 Hz, 1 H), 2.80 (dt, J = 3.1, 11.3 Hz, 1 H), 2.63 (dt, J = 2.5, 11.1 Hz, 1 H), 2.53 (dt, J = 3.2, 11.5 Hz, 2 H), 2.44 (s, 3 H), 2.09 (t, J = 11.0 Hz, 1 H), and 1.11 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.1, 133.0, 130.0, 129.7, 127.9, 124.3, 116.2, 56.5, 55.5, 51.7, 50.2, 45.8, 35.1, 21.7, and 19.9; Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{N}_2$: C, 61.61; H, 6.39; N, 12.68. Found: C, 61.57; H, 6.35; N, 12.47.

***cis*-3,6,7,11b-Tetrahydro-4-cyano-4H-pyrido[2,1-*a*]isoquinoline (18a):** Cycloaddition in this case was carried out at 120 $^{\circ}\text{C}$ for 36 h in toluene. Mp 130-131 $^{\circ}\text{C}$; IR (CH_2Cl_2) 3054, 2934, 2826, 2736, 1494, 1432, 1332, 1274, and 1129 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.31 (d, J = 7.6 Hz, 1 H), 7.16-7.23 (m, 2 H), 7.12 (dd, J = 7.0, 0.9 Hz, 1 H), 6.30 (d, J = 10.4 Hz, 1 H), 5.82-5.86 (m, 1 H), 4.39 (s, 1 H), 4.06 (dd, J = 6.1, 0.6 Hz, 1 H), 3.18-3.27 (m, 1 H), 2.97-3.02 (m, 2 H), 2.76-2.86 (m, 2 H), and 2.36-2.42 (m, 1 H); ^{13}C NMR (125 MHz, CDCl_3) δ 135.5, 133.9, 129.4, 127.9, 126.7, 126.2, 124.7, 122.3, 117.0, 56.4, 52.4, 51.0, 29.5, and 29.4; Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2$: C, 79.97; H, 6.71; N, 13.32. Found: C, 80.00; H, 7.02; N, 13.52.

***trans*-3,6,7,11b-Tetrahydro-4-cyano-4*H*-pyrido[2,1-*a*]isoquinoline (18b).** Mp 90-91 °C; IR (CH₂Cl₂) 3053, 2985, 2933, 2849, 1637, 1496, 1422, 1273, 1094, and 896 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.12-7.26 (m, 4 H), 7.12 (dd, *J* = 7.0, 0.9 Hz, 1 H), 5.93 (dt, *J* = 8.2, 2.0 Hz, 1 H), 5.77-5.82 (m, 1 H), 4.54 (br s, 1 H), 4.12 (dd, *J* = 11.0, 4.9 Hz, 1 H), 3.18-3.27 (m, 1 H), 2.92-3.05 (m, 4 H), 2.56-2.66 (m, 1 H), and 2.30-2.38 (m, 1 H); ¹³C NMR (125 MHz, CDCl₃) δ 135.9, 134.5, 129.8, 129.1, 126.9, 126.4, 126.2, 122.7, 119.2, 58.7, 51.1, 43.4, 29.3, and 25.7; Anal. Calcd for C₁₄H₁₄N₂: C, 79.97; H, 6.71; N, 13.32. Found: C, 79.62; H, 6.55; N, 13.10.

3-(*tert*-Butyldimethylsiloxy)-*cis*-3,4-didehydro-1-cyanoquinolizidine (19). Cycloaddition in this case was carried out at 120 °C for 25 h in toluene. Mp 61-62 °C; IR (CH₂Cl₂) 2933, 2857, 1678, 1472, 1372, 1287, 1256, 1212, 1171, 1127, 898, 835, 780, and 689 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 4.67 (app t, *J* = 1.8 Hz, 1 H), 3.81 (d, *J* = 5.5 Hz, 1 H), 2.86 (br d, *J* = 10.2 Hz, 1 H), 2.73-2.79 (m, 2 H), 2.49 (dt, *J* = 3.1, 11.5 Hz, 1 H), 2.16 (dt, *J* = 17.0, 1.8 Hz, 1 H), 1.76-1.79 (m, 1 H), 1.61-1.73 (m, 3 H), 1.38 (tq, *J* = 3.8, 12.8 Hz, 1 H), 1.25-1.34 (m, 1 H), 0.92 (s, 9 H), 0.17 (s, 3 H), and 0.16 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 145.4, 116.8, 107.1, 56.1, 53.7, 53.1, 33.9, 33.0, 25.9, 25.8, 24.3, 18.2, -4.2, and -4.4; Anal. Calcd for C₁₆H₂₈N₂OSi: C, 65.70; H, 9.65; N, 9.58. Found: C, 65.56; H, 9.63; N, 9.44.

3-(*tert*-Butyldimethylsiloxymethyl)-3,4-didehydroquinolizidine (21). A 25-mL, two-necked, round-bottomed flask equipped with a rubber septum and argon inlet adapter was charged with NaBH₃CN (0.187 g, 2.98 mmol) and 6 mL of acetonitrile. Acetic acid (0.34 mL, 0.36 g, 6.0 mmol) was added dropwise via syringe over 2 min. The resulting solution was stirred at rt for 30 min, and then a solution of nitrile **20** (0.152 g, 0.50 mmol) in 4 mL of acetonitrile was added over 2 min. The reaction mixture was stirred at rt for 20 h and then diluted with 30 mL of

1 M NaOH solution and 30 mL of CH₂Cl₂. The aqueous layer was separated and extracted with three 15-mL portions of CH₂Cl₂, and the combined organic layers were washed with 30 mL of saturated NaCl solution, dried over MgSO₄, filtered, and concentrated to provide 0.140 g of colorless oil. Column chromatography on 8 g of silica gel (elution with 1% Et₃N-10% EtOAc-hexanes) provided 0.129 g (91%) of **21** as a colorless oil: IR (film) 2930, 2855, 2797, 2740, 2709, 1463, 1441, 1390, 1360, 1294, 1252, 1216, 1187, 1153, 1132, 1116, 1066, 1007, 940, 836, 775, 733, and 665 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 5.39 (br s, 1 H), 4.04 (br s, 2 H), 2.81-2.89 (m, 2 H), 2.42 (br d, *J* = 11.0 Hz, 1 H), 2.28-2.38 (m, 2 H), 2.15 (ddd, *J* = 11.1, 11.1, 4.0 Hz, 1 H), 1.94-2.01 (m, 1 H), 1.76-1.81 (m, 1 H), 1.59-1.69 (m, 3 H), 1.25-1.40 (m, 2 H), 0.91 (s, 9 H), 0.07 (s, 3 H), and 0.06 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 135.5, 124.4, 66.5, 61.5, 56.2, 52.5, 32.4, 26.3, 26.1, 26.0, 25.1, 18.6, -5.1, and -5.2; HRMS [M+H]⁺: calcd for C₁₆H₃₂NOSi: 282.2248, found: 282.2253.

3-(*tert*-Butyldimethylsiloxymethyl)-*cis*-3,4-didehydro-1-(1-pentynyl)quinolizidine (22). A 10-mL, pear-shaped flask equipped with a rubber septum and argon inlet needle was charged with 1-pentyne (0.13 mL, 0.088 g, 1.3 mmol) and 4 mL of THF. Ethylmagnesium bromide solution (3.0 M in ether, 0.43 mL, 1.3 mmol) was then added via syringe over 1 min, and the reaction mixture was stirred at rt for 1 h. The resulting solution was then transferred via cannula over 2 min into a solution of nitrile **20** (0.132 g, 0.43 mmol) in 2 mL of THF. The reaction mixture was stirred at rt for 3.5 h and then diluted with 5 mL of satd aq NH₄Cl solution, 15 mL of water, and 15 mL of ether. The aqueous layer was separated and extracted with three 15-mL portions of ether, and the combined organic layers were washed with 25 mL of saturated NaCl solution, dried over K₂CO₃, filtered, and concentrated to provide 0.149 g of yellow oil. Column chromatography on 8 g of silica gel (gradient elution with 5-10% EtOAc-hexanes)

provided 0.114 g (76%) of **22** as a colorless oil: IR (film) 2931, 2855, 1462, 1360, 1325, 1292, 1255, 1225, 1193, 1153, 1072, 1005, 836, and 776 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.39 (br s, 1 H), 4.04 (br s, 2 H), 3.69 (d, $J = 4.9$ Hz, 1 H), 2.82 (br d, $J = 10.1$ Hz, 1 H), 2.66 (br d, $J = 11.3$ Hz, 1 H), 2.48-2.60 (m, 2 H), 2.16 (dt, $J = 7.0, 2.1$ Hz, 2 H), 2.07 (d, $J = 14.3$ Hz, 1 H), 1.61-1.79 (m, 4 H), 1.51 (sextet, $J = 7.3$ Hz, 2 H), 1.21-1.38 (m, 2 H), 0.98 (t, $J = 7.3$ Hz, 3 H), 0.91 (s, 9 H), and 0.06 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 132.9, 124.0, 85.0, 77.5, 66.6, 55.5, 53.6, 51.4, 32.6, 32.3, 26.2, 26.1, 25.1, 22.7, 20.9, 18.6, 13.7, -5.0, and -5.1; HRMS $[\text{M}+\text{H}]^+$: calcd for $\text{C}_{21}\text{H}_{37}\text{NOSi}$: 348.2717, found: 348.2708.