

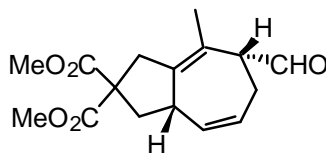
Appendix

On The regioselectivity of the Ru-Catalyzed Intramolecular [5+2] Cycloaddition

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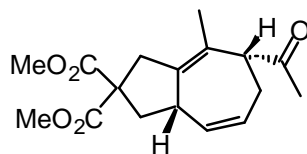
General procedure for ruthenium catalyzed [5+2] cycloadditions.

A 4 ml round bottom flask containing malonate ester **2a** (72 mg, 0.25 mmol) in 0.6 ml distilled acetone is degassed with argon for 5 min. To this solution is added CpRu(CH₃CN)₃PF₆ (11 mg, 0.025 mmol). The resulting orange solution is stirred for 30 min. Direct flash chromatography eluting with 5 % to 15 % diethyl ether in petroleum ether afforded **4a** (63 mg, 0.21 mmol, 83 %) as a colorless oil.



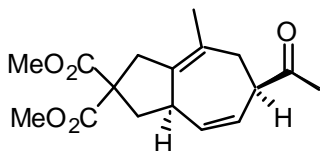
4a

4a: IR (film): 2955, 2850, 1734, 1437, 1274, 1202, 1163, 1078, 953, 885 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): δ 9.67 (d, J=1.8 Hz, 1H), 5.70 (dtd, J=2.7, 6.0 and 10.2 Hz, 1H), 5.61 (dt, J=2.2 and 10.5 Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.60 (m, 1H), 3.17 (m, 1H), 3.06 (d, J=17.2 Hz, 1H), 2.91 (d, J=1.8 and 17.2 Hz, 1H), 2.66 (m, 2 H), 2.32 (dt, J=5.7, 15.3 Hz, 1H), 2.04 (t, J=12.4 Hz, 1H), 1.66 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃): δ 202.8, 172.0, 171.8, 138.4, 134.5, 127.7, 124.3, 58.0, 55.0, 52.9, 52.8, 41.2, 41.0, 39.7, 26.0, 19.9. HRMS: Calc'd for C₁₆H₂₀O₅: 292.1311. Found: 292.1106.



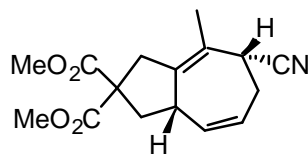
4c

4c: IR (film): 2955, 2918, 2851, 1735, 1715, 1435, 1357, 1273, 1236, 1202, 1165, 1076 cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.82 (ddd, $J=2.5, 6.0, 10.5$ Hz, 1H), 5.74 (ddd, $J=1.5, 2.5, 10.5$ Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.70 (m, 2H), 3.04 (d, $J=16.5$ Hz, 1H), 2.87 (dt, $J=2.0, 17.0$ Hz, 1H), 2.71 (dq, $J=2.5, 10.0$ Hz, 1H), 2.57 (m, 1H), 2.29 (m, 1H), 2.19 (s, 3H), 2.07 (q, $J=10.5$ Hz, 1H), 1.66 (d, $J=2.0$ Hz, 3H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3) of major isomer: δ 209.3, 172.0, 171.8, 134.6, 134.3, 127.6, 126.8, 58.1, 52.9, 52.8, 50.5, 41.2, 40.0, 39.4, 34.1, 29.6, 28.9. HRMS Calc'd for $\text{C}_{17}\text{H}_{22}\text{O}_5$: 306.1467. Found: 306.1457.



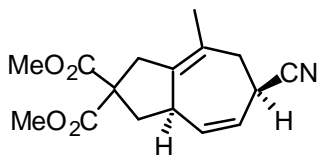
3c

Additional signals for minor regioisomer **3c**: $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.62 (m, 1H), 5.57 (d, $J=10.5$ Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.70 (m, 1H), 3.54 (d, $J=8.0$ Hz, 1H), 3.05 (d, $J=17.0$ Hz, 1H), 2.97 (d, $J=17.0$ Hz, 1H), 2.72 (ddd, $J=1.5, 8.0, 10.5$ Hz, 1H), 2.55 (dm, $J=13.5$ Hz, 1H), 2.31 (m, 1H), 2.16 (s, 3H), 2.08 (dd, $J=10.5, 13.0$ Hz, 1H), 1.59 (s, 3H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): δ 210.4, 172.1, 171.9, 138.3, 133.3, 127.7, 126.1, 58.3, 55.2, 52.9, 52.8, 41.3, 40.1, 39.4, 30.1, 29.7, 27.6.



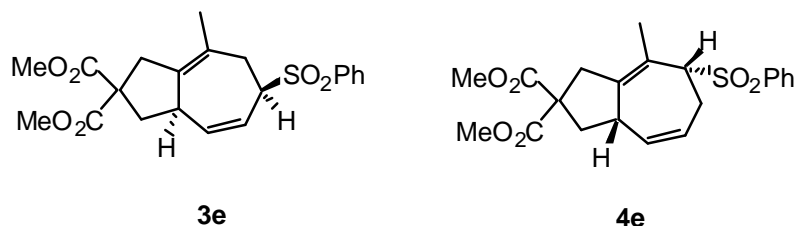
4d

4d: IR (film): 2921, 2851, 2234, 1733, 1456, 1435, 1270, 1201, 1165 cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.68 (m, 1H), 5.60 (d, $J=10.5$ Hz, 1H), 3.772 (s, 3H), 3.766 (s, 3H), 3.62 (m, 1H), 3.05 (d, $J=17.0$ Hz, 1H), 2.95 (d, $J=17.0$ Hz, 1H), 2.74 (m, 1H), 2.61 (m, 1H), 2.48 (m, 1H), 2.30 (m, 1H), 2.04 (t, $J=13.0$ Hz, 1H), 1.88 (s, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 171.7, 171.4, 137.3, 133.4, 126.4, 123.2, 120.4, 58.1, 52.9, 41.3, 39.6, 39.2, 33.8, 32.0, 29.7, 22.7. HRMS: Calc'd for $\text{C}_{16}\text{H}_{19}\text{O}_4\text{N}$: 289.1314. Found: 289.1313.

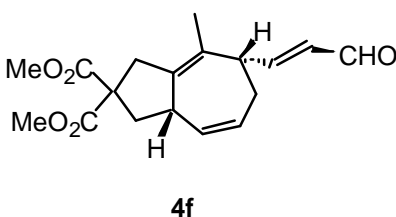


3d

Additional signals for minor regioisomer **3d**: $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.72 (dd, $J=11.0$ Hz, 1H), 5.60 (d, $J=10.5$ Hz, 1H), 3.768 (s, 3H), 3.766 (s, 3H), 3.56 (m, 1H), 3.05 (d, $J=17.0$ Hz, 1H), 2.95 (d, $J=17.0$ Hz, 1H), 2.74 (m, 2H), 2.64 (m, 1H), 2.20 (m, 1H), 2.05 (t, $J=11.0$ Hz, 1H), 1.82 (s, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 171.8, 171.5, 139.4, 135.6, 127.5, 125.5, 122.7, 58.1, 53.0, 41.2, 39.6, 39.7, 34.9, 30.0, 29.4, 22.0.

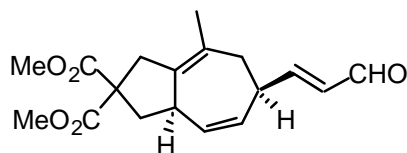


3e+4e: IR (film): 2958, 2927, 2859, 1732, 1601, 1581, 1448, 1276, 1200, 1131, 1074, cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 7.87 (m, 4H), 7.57 (m, 6H), 5.82 (m, 2H), 5.57 (m, 1H), 5.32 (dt, $J=10.5$ Hz, 1H), 4.11 (m, 2H), 3.762 (s, 3H), 3.759 (s, 3H), 3.747 (s, 3H), 3.742 (s, 3H), 3.46 (m, 4H), 3.06 (d, $J=17.0$ Hz, 1H), 2.95 (m, $J=16.5$ Hz, 1H), 2.93 (m, $J=15.0$ Hz, 1H), 2.78 (dm, $J=16.5$ Hz, 1H), 2.59 (m, 6H), 2.03 (s, 3H), 1.71 (s, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 171.9, 171.6, 160.3, 160.2, 144.6, 141.6, 141.5, 138.0, 137.3, 134.6, 133.6, 133.4, 133.1, 129.1, 128.8, 128.6, 126.3, 124.8, 123.0, 122.5, 70.5, 68.7, 63.4, 57.6, 52.9, 51.2, 51.0, 41.0, 40.9, 40.0, 39.3, 36.6, 31.5, 30.3, 29.7, 27.8, 27.4, 22.5. HRMS: Calc'd for $\text{C}_{15}\text{H}_{19}\text{O}_4$ ($\text{M-C}_6\text{H}_5\text{SO}_2^+$): 263.1278. Found: 263.1267.



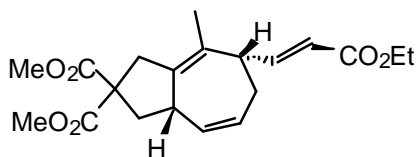
4f: IR (film): 2949, 2924, 2850, 1732, 1688, 1628, 1434, 1257, 1198, 1162, 1126, 1072, 979 cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 9.50 (d, $J=8.0$ Hz, 1H), 6.79 (dd, $J=7.5, 15.0$ Hz, 1H), 6.05 (dd, $J=8.0, 15.5$ Hz, 1H), 5.64 (m, 2H), 3.722 (s, 3H), 3.719 (s, 3H), 3.60 (m, 1H), 3.37 (m, 1H), 3.04 (d, $J=17.0$ Hz, 1H), 2.87 (m, 1H), 2.66 (m, 2H), 2.17 (m, 1H), 2.25 (m, 1H), 1.56 (s, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 194.1, 171.0, 160.0,

136.5, 134.5, 132.9, 128.8, 127.8, 125.5, 58.0, 52.8, 45.1, 41.2, 40.0, 39.8, 37.1, 30.4, 19.8. Anal. Calc'd for C₁₈H₂₂O₅: C, 67.91; H, 6.97. Found: C, 67.70; H, 6.74.



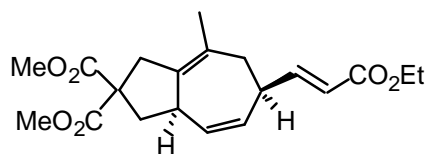
3f

Additional signals for minor regioisomer **3f**: ¹H-NMR (500 MHz, CDCl₃): δ 9.51 (d, J=8.0 Hz, 1H), 6.78 (dd, J=7.0, 15.5 Hz, 1H), 6.10 (dd, J=7.5, 17.0 Hz, 1H), 5.63 (m, 1H), 5.45 (m, 1H), 3.74 (s, 3 H), 3.72 (s, 3H), 3.60 (m, 1H), 3.26 (m, 1H), 2.97 (d, J=16.5 Hz, 1H), 2.85 (m, 1H), 2.75 (m, J=14.0 Hz, 1H), 2.66 (m, 1H), 1.95 (m, 2H), 1.55 (s, 3H). ¹³C-NMR (75 MHz, CDCl₃): δ 194.0, 172.1, 159.8, 136.5, 133.4, 132.5, 127.8, 127.2, 126.6, 52.3, 45.1, 41.6, 40.2, 40.0, 39.8, 39.1, 29.7, 22.6;



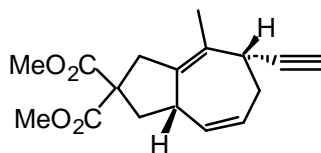
4g

4g: IR (film): 2956, 2926, 2855, 1733, 1710, 1646, 1436, 1368, 1258, 1162, 1047 cm⁻¹. ¹H-NMR (300 MHz, CDCl₃): δ 6.93 (dd, J=8.7, 15.9 Hz, 1H), 5.75 (d, J=15.6 Hz, 1H), 5.62 (m, 2 H), 4.18 (q, J=7.2 Hz, 2 H), 3.75 (s, 3H), 3.74 (s, 3H), 3.61 (m, 1H), 3.18 (m, 1H), 3.12 (d, J=16.8 Hz, 1H), 2.87 (d, J=17.4 Hz, 1H), 2.65 (m, 2H), 2.17 (m, 1H), 2.04 (m, 1H), 1.56 (s, 3H), 1.30 (t, J=7.2 Hz, 3H). ¹³C-NMR (75 MHz, CDCl₃): δ 167.3, 167.2, 161.9, 145.7, 131.2, 129.2, 123.4, 122.2, 116.7, 62.1, 55.5, 53.6, 48.0, 36.8, 35.1, 34.8, 34.3, 25.8, 24.9, 16.2. HRMS: Calc'd C₂₀H₂₆O₆: 362.1729. Found: 362.1724.



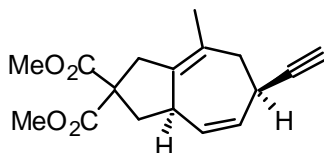
3g

Additional signals for minor regioisomer **3g**: $^1\text{H-NMR}$ (300 MHz, CDCl_3): δ 6.93 (dd, $J=8.7, 15.9$ Hz, 1H), 5.78 (d, $J=15.9$ Hz, 1H), 5.60 (m, 1H), 5.46 (m, 1H), 4.18 (q, $J=7.2$ Hz, 2H), 3.75 (s, 3H), 3.73 (s, 3H), 3.51 (m, 1H), 2.98 (d, $J=13.5$ Hz, 1H), 2.70 (d, $J=12.9$ Hz, 1H), 2.60 (m, 3H), 2.06 (m, 2H), 1.60 (s, 3H), 1.21 (t, $J=7.2$ Hz, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ 167.3, 167.1, 162.0, 146.3, 131.1, 128.3, 124.9, 123.3, 116.4, 59.5, 55.4, 53.3, 40.0, 36.5, 35.1, 34.9, 32.5, 24.9, 20.1, 17.7.



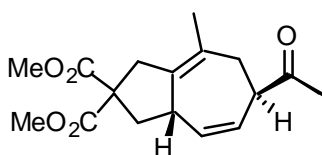
4h

4h: IR (film): 3288, 2954, 2917, 2851, 2112, 1733, 1435, 1275, 1257, 1201, 1164, 1071, cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.61 (ddd, $J=3.0, 6.0, 11.0$ Hz, 1H), 5.49 (dt, $J=2.0, 11.0$ Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.62 (m, 2H), 3.03 (d, $J=17.0$ Hz, 1H), 2.98 (d, $J=17.0$ Hz, 1H), 2.70 (m, 1H), 2.48 (d, $J=16.0$ Hz, 1H), 2.34 (m, 1H), 2.14 (d, $J=2.0$ Hz, 1H), 2.01 (t, $J=12.0$ Hz, 1H), 1.82 (s, 3H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): δ 171.9, 171.8, 136.5, 132.4, 128.0, 127.5, 85.7, 69.8, 52.85, 52.76, 41.5, 39.52, 39.50, 33.7, 32.4, 28.6, 18.5. HRMS: Calc'd for: $\text{C}_{17}\text{H}_{20}\text{O}_4$: 288.1362. Found: 288.1361.



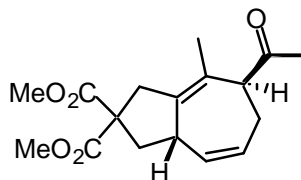
3h

Additional signals for minor regioisomer **3h**: $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.61 (ddd, $J=3.5, 6.5, 11.0$ Hz, 1H), 5.53 (d, $J=10.5$ Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.48 (m, 2H), 3.04 (d, $J=17.0$ Hz, 1H), 2.98 (d, $J=17.0$ Hz, 1H), 2.70 (m, 1H), 2.64 (d, $J=15.5$ Hz, 1H), 2.17 (m, $J=15.5$ Hz, 1H), 2.10 (d, $J=2.5$ Hz, 1H), 2.03 (t, $J=10.5$ Hz, 1H), 1.74 (s, 3H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): δ 172.0, 171.9, 135.1, 132.7, 130.0, 125.5, 86.2, 68.4, 58.3, 52.8, 41.4, 39.3, 39.2, 37.5, 30.3, 29.7, 22.5.



6b

6b: IR (film): 2955, 2922, 2859, 1736, 1434, 1261, 1202, 1163 cm^{-1} . $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.60 (dm, $J=12.0$ Hz, 1H), 5.56 (dm, $J=12.0$ Hz, 1H), 3.76 (s, 6H), 3.60 (m, 1H), 3.15 (d, $J=12.0$ Hz, 1H), 3.02 (m, 1H), 2.89 (m, 1H), 2.73 (m, 2H), 2.20 (s, 3H), 2.03 (m, 2H), 1.76 (s, 3H). $^{13}\text{C-NMR}$ (125 MHz, CDCl_3): δ 209.3, 171.9, 137.5, 133.3, 127.5, 126.8, 125.8, 58.4, 55.2, 52.8, 50.6, 41.7, 39.9, 39.4, 34.4, 29.7, 27.5. HRMS Calc'd for: $\text{C}_{17}\text{H}_{22}\text{O}_5$: 306.1467. Found: 306.1469.

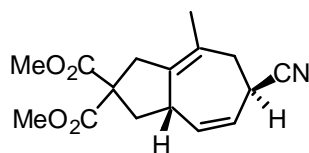


7b

Additional signals for minor regioisomer **7b**: $^1\text{H-NMR}$ (500 MHz, CDCl_3): δ 5.82 (ddd, $J=2.5, 6.0, 11.0$ Hz, 1H), 5.76 (ddd, $J=1.5, 2.5, 10.5$ Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.61 (m, 2H), 3.04 (d, $J=16.5$ Hz, 1H), 2.87 (dt, $J=2.0, 17.0$ Hz, 1H), 2.71 (dq, $J=2.5, 10.0$

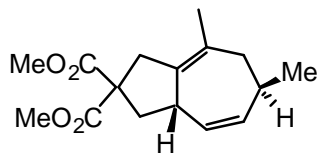
Hz, 1H), 2.54 (m, 1H), 2.29 (m, 1H), 2.16 (s, 3H), 2.05 (m, 1H), 1.59 (d, J=3.5 Hz, 3H).

^{13}C -NMR (125 MHz, CDCl_3): δ 209.3, 172.1, 134.6, 134.3, 130.9, 128.8, 127.8, 58.2, 58.1, 52.8, 50.5, 41.2, 39.6, 39.4, 34.1, 29.7, 27.6.



6d

6d: IR (film): 2954, 2855, 1783, 1435, 1258, 1204, 1165, 1062 cm^{-1} . ^1H -NMR (500 MHz, CDCl_3): δ 5.61 (dt, J=2.5, 11.5 Hz, 1H), 5.50 (dq, J=4.0, 11.5 Hz, 1H), 3.76 (s, 3H), 3.75 (s, 3H), 3.66 (bm, 1H), 3.33 (m, 1H), 2.98 (d, J=16.5 Hz, 1H), 2.93 (d, J=13.0 Hz, 1H), 2.85 (m, J=17.0 Hz, 1H), 2.73 (ddd, J=2.0, 8.5, 13.0 Hz, 1H), 2.24 (dt, J=1.5, 11.5 Hz, 1H), 1.96 (dd, J=11.0, 13.0 Hz, 1H), 1.73 (s, 3H). ^{13}C -NMR (125 MHz, CDCl_3): δ 171.61, 171.55, 138.9, 134.4, 126.4, 122.9, 120.8, 58.1, 52.9, 52.8, 41.5, 39.9, 38.9, 36.0, 29.7, 20.8. HRMS Calc'd for $\text{C}_{16}\text{H}_{19}\text{O}_4\text{N}$: 289.1314. Found: 289.1320.



6f

6f: IR (film): 2955, 2926, 2872, 1732, 1435, 1268, 1229, 1205, 1165, 1086, 1066 cm^{-1} . ^1H -NMR (500 MHz, CDCl_3): δ 5.33 (m, 2H), 3.744 (s, 3H), 3.738 (s, 3H), 3.55 (m, 1H), 3.00 (d, J=16.0 Hz, 1H), 2.87 (dq, J=2.0, 15.5 Hz, 1H), 2.71 (ddd, J=2.0, 8.5, 12.5 Hz, 1H), 2.46 (t, 12.5 Hz, 1H), 2.24 (m, 1H), 1.93 (dd, J=11.0, 12.5 Hz, 1H), 1.76 (m, J=2.5 Hz, 1H), 1.72 (d, J=1.0 Hz, 3H), 0.98 (d, J=7.0 Hz, 3H). ^{13}C -NMR (125 MHz, CDCl_3): δ

172.1, 172.0, 136.6, 135.4, 129.2, 129.1, 58.4, 52.7, 52.6, 42.0, 41.0, 39.7, 38.8, 31.1,
23.6, 21.0. HRMS Calc'd for C₁₆H₂₂O₄: 278.1518. Found: 278.1512.