Supporting Information

for

Rh(III)-catalyzed C−H activation/desymmetrization of diazabicycles with arenes: facile synthesis of functionalized cyclopentenes

Sunliang Cui,* Yan Zhang, and Qifan Wu

Institute of Materia Medica and College of Pharmaceutical Sciences,

Zhejiang University, Hangzhou 310058, P.R.China

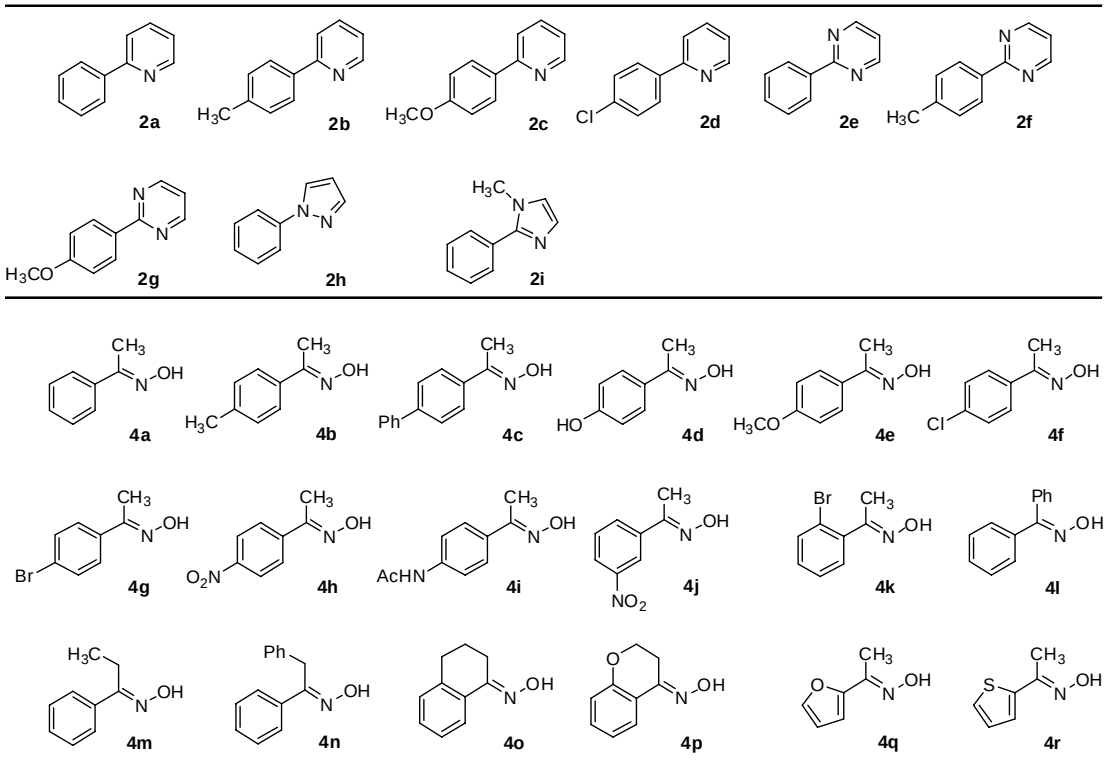
E-mail: slcui@zju.edu.cn

Contents

General Information:

Infrared spectra were obtained on a FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on BRUKER AVANCE III 500 or BRUKER AVANCE III 400 spectrometer. CD_3OD, acetone-*d6* and $CDCl_3$ were used as solvent. Chemical shifts were referenced relative to residual solvent signal (CD_3OD, ^{1}H NMR: δ 3.31 ppm, ^{13}C NMR: δ 49.0 ppm; acetone-*d6*, ^{1}H NMR: δ 2.05 ppm, ^{13}C NMR: δ 29.84 ppm; $CDCl_3$: ^{1}H NMR: δ 7.26 ppm, ^{13}C NMR: δ 77.0 ppm). The following abbreviations are used to describe peak patterns where appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants (*J*) are reported in Hertz (Hz). HRMS were performed on Agilent Technologies 6224 TOF LC/MS apparatus (ESI). Melting points were measured with micro melting point apparatus.

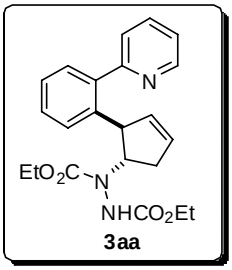
The diazabicycles **1** were prepared according to the literature,[1] while heterocycles **2** and oximes **4** were purchased or prepared according to literature report.[2] $[Cp^*RhCl_2]_2$, AgOAc, anhydrous CH_3OH were commercial available.



Typical Procedure:

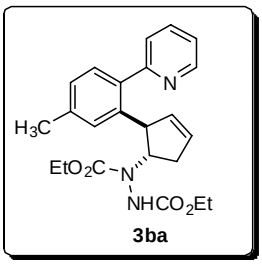
Typical procedure for desymmetrization: $[Cp^*RhCl_2]_2$ (2.5 mg, 2 mol%) and AgOAc (2.7 mg, 8 mol%) were added to a vial. MeOH (0.5 mL) was added and the solution was stirred for 10 min at room temperature. Afterwards, 2-phenylpyridine (31 mg, 0.2 mmol), diazabicycle **1a** (52.8 mg, 0.22 mmol), and additional MeOH (1 mL) were added. The reaction was kept at 60 ^oC under air. After completion, the solution was concentrated and subject to flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:3) as eluent to give product **3aa** as a colorless oil (64.8 mg, 82% yield).

Characterization of Products 3 and 5:



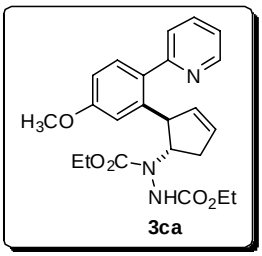
3aa

Diethyl 1-(2-(2-(pyridin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarbox--ylate (3aa). Colorless oil; ^1H NMR (CD_3OD, 500 MHz): δ= 8.63 (s, 1H), 7.90 (t, *J* = 6.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.43-7.31 (m, 5H), 5.78 (m, 1H), 5.58 (s, 1H), 4.97 (s, 1H), 4.31 (s, 1H), 4.11-3.98 (m, 4H), 2.67-2.52 (m, 2H), 1.26-1.10 (m, 6H) ppm; ^{13}C NMR (CD_3OD, 125 MHz): δ= 161.0, 158.6, 157.5, 149.4, 141.5, 138.7, 134.6, 131.0, 130.1, 129.0, 127.6, 126.7, 123.6, 70.1, 63.4, 62.8, 50.9, 36.0, 14.9, 14.7 ppm; HRMS (ESI) (*m/z*): calcd for $C_{22}H_{25}N_3O_4$ $[M+H]^+$ 396.1918, found 396.1933.



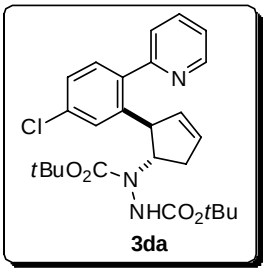
3ba

Diethyl 1-(2-(5-methyl-2-(pyridin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3ba). White solid; m.p.94-96 ^{o}C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 8.61 (s, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 6.0 Hz, 1H), 7.20-7.12 (m, 3H), 5.77 (s, 1H), 5.55 (s, 1H), 4.98 (s, 1H), 4.30 (s, 1H), 4.11-3.96 (m, 4H), 2.65-2.49 (m, 2H), 2.36 (s, 3H), 1.30-1.10 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 161.1, 158.5, 157.5, 149.3, 141.9, 140.0, 138.7, 138.6, 134.7, 131.1, 130.1, 129.5, 128.3, 126.7, 123.4, 70.0, 63.4, 62.8, 50.6, 36.0, 21.4, 14.9, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{27}N_3O_4$[M+H]$^{+}$ 410.2075; found 410.2074.



3ca

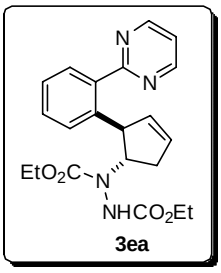
Diethyl 1-(2-(5-methoxy-2-(pyridin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine 1,2-dicarboxylate (3ca). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 8.61 (s, 1H), 7.87 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 6.0 Hz, 1H), 7.25 (d, *J* = 8.5 Hz, 1H), 6.89 (d, *J* = 7.0 Hz, 2H), 5.78 (m, 1H), 5.56 (s, 1H), 5.00 (s, 1H), 4.35 (s, 1H), 4.12-3.96 (m, 4H), 3.82 (s, 3H), 2.64-2.50 (m, 2H), 1.30-1.11 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 161.7, 160.9, 158.5, 157.5, 149.3, 138.7, 134.5, 134.2, 132.6, 130.3, 126.8, 123.2, 114.2, 113.1, 69.9, 63.4, 62.8, 55.8, 50.9, 35.9, 14.9, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{27}N_3O_5$ [M+H]$^{+}$ 426.2024; found 426.2031.



3da

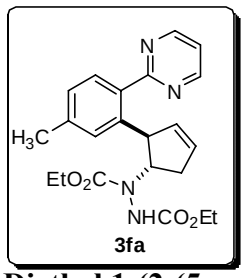
Di-*tert*-butyl 1-(2-(5-chloro-2-(pyridin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazi--ne-1,2-dicarboxylate (3da). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 8.66 (s, 1H), 7.92 (s, 1H), 7.51-7.33 (m, 5H), 5.80 (s, 1H), 5.52 (s, 1H), 4.29 (s, 1H),

2.61-2.48 (m, 2H), 1.50-1.22 (m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.9, 157.6, 156.6, 149.6, 140.2, 138.9, 136.0, 134.0, 132.8, 131.0, 129.0, 127.6, 126.7, 123.9, 120.1, 82.4, 81.9, 70.7, 67.2, 35.7, 28.6, 28.4; HRMS (ESI) (*m/z*): calcd for $C_{26}H_{32}ClN_3O_4$ $[M+H]^+$ 486.2154; found 486.2156.



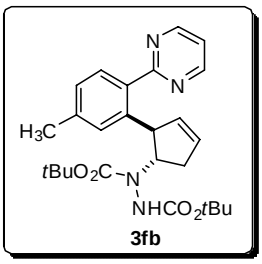
3ea

Diethyl 1-(2-(2-(pyrimidin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3ea). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 8.87 (d, *J* = 4.5 Hz, 2H), 7.63 (s, 1H), 7.47-7.33 (m, 4H), 5.80 (s, 1H), 5.57 (s, 1H), 4.59 (s, 1H), 4.15-3.93 (m, 4H), 2.71-2.53 (m, 2H), 1.30-1.07 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 168.4, 158.4, 143.5, 139.6, 134.6, 131.8, 131.0, 129.3, 127.4, 125.9, 125.2, 120.4, 69.1, 63.3, 62.8, 51.1, 36.2, 14.9, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{21}H_{24}N_4O_4$ $[M+H]^+$ 397.1871; found 397.1858.



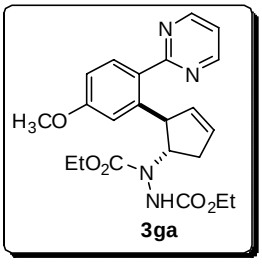
3fa

Diethyl 1-(2-(5-methyl-2-(pyrimidin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3fa). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 8.85 (d, *J* = 4.5Hz, 2H), 7.56-7.41 (m, 2H), 7.20-7.16 (m, 2H), 5.81 (d, *J* = 3.5 Hz, 1H), 5.55 (s, 1H), 5.05 (s, 1H), 4.60 (s, 1H), 4.14-3.93 (m, 4H), 2.71-2.51 (m, 2H), 2.38 (s, 3H), 1.34-1.27 (m, 6H); ^{13}C NMR (CD_3OD, 125 MHz): δ= 168.5, 158.4, 143.4, 141.2, 139.9, 136.8, 134.8, 132.0, 130.2, 129.9, 128.3, 125.9, 125.2, 120.2, 69.4, 63.3, 62.8, 50.8, 35.9, 21.4, 14.9, 14.5; HRMS (ESI) (*m/z*): calcd for $C_{22}H_{26}N_4O_4$ $[M+H]^+$ 411.2027; found 411.2044.



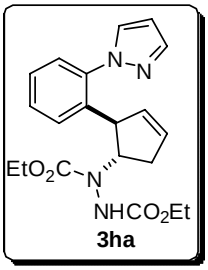
3fb

Di-*tert*-butyl 1-(2-(5-methyl-2-(pyrimidin-2-yl)phenyl)cyclopent-3-en-1-yl)hydra--zine-1,2-dicarboxylate (3fb). Colorless oil; ^{1}H NMR (acetone-*d6*, 400 MHz): δ= 8.92 (s, 2H), 8.26-8.06 (m, 1H), 7.73 (s, 1H), 7.47 (s, 1H), 7.26-7.17 (m, 2H), 5.79 (d, *J* = 2.8 Hz, 1H), 5.51 (s, 1H), 5.10-5.01 (m, 1H), 4.77 (s, 1H), 2.60 (s, 2H), 2.39 (s, 2H), 1.47-1.10 (m, 18H); ^{13}C NMR(acetone-*d6*, 100 MHz): δ= 167.7, 158.0, 156.2, 155.6, 143.2, 140.4, 136.9, 135.0, 132.3, 129.9, 127.9, 119.9, 80.6, 80.3, 67.8, 48.9, 30.5, 28.5, 21.4; HRMS (ESI) (*m/z*): calcd for $C_{26}H_{34}N_4O_4$ $[M+H]^+$ 467.2653; found 467.2666.



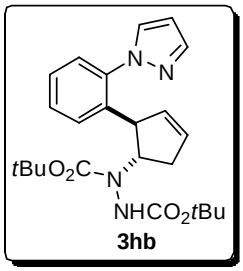
3ga

Diethyl 1-(2-(5-methoxy-2-(pyrimidin-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3ga). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 8.84 (d, *J* = 5.0Hz, 2H), 7.68 (s, 1H), 7.38 (t, *J* = 5.0Hz, 1H), 6.93-6.90 (m, 2H), 5.83 (d, *J* = 3.5 Hz, 1H), 5.57 (s, 1H), 5.04 (s, 1H), 4.74 (s, 1H), 4.14-3.91 (m, 4H), 3.84 (s, 3H), 2.71-2.52 (m, 2H), 1.34-1.27 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 168.1, 162.5, 158.7, 158.3, 157.8, 145.5, 134.6, 133.9, 132.0, 130.5, 125.2, 119.9, 114.6, 113.0, 69.3, 63.4, 62.8, 55.8, 51.1, 36.1, 14.9, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{22}H_{26}N_4O_5$ $[M+H]^+$ 427.1976; found 427.1993.



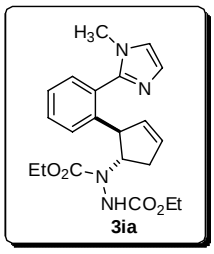
3ha

Diethyl 1-(2-(2-(1H-pyrazol-1-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3ha). White solid; m.p. 94-96 °C; ^{1}H NMR (acetone-*d6*, 400 MHz): δ= 7.87 (s, 1H), 7.74 (s, 1H), 7.49 (m, 2H), 7.37 (m, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 6.52 (s, 1H), 5.81 (s, 1H), 5.49 (m, 1H), 4.97 (m, 1H), 4.14-3.95 (m, 5H), 2.59 (br, 2H), 1.24-0.94 (m, 6H); ^{13}C NMR(acetone-*d6*, 100 MHz): δ= 157.0, 156.3, 141.1, 140.7, 140.2, 133.6, 132.9, 130.7, 129.9, 129.7, 128.1, 127.3, 107.5, 68.8, 62.3, 61.9, 47.3, 35.8, 14.8, 14.7; HRMS (ESI) (*m/z*): calcd for $C_{20}H_{24}N_4O_4$ $[M+H]^+$ 385.1871; found 385.1856.



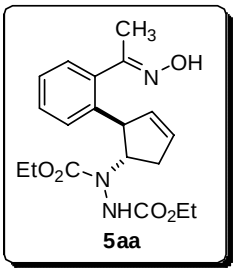
3hb

Di-*tert*-butyl 1-(2-(2-(1H-pyrazol-1-yl)phenyl)cyclopent-3-en-1-yl)hydrazine-1,2-dicarboxylate (3hb). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.82 (s, 1H), 7.74 (s, 1H), 7.47 (t, *J* = 4.0 Hz, 2H), 7.37 (s, 1H), 7.28 (d, *J* =7.5 Hz, 1H), 6.54 (s, 1H), 5.81 (s, 1H), 5.51(s, 1H), 4.93 (s, 1H), 3.98 (s, 1H), 2.62-2.48(m, 2H), 1.47-1.39(m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 157.7, 156.5, 152.6, 141.4, 140.8, 133.6, 131.0, 130.6, 130.1, 129.8, 128.4, 127.8, 107.8, 84.6, 82.1, 70.7, 67.2, 35.9, 28.6, 28.4; HRMS (ESI) (*m/z*): calcd for $C_{24}H_{32}N_4O_4$ $[M+H]^+$ 441.2497; found 441.2484.



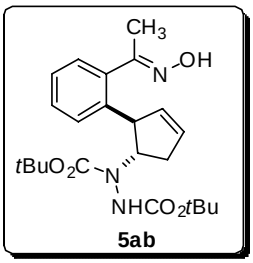
3ia

Diethyl 1-(2-(2-(1-methyl-1H-imidazol-2-yl)phenyl)cyclopent-3-en-1-yl)hydrazine 1,2-dicarboxylate (3ia). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.50-7.27 (m, 4H), 7.20-7.06 (m, 2H), 5.78 (s, 1H), 5.58 (s, 1H), 4.11-3.98 (m, 5H), 3.50 (s, 3H), 2.62-2.48 (m, 2H), 1.31-1.15 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 158.6, 157.4, 148.3, 144.9, 133.9, 131.6, 131.2, 130.9, 130.5, 129.3, 127.7, 127.6, 123.0, 69.9, 63.4, 62.7, 50.9, 35.7, 34.1, 14.9, 14.7; HRMS (ESI) (*m/z*): calcd for $C_{21}H_{26}N_4O_4$ $[M+H]^+$ 399.2027; found 399.2024.



5aa

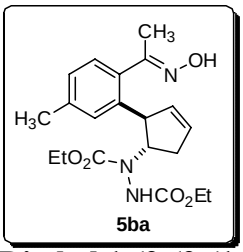
Diethyl 1-(2-(2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en-1-yl)hydrazine 1,2-dicarboxylate (5aa). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.36-7.20 (m, 4H), 5.85 (s, 1H), 5.62 (s, 1H), 4.31 (s, 1H), 4.11 (m, 4H), 2.73-2.59 (m, 2H), 2.20 (s, 3H), 1.30 (m, 6H); ^{13}C NMR (CD_3OD, 100MHz): δ= 159.0, 158.8, 157.6, 142.7, 139.2, 134.5, 130.4, 129.8, 129.4, 128.9, 127.4, 69.1, 63.4, 62.9, 51.7, 36.4, 17.1, 14.9, 14.8; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{25}N_3O_5$ $[M+H]^+$ 376.1867; found 376.1869.



5ab

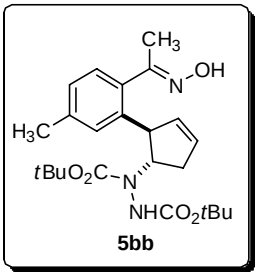
Di-*tert*-butyl 1-(2-(2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en-1-yl)hydra--zine-1,2-dicarboxylate (5ab). White solid; m.p. 59-61 °C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.33-7.19 (m, 4H), 5.83 (m, 1H), 5.57 (br, 1H), 4.24 (br, 1H), 2.66-2.52 (m, 2H), 2.18 (s, 3H), 1.50-1.29 (m, 18H); ^{13}C NMR (CD_3OD, 100MHz): δ= 158.6, 157.8, 156.6, 152.6, 143.0, 139.3, 134.4, 130.5, 129.8, 129.2, 127.4, 82.2, 70.3, 51.6, 36.2,

28.6, 28.4, 17.2; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{33}N_3O_5$ $[M+H]^+$ 432.2493; found 432.2478.



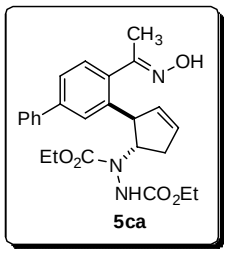
5ba

Diethyl 1-(2-(2-(1-(hydroxyimino)ethyl)-5-methylphenyl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5ba). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.06 (m, 3H), 5.82 (m, 1H), 5.58 (br, 1H), 4.28-4.01 (m, 5H), 2.70-2.50 (m, 2H), 2.31 (s, 3H), 2.16 (s, 3H), 1.34-1.18 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.0, 157.6, 142.5, 139.7, 136.3, 134.6, 130.3, 129.3, 128.2, 69.1, 63.4, 62.9, 51.5, 36.3, 21.4, 17.1, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{20}H_{27}N_3O_5$ $[M+H]^+$ 390.2024; found 390.2033.



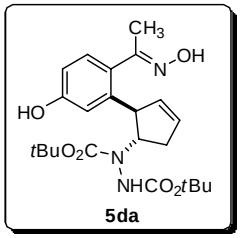
5bb

Di-*tert*-butyl 1-(2-(2-(1-(hydroxyimino)ethyl)-5-methylphenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5bb). White solid; m.p. 58-60 ^{o}C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.07 (m, 3H), 5.82 (br, 1H), 5.56 (br, 1H), 4.24 (br, 1H), 2.65-2.49 (m, 2H), 2.32 (s, 3H), 2.16 (s, 3H), 1.52-1.12 (m, 18H); ^{13}C NMR (CD_3OD, 100MHz): δ= 158.6, 158.0, 156.7, 142.7, 139.6, 136.5, 134.6, 130.3, 129.6, 129.2, 128.1, 82.2, 70.4, 36.2, 28.6, 21.4, 17.2; HRMS (ESI) (*m/z*): calcd for $C_{24}H_{35}N_3O_5$ $[M+H]^+$ 446.2650; found 446.2655.



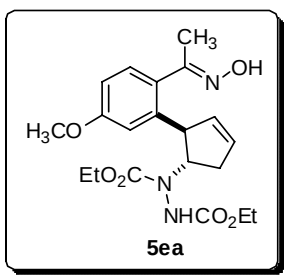
5ca

Diethyl 1-(2-(4-(1-(hydroxyimino)ethyl)-[1,1'-biphenyl]-3-yl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5ca). White solid; m.p.147-149 ^{o}C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.59 (d, *J*= 7.5 Hz, 2H), 7.50 (d, *J* = 6.5 Hz, 2H), 7.43 (t, *J*= 7.5Hz, 2H), 7.35-7.28 (m, 2H), 5.87 (s, 1H), 5.66 (s, 1H), 4.97 (br, 1H), 4.39 (br, 1H), 4.18-4.02 (m, 4H), 2.73-2.59 (m, 2H), 2.22 (s, 3H), 1.30-1.27 (m, 6H); ^{13}C NMR (CD_3OD, 125 MHz): δ= 159.0, 158.5, 157.7, 143.1, 142.8, 141.9, 138.2, 134.4, 130.6, 130.1, 129.9, 128.6, 128.0, 127.5, 126.1, 69.0, 63.5, 62.9, 51.7, 36.2, 16.8, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{25}H_{29}N_3O_5$ $[M+H]^+$: 452.2180, found: 452.2173.



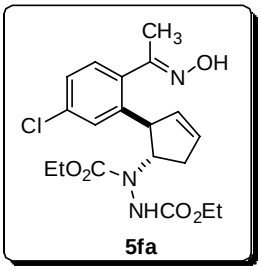
5da

Di-*tert*-butyl 1-(2-(5-hydroxy-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en-1--yl)hydrazine-1,2-dicarboxylate (5da). White solid; m.p.127-129 ^{o}C; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.03 (d, *J*= 8.4 Hz, 1H), 6.88-6.33 (m, 2H), 5.81 (br, 1H), 5.55 (br, 1H), 4.25 (br, 1H), 2.62-2.48 (m, 2H), 2.15 (s, 3H), 1.48-1.29 (m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.0, 157.9, 156.5, 144.5, 134.6, 130.6, 130.3, 115.4, 114.6, 113.4, 82.3, 70.4, 51.5, 36.1, 28.5, 17.3; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{33}N_3O_6$ $[M+H]^+$ 448.2442; found 448.2437.



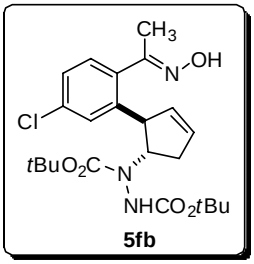
5ea

Diethyl 1-(2-(2-(1-(hydroxyimino)ethyl)-5-methoxyphenyl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5ea). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.13 (d, *J* = 8.4 Hz, 1H), 6.80 (m, 2H), 5.83 (d, *J* = 3.2 Hz, 1H), 5.60 (br, 1H), 4.33 (s, 1H), 4.17 (m, 4H), 3.77 (s, 3H), 2.69-2.55 (m, 2H), 2.16 (s, 3H), 1.30-1.25 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 161.3, 159.0, 158.7, 157.6, 144.3, 134.3, 131.7, 130.8, 130.5, 114.1, 112.9, 69.0, 63.7, 62.9, 55.7, 51.6, 36.2, 17.2, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{20}H_{27}N_3O_6$ $[M+H]^+$ 406.1973; found 406.1972.



5fa

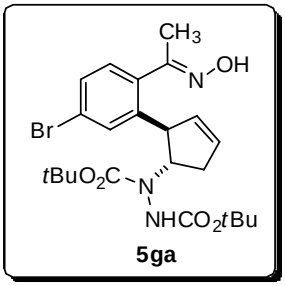
Diethyl 1-(2-(5-chloro-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5fa). Yellow solid; m.p. 119-120 °C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.25-7.18 (m, 3H), 5.88 (s, 1H), 5.58 (s, 1H), 4.84 (m, 1H), 4.32 (s, 1H), 4.16 (m, 4H), 2.71-2.57 (m, 2H), 2.16 (s, 3H), 1.34-1.17 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.0, 157.6, 145.2, 137.9, 135.5, 133.7, 131.1, 128.9, 127.6, 68.1, 63.5, 62.9, 51.9, 36.4, 16.8, 14.7, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{24}ClN_3O_5$ $[M+H]^+$ 410.1477; found 410.1487.



5fb

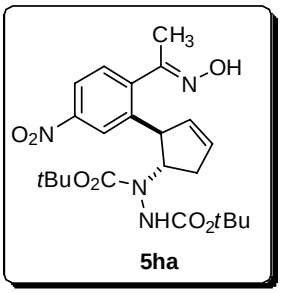
Di-*tert*-butyl 1-(2-(5-chloro-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en-1--yl)hydrazine-1,2-dicarboxylate (5fb). White solid; m.p. 143-145 °C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.25-7.20 (m, 3H), 5.89 (m, 1H), 5.56 (br, 1H), 4.26 (br, 1H), 2.66-2.56 (m, 2H), 2.17 (s, 3H), 1.50-1.29 (m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 157.9, 156.6, 152.6, 145.3, 138.1, 135.5, 133.7, 131.1, 129.2, 127.5, 82.4, 70.0,

66.4, 51.7, 36.1, 28.6, 28.4, 16.8; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{32}ClN_3O_5$ $[M+H]^+$ 466.2103; found 466.2127.



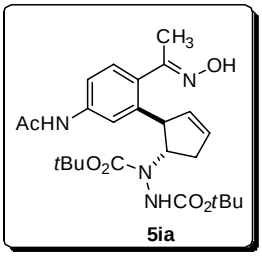
5ga

Di-*tert*-butyl 1-(2-(5-bromo-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5ga). White solid; m.p.161-163 ^oC; ^1H NMR (CD_3OD, 500 MHz): δ= 7.40 (d, *J* = 6.0 Hz, 2H), 7.13 (d, *J* = 5.5 Hz, 1H), 5.86 (m, 1H), 5.56 (br, 1H), 4.22 (br, 1H), 2.64-2.55 (m, 2H), 2.17 (s, 3H), 1.48-1.17 (m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 157.9, 156.5, 145.7, 138.5, 133.7, 132.1, 131.3, 130.5, 123.7, 82.5, 82.0, 70.1, 51.7, 36.1, 28.6, 28.4, 16.9; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{32}BrN_3O_5$ $[M+H]^+$ 510.1598; found 510.1601.



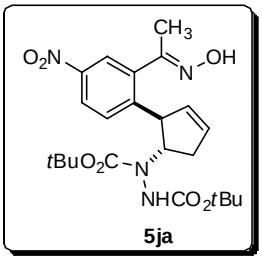
5ha

Di-*tert*-butyl 1-(2-(2-(1-(hydroxyimino)ethyl)-5-nitrophenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5ha). Yellow solid; m.p.177-179 ^oC; ^1H NMR (CD_3OD, 400 MHz): δ= 8.120 (m, 2H), 7.47 (m, 1H), 5.92 (m, 1H), 5.62 (br, 1H), 4.40 (br, 1H), 2.72-2.57 (m, 2H), 2.22 (s, 3H), 1.48-1.29 (m, 18H); ^{13}C NMR (CD_3OD, 100MHz): δ= 156.6, 155.6, 154.4, 148.0, 144.7, 143.5, 131.8, 131.6, 129.1, 123.2, 122.8, 121.1, 81.6, 81.1, 69.3, 50.9, 35.6, 28.1, 16.5, 16.2; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{32}N_4O_7$ $[M+H]^+$ 477.2344; found 477.2351.



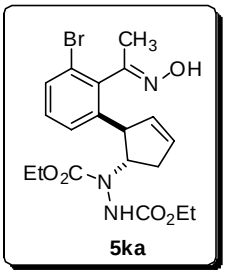
5ia

Di-*tert*-butyl 1-(2-(5-acetamido-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent--3-en-1-yl)hydrazine-1,2-dicarboxylate (5ia). White solid; m.p.139-141 ^{o}C; ^{1}H NMR (acetone-*d6*, 400 MHz): δ= 9.24 (s, 1H), 8.01 (s, 1H), 7.66 (s, 1H), 7.41-7.35 (m, 1H), 7.16 (br, 1H), 5.81 (br, s, 1H), 5.57 (br, s, 1H), 4.78 (br, 1H), 4.49-4.36 (m, 1H), 2.58 (br, 2H),2.17 (s, 3H), 2.08 (s, 3H), 1.44-1.29 (m, 18H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ= 169.0, 156.6, 156.4, 156.0, 139.0, 132.8, 130.1, 128.7, 118.6, 117.8, 81.9, 81.0, 28.2, 24.3, 16.8, 16.2; HRMS (ESI) (*m/z*): calcd for $C_{25}H_{36}N_4O_6$ $[M+H]^+$ 489.2708; found 489.2704.



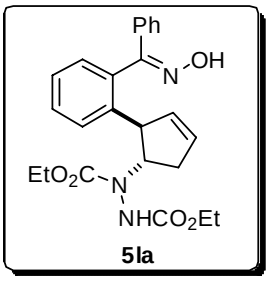
5ja

Di-*tert*-butyl 1-(2-(2-(1-(hydroxyimino)ethyl)-4-nitrophenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5ja). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 8.17 (d, *J* = 8.0 Hz, 1H), 8.07 (s, 1H), 7.52 (br, 1H), 5.90(m, 1H), 5.59 (br, s, 1H), 4.38 (m, 1H), 2.74-2.56 (m, 2H), 2.24 (s, 3H), 1.48-1.28 (m, 18H); ^{13}C NMR (CD_3OD, 100MHz): δ= 158.0, 156.5, 151.4, 147.6, 140.6, 133.2, 131.8, 130.6, 124.4, 124.3, 82.3, 66.6, 52.6, 36.0, 28.2, 16.2; HRMS (ESI) (*m/z*): calcd for $C_{23}H_{32}N_4O_7$[$M+H]^+$ 477.2344; found 477.2339.

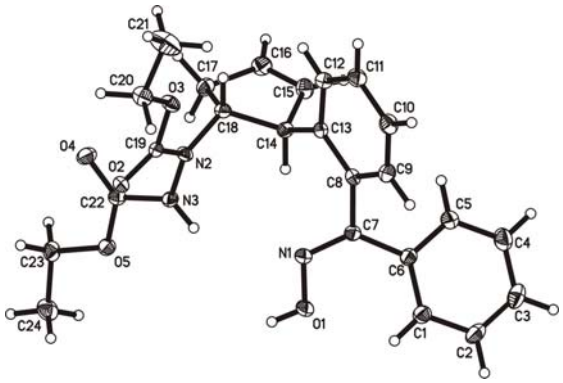


5ka

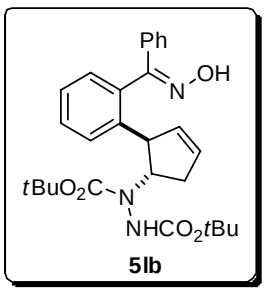
Diethyl 1-(2-(3-bromo-2-(1-(hydroxyimino)ethyl)phenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5ka). White solid; m.p. 146-147 °C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.49 (d, *J* =5.0 Hz, 1H), 7.25 (m, 2H), 5.84 (m, 1H), 5.56 (m, 1H), 4.96 (s, 1H), 4.16-4.04 (m, 5H), 2.80-2.60 (m, 2H), 2.13 (s, 3H), 1.34-1.17 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.0, 158.1, 157.4, 146.2, 139.6, 139.3, 133.5, 131.8, 131.2, 127.9, 124.1, 66.9, 63.5, 62.8, 54.8, 36.7, 16.8, 14.8, 14.7; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{24}BrN_3O_5$ $[M+H]^+$ 454.0972; found 454.0943.



5la



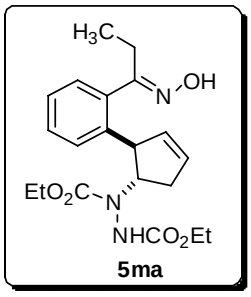
Diethyl 1-(2-(2-((hydroxyimino)(phenyl)methyl)phenyl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5la). White solid; m.p. 70-72 °C; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.56 (d, *J* = 3.6 Hz, 2H), 7.40-7.30 (m, 5H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.17 (s, 1H), 5.73 (br, 1H), 5.40 (br, 1H), 4.25 (br, 1H), 4.13 (m, 4H), 2.69-2.53 (m, 2H), 1.34-1.03 (m, 6H); ^{13}C NMR (CD_3OD, 100MHz): δ= 158.9, 157.7, 157.4, 144.0, 138.3, 135.3, 134.4, 131.5, 131.3, 130.5, 130.3, 130.2, 129.7, 129.1, 128.9, 127.3, 69.1, 63.5, 63.0, 51.5, 36.5, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{24}H_{27}N_3O_5$ $[M+H]^+$: 438.2024; found 438.2023.



5lb

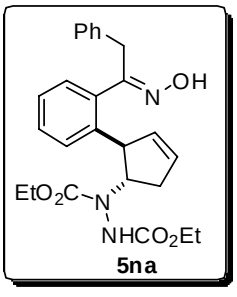
Di-*tert*-butyl 1-(2-(2-((hydroxyimino)(phenyl)methyl)phenyl)cyclopent-3-en--1-yl)hydrazine-1,2-dicarboxylate (5lb). White solid; m.p. 80-82 °C; ^{1}H NMR

(CD_3OD, 400 MHz): δ= 7.88 (s, 0.2 H, NH), 7.57 (br, 2H), 7.43-7.36 (m, 5H), 7.26-7.14 (m, 2H), 5.73(br, 1H), 5.39 (m, 1H), 4.89 (m, 1H), 4.16 (br, 1H), 2.60-2.50 (m, 2H), 1.54-1.24 (m, 18H); ^{13}C NMR (CD_3OD, 100MHz): δ= 157.6, 156.5, 152.6, 144.0, 138.4, 135.3, 134.4, 131.4, 131.2, 130.3, 130.2, 129.6, 129.3, 129.0, 127.3, 82.1, 70.1, 66.8, 51.2, 36.3, 28.6, 28.4; HRMS (ESI) (*m/z*): calcd for $C_{28}H_{35}N_3O_5$[M+H]$^+$ 494.2650; found 494.2634.



5ma

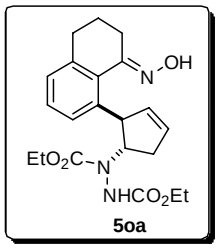
Diethyl 1-(2-(2-(1-(hydroxyimino)propyl)phenyl)cyclopent-3-en-1-yl) hydra--zine-1,2-dicarboxylate (5ma). White solid; m.p. 87-89 °C; ^1H NMR (CD_3OD, 500 MHz): δ= 7.33 (t, *J* =7.5 Hz, 1H), 7.23 (m, 2H), 7.14 (d, *J* =7.5Hz, 1H), 5.82 (d, *J* =3.5 Hz, 1H), 5.57 (m, 1H), 4.93 (m, 1H), 4.15-3.99 (m, 5H), 2.76-2.62 (m, 4H), 1.34-1.21 (m, 6H), 0.98 (t, *J* = 7.5Hz, 3H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 163.6, 159.0, 157.6, 143.2, 137.7, 134.5, 130.4, 129.9, 129.6, 128.8, 127.3, 69.5, 63.4, 62.9, 51.9, 36.4, 24.3, 14.8, 14.6, 9.8; HRMS (ESI) (*m/z*): calcd for $C_{20}H_{27}N_3O_5$ [M+H]$^+$ 390.2024; found 390.2012.



5na

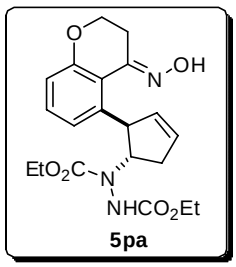
Diethyl 1-(2-(2-(1-(hydroxyimino)-2-phenylethyl)phenyl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5na). Colorless oil; ^1H NMR (CD_3OD, 400 MHz): δ= 7.28 (t, *J*= 7.2 Hz, 1H), 7.16-7.00 (m, 8H), 5.70 (s, 1H), 5.11 (m, 1H), 4.42 (d, *J*= 14.0

Hz, 1H), 4.18-3.70 (m, 6H), 2.65-2.54 (m, 2H), 1.40-1.14 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 160.2, 159.0, 157.9, 143.5, 137.6, 134.7, 130.7, 129.9, 129.4, 128.8, 127.5, 127.1, 69.8, 63.5, 63.1, 51.3, 37.3, 36.1, 30.8, 15.0, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{25}H_{29}N_3O_5$ $[M+H]^+$ 452.2180; found 452.2181.



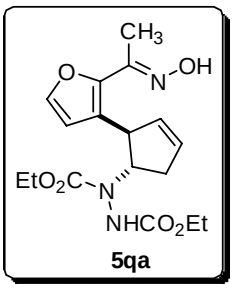
5oa

Diethyl 1-(2-(8-(hydroxyimino)-5,6,7,8-tetrahydronaphthalen-1-yl)cyclopent-3--en-1-yl)hydrazine-1,2-dicarboxylate (5oa). White solid; m.p. 144-146 ^{o}C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.17 (t, *J* = 7.0 Hz, 2H), 7.03 (d, *J* = 6.5 Hz, 1H), 5.80 (s, 1H), 5.59 (br, 1H), 5.11(br, 1H), 4.82 (m, 1H), 4.18-3.91 (m, 4H), 2.79-2.53 (m, 6H), 1.80-1.66 (m, 2H), 1.34-1.02 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.1, 157.7, 143.6, 143.3, 135.1, 131.5, 129.5, 127.7, 126.9, 69.2, 63.4, 63.0, 50.3, 36.2, 32.2, 26.2, 22.5, 14.8, 14.5; HRMS (ESI) (*m/z*): calcd for $C_{21}H_{27}N_3O_5$ $[M+H]^+$ 402.2024; found 402.2029.



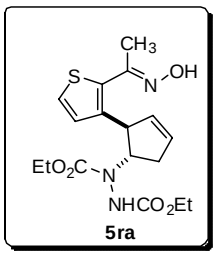
5pa

Diethyl 1-(2-(4-(hydroxyimino)chroman-5-yl)cyclopent-3-en-1-yl)hydrazine--1,2-dicarboxylate (5pa). White solid; m.p. 151-152 ^{o}C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.16 (s, 1H), 6.89 (s, 1H), 6.75 (d, *J*= 6.0 Hz, 1H), 5.81 (s, 1H), 5.58 (s, 1H), 5.39 (br, 1H), 4.19-4.00 (m, 6H), 3.10-2.98 (m, 2H), 2.69-2.54 (m, 2H), 1.31-1.19 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.4, 158.0, 152.9, 145.2, 134.7, 130.8, 129.9, 122.7, 119.8, 117.1, 66.1, 63.4, 63.0, 50.8, 36.2, 26.3, 14.8, 14.5; HRMS (ESI) (*m/z*): calcd for $C_{20}H_{25}N_3O_6$ $[M+H]^+$ 404.1816; found 404.1829.



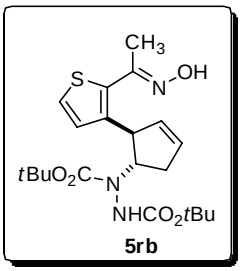
5qa

Diethyl 1-(2-(2-(1-(hydroxyimino)ethyl)furan-3-yl)cyclopent-3-en-1-yl)hydrazine--1,2-dicarboxylate (5qa). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.47 (m, 1H), 6.39 (s, 1H), 5.81 (m, 1H), 5.58 (m, 1H), 4.82 (m, 1H), 4.41 (m, 1H), 4.19-4.00 (m, 4H), 2.57-2.44 (m, 2H), 2.16 (s, 3H), 1.34-0.99 (m, 6H); ^{13}C NMR (CD_3OD, 125 MHz): δ= 160.5, 157.9, 143.5, 140.2, 135.4, 133.3, 130.8, 128.3, 112.5, 66.9, 63.7, 63.4, 63.0, 48.9, 35.5, 14.8, 14.7; HRMS (ESI) (*m/z*): calcd for $C_{17}H_{23}N_3O_6$ $[M+H]^+$ 366.1660; found 366.1643.



5ra

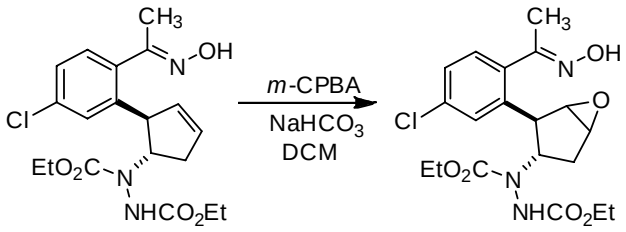
Diethyl 1-(2-(2-(1-(hydroxyimino)ethyl)thiophen-3-yl)cyclopent-3-en-1-yl)hydra--zine-1,2-dicarboxylate (5ra). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.34 (m, 1H), 6.93 (m, 1H), 5.78 (m, 1H), 5.58 (d, *J*= 4.0 Hz, 1H), 4.86 (m, 1H), 4.59 (s, 1H), 4.17-3.98 (m, 4H), 2.64-2.48 (m, 2H), 2.23 (s, 3H), 1.38-1.08 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.1, 157.8, 152.6, 142.9, 136.4, 134.0, 130.2, 129.3, 126.0, 67.3, 63.5, 63.0, 35.8, 16.3, 14.7, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{17}H_{23}N_3O_5S$ $[M+H]^+$ 382.1431; found 382.1437.



5rb

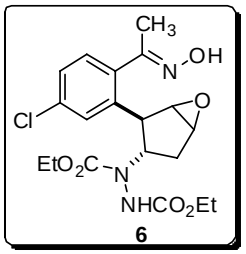
Di *tert*-butyl 1-(2-(2-(1-(hydroxyimino)ethyl)thiophen-3-yl)cyclopent-3-en-1-yl)-hydrazine-1,2-dicarboxylate (5rb). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.37 (m, 1H), 6.93 (m, 1H), 5.81 (m, 1H), 5.58 (br, 1H), 4.57 (m, 1H), 2.62-2.50 (m, 2H), 2.24 (s, 3H), 1.49-1.18 (m, 18H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 158.1, 156.8, 152.5, 143.3, 134.0, 130.4, 129.5, 126.5, 126.0, 82.3, 69.0, 47.2, 35.8, 28.6, 28.4, 16.4; HRMS (ESI) (*m/z*): calcd for $C_{21}H_{31}N_3O_5S$ $[M+H]^+$ 438.2057; found 438.2052.

Derivation of Product 5fa to 6 and 7:



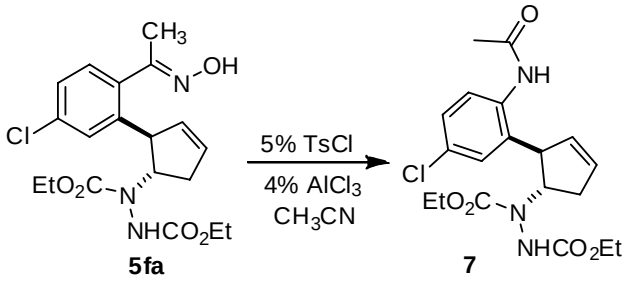
5fa **6**

To a vial was added **5fa** (82 mg, 0.2 mmol) and $NaHCO_3$ (34 mg, 0.4 mmol), DCM (2 mL) was then added. The solution was cooled to 0 ^{o}C and *m*-CPBA (81 mg, 85% purity, 0.4 mmol) was added in one portion. Afterwards, the reaction solution was slowly warmed to 15 ^{o}C and kept for 24 hours. After that, saturated Na_2SO_3 solution (2 mL) was added and the mixture was stirred for 15 min. The solution was diluted with DCM (10 mL) and water (5 mL) and then subject to separatory funnel. The aqueous layer was extracted with DCM for three times and the organic layer was combined, washed with saturated Na_2SO_3 solution, $NaHCO_3$ solution, brine, dried over anhydrous $MgSO_4$, concentrated under vacuum and subject to flash chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:3) as eluent to give product **6** as colorless oil (72 mg, 84.5% yield).



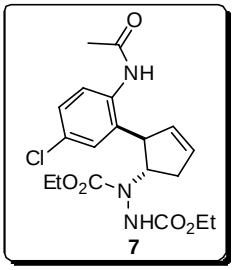
6

Diethyl 1-(2-(5-chloro-2-(1-(hydroxyimino)ethyl)phenyl)-6-oxabicyclo[3.1.0]--hexan-3-yl)hydrazine-1,2-dicarboxylate (6). Colorless oil; ^{1}H NMR (CD_3OD, 400 MHz): δ= 7.64 (s, 1H), 7.28 (m, 2H), 4.58 (m, 1H), 4.15-3.96 (m, 4H), 3.65 (m, 2H), 3.31 (m, 1H), 2.39 (q, *J* = 7.6 Hz, 1H), 2.22 (s, 3H), 1.96 (br, 1H), 1.45-1.11 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 158.9, 157.4, 140.4, 138.9, 135.1, 131.0, 129.4, 127.9, 63.6, 63.1, 60.6, 54.9, 44.6, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{24}ClN_3O_6$ $[M+H]^+$ 426.1427; found 426.1420.



5fa **7**

5fa (62 mg, 0.15 mmol), TsCl (2 mg) and $AlCl_3$ (1 mg) were added to Schlenk tube, vacuumed and refilled with argon for three times. Anhydrous CH_3CN (4 mL) was added and the solution was heated to reflux and kept for 1 hour. Then it was transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under vacuum. The purification was performed by flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:1) as eluent to give product **7** as colorless oil (46 mg, 74% yield).

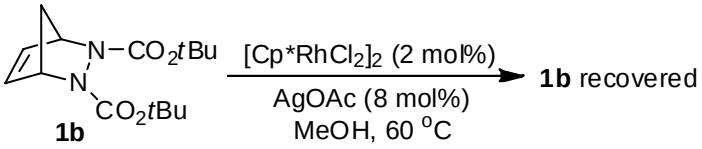


7

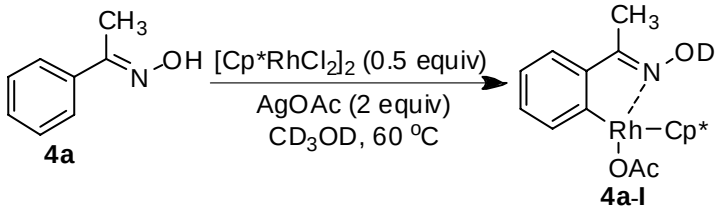
Diethyl 1-(2-(2-acetamido-5-chlorophenyl)cyclopent-3-en-1-yl)hydrazine-1,2-

dicarboxylate (7). Colorless oil; ^{1}H NMR (CD_3OD, 500 MHz): δ= 7.71 (br, 1H), 7.47-7.45 (m, 0.25H), 7.23-7.14 (m, 2H), 5.98 (s, 1H), 5.58 (s, 1H), 4.72 (s, 1H), 4.26-3.94 (m, 5H), 2.74-2.54 (m, 2H), 2.19 (s, 3H), 1.34-1.29 (m, 6H), ^{13}C NMR (CD_3OD, 100 MHz): δ= 172.5, 160.1, 157.5, 149.0, 139.3, 135.5, 132.6, 131.8, 129.5, 128.4, 127.8, 66.5, 63.8, 63.3, 50.5, 36.2, 23.6, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{24}ClN_3O_5$ $[M+H]^+$ 410.1477; found 410.1460.

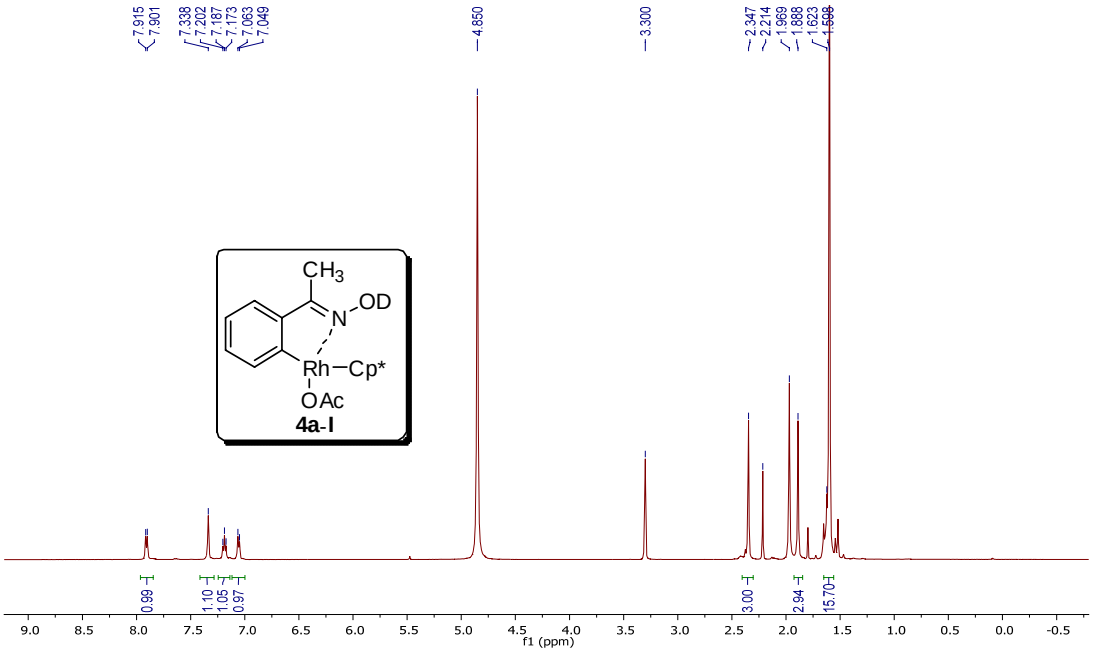
Control Experiments:

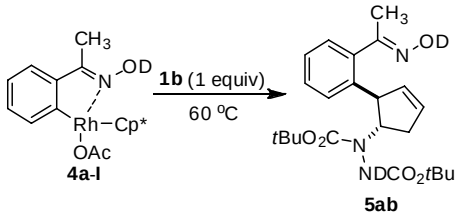


$[Cp^*RhCl_2]_2$ (1.2 mg, 2 mol%), AgOAc (1.4 mg, 8 mol%) were added to a vial and MeOH (0.2 mL) was then added. The solution was stirred for 10 min, afterwards, diazabicycle **1b** (29.6 mg, 0.1 mmol) was added and the solution was kept at 60 °C for 8h. TLC analysis showed it was recovered and no new product was observed.

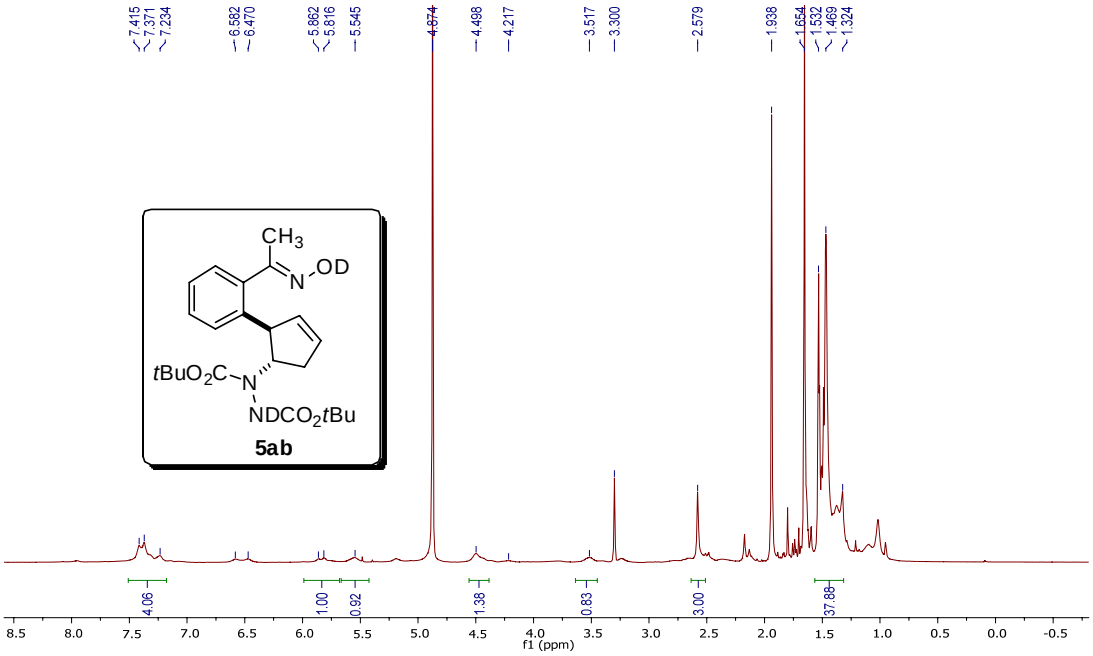


$[Cp^*RhCl_2]_2$ (6.2 mg, 0.01 mmol), AgOAc (6.7 mg, 0.04 mmol) and **4a** (2.7 mg, 0.02 mmol) were added to a NMR tube and CD_3OD (0.5 mL) was then added. The NMR tube was kept at 60 °C in oil bath for 1h. ^{1}H NMR analysis showed **4a** was consumed and the intermediate **4a-I** was formed.



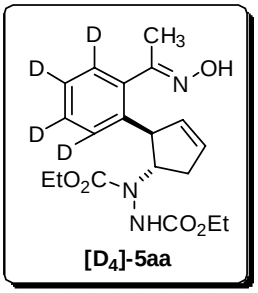


To the NMR tube was then added diazabicycle **1b** (6 mg, 0.02 mmol) and it was kept at 60 ^{o}C in oil bath for 1h. ^{1}H NMR analysis showed **4a-I** was consumed and the product **5ab** was formed.



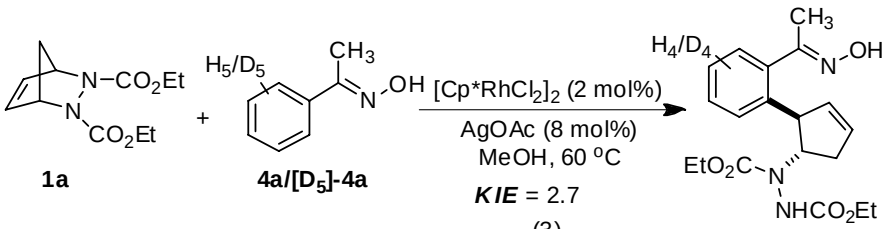
Kinetic Isotope Effect Study:

[D_4]-**5aa** was prepared according to general procedure in 87% yield.



[D_4]-5aa

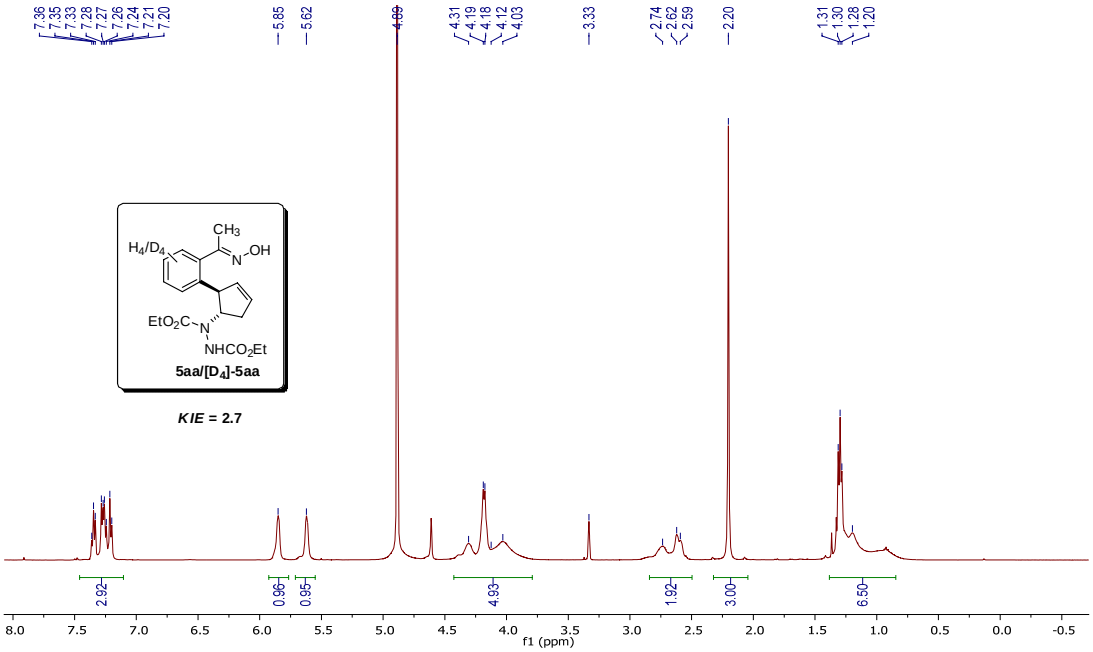
White solid; m.p. 132-134 °C; ^{1}H NMR (CD_3OD, 500 MHz): δ= 5.83 (s, 1H), 5.60 (s, 1H), 4.29-4.01 (m, 5H), 2.71-2.52 (m, 2H), 2.18 (s, 3H), 1.31-1.26 (m, 6H); ^{13}C NMR (CD_3OD, 100 MHz): δ= 159.1, 158.9, 157.6, 142.6, 139.1, 134.5, 130.4, 129.1, 127.1, 125.2, 68.9, 63.5, 62.9, 51.7, 36.4, 17.1, 14.8, 14.6; HRMS (ESI) (*m/z*): calcd for $C_{19}H_{21}D_4N_3O_5$ $[M+H]^+$ 380.2114; found 380.2123.



1a **4a/[D_5]-4a** **5aa/[D_4]-5aa**

parallel experiments

Following general procedure, [Cp*$RhCl_2$]$_2$ (1.2 mg, 2 mol%), AgOAc (1.3 mg, 8 mmol%) were added to a vial. MeOH (0.2 mL) was added and the solution was stirred at RT for 10min. Afterwards, diazabicycle **1a** (24 mg, 0.1 mmol) and oxime **4a** (13.5 mg, 0.1 mmol) was added, followed by addition of MeOH (0.6 mL). In another reaction vial, [D_5]-**4a** (14 mg, 0.1 mmol) was used instead of **4a**. The two reactions were kept at 60 °C for 5 min. Then they were diluted with DCM and combined. Silica gel was added and all the solvent were concentrated under vacuum. The residue was subject to flash chromatography to isolate the products (70% for combing yield) and the value of K_H/K_D was obtained based on ^{1}HNMR.



Reference:

1 (a) F. Menard, C. F. Weise, M. Lautens, *Org. Lett*. **2007**, *9*, 5365; (b) F. Menard, M. Lautens, *Angew. Chem. Int. Ed*. **2008**, *47*, 2085.

2 X. Chen, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 6790.