Tandem Nazarov Cyclization-Michael Addition Sequence Catalyzed by an Ir (III) Complex

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I. Experimental Details

I-a. General Procedures and Materials. Methanol- d_4 , chloroform- d and dichloromethane- d_2 were purchased from Cambridge Isotope. Aromatic nitrostyrenes were obtained from commercial sources and were used as received. Purification of reaction products was carried out by column chromatography using Silica Gel (40-140 mesh). TLC visualization was accomplished using UV light or with KMnO_4 solution. Dichloromethane, dichloroethane, diethyl-ether, hexanes and tetrahydrofuran were purified as described by Grubbs.¹ All NMR spectra were recorded on either an Avance 400 or Avance 500 MHz spectrometer. ^1H and ^{13}C chemical shifts (δ in ppm) are relative to tetramethylsilane and referenced using chemical shifts of residual solvent resonances. ^{31}P chemical shifts (δ in ppm) are relative to an external 85% solution of phosphoric acid in the appropriate solvent. Data are reported as s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, m = multiplet, b = broad, and dd = doublet of doublets with integration and coupling constant(s) given in Hz. Infrared spectra were recorded on 8400S Shimadzu FTIR spectrometer. High-resolution mass spectra were obtained using a ThermoFinnigan MAT95XL high resolution magnetic sector mass spectrometer at the Chemistry Mass Spectrometry Facility at the University of Buffalo. Unless otherwise stated, all reactions and manipulations were performed in dry glassware under a nitrogen atmosphere using either standard Schlenk techniques or an inert-atmosphere glovebox.

-b. Syntheses of the Catalyst, Nazarov substrates and nitrostyrene: The following compounds were made according to literature procedures: $[\text{IrMe}(\text{CO})(\text{dppe})(\text{DIB})](\text{BAr}^f_4)_2$,² the different Nazarov substrates,³ and *n*-propylnitrostyrene.⁴

II. General Procedure and Characterization data

II-a. General Procedure for the $[\text{IrMe}(\text{CO})(\text{dppe})(\text{DIB})](\text{BAr}^{\text{f}}_4)_2$ - Catalyzed Tandem

Nazarov Cyclization-Michael Addition. In a glovebox, a three neck flask equipped with a stir bar and reflux condenser was charged with $[\text{IrMe}(\text{CO})(\text{dppe})(\text{DIB})](\text{BAr}^{\text{f}}_4)_2$ (16.4 mg, 0.006 mmol), the Nazarov substrate (0.15 mmol), the nitroalkene Michael acceptor (0.30 mmol), *N*-ethylpiperidine (0.015 mmol) and 1, 2-dichloroethane (0.75 mL). The reaction solution was stirred at 40 °C under nitrogen. The volatile components were then removed under reduced pressure and the crude reaction product was purified by column chromatography using ethyl acetate/hexanes (1:1).

II-b. Characterization data for 4a – 4i

Methyl 5-(4-methoxyphenyl)-6-(2-nitro-1-phenylethyl)-7-oxo-2,3,4,5,6,7-

hexahdropenta[b]pyran-6-carboxylate 4a. ^1H NMR (500 MHz, CDCl_3) at 25 °C: δ 7.38-7.30 (m, 5H), 7.06 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 5.31 (dd, J = 13.0, 11.6 Hz, 1H), 4.90 (dd, J = 13.0, 2.8 Hz, 1H), 4.51 (dd, J = 11.6, 2.8 Hz, 1H), 4.21 (m, 1H), 4.10 (m, 1H), 3.87 (s, 3H), 3.67 (s, 1H), 3.30 (s, 3H), 2.16 (m, 1H), 1.93 (m, 1H), 1.71 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) at 25 °C: δ 196.8, 169.4, 159.3, 152.1, 145.9, 134.1, 130.3, 130.3, 128.6, 128.6, 127.1, 113.8, 77.1, 67.1, 64.1, 55.2, 52.3, 52.1, 48.3, 22.1, 21.0; IR (cell, CH_2Cl_2 , cm^{-1}) 2950, 2837, 1737, 1710, 1657, 1553, 1512, 1250, 1130, 1037, 841, 798, 706; HRMS (ES^+): Calculated for $\text{C}_{25}\text{H}_{25}\text{O}_7\text{NNa}$ ($\text{M} + \text{Na}$) $^+$ 474.1523, Found: 474.1538.

Methyl 5-(4-bromophenyl)-6-(1-(4-methoxyphenyl)-2-nitroethyl)-7-oxo-

2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate 4b. ^1H NMR (400 MHz, CDCl_3) at 25 °C: δ 7.47 (d, J = 8.4 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 8.4 Hz, 2H), 6.86 (d, J = 8.4 Hz, 2H), 5.25 (dd, J = 13.0, 11.6 Hz, 1H), 4.83 (dd, J = 13.0, 3.2 Hz, 1H), 4.43 (dd, J = 11.6, 3.2 Hz, 1H), 4.12 (m, 1H), 4.04 (m, 1H), 3.81 (s, 3H), 3.60 (s, 1H), 3.23 (s, 3H), 2.10 (m, 1H), 1.87 (m, 1H), 1.61 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) at 25 °C: δ 196.4, 169.1, 159.4, 152.1, 145.8, 133.4, 131.8, 131.8, 130.2, 126.8, 122.7, 113.8, 77.1, 67.1, 64.0, 55.2, 52.3, 52.1, 47.7, 22.2, 21.0; IR (cell, CH_2Cl_2 , cm^{-1}) 2951, 2837, 1736, 1709, 1649, 1553, 1512, 1248, 1130, 1038, 841, 749; HRMS (ES^+): Calculated for $\text{C}_{25}\text{H}_{24}\text{O}_7\text{NBrNa}$ ($\text{M} + \text{Na}$) $^+$ 554.0608, Found: 554.0607.

Methyl 5-(4-methoxyphenyl)-6-(1-(4-methoxyphenyl)-2-nitroethyl)-7-oxo-

2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate 4c. ^1H NMR (500 MHz, CDCl_3) at 25 °C: δ 7.20 (d, J = 8.5 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 6.86 (d, J = 7.5 Hz, 2H), 6.83 (d, J = 7.5 Hz, 2H), 5.24 (dd, J = 13.5, 11.5 Hz, 1H), 4.81 (dd, J = 13.5, 3.0 Hz, 1H), 4.40 (dd, J = 11.5, 3.0 Hz, 1H), 4.13 (m, 1H), 4.01 (m, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.67 (s, 1H), 3.21 (s, 3H), 2.08 (m, 1H), 1.84 (m, 1H), 1.64 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 197.5, 170.1, 160.2, 160.0, 152.8, 146.5, 131.6, 131.0, 127.9, 126.6, 114.7, 114.4, 78.0, 77.61, 67.7, 65.0, 55.9, 52.8, 52.6, 48.3, 22.8, 21.7; IR (cell,

CH₂Cl₂, cm⁻¹) 2951, 2837, 1736, 1706, 1649, 1553, 1512, 1250, 1180, 1038, 841; HRMS (ES⁺):

Calculated for C₂₆H₂₇O₈NNa (M + Na)⁺ 504.1629, Found: 504.1618.

Methyl 6-(1-(furan-2-yl)-2-nitroethyl)-5-(4-methoxyphenyl)-7-oxo-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4d. ¹H NMR (400 MHz, CDCl₃) at 25 °C: δ 7.36 (d, *J* = 1.6 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.8 Hz, 2H), 6.35 (d, *J* = 3.2 Hz, 1H), 6.32 (dd, *J* = 3.2, 1.6 Hz, 1H), 5.24 (dd, *J* = 14.0, 11.2 Hz, 1H), 4.77 (dd, *J* = 14.0, 3.2 Hz, 1H), 4.62 (dd, *J* = 11.2, 3.2 Hz, 1H), 4.14 (m, 1H), 4.08 (m, 1H), 3.85 (s, 1H), 3.81 (s, 3H), 3.19 (s, 3H), 2.12 (m, 1H), 1.89 (m, 1H), 1.78 (m, 2H); ¹³C{¹H} NMR (125 MHz, CDCl₃) at 25 °C: δ 197.5, 171.3, 162.4, 158.2, 156.8, 142.4, 131.6, 129.4, 120.9, 116.6, 110.8, 106.4, 75.0, 71.6, 66.7, 56.0, 52.9, 47.2, 31.2, 26.1, 21.7; IR (cell, CH₂Cl₂, cm⁻¹) 2953, 2837, 1734, 1713, 1651, 1557, 1512, 1252, 1134, 1040, 843, 737; HRMS (ES⁺): Calculated for C₂₃H₂₃O₈NNa (M + Na)⁺ 464.1316, Found: 464.1306.

Methyl 5-(4-methoxyphenyl)-6-(1-nitropentan-2-yl)-7-oxo-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4e. ¹H NMR (400 MHz, CDCl₃) at 25 °C: δ 7.02 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 4.51 (dd, *J* = 13.0, 3.2 Hz, 1H), 4.42 (dd, *J* = 11.2, 3.2 Hz, 1H), 4.14 (m, 1H), 4.01 (m, 1H), 3.81 (s, 3H), 3.35 (s, 1H), 3.12 (s, 3H), 2.5 (m, 1H), 2.12 (m, 1H), 1.89 (m, 1H), 1.78 (m, 2H), 1.33 (quint, *J* = 3.5 Hz, 2H), 1.25 (quint, *J* = 3.5 Hz, 2H), 0.96 (t, *J* = 3.5 Hz, 3H);

$^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 194.9, 171.2, 162.4, 157.9, 132.2, 129.2, 119.6, 114.1, 75.1, 71.1, 65.6, 55.9, 52.2, 32.5, 29.8, 26.2, 25.3, 21.7, 19.3, 14.4; IR (cell, CH_2Cl_2 , cm^{-1}) 2956, 2836, 1740, 1713, 1649, 1553, 1512, 1250, 1122, 1034, 837, 733; HRMS (ES^+): Calculated for $\text{C}_{22}\text{H}_{27}\text{O}_7\text{NNa}$ ($\text{M} + \text{Na}$) $^+$ 440.4529, Found: 440.4521.

Methyl 5-(furan-2-yl)-6-(2-nitro-1-phenylethyl)-7-oxo-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4f. ^1H NMR (500 MHz, CDCl_3) at 25 °C: δ 7.36 (d, J = 1.6 Hz, 1H), 7.18-7.05 (m, 5H), 6.34 (d, J = 3.2 Hz, 1H), 6.28 (dd, J = 3.2, 1.6 Hz, 1H), 5.23 (dd, J = 13.6, 11.2 Hz, 1H), 4.77 (dd, J = 13.6, 3.2 Hz, 1H), 4.60 (dd, J = 11.2, 3.2 Hz, 1H), 4.13 (m, 1H), 4.08 (m, 1H), 3.85 (s, 1H), 3.17 (s, 3H), 2.11 (m, 1H), 1.86 (m, 1H), 1.78 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 195.3, 169.6, 152.9, 150.4, 143.3, 142.7, 142.2, 134.4, 128.6, 111.0, 109.6, 109.2, 77.6, 67.1, 56.3, 52.7, 48.0, 46.8, 22.1, 21.2; IR (cell, CH_2Cl_2 , cm^{-1}) 2953, 2836, 1736, 1713, 1653, 1553, 1435, 1379, 1238, 737, 704; HRMS (ES^+): Calculated for $\text{C}_{22}\text{H}_{21}\text{O}_7\text{NNa}$ ($\text{M} + \text{Na}$) $^+$ 434.1210, Found: 434.1199.

Methyl 6-(1-(4-bromophenyl)-2-nitroethyl)-5-(furan-2-yl)-7-oxo-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4g. ^1H NMR (500 MHz, CDCl_3) at 25 °C: δ 7.46 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 1.2 Hz, 1H), 7.17 (d, J = 8.5 Hz, 2H), 6.35 (dd, J = 1.2, 3.0 Hz, 1H), 6.10 (d,

$J = 1.0$ Hz, 1H), 5.30 (dd, $J = 14, 11.5$ Hz, 1H), 4.86 (dd, $J = 14, 3.0$ Hz, 1H), 4.46 (dd, $J = 11.5, 3.0$ Hz, 1H), 4.15 (m, 1H), 4.06 (m, 1H), 3.81 (s, 1H), 3.46 (s, 3H), 2.20 (m, 1H), 1.90 (m, 1H), 1.76 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 195.3, 169.6, 152.9, 150.4, 143.3, 142.2, 134.4, 132.5, 131.9, 123.2, 111.0, 109.2, 77.5, 76.6, 67.1, 52.7, 48.1, 46.7, 22.6, 21.2; IR (cell, CH_2Cl_2 , cm^{-1}) 2961, 2839, 1738, 1713, 1651, 1553, 1514, 1300, 1225, 1183, 1038, 802, 741; HRMS (ES^+): Calculated for $\text{C}_{22}\text{H}_{20}\text{O}_7\text{NBrNa}$ ($\text{M} + \text{Na}$) $^+$ 512.0315, Found: 512.0316.

Methyl 5-(furan-2-yl)-6-(1-(4-methoxyphenyl)-2-nitroethyl)-7-oxo-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4h. ^1H NMR (400 MHz, CDCl_3) at 25 °C: δ 7.49 (d, $J = 1.2$ Hz, 1H), 7.29 (d, $J = 8.8$ Hz, 2H), 6.92 (d, $J = 8.8$ Hz, 2H), 6.44 (dd, $J = 1.2, 3.2$ Hz, 1H), 6.19 (d, $J = 1.2$ Hz, 1H), 5.38 (dd, $J = 13.6, 11.6$ Hz, 1H), 4.93 (dd, $J = 13.6, 3.2$ Hz, 1H), 4.52 (dd, $J = 11.6, 3.2$ Hz, 1H), 4.22 (m, 1H), 4.12 (m, 1H), 3.97 (s, 1H), 3.87 (s, 3H), 3.54 (s, 3H), 2.27 (m, 1H), 1.99 (m, 1H), 1.82 (m, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 196.6, 170.0, 160.2, 152.5, 150.1, 143.6, 143.5, 131.4, 126.5, 114.7, 111.2, 109.7, 77.6, 67.7, 63.9, 55.8, 53.4, 47.7, 46.9, 22.7, 21.6; IR (cell, CH_2Cl_2 , cm^{-1}) 2961, 2839, 1738, 1713, 1651, 1553, 1514, 1300, 1225, 1183, 1038, 802, 741; HRMS (ES^+): Calculated for $\text{C}_{23}\text{H}_{23}\text{O}_8\text{NNa}$ ($\text{M} + \text{Na}$) $^+$ 464.4310, Found: 464.4299.

Methyl 6-(2-nitro-1-phenylethyl)-7-oxo-5-styryl-2,3,4,5,6,7-

hexahydrocyclopenta[b]pyran-6-carboxylate 4i. ^1H NMR (400 MHz, CDCl_3) at 25 °C: δ 7.27-7.37 (m, 10H), 6.59 (d, J = 16 Hz, 1H), 5.88 (dd, J = 6.4, 9.2 Hz, 1H), 5.31 (dd, J = 2.4, 13.6 Hz, 1H), 5.01 (dd, J = 2.4, 13.6 Hz, 1H), 4.47 (dd, J = 2.4, 11.2 Hz, 1H), 4.12 (m, 1H), 3.98 (m, 1H), 3.73 (s, 3H), 3.28 (d, J = 9.2 Hz, 1H), 2.17 (m, 1H), 1.85 (m, 1H), 1.62 (m, 2H) $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3) at 25 °C: δ 196.2, 169.8, 151.2, 146.4, 136.0, 135.9, 134.2, 129.5, 128.7, 128.6, 128.5, 128.2, 126.3, 123.8, 77.1, 67.0, 62.9, 52.7, 50.3, 47.8, 22.3, 21.2; IR (cell, CH_2Cl_2 , cm^{-1}) 2956, 2833, 1733, 1710, 1655, 1550, 1510, 1250, 1233, 1118, 1005, 841, 798, 700 ; HRMS (ES^+): Calculated for $\text{C}_{26}\text{H}_{25}\text{O}_6\text{NNa}$ ($\text{M} + \text{Na}$) $^+$ 470.1574, Found: 470.1579.

II-c. ^1H NMR spectrum of methyl 5-(4-methoxyphenyl)-6-(2-nitro-1-phenylethyl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate (**4a**).

II-d. $^{13}\text{C}\{^1\text{H}\}$ (a), $^{13}\text{C}/\text{DEPT}135$ (b) and $^{13}\text{C}/\text{DEPT}90$ (c) NMR spectra of methyl 5-(4-methoxyphenyl)-6-(2-nitro-1-phenylethyl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate (**4a**).

(a)

(b)

(c)

II-e. ^1H NMR spectrum of methyl 6-(1-(4-bromophenyl)-2-nitroethyl)-5-(4-methoxyphenyl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[*b*]pyran-6-carboxylate (**4b**).

II-f. $^{13}\text{C}\{^1\text{H}\}$ (a), $^{13}\text{C}/\text{DEPT}135$ (b) and $^{13}\text{C}/\text{DEPT}90$ (c) NMR spectra of methyl 6-(1-(4-bromophenyl)-2-nitroethyl)-5-(4-methoxyphenyl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate (**4b**).

(a)

(b)

(c)

II-g. ^1H NMR spectrum of methyl 6-(1-(4-bromophenyl)-2-nitroethyl)-5-(furan-2-yl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate (**4g**).

II-h. $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of methyl 6-(1-(4-bromophenyl)-2-nitroethyl)-5-(furan-2-yl)-7-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran-6-carboxylate (**4g**).

II-i. Fractional recrystallization of tandem product 4b:

¹H NMR spectrum in CDCl₃ of product **4b**.

¹H NMR spectrum in CDCl₃ of the white solid precipitated out after dissolving oily product **4b** in ethyl acetate/hexanes (2:3).

¹H NMR spectrum in CDCl₃ of the white solid obtained after second fractional recrystallization from ethyl acetate/hexanes (2:3).

III. X-Ray Crystal Structures of product **4b** and **4g**

1. An ORTEP32/pov-ray representation of **4b** showing 50% probability ellipsoids. For clarity selected H atoms are shown.

2. An ORTEP32/pov-ray representation of **4g** showing 50% probability ellipsoids. For clarity selected H atoms are shown.

IV. References for supporting information:

- (1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.
- (2) Albietz, P. J.; Cleary, B. P.; Paw, W.; Eisenberg, R. *Inorg. Chem.* **2002**, *41*, 2095-2108.
- (3) He, W.; Sun, X.; Frontier, A. J. *J. Am. Chem. Soc.* **2003**, *125*, 14278-14279.
- (4) Lucet, D.; Sabelle, S.; Kostelitz, O; Gall, T. L.; Mioskowski, C. *Eur. J. Org. Chem.* **1999**, 2583-2581.