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SUPPORTING INFORMATION

Title: BINOLate–Magnesium Catalysts for Enantioselective Hetero-Diels–Alder Reaction of Danishefsky's Diene with Aldehydes

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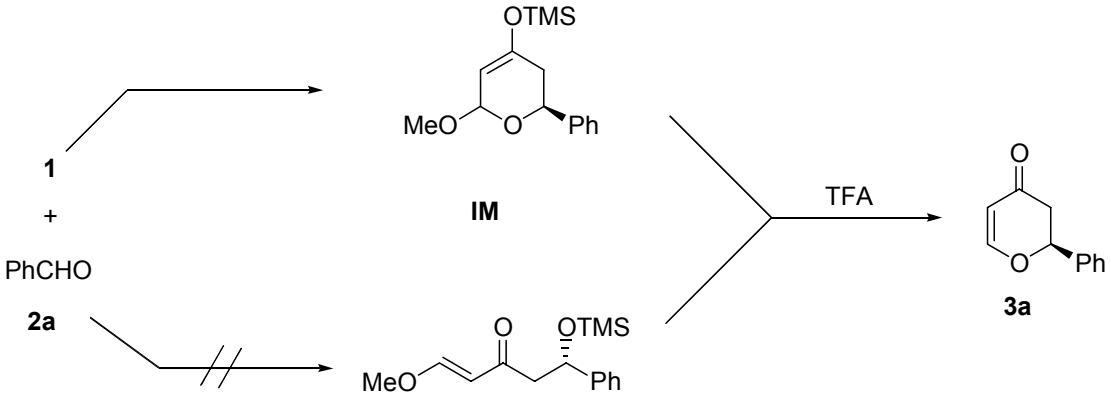
Ref. No.: O200701223

Investigation on HDA Reaction Pathway: Isolation and Characterization of the Primary HDA Adduct



To a 1.5-mL polypropylene microtube were added 0.025 M toluene solution of **4a** (0.02 mmol, 0.8 mL) and 1 M solution of Bu_2Mg in heptane (0.03mmol, 30 μL). The mixture was kept at room temperature for 0.5 h and then freshly distilled benzaldehyde (21.2 mg, 0.20 mmol) was added. Danishefsky' diene (34.4 mg, 0.20 mmol) was charged after the reaction mixture was kept at room temperature for 10 min. The reaction mixture was concentrated after 24 h and the crude material was purified by flash chromatography on silica gel with hexanes/ethyl acetate = 8:1 as an eluent to afford a colorless oil and submit to NMR analysis. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45-7.28 (m, 5H), 5.36-5.35 (m, 1H), 4.89-4.88 (m, 1H), 4.76 (dd, *J* = 3.6, 1.1 Hz, 1H), 3.52 (s, 1H), 2.40-2.30 (m , 1H), 2.26-2.24 (m, 1H), 0.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.0, 141.2, 128.3, 127.5, 125.5, 103.2, 99.5, 73.3, 54.6, 37.7, 0.12.

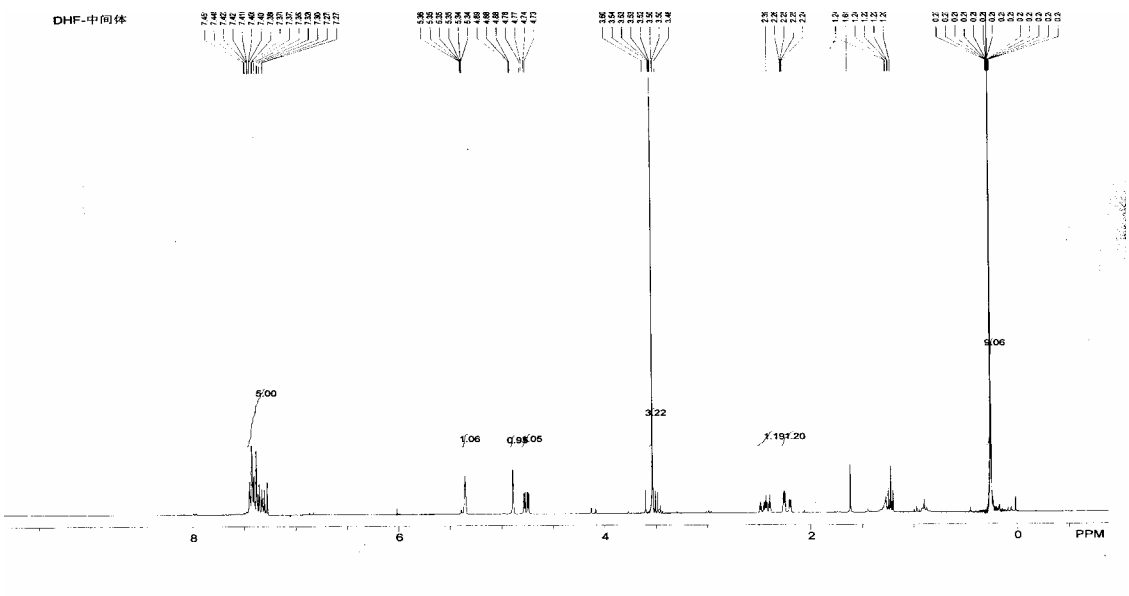


Figure S1. ^{1}H NMR spectrum for the isolated primary HDA product (IM)

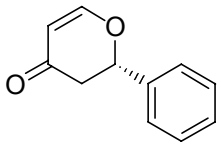
Table S1. Investigation of nonlinear effect in the enantioselective HDA reaction of Danishefsky's diene with benzaldehyde using 4a-Mg catalyst[a]

entry	Ee (ligand) [b]	Yield (%)[c]	Ee (%)[d]
1	**0**	58	0
2	14	74	38
3	30	85	63
4	48	85	79
5	68	>99	87
6	83	>99	89
7	100	>99	94

[a] All the reactions were conducted under the experimental conditions shown in Table 2 with the variation of ee of BINOL ligand. [b] Enantiomeric excesses of ligand were determined by HPLC on Chiralcel OD column. [c] Determined by HPLC with biphenyl as an internal standard. [d] Enantiomeric excesses of product 3a were determined by HPLC on Chiralcel OD column. The configuration was determined to be *S* by retention time of HPLC in comparison with that of an authentic sample.

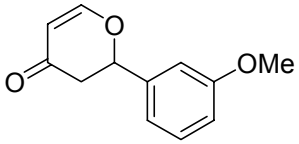
Spectroscopic Data and Chiral HPLC Assay Parameters for 4c-Catalyzed HDA Products 3a-n

(S)-2-Phenyl-2, 3-dihydro-4H-pyran-4-one **3a**



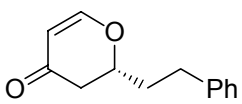
>99% yield, 99% ee. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (d, *J* = 6.6 Hz, 1H), 7.46-7.32 (m, 5H), 5.51 (dd, *J* = 5.7, 1.2 Hz, 1H), 5.41 (dd, *J* = 14.2, 3.4 Hz, 1H), 2.95-2.84 (m, 1H), 2.68-2.60 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.2, 163.2, 137.8, 128.9, 128.8, 126.1, 107.4, 81.0, 43.4.The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 90:10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 15.4 min (*S*, major), t_{R2} = 18.1 min (*R*, minor).

2-(3-Methoxyphenyl)-2, 3-dihydro-4H-pyran-4-one **3b**



>99% yield, 97% *ee*. $[\alpha]_D^{20}$ +58.0° (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, *J* = 6.0 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 1H), 7.00-6.92 (m, 3H), 5.54 (d, *J* = 5.7 Hz, 1H), 5.42 (dd, *J* = 14.4, 3.3 Hz, 1H), 3.85 (s, 3H), 2.96-2.86 (m, 1H), 2.71-2.64 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 22.3 min (major), t_{R2} = 28.7 min (minor).

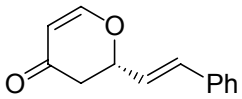
(R)-2-Phenylethyl-2, 3-dihydro-4H-pyran-4-one **3c**



>99% yield, 80% ee, $[\alpha]_D^{20}$ +47.8° (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.39 (d, *J* = 6.0Hz, 1H), 7.33-7.12 (m, 5H), 5.41 (dd, *J* = 6.0, 0.9 Hz, 1H),

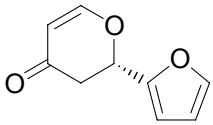
4.42-4.37 (m, 1H), 2.87-2.80 (m, 2H), 2.61-2.41 (m, 2H), 2.20-2.13 (m, 1H), 2.01-1.94 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 90:10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 18.1 min (*R*, major), t_{R2} = 27.4 min (*S*, minor).

(S)-2-(E-Styryl)-2, 3-dihydro-4H-pyran-4-one **3d**



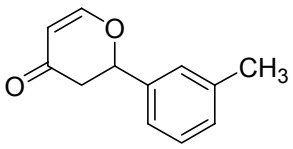
>99% yield, 97% ee, $[\alpha]_D^{20}$ +142.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43-7.26 (m, 6H), δ 6.72 (d, *J* = 15.9 Hz, 1H), 6.31 (dd, *J* = 15.9, 6.6 Hz, 1H), 5.47 (d, *J* = 5.7 Hz, 1H), 5.10-5.05 (m, 1H), 2.79-2.58 (m, 2H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 19.2 min (major), t_{R2} = 37.5 min (minor).

(S)-2-(2-Furyl)-2,3-dihydro-4H-pyran-4-one **3e**



>99% yield, 93% ee; $[\alpha]_D^{20}$ +283.5° (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 (d, *J* = 1.2 Hz, 1H), 7.37 (d, *J* = 6.0 Hz, 1H), 6.45-6.40 (m, 2H), 5.51-5.44 (m, 2H), 3.14-3.04 (m, 1H), 2.76-2.69 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 95: 5, flow rate = 0.5 mL/min, UV detection at λ = 254 nm; t_{R1} = 34.0 min (*R*, minor), t_{R2} = 37.6 min (*S*, major).

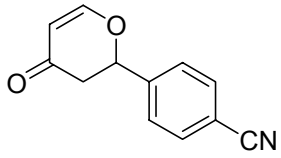
2-(3-Tolyl)-2, 3-dihydro-4H-pyran-4-one **3f**



>99% yield, 97% *ee*; $[\alpha]_D^{20}$ +67.8° (c = 1.08, $CHCl_3$);^{1}H NMR (300 MHz,

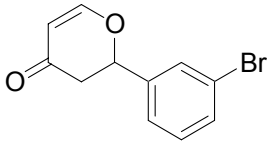
$CDCl_3$): δ 7.47 (d, *J* = 6.0 Hz, 1H), 7.33-7.26 (m, 2H), 7.25-7.17 (m, 2H), 5.52 (d, *J* = 6.3 Hz, 1H), 5.38 (d, *J* = 14.1 Hz, 1H), 2.96-2.86 (m, 1H), 2.68-2.61 (m, 1H), 2.39 (s, 3H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol = 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 10.6 min (major), t_{R2} = 12.0 min (minor).

2-(4-Cyanophenyl)-2, 3-dihydro-4H-pyran-4-one **3g**



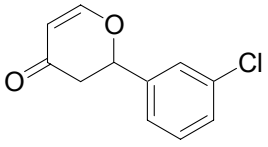
80.0% yield, 85% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (dd, *J* = 6.6, 1.2 Hz, 2H), 7.59-7.52 (m, 3H), 5.58-5.10 (m, 2H), 2.89-2.79 (m, 1H), 2.74-2.67 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 37.3 min (major), t_{R2} = 45.0 min (minor).

2-(3-Bromophenyl)-2, 3-dihydro-4H-pyran-4-one **3h**



>99% yield, 91% *ee*; $[\alpha]_D^{20}$ +54.6° (c = 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (s, 1H), 7.59-7.52 (m, 2H), 7.36-7.31 (m, 2H), 5.59 (d, *J* = 6.00 Hz, 1H), 5.42 (dd, *J* = 14.8, 3.6 Hz, 1H), 2.96-2.86 (m, 1H), 2.74-2.67 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 13.9 min (major), t_{R2} = 17.6 min (minor).

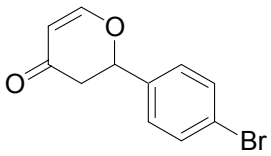
2-(3-Chlorophenyl)-2,3-dihydro-4H-pyran-4-one **3i**



>99% yield, 94% *ee*; $[\alpha]_D^{20}$ +55.5° (c = 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$):

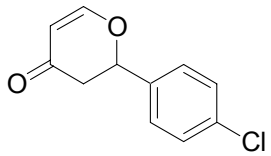
δ 7.49 (d, *J* = 5.7 Hz 1H), 7.43 -7.26 (m, 4H), 5.55 (d, *J* = 6.3 Hz, 1H), 5.42 (d, *J* = 14.1 Hz, 1H), 2.93-2.82 (m, 1H), 2.71-2.64 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 13.1 min (major), t_{R2} = 16.6 min (minor).

2-(4-Bromophenyl)-2, 3-dihydro-4H-pyran-4-one **3*j***



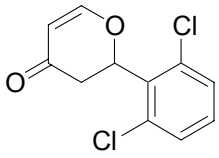
>99% yield, 95% *ee*; $[\alpha]_D^{20}$ +112.4° (c = 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (dd, *J* = 6.9, 1.8 Hz, 2H), 7.47 (d, *J* = 6.0 Hz, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 5.53 (dd, *J* = 6.0, 1.2 Hz, 1H), 5.39 (dd, *J* = 11.4, 3.6 Hz, 1H), 2.91-2.80 (m, 1H), 2.68-2.60 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 14.4 min (major), t_{R2} = 18.0 min (minor).

2-(4-Chlorophenyl)-2, 3-dihydro-4H-pyran-4-one **3k**



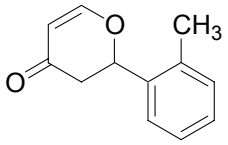
>99% yield, 91% *ee*; $[\alpha]_D^{20}$ +59.6° (c = 1.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 6.0 Hz, 1H), 7.45-7.36 (m, 4H), 5.56 (d, *J* = 6.3 Hz, 1H), 5.43 (dd, *J* = 14.1, 3.6Hz, 1H), 2.94-2.84 (m, 1H), 2.71-2.64 (m, 1H). The enantiomeric excess was determined by HPLC on Chiralcel OD column, hexane: isopropanol 90: 10, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 13.0 min (major), t_{R2} = 15.6 min (minor).

2-(2,6-Dichlorophenyl)-2, 3-dihydro-4H-pyran-4-one **3l**



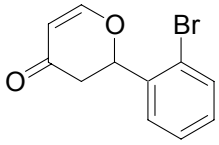
91.0% yield, 94% *ee*; $[\alpha]_D^{20}$ –13.6° (c = 1.08, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 7.49 (dd, *J* = 6.6, 0.6 Hz, 1H), 7.39-7.37 (m, 2H), 7.26 (t, *J* = 9.0 Hz, 1H), 6.23 (dd, *J* = 15.6, 4.2Hz, 1H), 5.54 (dd, *J* = 6.3, 1.2 Hz, 1H), 3.54 (dd, *J* = 17.1, 15.6 Hz, 1H), 2.52-2.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.5, 163.1, 135.3, 132.0, 130.7, 129.8, 107.3, 77.6, 38.8. The enantiomeric excess was determined by HPLC on Chiralpak AD column, hexane: isopropanol 99.5: 0.5, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 28.1 min (minor), t_{R2} = 33.5 min (major).

(S)-2-2-Tolyl -2, 3-dihydro-4H-pyran-4-one **3m**



>99% yield, 96% ee; $[\alpha]_D^{20}$ +32.4° (c = 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 6.0 Hz, 1H), 7.49-7.46 (m, 1H), 7.30-7.27 (m, 2H), 7.23-7.21 (m, 1H), 5.63 (dd, *J* = 14.4, 3.0 Hz, 1H), 5.55 (d, *J* = 6.0 Hz, 1H), 2.94-2.84 (m, 1H), 2.64-2.57 (m, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.4, 163.5, 135.8, 135.0, 130.8, 128.7, 126.5, 125.7, 107.2, 78.4, 43.3, 18.9. The enantiomeric excess was determined by HPLC on Chiralpak AD column, hexane:isopropanol 85:15, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 34.0 min (minor, *R*), t_{R2} = 48.3 min (major, *S*).

2-(2-Bromophenyl)-2, 3-dihydro-4H-pyran-4-one **3n**



>99% yield, 88% ee; $[\alpha]_D^{20}$ -95.9° (c = 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$):

δ 7.61 (d, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 6.6 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.28-7.23 (m, 1H), 5.80(dd, *J* = 14.4, 3.9 Hz, 1H), 5.58 (d, *J* = 6.0 Hz, 1H), 2.89-2.82 (m, 1H), 2.76-2.65 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.6, 163.1, 137.4, 133.0, 130.1, 128.0, 127.3, 121.4, 107.6, 80.2, 42.2. The enantiomeric excess was determined by HPLC on Chiralpak AD column, hexane:isopropanol 85:15, flow rate = 1.0 mL/min, UV detection at λ = 254 nm; t_{R1} = 29.6 min (minor), t_{R2} = 53.7 min (major).