Supporting Information
for
Lewis Acid-Assisted Ring-Closing Metathesis of Chiral Diallylamines: An
Efficient Approach to Enantiopure Pyrrolidine Derivatives

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General Methods

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Methanol was distilled from sodium prior to use. Sulphorous oxychloride was freshly distilled. Acetonitrile, dichloromethane were freshly distilled from calcium hydride. Column chromatography was performed using 200-300 mesh silica gel. IR were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr film with absorption in cm^{-1} . ¹HNMR spectra were recorded on Varian Mercury 400 (400 MHz) spectrophotometers. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (CDCl_3 : δ 7.26). Data are reported as follows: chemical shift, multiplicity (s= singlet, d= doublet, t= triplet, q= quartet, br= broad, m= multiplet), coupling constants (Hz). ¹³CNMR spectra were recorded on Varian Mercury 400 (100 MHz) with complete proton decoupling spectrophotometers (CDCl_3 : 77.7). Enantiomer ratios were determined by chiral HPLC (Chiralpak AD-H (4.6mm x 250mm)), in comparison with authentic racemic materials. Mass spectra were measured on a Finnigan Trace MS spectrometer. Elementary analyses were taken on a Vario EL elementary analysis instrument. Rotations were taken on a Perkin Elmer Model 341 Polarimeter. Esterification of amino acids was performed according to the literature procedure¹.

General Procedure for the Preparation of Precursors of Diallylamines:

All precursors were prepared analogous to the following procedure: To a solution of the L-amino acid methyl ester hydrochloride(20mmol) in acetonitrile(100mL) at room temperature was added sodium bicarbonate(80mmol), followed by adding 3-bromo-propene(44mmol), then began to heat it to 70 °C. The reaction solution was stirred at this temperature for 24 hours. The mixture was allowed to cool to room temperature. The solvent was evaporated and the oily residue was purified with flash chromatography to give diallylamines in good to excellent yields(71-91%).

Methyl 2-diallylamino-3-phenyl-propionate² (4): 4.72g, 18.21mmol, yield: 91%. **IR** (neat) 1733cm⁻¹; **¹HNMR** (400 MHz, CDCl₃): 7.21-7.09 (m, 5H), 5.63-5.61 (m, 2H), 5.10-5.01 (m, 4H), 3.64 (t, 1H, J=7.6 Hz), 3.57 (s, 3H), 3.32-2.96 (m, 4H), 2.88-2.79 (m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 172.9, 138.4, 136.2, 129.3, 128.1, 126.2, 117.2, 63.7, 53.4, 51.1, 35.6; **MS** (ESI⁺) m/z 259 (M⁺); Analysis calculated for C₁₆H₂₁NO₂: C, 74.10, H, 8.16, N, 5.40. Found: C, 74.59; H, 8.45; N, 4.92; [α]_D²⁰ = -39.94 ° (C = 1.02, CHCl₃).

Methyl 2-diallylamino-propionate (16): **IR** (neat) 1737cm⁻¹; **¹HNMR** (400 MHz, CDCl₃): 5.80-5.72 (m, 2H), 5.21-5.09 (m, 4H), 3.68 (s, 3H), 3.52 (t, 1H, J =7.6Hz), 3.37-3.32 (m, 1H), 3.05-3.00 (m, 2H), 1.70-1.50 (m, 3H), 0.91-0.87 (m, 6H); **¹³CNMR** (100 MHz, CDCl₃): 174.3, 136.2, 117.1, 57.1, 53.4, 51.2, 14.4; **MS** (ESI⁺) m/z 183 (M⁺); Analysis calculated for C₁₀H₁₇NO₂: C, 65.54, H, 9.35, N, 7.64. Found: C, 65.26; H, 8.85; N, 7.15; [α]_D²⁰ = -60.02 ° (C = 1.0, CHCl₃).

Methyl 2-diallylamino-4-methyl-pentionate (18): 3.51g, 16.61mmol, yield: 83%. **IR** (neat) 1737cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 5.78-5.70 (m, 2H), 5.21-5.09 (m, 4H), 3.69 (s, 3H), 3.44-3.08 (m, 2H), 2.96 (d, 1H), 2.85-2.80 (m, 2H), 2.06-2.01(m, 1H), 0.96 (d,3H), 0.85 (d,3H); **¹³CNMR** (100 MHz, CDCl₃): 174.0, 136.6, 116.9, 59.6, 53.3, 50.8, 38.4, 24.5, 22.9, 21.9; **MS** (ESI⁺) m/z 225 (M⁺); Analysis calculated for C₁₃H₂₃NO₂: C, 69.29, H, 10.29, N, 6.22. Found: C, 69.18; H, 10.34; N, 6.13; [α]_D²⁰ = -61.49 ° (C = 1.21, CHCl₃).

Dimethyl 2-diallylamino-succinate (20): 3.95g, 16.39mmol, yield: 82%. **IR** (neat) 1737cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 5.78-5.70 (m, 2H), 5.22-5.12 (m, 4H), 4.01 (t, 1H, J=7.6Hz), 3.73 (s, 3H), 3.68 (s, 3H), 3.28-3.05 (m, 4H), 3.05-3.57 (m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 172.2, 171.6, 135.9, 117.4, 58.2, 53.7, 51.6, 51.4, 34.6; **MS** (ESI⁺) m/z 241 (M⁺); Analysis calculated for C₁₃H₂₃NO₂: C, 69.29, H, 10.29, N, 6.22. Found: C, 69.18; H, 10.34; N, 6.13; [α]_D²⁰ = -60.24 ° (C = 1.0, CHCl₃).

Methyl 2-diallylamino-3-indolyl- propionate (22): 5.13g, 17.24mmol, yield: 86%. **IR** (neat) 1737cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 7.97 (s, 1H), 7.60-7.58 (d, 1H), 7.36-7.34 (d, 1H), 7.18 (t, 1H), 7.12 (t, 1H), 7.04 (s, 1H), 5.84-5.74 (m, 2H), 5.22-5.10 (m, 4H), 3.86-3.60 (m, 1H), 3.47 (s, 3H), 3.47-3.42 (m, 2H), 3.32-3.26 (m, 1H), 3.14-3.01 (m, 3H); **¹³CNMR** (100 MHz, CDCl₃): 173.2, 136.1, 135.9, 127.3, 122.7, 121.7, 119.1, 118.6, 117.4, 111.9, 111.0, 62.8, 53.5, 51.0, 25.3; **MS** (ESI⁺) m/z 299 (M⁺); Analysis calculated for C₁₈H₂₂N₂O₂: C, 72.46, H, 7.43, N, 9.39. Found: C, 72.06; H, 7.66; N, 9.27; [α]_D²⁰ = -4.03 ° (C = 1.07, CHCl₃).

Dimethyl 2-diallylamino-pentanedioate (24): 3.62g, 14.18mmol, yield: 71%. **IR** (neat) **IR** (CHCl₃) 1730, 1732cm⁻¹ (C=O) **¹HNMR** (400 MHz, CDCl₃): 5.74-5.72 (m, 2H), 5.20-5.09 (m, 4H), 3.70 (s,3H), 3.47 (t, 1H, J=7.4Hz), 3.34-3.01 (m, 4H), 2.44-2.40 (m, 2H), 2.03-1.96 (m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 173.7, 173.1, 136.3, 117.2,

60.3, 53.2, 51.5, 51.1, 30.6, 24.3; **MS** (ESI⁺) m/z 255 (M⁺); Analysis calculated for C₁₃H₂₁NO₄: C, 61.16, H, 8.29, N, 5.49. Found: C, 61.37; H, 8.34; N, 5.32; [α]_D²⁰ = -62.92 ° (C = 0.45, CHCl₃).

General Procedure for Ring Closing Metathesis: Synthesis of Pyrrolidine Derivatives.

A typical procedure for the ring closing metathesis is as follows: precursor diallylamine (3mmol) was dissolved in freshly distilled and degassed dichloromethane(30mL) under nitrogen atmosphere. This solution was degassed again using nitrogen and then Ti(OPr-i)₄ (0.27mL, 0.9mmol) was added by syringe. After stirring for 0.5 hour at room temperature, ruthenium catalyst **10**(0.127mg, 0.15mmol) dissolved in dichloromethane was added by syringe. After 2-13 hours of reflux, the reaction was complete as indicated by TLC. Saturated sodium bicarbonate was added to quench the reaction, the organic layer was separated and the aqueous layer was extracted with dichloromethane. The combined organic layers were dried over anhydrous magnesium sulfate for several hours, and then filtrated. The solution was concentrated via rotavapor. Flash column chromatography of the crude oil gave the corresponding pyrrolidine derivatives.

Methyl 2-(2,5-Dihydro-pyrrol-yl)-3-phenyl- propionate (13): 0.65g, 2.80mmol, yield: 93%. **IR** (neat) 1732cm⁻¹(C=O); ¹**H**NMR (400 MHz, CDCl₃): 7.28-7.20 (m, 5H), 5.78 (s, 2H), 3.78-3.65 (m, 5H), 3.60 (s, 3H), 3.08-3.03 (m, 2H); ¹³**C**NMR (100 MHz, CDCl₃): 172.6, 137.7, 128.8, 128.2, 126.9, 126.3, 66.5, 56.3, 51.2, 37.3; **MS** (ESI⁺) m/z 231 (M⁺); Analysis calculated for C₁₄H₁₇NO₂: C, 72.70, H, 7.41, N, 6.06. Found: C, 72.39; H, 7.09; N, 5.95; [α]_D²⁰ = +36.85 ° (C = 1.35, CHCl₃). The enantiomeric ratio was determined to be >99% by HPLC analysis using a Chiralpak AD-H column (3:97 isopropyl/hexanes, 0.5mL/min); t_r = 13.3 min.

1-(1-Methoxycarbonyl-ethyl)-2,5-dihydro-1H-pyrrolium chloride (17): 0.45g, 2.34mmol, yield: 78%. **IR** (CHCl₃) 1748cm⁻¹ (C=O); ¹**H**NMR (400 MHz, CDCl₃): 13.58 (br s, 1H), 5.88 (s, 2H), 4.57 (br, 1H), 4.51 (br, 1H), 4.40-4.25 (m, 2H), 3.40 (1M1, 1H), 3.85 (s, 3H), 1.80 (s, 3H), 1.79 (s, 3H); ¹³**C**NMR (100 MHz, CDCl₃): 168.2, 124.4, 59.2, 53.0, 14.4; **MS** (ESI⁺) m/z 191 (M⁺); Analysis calculated for C₇H₁₂NO₂: C, 47.33, H, 6.81, N, 7.89. Found: C, 47.21; H, 6.96; N, 7.81; [α]_D¹⁵ = + 5.76 ° (C = 0.66, CHCl₃).

Methyl 2-(2,5-Dihydro-pyrrol-1-yl)-4-methyl-pentionate (19): 0.53g, 2.67mmol, yield: 89%. **IR** (neat) 1737cm⁻¹ (C=O); ¹**H**NMR (400 MHz, CDCl₃): 5.77 (s, 2H), 3.77-3.73 (m, 2H), 3.71 (s, 3H), 3.60-3.65 (m, 2H), 3.52-3.49 (t, 1H, J=7.4Hz), 1.72-1.55 (m, 3H), 0.95-0.92 (m, 6H); ¹³**C**NMR (100 MHz, CDCl₃): 174.1, 127.0, 62.1, 55.9, 51.1, 40.3, 24.9, 22.5, 22.4 (After hydrolysis to the corresponding acid); **MS** (ESI⁺) m/z 197(M⁺); Analysis calculated for C₁₁H₁₉NO₂: C, 66.97, H, 9.71, N, 7.10. Found: C, 66.85; H, 9.65; N, 7.24(After hydrolysis to the corresponding acid); [α]_D¹⁵ = + 7.93 ° (C = 1.03, CHCl₃).

Dimethyl 2-(2,5-Dihydro-pyrrol-1-yl)- succinate (21): 0.52g, 2.46mmol, yield: 82%. **IR** (CHCl₃) 1735cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 5.75 (s, 2H), 3.40 (t, 1H, J=7.6Hz), 3.74-3.65 (m, 10H, two singles at 3.72 and 3.70 inside) 2.93-2.68 (m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 172.0, 171.5, 127.0, 60.0, 56.0, 51.8, 35.8; **MS** (ESI⁺) m/z 213(M⁺) 214 (M+1); Analysis calculated for C₁₀H₁₅NO₄: C, 56.33, H, 7.09, N, 6.57. Found: C, 56.22; H, 7.11; N, 6.64; [α]¹⁵_D = -30.13 ° (C = 0.92, CHCl₃).

Methyl 2-(2,5-Dihydro-pyrrol-1-yl)-3-(1H-indol-3-yl)-propionate (23): 0.64g, 2.38mmol, yield: 79%. **IR** (CHCl₃) 1721cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 8.13 (br s, 1H), 7.63-7.61 (d, 1H), 7.36-7.35 (d, 1H), 7.34-7.08 (m, 3H), 5.81 (s, 2H), 3.83-3.61 (m, 5H), 3.56 (s, 3H), 3.32-3.16 (m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 173.3, 136.0, 127.1, 127.0, 122.8, 121.4, 118.8, 111.2, 110.6, 66.1, 56.4, 51.2, 27.2. **MS** (ESI⁺) m/z 270 (M⁺). Analysis calculated for C₁₆H₁₈N₂O₂: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.93; H, 6.93; N, 9.90; [α]¹⁵_D = + 24.59 ° (C = 1.16, CHCl₃).

Dimethyl 2-(2,5-Dihydro-pyrrol-1-yl)- pentanedioate (25): 0.54 g, 2.37mmol, yield: 79%. **IR** (CHCl₃) 1729, 1731cm⁻¹ (C=O); **¹HNMR** (400 MHz, CDCl₃): 5.77 (s, 2H), 3.74-3.63 (m, 10H, two singles at 3.69 and 3.63 inside), 3.49 (t, 1H, J=7.4Hz), 2.48-2.44 (m, 2H), 2.13-2.03(m, 2H); **¹³CNMR** (100 MHz, CDCl₃): 173.2, 172.8, 126.8, 62.8, 55.8, 51.3, 51.1, 30.3, 26.0. **MS** (ESI⁺) m/z 228 (M+1); Analysis calculated for C₁₁H₁₇NO₄: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.26; H, 7.59; N, 5.88; [α]¹⁵_D = -15.19 ° (C = 0.71, CHCl₃).

References

1. Zamudio-Rivera, L. S.; Beltran, H. I.; Farfan, N. *Org. Prep. Proced. Int.* **2001**, 33, 341.
2. Laguzza, B. C.; Ganem, B. *Tetrahedron Lett.* **1981**, 22, 1483.

0721a cdc13

Pulse Sequence: zgpg30

yybz c13 cdcl3
Pulse Sequence: szput

37-47

Pulse Sequence: zgpg30

$C_{10}H_{17}NO_2$
Mol. Wt.: 183.2

yy47 c13

Pulse Sequence: zgpg30

$C_{10}H_{11}NO_2$
Mol. Wt.: 183.2

yy61 c6c13
Pulse Sequence: zgpg1

$C_{13}H_{23}NO_2$
Mol. Wt.: 225.3

yy61 c13

Pulse Sequence: szput

STANDARD IN OBSERVE

exptl stdin

SAMPLE DEC. 6 VT
 date Apr 4 2003 dfrq 299.868
 solvent CDCl3 d1n H1
 file exp d1p 36
 title exp d1p 0
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 sfrq 299.868 dm H1
 tn H1 dm H1
 at 1.820 dm PROCESSING
 np 16364 wfile 7900
 sw 4500.5 wfile
 fb 2800 proc
 bs 18 fm not used
 tpwr 56
 pw 14.0 werr react
 d1 3.000 wexp
 tof 0 wds
 nt 8 wnt
 ct 8
 alock n
 gain not used
 flags
 11 n
 in n
 dp y
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 vs 150
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 wc 250
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 ls 500.00
 f1 754.6
 f1p 0
 th 2
 ins 100.000
 nm cdc ph

yy52 cdc13

Pulse Sequence: szpu1

Pulse Sequence: zgpg30

yy66 cdc13
Pulse Sequence: szpu1

yy66 c13 cdc13
Pulse Sequence: zgpg30

$C_{11}H_{19}NO_2$
Mol. Wt.: 197.3

qy-53 c6c19
Pulse Sequence: szpu1

gvs3 cdc13 c13
Pulse Sequence: zgpg30

QY59 cdc13
Pulse Sequence: zgpg30

5.805

0.008
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 -0.008

QY59 cdc13 c13
Pulse Sequence: zgpg30

qy56b cdcl3
Pulse Sequence: zgpg30

q55db c6c13 c13
Pulse Sequence: s2pu1

L- Conformation

Injection Date : 12/22/2004 5:16:06 PM   Seq. Line : 1
Sample Name : yy-67   Location : Vial 2
Acq. Operator : liuhui   Inj : 1
Acq. Instrument : Instrument 2   Inj Volume : 5 µl
Different Inj Volume from Sequence !   Actual Inj Volume : 1 µl
Acq. Method : C:\HPCHEM\2\METHODS\97HEX254.M
Last changed : 12/21/2004 2:50:26 PM by liuhui
Analysis Method : C:\HPCHEM\2\METHODS\97HEX254.M
Last changed : 12/22/2004 5:10:26 PM by liuhui
(modified after loading)

97%hexane, 254nm, 60min, AD column.

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: WVD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	13.260	BB	0.2221	827.72388	56.43924	100.0000

Totals :   827.72388   56.43924

Results obtained with enhanced integrator!

*** End of Report ***

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Injection Date   : 12/21/2004 2:51:54 PM      Seq. Line :    1
Sample Name     : yy-64                      Location  : Vial 1
Acq. Operator   : liuhui                     Inj       :    1
Acq. Instrument : Instrument 2                Inj Volume: 5 µl
Acq. Method     : C:\HPCHEM\2\METHODS\97HEX254.M
Last changed    : 12/21/2004 3:49:01 PM by liuhui
                  (modified after loading)
Analysis Method : C:\HPCHEM\2\METHODS\97HEX254.M
Last changed    : 12/22/2004 5:10:26 PM by liuhui
                  (modified after loading)

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97%hexane, 254nm, 60min, AD column.

VWD1 A, Wavelength=254 nm (YANGQI-1\YY-64.D)

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                        Area Percent Report
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Sorted By      : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
Use Multiplier & Dilution Factor with ISTDs

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Signal 1: VWD1 A, Wavelength=254 nm

Peak #	RetTime [min]	Type	Width [min]	Area mAU	Height [mAU]	Area %
1	12.105	PV	0.2167	1501.27441	105.67200	50.2818
2	13.323	VB	0.2331	1484.44971	96.60988	49.7182

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Totals :                2985.72412  202.28188
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Results obtained with enhanced integrator!

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*** End of Report ***

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