Organic Letters

SUPPORTING INFORMATION

D. L. Comins*, Stefan Schilling and Yanchen Zhang
Dept. of Chemistry, NCSU, Raleigh, NC 27695-8204

"Asymmetric Synthesis of 3-Substituted Isoindolinones: Application to the Total Synthesis of (+)-Lennoxamine"

- I.** General experimental procedures for **3,4** (1 page)
- II.** Characterization data for **2,3,4e-f,5,11 and 13-18** (17 pages).
- III.** ORTEP plot for **3d** (1 page).

Total pages of supporting information: (20).

Supporting Information

General Experimental

General procedure for the preparation of 3-substituted *N*-((((1*S*,2*R*)-2-(1-methyl-1-phenylethyl)cyclohexyl)oxy)carbonyl)-2,3-dihydroisoindol-1-ones **3.** To a cooled (- 78 °C) solution of 0.30 mmol of sodium bis(trimethylsilyl)amide in 3 mL of THF was cannulated 0.27 mmol of **2** in 2 mL of THF. After 45 min, 2.7 mmol of electrophile was added dropwise. After 1 h at -78 C, the reaction was quenched with 0.60 mmol of acetic acid followed by 5 mL of aqueous saturated NaHCO₃. The aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The crude product was purified by radial PLC (silica gel, EtOAc / hexane) to give **3**.

General procedure for the preparation of (3*S*)-3-alkyl-2,3-dihydroisoindol-1-ones **4.** To a solution of 0.2 mmol of compound **3** in 3 mL of methanol was added 1.0 mL of Mg(OMe)₂ (7.4 wt% in methanol, 0.88 mmol). After 3 h at rt, the mixture was concentrated under reduced pressure. The residue was redissolved in EtOAc, and washed with aqueous saturated NH₄Cl. The aqueous layer was extracted with EtOAc. The combined organic extracts were washed with brine, dried over MgSO₄, and concentrated under reduced pressure. The crude product was purified by radial PLC (silica gel, EtOAc / hexane)) to give the 3-substituted 2,3-dihydro-isoindol-1-one **4**.

Compound Name: *N*-[(((1*S*, 2*R*)-2-(1-methyl-1-phenylethyl)cyclohexyl)oxy)carbonyl]-2,3-dihydroisoindol-1-one

Compound No: **2**

Notebook Pg(s): zyc1-015y

Formula: C₂₄H₂₇NO₃
Molecular Weight: 377.4761
Yields(s): 86 %
Appearance: white solid
Stability: stable
mp/bp: 123 °C
[α]²³_D: +42° (c 0.43, CHCl₃)

Elemental Analysis (Atlantic Microlabs, Inc.)		%C	%H	%N	%__O__
	Calculated:	76.36	7.21	3.71	12.72
	Found:	76.11	7.28	3.68	

HRMS: Calculated

Found

IR (thin film): cm⁻¹ 2928, 2862, 1744, 1706, 1357, 1330, 1297 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.21-1.40 (m, 10H), 1.75 (m, 2H), 1.92-1.96 (m, 2H), 2.21(m, 1H), 3.38 (d, 1H, *J* = 1.7 Hz), 5.00 (m, 1H), 6.84 (t, 1H, *J* = 7.2 Hz), 7.11(t, 2H, *J* = 7.6 Hz), 7.31(m, 3H), 7.46 (t, 1H, *J* = 7.4 Hz), 7.60 (t, 1H, *J* = 7.4 Hz), 7.88 (d, 1H, *J* = 7.6 Hz)

¹³C-NMR (75 MHz) δ 23.2, 24.9, 26.0, 27.1, 29.9, 33.8, 39.9, 48.5, 51.4, 76.7, 123.0, 124.9, 125.2, 125.6, 128.0, 128.5, 131.3, 133.6, 141.2, 150.2, 152.4, 166.7

Literature References:

Compound Name: (3*S*)-3-Allyl-*N*-[(((1*S*,2*R*)-2-(1-methyl-1-phenylethyl)cyclohexyl)oxy)carbonyl]-2,3-dihydro-isoindol-1-one

Compound No: **3a**

Notebook Pg(s): zyc1-061W

Formula: C₂₇H₃₁NO₃

Molecular Weight: 417.5400

Yields(s): 83%

Appearance: clear oil

Stability: stable

mp/bp:

[α]_D³⁰ +35° (c 1.35, CHCl₃)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	76.67	7.48	3.35	
Found:				

HRMS: Calculated 418.2382 Found 418.2398

IR (thin film): 2925, 1740, 1708, 1357, 1331, 1288, 1257 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.17 -1.38 (m, 10H), 1.77 (m, 2H), 1.94 -2.06 (m, 2H), 2.23 (m, 1H), 2.29 (t, 2H, *J* = 5.8 Hz), 3.55 (s, 1H), 4.90 (t, 2H, *J* = 16.5 and 8.6 Hz), 5.00 (m, 1H), 5.19 (m, 1H), 6.76 (t, 1H, *J* = 7.2 Hz), 7.05 (t, 2H, *J* = 7.7 Hz), 7.28 (m, 3H), 7.45 (t, 1H, *J* = 7.5 Hz), 7.60 (t, 1H, *J* = 7.5 Hz), 7.86 (d, 1H, *J* = 7.5 Hz)

¹³C-NMR (75 MHz) δ 22.9, 24.8, 26.1, 27.0, 29.9, 33.8, 37.2, 39.8, 51.6, 58.5, 76.6, 119.6, 122.6, 124.8, 124.9, 125.4, 127.9, 128.5, 130.7, 133.5, 145.1, 159.6, 152.5, 166.8

Literature References:

Compound Name: (3*S*)-3- Benzyl - *N*-[(((1*S*, 2*R*) -2- (1-methyl -1 -phenylethyl) cyclohexyl)oxy) carbonyl)
-2,3- dihydro - isoindol -1- one

Compound No: **3b**

Notebook Pg(s): zyc1-067Y

Formula: C₃₁H₃₃NO₃

Molecular Weight: 467.5987

Yields(s): 89 %

Appearance: white solid

Stability: stable

mp/bp: 117-119 °C

[α]_D³⁰ +91° (c, 0.7, CHCl₃),

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	79.63	7.11	3.00	10.26
Found:	79.65	7.23	3.10	

HRMS: Calculated

Found

IR (thin film): 2931, 1748, 1707, 1366, 1325, 1255, 1208 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.24 -1.45 (m, 10H), 1.80 (m, 2H), 2.00-2.12 (m, 2H), 2.29 (m, 1H), 2.63(dd, 1H, *J* = 8.6 & 13.3 Hz), 3.22 (dd, 1H, *J* = 13.3 & 2.6 Hz), 3.69 (d, 1H, *J* = 6.5 Hz), 5.11(m, 1H), 6.65 (t, 1H, *J* = 7.2 Hz), 6.74 (d, 1H, *J* = 7.5 Hz) 6.82 (t, 1H, *J* = 3.4 Hz), 7.00 (t, 2H, *J* = 7.6 Hz), 7.18 (m, 3H), 7.34 (d, 2H, *J* = 8.1 Hz), 7.37-7.49 (m, 2H), 7.77 (d, 1H, *J* = 7.4 Hz)

¹³C-NMR (75 MHz) δ 22.7, 24.9, 26.1, 27.0, 29.8, 30.1, 34.0, 39.6, 39.8, 51.9, 59.9, 76.7, 123.2, 124.9, 125.4, 127.0, 127.9, 128.4, 129.8, 130.4, 133.1, 135.5, 145.1, 149.6, 152.6, 166.6

Literature References:

Compound Name: (3*S*)- 3- Isopropyl - *N*-[(((1*S*, 2*R*) -2- (1-methyl -1 -phenylethyl)cyclohexyl)oxy)carbonyl)
-2,3-dihydro -isoindol -1- one

Compound No: **3c**

Notebook Pg(s): zyc1- 061Y

Formula: C₂₇H₃₃NO₃

Molecular Weight: 419.5559

Yields(s): 76 %

Appearance: white solid

Stability: stable

mp/bp: 155- 157 °C

[α]²⁸_D +79° (c, 0.445, CHCl₃),

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	77.29	7.93	3.34	11.44
Found:	77.20	7.89	3.28	

HRMS: Calculated

Found

IR (thin film): 2963, 2931, 1747, 1704, 1468, 1372, 1329, 1280 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 0.29 (d, 3H, *J* = 6.8 Hz), 1.00 (d, 3H, *J* = 7.1 Hz), 1.17- 1.36 (m, 10H), 1.77 (m, 2H), 1.98 (m, 2H), 2.20 (m, 2H), 3.47(d, 1H, *J* = 2.0 Hz), 4.99 (m, 1H), 6.73 (t, 1H, *J* = 7.2 Hz), 7.00 (t, 2H, *J* = 7.7 Hz), 7.28 (m, 3H), 7.47 (t, 1H, *J* = 7.3 Hz), 7.58 (t, 1H, *J* = 7.2 Hz), 7.89 (d, 1H, *J* = 7.7 Hz)

¹³C-NMR (75 MHz) δ 15.2, 19.6, 23.0, 24.9, 26.1, 27.0, 29.9, 30.5, 33.7, 39.8, 51.7, 64.0, 76.7, 123.6, 124.9, 125.1, 125.4, 127.9, 128.4, 131.5, 133.0, 143.8, 149.8, 152.5, 167.1

Literature References:

Compound Name: (3*S*)-3-Methyl - *N*-[(((1*R**, 2*S**) -2- (1-methyl -1 -phenylethyl) - cyclohexyl)-oxy) carbonyl)
-2,3- dihydro - isoindol -1- one

Compound No: **3d**
Notebook Pg(s): zyc1- 059Y

Formula: C₂₅H₂₉NO₃

Molecular Weight: 391.5027

Yields(s): 86 %

Appearance: white solid

Stability: stable

mp/bp: 151-152 °C

[α]_D²⁸ +37.7° (c, 0.86, CHCl₃)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	76.70	7.47	3.58	12.26
Found:	76.77	7.50	3.62	

HRMS: Calculated Found

IR (thin film): 2919, 2860, 1743, 1707, 1372, 1349, 1331, 1284, 1255 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.20 (m, 5H), 1.27 (d, 3H, *J* = 6.5 Hz), 1.38 (m, 5H), 1.77 (m, 2H), 2.01 (m, 2H), 2.21(m, 2H), 3.51(q, 1H, *J* = 6.2 Hz), 5.00 (m, 1H), 6.72 (t, 1H, *J* = 7.2 Hz), 7.03 (t, 2H, *J* = 7.6 Hz), 7.28 (m, 3H), 7.45 (t, 1H, *J* = 7.5 Hz), 7.61 (t, 1H, *J* = 7.4 Hz), 7.87 (d, 1H, *J* = 7.7 Hz)

¹³C-NMR (75 MHz) δ 20.5, 22.6, 24.9, 26.1, 27.0, 30.2, 33.7, 39.8, 51.6, 55.6, 76.5, 122.3, 124.8, 125.0, 125.4, 127.9, 128.4, 129.9, 133.7, 147.2, 149.8, 152.4, 166.7

Literature References:

Compound Name: (3*S*)-3-Propargyl-*N*-[(((1*S*,2*R*)-2-(1-methyl-1-phenylethyl)-cyclohexyl)-oxy)carbonyl]-2,3-dihydro-isoindol-1-one

Compound No: **3e**

Notebook Pg(s): zycll- 06Y

Formula: C₂₇H₂₉NO₃

Molecular Weight: 415.5241

Yields(s): 84%

Appearance: white solid

Stability: stable

mp/bp: 153 - 154 °C
(ethylacetate / hexane)

[α]_D³⁰ +90° (c 1.28, CH₂Cl₂)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	78.04	7.03	3.37	11.55
Found:	77.93	7.04	3.39	

HRMS: Calculated

Found

IR (thin film): 3303, 3056, 2933, 2859, 1747, 1704, 1356, 1333, 1295, 1258 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.21 (m, 3H), 1.27 (m, 2H), 1.38 (m, 5H), 1.80 (m, 3H), 2.00 (m, 2H), 2.23 (m, 1H), 2.61 (m, 2H), 3.54 (s, 1H), 4.99 (m, 1H), 6.79 (t, 1H, *J* = 7.2 Hz), 7.06 (t, 2H, *J* = 7.6 Hz), 7.30 (d, 2H, *J* = 7.7 Hz), 7.48 (m, 2H), 7.62 (t, 1H, *J* = 7.4 Hz), 7.88 (d, 1H, *J* = 7.7 Hz)

¹³C-NMR (75 MHz) δ 22.8, 24.1, 24.9, 26.1, 27.0, 30.1, 33.7, 39.8, 51.5, 56.9, 72.1, 78.0, 122.8, 124.9, 125.4, 128.0, 128.9, 130.7, 133.7, 144.3, 149.4, 152.5, 166.6

Literature References:

Compound Name: (3*S*)-3-(4-Chlorobutyl)-*N*-((((1*S*,2*R*)-2-(1-methyl-1-phenylethyl)-cyclohexyl)-oxy)carbonyl)-2,3-dihydro-isoindol-1-one

Compound No: **3f**

Notebook Pg(s): zycl- 099w

Formula: C₂₈H₃₄ClNO₃

Molecular Weight: 468.0272

Yields(s): 74%

Appearance: colorless oil

Stability: stable

mp/bp:

[α]_D³⁰ +47° (c 0.80, CH₂Cl₂)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	71.85	7.32	2.99	
Found:				

HRMS: Calculated for C₂₈H₃₄ClNO₃: 468.2305 [M+H]⁺ . Found: 468.2326 [M+H]⁺

IR (thin film): 2933, 2861, 1746, 1711, 1360, 1332, 1294, 1257 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 0.88 (m, 1H), 1.20 (m, 4H), 1.25 (m, 3H), 1.37 (m, 4H), 1.59 (m, 2H), 1.76 (m, 4H), 1.99 (m, 2H), 2.21 (m, 1H), 3.36 (dt, 2H, *J* = 6.5 and 1.9 Hz), 3.52 (m, 1H), 5.00 (m, 1H), 6.73 (t, 1H, *J* = 7.2 Hz), 7.03 (t, 2H, *J* = 7.5 Hz), 7.27 (m, 3H), 7.47 (t, 1H, *J* = 7.5 Hz), 7.62 (t, 1H, *J* = 7.4 Hz), 7.88 (d, 1H, *J* = 7.5 Hz)

¹³C-NMR (75 MHz) δ 20.1, 22.5, 24.7, 25.9, 26.8, 30.0, 31.9, 32.3, 33.6, 39.6, 44.3, 51.5, 58.7, 76.5, 122.2, 124.7, 125.0, 125.3, 127.8, 128.4, 130.5, 133.6, 145.3, 149.5, 152.4, 166.9

Literature References:

Compound Name: (3*S*)-3-Propargyl-2,3-dihydroisoindol-1-one

Compound No: **4e**

Notebook Pg(s): zycll- 04w

Formula: C₁₁H₉NO

Molecular Weight: 171.20

Yields(s): 93%

Appearance: white solid

Stability: stable

mp/bp: 179-180 °C

[α]_D²⁸ -57° (c 0.43, CH₂Cl₂)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	77.17	5.30	8.18	
Found:	76.89	5.36	8.28	

HRMS: Calculated

Found

IR (thin film): 3234, 2967, 1698, 1660, 1469, 1417, 1304, 1213 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.51 (d, 3H, *J* = 6.7 Hz), 4.70 (q, 1H, *J* = 6.7 Hz), 6.85 (s, 1H), 7.46 (m, 2H), 7.58 (t, 1H, *J* = 7.2 Hz), 7.85 (d, 1H, *J* = 7.5 Hz)

¹³C-NMR (75 MHz) δ 20.4, 52.9, 122.3, 123.7, 128.1, 131.9, 149.2, 171.4

Literature References:

Compound Name: (3*S*)-3-(4-Chlorobutyl)-2,3-dihydroisoindol-1-one

Compound No: **4f**

Notebook Pg(s): zycl- 100Y

Formula: C₁₂H₁₄ClNO

Molecular Weight: 223.6984

Yields(s): 90%

Appearance: white solid

Stability: stable

mp/bp: 201-202 °C
(EtOAc / hexane)

[α]_D²³ -44° (c 0.40, CH₂Cl₂)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	64.43	6.31	6.26	
Found:	64.22	6.38	6.21	

HRMS:

IR (thin film): 3224, 2936, 2865, 1694, 1469, 1420, 1361, 1312 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.49 (m, 1H), 1.69 (m, 2H), 1.81 (m, 2H), 1.99 (m, 1H), 3.53 (t, 2H, *J* = 6.5 Hz), 4.66 (t, 1H, *J* = 5.7 Hz), 7.31 (s, 1H), 7.47 (dd, 2H, *J* = 14.7 and 7.5 Hz), 7.58 (t, 1H, *J* = 7.5 Hz), 7.85 (d, 1H, *J* = 7.5 Hz)

¹³C-NMR (75 MHz) δ 22.9, 32.6, 34.0, 44.7, 56.8, 122.6, 124.1, 128.4, 132.1, 147.5, 171.3.

Literature References:

Compound Name: (S)-Lennoxamine

Compound No: 5

Notebook Pg(s): zycll-57w, SSII-44y

Formula: $C_{20}H_{19}NO_5$
Molecular Weight: 353.37
Yields(s): 99 %
Appearance: white solid
Stability: stable
mp/bp: 232-234 °C
 $[\alpha]^{23}_D$ +28° (c 1.0, $CHCl_3$)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	67.98	5.42	3.96	
Found:				

HRMS Calcd. for $C_{20}H_{20}O_5$: 354.1341 $[M + H]^+$. Found: 354.1339 $[M + H]^+$

IR (thin film): 2916, 2848, 1680, 1494, 1486, 1293, 1288, 1035 cm^{-1}

NMR ($CDCl_3$):

1H -NMR (400 MHz) δ 7.17 (d, $J = 8.0$ Hz, 1H), 7.13 (d, $J = 8.0$ Hz, 1H), 6.78 (s, 1H), 6.70 (s, 1H), 5.96 (d, $J = 1.2$ Hz, 1H), 5.95 (d, $J = 1.2$ Hz, 1H), 4.74 (m, 1H), 4.30 (d, $J = 9.6$ Hz, 1H), 4.10 (s, 3H), 3.91 (s, 3H), 3.10 (dd, $J = 14.6, 1.4$ Hz, 1H), 2.91 (m, 2H), 2.82 (m, 2H)

^{13}C -NMR (100 MHz) δ 165.4, 152.9, 147.5, 146.6, 146.3, 138.4, 135.1, 131.2, 124.4, 117.3, 116.4, 110.6, 110.5, 101.3, 62.8, 60.4, 57.0, 42.9, 41.3, 36.2

Literature References:

For the isolation of racemic lennoxamine from *Berberis darwinii*, see: (a) Valencia, E.; Freyer, A. J.; Shamma, M.; Fajardo, V. *Tetrahedron Lett.* **1984**, 25, 599. For recent racemic total syntheses and leading references, see: (b) Sahakitpichan, P.; Ruchirawat, S.; *Tetrahedron* **2004**, 60, 4169. (c) Kim, G.; Kim, J. H.; Kim, W. -j.; Kim, Y. A. *Tetrahedron Lett.* **2003**, 44, 8207. (d) Koseki, Y.; Katsura, S.; Kusano, S.; Sakata, H.; Sato, H.; Monzene, Y.; Nagasaka, T. *Heterocycles* **2003**, 59, 527. (e) Padwa, A.; Beall, L. S.; Eidell, C. K.; Worsencroft, K. J. *J. Org. Chem.* **2001**, 66, 2414. (f) Fuchs, J. R.; Funk, R. L. *Org. Lett.* **2001**, 3, 3923 and references cited therein.

Compound Name: 6,7-Dimethoxy-*N*-((((1*S*, 2*R*) - 2 - (1-methyl-1-phenylethyl)cyclohexyl)oxy) carbonyl) - 2,3- dihydroisoindol - 1-one

Compound No: 11

Notebook Pg(s): zycII-062W

Formula: $C_{26}H_{31}NO_5$
Molecular Weight: 437.5281
Yields(s): 75 %
Appearance: clear oil
Stability: stable
mp/bp:
 $[\alpha]^{23}_D$ +38° (c 0.5, $CHCl_3$)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	71.37	7.14	3.20	
Found:				

HRMS Calcd. for $C_{26}H_{31}O_5$ 438.2230 $[M + H]^+$. Found: 438.2221 $[M + H]^+$

IR (thin film): 2934, 2860, 1755, 1642, 1495, 1445, 1229, 1015, 765, 699 cm^{-1}

NMR ($CDCl_3$):

1H -NMR (300 MHz) δ 1.21 (m, 5H), 1.39 (s, 4H), 1.73 (m, 3H), 1.95 (m, 2H), 2.21(m, 1H), 3.37 (d, 1H, $J = 16.5$ Hz), 3.89 (s, 3H), 4.06 (s, 3H), 4.08 (d, 1H, $J = 16.5$ Hz), 4.98 (m, 1H), 6.88 (m, 2H), 7.14 (m, 3H), 7.31 (s, 1H), 7.33 (s, 1H)

^{13}C -NMR (75 MHz) δ 23.2, 24.9, 26.0, 27.1, 29.9, 33.8, 39.9, 48.5, 51.4, 76.7, 123.0, 124.9, 125.2, 125.6, 128.0, 128.5, 131.3, 133.6, 141.2, 150.2, 152.4, 166.7

Literature References:

Compound Name: 5-Bromo-6-(2-methoxyvinyl)benzo[1,3]dioxole

Compound No: 13

Notebook Pg(s): yzcll-24w, SSII-14w

Formula: $C_{10}H_9BrO_3$

Molecular Weight: 257.081

Yields(s): 96%

Appearance: clear oil

Stability:

mp/bp:

$[\alpha]^{23}_D$

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	% O
Calculated:	46.72	3.53		18.67
Found:				

HRMS Calcd. for $C_{10}H_9BrO_3$ 255.9735 $[M + H]^+$. Found: 255.9738 $[M + H]^+$

IR (thin film): 2934, 2897, 1637, 1503, 1477, 1231, 1122, 1039 cm^{-1}

NMR ($CDCl_3$):

1H -NMR (300 MHz) δ 3.71 (m, 3H), 3.77 (m, 3H, isomer), 5.52 (d, 1H, $J = 7.2$ Hz), 5.95 (s, 2H), 6.02 (d, 1H, $J = 12.8$ Hz), 6.16 (d, 1H, $J = 7.2$ Hz), 6.82 (s, 1H), 6.86 (d, 1H, $J = 12.8$ Hz)

^{13}C -NMR (75 MHz) δ 56.6, 60.8, 101.6, 101.7, 104.0, 104.7, 105.4, 109.8, 112.5, 112.8, 128.6, 129.6, 133.7, 134.0, 148.1, 149.7

Literature References:

Compound Name: [6-(2-Methoxyvinyl)benzo-[1,3-dioxol-5-yl]-methanol

Compound No: 14

Notebook Pg(s): zycll-30w

Formula: C₁₁H₁₂O₄

Molecular Weight: 208.211

Yields(s): 85%

Appearance: clear oil

Stability:

mp/bp:

[α]²³_D

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	% O
Calculated:	63.45	5.81		30.74
Found:				

HRMS Calcd. for C₁₁H₁₂O₄ 208.0736 [M + H]⁺. Found: 208.0737 [M + H]⁺

IR (thin film): 3380, 2934, 2894, 1643, 1504, 1485, 1261, 1135, 1040 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 3.70 (s, 3H), 3.75 (s, 3H, isomer), 4.62 (d, 2H, *J* = 4.0 Hz), 5.41 (d, 1H, *J* = 7.0 Hz), 5.94 (s, 2H), 6.04 (d, 1H, *J* = 27.8 Hz), 6.16 (d, 1H, *J* = 7.0 Hz), 6.81 (m, 1H), 6.85 (m, 1H)

¹³C-NMR (75 MHz) δ 56.8, 60.6, 63.4, 63.6, 101.0, 101.7, 102.0, 105.9, 109.1, 109.7, 127.9, 128.9, 130.9, 131.4, 147.6, 149.5

Literature References:

Compound Name: [6-(2-Methoxyethyl)-benzo[1,3]dioxol-5-yl]-methanol

Compound No: 15

Notebook Pg(s): zycll-46w

Formula: C₁₁H₁₄O₄

Molecular Weight: 210.23

Yields(s): 82%

Appearance: white solid

Stability:

mp/bp: 73 °C

[α]²³_D

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	% O
Calculated:	62.85	6.71		30.44
Found:	62.83	6.86		

IR (thin film): 3380, 2934, 2894, 1643, 1504, 1485, 1261, 1135, 1040 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 2.86 (t, 2H, *J* = 5.8 Hz), 3.29 (s, 3H), 3.57 (t, 2H, *J* = 5.8 Hz), 4.48 (d, 2H, *J* = 5.9 Hz), 5.91 (s, 2H), 6.78 (s, 1H), 6.80 (s, 1H)

¹³C-NMR (75 MHz) δ 32.9, 59.0, 62.9, 73.7, 101.1, 109.7, 110.1, 131.7, 133.4, 146.3, 147.6.

Literature References:

Compound Name: 5-Bromomethyl-6-(2-methoxyethyl)benzo[1,3]dioxole

Compound No: 16

Notebook Pg(s): zycll-46w

Formula: $C_{11}H_{13}BrO_3$

Molecular Weight: 273.12

Yields(s): 99% crude

Appearance: oil

Stability: unstable: used directly in the next step

mp/bp:

$[\alpha]^{23}_D$

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	% O
Calculated:	48.37	4.80		17.57
Found:				

IR (thin film):

NMR ($CDCl_3$):

1H -NMR (300 MHz) δ 2.86 (t, 2H, $J = 5.8$ Hz), 3.29 (s, 3H), 3.57 (t, 2H, $J = 5.8$ Hz), 4.48 (s, 2H), 5.91 (s, 2H), 6.78 (s, 1H), 6.80 (s, 1H)

^{13}C -NMR (75 MHz) δ

Literature References:

Compound Name: (3S)- 4,5-Dimethoxy-1-[6-(2-methoxyethyl)benzo[1,3]dioxol-5-ylmethyl]-3-oxo-1,3-dihydroisindole-2-carboxylic acid (1*S*,2*R*)-2-(1-methyl-1-phenylethyl)cyclohexyl ester

Compound No: 17

Notebook Pg(s): zycll-51y, SSII-39w

Formula: C₃₇H₄₃NO₈
Molecular Weight: 629.74
Yields(s): 56 %
Appearance: white solid
Stability: stable
mp/bp: 149-150 °C
[α]²³_D: +93° (c 0.95, CHCl₃)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	70.57	6.88	2.22	
Found:	70.16	7.01	2.30	

IR (thin film): 2931, 1777, 1498, 1488, 1362, 1328, 1268, 1219, 1176, 1112, 1038, 1018 cm⁻¹

NMR (CDCl₃):

¹H-NMR (300 MHz) δ 1.23 (m, 5H), 1.39 (m, 5H), 1.77 (m, 2H), 2.01 (m, 2H), 2.24(m, 1H), 2.55 (m, 2H), 3.27 (s, 3H), 3.30 (m, 2H), 3.49(m, 1H), 3.86 (s, 3H), 4.07 (m, 4H), 5.10 (m, 1H), 5.98(s, 2H), 6.36 (s, 1H), 6.60 (t, 1H, J = 7.2 Hz), 6.95 (m, 4H), 7.31 (s, 1H), 7.33 (s, 1H)

¹³C-NMR (75 MHz) δ 14.4, 22.4, 25.0, 26.0, 27.0, 30.3, 33.2, 33.7, 37.8, 39.8, 51.8, 56.8, 58.5, 58.9, 60.6, 62.7, 73.4, 76.6, 101.2, 110.0, 111.1, 117.7, 118.9, 122.4, 125.0, 125.5, 127.9, 131.1, 137.8, 146.1, 146.8, 148.3, 149.6, 152.05, 152.6, 164.8

Literature References:

Compound Name: (3S)-3-[6-(2-Hydroxyethyl)benzo[1,3]dioxol-5-ylmethyl]-6,7-dimethoxy-2,3-dihydro-isoindol-1-one

Compound No: 18

Notebook Pg(s): SSII-44w

Formula: $C_{20}H_{21}NO_6$
Molecular Weight: 371.38
Yields(s): 60 %
Appearance: oil
Stability: stable
mp/bp:
 $[\alpha]^{23}_D$ -40° (c 1.0, $CHCl_3$)

Elemental
Analysis
(Atlantic Microlabs, Inc.)

	%C	%H	%N	%__O__
Calculated:	64.68	5.70	3.77	
Found:				

HRMS Calcd. for $C_{20}H_{22}O_6$: 372.1447 $[M + H]^+$. Found: 372.1463 $[M + H]^+$

IR (thin film): 3388, 2929, 1688, 1488, 1267, 1041 cm^{-1}

NMR ($CDCl_3$):

1H -NMR (400 MHz) δ 7.40 (s, 1H), 7.10 (d, $J = 8.4$ Hz, 1H), 7.00 (d, $J = 8.4$ Hz, 1H), 6.75 (s, 1H), 6.68 (s, 1H), 5.90 (d, $J = 1.6$ Hz, 1H), 5.87 (d, $J = 1.2$ Hz, 1H), 4.64 (dd, $J = 9.2, 4.8$ Hz, 1H), 4.05 (s, 3H), 3.90 (s, 3H), 3.86 (m, 2H), 3.12 (dd, $J = 13.6, 4.8$ Hz, 1H), 2.89-2.72 (m, 4H)

^{13}C -NMR (100 MHz) δ 169.2, 152.6, 147.6, 147.0, 146.5, 140.7, 130.9, 129.2, 124.3, 117.8, 117.0, 110.2, 110.0, 101.2, 63.2, 62.6, 57.3, 56.9, 38.8, 35.3

Literature References:

This structure is the enantiomer of **3d** prepared from the (-)-TCC-carbamate (-)-**2**.