Organic Letters

SUPPORTING INFORMATION

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"A Six-Step Asymmetric Synthesis of (+)-Hyperaspine"

- I.** Characterization data for compounds **1** and **3-8** (7 pages).
- II.** Comparison tables of NMR data for synthetic **1** (1 page).

Total pages of supporting information: (9).

Data Sheet- James J. Sahn

Compound: (2*S*)-1-[(1*S*,2*R*)-(α-Cumyl)cyclohexyloxycarbonyl]-2-(2-ketopropyl)-5-triisopropylsilyl-2,3-dihydro-4-pyridone

Compound No: 3

Notebook Pg(s): JJS-1-75W, JJS-1-87W

Formula: C₃₃H₅₁NO₄Si

Molecular Weight: 553.835

Yield: 72% (de 93%, crude)

Appearance: white solid

Stability: stable

Mp: 138 - 139 °C

[α]_D³⁰ + 75 (c 0.35, CHCl₃)

Elemental analysis (Atlantic Microlabs)	%C			%H			%N		
	Calculated								
	Found								

HRMS

Calculated: 554.3666

Found: 554.3699

Enantiomer of known compound, see reference below*.

IR (thin film, neat, NaCl): 2938, 2862, 1719, 1560, 1387, 1328, 1248 cm⁻¹.

NMR (CDCl₃):

(¹H, 400 MHz): δ 7.65 (bs, 1 H), 7.36 (m, 4 H), 7.81 (m, 1 H), 4.88 (m, 1 H), 3.48 (m, 1 H), 2.50 (m, 2H), 2.20 (m, 2H), 2.02 (s, 3H), 1.60-2.00 (m, 4H), 1.00-1.40 (m, 32 H).

(¹³C, 100 MHz): δ 204.88, 196.76, 152.40, 151.82, 147.59, 128.40, 125.26, 110.47, 78.33, 51.14, 48.10, 43.76, 40.73, 39.63, 33.75, 31.12, 30.95, 26.95, 25.93, 24.85, 21.87, 19.11, 19.05, 11.49, 10.94.

*Literature reference(s): Comins, D.; Hong, H. *J. Org. Chem.* **1993**, 58, 5035.

Data Sheet- James J. Sahn

Compound: (2*S*)-[(2*S*)-Hydroxypropyl]-5-(triisopropylsilyl)-2,3-dihydro-1*H*-pyridin-4-one

Compound No: 4

Notebook Pg(s): JJS-1-76W, JJS-1-77Y, JJS-1-88W

Formula: C₁₇H₃₃NO₂Si

Molecular Weight: 311.535

Yield(s): 80%

Appearance: fine, white needles

Stability: stable

Mp: 169-170 °C

$[\alpha]_D^{29}$ -178 (*c* 2.75, MeOH)

		%C	%H	%N
Elemental analysis (Atlantic Microlabs)	Calculated	65.54	10.68	4.50
	Found	65.59	10.63	4.49

HRMS	Calculated: 312.2359	Found: 312.2376
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IR (thin film, neat, NaCl): 3429, 2959, 1651, 1316 cm⁻¹.

NMR (CDCl₃):

(¹H, 300 MHz): δ 7.21 (d, 1 H, *J* = 5.4 Hz), 6.60 (bs, 1 H), 4.07 (m, 1 H), 3.79 (m, 1H), 2.35 (m, 2H), 1.65 (m, 2 H), 1.27 (m, 6 H), 1.02 (m, 18 H).

(¹³C, 75 MHz): δ 205.0, 156.7, 112.3, 69.6, 53.9, 44.3, 42.7, 25.7, 19.2, 11.5.

Literature reference(s): Comins, D.; Hong, H. *J. Org. Chem.* **1993**, 58, 5035.

Data Sheet- James J. Sahn

Compound: (3*S*,4*aS*)-3-Methyl-7-(triisopropylsilanyl)-3,4,4*a*,5-tetrahydro-pyrido[1,2-*c*][1,3]oxazine-1,6-dione

Compound No: **5**

Notebook Pg(s): JJS-2-05W

Formula: C₁₈H₃₁NO₃Si

Molecular Weight: 337.2073

Yield(s): 55%

Appearance: white solid

Stability: stable

Mp: 109 – 110 °C

[α]_D³² -235 (*c* 0.4, CHCl₃)

	%C	%H	%N
Elemental analysis (Atlantic Microlabs)	Calculated		
	Found		

HRMS

Calculated: 338.2151

Found: 338.2170

IR (thin film, neat, NaCl): 2944, 2866, 1729, 1653, 1560, 1270 cm⁻¹.

NMR (CDCl₃):

(¹H, 300 MHz): δ 8.02 (s, 1 H), 4.57 (m, 1 H), 4.08 (m, 1 H), 2.50 (m, 2 H), 2.21 (m, 1 H), 1.86 (m, 1 H), 1.60 – 1.20 (m, 6 H).

(¹³C, 75 MHz): δ 195.88, 150.33, 149.06, 114.32, 74.44, 53.33, 43.06, 36.12, 21.26, 19.00, 11.28.

Literature reference(s): none

Data Sheet- James J. Sahn

Compound: (3*S*,4*aS*)-3-Methyl-7-(triisopropyl-silanyl)-3,4,4*a*,5-tetrahydro-pyrido[1,2-*c*][1,3]oxazin-6-one

Compound No: **6**

Notebook Pg(s): JJS-1-57Y

Formula: C₁₈H₃₃NO₂Si

Molecular Weight: 323.228

Yield(s): 82%

Appearance: white solid

Stability: stable

Mp: 62-63 °C

[α]_D³⁰ -114 (*c* 0.35, MeOH)

Elemental analysis (Atlantic Microlabs)	%C			%H			%N		
	Calculated								
	Found								

HRMS

Calculated: 324.2359	Found: 324.2360
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IR (thin film, neat, NaCl): 2942, 2863, 1650, 1634, 1367 cm⁻¹.

NMR (CDCl₃):

(¹H, 400 MHz): δ 6.91 (s, 1 H), 4.81 (d, 1 H, *J* = 10 Hz), 4.55 (d, 1 H, *J* = 10 Hz), 3.69 (m, 2 H), 2.71 (dd, 1 H, *J* = 16.2 Hz and 6.6 Hz), 2.30 (dd, 1 H, *J* = 15.8 Hz and 7.4 Hz), 1.69 (q, 1 H), 1.51 (dt, 1 H, *J* = 13.2 Hz and 2.4 Hz), 1.25 (m, 6 H), 1.02 (d, 18 H, *J* = 10 Hz).

(¹³C, 100 MHz): δ 195.71, 157.12, 103.26, 83.55, 73.68, 55.59, 42.52, 37.04, 21.62, 19.15, 11.32.

Literature reference(s):

Data Sheet- James J. Sahn

Compound: (3*S*,4*aS*)-3-Methyl-3,4,4*a*,5-tetrahydro-pyrido[1,2-*c*][1,3]oxazin-6-one

Compound No: 7

Notebook Pg(s): JJS-1-79W

Formula: C₉H₁₃NO₂

Molecular Weight: 167.205

Yield(s): 97%

Appearance: oil

Stability: stable

Mp: N/A

[α]_D²⁸ -226 (*c* 2.15, MeOH)

	%C		%H	%N
Elemental analysis (Atlantic Microlabs)	Calculated			
	Found			

HRMS	Calculated: 168.1025	Found: 168.1016
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IR (thin film, neat, NaCl): 1635, 1595, 1456, 1403, 1236, 1170 cm⁻¹.

NMR (CDCl₃):

(¹H, 300 MHz): δ 6.93 (d, 1H, *J* = 7.65 Hz), 5.04 (d, 1 H, *J* = 7.65 Hz.), 4.76 (d, 1 H, *J* = 9.9 Hz.), 4.52 (d, 1 H, *J* = 9.9 Hz), 3.69 (m, 2 H), 2.70 (m, 1 H), 2.22 (m, 1 H), 1.74 (q, 1 H), 1.48 (dt, 1 H, *J* = 13.8 Hz and 2.6 Hz), 1.21 (d, 3 H, *J* = 6.3 Hz).

(¹³C, 75 MHz): δ 191.96, 151.90, 101.69, 83.31, 73.76, 55.79, 41.72, 36.89, 21.50.

Literature reference(s):

Data Sheet- James J. Sahn

Compound: (3*S*,4*aS*,8*S*)-3-Methyl-8-pentylhexahydropyrido[1,2-*c*][1,3]oxazin-6-one

Compound No: 8

Notebook Pg(s): JJS-1-90W

Formula: C₁₄H₂₅NO₂

Molecular Weight: 239.354

Yield(s): 92%

Appearance: clear oil

Stability: stable

Mp: N/A

$[\alpha]_D^{32} + 45$ (*c* 0.7, MeOH)

	%C	%H	%N
Elemental analysis (Atlantic Microlabs)	Calculated		
	Found		

HRMS	Calculated:	Found:
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Known compound; see reference below*.

IR (thin film, neat, NaCl): 2956, 2932, 2861, 1717, 1212 cm⁻¹.

NMR (CDCl₃):

(¹H, 300 MHz): δ 4.76 (d, 1 H, *J* = 10.2 Hz), 4.29 (d, 1 H, *J* = 10.2 Hz) 3.62 (m, 1 H), 3.46 (m, 1 H), 3.35 (m, 1 H), 2.68 (ddd, 1 H, *J* = 14.3 Hz, 5.6 Hz and 2.0 Hz), 2.46 (ddd, 1 H, *J* = 13.6, 8.9 and 2.0), 2.35 (ddd, 1 H, *J* = 13.6, 8.9 and 1.5 Hz), 2.16 (ddd, 1 H, *J* = 14.3, 4.7 and 2.1 Hz), 1.67-1.18 (m, 13 H), 0.87 (t, 3H, *J* = 6.8 Hz).

(¹³C, 75 MHz): δ 209.20, 81.52, 73.59, 56.32, 53.43, 47.04, 45.94, 35.87, 32.24, 30.96, 24.66, 22.80, 21.84, 14.22.

*Literature reference(s): Ma, D.; Zhu, W. *Org. Lett.* **2003**, 5, 5063.

Data Sheet – James J. Sahn

Compound: (+)-Hyperaspine

Compound No: **1**

Notebook Pg(s): JJS-1-99Y

Formula: C₁₉H₃₀N₂O₃

Molecular Weight: 334.4531

Yield(s): 50%

Appearance: oil

Stability: stable

m.p.: N/A

$[\alpha]_D^{32} + 65$ (c 0.20, MeOH)

	%C	%H	%N
Elemental analysis (Atlantic Microlabs)	Calculated		
	Found		

HRMS	Calculated:	Found:
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Known compound; see reference below.

IR (thin film, neat, NaCl): 3305, 2930, 2861, 1699 cm⁻¹.

NMR (CD₂Cl₂):

(¹H, 300 MHz): δ 9.15 (bs, 1 H), 6.96 (m, 1 H), 6.87 (m, 1 H), 6.25 (m, 1 H), 5.12 (m, 1 H), 4.78 (d, 1 H, *J* = 10.8 Hz), 4.22 (d, 1 H, *J* = 10.8 Hz), 3.62 (m, 1 H), 3.40 (m, 1 H), 3.19 (m, 1 H), 2.08 (m, 1 H), 1.90 – 1.02 (m, 16 H), 0.89 (m, 3 H).

(¹³C, 75 MHz): δ 160.82, 123.23, 122.99, 115.52, 110.71, 80.90, 74.12, 68.81, 55.65, 49.42, 36.68, 36.38, 33.39, 32.54, 32.48, 24.48, 22.86, 22.17, 14.29.

Literature reference(s): Ma, D.; Zhu, Wei. *Org. Lett.* **2003**, 5063.
Pradhar, S. *Tetrahedron*, **1986**, 42, 6351.

Comparison Tables of NMR Data for 1

^1H NMR for (+)-Hyperaspine (1)

<u>Literature</u> *	<u>Our Synthetic 1</u>
(CD ₂ Cl ₂ , 300 MHz)	(CD ₂ Cl ₂ , 300 MHz)
9.64 (br s, 1 H)	9.15 (br s, 1 H)
6.96 (m, 1 H)	6.96 (m, 1 H)
6.87 (m, 1 H)	6.87 (m, 1 H)
6.25 (m, 1 H)	6.25 (m, 1 H)
5.10 (m, 1 H)	5.12 (m, 1 H)
4.77 (d, 1 H, $J = 10.8$ Hz)	4.78 (d, 1 H, $J = 10.8$ Hz)
4.22 (d, 1 H, $J = 10.8$ Hz)	4.22 (d, 1 H, $J = 10.8$ Hz)
3.61 (m, 1 H)	3.62 (m, 1 H)
3.38 (m, 1 H)	3.40 (m, 1 H)
3.16 (m, 1 H)	3.19 (m, 1 H)
1.86 (m, 1 H)	2.08 (m, 1 H)
1.67-1.15 (m, 16 H)	1.90-1.02 (m, 16 H)
0.86 (m, 3 H)	0.89 (m, 3 H)

^{13}C NMR for (+)-Hyperaspine (1)

<u>Literature</u> *	<u>Our Synthetic 1</u>
(CD ₂ Cl ₂ , 75 MHz)	(CD ₂ Cl ₂ , 75 MHz)
161.1	160.8
124.0	123.2
123.5	123.0
115.6	115.5
111.0	110.7
81.4	80.9
74.6	74.1
69.5	68.8
56.2	55.7
49.9	49.4
37.3	36.7
37.0	36.4
33.9	33.4
33.1	32.5
33.0	32.5
24.9	24.5
23.4	22.9
22.5	22.2
14.6	14.3

* Ma, D; Zhu, W.; *Org. Lett.* **2003** 5, 5063.