### **Supporting Information**

### Enantioselective Synthesis of Pyranonaphthoquinone Antibiotics using a CBS Reduction/ Cross-metathesis/ oxa-Michael Strategy<sup>†</sup>

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(±)-2-(1-(*tert*-Butyldimethylsilyloxy)ethyl)-1,4-dimethoxynaphthalene (11b). To a solution of alcohol 11a (1.14 g, 4.9 mmol) in dry DMF (15 mL) was added TBDMSCl (1.11 g, 7.3 mmol), imidazole (0.67 g, 9.8 mmol), and DMAP (0.12 g, 0.98 mmol). The reaction mixture was stirred under nitrogen at room temperature for 24 hours. The solution was quenched by the addition of sat. aq. NaHCO<sub>3</sub> (50 mL) and extracted with EtOAc ( $3 \times 50$  mL). The combined organic extracts were dried over MgSO<sub>4</sub> and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 5:1) gave TBDMS ether 11b (1.7 g, 100%) as a colourless solid: mp 53-57 °C; IR (film)  $v_{max}$ /cm<sup>-1</sup> 3071, 2953, 2928, 2857, 1629, 1592, 1452, 1369, 1247, 1212, 1127, 1085, 999, 896, 828, 764; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.28 (1 H, d, *J* = 7.7 Hz, 5-H or 8-H), 8.05 (1 H, d, *J* = 8.4 Hz, 5-H or 8-H), 7.57-7.46 (2 H, m, 6-H and 7-H), 7.07 (1 H, s, 3-H), 5.47 (1 H, q, *J* = 6.3 Hz, CHOSi), 4.03 (3 H, s OCH<sub>3</sub>), 3.94 (3 H, s, OCH<sub>3</sub>), 1.53 (3 H, d, *J* = 6.3 Hz, CH<sub>3</sub>), 0.96 (9 H, s, <sup>1</sup>Bu), 0.14 (3 H, s, SiCH<sub>3</sub>), 0.01 (3 H, s, SiCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  152.1 (C-Ar), 144.3 (C-Ar), 134.9 (C-Ar), 128.2 (C-Ar), 126.4 (CH-Ar), 125.9 (C-Ar), 125.0 (CH-Ar), 122.4 (CH-Ar), 121.9 (CH-Ar), 101.8 (CH-Ar), 65.3 (CHOSi), 62.1 (OCH<sub>3</sub>), 55.6 (OCH<sub>3</sub>), 26.6 (CH<sub>3</sub>), 25.9 (3 × CH<sub>3</sub>), 18.3 (<u>C</u>(CH<sub>3</sub>)<sub>3</sub>), -4.8 (SiCH<sub>3</sub>), -4.8 (SiCH<sub>3</sub>); MS (ESI) *m*/z 369 ([M-Na]<sup>+</sup>, 12%), 299 (10), 215 (100), 186 (58); HRMS (ESI) *m*/z for C<sub>20</sub>H<sub>30</sub>NaO<sub>3</sub>Si<sup>+</sup> [M-Na]<sup>+</sup> calcd 369.1856, found 369.1844.

(±)-2-(1-(*tert*-Butyldimethylsilyloxy)ethyl)-1,4-naphthoquinone (9b). To a stirred solution of TBDMS ether 11b (0.2 g, 0.6 mmol) in acetonitrile (5 mL) was added a solution of CAN (0.63 g, 1.2 mmol) in water (1 mL). The solution was stirred at room temperature for 5 minutes and then diluted with water (30 mL). The reaction mixture was extracted with EtOAc ( $3 \times 30$  mL). The combined organic extracts were washed with sat. aq. NaHCO<sub>3</sub> (30 mL), dried over MgSO<sub>4</sub> and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 30:1) gave naphthoquinone 9b (0.14 g, 75%) as a yellow oil: IR (film)  $v_{max}$ /cm<sup>-1</sup> 2956, 2930, 2857, 1662, 1620, 1596, 1298, 1249, 1112, 893, 830, 776; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.02-7.99 (2 H, m, 5-H and 8-H), 7.68-7.65 (2 H,

m, 6-H and 7-H), 7.05 (1 H, s, 3-H), 4.99 (1 H, q, J = 6.4 Hz, CHOSi), 1.35 (3 H, d, J = 6.4 Hz, CH<sub>3</sub>), 0.87 (9 H, s, <sup>t</sup>Bu), 0.06 (3 H, s, SiCH<sub>3</sub>), 0.01 (3 H, s, SiCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  185.3 (C=O), 184.7 (C=O), 155.0 (C-Ar), 133.7 (CH-Ar), 133.5 (CH-Ar), 132.9 (CH-Ar), 132.2 (C-Ar), 132.0 (C-Ar), 126.2 (CH-Ar), 126.0 (CH-Ar), 64.7 (CHOSi), 25.7 (3 × CH<sub>3</sub>), 24.8 (CH<sub>3</sub>), 18.1 (<u>C</u>(CH<sub>3</sub>)<sub>3</sub>), -5.0 (SiCH<sub>3</sub>), -5.1 (SiCH<sub>3</sub>); MS (ESI) m/z 339 ([M-Na]<sup>+</sup>, 50%), 317 ([M-H]<sup>+</sup>, 58), 185 (100); HRMS (ESI) m/z for C<sub>18</sub>H<sub>25</sub>O<sub>3</sub>Si<sup>+</sup> [M-H]<sup>+</sup> calcd 317.1567, found 317.1567.

(±)-2-(1-(Ethoxymethoxy)ethyl)-1,4-dimethoxynaphthalene (11c). To a solution of alcohol 11a (0.5 g, 2.2 mmol) and DIPEA (1.5 mL, 8.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (21 mL) was added ethoxymethyl chloride (0.4 mL, 4.3 mmol) and DMAP (50 mg, 4.3 mmol). The solution was stirred under nitrogen at room temperature for 2 days. The solution was quenched with sat. aq. NH<sub>4</sub>Cl (50 mL). The layers were separated and the aqueous phase extracted with EtOAc ( $3 \times 50$  mL). The combined organic extracts were washed with brine (50 mL), dried over MgSO<sub>4</sub> and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 5:1) gave EOM ether **11c** (0.56 g, 90%) as a colourless oil: IR (film)  $v_{max}$ /cm<sup>-1</sup> 2975, 2934, 1596, 1459, 1365, 1213, 1088, 997, 846, 768; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.31-8.29 (1 H, d, J = 8.4 Hz, 5-H or 8-H), 8.09 (1 H, d, J = 7.8 Hz, 5-H or 8-H), 7.57-7.47 (2 H, m, 6-H and 7-H), 6.92 (1 H, s, 3-H), 5.50 (1 H, q, J = 6.8 Hz, CHOEOM), 4.73 (1 H, d, J = 6.6 Hz, OCH<sub>2</sub>O), 4.66 (1 H, d, J = 6.6 Hz, OCH<sub>2</sub>O), 4.01 (3 H, s, OCH<sub>3</sub>), 3.96 (3 H,s, OCH<sub>3</sub>), 3.83-3.74 (1 H, m, OCH<sub>2</sub>CH<sub>3</sub>), 3.61-3.53 (1 H, m, OCH<sub>2</sub>CH<sub>3</sub>), 1.60 (3 H, d, J = 6.8 Hz,CH<sub>3</sub>), 1.23 (3H, t, J = 7.2 Hz, OCH<sub>2</sub>CH<sub>3</sub>); 1<sup>3</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  152.2 (C-Ar), 146.4 (C-Ar), 130.9 (C-Ar), 128.2 (C-Ar), 126.4 (CH-Ar), 126.1 (C-Ar) 125.2 (CH-Ar), 122.2 (CH-Ar), 121.8 (CH-Ar) 101.0 (3-C), 92.6 (OCH<sub>2</sub>O), 67.3 (CHOEOM), 63.1 (OCH<sub>2</sub>CH<sub>3</sub>), 62.3 (OCH<sub>3</sub>), 55.4 (OCH<sub>3</sub>), 23.0 (CH<sub>3</sub>), 1.50 (OCH<sub>2</sub>CH<sub>3</sub>); MS (ESI) *m*/z 313 ([M-Na]<sup>+</sup>, 35%), 215 (100), 186 (40); HRMS (ESI) *m*/z for C<sub>17</sub>H<sub>22</sub>NaO<sub>4</sub><sup>+</sup> [M-Na]<sup>+</sup> calcd 313.1410, found 313.1413.

(±)-2-(1-(Ethoxymethoxy)ethyl)-1,4-naphthoquinone (9c). To a stirred solution of EOM ether 11c (0.48 g, 1.6 mmol) in acetonitrile (4.2 mL) was added a solution of CAN (1.8 g, 3.3 mmol) in water (4.2 mL). The solution was stirred at room temperature for 15 minutes then diluted with water (25 mL). The reaction mixture was extracted with EtOAc ( $3 \times 25$  mL). The combined organic extracts were washed with brine (25 mL), dried over MgSO<sub>4</sub> and concentrated *in vacuo*. Purification by column chromatography (hexanes-EtOAc 7:1) gave quinone 9c (0.37 g, 86%) as a yellow oil: IR (film)  $v_{max}/cm^{-1}$  2931, 2856, 1722, 1653, 1355,1260, 1082, 1014, 969, 826; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.04-7.99 (2 H, m, 5-H and 8-H), 7.74-7.70 (2 H, m, 6-H and 7-H), 7.03 (1 H, s, 3-H), 5.01 (1 H, q, *J* = 6.5 Hz, CHOEOM), 4.79 (1 H, d, *J* = 6.9 Hz, OCH<sub>2</sub>O), 4.71 (1 H, d, *J* = 6.9 Hz, OCH<sub>2</sub>O), 3.73-3.55 (2 H, m, OCH<sub>2</sub>CH<sub>3</sub>), 1.46 (3 H, d, *J* = 6.5 Hz, ArCHCH<sub>3</sub>), 1.19 (3 H, t, *J* = 7.1 Hz, OCH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  184.6 (C=O), 184.0 (C=O), 152.1 (2-C), 133.3 (CH-Ar), 133.2 (CH-Ar), 132.6 (3-C), 131.8 (C-Ar), 131.5 (C-Ar), 125.9 (CH-Ar), 125.6 (CH-Ar), 93.3 (OCH<sub>2</sub>O), 67.9 (CHOEOM), 63.2 (O<u>C</u>H<sub>2</sub>CH<sub>3</sub>), 21.4 (CH<sub>3</sub>), 14.7 (OCH<sub>2</sub><u>C</u>H<sub>3</sub>); MS (ESI) *m*/z 283 ([M-Na]<sup>+</sup>,100%), 185 (20); HRMS (ESI) *m*/z for C<sub>15</sub>H<sub>16</sub>NaO<sub>4</sub><sup>+</sup> [M-Na]<sup>+</sup> calcd. 283.0941, found 283.0935.





## Sequence:Racemic 65 35 IC Operator:Chemistry Timebase:NP\_HPLC

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1 Racemi	c 65 35 IC			
ample Name: ïal Number: ample Type: ontrol Program: uantif. Method: 'ecording Time: 'un Time (min):	Racemic 65 35 IC 2 unknown ZEW085 65_35 default 2/12/2010 10:57 38.50		Injection Volume: Channel: Wavelength: Bandwidth: Bandwidth: Dilution Factor: Sample Weight: Sample Amount:	20.0 UV_VIS_2 254 n.a. 1.0000 1.0000 1.0000
	11a OMe OHe OH	9.153 9.153		WVL:254 nm
-50	5.0 7.5	10.0 12.5	15.0 17.5 20.0	22.5 25.0

No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
-	9.15	n.a.	359.864	74.678	49.92	n.a.	BMB*
2	10.19	n.a.	326.938	74.929	50.08	n.a.	BMB*
Total:			686.802	149.607	100.00	0.000	

22.5

10.0 12.5 Retention Time [min]

7.5

2.5





1 ChiralS	ummer3 IC 65 35		
Sample Name:	ChiralSummer3 IC 65 35	Injection Volume:	20.0
Vial Number:	2	Channel:	
Sample Type:	unknown	Wavelength:	254
Control Program:	alcohol 65_35	Bandwidth:	n.a.
Quantif. Method:	default	Dilution Factor:	1.0000
Recording Time:	12/1/2010 14:16	Sample Weight:	1.0000
Run Time (min):	21.55	Sample Amount:	1.0000



 				_	_
	Type		BMB*	BMB*	
	Amount		n.a.	n.a.	0.000
	Rel.Area	%	<u> 99.65</u>	0.35	100.00
	Area	mAU <sup>*</sup> min	28.446	0.100	28.545
	Height	mAU	148.492	0.570	149.061
	eak Name				
	Pe		n.a.	n.a.	
	Ret.Time	min	9.09	10.11	
	No.		-	2	Fotal:

default/Integration

































# Sequence: Cis Acid IC 65 35 2 Operator:Chemistry Timebase:NP\_HPLC

Page 1-1 12:52 PM

2/4/2011

UV\_VIS\_1 1.0000 1.0000 1.0000 20.0 210 n.a. Injection Volume: Sample Amount: Sample Weight: Dilution Factor: Wavelength: Bandwidth: Channel: Cis Acid IC 65 35 2 65 35 2 2 2/4/2011 12:20 35 35 **Cis Acid IC** alcohol 65\_ unknown 65 default 30.07 **Cis Acid IC** 2 Control Program: Quantif. Method: Recording Time: Run Time (min): Sample Name: Sample Type: Vial Number: 400-1mAU 

![](_page_21_Figure_2.jpeg)

[UAm] sonsdroadA

No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
1	13.02	n.a.	283.761	529.741	82.64	n.a.	BMb*
2	20.93	n.a.	38.272	111.280	17.36	n.a.	bMB*
Total:			322.033	641.021	100.00	0.000	

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### Sequence: Cis Acid IC 65 35 3 Operator:Chemistry Timebase:NP\_HPLC

Operator:Chemistry	/ Timebase:NP_HPLC Sequ	ence:Cis Acid IC 65 35 3	2/4/2	Page 1-1 011 1:29 PM
1 Cis Aci	d IC 65 35 3			
Sample Name: Vial Number: Sample Type: Control Program: Quantif. Method: Recording Time: Run Time (min):	Cis Acid IC 65 35 3 2 unknown alcohol 65_35 default 2/4/2011 12:55 31.00	Injection Volume: Channel: Wavelength: Bandwidth: Dilution Factor: Sample Weight: Sample Amount:	20.0 UV_VIS_1 210 n.a. 1.0000 1.0000 1.0000	
400 350	ö	s Acid IC 65 35 3	WUL:210 nm	
(UAm) sonschozdA	12.927	OMe CH <sub>3</sub> (+)-17 OMe 9.e.=98%		

-100	-							min
	10.0 12.		14.0 16.0	18.0 Retention Ti	20.0 me [min]	22.0	24.0 26.0	28.0
No.	Ret.Time		Peak Name	Height	Area	Rel.Area	Amount	Type
	min			mAU	mAU*min	%		
-	12.93	n.a.		292.266	552.464	99.61	n.a.	BMb*
2	21.46	n.a.		0.822	2.186	0.39	n.a.	bMB*
Total:				293.088	554.650	100.00	0.000	

Chromeleon (c) Dionex 1996-2006 Version 6.80 SR5 Build 2413 (137116)

![](_page_23_Figure_1.jpeg)

![](_page_24_Figure_1.jpeg)

![](_page_25_Figure_1.jpeg)

![](_page_26_Figure_1.jpeg)

![](_page_27_Figure_1.jpeg)

![](_page_28_Figure_1.jpeg)

![](_page_29_Figure_1.jpeg)

![](_page_30_Figure_1.jpeg)

![](_page_31_Figure_0.jpeg)

![](_page_32_Figure_1.jpeg)

![](_page_33_Figure_1.jpeg)

![](_page_34_Figure_1.jpeg)

![](_page_35_Figure_1.jpeg)

![](_page_36_Figure_1.jpeg)

![](_page_37_Figure_1.jpeg)

![](_page_38_Figure_1.jpeg)

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![](_page_39_Figure_1.jpeg)

Sequence:Deoxydihydrokalafungin IC 90 10 THF rac 5 Page 1-1 3/31/2011 12:57 PM Operator:Chemistry Timebase:NP\_HPLC

1 Deoxyd	ihydrokalafungin IC 90 10 TH	F rac 5	
Sample Name: Vial Number: Sample Type: Control Program: Quantif. Method: Recording Time: Run Time (min):	Deoxydihydrokalafungin IC 90 10 THF r 2 unknown alcohol 65_35 default 3/31/2011 11:01 112.54	ac £ Injection Volume: Channel: Wavelength: Bandwidth: Dilution Factor: Sample Amount: Sample Amount:	20.0 UV_VIS_2 254 n.a. 1.0000 1.0000 1.0000
100- 120 Deoxydihydrokala 60- 60- 20- 20- 20- 20- 5.	Iungin IC 90 10 THF rac 5 #1 [modified by Chemistry] $\begin{array}{c} & & \\ & &$	2 - 76.953 3 CO <sub>2</sub> H	UV_VIS_2 WVL:254 nm
- -			

No.	Ret.Time	а.	eak Name	Height	Area	Rel.Area	Amount	Type
	min			mAU	mAU*min	%		
L	72.25	n.a.		20.470	56.335	12.00	n.a.	BM *
2	76.95	n.a.		109.956	413.018	88.00	n.a.	MB*
Total:				130.426	469.353	100.00	0.000	

113 113

100

-6

-8

-2

-8

-20

-9

-8

2-2

-9-

-20+

![](_page_40_Figure_5.jpeg)

Sequence:Deoxydihydrokalafungin IC 90 10 THF rac chiral late8age 1-1 3/31/2011 5:37 PM Operator:Chemistry Timebase:NP\_HPLC

1 Deoxydi	ihydrokalafungin IC 90 10 THF rac c	chiral latest	
sample Name:	Deoxydihydrokalafungin IC 90 10 THF rac c Inject	tion Volume:	20.0
fial Number:	2 Char	nnel:	
sample Type:	unknown Wave	elength:	254
Control Program:	alcohol 65_35 Band	dwidth:	n.a.
Quantif. Method:	default Diluti	ion Factor:	1.0000
Recording Time:	3/31/2011 14:35 Sam	ple Weight:	1.0000
tun Time (min):	89.28 Sam	ple Amount:	1.0000

![](_page_41_Figure_2.jpeg)

No.	Ret.Time	Peak Name	Height	Area	Rel.Area	Amount	Type
	min		mAU	mAU*min	%		
-	69.67	n.a.	5.266	8.214	0.55	n.a.	BMb*
2	72.83	n.a.	426.188	1478.830	99.45	n.a.	bMB*
Total:			431.454	1487.044	100.00	0.000	