Appendix 3

X-Ray Crystallography Reports Relevant to Chapter 3: Enantioselective Total Synthesis of (+)-Nocardioazines A and B[†]

[†] The work disclosed in this appendix for the X-ray crystallographic analysis of **277** completed entirely by Larry Henling and Dr. Michael Day in the Caltech X-ray crystallography lab.

Figure A3.1. *Macrocyclic alkene* ***277****. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 997790.*

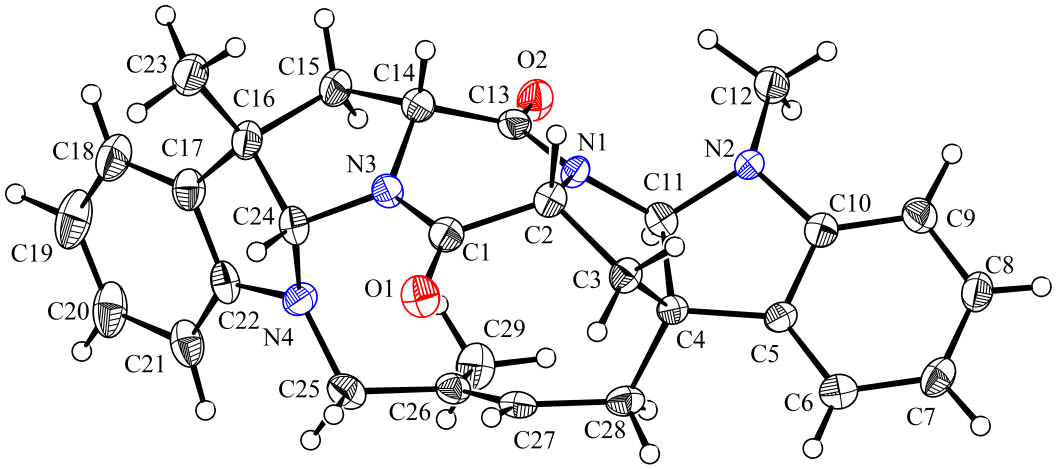

Table A3.1. *Crystal data and structure refinement for macrocyclic alkene* ***277*** *(CCDC 997790).*

Empirical formula	$C_{29}\ H_{30}\ N_4\ O_2$
Formula weight	466.57
Crystallization solvent	DCM/Pentane
Crystal shape	blade
Crystal color	colourless
Crystal size	0.03 x 0.2 x 0.36 mm

Data Collection

Preliminary photograph(s)	rotation	
Type of diffractometer	Bruker APEX-II CCD	
Wavelength	0.71073 Å MoK	
Data collection temperature	100.15 K	
Theta range for 5293 reflections used in lattice determination	2.40 to 20.69°	
Unit cell dimensions	a = 8.2481(3) Å b = 12.7097(5) Å c = 22.8106(8) Å	a= 90° b= 90° g = 90°
Volume	2391.26(15) $Å^3$	
Z	4	
Crystal system	orthorhombic	
Space group	P 21 21 21 (# 19)	
Density (calculated)	1.296 g/cm^3	
F(000)	992	
Theta range for data collection	2.4 to 29.4°	
Completeness to theta = 25.000°	99.9%	
Index ranges	-11 £ h £ 10, -16 £ k £ 16, -30 £ l £ 29	
Data collection scan type	and scans	
Reflections collected	42025	
Independent reflections	5687 [R_{int}= 0.1002]	
Reflections > 2s(I)	3486	
Average s(I)/(net I)	0.1114	
Absorption coefficient	0.08 mm^{-1}	
Absorption correction	None	
Max. and min. transmission	1.0000 and 0.8355	

Table A3.1 (cont.)

Structure solution and Refinement

Primary solution method	dual
Secondary solution method	?
Hydrogen placement	?
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5687 / 0 / 437
Treatment of hydrogen atoms	refall
Goodness-of-fit on F^2	1.13
Final R indices [I>2s(I), 3486 reflections]	R1 = 0.0522, *w*R2 = 0.0632
R indices (all data)	R1 = 0.1217, *w*R2 = 0.0725
Type of weighting scheme used	calc
Weighting scheme used	
Max shift/error	0.000
Average shift/error	0.000
Absolute structure parameter	0.6(8)
Extinction coefficient	0.0112(8)
Largest diff. peak and hole	0.21 and -0.23 e·$Å^{-3}$

Programs Used

Cell refinement	?
Data collection	?
Data reduction	SAINT v8.27A (Bruker, 2012)
Structure solution	
Structure refinement	
Graphics	

Table A3.2. *Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for macrocyclic alkene* ***277*** *(CCDC 997790). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.*

	x	y	z	U_{eq}
O(1)	7309(2)	5733(2)	8607(1)	29(1)
O(2)	12123(2)	5018(2)	10081(1)	30(1)
N(1)	9738(3)	5862(2)	9901(1)	20(1)
N(3)	9952(3)	5296(2)	8768(1)	21(1)
N(2)	9195(3)	6507(2)	10884(1)	21(1)
N(4)	9753(3)	3417(2)	8592(1)	24(1)
C(26)	7924(3)	3412(2)	9447(1)	22(1)
C(13)	11173(4)	5437(2)	9738(1)	22(1)
C(6)	4946(4)	6119(2)	11133(1)	25(1)
C(10)	7760(3)	6589(2)	11204(1)	21(1)
C(11)	8986(3)	5648(2)	10462(1)	20(1)
C(5)	6497(3)	6100(2)	10906(1)	20(1)
C(22)	10876(4)	2697(2)	8370(1)	24(1)
C(24)	10142(3)	4459(2)	8346(1)	24(1)
C(1)	8540(4)	5774(2)	8907(1)	24(1)
C(27)	6821(3)	4127(2)	9606(1)	24(1)
C(8)	5939(4)	7100(3)	11959(2)	28(1)
C(9)	7532(4)	7080(2)	11738(1)	26(1)
C(16)	11970(3)	4392(2)	8235(1)	26(1)
C(28)	6452(4)	4540(2)	10204(1)	24(1)
C(25)	8138(4)	3156(3)	8800(1)	28(1)
C(4)	7146(3)	5638(2)	10344(1)	18(1)
C(3)	7000(4)	6423(2)	9821(1)	22(1)
C(17)	12209(4)	3228(2)	8137(1)	27(1)
C(2)	8613(3)	6375(2)	9487(1)	21(1)
C(14)	11466(3)	5529(3)	9087(1)	24(1)
C(7)	4685(4)	6635(2)	11664(1)	27(1)
C(18)	13463(4)	2675(3)	7887(1)	36(1)
C(12)	10752(4)	6581(3)	11188(2)	28(1)
C(29)	9013(4)	2825(3)	9858(2)	33(1)
C(15)	12677(4)	4735(3)	8837(2)	29(1)
C(21)	10792(4)	1611(3)	8356(1)	31(1)
C(23)	12541(5)	5104(3)	7738(2)	34(1)
C(20)	12072(5)	1067(3)	8094(1)	39(1)
C(19)	13375(5)	1583(3)	7862(2)	45(1)

Table A3.3. *Bond lengths [Å] and angles [°] for macrocyclic alkene* ***277*** *(CCDC 997790).*

O(1)-C(1)	1.227(3)
O(2)-C(13)	1.228(3)
N(1)-C(13)	1.353(3)
N(1)-C(11)	1.447(3)
N(1)-C(2)	1.477(3)
N(3)-C(24)	1.445(3)
N(3)-C(1)	1.351(3)
N(3)-C(14)	1.475(4)
N(2)-C(10)	1.395(3)
N(2)-C(11)	1.466(3)
N(2)-C(12)	1.462(4)
N(4)-C(22)	1.397(3)
N(4)-C(24)	1.473(3)
N(4)-C(25)	1.453(4)
C(26)-C(27)	1.336(4)
C(26)-C(25)	1.521(4)
C(26)-C(29)	1.498(4)
C(13)-C(14)	1.510(4)
C(6)-H(6)	0.92(2)
C(6)-C(5)	1.380(4)
C(6)-C(7)	1.396(4)
C(10)-C(5)	1.390(4)
C(10)-C(9)	1.381(4)
C(11)-H(11)	1.04(2)
C(11)-C(4)	1.541(4)
C(5)-C(4)	1.509(4)
C(22)-C(17)	1.396(4)
C(22)-C(21)	1.383(4)
C(24)-H(24)	1.03(3)
C(24)-C(16)	1.531(4)
C(1)-C(2)	1.529(4)
C(27)-H(27)	1.04(3)
C(27)-C(28)	1.493(4)
C(8)-H(8)	0.90(3)
C(8)-C(9)	1.407(4)
C(8)-C(7)	1.367(4)
C(9)-H(9)	1.01(3)
C(16)-C(17)	1.509(4)
C(16)-C(15)	1.554(4)
C(16)-C(23)	1.524(4)
C(28)-H(28A)	1.00(3)
C(28)-H(28B)	0.94(2)
C(28)-C(4)	1.541(4)
C(25)-H(25A)	1.05(3)
C(25)-H(25B)	1.02(3)
C(4)-C(3)	1.560(4)
C(3)-H(3A)	1.03(3)
C(3)-H(3B)	0.98(3)
C(3)-C(2)	1.534(4)

C(17)-C(18)	1.374(4)
C(2)-H(2)	1.10(3)
C(14)-H(14)	0.99(2)
C(14)-C(15)	1.530(4)
C(7)-H(7)	0.95(3)
C(18)-H(18)	0.94(3)
C(18)-C(19)	1.391(5)
C(12)-H(12A)	0.98(4)
C(12)-H(12B)	1.10(3)
C(12)-H(12C)	1.00(3)
C(29)-H(29A)	1.00(3)
C(29)-H(29B)	1.04(3)
C(29)-H(29C)	1.01(3)
C(15)-H(15A)	1.05(3)
C(15)-H(15B)	0.97(3)
C(21)-H(21)	0.98(3)
C(21)-C(20)	1.397(5)
C(23)-H(23A)	1.05(3)
C(23)-H(23B)	1.03(3)
C(23)-H(23C)	1.05(3)
C(20)-H(20)	0.97(3)
C(20)-C(19)	1.366(5)
C(19)-H(19)	1.10(3)

C(13)-N(1)-C(11)	122.9(2)
C(13)-N(1)-C(2)	123.4(2)
C(11)-N(1)-C(2)	112.3(2)
C(24)-N(3)-C(14)	112.6(2)
C(1)-N(3)-C(24)	125.5(2)
C(1)-N(3)-C(14)	121.6(2)
C(10)-N(2)-C(11)	107.5(2)
C(10)-N(2)-C(12)	119.6(2)
C(12)-N(2)-C(11)	117.6(3)
C(22)-N(4)-C(24)	107.9(2)
C(22)-N(4)-C(25)	125.2(2)
C(25)-N(4)-C(24)	122.0(2)
C(27)-C(26)-C(25)	119.2(3)
C(27)-C(26)-C(29)	125.2(3)
C(29)-C(26)-C(25)	115.6(3)
O(2)-C(13)-N(1)	123.8(3)
O(2)-C(13)-C(14)	123.8(3)
N(1)-C(13)-C(14)	112.3(2)
C(5)-C(6)-H(6)	121.4(15)
C(5)-C(6)-C(7)	118.5(3)
C(7)-C(6)-H(6)	120.0(15)
C(5)-C(10)-N(2)	110.2(2)
C(9)-C(10)-N(2)	127.6(3)
C(9)-C(10)-C(5)	122.1(3)
N(1)-C(11)-N(2)	113.0(2)
N(1)-C(11)-H(11)	107.5(13)
N(1)-C(11)-C(4)	105.6(2)
N(2)-C(11)-H(11)	113.3(13)
N(2)-C(11)-C(4)	103.7(2)

C(4)-C(11)-H(11)	113.4(13)
C(6)-C(5)-C(10)	120.2(3)
C(6)-C(5)-C(4)	130.8(3)
C(10)-C(5)-C(4)	108.9(2)
C(17)-C(22)-N(4)	110.0(3)
C(21)-C(22)-N(4)	129.0(3)
C(21)-C(22)-C(17)	120.9(3)
N(3)-C(24)-N(4)	112.6(2)
N(3)-C(24)-H(24)	110.4(15)
N(3)-C(24)-C(16)	105.0(2)
N(4)-C(24)-H(24)	110.2(15)
N(4)-C(24)-C(16)	103.1(2)
C(16)-C(24)-H(24)	115.3(14)
O(1)-C(1)-N(3)	124.3(3)
O(1)-C(1)-C(2)	122.5(3)
N(3)-C(1)-C(2)	113.2(2)
C(26)-C(27)-H(27)	116.2(15)
C(26)-C(27)-C(28)	128.8(3)
C(28)-C(27)-H(27)	114.9(15)
C(9)-C(8)-H(8)	118(2)
C(7)-C(8)-H(8)	120(2)
C(7)-C(8)-C(9)	121.6(3)
C(10)-C(9)-C(8)	116.7(3)
C(10)-C(9)-H(9)	124.6(15)
C(8)-C(9)-H(9)	118.7(15)
C(24)-C(16)-C(15)	102.0(2)
C(17)-C(16)-C(24)	102.0(2)
C(17)-C(16)-C(15)	110.9(3)
C(17)-C(16)-C(23)	115.6(3)
C(23)-C(16)-C(24)	113.2(3)
C(23)-C(16)-C(15)	111.9(3)
C(27)-C(28)-H(28A)	111.3(15)
C(27)-C(28)-H(28B)	107.9(14)
C(27)-C(28)-C(4)	115.5(2)
H(28A)-C(28)-H(28B)	105(2)
C(4)-C(28)-H(28A)	108.9(15)
C(4)-C(28)-H(28B)	107.4(14)
N(4)-C(25)-C(26)	112.0(2)
N(4)-C(25)-H(25A)	105.5(15)
N(4)-C(25)-H(25B)	110.0(15)
C(26)-C(25)-H(25A)	110.1(15)
C(26)-C(25)-H(25B)	113.2(15)
H(25A)-C(25)-H(25B)	106(2)
C(11)-C(4)-C(3)	101.8(2)
C(5)-C(4)-C(11)	101.3(2)
C(5)-C(4)-C(28)	113.3(2)
C(5)-C(4)-C(3)	112.0(2)
C(28)-C(4)-C(11)	114.2(2)
C(28)-C(4)-C(3)	113.1(2)
C(4)-C(3)-H(3A)	112.4(14)
C(4)-C(3)-H(3B)	109.9(16)
H(3A)-C(3)-H(3B)	105(2)
C(2)-C(3)-C(4)	106.7(2)

C(2)-C(3)-H(3A)	112.7(14)
C(2)-C(3)-H(3B)	109.9(16)
C(22)-C(17)-C(16)	108.4(2)
C(18)-C(17)-C(22)	120.2(3)
C(18)-C(17)-C(16)	131.4(3)
N(1)-C(2)-C(1)	111.0(2)
N(1)-C(2)-C(3)	104.2(2)
N(1)-C(2)-H(2)	107.6(12)
C(1)-C(2)-C(3)	114.5(2)
C(1)-C(2)-H(2)	107.6(12)
C(3)-C(2)-H(2)	111.8(12)
N(3)-C(14)-C(13)	109.5(2)
N(3)-C(14)-H(14)	109.1(13)
N(3)-C(14)-C(15)	103.7(2)
C(13)-C(14)-H(14)	108.5(13)
C(13)-C(14)-C(15)	114.9(3)
C(15)-C(14)-H(14)	110.9(13)
C(6)-C(7)-H(7)	121.6(16)
C(8)-C(7)-C(6)	120.8(3)
C(8)-C(7)-H(7)	117.6(16)
C(17)-C(18)-H(18)	119.5(17)
C(17)-C(18)-C(19)	119.2(3)
C(19)-C(18)-H(18)	121.3(17)
N(2)-C(12)-H(12A)	106(2)
N(2)-C(12)-H(12B)	109.3(16)
N(2)-C(12)-H(12C)	110.4(15)
H(12A)-C(12)-H(12B)	114(3)
H(12A)-C(12)-H(12C)	108(2)
H(12B)-C(12)-H(12C)	109(2)
C(26)-C(29)-H(29A)	112.3(18)
C(26)-C(29)-H(29B)	109.6(16)
C(26)-C(29)-H(29C)	107.2(18)
H(29A)-C(29)-H(29B)	110(3)
H(29A)-C(29)-H(29C)	113(3)
H(29B)-C(29)-H(29C)	104(2)
C(16)-C(15)-H(15A)	112.7(15)
C(16)-C(15)-H(15B)	110.2(17)
C(14)-C(15)-C(16)	105.7(2)
C(14)-C(15)-H(15A)	105.3(15)
C(14)-C(15)-H(15B)	107.0(17)
H(15A)-C(15)-H(15B)	115(2)
C(22)-C(21)-H(21)	127.2(16)
C(22)-C(21)-C(20)	117.7(3)
C(20)-C(21)-H(21)	114.9(16)
C(16)-C(23)-H(23A)	108.3(17)
C(16)-C(23)-H(23B)	109.8(17)
C(16)-C(23)-H(23C)	112.1(16)
H(23A)-C(23)-H(23B)	106(2)
H(23A)-C(23)-H(23C)	115(2)
H(23B)-C(23)-H(23C)	105(2)
C(21)-C(20)-H(20)	119.2(18)
C(19)-C(20)-C(21)	121.6(4)
C(19)-C(20)-H(20)	119.2(18)

C(18)-C(19)-H(19)	120.2(16)
C(20)-C(19)-C(18)	120.3(3)
C(20)-C(19)-H(19)	119.4(16)

Symmetry transformations used to generate equivalent atoms.

Table A3.4. *Anisotropic displacement parameters ($Å^2 x\ 10^4$) for for macrocyclic alkene* ***277*** *(CCDC 997790). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	299(12)	311(13)	263(12)	14(10)	-58(10)	52(10)
O(2)	204(11)	433(14)	277(12)	-44(11)	-10(10)	68(10)
N(1)	188(13)	226(14)	175(13)	3(11)	42(11)	-1(11)
N(3)	205(14)	224(15)	209(14)	-27(11)	-13(12)	16(12)
N(2)	171(14)	250(15)	209(13)	-43(12)	34(11)	-26(11)
N(4)	232(15)	191(14)	288(14)	-7(12)	66(11)	-5(12)
C(26)	220(16)	170(16)	266(16)	-8(14)	1(14)	-16(15)
C(13)	168(17)	233(18)	259(18)	-42(15)	2(14)	-13(14)
C(6)	229(19)	238(18)	283(19)	29(15)	-12(17)	11(15)
C(10)	249(17)	163(15)	218(16)	34(15)	12(15)	19(14)
C(11)	224(16)	187(18)	203(17)	0(15)	-36(14)	29(14)
C(5)	179(17)	186(18)	231(17)	13(13)	27(14)	-2(13)
C(22)	315(19)	251(19)	169(16)	-32(15)	-37(15)	77(16)
C(24)	285(18)	239(18)	200(17)	-45(15)	-3(15)	37(15)
C(1)	257(18)	196(18)	252(18)	13(15)	13(15)	7(15)
C(27)	185(17)	237(19)	282(19)	-3(15)	-24(15)	-66(14)
C(8)	320(20)	283(19)	236(19)	-29(16)	66(16)	16(17)
C(9)	297(19)	230(18)	254(18)	-18(15)	7(15)	-29(15)
C(16)	288(18)	266(18)	217(16)	-27(15)	52(14)	22(15)
C(28)	164(19)	239(19)	320(20)	8(16)	1(15)	-10(14)
C(25)	266(19)	230(20)	330(20)	-47(16)	-38(16)	-4(15)
C(4)	173(15)	180(16)	202(16)	3(13)	5(12)	-6(14)
C(3)	210(18)	194(18)	243(17)	0(15)	24(15)	47(15)
C(17)	331(19)	260(20)	208(17)	9(14)	9(15)	46(16)
C(2)	222(17)	203(19)	206(16)	32(14)	8(14)	36(13)
C(14)	221(17)	250(20)	253(18)	-28(16)	11(14)	-4(15)
C(7)	270(20)	252(18)	296(19)	20(16)	95(17)	53(15)
C(18)	390(20)	350(20)	330(20)	-13(18)	129(18)	69(19)
C(12)	222(19)	370(20)	246(18)	-38(19)	-22(16)	6(17)
C(29)	380(20)	290(20)	320(20)	18(19)	14(18)	99(19)
C(15)	223(19)	360(20)	278(19)	-79(17)	54(16)	11(16)
C(21)	480(20)	220(20)	229(18)	-13(16)	2(17)	52(19)
C(23)	400(30)	290(20)	320(20)	-24(17)	108(18)	-16(17)
C(20)	620(30)	260(20)	290(20)	5(17)	109(19)	140(20)
C(19)	530(30)	440(30)	380(20)	-10(20)	159(19)	230(20)

Table A3.5. *Hydrogen coordinates (x 10^3) and isotropic displacement parameters ($Å^2$x 10^3) for macrocyclic alkene* ***277*** *(CCDC 997790).*

	x	y	z	U_{iso}
H(6)	408(3)	584(2)	1093(1)	11(7)
H(11)	943(3)	493(2)	1061(1)	14(7)
H(24)	944(3)	460(2)	798(1)	31(8)
H(27)	618(3)	448(2)	927(1)	34(9)
H(8)	580(3)	733(2)	1233(1)	39(10)
H(9)	842(3)	743(2)	1197(1)	32(9)
H(28A)	681(3)	404(2)	1051(1)	25(8)
H(28B)	532(3)	458(2)	1024(1)	8(7)
H(25A)	801(3)	235(2)	873(1)	29(8)
H(25B)	729(3)	350(2)	854(1)	31(8)
H(3A)	601(3)	626(2)	956(1)	20(7)
H(3B)	682(3)	714(2)	997(1)	31(8)
H(2)	909(3)	716(2)	939(1)	20(7)
H(14)	1181(3)	626(2)	900(1)	6(7)
H(7)	364(3)	667(2)	1184(1)	22(8)
H(18)	1437(3)	304(2)	774(1)	26(9)
H(12A)	1073(4)	724(3)	1141(2)	73(13)
H(12B)	1174(4)	654(2)	1086(1)	56(10)
H(12C)	1087(3)	599(2)	1148(1)	17(7)
H(29A)	891(4)	308(3)	1027(2)	55(11)
H(29B)	1021(4)	289(2)	972(1)	48(10)
H(29C)	876(3)	205(3)	981(1)	50(10)
H(15A)	1271(3)	412(2)	914(1)	30(8)
H(15B)	1370(4)	511(2)	878(1)	37(9)
H(21)	990(3)	117(2)	849(1)	31(9)
H(23A)	1381(4)	506(2)	772(1)	39(9)
H(23B)	1227(4)	587(3)	784(1)	50(10)
H(23C)	1192(3)	495(2)	734(1)	42(9)
H(20)	1204(3)	31(2)	808(1)	40(10)
H(19)	1440(4)	112(2)	768(1)	50(10)

Table A3.6*. Hydrogen bonds for macrocyclic alkene* ***277*** *[Å and °]. (CCDC 997790).*

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(12)-H(12B)...O(2)	1.10(3)	2.65(3)	3.406(4)	125(2)

Symmetry transformations used to generate equivalent atoms.