An Easy Approach to Optically Active α -Amino Phosphonic Acid Derivatives by Chiral Zn(II) Catalyzed Enantioselective Amination of Phosphonates

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Supporting Information

Contents:

- Experimental Section
- Representative Results from the Screening of Different Catalysts, Solvents and Additives for the Amination Reaction
- NMR Spectra and HPLC Chromatograms for the Products
- Absolute Configuration and Proposed Intermediate

Experimental Section.

General Methods. ^1H and ^{13}C NMR spectra were recorded on a Varian AS 400 spectrometer, running at 400 MHz and 100 MHz, respectively, in CDCl_3 as the solvent. Chemical shifts were reported in the δ scale relative to residual CHCl_3 (7.26 ppm) for ^1H NMR and to the central line of CDCl_3 (77.0 ppm) for ^{13}C NMR. ^1H and ^{13}C NMR spectra are reported and not described due to the presence of the signals of several rotameric isomers. ^1H NMR spectra were recorded also at 60 °C. ^{13}C NMR spectra were acquired on a broad band decoupled mode. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionisation techniques. Flash column chromatography (FC) was carried out using the Merck silica gel 60 (230-400 mesh). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AD or Daicel Chiralcel OJ/OD columns). Racemic samples were obtained using an equimolar mixture of (*S*)-(-)-2,2'-isopropylidene-bis(4-phenyl-2-oxazoline) and (*R*)-(+)-2,2'-isopropylidene-bis(4-phenyl-2-oxazoline) as a ligand.

Materials. CH_2Cl_2 was distilled from CaH_2 prior to use. All commercially available reagents were used as received. β -Ketophosphonates **1a-d**,¹ **1e**² and **1g,h**³ were prepared according to literature procedures.

General Procedure for the Catalytic Asymmetric Amination of β -Ketophosphonates 1a-h: In a flame dried Schlenk tube equipped with a magnetic stirring bar, $\text{Zn}(\text{OTf})_2$ (7.3 mg, 0.02 mmol) and (*S*)-(-)-2,2'-isopropylidene-bis(4-phenyl-2-oxazoline) (7.4 mg, 0.022 mmol) were added. The solid mixture was stirred under vacuum for 1 h, and then the Schlenk tube was filled with N_2 . Dry CH_2Cl_2 (2 mL) was added, and the resulting colourless solution was stirred for 1 h. β -Ketophosphonates **1a-h** (0.2 mmol) were then added, followed by azodicarboxylates **2a** or **2b** (0.3 mmol). After 48 h stirring at room temperature, the products **3a-i** were isolated by FC on silica gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixtures).

¹ Truel, I.; Mohamed-Hachi, A.; Aboud-Jaudet, E.; Collignon, N. *Synth. Commun.* **1997**, 27, 1165.

² Clark, R. D.; Kozar, L. G.; Heathcock, C. H. *Synthesis* **1975**, 635.

³ Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, 52, 4185.

***N,N'*-Bis(ethoxycarbonyl)-1-hydrazino-1-methyl-2-oxo-2-phenylethyl phosphonic acid diethyl ester (3a).** Following the general procedure, compound **3a** was obtained as a colourless oil in 75%

yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min $\tau_{\text{major}} = 16.1$ min; $\tau_{\text{minor}} = 9.5$ min); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{19}\text{H}_{29}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 467.1554, found: 467.1554; $[\alpha]_{\text{D}}^{\text{rt}} = -103$ ($c = 0.72$ in CHCl_3), 92% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-1-methyl-2-oxo-2-phenylethyl phosphonic acid diethyl ester (3b).** Following the general procedure, compound **3b** was obtained as a colourless oil in 85% yield.

The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 85/15, flow rate 1.0 mL/min $\tau_{\text{major}} = 21.3$ min; $\tau_{\text{minor}} = 10.9$ min); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{29}\text{H}_{33}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 591.1867, found: 591.1899; $[\alpha]_{\text{D}}^{\text{rt}} = -82$ ($c = 0.44$ in CHCl_3), 92% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-1-methyl-2-naphthalen-2-yl-2-oxo-ethyl phosphonic acid diethyl ester (3c).** Following the general procedure, compound **3c** was obtained as a white solid in

93% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 85/15, flow rate 1.0 mL/min $\tau_{\text{major}} = 33.1$ min; $\tau_{\text{minor}} = 13.2$ min); m.p. = 39-42 °C; ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{33}\text{H}_{35}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 641.2023, found: 641.2321; $[\alpha]_{\text{D}}^{\text{rt}} = -75$ ($c = 0.36$ in CHCl_3), 92% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-1-methyl-2-oxo-3-phenyl-propyl phosphonic acid diethyl ester (3d).** Following the general procedure, compound **3d** was obtained as a colourless oil in

60% yield. The ee of the product was determined by HPLC using a Daicel Chiralcel OD column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min $\tau_{\text{major}} = 12.8$ min; $\tau_{\text{minor}} = 18.0$

min); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{30}\text{H}_{35}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 605.2023, found: 605.2019; $[\alpha]_{\text{D}}^{\text{rt}} = -25$ ($c = 0.50$ in CHCl_3), 95% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-methyl-2-oxo-ethyl phosphonic acid diethyl ester (3e).** Following the general procedure, compound **3e** was obtained as a white solid in 75% yield. The ee of the product was determined on the corresponding oxazolidinone (*vide infra*); m.p. = 85-88 °C; ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 529.1710, found: 529.1738; $[\alpha]_{\text{D}}^{\text{rt}} = -29$ ($c = 0.37$ in CHCl_3), 85% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-2-oxo-2-phenylethyl-1-prop-2-en phosphonic acid diethyl ester (3f).** Following the general procedure and prolonging the reaction time to 96 h compound **3f** was obtained as a colourless oil in 85% yield. The ee of the product was determined on the corresponding oxazolidinone (*vide infra*); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{31}\text{H}_{35}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 617.2023, found: 617.2020; $[\alpha]_{\text{D}}^{\text{rt}} = -56$ ($c = 0.35$ in CHCl_3), 97% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-methyl-2-oxo-2-phenyl-ethyl phosphonic acid dimethyl ester (3g).** Following the general procedure, compound **3g** was obtained as a white solid in 97% yield, after chromatography on silica gel. The ee of the product was determined by HPLC using a Daicel Chiralcel OJ column (n -hexane/ i -PrOH = 85/15, flow rate 1.0 mL/min $\tau_{\text{major}} = 27.2$ min; $\tau_{\text{minor}} = 13.8$ min); m.p. = 38-40 °C; ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{29}\text{H}_{33}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 591.1867, found: 591.1899; $[\alpha]_{\text{D}}^{\text{rt}} = -106$ ($c = 0.45$ in CHCl_3), 95% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-2-oxo-cyclopentyl phosphonic acid diethyl ester (3h).** Following the general procedure, compound **3h** was obtained as colourless oil in 98% yield. The ee of the product was determined by HPLC using a Daicel Chiralcel OD column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min $\tau_{\text{major}} = 8.9$ min; $\tau_{\text{minor}} = 20.6$ min); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{25}\text{H}_{31}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 541.1710, found: 541.1712; $[\alpha]_{\text{D}}^{\text{rt}} = +41$ ($c = 0.22$ in CHCl_3), 95% ee.

***N,N'*-Bis(benzyloxycarbonyl)-1-hydrazino-2-oxo-cyclohexyl phosphonic acid diethyl ester (3i).** Following the general procedure, compound **3i** was obtained as colourless oil in 98% yield. The ee of the product was determined by HPLC using a Daicel Chiralcel OD column (*n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min $\tau_{\text{major}} = 28.4$ min; $\tau_{\text{minor}} = 35.7$ min); ^1H NMR (CDCl_3) see below; ^{13}C NMR (CDCl_3) see below; HRMS $\text{C}_{26}\text{H}_{33}\text{N}_2\text{O}_8\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 555.1867, found: 555.1887; $[\alpha]_{\text{D}}^{\text{rt}} = -27$ ($c = 0.61$ in CHCl_3), 94% ee.

(3-Benzyloxycarbonylamino-4-methyl-2-oxo-5-phenyl-oxazolidin-4-yl)-phosphonic acid diethyl ester (4). Compound **3b** (461 mg, 0.33 mmol) was dissolved in dry Et_2O (3 mL) and the resulting solution cooled to -24 °C. LiBH_4 (36 mg, 1.65 mmol) was added in small portions and the mixture was stirred for 3 h at -24 °C. The reaction mixture was then warmed to room temperature and 5 mL of H_2O were added. The aqueous suspension was extracted three times with EtOAc. The organic phase was washed with brine, dried on Na_2SO_4 , filtered and concentrated *in vacuo*. The crude product was purified by FC on silica gel ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ mixtures) to give compound **4** (252 mg) as a colorless oil in 67% yield and as a single diastereoisomer. ^1H NMR (CDCl_3) see below; HRMS $\text{C}_{22}\text{H}_{27}\text{N}_2\text{O}_7\text{P}$ $[\text{M}+\text{Na}]^+$; calculated: 485.1454 found: 485.1455.

(4-Allyl-3-benzyloxycarbonylamino-2-oxo-5-phenyl-oxazolidin-4-yl)-phosphonic acid diethyl ester. Following the procedure used for compound **4**, the title compound was obtained in 29% yield as pale yellow

oil and as a single diastereoisomer. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min $\tau_{\text{major}} = 24.2$ min; $\tau_{\text{minor}} = 31.5$ min). ^1H NMR (CDCl_3) see below; HRMS $\text{C}_{24}\text{H}_{29}\text{N}_2\text{O}_7\text{P}$ $[\text{M}+\text{Na}]^+$ calculated: 511.1610, found: 511.1614, 97% ee.

(4-Methyl-2-oxo-5-phenyl-oxazolidin-4-yl)-phosphonic acid diethyl

ester. (5). To a solution of compound **3b** (69 mg, mmol) in MeOH (4 mL)

10% Pd/C (25 mg) was added. The flask was filled with H_2 from a balloon and the mixture was stirred for 2 h at room temperature. The reaction mixture was filtered through a short pad of Celite and the pad washed with MeOH. After removal of the solvent *in vacuo*, the oily residue was dissolved in AcOH (6 mL) and 1M HCl (2 mL) was added, followed by NaNO_2 (40 mg) dissolved in H_2O (1 mL). The mixture was refluxed at $110\text{ }^\circ\text{C}$ for 90 min, then cooled to room temperature. 30 mL sat. NaHCO_3 and solid Na_2CO_3 were then added to adjust the pH value to 7. The water phase was extracted three times by EtOAc and the combined organic phases were washed three times by sat. NaHCO_3 , H_2O and brine subsequently and dried with Na_2SO_4 . After filtration and removal of the solvents, compound **5** (30 mg) was obtained as a pale yellow oil in 60% yield. The ee of the product was determined by HPLC using a Daicel Chiralpak AD column (*n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min $\tau_{\text{minor}} = 20.8$ min; $\tau_{\text{major}} = 22.9$ min). ^1H NMR (CDCl_3) δ 7.45-7.32 (m, 5H), 6.01 (br s, 1H), 5.38 (d, $J = 28.8$ Hz, 1H), 4.02-3.65 (m, 4H), 1.74 (d, $J = 13.2$ Hz, 3H), 1.20 (t, $J = 7.2$ Hz, 3H), 1.04 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR δ 157.4, 133.0, 128.9, 128.0, 126.8, 86.1, 63.8, 63.7, 62.6, 62.5, 22.1, 22.0, 16.4, 16.0; HRMS $\text{C}_{14}\text{H}_{20}\text{NO}_5\text{P}$ $[\text{M}+\text{Na}]^+$; calculated: 336.0977 found: 336.0978; $[\alpha]_{\text{D}}^{25} = -34$ ($c = 2.3$ in CHCl_3), 92% ee.

Some representative Results from the Screening of Different Catalysts and Solvents and Additives for the Catalytic Amination Reaction of 1a with 2a and 2b.

Entry	Catalyst	Azodicarboxylate	Solvent	Additive	Conversion ^a	Ee ^b
1		2a	CH ₂ Cl ₂		<10	/
2		2a	Et ₂ O		<10	/
3		2a	CH ₂ Cl ₂		50	20
4		2a	Et ₂ O		60	0
5		2a	THF		20	12
6		2a	CH ₂ Cl ₂		57	19
7		2a	CH ₂ Cl ₂		52	0
8		2a	CH ₂ Cl ₂	4 Å MS	>90	29
9		2a	CH ₂ Cl ₂	4 Å MS	80	91
10		2a	Toluene		80	79

11	4c	2a	THF		85	86
12	4c	2a	CHCl ₃		66	85
13	4c	2b	CH ₂ Cl ₂	Et ₃ N(10 mol%)	80 ^c	92

^a Determined by ¹H NMR spectroscopy. ^b Determined by chiral stationary phase HPLC. ^c 48h reaction.

rac-3a

Report Method: Default Report Printed: 18:23:21 05 July 2004 Page: 3/2

(-)-3a

Report Method: Default Report Printed: 6:09:23 PM 7/5/2004 Page: 2 of 2

Report Method: Default Report Printed: 05 July 2004

Report Method: Default Report Printed: 6:09:23 PM 7/5/2004

Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training19

SAMPLE INFORMATION

Sample Name: luca89_AD30_85-15
 Kube: 10
 Flow: 10.00 µl
 Injection Volume: 10.00 µl
 Run Time: 50.0 Minutes
 Solvent: 50:50
 Date Acquired: 19 May 2004 16:34:16
 Date Processed: 19 May 2004 17:04:31
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

rac-3b

Report Method: Default Report

Printed 16:29:22 26 June 2004

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Reported by User: Luca Bernardi (Luca)

Project Name: Training19

Individual Sample Report

Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training19

SAMPLE INFORMATION

Sample Name: luca100_AD30_85-15
 Kube: 10
 Flow: 10.00 µl
 Injection Volume: 10.00 µl
 Run Time: 70.0 Minutes
 Solvent: 50:50
 Date Acquired: 25 May 2004 12:04:00
 Date Processed: 25 May 2004 12:41:11
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

(-)-3b

Report Method: Default Report

Printed 16:31:29 26 June 2004

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Reported by User: Luca Bernardi (Luca)

Project Name: Training19

Individual Sample Report

Report Method: Default Report

Printed 16:29:22

26 June 2004

Report Method: Default Report

Printed 16:31:29

26 June 2004

3c

¹³C NMR (100 MHz, CDCl₃, r.t.)

ppm (f1)

M

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

SAMPLE INFORMATION

Sample Name: lucad1_AD30_85:15
Sample Type: Unknown
Injection #: 24
Injection Volume: 100.00 µl
Run Time: 100.0 Minutes
Sample Set Name: group

Acquired By: group
Date Acquired: 6/26/2004 4:50:51 PM
Acq. Method Set: 85_15_10
Date Processed: 6/26/2004 5:43:09 PM
Processing Method: LC MS
Channel Name: WtWn Ch1
Proc. Cont. Descr.: 85_15_10

RET	Area	% Area	Height
1	13.456	54074458	50.61
2	33.932	62816825	49.39

rac-3c

Report Method: Default Report

Printed 5:43:29 PM 6/26/2004

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M

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

SAMPLE INFORMATION

Sample Name: lucad107_AD30_85:15
Sample Type: Unknown
Injection #: 8
Injection Volume: 100.00 µl
Run Time: 100.0 Minutes
Sample Set Name: group

Acquired By: group
Date Acquired: 6/11/2004 4:52:26 PM
Acq. Method Set: 85_15_10
Date Processed: 6/11/2004 5:37:30 PM
Processing Method: LC MS
Channel Name: WtWn Ch1
Proc. Cont. Descr.: 85_15_10

RET	Area	% Area	Height
1	13.194	2094960	3.96
2	33.958	60776375	98.04

(-)-3c

Report Method: Default Report

Printed 5:47:57 PM 6/26/2004

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M

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

Spectrum Index Plot

Report Method: Default Report

Printed 5:43:29 PM 6/26/2004

M

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

Spectrum Index Plot

Report Method: Default Report

Printed 5:47:57 PM 6/26/2004

3d

^{13}C NMR (100 MHz, CDCl_3 , r.t.)

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

SAMPLE INFORMATION

Sample Name: lucad7_CD18_90:10
 Sample Type: Unknown
 Vial: 1
 Injection #: 6
 Injection Volume: 100.00 μl
 Run Time: 100.0 Minutes
 Sample Set Name:
 Acquired By: group
 Date Acquired: 6/20/2004 5:53:02 PM
 ACS Method Set: 90_10_10
 Date Processed: 6/20/2004 6:37:49 PM
 Processing Method: LQ PQ
 Channel Name: Wvln Ch1
 Phys. Chnl. Descr.: ERM 210.4 nm

rac-3d

Report Method: Default Report

Printed 6:20:32 PM 6/27/2004

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Individual Sample Report

Reported by User: group (group)

Project Name: Luca

SAMPLE INFORMATION

Sample Name: lucad8bis_CD18_90:10
 Sample Type: Unknown
 Vial: 1
 Injection #: 25
 Injection Volume: 100.00 μl
 Run Time: 100.0 Minutes
 Sample Set Name:
 Acquired By: group
 Date Acquired: 6/26/2004 7:13:20 PM
 ACS Method Set: 90_10_10
 Date Processed: 6/26/2004 7:47:33 PM
 Processing Method: LQ PQ
 Channel Name: Wvln Ch1
 Phys. Chnl. Descr.: ERM 210.4 nm

(-)-3d

Report Method: Default Report

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Individual Sample Report

Reported by User: group (group)

Project Name: Luca

Spectrum Index Plot

Report Method: Default Report

Printed 6:20:32 PM 6/27/2004

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

Spectrum Index Plot

Report Method: Default Report

Printed 6:05:21 PM 6/27/2004

3e

^1H NMR (400 MHz, CDCl_3 , r.t.)

3e

^1H NMR (400 MHz, CDCl_3 , 60°C)

3g

¹³C NMR (100 MHz, CDCl₃, r.t.)

ppm (f1)

Individual Sample Report

Individual Sample Report

Individual Sample Report

Individual Sample Report

SAMPLE INFORMATION				SAMPLE INFORMATION			
Sample Name:	luca150_OJ31_80-20	Acquired By:	Luca	Sample Name:	luca148_OJ31_85-15	Acquired By:	Luca
Kilobits:		Date Acquired:	12 July 2004 14:14:17	Kilobits:		Date Acquired:	12 July 2004 17:46:30
Flow:		Anal. Method set:	85_15_10	Flow:		Anal. Method set:	85_15_10
Injection Volume:	10.00 ul	Date Processed:	12 July 2004 15:23:27	Injection Volume:	10.00 ul	Date Processed:	12 July 2004 18:15:06
Run Time:	60.0 Minutes	Processing Method:	Training_process_method	Run Time:	100.0 Minutes	Processing Method:	Training_process_method
Solvent:		Channel Name:	Extract 254.0	Solvent:		Channel Name:	Extract 254.0

RET	Area	% Area	Height
1 13.613	400381.36	85.13	0.297
2 27.161	526125.06	14.87	0.059

rac-3g

RET	Area	% Area	Height
1 13.613	767752.7	84.47	0.797
2 27.161	3116365.28	15.53	0.41550

(-)-3g

Report Method: Default Report Printed: 15:29:20 12 July 2004

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Report Method: Default Report Printed: 19:15:45 12 July 2004

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Individual Sample Report

Individual Sample Report

Individual Sample Report

Individual Sample Report

Report Method: Default Report

Printed: 15:29:20

12 July 2004

Report Method: Default Report

Printed: 19:15:45

12 July 2004

¹³C NMR (100 MHz, CDCl₃, r.t.)

ppm (t1)

Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training10

SAMPLE INFORMATION

Sample Name: luca119_OD19_90-10
 Columns:
 Flow:
 Injection Volume: 10.00 µl
 Run Time: 70.0 Minutes
 Solvent:
 Acquired By: Luca
 Date Acquired: 14 June 2004 13:48:48
 Acq. Method:
 Date Processed: 14 June 2004 14:28:32
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

RET	Area	% Area	Height
1 8.600	5470460	47.27	1445210
2 18.979	61002781	52.73	667230

rac-3h

Report Method: Default Report

Printed 10:07:15 26 June 2004

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Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training10

Report Method: Default Report

Printed 10:07:15 26 June 2004

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Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training10

SAMPLE INFORMATION

Sample Name: luca120ba_b_OD19_90-10
 Columns:
 Flow:
 Injection Volume: 10.00 µl
 Run Time: 40.0 Minutes
 Solvent:
 Acquired By: Luca
 Date Acquired: 26 June 2004 18:42:48
 Acq. Method:
 Date Processed: 26 June 2004 19:15:12
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

RET	Area	% Area	Height
1 8.334	32080870	97.89	1104471
2 20.620	618277	2.41	11000

(+)-3h

Report Method: Default Report

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Individual Sample Report

Reported by User: Luca Bernardi (Luca)

Project Name: Training10

Report Method: Default Report

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¹³C NMR (100 MHz, CDCl₃, r.t.)

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

SAMPLE INFORMATION

Sample Name:	luca130_OD19_95.5	Acquired By:	group
Sample Type:	Unknown	Date Acquired:	6/29/2004 4:13:50 PM
Vial:	1	Acq. Method Set:	95_5_10
Injection #:	1	Date Processed:	6/29/2004 5:22:40 PM
Injection Volume:	10.00 uL	Processing Method:	LC PQ
Run Time:	100.0 Minutes	Channel Name:	WIn Ch1
Sample Set Name:		Proc. Chnl. Descr.:	PDA 210.4 nm

RET	Area	% Area	Height
1 28.425	20294055	49.04	189213
2 35.650	21084554	50.96	145510

rac-3i

Report Method: Default Report

Printed 2:11:56 PM 6/29/2004

Page: 2 of 2

Individual Sample Report

Reported by User: group (group)

Project Name: Luca

Spectrum Index Plot

Report Method: Default Report

Printed 2:11:56 PM 6/29/2004

Individual Sample Report

Reported by User: group (group)

Project Name: ThomasP

SAMPLE INFORMATION

Sample Name:	luca131bis.b.OD19_95.5	Acquired By:	group
Sample Type:	Unknown	Date Acquired:	6/29/2004 12:08:34 PM
Vial:	1	Acq. Method Set:	95_5_10
Injection #:	13	Date Processed:	6/29/2004 1:00:36 PM
Injection Volume:	10.00 uL	Processing Method:	LC PQ
Run Time:	100.0 Minutes	Channel Name:	WIn Ch1
Sample Set Name:		Proc. Chnl. Descr.:	PDA 210.4 nm

RT	Area	% Area	Height
1 28.425	54552196	97.18	503221
2 35.650	1583552	2.82	13487

(-)-3i

Spectrum Index Plot

Report Method: ThomasP

Printed 1:00:52 PM 6/29/2004

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^1H NMR (400 MHz, CDCl_3 , 60°C)

ppm (f1)

Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training1

SAMPLE INFORMATION

Sample Name: G229
Kubota AD-30
Flow 1.0
Injection Volume: 10.00 μl
Run Time: 60.0 Minutes
Solvent 90-10
Acquired By: wei
Date Acquired: 27 June 2004 13:06:47
Date Processed: 10 July 2004 17:49:44
Processing Method: Training_process_method
Channel Name: Extract 254.0

RET	Area	% Area	Height
1	23.968	80.06790	49.10
2	31.132	19.93210	50.90

Report Method: Default Report

Printed 17:50:22 16 July 2004

Page 2 of 2

Reported by User: Wei Zhuang (wei)

Project Name: Training2

Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training1

SAMPLE INFORMATION

Sample Name: G229
Kubota AD-30
Flow 1.0
Injection Volume: 10.00 μl
Run Time: 60.0 Minutes
Solvent 90-10
Acquired By: wei
Date Acquired: 28 June 2004 17:10:05
Date Processed: 10 July 2004 17:55:23
Processing Method: Training_process_method
Channel Name: Extract 254.0

RET	Area	% Area	Height
1	24.271	88.73	49.10
2	31.473	11.27	50.90

Report Method: Default Report

Printed 17:55:57 16 July 2004

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Reported by User: Wei Zhuang (wei)

Project Name: Training2

Individual Sample Report

Report Method: Default Report

Printed 17:50:22

16 July 2004

Report Method: Default Report

Printed 17:55:57

16 July 2004

Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training1

SAMPLE INFORMATION

Sample Name: G2332-1
 Kubeone AD-30
 Flow: 1.0
 Injection Volume: 10.00 µl
 Run Time: 30.0 minutes
 Solvent: 90-10
 Acquired By: wei
 Date Acquired: 30 June 2004 12:02:30
 Auto Method Set: 90_10_10
 Date Processed: 10 July 2004 17:42:13
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

RT	Area	% Area	Height
1 21.413	5851609	51.39	149590
2 23.281	5481130	48.61	130873

Report Method: Default Report

Printed 17:42:50 10 July 2004

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Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training1

SAMPLE INFORMATION

Sample Name: G2280
 Kubeone AD-30
 Flow: 1.0
 Injection Volume: 10.00 µl
 Run Time: 30.0 minutes
 Solvent: 90-10
 Acquired By: wei
 Date Acquired: 30 June 2004 12:00:39
 Auto Method Set: 90_10_10
 Date Processed: 10 July 2004 17:47:32
 Processing Method: Training_process_method
 Channel Name: Extract 254.0

RT	Area	% Area	Height
1 20.829	8890380	3.85	19074
2 22.887	22225152	96.15	450046

Report Method: Default Report

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Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training

Report Method: Default Report

Printed 04:00

10 July 2004

Individual Sample Report

Reported by User: Wei Zhuang (wei)

Project Name: Training

Report Method: Default Report

Printed 04:00

10 July 2004

Determination of the absolute configuration of 5. The absolute configuration of **5** was determined by the X-ray crystallography of the optically pure [3-(4-chlorobenzoylamino)-4-methyl-2-oxo-5-phenyl-oxazolidin-4-yl]-phosphonic acid diethyl ester **6**.

X-Ray work: Crystals of $C_{21}H_{24}ClN_2O_6P$, are monoclinic, $P2_1$, with unit cell: $a = 10.5320(9)\text{\AA}$, $b = 7.3532(7)\text{\AA}$, $c = 15.228(1)\text{\AA}$, $V = 1107.67(16)\text{\AA}^3$, $Z = 2$. Data were collected at 100K on a SMART diffractometer with CCD detector. The structure was solved by direct methods and refined by least squares methods to final $R = 0.044$, $R_w = 0.049$, $GOF = 0.942$ using 3199 reflections with $I > 3\sigma(I)$, 280 parameters refined. Least squares refinement included a parameter according to Rogers⁴ refined against all 3199 significant reflections including 749 Bijvoet pairs, determining the chirality.

⁴ Rogers, D. *Acta Cryst.* **1981**, *A37*, 734.

Proposed intermediate for the enantioselective approach of the amination reagent.