Supplementary Material (ESI) for
New Journal of Chemistry

Supporting information

High diastereoselective synthesis of novel bis α-aminophosphonates by lipase catalytic promiscuity

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Content:

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1. General information:

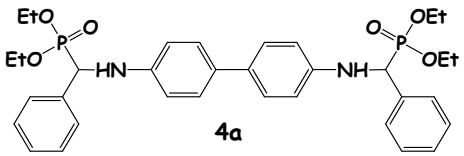
All starting materials and reagents used in this study were obtained commercially from Aldrich and Acros and were used without purification. Various commercially available lipases were screened: lipase from *Porcine pancreas* type II (*PPL*; LA = 100-500 U/mg), Rabbit Gastric Lipase (*RGL;* LA > 1170 U/mg), *Candida Cylindracea* lipase (*CCL*, LA = 3.85 U/mg), *Pseudomonas Cepacia* lipase (*PCL*; LA > 30 000 U/mg), and the *Candida antarctica* lipase fraction B immobilized on acrylic resin (*CAL-B*; LA > 10 000 U/mg). All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25-mm Merck silica gel plates (60F-254) using ultraviolet light (254 nm) as the visualizing agent and $KMnO_4$ solution as developing agents. ^{1}H NMR and ^{13}C NMR spectra were recorded with Bruker spectrometers (360 MHz, 300 MHz and 250 MHz for 1H, 90 MHz, 75 MHz and 63 MHz for ^{13}C and 101 MHz and 121 MHz for ^{31}P). Chemical shifts were reported downfield from $CDCl_3$ (δ = 7.26 ppm). For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent of $CDCl_3$ (δ = 77 ppm) used as internal reference. Coupling constants (J) are given in hertz. Following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal. Melting points were measured using Buchi Melting Point B-545. Mass spectra were recorded with a MicrOTOF-Q Bruker spectrometer using electrospray ionization (ESI) analysis.

2. General procedure for synthesis of bis *α*-aminophosphonates 4a-4k:

To the stirred mixture of aromatic aldehyde (2 mmol), benzidine (184 mg, 1 mmol) and diethylphosphite (331.2 mg, 2.4 mmol) in THF (2ml), the *CAL-B* (50 mg) was added. The reaction was stirred at 50°C for 30 minutes. After the reaction proceeded to completion, the lipase was removed by filtration. The two diastereoismers mixture was separated by column chromatography using ethyl acetate /hexane: 90/10 as eluent. Complete experimental data have been provided (NMR spectra and HRMS).

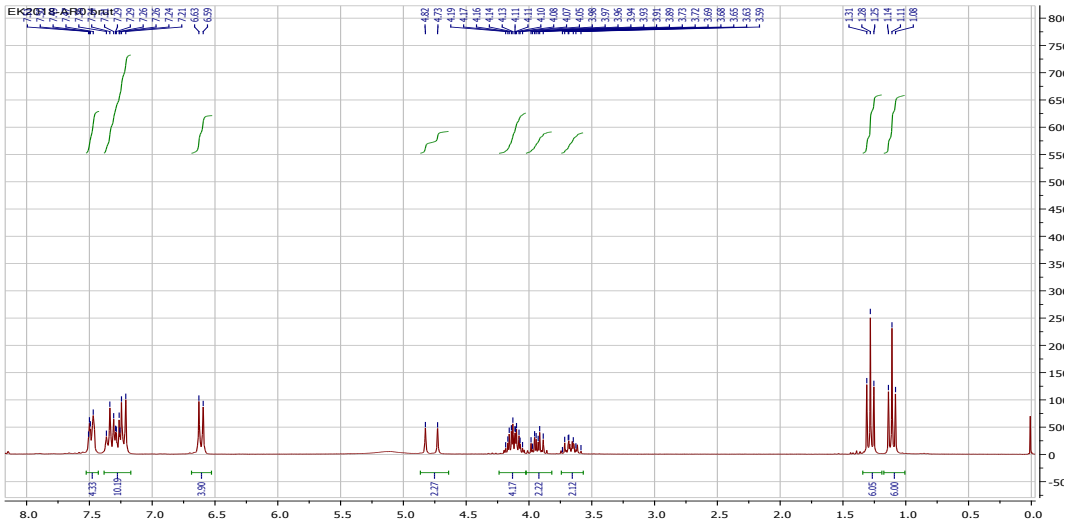
3. ^{1}H, ^{13}C and ^{31}P NMR data:

Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(phenyl) methylene] bisphosphonate 4a



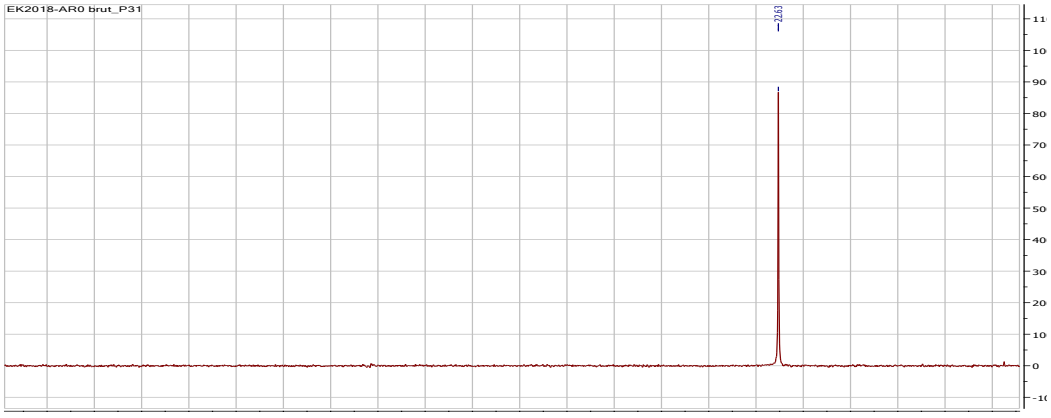
4a

^{1}H NMR (250 MHz, $CDCl_3$)

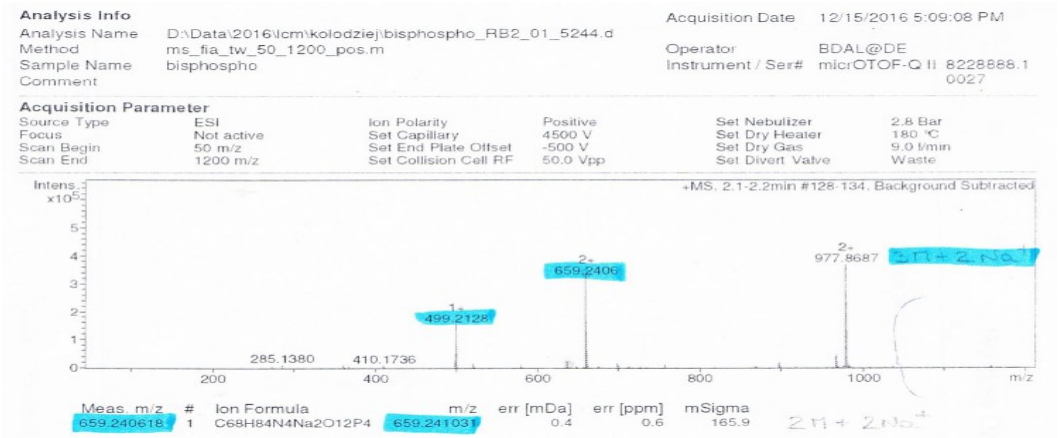


^{13}C NMR (91 MHz, $CDCl_3$)

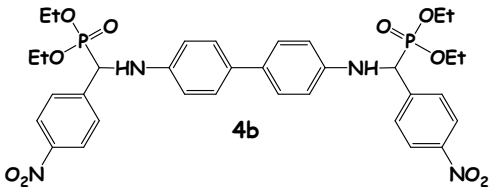
^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

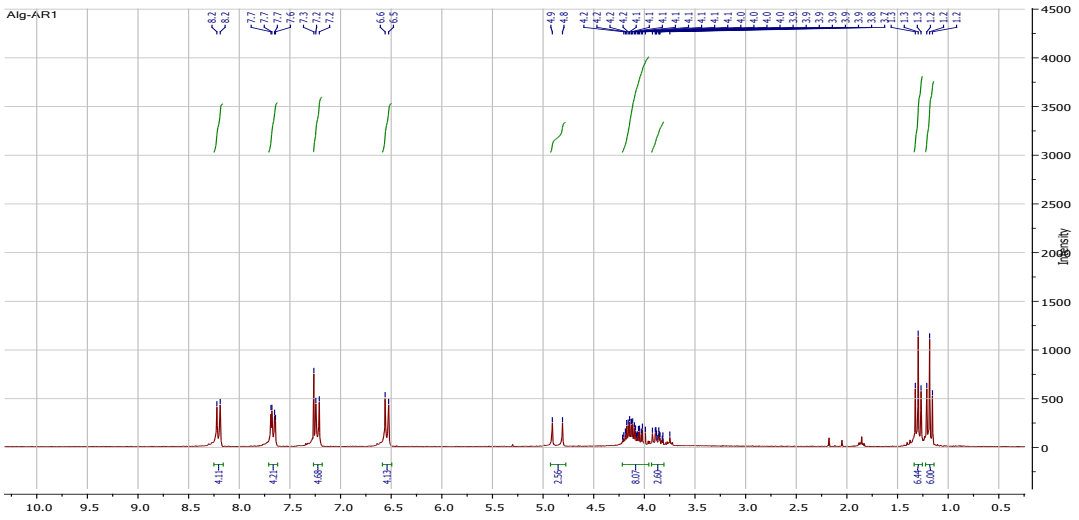


Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(4-nitrophenyl)methylene]bisphosphonate 4b

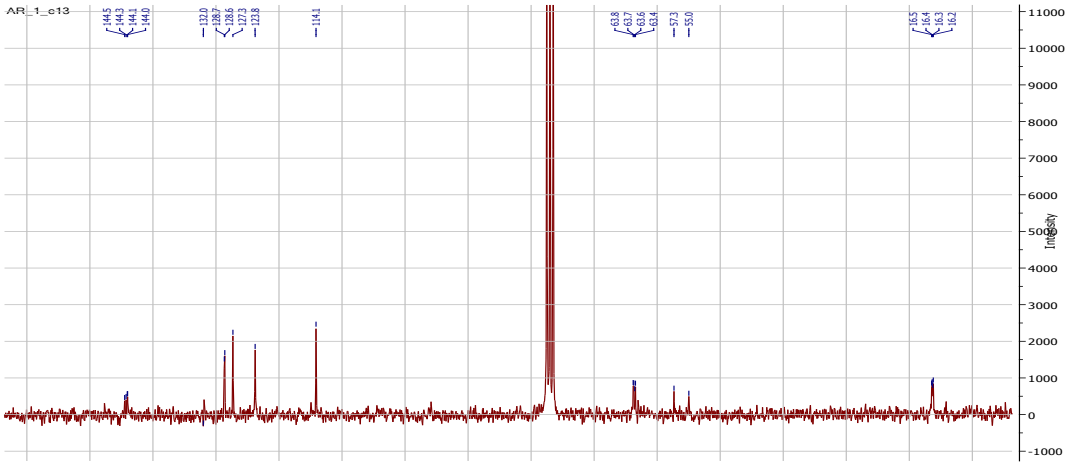


4b

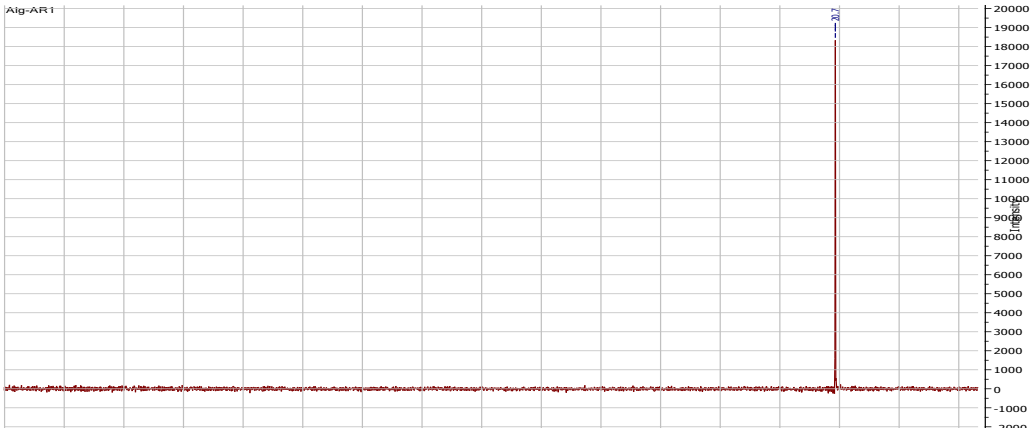
^{1}H NMR (250 MHz, $CDCl_3$)



^{13}C NMR (91 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

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Comment			

Acquisition Parameter

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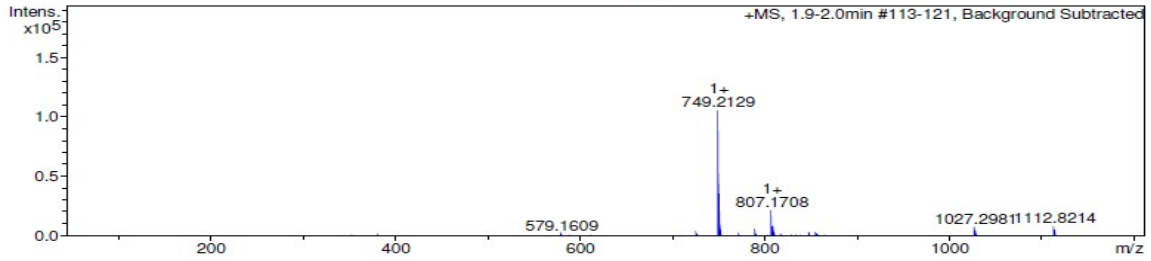

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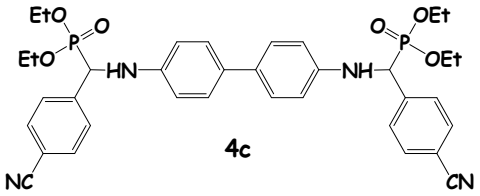
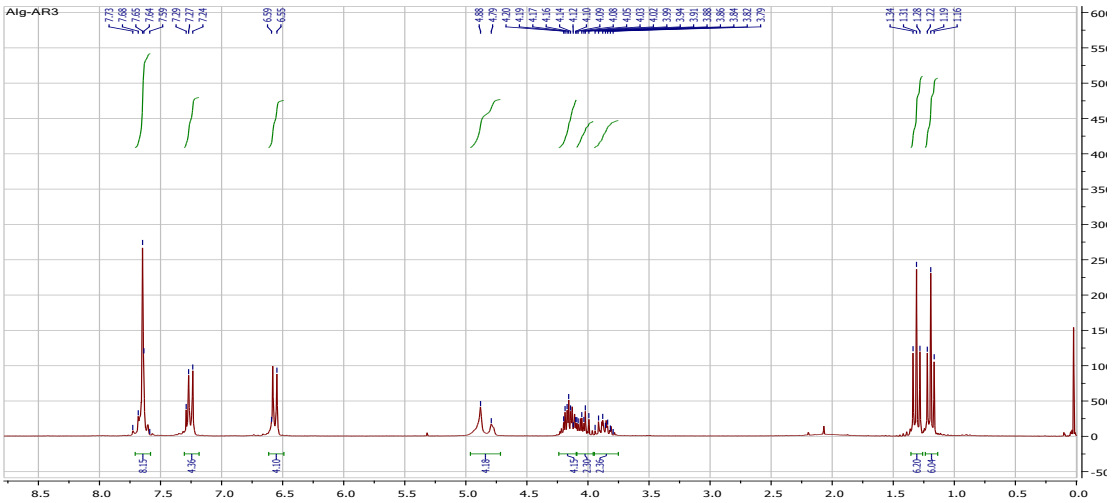
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(4-cyanophenyl) methylene] bisphosphonate 4c

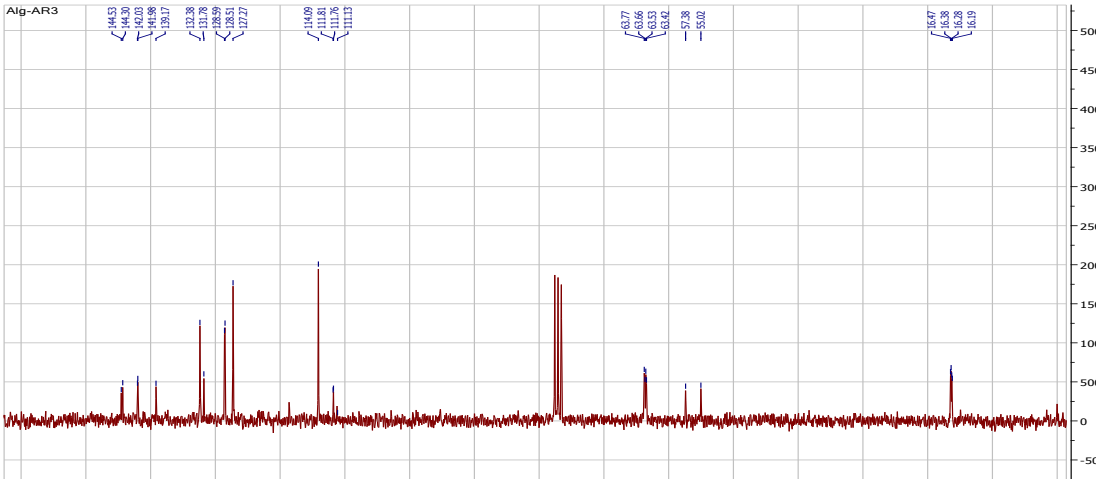


4c

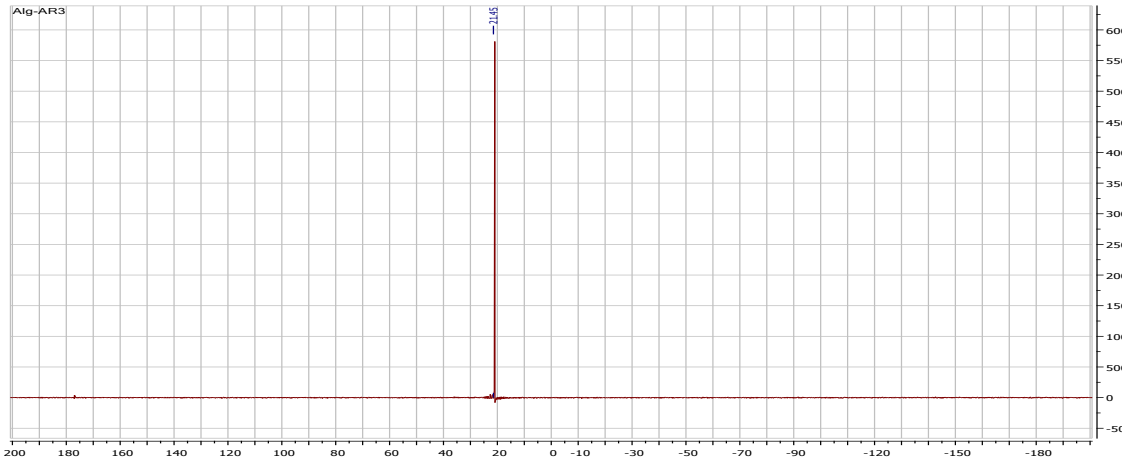
NMR ^1H (250 MHz, $CDCl_3$, 25°C)



NMR ^{13}C (63 MHz, $CDCl_3$, 25°C)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

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Comment		Instrument / Ser#	micrOTOF-Q II 8228888.10027

Acquisition Parameter

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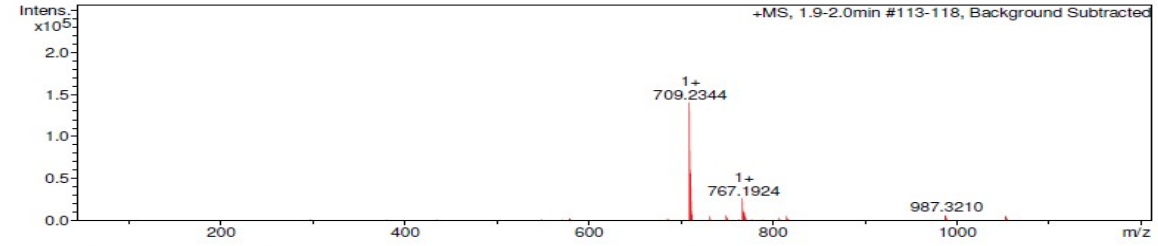
Scan End	1200 m/z	Set Collision Cell RF	50.0 Vpp	Set Divert Valve	Waste



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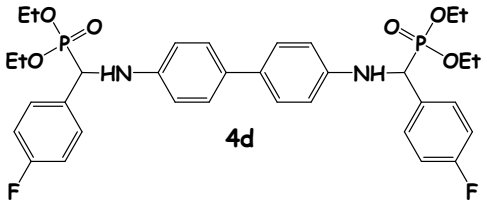
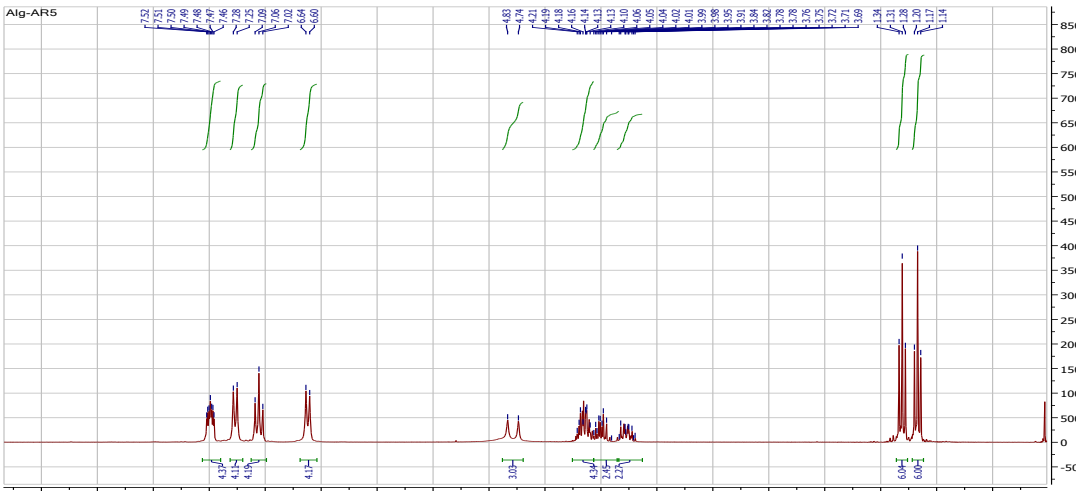
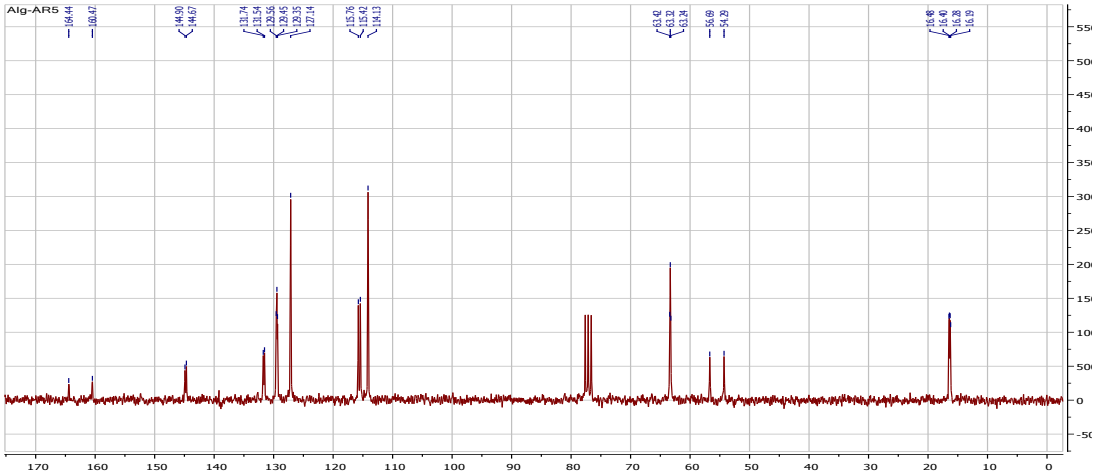
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(4-fluorophenyl) methylene] bisphosphonate 4d



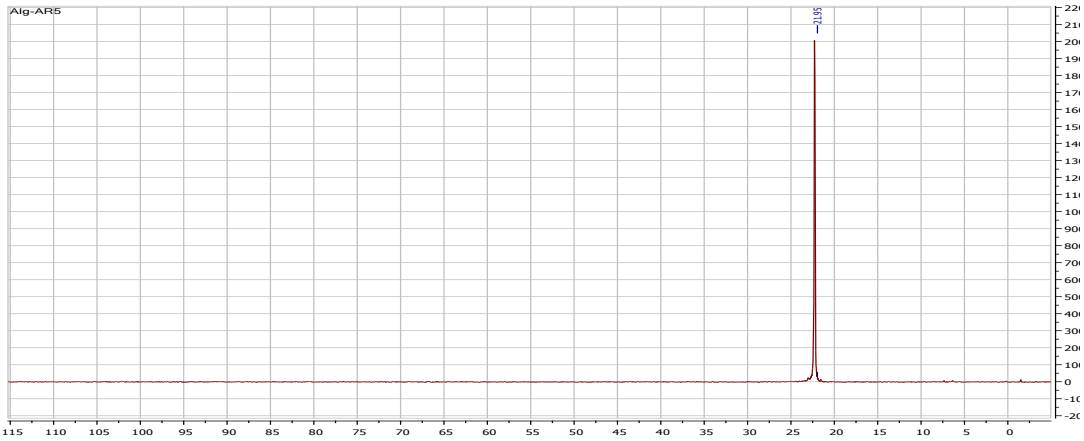
^{1}H NMR (250 MHz, $CDCl_3$, 25°C)



^{13}C NMR (63 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



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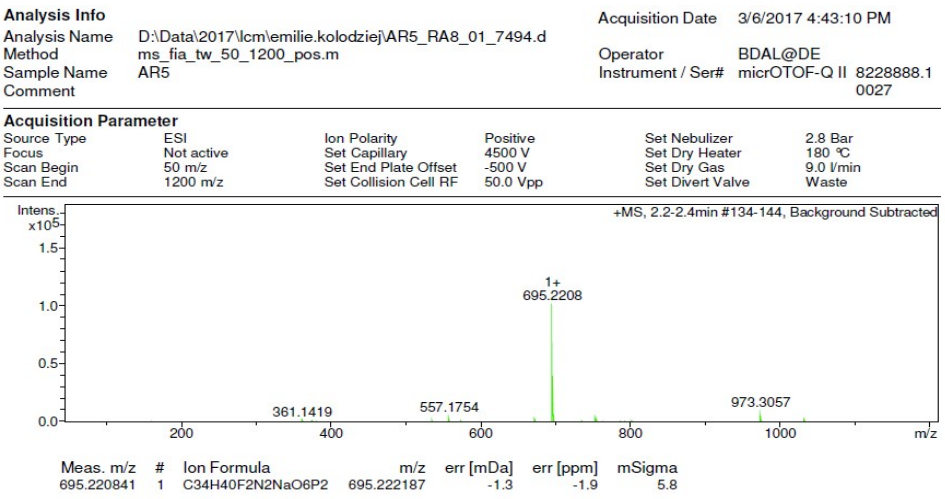
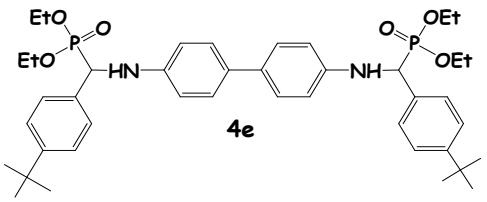
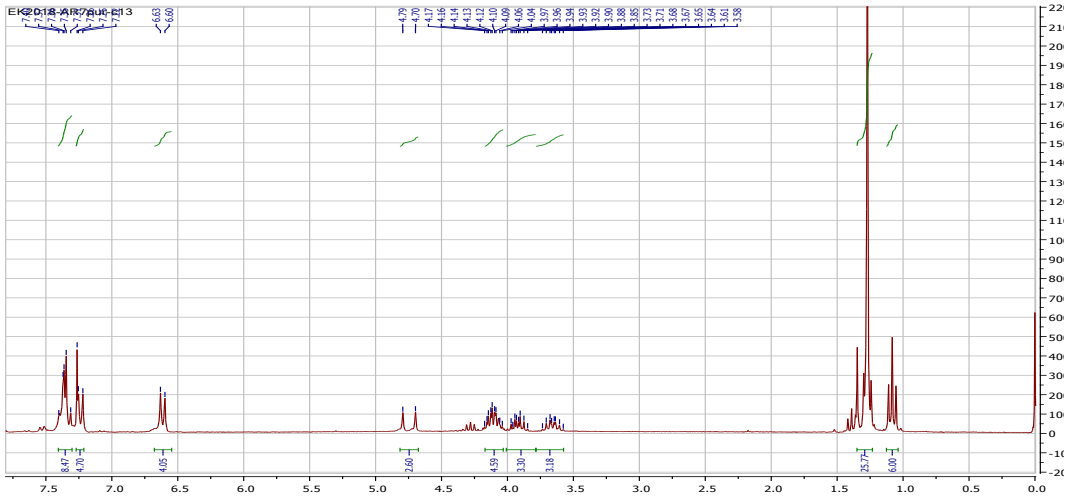


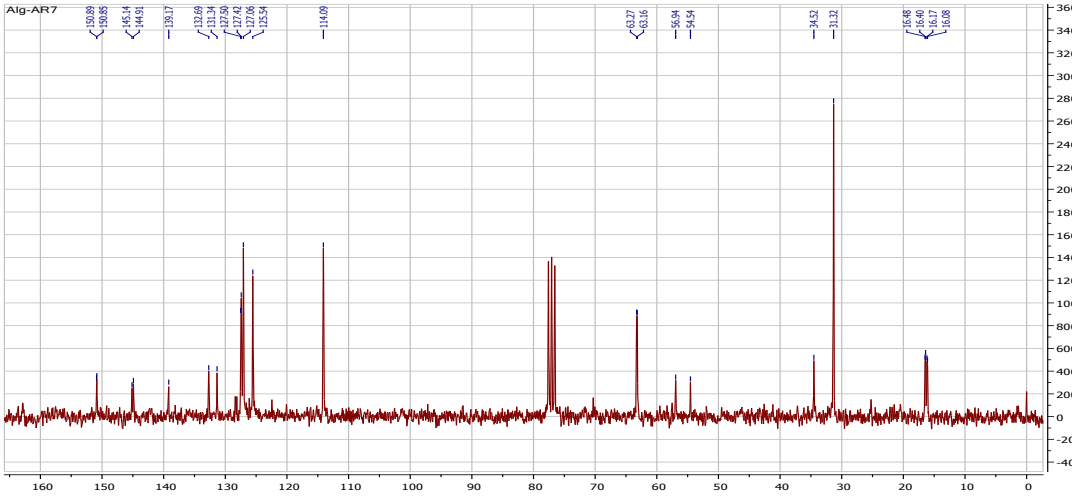
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[4-(*tert*-butyl)phenyl) methylene] bisphosphonate 4e



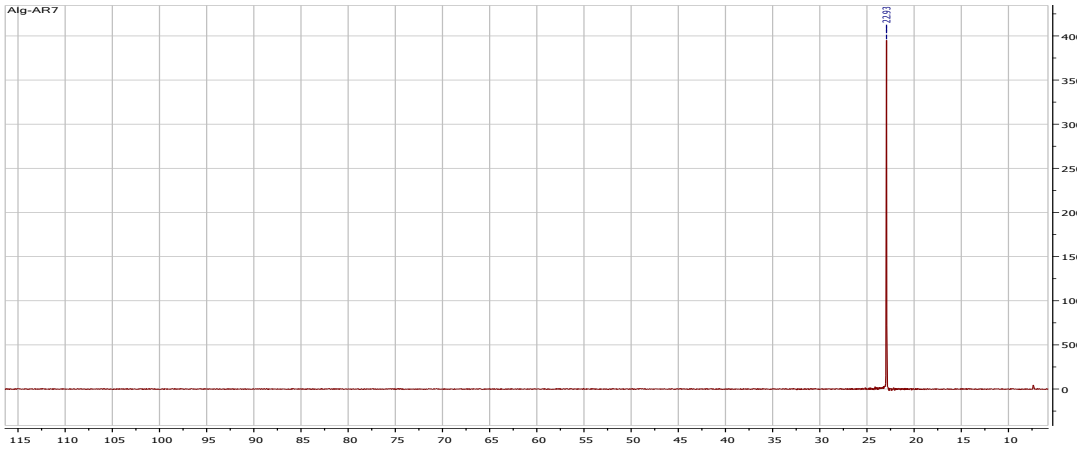
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



^{13}C NMR (63 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



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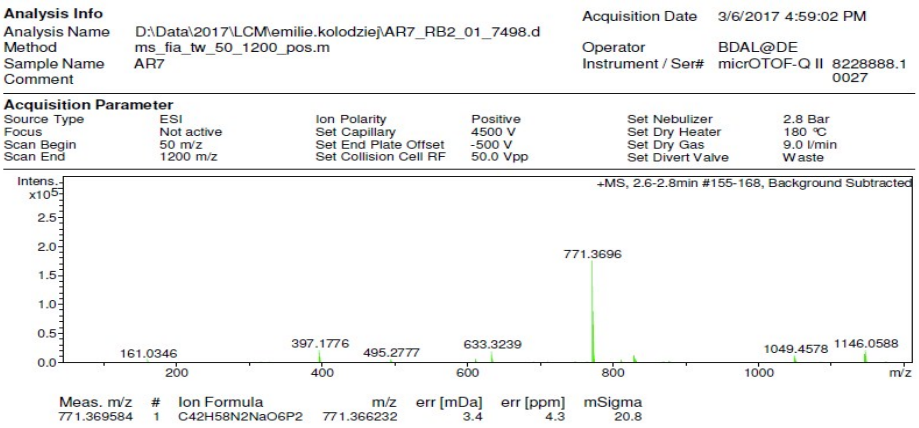

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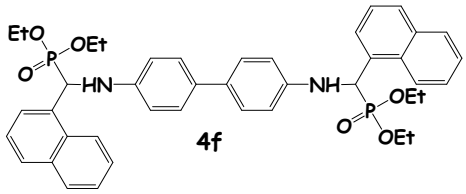
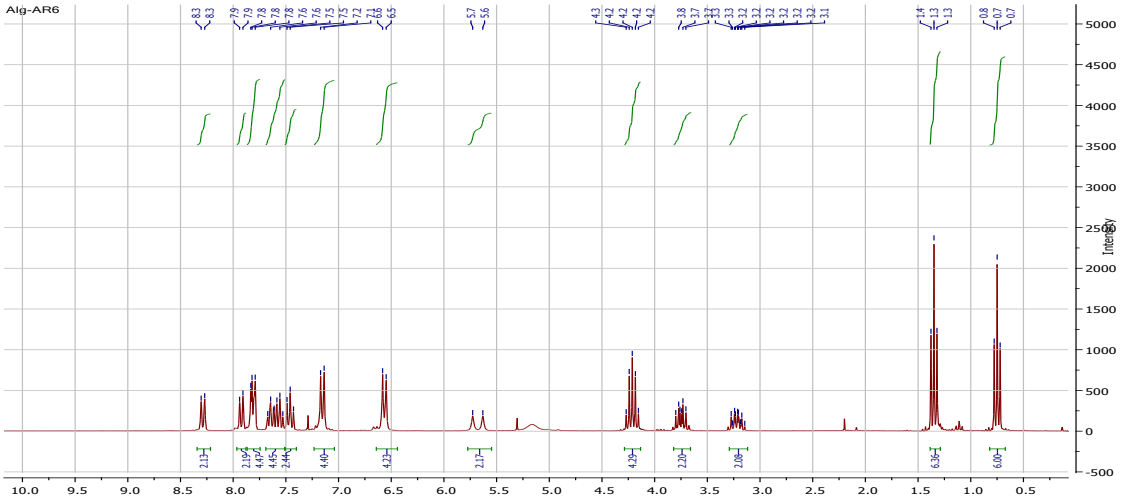
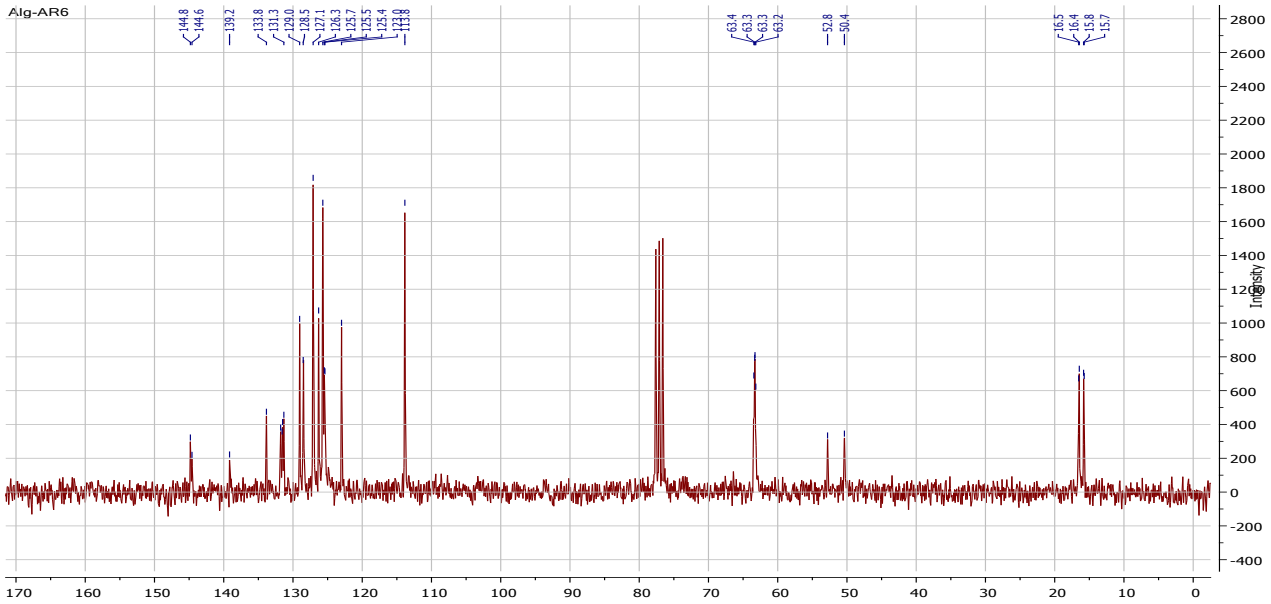


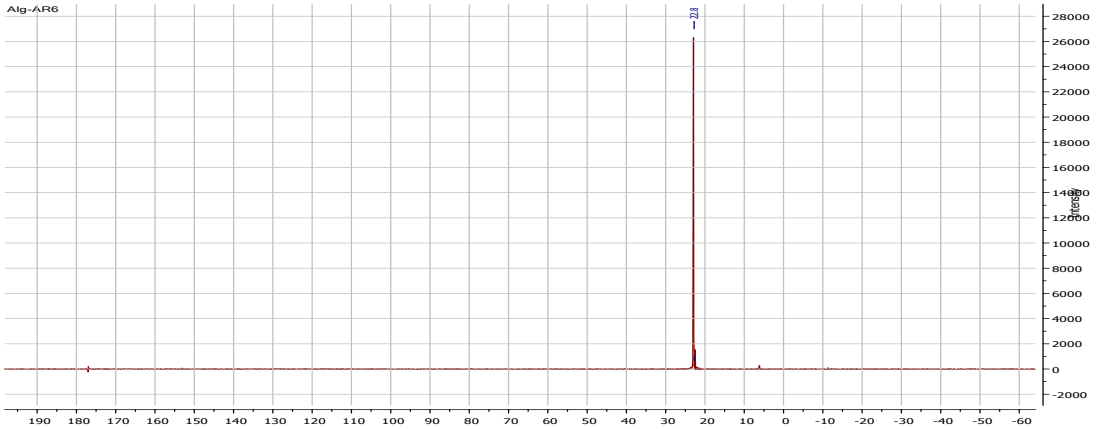
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



^{13}C NMR (63 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

Analysis Info

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Sample Name	AR6	Operator	BDAL@DE
Comment		Instrument / Ser#	micrOTOF-Q II 8228888.10027

Acquisition Parameter

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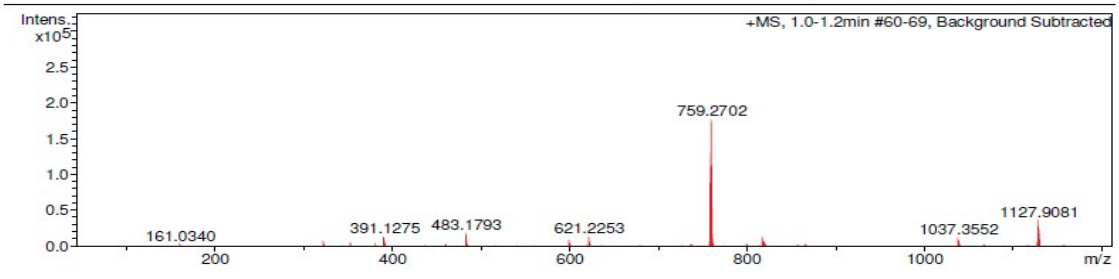
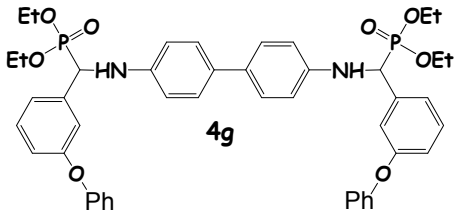
Scan End	1200 m/z	Set Collision Cell RF	50.0 Vpp	Set Divert Valve	Waste

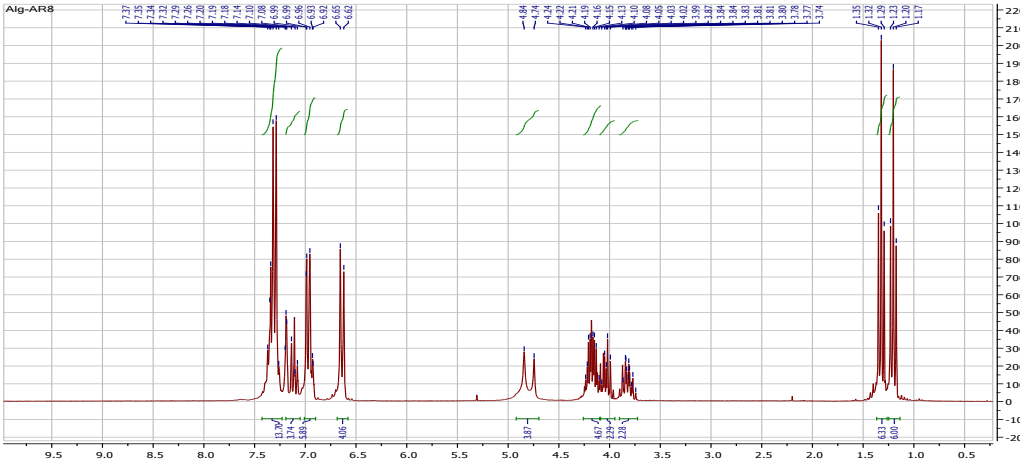


Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma
759.270194	1	C42H46N2NaO6P2	759.272331	-2.1	-2.8	15.9

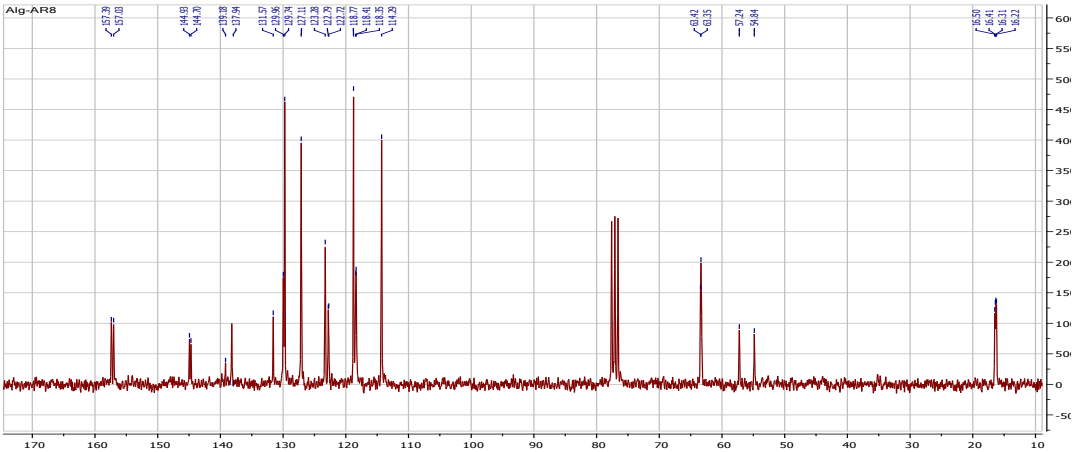
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(3-phenoxyphenyl) methylene] bisphosphonate 4g



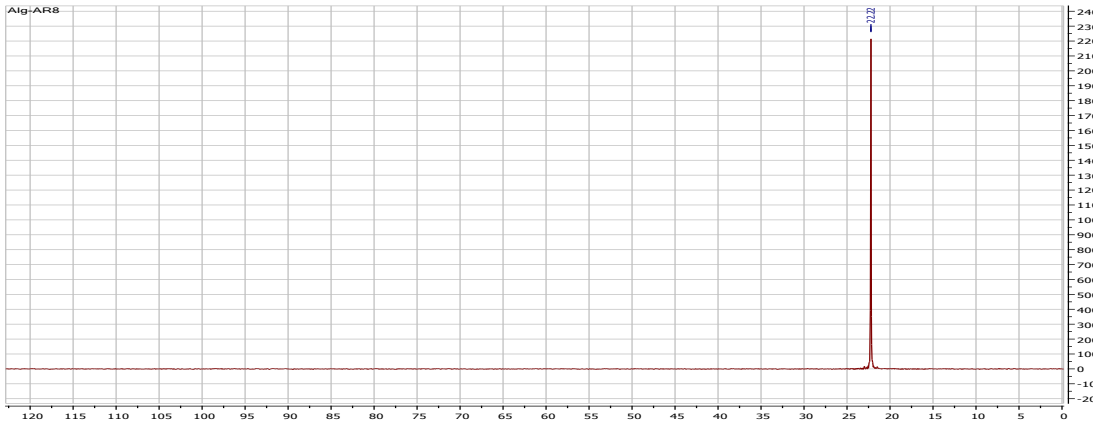
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



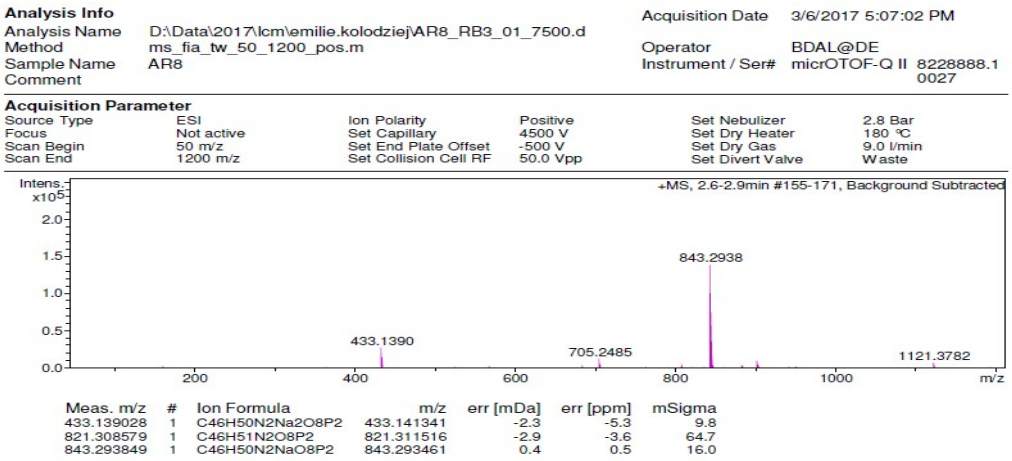
^{13}C NMR (63 MHz, $CDCl_3$)



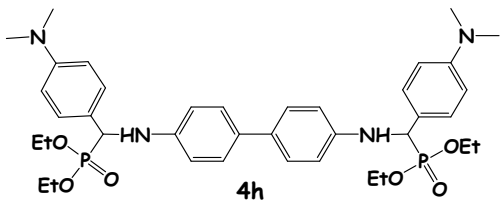
^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

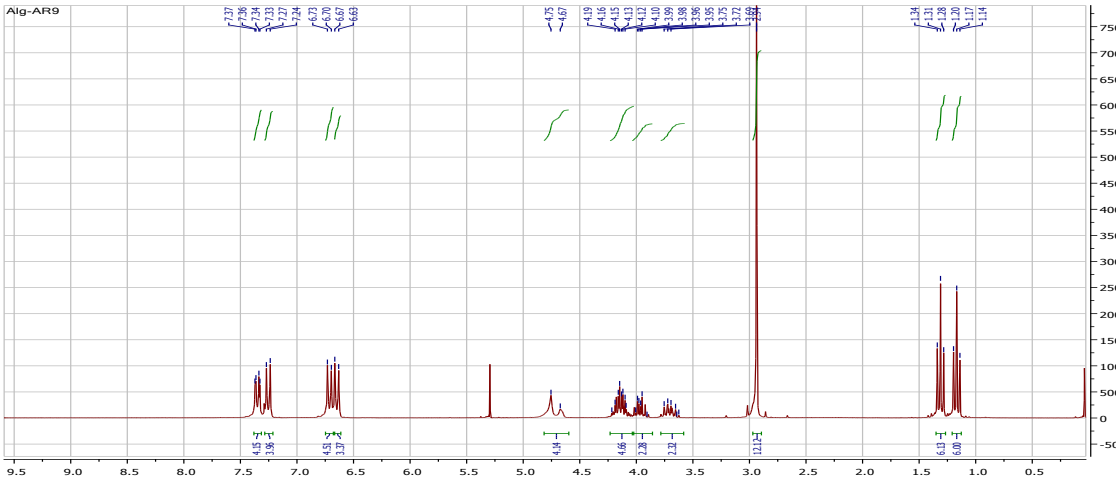


Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(4-dimethylaminophenyl) methylene] bisphosphonate 4h

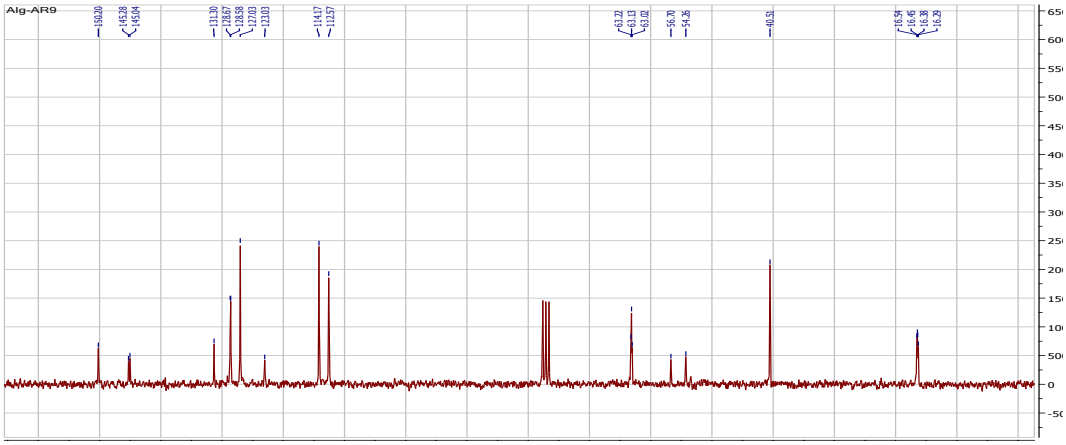


4h

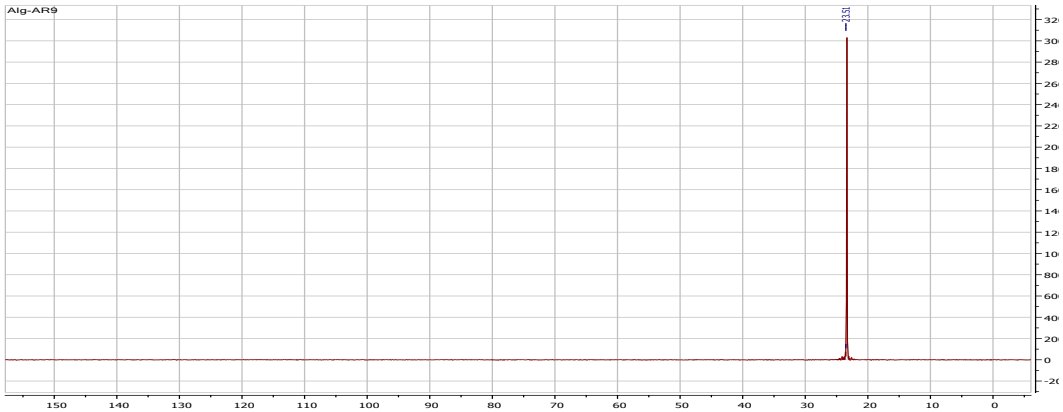
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



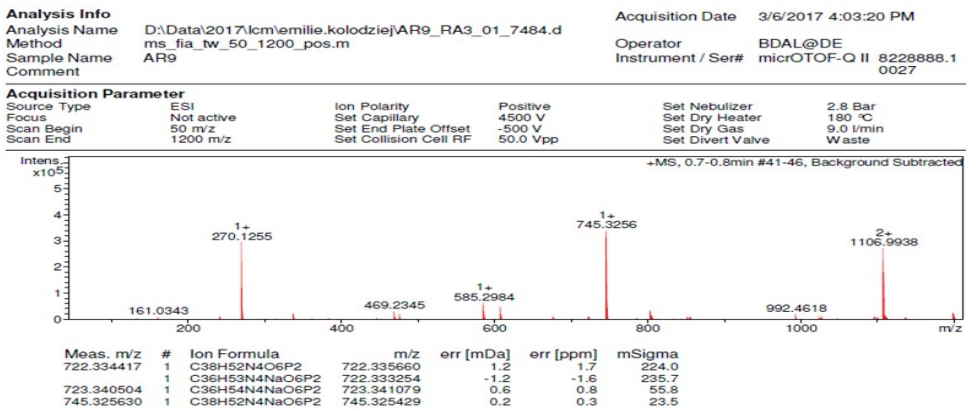
^{13}C NMR (63 MHz, $CDCl_3$)



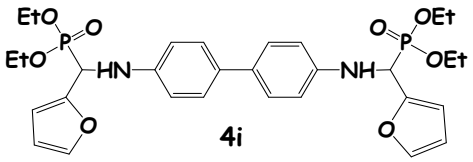
^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



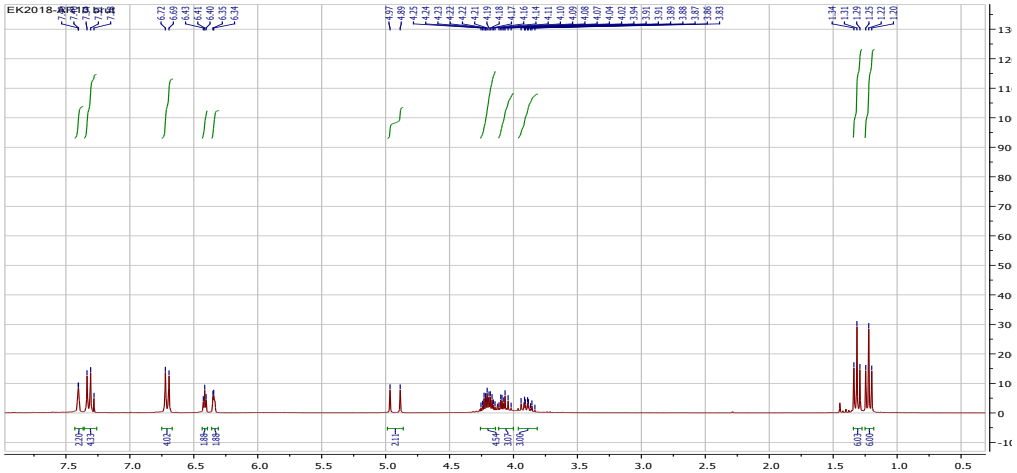
HRMS (ESI)



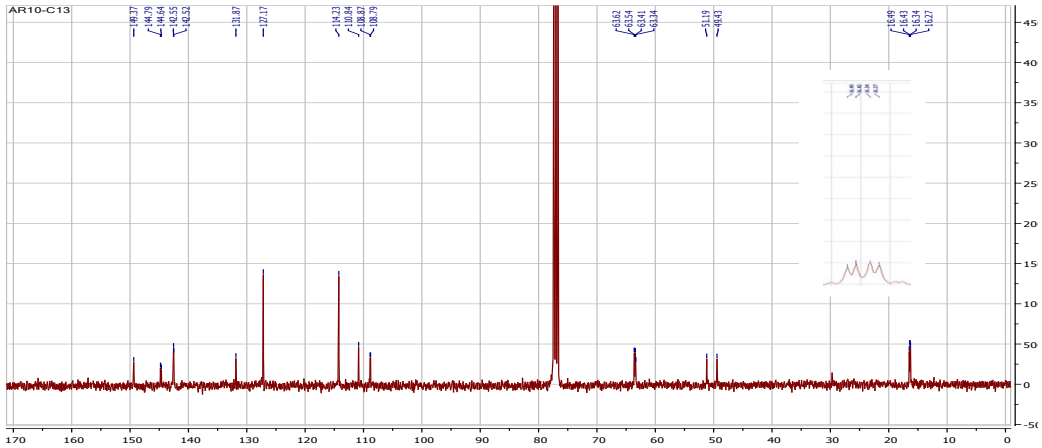
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[(furan-2ylmethylene] bisphosphonate 4i



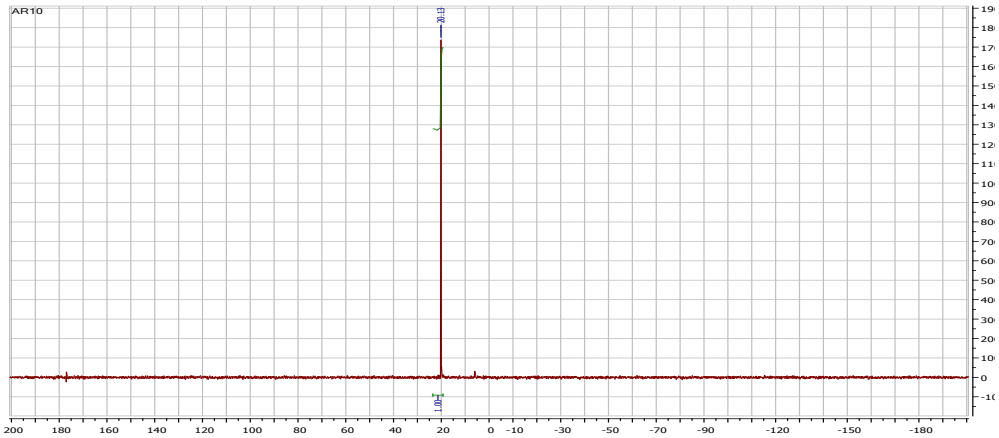
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



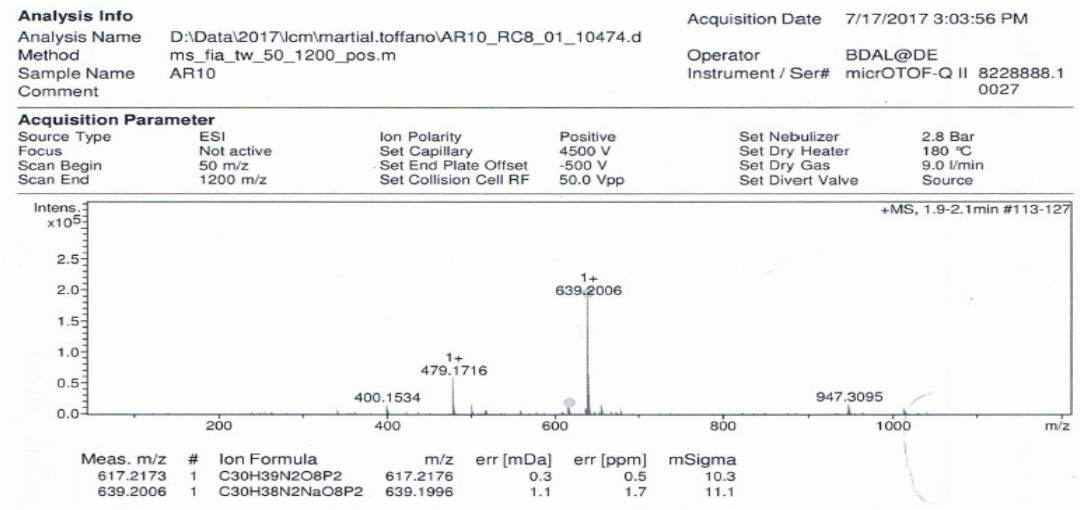
^{13}C NMR (63 MHz, $CDCl_3$)



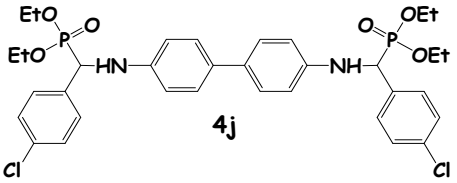
^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)

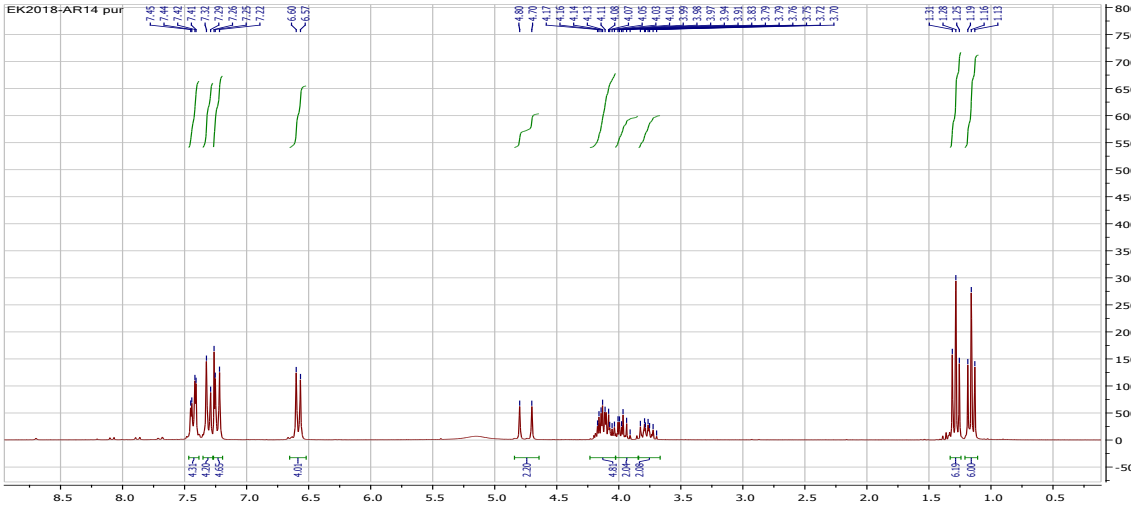


Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[4-chlorophenyl) methylene] bis phosphonate 4j

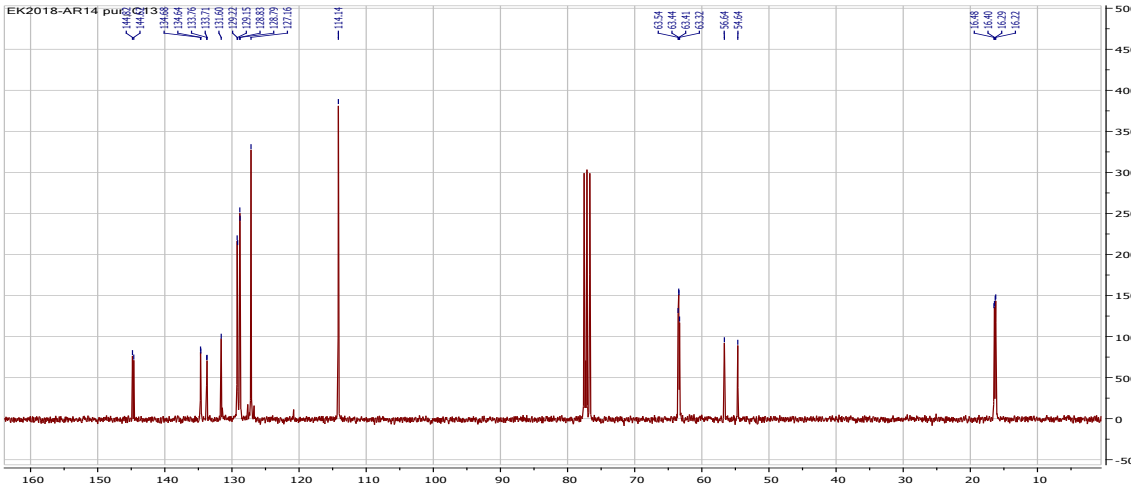


4j

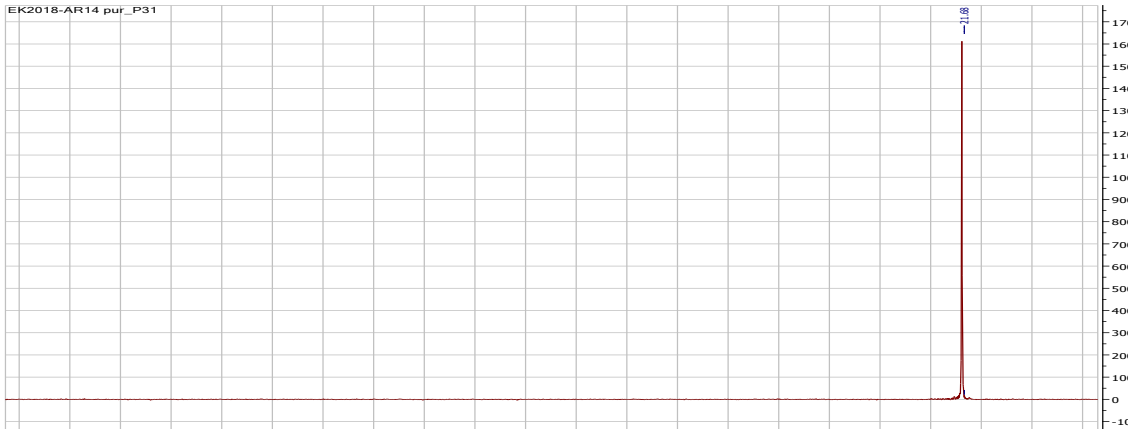
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



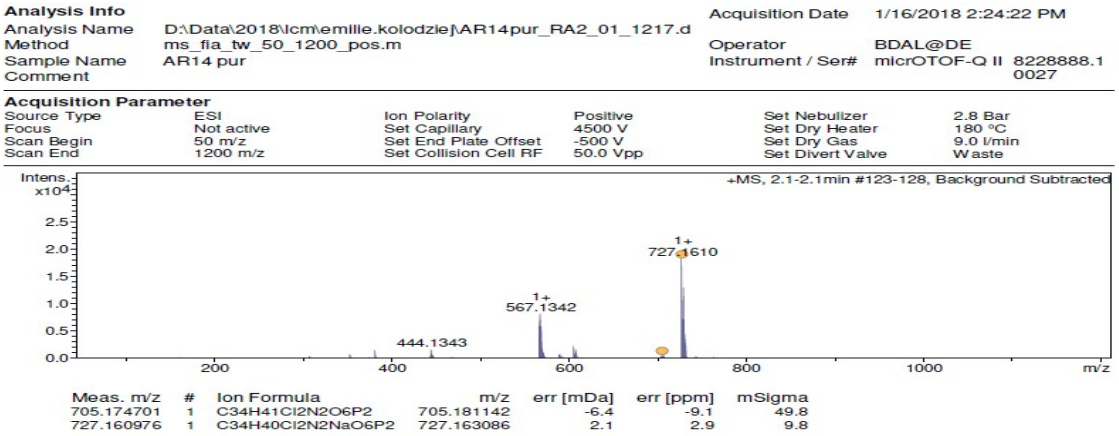
^{13}C NMR (63 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



HRMS (ESI)



Analysis Info

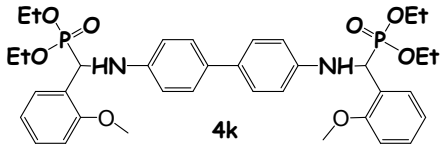
Analysis Name	D:\Data\2018\lcm\emilie.kolodziej\AR14pur_RA2_01_1217.d	Acquisition Date	1/16/2018 2:24:22 PM
Method	ms_fia_tw_50_1200_pos.m	Operator	BDAL@DE
Sample Name	AR14 pur	Instrument / Ser#	micrOTOF-Q II 8228888.1 0027
Comment			

Acquisition Parameter

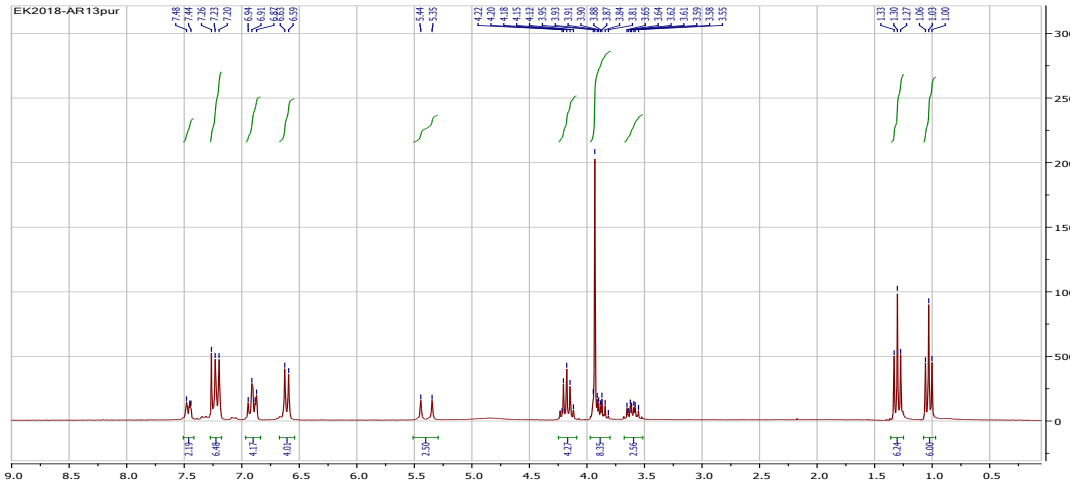
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.8 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	9.0 l/min
Scan End	1200 m/z	Set Collision Cell RF	50.0 Vpp	Set Divert Valve	Waste

Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma
705.174701	1	C34H41Cl2N2O6P2	705.181142	-6.4	-9.1	49.8
727.160976	1	C34H40Cl2N2NaO6P2	727.163086	2.1	2.9	9.8

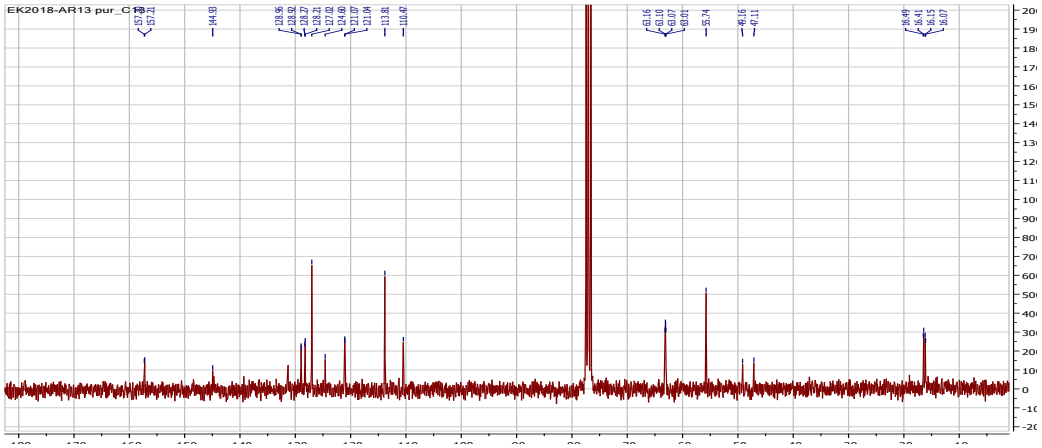
Tetraethyl [(4,1-phenylene) bis(azanediyl)] bis[2-methoxyphenyl) methylene] bisphosphon-ate 4k



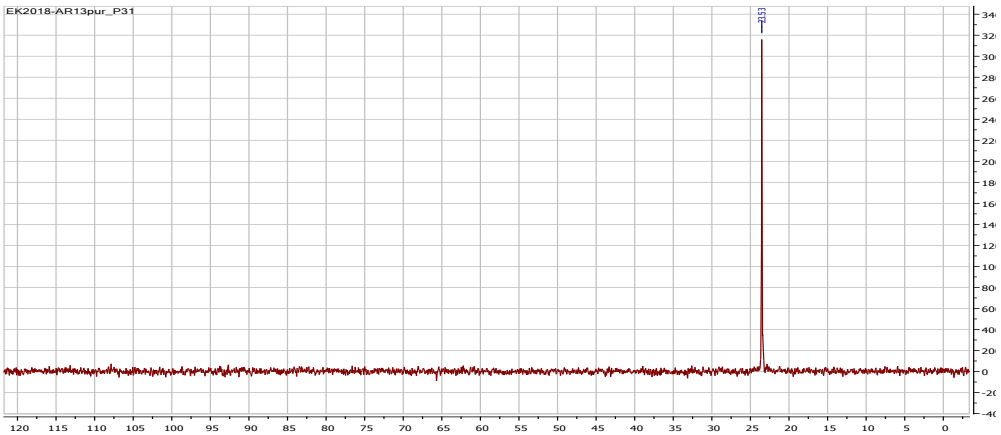
NMR ^{1}H (250 MHz, $CDCl_3$, 25°C)



^{13}C NMR (63 MHz, $CDCl_3$)



^{31}P NMR (121 MHz, $CDCl_3$, 25°C)



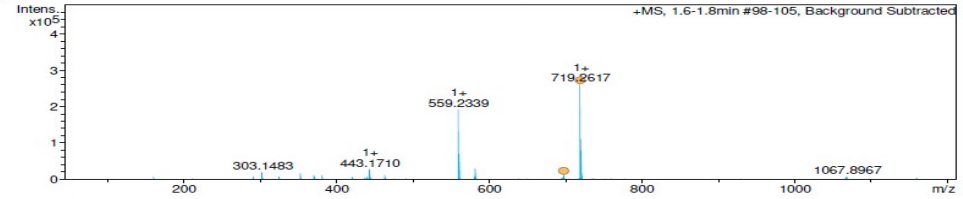
HRMS (ESI)

Analysis Info

Analysis Name	D:\Data\2018\lcm\emilie.kolodziej\AR13pur_RA5_01_1227.d	Acquisition Date	1/16/2018 3:12:08 PM
Method	ms_fia_tw_50_1200_pos.m	Operator	BDAL@DE
Sample Name	AR13 pur	Instrument / Ser#	micrOTOF-Q II 8228888.10027
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	2.8 Bar
Focus	Not active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	9.0 l/min
Scan End	1200 m/z	Set Collision Cell RF	50.0 Vpp	Set Divert Valve	Waste



Meas. m/z	#	Ion Formula	m/z	err [mDa]	err [ppm]	mSigma
697.277701	1	C36H47N2O8P2	697.280216	-2.5	-3.6	18.8
719.261678	1	C36H46N2NaO8P2	719.262160	-0.5	-0.7	10.9