

Synthesis and catalytic activity of fluoros chiral primary amine-thioureas

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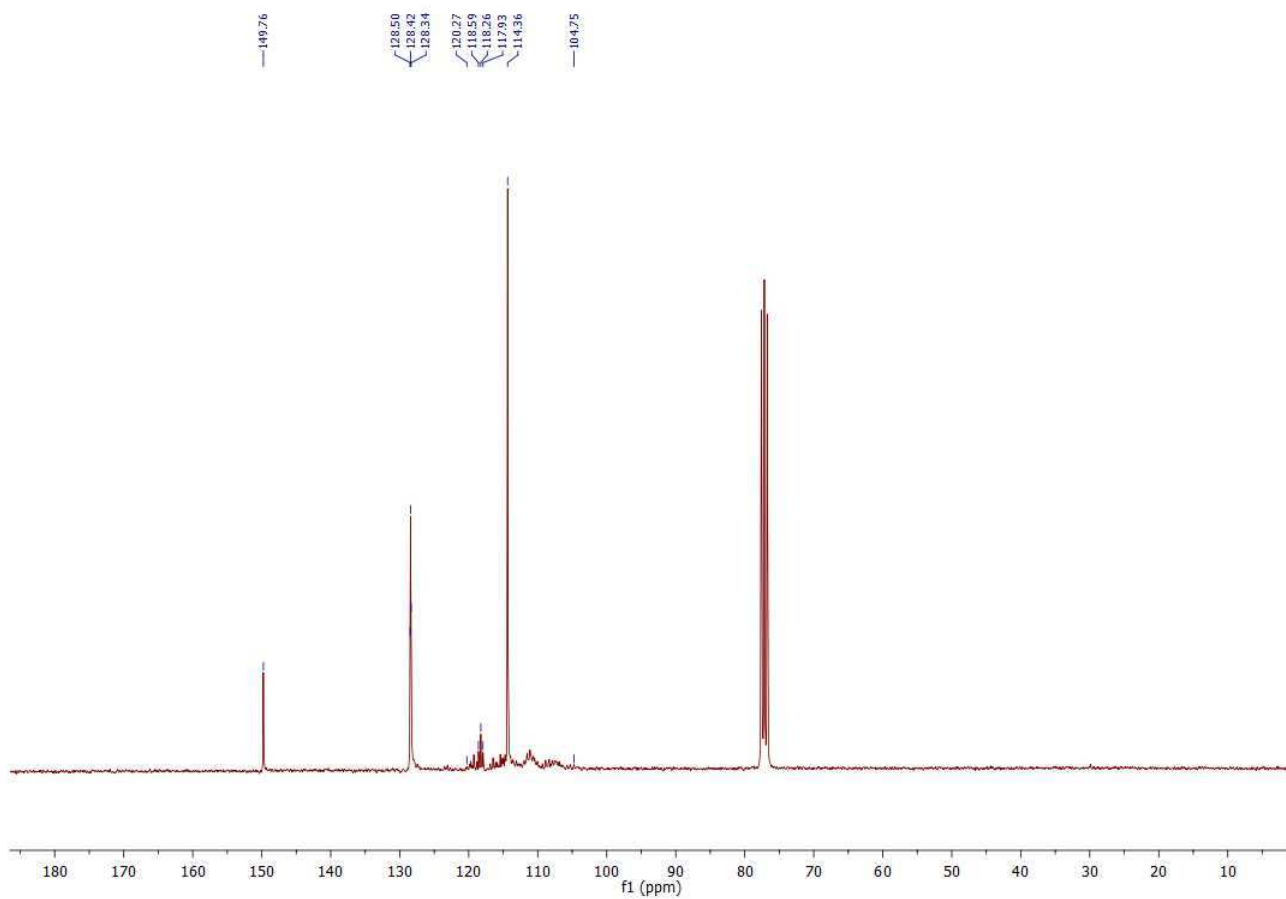
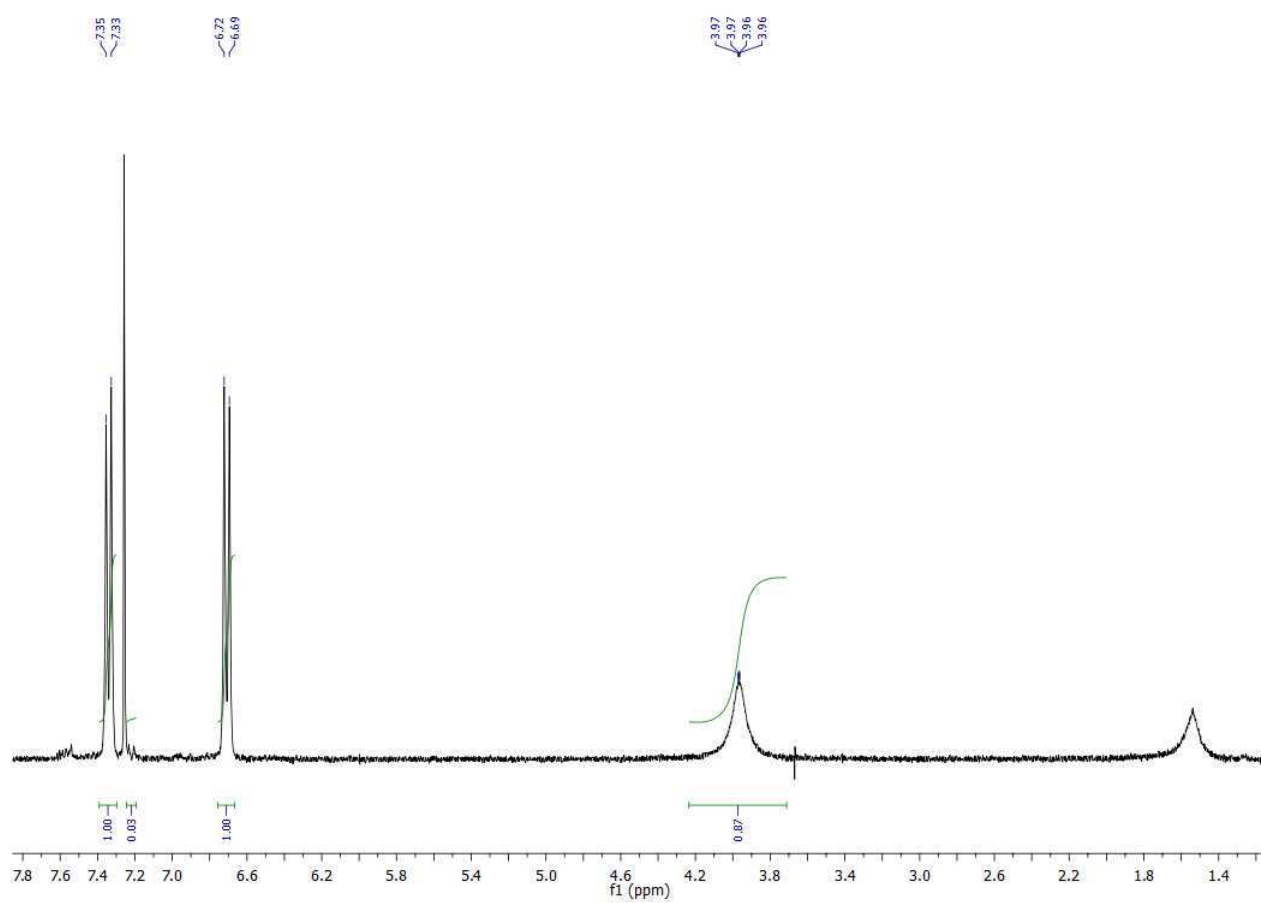
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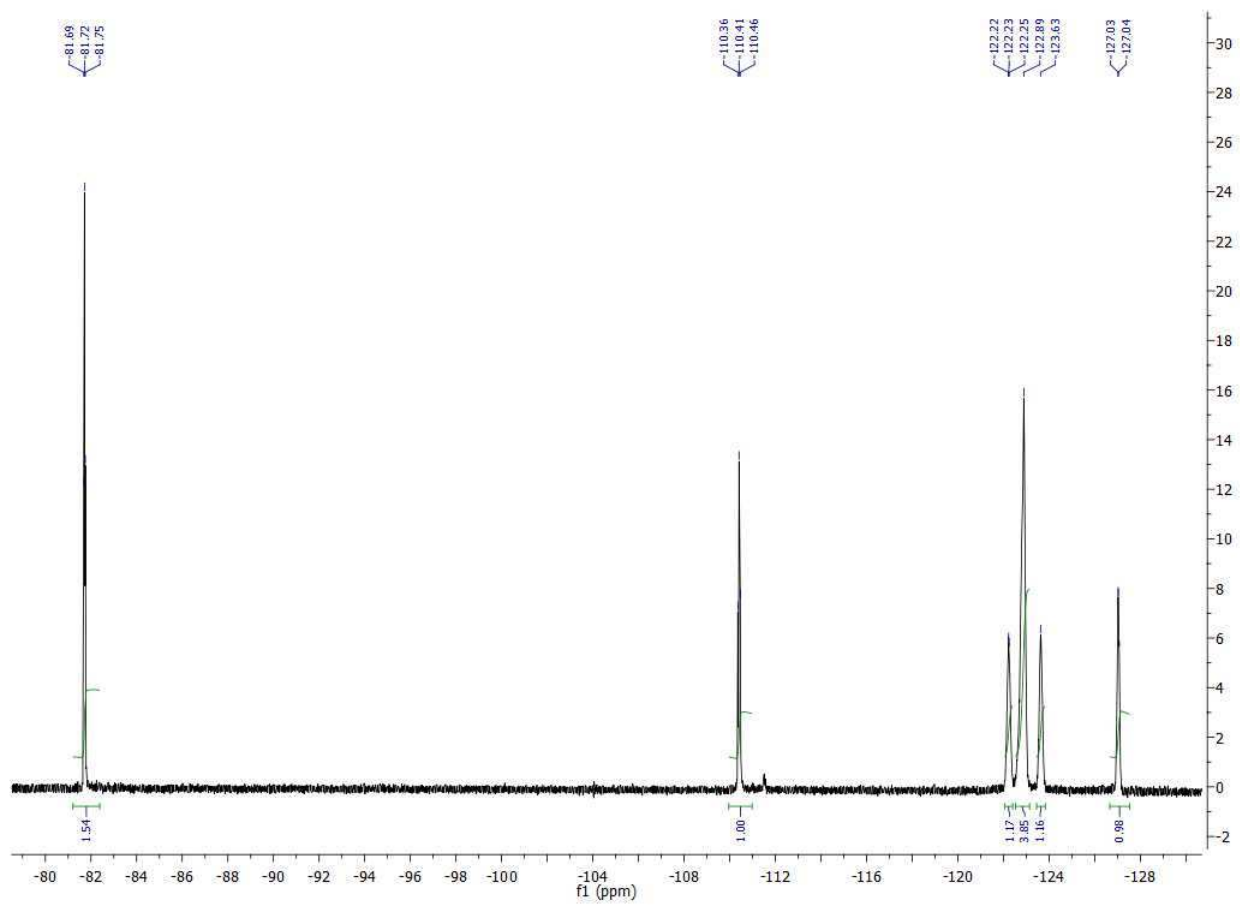
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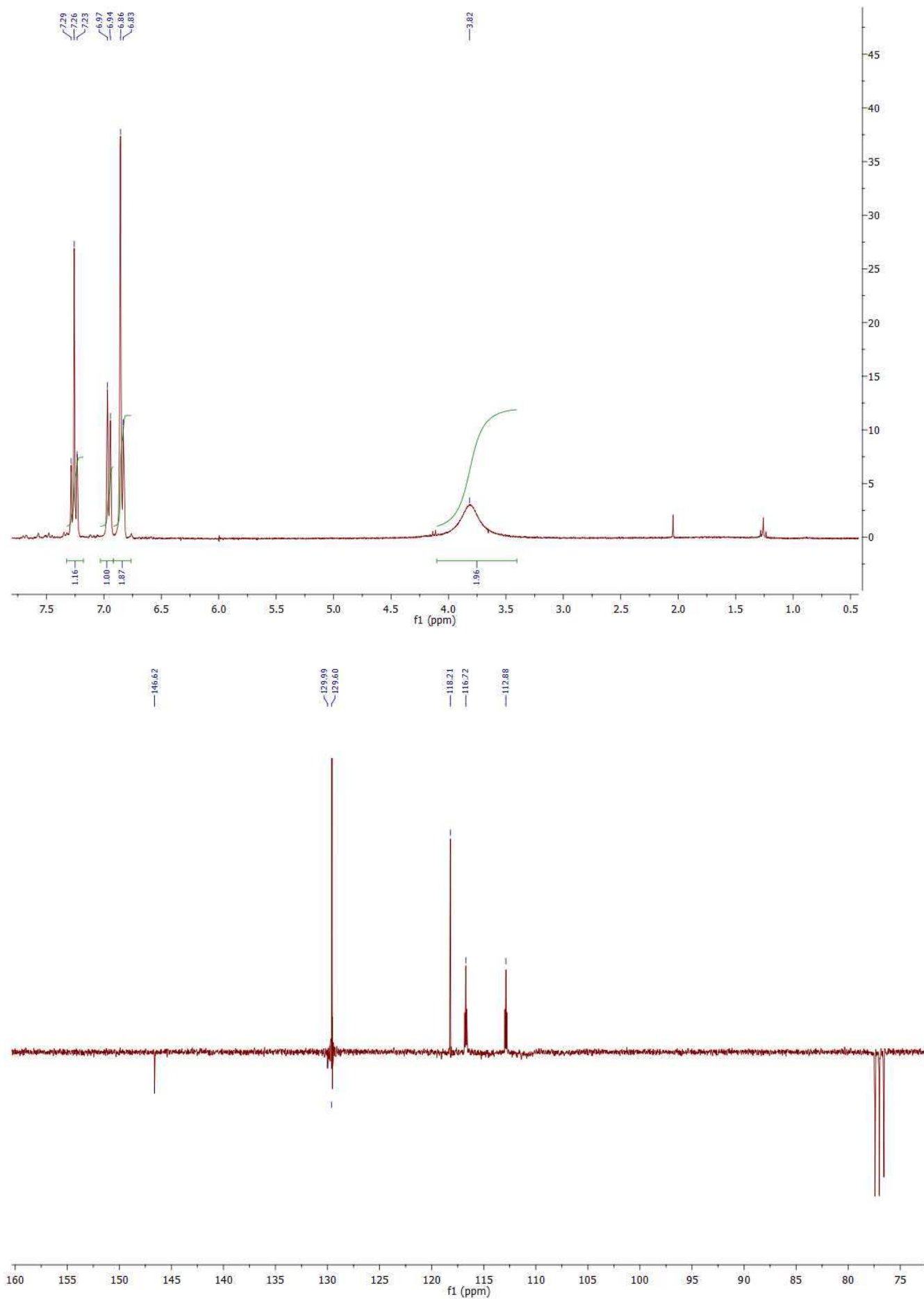
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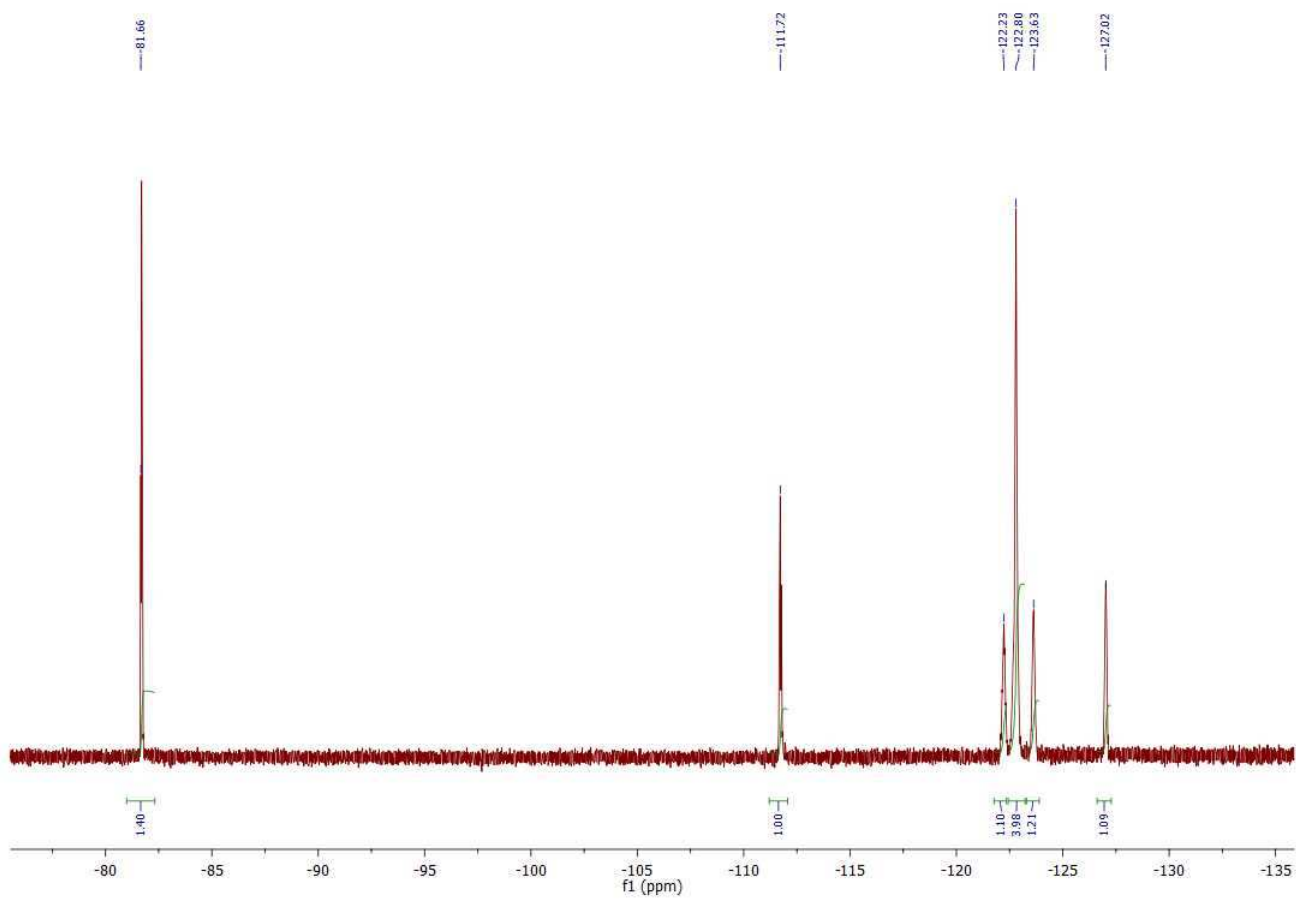
4-(*n*-Perfluorooctyl)aniline (5):



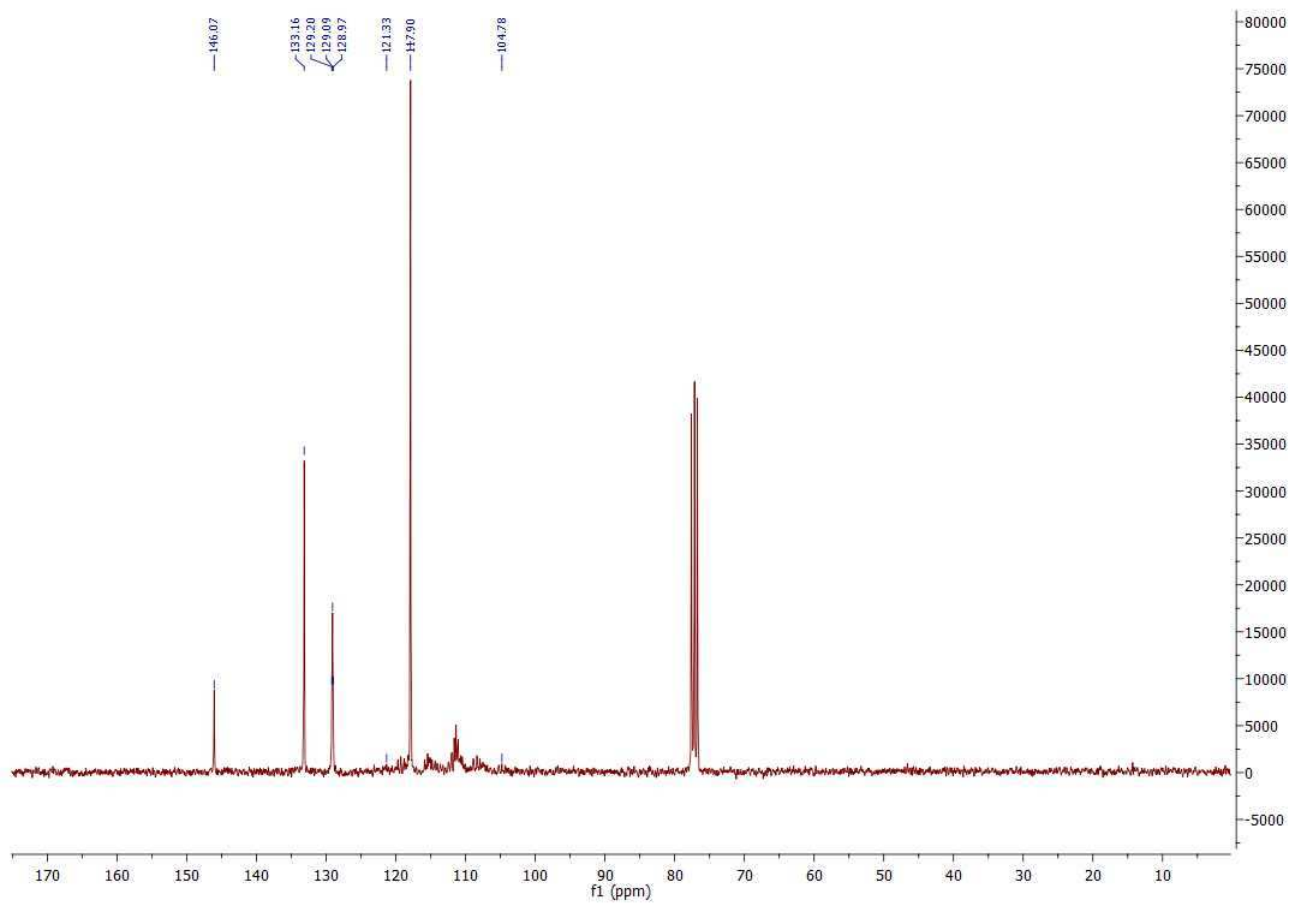
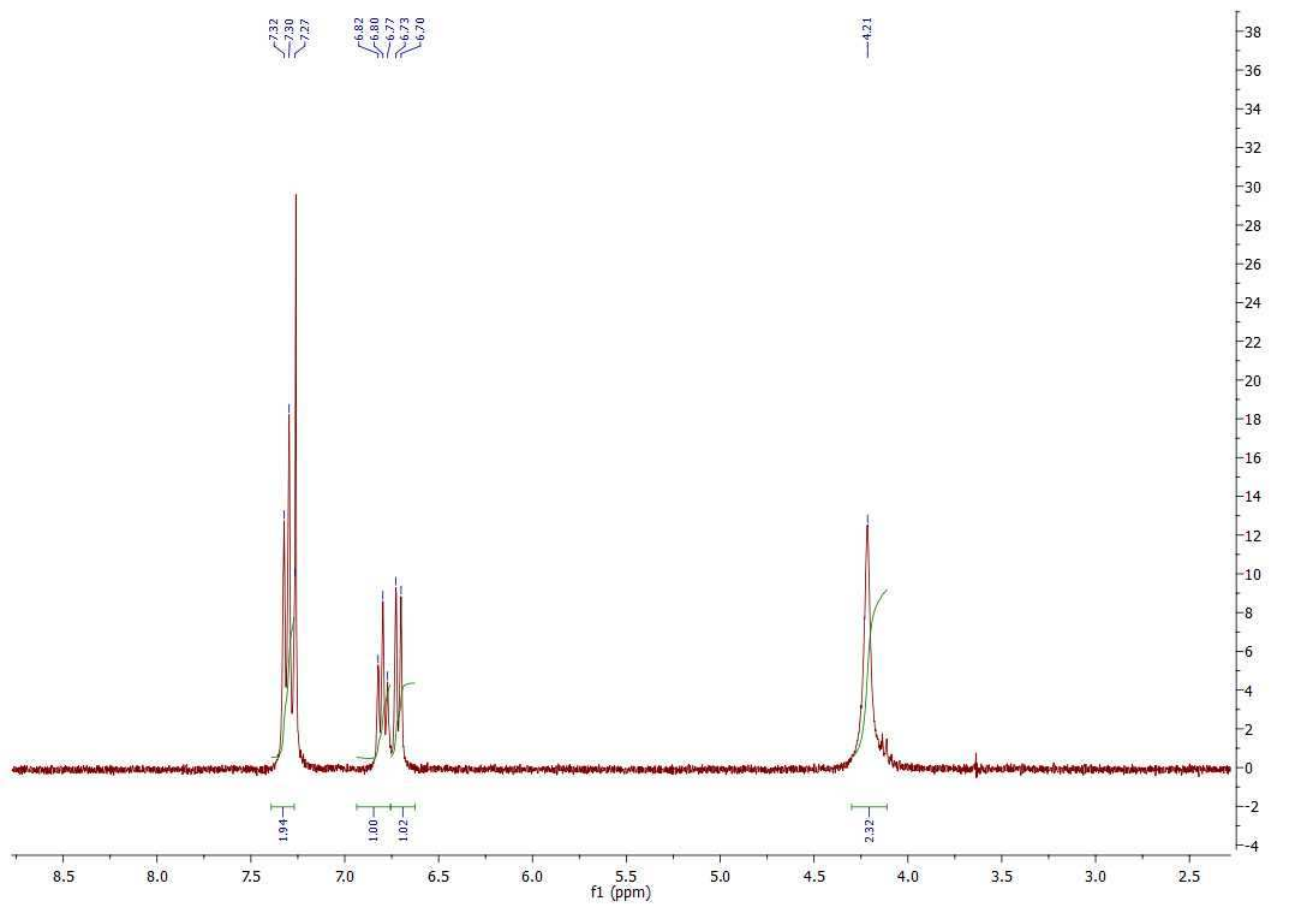


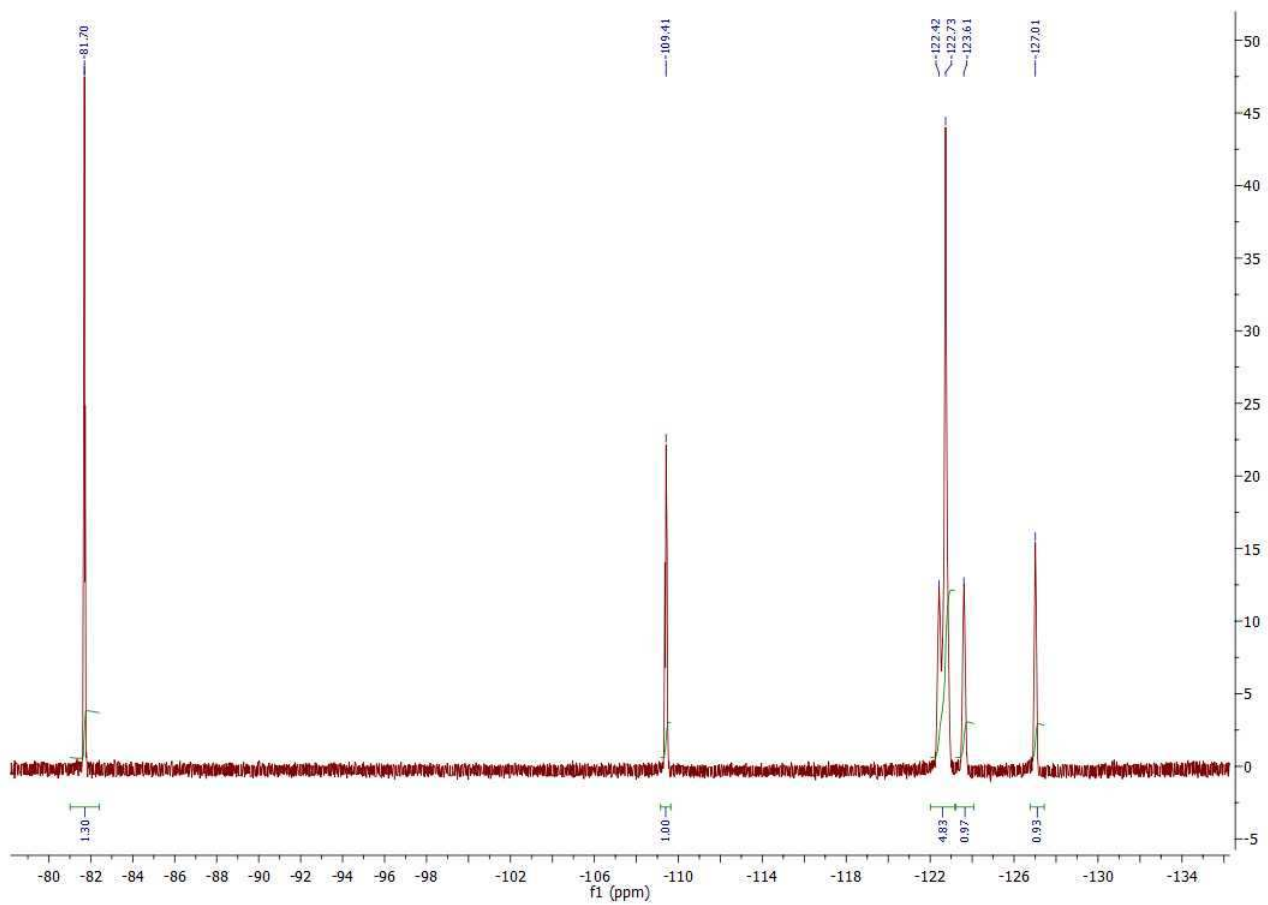
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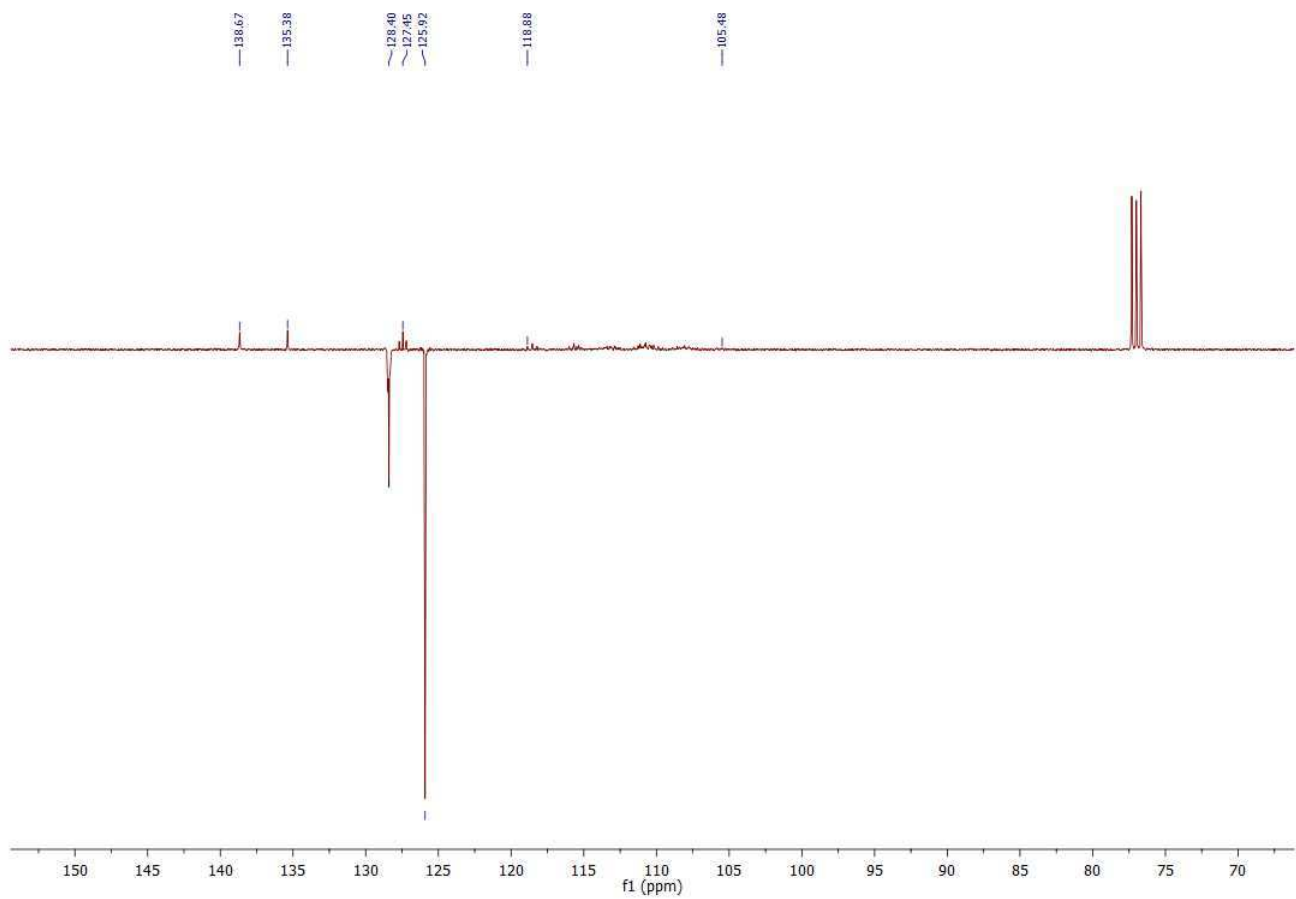
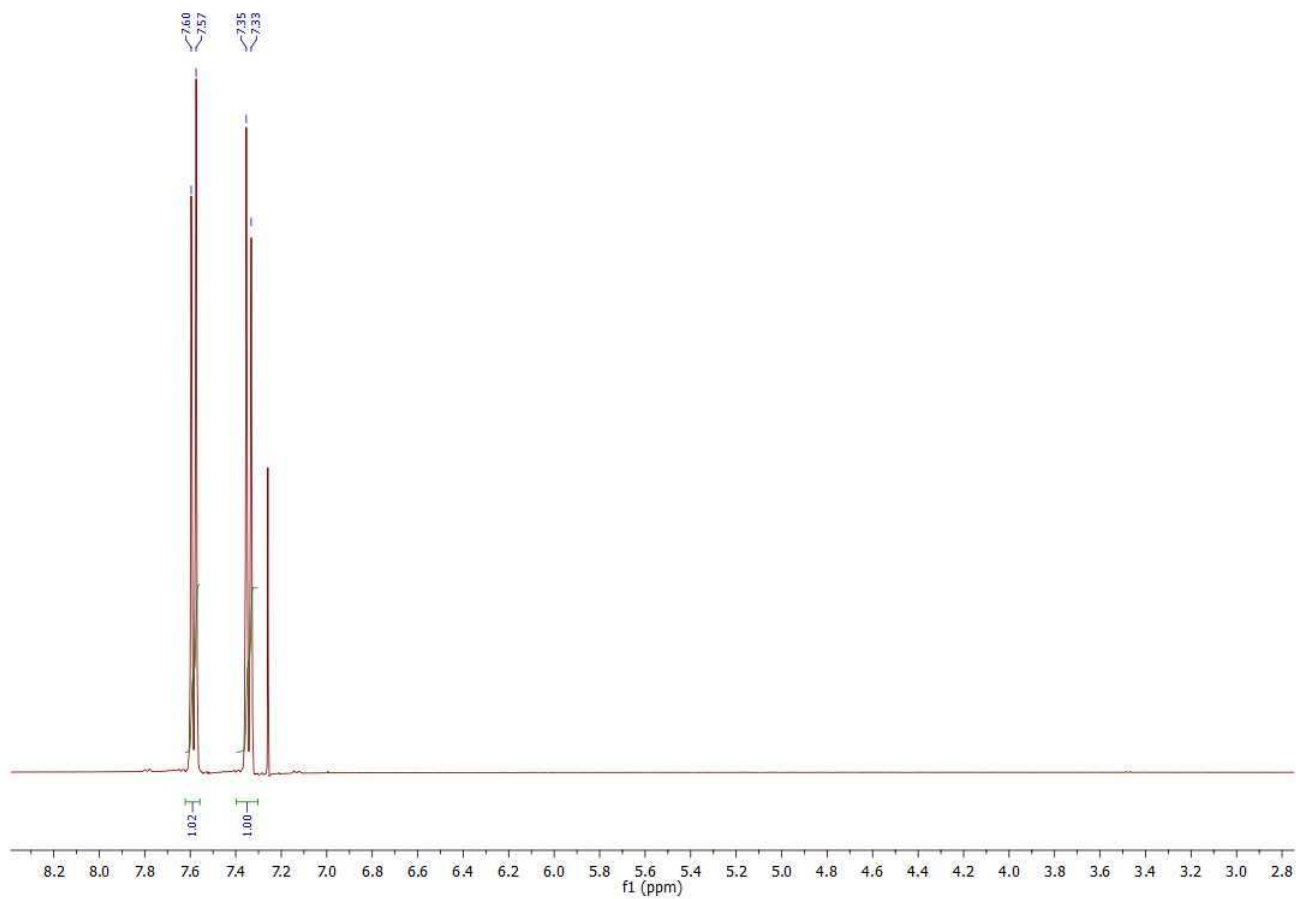


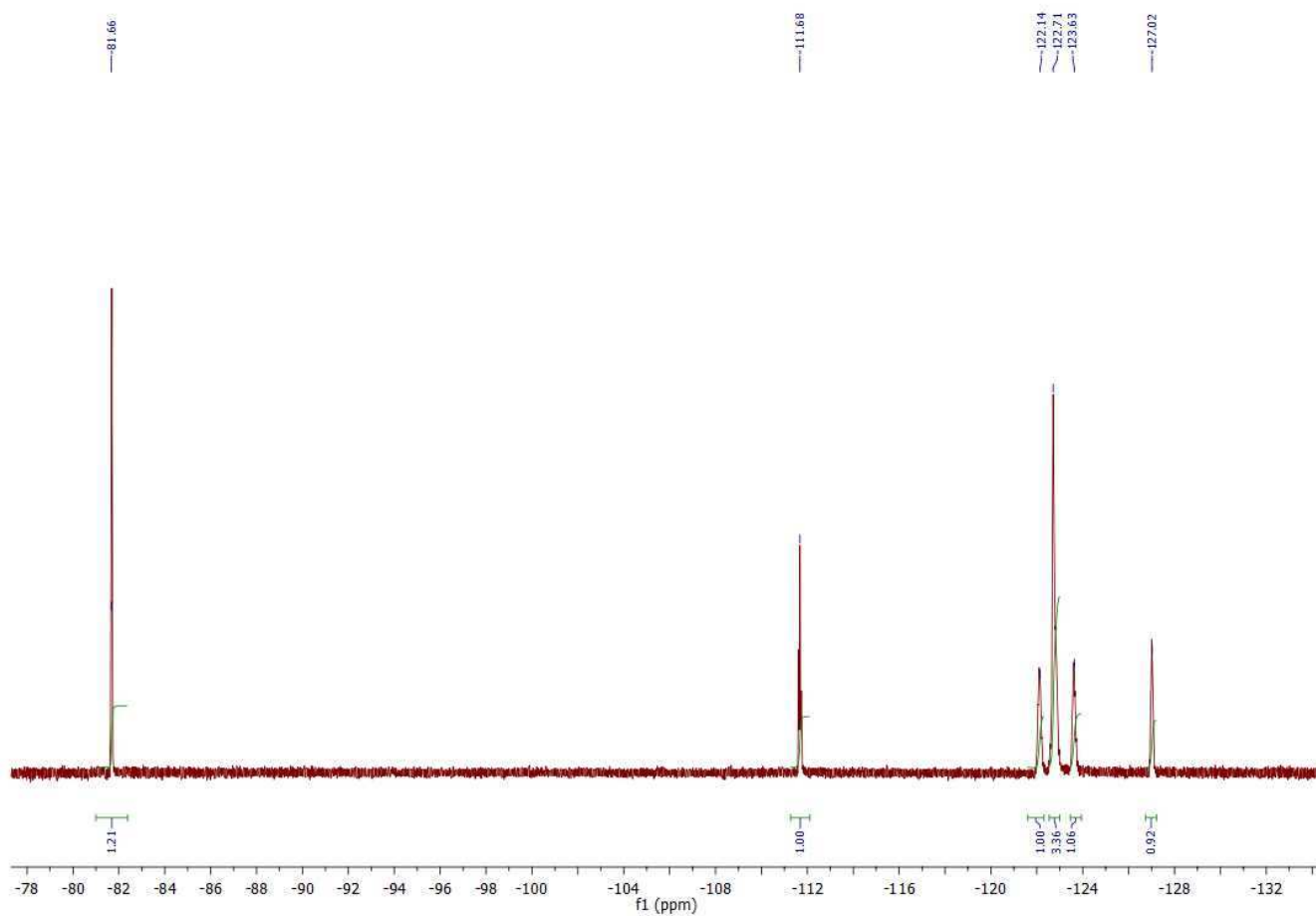
2-(*n*-Perfluorooctyl)aniline (7):



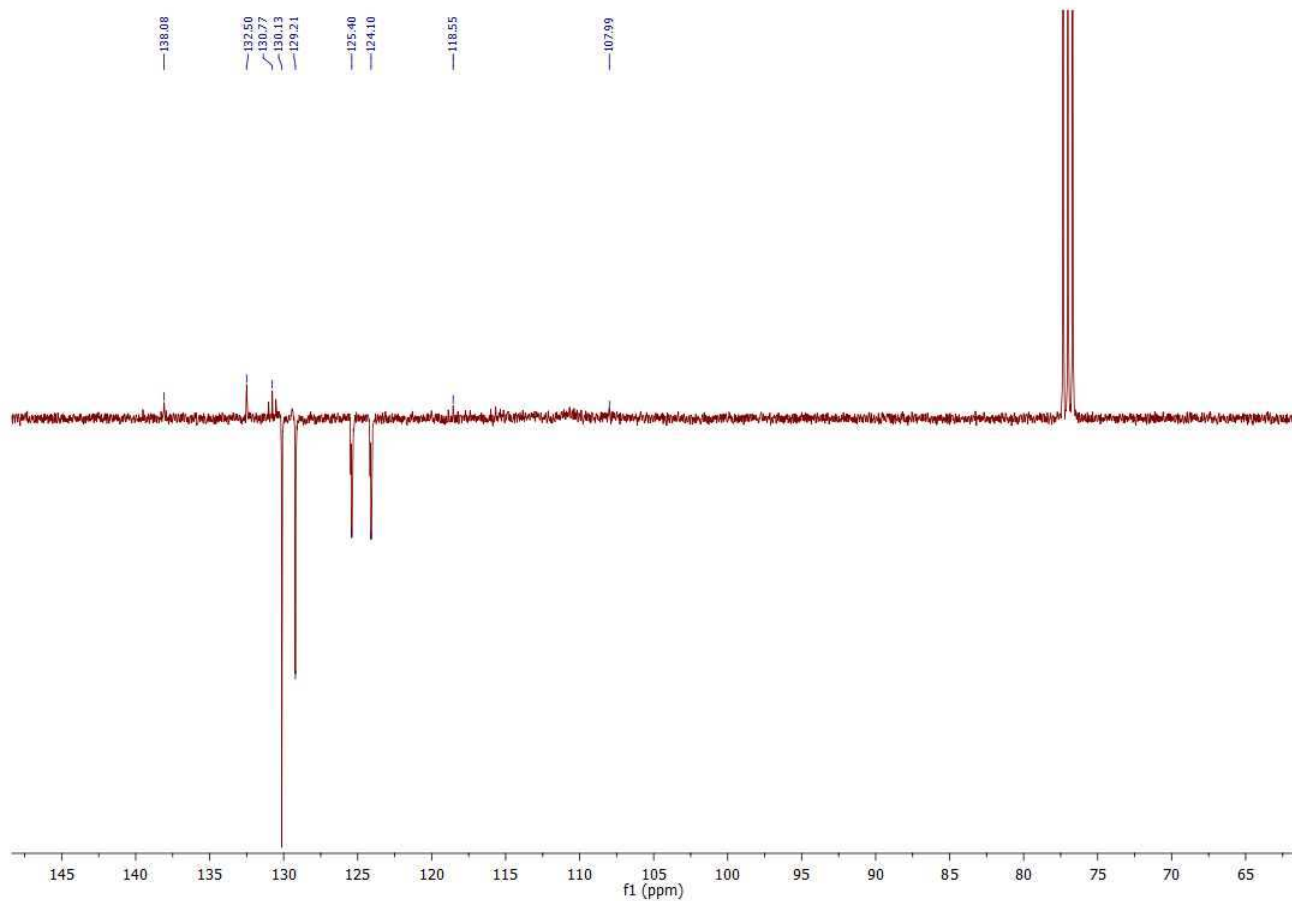
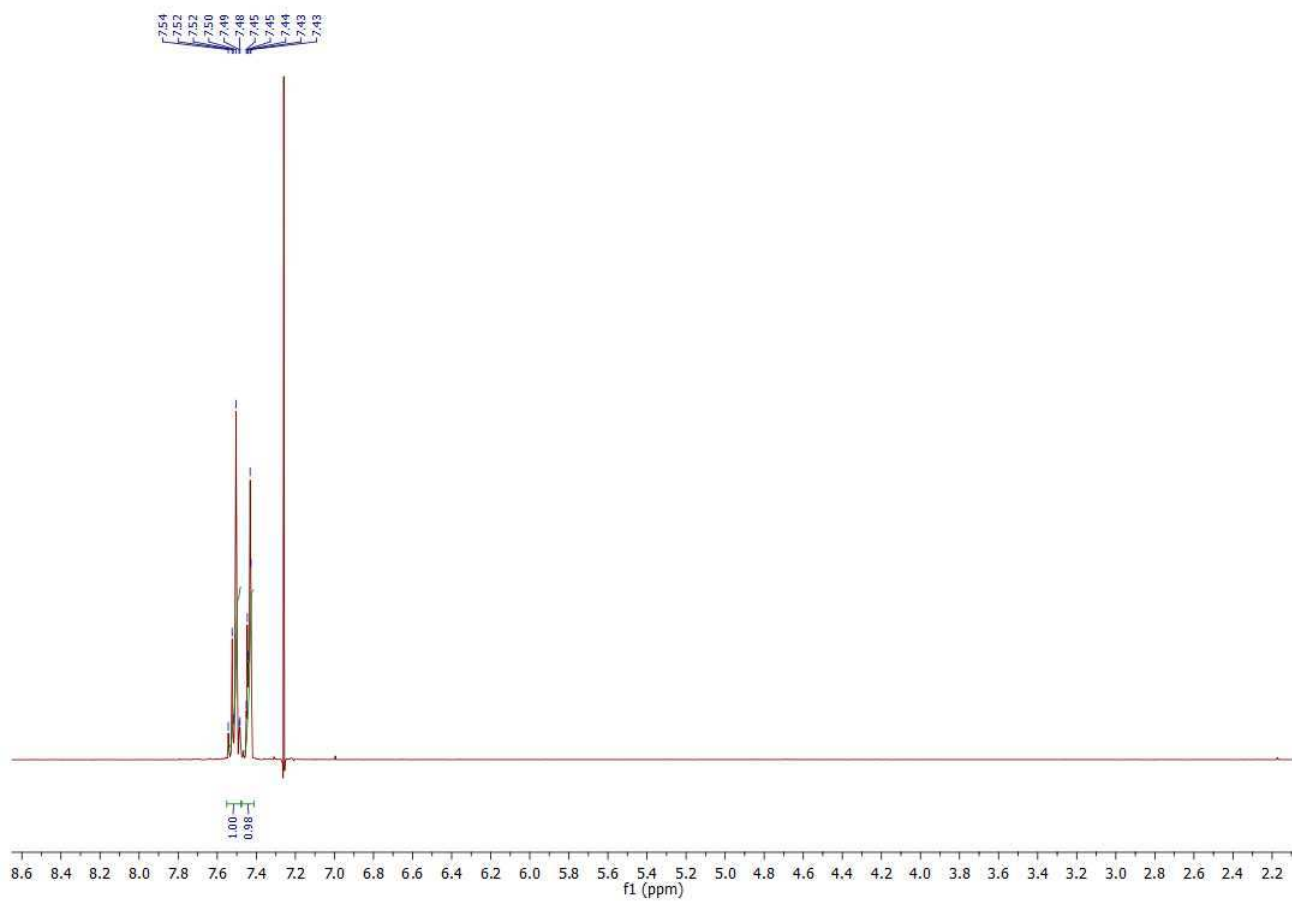


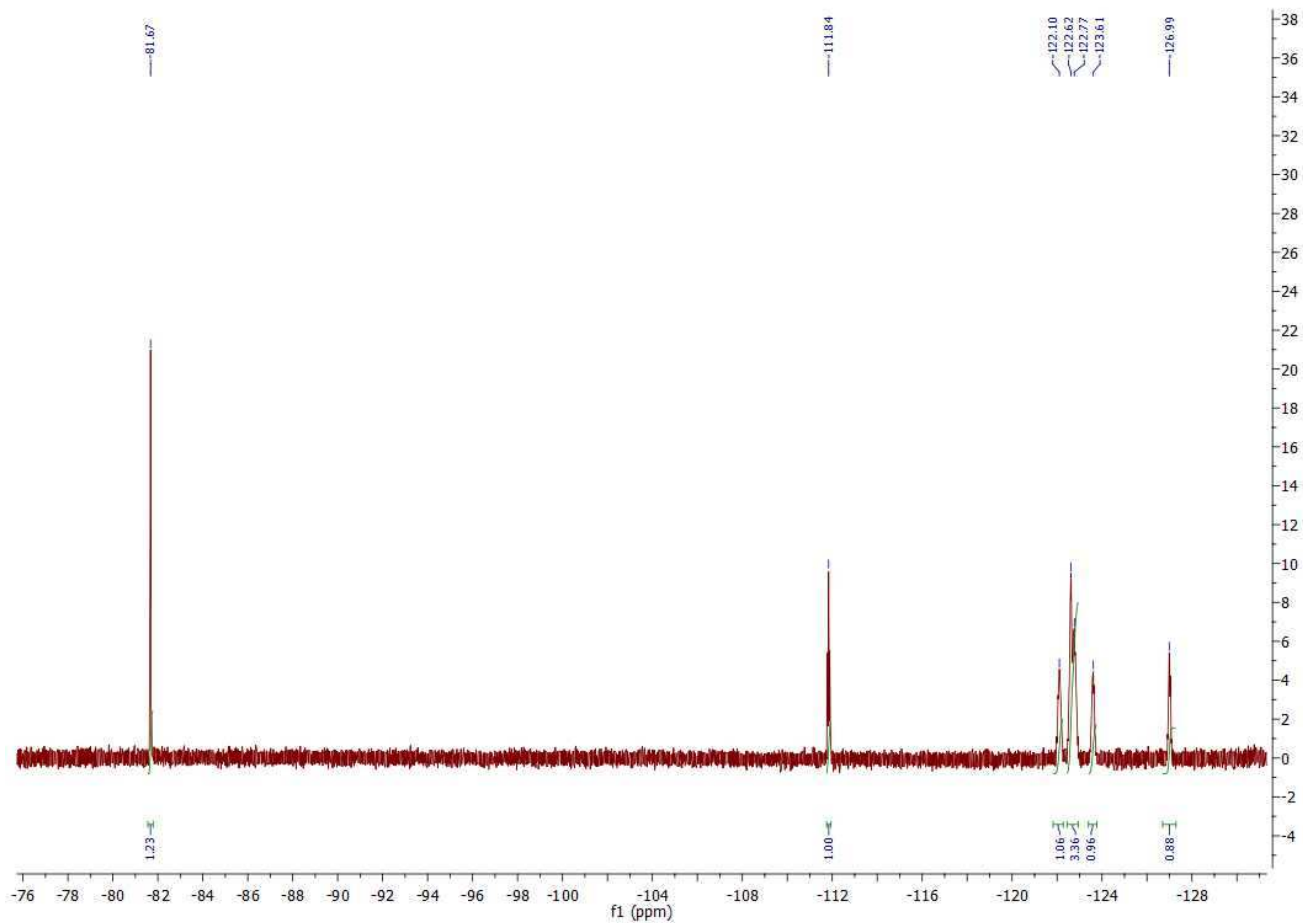
Isothiocyanato-4-(*n*-perfluorooctyl)benzene (8):



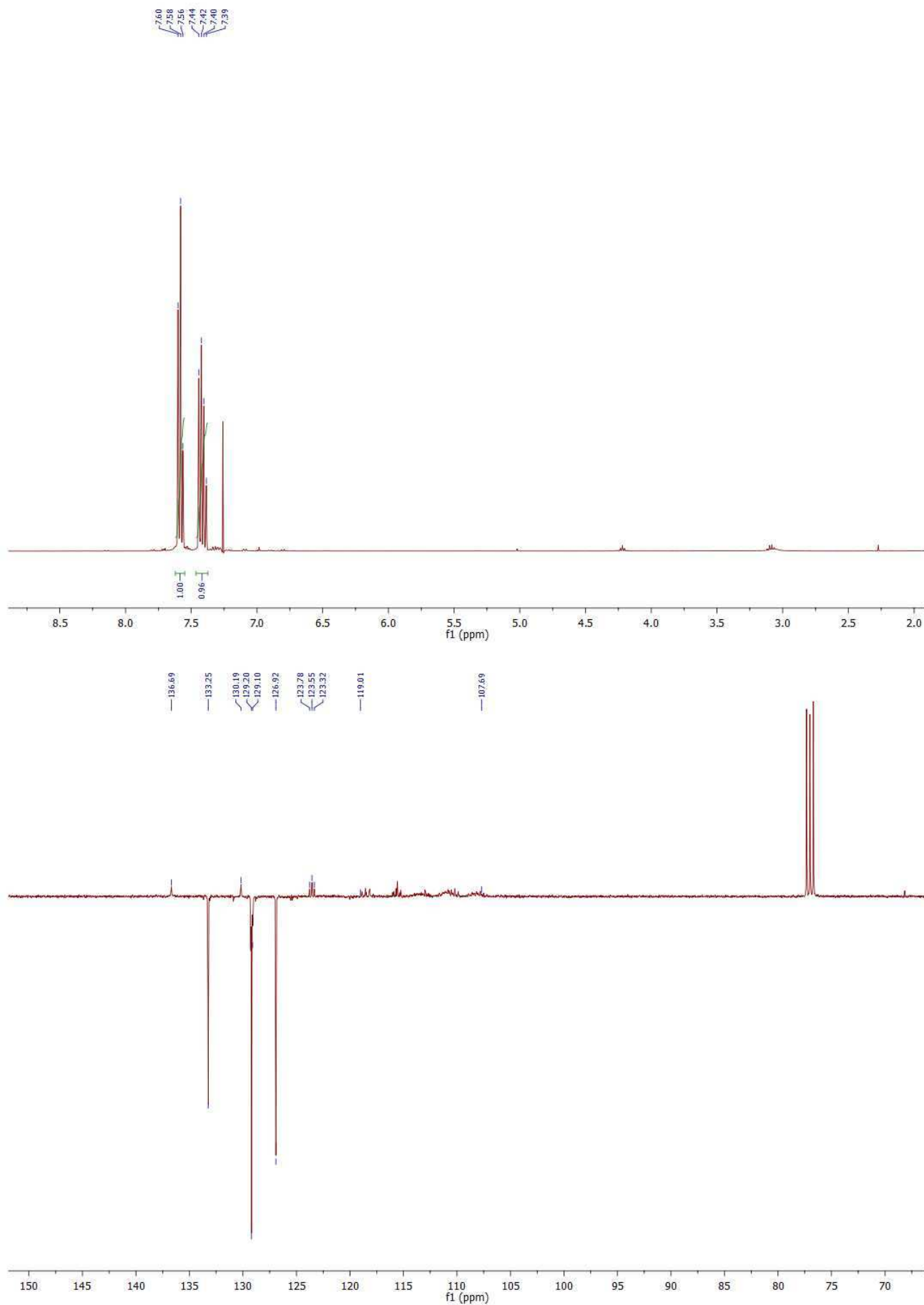


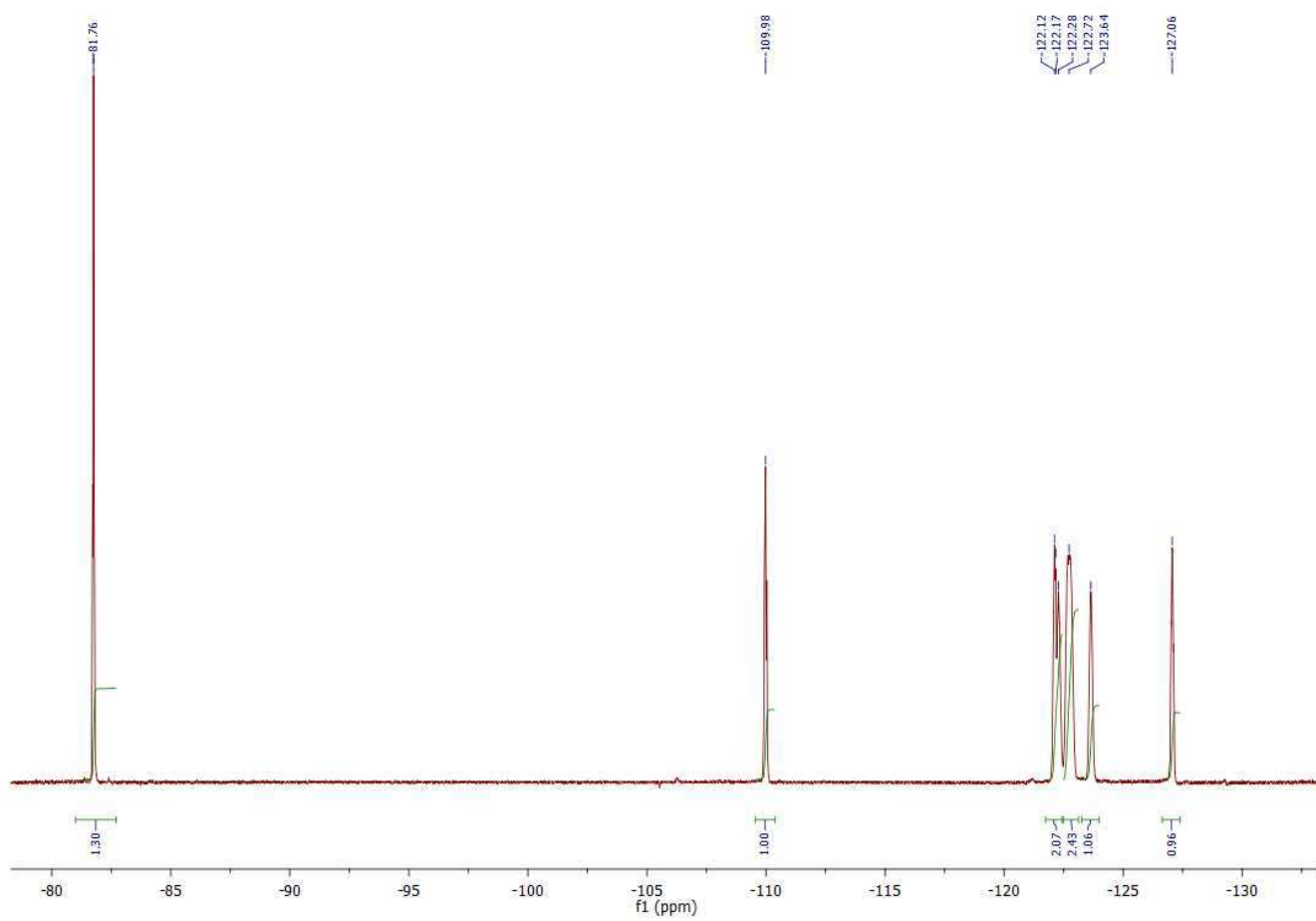
Isothiocyanato-3-(*n*-perfluorooctyl)benzene (9):



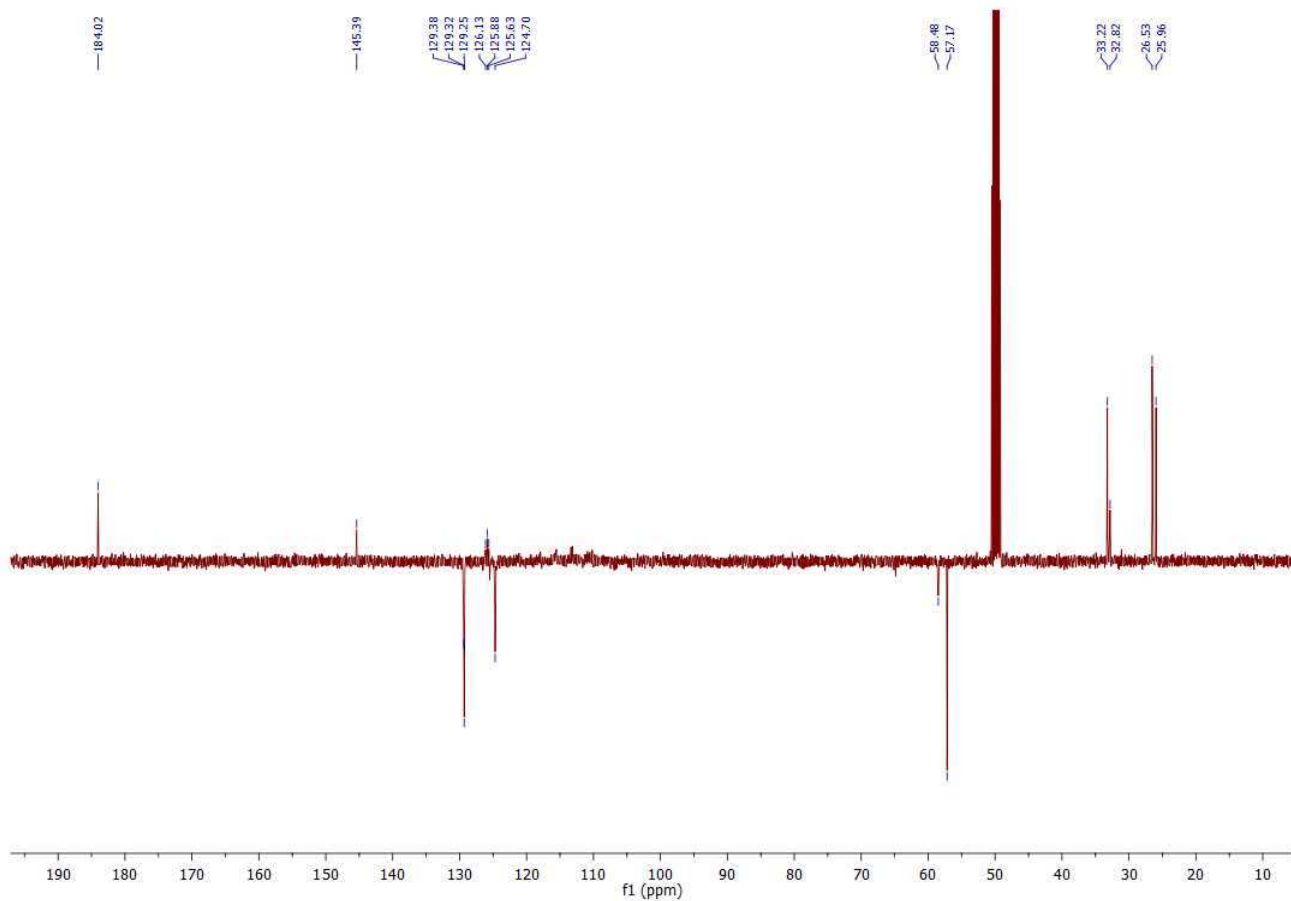
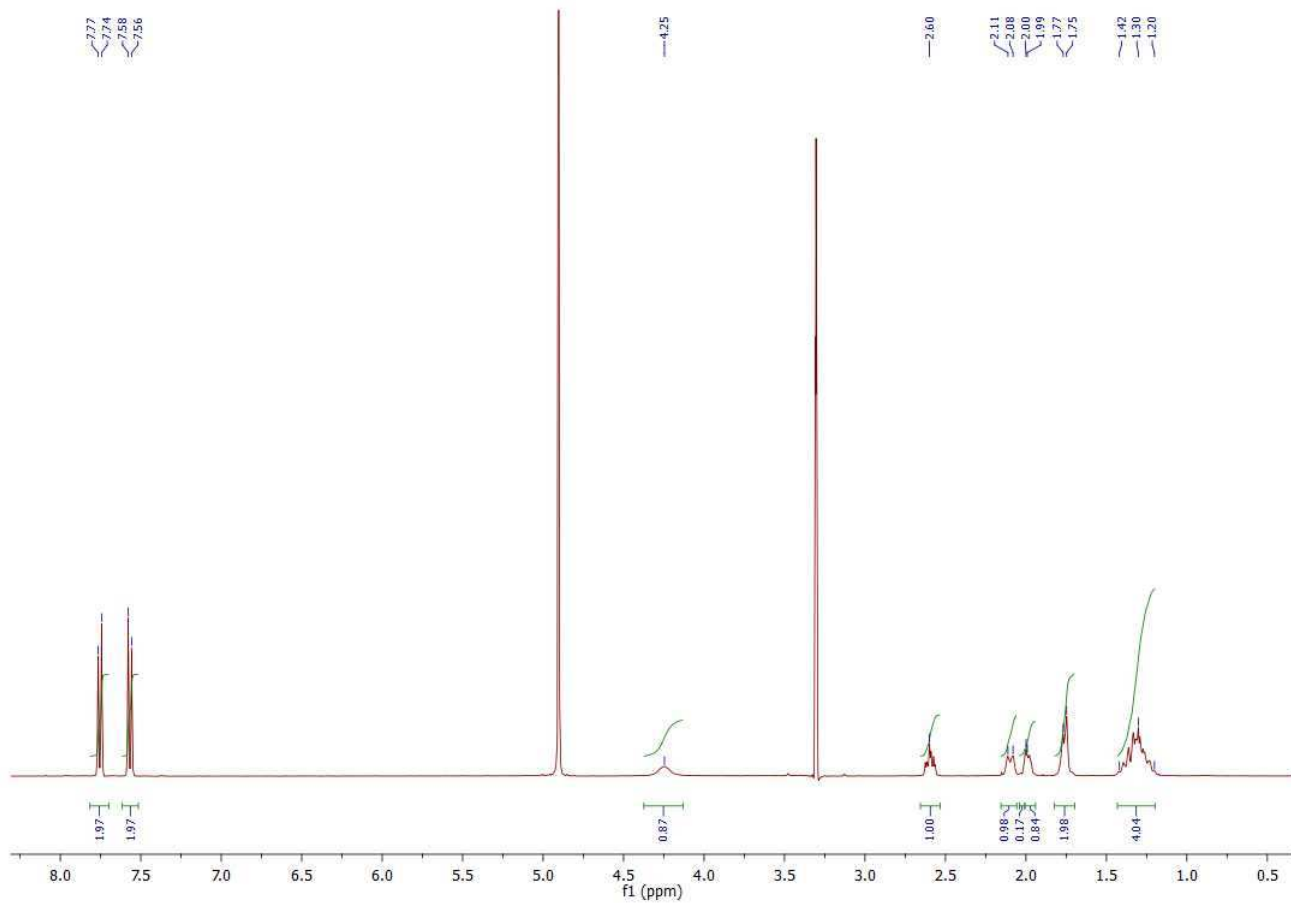


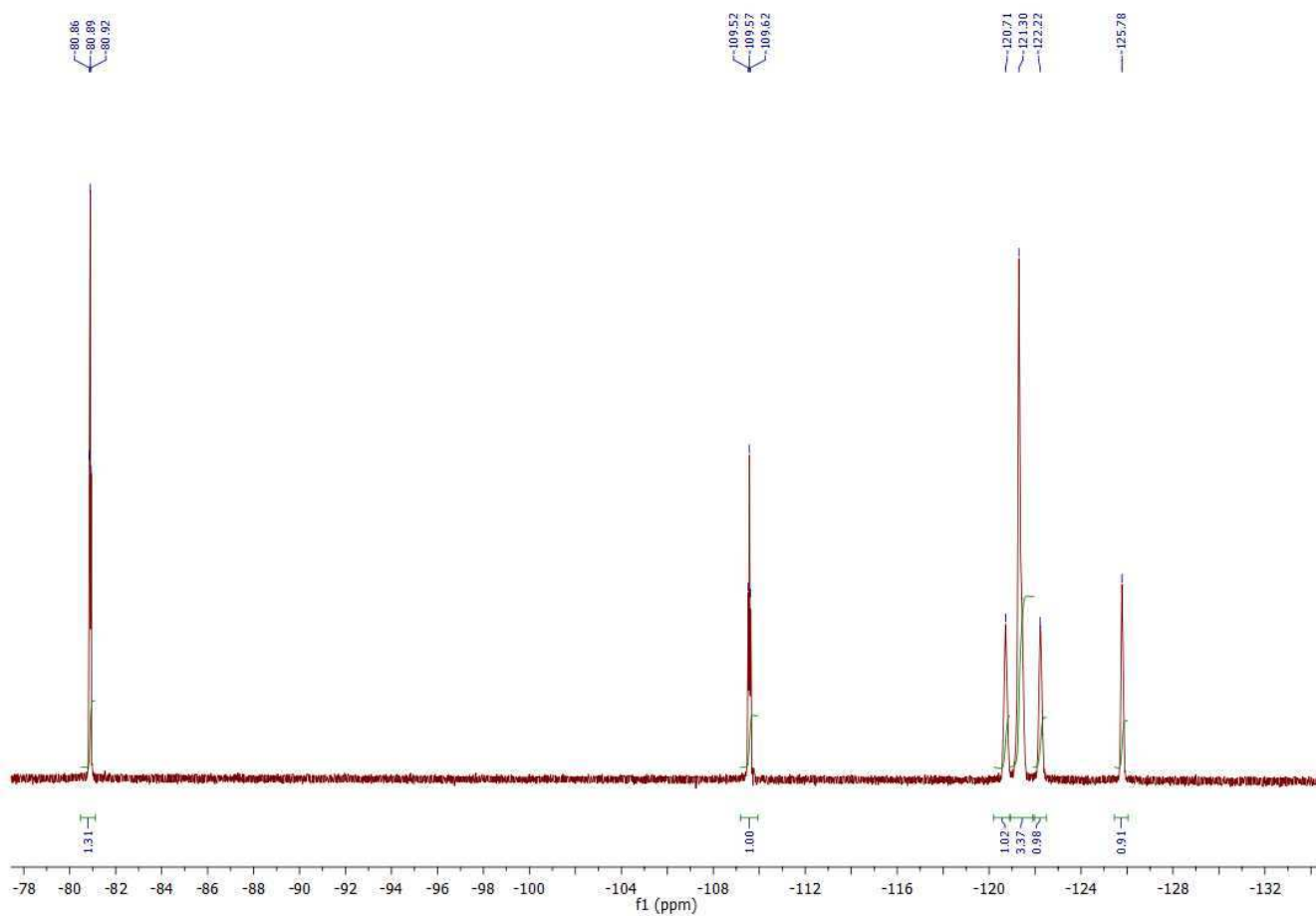
Isothiocyanato-2-(*n*-perfluorooctyl)benzene (10):



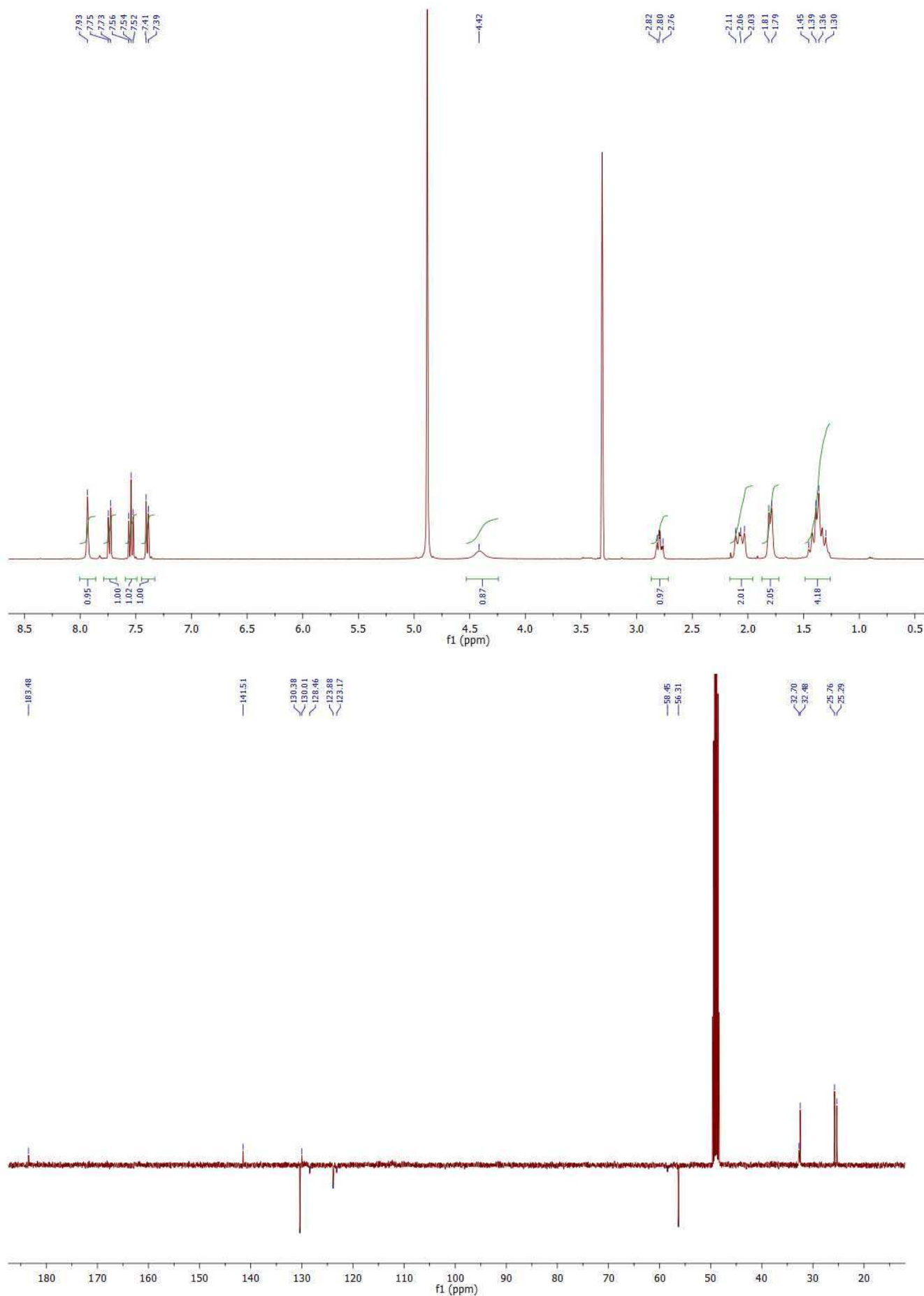


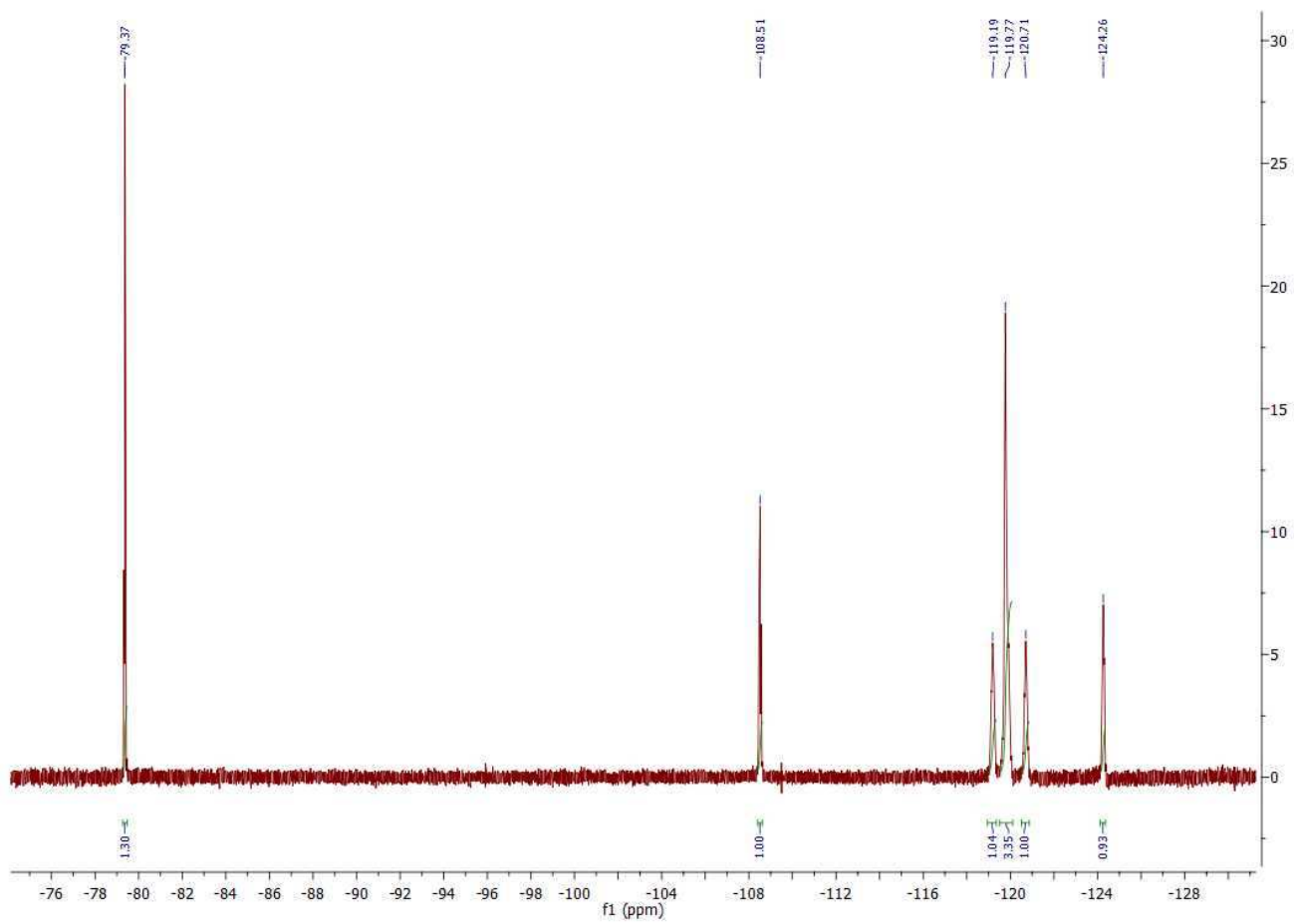
1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[4-(*n*-Perfluorooctyl)phenyl]thiourea (1):



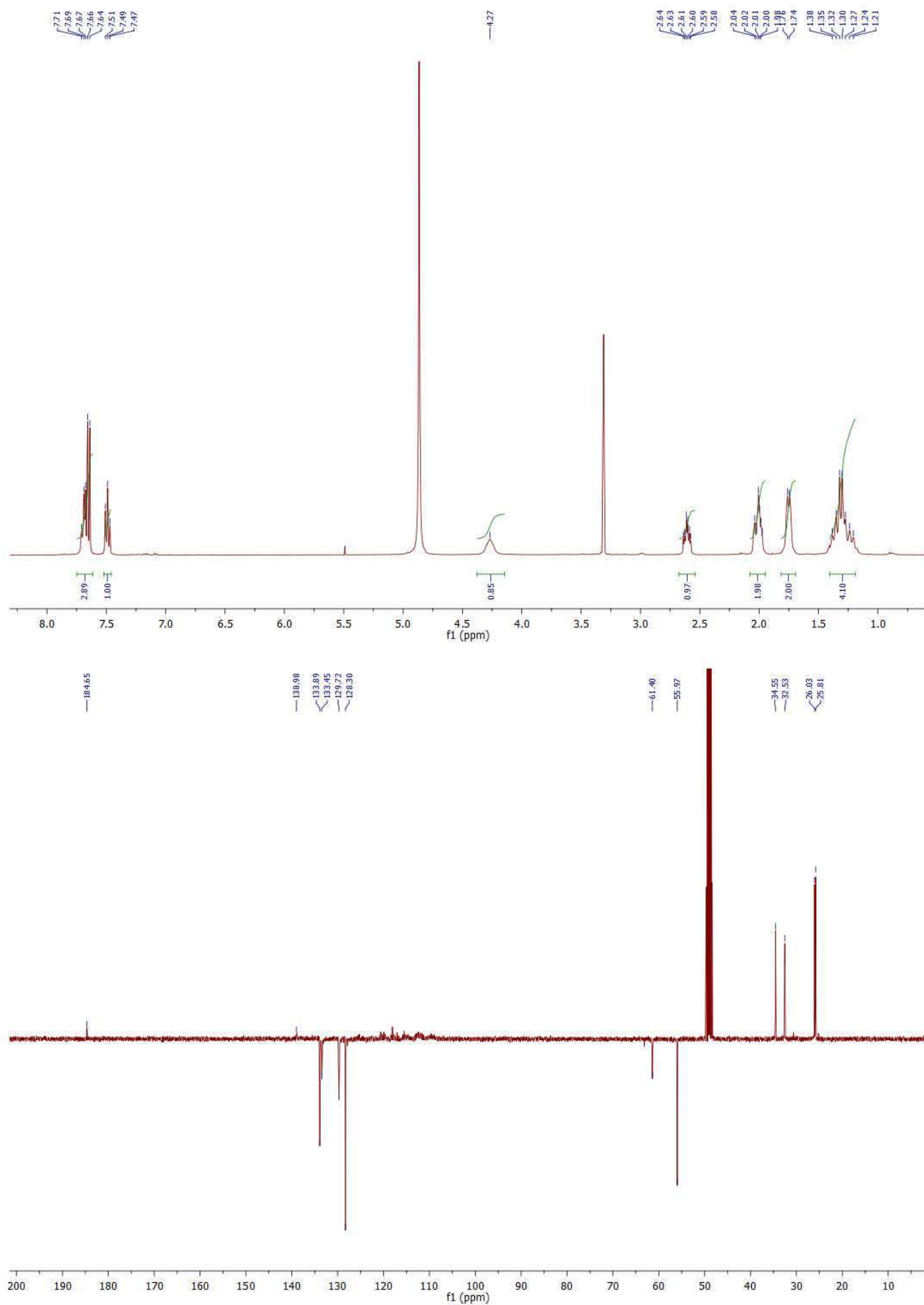


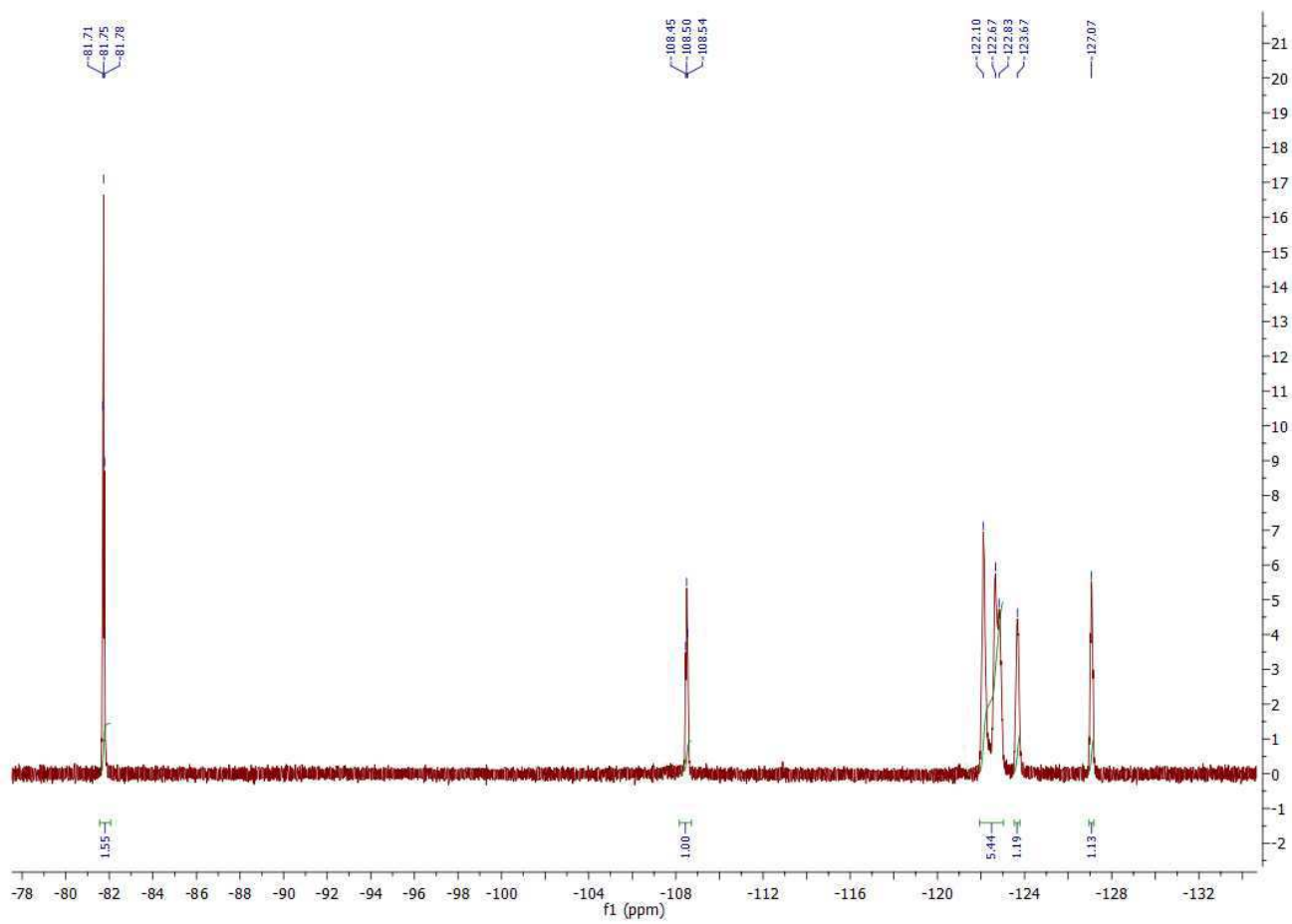
1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[3-(*n*-Perfluorooctyl)phenyl]thiourea (2):



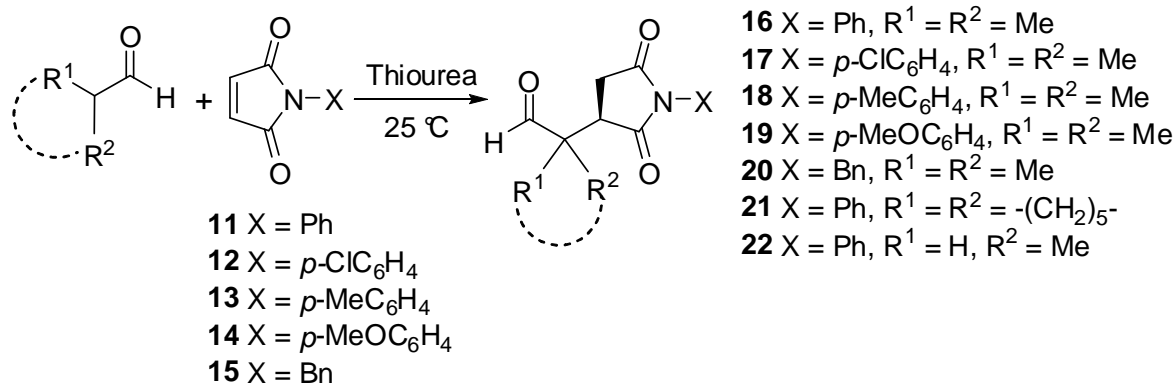


1-[(1*R*,2*R*)-2-Aminocyclohexyl]-3-[2-(*n*-Perfluorooctyl)phenyl]thiourea (3):





Michael addition of aldehydes to *N*-substituted maleimides.

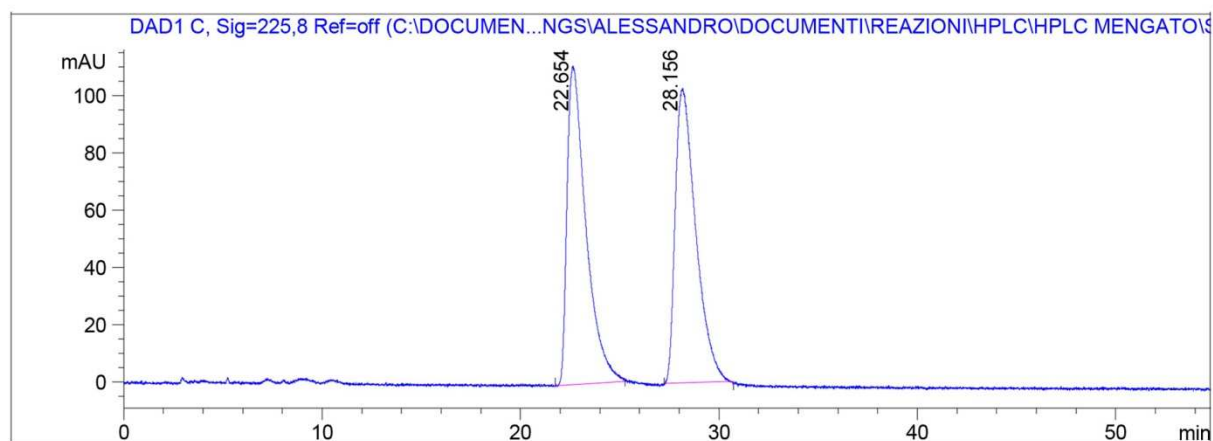


N-substituted maleimides **11**,^[1] **12-14**,^[2] **15**^[3] were synthesized as described in the literature. Reaction products **16-22** are known compounds and their spectroscopic data were in full agreement with those reported in the literature.^[4,5] For compounds **16-21** configuration of the major enantiomer obtained was established by comparison of measured HPLC retention times and optical rotations with those reported in the literature. Compound **22** was obtained as a mixture of diastereomers in a 1.4/1 ratio as evaluated by ¹H NMR analysis of the crude reaction product. In this case, configurations of the major enantiomers obtained were not established. HPLC conditions are here reported:

2-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-2-methylpropanal (16)

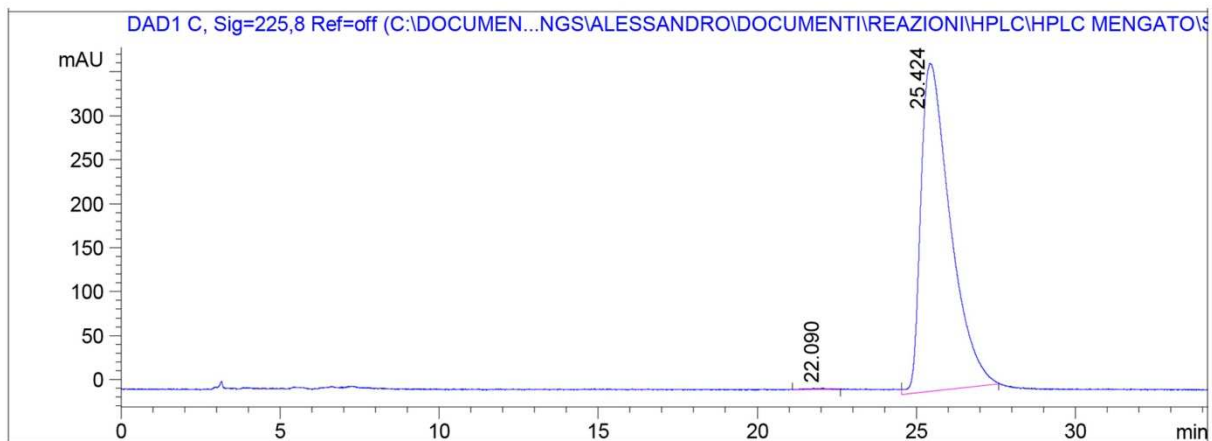
OD-H column, 225 nm, Hexane/2-Propanol = 75:25, flow rate = 1 mL*min⁻¹.

Racemic mixture



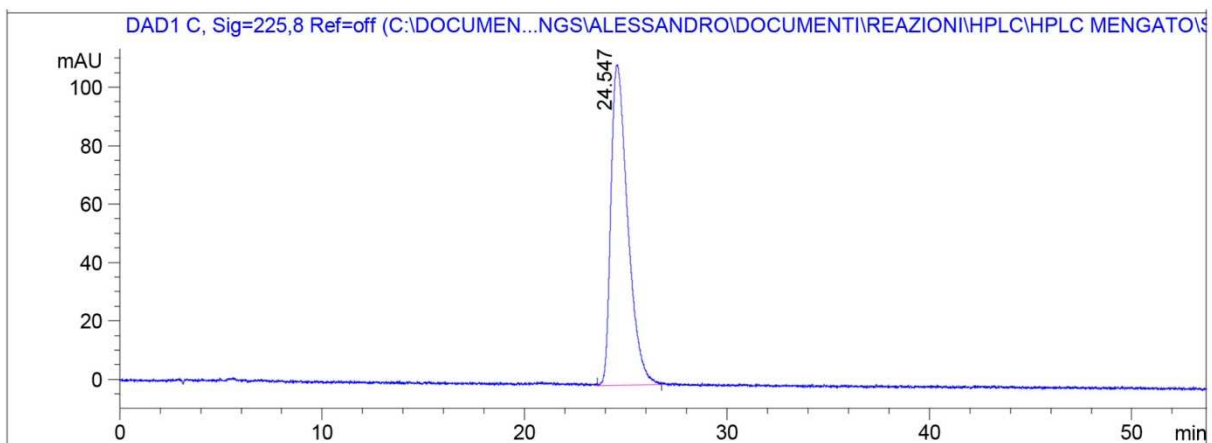
Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	22.654	MM	1.101	7358.084	49.891	
2	28.156	MM	1.196	7390.351	50.109	

Catalyst 4 (Table 2, entry 1)



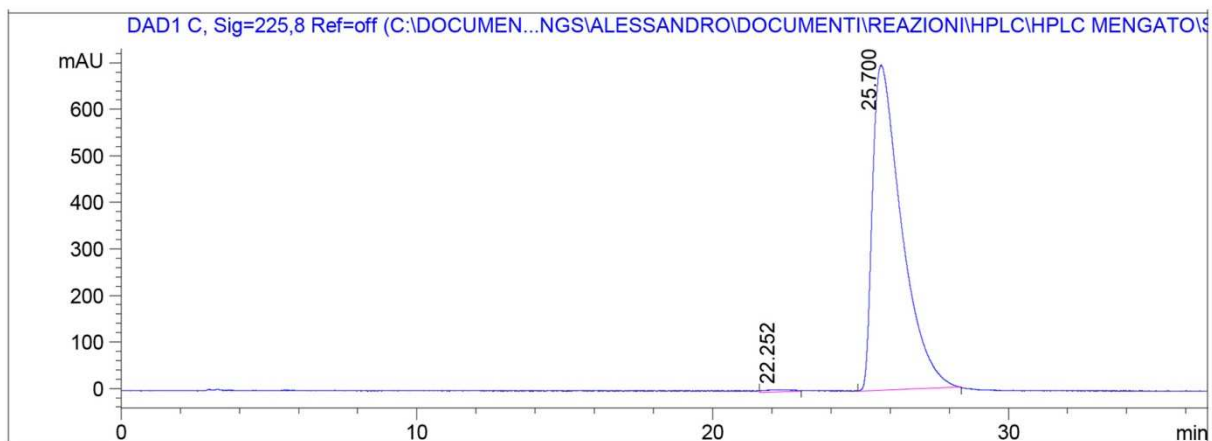
Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	22.090	MM	0.448	39.901	0.166	
2	25.424	MM	1.072	24008.732	99.834	

Catalyst 1 (Table 2, entry 2)



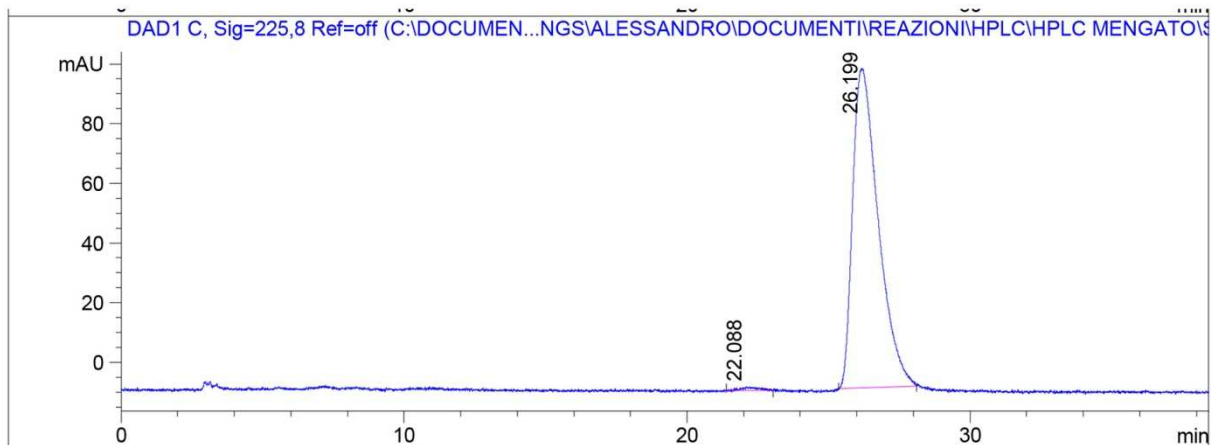
Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	24.547	MM	0.963	6348.832	100.000	

Catalyst 2 (Table 2, entry 3)



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	22.252	MM	0.989	279.155	0.583	
2	25.700	MM	1.135	47629.547	99.417	

Catalyst 3 (Table 2, entry 4)

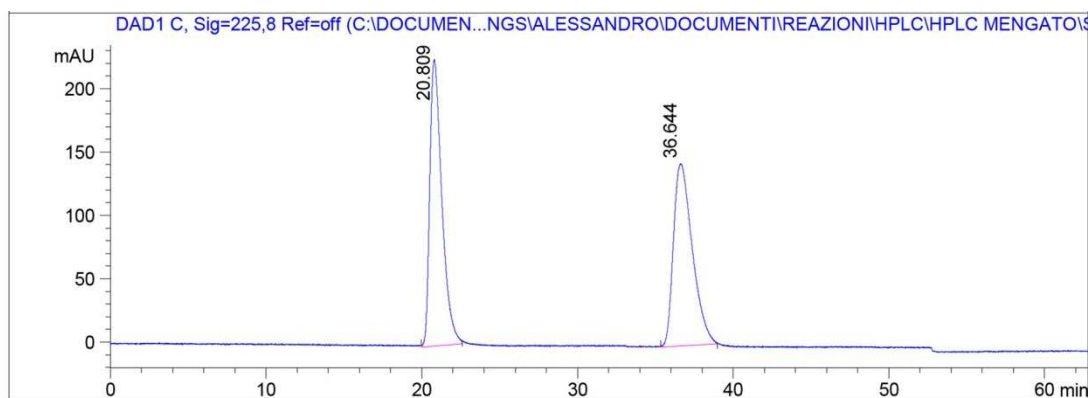


Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	22.088	MM	0.654	52.540	0.775	
2	26.199	MM	1.046	6727.118	99.225	

2-(1-(4-Chlorophenyl)-2,5-dioxopyrrolidin-3-yl)-2-methylpropanal (17)

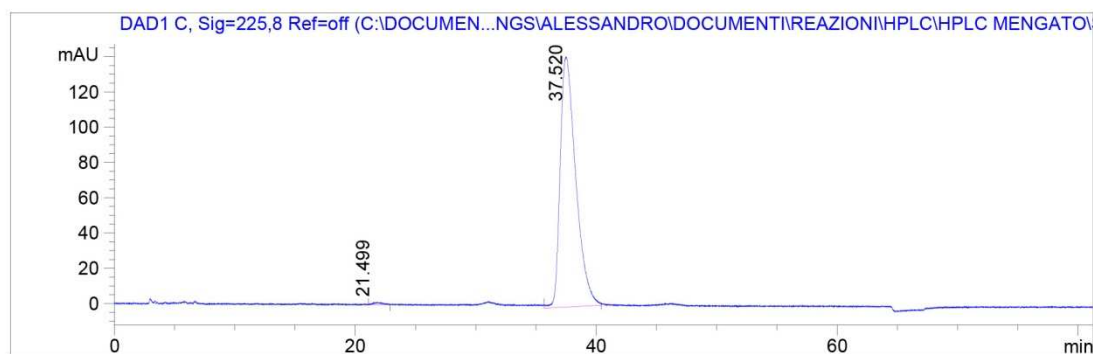
OD-H column, 225 nm, Hexane/2-Propanol = 75:25, flow rate = 1 mL*min⁻¹.

Racemic mixture



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	20.809	MM	0.897	12158.909	50.140	
2	36.644	MM	1.401	12090.836	49.860	

Catalyst 1 (Table 3, entry 1)

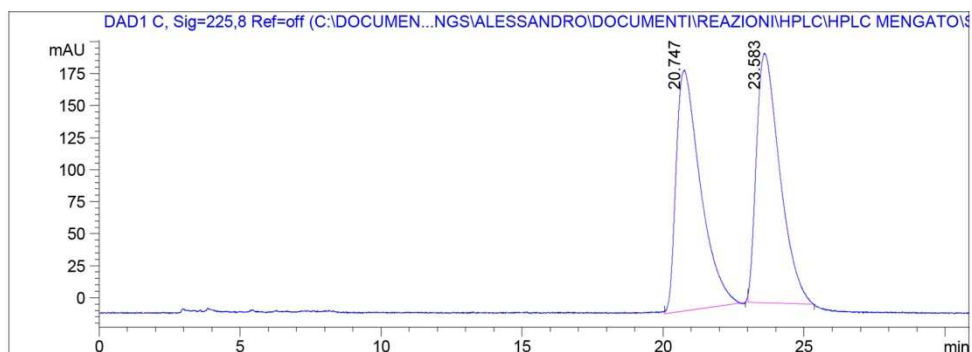


Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	21.499	MM	0.702	72.311	0.564	
2	37.520	MM	1.496	12750.869	99.436	

2-(2,5-Dioxo-1-p-tolylpyrrolidin-3-yl)-2-methylpropanal (18)

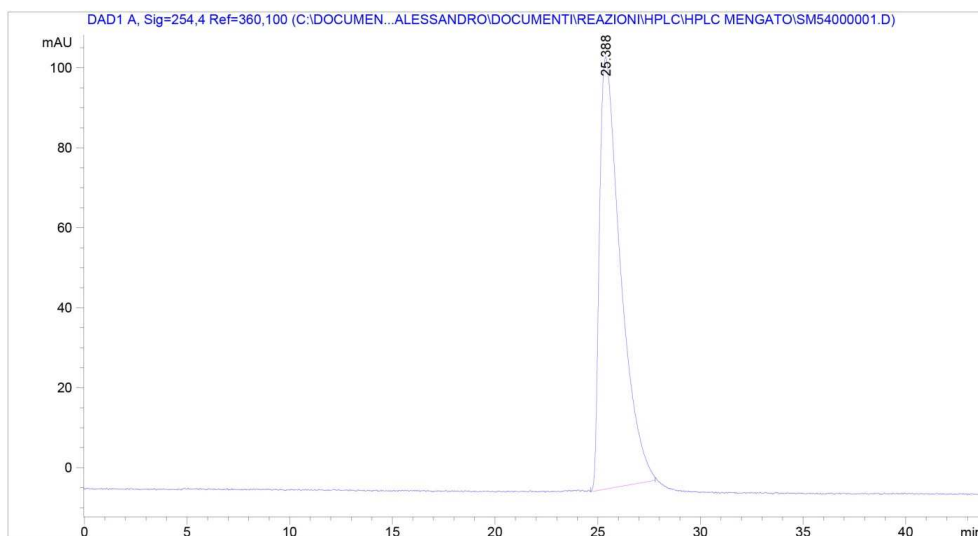
OD-H column, 225 nm, Hexane/2-Propanol = 75:25, flow rate = 1 mL*min⁻¹.

Racemic mixture



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	20.747	MM	1.000	11303.103	50.091	
2	23.583	MM	0.963	11262.214	49.909	

Catalyst 1 (Table 3, entry 2)

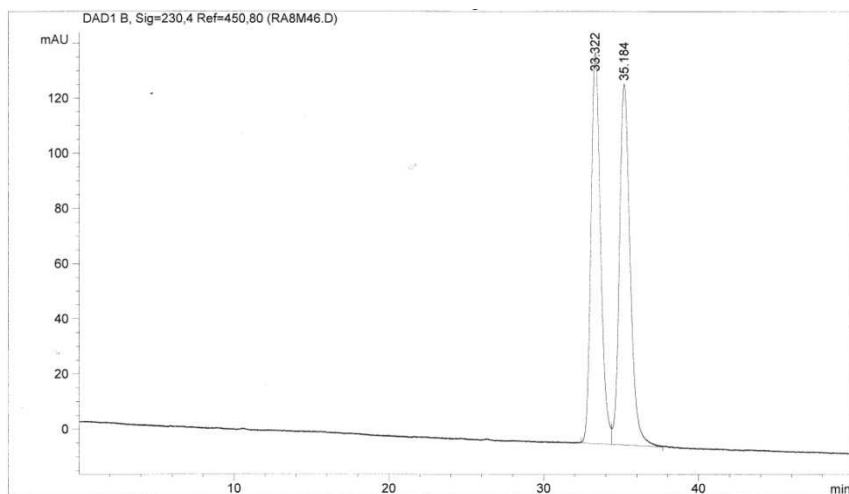


RetTime [min]	k'	Area [mAU*s]	Height [mAU]	Symm.	Width [min]	Plates	Resol	Select
							ution	ivity
25.388	-	7703.85693	108.12427	0.39	1.0733	3099	-	-

2-(1-(4-Methoxyphenyl)-2,5-dioxopyrrolidin-3-yl)-2-methylpropanal (19)

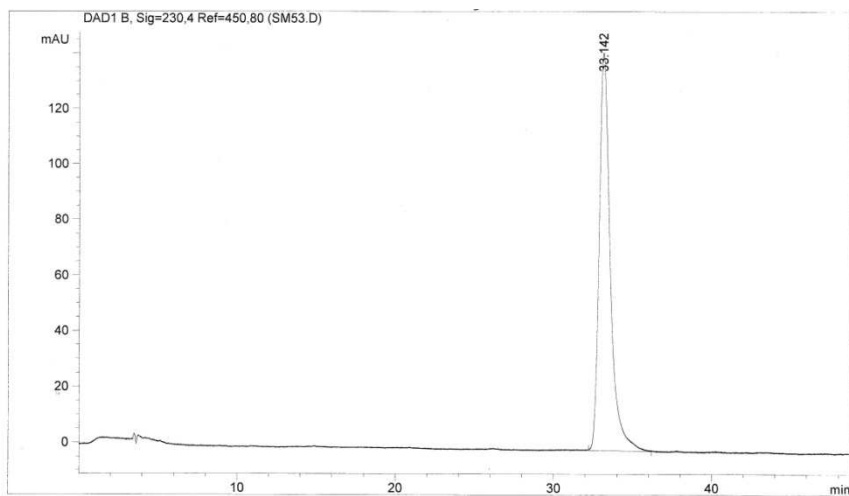
Chiralpak AS-3 column, 230 nm, Hexane/Ethanol = 80:20, flow rate = 0.8 mL*min⁻¹.

Racemic mixture



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.322	BV	0.6676	6122.04688	141.81790	49.2914
2	35.184	VB	0.7373	6298.06445	130.90422	50.7086

Catalyst 1 (Table 3, entry 3)

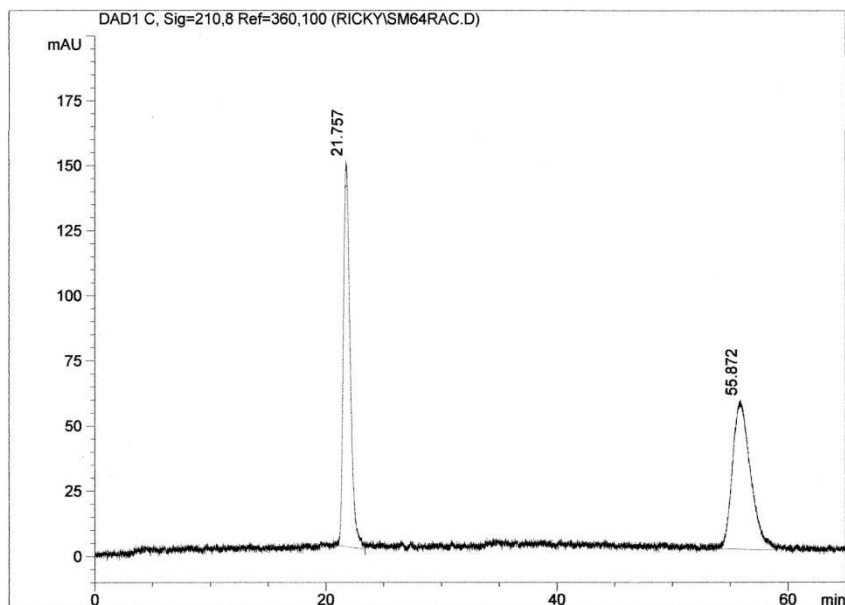


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	33.142	BB	0.7350	6988.18213	142.78363	100.0000

2-(1-Benzyl-2,5-dioxypyrrolidin-3-yl)-2-methylpropanal (20)

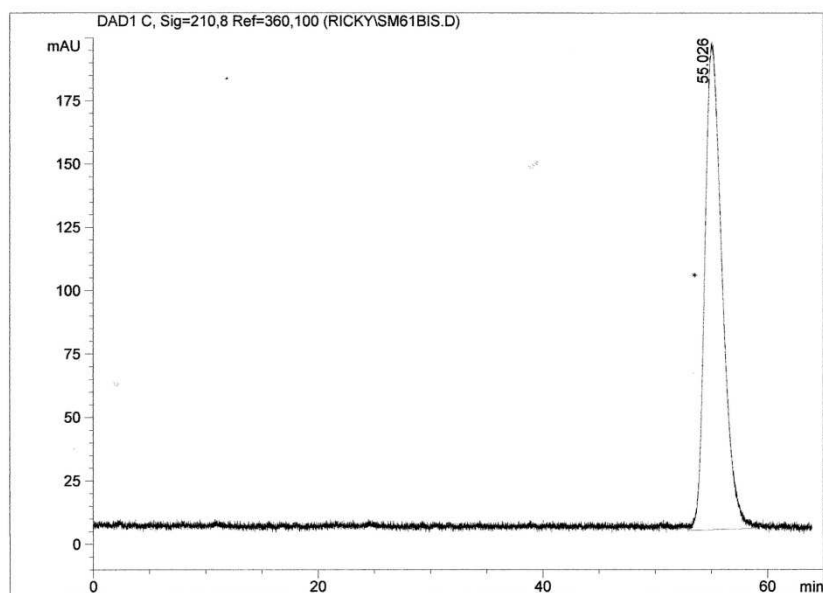
AD column, 210 nm, Hexane/2-Propanol = 80:20, flow rate = 0.5 mL*min⁻¹.

Racemic mixture



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	21.757	MM	0.683	6073.346	49.683	
2	55.872	MM	1.794	6150.751	50.317	

Catalyst 1 (Table 3, entry 4)

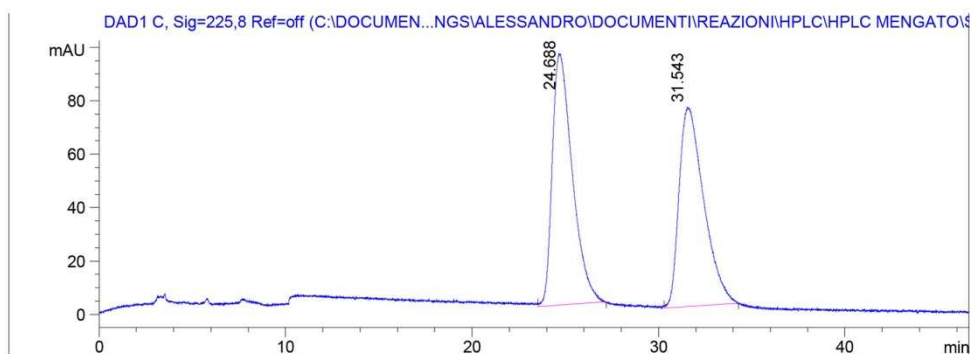


Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	55.026	MM	1.781	20629.014	100.000	

1-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)cyclohexanecarbaldehyde (21)

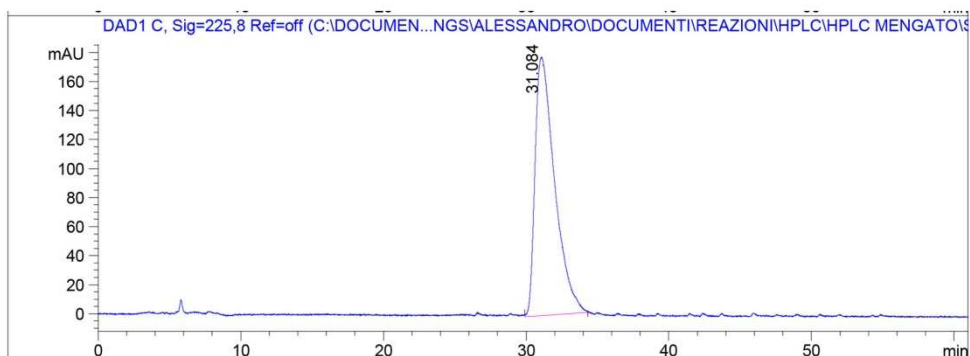
OD-H column, 225 nm, Hexane/2-Propanol = 75:25, flow rate = 1 mL*min⁻¹.

Racemic mixture



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	24.688	MM	1.248	7053.496	50.666	
2	31.543	MM	1.531	6868.023	49.334	

Catalyst 1 (Table 3, entry 5)

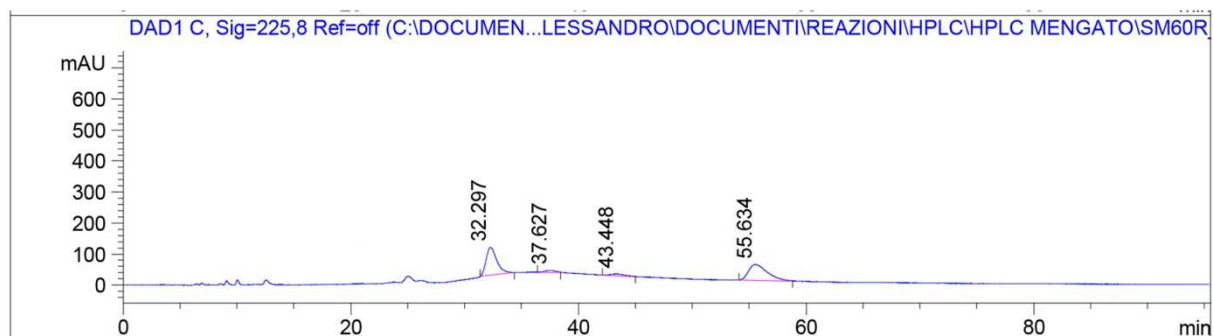


Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	31.084	MM	1.591	17015.232	100.000	

2-(2,5-dioxo-1-phenylpyrrolidin-3-yl)propanal (22)

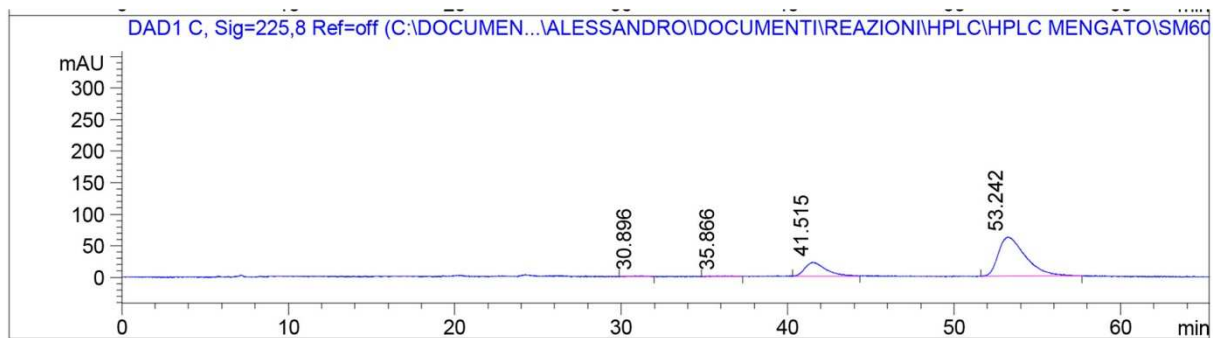
AD column, 225 nm, Hexane/2-Propanol = 4:1, flow rate = 0.5 mL*min⁻¹.

Racemic diastomeric mixture



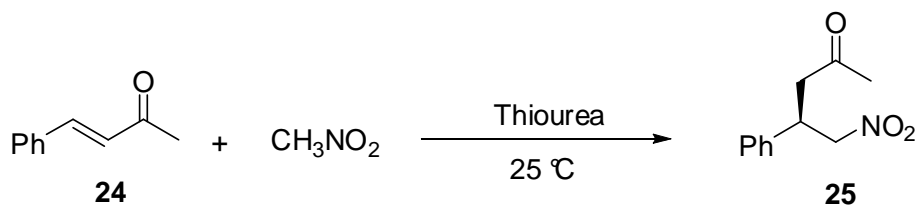
Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	32.297	MM	1.093	5938.101	46.125	
2	37.627	MM	1.088	472.320	3.669	
3	43.448	MM	1.457	594.905	4.621	
4	55.634	MM	1.890	5868.683	45.586	

Catalyst 1 (Table 3, entry 6)



Peak #	RT [min]	Type	Width [min]	Area	Area %	Name
1	30.896	MM	0.799	57.647	0.627	
2	35.866	MM	1.003	75.150	0.817	
3	41.515	MM	1.448	1911.132	20.788	
4	53.242	MM	1.905	7149.464	77.767	

Michael addition of nitromethane to 4-phenylbut-3-en-2-one (24).

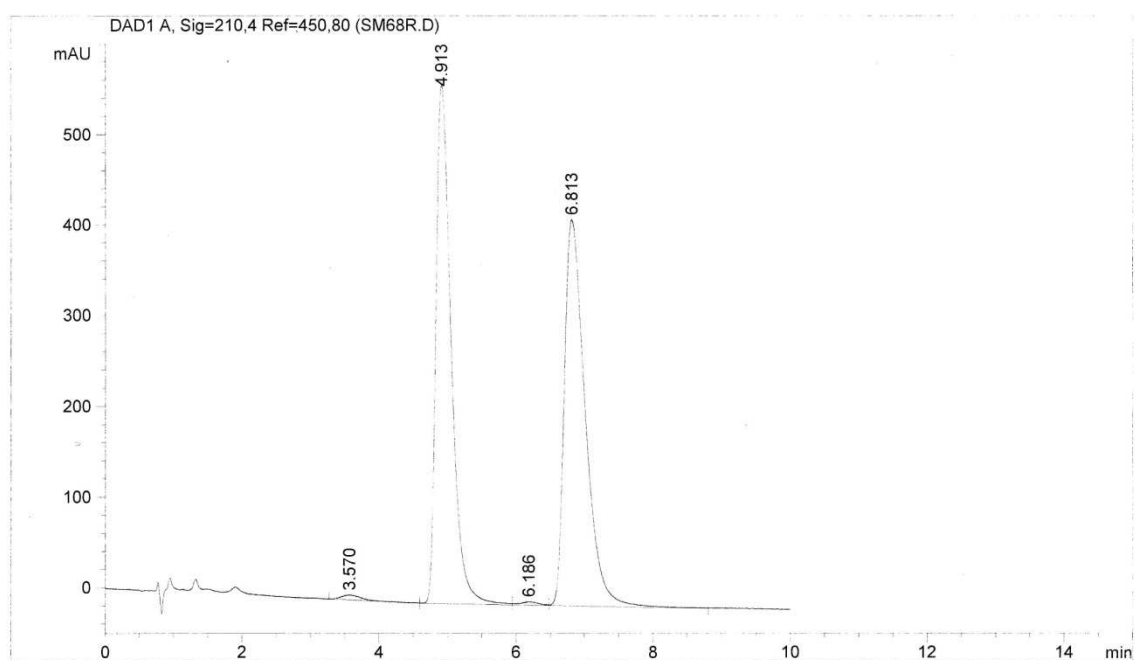


4-Phenylbut-3-en-2-one **24** and nitromethane were used as received. Spectroscopic data of product **25** were in full agreement with those reported in the literature.^[6] Configuration of the major enantiomer obtained was established by comparison of measured optical rotation with the literature value. HPLC conditions are here reported:

5-Nitro-4-(*R*)-phenylpentan-2-one (25)

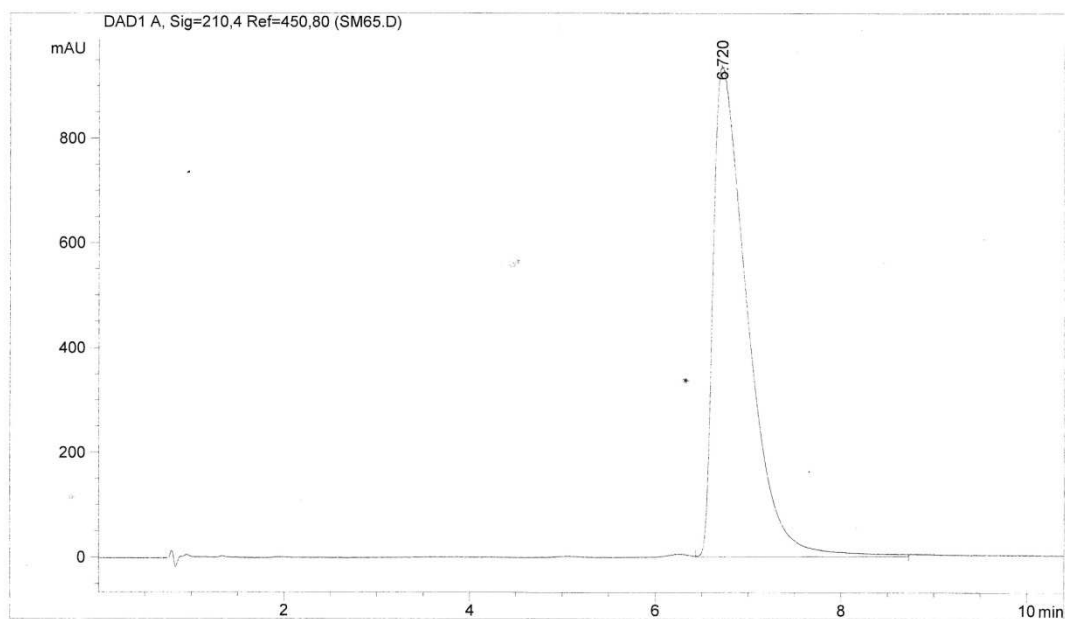
Lux3 Cellulose-3 column, 210 nm, Hexane/2-Propanol = 75:25, flow rate = 0,8 mL*min⁻¹.

Racemic mixture



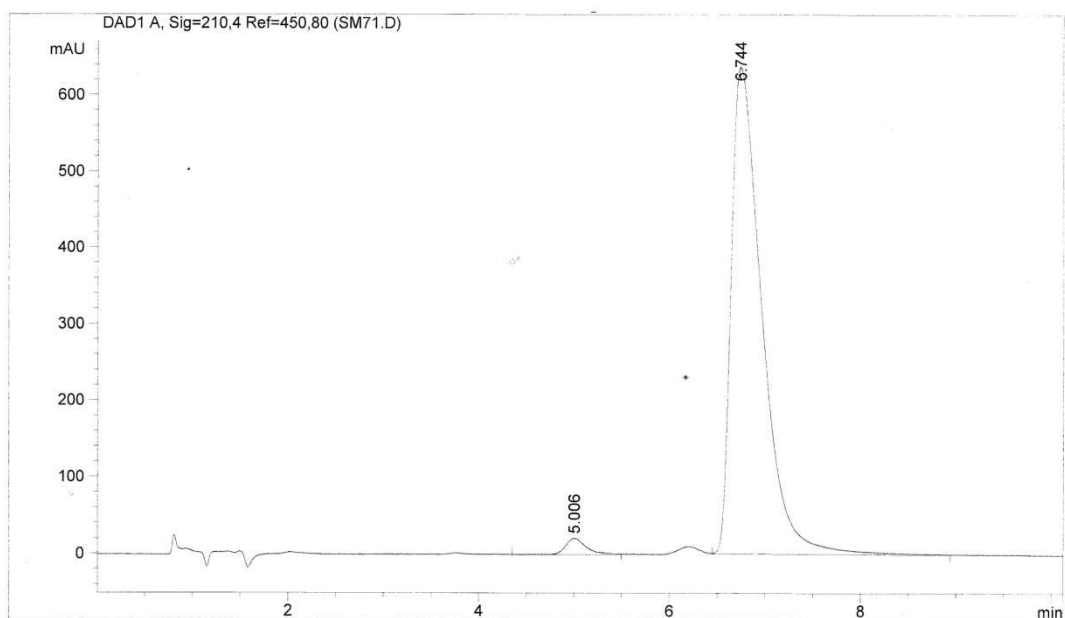
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.570	PP	0.2545	101.60098	5.23443	0.5670
2	4.913	VV	0.2349	8748.62598	570.67963	48.8221
3	6.186	VV	0.2373	65.33559	3.44477	0.3646
4	6.813	VP	0.3227	9003.83789	425.84299	50.2463

Catalyst 1 (Table 4, entry 1)



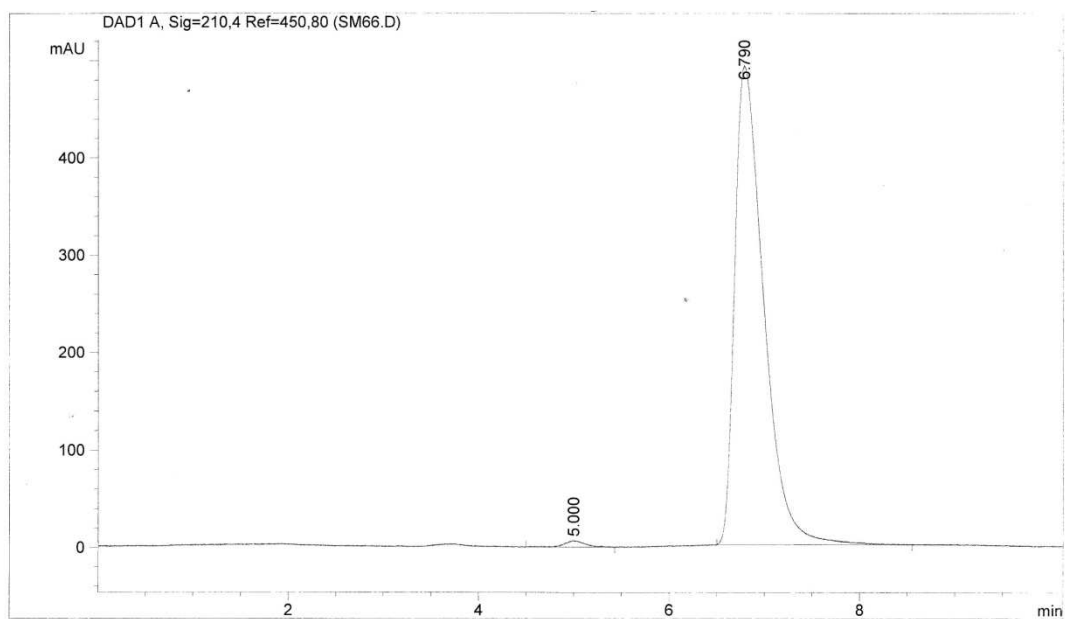
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.720	VV	0.3823	2.39279e4	935.97913	100.0000

Catalyst 2 (Table 4, entry 2)



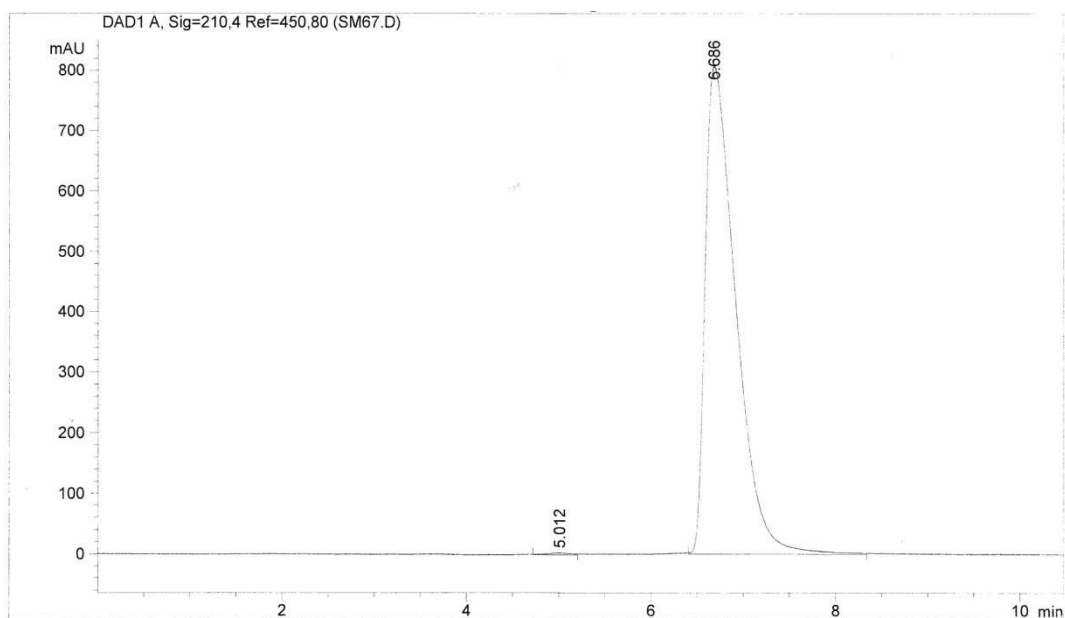
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.006	VBA	0.2313	324.16934	21.09611	2.2354
2	6.744	BV	0.3321	1.41776e4	635.90295	97.7646

Catalyst 3 (Table 4, entry 3)



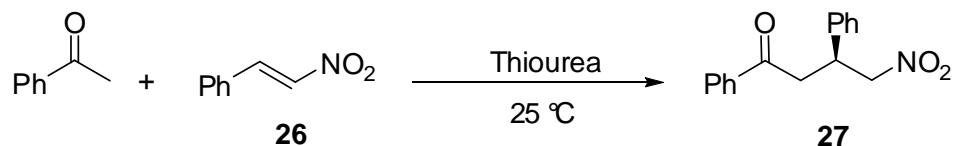
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.000	PP	0.2112	95.65063	6.22886	0.9114
2	6.790	BB	0.3232	1.03987e4	490.81140	99.0886

Catalyst 4 (Table 4, entry 4)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.012	VV	0.2503	56.15127	3.23751	0.3014
2	6.686	BV	0.3488	1.85742e4	806.29791	99.6986

Michael addition of acetophenone to *trans*- β -nitrostyrene (26**).**

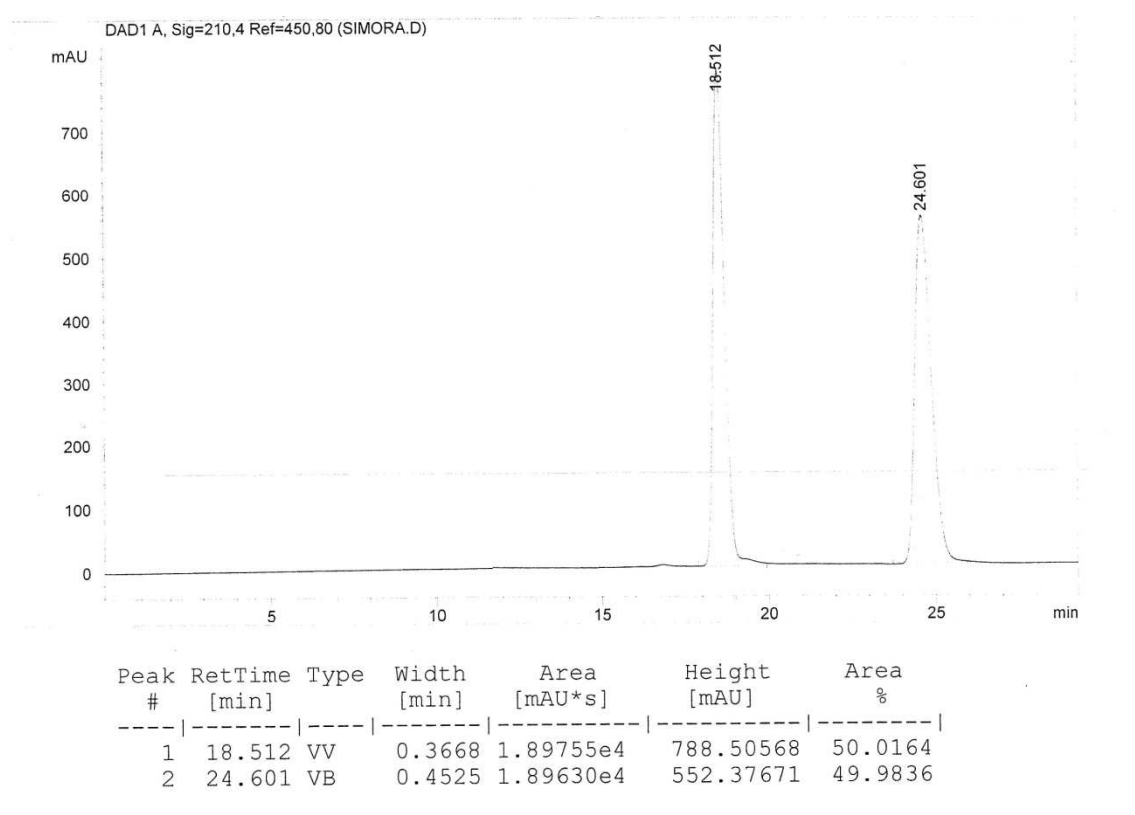


Acetophenone was distilled prior to use, *trans*- β -nitrostyrene **26** was used as received. Spectroscopic data of product **27** were in full agreement with those reported in the literature.^[7] Configuration of the major enantiomer obtained was established by of comparison of measured optical rotation with the literature value. HPLC conditions employed are here reported:

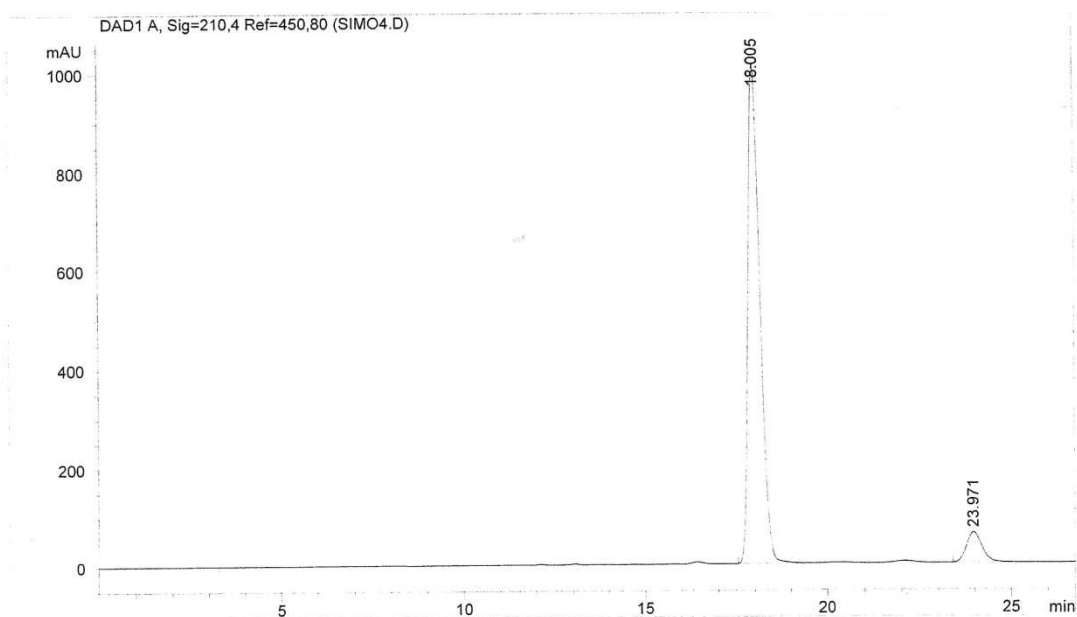
5-Nitro-4-(*S*)-phenylpentan-2-one (25**)**

Chiralpak AS-3 column, 210 nm, Hexane/2-Propanol = 80:20, flow rate = 0,8 mL*min⁻¹.

Racemic mixture

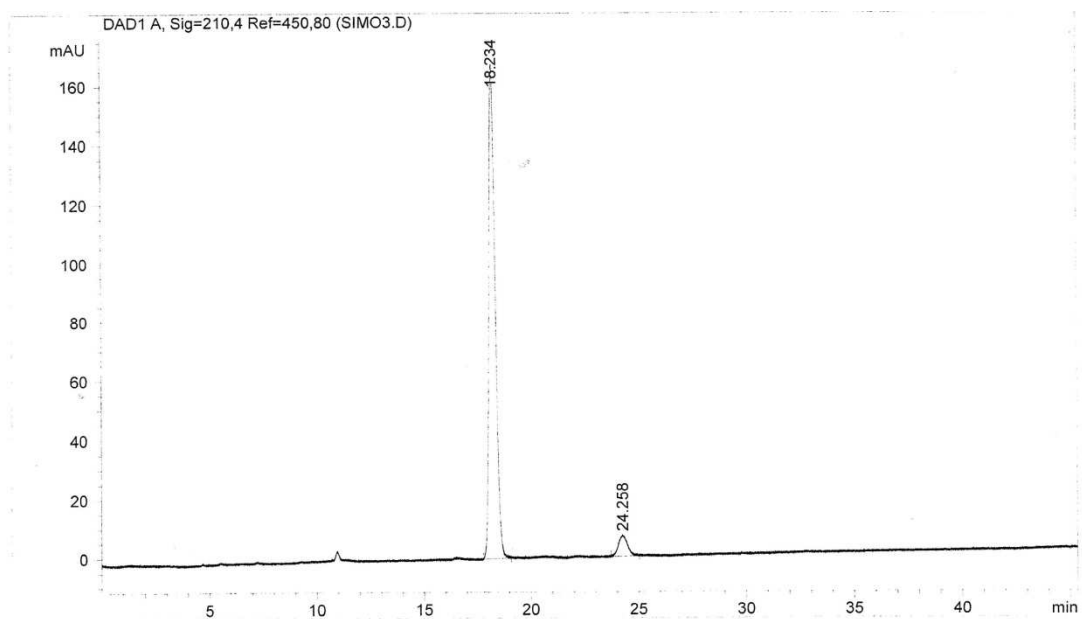


Catalyst 1 (Table 4, entry 1)



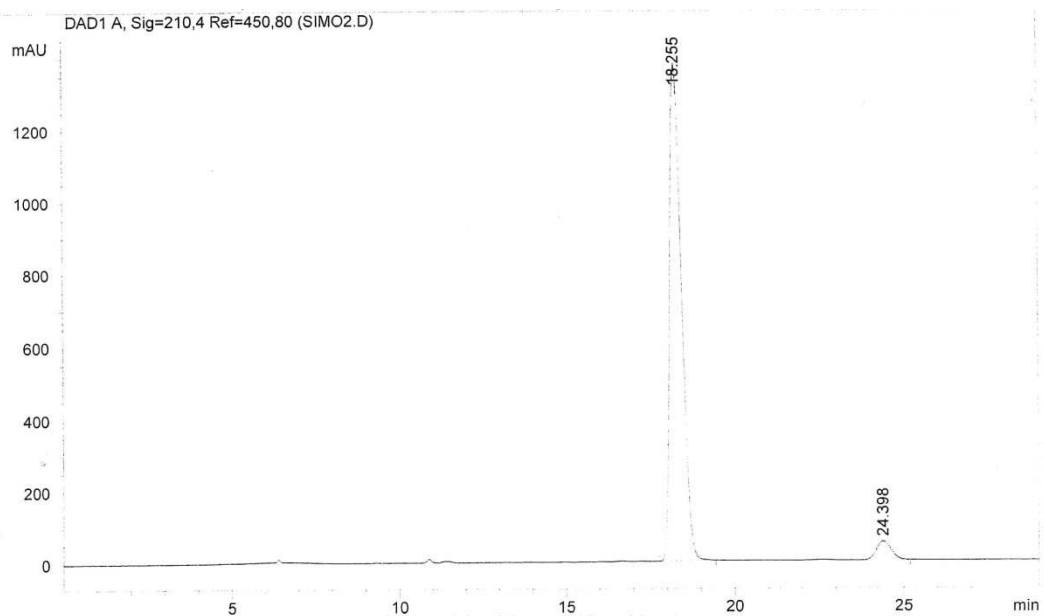
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.005	BB	0.3645	2.32832e4	1011.58948	92.5428
2	23.971	BB	0.4684	1876.19019	62.11470	7.4572

Catalyst 2 (Table 4, entry 2)



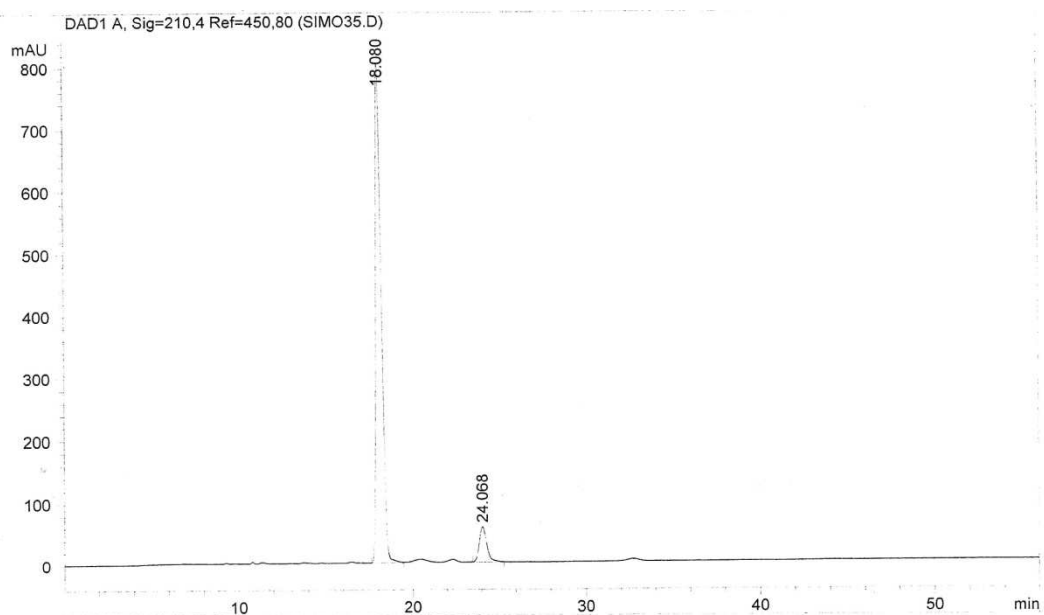
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.234	BB	0.3351	3598.36377	167.19955	94.4698
2	24.258	BB	0.3951	210.64456	7.08080	5.5302

Catalyst 3 (Table 4, entry 3)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.255	PB	0.3687	3.34391e4	1370.39233	95.4233
2	24.398	VV	0.3629	1603.80408	52.13010	4.5767

Catalyst 4 (Table 4, entry 4)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.080	BB	0.3584	1.82799e4	800.46173	91.1947
2	24.068	BB	0.4778	1765.00549	56.91182	8.8053

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