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SUPPORTING INFORMATION

Zinc (II)-Mediated Diastereoselective Passerini Reactions of Biocatalytically Desymmetrized Renewable Inputs

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Details on previous desymmetrizations of 2,5-bis(hydroxymethyl)tetrahydrofuran 3 and on the determination of absolute configuration

The enzymatic monoacylation of **3** was not previously reported. On the other hand, the enzymatic monohydrolysis of diesters of **3**, such as **S1** and **5**, has been previously described.

Naemura et al.[1] reported the monohydrolysis of diacetate **S1** with PLE to give (–)-**S2**, and its conversion into (+)-**S3**. These authors initially determined for (+)-**S3** an ee of 96% by a simple comparison of the polarimetric value with that reported by Jones,[2] but later corrected it to 51%.[3]

In 1990, Prasad *et al*[4] reported the hydrolysis of dibutyrate **5** with various lipases. The best results were obtained using lipase from *Mucor javanicus* (Fluka). This outcome was confirmed by our optimization, that selected lipase Amano M (again from *Mucor javanicus*) as the best enzyme. The ee reported by Prasad (> 99%) is probably slightly over evaluated, since the reported $[\alpha]_D$ (+16.0) is lower than the one measured by us on a sample of the enantiomer with 99% ee (–17.1). In our hands, we obtained a monobutyrate with 94% ee, and $[\alpha]_D$ = +16.2. It should be noted that Prasad determined the ee by ^{1}H NMR in the presence of Eu(hfc)$_3$ and we think that with this method, also due to the fact that in the monobutyrate there are no singlets, the detection limit of the minor enantiomer should be around 3%.

The absolute configuration of (+)-**4** and (–)-**4** obtained by us was assessed by polarimetric comparison with the value reported by Prasad *et al.* for (+)-**4**.

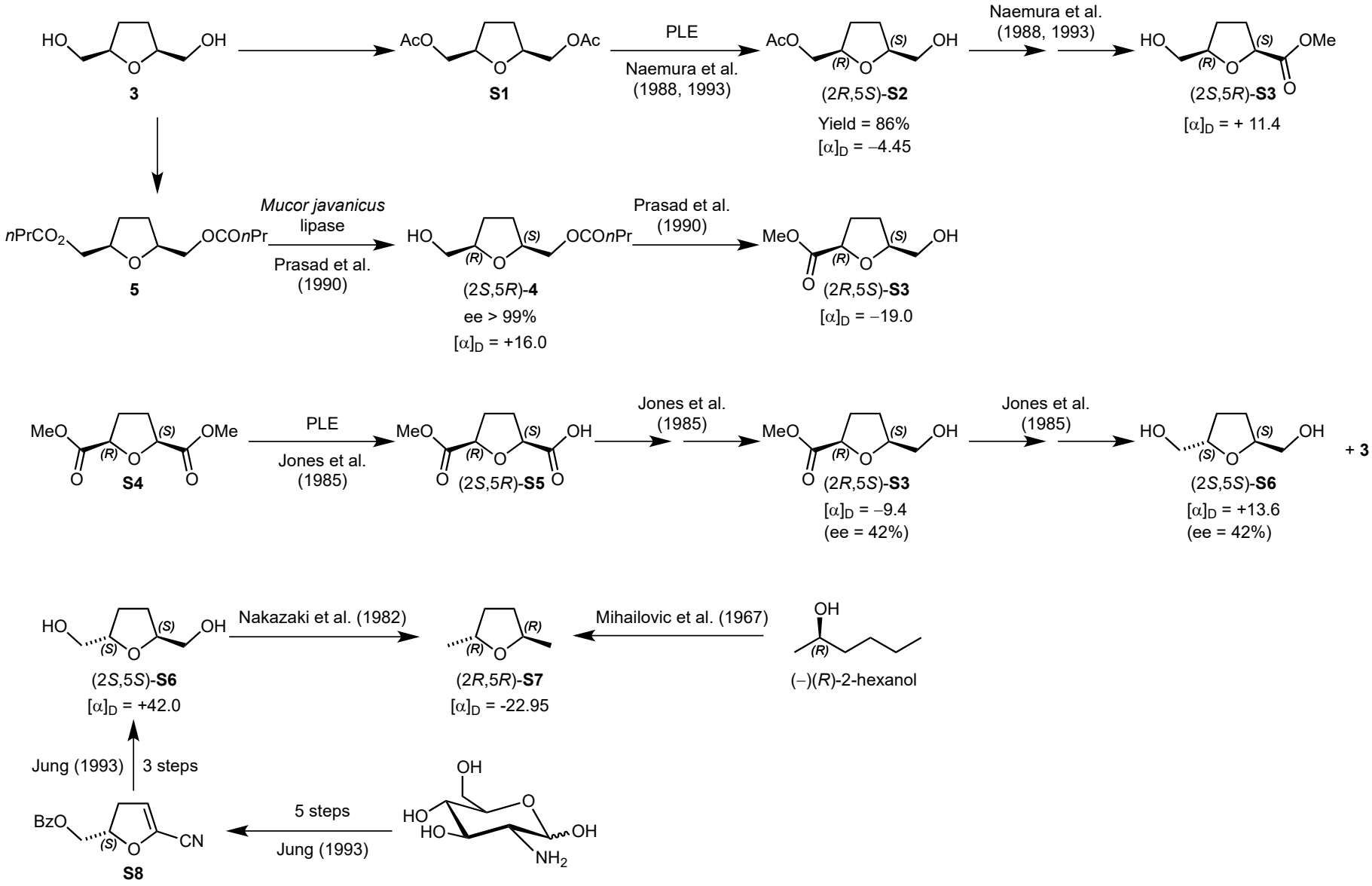
Prasad and coworkers have established the absolute configuration of (+)-(2*S*,5*R*)-**4** by its conversion into (–)(2*R*,5*S*)-**S3**.[4] In turn, the absolute configuration of (–)(2*R*,5*S*)-**S3** was previously demonstrated by Jones,[2] who reported the chemoenzymatic synthesis of (–)-**S3** (42% ee) through hydrolytic desymmetrization of diester **S4**. In order to determine the absolute configuration, he converted (–)-**S3** into known (+)-**S6**. This was done by epimerization at the α position of the ester, followed by $LiAlH_4$ reduction. The mixture of (+)-**S6** and *meso* **3** was separated and (+)-**S6** was recognized as (*S,S*) by polarimetric comparison with the enantiomerically pure compound previously described.[5]

(+)-**S6** was indeed chemically correlated to (–)-**S7**.[5] Moreover, (–)-**S7** was obtained by enantioretentive oxidation of (–)-(*R*)-2-hexanol.[6] Note that in the paper by Mihailovic et al.[6] the formula of (–)(*R*,*R*)-**S7** is erroneously depicted. However, since it derives from (*R*)-2-hexanol, it must necessarily have the (*R,R*) configuration.

The absolute configuration of (+)(*S,S*)-**S6** was also confirmed by Jung *et al.*, who obtained it in 8 steps starting from D-glucosamine.[7]

(1) K. Naemura, N. Takahashi, H. Chikamatsu, *Chem. Lett.* **1988**, *17*, 1717-1720.
(2) J. B. Jones, R. S. Hinks, P. G. Hultin, *Can. J. Chem.* **1985**, *63*, 452-456.
(3) K. Naemura, R. Fukuda, N. Takahashi, M. Konishi, Y. Hirose, Y. Tobe, *Tetrahedron: Asymm.* **1993**, *4*, 911-918.
(4) H. Estermann, K. Prasad, M. J. Shapiro, O. Repic, G. E. Hardtmann, J. J. Bolsterli, M. D. Walkinshaw, *Tetrahedron Lett.* **1990**, *31*, 445-448.
(5) M. Nakazaki, K. Naemura, M. Makimura, A. Matsuda, T. Kawano, Y. Ohta, *J. Org. Chem.* **1982**, *47*, 2429-2435.

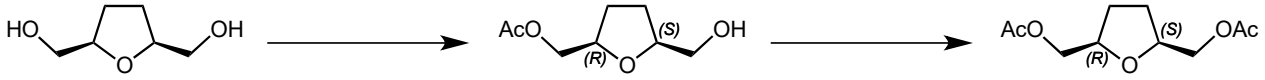
(6) M. L. Mihailović, R. I. Mamuzić, L. Žigić-Mamuzić, J. Bošnjak, Ž. Čeković, *Tetrahedron* **1967**, *23*, 215-226.
(7) M. E. Jung, I. D. Trifunovich, A. W. Sledeski, *Heterocycles* **1993**, *35*, 273-280.



Optimization of the enzymatic acylation of diol 3

***General note to the two following tables**:* "As usual for desymmetrization reactions of this type, conversion is defined as the percentage of acylated hydroxy groups. Thus, conversion = ([**S1**] + [**S2**]/2)/[starting **3**] or ([**5**]*2 + [**4**])/[starting **3**]*2. Therefore, for example, at 100% conversion, all **3** is converted into diacetate **S2**, whereas, at 50% conversion, the amounts of diol **3** and diacetate **S2** are equal and the yield of **S1** is highest. Pushing the reaction at conversions higher than 50% is known to increase the ee of monoester, at the expense of the yield, thanks to a kinetic resolution, which follows the first enantioselective monoacylation. For this reason, it is important to correlate e.e. with conversion. On the other hand, the yield of monoester depends on conversion (it is maximum at 50% conversion), but also on substrate selectivity. In other words, ideally, at 50% conversion one should have 100% monoester and no diol and no diester, because monoester is a poorer substrate than diol. In the reality, substrate selectivity is never so high, and thus, at 50% conversion, some starting diol and some diester are detected. The analytical yield is therefore very useful, during optimization, in order to have an idea of substrate selectivity.

Initially we investigated the enzymatic acetylation of **3**. After a preliminary screening, lipase Amano PS immobilized on celite was selected for further optimization.



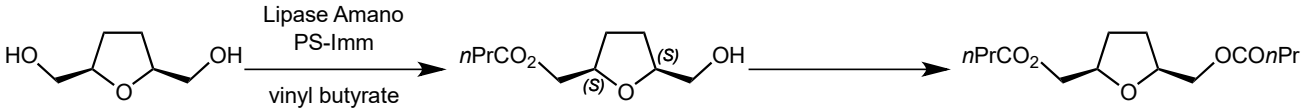
3 (2*R*,5*S*)-**S2** **S1**

Entry	Enzyme	Acyl donor[a]	Solvent	Enzyme quantity	Conc.	Temp.	Time	Conv (%)[b]	% **3**[c]	% **S2**[c]	% **S1**[c]	Analytical yield[d]	ee[e]
1	Amano PS-Imm	vinyl acetate	THF	0.2 g / g **3**	0.2 M	rt	6.5 h	68	4	56	40	53%	85%
2	Amano PS-Imm	vinyl acetate	THF	0.2 g / g **3**	0.2 M	0 °C	4.5 h	41	26	66	8	56%	88%
3	Amano PS-Imm	vinyl acetate	THF	0.2 g / g **3**	0.2 M	0 °C	4.5 h	41	26	66	8	56%	88%
4	Amano PS-Imm	phenyl acetate	THF	0.2 g / g **3**	0.2 M	0 °C	8 h	54	16	60	24	54%	86%
5	Amano PS-Imm	vinyl acetate	THF	0.2 g / g **3**	0.05 M	rt	8 h	46	23	62	15	58%	85%
6	Amano PS-Imm	vinyl acetate	*i*Pr$_2$O	0.2 g / g **3**	0.05 M	0 °C	3.5 h	54	14	64	22	58%	90%
7	Amano PS-Imm	isopropenyl acetate	*i*Pr$_2$O	0.2 g / g **3**	0.05 M	0 °C	6.5 h	56	10	68	22	63%	88%

[a] 5 Equivalents. [b] Defined as ([**S1**] + [**S2**]/2)/[starting **3**]. [c] Molar ratios, determined by ^{1}H NMR on the crude product, which contained only **3**, **S2** and **S1**. [d] Analytical yield based on ^{1}H-NMR with 2,5-dimethylfuran as internal standard. [e] Determined by HPLC on a chiral stationary phase.

Both ees and yields were unsatisfactory. The low yield is due to a poor substrate selectivity. At 50% conversion, substantial amounts of **3** and **S1** were present, as shown in the Table. However, the use of *i*Pr$_2$O as solvent showed a slight improvement in ee.

We then passed on to explore the related butyrylation reaction.



3 (2*R*,5*S*)-**4** **5**

Entry	Additive	Solvent	Enzyme quantity	Conc.	Temp.	Time	Conv (%)[b]	% 3[c]	% 4[c]	% 5[c]	Analytical yield[d]	ee[e]
1	none	THF	0.2 g / g **3**[f]	0.2 M	rt	5 h	63	12	50	38	30%	95%
2	none	THF	0.2 g / g **3**[f]	0.2 M	0° C	4 h	53	13	68	19	65%	93%
3	none	*i*Pr$_2$O	0.2 g / g **3**[f]	0.2 M	rt	2.2 h	68	3	58	39	53%	97%
4	none	*i*Pr$_2$O	0.2 g / g **3**[f]	0.2 M	0 °C	4 h	37	28	70	2	67%	94%
5	none	*i*Pr$_2$O	0.2 g / g **3**[f]	0.2 M	0 °C	5.5 h	50	8	84	8	80%	96%
6	none	*i*Pr$_2$O	0.2 g / g **3**[f]	0.2 M	0 °C	7 h	65	0	70	30	70%[e]	98%
7	none	*i*Pr$_2$O	0.2 g / g **3**[f]	0.2 M	–15 °C	7 h	32	38	60	2	54%	92%
8	none	*i*Pr$_2$O + 5% THF	0.2 g / g **3**[f]	0.1 M	0 °C	30 h	21	60	38	2	31%	90%
9	none	*i*Pr$_2$O + 20% THF	0.4 g / g **3**[f]	0.1 M	0 °C	15 h	45	20	70	10	61%	94%
10	none	*i*Pr$_2$O + 20% CH_2Cl_2	0.4 g / g **3**[f]	0.1 M	0 °C	62 h	59	3	76	21	70%[e]	99%
11	mol. sieves[a]	*i*Pr$_2$O + 20% CH_2Cl_2	0.4 g / g **3**[f]	0.1 M	0 °C	20 h	59	3	76	21	72%[e]	99%
12	mol. sieves[a]	*i*Pr$_2$O + 20% CH_2Cl_2	0.4 g / g **3**[f]	0.1 M	0 °C	14 h	50	6	88	6	82%[e]	96%

[a] 5 Equivalents. [b] Defined as ([**5**]*2 + [**4**])/[starting **3**]*2. [c] Molar ratios, determined by ^{1}H NMR on the crude product, which contained only **3**, **4** and **5**. [d] Analytical yield based on ^{1}H-NMR with 2,5-dimethylfuran as internal standard. [e] Determined by HPLC on a chiral stationary phase. [f] 1 g of this supported catalyst corresponds to 0.223 g of native Amano PS. Therefore 0.2 g corresponds to 0.045 g of enzyme, and 0.4 g corresponds to 0.089 g (8.9% w/w).

In general, the reaction was more enantioselective than the corresponding acetylation. Di-*iso*-propyl ether gave higher rates and better enantioselectivity than THF. The enantiomeric excess tends to increase when conversion goes beyond 50%, because of favorable kinetic resolution of intermediate **4** during its conversion into **5**. The reaction of entry 6 was nearly perfect, but it was poorly reproducible in

terms of rate on upscaling, probably because of the presence of variable amounts of water and of poor solubility of diol **3** in di-*iso*-propyl ether. Therefore, conditions of entry 11 are the ideal ones, because the reaction times are more reproducible.

The optimized conditions use 400 mg of supported enzyme (corresponding to 89 mg of received Amano PS) per gram of substrate (8.9% w/w). It should be noted that the work-up is very simple. By filtration on a sintered funnel one can recover the supported enzyme, which showed no loss in activity upon three times reuse. The mother liquors, on evaporation to dryness, give crude monobutyrate contaminated with some diol **3** and dibutyrate **5**, depending on conversion.

Optimization of Passerini reaction to give 7a

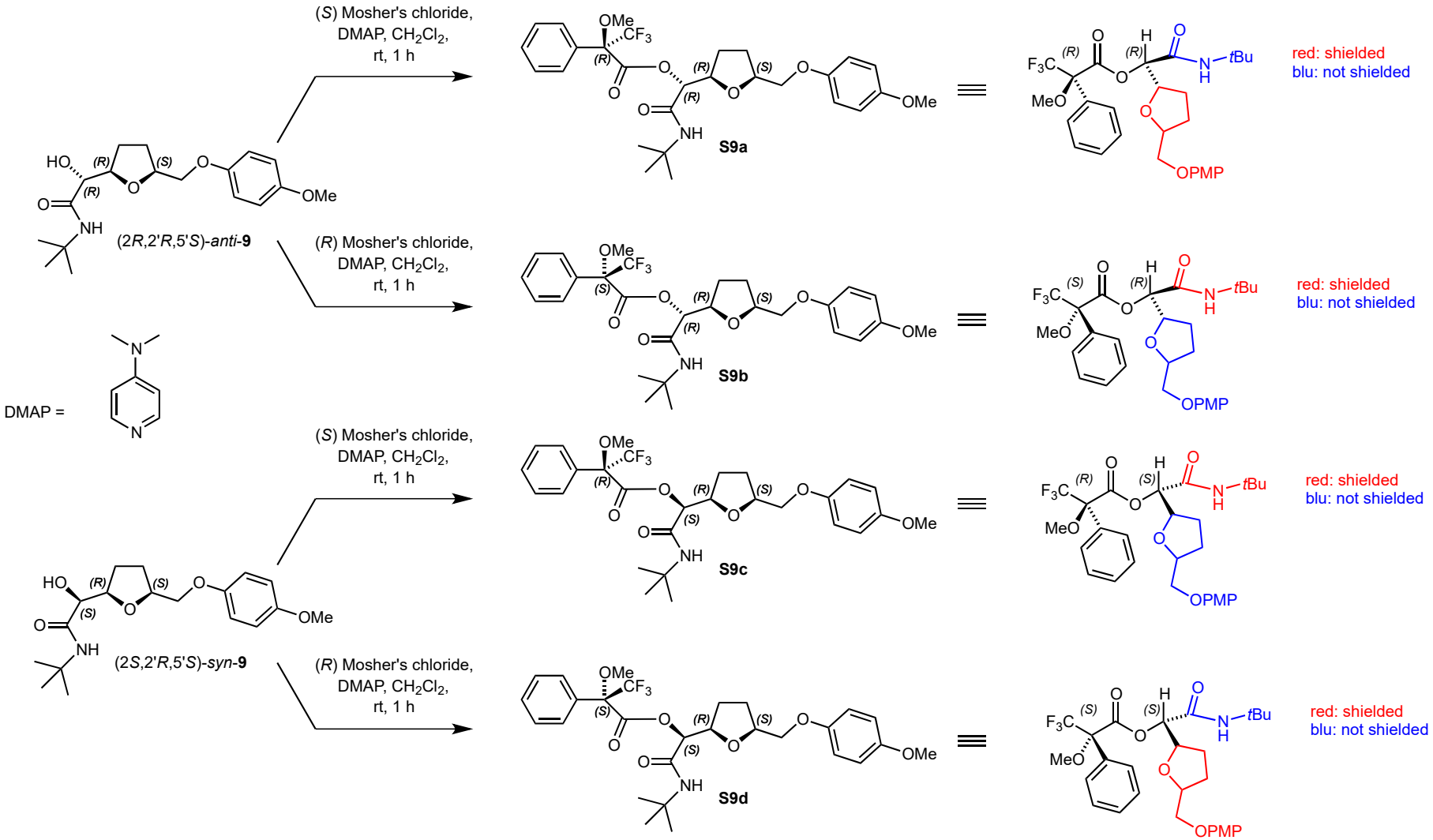
Entry	Prep. of **6**[a]	Solvent	Additive (equiv.)	Mode of addition[b]	Temp (° C)	Time (min)	Yield %[c]	Yield determination	dr (anti:syn)[d]
1	**A**	THF/CH_2Cl_2 1:1	none	**D**	20	40	93	Isolated	59:41
2	**A**	THF/CH_2Cl_2 1:1	none	**D**	–78	205	27	NMR	58:42
3	**A**	THF/CH_2Cl_2 1:1	$MgCl_2$ (1)	**D**	20	30	77	NMR	65:35
4	**A**	THF/CH_2Cl_2 1:1	$MgBr_2$ (1)	**D**	20	90	48	NMR	63:37
5	**A**	THF/CH_2Cl_2 1:1	CuBr (1)	**D**	20	30	-	NMR	-
6	**A**	THF/CH_2Cl_2 1:1	$CuBr_2$ (1)	**D**	20	60	9	NMR	58:42
7	**A**	THF/CH_2Cl_2 1:1	$BF_3{\cdot}Et_2O$ (1)	**D**	20	40	13	NMR	61:39
8	**A**	THF/CH_2Cl_2 1:1	$Yb(OTf)_3$ (1)	**D**	20	90	5	NMR	57:43
9	**A**	THF/CH_2Cl_2 1:1	$Ti(O\textit{i}Pr)_4$ (1)	**D**	20	40	50	NMR	68:32
10	**A**	THF/CH_2Cl_2 1:1	$Zn(OTf)_2$ (1)	**D**	20	90	47	NMR	57:43
11	**A**	THF/CH_2Cl_2 1:1	$ZnCl_2$ (1)	**D**	20	60	59	NMR	63:37
12	**A**	THF/CH_2Cl_2 1:1	ZnI_2 (1)	**D**	20	60	85	NMR	64:36
13	**A**	THF/CH_2Cl_2 1:1	ZnI_2 (1)	**D**	-78	120	36	NMR	65:35
14	**A**	THF/CH_2Cl_2 1:1	$ZnBr_2$ (1)	**D**	20	40	60	NMR	71:29
16	**B**	toluene	none	**D**	20	60	69	NMR	62:38
17	**B**	toluene	$ZnBr_2$ (1)	**D**	20	60	61	NMR	72:28
18	**B**	trifluorotoluene	none	**D**	20	60	74	NMR	60:40
19	**B**	trifluorotoluene	$ZnBr_2$ (1)	**D**	20	60	80	NMR	72:28
20	**B**	CH_2Cl_2	none	**D**	20	60	99	NMR	59:41
21	**B**	CH_2Cl_2	$ZnBr_2$ (1)	**D**	20	60	32	NMR	64:36
22	**B**	$CHCl_3$	none	**D**	20	75	78	NMR	63:37
23	**B**	$CHCl_3$	$ZnBr_2$ (1)	**D**	20	60	60	NMR	64:36
24	**B**	THF	none	**D**	20	60	77	NMR	62:38
25	**B**	THF	$ZnBr_2$ (1)	**D**	20	60	56	NMR	71:29
26	**B**	Et_2O	none	**D**	20	60	74	NMR	62:38

Entry	Prep. of **6**[a]	Solvent	Additive (equiv.)	Mode of addition[b]	Temp (° C)	Time (min)	Yield %[c]	Yield determination	dr (anti:syn)[d]
27	**B**	Et_2O	$ZnBr_2$ (1)	**D**	20	60	78	NMR	72:28
28	**B**	dimethyl carbonate	none	**D**	20	60	99	NMR	63:37
29	**B**	dimethyl carbonate	$ZnBr_2$ (1)	**D**	20	90	48	NMR	65:35
30	**B**	CH_3CN	none	**D**	20	60	68	NMR	56:44
31	**B**	CH_3CN	$ZnBr_2$ (1)	**D**	20	90	56	NMR	62:38
32	**B**	MeOH	none	**D**	20	270	30	NMR	63:37
33	**B**	MeOH	$ZnBr_2$ (1)	**D**	20	240	46	NMR	73:27
34	**B**	*i*Pr_2O	none	**D**	20	90	94	NMR	62:38
35	**B**	*i*Pr_2O	$ZnBr_2$ (1)	**D**	20	90	85	NMR	76:24
36	**B**	*i*Pr_2O/THF 9:1	$ZnBr_2$ (1)	**D**	20	90	80	NMR	72:28
37	**B**	*i*Pr_2O	$ZnBr_2$ (0.4)	**D**	20	120	85	NMR	76:24
38	**B**	*i*Pr_2O	$ZnBr_2$ (0.4)	**E**	20	180	57	NMR	72:28
39	**B**	*i*Pr_2O	$ZnBr_2$ (0.4)	**F**	20	180	68	NMR	80:20
40	**B**	*i*Pr_2O	$ZnBr_2$ (0.4)	**G**	20	180	88	NMR	79:21
41	**B**	*i*Pr_2O	$ZnBr_2$ (0.4)	**G**	20	180	77	isolated	79:21
42	**C**	*i*Pr_2O	$ZnBr_2$ (0.4)	**G**	20	180	82	isolated	81:19

[a] **A**: oxidation was performed with TEMPO/$PhI(OAc)_2$ system, and the following Passerini was carried out in a one-pot manner. Yield is determined from alcohol **4**. **B**: oxidation was performed with TEMPO/$PhI(OAc)_2$ system, and the aldehyde purified by chromatography. Yield is determined from aldehyde **6**; **C**: oxidation was performed with Swern methodology, the aldehyde purified by chromatography, and thoroughly dried on molecular sieves. Yield is determined from aldehyde **6**. [b] **D**: all reagents added together in a short time; **E**: isocyanide added slowly (during 2 h) to the mixture of aldehyde, $ZnBr_2$ and carboxylic acid; **F**: aldehyde added slowly (during 2 h) to the mixture of isocyanide, $ZnBr_2$ and carboxylic acid **G**: aldehyde and carboxylic acid mixed together and added slowly (during 2 h) to the mixture of isocyanide and $ZnBr_2$. [c] Overall yield of the two diastereomers. NMR yield was determined by ^{1}H NMR of the crude in the presence of 2,5-dimethylfuran as internal standard. The precision of the method was assessed by preparing a series of solutions by mixing the standard with variable amounts of pure product **7a** and examining them at ^{1}H NMR. By comparing the real molar % of **7a** in these mixtures (determined by weight) and the ratios determined by NMR we obtained errors always < 3%. [d] Determined by ^{1}H-NMR analysis on the crude product, by integration of the signals of C*H*-OAc of the two diastereomers.

The conditions of entry 42, compared to those of entries 40 or 41 were thus selected by us as the best ones. Despite, at first sight, entry 40 gave a better yield, the conditions of entry 42 bring about a better reproducibility and a cleaner crude. While the 81:19 diastereomeric ratio seems not excellent, we must consider that we started from poor dr of 59:41 under the standard Passerini conditions.

Mosher's ester analysis to establish the absolute configuration of compounds *anti* and *syn*-7a



As shown in the Scheme above, both diastereomers of alcohols **9** were converted into the corresponding Mosher's esters **S9a,b** and **S9c,d** by reaction with (*R*) or (*S*) Mosher's chloride.

The method by Mosher is based on the chemical shifts of the protons of the groups bound to the stereogenic centers. According to the expected preferred conformations, the anisotropic shielding effect of the phenyl group is exerted on one of the two groups. The table below reports the most diagnostic chemical shift for the four diastereomers **S9a-d**.

	chemical shifts ($CDCl_3$)			
Signal	Compound **S9a**	Compound **S9b**	Compound **S9c**	Compound **S9d**
($C\mathit{H}_3$)$_3$C	1.24	1.22	1.20	1.29
N*H*	6.19	5.91	5.63	5.93
H-2'	4.31	4.40	4.27	4.34

In particular, the chemical shifts of the isocyanide derived portion is fully in agreement with the proposed absolute configuration. For the tetrahydrofuran portion we examined the H-2' proton. While for **S9a** and **S9b** also these chemical shifts are in line with the expected effect, for **S9c** and **S9d** the effect seems opposite. However, in this fragment, prediction of the shielding effects is more difficult, because also the *p*-methoxyphenyl group could provoke shielding effects, which clearly depend on the overall conformation of the molecule.

Here we report the complete ^{1}H NMR data of Mosher esters

S9a. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.68-7.60 (2 H, m, aromatics), 7.46-7.38 (3 H, aromatics), 6.85 (4 H, s, aromatics of anisyl), 6.19 (1 H, br s, NH), 5.18 (1 H, d, J = 6.7 Hz, C*H*OC=O), 4.36-4.27 (2 H, m, 2'-H, 5'-H), 3.97 (1 H, dd, J = 9.9, 3.9 Hz, C*H*HOAn), 3.82 (1 H, dd, J = 9.9, 4.5 Hz, C*H*HOAn), 3.78 (3 H, s, CH_3O), 3.62 (3 H, q, J = 0.9 Hz, CH_3O Mosher), 2.00-1.77 (4 H, m, 3'-H, 4'-H), 1.24 (9 H, s, C(CH_3)$_3$)).

S9b. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.61-7.54 (2 H, m, aromatics), 7.42-7.35 (3 H, aromatics), 6.81 (4 H, s, aromatics of anisyl), 5.91 (1 H, br s, NH), 5.43 (1 H, d, J = 4.5 Hz, C*H*OC=O), 4.40 (dt, J = 4.5, 6.9 Hz, 2'-H), 4.35-4.26 (1 H, m, 5'-H), 3.88, 3.86 (2 H, AB part of ABX system, J_{AB} = 9.8, J_{AX} = 5.4, J_{BX} = 4.5 Hz, CH_2OAn), 3.77 (3 H, s, CH_3O), 3.55 (3 H, q, J = 0.9 Hz, CH_3O Mosher), 2.06-1.95 (3 H, m, 3-H, 4-H), 1.90-1.78 (1 H, m, 3-H, 4-H),1.22 (9 H, s, C(CH_3)$_3$)).

S9c. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.63-7.55 (2 H, m, aromatics), 7.44-7.35 (3 H, aromatics), 6.80 (4 H, s, aromatics of anisyl), 5.64 (1 H, br s, NH), 5.23 (1 H, d, J = 6.6 Hz, C*H*OC=O), 4.34-4.22 (2 H, m, 2'-H, 5'-H); 3.88, 3.85 (2 H, AB part of ABX system, J_{AB} = 9.8, J_{AX} = 4.8, J_{BX} = 5.7 Hz, CH_2OAn), 3.76 (3 H, s, CH_3O), 3.55 (3 H, q, J = 0.9 Hz, CH_3O Mosher), 2.16-1.98 (3 H, m, 3-H, 4-H), 1.89-1.72 (1 H, m, 3-H, 4-H),1.20 (9 H, s, C(CH_3)$_3$)).

S9d. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.61-7.54 (2 H, m, aromatics), 7.45-7.33 (3 H, aromatics), 6.81 (4 H, s, aromatics of anisyl), 5.93 (1 H, br s, NH), 5.24 (1 H, d, J = 4.6 Hz, C*H*OC=O), 4.34 (dt, J = 4.6, 6.5 Hz, 2'-H), 4.29-4.18 (1 H, m, 5'-H), 3.83, 3.80 (2 H, AB part of ABX system, J_{AB} = 9.8, J_{AX} = 4.7, J_{BX} = 6.1 Hz, CH_2OAn), 3.77 (3 H, s, CH_3O), 3.53 (3 H, q, J = 0.9 Hz, CH_3O Mosher), 2.07-1.83 (3 H, m, 3-H, 4-H), 1.74-1.61 (1 H, m, 3-H, 4-H),1.29 (9 H, s, C(CH_3)$_3$)).

HPLC and NMR determination of enantiomeric excesses and diastereomeric ratios

```
Colonna Chirale Chiral Pak AD 250x4,6mm senza precolonn
a, Campione GP03 racemo (Conc,: 400ug/ml Exane/isoPrOH
83:17) flusso 0,5ml/min, T= 26°C term.ON, vinj=20ul,Dad
 226nm,  isocr. A=Esano=95% B=isoPrOH=5%

======================================================================
Injection Date  : 7/6/2016 10:03:23 AM
Sample Name     : GP03 racemo                  Location : Vial 1
Acq. Operator   : AeV
Acq. Instrument : stanza306new                Inj Volume : 20 µl
Acq. Method     : C:\HPCHEM\1\METHODS\CHIRAL.M
Last changed    : 7/6/2016 10:00:23 AM by AeV
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\CHIRAL.M
Last changed    : 7/6/2016 12:24:39 PM by AeV
                  (modified after loading)
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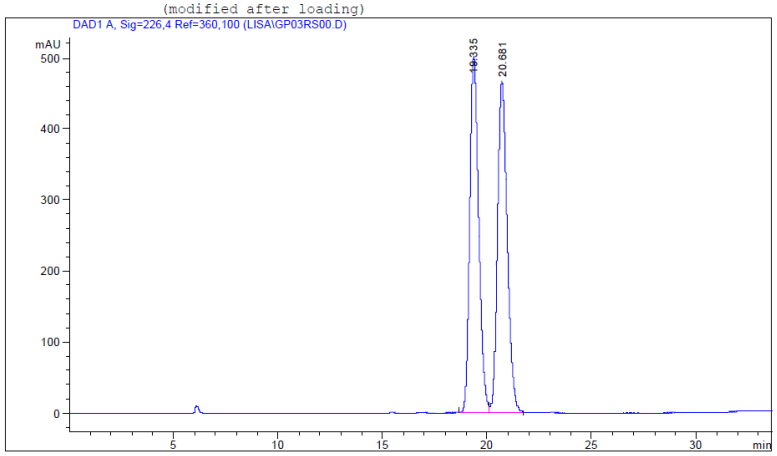


```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=226,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  19.335 BV    0.4515 1.49606e4   502.27441  49.9223
   2  20.681 VB    0.4740 1.50072e4   466.87311  50.0777
```

RACEMIC 4

```
Colonna Chirale ChiralPak AD 250x4,6mm senza precolonna
, Campione AC_003(Conc.:200ug/ml Exane:IsoPOH 9-1)) flu
sso 0,5ml/min, T= 26°C term.ON, vinj=20ul, Dad 226nm,
isocr A=Esano B=isoprOH, A=95%, B=5%

======================================================================
Injection Date  : 1/7/2006 8:12:01 AM
Sample Name     : AC 003                       Location : Vial 1
Acq. Operator   : AeV( Lisa)
Acq. Instrument : stanza306new                Inj Volume : 20 µl
Acq. Method     : C:\HPCHEM\1\METHODS\CHIRAL.M
Last changed    : 1/7/2006 8:25:33 AM by AeV( Lisa)
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\CHIRAL.M
Last changed    : 1/7/2006 8:42:34 AM by AeV( Lisa)
                  (modified after loading)
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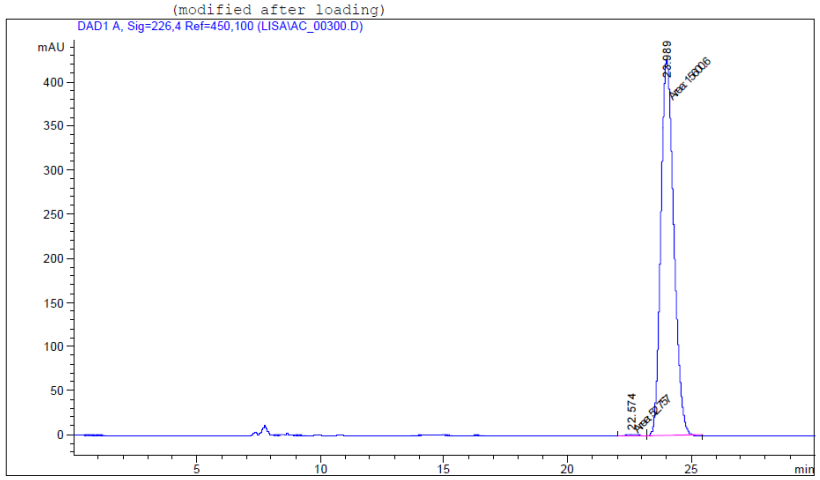
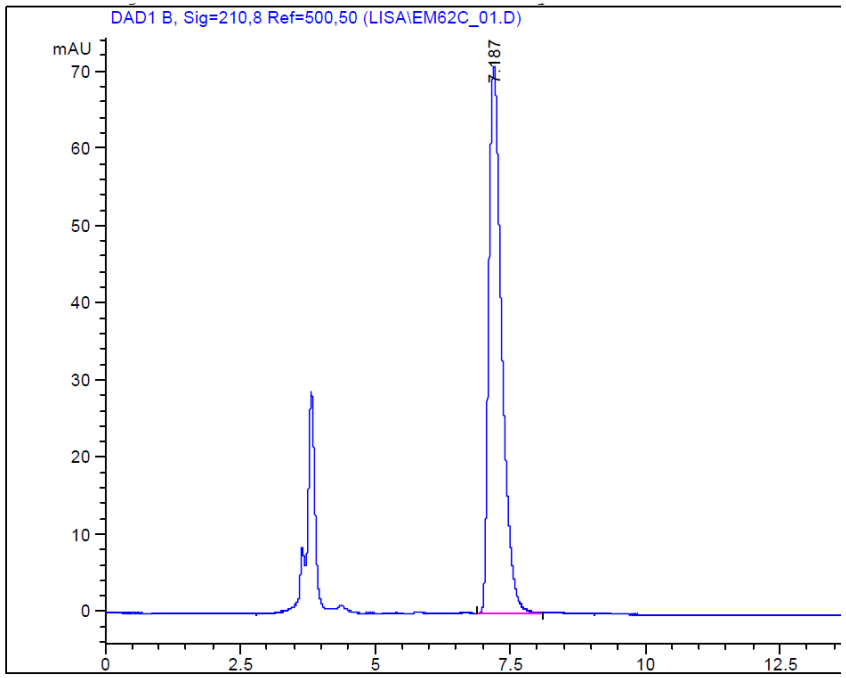


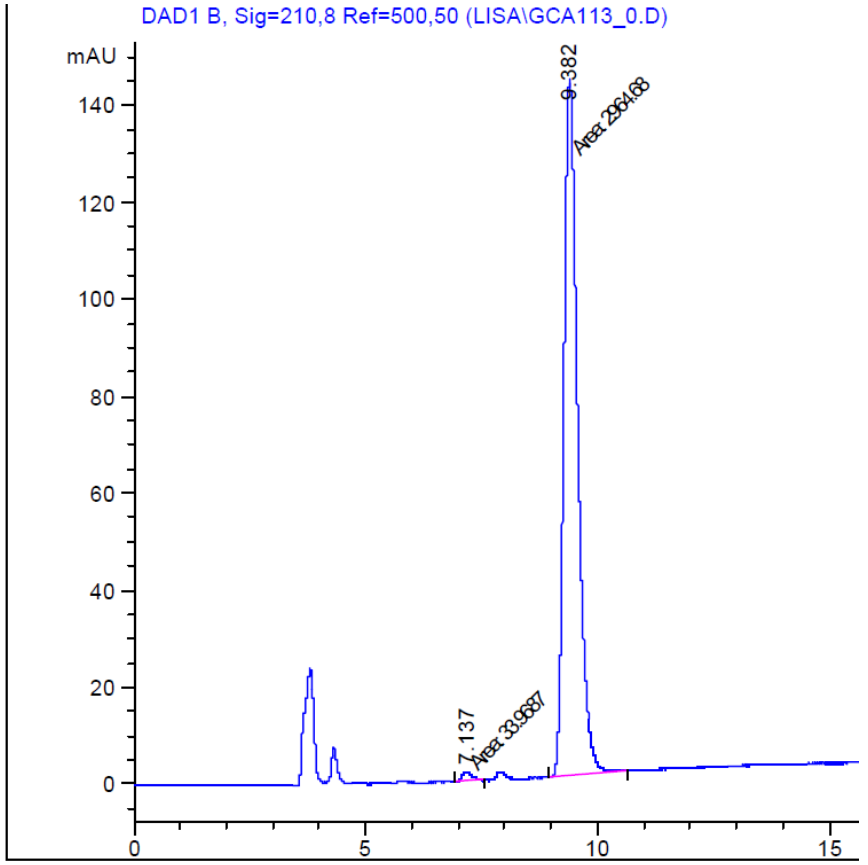

```
======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 A, Sig=226,4 Ref=450,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  22.574 MM    0.5072   52.75705    1.73360   0.3370
   2  23.989 MM    0.6087 1.56006e4   427.17075  99.6630
```

(–)-**4** from enzymatic butyrylation of **3**

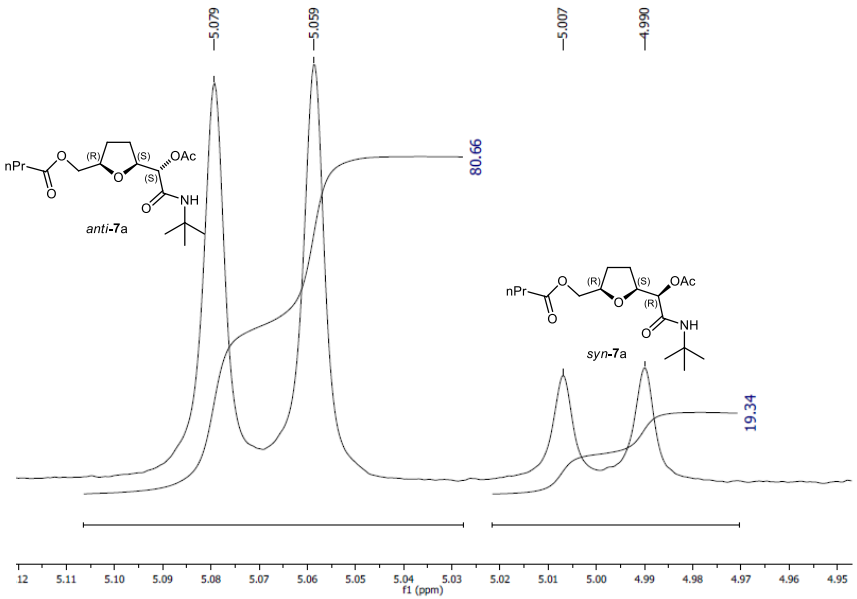
***Anti*-10**

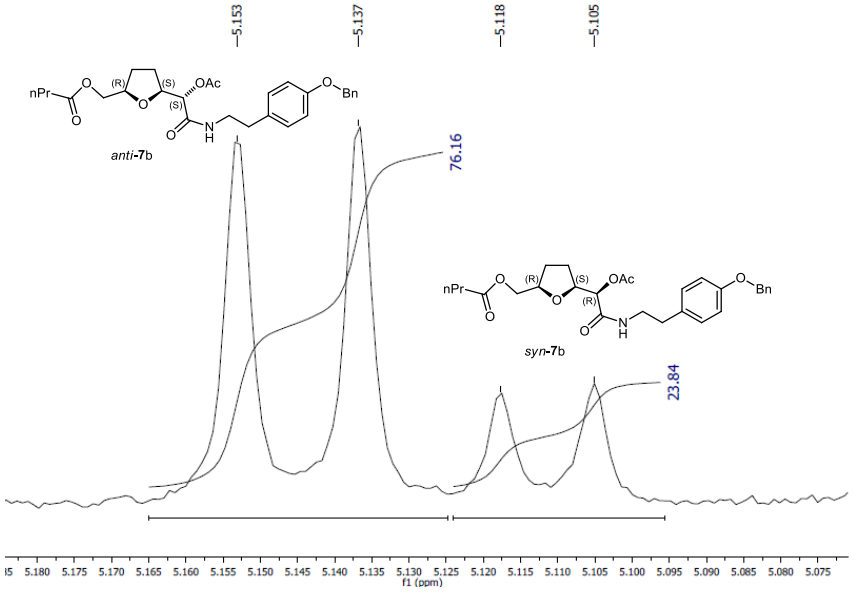


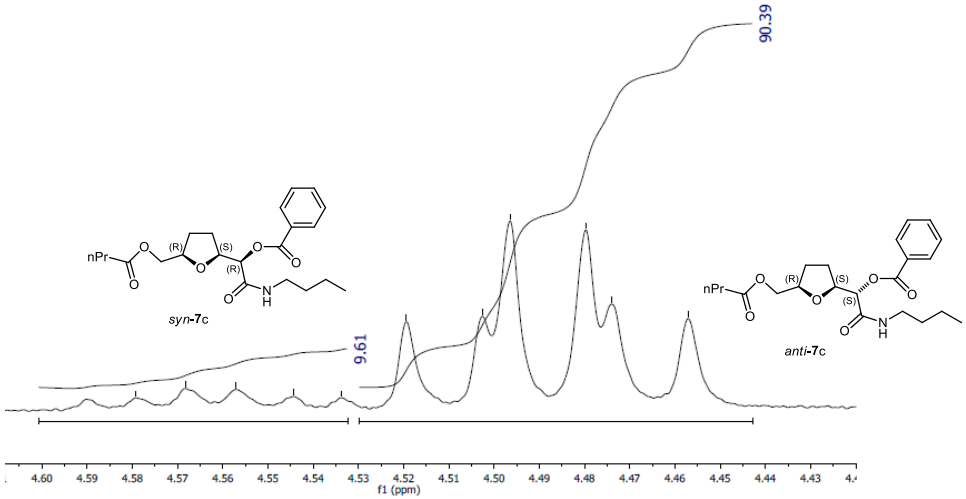
***Anti-ent*-10**

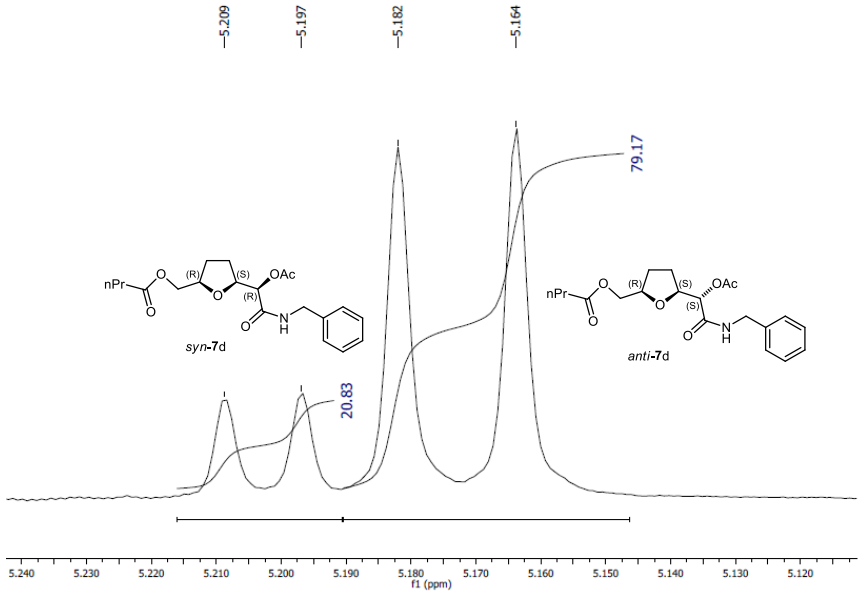


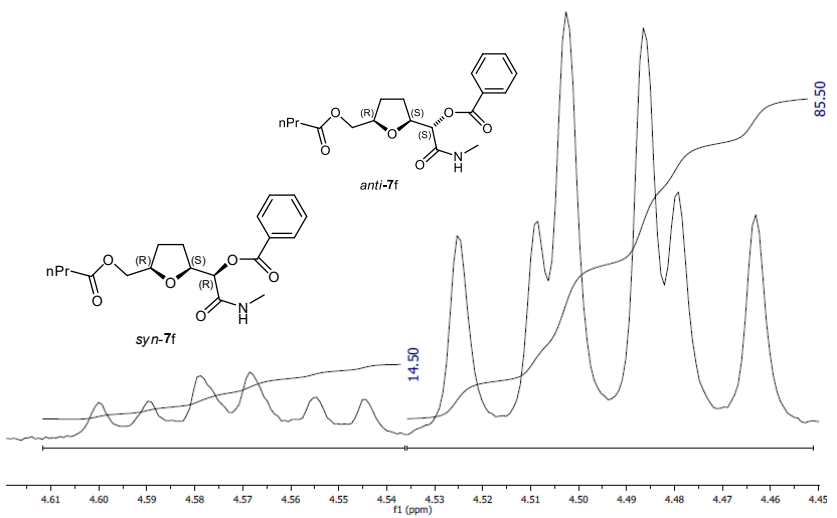
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.137	MM	0.2922	33.96866	1.93753	1.1328
2	9.382	MM	0.3429	2964.68018	144.10350	98.8672

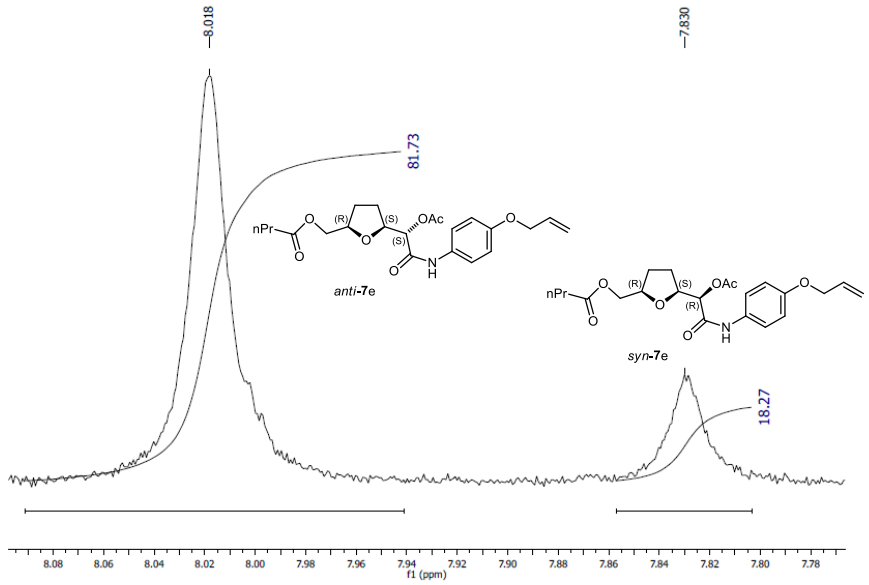

5.079
5.059
5.007
4.990
80.66
19.34
anti-7a
syn-7a
f1 (ppm)

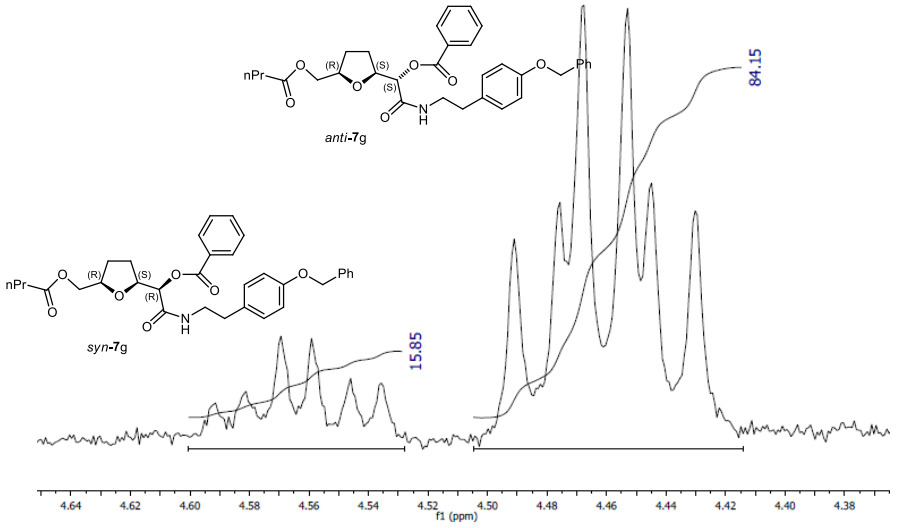

5.153
5.137
5.118
5.105
76.16
23.84
anti-7b
syn-7b
f1 (ppm)

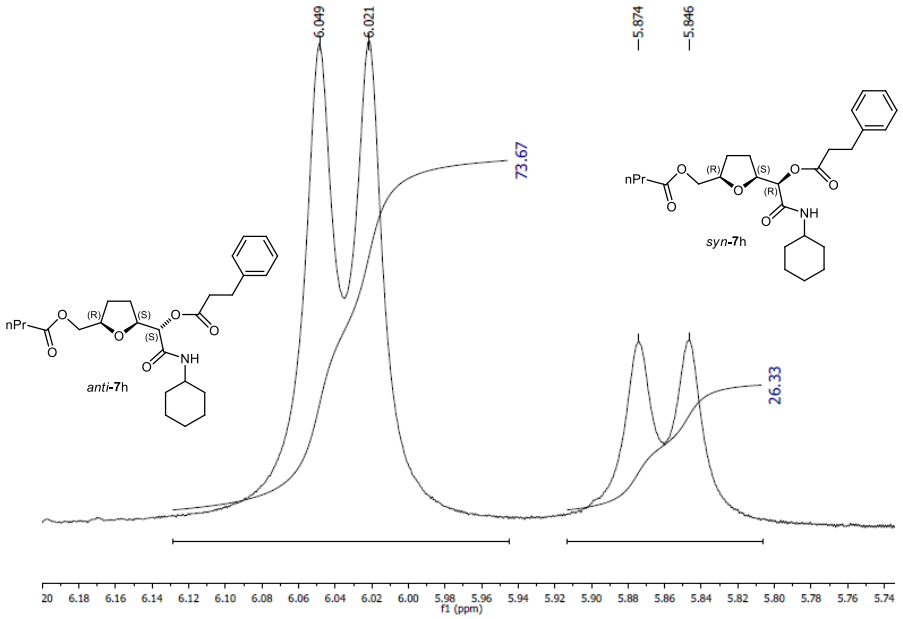

4.579
4.568
4.557
4.544
4.534
4.519
4.503
4.496
4.480
4.474
4.457
90.39
9.61
syn-7c
anti-7c
f1 (ppm)

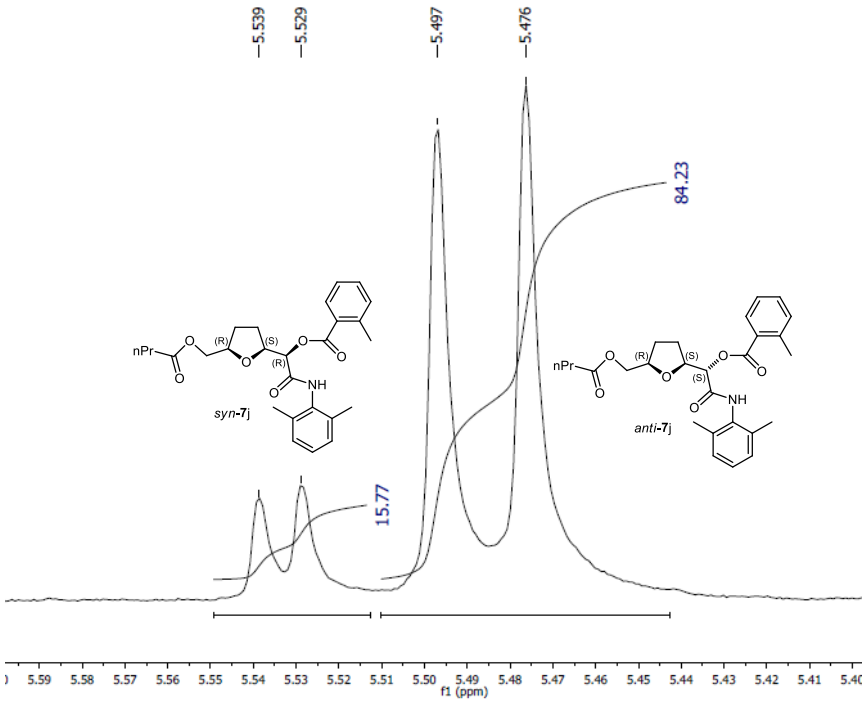

5.209
5.197
5.182
5.164
79.17
20.83
syn-7d
anti-7d
5.240 5.230 5.220 5.210 5.200 5.190 5.180 5.170 5.160 5.150 5.140 5.130 5.120
f1 (ppm)

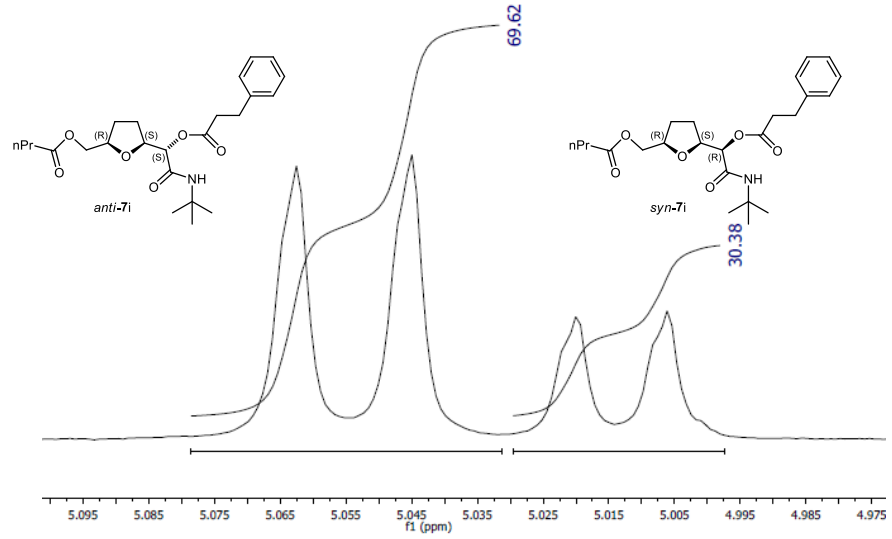

85.50
anti-7f
syn-7f
14.50
4.61 4.60 4.59 4.58 4.57 4.56 4.55 4.54 4.53 4.52 4.51 4.50 4.49 4.48 4.47 4.46 4.45
f1 (ppm)

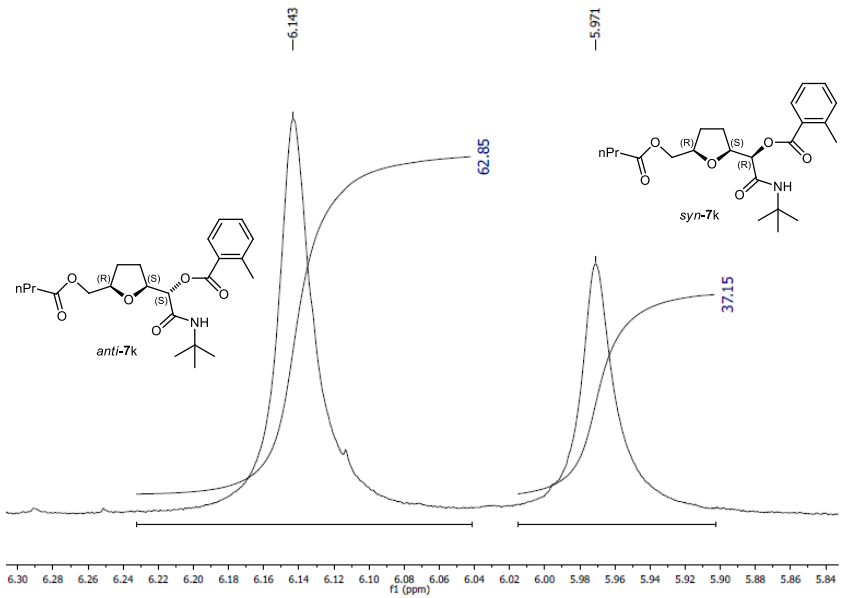

8.018
7.830
81.73
18.27
anti-7e
syn-7e
8.08 8.06 8.04 8.02 8.00 7.98 7.96 7.94 7.92 7.90 7.88 7.86 7.84 7.82 7.80 7.78
f1 (ppm)

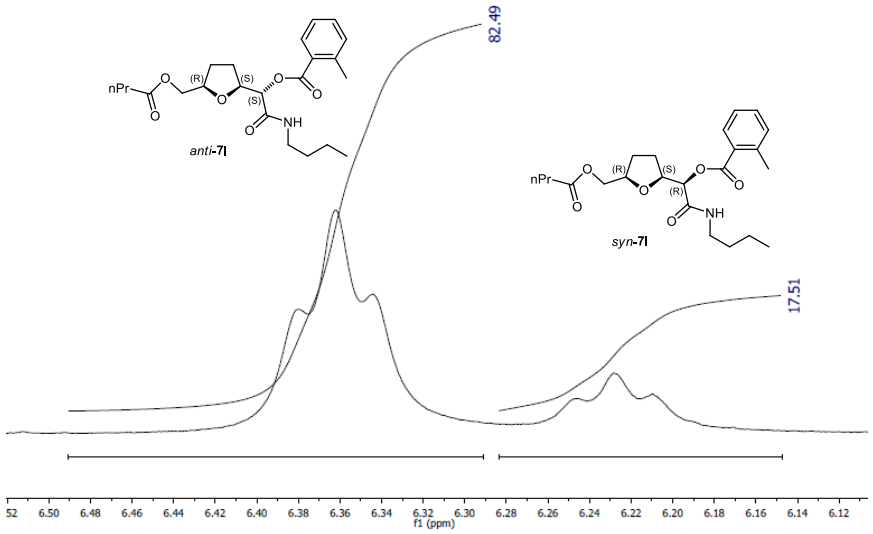

84.15
anti-7g
syn-7g
15.85
4.64 4.62 4.60 4.58 4.56 4.54 4.52 4.50 4.48 4.46 4.44 4.42 4.40 4.38
f1 (ppm)


6.049
6.021
5.874
5.846
73.67
26.33
anti-7h
syn-7h
f1 (ppm)

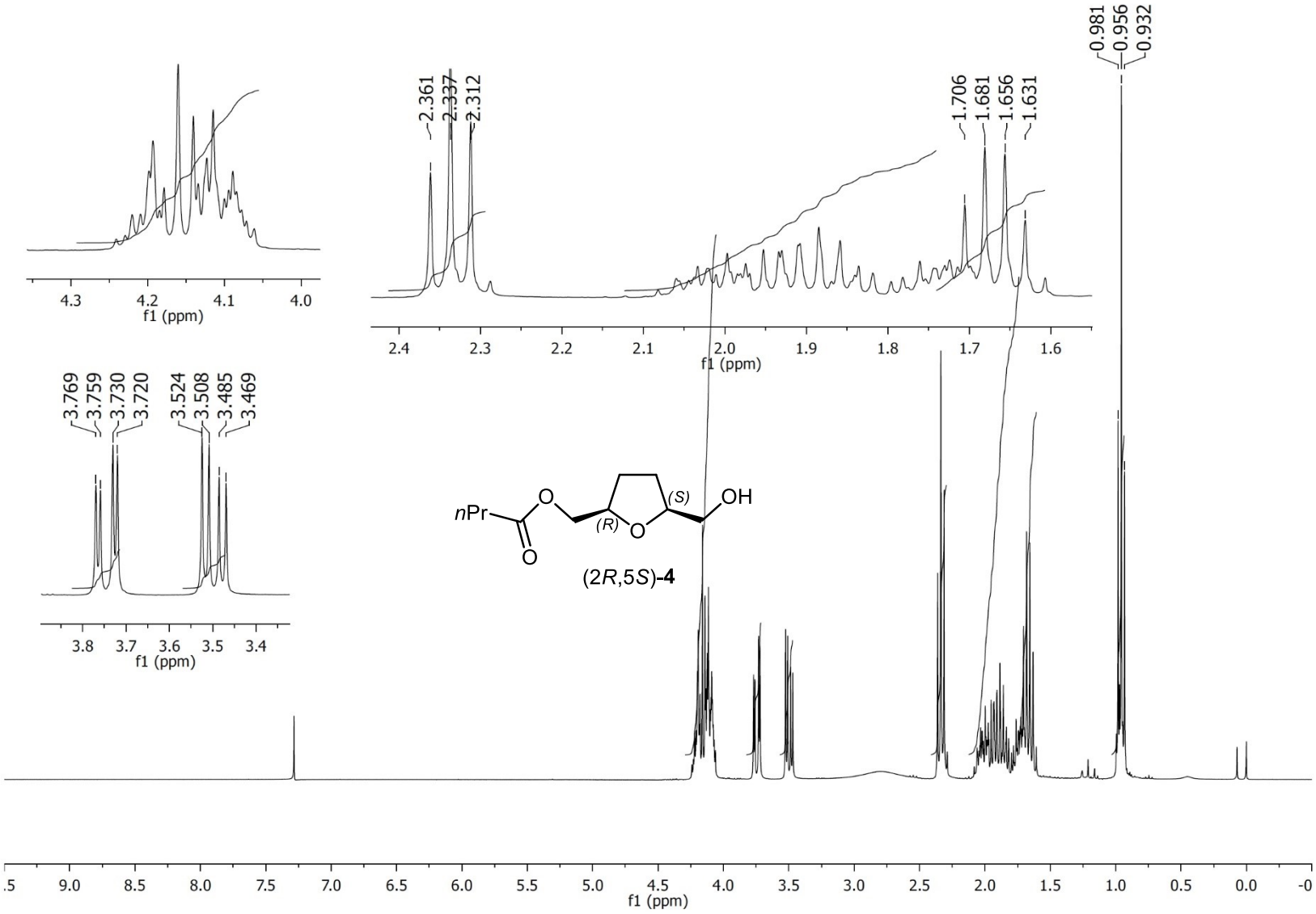

5.539
5.529
5.497
5.476
84.23
15.77
syn-7j
anti-7j
f1 (ppm)

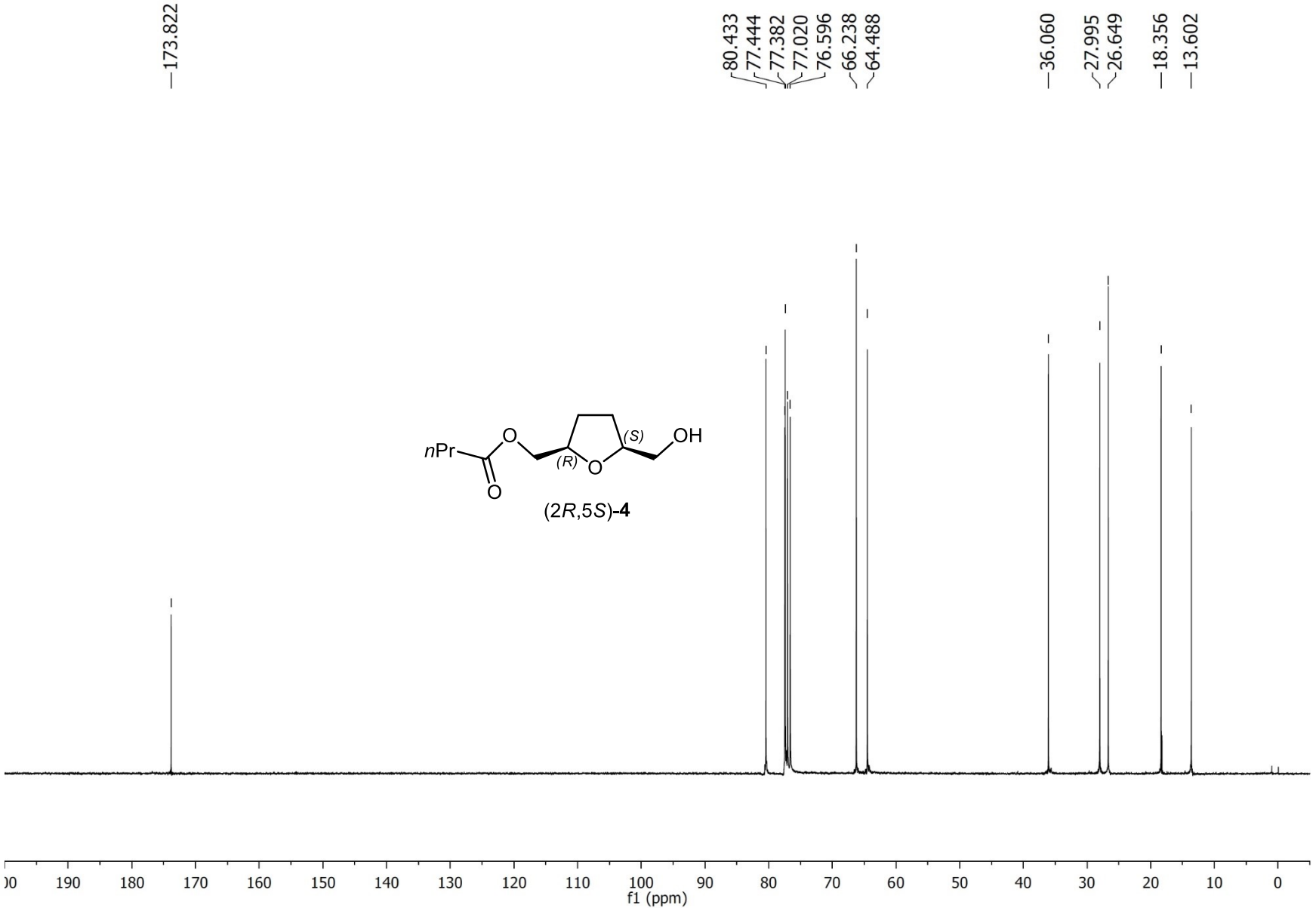

69.62
30.38
anti-7i
syn-7i
f1 (ppm)

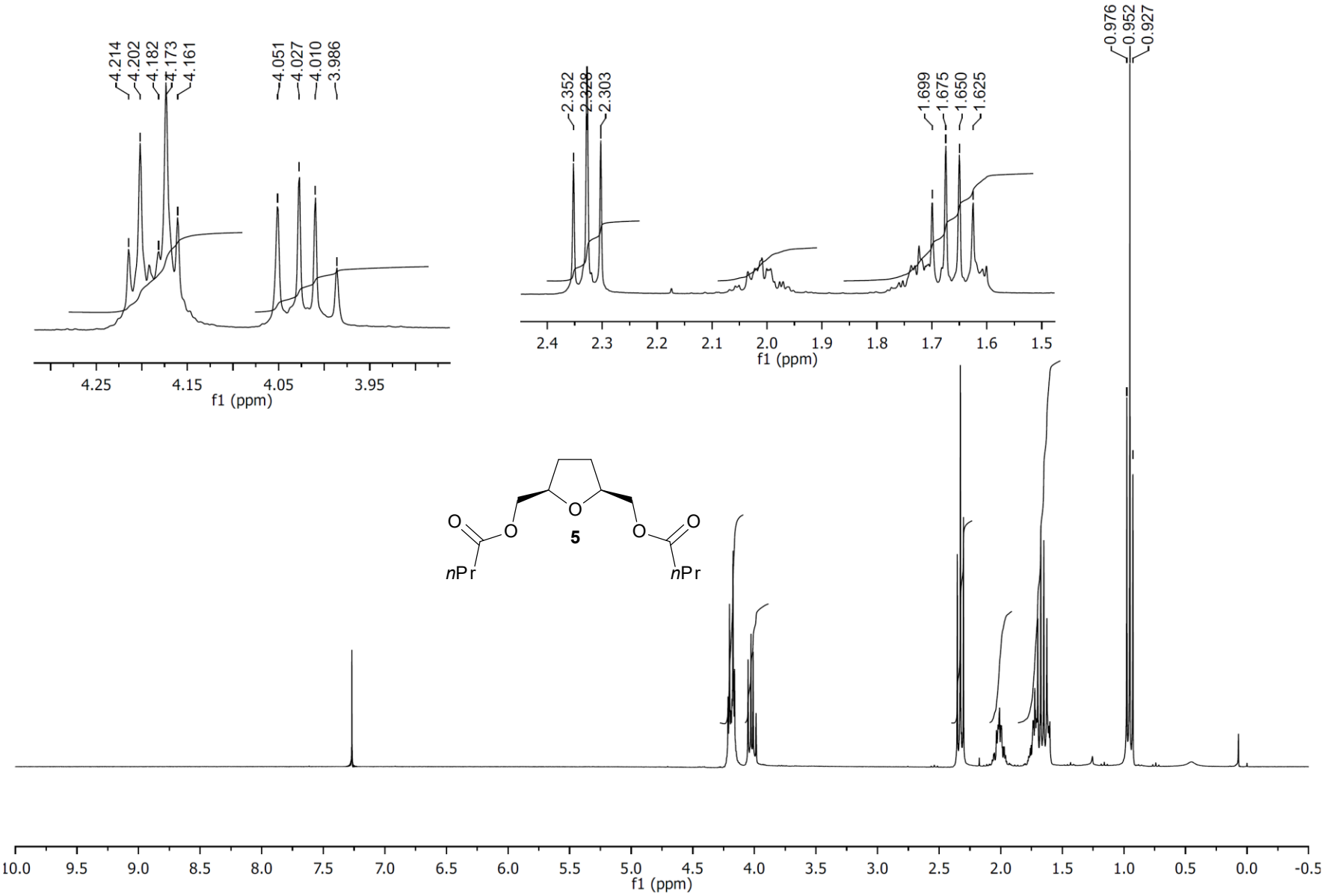

6.143
5.971
62.85
37.15
anti-7k
syn-7k
6.30 6.28 6.26 6.24 6.22 6.20 6.18 6.16 6.14 6.12 6.10 6.08 6.06 6.04 6.02 6.00 5.98 5.96 5.94 5.92 5.90 5.88 5.86 5.84
f1 (ppm)

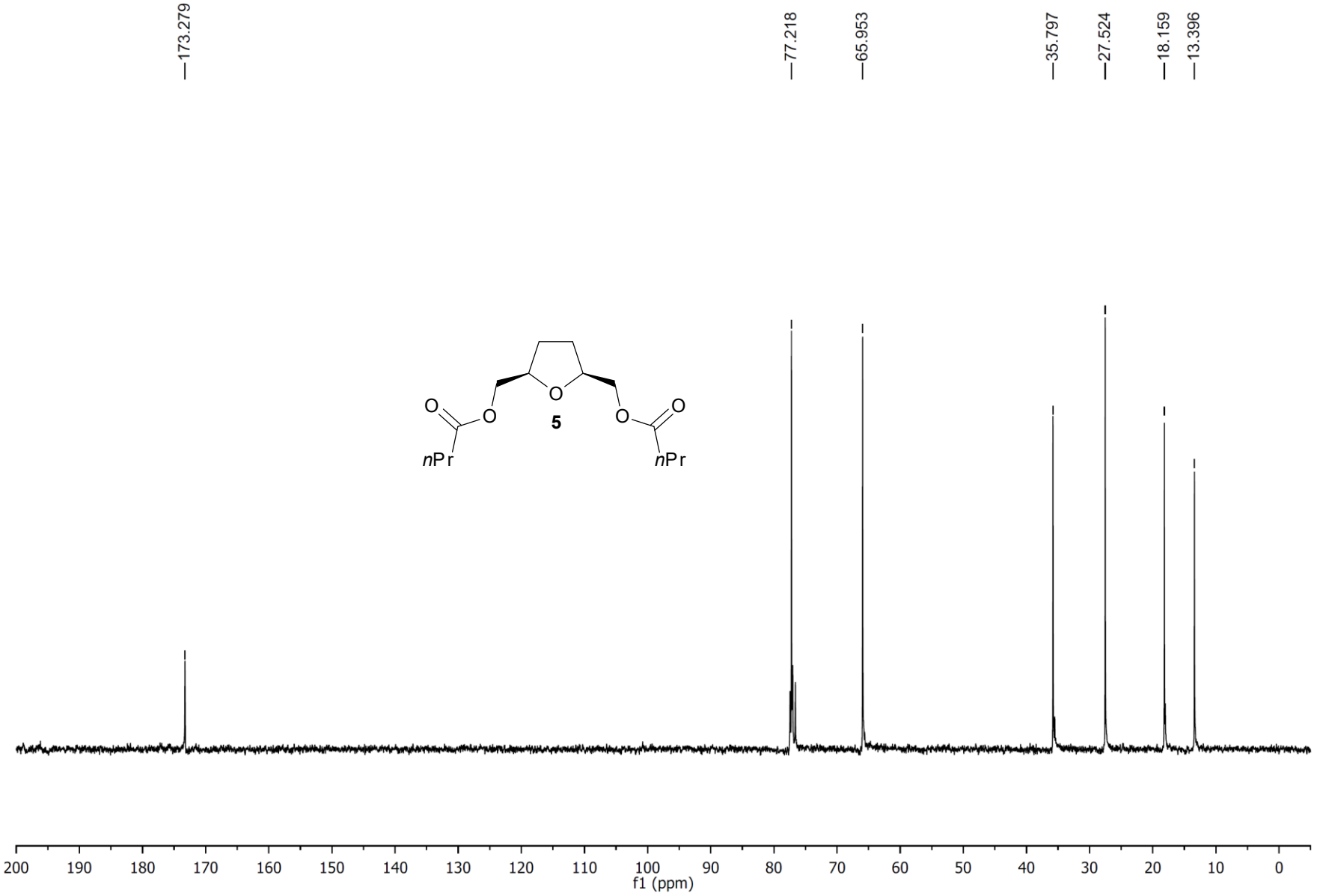

82.49
17.51
anti-7l
syn-7l
52 6.50 6.48 6.46 6.44 6.42 6.40 6.38 6.36 6.34 6.32 6.30 6.28 6.26 6.24 6.22 6.20 6.18 6.16 6.14 6.12
f1 (ppm)

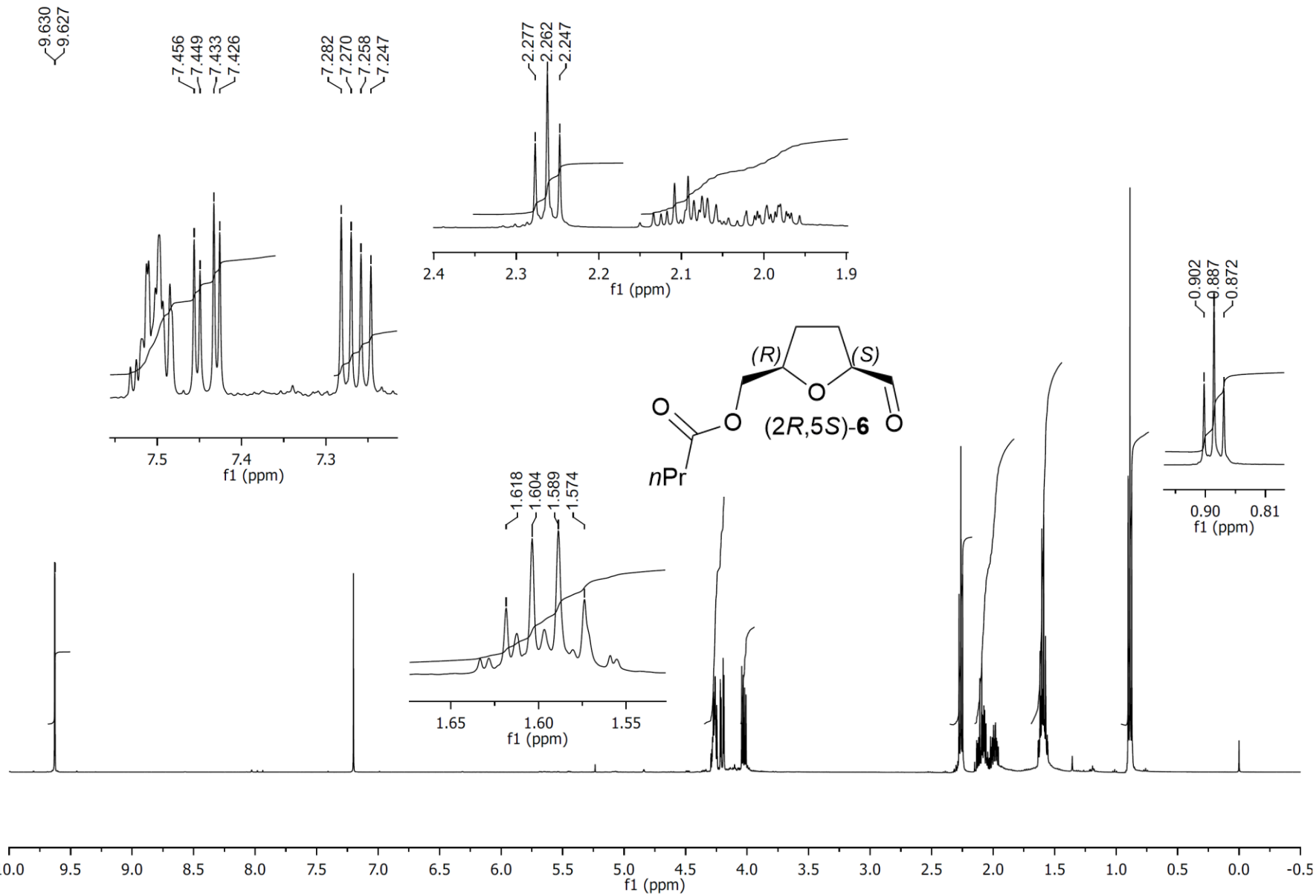
^{1}H and ^{13}C NMR spectra of all new compounds

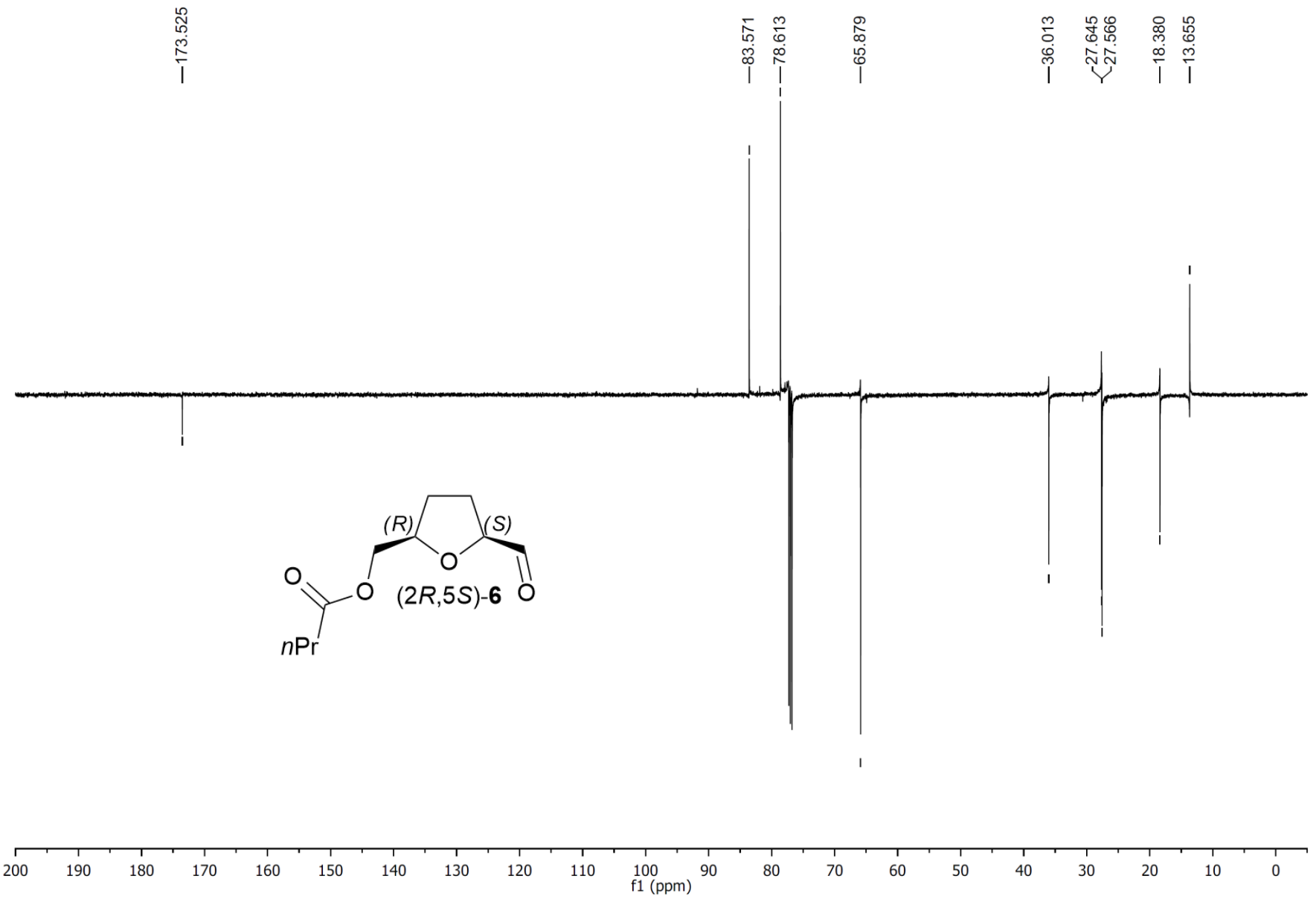


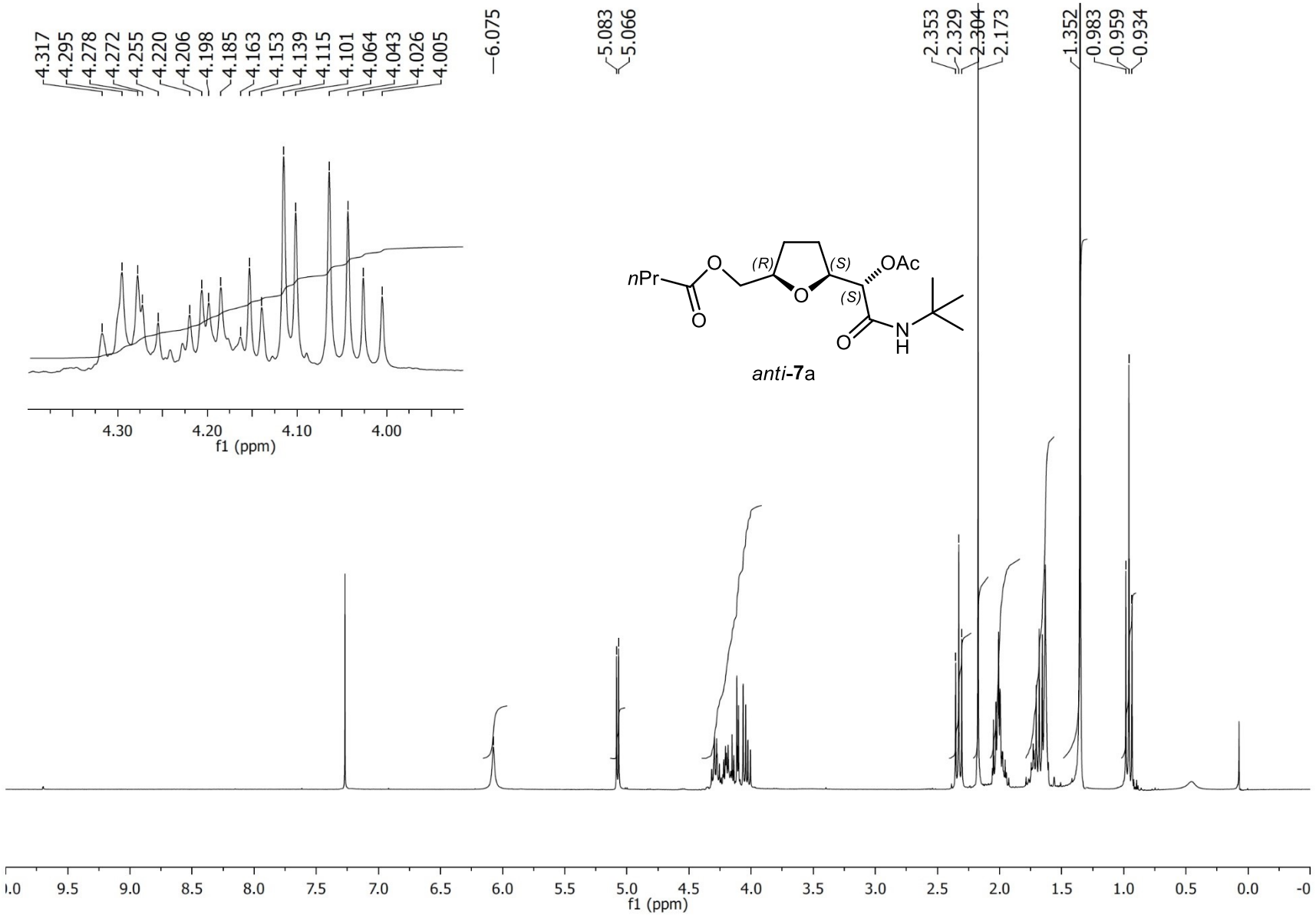

173.822
80.433
77.444
77.382
77.020
76.596
66.238
64.488
36.060
27.995
26.649
18.356
13.602
nPr
O
O
(R)
O
(S)
OH
(2R,5S)-4
f1 (ppm)

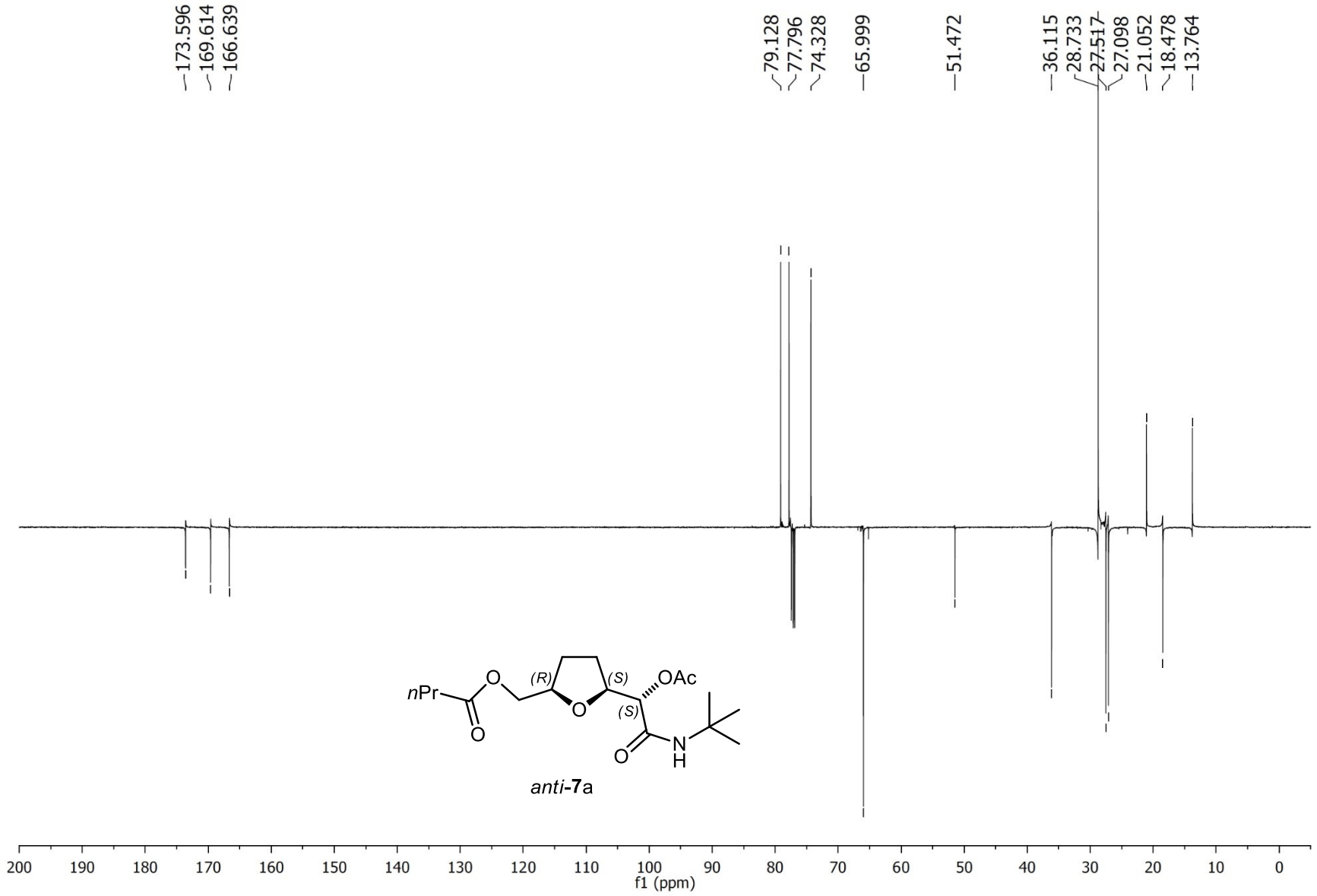

4.214
4.202
4.182
4.173
4.161
4.051
4.027
4.010
3.986
4.25
4.15
4.05
3.95
f1 (ppm)
2.352
2.328
2.303
1.699
1.675
1.650
1.625
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
f1 (ppm)
0.976
0.952
0.927
O
O
O
O
O
O
nPr
nPr
5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

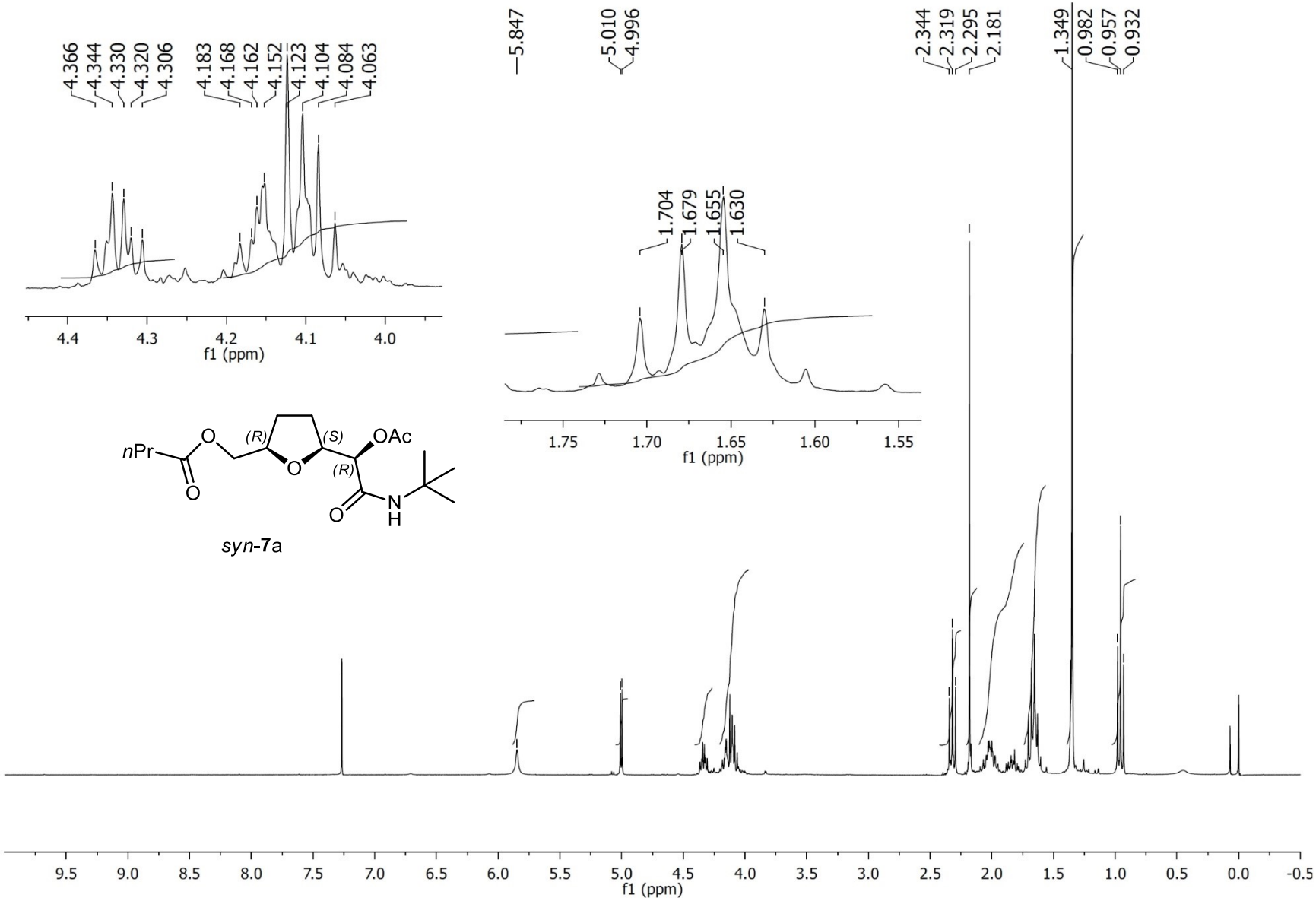

173.279
77.218
65.953
35.797
27.524
18.159
13.396
O
O
O
O
O
O
nPr
nPr
5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.630
9.627
7.456
7.449
7.433
7.426
7.282
7.270
7.258
7.247
2.277
2.262
2.247
1.618
1.604
1.589
1.574
0.902
0.887
0.872
(R)
(S)
O
O
O
O
O
nPr
(2R,5S)-6
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

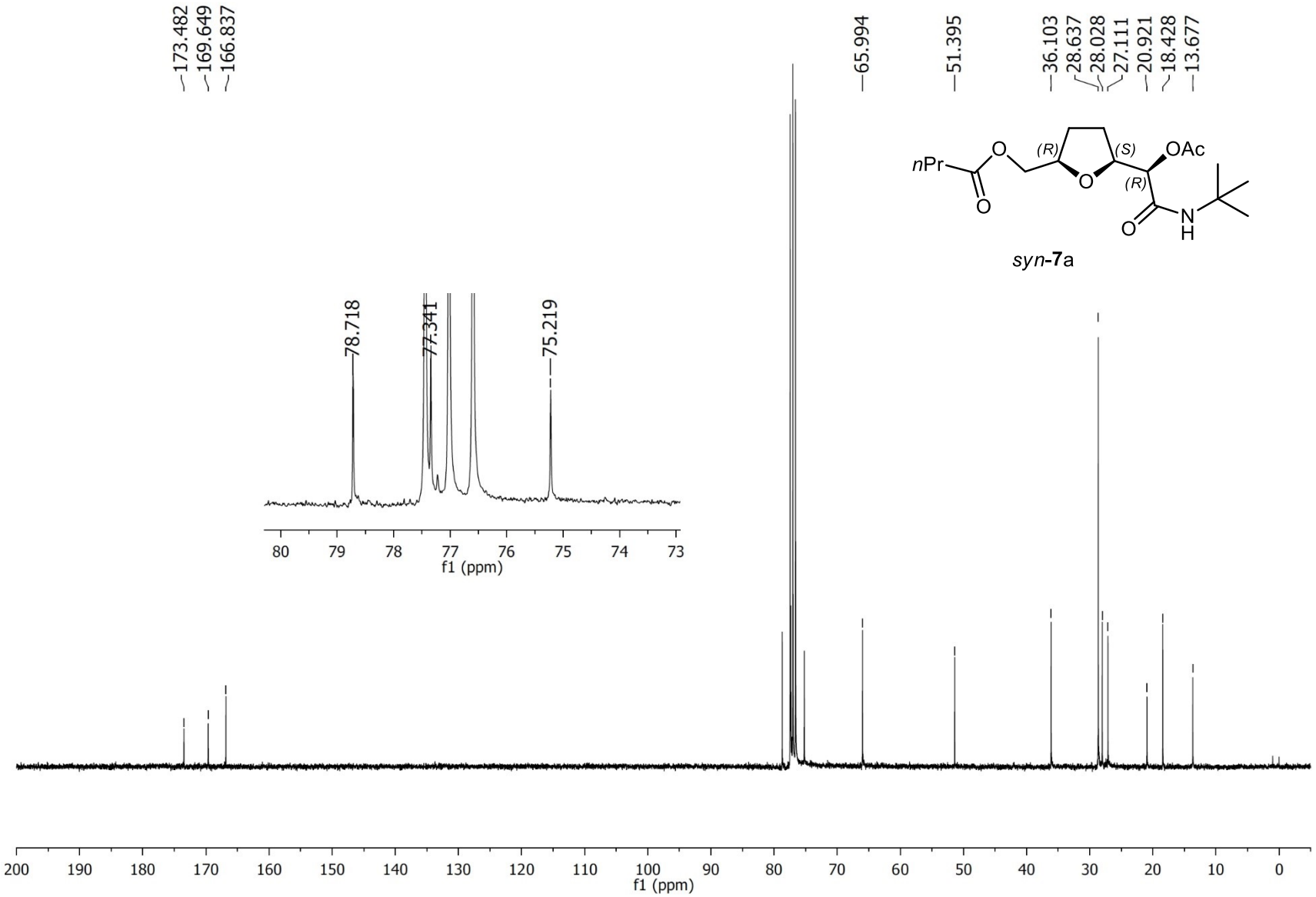

173.525
83.571
78.613
65.879
36.013
27.645
27.566
18.380
13.655
(R)
(S)
O
O
O
O
nPr
(2R,5S)-6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

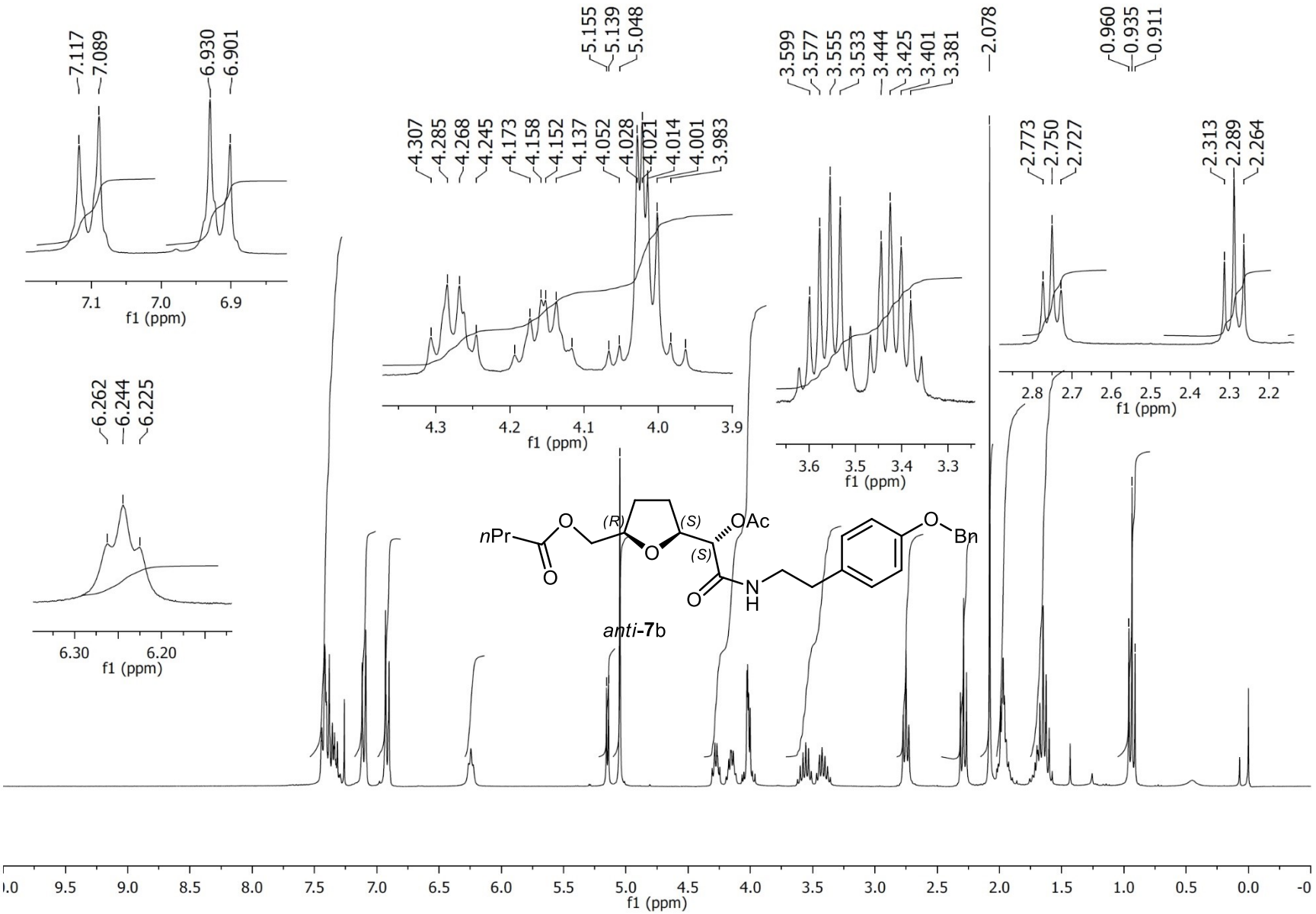

4.317
4.295
4.278
4.272
4.255
4.220
4.206
4.198
4.185
4.163
4.153
4.139
4.115
4.101
4.064
4.043
4.026
4.005
6.075
5.083
5.066
2.353
2.329
2.304
2.173
1.352
0.983
0.959
0.934
nPr
O
O
(R)
O
(S)
OAc
(S)
O
N
H
anti-7a
4.30
4.20
4.10
4.00
f1 (ppm)
f1 (ppm)

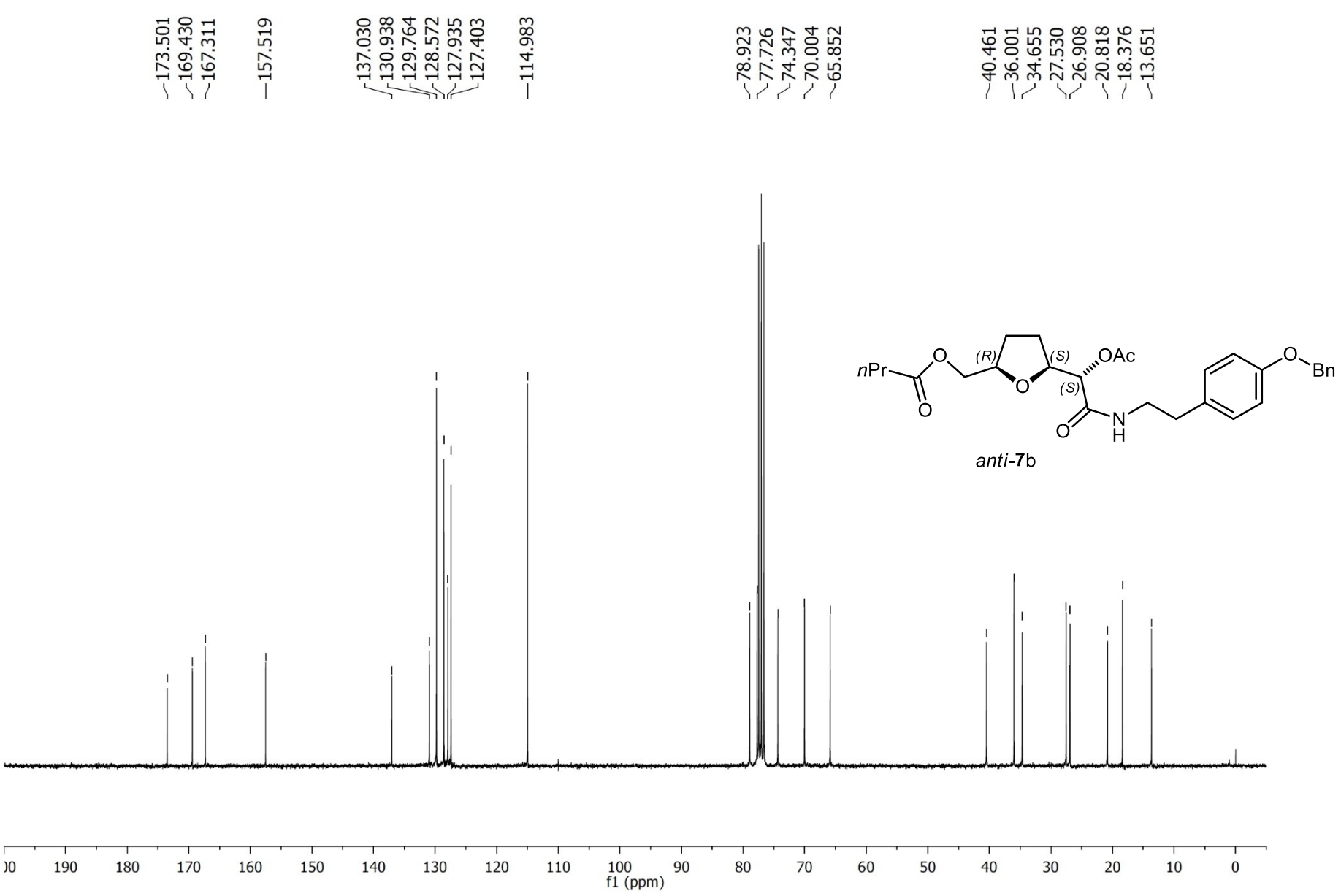

173.596
169.614
166.639
79.128
77.796
74.328
65.999
51.472
36.115
28.733
27.517
27.098
21.052
18.478
13.764
nPr
O
O
(R)
O
(S)
(S)
OAc
O
N
H
anti-7a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

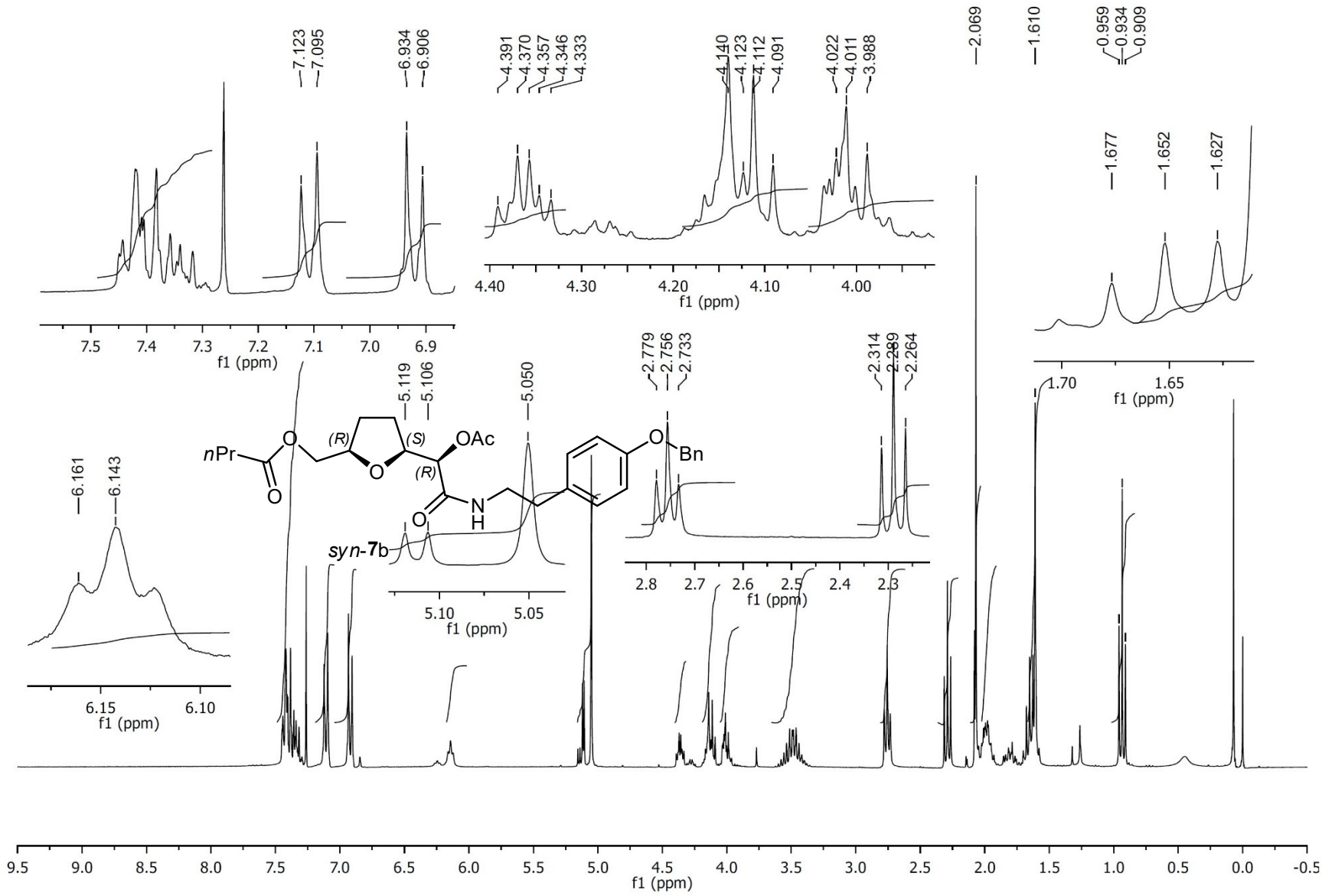

4.366
4.344
4.330
4.320
4.306
4.183
4.168
4.162
4.152
4.123
4.104
4.084
4.063
4.4
4.3
4.2
4.1
4.0
f1 (ppm)
5.847
5.010
4.996
2.344
2.319
2.295
2.181
1.349
0.982
0.957
0.932
1.704
1.679
1.655
1.630
1.75
1.70
1.65
1.60
1.55
f1 (ppm)
nPr
O
O
(R)
O
(S)
OAc
(R)
O
N
H
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

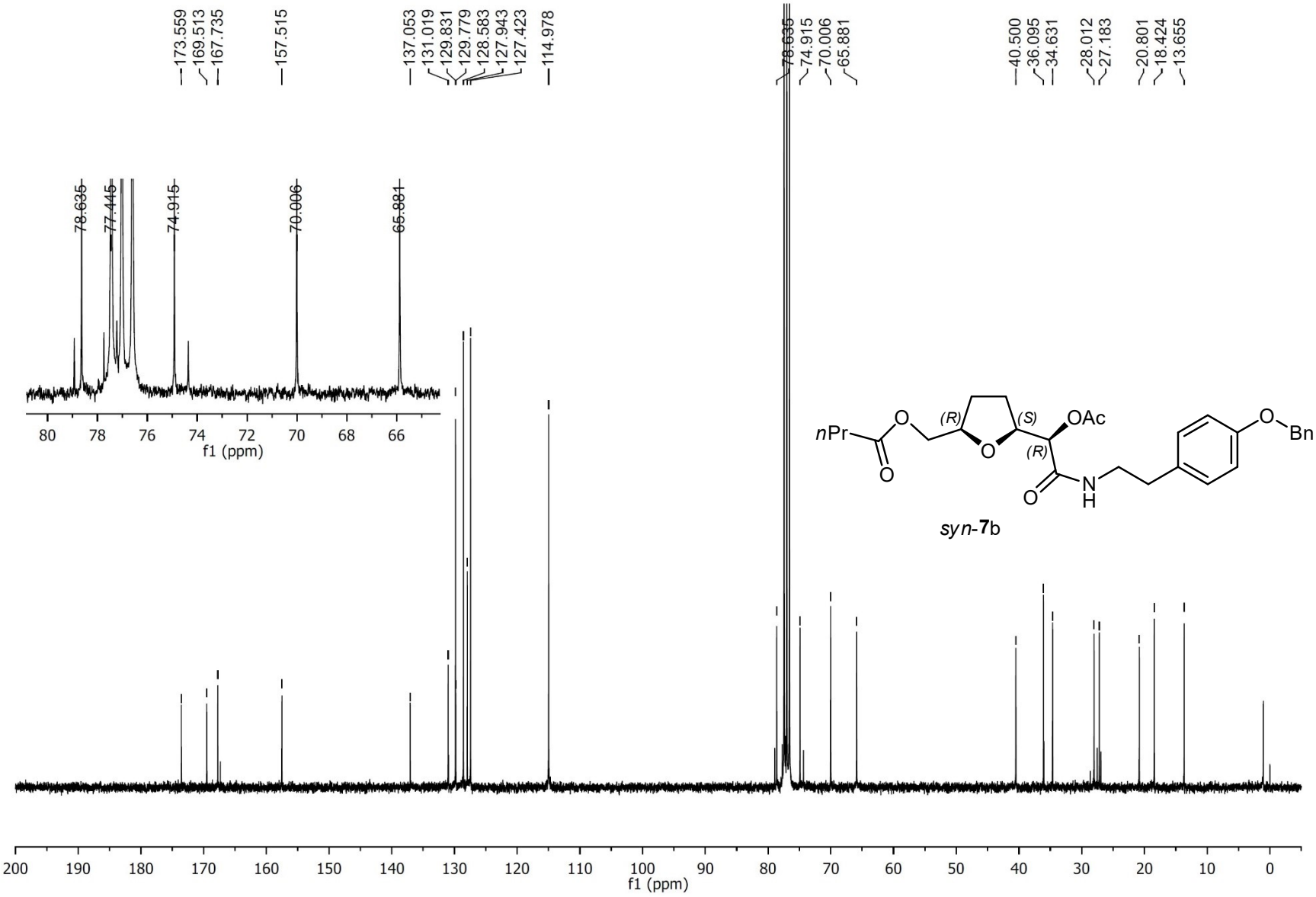
syn-**7**a


173.482
169.649
166.837
65.994
51.395
36.103
28.637
28.028
27.111
20.921
18.428
13.677
78.718
77.341
75.219
nPr
O
O
(R)
O
(S)
OAc
(R)
O
N
H
syn-7a
f1 (ppm)
f1 (ppm)


7.117
7.089
6.930
6.901
6.262
6.244
6.225
5.155
5.139
5.048
4.307
4.285
4.268
4.245
4.173
4.158
4.152
4.137
4.052
4.028
4.021
4.014
4.001
3.983
3.599
3.577
3.555
3.533
3.444
3.425
3.401
3.381
2.078
0.960
0.935
0.911
2.773
2.750
2.727
2.313
2.289
2.264
f1 (ppm)
nPr
OAc
OBn
(R)
(S)
(S)
anti-7b


173.501
169.430
167.311
157.519
137.030
130.938
129.764
128.572
127.935
127.403
114.983
78.923
77.726
74.347
70.004
65.852
40.461
36.001
34.655
27.530
26.908
20.818
18.376
13.651
nPr
O
O
(R)
O
(S)
OAc
(S)
O
N
H
O
Bn
anti-7b
f1 (ppm)


7.123
7.095
6.934
6.906
4.391
4.370
4.357
4.346
4.333
4.140
4.123
4.112
4.091
4.022
4.011
3.988
2.069
1.610
0.959
0.934
0.909
1.677
1.652
1.627
5.119
5.106
5.050
2.779
2.756
2.733
2.314
2.289
2.264
6.161
6.143
nPr
O
(R)
(S)
OAc
(R)
N
H
Bn
syn-7b
f1 (ppm)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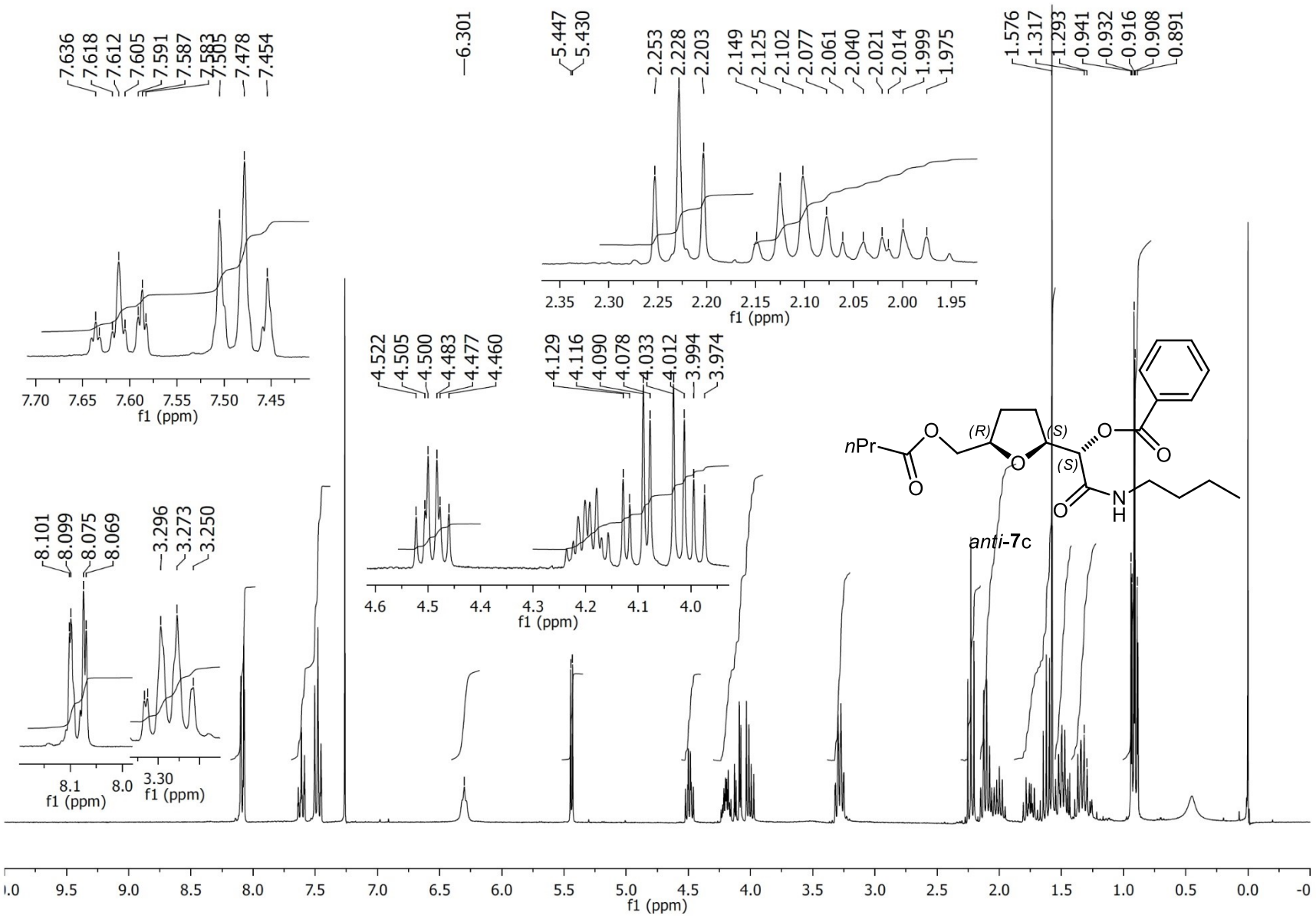
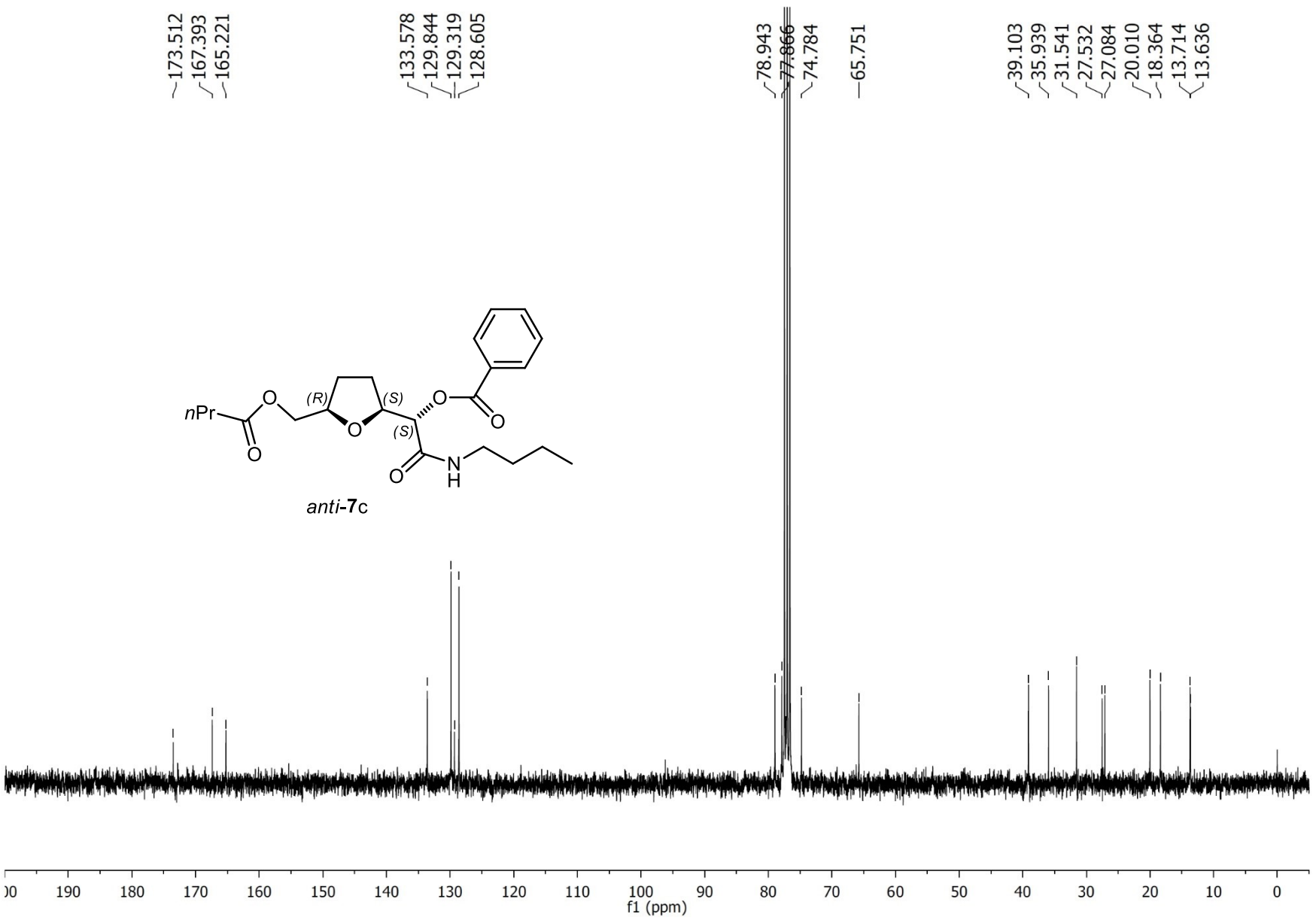
169.513
167.735
157.515
137.053
131.019
129.831
129.779
128.583
127.943
127.423
114.978
78.636
74.915
70.006
65.881
40.500
36.095
34.631
28.012
27.183
20.801
18.424
13.655
78.635
77.445
74.915
70.006
65.881
80 78 76 74 72 70 68 66
f1 (ppm)
nPr
O
O
(R)
(S)
OAc
O
(R)
O
N
H
O
Bn
syn-7b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.636
7.618
7.612
7.605
7.591
7.587
7.583
7.505
7.478
7.454
6.301
5.447
5.430
2.253
2.228
2.203
2.149
2.125
2.102
2.077
2.061
2.040
2.021
2.014
1.999
1.975
1.576
1.317
1.293
0.941
0.932
0.916
0.908
0.891
4.522
4.505
4.500
4.483
4.477
4.460
4.129
4.116
4.090
4.078
4.033
4.012
3.994
3.974
8.101
8.099
8.075
8.069
3.296
3.273
3.250
nPr
(R)
(S)
(S)
anti-7c
f1 (ppm)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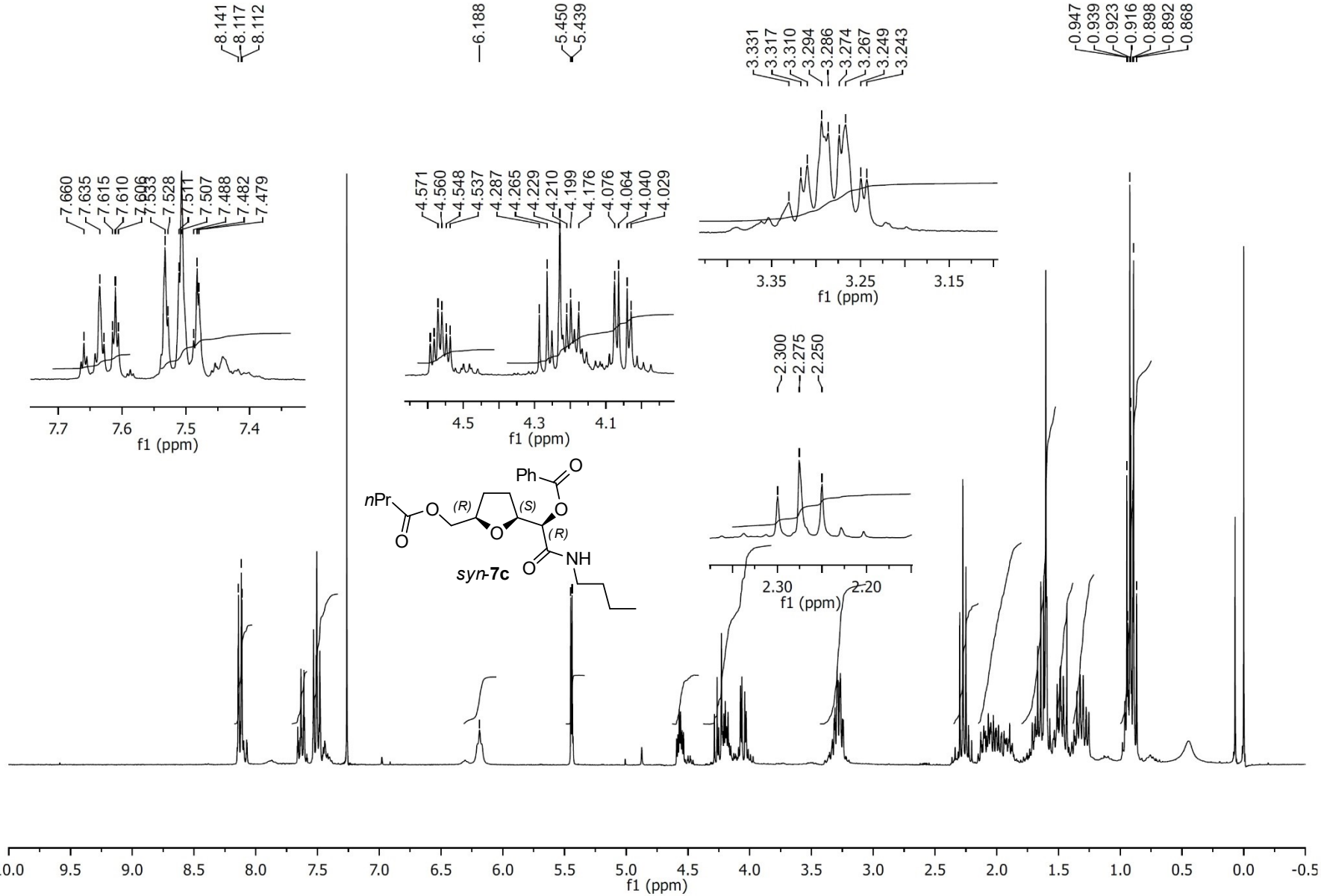
167.393
165.221
133.578
129.844
129.319
128.605
78.943
77.866
74.784
65.751
39.103
35.939
31.541
27.532
27.084
20.010
18.364
13.714
13.636
nPr
(R)
(S)
(S)
anti-7c
f1 (ppm)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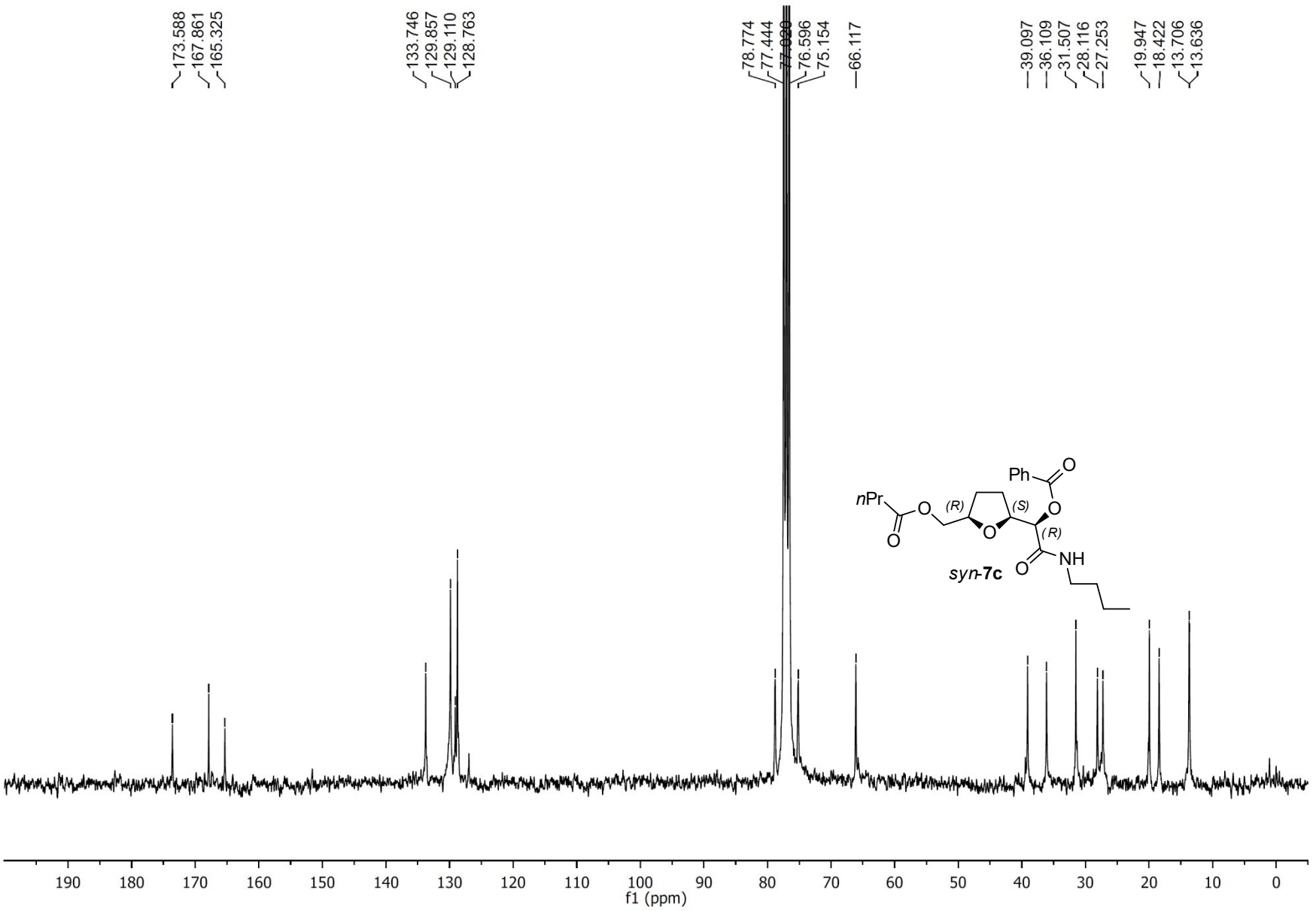
8.117
8.112
6.188
5.450
5.439
3.331
3.317
3.310
3.294
3.286
3.274
3.267
3.249
3.243
0.947
0.939
0.923
0.916
0.898
0.892
0.868
7.660
7.635
7.615
7.610
7.606
7.533
7.528
7.511
7.507
7.488
7.482
7.479
4.571
4.560
4.548
4.537
4.287
4.265
4.229
4.210
4.199
4.176
4.076
4.064
4.040
4.029
2.300
2.275
2.250
Ph
nPr
(R)
(S)
(R)
NH
syn-7c
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5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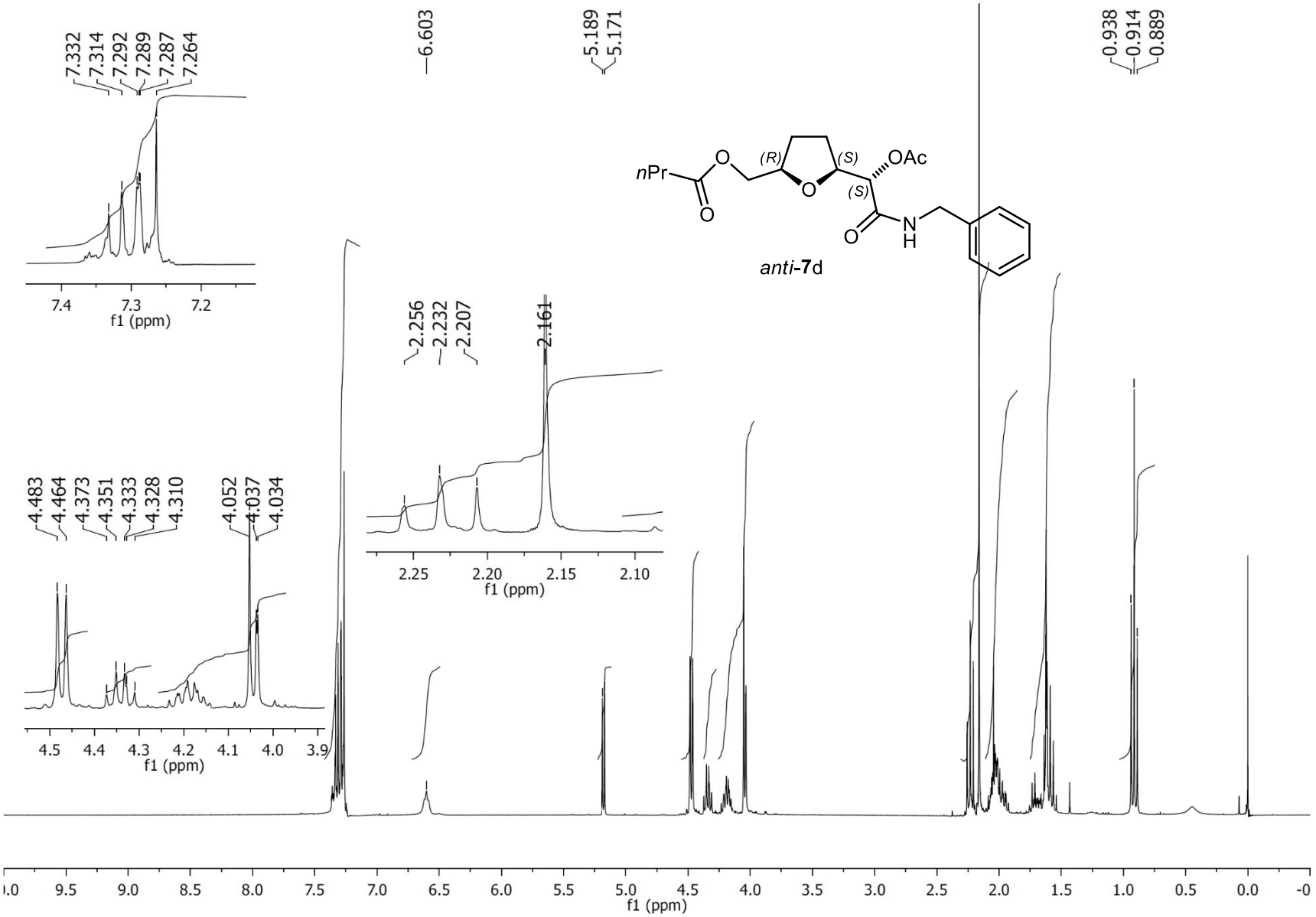
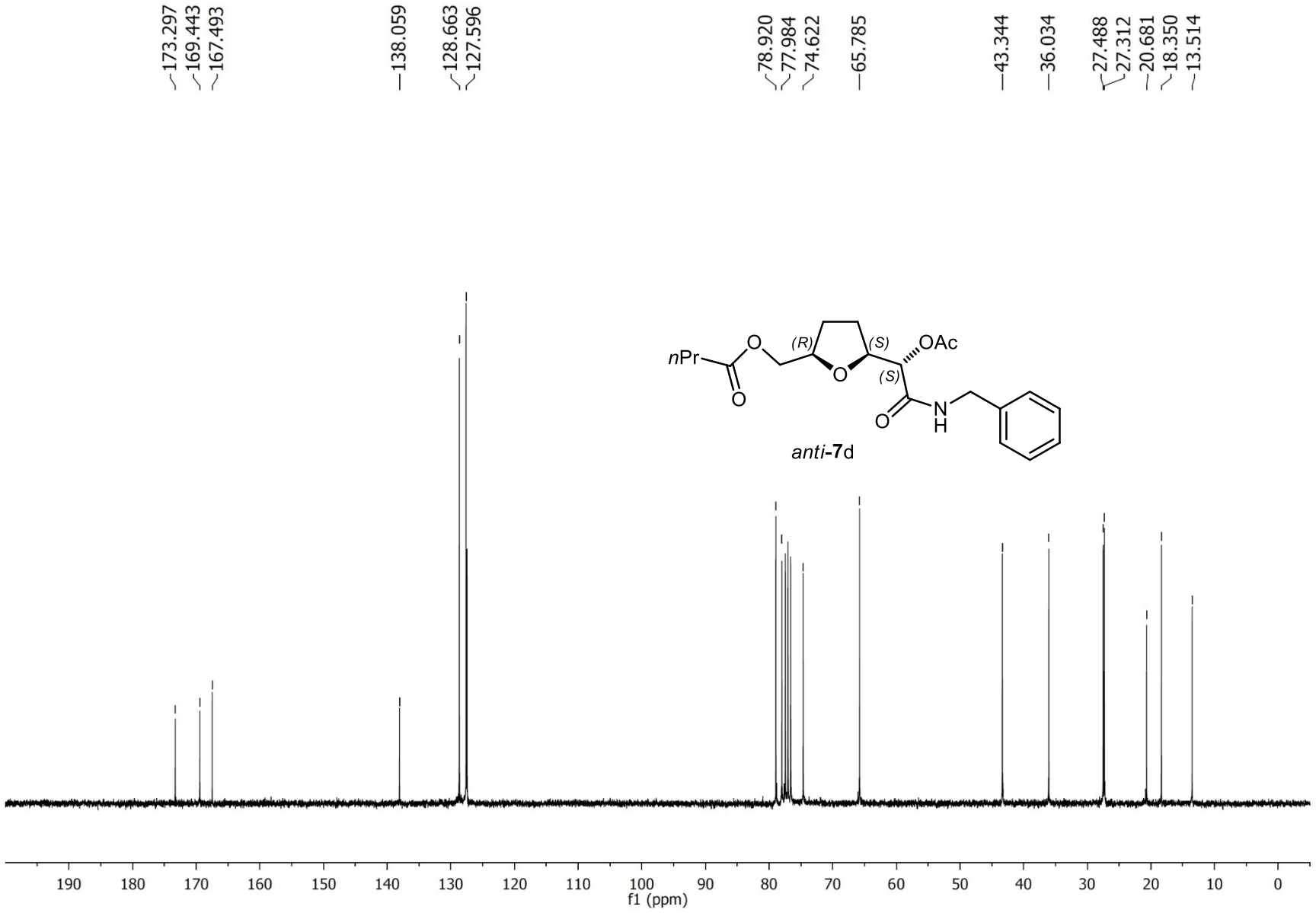
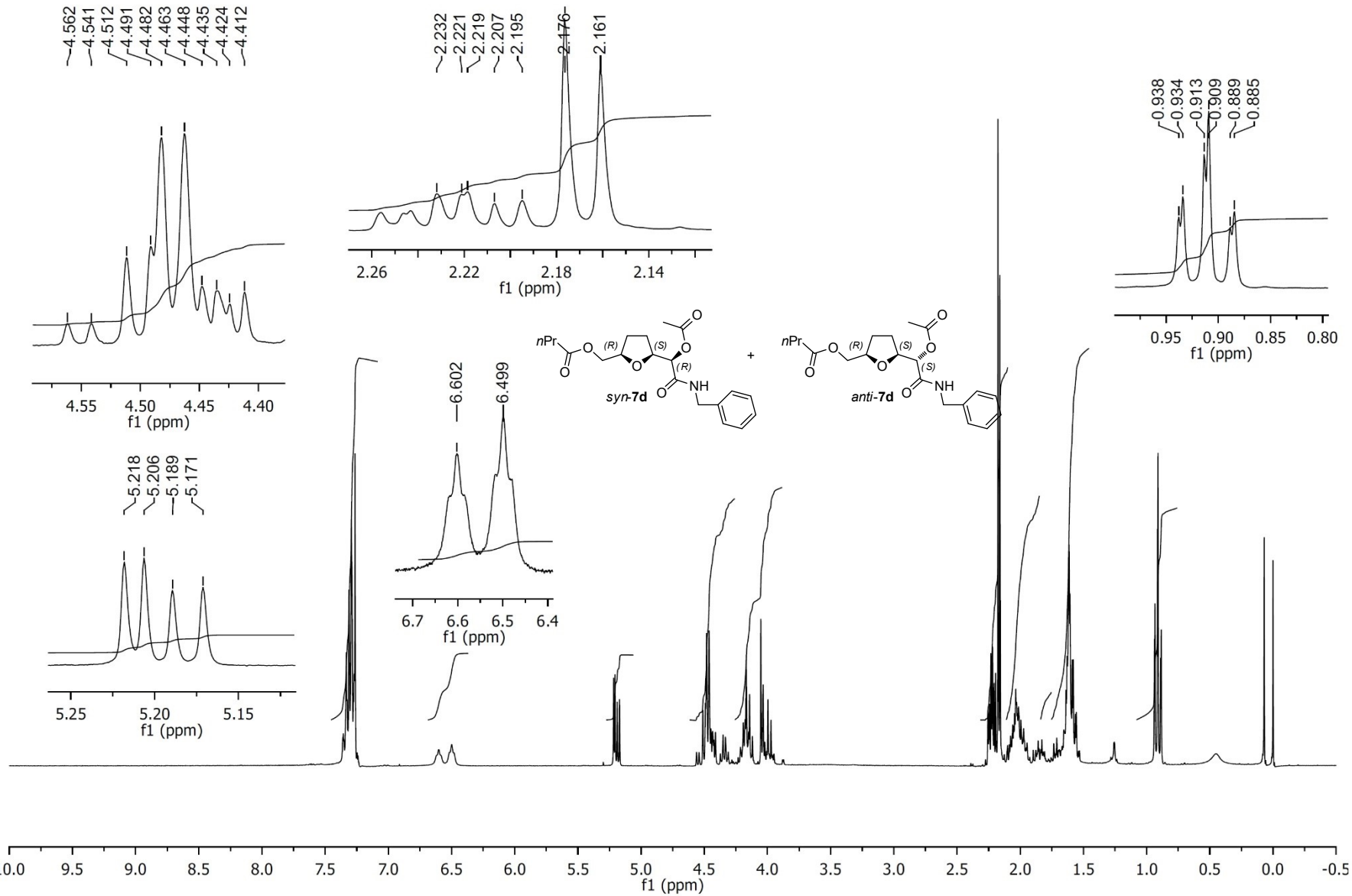
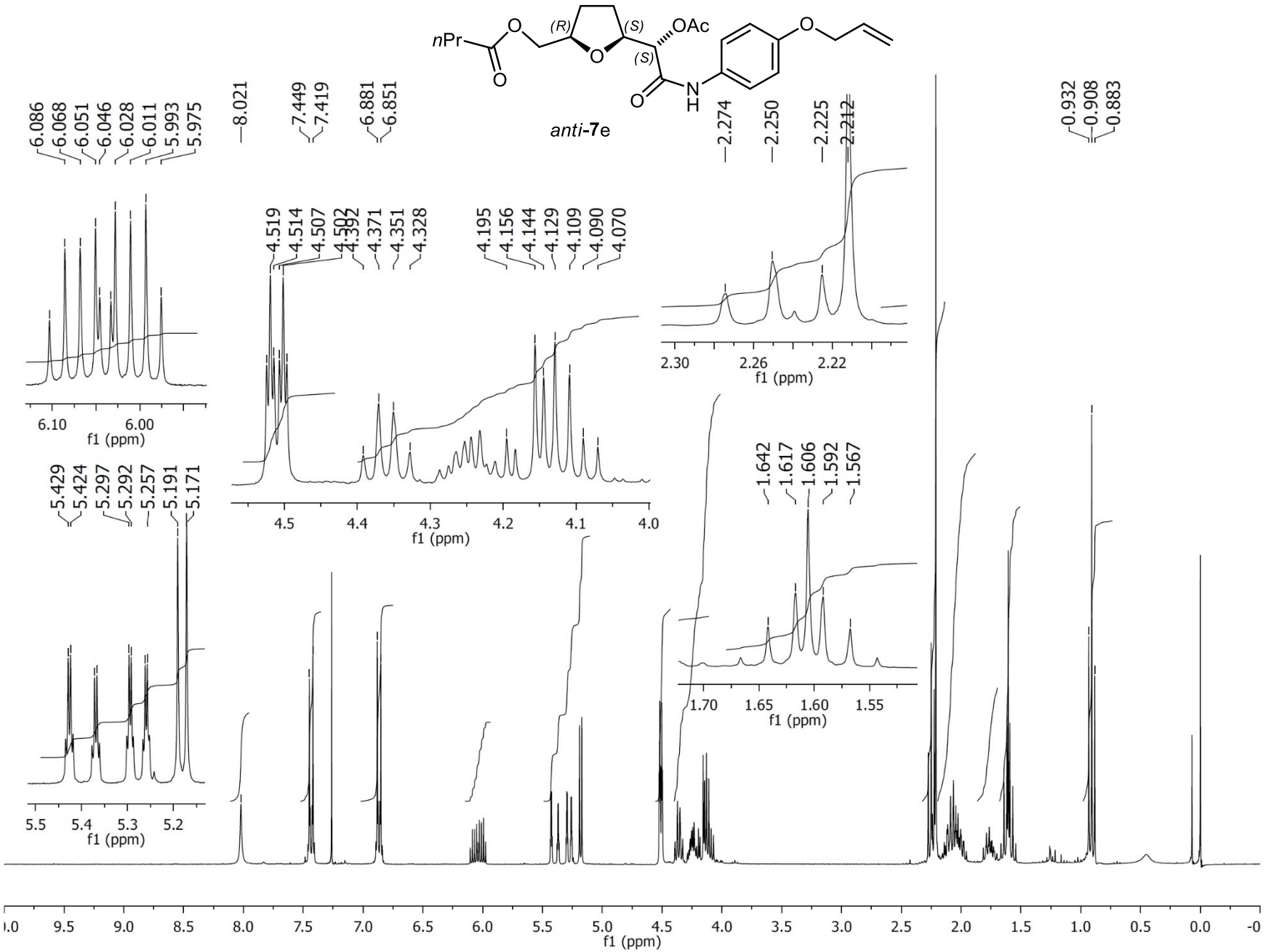
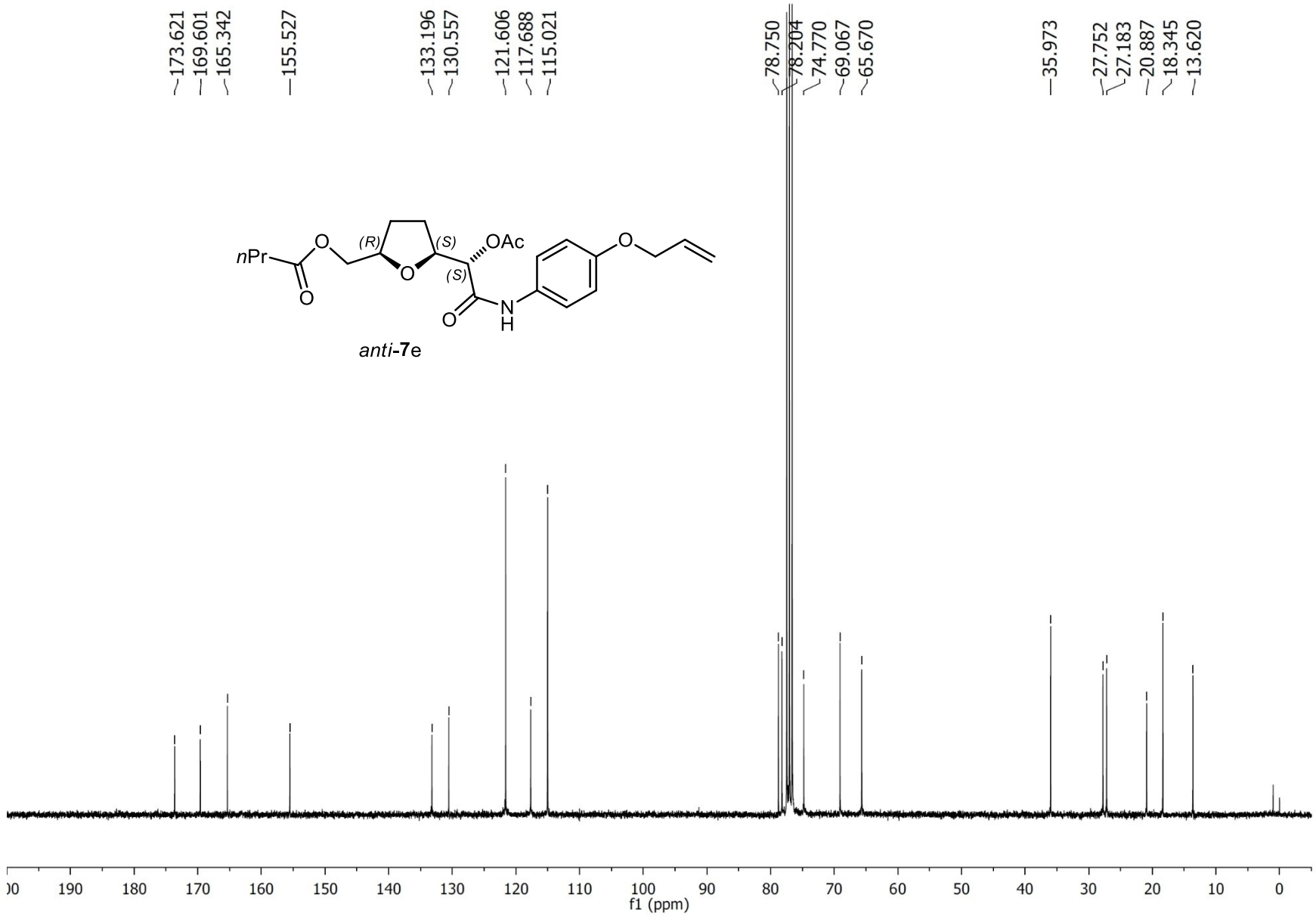
167.861
165.325
133.746
129.857
129.110
128.763
78.774
77.444
77.020
76.596
75.154
66.117
39.097
36.109
31.507
28.116
27.253
19.947
18.422
13.706
13.636
nPr
Ph
(R)
(S)
(R)
NH
syn-7c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.332
7.314
7.292
7.289
7.287
7.264
6.603
5.189
5.171
0.938
0.914
0.889
nPr
O
O
(R)
O
(S)
OAc
(S)
O
N
H
anti-7d
2.256
2.232
2.207
2.161
4.483
4.464
4.373
4.351
4.333
4.328
4.310
4.052
4.037
4.034
f1 (ppm)

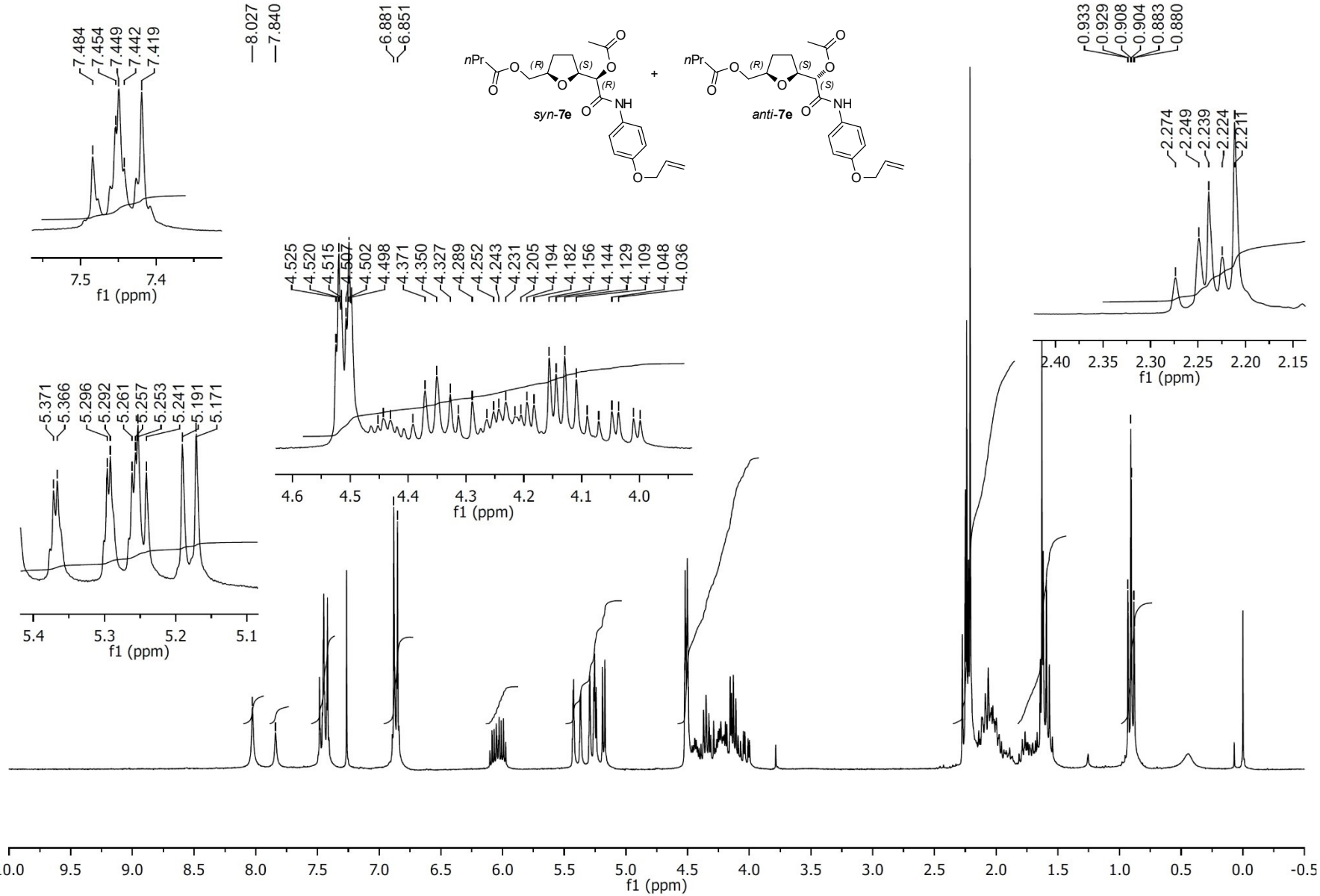

173.297
169.443
167.493
138.059
128.663
127.596
78.920
77.984
74.622
65.785
43.344
36.034
27.488
27.312
20.681
18.350
13.514
nPr
O
O
(R)
O
(S)
OAc
(S)
O
N
H
anti-7d
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

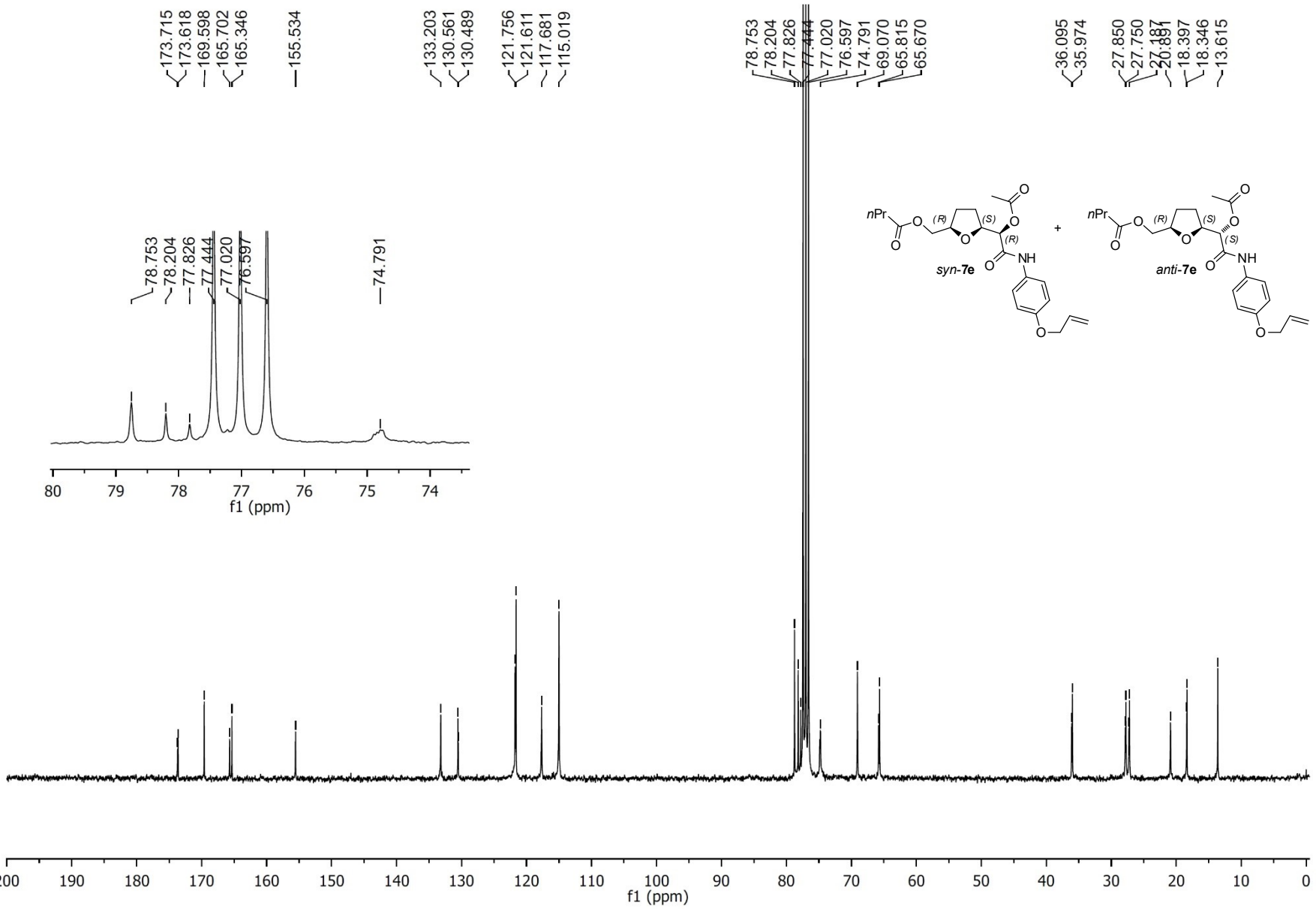

4.562
4.541
4.512
4.491
4.482
4.463
4.448
4.435
4.424
4.412
4.55 4.50 4.45 4.40
f1 (ppm)
2.232
2.221
2.219
2.207
2.195
2.176
2.161
2.26 2.22 2.18 2.14
f1 (ppm)
0.938
0.934
0.913
0.909
0.889
0.885
0.95 0.90 0.85 0.80
f1 (ppm)
5.218
5.206
5.189
5.171
5.25 5.20 5.15
f1 (ppm)
6.602
6.499
6.7 6.6 6.5 6.4
f1 (ppm)
nPr
(R)
(S)
(R)
NH
syn-7d
+
anti-7d
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


nPr
(R)
(S)
OAc
(S)
O
N
H
anti-7e
8.021
7.449
7.419
6.881
6.851
6.086
6.068
6.051
6.046
6.028
6.011
5.993
5.975
4.519
4.514
4.507
4.392
4.371
4.351
4.328
4.195
4.156
4.144
4.129
4.109
4.090
4.070
2.274
2.250
2.225
2.212
0.932
0.908
0.883
5.429
5.424
5.297
5.292
5.257
5.191
5.171
1.642
1.617
1.606
1.592
1.567
f1 (ppm)


173.621
169.601
165.342
155.527
133.196
130.557
121.606
117.688
115.021
78.750
78.204
74.770
69.067
65.670
35.973
27.752
27.183
20.887
18.345
13.620
nPr
O
O
(R)
O
(S)
OAc
(S)
O
N
H
O
f1 (ppm)

anti-**7**e


7.484
7.454
7.449
7.442
7.419
8.027
7.840
6.881
6.851
0.933
0.929
0.908
0.904
0.883
0.880
2.274
2.249
2.239
2.224
2.211
4.525
4.520
4.515
4.507
4.502
4.498
4.371
4.350
4.327
4.289
4.252
4.243
4.231
4.205
4.194
4.182
4.156
4.144
4.129
4.109
4.048
4.036
5.371
5.366
5.296
5.292
5.261
5.257
5.253
5.241
5.191
5.171
nPr
(R)
(S)
(R)
NH
syn-7e
+
anti-7e
f1 (ppm)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173.618
169.598
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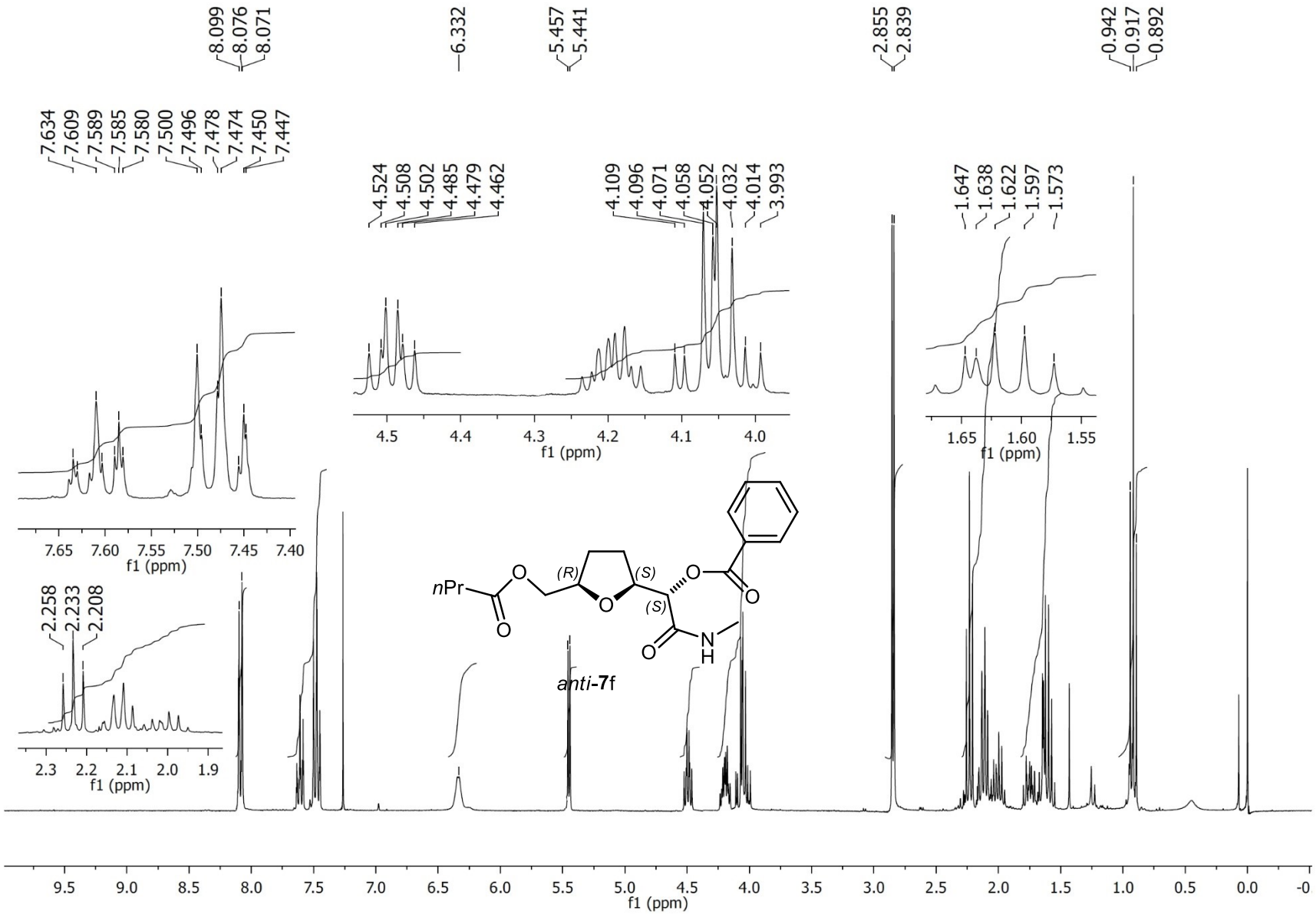
165.346
155.534
133.203
130.561
130.489
121.756
121.611
117.681
115.019
78.753
78.204
77.826
77.444
77.020
76.597
74.791
69.070
65.815
65.670
36.095
35.974
27.850
27.750
27.187
20.891
18.397
18.346
13.615
nPr
(R)
(S)
(R)
NH
syn-7e
+
nPr
(R)
(S)
(S)
NH
anti-7e
f1 (ppm)
f1 (ppm)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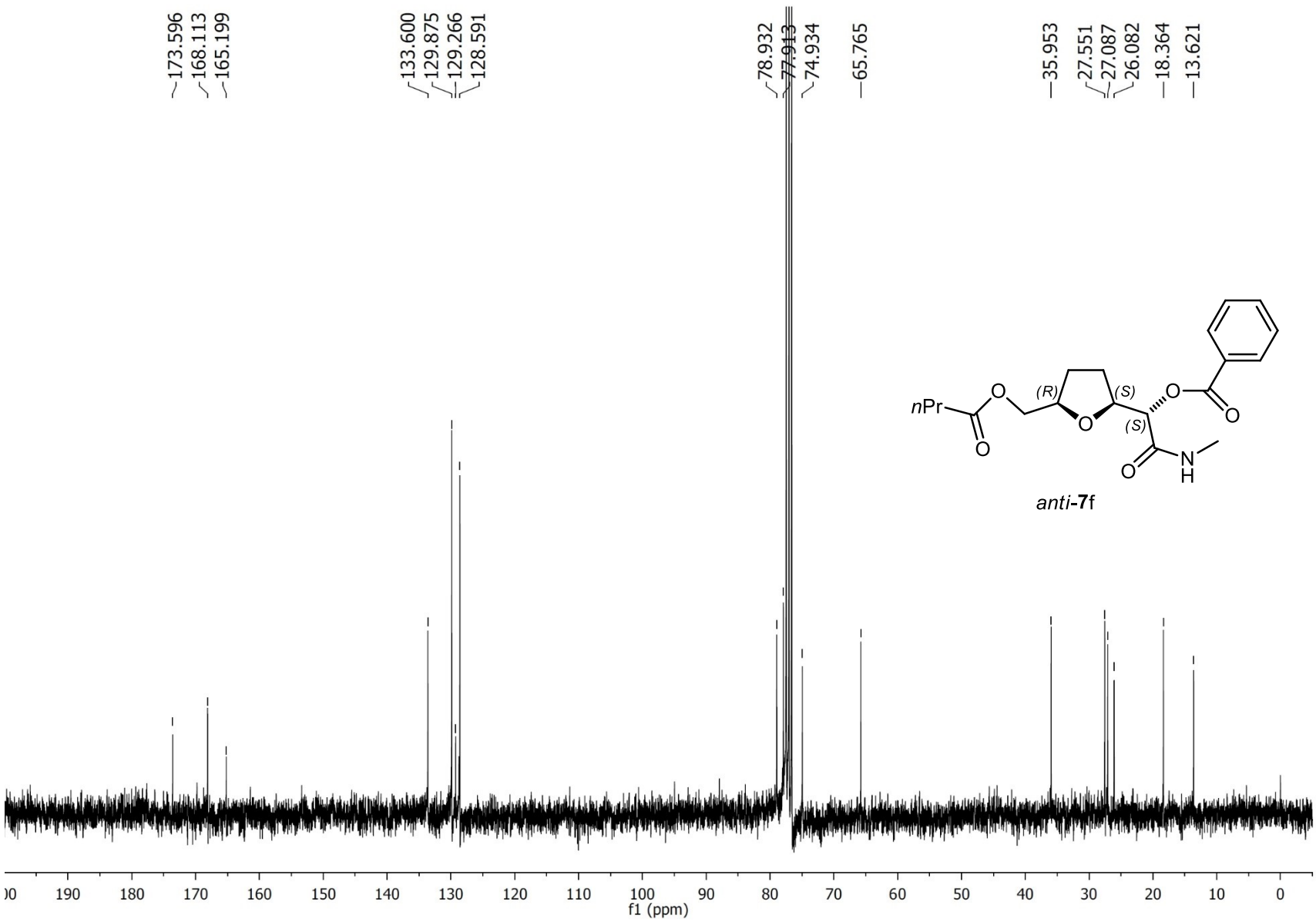
8.076
8.071
6.332
5.457
5.441
2.855
2.839
0.942
0.917
0.892
7.634
7.609
7.589
7.585
7.580
7.500
7.496
7.478
7.474
7.450
7.447
4.524
4.508
4.502
4.485
4.479
4.462
4.109
4.096
4.071
4.058
4.052
4.032
4.014
3.993
1.647
1.638
1.622
1.597
1.573
2.258
2.233
2.208
nPr
(R)
(S)
(S)
anti-7f
f1 (ppm)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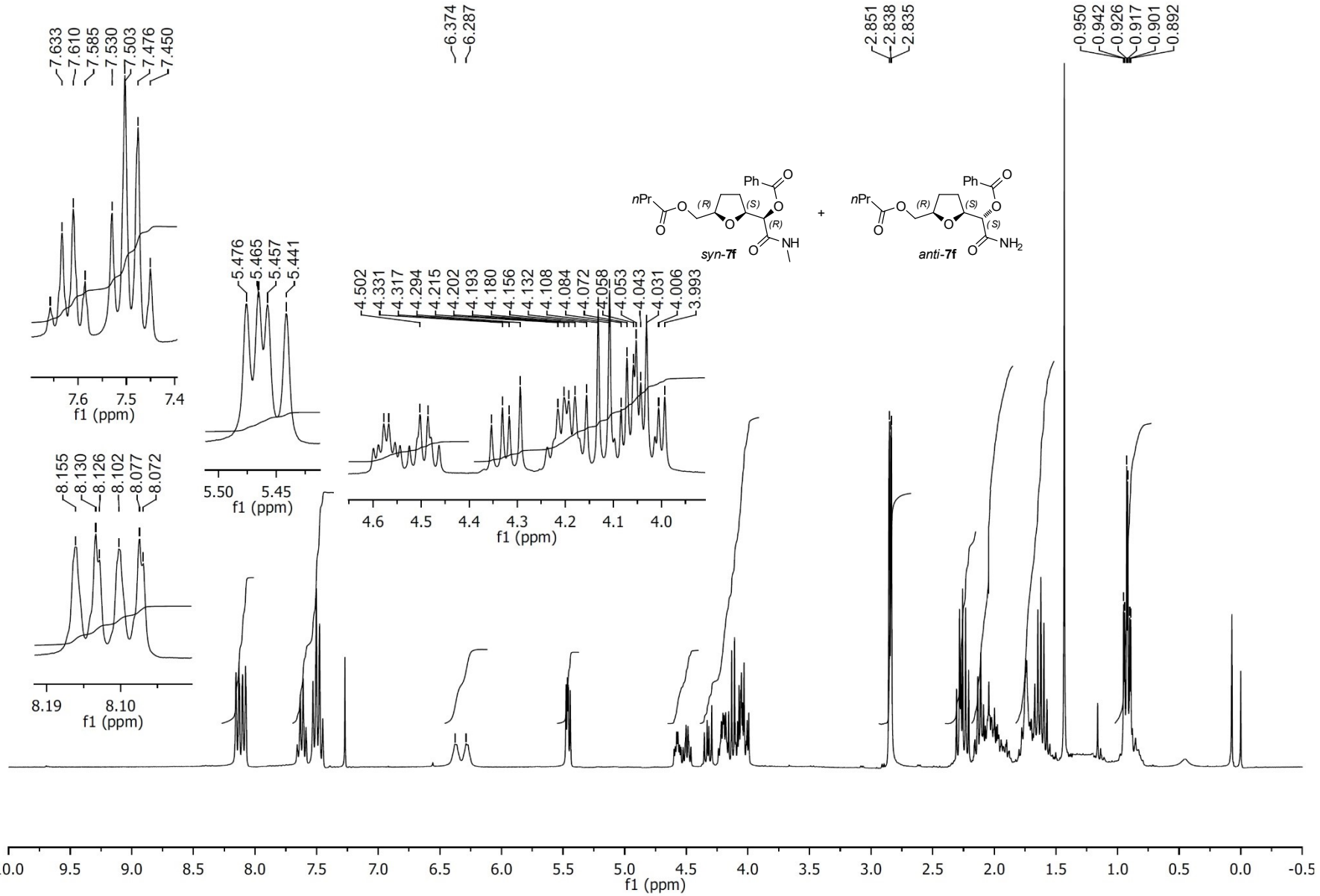
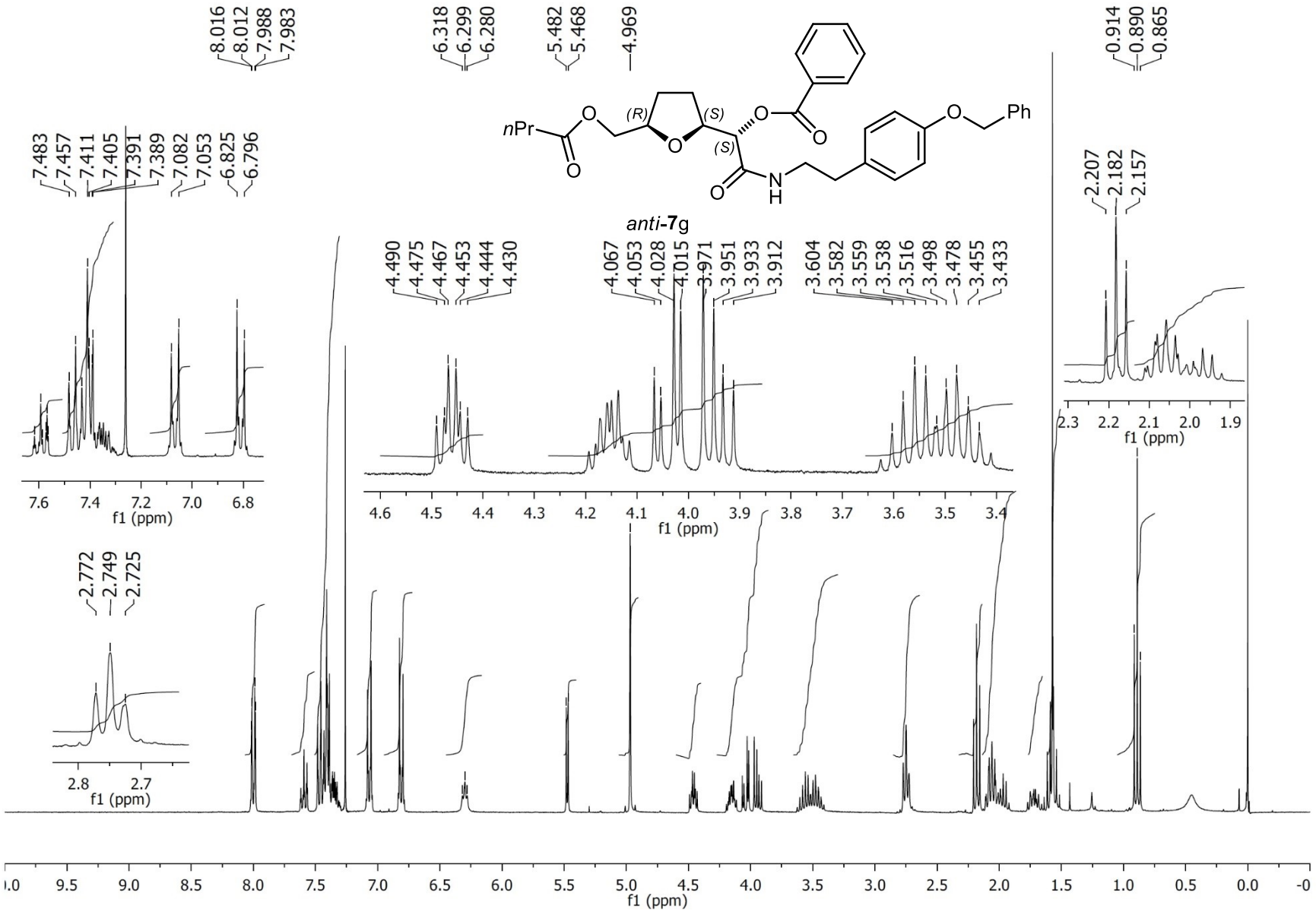
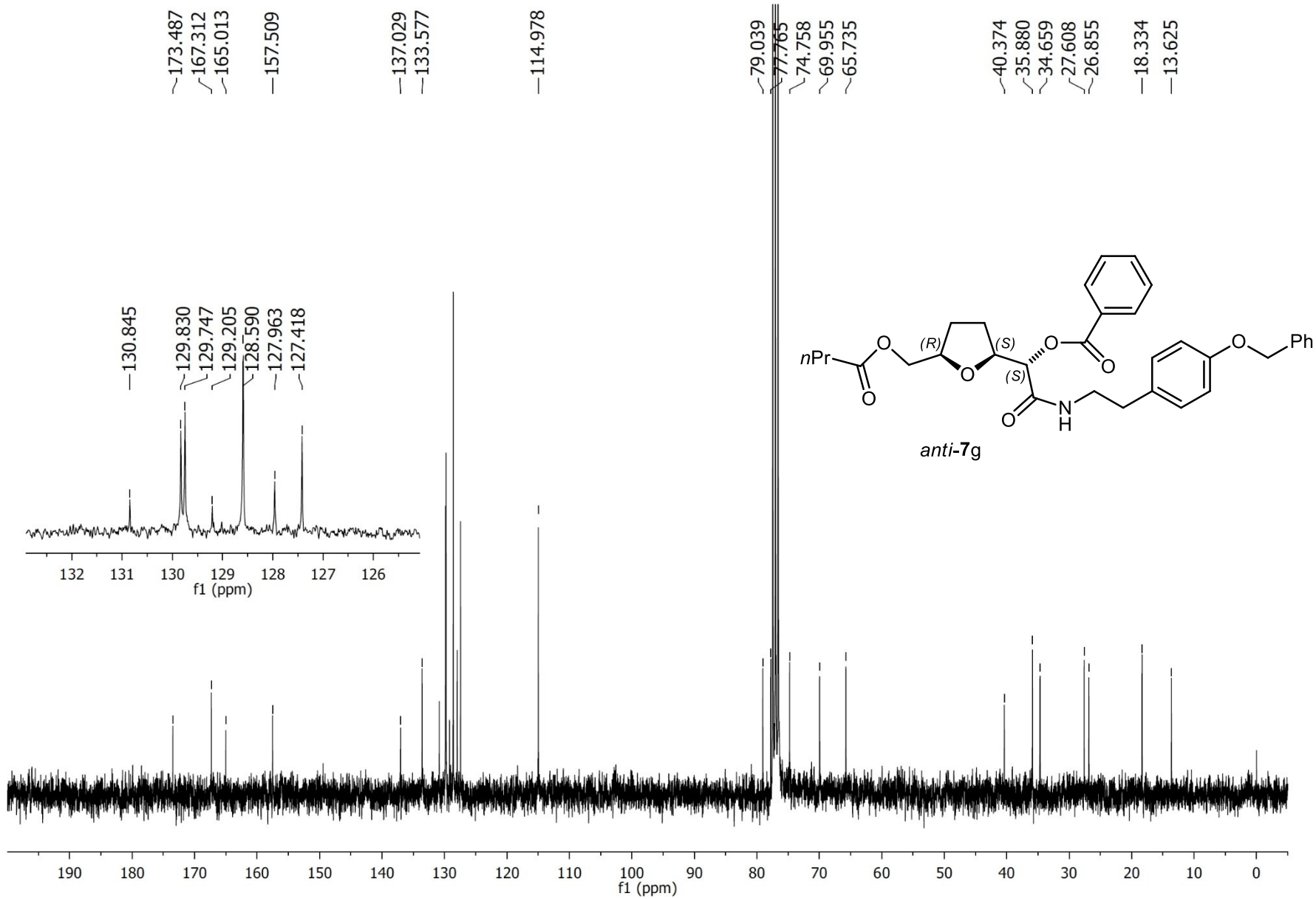
165.199
133.600
129.875
129.266
128.591
78.932
77.913
74.934
65.765
35.953
27.551
27.087
26.082
18.364
13.621
nPr
(R)
(S)
(S)
anti-7f
f1 (ppm)


7.633
7.610
7.585
7.530
7.503
7.476
7.450
6.374
6.287
2.851
2.838
2.835
0.950
0.942
0.926
0.917
0.901
0.892
5.476
5.465
5.457
5.441
4.502
4.331
4.317
4.294
4.215
4.202
4.193
4.180
4.156
4.132
4.108
4.084
4.072
4.058
4.053
4.043
4.031
4.006
3.993
8.155
8.130
8.126
8.102
8.077
8.072
nPr
Ph
(R)
(S)
(R)
NH
syn-7f
+
anti-7f
NH2
f1 (ppm)


8.016
8.012
7.988
7.983
6.318
6.299
6.280
5.482
5.468
4.969
0.914
0.890
0.865
7.483
7.457
7.411
7.405
7.391
7.389
7.082
7.053
6.825
6.796
2.207
2.182
2.157
4.490
4.475
4.467
4.453
4.444
4.430
4.067
4.053
4.028
4.015
3.971
3.951
3.933
3.912
3.604
3.582
3.559
3.538
3.516
3.498
3.478
3.455
3.433
2.772
2.749
2.725
nPr
(R)
(S)
(S)
Ph
anti-7g
f1 (ppm)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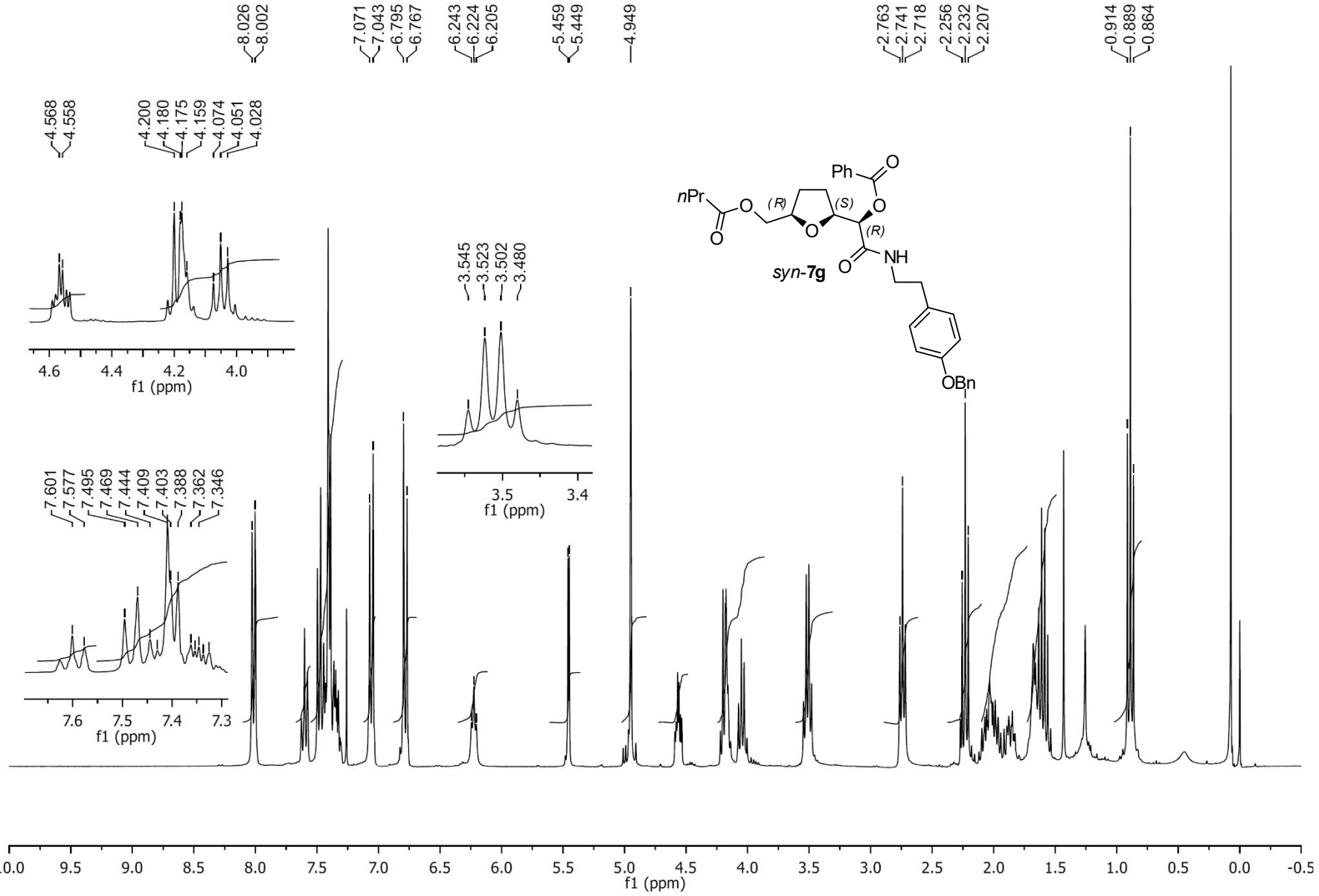
137.029
133.577
114.978
79.039
77.765
74.758
69.955
65.735
40.374
35.880
34.659
27.608
26.855
18.334
13.625
130.845
129.830
129.747
129.205
128.590
127.963
127.418
132 131 130 129 128 127 126
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
nPr
(R)
(S)
(S)
Ph
anti-7g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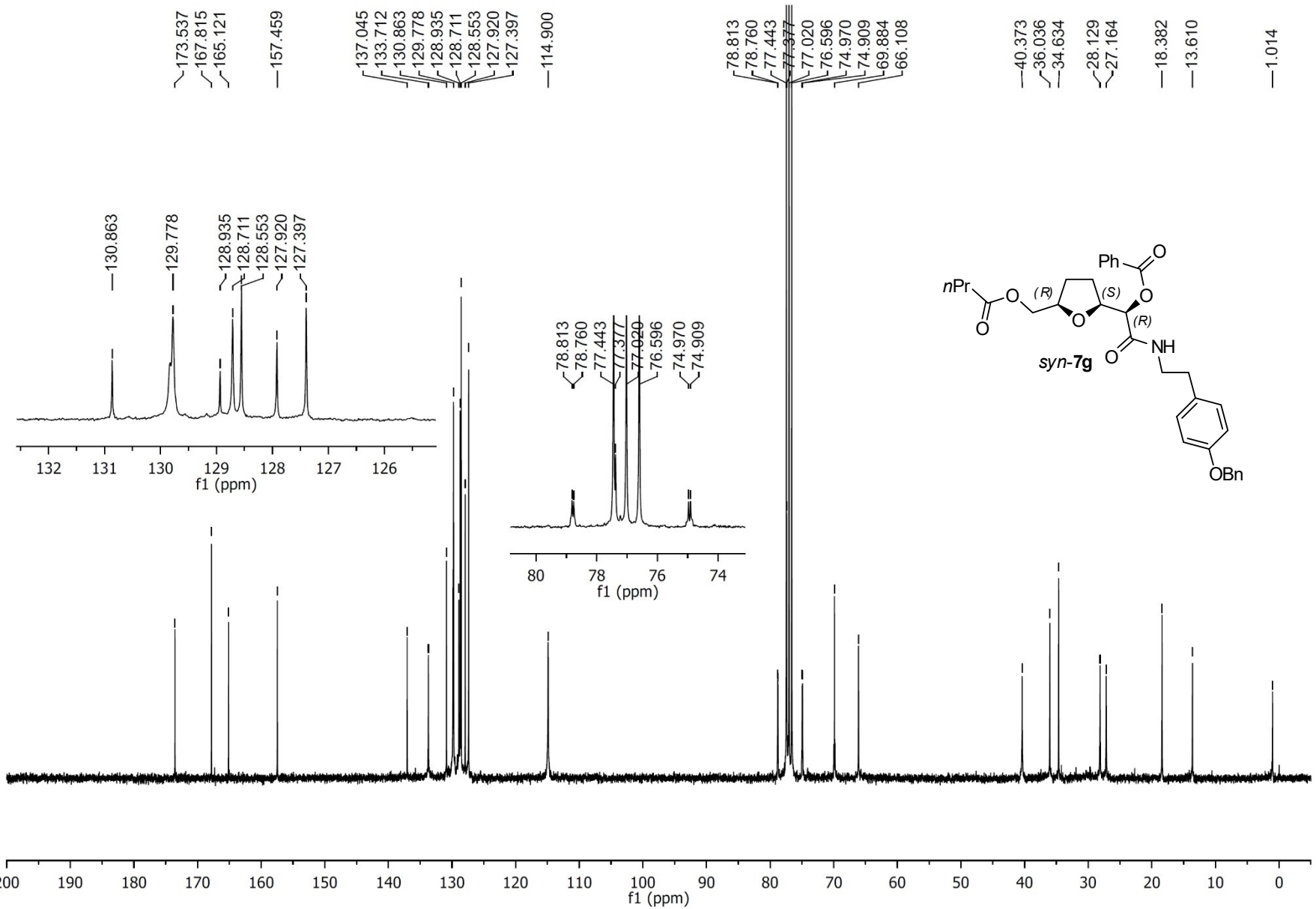
6.767
6.243
6.224
6.205
5.459
5.449
4.949
2.763
2.741
2.718
2.256
2.232
2.207
0.914
0.889
0.864
4.568
4.558
4.200
4.180
4.175
4.159
4.074
4.051
4.028
3.545
3.523
3.502
3.480
7.601
7.577
7.495
7.469
7.444
7.409
7.403
7.388
7.362
7.346
Ph
nPr
(R)
(S)
(R)
NH
OBn
syn-7g
f1 (ppm)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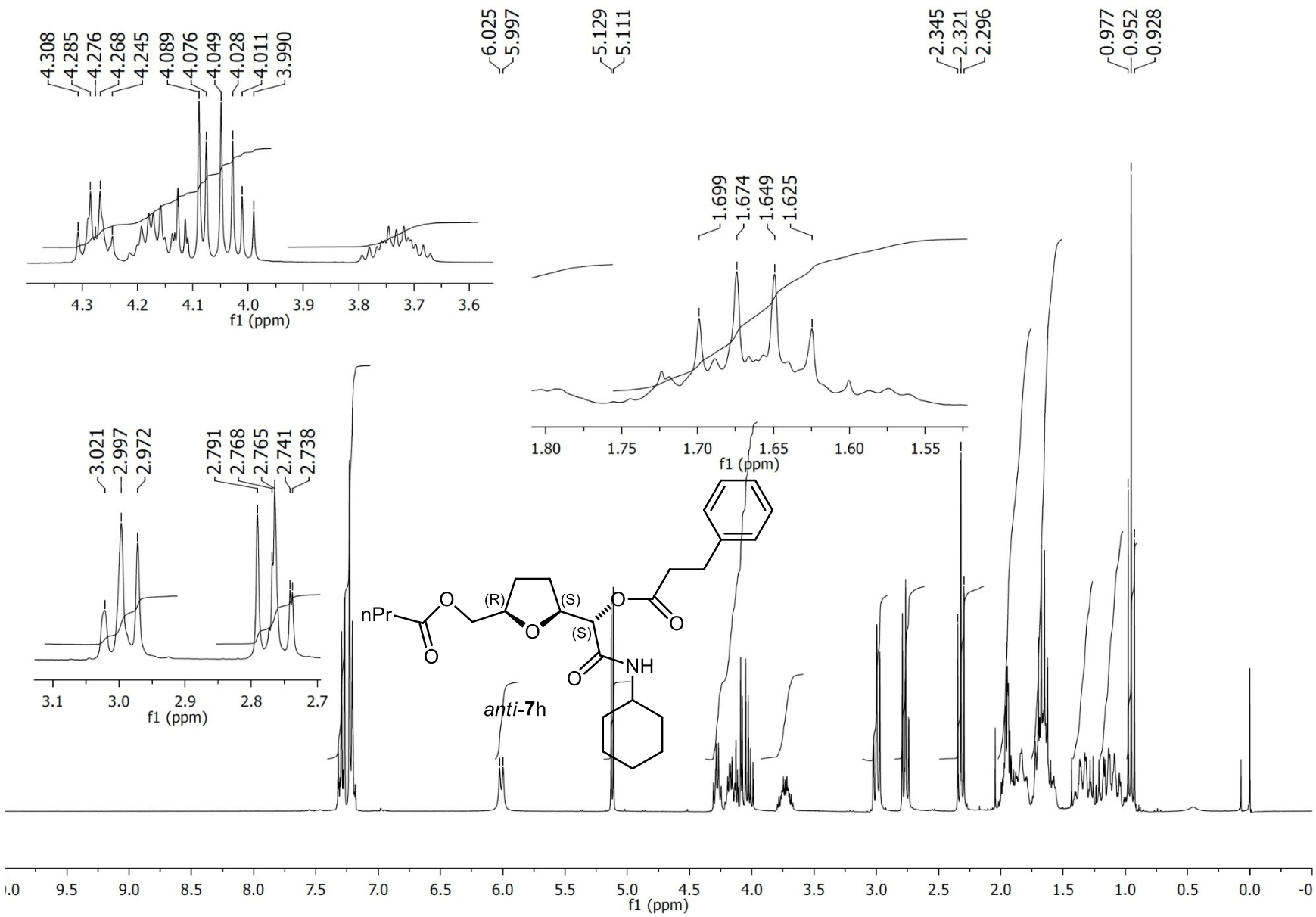
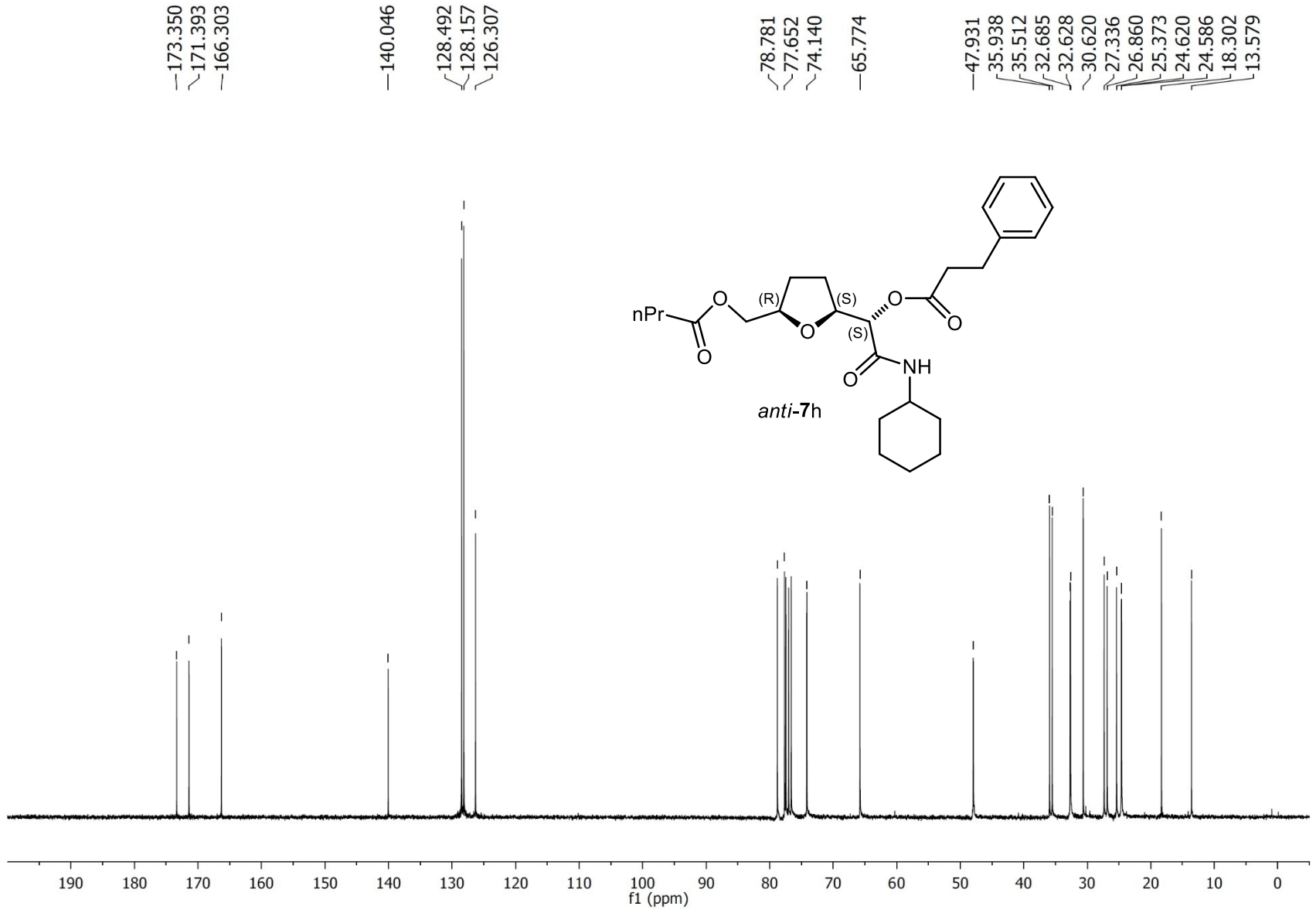
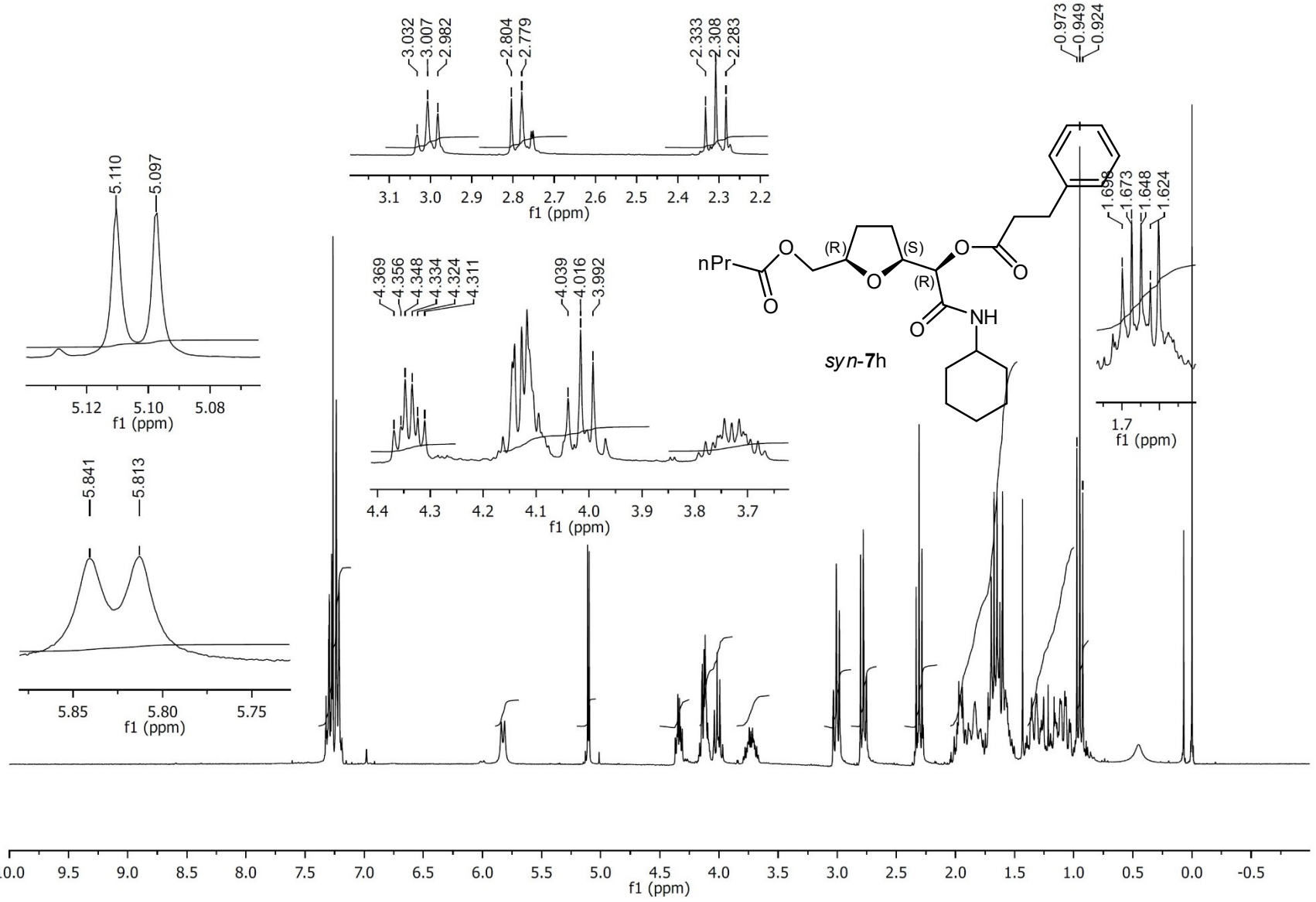
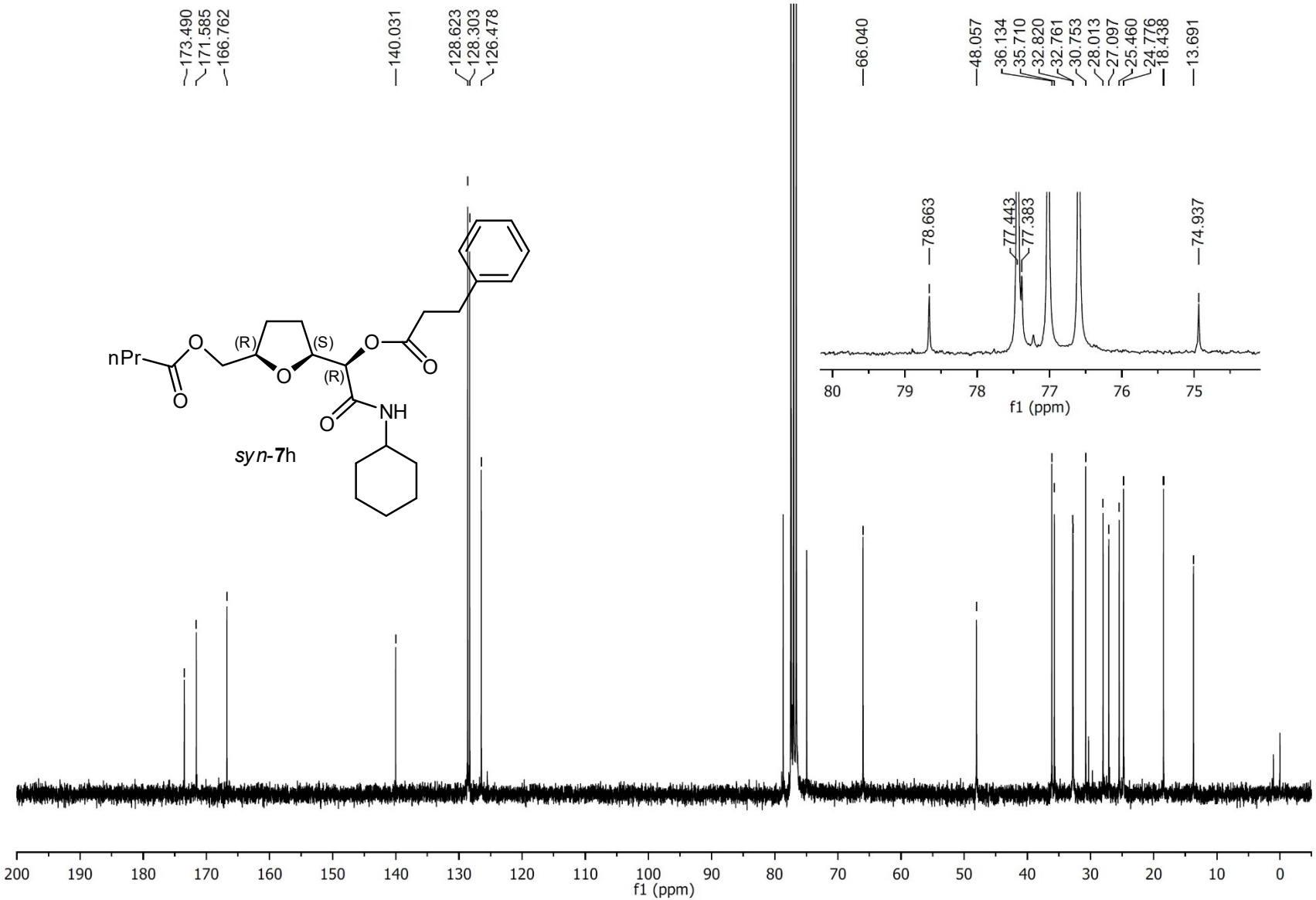
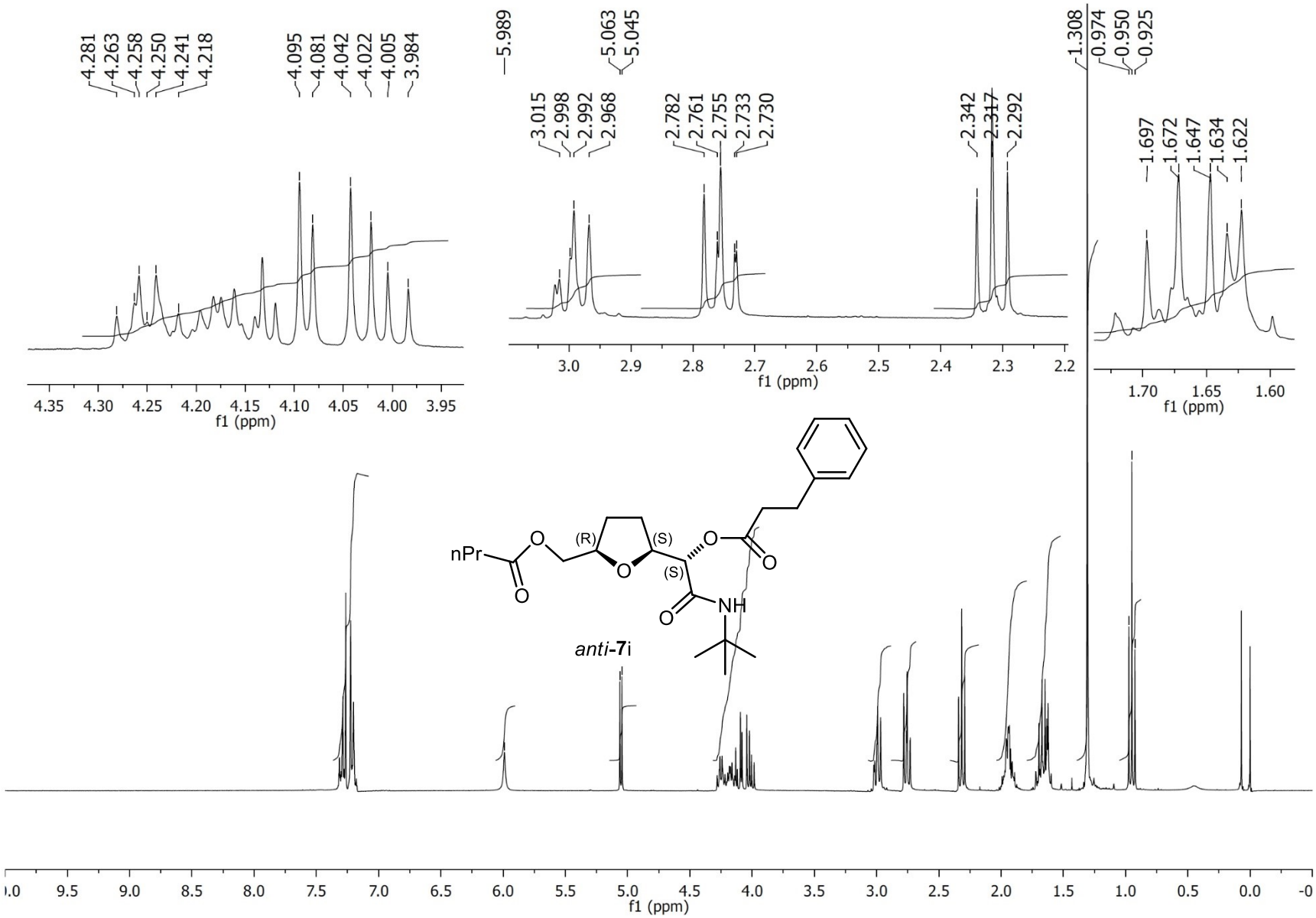
167.815
165.121
157.459
137.045
133.712
130.863
129.778
128.935
128.711
128.553
127.920
127.397
114.900
78.813
78.760
77.443
77.377
77.020
76.596
74.970
74.909
69.884
66.108
40.373
36.036
34.634
28.129
27.164
18.382
13.610
1.014
f1 (ppm)
nPr
Ph
(R)
(S)
(R)
NH
OBn
syn-7g

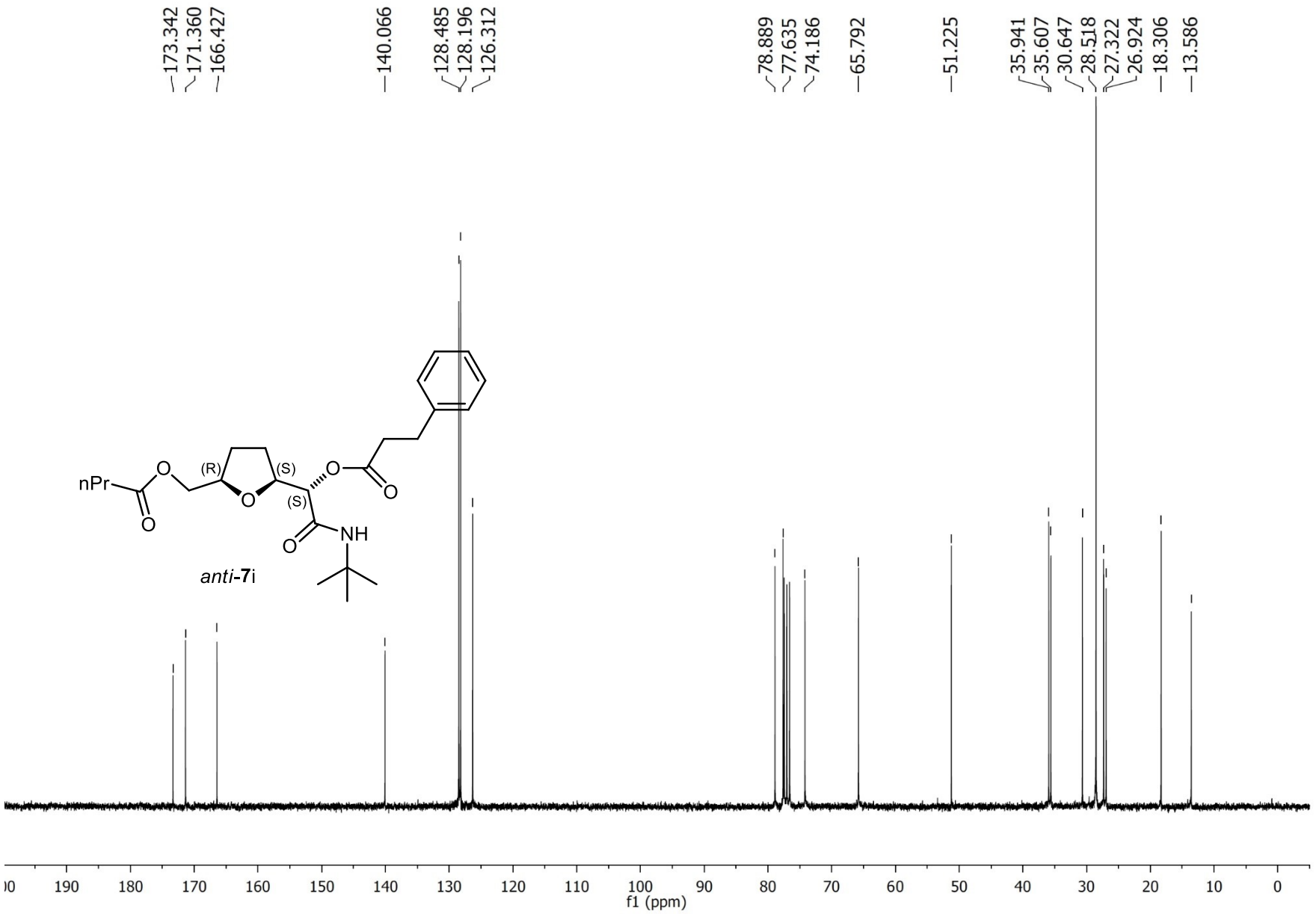

4.308
4.285
4.276
4.268
4.245
4.089
4.076
4.049
4.028
4.011
3.990
6.025
5.997
5.129
5.111
2.345
2.321
2.296
0.977
0.952
0.928
1.699
1.674
1.649
1.625
3.021
2.997
2.972
2.791
2.768
2.765
2.741
2.738
f1 (ppm)
nPr
(R)
(S)
(S)
NH
anti-7h

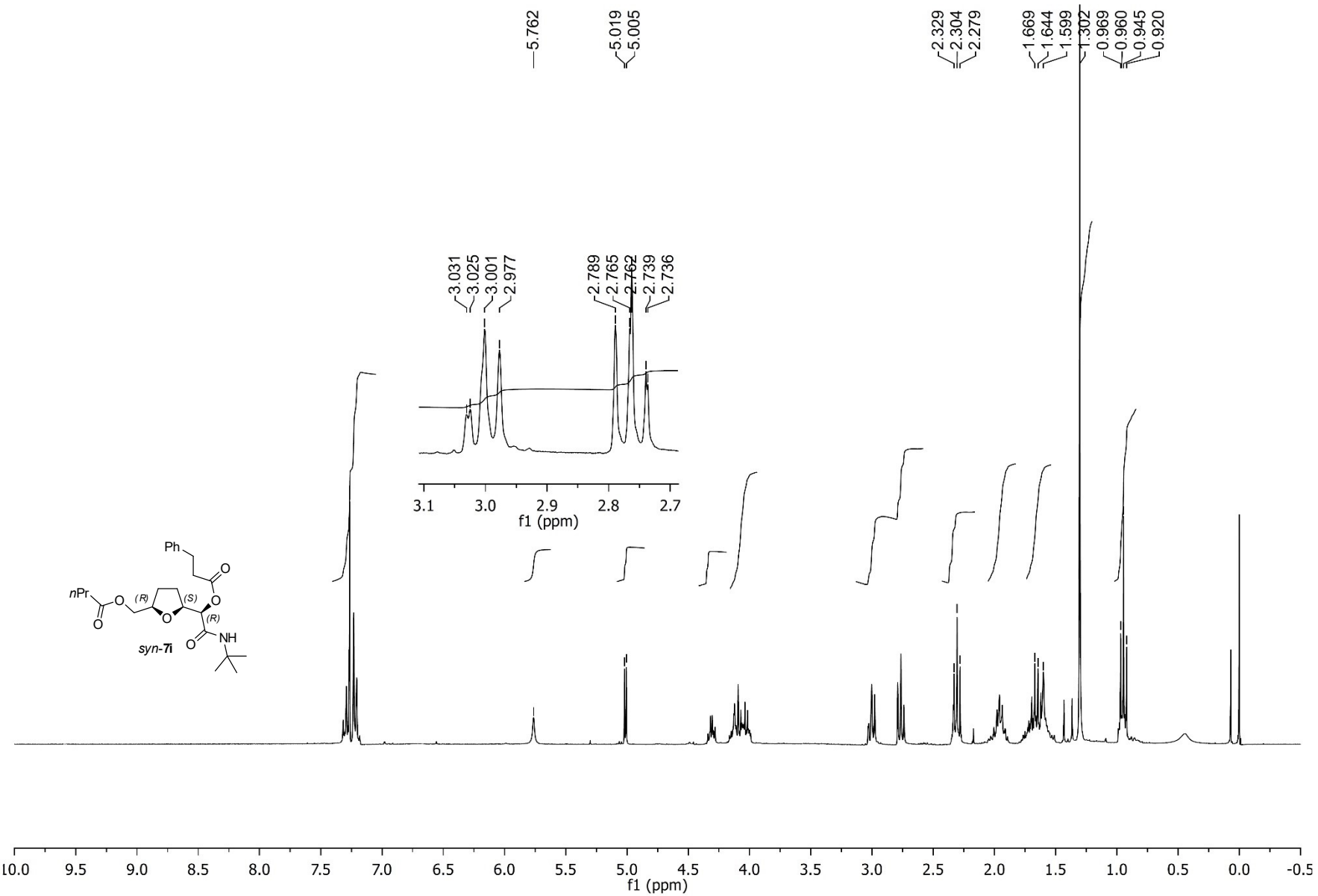

173.350
171.393
166.303
140.046
128.492
128.157
126.307
78.781
77.652
74.140
65.774
47.931
35.938
35.512
32.685
32.628
30.620
27.336
26.860
25.373
24.620
24.586
18.302
13.579
nPr
O
O
(R)
O
(S)
(S)
O
O
O
NH
anti-7h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

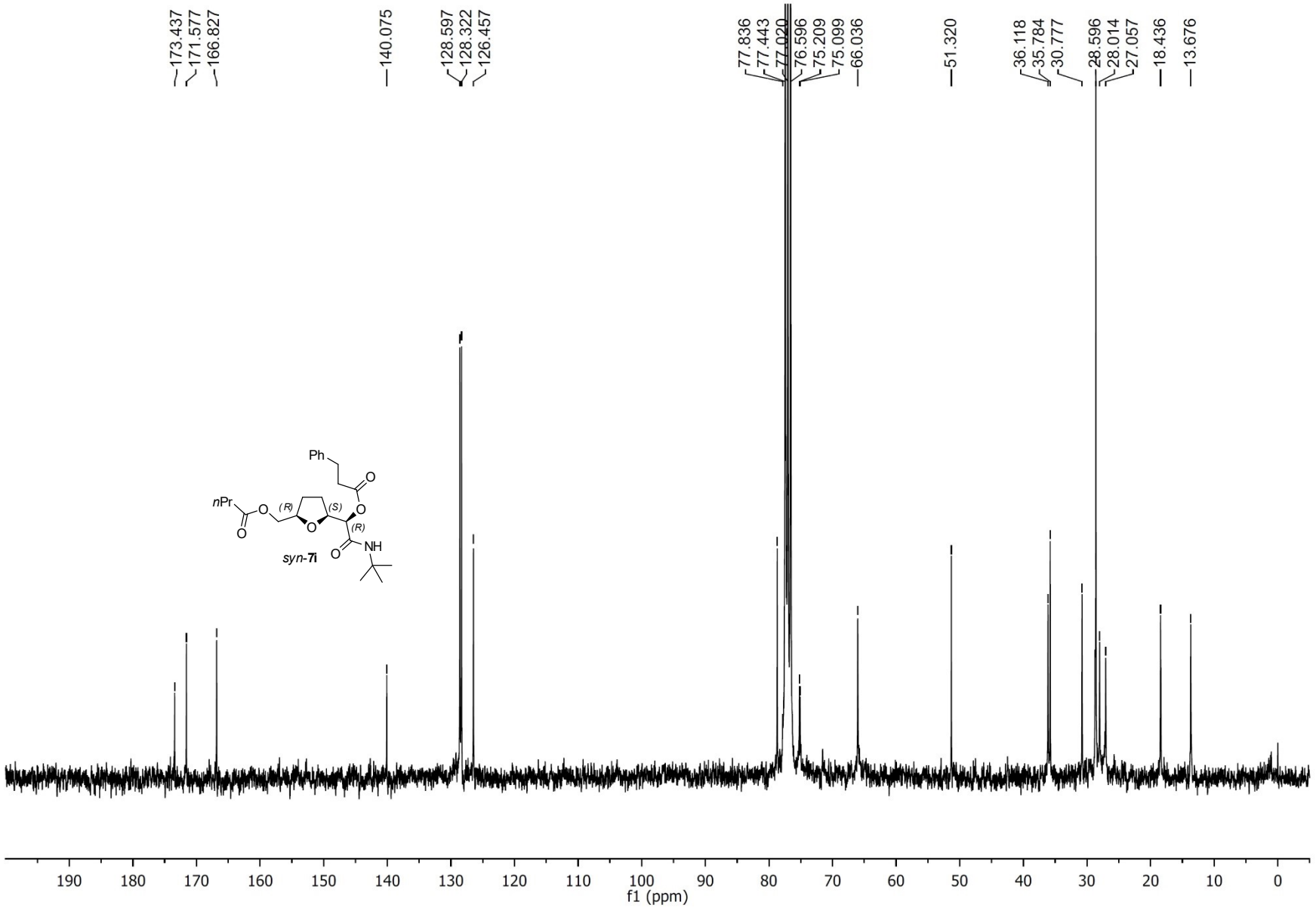

3.032
3.007
2.982
2.804
2.779
2.333
2.308
2.283
0.973
0.949
0.924
5.110
5.097
4.369
4.356
4.348
4.334
4.324
4.311
4.039
4.016
3.992
1.698
1.673
1.648
1.624
5.841
5.813
nPr
(R)
(S)
(R)
NH
syn-7h
f1 (ppm)

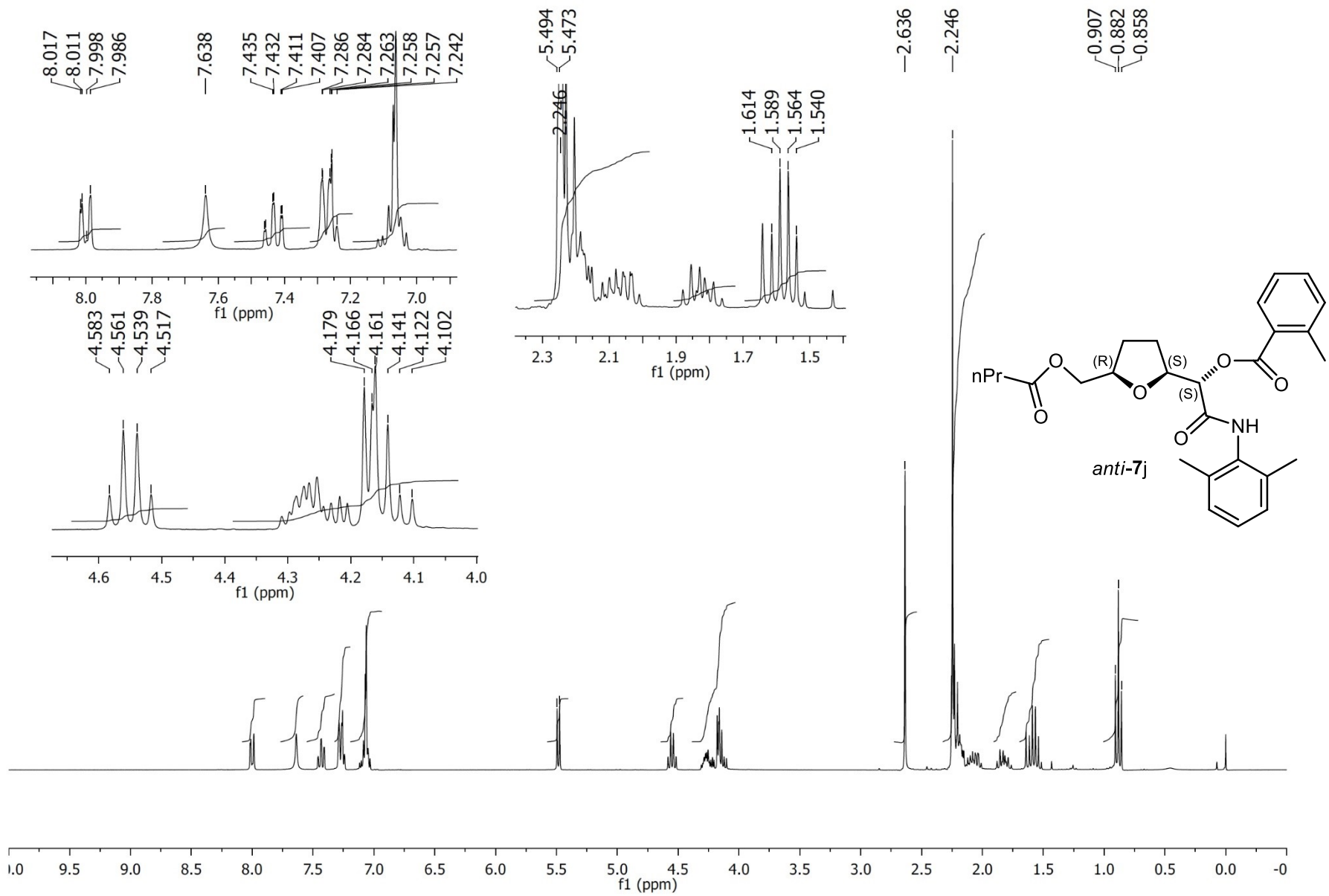

173.490
171.585
166.762
140.031
128.623
128.303
126.478
66.040
48.057
36.134
35.710
32.820
32.761
30.753
28.013
27.097
25.460
24.776
18.438
13.691
78.663
77.443
77.383
74.937
nPr
O
(R)
(S)
O
O
(R)
O
O
NH
syn-7h
80
79
78
77
76
75
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

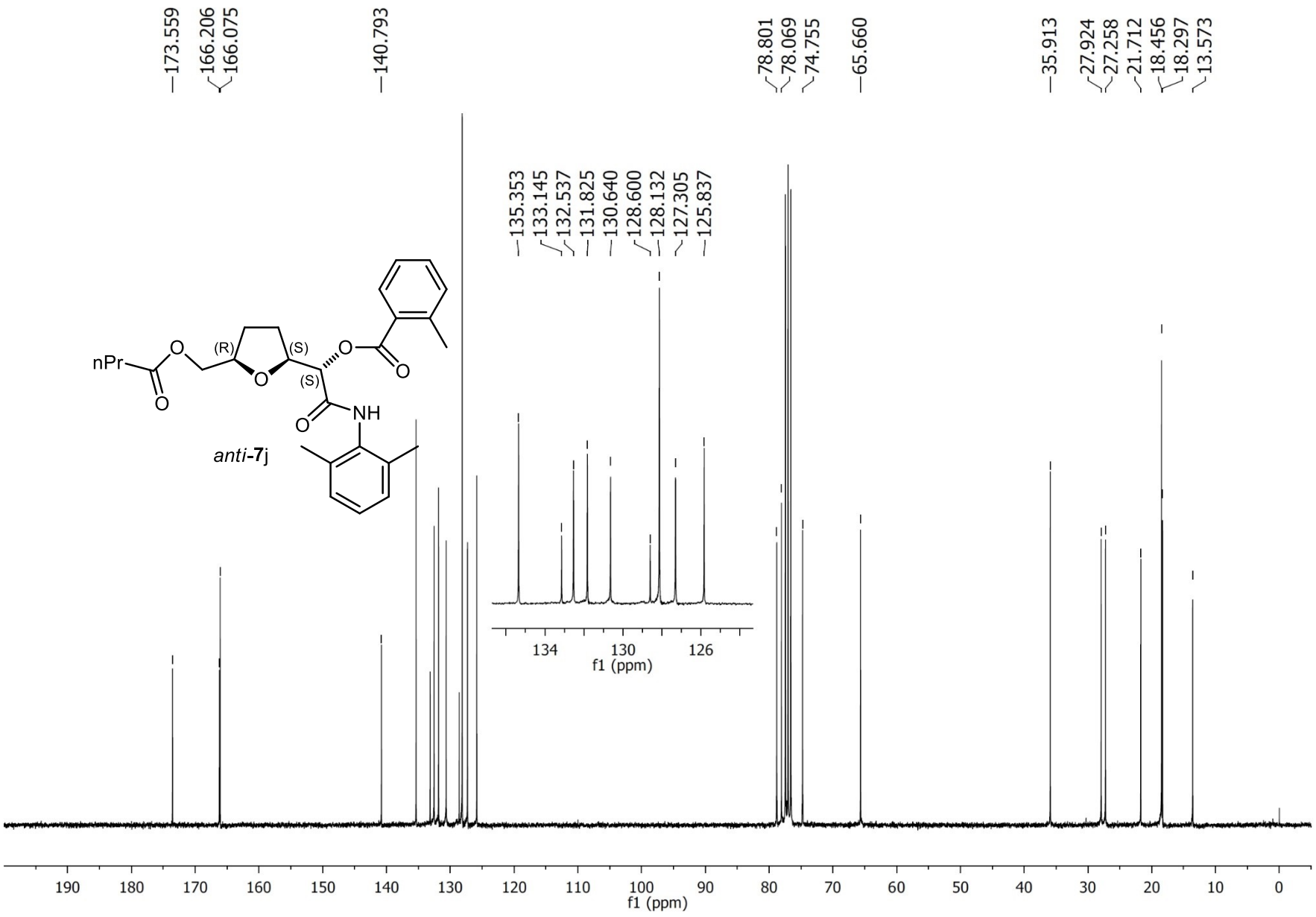

4.281
4.263
4.258
4.250
4.241
4.218
4.095
4.081
4.042
4.022
4.005
3.984
5.989
5.063
5.045
3.015
2.998
2.992
2.968
2.782
2.761
2.755
2.733
2.730
2.342
2.317
2.292
1.308
0.974
0.950
0.925
1.697
1.672
1.647
1.634
1.622
f1 (ppm)
nPr
(R)
(S)
(S)
NH
anti-7i

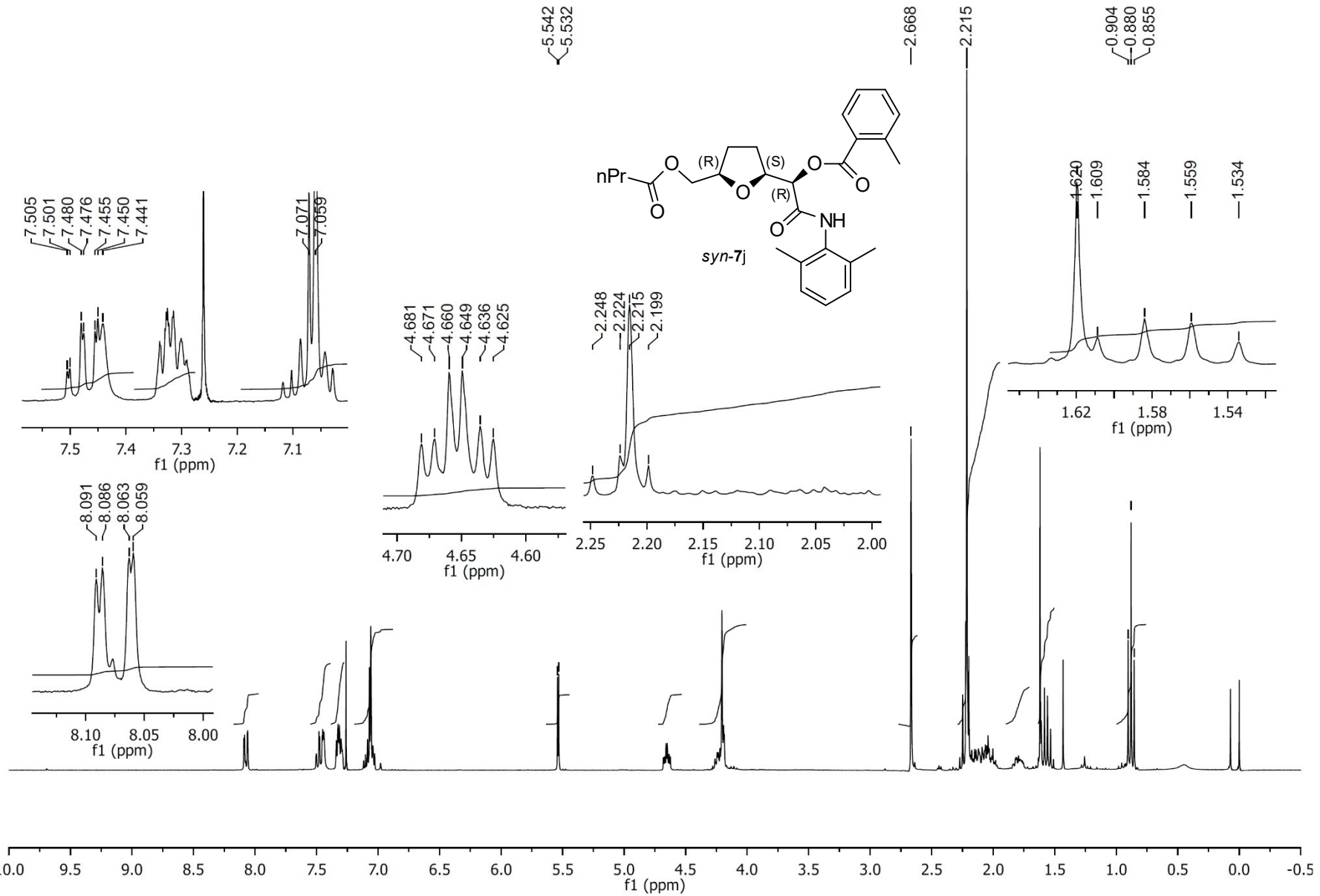

173.342
171.360
166.427
140.066
128.485
128.196
126.312
78.889
77.635
74.186
65.792
51.225
35.941
35.607
30.647
28.518
27.322
26.924
18.306
13.586
nPr
O
O
(R)
O
(S)
O
O
(S)
O
NH
anti-7i
f1 (ppm)

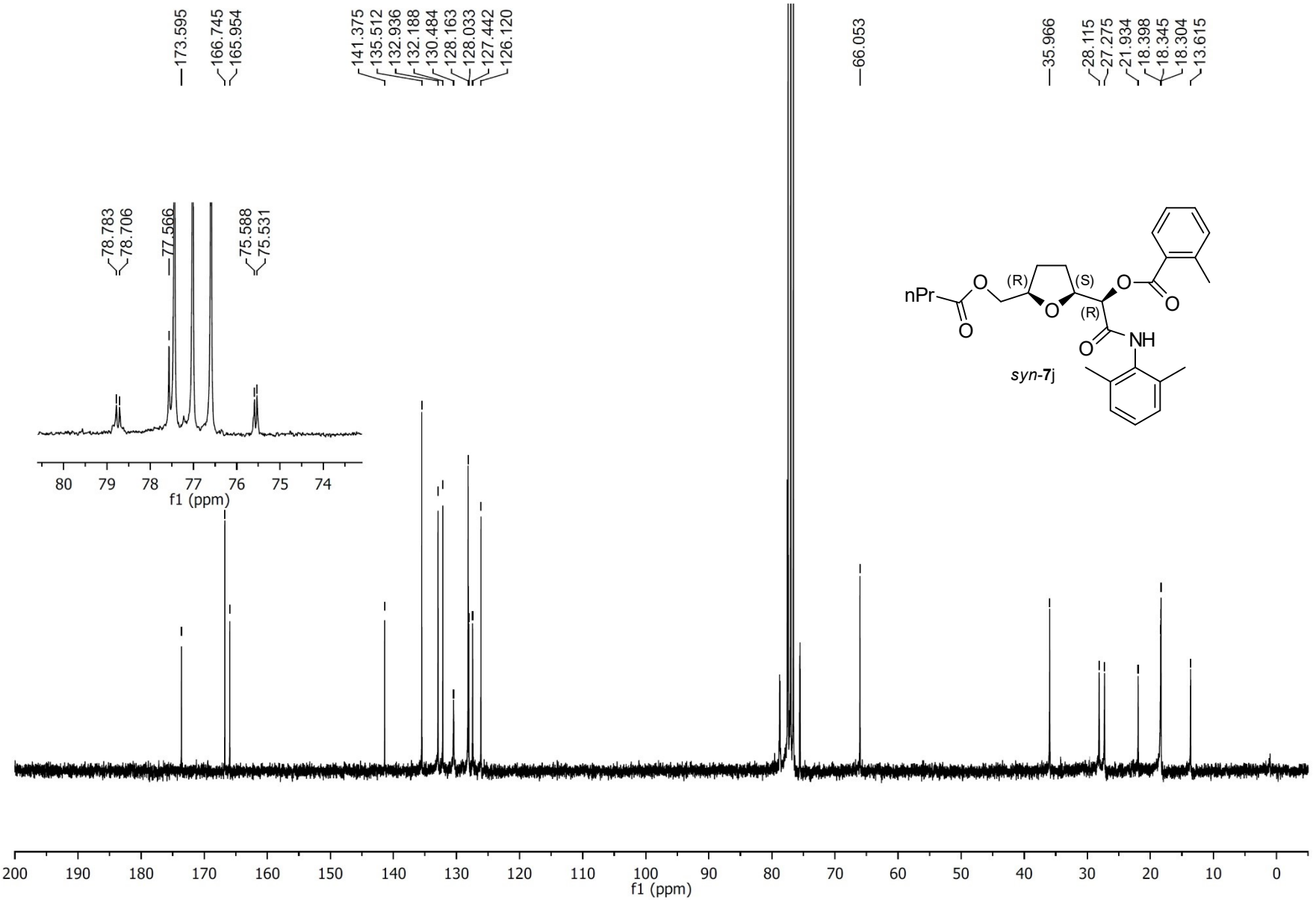

5.762
5.019
5.005
2.329
2.304
2.279
1.669
1.644
1.599
1.302
0.969
0.960
0.945
0.920
3.031
3.025
3.001
2.977
2.789
2.765
2.762
2.739
2.736
3.1
3.0
2.9
2.8
2.7
f1 (ppm)
Ph
nPr
(R)
(S)
(R)
NH
syn-7i
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

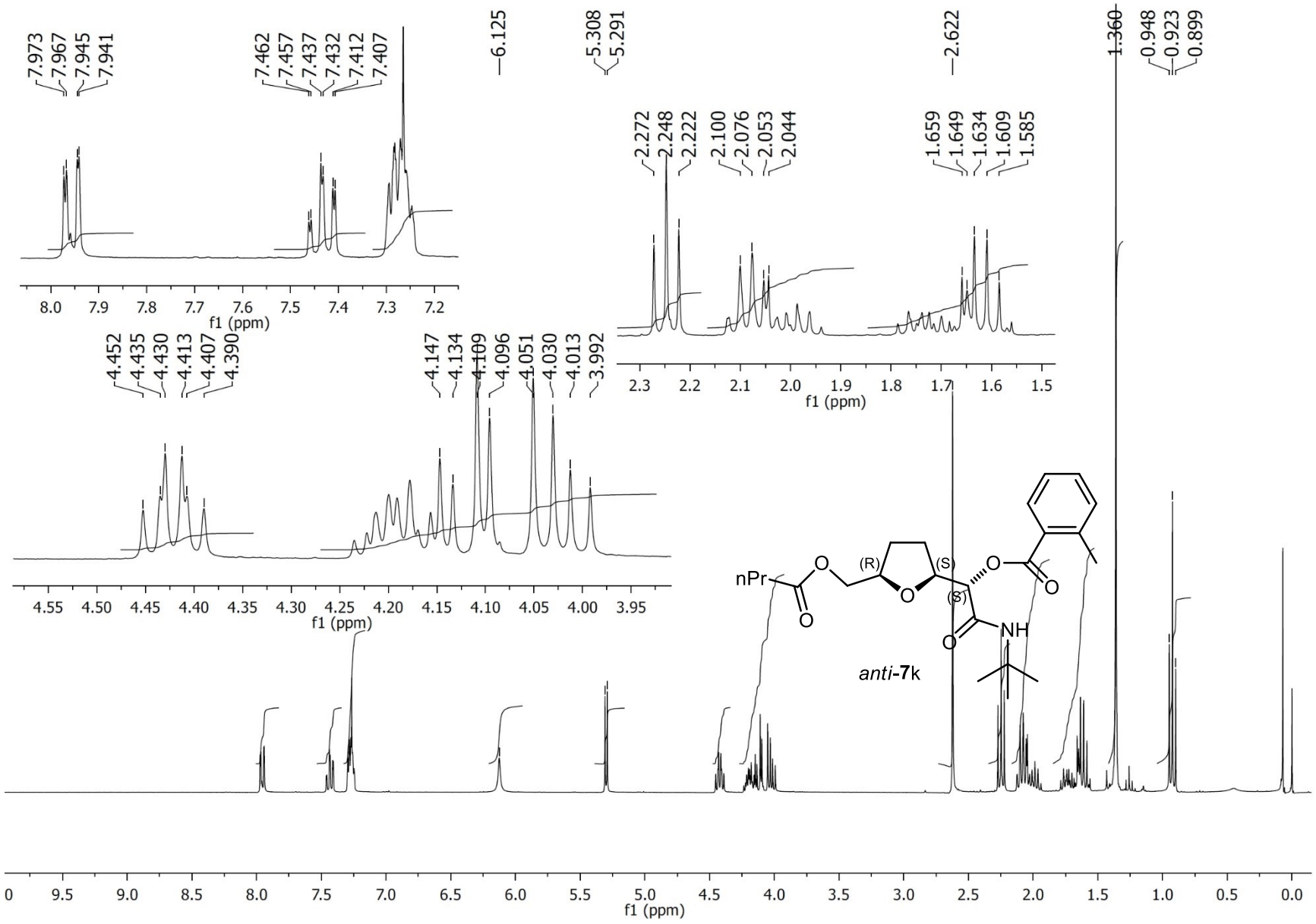

173.437
171.577
166.827
140.075
128.597
128.322
126.457
77.836
77.443
77.020
76.596
75.209
75.099
66.036
51.320
36.118
35.784
30.777
28.596
28.014
27.057
18.436
13.676
Ph
nPr
(R)
(S)
(R)
syn-7i
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

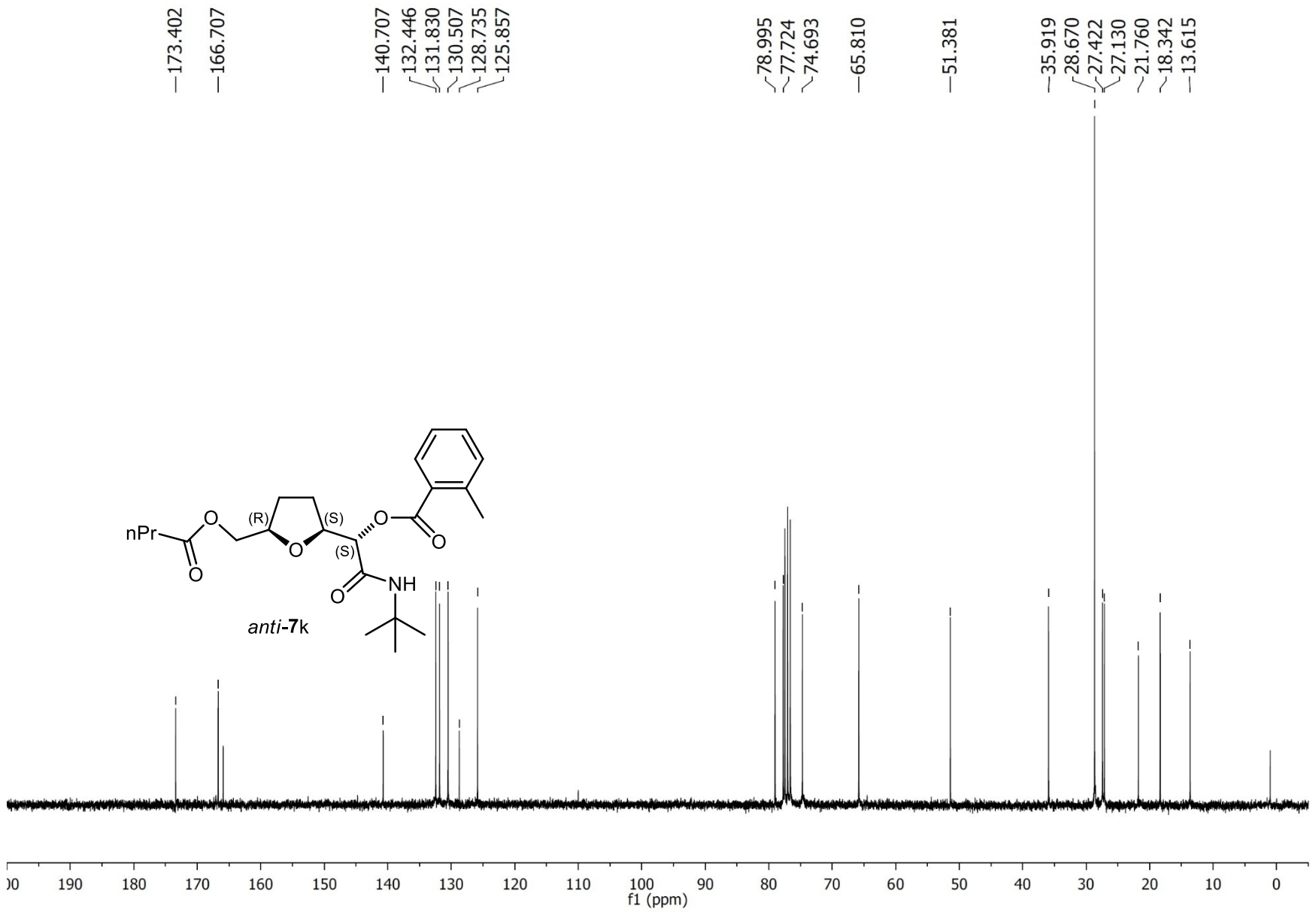

8.017
8.011
7.998
7.986
7.638
7.435
7.432
7.411
7.407
7.286
7.284
7.263
7.258
7.257
7.242
8.0
7.8
7.6
7.4
7.2
7.0
f1 (ppm)
5.494
5.473
2.246
1.614
1.589
1.564
1.540
2.3
2.1
1.9
1.7
1.5
f1 (ppm)
2.636
2.246
0.907
0.882
0.858
4.583
4.561
4.539
4.517
4.179
4.166
4.161
4.141
4.122
4.102
4.6
4.5
4.4
4.3
4.2
4.1
4.0
f1 (ppm)
nPr
O
O
(R)
O
(S)
(S)
O
O
O
NH
anti-7j
f1 (ppm)

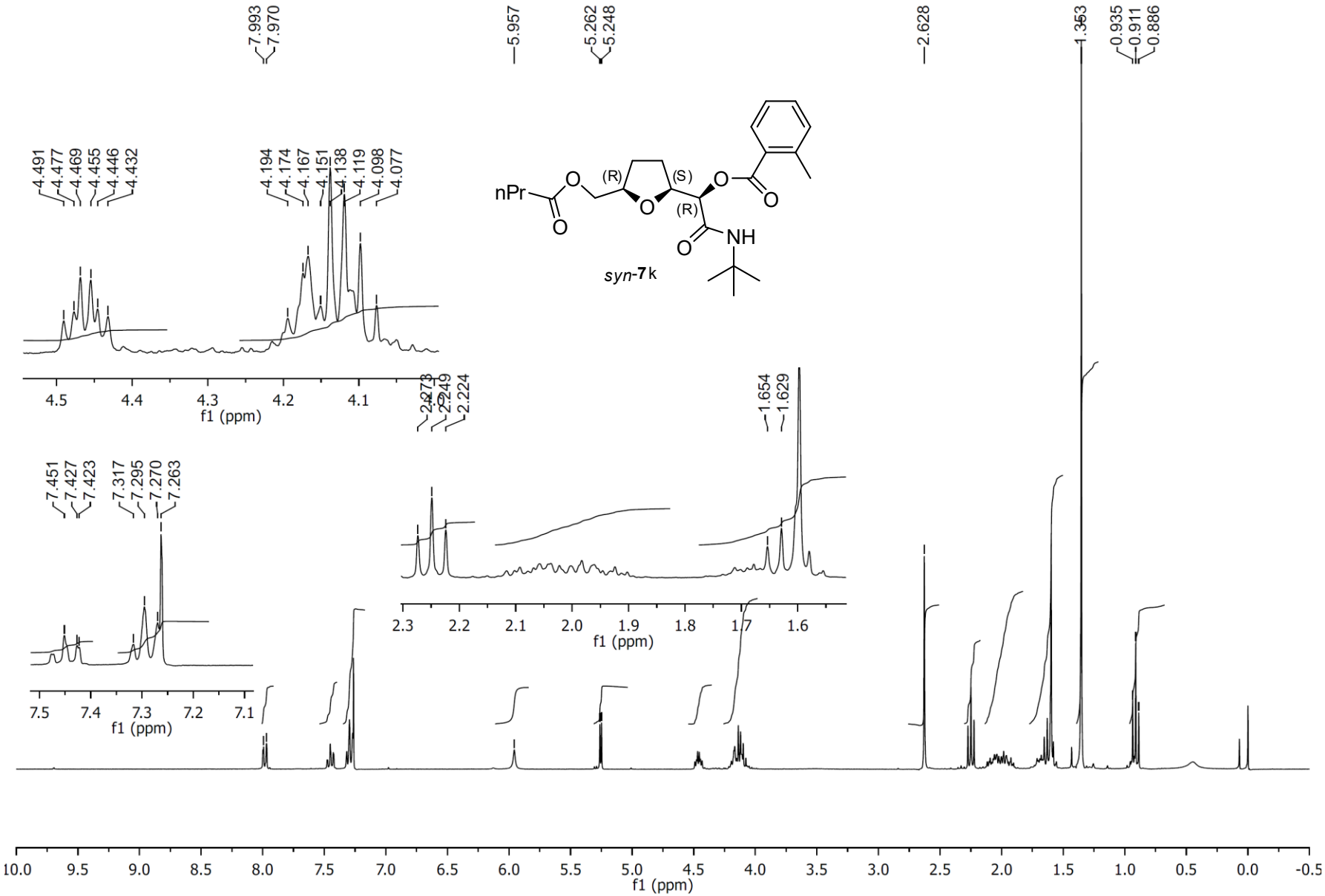

173.559
166.206
166.075
140.793
78.801
78.069
74.755
65.660
35.913
27.924
27.258
21.712
18.456
18.297
13.573
135.353
133.145
132.537
131.825
130.640
128.600
128.132
127.305
125.837
nPr
(R)
(S)
(S)
NH
anti-7j
134
130
126
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

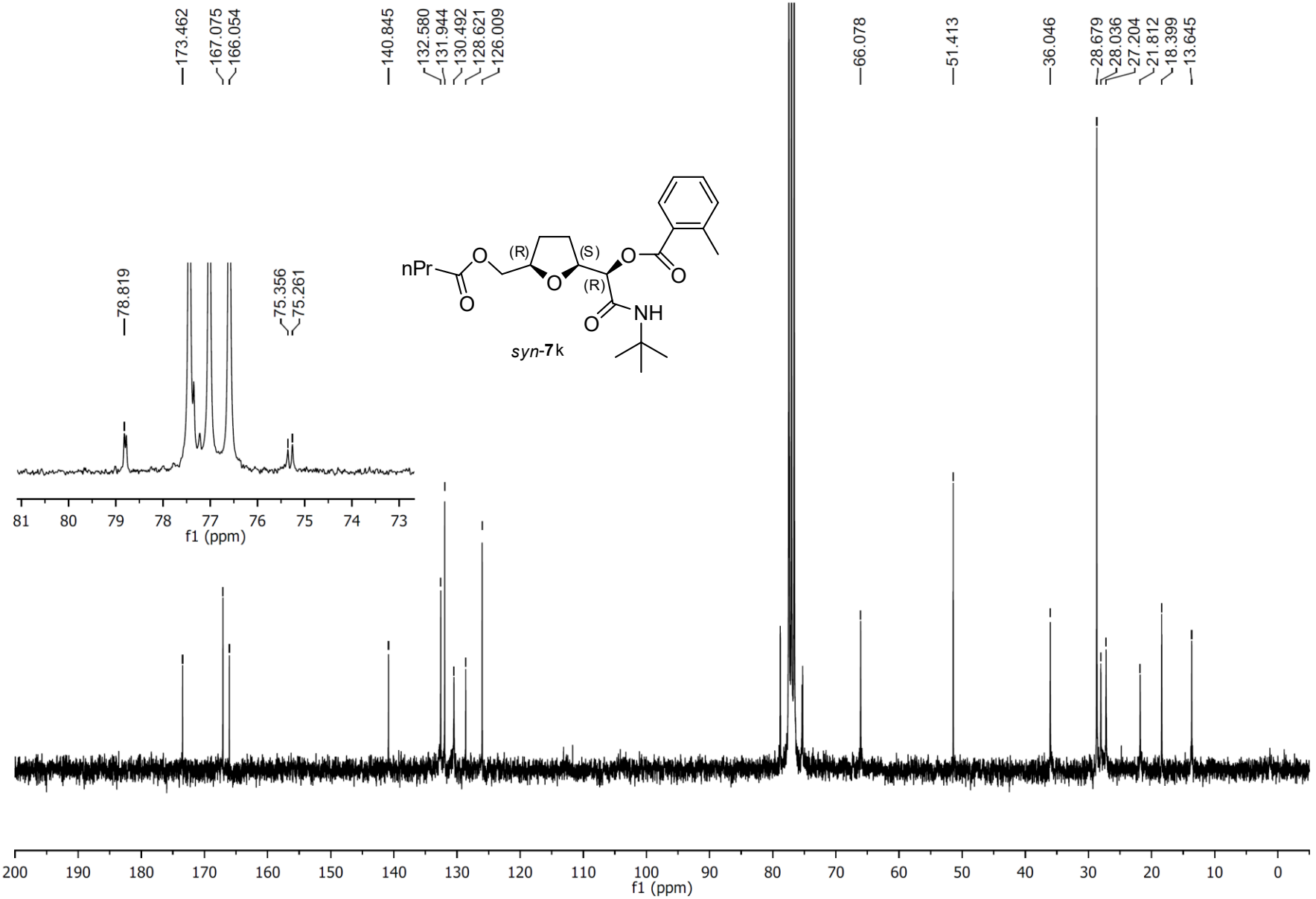

5.542
5.532
2.668
2.215
0.904
0.880
0.855
nPr
(R)
(S)
(R)
NH
syn-7j
7.505
7.501
7.480
7.476
7.455
7.450
7.441
7.071
7.059
4.681
4.671
4.660
4.649
4.636
4.625
2.248
2.224
2.215
2.199
1.620
1.609
1.584
1.559
1.534
8.091
8.086
8.063
8.059
f1 (ppm)

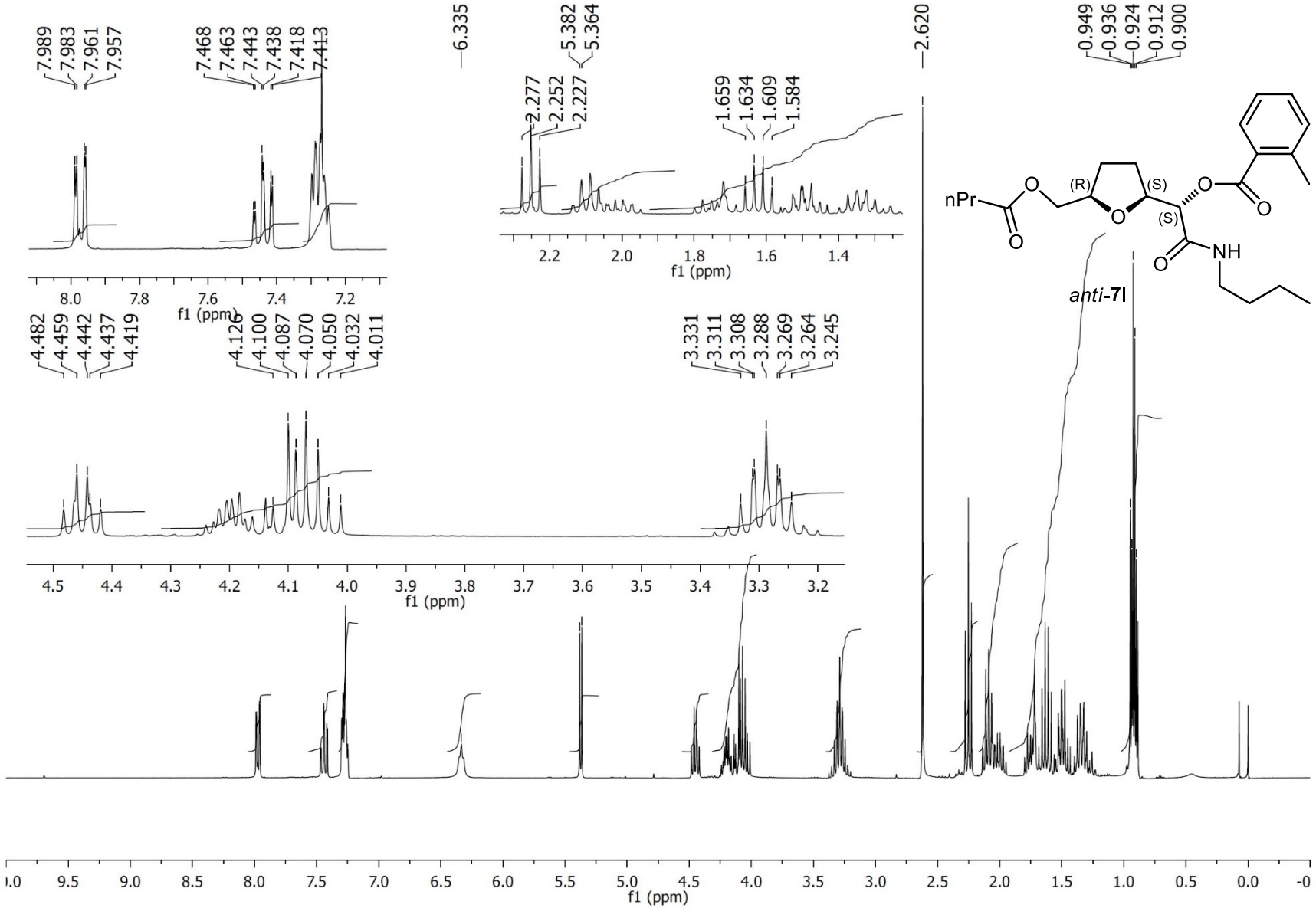

173.595
166.745
165.954
141.375
135.512
132.936
132.188
130.484
128.163
128.033
127.442
126.120
66.053
35.966
28.115
27.275
21.934
18.398
18.345
18.304
13.615
78.783
78.706
77.566
75.588
75.531
f1 (ppm)
nPr
(R)
(S)
(R)
NH
syn-7j
f1 (ppm)

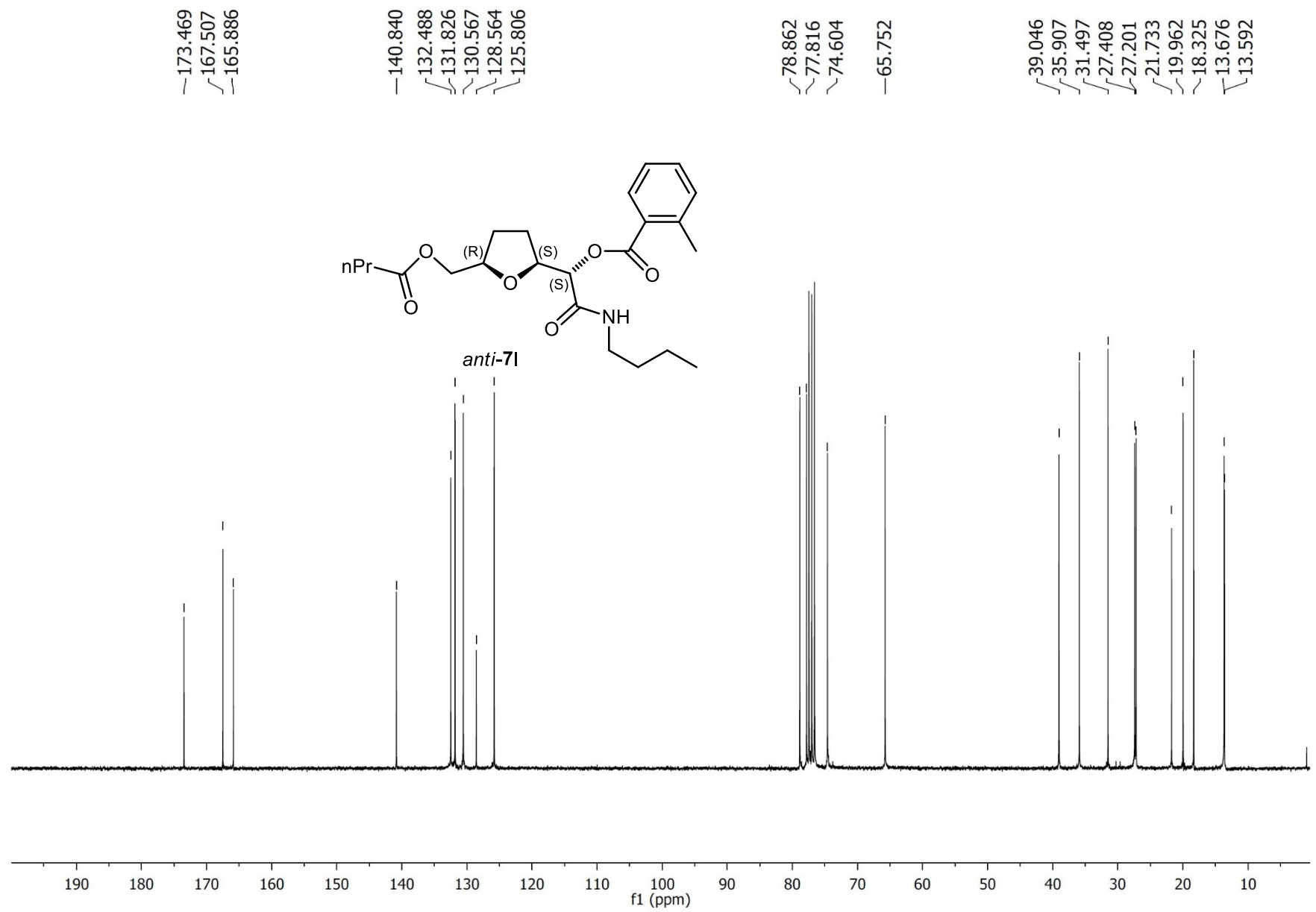

7.973
7.967
7.945
7.941
7.462
7.457
7.437
7.432
7.412
7.407
6.125
5.308
5.291
2.622
1.360
0.948
0.923
0.899
2.272
2.248
2.222
2.100
2.076
2.053
2.044
1.659
1.649
1.634
1.609
1.585
4.452
4.435
4.430
4.413
4.407
4.390
4.147
4.134
4.109
4.096
4.051
4.030
4.013
3.992
f1 (ppm)
nPr
(R)
(S)
(S)
NH
anti-7k

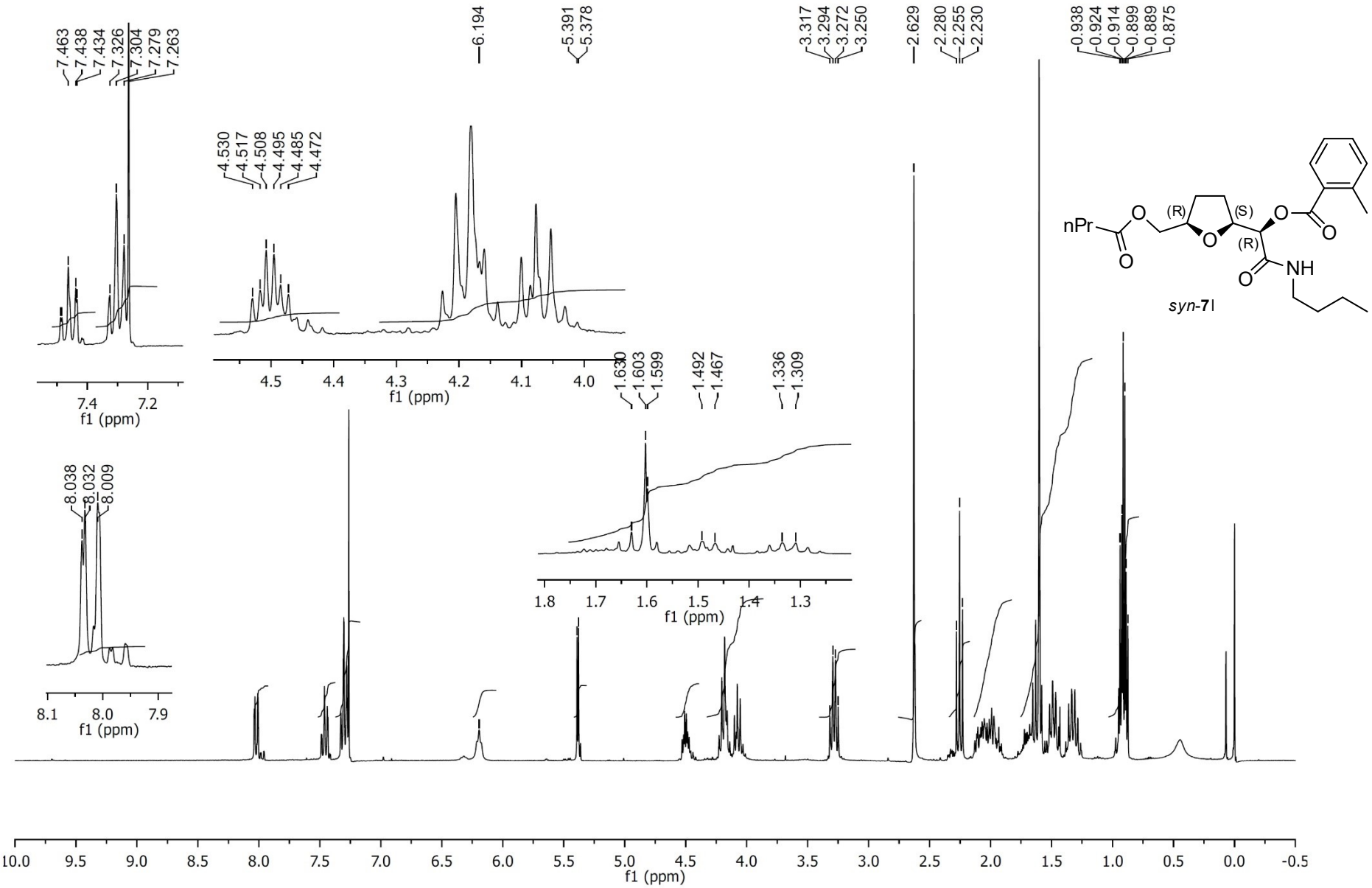

173.402
166.707
140.707
132.446
131.830
130.507
128.735
125.857
78.995
77.724
74.693
65.810
51.381
35.919
28.670
27.422
27.130
21.760
18.342
13.615
nPr
O
O
(R)
O
(S)
(S)
O
O
O
NH
anti-7k
f1 (ppm)

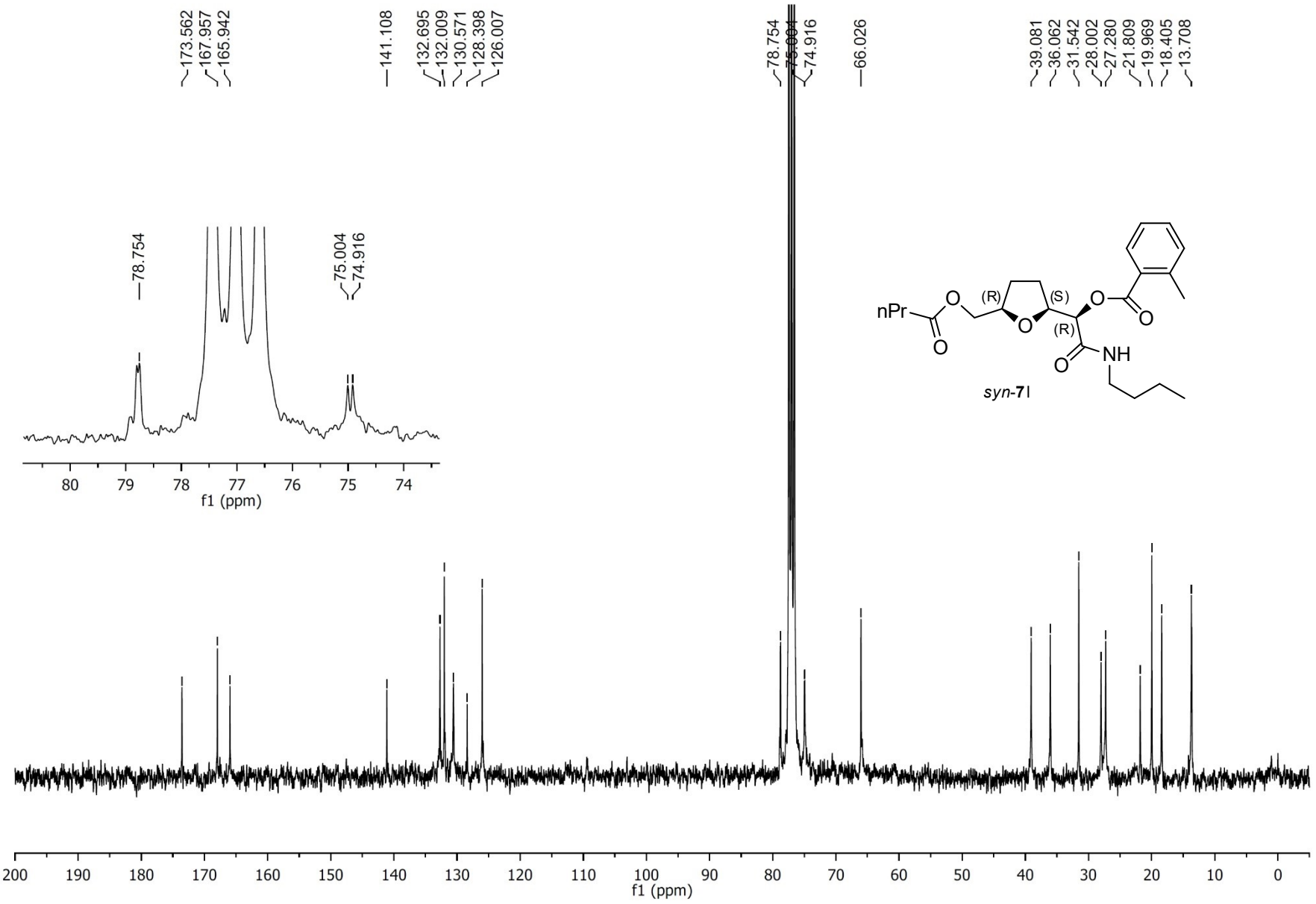

7.993
7.970
5.957
5.262
5.248
2.628
1.353
0.935
0.911
0.886
4.491
4.477
4.469
4.455
4.446
4.432
4.194
4.174
4.167
4.151
4.138
4.119
4.098
4.077
nPr
(R)
(S)
(R)
NH
syn-7k
2.273
2.249
2.224
1.654
1.629
7.451
7.427
7.423
7.317
7.295
7.270
7.263
f1 (ppm)

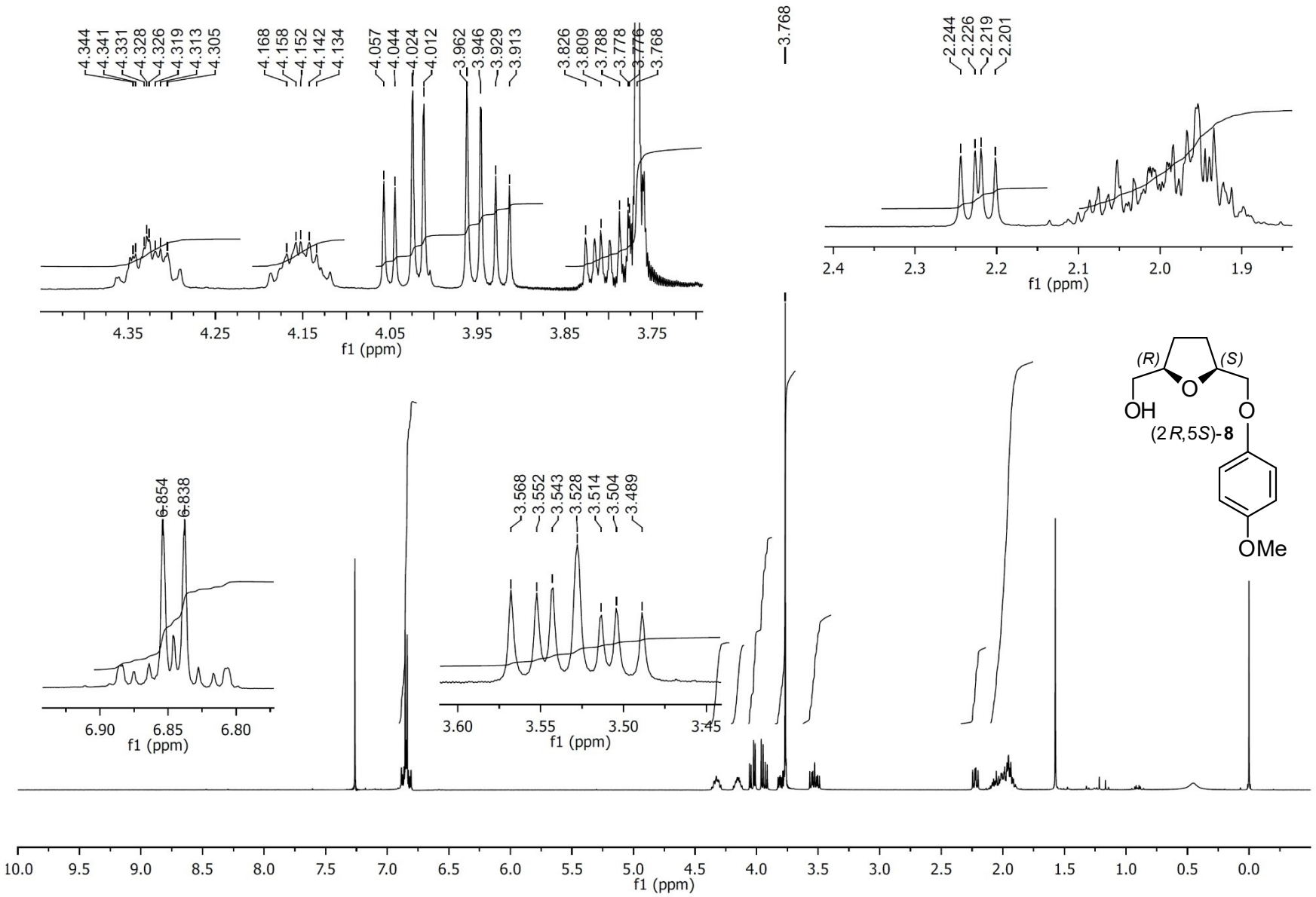

173.462
167.075
166.054
140.845
132.580
131.944
130.492
128.621
126.009
66.078
51.413
36.046
28.679
28.036
27.204
21.812
18.399
13.645
78.819
75.356
75.261
nPr
(R)
(S)
(R)
NH
syn-7k
f1 (ppm)

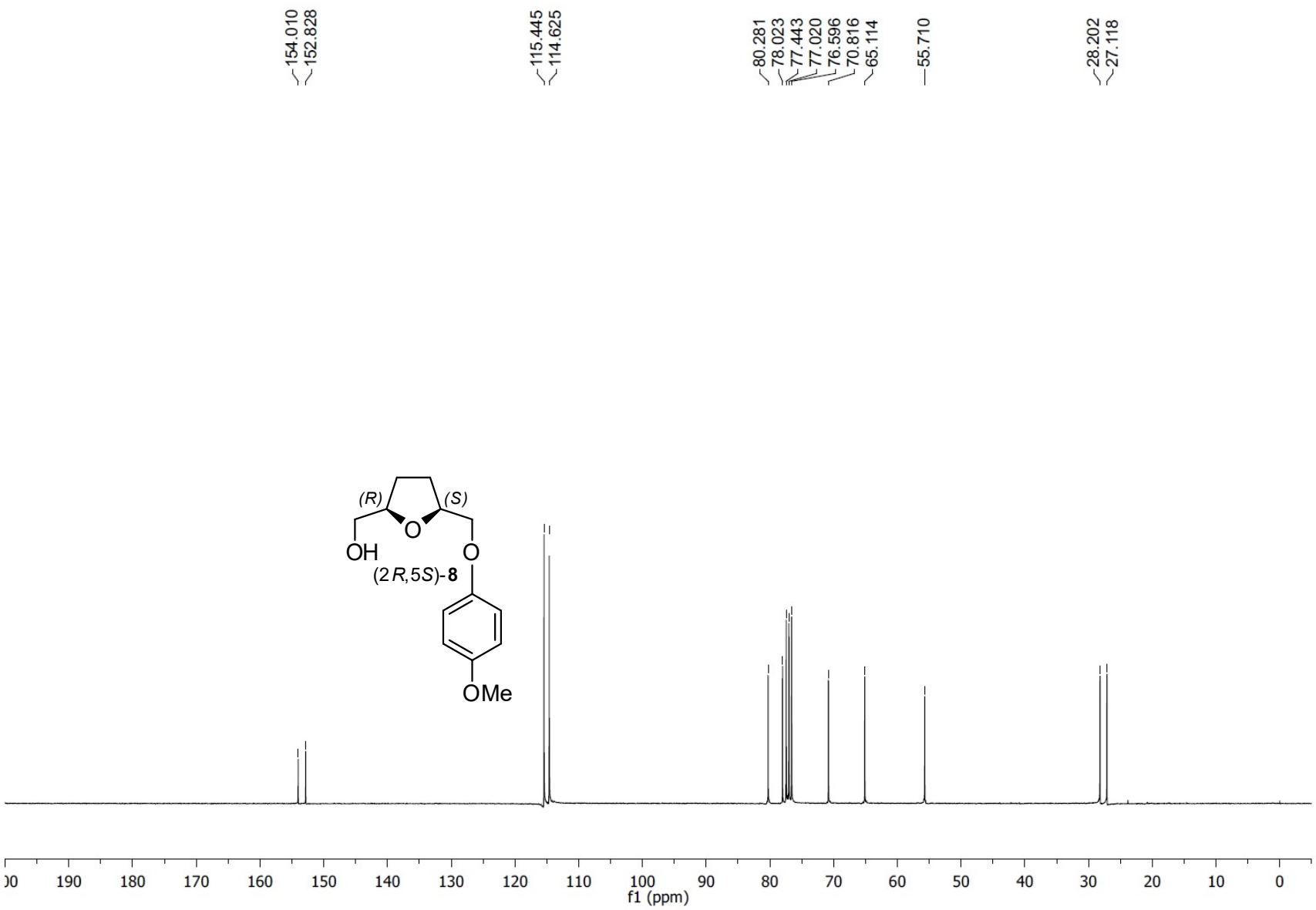

7.989
7.983
7.961
7.957
7.468
7.463
7.443
7.438
7.418
7.413
6.335
5.382
5.364
2.620
0.949
0.936
0.924
0.912
0.900
2.277
2.252
2.227
1.659
1.634
1.609
1.584
4.482
4.459
4.442
4.437
4.419
4.126
4.100
4.087
4.070
4.050
4.032
4.011
3.331
3.311
3.308
3.288
3.269
3.264
3.245
nPr
(R)
(S)
(S)
NH
anti-7l
f1 (ppm)

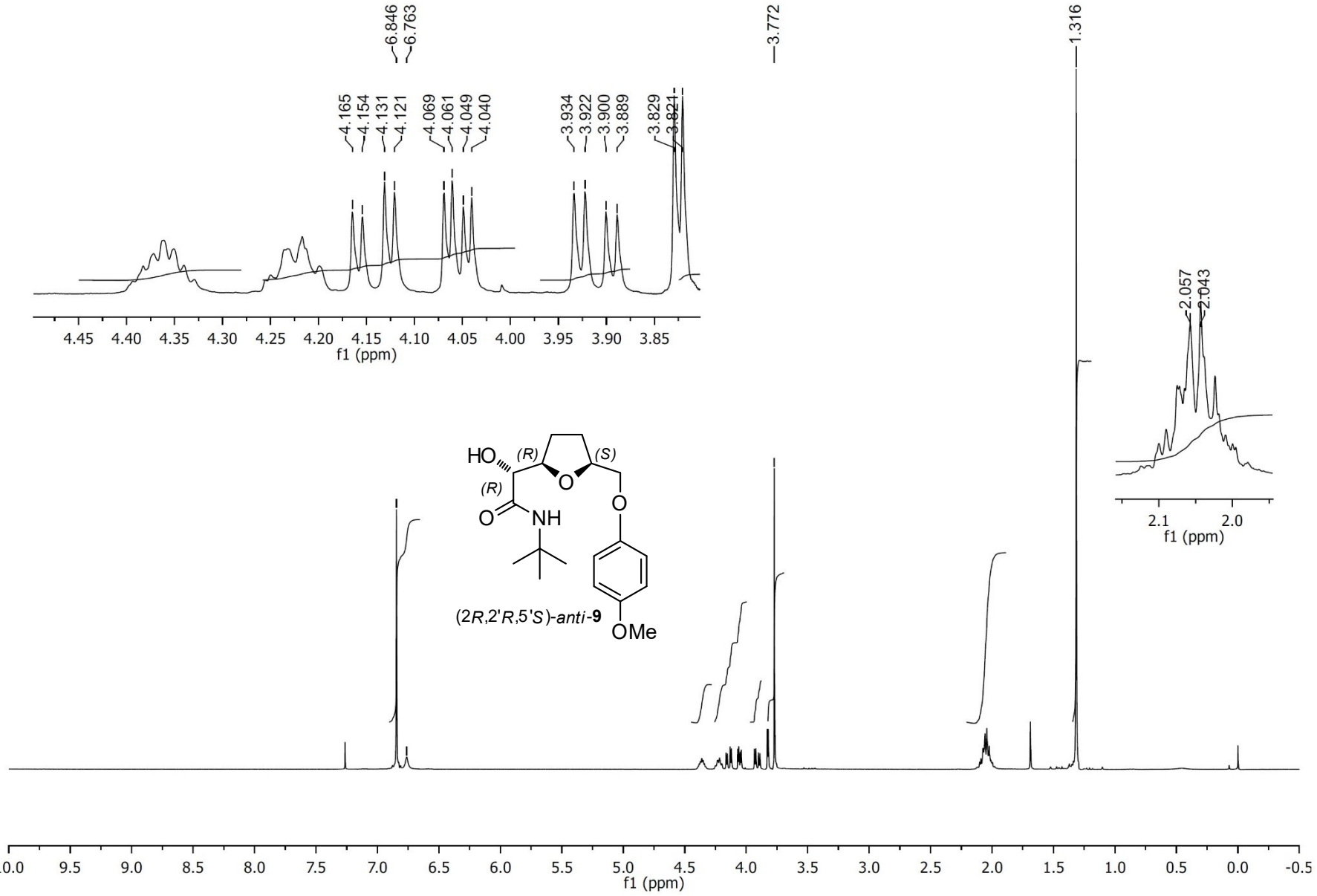

173.469
167.507
165.886
140.840
132.488
131.826
130.567
128.564
125.806
78.862
77.816
74.604
65.752
39.046
35.907
31.497
27.408
27.201
21.733
19.962
18.325
13.676
13.592
nPr
O
O
(R)
O
(S)
(S)
O
O
O
NH
anti-7l
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

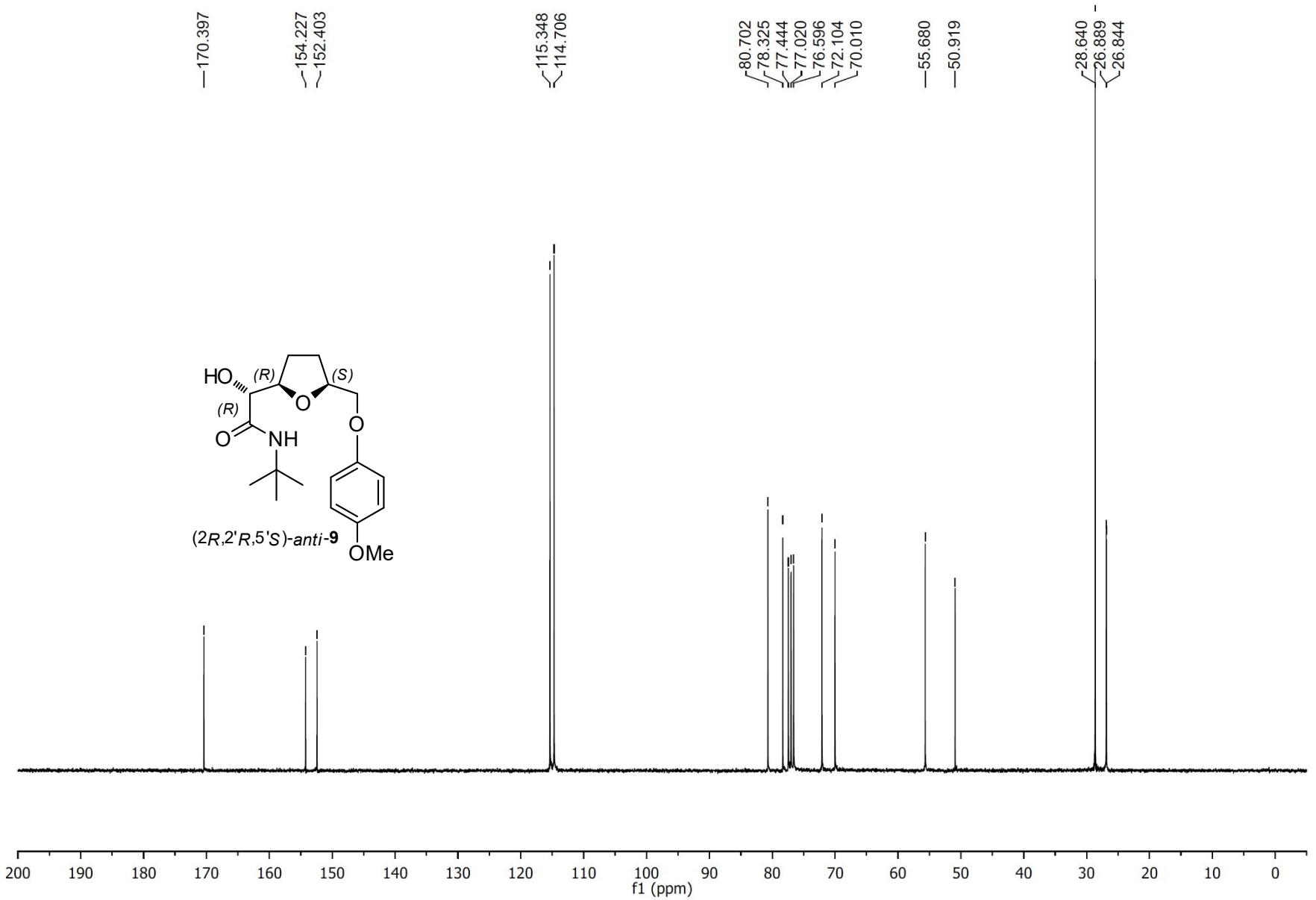

7.463
7.438
7.434
7.326
7.304
7.279
7.263
6.194
5.391
5.378
3.317
3.294
3.272
3.250
2.629
2.280
2.255
2.230
0.938
0.924
0.914
0.899
0.889
0.875
4.530
4.517
4.508
4.495
4.485
4.472
1.630
1.603
1.599
1.492
1.467
1.336
1.309
8.038
8.032
8.009
f1 (ppm)
nPr
(R)
(S)
(R)
NH
syn-7l

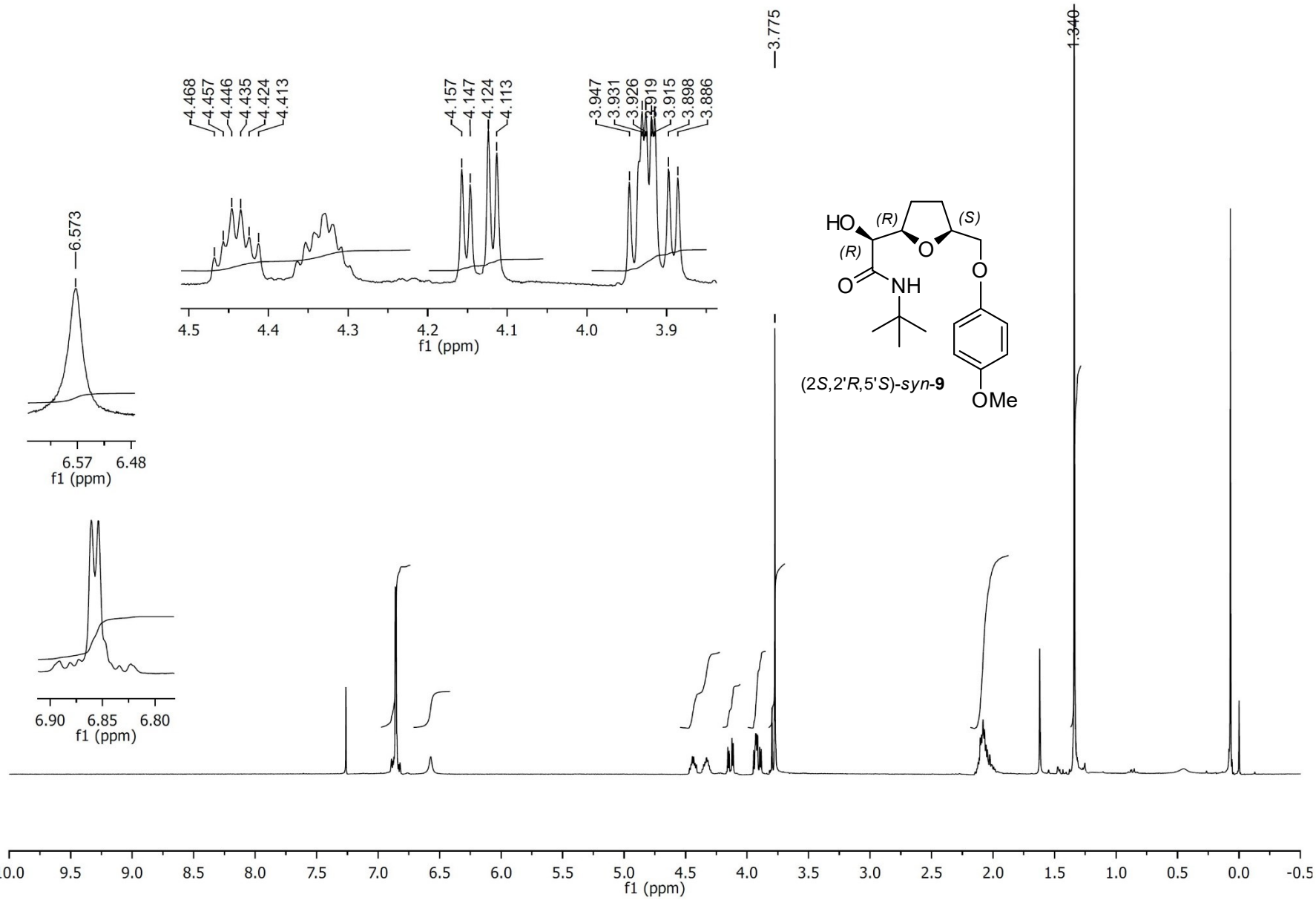

173.562
167.957
165.942
141.108
132.695
132.009
130.571
128.398
126.007
78.754
75.001
74.916
66.026
39.081
36.062
31.542
28.002
27.280
21.809
19.969
18.405
13.708
78.754
75.004
74.916
80
79
78
77
76
75
74
f1 (ppm)
nPr
O
O
(R)
O
(S)
O
O
(R)
O
NH
syn-7l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

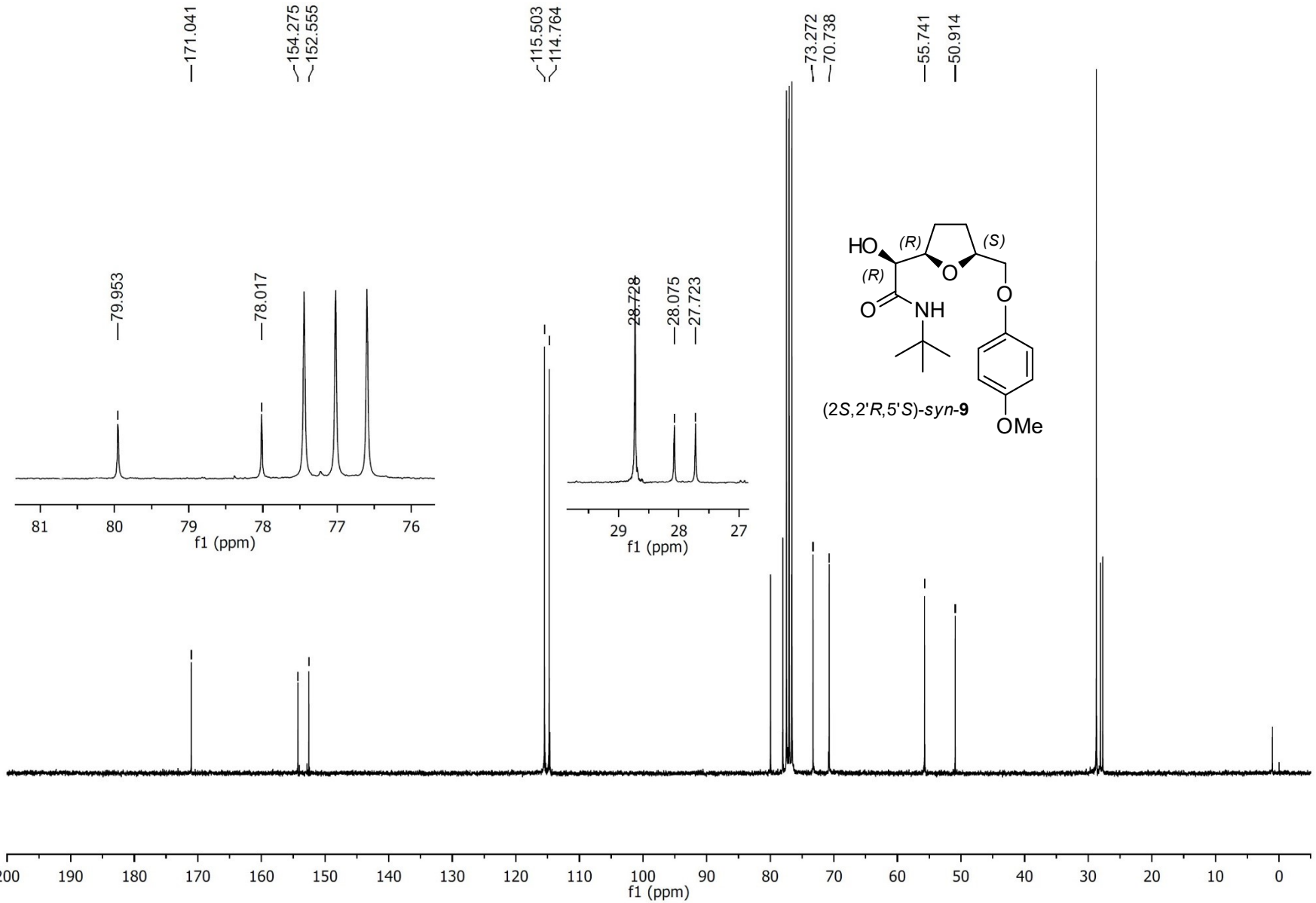

4.344
4.341
4.331
4.328
4.326
4.319
4.313
4.305
4.168
4.158
4.152
4.142
4.134
4.057
4.044
4.024
4.012
3.962
3.946
3.929
3.913
3.826
3.809
3.788
3.778
3.776
3.768
3.768
2.244
2.226
2.219
2.201
6.854
6.838
3.568
3.552
3.543
3.528
3.514
3.504
3.489
f1 (ppm)
(R)
(S)
OH
O
(2R,5S)-8
OMe

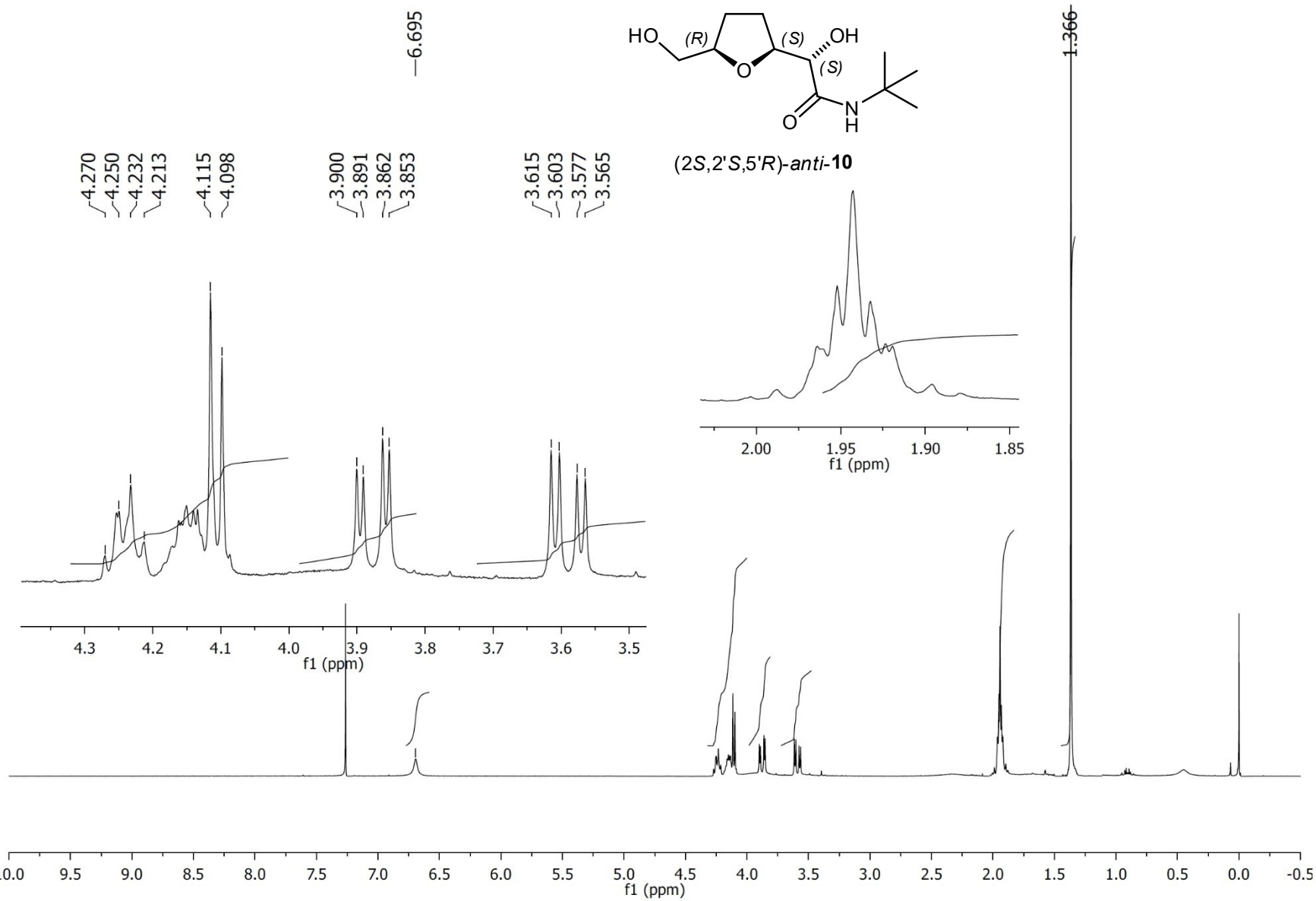

154.010
152.828
115.445
114.625
80.281
78.023
77.443
77.020
76.596
70.816
65.114
55.710
28.202
27.118
(R)
(S)
O
OH
O
(2R,5S)-8
OMe
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

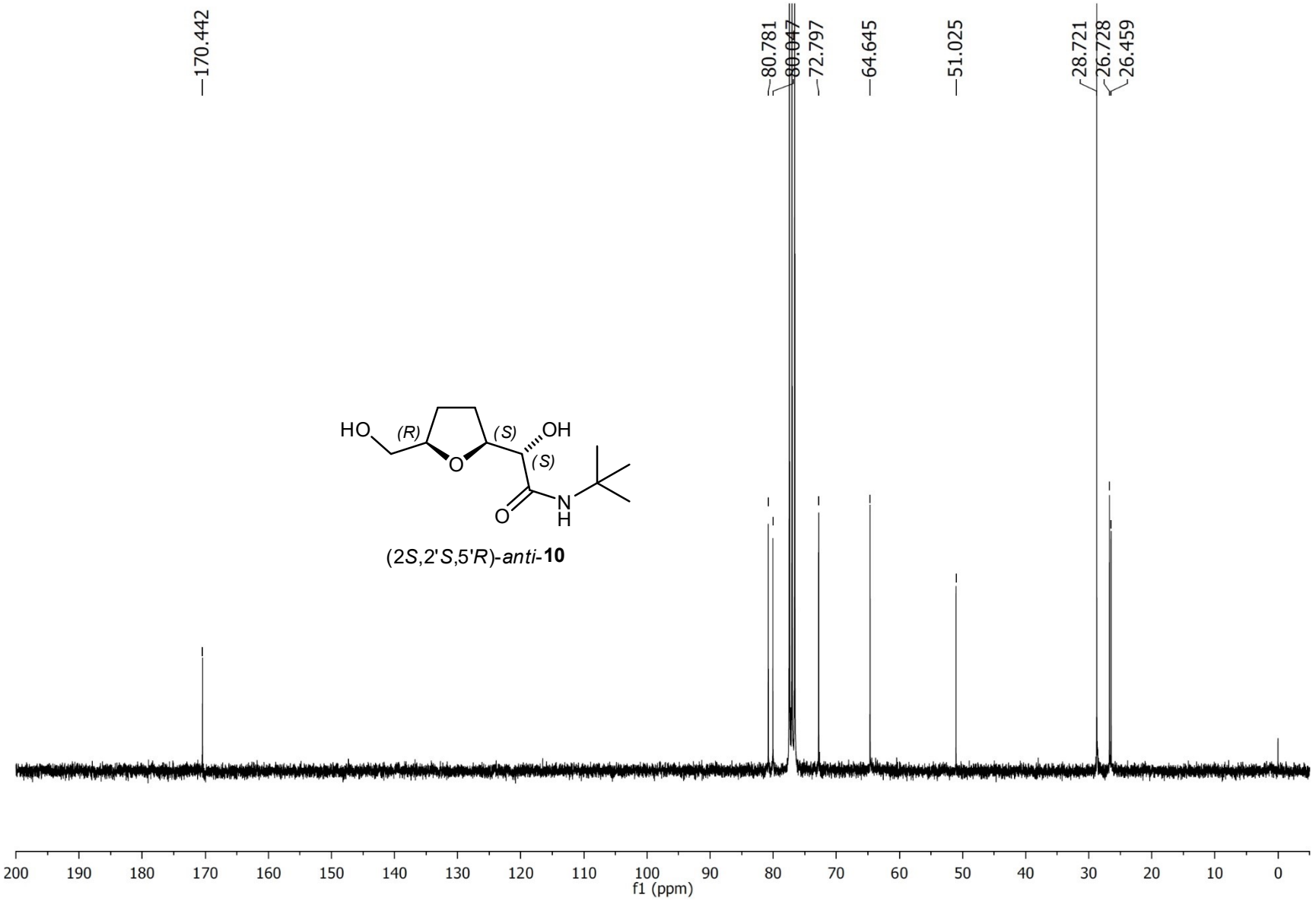

6.846
6.763
4.165
4.154
4.131
4.121
4.069
4.061
4.049
4.040
3.934
3.922
3.900
3.889
3.829
3.821
3.772
1.316
2.057
2.043
4.45 4.40 4.35 4.30 4.25 4.20 4.15 4.10 4.05 4.00 3.95 3.90 3.85
f1 (ppm)
2.1 2.0
f1 (ppm)
HO
(R)
(S)
(R)
O
O
NH
O
OMe
(2R,2'R,5'S)-anti-9
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

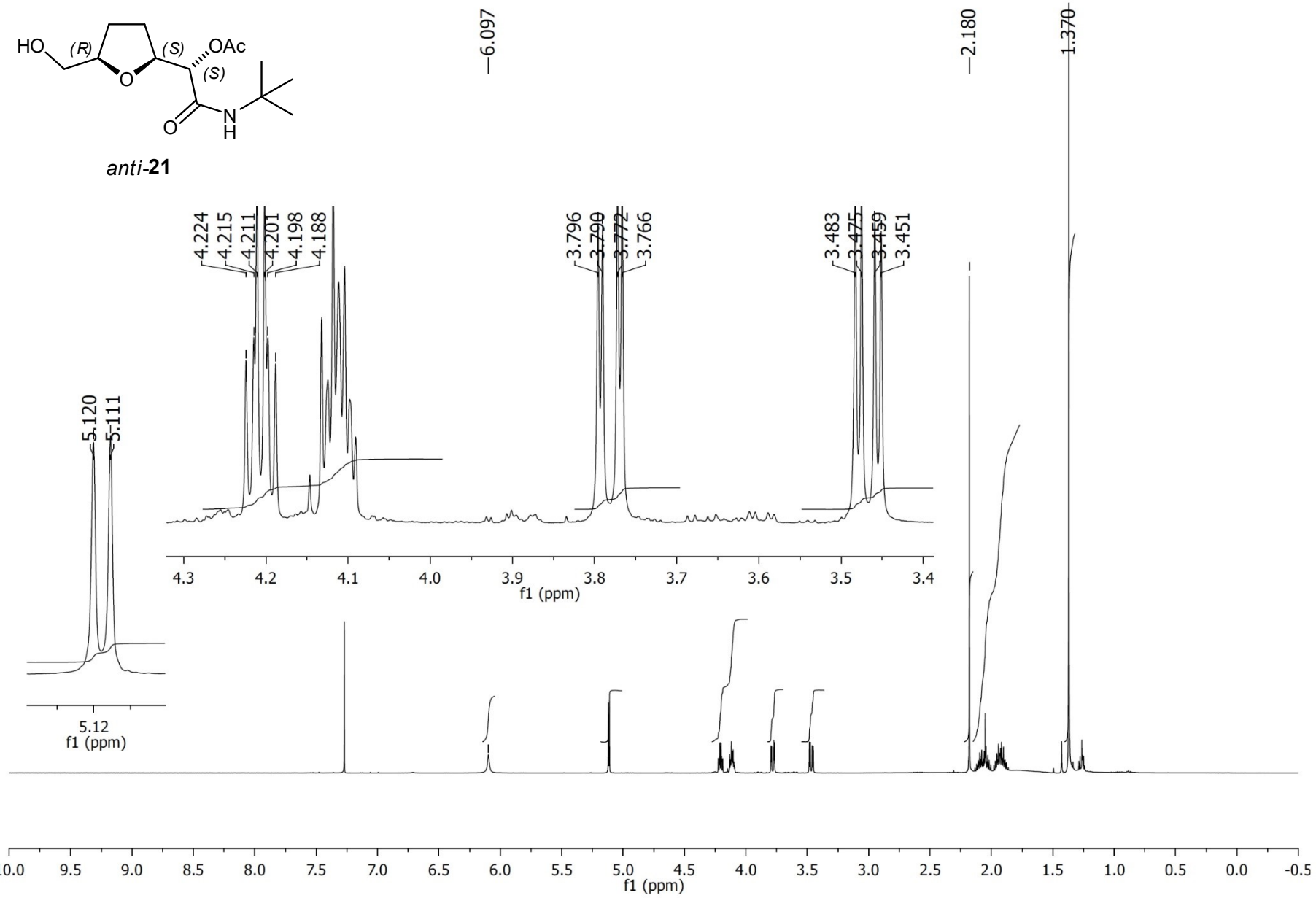

170.397
154.227
152.403
115.348
114.706
80.702
78.325
77.444
77.020
76.596
72.104
70.010
55.680
50.919
28.640
26.889
26.844
HO
(R)
(S)
(R)
O
O
NH
O
OMe
(2R,2'R,5'S)-anti-9
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

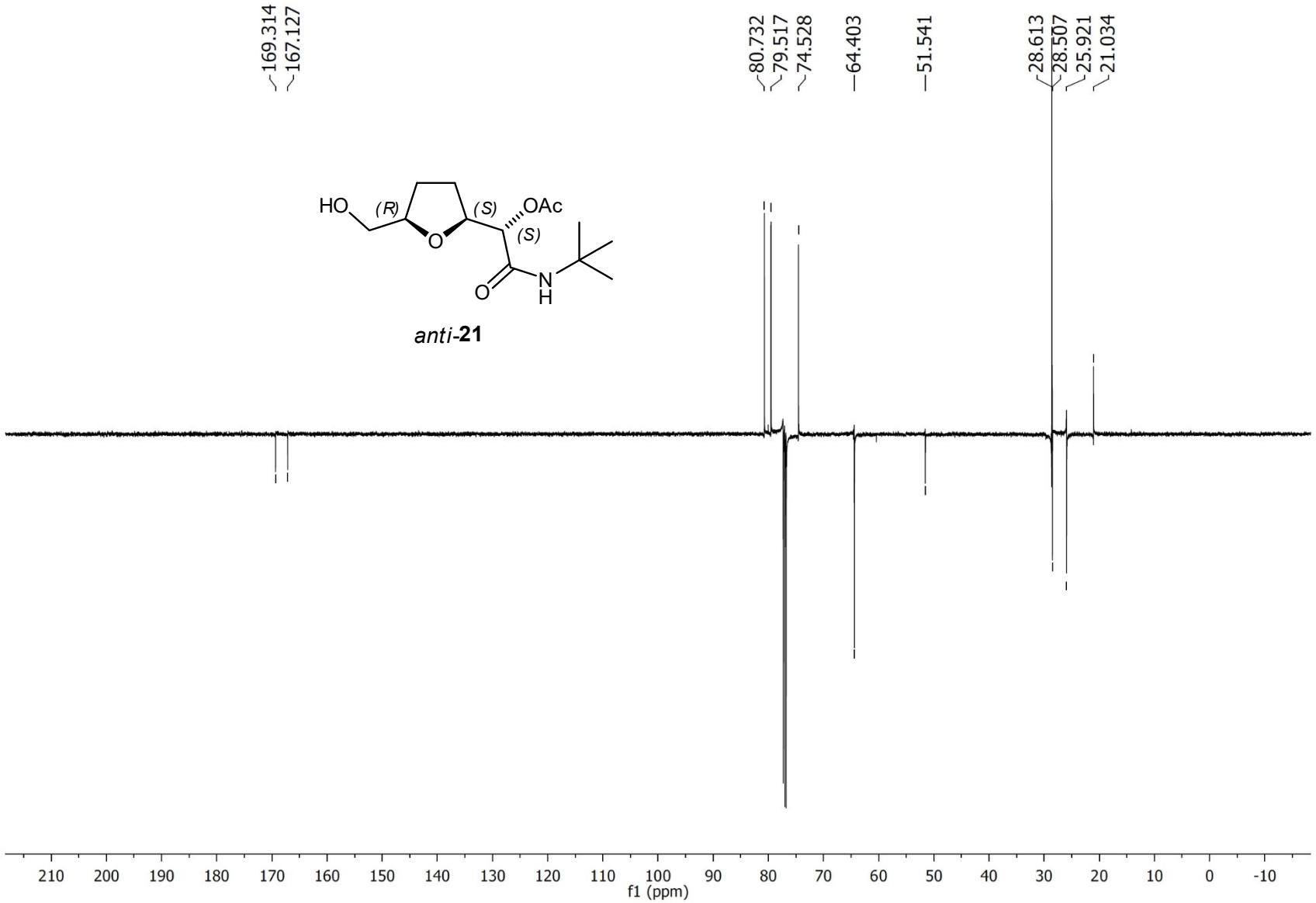

4.468
4.457
4.446
4.435
4.424
4.413
4.157
4.147
4.124
4.113
3.947
3.931
3.926
3.919
3.915
3.898
3.886
3.775
1.340
6.573
HO
(R)
(S)
(R)
O
O
NH
O
OMe
(2S,2'R,5'S)-syn-9
4.5
4.4
4.3
4.2
4.1
4.0
3.9
f1 (ppm)
6.57
6.48
f1 (ppm)
6.90
6.85
6.80
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

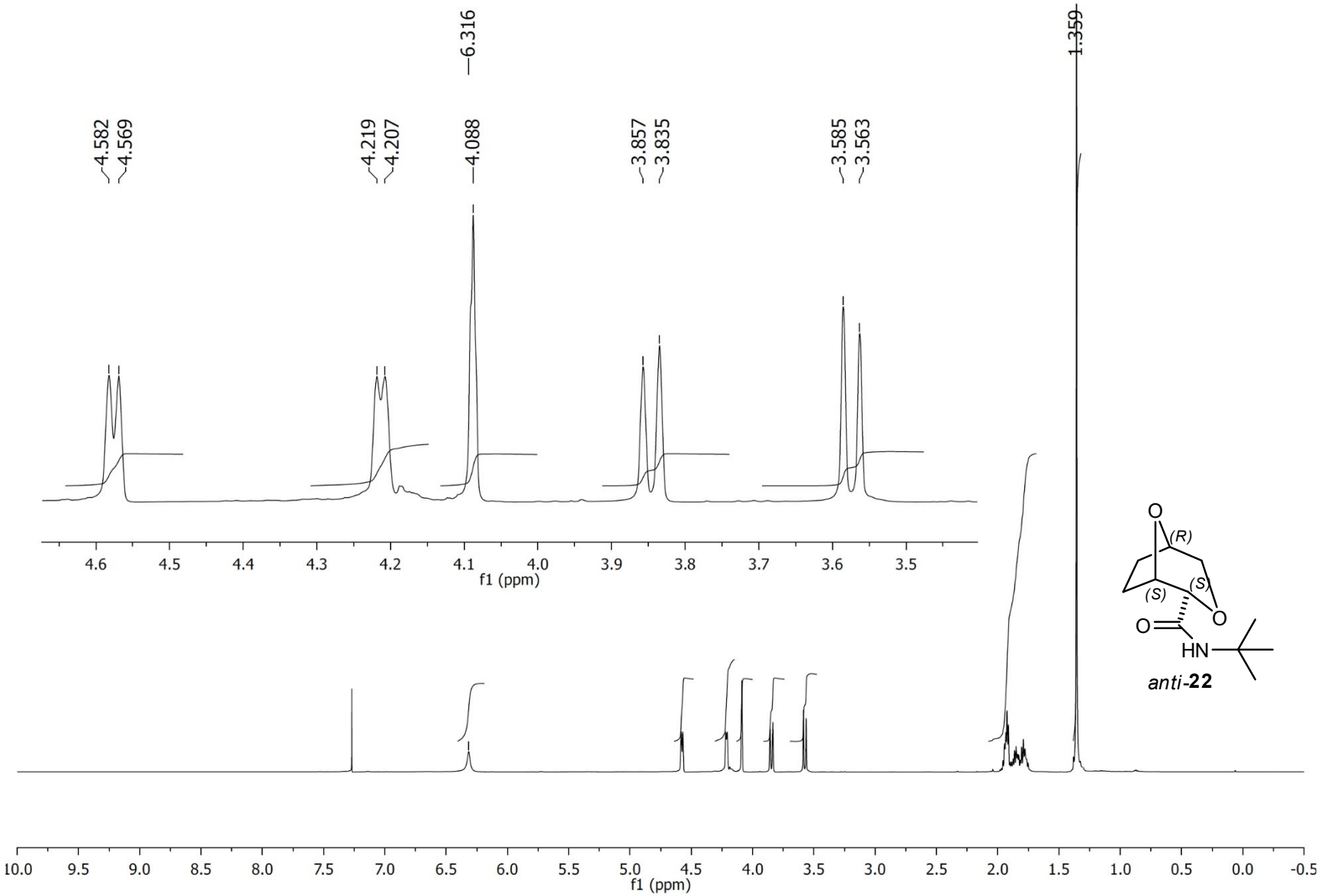

171.041
154.275
152.555
115.503
114.764
73.272
70.738
55.741
50.914
79.953
78.017
28.728
28.075
27.723
HO
(R)
(S)
(R)
O
O
NH
O
OMe
(2S,2'R,5'S)-syn-9
f1 (ppm)
f1 (ppm)
f1 (ppm)

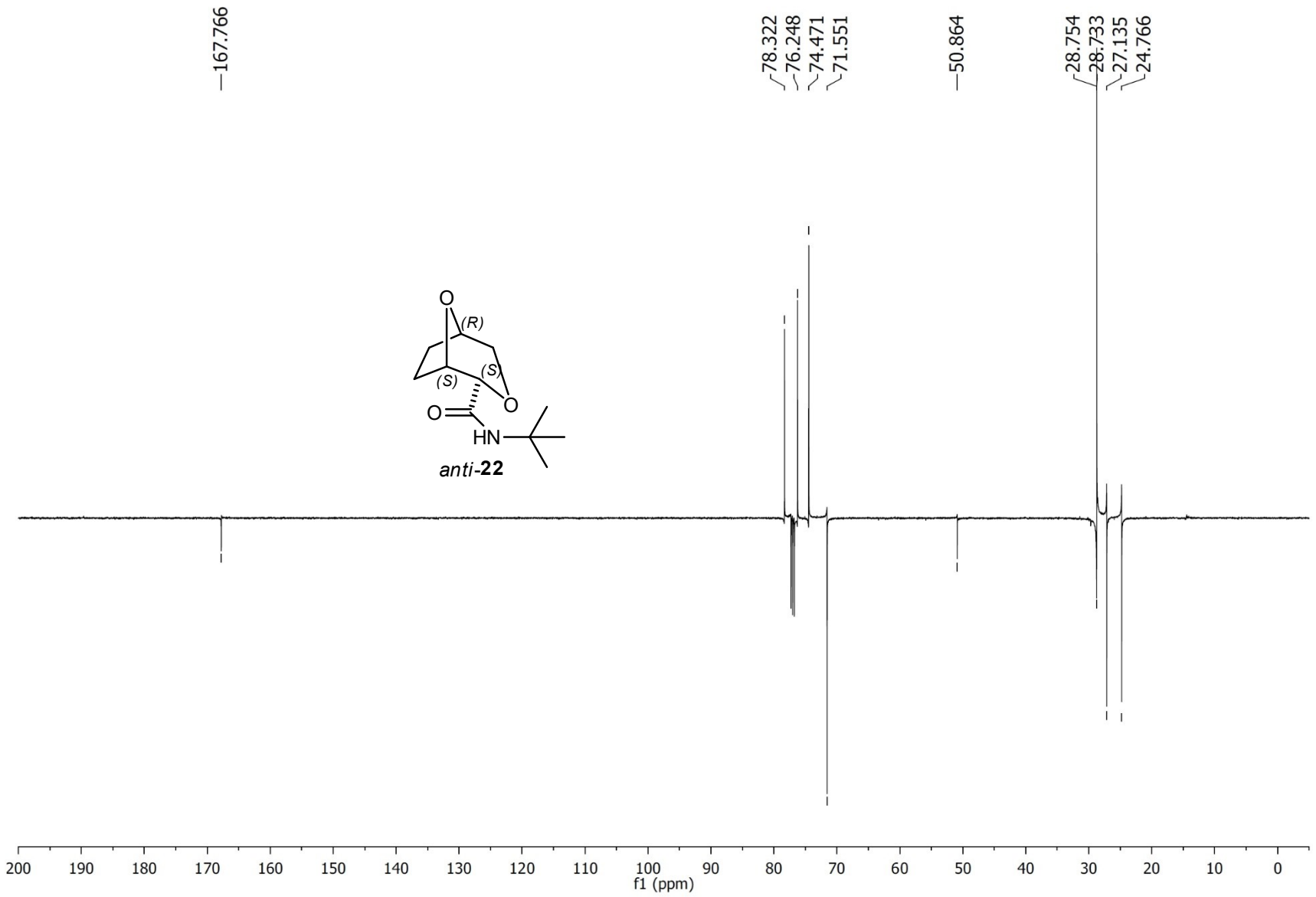

6.695
1.366
4.270
4.250
4.232
4.213
4.115
4.098
3.900
3.891
3.862
3.853
3.615
3.603
3.577
3.565
HO
(R)
O
(S)
OH
(S)
N
H
O
(2S,2'S,5'R)-anti-10
f1 (ppm)
f1 (ppm)
f1 (ppm)

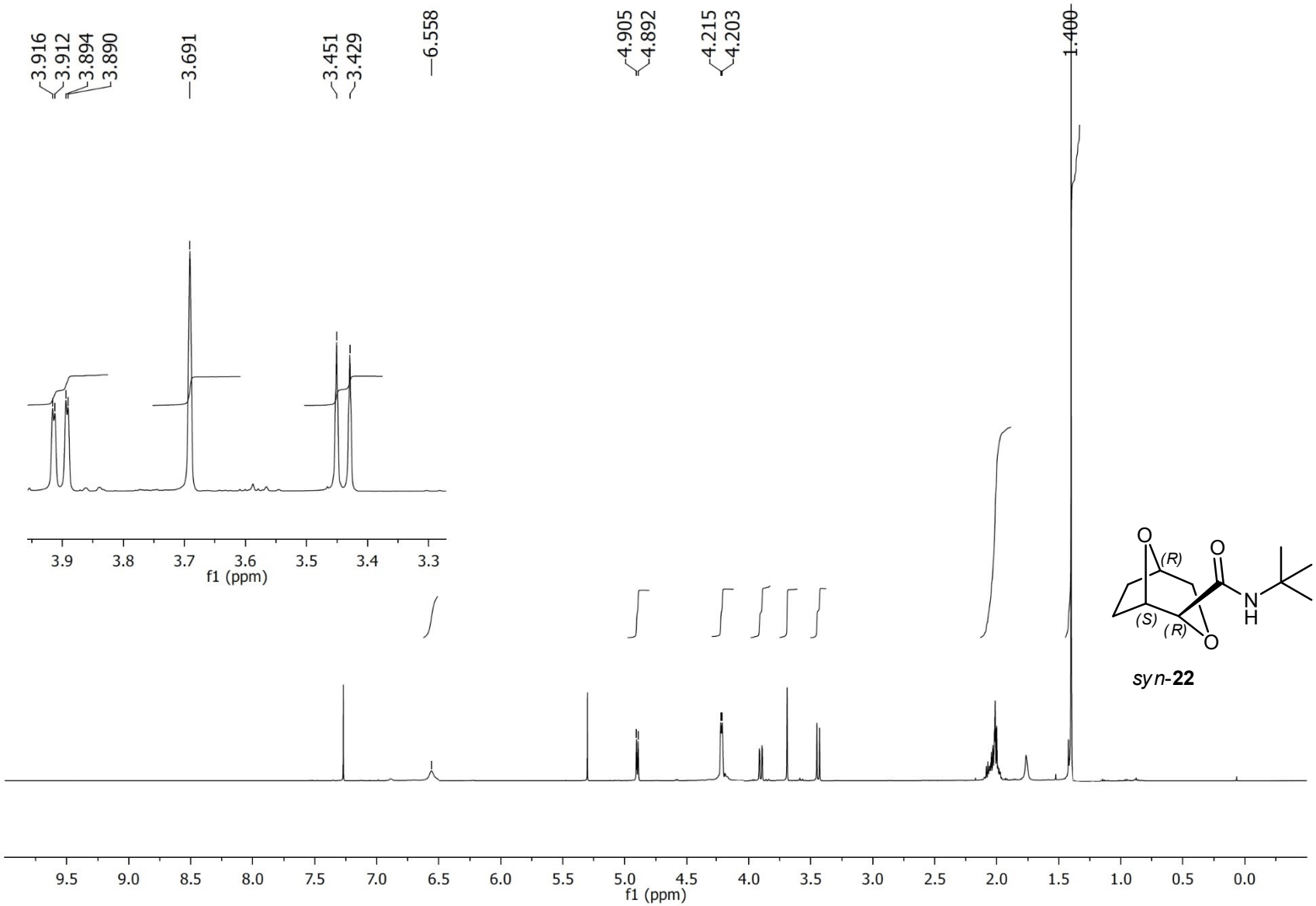

170.442
80.781
80.047
72.797
64.645
51.025
28.721
26.728
26.459
HO
(R)
(S)
OH
(S)
O
O
N
H
(2S,2'S,5'R)-anti-10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HO
(R)
(S)
OAc
(S)
O
O
N
H
anti-21
6.097
2.180
1.370
4.224
4.215
4.211
4.201
4.198
4.188
3.796
3.790
3.772
3.766
3.483
3.475
3.459
3.451
5.120
5.111
5.12
f1 (ppm)
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

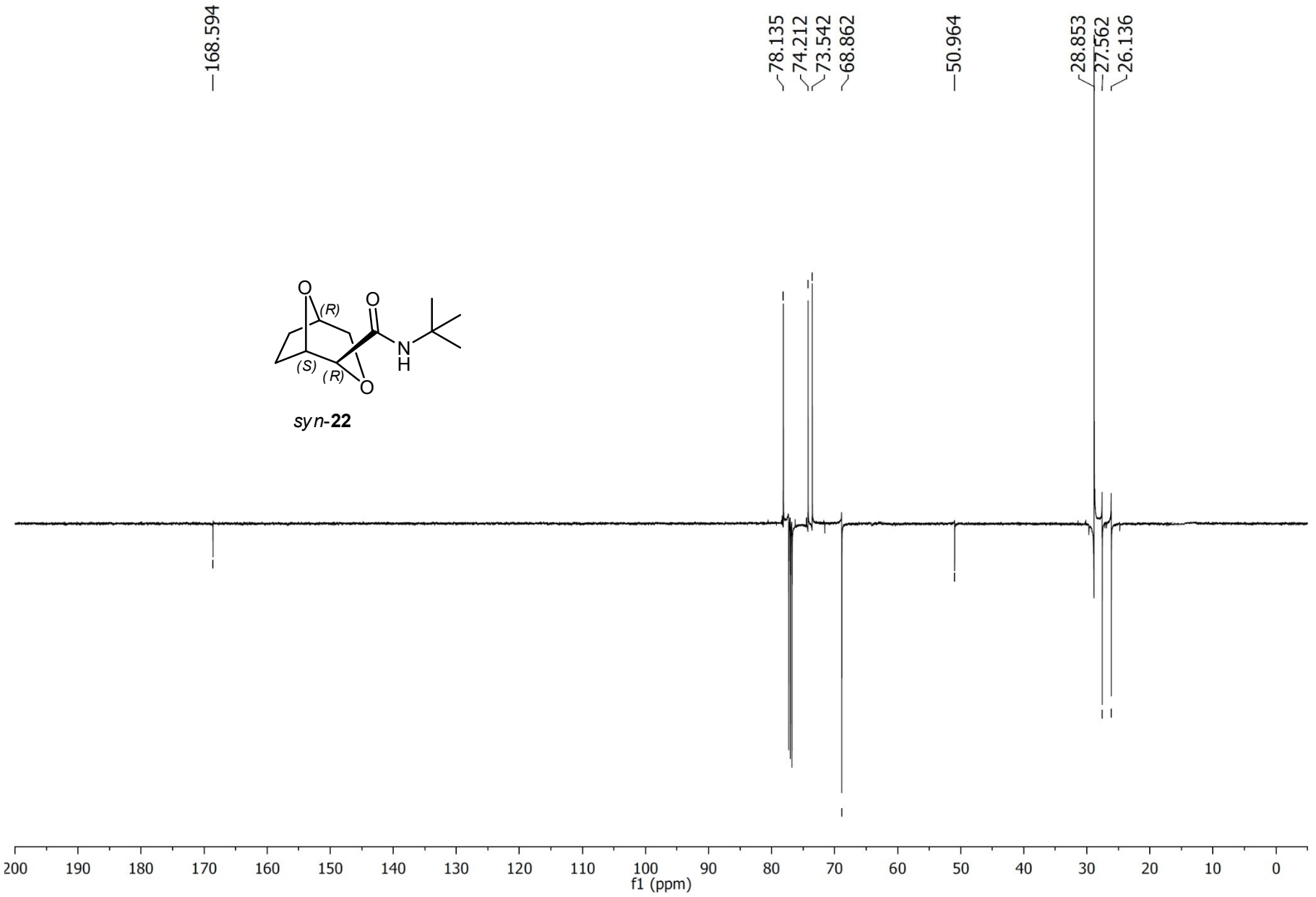

169.314
167.127
80.732
79.517
74.528
64.403
51.541
28.613
28.507
25.921
21.034
HO
(R)
(S)
OAc
(S)
O
O
N
H
anti-21
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


4.582
4.569
4.219
4.207
4.088
6.316
3.857
3.835
3.585
3.563
1.359
f1 (ppm)
f1 (ppm)
(R)
(S)
(S)
O
O
O
HN
anti-22

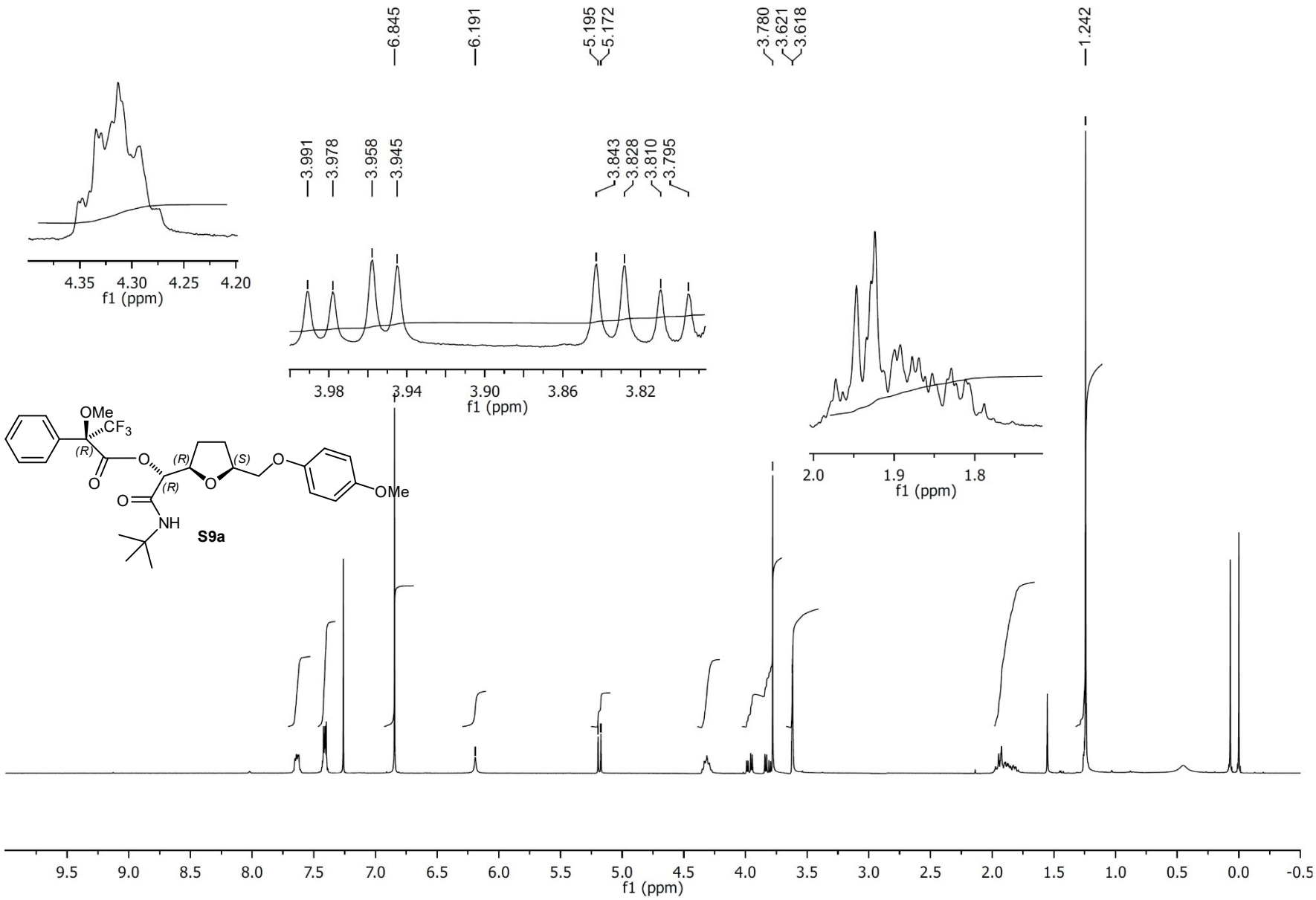

167.766
78.322
76.248
74.471
71.551
50.864
28.754
28.733
27.135
24.766
O
(R)
(S)
(S)
O
O
HN
anti-22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

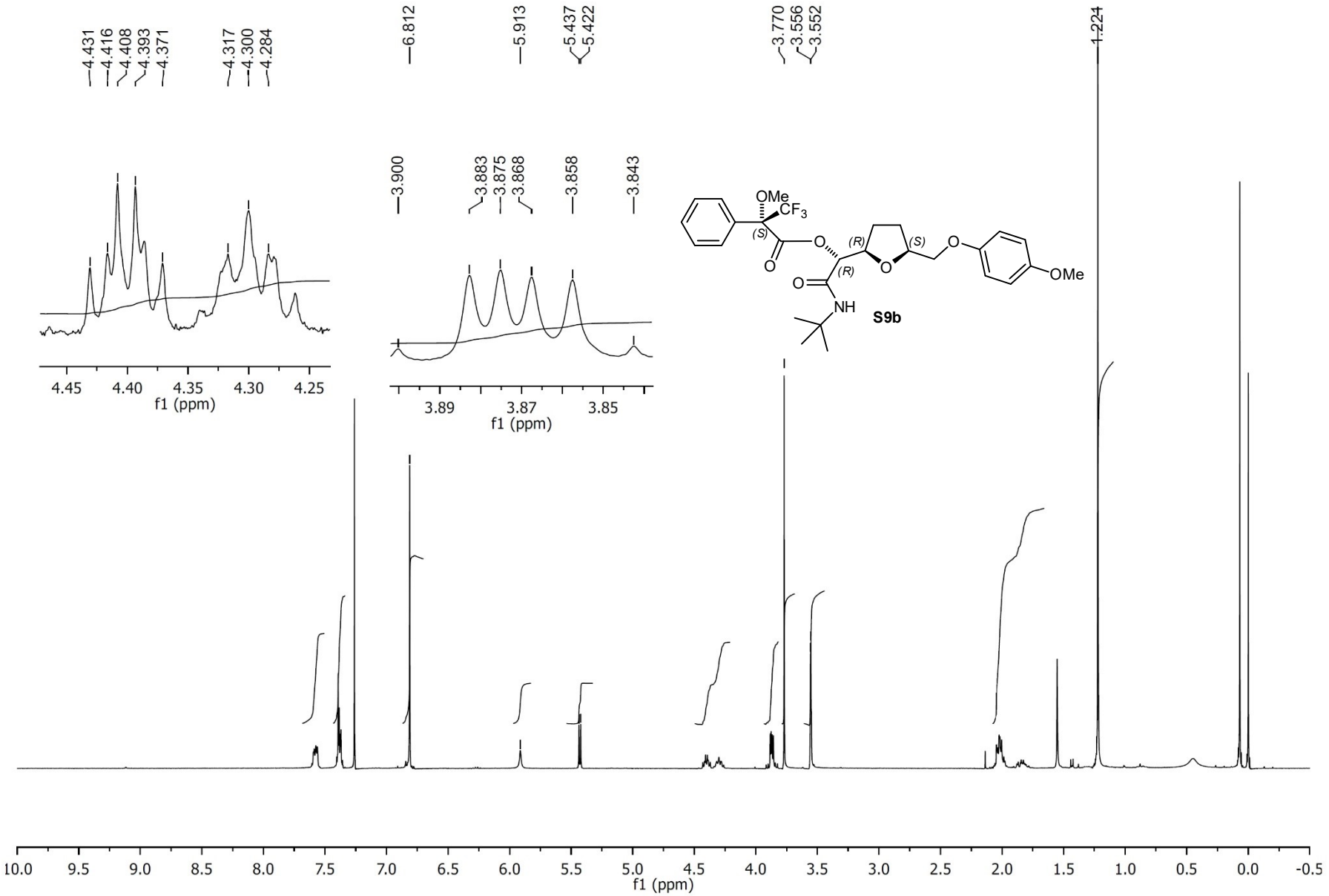

3.916
3.912
3.894
3.890
3.691
3.451
3.429
6.558
4.905
4.892
4.215
4.203
1.400
f1 (ppm)
f1 (ppm)
O
(R)
O
N
H
(S)
(R)
O

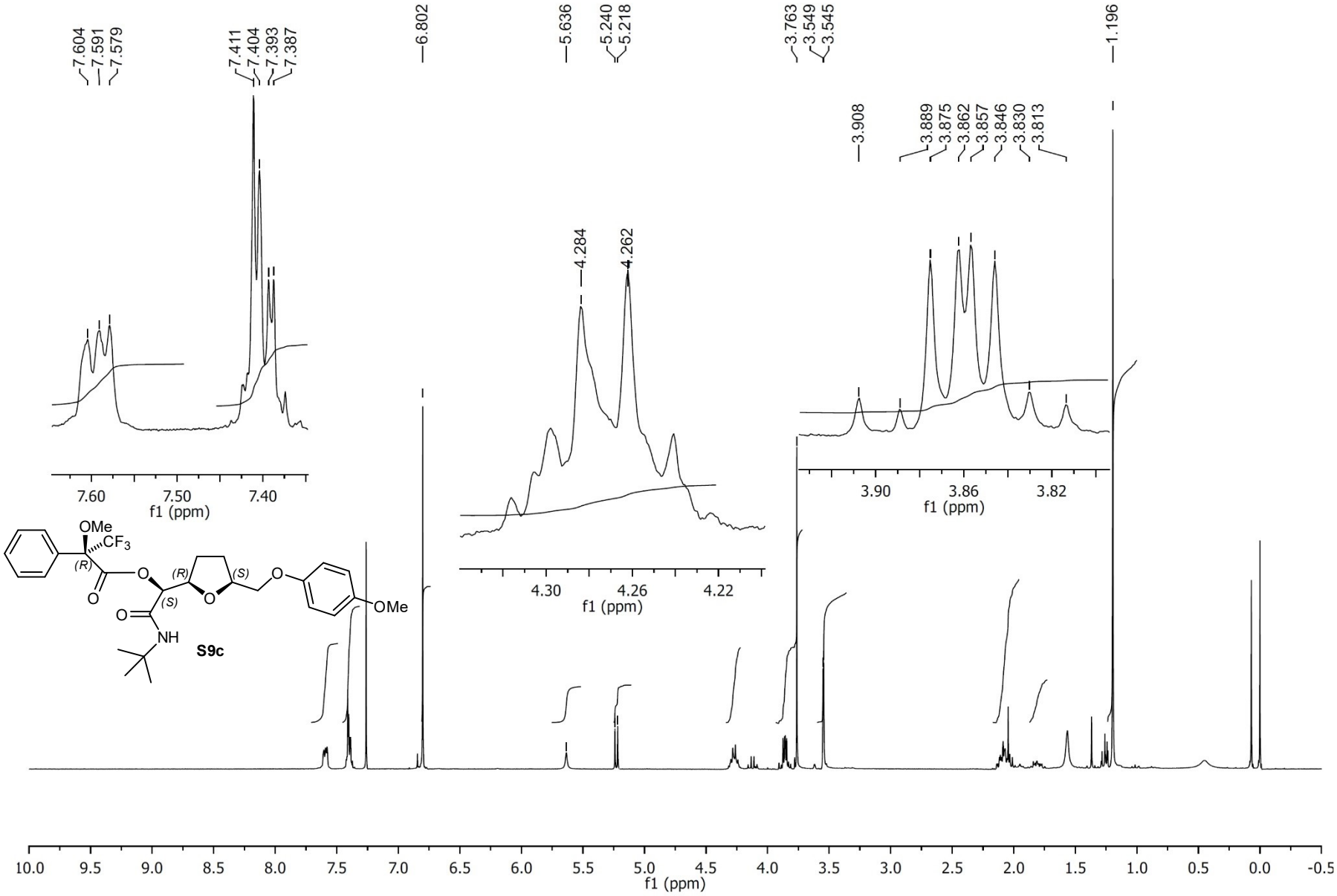
syn-**22**

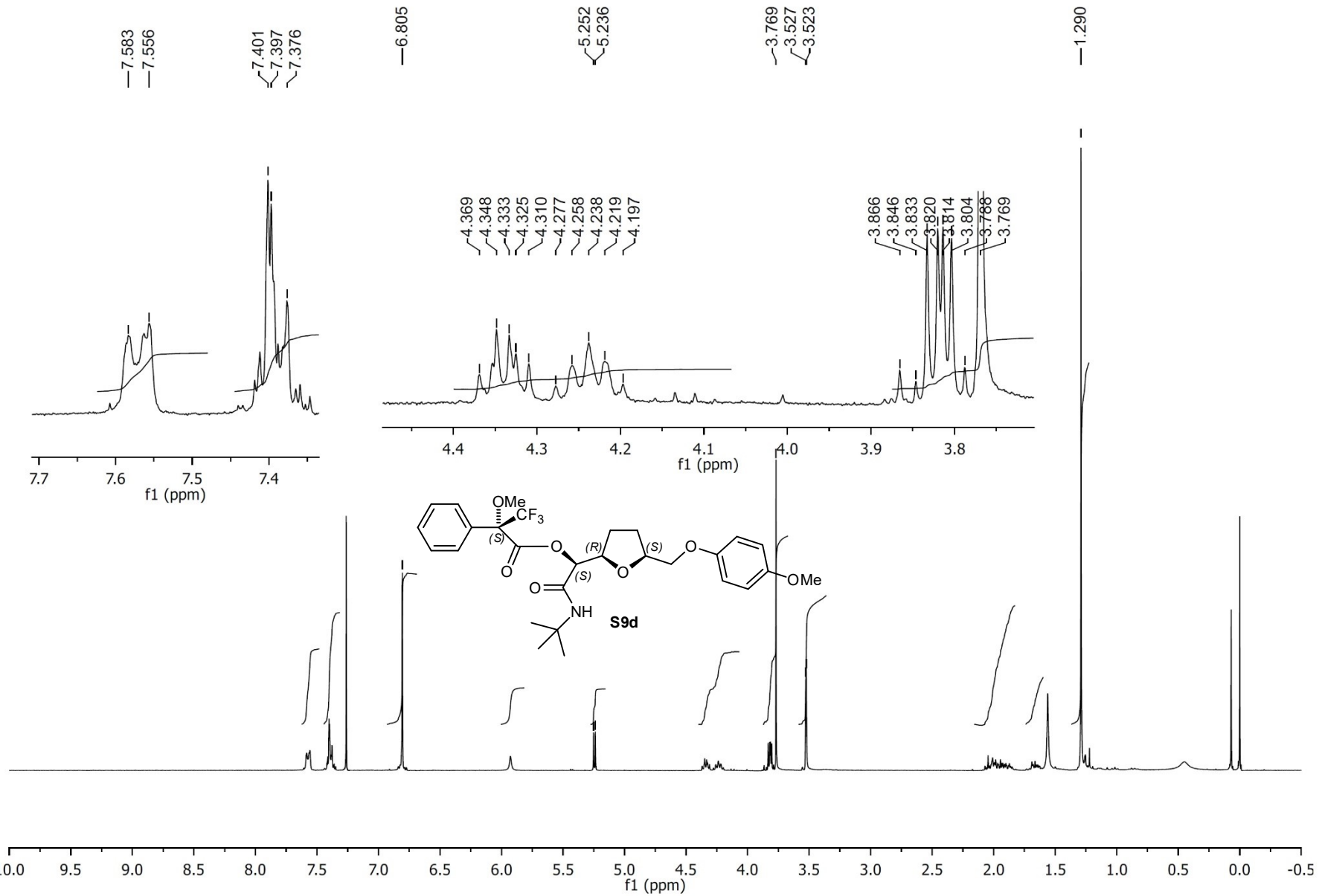

168.594
78.135
74.212
73.542
68.862
50.964
28.853
27.562
26.136
O
(R)
O
N
H
(S)
(R)
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

syn-**22**


6.845
6.191
5.195
5.172
3.780
3.621
3.618
1.242
3.991
3.978
3.958
3.945
3.843
3.828
3.810
3.795
4.35 4.30 4.25 4.20
f1 (ppm)
3.98 3.94 3.90 3.86 3.82
f1 (ppm)
2.0 1.9 1.8
f1 (ppm)
OMe
CF3
(R)
(R)
(S)
(R)
O
NH
OMe
S9a
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


4.431
4.416
4.408
4.393
4.371
4.317
4.300
4.284
6.812
5.913
5.437
5.422
3.770
3.556
3.552
1.224
3.900
3.883
3.875
3.868
3.858
3.843
OMe
CF3
(S)
O
O
(R)
(R)
O
(S)
O
OMe
O
NH
S9b
4.45
4.40
4.35
4.30
4.25
f1 (ppm)
3.89
3.87
3.85
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


7.604
7.591
7.579
7.411
7.404
7.393
7.387
6.802
5.636
5.240
5.218
4.284
4.262
3.908
3.889
3.875
3.862
3.857
3.846
3.830
3.813
3.763
3.549
3.545
1.196
7.60
7.50
7.40
f1 (ppm)
4.30
4.26
4.22
f1 (ppm)
3.90
3.86
3.82
f1 (ppm)
OMe
CF3
(R)
(R)
(S)
(S)
O
O
O
O
O
NH
OMe
S9c
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


7.583
7.556
7.401
7.397
7.376
6.805
5.252
5.236
3.769
3.527
3.523
1.290
4.369
4.348
4.333
4.325
4.310
4.277
4.258
4.238
4.219
4.197
3.866
3.846
3.833
3.820
3.814
3.804
3.788
3.769
f1 (ppm)
OMe
CF3
(S)
(R)
(S)
(S)
O
NH
OMe
S9d