Supporting Information

Synthesis of Caeliferins, Elicitors of Plant Immune Responses: Accessing Lipophilic Natural Products via Cross Metathesis

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1. 2D NMR spectroscopic analysis

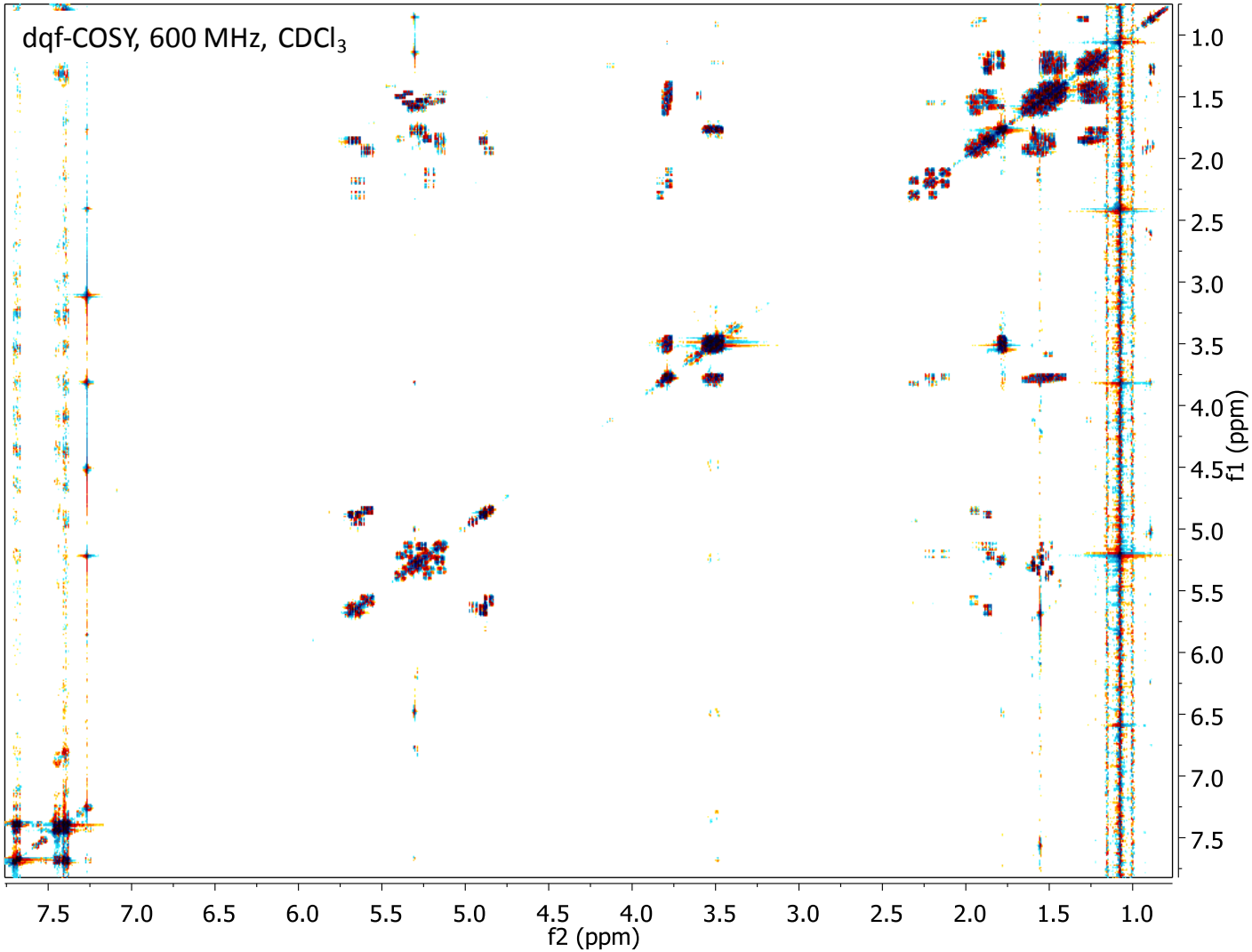


Figure S1a. dqfCOSY spectrum of the mixture of **17**, its isomers (**17a** and **17b**), and homologues (**17c**-**17i**) (600 MHz, $CDCl_3$). This sample was obtained via THP-protection of **9** isolated from CM reaction of **8** and **9** using G-II (0.05 equiv) and 1,4-benzoquinone (0.10 equiv).

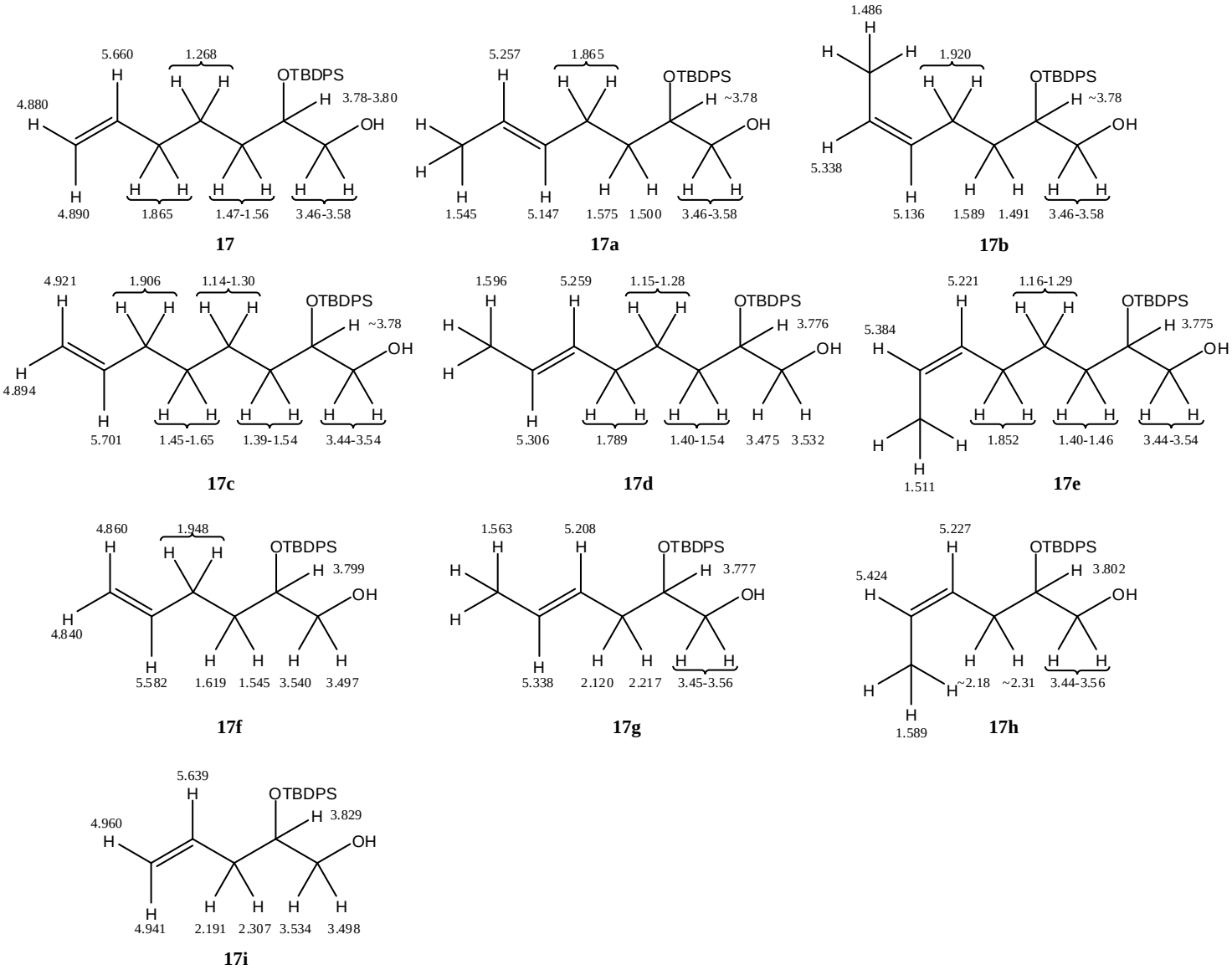
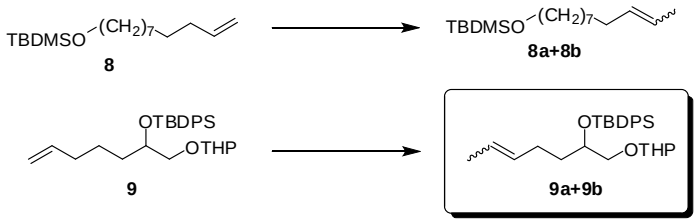


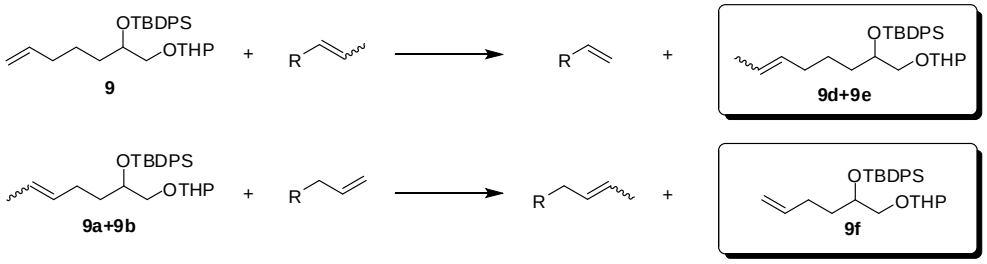
Figure S1b. Structures of compounds **17** and **17a-17i** as obtained from CM of **8** with **9** with G-II (0.05 equiv) and 1,4-benzoquinone (0.10 equiv).

2. Proposed isomerization and homologation pathways

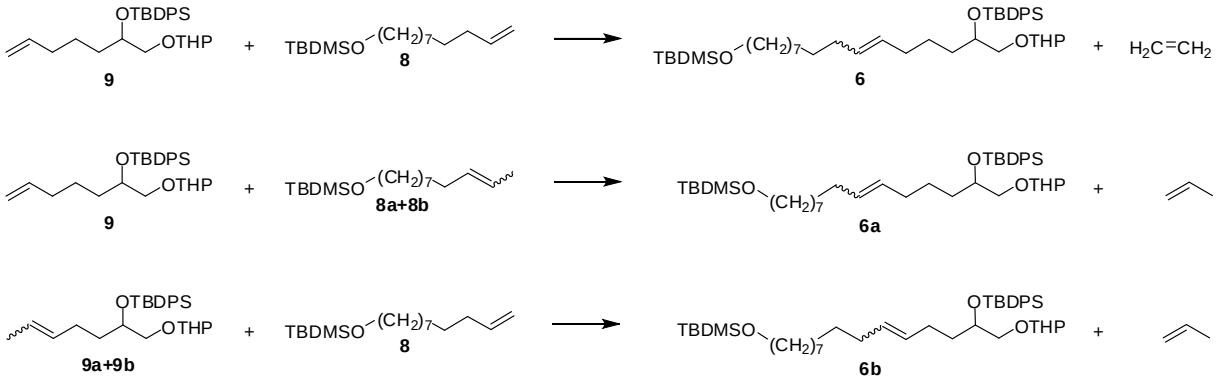
A. Isomerization of Starting Materials



B. Metathesis: Homologation of Isomerized Starting Materials



C. Metathesis: Formation of Product and its Nor-Homologues



D. Further Isomerization and Homologation

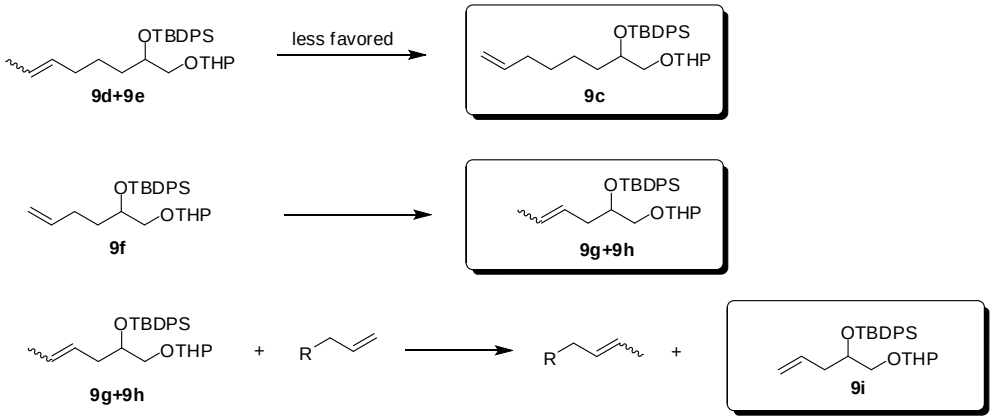


Figure S2. Proposed isomerization and homologation pathways in the cross metathesis of **8** and **9** with G-II (0.05 equiv) and 1,4-benzoquinone (0.10 equiv), based on analysis of dqfCOSY and ESI^+-MS spectra of reaction mixtures. Boxed: isomerization products of **9** and its homologues as detected in the dqfCOSY analysis of their THP-deprotected derivatives, **17** (see Figure S1).

3. Experimental

3.1 Instrumentation and general procedures

NMR spectra were recorded on Varian INOVA 600 (600 MHz), Varian INOVA 500 (500 MHz), or Varian INOVA 400 (400 MHz) spectrometers in Cornell University's NMR facility. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to residual solvent peaks (δ 2.05 ppm for acetone-d_6, 7.26 ppm for $CDCl_3$, 3.31 ppm for CD_3OD, 4.79 ppm for D_2O). NMR-spectroscopic data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR chemical shifts are reported in ppm (δ) relative to $CHCl_3$ (δ 77.2) in $CDCl_3$, CH_3OH (δ 49.0) in CD_3OD, and CH_3OH (δ 49.0) in D_2O). Positive-ion electrospray ionization mass spectra (ESI^+-MS) were obtained on a Micromass Quattro II mass spectrometer using MassLynx software. Optical rotations were measured on a Perkin Elmer 241 polarimeter. Solvents used for taking optical rotations (water, methanol, chloroform) were not further purified prior to use. Thin-layer chromatography (TLC) was performed using J. T. Baker Silica Gel IB2-F. Flash chromatography was performed using Teledyne Isco CombiFlash systems and Teledyne Isco RediSep Rf silica columns. Unless stated otherwise, reagents were purchased from Sigma-Aldrich and used without further purification. *N*,*N*-dimethylformamide (DMF), dichloromethane (DCM), dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF) were dried over 4 Å molecular sieves prior to use.

3.2 Cross metathesis test reactions

3.2.1 General procedure for CM test reactions[3]

A Schlenk flask was flame-dried under vacuum and charged with argon. Starting materials were added as solutions in dry DCM (2 ml of solvent per 0.1 mmol of compound **9**) and the resulting mixture was stirred for 10 min. Next, the catalyst was added and the reaction flask was brought to 40 °C with stirring. The reaction was stirred at 40 °C under argon and monitored by TLC and ESI^+-MS.

MS samples were prepared by diluting a small aliquot of the CM reaction into methanol, followed by filtration over a pad of silica. The filtered sample was evaporated to dryness under reduced pressure (<0.1 Torr) and re-suspended in methanol. The sample was then directly injected into the MS, monitoring a mass range of *m/z* 250-1000.

3.2.2 The effect of 1,4-benzoquinone[4]

Test CM reactions with catalysts G-I, G-II, and HG-II were conducted as outlined in **3.1.1** above, using mixtures of starting materials **8** and **9** in ratios of 5:1 respectively. Generally, test reactions were performed using 0.2 mmol of **9** and 0.01 mmol of catalyst.

After 2 h, ESI^+-MS analysis of the G-II and HG-II reaction mixtures revealed 30-35% conversion of starting material **9** and formation of corresponding amounts of product **6**, as well as significant amounts of homologues of both reactant and product. Chain-shortened derivatives of **6** accounted for 5-15% of products at this time point. Using G-I, 15-20% of **9** was consumed after 2 h, and corresponding amounts of **6** were detected.

After 20 h, ESI^+-MS analysis of the G-II and HG-II reaction mixtures revealed more than 65% conversion of **9**. Remaining starting materials **8** and **9** as well as product **6** were accompanied by significant amounts of nor-homologues, in addition to trace amounts of chain-extended variants. To investigate whether the production of these unwanted nor-homologues could be suppressed by the inclusion of 1,4-benzoquinone (1,4-BQ), a second series of reactions was performed, with addition of a 0.02 mmol solution of BQ in DCM to the reaction mix prior to the addition of the catalyst (Table S3).

Table S3. Reaction conditions for test CM of **8** and **9**. All reactions were carried out at least twice using two different batches of catalyst.

Catalyst	Amount of Catalyst	Amount of 9	Amount of 8	Amount of 1,4-benzoquinone	Solvent (DCM)	Conversion of 9
G-II	0.012 mmol	0.24 mmol	1.18 mmol	0.024 mmol	11 mL	65%
G-II	0.012 mmol	0.24 mmol	1.18 mmol	-	10 mL	90%
HG-II	0.016 mmol	0.32 mmol	1.60 mmol	0.032 mmol	11 mL	70%
HG-II	0.016 mmol	0.32 mmol	1.60 mmol	-	10 mL	90%
G-I	0.012 mmol	0.24 mmol	1.22 mmol	0.024 mmol	11 mL	50%
G-I	0.012 mmol	0..24 mmol	1.22 mmol	-	10 mL	60%

Figure S3 shows the ESI^+-MS spectra of samples from the reaction of **8** and **9** after 20 h, using either G-II, HG-II or G-I, in the presence or absence of 1-4-benzoquinone. Using G-II without BQ resulted in the generation of up to 60% of isomerization, CH_2-insertion and -deletion products. The inclusion of BQ with G-II in the CM reaction reduced the formation homologues to about 40%. In the case of HG-II, 40-50% of product **6** and starter **9** were converted to their respective homologues. Similarly to G-II, homologation process was suppressed to 10% by

addition of BQ. Comparatively small amounts of nor-homologues were found in the BQ-free CM using G-I, and addition of 1,4-BQ to G-I reaction suppressed homolog formation below the detection limit (less than 0.5% homologation). It should be noted that the MS analyses only reveal the extent of homologation, but not double bond isomerization. Therefore, products and starting materials isolated from CM reactions with all three catalysts were additionally analyzed by ^{1}H NMR, which revealed 5-50% of double bond isomerization, except for the case of using G-I in combination with 1,4-BQ. 2D-NMR spectroscopic experiments are described in the following section.

Similar results were obtained test CM reaction of **7** and **9** (Table S4, Figure S4).

Table S4. Reaction conditions for test CM of **7** and **9**. All reactions were carried out at least twice using two different batches of catalyst.

Catalyst	Amount of Catalyst	Amount of 9	Amount of 7	Amount of 1,4-benzoquinone	Solvent (DCM)	Conversion of 9
G-II	0.012 mmol	0.24 mmol	1.18 mmol	0.024 mmol	11 mL	70%
G-II	0.012 mmol	0.24 mmol	1.18 mmol	-	10 mL	65%
HG-II	0.016 mmol	0.32 mmol	1.60 mmol	0.032 mmol	11 mL	65%
HG-II	0.016 mmol	0.32 mmol	1.60 mmol	-	10 mL	65%
G-I	0.012 mmol	0.24 mmol	1.22 mmol	0.024 mmol	11 mL	65%
G-I	0.012 mmol	0..24 mmol	1.22 mmol	-	10 mL	75%

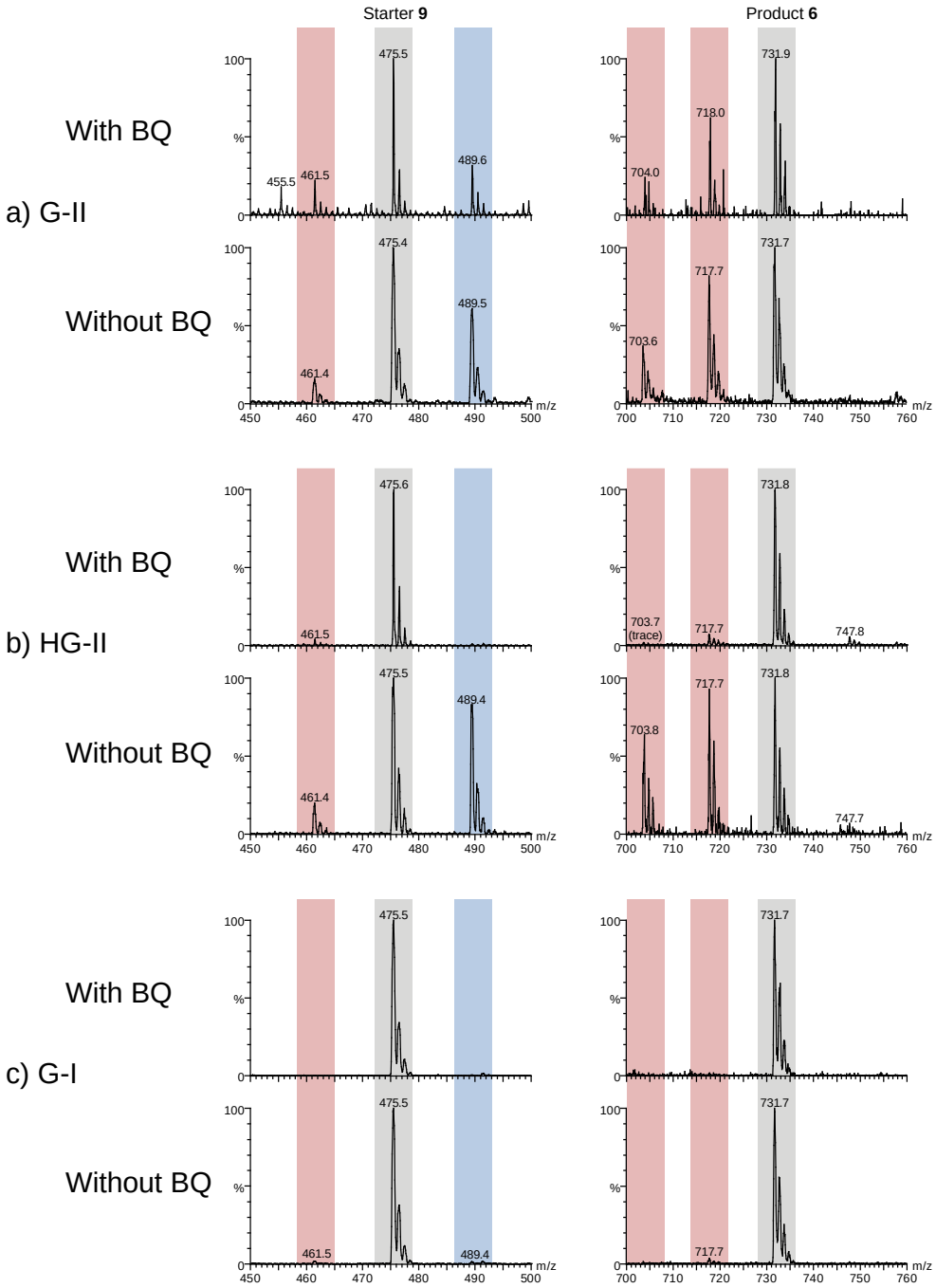


Figure S3. ESI$^+$-MS spectra of CM reaction mixtures showing [M+Na$^+$] for starter **9** (*m/z* 475.3) and product **6** (*m/z* 731.5). Ion signals corresponding to chain shortened and chain extended homologues are shown in red and blue, respectively. All reactions were carried out with 0.05 equiv. of catalyst at 40 °C for 20 h. For reactions with BQ, 0.1 equiv of 1,4-benzoquinone was added to the reaction. Conditions: (a) G-II catalyst; (b) HG-II catalyst; (c) G-I catalyst. For specific reaction conditions see ***Table S3.***

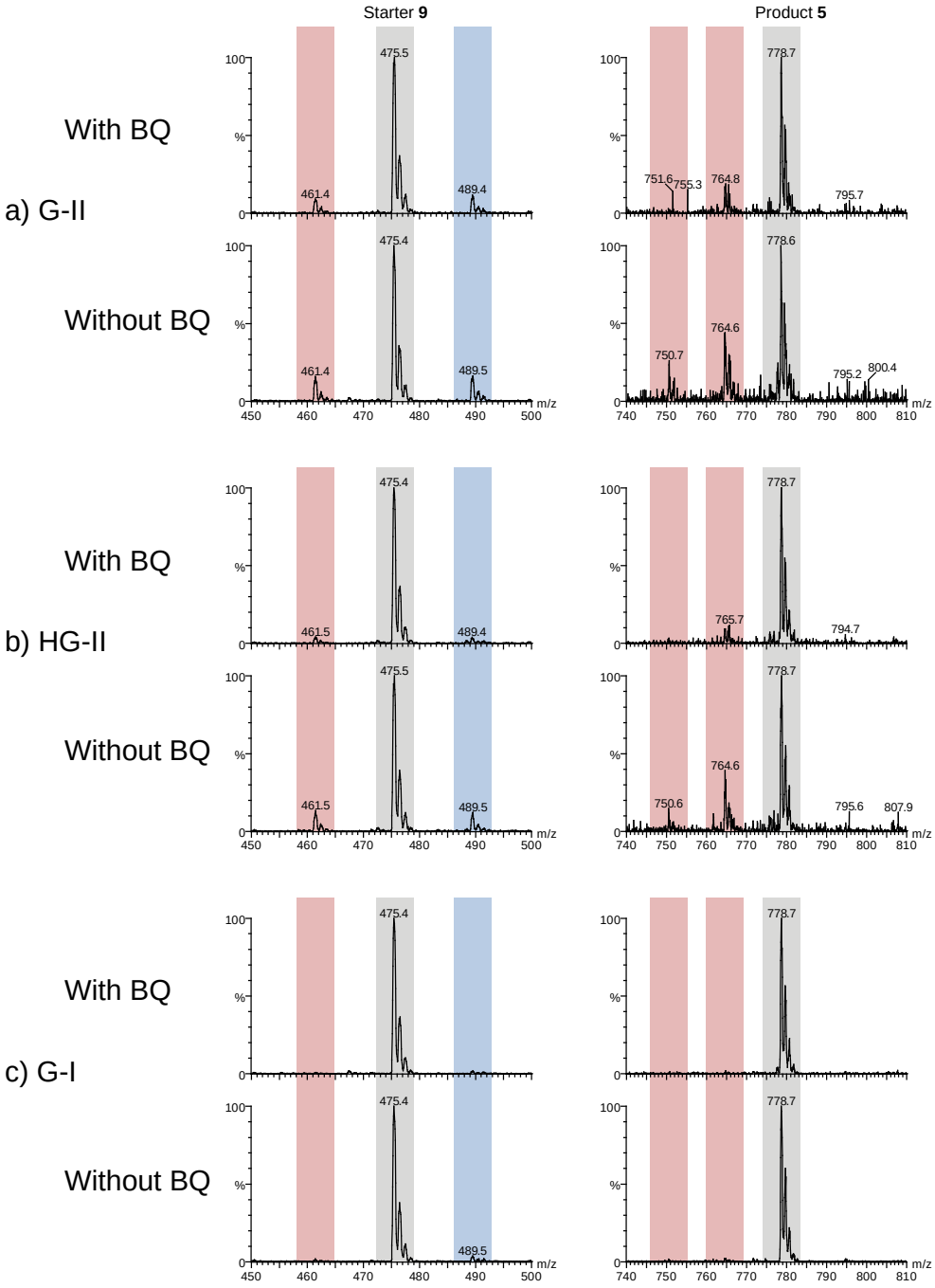


Figure S4. ESI$^+$-MS spectra of CM reaction mixtures showing [M+Na$^+$] for starter **9** (*m/z* 475.3) and product **5** (*m/z* 778.4). Ion signals corresponding to chain shortened and chain extended homologues are shown in red and blue, respectively. All reactions were carried out with 0.05 equiv. of catalyst at 40 °C for 20 h. For reactions with BQ, 0.1 equiv of 1,4-benzoquinone was added to the reaction. Conditions: (a) G-II catalyst; (b) HG-II catalyst; (c) G-I catalyst. For specific reaction conditions see ***Table S4.***

3.2.3 2D NMR-spectroscopic characterization of isomerization products

High resolution dqfCOSY NMR analysis[5] of products from a G-II reaction (as above, reaction time 20 h) with **8**, **9** and 1,4-benzoquinone were conducted after THP-deprotecting the mixture of recovered **9** and its homologues and isomers. For this purpose, the CM reaction was filtered over a pad of silica and evaporated *in vacuo*. This crude mixture was then dissolved in Et_2O and anhydrous $MgBr_2$ (5 equiv.) was added with stirring. After stirring overnight, the reaction was cooled to 0 °C and quenched by addition of 5% $NaHCO_3$ (10 equiv) in distilled H_2O. Cold pentane was added and the mixture was stirred for 15 min, during which time a voluminous white precipitate of $Mg(OH)_2$ formed. Subsequently, the organic layer was decanted and the reaction flask rinsed with pentane. The combined organic solutions were dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (EtOAc:hexanes, 1:9). Fractions containing **17**, its isomers, and homologues were combined, evaporated *in vacuo,* and characterized via dqfCOSY spectra (Figure 2 and Figure S1a).

3.2.4 Alkene chain lengths and degree of homologation

CM test reactions using **7** and **9** or **8** and **9** showed that the degree of isomerization was dependent on the activity of the catalyst (section 3.2.2). We further observed that homologation and isomerization were generally less prevalent in the synthesis of **5** (via CM of **7** and **9**) than in the preparation of **6** (via CM of **8** and **9)**. To investigate the effect of specific features of CM starting materials on isomerization and homologation, we conducted the additional test reactions shown in Figure S5 (for conditions, see Tables S5-S7).

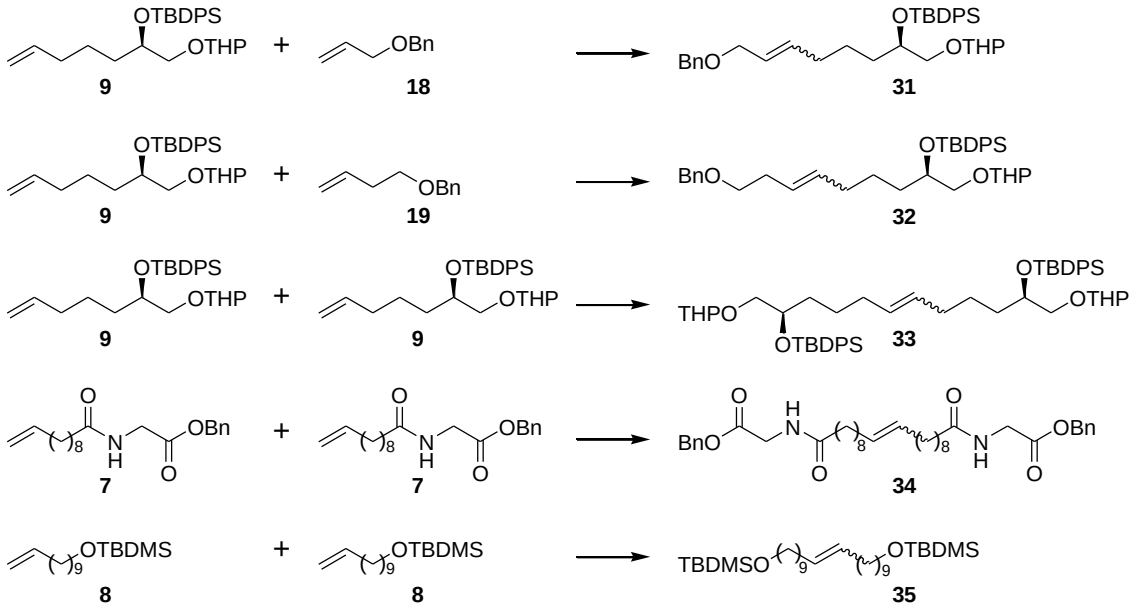


Figure S5. Additional test metathesis reactions.

Table S5. Reaction conditions for CM of **9** and **18**, **9** and **19**, and homodimerization of **9** using G-II catalyst without 1,4-benzoquinone.

Catalyst	Amount of Catalyst	Amount of 9	Amount of second substrate	Solvent (DCM)	Conversion of 9
G-II	0.012 mmol	0.24 mmol	**18,** allyl benzyl ether 1.18 mmol	10 mL	40%
G-II	0.012 mmol	0.24 mmol	**19**, homoallyl benzyl ether 1.18 mmol	10 mL	40%
G-II	0.012 mmol	0.24 mmol	-	8 mL	80%

Table S6. Reaction conditions for test CM of homodimerization of **7**.

Catalyst	Amount of Catalyst	Amount of 7	Amount of 1,4-benzoquinone	Solvent (DCM)	Conversion of 7
G-II	0.024 mmol	0.24 mmol	0.024 mmol	8 mL	80%
G-II	0.024 mmol	0.24 mmol	-	7 mL	90%
HG-II	0.016 mmol	0.32 mmol	0.032 mmol	8 mL	70%
HG-II	0.016 mmol	0.32 mmol	-	7 mL	90%
G-I	0.012 mmol	0.24 mmol	0.024 mmol	6 mL	70%
G-I	0.012 mmol	0.24 mmol	-	5 mL	80%

Table S7. Reaction conditions for test CM of homodimerization of **8**.

Catalyst	Amount of Catalyst	Amount of 8	Amount of 1,4-benzoquinone	Solvent (DCM)	Conversion of 8
G-II	0.012 mmol	0.24 mmol	0.024 mmol	8 mL	80%
G-II	0.012 mmol	0.24 mmol	-	7 mL	90%
HG-II	0.016 mmol	0.32 mmol	0.032 mmol	8 mL	80%
HG-II	0.016 mmol	0.32 mmol	-	7 mL	90%
G-I	0.012 mmol	0.24 mmol	0.024 mmol	8 mL	80%
G-I	0.012 mmol	0.24 mmol	-	7 mL	80%

Homologation of remaining starting materials or products was detected in the homodimerization of **9** as well as in CM of **9** with **18** using G-II as catalyst (Figure S6). Upon the addition of 1,4-BQ to these short chain CM reactions, full suppression of homolog formation was achieved, which was verified by ESI^+-MS. In contrast, homodimerization of long-chain substrates **7** and **8** resulted in extensive homologation when using G-II catalyst. Smaller quantities of homologues were observed when using HG-II and G-I catalysts (Figures S7, S8). Addition of 1,4-benoquinone reduced homologation extent, but in case of the homodimerization of **8** did not fully suppress homologation, even when using the least active G-I catalyst (Figure S8). Comparing the reaction series that resulted in significant homologation and isomerization (Figures S3, S4, S6-S8), the degree of homologation strongly correlates with the chain lengths of the reactants. Reaction times and conversion of starting materials was roughly similar for all reactions (see Tables S3-S7).

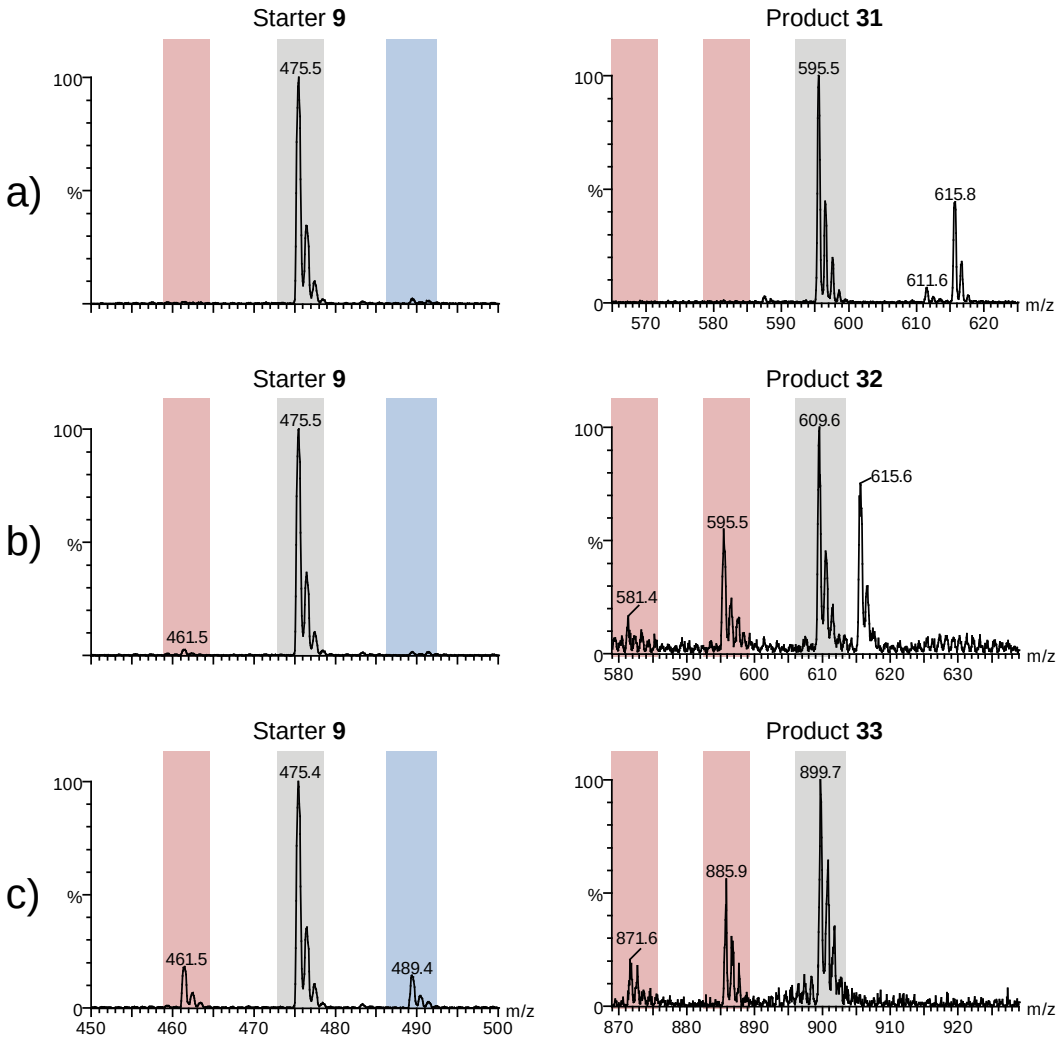


Figure S6. ESI$^+$-MS analysis of CM test reactions of (a) **9** and **18**, (b) **9** and **19**, and (c) the homodimerization of **9**, using G-II catalyst without benzoquinone. For each reaction [M+Na$^+$] for starter **9** (*m/z* 475.3) and the products [**31** (*m/z* 595.3), **32** (*m/z* 609.3), and **33** (*m/z* 899.5)] are shown, along with signals representing varying quantities of homologues and norhomologues. All reactions were carried out with 0.05 equiv. of G-II catalyst at 40 °C for 20 h. For specific reaction conditions see ***Table S5***.

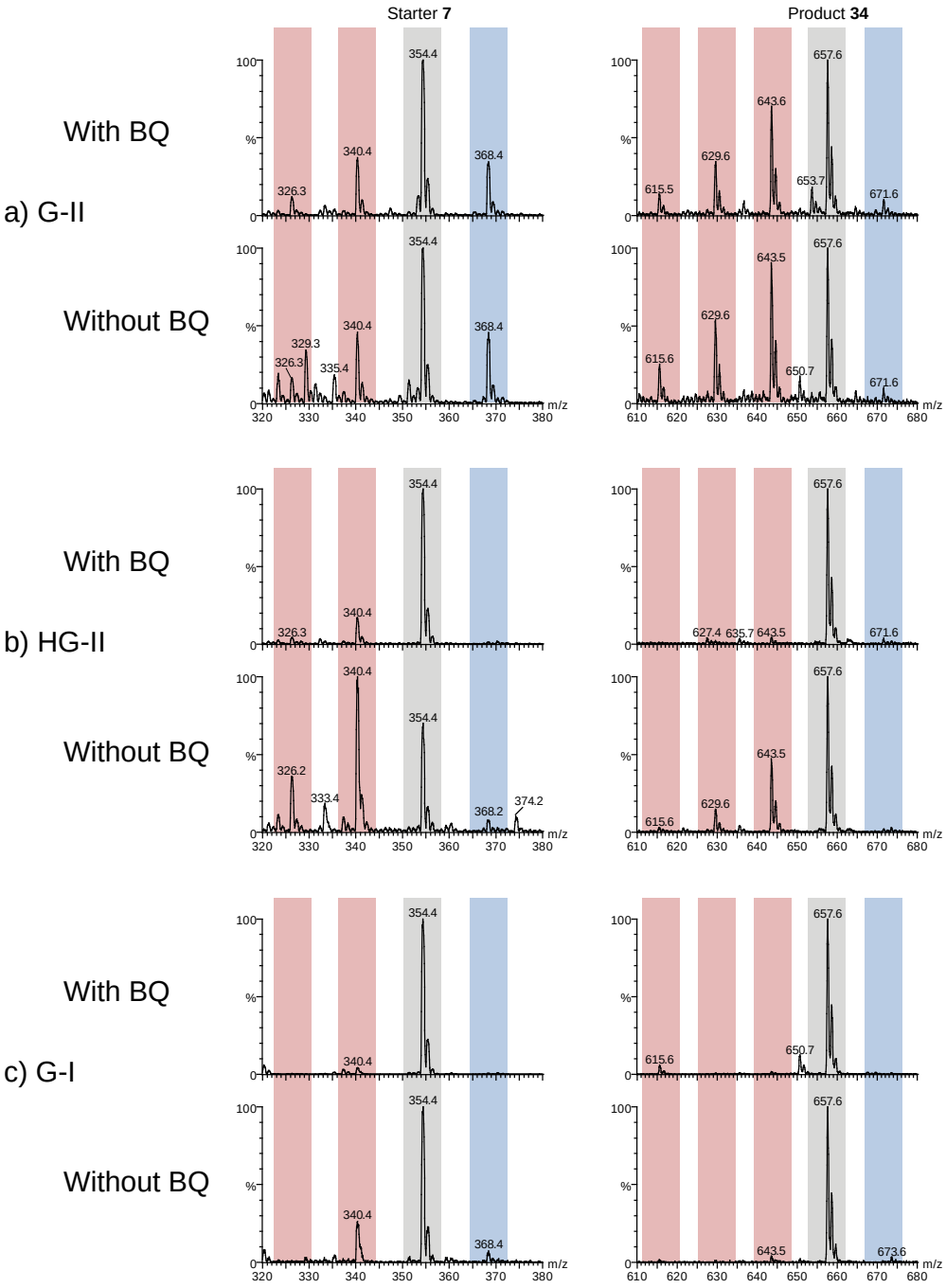


Figure S7. ESI^{+}-MS spectra of CM reaction mixtures showing [M+Na^{+}] for starter **7** **(***m/z* 354.2) and product **34** **(***m/z* 657.4). Ion signals corresponding to chain shortened and chain extended homologues are shown in red and blue, respectively. All reactions were carried out with 0.05 equiv. of catalyst at 40 °C for 20 h. For reactions with BQ, 0.1 equiv of 1,4-benzoquinone was added to the reaction. Conditions: (a) G-II catalyst; (b) HG-II catalyst; (c) G-I catalyst. For specific reaction conditions see ***Table S6.***

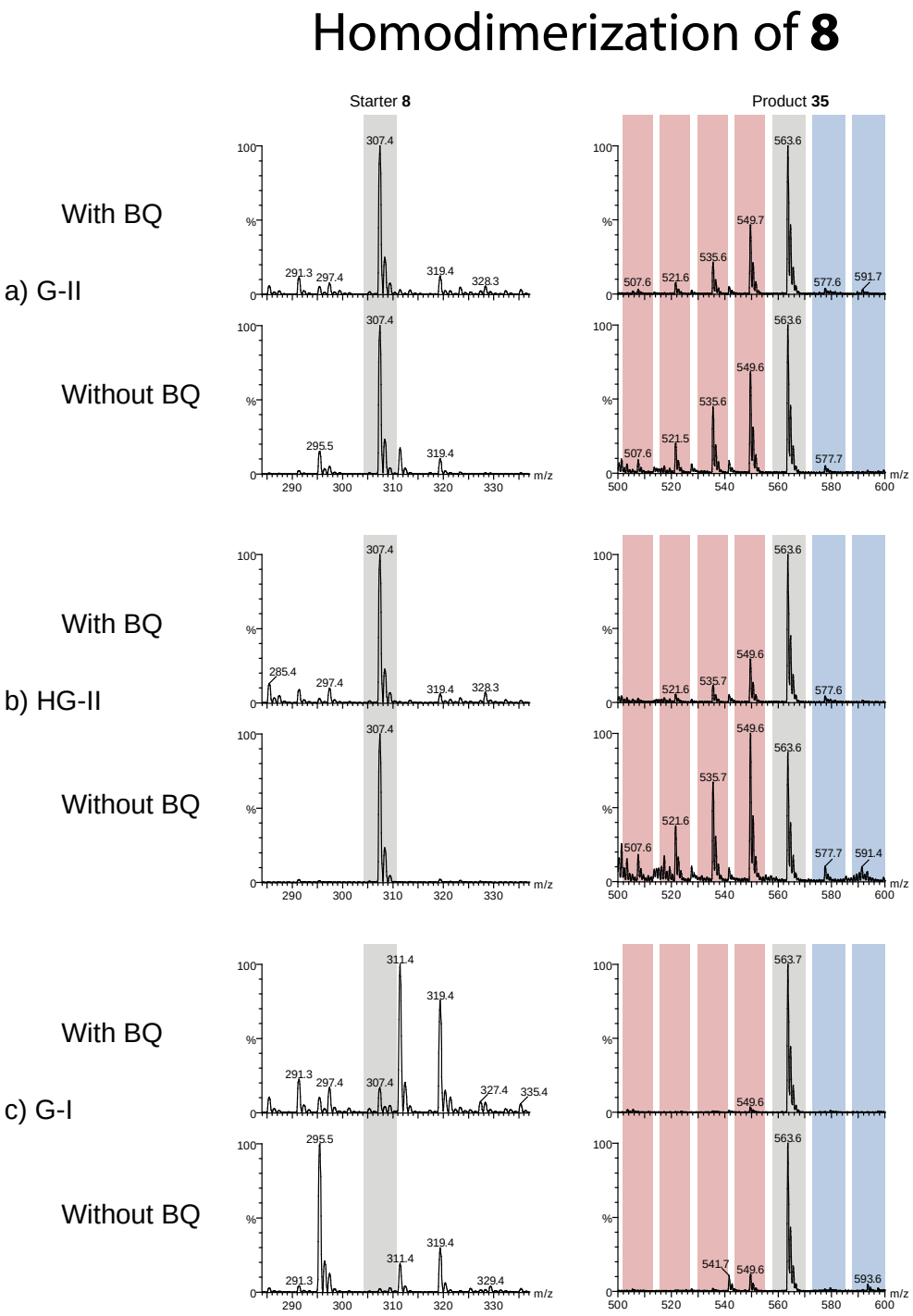
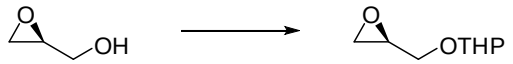


Figure S8. ESI^{+}-MS spectra of CM reaction mixtures showing [M+Na^{+}] for starter **8** (*m/z* 307.2) and product **35** (*m/z* 563.5). Ion signals corresponding to chain shortened and chain extended homologues are shown in red and blue, respectively. All reactions were carried out with 0.05 equiv. of catalyst at 40 °C for 20h. For reactions with BQ, 0.1 equiv of 1,4-benzoquinone was added to the reaction. Conditions: (a) G-II catalyst; (b) HG-II catalyst; (c) G-I catalyst. For specific reaction conditions see ***Table S7.*** Note: in contrast to all other substrates surveyed, remaining starting material **8** was *not* accompanied by significant amounts of chain-shortened or elongated derivatives, neither in this homodimerization reaction (see this Figure), nor in CM with compound **9**, despite the fact that reaction of **8** resulted in the largest percentages of homologated products.

3.3 Synthesis of (*R*)-1

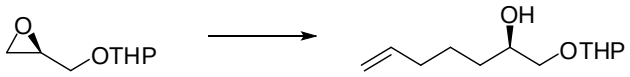
3.3.1 2-((*S*)-Oxiran-2-ylmethoxy)tetrahydro-2H-pyran ((*S*)-11):



***(S)*-10** ***(S)*-11**

To a 500 mL round bottom flask, (*S*)-(–)-glycidol **(*S*)-10** (10.0 g, 135 mmol, 97% *ee*) and DCM (450 mL) were added. To this mixture, 3,4-dihydropyran (56.8 g, 74.9 mmol, 5.0 equiv) and *p*-toluenesulfonic acid (260 mg, 1.34 mmol, 0.01 equiv) were added with stirring. The mixture turned a light purple color and stirred for 2 h. Subsequently, saturated aqueous $NaHCO_3$ solution (570 mL) was added to the reaction mixture and stirring was continued for 10 min. The organic layer was separated, and the aqueous layer extracted with two 50ml-portions of DCM. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:2) yielding **(*S*)-11** as a yellow oil (18.9 g, 120 mmol, 89% yield). **^{1}H NMR (400 MHz, acetone-d_6):** δ 4.65-4.60 (m, 1H), 3.90-3.85 (dd, *J* = 11.7, 3.0 Hz, 0.5H), 3.85-3.75 (m, 1H), 3.67-3.61 (dd, *J* = 11.6, 3.2 Hz, 0.5H), 3.59-3.53 (dd, *J* = 11.6, 5.6 Hz, 0.5H), 3.48-3.41 (m, 1H), 3.33-3.26 (dd, *J* = 11.7, 6.5 Hz, 0.5H), 3.13-3.07 (m, 1H), 2.73-2.69 (dd, *J* = 5.2, 4.1 Hz, 1H), 2.59-2.50 (m, 1H), 1.87-1.41 (m, 6H) ppm.

3.3.2 (2*R*)-1-(Tetrahydro-2H-pyran-2-yloxy)hept-6-en-2-ol ((*R*)-12):

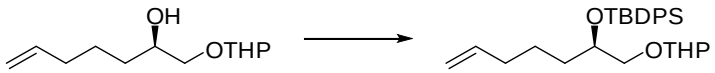


(*S*)-11 **(*R*)-12**

A multi-neck round bottom flask was flame-dried under vacuum and charged with argon. Magnesium (3.0 g, 123.9 mmol, 5.0 equiv) was placed into the round bottom flask and activated by heating the flask to 80 °C and stirring with a large stir-bar for 30 min. After cooling the flask with the activated magnesium to r.t., THF (36 mL) and a few iodine crystals were placed into the flask. A 100 mL dropping funnel was fitted to the multi-neck round bottom flask, and 4-bromobut-1-ene (10 g, 74.1 mmol, 3.0 equiv) and THF (36 mL) were placed into the dropping funnel. A few drops of the 4-bromobut-1-ene/THF solution were added to the Mg-containing

suspension and stirred gently until the brown iodine color disappeared and the mixture turned clear. Subsequently, the remaining 4-bromobut-1-ene/THF solution was added dropwise to the reaction mixture over a period of 1 h. Following the completion of addition, the mixture stirred for an additional 25 min. Then, the mixture was cooled to -40 °C, copper iodide (0.36 g, 1.9 mmol, 0.07 equiv) was added, and the resulting mixture was stirred for 20 min[6]. Subsequently, the reaction was warmed to -10 °C and stirred for another 10 min. The resulting purple-back mixture was cooled again to -40 °C and stirred for 25 min at this temperature. Next, a solution of **(*S*)-11** (4.05 g, 25.6 mmol) in THF (36 mL) was added dropwise over a period of 20 min. The mixture was gradually warmed to r.t and allowed to stir overnight. Subsequently, the reaction mixture was cooled to 0 °C, and pre-cooled (0 °C) saturated aqueous NH_4Cl solution (180 mL) was added, followed by stirring for 25 min. The resulting aquamarine-colored mixture was extracted with Et_2O (3 × 100 mL), and the combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:2) yielding **(*R*)-12** as a colorless oil (4.16 g, 19.4 mmol, 76% yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.81 (ddtd, *J* = 0.8, 6.7, 10.3, 17.1 Hz, 1H), 5.05-4.97 (m, 1H), 4.97-4.92 (m, 1H), 4.59-4.54 (m, 1H), 3.95-3.85 (m, 1H), 3.81-3.72 (m, 1.5H), 3.64 (dd, *J* = 2.55, 10.89 Hz, 0.5H) 3.57-3.47 (m, 1.5H), 3.37-3.31 (dd, *J* = 8.2, 10.8 Hz, 0.5H), 3.18 (d, *J* = 2.8 Hz, 0.5H), 2.64 (d, *J* = 4.0 Hz, 0.5H), 2.15-2.02 (m, 2H), 1.90-1.69 (m, 2H), 21.64-1.36 (m, 8H) ppm. ESI-MS *(m/z)*: [M+Na$^+$] calcd. for $C_{12}H_{22}O_3Na$: 237.15; found 237.1.

3.3.3 (2*R*)-(*t*-Butyldimethylsilyloxy)-1-(tetrahydro-2H-pyran-2-yloxy)hept-6-ene ((*R*)-9):

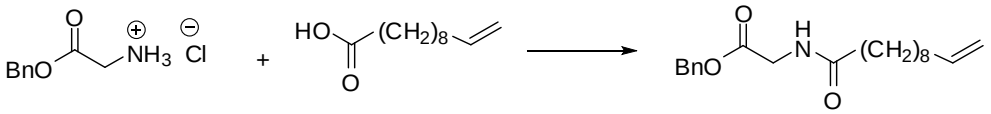


(*R*)-12 **(*R*)-9**

A round bottom flask was flame-dried under vacuum and charged with argon. Alcohol **(*R*)-12** (3.0 g, 14.0 mmol), imidazol (1.43 g, 21.0 mmol, 1.5 equiv) and dry DMF (20 mL) were added. The mixture was cooled to 0 °C and stirred for 10 min. To the cooled reaction flask, *tert*-butylchlorodiphenylsilane (TBDPSCl) (6.7 mL, 26.3 mmol, 1.9 equiv) was added. The reaction was warmed to r.t. and stirred overnight. The reaction was quenched with saturated aqueous NaCl solution (230 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:2) yielding **(*R*)-9** as a colorless oil (5.91 g, 13.1 mmol, 93%

yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.74-7.67 (m, 4H), 7.44-7.32 (m, 6H), 5.71 (ddt, *J*=6.6, 10.3, 17.1 Hz, 1H), 4.95-4.87 (m, 2H), 4.49-4.46 (m, 0.5H), 4.36-4.34 (m, 0.5H), 3.94-3.86 (m, 1H), 3.75-3.67 (m, 1H), 3.65-3.61 (m, 1H), 3.44-3.37 (m, 1H), 3.32-3.26 (m, 1H), 1.95-1.88 (m, 2H), 1.77-1.60 (m, 1H), 1.56-1.35 (m, 8H), 1.31-1.24 (m, 1H), 1.04 (d, *J* = 6.7 Hz, 9H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$):** δ 138.8, 114.3, 98.8, 72.2, 70.9, 61.8, 33.8, 33.7, 30.1, 27.0 (3C), 25.4, 24.0, 19.4, 19.2 ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{28}H_{40}O_3SiNa$: 475.26; found 475.4. $[\alpha]^{22}_D$ = +5.5 (*c* 0.01, chloroform).

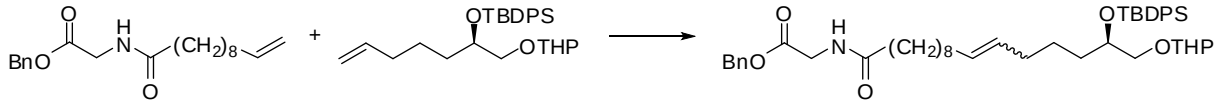
3.3.4 *N*-(Undec-10-enoyl)glycine benzyl ester (7):



13 **14** **7**

This compound was prepared as described by Xu et al.[1]

3.3.5 *N*-[15*R*-(*t*-Butyldiphenylsilyloxy)-16-(tetrahydro-2H-pyran-2-yloxy)hexadec-10-enoyl] glycine benzyl ester ((*R*)-5):

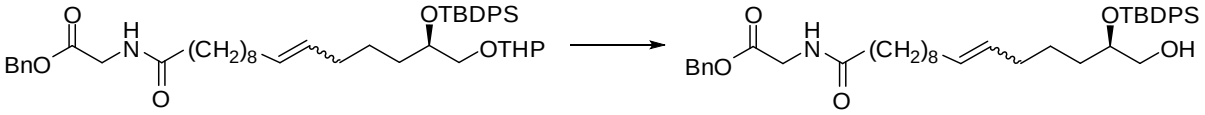


7 **(*R*)-9** **(*R*)-5**

A Schlenk flask was flame-dried under vacuum and charged with argon. To the flask, **(*R*)-9** (1.99 g, 4.4 mmol) and dry DCM (45 mL) were added. This mixture was stirred for 10 min, at which time benzyl 2-undec-10-enamidoacetate **7** (7.28 g, 22.0 mmol, 5.0 equiv) was added. This mixture was stirred for 10 min. Subsequently, Grubb's 1st Generation (G-I) catalyst (180 mg, 0.22 mmol, 0.05 equiv) was added to the mixture. The reaction flask was brought to 40 °C and the purple mixture was allowed to stir for 12 h during which time the reaction was monitored by TLC (EtOAc:toluene, 1:2) and ESI^+-MS. The reaction mixture was then filtered through silica. The resulting residue was concentrated *in vacuo* and was purified by silica gel flash chromatography (EtOAc:toluene, 1:4) yielding **(*R*)-5** as a colorless oil (950 mg, 1.25 mmol, 40% yield, 1:4 cis:trans ratio). 18% of unreacted **(*R*)-9** was recovered and could be used for subsequent reactions. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.73-7.67 (m, 4H), 7.43-7.32 (m, 9H), 7.27-7.23 (m, 1H), 7.19-7.14 (m, 1H), 5.96-5.88 (m, 1H), 5.34-5.22 (m, 2H), 5.19 (s, 2H), 4.49-

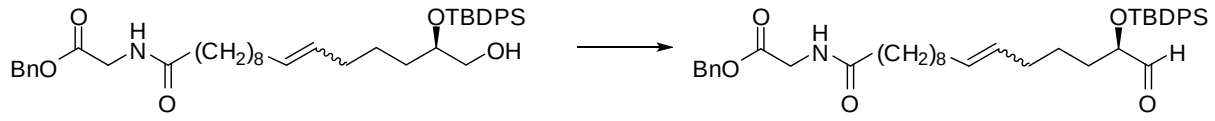
4.46 (m, 0.5H), 4.37-4.33 (m, 0.5H), 4.09 (d, *J* = 5.2 Hz, 2H), 3.94-3.84 (m, 1H), 3.75-3.67 (m, 1H), 3.65-3.59 (m, 1H), 3.44-3.36 (m, 1H), 3.31-3.25 (m, 1H), 2.25-2.20 (m, 2H), 1.98-1.80 (m, 4H), 1.75-1.19 (m, 22H), 1.07-1.03 (m, 9H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{46}H_{65}NO_6SiNa$: 778.45; found 778.4.

3.3.6 *N*-[15*R*-(*t*-Butyldiphenylsilyloxy)-16-hydroxyhexadec-10-enoyl]glycine benzyl ester ((*R*)-20):



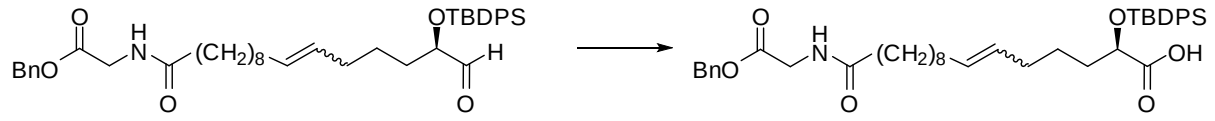
To a round bottom flask, **(*R*)-5** (390 mg, 0.52 mmol) and Et_2O (10 mL) were added. To this stirred mixture, anhydrous $MgBr_2$ (480 mg, 2.59 mmol, 5.0 equiv) was added and stirring was continued for 6 h. Subsequently, the reaction was cooled to 0 °C and quenched with $NaHCO_3$ (480 mg, 5.69 mmol, 11.0 equiv) in distilled H_2O (20 mL). Pentane (12 mL) were added to the reaction mixture and stirring was continued for 15 min. While stirring, large quantities of $Mg(OH)_2$ precipitated from the aqueous layer. The organic layer was decanted and the reaction flask washed with pentane (2 × 20 mL). The combined organic solutions were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:toluene, 1:2) yielding **(*R*)-20** as a colorless oil (210 mg, 0.32 mmol, 61% yield). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.69-7.62 (m, 5H), 7.46-7.29 (m, 10H), 6.00-5.92 (m, 1H), 5.33-5.18 (m, 2H), 5.19 (s, 2H), 4.09 (d, *J*=5.2 Hz, 2H), 3.80-3.73 (m, 1H), 3.56-3.43 (m, 2H), 2.26-2.19 (m, 2H), 1.96-1.74 (m, 4H), 1.69-1.57 (m, 2H), 1.56-1.37 (m, 2H), 1.35-1.12 (m, 12H), 1.07 (s, 9H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$):** δ 173.2, 170.0, 135.84, 135.75 (4C), 135.71, 135.1, 133.9, 133.8, 129.7 (2C), 128.7, 128.5 (2C), 128.4 (2C), 127.7, 127.6, 130.7, 129.6, 74.0, 67.2, 66.0, 41.3, 36.39, 36.40, 33.0, 32.5, 32.4, 29.4, 29.3-29.2 (2C), 29.2, 27.0 (3C), 25.5, 25.0, 19.3 ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{41}H_{57}NO_5SiNa$: 694.39; found 694.0.

3.3.7 *N*-[15*R*-(*t*-Butyldiphenylsilyloxy)-16-oxohexadec-10-enoyl]glycine benzyl ester ((*R*)-21):



A Schlenk flask was flame-dried under vacuum and charged with argon. **(*R*)-20** (240 mg, 0.36 mmol) and dry DCM (6.1 mL) were added under argon. This stirred mixture was cooled to 0 °C, *N*,*N*-diisopropylethylamine (150 µL, 1.07 mmol, 3.0 equiv) was added, and stirring was continued for 15 min. In a separate flame-dried and argon-charged Schlenk flask, a mixture of SO_3-pyridine complex (860 mg) and dry DMSO (10 mL) was prepared. Consequently, a portion of the SO_3-pyridine/DMSO mixture (2.2 mL, 1.18 mmol, 3.3 equiv) was added to the reaction flask at 0 °C. This reaction was allowed to stir for 1.5 h, at which time the reaction was quenched with saturated aqueous NaCl solution (10 mL) and extracted with DCM (2 × 10 mL) and then with EtOAc (2 × 10 mL). The combined organic extracts were dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (EtOAc:toluene, 1:3) yielding **(*R*)-21** as a colorless oil (200 mg, 0.29 mmol, 83% yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 9.58-9.55 (m, 1H), 7.66-7.61 (m, 5H), 7.46-7.32 (m, 10H), 5.99-5.91 (m, 1H), 5.37-5.22 (m, 2H), 5.19 (s, 2H), 4.09 (d, *J* = 5.2 Hz, 2H), 4.03 (td, *J* = 5.9, 1.6 Hz, 1H), 2.34-2.21 (m, 2H), 1.97-1.84 (m, 4H), 1.65-1.19 (m, 16H), 1.11 (s, 9H) ppm. ESI-MS *(m/z)*: [M+CH_3OH+Na^+] calcd. for $C_{42}H_{59}NO_6SiNa$: 724.40; found 724.1.

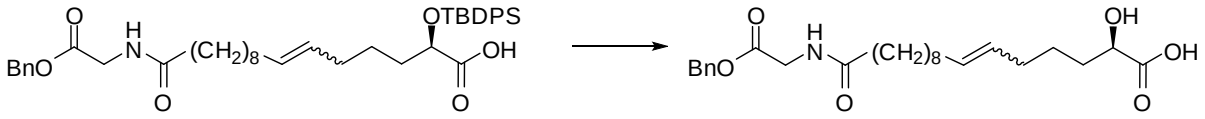
3.3.8 *N*-[15*R*-(t-Butyldiphenylsilyloxy)-15-carboxypentadec-10-enoyl]glycine benzyl ester ((*R*)-15):



In an Erlenmeyer flask, a buffer solution was prepared from NaH_2PO_4 (8.938 g) in distilled-H_2O (160 mL). To a round bottom flask, aldehyde **(*R*)-21** (680 mg, 1.0 mmol), *t*-butanol (37.0 mL), and a freshly distilled 2-methylbut-2-ene (18.0 mL) were added, and the reaction flask was brought to 0 °C. To this mixture, a portion of the prepared buffer solution (34.0 mL) was added in one portion. In a separate flask, a fresh oxidant solution was prepared by mixing $NaClO_2$ (2.0

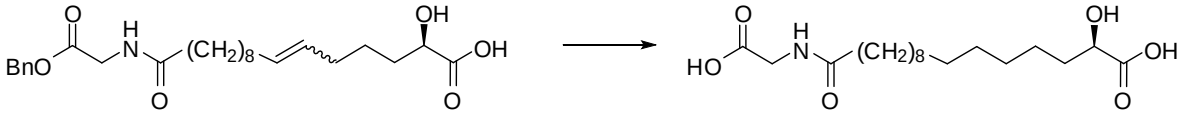
g) and buffer solution (34.0 mL). Immediately after preparation, the oxidant solution was added via Pasteur pipette to the reaction mixture stirred at 0 °C. The reaction was stirred for 10 min at 0 °C, followed by stirring for 3 h at r.t. The reaction was quenched by addition of dimethyl sulfide (DMS) (5.5 mL) and the remaining buffer solution and then brought to pH = 4 using citric acid solution (citric acid:H_2O, 1:10, *{w:v}*). The resulting mixture was extracted with EtOAc (3 × 100 mL), and the combined organic extracts were dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (EtOAc:toluene, 1:3) yielding **(*R*)-15** as a colorless oil (660 mg, 96% yield). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.68-7.59 (m, 5H), 7.49-7.32 (m, 10H), 6.11-6.04 (m, 1H), 5.35-5.19 (m, 2H), 5.19 (s, 2H), 4.34-4.29 (m, 1H), 4.14-4.04 (m, 2H), 2.27-2.20 (m, 2H), 1.97-1.81 (m, 4H), 1.72-1.41 (m, 6H), 1.34-1.19 (m, 10H), 1.12 (s, 9H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{41}H_{55}NO_6SiNa$: 708.37; found 708.1.

3.3.9 *N*-(15-Carboxy-15*R*-hydroxypentadec-10-enoyl)glycine benzyl ester ((*R*)-22):



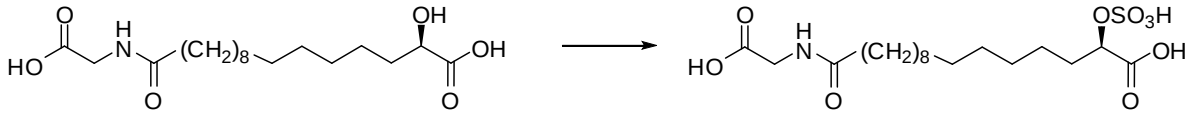
To a stirred solution of **(*R*)-15** (230 mg, 0.42 mmol) in acetonitrile (5 mL) at 0 °C was added 40% HF (2 drops). The reaction was allowed to warm to r.t. and stirred for 18 h. Subsequently, the reaction was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ solution (20 drops). The resulting mixture was concentrated *in vacuo* and was purified by C18 reverse-phase flash chromatography, using a water/acetonitrile gradient as solvents to yield **(*R*)-22** (170 mg, 0.37 mmol, 90% yield).**^{1}H NMR (500 MHz, CD_3OD):** δ 7.39-7.29 (m, 5H), 5.46-5.31 (m, 2H), 5.17 (s, 2H), 4.09-4.00 (m, 1H), 3.96 (s, 2H), 2.27-2.21 (m, 2H), 2.11-1.94 (m, 4H), 1.82-1.70 (m, 1H), 1.67-1.55 (m, 3H), 1.53-1.43 (m, 2H), 1.38-1.23 (m, 10H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{25}H_{37}NNO_6Na$: 470.25; found 470.5.

3.3.10 *N*-(15-Carboxy-15*R*-hydroxypentadecanoyl)glycine ((*R*)-23):



A Schlenk flask was flame-dried under vacuum and charged with argon. To the Schlenk flask, 10 wt % Pd/C (17 mg) and EtOH (4 mL) were added. The reaction flask was flushed briefly with argon and subsequently with H_2 gas for 5 min. The H_2 flow was reduced and acid **(*R*)-22** (19 mg, 0.04 mmol) was added to the Pd/C/EtOH mixture. The reaction was stirred for 10 h under H_2. Subsequently, the mixture was filtered through silica, using methanol to (50 ml) for elution. The combined filtrates were concentrated *in vacuo* and purified by C-18 reverse-phase flash chromatography, using a water/acetonitrile solvent gradient, to yield **(*R*)-23** (13 mg, 0.36 mmol, 85% yield). **^{1}H NMR (500 MHz, CD_3OD):** δ 4.09-4.04 (m, 1H), 3.86 (s, 2H), 2.28-2.21 (m, 2H), 1.80-1.70 (m, 1H), 1.68-1.57 (m, 3H), 1.48-1.21 (m, 20H) ppm. **^{13}C NMR (151 MHz, CD_3OD):** δ 178.3, 176.3, 173.5, 71.4, 41.9, 36.5, 35.2, 30.4-30.3 (6C), 30.3, 30.1, 26.0, 26.5, 25.8 ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{18}H_{33}NO_6Na$: 382.22; found 382.3. $[\alpha]^{22}_D$ = +5.5 (*c* 0.002, methanol).

3.3.11 *N*-(15-carboxy-15*R*-sulfooxypentadecanoyl) glycine ((*R*)-1):

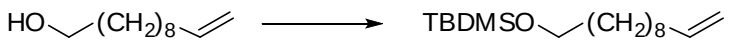


A Schlenk flask was flame-dried under vacuum and charged with argon. The acid **(*R*)-23** (32 mg, 0.09 mmol) and dry DMF (6.6 mL) were added to the flask. In a separate Schlenk flask, a solution of SO_3DMF complex (320 mg) in dry DMF (3 mL) was prepared. A portion of the SO_3DMF solution (0.8 mL, 0.54 mmol, 6.0 equiv) was added to the alcohol/DMF mixture at 0 °C. The reaction was stirred for 30 min at 0 °C and then for 20 min at r.t. Subsequently, the reaction flask was cooled again to 0 °C and quenched with a solution of $KHCO_3$ (110 mg, 1.1 mmol, 12.0 equiv) in distilled H_2O (3 mL), resulting in a yellow mixture with pH = 4. This mixture was concentrated under reduced pressure, and the residue purified by silica gel flash chromatography (solvents: DCM with 1% AcOH and acetonitrile containing 1% AcOH and 5% distilled H_2O in a ratio of 2:1) to yield **(*R*)-1** as a white solid (28 mg, 0.06 mmol, 71% yield). **^{1}H**

NMR (500 MHz, D_2O): δ 4.52-4.47 (m, 1H), 3.70 (s, 2H), 2.27-2.22 (m, 2H), 1.79-1.65 (m, 2H), 1.60-1.49 (m, 2H), 1.40-1.00 (m, 20H) ppm. **^{13}C NMR (151 MHz and 126 MHz, D_2O):** δ 178.0, 176.9, 176.5, 77.9, 41.7, 35.4, 31.9, 28.6-28.2 (8C), 27.9, 25.1, 23.9 ppm. ESI-MS *(m/z)*: [M-H] calcd. for $C_{18}H_{32}NO_9S$: 358.22; found 358.4. $[\alpha]^{22}_D$ = +15.6 (*c* 0.002, methanol).

3.4 Synthesis of (*R*)-3, (*R*)-4, and (*S*)-4

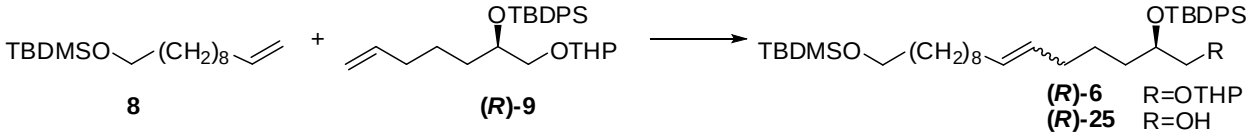
3.4.1 *O*-(*t*-Butyldimethylsilyl)undec-10-enol (8):



24 **8**

To a stirred solution of alcohol **24** (5.0 g, 29.4 mmol) and imidazol (3.0 g, 44.0 mmol, 1.5 equiv) in dry DMF (20 mL) at 0 °C was added *tert*-butylchlorodimethylsilane (TBDMSCl) (7.08 g, 47.0 mmol, 1.6 equiv), and the mixture was stirred overnight at r.t. The reaction was quenched with saturated aqueous NaCl solution (60 mL) and extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:2) yielding **8** as a colorless oil (7.64 g, 26.9 mmol, 92% yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 5.81 (ddt, *J* = 17.1, 10.2, 6.7 Hz, 1H), 5.01-4.97 (m, 1H), 4.94-4.91 (m, 1H), 3.595 (t, *J* = 6.7 Hz, 2H), 2.07-2.01 (m, 2H), 1.54-1.47 (m, 2H), 1.40-1.34 (m, 2H), 1.33-1.24 (m, 10H), 0.89 (s, 9H), 0.05 (s, 6H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$):** δ 139.2, 114.2, 63.3, 33.8, 32.8, 29.5-29.4 (2C), 29.4, 29.2, 28.9, 26.0 (3C), 25.8, 18.4, -5.3 (2C) ppm.

3.4.2 16-(*t*-Butyldimethylsilyloxy)-2*R*-(*t*-butyldiphenylsilyloxy)hexadec-6-enol ((*R*)-25):

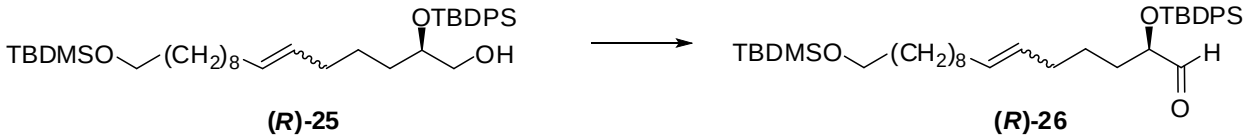


A Schlenk flask was flame-dried under vacuum and charged with argon. To this flask, a solution of **(*R*)-9** (0.76 g, 1.68 mmol) in dry DCM (18 mL), a solution of benzoquinone (36 mg, 0.34 mmol, 0.2 equiv) in dry DCM (1.5 mL), and a solution of **8** (2.38 g, 8.39 mmol, 5.0 equiv) in DCM (2 ml) was added. All solutions were prepared under argon. The resulting mixture was stirred for 10 min and Grubb's 1st Generation (G-I) catalyst (138 mg, 0.17 mmol, 0.1 equiv) was added. Following the addition of the catalyst, the reaction was brought to 40 °C and the purple mixture was stirred for 20 h. The reaction was monitored by TLC (EtOAc:hexanes, 1:9) and ESI$^+$-MS. Subsequently, the reaction mixture was cooled to r.t. and filtered over a small pad of silica. The filtrate was concentrated *in vacuo* and partially purified by silica gel flash chromatography (EtOAc:hexanes, 1:9), yielding a mixture (1.39 g) of desired (*R*)-**6,** starting material (*R*)-**9,** starting material 8, and homodimer of **8.** The ratio of the THP group protons for (*R*)-**6** and (*R*)-**9** was 1.8:1 as determined by NMR-spectroscopic analysis, corresponding to 65% yield of **(*R*)-6**. This mixture was not purified further at this stage and instead directly subjected to THP-deprotection using $MgBr_2$.

For this purpose, the crude mixture (1.39 g, 1.96 mmol) was dissolved in Et_2O (24 mL) and anhydrous $MgBr_2$ (1.85 g, 10.1 mmol, 5.1 equiv) was added with stirring. After stirring overnight, the reaction was cooled to 0 °C and quenched by addition of a solution of $NaHCO_3$ (1.69 g, 20.1 mmol, 10.2 equiv) in distilled H_2O (34 mL). Cold pentane (24 mL) were added and the mixture was stirred for 15 min, during which time a voluminous white precipitate of $Mg(OH)_2$ formed. Subsequently, the organic layer was decanted and the reaction flask rinsed with pentane (2 × 30 mL). The combined organic solutions were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:9) yielding **(*R*)-25** as a colorless oil (476 mg, 0.73 mmol, 45% yield over two steps). 130 mg (0.35 mmol, 20%) of THP-deprotected **9** was recovered from the deprotection, giving **(*R*)-25** in 55% yield over two steps based on consumed **9**. **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.70-7.65 (m, 4H), 7.46-741. (m, 2H), 7.40-7.34 (m, 4H), 5.33-5.15 (m, 2H), 3.80-3.75 (m, 1H), 3.593 (t, *J* = 6.7 Hz, 2H), 3.56-3.44 (m, 2H), 1.94-1.88 (m, 2H), 1.86-1.76 (m, 2H), 1.54-1.39 (m,

4H), 1.33-1.17 (m, 14H), 1.07 (s, 9H), 0.89 (s, 9H), 0.05 (s, 6H) ppm. **^{13}C NMR (151 MHz, $CDCl_3$):** δ 135.8 (4C), 133.9 (2C), 130.8, 129.7 (2C), 129.6, 127.7 (4C), 74.0, 66.0, 63.3, 33.0, 32.9, 32.6, 32.4, 29.6-29.5 (2C), 29.53, 29.45, 27.10, 27.05 (3C), 26.0 (3C), 25.8, 25.2, 19.5, 18.4, -5.3 (2C) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{38}H_{64}O_3Si_2Na$: 647.43; found 647.2.

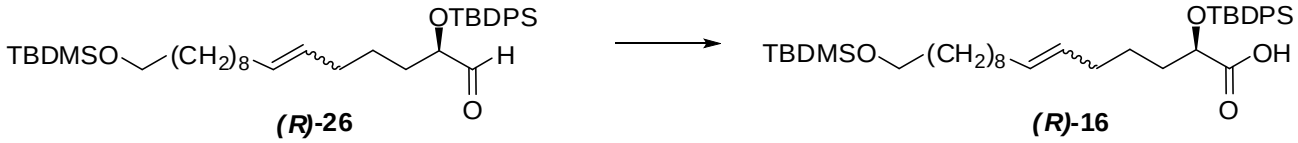
3.4.3 16-(*t*-Butyldimethylsilyloxy)-2*R*-(*t*-butyldiphenylsilyloxy)hexadec-6-enal ((*R*)-26):



(*R*)-25 **(*R*)-26**

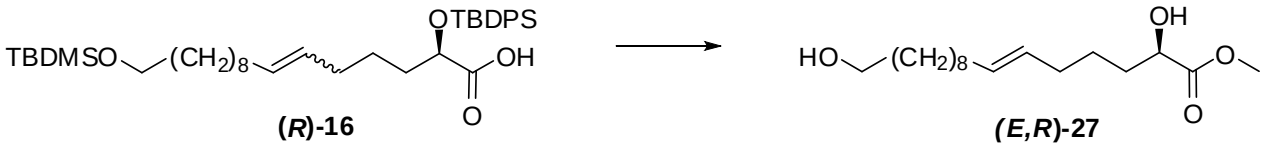
A Schlenk flask was flame-dried under vacuum and charged with argon. Alcohol **(*R*)-25** (0.8 g, 1.28 mmol) and dry DCM (15 mL) were placed into the flask under argon. The stirred reaction mixture was cooled to 0 °C, at which time *N*,*N*-diisopropylethylamine (0.6 mL, 4.1 mmol, 3.2 equiv) was added. The mixture was stirred for 15 min. In a separate flame-dried and argon-charged Schlenk flask, a mixture of SO_3-pyridine complex (1.42 g, 8.9 mmol) and dry DMSO (8.8 mL) was prepared under argon atmosphere. Subsequently, a portion of the SO_3-pyridine/DMSO mixture (4 mL, 4.09 mmol, 3.2 equiv) was added dropwise to the reaction flask at 0 °C. This mixture was stirred for another 1.5 h, at which time the reaction was quenched with saturated aqueous NaCl solution (20 mL), followed by extraction with DCM (2 × 10 mL) and EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, concentrated *in vacuo*, and the residue was purified by silica gel flash chromatography (EtOAc:hexanes, 1:9) yielding **(*R*)-26** as a colorless oil (746 mg, 1.2 mmol, 93% yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 9.58-9.55 (m, 1H), 7.66-7.61 (m, 4H), 7.46-7.41 (m, 2H), 7.40-7.35 (m, 4H), 5.37-5.21 (m, 2H), 4.02 (dt, *J* = 1.6, 5.8 Hz, 1H), 3.60 (t, *J* = 6.7 Hz, 2H), 1.96-1.86 (m, 4H), 1.68-1.55 (m, 3H), 1.53-1.48 (m, 2H), 1.48-1.40 (m, 1H), 1.39-1.23 (m, 12H), 1.11 (s, 9H), 0.89 (s, 9H), 0.05 (s, 6H) ppm. ESI-MS *(m/z)*: [M+CH_3OH+Na^+] calcd. for $C_{39}H_{66}O_4Si_2Na$: 677.44; found 677.1.

3.4.4 16-(*t*-Butyldimethylsilyloxy)-2*R*-(*t*-butyldiphenylsilyloxy)hexadec-6-enoic acid ((*R*)-16):



A buffer solution was prepared from NaH_2PO_4 (8.17 g) and distilled H_2O (150 mL). A stirred mixture of aldehyde **(*R*)-26** (547 mg, 0.88 mmol), *t*-BuOH (33.5 mL), and freshly distilled solution of 2-methylbut-2-ene (16.7 mL) was cooled to 0 °C, and 30 mL of the prepared buffer solution was added. Separately, a fresh oxidant solution was prepared by dissolving $NaClO_2$ (1.79 g) in buffer solution (34 mL). Immediately following preparation, the oxidant solution was added drop-wise to the reaction mixture. The reaction was allowed to stir for 10 min at 0 °C and then for 3 h at r.t. The reaction was quenched by addition of DMS (3 mL) and the remaining buffer solution. The reaction mixture was then brought to pH = 4 using a citric acid solution (citric acid:H_2O, 1:10, *{w:v}*). The resulting mixture was extracted with EtOAc (3 × 50 mL) and the combined organic extracts were dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (EtOAc:hexanes, 1:9) yielding **(*R*)-16** as a colorless oil (490 mg, 0.77 mmol, 88% yield). **^{1}H NMR (600 MHz, $CDCl_3$):** δ 7.67-7.58 (m, 4H), 7.49-7.36 (m, 6H), 5.45-5.15 (m, 2H), 4.35-4.29 (m, 1H), 3.60 (t, *J* = 6.7 Hz, 2H), 1.99-1.77 (m, 4H), 1.71-1.41 (m, 6H), 1.35-1.19 (m, 12H), 1.12 (s, 9H), 0.89 (s, 9H), 0.05 (s, 6H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{38}H_{62}O_4Si_2Na$: 661.41; found 661.3.

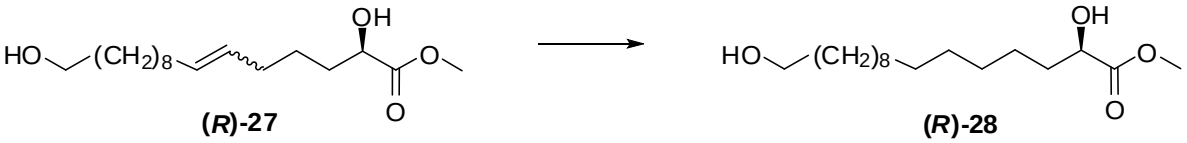
3.4.5 16-(*t*-Butyldimethylsilyloxy)-2*R*-(*t*-butyldiphenylsilyloxy)hexadec-6-enoic acid ((*R*)-16):



Acid **(*R*)-16** (556 mg, 0.87 mmol) was dissolved in acetonitrile (10 mL) at 0 °C and 40% HF (28 drops, 0.2 mL) was added with stirring. The reaction was allowed to warm to r.t. and stirred for 40 h. Subsequently, the reaction was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ solution (5 mL). The resulting mixture was extracted with ether (3 x 20 ml) and the combined ether extracts were concentrated *in vacuo*, filtered over a pad of silica (ethylacetate/hexanes) and used for the next step without further purification. The deprotected

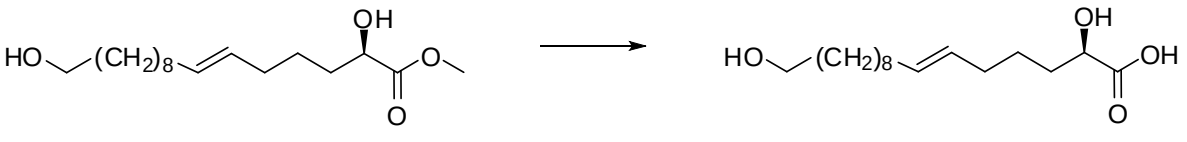
acid was methylated as follows: the acid was dissolved in a mixture of 3:2 toluene:MeOH, and trimethylsilyldiazomethane (2 M in ether, 0.65 mL, 1.31 mmol, 1.5 equiv) was added until a yellow color persisted. The reaction mixture was concentrated *in vacuo* and purified by silica gel flash chromatography (MeOH:DCM, 1:10) to yield **(*R*)-27** (193 mg, 0.67 mmol, 77% yield over two steps). An $AgNO_3$ impregnated on silica column[2] was used to obtain (**2*R*,6*E*)-27** with >95% 6*E* configuration. **^{1}H NMR (600 MHz, CD_3OD):** δ 5.44-5.33 (m, 2H), 4.17-4.13 (m, 1H), 3.79 (s, 3H), 3.66-3.61 (m, 2H), 2.702 (d, *J* = 5.8 Hz, 1H), 2.04-1.94 (m, 4H), 1.82-1.75 (m, 1H), 1.67-1.59 (m, 1H), 1.54-1.39 (m, 2H), 1.38-1.22 (m, 14H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{17}H_{32}O_4Na$: 323.22; found 323.3.

3.4.6 16-(*t*-Butyldimethylsilyloxy)-2*R*-(*t*-butyldiphenylsilyloxy)hexadec-6-enoic acid ((*R*)-16):



A Schlenk flask was flame-dried under vacuum and charged with argon, and Pd/C (34mg) and EtOH (15 mL) were added. The reaction flask was briefly flushed with argon and subsequently flushed with H_2 gas for 15 min. The H_2 flow was reduced and **(*R*)-27** (38 mg, 0.13 mmol, mixture of cis/trans), dissolved in ethanol (5 mL) was added. The reaction was allowed to stirred for 30 h under H_2. Subsequently, the mixture was filtered through a pad of silica with EtOH (50 mL). The resulting mixture was concentrated *in vacuo* to yield **(*R*)-28** (35 mg, 0.12 mmol, 91% yield). **^{1}H NMR (600 MHz, CD_3OD):** δ 4.13 (dd, *J* = 4.5, 7.9 Hz, 1H), 3.72 (s, 3H), 3.54 (t, *J* = 6.7 Hz, 2H), 1.77-1.69 (m, 1H), 1.68-1.58 (m, 1H), 1.56-1.49 (m, 2H), 1.45-1.24 (m, 22H) ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{17}H_{34}O_4Na$: 325.24; found 325.1.

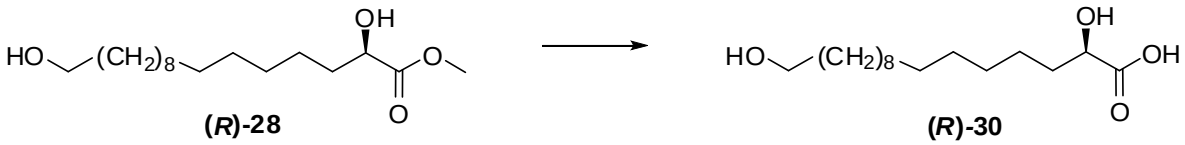
3.4.7 2*R*,16-Dihydroxyhexadec-(6*E*)-enoic acid ((*R*)-29):



To a stirred solution of **((2*R*,6*E*)-27)** (24 mg, 0.08 mmol) in a mixture of THF:MeOH:H_2O (2:2:1, *{v:v:v}*, 3 mL) LiOH (48 mg, 2.0 mmol, 25 equiv) was added at r.t. After stirring for 5 h, the

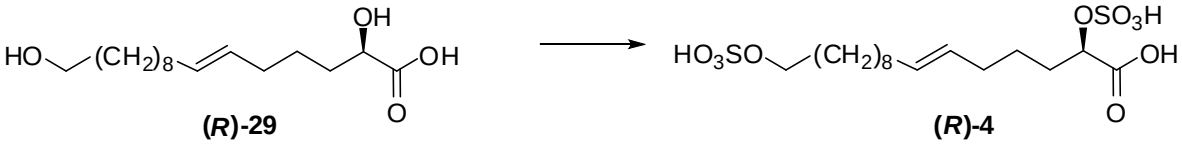
reaction was acidified to pH = 1 using 0.25 M aqueous HCl and extracted with EtOAc (3 × 6 mL). The combined organic extracts were washed with 0.25 M aqueous HCl (6 mL) and brine (6 mL), dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (MeOH:DCM with 0.2% AcOH, 1:9) to yield **(*R*)-29** as a white solid (20 mg, 0.07 mmol, 87% yield). **^{1}H NMR (600 MHz, CD_3OD):** δ 5.46-5.33 (m, 2H), 4.10 (dd, *J* = 4.3,7.8 Hz, 1H), 3.54 (t, *J* = 6.7 Hz, 2H), 2.11-1.95 (m, 4H), 1.83-1.72 (m, 1H), 1.68-1.59 (m, 1H), 1.56-1.44 (m, 4H), 1.39-1.28 (m, 12H) ppm. **^{13}C NMR (151 MHz, CD_3OD):** δ 177.7, 131.8, 130.6, 71.1, 62.7, 34.6, 33.4, 33.1, 30.4, 30.4-30.2 (5C), 26.7, 25.9 ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{16}H_{30}O_4Na$: 309.20; found 309.2. $[\alpha]^{22}_D$ = -0.4 (*c* 0.02, methanol).

3.4.8 2*R*,16-Dihydroxyhexadecanoic acid ((*R*)-30):



To stirred solution of **(*R*)-28** (35 mg, 0.116 mmol) in a mixture of THF:MeOH:H_2O 2:2:1 *{v:v:v}* (4.5 mL) LiOH (71 mg, 2.96 mmol, 25.5 equiv) was added at r.t. After stirring for 5 h, the reaction was acidified to pH = 1 using 0.25 M aqueous HCl and extracted with EtOAc (3×10 mL). The combined organic extracts were washed with 0.25M HCl (10 mL) and brine (10 mL), dried over Na_2SO_4, concentrated *in vacuo*, and purified by silica gel flash chromatography (MeOH:DCM with 0.2% AcOH, 1:9) to yield **(*R*)-30** as a white solid (29 mg, 0.10 mmol, 87% yield). **^{1}H NMR (600 MHz, CD_3OD):** δ 4.09 (dd, *J* = 4.4, 7.8 Hz, 1H), 3.54 (t, *J* = 6.7 Hz, 2H), 1.80-1.72 (m, 1H), 1.68-1.59 (m, 1H), 1.57-1.49 (m, 2H), 1.48-1.16 (m, 22H) ppm. **^{13}C NMR (151 MHz, CD_3OD):** δ 177.8, 71.2, 62.73, 35.2, 35.1, 33.4, 30.4-30.2 (5C), 30.31, 30.25, 30.20, 26.7, 25.9 ppm. ESI-MS *(m/z)*: [M+Na^+] calcd. for $C_{16}H_{32}O_4Na$: 311.22; found 311.2. $[\alpha]^{22}_D$ = -1.2 (*c* 0.01, methanol).

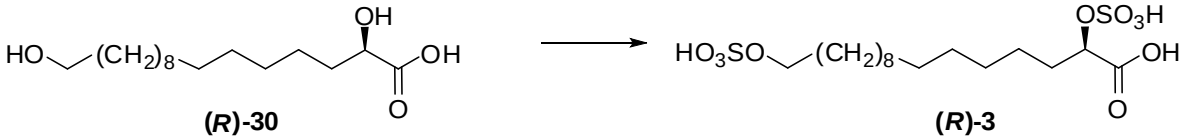
3.4.9 2*R*,16-Disulfooxyhexadec-(6*E*)-enoic acid ((*R*)-4):



A Schlenk flask was flame-dried under vacuum and charged with argon. The acid **(*R*)-29** (20 mg, 0.07 mmol) and dry DMF (3 mL) were added to the flask. In a separate Schlenk flask, a solution of SO_3DMF complex (290 mg) in dry DMF (2 mL) was prepared. A portion of the SO_3DMF solution (0.75 mL, 0.7 mmol, 10.0 equiv) was added to the alcohol/DMF mixture at 0 °C and the resulting mixture was stirred for 30 min. The reaction was then allowed to warm to r.t. and stirred for an additional 20 min. Subsequently, the reaction flask was brought back to 0 °C and quenched by addition of a solution of $KHCO_3$ (142 mg, 1.42 mmol, 20.3 equiv) in distilled H_2O (1 mL). The resulting yellow mixture was checked to be at pH = 6, concentrated *in vacuo*, and purified by silica gel flash chromatography (DCM with 1% AcOH:MeOH, 1:1) to yield **(*R*)-4** as a white solid (17 mg, 0.04 mmol, 54% yield). **^{1}H NMR (600 MHz, CD_3OD):** δ 5.45-5.34 (m, 2H), 4.69-4.58 (m, 1H), 3.99 (t, *J* = 6.6 Hz, 2H), 2.19-1.94 (m, 4H), 1.91-1.82 (m, 1H), 1.82-1.73 (m, 1H), 1.69-1.62 (m, 2H), 1.57-1.49 (m, 2H), 1.44-1.37 (m, 2H), 1.37-1.26 (m, 10H) ppm. **^{13}C NMR (151 MHz, CD_3OD):** δ 182.2, 131.3, 130.8, 80.4, 68.8, 33.6, 33.4, 33.1, 30.2, 30.4-30.1 (5C), 26.6, 26.1 ppm. ESI-MS *(m/z)*: [(M-2H)/2] calcd. for $(C_{16}H_{28}O_{10}S_2)/2$: 222.06; found 222.9. $[\alpha]^{22}_D$ = +3.2 (*c* 0.004, water).

(*S*)-4 was prepared in the same manner as **(*R*)-4** starting with (*R*)-(+)-glycidol.
$[\alpha]^{22}_D$ = -1.2 (*c* 0.005, water)

3.4.10 2*R*,16-Disulfooxyhexadecanoic acid ((*R*)-3):

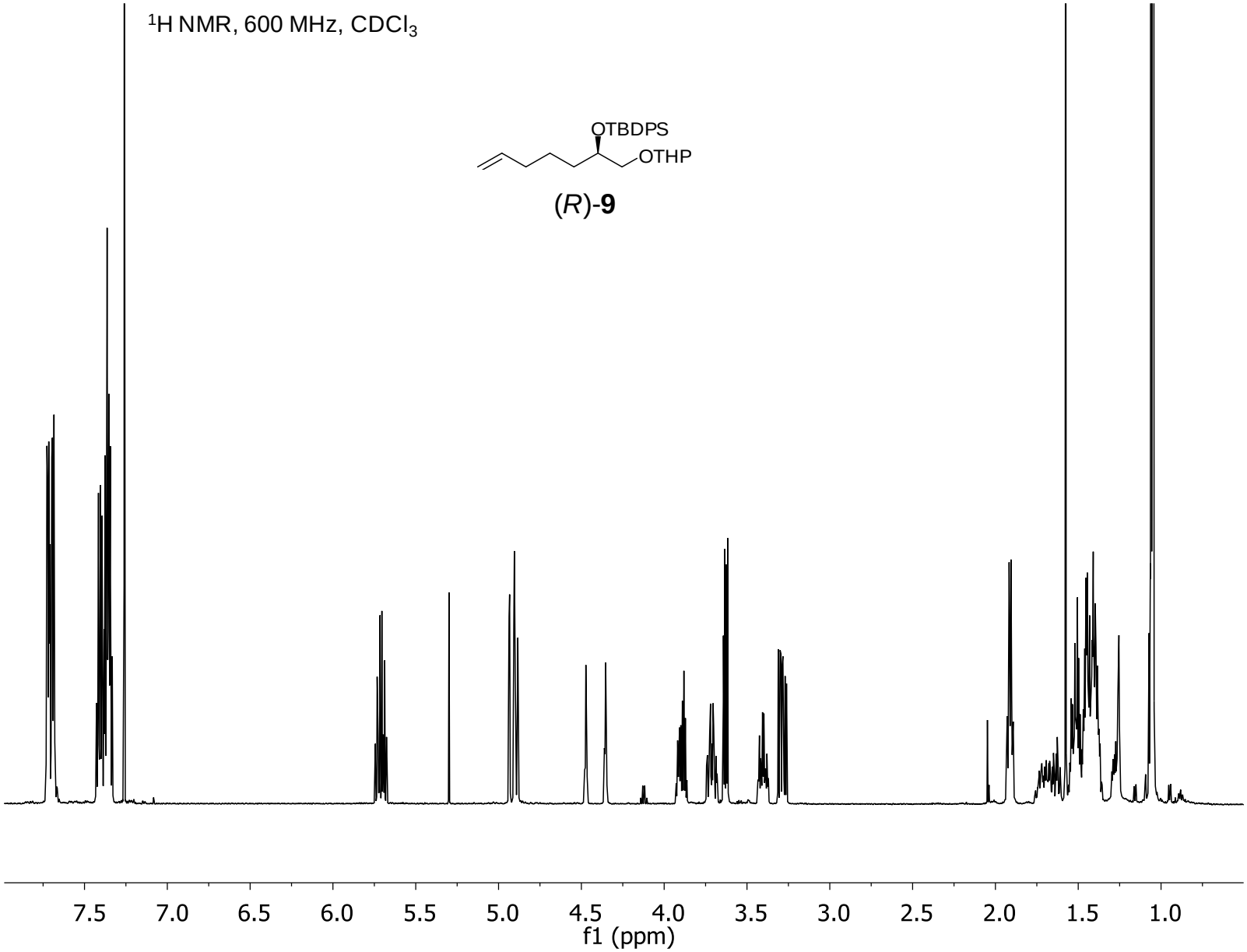


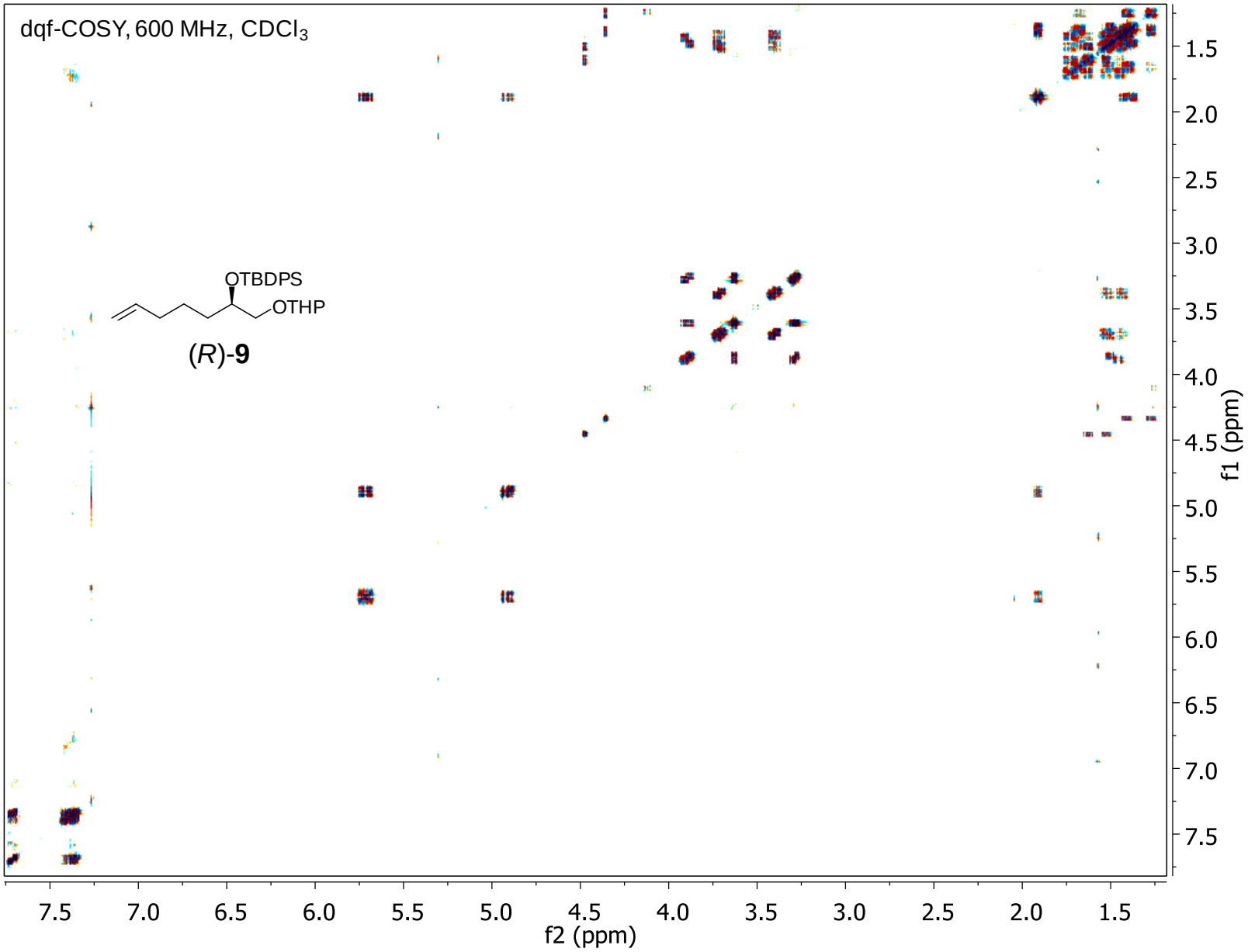
A Schlenk flask was flame-dried under vacuum and charged with argon. The acid **(*R*)-30** (16 mg, 0.06 mmol) and dry DMF (3 mL) were added to the flask. In a separate Schlenk flask, a solution of SO_3DMF complex (300 mg) in dry DMF (2 mL) was prepared. A portion of the SO_3DMF solution (0.6 mL, 0.59 mmol, 10.6 equiv) was added to the alcohol/DMF mixture at 0 °C and the resulting mixture was stirred for 30 min. The reaction was allowed to warm to r.t. and stirred for an additional 20 min. Subsequently, the reaction flask was brought back to 0 °C and quenched by addition of a solution of $KHCO_3$ (112 mg, 1.12 mmol, 20.0 equiv) in distilled H_2O (0.56 mL). The resulting yellow mixture was checked to be at pH = 6, concentrated *in vacuo*, and purified by silica gel flash chromatography (DCM with 1% AcOH : MeOH, 1:1) to yield **(*R*)-3** as a white solid (17 mg, 0.04 mmol, 68% yield). **^{1}H NMR (600 MHz, CD_3OD):** δ 4.66-4.58 (m, 1H), 3.99 (t, *J* = 6.6 Hz, 2H), 1.89-1.81 (m, 1H), 1.81-1.73 (m, 1H), 1.69-1.62 (m, 2H), 1.51-1.26 (m, 22H) ppm. **^{13}C NMR (151 MHz, CD_3OD):** δ 182.2, 80.2, 68.8, 33.9, 30.6-30.2 (7C), 30.3, 30.2, 30.1, 26.6, 26.0 ppm. ESI-MS *(m/z)*: [(M-2H)/2] calcd. for ($C_{16}H_{30}O_{10}S_2$)/2: 223.07; found 223.1. [(M-3H+Na^+)/2] calcd. for ($C_{16}H_{29}NaO_{10}S_2$)/2: 234.06; found 234.0. $[\alpha]^{22}_D$ = +1.9 (*c* 0.008, water)

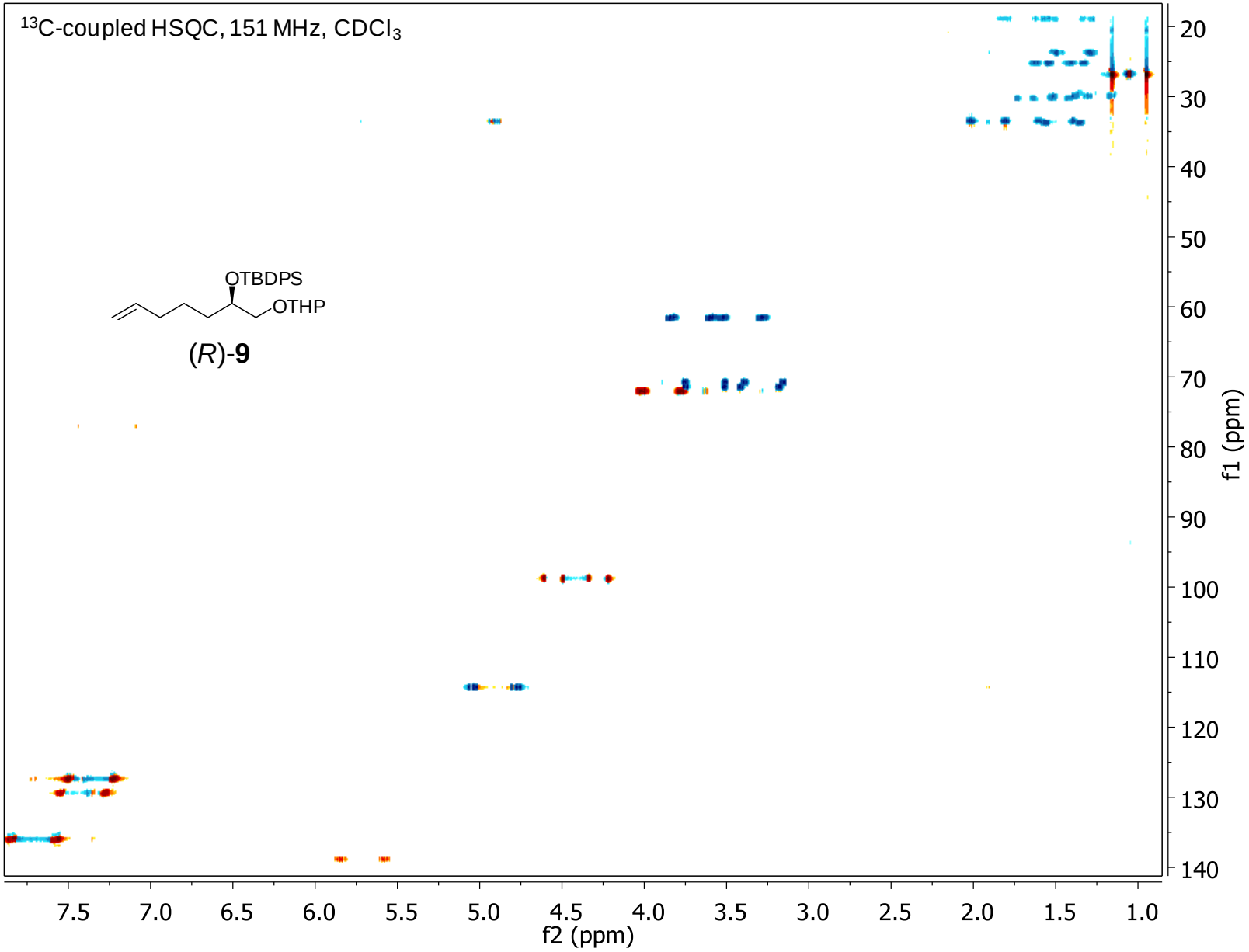
3.5 Bioassays with synthetic caeliferins in Arabidopsis[7]

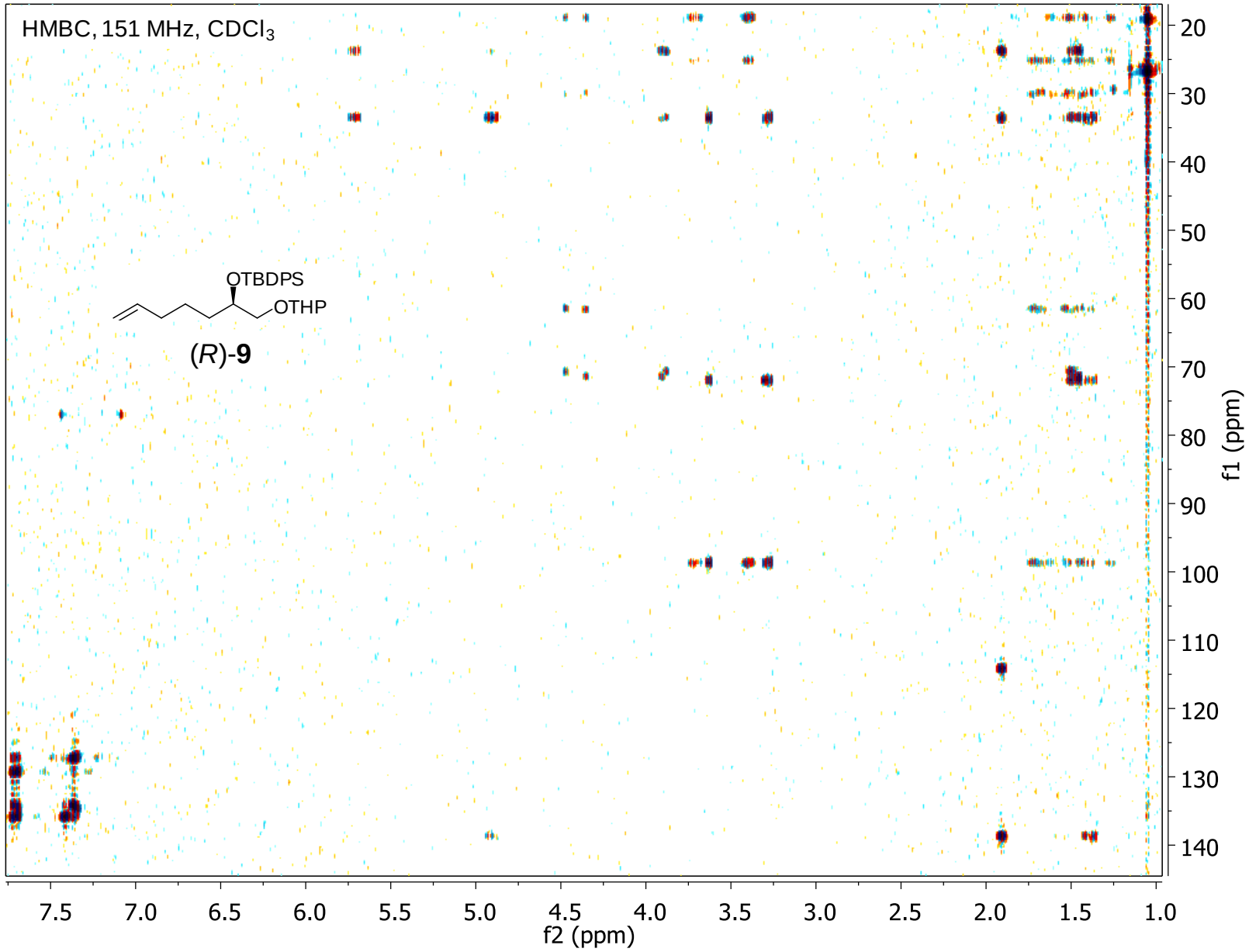
Arabidopsis thaliana Columbia (Col-O) were germinated in MetroMix® 200 (Sun Gro Horticulture Distribution, Inc) supplemented with 14-14-14 Osmocote (Scotts Miracle-Gro) . Plants were maintained in a walk-in growth chamber with a 12-h photoperiod, approximately 130 $\mu mol^{-2}\ s^{-1}$ of photosynthetically active radiation supplied by supplemental lighting, 65% relative humidity, and constant temperature of 21°C. One month old plants were treated with caeliferins at concentration of 22 nmol μl^{-1}. The adaxial sides of the 3 largest fully expanded leaves were scratched with a razor removing 5-10% of the waxy cuticle. The damage sites included the central leaf tip spanning both sides of the midrib and two midbasal sections on opposite sides of the midrib. Test solutions of 5 µl $plant^{-1}$ or 50 mM Na_2HPO_4 buffer (pH 8) alone were immediately applied and dispersed over the damage sites. Leaves remained on the intact plants for 1 h before shoot excision, sampling and GC analyses. Excised shoots were sealed in 6 mL tubes for an additional 1 hr before headspace sampling as described[7]. All experiments were carried out in four independent replicates for each synthetic sample.

4. NMR Spectra

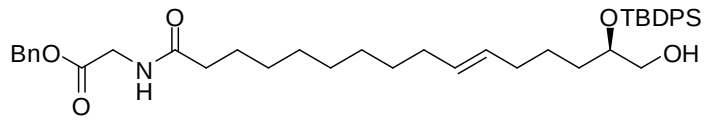

^{1}H NMR, 600 MHz, $CDCl_3$
OTBDPS
OTHP
(*R*)-**9**
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


dqf-COSY, 600 MHz, CDCl3
OTBDPS
OTHP
(R)-9
f2 (ppm)
f1 (ppm)

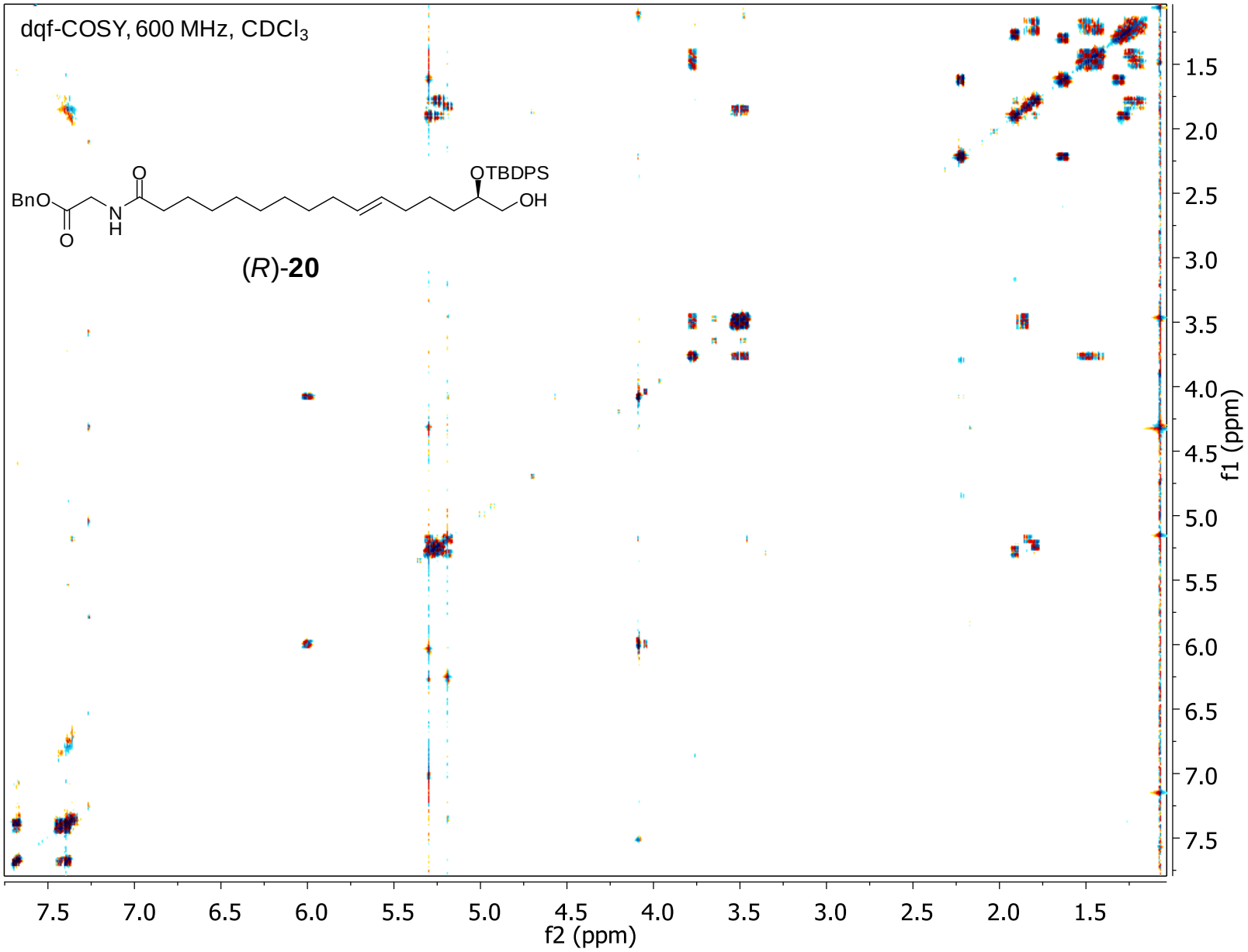

^{13}C-coupled HSQC, 151 MHz, $CDCl_3$
OTBDPS
OTHP
(*R*)-**9**
f1 (ppm)
f2 (ppm)

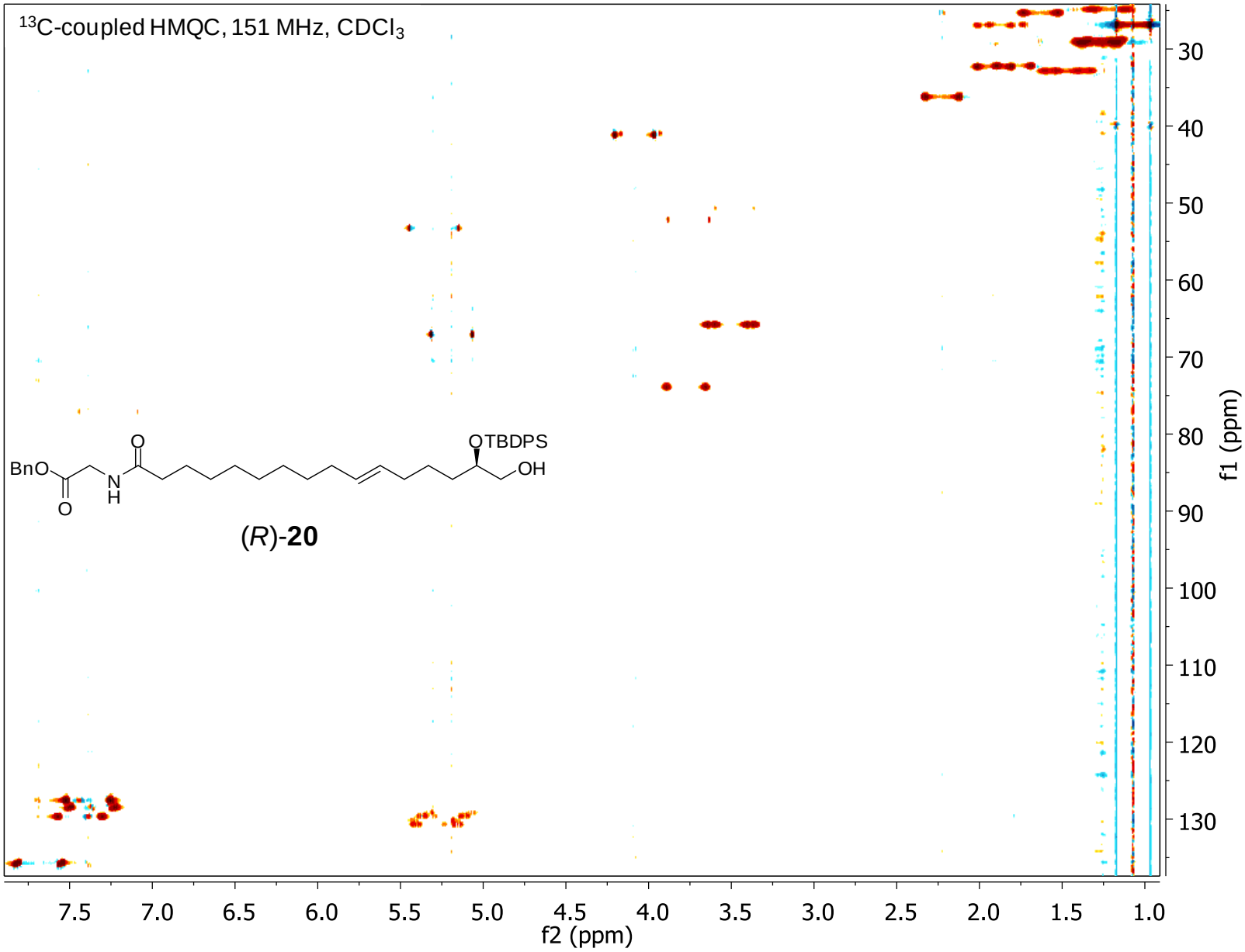

HMBC, 151 MHz, CDCl3
OTBDPS
OTHP
(R)-9
f2 (ppm)
f1 (ppm)

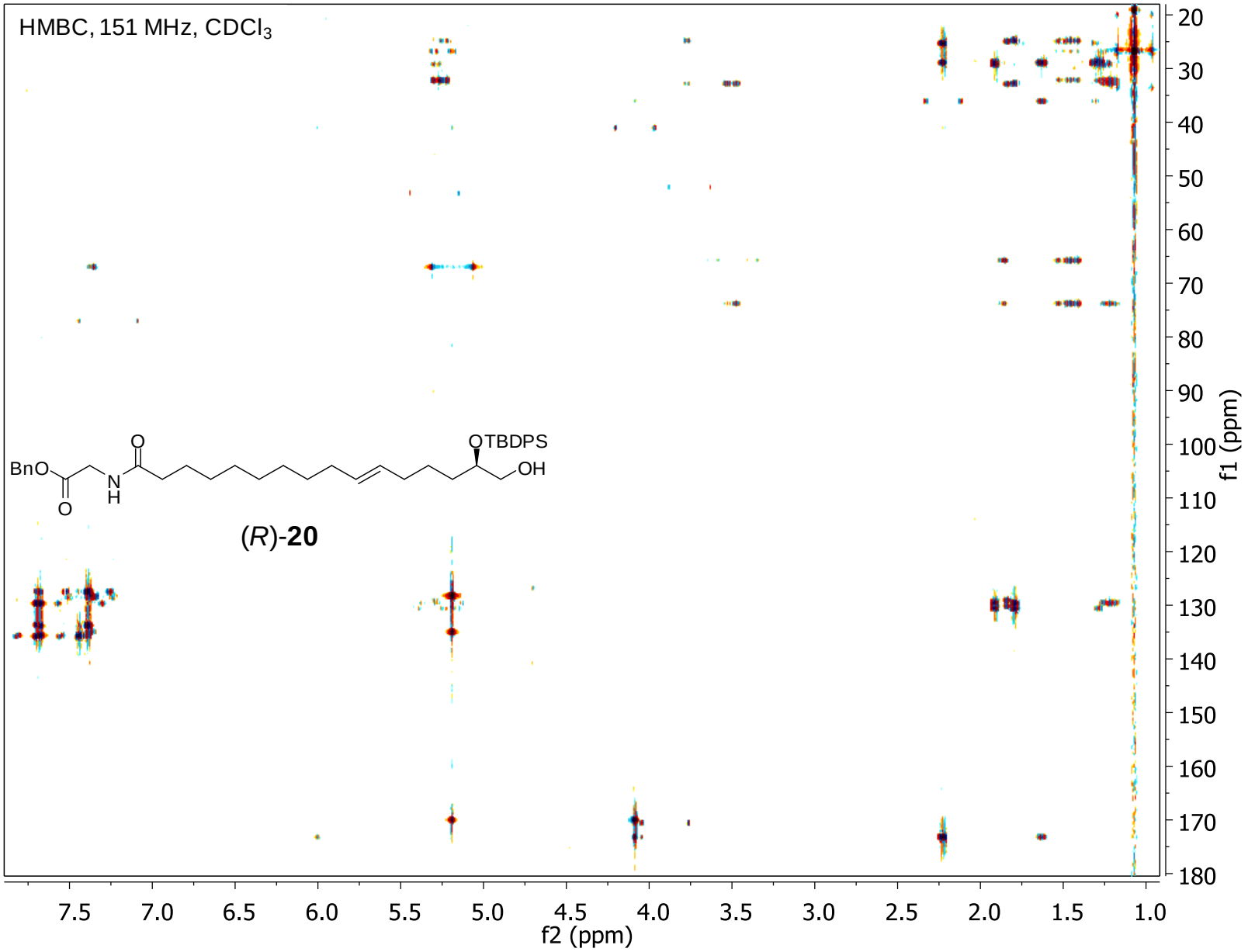
^{1}H NMR, 600 MHz, $CDCl_3$

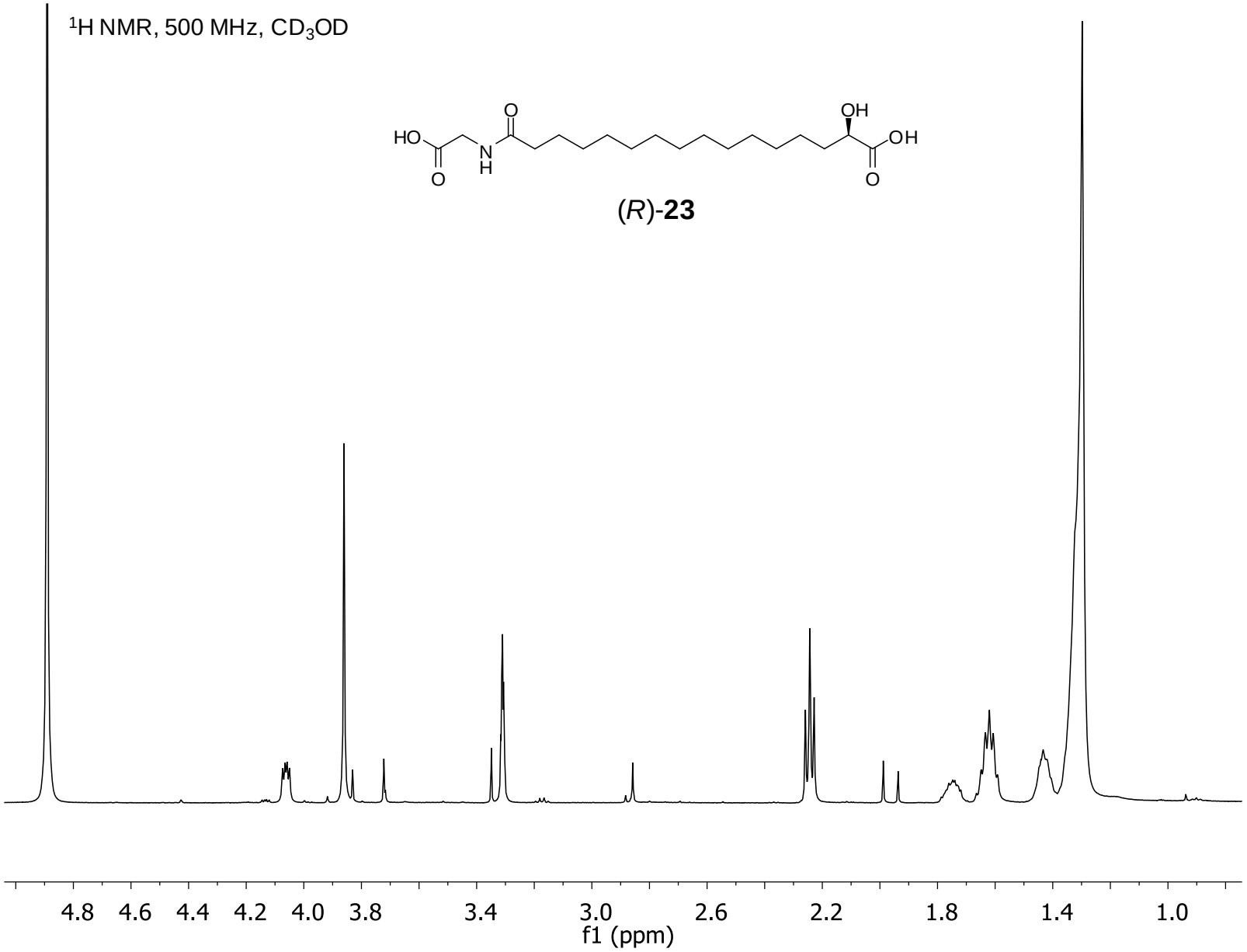


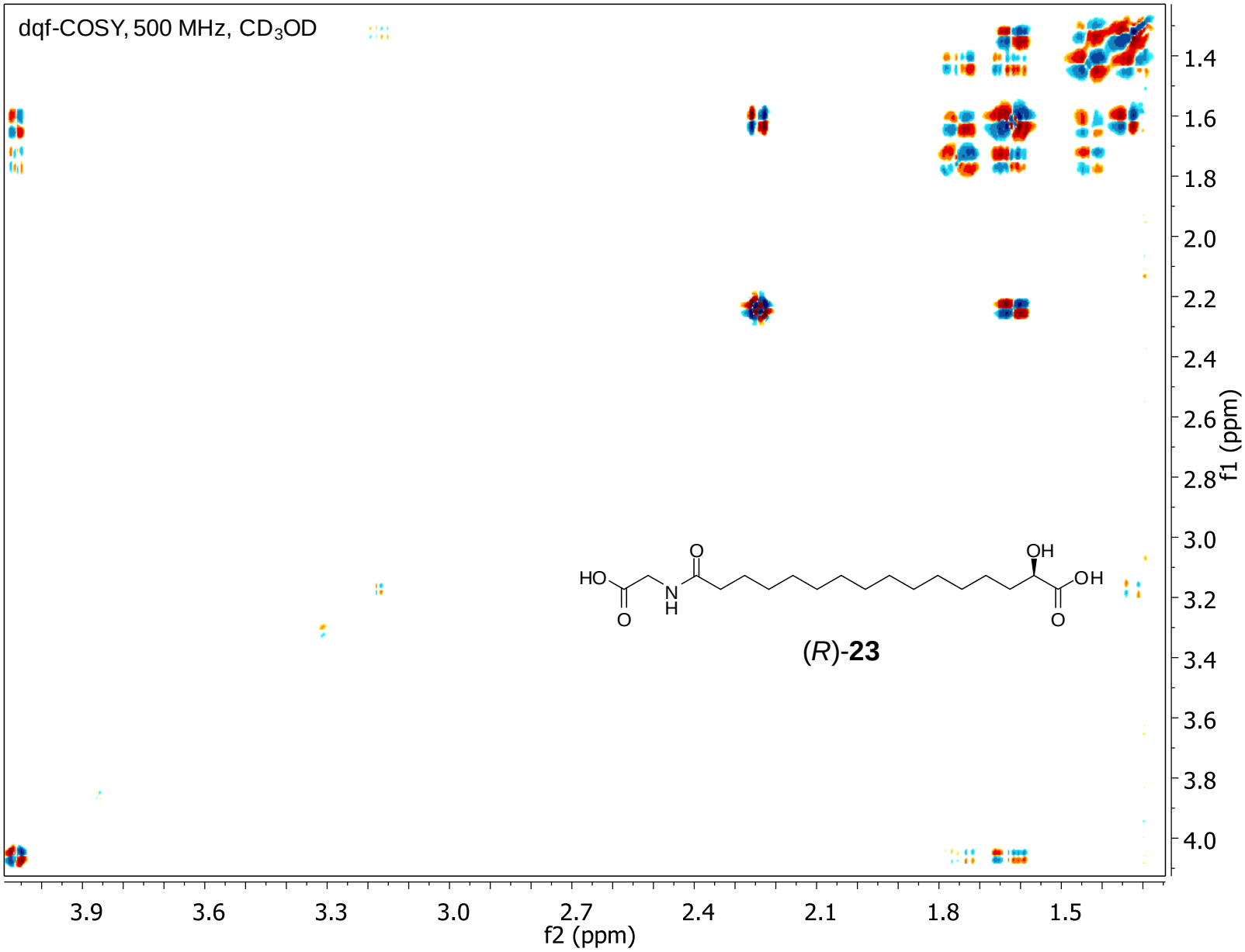
(*R*)-**20**

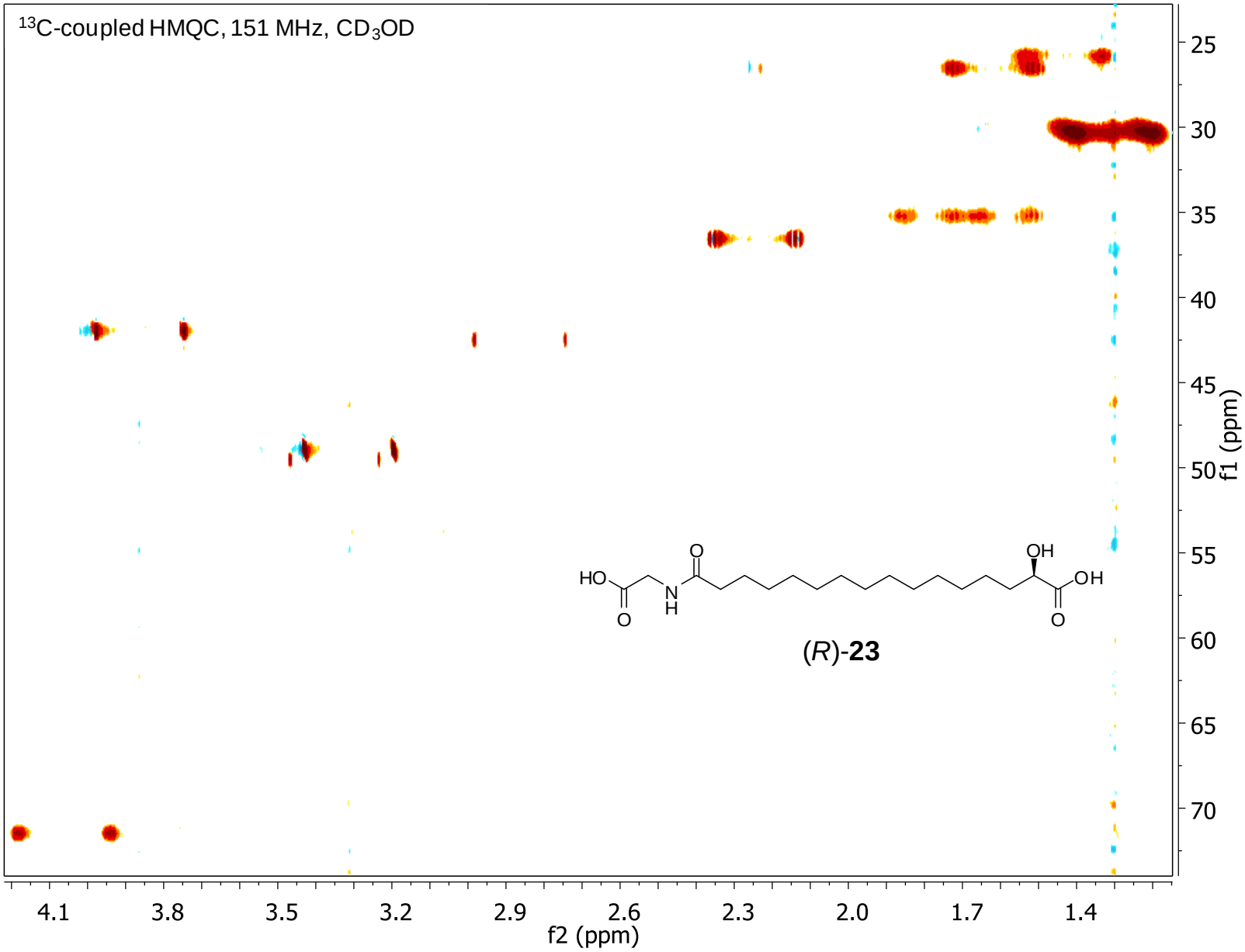

dqf-COSY, 600 MHz, CDCl3
BnO
O
N
H
O
OTBDPS
OH
(R)-20
f2 (ppm)
f1 (ppm)


^{13}C-coupled HMQC, 151 MHz, $CDCl_3$
BnO
O
N
H
O
OTBDPS
OH
(*R*)-**20**
f2 (ppm)
f1 (ppm)

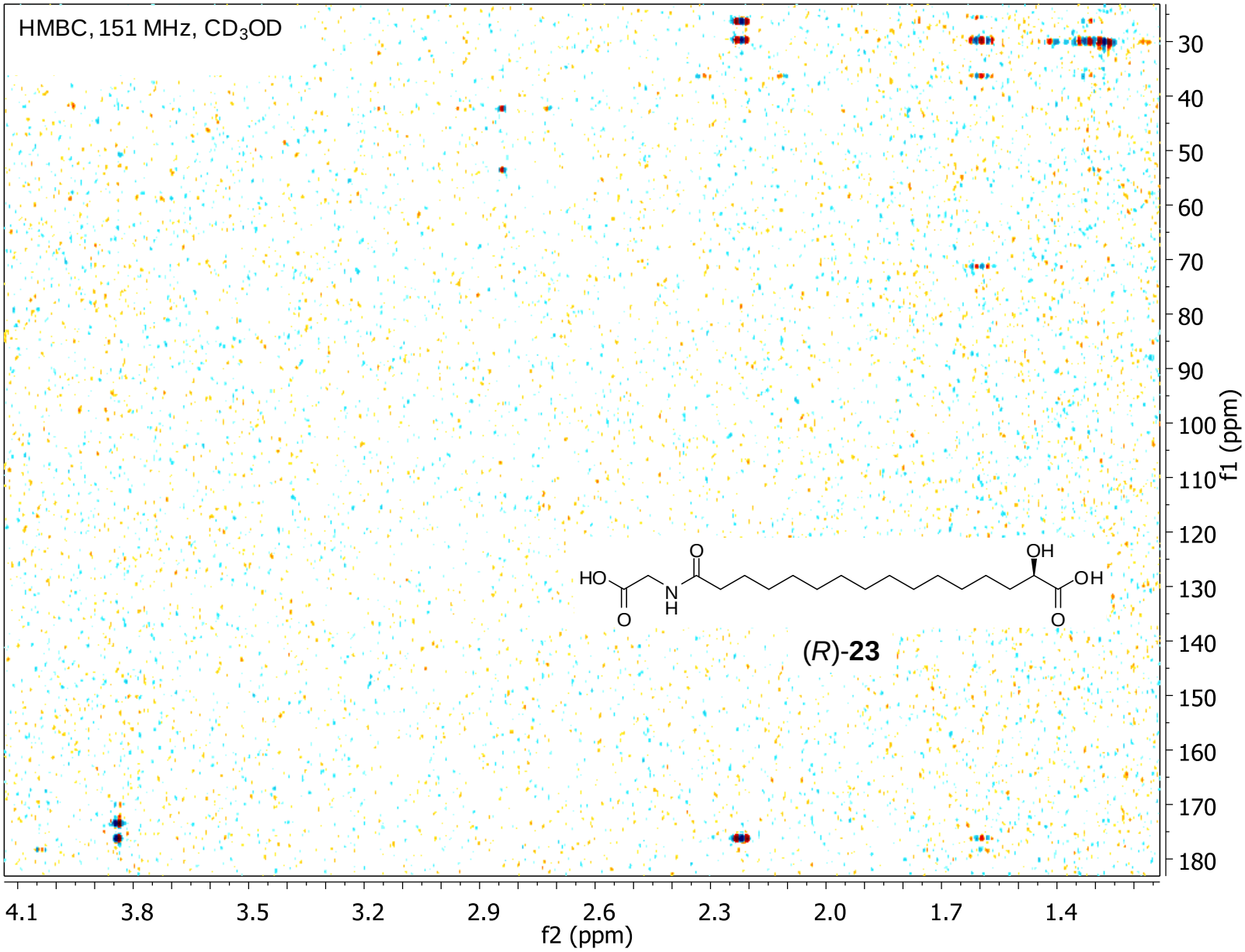

HMBC, 151 MHz, $CDCl_3$
BnO
O
N
H
O
OTBDPS
OH
(*R*)-**20**
f2 (ppm)
f1 (ppm)

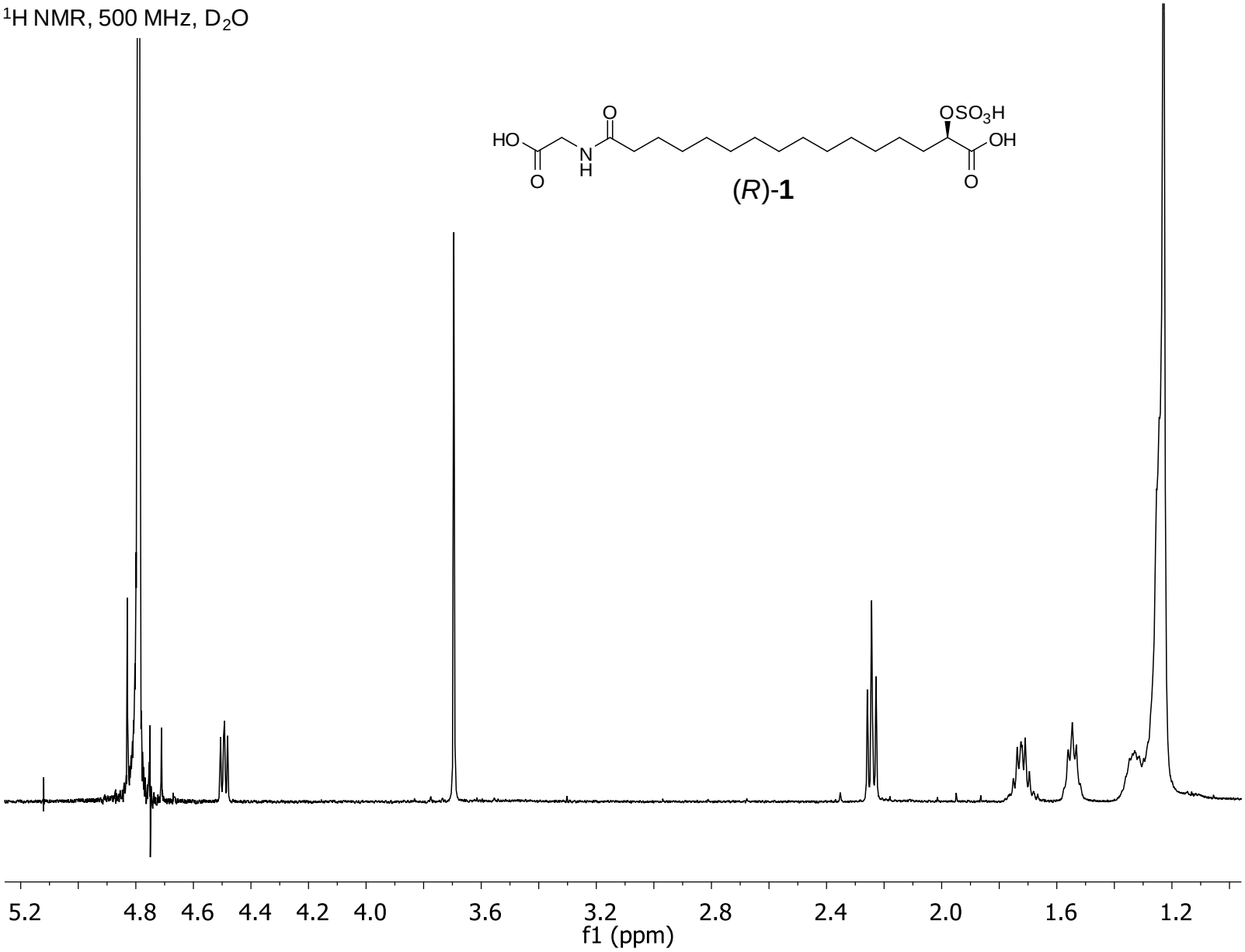

1H NMR, 500 MHz, CD3OD
HO
O
N
H
O
OH
OH
O
(R)-23
4.8
4.6
4.4
4.2
4.0
3.8
3.4
3.0
2.6
2.2
1.8
1.4
1.0
f1 (ppm)

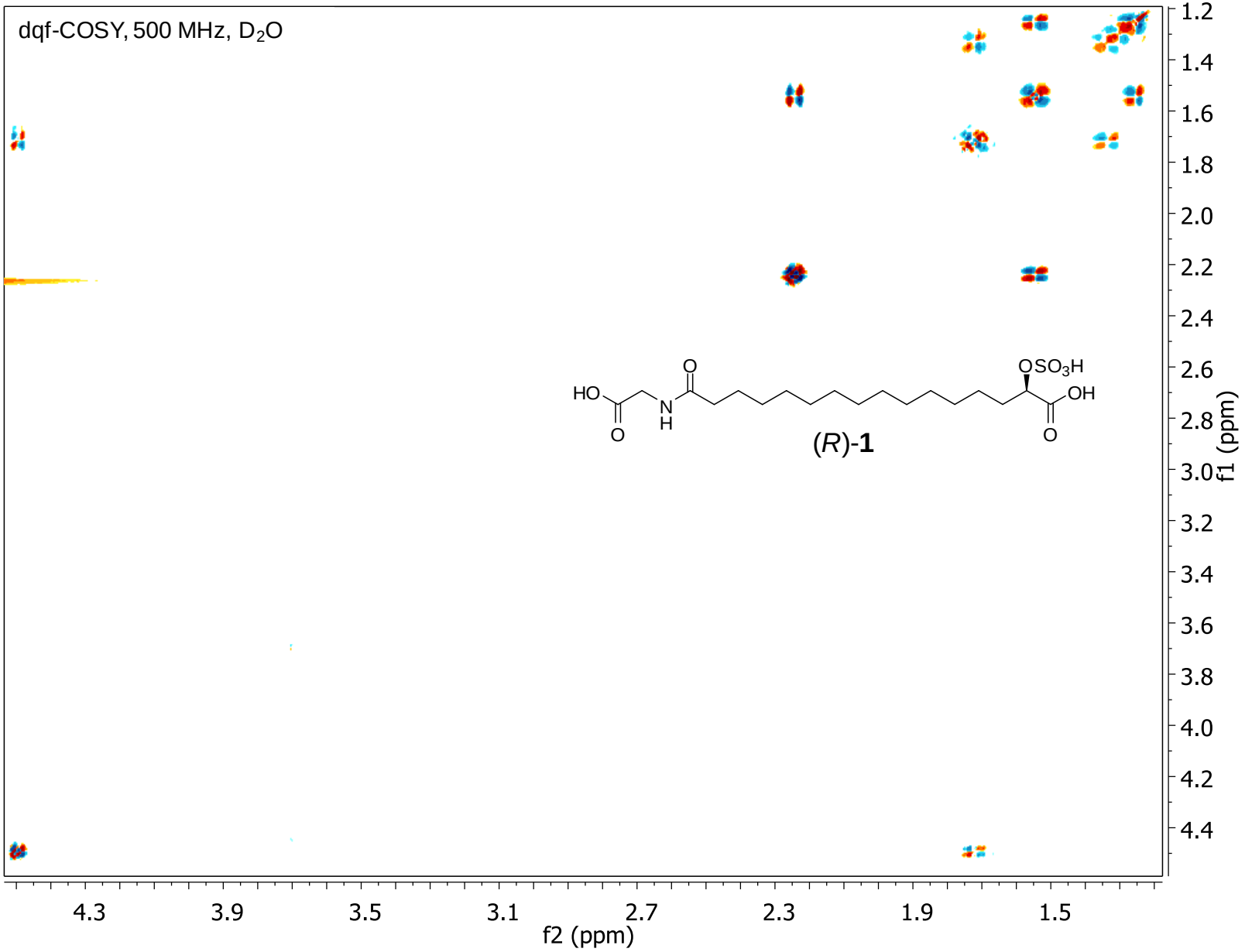

dqf-COSY, 500 MHz, CD3OD
HO
O
N
H
O
O
OH
OH
O
(R)-23
f1 (ppm)
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
3.9
3.6
3.3
3.0
2.7
2.4
2.1
1.8
1.5
f2 (ppm)

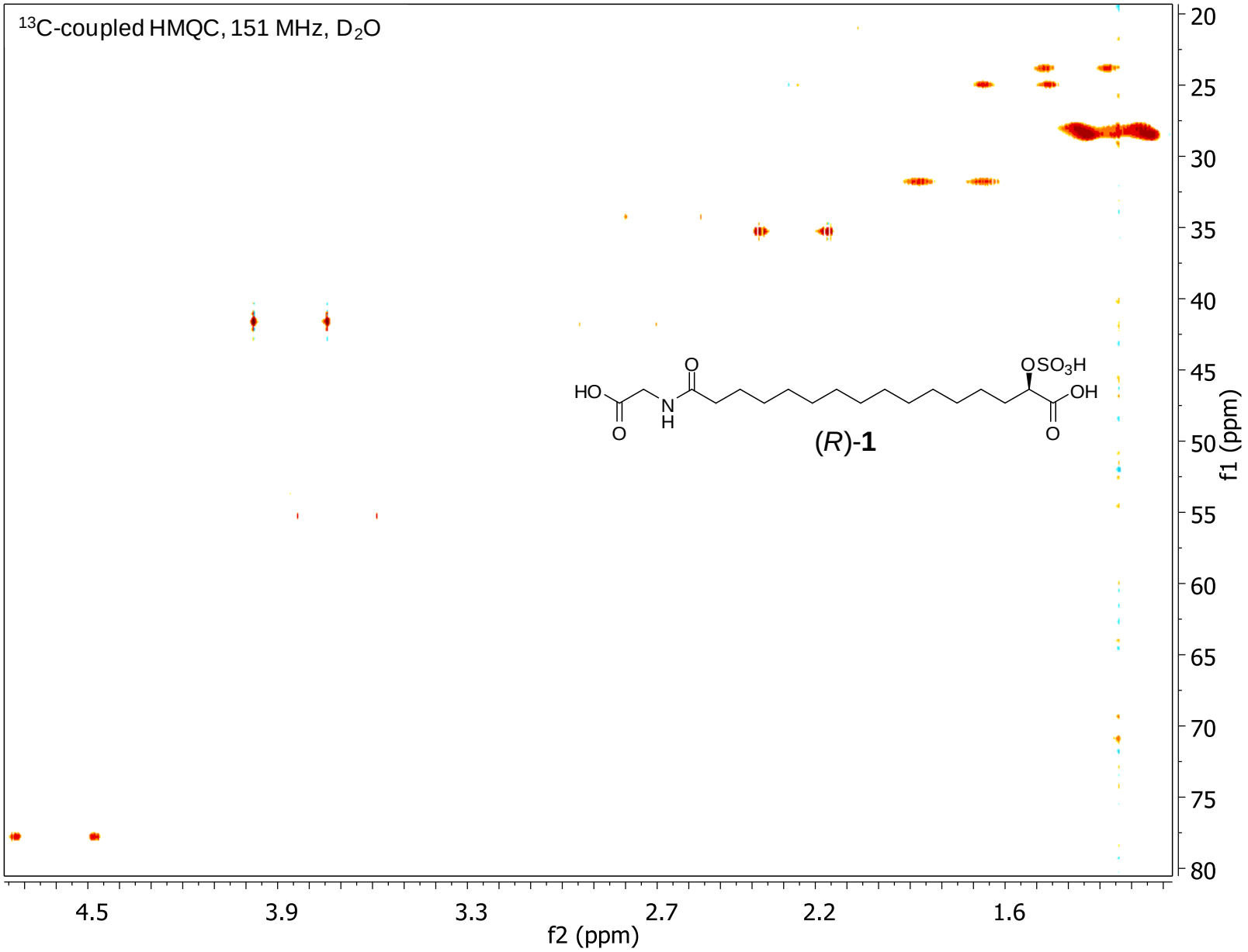

^{13}C-coupled HMQC, 151 MHz, CD_3OD
25
30
35
40
45
50
55
60
65
70
f1 (ppm)
4.1
3.8
3.5
3.2
2.9
2.6
2.3
2.0
1.7
1.4
f2 (ppm)
HO
O
N
H
O
OH
OH
O

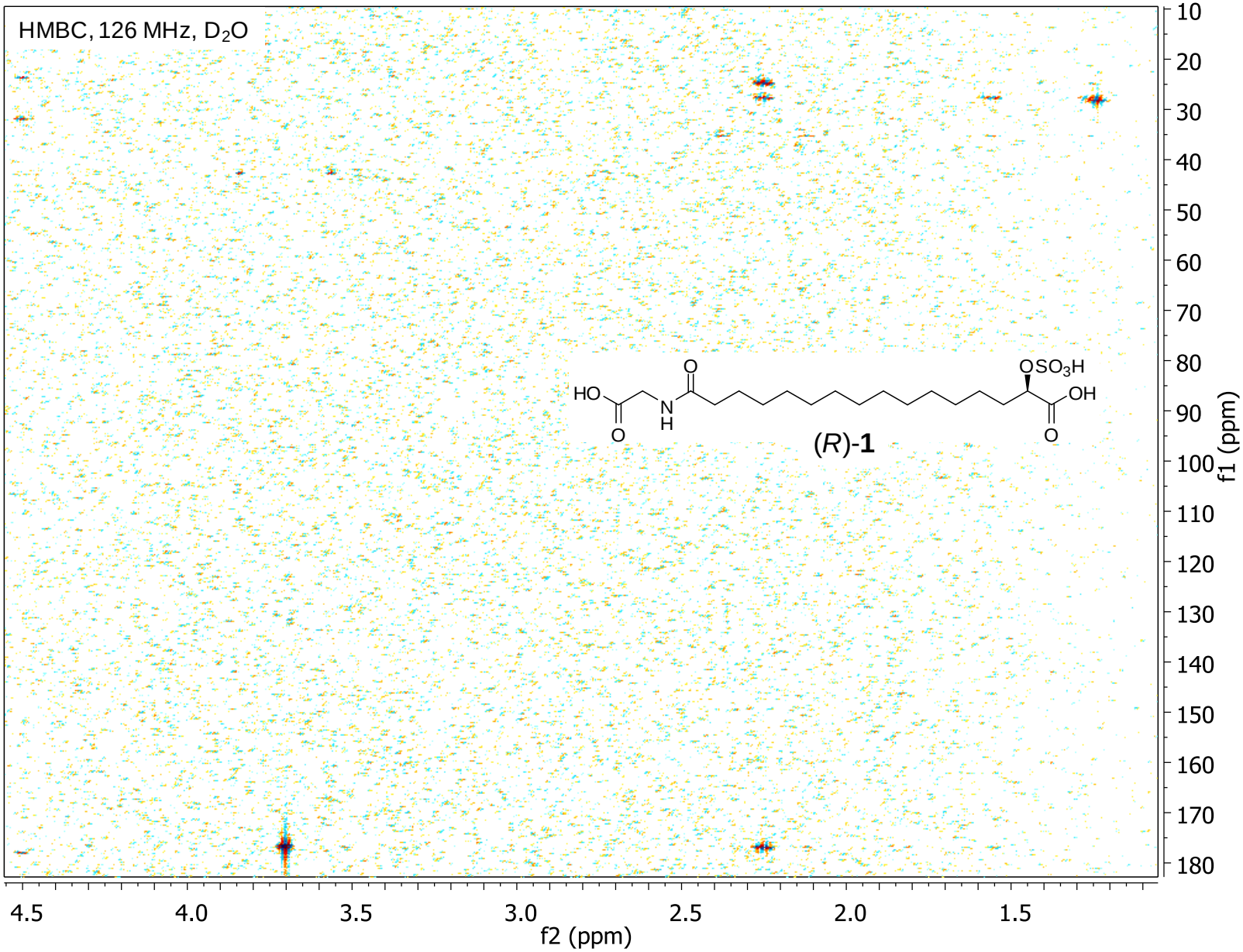
(*R*)-**23**


HMBC, 151 MHz, CD3OD
HO
O
N
H
O
O
OH
OH
(R)-23
f1 (ppm)
f2 (ppm)
4.1
3.8
3.5
3.2
2.9
2.6
2.3
2.0
1.7
1.4
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

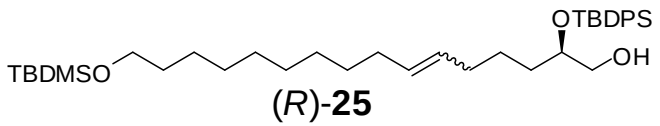

^{1}H NMR, 500 MHz, D_2O
HO
O
N
H
O
O
OSO$_3$H
OH
O
(*R*)-**1**
5.2
4.8
4.6
4.4
4.2
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
f1 (ppm)


dqf-COSY, 500 MHz, D2O
HO
O
N
H
O
OSO3H
OH
O
(R)-1
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0
4.2
4.4
f1 (ppm)
4.3
3.9
3.5
3.1
2.7
2.3
1.9
1.5
f2 (ppm)

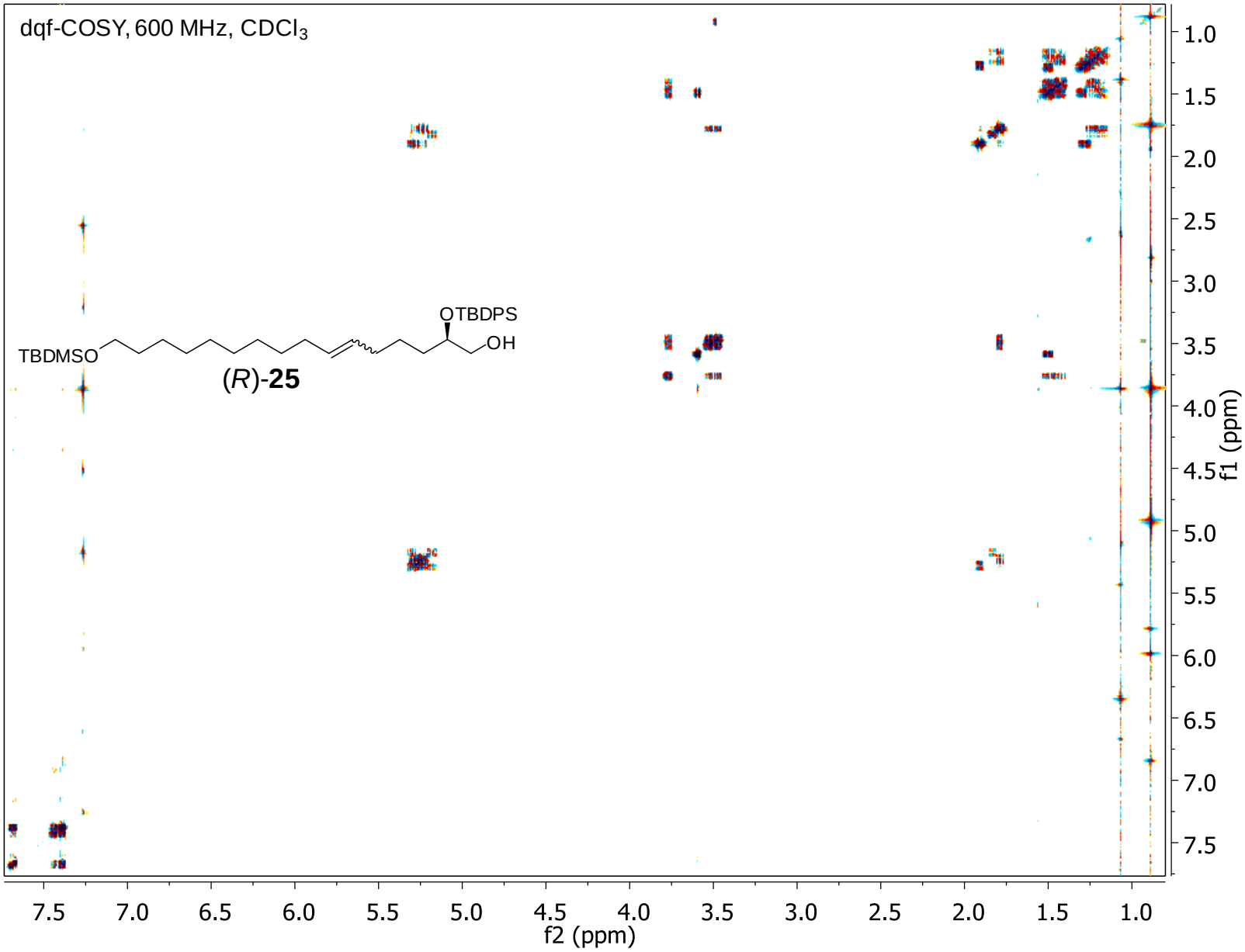

^{13}C-coupled HMQC, 151 MHz, D_2O
HO
O
N
H
O
OSO$_3$H
OH
O
(*R*)-**1**
20
25
30
35
40
45
50
55
60
65
70
75
80
f1 (ppm)
4.5
3.9
3.3
2.7
2.2
1.6
f2 (ppm)

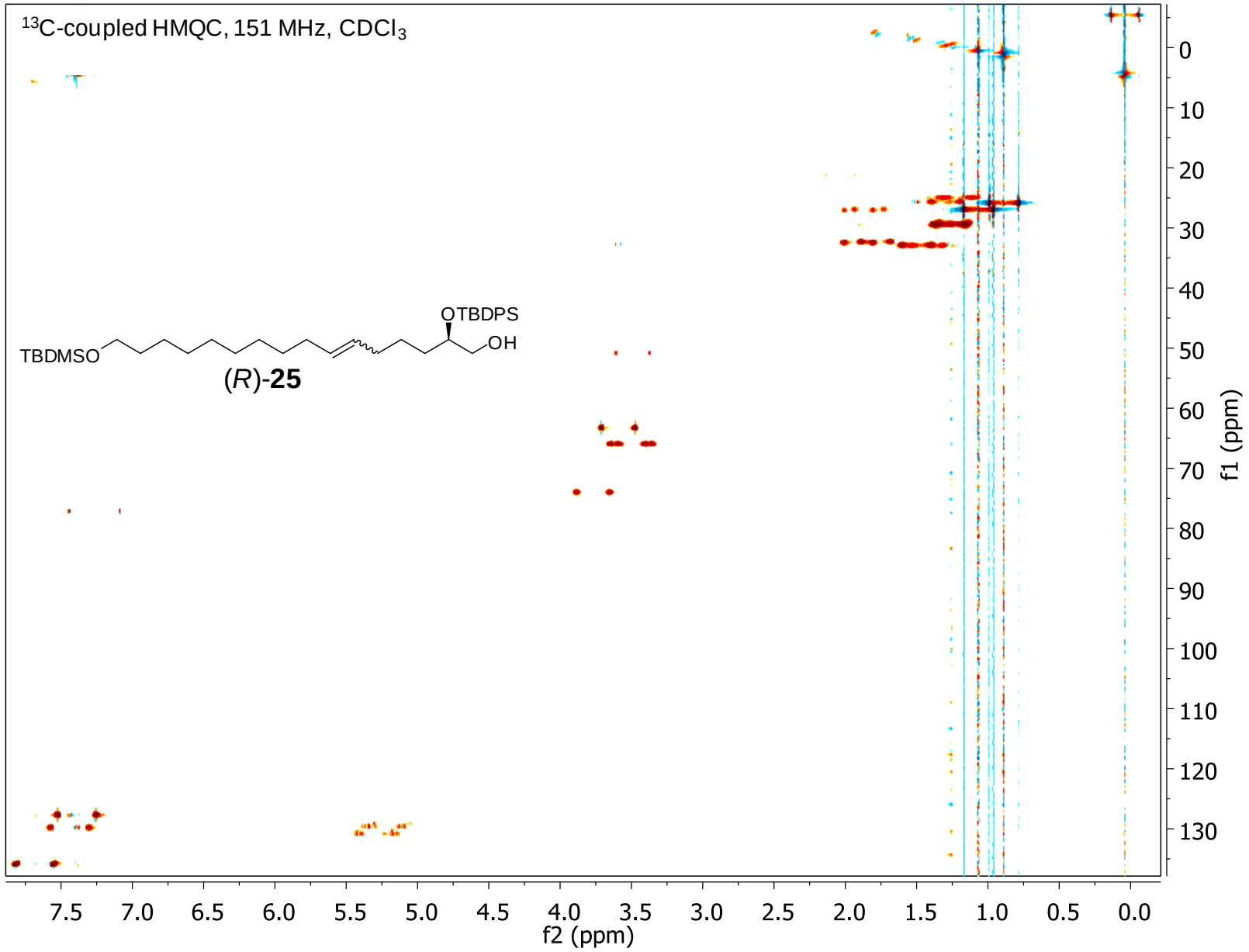

HMBC, 126 MHz, D2O
HO
O
N
H
O
OSO3H
OH
O
(R)-1
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f2 (ppm)

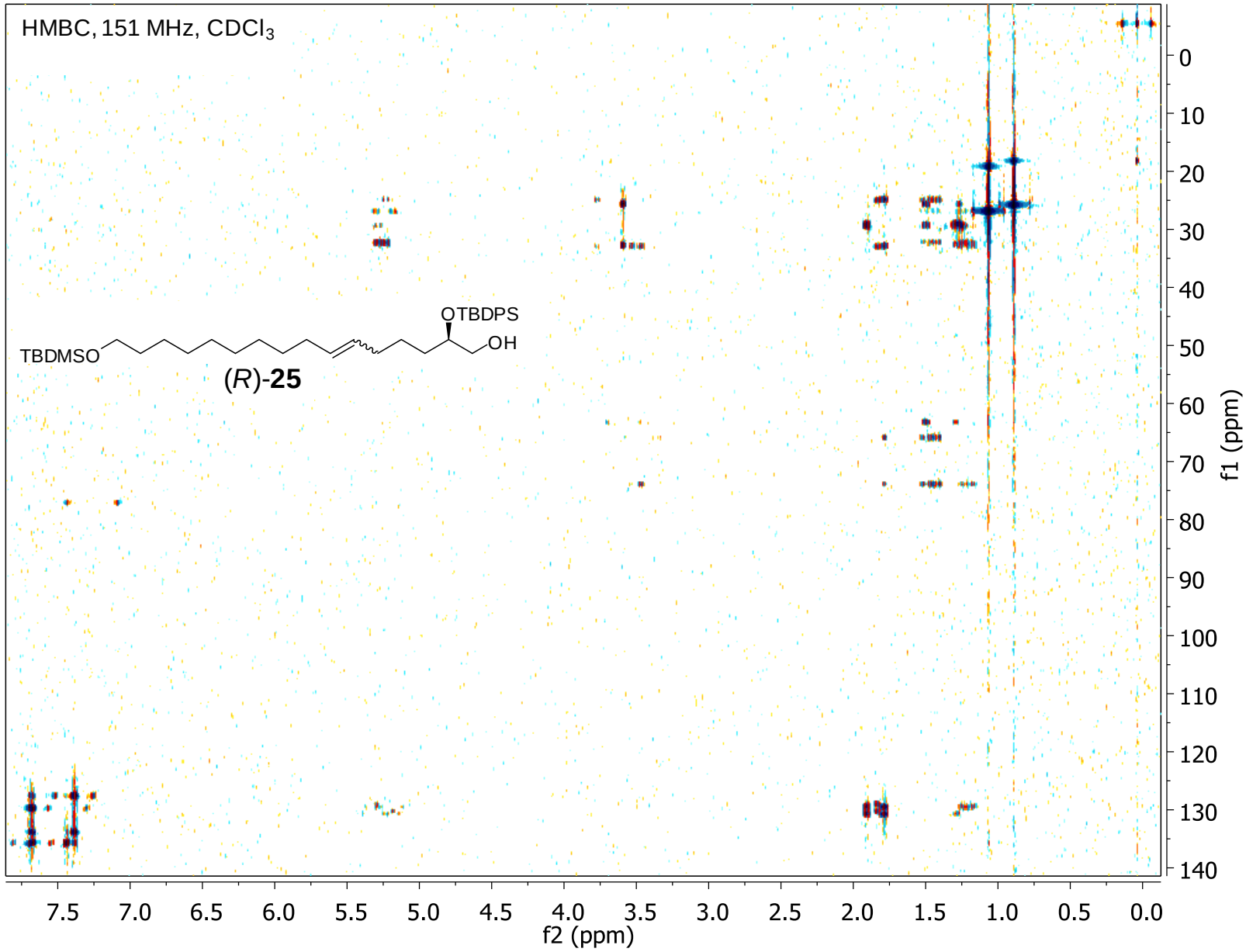
^{1}H NMR, 600 MHz, $CDCl_3$



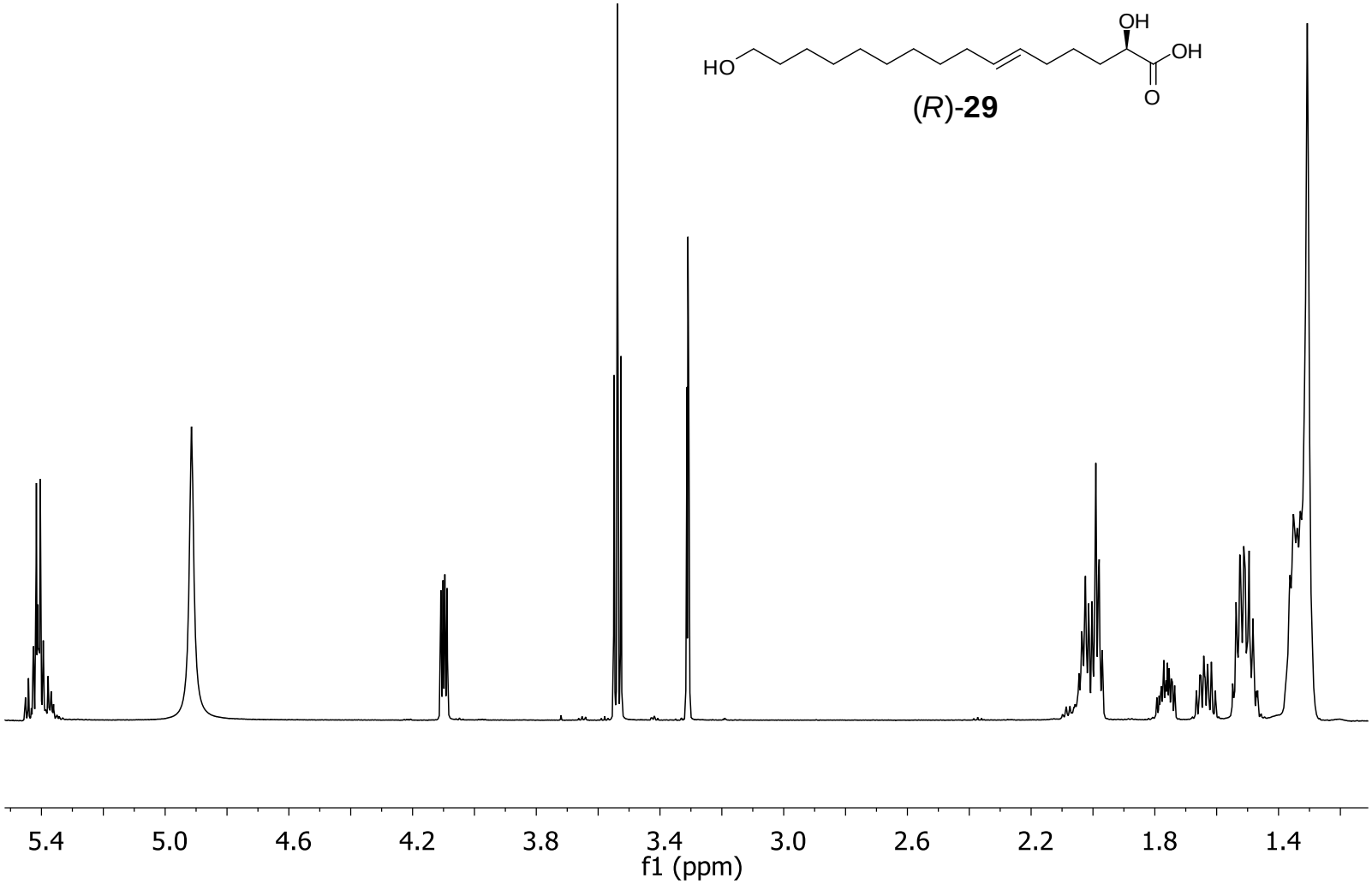
(*R*)-**25**

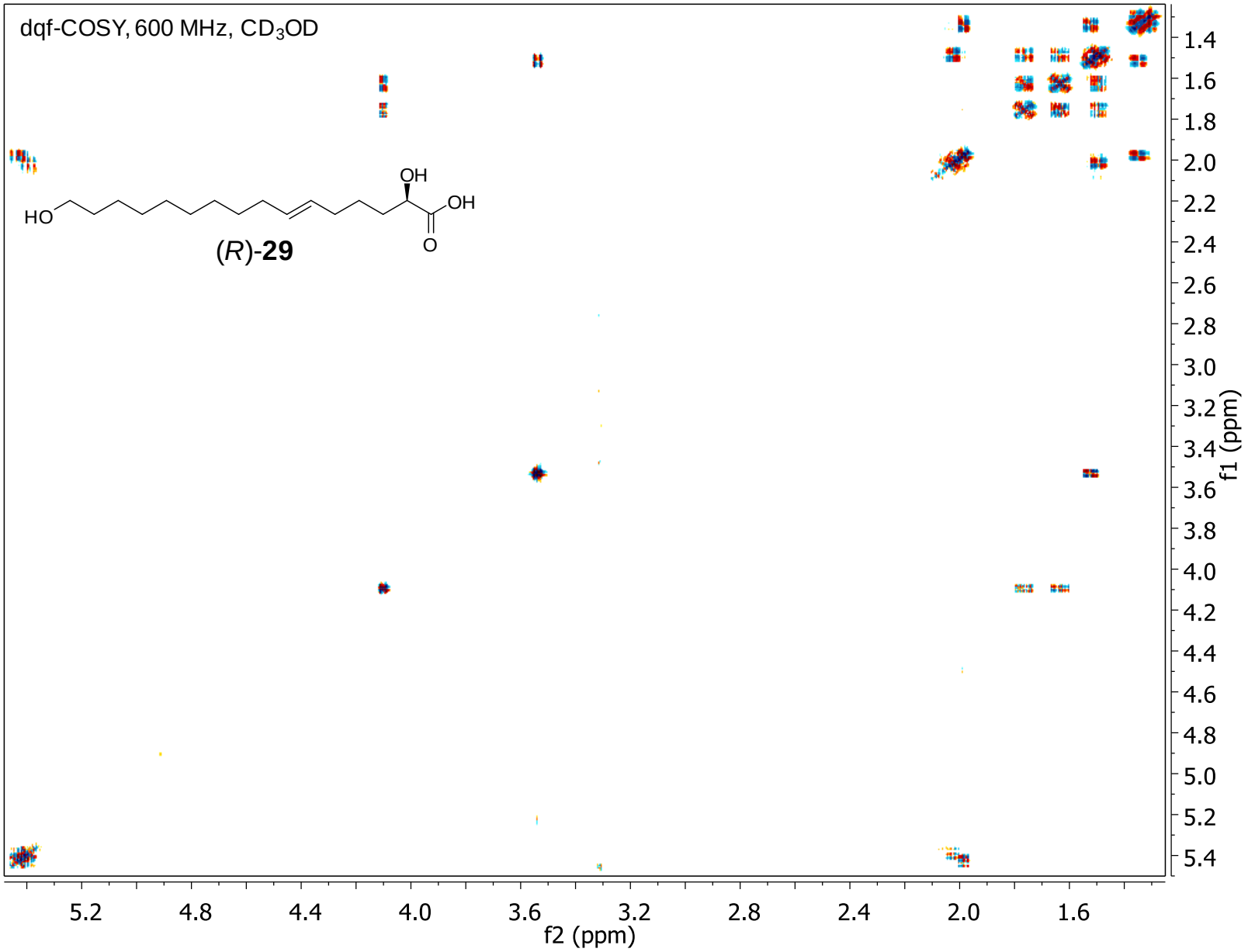

dqf-COSY, 600 MHz, CDCl3
OTBDPS
TBDMSO
OH
(R)-25
f2 (ppm)
f1 (ppm)

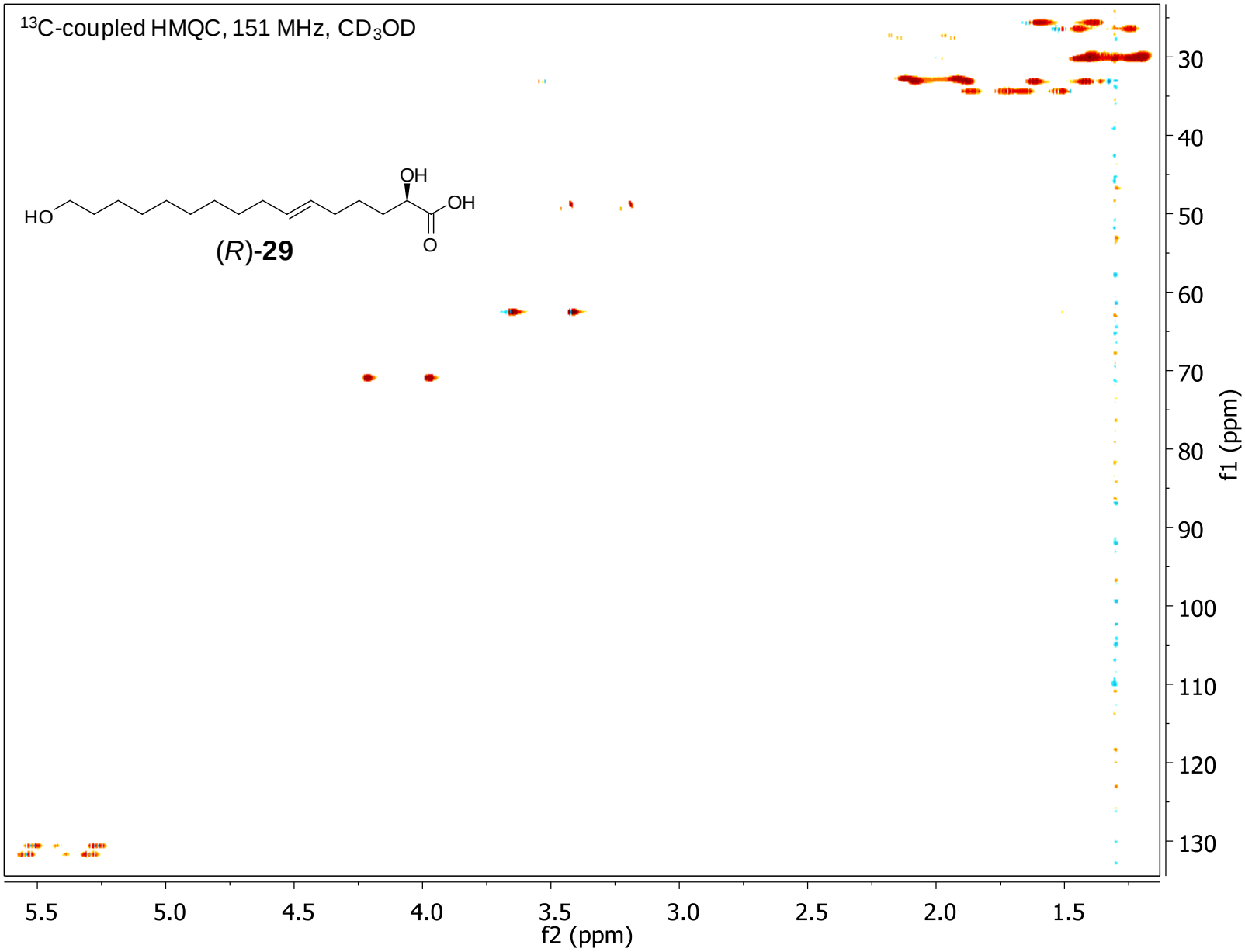

^{13}C-coupled HMQC, 151 MHz, $CDCl_3$
OTBDPS
OH
TBDMSO
(*R*)-**25**
f2 (ppm)
f1 (ppm)

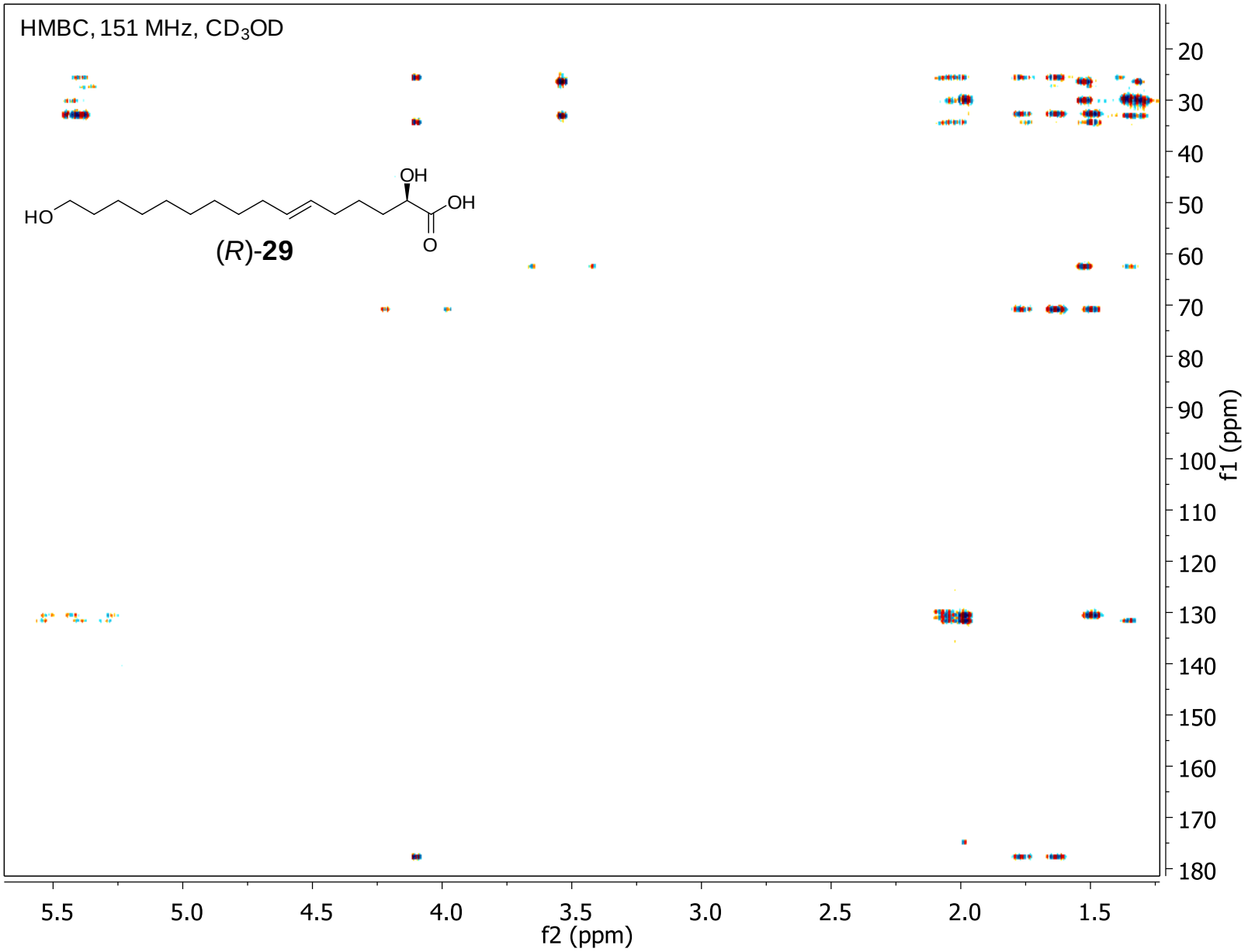

HMBC, 151 MHz, CDCl3
TBDMSO
OTBDPS
OH
(R)-25
f2 (ppm)
f1 (ppm)

^{1}H NMR, 600 MHz, CD_3OD

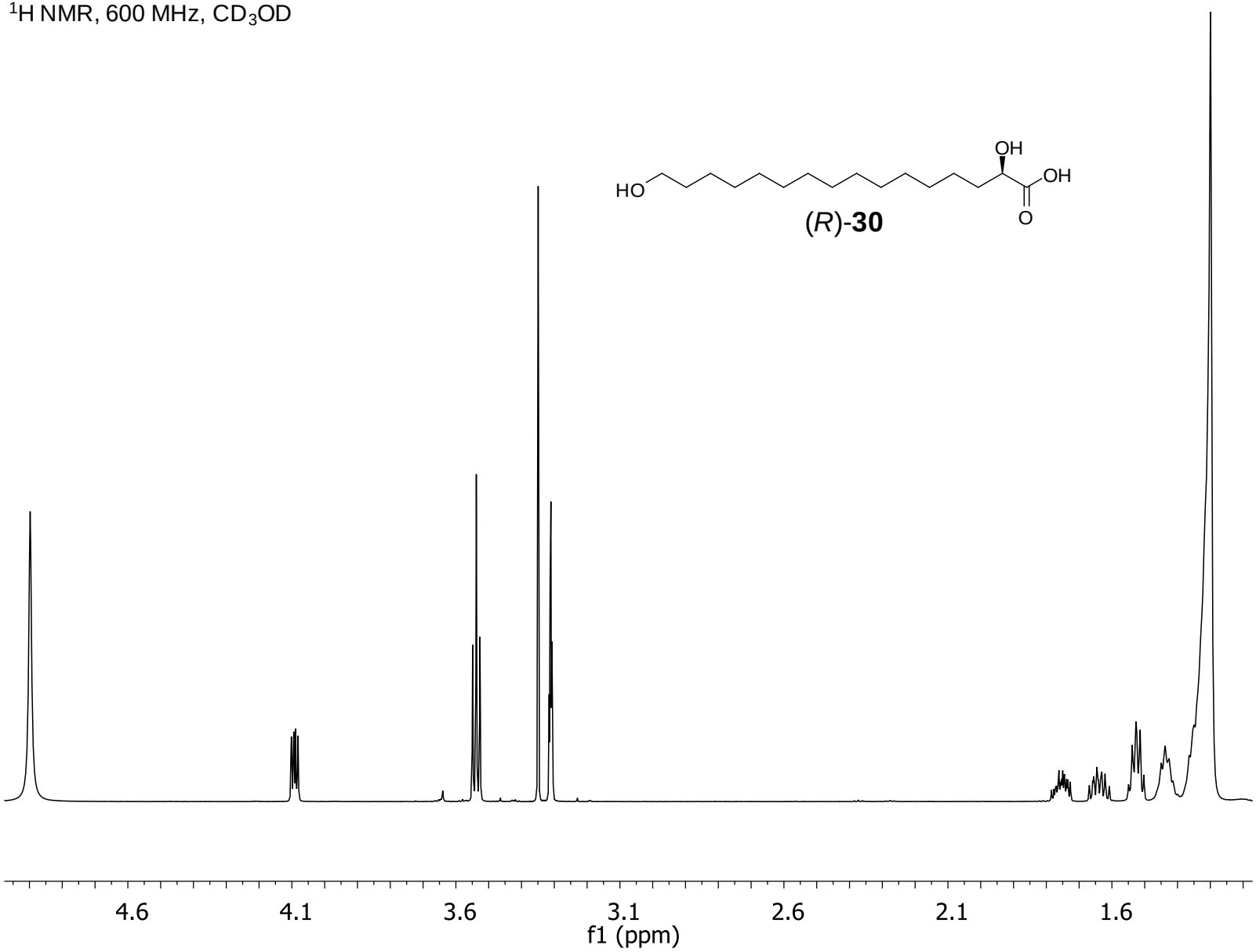


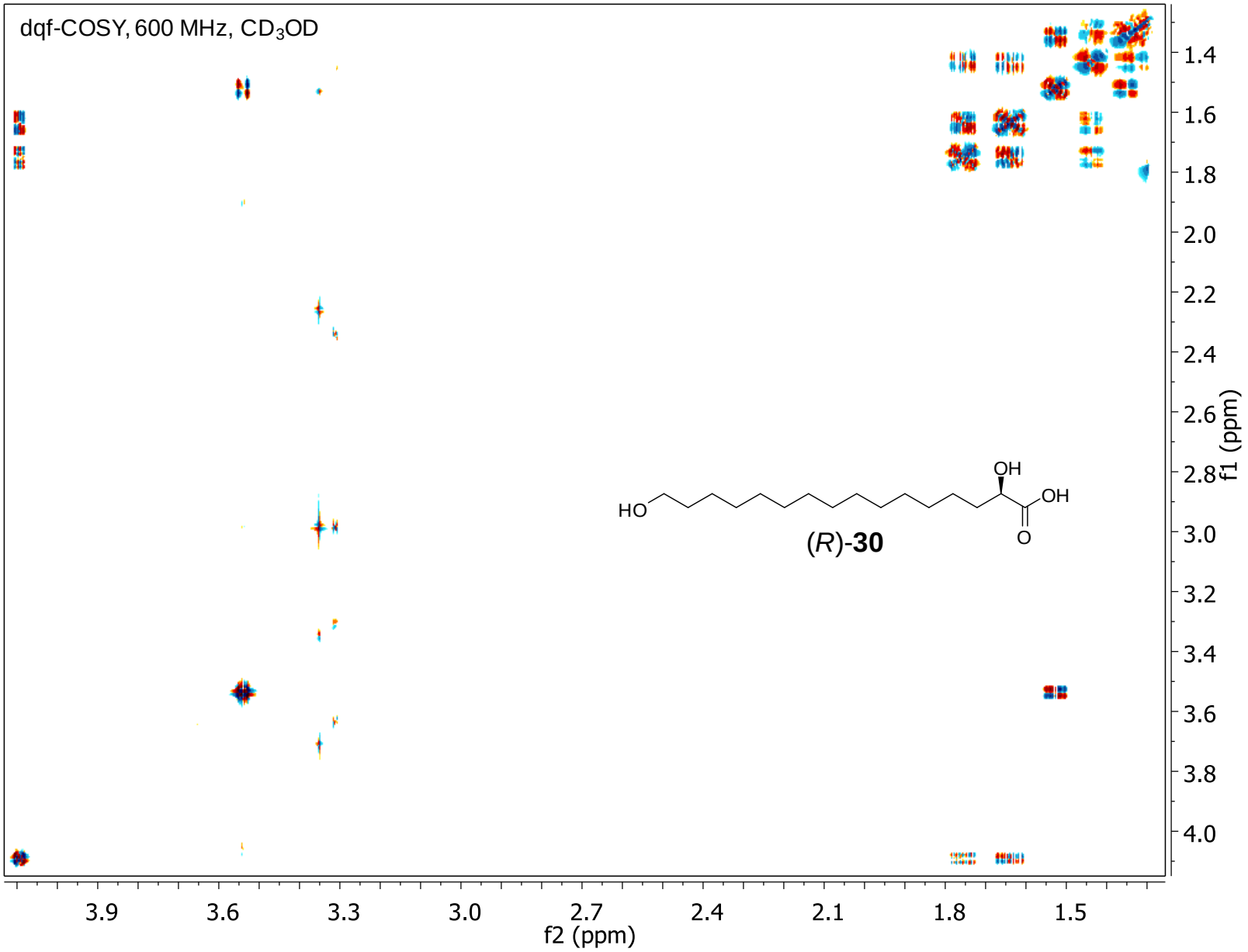

dqf-COSY, 600 MHz, CD3OD
HO
OH
OH
O
(R)-29
f2 (ppm)
f1 (ppm)

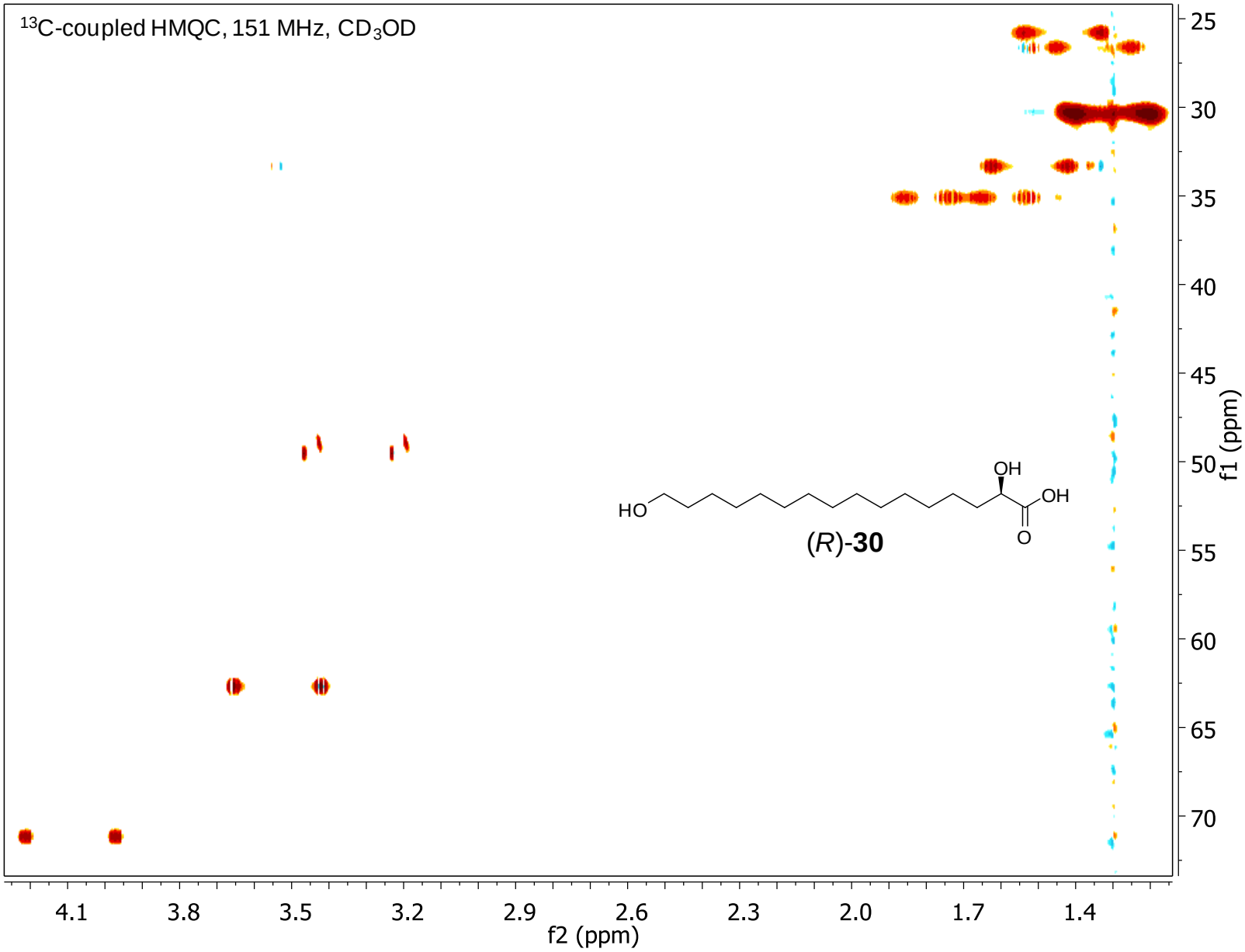

^{13}C-coupled HMQC, 151 MHz, CD_3OD
HO
OH
OH
O
(*R*)-**29**
f1 (ppm)
f2 (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
30
40
50
60
70
80
90
100
110
120
130

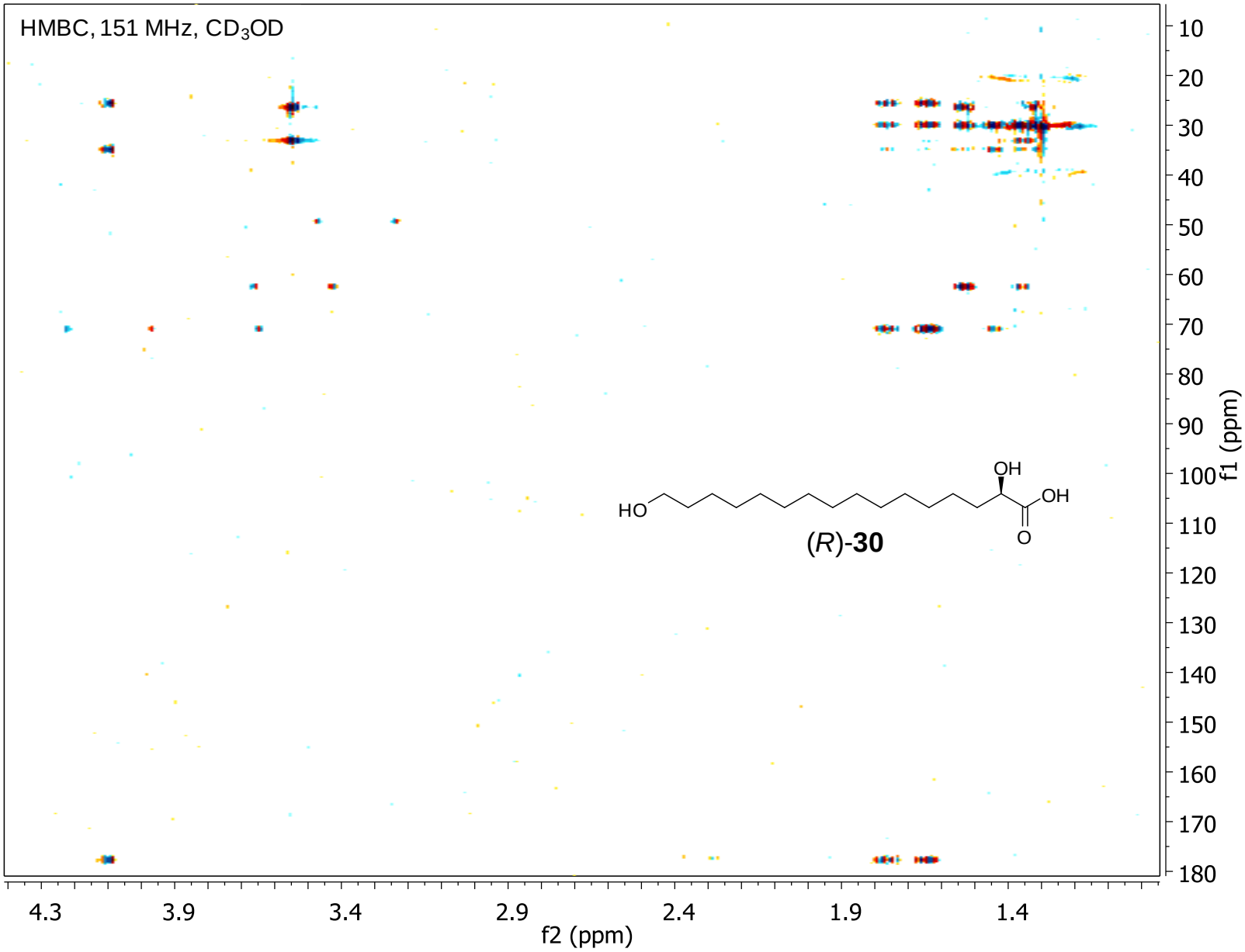

HMBC, 151 MHz, CD_3OD
HO
OH
OH
O
(*R*)-**29**
f1 (ppm)
f2 (ppm)

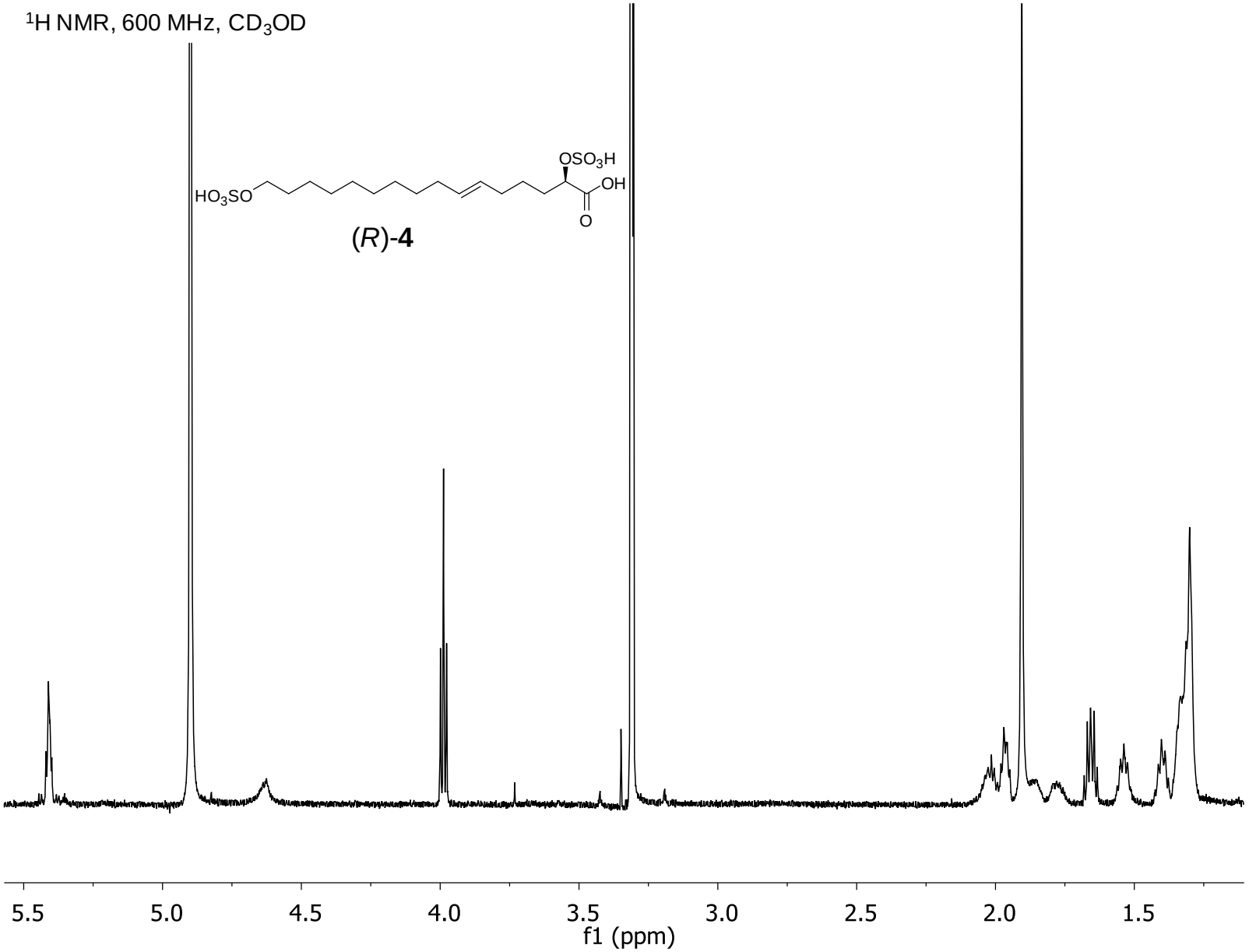
^{1}H NMR, 600 MHz, CD_3OD

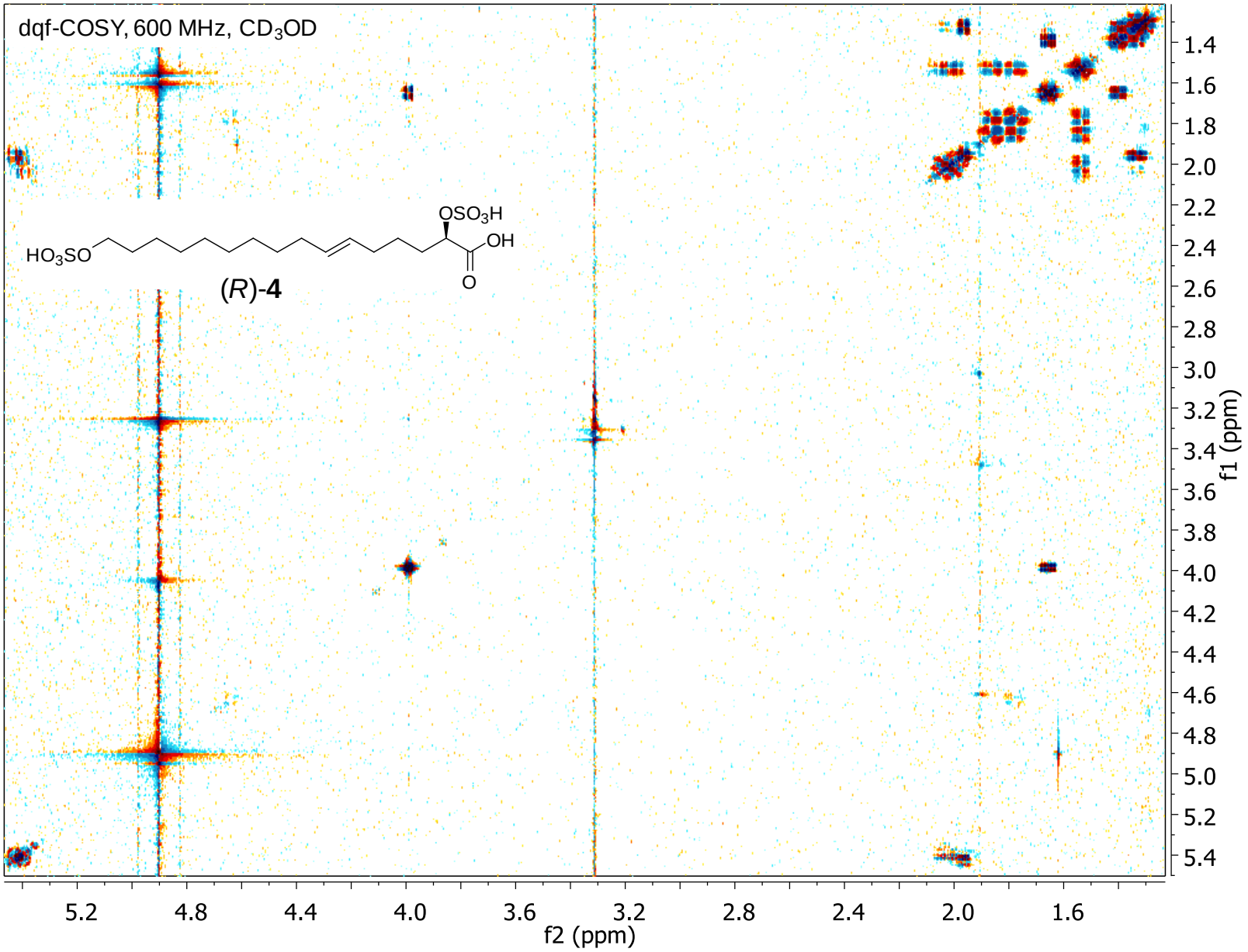


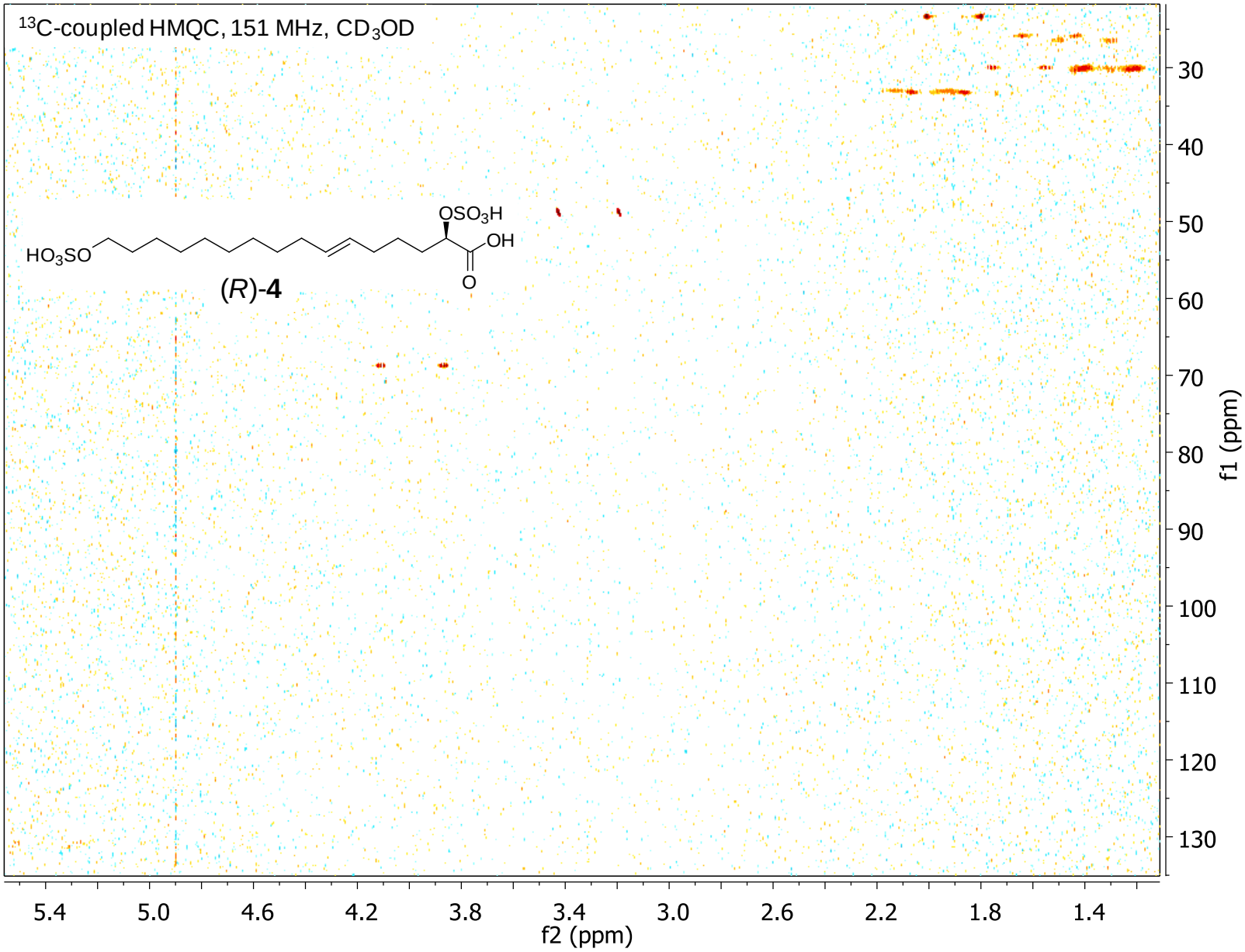

dqf-COSY, 600 MHz, CD3OD
HO
OH
OH
O
(R)-30
f2 (ppm)
f1 (ppm)
3.9
3.6
3.3
3.0
2.7
2.4
2.1
1.8
1.5
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
3.2
3.4
3.6
3.8
4.0

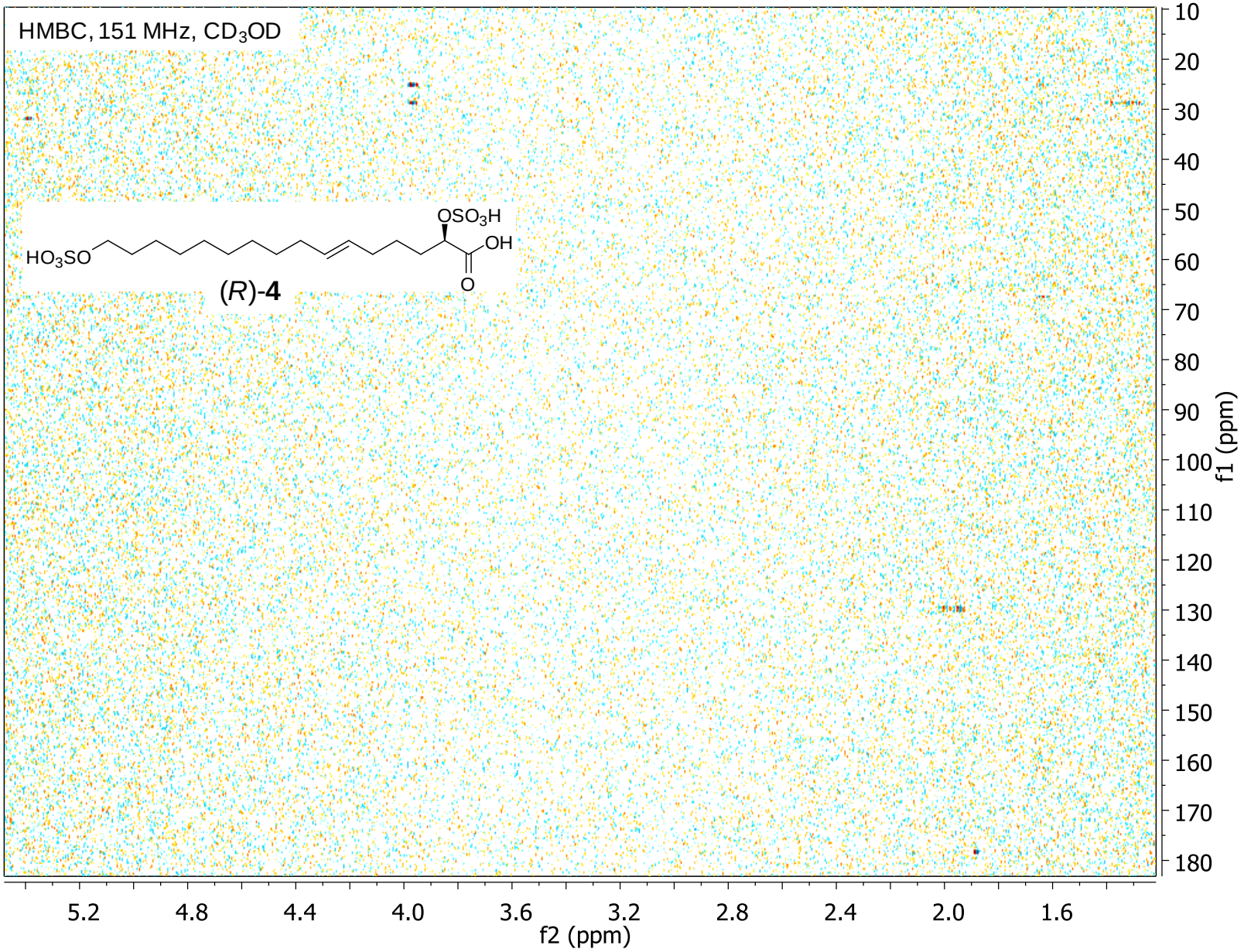

^{13}C-coupled HMQC, 151 MHz, CD_3OD
HO
OH
OH
O
(*R*)-**30**
f1 (ppm)
25
30
35
40
45
50
55
60
65
70
4.1
3.8
3.5
3.2
2.9
2.6
2.3
2.0
1.7
1.4
f2 (ppm)

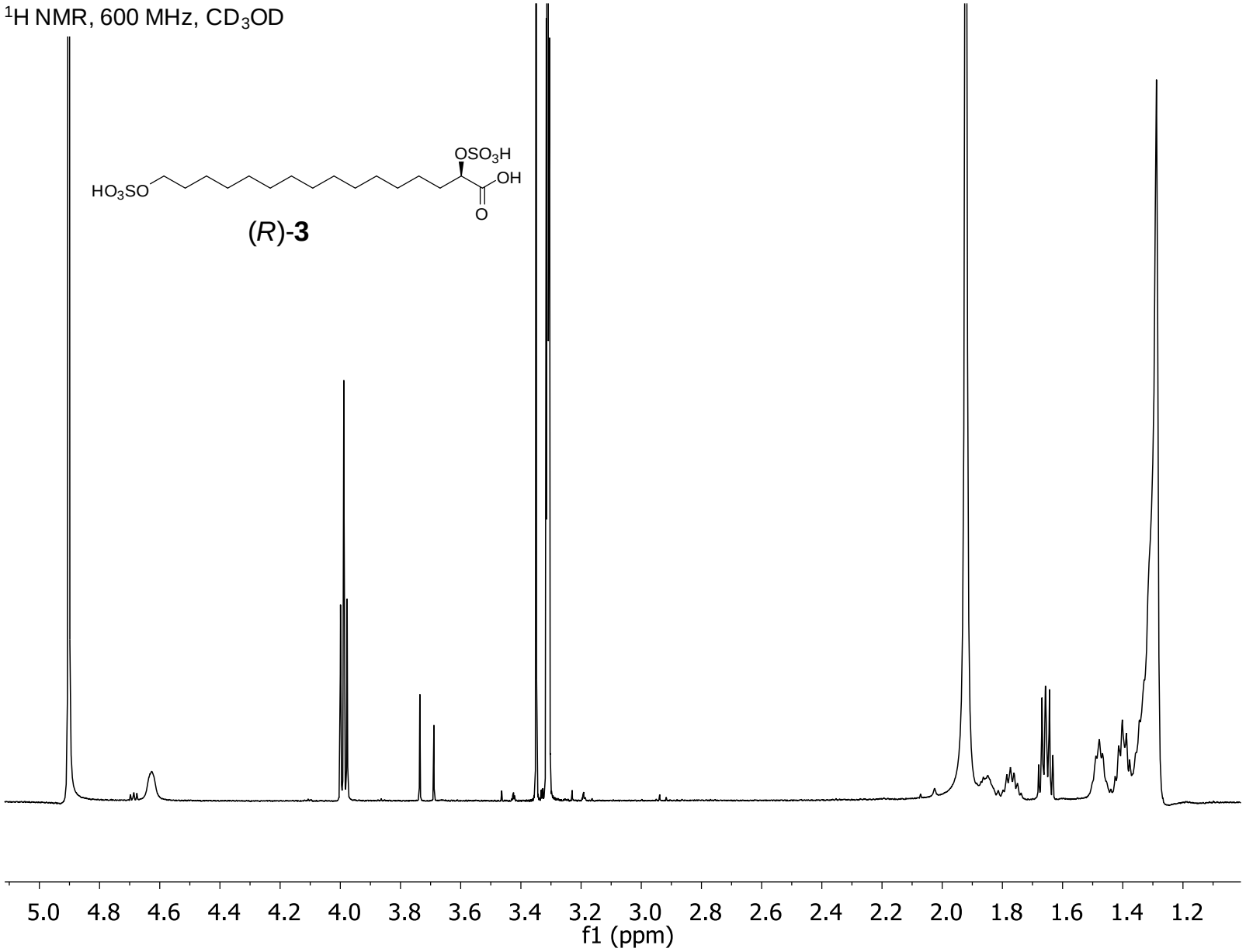

HMBC, 151 MHz, CD3OD
HO
OH
OH
O
(R)-30
f1 (ppm)
f2 (ppm)
4.3
3.9
3.4
2.9
2.4
1.9
1.4
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

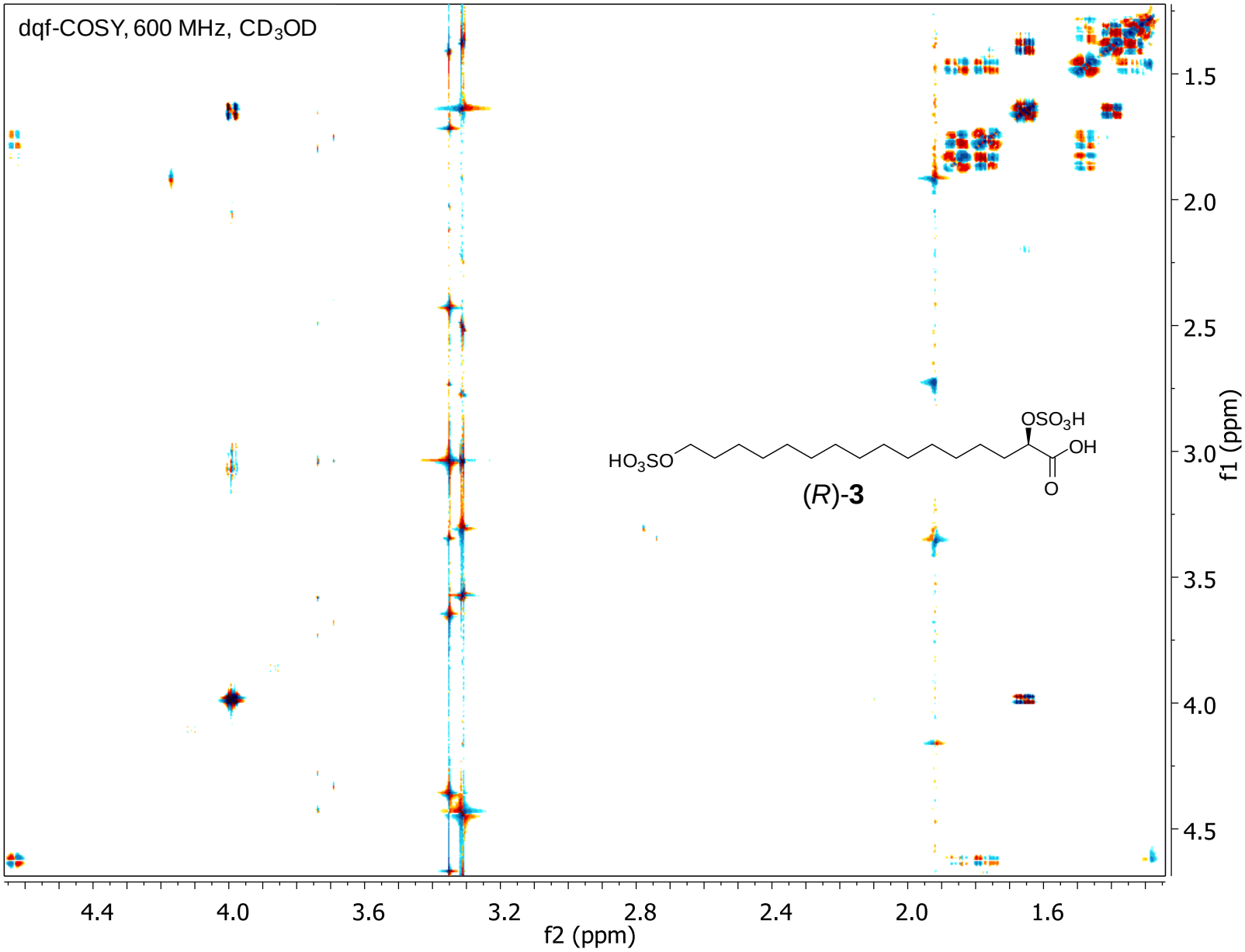

^{1}H NMR, 600 MHz, CD_3OD
HO_3SO
OSO_3H
OH
O
(*R*)-**4**
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

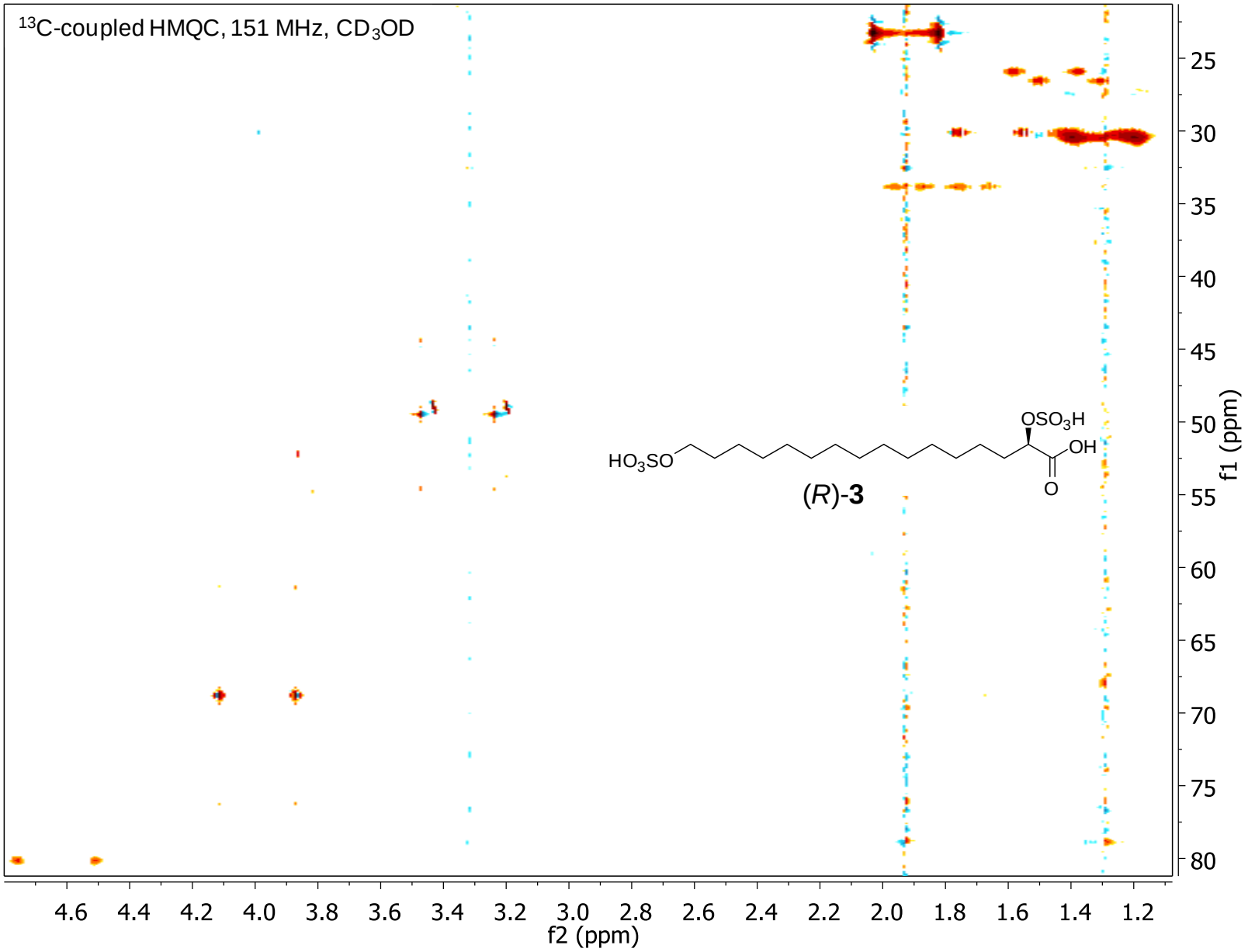

dqf-COSY, 600 MHz, CD3OD
HO3SO
OSO3H
OH
O
(R)-4
f2 (ppm)
f1 (ppm)

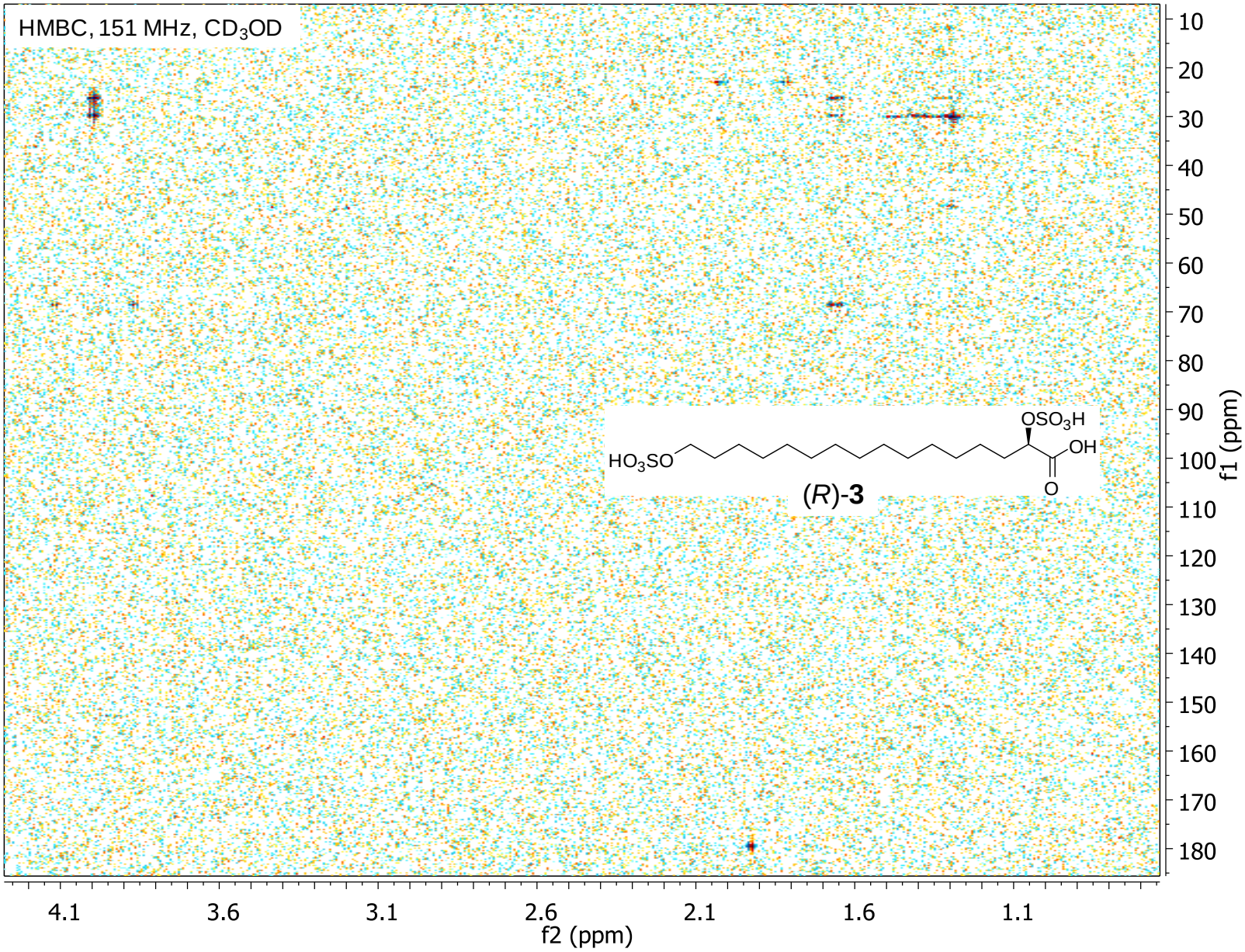

^{13}C-coupled HMQC, 151 MHz, CD_3OD
HO_3SO
OSO_3H
OH
O
(*R*)-**4**
30
40
50
60
70
80
90
100
110
120
130
f1 (ppm)
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
1.8
1.4
f2 (ppm)


HMBC, 151 MHz, CD3OD
HO3SO
OSO3H
OH
O
(R)-4
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
f2 (ppm)


^{1}H NMR, 600 MHz, CD_3OD
HO_3SO
OSO_3H
OH
O
(*R*)-**3**
5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
f1 (ppm)


dqf-COSY, 600 MHz, CD3OD
HO3SO
OSO3H
OH
O
(R)-3
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
f2 (ppm)
1.5
2.0
2.5
3.0
3.5
4.0
4.5
f1 (ppm)


^{13}C-coupled HMQC, 151 MHz, CD_3OD
HO_3SO
OSO_3H
OH
O
(*R*)-**3**
f1 (ppm)
f2 (ppm)
25
30
35
40
45
50
55
60
65
70
75
80
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2


HMBC, 151 MHz, CD3OD
HO3SO
OSO3H
OH
O
(R)-3
f1 (ppm)
f2 (ppm)
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
4.1
3.6
3.1
2.6
2.1
1.6
1.1

References

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(4) Hong, S. H.; Sanders, D. P.; Lee, C. W.; Grubbs, R. H. *J. Am. Chem. Soc.* **2005**, *127*, 17160-17161
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