Toward Catalytic, Enantioselective Chlorolactonization of 1,2-Disubstituted Styrenyl Carboxylic Acids

Scott E. Denmark*, Pavel Ryabchuk, Matthew T. Burk and Bradley B. Gilbert

Department of Chemistry, University of Illinois Urbana-Champaign, Urbana, IL 61801

SUPPORTING INFORMATION

TABLE OF CONTENTS **PAGE**

General Experimental

All reactions were performed in oven (160 °C) and/or flame-dried glassware under an atmosphere of dry argon unless otherwise noted. Reaction solvents dichloromethane, toluene, DMF and THF (HPLC grade) were dried by percolation through neutral alumina in a solvent dispensing system. 1,1,1,3,3,3-Hexafluoro-2-propanol was dried over 3Å molecular sieves. Deuterochloroform and deuterodichloromethane were dried over 4Å molecular sieves before use. Triethylamine and pyridine were distilled from CaH_2.

ACS reagent grade ethyl acetate, dichloromethane and hexanes used for chromatography and recrystallization were purchased from Fisher. Column chromatography was performed using Merck grade 9385, 60 Å silica gel. Visualization was accomplished by UV light, potassium permanganate ($KMnO_4$) or iodine vapor. R_f values reported were measured using a 10 × 2 cm TLC plate in a developing chamber containing the solvent system described. Analytical and preparative thin-layer chromatography was performed on Merck silica gel plates with F-254 indicator.

Dibutyl sulfide, diphenyl sulfide, 1,3-diphenylimidazolidine-2-thione, quinuclidine, diphenyl selenide, tosyl amide, 2,4,6-trimethylaniline, diphenyl phosphoramide, tetrabutylammonium iodide, tetrabutylammonium acetate were purchased from commercial suppliers and used without further purification. Triethylamine and pyridine were distilled from CaH_2 prior to use.

^{1}H NMR, ^{13}C NMR spectra were recorded on 400 or 500 MHz NMR spectrometers (400 or 500 MHz, ^{1}H; 126 MHz, ^{13}C). Spectra were referenced to residual $CHCl_3$ (7.26 ppm ^{1}H; 77.00 ppm ^{13}C) or CD_2Cl_2 (5.32 ppm ^{1}H; 54.24 ppm ^{13}C). Assignments were obtained by reference to COSY and HMQC correlations. Chemical shifts are reported in ppm, multiplicities are indicated

by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), hep (heptet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. EI and ESI mass spectra mass spectral data are reported in the form of (*m*/*z*) versus intensity. Infrared spectra (IR) were using ATR and peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m (medium, 34-66%); w (weak, 0-33%). Melting points (mp) were determined in sealed tubes and are corrected. Analytical supercritical fluid chromatography was performed with spectrophotometric detection at 220 nm using Daicel Chiralpak OD and AS columns. Analytical gas chromatography was performed using 30-m Astec G TA or B PH (ChiraldexTM) columns. Analytical high performance liquid chromatography (HPLC) was performed using a built-in photometric detector (220 nm, 254 nm). Chiral separations were performed using a Chirapak ® AD column.

Literature Preparations

(E)-5-Phenyl-4-pentenoic acid **8** was prepared by Claisen rearrangement according to the procedure of Gao and co-workers.[1] 4-phenylpent-4-enoic acid was prepared by Wittig reaction according to the procedure of Borhan and co-workers.[2] Dibutyl selenide,[3] $Cy_3P{=}S$,[4] $Bu_3P{=}S$,[5] $(Me_2N)_3P{=}S$[6], $Bu_3P{=}Se$[7], $(Me_2N)_3P{=}Se$[7] were prepared by reaction of their parent phosphines with elemental S or Se according to the procedures specified. 1-Chlorobenzatriazole was prepared according the procedure of Cava and co-workers.[8]

Chlorolactonizations

Lewis Base Survey.

General procedure (Table 1). An 5-mm, oven-dried NMR tube equipped with a septum was charged with chlorinating agent (0.24 mmol, 1.2 equiv) and then the tube was purged with

Ar through a needle. Deuterochloroform (with 1% v/v TMS) (1.0 mL) was added via syringe and then the tube was agitated with a vortex mixer. **8** (35.2 mg, 0.2 mmol, 1.0 equiv) was added as a solid and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then a Lewis base was added and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy after 20 h. Conversion of **8** and yields of **9** and respectively were calculated by comparing the integrated area of the signal of tetramethylsilane standard (δ 0.0 (s, 12H)) with the signal for H-6 of **9** (δ 5.49 (d, J = 5.8 Hz, 1H)) and H-5 of **9** (δ 6.45 (d, J = 15.8 Hz, 1H)).

Table 1, Entry 5

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and $(Me_2N)_3P{=}S$ (3.9 mg, 0.02 mmol, 0.1 equiv). Yield of 30% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 6

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and $Ph_3P{=}S$ (5.9 mg, 0.02 mmol, 0.1 equiv). Yield of 23% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 7

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and $Bu_3P{=}S$ (4.7 mg, 0.02 mmol, 0.1 equiv). Yield of 21% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 8

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and $(Me_2N)_2C{=}S$ (2.6

mg, 0.02 mmol, 0.1 equiv). Yield of 29% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 9

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and 1,3-diphenylimidazolidine-2-thione (5.1 mg, 0.02 mmol, 0.1 equiv). Yield of 25% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 10

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and 1,3-$(Me_2N)_3P$=Se (4.9 mg, 0.02 mmol, 0.1 equiv). Yield of 25% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 11

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and Cy_3P=Se (7.2 mg, 0.02 mmol, 0.1 equiv). Yield of 22% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 12

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and Ph_2Se (4.6 mg, 0.02 mmol, 0.1 equiv). Yield of 0% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 13

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and Bu_2Se (3.9 mg, 0.02 mmol, 0.1 equiv). Yield of 0% was observed by ^{1}H NMR spectroscopy after 20 h.

Table 1, Entry 14

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and Bu_2S (2.9 mg, 0.02 mmol, 0.1 equiv). Yield of 38% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 15

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and Ph_2S (3.7 mg, 0.02 mmol, 0.1 equiv). Yield of 13% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 16

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and 2,4,6-trimethyl aniline (2.7 mg, 0.02 mmol, 0.1 equiv). Yield of 5% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 17

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and $TsNH_2$ (3.4 mg, 0.02 mmol, 0.1 equiv). Yield of 0% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 18

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and diphenyl phosphoramide (5.0 mg, 0.02 mmol, 0.1 equiv). Yield of 0% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 19

According to General Procedure, an NMR tube was charged with NCS (31.7 mg, 0.24

mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and quinuclidine (2.2 mg, 0.02 mmol, 0.1 equiv). Yield of 45% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 20

According to General Procedure, an NMR tube was charged with NCP (43.6 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and quinuclidine (2.2 mg, 0.02 mmol, 0.1 equiv). Yield of 72% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 21

According to General Procedure, an NMR tube was charged with DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and quinuclidine (2.2 mg, 0.02 mmol, 0.1 equiv). Yield of 96% was observed by ^1H NMR spectroscopy after 20 h.

Table 1, Entry 22

According to General Procedure, an NMR tube was charged with 1-CBT (36.8 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and quinuclidine (2.2 mg, 0.02 mmol, 0.1 equiv). Yield of 77% was observed by ^1H NMR spectroscopy after 20 h.

Chiral Lewis Base Survey

General Procedure (Scheme 8): A 5-mm, oven-dried NMR tube equipped with a septum was charged with 1-CBT (10 mg, 0.078 mmol, 1.2 equiv) and 1,2,4,5-$C_6H_2Cl_4$ (10.2 mg). The tube was then purged with Ar through a needle. Deuterochloroform (600 μL) was added via syringe and then the tube was agitated with a vortex mixer. **8** (12.1 mg, 0.066 mmol) was added as a solid and then the tube was agitated with a vortex mixer. Solution of $(DHQD)_2PHAL$ (5.0 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv) was added via syringe and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^1H NMR spectroscopy after 1 h and 24 h. After 24 h, a solution of butyl vinyl ether in ethanol (15 vol%, 100 μL) was added

to quench the reaction. The resulting solution was concentrated in vacuo (23 ºC, 6 mmHg). The residue was purified by column chromatography (silica gel (1 g), 1 cm diam, hexane/CH_2Cl_2, 20:80) to afford 8.8 mg (66%) of **9** as a colorless oil.

SFC: (5*R*,6*S*)/(5*S*,6*R*)-**9**, t_R 7.0 min (45.0%); (5*S*,6*R*)/(5*R*,6*S*)-**9**, t_R 11.5 min (55.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Nicotine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and Nicotine (1.0 μL 0.0065 mmol, 0.1 equiv). A yield of 39% was observed by ^{1}H NMR spectroscopy after 24 h. The reaction was quenched after 24 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 6.5 mg (45%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (49.6%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.4%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Dihydrocinchonidine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a suspension of dihydrocinchonidine (1.9 mg in 150 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 93% was observed by ^{1}H NMR spectroscopy after 26 h. The reaction was quenched after 26 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 11.9 mg (89%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (48.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (52.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Quinidine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078

mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a solution of quinidine (1.9 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 87% was observed by ^{1}H NMR spectroscopy after 2 h. The reaction was quenched after 3 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 10.5 mg (77%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (48.8%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (51.2%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Cinchonine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (300 μL), **8** (11.2 mg, 0.066 mmol), and a a suspension of cinchonine (1.9 mg in 300 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 95% was observed by ^{1}H NMR spectroscopy after 0.8 h. The reaction was quenched after 3 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 9.3 mg (67%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (49.4%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.6%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Quinine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a solution of quinine (2.1 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 82% was observed by ^{1}H NMR spectroscopy after 2 h. The reaction was quenched after 2 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 10.4 mg (76%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (49.4%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.6%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of Cinchonidine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and cinchonidine (1.9 mg, 0.0065 mmol, 0.1 equiv). A yield of 81% was observed by ^{1}H NMR spectroscopy after 2.2 h. The reaction was quenched after 3 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 8.0 mg (56%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (48.4%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (51.6%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of O-Methylcinchonidine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (550 μL), **8** (11.2 mg, 0.066 mmol), and a solution of *O*-methylcinchonidine (2.0 mg in 100 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 81% was observed by ^{1}H NMR spectroscopy after 2.2 h. The reaction was quenched after 3 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 8.0 mg (56%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (49.5%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.5%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of (*1R,3S,5aS,7aS,7bR*)-Octahydro-1-benzyloxy-1-phenyl-7b-methyl-2H-cyclopenta[gh]pyrrolizine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a solution of catalyst (2.1 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 96% was observed by ^{1}H NMR spectroscopy after 2 h. The reaction was quenched after 3 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 8.5 mg (62%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (51.1%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (48.9%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of *(R,R)*-N,N,N',N'-Tetramethylcyclohexanediamine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a solution of catalyst (2.1 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 73% was observed by ^{1}H NMR spectroscopy after 22.5 h. The reaction was quenched after 24 h to afford after chromatography (silica gel (1 g), CH_2Cl_2) 8.5 mg (62%) of **9**.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (52.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (48.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with 1-CBT in the presence of (-)-Sparteine.

According to General Procedure, an NMR tube was charged with 1-CBT (12 mg, 0.078 mmol , 1.2 equiv), 1,2,4,5-$C_6H_2Cl_2$ (11.1 mg), $CDCl_3$ (600 μL), **8** (11.2 mg, 0.066 mmol), and a solution of catalyst (2.1 mg in 50 μL of $CDCl_3$, 0.0065 mmol, 0.1 equiv). A yield of 47% was observed by ^{1}H NMR spectroscopy after 22.5 h. The reaction was quenched after 24 h.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (52.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (48.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with DCDMH in the presence of 15.

According to General Procedure, an NMR tube was charged with DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and C_3-symmetric quinuclidine **15** (6.8 mg, 0.02 mmol, 0.1 equiv). A yield of 29% was observed by ^{1}H NMR spectroscopy after 21 h. The reaction was quenched after 24 h.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (50.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with DCDMH in the presence of 19.

According to General Procedure, an NMR tube was charged with DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and C_3-symmetric quinuclidine **19** (6.8 mg, 0.02 mmol, 0.1 equiv). A yield of 22% was observed by ^{1}H NMR spectroscopy after 21 h. The reaction was quenched after 24 h.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (50.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of 8 with DCDMH in the presence of 20.

According to General Procedure, an NMR tube was charged with DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv), $CDCl_3$ (1.0 mL) and **8** (35.2 mg, 0.2 mmol, 1.0 equiv) and diphenyl quinuclidine **20** (5.3 mg, 0.02 mmol, 0.1 equiv). A yield of 75% was observed by ^{1}H NMR spectroscopy after 1.5 h. The reaction was quenched after 3 h.

SFC: (5*R*,6*S*)/(5*S*,6*R*) -**9**, t_R 7.0 min (50.0%); (5*S*,6*R*)/(5*R*,6*S*) -**9**, t_R 11.5 min (50.0%); (Chirapak AD, 125 bar, 3 mL/min, 5% MeOH in CO_2).

Chlorolactonization of Model Substrates.

Chlorolactonization of 22 with DCDMH in the presence of quinuclidine (Scheme 11).

An 5-mm, oven-dried NMR tube equipped with a septum was charged with DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv) and then the tube was purged with Ar through a needle. Deuterochloroform (with 1% v/v TMS) (1.0 mL) was added via syringe and then the tube was agitated with a vortex mixer. **22** (58.1 mg, 0.2 mmol, 1.0 equiv) was added as an oil and then the

tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then quinuclidine (5.3 mg, 0.02 mmol, 0.1 equiv was added and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy after 12 h. A yield of 3% was calculated by comparing the integrated area of the signal of tetramethylsilane standard (δ 0.0 (s, 12H)) with the signal for H-6 of **9** (δ 5.49 (d, J = 5.8 Hz, 1H)).

Chlorolactonization of 23 with DCDMH in the absence of the catalyst (Table 2, Entry 1).

A 5-mm, oven-dried NMR tube equipped with a septum was charged with **23** (83.5 mg, 0.2 mmol, 1.0 equiv) and then the tube was purged with Ar through a needle. Deuteriochloroform (with 1% v/v TMS) (1.0 mL) was added via syringe and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv) was added and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy after 2.5 h. Yields of 46% for **9** and 17 % for **24** were calculated by comparing the integrated area of the signal of tetramethylsilane standard (δ 0.0 (s, 12H)) with the signal for H-6 of **9** (δ 5.49 (d, J = 5.8 Hz, 1H)) and H-6 of **9** (δ 5.07 (d, J = 5.5 Hz, 1H)) correspondingly.

Chlorolactonization of 23 with DCDMH in the presence of 20 (Table 2, Entry 2).

A 5-mm, oven-dried NMR tube equipped with a septum was charged with **23** (83.5 mg, 0.2 mmol, 1.0 equiv) and diphenyl quinuclidine **20** (5.3 mg, 0.02 mmol, 0.1 equiv), then the tube was purged with Ar through a needle. Deuteriochloroform (with 1% v/v TMS) (1.0 mL) was added via syringe and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv) was

added and the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy after 2.5 h. Yields of 48% for **9** and 16 % for **24** were calculated by comparing the integrated area of the signal of tetramethylsilane standard (δ 0.0 (s, 12H)) with the signal for H-6 of **9** (δ 5.49 (d, J = 5.8 Hz, 1H)) and H-6 of **9** (δ 5.07 (d, J = 5.5 Hz, 1H)) correspondingly.

Chlorolactonization of 23 with DCDMH in the presence of quinuclidine (Table 2, Entry 3).

A 5-mm, oven-dried NMR tube equipped with a septum was charged with **23** (83.5 mg, 0.2 mmol, 1.0 equiv) and quinuclidine (2.2 mg, 0.02 mmol, 0.1 equiv), then the tube was purged with Ar through a needle. Deuteriochloroform (with 1% v/v TMS) (1.0 mL) was added via syringe and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then DCDMH (47.3 mg, 0.24 mmol, 1.2 equiv) was added and the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy after 20 min. Yields of 76% for **9** and 19 % for **24** were calculated by comparing the integrated area of the signal of tetramethylsilane standard (δ 0.0 (s, 12H)) with the signal for H-6 of **9** (δ 5.49 (d, J = 5.8 Hz, 1H)) and H-6 of **9** (δ 5.07 (d, J = 5.5 Hz, 1H)) correspondingly.

General Procedure. Solvolytic Substitution with 25 (Table 3).

A 5-mm, oven-dried NMR tube equipped with a septum was charged with tetrabutylammonium acetate (1.0 – 20.0 equiv), then the tube was purged with Ar through a needle. HFIP (0.25 mL) and deuteriodichloromethane (0.25 mL) were added via syringe and then the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy and then **25** (11.7 mg, 0.05 mmol, 1.0 equiv) was added via syringe and the tube was agitated with a vortex mixer. The reaction mixture was analyzed by ^{1}H NMR spectroscopy;

conversion of starting material **25** was monitored by the disappearance of diagnostic benzylic proton signal of **25** δ 5.69 (d, *J* = 5.45 Hz, 1H). Diastereomeric ratio of products *anti*–**26**/*syn*–**26** was calculated by comparing the integrated areas of benzylic signals: δ 5.91 (d, *J* = 5.3 Hz, 1H) for *anti*–**26** and δ 5.84 (d, J = 7.2 Hz, 1H) for *syn*–**26** correspondingly.

Table 3, Entry 1.

According to General Procedure, an NMR tube was charged with tetrabutylammonium acetate (13 mg, 0.05 mmol, 1.0 equiv), HFIP (0.25 mL), deuteriodichloromethane (0.25 mL) and **25** (11.7 mg, 0.05 mmol, 1.0 equiv). The reaction mixture was analyzed by ^{1}H NMR spectroscopy; full conversion was achieved after 15 minutes. Diastereomeric ratio of products *anti*–**26**/*syn*–**26** was determined to be 62:38 and was constant during the course of the reaction.

Table 3, Entry 2.

According to General Procedure, an NMR tube was charged with tetrabutylammonium acetate (26.0 mg, 0.1 mmol, 2.0 equiv), HFIP (0.25 mL), deuteriodichloromethane (0.25 mL) and **25** (11.7 mg, 0.05 mmol, 1.0 equiv). The reaction mixture was analyzed by ^{1}H NMR spectroscopy; full conversion was achieved after 17 minutes. Diastereomeric ratio of products *anti*–**26**/*syn*–**26** was determined to be 60:40 and was constant during the course of the reaction.

Table 3, Entry 3.

According to General Procedure, an NMR tube was charged with tetrabutylammonium acetate (64.9 mg, 0.25 mmol, 5.0 equiv), HFIP (0.25 mL), deuteriodichloromethane (0.25 mL) and **25** (11.7 mg, 0.05 mmol, 1.0 equiv). The reaction mixture was analyzed by ^{1}H NMR spectroscopy; full conversion was achieved after 70 minutes. Diastereomeric ratio of products *anti*–**26**/*syn*–**26** was determined to be 62:38 and was constant during the course of the reaction.

Table 3, Entry 4.

According to General Procedure, an NMR tube was charged with tetrabutylammonium acetate (129.7 mg, 0.5 mmol, 10.0 equiv), HFIP (0.25 mL), deuteriodichloromethane (0.25 mL) and **25** (11.7 mg, 0.05 mmol, 1.0 equiv). The reaction mixture was analyzed by ^{1}H NMR spectroscopy; 76% conversion was achieved after 48 h. Diastereomeric ratio of products *anti*–**26**/*syn*–**26** was determined to be 62:38 and was constant during the course of the reaction.

Table 3, Entry 5.

According to General Procedure, an NMR tube was charged with tetrabutylammonium acetate (259.5 mg, 1.0 mmol, 20.0 equiv), HFIP (0.25 mL), deuteriodichloromethane (0.25 mL) and **25** (11.7 mg, 0.05 mmol, 1.0 equiv). The reaction mixture was analyzed by ^{1}H NMR spectroscopy; no conversion was achieved after 48 h.

References

(1) Wang, M.; Gao, L. X.; Mai, W. P.; Xia, A. X.; Wang, F.; Zhang, S. B. *J. Org. Chem.* **2004**, *69*, 2874.

(2) Zheng, T.; Narayan, R. S.; Schomaker, J. M.; Borhan, B. *J. Am. Chem. Soc.* **2005**, *127*, 6946.

(3) Krief, A.; Trabelsi, M.; Dumont, W.; Derock, M. *Synlett* **2004**, *10*, 1751.

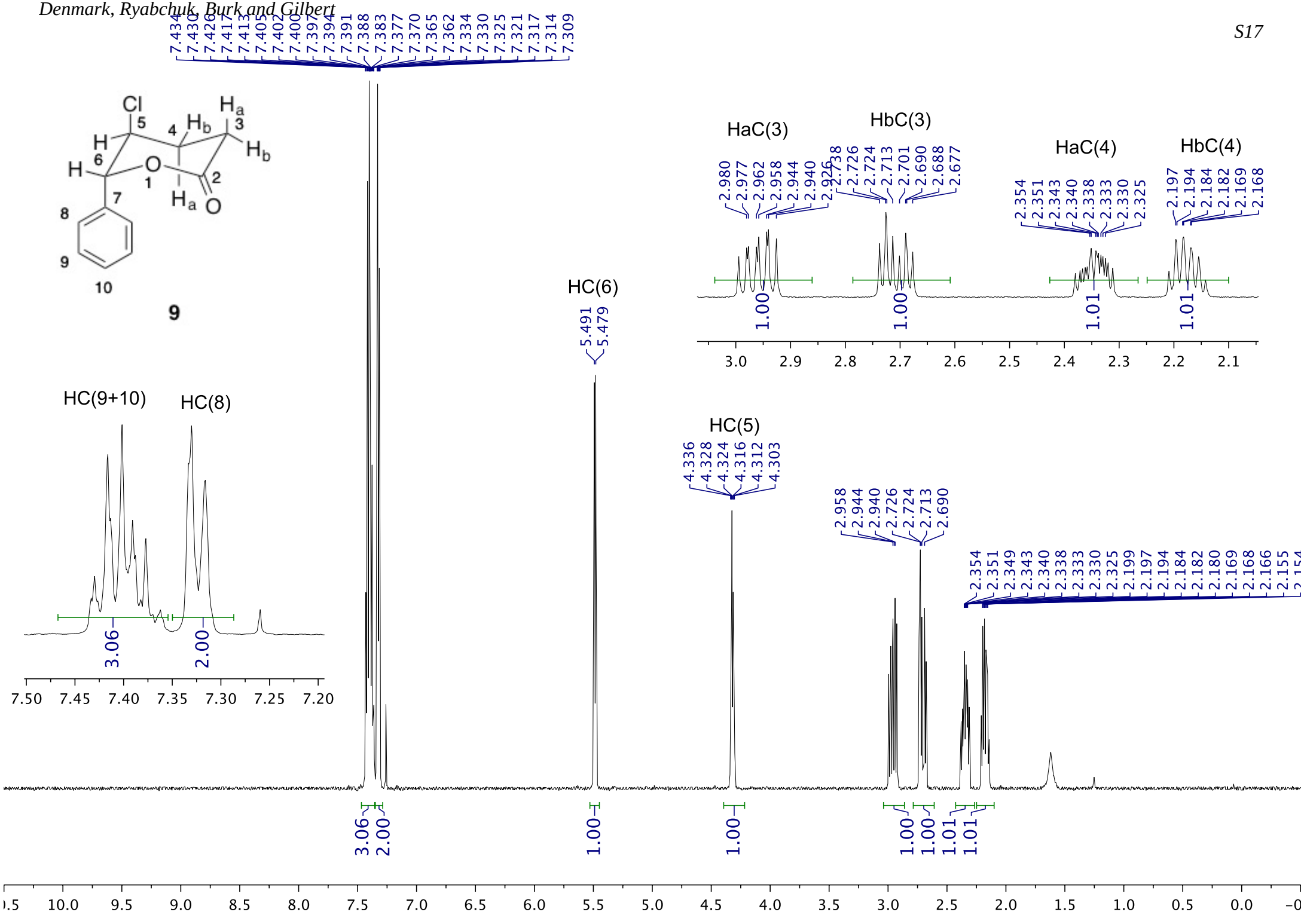
(4) Janssen, R. A. J.; Kingma, J. A. J. M.; Buck, H. M. *J. Am. Chem. Soc.* **1988**, *110*, 3018.

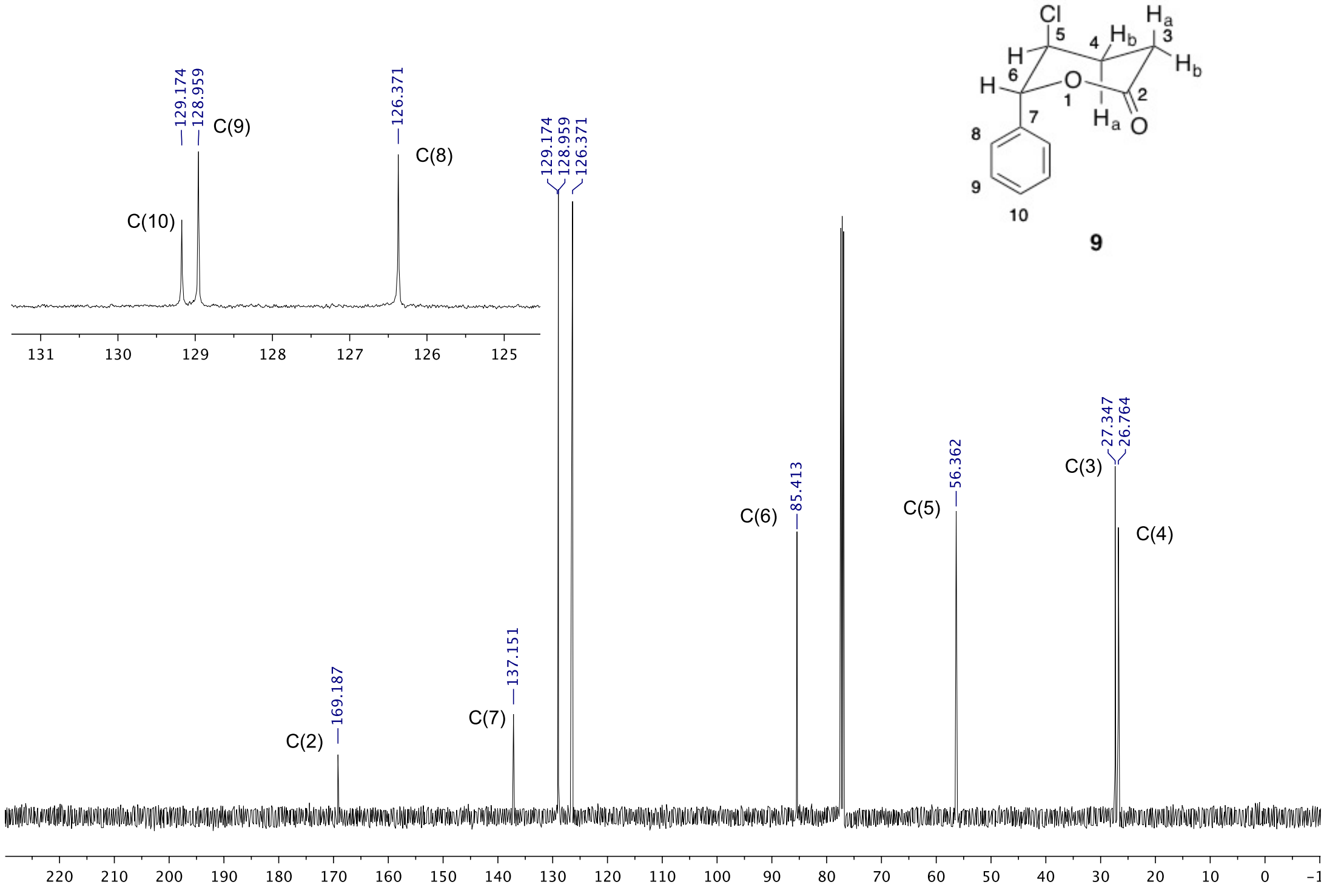
(5) Schmutzler, R. *Inorg. Chem.* **1964**, *3*, 421.

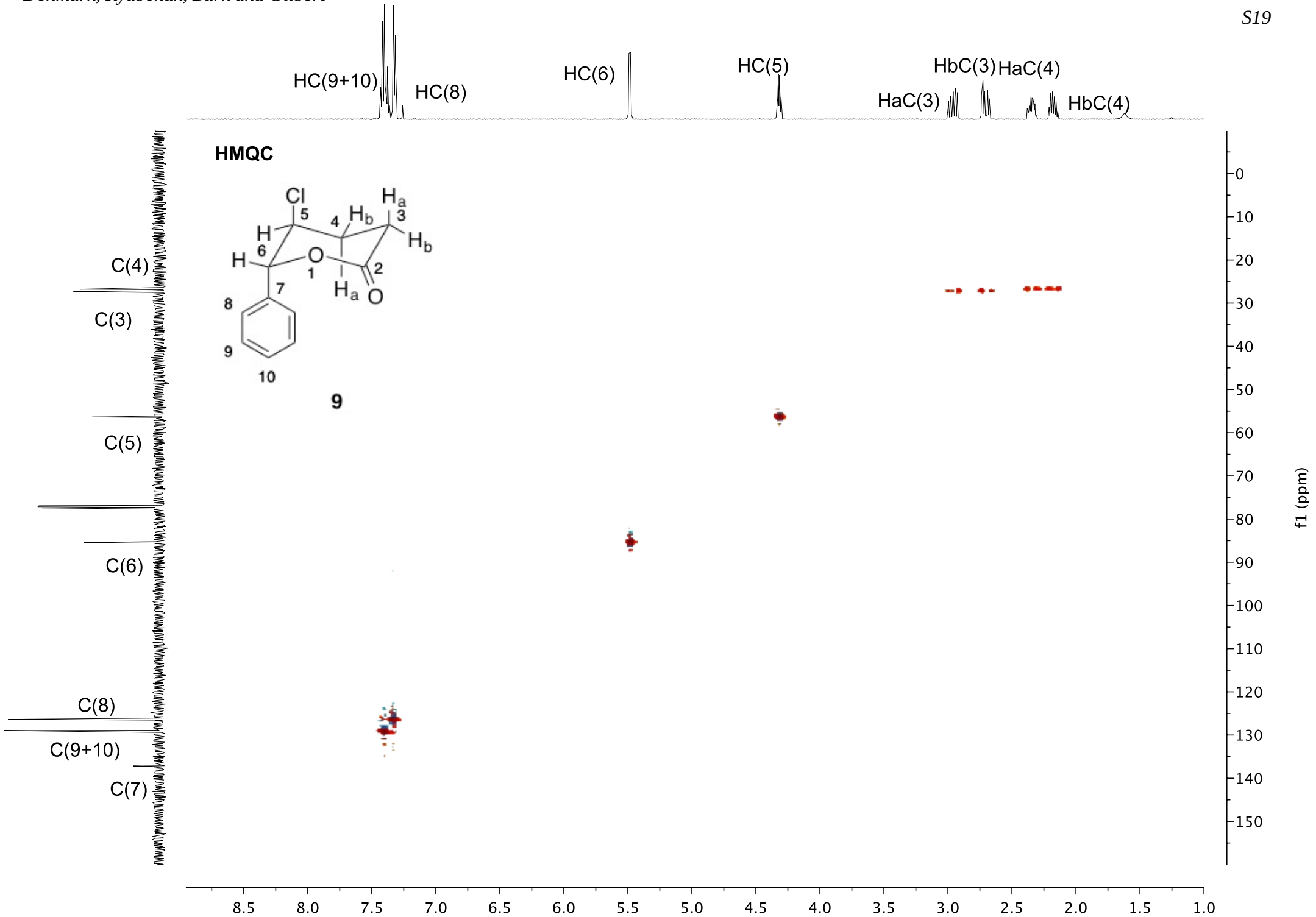
(6) Haynes, R. K.; Indorato, C. *Aust. J. Chem.* **1984**, *37*, 1183.

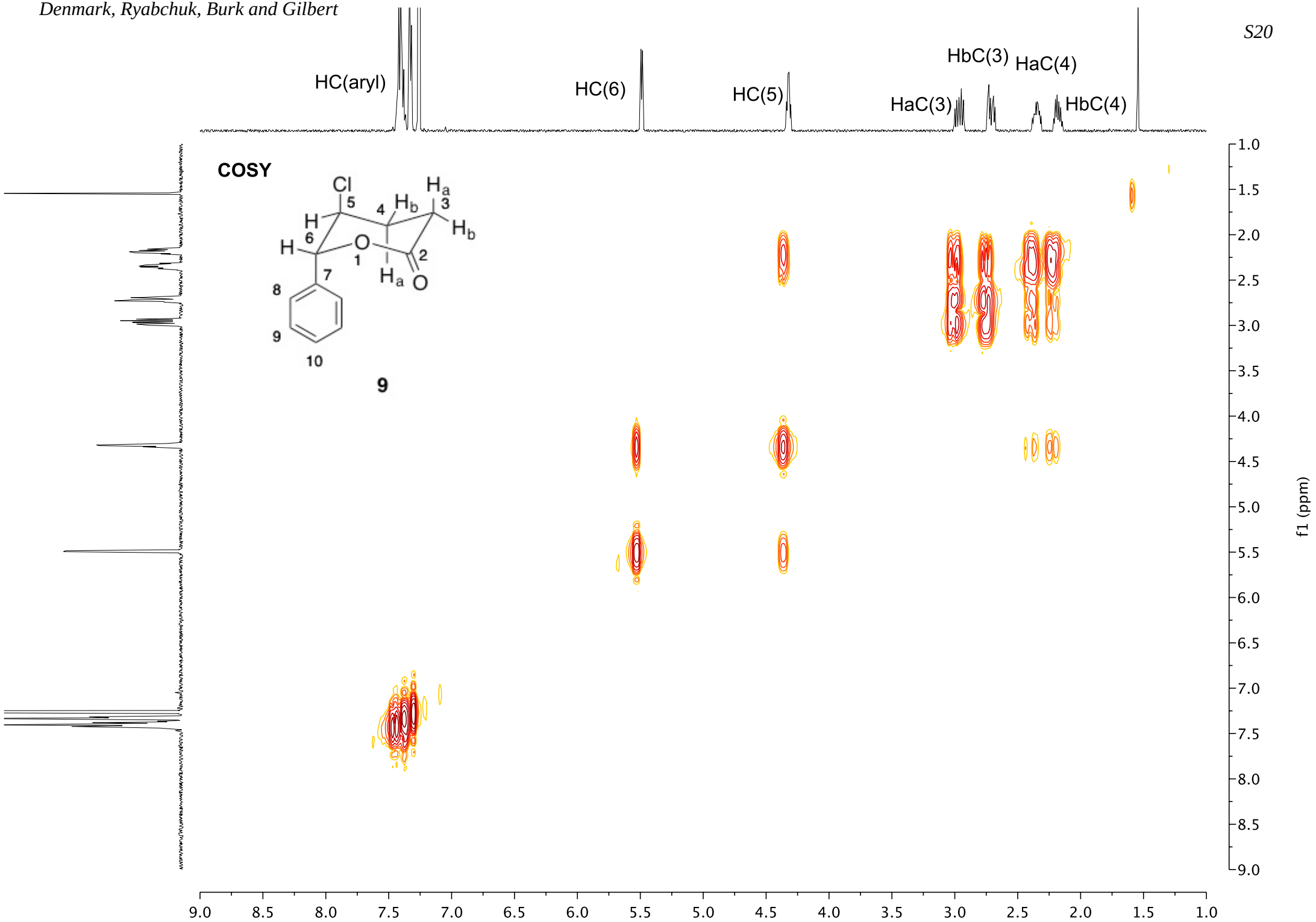
(7) Sova, M.; Mravljak, J.; Kovač, A.; Pečar, S.; Časar, Z.; Gobec, S. *Synthesis* **2010**, *2010*, 3433.

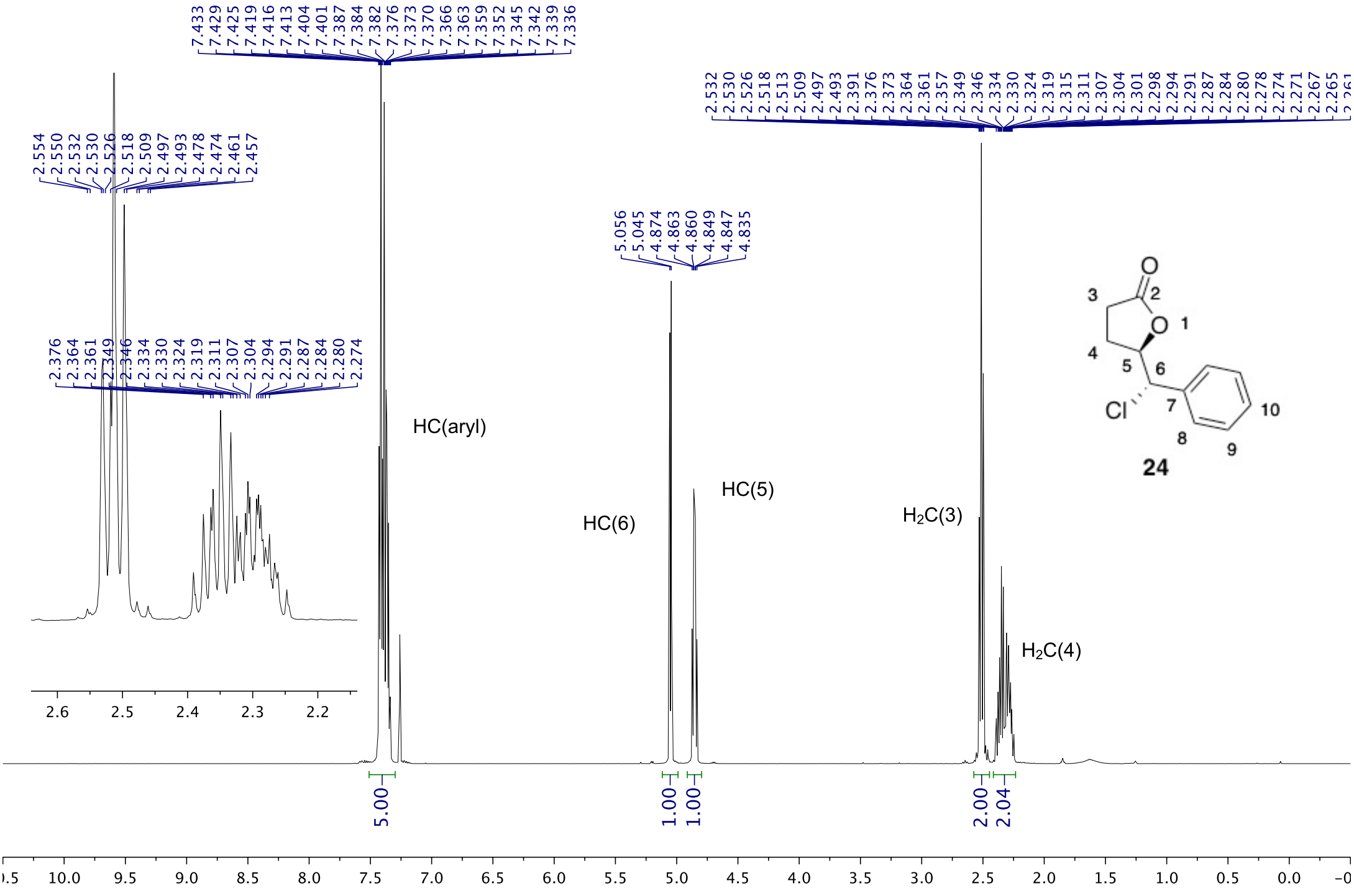
(8) Hughes, T. V.; Hammond, S. D.; Cava, M. P *J. Org. Chem.* **1998**, *63*, 401.

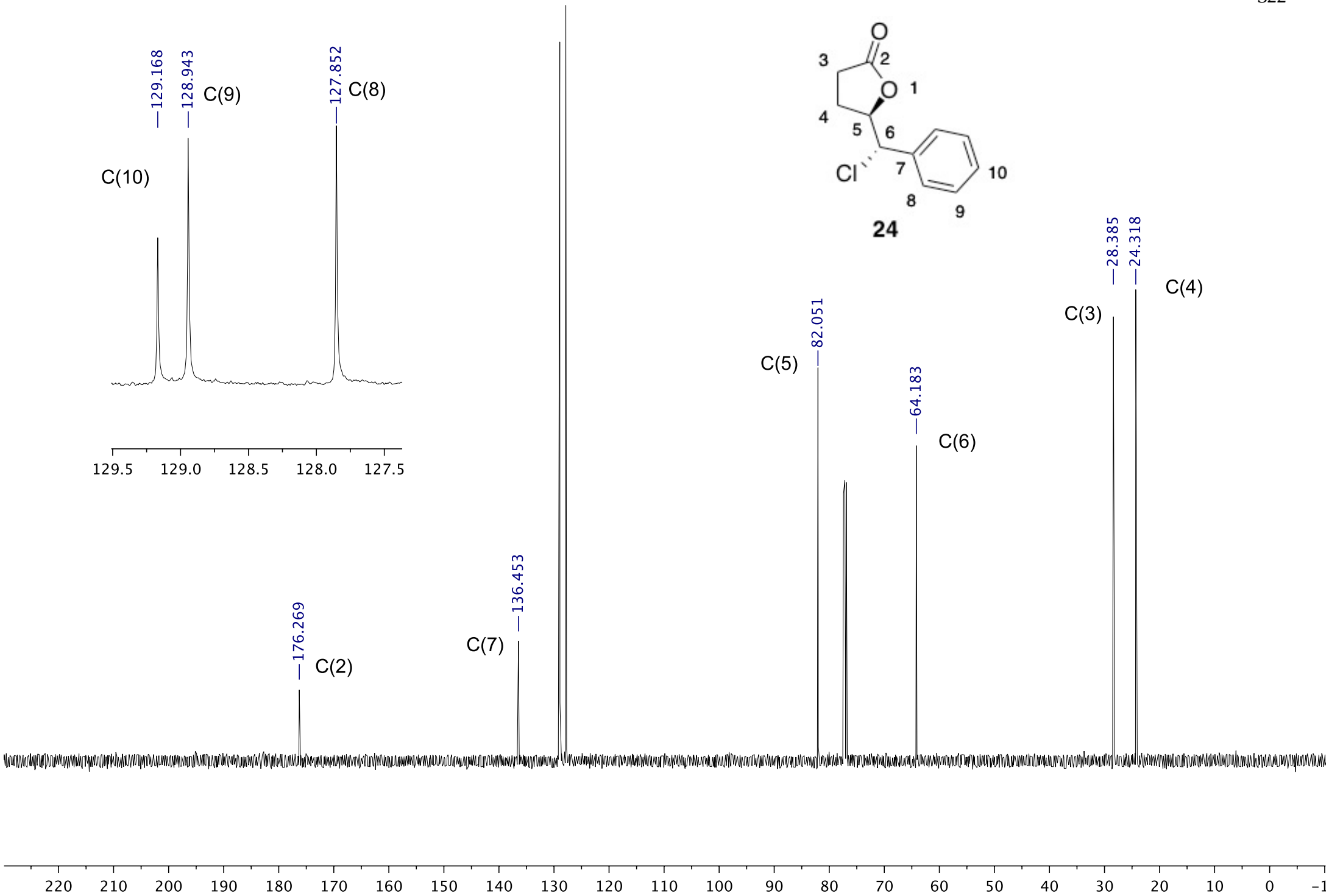

Cl
5
4
Hb
Ha
3
H
Hb
H
6
O
1
2
7
Ha
O
8
9
10
9
HaC(3)
HbC(3)
HaC(4)
HbC(4)
HC(6)
HC(9+10)
HC(8)
HC(5)
1.00
1.00
1.01
1.01
3.06
2.00
1.00
1.00
1.00
1.01
1.01

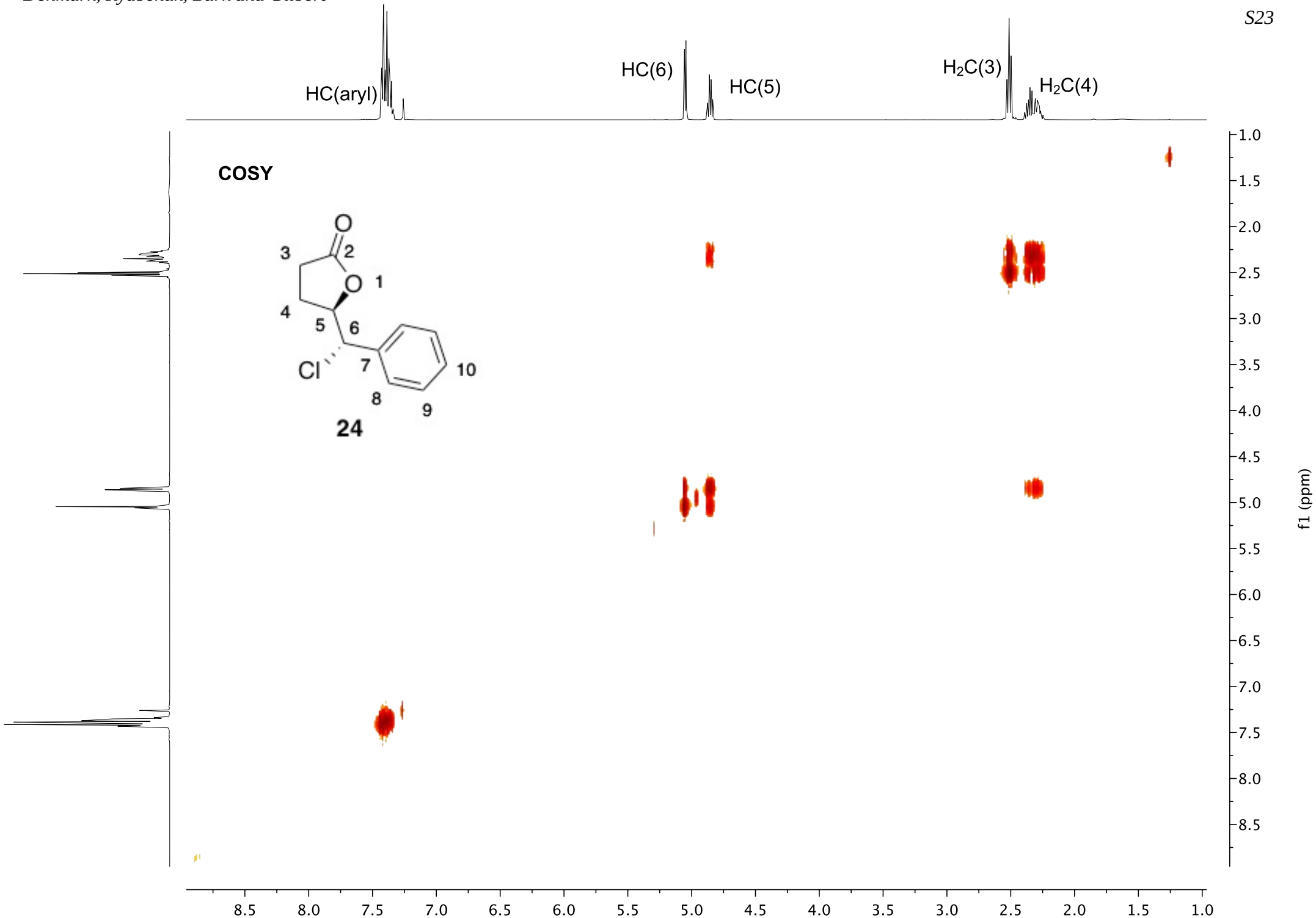

129.174
128.959
C(9)
126.371
C(8)
C(10)
131
130
129
128
127
126
125
129.174
128.959
126.371
Cl
5
4
H_b
H_a
3
H
6
H_b
H
O
1
2
7
H_a
O
8
9
10
9
C(2)
169.187
137.151
C(7)
C(6)
85.413
C(5)
56.362
C(3)
27.347
26.764
C(4)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1

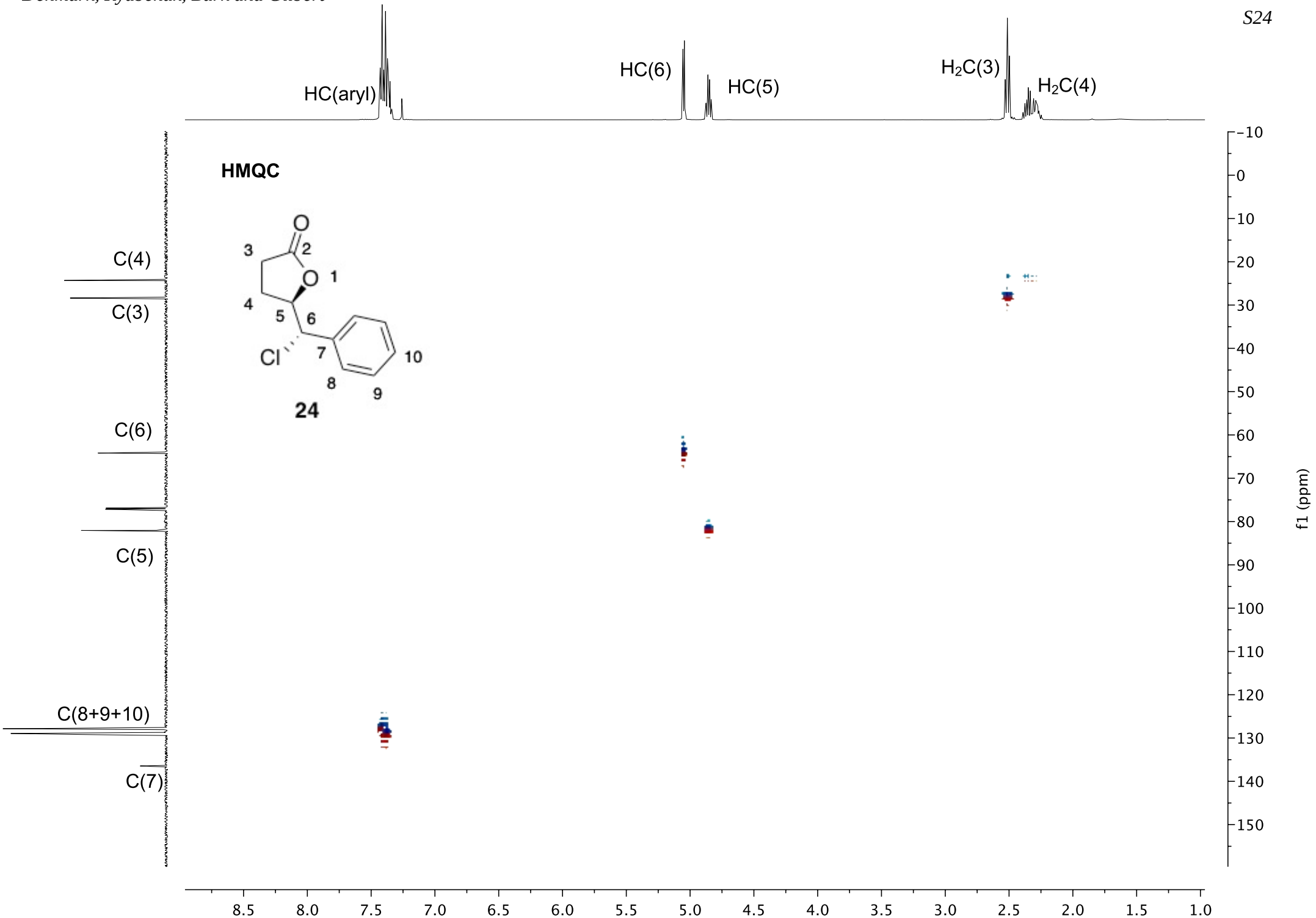

HC(9+10)
HC(8)
HC(6)
HC(5)
HbC(3)
HaC(4)
HaC(3)
HbC(4)
HMQC
Cl
5
4
H_b
H_a
3
H_b
H
6
H
O
1
2
7
H_a
O
8
9
10
9
C(4)
C(3)
C(5)
C(6)
C(8)
C(9+10)
C(7)
f1 (ppm)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

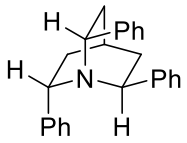

HC(aryl)
HC(6)
HC(5)
HaC(3)
HbC(3)
HaC(4)
HbC(4)
COSY
Cl
5
4
Hb
Ha
3
Hb
H
6
H
O
1
2
7
Ha
O
8
9
10
9
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0


HC(aryl)
HC(6)
HC(5)
H2C(3)
H2C(4)
5.00
1.00
1.00
2.00
2.04
Cl
24

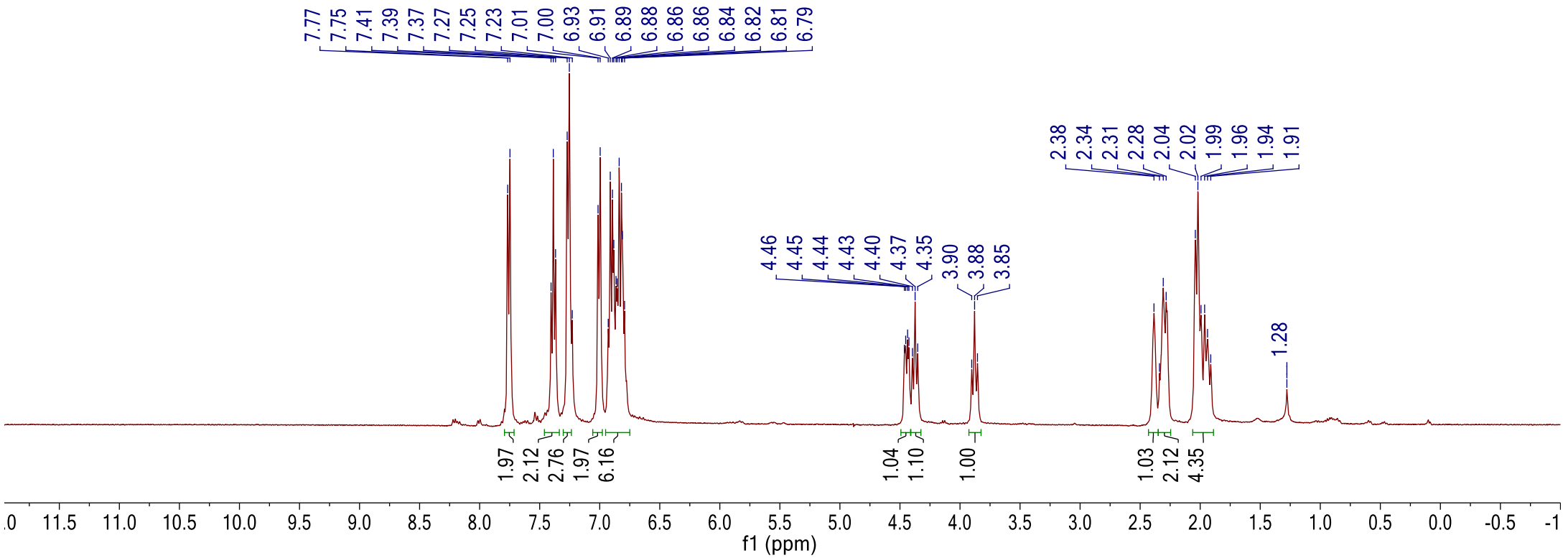

129.168
128.943
C(9)
127.852
C(8)
C(10)
129.5
129.0
128.5
128.0
127.5
O
2
3
O
1
4
5
6
Cl
7
10
8
9
24
28.385
24.318
C(4)
C(3)
82.051
C(5)
64.183
C(6)
176.269
C(2)
136.453
C(7)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1

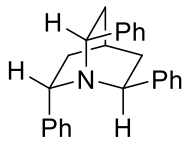

HC(aryl)
HC(6)
HC(5)
H2C(3)
H2C(4)
COSY
O
2
3
O
1
4
5
6
Cl
7
10
8
9
24
f1 (ppm)
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5


HC(aryl)
HC(6)
HC(5)
H2C(3)
H2C(4)
HMQC
C(4)
C(3)
C(6)
C(5)
C(8+9+10)
C(7)
24
f1 (ppm)

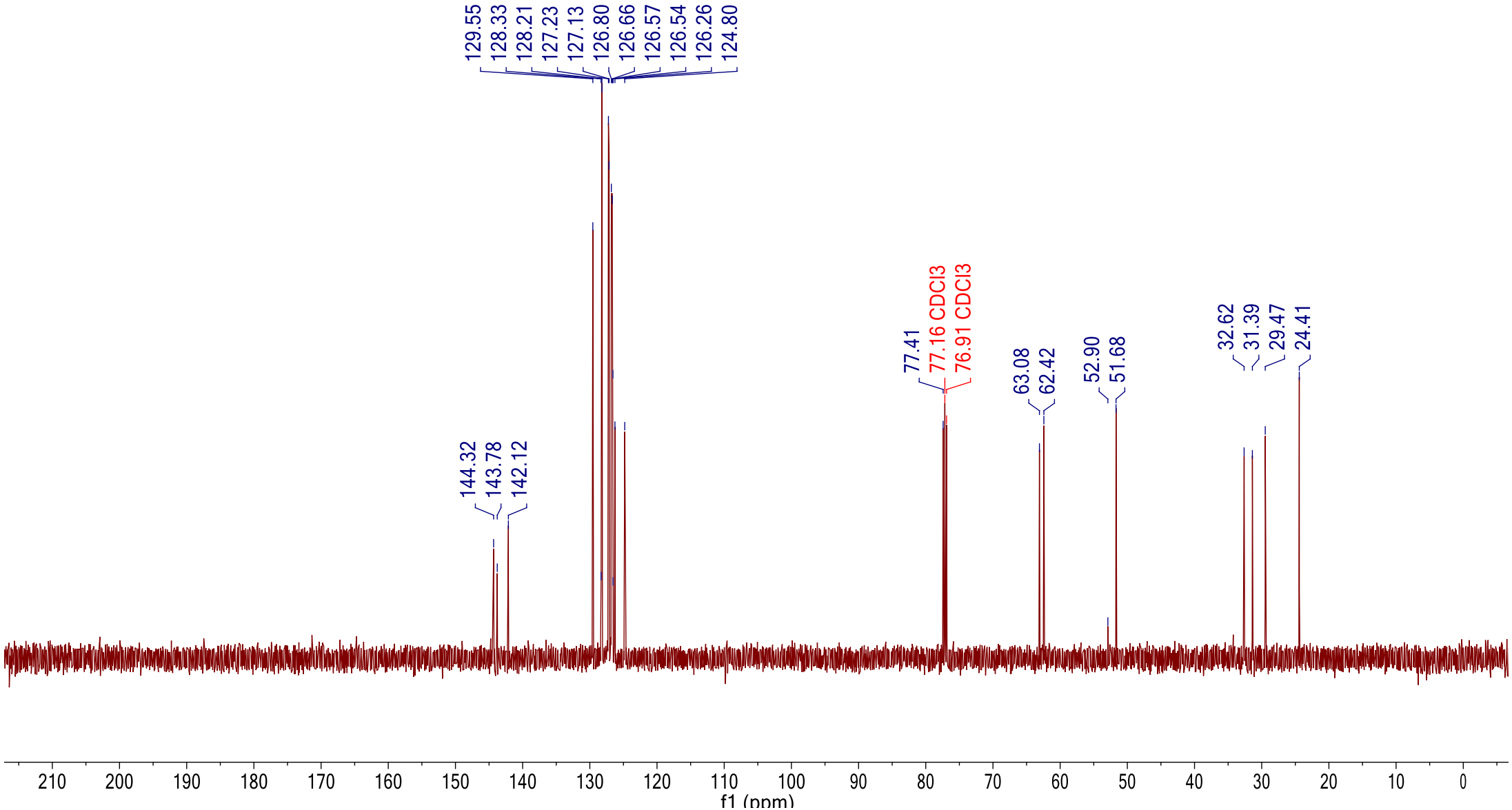

H
Ph
H
N
Ph
Ph
H

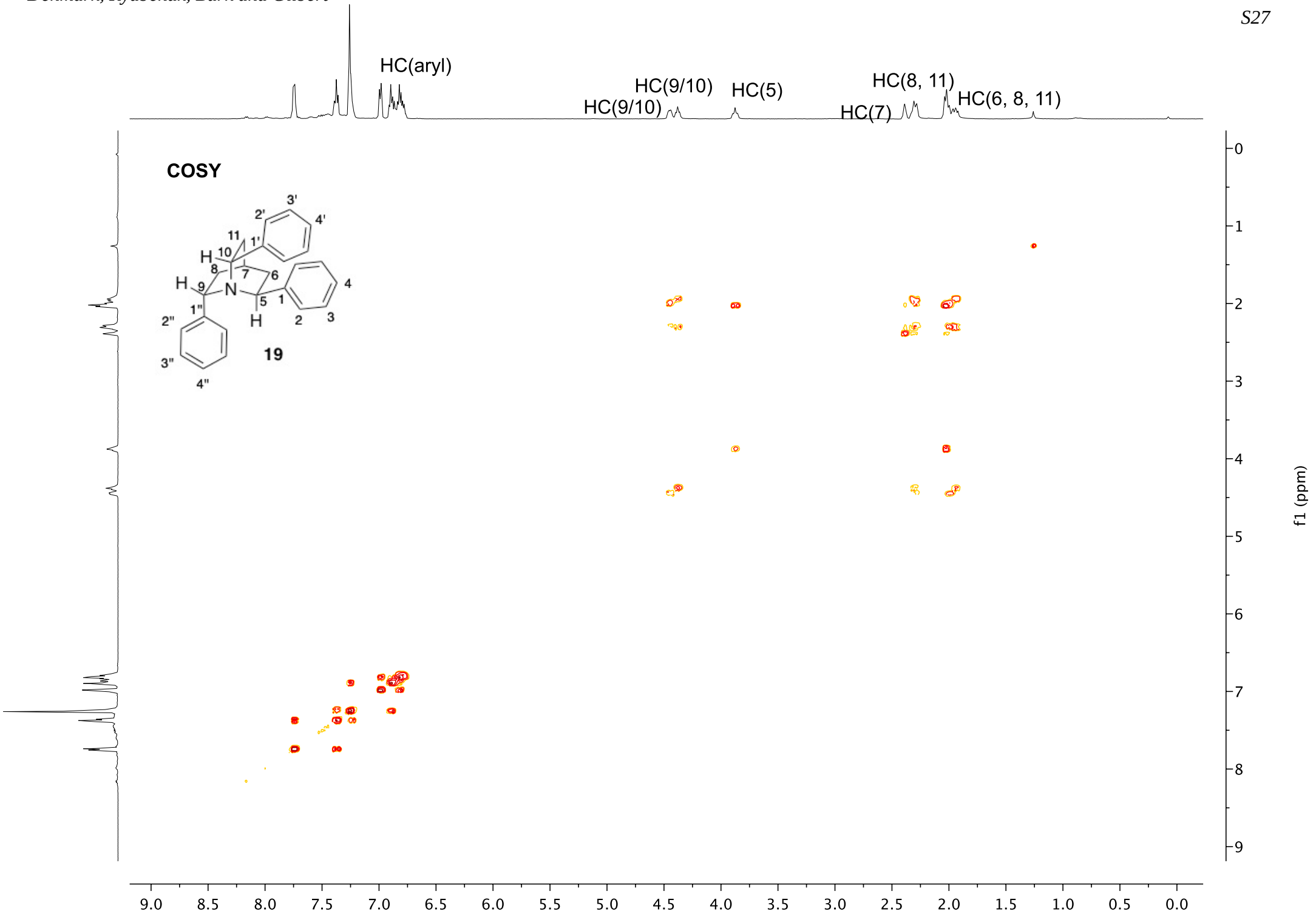
19

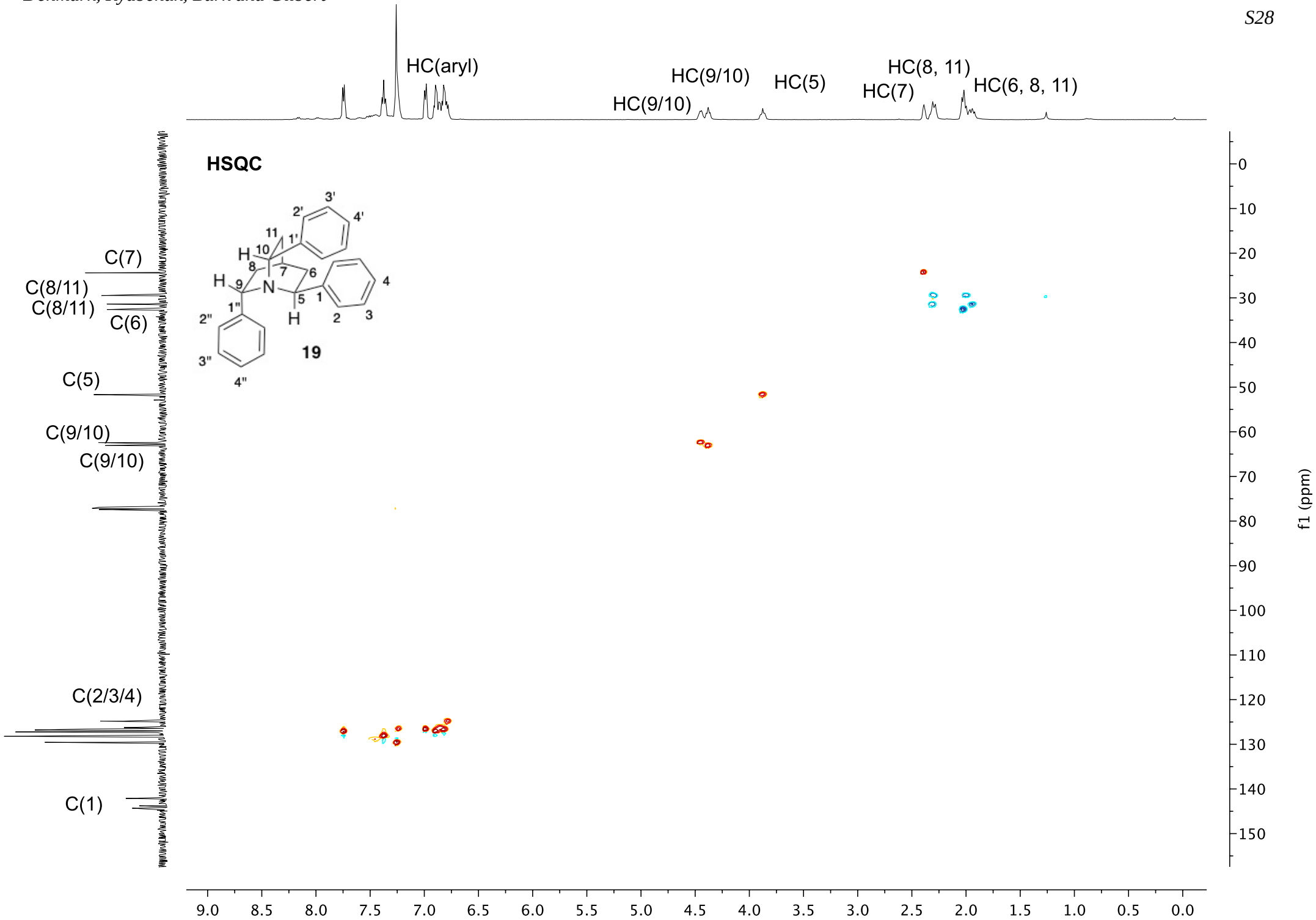

7.77
7.75
7.41
7.39
7.37
7.27
7.25
7.23
7.01
7.00
6.93
6.91
6.89
6.88
6.86
6.86
6.84
6.82
6.81
6.79
4.46
4.45
4.44
4.43
4.40
4.37
4.35
3.90
3.88
3.85
2.38
2.34
2.31
2.28
2.04
2.02
1.99
1.96
1.94
1.91
1.28
1.97
2.12
2.76
1.97
6.16
1.04
1.10
1.00
1.03
2.12
4.35
f1 (ppm)

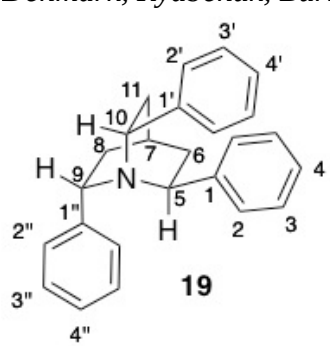

H
Ph
H
N
Ph
Ph
H

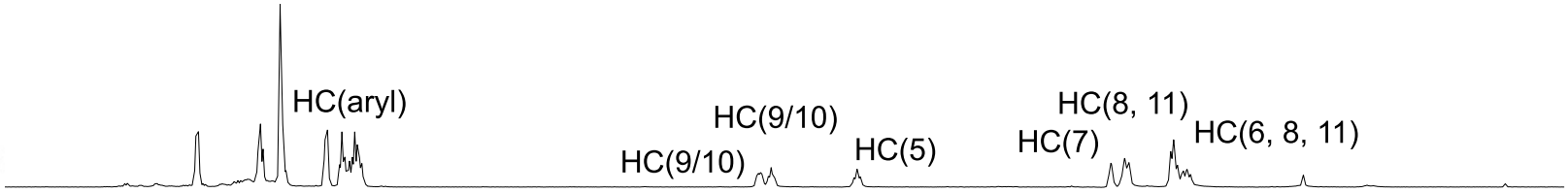
19


129.55
128.33
128.21
127.23
127.13
126.80
126.66
126.57
126.54
126.26
124.80
144.32
143.78
142.12
77.41
77.16 CDCl3
76.91 CDCl3
63.08
62.42
52.90
51.68
32.62
31.39
29.47
24.41
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

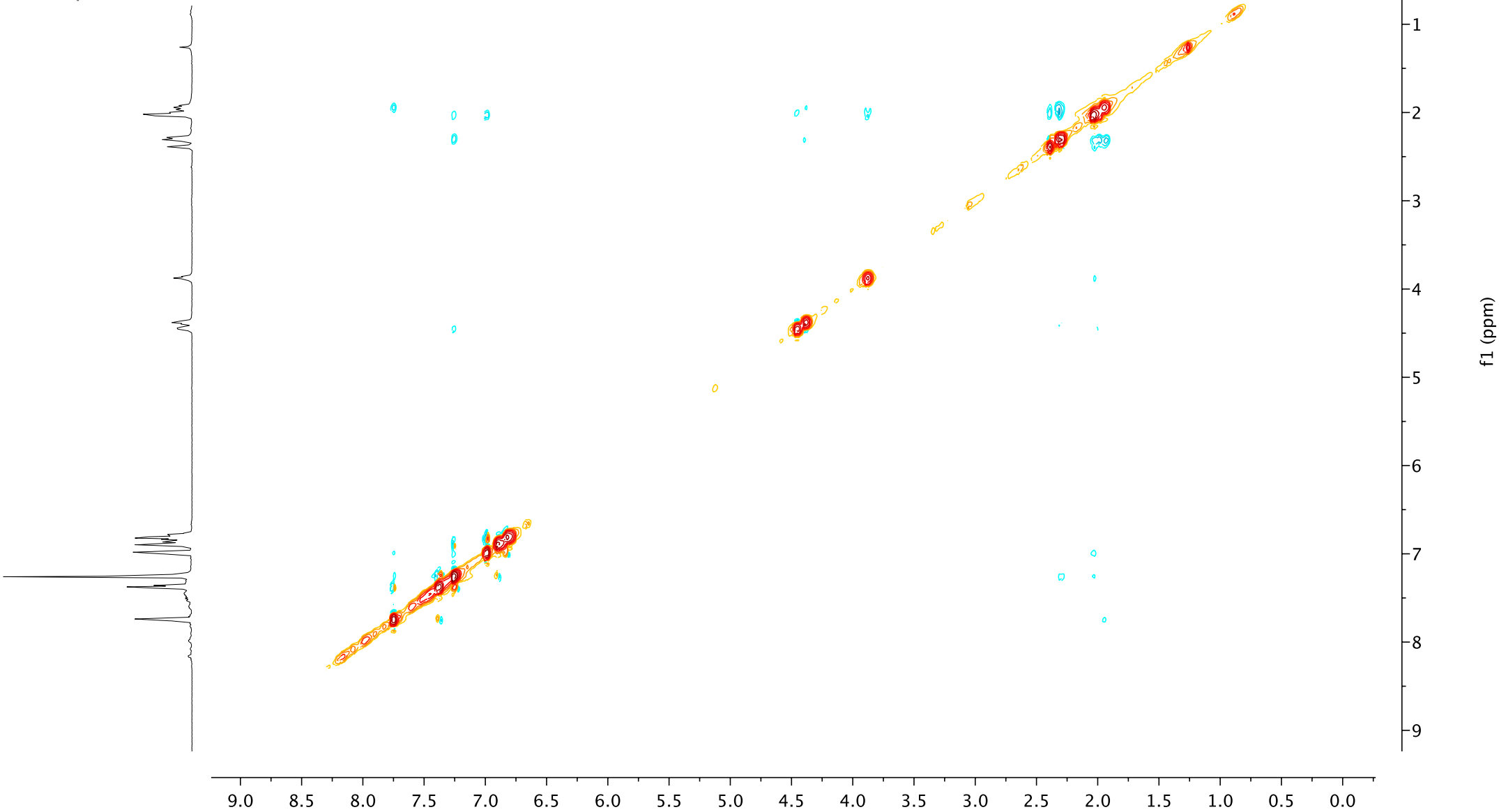

HC(aryl)
HC(9/10)
HC(9/10)
HC(5)
HC(7)
HC(8, 11)
HC(6, 8, 11)
COSY
19
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

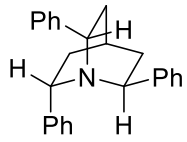

HC(aryl)
HC(9/10)
HC(9/10)
HC(5)
HC(7)
HC(8, 11)
HC(6, 8, 11)
HSQC
C(7)
C(8/11)
C(8/11)
C(6)
C(5)
C(9/10)
C(9/10)
C(2/3/4)
C(1)
19
f1 (ppm)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


19

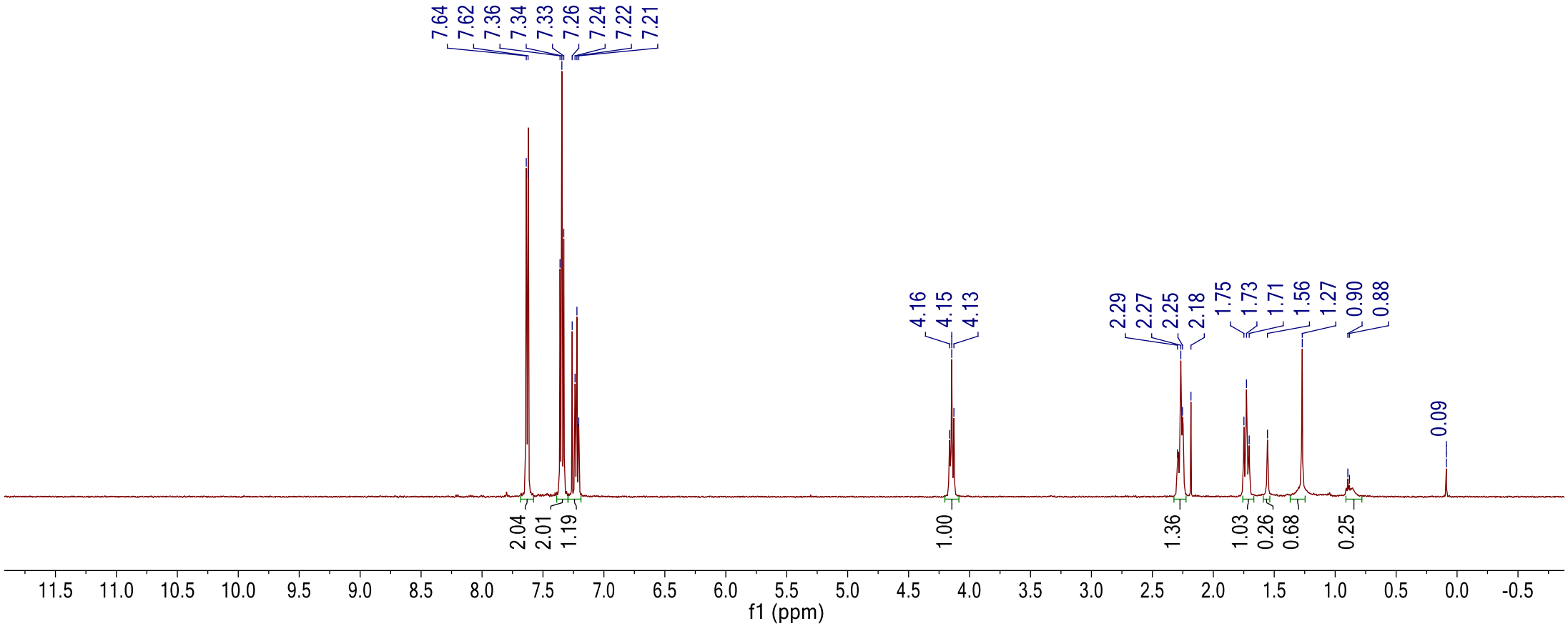

HC(aryl)
HC(9/10)
HC(9/10)
HC(5)
HC(7)
HC(8, 11)
HC(6, 8, 11)

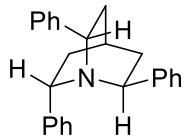
NOESY


f1 (ppm)
0
1
2
3
4
5
6
7
8
9
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

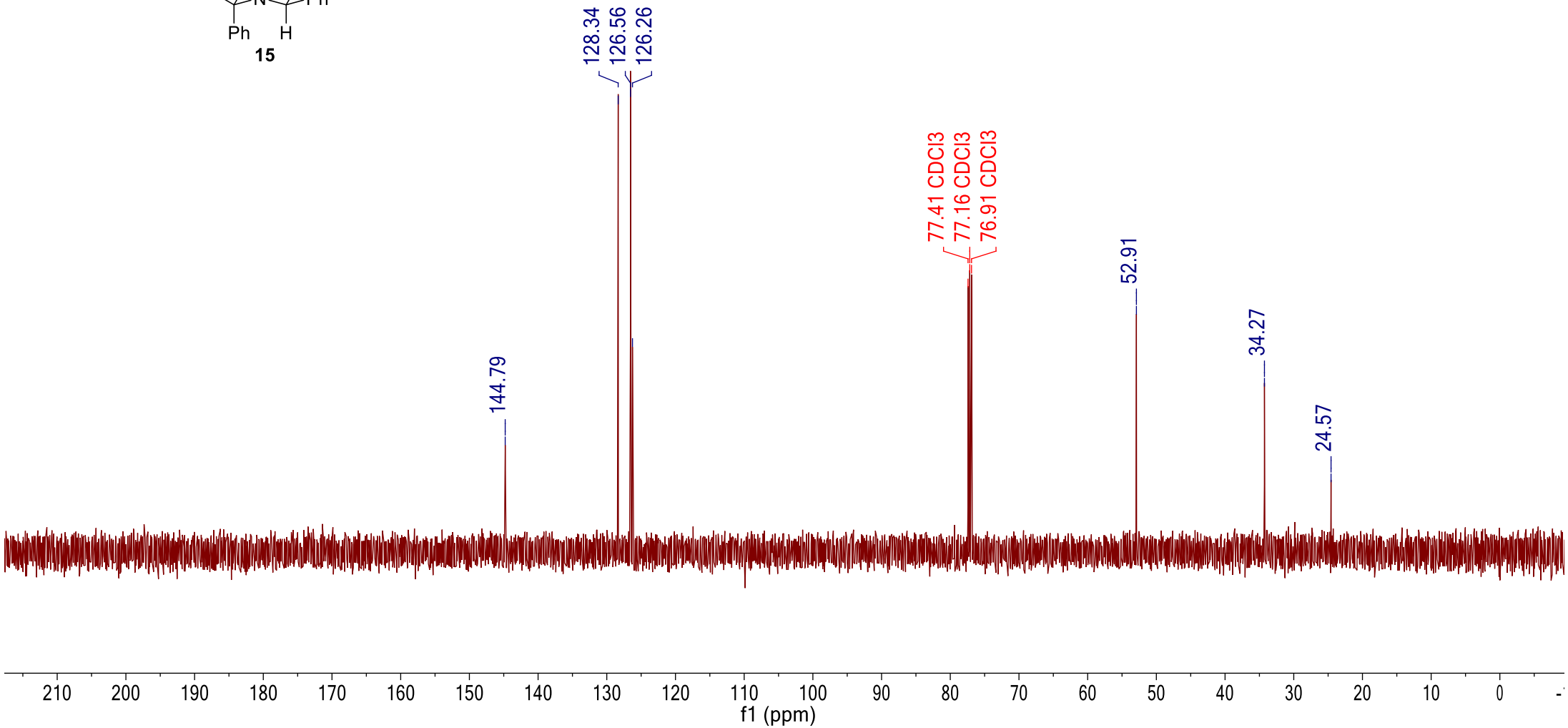

Ph
H
H
N
Ph
Ph
H

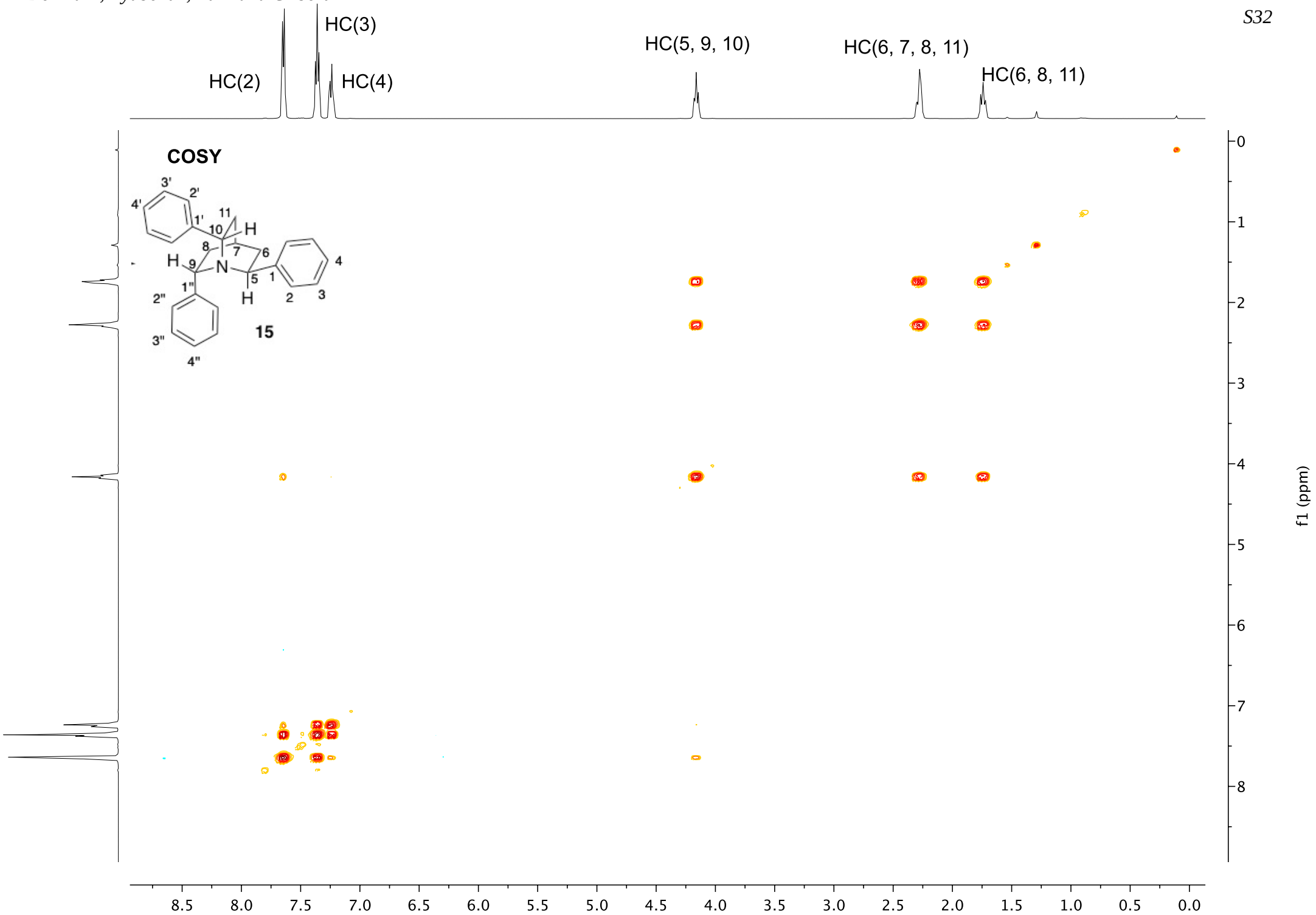
15

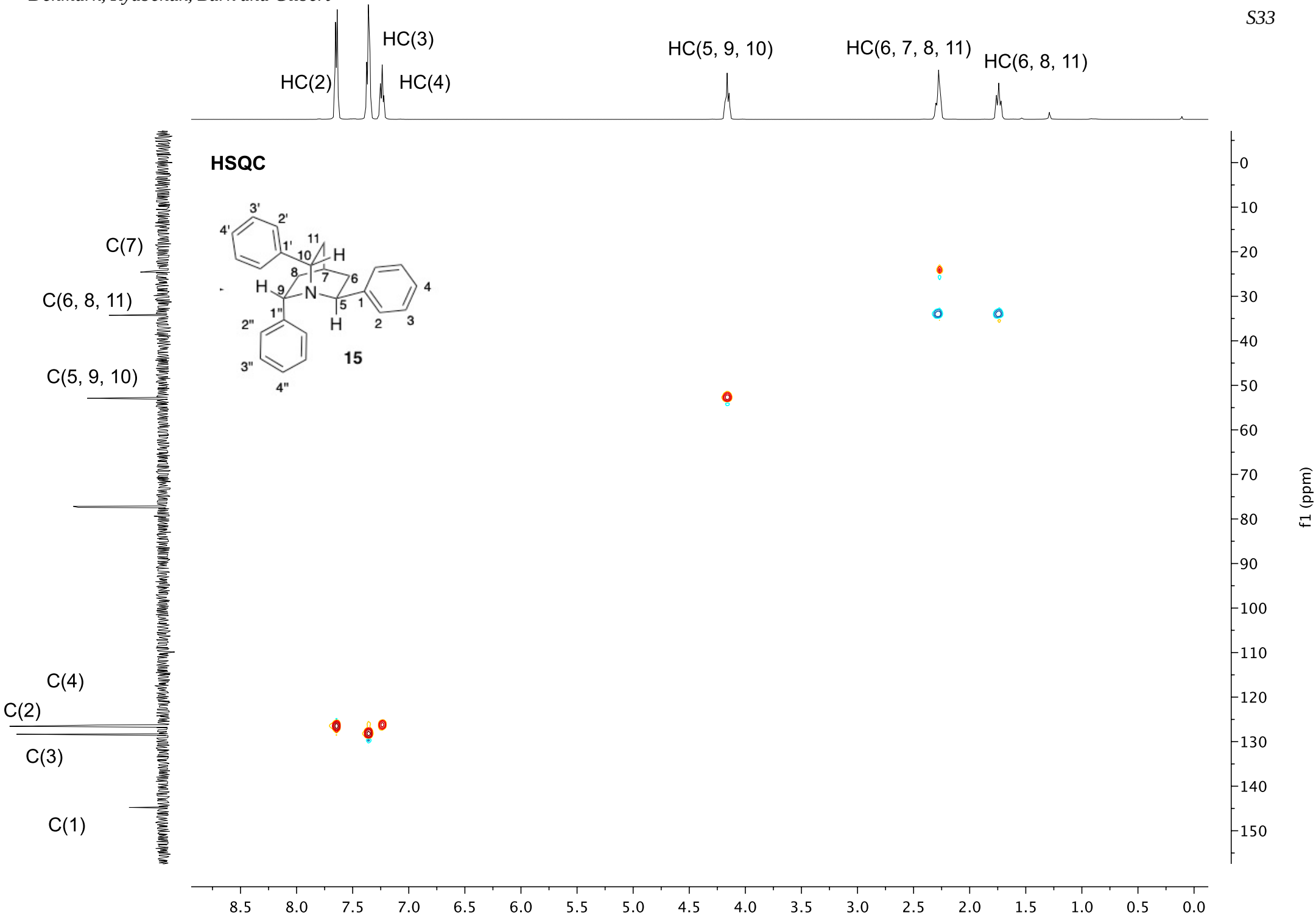

7.64
7.62
7.36
7.34
7.33
7.26
7.24
7.22
7.21
4.16
4.15
4.13
2.29
2.27
2.25
2.18
1.75
1.73
1.71
1.56
1.27
0.90
0.88
0.09
2.04
2.01
1.19
1.00
1.36
1.03
0.26
0.68
0.25
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

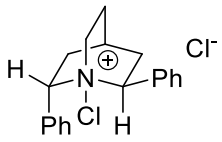

Ph
H
H
N
Ph
Ph
H

15

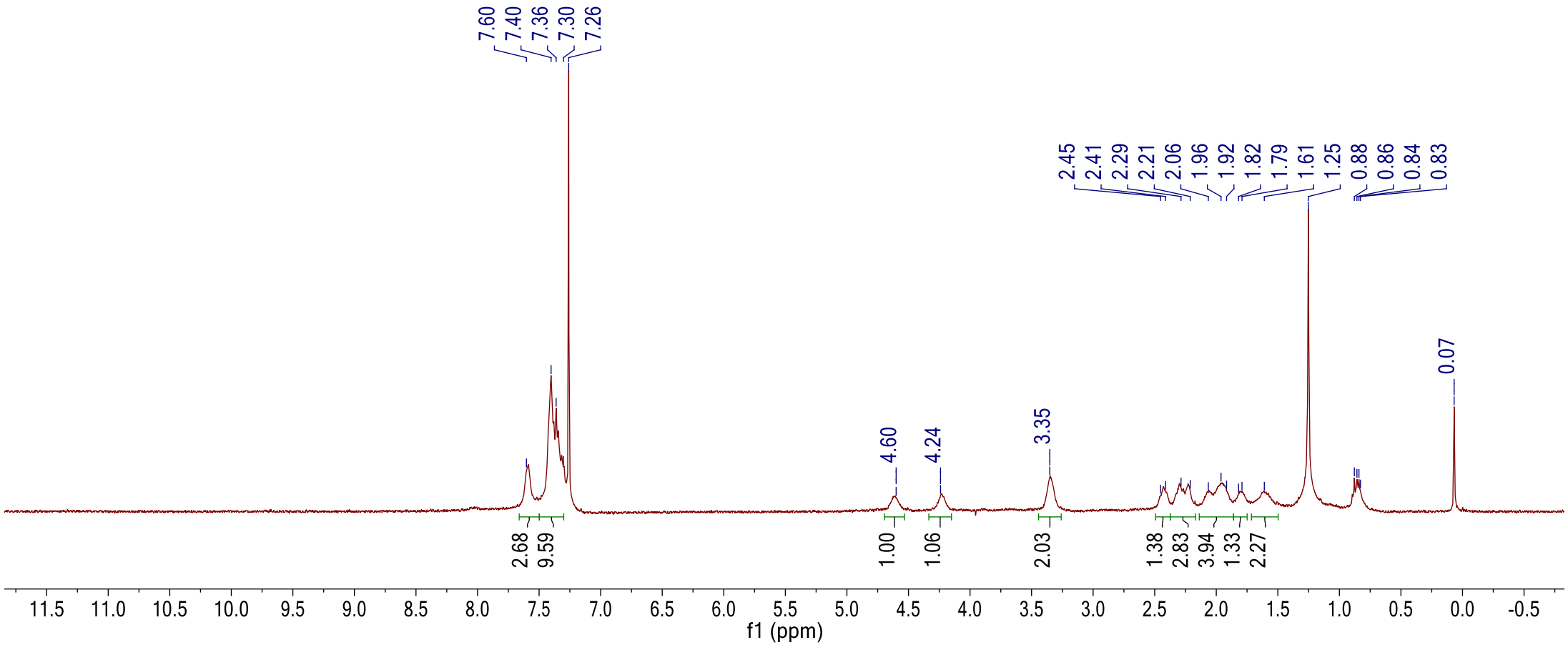

128.34
126.56
126.26
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
144.79
52.91
34.27
24.57
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

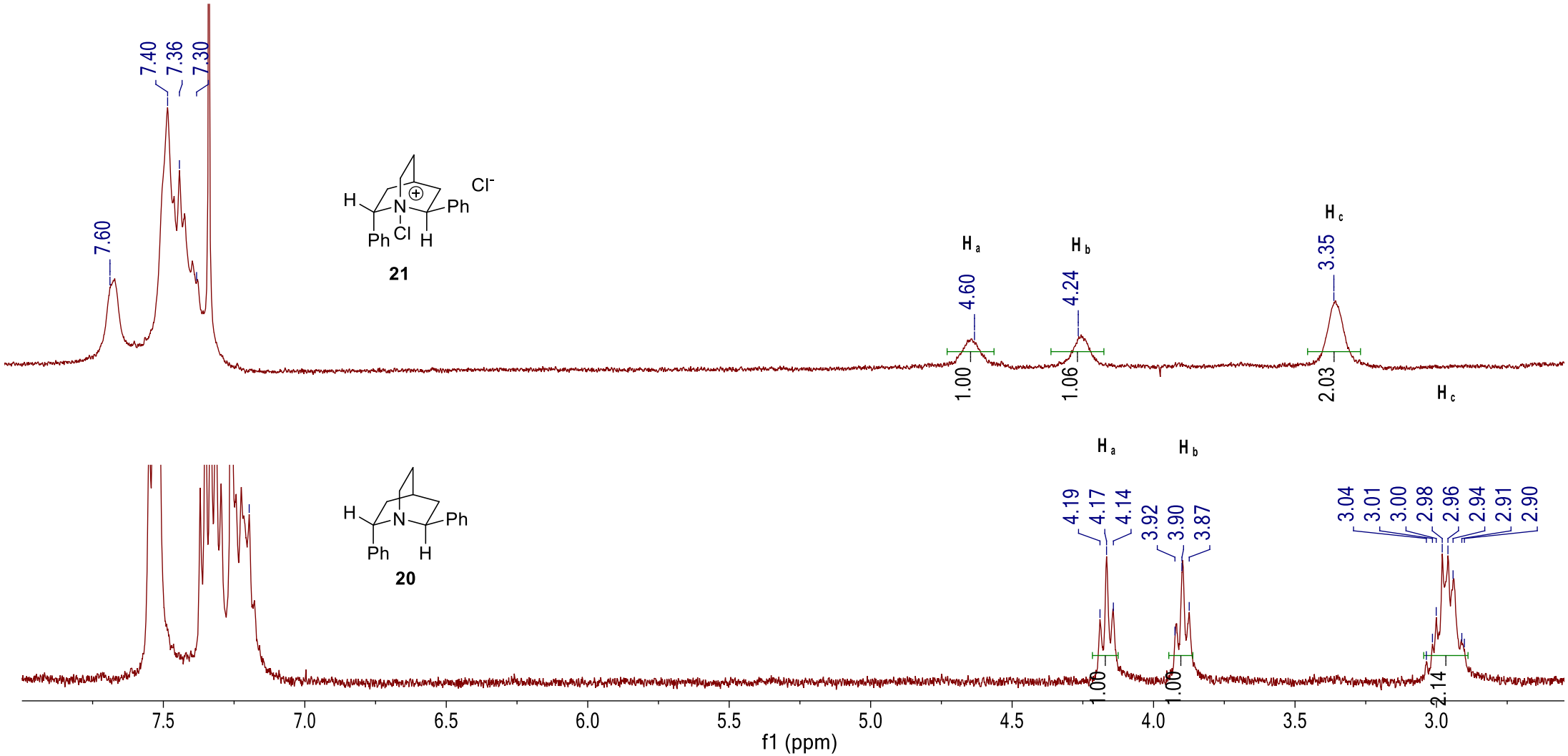

HC(2)
HC(3)
HC(4)
HC(5, 9, 10)
HC(6, 7, 8, 11)
HC(6, 8, 11)
COSY
15
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

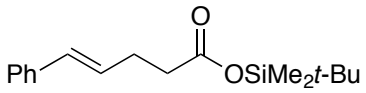

HC(2)
HC(3)
HC(4)
HC(5, 9, 10)
HC(6, 7, 8, 11)
HC(6, 8, 11)
HSQC
C(7)
C(6, 8, 11)
C(5, 9, 10)
C(4)
C(2)
C(3)
C(1)
15
f1 (ppm)


H
N
Cl
Ph
Ph
Cl
H

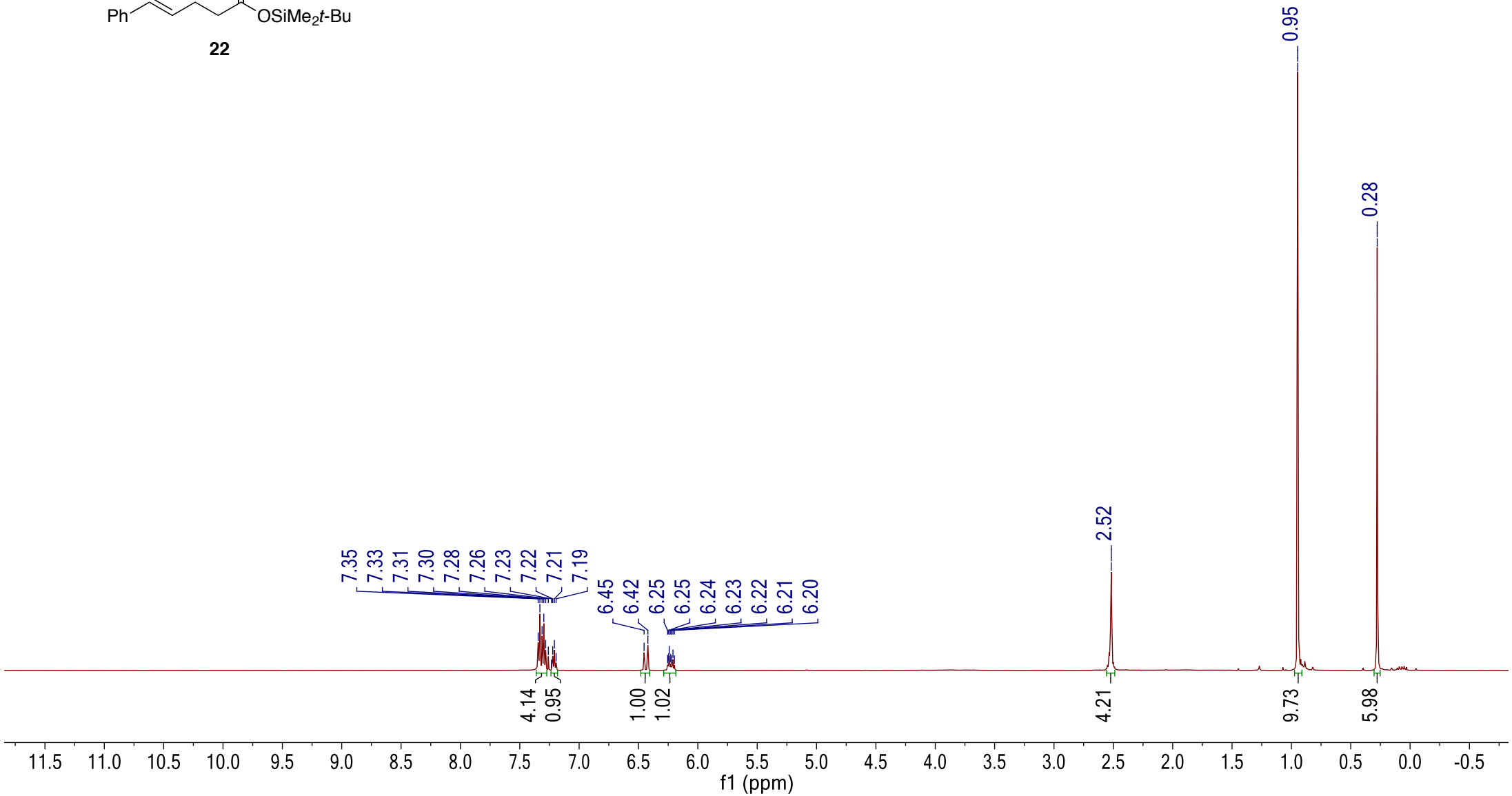
21

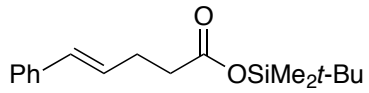

7.60
7.40
7.36
7.30
7.26
2.45
2.41
2.29
2.21
2.06
1.96
1.92
1.82
1.79
1.61
1.25
0.88
0.86
0.84
0.83
0.07
4.60
4.24
3.35
2.68
9.59
1.00
1.06
2.03
1.38
2.83
3.94
1.33
2.27
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


7.60
7.40
7.36
7.30
H
N
Cl
Ph
Ph
H
Cl⁻
21
Ha
Hb
Hc
4.60
4.24
3.35
1.00
1.06
2.03
Hc
Ha
Hb
4.19
4.17
4.14
3.92
3.90
3.87
3.04
3.01
3.00
2.98
2.96
2.94
2.91
2.90
1.00
1.00
2.14
20
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f1 (ppm)


O
Ph
OSiMe2t-Bu

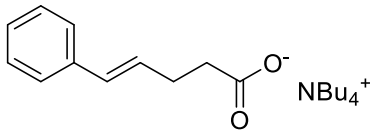
22


0.95
0.28
2.52
7.35
7.33
7.31
7.30
7.28
7.26
7.23
7.22
7.21
7.19
6.45
6.42
6.25
6.25
6.24
6.23
6.22
6.21
6.20
4.14
0.95
1.00
1.02
4.21
9.73
5.98
11.5
11.0
10.5
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)

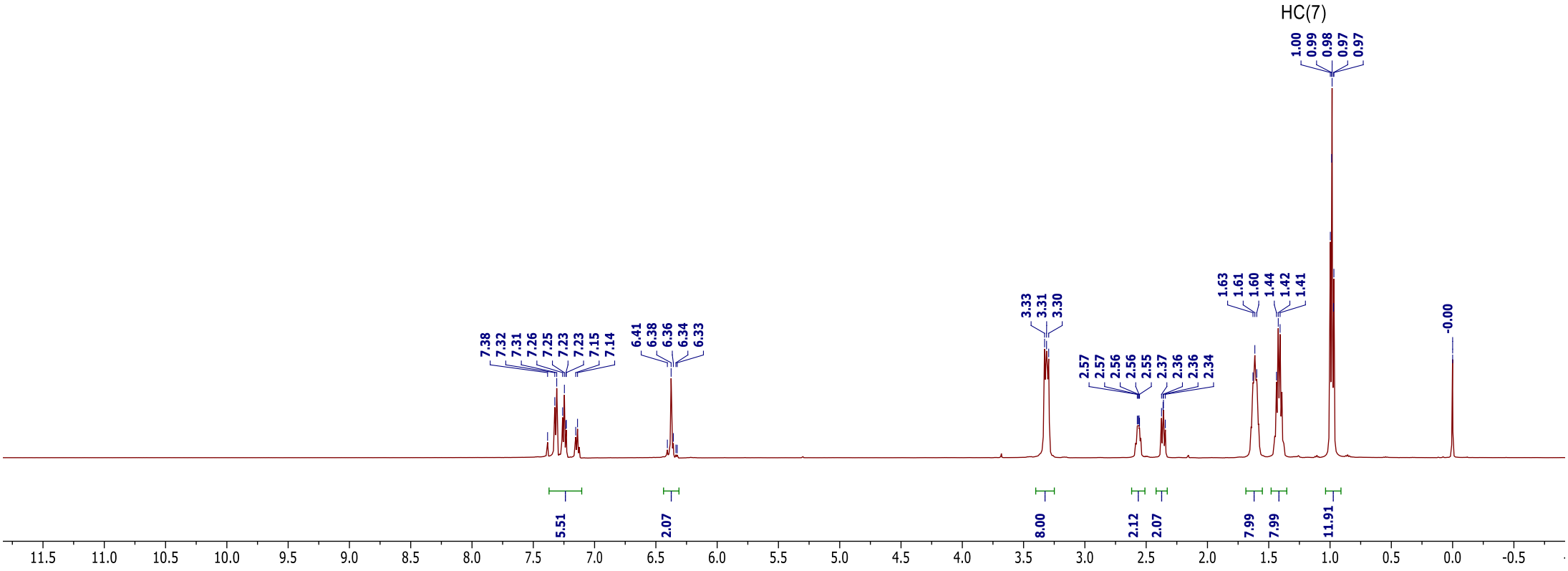

O
Ph
OSiMe2t-Bu

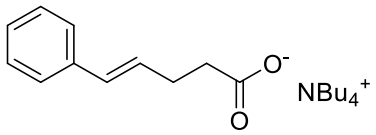
22

35.82
28.63
25.69
25.68
137.53
130.94
128.73
128.60
127.20
126.14
4.65
77.41
77.16
76.91
17.73
173.49
f1 (ppm)

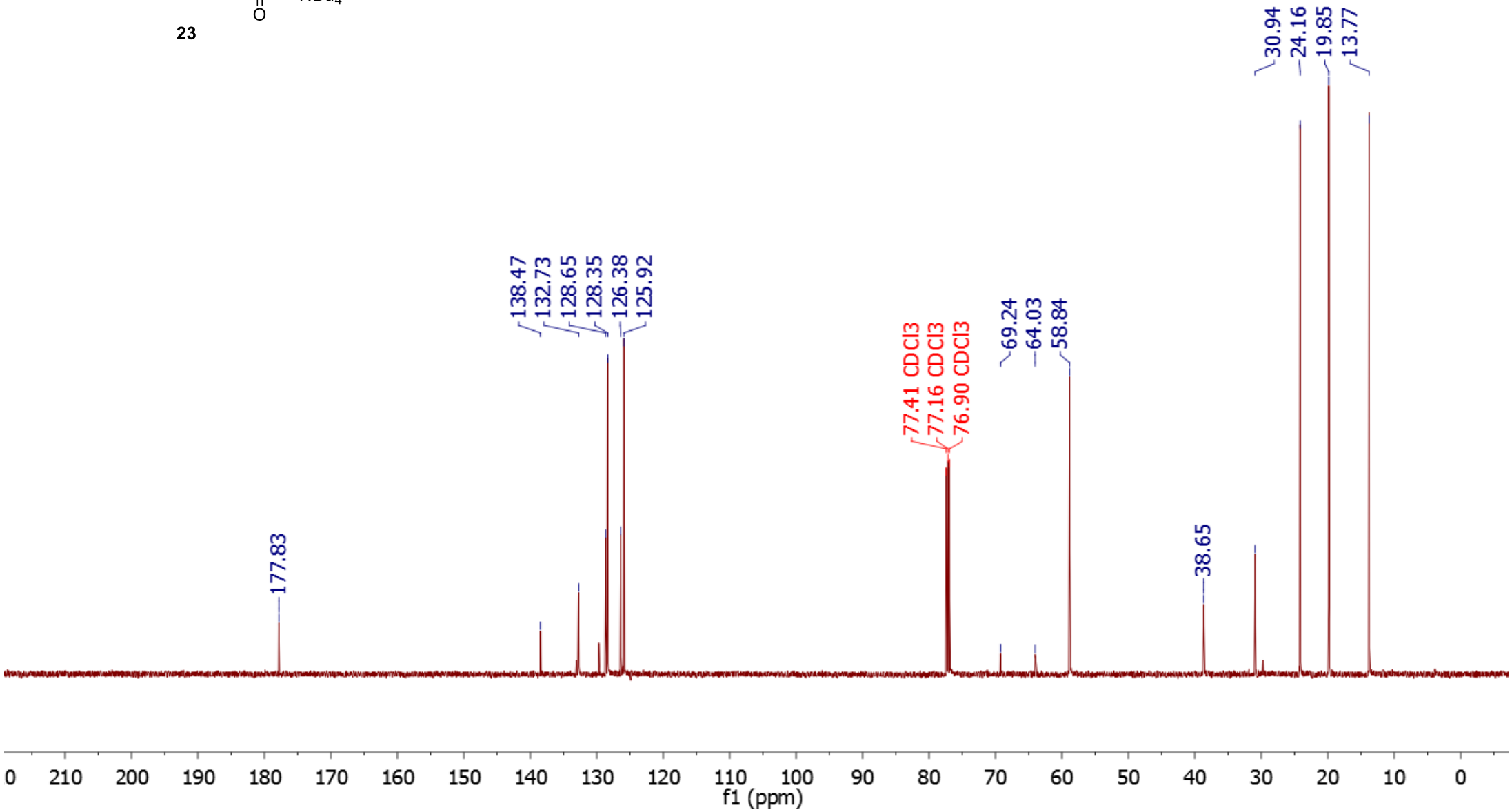

O-
NBu4+
O

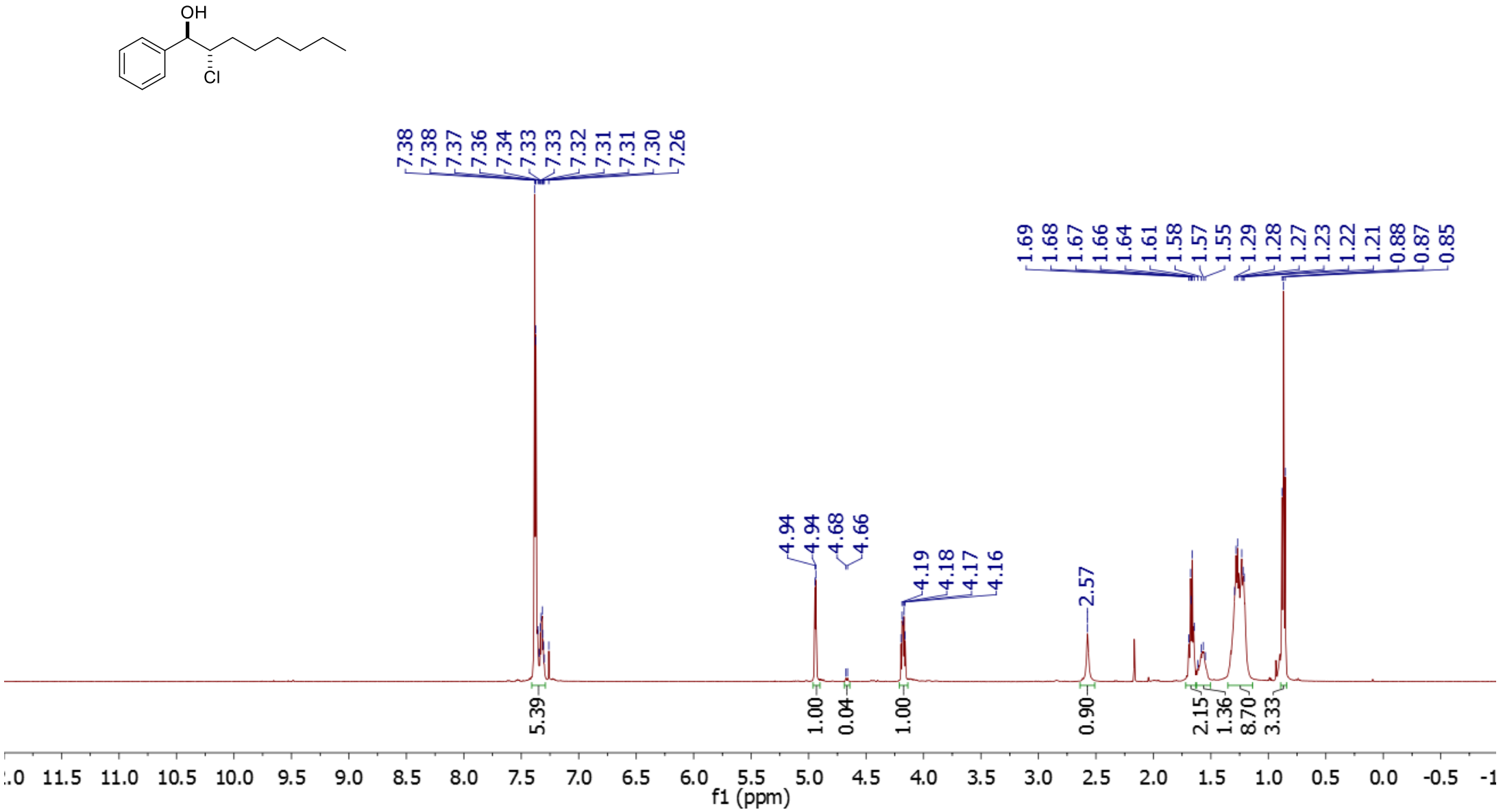
23

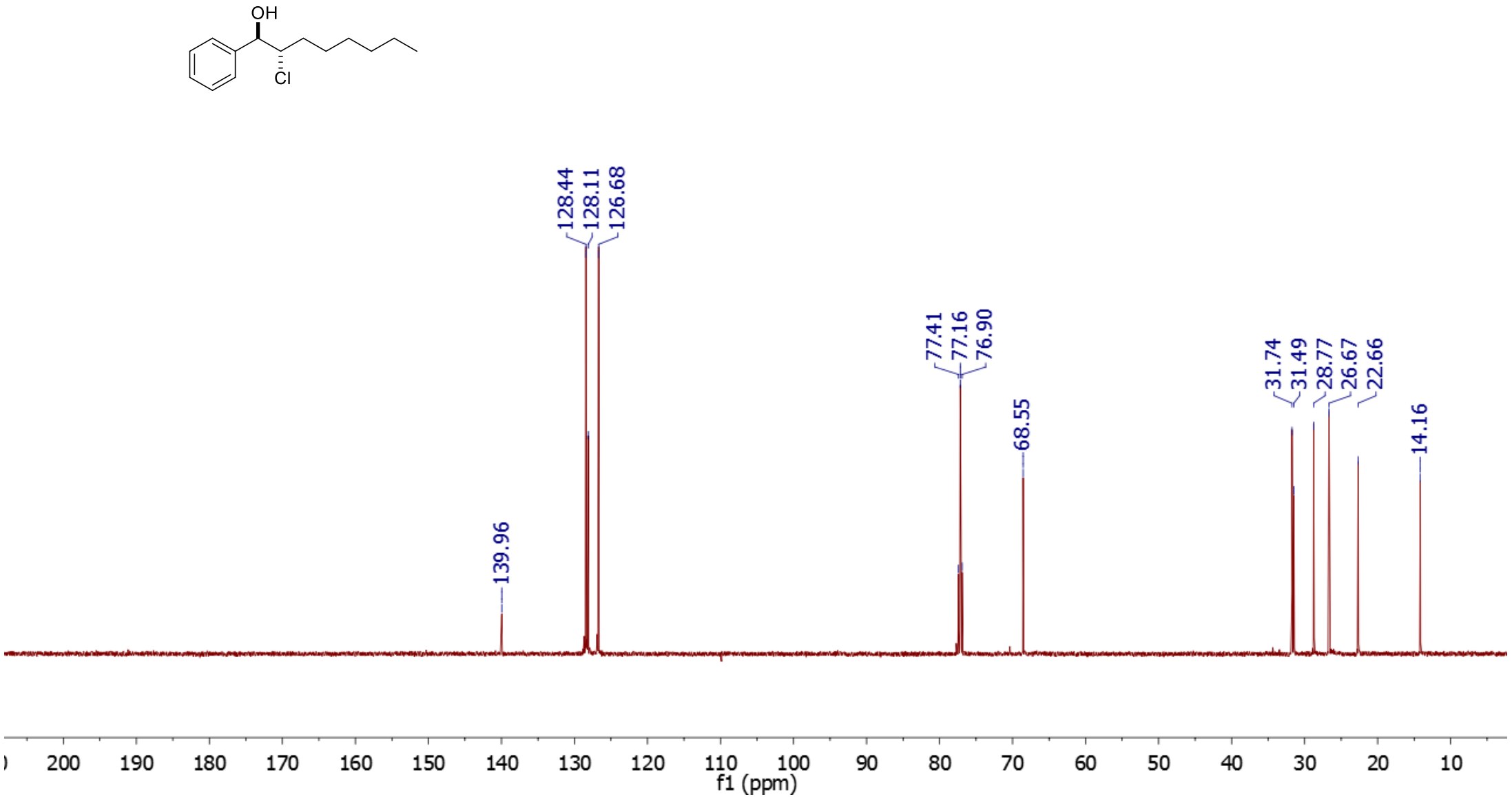

HC(7)
1.00
0.99
0.98
0.97
0.97
7.38
7.32
7.31
7.26
7.25
7.23
7.23
7.15
7.14
6.41
6.38
6.36
6.34
6.33
3.33
3.31
3.30
2.57
2.57
2.56
2.56
2.55
2.37
2.36
2.36
2.34
1.63
1.61
1.60
1.44
1.42
1.41
-0.00
5.51
2.07
8.00
2.12
2.07
7.99
7.99
11.91
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

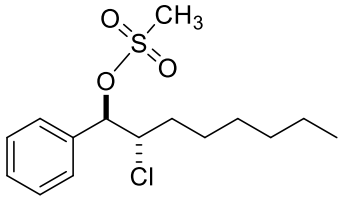

O-
NBu4+
O

23


30.94
24.16
19.85
13.77
138.47
132.73
128.65
128.35
126.38
125.92
77.41 CDCl3
77.16 CDCl3
76.90 CDCl3
69.24
64.03
58.84
38.65
177.83
0 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

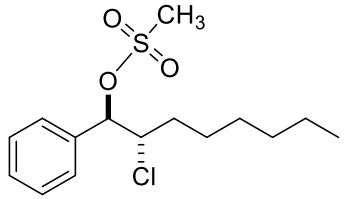

OH
Cl
7.38
7.38
7.37
7.36
7.34
7.33
7.33
7.32
7.31
7.31
7.30
7.26
1.69
1.68
1.67
1.66
1.64
1.61
1.58
1.57
1.55
1.29
1.28
1.27
1.23
1.22
1.21
0.88
0.87
0.85
4.94
4.94
4.68
4.66
4.19
4.18
4.17
4.16
2.57
5.39
1.00
0.04
1.00
0.90
2.15
1.36
8.70
3.33
f1 (ppm)


OH
Cl
128.44
128.11
126.68
77.41
77.16
76.90
68.55
31.74
31.49
28.77
26.67
22.66
14.16
139.96
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

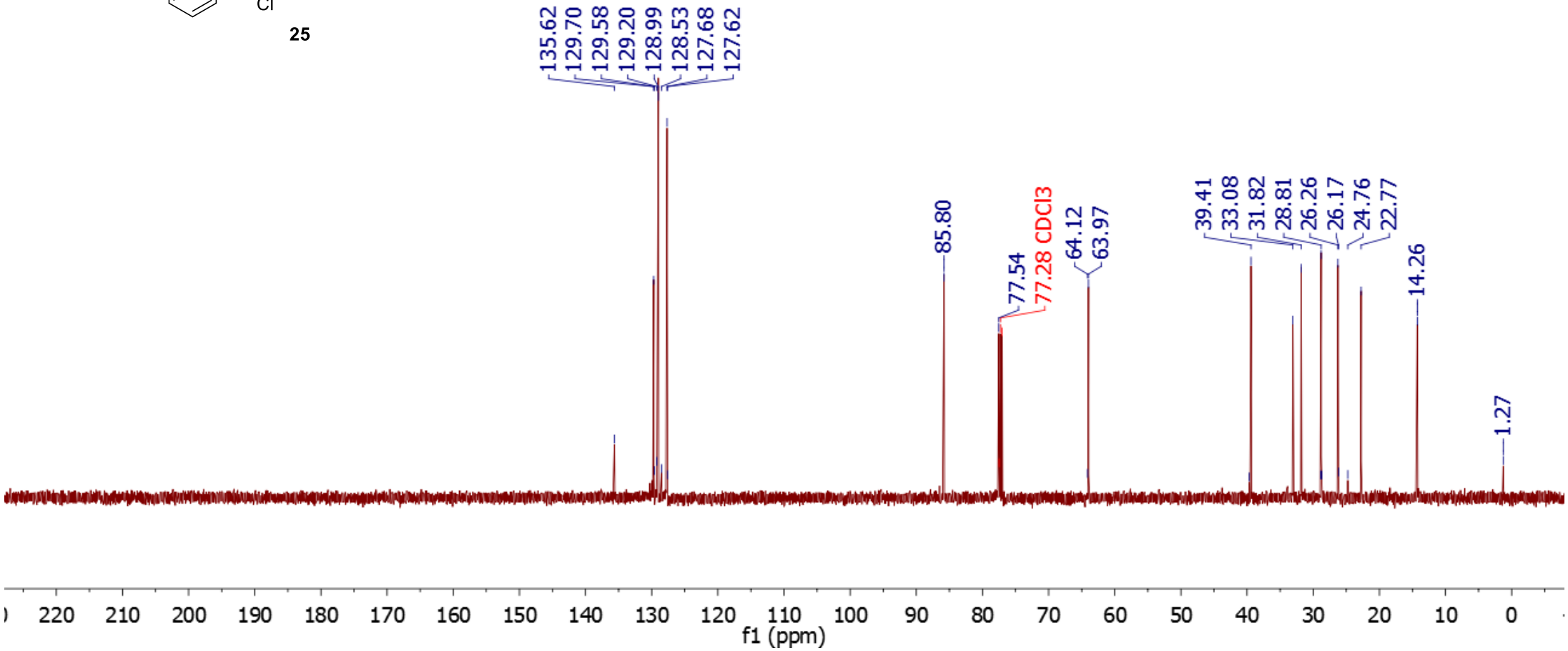

O
S
CH3
O
O
Cl

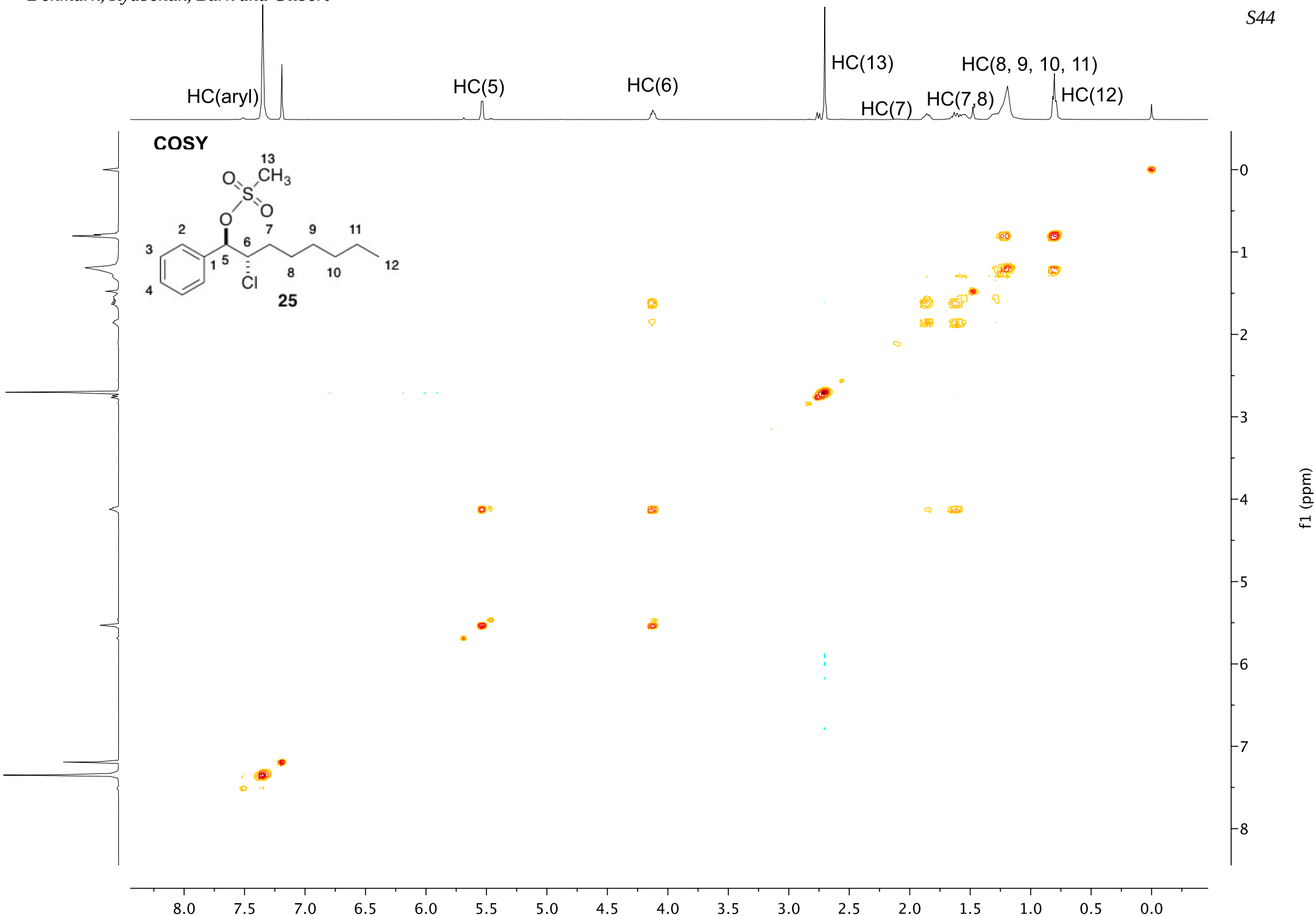
25

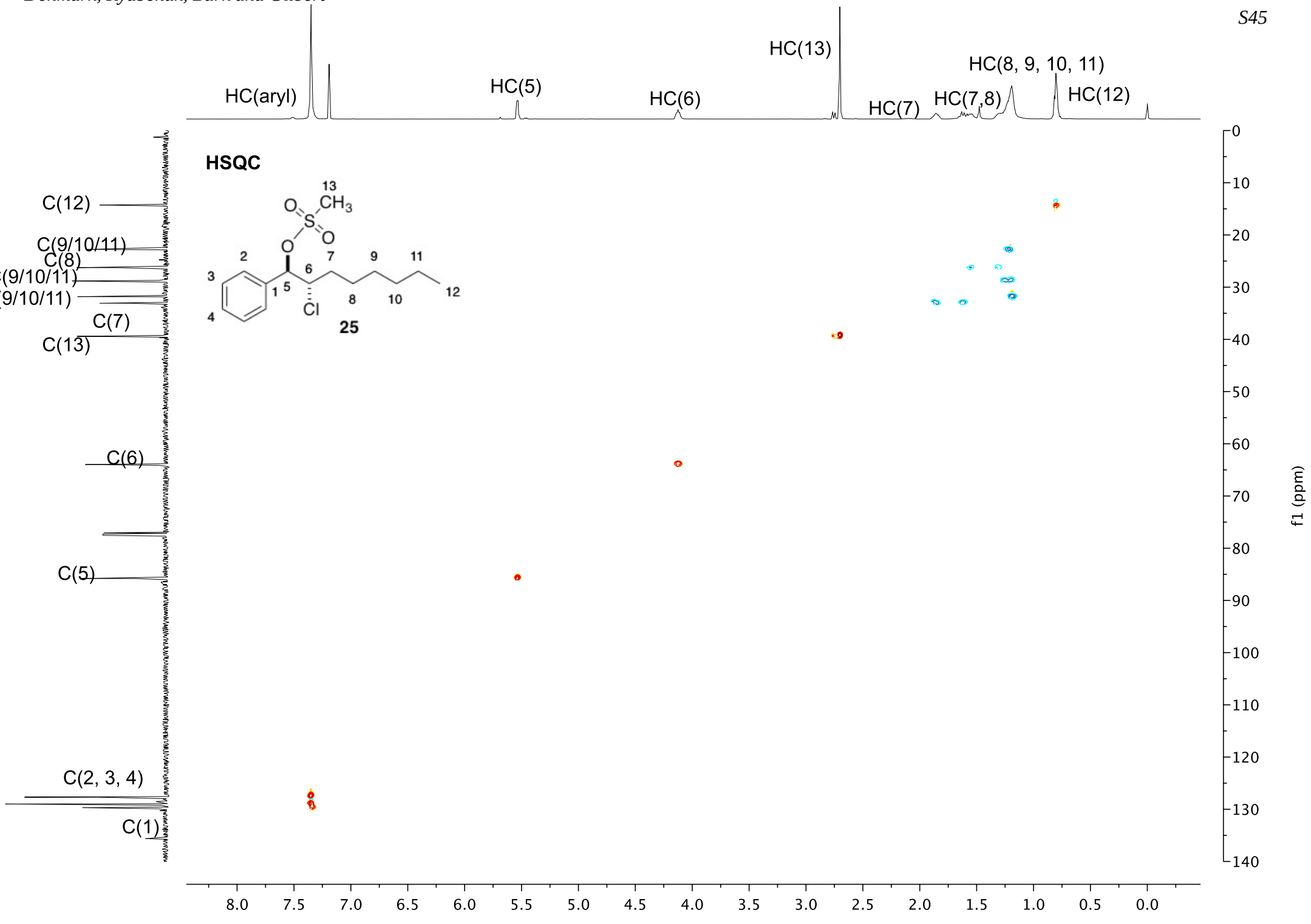
5.61
5.60
5.54
5.53
4.22
4.21
4.20
4.20
4.19
4.18
4.18
1.00
1.10
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0
f1 (ppm)
7.43
7.42
7.42
7.41
7.41
7.26
2.83
2.81
2.77
2.76
1.31
1.30
1.29
1.28
1.28
1.27
1.27
1.26
1.26
1.25
1.24
1.24
0.89
0.87
0.86
0.07
5.56
1.00
1.10
0.38
3.11
1.03
2.34
8.76
3.61
0 11.5 11.0 10.5 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 -1
f1 (ppm)

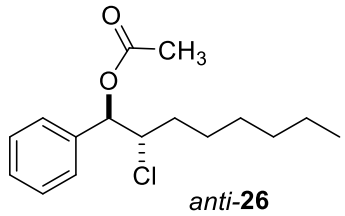

O
CH3
S
O
O
Cl

25

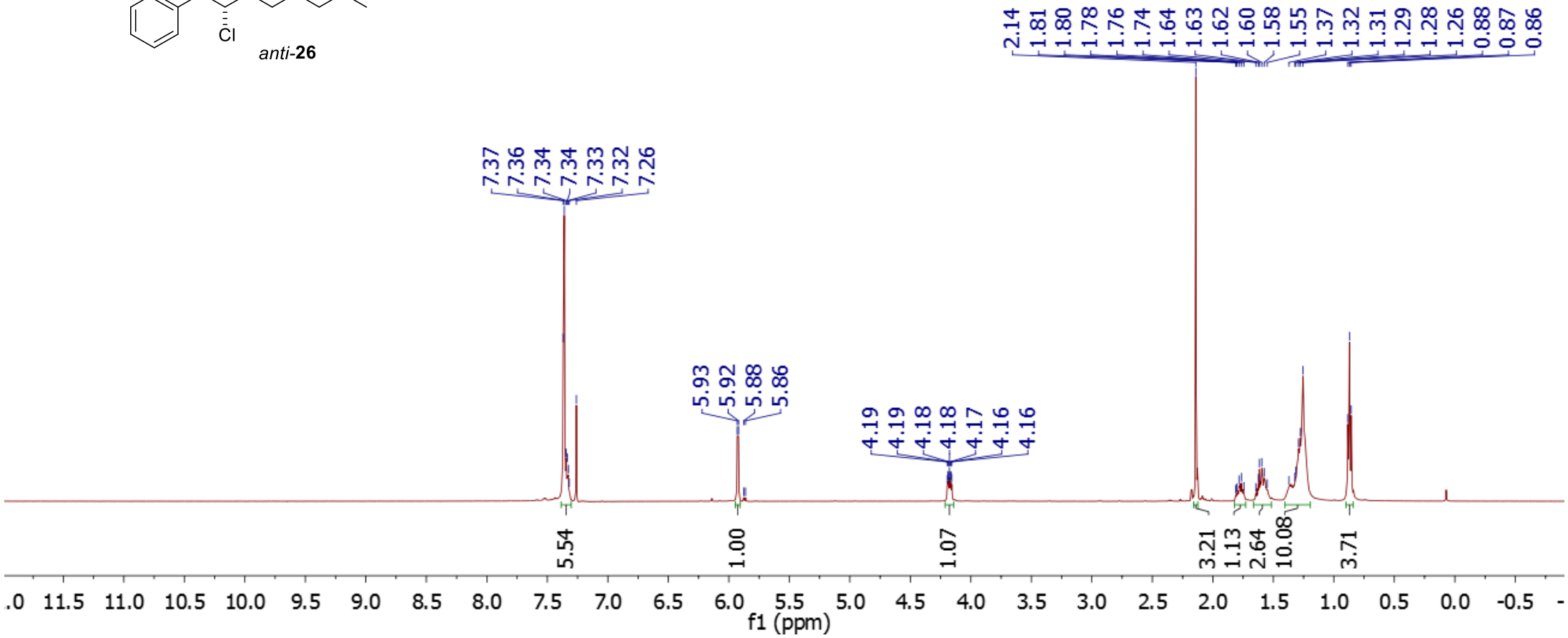

135.62
129.70
129.58
129.20
128.99
128.53
127.68
127.62
85.80
77.54
77.28 CDCl3
64.12
63.97
39.41
33.08
31.82
28.81
26.26
26.17
24.76
22.77
14.26
1.27
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

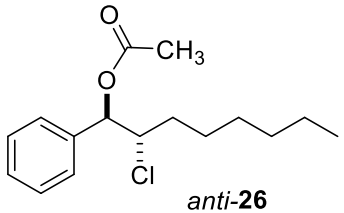

HC(aryl)
HC(5)
HC(6)
HC(13)
HC(7)
HC(7,8)
HC(8, 9, 10, 11)
HC(12)
COSY
13
CH3
O
S
O
O
2
7
9
11
3
6
1
5
12
8
10
4
Cl
25
f1 (ppm)
0
1
2
3
4
5
6
7
8
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


HC(aryl)
HC(5)
HC(6)
HC(13)
HC(7)
HC(7,8)
HC(8, 9, 10, 11)
HC(12)
HSQC
C(12)
C(9/10/11)
C(8)
C(9/10/11)
C(9/10/11)
C(7)
C(13)
C(6)
C(5)
C(2, 3, 4)
C(1)
25
f1 (ppm)

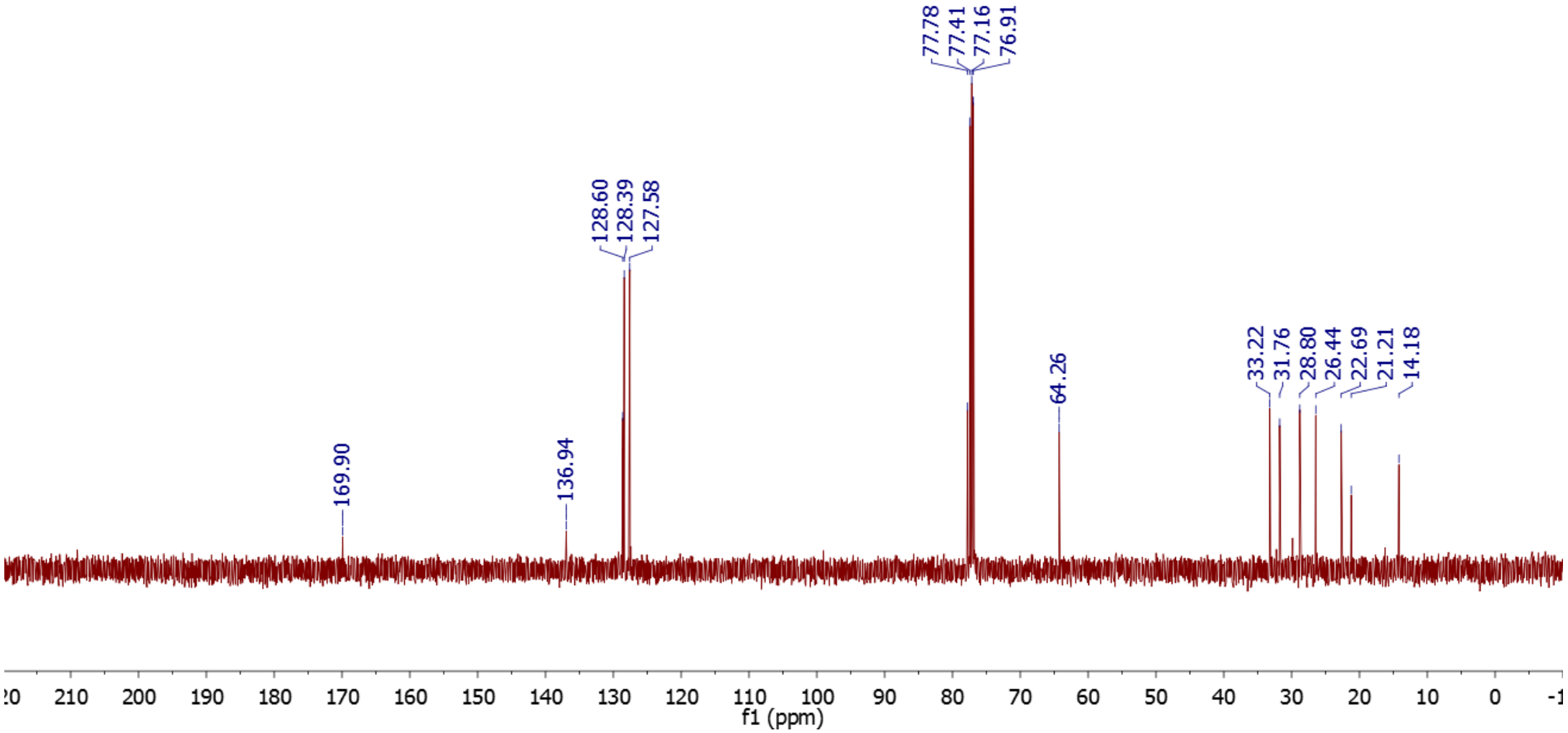

O
CH3
O
Cl

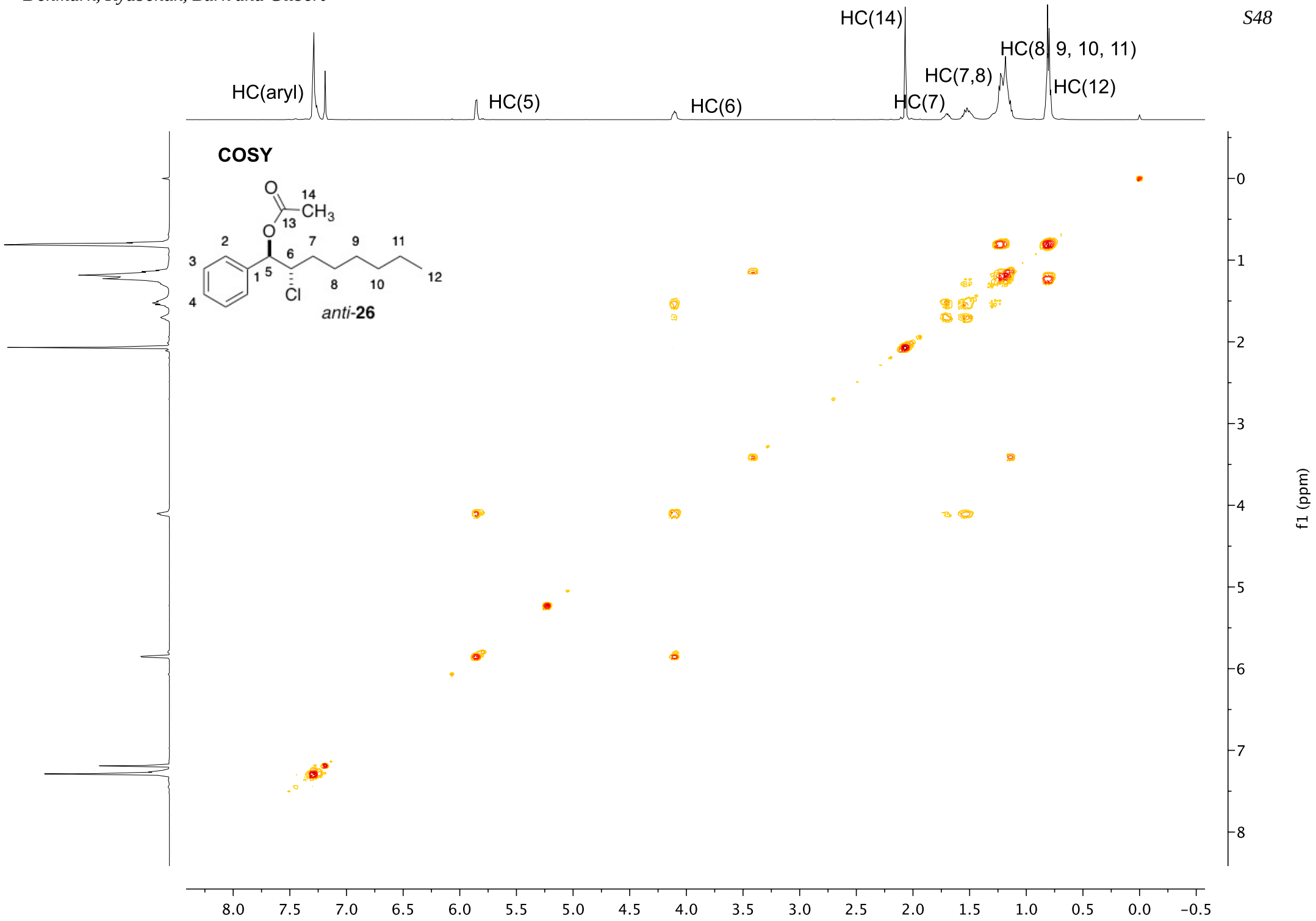
anti-**26**

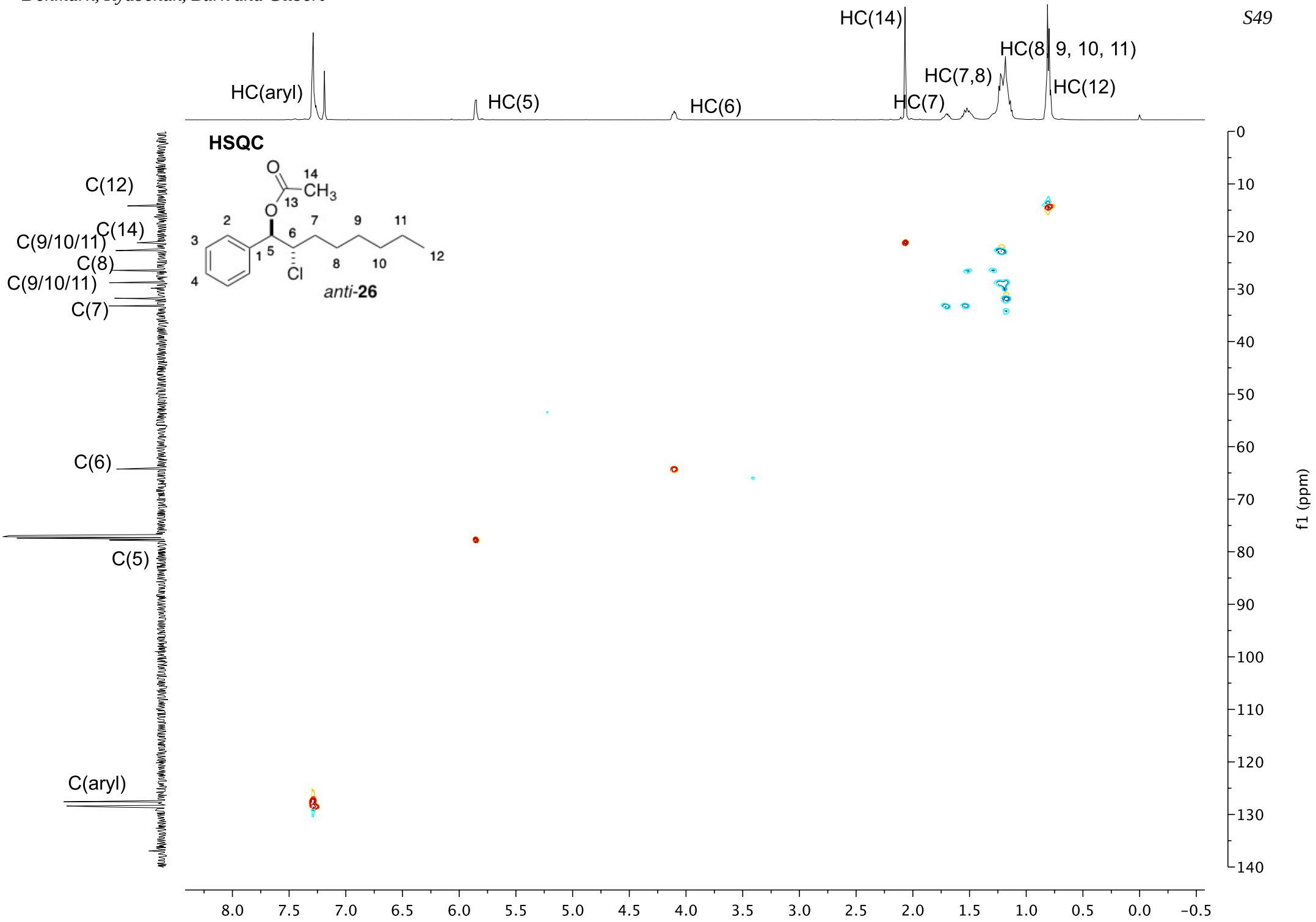

2.14
1.81
1.80
1.78
1.76
1.74
1.64
1.63
1.62
1.60
1.58
1.55
1.37
1.32
1.31
1.29
1.28
1.26
0.88
0.87
0.86
7.37
7.36
7.34
7.34
7.33
7.32
7.26
5.93
5.92
5.88
5.86
4.19
4.19
4.18
4.18
4.17
4.16
4.16
5.54
1.00
1.07
3.21
1.13
2.64
10.08
3.71
f1 (ppm)

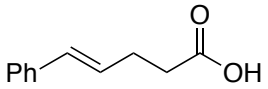

O
CH3
O
Cl

anti-**26**

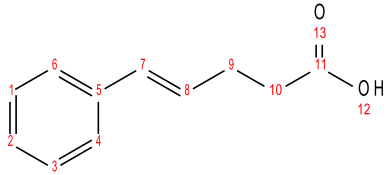

77.78
77.41
77.16
76.91
128.60
128.39
127.58
169.90
136.94
64.26
33.22
31.76
28.80
26.44
22.69
21.21
14.18
f1 (ppm)

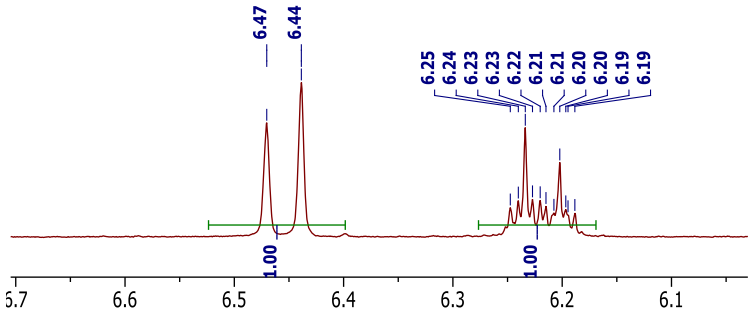

HC(14)
HC(8, 9, 10, 11)
HC(7,8)
HC(12)
HC(aryl)
HC(5)
HC(6)
HC(7)
COSY
anti-26
f1 (ppm)

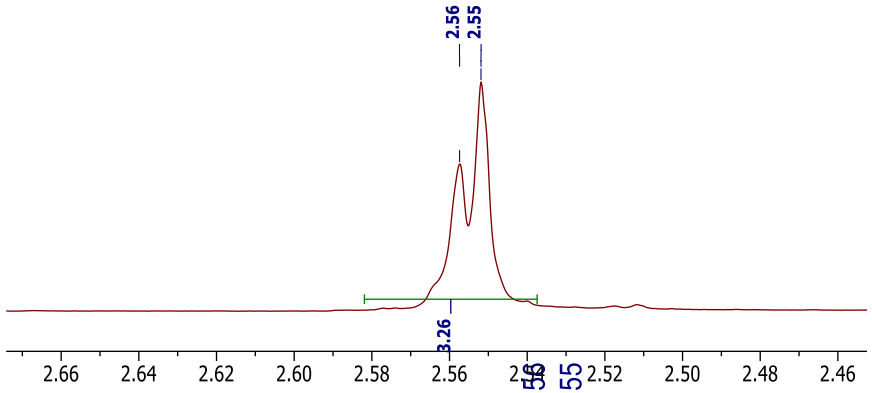

HC(14)
HC(8, 9, 10, 11)
HC(7,8)
HC(12)
HC(aryl)
HC(5)
HC(6)
HC(7)
HSQC
C(12)
C(14)
C(9/10/11)
C(8)
C(9/10/11)
C(7)
C(6)
C(5)
C(aryl)
anti-26
f1 (ppm)

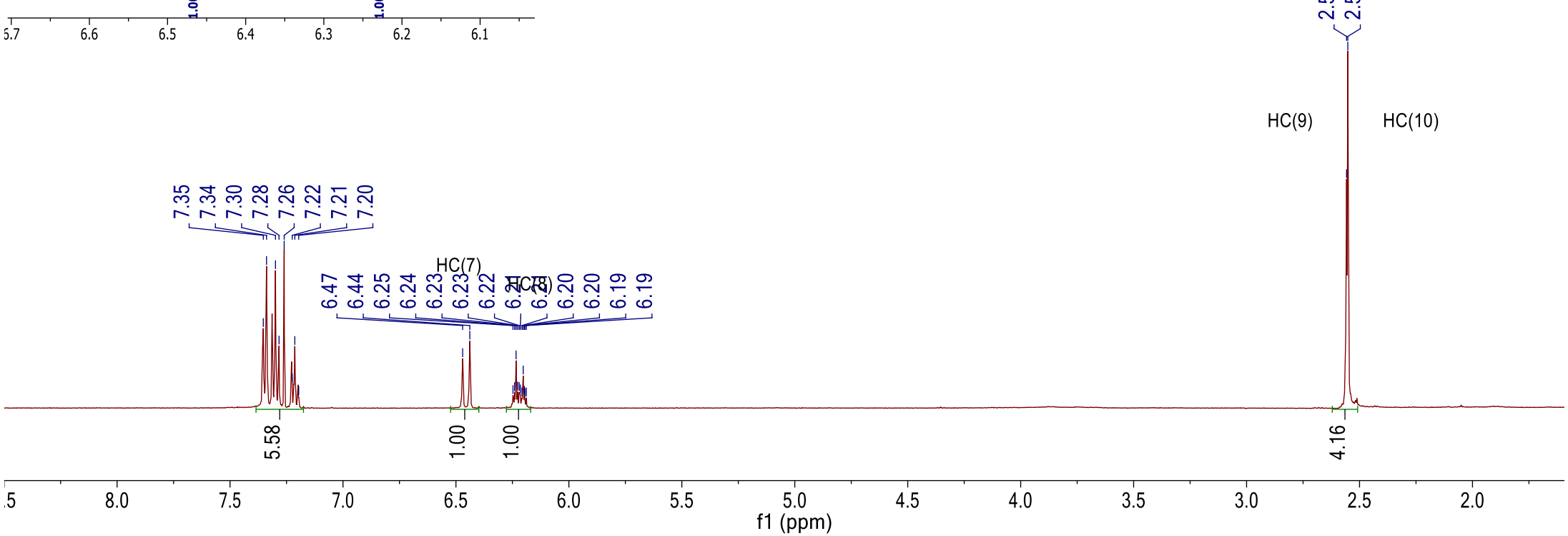

O
Ph
OH

8

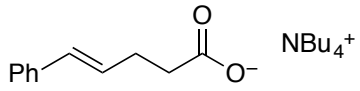

O
13
OH
12


6.47
6.44
6.25
6.24
6.23
6.23
6.22
6.21
6.21
6.20
6.20
6.19
6.19
1.00
1.00

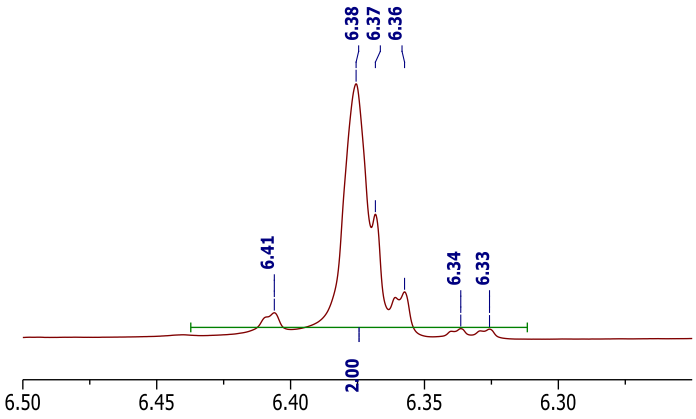

2.56
2.55
3.26

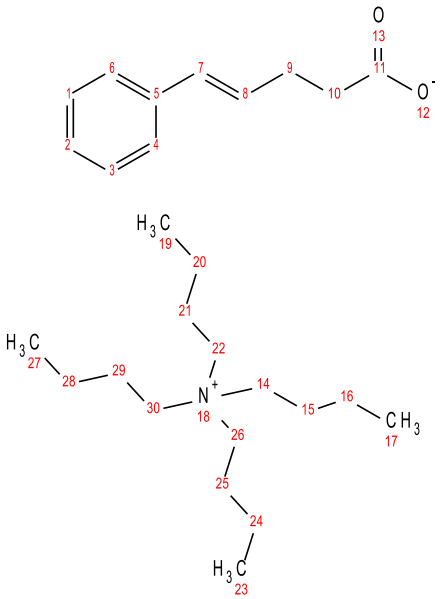

7.35
7.34
7.30
7.28
7.26
7.22
7.21
7.20
6.47
6.44
6.25
6.24
6.23
6.23
6.22
6.21
6.20
6.20
6.19
6.19
HC(7)
HC(8)
HC(9)
HC(10)
2.56
2.55
5.58
1.00
1.00
4.16
f1 (ppm)

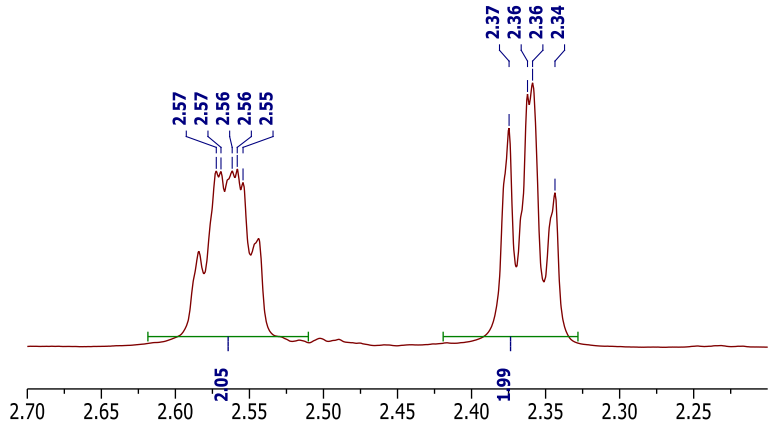
)4-56-0min
ˆANDARD PROTON PARAMETERS

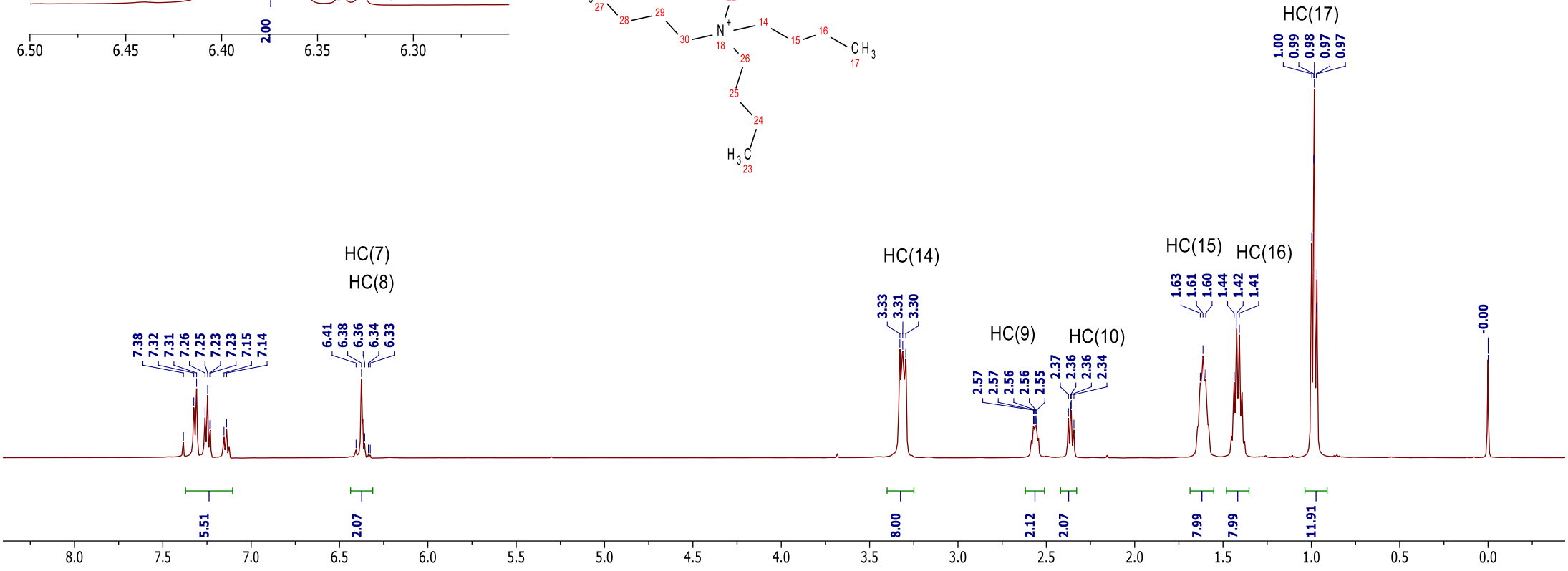


23

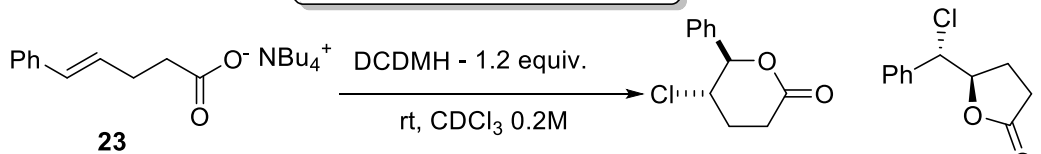






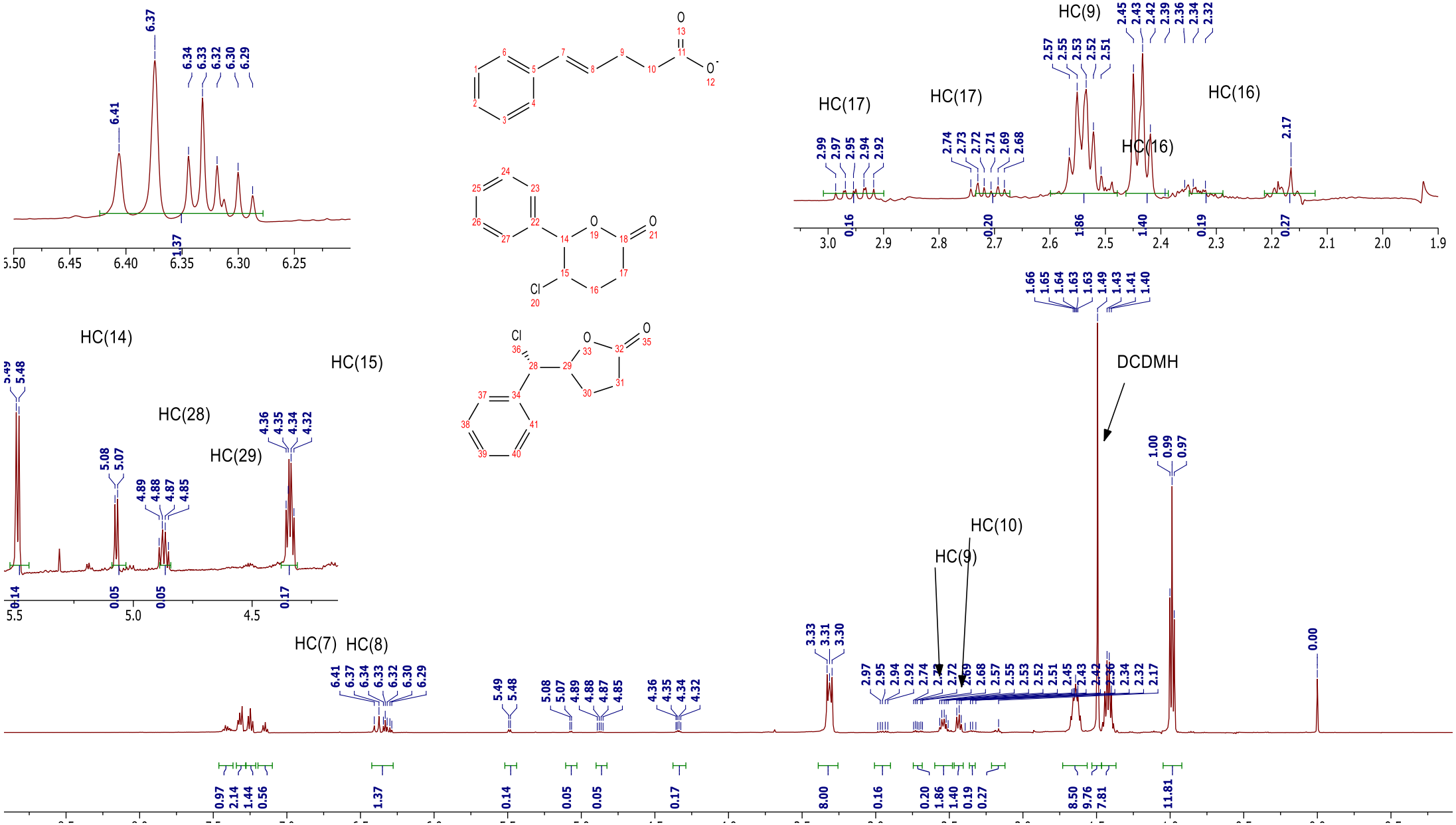


Entry 1, Table 2 - 10 min

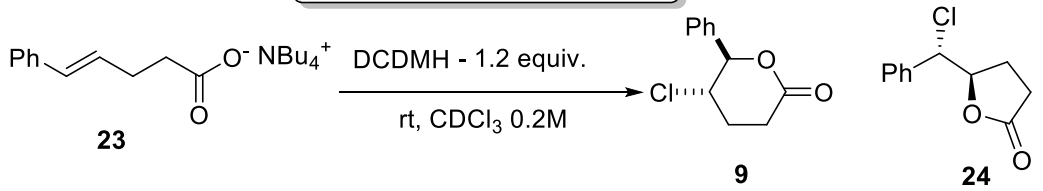


23 **9** **24**

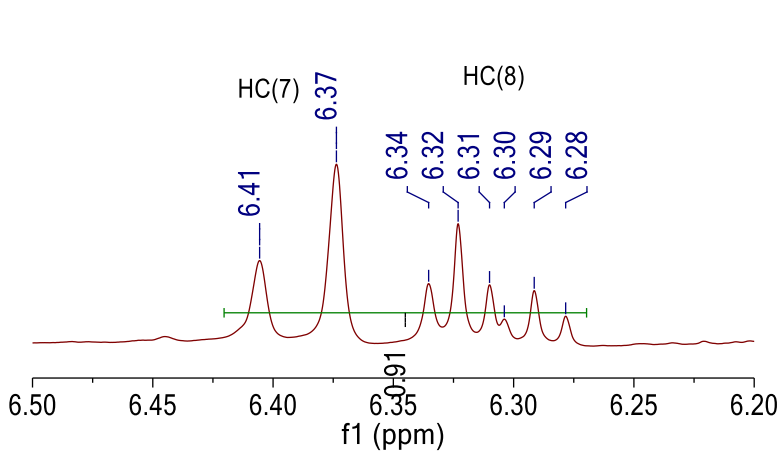
P4-56-10min-nocat
TANDARD PROTON PARAMETERS

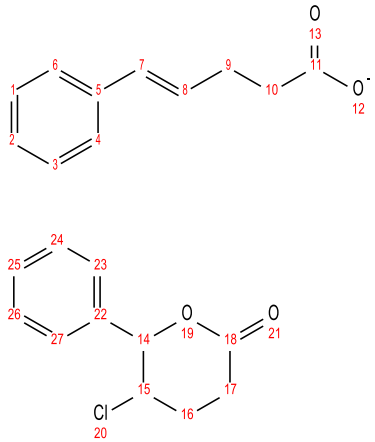


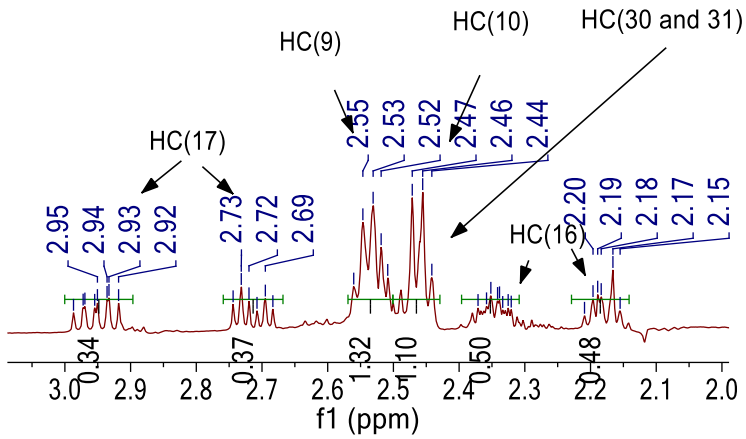
Entry 1, Table 2 - 1 h

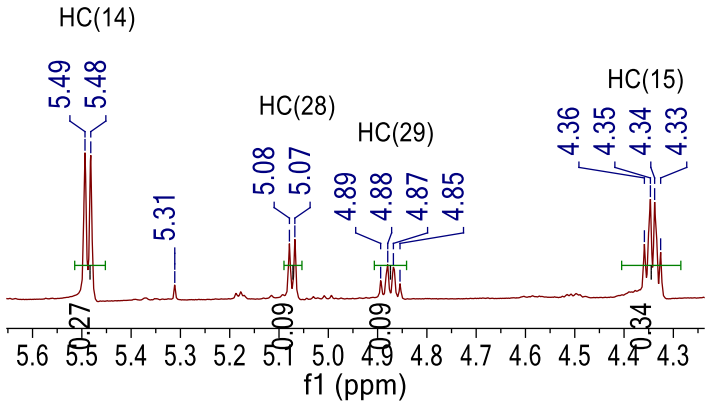


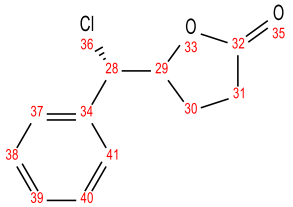
RP4-56-1h-nocat
STANDARD PROTON PARAMETERS



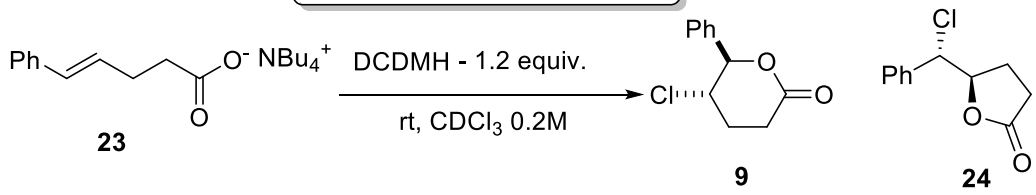




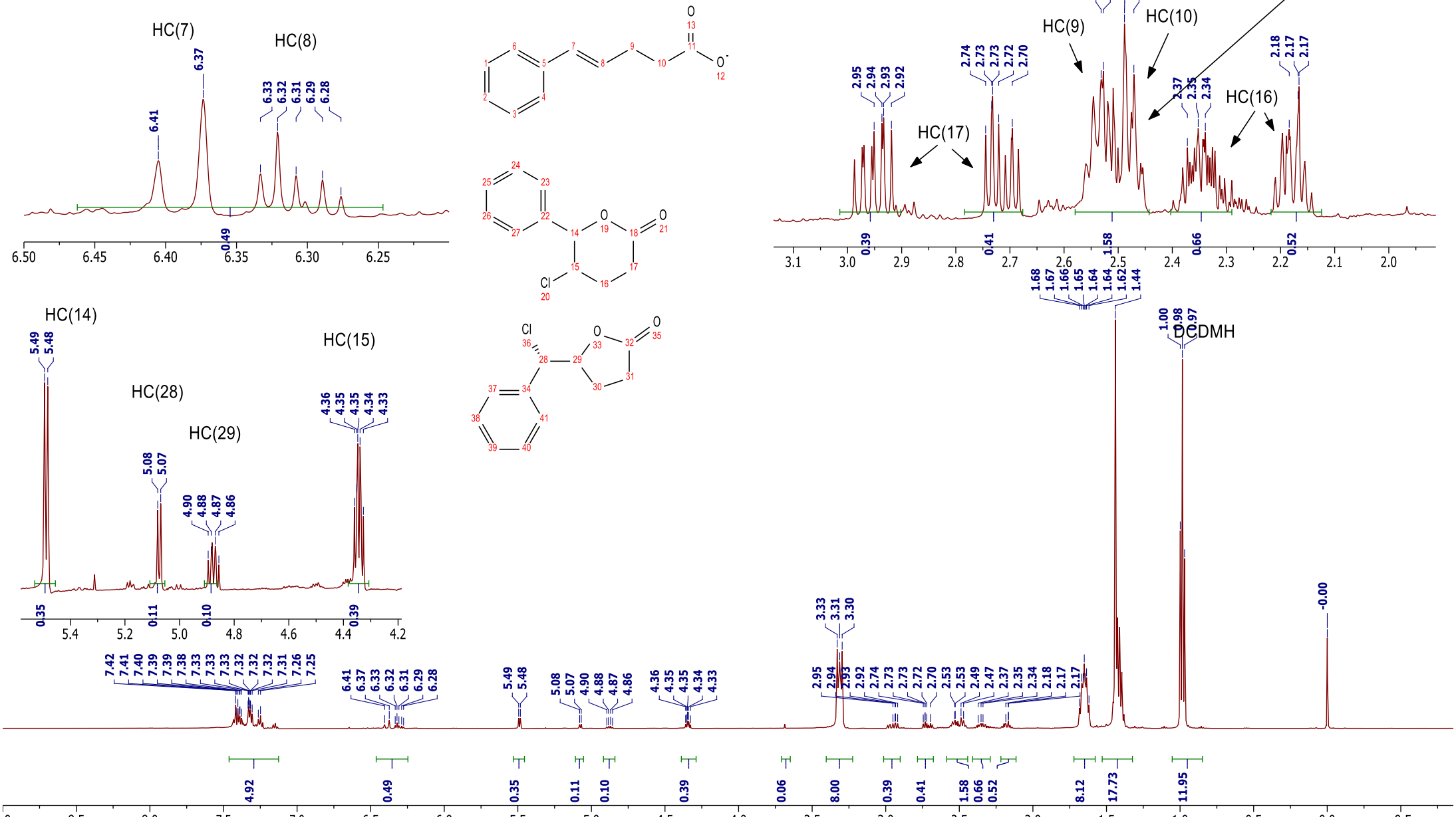




Entry 1, Table 2 - 2.5 h



RP4-56-2.5-nocat
STANDARD PROTON PARAMETERS



Entry 3, Table 2 - 3 min