Supporting Information for

An Isotopic Probe to Follow the Stereochemical Course of Dehydratase Reactions in Polyketide and Fatty Acid Biosynthesis

Synthetic procedures

Synthesis of ethyl (2-^{13}C)cinnamate (26a). To a solution of diisopropylamine (1.60 mL, 11.1 mmol) in THF (17 mL) was added BuLi (6.90 mL, 1.6 M in hexane, 11.1 mmol) dropwise at 0 °C under Ar. After 1 h, the mixture was cooled to –78 °C and triethyl (2-^{13}C)phosphonoacetate (2.50 g, 11.1 mmol) was added dropwise. The reaction mixture was allowed to stir at –78 °C for 45 min, and then benzaldehyde (1.10 g, 11.1 mmol) was added dropwise. Stirring was continued at –78 °C for 6 h. The mixture was allowed to warm to room temperature and poured onto H_2O (30 mL). The aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic layers were dried with $MgSO_4$ and concentrated to dryness. The residue was purified through silica gel column chromatography (pentane/Et_2O, 15:1-5:1) to afford ethyl (2-^{13}C)cinnamate (**26a**)[1] as a colourless solid (1.75 g, 9.9 mmol, 89 % yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.69 (dd, $^3J_{H,H}$ = 16.0 Hz, $^4J_{H,H}$ = 3.1 Hz, 1H), 7.53 (m, 2H), 7.38 (m, 3H), 6.44 (dd, $^1J_{C,H}$ = 161.8 Hz, $^3J_{H,H}$ = 16.0 Hz, 1H), 4.27 (q, $^3J_{H,H}$ = 7.1 Hz, 2H), 1.34 (t, $^3J_{H,H}$ = 7.1 Hz, 3H) ppm (Figure S1); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 167.1 (d, $^1J_{C,C}$ = 76.2 Hz, C), 144.7 (d, $^1J_{C,C}$ = 71.5 Hz, CH), 134.6 (C), 130.4 (d, $^5J_{C,C}$ = 1.1 Hz, CH), 129.0 (2xCH), 128.2 (d, $^3J_{C,C}$ = 4.8 Hz, 2xCH), 118.4 (^{13}CH), 60.6 (d, $^3J_{C,C}$ = 1.5 Hz, CH_2), 14.5 (CH_3) ppm (Figure S2).

Synthesis of (2-^{13}C,3-^{2}H)cinnamate (26b). The same procedure was used to prepare **26b**. Starting material triethyl (2-^{13}C)phosphonoacetate: 3.64 g (16.16 mmol), yield of **26b**: 2.64 g (14.81 mmol, 92%).^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.53 (m, 2H), 7.39 (m, 3H), 6.43 (dt, $^1J_{C,H}$ = 161.9 Hz, $^3J_{H,D}$ = 2.4 Hz, 1H), 4.27 (q, $^3J_{H,H}$ = 7.1 Hz, 2H), 1.34 (t, $^3J_{H,H}$ = 7.1 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 167.1 (d, $^1J_{C,C}$ = 76.0 Hz, C), 144.1 (dt, $^1J_{C,C}$ = 71.5 Hz, $^1J_{C,D}$ = 24.0 Hz, CD), 134.6 (C), 130.4 (d, $^5J_{C,C}$ = 1.1 Hz, CH), 129.0 (2xCH), 128.2 (d, $^3J_{C,C}$ = 4.9 Hz, 2xCH), 118.3 (^{13}CH), 60.6 (d, $^3J_{C,C}$ = 1.4 Hz, CH_2), 14.5 (CH_3) ppm.

Synthesis of (2-^{13}C)cinnamyl alcohol (15a). To a solution of ethyl (2-^{13}C)cinnamate (**26a**) (1.75 g, 9.9 mmol) in THF (27 mL) was added DIBAL-H (21.50 mL, 1 M in hexane, 21.5 mmol) dropwise at 0 °C under Ar. The reaction mixture was stirred for 0.5 h, then saturated potassium sodium tartrate solution (30 mL) was added and stirring was continued for 1 h. The aqueous layer was extracted with Et_2O (3 x 30 mL). The combined organic layers were dried with $MgSO_4$ and concentrated to dryness. Purification of the crude product by column chromatography on silica gel (cyclohexane/EtOAc, 3:1) gave (2-^{13}C)cinnamyl alcohol (**15a**)[2] as a colorless solid (1.20 g, 8.89 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.39 (m, 2H), 7.32 (m, 2H), 7.25 (m, 1H), 6.62 (ddd, $^3J_{H,H}$ = 16.2 Hz, $^4J_{H,H}$ = 1.2 Hz, $^2J_{C,H}$ = 1.2 Hz, 1H), 6.36 (ddt, $^1J_{C,H}$ = 151.6 Hz, $^3J_{H,H}$ = 16.1 Hz, $^3J_{H,H}$ = 5.5 Hz, 1H), 4.33 (dddd, $^3J_{H,H}$ = 5.5 Hz, $^3J_{H,H}$ = 5.5 Hz, $^2J_{C,H}$ = 5.5 Hz, $^4J_{H,H}$ = 1.2 Hz, 2H), 1.51 (td, $^3J_{H,H}$ = 5.5 Hz, $^3J_{C,H}$ = 2.3 Hz, OH) ppm (Figure S3); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.8 (C), 131.3 (d, $^1J_{C,C}$ = 72.5 Hz, CH), 128.7 (2xCH), 128.5 (^{13}CH), 127.8 (d, $^5J_{C,C}$ = 1.1 Hz, CH), 126.6 (d, $^3J_{C,C}$ = 4.6 Hz, 2xCH), 63.9 (d, $^1J_{C,C}$ = 46.9 Hz, CH_2) ppm (Figure S4).

Synthesis of (2-^{13}C,3-^{2}H)cinnamyl alcohol (15b). The same procedure was used to convert (2-^{13}C,3-^{2}H)cinnamyl alcohol (**26b**) into **15b**. Starting material **26b**: 2.60 g (14.6 mmol), yield of **15b**: 1.67 g (12.2 mmol, 84%).^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.39 (m, 2H), 7.32 (m, 2H), 7.25 (m, 1H), 6.36 (dddt, $^1J_{C,H}$ = 152.8 Hz, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 2.8 Hz, $^3J_{H,D}$ = 2.4 Hz, 1H), 4.33 (dd, $^3J_{H,H}$ = 5.8 Hz, $^2J_{C,H}$ = 3.4 Hz, 2H), 1.51 (brs, OH) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.7 (C), 130.9 (dt, $^1J_{C,C}$ = 72.5 Hz, $^1J_{C,D}$ = 22.8 Hz, CD), 128.7 (2xCH), 128.5 (^{13}CH), 127.9 (d, $^5J_{C,C}$ = 1.0 Hz, CH), 126.6 (d, $^3J_{C,C}$ = 4.7 Hz, 2xCH), 63.9 (d, $^1J_{C,C}$ = 46.8 Hz, CH_2) ppm.

Synthesis of (2*S*,3*S*)-(3-phenyloxiranyl)methanol ((2*S*,3*S*)-16).[3] To a solution of L-(+)-diisopropyl tartrate (0.60 mL, 2.9 mmol) in anhydrous CH_2Cl_2 (60 mL) at –20 °C, 3 g of activated powdered 4 Å molecular sieves were added. A solution of *t*-butylhydroperoxide (TBHP) in decane (5–6 M, 8.40 mL, 47 mmol) was slowly added, followed by adding Ti(O*i*Pr)$_4$ (0.75 mL, 2.5 mmol) dropwise. The mixture was

allowed to stir at –20 °C for 0.5 h and then a solution of cinnamyl alcohol (3.00 g, 22.4 mmol) in CH_2Cl_2 (20 mL) was added dropwise over 30 min. After 3 h at –20 °C, the reaction was quenched with 10% aqueous solution of NaOH saturated with NaCl (3 mL). After diethyl ether (50 mL) was added, the mixture was allowed to warm to 10 °C. Stirring was maintained at 10 °C, while $MgSO_4$ (6 g) and celite (1.5 g) were added. After another 15 min of stirring, the solution was filtered through a pad of celite and extracted with diethyl ether (50 mL × 3). The combined organic layers were concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (cyclohexane/EtOAc, 4:1) to give the epoxide (2*S*,3*S*)-**16** (2.30 g, 15.3 mmol, 69%, 96% *ee*) as a colourless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.32 (m, 3H), 7.13 (m, 2H), 4.06 (br d, $^2J_{H,H}$ = 12.7 Hz, 2H), 3.93 (d, $^3J_{H,H}$ = 2.2 Hz, 1H), 3.81 (ddd, $^2J_{H,H}$ = 12.4 Hz, $^3J_{H,H}$ = 7.7 Hz, $^3J_{H,H}$ = 3.8 Hz, 1H), 3.23 (ddd, $^3J_{H,H}$ = 3.7 Hz, $^3J_{H,H}$ = 2.3 Hz, $^3J_{H,H}$ = 2.3 Hz, 1H) ppm (Figure S5); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.8 (C), 128.7 (2xCH), 128.5 (CH), 125.9 (2xCH), 62.5 (CH), 61.4 (CH_2), 55.7 (CH) ppm (Figure S6). Optical rotary power: $[\alpha]_D^{25}$ = –14.9 (*c* 0.7, $CHCl_3$), lit. $[\alpha]_D^{25}$ = –49.3 (*c* 2.4, $CHCl_3$).[3]

Synthesis of (2*S*,3*S*)-16aa, (2*S*,3*S*)-16ba, (2*R*,3*R*)-16ab, and (2*R*,3*R*)-16bb. The same procedure was used to convert (2-^{13}C)cinnamyl alcohol (**15a**) into (2*S*,3*S*)-**16aa** and (2-^{13}C,3-^{2}H)cinnamyl alcohol (**15b**) into (2*S*,3*S*)-**16ba**, while the analogous procedure with D-(–)-diisopropyl tartrate was used for the conversion of **15a** into (2*R*,3*R*)-**16ab** and of **15b** into (2*R*,3*R*)-**16bb**.

(2*S*,3*S*)-16aa. Starting material **15a**: 600 mg (4.44 mmol), yield of **16aa**: 577 mg (3.82 mmol, 86%, 96% *ee*). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.33 (m, 5H), 4.05 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 5.0 Hz, $^2J_{C,H}$ = 2.4 Hz, $^3J_{H,H}$ = 2.4 Hz, 1H), 3.93 (dd, $^2J_{C,H}$ = 2.2 Hz, $^3J_{H,H}$ = 2.2 Hz, 1H), 3.81 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 7.8 Hz, $^3J_{H,H}$ = 3.8, $^2J_{C,H}$ = 2.1 Hz, 1H), 3.23 (dddd, $^1J_{C,H}$ = 173.8 Hz, $^3J_{H,H}$ = 3.9 Hz, $^3J_{H,H}$ = 2.3 Hz, $^3J_{H,H}$ = 2.3 Hz, 1H), 1.85 (ddd, $^3J_{H,H}$ = 7.5 Hz, $^3J_{H,H}$ =5.3 Hz, $^3J_{C,H}$ = 2.2 Hz, OH) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.8 (d, $^2J_{C,C}$ = 0.8 Hz, C), 128.7 (2xCH), 128.5 (CH), 125.9 (d, $^3J_{C,C}$ = 1.5 Hz, 2xCH), 62.5 (^{13}CH), 61.3 (d, $^1J_{C,C}$ = 45.5 Hz, CH_2), 55.7 (d, $^1J_{C,C}$ = 30.2 Hz, CH) ppm. Optical rotation: $[\alpha]_D^{25}$ = –16.4 (*c* 0.25, $CHCl_3$).

(2*S*,3*S*)-16ba. Starting material **15b**: 545 mg (4.03 mmol), yield of **16ba**: 578 mg (3.82 mmol, 94%, 96% *ee*). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.32 (m, 5H), 4.05 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 5.0, $^3J_{H,H}$ = 2.4 Hz, $^2J_{C,H}$ = 2.4 Hz, 1H), 3.81 (dddd, $^2J_{H,H}$ = 12.8 Hz, $^3J_{H,H}$ = 7.8 Hz, $^3J_{H,H}$ = 3.8 Hz, $^2J_{C,H}$ = 2.1 Hz, 1H), 3.23 (ddd, $^1J_{C,H}$ = 173.7 Hz, $^3J_{H,H}$ = 3.8 Hz, $^3J_{H,H}$ = 2.4 Hz, 1H), 1.82 (ddd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 5.3 Hz, $^3J_{C,H}$ = 2.2 Hz, OH) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.7 (d, $^2J_{C,C}$ = 0.5 Hz, C), 128.7 (2xCH), 128.5 (CH), 125.9 (d, $^3J_{C,C}$ = 1.5 Hz, 2xCH), 62.4 (^{13}CH), 61.3 (d, $^1J_{C,C}$ = 45.6 Hz, CH_2), 55.3 (dt, $^1J_{C,C}$ = 30.4 Hz, $^1J_{C,D}$ = 26.9 Hz, CD) ppm. Optical rotation: $[\alpha]_D^{25}$ = –17.2 (*c* 0.30, $CHCl_3$).

(2*R*,3*R*)-16ab. Starting material **15a**: 580 mg (4.29 mmol), yield of **16ab**: 529 mg (3.50 mmol, 82%, 80% *ee*). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.33 (m, 5H), 4.05 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 5.2, $^3J_{H,H}$ = 2.4 Hz, $^2J_{C,H}$ = 2.4 Hz, 1H), 3.93 (dd, $^3J_{H,H}$ = 2.2 Hz, $^2J_{C,H}$ = 2.2 Hz, 1H), 3.81 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 7.8 Hz, $^3J_{H,H}$ = 3.8 Hz, $^2J_{C,H}$ = 2.1 Hz, 1H), 3.23 (dddd, $^1J_{C,H}$ = 173.8 Hz, $^3J_{H,H}$ = 3.8 Hz, $^3J_{H,H}$ = 2.3 Hz, $^3J_{H,H}$ = 2.3 Hz, 1H), 1.75 (ddd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 5.2 Hz, $^3J_{C,H}$ = 2.2 Hz, OH) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.8 (d, $^2J_{C,C}$ = 0.6 Hz, C), 128.7 (2xCH), 128.5 (CH), 125.9 (d, $^3J_{C,C}$ = 1.6 Hz, 2xCH), 62.5 (^{13}CH), 61.3 (d, $^1J_{C,C}$ = 45.5 Hz, CH_2), 55.7 (d, $^1J_{C,C}$ = 30.1 Hz, CH) ppm. Optical rotation: $[\alpha]_D^{25}$ = +15.6 (*c* 0.25, $CHCl_3$).

(2*R*,3*R*)-16bb. Starting material **15b**: 822 mg (6.08 mmol), yield of **16bb**: 845 mg (5.59 mmol, 92%, 96% *ee*). ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 7.32 (m, 5H), 4.05 (dddd, $^2J_{H,H}$ = 12.8 Hz, $^3J_{H,H}$ = 5.0, $^3J_{H,H}$ = 2.4 Hz, $^2J_{C,H}$ = 2.4 Hz, 1H), 3.81 (dddd, $^2J_{H,H}$ = 12.7 Hz, $^3J_{H,H}$ = 7.7 Hz, $^3J_{H,H}$ = 3.8 Hz, $^2J_{C,H}$ = 2.1 Hz, 1H), 3.23 (ddd, $^1J_{C,H}$ = 173.7 Hz, $^3J_{H,H}$ = 3.8 Hz, $^3J_{H,H}$ = 2.4 Hz, 1H), 1.79 (ddd, $^3J_{H,H}$ = 7.6 Hz, $^3J_{H,H}$ = 5.2 Hz, $^3J_{C,H}$ = 2.2 Hz, OH) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 136.7 (d, $^2J_{C,C}$ = 0.5 Hz, C), 128.7 (2xCH), 128.5 (CH), 125.9 (d, $^3J_{C,C}$ = 1.5 Hz, 2xCH), 62.4 (^{13}CH), 61.3 (d, $^1J_{C,C}$ = 45.4 Hz, CH_2), 55.3 (dt, $^1J_{C,C}$ = 30.1 Hz, $^1J_{C,D}$ = 26.9 Hz, CD) ppm. Optical rotation: $[\alpha]_D^{25}$ = +21.3 (*c* 0.3, $CHCl_3$).

Synthesis of Mosher esters of 16. For determination of the enantiomeric excesses of the epoxides **16**, unlabelled (2*S*,3*S*)-**16** and all four labelled compounds **16aa**, **16ba**, **16ab** and **16bb** were converted into their Mosher esters, followed by ^{1}H-NMR spectroscopy. Peak integrations gave then access to the *ee* values. Epoxide (2*S*,3*S*)-**16** (1 mg) was dissolved in CH_2Cl_2 (1 mL). Then (*S*)-Mosher chloride (2 µL) and pyridine (2 µL) were added. The mixture was stirred for 2 h at room temperature. The solvent was evaporated under reduced pressure. The crude product was purified by column chromatography to obtain the Mosher ester of (2*S*,3*S*)-**16** that was analysed by ^{1}H-NMR spectroscopy (Figure S7). The same

procedure was used to convert **16aa**, **16ba**, **16ab** and **16bb** with (*S*)-Mosher chloride to obtain their corresponding Mosher esters, followed by ^{1}H-NMR analysis (Figure S8).

Synthesis of (2*S*,3*S*)-2-(bromomethyl)-3-phenyloxirane ((2*S*,3*S*)-17).[4] To a stirred solution of (2*S*,3*S*)-**16** (2.30 g, 15.3 mmol) and CBr_4 (5.70 g, 17.2 mmol) in CH_2Cl_2 (56 mL) was added dropwise a solution of PPh_3 (4.10 g, 15.3 mmol) in CH_2Cl_2 (25 mL) at 0 °C under Ar. The mixture was stirred at 0 °C for 4 h. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (cyclohexane/EtOAc, 20:1) to give (2*S*,3*S*)-**17** (2.94 g, 13.8 mmol, 90%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.35 (m, 3H), 7.28 (m, 2H), 3.82 (d, $^3J_{H,H}$ = 1.9 Hz, 1H), 3.51 (d, $^3J_{H,H}$ = 5.8 Hz, 2H), 3.32 (td, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.9 Hz, 1H) ppm (Figure S9); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.1 (C), 128.8 (3xCH), 125.8 (2xCH), 61.1 (CH), 60.5 (CH), 32.0 (CH_2) ppm (Figure S10). Optical rotation: $[\alpha]_D^{25}$ = –16.4 (*c* 0.25, $CHCl_3$).

Synthesis of (2*R*,3*S*)-17aa, (2*R*,3*S*)-17ba, (2*S*,3*R*)-17ab, and (2*S*,3*R*)-17bb. The same procedure was used to convert (2*S*,3*S*)-**16aa**, (2*S*,3*S*)-**16ba**, (2*R*,3*R*)-**16ab**, and (2*R*,3*R*)-**16bb**.
(2*R*,3*S*)-17aa. Starting material (2*S*,3*S*)-**16aa**: 577 mg (3.82 mmol), yield of **17aa**: 568 mg (2.65 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.36 (m, 3H), 7.28 (m, 2H), 3.82 (dd, $^3J_{H,H}$ = 1.8 Hz, $^2J_{C,H}$ = 1.5 Hz, 1H), 3.51 (m, 2H), 3.32 (tdd, $^3J_{H,H}$ = 5.8, $^3J_{H,H}$ = 1.9 Hz, $^1J_{C,H}$ = 186.9 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.1 (d, $^2J_{C,C}$ = 1.0 Hz, C), 128.7 (3xCH), 125.8 (d, $^3J_{C,C}$ = 1.6 Hz, 2xCH), 61.1 (^{13}CH), 60.5 (d, $^1J_{C,C}$ = 29.1 Hz, CH), 32.0 (d, $J_{C,C}$ = 47.2 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = –13.0 (*c* 0.3, $CHCl_3$).
(2*R*,3*S*)-17ba. Starting material (2*S*,3*S*)-**16ba**: 578 mg (3.82 mmol), yield of **17ba**: 468 mg (2.19 mmol, 57%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.35 (m, 3H), 7.28 (m, 2H), 3.51 (m, 2H), 3.32 (dt, $^1J_{C,H}$ = 187.3 Hz, $^3J_{H,H}$ = 5.8 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.1 (d, $^2J_{C,C}$ = 1.0 Hz, C), 128.7 (3xCH), 125.8 (d, $^3J_{C,C}$ = 1.2 Hz, 2xCH), 61.0 (^{13}CH), 60.5 (dt, $^1J_{C,C}$ = 29.1 Hz, $^1J_{C,D}$ = 26.5 Hz, CD), 32.0 (d, $^1J_{C,C}$ = 47.2 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = –18.6 (*c* 0.3, $CHCl_3$).
(2*S*,3*R*)-17ab. Starting material (2*R*,3*R*)-**16ab**: 272 mg (1.81 mmol), yield of **17ab**: 328 mg (1.53 mmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.35 (m, 3H), 7.28 (m, 2H), 3.82 (dd, d, $^3J_{H,H}$ = 1.9 Hz, $^2J_{C,H}$ = 1.5, 1H), 3.51 (m, 2H), 3.32 (tdd, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 1.9 Hz, $^1J_{C,H}$ = 186.8 Hz, H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.1 (d, $^2J_{C,C}$ = 0.8 Hz, C), 128.8 (3xCH), 125.8 (d, d, $^3J_{C,C}$ = 1.6 Hz, 2xCH), 61.1 (^{13}CH), 60.5 (d, $^1J_{C,C}$ = 29.1 Hz, CH), 32.0 (d, $^1J_{C,C}$ = 47.2 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = +13.5 (*c* 0.3, $CHCl_3$).
(2*S*,3*R*)-17bb. Starting material (2*R*,3*R*)-**16bb**: 826 mg (5.46 mmol), yield of **17bb**: 1.11 g (5.17 mmol, 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.35 (m, 3H), 7.28 (m, 2H), 3.52 (dd, $^2J_{C,H}$ = 2.6 Hz, $^3J_{H,H}$ = 5.6 Hz, 2H), 3.31 (ddd, $^1J_{C,H}$ = 186.8 Hz, $^3J_{H,H}$ = 5.8 Hz, $^3J_{H,H}$ = 5.8 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 136.1 (d, $^2J_{C,C}$ = 0.6 Hz, C), 128.8 (3xCH), 125.8 (d, $^3J_{C,C}$ = 1.6 Hz, 2xCH), 61.0 (^{13}CH), 60.1 (dt, $^1J_{C,C}$ = 28.9 Hz, $^1J_{C,D}$ = 26.5 Hz, CD), 32.0 (d, $^1J_{C,C}$ = 47.3 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = +15.4 (*c* 0.28, $CHCl_3$).

Synthesis of (2*S*,3*R*)-(3-^{2}H)-1-bromo-3-phenylpropan-2-ol ((2*S*,3*R*)-18).[5] A mixture of (2*S*,3*S*)-**17** (1.00 g, 4.71 mmol) and Pd/C (600 mg, 5% Pd) in CH_3OH (100 mL) was stirred in a D_2 atmosphere (balloon) for 1 h with ice cooling. At the end of the reaction the catalyst was removed by filtration and the solvents were evaporated to obtain the product (2*S*,3*R*)-**18** (790 mg, 3.66 mmol, 78%) without purification.[6] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.33 (m, 2H), 7.25 (m, 3H), 4.02 (ddd, $^3J_{H,H}$ = 6.6 Hz, $^3J_{H,H}$ = 6.6 Hz, $^3J_{H,H}$ = 3.7 Hz, 1H), 3.52 (dd, $^2J_{H,H}$ = 10.4, $^3J_{H,H}$ = 3.8 Hz, 1H), 3.40 (dd, $^2J_{H,H}$ = 10.4, $^3J_{H,H}$ = 6.3 Hz, 1H), 2.90 (dm, $^3J_{H,H}$ = 6.8, 1H) ppm (Figure S11); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 137.1 (C), 129.5 (2xCH), 128.9 (2xCH), 127.0 (CH), 72.0 (CH), 41.2 (t, $^1J_{C,D}$ = 19.4 Hz, CHD), 39.3 (CH_2) ppm (Figure S12). Optical rotation: $[\alpha]_D^{25}$ = –17.7 (*c* 0.3, $CHCl_3$).

Synthesis of (2*R*,3*R*)-18aa, (2*R*,3*S*)-18ba, (2*S*,3*S*)-18ab, and (2*S*,3*R*)-18bb. The same procedure was used to convert (2*R*,3*S*)-**17aa**, (2*R*,3*S*)-**17ba**, (2*S*,3*R*)-**17ab**, and (2*S*,3*R*)-**17bb**.
(2*R*,3*R*)-18aa. Starting material (2*R*,3*S*)-**17aa**: 534 mg (2.49 mmol), yield of **18aa**: 375 mg (1.74 mmol, 69%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.31 (m, 5H), 4.02 (dddd, $^1J_{C,H}$ = 146.5 Hz, $^3J_{H,H}$ = 6.5 Hz, $^3J_{H,H}$ = 6.5 Hz, $^3J_{H,H}$ = 3.7 Hz, 1H), 3.52 (ddd, $^2J_{H,H}$ = 10.5 Hz, $^3J_{H,H}$ = 3.8 Hz, $^2J_{C,H}$ = 1.7 Hz, 1H), 3.40 (ddd, $^2J_{H,H}$ = 10.3 Hz, $^3J_{H,H}$ = 6.2 Hz, $^2J_{C,H}$ = 2.7 Hz, 1H), 2.90 (m, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 137.1 (d, $^2J_{C,C}$ = 1.0 Hz, C), 129.5 (d, $^2J_{C,C}$ = 1.3 Hz, 2xCH), 128.9 (2xCH), 127.0 (CH), 72.0 (^{13}CH), 41.2 (dt, $^1J_{C,C}$ = 37.1 Hz, $^1J_{C,D}$ = 19.4 Hz, CHD), 39.3 (d, $^1J_{C,C}$ = 39.0 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = –16.1 (*c* 0.3, $CHCl_3$).

(2*R*,3*S*)-18ba. Starting material (2*R*,3*S*)-**17ba**: 468 mg (2.19 mmol), yield of **18ba**: 400 mg (1.85 mmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.28 (m, 5H), 4.02 (ddddd, $^{1}J_{C,H}$ = 146.3 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 5.2 Hz, $^{3}J_{H,H}$ = 3.9 Hz, 1H), 3.53 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 3.8 Hz, $^{2}J_{C,H}$ = 1.7 Hz, 1H), 3.40 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 2.7 Hz, 1H), 2.89 (ddt, $^{3}J_{H,H}$ = 6.2 Hz, $^{2}J_{C,H}$ = 4.1 Hz, $^{2}J_{H,D}$ = 1.9 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 137.1 (d, $^{2}J_{C,C}$ = 1.4 Hz, C), 129.5 (d, $^{3}J_{C,C}$ = 1.6 Hz, 2xCH), 128.9 (2xCH), 127.0 (d, $^{5}J_{C,C}$ = 0.6 Hz, CH), 71.9 (^{13}CH), 41.2 (dt, $^{1}J_{C,C}$ = 36.9 Hz, $^{1}J_{C,D}$ = 19.6 Hz, CHD), 39.3 (d, $^{1}J_{C,C}$ = 39.0 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = –17.4 (*c* 0.3, $CHCl_3$).
(2*S*,3*S*)-18ab. Starting material (2*S*,3*R*)-**17ab**: 328 mg (1.53 mmol), yield of **18ab**: 256 mg (1.18 mmol, 77%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.28 (m, 5H), 4.02 (dddd, $^{1}J_{C,H}$ = 146.3 Hz, $^{3}J_{H,H}$ = 6.6 Hz, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 3.8 Hz, 1H), 3.52 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 3.8 Hz, $^{2}J_{C,H}$ = 1.7 Hz, 1H), 3.39 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 2.7 Hz, 1H), 2.90 (ddt, $^{3}J_{H,H}$ = 6.7 Hz, $^{2}J_{C,H}$ = 6.7 Hz, $^{2}J_{H,D}$ = 2.2 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 137.0 (d, $^{2}J_{C,C}$ = 1.0 Hz, C), 129.3 (2xCH), 128.7 (2xCH), 126.9 (d, $^{5}J_{C,C}$ = 0.6 Hz, CH), 71.8 (^{13}CH), 41.1 (dt, $^{1}J_{C,C}$ = 36.8 Hz, $^{1}J_{C,D}$ = 19.5 Hz, CHD), 39.2 (d, $^{1}J_{C,C}$ = 38.8 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = +18.9 (*c* 0.3, $CHCl_3$).
(2*S*,3*R*)-18bb. Starting material (2*S*,3*R*)-**17bb**: 300 mg (1.40 mmol), yield of **18bb**: 220 mg (1.02 mmol, 72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.28 (m, 5H), 4.03 (ddddd, $^{1}J_{C,H}$ = 146.5 Hz, $^{3}J_{H,H}$ = 6.6 Hz, $^{3}J_{H,H}$ = 6.6 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 5.2 Hz, $^{3}J_{H,H}$ = 3.8 Hz, 1H), 3.53 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 3.8 Hz, $^{2}J_{C,H}$ = 1.7 Hz, 1H), 3.40 (ddd, $^{2}J_{H,H}$ = 10.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 2.7 Hz, 1H), 2.89 (ddt, $^{3}J_{H,H}$ = 6.4 Hz, $^{2}J_{C,H}$ = 4.2 Hz, $^{2}J_{H,D}$ = 2.0 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 137.0 (d, $^{2}J_{C,C}$ = 1.1 Hz, C), 129.3 (d, $^{3}J_{C,C}$ = 1.6 Hz, 2xCH), 128.7 (2xCH), 126.9 (CH), 71.8 (^{13}CH), 41.1 (dt, $^{1}J_{C,C}$ = 36.9 Hz, $^{1}J_{C,D}$ = 19.6 Hz, CHD), 39.2 (d, $^{1}J_{C,C}$ = 38.8 Hz, CH_2) ppm. Optical rotation: $[\alpha]_D^{25}$ = +16.6 (*c* 0.3, $CHCl_3$).

Synthesis of (2*S*,3*R*)-(3-^{2}H)-1-bromo-3-phenylpropan-2-yl acetate ((2*S*,3*R*)-19). A mixture of (2*S*,3*R*)-**18** (790 mg, 3.7 mmol) in acetyl chloride (30 mL) was stirred at room temperature overnight. The mixture was then concentrated under reduced pressure and the residue was purified by column chromatography on silica gel (cyclohexane/EtOAc, 20:1) to give the ester (2*S*,3*R*)-**18** (920 mg, 3.56 mmol, 97%) as a colourless oil.[7] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.27 (m, 5H), 5.17 (ddd, $^{3}J_{H,H}$ = 6.3 Hz, $^{3}J_{H,H}$ = 5.0 Hz, $^{3}J_{H,H}$ = 4.6 Hz, 1H), 3.49 (ddd, $^{2}J_{H,H}$ = 10.9, $^{3}J_{H,H}$ = 4.6 Hz, 1H), 3.37 (dd, $^{2}J_{H,H}$ = 10.9 Hz, $^{3}J_{H,H}$ = 5.0 Hz, 1H), 2.99 (br d, $^{3}J_{H,H}$ = 6.4 Hz, 1H), 2.07 (s, 3H) ppm (Figure S13); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.2 (C), 136.0 (C), 129.4 (2xCH), 128.6 (2xCH), 127.0 (CH), 72.9 (CH), 38.1 (t, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 33.4 (CH_2), 21.0 (CH_3) ppm (Figure S14). Optical rotation: $[\alpha]_D^{25}$ = +0.83 (*c* 0.12, $CHCl_3$), lit. for unlabelled (*S*)-**19**: $[\alpha]_D^{20}$ = –1.2 (*c* 2.07, $CHCl_3$).[7]

Synthesis of (2*R*,3*R*)-19aa, (2*R*,3*S*)-19ba, (2*S*,3*S*)-19ab, and (2*S*,3*R*)-19bb. The same procedure was used to convert (2*R*,3*R*)-**18aa**, (2*R*,3*S*)-**18ba**, (2*S*,3*S*)-**18ab**, and (2*S*,3*R*)-**18bb**.
(2*R*,3*R*)-19aa. Starting material (2*R*,3*R*)-**18aa**: 375 mg (1.74 mmol), yield of **19aa**: 368 mg (1.43 mmol, 82%). ^{1}H NMR (500 MHz, C_6D_6): δ_H 7.04 (m, 5H), 5.10 (dddd, $^{1}J_{C,H}$ = 149.8 Hz, $^{3}J_{H,H}$ = 6.0 Hz, $^{3}J_{H,H}$ = 5.0 Hz, $^{3}J_{H,H}$ = 4.4 Hz, 1H), 3.13 (ddd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 4.3 Hz, $^{2}J_{C,H}$ = 2.3 Hz, 1H), 2.96 (ddd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 5.0, $^{2}J_{C,H}$ = 1.7 Hz, 1H), 2.74 (m, 1H), 1.60 (d, $^{4}J_{C,H}$ = 0.4 Hz, 3H) ppm; ^{13}C NMR (126 MHz, C_6D_6): δ_C 169.4 (d, $^{2}J_{C,C}$ = 2.5 Hz, C), 136.5 (C), 129.7 (d, $^{3}J_{C,C}$ = 1.3 Hz, 2xCH), 128.8 (2xCH), 127.1 (CH), 72.0 (^{13}CH), 38.3 (dt, $^{1}J_{C,C}$ = 38.3 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 33.8 (d, $^{1}J_{C,C}$ = 41.0 Hz, CH_2), 20.4 (d, $^{3}J_{C,C}$ = 1.3 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +1.8 (*c* 0.8, $CHCl_3$).
(2*R*,3*S*)-19ba. Starting material (2*R*,3*S*)-**18ba**: 400 mg (1.85 mmol), yield of **19ba**: 430 mg (1.67 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.27 (m, 5H), 5.17 (dddd, $^{1}J_{C,H}$ = 150.2 Hz, $^{3}J_{H,H}$ = 6.9 Hz, $^{3}J_{H,H}$ = 4.8 Hz, $^{3}J_{H,H}$ = 4.8 Hz, 1H), 3.49 (ddd, $^{2}J_{H,H}$ = 10.9 Hz, $^{3}J_{H,H}$ = 4.5 Hz, $^{2}J_{C,H}$ = 2.3 Hz, 1H), 3.37 (ddd, $^{2}J_{H,H}$ = 10.9 Hz, $^{3}J_{H,H}$ = 5.0 Hz, $^{2}J_{C,H}$ = 1.8 Hz, 1H), 2.99 (ddt, $^{3}J_{H,H}$ = 4.9 Hz, $^{2}J_{C,H}$ = 4.9 Hz, $^{2}J_{H,D}$ = 2.1 Hz, 1H), 2.06 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.3 (d, $^{2}J_{C,C}$ = 2.6 Hz, C), 136.2 (C), 129.6 (d, $^{3}J_{C,C}$ = 1.7 Hz, 2xCH), 128.8 (2xCH), 127.1 (CH), 73.1 (^{13}CH), 38.3 (dt, $^{1}J_{C,C}$ = 38.3 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 33.5 (d, $^{1}J_{C,C}$ = 41.2 Hz, CH_2), 21.1 (d, $^{3}J_{C,C}$ = 1.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +2.2 (*c* 1.0, $CHCl_3$).
(2*S*,3*S*)-19ab. Starting material (2*S*,3*S*)-**18ab**: 256 mg (1.18 mmol), yield of **19ab**: 260 mg (1.00 mmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.27 (m, 5H), 5.17 (dddd, $^{1}J_{C,H}$ = 150.2 Hz, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 4.8 Hz, $^{3}J_{H,H}$ = 4.8 Hz, 1H), 3.49 (ddd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 4.5 Hz, $^{2}J_{C,H}$ = 2.4 Hz, 1H), 3.37 (ddd, $^{2}J_{H,H}$ = 10.9 Hz, $^{3}J_{H,H}$ = 5.0 Hz, $^{2}J_{C,H}$ = 1.8 Hz, 1H), 3.00 (ddt, $^{3}J_{H,H}$ = 7.9 Hz, $^{2}J_{C,H}$ = 6.6 Hz, $^{2}J_{H,D}$ = 5.1 Hz, 1H), 2.07 (d, $^{4}J_{C,H}$ = 0.6 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.3 (d, $^{2}J_{C,C}$ = 2.5 Hz, C), 136.2 (C), 129.6 (d, $^{3}J_{C,C}$

= 1.6 Hz, 2xCH), 128.8 (2xCH), 127.1 (CH), 73.1 (^{13}CH), 38.3 (dt, $^{1}J_{C,C}$ = 38.4 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 33.5 (d, $^{1}J_{C,C}$ = 41.2 Hz, CH_2), 21.1 (d, $^{3}J_{C,C}$ = 1.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –1.5 (*c* 1.2, $CHCl_3$).
(2*S*,3*R*)-19bb. Starting material (2*S*,3*R*)-**18bb**: 144 mg (0.67 mmol), yield of **19bb**: 155 mg (0.60 mmol, 90%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.27 (m, 5H), 5.17 (dddd, $^{1}J_{C,H}$ = 150.2 Hz, $^{3}J_{H,H}$ = 6.9 Hz, $^{3}J_{H,H}$ = 4.8 Hz, $^{3}J_{H,H}$ = 4.8 Hz, 1H), 3.49 (ddd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 4.5 Hz, $^{2}J_{C,H}$ = 2.3 Hz, 1H), 3.38 (ddd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 5.0 Hz, $^{2}J_{C,H}$ = 1.8 Hz, 1H), 2.99 (ddt, $^{3}J_{H,H}$ = 4.9 Hz, $^{2}J_{C,H}$ = 4.9 Hz, $^{2}J_{H,D}$ = 2.1 Hz, 1H), 2.07 (d, $^{4}J_{C,H}$ = 0.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.3 (d, $^{2}J_{C,C}$ = 2.6 Hz, C), 136.1 (C), 129.4 (d, $^{3}J_{C,C}$ = 1.7 Hz, 2xCH), 128.6 (2xCH), 127.0 (CH), 72.9 (^{13}CH), 38.1 (dt, $^{1}J_{C,C}$ = 38.4 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 33.4 (d, $^{1}J_{C,C}$ = 41.0 Hz, CH_2), 21.1 (d, $^{3}J_{C,C}$ = 1.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –2.0 (*c* 1.5, $CHCl_3$).

Synthesis of (1*R*,2*S*)-(1-^{2}H)-1-phenylpropan-2-yl acetate ((1*R*,2*S*)-20).[8a] A solution of (2*R*,3*R*)-**19** (920 mg, 3.56 mmol), AIBN (3.60 mL, 0.7 mmol) and $(SiMe_3)_3SiH$ (1.30 mL, 4.3 mmol) in dry benzene (22 mL) was irradiated with UV light under argon. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was purified through silica gel column chromatography with cyclohexane / EtOAc (10:1) to elute the product (1*R*,2*S*)-**20** (1.40 g), contaminated with $(SiMe_3)_3SiH$. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.23 (m, 5H), 5.11 (dq, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 2.91 (dt, $^{3}J_{H,H}$ = 6.5 Hz, $^{2}J_{H,D}$ = 2.1 Hz, 1H), 2.00 (s, 3H), 1.21 (d, $^{3}J_{H,H}$ = 6.3 Hz, 3H) ppm (Figure S15); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.7 (C), 137.7 (C), 129.6 (2xCH), 128.5 (2xCH), 126.6 (CH), 71.6 (CH), 42.0 (t, $^{1}J_{C,D}$ = 19.5 Hz, CHD), 21.5 (CH_3), 19.6 (CH_3) ppm (Figure S16). Optical rotation: $[\alpha]_D^{25}$ = +2.5 (*c* 0.2, $CHCl_3$), lit. for unlabelled (*R*)-**20**: $[\alpha]_D^{20}$ = –3.35 (*c* 0.62, CH_2Cl_2).[8b]

Synthesis of (1*R*,2*S*)-20aa, (1*S*,2*S*)-20ba, (1*S*,2*R*)-20ab, and (1*R*,2*R*)-20bb. The same procedure was used to convert (2*R*,3*R*)-**19aa**, (2*R*,3*S*)-**19ba**, (2*S*,3*S*)-**19ab**, and (2*S*,3*R*)-**19bb**.
(1*R*,2*S*)-20aa. Starting material (2*R*,3*R*)-**19aa**: 368 mg (1.43 mmol), yield of **20aa**: 472 mg. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.23 (m, 5H), 5.11 (ddq, $^{1}J_{C,H}$ = 149.0 Hz, $^{3}J_{H,H}$ = 6.5 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 2.91 (ddt, $^{3}J_{H,H}$ = 6.5 Hz, $^{2}J_{C,H}$ = 6.5 Hz, $^{2}J_{H,D}$ = 2.0 Hz, 1H), 2.00 (s, 3H), 1.22 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.7 (d, $^{2}J_{C,C}$ = 2.5 Hz, C), 137.7 (C), 129.6 (d, $^{3}J_{C,C}$ = 1.4 Hz, 2xCH), 128.5 (2xCH), 126.6 (CH), 71.6 (^{13}CH), 42.1 (dt, $^{1}J_{C,C}$ = 37.9 Hz, $^{1}J_{C,D}$ = 19.3 Hz, CHD), 21.5 (CH_3), 19.5 (d, $^{1}J_{C,C}$ = 39.8 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +1.2 (*c* 0.2, $CHCl_3$).
(1*S*,2*S*)-20ba. Starting material (2*R*,3*S*)-**19ba**: 410 mg (1.59 mmol), yield of **20ba**: 799 mg. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.24 (m, 5H), 5.10 (ddq, $^{1}J_{C,H}$ = 149.0 Hz, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 6.4 Hz, 1H), 2.73 (ddt, $^{3}J_{H,H}$ = 6.7 Hz, $^{2}J_{C,H}$ = 4.3 Hz, $^{2}J_{H,D}$ = 2.1 Hz, 1H), 2.00 (s, 3H), 1.21 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.7 (d, $^{2}J_{C,C}$ = 2.6 Hz, C), 137.7 (C), 129.6 (d, $^{3}J_{C,C}$ = 1.7 Hz, 2xCH), 128.5 (2xCH), 126.6 (CH), 71.6 (^{13}CH), 42.0 (dt, $^{1}J_{C,C}$ = 37.8 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 21.5 (CH_3), 19.6 (d, $^{1}J_{C,C}$ = 39.5 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +2.0 (*c* 0.3, $CHCl_3$).
(1*S*,2*R*)-20ab. Starting material (2*S*,3*S*)-**19ab**: 260 mg (1.00 mmol), yield of **20ab**: 325 mg. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 7.24 (m, 5H), 5.11 (ddq, $^{1}J_{C,H}$ = 149.1 Hz, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 6.4 Hz, 1H), 2.91 (ddt, $^{3}J_{H,H}$ = 6.5 Hz, $^{2}J_{C,H}$ = 6.5 Hz, $^{2}J_{H,D}$ = 2.0 Hz, 1H), 2.00 (s, 3H), 1.21 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 170.7 (d, $^{2}J_{C,C}$ = 2.6 Hz, C), 137.7 (d, $^{2}J_{C,C}$ = 1.5 Hz, C), 129.6 (d, $^{3}J_{C,C}$ = 1.6 Hz, 2xCH), 128.5 (d, $^{4}J_{C,C}$ = 0.5 Hz, 2xCH), 126.6 (d, $^{5}J_{C,C}$ = 0.8 Hz, CH), 71.6 (^{13}CH), 42.0 (dt, $^{1}J_{C,C}$ = 37.9 Hz, $^{1}J_{C,D}$ = 19.5 Hz, CHD), 21.5 (CH_3), 19.6 (d, $^{1}J_{C,C}$ = 39.6 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –3.2 (*c* 0.5, $CHCl_3$).
(1*R*,2*R*)-20bb. Starting material (2*S*,3*R*)-**19bb**: 200 mg (0.77 mmol), yield of **20bb**: 235 mg. ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 7.23 (m, 5H), 5.10 (ddq, $^{1}J_{C,H}$ = 149.0 Hz, $^{3}J_{H,H}$ = 6.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 2.73 (ddt, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.0 Hz, $^{2}J_{H,D}$ = 1.9 Hz, 1H), 1.99 (s, 3H), 1.21 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.2 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 170.7 (d, $^{2}J_{C,C}$ = 2.6 Hz, C), 137.7 (d, $^{2}J_{C,C}$ = 1.5 Hz, C), 129.6 (d, $^{3}J_{C,C}$ = 1.7 Hz, 2xCH), 128.5 (2xCH), 126.6 (d, $^{5}J_{C,C}$ = 0.9 Hz, CH), 71.6 (^{13}CH), 42.0 (dt, $^{1}J_{C,C}$ = 37.9 Hz, $^{1}J_{C,D}$ = 19.7 Hz, CHD), 21.5 (CH_3), 19.6 (d, $^{1}J_{C,C}$ = 39.5 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –1.3 (*c* 0.3, $CHCl_3$).

Synthesis of (2*S*,3*S*)-(2-^{2}H)-3-acetoxybutanoic acid ((2*S*,3*S*)-21).[9,10] To a solution of (2*S*,3*S*)-**20** (1.40 g) in CCl_4 (20 mL), CH_3CN (20 mL) and phosphate buffer (30 mL, pH = 7), H_5IO_6 (16.5 g, 72.4 mmol) was added and the mixture was stirred for 1 h at room temperature. After cooling to 10 °C, $RuCl_3$ (72 mg, 0.4 mmol) was added. The mixture was stirred overnight at that temperature, and then diethyl ether (40 ml) was added under vigorous stirring for 10 min. The mixture was extracted with diethyl ether (3

x 80 mL). The combined organic layers were evaporated to 10 mL, extracted with NH_3 H_2O (2 mL) and with H_20 (10 mL x 3). The combined water phases were acidified by adding 1 M HCl (5 mL), followed by extraction with Et_20 (50 mL x 3). The combined organic extracts were dried with $MgSO_4$ and concentrated in vacuo obtain the product (2*S*,3*S*)-**21** (351 mg, 2.39 mmol, 67% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.26 (dq, $^3J_{H,H}$ = 7.4 Hz, $^3J_{H,H}$ = 6.4 Hz, 1H), 2.67 (dt, $^3J_{H,H}$ = 7.4 Hz, $^2J_{H,D}$ = 2.1 Hz, 1H), 2.03 (s, 3H), 1.32 (d, $^3J_{H,H}$ = 6.4 Hz, 3H) ppm (Figure S17); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 175.9 (C), 170.5 (C), 67.0 (CH), 40.1 (t, $J_{C,D}$ = 19.6 Hz, CHD), 21.2 (CH_3), 19.8 (CH_3) ppm (Figure S18). Optical rotation: $[\alpha]_D^{25}$ = +1.7 (*c* 1.5, $CHCl_3$), lit. $[\alpha]_D^{24}$ = +3.6 (*c* 10.175, EtOH).[11]

Synthesis of (2*S*,3*S*)-21aa, (2*R*,3*S*)-21ba, (2*R*,3*R*)-21ab, and (2*R*,3*R*)-21bb. The same procedure was used to convert (1*R*,2*S*)-**20aa**, (1*S*,2*S*)-**20ba**, (1*S*,2*R*)-**20ab**, and (1*R*,2*R*)-**20bb**.
(2*S*,3*S*)-21aa. Starting material (1*R*,2*S*)-**20aa**: 472 mg, yield of **21aa**: 135 mg (0.92 mmol, 64% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.26 (ddq, $^1J_{C,H}$ = 151.4 Hz, $^3J_{H,H}$ = 7.4 Hz, $^3J_{H,H}$ = 6.4 Hz, 1H), 2.67 (m, 1H), 2.04 (s, 3H), 1.32 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 175.9 (C), 170.6 (d, $^2J_{C,C}$ = 2.5 Hz, C), 67.1 (^{13}CH), 40.2 (dt, $^1J_{C,C}$ = 39.9 Hz, $^1J_{C,D}$ = 19.6 Hz, CHD), 21.3 (CH_3), 19.9 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +2.0 (*c* 1.0, $CHCl_3$).
(2*R*,3*S*)-21ba. Starting material (1*S*,2*S*)-**20ba**: 799 mg, yield of **21ba**: 151 mg (1.03 mmol, 62% over two steps). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.26 (ddq, $^1J_{C,H}$ = 151.5 Hz, $^3J_{H,H}$ = 6.3 Hz, $^3J_{H,H}$ = 6.2 Hz, 1H), 2.54 (ddt, $^3J_{H,H}$ = 6.2 Hz, $^2J_{C,H}$ = 2.9 Hz, $^3J_{H,D}$ = 2.9 Hz, 1H), 2.04 (s, 3H), 1.32 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 175.5 (C), 170.5 (d, $^2J_{C,C}$ = 2.4 Hz, C), 67.1 (^{13}CH), 40.1 (dt, $^1J_{C,C}$ = 39.6 Hz, $^1J_{C,D}$ = 20.0 Hz, CHD), 21.3 (CH_3), 20.0 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +1.8 (*c* 1.2, $CHCl_3$).
(2*R*,3*R*)-21ab. Starting material (1*S*,2*R*)-**20ab**: 325 mg, yield of **21ab**: 70 mg (0.47 mmol, 47% over two steps). ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 5.26 (ddq, $^1J_{C,H}$ = 151.4 Hz, $^3J_{H,H}$ = 7.4 Hz, $^3J_{H,H}$ = 6.4 Hz, 1H), 2.68 (ddt, $^3J_{H,H}$ = 7.2 Hz, $^2J_{C,H}$ = 2.2 Hz, $^3J_{H,D}$ = 2.2 Hz, 1H), 2.04 (d, $^4J_{C,H}$ = 0.5 Hz, 3H), 1.32 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 175.4 (C), 170.5 (d, $^2J_{C,C}$ = 2.5 Hz, C), 67.1 (^{13}CH), 40.1 (dt, $^1J_{C,C}$ = 39.7 Hz, $^1J_{C,D}$ = 19.5 Hz, CHD), 21.3 (d, $^3J_{C,C}$ = 1.1 Hz, CH_3), 19.9 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –1.1 (*c* 0.8, $CHCl_3$).
(2*R*,3*R*)-21bb. Starting material (1*R*,2*R*)-**20bb**: 235 mg, yield of **21bb**: 84 mg (0.57 mmol, 74% over two steps). ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 5.26 (ddq, $^1J_{C,H}$ = 151.4 Hz, $^3J_{H,H}$ = 6.2 Hz, $^3J_{H,H}$ = 6.1 Hz, 1H), 2.53 (ddt, $^3J_{H,H}$ = 5.5 Hz, $^2J_{C,H}$ = 3.5 Hz, $^3J_{H,D}$ = 2.2 Hz, 1H), 2.03 (d, $^4J_{C,H}$ = 0.5 Hz, 3H), 1.32 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.3 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 176.1 (C), 170.6 (C), 67.1 (^{13}CH), 40.2 (dt, $^1J_{C,C}$ = 39.7 Hz, $^1J_{C,D}$ = 19.9 Hz, CHD), 21.3 (d, $^3J_{C,C}$ = 1.1 Hz, CH_3), 19.9 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –1.3 (*c* 0.9, $CHCl_3$).

Synthesis of (2*S*,3*S*)-(2-^{2}H)-3-hydroxybutanoic acid ((2*S*,3*S*)-22). To a solution of (2*S*,3*S*)-**21** (351 mg, 2.39 mmol) in methanol (5 mL), LiOH (170 mg, 7.0 mmol) was added and the mixture was stirred for 1 h. The mixture was acidified by adding 1 M HCl (1 mL), followed by extraction with Et_20 (20 mL x 3). The combined extracts were dried with $MgSO_4$ and concentrated to yield the product (2*S*,3*S*)-**22** (150 mg, 1.43 mmol, 60%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 4.23 (m, 1H), 2.48 (m, 1H), 1.26 (dd, $^3J_{H,H}$ = 6.3 Hz, $^4J_{H,H}$ = 0.7 Hz, 3H) ppm (Figure S19); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 177.2 (C), 64.3 (CH), 42.3 (t, $^1J_{C,D}$ = 19.5 Hz, CHD), 22.5 (CH_3) ppm (Figure S20). Optical rotation: $[\alpha]_D^{25}$ = +6.9 (*c* 0.32, $CHCl_3$), lit. $[\alpha]_D^{25}$ = +4.1 (*c* 2.70, MeOH).[12]

Synthesis of (2*S*,3*S*)-22aa, (2*R*,3*S*)-22ba, (2*R*,3*R*)-22ab, and (2*R*,3*R*)-22bb. The same procedure was used to convert (2*S*,3*S*)-**21aa**, (2*R*,3*S*)-**21ba**, (2*R*,3*R*)-**21ab**, and (2*R*,3*R*)-**21bb**.
(2*S*,3*S*)-22aa. Starting material (2*S*,3*S*)-**21aa**: 135 mg (0.92 mmol), yield of **22aa**: 68 mg (0.65 mmol, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 4.23 (ddq, $^1J_{C,H}$ = 145.2 Hz, $^3J_{H,H}$ = 9.0 Hz, $^3J_{H,H}$ = 6.3 Hz, 1H), 2.49 (ddt, $^3J_{H,H}$ = 9.0 Hz, $^2J_{C,H}$ = 5.8 Hz, $^3J_{H,D}$ = 2.4 Hz, 1H), 1.27 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 176.4 (C), 64.3 (CH), 42.2 (dt, $^1J_{C,C}$ = 37.3 Hz, $^1J_{C,D}$ = 19.1 Hz, CHD), 22.6 (d, $^1J_{C,C}$ = 39.4 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +8.1 (*c* 0.25, $CHCl_3$).
(2*R*,3*S*)-22ba. Starting material (2*R*,3*S*)-**21ba**: 82 mg (0.56 mmol), yield of **22ba**: 30 mg (0.29 mmol, 51%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 4.22 (ddq, $^1J_{C,H}$ = 144.1 Hz, $^3J_{H,H}$ = 9.0 Hz, $^3J_{H,H}$ = 6.4 Hz, 1H), 2.55 (m, 1H), 1.27 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 177.2 (C), 64.3 (CH),

42.2 (dt, $^{1}J_{C,C}$ = 37.1 Hz, $^{1}J_{C,D}$ = 19.8 Hz, CHD), 22.6 (d, $^{1}J_{C,C}$ = 39.3 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +7.3 (*c* 0.3, $CHCl_3$).

(2*R*,3*R*)-22ab. Starting material (2*R*,3*R*)-**21ab**: 70 mg (0.47 mmol), yield of **22ab**: 35 mg (0.33 mmol, 70%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 4.23 (ddq, $^{1}J_{C,H}$ = 145.3 Hz, $^{3}J_{H,H}$ = 9.0 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 2.49 (ddt, $^{3}J_{H,H}$ = 8.3 Hz, $^{2}J_{C,H}$ = 3.7 Hz, $^{3}J_{H,D}$ = 2.0 Hz, 1H), 1.27 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 177.4 (C), 64.3 (CH), 42.2 (dt, $^{1}J_{C,C}$ = 38.0 Hz, $^{1}J_{C,D}$ = 19.6 Hz, CHD), 22.6 (d, $^{1}J_{C,C}$ = 39.3 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –8.4 (*c* 0.27, $CHCl_3$).

(2*R*,3*R*)-22bb. Starting material (2*R*,3*R*)-**21bb**: 84 mg (0.57 mmol), yield of **22bb**: 40 mg (0.38 mmol, 67%). ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 4.21 (m, 1H), 2.55 (ddt, $^{3}J_{H,H}$ = 8.3 Hz, $^{2}J_{C,H}$ = 5.5 Hz, $^{3}J_{H,D}$ = 2.6 Hz, 1H), 1.27 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 175.1 (C), 64.3 (CH), 42.0 (dt, $^{1}J_{C,C}$ = 37.6 Hz, $^{1}J_{C,D}$ = 19.6 Hz, CHD), 22.7 (d, $^{1}J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –10.3 (*c* 0.35, $CHCl_3$).

Synthesis of (2*R*,3*S*)-(2-^{2}H)butane-1,3-diol ((2*R*,3*S*)-23). A solution of (2*S*,3*S*)-**22** (150 mg, 1.43 mmol) in THF (0.5 mL) was added dropwise to a solution of $BH_3{\cdot}Me_2S$ (165 µL, 1.7 mmol) in THF (1 mL) under ice cooling, followed by stirring the mixture overnight. The reaction was quenched by the addition of H_2O (2 mL) and extracted with Et_20 (10 mL x 3). The combined extracts were dried with $MgSO_4$ and concentrated in vacuo to get the product (2*R*,3*S*)-**23**. ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 4.18 (dq, $^{3}J_{H,H}$ = 9.4 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 4.06 (dd, $^{2}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 4.9 Hz, 1H), 3.98 (dd, $^{2}J_{H,H}$ = 10.9 Hz, $^{3}J_{H,H}$ = 6.7 Hz, 1H), 1.66 (m, 1H), 1.28 (d, $^{3}J_{H,H}$ = 6.3 Hz, 3H) ppm (Figure S21); ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 68.8 (CH), 62.0 (CH_2), 33.8 (t, $^{1}J_{C,D}$ = 18.3 Hz, CHD), 22.9 (CH_3) ppm (Figure S22).[13]

Synthesis of (2*R*,3*S*)-(2-^{2}H)butane-1,3-diol ((2*R*,3*S*)-24).[14,15] A mixture of (2*S*,3*S*)-**23** (129 mg, 1.4 mmol), benzaldehyde (150 mg, 14 mmol), *p*-toluenesulfonic acid monohydrate (27 mg, 0.14 mmol) and $MgSO_4$ (344 mg, 2.8 mmol) in 1.5 mL of CH_2Cl_2 was stirred for 6 hours at room temperature. Then the reaction mixture was filtered, the organic layer was washed with sat. aq. $NaHCO_3$ and sat. aq. Na_2SO_3. The organic layer was dried with $MgSO_4$ and concentrated to give a mixture consisting of the desired benzylidene acetal (2*R*,3*S*)-**24** and benzaldehyde (35 mg, ^{1}H-NMR ratio: 1/6) which was analysed without further purification. ^{1}H NMR (700 MHz, C_6D_6): δ_H 7.70 (ddd, $^{3}J_{H,H}$ = 7.8 Hz, $^{4}J_{H,H}$ = 1.4 Hz, $^{4}J_{H,H}$ = 0.6 Hz, 2H), 7.20 (dd, $^{3}J_{H,H}$ = 8.4 Hz, $^{3}J_{H,H}$ = 7.0 Hz, 2H), 7.12 (m, 1H), 5.38 (s, 1H), 3.94 (dd, $^{3}J_{H,H}$ = 11.3 Hz, $^{3}J_{H,H}$ = 5.0 Hz, 1H), 3.49 (m, overlap, 1H), 3.48 (m, overlap, 1H), 1.50 (dd, $^{3}J_{H,H}$ = 12.6 Hz, $^{3}J_{H,H}$ = 11.0 Hz, $^{3}J_{H,H}$ = 4.9 Hz, $^{2}J_{H,D}$ = 1.8 Hz, 1H), 1.11 (d, $^{3}J_{H,H}$ = 6.2 Hz, 3H) ppm (Figure S23); ^{13}C NMR (176 MHz, C_6D_6): δ_C 140.0 (C), 128.2 (2xCH), 128.0 (CH), 126.8 (2xCH), 101.5 (CH), 73.2 (CH), 66.9 (CH_2), 32.8 (t, $^{1}J_{C,D}$ = 19.8 Hz, CHD), 21.9 (CH_3) ppm (Figure S24).[16] Optical rotation: $[\alpha]_D^{25}$ = +13.4 (*c* 0.5, $CHCl_3$).

Synthesis of *S*-(2-acetamidoethyl) (2-^{13}C,3-^{2}H)-(2*S*,3*S*)-3-hydroxybutanethioate ((2*S*,3*S*)-27aa).[17] (2*S*,3*S*)-**22aa** (68 mg, 0.65 mmol) was dissolved in CH_2Cl_2 (11 mL). DMAP (14 mg, 0.11 mmol), EDC·HCl (140 mg, 0.73 mmol) and N-acetylcysteamine (78 mg, 0.65 mmol) were added to this solution. The mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc) to yield (2*S*,3*S*)-**27aa** (47 mg, 0.23 mmol, 35%).[18] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.82 (br s, NH), 4.25 (ddq, $^{1}J_{C,H}$ = 145.5 Hz, $^{3}J_{H,H}$ = 8.8 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 3.46 (m, 2H), 3.05 (m, 2H), 2.69 (ddt, $^{3}J_{H,H}$ = 8.4 Hz, $^{2}J_{C,H}$ = 5.9 Hz, $^{3}J_{H,D}$ = 2.2 Hz, 1H), 1.98 (s, 3H), 1.24 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.5 Hz, 3H) ppm (Figure S30); ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 199.6 (C), 170.6(C), 65.2 (^{13}CH), 52.2 (dt, $^{1}J_{C,C}$ = 36.0 Hz, $^{1}J_{C,D}$ = 19.9 Hz, CHD), 39.5 (CH_2), 29.0 (CH_2), 23.4 (CH_3), 22.8 (d, $^{1}J_{C,C}$ = 39.2 Hz, CH_3) ppm (Figure S31). Optical rotation: $[\alpha]_D^{25}$ = +8.0 (*c* 0.3, $CHCl_3$), lit. $[\alpha]_D^{25}$ = +27.9 (*c* 1.0, $CHCl_3$).[18]

Synthesis of (2*R*,3*S*)-27ba, (2*R*,3*R*)-27ab, and (2*S*,3*R*)-27bb. The same procedure was used to convert (2*R*,3*S*)-**22ba**, (2*R*,3*R*)-**22ab**, and (2*R*,3*R*)-**22bb**.

(2*R*,3*S*)-27ba. Starting material (2*R*,3*S*)-**22ba**: 30 mg (0.29 mmol), yield of **27ba**: 22 mg (0.11 mmol, 37%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.85 (br s, NH), 4.29 (ddq, $^{1}J_{C,H}$ = 145.5 Hz, $^{3}J_{H,H}$ = 8.8 Hz, $^{3}J_{H,H}$ = 6.3 Hz, 1H), 3.46 (m, 2H), 3.06 (m, 2H), 2.72 (m, 1H), 1.98 (s, 3H), 1.24 (dd, $^{3}J_{H,H}$ = 6.3 Hz, $^{2}J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 199.6 (C), 170.7 (C), 65.2 (^{13}CH), 52.1 (dt, $^{1}J_{C,C}$ = 36.2 Hz, $^{1}J_{C,D}$ = 19.9

Hz, CHD), 39.5 (CH_2), 29.0 (CH_2), 23.3 (CH_3), 22.8 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = +16.8 (*c* 0.5, $CHCl_3$).[18]

(2*R*,3*R*)-27ab. Starting material (2*R*,3*R*)-**22ab**: 35 mg (0.33 mmol), yield of **27ab**: 22 mg (0.11 mmol, 32%). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 5.95 (br s, NH), 4.26 (ddq, $^1J_{C,H}$ = 145.5 Hz, $^3J_{H,H}$ = 8.7 Hz, $^3J_{H,H}$ = 6.3 Hz, 1H), 3.45 (m, 2H), 3.04 (m, 2H), 2.68 (ddt, $^3J_{H,H}$ = 8.4 Hz, $^2J_{C,H}$ = 5.9 Hz, $^3J_{H,D}$ = 2.2 Hz, 1H), 1.97 (s, 3H), 1.23 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 199.5 (C), 170.7 (C), 65.2 (^{13}CH), 52.3 (dt, $^1J_{C,C}$ = 36.0 Hz, $^1J_{C,D}$ = 19.5 Hz, CHD), 39.4 (CH_2), 28.9 (CH_2), 23.3 (CH_3), 22.8 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –10.2 (*c* 0.6, $CHCl_3$), lit. $[\alpha]_D^{25}$ = –27.2 (*c* 1.0, $CHCl_3$).[18]

(2*S*,3*R*)-27bb. Starting material (2*R*,3*R*)-**22bb**: 40 mg (0.38 mmol), yield of **27bb**: 21 mg (0.10 mmol, 27%). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 5.92 (br s, NH), 4.24 (ddq, $^1J_{C,H}$ = 145.0 Hz, $^3J_{H,H}$ = 8.9 Hz, $^3J_{H,H}$ = 6.1 Hz, 1H), 3.44 (m, 2H), 3.04 (m, 2H), 2.71 (m, 1H), 1.96 (s, 3H), 1.23 (dd, $^3J_{H,H}$ = 6.3 Hz, $^2J_{C,H}$ = 4.5 Hz, 3H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 199.5 (d, $^2J_{C,C}$ = 2.4 Hz, C), 170.6 (C), 65.1 (^{13}CH), 52.3 (dt, $^1J_{C,C}$ = 36.1 Hz, $^1J_{C,D}$ = 20.0 Hz, CHD), 39.4 (CH_2), 29.0 (CH_2), 23.3 (CH_3), 22.8 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm. Optical rotation: $[\alpha]_D^{25}$ = –18.8 (*c* 0.8, $CHCl_3$).[18]

Synthesis of *S*-(2-acetamidoethyl) (*E*)-but-2-enethioate (28a).[17] (*E*)-But-2-enoic acid (100 mg, 1.16 mmol) was dissolved in CH_2Cl_2 (20 mL). DMAP (28 mg, 0.23 mmol), EDC·HCl (245 mg, 1.28 mmol) and N-acetylcysteamine (143 mg, 1.16 mmol) were added to this solution. The mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc) to yield **28a** (170 mg, 0.91 mmol, 78%). ^{1}H NMR (700 MHz, C_6D_6): δ_H 6.73 (dq, $^3J_{H,H}$ = 15.4 Hz, $^3J_{H,H}$ = 6.9 Hz, 1H), 5.91 (dq, $^3J_{H,H}$ = 15.4 Hz, $^4J_{H,H}$ = 1.7 Hz, 1H), 3.24 (td, $^3J_{H,H}$ = 6.8 Hz, $^3J_{H,H}$ = 5.8 Hz, 2H), 2.88 (t, $^3J_{H,H}$ = 6.8 Hz, 2H), 1.48 (s, 3H), 1.22 (dd, $^3J_{H,H}$ = 6.9 Hz, $^3J_{H,H}$ = 1.7 Hz, 3H) ppm (Figure S32); ^{13}C NMR (176 MHz, C_6D_6): δ_C 189.3 (C), 168.9 (C), 141.1 (CH), 130.2 (CH), 39.8 (CH_2), 28.5 (CH_2), 22.7 (CH_3), 17.4 (CH_3) ppm (Figure S33).

Synthesis of *S*-(2-acetamidoethyl) (*Z*)-but-2-enethioate (29a).[19] A mixture of but-2-ynoic acid (100 mg, 1.19 mmol), quinoline (5 mg, 0.04 mmol) and Lindlar's catalyst (23 mg) in Et_2O (10 mL) was stirred in a H_2 atmosphere for 1 h at room temperature. The catalyst was removed by filtration and the solvents were evaporated. The product (*Z*)-but-2-enoic acid (40 mg, 0.46 mmol, 39%) was obtained by column chromatography on silica gel (n-pentane / Et_2O, 2:1). ^{1}H NMR (700 MHz, $CDCl_3$): δ_H 6.47 (dq, $^3J_{H,H}$ = 11.5 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H), 5.83 (dq, $^3J_{H,H}$ = 11.6 Hz, $^4J_{H,H}$ = 1.8 Hz, 1H), 2.16 (dd, $^3J_{H,H}$ = 7.3 Hz, $^3J_{H,H}$ = 1.8 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$): δ_C 172.0 (C), 148.0 (CH), 120.2 (CH), 15.8 (CH_3) ppm.

A mixture of (*Z*)-but-2-enoic acid (20 mg, 0.23 mmol) and triethylamine (47 mg, 0.46 mmol) in CH_2Cl_2 (2 mL) was stirred for 10 min with ice cooling. $ClCO_2Et$ (50 mg, 0.46 mmol) was added to this solution. After 2 h, N-acetylcysteamine (29 mg, 0.23 mmol) was added. The mixture was stirred for 3 h at room temperature and then concentrated under reduced pressure. The residue was purified by HPLC to yield **29a** (6 mg, 0.03 mmol, 14%). ^{1}H NMR (700 MHz, C_6D_6): δ_H 5.86 (dq, $^3J_{H,H}$ = 11.2 Hz, $^4J_{H,H}$ = 1.7 Hz, 1H), 5.51 (dq, $^3J_{H,H}$ = 11.3 Hz, $^3J_{H,H}$ = 7.3 Hz, 1H), 3.21 (td, $^3J_{H,H}$ = 6.5 Hz, $^3J_{H,H}$ = 6.4 Hz, 2H), 2.84 (t, $^3J_{H,H}$ = 6.7 Hz, 2H), 1.92 (dd, $^3J_{H,H}$ = 7.3 Hz, $^3J_{H,H}$ = 1.8 Hz, 3H), 1.47 (s, 3H) ppm (Figure S34); ^{13}C NMR (176 MHz, C_6D_6): δ_C 199.6 (C), 170.6(C), 65.2 (^{13}CH), 52.2 (dt, $^1J_{C,C}$ = 36.0 Hz, $^1J_{C,D}$ = 19.9 Hz, CHD), 39.5 (CH_2), 29.0 (CH_2), 23.4 (CH_3), 22.8 (d, $^1J_{C,C}$ = 39.2 Hz, CH_3) ppm (Figure S35).

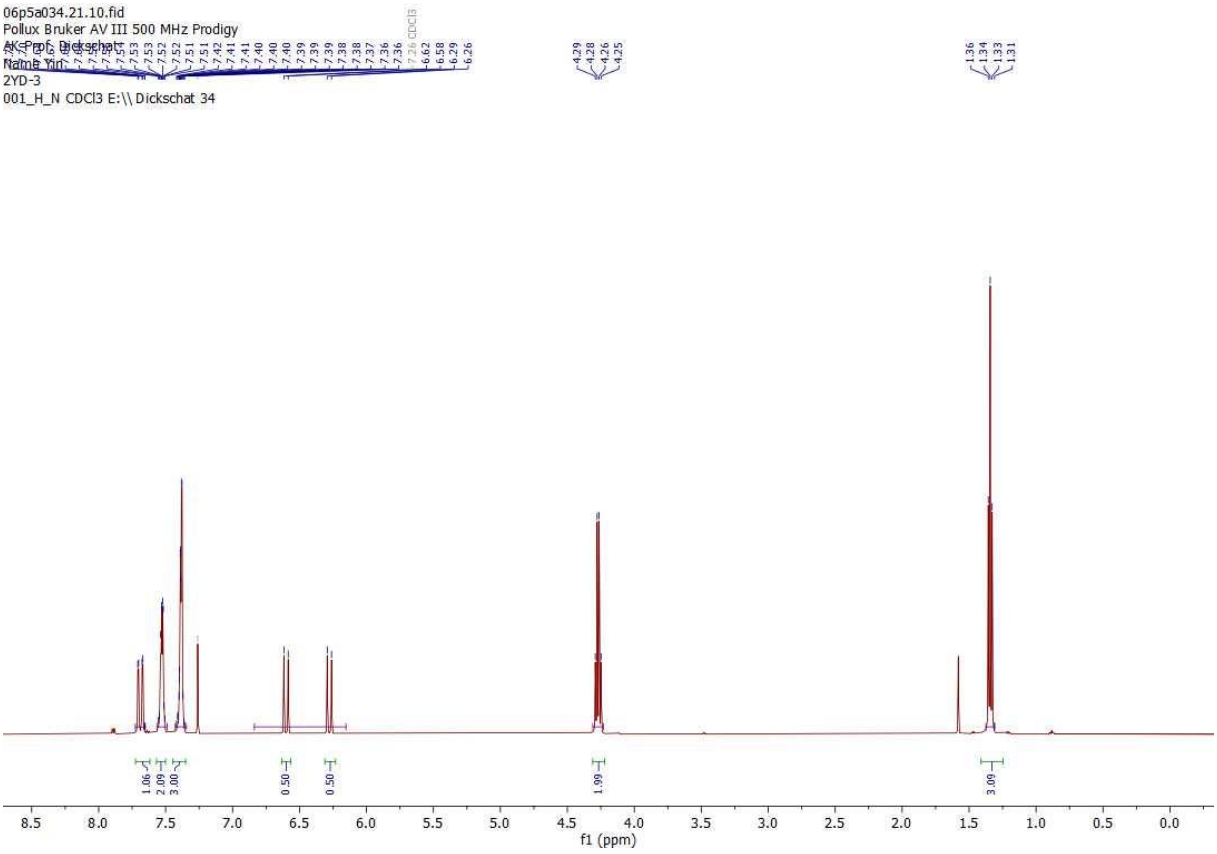

Figure S1. ^{1}H NMR (500 MHz, $CDCl_3$) of **26a**.

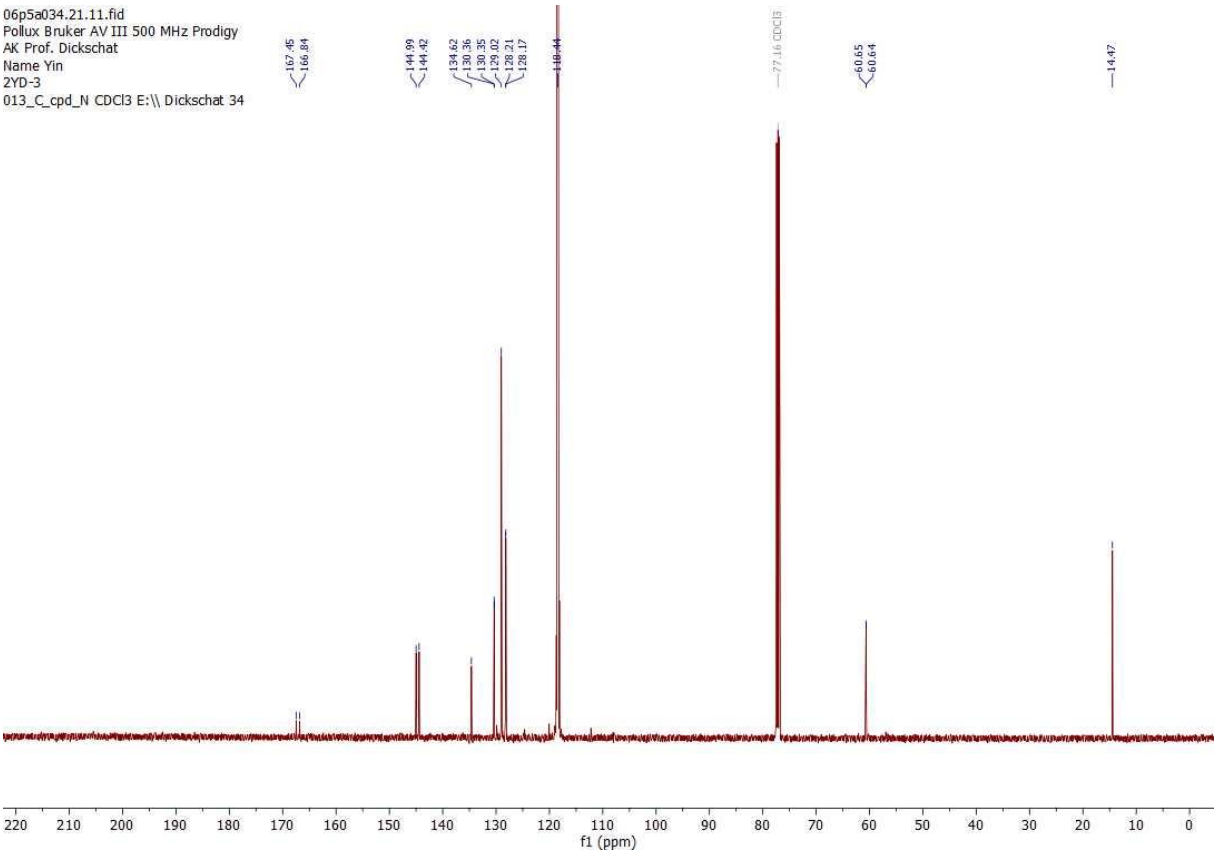

Figure S2. ^{13}C NMR (126 MHz, $CDCl_3$) of **26a**.

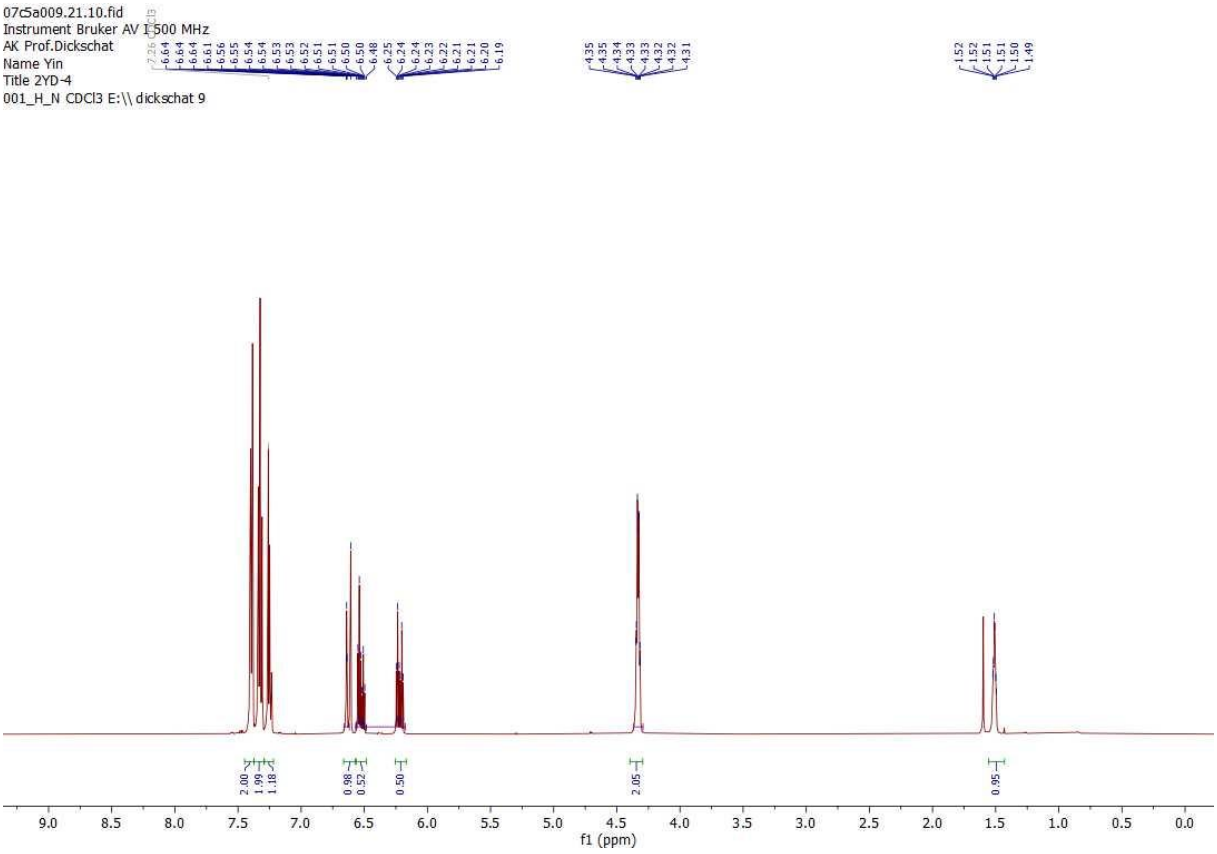

Figure S3. ^{1}H NMR (500 MHz, $CDCl_3$) of **15a**.

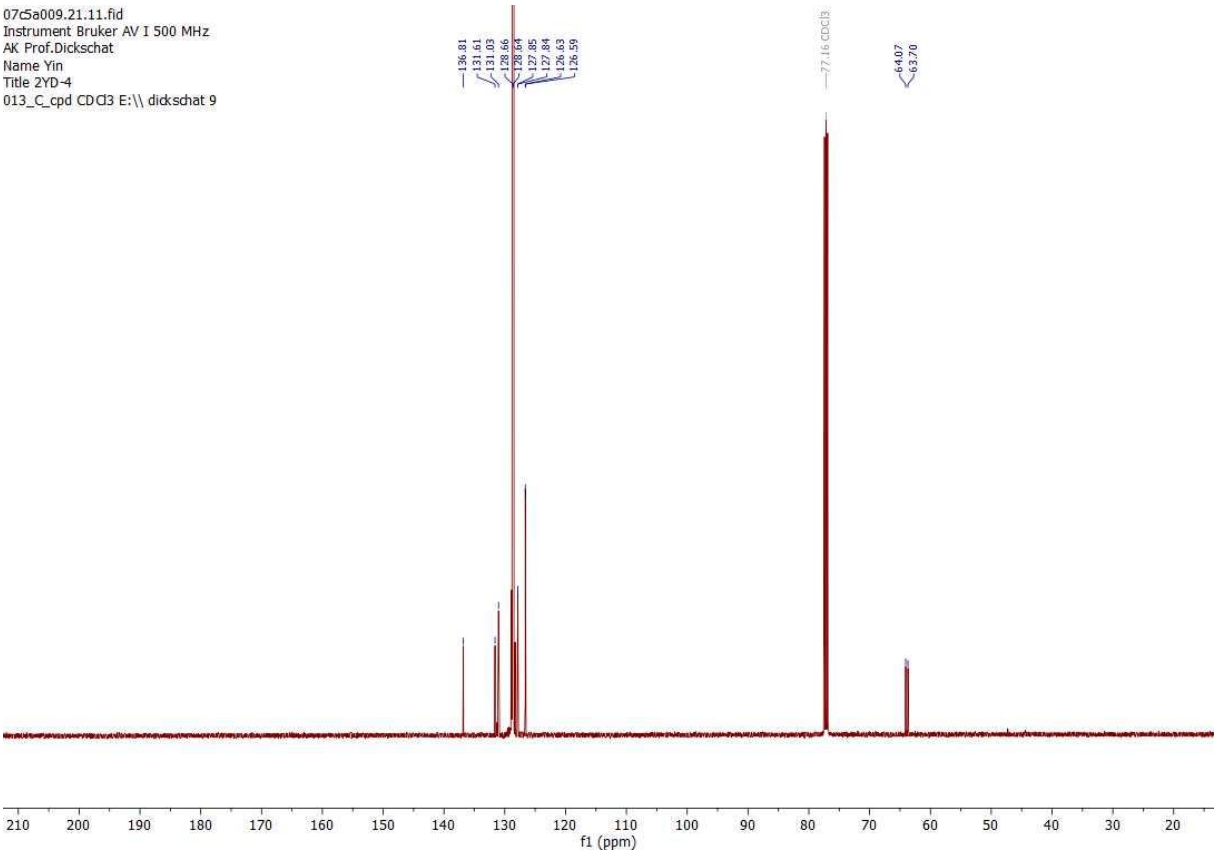

Figure S4. ^{13}C NMR (126 MHz, $CDCl_3$) of **15a**.

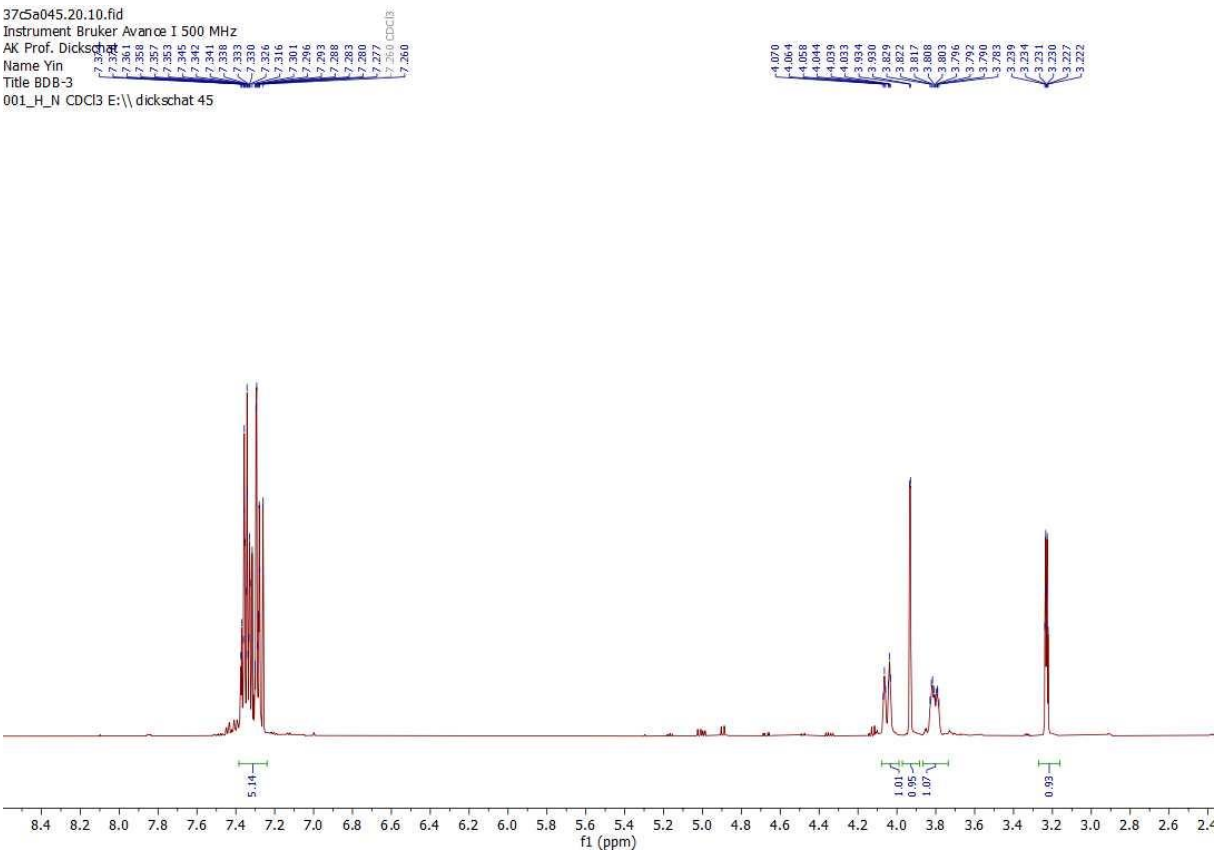

Figure S5. ^{1}H NMR (500 MHz, $CDCl_3$) of **16**.

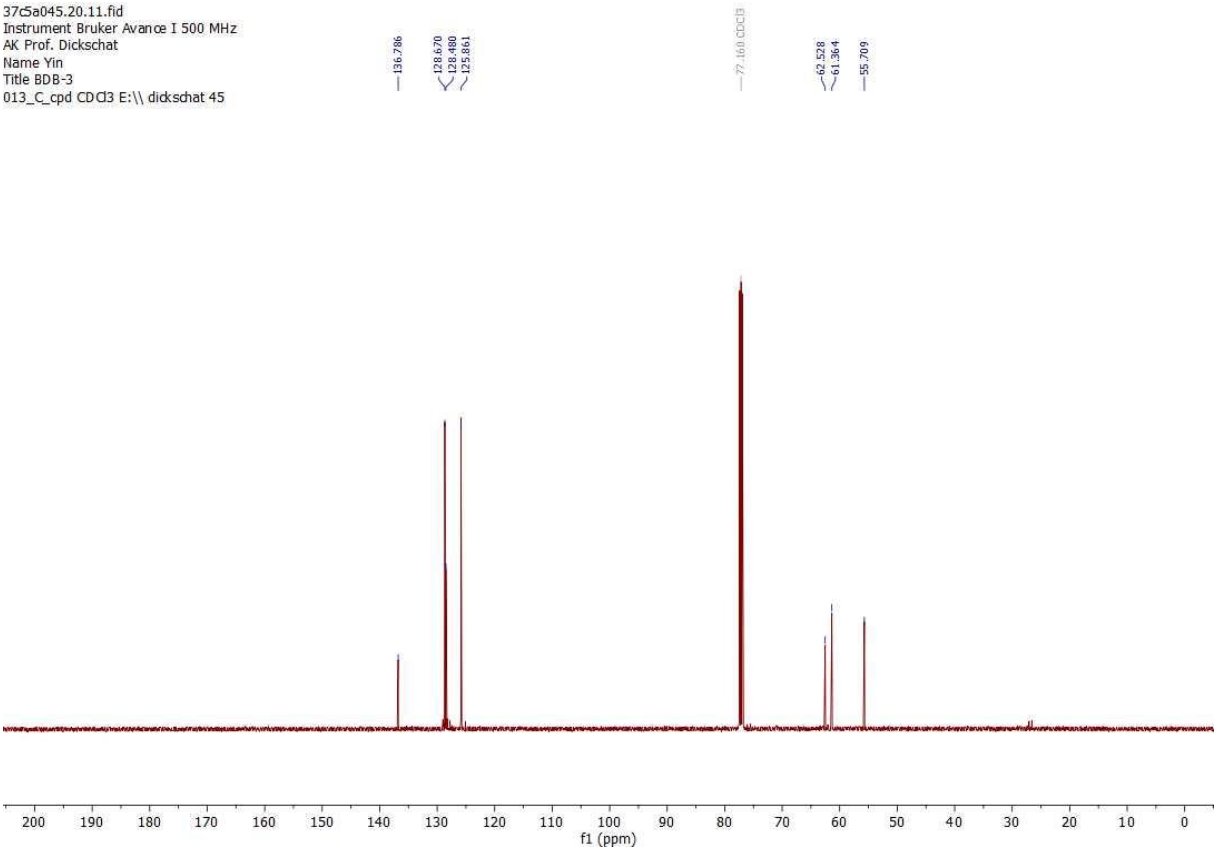

Figure S6. ^{13}C NMR (126 MHz, $CDCl_3$) of **16**.

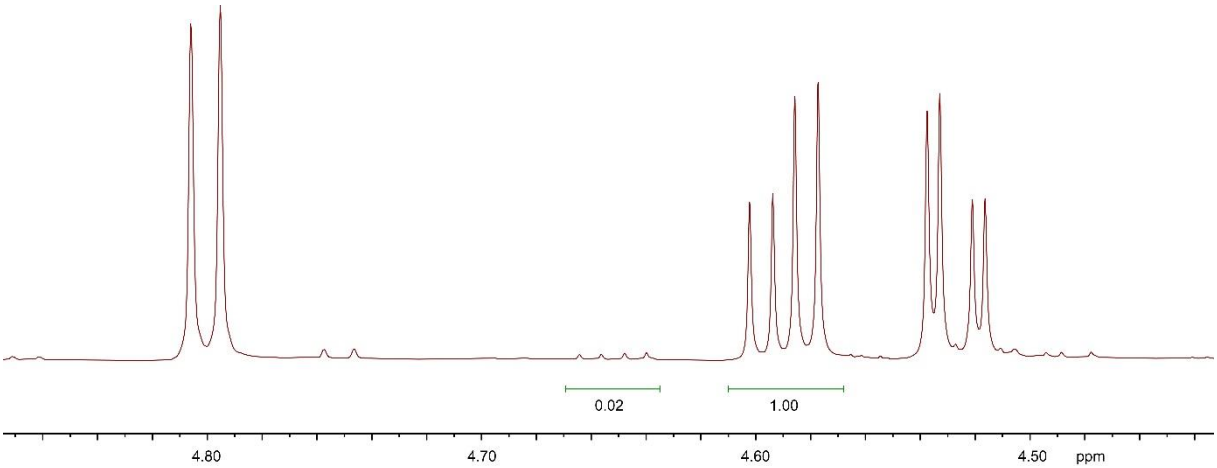

Figure S7. ^{1}H NMR (700 MHz, $CDCl_3$) for the Mosher ester obtained from **16** and (*S*)-Mosher chloride.

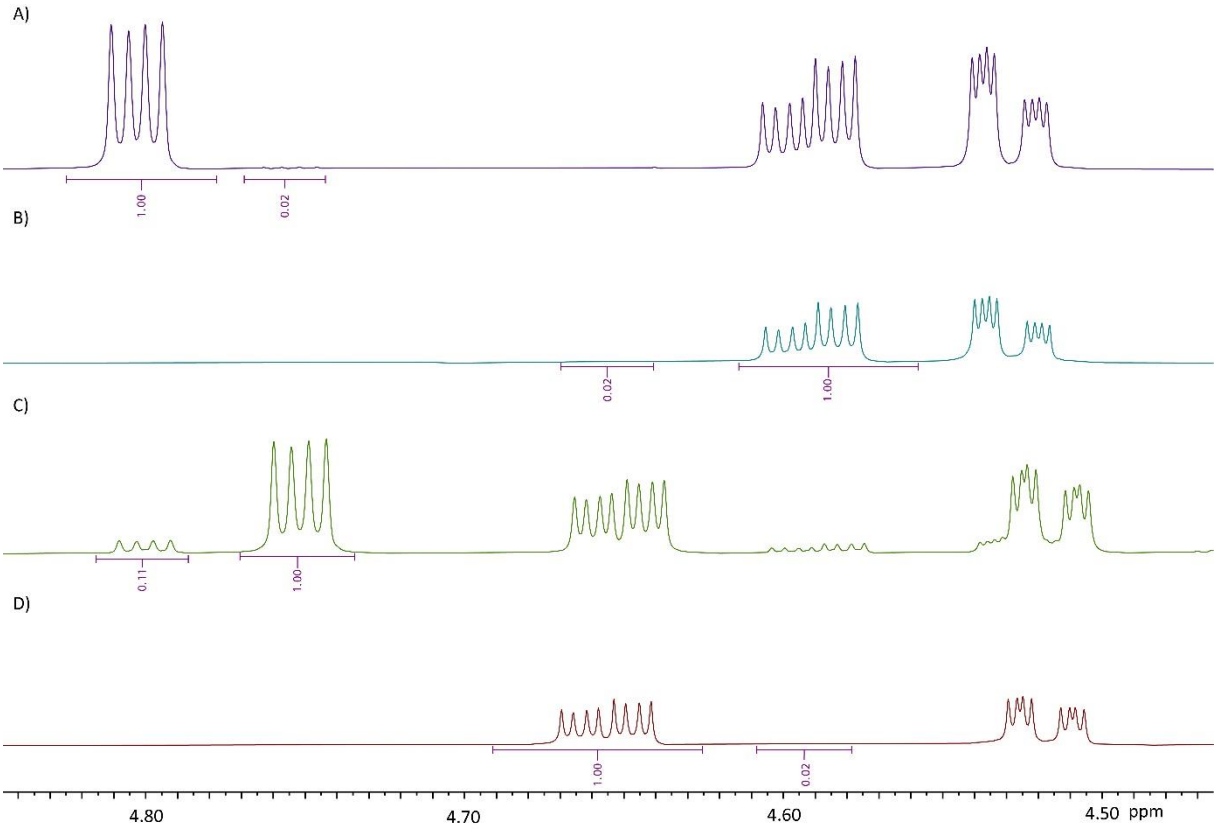

Figure S8. ^{1}H NMR (700 MHz, $CDCl_3$) for the Mosher esters obtained from (*S*)-Mosher chloride and A) **16aa**, B) **16ba**, C) **16ab**, and D) **16bb**.

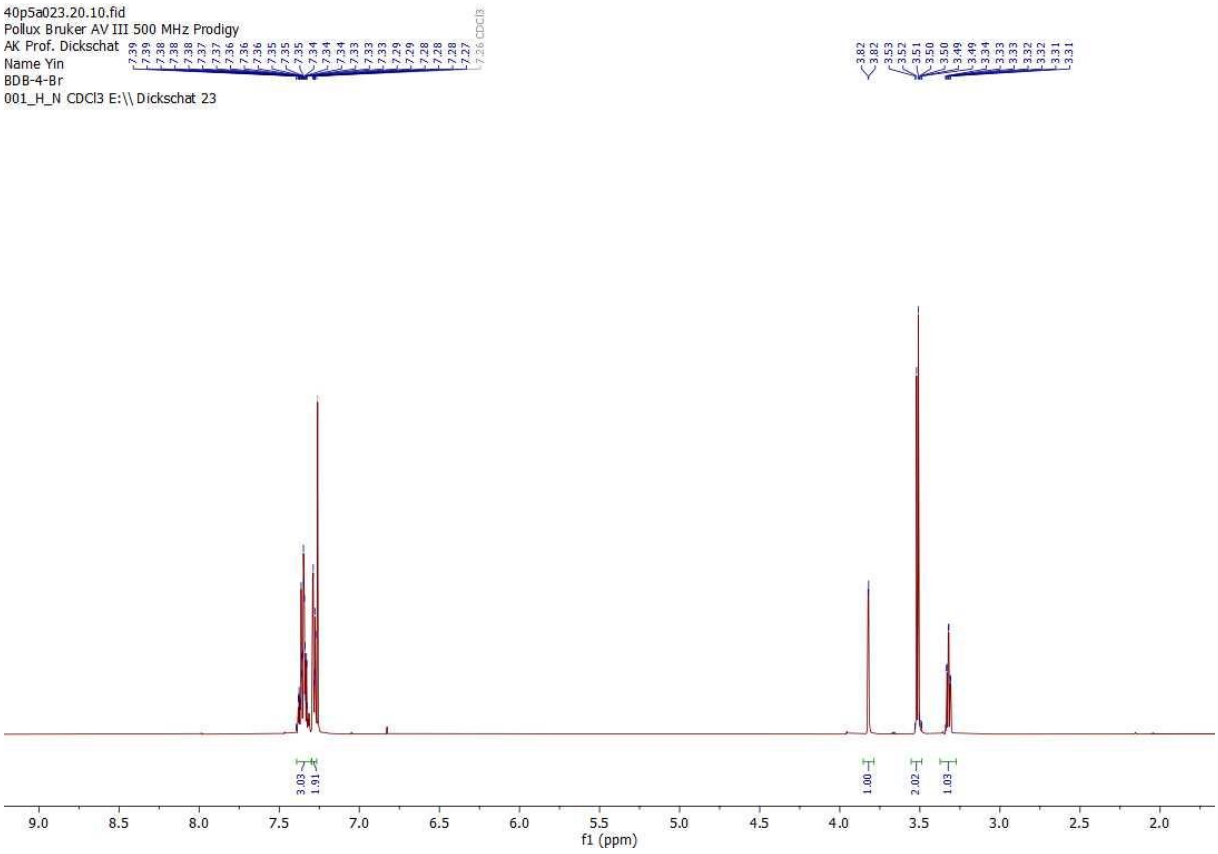

Figure S9. ^{1}H NMR (500 MHz, $CDCl_3$) of **17**.

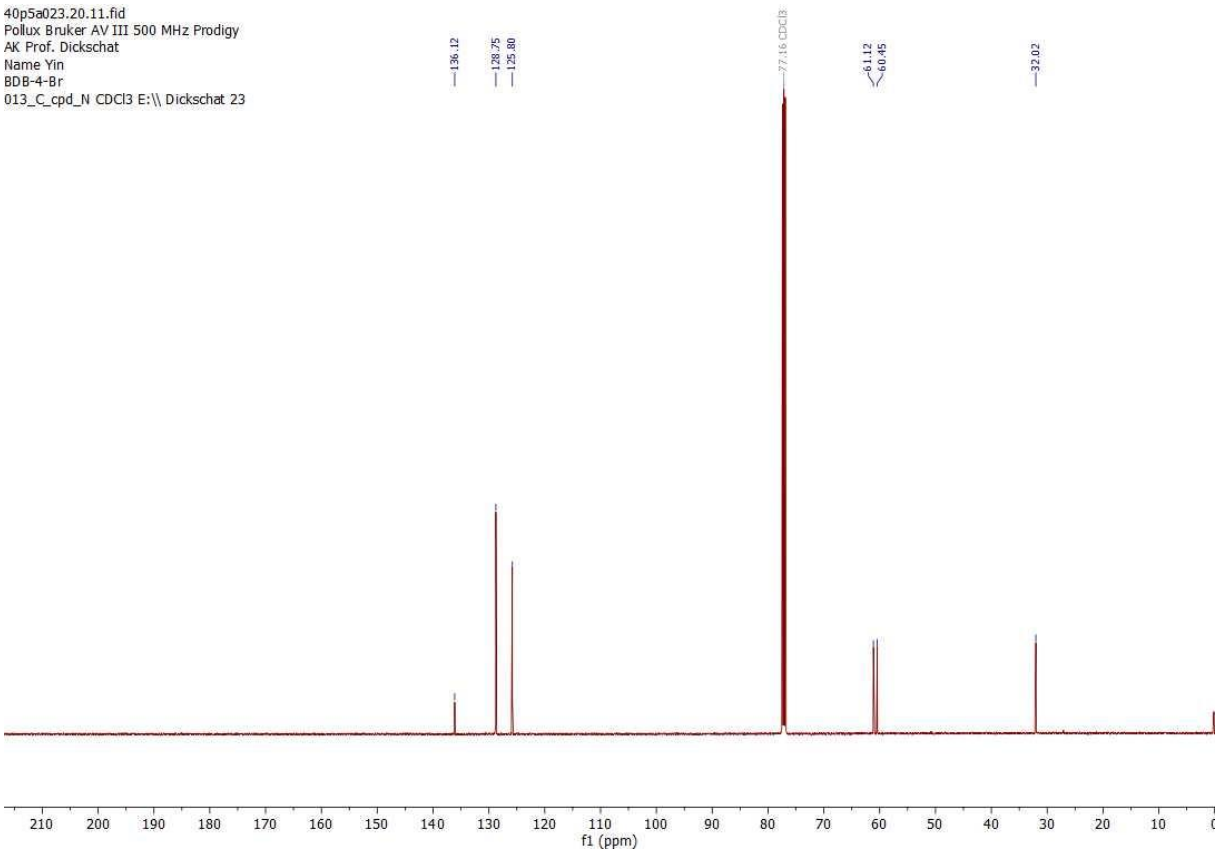

Figure S10. ^{13}C NMR (126 MHz, $CDCl_3$) of **17**.

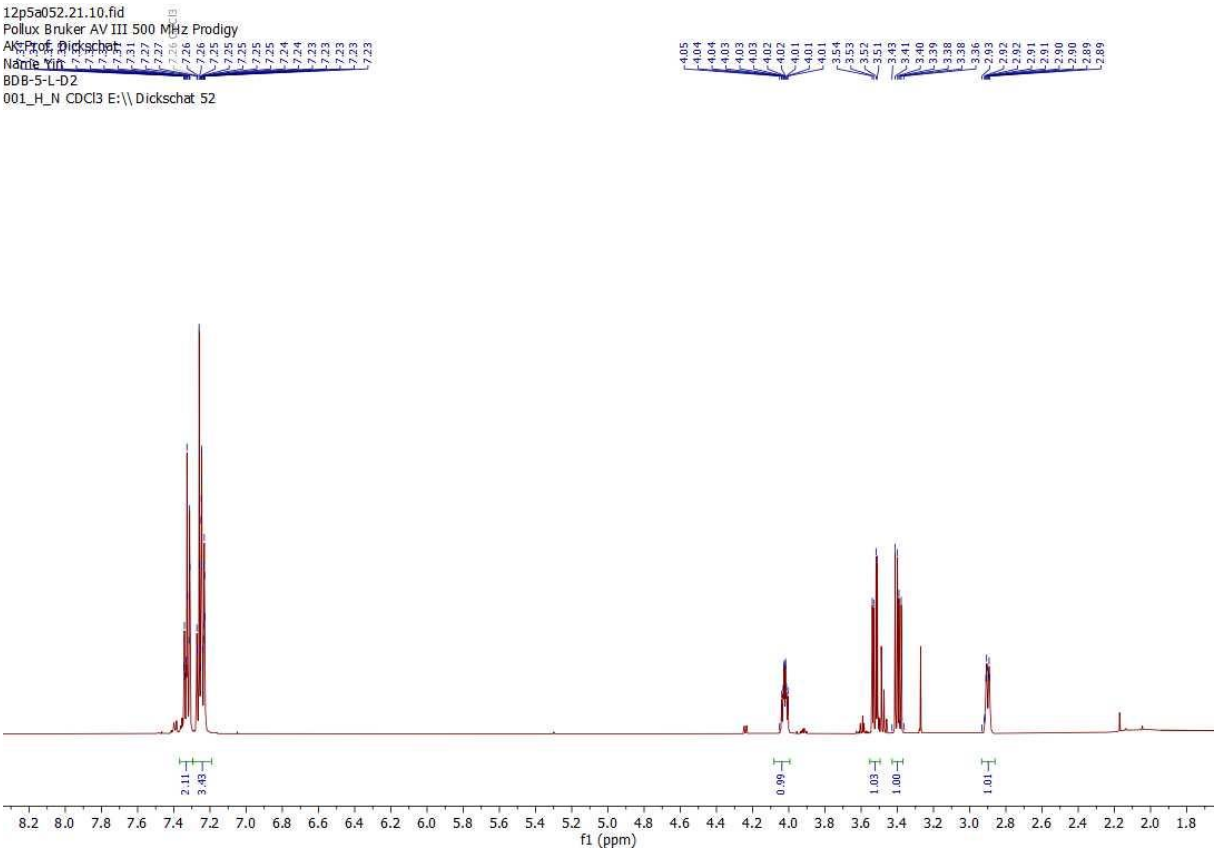

Figure S11. ^{1}H NMR (500 MHz, $CDCl_3$) of **18**.

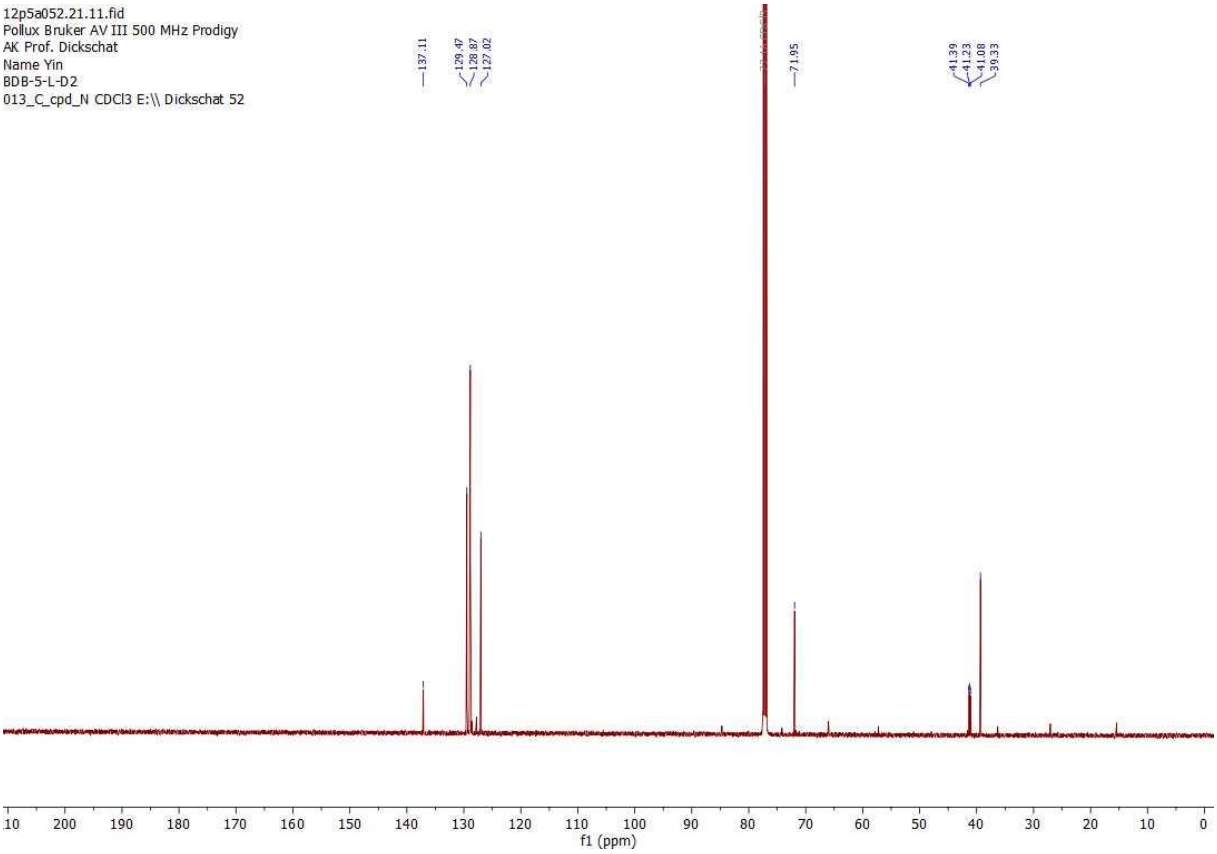

Figure S12. ^{13}C NMR (126 MHz, $CDCl_3$) of **18**.

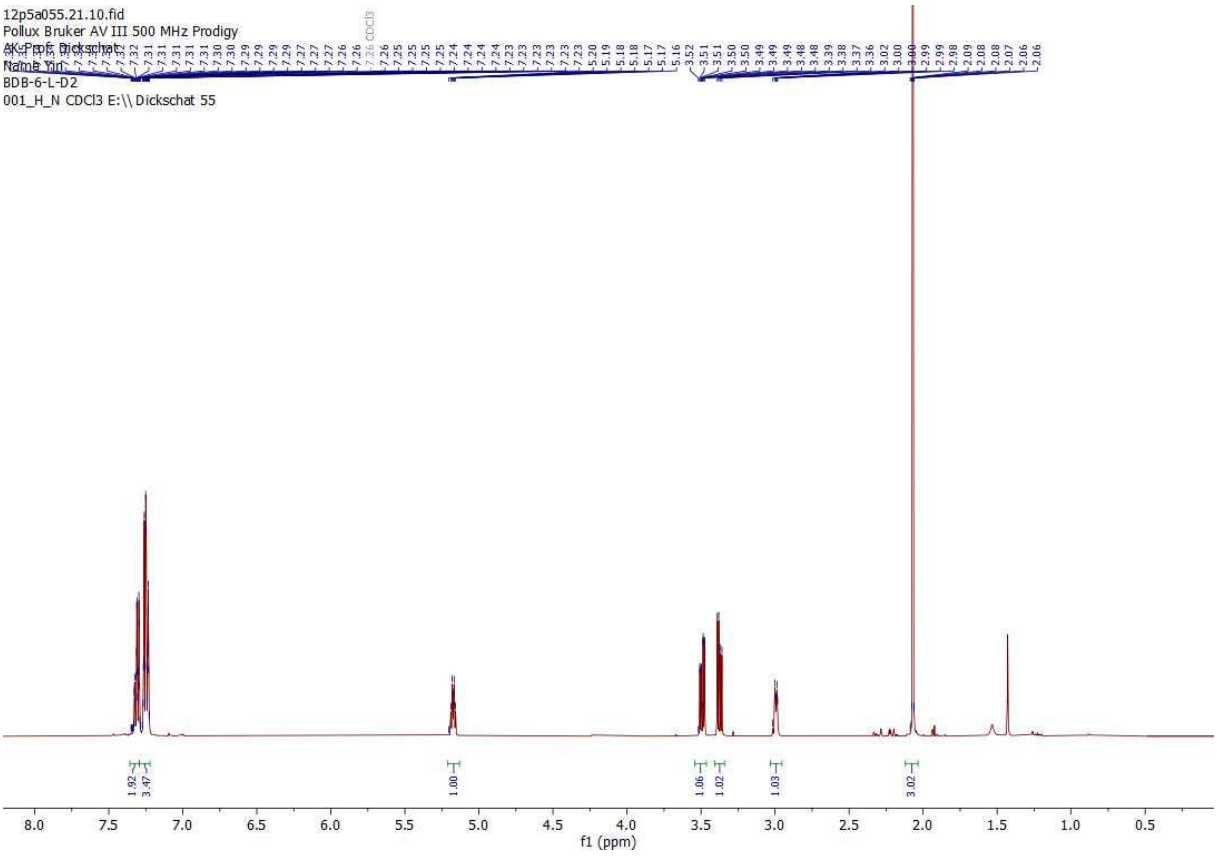

Figure S13. ^{1}H NMR (500 MHz, $CDCl_3$) of **19**.

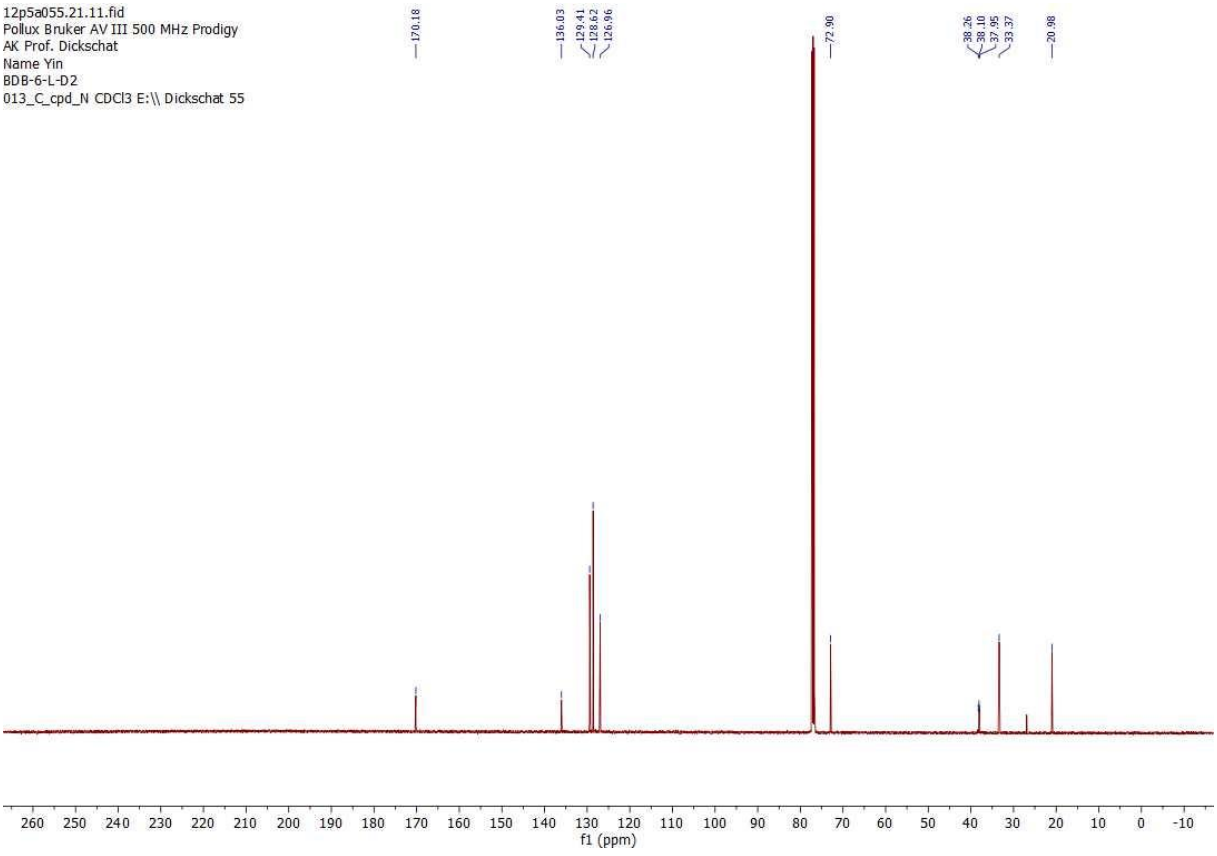

Figure S14. ^{13}C NMR (126 MHz, $CDCl_3$) of **19**.

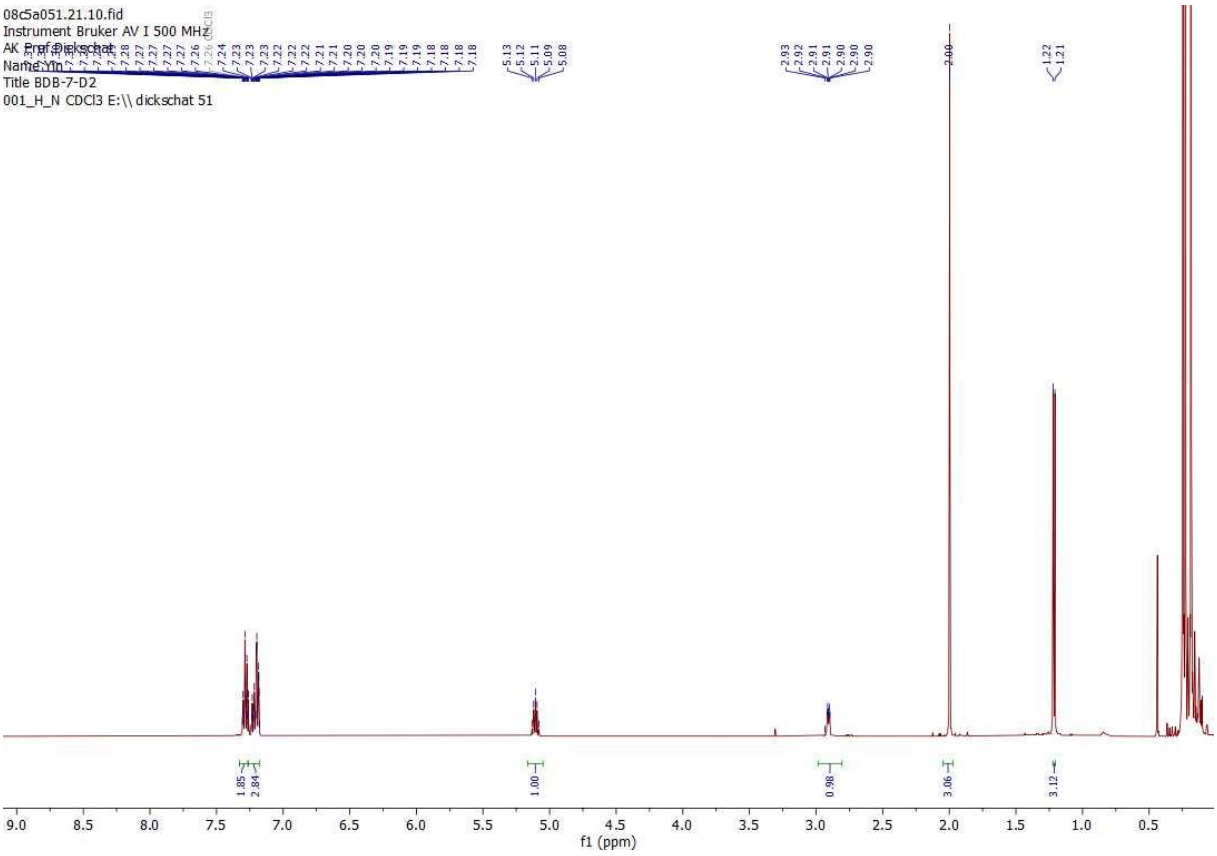

Figure S15. ^{1}H NMR (500 MHz, $CDCl_3$) of **20**.

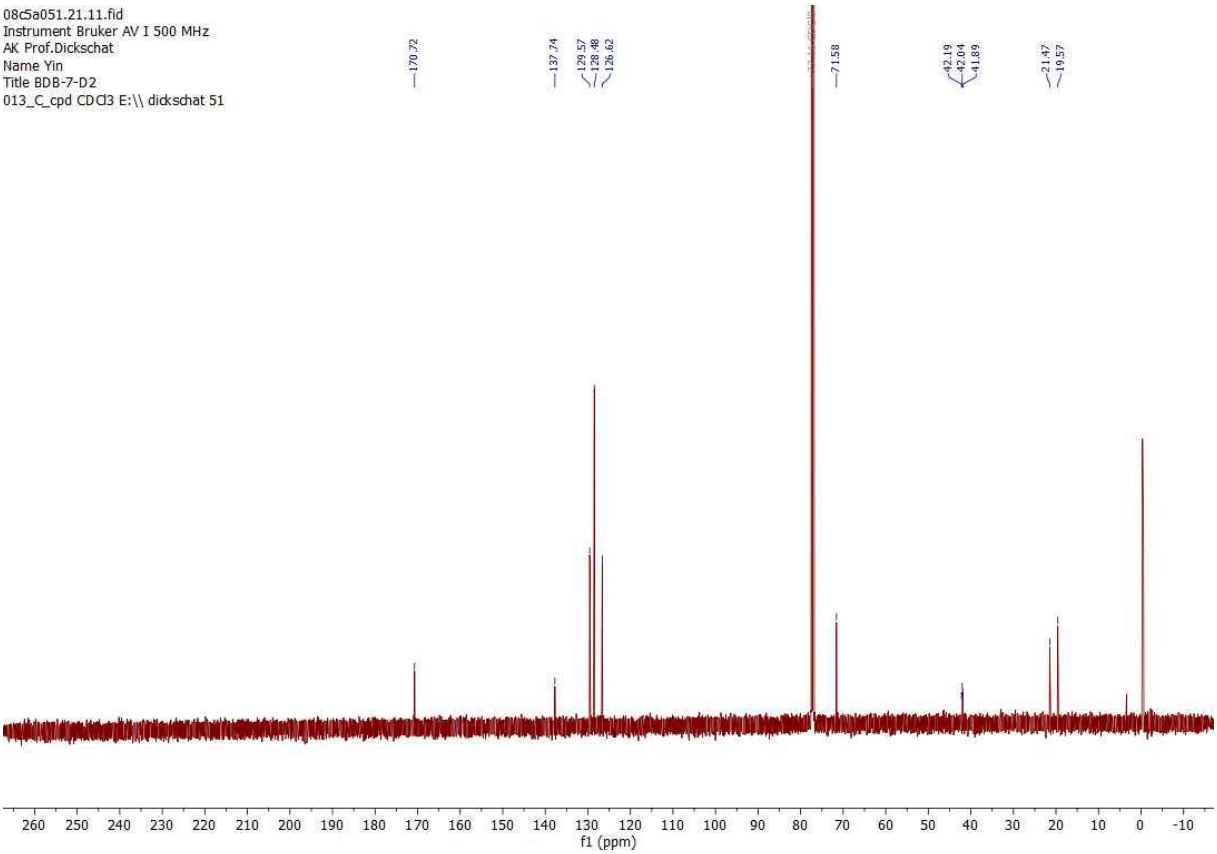

Figure S16. ^{13}C NMR (126 MHz, $CDCl_3$) of **20**.

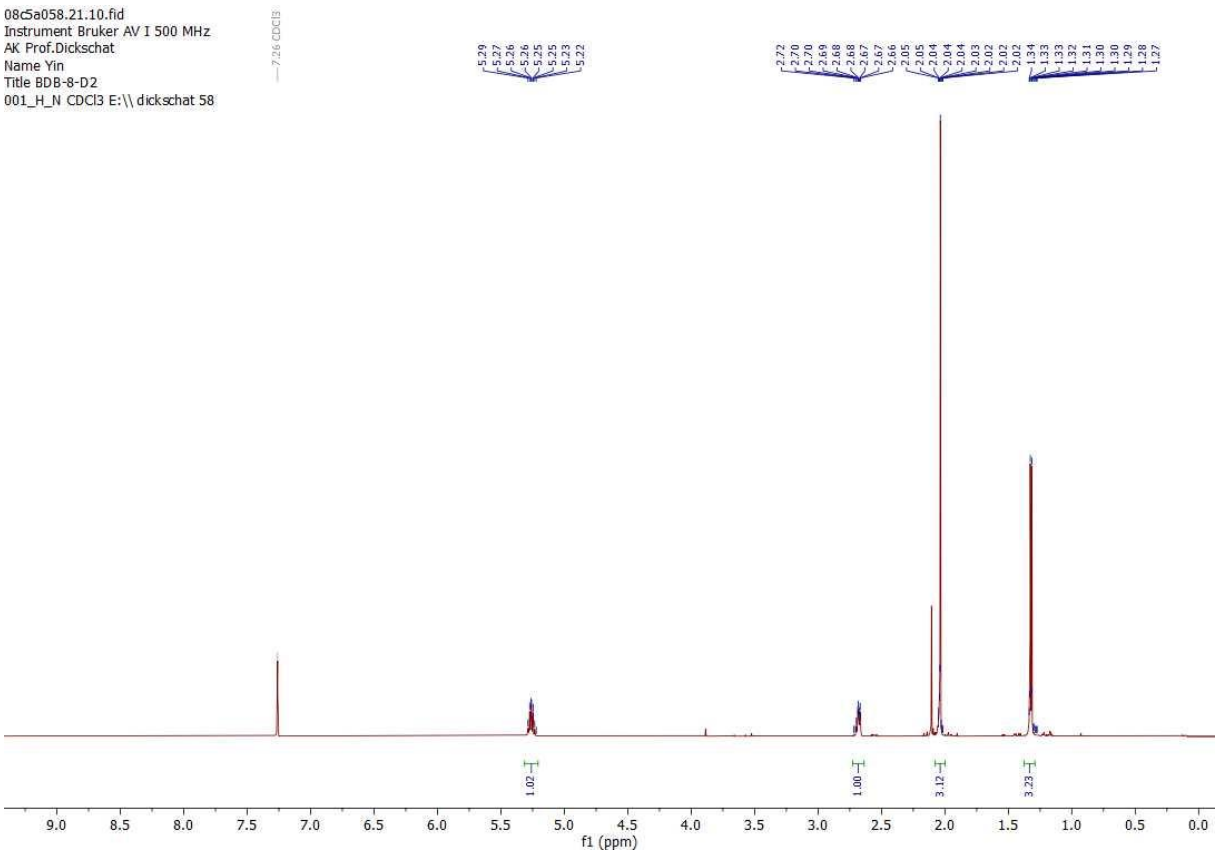

Figure S17. ^{1}H NMR (500 MHz, $CDCl_3$) of **21**.

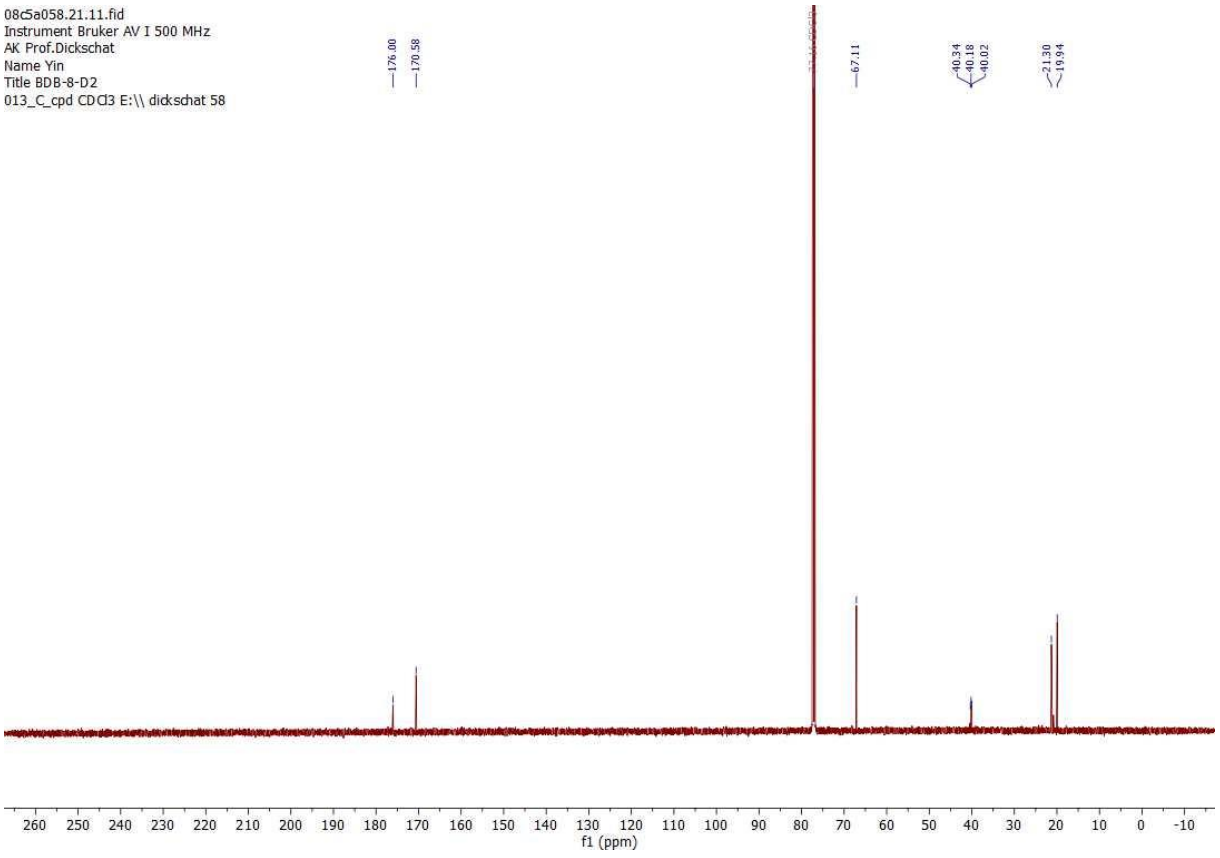

Figure S18. ^{13}C NMR (126 MHz, $CDCl_3$) of **21**.

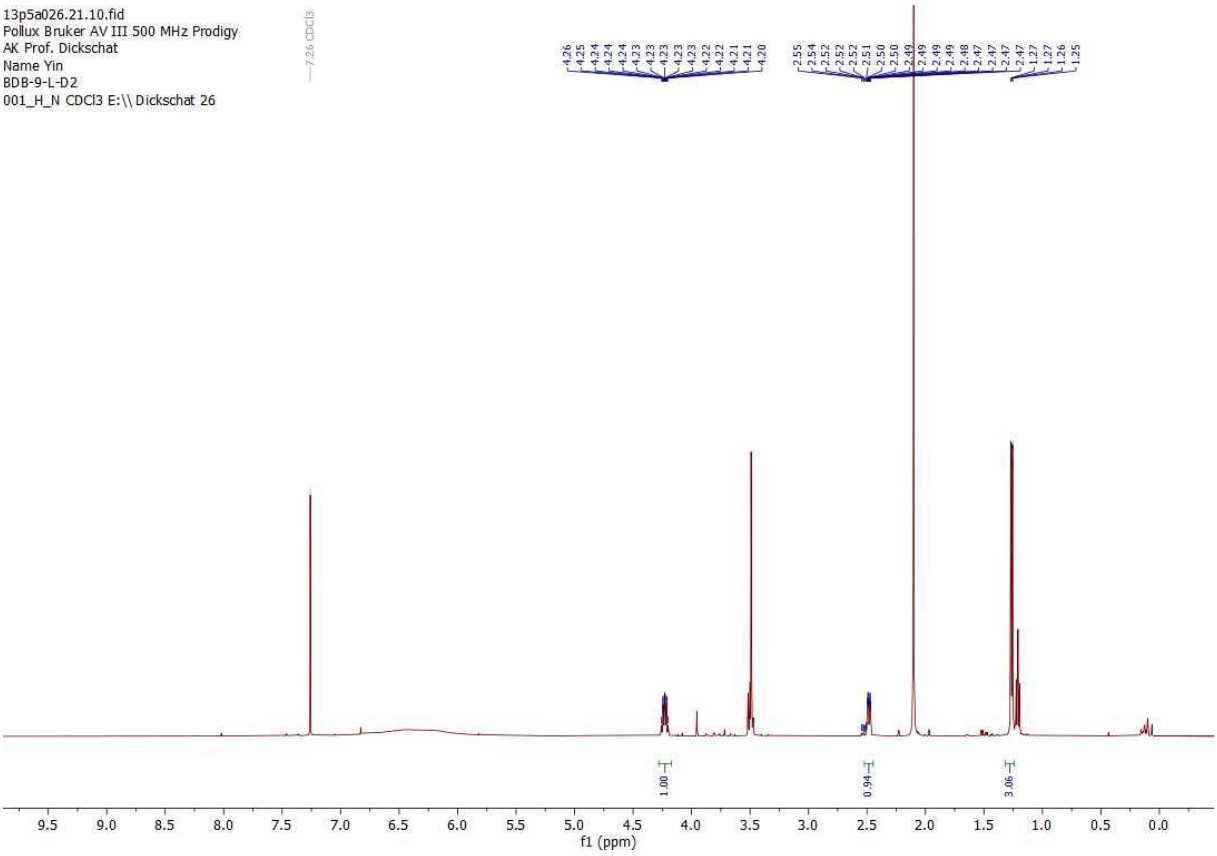

Figure S19. ^{1}H NMR (500 MHz, $CDCl_3$) of **22**.

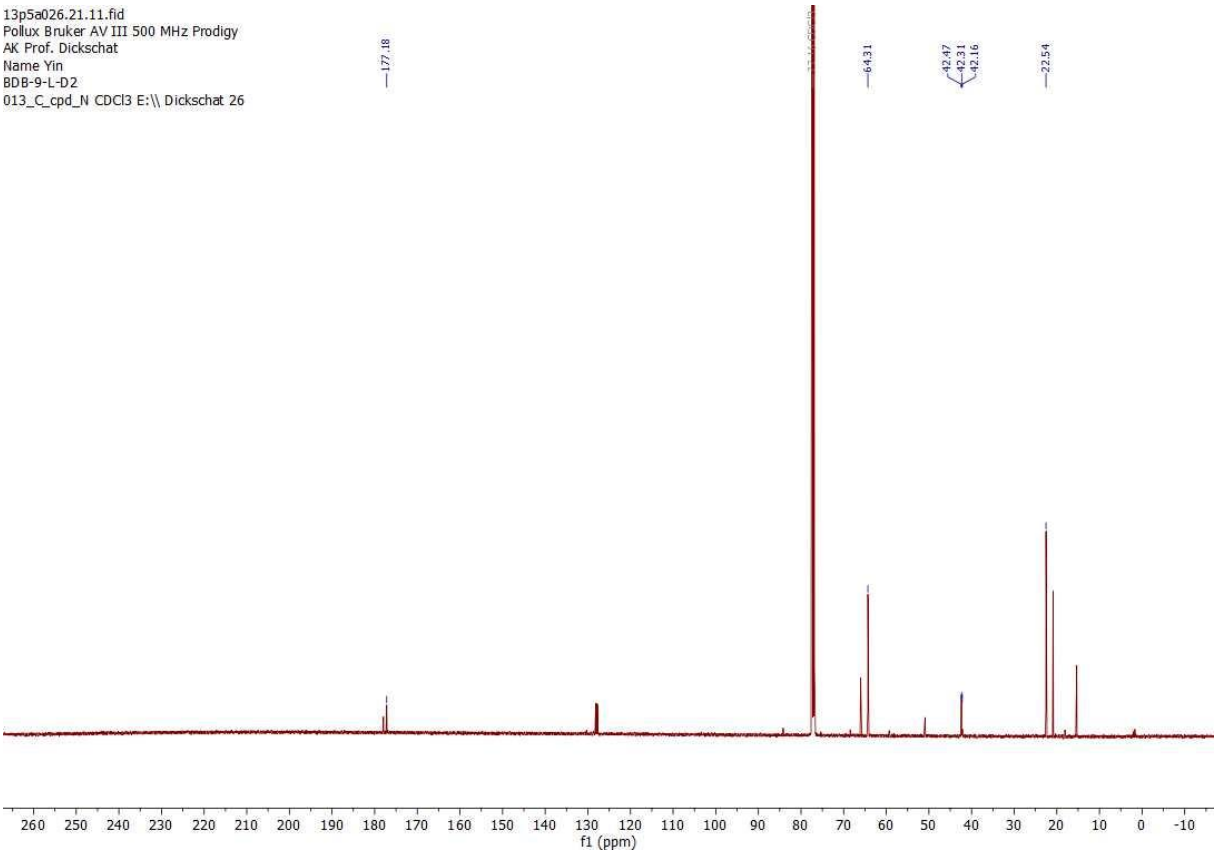

Figure S20. ^{13}C NMR (126 MHz, $CDCl_3$) of **22**.

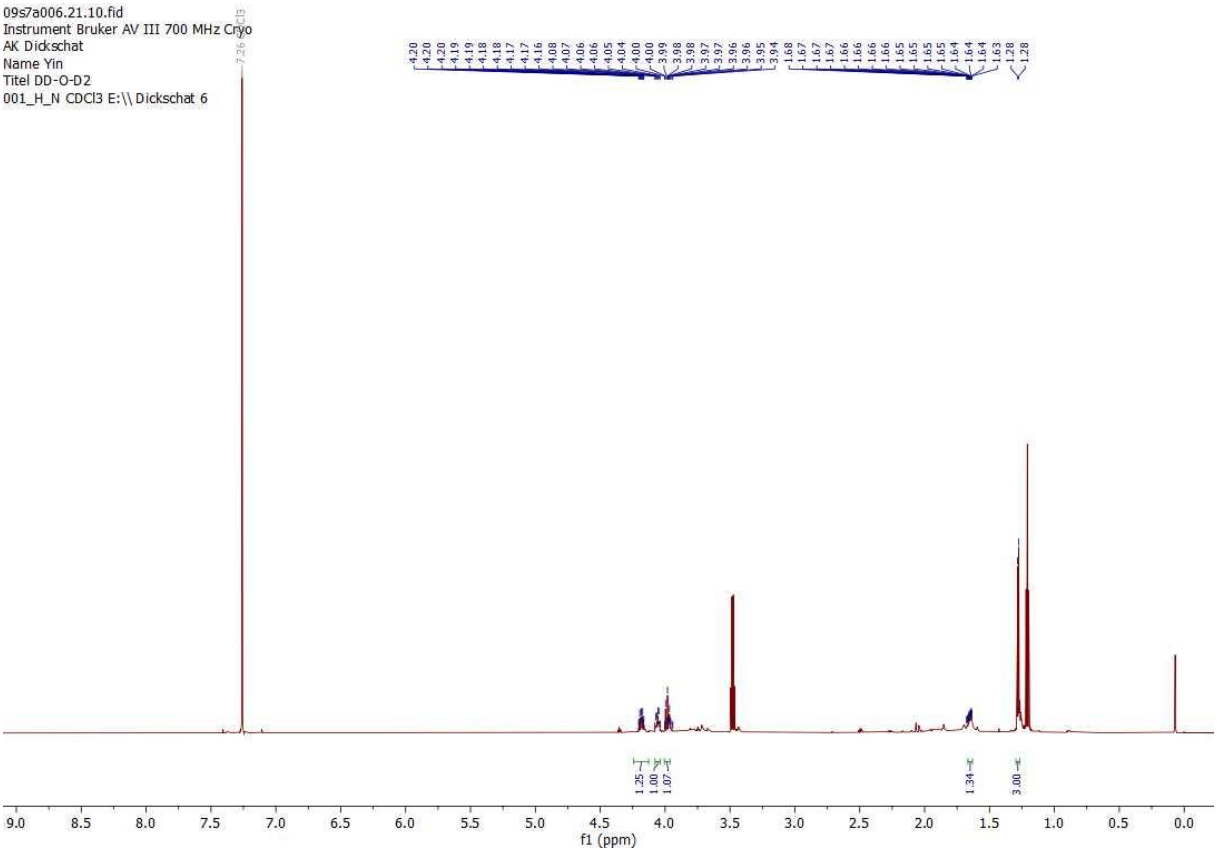

Figure S21. ^{1}H NMR (700 MHz, $CDCl_3$) of **23**.

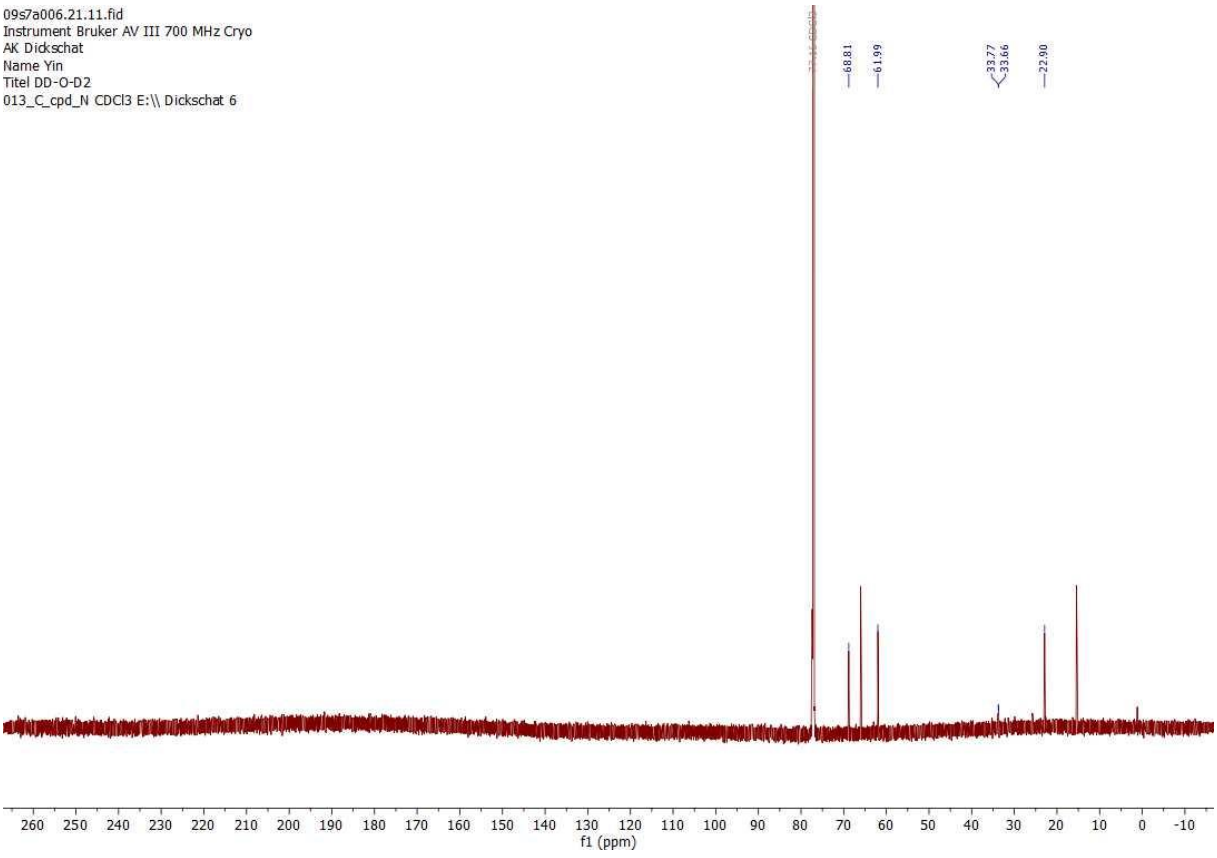

Figure S22. ^{13}C NMR (176 MHz, $CDCl_3$) of **23**.

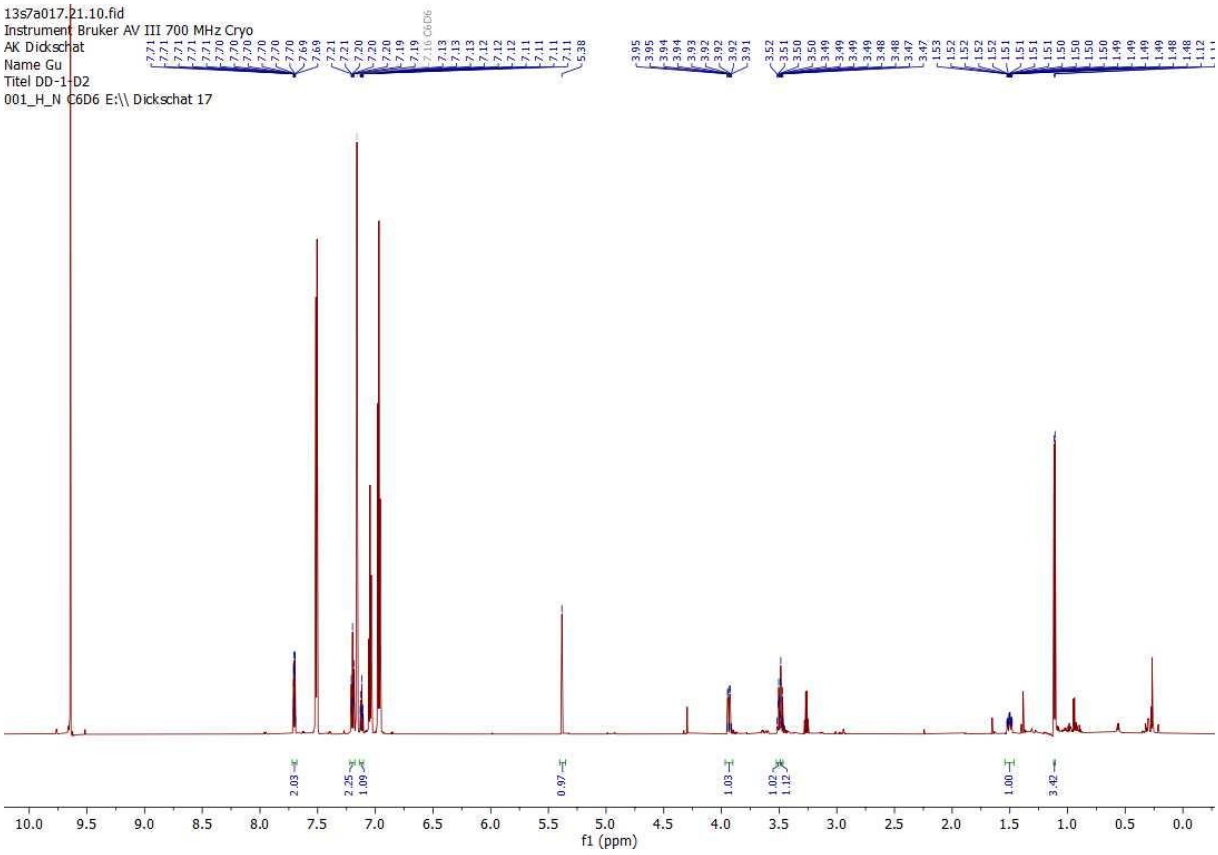

Figure S23. ^{1}H NMR (700 MHz, C_6D_6) of **24**.

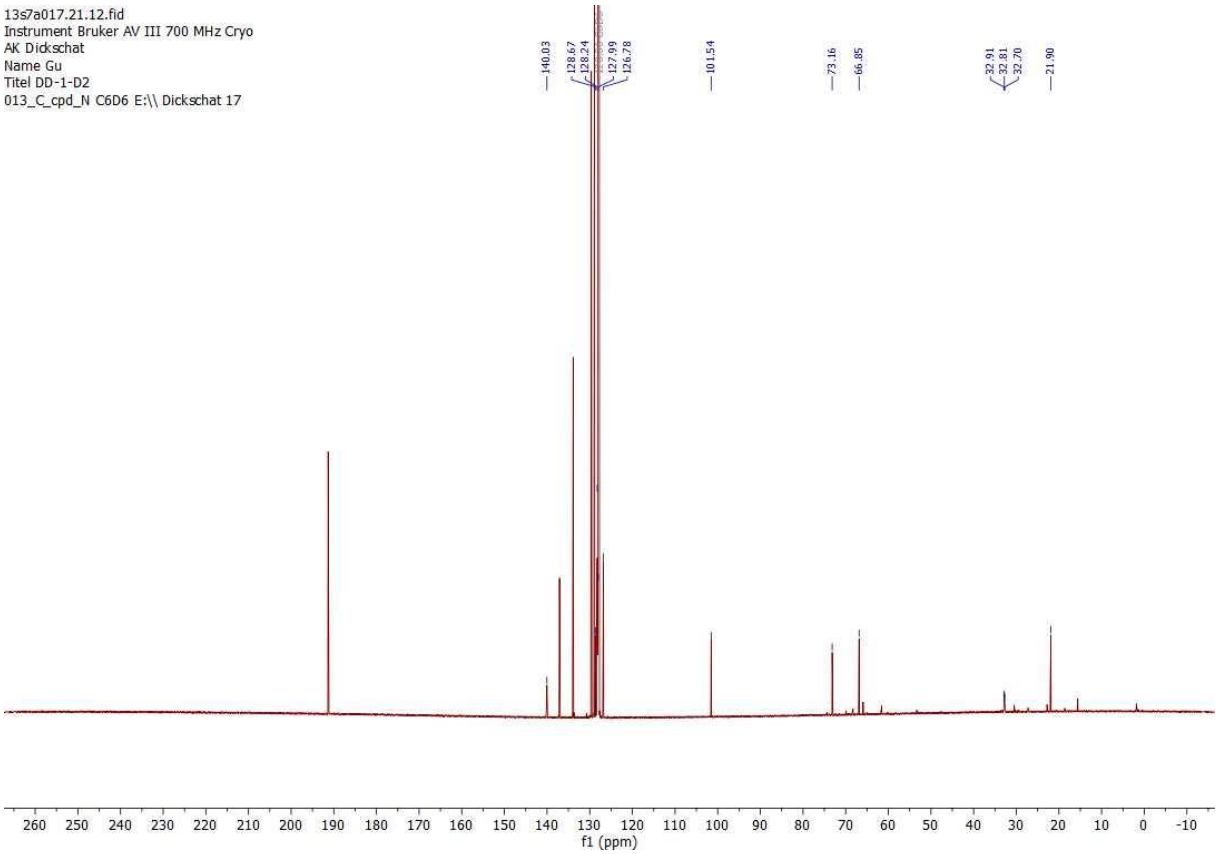

Figure S24. ^{13}C NMR (176 MHz, C_6D_6) of **24**.

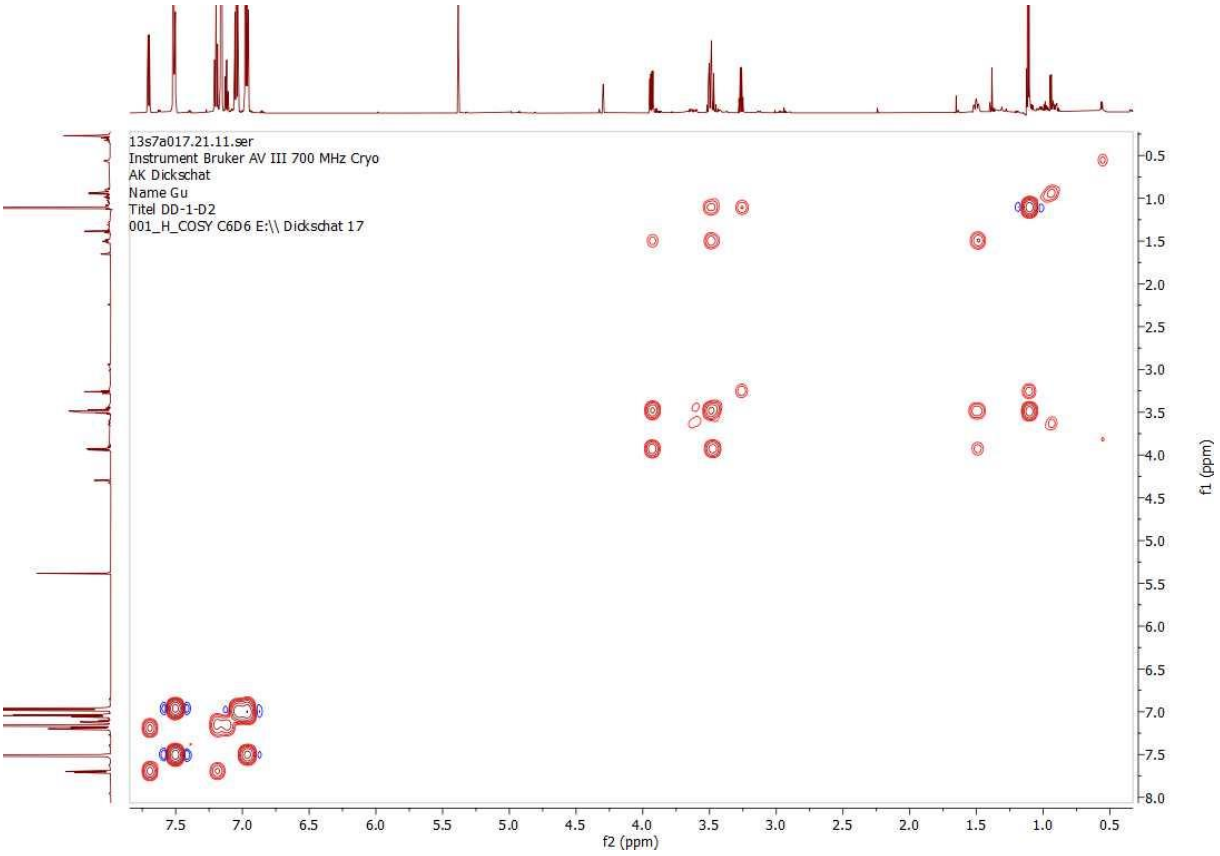

Figure S25. HSQC spectrum (C_6D_6) of **24**.

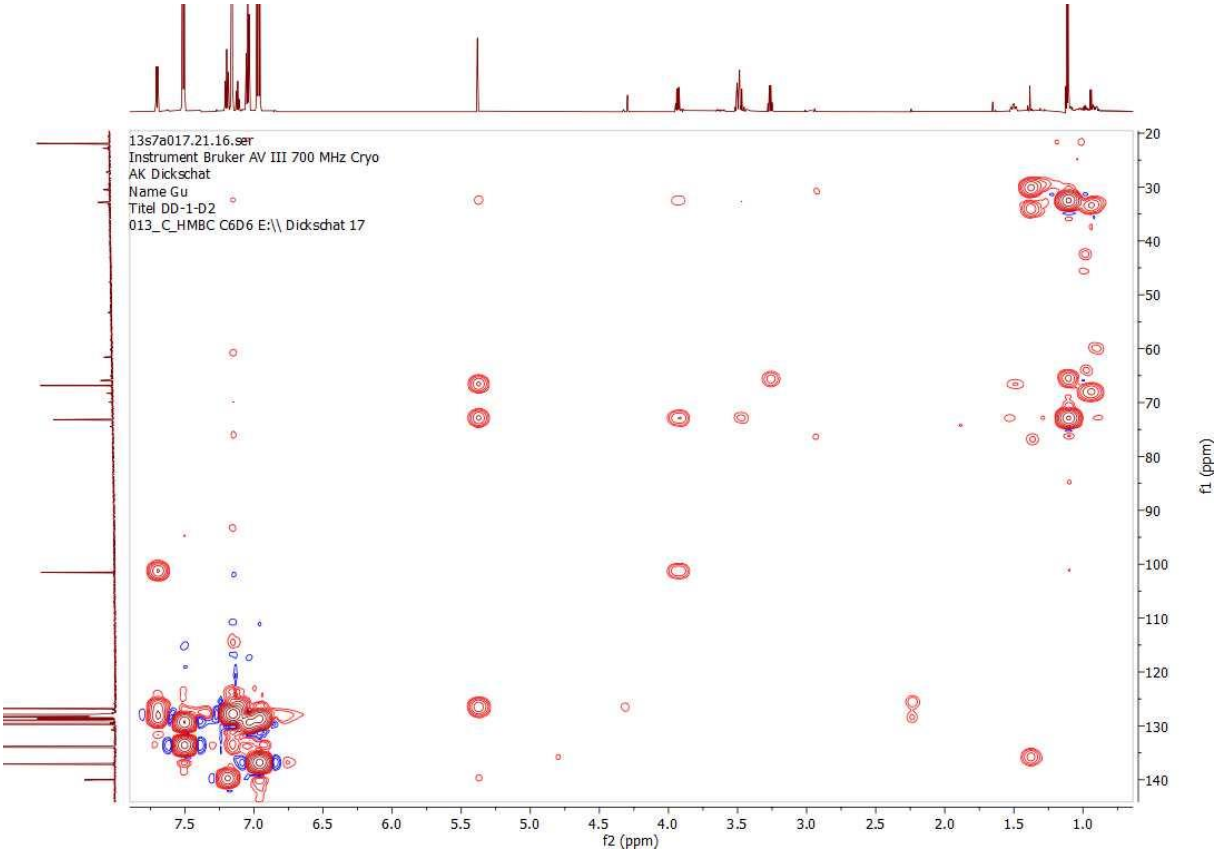

Figure S26. HMBC spectrum (C_6D_6) of **24**.

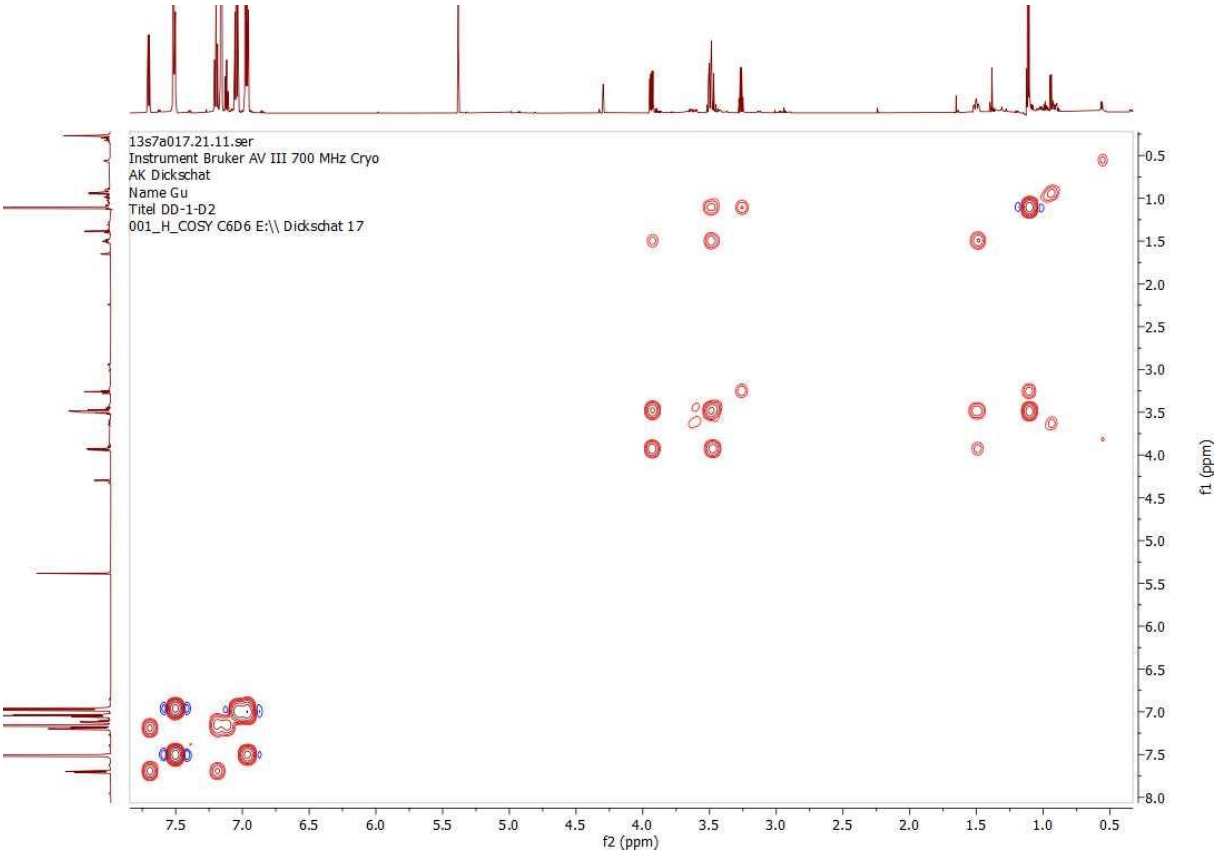

Figure S27. ^{1}H-^{1}H COSY spectrum (700 MHz, C_6D_6) of **24**.

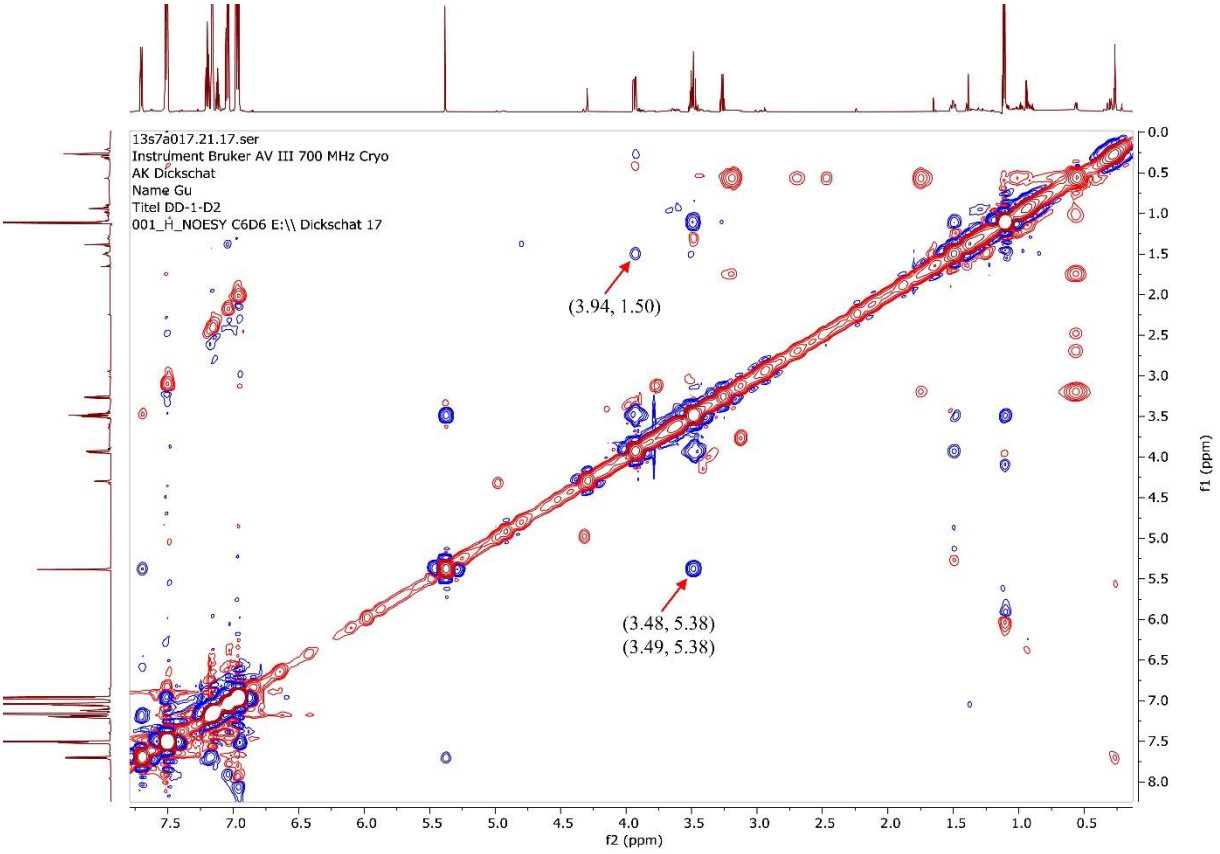

Figure S28. NOESY spectrum (700 MHz, C_6D_6) of **24**.

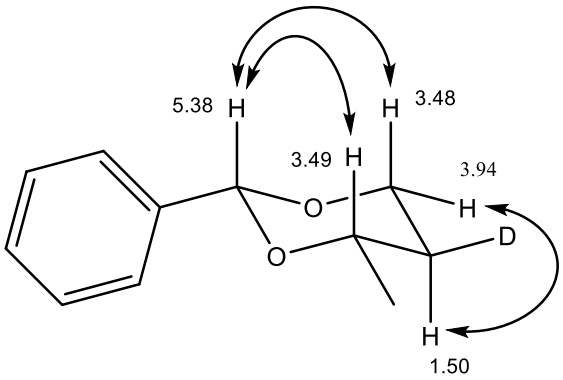

Figure S29. NOESY correlations of **24**.

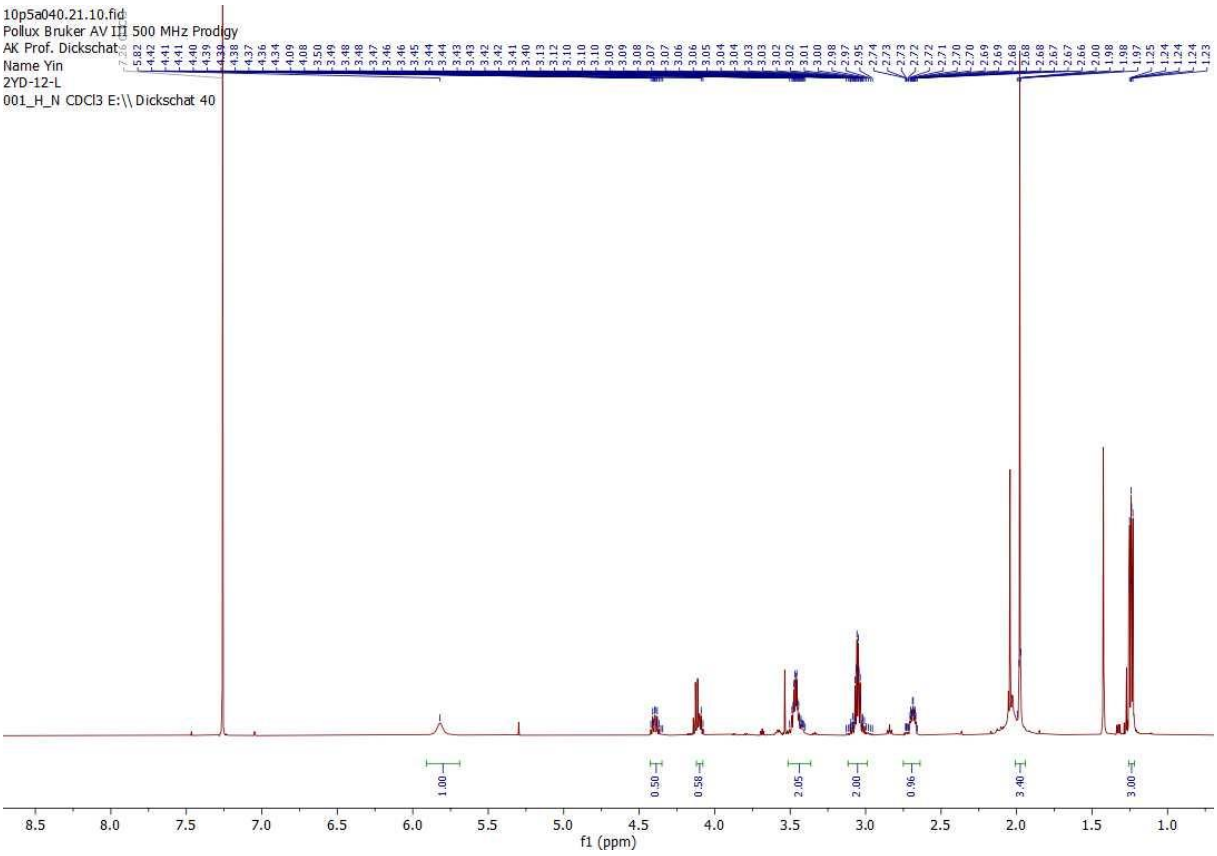

Figure S30. ^{1}H NMR (500 MHz, $CDCl_3$) of **27aa**.

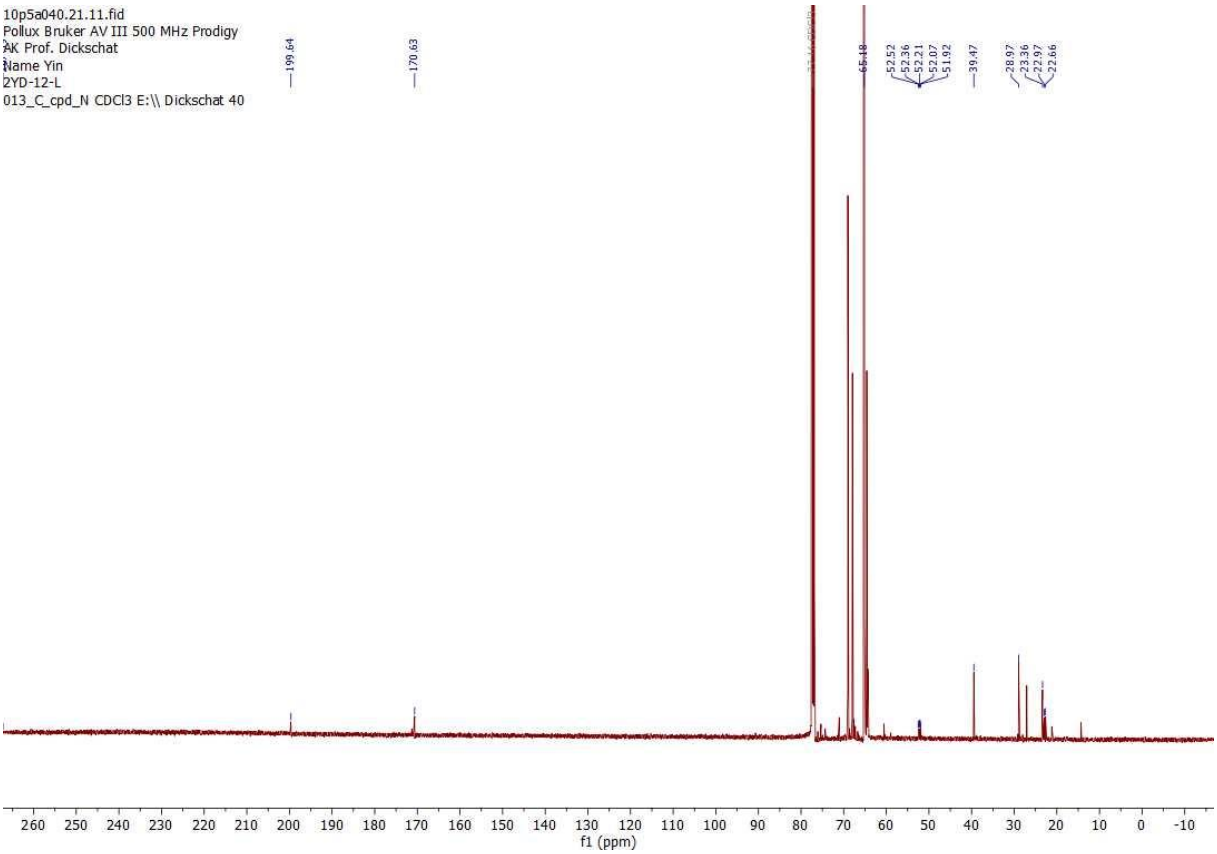

Figure S31. ^{13}C NMR (126 MHz, $CDCl_3$) of **27aa**.

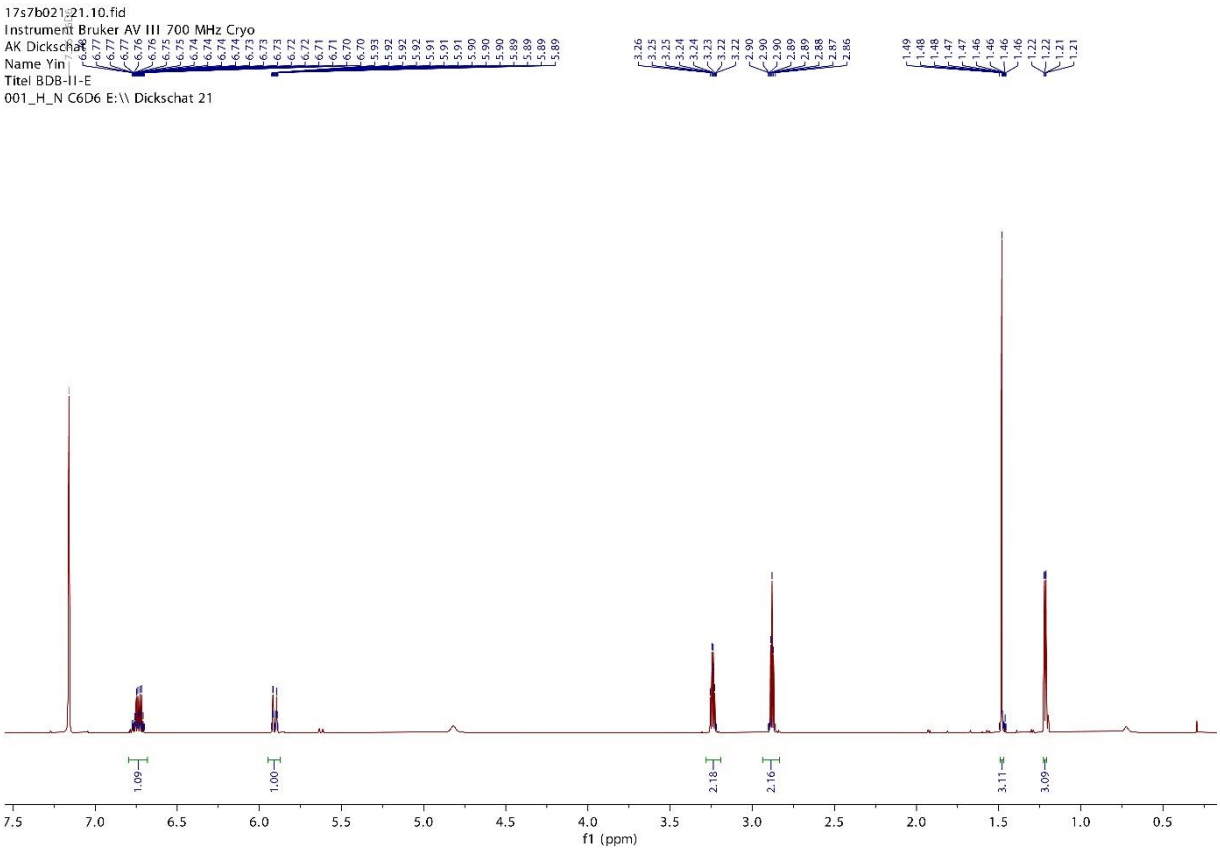

Figure S32. ^{1}H NMR (700 MHz, C_6D_6) of **28a**.

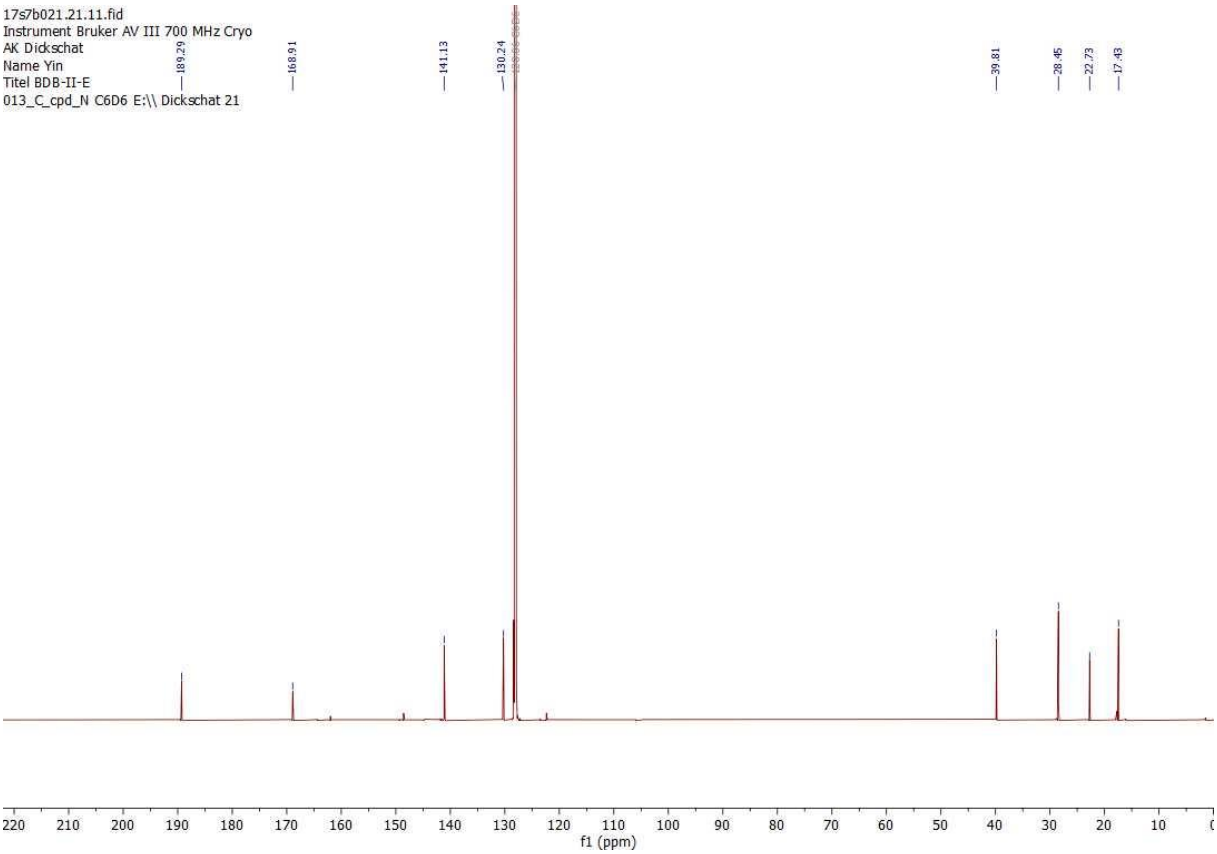

Figure S33. ^{13}C NMR (176 MHz, C_6D_6) of **28a**.

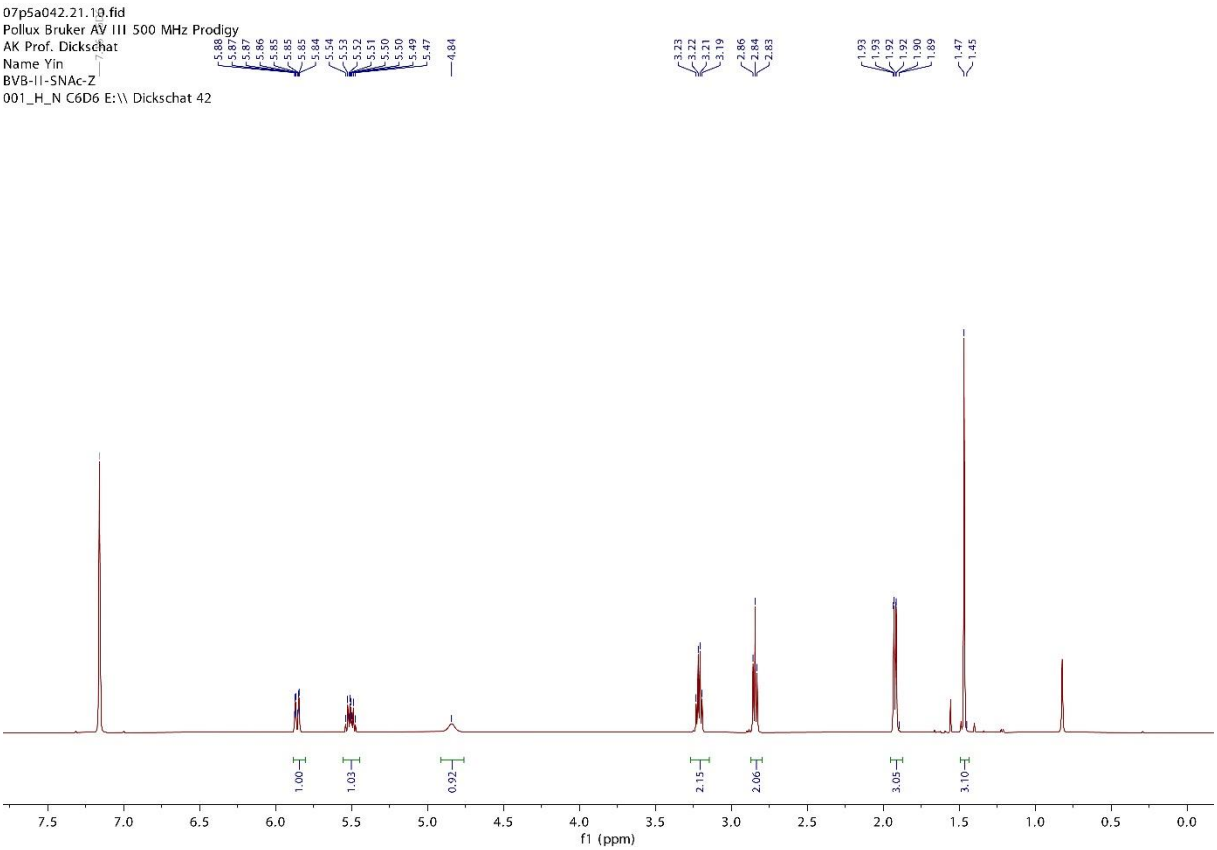

Figure S34. ^{1}H NMR (700 MHz, C_6D_6) of **29a**.

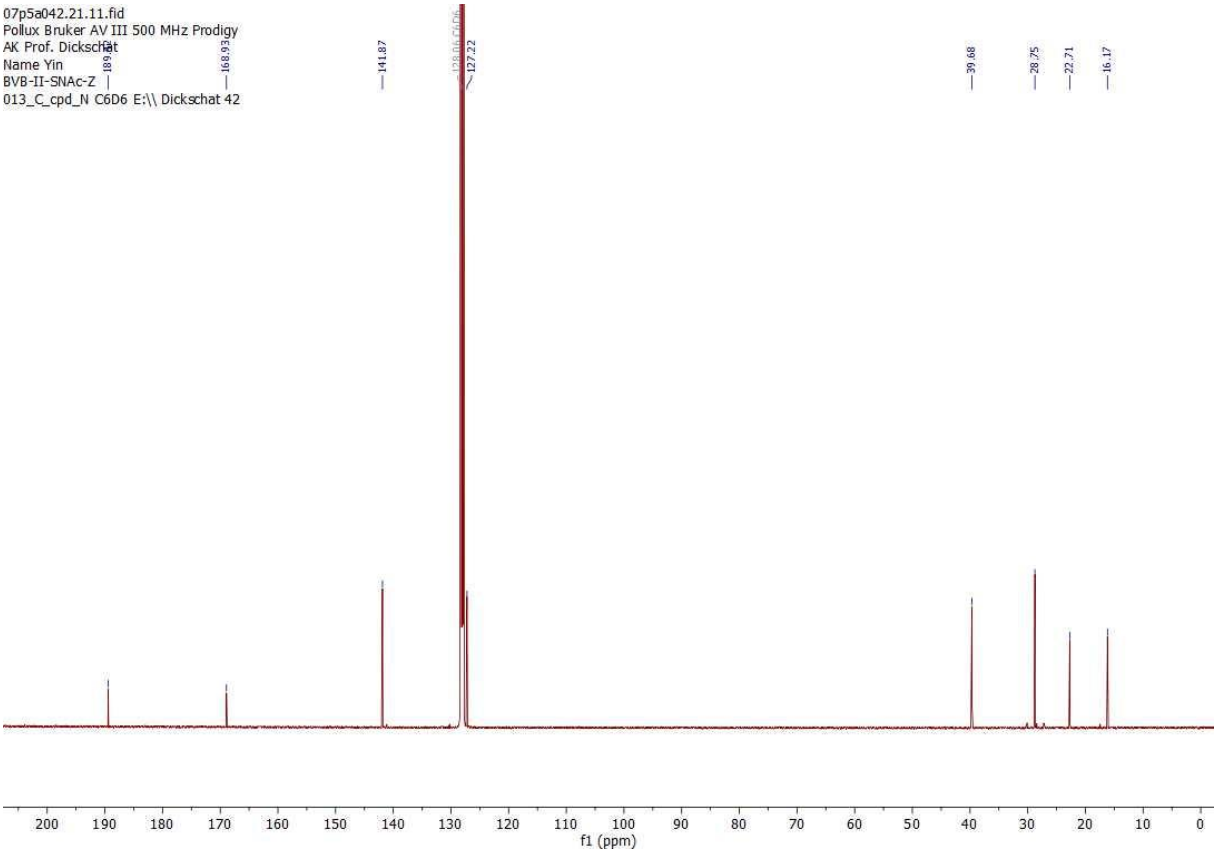

Figure S35. ^{13}C NMR (176 MHz, C_6D_6) of **29a**.

Strains and culture conditions

Streptomyces parvulus Tü4055 was grown on 65 GYM liquid medium (4.0 g glucose, 4.0 g yeast extract, 4.0 g malt extract, 1 L water, pH 7.2) at 30 °C. *Escherichia coli* (K12 and BL21) were grown on LB liquid medium at 37 °C. *Saccharomyces cerevisiae* was grown on YPAD liquid medium (20 g glucose, 10 g yeast extract, 20 g peptone, 40 mg adenine sulfate dehydrate, 1 L water) at 30 °C.

Gene cloning

For gene cloning, genomic DNA (gDNA) of *S. parvulus* Tü4055 and of *E. coli* K12 was isolated from freshly grown cultures in liquid medium (100 mL). The cultures were centrifuged at 8000 x g and the supernatant was discarded. The cells were resuspended in SET buffer (5 mL; 75 mM NaCl, 25 mM EDTA, 20 mM Tris HCl, pH 8.0), then lysozyme solution (100 µL; 50 mg mL^{-1}) was added and the mixture was incubated for 30 min at 37 °C. To this mixture, proteinase K solution (100 µL; 50 mg mL^{-1}) and 10 % SDS (600 µL) were added and incubation was carried on for 1 h at 55 °C. Phenol/chloroform/ isoamyl alcohol (25:24:1, 5 mL) was added, the phases were mixed, followed by centrifugation at top speed (14600 rpm) for 5 min. The aqueous layer was transferred to a fresh tube and the DNA was precipitated by addition of 3 M NaOAc (0.1 vol) and ethanol (0.6 vol). The DNA was spun down, washed with 70 % ethanol, centrifuged again and dried overnight. The dry DNA was dissolved in nuclease free water to a final concentration of approximately 1000 ng/µL.

Polymerase chain reactions (PCR) were performed according to a standard 3-step PCR protocol provided by the supplier of Q5 high-fidelity DNA polymerase (New England Biolabs, Ipswich, MA, USA). The desired dehydratase gene sequences from the borrelidin biosynthetic gene cluster (AJ580915) were amplified by PCR using gDNA of *S. parvulus* as template with the primers YZ074_BorDH2_1_Fw and YZ075_BorDH2_1_Rv (for BorDH2), YZ088_BorDH3_Fw and YZ089_BorDH3_Rv (for BorDH3), and with YZ092_BorDH5_Fw and YZ093_BorDH5_Rv (for BorDH5) (Table S1).[20] The FabZ gene (WP_152065349)[21] was amplified by PCR using gDNA from *E. coli* K12 DSM 18039 and primers YZ122_FabZ_Fw and YZ122_FabZ_Rv. PCR conditions were: initial denaturation at 98 °C, 30 sec; 3-step cycle: 98 °C, 10 sec; 60.3 °C, 30 sec; 72 °C, 30 sec; repeated 35 times; final elongation at 72 °C, 2 min. The obtained products were elongated with homology arms by PCR using the primers YZ078_BorDH2_2_LFw and YZ079_BorDH2_2_LRv (for BorDH2), YZ090_BorDH3_LFw and YZ091_BorDH3_LRv (for BorDH3), YZ094_BorDH5_LFw and YZ095_BorDH5_LRv (for BorDH5), YZ124_FabZ_LFw and YZ124_FabZ_LRv (for FabZ), respectively, under the same PCR conditions as mentioned above.

Homologous recombination in yeast was then carried out using the elongated PCR products in combination with the pYE-Express shuttle vector[22] (linearised via digestion with HindIII and EcoRI), through the standard protocol using LiOAc, polyethylene glycol and salmon sperm DNA.[22] Transformed yeast cultures were grown on SM-URA agar plates (425 mg yeast nitrogen base, 1.25 g ammonium sulphate, 5 g glucose, 192.5 mg nutritional supplement minus uracil, 5 g agar, 250 mL water) at 28 °C for 3 days and colonies were collected to obtain the recombined plasmid using the Zymoprep Yeast Plasmid Miniprep II kit (Zymo Research, Irvine, CA, USA). The isolated plasmid was used for electroporation of *E. coli* BL21(DE3) electrocompetent cells, which were grown overnight at 37 °C on LB agar plates. Single colonies were picked and inoculated in LB medium (10 mL) with kanamycin (10 µL; 50 mg mL^{-1}) and grown for 12 h to isolate plasmid DNA. The correct insertion of the desired genes was checked by PCR and by sequencing to obtain the plasmids pYE-BorDH2, pYE-BorDH3 and pYE-BorDH5.

LkcB (ADN64232),[23] FosDH1 (HQ434551, coding sequence for amino acids A1992 to G2294 of module 1) and FosDH2 (HQ434551, coding sequence for amino acids A947 to A1232 of module 2)[19] were codon optimised for expression in *E. coli*, synthesised and cloned into pET-28b(+) (LkcB) and pET-28a(+) (FosDH1 and FosDH2) by BioCat GmbH (Heidelberg, Germany).

For cloning of *ShawDH1* and *ShawDH2* genes, genomic DNA of *S. hawaiiensis* NRRL 15010 was isolated using the NucleoSpin Microbial DNA Kit (Macherey-Nagel) following the manufacturer`s instructions. DNA fragments encoding ShawDH1 and ShawDH2 were amplified by PCR from the genomic DNA using Q5 high-fidelity DNA polymerase and the primer pairs ShawDH1_NdeI_fw/ShawDH1_HindIII_rv and ShawDH2_NdeI_fw/ShawDH2_HindIII_rv, respectively. The PCR products were each ligated into the vector pET-28a(+), which was previously linearized with NdeI and HindIII. The PCR products were verified by Sanger sequencing (Eurofins Genomics).

Table S1. Primers used for gene cloning.

Primer	Sequence[a]
YZ074_BorDH2_1_Fw	CTTCCAGCACCAGCACTACTGGATGATG
YZ075_BorDH2_1_Rv	CAGTCGACCCGGAACAGTGAGTC
YZ078_BorDH2_2_LFw	GGCAGCCATATGGCTAGCATGACTGGTGGAATGAACACCGGAAGTGCCGC
YZ079_BorDH2_2_LRv	TCTCAGTGGTGGTGGTGGTGGTGCTCGAGTCAGTCGACCCGGAACAGTTAGTCG
YZ088_BorDH3_Fw	CACCCTGCCGGAGACGTGAC
YZ089_BorDH3_Rv	TTACCAGGGCTTCGTGCCGCGTT
YZ090_BorDH3_LFw	GGCAGCCATATGGCTAGCATGACTGGTGGACACCCTGCCGGAGACGTGAC
YZ091_BorDH3_LRv	TCTCAGTGGTGGTGGTGGTGGTGCTCGAGTTTAGCCCGCCCGCC
YZ092_BorDH5_Fw	TCCCGCACCGGGAACCTCAA
YZ093_BorDH5_Rv	TTACTCGGGCCGCTTCACGGTCA
YZ094_BorDH5_LFw	GGCAGCCATATGGCTAGCATGACTGGTGGATCCCGCACCGGGAACCTCAA
YZ095_BorDH5_LRv	TCTCAGTGGTGGTGGTGGTGGTGCTCGAGTTTACTCGGGCCGCTTCACGGTCA
YZ122_FabZ_Fw	TTGACTACTAACACTCATACTCTGCAG
YZ123_FabZ_Rv	TCAGGCCTCCCGGCTACGA
YZ124_FabZ_LFw	GGCAGCCATATGGCTAGCATGACTGGTGGATTGACTACTAACACTCATACTCTGCAG
YZ125_FabZ_LRv	TCTCAGTGGTGGTGGTGGTGGTGCTCGAGTTCAGGCCTCCCGGCTACGA
ShawDH1_NdeI_fw	GAGCTGCATATGACCGCGAAGATCTCC
ShawDH1_HindIII_rv	GATTAAGCTTCGTCTCAGGCCAGCCGCAC
ShawDH2_NdeI_fw	GATTACATATGGCAGAGCCGAGG
ShawDH2_HindIII_rv	GTTAAAGCTTCTCAGAAGTAGTAGCGCG

[a] Homology arms for recombination in yeast fitting to pYE-Express are underlined.

Gene expression and protein purification

E. coli BL21(DE3) cells harboring the corresponding pYE-Express/pET-28 derived plasmids were used to inoculate a preculture in LB medium (10 mL) supplied with kanamycin (50 μg/mL final concentration), which was grown with shaking at 37 °C overnight. The precultures were used to inoculate main cultures (1/100) in LB medium with kanamycin (50 μg/mL final concentration) and the cells were grown with shaking at 37 °C until OD_{600} = 0.4 – 0.6 was reached. The cultures were cooled down to 18 °C, before IPTG (0.4 mM final concentration) was added to induce expression. The cultures were shaken at the same temperature overnight and then centrifuged (3500 x g, 40 min, 4 °C). The medium was discarded and the cell pellet was resuspended in binding buffer (10 mL/L culture; 40 mM Tris-HCl, 100 mM NaCl, pH 7.8, 4 °C). The cells were lysed by ultrasonication (5 x 1 min). The cell debris was spun down (top speed, 10 min, 4 °C) and the soluble protein fraction was filtrated and loaded onto a Ni^{2+}-NTA affinity chromatography column (Ni-NTA superflow, Qiagen, Venlo, Netherlands). The bound target protein was washed with wash buffer (2 x 10 mL/L culture; 40 mM Tris-HCl, 100 mM NaCl, 50 mM imidazole, pH 7.8, 4 °C) and desorbed from the stationary phase with elution buffer (1 x 10 mL/L culture; 40 mM Tris-HCl, 100 mM NaCl, 500 mM imidazole, pH 7.8, 4 °C) with fractionation. The fractions were analysed by SDS-PAGE (Figure S36) and fractions containing pure protein were pooled and used for incubation experiments. Protein concentrations obtained by this procedure were 1.6 mg/mL for BorDH2, 2.3 mg/mL for BorDH3 and 2.8 mg/mL for BorDH5. Finally, the eluate was concentrated, the buffer was replaced by incubation buffer (25 mM HEPES, 100 mM NaCl, pH 7.5). The same protocol was used for the purification of the other proteins (FosDH1, FosDH2, FabZ, LkcB and ShawDH2). For ShawDH1 expression, the strain was *E. coli* BL21(DE3) transformed with plasmid pGro7, additionally supplemented with arabinose (500 mg/L) to induce expression of the GroEL/ES chaperone.[24]

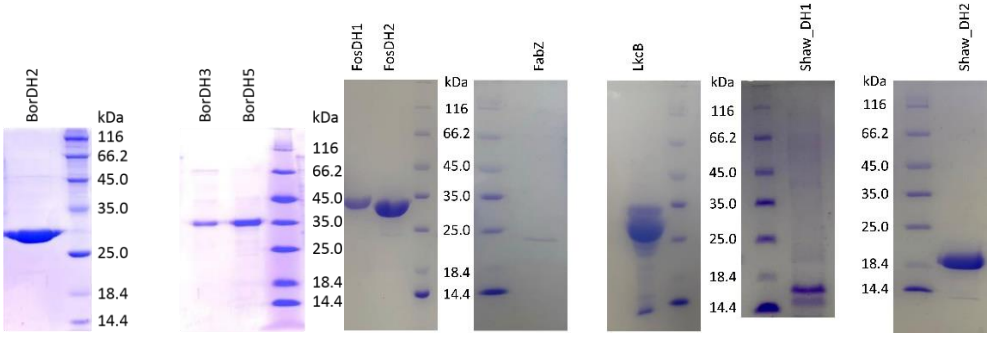

Figure S36. SDS-PAGE analysis of all recombinant enzymes used in this study. The theoretical molecular weights of target proteins are 34.6 kDa (BorDH2), 34.0 kDa (BorDH3), 34.2 kDa (BorDH5), 33.3 kDa (FosDH1), 33.1 kDa (FosDH2), 19.8 kDa (FabZ), 30.4 kDa (LkcB), 15.2 kDa (ShawDH1) and 16.5 kDa (ShawDH2).

Activity assays

Activity assays were carried out in a total volume of 100 μL containing 1 mg (0.1 mg for labelled compound) SNAC thioesters **27**, 25 mM HEPES pH 7.5, 100 mM NaCl and up to 8 mg/mL of the corresponding enzyme BorDH2 (6.2 mg/mL), BorDH3 (7.2 mg/mL), BorDH5 (5.6 mg/mL), LkcB (7.3 mg/mL), FabZ (7.8 mg/mL), FosDH1 (6.9 mg/mL), FosDH2 (6.1 mg/mL), ShawDH1(6.0 mg/mL) and ShawDH2(6.0 mg/mL). Reactions were incubated at 30 °C for 16 h and extracted with 0.6 mL of C_6D_6.[20] After extraction the sample was analysed by NMR. All traces were compared to authentic standards. The configuration of the reaction product was determined by ^{1}H NMR and ^{13}C NMR.

BorDH2 nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAG
CATGACTGGTGGAATGAACACCGGAAGTGCCGCCGAGCCGGCGGAGCTGGGGCTCGGCGATGCCCGTC
ATCCGCTGCTCGGTTCCGTCGTCACCGTCGCGGGGGACGACAAGGTCGTCTTCGCCGGGCGGCTGGCG
CTGCGCACACACCCCTGGCTGGCCGACCACACCGTGCTCGACGCGGTCTTGCTGCCCGCTACGGCCTT
CCTCGAACTGGCCGTGCGCGCCGGTGAGGAGGTGAGCTGTCCGGTCGTACACGACCTGACGCTGCACC
GACCGCTGGTCGTACCCGAGCGGGGCGCCGTGCAGGTACAGATGGCTGTGGGCGCACCGGAAGCCGAT
GGGCGACGTGAGGTCCGGGTGTACTCCCGCCCCGACGACGACGCGGAGCACGAGTGGACGCTGCACGC
CGCTGGACTGCTGGCGTCGGCCGCCACGGCGGAGCCCGCCGTGGCGGCCGGTGCCTGGCCGCCGCCGG
AGGCGCAGGCCGTGGACCTCGACGGCTTCTACGCCGGACTCGCCGAGCACGGCTACCACTACGGCCCG
CTGTTCCAGGGCGTCCGGGCCGCGTGGCGGCTGGGCGACGACGTTCTCGCCGAGATCGTGCTGCCCGA
GGCGGCCGGCGCCGACGCCGCCCGGTACGGCATGCATCCGGCCCTGCTCGACGCCGTCCTGCACGCGG
CACGGCTGGGCGCCTTCCGTGAGCGGTCGGAGGAGAAGTACCTGCCGTTCGCCTGGGAAGGCGTGACC
CTGCGTACCAGGGGAGCGACCGCCGTACGTGCTCGAATCTCCCGGGCCGGTACCGACGCCATCCGGCT
GGACGTCACCGACACCGCGGACCGGCCGGTCCTCACGGCCGAATCGCTCACGCTGCGACCGGTCTCCG
CCGGTCAGCTCATGGCCGTCCCGCGCGACTAA

BorDH2 amino acid sequence

MGSSHHHHHHSSGLVPRGSHMASMTGGMNTGSAAEPAELGLGDARHPLLGSVVTVAGDDKVVFAGRLA
LRTHPWLADHTVLDAVLLPATAFLELAVRAGEEVSCPVVHDLTLHRPLVVPERGAVQVQMAVGAPEAD
GRREVRVYSRPDDDAEHEWTLHAAGLLASAATAEPAVAAGAWPPPEAQAVDLDGFYAGLAEHGYHYGP
LFQGVRAAWRLGDDVLAEIVLPEAAGADAARYGMHPALLDAVLHAARLGAFRERSEEKYLPFAWEGVT
LRTRGATAVRARISRAGTDAIRLDVTDTADRPVLTAESLTLRPVSAGQLMAVPRD*

BorDH3 nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAG
CATGACTGGTGGACACCCTGCCGGAGACGTGACCGCCGTCGGTCTCACAGAGGCCGGTCACGCGTTCG
TGCCGGCGGCGGTCGACCTGCCGGACGGGCAGCGGGTCTGGACGGGACGACTGTCGCTTCCCTCCTAC
CCGTGGCTGGCCGATCATCAGGTGCTCGGGCAGGTGCTGCTCCCCGGCGTGGTCTGGGTCGAACTCGC
CCTGCACGCGGGGCACCAGGCCGGATGCGACTCTGTCGATGAGCTCACCCTACAGTCGCCGCTCGTGC
TCGGTGCGTCCGACACCGTACAGGTGAGGGTCGTCGTCACGGAGACCGAAGAGCCCGGCACCCGCACC
GTGTCGATGCACTCGCGCCGTGACGACGGCAGCTGGGTGACTCACGCCGAGGGGATCCTCGGGGCGGG
CGGGCCGCCGCCGGAGCCGCTGCCGGAATGGCCGCCGACCGGCGCCATGCCCCTCGATGTCGAGGGCT
TCTACGACGAGCTCGCGGCGGGCGGCTACCACTACGGGCCTCAGTTCCGCTGCCTGCGGCGCGCCTGG
CGTGCCGGTGAGGATCTCGTCGCCGAGATCTCGCTGCCGGAGGGCACCGACGTCGATGCGTACGGCCT
GCACCCTGGACTCTTCGACGCGGCGGTGCACAGCGTGGCCTGCGCCCGGACGAGCGCGGGGGCCGGCG
ATGACGGTCCCCGGCTGCCGTTCGCCTTCTCGGACGTCCGGCTCTTCGCGACCGGGGTGACCTCGCTA
CGGGTCCGGATCGATCCGCAGAACTCCTCGTGGCAGGCGTGGGACGAATCCGGGCTGCCGGTCCTCAC
CATCGGGCGGCTCGCCGGCCGGCCTGTCGACGCCGATCAGTTCGCCGTGCGGCGGGCGGGCCTGTTCC
GGGTCGACTGA

BorDH3 amino acid sequence

MGSSHHHHHHSSGLVPRGSHMASMTGGHPAGDVTAVGLTEAGHAFVPAAVDLPDGQRVWTGRLSLPSY
PWLADHQVLGQVLLPGVVWVELALHAGHQAGCDSVDELTLQSPLVLGASDTVQVRVVVTETEEPGTRT
VSMHSRRDDGSWVTHAEGILGAGGPPPEPLPEWPPTGAMPLDVEGFYDELAAGGYHYGPQFRCLRRAW
RAGEDLVAEISLPEGTDVDAYGLHPGLFDAAVHSVACARTSAGAGDDGPRLPFAFSDVRLFATGVTSL
RVRIDPQNSSWQAWDESGLPVLTIGRLAGRPVDADQFAVRRAGLFRVD*

BorDH5 nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAG
CATGACTGGTGGATCCCGCACCGGGAACCTCAACATGGCCGGGCTGGTCGAAGCCGGACATGAAATCC
TGCCCGCCGCAGTGGAGTTGCCCGGAGAGCAGTGGGTGTGGACCGGCGAGCTGTCGCTCTCCGCGTAC
CCGTGGCTGGCCGATCACCAGGTGCTCGGGCAGACCCTGGTGCCGGGCGTGGCGTGGGTCGAACTCGC
CCTGCACGCGGGCCACCAGCTCGGTTTCGGATCCGTCGAGGAACTCACCCTGCAGGCACCGCTCGTGC

TCGGCGAGTCCGACGCCGTGCAGGTCAGAGTCGTTGTCTCCGATCTCGGGGAGAGTGATCGCCGGGCA
GTGTCGGTGCACTCGCGTGGTGACGACCAGACGTGGGTGACCCATGCGGAGGGATTCCTCACCGCGAA
AGGGGCGCAGCCGGAGACCATGGCCGTGTGGCCGCCGTCCGGTGCGGAGCCGGTGGAGGCTGACGGGT
TCTACGAACGCCTCGCCGATGCGGGGTACCACTATGGCCCGGTCTTCCAGGGCGTGAGCAAGGTCTGG
CGAGCTGGCGAGGAGATCTACGCCGAGGTCGGGCTGCTCGACGACGCCGACGTGGACGGCTTCGGCAT
CCACCCCGCCCTGCTCGACGCCGCCCTGCAGACCGCCTACGTCGCCCAACGGGGCCCCGCAGAGACGA
AGTTGCCTTTCGCGTTCGGCGATGTACAGCTGTTCGCCACCGGTGCCCGGTCGCTCCGCGTACGGGTC
TCGCCGGCCGCTCAGCAGGGGATGGCGTGGGAGGCCTGGGACCCCACCGGACTTCCGGTGTTCTCCCT
CGGGTACCTGGCGACCCGGCCGGTCGACCGCGGCCAGCTGACCGTGAAGCGGCCCGAGCTGTTCCGGG
TCGACTGA

BorDH5 amino acid sequence

MGSSHHHHHHSSGLVPRGSHMASMTGGSRTGNLNMAGLVEAGHEILPAAVELPGEQWVWTGELSLSAY
PWLADHQVLGQTLVPGVAWVELALHAGHQLGFGSVEELTLQAPLVLGESDAVQVRVVVSDLGESDRRA
VSVHSRGDDQTWVTHAEGFLTAKGAQPETMAVWPPSGAEPVEADGFYERLADAGYHYGPVFQGVSKVW
RAGEEIYAEVGLLDDADVDGFGIHPALLDAALQTAYVAQRGPAETKLPFAFGDVQLFATGARSLRVRV
SPAAQQGMAWEAWDPTGLPVFSLGYLATRPVDRGQLTVKRPELFRVD*

FosDH1 nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTGG
TTTGACTGGTACCCCTCACCCACTGTTGGCCGCTGCAGTAGAATTGCCTGAGGGTGGCGGTTTCGTTC
ACACGGGTCGTATCGGCACCCTGACTCATCCGTGGCTGGCTGATCACGCAATTCATGGCACCACGTTG
CTGCCGGGTACCGCGCTGCTGGATCTGGTTCTGCACGCAGCGAGCGATGGTGCGGGTGAGCACCCGGC
GGTTGCGGAGCTGGCTCTGCAAGCGCCGCTGGTCCTGCCGGGTGAACGTGGCGTTGATATTCGTGTCA
CGGTCCAAGAAGCGGACGAGAGCGGCCTGCGTGCATTCGCGGTGCACAGCCGTCCGGCGCCGGCTGGT
GACGATGCGTCCGGCAGCTCTAGCTGGACCCGCCATGCCAGCGGTGCGCTGGGCCCGACGGAAGCGCC
GGATGCGGCCGACCGTGCGCCACAGTGGCCACCGGCGGATGCCGCCCCGGTCGACCTGACGGACCTGT
ATCCGGCGCTGGCACTGACCGGTTACGAGTACGGTCCGGACTTCCGCCTGTTAACCGCCGCATGGCGC
ACGGATGACGATGTCTTTGCTCAGGTTGAGCTTGGCGACGACGCAGCGGCGTCTGACGATGTTGACCG
TTTTAGCGTGCATCCGGCACTGTTGGACGCATCCCTCCACGCGTTGTTGCGTAGCGGTCTGCTGGCGG
ATGGCGTTTCTGGCACCGACGCCAGCGGCACGCTGCTGCCGTTCAGCTGGGGTGACGTGGCACTGCAC
GCCCTGGGCGCGACGGCACTGCGCGTGCGTTTCACCCGCACCGGTCCGACCACCGTGCGCGTGGTCGC
CTCGGACCCGAGCGGTGCACTGATCCTGACCGCGGGTGAACTGAGCCTGCGTCCGGTTGTGCTGGACC
GTCTGAGCGATGGTAGCGGCTAA

FosDH1 amino acid sequence

MGSSHHHHHHSSGLVPRGSHMAGLTGTPHPLLAAAVELPEGGGFVHTGRIGTLTHPWLADHAIHGTTL
LPGTALLDLVLHAASDGAGEHPAVAELALQAPLVLPGERGVDIRVTVQEADESGLRAFAVHSRPAPAG
DDASGSSSWTRHASGALGPTEAPDAADRAPQWPPADAAPVDLTDLYPALALTGYEYGPDFRLLTAAWR
TDDDVFAQVELGDDAAASDDVDRFSVHPALLDASLHALLRSGLLADGVSGTDASGTLLPFSWGDVALH
ALGATALRVRFTRTGPTTVRVVASDPSGALILTAGELSLRPVVLDRLSDGSG*

FosDH2 nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCGGG
TGCCGACGCACTGCCGCATCCGATGCTGAGCCAACGTACTGATCTGCCGGGTGGTGGCGGCGTACTGT
TTAGCGGTCGTCTGGCTCCGGGCACGGACCCGTGGCTGCCGGATCACGCGGTGATGGGTACGCTGCTG
CTGCCGGGTACCGGCTTCGTGGAGTTGGCCCTGGAGGCGGCACGTGCAGTGGGTGCAGGTCGTGTGGA
GGAGCTGGTCCTGCGTGCGCCAATGGTTTTTCCGGGTGGTCGTGCGCGCGATTTGCAGGTCTGGGTCG
CACCGGACCAGGGTGGTGAACGTGAACTGTTGATTCGCACGCGCACCCCGGGTGAAGATTGGACCCTG
CACGCGACTGGCGTTGTCACGGCGAGCCGCGTTGACACCGATGGTTTTACGCCGGACTGGACCGGCGC
TGTTTGGCCTCCGGCAGGCGCCGAGCAGATTCCGGGCGATACCTTCTACCCTGACCTGGCAGAGCGCG
GCTATGAGTACGGTCCGGCGTTCCGTTCGGTCAAAGCGCTGTGGCGTCGTGGTGATGACCTGTTCGCA
GAAGTCGTCCTGCCGGAAGATCAGCCATACGGTTTTGGCGCGCATCCAGCGCTGCTGGACGCATCTTT
GCACGCCCTGCCGATCACCCGTAGCTTCTATGAAACGGACGATGAGGTGCGCTTGCCGTTTTCCTTCG

GTGGTGTTAGCTTGTTCGCCACCGACGTGCGCCGTGTTCGTGTTCGTCTGCGTCCGCGTCCGGAGGCG
ACCAGCGTGTGGATCACCGACGCGGCTGGCACCCCGGTGCTGGCGATGGAAAGCCTGATCCTGCGCGC
TGTTGAACGCACGCAACTGCAAGCGGCGGAGGGCGCCTAA

FosDH2 amino acid sequence

MGSSHHHHHHSSGLVPRGSHMAGADALPHPMLSQRTDLPGGGGVLFSGRLAPGTDPWLPDHAVMGTLL
LPGTGFVELALEAARAVGAGRVEELVLRAPMVFPGGRARDLQVWVAPDQGGERELLIRTRTPGEDWTL
HATGVVTASRVDTDGFTPDWTGAVWPPAGAEQIPGDTFYPDLAERGYEYGPAFRSVKALWRRGDDLFA
EVVLPEDQPYGFGAHPALLDASLHALPITRSFYETDDEVRLPFSFGGVSLFATDVRRVRVRLRPRPEA
TSVWITDAAGTPVLAMESLILRAVERTQLQAAEGA*

FabZ nucleotide sequence

ATGGGCAGCAGCCATCATCATCATCATCACAGCAGCGGCCTGGTGCCGCGCGGCAGCCATATGGCTAG
CATGACTGGTGGATTGACTACTAACACTCATACTCTGCAGATTGAAGAGATTTTAGAACTTCTGCCGC
ACCGTTTCCCGTTCTTACTGGTGGATCGCGTGCTGGATTTTGAAGAAGGTCGTTTTCTGCGCGCAGTA
AAAAATGTCTCTGTCAATGAGCCATTCTTCCAGGGCCATTTCCCTGGAAAACCGATTTTCCCGGGTGT
GCTGATTCTGGAAGCAATGGCACAGGCAACAGGTATTCTGGCGTTTAAAAGCGTAGGAAAACTGGAAC
CGGGTGAGCTGTACTACTTCGCTGGTATTGACGAAGCGCGCTTCAAGCGCCCGGTCGTGCCTGGCGAT
CAAATGATCATAGAAGTCACTTTCGAAAAAACGCGCCGCGGCCTGACCCGTTTTAAAGGGGTTGCTCT
GGTCGATGGTAAAGTAGTTTGCGAAGCAACGATGATGTGTGCTCGTAGCCGGGAGGCCTGA

FabZ amino acid sequence

MGSSHHHHHHSSGLVPRGSHMASMTGGLTTNTHTLQIEEILELLPHRFPFLLVDRVLDFEEGRFLRAV
KNVSVNEPFFQGHFPGKPIFPGVLILEAMAQATGILAFKSVGKLEPGELYYFAGIDEARFKRPVVPGD
QMIIEVTFEKTRRGLTRFKGVALVDGKVVCEATMMCARSREA*

LkcB nucleotide sequence

ATGACCACCCGTGCAGATCAGACCGCAGGCCCGGCCGCAGTGGAACCTCCTCGTCTGCTGGATACCGG
CGAACCGGATACCTTTCGTGTGCCGATTGAAACCGGTCATCCGTATCTGGCACAGCATCTGGTTCAGG
GCCGCCGCGTTCTGCCGGGTGTTGCATGCCTGGAAATGGCCCTGCGTGGTGCAGCCCGCGTGCGTCCT
GGTGCACGTCCTTTTGCCGTTCGTGATGCCGCCTGGCTGCGCCCTGTGTATGGCGATGAACCGCTGGA
TGAACTGAGTGTTGCCTTTCGCACCGCCCCGGGCGCCAGAGAAACCGATTATACCGTTACCAATCGTG
GTGCCCTGTGCGCAATGGGCACCCTGCTGTTTGAACCGCAGGATCGCGCCGTGGCCGTTGGTCTGGAA
GTGCGCGATGAAATTTGTGCCCATACCCGCAGTCATCTGACCCGCGCAGAAATCTATGAAGAATTTTC
TAATATGGGCATCGATTATGGCCCGTATTTTCGTCGTAATAGTTATGTGCAGCGCCATGGCCAGCGTA
GTCTGGCCTGGCTGAGTCATAATGATGGCACCCGCATTGGTCTGGTGAATCTGCTGGATTGTGCATTT
CAGAGTGGCATGGCCATTAGTATTGGCGAACATCGCGATAGTCTGATGCCGTTTAGTATGGGCCATAT
GGTTTTTCATGCCCCGACCCGCTTTCCGCTGGGTAGCGCATTTGTTCTGACCGAAAAACTGAGCCCGT
TTCGTACCAATTTTACCCTGTTTGATGAAGATTATGAGCCGCTGCTGAGCGTTTTTGATCTGGGTGTG
AAACCGGCACTGAAGCTTGCGGCCGCACTCGAGCACCACCACCACCACCACTGA

LkcB amino acid sequence

MTTRADQTAGPAAVEPPRLLDTGEPDTFRVPIETGHPYLAQHLVQGRRVLPGVACLEMALRGAARVRP
GARPFAVRDAAWLRPVYGDEPLDELSVAFRTAPGARETDYTVTNRGALCAMGTLLFEPQDRAVAVGLE
VRDEICAHTRSHLTRAEIYEEFSNMGIDYGPYFRRNSYVQRHGQRSLAWLSHNDGTRIGLVNLLDCAF
QSGMAISIGEHRDSLMPFSMGHMVFHAPTRFPLGSAFVLTEKLSPFRTNFTLFDEDYEPLLSVFDLGV
KPALKLAAALEHHHHHH*

ShawDH1 nucleotide sequence

ATGACCGCGAAGATCTCCTACGCCGACGTCGAGGTCGGCACCGAACTGCCCGCGCAGACCTTCCCCGT
GACCCGCGAGACCCTCGTCCGGTACGCGGGCGCCTCCGGCGACTTCAACCCGATCCACTGGAACGAGA
AGTTCGCCAAGGAGGTCGGCCTGCCGGACGTCATCGCGCACGGCATGTTCACCATGGCCGAGGCGATC
CGCGTGGTCACCGACTGGACCGGCGACCCGGGCGCGGTCGTCGAGTACGGCGTCCGCTTCACCAAGCC
GGTCGTCGTCCCGAACGACGGCCAGGGCGCTGTGATCGAGGTCGCCGGCAAGGTCGCCGCCAAGCTCG

ACGACAACACGGTCCGCGTGGACCTGACGGCGACCAGCGCAGGGCAGAAGGTGCTGGGCATGTCCAGG
GCGGTCGTGCGGCTGGCCTGA

ShawDH1 amino acid sequence

MTAKISYADVEVGTELPAQTFPVTRETLVRYAGASGDFNPIHWNEKFAKEVGLPDVIAHGMFTMAEAI
RVVTDWTGDPGAVVEYGVRFTKPVVVPNDGQGAVIEVAGKVAAKLDDNTVRVDLTATSAGQKVLGMSR
AVVRLA*

ShawDH2 nucleotide sequence

ATGGCAGAGCCGAGGATCTTCACGTCCGTCGACGACCTGAAGTCGGCGGTGGGCGAACAACTGGGGTA
CACCGACTGGCTCGACATCGACCAGAAGCGGATCGACCTCTTCGCGGAGGCCACCGGCGACCACCAGT
GGATCCACGTCGACCCGGAGAAGGCCGCCGCGGGCCCCTTCGGCACCACCATCGCGCACGGCTATCTG
ACCCTGTCGCTGCTGCCCCTCTTCGGACCGCAGCTGATCGCCGTCGAGGACGTGAAGATGGGCGTCAA
CTACGGCACGAACAAGGTGCGTTTCCCCGCCCCGGTCCCCGTCGGCTCCCGTCTGCGCGCCACCGCGA
CGATCAGCGCGGTCGACGAGGTGCCCGGTGGCGTCCAGGTGGCCGTCGCCTTCAGCGTCGAACGCGAG
GGCGGCGACAAGCCGGTCTGCGTCGCCGAGTCCGTGGCGCGCTACTACTTCTGA

ShawDH2 amino acid sequence

MAEPRIFTSVDDLKSAVGEQLGYTDWLDIDQKRIDLFAEATGDHQWIHVDPEKAAAGPFGTTIAHGYL
TLSLLPLFGPQLIAVEDVKMGVNYGTNKVRFPAPVPVGSRLRATATISAVDEVPGGVQVAVAFSVERE
GGDKPVCVAESVARYYF*

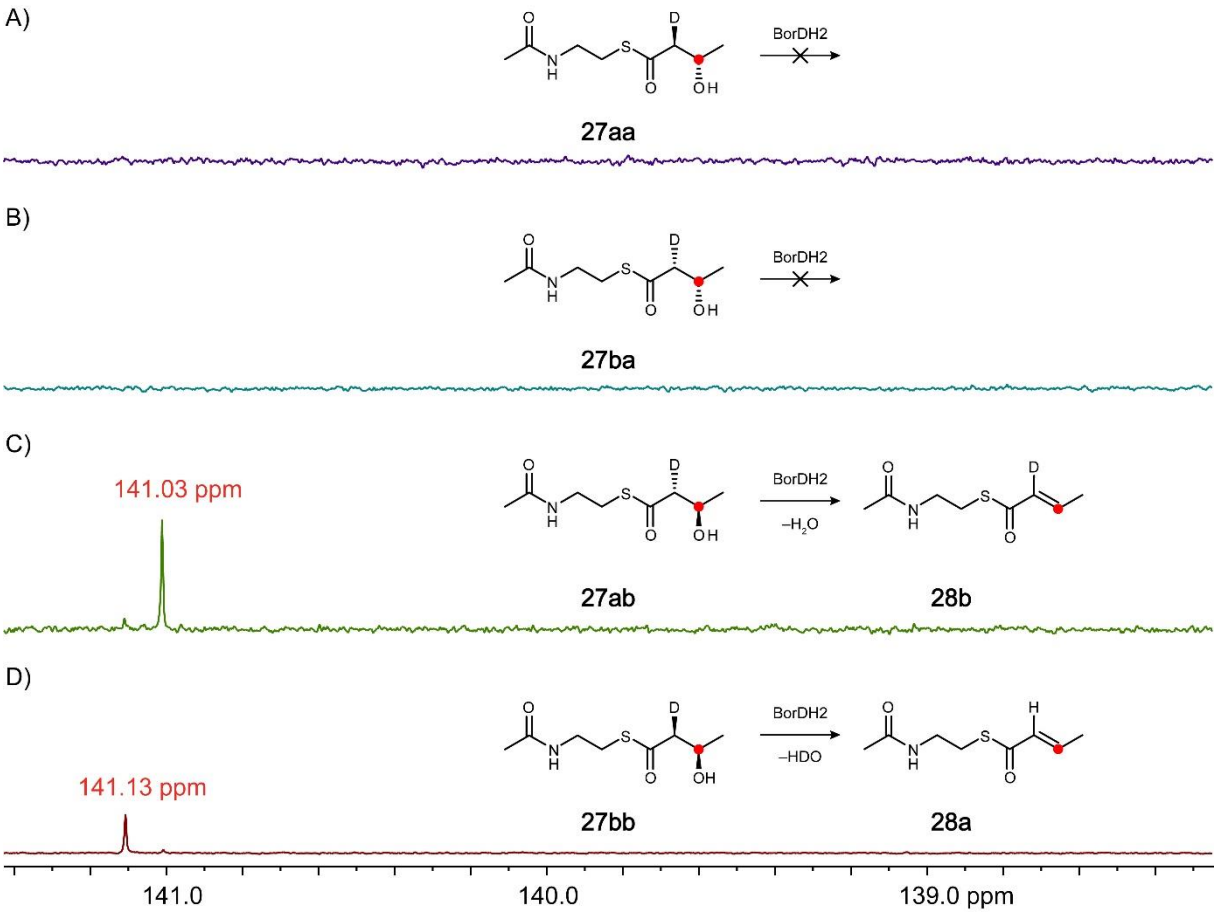

Figure S37. BorDH2 enzyme reaction with **27**.

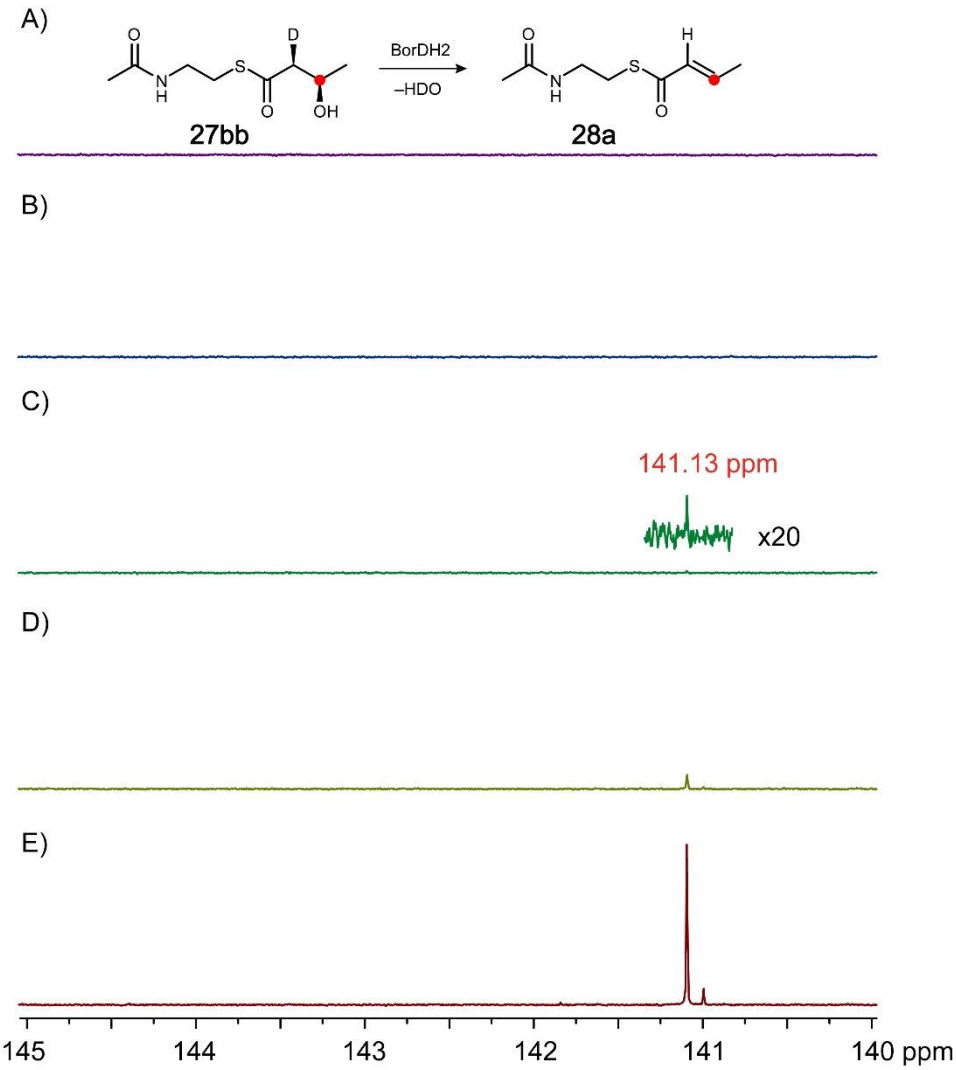

Figure S38. BorDH2 enzyme reaction with different concentrations of **27bb**. A) 0.0001 mg, B) 0.001 mg, C) 0.01 mg, D) 0.1 mg, E) 1 mg.

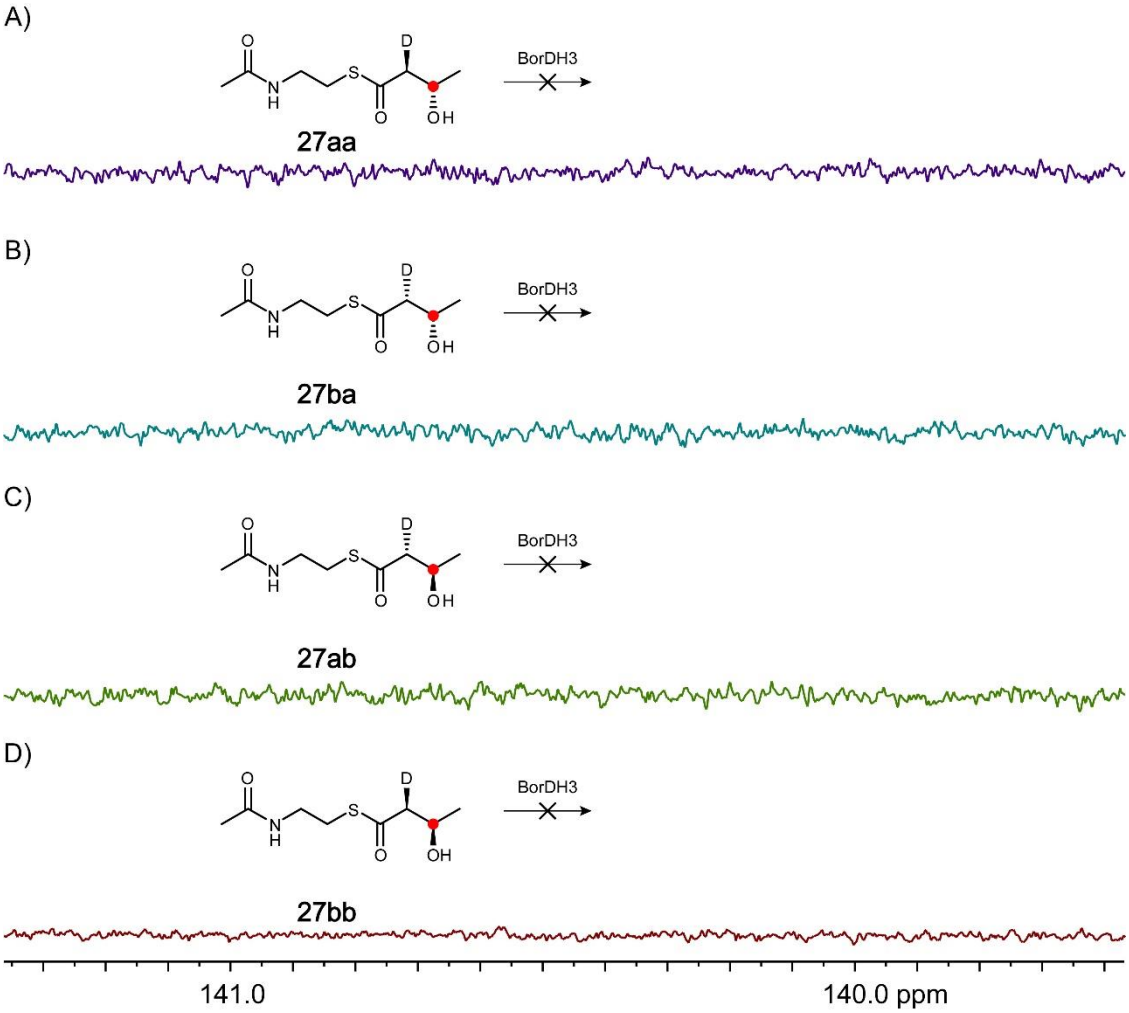

Figure S39. BorDH3 enzyme reaction with **27**.

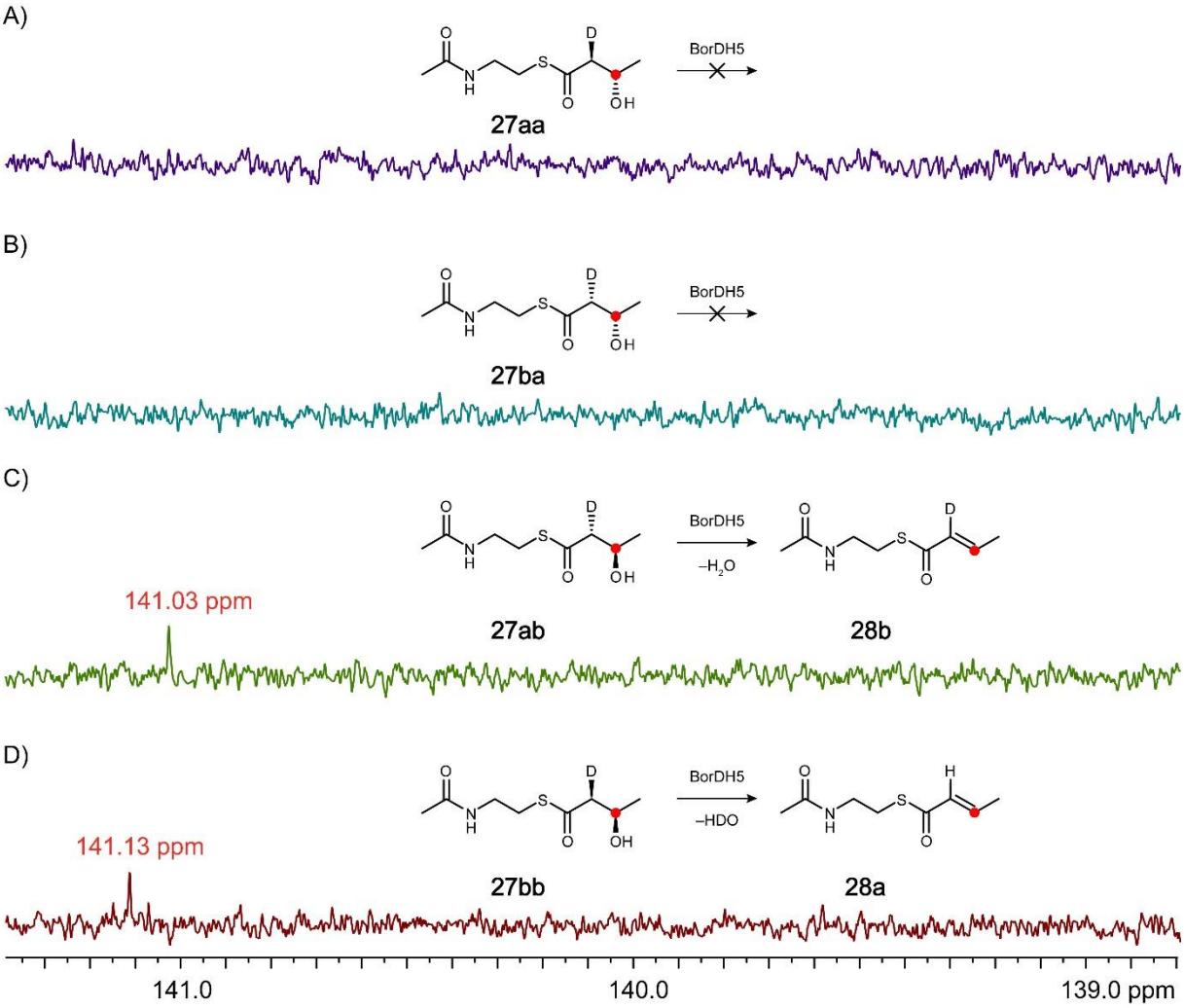

Figure S40. BorDH5 enzyme reaction with **27**.

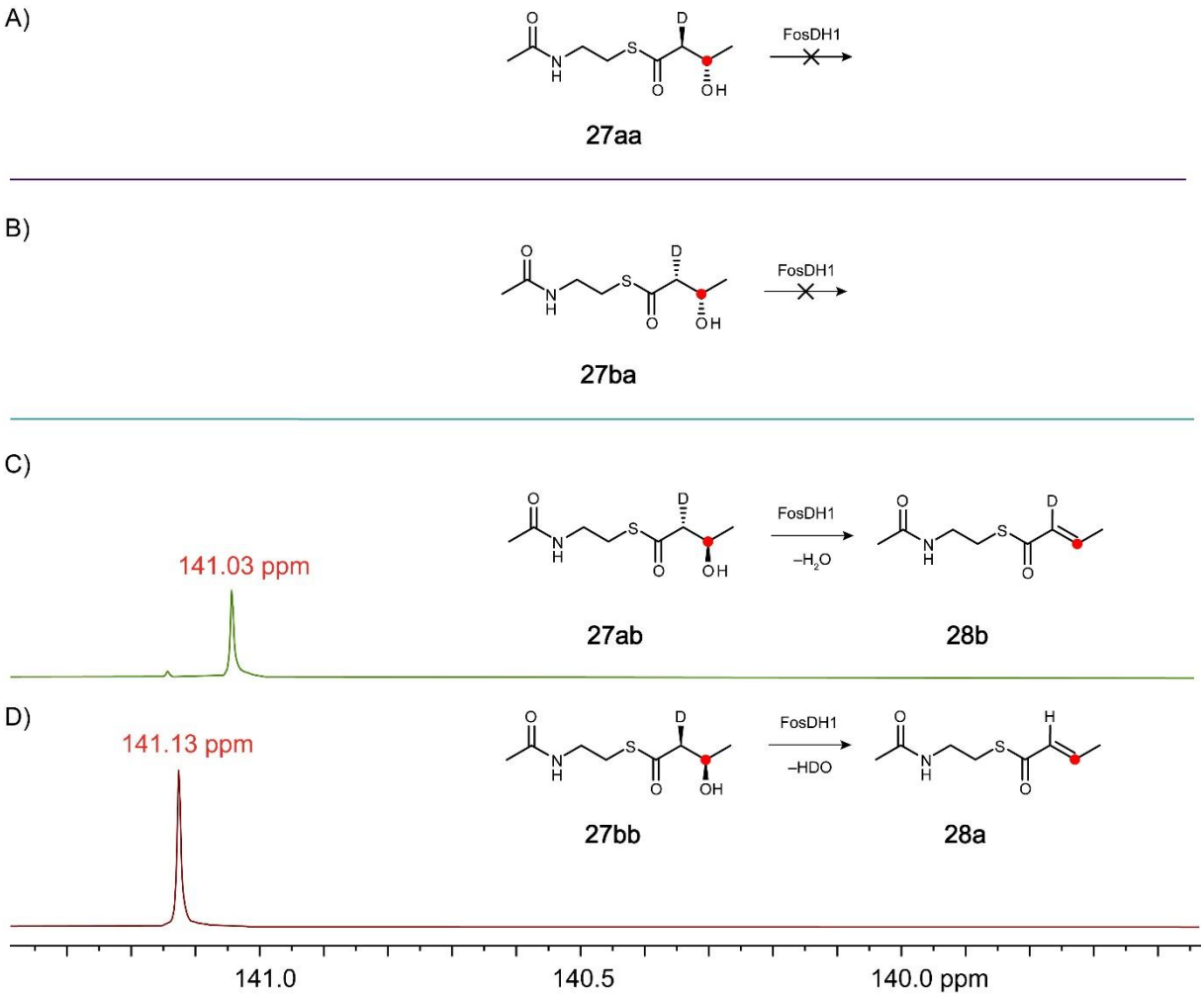

Figure S41. FosDH1 enzyme reaction with **27**.

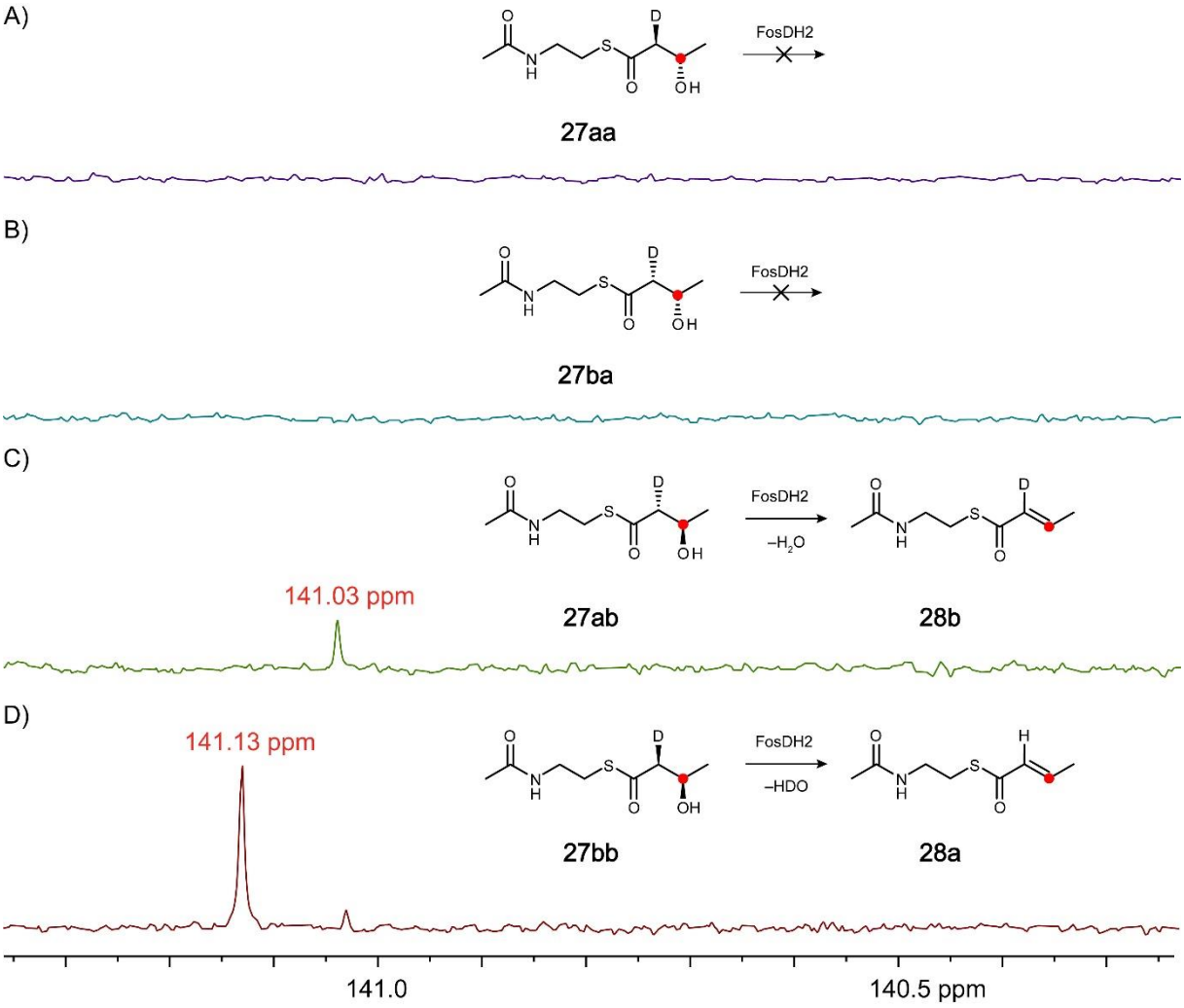

Figure S42. FosDH2 enzyme reaction with **27**.

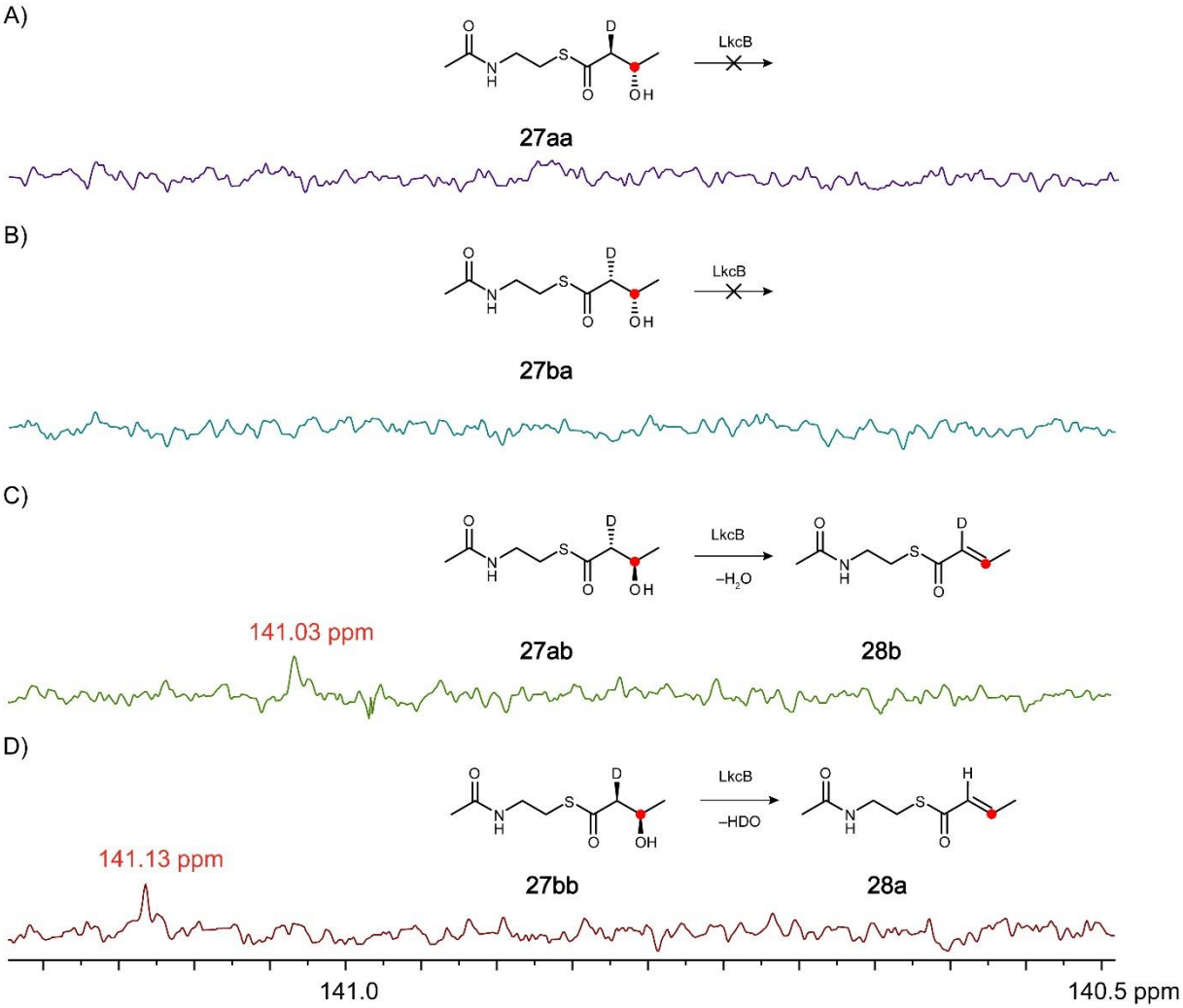

Figure S43. LkcB enzyme reaction with **27**.

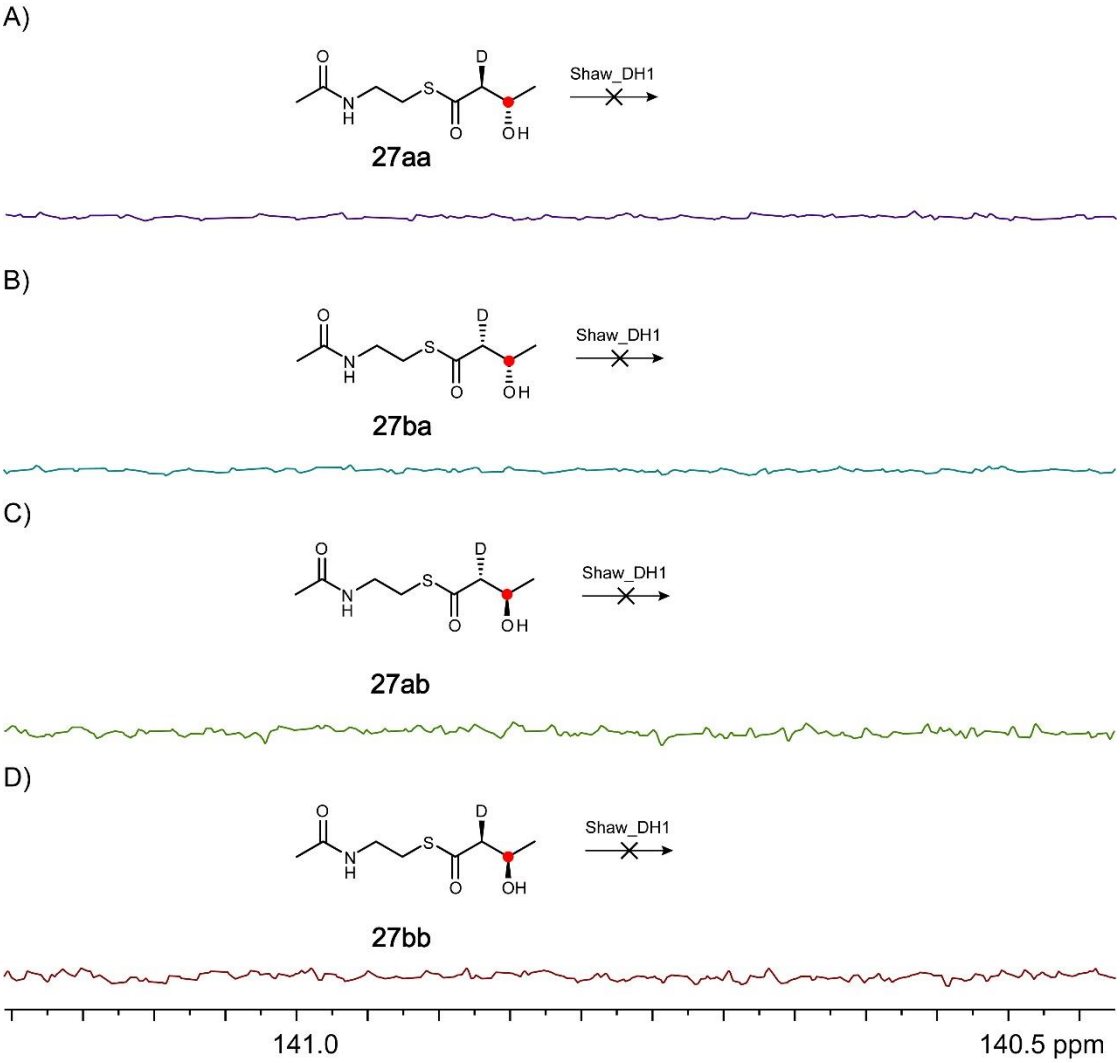

Figure S44. ShawDH1 enzyme reaction with **27**.

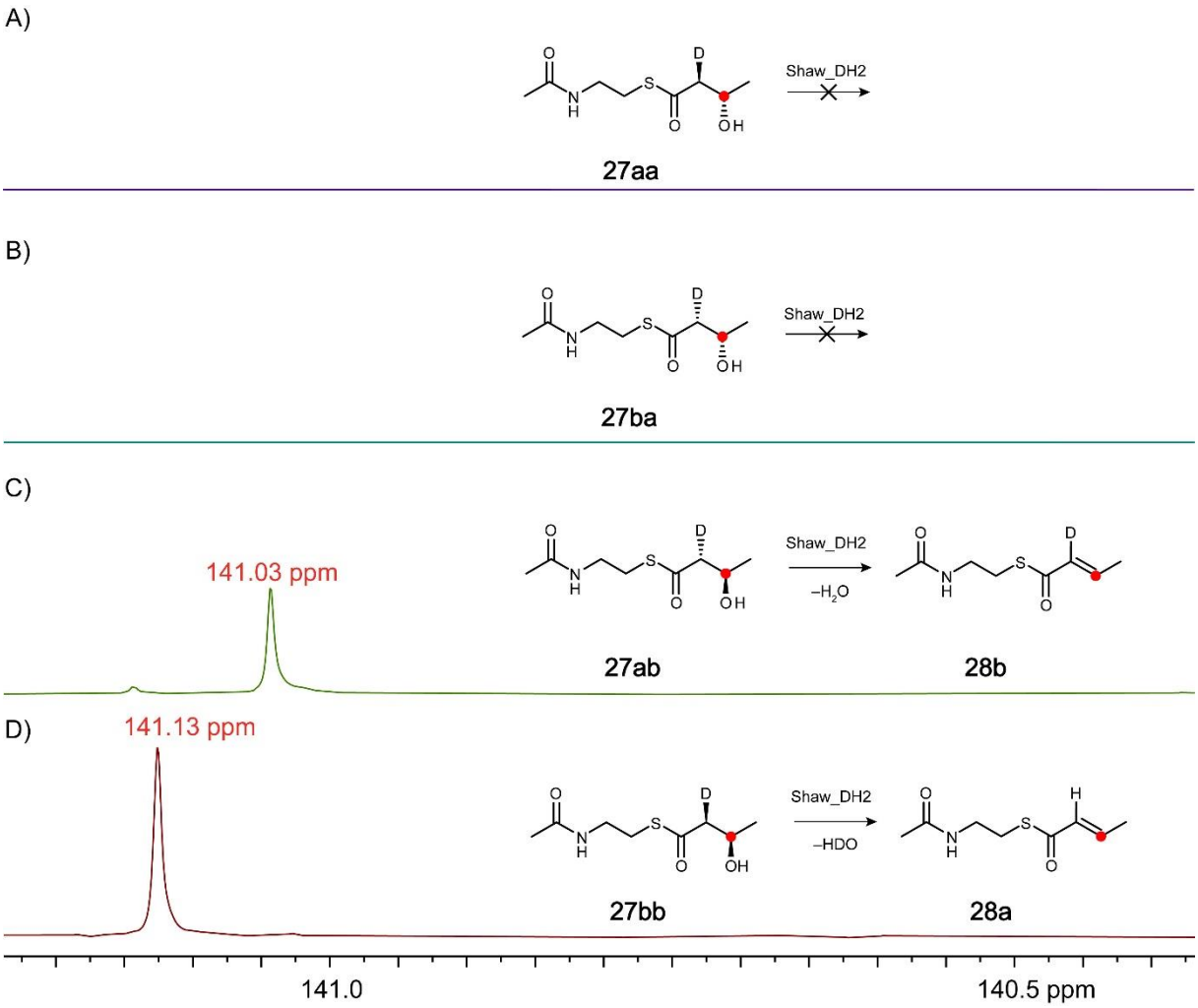

Figure S45. ShawDH2 enzyme reaction with **27**.

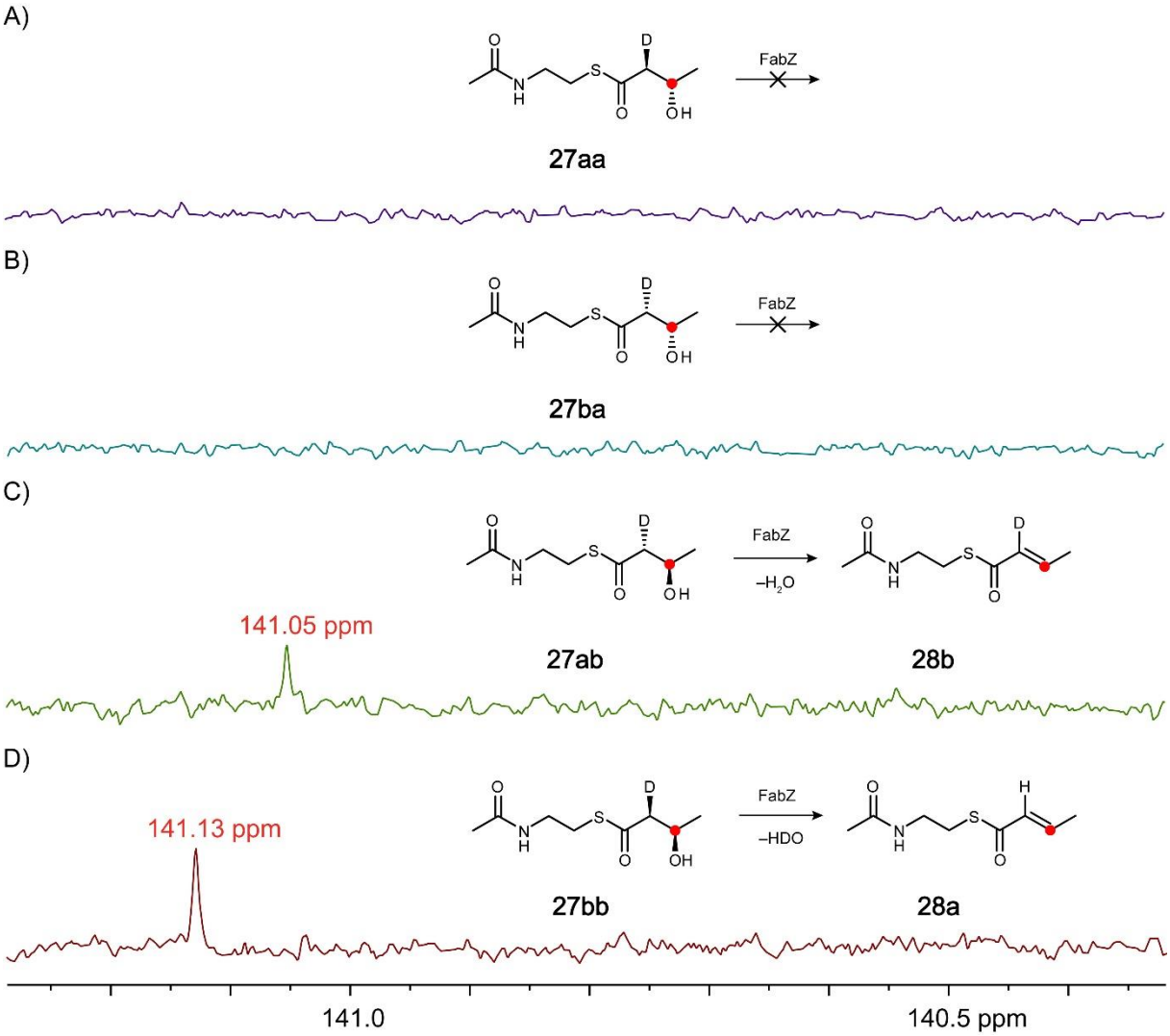

Figure S46. FabZ enzyme reaction with **27**.

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