Supplementary Material

Racemic Synthesis of Linderuca C from lignin derived starting materials

Daniel J. Davidson[a], Oliver Lynard[a], Daniel M. Miles-Barrett[a], Geraud N. Sansom[a]*, Filomena Tedesco[a], Fraser Watson[a], Nicholas J. Westwood[a]*

[a]School of Chemistry and Biomedical Sciences Research Complex, University of St Andrews and EaStCHEM, North Haugh, St Andrews, Fife, KY16 9ST, UK.
**Email: gns6@st-andrews.ac.uk and njw3@st-andrews.ac.uk*

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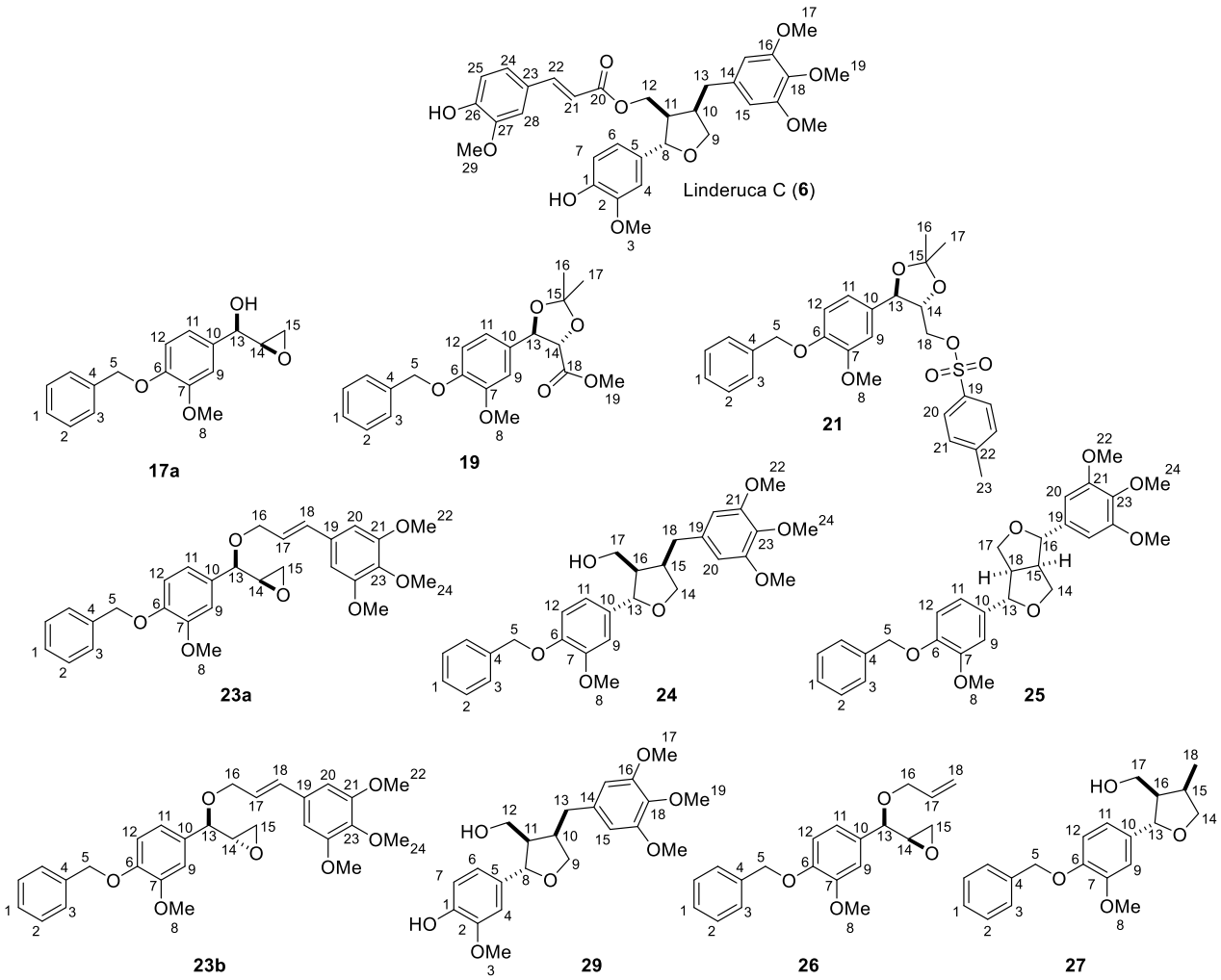
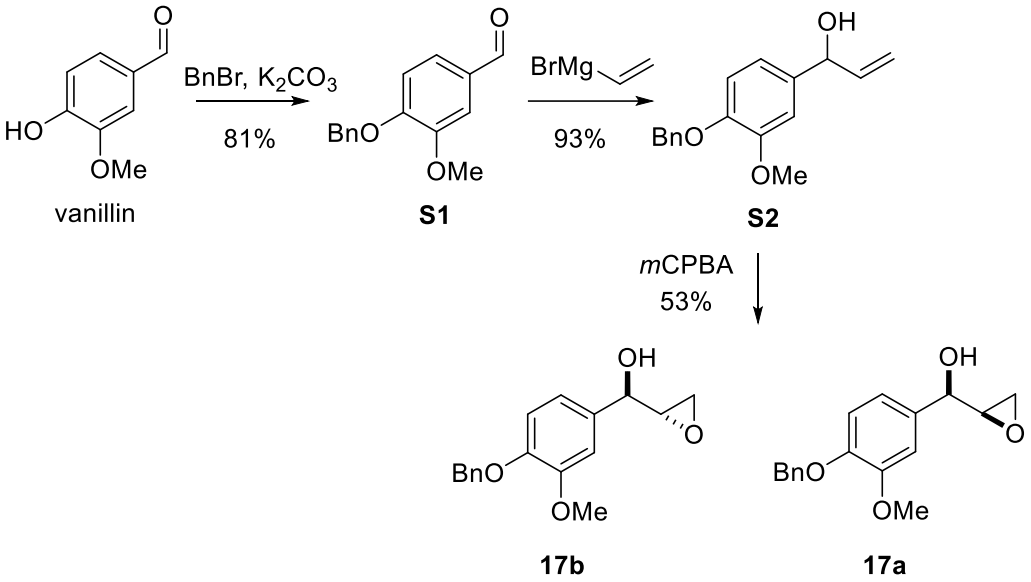


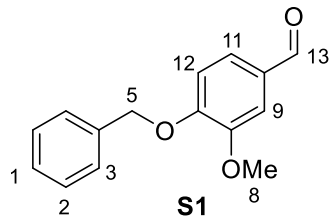
Figure S1. Numbering system used for NMR assignments in Experimental Section.

Synthesis Procedure for Diastereomer Mixture 17ab.



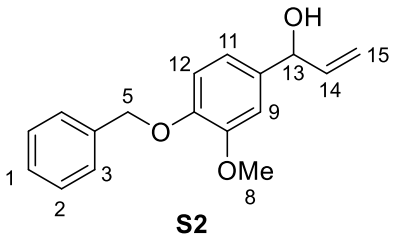
Scheme S1. Synthetic route used to prepare diastereomeric mixture of **17ab**.

4-(Benzyloxy)-3-methoxybenzaldehyde (S1).[1]



A flask was charged with vanillin (20.0 g, 0.132 mol, 1.00 eq.), K_2CO_3 (36.4 g, 0.264 mol, 2.00 eq.), benzyl bromide (17.2 cm^3, 0.145 mol, 1.10 eq.) and MeCN (330 mL). The resultant mixture was stirred at reflux for 4 hours. The reaction was cooled to room temperature, diluted with Et_2O (400 mL) and filtered under vacuum. The supernatant was evaporated under reduced pressure, and the resulting solid recrystallised from EtOH to give **S1** (25.9 g, 0.107 mol, 81%) as white crystals. Analytical data were consistent with that previously reported.[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.95 (s, 3H, H-8), 5.25 (s, 2H, H-5), 6.99 (d, *J* = 8.2 Hz, 1H, H-12), 7.30 – 7.47 (m, 7H, H-1, H-2, H-3, H-9, H-11), 9.84 (s, 1H, H-13).

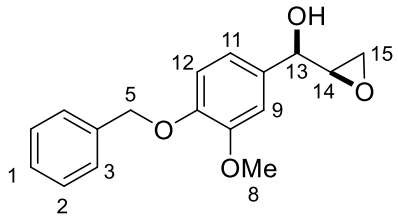
1-(4-(Benzyloxy)-3-methoxyphenyl)prop-2-en-1-ol (S2).[2]



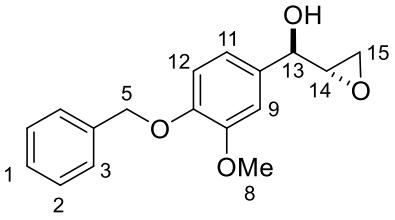
A solution of **S1** (5.08 g, 21.0 mmol, 1.00 eq.) in dry THF (210 mL) was cooled to 0˚C, and vinyl magnesium bromide (1.0 M solution in THF, 26.3 mL, 26.3 mmol, 1.25 eq.) was added dropwise *via* cannula. The reaction

mixture was then warmed to room temperature and stirred for 1 hour. The reaction was quenched using $NH_4Cl_{(aq)}$ (150 mL) and extracted using EtOAc (2 x 200 mL). The combined organic extracts were dried ($MgSO_4$) and evaporated under reduced pressure. Purification on silica gel (0-40% EtOAc in pet ether) gave **S2** (5.26 g, 19.5 mmol, 93%) as a pale yellow oil. Analytical data were consistent with that previously reported.[2] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.90 (s, 3H, H-8), 5.12 – 5.17 (m, 3H, H-5, H-13), 5.19 (ddd, *J* = 10.3, 1.4, 1.4 Hz, 1H, H_b-15), 5.35 (ddd, *J* = 17.1, 1.5, 1.5 Hz, 1H, H_a-15), 6.04 (ddd, *J* = 17.0, 10.3, 5.9 Hz, 1H, H-14), 6.81 – 6.87 (m, 2H, H-11, H-12), 6.94 (d, *J* = 1.8 Hz, 1H, H-9), 7.28 – 7.33 (m, 1H, H-1), 7.33 – 7.39 (m, 2H, H-2), 7.41 – 7.45 (m, 2H, H-3).

Rel-(*R*)-(4-(benzyloxy)-3-methoxyphenyl(*R*)-oxiran-2-yl)methanol (17a) and *Rel*-(*S*)-(4-(benzyloxy)-3-methoxyphenyl)((*R*)-oxiran-2-yl)methanol (17b).[3]



17a

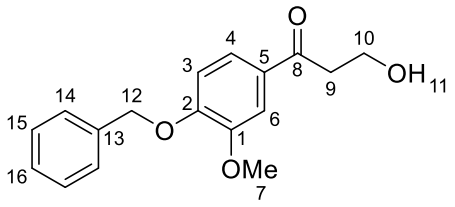


17b

A solution of **S2** (5.26 g, 19.5 mmol, 1.00 eq.) in $CHCl_3$ (195 mL) was cooled to 0˚C. To this was added *m*CPBA (4.37 g, 25.3 mmol, 1.30 eq.) portion wise over 30 minutes. The reaction was stirred at 0˚C for 4 hours, before quenching with a 1 : 1 $Na_2SO_{3(aq)}$ and $NaHCO_{3(aq)}$ solution (200 mL). The reaction was partitioned and the organic layer washed with H_2O (1 x 150 mL) and brine (1 x 150 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification on silica gel (0-40% EtOAc in pet ether) gave **17a** and **17b** (*d.r.* 1:1, 2.96 g, 10.3 mmol, 53%) as an orange solid. Analytical data were consistent with that previously reported.[3] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.78 (dd, *J* = 5.0, 4.0 Hz, 1H, H_b-15 in **17b**), 2.81 (dd, *J* = 4.9, 2.7 Hz, 1H, H_b-15 in **17a**), 2.85 (dd, *J* = 4.8, 4.1 Hz, 1H, H_a-15 in **17a**), 2.96 (ddd, *J* = 5.0, 2.8, 0.6 Hz, 1H, H_a-15 in **17b**), 3.19 – 3.24 (m, 2H, H-14 in **17a** & **17b**), 3.91 (s, 3H, H-8 in **17b**), 3.92 (s, 3H, H-8 in **17a**), 4.42 (t, *J* = 5.1 Hz, 1H, H-13 in **17a**), 4.86 (t, *J* = 2.6 Hz, 1H, H-13 in **17b**), 5.16 (s, 4H, H-5 in **17a** & **17b**), 6.85 – 6.88 (m, 3H, H-11 in **17a** & **17b**, H-12 in **17a**), 6.96 (d, *J* = 1.6 Hz, 1H, H-12 in **17b**), 7.01 (d, *J* = 1.5 Hz, 2H, H-9 in **17a** & **17b**), 7.27 – 7.47 (m, 10H, H-1, H-2, H-3 in **17a** & **17b**).

Analytical Data for known compounds prepared during this work.

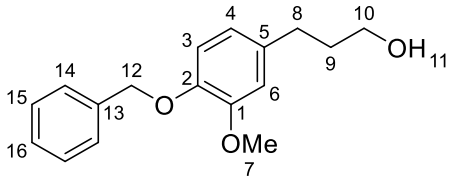
1-(4-(benzyloxy)-3-methoxyphenyl)-3-hydroxypropan-1-one (10).[4]



10

3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)propan-1-one **1** (0.012 g, 0.0607 mmol, 1 eq.) and K_2CO_3 (0.017 g, 0.121 mmol, 2.0 eq.) were suspended in acetone (5 mL) and benzyl bromide (0.014 mL, 0.121 mmol, 2 eq.) was added and the mixture heated to reflux for 20 hours. The mixture was cooled, filtered, solvent removed under reduced pressure and the crude product purified by flash chromatography on silica gel eluting with ethyl acetate/hexane (0-50%) to afford **10** (0.017 g, 99%) as an amorphous pale yellow wax. Spectral data was in agreement with previous reports.[4] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.17 (t, *J* = 5.3 Hz, 2H, H-9), 3.94 (s, 3H, H-7), 4.01 (t, *J* = 5.2 Hz, 2H, H-10), 5.24 (s, 2H, H-12), 6.90 (d, *J* = 8.3 Hz, 1H, H-3), 7.30 – 7.35 (m, 1H, H-16), 7.36 – 7.41 (m, 2H, H-15), 7.41 – 7.45 (m, 2H, H-14), 7.51 (dd, *J* = 8.4, 2.1 Hz, 1H, H-4), 7.54 (d, *J* = 2.0 Hz, 1H, H-6).

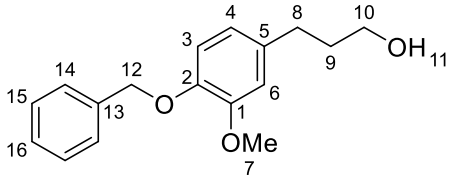
3-(4-(benzyloxy)-3-methoxyphenyl)propan-1-ol (11).[5]



11

Dihydroconiferyl alcohol **3** (0.31 g, 1.70 mmol, 1 eq.) and K_2CO_3 (0.46 g, 3.36 mmol, 2.0 eq.) were suspended in acetone (15 mL) and benzyl bromide (0.22 mL, 1.85 mmol, 1.1 eq.) was added and the mixture heated to reflux for 12 hours. The mixture was cooled, filtered, solvent removed under reduced pressure and the crude product purified by flash chromatography on silica gel eluting with ethyl acetate/hexane (0-50%) to afford 3-(4-(benzyloxy)-3-methoxyphenyl)propan-1-ol **11** (0.45 g, 97%) as an amorphous pale yellow wax. Spectral data was in agreement with previous reports.[5] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.82 – 1.92 (m, 2H, H-9), 2.65 (t, *J* = 7.4 Hz, 2H, H-8), 3.67 (t, *J* = 6.4 Hz, 2H, H-10), 3.88 (s, 3H, H-7), 5.13 (s, 2H, H-12), 6.67 (dd, *J* = 8.1, 2.0 Hz, 1H, H-4), 6.75 (d, *J* = 2.1 Hz, 1H, H-6), 6.81 (d, *J* = 8.1 Hz, 1H, H-3), 7.27 – 7.32 (m, 1H, H-16), 7.33 – 7.39 (m, 2H, H-15), 7.41 – 7.46 (m, 2H, H-14).

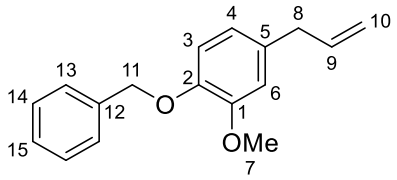
3-(4-(benzyloxy)-3-methoxyphenyl)propan-1-ol (11).[5]



11

1-(4-(benzyloxy)-3-methoxyphenyl)-3-hydroxypropan-1-one **10** (100.0 mg, 0.35 mmol, 1.00 eq.) was dissolved in dry THF (10 mL) and $BF_3.OEt_2$ (0.26 mL, 2.11 mmol, 6.00 eq.) added. Sodium cyanoborohydride (105.9 mg, 1.69 mmol, 4.80 eq.) was added portionwise and the resulting suspension stirred at room temperature for 12 hours then heated to 50 °C for 6 hours. The reaction was quenched by the addition of sat. aq. sodium bicarbonate (15 mL), extracted with ethyl acetate (3 x 5 mL), washed with brine (1 x 10 mL), dried over $MgSO_4$ and the volatiles removed under reduced pressure. Purified by flash column chromatography on silica gel, eluting with ethyl acetate/hexane (0-70%) to afford 3-(4-(benzyloxy)-3-methoxyphenyl)propan-1-ol **11** (61.3 mg, 64%) as an amorphous pale yellow wax. ^{1}H NMR analysis was consistent with that reported in the Supplementary Section above for the alternative synthesis of **11**.

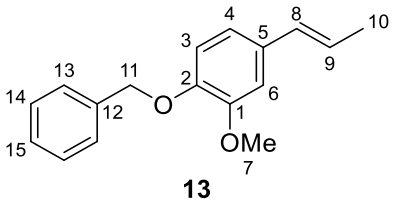
4-allyl-1-(benzyloxy)-2-methoxybenzene (12).[6]



12

2-nitrophenyl selenocyanate (125.2 mg, 0.55 mmol, 1.50 eq.) was dissolved in dry THF (8 mL) under N_2 and **11** (115 mg, 0.37 mmol, 1.00 eq.) dissolved in dry THF (2 mL) was added at room temperature. Tributyl phosphine (0.14 mL, 0.56 mmol, 1.50 eq.) was added slowly dropwise and the resulting mixture stirred at room temperature for 1 hour until starting material had been consumed as judged by TLC analysis. Quenched by addition of sat. aq. sodium bicarbonate (10 mL), extracted with diethyl ether (3 x 10 mL), washed with brine (1 x 10 mL), dried over $MgSO_4$ and volatiles removed under reduced pressure. The crude intermediate was used in the next step with no further purification. Crude intermediate was dissolved in diethyl ether (10 mL) and sodium bicarbonate (173.4 mg, 2.06 mmol, 5.5 eq.) added, followed by H_2O_2 (30% aq. solution, 6 mL) and stirred at room temperature for 1 hour until complete as judged by TLC. Quenched with sat. aq. ammonium chloride (10 mL), extracted with diethyl ether (3 x 10 mL), washed with brine (1 x 10 mL), dried over $MgSO_4$ and volatiles removed under reduced pressure. Purified by flash column chromatography on silica gel, eluting with ethyl acetate/hexane (0-30%) to afford 4-allyl-1-(benzyloxy)-2-methoxybenzene **12** (51.4 mg, 54%) as a yellow oil. Spectral data was in agreement with previous reports.[6] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.33 (dt, *J* = 6.7, 1.6 Hz, 2H, H-8), 3.88 (s, 3H, H-7), 5.04 – 5.12 (m, 2H, H-10), 5.14 (s, 2H, H-11), 5.90 – 6.03 (m, 1H, H-9), 6.64 – 6.70 (m, 1H, H-4), 6.72 – 6.76 (m, 1H, H-6), 6.82 (dd, *J* = 8.2, 2.0 Hz, 1H, H-3), 7.27 – 7.32 (m, 1H, H-15), 7.34 – 7.40 (m, 2H, H-14), 7.41 – 7.48 (m, 2H, H-13).

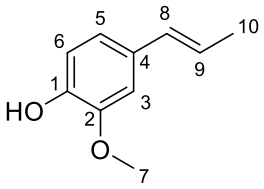
1-(benzyloxy)-2-methoxy-4-(prop-1-en-1-yl)benzene (13).



13

Benzylated eugenol **12** (254.2 mg, 1.00 mmol, 1.00 eq.) was dissolved in dry EtOH (8 mL) in a sealed pressure tube and degassed with N_2. Pre-dried $MgCl_2.6H_2O$ (20.8 mg, 0.10 mmol, 10 mol%) was added followed by $RuH_2(CO)(PPh_3)_3$ (49.7 mg, 0.05 mmol, 5 mol%) and the pressure tube sealed and heated to 80 °C for 1 hour. Cooled to room temperature, filtered through a pad of Celite, solvent removed under reduced pressure and purified by flash chromatography on silica gel eluting with 0-50% ethyl acetate/hexane to afford 1-(benzyloxy)-2-methoxy-4-(prop-1-en-1-yl)benzene **13** (241.6 mg, 95 % *E*/*Z* 95:5) as an amorphous white solid. Spectral data was in agreement with previous reports.[7] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.86 (dd, *J* = 6.6, 1.7 Hz, 3H, H-10), 3.90 (s, 3H, H-7), 5.14 (s, 2H, H-11), 6.10 (dq, *J* = 15.7, 6.6 Hz, 1H, H-9), 6.33 (dq, *J* = 15.6, 1.4 Hz, 1H, H-8), 6.80 (m, 2H, H-4, H-6), 6.91 (d, *J* = 1.6 Hz, 1H, H-3), 7.27 – 7.32 (m, 1H, H-15), 7.33 – 7.39 (m, 2H, H-14), 7.41 – 7.45 (m, 2H, H-13).

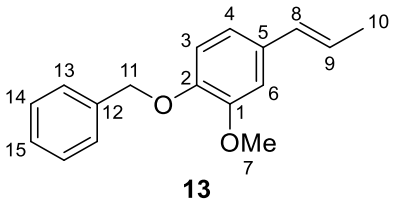
(*E*)-2-methoxy-4-(prop-1-en-1-yl)phenol (16).



16

To a suspension of DDQ (0.854 g, 3.76 mmol, 1.25 eq.) in dry dioxane (5 mL), a solution of propyl guaiacol **4** (0.482 mL, 3.01 mmol, 1.00 eq.) in dry dioxane (5 mL) and AcOH (17.0 µL, 0.301 mmol, 0.10 eq.) were added. The resultant mixture was stirred for 16 hours at room temperature under a nitrogen atmosphere, before the addition of 1 M NaOH (6.02 mL). The resultant biphasic mixture was stirred for 1 hour at room temperature. Then, the resulting mixture was acidified to pH 1 with 1 M HCl. The aqueous phase was extracted with EtOAc (3 x 50 mL), and the combined organic extracts were washed with brine (1 x 20 mL), dried over $MgSO_4$, filtered, and concentred under reduced pressure. Purification on silica gel (0-30% EtOAc in hexane) gave **16** (0.140 g, 0.874 mmol, 29%, *E*/*Z* 95:5) as a colourless oil. Analytical data were in accordance with the literature.[8] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.86 (dd, *J* = 6.6, 1.7 Hz, 3H, H-10) , 3.90 (s, 3H, H-7) , 6.08 (dq, *J* = 15.7, 6.6 Hz, 1H, H-9) , 6.32 (dt, *J* = 15.6, 1.7 Hz, 1H, H-8), 6.81 – 6.88 (m, 3H, H-3, H-5, H-6).

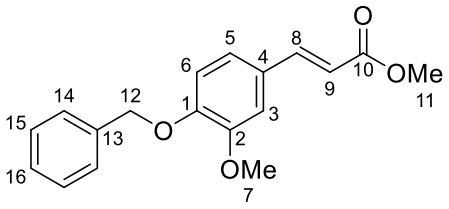
1-(benzyloxy)-2-methoxy-4-(prop-1-en-1-yl)benzene (13).[9]



13

Isoeugenol **16** (2.01 g, 12.2 mmol, 1 eq.) and K_2CO_3 (3.70 g, 26.80 mmol, 2.20 eq.) were suspended in acetone (40 mL) and benzyl bromide (1.60 mL, 13.45 mmol, 1.10 eq.) was added and the mixture heated to reflux for 12 hours. The mixture was cooled, filtered, solvent removed under reduced pressure and the crude product purified by flash chromatography on silica gel eluting with ethyl acetate/hexane (0-50%) to afford 1-(benzyloxy)-2-methoxy-4-(prop-1-en-1-yl)benzene **13** (3.10 g, 12.1 mmol, 99%, *E*/*Z* 95:5). ^{1}H NMR analysis was consistent with that reported for the alternative synthesis of **13**.

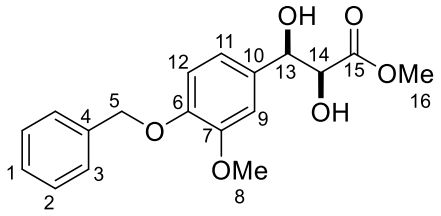
Methyl 3-(4-(benzyloxy)-3-methoxyphenyl)acrylate (14).[10,11]



14

Based on a literature procedure,[10] **13** (500.9 mg, 1.97 mmol, 1 eq.) and methyl acrylate (0.71 mL, 7.88 mmol, 4 eq.) were dissolved in DCE (8 mL) under N_2 atmosphere in a sealed tube and degassed for 10 minutes. Hoveyda-Grubbs II catalyst **15** (11.4 mg, 0.02 mmol, 1 mol%) in DCE (2 mL) was added under N_2 atmosphere and the reaction vessel sealed, heated to 70 °C for 16 hours then cooled to room temperature and volatiles removed under reduced pressure. Crude mixture purified by flash chromatography on silica gel eluting with ethyl acetate/hexane (0-50%) to afford methyl 3-(4-(benzyloxy)-3-methoxyphenyl)acrylate **14** (238.4 mg, 73% based on recovered SM, E/Z 85:15). Spectral data was in agreement with previous reports.[32] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.80 (s, 3H, H-11), 3.92 (s, 3H, H-7), 5.19 (s, 2H, H-12), 6.30 (d, *J* = 15.9 Hz, 1H, H-9), 6.83 – 6.90 (m, 1H, H-6), 7.01 – 7.08 (m, 2H, H-3, H-5), 7.28 – 7.34 (m, 1H, H-16), 7.34 – 7.40 (m, 2H, H-15), 7.41 – 7.47 (m, 2H, H-14), 7.62 (d, *J* = 15.9 Hz, 1H, H-8).

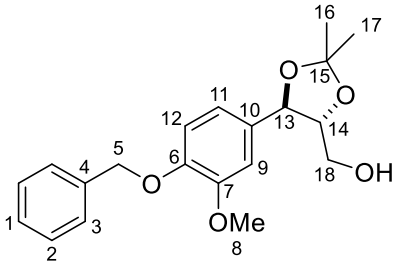
***Rel*-methyl (2*S*,3*R*)-3-(4-(benzyloxy)-3-methoxyphenyl)-2,3-dihydroxypropanoate (18).[12]**



18

A flask was charged with **14** (5.01 g, 16.8 mmol, 1.00 eq), citric acid (2.42 g, 12.6 mmol, 0.750 eq), NMO (2.95 g, 25.2 mmol, 1.10 eq), OsO_4 (2.5 wt% solution in ^tBuOH, 0.2 cm^3, catalytic) and a 3 : 3 : 1 mixture of MeCN : acetone : H_2O (168 cm^3, 0.1 M solution). The reaction was stirred at room temperature overnight, or until no more starting material could be observed (in cases where the reaction was incomplete after 16 hours, small quantities of extra OsO_4 were added to complete the reaction). The reaction was then quenched by addition of $Na_2SO_{3(aq)}$ (170 cm^3), then stirred vigorously for 30 minutes. The solvents were removed under reduced pressure and the aqueous phase was extracted using EtOAc (3 x 150 cm^3). The combined organic exctracts were dried (Na_2SO_4) and concentrated *in vacuo*. Purification on silica gel (0-80% EtOAc in hexane) afforded **18** (5.23 g, 16.3 mmol, 94%) as a colourless oil. Analytical data were consistent with a previous report.[12] ^1H NMR (500 MHz, $CDCl_3$): δ_H 2.63 (d, *J* = 6.8 Hz, 1H, –OH), 3.07 (d, *J* = 5.9 Hz, 1H, –OH), 3.81 (s, 3H, H-16), 3.90 (s, 3H, H-8),.4.35 (dd, *J* = 5.9, 2.9 Hz, 1H, H-13), 4.94 (dd, *J* = 6.7, 3.0 Hz, 1H, H-14), 5.16 (s, 2H, H-5), 6.84-6.88 (m, 2H, H-11, H-12), 6.99 (app br s, 1H, H-9), 7.27 – 7.33 (m, 1H, H-1), 7.34 – 7.39 (m, 2H, H-2), 7.41 – 7.45 (m, 2H, H-3).

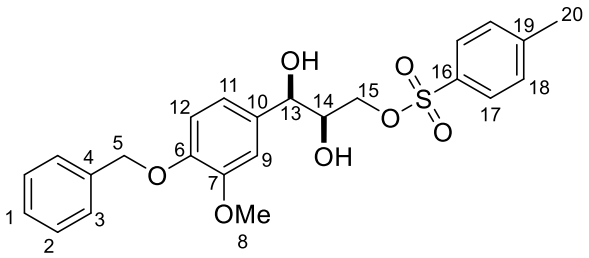
***Rel*-((4*R*,5*R*)-5-(4-(benzyloxy)-3-methoxyphenyl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (20).[13]**



20

See Experimental Section (synthesis of **21**) of manuscript for experimental procedure: ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.52 (s, 3H, 1 x acetal Me), 1.58 (s, 3H, 1 x acetal Me), 3.59 – 3.65 (m, 1H, H-14), 3.82 – 3.89 (m, 2H, H-18), 3.90 (s, 3H, H-8), 4.84 (d, *J* = 8.7 Hz, 1H, H-13), 5.15 (s, 2H, H-5), 6.88-6.84 (m, 2H, H-11, H-12), 6.95 (d, *J* = 1.2 Hz, 1H, H-9), 7.27 – 7.32 (m, 1H, H-1), 7.33 – 7.39 (m, 2H, H-2), 7.41 – 7.44 (m, 2H, H-3).

***Rel*-(2*R*,3*R*)-3-(4-(benzyloxy)-3-methoxyphenyl)-2,3-dihydroxypropyl 4-methylbenzene-sulfonate (22).[14]**

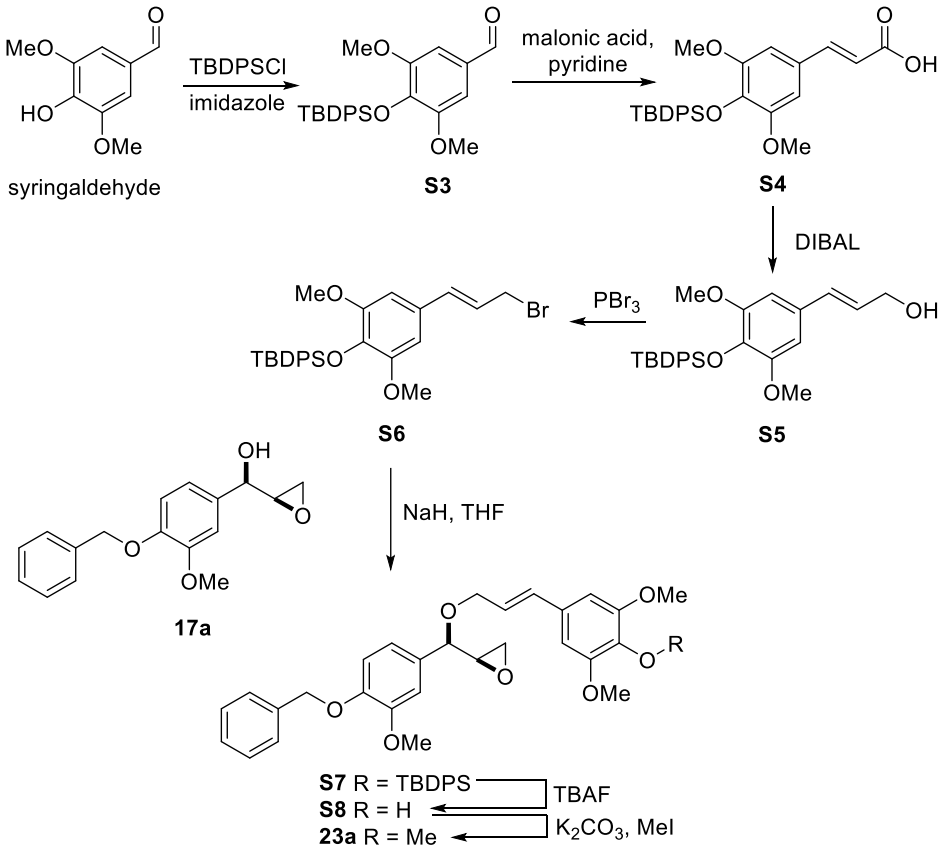


22

See Experimental Section (synthesis of **17a**) of manuscript for experimental procedure. **22** was used without purification: ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 2.44 (s, 3H, H-20), 2.72 (s, 1H, –OH), 2.77 (s, 1H, –O<u>H</u>), 3.83 – 3.95 (m, 5H, H-8, H-14, H_b-15), 3.99 – 4.05 (m, 1H, H_a-15), 4.60 (d, *J* = 6.1 Hz, 1H, H-13), 5.14 (s, 2H, H-5), 7.71 – 7.78 (m, 2H, H-17), 6.73 (dd, *J* = 8.3, 2.0 Hz, 1H, H-11), 6.81 (d, *J* = 8.2 Hz, 1H, H-12), 6.89 (d, *J* = 2.0 Hz, 1H, H-9), 7.29 – 7.34 (m, 3H, H-1, H-18), 7.34 – 7.40 (m, 2H, H-2), 7.41 – 7.46 (m, 2H, H-3).

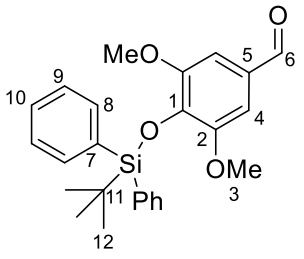
See below for experimental details for the synthesis of **28**.

Synthesis procedures and analytical data for 23a from 17a.



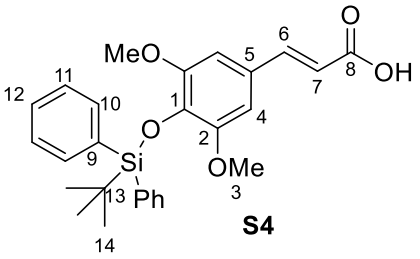
Scheme S2. Alternative route to **23a** taking advantage of the relative ease of synthesis and isolation of **S6**.

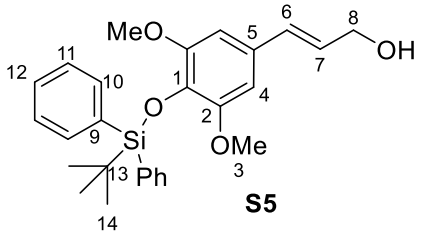
4-((tert-butyldiphenylsilyl)oxy)-3,5-dimethoxybenzaldehyde (S3).[15]



To a flask was added commercially available syringaldehyde (4.53, 1.02 g, 5.59 mmol, 1.00 eq), imidazole (950 mg, 14.0 mmol, 2.50 eq.), TBDPS-Cl (1.5 mL, 6.14 mmol, 1.10 eq.) and DCM (56 mL, 0.1 M solution), and the reaction was stirred overnight at room temperature, before quenching by addition of saturated $NH_4Cl_{(aq)}$ (55 mL). The layers were separated, and the aqueous phase extracted using DCM (2 x 50 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-25% EtOAc in pet ether) afforded **S3** (1.97 g, 4.68 mmol, 84%) as a viscous, colourless oil. Analytical data were consistent with that previously reported.[15] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.10 (s, 9H, H-12), 3.50 (s, 6H, H-3), 6.97 (s, 2H, H-4), 7.27 – 7.46 (m, 6H, H-9, H-10), 7.68 (dd, *J* = 8.0, 1.5 Hz, 4H, H-8), 9.76 (s, 1H, H-6).

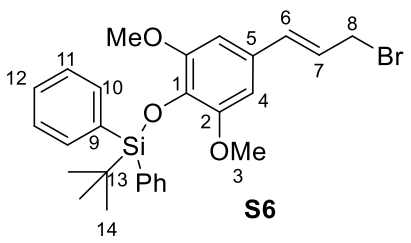
(*E*)-3-(4-((tert-butyldiphenylsilyl)oxy)-3,5-dimethoxyphenyl)prop-2-en-1-ol (S5).

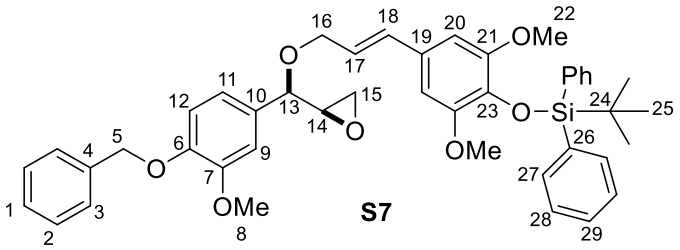




A flask was charged with **S3** (1.97 g, 4.68 mmol, 1.00 eq), malonic acid (731 mg, 7.02 mmol, 1.50 eq.), aniline (drop, catalytic) and pyridine (2.3 mL, 2.0 M solution), and the reaction mixture was stirred at 60˚C overnight. The reaction was quenched by pouring on ice and concentrated HCl (4 mL), and left to precipitate. The resulting suspension was filtered under vacuum, and (*E*)-3-(4-((*tert*-butyldiphenylsilyl)oxy)-3,5-dimethoxyphenyl)acrylic acid (**S4**) was taken on without further purification. A flame-dried flask containing **S4** (4.07 g, 8.55 mmol, 1.00 eq.) in dry THF (86 mL, 0.1 M solution) under a nitrogen atmosphere was cooled to 0˚C, and to it was added DIBAL-H (1.2 M solution in hexanes, 14.2 mL, 17.1 mmol, 2.10 eq.) dropwise. The reaction was warmed to room temperature, and stirred for 1 hour. The reaction was quenched by cooling to 0˚C, followed by slow addition of MeOH (75 mL) and water (10 mL) until no change could be observed. The suspension was filtered under vacuum, and the supernatant concentrated under reduced pressure. Purification on silica gel (0-40% EtOAc in hexane) afforded **S5** (3.33 g, 7.56 mmol, 89%) as a colourless, viscous oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.09 (s, 9H, H-14), 1.36 (t, *J* = 5.8 Hz, 1H, –OH), 3.44 (s, 6H, H-3), 4.28 (td, *J* = 5.8, 1.4 Hz, 2H, H-8), 6.19 (dt, *J* = 15.8, 6.0 Hz, 1H, H-7), 6.43 – 6.51 (m, 3H, H-4, H-6), 7.28 – 7.40 (m, 6H, H-11, H-12), 7.66 – 7.74 (m, 4H, H-10). ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 20.3 (C-13), 26.9 (C-14), 55.3 (C-3), 64.0 (C-8), 103.5 (C-4), 103.8 (C-1), 126.6 (C-7), 127.2 (C-11), 129.2 (C-12), 129.4 (C-5), 132.0 (C-6), 134.6 (C-9), 135.3 (C-10), 151.1 (C-2).

(4-((*E*)-3-((*R*)-(4-(benzyloxy)-3-methoxyphenyl)((*R*)-oxiran-2-yl)methoxy)prop-1-en-1-yl)-2,6-dimethoxyphenoxy)(*tert*-butyl)diphenylsilane (S7).

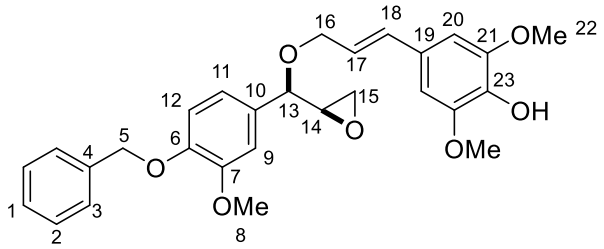




A flask containing **S5** (3.33 g, 7.56 mmol, 1.00 eq.) and dry Et_2O (76 mL, 0.1 M solution) was cooled to 0˚C, and to it was added PBr_3 (0.8 mL, 9.08 mmol, 1.20 eq.) dropwise in the absence of light. The reaction was stirred in darkness at 0˚C for 1 hour, before quenching by pouring over ice and water (75 mL). The aqueous phase was extracted with hexane (2 x 40 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure to give (*E*)-(4-(3-bromoprop-1-en-1-yl)-2,6-dimethoxyphenoxy)(*tert*-butyl)diphenylsilane (**S6**), which was taken on without further purification. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.08 (s, 9H, H-14), 3.44 (s, 6H, H-3), 4.15 (dd, *J* = 7.9, 1.0 Hz, 2H, H-8), 6.21 (dt, *J* = 15.6, 7.9 Hz, 1H, H-7), 6.45 (s, 2H, H-4), 6.50 (d, *J* = 15.5 Hz, 1H, H-6), 7.28 – 7.33 (m, 4H, H-11), 7.34 – 7.40 (m, 2H, H-12), 7.67 – 7.72 (m, 4H, H-10). A flame-dried flask was charged with **17a** (497 mg, 1.74 mmol, 1.00 eq.), in THF (17 mL, 0.1 M solution) under a nitrogen atmosphere. The solution was cooled to 0˚C, and to it was added NaH (60%

dispersion, 209 mg, 5.21 mmol, 3.00 eq.), and the resultant suspension was stirred at 0˚C for 30 minutes. To this mixture was added **S6** (1.06 g, 2.08 mmol, 1.2 eq) in dry THF (2 mL, 1 M solution). The reaction was warmed to room temperature and stirred for 1 hour, until no more starting material could be observed by TLC. The reaction was quenched by addition of $NH_4Cl_{(aq)}$ and the layers were separated. The aqueous phase was extracted using EtOAc, the combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-40% EtOAc in hexane) to give **S7** (987 mg, 1.38 mmol, 79%) as a colourless amorphous solid. **S7** was determined to be relatively unstable so only ^{1}H NMR characterisation was performed, and the material carried directly onto the following reaction. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.08 (s, 9H, H-25), 2.60 (dd, *J* = 4.9, 2.7 Hz, 1H, H_b-15), 2.74 (dd, *J* = 4.8, 4.2 Hz, 1H, H_a-15), 3.22 (ddd, *J* = 6.7, 4.2, 2.7 Hz, 1H, H-14), 3.43 (s, 6H, H-22), 3.90 (s, 3H, H-8), 4.03 (d, *J* = 6.5 Hz, 1H, H-13), 4.05 – 4.20 (m, 2H, H-16), 5.16 (s, 2H, H-5), 6.12 (dt, *J* = 15.8, 6.3 Hz, 1H, H-17), 6.37 – 6.46 (m, 3H, H-18, H-20), 6.80 (dd, *J* = 8.2, 1.9 Hz, 1H, H-11), 6.87 (d, *J* = 8.2 Hz, 1H, H-12), 6.94 (d, *J* = 1.9 Hz, 1H, H-9), 7.27 – 7.40 (m, 10H, H-2, H-3, H-28, H-29), 7.41 – 7.48 (m, 2H, H-1 or H-27), 7.67 – 7.73 (m, 4H, H-27).

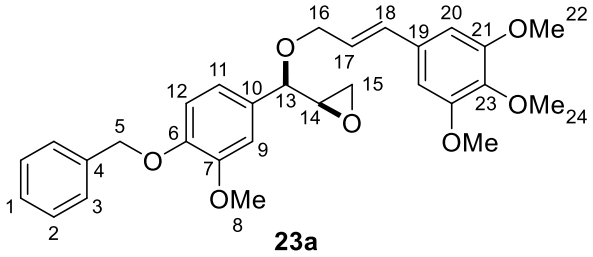
Rel-4-((*E*)-3-((*R*)-(4-(benzyloxy)-3-methoxyphenyl)((*R*)-oxiran-2-yl)methoxy)prop-1-en-1-yl)-2,6-dimethoxyphenol (S8).



S8

A flame-dried flask was charged with **S7** (1.42 g, 1.98 mmol, 1.00 eq.) and dry THF (20 mL, 0.1 M solution) under a nitrogen atmosphere. The solution was cooled to 0˚C, and to it was added TBAF (1.0 M solution in THF, 2.4 mL, 2.37 mmol, 1.20 eq.). The reaction was warmed to room temperature and stirred for 16 hours. The reaction was quenched with brine (25 mL) and diluted with Et_2O (25 mL). The layers were separated, the aqueous phase was extracted with Et_2O (2 x 25 mL), the organic phases were combined, dried ($MgSO_4$) and concentrated *in vacuo*. Purification on silica gel (0-70% EtOAc in pet ether) gave **S8** (787 mg, 1.65 mmol, 83%) as a colourless amorphous solid. IR (oil, ATR-FTIR, ν_{max}, cm^{-1}): 2936, 2361, 1732, 1680, 1605, 1512, 1454, 1422, 1375, 1333, 1260, 1217, 1136, 1111, 1032, 966, 912, 854, 804, 741, 696, 627. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.61 (dd, *J* = 4.9, 2.7 Hz, 1H, H_a-15), 2.75 (dd, *J* = 4.9, 4.2 Hz, 1H, H_b-15), 3.24 (ddd, *J* = 6.7, 4.2, 2.7 Hz, 1H, H-14), 3.89 (s, 6H, H-22), 3.91 (s, 3H, H-8), 4.04 (d, *J* = 6.7 Hz, 1H, H-13), 4.12 (ddd, *J* = 12.4, 6.5, 1.4 Hz, 1H, H_a-16), 4.19 (ddd, *J* = 12.4, 6.0, 1.5 Hz, 1H, H_b-16), 5.16 (s, 2H, H-5), 5.54 (s, 1H, Ar–OH), 6.17 (dt, *J* = 15.8, 6.3 Hz, 1H, H-17), 6.47 (dt, *J* = 15.8, 1.3 Hz, 1H, H-18), 6.61 (s, 2H, H-20), 6.81 (dd, *J* = 8.3, 2.0 Hz, 1H, H-11), 6.88 (d, *J* = 8.2 Hz, 1H, H-12), 6.96 (d, *J* = 1.9 Hz, 1H, H-9), 7.29 – 7.33 (m, 1H, H-1), 7.35 – 7.40 (m, 2H, H-2), 7.42 – 7.46 (m, 2H, H-3). ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 44.6 (C-15), 55.5 (C-14), 56.2 (C-8), 56.4 (C-22), 69.6 (C-16), 71.1 (C-5), 82.5 (C-13), 103.4 (C-20), 110.5 (C-9), 113.8 (C-12), 119.7 (C-11), 124.0 (C-17), 127.4 (C-3), 128.0 (C-1), 128.3 (C-19), 128.7 (C-2), 131.3 (C-10), 133.0 (C-18), 134.8 (C-23), 137.2 (C-4), 147.2 (C-21), 148.4 (C-6), 150.0 (C-7). Found, *m/z*: 501.1869 $[M+Na]^+$. $C_{28}H_{30}O_7Na$. Calculated, *m/z*: 501.1884.

***Rel*-(*R*)-2-((*R*)-(4-(benzyloxy)-3-methoxyphenyl)(((*E*)-3-(3,4,5-trimethoxyphenyl)allyl)oxy)methyl)oxirane-(23a).**



23a

Anhydrous potassium carbonate (59.2 mg, 0.428 mmol, 2.0 eq.) was weighed into a dry flask. **S8** (100.0 mg, 0.209 mmol, 1.00 eq.) was dissolved in dry acetone (10 cm^3, 0.021 M) and added to the flask containing potassium carbonate. Methyl iodide (296.4 mg, 2.09 mmol, 10 eq.) was injected into the reaction and it was stirred at room temperature overnight. After 24 hours, the reaction mixture was filtered and solid washed with an additional 10 cm^3 of acetone. Solvent of filtrate was removed under reduced pressure giving crude product. Purification on silica gel (30% EtOAc in hexane) afforded **23a** (17.3 mg, 0.0351 mmol, 17%) as a colourless, amorphous solid. IR (oil, ATR-FTIR, ν_{max}, cm^{-1}): 2927, 1722, 1581, 1506, 1452, 1417, 1334, 1122, 1004. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.61 (dd, *J* = 4.9, 2.7 Hz, 1H, H_a-15), 2.76 (dd, *J* = 4.5 Hz, 1H, H_b-15), 3.24 (ddd, *J* = 6.6, 4.2, 2.6 Hz, 1H, H-14), 3.84 (s, 3H, H-24), 3.86 (s, 6H, H-22), 3.91 (s, 3H, H-8), 4.04 (d, *J* = 6.5 Hz, 1H, H-13), 4.14 (ddd, *J* = 12.6, 6.4, 1.5 Hz, 1H, H_a-16), 4.20 (ddd, *J* = 12.6, 5.8, 1.7 Hz, 1H, H_b-16), 5.16 (s, 2H, H-5), 6.22 (dt, *J* = 15.8, 6.1 Hz, 1H, H-17), 6.49 (dt, *J* = 15.9, 1.6 Hz, 1H, H-18), 6.60 (s, 2H, H-20), 6.81 (dd, *J* = 8.1, 2.0 Hz, 1H, H-11), 6.88 (d, *J* = 8.2 Hz, 1H, H-12), 6.96 (d, *J* = 2.0 Hz, 1H, H-9), 7.27 – 7.35 (m, 1H, H-1), 7.34 – 7.41 (m, 2H, H-2), 7.42 – 7.47 (m, 2H, H-3). ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 44.6 (C-15), 55.5 (C-14), 56.2 (C-22), 56.2 (C-8), 61.1 (C-24), 69.5 (C-16), 71.1 (C-5), 82.6 (C-13), 103.6 (C-20), 110.5 (C-9), 113.8 (C-12), 119.7 (C-11), 125.5 (C-17), 127.4 (C-3), 128.0 (C-1), 128.7 (C-2), 131.2 (C-10), 132.5 (C-19), 132.7 (C-18), 137.2 (C-4), 138.0 (C-23), 148.4 (C-6), 150.0 (C-7), 153.4 (C-21). Found, *m/z*: 515.2028 $[M+Na]^+$. $C_{29}H_{32}O_7Na$. Calculated, *m/z*: 515.2040.

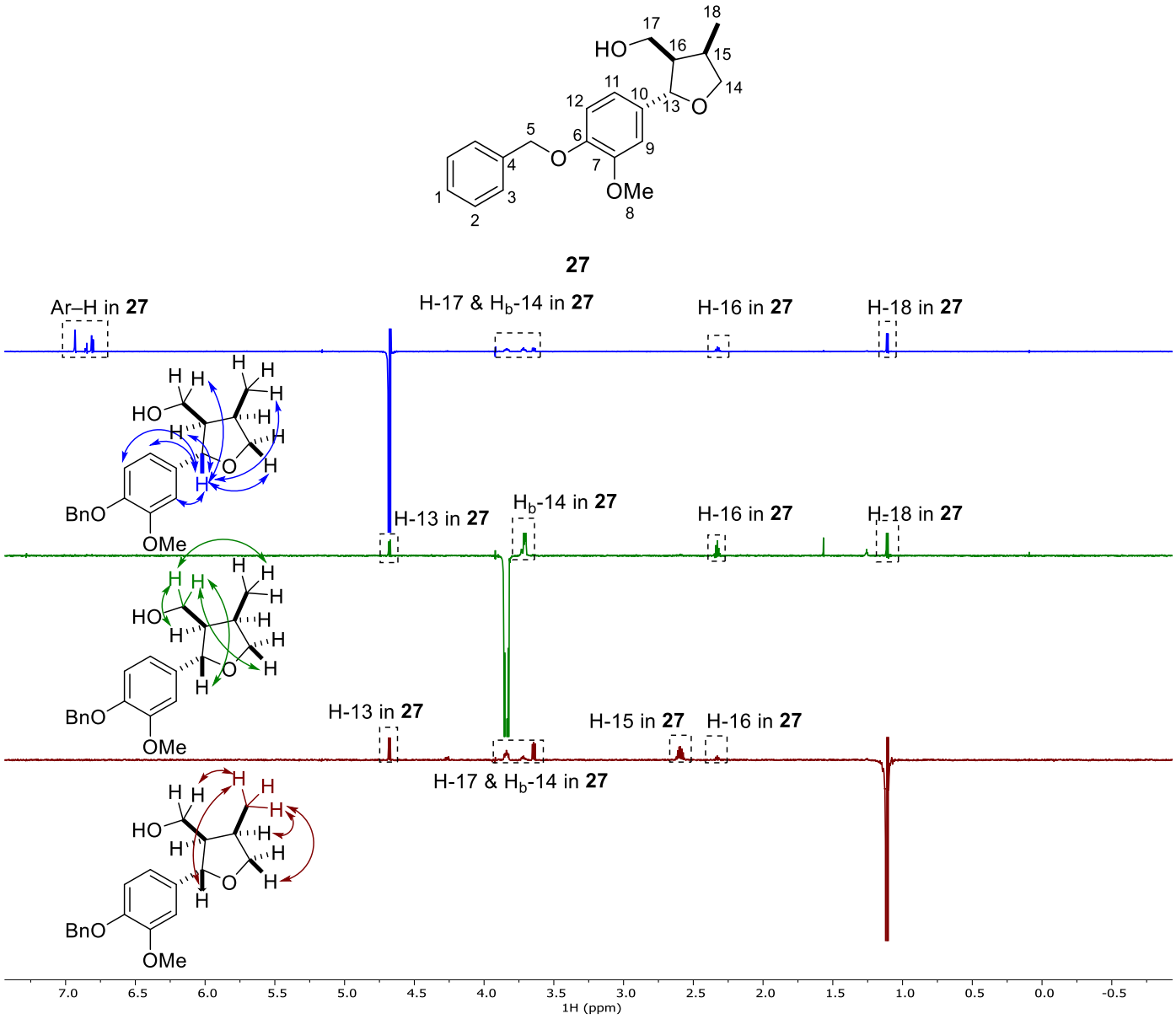
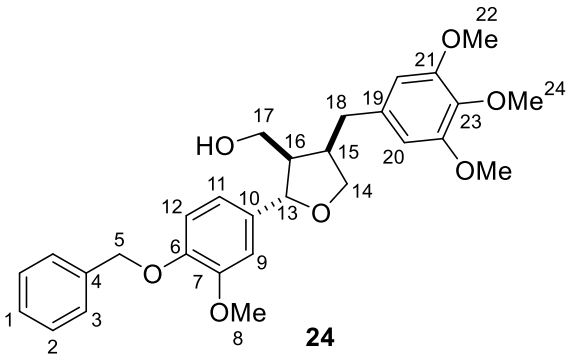
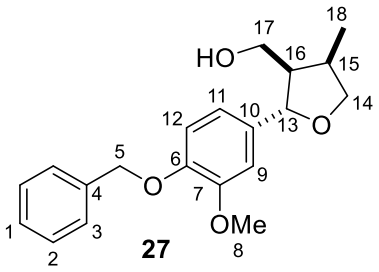


Figure S2. nOe studies on **27**. Frequencies corresponding to the signals for H-13 (top spectrum), H-17 (middle spectrum) and Me-18 (bottom spectra) were irradiated. Observed nOe correlations are highlighted and are consistent with: (i) CH_2-17 and Me-18, (ii) CH-13 and CH_2-17 and (iii) CH-13 and Me-18 being in close proximity and hence on the same face in **27**. This is consistent with the assigned stereochemistry of **27**.

Table S1 – ^{1}H NMR assignment comparison between relevant protons of **24** and **27** in $CDCl_3$. Right & left column show chemical shift in ppm, followed by multiplicity of the signal; *J* values shown in brackets for relavant peaks. Middle column lists assigned proton signals



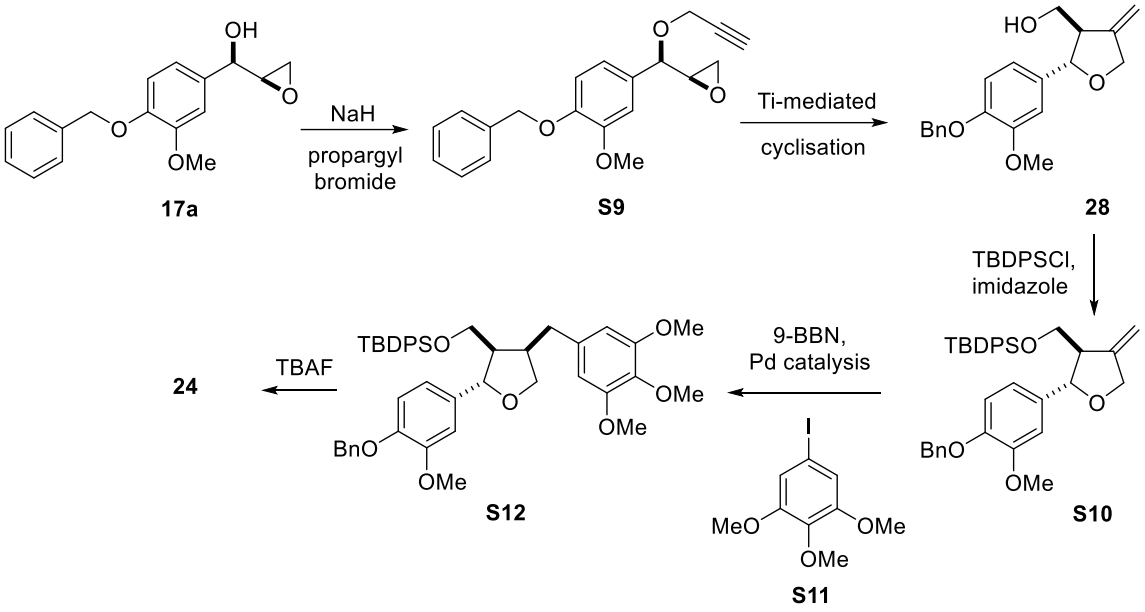
24



27

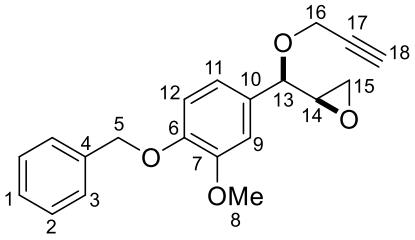
(**24**) Chemical Shift (δ_H in ppm) in $CDCl_3$, Multiplicity and *J* Value	Proton in (**24**) & (**27**)	(**27**) Chemical Shift (δ_H in ppm) in $CDCl_3$, Multiplicity and *J* Value
7.41 – 7.45 m	H-3	7.40 – 7.46 m
7.33 – 7.38 m	H-2	7.36 – 7.38 m
7.27 – 7.23 m	H-1	7.27 – 7.31 m
6.91 d (2.0)	H-9	6.91 d (2.0)
6.84 d (8.2)	H-12	6.83 d (8.1)
6.79 dd (8.2, 2.0)	H-11	6.79 dd (8.2, 2.0)
6.40 s	H-20	N.A.
5.15 s	H-5	5.14 s
4.79 d (6.7)	H-13	4.66 d (7.3)
4.06 dd (8.6, 6.5)	H_a-14	4.24 dd (8.4, 6.6)
3.75-3.95 m	H-8	3.90 s
3.75-3.95 m	H_a-17	3.82 ddd (10.7, 7.3, 4.9)
3.75-3.95 m	H_b-17	3.69 ddd (10.6, 6.3, 4.4)
3.75-3.95 m	H_b-14	3.62 dd (8.4, 5.6)
3.75-3.95 m	H-22	N.A.
3.75-3.95 m	H-24	N.A.
2.94 dd (13.5, 4.9)	H_a-18	1.09 d (7.1)
2.70 – 2.79 m	H-15	2.52 – 2.62 m
2.55 dd (13.5, 10.9)	H_b-18	N.A.
2.39 – 2.48 m	H-16	2.29 – 2.31 m

Alternative Synthesis of 24 via 28 inspired by a literature route.[16]



Scheme S3. Alternative route used to prepare further quantities of compound **24**. [16]

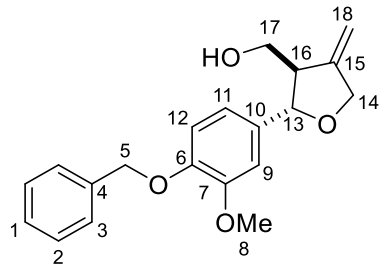
***Rel*-(*R*)-2-((*R*)-(4-(benzyloxy)-3-methoxyphenyl)(prop-2-yn-1-yloxy)methyl)oxirane (S9).[3]**



S9

A flame-dried flask containing the **17a** (588 mg, 2.06 mmol, 1.00 eq.) in dry THF (20 mL) under a nitrogen atmosphere was cooled to 0˚C, and to it was added NaH (60% dispersion, 247 mg, 6.17 mmol, 3.00 eq.), and the resultant suspension was stirred at 0˚C for 30 minutes. To this mixture was added propargyl bromide (80% solution in toluene, 459 mg, 3.09 mmol, 1.50 eq.). The reaction was then warmed to room temperature, and stirred for 1 hour. The reaction was quenched by addition of $NH_4Cl_{(aq)}$ (20 mL) and the layers were partitioned. The aqueous phase was extracted using EtOAc (3 x 25 mL), the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-30% EtOAc in pet ether) gave **S9** (482 mg, 1.49 mmol, 73%) as a white, amorphous solid. Analytical data were consistent with that previously reported. [3] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.43 (dd, *J* = 2.4, 2.4 Hz, 1H, H-18), 2.64 (dd, *J* = 4.9, 2.6 Hz, 1H, H_b-15), 2.75 (dd, *J* = 4.9, 4.2 Hz, 1H, H_a-15), 3.23 (ddd, *J* = 6.5, 4.2, 2.7 Hz, 1H, H-14), 3.91 (s, 3H, H-8), 4.06 (dd, *J* = 15.7, 2.4 Hz, 1H, H_b-16), 4.22 (d, *J* = 6.3 Hz, 1H, H-13), 4.26 (dd, *J* = 15.7, 2.4 Hz, 1H, H_a-16), 5.16 (s, 2H, H-5), 6.81 (dd, *J* = 8.2, 2.0 Hz, 1H, H-11), 6.87 (d, *J* = 8.2 Hz, 1H, H-12), 6.94 (d, *J* = 1.9 Hz, 1H, H-9), 7.28 – 7.34 (m, 1H, H-1), 7.34 – 7.39 (m, 2H, H-2), 7.42 – 7.46 (m, 2H, H-3).

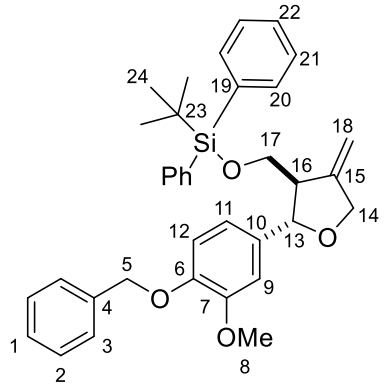
***Rel*-((2*S*,3*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-4-methylenetetrahydrofuran-3-yl)methanol (28).[3]**



28

A flame-dried Schlenk flask was charged with $TiCp_2Cl_2$ (1.42 g, 5.70 mmol, 2.50 eq.) under a nitrogen atmosphere and to this was added dry, degassed THF (23 mL), followed by freshly activated[3,17,18] Zn dust (1.48 g, 22.8 mmol, 10.0 eq.). The resultant suspension was stirred for 1 hour at room temperature. Stirring was stopped to allow excess Zn dust to settle to the bottom of the flask. The supernatant was then added *via* cannula to a solution of **S9** (739 mg, 2.28 mmol, 1.00 eq.) in dry degassed THF (10 mL) and the reaction mixture was stirred at room temperature for 1 hour. The mixture was quenched using 10% aqueous H_2SO_4 (10 mL) and diluted with EtOAc (50 mL). The reaction was partitioned and the organic layer washed with H_2O (1 x 25 mL) followed by $NaHCO_{3(aq)}$ (1 x 25 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification on silica gel (0-40% EtOAc in pet ether) gave **28** (397 mg, 1.22 mmol, 52%) as a colourless oil. Analytical data were consistent with that previously reported.[3] ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.76-2.80 (m, 1H, H-16), 3.73 (dd, *J* = 11.3, 4.7 Hz, 1H, H_b-17), 3.87 (dd, *J* = 11.3, 5.4 Hz, 1H, H_a-17), 3.90 (s, 3H, H-8), 4.39-4.43 (m, 1H, H_b=14), 4.59-4.63 (m, 1H, H_a-14), 4.78 (d, *J* = 7.5 Hz, 1H, H-13), 5.05-5.09 (m, 1H, H_b-18), 5.09-5.13 (m, 1H, H_a-18), 5.15 (s, 2H, H-5), 6.83 – 6.87 (m, 2H, H-11, H-12), 6.96 (d, *J* = 1.2 Hz, 1H, H-9), 7.27 – 7.32 (m, 1H, H-1), 7.34 – 7.38 (m, 2H, H-2), 7.41-7.45 (m, 2H, H-3).

(((2*S*,3*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-4-methylenetetrahydrofuran-3-yl)methoxy)-(*tert*-butyl)diphenylsilane (S10).

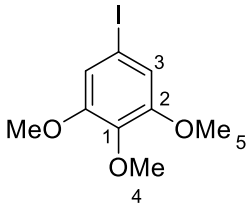


S10

To a flask was added **28** (397 mg, 1.22 mmol, 1.00 eq.), TBDPSCl (0.4 mL, 1.46 mmol, 1.20 eq.), imidazole (166 mg, 2.44 mmol, 2.00 eq.), 4-DMAP (14 mg, 0.122 mmol, 10.0 mol%) and DCM (12 mL). The reaction was stirred at room temperature for 16 hours, and subsequently quenched with saturated $NH_4Cl_{(aq)}$ (15 mL). The layers were partitioned and the aqueous phase was extracted with Et_2O (3 x 15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification on silica gel (0-15% EtOAc in pet ether) gave **S10** (612 mg, 1.09 mmol, 89%) as a viscous, colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.04 (s, 9H, H-

24), 2.79 – 2.86 (m, 1H, H-16), 3.78 (dd, *J* = 10.3, 5.2 Hz, 1H, H_b-17), 3.83 (dd, *J* = 10.4, 6.5 Hz, 1H, H_a-17), 3.87 (s, 3H, H-8), 4.41-4.45 (m, 1H, H_b-14), 4.56-4.60 (m, 1H, H_a-14), 4.94 (d, *J* = 6.6 Hz, 1H, H-13), 4.96-5.00 (m, 1H, H_b-18), 5.01-5.05 (m, 1H, H_a-18), 5.17 (s, 2H, H-5), 6.79 (dd, *J* = 8.3, 1.9 Hz, 1H, H-11), 6.83 (d, *J* = 8.2 Hz, 1H, H-12), 6.93 (d, *J* = 1.9 Hz, 1H, H-9), 7.30 – 7.34 (m, 1H, H-1), 7.34 – 7.49 (m, 10H, H-2, H-3, H-21, H-22), 7.67 – 7.61 (m, 4H, H-20). ^{13}C NMR (126 MHz, $CDCl_3$): δ_C 19.4 (C-23), 27.0 (C-24), 54.1 (C-16), 56.1 (C-8), 64.2 (C-17), 71.2 (C-5), 71.7 (C-14), 83.7 (C-13), 105.2 (C-18), 110.0 (C-9), 113.9 (C-12), 118.8 (C-11), 127.4 (C-3), 127.8 (C-2), 127.9 (C-1), 128.7 (C-21), 129.8 (C-22), 133.6 (C-19), 134.9 (C-10), 135.8 (C-20), 137.4 (C-4), 147.7 (C-6), 149.1 (C-15), 149.8 (C-7). Found, *m/z*: 587.2599 $[M+Na]^+$. $C_{36}H_{40}O_4SiNa$. Calculated, *m/z*: 587.2594.

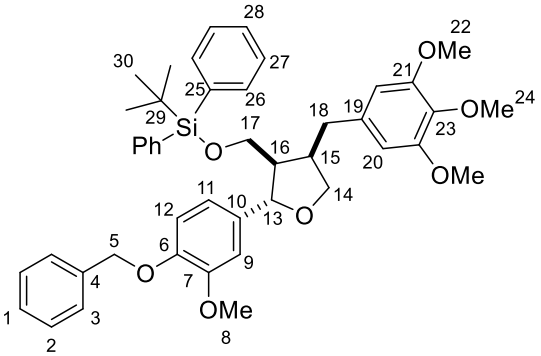
5-Iodo-1,2,3-trimethoxybenzene (S11).[19]



S11

Commercially available 3,4,5-Trimethoxyaniline (504 mg, 2.75 mmol, 1.00 eq.) was taken up in THF (5 mL) and 4 M $HCl_{(aq)}$ (7.0 mL) and the solution was cooled to 0˚C. To this was added $NaNO_2$ (228 mg, 3.31 mmol, 1.20 eq.) as a solution in H_2O (2.5 mL) dropwise, and the resultant mixture was stirred for 20 minutes, before addition of NaI (1.03 g, 6.89 mmol, 2.50 eq.) as a solution in H_2O (2.5 mL). The reaction was stirred at 0˚C for 10 further minutes, before warming to room temperature and stirring for 1 hour. The reaction was quenched by addition of 1 M $Na_2S_2O_{3(aq)}$. The reaction was extracted with EtOAc (3 x 20 mL) and the combined organic layers were washed with H_2O (30 mL) and brine (30 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-15% EtOAc in pet ether) afforded **S11** (703 mg, 2.39 mmol, 87%) as an orange powder. Analytical data were in accordance with that previously reported. [19] ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 3.82 (s, 3H, H-4), 3.84 (s, 6H, H-5), 6.89 (s, 2H, H-3).

***Rel*-(((2*S*,3*R*,4*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-4-(3,4,5-trimethoxybenzyl)tetrahydro-furan-3-yl)methoxy)(*tert*-butyl)diphenylsilane (S12).**

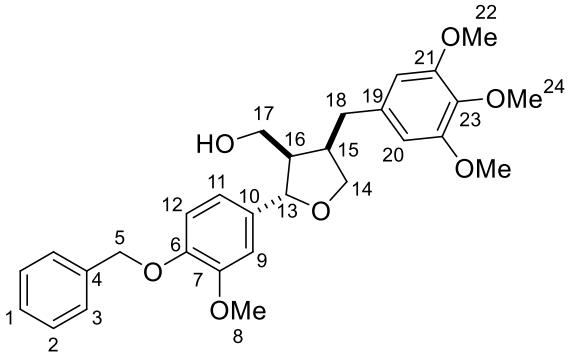


S12

A flame-dried flask was charged with **S10** (118 mg, 0.210 mmol, 1.00 eq.), evacuated and back-filled with N_2. To this was added 9-BBN (0.5 M solution in THF, 0.6 mL, 0.315 mmol, 1.50 eq.), and the reaction mixture was

stirred at 40˚C for 16 hours, then cooled to room temperature, before addition of 1 M NaOH (0.6 mL, excess). The resultant biphasic mixture was stirred for 15 minutes, then 5-iodo-1,2,3-trimethoxybenzene (**S11**, 80.0 mg, 0.273 mmol, 1.30 eq.) and $Pd(dppf)Cl_2$ (5.00 mg, 0.006 mmol, 3.00 mol%) were added, and the reaction was stirred for 24 hour at room temperature. The mixture was then diluted with Et_2O (5 mL) and brine (5 mL). The aqueous layer was extracted with Et_2O (3 x 5 mL), and finally the combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-30% EtOAc in pet. ether) gave **S12** (119 mg, 0.163 mmol, 77%) as a viscous, colourless oil. IR (oil, ATR-FTIR, ν_{max}, cm^{-1}): 2932, 1128, 702; ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.08 (s, 9H, H-30), 2.40-2.44 (m, 1H, H-15), 2.51 (dd, *J* = 13.4, 11.0 Hz, 1H, H_a-18), 2.68-2.72 (m, 1H, H-16), 2.88 (dd, *J* = 13.4, 4.8 Hz, 1H, H_b-18), 3.76 (dd, *J* = 8.5, 6.8 Hz, 1H, H_a-14), 3.78 – 3.85 (m, 13H, H-8, H_a-17, H-22, H-24), 3.87-3.91 (m, 1H, H_b-17), 4.02 (dd, *J* = 8.5, 6.5 Hz, 1H, H_b-14), 4.91 (d, *J* = 5.9 Hz, 1H, H-13), 5.14 (s, 2H, H-5), 6.34 (s, 2H, H-20), 6.66 (dd, *J* = 8.3, 2.0 Hz, 1H, H-11), 6.78 (d, *J* = 8.2 Hz, 1H, H-12), 6.81 (d, *J* = 2.0 Hz, 1H, H-9), 7.27 – 7.32 (m, 1H, H-1), 7.35 (dt, *J* = 8.2, 7.0 Hz, 6H, H-2, H-27), 7.38 – 7.45 (m, 4H, H-3, H-28), 7.62 – 7.67 (m, 4H, H-26). Found, *m/z*: 755.3355 $[M+Na]^+$. $C_{45}H_{52}O_7SiNa$. Calculated, *m/z*: 755.3380.

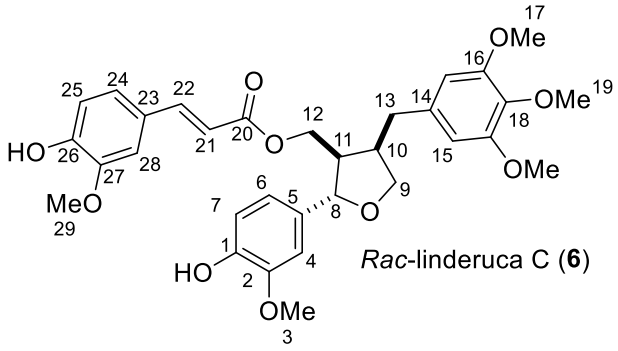
Rel-((2*S*,3*R*,4*R*)-2-(4-(benzyloxy)-3-methoxyphenyl)-4-(3,4,5-trimethoxybenzyl)tetrahydro-furan-3-yl)methanol (24).



24

A flame-dried flask was charged with **S12** (119 mg, 0.163 mmol, 1.00 eq.) and dry THF (1.6 mL) under a nitrogen atmosphere. The solution was cooled to 0˚C, and to it was added TBAF (1.0 M solution in THF, 0.20 mL, 0.195 mmol, 1.20 eq.). The reaction was warmed to room temperature, stirred for 16 hours, then diluted with Et_2O (5 mL) and brine (5 mL). The layers were partitioned and the aqueous phase extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification on silica gel (0-50% EtOAc in pet. ether) gave **24** (68.4 mg, 0.139 mmol, 85%) as a colourless oil. ^1H NMR analysis was consistent with that reported in the Experimental Section for the alternative synthesis of **24**.

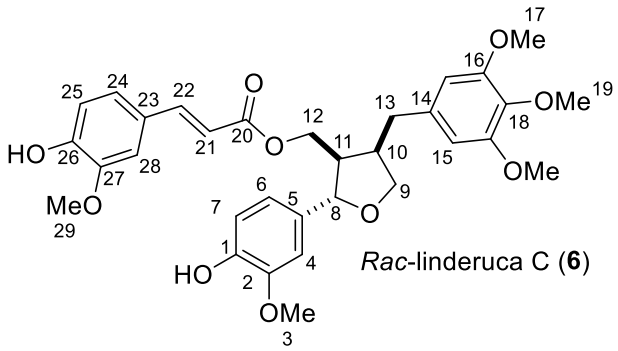
Table S2 – ^{1}H NMR assignment comparison between linderuca C (**6**) in CD_3OD[39] with the obtained sample of *rac*-linderuca C (**6**) in CD_3OD from this investigation. Right & left column show chemical shift in ppm, followed by multiplicity of the signal; *J* values shown in brackets for relative peaks. Middle column lists assigned proton signals



Rac-linderuca C (**6**)

Literature Chemical Shift (δ_H in ppm) in CD_3OD[39] (500 MHz)	Proton in Linderuca C (**6**)	Obtained Chemical Shift (δ_H in ppm) in CD_3OD (700 MHz)
7.38 d (16.0)	H-22	7.39 d (15.9)
7.09 d (2.0)	H-28	7.11 d (1.9)
6.99 dd (8.5, 2.0)	H-24	7.01 dd (8.2, 2.0)
6.90 d (2.0)	H-4	6.94 d (1.9)
6.81 dd (8.0, 2.0)	H-6	6.83 dd (8.1, 2.0)
6.79 d (8.5)	H-25	6.80 d (8.2)
6.76 d (8.0)	H-7	6.78 d (8.1)
6.58 s	H-15	6.55 s
6.23 d (16.0)	H-21	6.23 d (15.9)
4.80 d (7.0)	H-8	4.80 d (7.5)
4.50 dd (12.0, 6.0)	H_a-12	4.50 dd (11.2, 6.6)
4.29 dd (12.0, 8.0)	H_b-12	4.27 dd (11.2, 7.7)
4.12 dd (8.0, 7.0)	H_a-9	4.08 dd (8.5, 6.3)
3.89 s	H-29	3.90 s
3.81 s	H-3	3.82 s
3.81 s	H-17	3.81 s
3.78 dd (8.0, 6.5)	H_b-9	3.76 dd (8.5, 5.6)
3.78 s	H-19	3.72 s
2.92 dd (13.5, 5.0)	H_a-13	2.92 dd (13.4, 5.4)
2.87 m	H-10	2.84-2.90 m
2.66 m	H-11	2.66-2.71 m
2.57 dd (13.5, 11.0)	H-13	2.61 dd (13.4, 10.4)

Table S3 – ^{13}C NMR assignment comparison between linderuca C (**6**) in CD_3OD[39] with the obtained sample of *rac*-linderuca C (**6**) in CD_3OD from this investigation. Right & left column show chemical shift in ppm. Middle column lists assigned proton signals



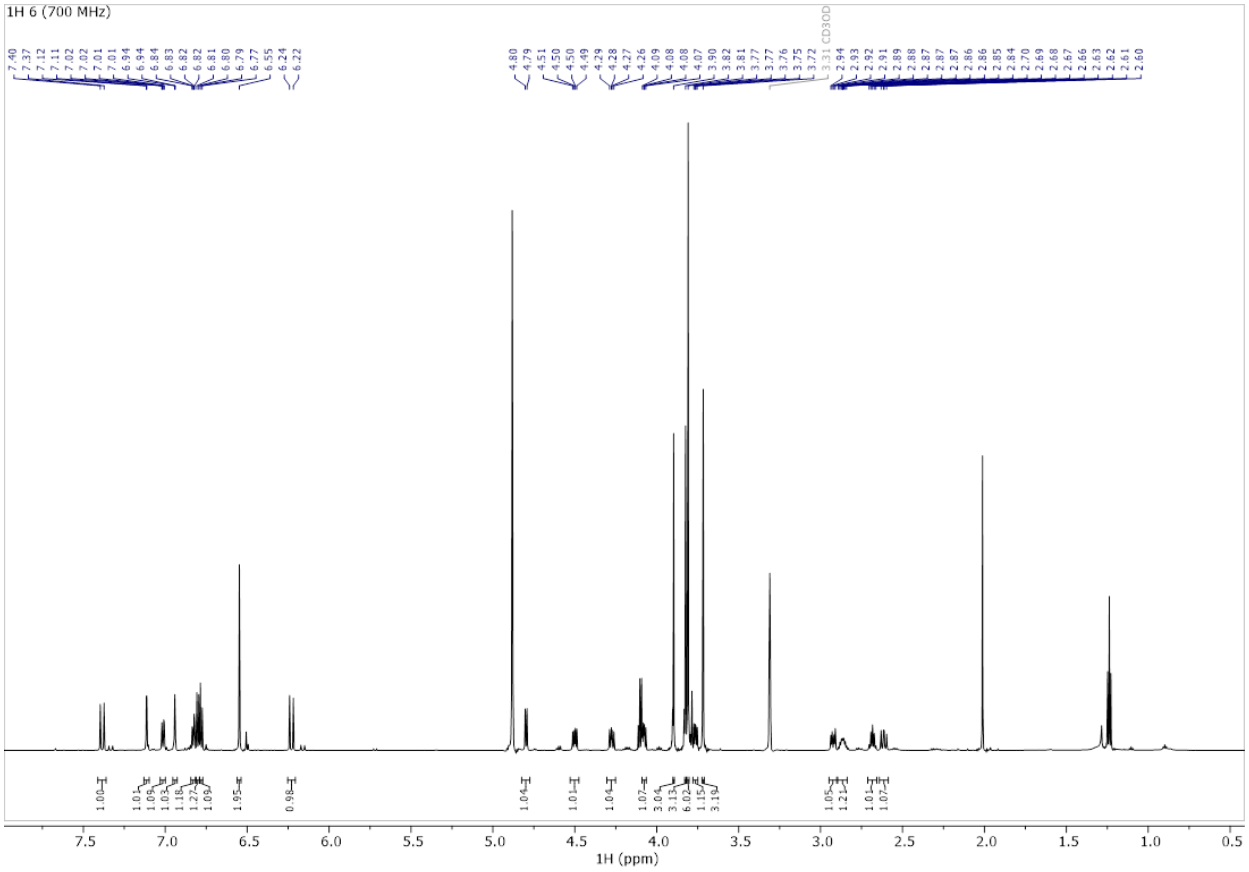
Rac-linderuca C (**6**)

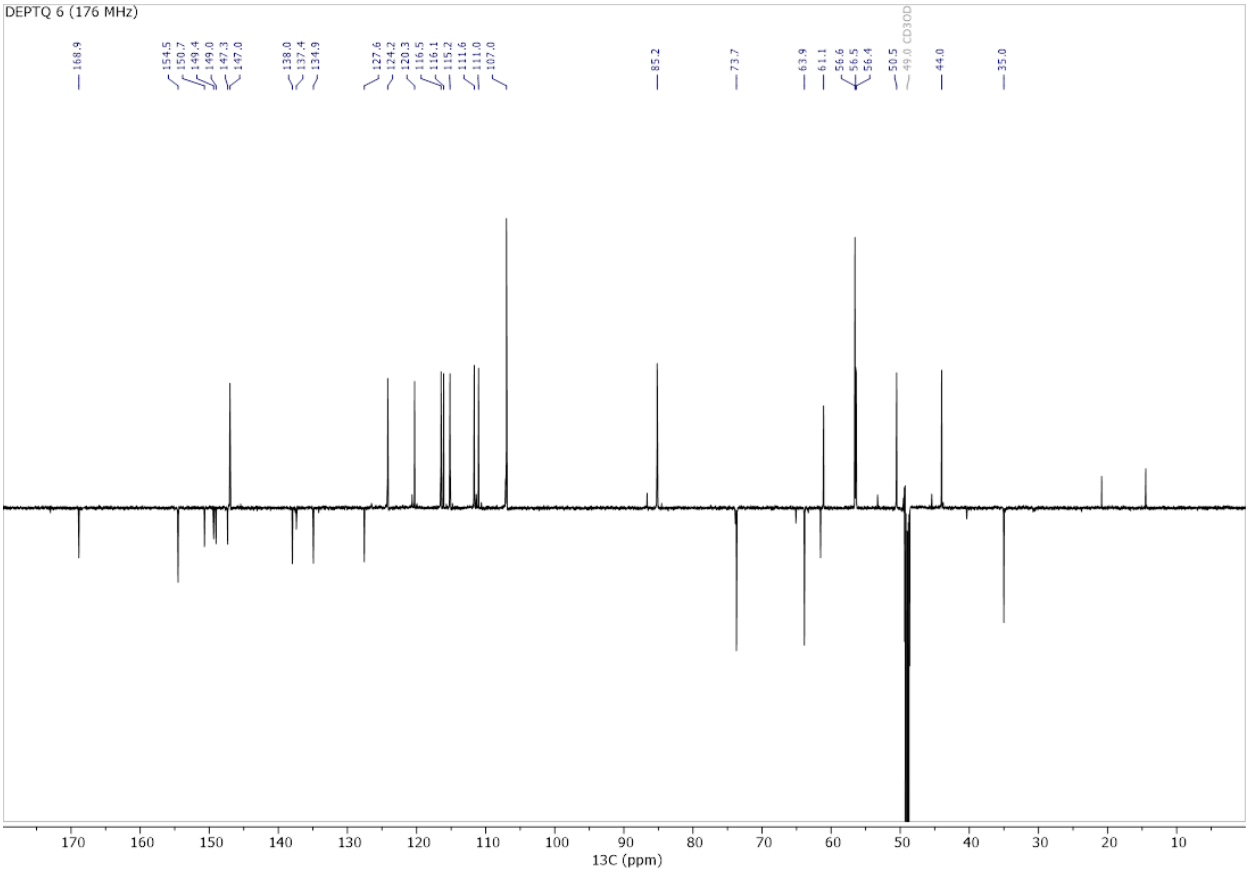
Literature Chemical Shift (δ_C in ppm) in CD_3OD[39] (126 MHz)	Literature Carbon Assignments in Linderuca C (**6**)	Obtained Chemical Shift (δ_C in ppm) in CD_3OD (176 MHz)	Corrected Carbon Assignments in Linderuca C (**6**)
167.6	C-20	168.9	C-20
153.3	C-16	154.5	C-16
149.2	C-2	150.7	C-2 or C-26 or C27[a]
148.1	C-26	149.4	C-2 or C-26 or C27[a]
147.7	C-27	149.0	C-2 or C-26 or C27[a]
147.3	C-1	147.3	C-1
145.8	C-22	147.0	C-22
136.9	C-18	138.0	C-14 or C-18[a]
136.8	C-14	137.4	C-14 or C-18[a]
135.3	C-5	134.9	C-5
126.3	C-23	127.6	C-23
122.9	C-24	124.2	C-24
120.4	C-6	120.3	C-6
116.2	C-7	116.5	C-7 or C-25[a]
115.3	C-25	116.1	C-7 or C-25[a]
114.0	C-21	115.2	C-21
110.6	C-28	111.6	C-28
110.3	C-4	111.0	C-4
106.0	C-15	107.0	C-15
84.1	C-8	85.2	C-8
73.0	C-9	73.7	C-9
62.8	C-12	63.9	C-12
60.4	C-19	61.1	C-19
55.6	C-17	56.6	C-17
55.6	C-29	56.5	C-29
55.6	C-3	56.4	C-3
49.5	C-11	50.5	C-11
42.8	C-10	44.0	C-10
33.8	C-13	35.0	C-13

[a]Carbon peaks are indistinguishable and could reasonably be assigned any of these carbons.

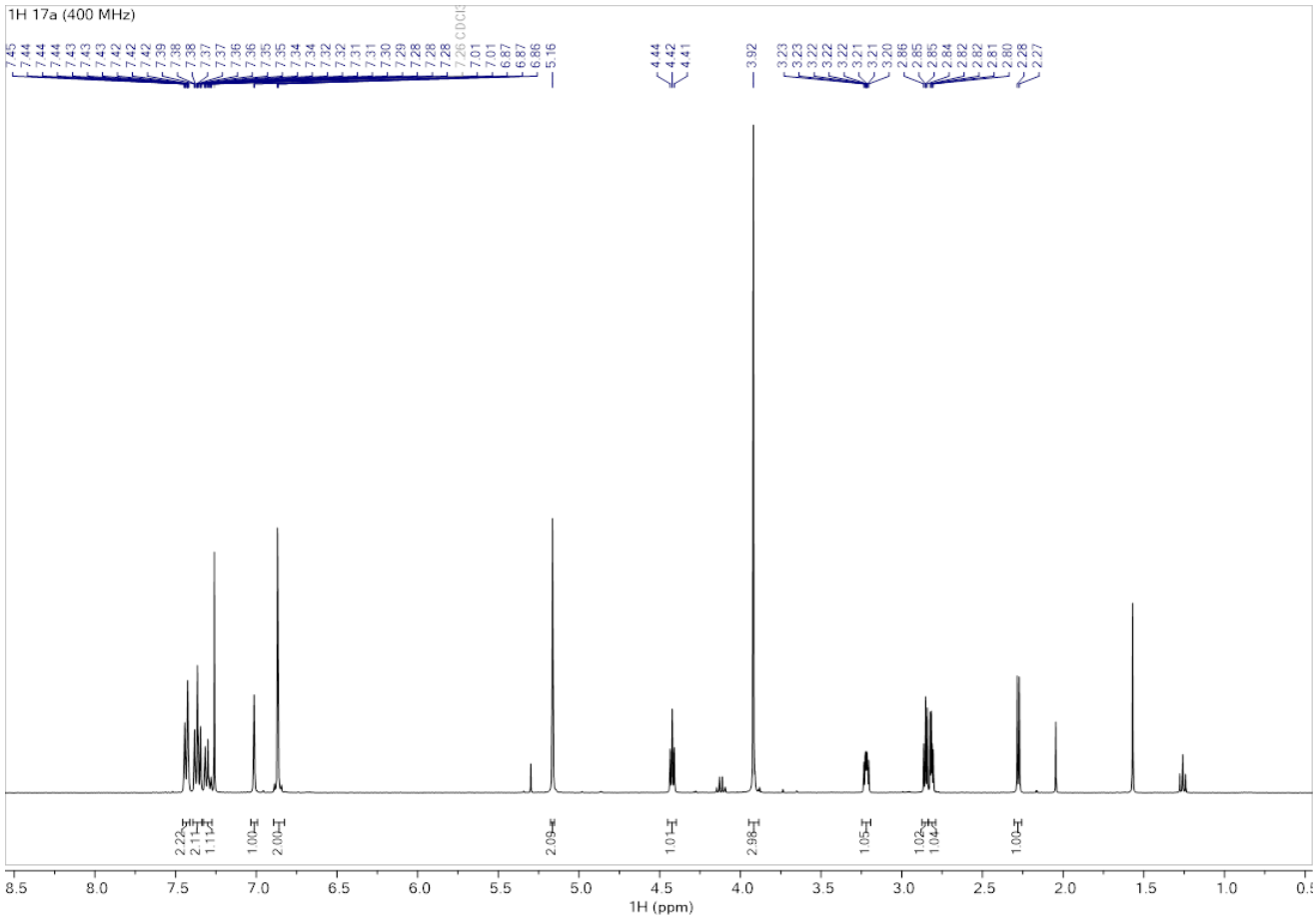
NMR Spectra for Novel and Key Compounds:

NMR spectra for compound 6.

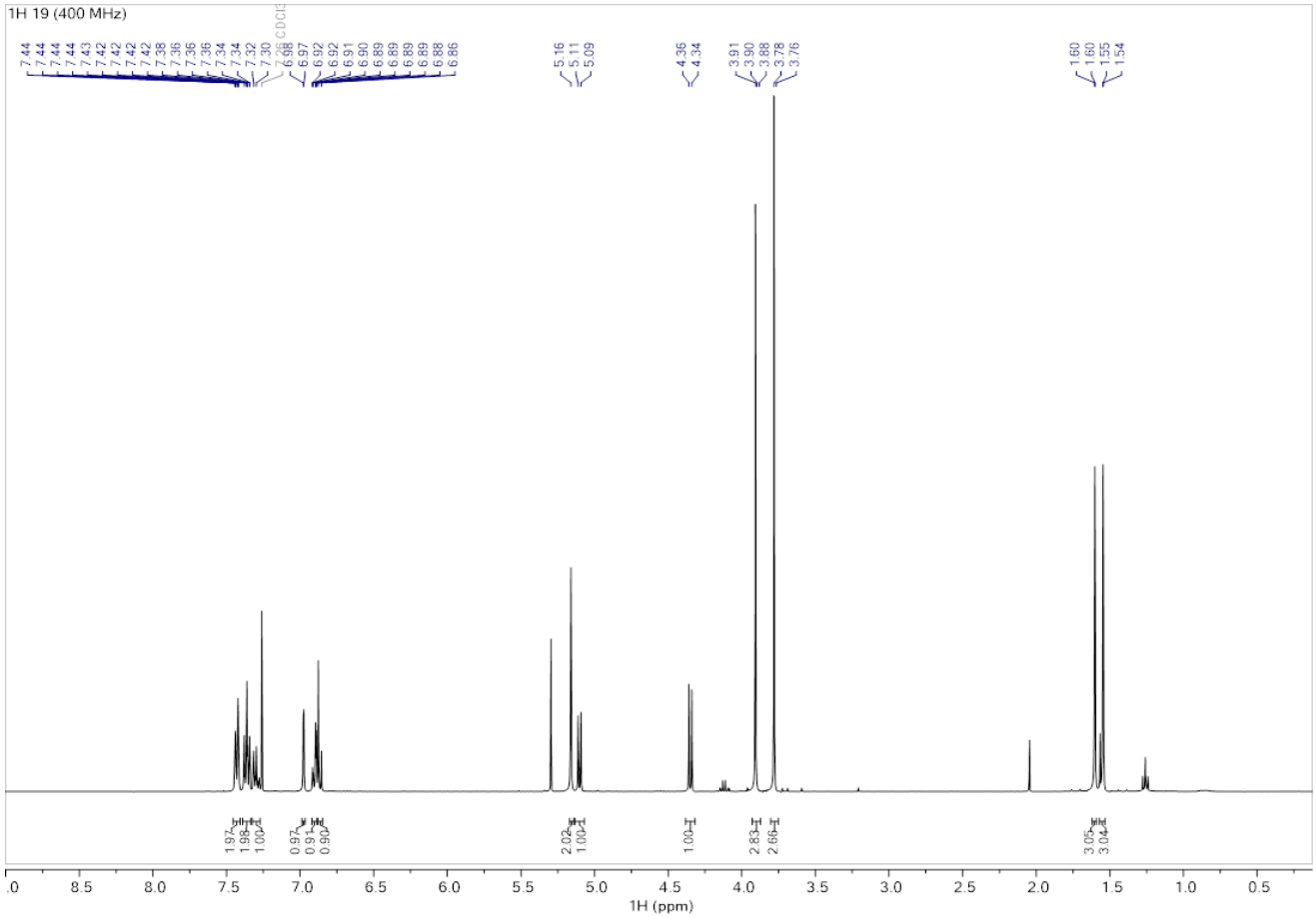


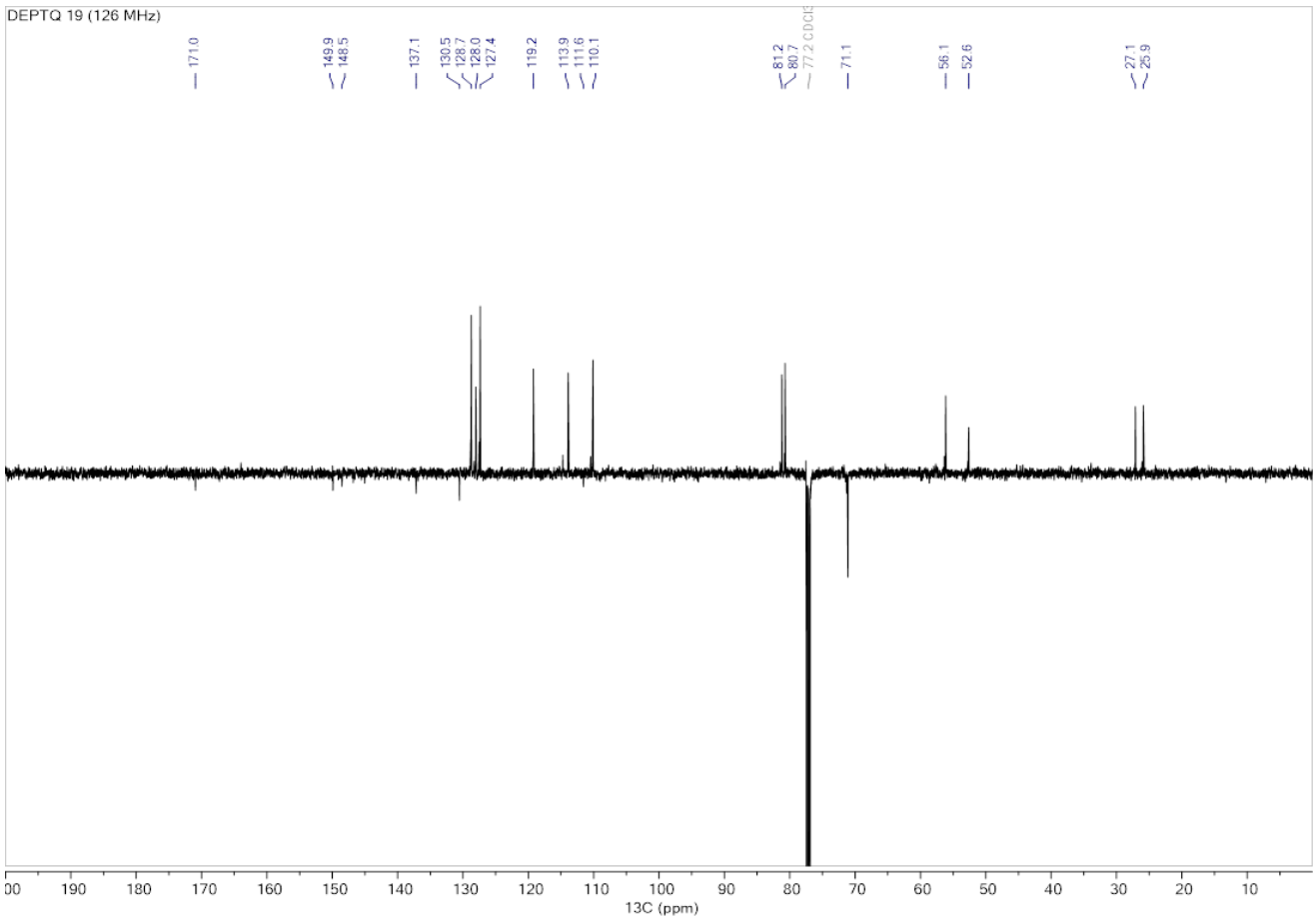


NMR spectra for compound 17a.

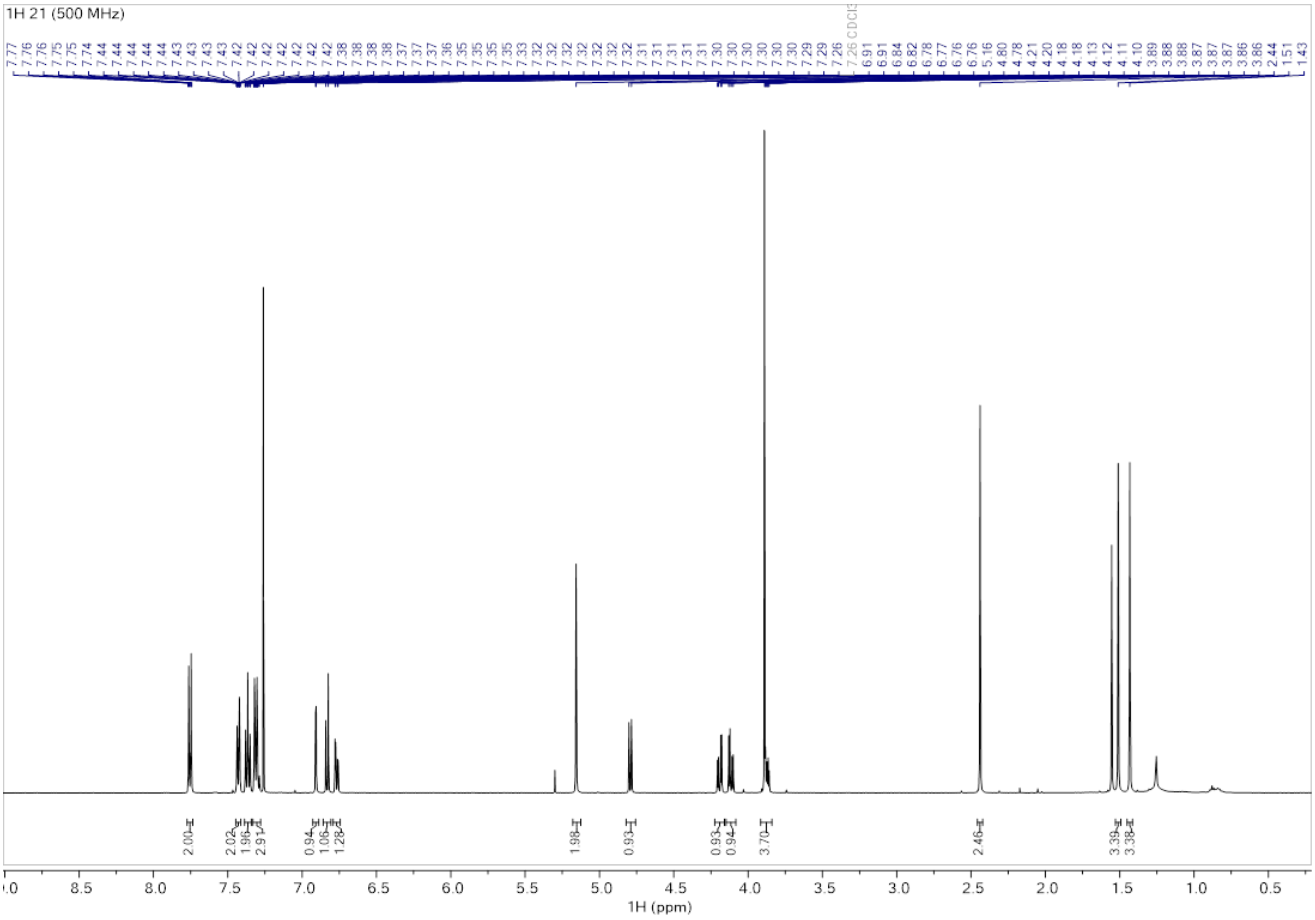


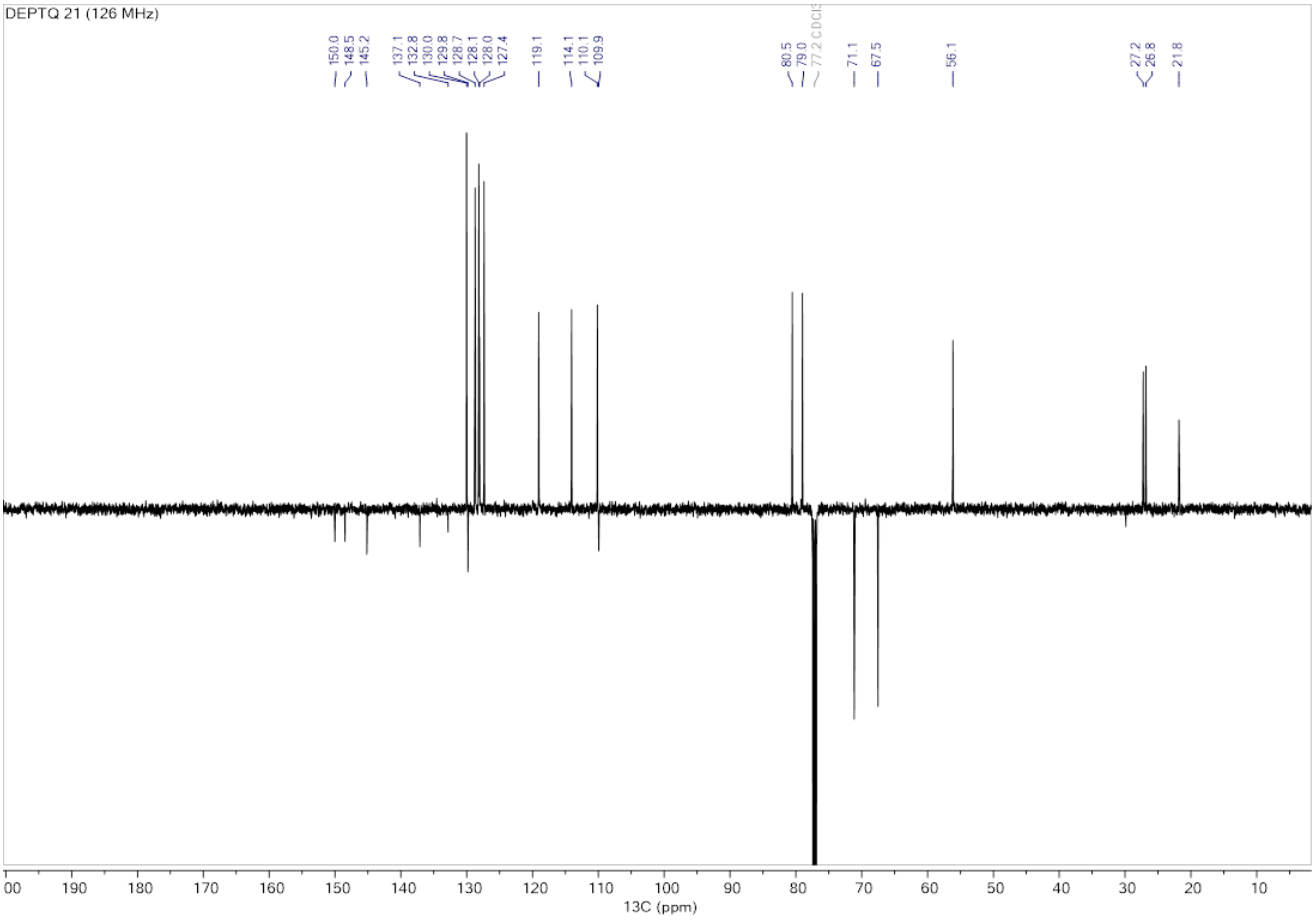
NMR spectra for compound 19.



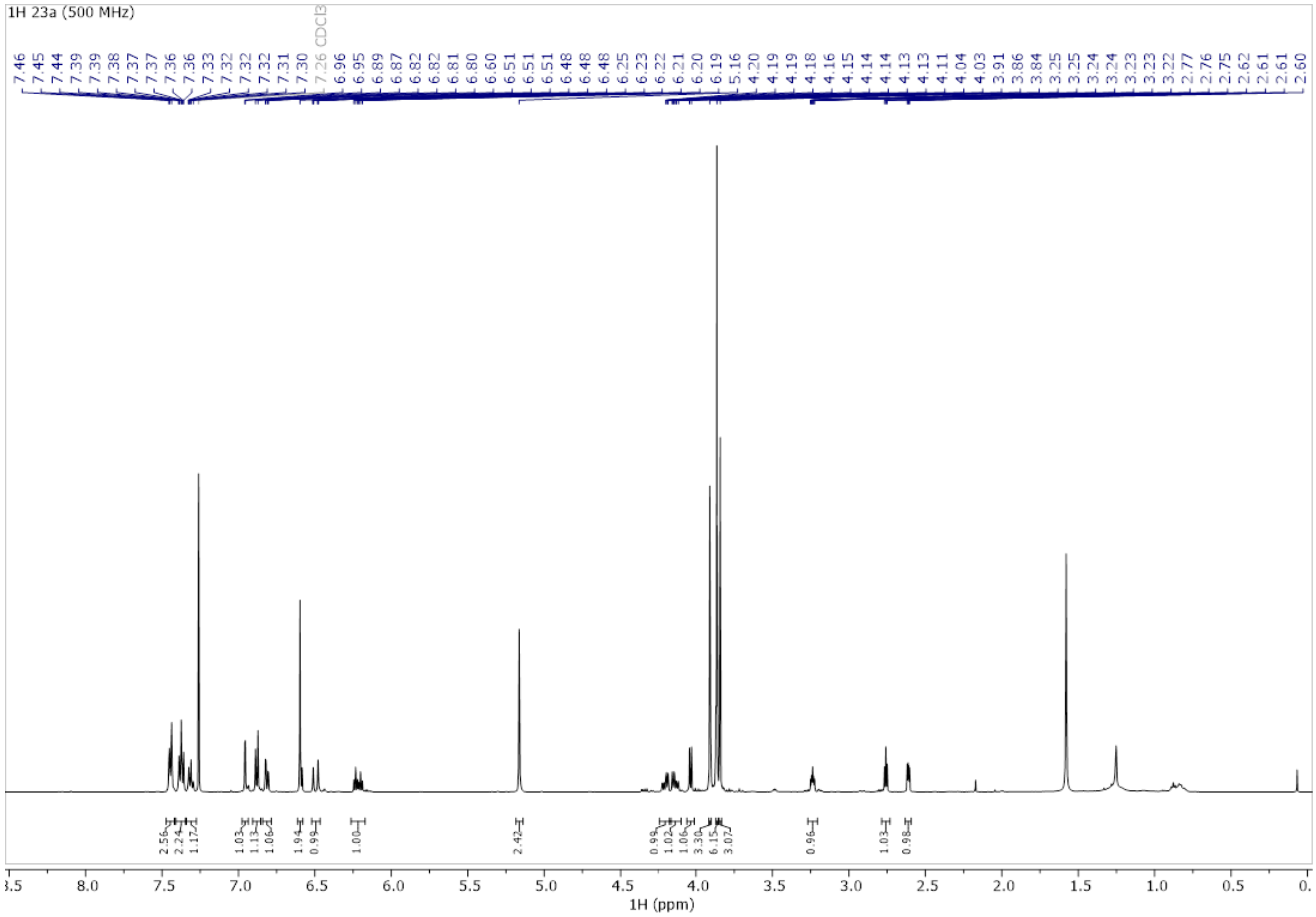


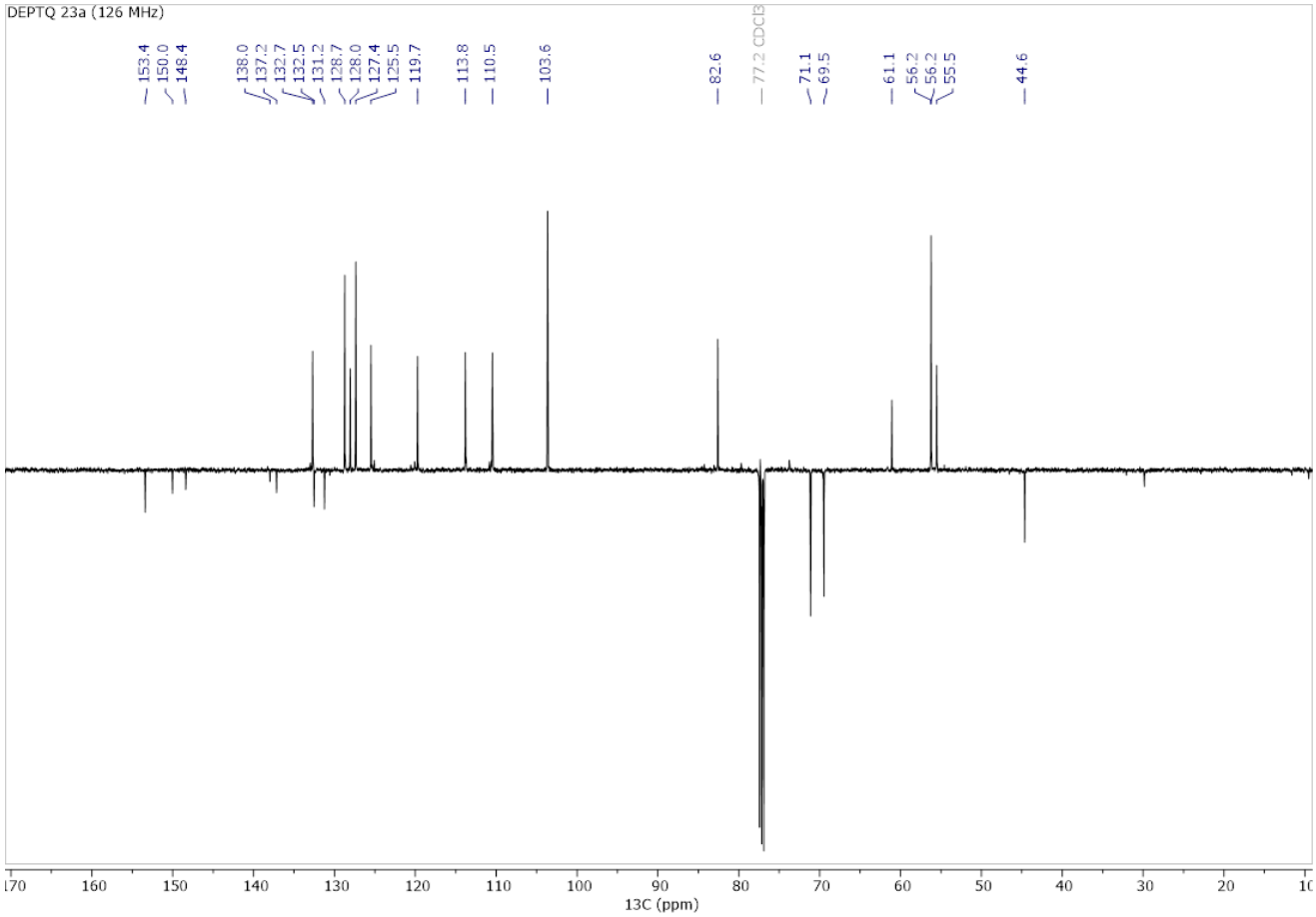
NMR spectra for compound 21.



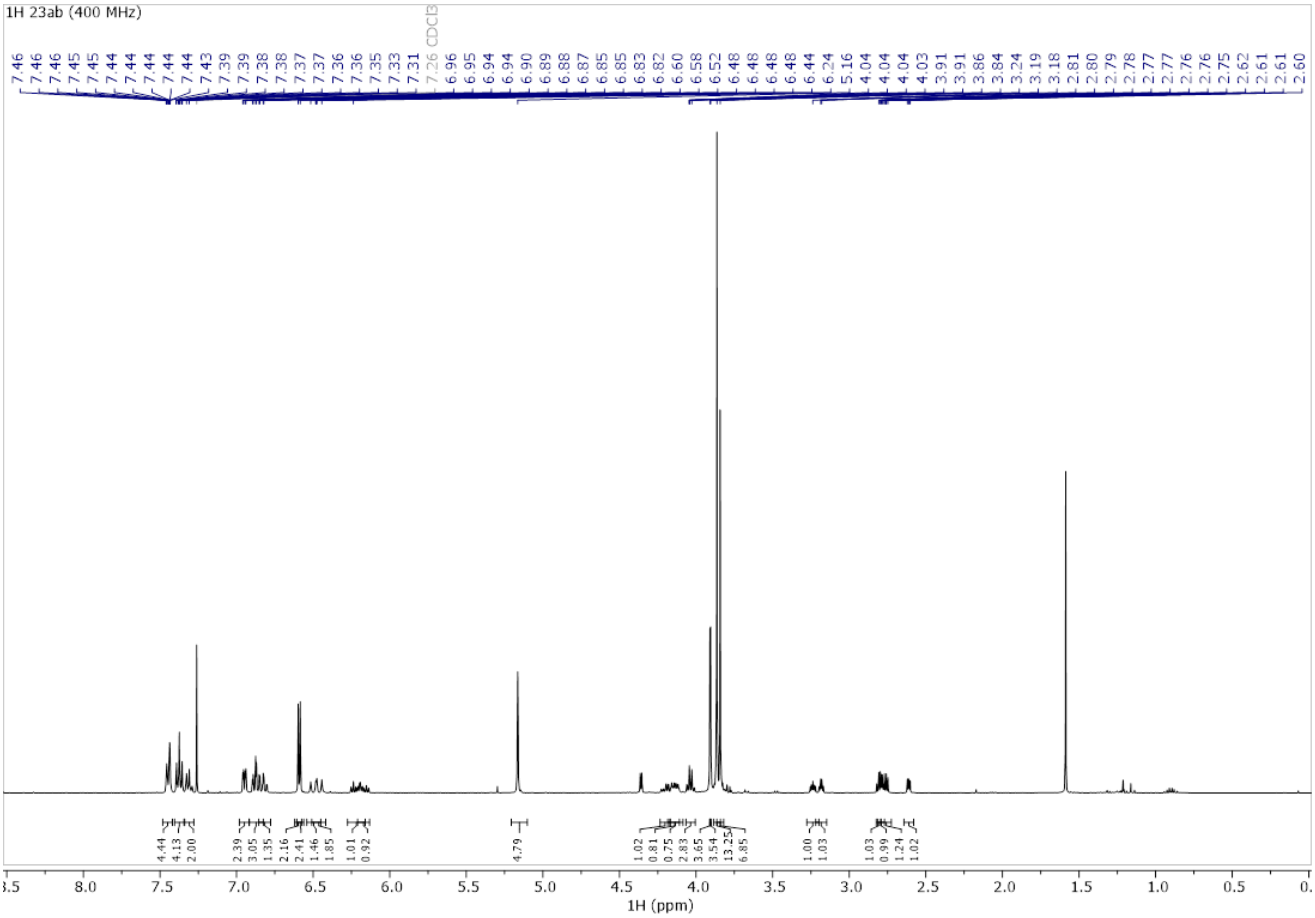


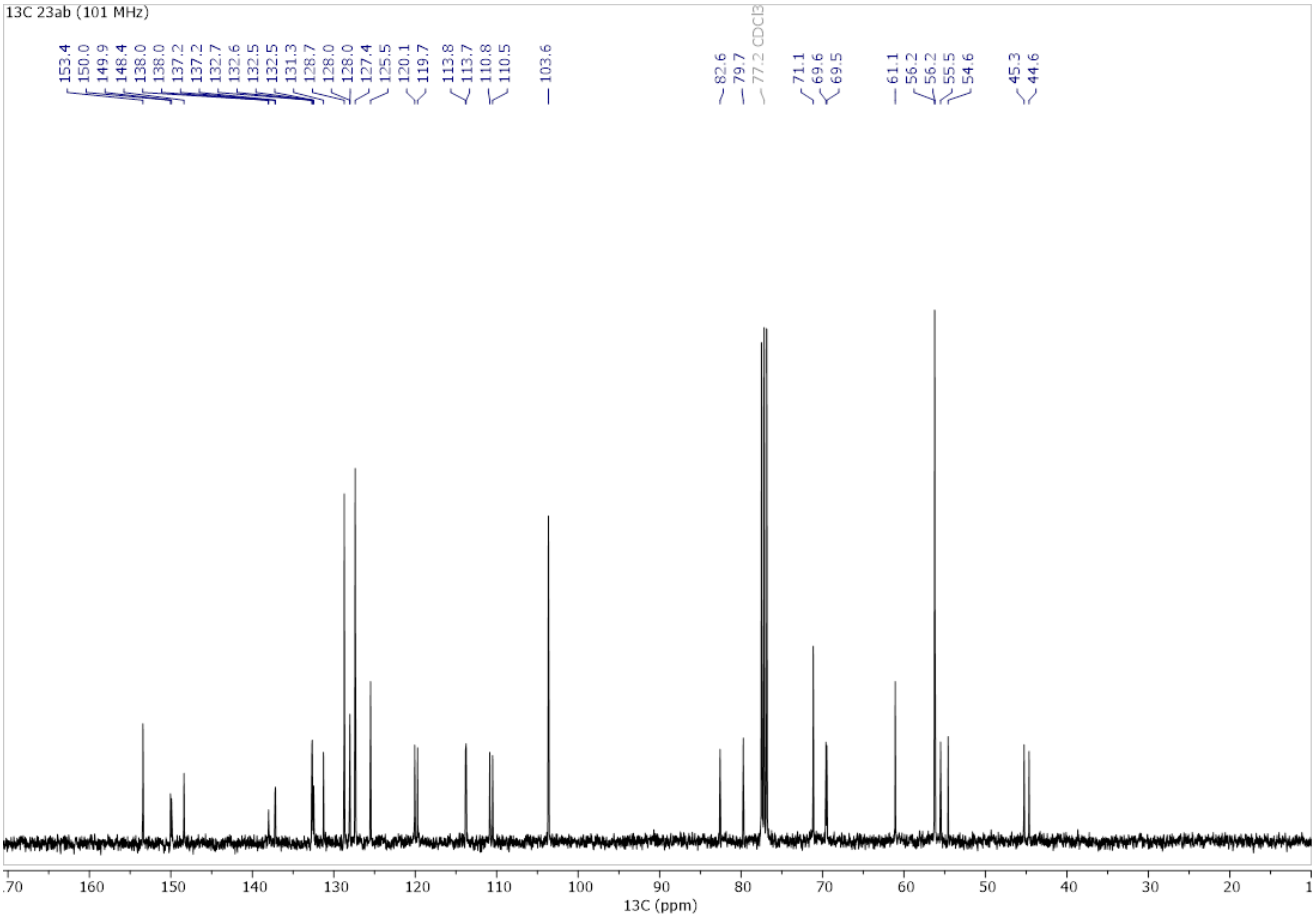
NMR spectra for compound 23a.



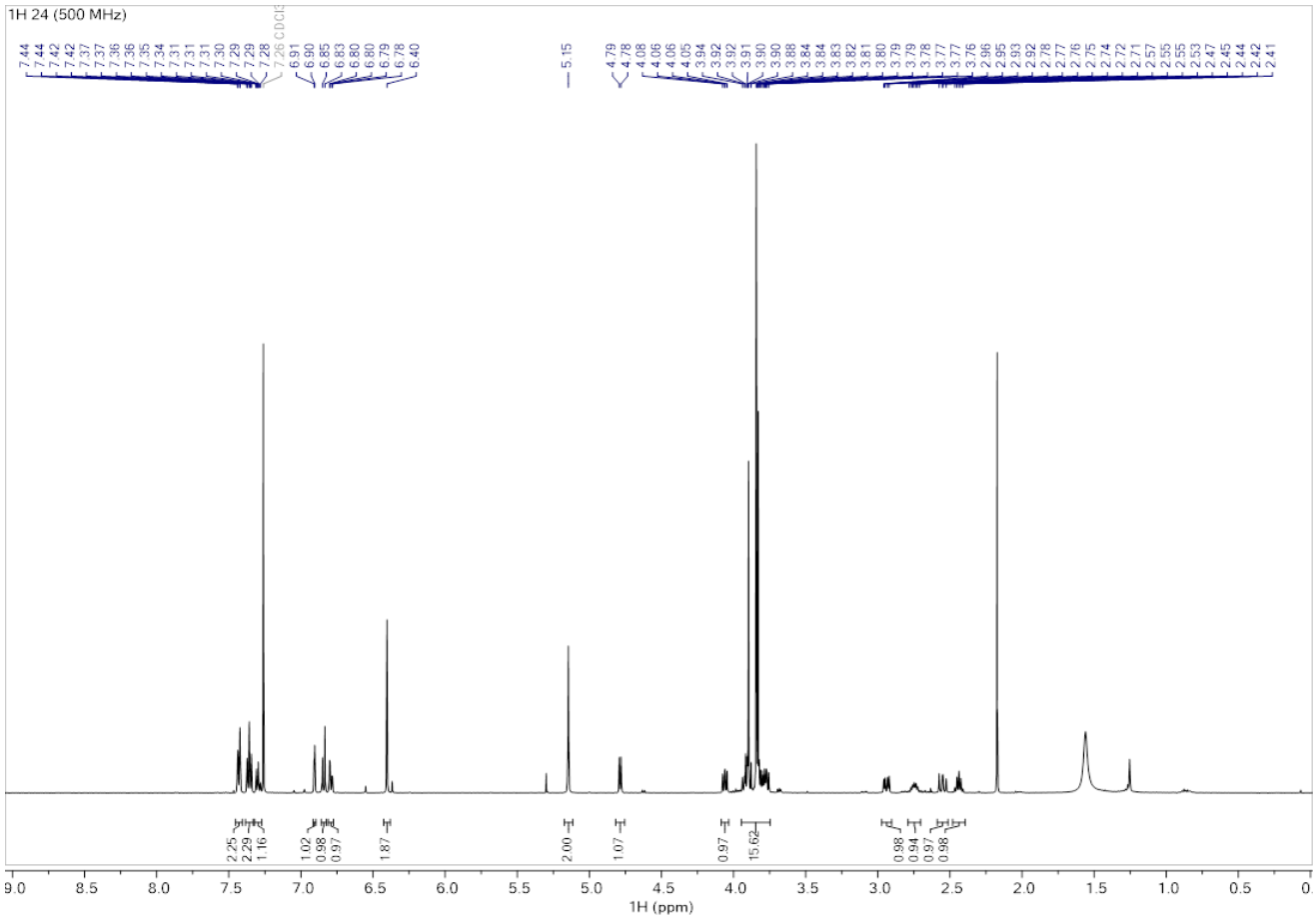


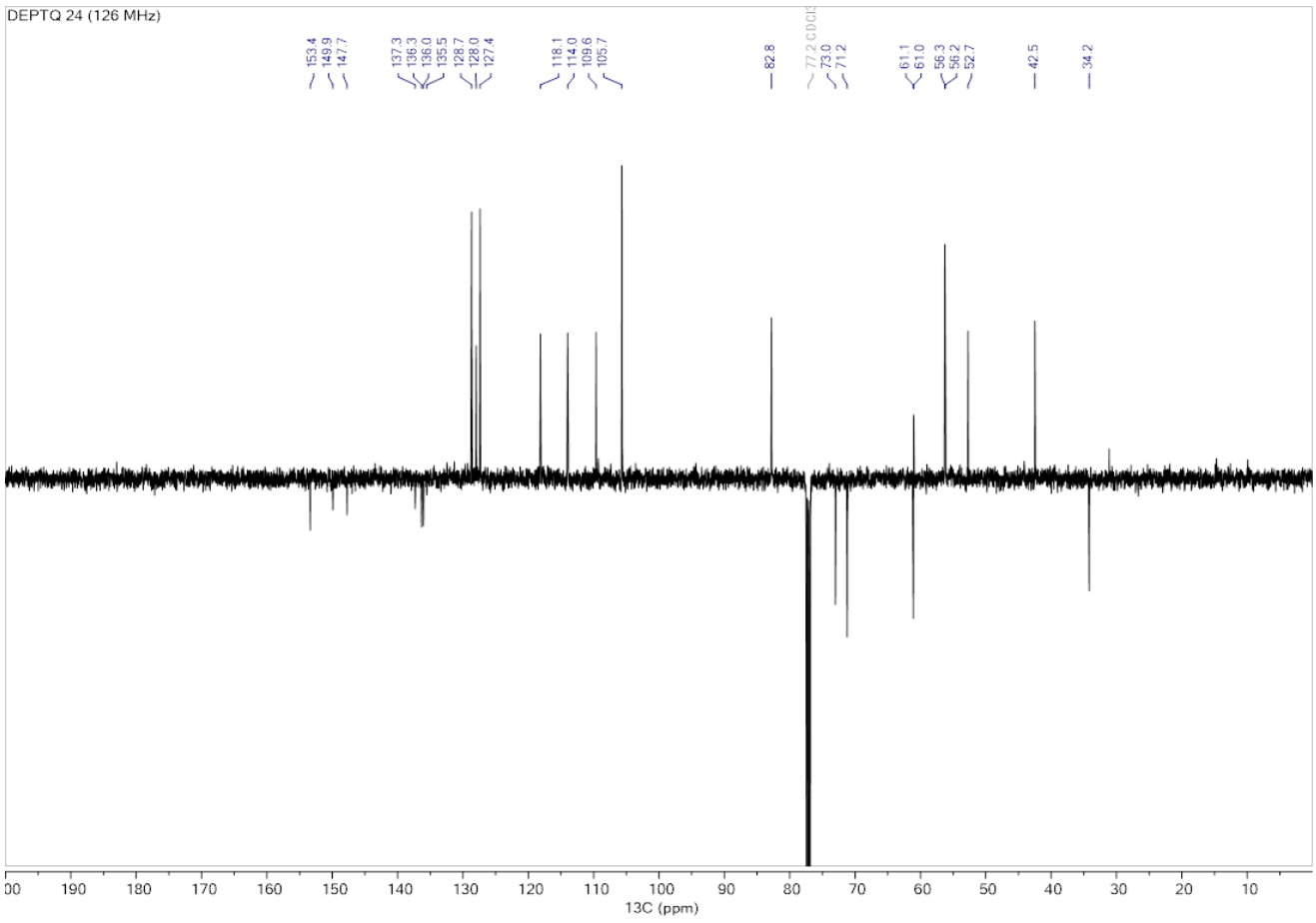
NMR spectra for compound 23ab.



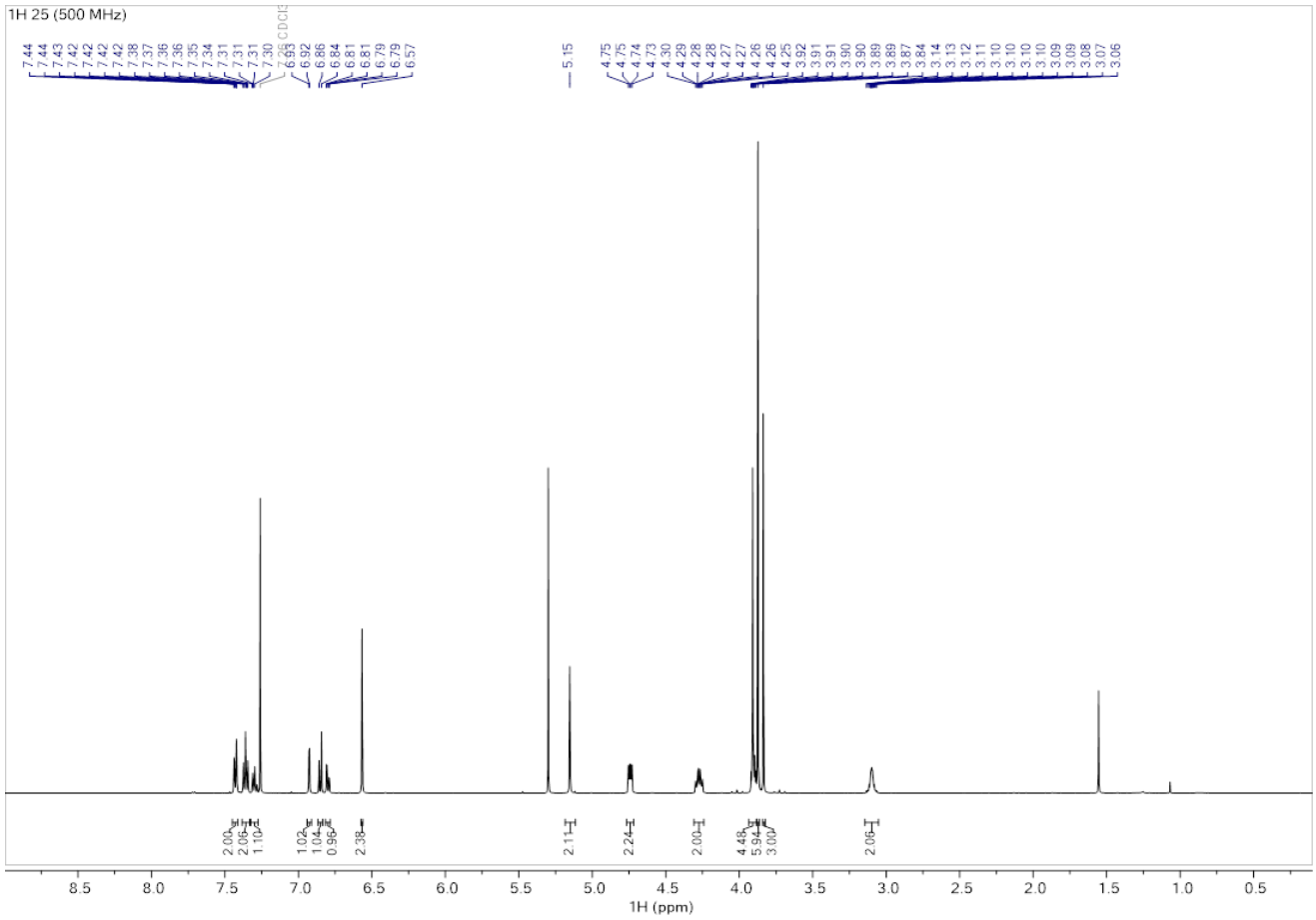


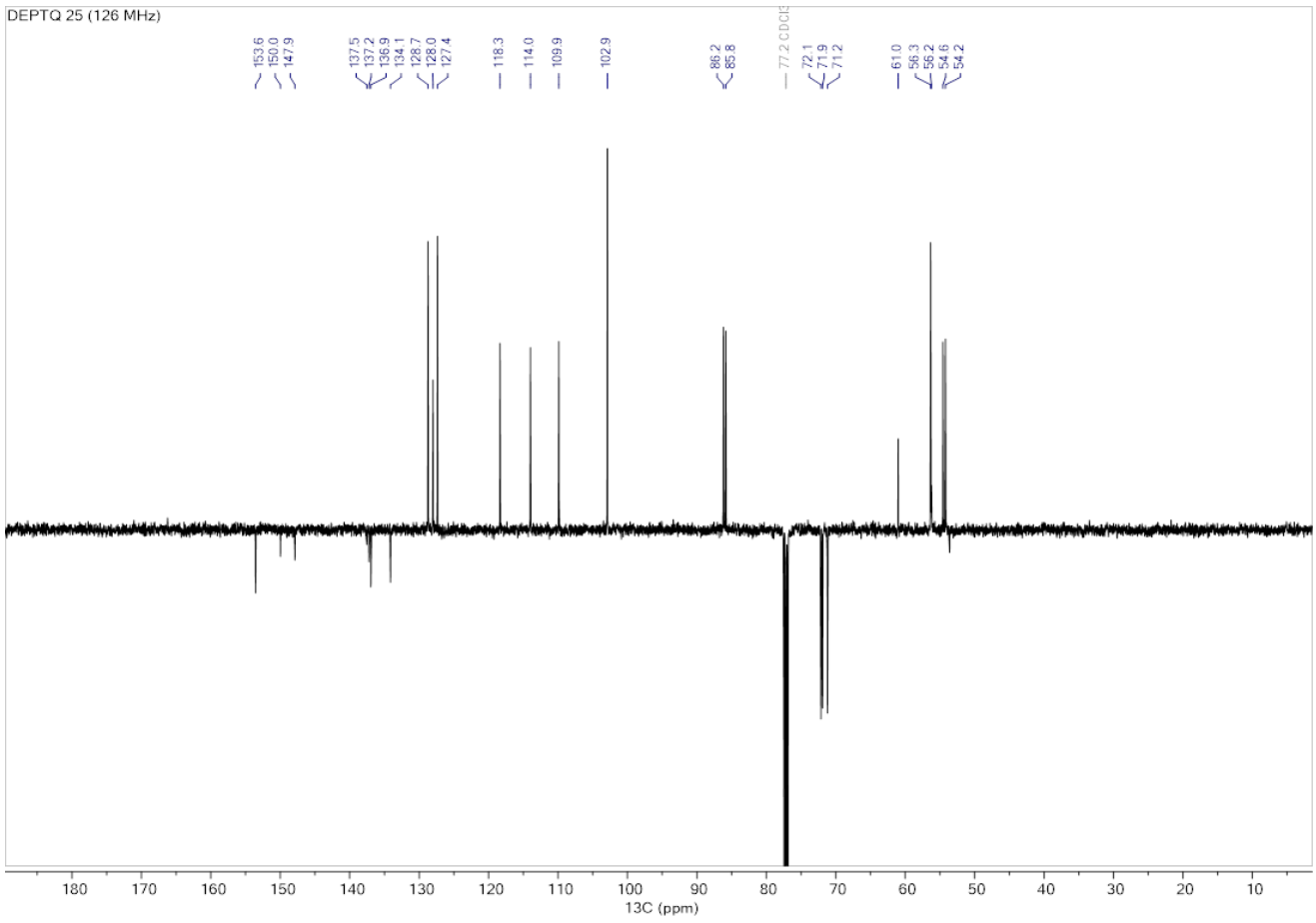
NMR spectra for compound 24.



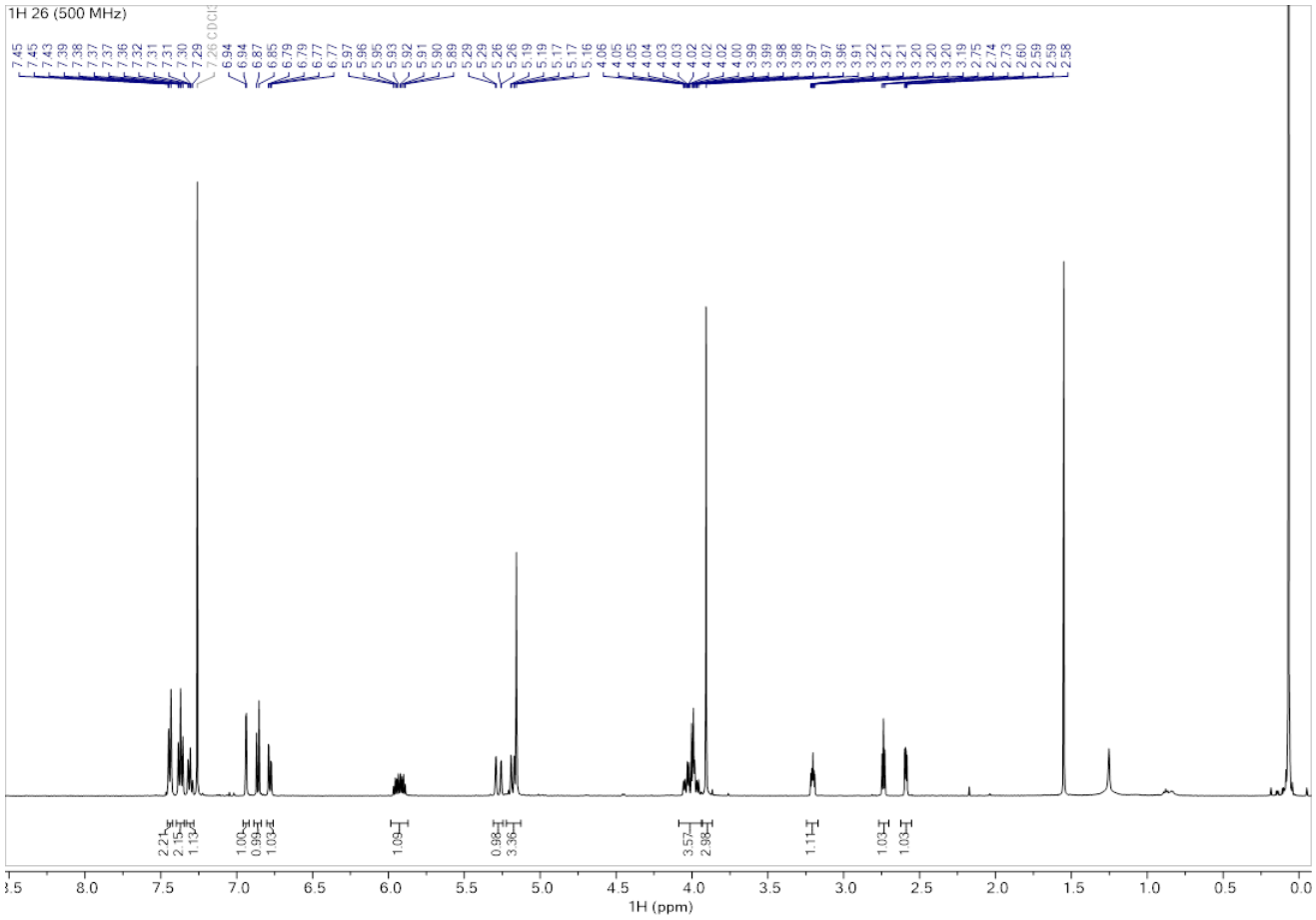


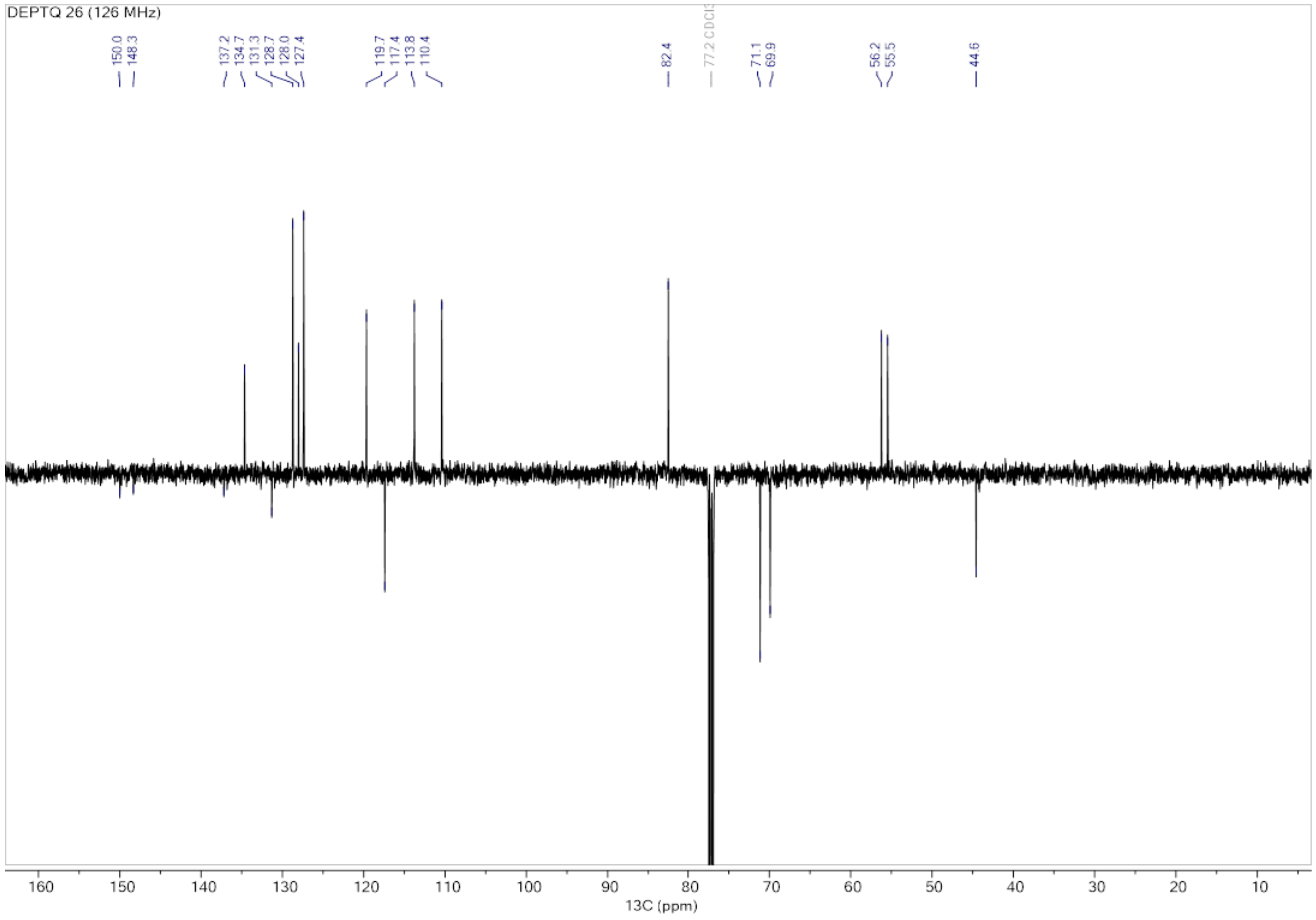
NMR spectra for compound 25.



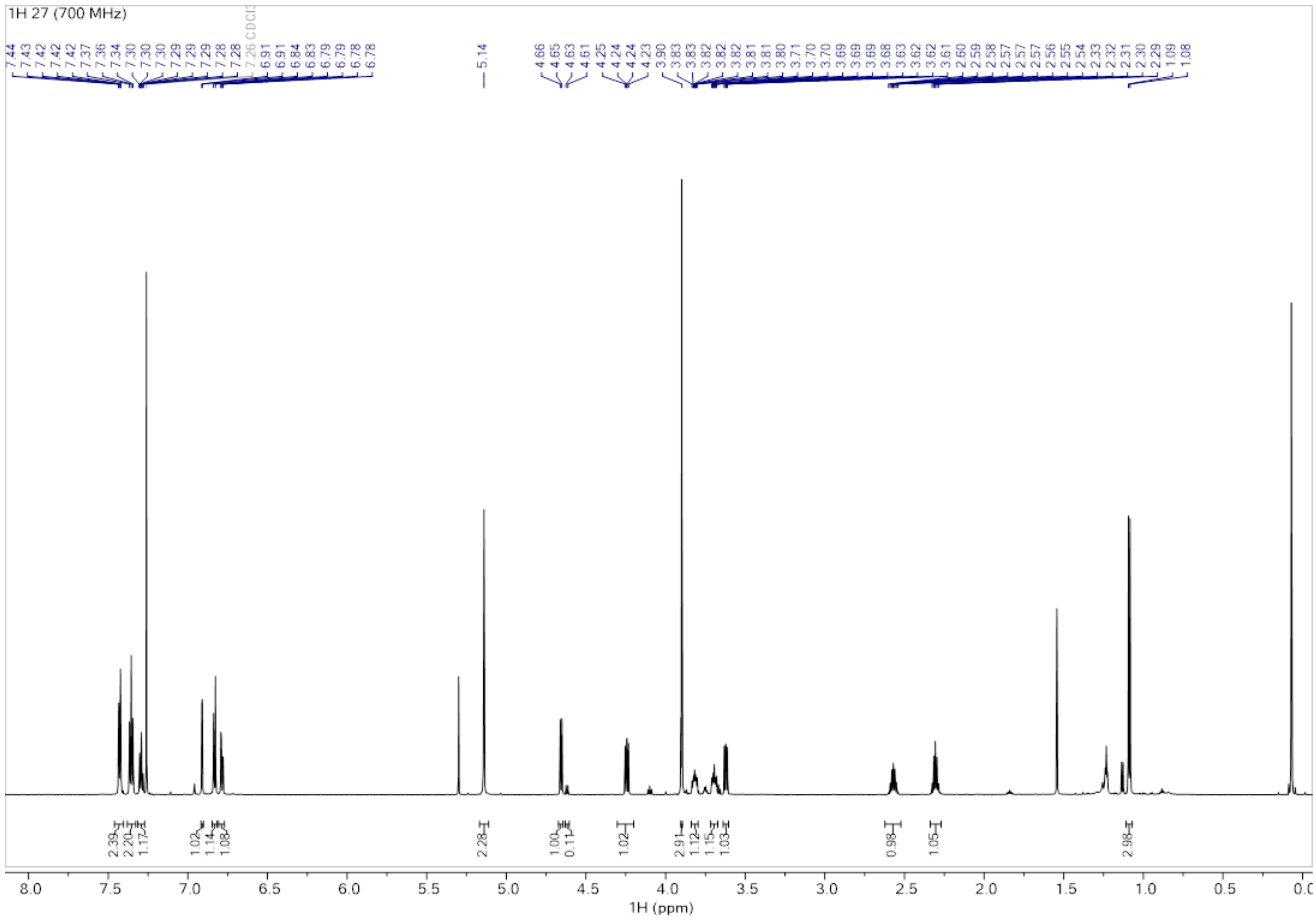


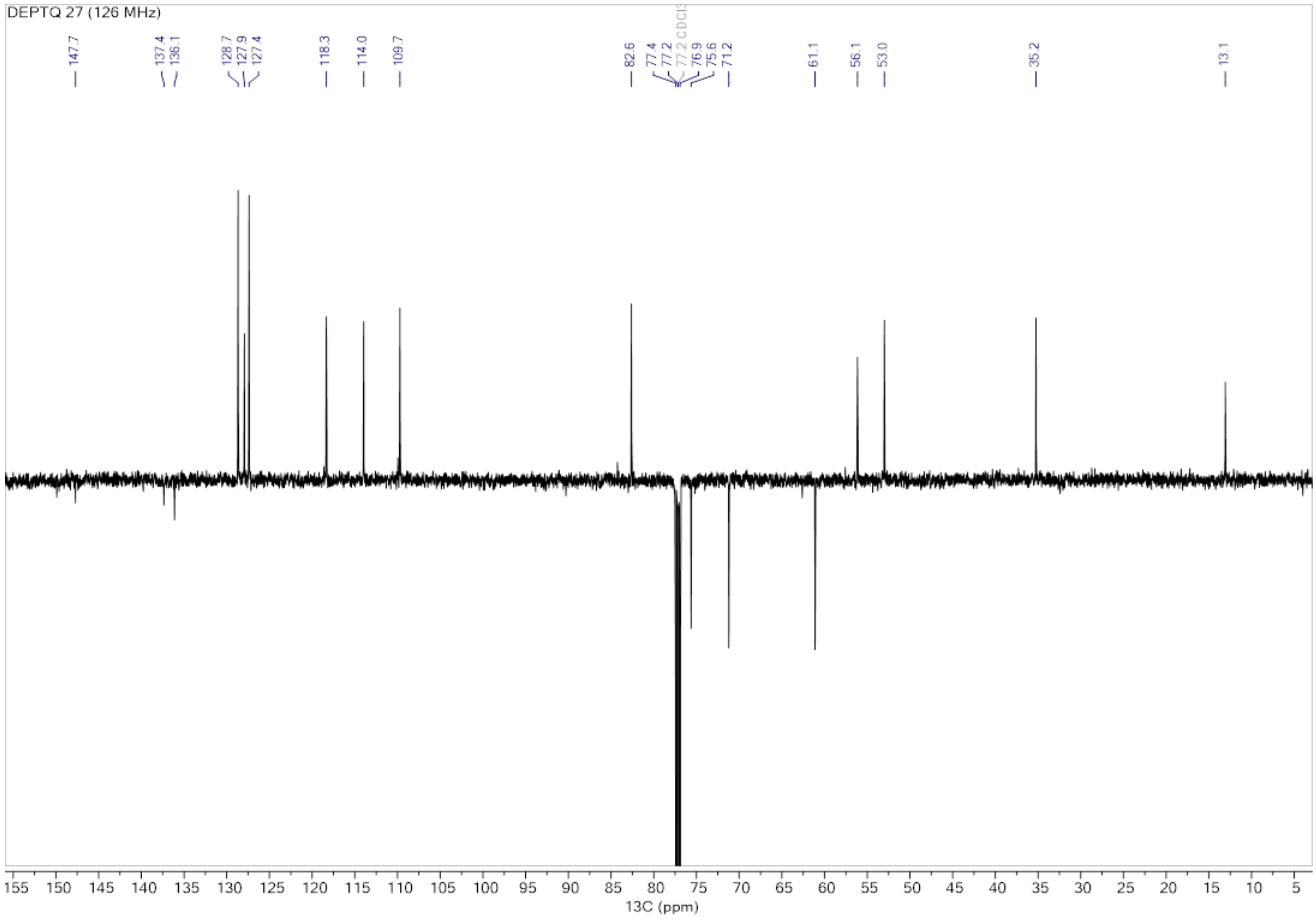
NMR spectra for compound 26.



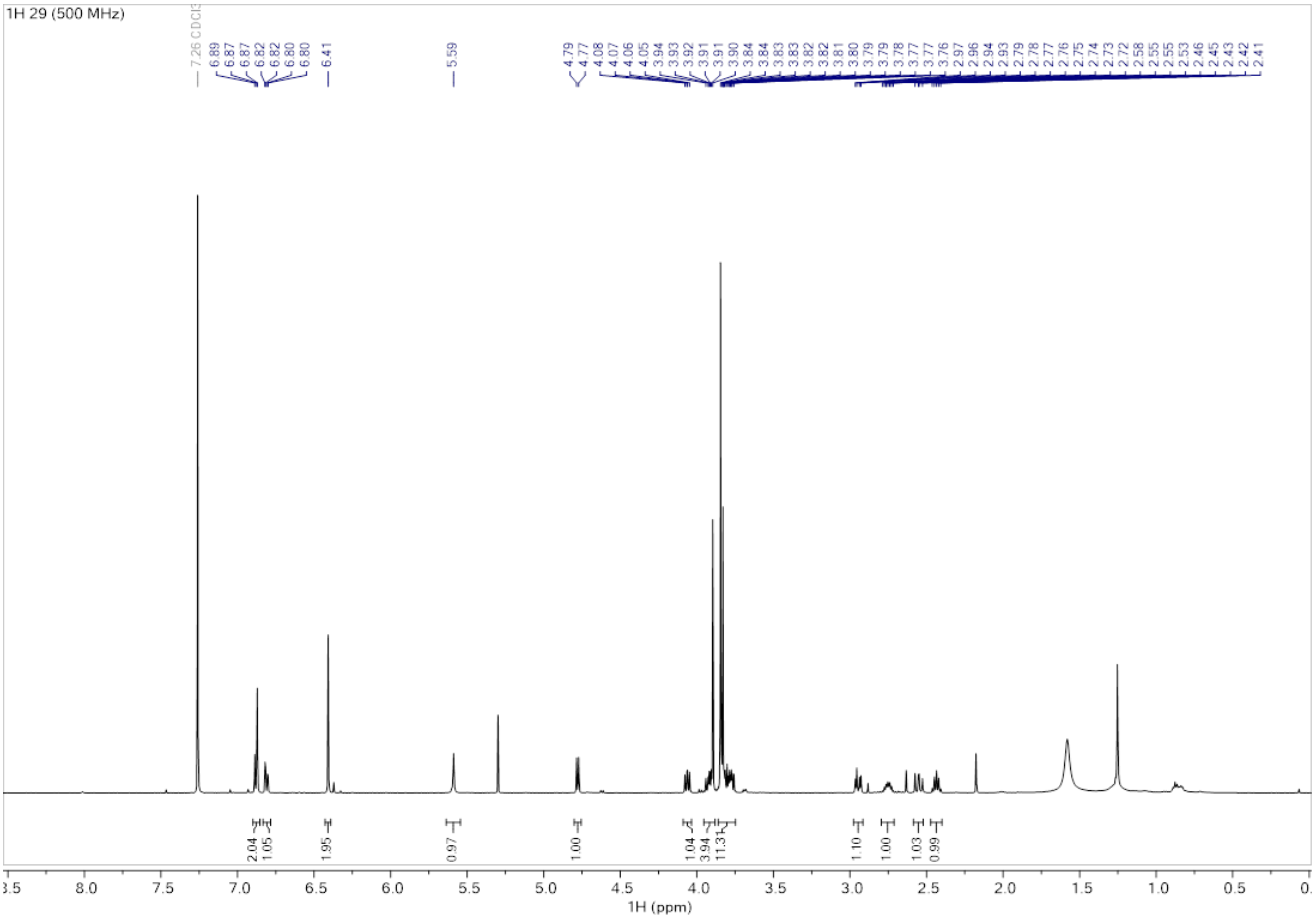


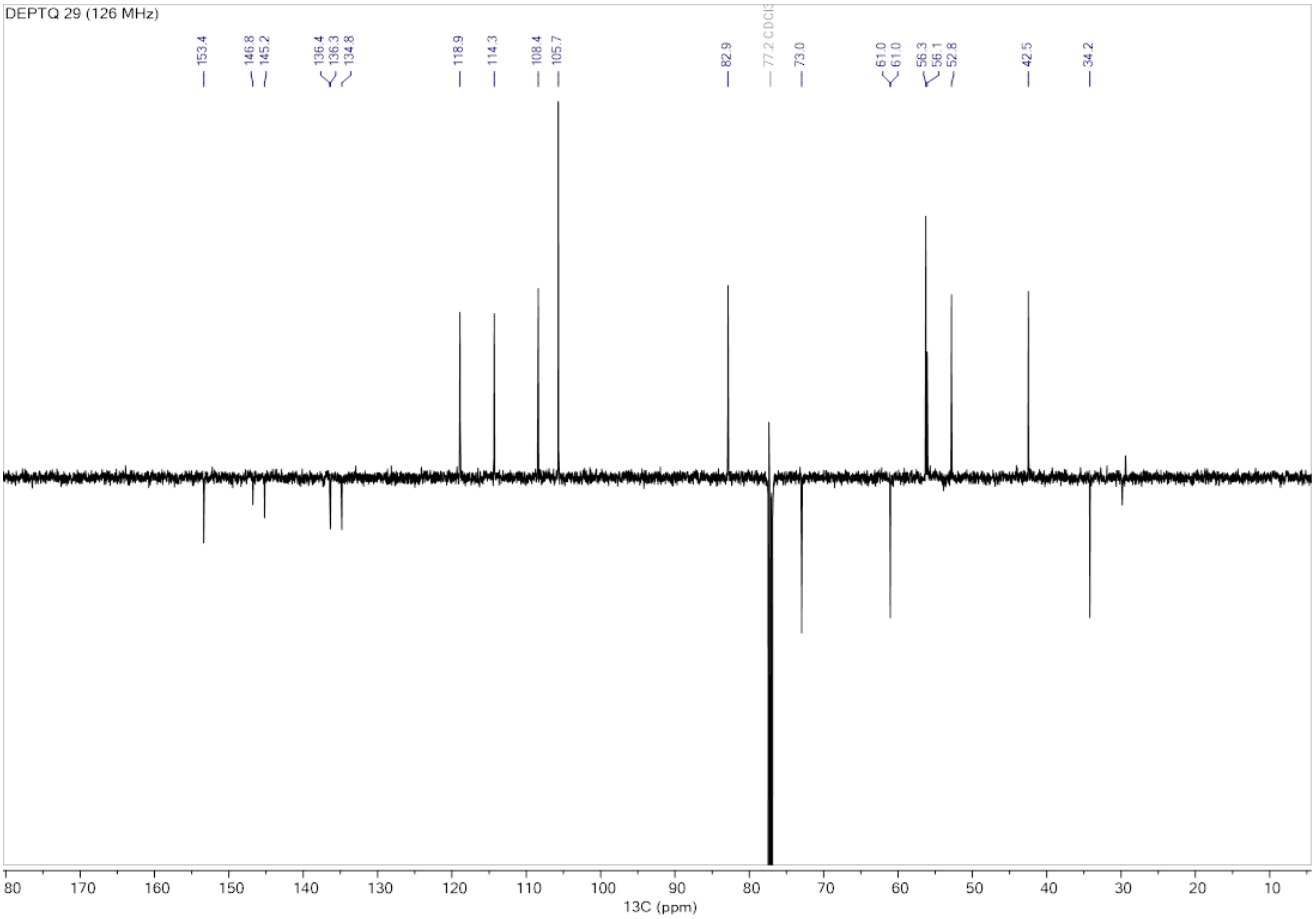
NMR spectra for compound 27.





NMR spectra for compound 29.





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