Electronic Supplementary Information

Diastereoisomeric enrichment of 1,4–enediols and H_2–splitting inhibition on Pd–supported catalysts

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Experimental Section.

– General.

Glassware was dried in an oven at 175 ºC before use. Reagents and solvents were obtained from commercial sources and were used without further purification otherwise indicated. Products were characterized by gas chromatography– mass spectrometry and ^{1}H, ^{13}C and DEPT liquid nuclear magnetic resonance, and the resulting spectra compared with the given literature. The metal content of the samples was determined by inductively coupled plasma–atomic emission spectroscopy (ICP–AES). Solids were disaggregated in aqua regia and later diluted before analysis.

– Physical techniques.

Gas chromatography–mass spectrometry. Gas chromatographic analyses were performed in an instrument equipped with a 25 cm capillary column of 5% phenylmethylsilicone. *N*–dodecane was used as an external standard. Gas chromatography–mass spectrometry analyses were performed on a spectrometer equipped with the same column as the GC and operated under the same conditions.

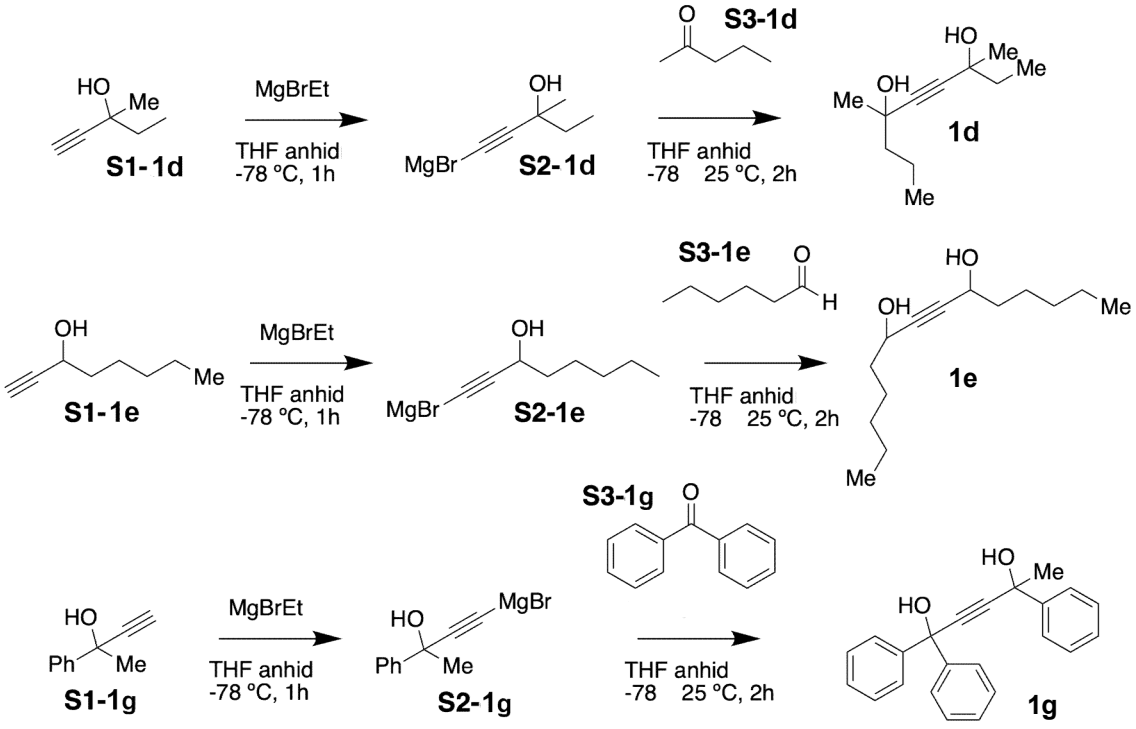
Nuclear magnetic resonance. ^{1}H, ^{13}C and distortionless enhancement by polarization transfer (DEPT) liquid nuclear magnetic resonance (NMR) measurements, and also 2D–nuclear Overhauser enhancement spectroscopy (NOESY), were recorded on a 400 MHz Bruker Avance instrument at room temperature, using deuterated chloroform as a solvent, which contains TMS as internal standard.

Raman spectroscopy. The Raman spectra of the Lindlar and Pd/C catalysts with or without **2a**/**3a** were obtained with an excitation wavelength of 514 nm in a Renishaw inVia spectrometer, under a stream of H_2.

H_2 / D_2. A fixed–bed reactor was loaded with 2–5 mg of catalyst. After maintaining an argon flow rate of 18 ml/min for 20 min, 1 ml/min H_2 and 1 ml/min D_2 were added to the argon stream (total flow rate of 20 ml/min). This mixture of Ar, H_2 and D_2 was flowed for 15 min through the reactor bypass to calibrate the signal and then approximately 15 min through the fixed bed to obtain the measurement. The pressure was kept constant at 1 bar, and the temperature was maintained at 30 °C throughout the experiment. The compounds at the reactor exit (H_2, D_2, H–D) were quantified by on–line mass spectroscopy (m/z = 2, 4 and 3, respectively).

– Reaction procedures.

*Synthesis of cis–1,4–acetylene diols **1d, 1e and 1g***. To synthesize diol **1d**, 8 mmol of 3–methyl–1–pentin–3–ol (**S1–1d**) were dissolved in 15 mL of anhydrous THF and the mixture was stirred and cooled to –78 °C in a dry ice bath. Then, 3 equivalents of ethylmagnesium bromide were introduced dropwise, considering that part of it is deactivated in contact with alcohol, to form the intermediate (**S2–1d**). After 1 h, 1.2 equivalents of 2–pentanone (**S3–1d**) were added and the dry ice bath was removed, allowing the reaction to reheat to room temperature. The reaction was left to stir for 2 h and then neutralized in 15 mL of water. The mixture was extracted with CH_2Cl_2, dried over $MgSO_4$ and purified by column chromatography. The final yield of 37 was 93%. The same procedure was followed to synthesize substrate **1e**, using 5 mmol of 1–octin–3–ol (**S1–1e**), and 1.2 equivalents of 1–hexanal (**S3–1e**). Final yield of 90%. The same procedure was followed to synthesize the substrate **1g**, using 5 mmol of 2–phenyl–3–butyn–2–ol (**S1–1g**), and 1.2 equivalents of benzophenone (**S3–1g**). Final yield of 71%. The remaining diols (**1a**, **1b**, **1c** and **1f**) were purchased from commercial sources.



*Synthesis of trans–2,4,7,9–tetrametyl–5–decen–4,7–diol (**4a**)*. 500 mg (2.2 mmol) of **1a** were dissolved in 15 mL of anhydrous THF and the mixture was stirred and cooled to 0 °C in an ice bath. Then, 4 equivalents of $LiAlH_4$ in a 2 M solution in THF were introduced

dropwise (4.4 mL). The progress of the reaction was constantly measured by taking reaction aliquots, neutralizing them in water, extracting them in THF and monitoring the GC conversion. The reaction reached full conversion after 90 minutes, and was at that point neutralized in 15 mL of water. The mixture was extracted with CH_2Cl_2, dried over $MgSO_4$. Final yield of 95% for **4a** (*trans*).

Semi–hydrogenation reactions. All the hydrogenation reactions were performed in a 6–mL round bottom vial with a stirring magnet, in 0.5 mL of ethanol or toluene, and 0.3 mmol of starting material, otherwise stated. The reactions were conducted at 30–65 ºC and stirred at 450 rpm, in a H_2 pressurized atmosphere of 3 bars. At the start of the reaction, the alkyne: H_2 molar ratio was roughly 1–2.5, and enough H_2 was always present to fully hydrogenate the alkyne to the corresponding alkane. The catalytic Pd amount was adjusted for each catalyst in order to precisely measure the initial rate for any substrate, i.e. Pd–$(CaCO_3)_n$ (0.003 mol%), c–Pd/TiS catalyst (0.015 mol% Pd), Pd/C catalyst (0.04 mol%) and the Lindlar catalyst (0.15 mol%) for TMDD **1a**. Yields were obtained by combined gas chromatography, gas chromatography–mass spectrometry and nuclear magnetic resonance, and the latter were used to identify the products.

Reuses. Reactions were performed and analyzed following the above procedure; conditions: 3 bar H_2, 0.6 M **1a** and 65 ºC. After reaction, the solid catalyst was recovered by either gravity filtration or centrifugation (3000 rpm), washed with ethanol and centrifugated again, and weighed for the next use.

$H_2O(^{18}O)$ isotopic exchange. The reaction was performed in a 6–mL round bottom vial with a stirring magnet, in 0.1 mL of H_2O or $H_2{}^{18}O$, with 70 mg (0.3 mmol) of TMDD **1a** or 72 mg (0.3 mmol) of alkenediols **2a/3a**, and Lindlar catalyst (2 mg), in the presence or not of and H_2 (pressurized atmosphere of 3 bars). The reactions were conducted at 65 ºC, stirred at 450 rpm, and monitored by gas chromatography–mass spectrometry.

Typical poisoning experiment. The hydrogenation reaction was performed in a 6–mL round bottom vial with a stirring magnet, in 0.5 mL of ethanol or toluene, and 70 mg (0.3 mmol) of TMDD **1a**. Previously, the Lindlar cat. (2 mg) and alkenediols **2a/3a** (60 mg, 0.25 mmol) were mixed. The reactions were conducted at 60 ºC and stirred at 450 rpm, in a H_2 pressurized atmosphere of 3 bars, during 90 min. The reaction mas monitored by gas chromatography.

Tables.

Table S1. Semi–hydrogenation reaction of TMDD **1a** performed with different solvents (1 M, 0.3 mL solvent, 65 ºC, 10 bar H_2, 1 mg Lindlar cat., 12 h; see Table 1 in the main text). The mass balance is completed with dihydroxylation products.

Solvent	Conversion (%)	Alkene selectivity (%)	Diastereoisomeric ratio	Alkane selectivity (%)
Solventless	99.9	86.1	1:1.3	1.6
Ethanol	100.0	84.2	1:2.0	1.3
Heptane	100.0	86.3	1:2.0	0.4
Isopropanol	100.0	41.1	1:1.9	31.4
Toluene	100.0	88.7	1:2.5	0.0
Water	94.4	90.8	1:1.4	0.0

Table S2. Semi–hydrogenation reaction of TMDD **1a** performed with different catalysts (0.6 M, 0.5 mL EtOH, 65 ºC, 3 bar H_2, 3 h; see Table 1 in the main text).

Catalyst (metal content)	Cat. weight (mg)	Alkyne (%)	Alkenes (%)	Alkane (%)	–1OH (%)	–2OHs (%)
Lindlar (5 wt%)	1.0	0.4	86.4	7.9	4.8	0.5
c–Pd/TiS (0.5 wt%)	1.1	0.4	92.6	5.3	1.2	0.4
Pd–$(CaCO_3)_n$ (0.1 wt%)	1.0	0.0	95.4	0.0	1.2	3.4
Pd/C (1 wt%)	1.4	0.0	23.6	16.4	45.1	15
Pt/C (1 wt%)	1.1	0.0	47.8	9.8	27.5	14.8
Ni–Raney	5.0	0.0	45.9	25.9	14.4	13.8

Table S3. Semi–hydrogenation reaction of different 1,4–acetylene diols **1b–g** catalyzed by the Lindlar catalyst (0.15 mol%) under the reaction conditions indicated in Figure in the main text and also below. [a] 60% alkene, 7% alkane and 33% hydrogenolysis.

Entry	1,4–Acetylene diol	T (°C)	Conversion (%)	Alkene selectivity (%)	*cis*/*trans*	meso/*DL*
1	**1a**	65	100	96	96/4	67.0/33.0
2	**1b**	30	100	99	95/5	–
3	**1c**	30	96	100	97/3	60.3/39.7
4	**1d**	30	100	99	95/5	59.7/40.4
5[a]	**1e**	30	80	60	85/15	53.5/46.5
6	**1f**	65	100	99	95/5	–
7	**1g**	65	98	86	94/6	Not observed

Table S4. Results for the reaction of alkyne **1a** and alkenes **2a**/**3a** with $H_2O(^{18}O)$ (15 equivalents) in the presence of the Lindlar catalyst (0.15 mol%), followed by GC–MS. Isotopic incorporation is not observed in any case without the Lindlar catalyst.

		Water	1a-^{18}O	2a–3a-^{18}O	^{18}O incorporated (%)
Without H_2	Alkyne **1a**	^{16}O	0.0	–	48.7
		^{18}O	48.7	–	
	Alkenes **2a/3a**	^{16}O	–	14.6	5.6
		^{18}O	–	20.2	

Table S5. Semi–hydrogenation reaction of phenylacetylene performed with different palladium catalysts in the presence or not of **2a**/**3a** (0.6 M, 0.5 mL toluene, 60 ºC, 3 bar H_2, 5 h). Conversion is 100% in all cases.

Catalyst (metal content)	2a/3a	mol% Pd	Styrene	Ethylbenzene
Lindlar (5 wt%)	No	0.19	2.7	97.3
Pd/C (1 wt%)		0.04	0.0	100.0
Lindlar (5 wt%)	Mixed with catalyst	0.19	41.2	58.8
Pd/C (1 wt%)		0.03	0.0	100.0
Lindlar (5 wt%)	Added in solution	0.20	51.2	48.8
Pd/C (1 wt%)		0.04	11.8	88.2

Figures.

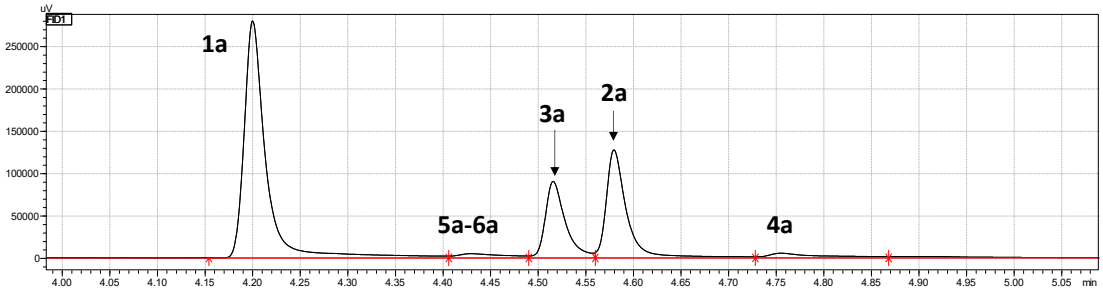


Figure S1. Gas chromatogram for the semi–hydrogenation reaction of TMDD **1a** (Table 1 in the main text, entry 1).

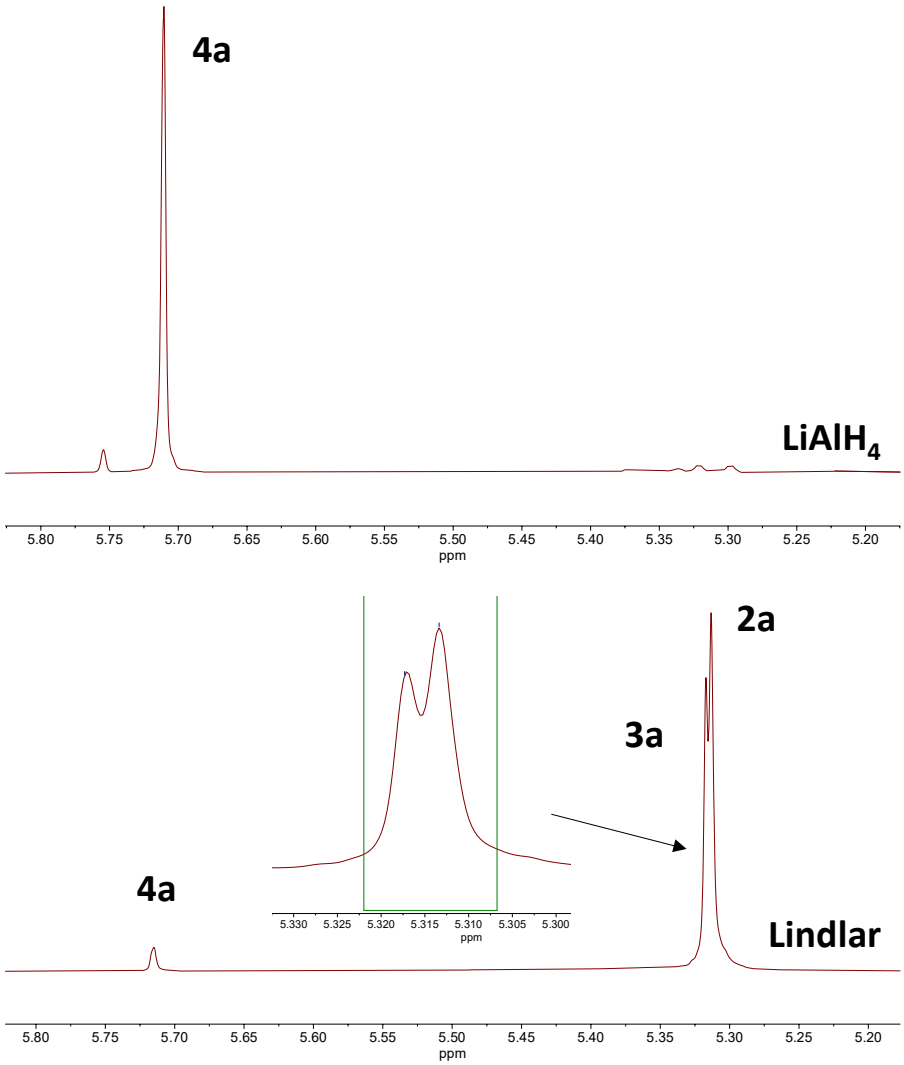


Figure S2. Bottom: ^{1}H NMR spectrum of the isolated products from the semi–hydrogenation reaction of TMDD **1a** (Table 1 in the main text, entry 1), the inset magnifies the diasteroisomer area. Top: ^{1}H NMR spectrum of the isolated products from the reaction of **1a** with $LiAlH_4$.

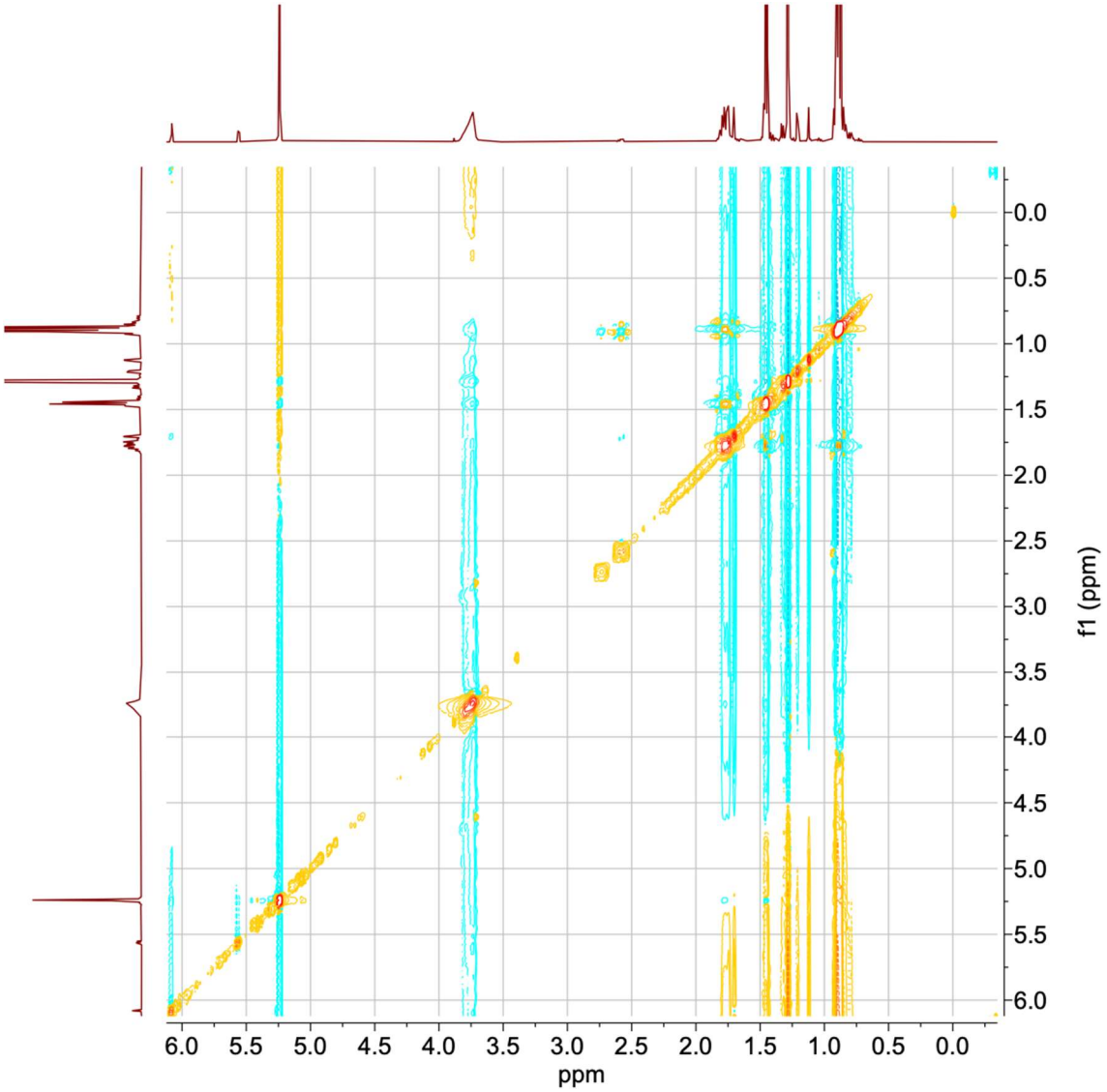


Figure S3. a) NOESY 2D NMR of alkenediol *cis*–**2a+3a**.

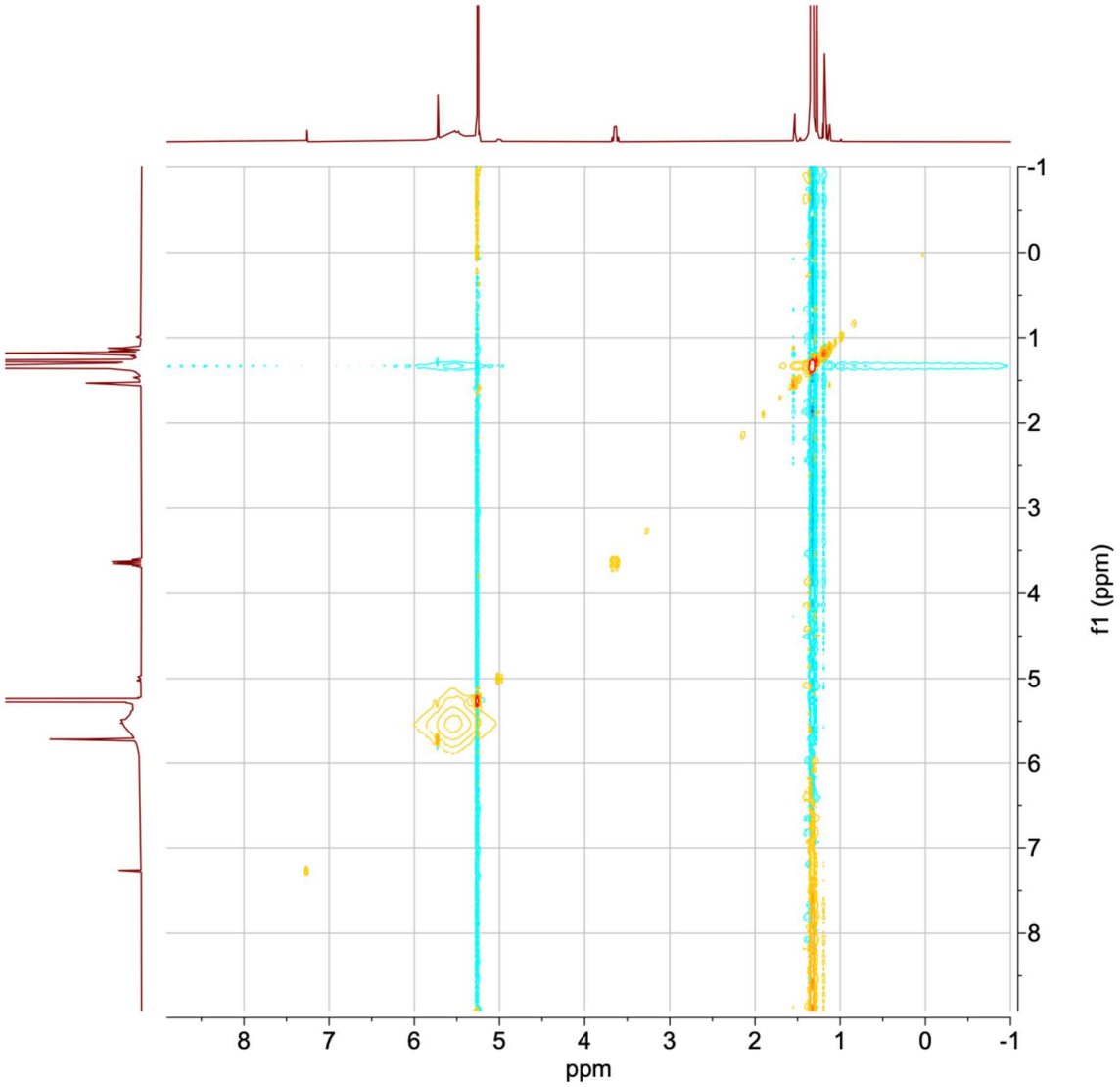


Figure S3. b) NOESY 2D NMR of alkenediol *cis*–**2b**+**3b**.

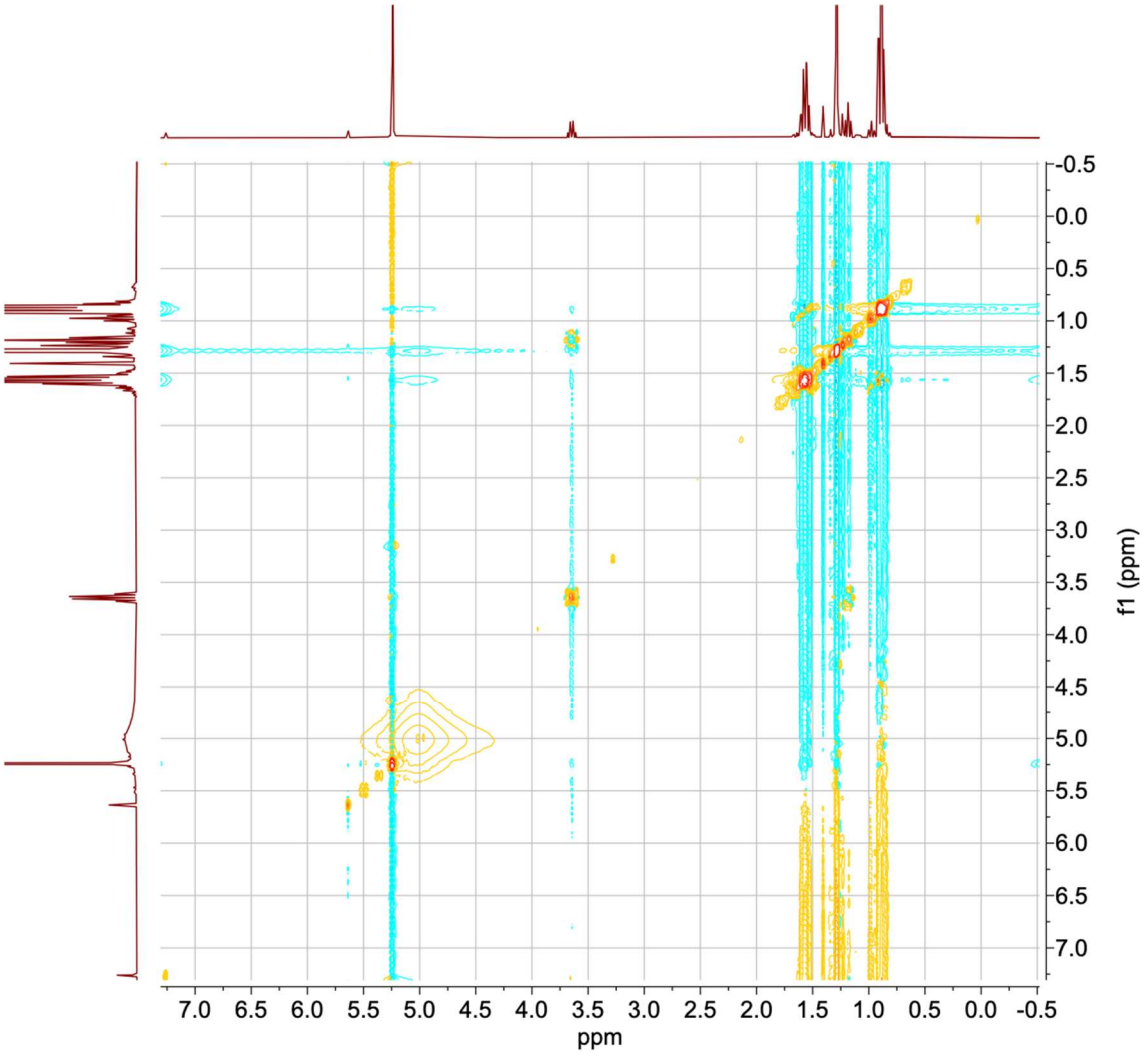


Figure S3. c) NOESY 2D NMR of alkenediol *cis*–**2c+3c**.

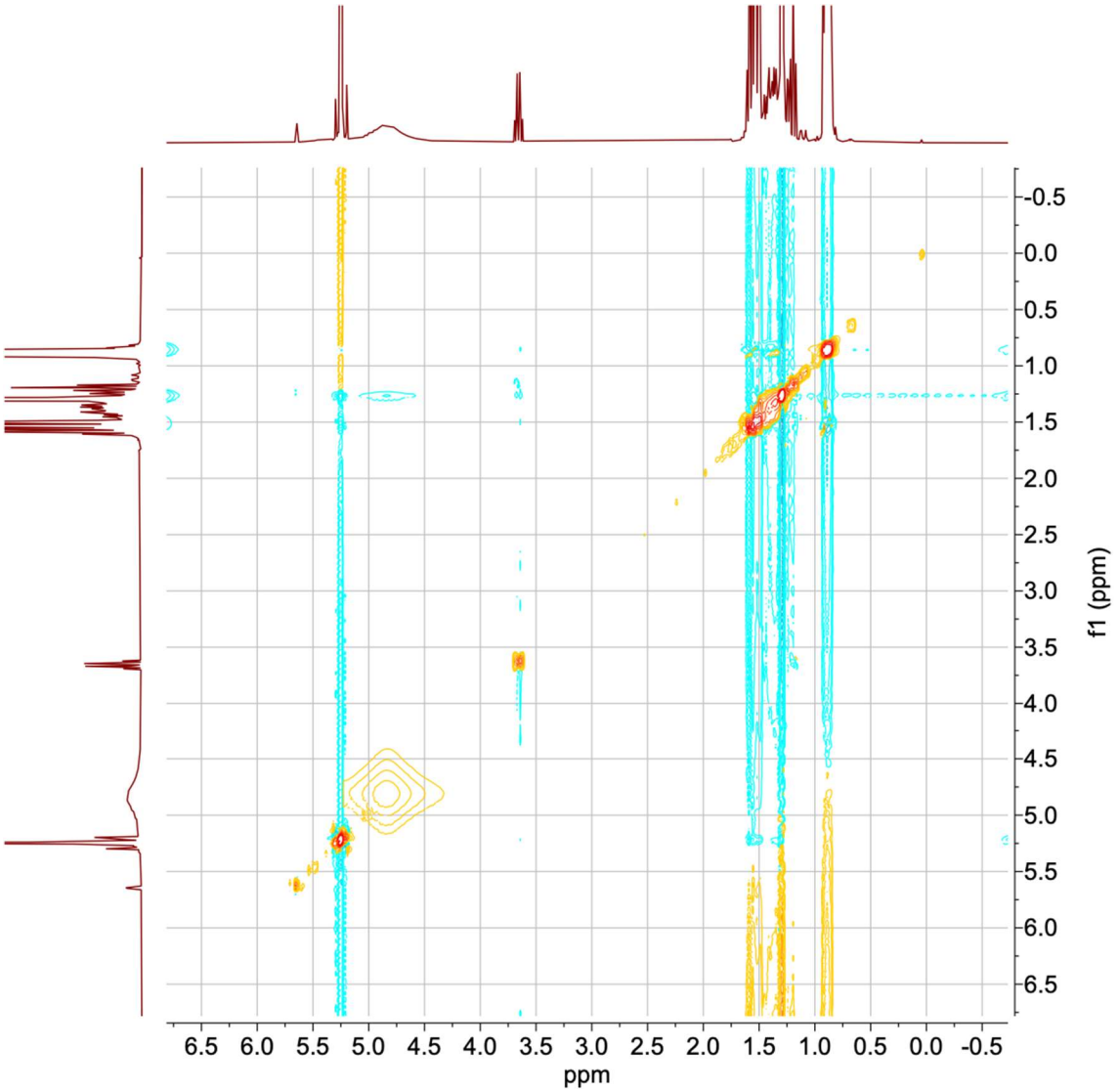


Figure S3. d) NOESY 2D NMR of alkenediol *cis*–**2d+3d**.

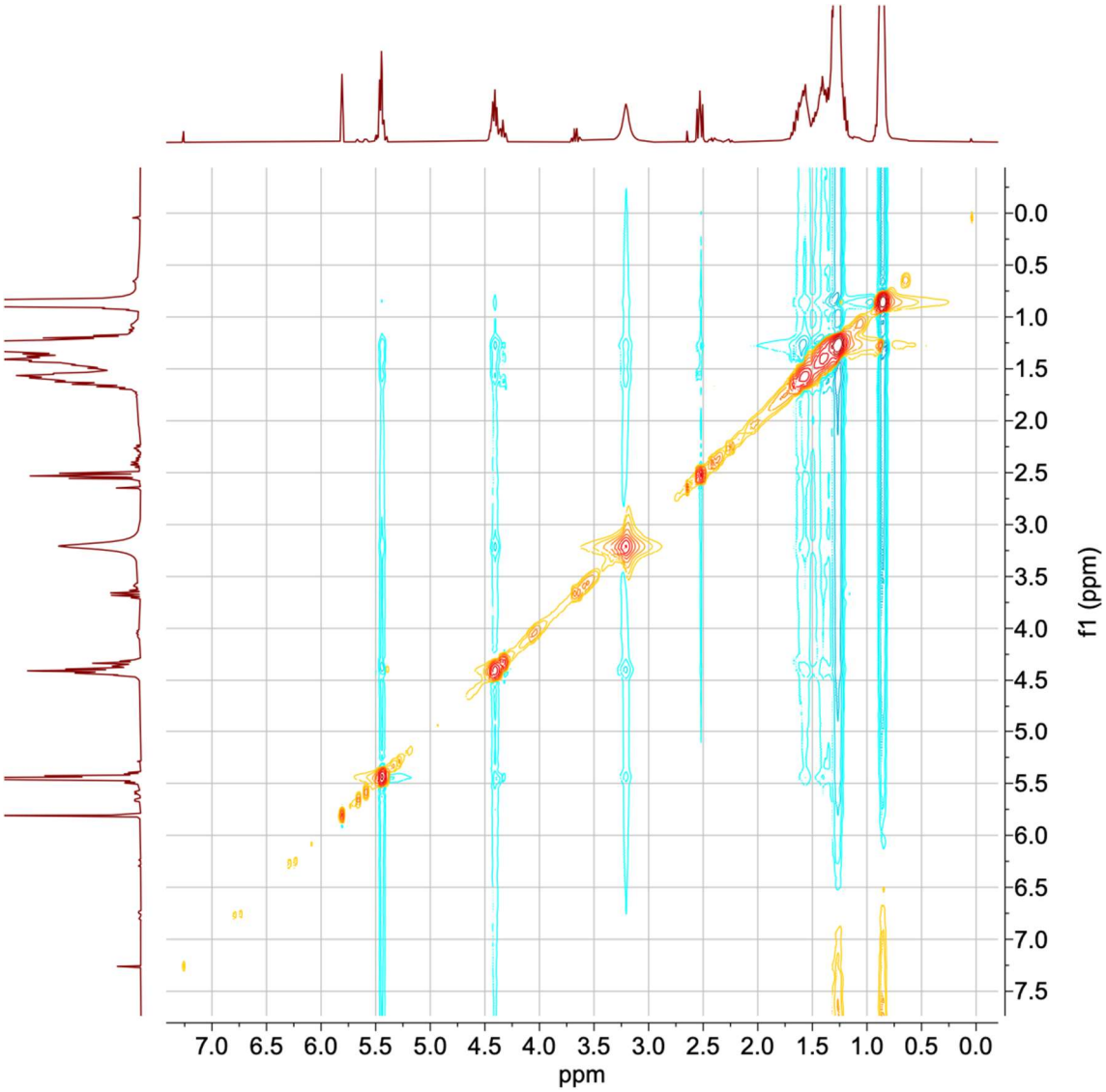


Figure S3. e) NOESY 2D NMR of alkenediol **2e+3e**.

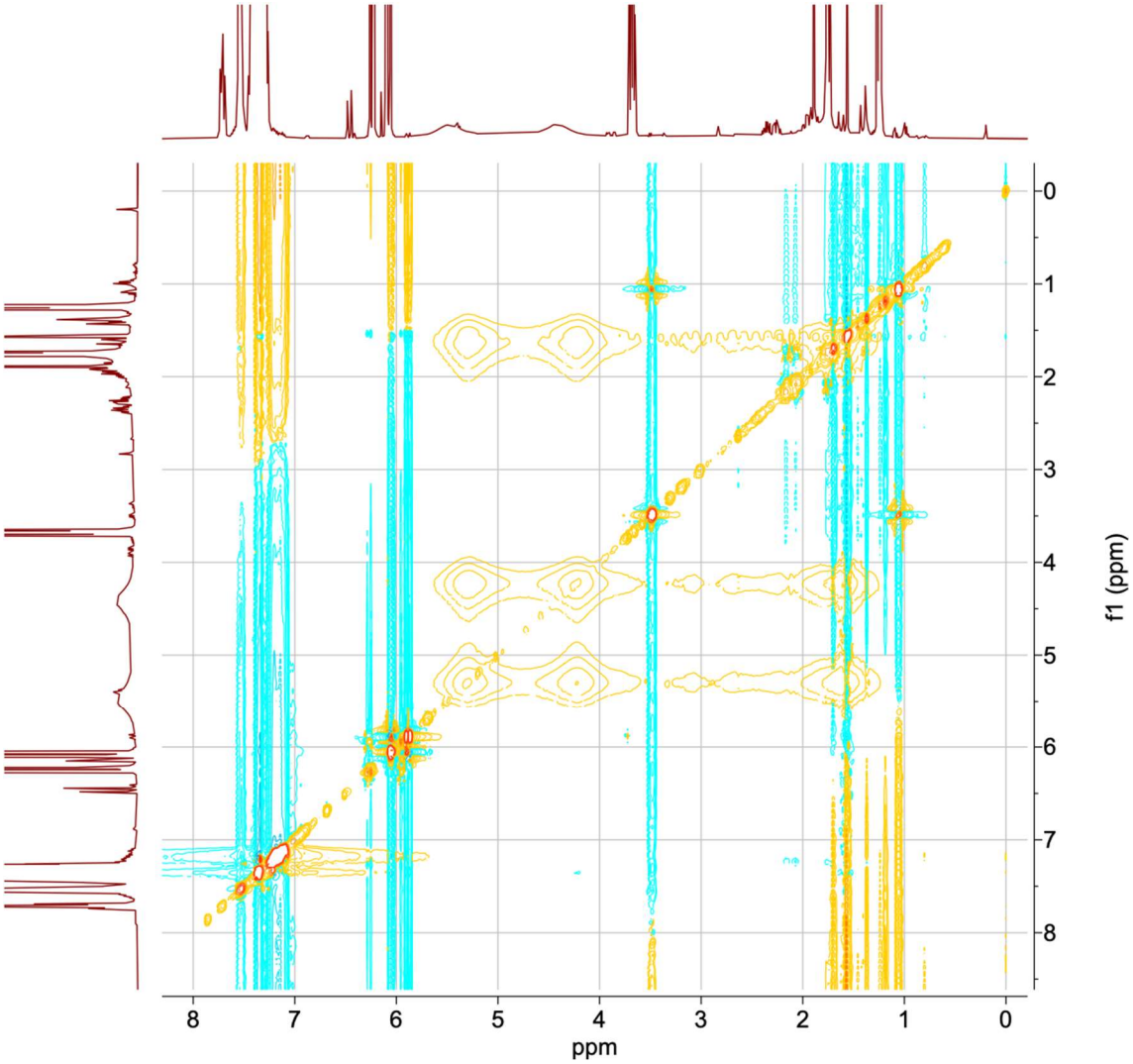


Figure S3. f) 2D–NOESY of alkenediol **2g+3g**.

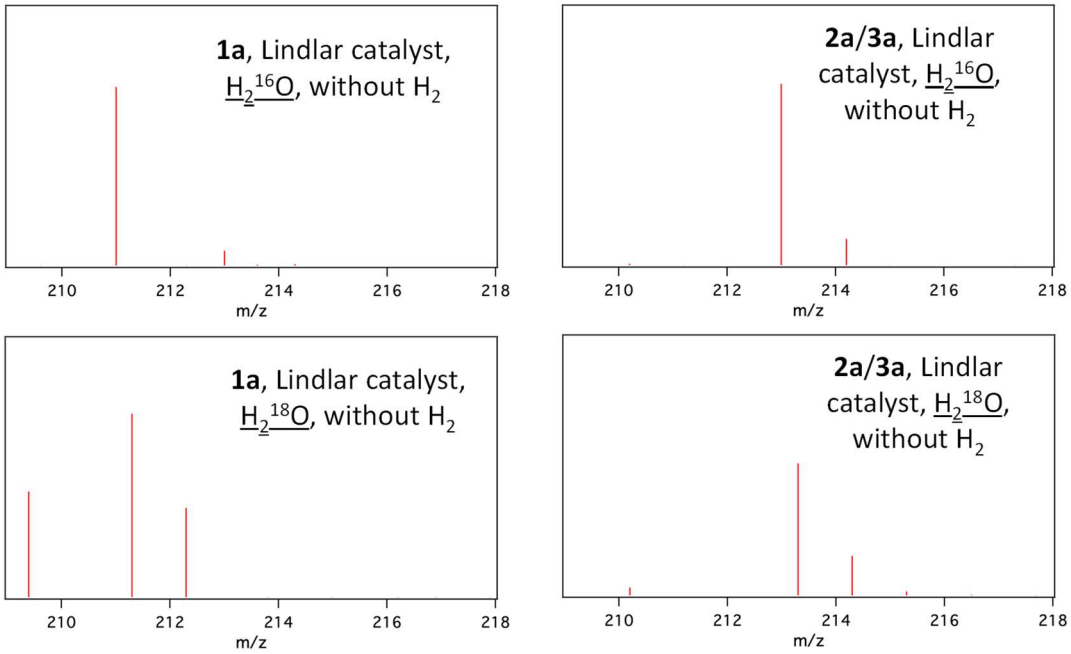


Figure S4. GC–MS spectra for the reaction of alkyne **1a** (left) and alkenes **2a**/**3a** (right) with $H_2O(^{18}O)$ (15 equivalents) in the presence of the Lindlar catalyst (0.15 mol%).

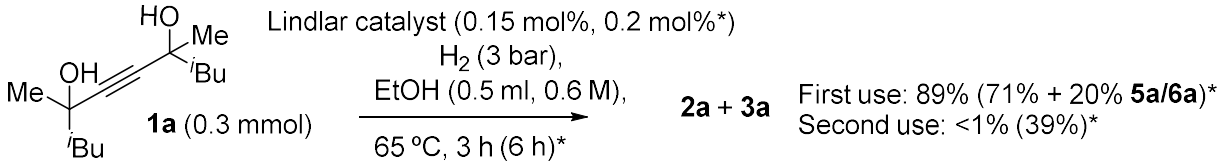


Figure S5. Results for the semi–hydrogenation reaction of TMDD **1a** catalyzed by the Lindlar catalyst in ethanol, under the indicated reaction conditions, before and after recovering the solid catalyst by simple filtration and washings with ethanol. * Denotes a second experiment with more Pd catalyst and reaction time.

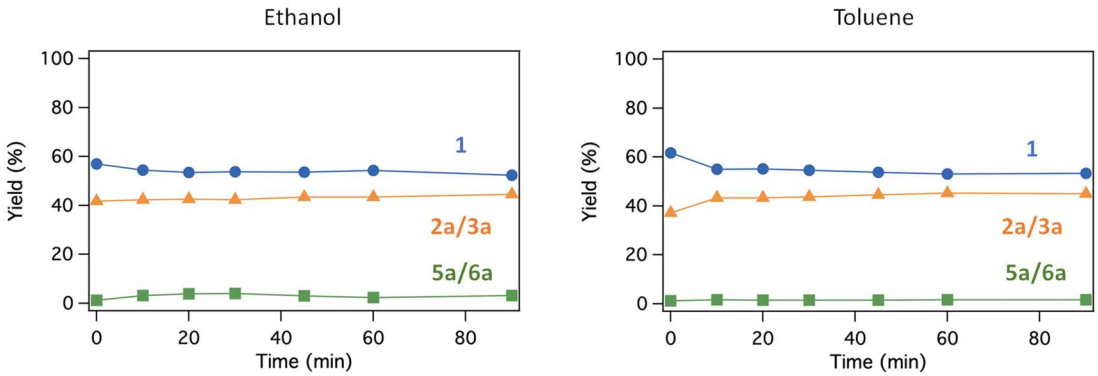


Figure S6. Kinetic results for the semi–hydrogenation reaction of TMDD **1a** (60%) mixed with the alkene products **2a**/**3a** (40%) catalyzed by the Lindlar catalyst in ethanol (left) or toluene solvent (right), under the indicated reaction conditions in Table 1 of the main text.

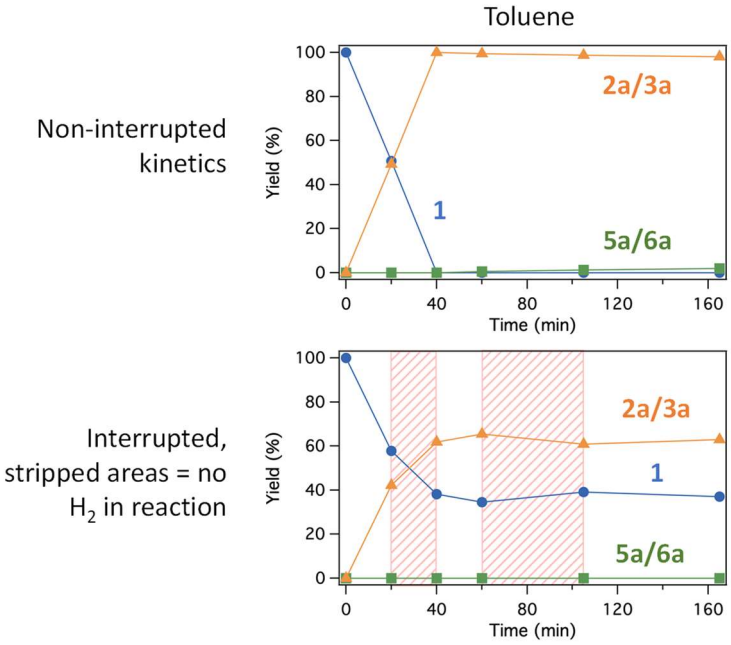


Figure S7. Kinetics for the semi–hydrogenation reaction of TMDD **1a** catalyzed by the Lindlar catalyst in toluene instead than in ethanol solvent, under the indicated reaction conditions in Figure 3 of the main text.

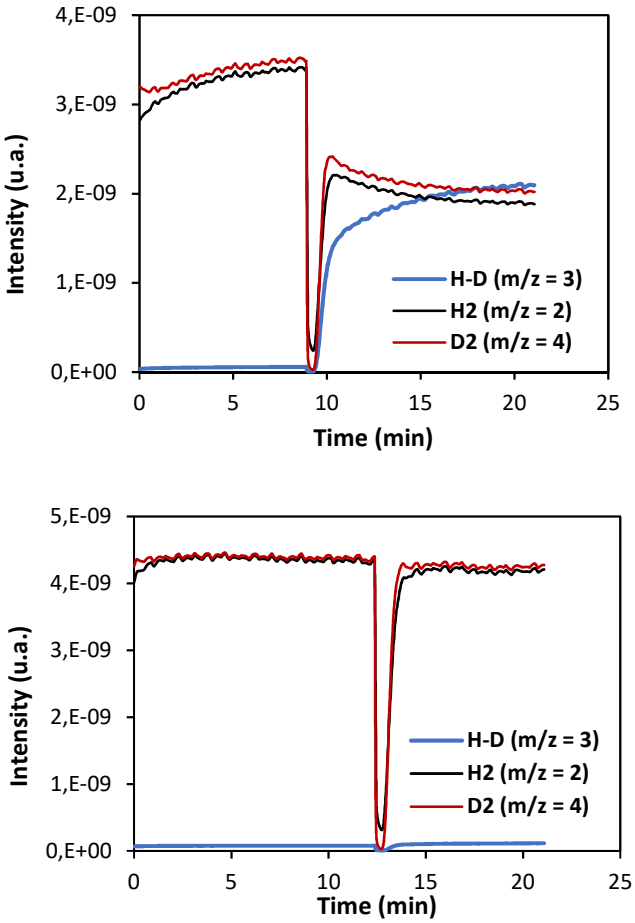


Figure S8. H_2–D_2 isotopic exchange experiments, at 30 ºC, for the fresh Pd/C catalyst (top) and poisoned Pd/C catalyst, with the **2a**+**3a** mixture (bottom).

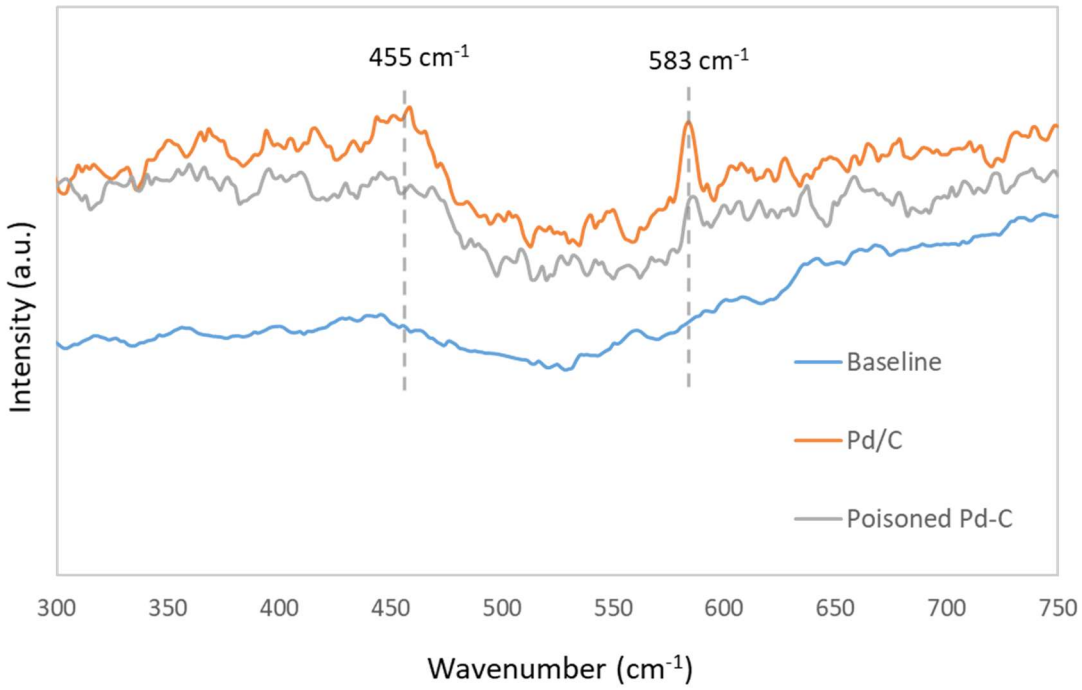


Figure S9. Raman spectra of a commercial sample of Pd/C under a flow of H_2, previously treated (gray) or not (orange) with the 1,4 enediols **2a**/**3a**. It can be seen how the signals assigned to the Pd–H bonds formed after H_2 splitting on the Pd sites, at 455 and 583 cm^{-1}, are much smaller in the treated material, and do not appear in the baseline spectra (blue), measured with the same catalyst under argon.

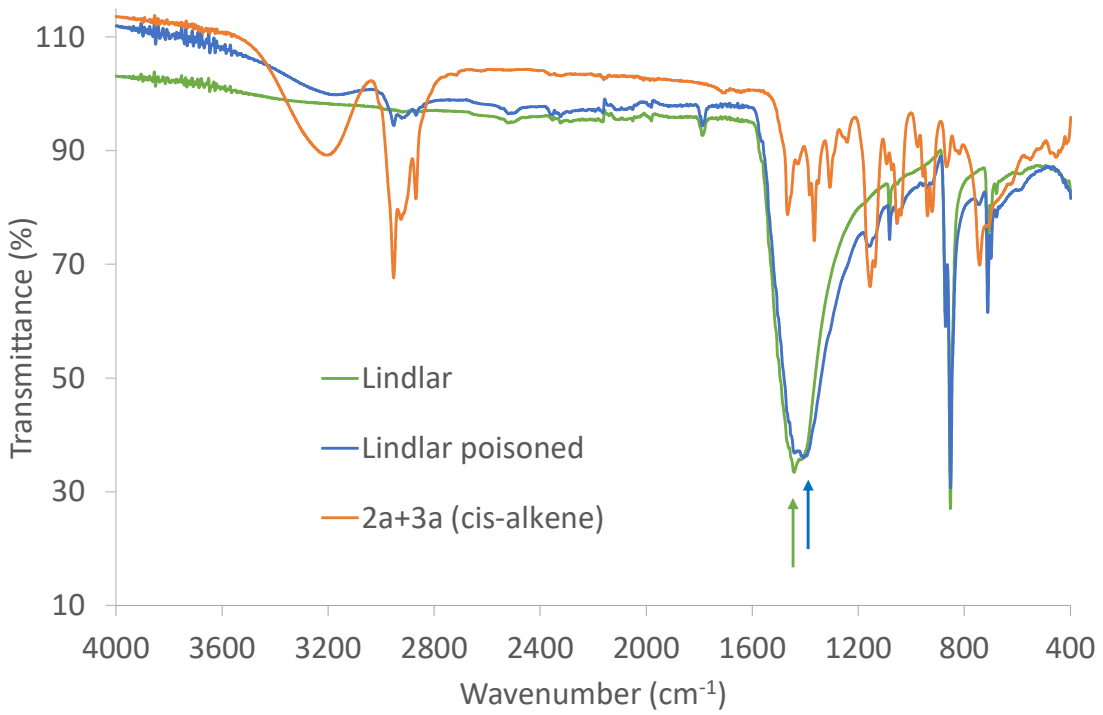


Figure S10. Fourier-transformed infrared (FT-IR) spectra of the Lindlar catalyst before and after adding the 1,4 enediols **2a/3a**. For the sake of comparison, the spectrum of neat 1,4 enediols **2a/3a** is also shown. The arrows indicate the change in the carbonate band.

Substrate	Pd Lattice	E_{ads} (Kcal·mol^{-1})
1a	111	-4.6
	100	-23.9
	110	-15.2
2a	111	-32.9
	100	-19.3
	110	-13.1
1h	111	-14.9
	100	-17.9
	110	-8.3

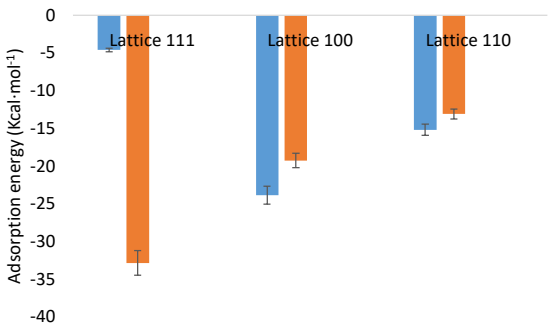


Figure S11. Calculated adsorption energies of **1a**, **2a** and 2-butyn-1,4-diol **1h** on different Pd crystal slabs [(100), (110) and (111)] (left) and graphical comparison of the relative adsorption energies for **1a** and **2a**. The graph neural network GAME–Net was employed (see Ref. 39 in the main text). Error bars account for a 5% uncertainty.

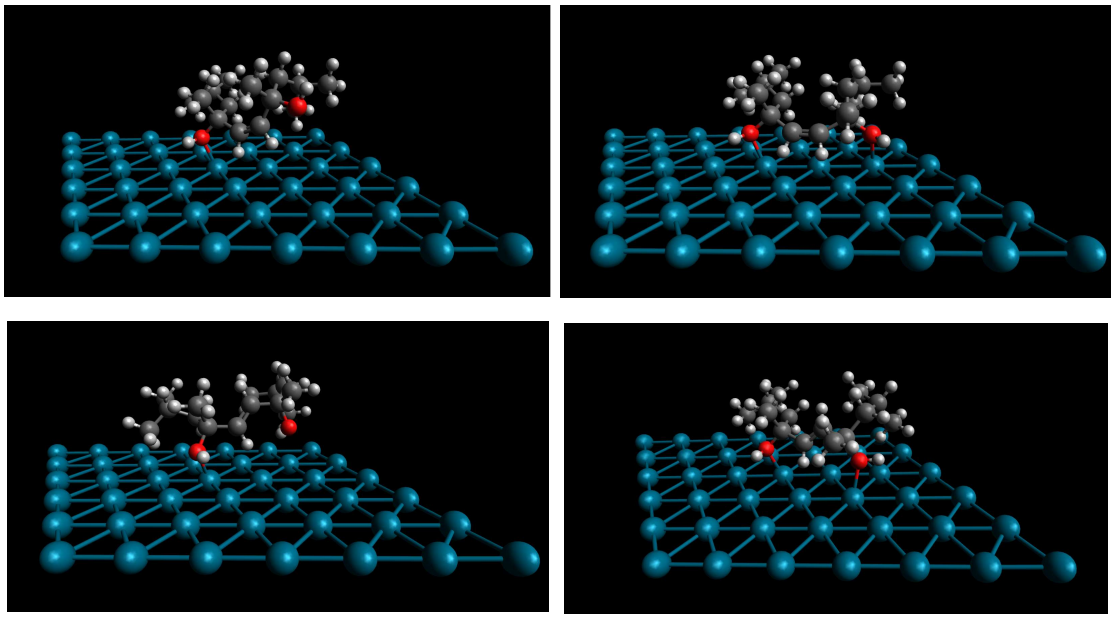


Figure S12. Modelling of alkenes **2a** (*cis*, top) and **4a** (*trans*, bottom) on a Pd (111) slab, with either one (left) or the two OH groups bound to Pd (right). Color code: Pd blue spheres, C grey spheres, H white spheres and O red spheres.

Reactant and product characterization.

^{1}H NMR of synthesized 1,4–alkynediols 1d, 1e, 1g.

^{1}H NMR **1d** (400 MHz, $CDCl_3$)
δ 2.20 – 2.00 (s, broad, 2H), 1.74 – 1.57 (m, 4H), 1.54 – 1.40 (m, 2H), 1.46 (s, 3H), 1.45 (s, 3H), 1.01 (s, 3H), 0.95 (s, 3H).

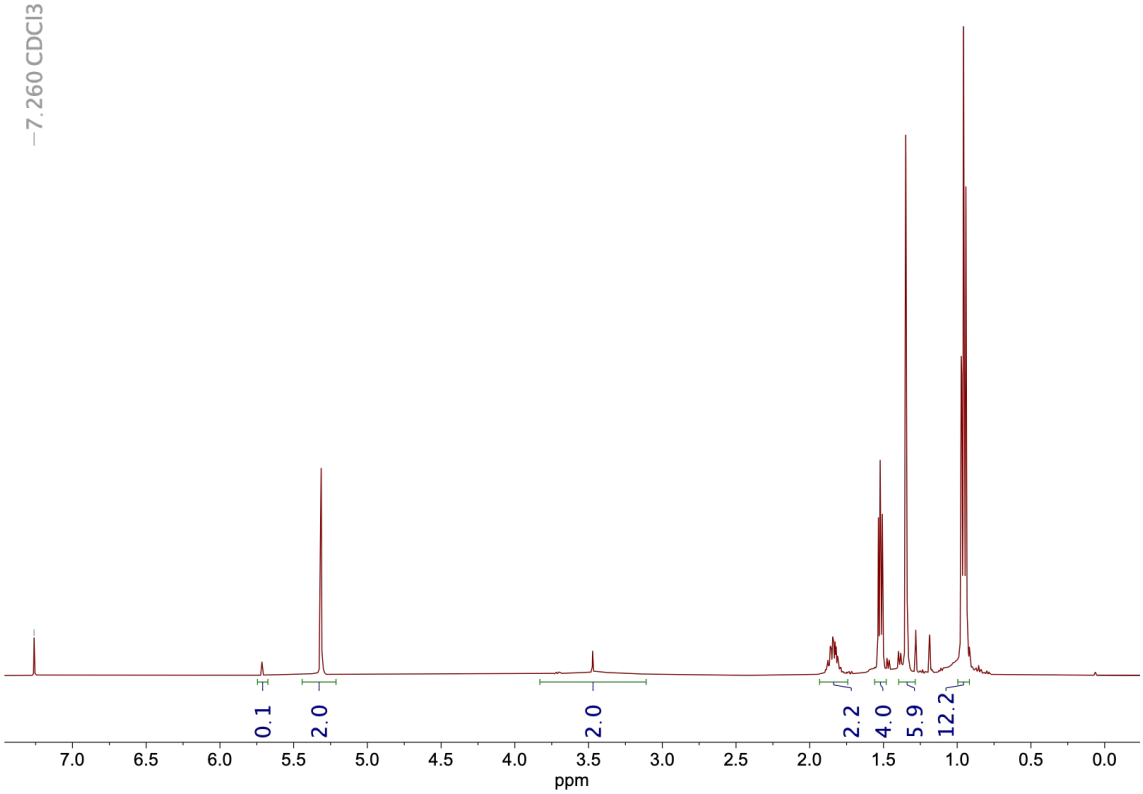
^{1}H NMR **1e** (400 MHz, $CDCl_3$) δ 4.39
(dt, J = 5.9, 1.7 Hz, 2H), 2.50 (s, broad 2H), 1.80 – 1.56 (m, 3H), 1.43 (m, 3H), 1.37 – 1.23 (m, 8H), 0.92 – 0.85 (dt, J = 7.0, 6H).

^{1}H NMR **1g** (300 MHz, $CDCl_3$)
δ 7.59 – 7.50 (m, 6H), 7.30 – 7.15 (s, 9H), 1.76 (s, 3H). Hydroxyl groups were not observe don the starting product (**1g**) but could be observed on the semi–hydrogenated product (**2g+3g**).

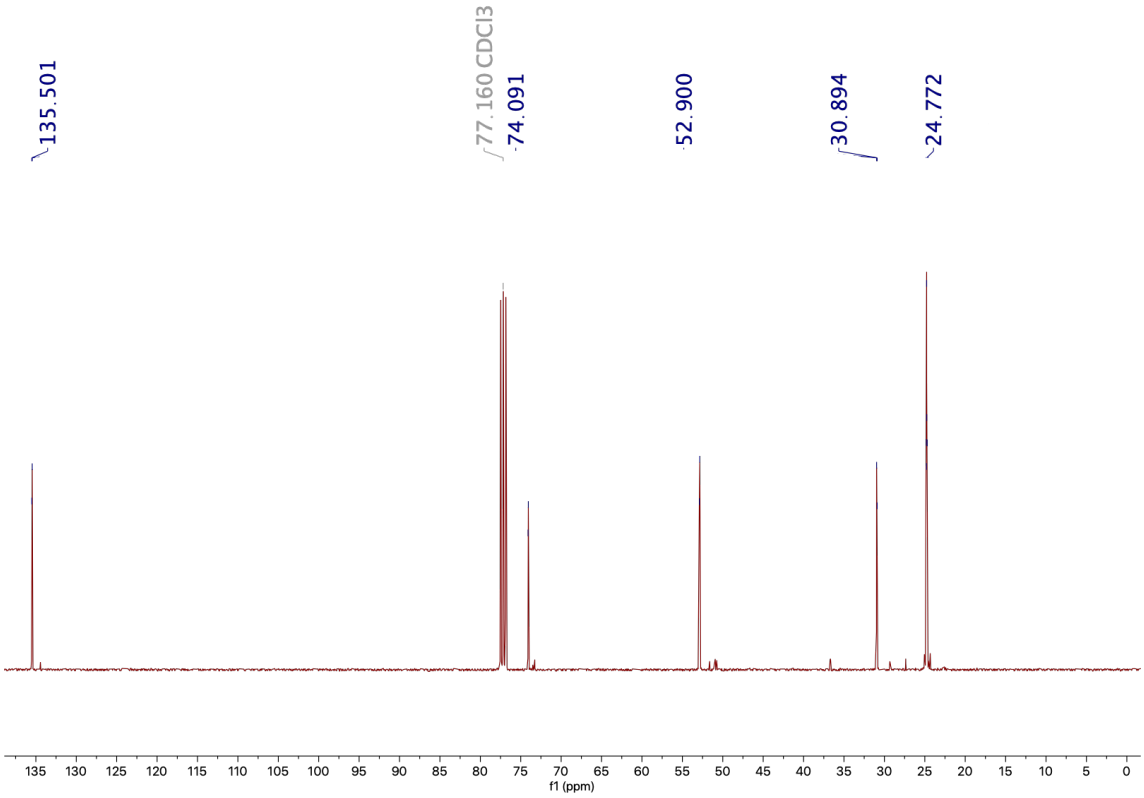
^{1}H NMR of synthesized 4a (*trans*–) from alkynediol 1a with $LiAlH_4$

^{1}H NMR **4a** (401 MHz, $CDCl_3$) δ 5.72 (ds, 2H), 1.87 – 1.74 (m, 2H), 1.46 (m, 4H), 1.28 (s, 6H), 0.92 (m, 6 Hz, 12H). Hydroxyl groups were not observed for this product, but could be observed for the *cis*– counterpart.

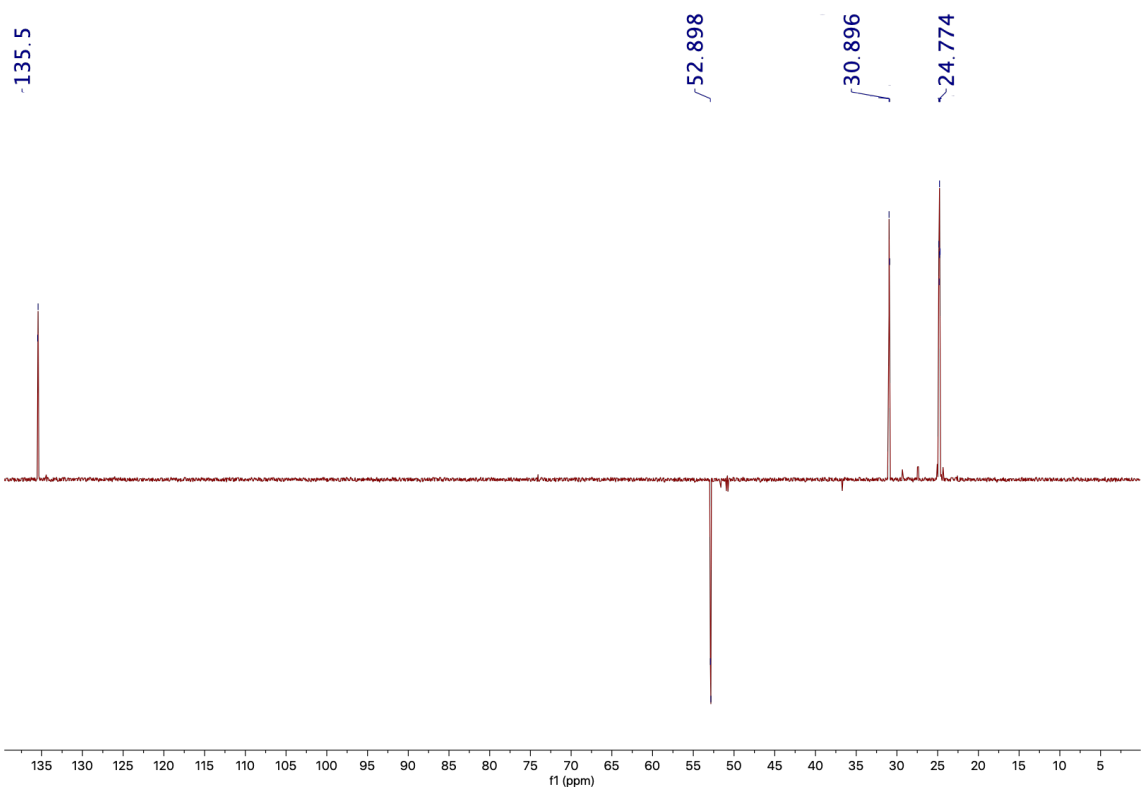
^{1}H, ^{13}C and DEPT 135 NMR spectra of *cis*–alkenediols as diastereoisomeric mixtures from hydrogenation with molecular H_2 and Lindlar catalyst.



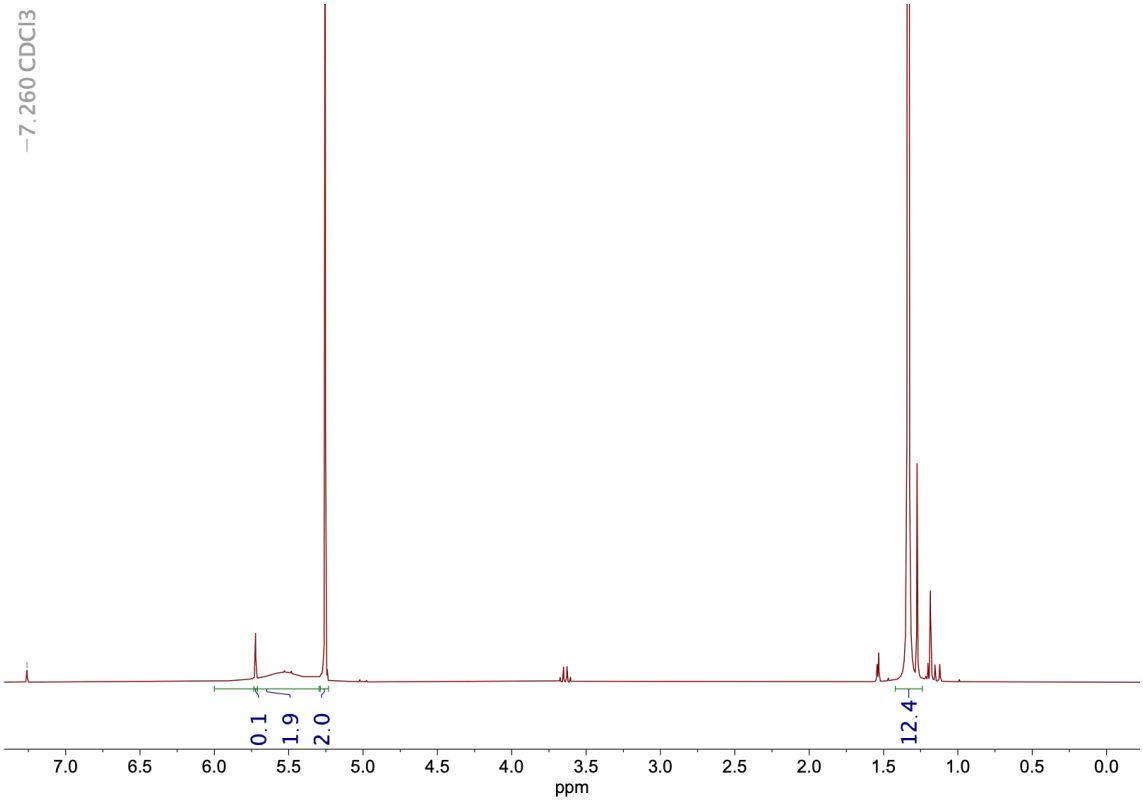
^{1}H NMR **2a+3a**: (401 MHz, $CDCl_3$) δ 5.72 (ds, 0.1H (*trans*, 2H)), 5.32 (ds, 2H), 3.47 (s, broad 2H), 1.92 – 1.77 (m, 2H), 1.52 (dd, J = 6.0, 5.0 Hz, 4H), 1.35 (ds, 6H), 0.97 (dt, 6 Hz, 12H).



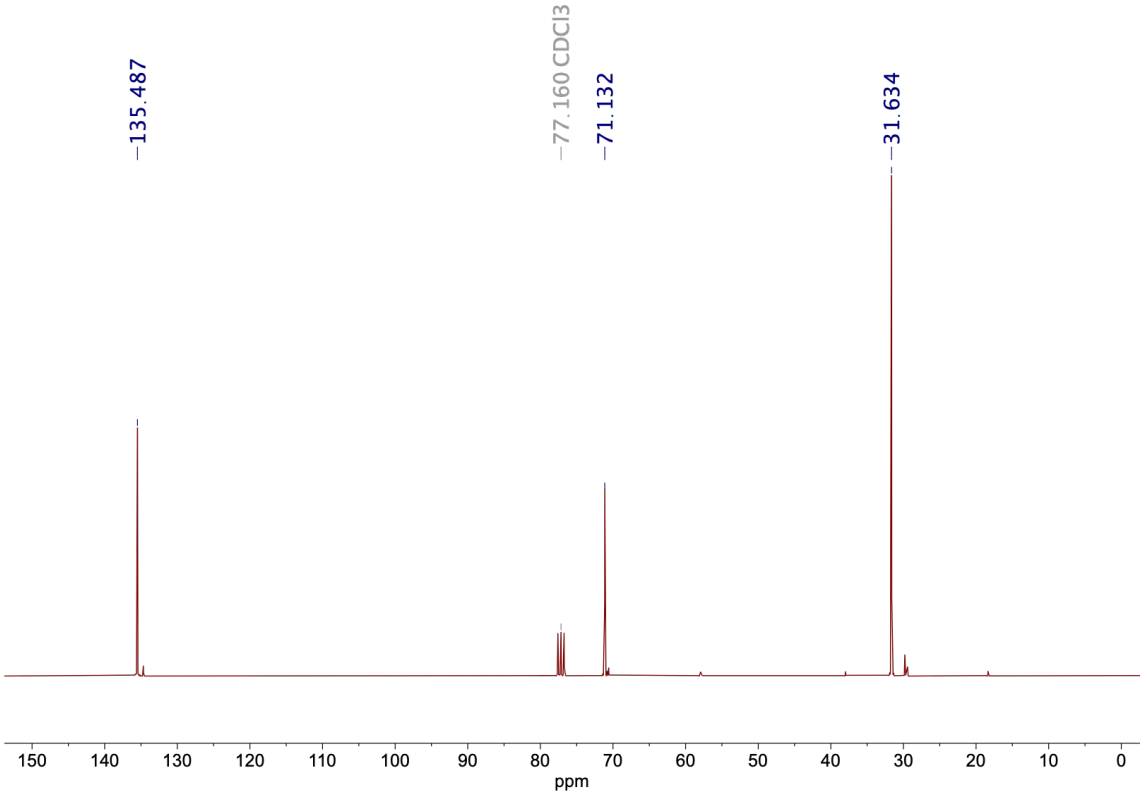
^{13}C NMR **2a**+**3a**: (75 MHz, $CDCl_3$) δ 135.50, 74.09, 52.90, 30.96, 30.89, 24.77.



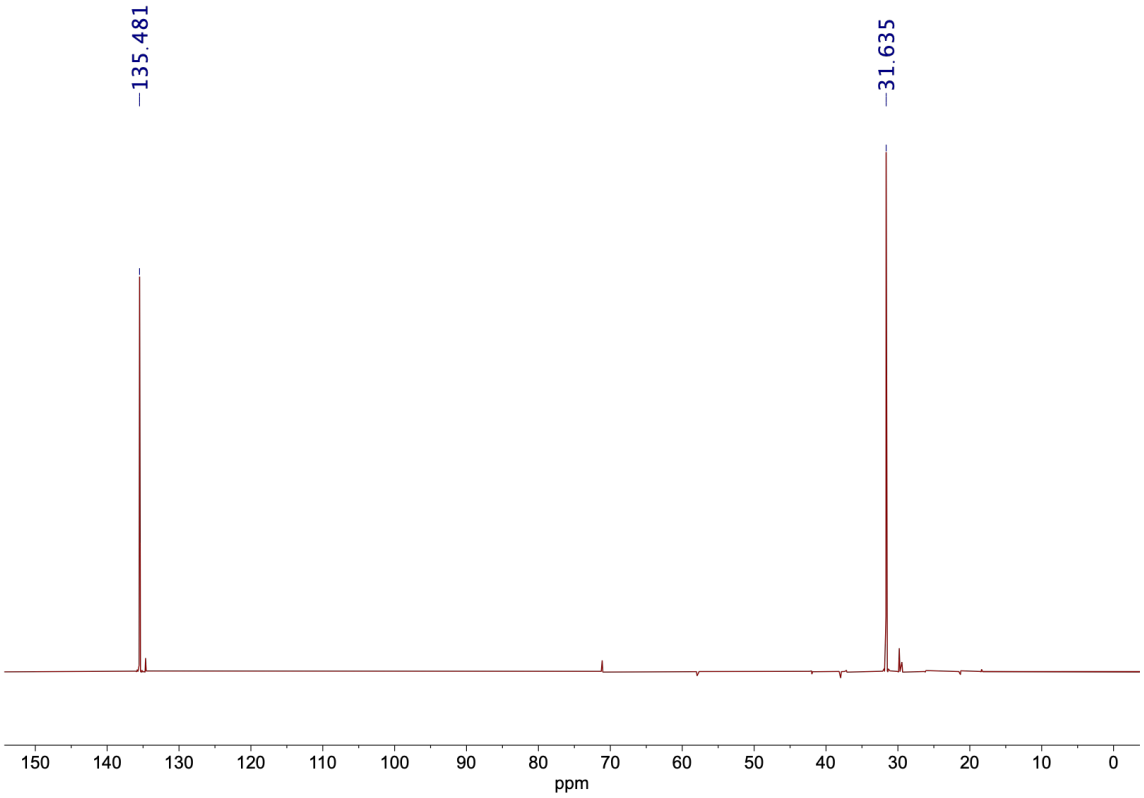
DEPT 135 NMR **2a**+**3a**.



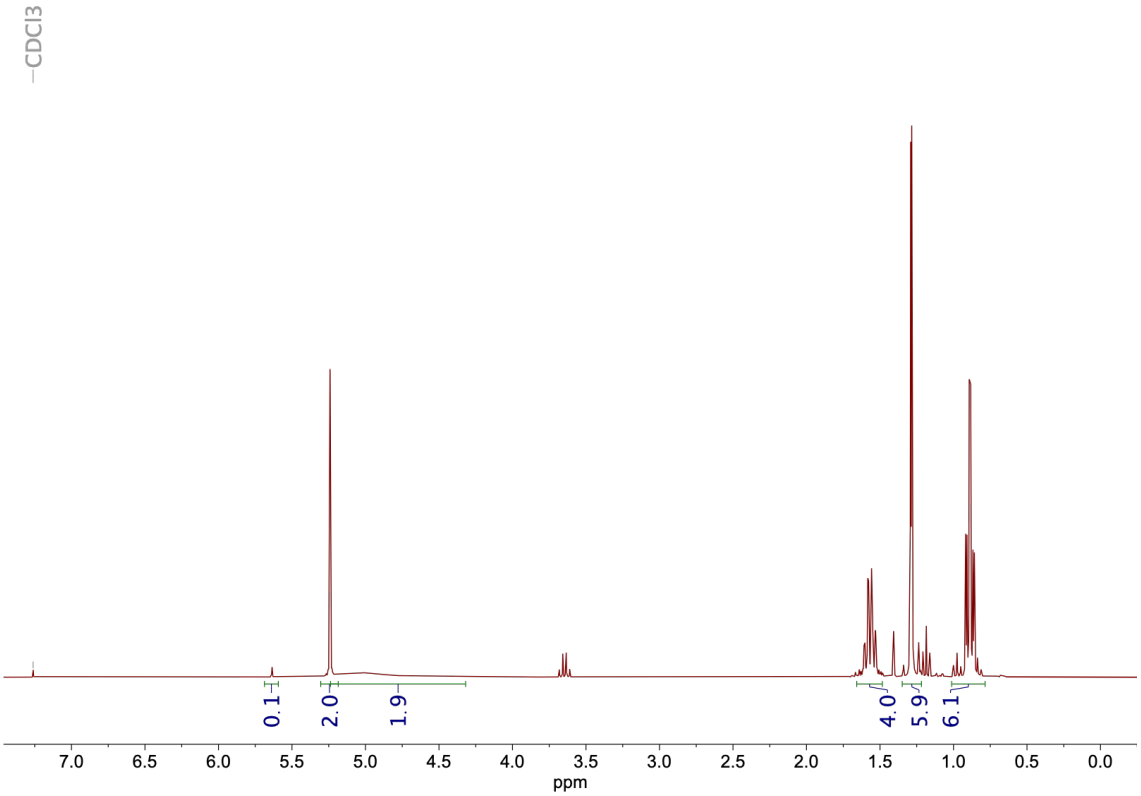
^{1}H NMR **2b**+**3b**: (401 MHz, $CDCl_3$) δ 5.72 (s, 0.1H (*trans* 2H)), 5.80–5.30 (s, broad, 2H), 5.26 (s, 2H), 1.33 (s, 12H).



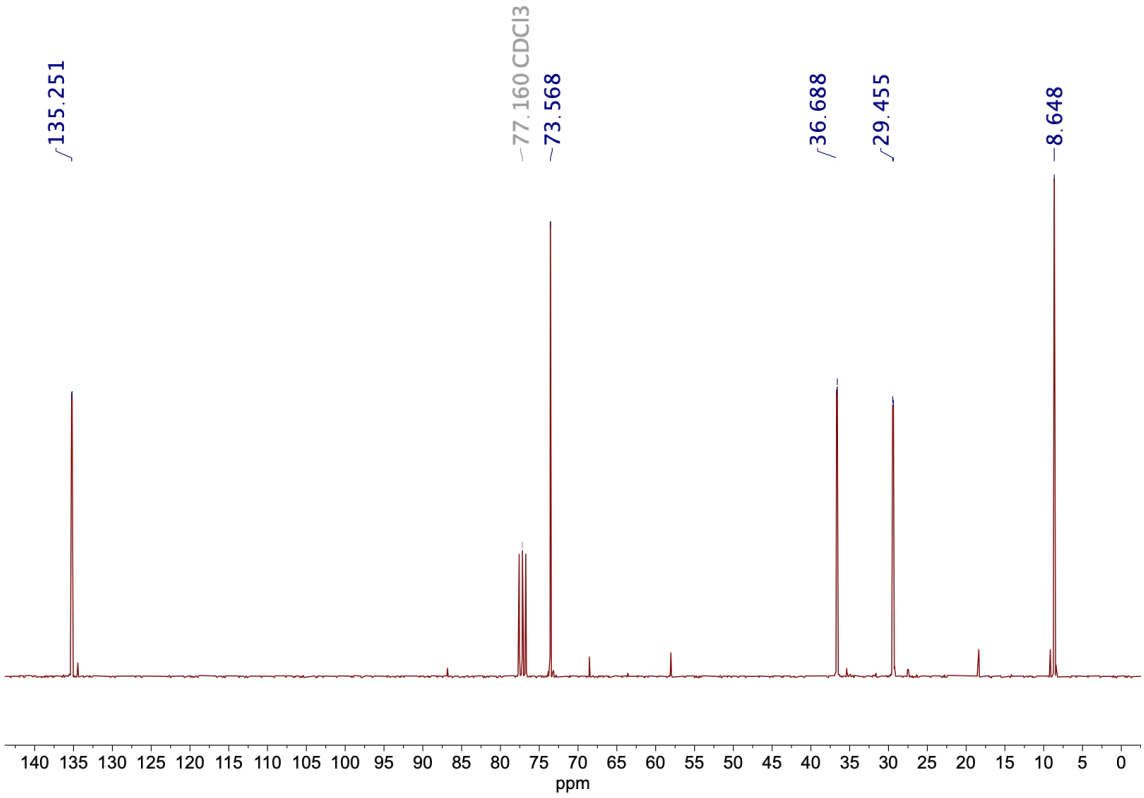
^{13}C NMR **2b**+**3b:** (75 MHz, $CDCl_3$) δ 135.49, 71.13, 31.63.



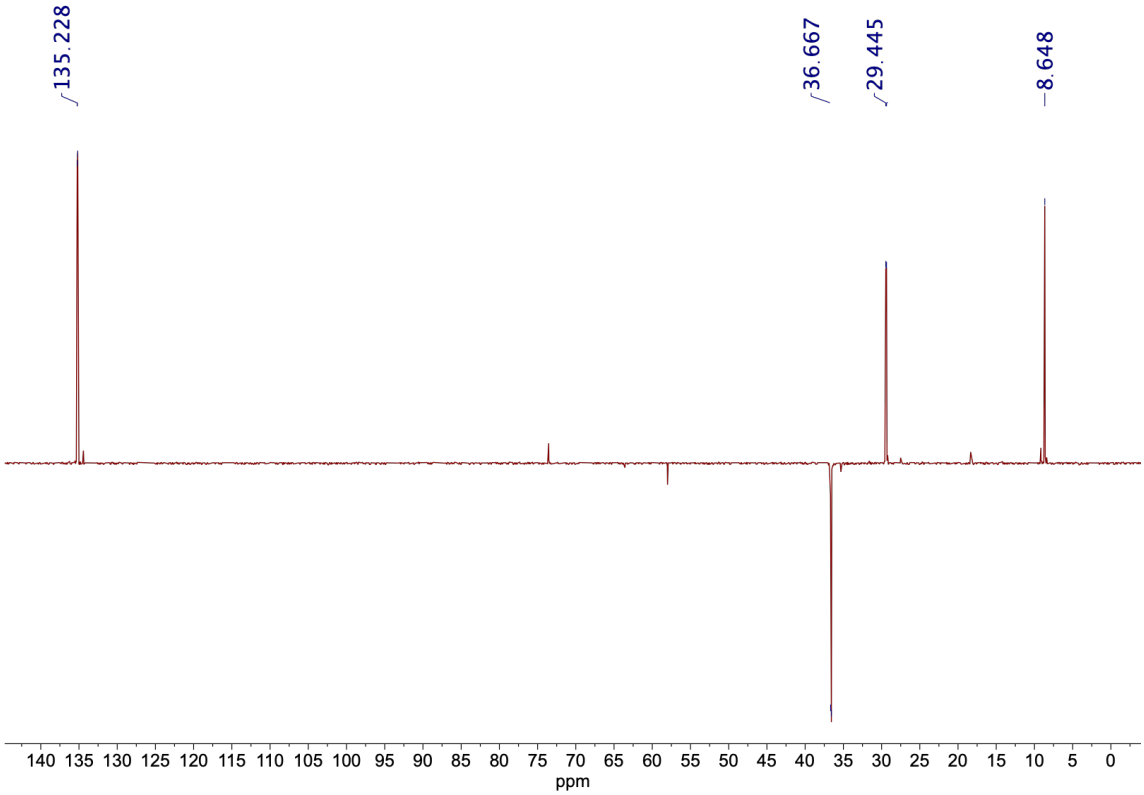
DEPT 135 NMR **2b**+**3b**.



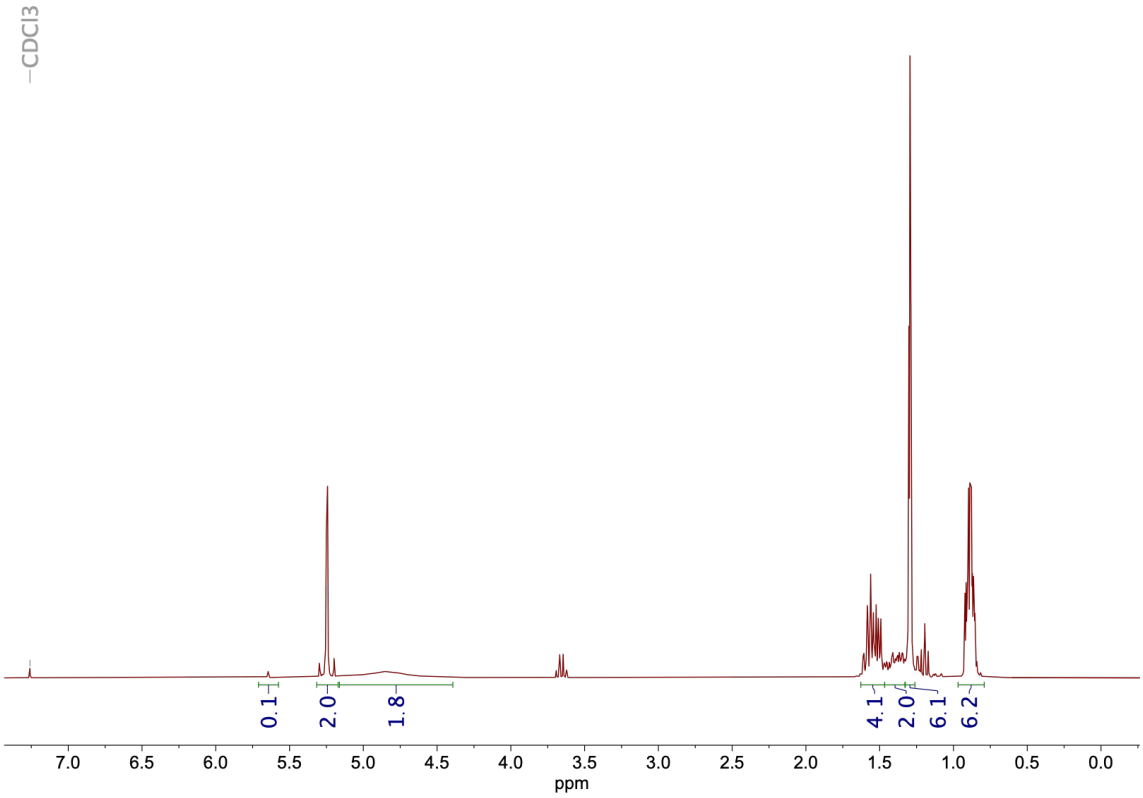
^{1}H NMR **2c**+**3c**: (401 MHz, $CDCl_3$) δ 5.64 (ds, 0.1H (*trans*, 2H)), 5.24 (ds, 2H), 5.01 (s, broad, 2H), 1.56 (dq, 4H), 1.29 (ds, 6H), 0.89 (dt, 6H).



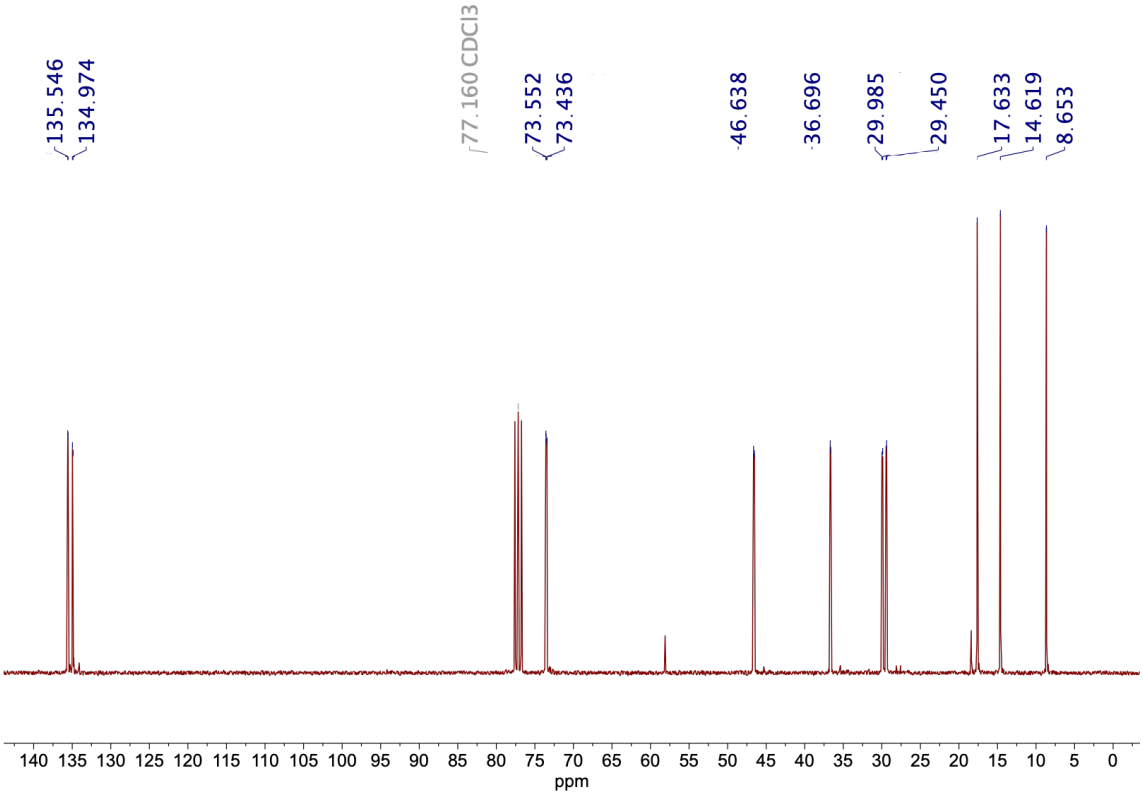
^{13}C NMR **2c+3c:** (75 MHz, $CDCl_3$) δ 135.25, 73.57, 36.69, 29.45, 8.65.



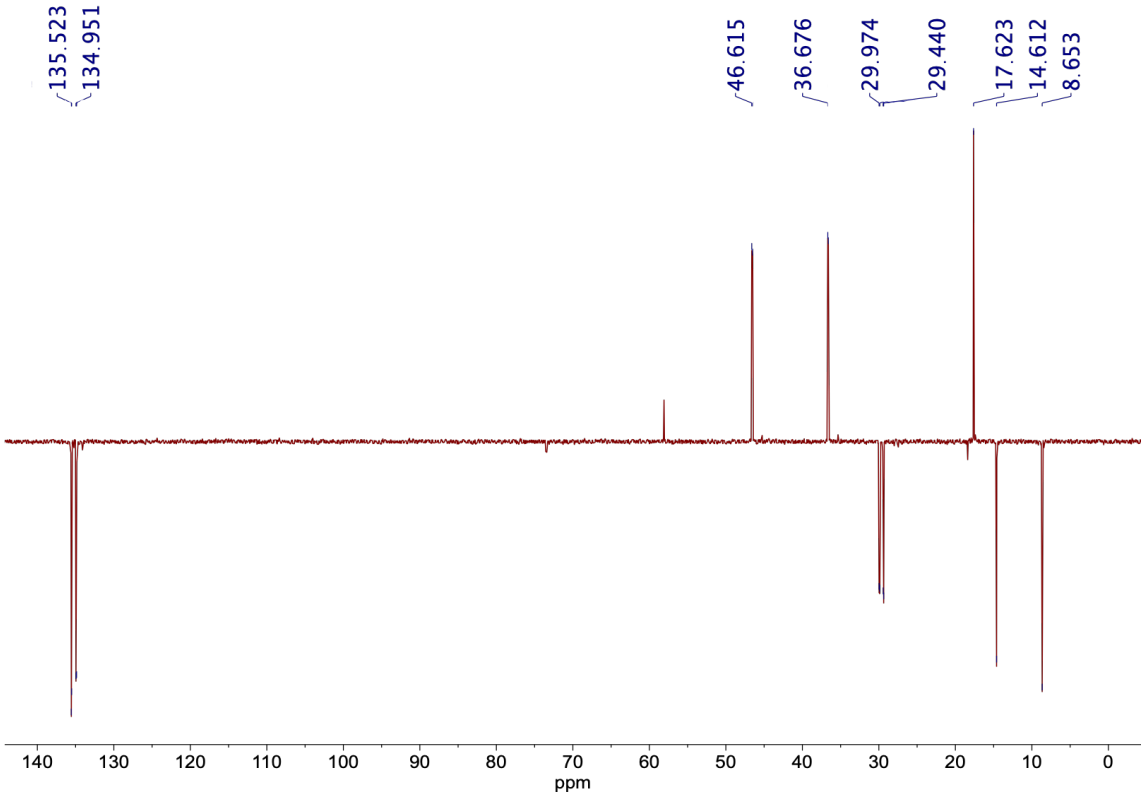
DEPT 135 NMR **2c+3c**.



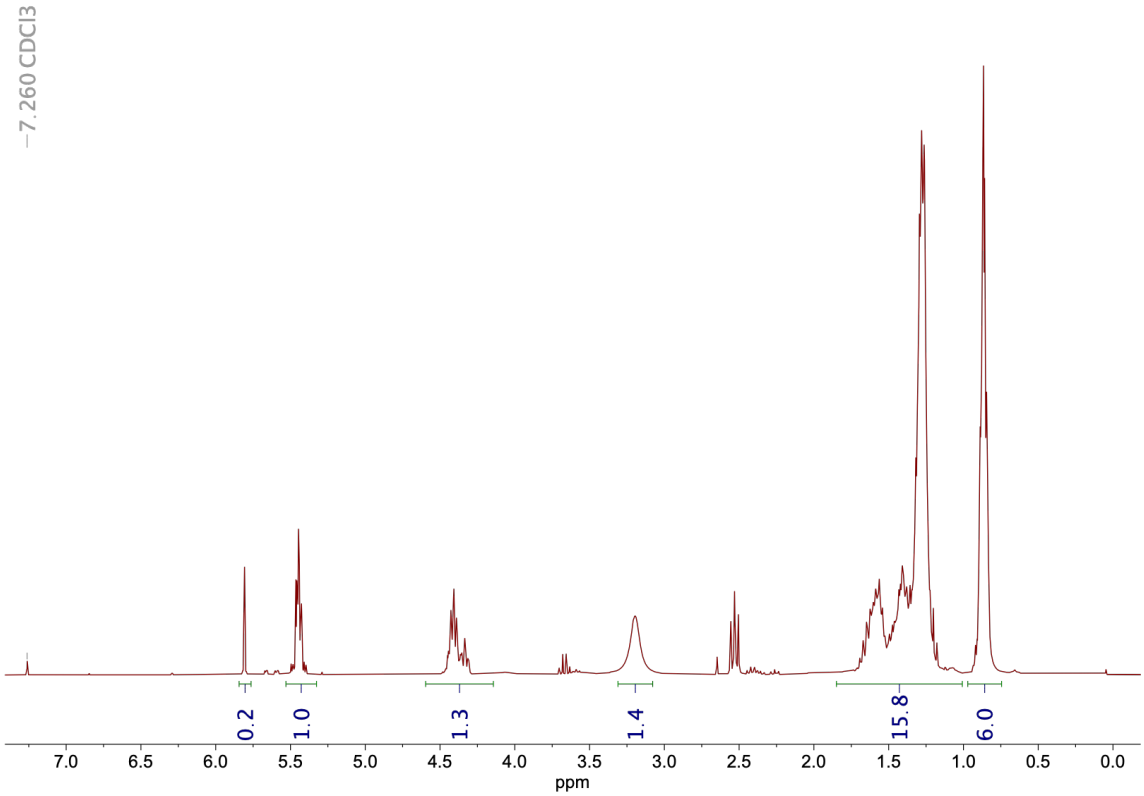
^{1}H NMR **2d+3d**: δ 5.65 (ds, 0.1H (*trans*, 2H)), 5.25 (ds, 2H), 5.24 (s, 2H), 4.84 (s, broad, 2H), 1.64 – 1.48 (m, 4H), 1.48 – 1.32 (m, 2H), 1.29 (dds, 6H), 0.89 (m, 6H).



^{13}C NMR **2d+3d:** (75 MHz, $CDCl_3$) δ 135.58, 134.97, 73.57, 73.44, 46.64, 36.70, 29.98, 29.45, 17.63, 14.62, 8.65.

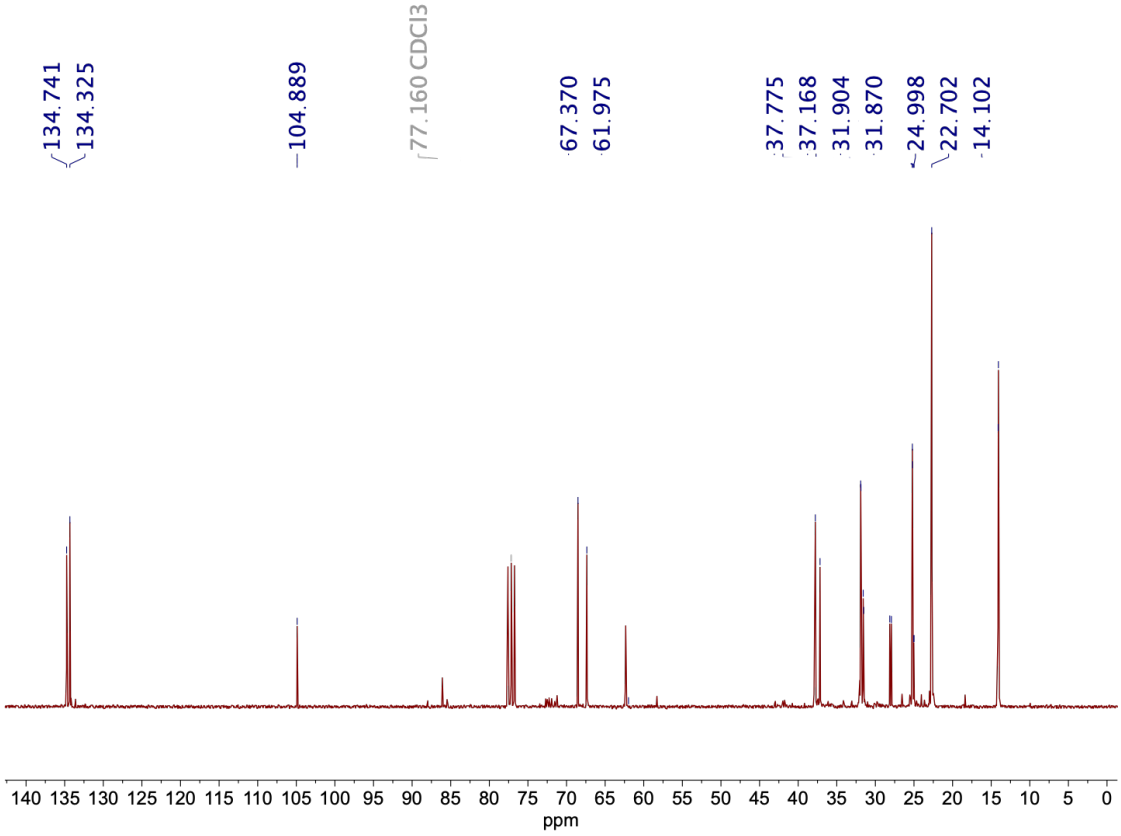


DEPT 135 NMR **2d+3d**.

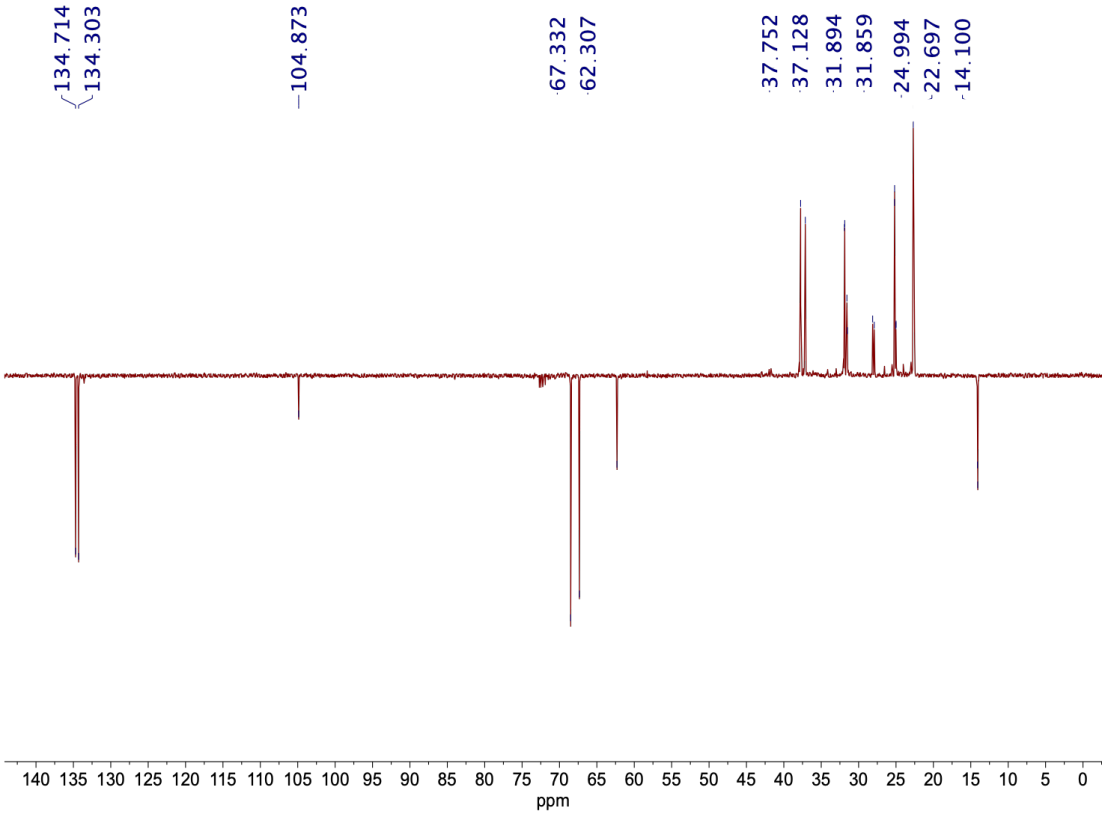


^{1}H NMR **2e+3e**: (401 MHz, $CDCl_3$) δ 5.81 (s, 0.2H (*trans*, 2H)), 5.45 (dq, 1H, (*cis* 2H)), 4.41 (m, 1.3H (alkene, 2H)), 3.19 (s, broad, 1.4H (alkene, 2H)), 1.40 (m, 16H), 0.87 (m, 6H). Integrals normalized by the signal of the methyl group (6H). According to these assignments, we know that 1.3/2 (4.41 ppm signal) divided by 6/6 (0.87 ppm signal),

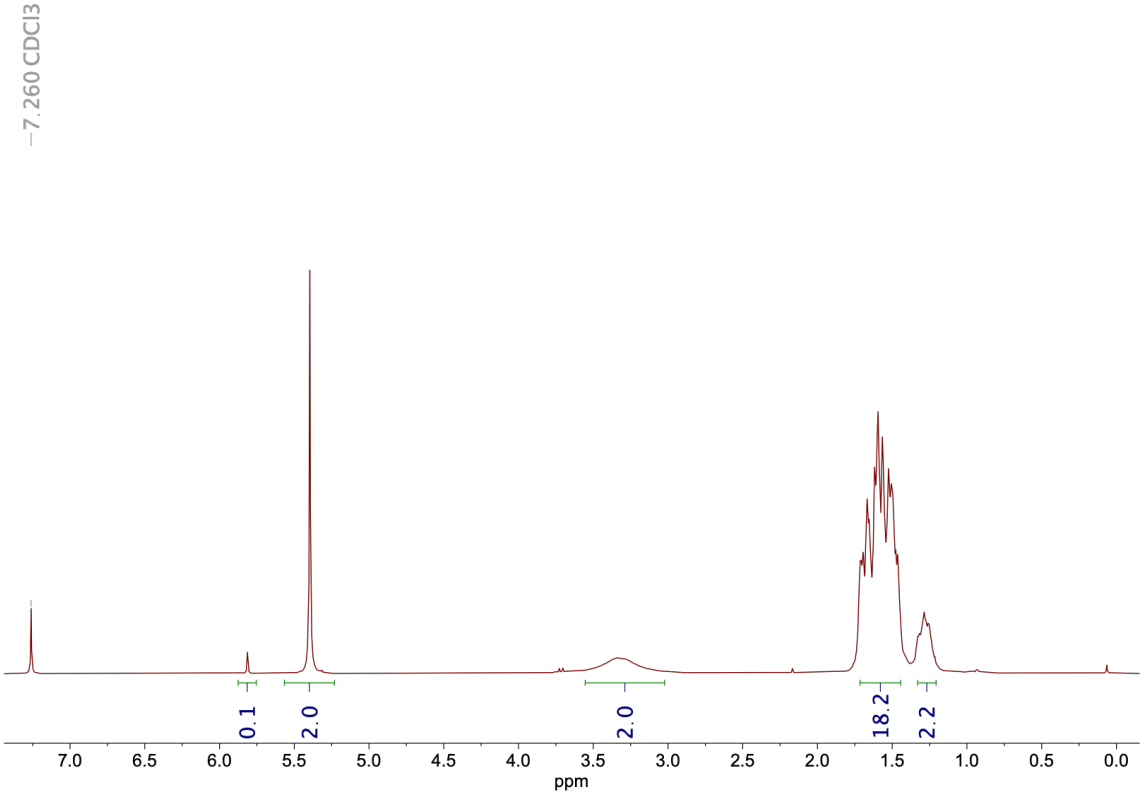
approximately 60% of the mixture is the alkene, and that all of the alkene contains both hydroxyl groups (3.19 ppm signal).



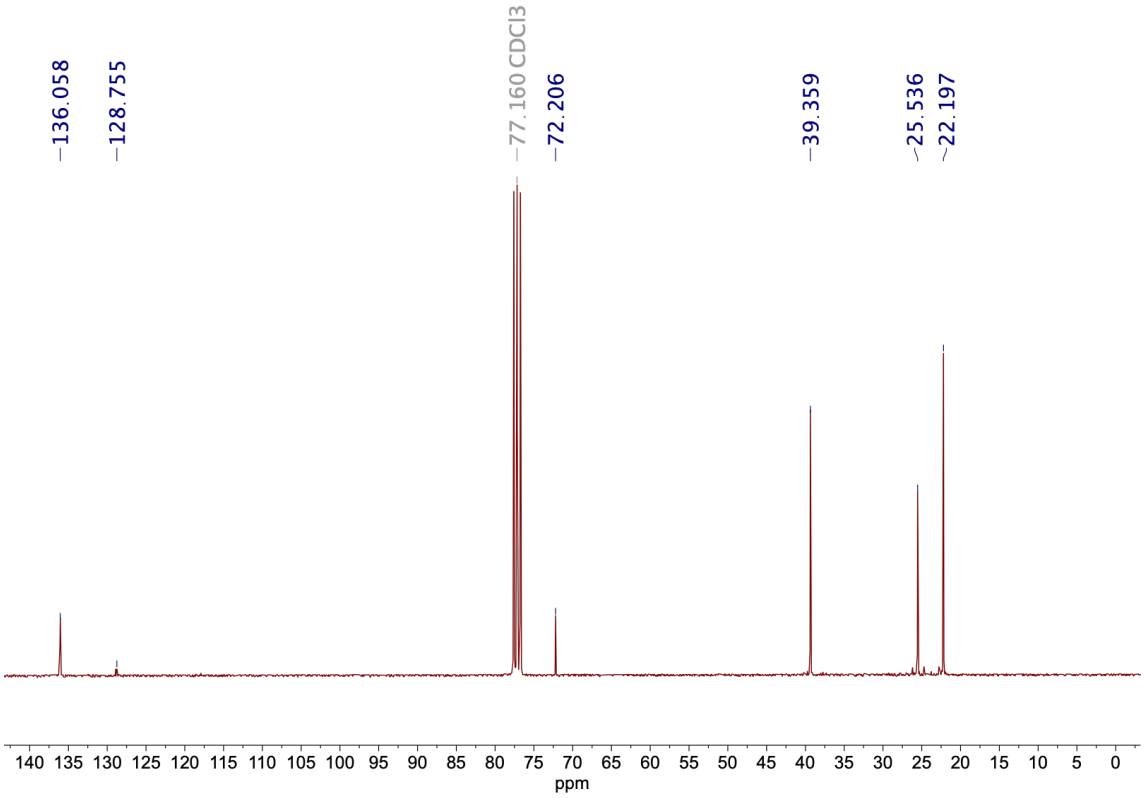
^{13}C NMR **2e+3e:** (75 MHz, $CDCl_3$) δ 134.74, 134.33, 104.89, 67.37, 61.98, 37.77, 37.17, 31.90, 31.87, 25.00, 22.70, 14.10.



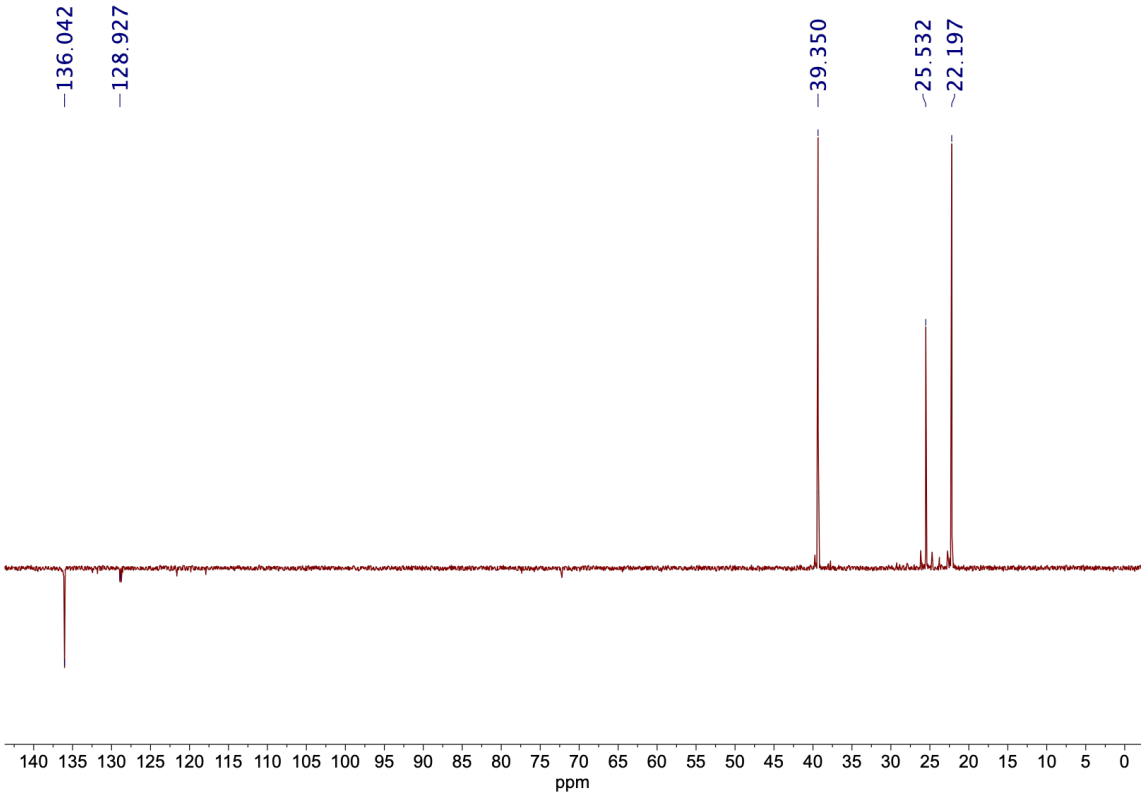
DEPT 135 NMR **2e+3e**.



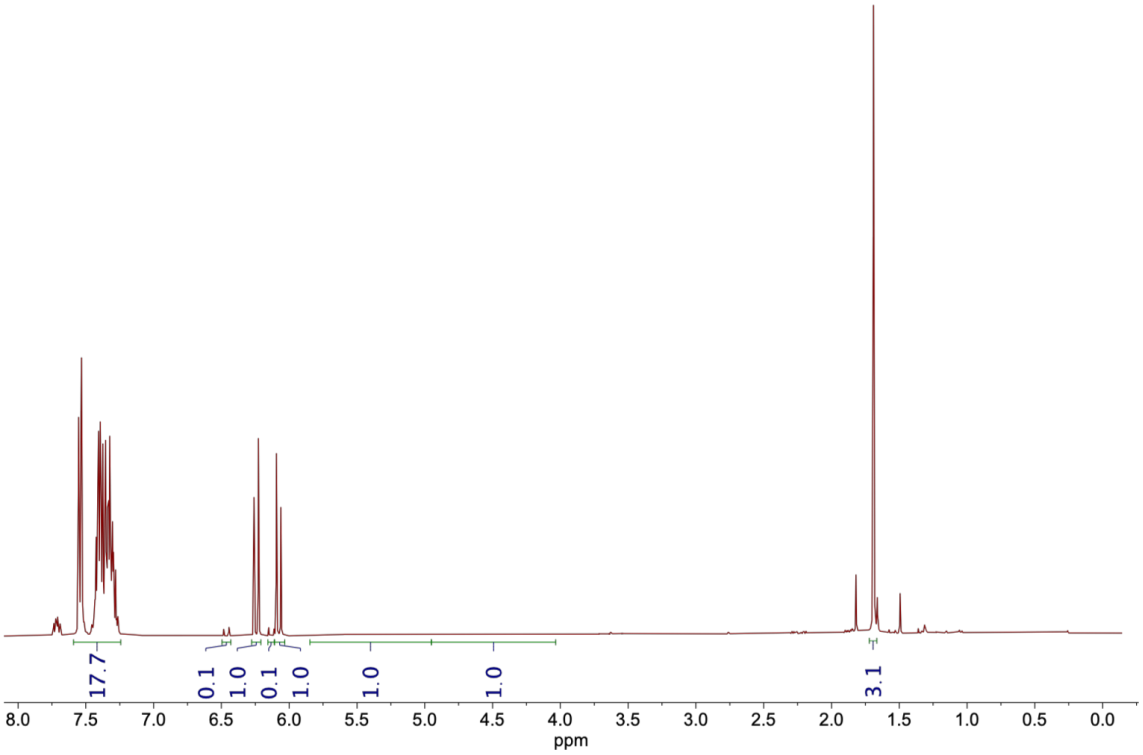
^{1}H NMR **2f+3f**: (401 MHz, $CDCl_3$) δ 5.81 (s, 0.1H (*trans*, 2H)), 5.38 (s, 2.0H), 3.33 (s, broad, 2H), 1.58 (m, 18H), 1.25 (m, 2H).



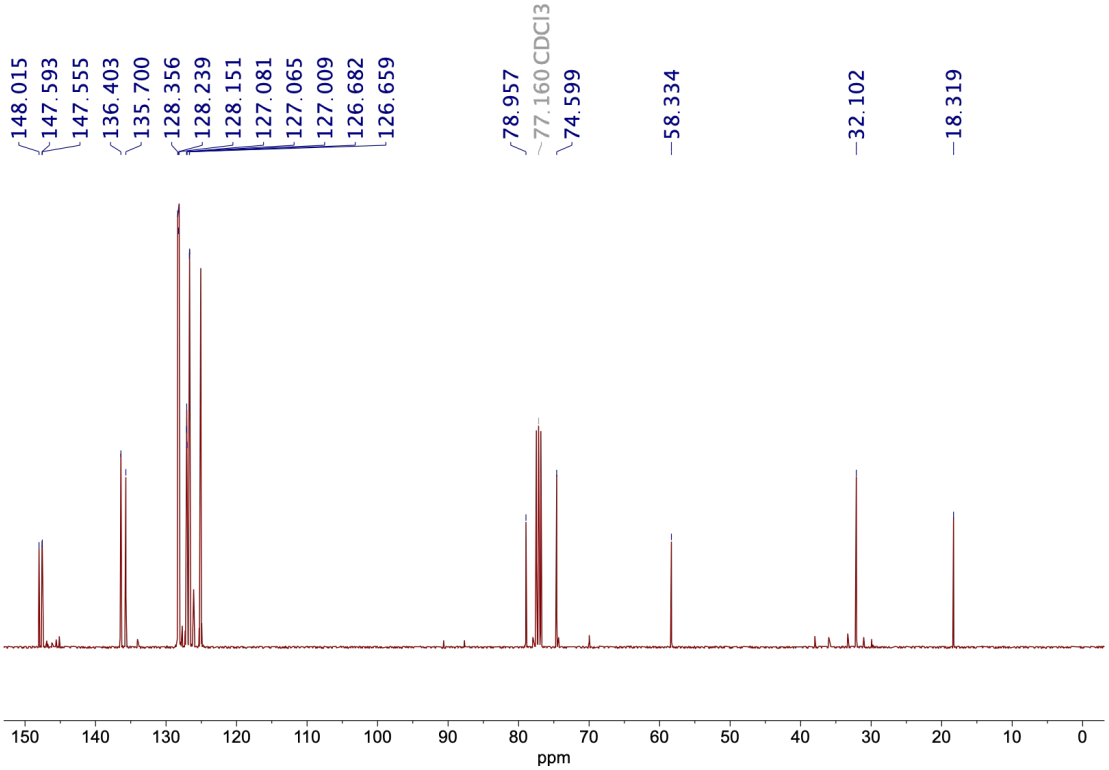
^{13}C NMR **2f+3f:** (75 MHz, $CDCl_3$) δ 136.06, 128.75 (*trans*), 72.21, 39.36, 25.54, 22.20.



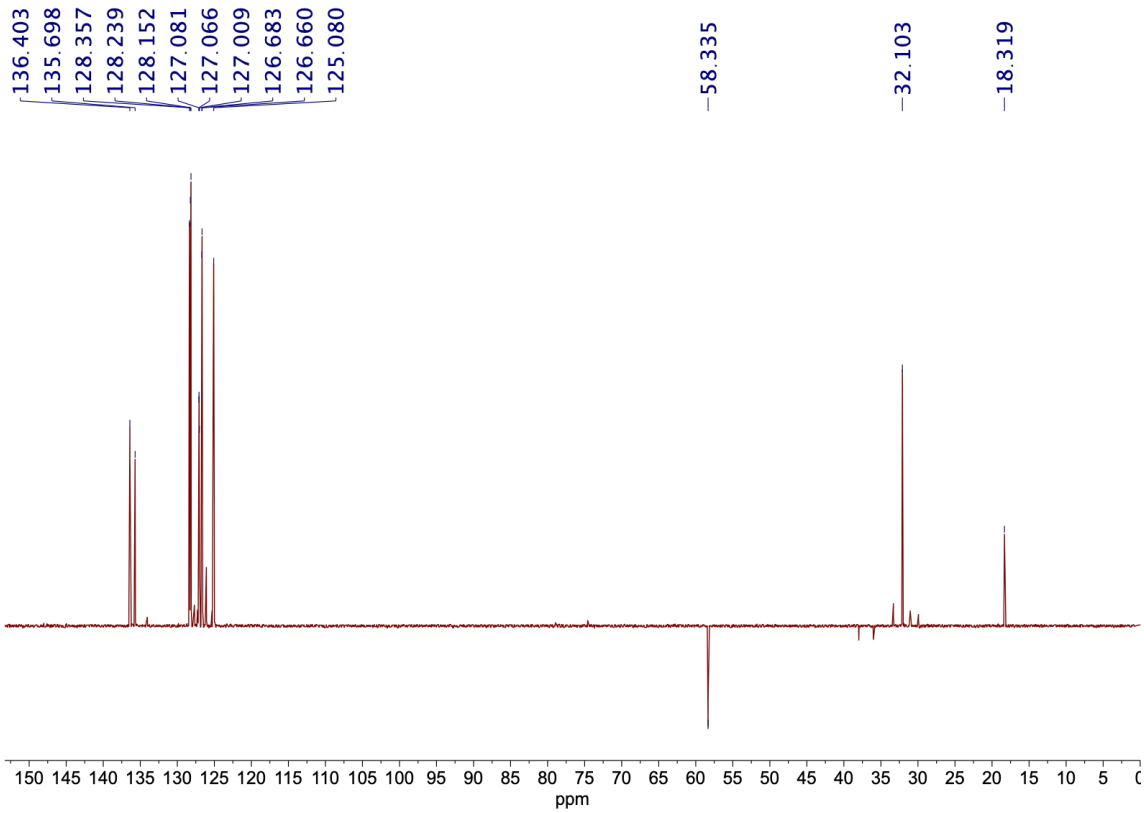
DEPT 135 NMR **2f+3f**.



^{1}H NMR **2g+3g**: (401 MHz, $CDCl_3$) δ 7.37 (m, 15H + chloroform peak), 6.46 (d, J = 15.6 Hz, 0.1H (*trans*, 1H)), 6.24 (d, J = 13.0 Hz, 1H), 6.13 (d, J = 15.6 Hz, 0.1H (*trans*, 1H)), 6.08 (d, J = 13.0 Hz, 1H), 5.48 (s, broad, 1H), 4.43 (s, broad, 1H), 1.76 (s, 3H).



^{13}C NMR **2g+3g**: (75 MHz, $CDCl_3$) δ 148.02, 147.59, 147.55, 136.40, 135.70, 128.36, 128.24, 128.15, 127.08, 127.07, 127.01, 126.68, 126.66, 78.96, 74.60, 32.10. Peaks at 58.33 (CH_2, according to DEPT 135) and 18.32 (CH o CH_3, according to DEPT 135) are impurities.



DEPT 135 NMR **2g+3g**