

Computer Vision for Non-contact Monitoring of Catalyst Degradation and Product Formation Kinetics

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Abstract: We report a computer vision strategy for the extraction and colorimetric analysis of catalyst degradation and product-formation kinetics from video footage. The degradation of palladium(II) pre-catalyst systems to form 'Pd black' is investigated as a widely relevant case study for catalysis and materials chemistries. Beyond the study of catalysts in isolation, investigation of Pd-catalyzed Miyaura borylation reactions revealed informative correlations between colour parameters (most notably ΔE , a colour-agnostic measure of contrast change) and the concentration of product measured by off-line analysis (NMR and LC-MS). The breakdown of such correlations helped inform conditions under which reaction vessels were compromised by air ingress. These findings present opportunities to expand the toolbox of non-invasive analytical techniques, operationally cheaper and simpler to implement than common spectroscopic methods. The approach introduces the capability of analyzing the macroscopic 'bulk' for the study of reaction kinetics in complex mixtures, in complement to the more common study of microscopic and molecular specifics.

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General Considerations

All reagents were purchased from commercial suppliers (Sigma Aldrich, Thermo Fisher Scientific, Fluorochem, VWR, or Alfa Aesar) and used without further purification unless stated otherwise.

Dry solvents were obtained from a PureSolv SPS-400-5 Solvent Purification System.

Infrared (IR) spectra were recorded on a Thermo Fisher Nicolet iS5. All spectra were taken from neat samples and absorptions are listed in cm^{-1} .

^1H , ^{13}C , and ^{31}P , NMR spectra for structural analysis and single point degradation studies were recorded on a Bruker AV3-400 spectrometer at 400 MHz, 101 MHz, and 162 MHz, respectively. All spectra were recorded at ambient temperature using standard pulse methods. Chemical shifts are recorded in ppm with respect to residual solvent peak, and multiplicities are denoted as: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin) or multiplet (m).

LC-MS spectra were obtained on the Agilent 6130 LC-MS instrument. Using 5 mM ammonium acetate in water/acetonitrile as eluent, and the substances can be detected under 214 nm.

Video data, serving as input for computer vision analysis, were collected using the following cameras:

- Raspberry Pi camera module v2 connected to a Raspberry Pi model 3B
- Panasonic HC-W580EB-K Full-HD Palm sized Camcorder
- GoPro HERO6 Camera

The camera used is specified in the specific procedures below, where necessary.

Minimal lighting control was provided by a Gleading 22x22x24cm Mini Portable Photography Studio Light Tent LightRoom Light Box Kit with LED Light. Hotplate stirrer and flasks were kept in the most central position inside the lightbox to minimise the impact on subtle changes due to positioning. The exception to this was in the case of results described in manuscript Scheme 5 (bottom right panel), where positioning was more deliberately explored.

All video footage was captured using the standard camera settings (e.g. 30 frames per second, 1920x1080 or 1080p resolution), where possible. Wherever the maximum video recording was shorter than the time of the reaction, the collected video clips were combined into a single video file before analysis.

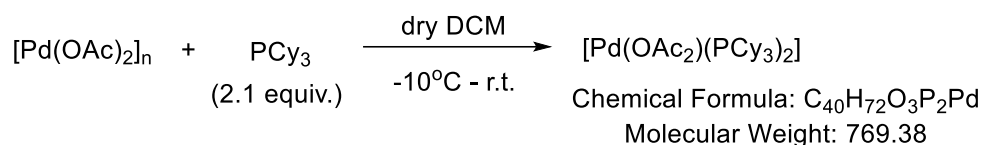
Video analysis was performed using the developmental video analysis software, *Kineticolor*. An early electrochemically-focused application of this software has been reported in the literature.^[5] All video data in this report were analysed using the March 2022 version of the software.

All videos were analysed by breaking videos into their constituent frames, and each frame being analysed, at the pixel level, in turn. A user-selected region of interest was analysed, averaging all pixel values in the selected range. All background data outside the selected region was ignored in the analysis. Data were analysed according to a user-selected number of frames to be skipped. The analysed frames were curated in plots of various colour components versus time to enable semi-quantitative and comparative kinetic analysis between different video analysis datasets.

Extracted colour data were provided from across a common subset of colour models, namely: RGB, HSV, CIE-L*a*b*, and CIE-XYZ. For the purposes of this report, analysis primarily focused on plots of Delta E versus time. Delta E is the colour-independent measure of contrast, measured as the Euclidean distance between two colours in the CIE_L*a*b* colour space.^[6]

Experimental Procedures

Synthesis of Pd catalyst precursor [(PCy₃)₂Pd(OAc)₂]^[1]



Pd(OAc)₂ (90 mg, 0.4 mmol) was added into an oven-dried 20 mL Schlenk tube containing dry DCM (2 mL) and stirrer bar. The mixture was cooled to -10 °C in a salt-ice bath and stirred for 1 h under an argon atmosphere. Then a solution of PCy₃ (225 mg, 0.8 mmol) in dry DCM (4 mL) was added dropwise at -10 °C over 15 mins. The resulting yellow mixture was stirred for another 3 h, and the temperature was allowed to gradually increase to room temperature. The reaction mixture was transferred to a round bottom flask and the majority of the solvent was removed under vacuum before petroleum ether (20 mL) was added and then the residue collected by filtration. The residue was dried under high vacuum for overnight. The final product [(PCy₃)₂Pd(OAc)₂] was obtained as pale yellow solid (229 mg, 73% yield) .

¹H NMR (400 MHz, CDCl₃): 2.02 (d, ²J = 12.1 Hz, 12H), 1.89 – 1.79 (m, 24H), 1.73 – 1.64 (m, 18H), 1.31 – 1.17 (m, 18H).

¹³C NMR (101 MHz, CDCl₃): δ 174.7, 32.6 (t, ³J = 8.7 Hz), 28.9, 27.6 (t, ³J = 5.3 Hz), 26.1, 23.2.

³¹P NMR (162 MHz, CDCl₃): δ 21.62

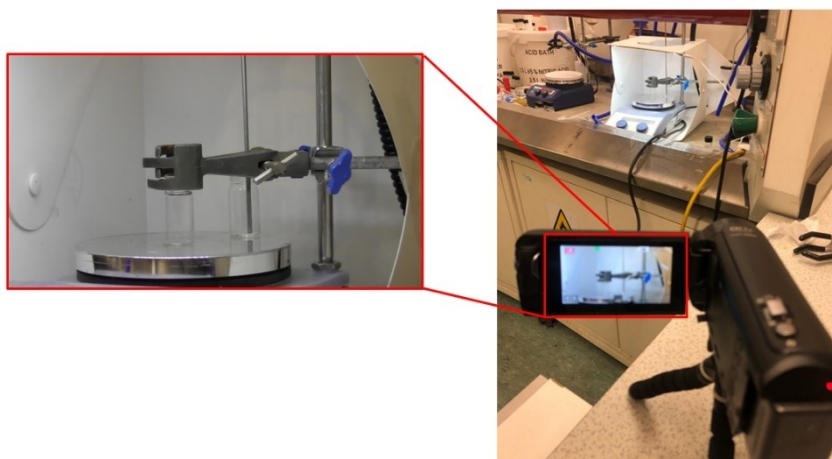
Infrared Spectrum (cm⁻¹): 2942, 2886, 1634, 1454, 1368, 1311, 1007, 852, 741, 688

General procedure A - degradation of Pd catalyst

[(PCy₃)₂Pd(OAc)₂] and B₂Pin₂ were added to separate vials, and dissolved in 1 mL solvent (toluene or THF). Both solutions were heated to a specific temperature, recording using a thermocouple (K-Digital Thermometer Re5881), then the pre-catalyst solution was added into the other vial in one portion using a syringe. NOTE: The camera was turned on before the transfer of pre-catalyst in order to effectively capture time-zero for the reaction. The final reaction mixture was then stirred at the specified temperature for the time required to capture the main colorimetric events necessary for computer vision analysis.

Laboratory setup:

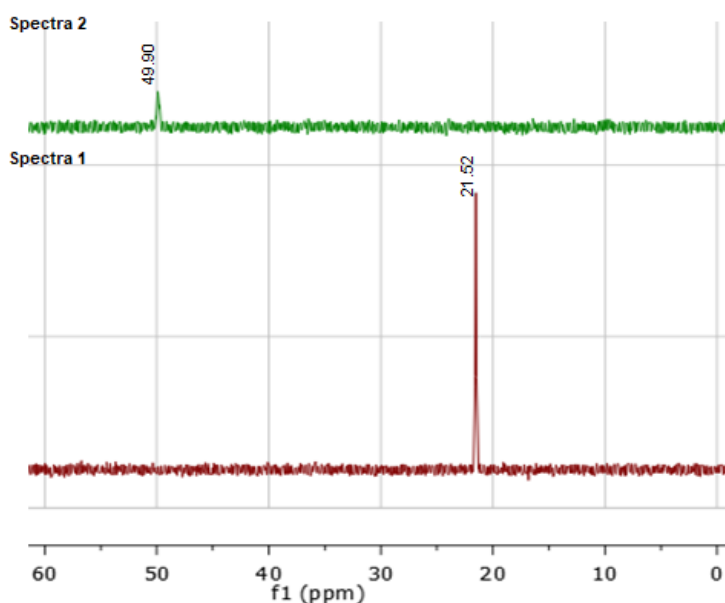
The hotplate was placed in a lightbox with lamp switched on. The hotplate temperature was programmed by immersing its thermometer rod inside a 4 dram (~15 mL) vial of paraffin oil placed on the hotplate. Measuring the temperature of the oil instead of the metal hotplate itself allowed a more stable operating temperature to be obtained via the temperature feedback control on the hotplate.



Scheme S1. Representative set-up for monitoring catalyst degradation.

Exploratory analysis of Pd catalyst degradation – manuscript Scheme 3

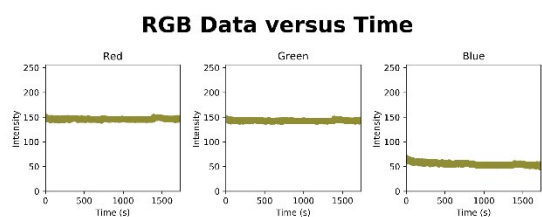
The spectra in Scheme S2 highlighted that the phosphine groups were in a different environment therefore the species present before and after deactivation were chemically different. Spectrum 1 (before reaction) highlighted a chemical shift of 21.52 ppm which matched the literature value for the $\text{trans}[(\text{PCy}_3)_2\text{Pd}(\text{OAc})_2]$ complex.^[1] If the active Pd(0) complex had formed, a peak around 39 ppm would have been observed.^[2,3] Spectrum 2 (after reaction) illustrated a higher chemical shift of 49.90 ppm which was characteristic of a phosphine oxide peak, indicating that $\text{Cy}_3\text{P}=\text{O}$ had formed – not $\text{Pd}(\text{PCy}_3)_2$.^[4] This structural information suggested that the phosphine ligands had oxidised in air, thus detached from the Pd centre, accelerating the formation of elemental palladium.



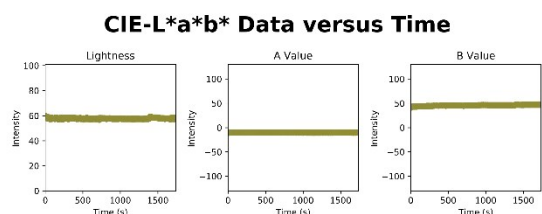
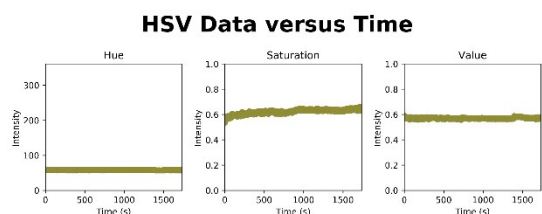
Scheme S2. ^{31}P NMR spectra in CDCl_3 . Spectrum 1 = $[(\text{PCy}_3)_2\text{Pd}(\text{OAc})_2]$ in toluene; Spectrum 2 = post-reaction mixture.

Additional exploration of base effects in isolated catalyst degradation studies

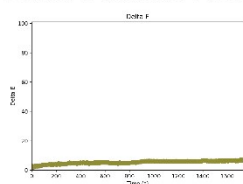
$[(PCy_3)_2Pd(OAc)_0]$ (0.015 mmol), KOAc (0.3 mmol, 20 equiv.), toluene (2 mL), 70 °C, 250 rpm. The mixture was stirred for 30 mins, and no obvious formation of 'Pd black' was observed.



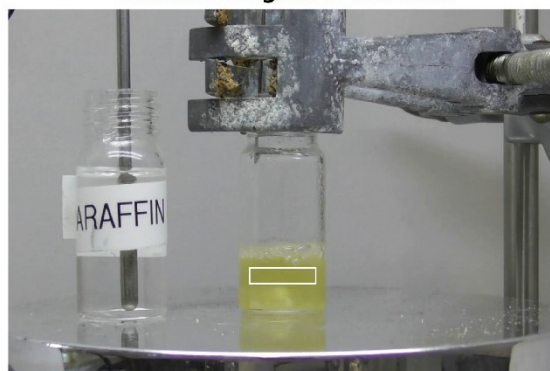
Kineticolor



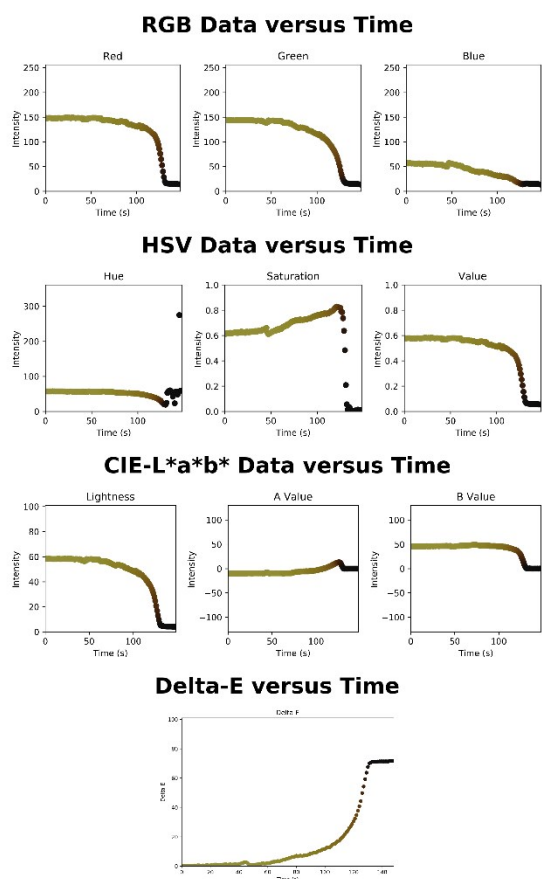
Delta-E versus Time



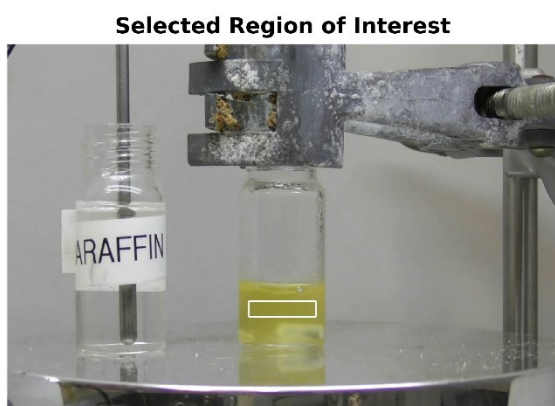
Selected Region of Interest



Then B_2Pin_2 (20 mg in 0.2 mL toluene) was added, 'Pd' black' was soon formed.



Kineticolor



Further Data and Discussion for manuscript Scheme 4

Panasonic camera

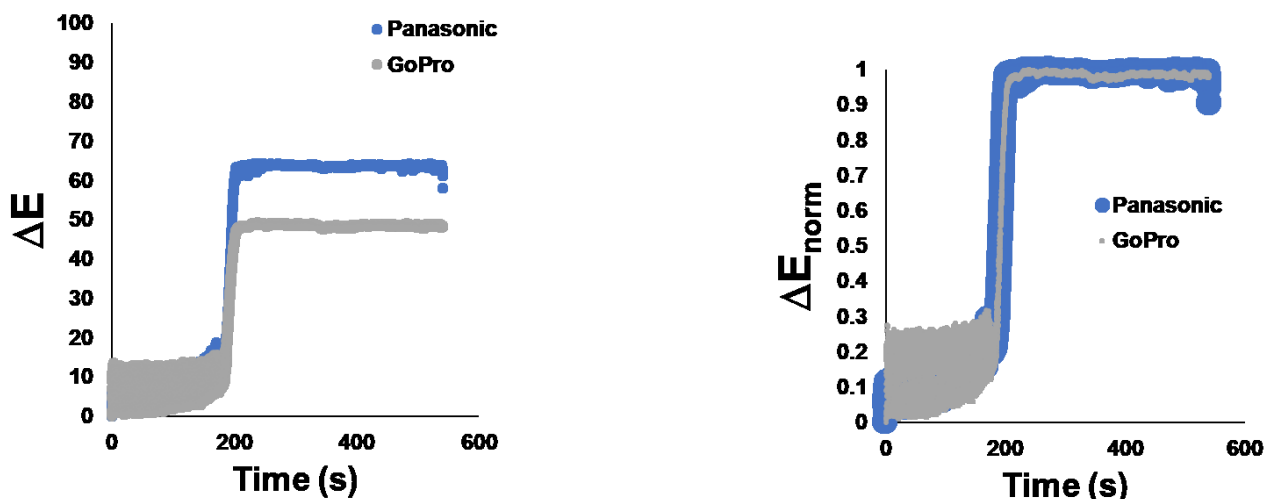
Following **General Procedure A**, $[(PCy_3)_2Pd(OAc)_2]$ (7.85 mg, 0.01 mmol) and B_2Pin_2 (25.4 mg, 0.1 mmol) was added in separate vials, and dissolved in toluene (2 mL). Both solutions were heated to 70 °C, then the pre-catalyst solution was quickly added into the vials containing B_2Pin_2 (**Panasonic Camcorder** was turned on before the transfer). The mixtures were then stirred at 250 RPM and monitored at 70 °C for 10 minutes.

GoPro camera

Following **General Procedure A**, $[(PCy_3)_2Pd(OAc)_2]$ (0.11 g, 0.015 mmol) and B_2Pin_2 (0.051 g, 0.2 mmol) was added in separate vials, and dissolved in toluene (2 mL). Both solutions were heated to 70 °C, then the pre-catalyst solution was quickly added into the vials containing B_2Pin_2 (**GoPro** was turned on before the transfer). The mixtures were then stirred at 250 RPM and monitored at 70 °C for 10 minutes.

Further Discussion for manuscript Scheme 5 – camera choice and positioning

Above discussion attends use of more than one camera (hardware) from which data are extracted using Kineticolor (software). As shown in Scheme S3 below, the raw data outputs from each camera pointed at the same reaction can be normalised to account for any lighting and sensor differences reaching and within each camera, respectively.



Scheme S3. Comparison of computer vision analysis of the same reaction with two different cameras from two different angles. Left: raw data. Right: Normalised data.

Degradation experiments run under different B_2Pin_2 concentration – manuscript Scheme 5 (bottom left)

The experiments are carried out following **General Procedure A**, using 0.011 g $[(PCy_3)_2Pd(OAc)_2]$ (0.015 mmol) and treated with 13.3 equiv. (0.051 g 0.2 mmol), 20 equiv. (0.076 g, 0.3 mmol), 26.67 equiv. (0.102 g, 0.4 mmol), 33.3 equiv. (0.127 g, 0.5 mmol) B_2Pin_2 separately. Both solutions were heated to 70 °C prior to mixing. The pre-catalyst solution was quickly added into the vials containing B_2Pin_2 . The mixtures were stirred at 250 RPM and monitored by **GoPro**. Reactions of each concentration of B_2Pin_2 were repeated 3 times.

Degradation experiments run under different temperature – manuscript Scheme 5 (top middle)

The experiments are carried out following **General Procedure A**, using 0.011 g $[(PCy_3)_2Pd(OAc)_2]$ (0.015 mmol) and 0.076g B_2Pin_2 (20 equiv., 0.3 mmol), dissolving in 1 mL toluene separately. Both solutions were brought to desired temperature (80 °C, 60 °C, 40 °C and r.t.) prior to mixing. The pre-catalyst solution was quickly added into the vials containing B_2Pin_2 . The mixture were stirred at 250 RPM and monitored by **GoPro**.

Degradation experiments run under different pre-catalyst concentration – manuscript Scheme 5 (bottom middle)

The experiments are carried out following **General Procedure A**, using 0.076g B_2Pin_2 (0.3 mmol) and different amount of pre-catalyst $[(PCy_3)_2Pd(OAc)_2]$ (5 mol%: 11.8 mg, 0.015 mmol; 13.3 mol%: 30 mg, 0.04 mmol; 33.3 mol%: 75 mg, 0.1 mmol), dissolving in 1 mL toluene separately. Both solutions were heated to 70 °C prior to mixing. The pre-catalyst solution was quickly added into the vials containing B_2Pin_2 , and the resulting mixture were monitored by **Raspberry Pi camera module v2**.

Degradation experiments run in triplicate on one hotplate – manuscript Scheme 5 (bottom right)
 $[(PCy_3)_2Pd(OAc)_2]$ (7.85 mg, 0.01 mmol) and B_2Pin_2 (25.4 mg, 0.1 mmol) were added in separate vials, and dissolved in toluene (2 mL). This was done 3 times following **General Procedure A**. All six solutions

were heated to 70 °C, then the pre-catalyst solution was quickly added into the vials containing B₂Pin₂ solution one by one (Camcorder was turned on before the transfer). The three mixtures were then stirred and monitored at 70 °C for 10 minutes.

Laboratory setup:

The hotplate was placed in a lightbox and its thermometer rod was placed inside a large vial of paraffin oil on the hotplate.

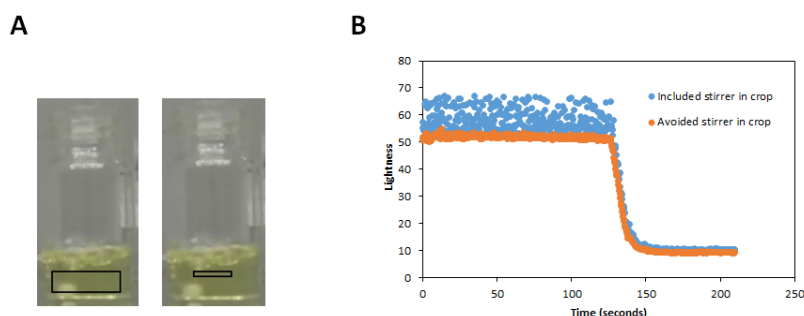


Scheme S4. The setup of 3-in-1 degradation reaction.

Comparison between small and large region of interest crop:

The experiments are carried out following **General Procedure A**, using 0.0112 g [(PCy₃)₂Pd(OAc)₂] (0.015 mmol) and 0.0762 g B₂Pin₂ (0.3 mmol, 20 equiv.), dissolving in 1 mL toluene separately. Both solutions were heated to 70 °C prior to mixing. The pre-catalyst solution was quickly added into the vials containing B₂Pin₂. The mixture were stirred at 250 RPM and monitored by **GoPro**.

Below, the images are from the first frame of the video. The picture on the left highlights a crop covering the majority of the area of interest, evidently including the white stirrer bar. Since the stirrer was continuously moving, it affected the observed colour and thus the colour kinetics graph produced. The graphical results in Scheme S5 highlight the variance between analyses of the left- versus right-hand side crop. The smaller crop was selected to purposely avoid the stirrer bar while still only including the reaction mixture.



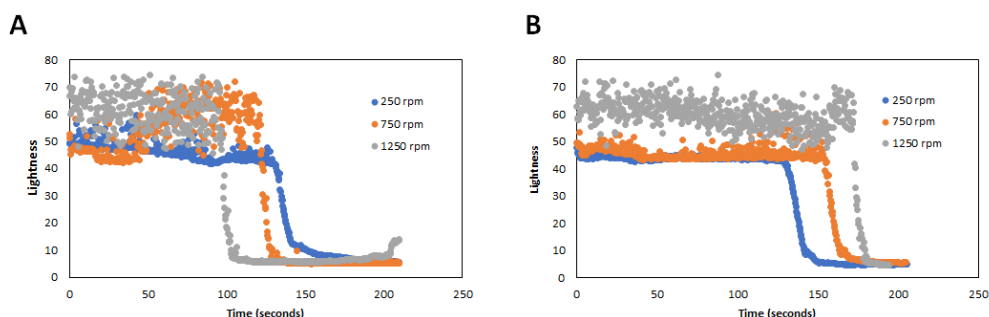
Scheme S5. A: Different crop sizes analysed, LHS - includes stirrer bar, RHS - excludes stirrer bar. **B:** Analysis of stirrer bar interference on the L* versus time plot.

It was believed that the faster the stirring speed, the faster the solid nanoparticles forming would aggregate together, producing this observed cluster of elemental palladium quicker. In a heterogeneous nature, tiny solid particulates present can act as a support (i.e. a nucleation site) for particles to bind to and start a cluster. Therefore, with vigorous stirring, it was possible that minuscule shards of glass from the vial could have been acting as this support, thus increasing the rate of Pd nanoparticle aggregation. However, when this experiment was repeated, an opposed trend appeared (Scheme S6) – suggesting that increasing the stirring speed decreased the rate of Pd black formation.

Further Data and Discussion for manuscript Scheme 5 – stirrer speed analysis (not shown in manuscript)

The experiments are carried out following **General Procedure A**, using 0.0112 g $[(PCy_3)_2Pd(OAc)_2]$ (0.015 mmol) and 0.076 g B_2Pin_2 (0.3 mmol), dissolving in 1 mL toluene separately. Both solutions were heated to 70 °C prior to mixing. The pre-catalyst solution was quickly added into the vials containing B_2Pin_2 . The mixture were stirred at different stirring speed (250, 750 and 1250 RPM) and monitored by **GoPro**. Reactions carried out at a given stirrer speed were each repeated 3 times.

Results



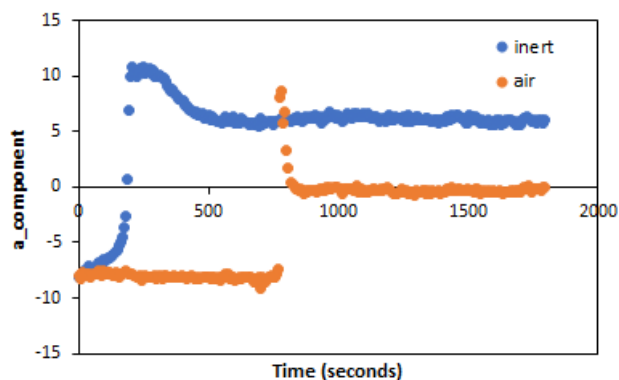
Scheme S6. Stirrer speed analysis (**A**: run 1, **B**: run 2) with the L^* versus time plots.

Recording Inert- versus Open-atmosphere Effects – manuscript Scheme 6

Conditions: $[(PCy_3)_2Pd(OAc)_2]$ (0.0336 g, 0.05 mmol), B_2Pin_2 (0.2286 g, 0.90 mmol), toluene (6 mL) using dry toluene for under argon, 56 °C, 600 rpm. Left Schlenk: under argon. Right Schlenk: under air. The reaction is recorded by GoPro.

The inert system began turning brown within seconds whereas the mixture in air took minutes for any colour change to occur. Intriguingly, the colour transition was significantly more gradual under inert

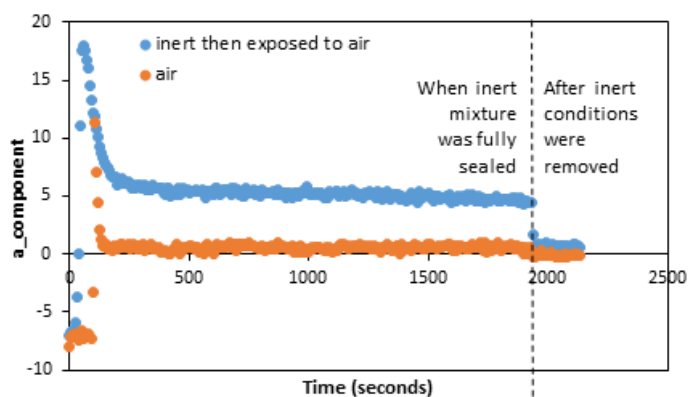
conditions and the colour after 30 minutes evidently remained brown as the mixture was still transparent. The air mixture followed the trend expected by a sudden colour change computed as the sharp decline in the orange curve due to Pd black formation. Furthermore, it instantly dropped below the blue curve indicating that it was much darker in colour (opaque mixture) than the inert reaction mixture. This provided evidence to support the visual observation that the mixture under argon remained brown in colour. Potentially, a more enhanced proof of this brown colour, was portrayed after analysis of the a^* component graph in Scheme S7.



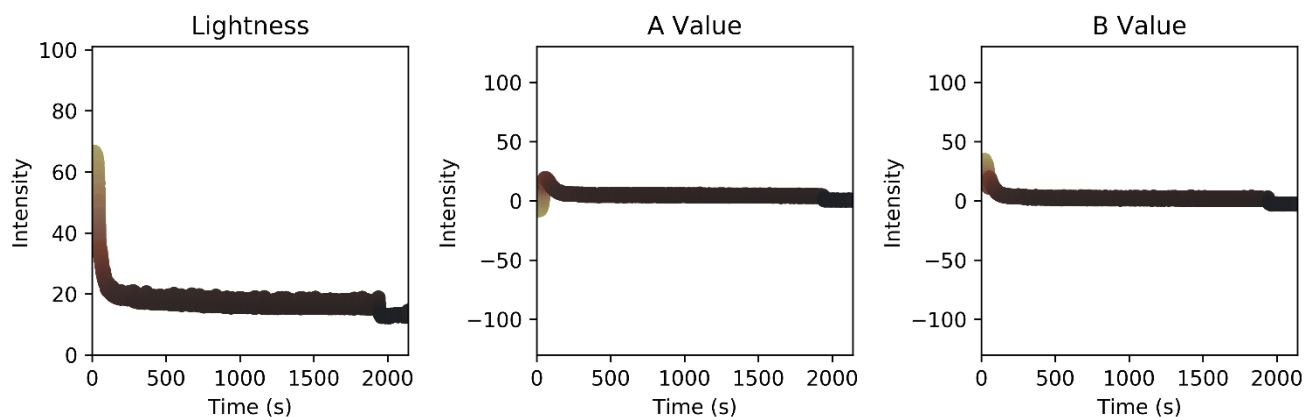
Scheme S7. Argon-inerted versus air analysis with the a^* versus time plots.

Conditions: $[(PCy_3)_2Pd(OAc)_2]$ (0.05 mmol), B_2Pin_2 (0.90 mmol), toluene (6 mL), 70 °C, 600 rpm. Left Schlenk: under argon. Right Schlenk: under air.

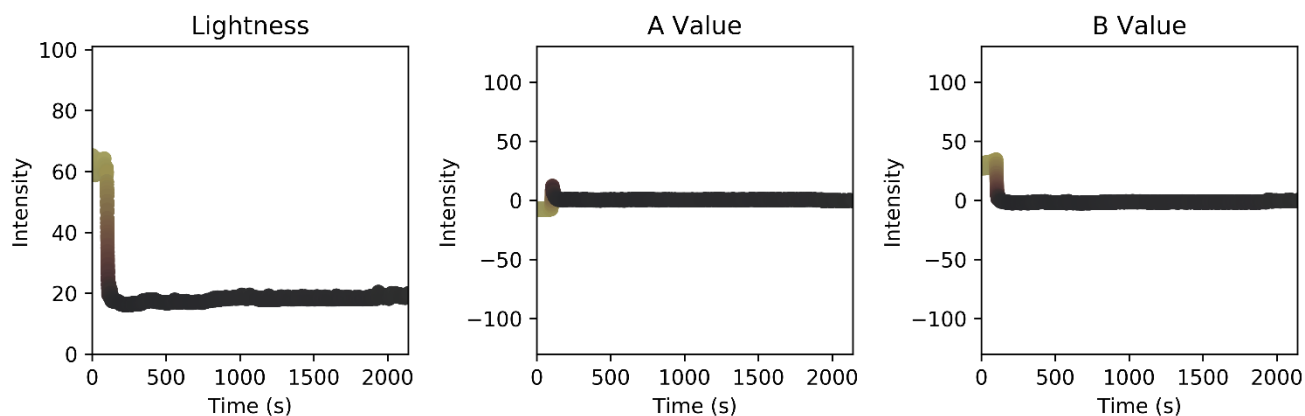
The experiment was then executed at a higher temperature of 70 °C and results displayed a similar trend to those at the lower temperature. The difference was that both reactions occurred much faster and therefore was difficult to closely see the initial contrast between the air and inert system. An extra experiment of curiosity, was what then happened to the inert reaction mixture when it was exposed to air. After 30 minutes of leaving this brown solution under flow of argon, the rubber cap was removed and the GoPro recording was restarted. Scheme S8 illustrates the results effectively – showing how the brown solution instantly turned black as Pd nanoparticles started to aggregate immediately after it was in contact with air.



Argon:



Air:



Scheme S8. Change in colour when reaction under inert conditions was suddenly exposed to air.

Applying computer vision kinetics to Pd-catalysed Borylation – manuscript Scheme 7

Optimization process:

As off-line analysis (NMR and LC-MS) was used, the reaction solvent needed to be compatible with deuterated solvent for the NMR component of offline analysis. As such, DMSO-d₆ was the first choice for its affordable price and no overlay with the internal standard in NMR.

1,4-dioxane was applied as co-solvent to assist the dissolving of the Pd(II) pre-catalyst. However, when 1,4-dioxane was applied as the sole solvent, it was found to be slightly volatile at 70 °C, which was not ideal for reliable calculation of analyte concentration or video analysis. Therefore, the combination of DMSO and 1,4-dioxane is selected as the reaction solvent.

This kinetic information can also be concluded from the time-trend plots based on three colour models (Scheme S9). It can be found that an abrupt change of colour occurred near the end of the monitoring period (5 h), which is most noticeable in the plot of Hue value. In reality, this is only caused by the change of lightening conditions that the lightbox and the light of fume hood are switched off after taking the last sample.

Procedure of Miyaura borylation under argon and exposed to air (manuscript Scheme 7)

The hot plate was placed in a lightbox with lamp switched on, a Spyder Checkr® 24 standard-colour chart was placed at the back of the lightbox. To two 20 mL Schlenk tubes was added the following chemicals: bromobenzene (157 mg, 1 mmol), B₂Pin₂ (305 mg, 1.2 mmol), KOAc (294 mg, 3 mmol) and 1,3,5-trimethoxybenzene (84 mg, 0.5 mmol). After the addition of 3 mL DMSO to each Schlenk tube, the mixtures were heated to 70 °C, one under argon and one exposed to air. To another vial was added [(PCy₃)₂Pd(OAc)₂] (7.8 mg, 0.01 mmol) in 1,4-dioxane and DMSO (2 mL total, 1 mL dioxane:1 mL DMSO). This catalyst solution was purged with argon and then heated for 5 mins to 70 °C. The Panasonic camcorder was turned on (making sure the white colour tile was captured in the same frame as the reaction vessel), then half the pre-heated catalyst solution was quickly added into one of the two Schlenk tubes using a syringe. The other half of the catalyst solution was added to the second Schlenk. Each reaction therefore used 0.005 mmol of Pd precatalyst (0.5 mol% relative to bromobenzene). Both reactions were stirred at 70 °C for 5 h at 600 rpm stirrer speed.

NOTE - the camcorder was kept on constant mains power throughout the processes to avoid battery issues.

Sampling:

0.15 mL of reaction mixture was taken for off-line analysis using a syringe (NMR and LC-MS) at 0, 30, 60, 120, 200 mins.

The syringe was washed with 1:5 methanol/acetone mixture and dried with compressed air prior to taking the next sample.

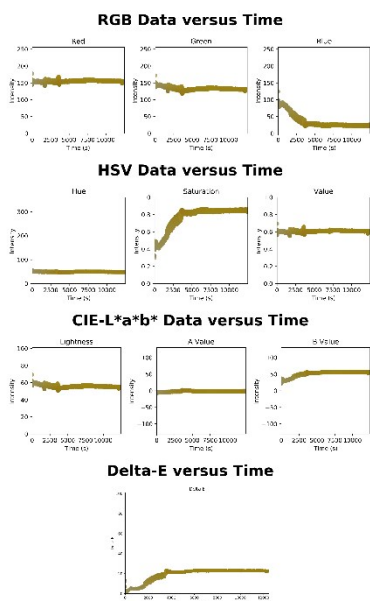
Preparation of NMR sample:

About 0.1 mL of reaction mixture was added into 0.3 mL DMSO-d₆

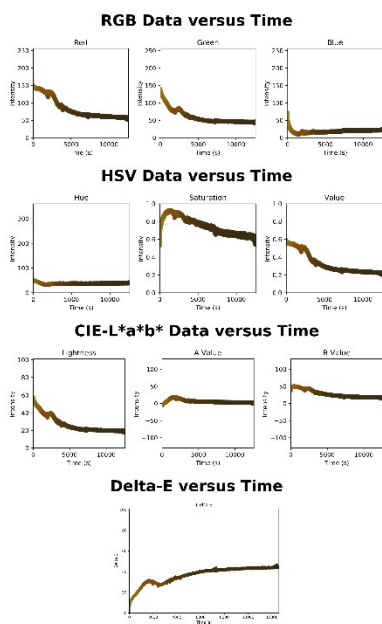
Preparation of LC-MS sample:

1 – 2 drops of reaction mixture were added into the LC-MS sample vial and diluted with 1.4 mL of mobile phase solution (5 mM ammonium acetate in water/acetonitrile 50:50)

Computer vision outputs:



Kineticolor



Kineticolor



Scheme S9. The time-based results in 9 colour parameters (upper: RGB, middle: HSV, bottom: L*a*b* and ΔE). Top: argon-protected reaction. Bottom: air-exposed reaction.

Table S1. ¹H NMR and LC-MS data relating to samples co-plotted with colour data on manuscript Scheme 7.

	Time/min	NMR Results				Volume/ mL	LCMS Results	
		Product/%	Substrate/%	Product/M	Substrate/M		Substrate/% Peak Area	Substrate/M
Argon Protected	0.00	0.00	93.88	0	0.2347	4	80.12	0.2003
	28.62	28.73	57.22	0.0746	0.1486	3.85	68.95	0.1791
	61.13	47.29	43.55	0.1278	0.1177	3.7	57.69	0.1559
	117.68	50.60	33.40	0.1425	0.0941	3.55	49.91	0.1406
	203.45	55.41	33.55	0.1630	0.0987	3.4	47.16	0.1387
Exposed to air	0.00	0.00	84.42	0	0.2110	4	78.63	0.1966
	32.77	26.05	53.83	0.0677	0.1398	3.85	63.97	0.1661
	64.95	29.84	50.59	0.0806	0.1367	3.7	61.08	0.1651
	121.88	27.56	47.38	0.0776	0.1335	3.55	60.83	0.1713
	207.38	29.99	46.63	0.0882	0.1371	3.4	62.69	0.1844

General Procedure of Miyaura borylation with preheated catalyst solution (manuscript Scheme 8)

The hot plate was placed in a lightbox with lamp switched on, a Spyder Checkr® 24 standard-colour chart was placed at the back of the lightbox. To a 20 mL Schlenk tube was added bromobenzene (314 mg, 2 mmol), B₂Pin₂ (610 mg, 2.4 mmol), KOAc (588 mg, 6 mmol) and 1,3,5-trimethoxybenzene (168.3 mg, 1 mmol) as an internal standard for subsequent offline NMR and LC analyses. After the addition of DMSO (6 mL), the mixture was heated to 70 °C under argon. To another vial was added [(PCy₃)₂Pd(OAc)₂] (7.8 mg, 0.01 mmol) in 1,4-dioxane and DMSO (2 mL total, 1 mL dioxane:1 mL DMSO). This catalyst solution was purged with argon and then heated for 2 mins to 70 °C. The Panasonic camcorder was turned on (making sure the white colour tile was captured in the same frame as the reaction vessel), then the pre-heated catalyst solution was quickly added into the mixture present in the 20 mL Schlenk tube using a syringe in one portion. The reaction was stirred at 70 °C and 600 rpm for 5 h.

NOTE – the camcorder was kept on constant mains power throughout the processes to avoid battery issues.

Sampling:

0.15 mL of reaction mixture was taken for off-line analysis by a syringe (NMR and LC-MS) at 0, 15, 30, 45, 60, 75, 90, 120, 150, 180, 240, 300 mins.

The syringe was washed with 1:5 methanol/acetone mixture and dried with compressed air prior to taking the next sample.

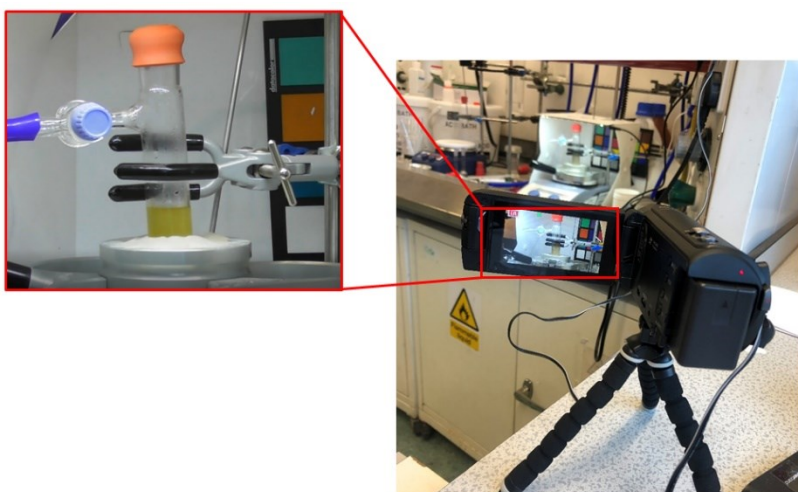
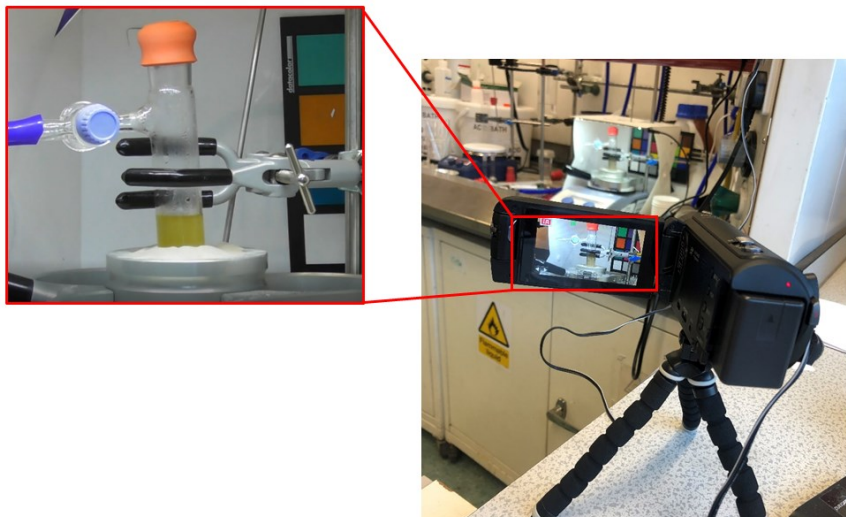
Preparation of NMR sample:

0.1 mL of reaction mixture was added into 0.3 mL DMSO-d₆

Preparation of LC-MS sample:

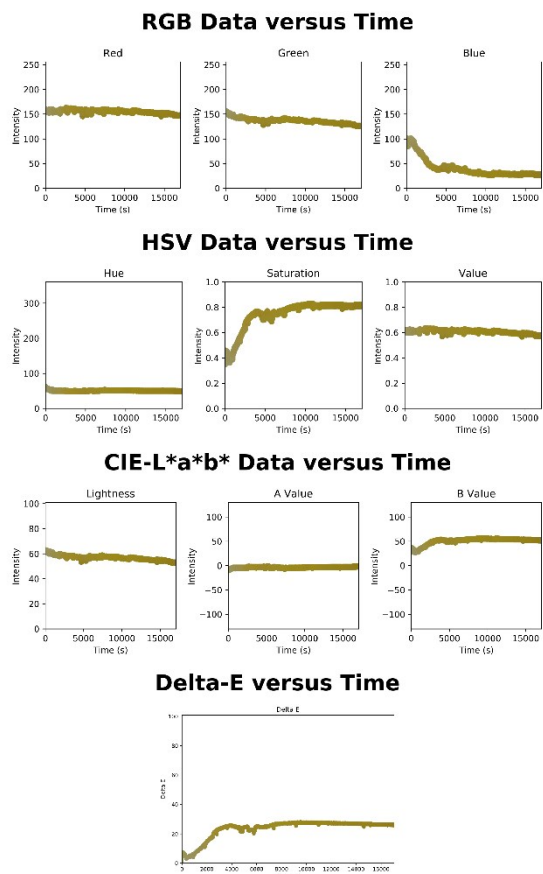
1 – 2 drops of reaction mixture were added into the LC-MS sample vial and diluted with 1.4 mL of mobile phase solution (5 mM ammonium acetate in 1:1 water/acetonitrile mixture).

Laboratory setup:



Scheme S10. The setup of Miyaura borylation reaction. The white colour tile must be included in the video for the calibration.

Computer vision outputs:



Kineticolor

Selected Region of Interest



Scheme S11. The time-based results in 9 colour parameters (upper: RGB, middle: HSV, bottom: L*a*b* and ΔE). Results for pre-heated set-up described immediately above.

Table S2. ¹H NMR and LC-MS data relating to samples co-plotted with colour data on manuscript Scheme 8.

	Time/min	NMR Results				Volume /mL	LCMS Results	
		Product/%	Substrate/%	Product/ M	Substrate/ M		Substrate/% Peak Area	Substrate/ M
Preheated Catalyst Solution	0.00	0.00	80.25	0	0.2145	8	74.82	0.2000
	15.40	14.21	58.39	0.0387	0.1590	7.85	56.15	0.1529
	31.07	29.83	45.30	0.0828	0.1258	7.7	44.20	0.1228
	46.85	40.39	38.14	0.1144	0.1080	7.55	39.21	0.1110
	61.00	46.16	32.49	0.1334	0.0939	7.4	33.99	0.0982
	77.75	52.03	26.91	0.1534	0.0794	7.25	28.93	0.0853
	96.38	56.29	23.55	0.1695	0.0709	7.1	25.25	0.0760
	123.17	58.43	20.58	0.1798	0.0633	6.95	23.50	0.0723
	152.75	57.54	21.41	0.1809	0.0673	6.8	22.42	0.0705
	183.12	58.05	21.13	0.1867	0.0679	6.65	24.90	0.0801
	243.60	58.45	21.21	0.1923	0.0698	6.5	23.36	0.0768
	287.80	58.62	20.89	0.1974	0.0703	6.35	22.79	0.0767
	Non-preheated Catalyst Solution	0	0.00	69.00	0	0.1803	8	67.59
15.75		13.93	52.00	0.0371	0.1385	7.85	49.56	0.1320
30.85		29.44	38.78	0.0799	0.1053	7.7	38.95	0.1057
45.4666 7		39.10	30.57	0.1083	0.0846	7.55	33.18	0.0919
61.65		46.15	24.03	0.1304	0.0679	7.4	26.45	0.0747
75.55		49.88	21.38	0.1438	0.0616	7.25	24.66	0.0711
90.43		56.16	18.24	0.1654	0.0537	7.1	21.21	0.0624
120.88		62.78	14.88	0.1889	0.0448	6.95	16.94	0.0510
150.88		63.54	13.32	0.1954	0.0409	6.8	16.97	0.0522
181.20		65.62	15.47	0.2063	0.0486	6.65	15.95	0.0501
239.87		64.68	14.53	0.2080	0.0467	6.5	16.52	0.0531
296.65		62.98	12.60	0.2073	0.0415	6.35	16.66	0.0549

Modified Procedure of Miyaura borylation with non-preheated catalyst solution (manuscript Scheme 8)

The hot plate was placed in a lightbox with lamp switched on, a Spyder Checkr® 24 standard-colour chart was placed at the back of the lightbox. To a 20 mL Schlenk tube was added bromobenzene (314 mg, 2 mmol), B₂Pin₂ (610 mg, 2.4 mmol), KOAc (588 mg, 6 mmol) and 1,3,5-trimethoxybenzene (168.3 mg, 1 mmol) as an internal standard for subsequent offline NMR and LC analyses. After the addition of DMSO (6 mL), the mixture was heated to 70 °C under argon. To another vial was added [(Pcy₃)₂Pd(OAc)₂] (7.8 mg, 0.01 mmol) in 1,4-dioxane and DMSO (2 mL total, 1 mL dioxane:1 mL DMSO). The Panasonic camcorder was turned on (making sure the white colour tile was captured in the same frame as the reaction vessel), then the **non-pre-heated** catalyst solution was quickly added into the mixture present in the 20 mL Schlenk tube using a syringe in one portion. The reaction was stirred at 70 °C and 600 rpm for 5 h.

NOTE - the camcorder was kept on constant mains power throughout the processes to avoid battery issues.

Sampling:

0.15 mL of reaction mixture was taken for off-line analysis by a syringe (NMR and LC-MS) at 0, 15, 30, 45, 60, 75, 90, 120, 150, 180, 240, 300 mins.

The syringe was washed with 1:5 methanol/acetone mixture and dried with compressed air prior to taking the next sample.

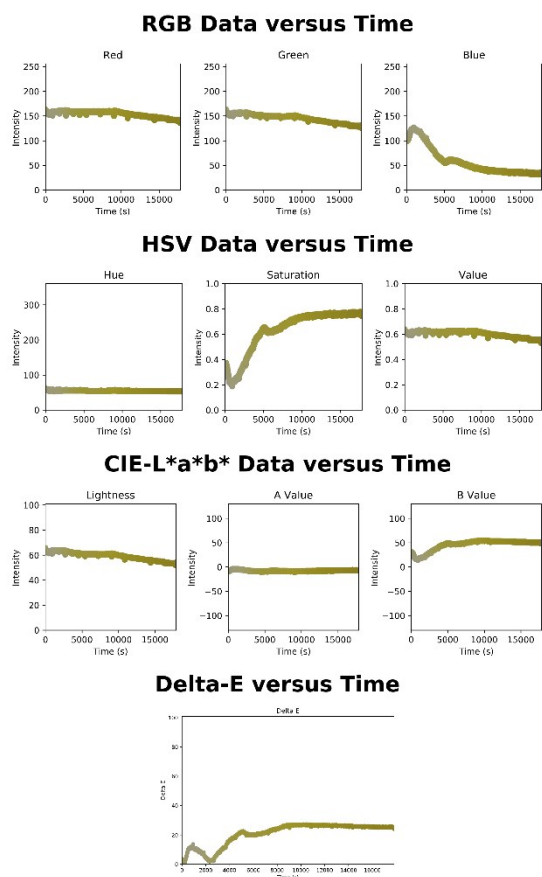
Preparation of NMR sample:

0.1 mL of reaction mixture were added into 0.3 mL DMSO-d6

Preparation of LC-MS sample:

1 – 2 drops of reaction mixture are added into the LC-MS sample vial and diluted with 1.4 mL of mobile phase solution (5 mM ammonium acetate in 1:1 water/acetonitrile mixture).

Computer Vision outputs:



Kineticolor

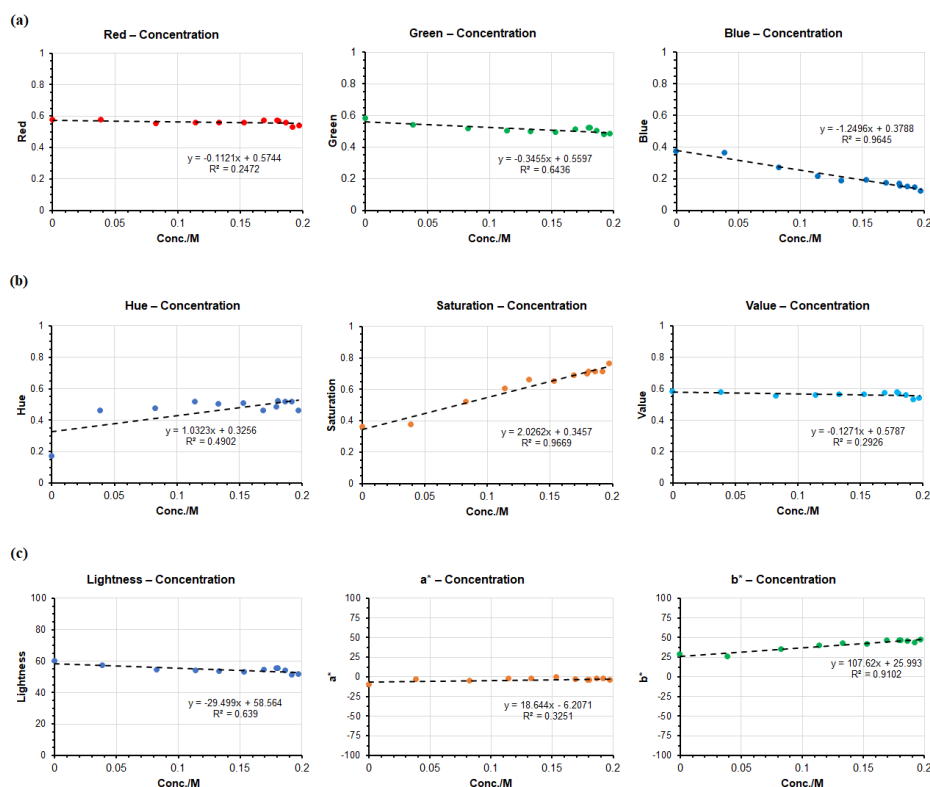
Selected Region of Interest



Scheme S12. The time-based results in 9 colour parameters (upper: RGB, middle: HSV, bottom: L*a*b* and ΔE). Results for non-pre-heated set-up described immediately above.

Investigating correlations between analytical datasets – manuscript Scheme 9

Overall, the concentration matches well with the 'Blue', 'Saturation' and 'b*' colour components, with R² values over 0.9. Before further explanation, it needs to be kept in mind that the colour of the reaction mixture becomes more yellow over time, that is from greenish-yellow to golden yellow, which is from greenish-yellow to gold-yellow. Therefore, the b* value of L*a*b* colour space, governing blue (negative value) and yellow (positive value), will increase as the transformation proceeds (see Scheme S13c), and the 'Blue' value of RGB model will reduce as yellow is the combination of 'Red' and 'Green' (Scheme S13a), and 'Saturation' value of HSV model increases over time indicating the colour is more close to its 'prime' colour – yellow (Scheme S13b), although it visually looks darker.



Scheme S13. Results of data correlations between concentration and colour parameters in a) RGB, b) HSV, c) L*a*b*. In all cases, liner trend lines are shown together with equations and R² values.

An example of the correlation process between ΔE and analysed NMR data are shown in Table S3, this data set was used to correlate the observed colour results from the reaction with the amount of product or substrate present (as percentage) derived from NMR and LC-MS off-line sample analysis.

Table S3: Data correlation between concentration and Kineticolor output

Entry	Off-line analysis				Kineticolor analysis				
	second	Product% by NMR	Substrate% by NMR	Substrate% by LCMS	seconds	blue	saturation	a_component	ΔE
1	924	14.209	58.391	56.147	924	0.3662	0.3974	-5.2480	4.5499
2	1864	29.827	45.301	44.204	1864	0.2772	0.5394	-5.4226	11.7136
3	2811	40.394	38.137	39.206	2811	0.1921	0.6826	-3.2115	20.4548
4	3660	46.162	32.493	33.994	3660	0.1613	0.7411	-3.1633	24.5010
5	4665	52.029	26.911	28.932	4665	0.1618	0.7296	-2.8852	22.8488
6	5783	56.290	23.547	25.251	5783	0.1790	0.6973	-5.4767	21.0621
7	7390	58.433	20.584	23.499	7390	0.1514	0.7563	-5.3939	25.6707
8	9165	57.541	21.405	22.422	9165	0.1261	0.7930	-4.5973	26.7544
9	10987	58.050	21.130	24.900	10987	0.1168	0.8057	-4.3861	26.9324
10	14616	58.447	21.212	23.357	14616	0.1210	0.7867	-3.9780	24.6605

Multivariate correlation analysis between colour and offline concentration datasets

As shown in **Figure S1**, the correlations between colour analysis and off-line analytical results (i.e. ^1H NMR or HPLC-determined concentrations) was evaluated after combining data sets. To extract the colour results at the time of taking off-line samples, the time data in each data set were compared to find the matched time points between the colour analysis and off-line analysis data sets. Thus, a new combined HPLC-NMR-colour data set was used for more in-depth correlation analyses. See **Table S3**. This combined dataset was then used to determine the R^2 value for all potential 2D correlations, which was used as a first approximation of exploring the colour parameters evidencing possible predictive power.

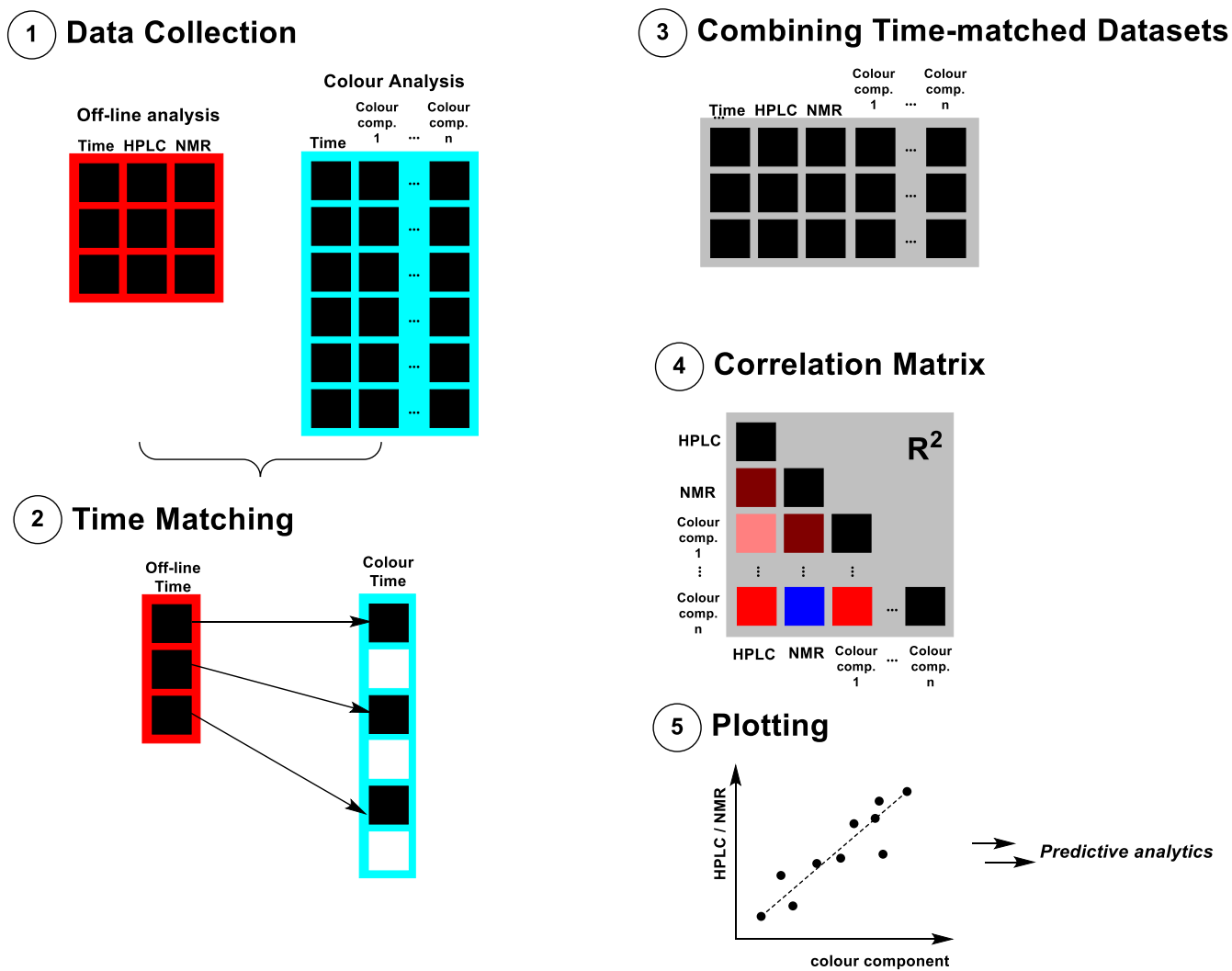


Figure S1 General workflow of data correlation and the determination of linearity

The predictive power of any single colour component/channel to estimate off-line concentration measurements was assessed using leave-one-out (LOO) cross-validation of the simple linear regression models calculated for all colour and concentration combinations. This process can be repeated for n times ($n =$ the number of samples), giving all possible linear models trained on $n-1$ datapoints for a given simple linear model. The final model is then calculated as the average of all models generated. The correlation coefficient for the relationship between off-line concentration and the concentration predicted by colour was then used to score the predictive power of that particular colour model. See **Figure S2**.

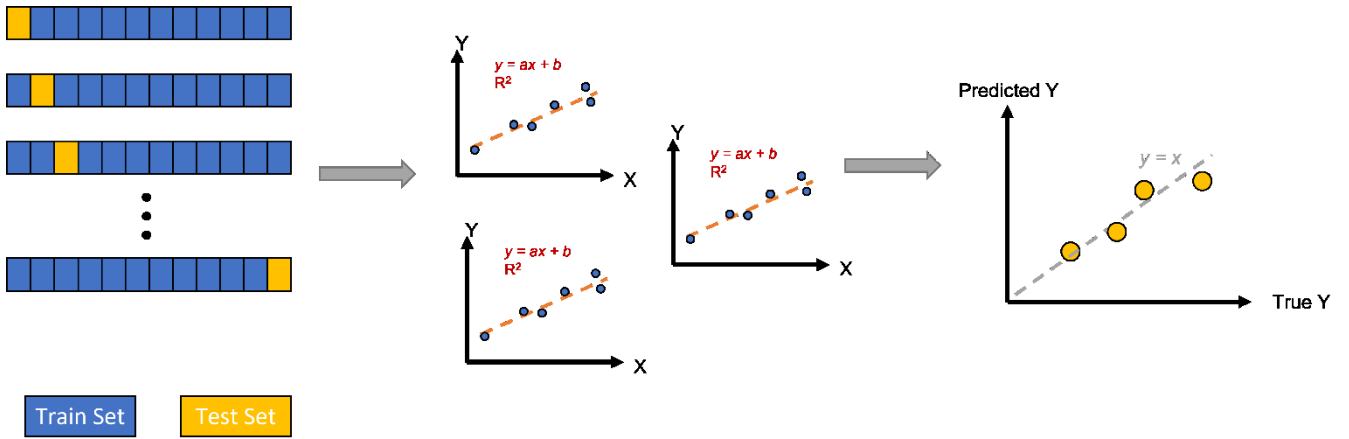


Figure S2 Schematic workflow of cross validation (leave-one-out)

Kinetic and Variable Time Normalisation Analysis (VTNA) to Investigate Catalyst Degradation

VTNA was carried out according to the procedure described by Bures.⁷ Assuming no degradation or decrease of catalyst concentration during reactions.

The hot plate was placed in a lightbox with lamp switched on. Light level (illuminance) in the box was controlled and measured using a light meter, a white background board was placed at the back of the lightbox. To a 20 mL Schlenk tube was added bromobenzene (314 mg, 2 mmol), B₂Pin₂ (610 mg, 2.4 mmol), KOAc (588 mg, 6 mmol) and 1,3,5-trimethoxybenzene (168.3 mg, 1 mmol) as an internal standard for subsequent offline NMR and HPLC analyses.

After the addition of DMSO (6 mL), the mixture was heated to 70 °C under argon, nitrogen, or air. To another vial was added [(PCy₃)₂Pd(OAc)₂] (3.9 mg, 0.005 mmol) in 1,4-dioxane and DMSO (2 mL total, 1 mL dioxane:1 mL DMSO). This catalyst solution was then heated for 2 mins to 70 °C. And this pre-heated catalyst solution was quickly added into the mixture presented in the 20 mL Schlenk tube using a syringe in one portion. The resulting mixture was stirred at 70 °C and 600 rpm for 5 hours.

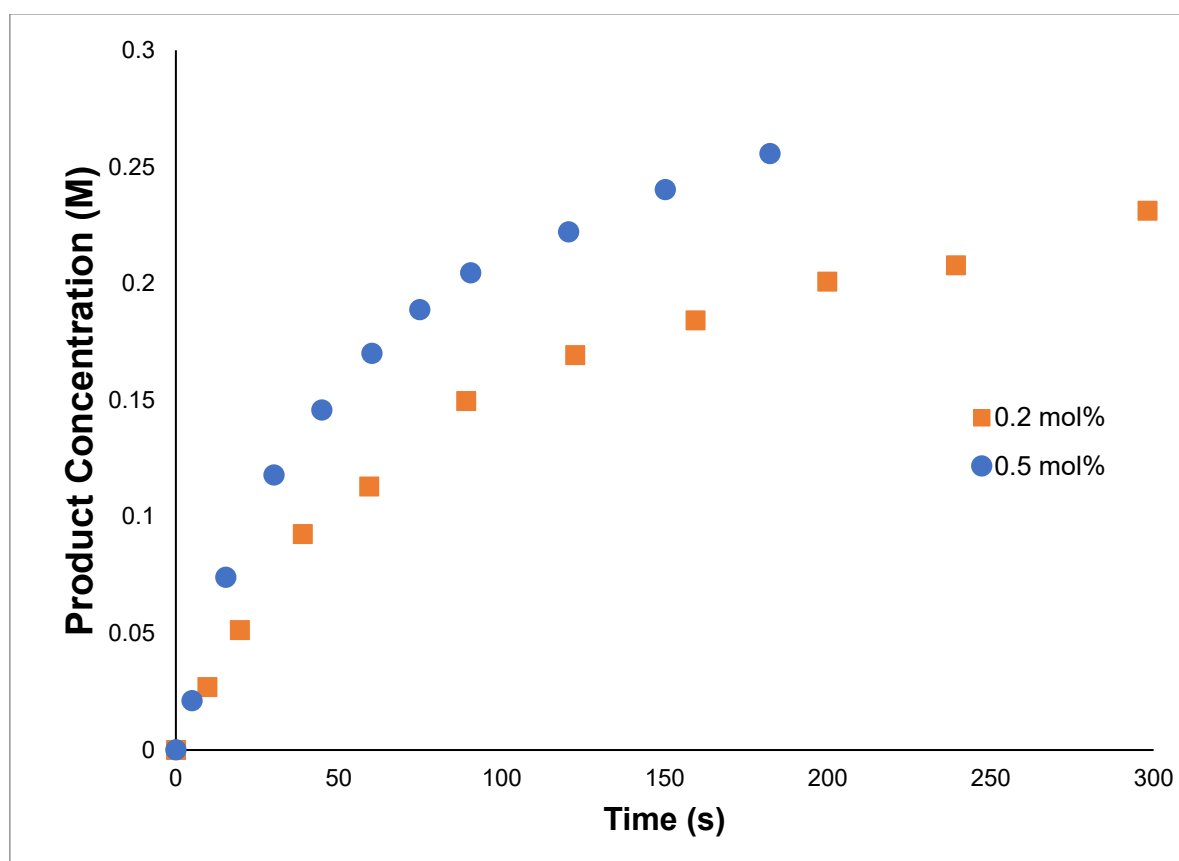
Time course plots under argon

0.2 mol% catalyst

Time/min	Product	[cat] ¹ .Δt	Σ[cat] ¹ .Δt
0	0	0	0
9.633333	0.026961	0.005519621	0.00552
19.633333	0.051389	0.00572971	0.011249
38.91667	0.092562	0.011048792	0.022298
59.31667	0.112962	0.011688609	0.033987
89.06667	0.149614	0.017045889	0.051033
122.5	0.169297	0.019156332	0.070189
159.45	0.184212	0.02117128	0.09136
199.85	0.200787	0.02314803	0.114508
239.3167	0.207808	0.022613257	0.137122
298.1	0.231171	0.033681148	0.170803

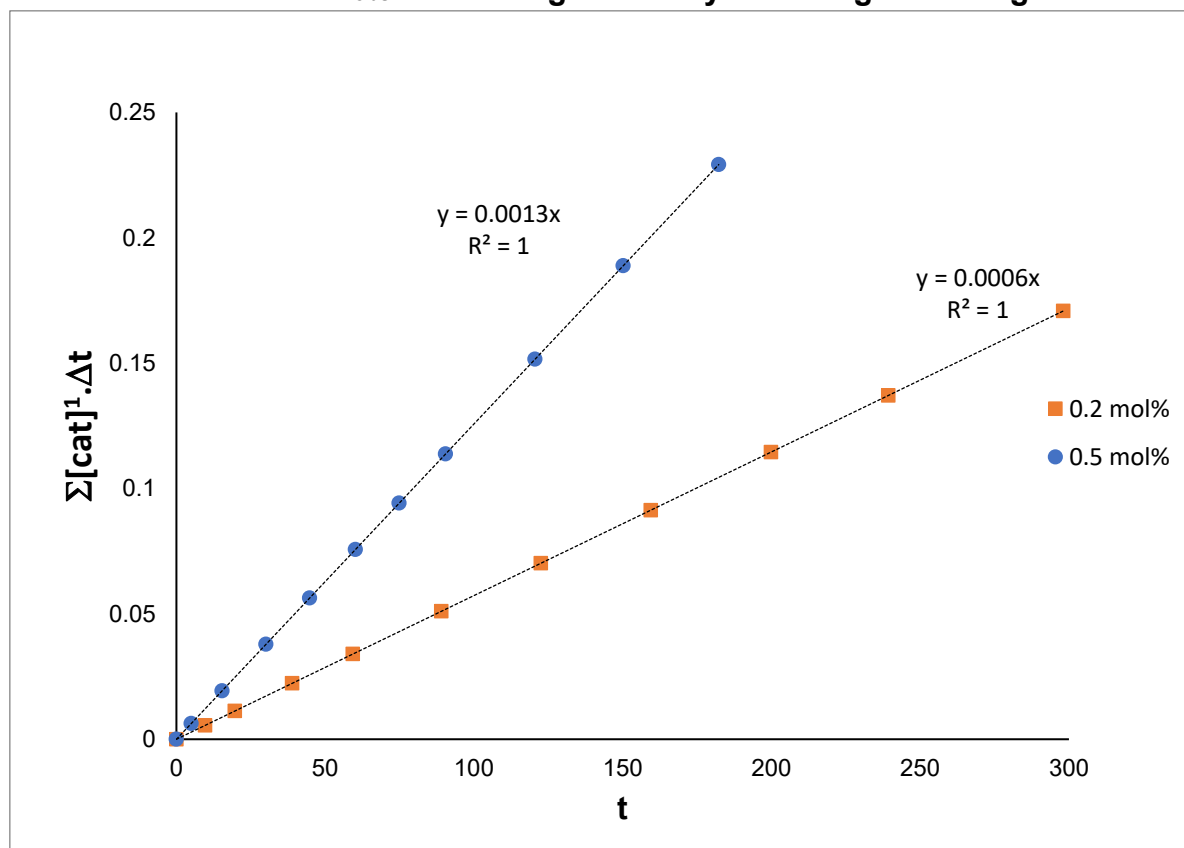
0.5 mol% catalyst

Time/min	Product	[cat] ¹ .Δt	Σ[cat] ¹ .Δt
0	0	0	0
4.966667	0.021076	0.006244854	0.006245
15.36667	0.073988	0.013076473	0.019321
30.11667	0.117836	0.018545959	0.037867
44.8	0.145709	0.018462135	0.056329
60.16667	0.169992	0.019321326	0.075651
74.88333	0.188748	0.018504047	0.094155
90.46667	0.204523	0.019593753	0.113749
120.5333	0.222048	0.037804417	0.151553
150.2	0.240207	0.037301476	0.188854
182.3	0.255614	0.040361035	0.229215



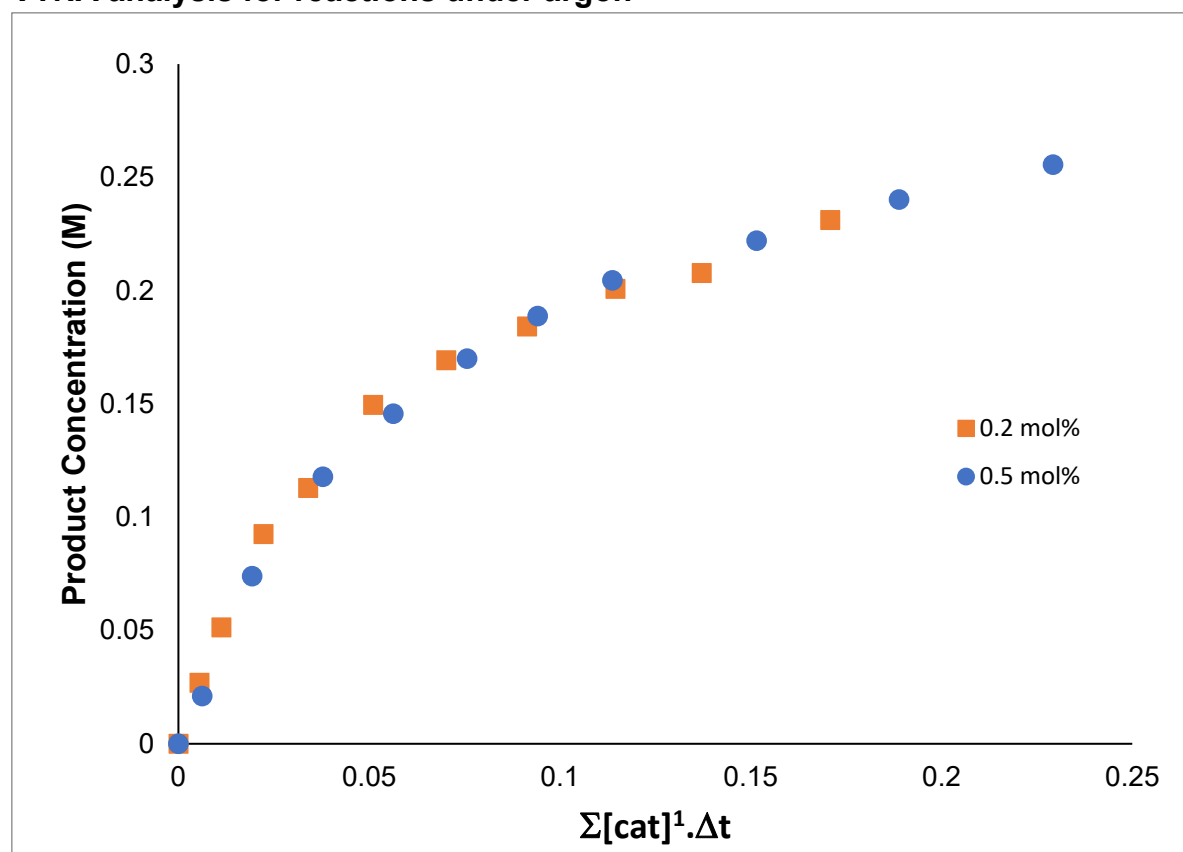
As expected, higher catalyst loading led to a qualitatively higher rate of product formation, reaching approximately 1.25x higher product conversion within the first 180 seconds.

Extraction of relative k_{obs} with change in catalyst loading under argon



As part of the VTNA analysis, the plot above assumes first order in catalyst. The relative k_{obs} derived from the gradient of each line suggests that the 2.5-fold increase in catalyst loading results in an approximately 2.2-fold increase in k_{obs} .

VTNA analysis for reactions under argon



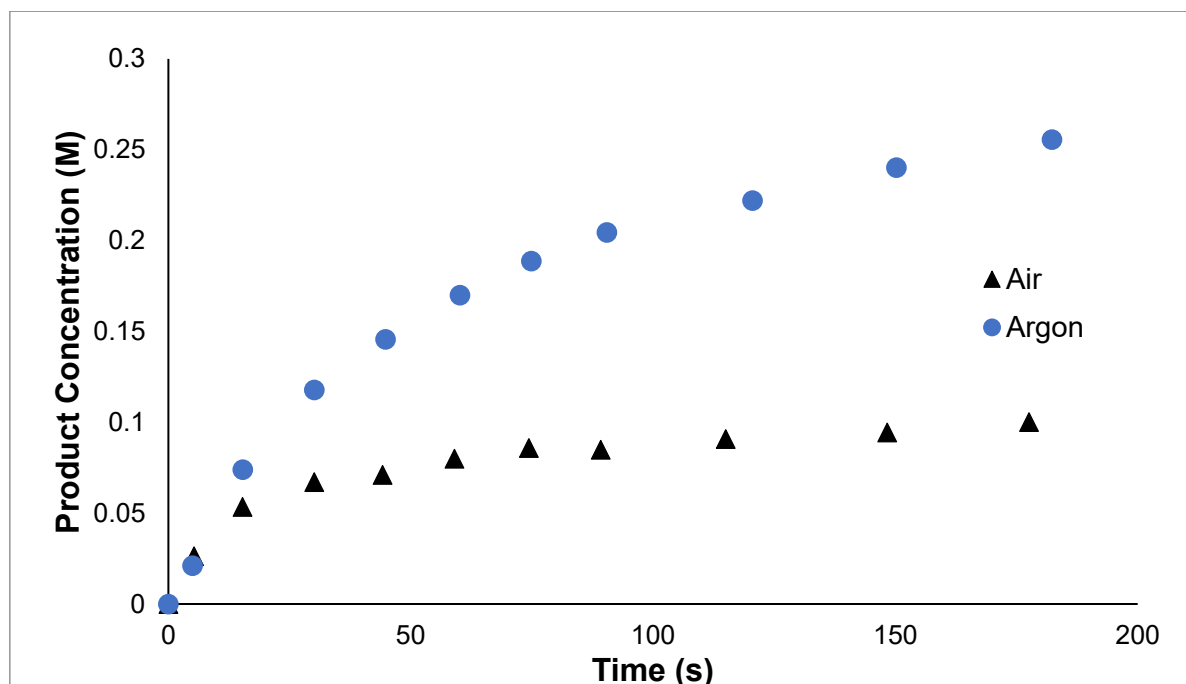
Formal VTNA analysis in the plot above maintains the assumption of the borylation being first order in catalyst. Indeed, visual inspection of the overlay for reactions at 0.2 and 0.5 mol% catalyst support this claim. The analysis also supports the assumption that negligible catalyst degradation takes place in the analysis time window.

Impact of removing argon protection

0.5 mol% catalyst under air (instead of argon)

Time/min	Product	[cat]¹.Δt	Σ[cat]¹.Δt
0	0	0	0
5.283333333	0.026368476	0.006643016	0.006643016
15.31666667	0.053486849	0.012615443	0.019258459
30.08333333	0.067142278	0.018566915	0.037825373
44.2	0.071093564	0.017749635	0.055575008
59.03333333	0.080036645	0.018650738	0.074225746
74.36666667	0.085942773	0.019279415	0.093505161
89.21666667	0.084927101	0.018671694	0.112176855
115	0.09087385	0.032418755	0.14459561
148.3166667	0.094439264	0.041890815	0.186486425

177.5833333	0.100168729	0.036798535	0.22328496
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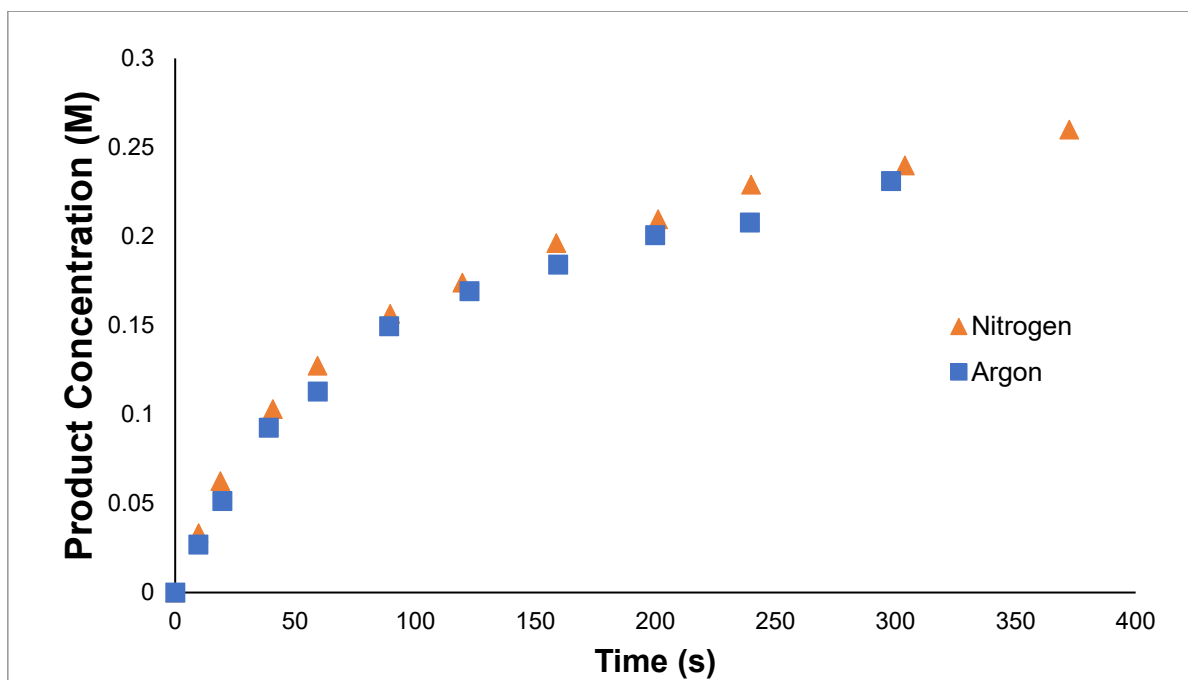


Consistent with observed blackening of the reaction mixture under air, calculated conversion to borylation product was approximately 2.5-fold lower at 180 seconds than for the same reaction under argon at 0.5 mol% catalyst loading.

Swapping argon for nitrogen

0.2 mol% catalyst under nitrogen (instead of argon)

Time/min	Product	[cat] ¹ .Δt	Σ[cat] ¹ .Δt
0	0	0	0
9.73333333	0.03339016	0.005422004	0.005422
18.8	0.06256074	0.005050634	0.01047264
40.68333333	0.10299269	0.012190224	0.02266286
59.3	0.12736269	0.010370511	0.03303337
89.55	0.15653127	0.016850919	0.04988429
119.6	0.17404899	0.016739508	0.0666238
158.733333	0.19623435	0.021799426	0.08842323
201.15	0.20964946	0.023628424	0.11205165
239.816667	0.22906645	0.021539467	0.13359112
303.9	0.23987403	0.035697953	0.16928907
372.35	0.26001831	0.038130427	0.2074195



Attending the practical considerations of industrial practitioners who may wish to apply these methods using nitrogen in place of comparatively more expensive argon, the above comparison of borylation under both inert gases revealed no concerns regarding catalyst degradation (0.2 mol% catalyst). This analysis is consistent with neither reaction – under argon or nitrogen – producing observable blackening of the bulk reaction mixture, as recorded by the video footage.

Mutual Information

Entropy: A measure of the uncertainty associated with a random variable. The more uncertain we are, the more we lack information.

Information: the capacity to reduce uncertainty.

Quantification of information pioneered by Claude Shannon in *A Mathematical Theory of Communication Bell System Technical Journal, 1948*).⁸

For $\mathbf{A} = (a_1..a_n)$, this could be (as a relevant example) time series, carrying an array of values occurring at specific times

Probabilities = $(p_1...p_n)$ where each

Self-information, $I(a_i) = \log (1/p_i)$

If a data-source has a low-probability value, the event carries more 'surprisal' than when the source data has high probability.

Shannon Entropy (H) defines the amount of uncertainty in a data source as:

$$H = - \sum_{i=1}^n p_i \cdot \log(p_i)$$

When working with one variable array, x , one must first consider how to calculate or source the value of the **marginal probability**, $P(x)$:

$$H(X) = - \sum_{i=1}^n P(x_i) \cdot \log P(x_i)$$

One way to estimate marginal probability is the **histogram approach**:

1. Find **min**, **max**, and **range** of values.
 2. Select number and size of **bins**.
 3. Segment the **range** using the **number of bins**, each bin being of equivalent size.
- The **marginal probabilities** to be summed are then the **frequency counts** falling within each histogram bin divided by the **total number of samples** (i.e. elements in the time series array).

$$P(x_i) = \frac{\text{no. elements in bin}}{\text{total no. elements in series}}$$

The **entropy** is then calculated based on the previous equation. If there are 10 histogram bins, the I ranges from 1 – 10.

The process repeats for the number of supposedly independent features to be compared.

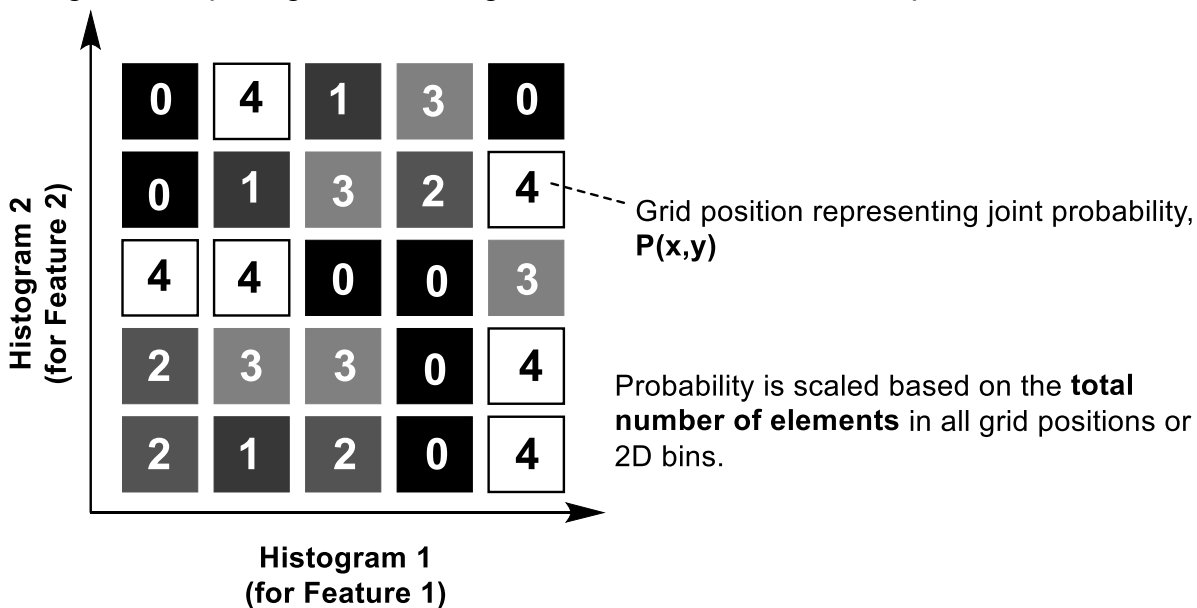
After calculating the **entropy** for each feature, one can then look to understand the **information** available in one feature when another feature is given. This is where **joint entropy** comes in.

Joint entropy of discrete random variables X and Y is the entropy of their pairing, **H(X,Y)**. By the same chord, we now need to consider **joint probability, P(x_i,y_i)** instead of **marginal probability**.

$$H(X,Y) = - \sum_{x \in X} \sum_{y \in Y} P(x,y) \cdot \log_2[P(x,y)]$$

Useful intuition builder: (X,Y) could represent the position of a **chess piece**. X stores row position, Y stores column position. The **entropy of the row of the piece** and the **entropy of the column of the piece** come together to represent the **entropy of the position of the piece**.

To estimate the **joint probabilities**, we can use 2D instead of 1D histograms. Each 1D histogram composing the 2D histogram can come from two 'independent' features.

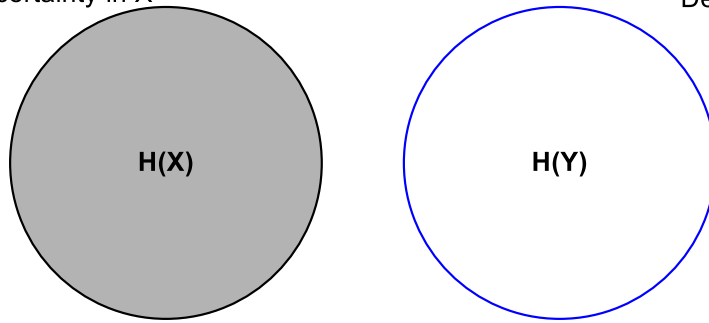


$$P(x,y) = \frac{\text{no. elements in 2D grid position}}{\text{total no. elements in the 2D grid}}$$

Taking all of this towards an understanding of the **mutual information** held between two features or variables demands a **Venn diagram** visualization of the entropies thus far formulated.

Degree of uncertainty in X

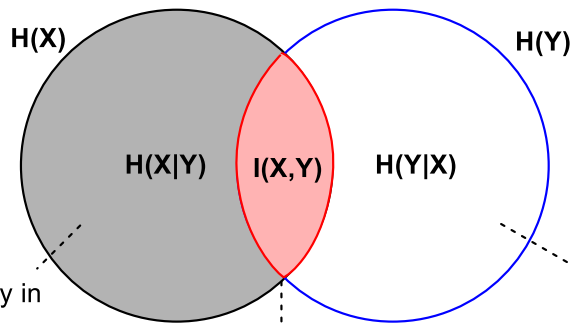
Degree of uncertainty in Y



No overlap => X and Y are completely independent of one another

Degree of uncertainty in X

Degree of uncertainty in Y



Remaining uncertainty in X, given Y

Remaining uncertainty in Y, given X

Overlap => the mutual information between X and Y

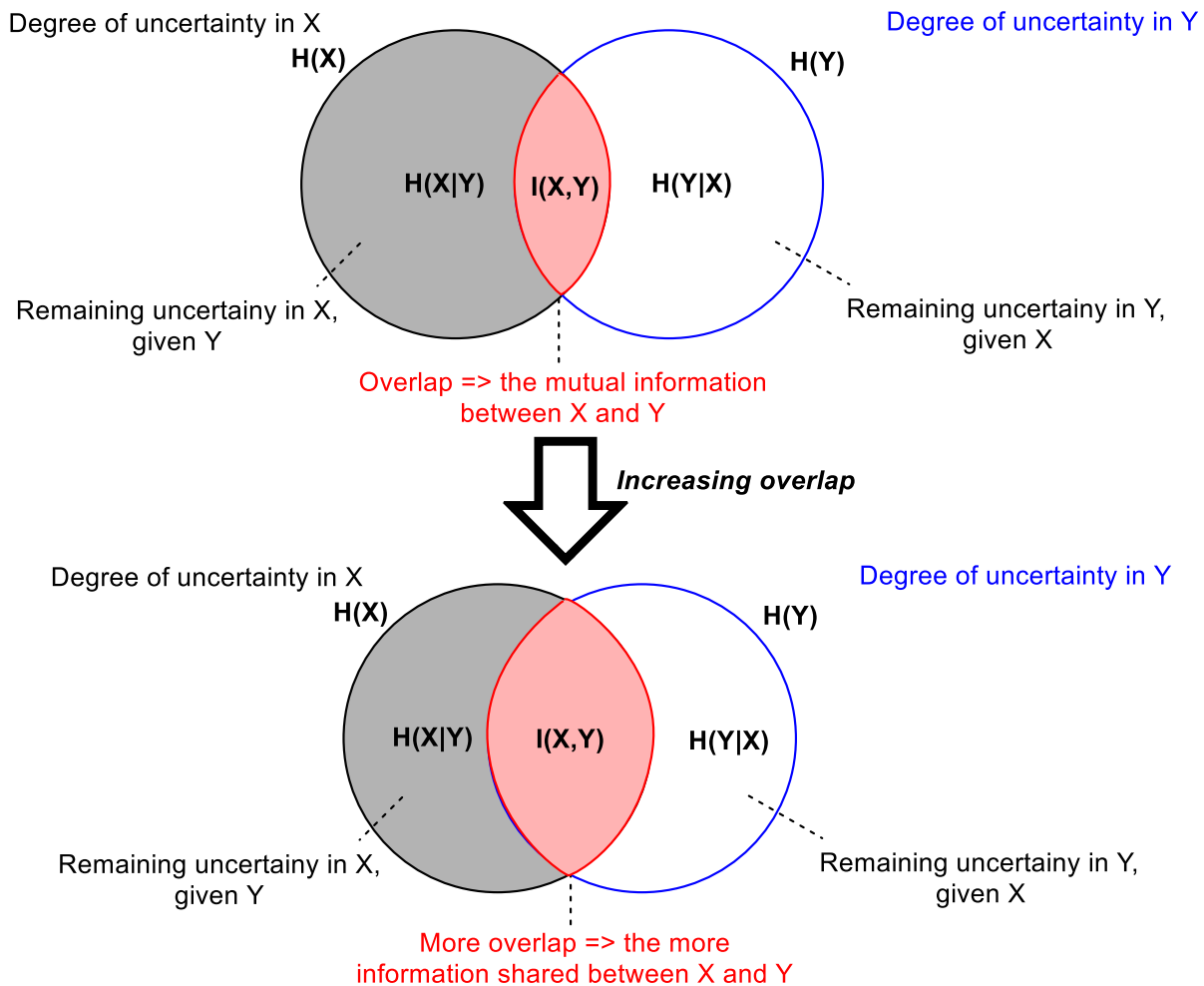
$$\begin{aligned}
 I(X; Y) &= H(X) - H(X|Y) \\
 I(X; Y) &= H(Y) - H(Y|X) \\
 I(X; Y) &= H(X) + H(Y) - H(X, Y) \\
 I(X; Y) &= H(X, Y) - H(X|Y) - H(Y|X)
 \end{aligned}$$

where, for example:

$$H(Y|X) = - \sum_{x \in X} \sum_{y \in Y} P(x, y) \cdot \log_2 \left[\frac{P(x, y)}{P(x)} \right] = P(x, y) \cdot \{ \log_2 [P(x, y)] - \log_2 [P(x)] \}$$

Some notes on reading these diagrams:

- As the overlap increases, the amount of shared information between X and Y increases. It does **NOT** mean there is any sort of additional transfer of information between X and Y:



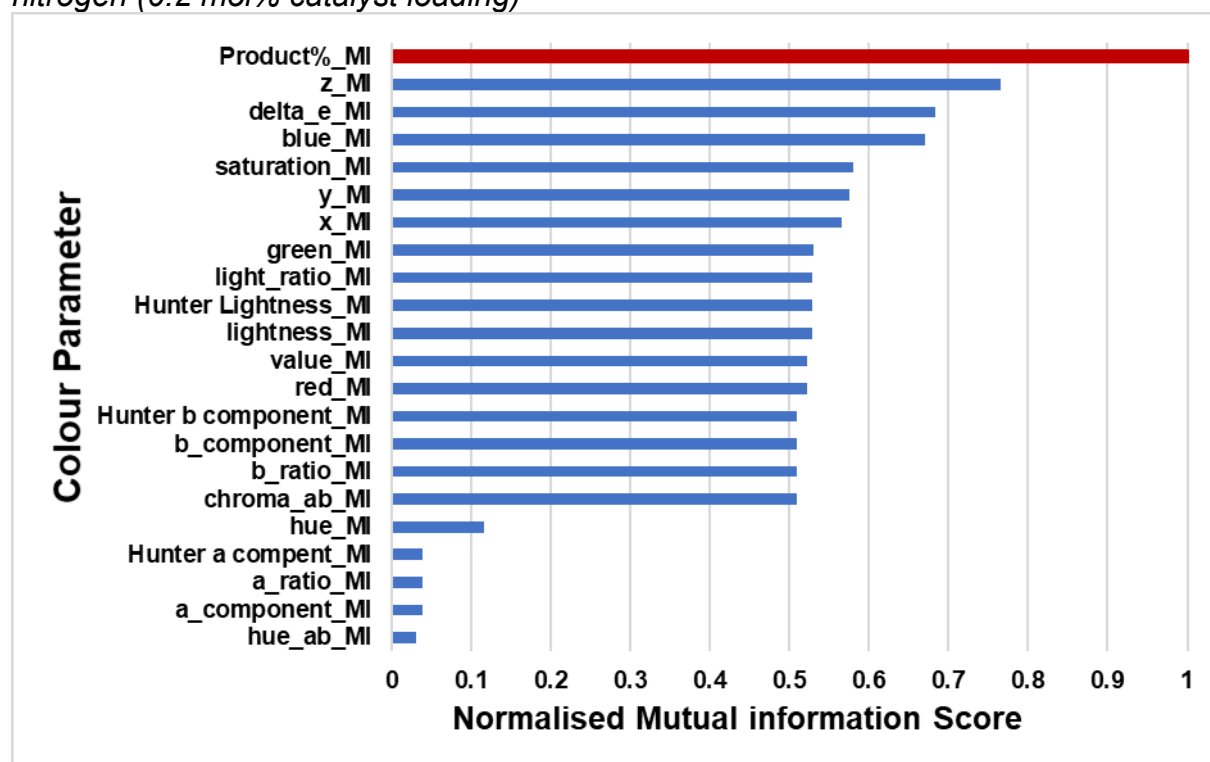
- When the **mutual information** is expressed using a *comma* between X and Y, it assumes the size of X and Y is the same. It also assumes we are only considering two features, X and Y. For example, X could be an array of HPLC samples over time. Y could be the subset of colour data at the same time points as HPLC samples, making arrays X and Y the same size.

The use of a semi-colon is more general (e.g. for **conditional mutual information** involving >2 features). The semi-colon denotes everything that is to be measured (left) given everything known (right).

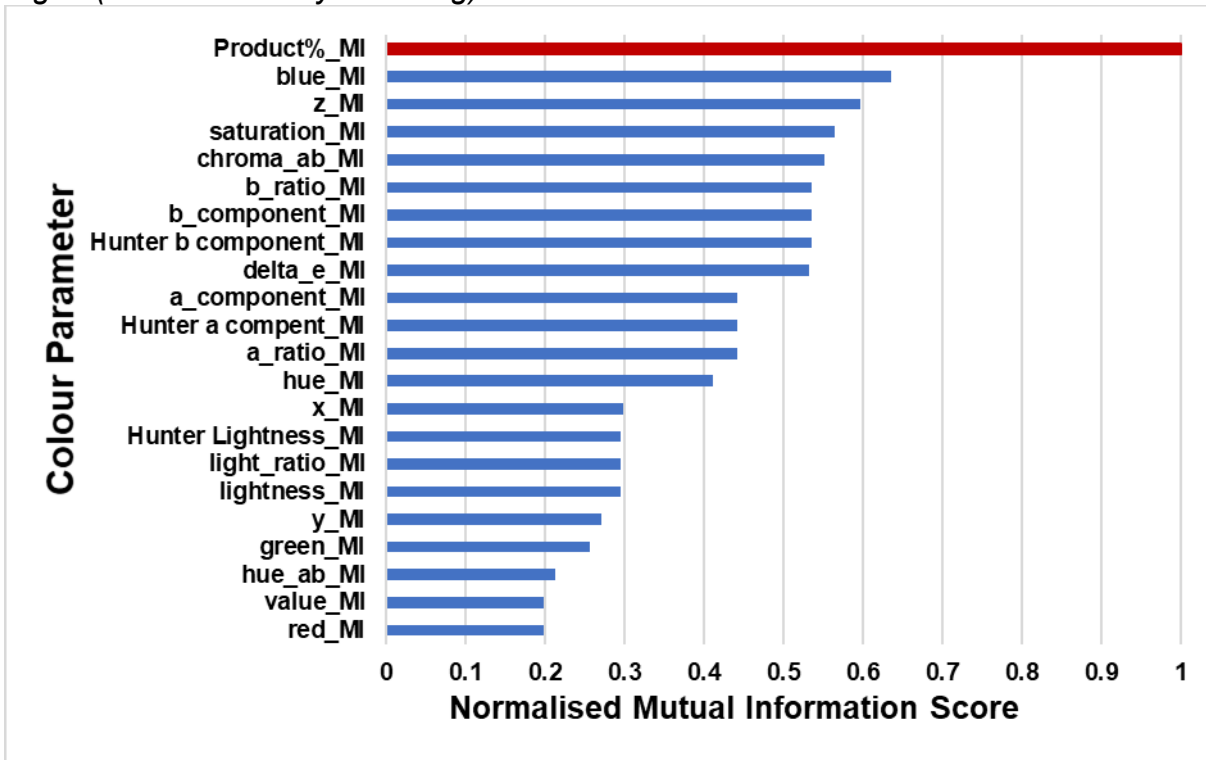
Employing the mutual information function (and default settings) in the Python library *Scikit Learn*, the off-line NMR-derived % product conversion was compared to all colour components extracted from reaction video files. All mutual information scores were scaled to the range 0 – 1 (where 1 is the maximum possible score, representing the highest likelihood of knowing something about one time series given an independent other).

In the graphs below, the mutual information between the off-line dataset with itself is coloured red, and has the benchmark value of 1 by definition.

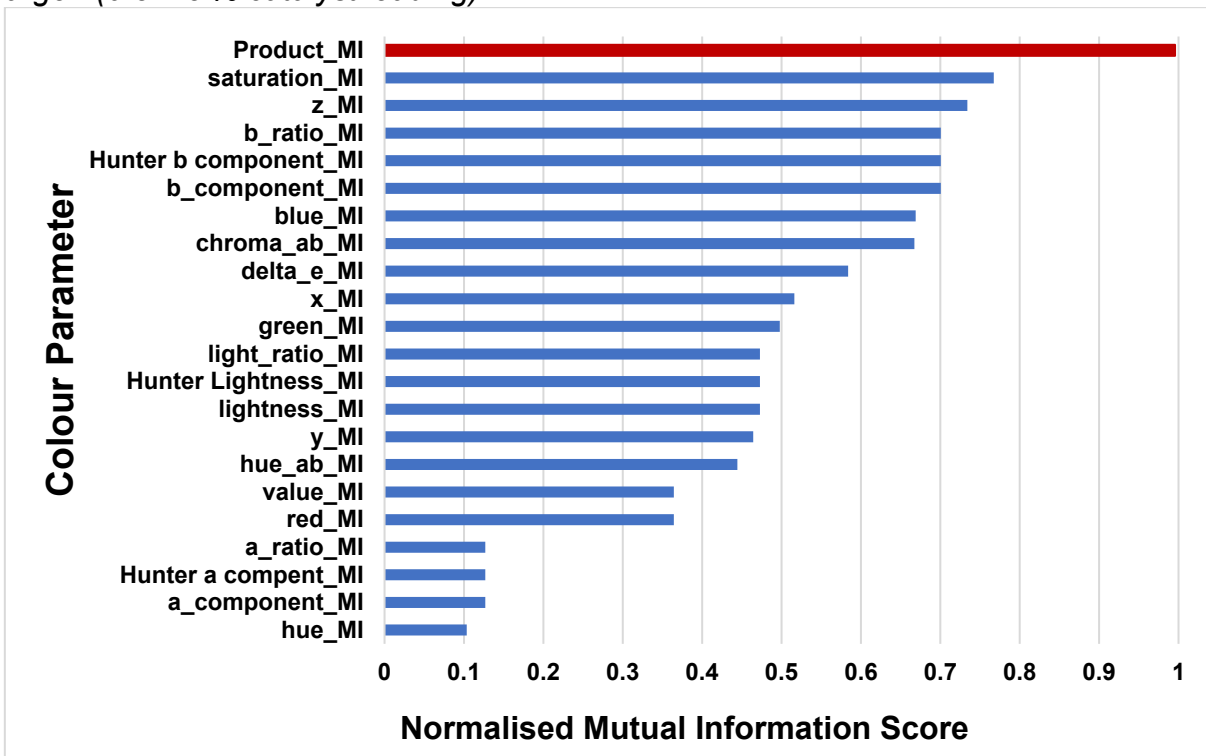
nitrogen (0.2 mol% catalyst loading)



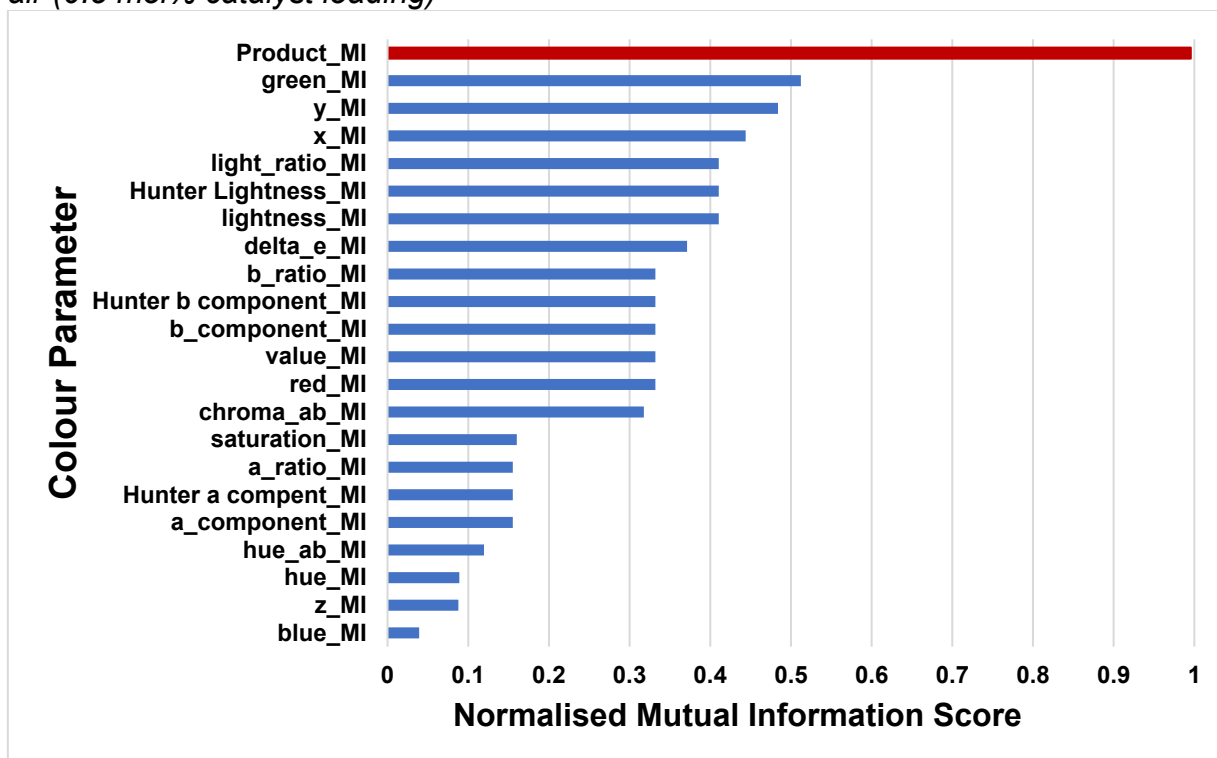
argon (0.2 mol% catalyst loading)



argon (0.5 mol% catalyst loading)

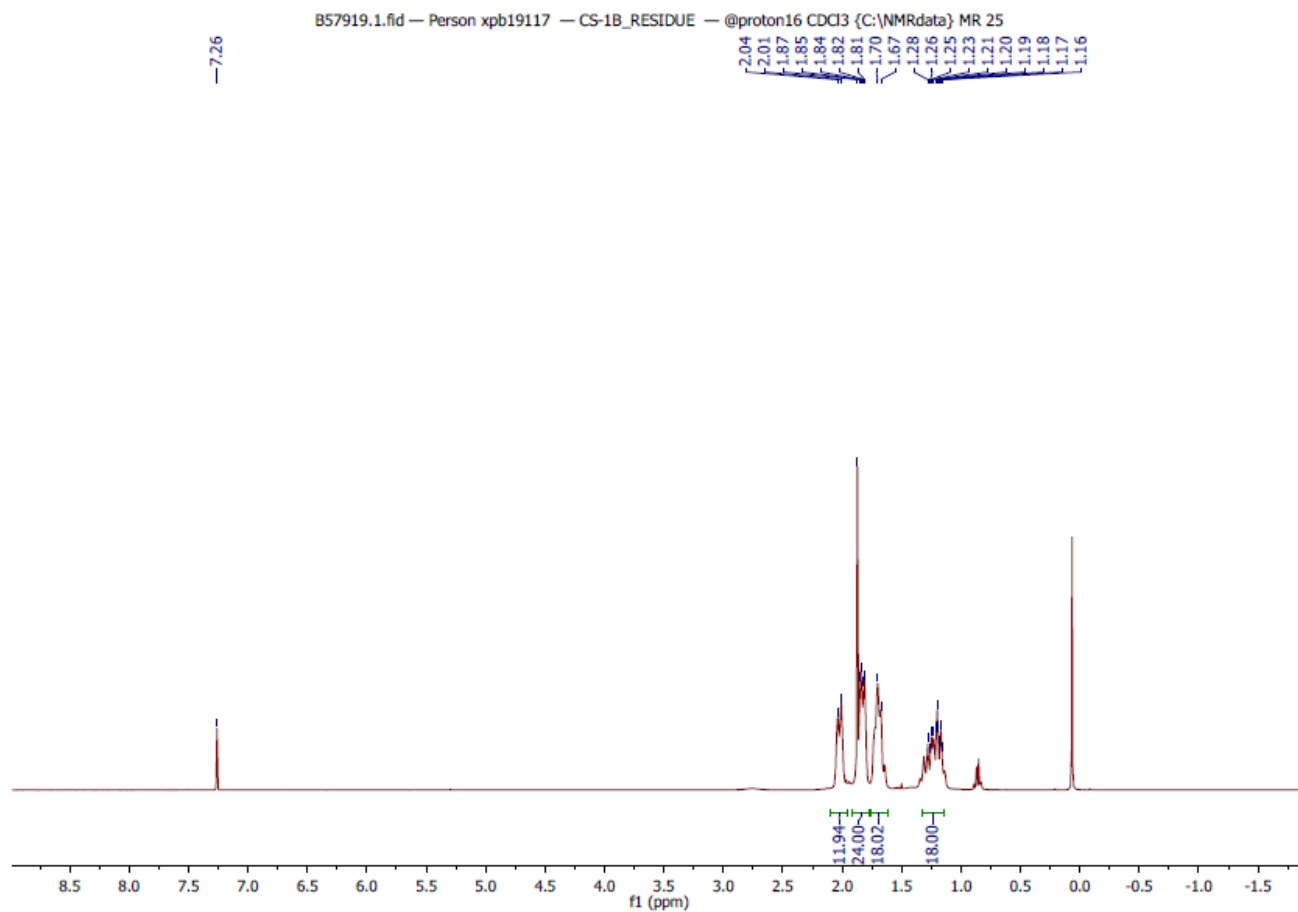


air (0.5 mol% catalyst loading)



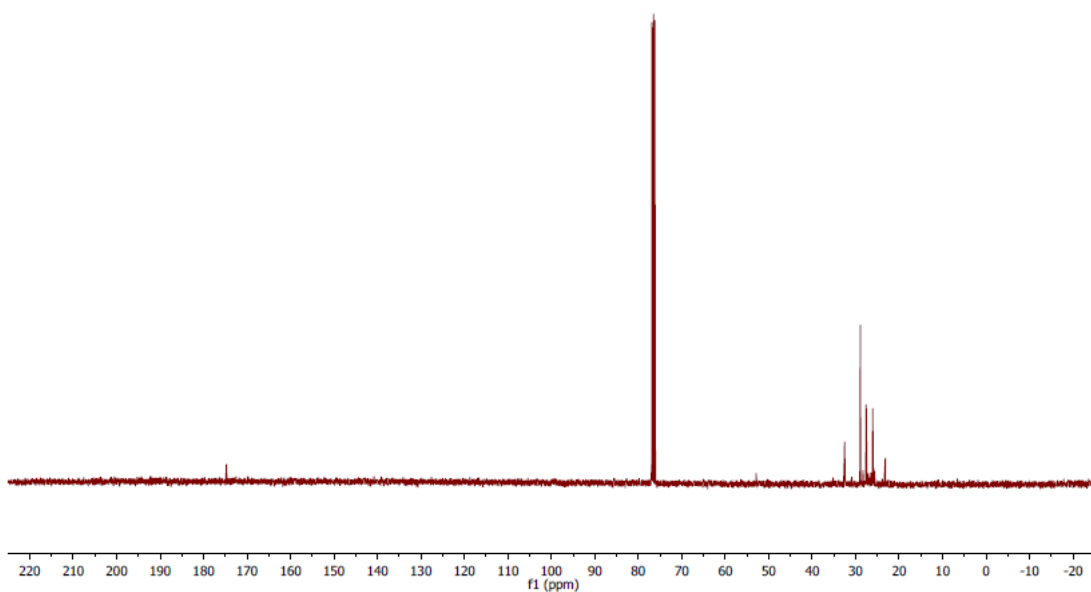
NMR Spectra

[Pd(OAc)₂(PCy₃)] – ¹H (CDCl₃)



[Pd(OAc)₂(PCy₃)] – ³¹P (CDCl₃)

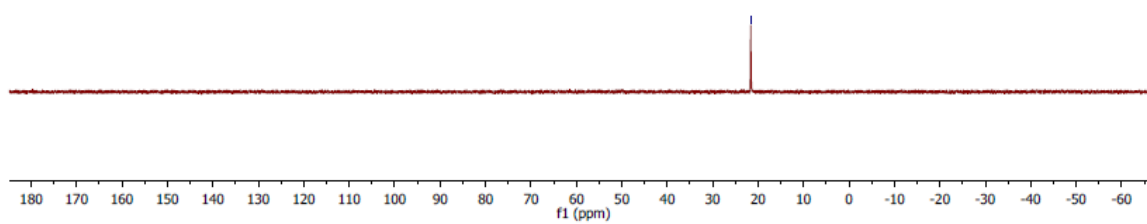
D320981.2.fid
Person xpb19117
CS-1B
13C_@ CDCl3 (C:\NMRdata) MR 5



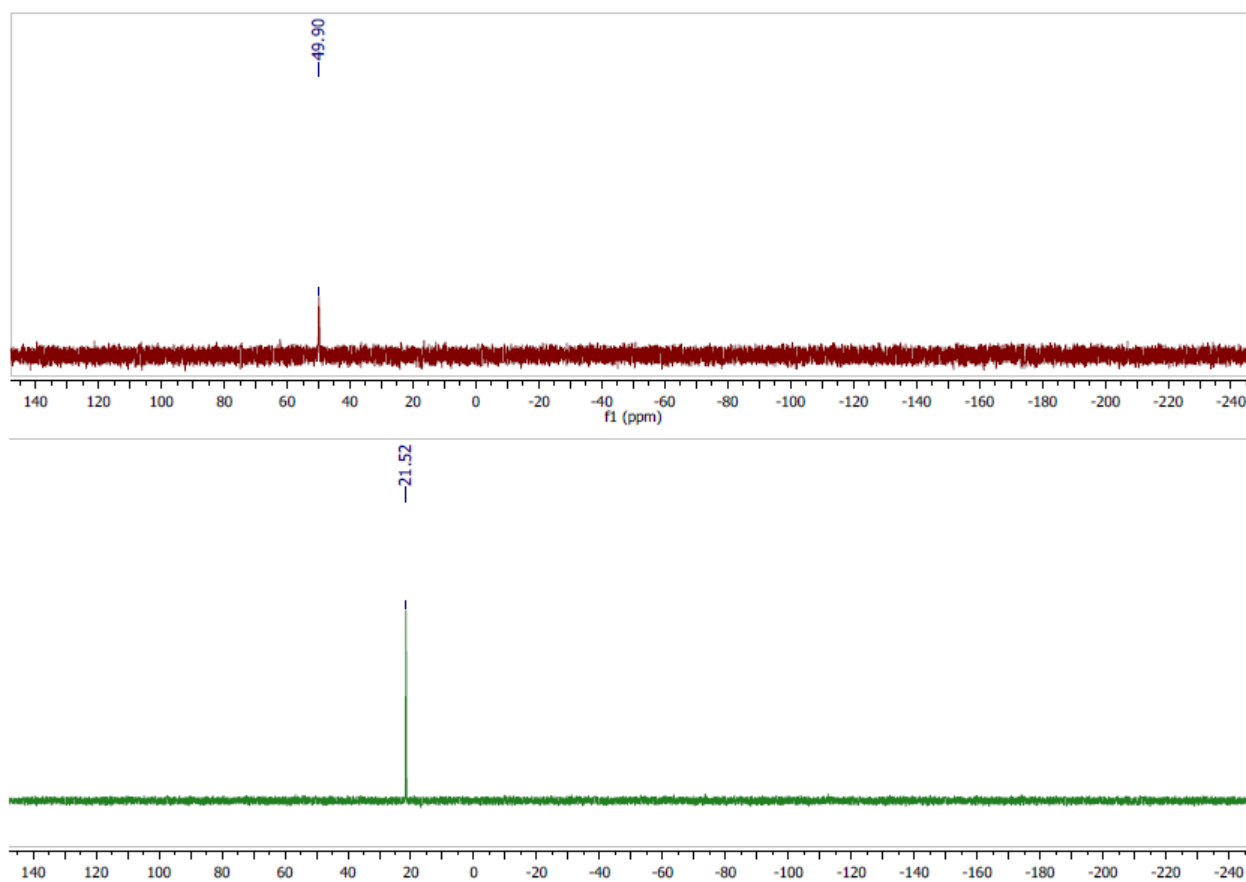
[Pd(OAc)₂(PCy₃)] – ³¹P (CDCl₃)

B57919.2.fid
Person xpb19117
CS-1B_RESIDUE
@31P CDCl3 (C:\NMRdata) MR 25

— 21.62

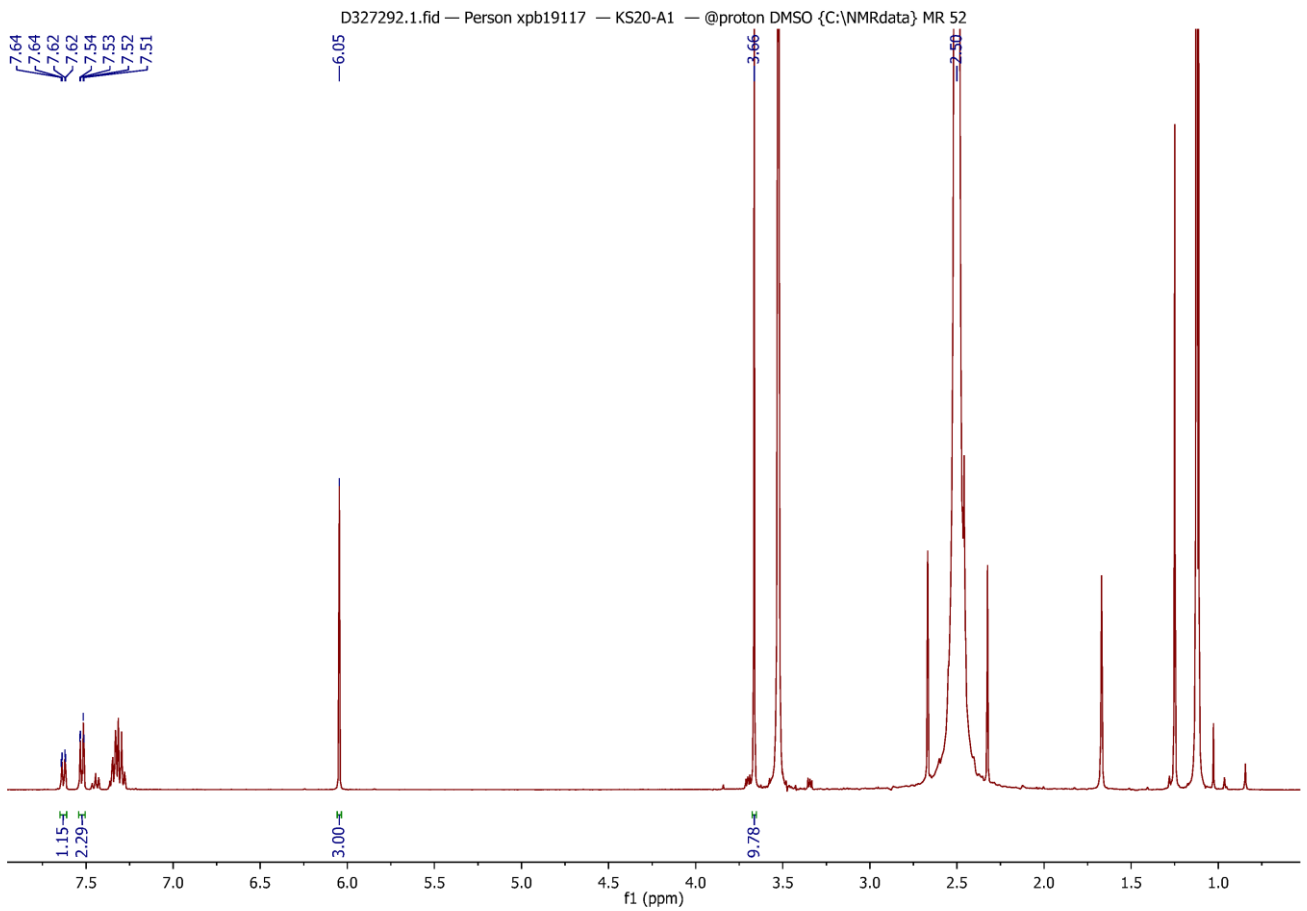
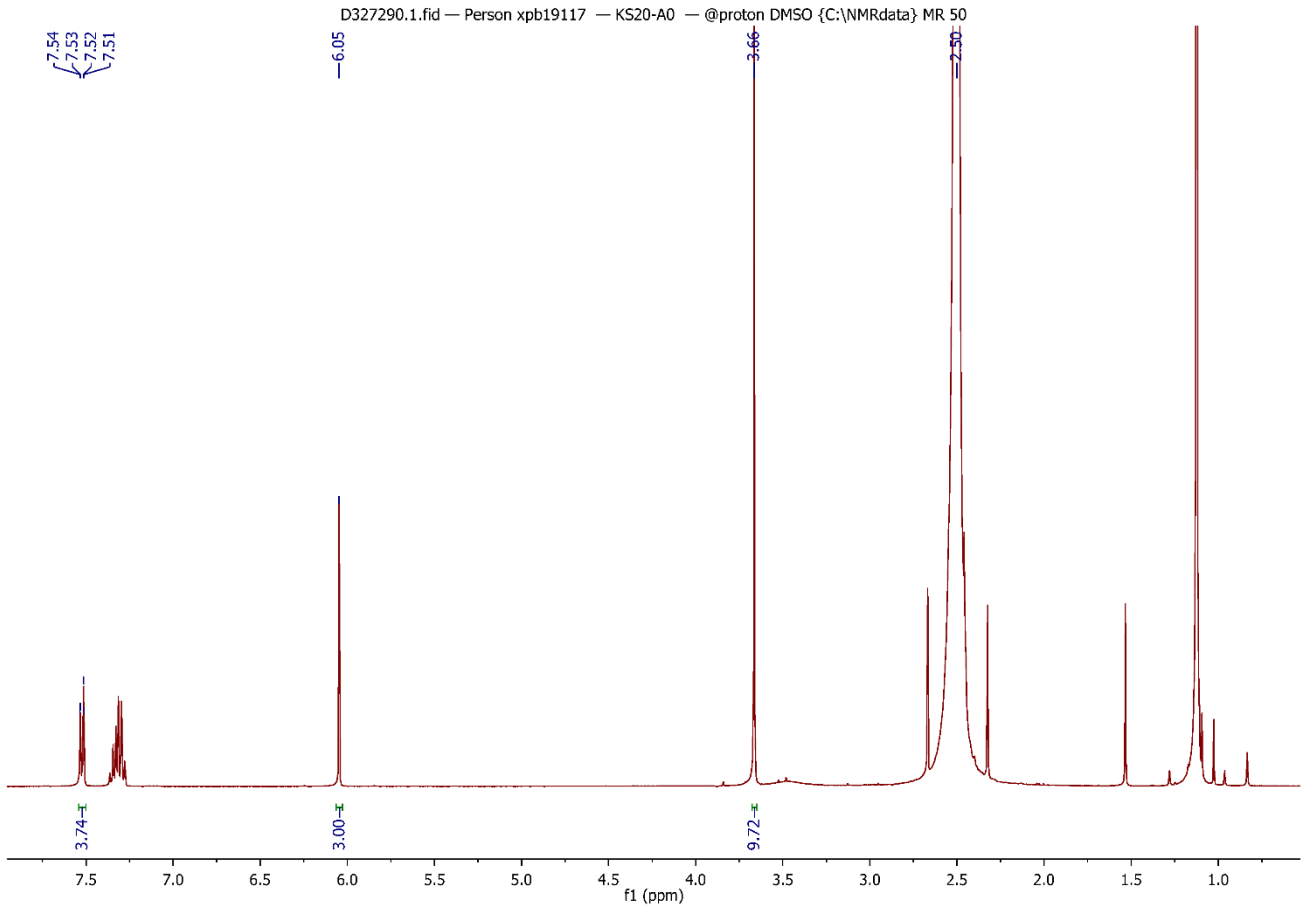


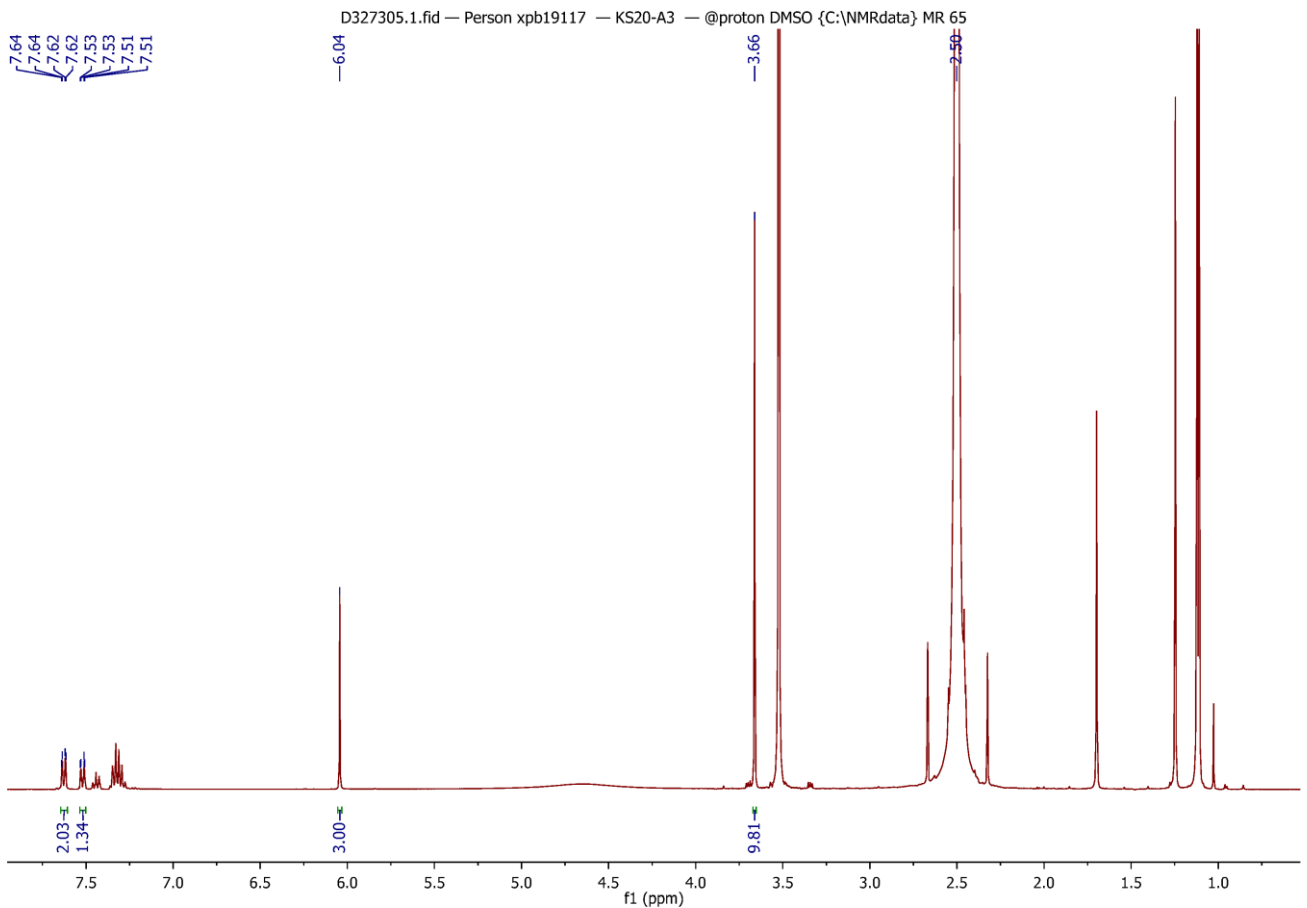
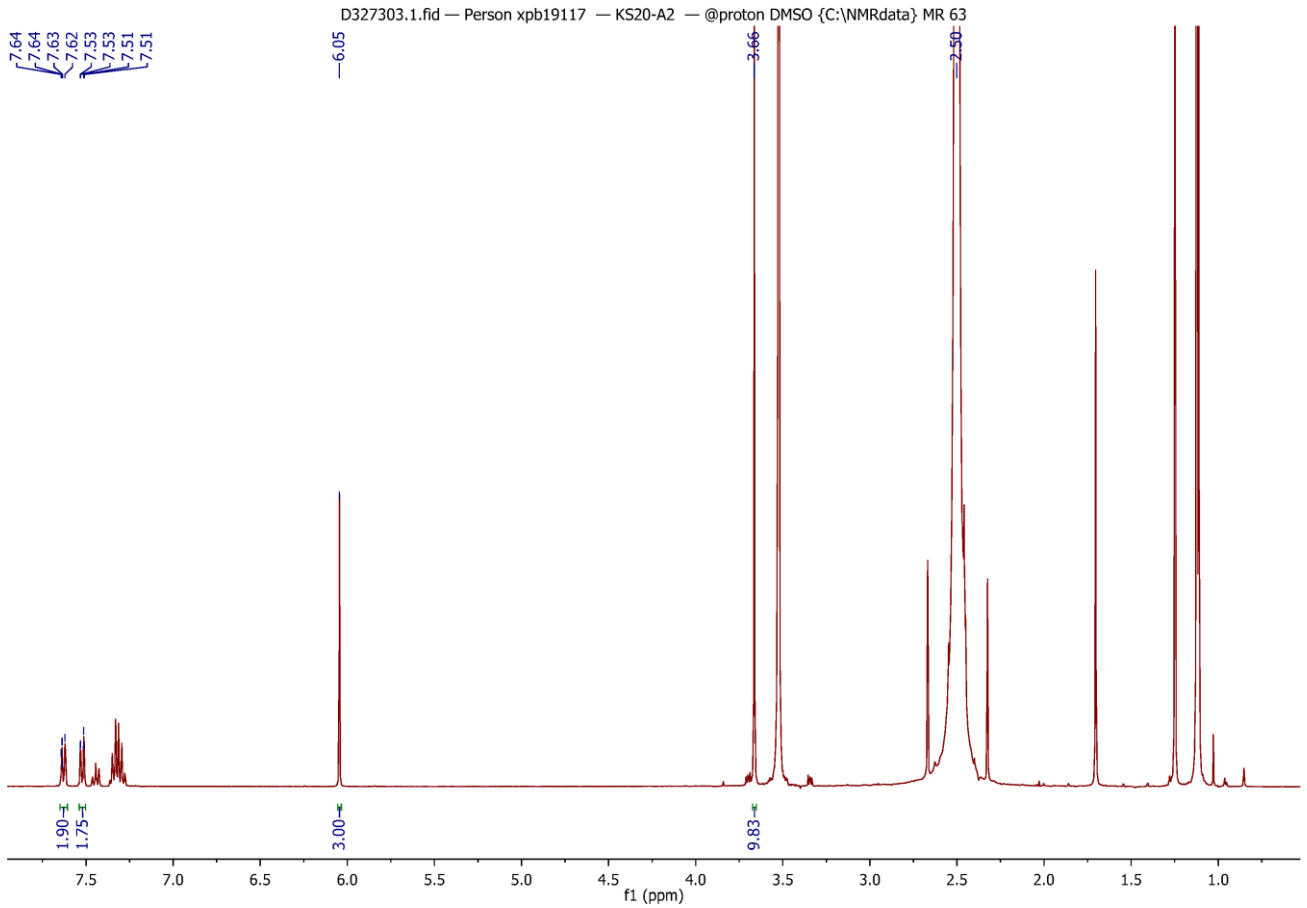
Isolated catalyst degradation – ^{31}P (CDCl_3) spectra for manuscript Scheme 3

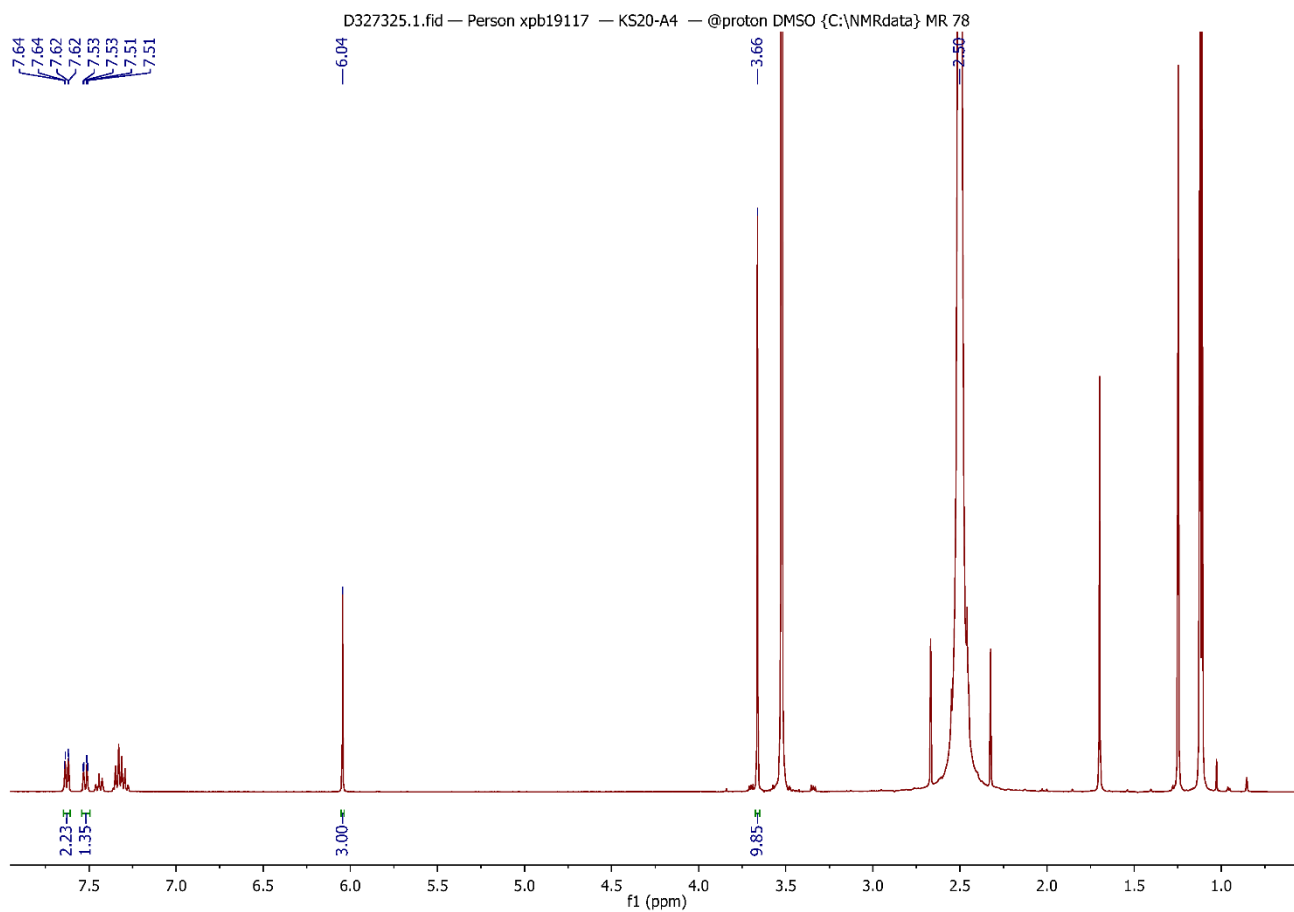


Miyaura borylation reaction samples – ^1H (DMSO-d_6) spectra for manuscript Scheme 7

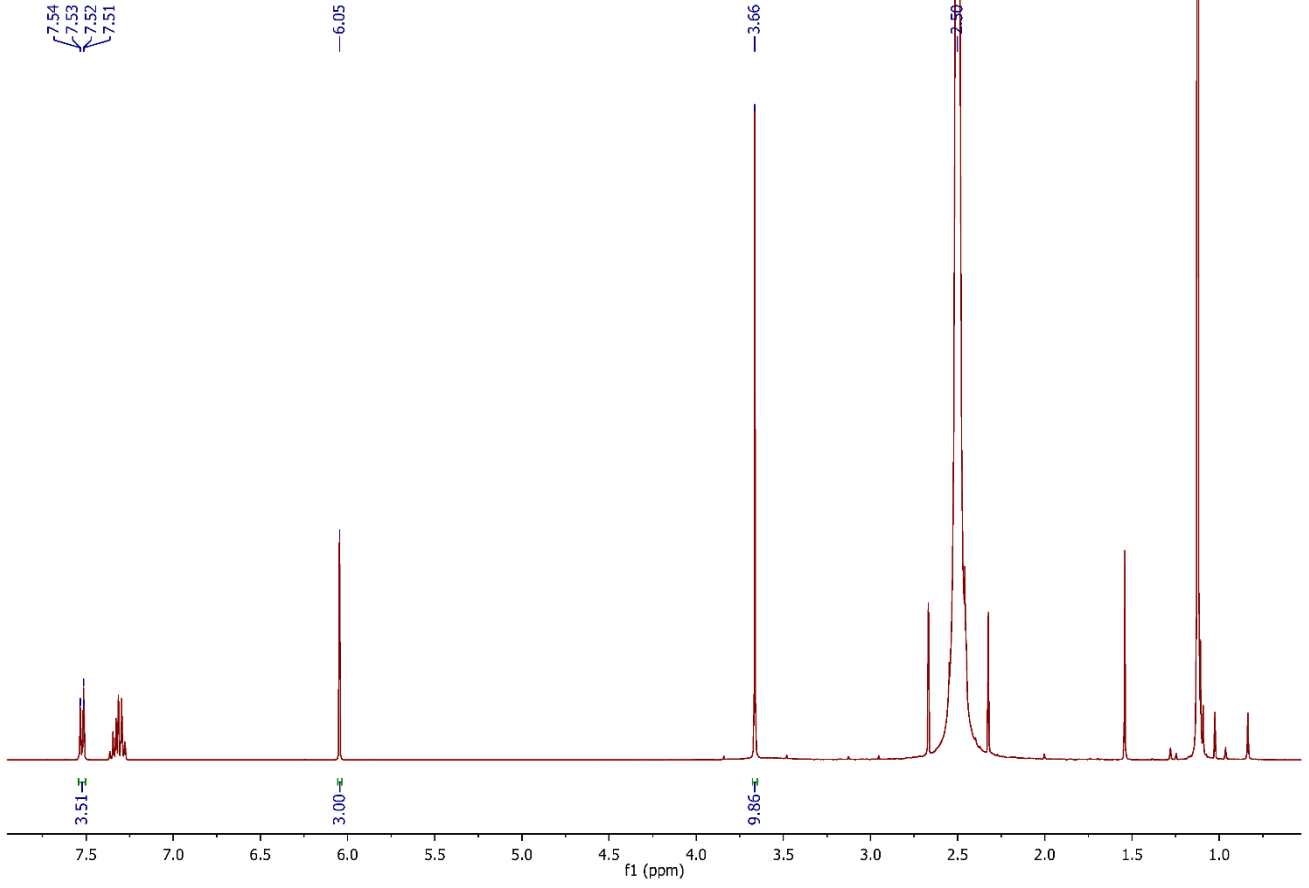
Reaction under Argon with 0.5 mol% catalyst loading:

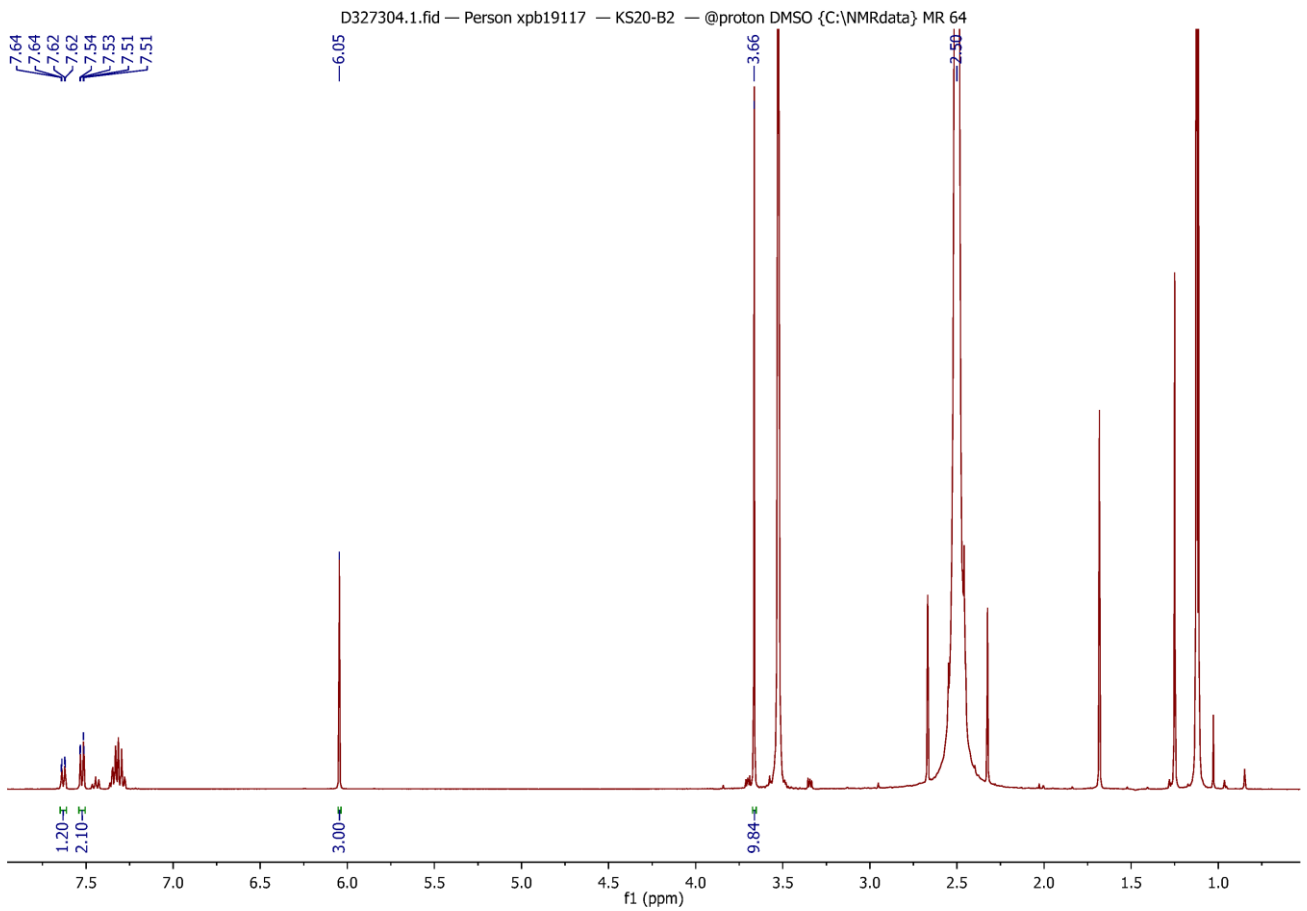
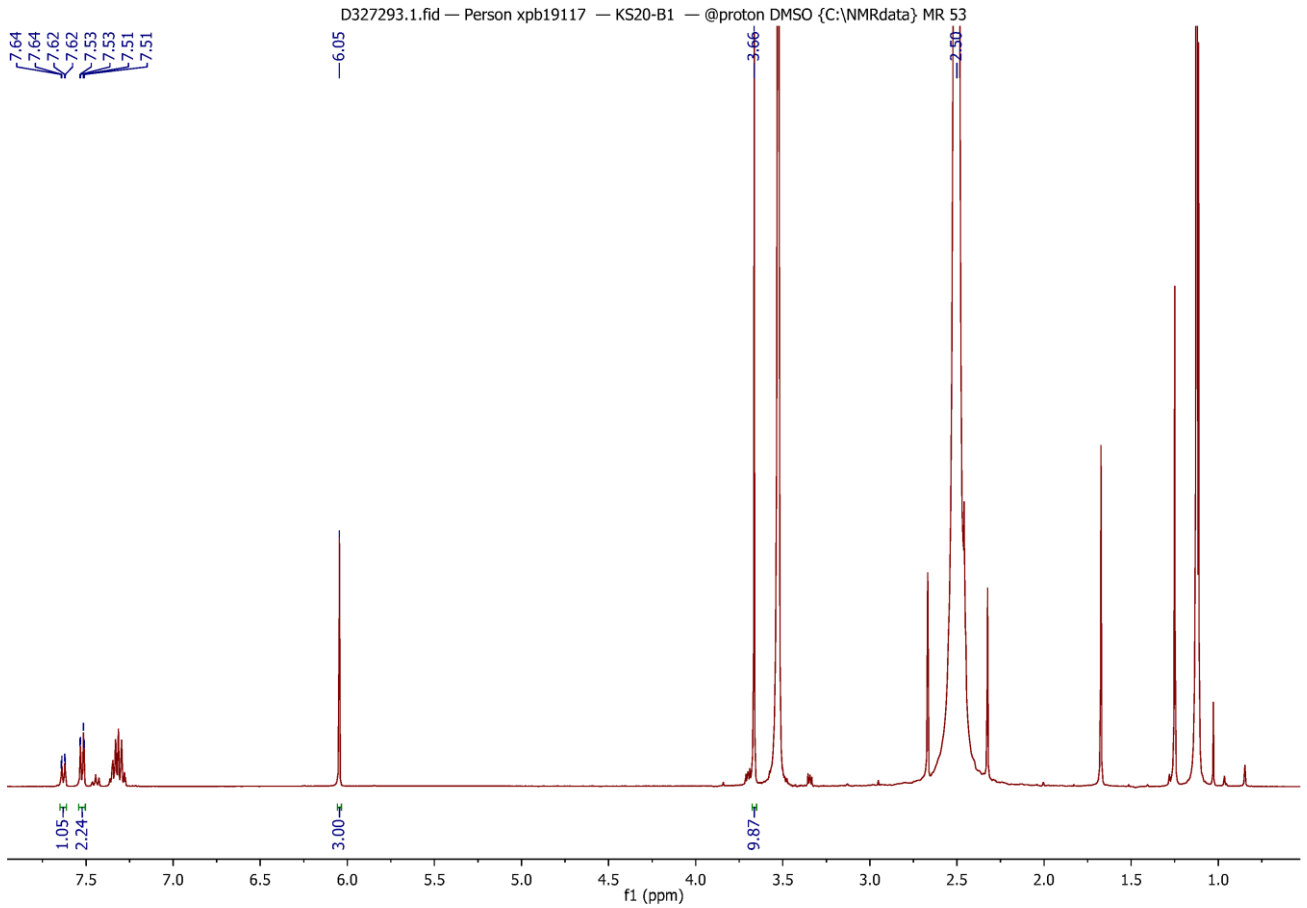


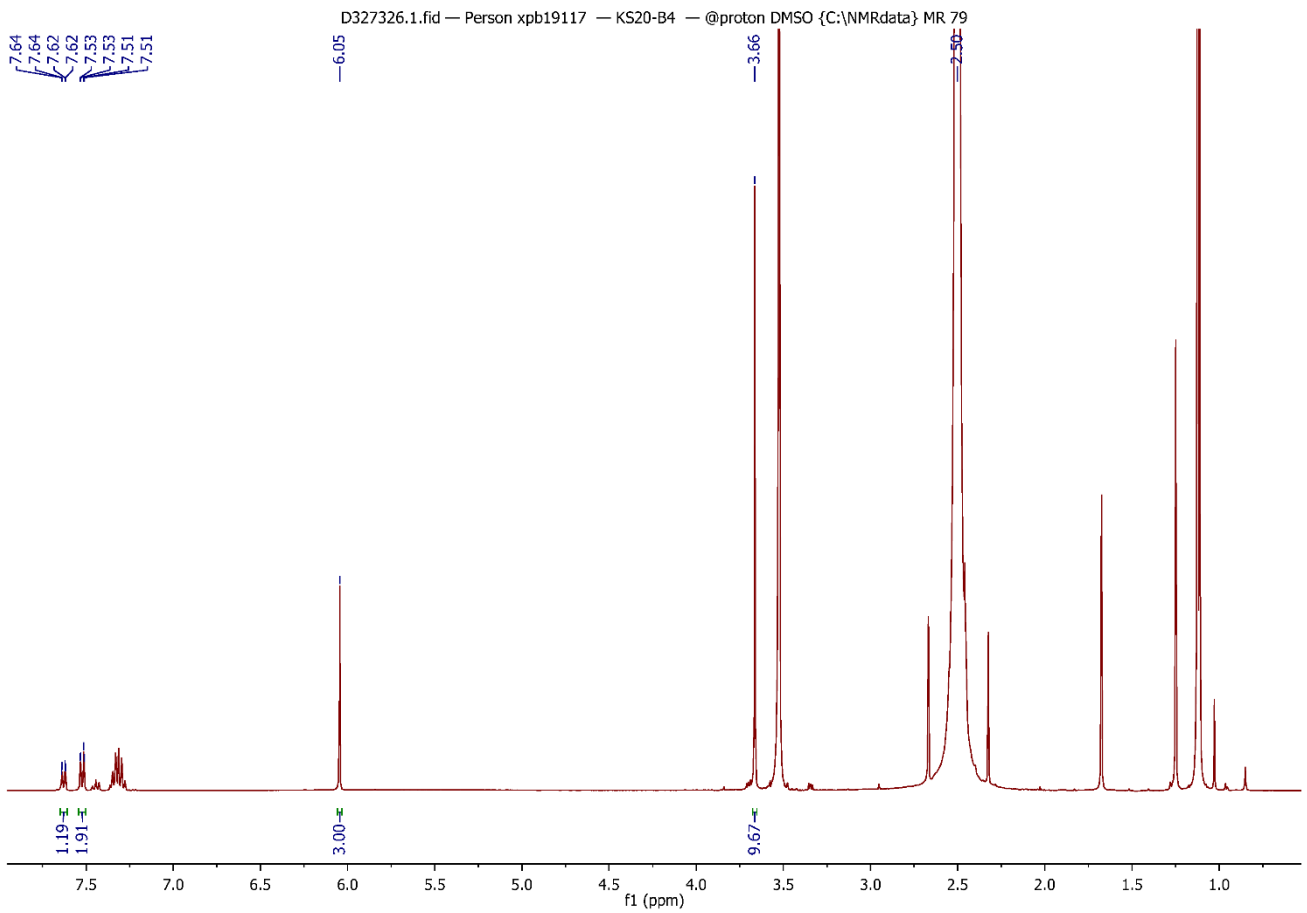
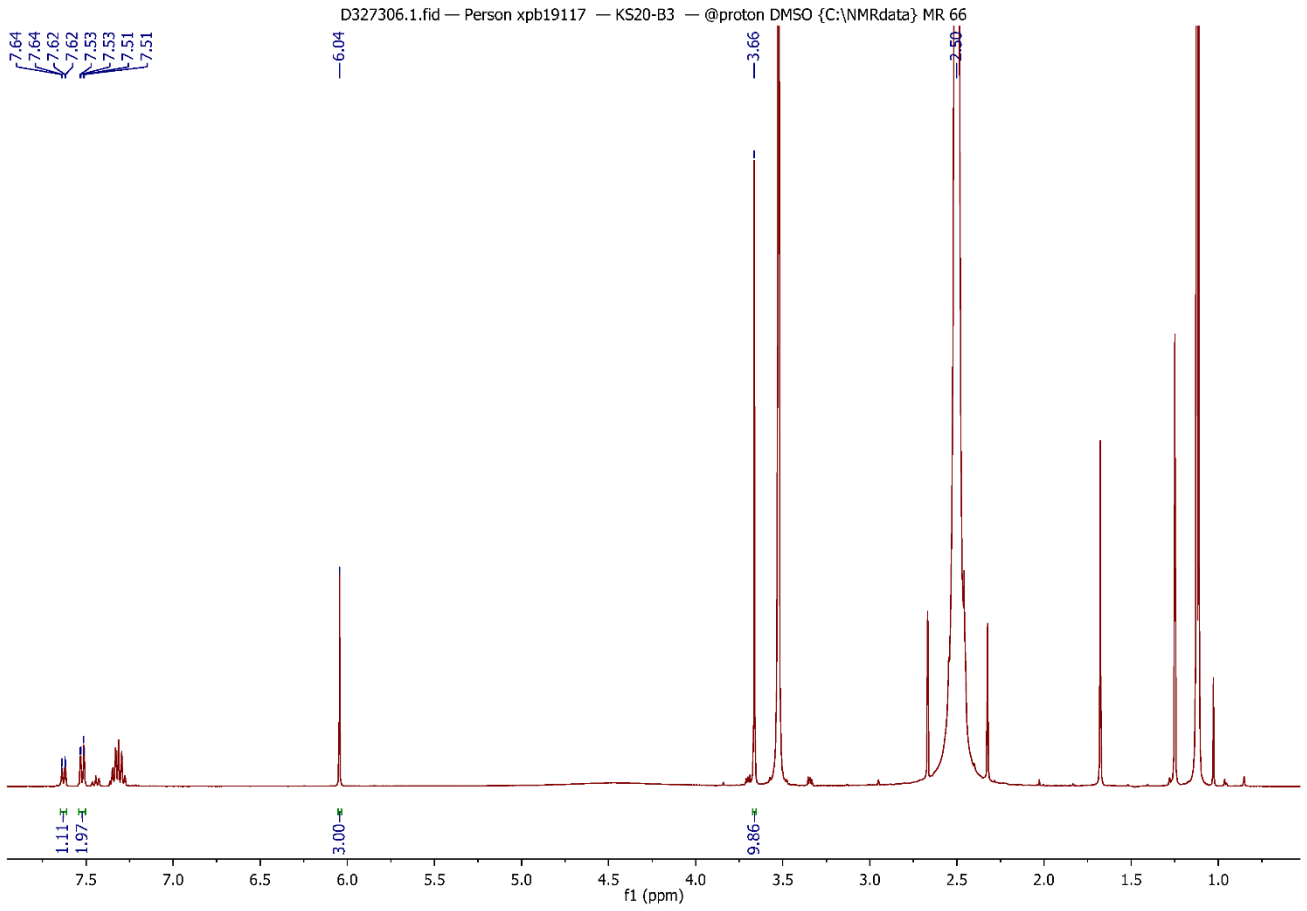




Reaction exposed to air with 0.5 mol% catalyst loading:

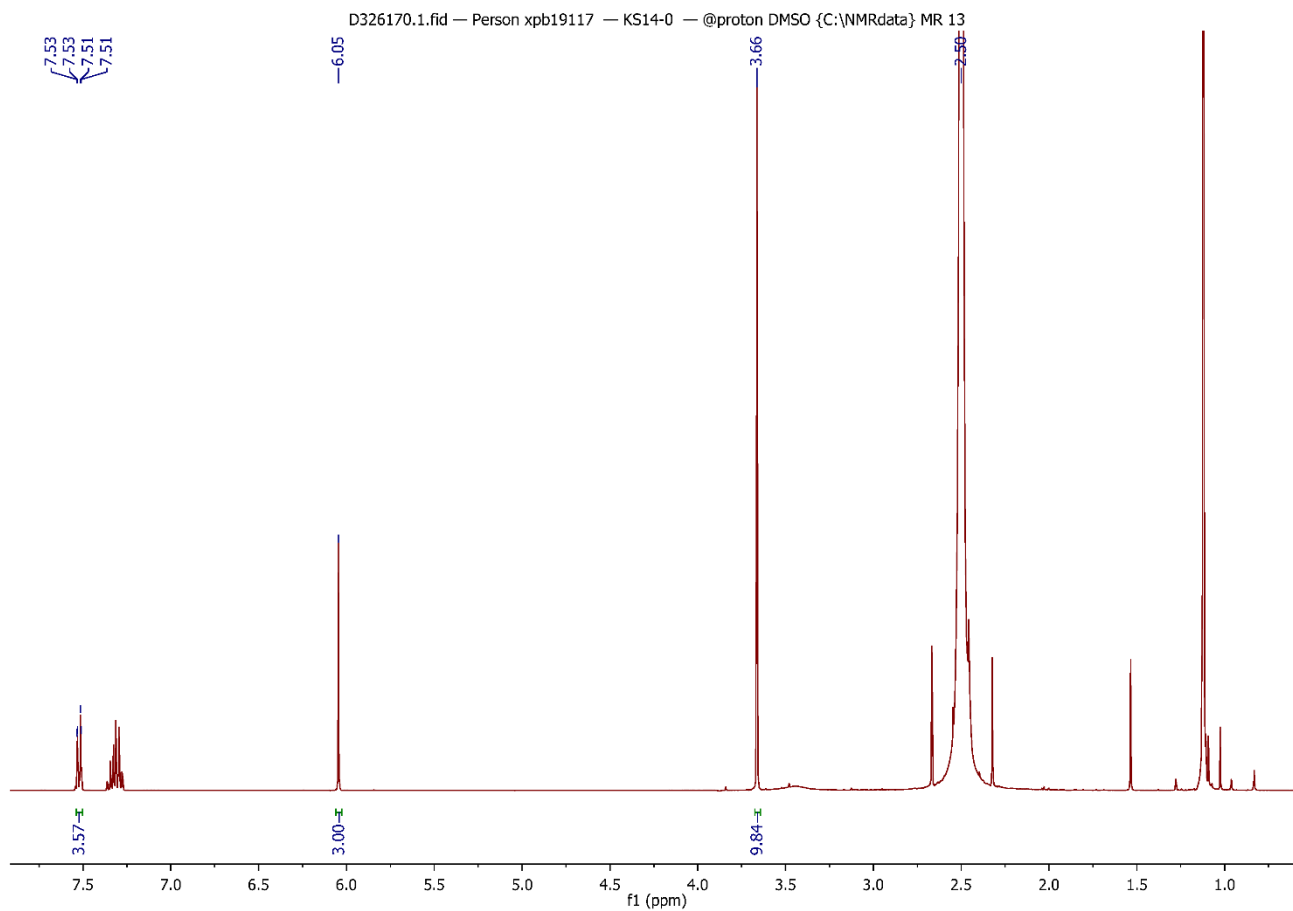


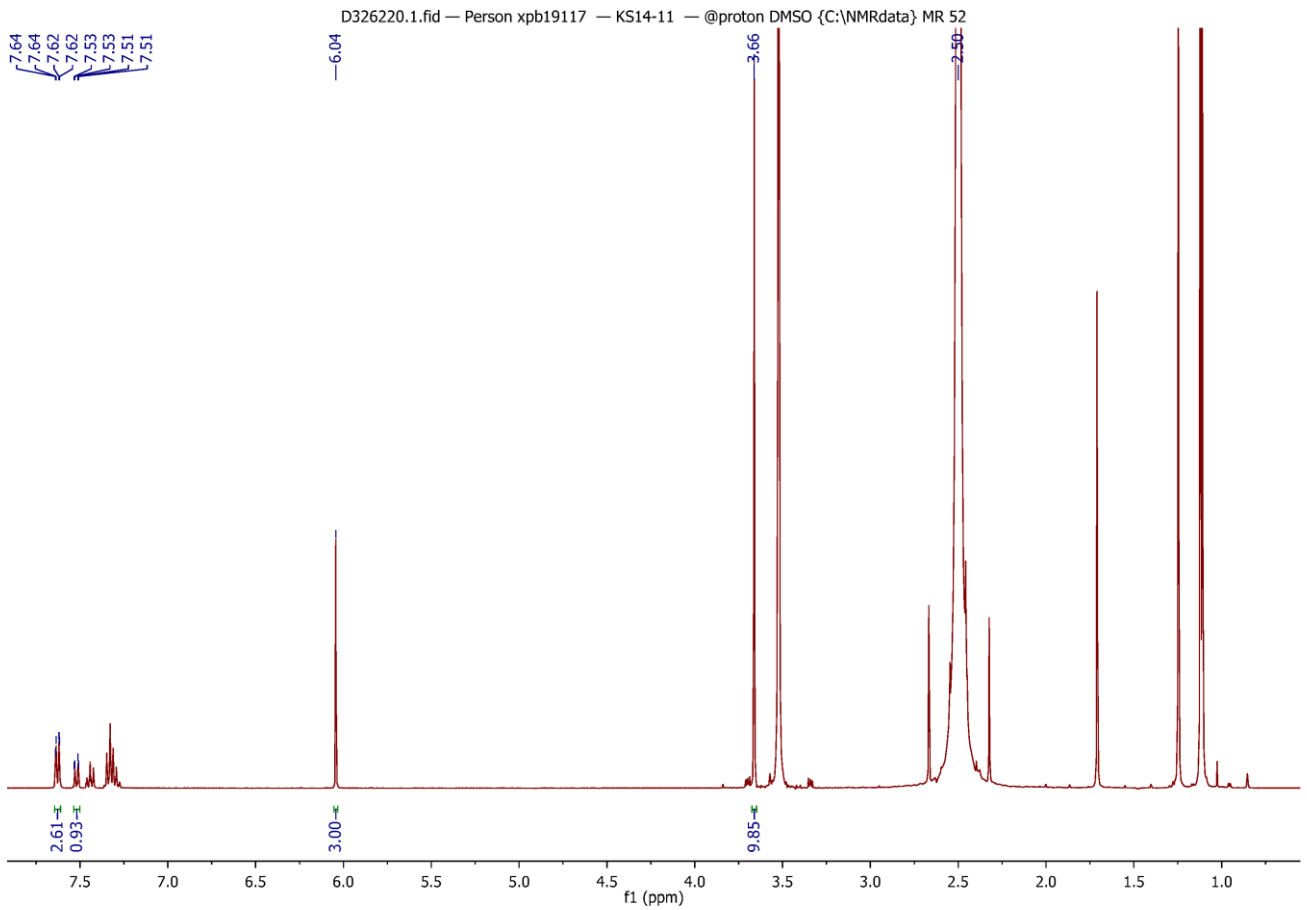
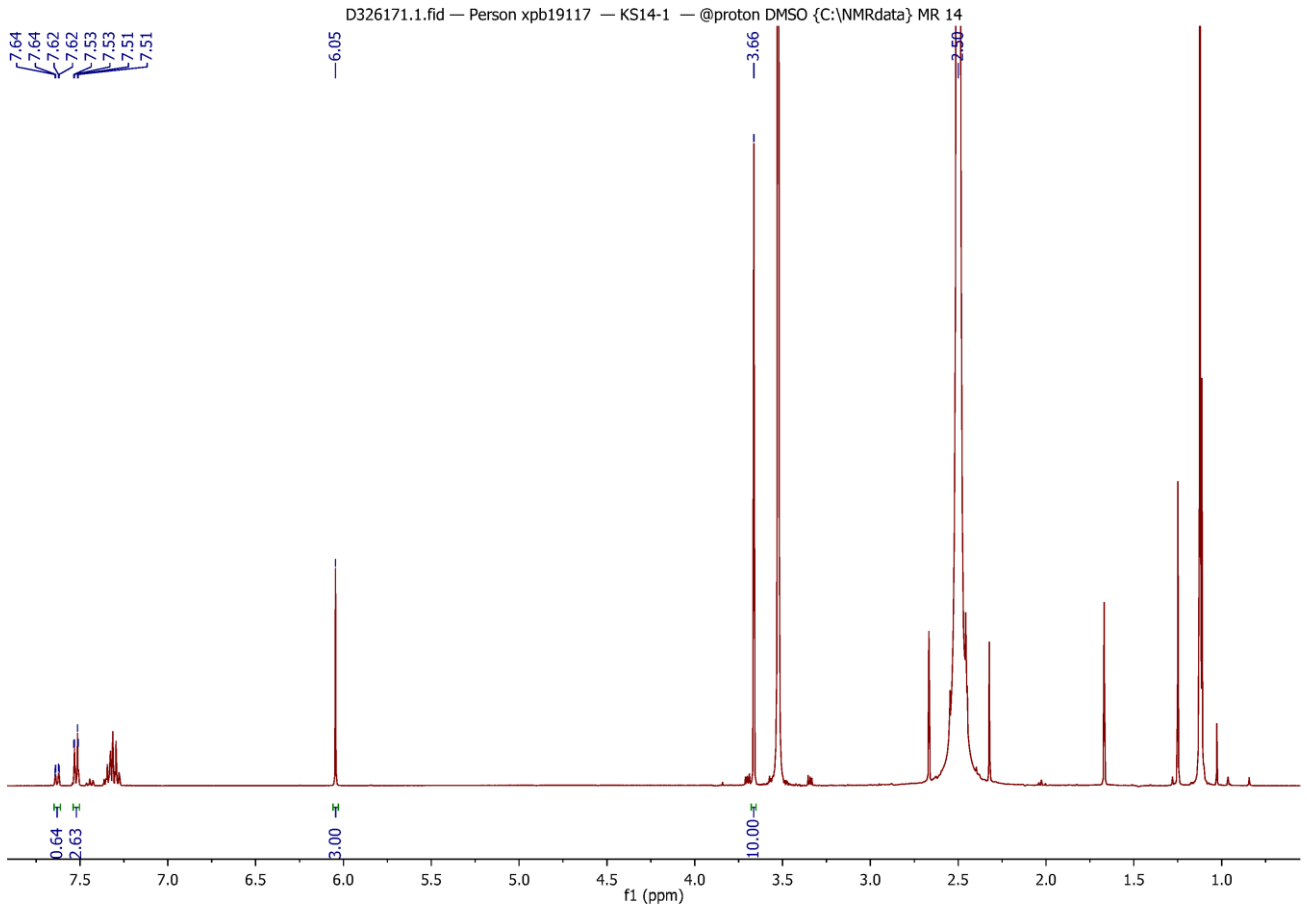


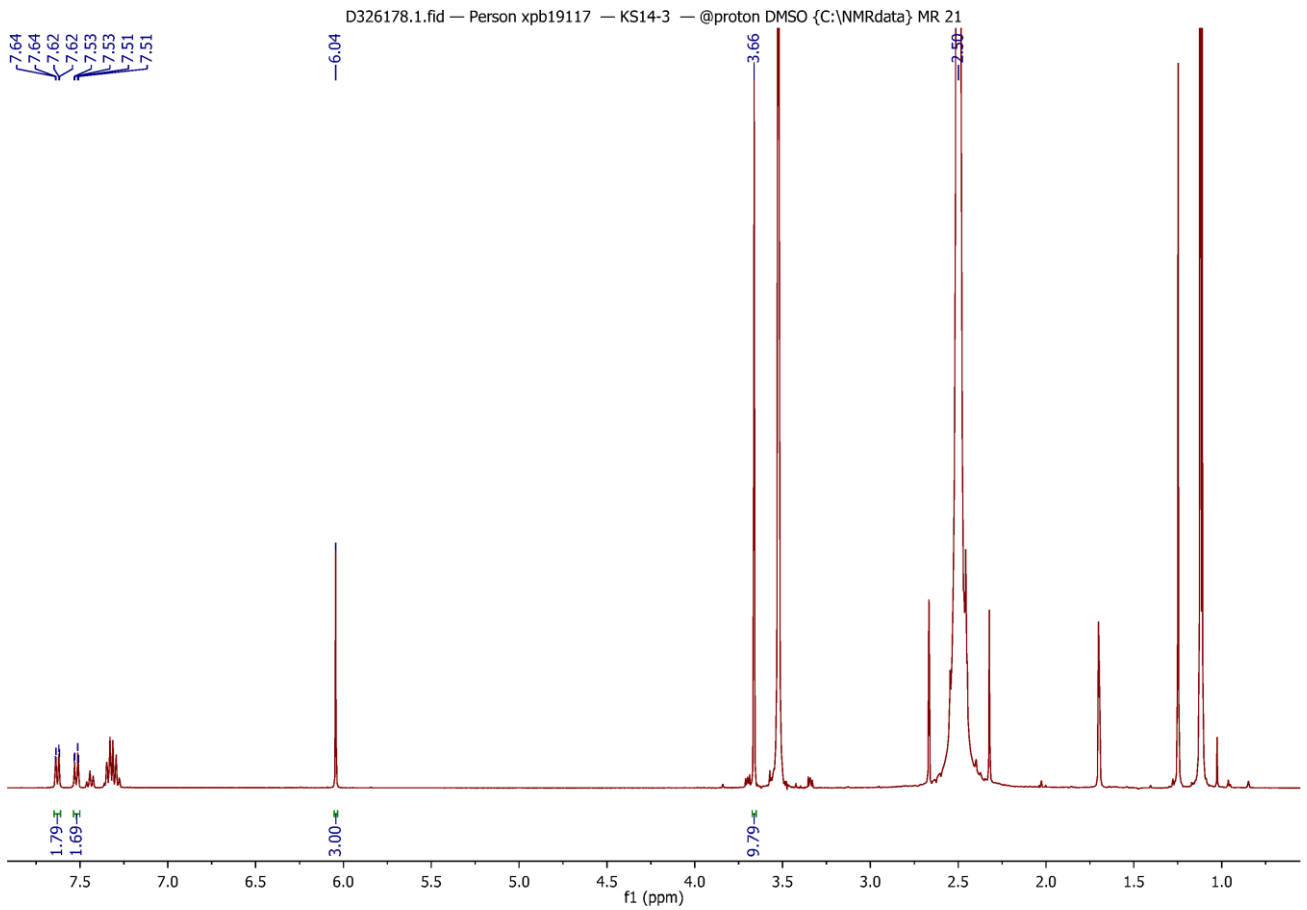
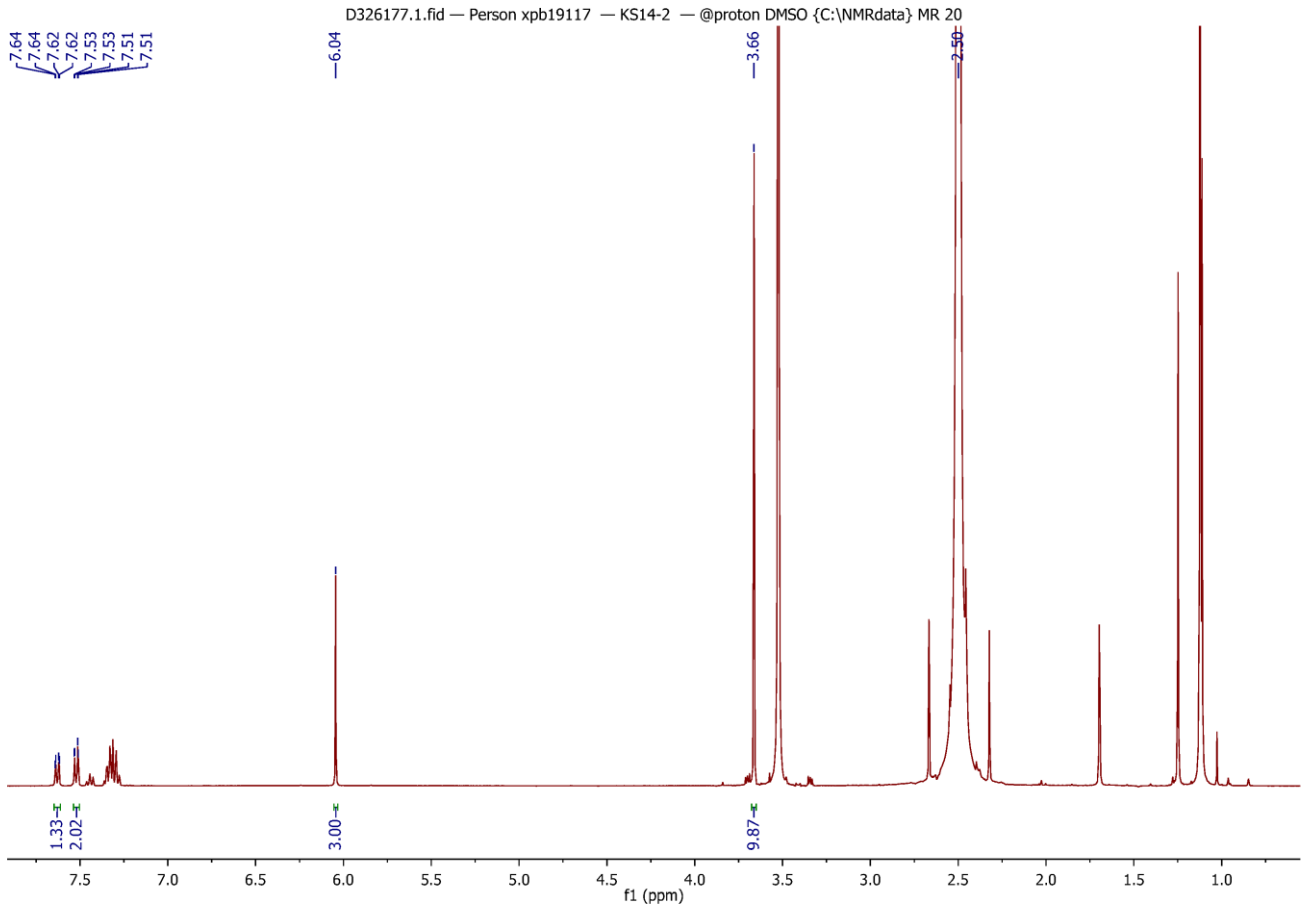


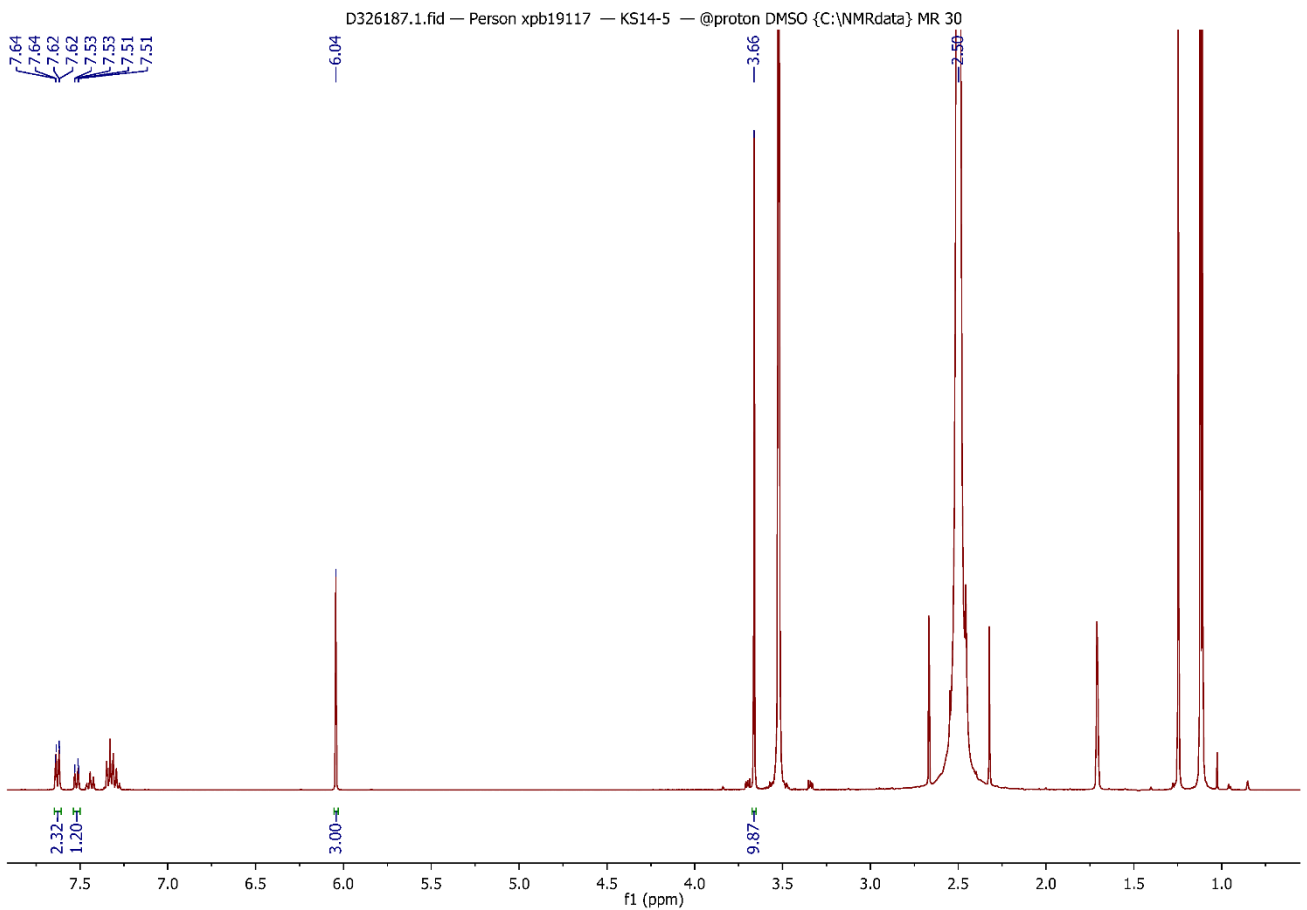
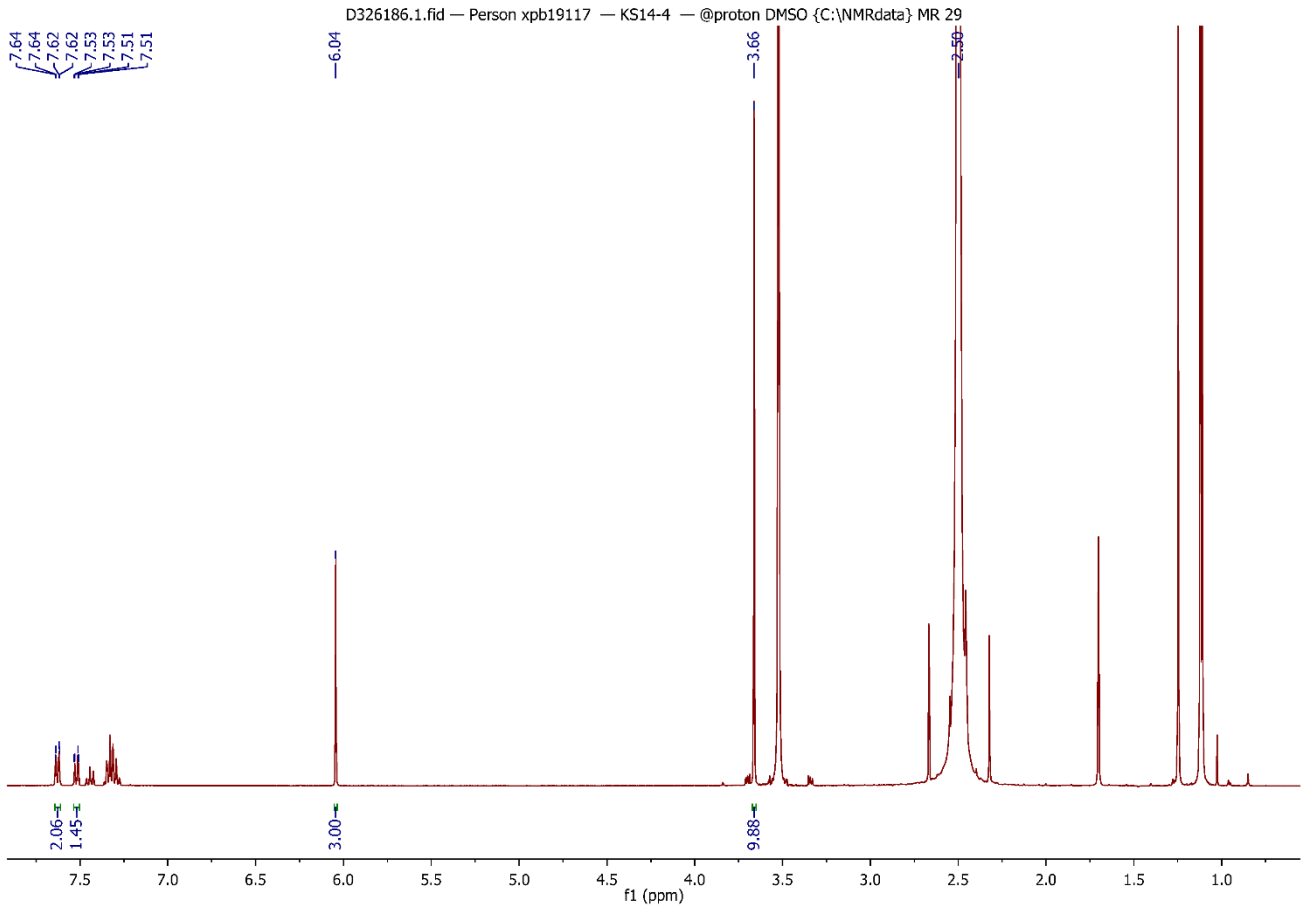
Miyaura borylation reaction samples – ^1H (DMSO- d_6) spectra for manuscript Scheme 8

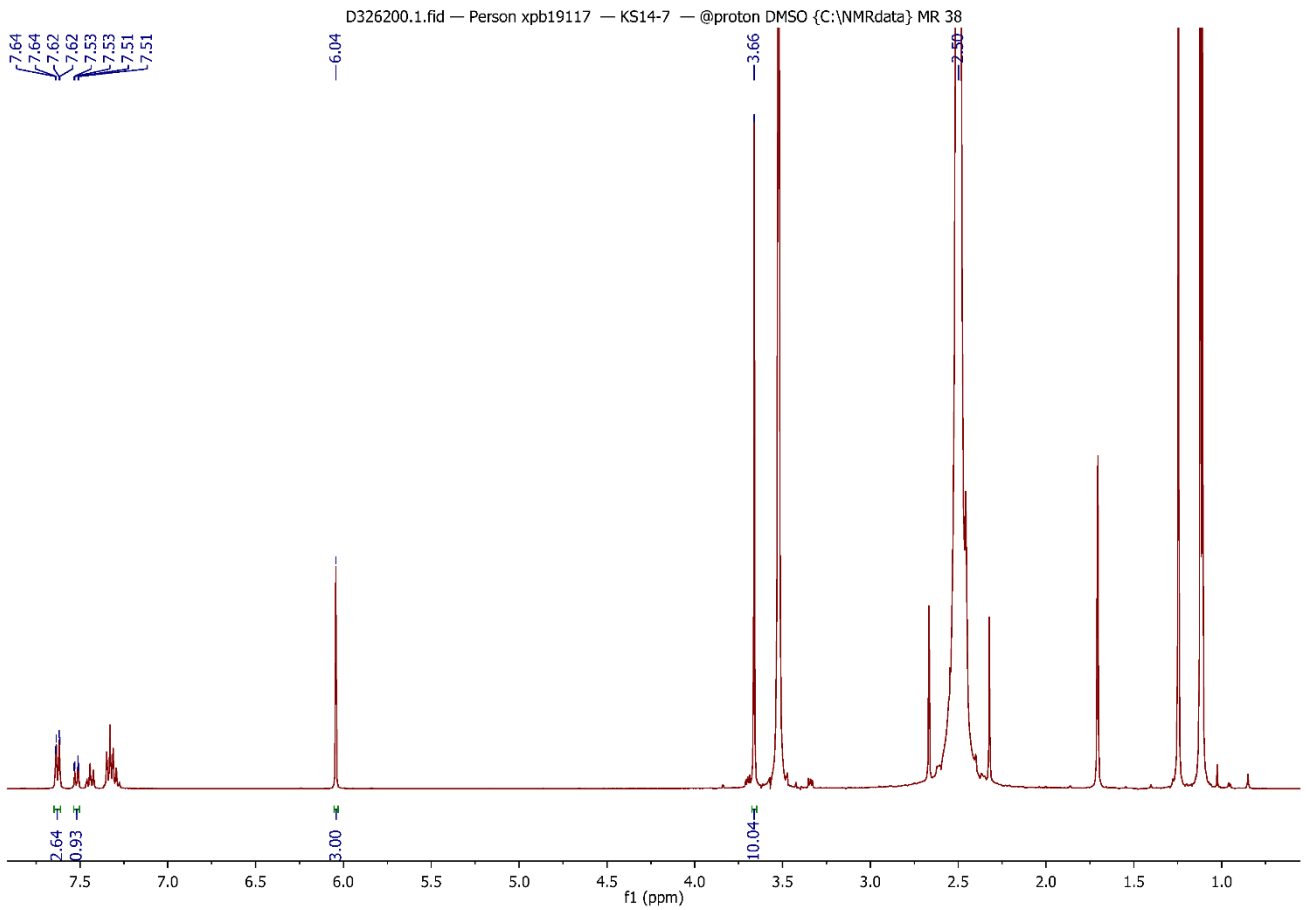
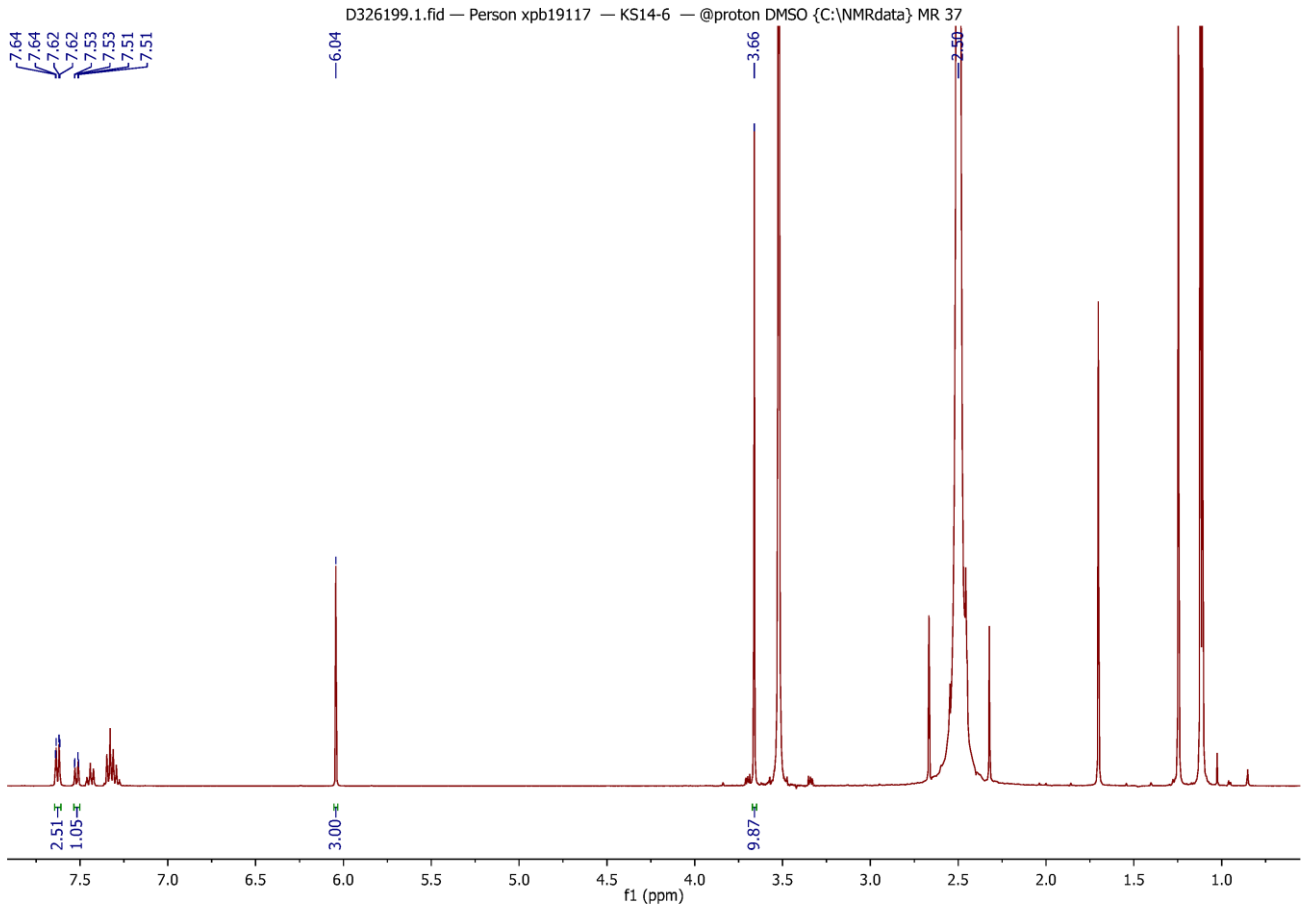
Part – A using pre-heated catalyst solution:

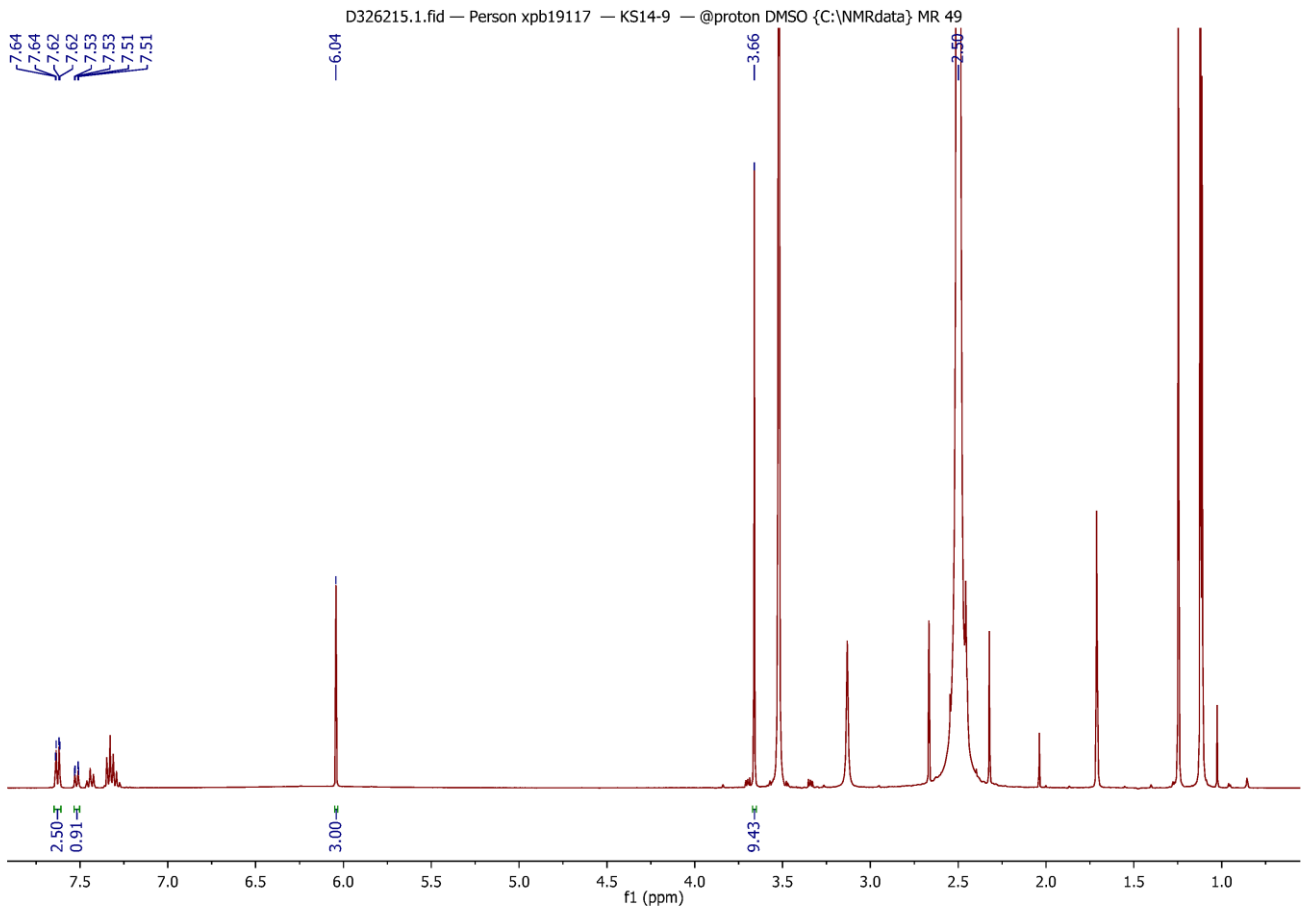
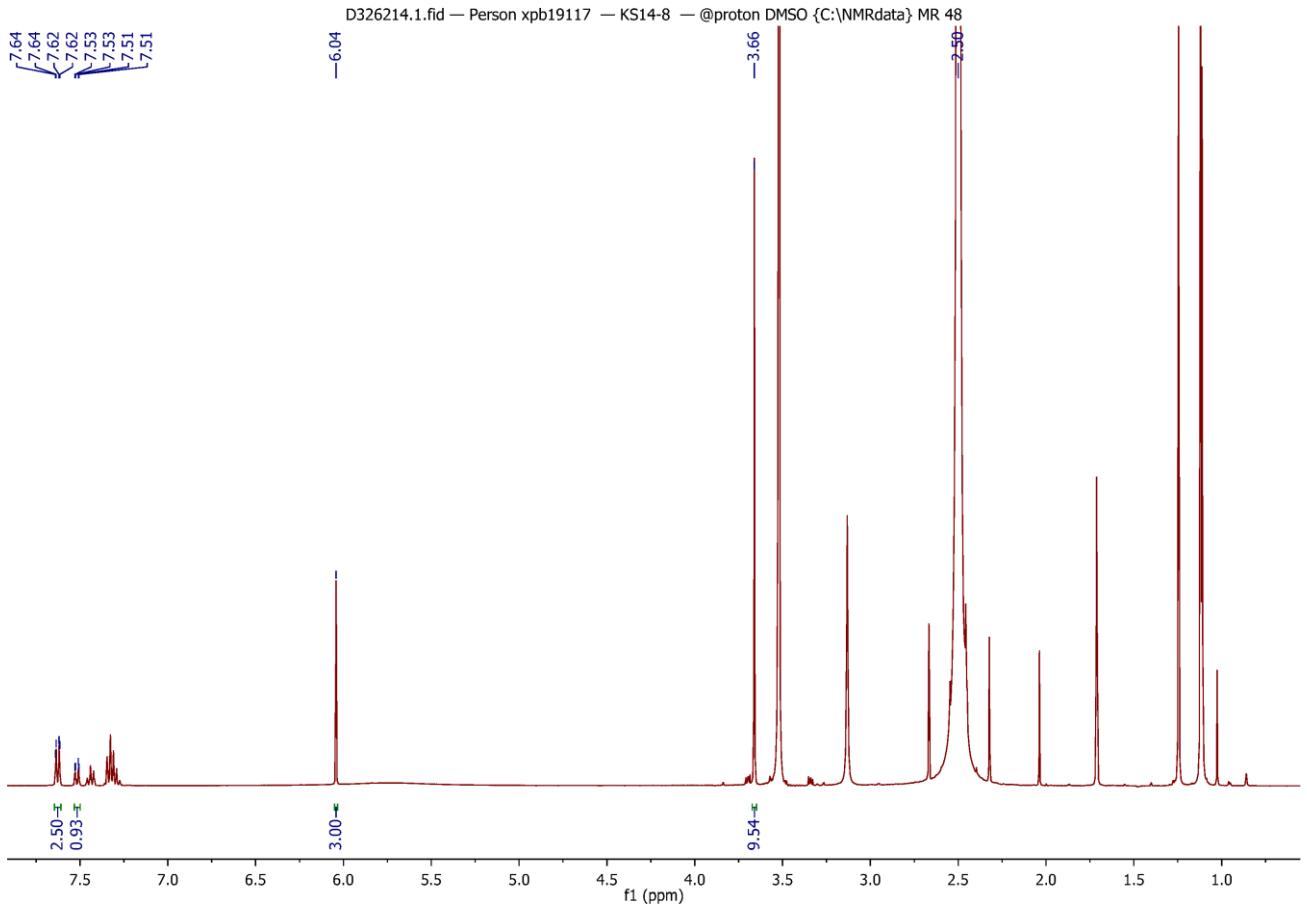


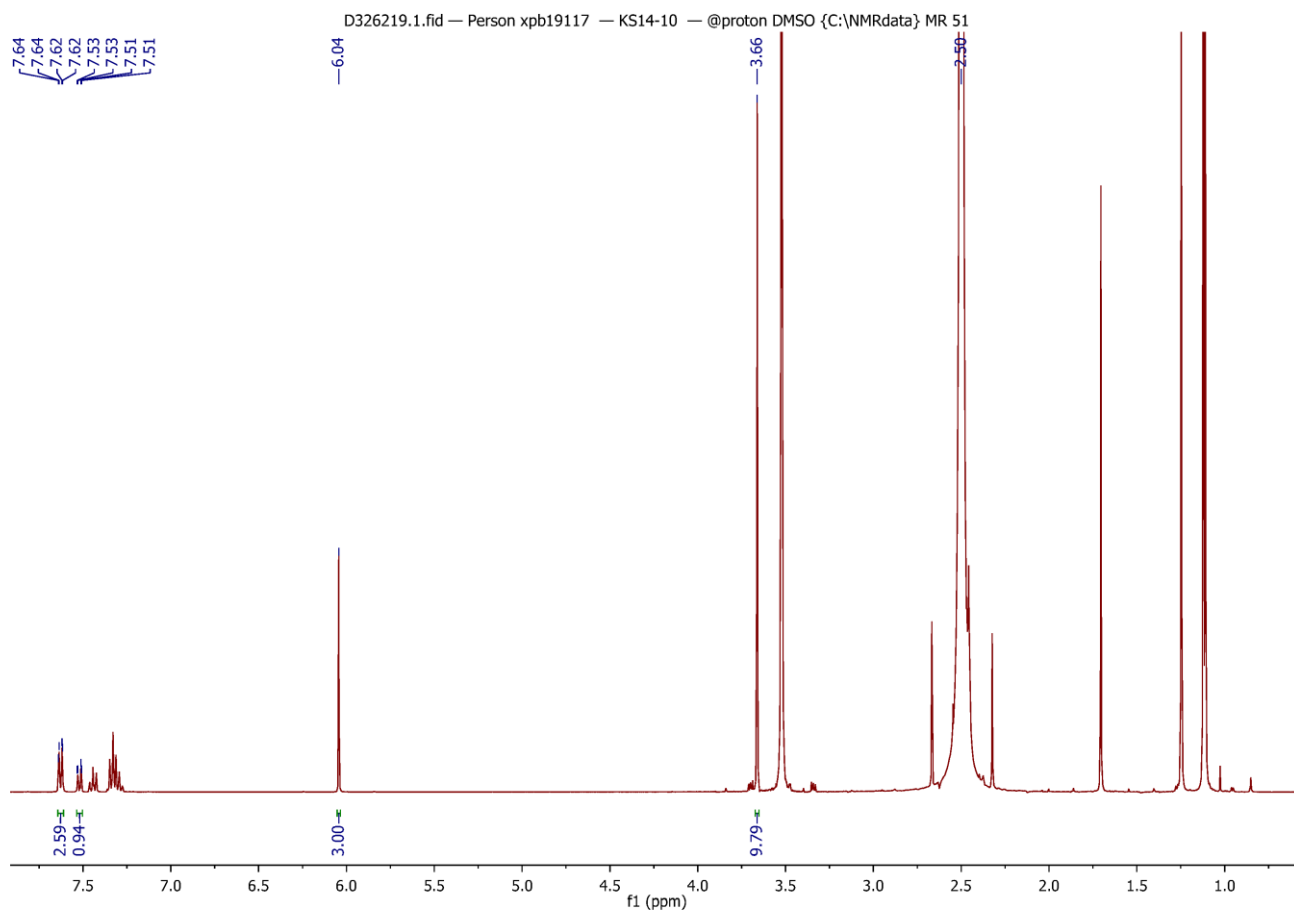




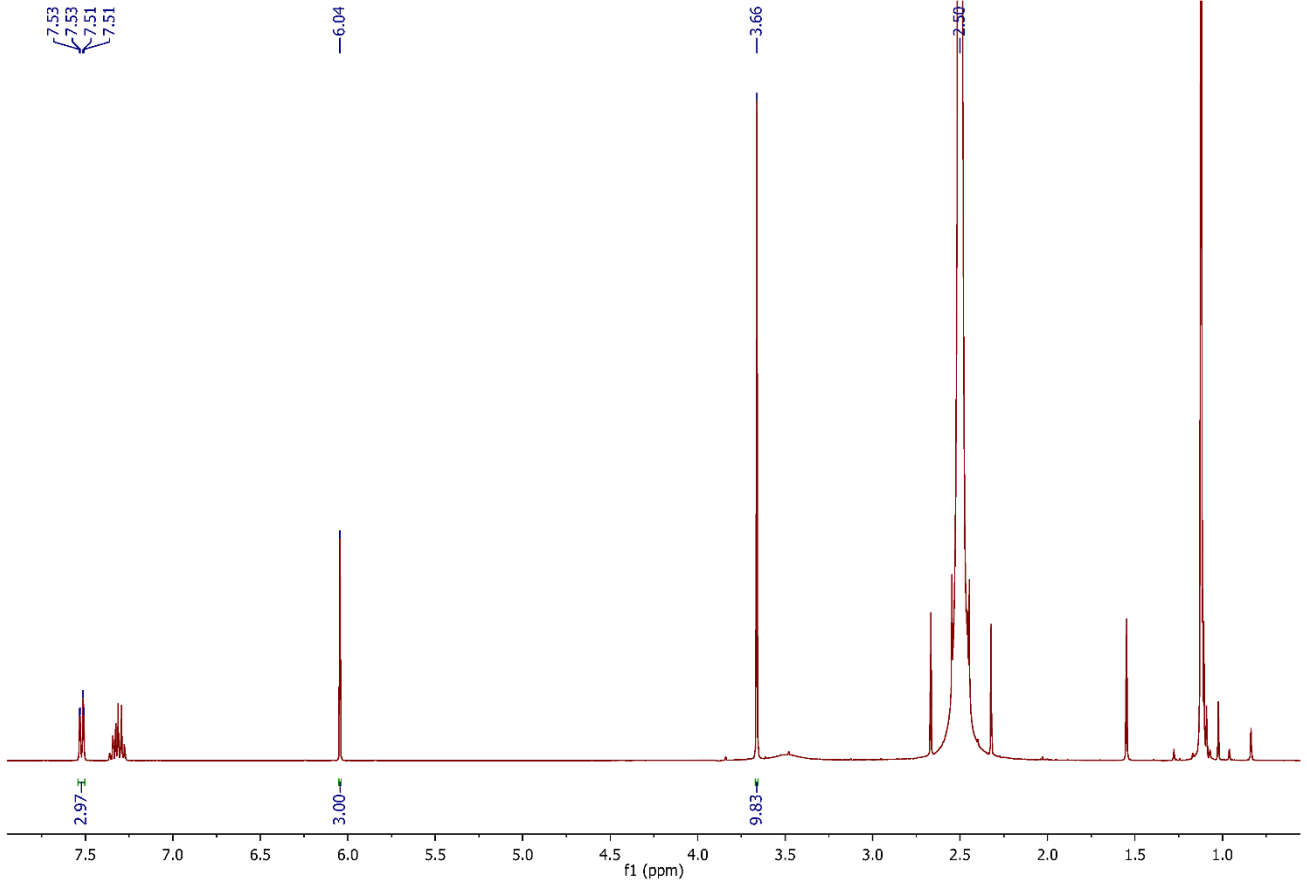


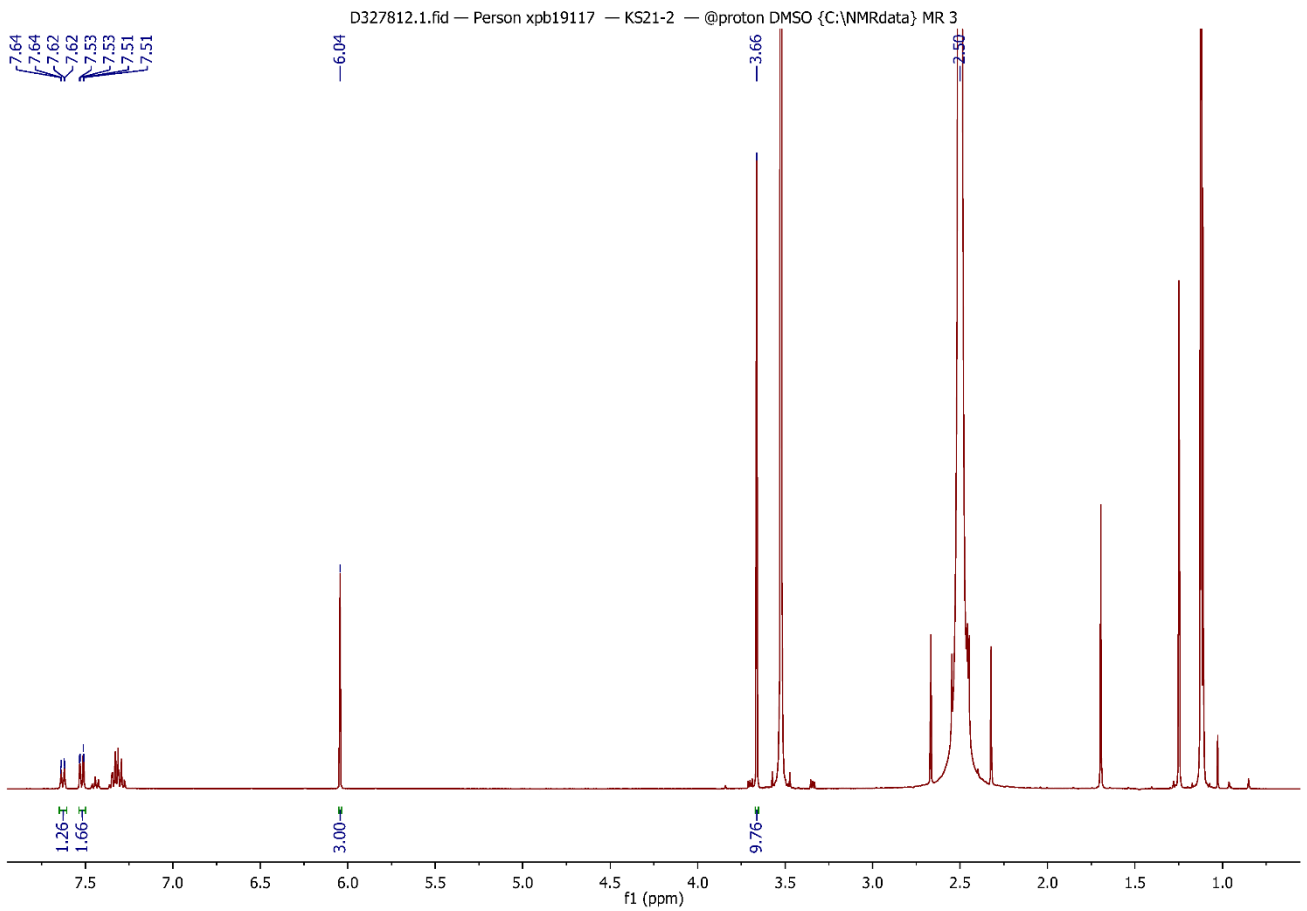
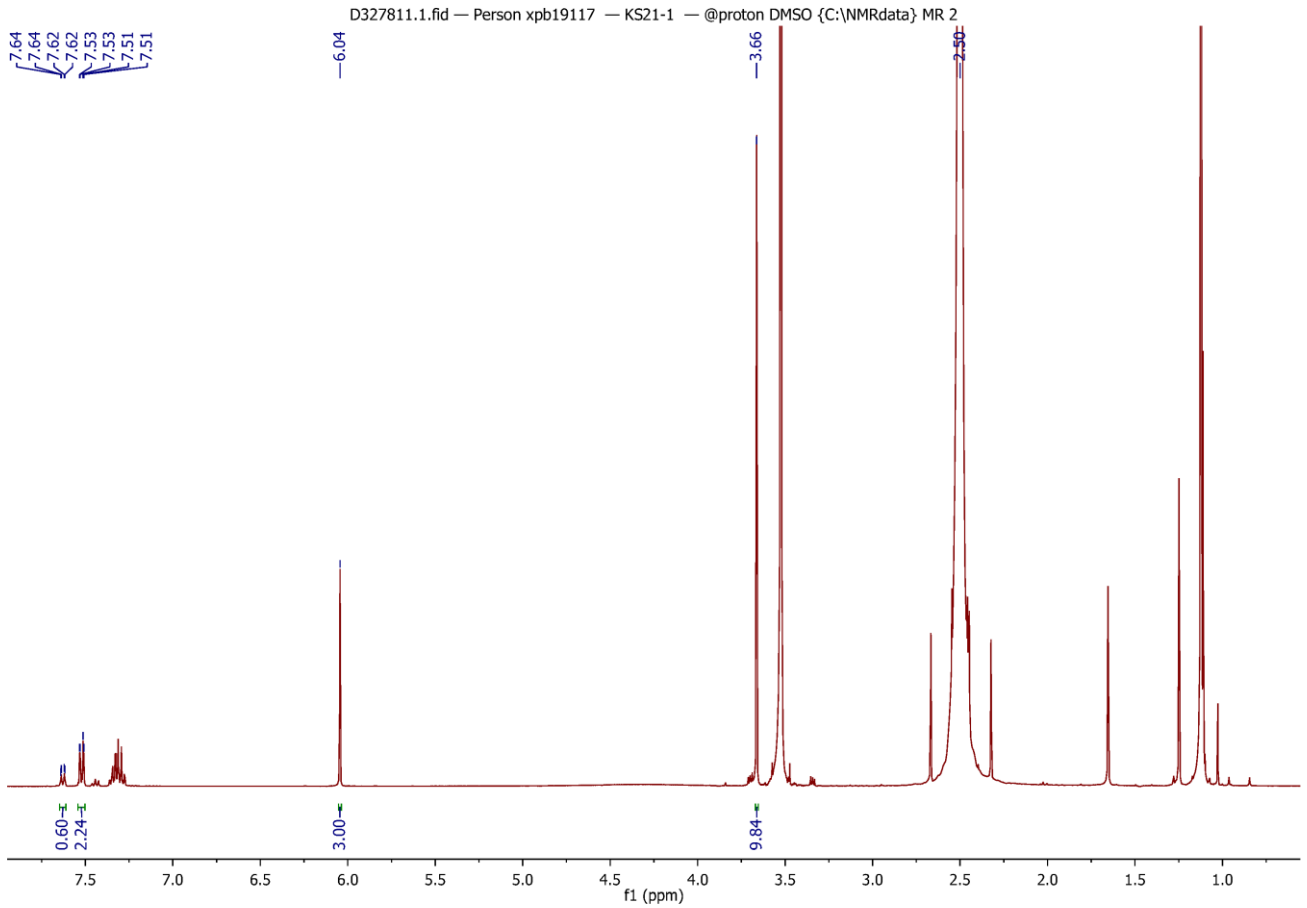


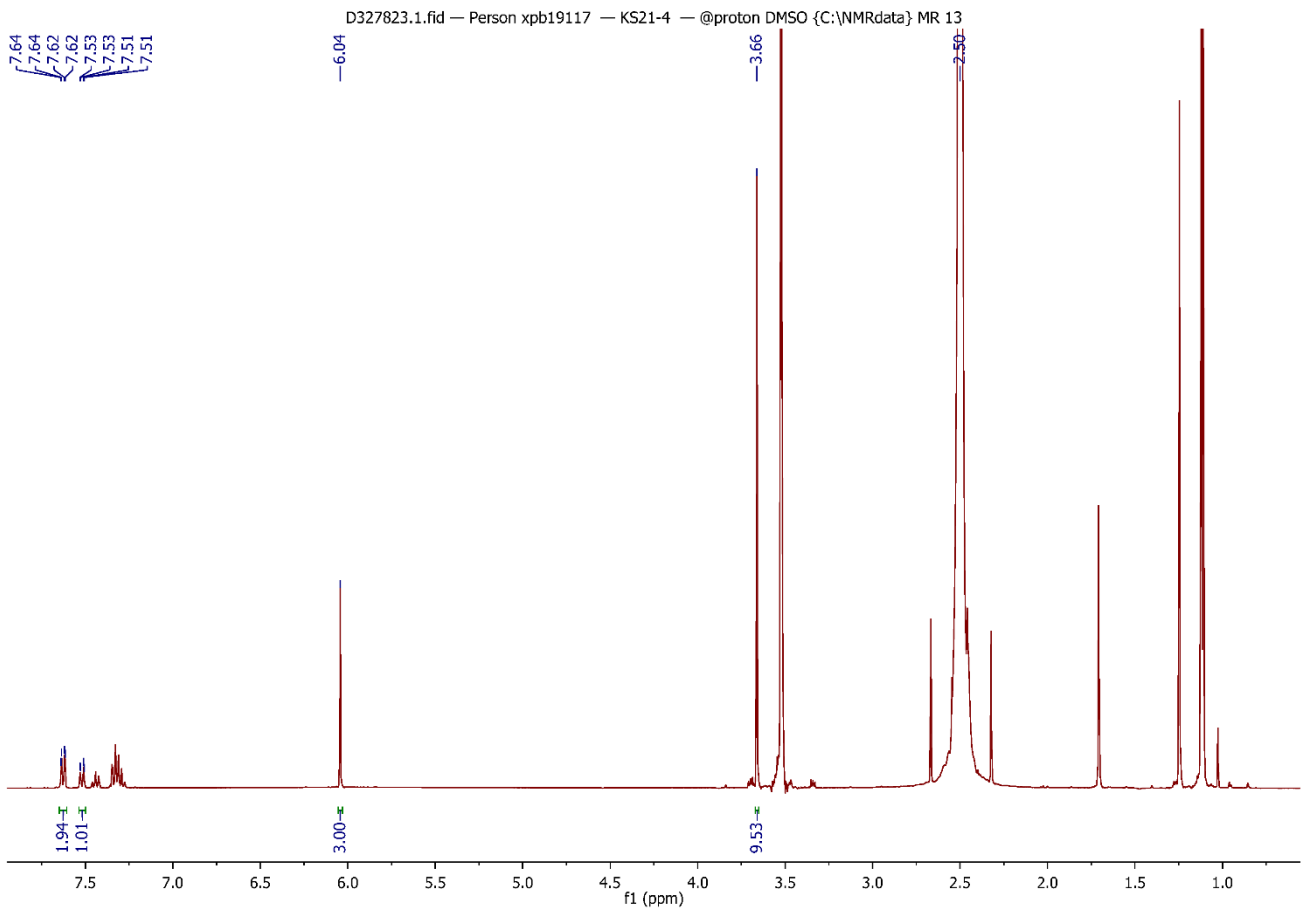
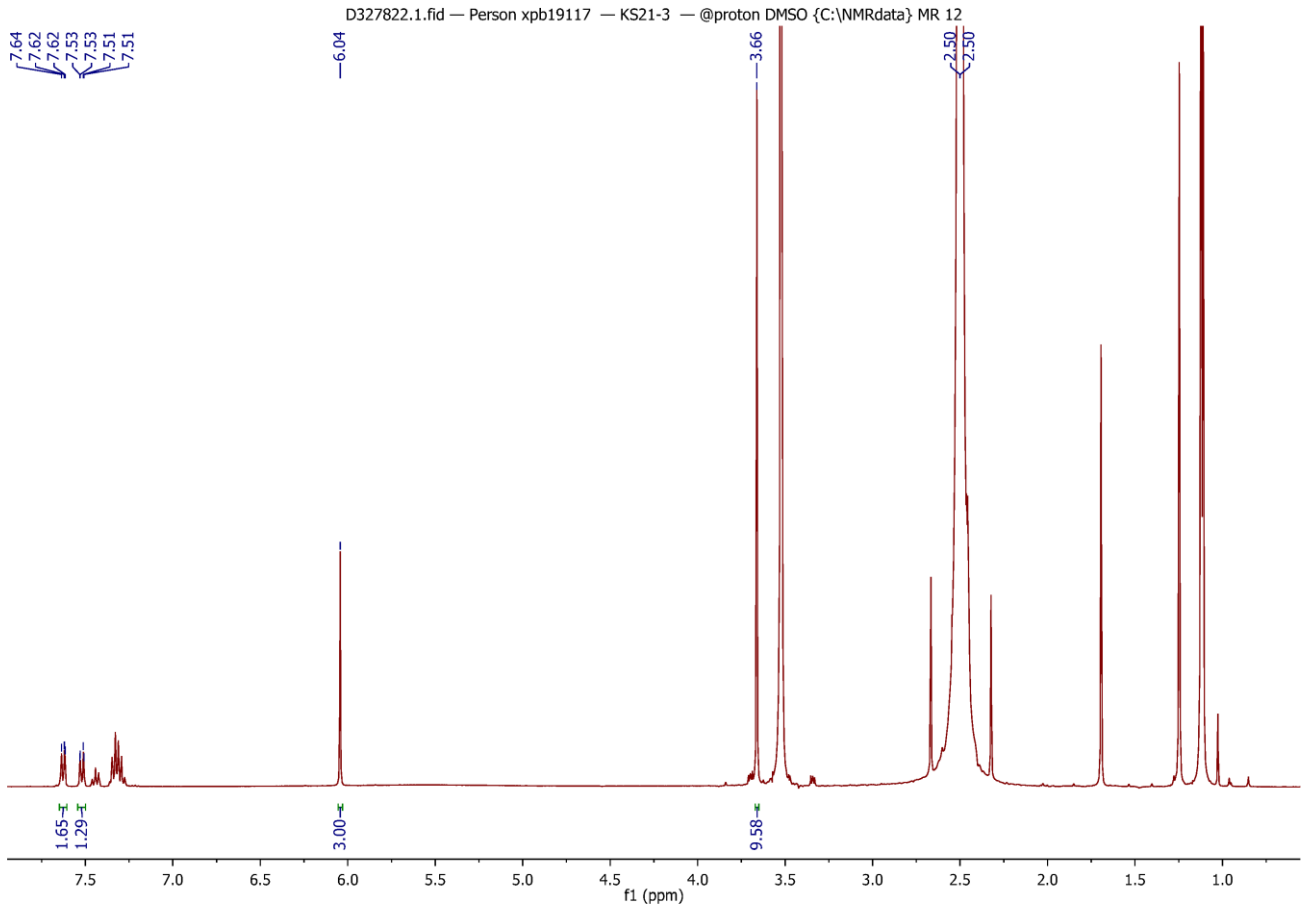


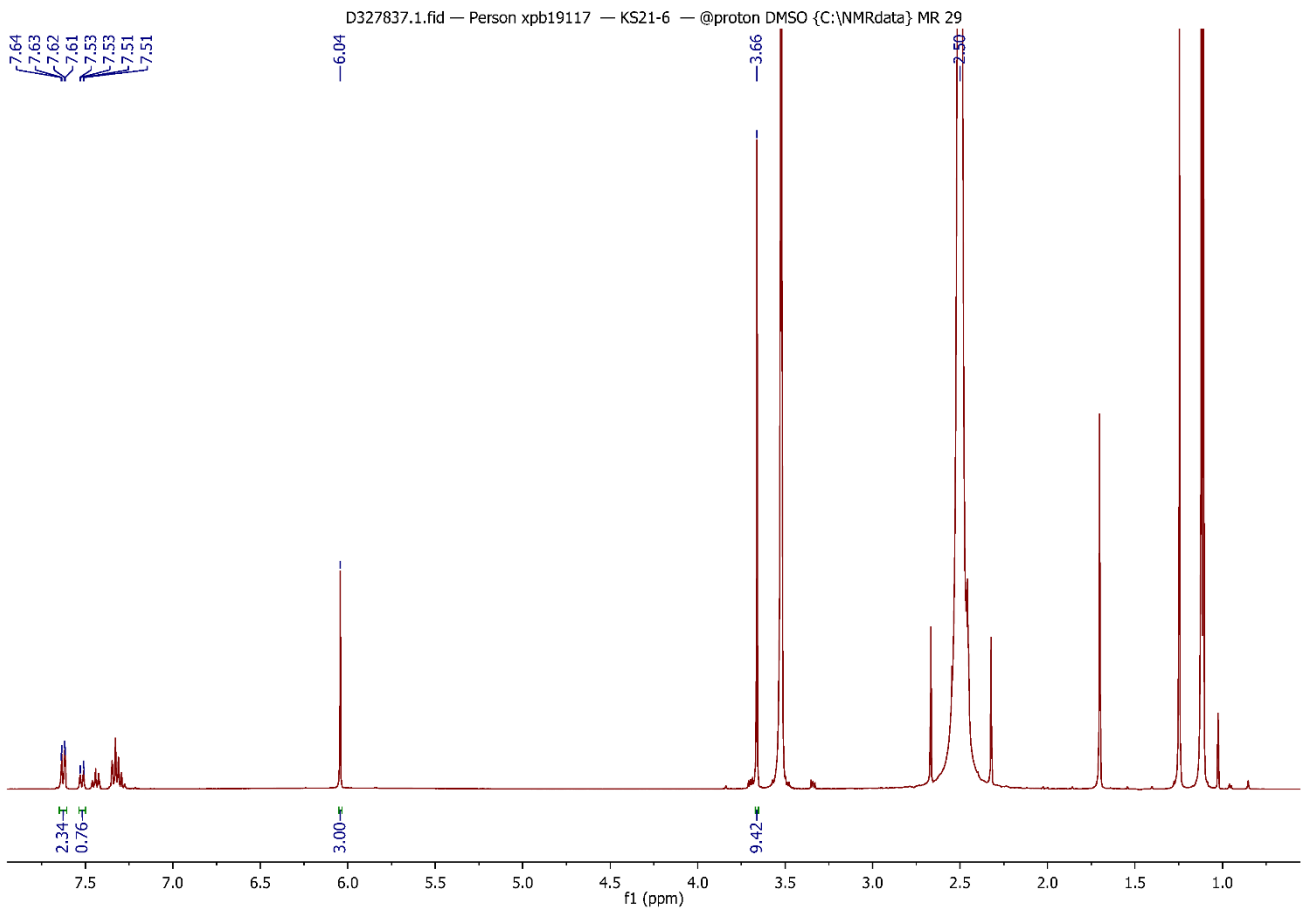
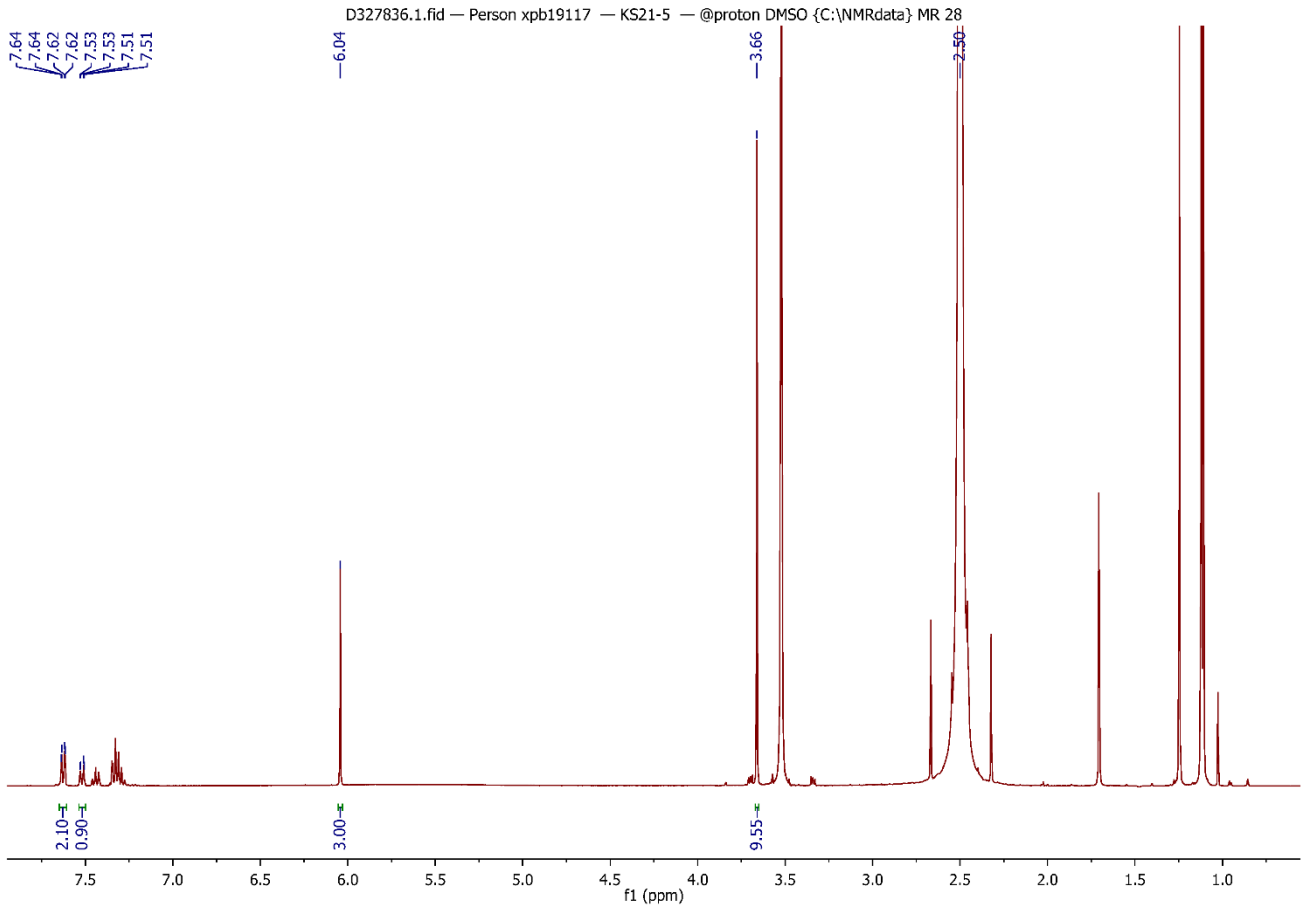


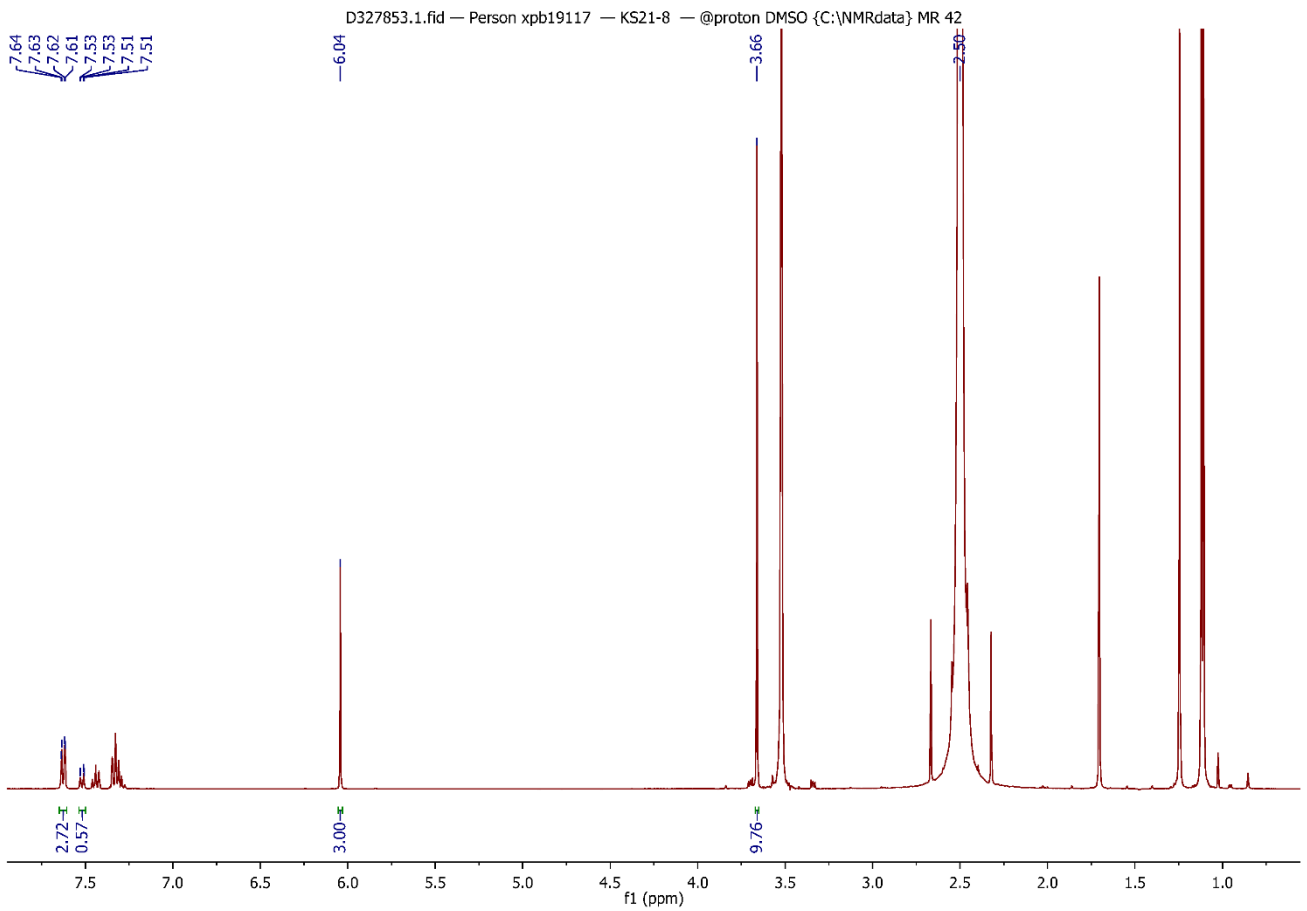
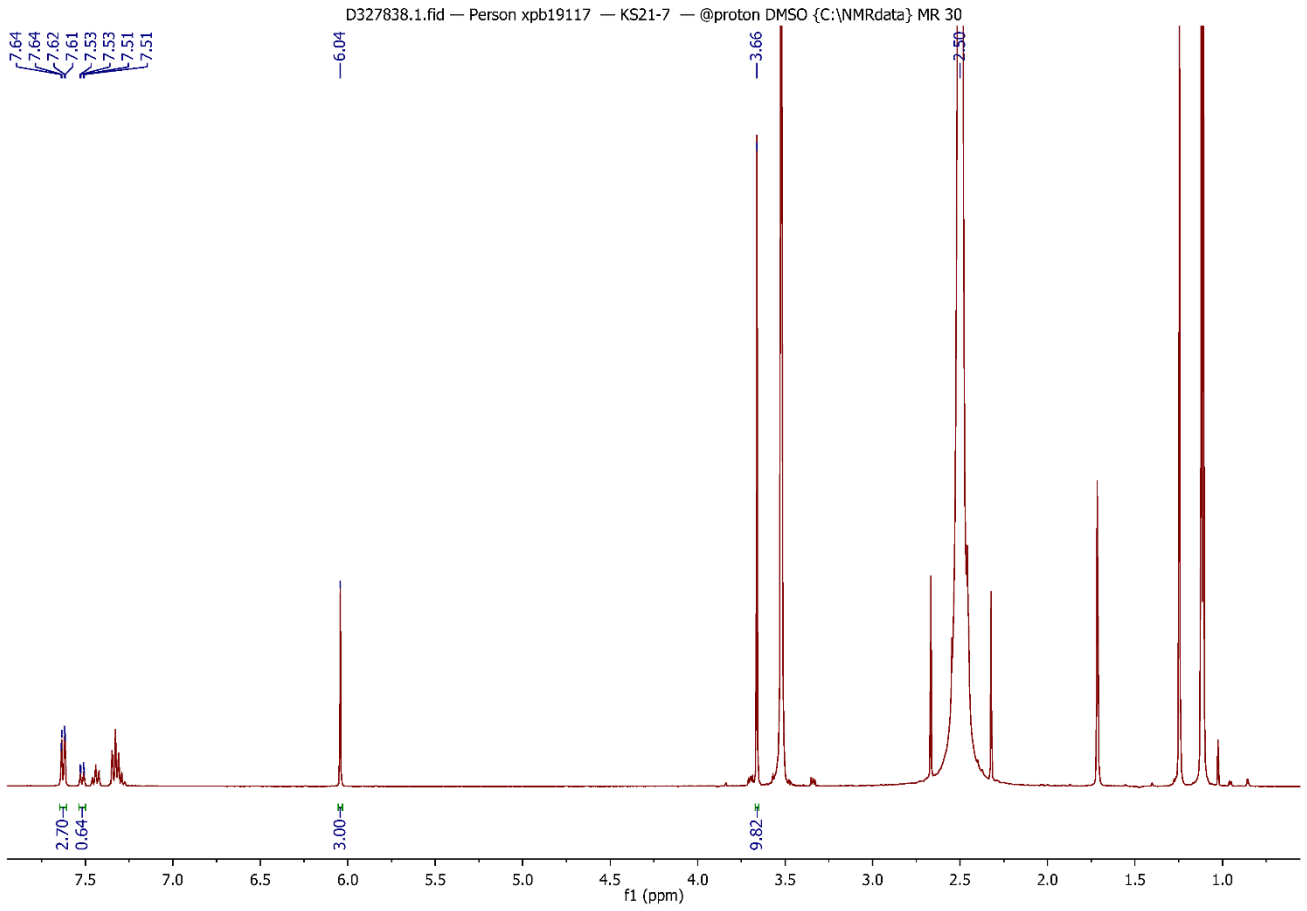
Part – B using non-preheated catalyst solution:

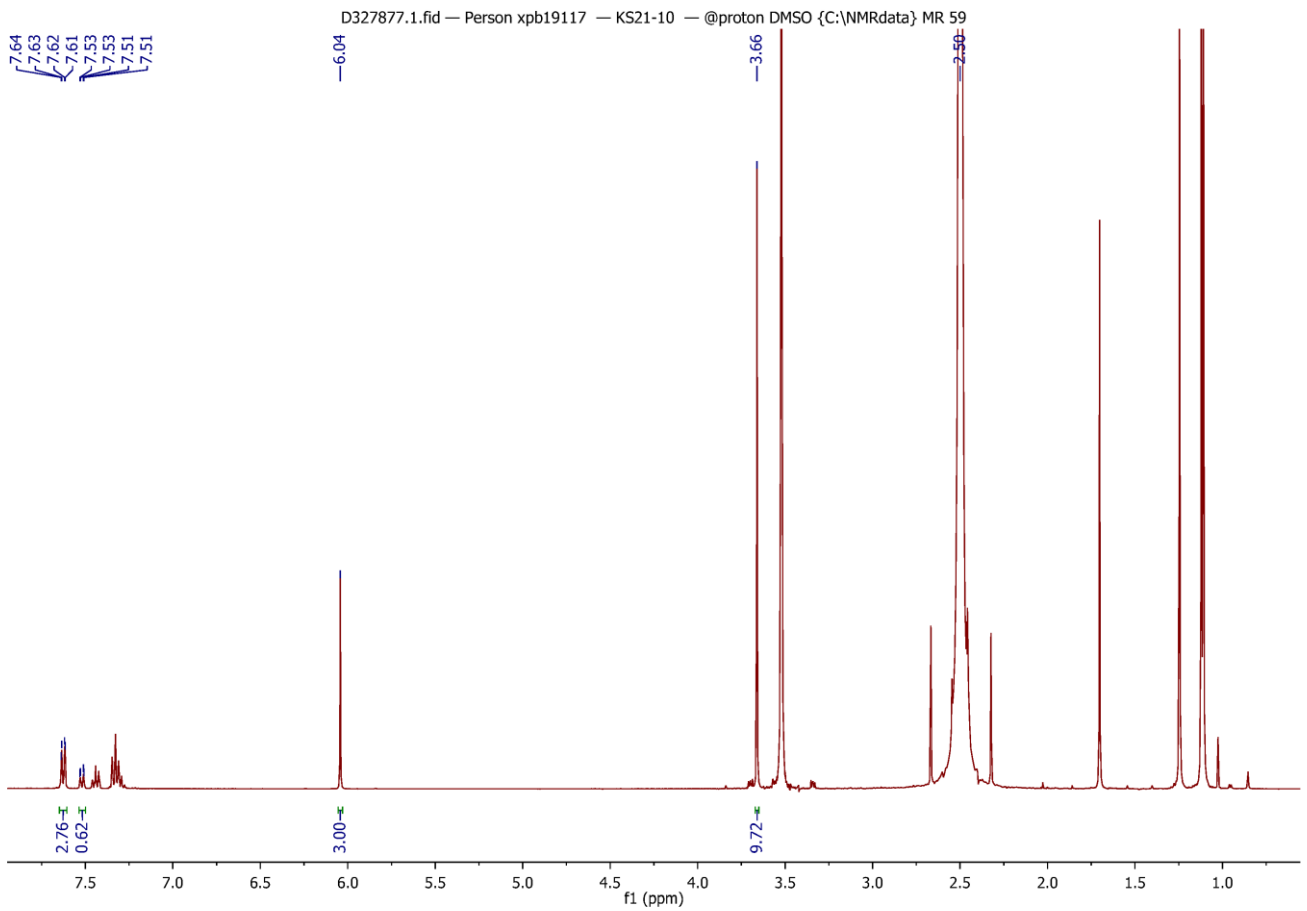
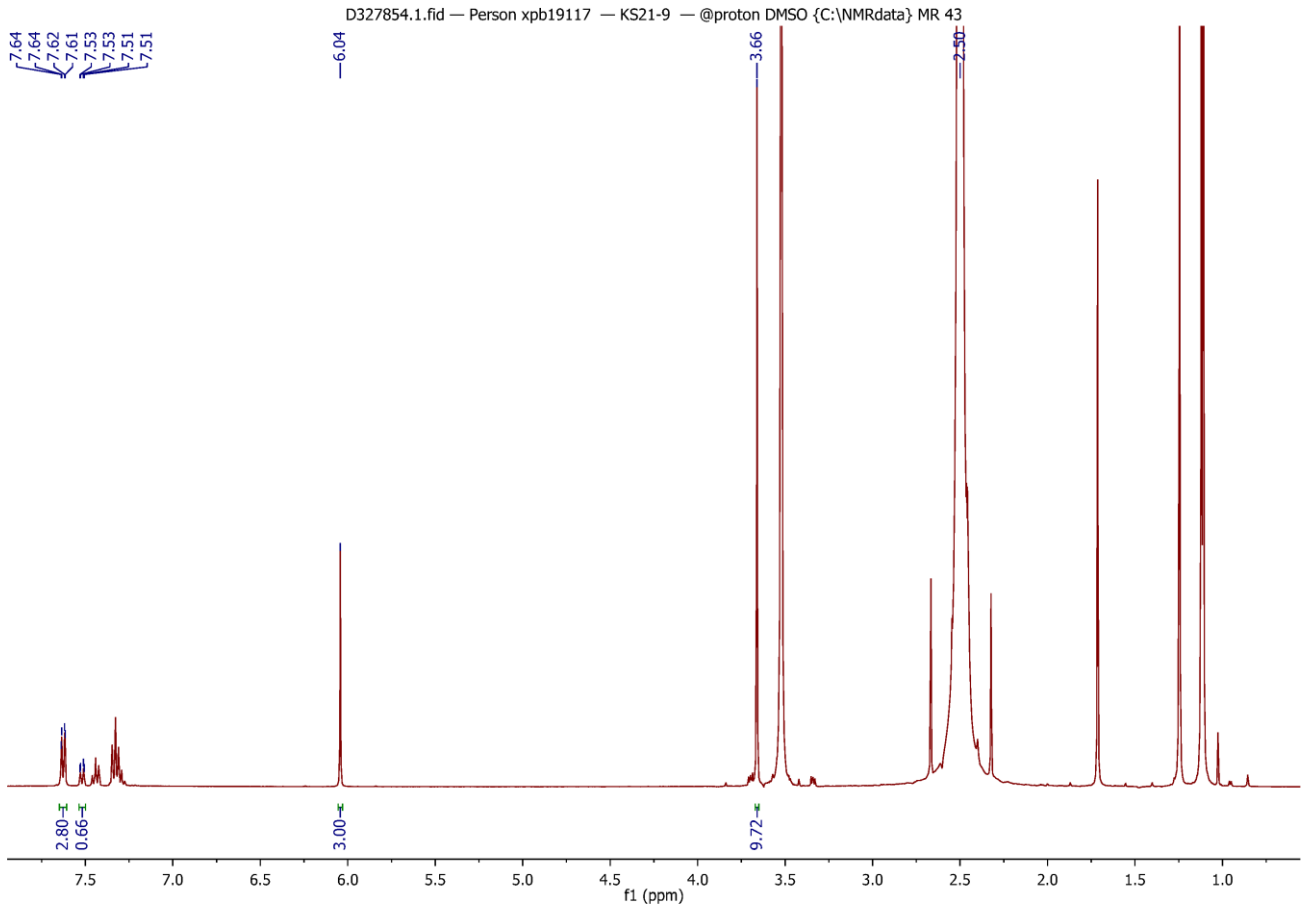


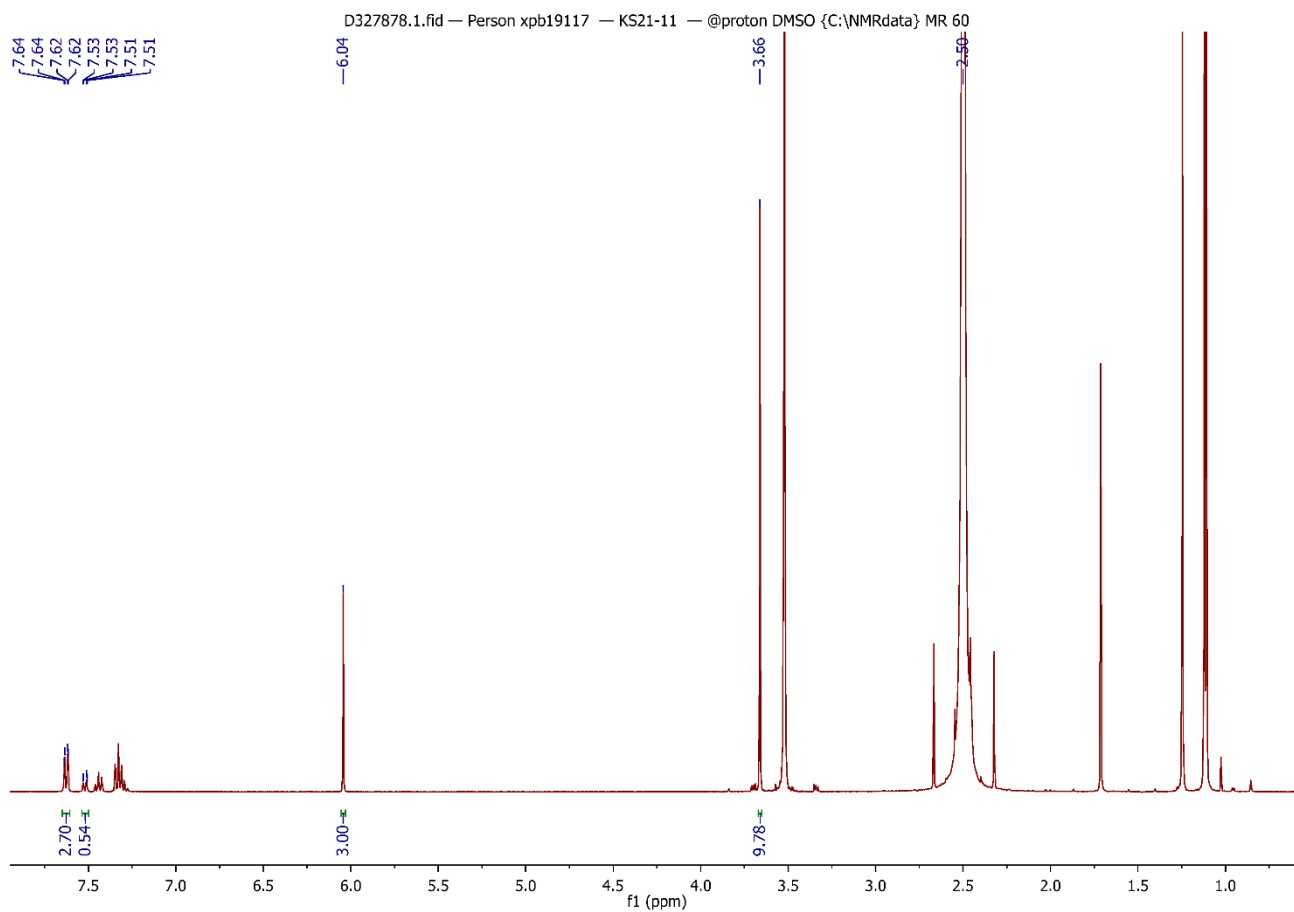






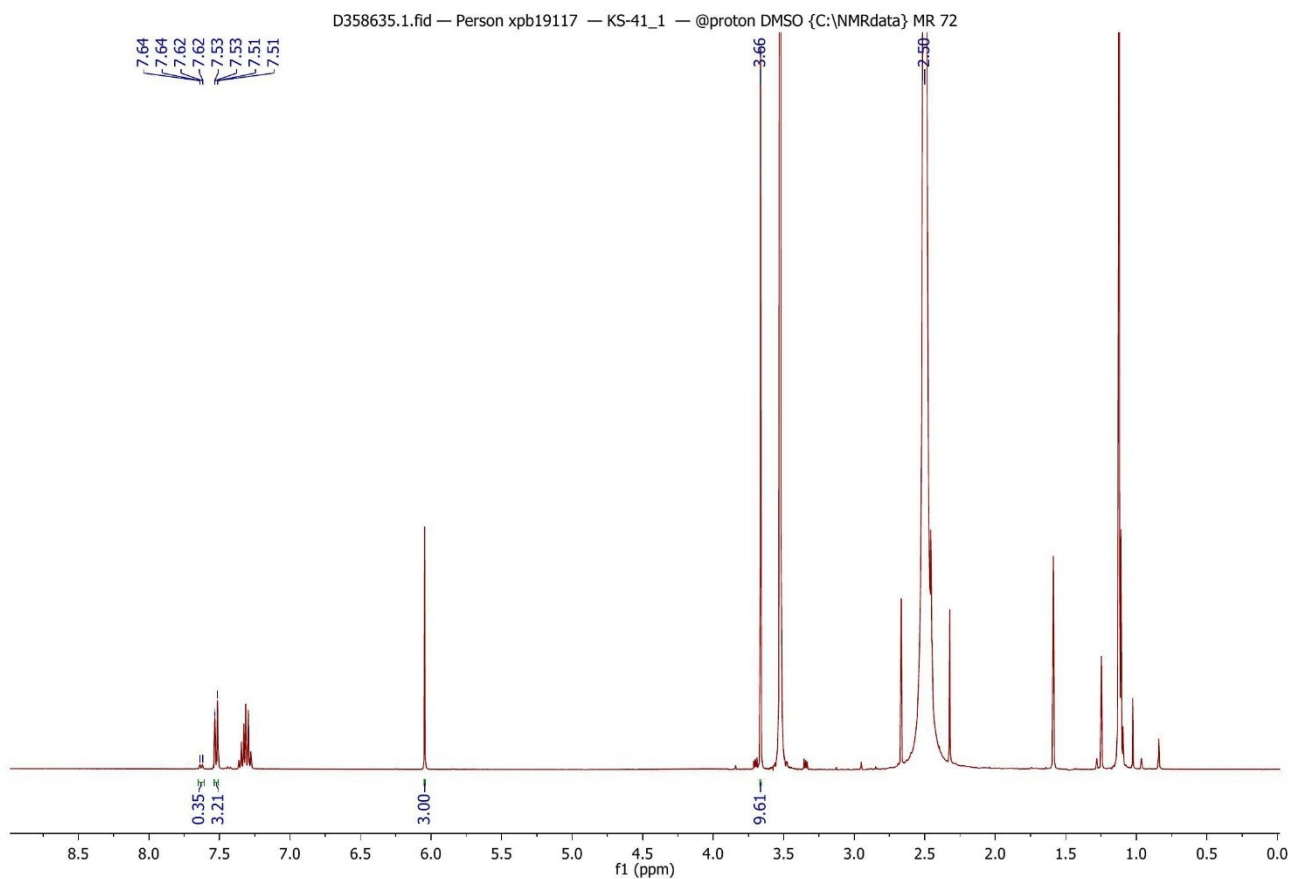
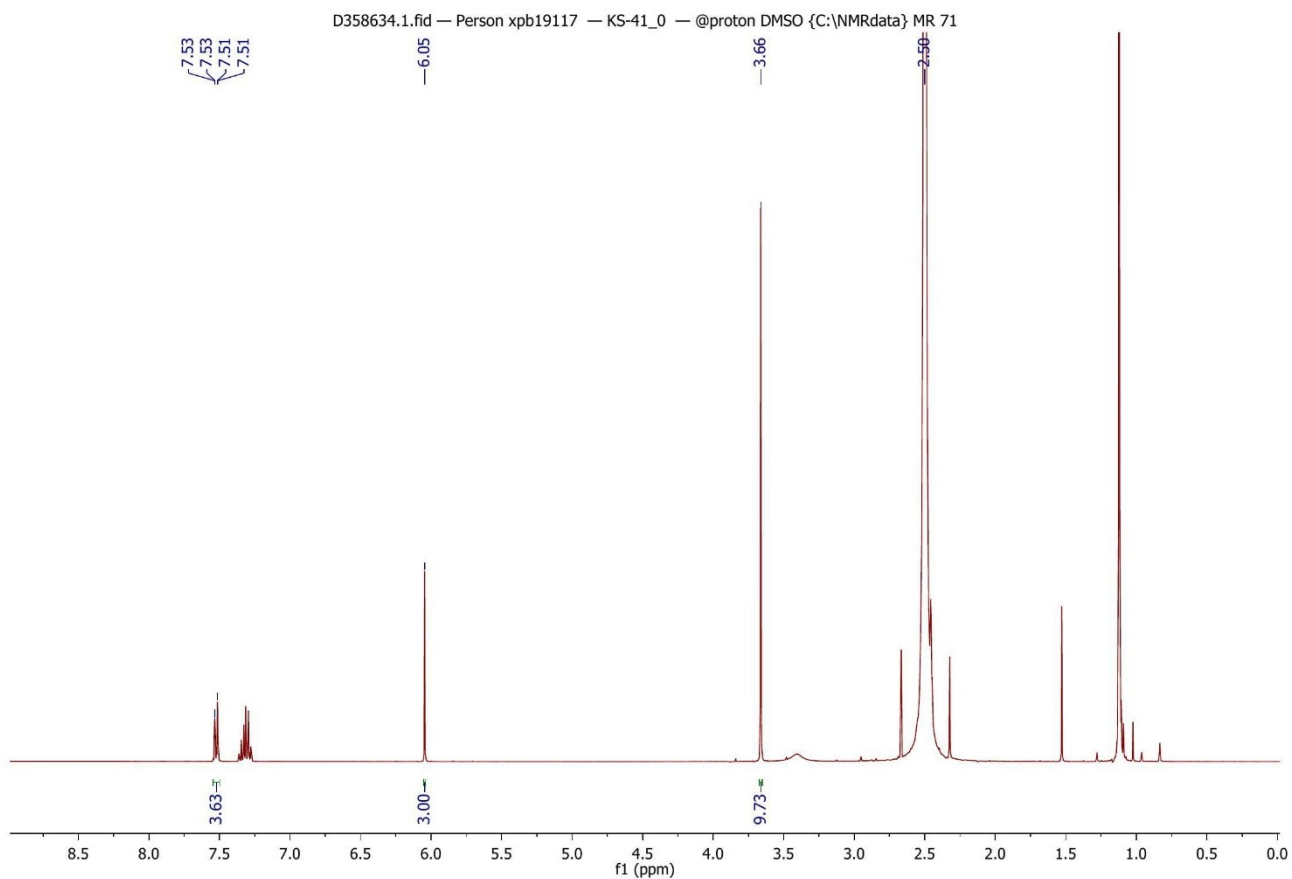


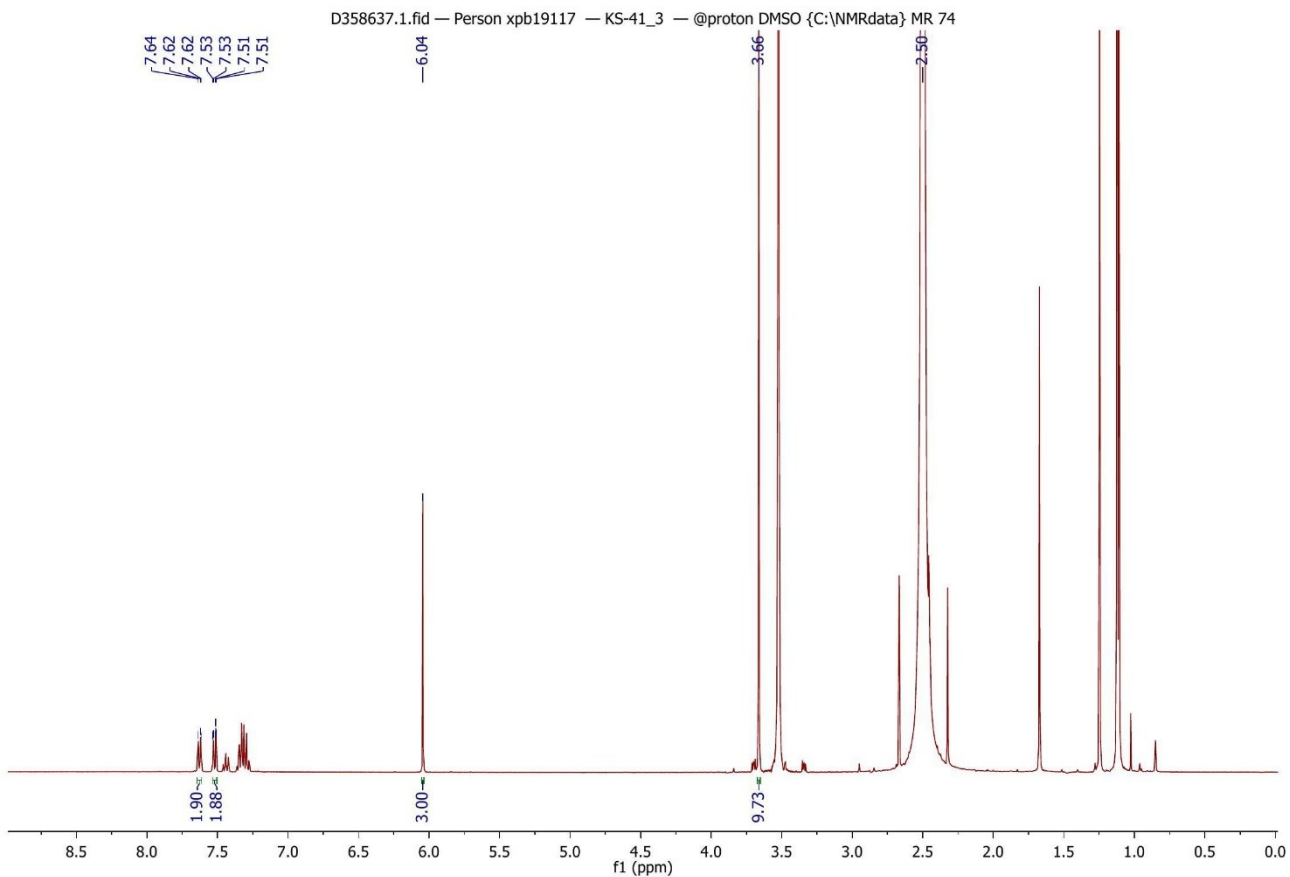
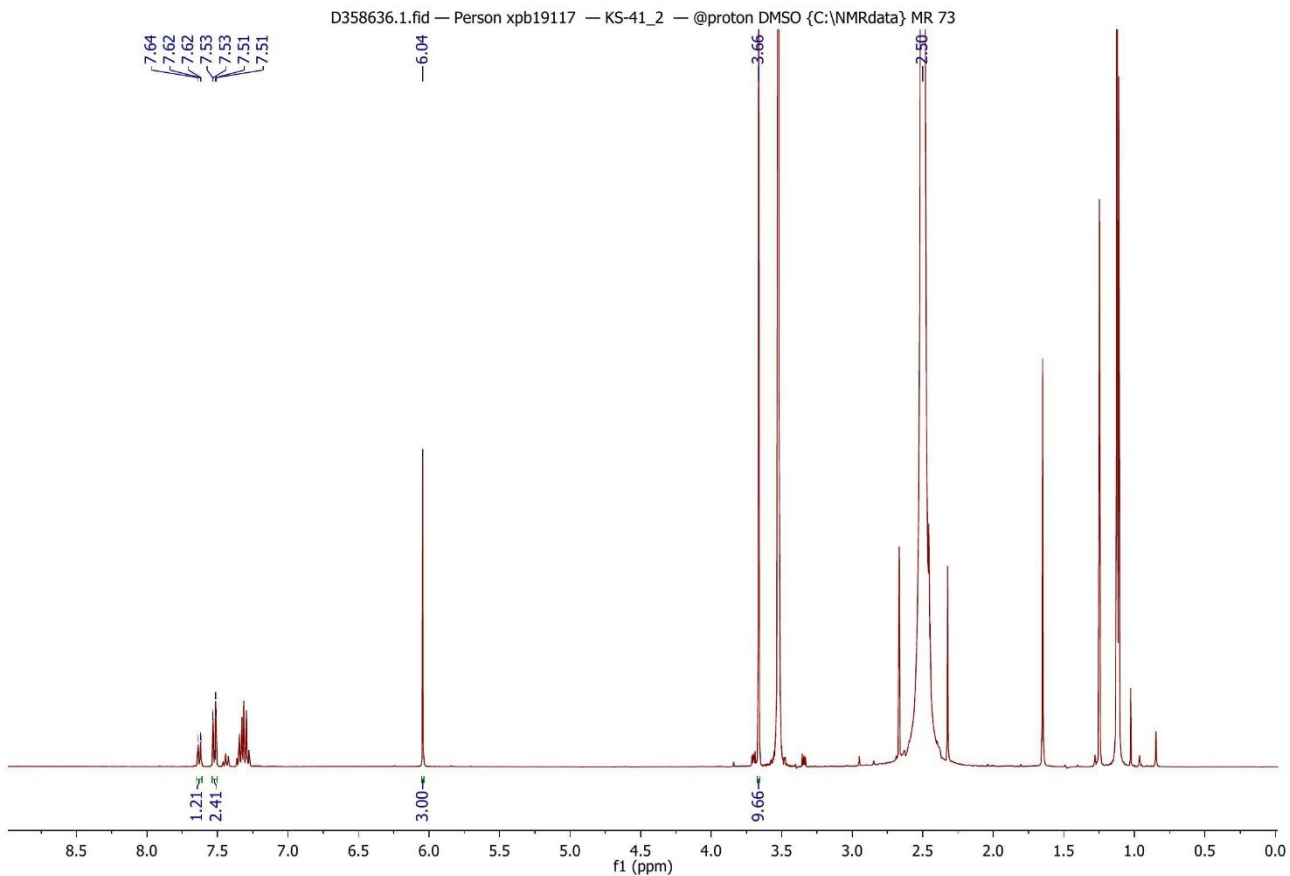


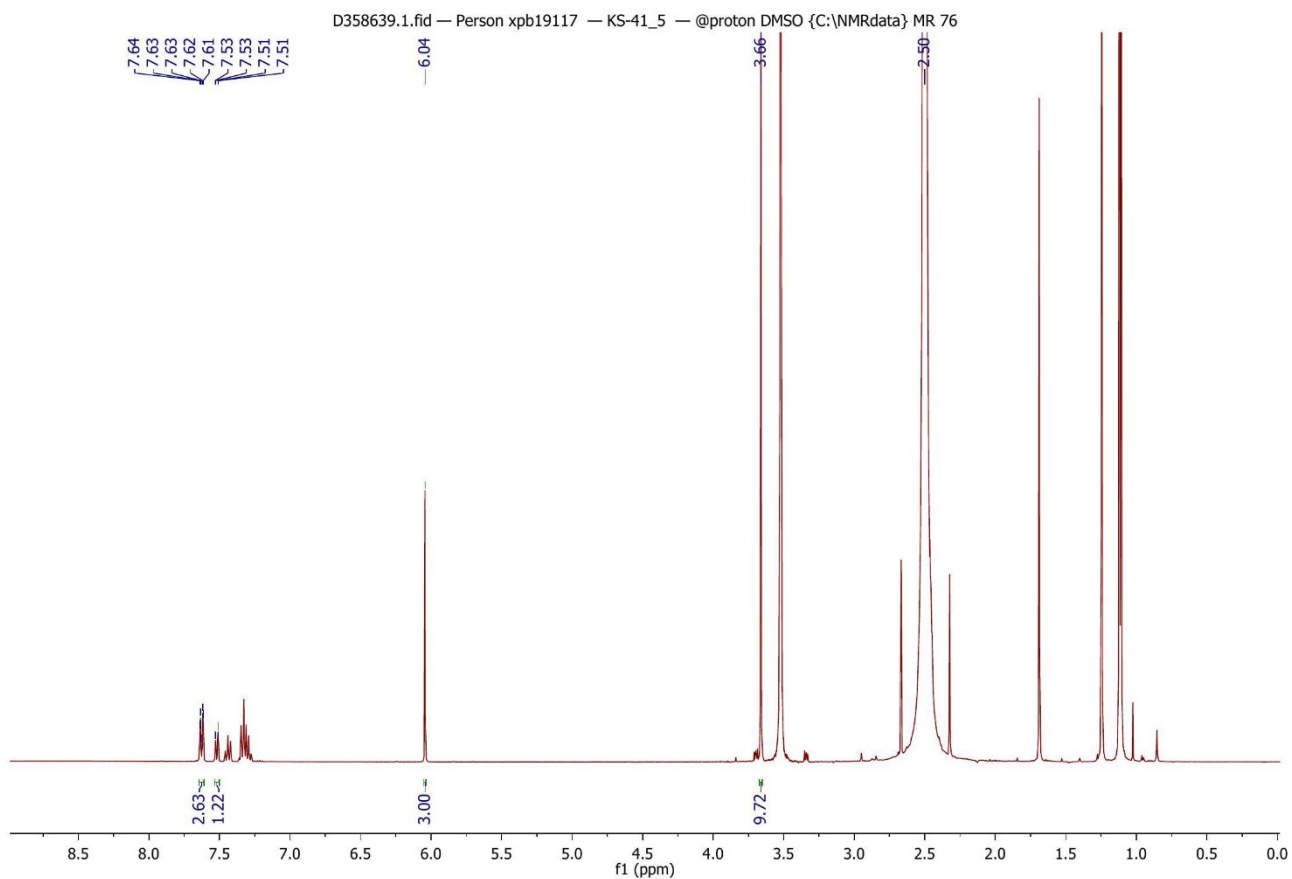
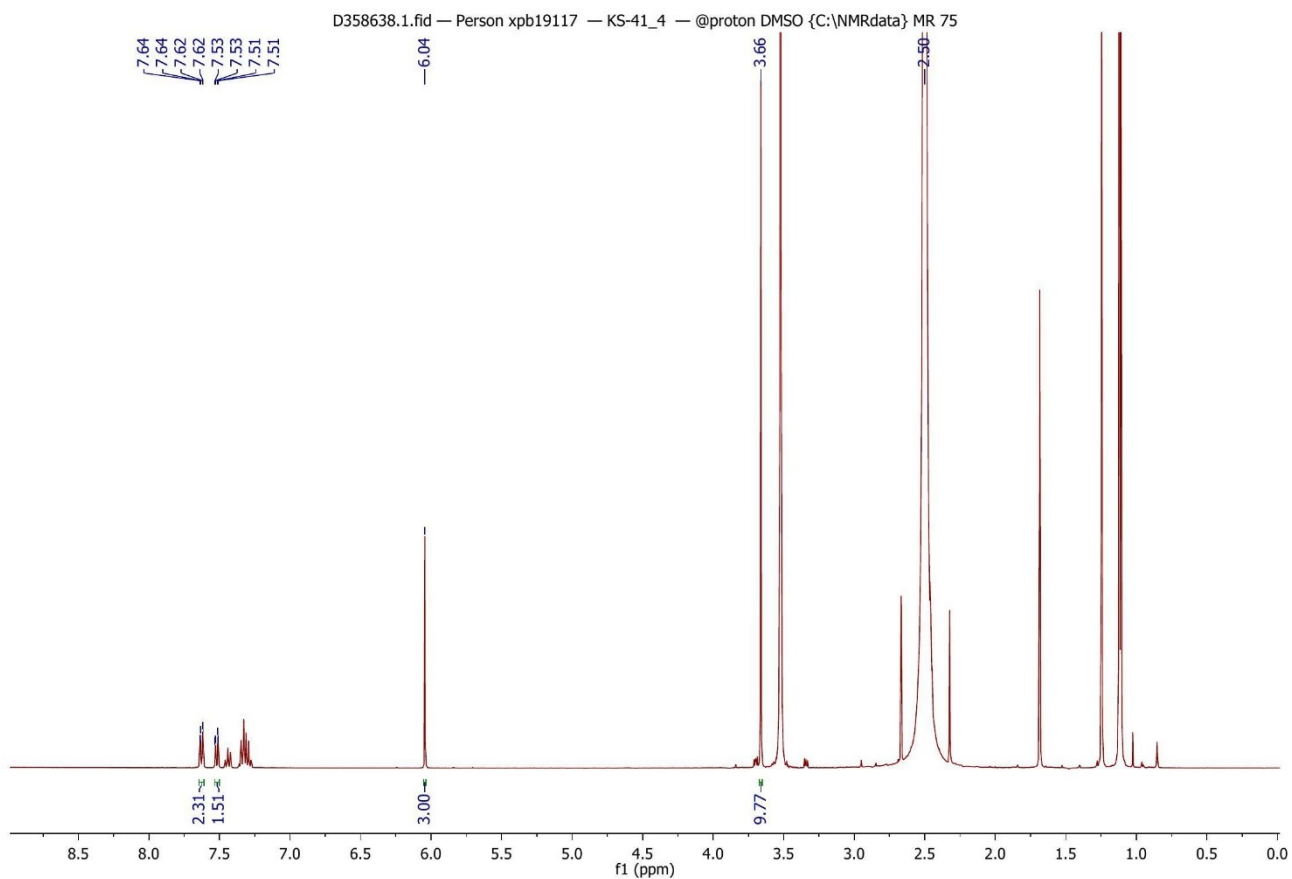


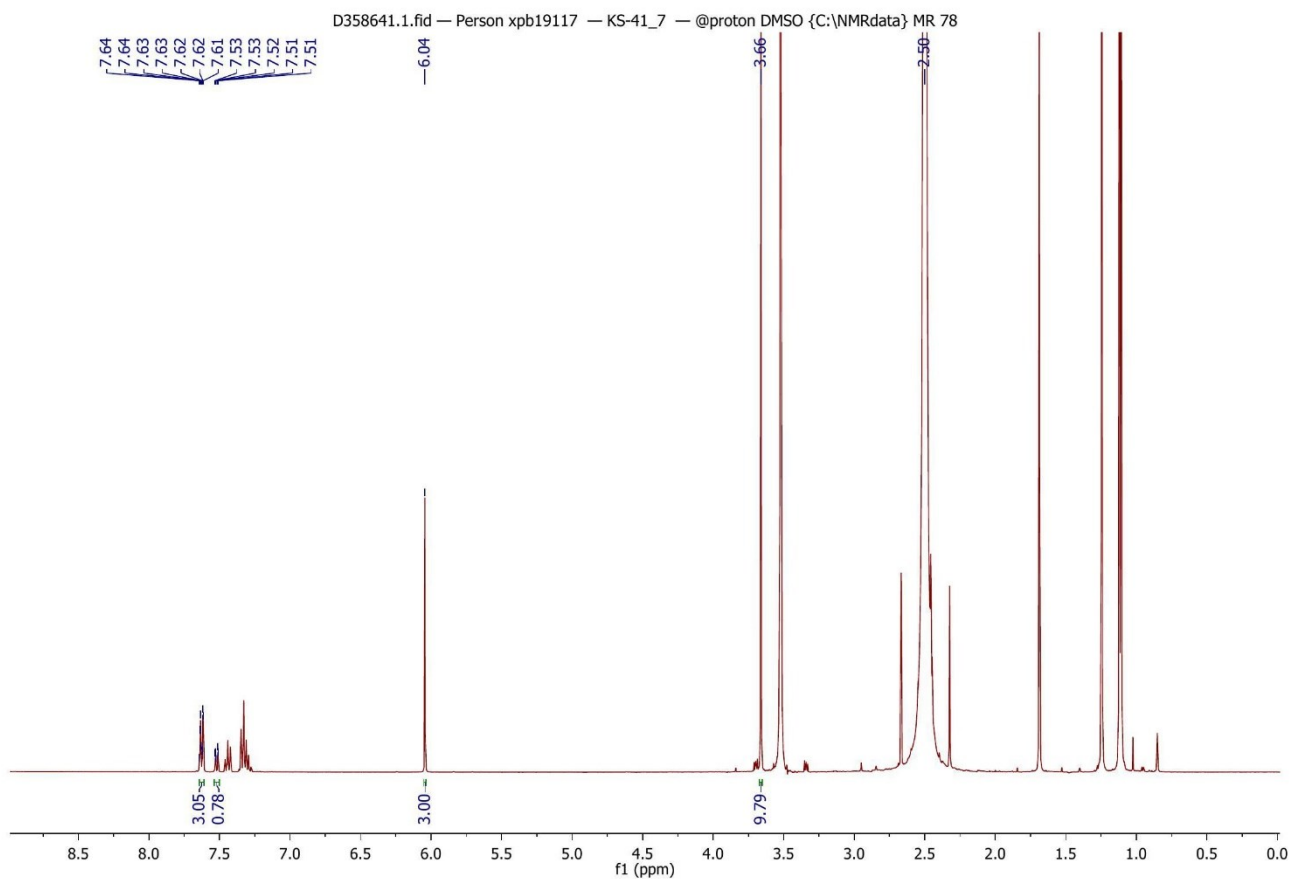
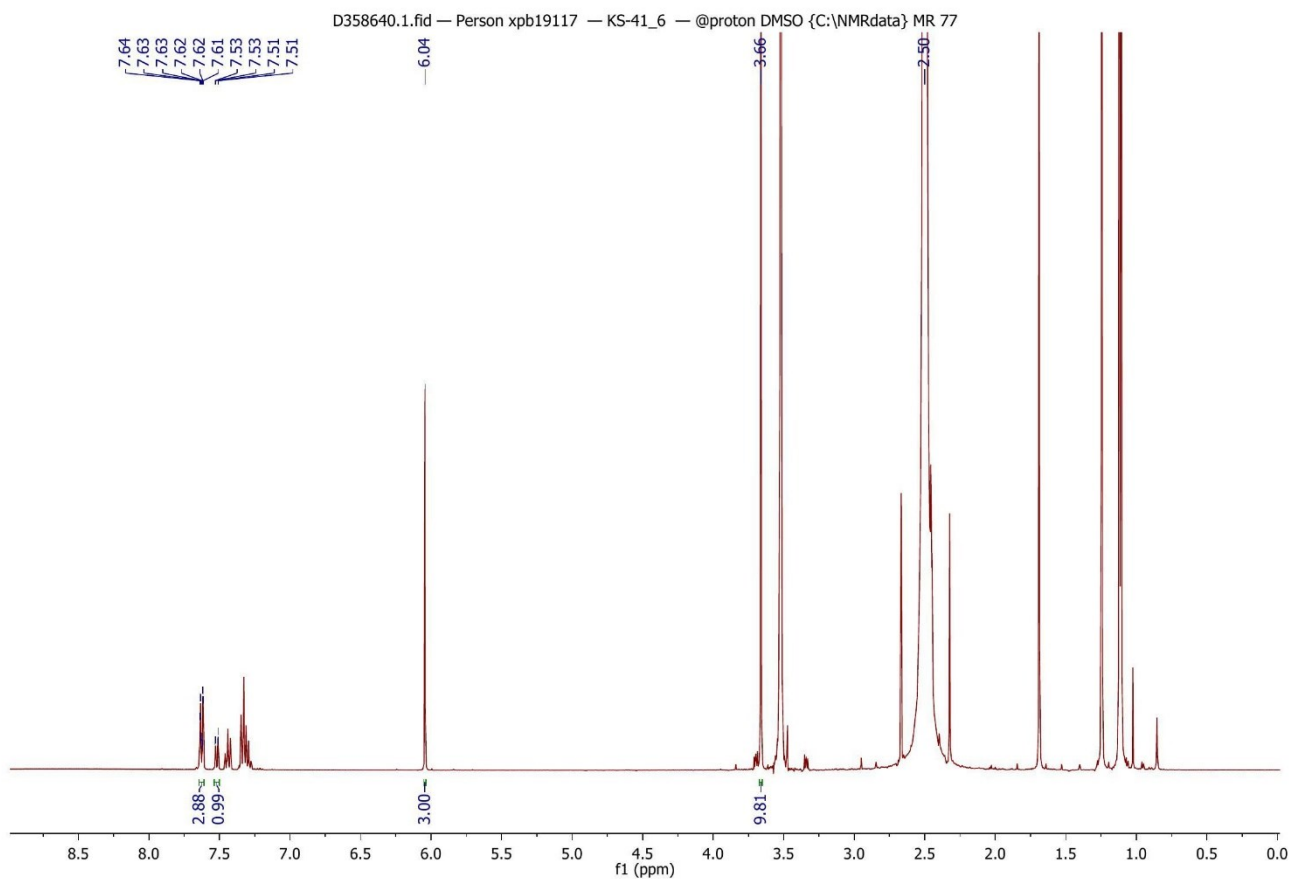
Miyaura borylation reaction samples – ^1H (DMSO- d_6) spectra for manuscript Scheme 9

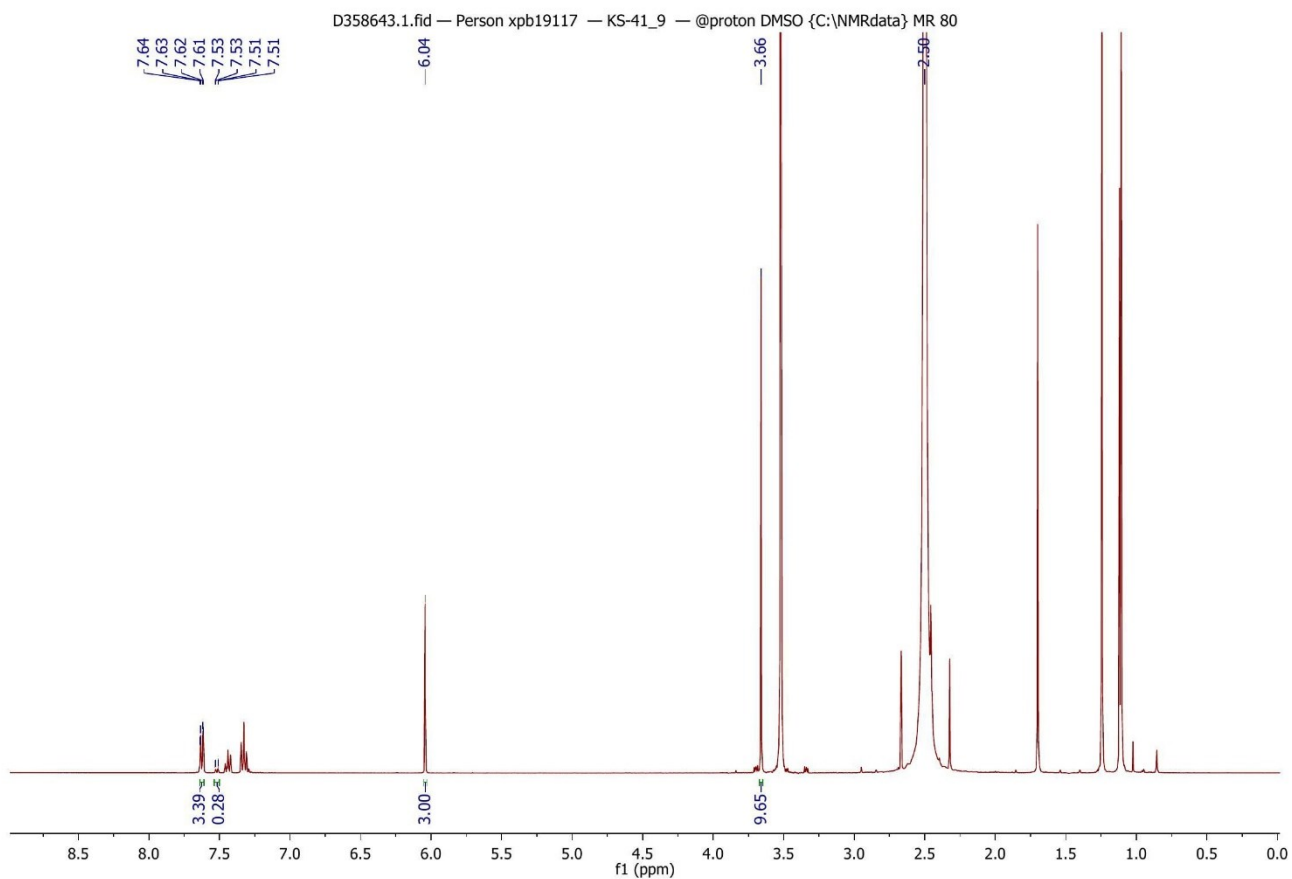
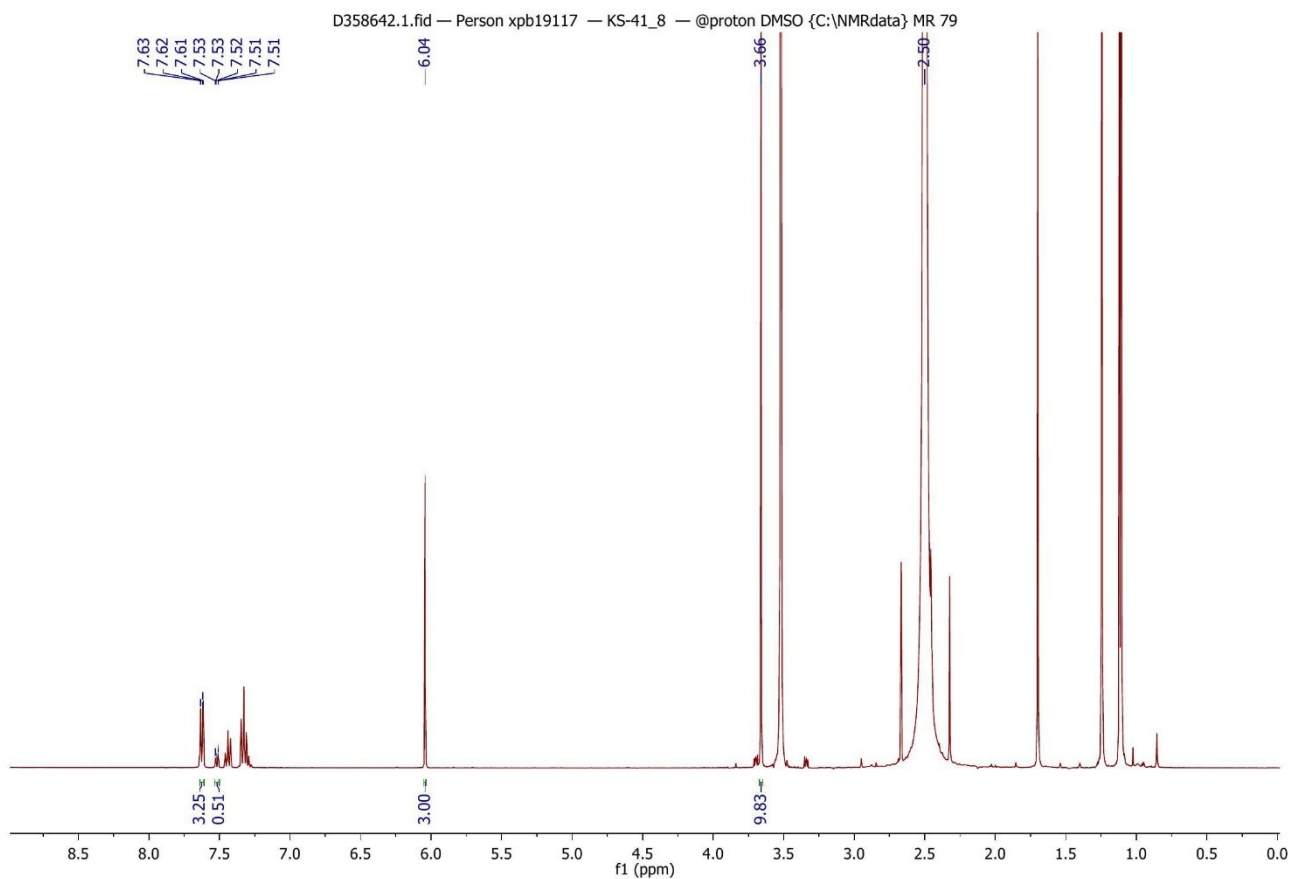
Reaction under Argon with 0.5 mol% catalyst loading:

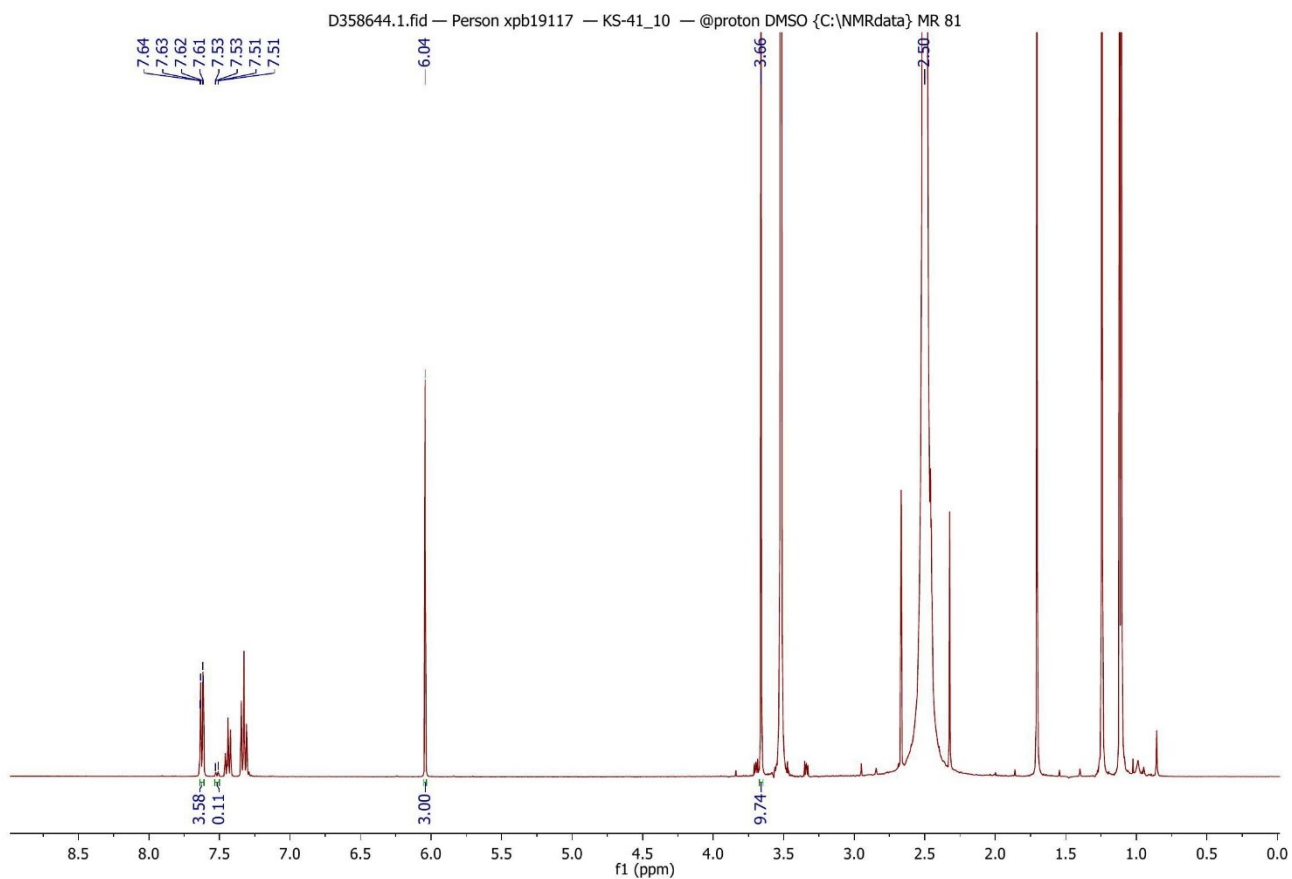




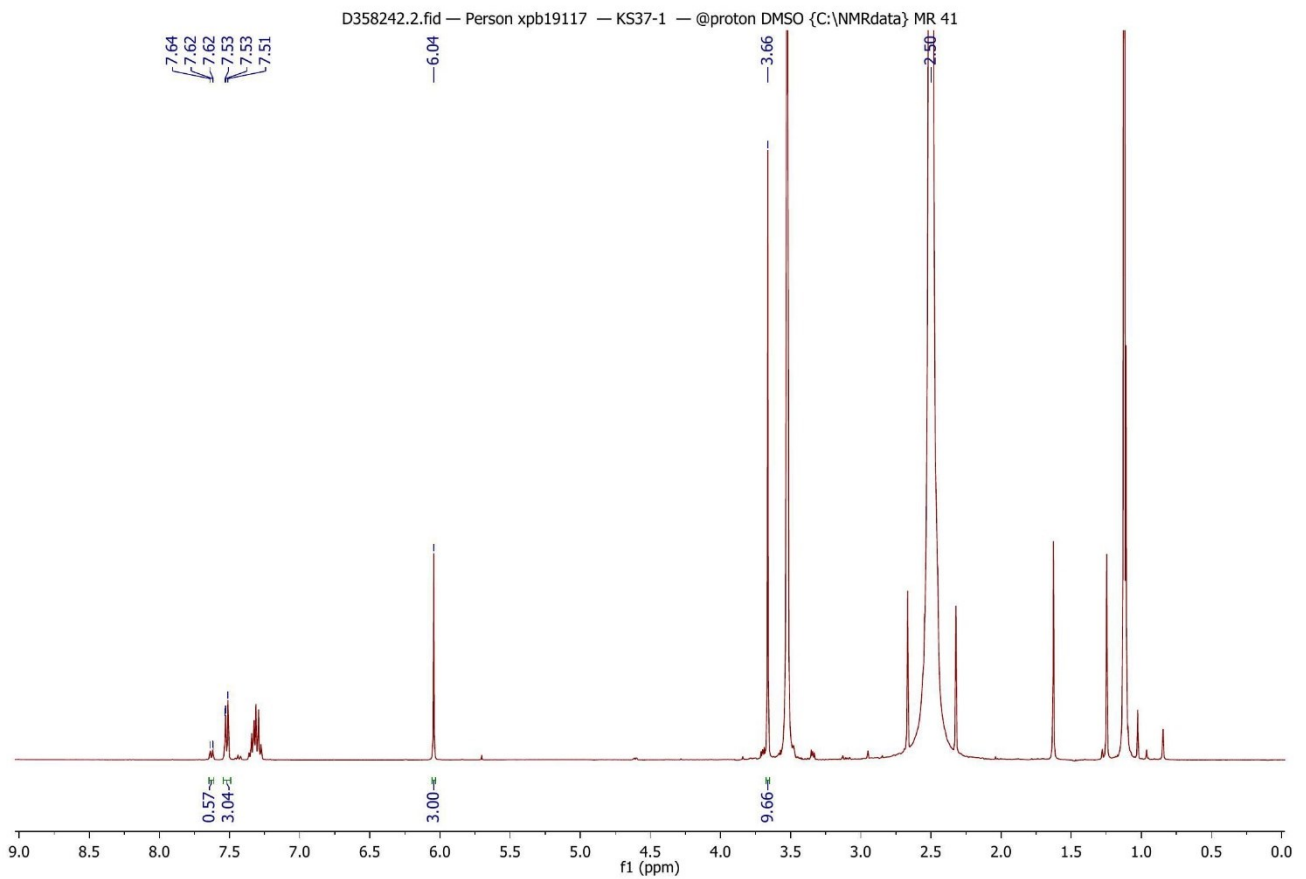
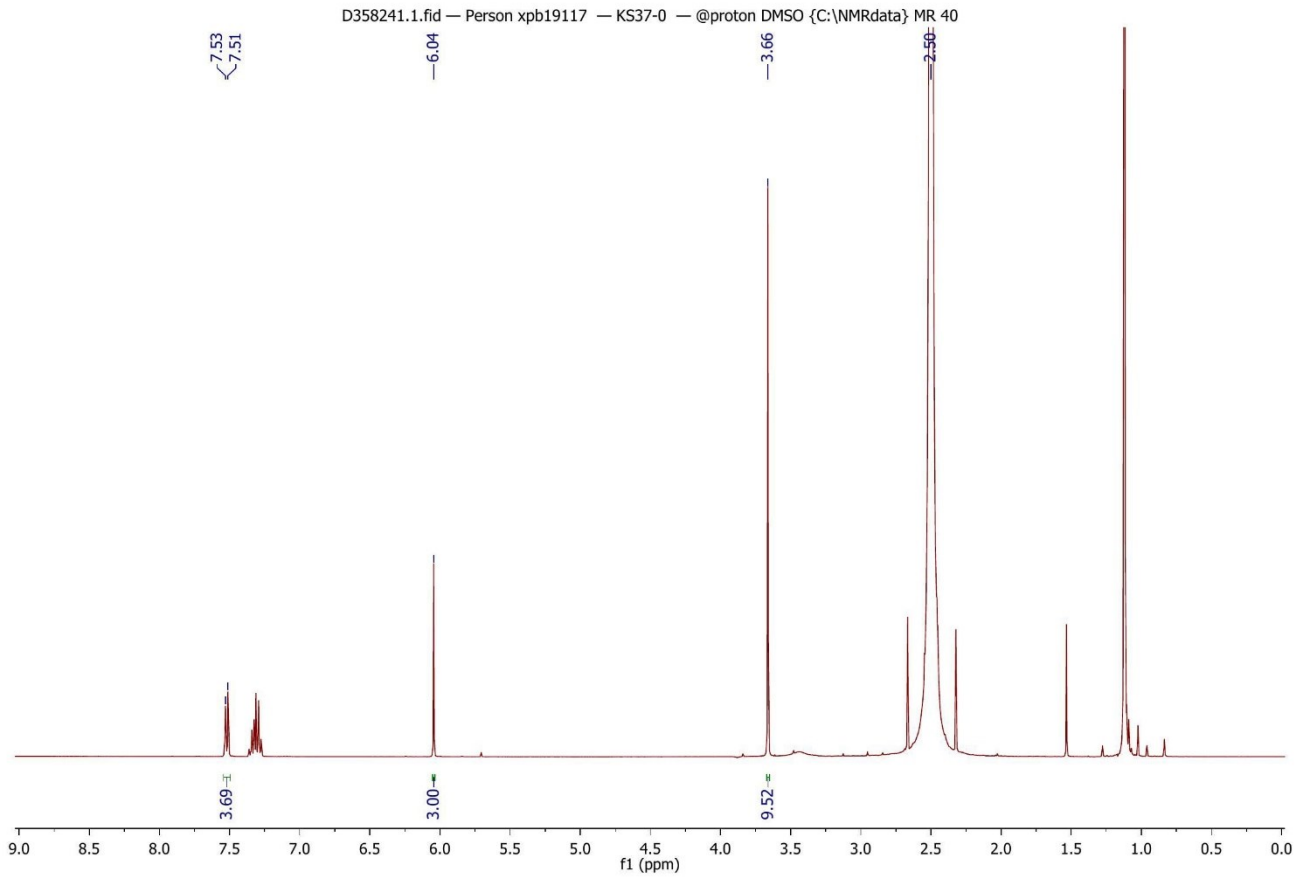


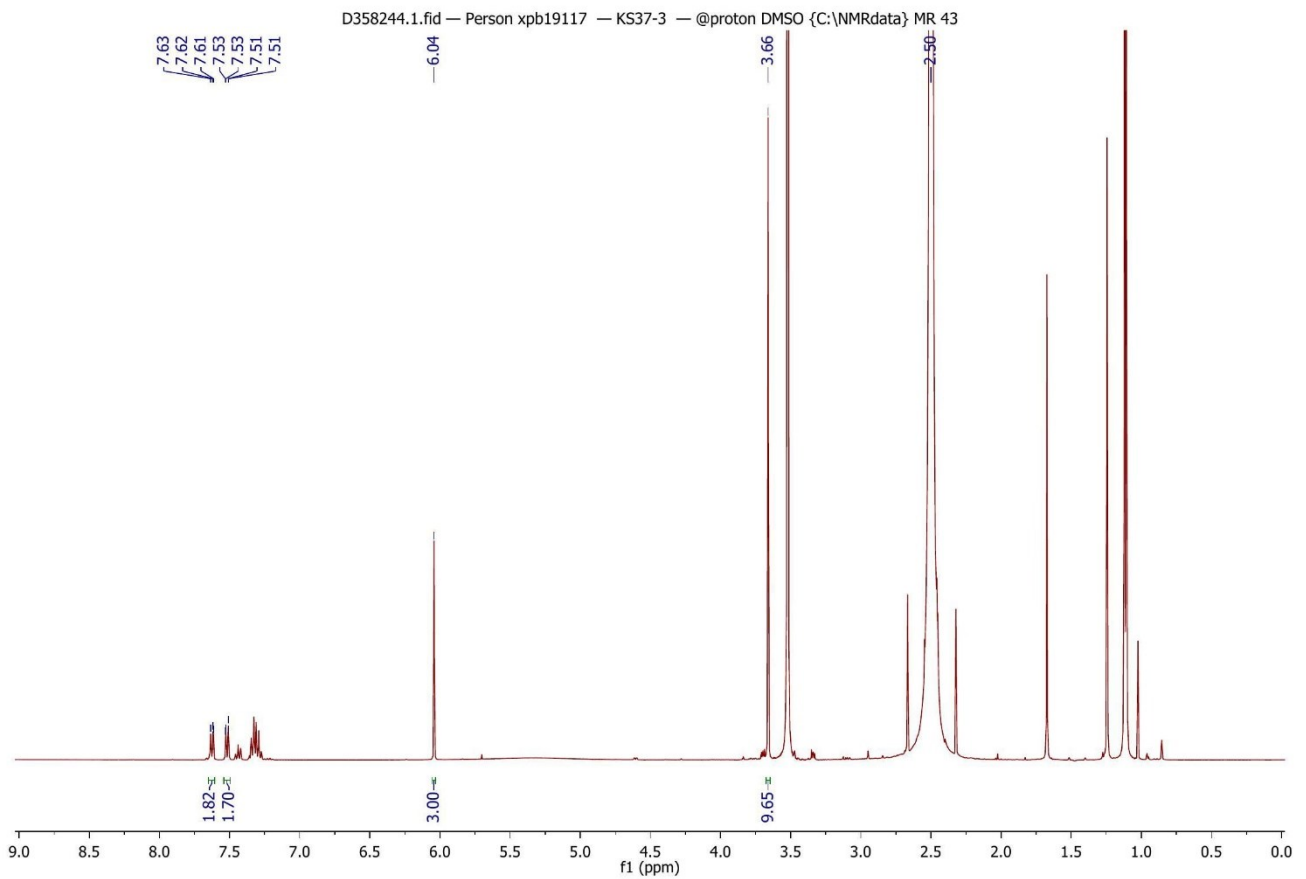
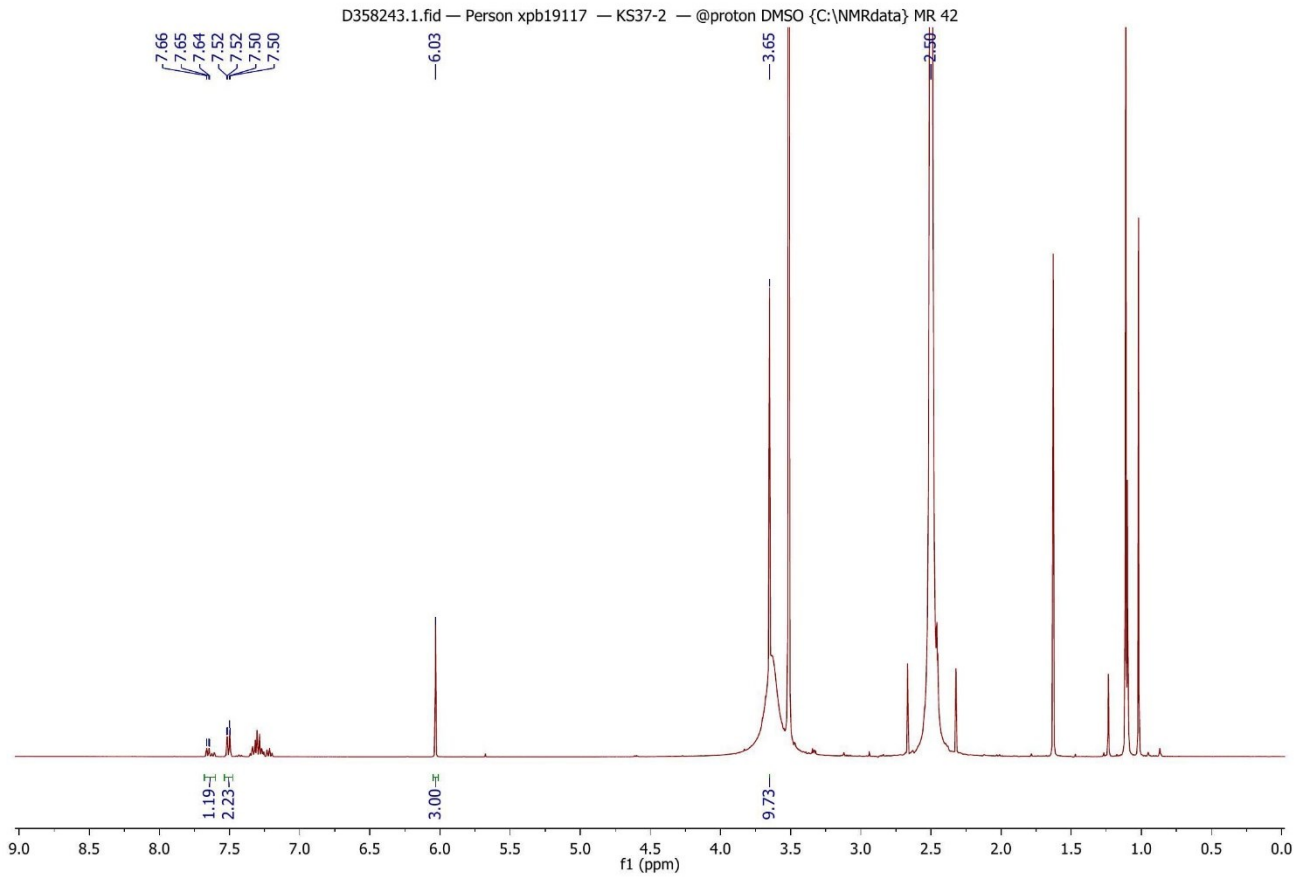


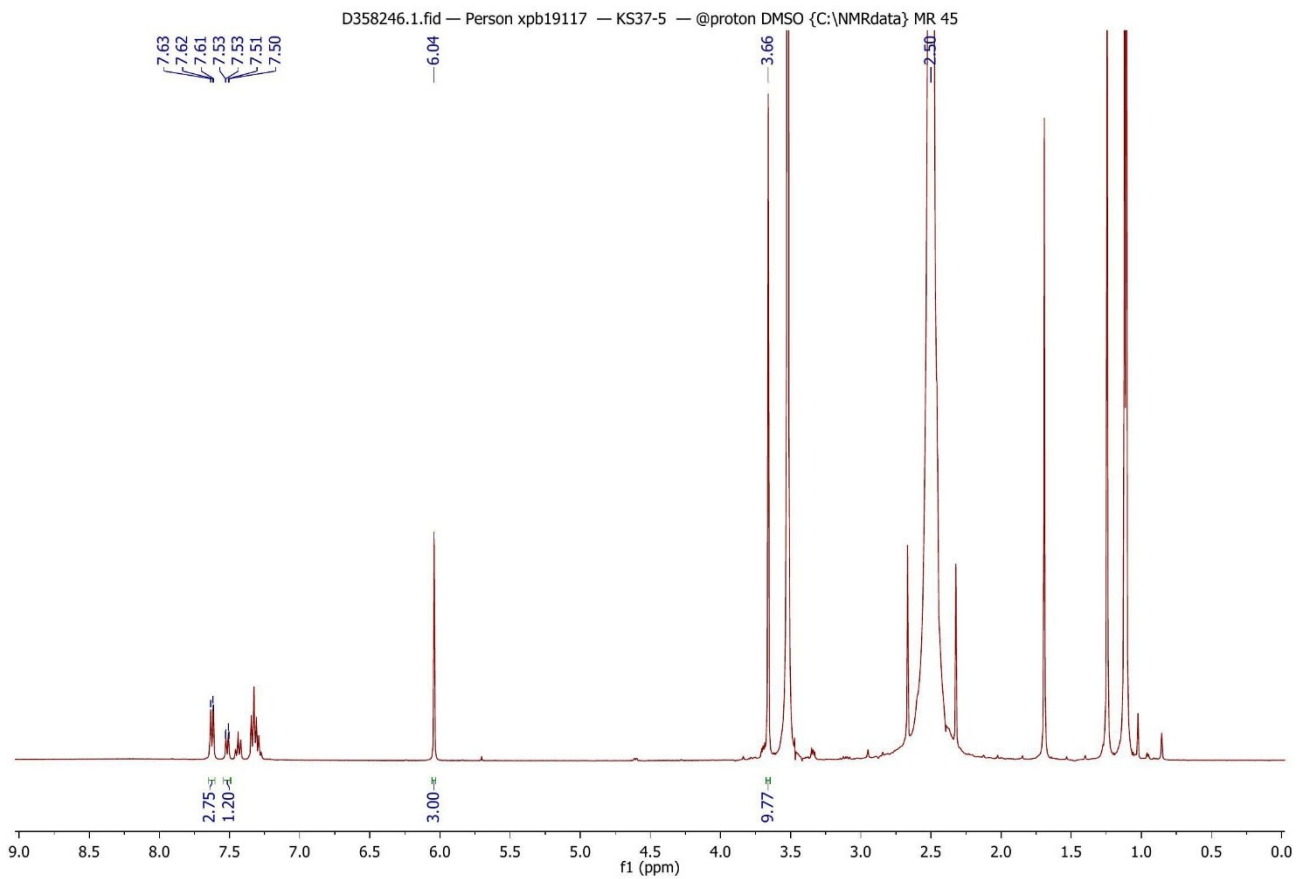
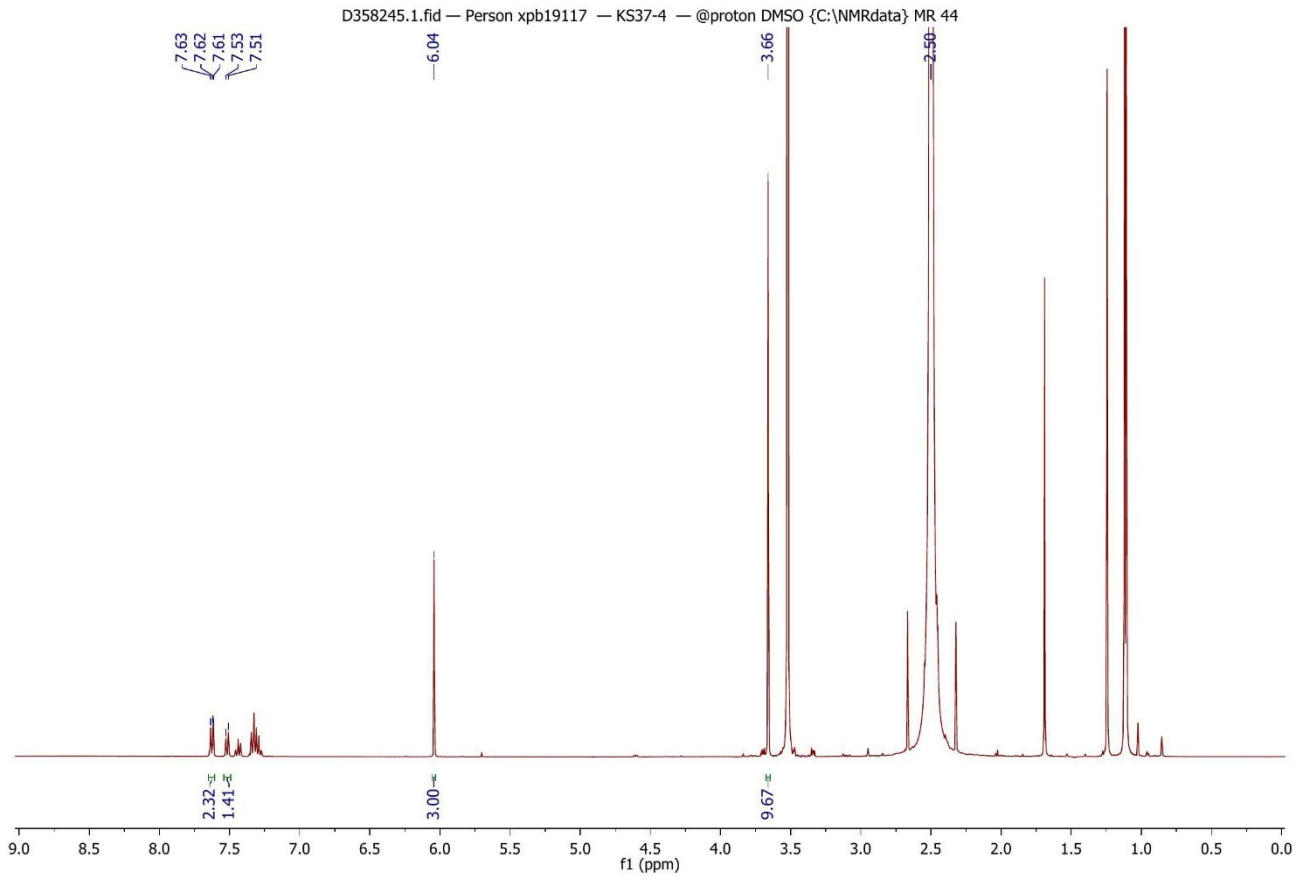


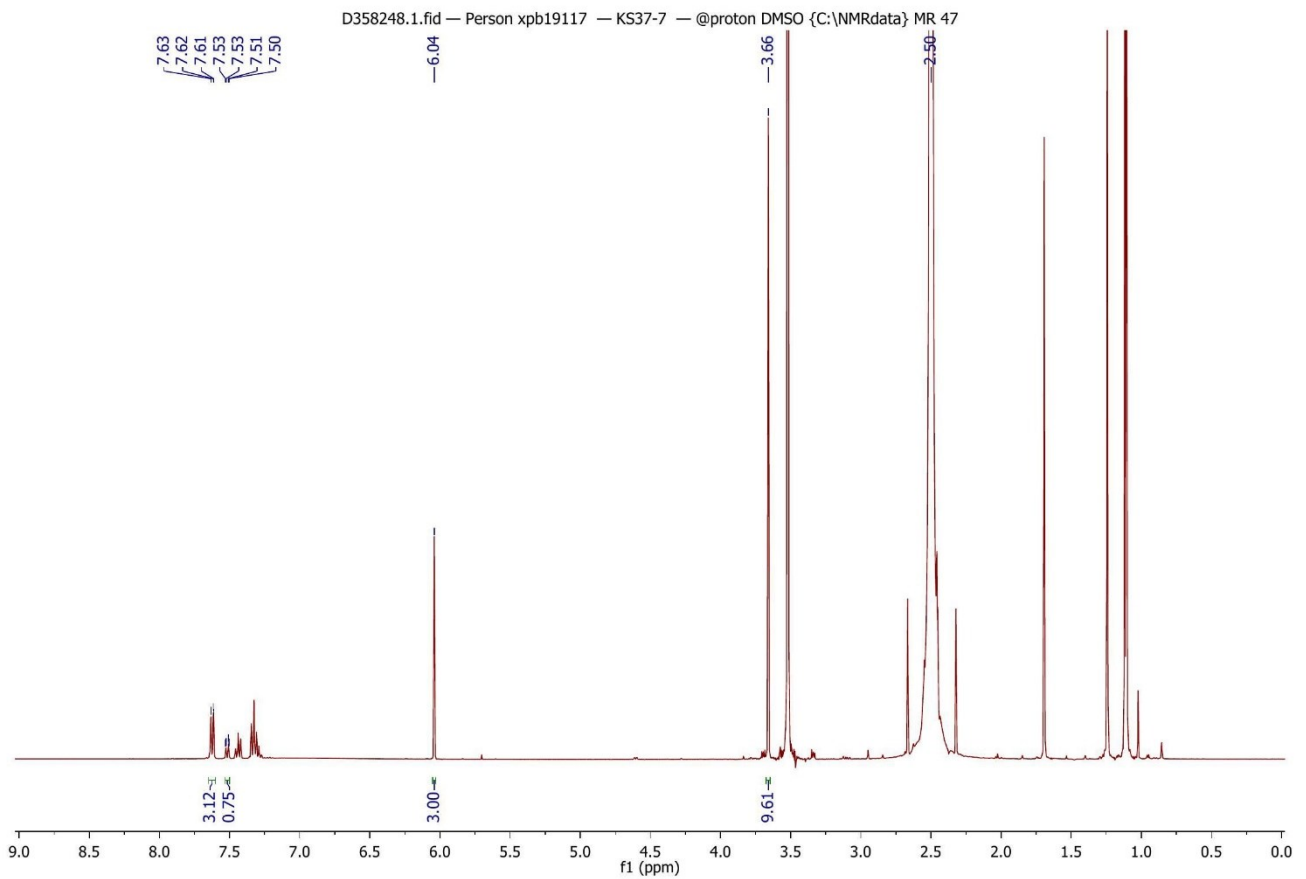
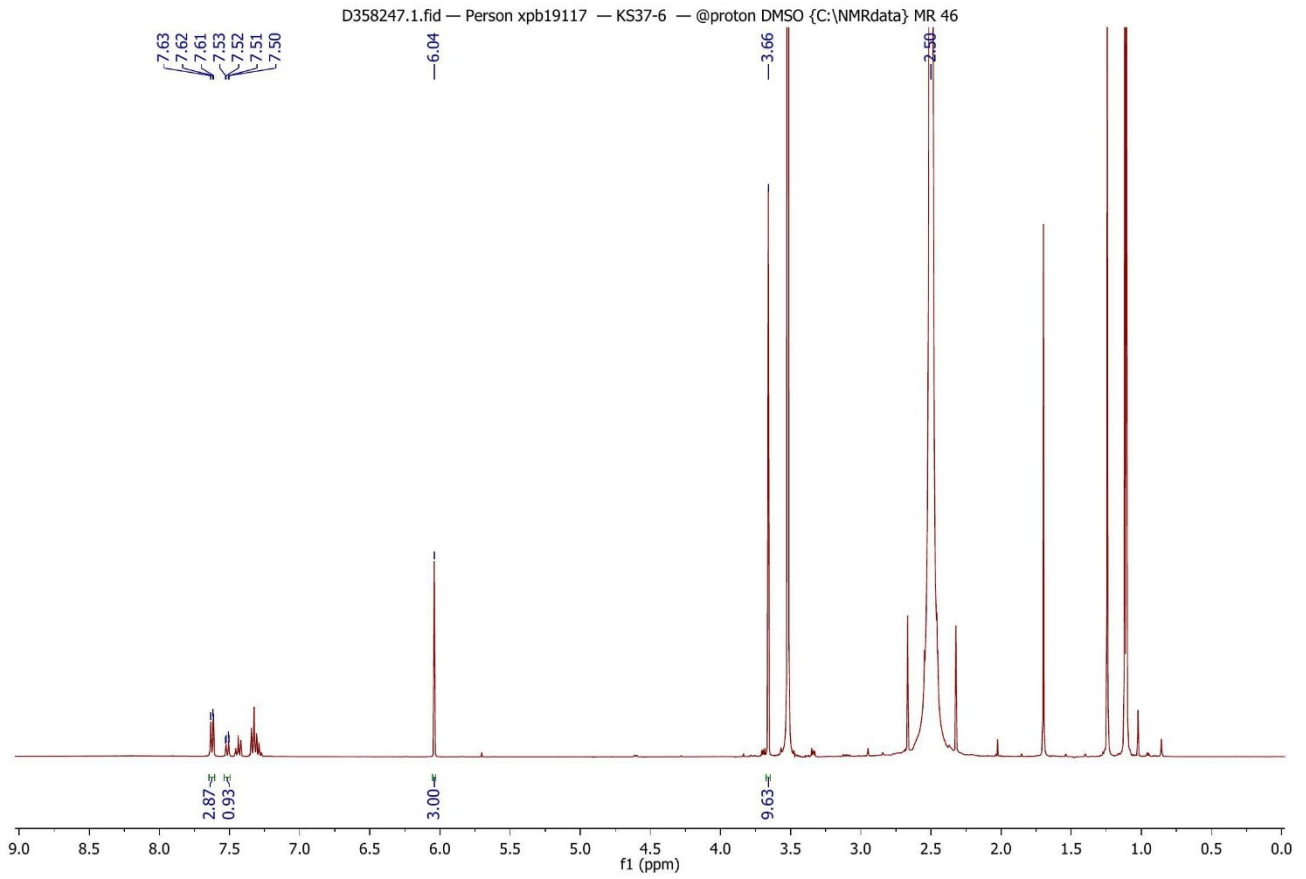


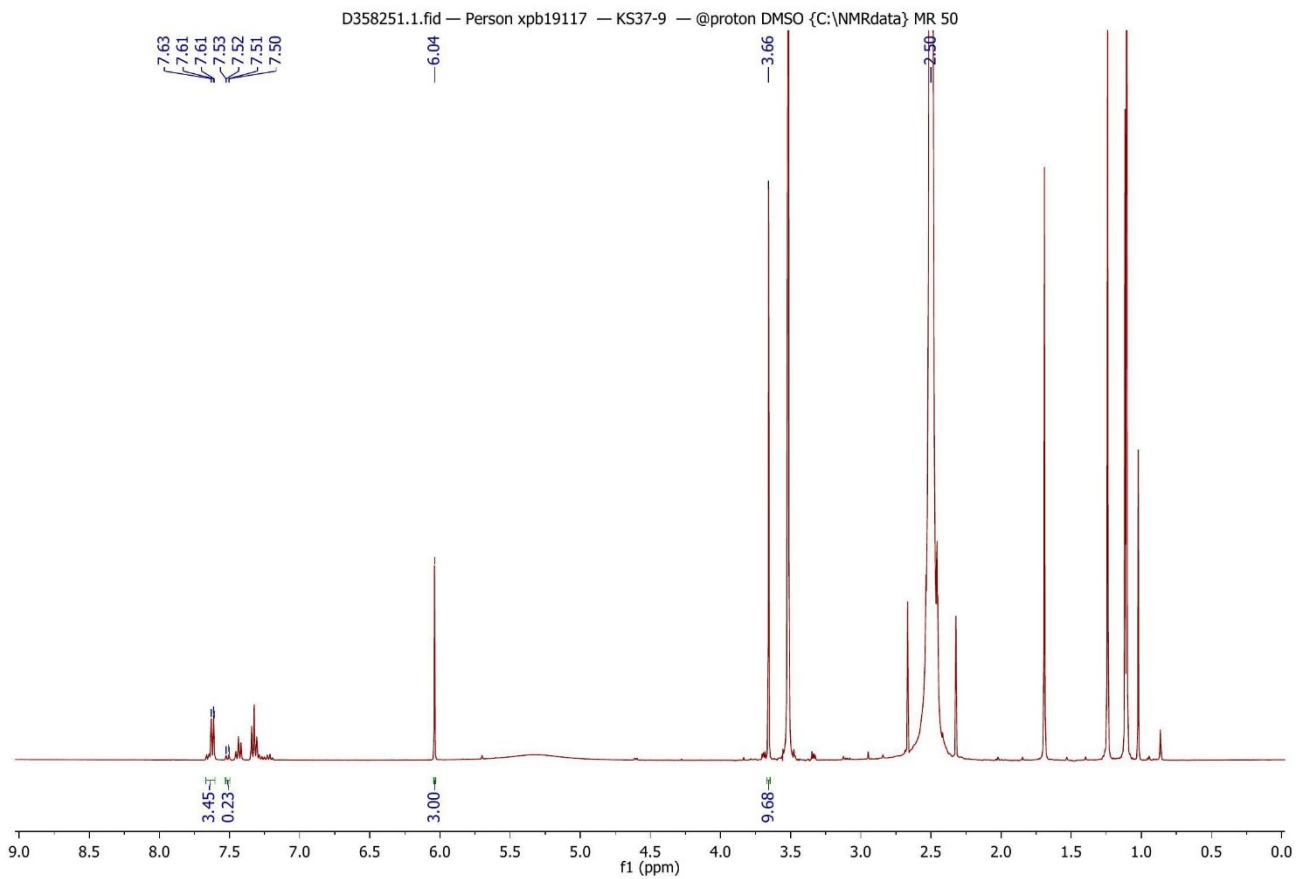
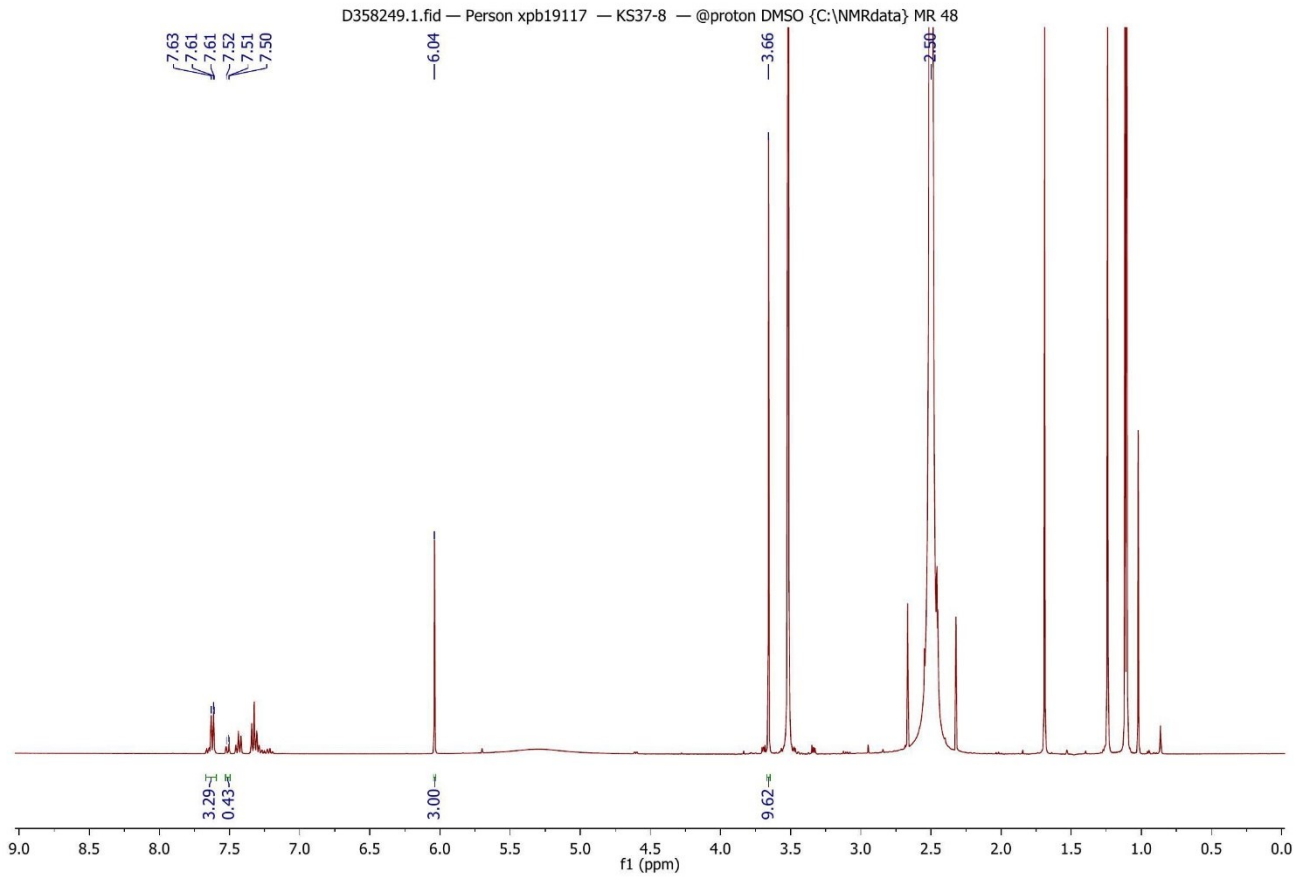
Reaction under Nitrogen with 0.5 mol% catalyst loading:

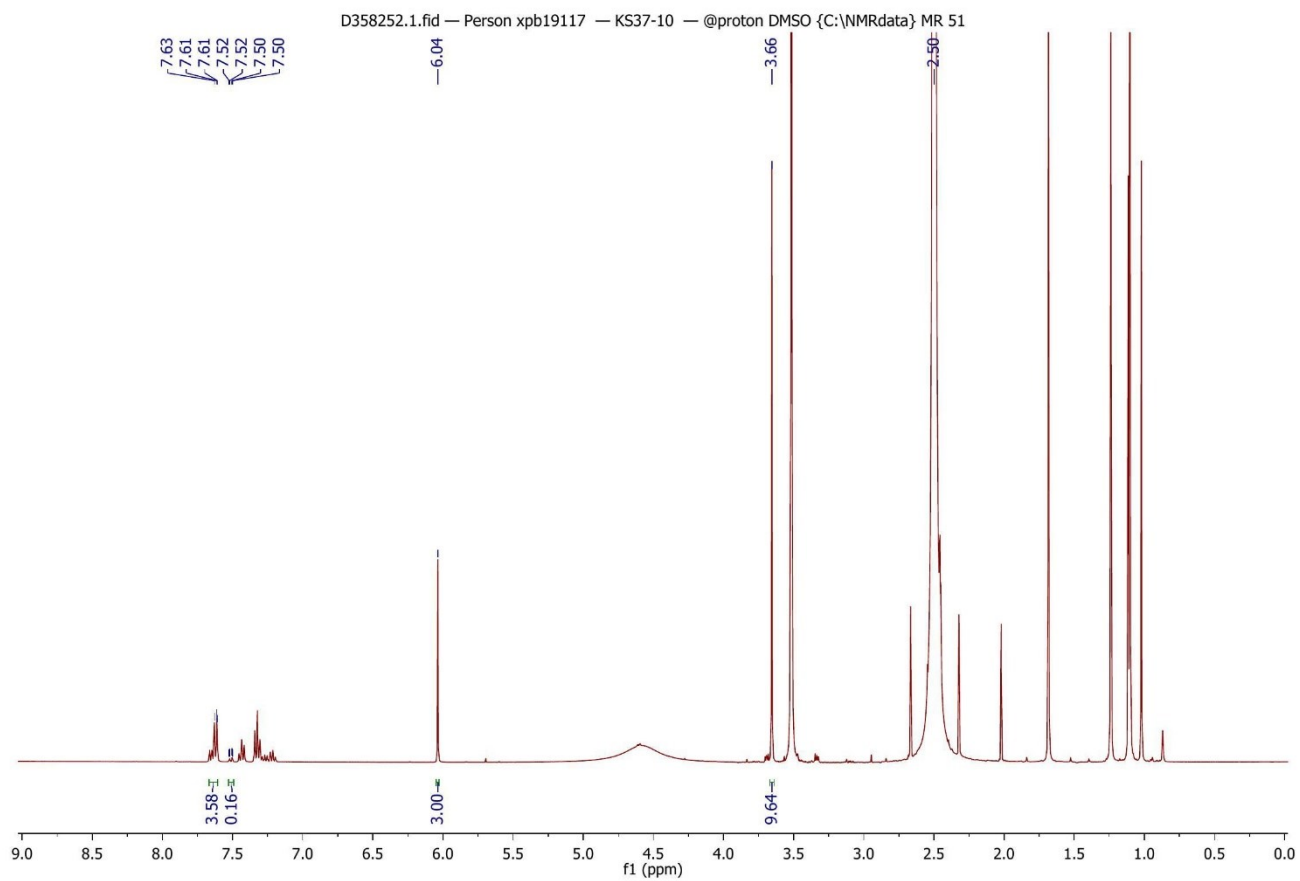




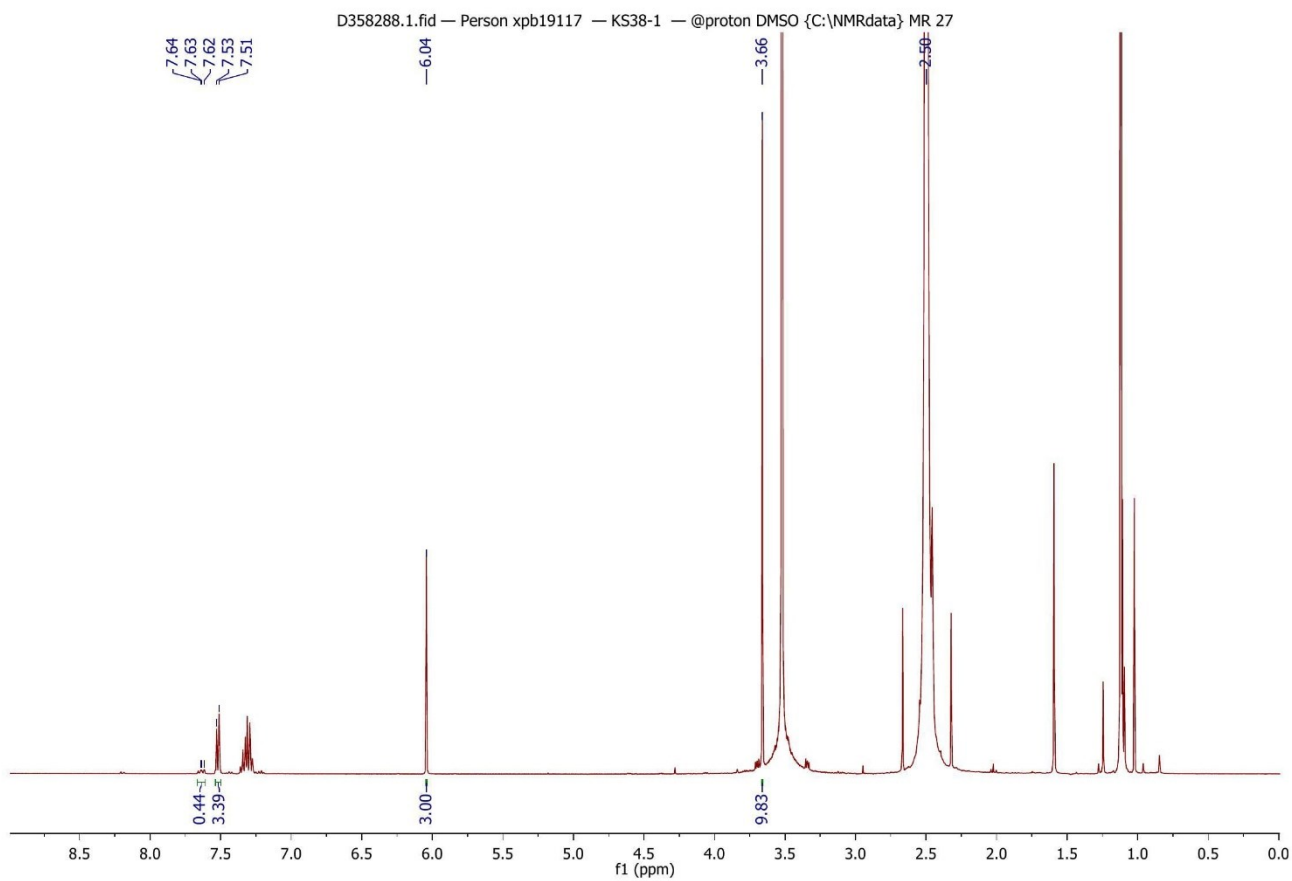
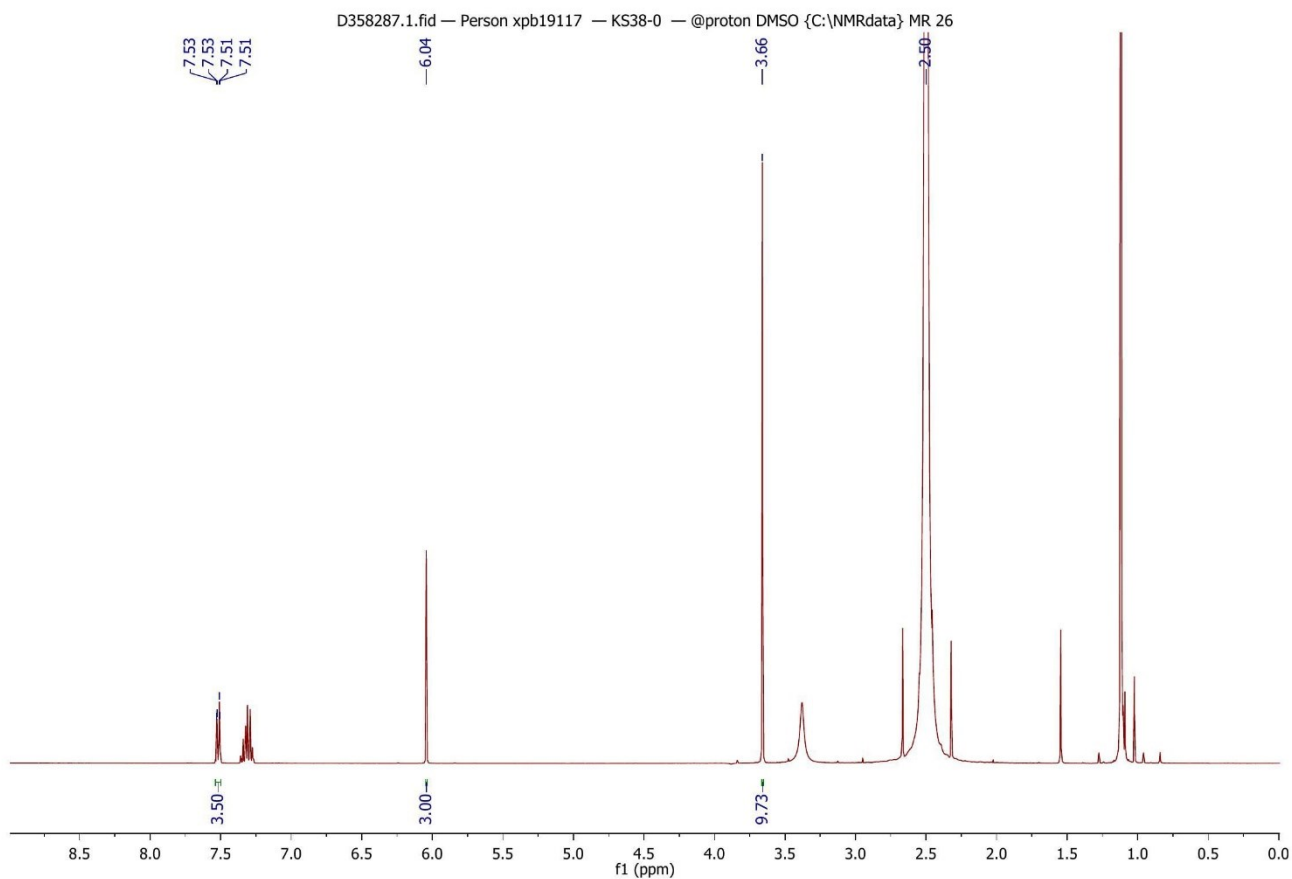


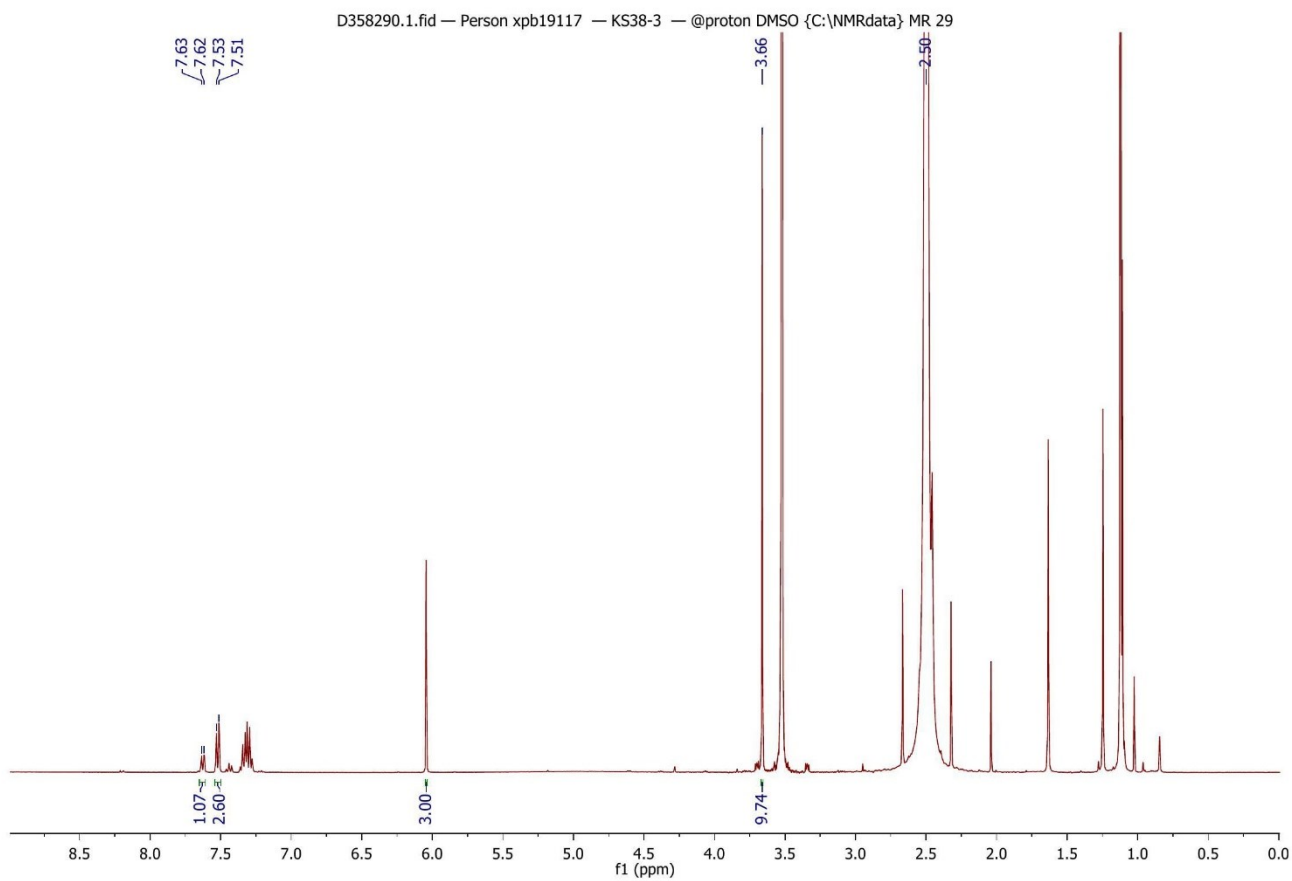
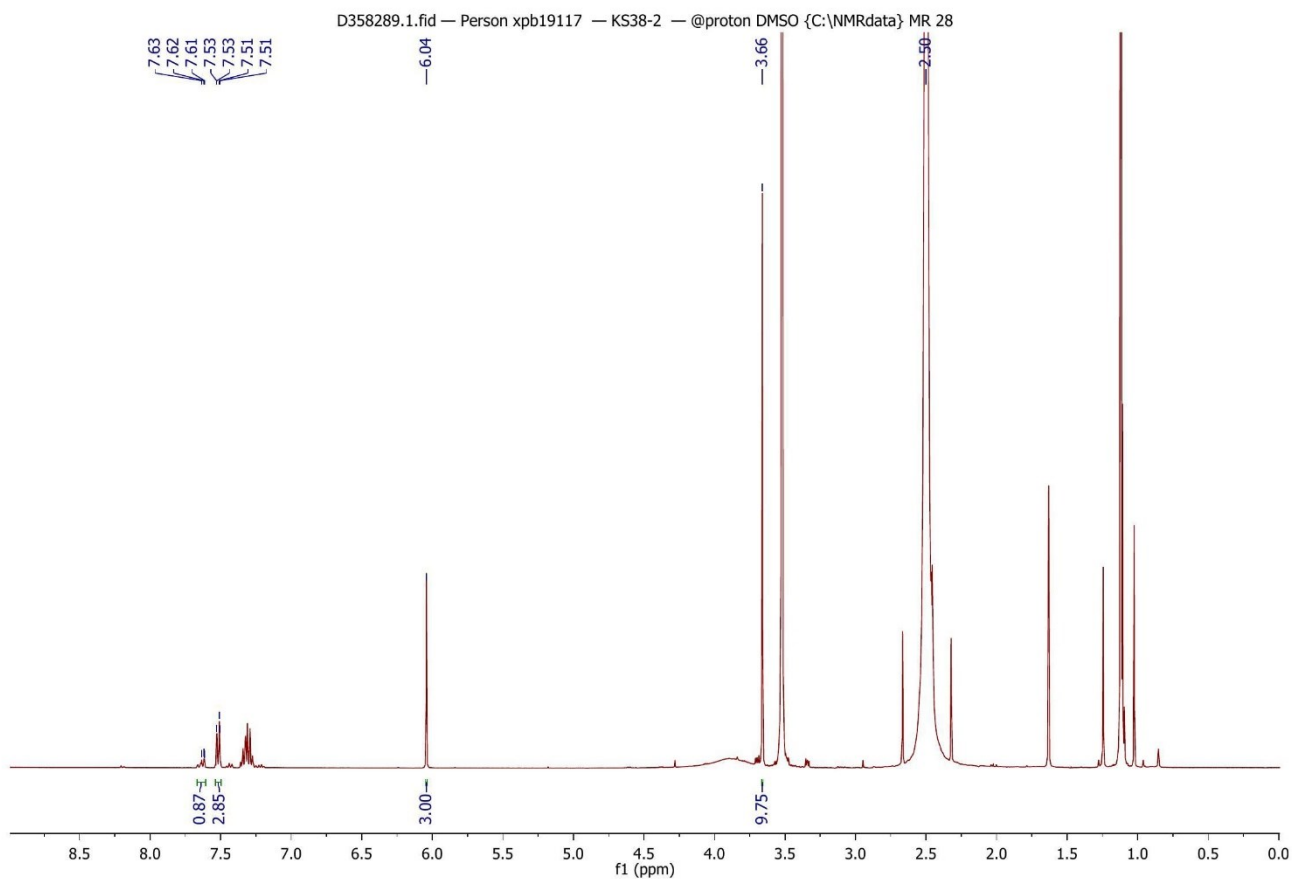


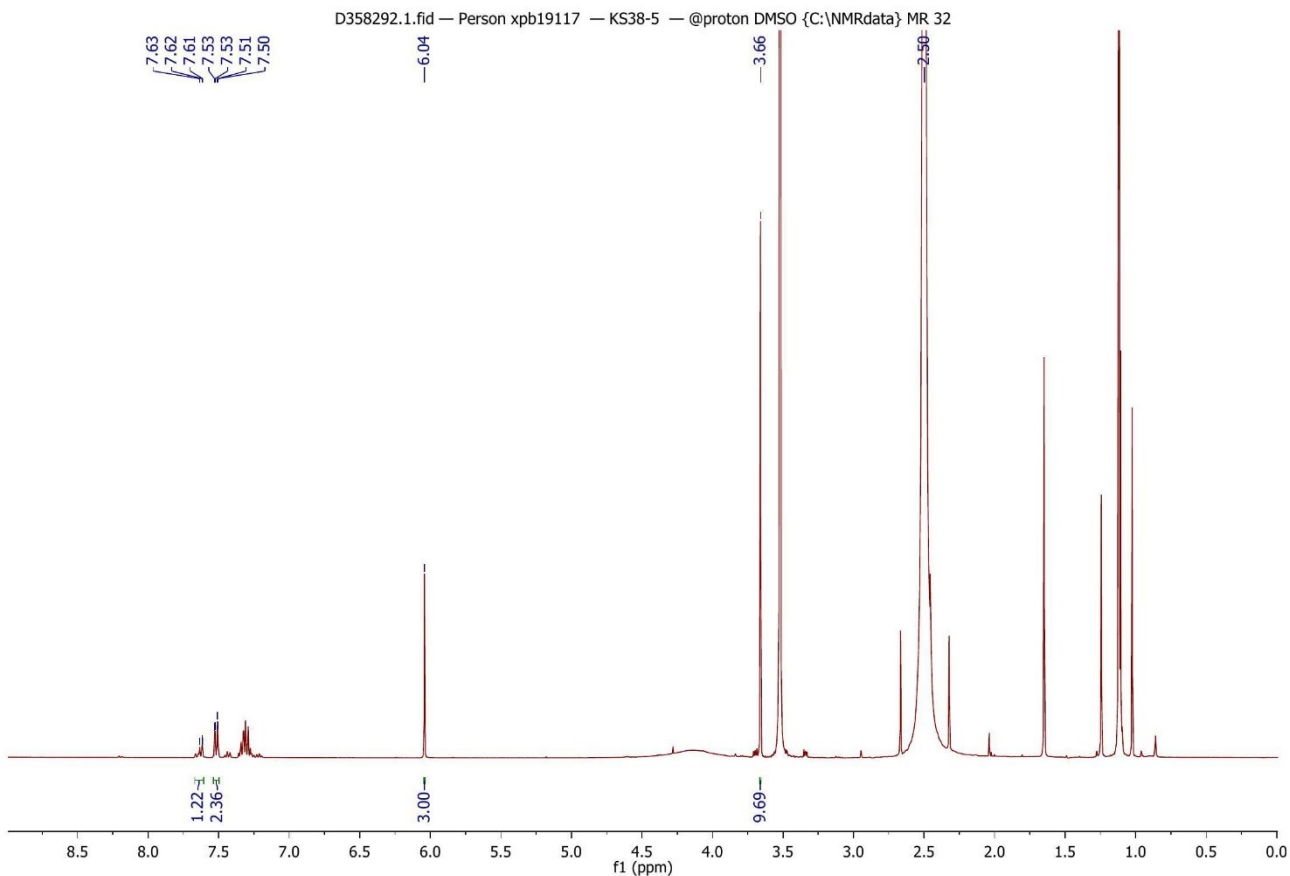
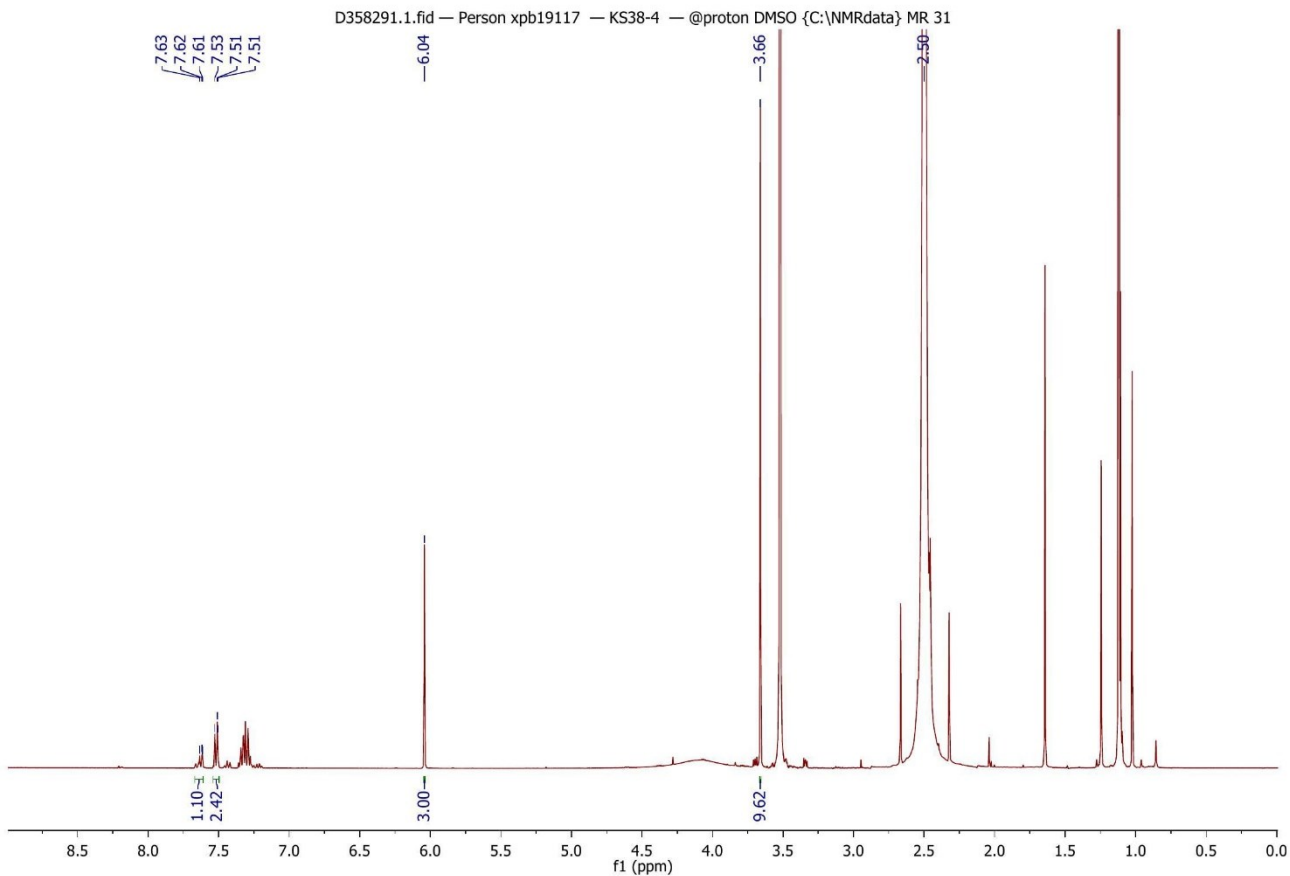


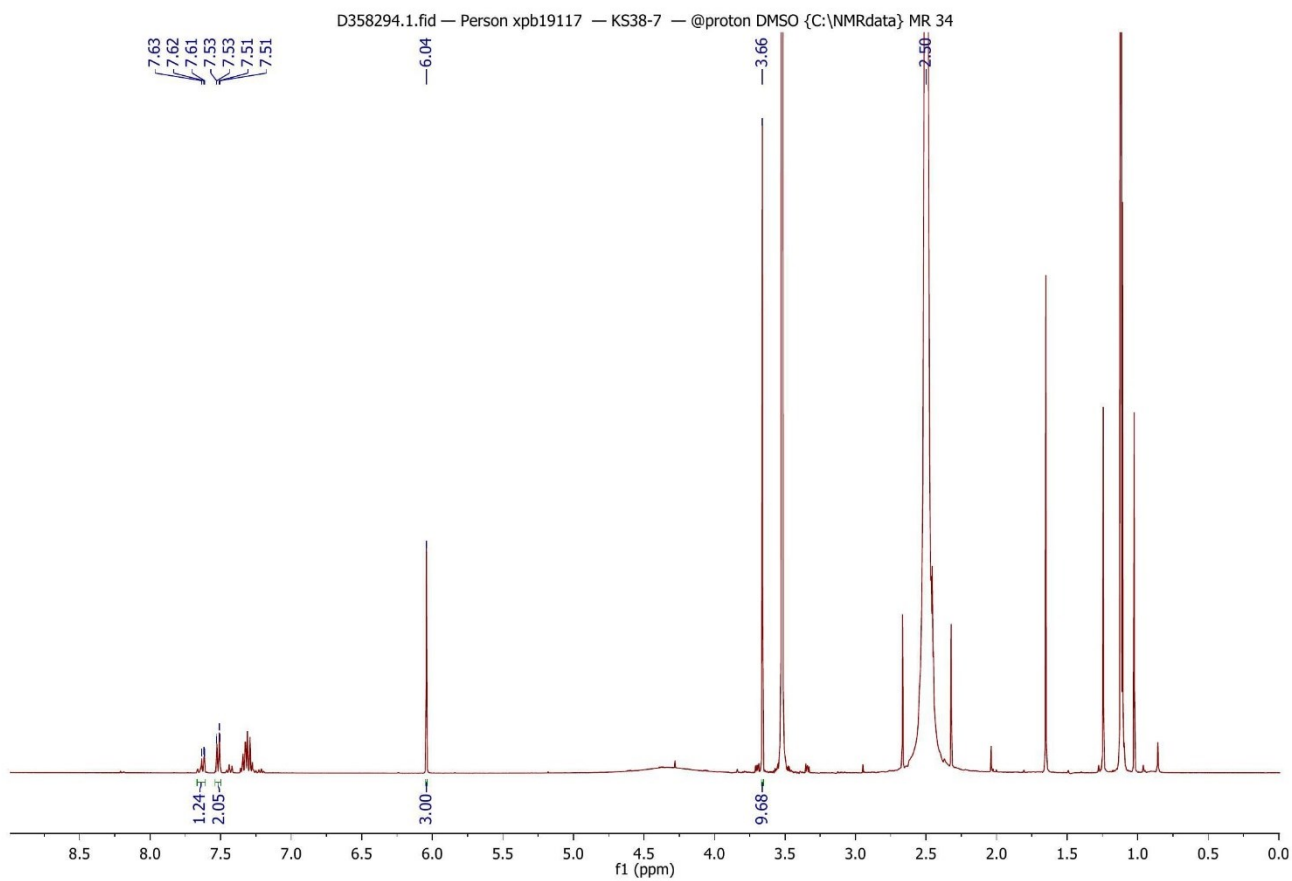
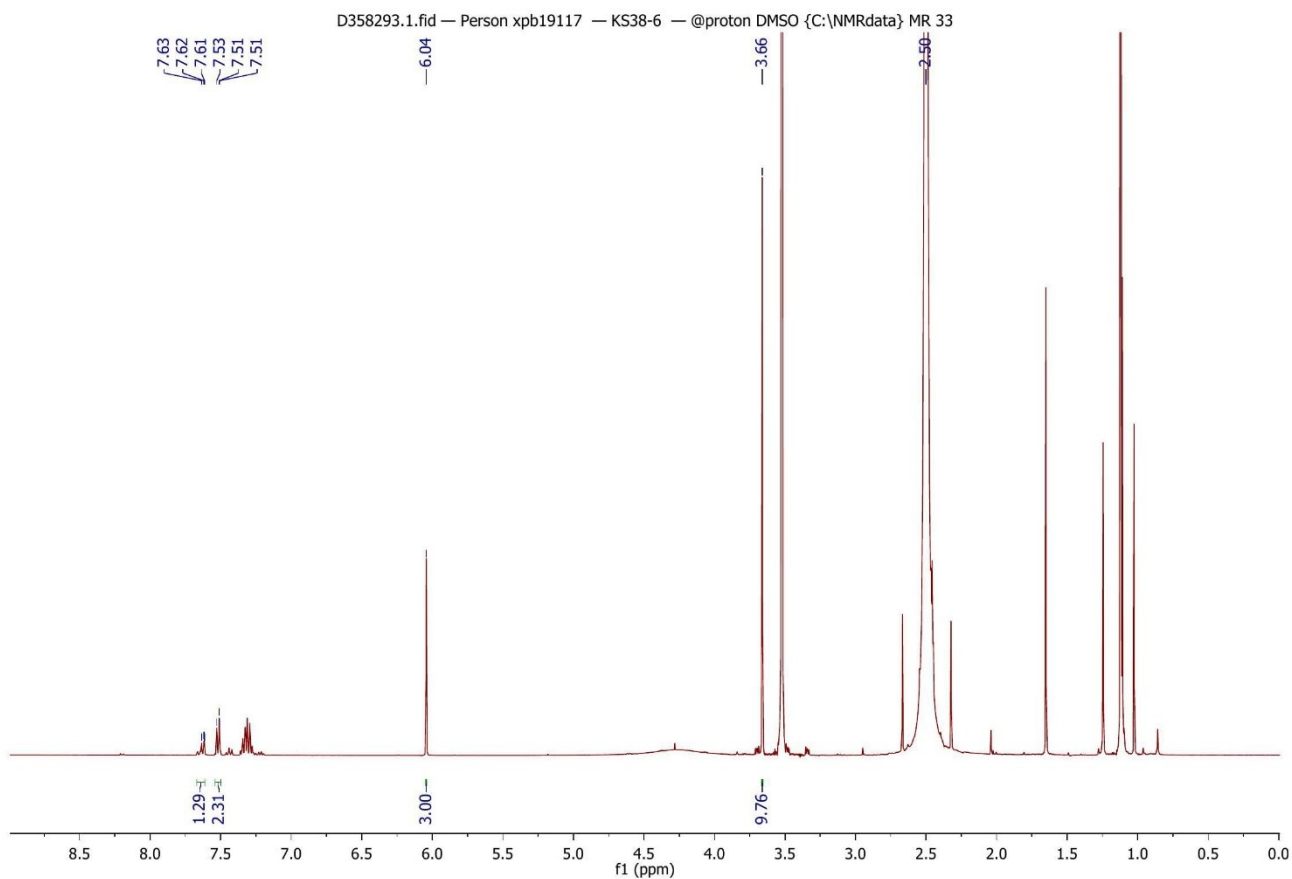


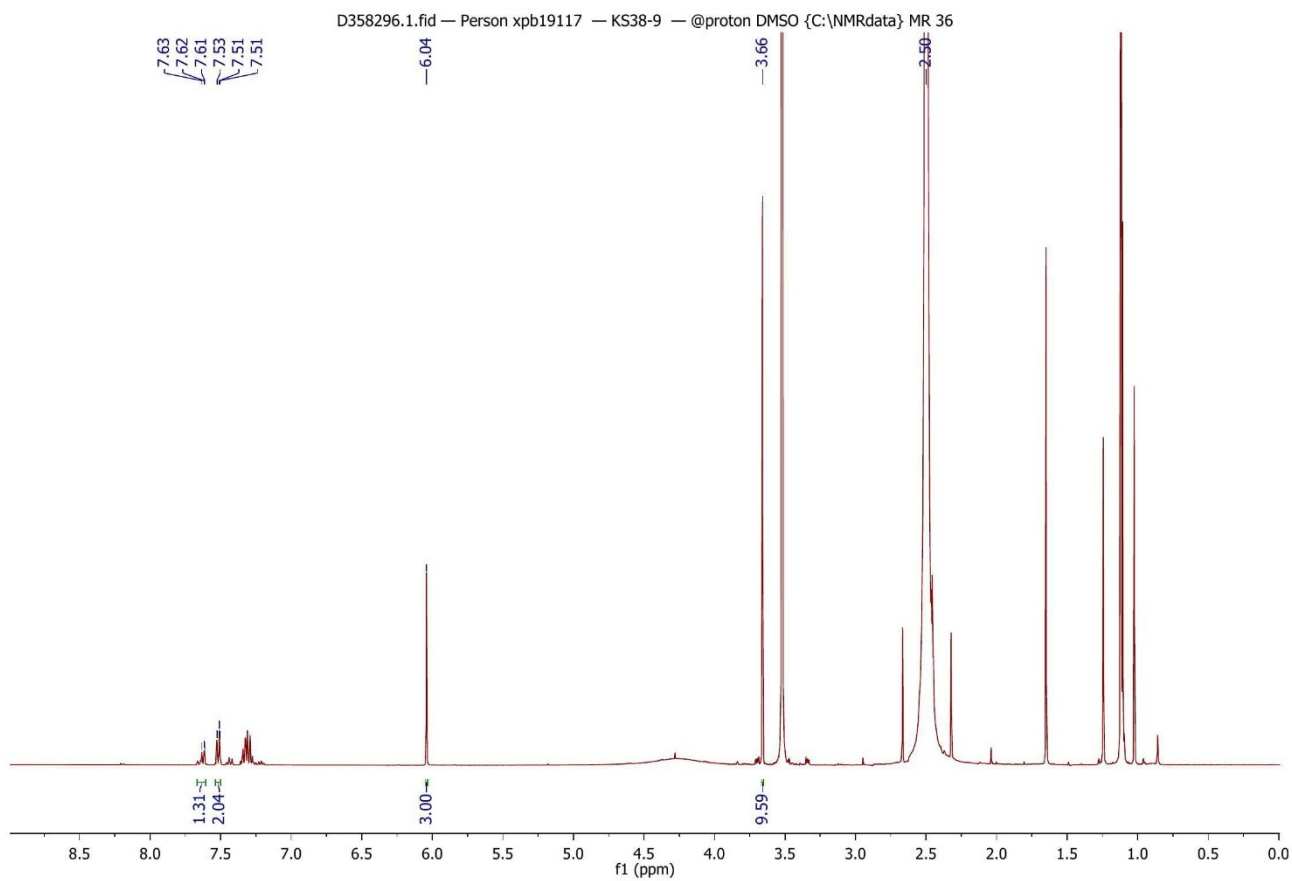
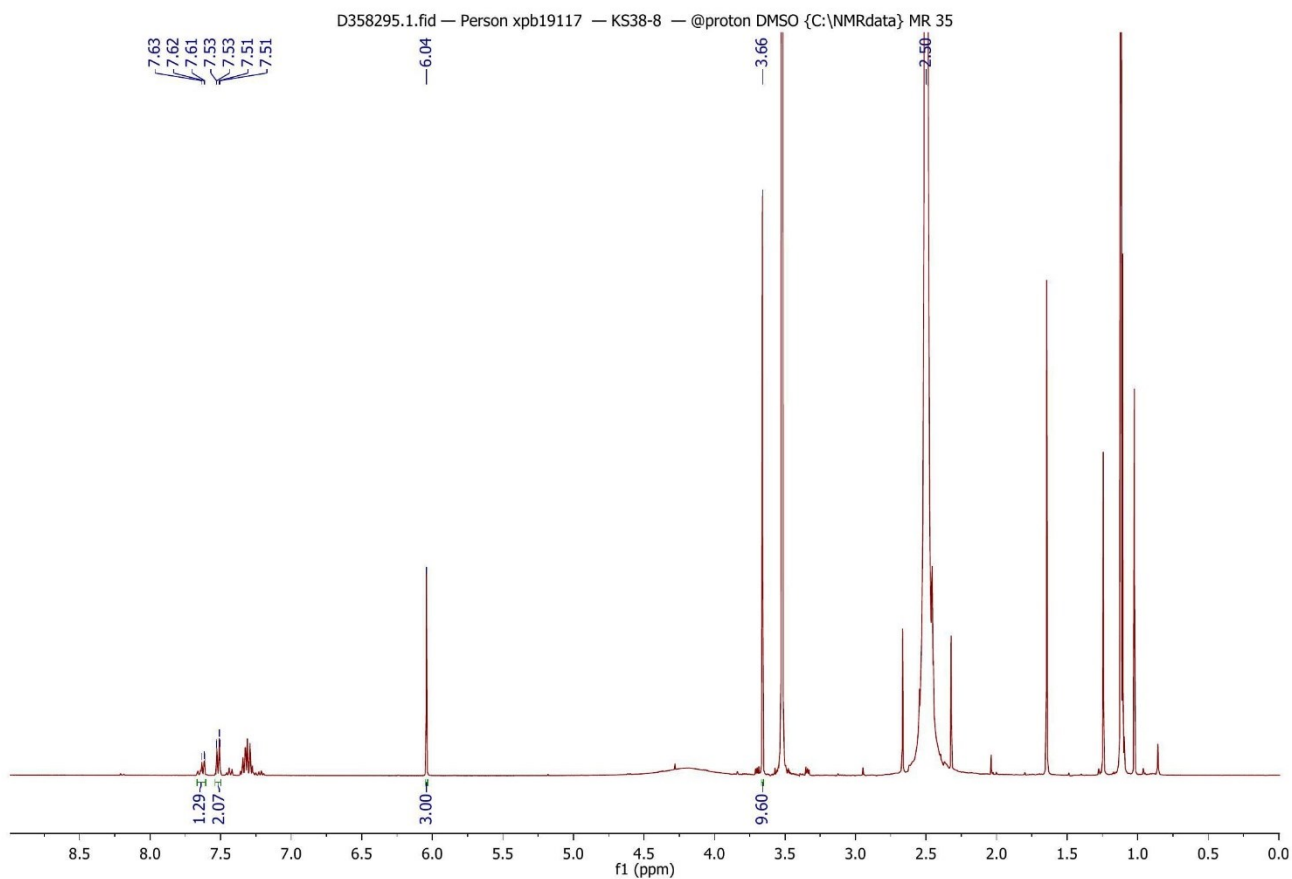
Reaction exposed to air with 0.5 mol% catalyst loading:

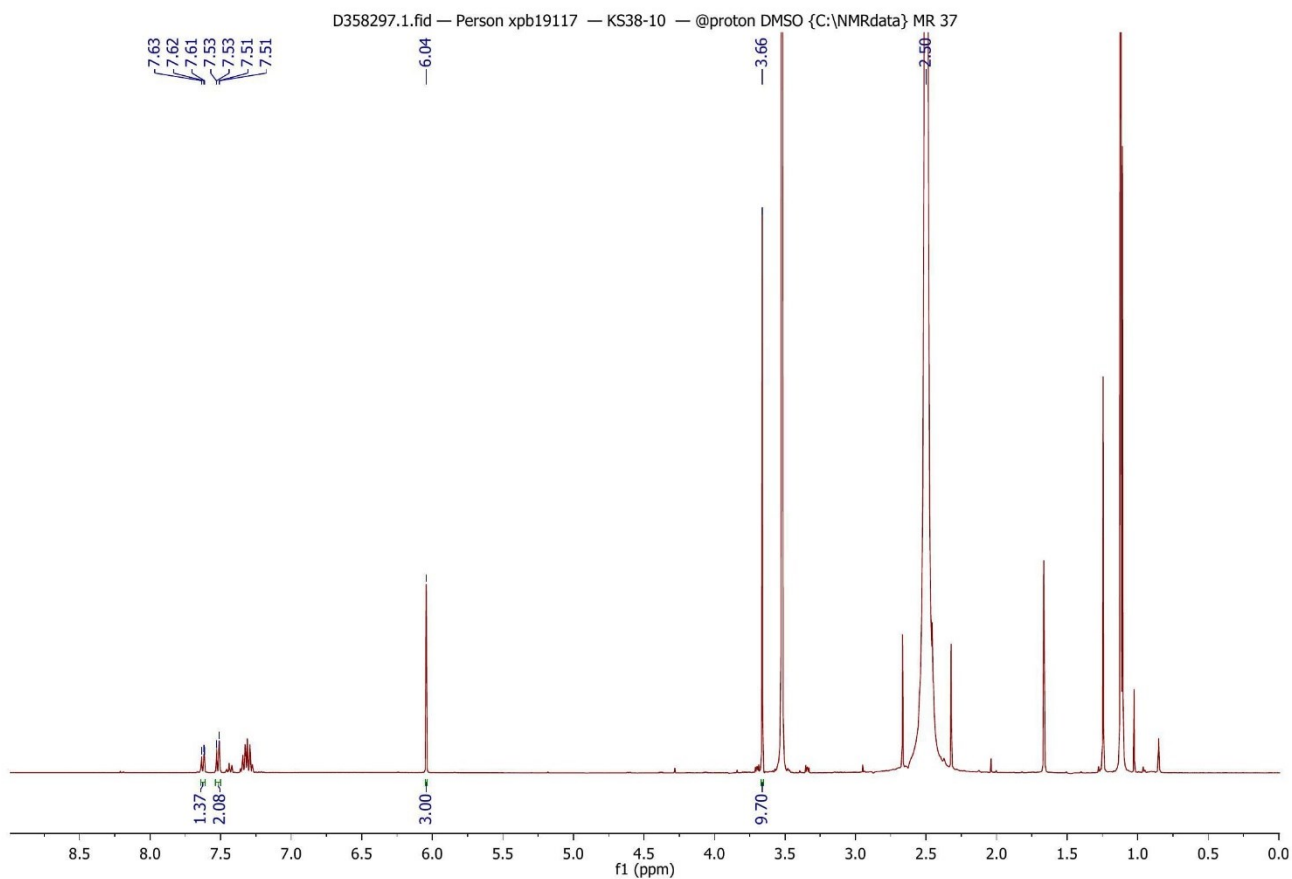






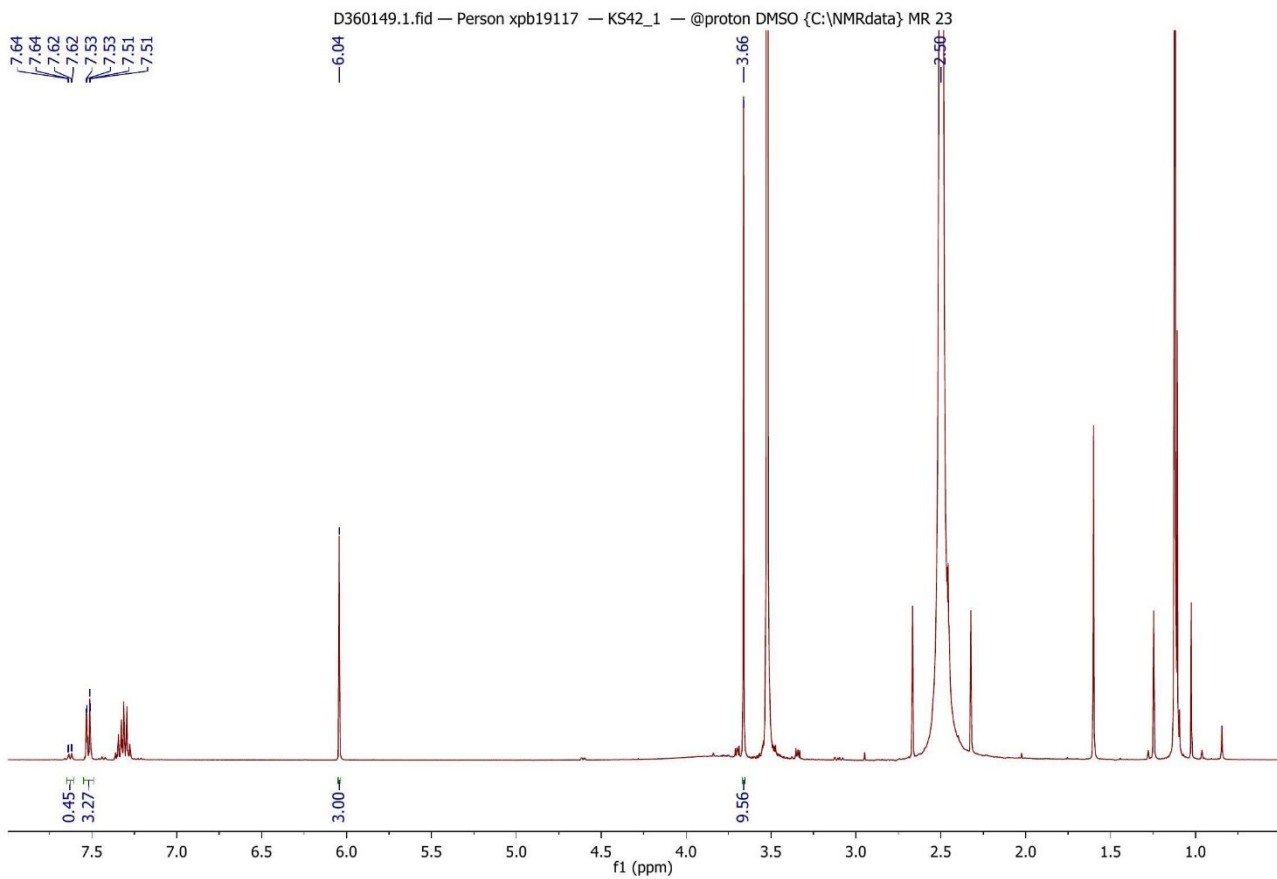
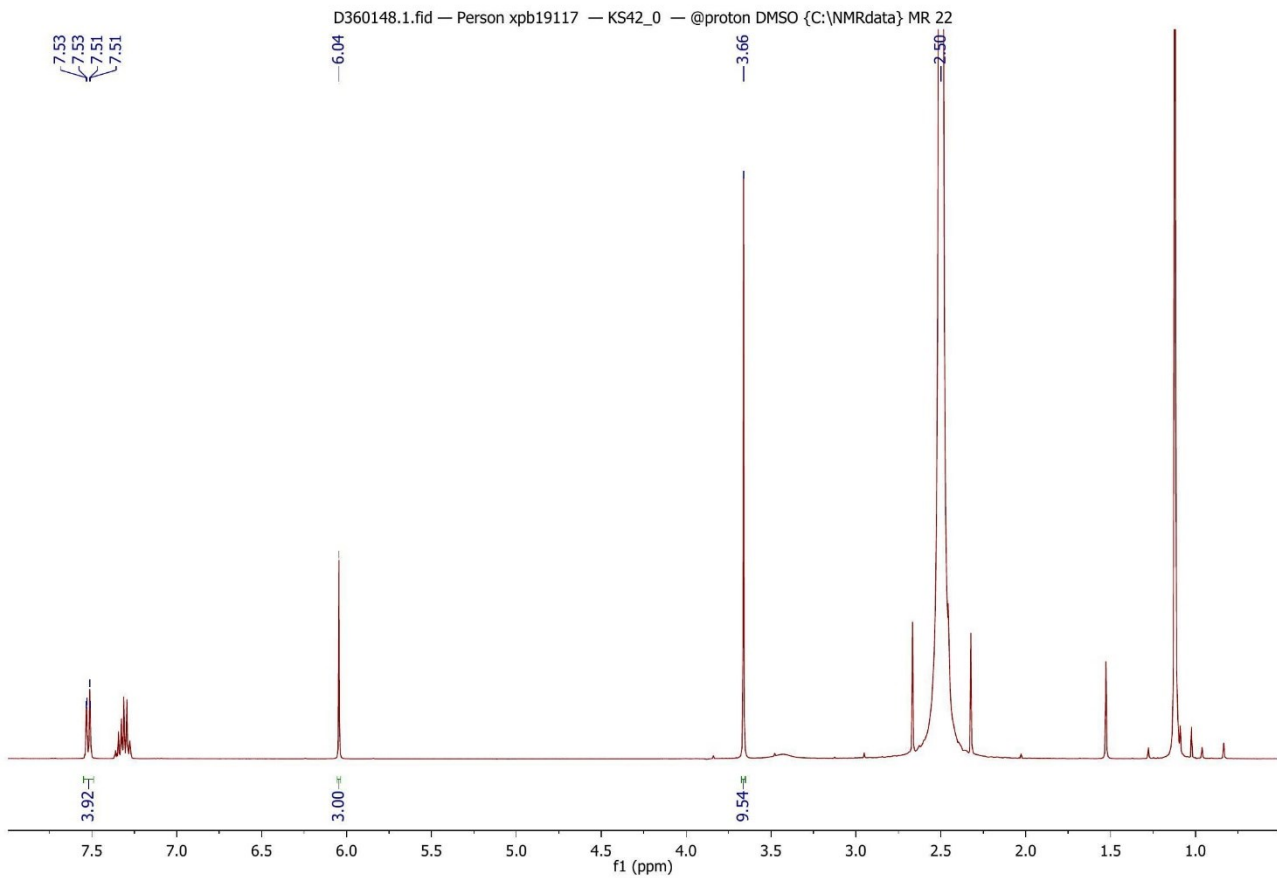


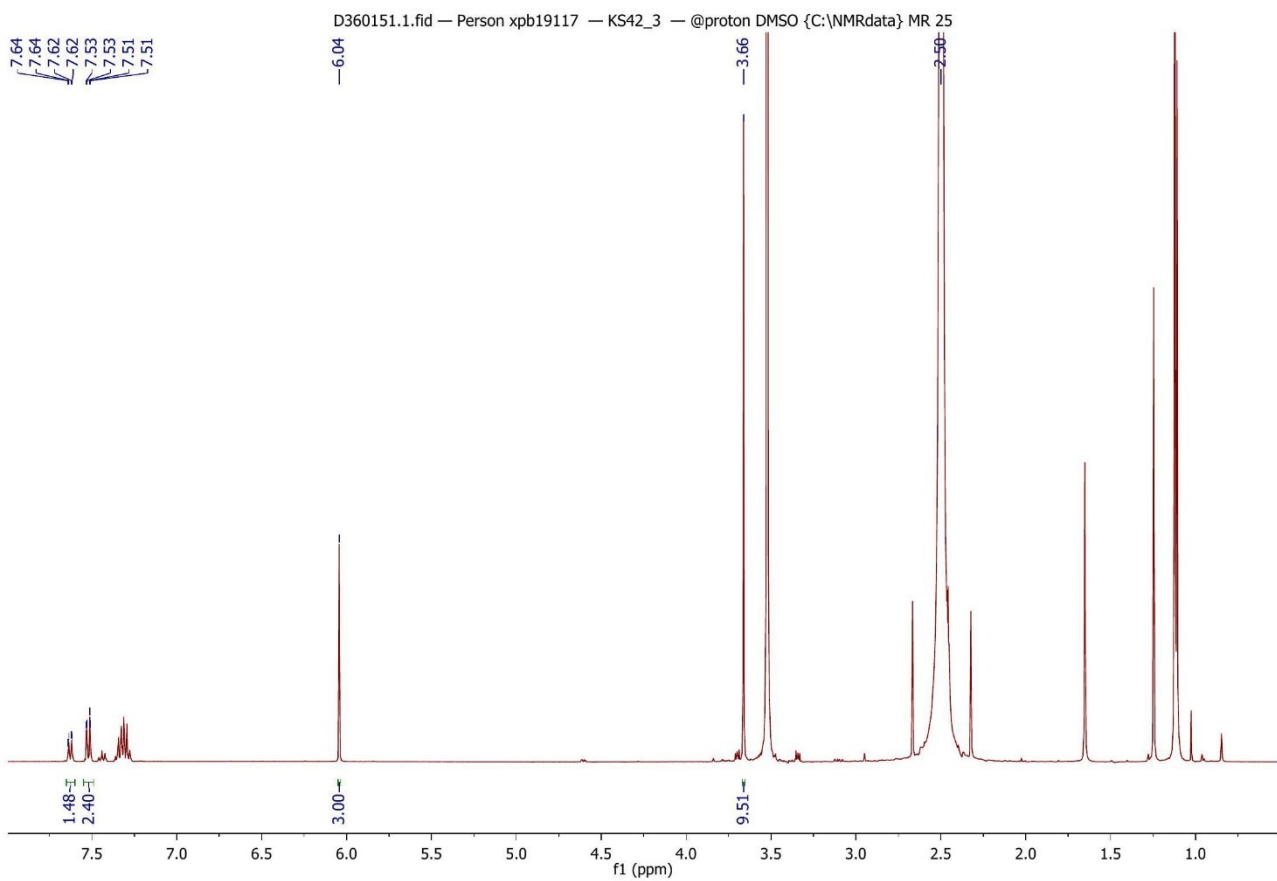
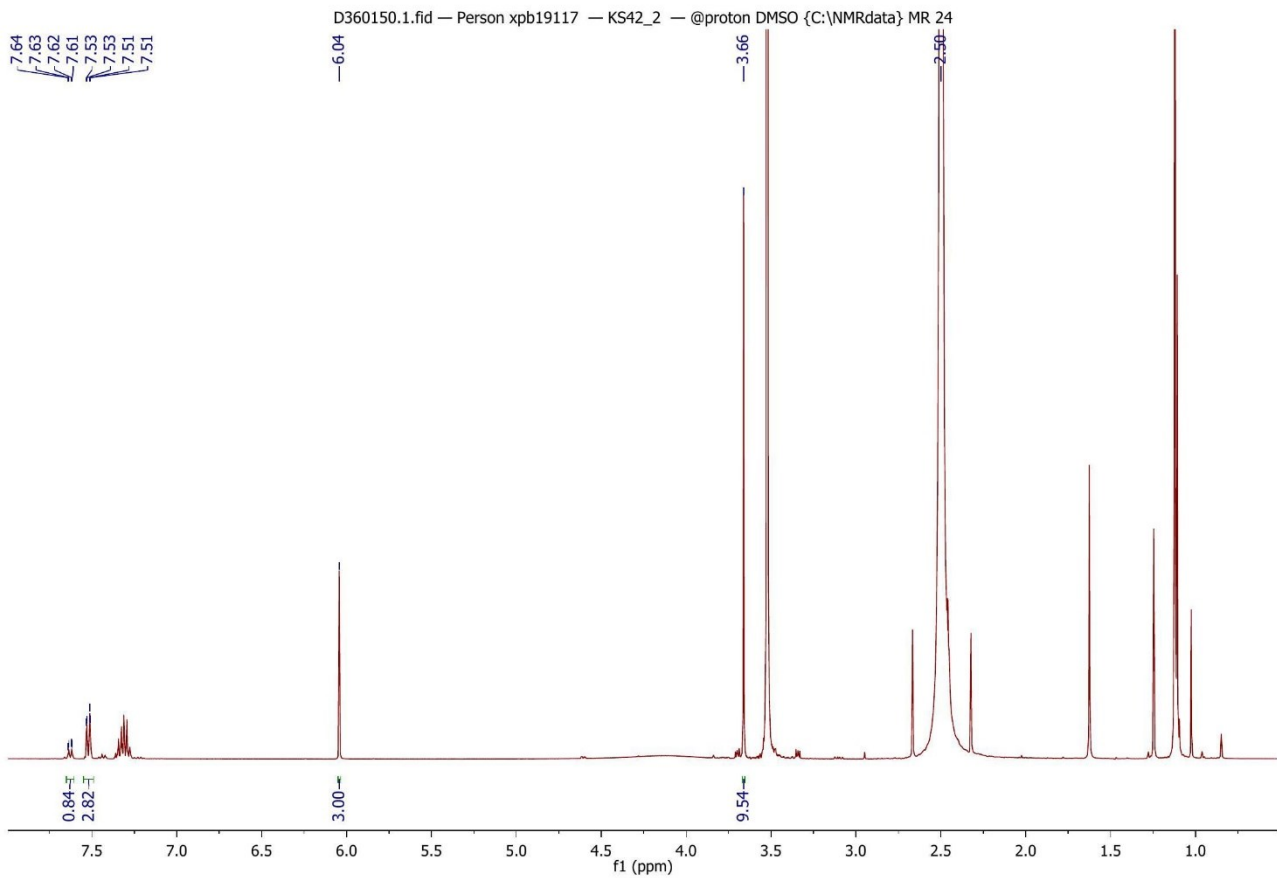


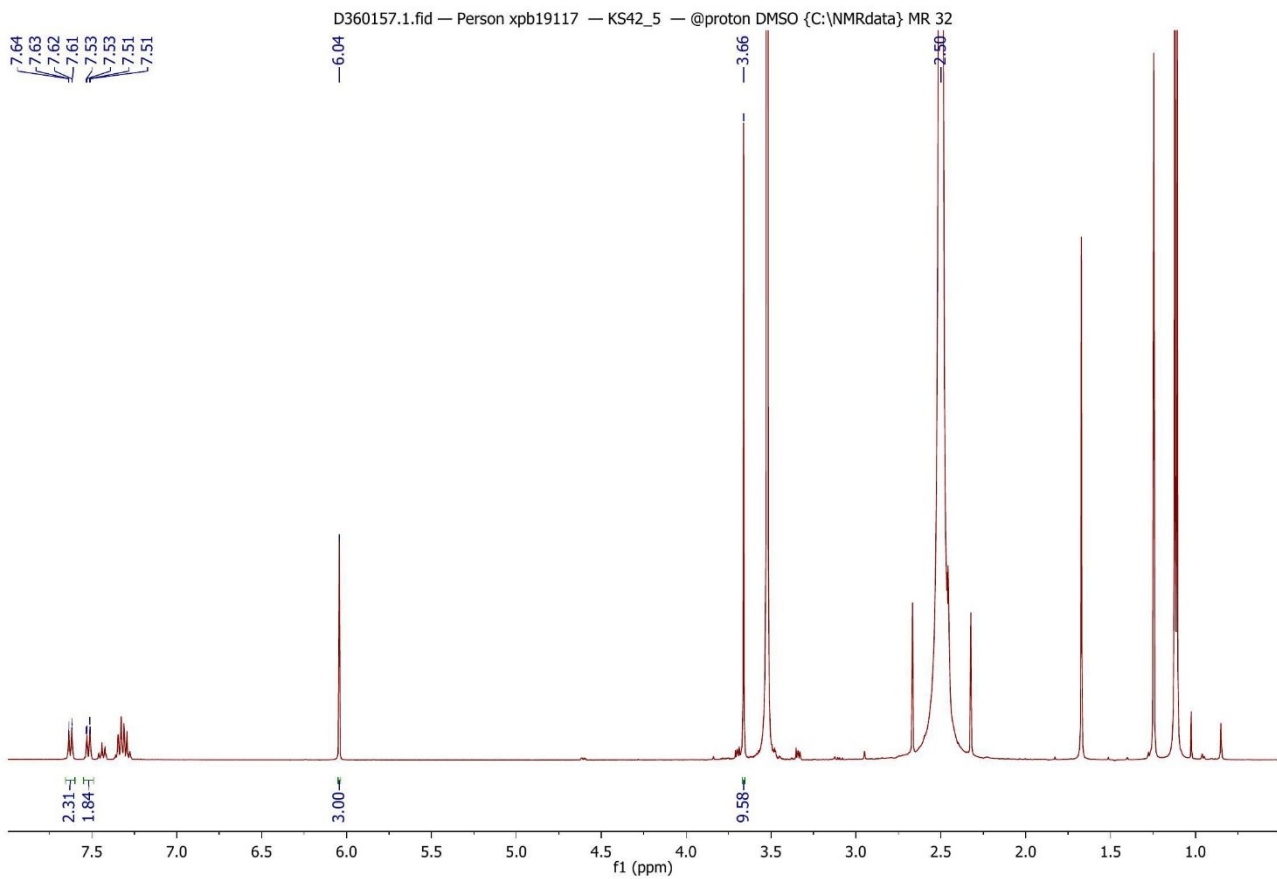
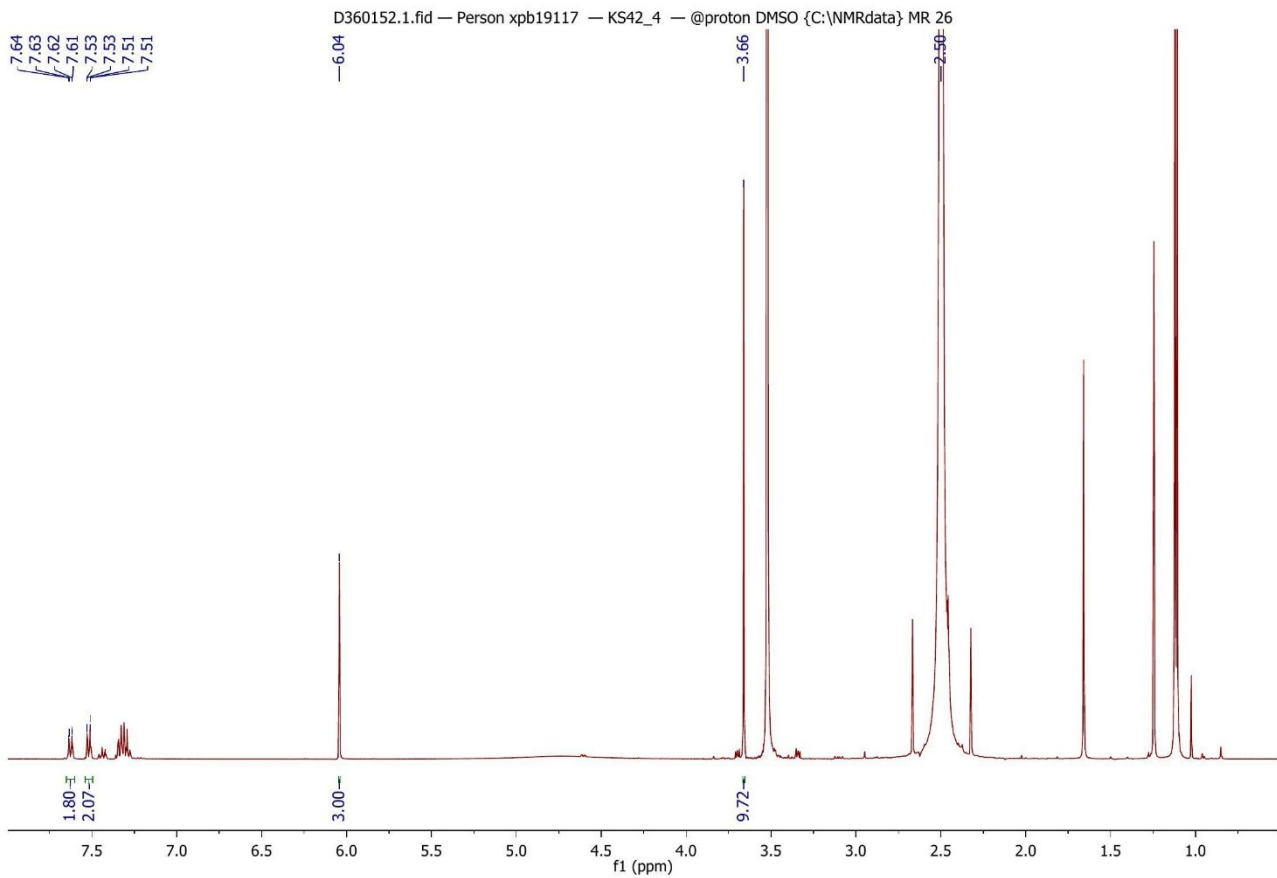


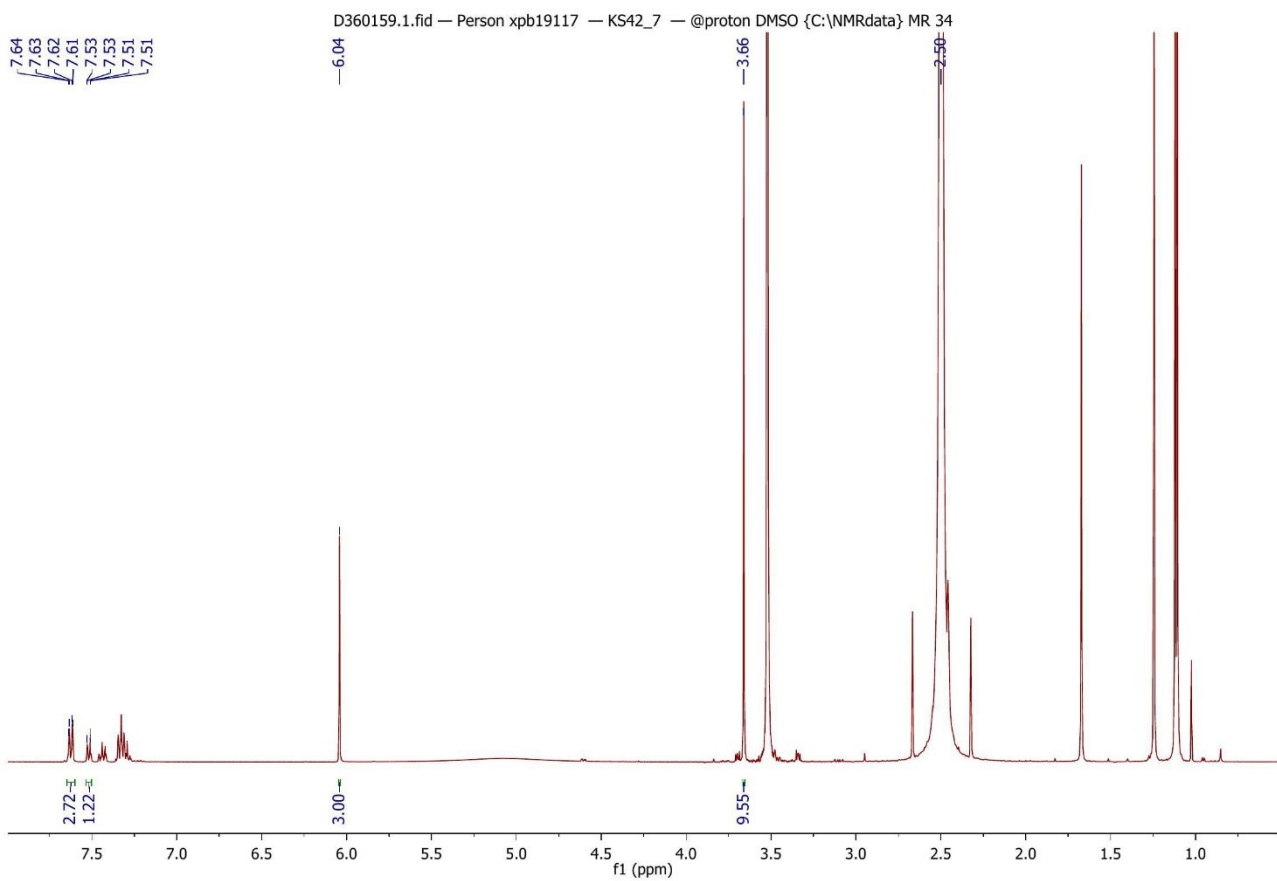
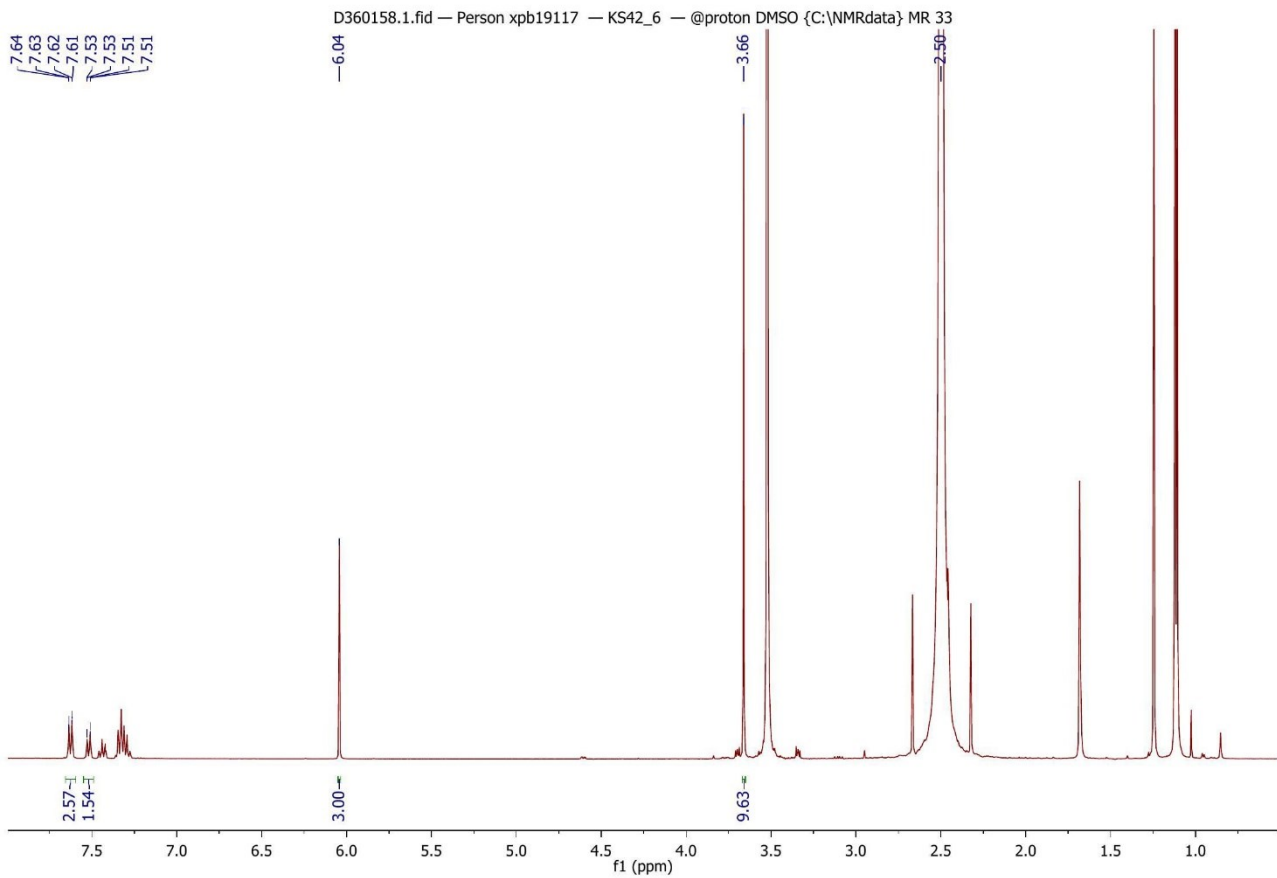
Miyaura borylation reaction samples – ^1H (DMSO- d_6) spectra for manuscript Scheme 10

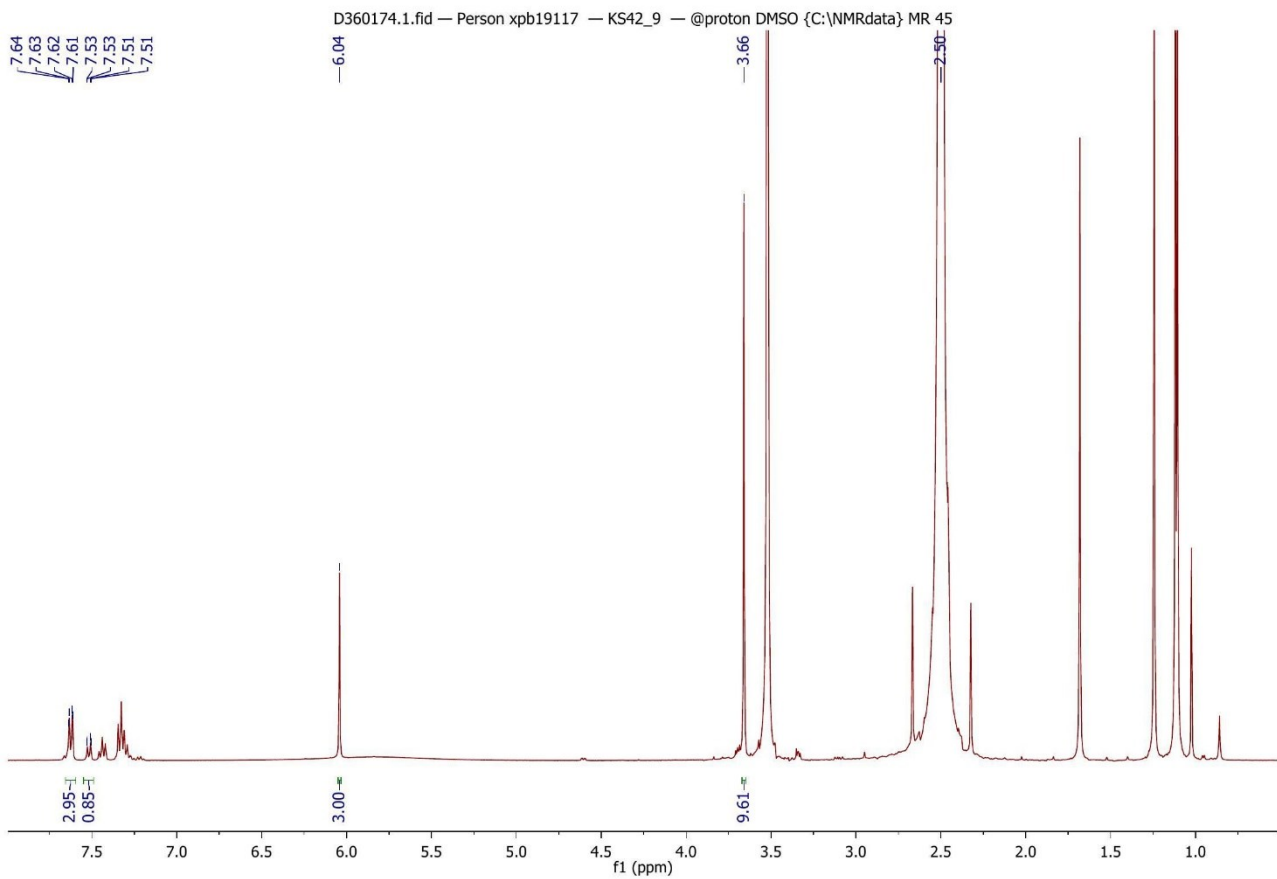
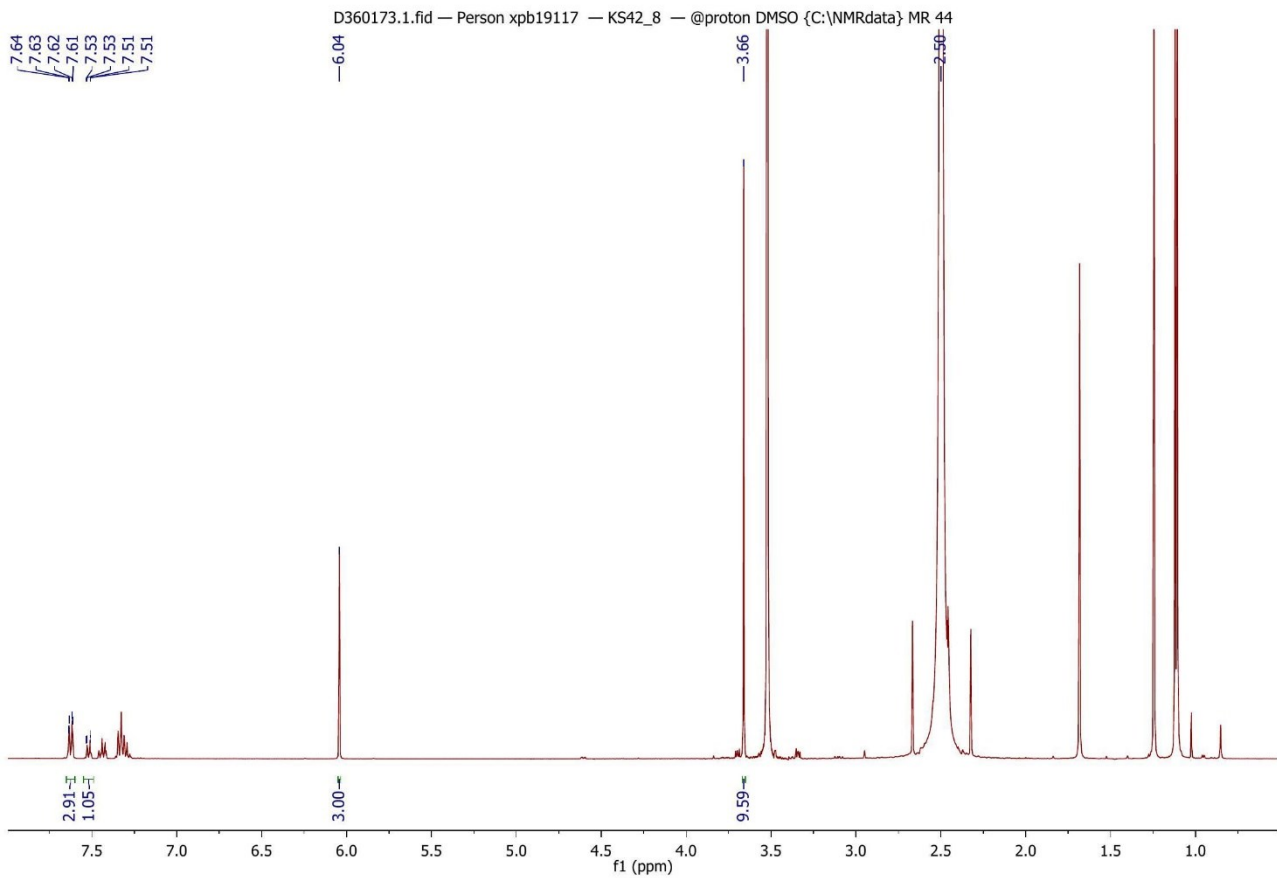
Reaction under Argon with 0.2 mol% catalyst loading:

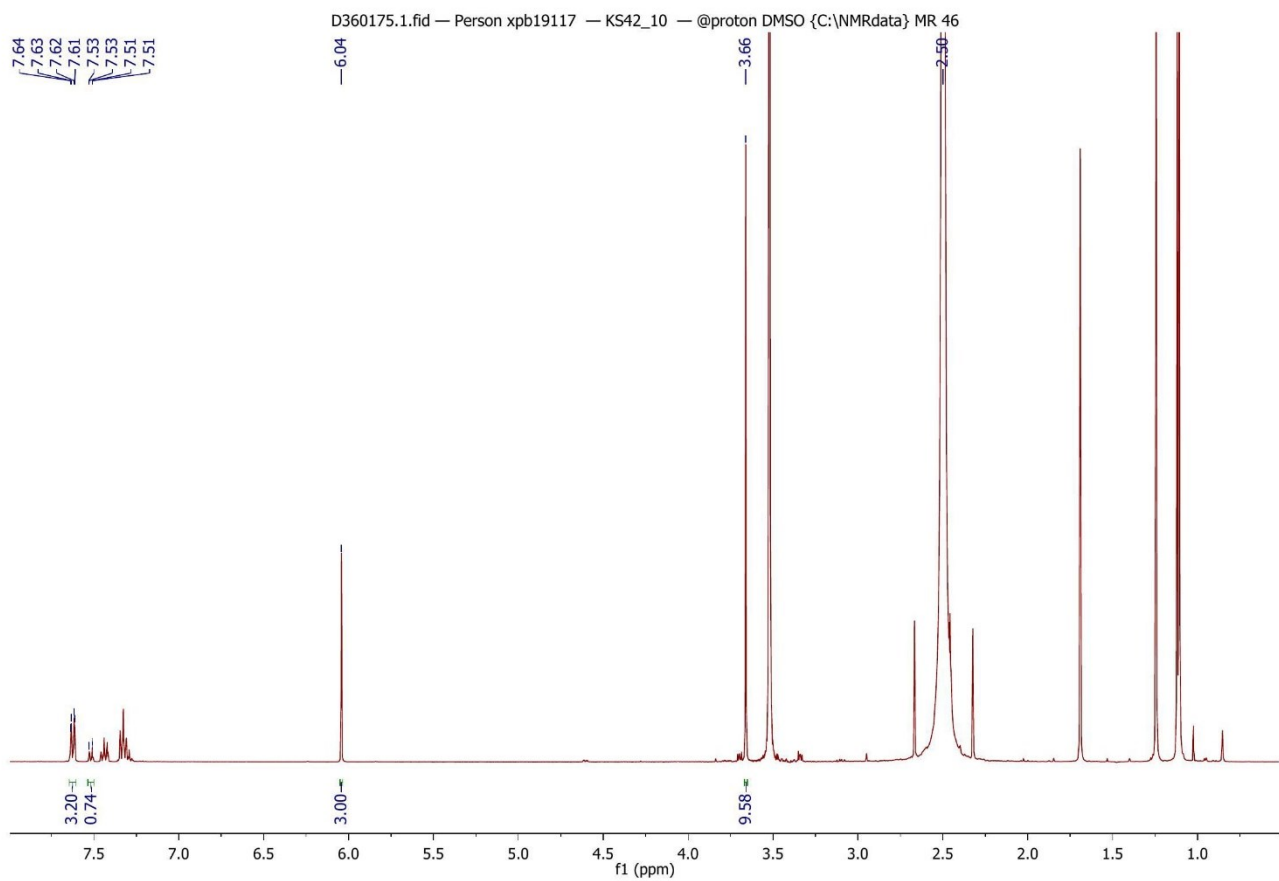




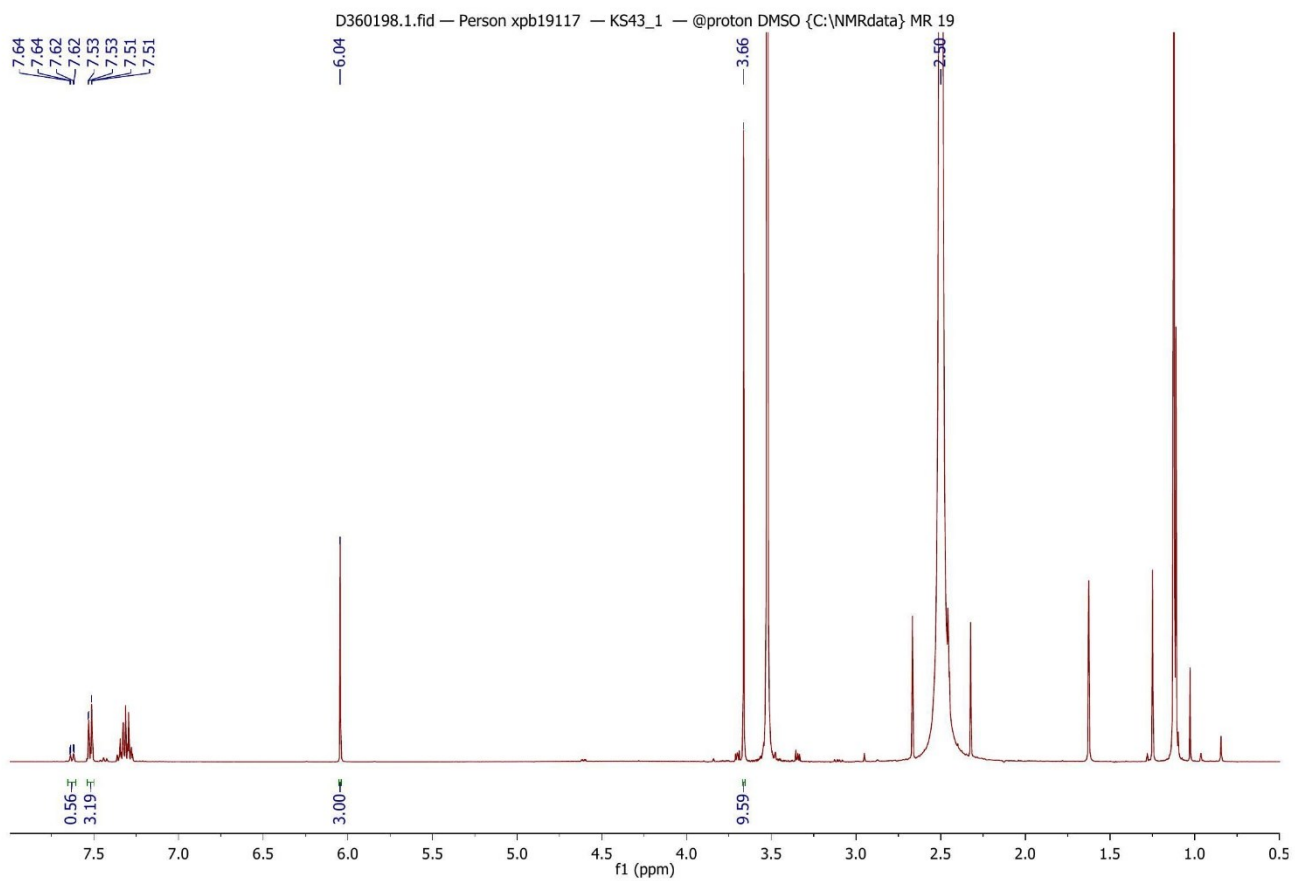
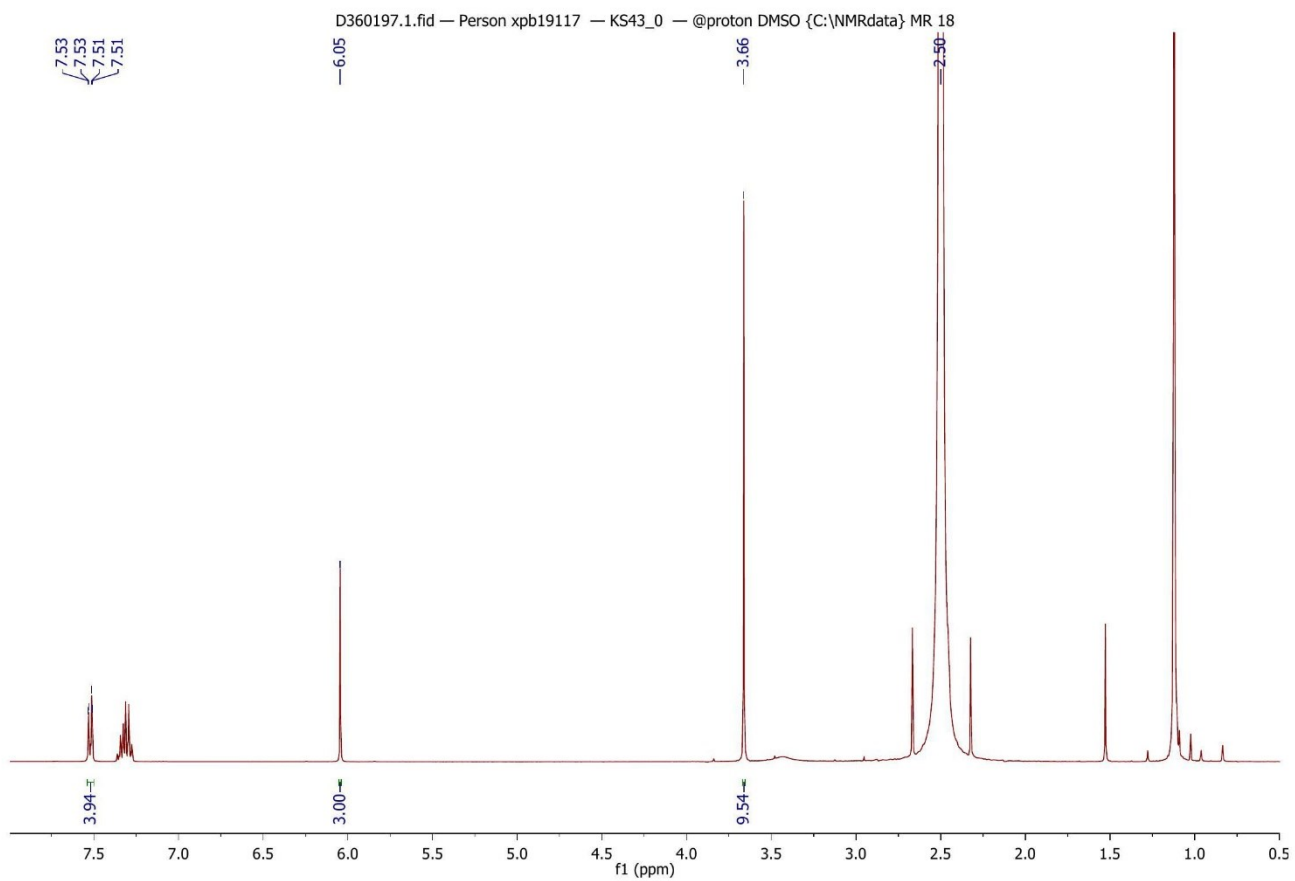


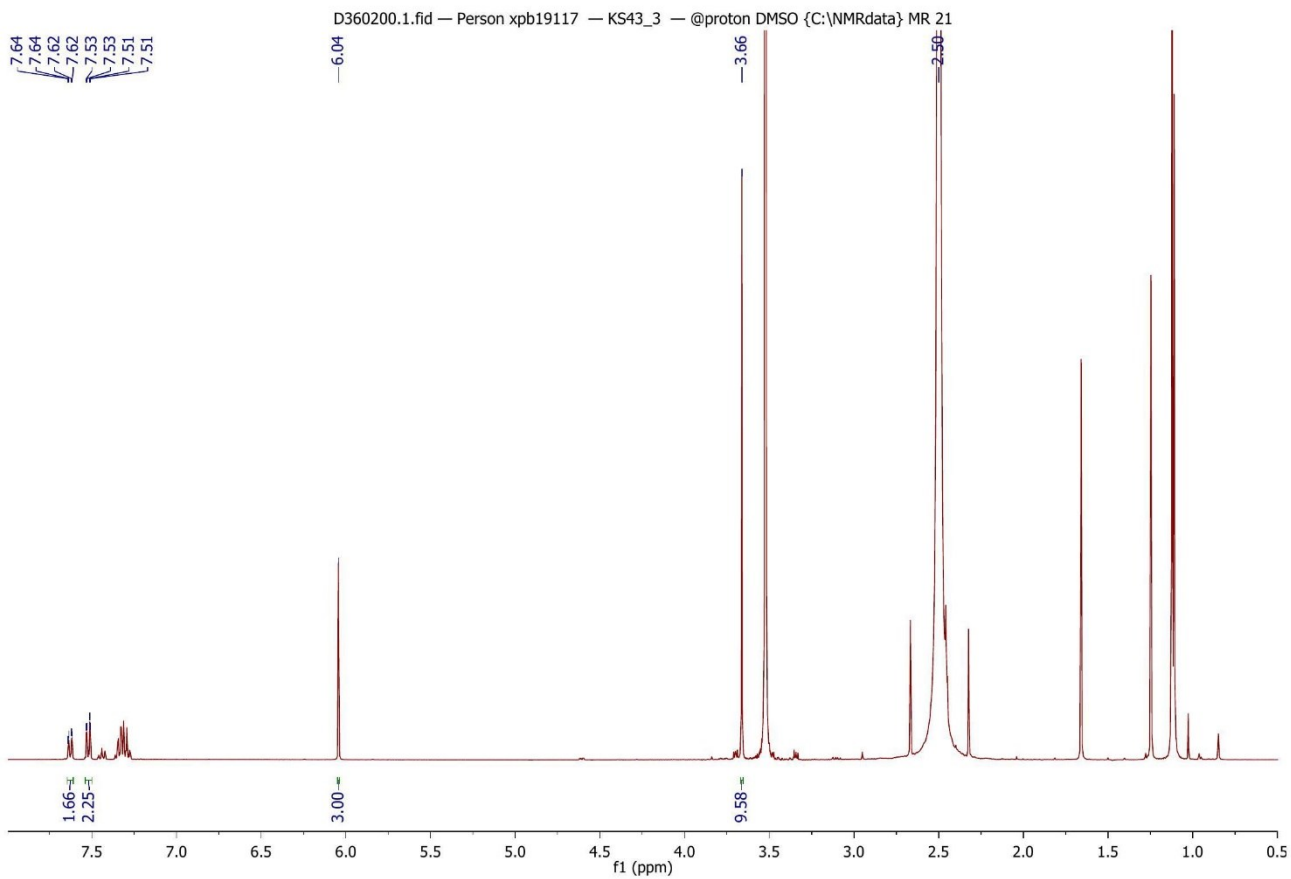
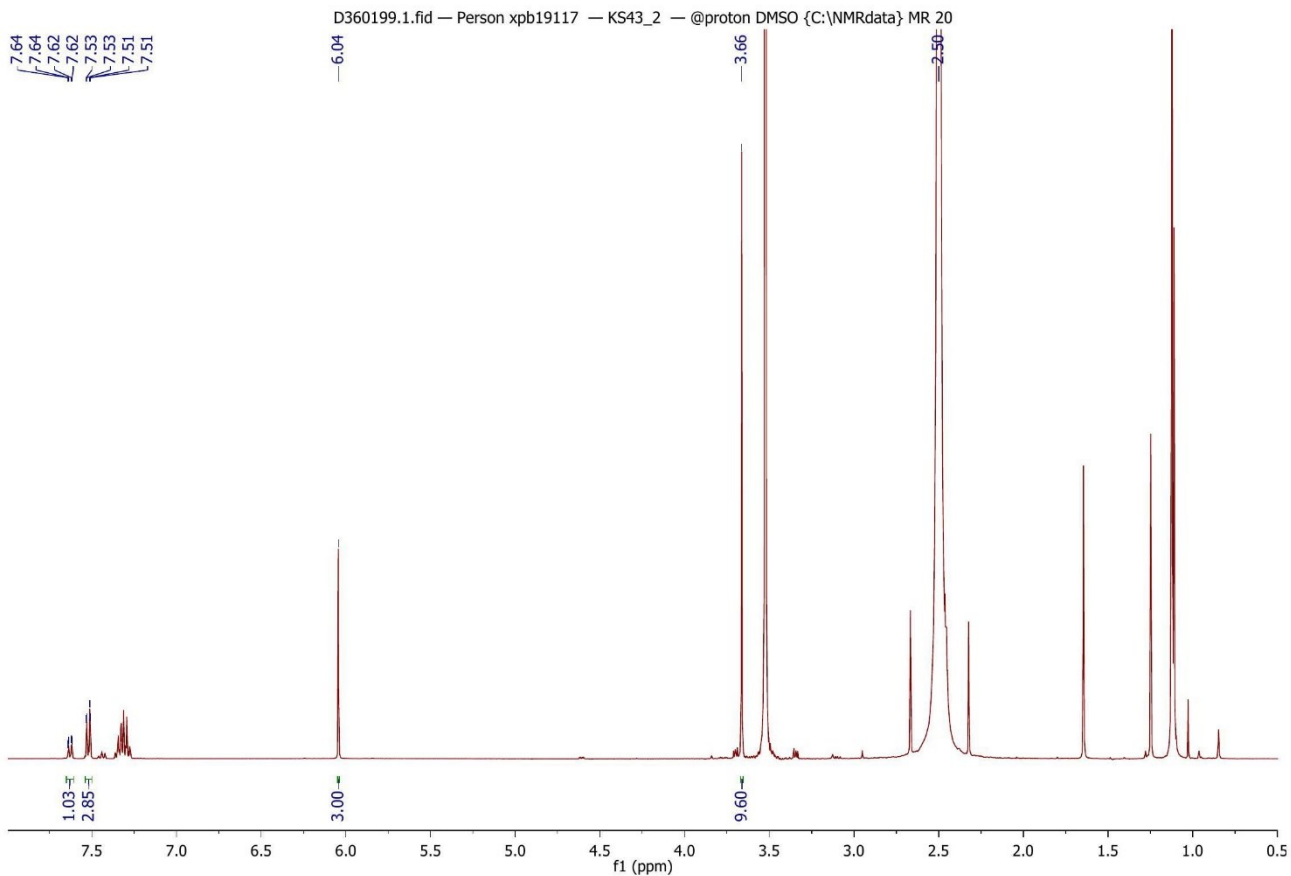


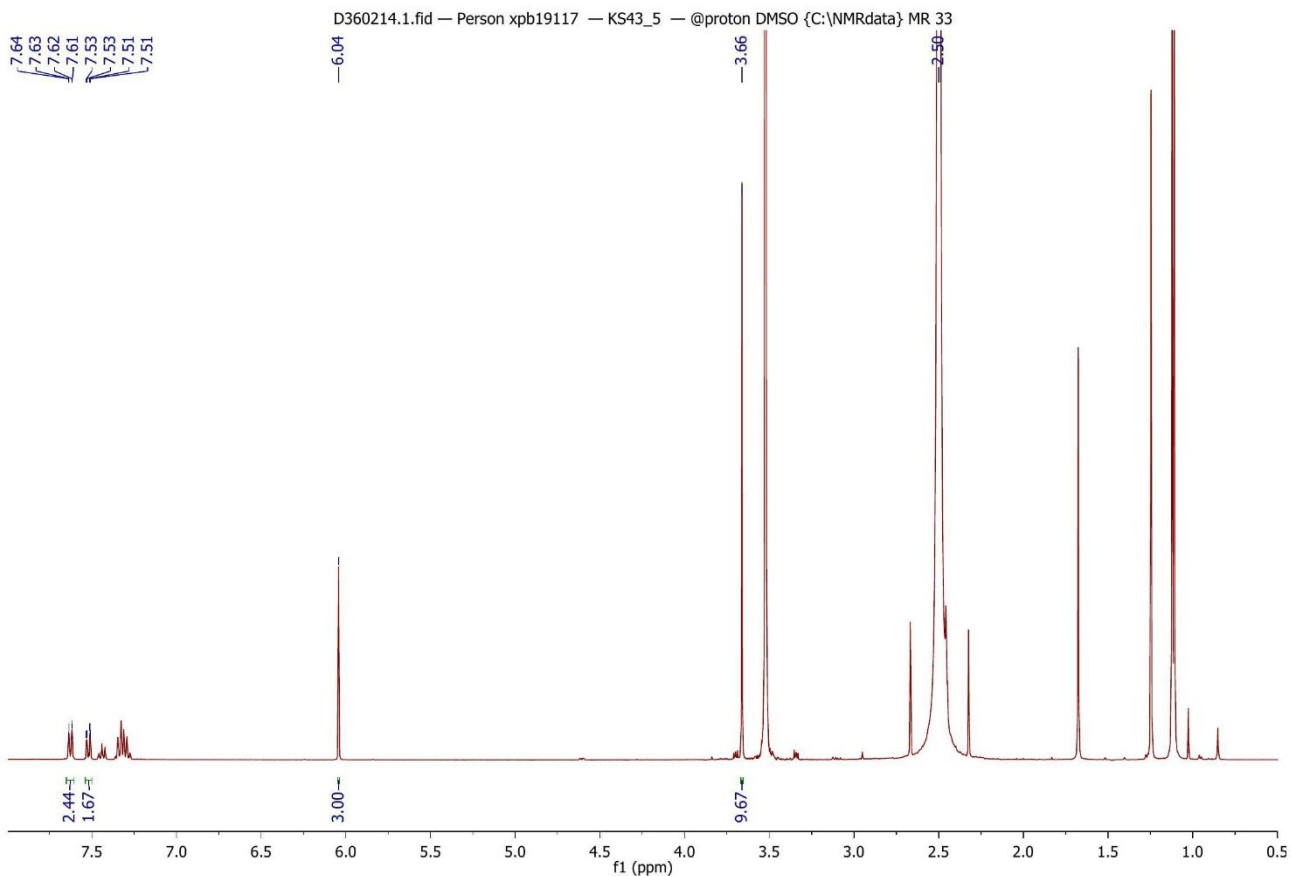
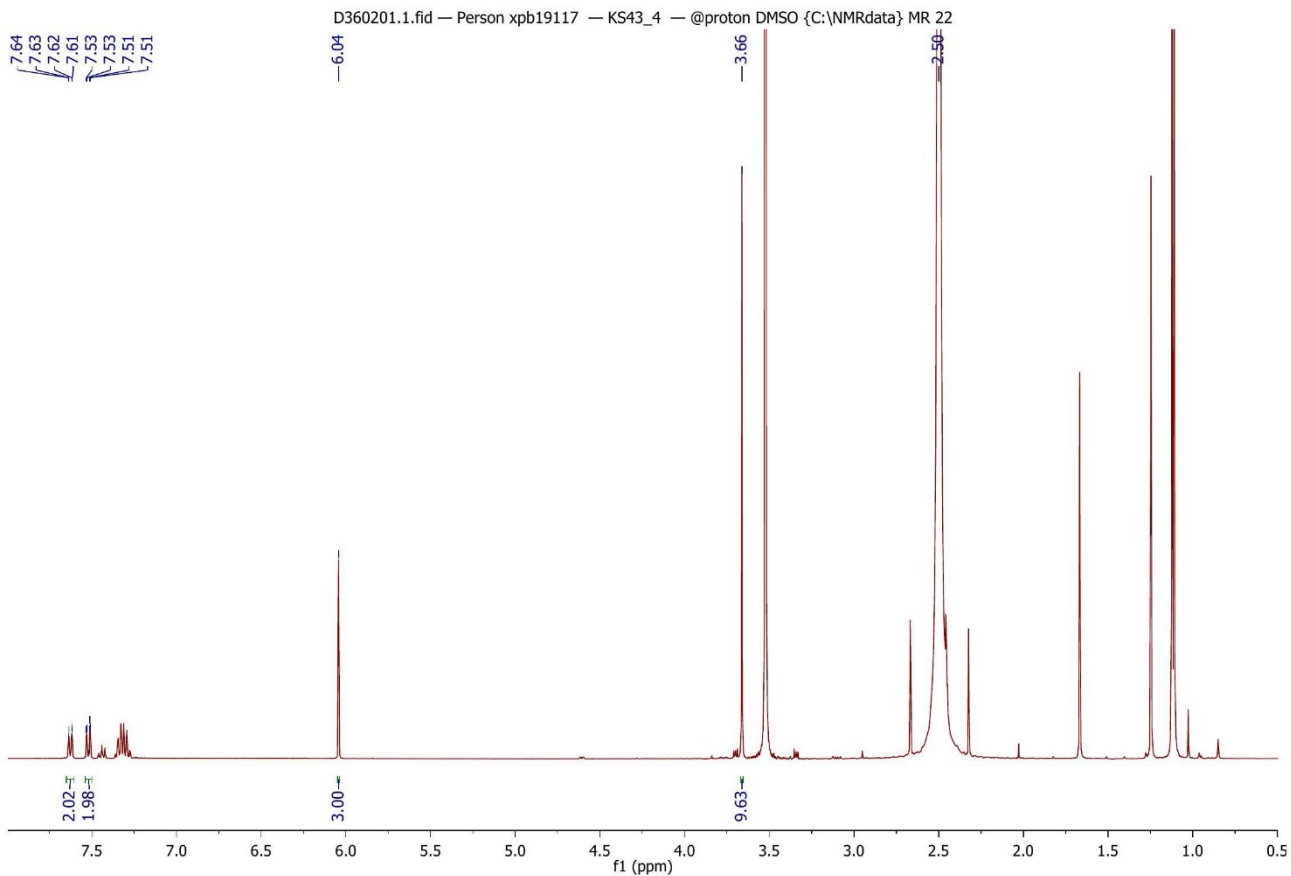


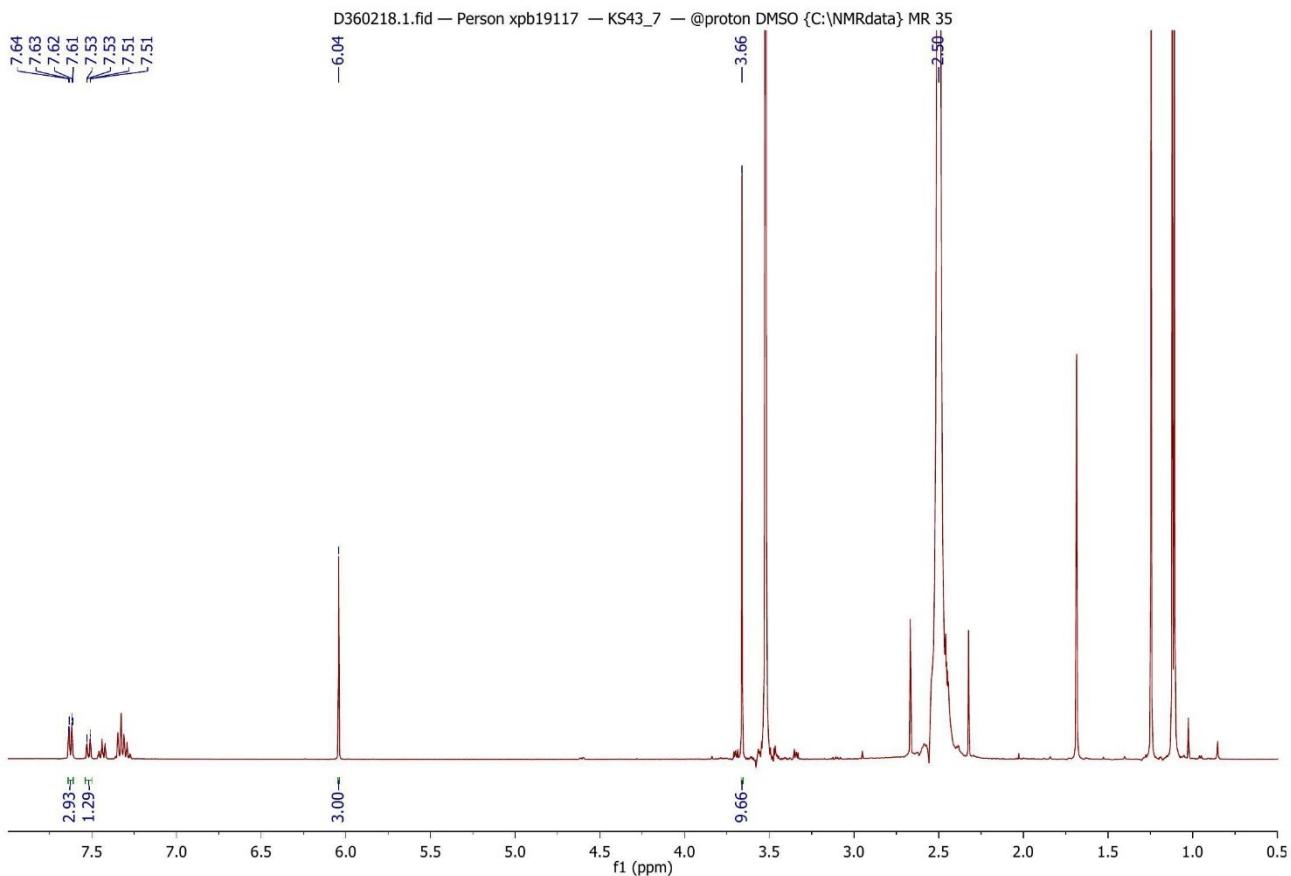
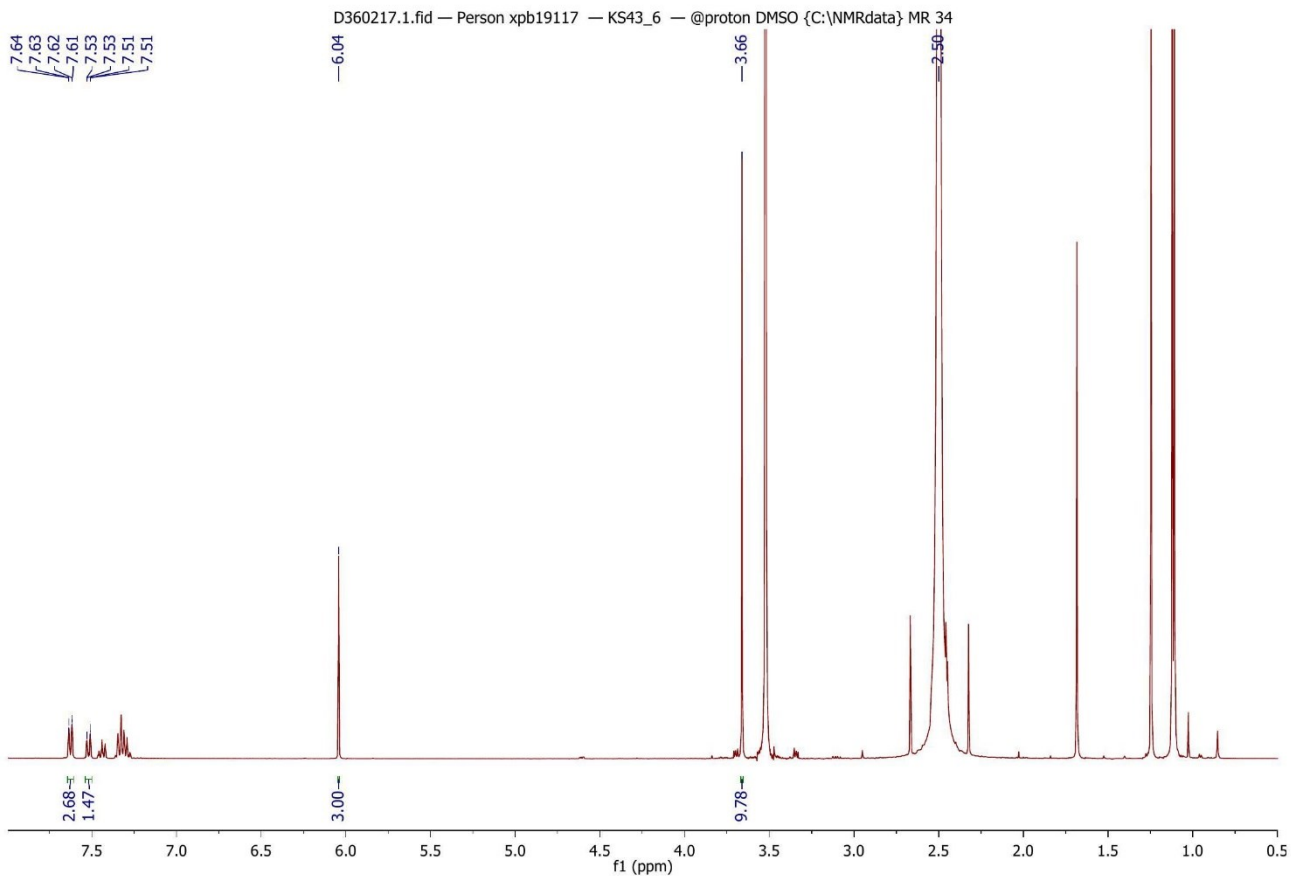


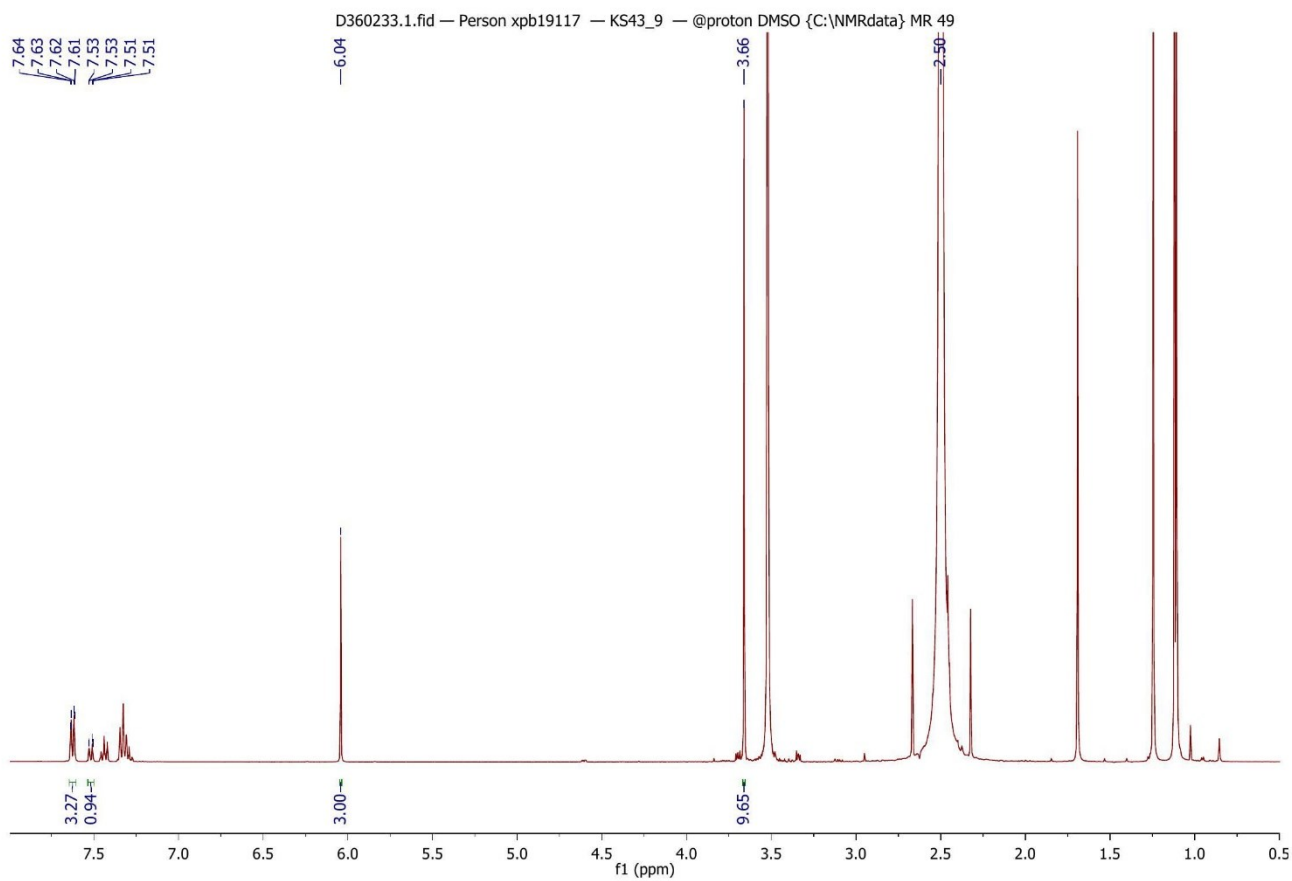
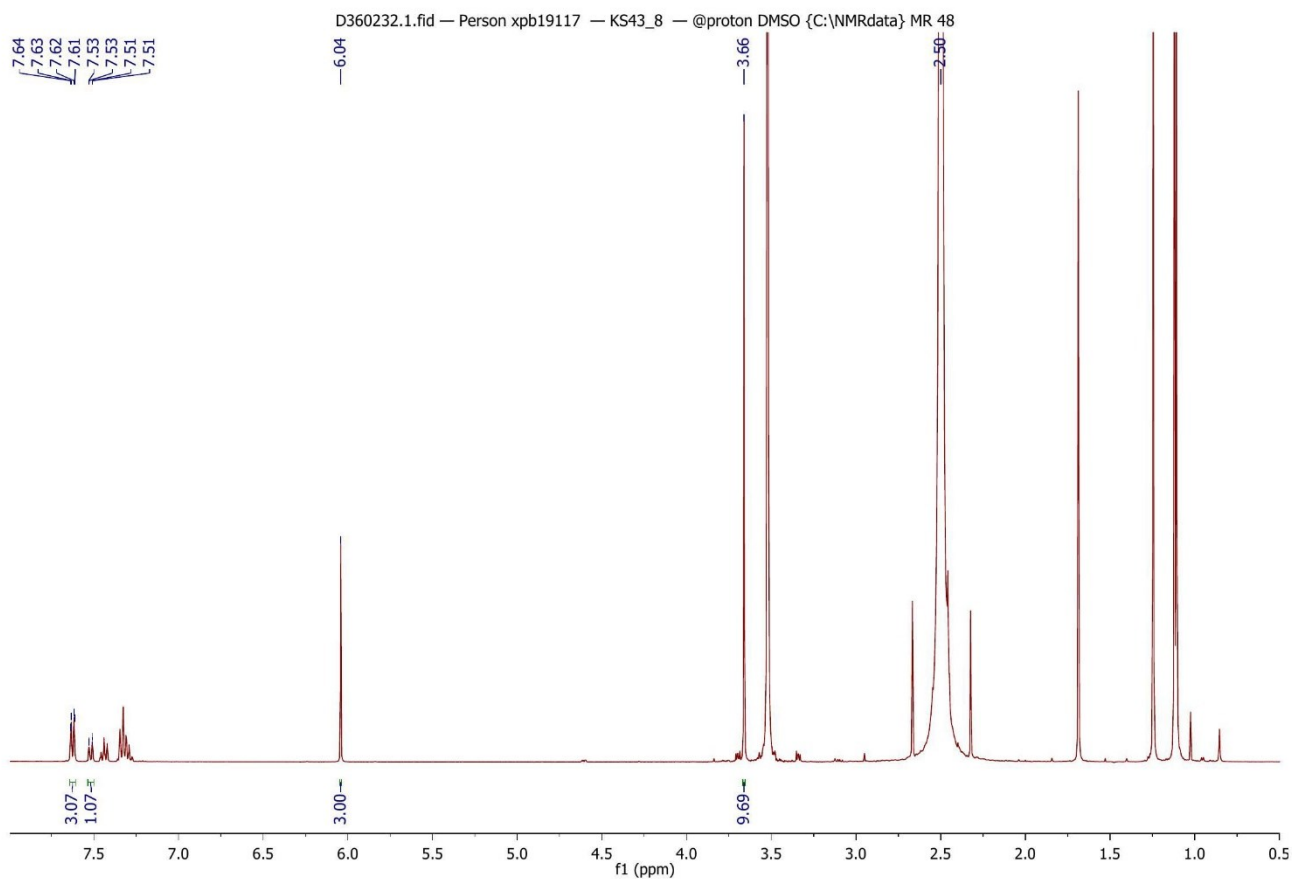
Reaction under Nitrogen with 0.2 mol% catalyst loading:

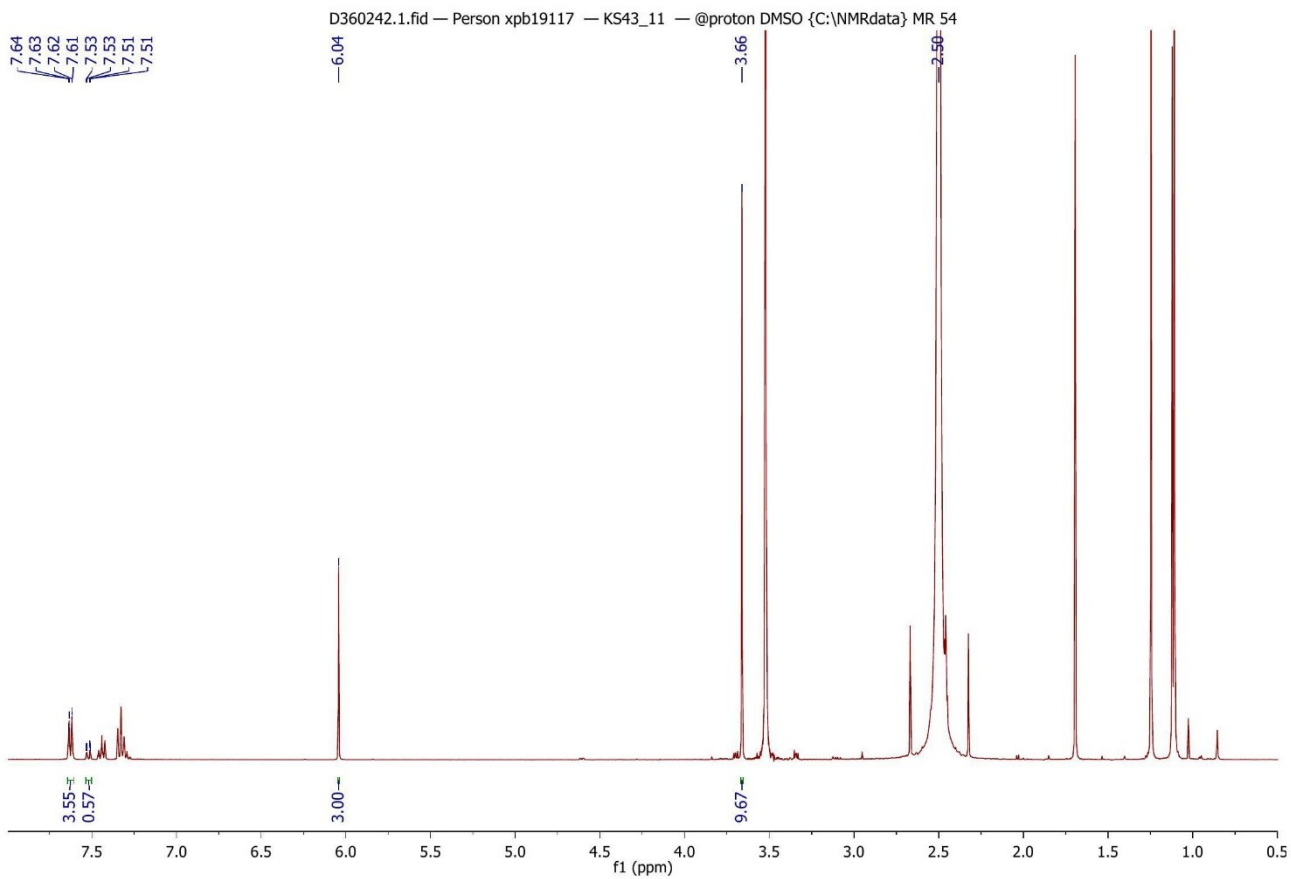
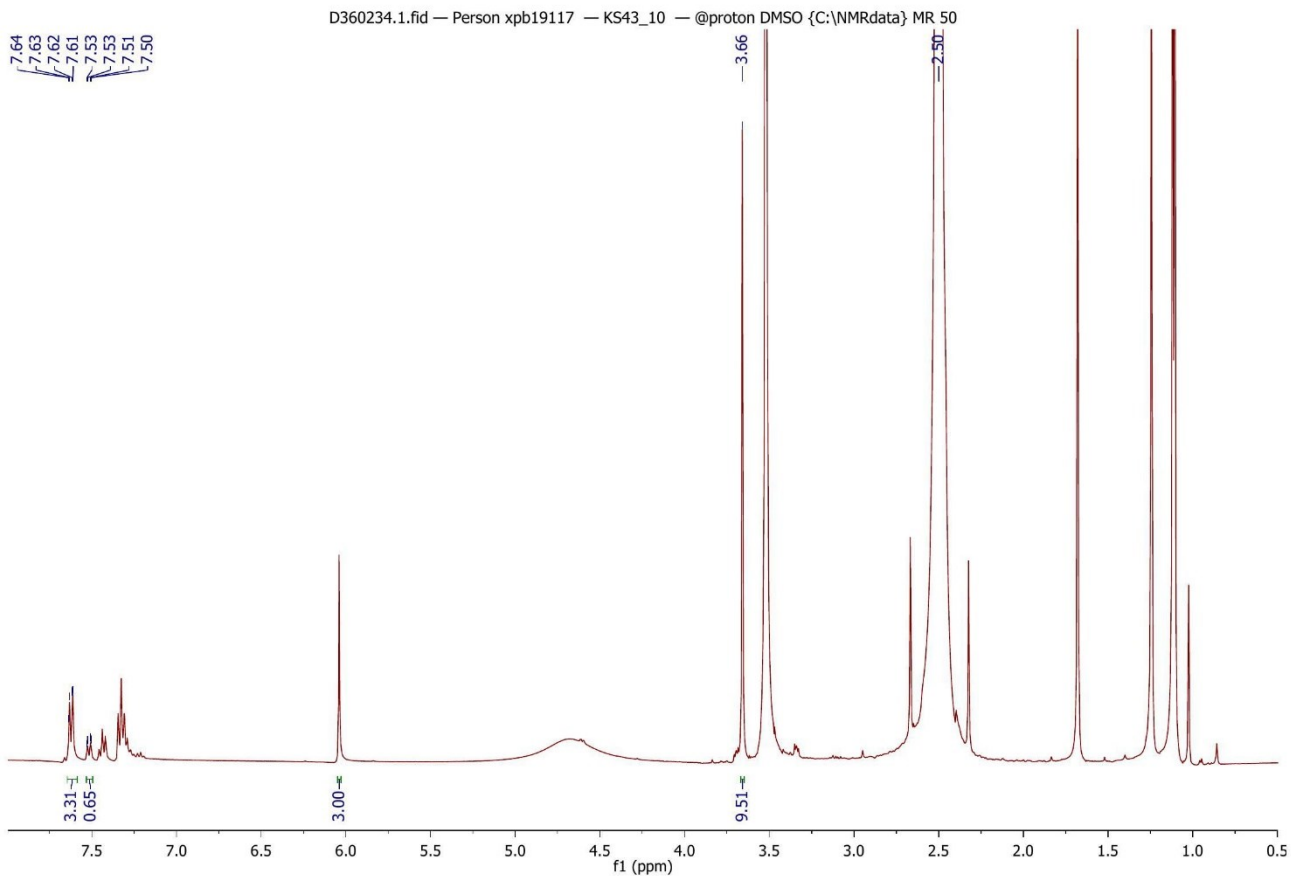












LC-MS Traces

All raw LC-MS trace outputs for Scheme 8 are provided in a separate supporting information document.

HPLC Traces

All raw LC-MS trace outputs for Scheme 9 and 10 are provided in a separate supporting information document.

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Martin Gildea: software; validation; formal analysis.

Martin H. Goodfellow: software; supervision.

Marc Reid: conceptualization; methodology; software; formal analysis; resources; data curation; writing (original draft); writing (review & editing); visualization; supervision; project administration; funding acquisition.