Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

Lactose Utilisation to Furan Carboxylates: A Novel Waste Source for Platform Molecules

Joseph Install[a], Anže Zupanc[a], Mikko Nikunen[b], Janne Jänis[b] Timo Repo*[a]

a) Department of Chemistry, University of Helsinki, A. I. Virtasen aukio 1, P.O. Box 55, 00014 Helsinki (Finland), E-mail: timo.repo@helsinki.fi.

b) Department of Chemistry, University of Eastern Finalnd, P.O. Box 111, FI-80101 Joesnsuu, Finland

*Corresponding author: timo.repo@helsinki.fi

1.0 Oxidation of Lactose to Mucate Esters

1.1 Nitric acid oxidation procedure

In a round-bottom flask 5g (14mmol) of lactose monohydrate is dissolved in 40mL of 35% HNO_3 with 5 mol% $Fe(NO_3)_3$ added, the solution was stirred (600rpm) and heated to 80°C for 24 hours. The resulting precipitate solution is diluted with deionised H_2O to a total volume of 100mL. The solution is then filtered under vacuo to obtain a white solid, mucic acid which is washed with water and ethyl acetate before it is dried in an oven overnight to remove moisture, then weighed and confirmed by ^1H & ^{13}C NMR spectroscopy. (2.28g yield 74.9%, conversion 100%)

All NMR spectra were recorded in $CDCl_3$ or DMSO dependant on solubility with a Bruker Varance 400 instrument (at 400 MHz) using Me_4Si as an internal standard. Chemical shifts are reported in ppm (δ) relative to $CDCl_3$ solvent residual peak for ^1H NMR (δ = 7.26 ppm) and solvent central line for ^{13}C NMR (δ = 77.16 ppm).

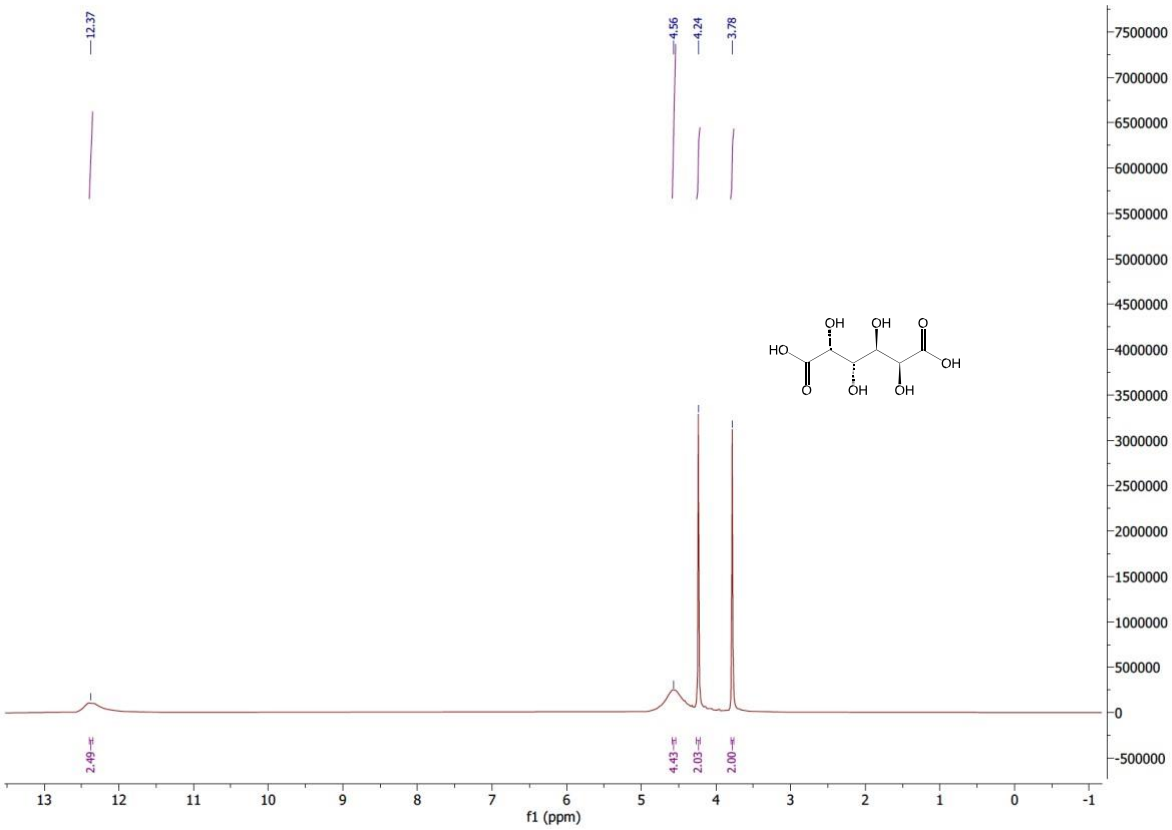

Figure SI1: ^1H NMR spectrum of mucic acid from oxidation of lactose: ^1H NMR (400 MHz, DMSO) δ 12.37 (s, 2H), 4.56 (s, 4H), 4.24 (s, 2H), 3.78 (s, 2H).

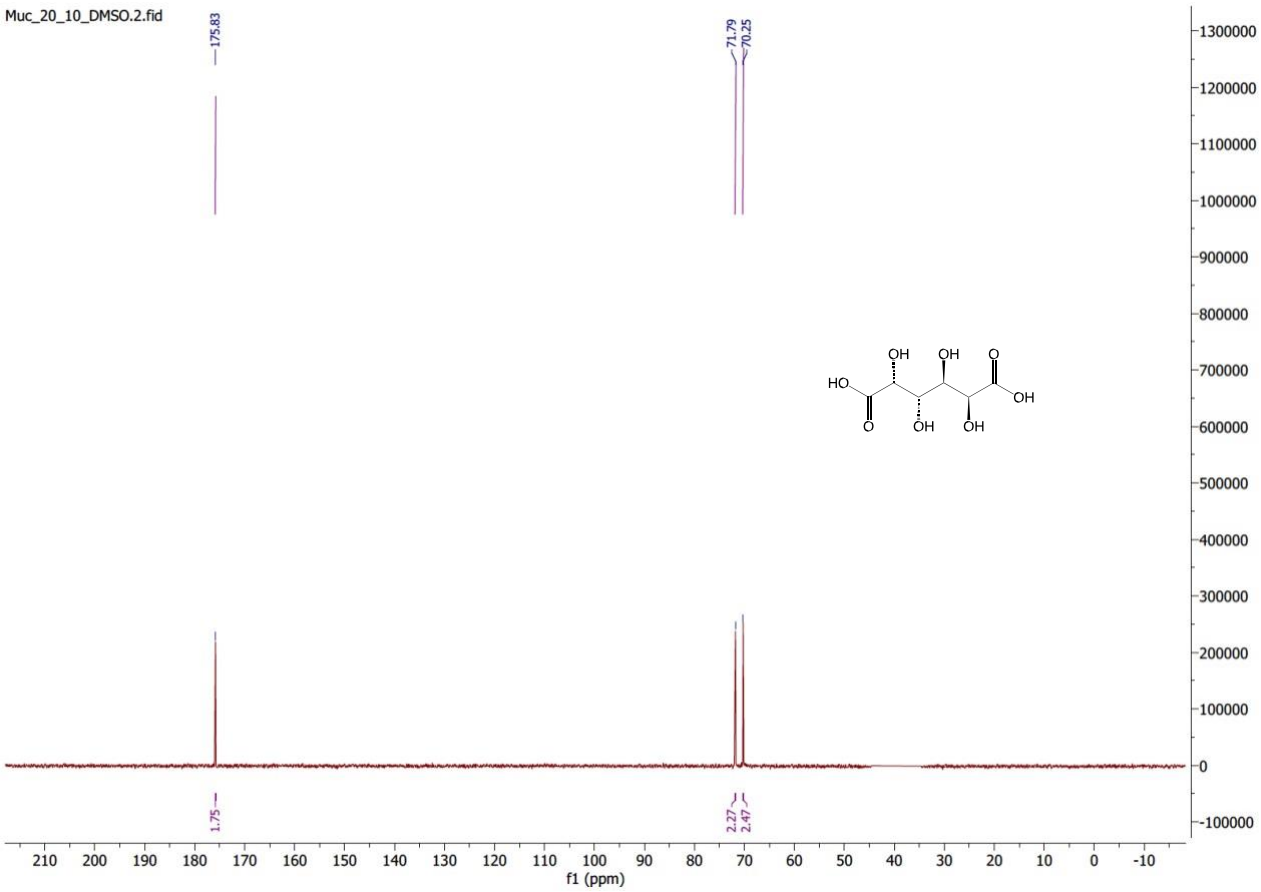

Figure SI2: 13C NMR spectrum of isolated mucic acid from oxidation of lactose: ^{13}C NMR (101 MHz, DMSO) δ 175.83, 71.79, 70.25.

1.2 High-Resolution Mass Spectrometry Analysis of Reaction Mixtures

Direct-infusion HRMS analyses with reaction mixtures after oxidation were performed on a 12-T Bruker solariX XR FT-ICR instrument, equipped with an Apollo-II electrospray ionization (ESI) source. The samples were diluted 1:1000 v/v with HPLC grade methanol and directly infused into the ion source by a syringe pump at a flow rate of 2 µL/min. All the ESI FT-ICR MS data were acquired at an *m*/*z* range of 90-1000 with 200 co-added (4 MWord) time-domain transients. The instrument was externally calibrated with sodium trifluoroacetate (STFA) clusters and Bruker DataAnalysis 5.0 was used for the data post-processing and analysis. The molecular formulae for each ion were obtained by using a SmartFormula tool implemented in DataAnalysis.

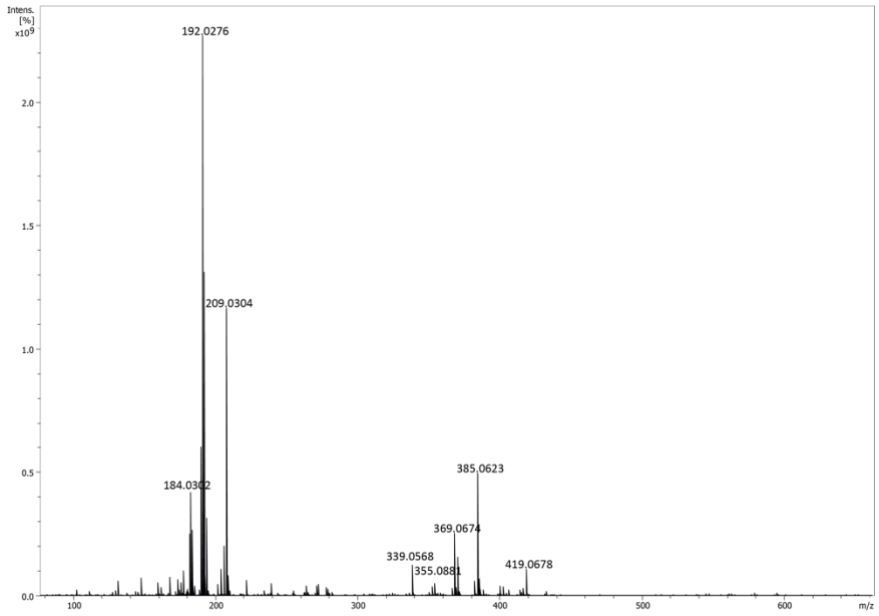

Figure SI3: Direct-infusion negative-ion ESI FT-ICR mass spectrum of the remaining compounds in the nitric acid oxidation mixture after the reaction and extraction of mucic acid.

Table SI1: Table of detected ions for nitric acid oxidation reaction mixture

Singly charged ions						
Meas. m/z	**Ion Formula**	**Molecular formula (assignment)**	**m/z**	**err [ppm]**	**DBE**	**Charge**
193.0355	C6H9O7	C6H10O7 **(glucuronic acid)**	193.0354	-0.5	2	-1
195.0511	C6H11O7	C6H12O7 **(gluconic/galactonic acid)**	195.051	-0.5	1	-1
209.0304	C6H9O8	C6H10O8 **(glucaric acid)**	209.0303	-0.4	2	-1
339.0568	C11H15O12	C11H16O12	339.0569	0.2	4	-1
369.0674	C12H17O13	C12H18O13	369.0675	0.1	4	-1
371.0831	C12H19O13	C12H20O13	371.0831	0.1	3	-1
385.0623	C12H17O14	C12H18O14	385.0624	0.2	4	-1

Doubly charged ions						
Meas. m/z	**Ion Formula**	**Molecular formula (assignment)**	**m/z**	**err [ppm]**	**DBE**	**Charge**
183.0224	C12H14O13	C12H16O13	183.0223	-0.6	5	-2
184.0302	C12H16O13	C12H18O13	184.0301	-0.6	4	-2
185.038	C12H18O13	C12H20O13	185.0379	-0.6	3	-2
191.0198	C12H14O14	C12H16O14	191.0197	-0.5	5	-2
192.0276	C12H16O14	C12H18O14	192.0276	-0.5	4	-2
207.0147	C12H14O16	C12H16O16	207.0146	-0.4	5	-2

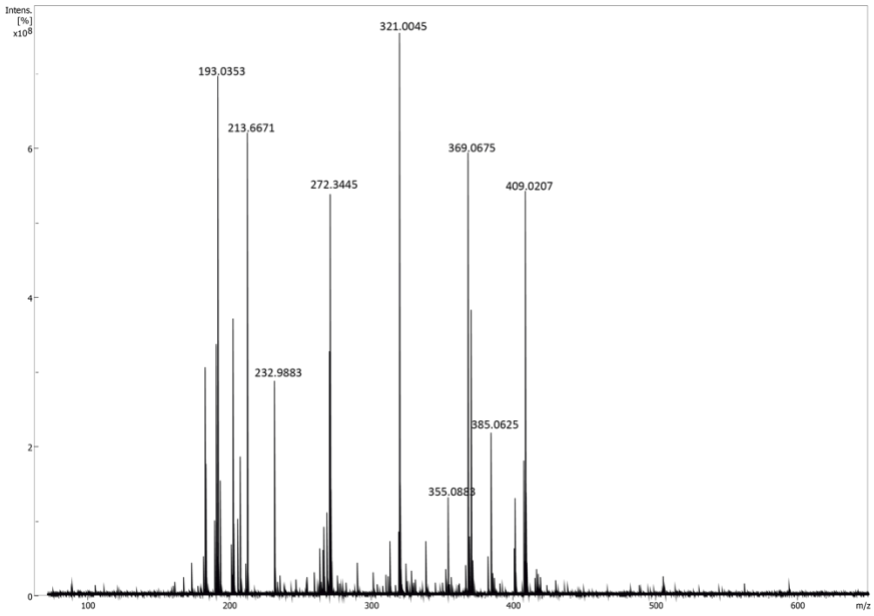

Figure SI4: Direct-infusion negative-ion ESI FT-ICR mass spectrum of the remaining compounds in the nitric acid oxidation mixture with 5mol% added TEMPO after reaction after the reaction and extraction of mucic acid.

Table SI2: Table of detected ions for nitric acid oxidation reaction mixture with 5mol% TEMPO added

Singly charged ions						
Meas. m/z	**Ion Formula**	**Molecular formula (assignment)**	**m/z**	**err [ppm]**	**DBE**	**Charge**
191.0196	C6H7O7	C6H8O7	191.0197	0.6	3	-1
193.0353	C6H9O7	C6H10O7 (glucuronic acid	193.0354	0.5	2	-1
195.0509	C6H11O7	C6H12O7 (gluconic/galactonic acid)	195.051	0.5	1	-1
209.0302	C6H9O8	C6H10O8 (glucaric acid)	209.0303	0.4	2	-1
355.0883	C12H19O12	C12H20O12	355.0882	-0.1	3	-1
369.0675	C12H17O13	C12H18O13	369.0675	-0.2	4	-1
371.0832	C12H19O13	C12H21O13	371.0831	-0.2	3	-1
385.0625	C12H17O14	C12H18O14	385.0624	-0.3	4	-1

Doubly charged ions						
Meas. m/z	**Ion Formula**	**Molecular formula**	**m/z**	**err [ppm]**	**DBE**	**Charge**
184.03	C12H16O13	C12H18O13	184.0301	0.7	4	-2
185.0378	C12H18O13	C12H20O13	185.0379	0.7	3	-2
191.0196	C12H14O14	C12H16O14	191.0197	0.6	5	-2
192.0274	C12H16O14	C12H18O14	192.0276	0.6	4	-2
207.0146	C12H14O16	C12H16O16	207.0146	0.4	5	-2

2.0 Esterification of mucic acid. Procedure and spectra

In a round bottom flask with stirring bar 10g of Mucic acid was added with p-Toluenesulfonic acid (21mol%) and 100mL of respective alcohol for the desired ester. The mixture was then refluxed for 24 hours. The resulting solution was then filtered under vacuo, washed with DI water before drying over night. The white crystals were weighed and analysed by ^{1}H & ^{13}NMR.

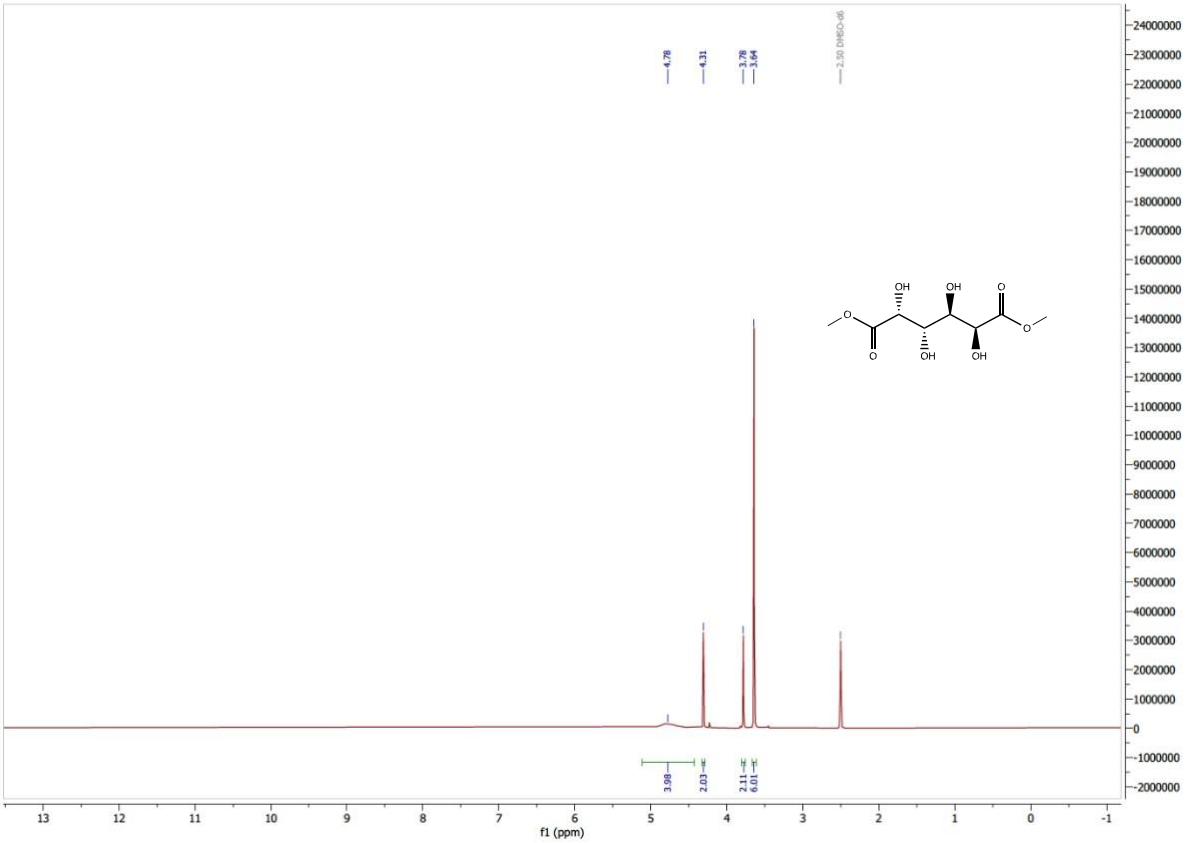

Figure SI5: ^{1}H NMR spectrum of mucic acid from oxidation of dimethyl mucate ester δ H (400 MHz, DMSO) 4.78 (4 H, br s), 4.31 (2 H, s), 3.78 (2 H, s), 3.64 (6 H, s).

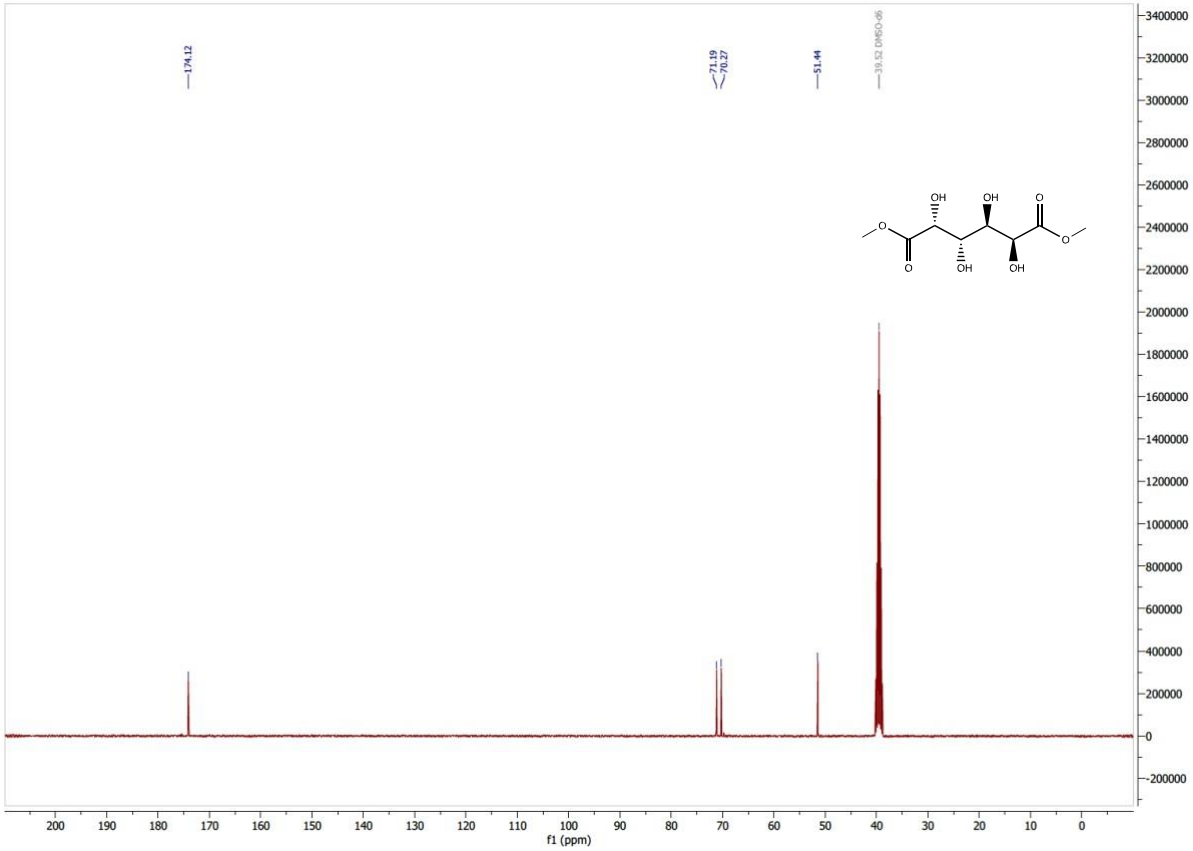

Figure SI6: 13C NMR spectrum of isolated mucic acid from oxidation of dimethyl mucate ester: δ C (101 MHz, DMSO) 174.1, 71.2, 70.3, 51.4.

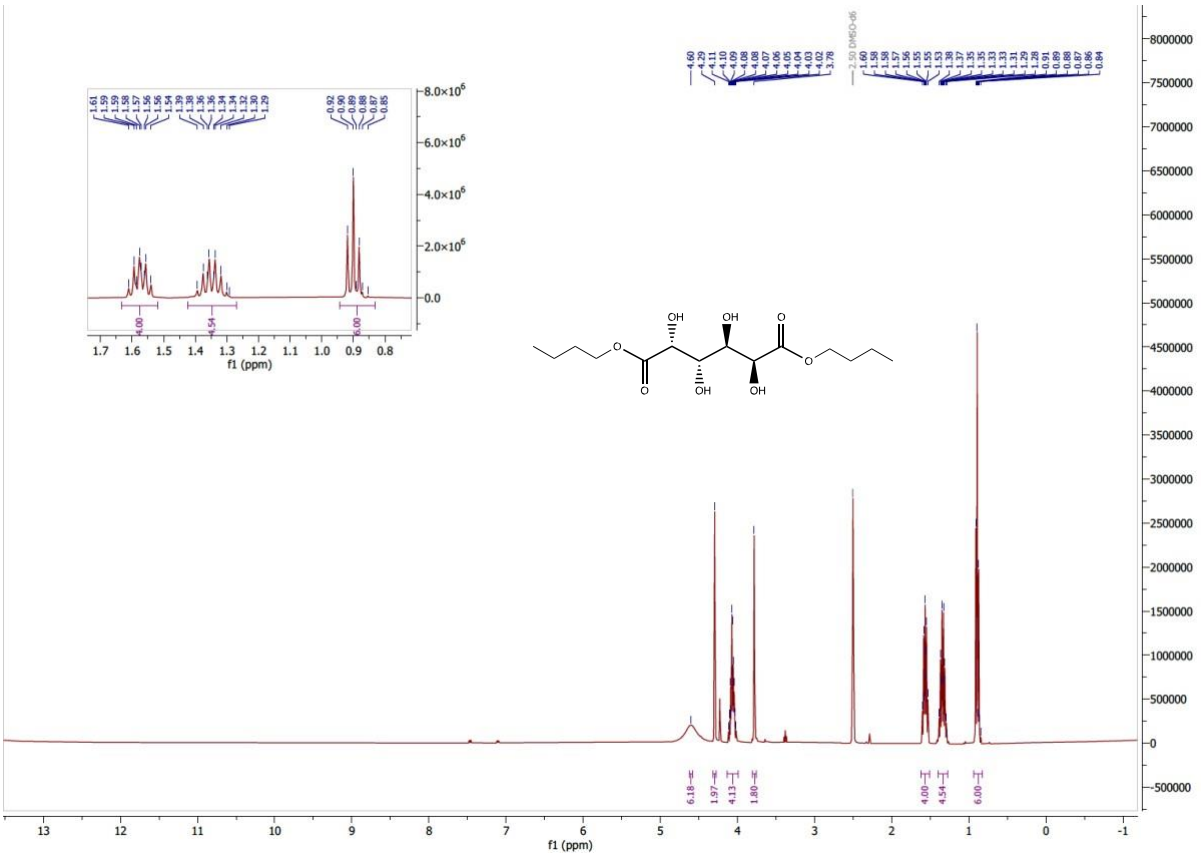

Figure SI7: ^{1}H NMR spectrum of mucic acid from oxidation of dibutyl mucate ester δ H (400 MHz, DMSO) 4.60 (4 H, br s), 4.29 (2 H, s), 4.14 – 3.99 (4 H, m), 3.78 (2 H, s), 1.62 – 1.51 (4 H, m), 1.41 – 1.26 (4 H, m), 0.89 (6 H, t, J 7.4).

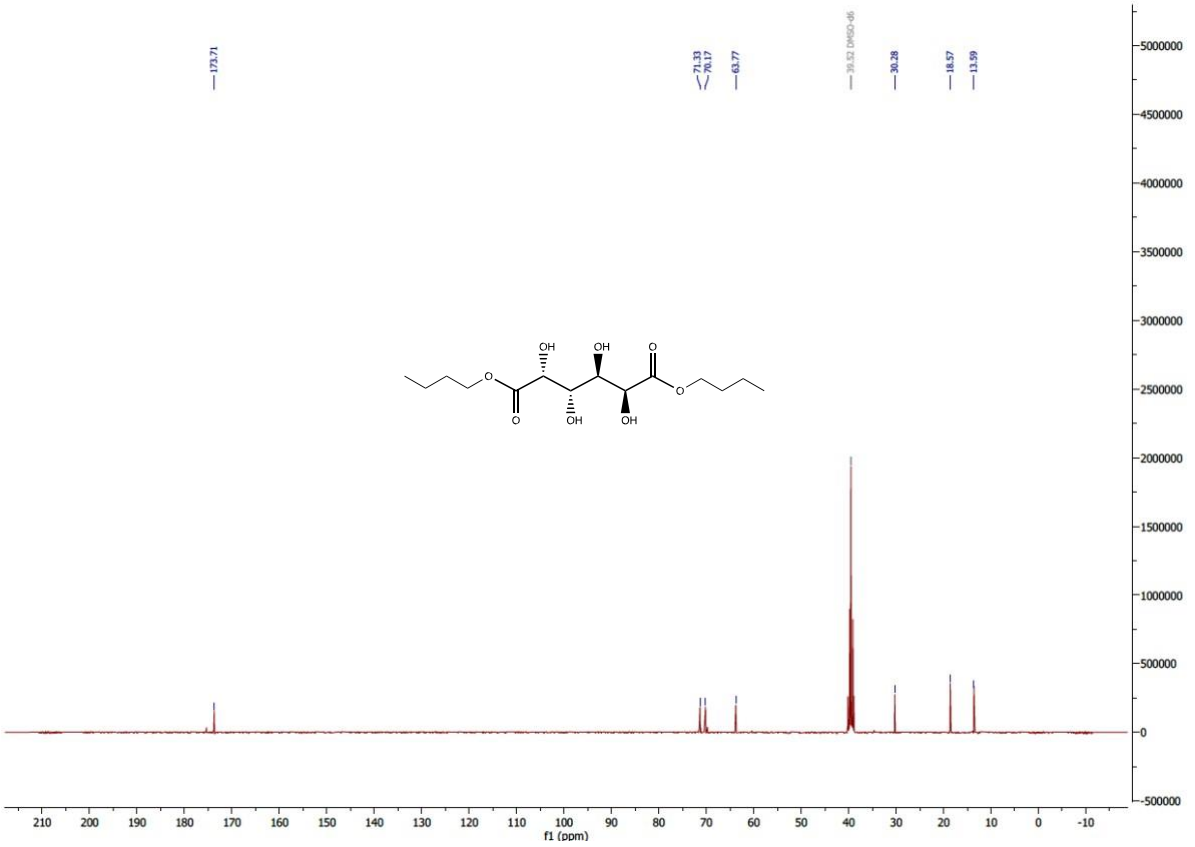

Figure SI8: 13C NMR spectrum of isolated mucic acid from oxidation of dibutyl mucate ester: δ C (101 MHz, DMSO) 173.7, 71.3, 70.2, 63.8, 30.3, 18.6, 13.6.

3.0 Dehydration of Mucate Esters

3.1 Dehydration of mucate esters to furan carboxylates general procedure

Inside an autoclave reactor 20mL vessel 0.3-0.4mmol of diesterified mucate ester, along with 15 mL respective alcohol (methanol for methyl esters and 1-butanol for butyl esters) and the selected acid catalyst are added. The vessel is then purged three times with N_2 before charging to the desired reaction pressure. A programmed reaction run is then initiated ramping to the desired temperature at 2.5°C/min before holding for desired reaction time. Once completed the reactor is water cooled to room temperature before returning to atmospheric pressure. The obtained solution is then centrifuged to separate and recover the catalyst, followed by sample preparation for GC-MS and GC-FID analysis to quantify the reaction products.

3.2 GC Analysis

The furan carboxylate esters were quantified using gas chromatography for peak definition and accuracy of quantification. For this an Agilent 6890N equipped with an autosampler and 5973N MSD detector and an Agilent 7890B GC equipped with flame ionisation detector was used for high quality detection and quantification. The column used in both instruments was an Agilent J&W GC HP Column, length 30m, diameter 0.25mm and 0.25um film. An internal standard of 2,3,5-trichloro benzene was used and quantifications made using external quantification with respect to the internal standard for high precision quantifications.

3.3 Zeolite dehydration experiments

Table SI3: Recorded yields from zeolite screening experiments. Reaction conditions: 0.4mmol dimethyl mucate, 50wt% zeolite, 15mL methanol, 10bar N_2 in a sealed reaction vessel.

Zeolite	Si:Al	Temperature / °C	Time / Hr	Yield 2,5MFDC 2b / mol%	Yield 2-MFC 3b/ mol%
Beta	30	220	1	12.2	13.2
Beta	30	220	3	30.1	25.0
Beta	30	220	10	1.5	2.6
Beta	360	220	3	17.4	18.8

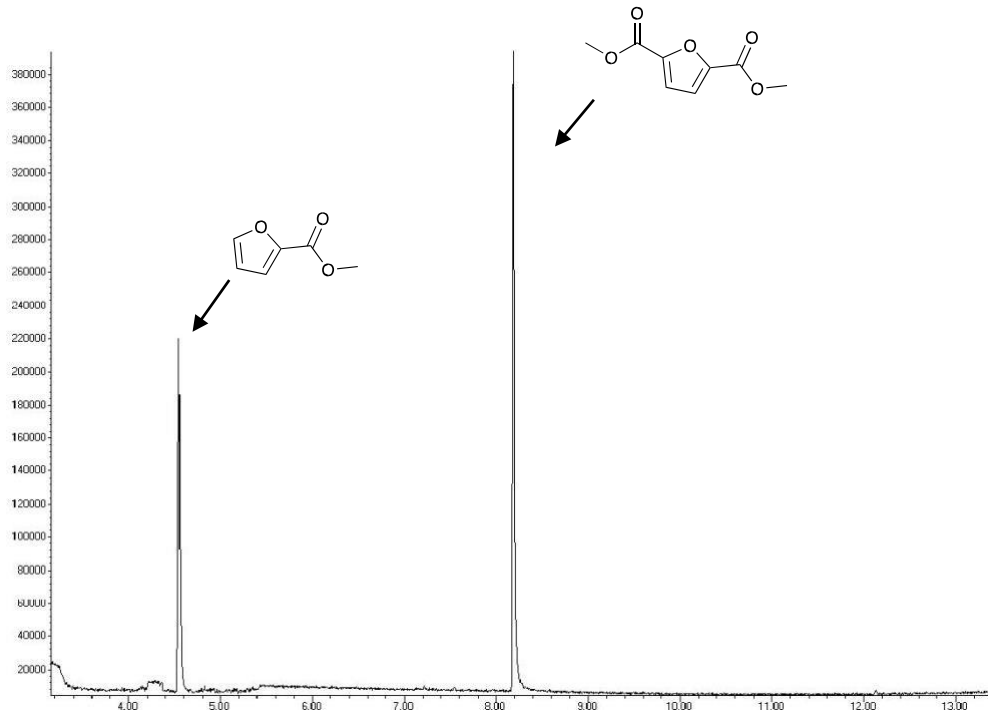

Figure SI9: Example GC spectra obtained on GC-MS Spectrometer for the reaction products **2b** and **3b** in ethyl acetetate

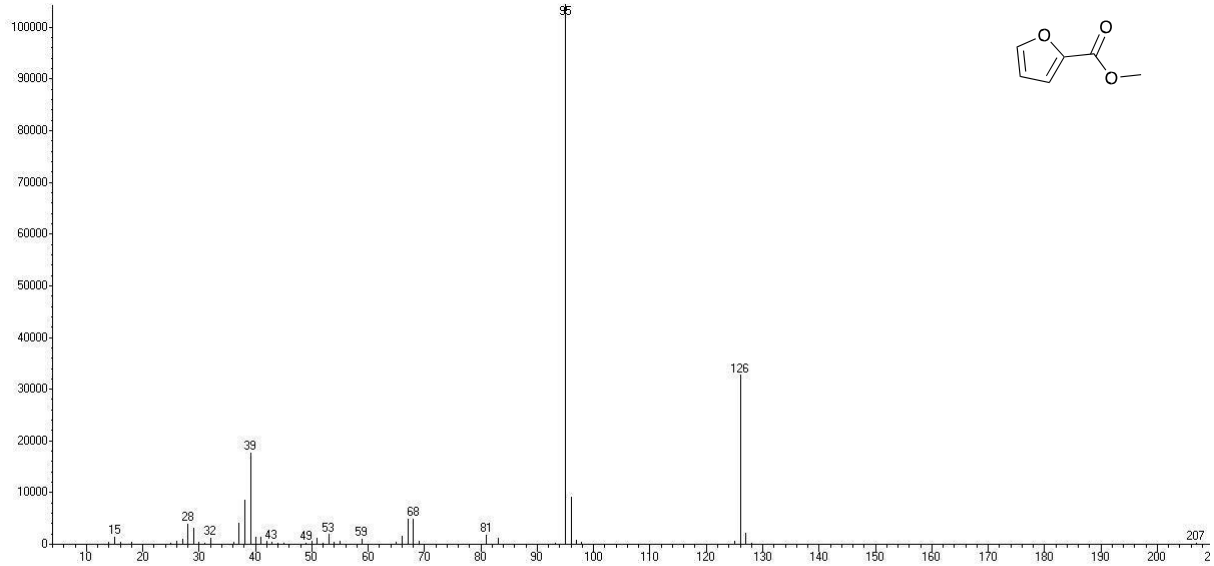

Figure SI10: Example MS spectra obtained on GC-MS Spectrometer for the reaction product **3b** using EI as ion source

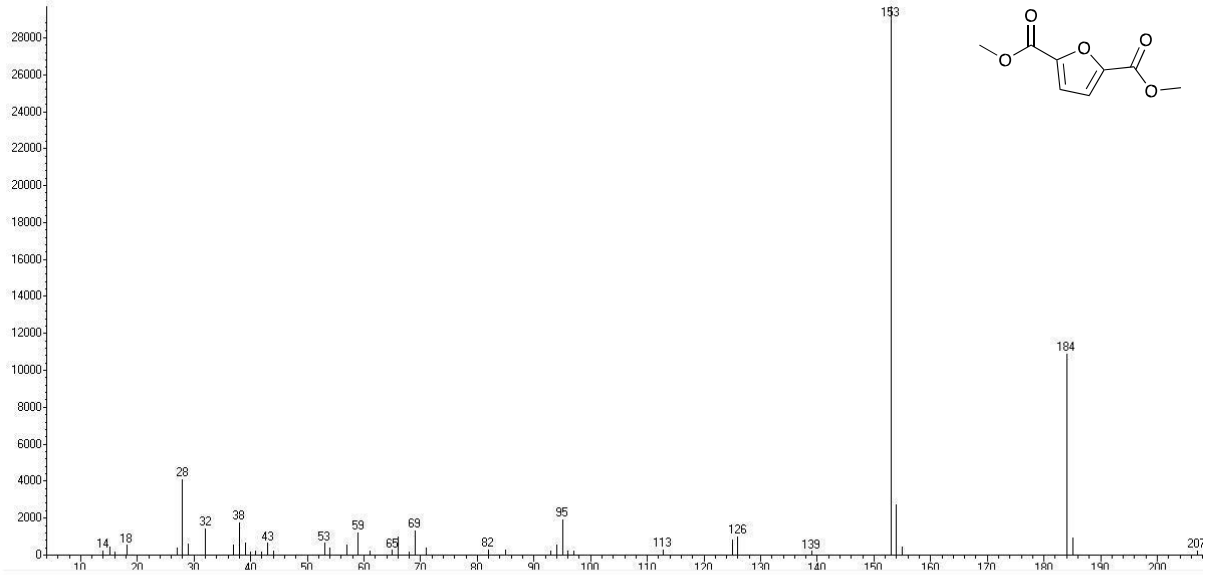

Figure SI11: Example MS spectra obtained on GC-MS Spectrometer for the reaction product **2b** using EI as ion source.

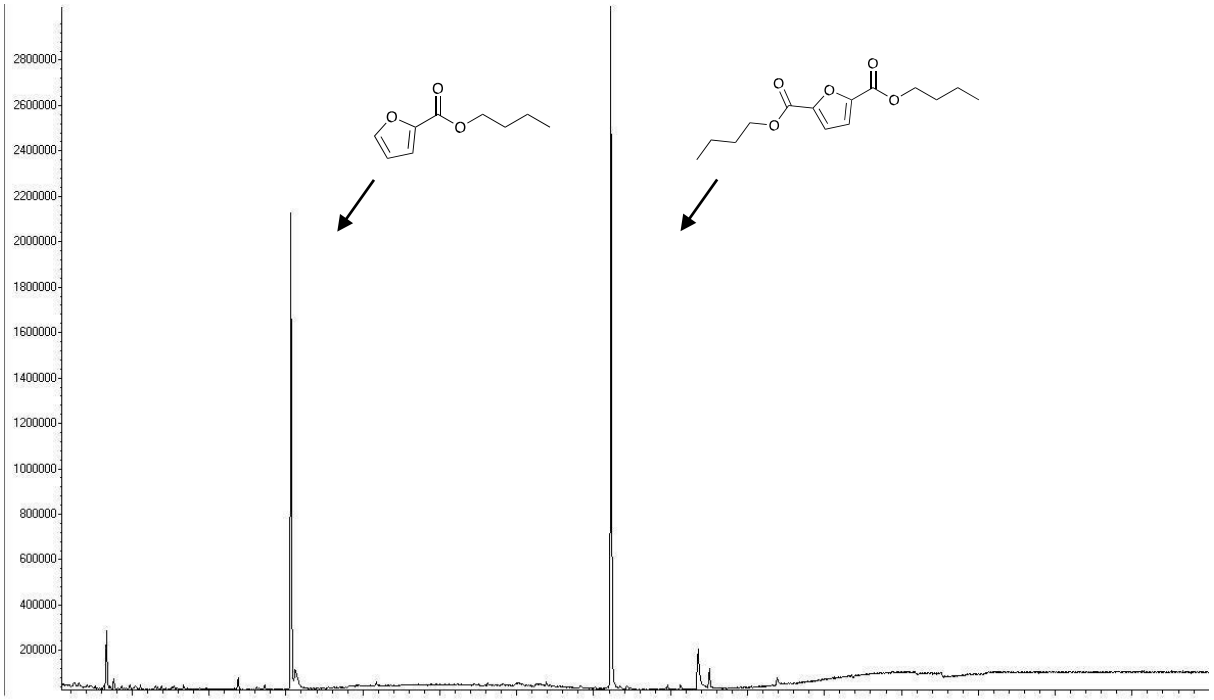

Figure SI12: Example GC spectra obtained on GC-MS Spectrometer for the reaction products **2c** and **3c** in ethyl acetate

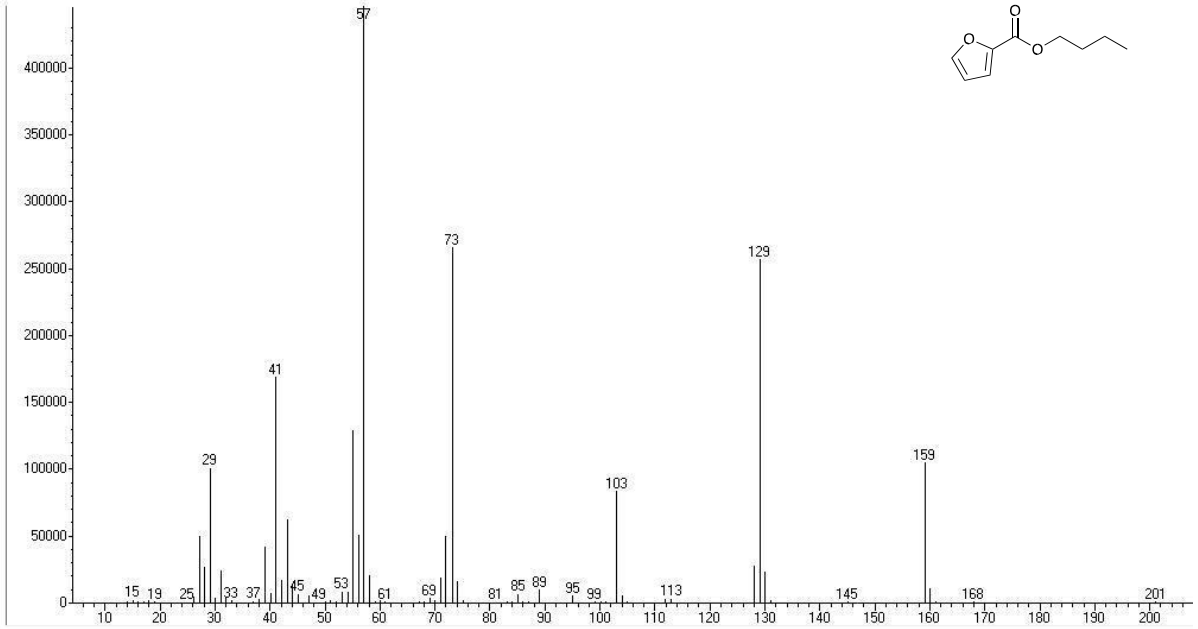

Figure SI13: Example MS spectra obtained on GC-MS Spectrometer for the reaction product **3c** using EI as ion source.

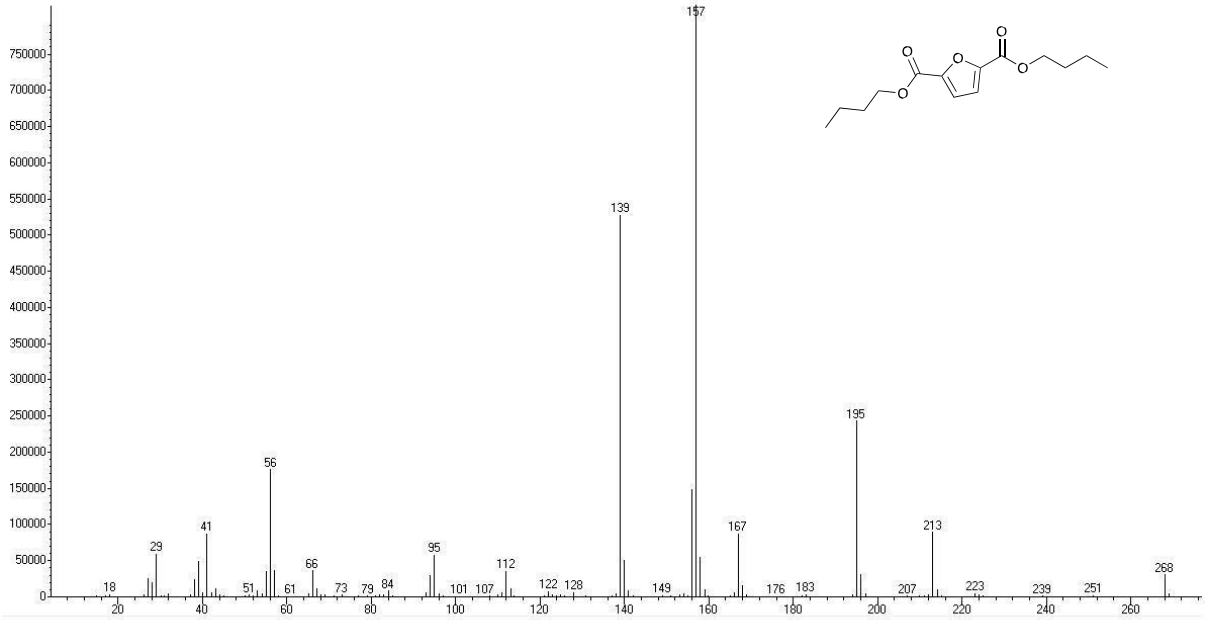

Figure SI14: Example MS spectra obtained on GC-MS Spectrometer for the reaction product **2c** using EI as ion source.

Compound **2c,** dibutyl furandicarboxylate was isolated via column chromatography using silica gel (40–63 µm; VWR Chemicals) as stationary and DCM as mobile phase.

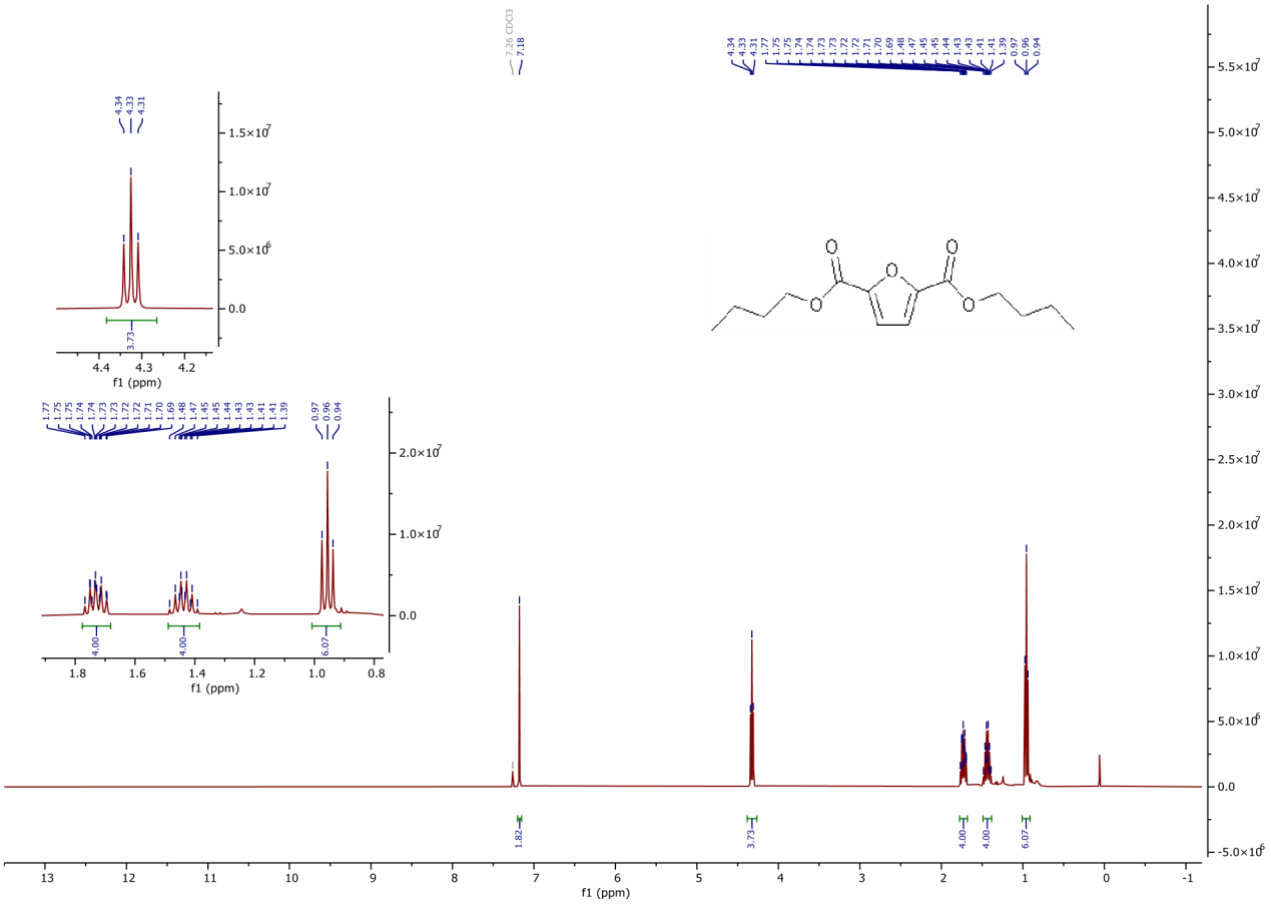

Figure SI15: ^{1}H NMR spectrum of isolated compound **2c**: δ ^{1}H (400 MHz, $CDCl_3$): 7.18 (2 H, s), 4.33 (4 H, t, J 6.7), 1.78–1.68 (4 H, m), 1.49–1.38 (4 H, m), 0.96 (6 H, t, J 7.4).

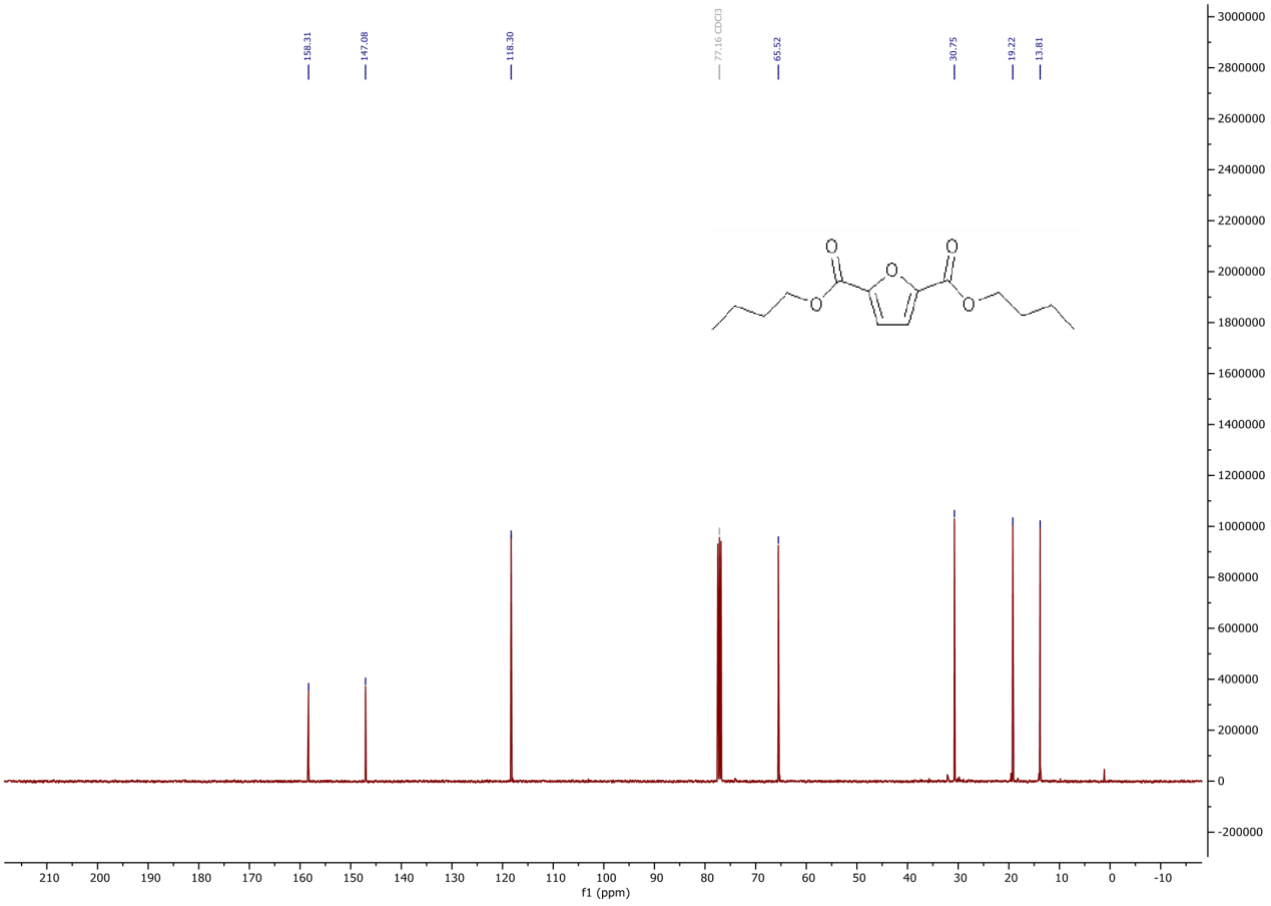

Figure SI16: 13C NMR spectrum of isolated compound **2c**: δ ^{13}C (101 MHz, $CDCl_3$): 158.3, 17.1, 118.3, 65.5, 30.7, 19.2, 13.8.

3.4 Design of Experiments Methods for Dehyrdation of Dibutyl Mucate Ester to dibutyl furandicarboxylate

D-Optimal Design for Optimised Results

As the dependence on time, temperature and catalyst loading was large for the dehydration reaction but the scope for the acceptable parameters were narrow, a D-Optimal (figure SI15) design was selected to precisely obtain the optimal conditions. All statistical models were generated using Umetrics Sartorius Modde Pro software and the contour plots presented in figure 3 were generated by the software.

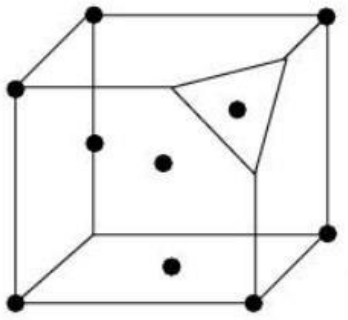

Figure SI 17: *D-optimal statistical design of the experimental region*

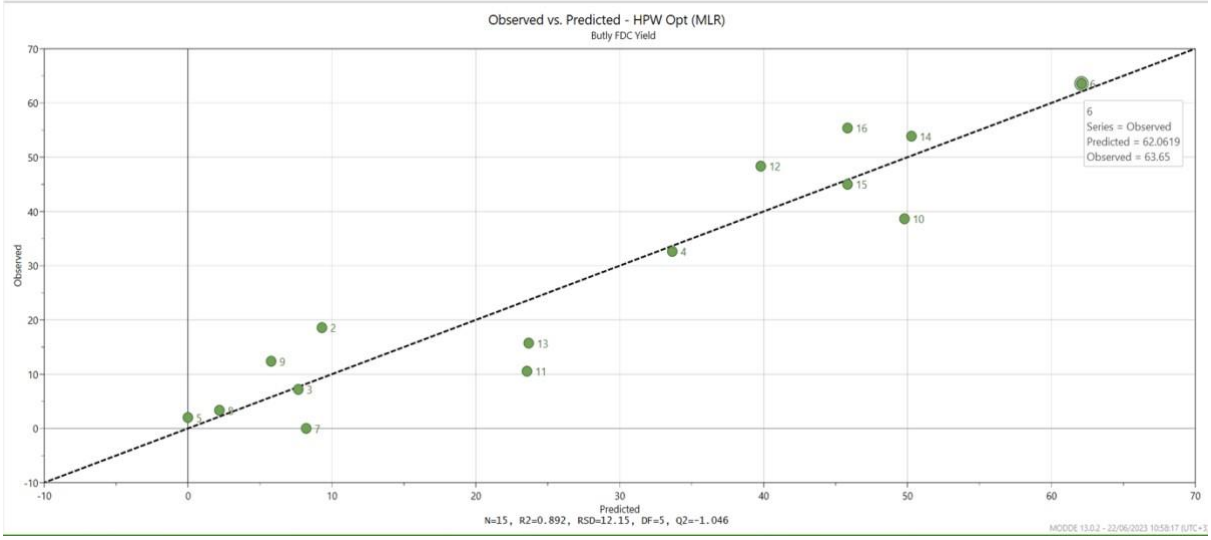

Figure SI18: Observed vs Predicted plot of the response for the yield of **2c** as a function of reaction time, temperature and catalytic loading.

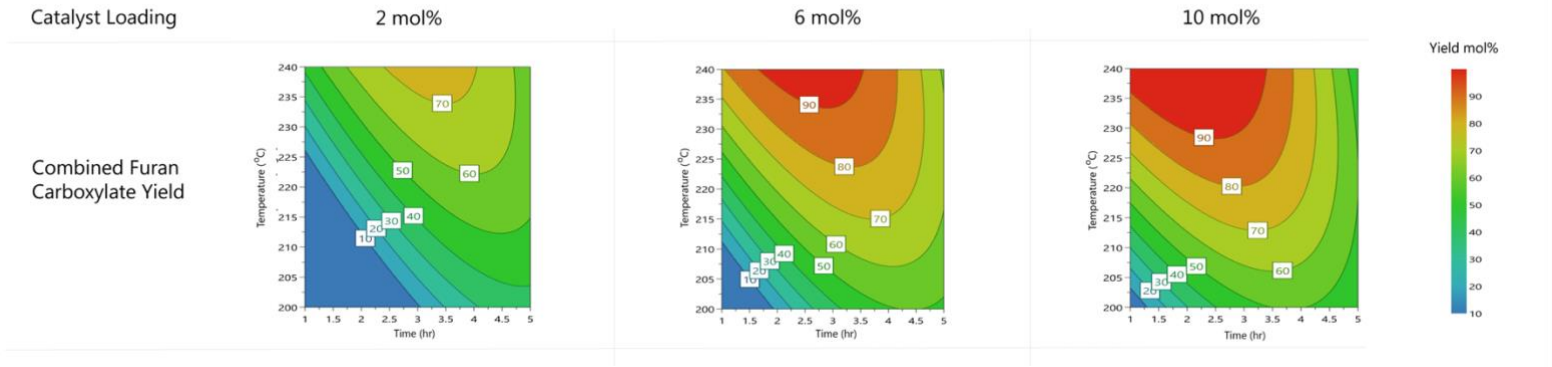

Figure SI19: *D-optimal of The effect of temperature (200-240°C), reaction time (1-5hr) and catalyst loading (2-10mol%) on the yield of Dibutyl-2,5-Furandicrbxoylate modelled with D-Optimal Design of Experiment model.*