Electronic Supplementary Material (ESI) for Reaction Chemistry & Engineering.

One-pot tandem synthesis of 5-ethoxymethylfurfural as a potential biofuel

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GENERAL TECHNIQUES

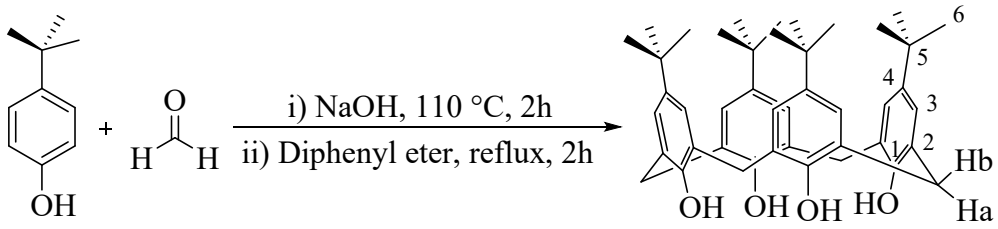
Analytical grade commercial solvents and reagents were purchased from Sigma-Aldrich, and used as received. Infrared spectra were recorded as neat using a FT-IR Varian 660 Fourier transform infrared spectrometer. Values are expressed in wavenumbers (cm^{-1}) and recorded in a range of 4000−400 cm^{-1}. NMR spectra were recorded at 25 °C in $CDCl_3$ on a Varian Mercury 300 spectrometer operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C. All chemical shifts are reported in parts per million (ppm) and were measured relative to the solvent in which the sample was analyzed ($CDCl_3$ δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR). Coupling constants (*J*) are reported in hertz (Hz). The chromatograms were obtained by gas chromatography coupled to a mass spectrometer, using a SHIMADZU GCMS-QP2010C Ultra mass spectrometer and the method with the following specifications: column Ultra Alloy 5, 30 m, DI 0.25 mm; helium carrier gas; injector temperature: 290 °C; the oven temperature was: 40 °C (2.0 min), with a ramp from 30 °C min^{-1} to 250 °C (maintained for 1.0 min). The percentage of EMF, HMF e EL yield (%) was calculated based on the calibration curve, using TMB as an internal standard. The conversion of fructose under optimal reaction conditions was determined using a system Thermo Scientific Accela LC liquid chromatograph (refractive index (RI) detector, auto-injector and Accela pump) (Thermo Fischer Scientific, TX, USA).

EXPERIMENTAL PROCEDURES

Synthesis of calix[*n*]arenes

Synthesis of the *p-tert*-butylcalix[4]arene

The synthesis of the *p-tert*-butylcalix[4]arene involving the condensation of the *p-tert*-butylphenol, formaldehyde solution with a basic medium and under heating, as shown in Scheme 1, following the methodology described by Gutsche et al [1]. The product was obtained as a white solid in 77% yield.



Scheme 1 Reaction for obtaining the *p-tert*-butylcalix[4]arene.

^{1}H NMR (300 MHz, $CDCl_3$): 1.21 (s, 36H, H-6), 3.48 (d, 4H, J = 12.4, CH_2-Ha), 4.28 (d, 4H, J = 12.4, CH_2-Hb), 7.05 (s, 8H, H-3), 10.34 (s, 4H, OH).

^{13}C NMR (75 MHz, $CDCl_3$): 31.4 (C-6), 32.7 (CH_2), 34.0 (C-5), 125.9 (C-3), 127.6 (C-2), 144.3 (C-4), 146.7 (C-1).

IR (ATR, cm^{-1}): 3150, 3057, 3024, 2952, 1737, 1605, 1480, 1456, 1391, 1362, 1231, 1200, 871, 814, 780.

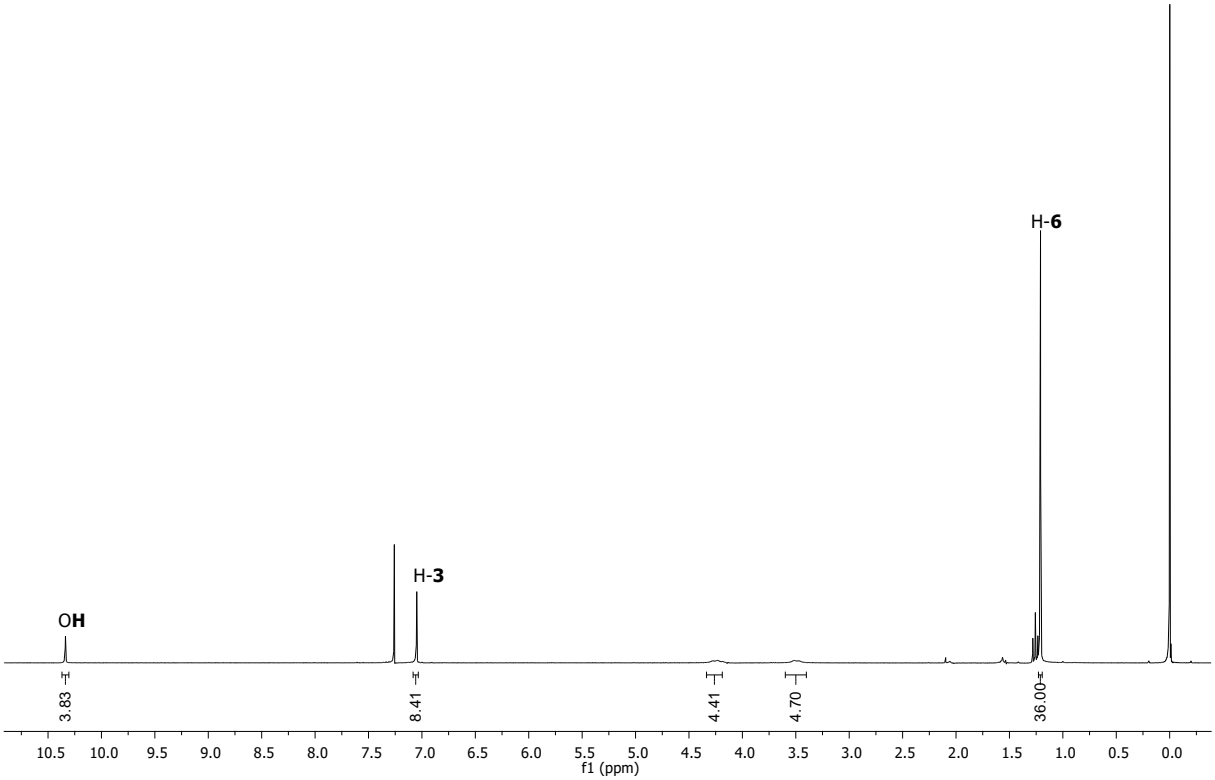


Fig. S1. ^{1}H NMR spectrum (300 MHz; $CDCl_3$) of the *p-tert*-butylcalix[4]arene.

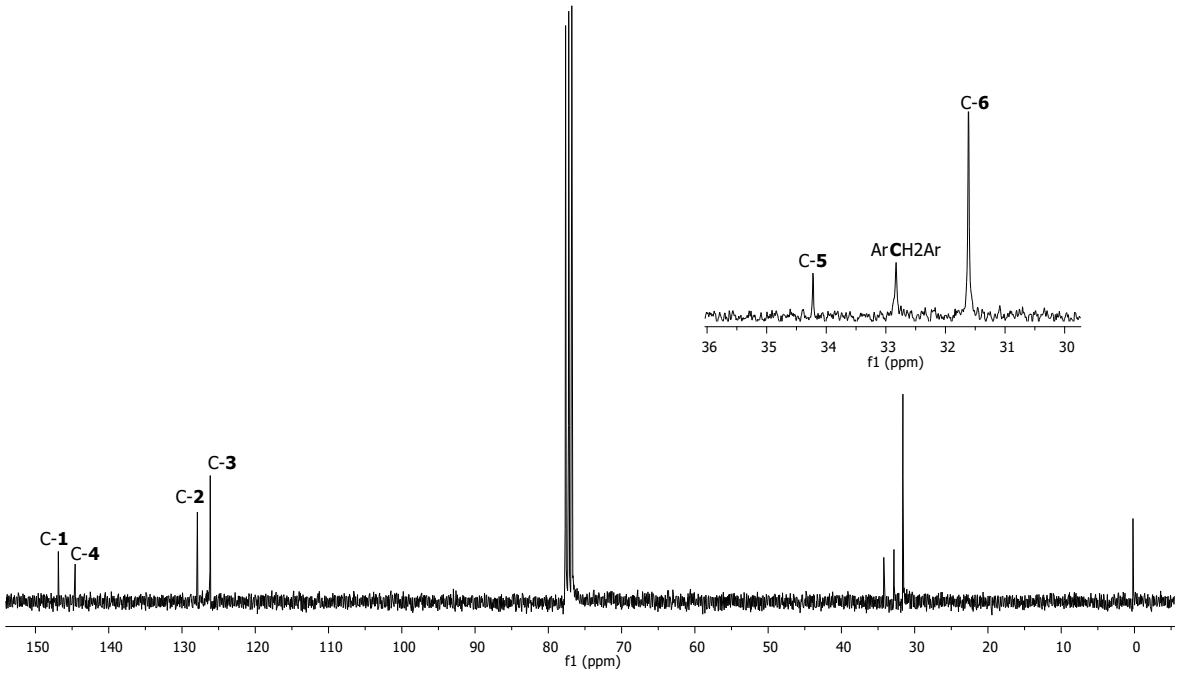


Fig. S2. ^{13}C NMR spectrum (75 MHz; $CDCl_3$) of the *p-tert*-butylcalix[4]arene.

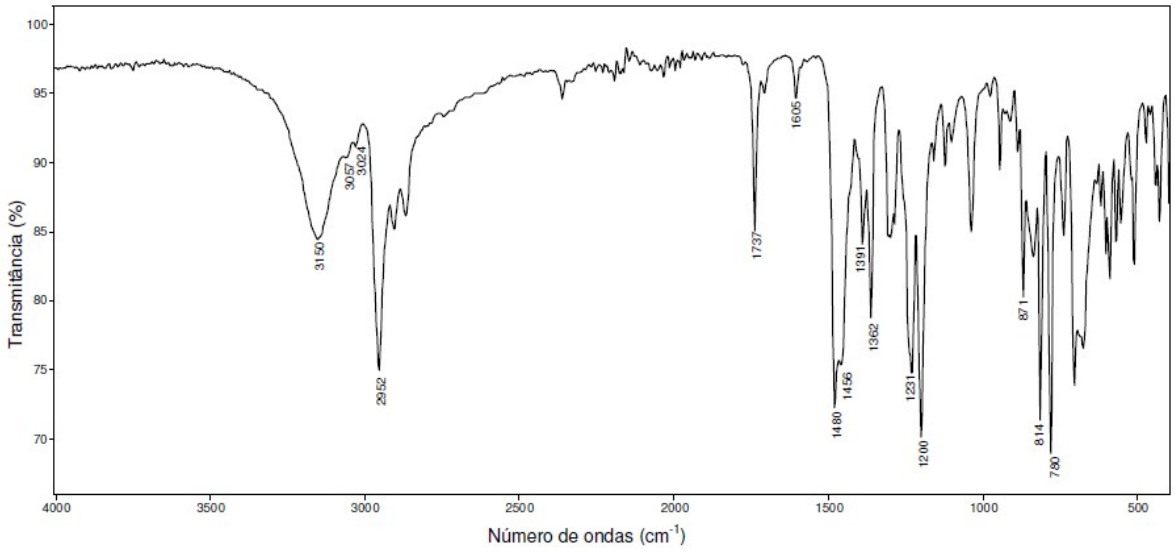
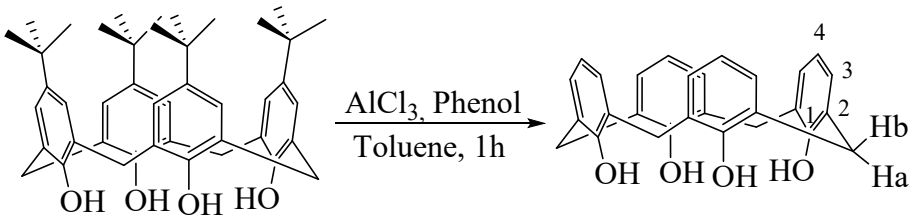


Fig. S3. *p-tert*-butylcalix[4]arene infrared spectrum.

Synthesis of the calix[4]arene

The synthesis of calix[4]arene was carried out using *p-tert*-butilcalix[4]arene, phenol and aluminum chloride anhydrous in toluene following the methodology described by Gutsche et al [2]. The system was kept under stirring and nitrogen atmosphere at room temperature for one hour (Scheme 2). The desired product, a white solid, was obtained in 81% yield after recrystallization in methanol-chloroform.



Scheme 2 Reaction for obtaining the calix[4]arene.

^{1}H NMR (300 MHz, $CDCl_3$): 3.56 (d, 4H, *J* = 12.6, H-a), 4.27 (d, 4H, *J* = 12.6, H-b), 6.79 (t, 4H, *J* = 7.5, H-4), 7.08 (d, 8H, *J* = 7.5 Hz, H-3), 10.23 (s, 4H, OH).

^{13}C NMR (75 MHz; $CDCl_3$): 31.9 (CH_2), 122.5 (C-4), 128.5 (C-2), 129.2 (C-3), 149.0 (C-1).

IR (ATR, cm^{-1}): 3152, 3092, 2935, 1593, 1466, 1447, 1410, 1369, 1238, 774, 749.

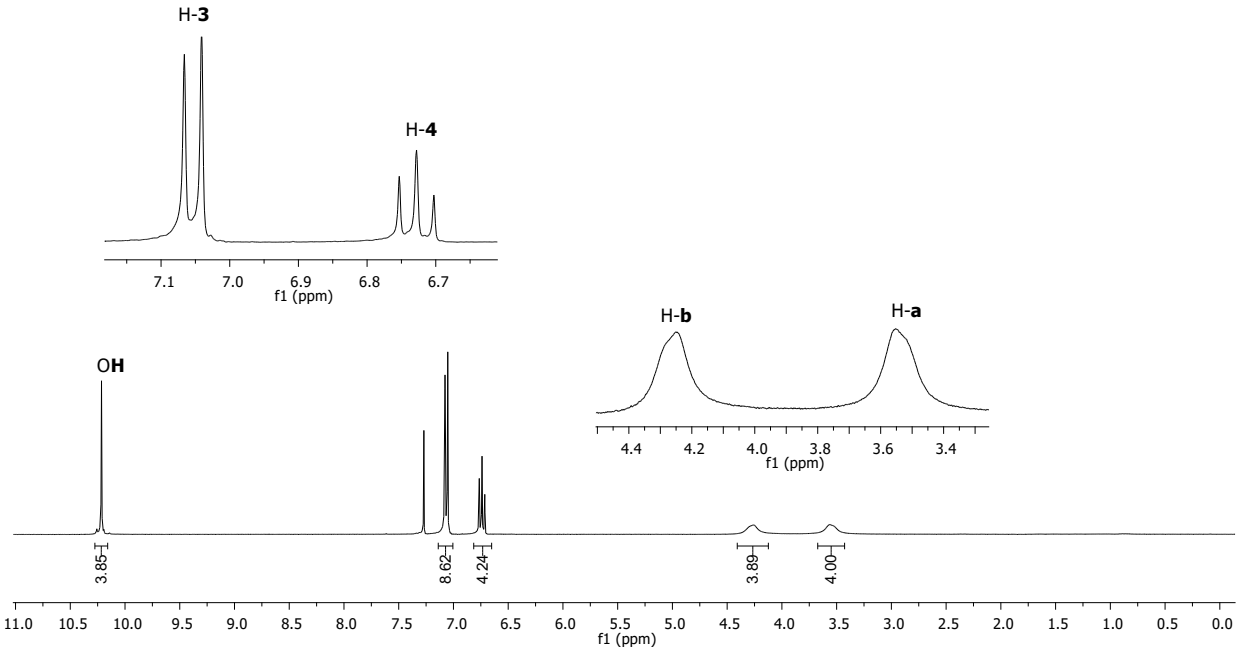


Fig. S4. ^{1}H NMR spectrum (300 MHz; $CDCl_3$) of the calix[4]arene.

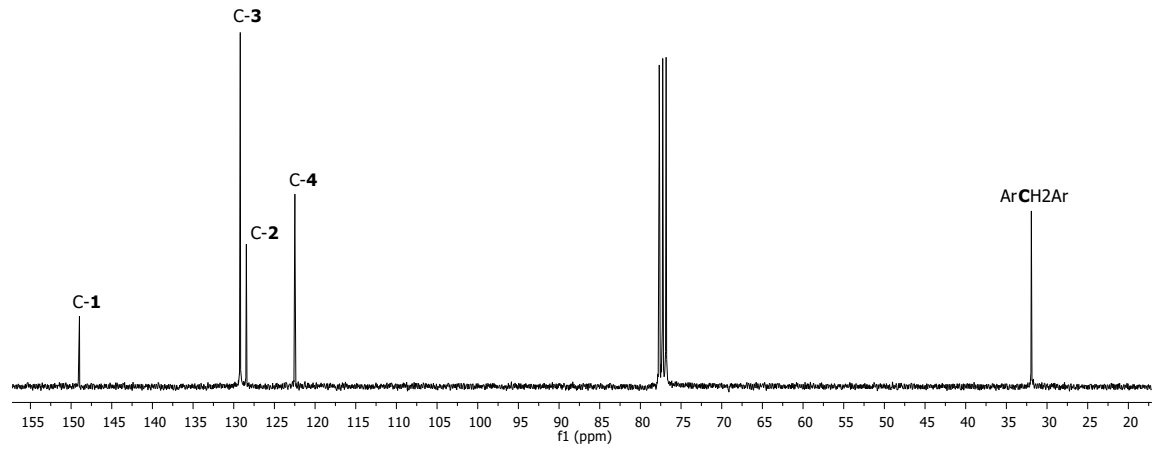


Fig. S5. ^{13}C NMR spectrum (75 MHz; $CDCl_3$) of the calix[4]arene.

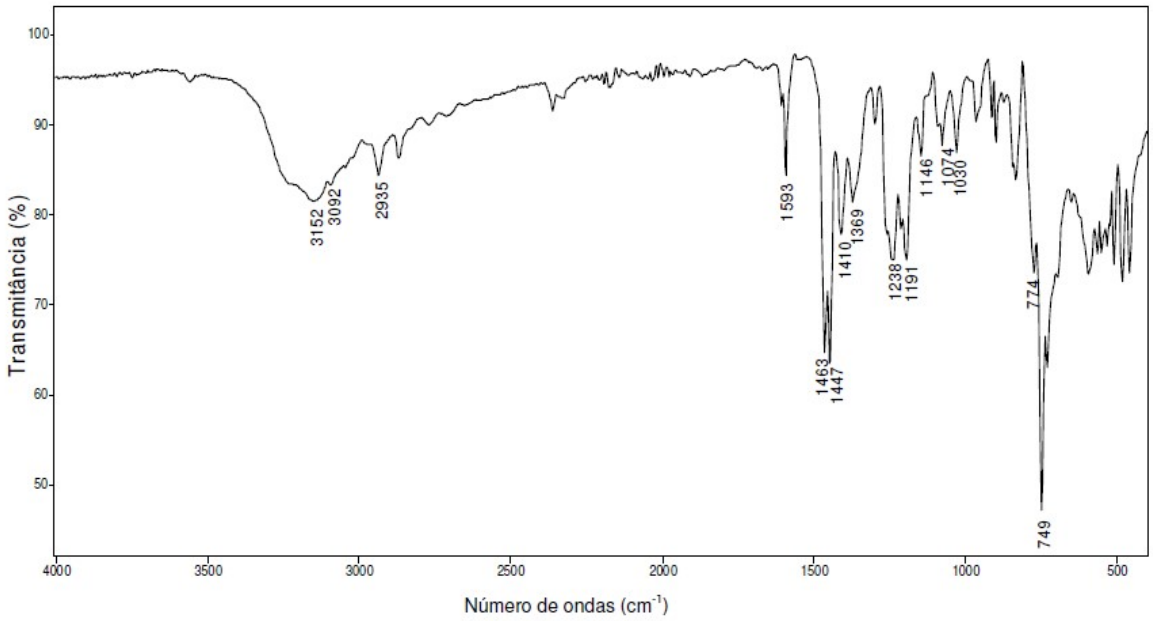
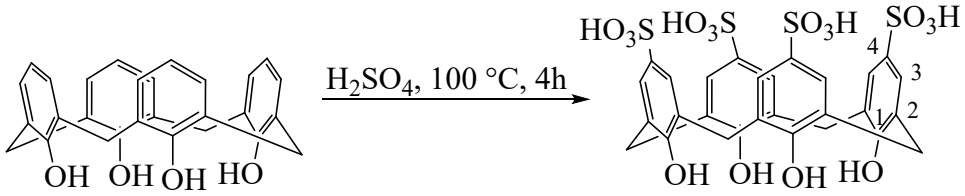


Fig. S6. calix[4]arene infrared spectrum.

Synthesis of the *p*-sulfonic acid calix[4]arene (CX4SO$_3$H)

Catalyst *p*-sulfonic acid calix[4]arene was conducted from calix[4]arene in the presence of concentrated sulfuric acid and heated for four hours as described by Gutsche et al[3] (Scheme 3). The product was obtained in 75% yield as a solid white.



Scheme 3 Reaction for obtaining of the *p*-sulfonic acid calix[4]arene (CX4SO$_3$H).

^{1}H NMR (300 MHz, D_2O): 3.84 (s, 8H, CH_2), 7.39 (s, 8H, H-3).

^{13}C NMR (75 MHz, D_2O): 30.7 (CH_2), 126.6 (C-3), 128.2 (C-2), 135.8 (C-4), 151.9 (C-1).

IR (ATR, cm^{-1}): 3182, 1705, 1636, 1599, 1455, 1147, 1117, 623.

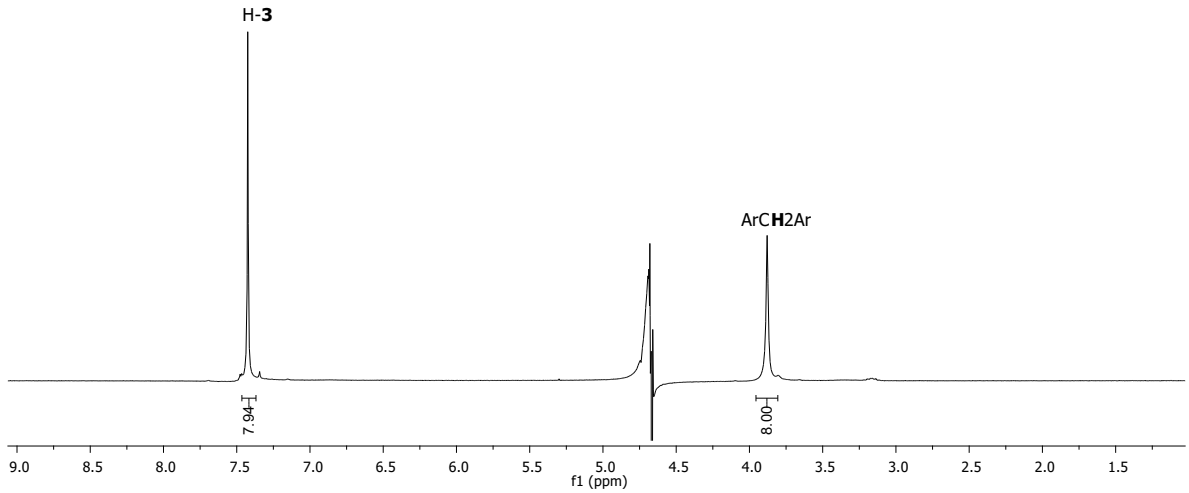


Fig. S7. ^{1}H NMR spectrum (300 MHz; D_2O) of the *p*-sulfonic acid calix[4]arene ($CX4SO_3H$).

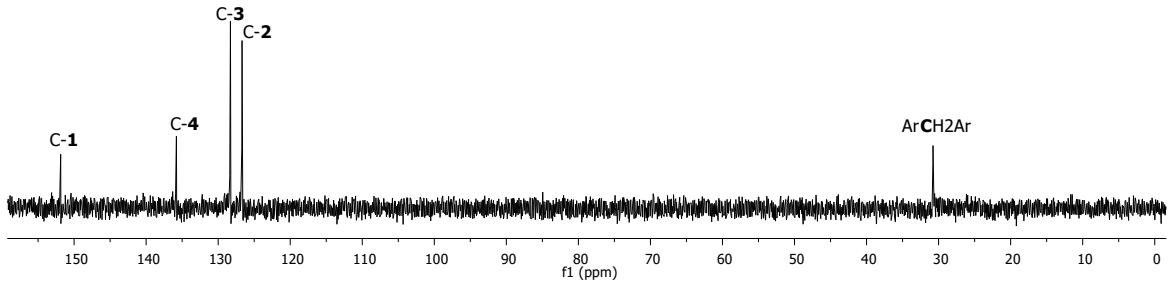


Fig. S8. ^{13}C NMR spectrum (75 MHz; D_2O) of the *p*-sulfonic acid calix[4]arene ($CX4SO_3H$).

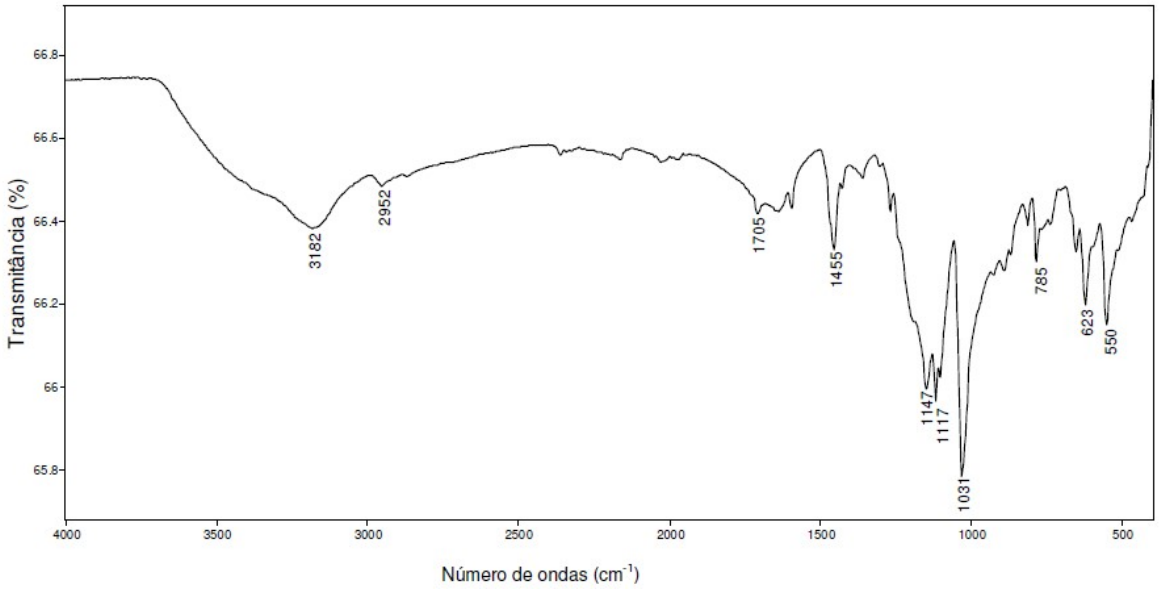


Fig. S9. *p*-Sulfonic acid calix[4]arene ($CX4SO_3H$) infrared spectrum.

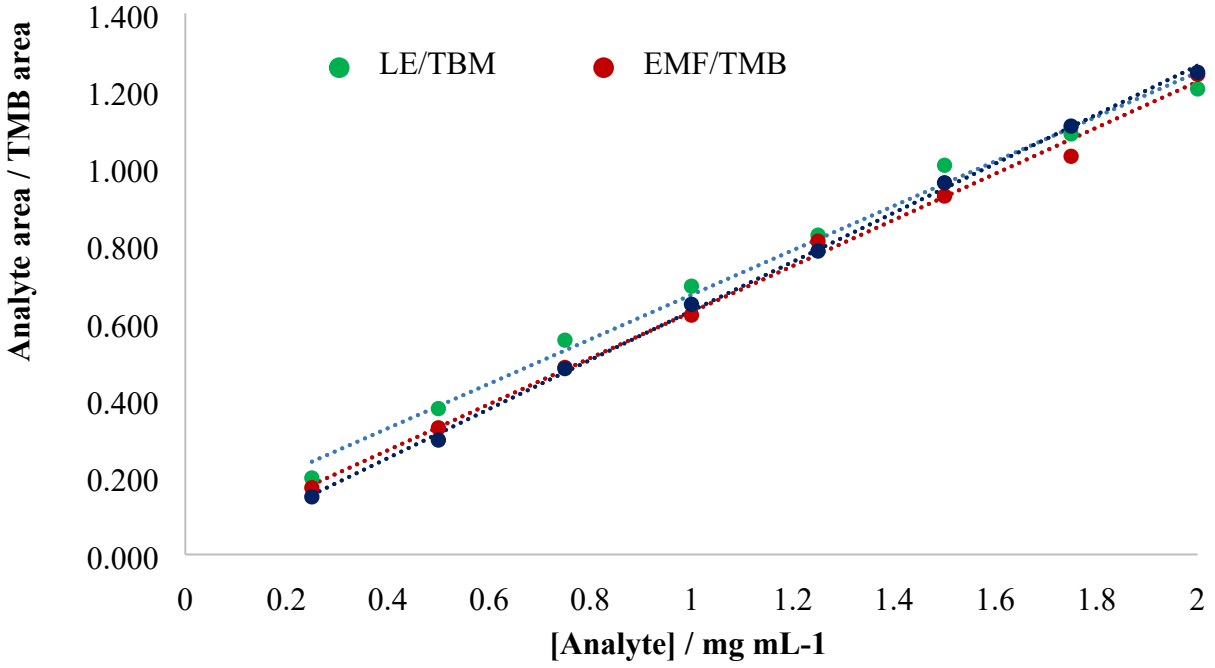
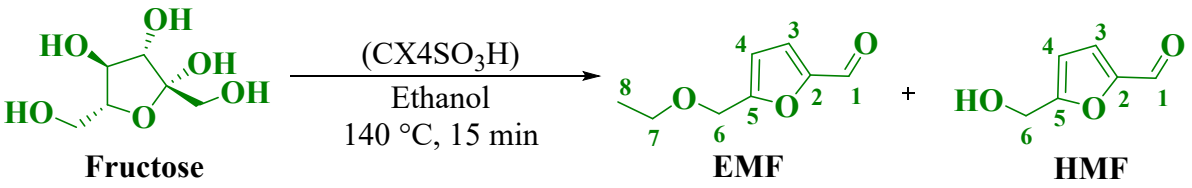


Fig. S10 calibration curves for LE, EMF and HMF with internal standard (TMB) in ethyl acetate.

5-Ethoxymethylfurfural (EMF) and 5-hydroxymethylfurfural (HMF)

An experiment was set up to produce the EMF and HMF for the construction of the calibration curve. 0.25 mmol of fructose, 1 mol% of $CX4SO_3H$ and 1.00 mL of ethanol were added in a reaction vessel (Scheme 4). The mixture was taken to a microwave reactor and heated to 140 °C for 15 mim. A mixture of EMF and HMF was obtained, which were isolated by silica gel column chromatography, using dichloromethane/diethyl ether (1:1) as the mobile phase.



Scheme 4 Synthesis of EMF and HMF.

EMF:

^{1}H NMR (300 MHz, $CDCl_3$): 1.23 (t, *J* = 7.0 Hz, 3H, H-8), 3.79 (q, *J* = 7.0 Hz, 2H, H-7), 4.52 (s, 2H, H-6), 6.51 (d, *J* = 3.5 Hz, 1H, H-4), 7.20 (d, *J* = 3.5 Hz, 1H, H-3), 9.61 (s, 1H, HC=O).

^{13}C NMR (75 MHz, $CDCl_3$): 15.0 (C-8), 64.8 (C-6), 66.6 (C-7), 111.0 (C-4), 122.0 (C-3), 153.0 (C-2), 158.8 (C-5), 177.7 (C-1).

GC/MS *m/z* (abundancy %): 154 (20, M+), 125 (100), 109 (90), 97 (95), 81 (40), 69 (30), 53 (35), 41 (30).

IR (ATR, cm^{-1}): 2972, 2866, 1673, 1520, 1186, 1095, 1019, 803.

HMF:

^{1}H NMR ($CDCl_3$, 300 MHz) 4.68 (s, 2H, H-6), 6.49 (d, J = 3.6 Hz, 1H, H-4), 7.20 (d, J = 3.6 Hz, 1H, H-3), 9.53 (s, 1H, HC=O).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 57.5 (C-6), 109.9 (C-4), 123.0 (C-3), 152.3 (C-2), 160.8 (C-5), 177.7 (C-1).

GC-MS *m/z* (abundancy %): 126 (55, M+), 97 (100), 69 (35), 41 (65).

IR (ATR, cm^{-1}): 3336, 2837, 1659, 1513, 1395, 1186, 1111, 764.

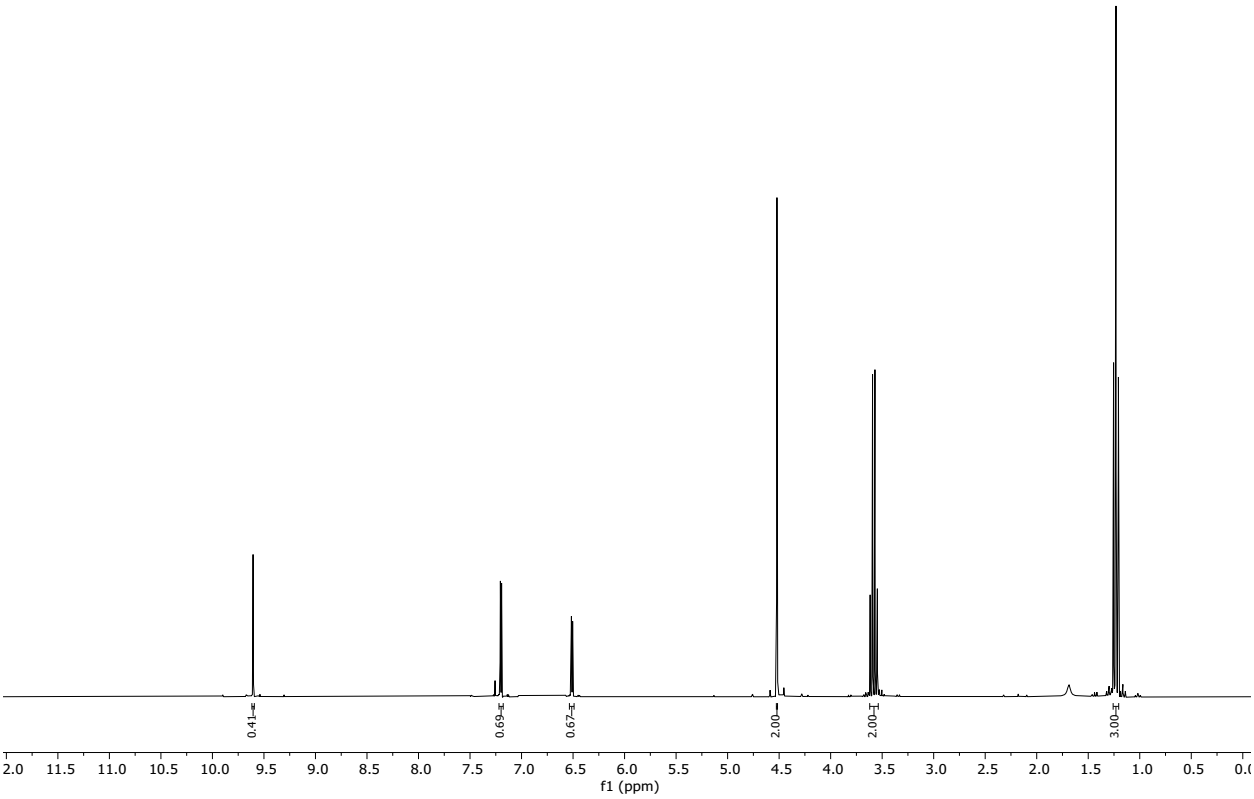


Fig. S11 ^{1}H NMR (300 MHz; $CDCl_3$) of EMF.

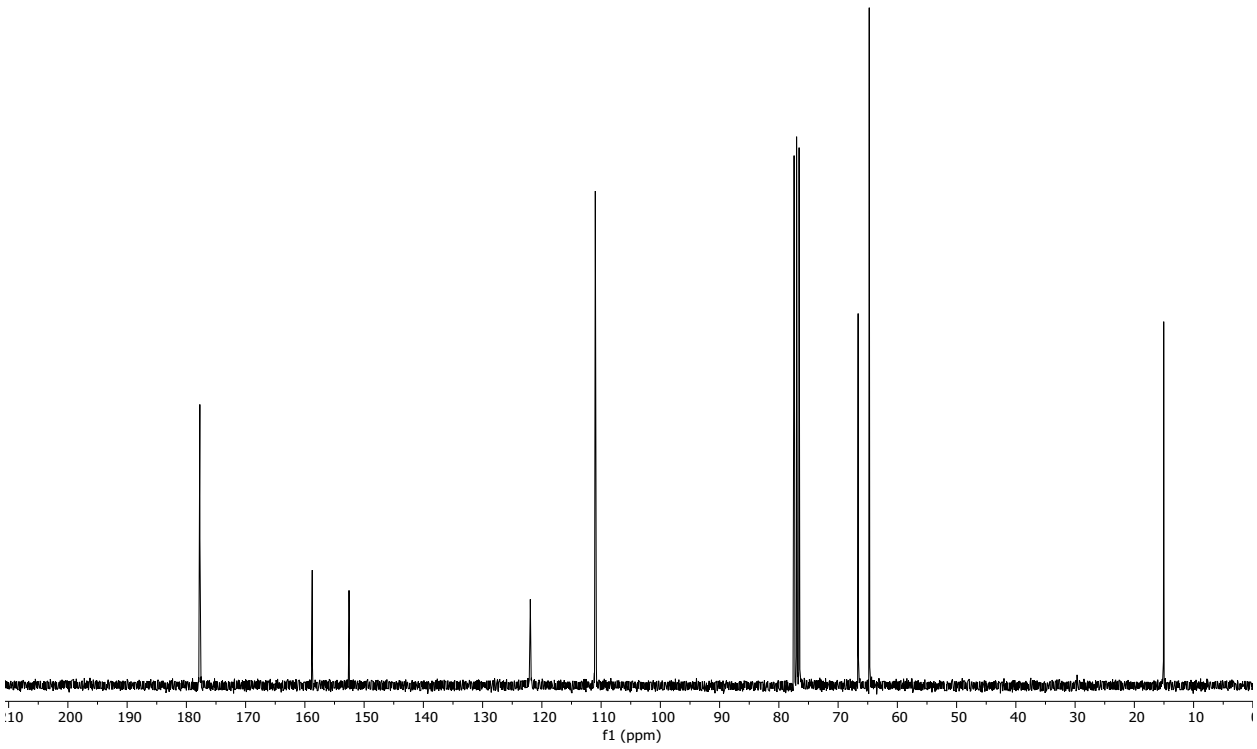


Fig. S12 ^{13}C NMR (75 MHz; $CDCl_3$) of EMF.

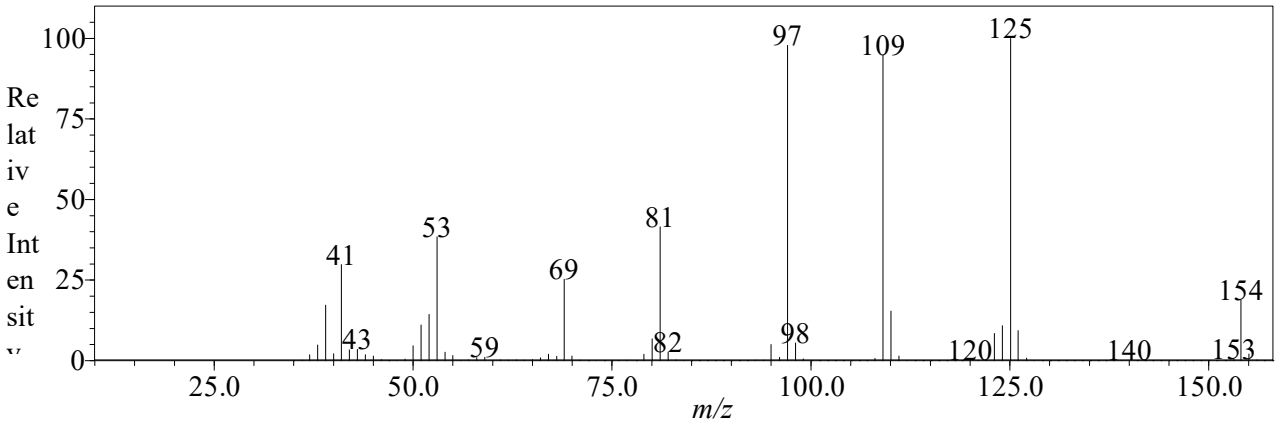


Fig. S13 EMF mass spectrum.

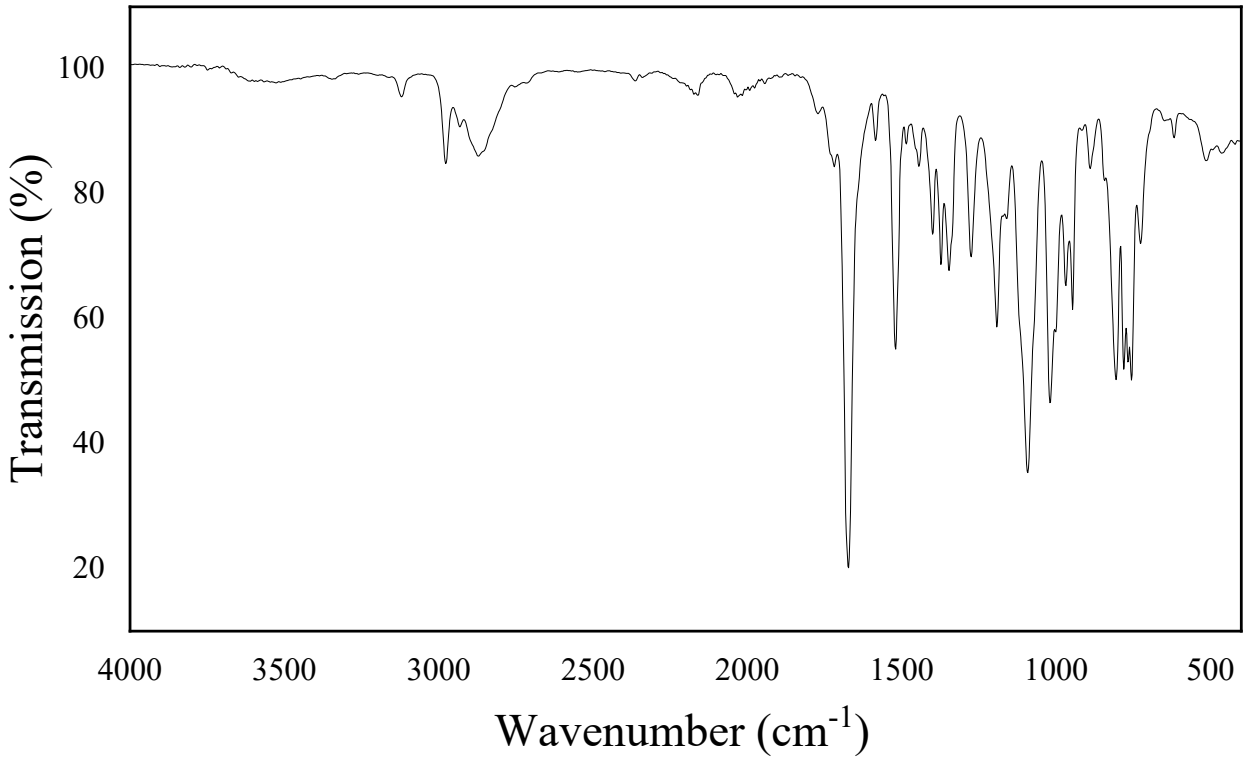


Fig. S14 EMF infrared spectrum.

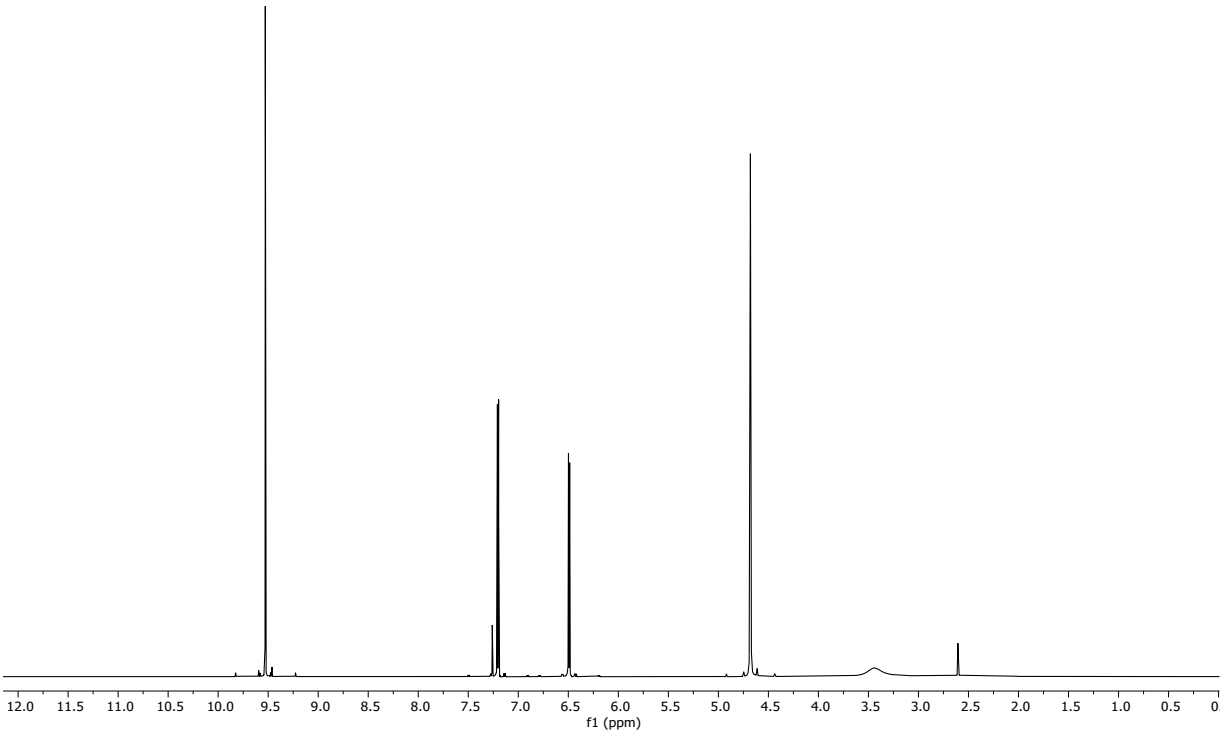


Fig. S15 ^{1}H NMR (300 MHz; $CDCl_3$) of 5-hidroxymethylfurfural.

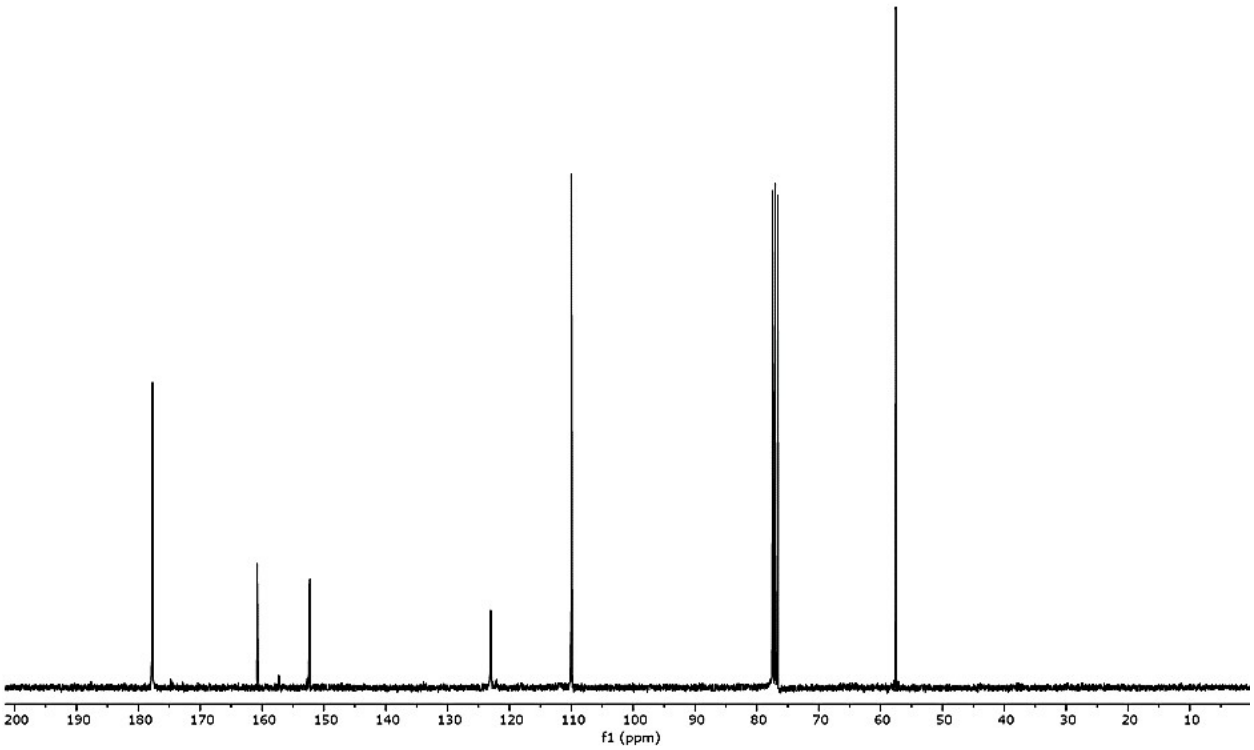


Fig. S16 ^{13}C NMR (75 MHz; $CDCl_3$) of 5-hydroxymethylfurfural.

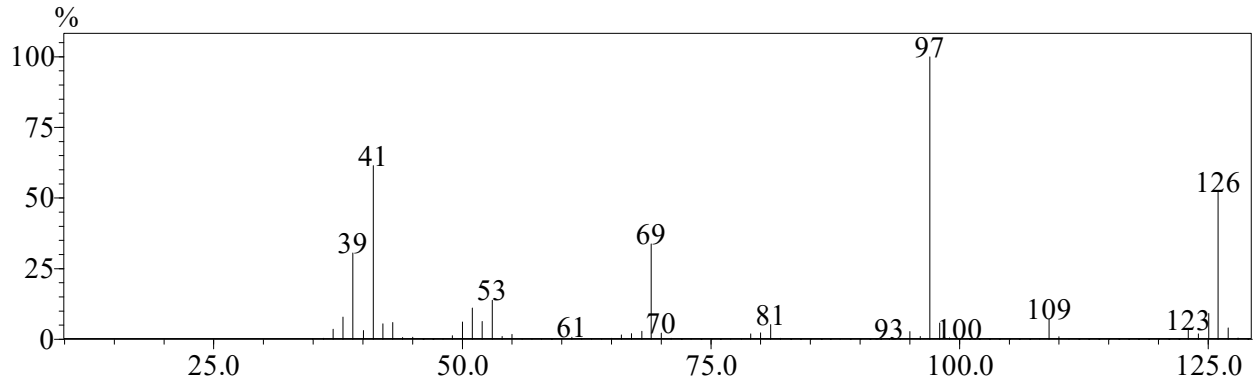


Fig. S17 5-hydroxymethylfurfural mass spectrum.

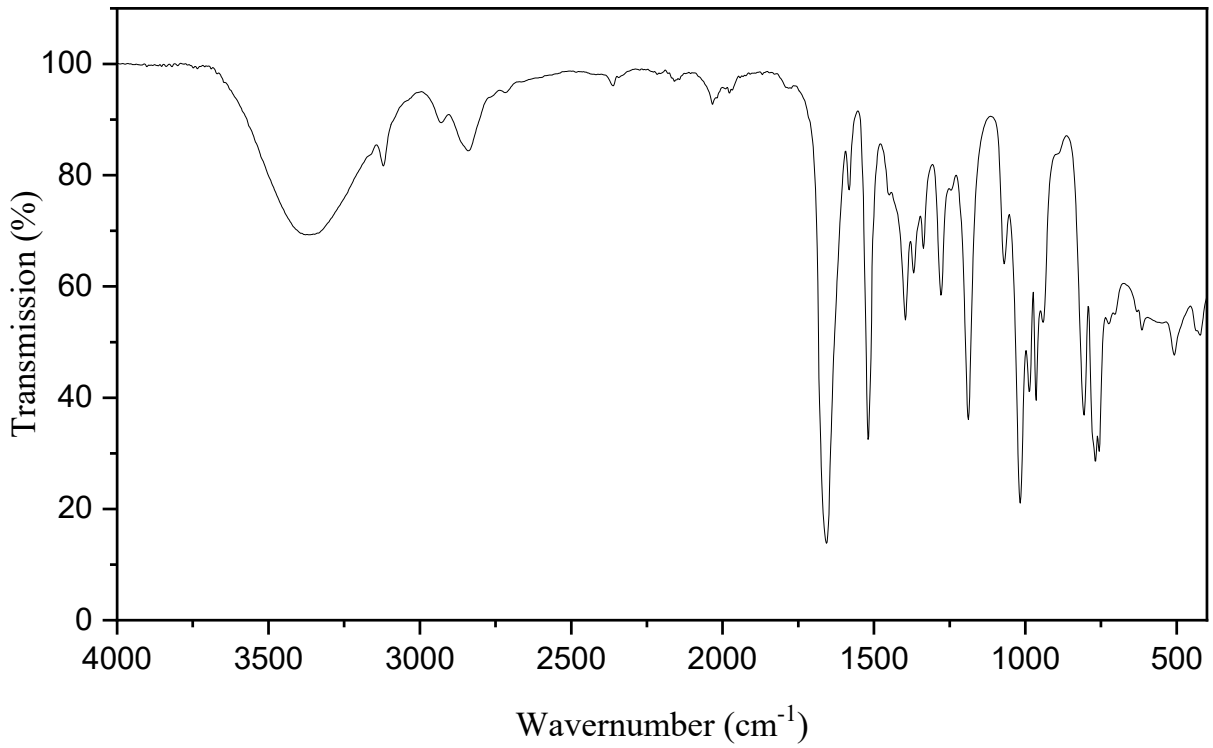
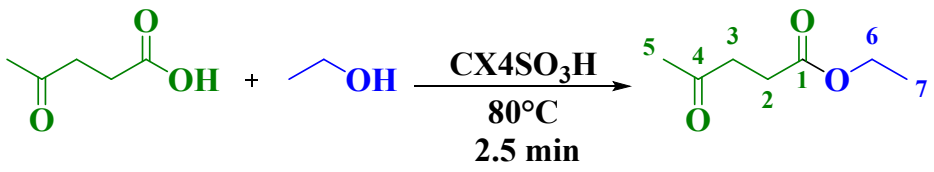


Fig. S18 5-hydroxymethylfurfural infrared spectrum.

Ethy Levulinate (EL)

An experiment to synthesize EL was set up according to the methodology already reported in the literature by Castro et al [4] (Scheme 5), in order to obtain the ester to build the calibration curve.



Scheme 5 Synthesis of EL.

^{1}**H NMR** (300 MHz, $CDCl_3$): 1.24 (t, *J* = 7.1 Hz, 3H, H-7), 2.18 (s, 3H, H-5), 2.56 (t, *J* = 7.0 Hz, 2H, H-3), 2.74 (t, *J* = 7.0 Hz, 2H, H-2), 4.12 (q, *J* = 7.1 Hz, 2H, H-6).

^{13}**C NMR** (75 MHz, $CDCl_3$): 14.1 (C-7), 28.0 (C-2), 29.9 (C-5), 37.9 (C-3), 60.6 (C-6), 172.7 (C-4), 206.7 (C-1).

GC/MS *m/z* (abundancy %): 144 (4, M+), 129 (21), 99 (71), 43 (100).

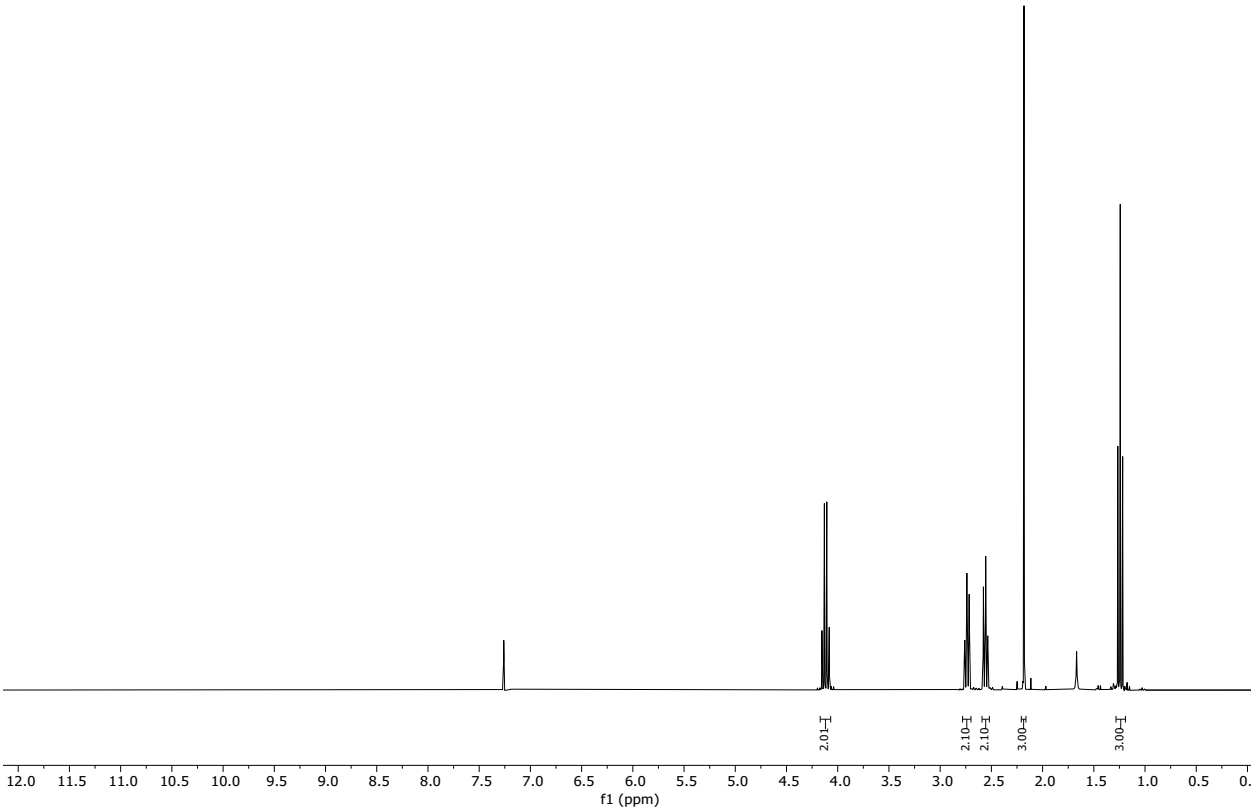


Fig. S19 ^{1}H NMR (300 MHz; $CDCl_3$) of EL.

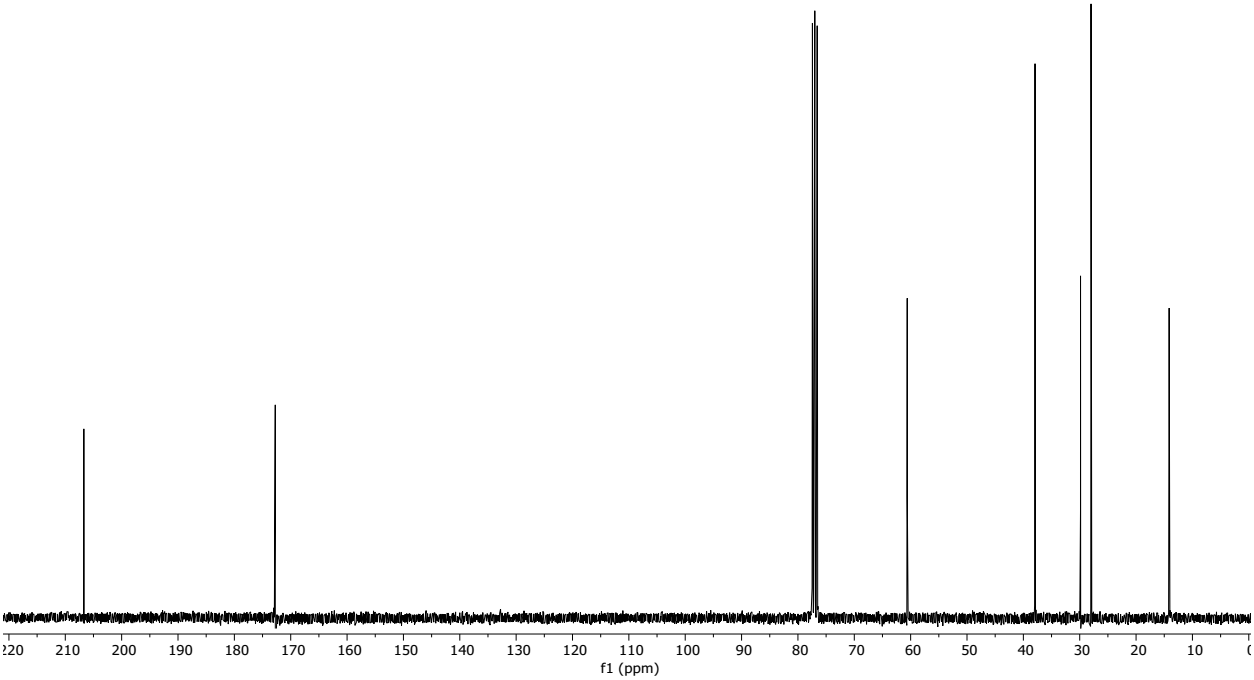


Fig. S20 ^{13}C NMR (75 MHz; $CDCl_3$) of EL.

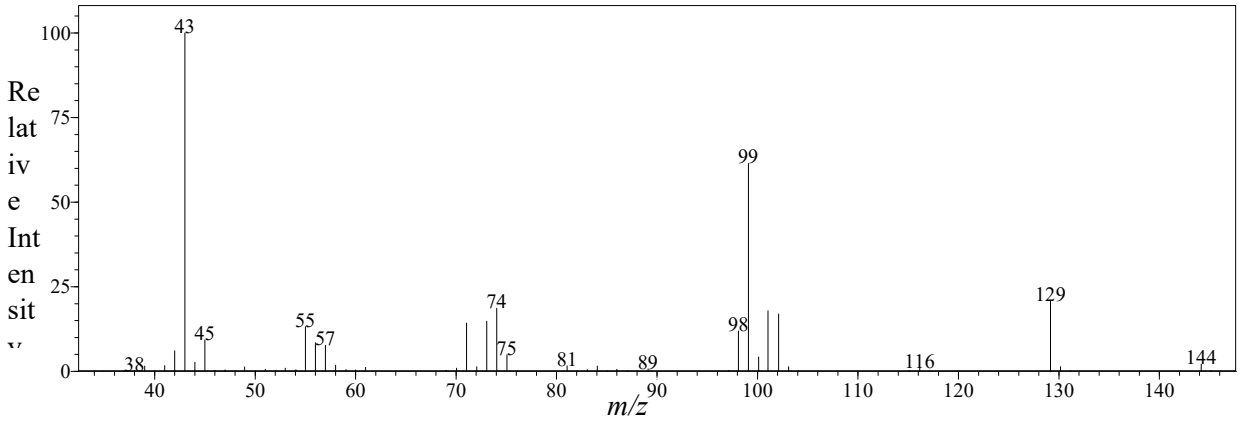


Fig. S21 EL mass spectrum.

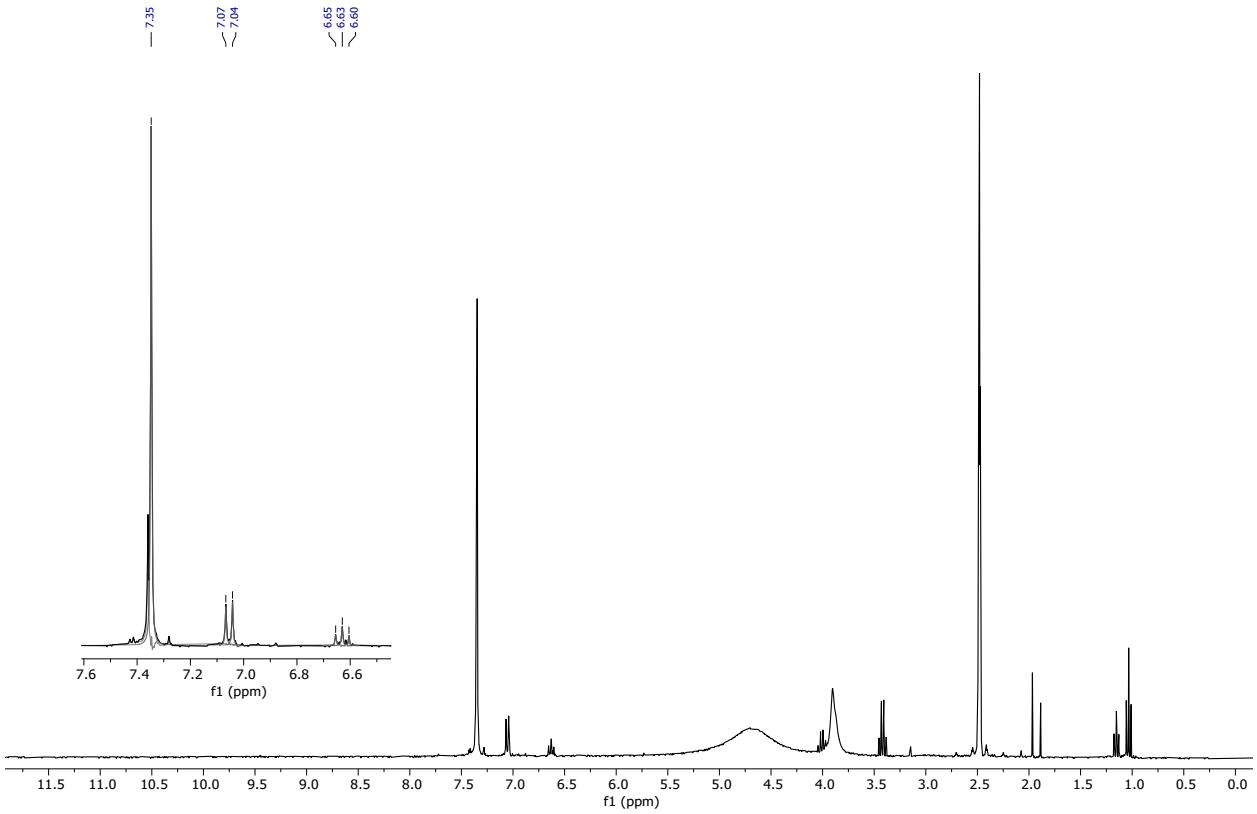


Fig. S22 ^{1}H NMR (300 MHz; DMSO-d_6) of $CX4SO_3H$ catalyst recovered after reaction.

Fructose conversion under optimal conditions

After determining the optimal conditions for converting fructose to EMF (140 °C, 20 min, 1.0 mol% $CX4SO_3H$), an experiment was carried out to determine the conversion of fructose. For this, after an experiment under optimized conditions, the entire reaction mixture was transferred to a 5 mL flask, which had its volume measured with Milli-Q water. After homogenization of this solution, it was filtered through a 45 μm cellulose acetate filter. Then, an aliquot with a volume of 20 μL was injected into a high performance liquid chromatography system with a refractive index detector (HPLC-RI), using a Thermo Scientific Accela LC liquid chromatograph (refractive index (RI) detector, auto-injector and Accela pump) (Thermo Fischer Scientific, TX, USA). The method used had the following specifications: column Rezex RFQ-Fast Acid H+ (8%) (100 x 7.8 mm), mobile phase H_2SO_4 5 mM, flow of 0.5 mL min^{-1}, oven temperature of 60 °C. After analysis, it was found that 99% of the fructose was converted under optimal reaction conditions.

References

(1) Gutsche, C.; Iqbal, M. P-Tert-Buthylcalix[4]Arene. *Org Synth* **1990**, *68*, 234.

(2) Casnati, A.; Ca', N. Della; Sansone, F.; Ugozzoli, F.; Ungaro, R. Enlarging the Size of Calix[4]Arene-Crowns-6 to Improve Cs +/K+ Selectivity: A Theoretical and Experimental Study. *Tetrahedron* **2004**, *60* (36), 7869–7876. https://doi.org/10.1016/j.tet.2004.06.058.

(3) Shinkai, S.; Mori, S.; Tsubaki, T.; Sone, T.; Manabe, O. New Syntheses of Calixarene-p-Sulphonates and p-Nitrocalixarenes. *J. CHEM. SOC. PERKIN TRANS.* **1987**, 2297–2299.

(4) Castro, G. A. D.; Fernandes, S. A. Microwave-Assisted Green Synthesis of Levulinate

Esters as Biofuel Precursors Using Calix[4]Arene as an Organocatalyst under Solvent-Free Conditions. *Sustain. Energy Fuels* **2021**, *5* (1), 108–111. https://doi.org/10.1039/d0se01257b.