Supplementary Information

Formation of a Renewable Amide, 3-acetamido-5-acetylfuran, via Direct Conversion of N-acetyl-D-glucosamine

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Contents:

S1. General Information

N-acetyl-D-glucosamine (95%) was purchased from Toronto Research Chemicals. 1-butyl-3-methylimidazolium chloride ([BMim]Cl), 1-butyl-2,3-dimethylimidazolium chloride ([BMmim]Cl), chlorobutane, bromoethane, 1-methylimidazole and silver acetate were purchased from Alfa-Aesar. All solvents and chemicals were used as obtained from commercial suppliers, unless otherwise indicated. Centrifugation was performed on an Eppendorf centrifuge 5430 (2500 rpm, 1 min).^{1}H and ^{13}C NMR spectra were recorded on Bruker 500 and 300 MHz spectrometers. Gas chromatography-mass spectrometry (GC-MS) was performed on an Agilent 7890A GC system coupled with an Agilent 5975C MS detector that was equipped with a capillary column DB-5 (column length: 30.0 m and column diameter: 0.25 mm). Microwave reactions were performed using a Biotage Initiator 2.5 microwave reactor (0.5 – 2.0 mL reaction volume vials. The 'very high' absorption level setting was used each time to ensure controlled heating of the reaction mixture. IR Spectra were recorded using a Bruker Alpha FTIR spectrometer (4 cm^{-1} resolution) using a diamond ATR single reflectance module (24 scans).

S2. Experimental Procedure

In a typical reaction: N-acetyl-D-glucosamine (0.100 g, 0.426 mmol) and [BMim]Cl (0.750 g) were placed in a MW vial. This mixture was warmed to 100 °C for 1 min using a water bath to melt the ionic liquid. The reaction mixture was subsequently loaded into a Biotage Initiator MW reactor and heated for an appropriate amount of time. HPLC grade EtOAc was used to extract the mixtures and prepare samples for analysis, as described below (S3). The given extracts ranged from pale yellow to golden brown.

For isolated yields: 3A5AF was purified using flash chromatography (FC) Biotage Isolera One. A silica column (SNAP cartridge, silica, 10 g) and a variable 200-400 nm wavelength detector at 254 and 293 nm were used. The sample was previously analyzed on SiO_2 TLC plates using a 50% ethyl acetate/hexanes mixture and the retention factor (R_f) obtained was transferred to the FC instrument. The R_f was 0.13. Samples of the product were combined. After evaporating the solvent using the evaporator at 50 °C until dryness, the dried residue was placed vacuum using a standard Schlenk line overnight. CHN microanalytical data (Canadian Microanalytical Service, Delta, BC) were in agreement with the formulation $C_8H_9NO_3$. For three reactions performed under identical conditions (Table 2, entry 4), isolated yields were 57-58%.

S3. 3A5AF Quantification Procedure

A typical reaction mixture was unsealed and an aliquot taken (ca. 5-10% w/w). 100 µL of (2.00 mg/mL) acetophenone (GC-internal standard) was added along with 500 µL of deionized water and 3.00 mL HPLC grade EtOAc. The reaction was centrifuged at 2,500 rpm for 1 min, and the organic layer decanted and kept. Two further extractions with 3.00 mL EtOAc were performed yielding a total of ca. 9.00 mL of extract, which was concentrated on a Buchi Rotavap yielding a pale yellow oil. This was diluted with 500 µL of EtOAc and analyzed via GC-MS (Agilent Technologies 5975C VL MSD) for quantification using the calibration curve shown below.

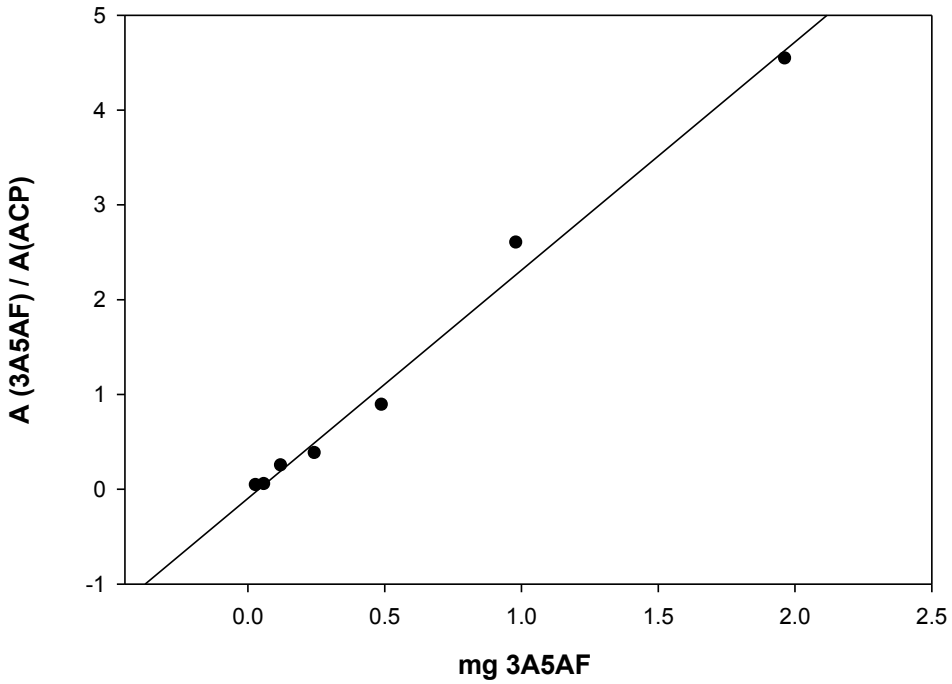


Fig. S3. Standard curve of authentic 3A5AF in Ethyl Acetate (R^2 = 0.9899), where ACP = acetophenone.

Analytical data for 3A5AF

^{1}H NMR δ_H (298K, 500 MHz, DMSO-d_6) 2.02 (s, 3H), 2.40 (s, 3H) 7.18 (d, J = 0.8 Hz, 1H), 8.18 (d, J = 0.8 Hz, 1H), 10.23 (s, 1H); ^{13}C NMR δ_C (298K, 75 MHz, DMSO-d_6) 22.81, 25.85, 110.99, 127.03, 135.25, 149.75, 167.88, 186.04; MS, *m/z* (% ion) 167 (49), 125 (88), 110 (100),

96 (15), 83 (17), 69(9), 54(13); HRMS, *m/z*: Anal. Calcd: 167.0582 (M^+) Found: 167.0584 (M^+); Selected IR data (KBr, cm^{-1}) 1668 (s).

S4. Sample GC Trace/ MS Spectrum

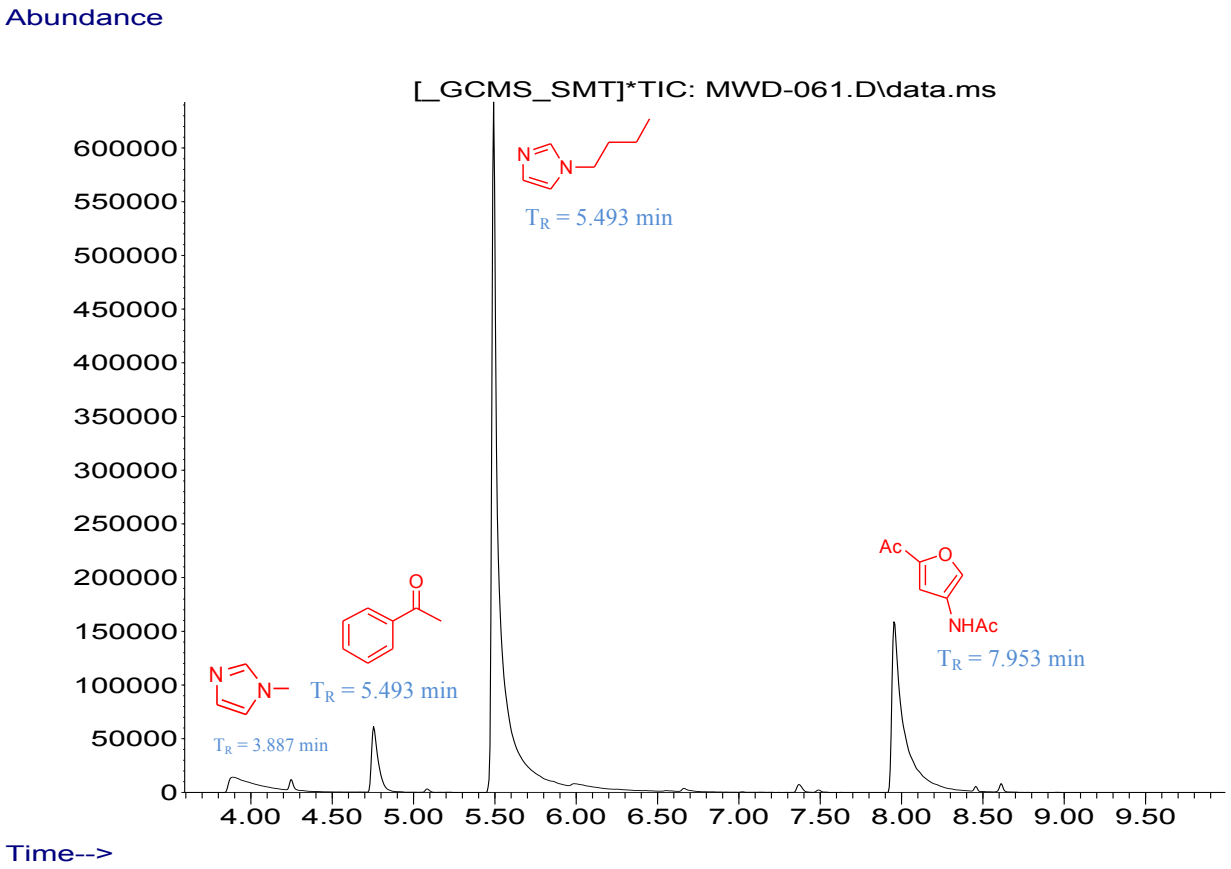


Fig. S4a. Sample GC-MS chromatogram of a representative reaction mixture producing 3A5AF from N-acetyl-D-glucosamine and 1-butyl-3-methylimidazolium chloride.

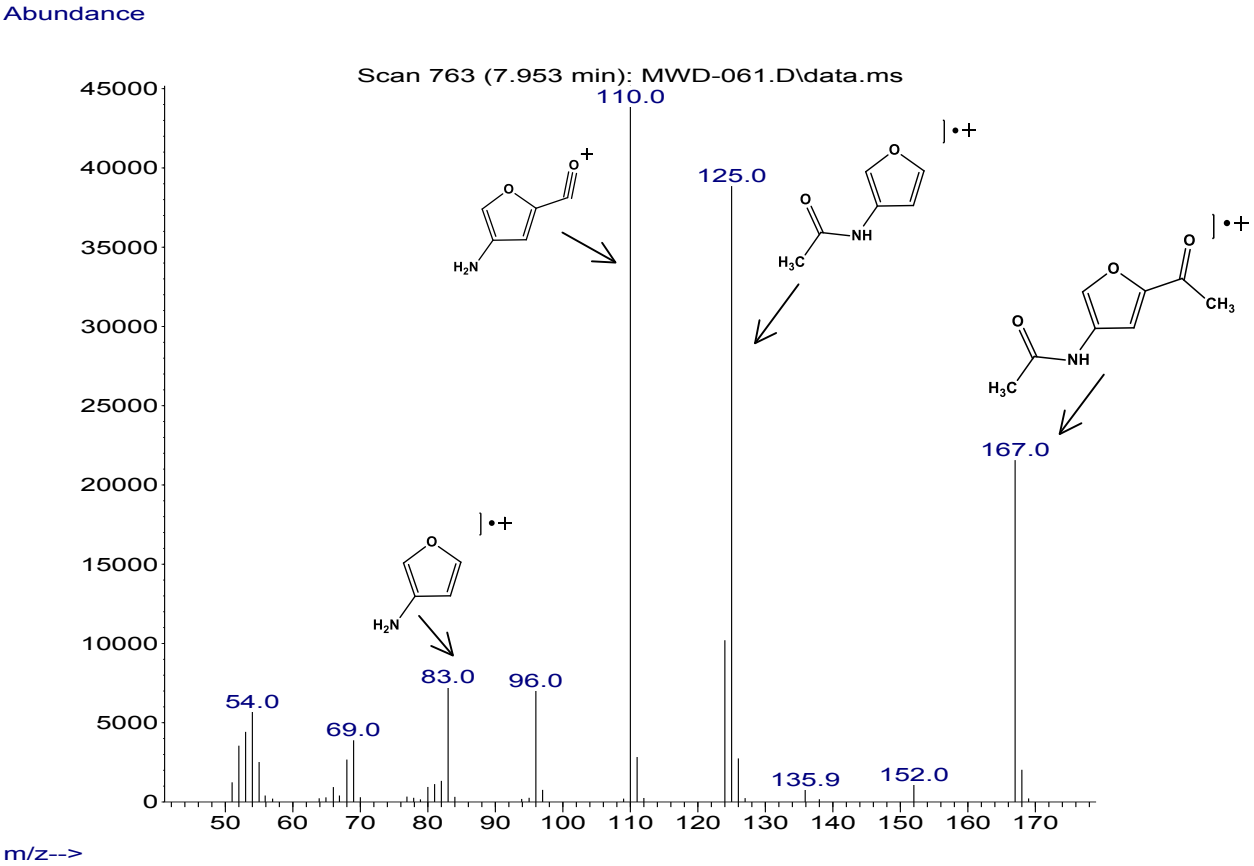
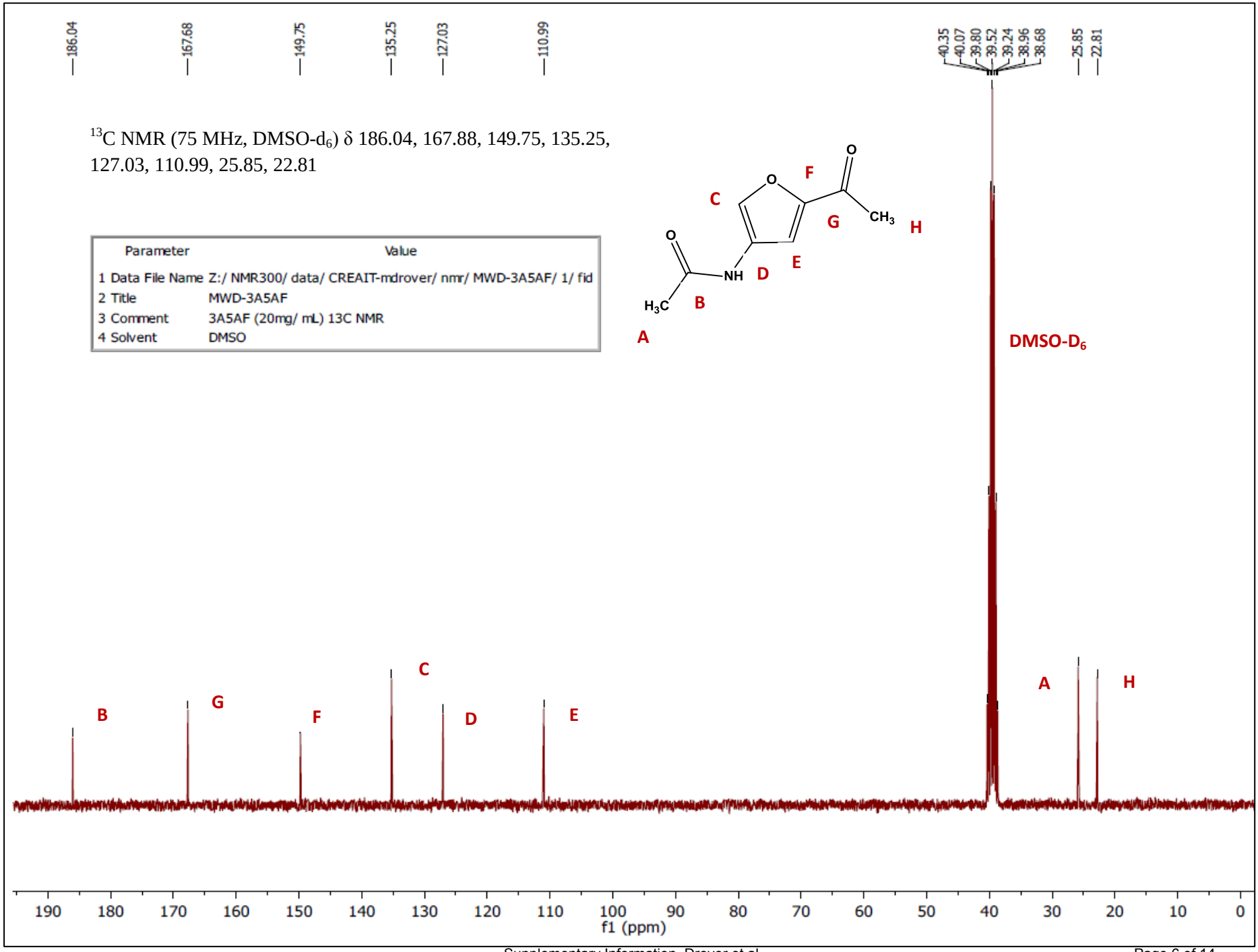
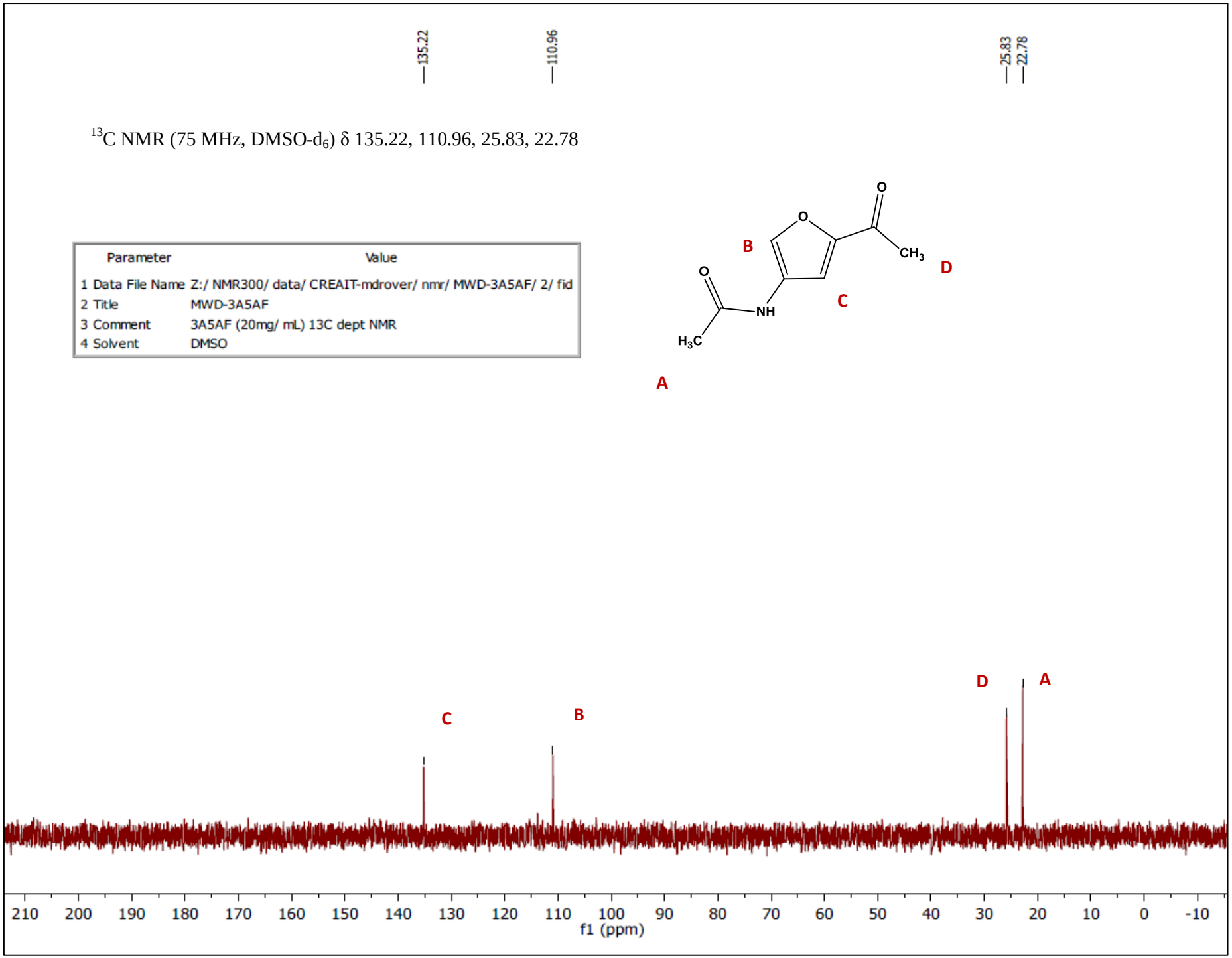
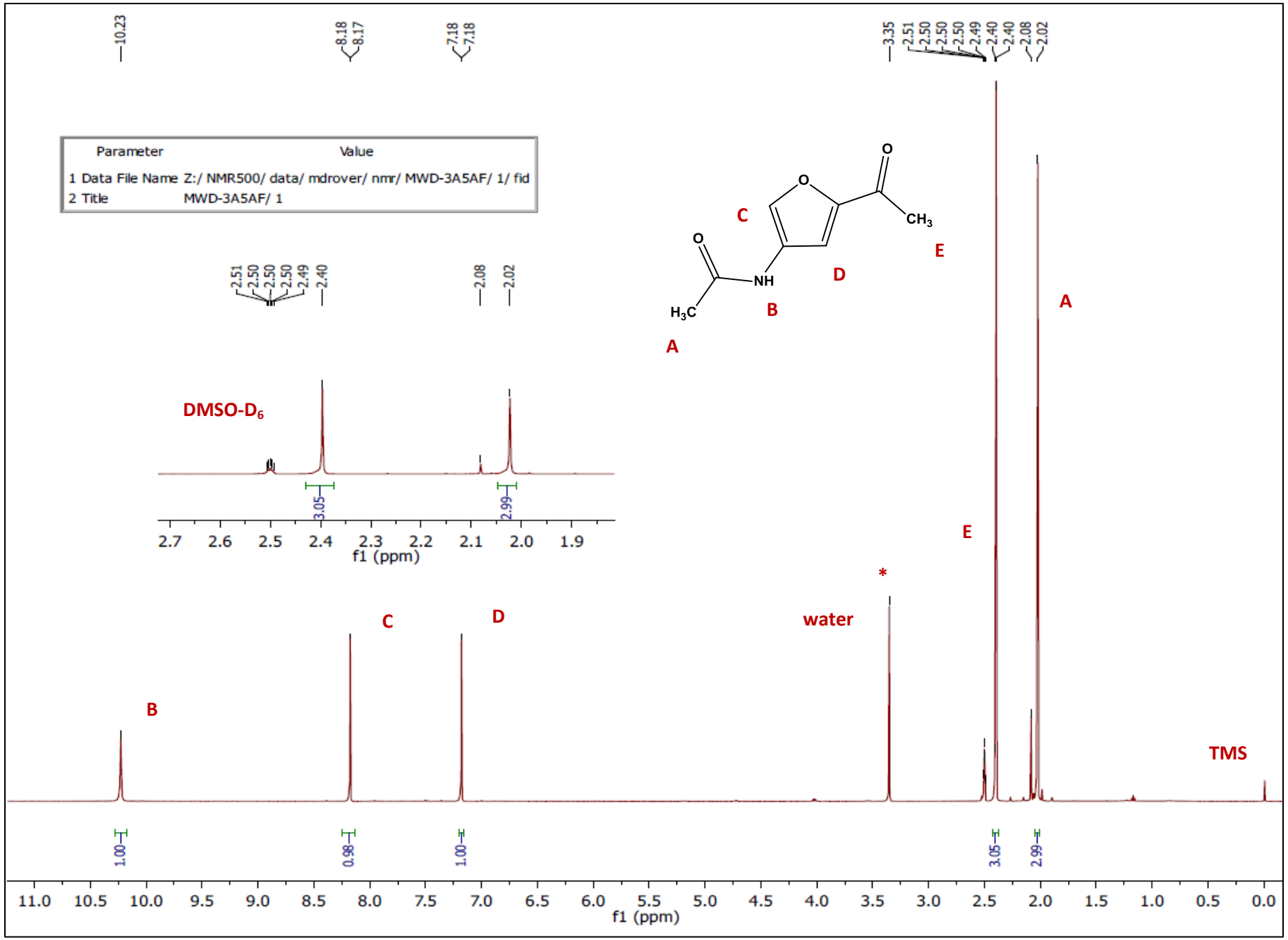


Fig. S4b. Sample MS chromatogram of 3A5AF showing both the base peak and molecular ion peak, along with other peaks of interest.







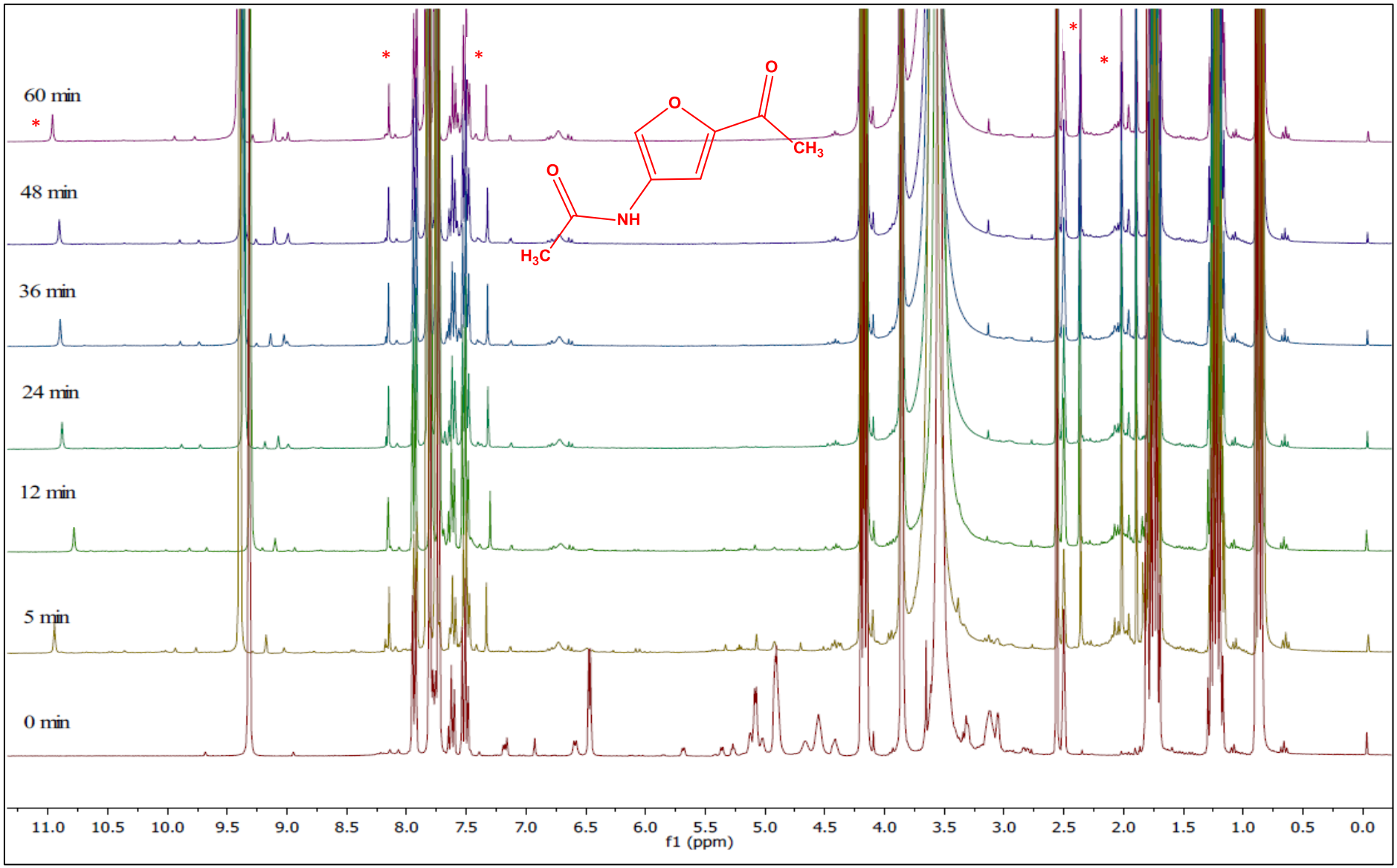
^{1}H NMR (500 MHz, DMSO-d_6) δ 10.23 (s, 1H), 8.18 (d, *J = 0.8Hz*, 1H), 7.18 (d, *J = 0.8 Hz*, 1H), 2.40 (s, 3H), 2.02 (s, 3H).

S6b. Timed Reaction at 200 ^{o}C (Sample Stacked ^{1}H NMR Spectra, see next page)

Strong peaks found between ca. 0.25 – 2.25, 4.25, 7.50 and 9.25 ppm are assigned to [BMim]Cl; mid-field peaks found in the 4.25 – 7.25 ppm region are characteristic peaks attributable to N-acetyl-D-glucosamine. The peaks at ca. 11.00, 7.25, 8.25, 2.40 and 2.00 ppm are typical signals of 3-acetamido-5-acetylfuran. As reaction time is increased the peaks in mid-field decrease in intensity, while those of the product begin to increase, and those of the ionic liquid remain the same. The spectra recorded after 24 mins shows the peaks of N-acetyl-D-glucosamine to be nearly gone. No other products were identifiable during this process. Likewise, resonances due to acetophenone are also present at ca. 2.51 and 7.50-7.75 ppm (used as an internal standard). Also note the above reaction consisted of 33wt% NAG (ca. 425 mg) in 1.00 g [BMim]Cl at 200 ^{o}C. * - Indicates product formation.

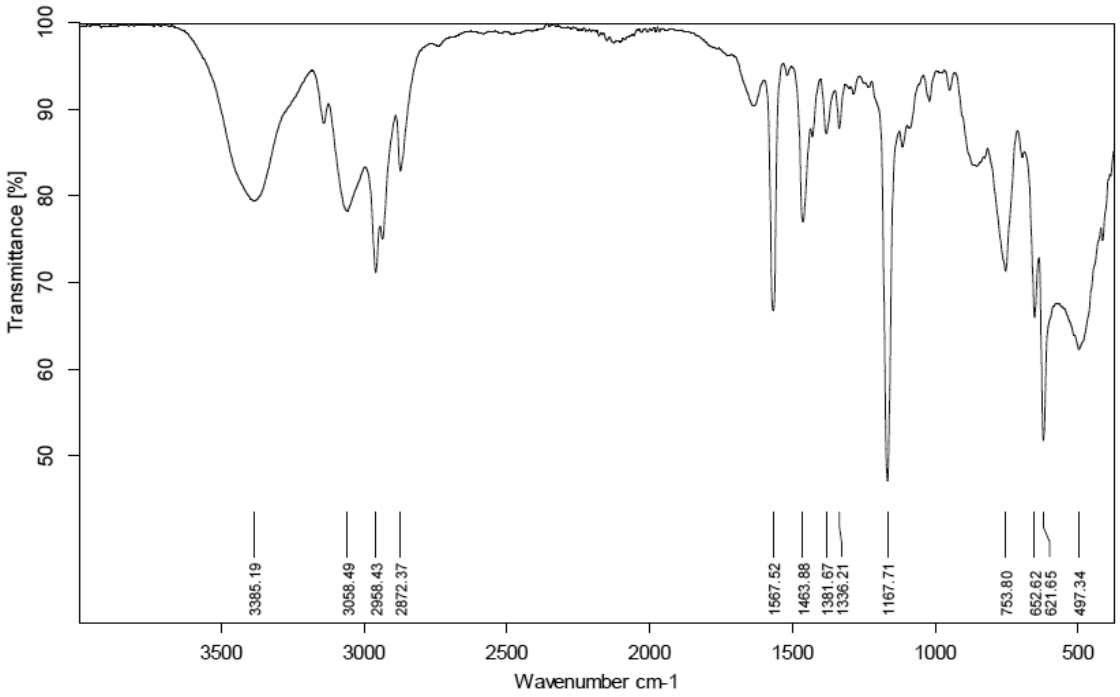
S6c. NMR Sample Preparation Procedure for Kinetic data

33 wt% of NAG (425 mg) was added to 1.00g of [BMim]Cl in a vial, and the reaction was heated using an oil bath at the given temperature for 2 h. After a given amount of time, an aliquot of the reaction mixture was removed (20-60 mg) and to it was added 3.00 μL (3.0-4.5 mg) of acetophenone in a small vial. To this, was added 500 μL of DMSO-d_6 and the appropriate NMR experiment run. With an accurately measured amount of reference material, the sugar (or material of interest) could be integrated to 1 and the $-CH_3$ group of acetophenone accordingly integrated. Bearing this in mind, the amount of sugar could be calculated at any given time, t, allowing for the plotting of first order rate plots, thereby affording a method to identify the activation energy for the decomposition of NAG.

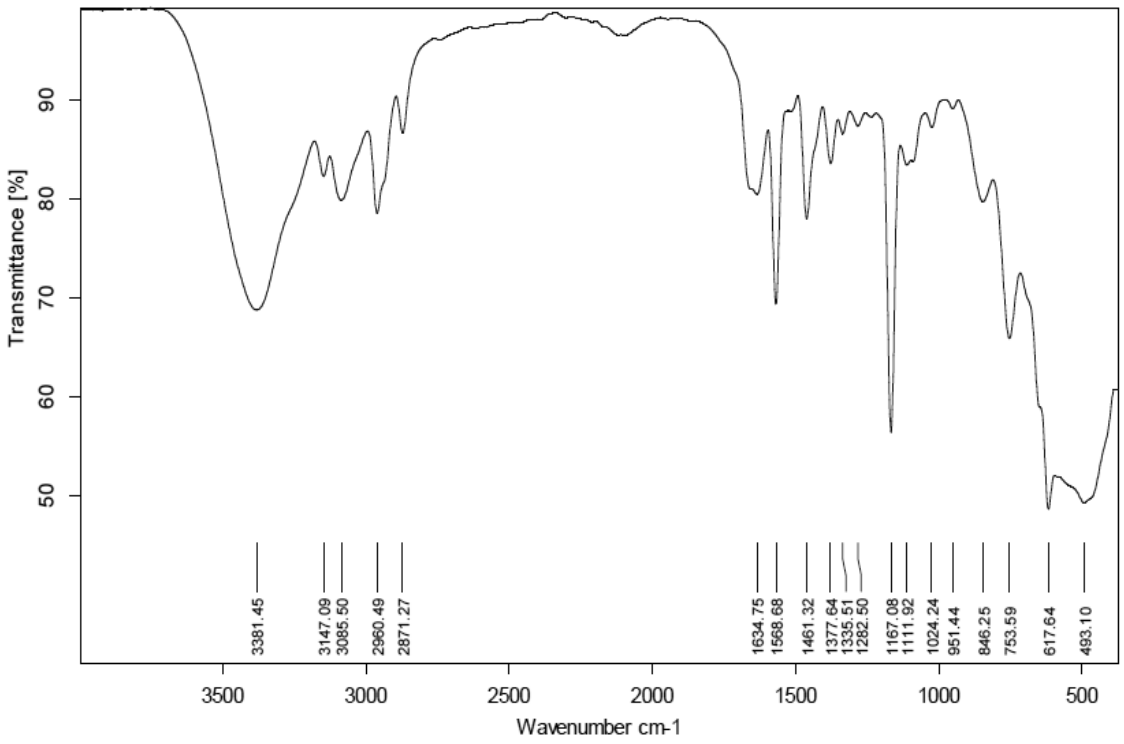


S7. Ionic Liquid Recyclability Study ([BMim]Cl before (a) and after (b) reaction)

a.

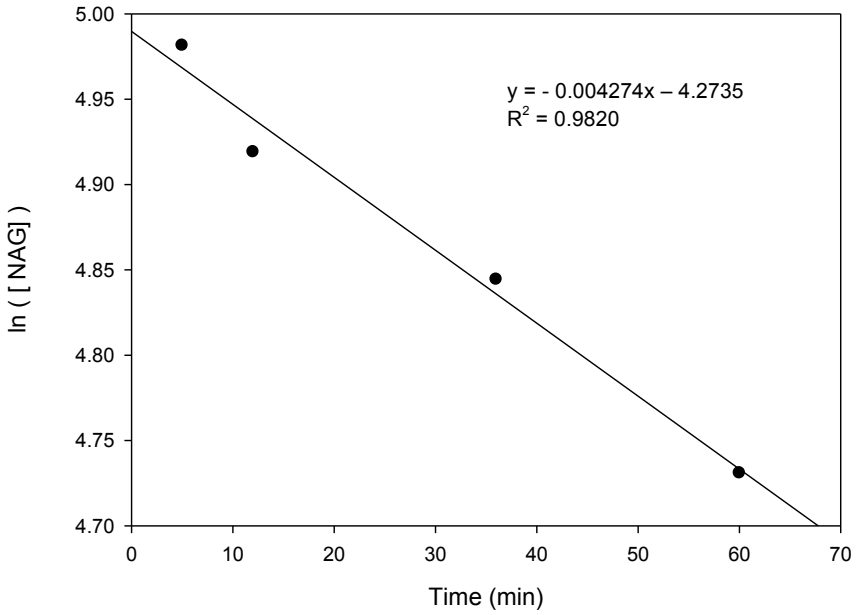


b.

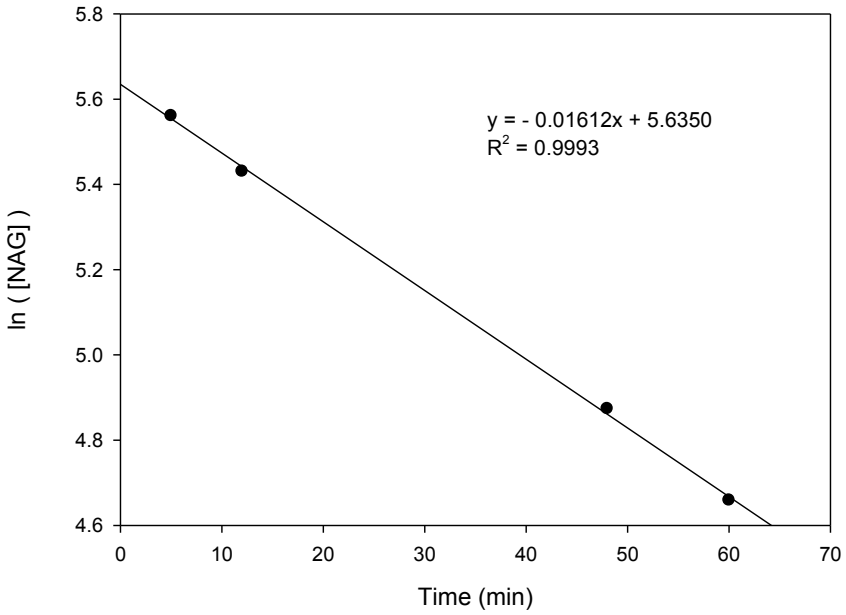


S8. First-Order Rate Plots at (a) 140, (b) 160, (c) 180 and (d) 200 ^{o}C

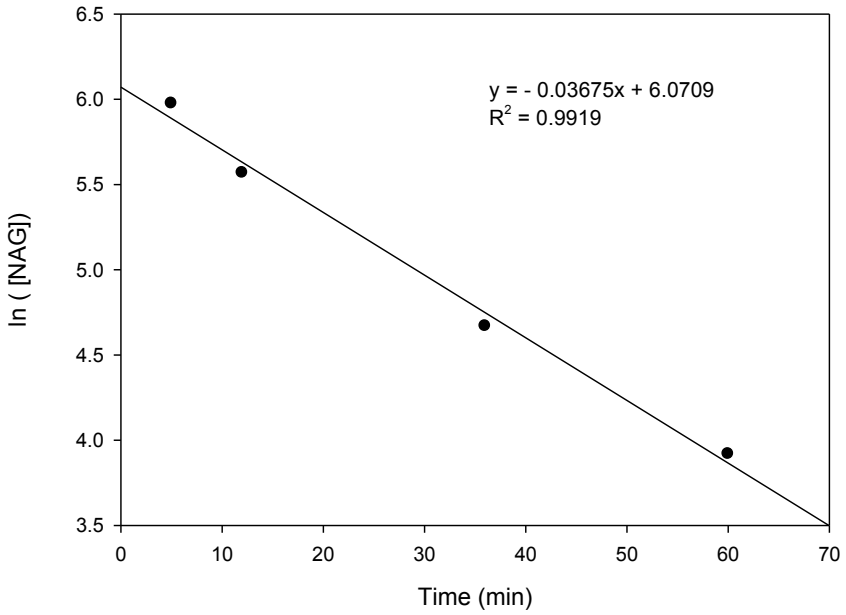
a.



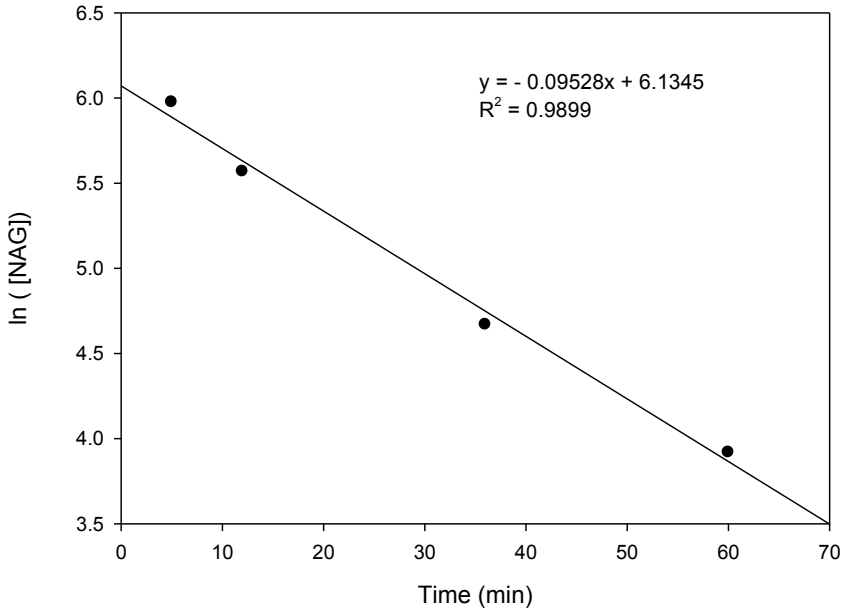
b.



c.



d.



S9. Kinetics Data Used for the Arrhenius Plot

Temperature (^{o}C)	Temperature (K)	1/ T (K^{-1})	K_{obs}	ln(k_{obs})
140	413	0.00242_0	0.004274	-5.4552
160	433	0.00230_9	0.01612	-4.1277
180	453	0.00220_7	0.03675	-3.3036
200	473	0.00211_4	0.09528	-2.3509