Supporting Information

Sonogashira Coupling Reactions in Biodegradable Ionic Liquids Derived from Nicotinic Acid

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Sonogashira Reactions

Starting materials were purchased from Sigma-Aldrich and had a purity of 96% or greater. Melting points were determined on an Electrothermal melting point apparatus and are uncorrected. All ^{1}H NMR spectra were recorded on a Bruker Avance DPX 300 spectrometer at 300.13 MHz. All ^{13}C NMR spectra were recorded on a Varian Unity Inova 600 spectrometer at 150.8 MHz, or on a Bruker Avance DPX 300 spectrometer at 75.4 MHz. Unless stated otherwise, $CDCl_3$ was used as the solvent for NMR samples. Low resolution electrospray mass spectra (LRMS) using electrospray ionisation (ESI) were obtained on a Micromass Platform II spectrometer. Unless otherwise stated, the cone voltage was 20 eV. Kinetics studies were performed using an Agilent 110 liquid chromatograph (LC) equipped with an Agilent – Zorbax reverse phase column (5 μm particle size; 4.6 mm x 150 mm). The ILs used as solvents for Sonogashira couplings were typically dried under high vacuum while heating at 60^{o}C.

1,2-Diphenylethyne. White solid. Yield 86%. mp 59–60 ^{o}C. ^{1}H NMR δ 7.42–7.47 (m, 6H), 7.61–7.64 (m, 4H). ^{13}C NMR δ 89.6 123.5, 128.5, 128.6, 131.8.

1-Methoxy-4-(phenylethynyl)benzene. White solid. Yield 47%. mp 56–58 ^{o}C. ^{1}H NMR δ 3.84 (s, 3H), 6.88–6.91 (m, 2H), 7.31–7.38 (m, 3H) 7.47–7.54 (m, 4H). ^{13}C NMR δ 55.5, 88.3, 89.6, 114.2, 115.6, 123.8, 128.1, 128.5, 131.7, 133.3, 159.8.

1-(4-(Phenylethynyl)phenyl)ethanone. White solid. Yield 88%. mp 95–97 ^{o}C. ^{1}H NMR δ 2.63 (s, 3H), 7.37–7.40 (m, 3H), 7.55–7.58 (m, 2H), 7.61–7.64 (m, 2H) 7.94–7.97 (m, 2H). ^{13}C NMR δ 26.8, 88.8, 92.9, 122.8, 128.4, 128.5, 128.6, 129.0, 131.9, 131.9, 136.3, 197.5.

1-Methyl-4-(phenylethynyl)benzene. White solid. Yield 60%. mp 66–68 ^{o}C. ^{1}H NMR δ 2.38 (s, 3H), 7.16–7.18 (d, J = 7.8 Hz, 2H), 7.32–7.37 (m, 3H), 7.43–7.45 (m, 2H) 7.51–7.55 (m, 2H). ^{13}C NMR δ 21.7, 88.9, 89.8, 120.4, 123.7, 128.3, 128.5, 129.3, 131.7, 131.8, 138.6.

Ethyl 4-(phenylethynyl)benzoate. Yellow solid. Yield 93%. mp 74–76 ^{o}C. ^{1}H NMR δ 1.39–1.44 (t, J = 7.1 Hz, 3H), 4.36–4.44 (q, J = 7.1 Hz, 2H), 7.35–7.39 (m, 3H), 7.54–7.61 (m, 4H), 8.02–8.05 (m, 2H), ^{13}C NMR δ 14.5, 61.3, 88.9, 92.5, 122.9, 128.1, 128.6, 128.9, 129.7, 130.0, 131.7, 131.9, 166.3.

2-(Phenylethynyl)naphthalene. White solid. Yield 78%. mp 111–113 ^{o}C, ^{1}H NMR δ 7.37–7.44 (m, 3H), 7.49–7.55 (m, 2H), 7.59–7.63 (m, 3H), 7.82–7.87 (m, 3H), 8.08–8.09 (m, 1H). ^{13}C NMR δ 90.0, 90.02, 120.8, 123.5, 126.8, 126.9, 128.0, 127.98, 128.2, 128.5, 128.6, 128.62, 131.6, 131.9, 133.0, 133.2.

(4-(Phenylethynyl)phenyl)methanol. White solid, Yield 72%. mp 119–121 ^{o}C, ^{1}H NMR δ 1.85 (br s, 1H), 4.71 (s, 2H), 7.35–7.37 (m, 5H), 7.53–7.56 (m, 4H), ^{13}C NMR δ 65.2, 89.4, 89.6, 122.7, 123.4, 127.0, 128.5, 128.6, 131.8, 132.0, 141.2.

4-(Phenylethynyl)phenyl acetate. White solid, Yield 81%. mp 101–103 ^{o}C. ^{1}H NMR δ 2.32 (s, 3H), 7.10–7.13 (d, J = 8.7 Hz, 2H), 7.36–7.38 (m, 3H), 7.54–7.59 (m, 4H). ^{13}C NMR δ 21.3, 88.7, 89.6, 121.1, 121.9, 123.2, 128.5, 128.5, 131.8, 132.9, 150.6, 169.3.

4-(Phenylethynyl)phenyl benzoate. White solid, Yield 76%. mp 121–123 ^{o}C. ^{1}H NMR δ 7.23–7.26 (m, 2H), 7.36–7.41 (m, 3H), 7.50–7.69 (m, 7H), 8.21–8.24 (m, 2H). ^{13}C NMR δ 88.8, 89.7, 121.2, 122.0, 123.3, 128.5, 128.53, 128.8, 129.4, 130.4, 131. 8, 133.0, 133.9, 150.9, 165.0.

1-Nitro-4-(phenylethynyl)benzene. Yellow solid. Yield 86%. mp 111–113 ^{o}C. ^{1}H NMR δ

7.38–7.43 (m, 3H), 7.56–7.59 (m, 2H), 7.66–7.70 (m, 2H), 8.21–8.26 (m, 2H). ^{13}C NMR δ 87.7, 94.9, 122.3, 123.8, 128.7, 129.5, 130.4, 132.0, 132.4, 147.1.

4-(Phenylethynyl)benzyl acetate. Yellow solid. Yield 93%. mp 57–59 ^{o}C. ^{1}H NMR δ 2.13 (s, 3H), 5.13 (s, 2H), 7.34–7.39 (m, 5H), 7.54–7.58 (m, 4H). ^{13}C NMR δ 21.1, 65.9, 89.1, 90.0, 123.2, 123.3, 128.2, 128.5, 131.7, 131.9, 136.1, 170.9.

Methyl 2-(benzoyloxy)-5-(phenylethynyl)-benzoate. White solid. Yield 79%. mp 128–130 ^{o}C. ^{1}H NMR δ 3.72 (s, 3H), 7.18–7.20 (d, J = 8.4 Hz, 1H), 7.31–7.33 (m, 3H), 7.46–7.53 (m, 4H) 7.58–7.63 (m, 1H) 7.68–7.71 (dd, J = 2.1, 8.4 Hz, 1H), 8.17–8.21 (m, 3H). ^{13}C NMR δ 52.5, 87.75, 90.6, 121.8, 122.9, 123.9, 124.5, 128.6, 128.8, 129.4, 130.5, 131.9, 133.9, 135.3, 136.7, 150.6, 164.5, 165.4.

1-(4-Methoxy-3-(phenylethynyl)phenyl)ethanone. Light brown solid. Yield 78%. mp 70–72 ^{o}C. ^{1}H NMR δ 2.58 (s, 3H), 3.97 (s, 3H), 6.93–6.96 (d, J = 8.7 Hz, 1H), 7.34–7.38 (m, 3H), 7.56–7.59 (m, 2H), 7.93–7.97 (dd, J = 2.1, 8.7 Hz, 1H), 8.11–8.12 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 26.5, 56.3, 84.8, 94.3, 110.4, 112.8, 123.2, 128.5, 128.6, 130.2, 130.6, 131.9, 134.4, 163.5, 196.4.

2-(Phenylethynyl)thiophene. White solid. Yield 98%. mp 46–48 ^{o}C. ^{1}H NMR δ 7.03–7.06 (m, 1H), 7.28–7.38 (m, 5H), 7.53–7.56 (m, 2H). ^{13}C NMR δ 82.8, 93.2, 123.1, 123.5, 127.3, 127.4, 128.55, 128.59, 129.4, 131.6, 132.1, 132.7.

3-(Phenylethynyl)thiophene. White solid. Yield 84%. mp 48–50 ^{o}C. ^{1}H NMR δ 7.23–7.25 (m, 1H), 7.30–7.41 (m, 4H), 7.55–7.59 (m, 3H). ^{13}C NMR δ 84.7, 89.1, 122.4, 123.4, 125.6,

128.4, 128.5, 128.8, 130.0, 131.7.

HPLC Method

The appearance of the carboxylic acid IL, the product of the base hydrolysis of the butyl nicotinate based ILs, was monitored using a Agilent 1100 series HPLC with PDA monitoring absorbance at a wavelength of 264 nm. The HPLC was equipped with a Zobax Bonus-RP 4.6 x 150 mm, 5 μm column maintained at a temperature of 20^{o}C. The mobile phase that gave adequate separation between the reactant IL and product IL was found to be 20% methanol, 20% acetonitrile and 60% water flowing at a rate of 0.500 mL/min. Note that all solvents were HPLC grade. The volume of sample injected was set at 5.00 μL. The runtime for each sample was 5 minutes with peak for the product IL appearing at 3.02 minutes.

The base hydrolyses of all four butyl nicotinate based ILs were performed in a 50% v/v methanol-water solutions to improve solubility of the ILs and to allow higher concentrations to be utilized and were monitored using the HPLC. For each reaction equimolar amounts of base and IL were used meaning that initially the reaction solution was 0.250mM in both the IL and base. This was done by transferring 20 μL of the 0.1250M solution of NaOH, with an Eppendorf, into a vial containing 10 mL of the 0.250 mM butyl nicotinate based IL. Each reaction was stirred with a stir bar and was performed at 22^{o}C. An initial sample of the 0.250 mM butyl nicotinate IL with no base was placed in the auto sampler and HPLC was set to run. The base was added to the vial, using an Eppendorf pipette, at the instant the initial sample was injected to into the HPLC so that time at t=0 corresponded to the injection time of the initial sample containing no base. The reaction was monitored by running aliquots of the reaction mixture through the HPLC consecutively with no time between runs. Each aliquot was 30 μL

and was transferred, with an Eppendorf, into a GC vial containing an Agilent 100 μL pulled point glass insert. After 10 aliquots were taken monitoring was ceased.

Standard Curve

Before each reaction, the nine different carboxylic acid IL solutions were run on the HPLC, under the same conditions, so that they could then be used to form a Beer-Lambert plot to relate the area under the carboxylic acid IL peak to the concentration of the carboxylic acid IL.

***n*-Butyl**

Time(s)	[1e]	[1a]	1/[1a]
0	0.00	0.25	4.00
421	0.18	0.07	14.02
837	0.22	0.03	37.79
1260	0.24	0.01	91.02
1679	0.24	0.01	172.73

Isobutyl

Time (s)	**[1e]**	**[1b]**	**1/[1b]**
0	0.00	0.25	4.00
419	0.16	0.09	11.54
839	0.19	0.06	17.89
1260	0.21	0.04	22.36
1674	0.21	0.04	24.78

***sec*-Butyl**

Time (s)	**[1e]**	**[1c]**	**1/[1c]**
0	0.00	0.25	4.00
424	0.10	0.15	6.52
845	0.15	0.10	9.80
1271	0.17	0.08	12.40
1692	0.18	0.07	13.86

***tert*-Butyl**

Time (s)	**[1e]**	**[1d]**	**1/[1d]**
0	0.00	0.25	4.00
418	0.02	0.23	4.28
838	0.03	0.22	4.53
1256	0.04	0.21	4.80
1673	0.05	0.20	4.96

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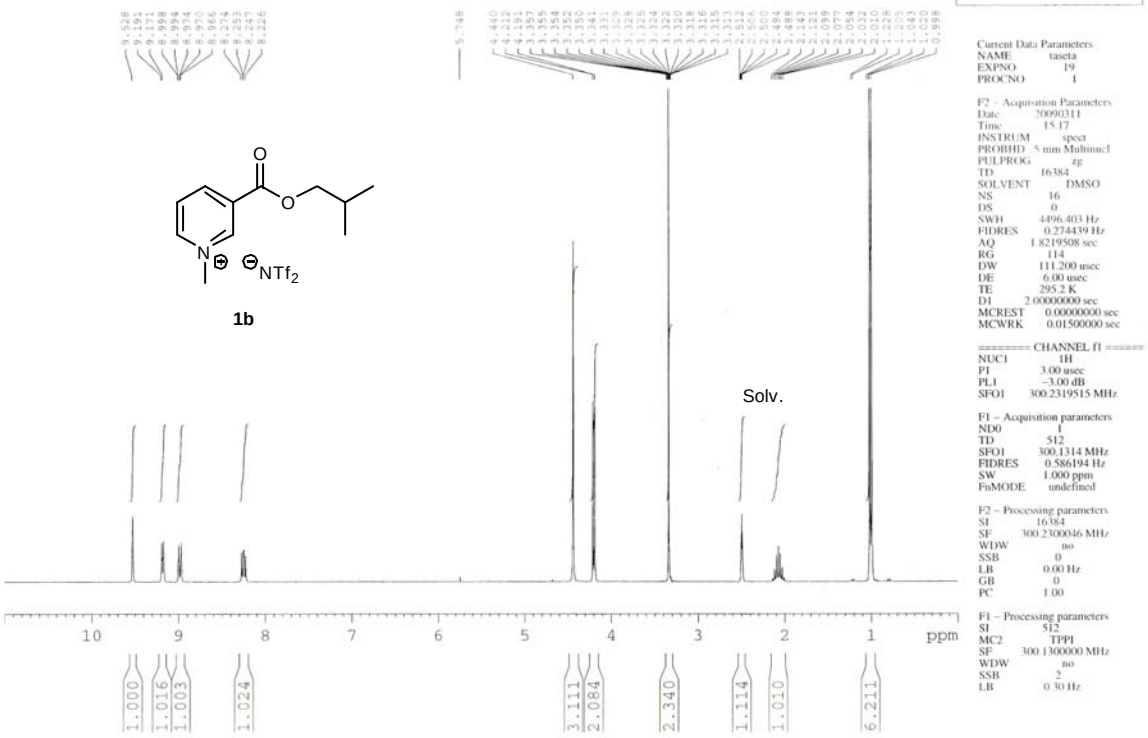

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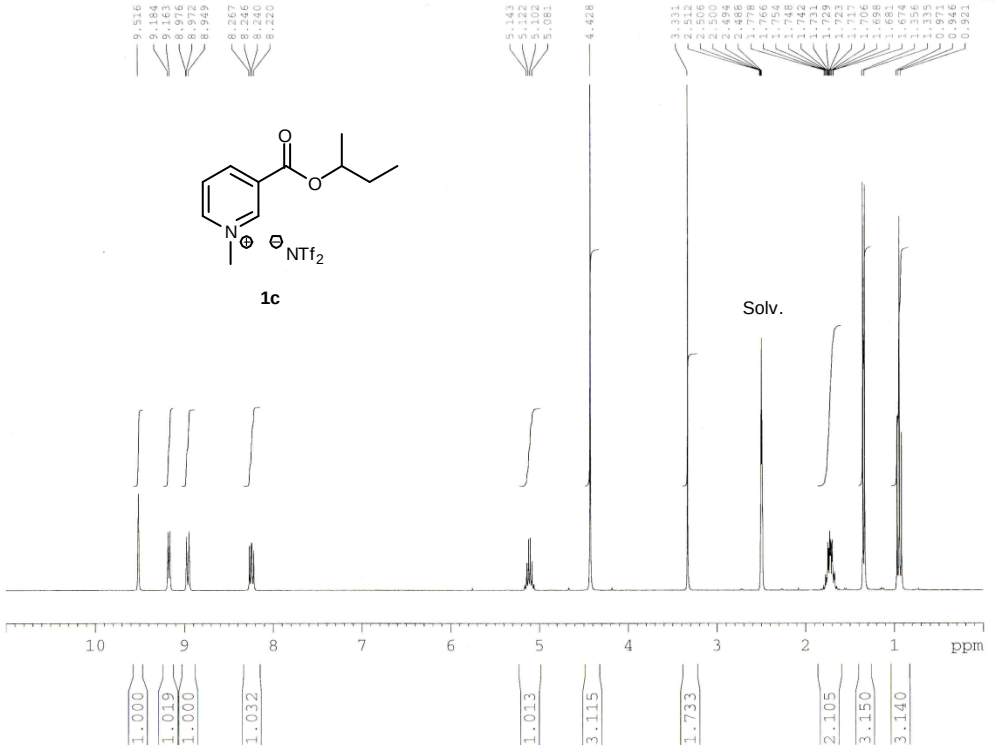

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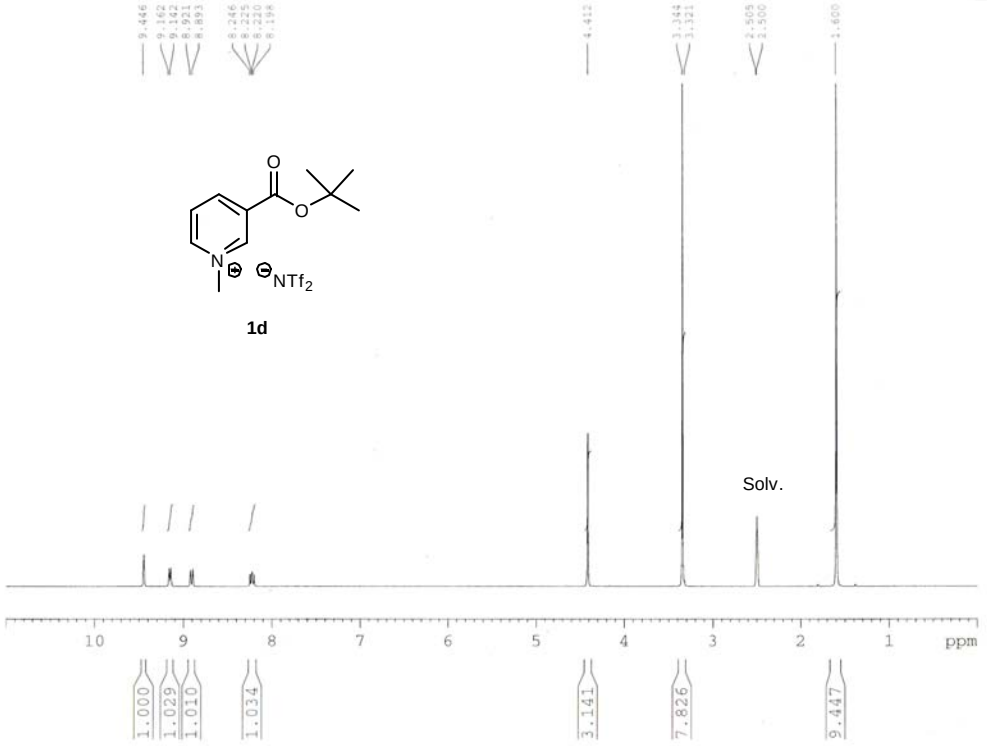

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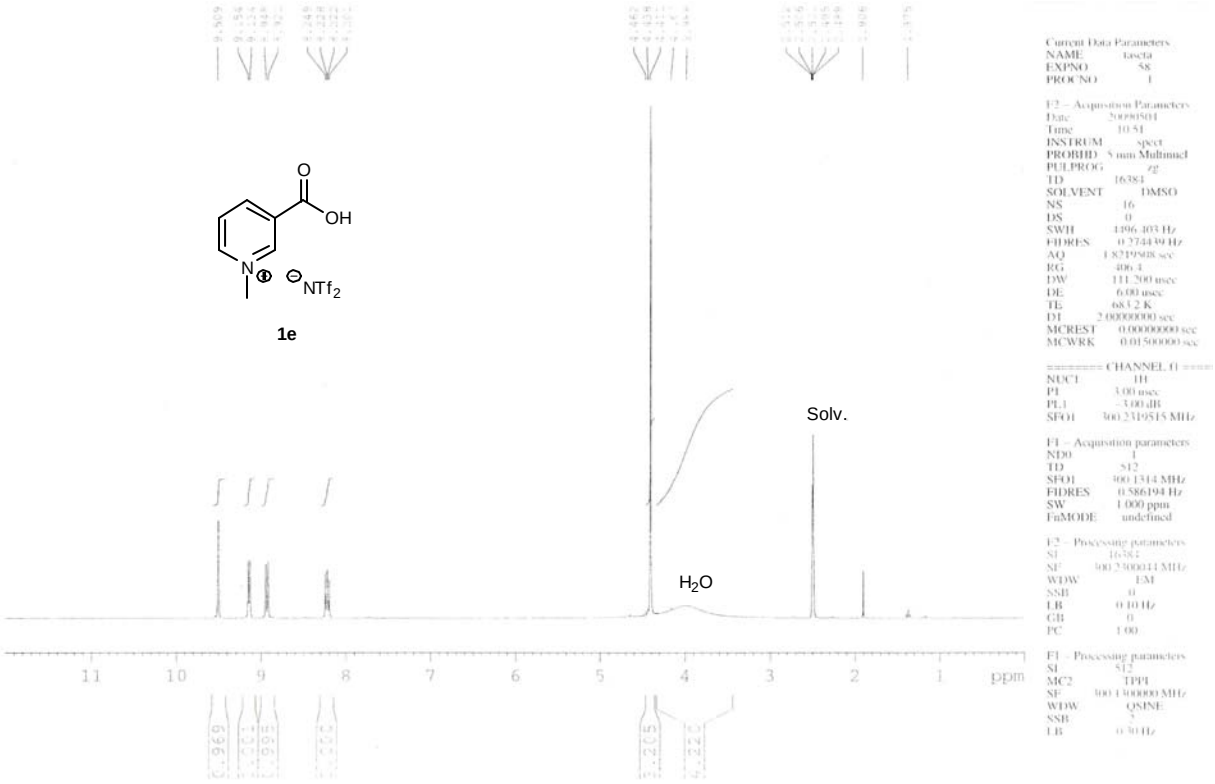
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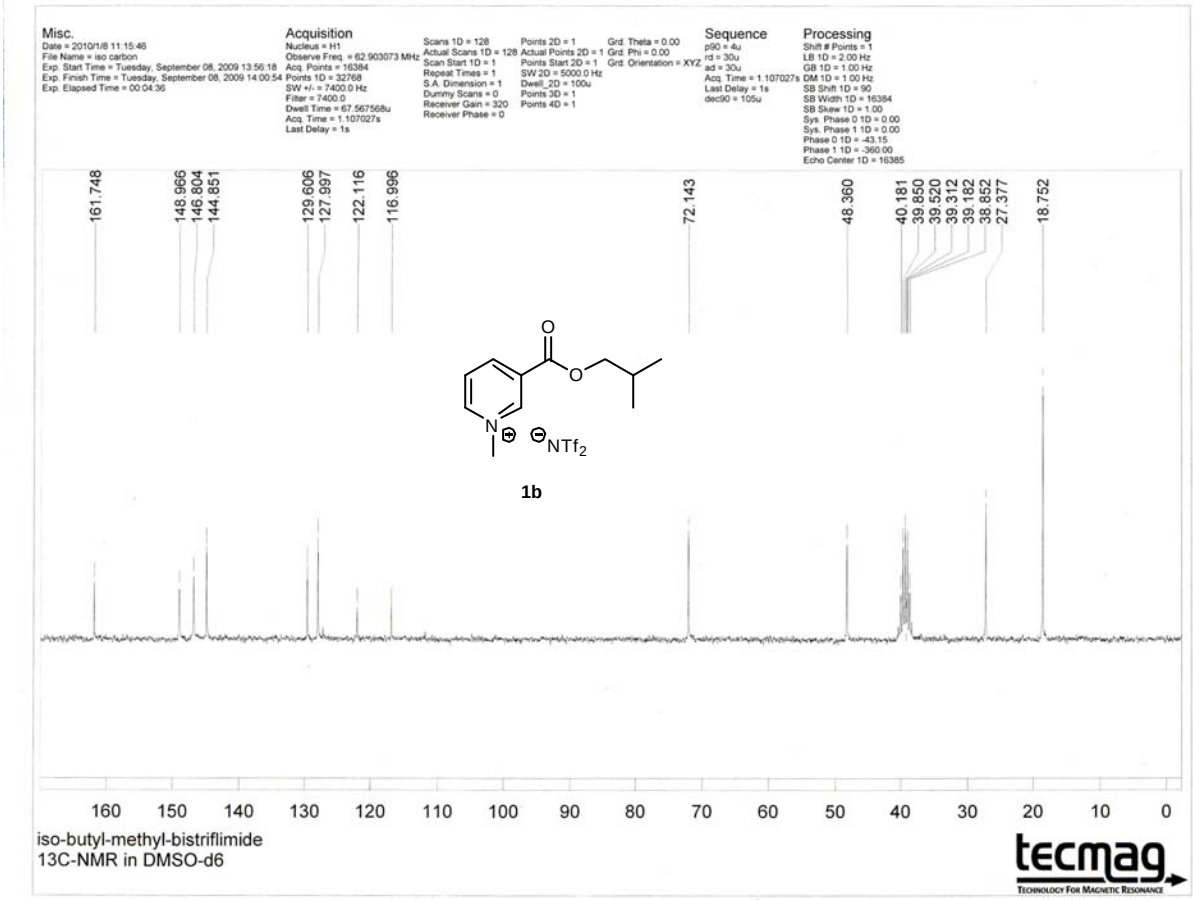
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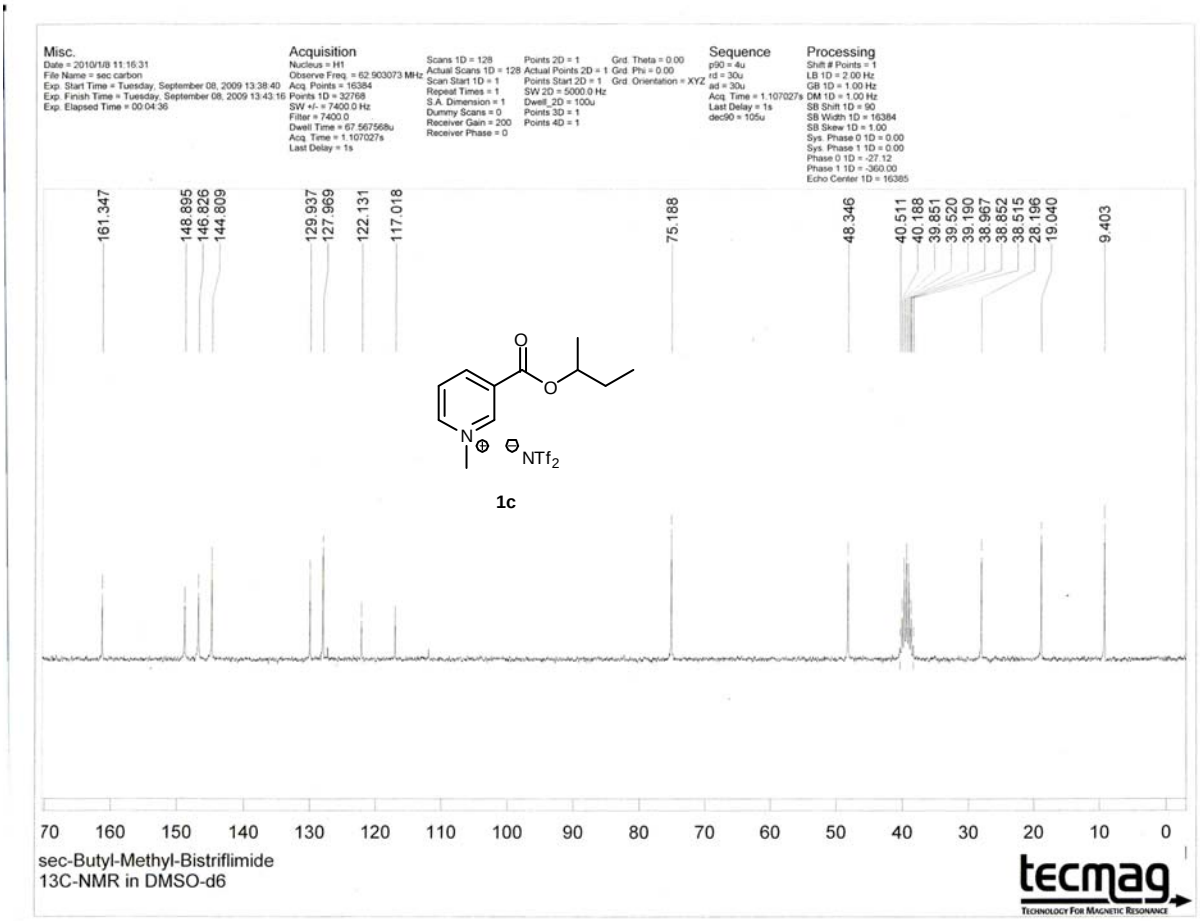
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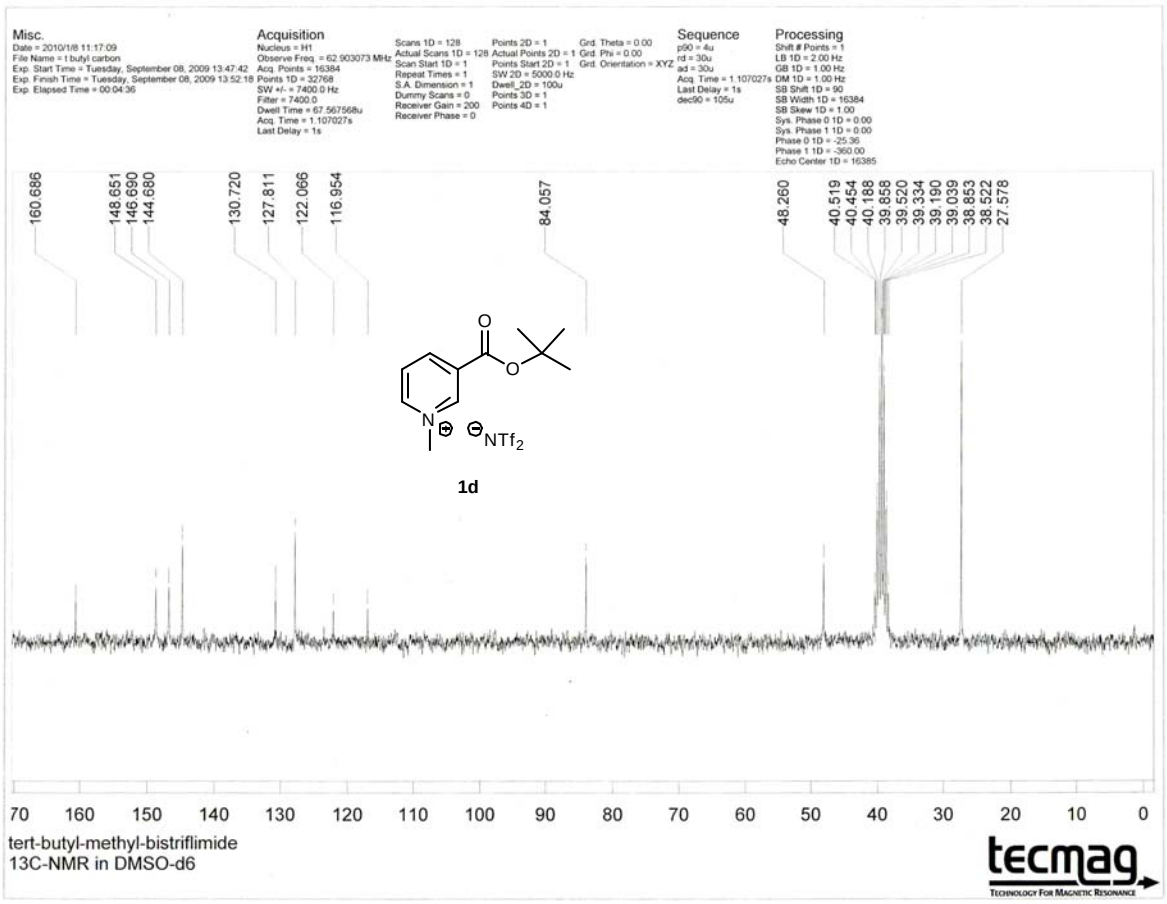
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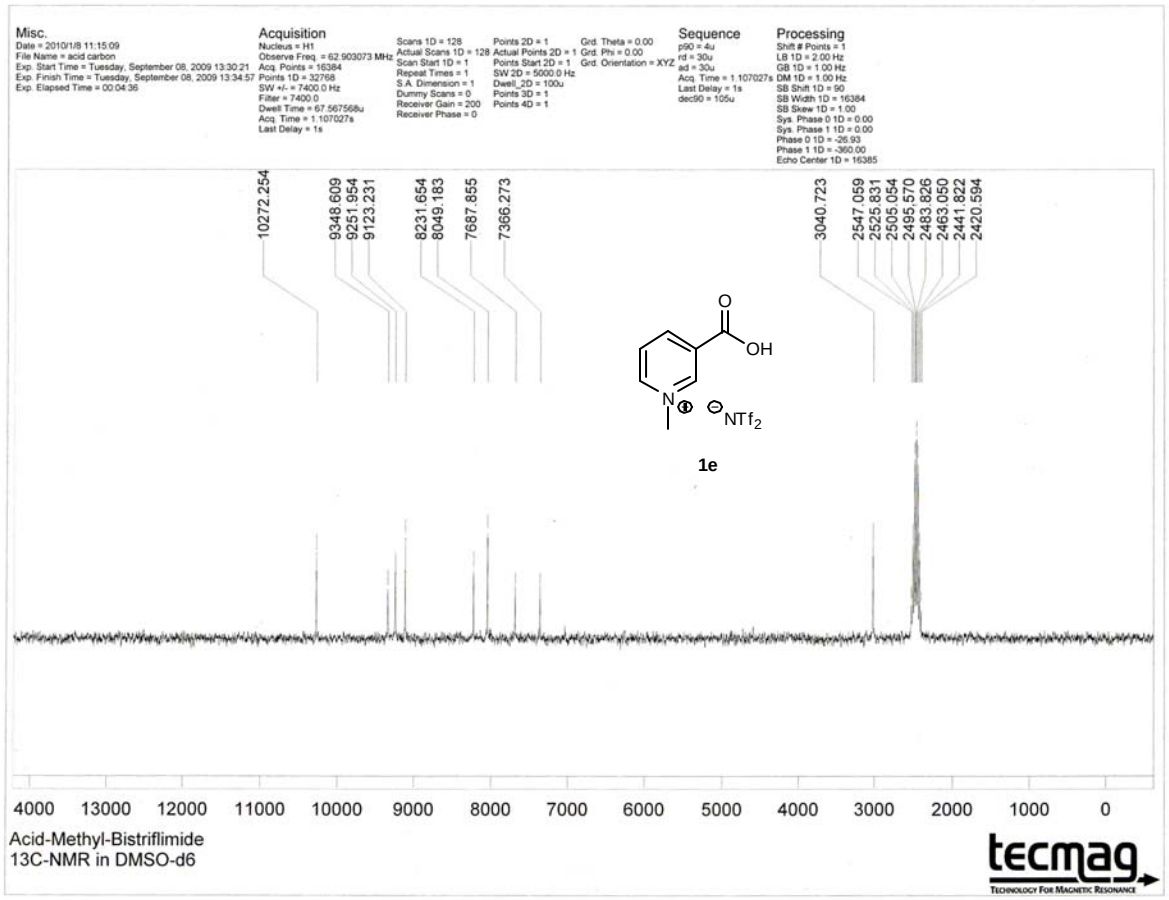
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2463.050
2441.822
2420.594
O
OH
N
⊖NTf2
1e
4000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Acid-Methyl-Bistriflimide
13C-NMR in DMSO-d6
tecmag
Technology For Magnetic Resonance