

Supplementary Information for

Cationic CH $\cdots\pi$ interactions as a Function of Solvation

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Table of Contents

General Experimental	3
Error Analysis:	4
Error Analyses Table	4
Synthesis of Balance 2	5
Synthesis of Balance 1	6
Table S1. Solvent polarity scales, Hunter’s H-bond parameters, and interaction energies determined from balances 1 and 1a.	7
Correlation Plots:	7
Figure S1. Correlation of interaction energies with solvents’ dielectric constant.	7
Figure S3. Correlation of interaction energies with solvents’ $E_T(30)$ values.	8
Computational Results⁴	9
The xyz coordinates for the folded conformer of Balance 1 optimized at B3LYP/6-31+G(d)-D3⁴	9
The xyz coordinates for the unfolded conformer of Balance 1 optimized at B3LYP/6-31+G(d)-D3	10
Crystallographic details	13
Table S2. Experimental details for X-ray Analysis	13
Figure S1. Ortep representation of 2 (50% probability level) with atom labels and showing disorder of cation.	15
Carbon and Proton NMR of Balance 2 precursor	16
Carbon and Proton NMR of Balance 2	17
Carbon and Proton NMR of Balance 1 precursor	18
Carbon and Proton NMR of Balance 1	19
Proton and Carbon-13 NMR of balance 3	20
Proton NMR of Balance 1 in various solvents	21
Proton NMR of balance 1 in acetic acid	21
Proton NMR of balance 1 in acetone	21
Proton NMR of balance 1 in acetonitrile	22
Proton NMR of balance 1 in DMF	22
Proton NMR of balance 1 in DMSO	23
Proton NMR of balance 1 in Methanol	23
Proton NMR of balance 1 in nitromethane	24
Proton NMR of balance 1 in Pyridine	24
MS Spectrum for Balances 1 and 1a	25
References	26

General Experimental

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware with magnetic stirring unless otherwise indicated. Reagents were purchased from commercial sources and used without further purification. Solvents for chemical reaction were dried. Purification of the reaction products was carried out by flash chromatography using silica gel 40-63 μm (230-400 mesh) unless otherwise stated. Reactions were monitored by ^1H NMR and/or thin layer chromatography. Visualization was accomplished with UV light, staining with 5% KMnO_4 followed by heating or with p-anisaldehyde in EtOH solution. NMR was recorded using a 400 MHz Bruker spectrometer. Chemical shifts were recorded in ppm (δ) using tetramethylsilane (C, H) as the internal reference. Data are reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; integration; coupling constant(s) in Hz). Melting points were measured with a Gallenkamp melting point apparatus.

Measurement of interaction energies (ΔG) and error analysis

The *folded/unfolded* ratios were measured by proton NMR spectra at room temperature ($\sim 25^\circ\text{C}$). The peak areas corresponding to the *ortho* methyl proton in the *folded* and *unfolded* states were integrated. The CH- π interaction energies were estimated from the equation: $\Delta G = -RT\ln K = -RT\ln[\textit{folded}]/[\textit{unfolded}]$.

Error Analysis:

The error in the folding energies was estimated systematically by including a 3% error in the relative integral of the smaller peak of the two conformer peaks. e.g. relative integrals of 0.1 to 1, would be 0.13 to 1 at one extreme and 0.07 to 1 at the other extreme with a 3% error applied. These max and min integrations are applied in the computation of the ΔG to determine the upper and lower limit of the conformational free energies. This approach ensures that small errors are associated with ΔG s that are close to zero.

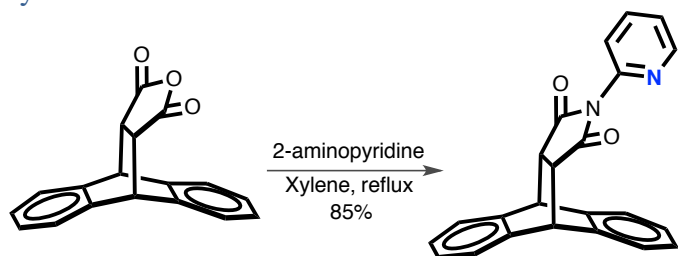
Multiple-linear regression was performed with *Statplus* program

Error Analyses Table

Solvents	Balance 1 (%)		3% Error Limits (Unfolded)		ΔG (with 3% errors) kcal/mol	
	Unfolded	Folded	upper	lower	upper	lower
DMSO	9	91	12	6	-1.21	-1.58
Pyridine	14	86	17	11	-0.97	-1.19
DMF	15	85	18	12	-0.93	-1.14
Acetone	16	84	19	13	-0.89	-1.08
Acetonitrile	18	82	20	16	-0.82	-0.98
Nitromethane	21	79	23	19	-0.72	-0.85
Methanol	21	79	23	19	-0.72	-0.85
Acetic acid	25	75	27	23	-0.60	-0.71

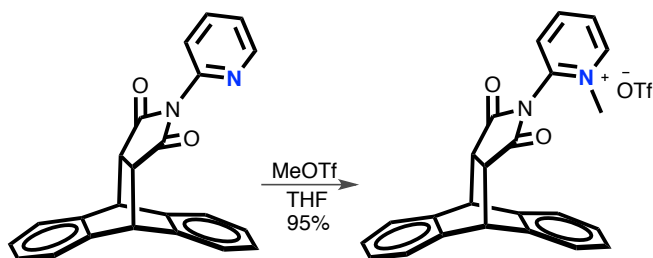
	Balance 1a (%)		3% Error Limits (Unfolded)		ΔG (with 3% errors) kcal/mol	
	Unfolded	Folded	upper	lower	upper	lower
DMSO	31	69	33	29	-0.44	-0.51
Pyridine	33	67	35	31	-0.38	-0.46
DMF	34	66	36	32	-0.36	-0.43
Acetone	35	65	37	33	-0.33	-0.40
Acetonitrile	35	65	37	33	-0.33	-0.40
Nitromethane	35	65	37	33	-0.33	-0.40
Methanol	36	64	38	34	-0.31	-0.37
Acetic acid	40	60	42	38	-0.21	-0.27

Synthesis of Balance 2



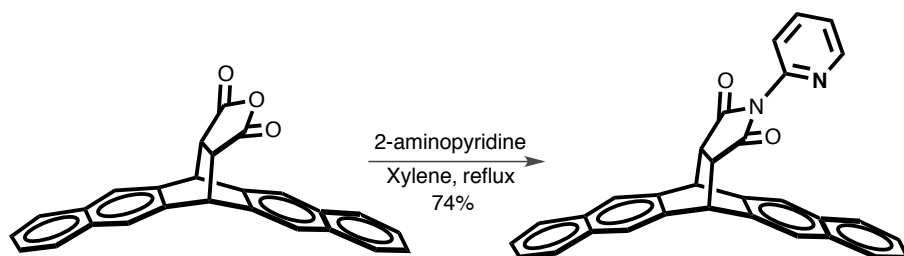
Procedure: Anhydride (350 mg, 1.27 mmol) and 2-aminopyridine (143 mg, 1.52 mmol) dissolved in ~4 ml xylene was refluxed for 3 days (monitored by NMR) after which the volume of xylene was reduced and the crude product purified by column chromatography to yield 380 mg (85%) of the imide product.

Proton NMR (400 MHz, DMSO-d₆): δ 3.50 (s, 2H), 4.89 (s, 2H), 6.03 – 6.05 (d, 1H, J = 7.6 Hz), 7.18 – 7.83 (m, 11H), 8.48 (d, 1H, J = 4.8 Hz). Carbon NMR (400 MHz, DMSO-d₆): δ 45.3, 47.4, 122.2, 124.9, 125.3, 126.9, 127.2, 139.2, 139.8, 142.1, 146.2, 150.0, 176.0. HRMS calcd for C₂₃H₁₆N₂O₂ [M]⁺ found 352.1213



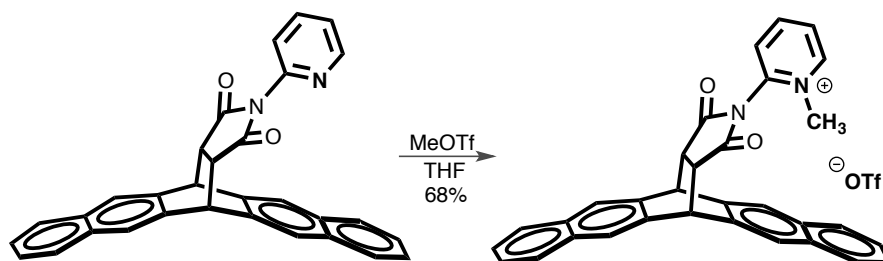
Procedure: Imide (100 mg, 0.28 mmol) was dissolved in 2 ml (1:1) THF-acetonitrile. After cooling for 5 mins using ice-water bath, MeOTf (460 mg, 2.8 mmol) in 1 ml THF was added dropwise and the reaction was stirred at room temperature. TLC indicated reaction completion after just 15 mins and the reaction was concentrated to a minimum volume and the crude product was purified by column chromatography with EtOAc-Methanol. Yield = 140 mg, 95%. Proton NMR (400 MHz, DMSO-d₆): δ 2.91 and 4.15 (s, 3H), 3.70 – 3.75 (s, 2H), 4.93 (s, 2H), 5.91 and 8.08 (d, 1H, J = 8.0 Hz), 7.10 – 7.63 (m, 8H), 7.45 (t, 1H), 8.63 and 8.74 (t, 1H), 9.00 and 9.14 (d, 1H, d = 6 Hz). Carbon NMR (400 MHz, acetone-d₆): δ 43.3, 45.2, 45.3, 48.3, 48.5, 119.6, 122.8, 124.5, 124.6, 125.2, 125.5, 126.8, 126.9, 127.5, 128.8, 129.0, 139.6, 140.1, 141.2, 141.7, 141.8, 148.4, 148.5, 148.6, 149.1, 174.4, 174.5. HRMS calcd for C₂₄H₁₉N₂O₂ [M]⁺ found 367.1442.

Synthesis of Balance 1



Procedure: Anhydride (165 mg, 0.44 mmol) and 2-aminopyridine (49 mg, 0.53 mmol) dissolved in ~2 ml xylene was refluxed for 3 days after which the volume of xylene was reduced and the crude product purified by column chromatography to yield 147mg (74%) of the imide product.

Proton NMR (400 MHz, CDCl_3): δ 3.61 (s, 2H), 5.17 (s, 2H), 5.72 (d, 1H, $J = 8$ Hz), 7.16 (m, 1H), 7.37 – 7.50 (m, 5H), 7.52 – 7.87 (m, 7H), 8.50 (d, 1H). Carbon NMR (400 MHz, CDCl_3): δ 45.6, 47.3, 121.6, 122.7, 123.0, 124.0, 125.5, 126.2, 126.3, 127.6, 127.8, 128.1, 132.6, 135.8, 138.1, 138.4, 145.6, 149.6, 175.7. HRMS calcd for $\text{C}_{31}\text{H}_{20}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 453.1598 found 453.1601



Procedure: Imide (150 mg, 0.33 mmol) was dissolved in 5 ml (1:1) THF-acetonitrile. After cooling for 5 mins using ice-water bath, MeOTf (542 mg, 3.3 mmol) in 1 ml THF was added dropwise and the reaction was stirred at room temperature. TLC indicated reaction completion after just 20 mins and the product was purified by column chromatography. Yield = 139 mg, 68%. Proton NMR (400 MHz, DMSO-d_6): δ 2.34 and 4.19 (s, 3H), 3.82 (s, 2H), 5.25 (s, 2H), 7.55 (m, 4H), 7.93 – 8.29 (m, 10H), 8.85 – 9.13 (m, 2H). Carbon NMR (400 MHz, acetone- d_6): δ 42.7, 45.2, 45.3, 45.5, 48.2, 48.2, 123.2, 123.9, 124.1, 126.2, 126.7, 126.7, 127.7, 127.8, 128.7, 129.0, 132.8, 136.9, 138.3, 146.6, 174.4 HRMS calcd for $\text{C}_{32}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}]^+$ 467.1754 found 467.1764.

Table S1. Solvent polarity scales, Hunter's H-bond parameters, and interaction energies determined from balances 1 and 1a.

solvents	α_s β_s		ϵ	μ	$E_T(30)$	% Folded		ΔG (kcal/mol)	
	α_s	β_s				1a	1	1a	1
DMSO	0.8	8.9	47.0	3.9	45.1	69	91	-0.47	-1.37
Pyridine	1.2	7.2	12.3	2.4	40.5	67	86	-0.42	-1.07
DMF	2.9	8.3	36.7	3.9	41.8	66	85	-0.39	-1.03
Acetone	1.5	5.7	20.7	1.7	51.7	65	84	-0.37	-0.98
Acetonitrile	1.7	5.1	36.6	3.5	45.6	65	82	-0.37	-0.90
Nitromethane	1.8	3.7	35.9	3.5	46.3	65	79	-0.37	-0.78
Methanol	2.7	5.3	32.6	1.7	55.4	64	79	-0.34	-0.78
Acetic acid	3.7	4.9	6.2	1.7	51.7	60	75	-0.24	-0.65

Symbols: ϵ = dielectric constant; μ = dipole moment in Debye unit; $E_T(30)$ = Reichardt's solvent polarity in kcal/mol;² α and β are Hunter's solvation parameters.³

Correlation Plots:

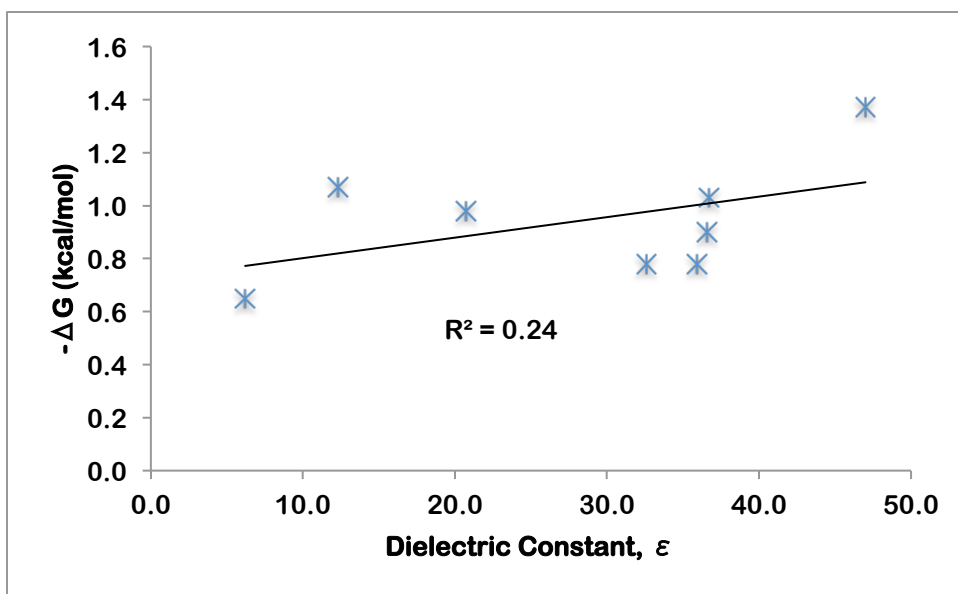


Figure S1. Correlation of interaction energies with solvents' dielectric constant.

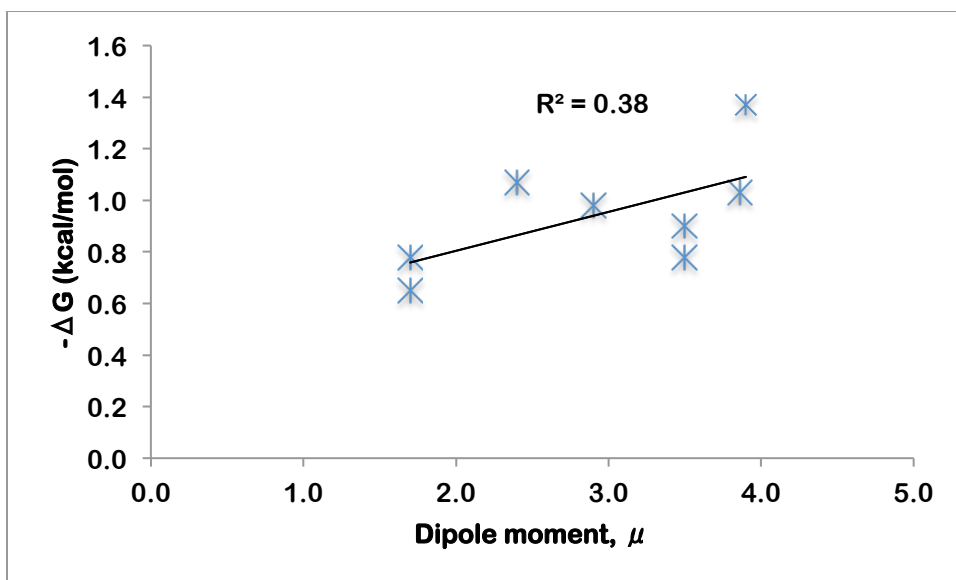


Figure S2. Correlation of interaction energies with solvents' dipole moment.

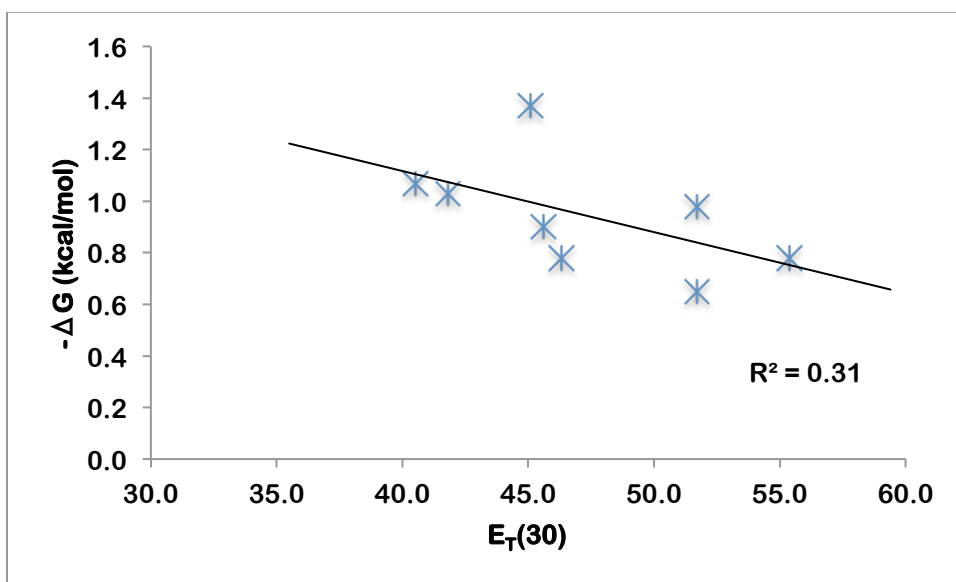


Figure S3. Correlation of interaction energies with solvents' $E_T(30)$ values.

Computational Results⁴

The xyz coordinates for the folded conformer of Balance 1 optimized at B3LYP/6-31+G(d)-D3⁴

H	-3.02056	5.4821	1.57605
C	-2.47141	4.74869	0.99287
H	-1.84351	3.6252	2.70917
C	-1.81555	3.71384	1.62596
C	-1.71988	3.9527	-1.17129
C	-1.08575	2.75114	0.87936
C	-2.42323	4.86917	-0.41796
C	-1.03625	2.87359	-0.55031
C	-0.41108	1.66342	1.50776
H	-2.93538	5.69425	-0.90446
H	-0.29669	1.98149	-2.38986
H	-1.67228	4.0502	-2.25326
C	0.27385	0.74334	0.75211
H	-0.43925	1.57746	2.59181
C	0.3051	0.85526	-0.67158
C	-0.32603	1.89625	-1.30561
C	1.04314	-0.45552	1.2734
H	1.03831	-0.51732	2.36348
C	1.05867	-0.27875	-1.3375
C	0.3811	-1.73742	0.65156
H	0.93779	-2.61672	0.9867
C	0.34364	-1.60439	-0.89309
H	0.8177	-2.45305	-1.39521
C	-1.05785	-1.88502	1.09253
C	-1.12579	-1.59172	-1.26622
O	-1.5049	-2.07	2.19804
O	-1.63789	-1.4769	-2.35527
N	-1.87788	-1.73296	-0.06642
C	-3.27043	-1.85278	-0.01946
C	-6.02968	-2.01603	0.02564
C	-3.88037	-3.03085	0.39389
N	-4.02841	-0.77202	-0.36049
C	-5.38079	-0.8574	-0.3593
C	-5.26927	-3.11788	0.42378
H	-3.25074	-3.86464	0.67915
H	-5.91085	0.03537	-0.66638
H	-5.75143	-4.03675	0.74135

H	-7.11325	-2.04374	0.01828
H	-4.14051	1.29838	-0.69221
C	-3.38111	0.51887	-0.70466
H	-2.62089	0.73914	0.04266
H	-2.92552	0.43947	-1.69084
C	2.44148	-0.40823	0.68787
H	3.61266	-0.50865	2.4793
C	3.61739	-0.44953	1.39294
C	3.63463	-0.29189	-1.4272
C	4.86535	-0.40833	0.70682
C	2.44979	-0.32734	-0.73638
C	4.87404	-0.32985	-0.72574
C	6.10301	-0.44249	1.40046
H	6.12533	-0.22965	-2.48929
H	3.64345	-0.22778	-2.51327
C	7.29728	-0.40194	0.71273
H	6.09478	-0.50001	2.48603
H	8.23798	-0.42821	1.2549
C	7.30594	-0.32515	-0.70126
H	8.25323	-0.29334	-1.23152
C	6.1202	-0.28978	-1.40384
H	1.06532	-0.19699	-2.42609

The xyz coordinates for the unfolded conformer of Balance 1 optimized at B3LYP/6-31+G(d)-D3.

H	-3.59295	5.19523	0.86092
C	-2.97641	4.43732	0.38623
H	-2.06961	3.80176	2.2243
C	-2.12698	3.66186	1.14758
C	-2.25057	3.31394	-1.63729
C	-1.30593	2.67344	0.54115
C	-3.03814	4.26211	-1.01869
C	-1.37065	2.49415	-0.88164
C	-0.45202	1.82927	1.30908
H	-3.70219	4.88675	-1.60917
H	-0.62642	1.34343	-2.56863
H	-2.29011	3.18456	-2.71606
C	0.30026	0.86054	0.69161
H	-0.42057	1.9476	2.38983
C	0.24748	0.69123	-0.72535
C	-0.57094	1.48457	-1.49158

C	1.15964	-0.1811	1.38066
H	1.18774	-0.05249	2.46422
C	1.08865	-0.47149	-1.21732
C	0.50895	-1.56982	1.01604
H	1.04108	-2.36825	1.53973
C	0.49894	-1.7591	-0.52355
H	1.06324	-2.63479	-0.85378
C	-0.94729	-1.56404	1.43735
C	-0.95468	-1.90958	-0.91376
O	-1.42658	-1.41136	2.53346
O	-1.43748	-2.09177	-2.00811
N	-1.73847	-1.73881	0.25971
C	-3.09519	-1.39793	0.21317
C	-5.77229	-0.75813	0.00079
C	-3.51283	-0.10592	0.5063
N	-3.99889	-2.3499	-0.14993
C	-5.31299	-2.03408	-0.26811
C	-4.86053	0.22244	0.40134
H	-2.76693	0.62798	0.78576
H	-5.96779	-2.83772	-0.5805
H	-5.18726	1.23583	0.61153
H	-6.82979	-0.54476	-0.10517
H	-4.43658	-4.37781	-0.45767
C	-3.55561	-3.73906	-0.42247
H	-3.02486	-3.76105	-1.37506
H	-2.8989	-4.0621	0.38569
C	2.53258	-0.17197	0.74376
H	3.76179	0.07784	2.48135
C	3.73023	-0.03738	1.39995
C	3.6527	-0.33136	-1.40817
C	4.95182	-0.03919	0.66762
C	2.49372	-0.32081	-0.67372
C	4.91246	-0.18752	-0.75914
C	6.21005	0.10287	1.30896
H	6.10159	-0.29714	-2.56469
H	3.6246	-0.44317	-2.49003
C	7.37821	0.09929	0.57693
H	6.23823	0.21591	2.38983
H	8.33486	0.20957	1.07915
C	7.33935	-0.04656	-0.83127

H	8.26655	-0.04676	-1.39681
C	6.13298	-0.1866	-1.48365
H	1.05849	-0.58283	-2.3029

Crystallographic details

Diffraction data were collected on a Bruker APEX II CCD diffractometer at 100 K using monochromatic Mo K α radiation with the omega scan technique. Data for torsion balance 2 were collected, its unit cell determined, and the data integrated and corrected for absorption and other systematic errors using the Apex2 suite of programs.[A] The space group was assigned and the structure was solved by direct methods using the SHELXTL suite of programs [B] and refined by full matrix least squares against F^2 with all reflections using Shelxl2014 [C] using the graphical interface Shelxle [D]. H atoms attached to carbon and nitrogen atoms were positioned geometrically and constrained to ride on their parent atoms, with carbon hydrogen bond distances of 0.95 Å for alkene and aromatic C-H, 1.00 and 0.98 Å for aliphatic C-H and CH₃ moieties, respectively. Methyl H atoms were allowed to rotate but not to tip to best fit the experimental electron density. $U_{\text{iso}}(\text{H})$ values were set to a multiple of $U_{\text{eq}}(\text{C/N})$ with 1.5 for CH₃ and 1.2 for C-H units, respectively. Large parts of the cation are disordered by a wiggling motion around the central axis of the cation. The two moieties were refined to have similar geometries (SAME command in Shelxl), and U_{ij} components of ADPs of disordered atoms were restrained to be similar when closer than 1.7 Å (SIMU command in Shelxl). Subject to these restraints the occupancy ratio refined to close to 1:1, 0.505(8) to 0.459(8), indicating correlated disorder with alternating moieties. No indication of obvious lower symmetry (monoclinic, triclinic) was observed (refinement in triclinic with four independent molecules required a disorder model for the cation similar to that used in the orthorhombic model).

The structure was refined as a 2-component inversion twin, Flack parameter 0.06(10).

Complete crystallographic data, in CIF format, have been deposited with the Cambridge Crystallographic Data Centre. **CCDC 1500195** contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Table S2. Experimental details for X-ray Analysis

	brt10_0m
Crystal data	
Chemical formula	C ₂₄ H ₁₉ N ₂ O ₂ ·CF ₃ O ₃ S
M_r	516.48
Crystal system, space group	Orthorhombic, $Pna2_1$
Temperature (K)	100
a, b, c (Å)	27.601 (10), 10.773 (4), 7.699 (3)
V (Å ³)	2289.3 (14)

Z	4
$F(000)$	1064
D_x (Mg m ⁻³)	1.499
Radiation type	Mo Ka
No. of reflections for cell measurement	8393
q range (°) for cell measurement	2.4–27.5
m (mm ⁻¹)	0.21
Crystal shape	Plate
Colour	Colourless
Crystal size (mm)	0.25 × 0.20 × 0.09
Data collection	
Diffractometer	Bruker AXS APEXII CCD diffractometer
Radiation source	fine focus sealed tube
Monochromator	Graphite
Scan method	w and phi scans
Absorption correction	Multi-scan, <i>SADABS2014/3</i> (Bruker, 2014)
T_{\min}, T_{\max}	0.692, 0.746
No. of measured, independent and observed [$I > 2s(I)$] reflections	41711, 6772, 5413
R_{int}	0.052
q values (°)	$q_{\max} = 30.2, q_{\min} = 1.5$
$(\sin q/l)_{\max}$ (Å ⁻¹)	0.709
Range of h, k, l	$h = -39\text{®}38, k = -15\text{®}15, l = -10\text{®}10$
Refinement	
$R[F^2 > 2s(F^2)], wR(F^2), S$	0.039, 0.091, 1.03
No. of reflections	6772
No. of parameters	511
No. of restraints	785

H-atom treatment	H-atom parameters constrained
$(D/s)_{\max}$	< 0.001
$D\rho_{\max}, D\rho_{\min}$ ($e \text{ \AA}^{-3}$)	0.24, -0.28
Absolute structure	Refined as an inversion twin.
Absolute structure parameter	0.06 (10)

Computer programs: Apex2 v2014.7-1 (Bruker, 2014), SAINT V8.34A (Bruker, 2013), SHELXS97 (Sheldrick, 2008), SHELXL2014/7 (Sheldrick, 2014), SHELXLE Rev714 (Hübschle *et al.*, 2011).

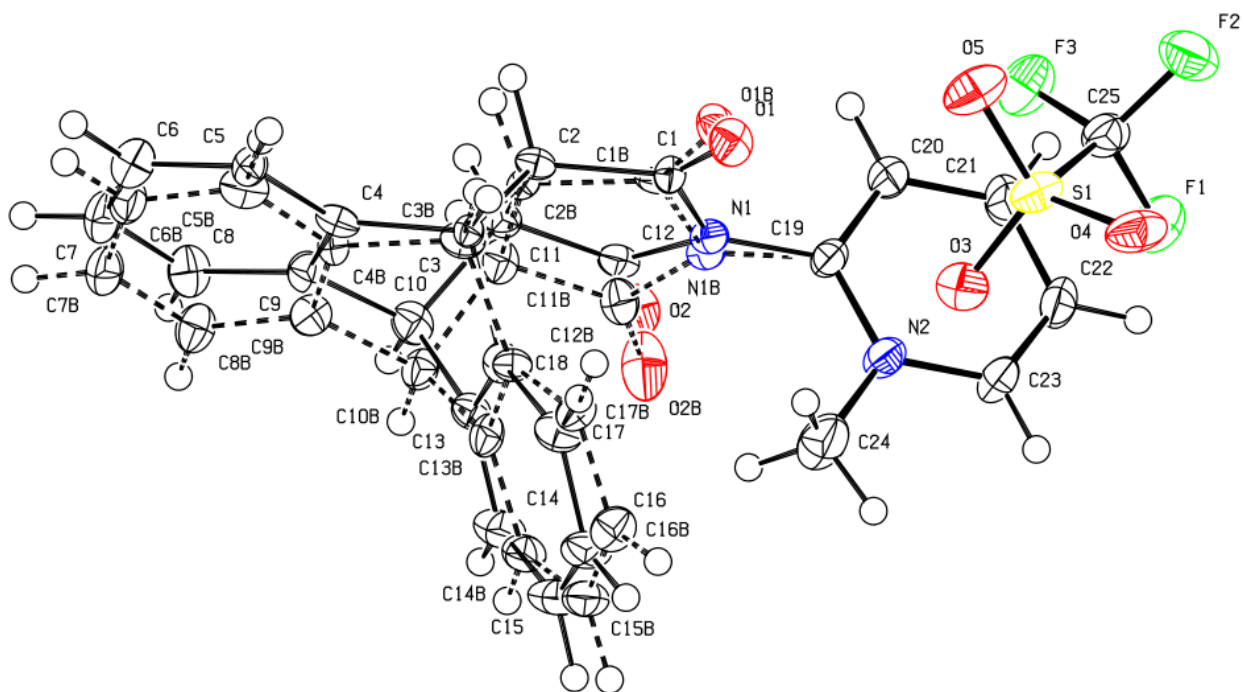
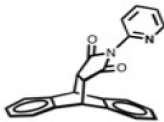
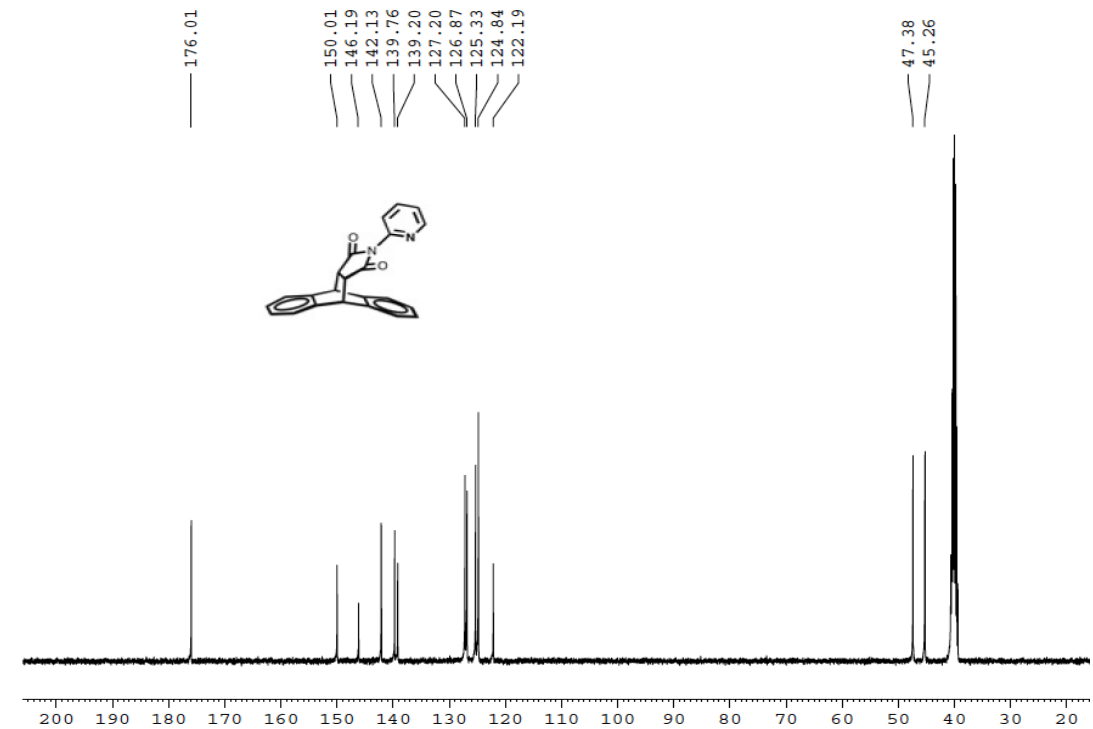
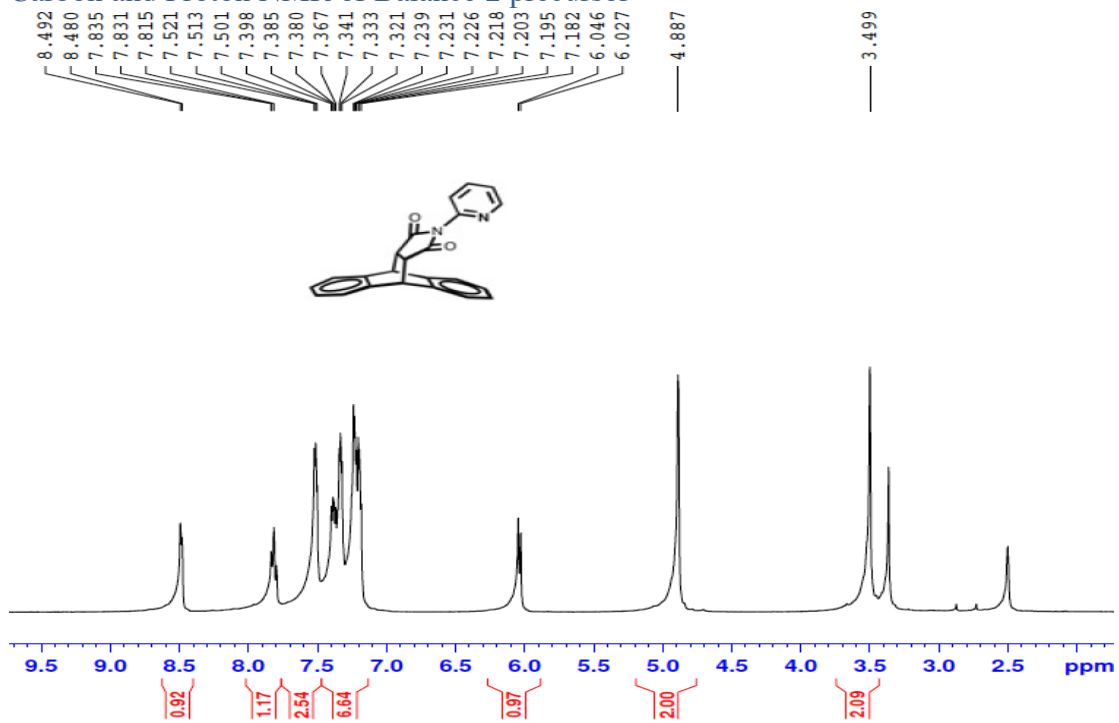
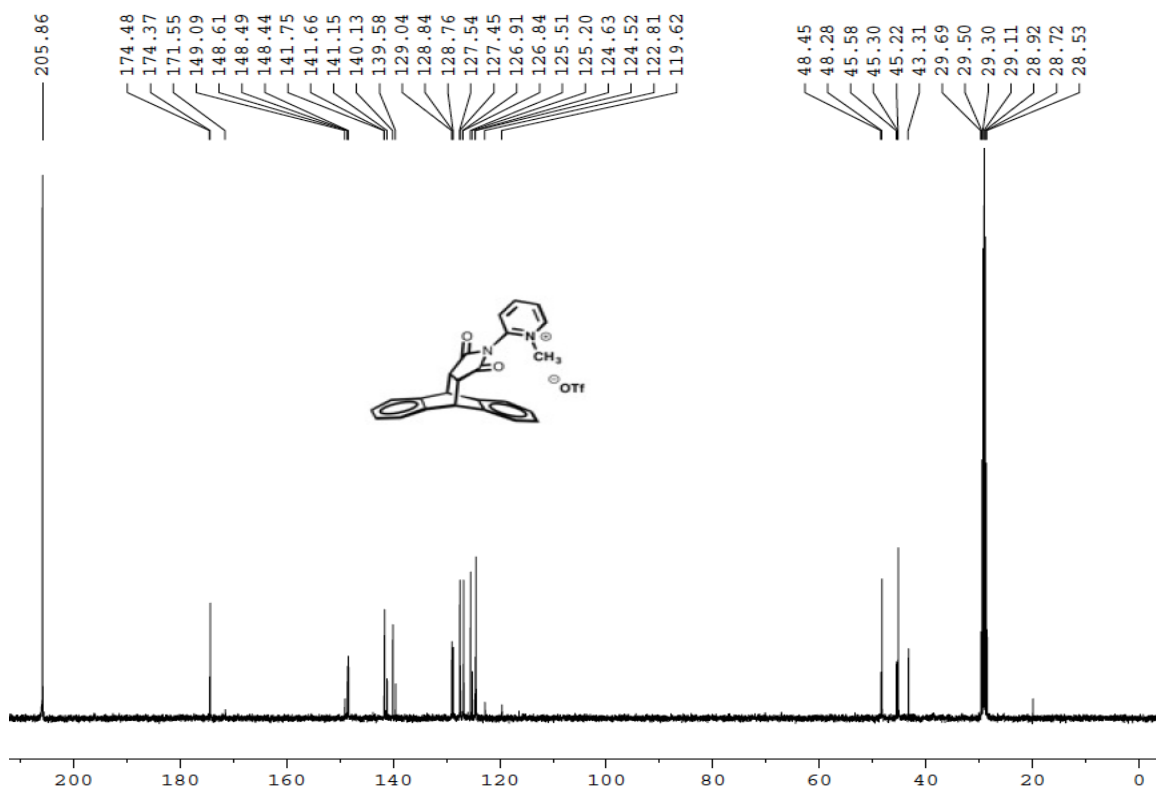
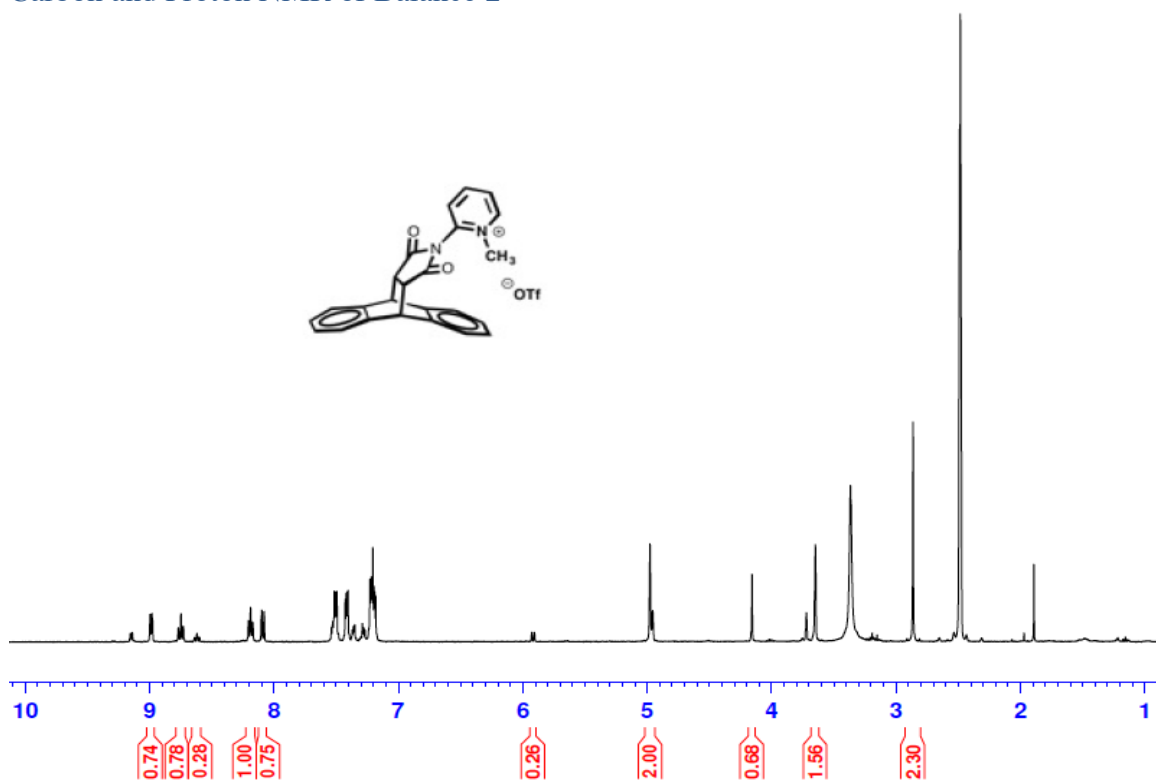


Figure S1. Ortep representation of **2** (50% probability level) with atom labels and showing disorder of cation.

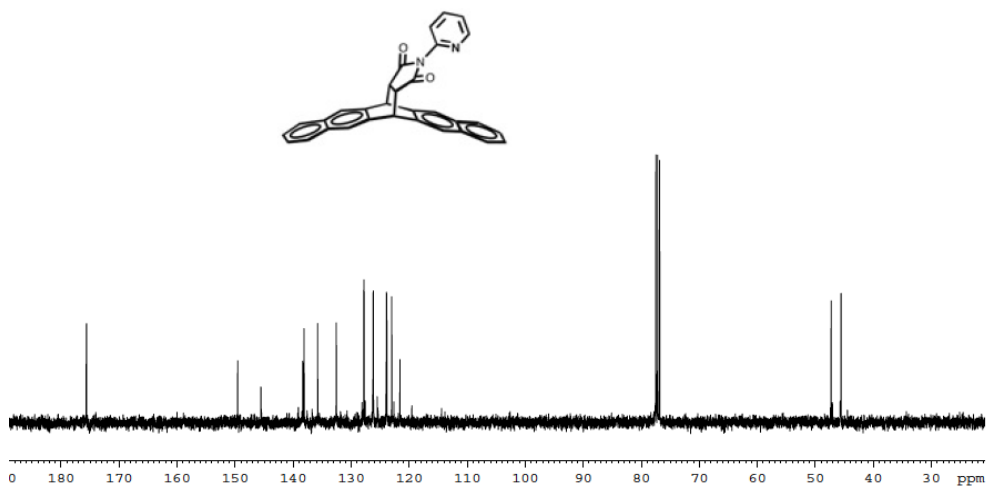
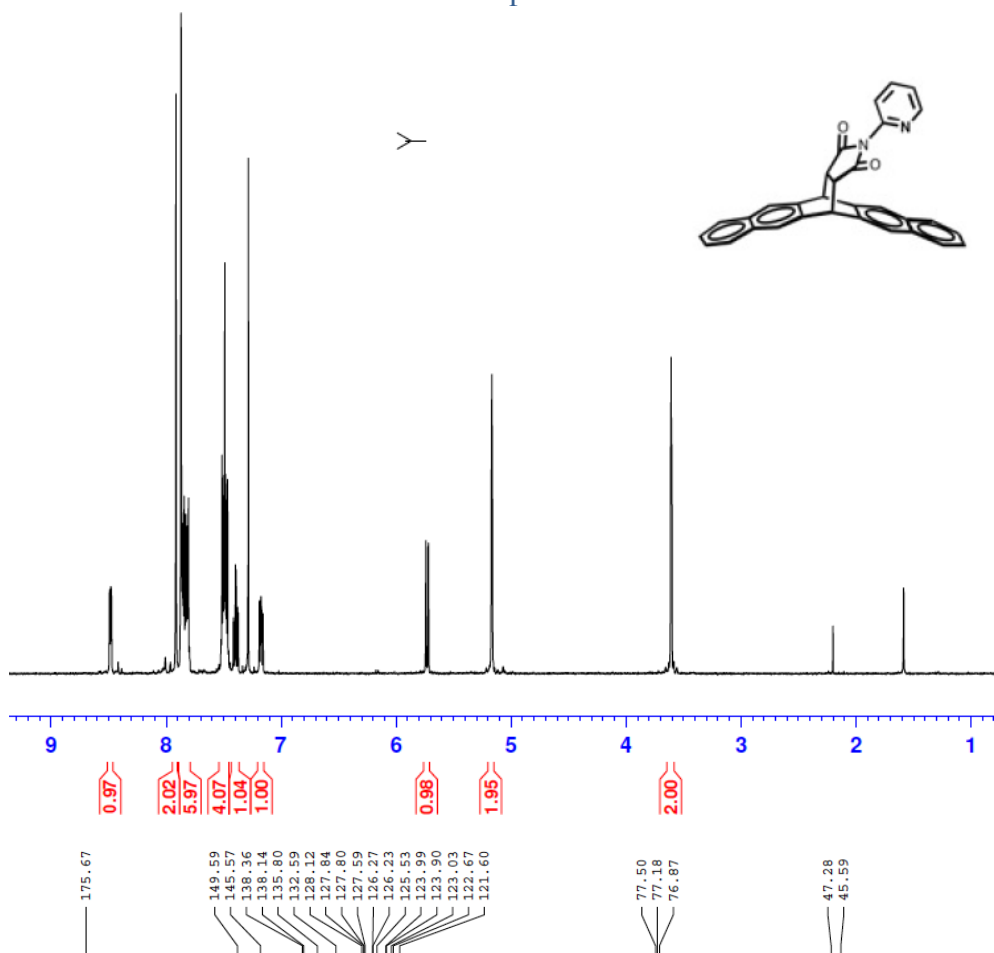
Carbon and Proton NMR of Balance 2 precursor



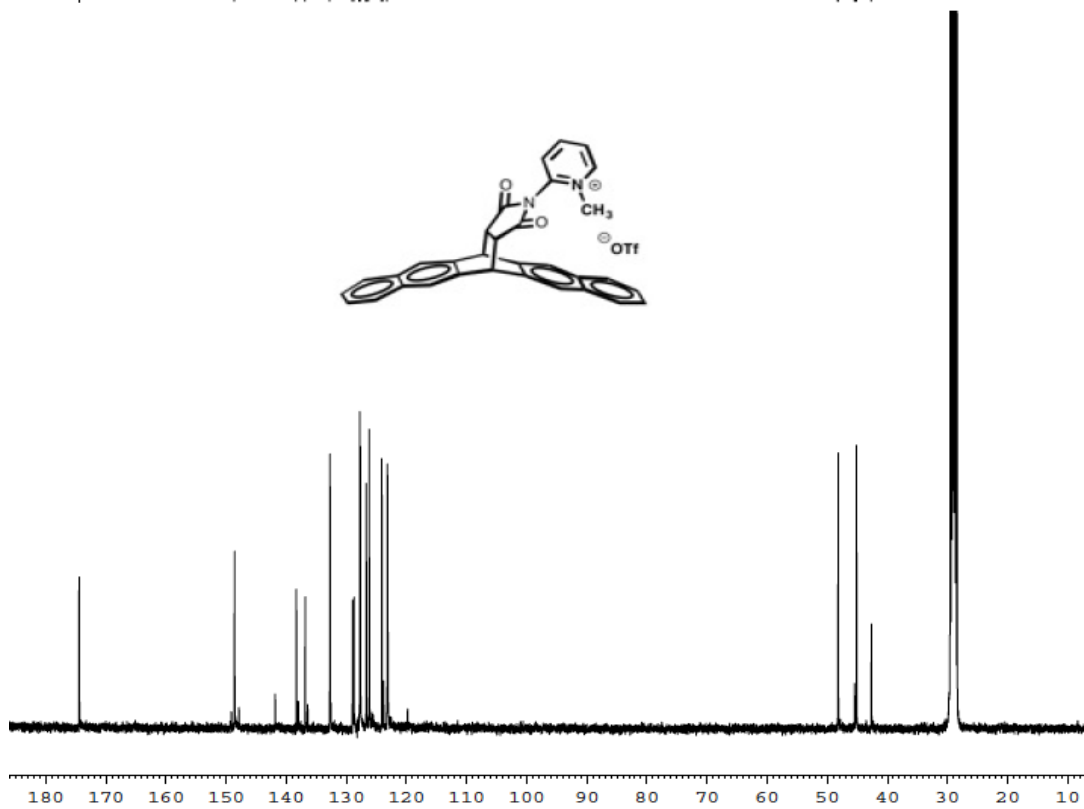
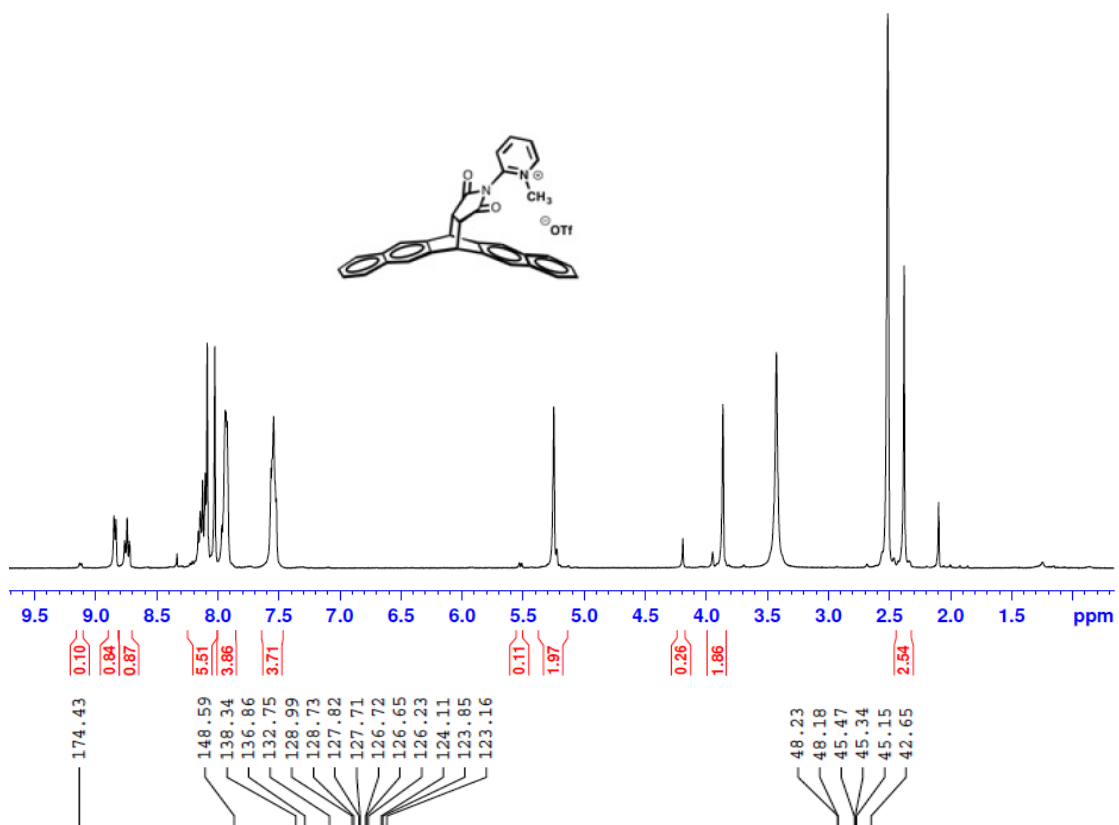
Carbon and Proton NMR of Balance 2



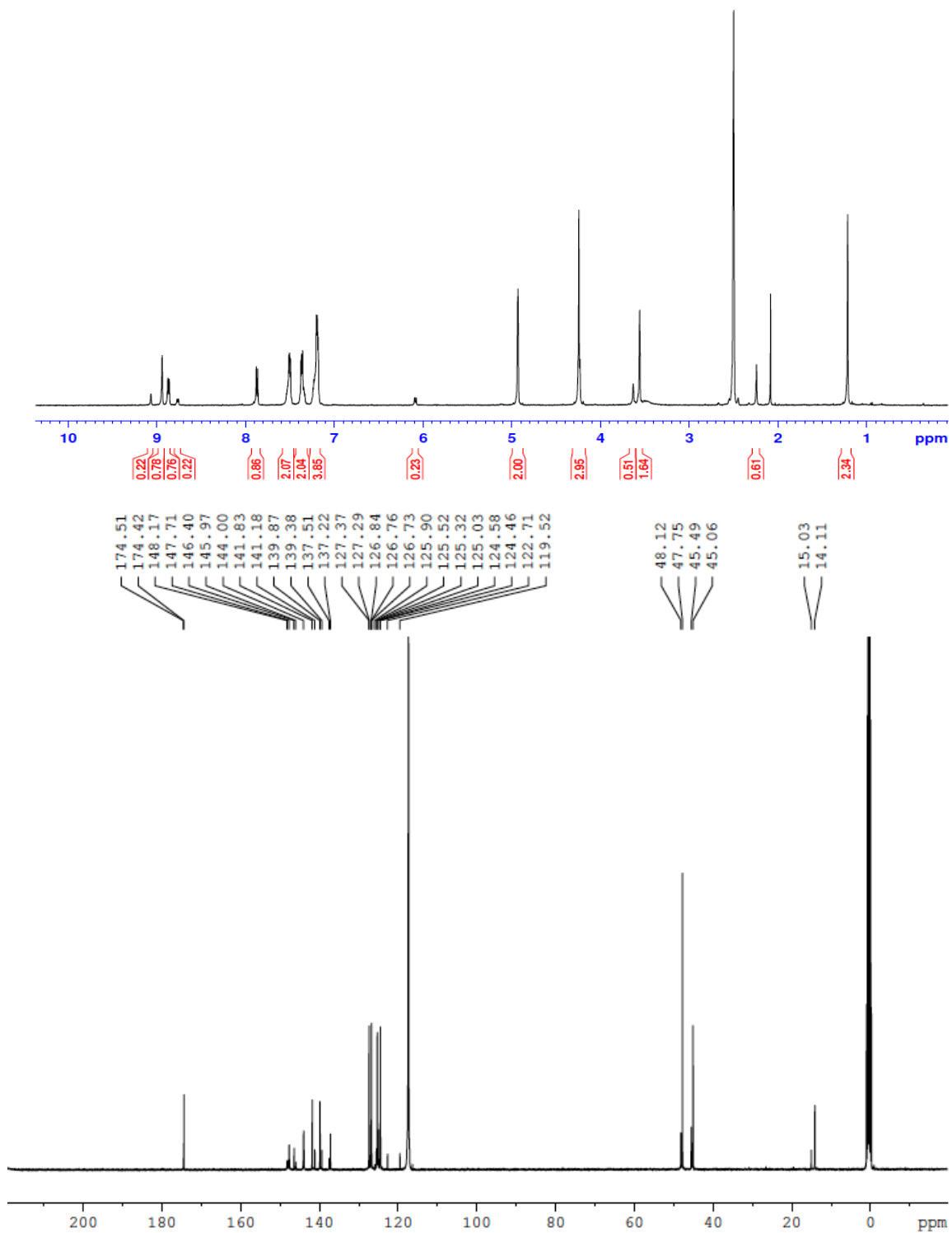
Carbon and Proton NMR of Balance 1 precursor



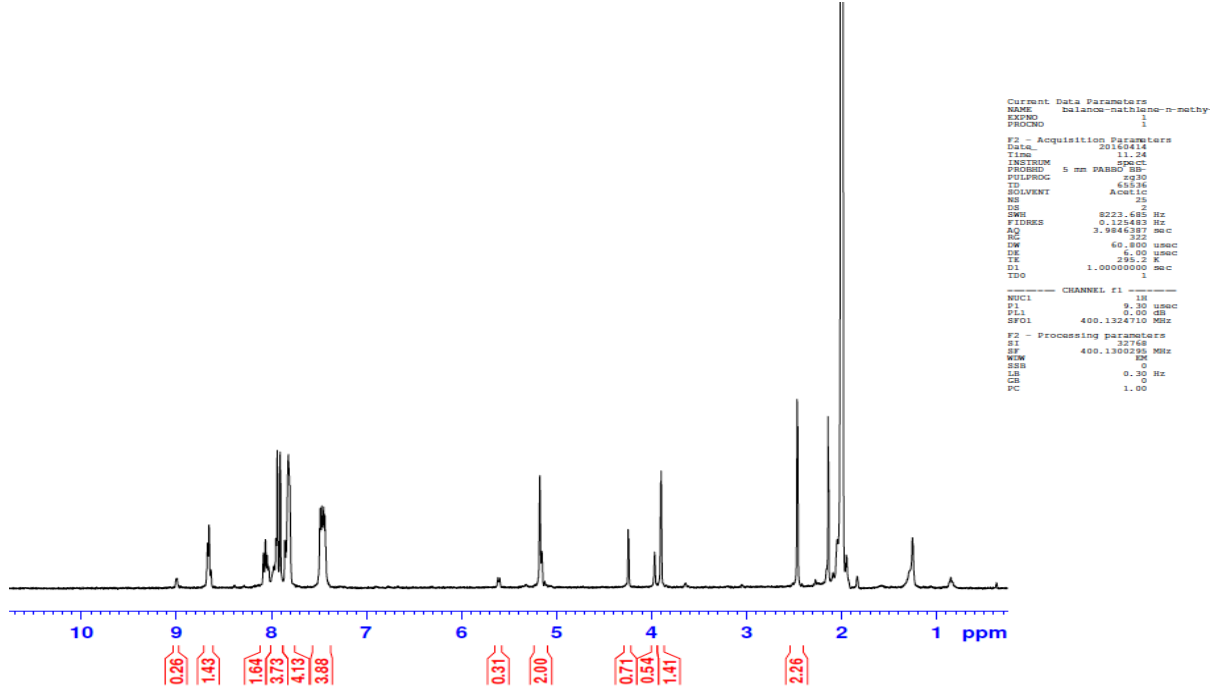
Carbon and Proton NMR of Balance 1



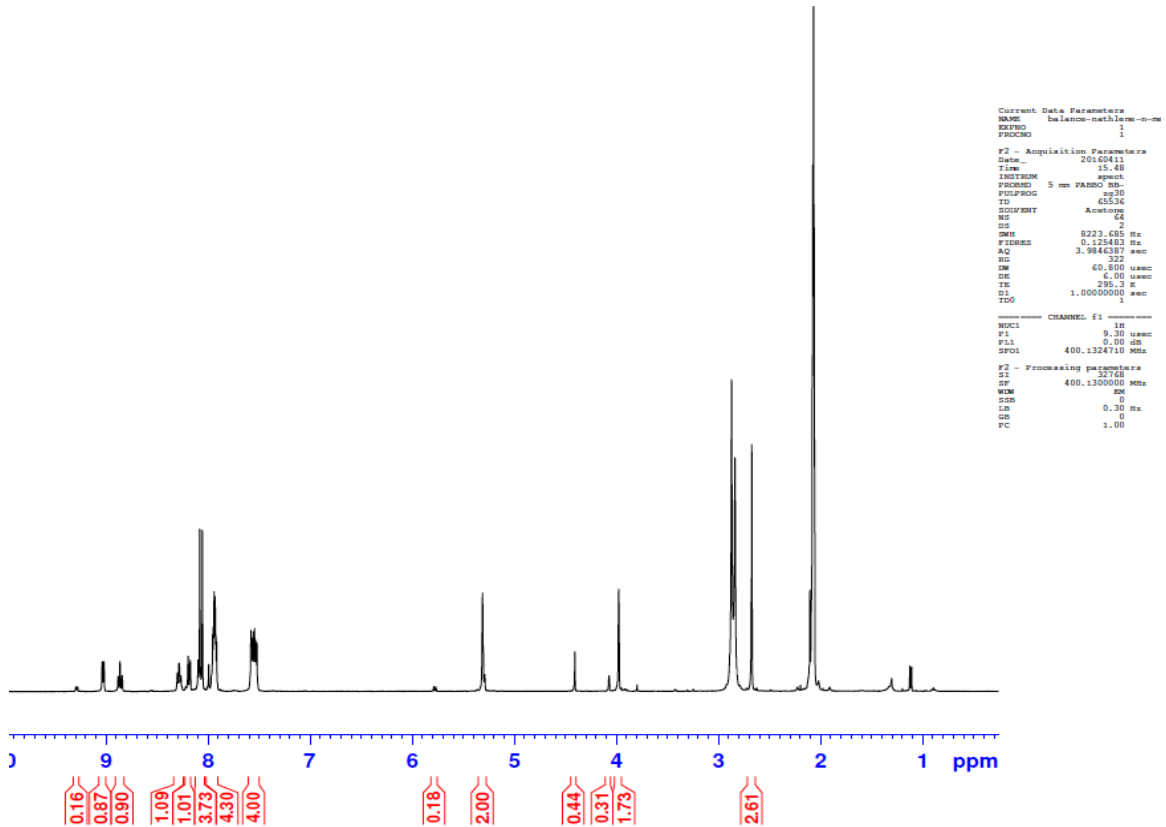
Proton and Carbon-13 NMR of balance 3



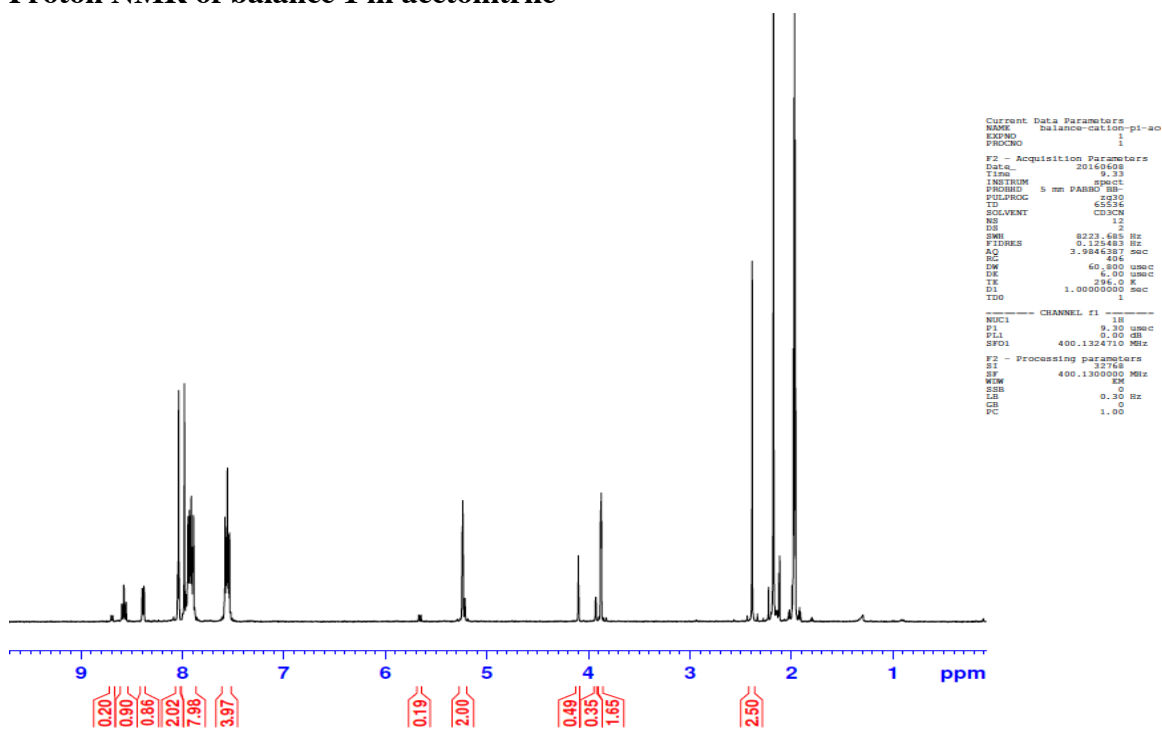
Proton NMR of Balance 1 in various solvents
Proton NMR of balance 1 in acetic acid



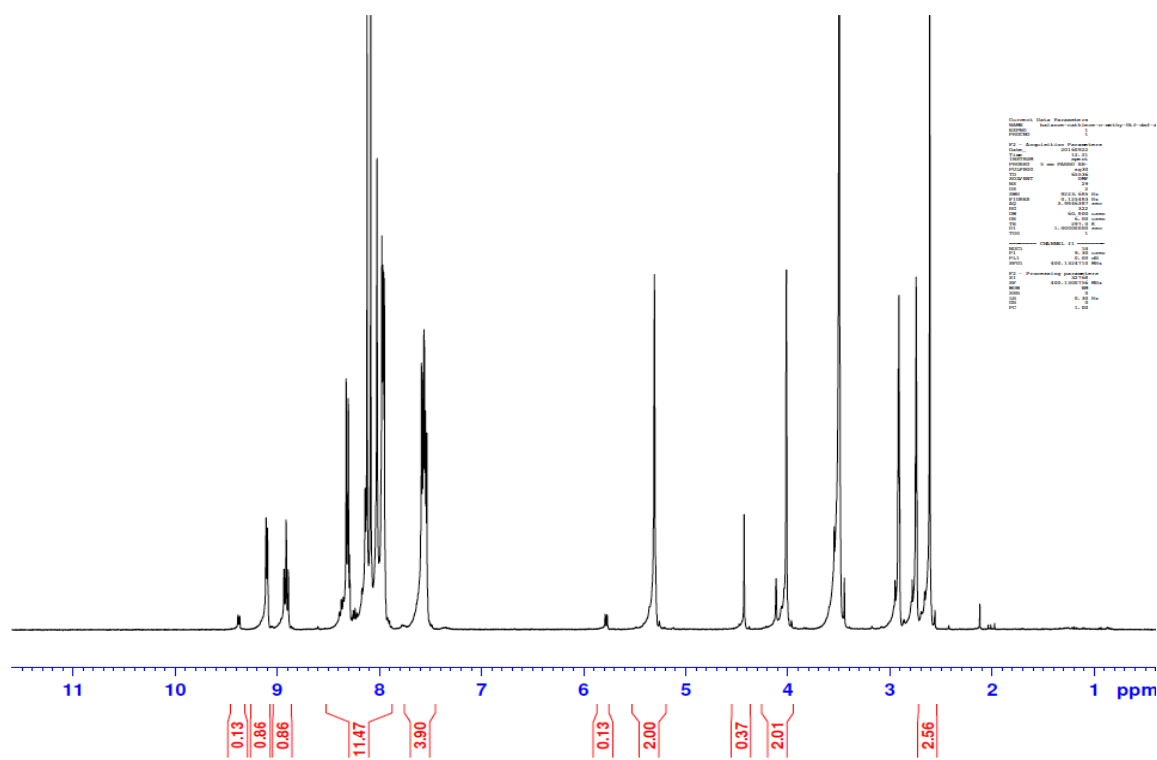
Proton NMR of balance 1 in acetone



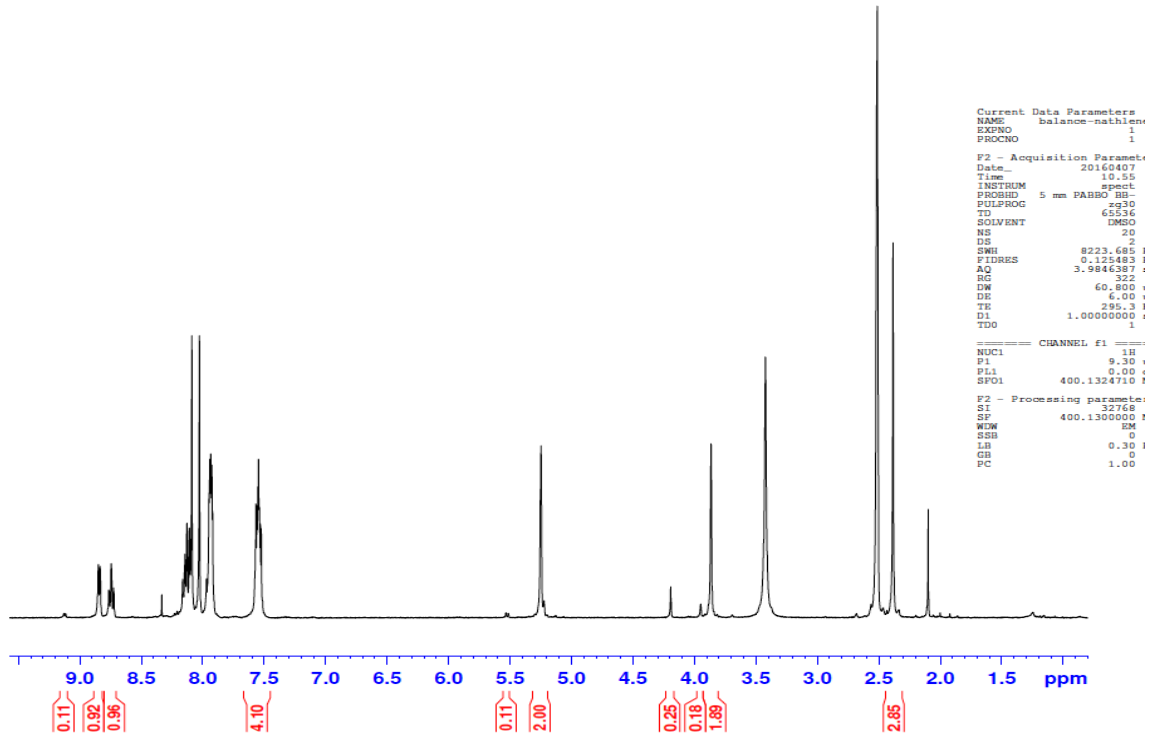
Proton NMR of balance 1 in acetonitrile



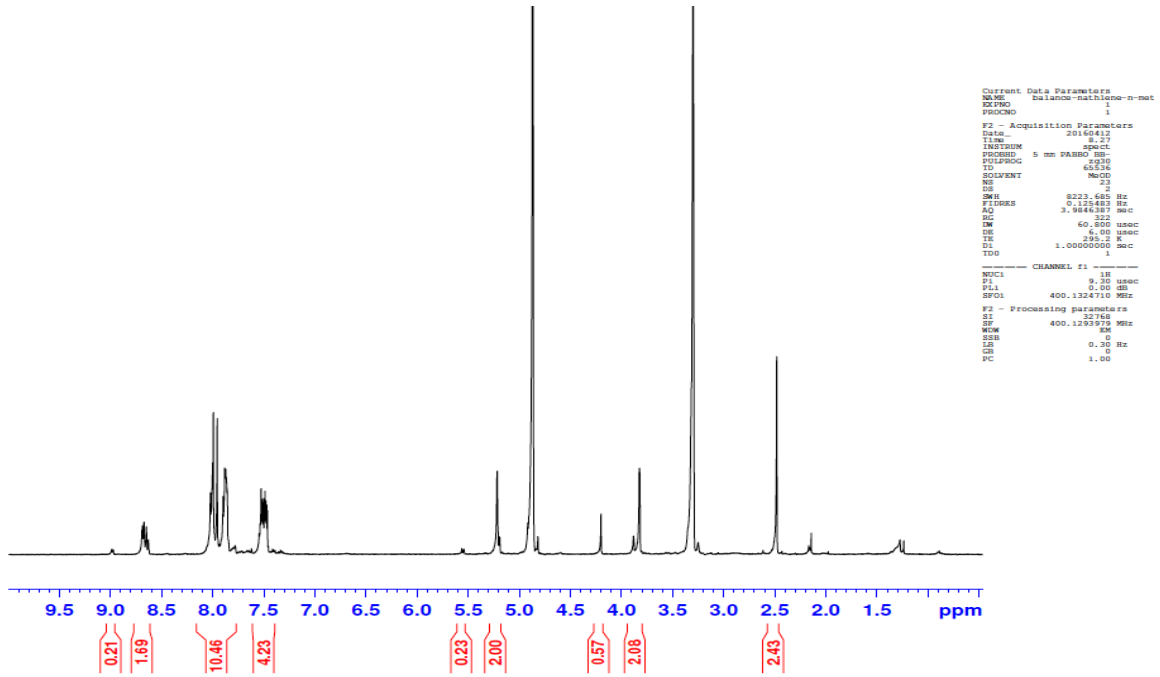
Proton NMR of balance 1 in DMF



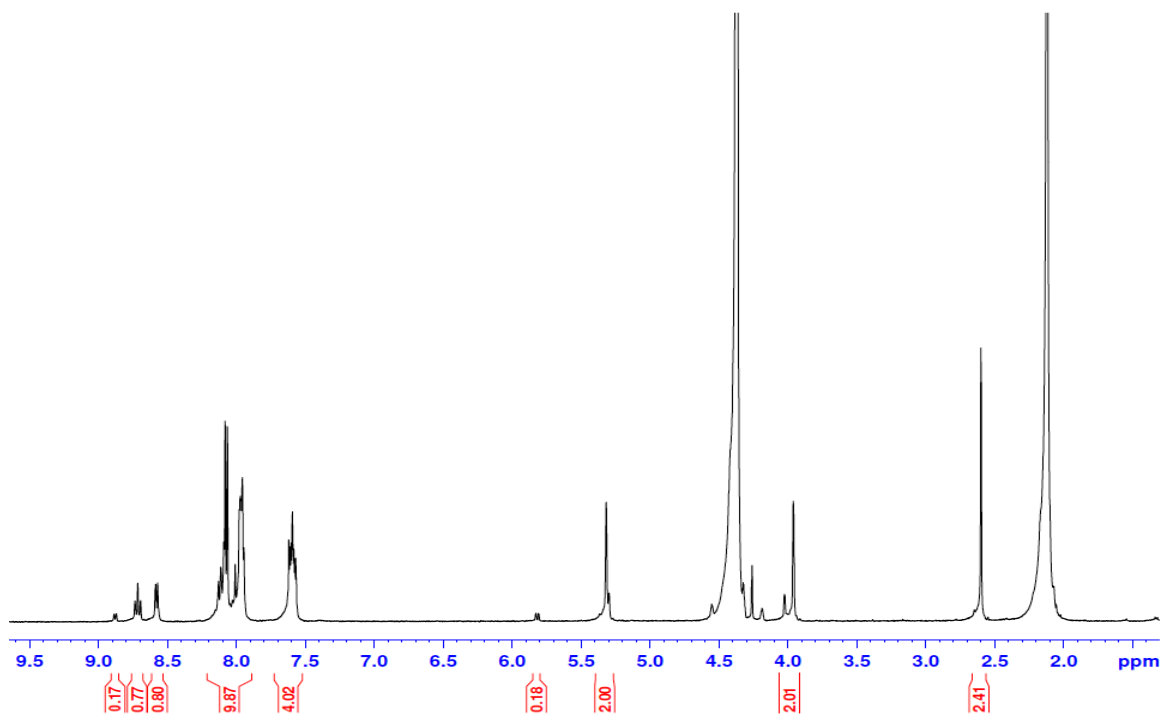
Proton NMR of balance 1 in DMSO



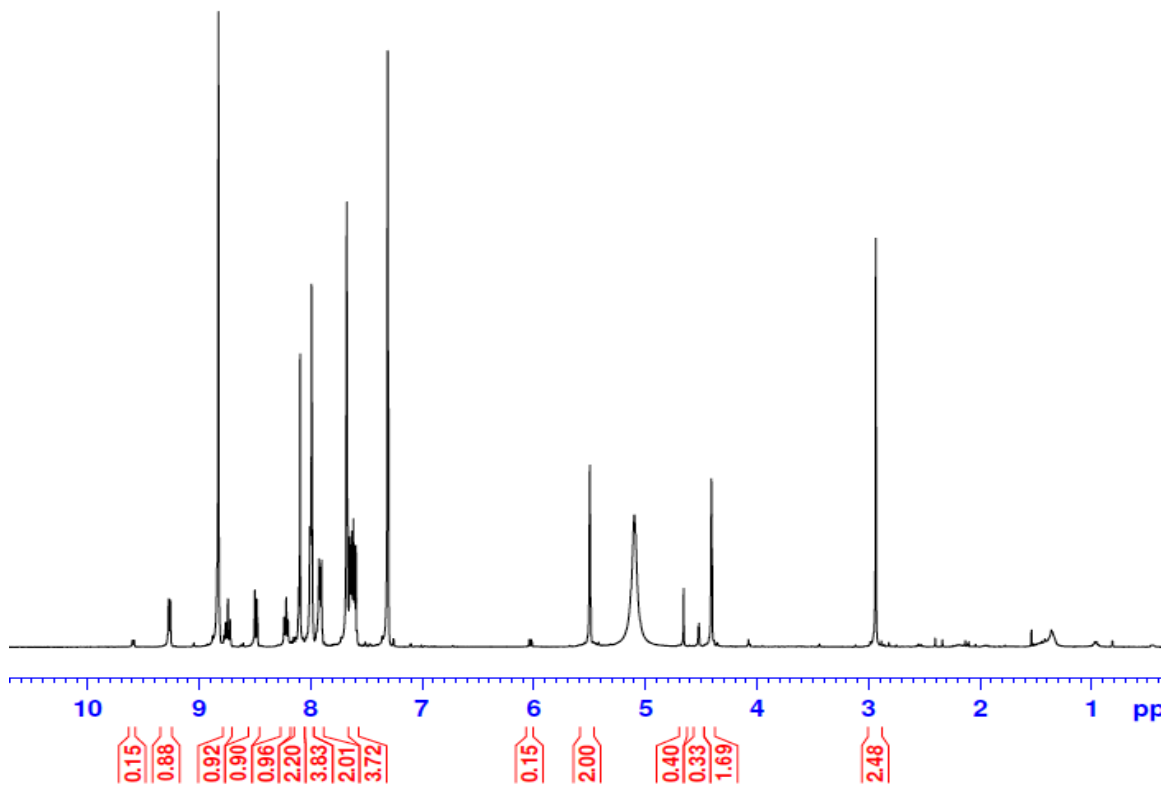
Proton NMR of balance 1 in Methanol



Proton NMR of balance 1 in nitromethane

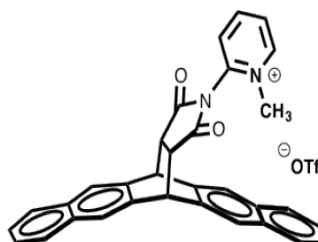
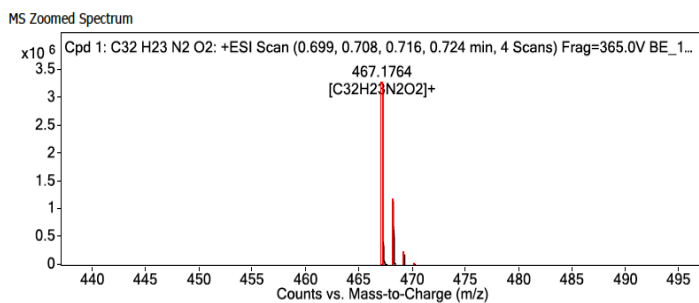
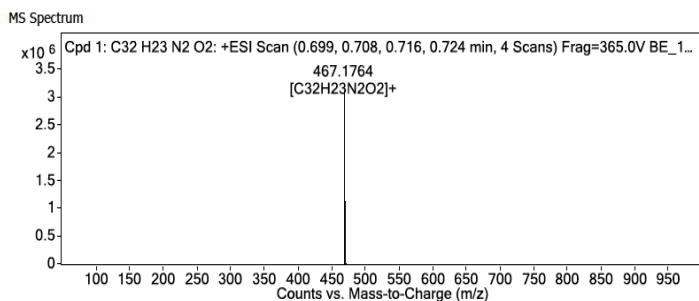


Proton NMR of balance 1 in Pyridine

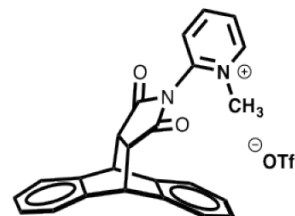
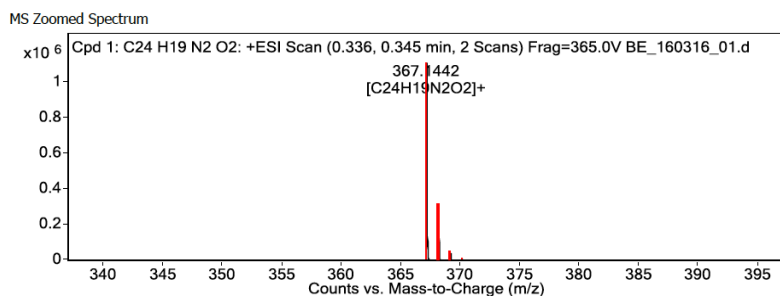
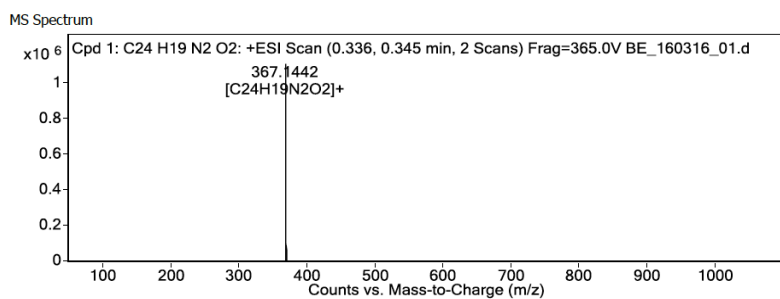


MS Spectrum for Balances 1 and 1a

Balance 1



Balance 1a



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