Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Elucidating Factors Leading to Acidolytic Degradation of Sterically Strained Oligoether Dendrons

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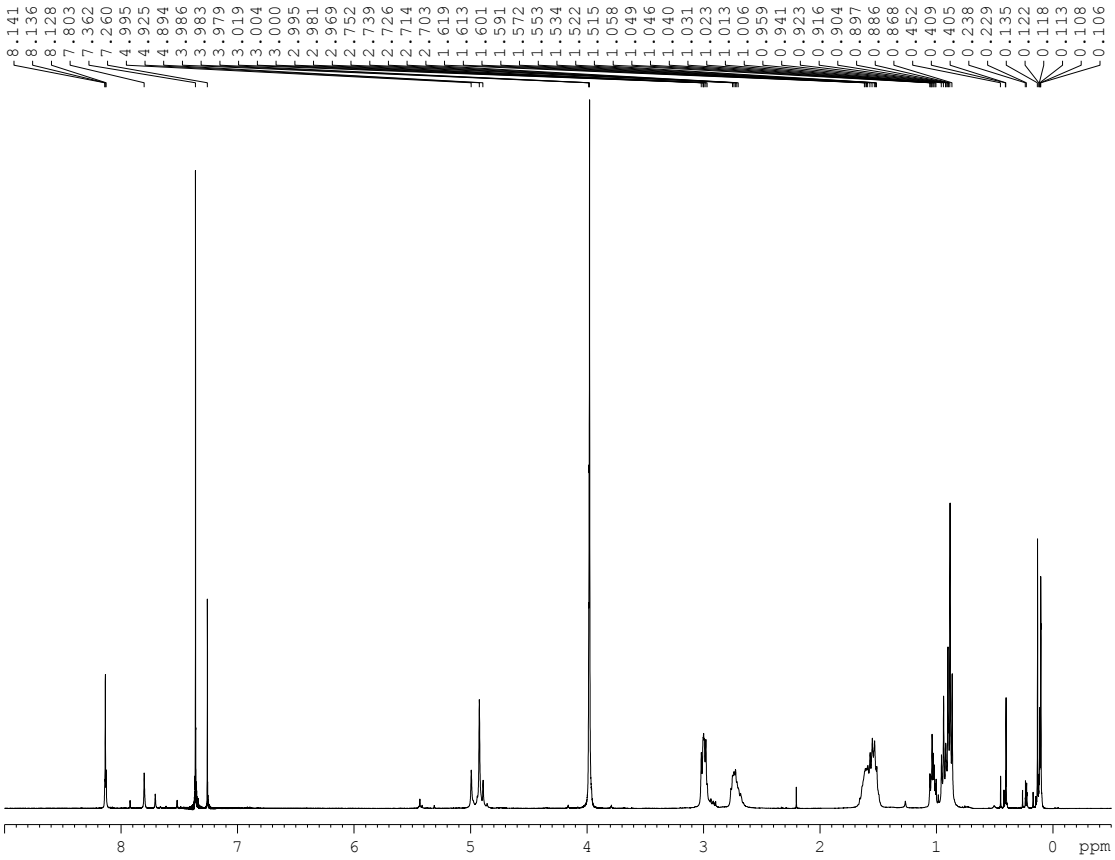
Supplementary Information

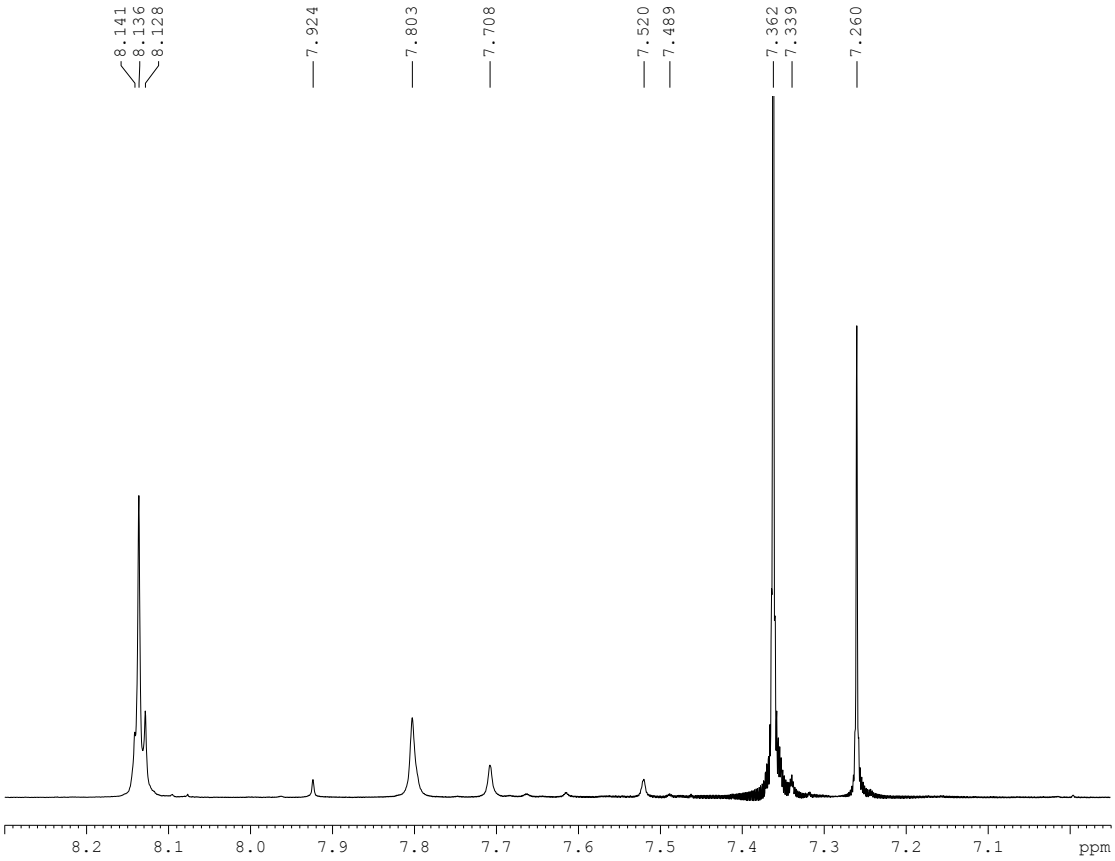
1. H NMR monitoring of the disassembly of G3(E) in a 9:1 $CDCl_3$:TFA mixture

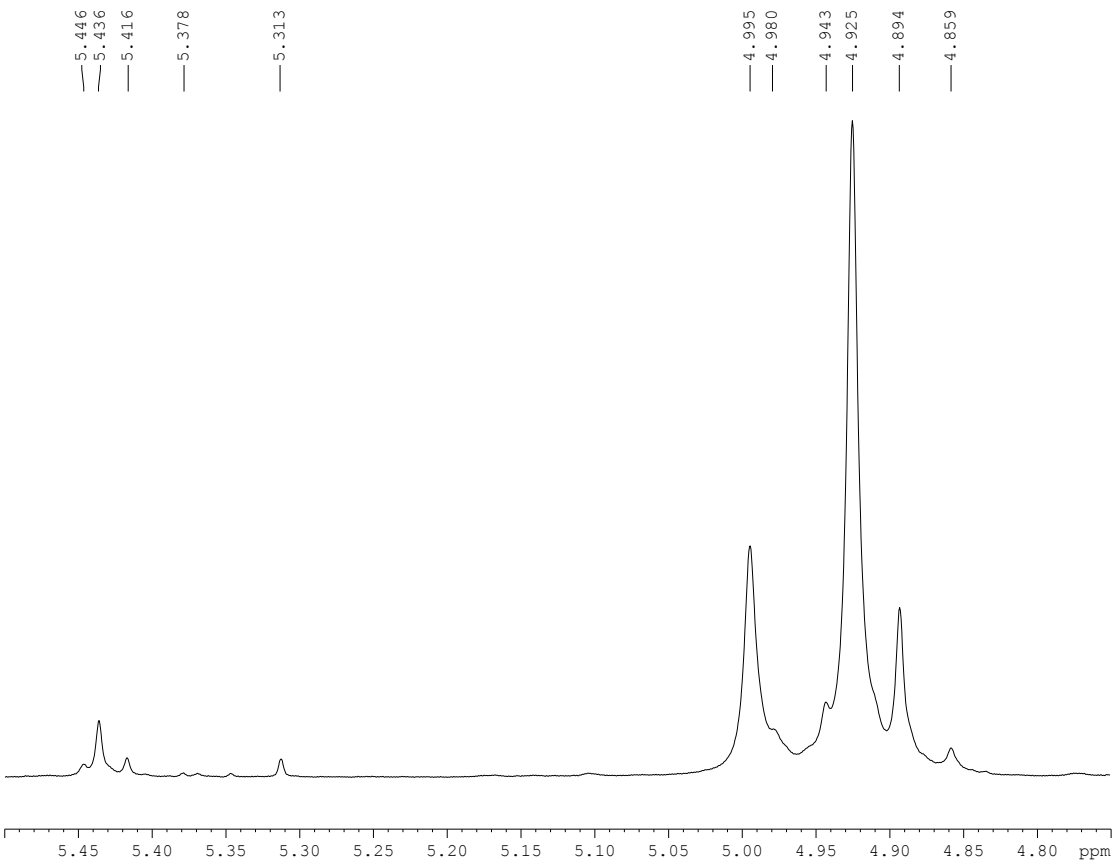
The monitoring measurements were carried out on Bruker AVANCE-400 spectrometer, with residual $CHCl_3$ (7.26 ppm), as calibration standard, and with benzene (7.36 ppm), as internal standard.

Signals at 0.1-0.5 ppm and 2.20 ppm – regular impurities observed in the cleavage solutions. Minor signal at 5.31 – unidentified impurity.

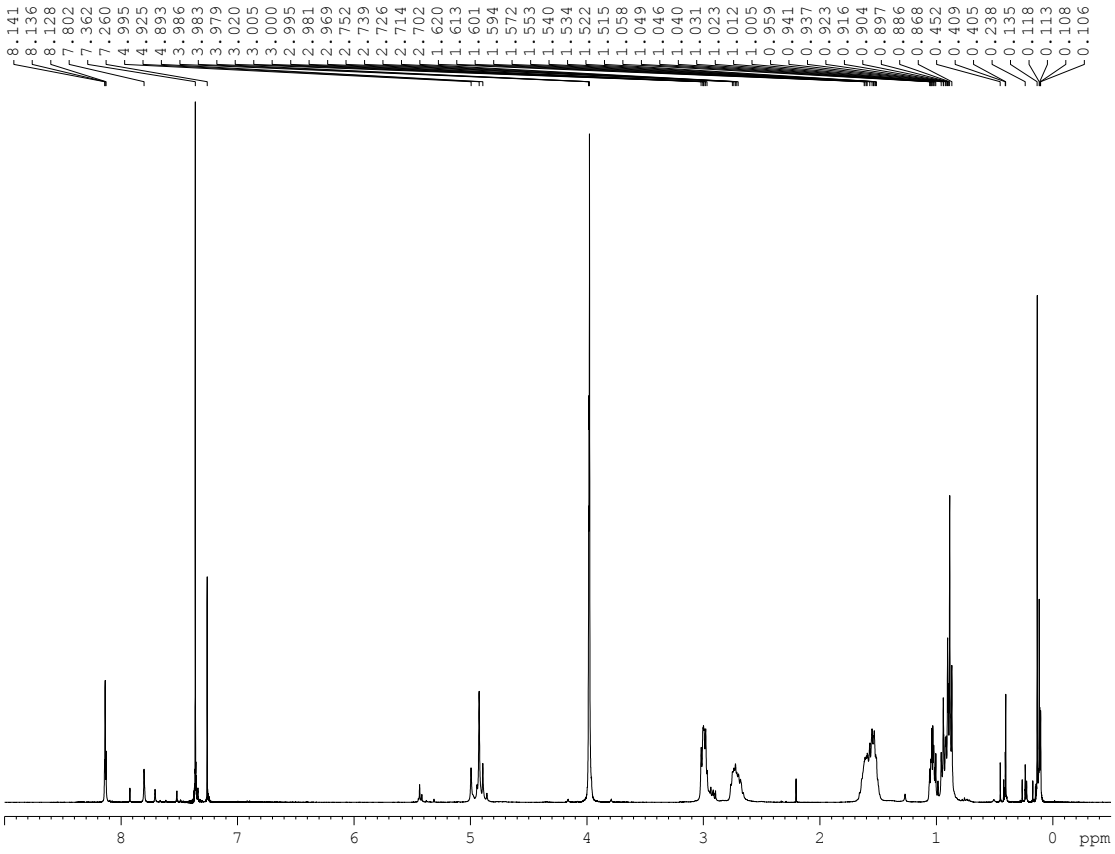
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 45 min.

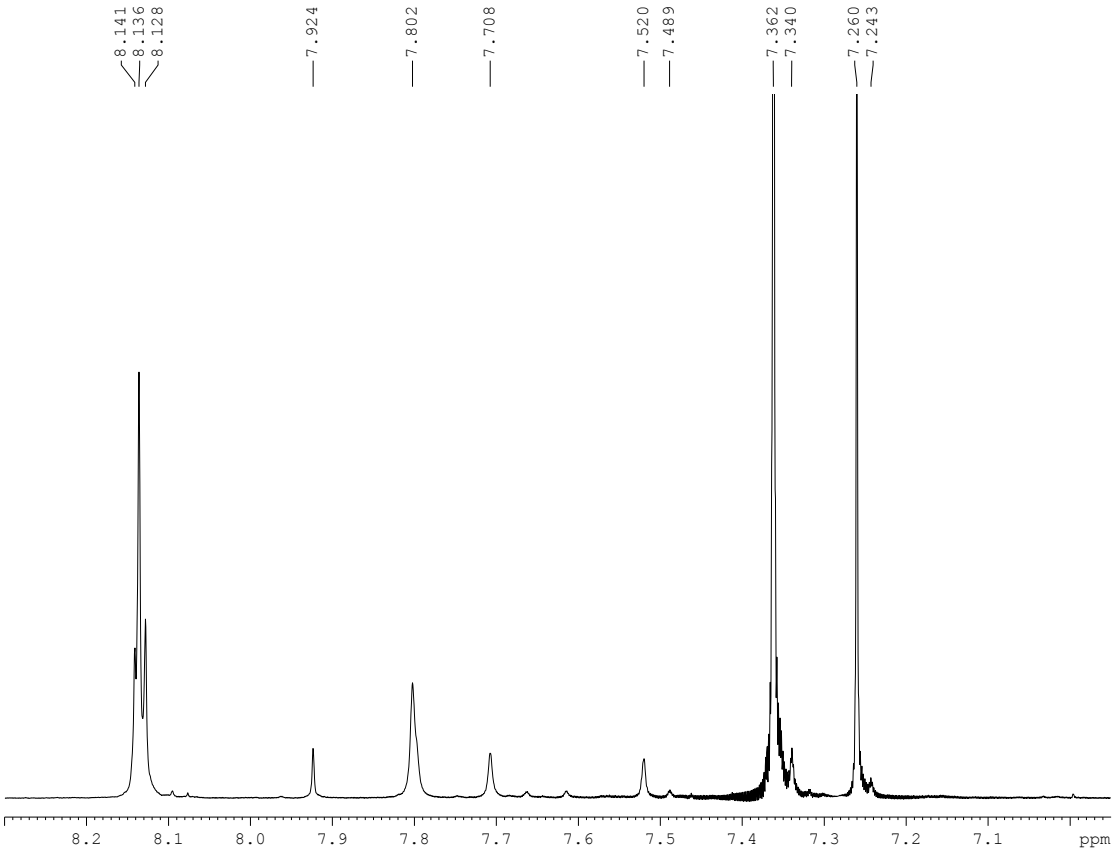


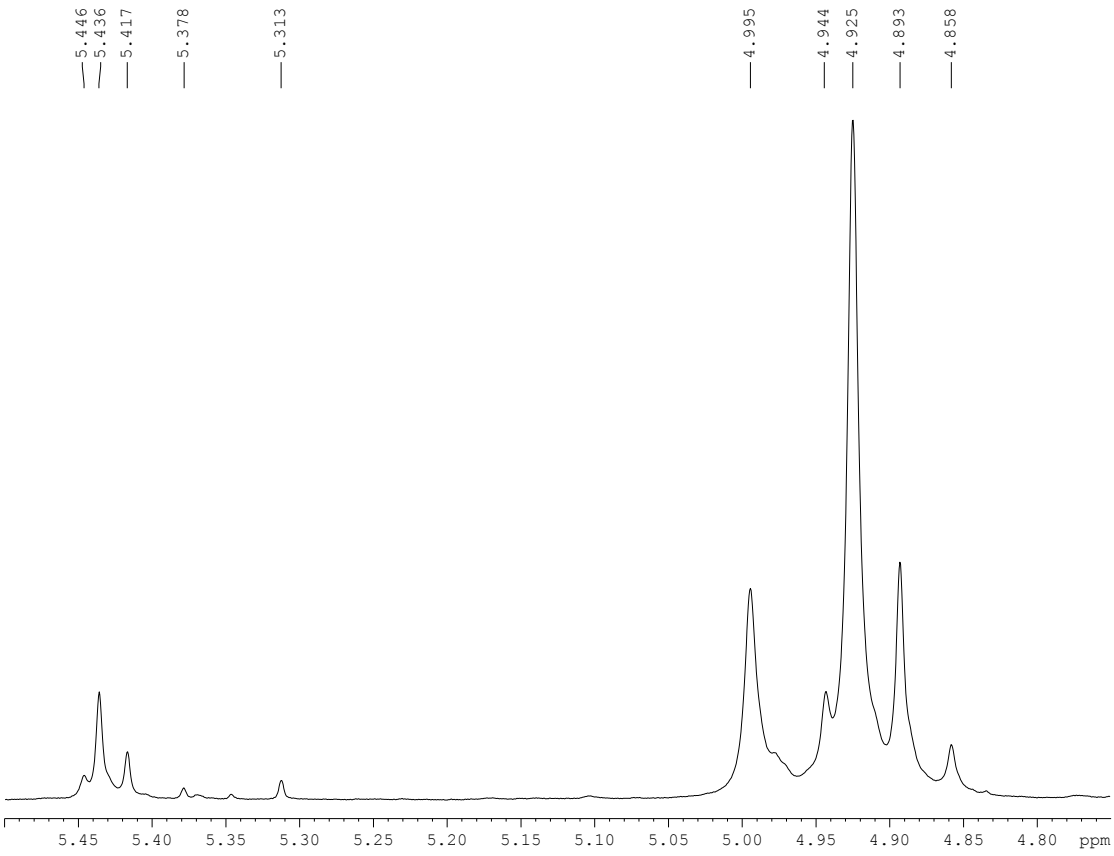



5.446
5.436
5.416
5.378
5.313
4.995
4.980
4.943
4.925
4.894
4.859
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

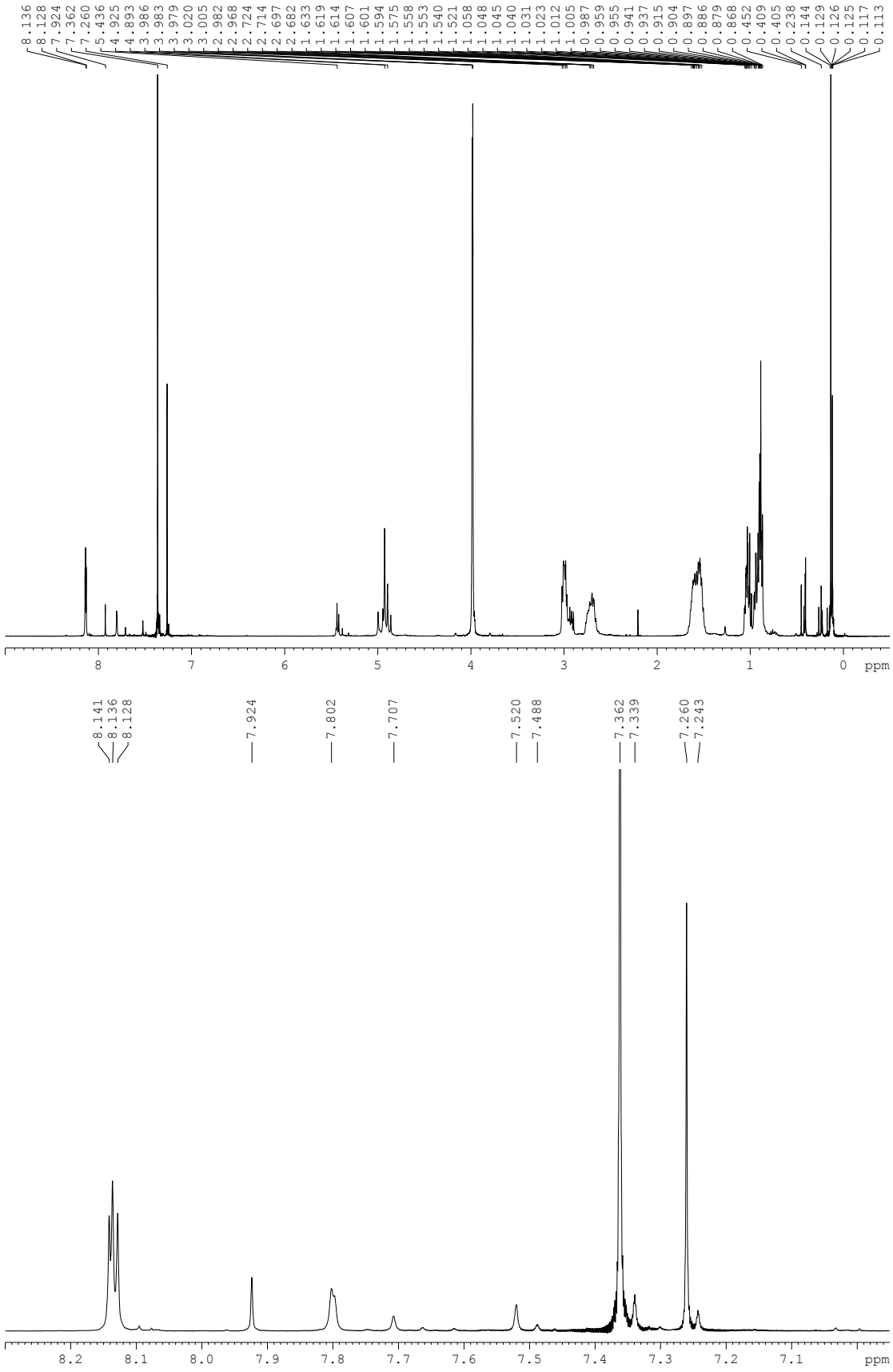
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 2 h.

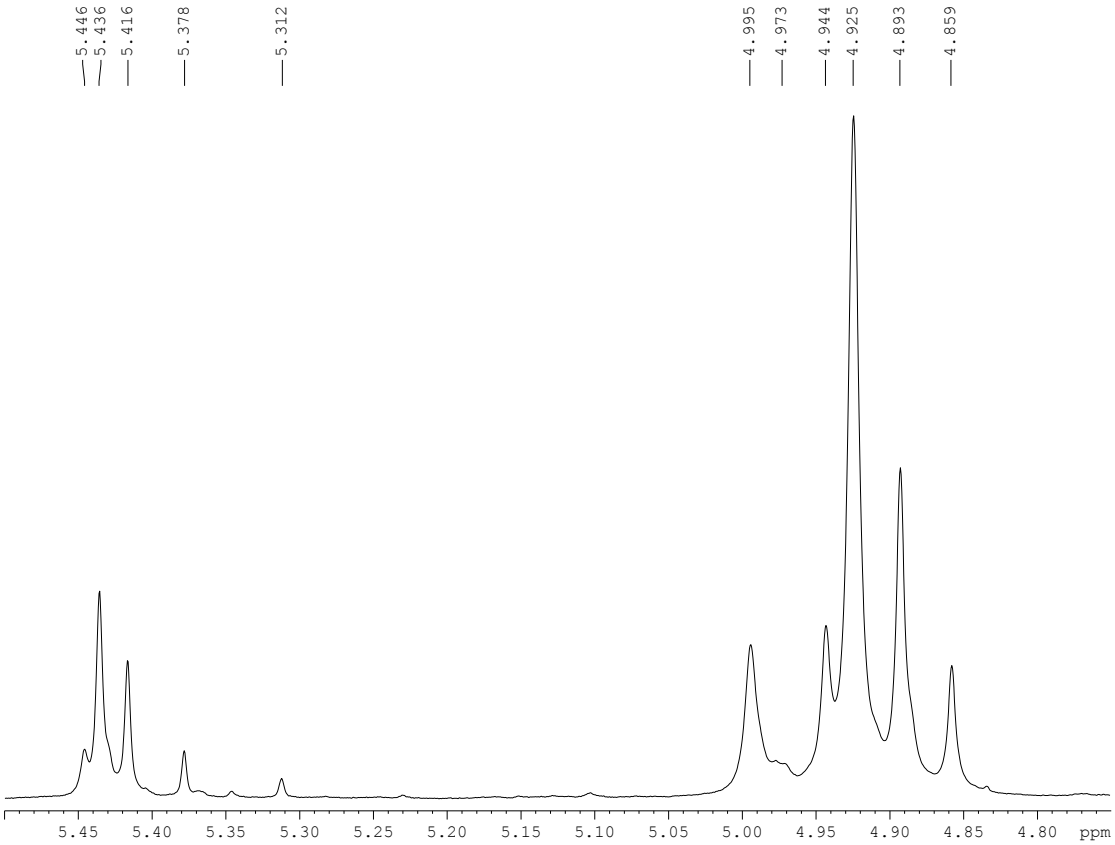




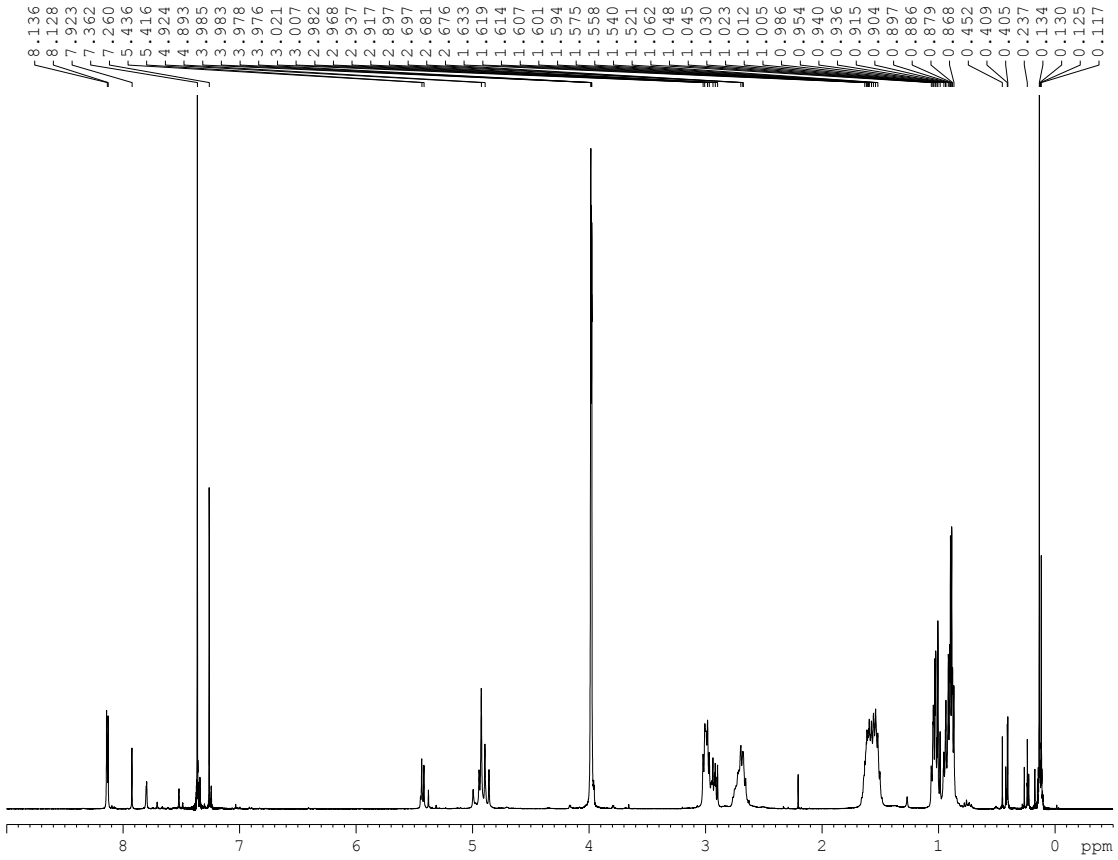

5.446
5.436
5.417
5.378
5.313
4.995
4.944
4.925
4.893
4.858
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

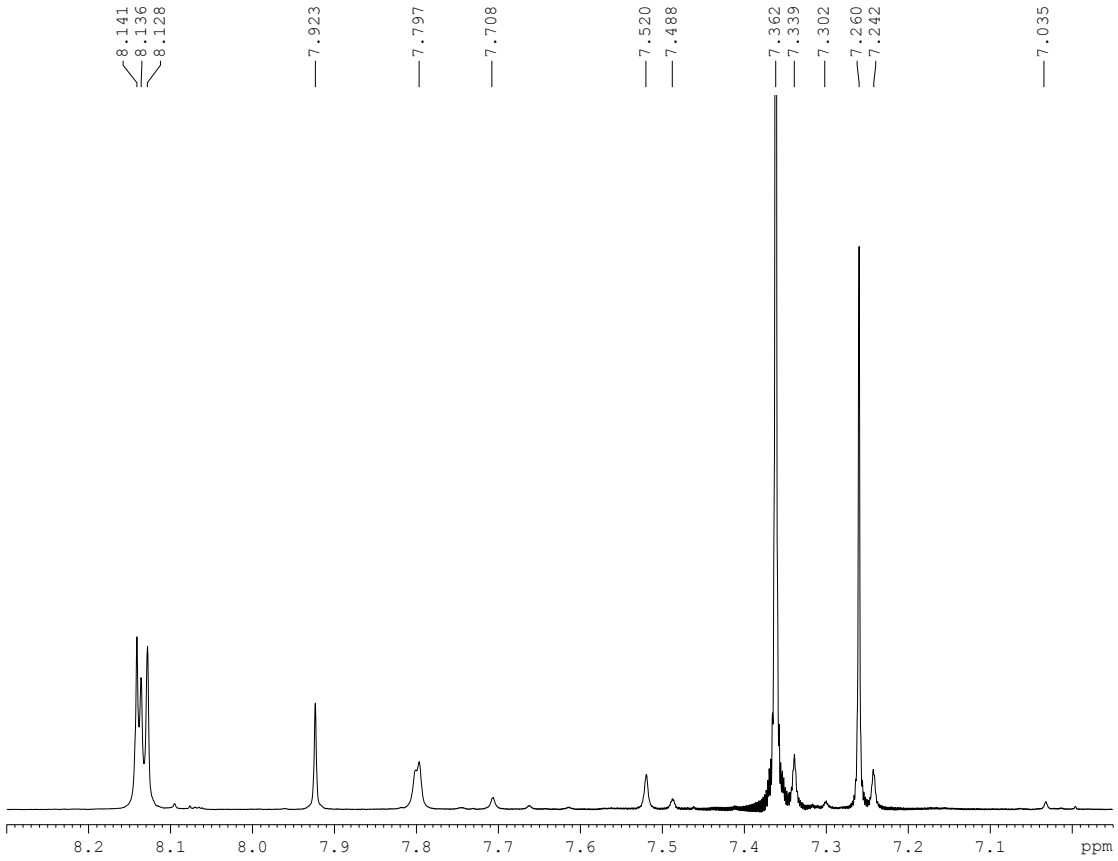
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 4 h.

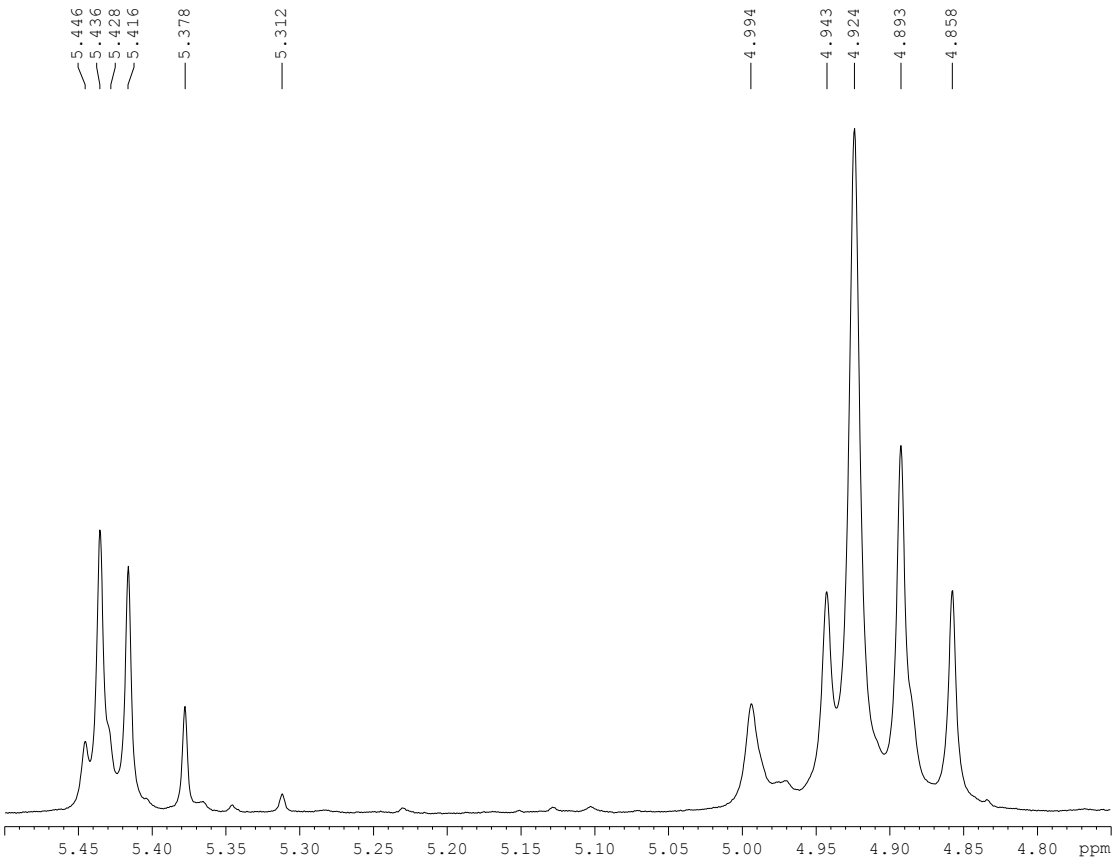



5.446
5.436
5.416
5.378
5.312
4.995
4.973
4.944
4.925
4.893
4.859
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

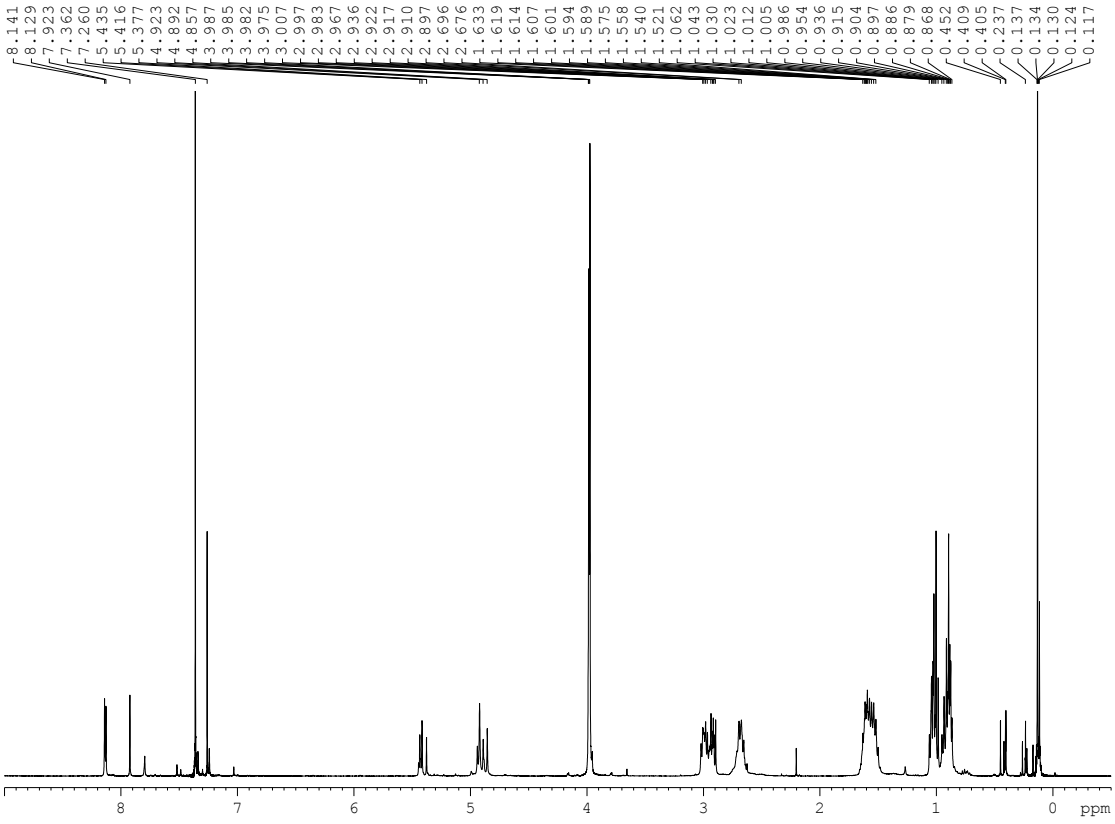
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 6 h.

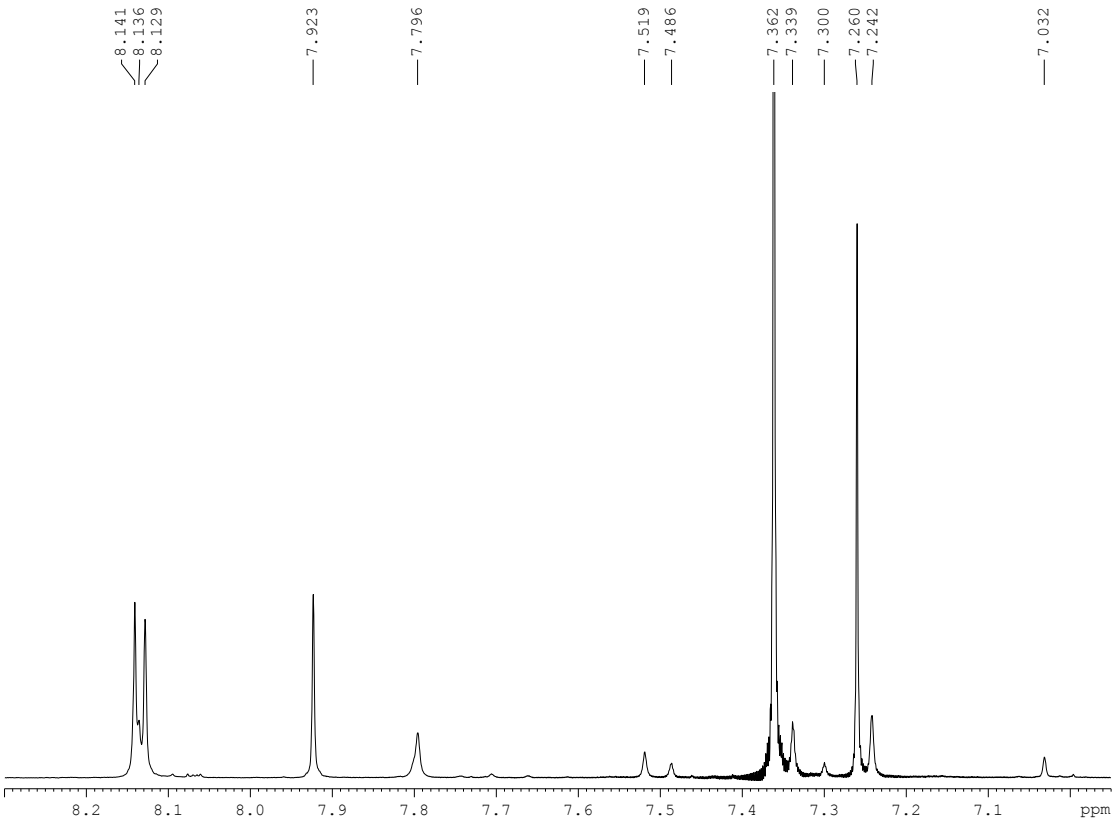


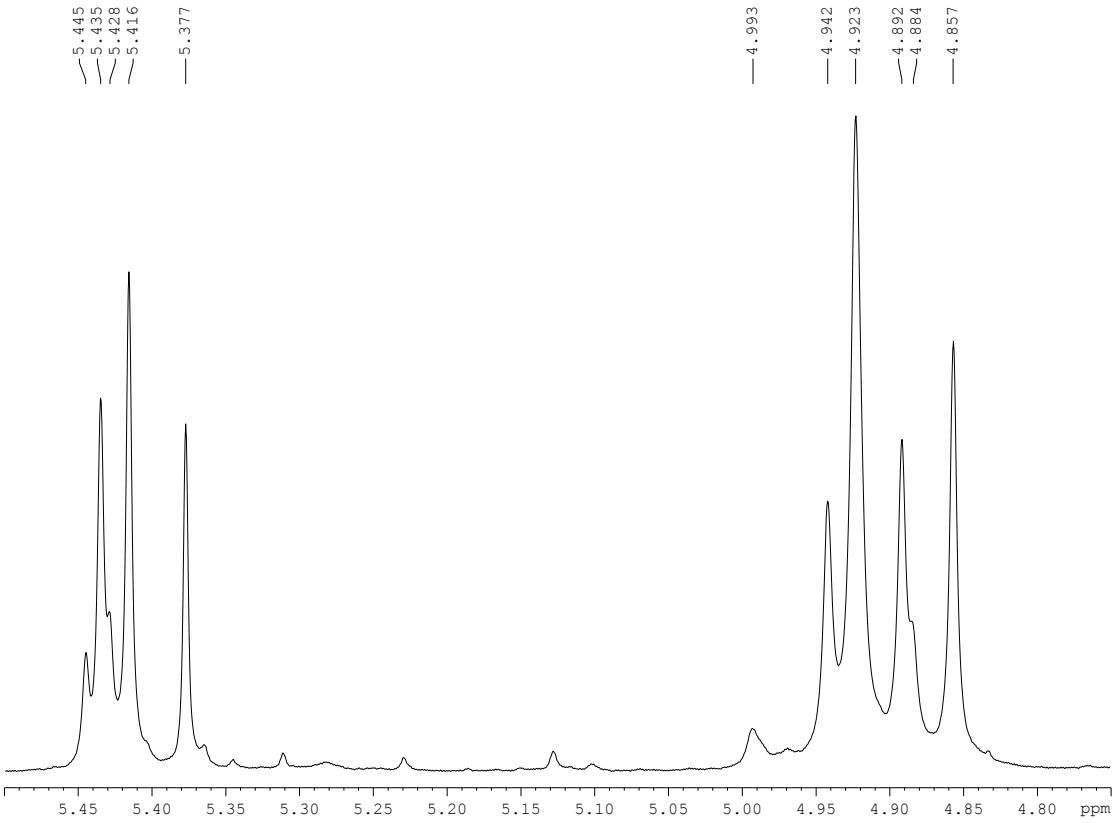



5.446
5.436
5.428
5.416
5.378
5.312
4.994
4.943
4.924
4.893
4.858
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

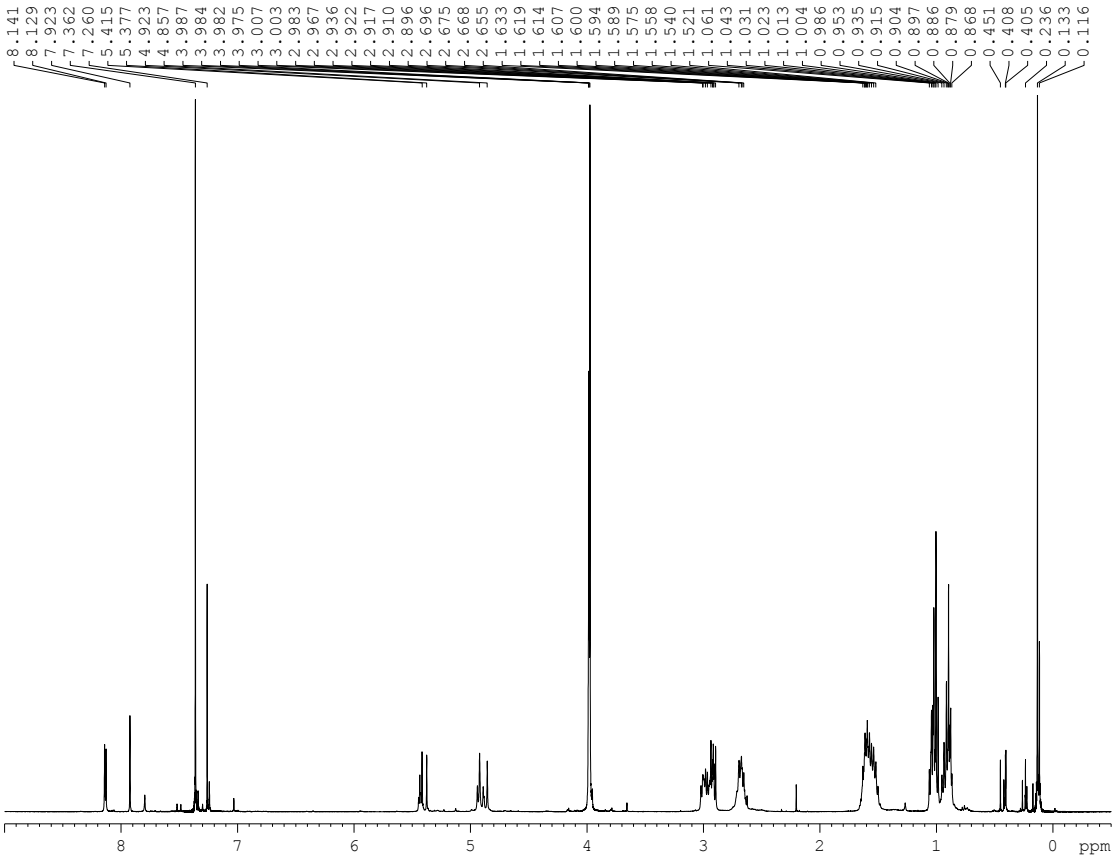
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 11 h.

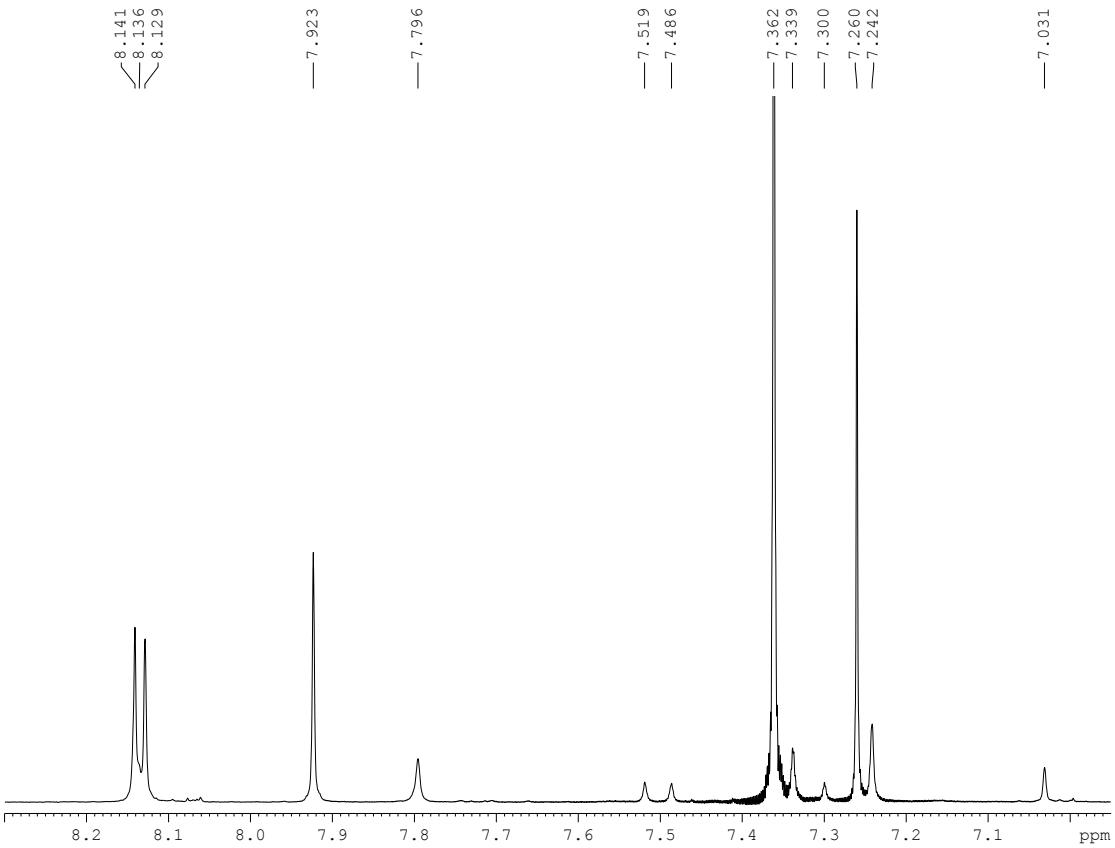


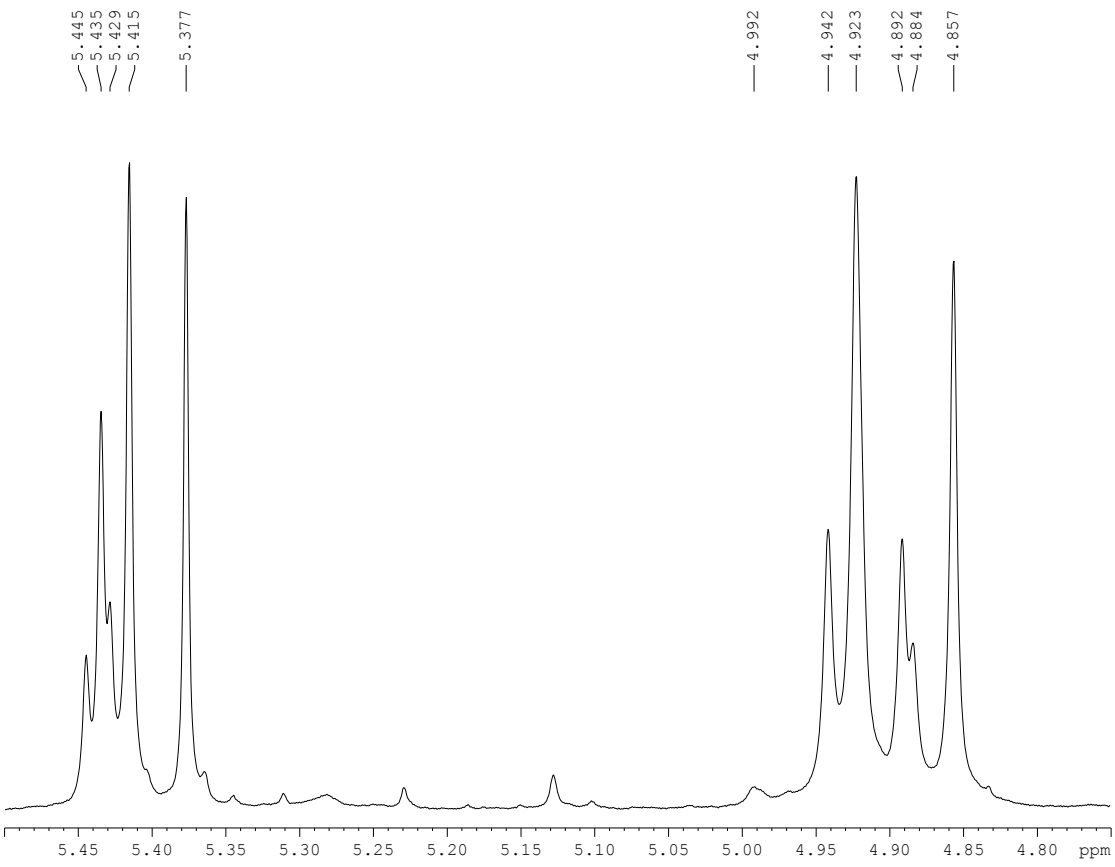



5.445
5.435
5.428
5.416
5.377
4.993
4.942
4.923
4.892
4.884
4.857
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

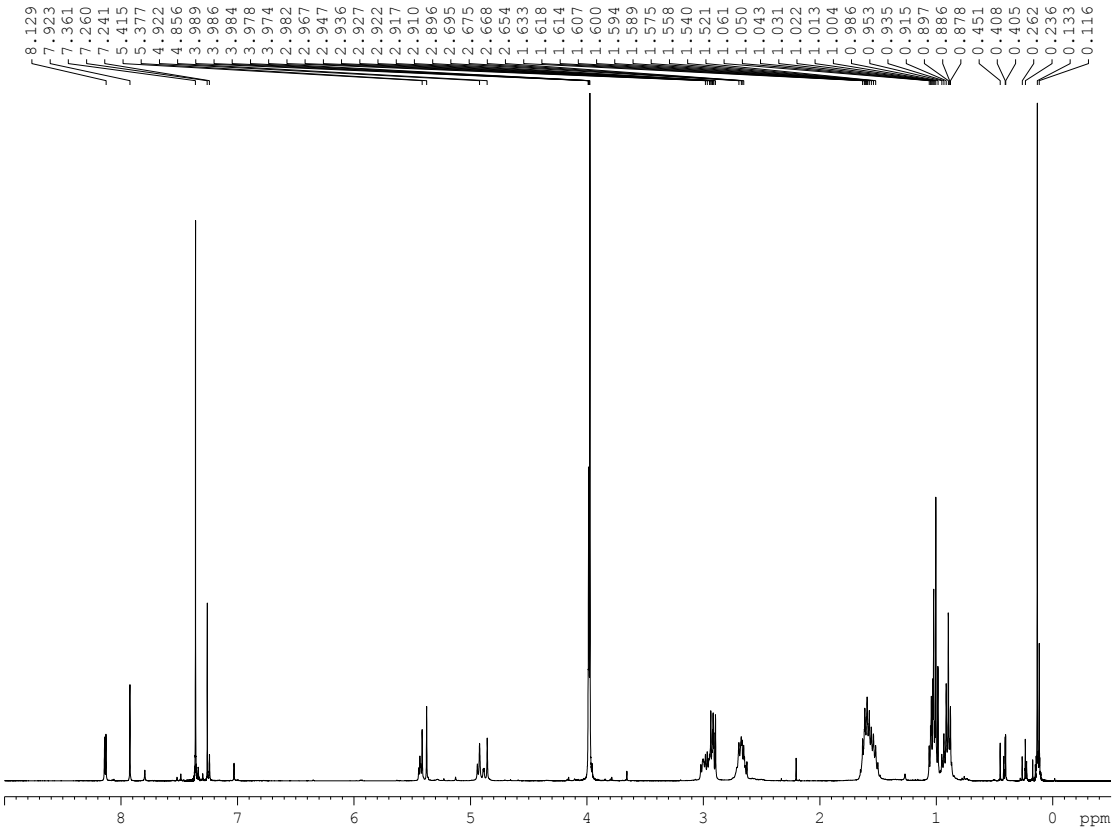
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 15 h.

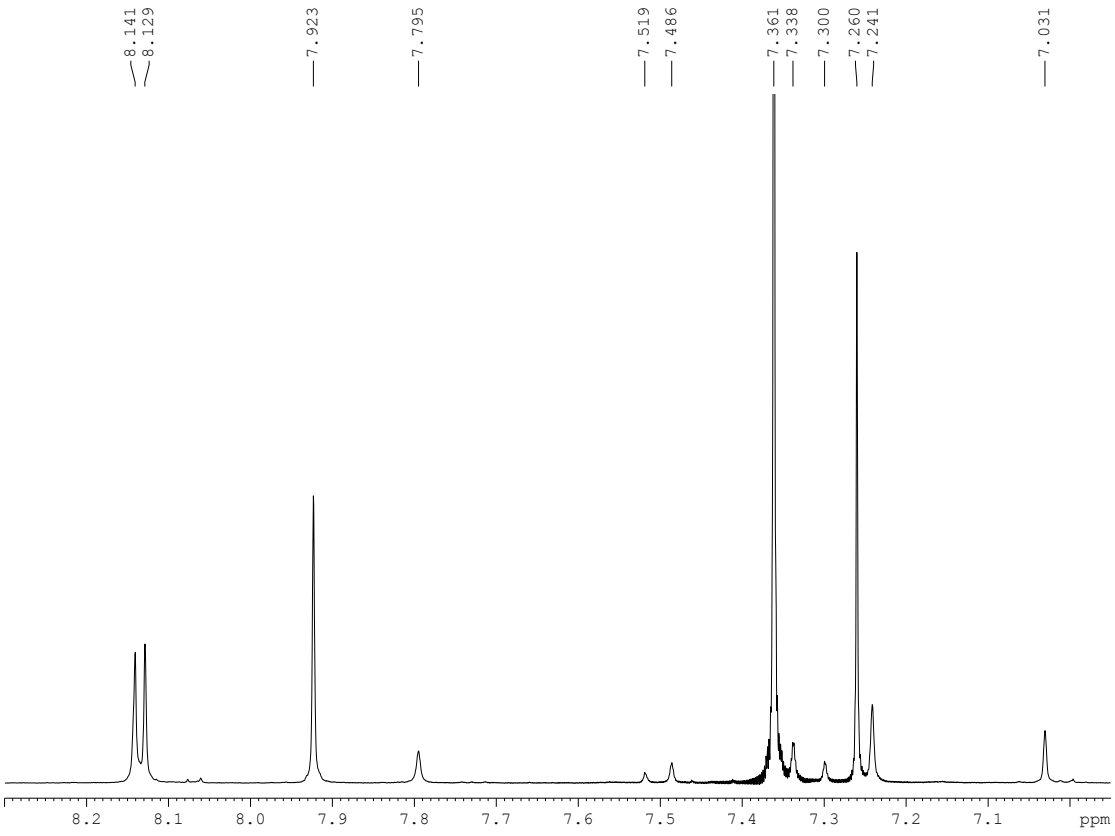


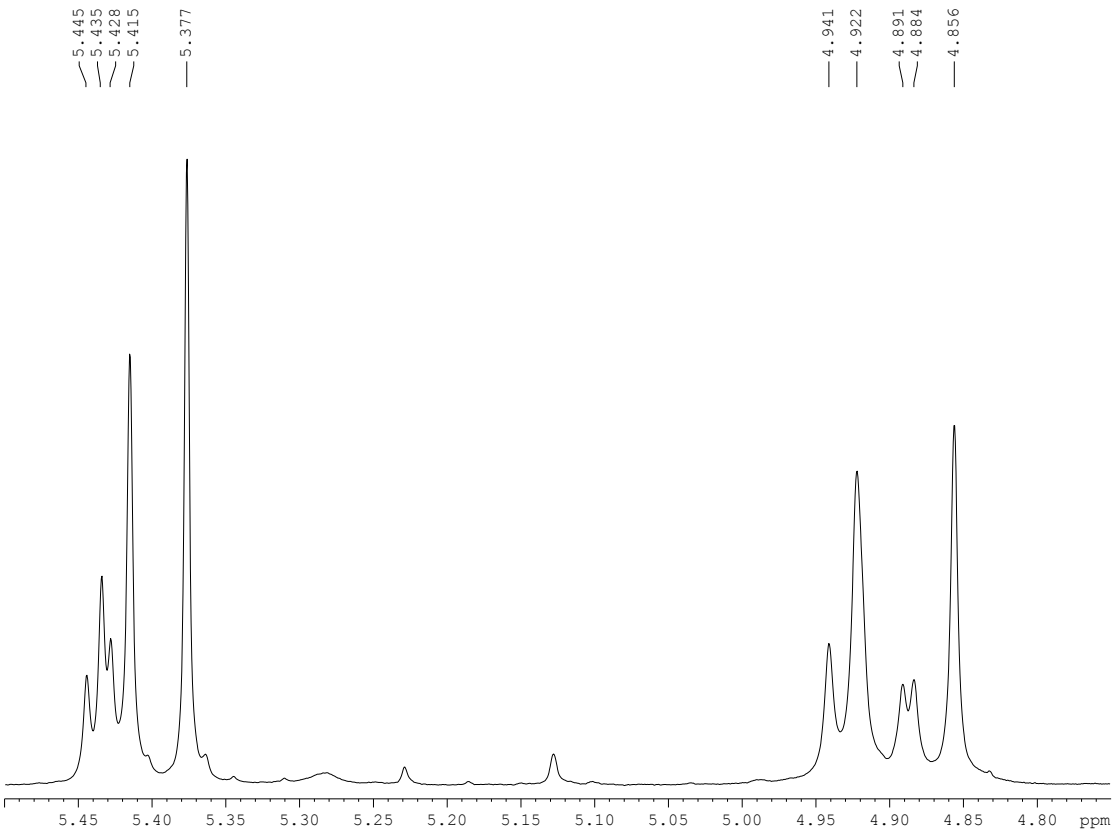



5.445
5.435
5.429
5.415
5.377
4.992
4.942
4.923
4.892
4.884
4.857
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

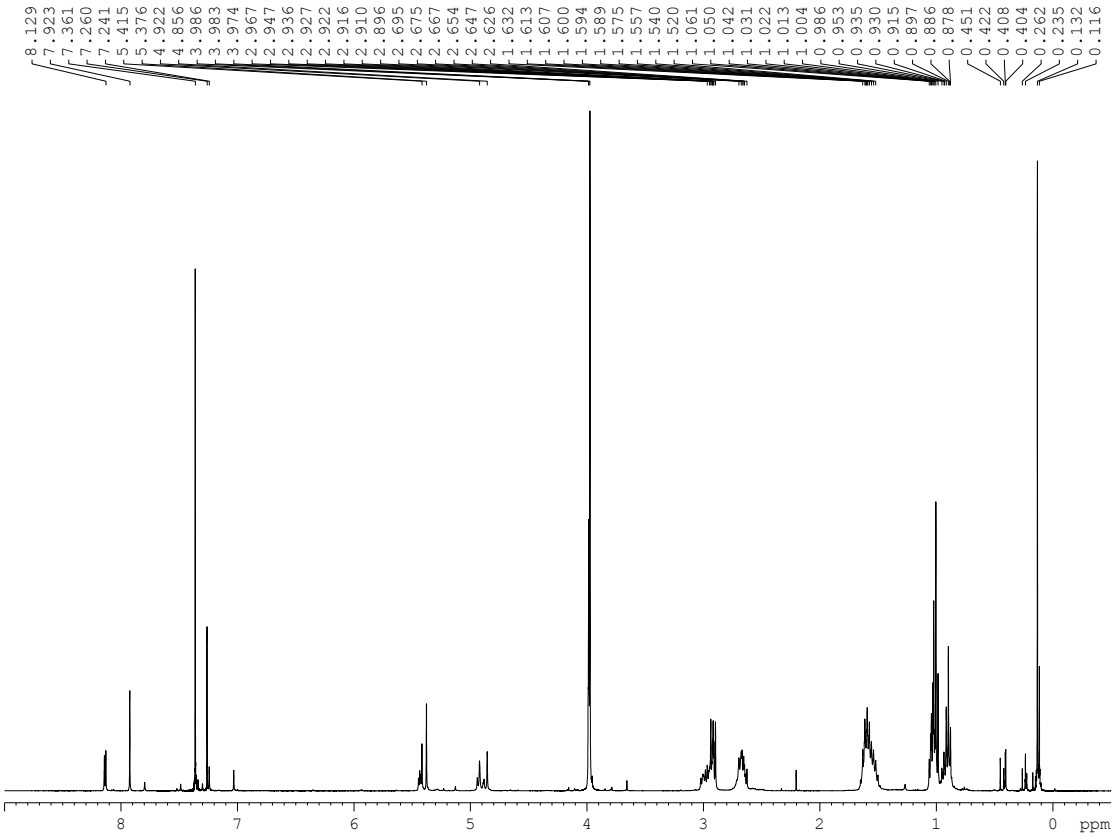
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 22 h.

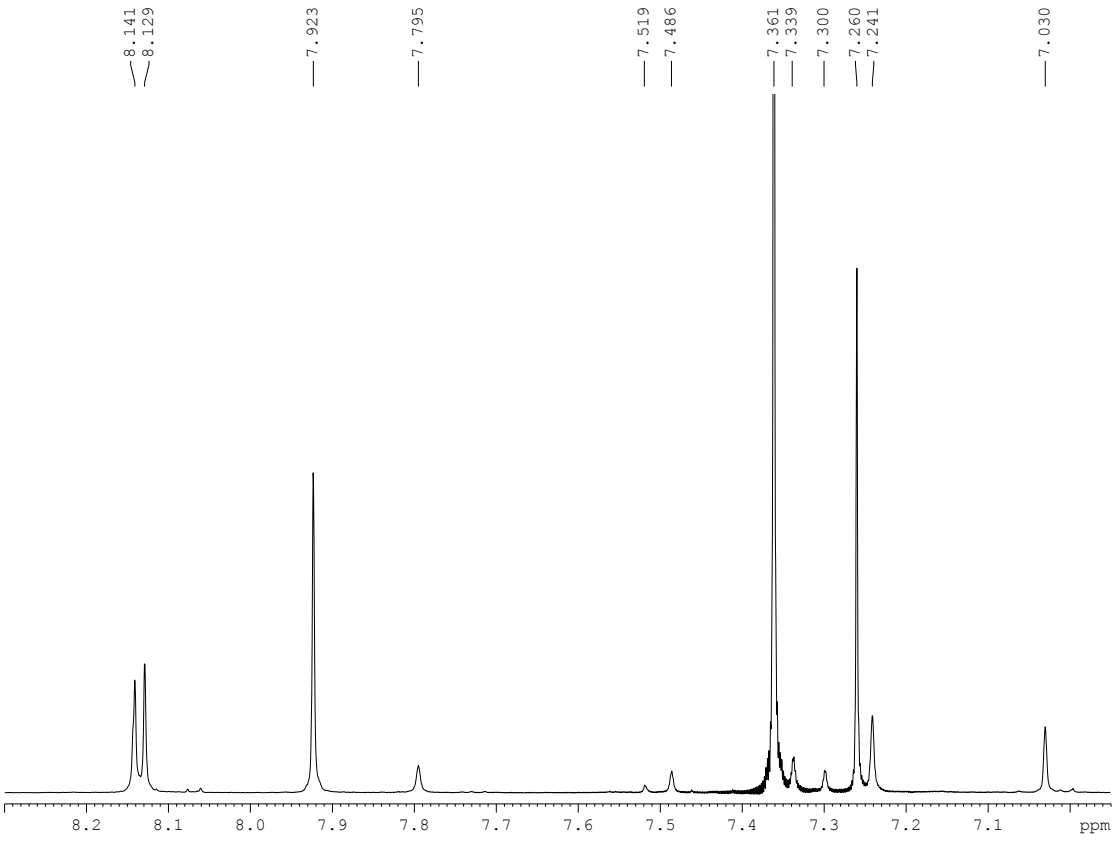


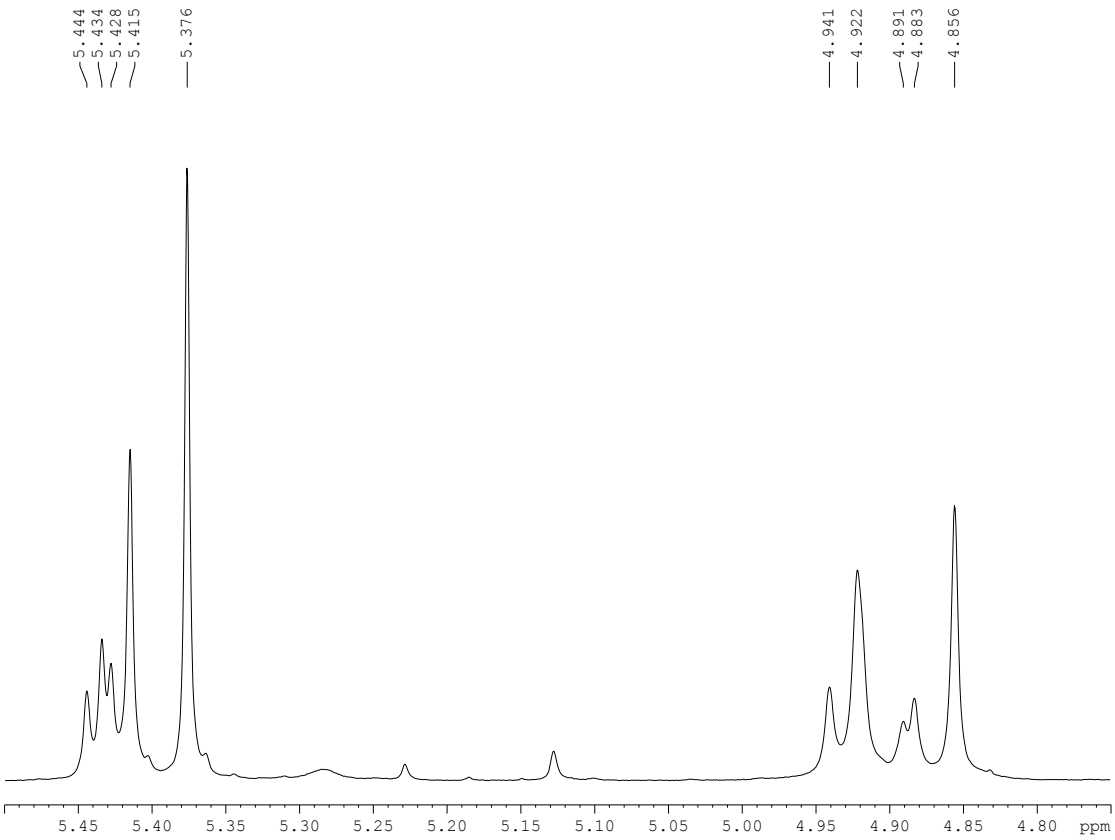



5.445
5.435
5.428
5.415
5.377
4.941
4.922
4.891
4.884
4.856
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

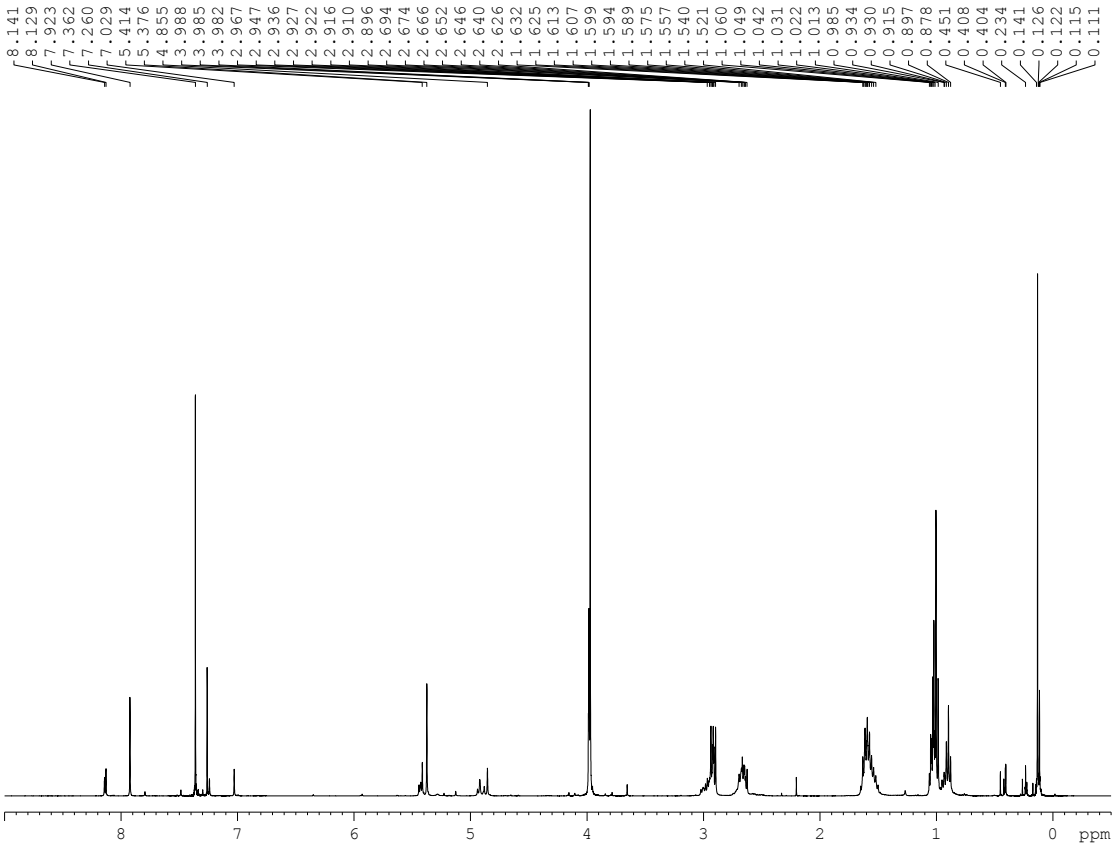
^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 27 h.

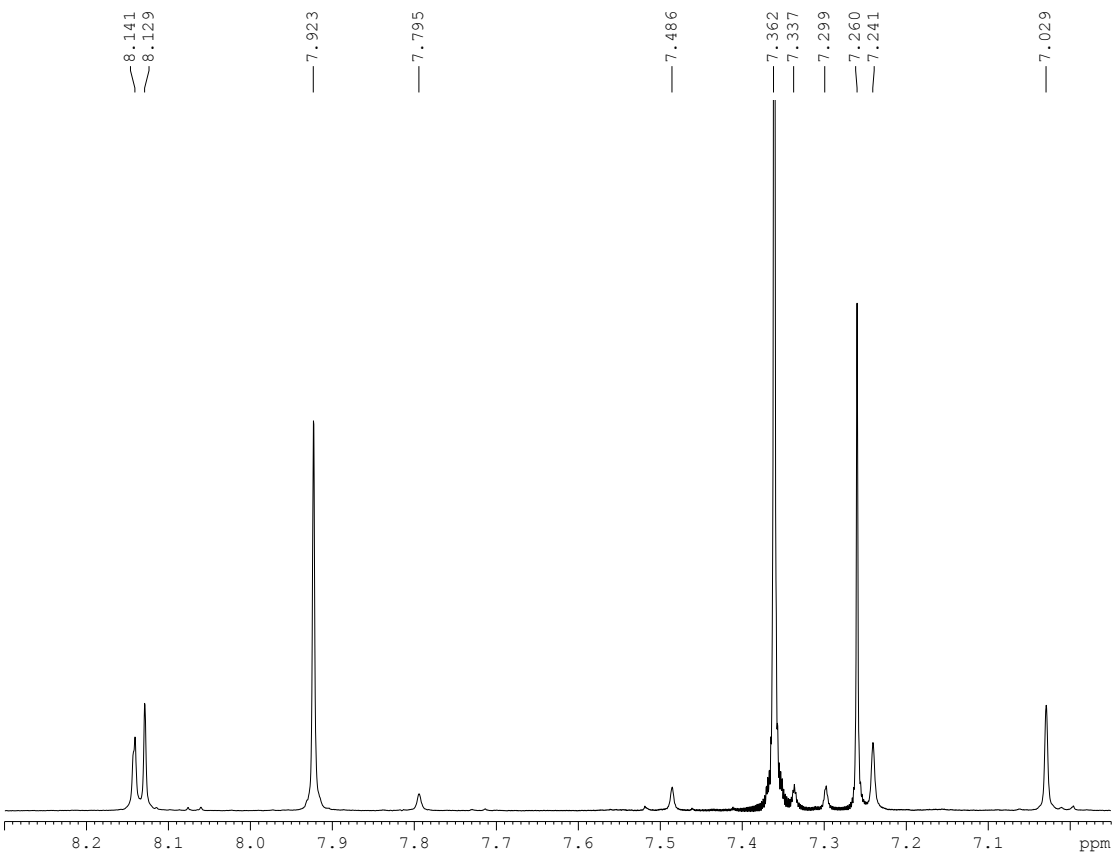


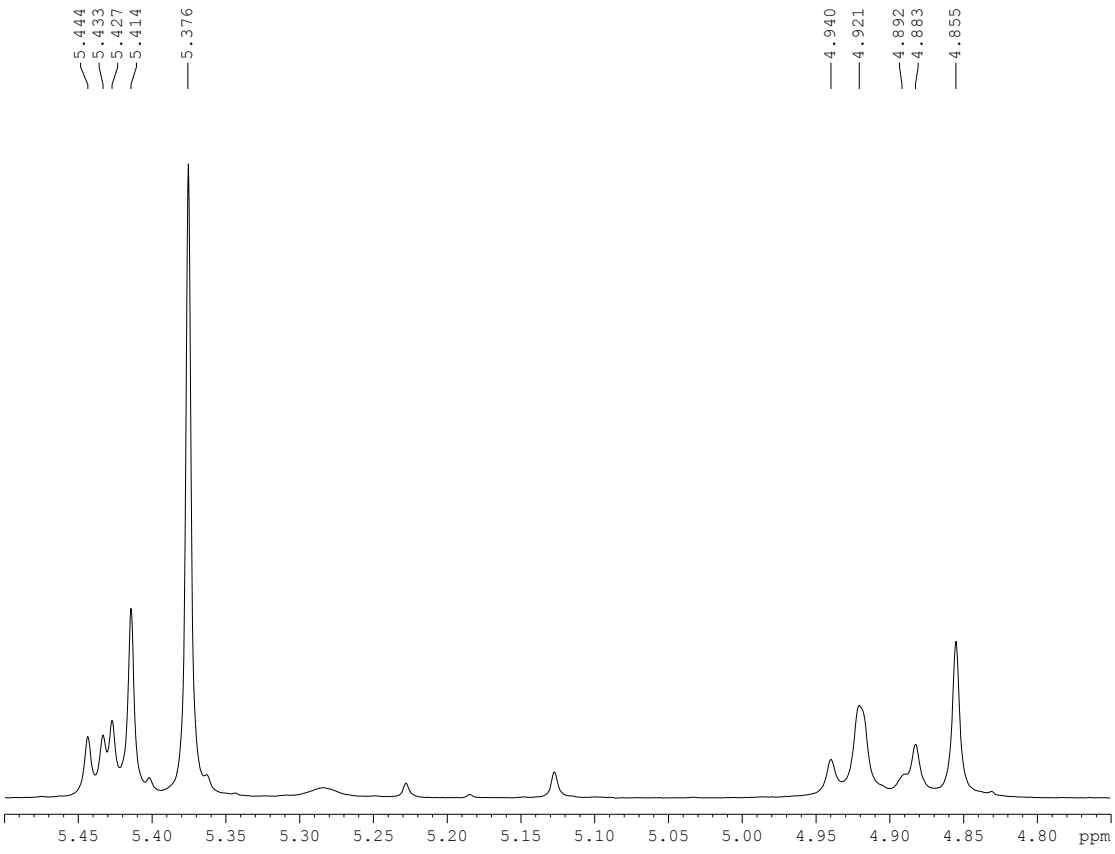



5.444
5.434
5.428
5.415
5.376
4.941
4.922
4.891
4.883
4.856
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

^{1}H-NMR of G3(E) in 9:1 $CDCl_3$:TFA solution after 42.5 h.





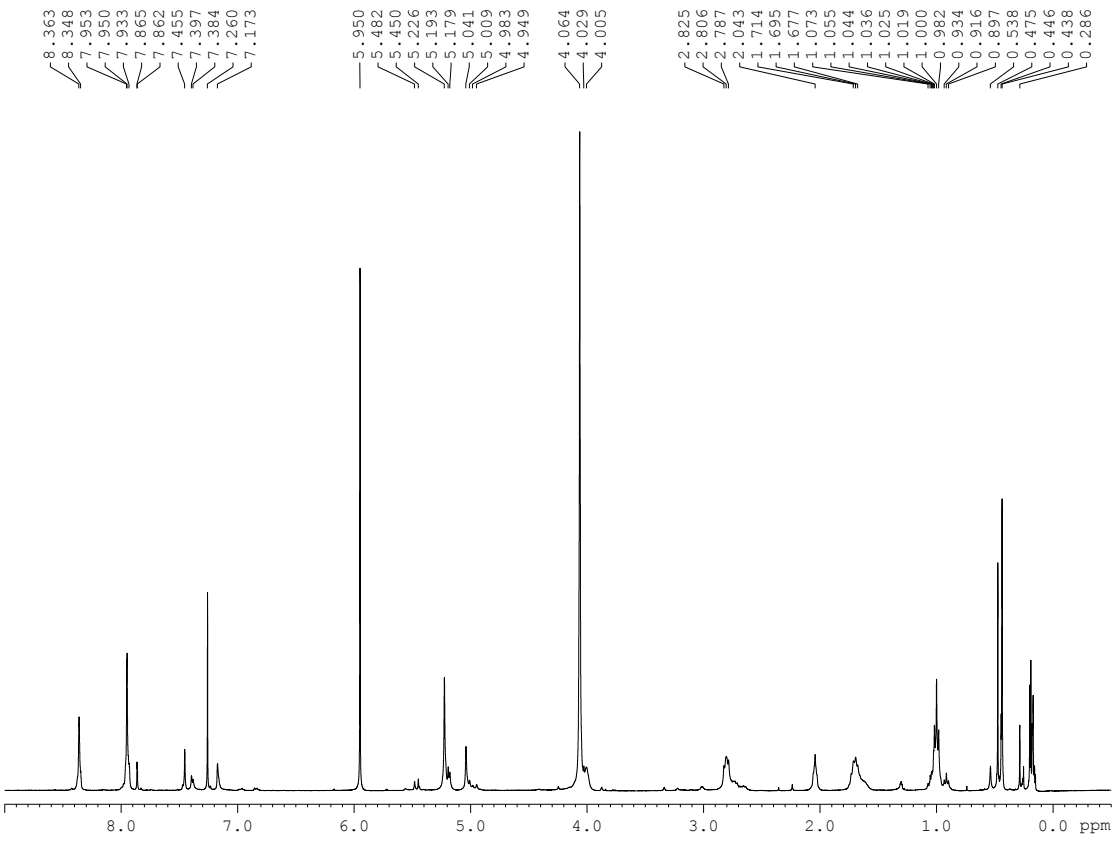

5.444
5.433
5.427
5.414
5.376
4.940
4.921
4.892
4.883
4.855
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
ppm

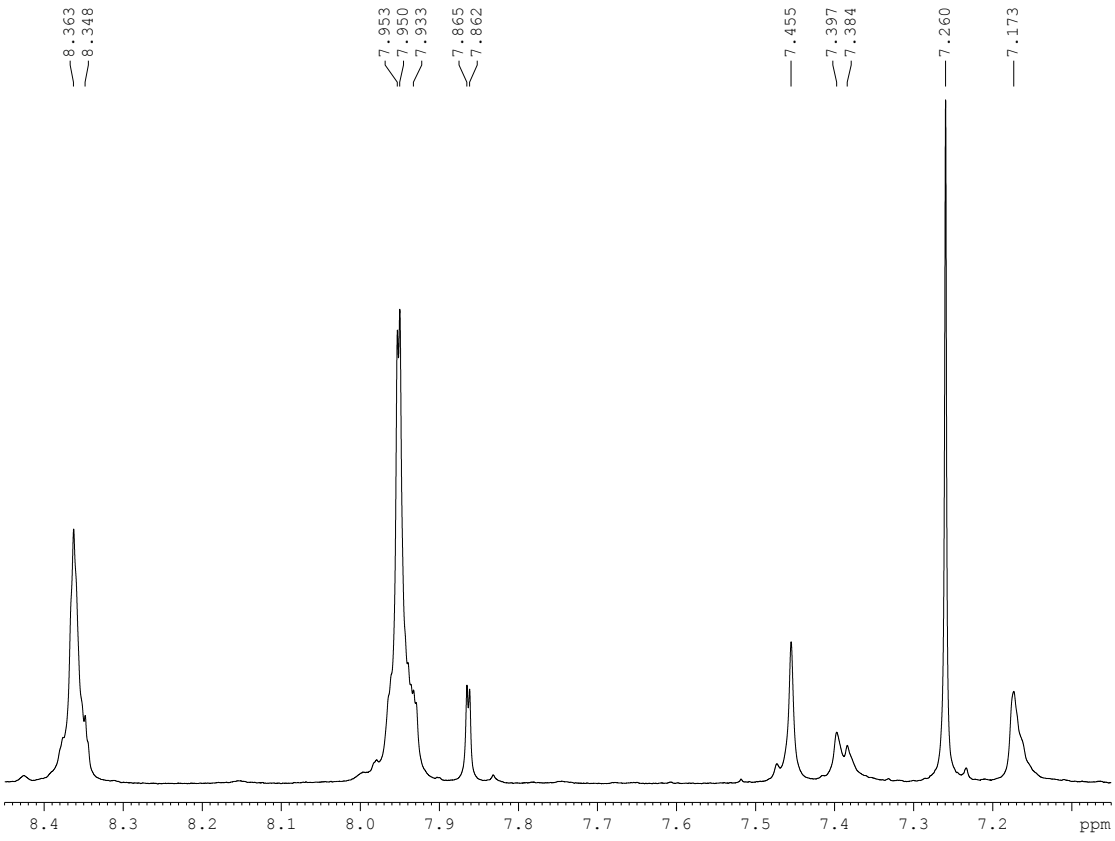
2. H NMR monitoring of the disassembly of G3des$_{1,3}$(E) in a 1:1 CDCl$_3$:TFA mixture

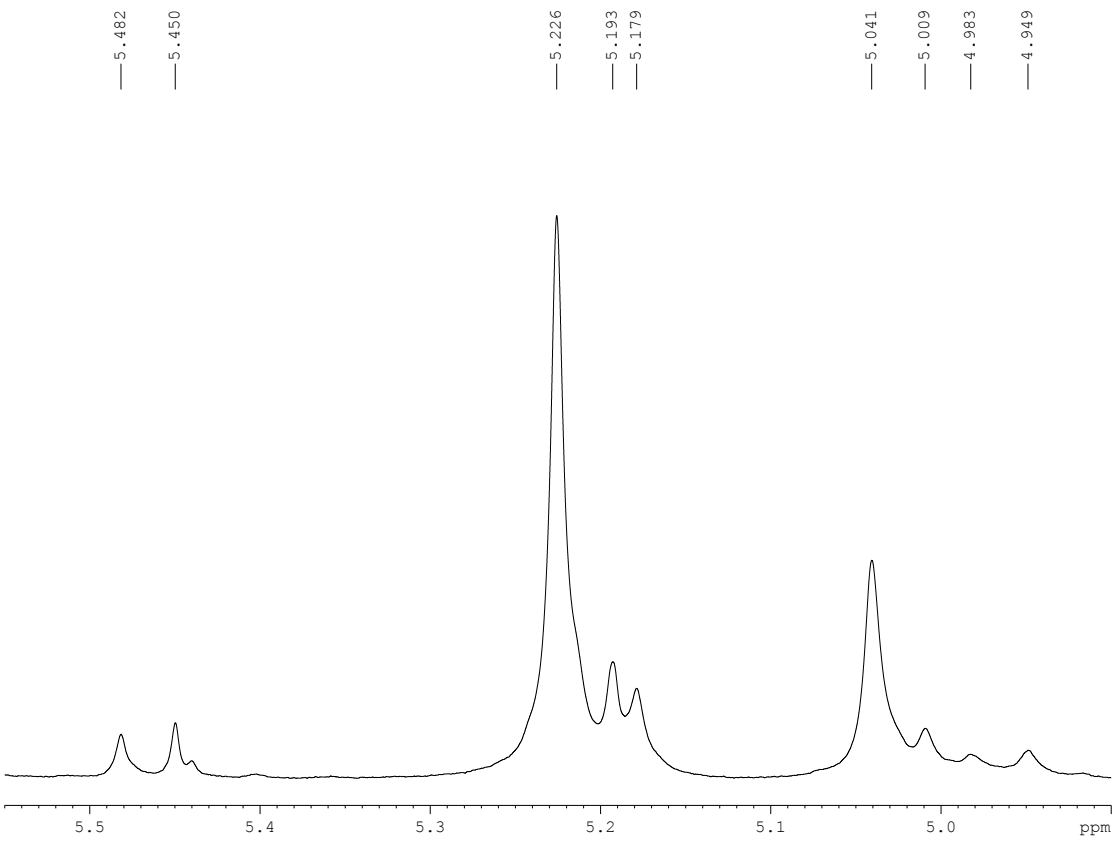
The monitoring measurements were carried out on Bruker AVANCE-400 spectrometer, with residual $CHCl_3$ (7.26 ppm), as calibration standard, and with 1,1,2,2-tetrachloroethane (5.95 ppm), as internal standard.

Signals at 0.15-0.55 ppm and 2.31 ppm – regular impurities observed in the cleavage solutions. Signals at 7.94, 7.11, 5.45, 5.44, 5.19, 5.18 at various stages of the monitoring are due to the impurity of **G2des$_2$(E)** and its decomposition products.[1]

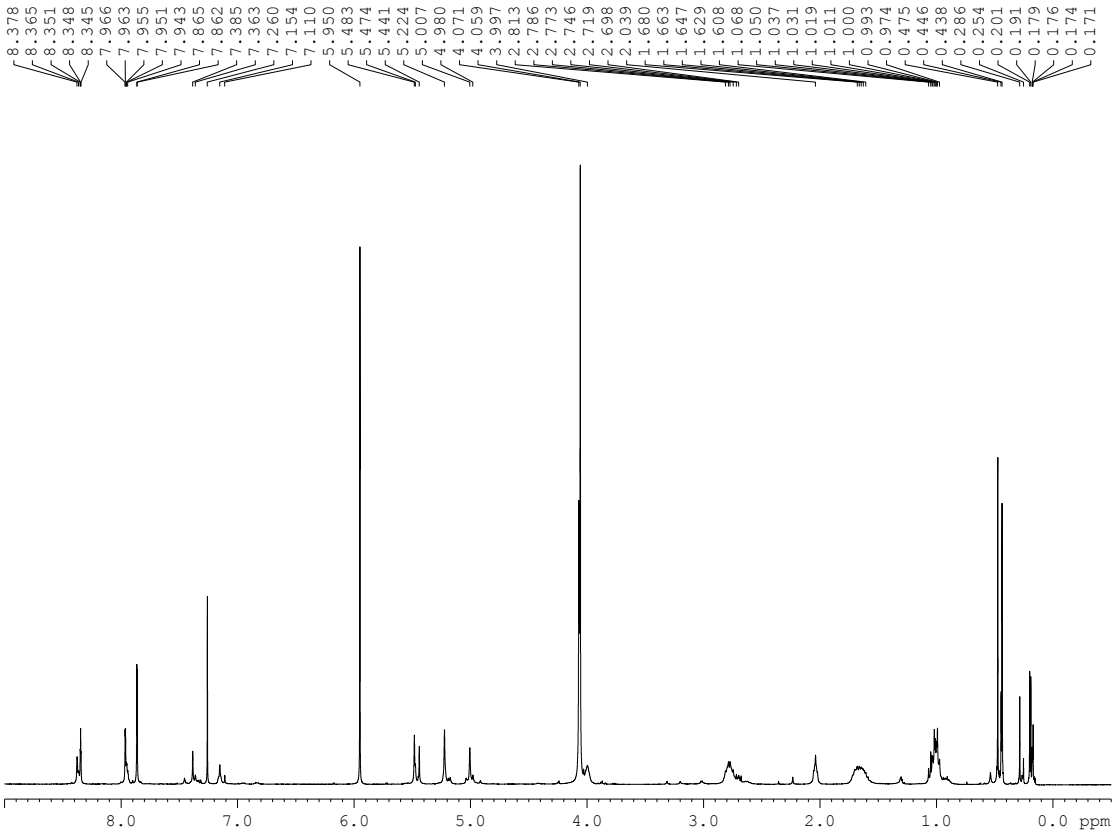
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 45 min.

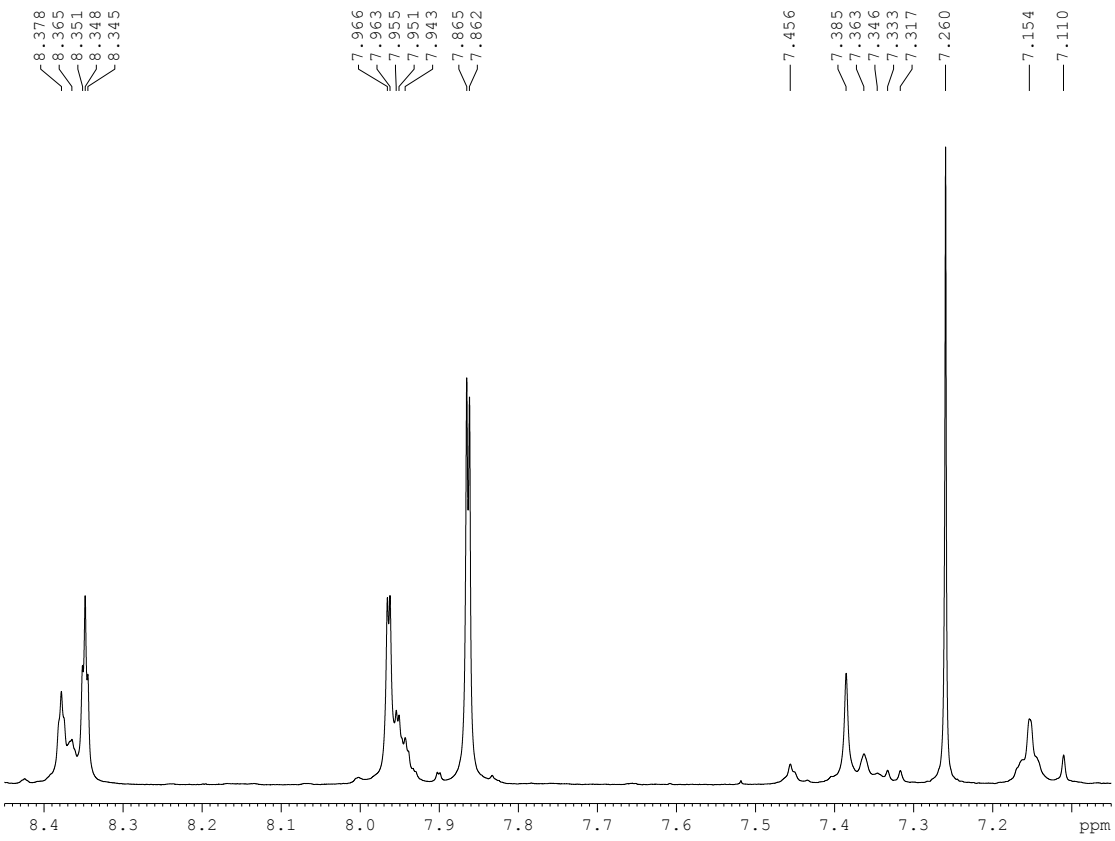


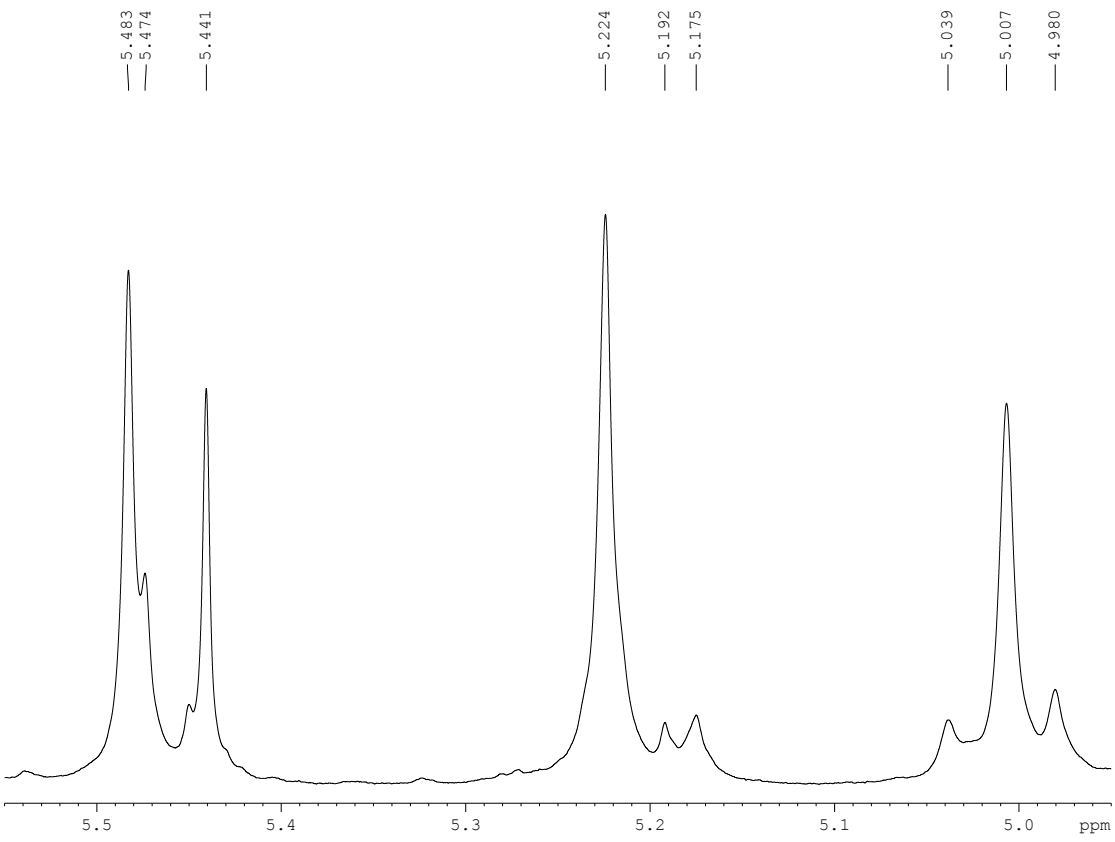



5.482
5.450
5.226
5.193
5.179
5.041
5.009
4.983
4.949
5.5
5.4
5.3
5.2
5.1
5.0
ppm

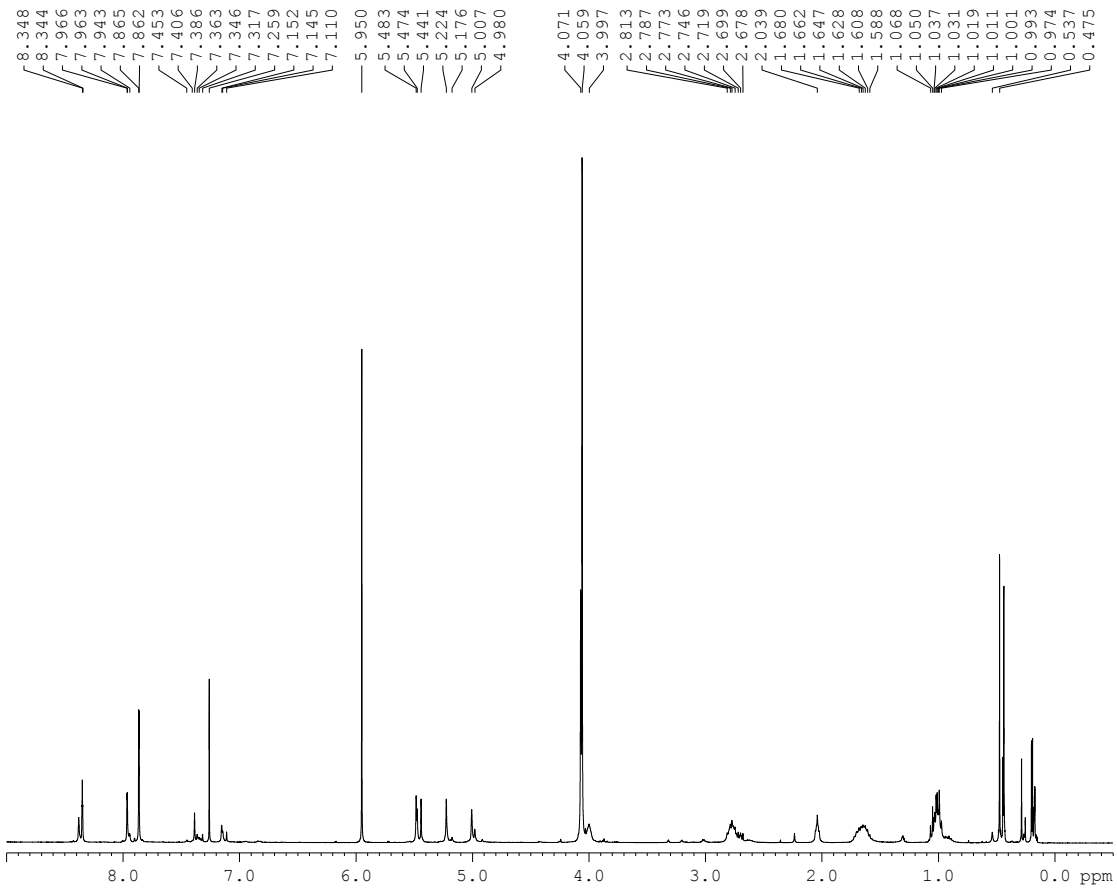
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 1 day.

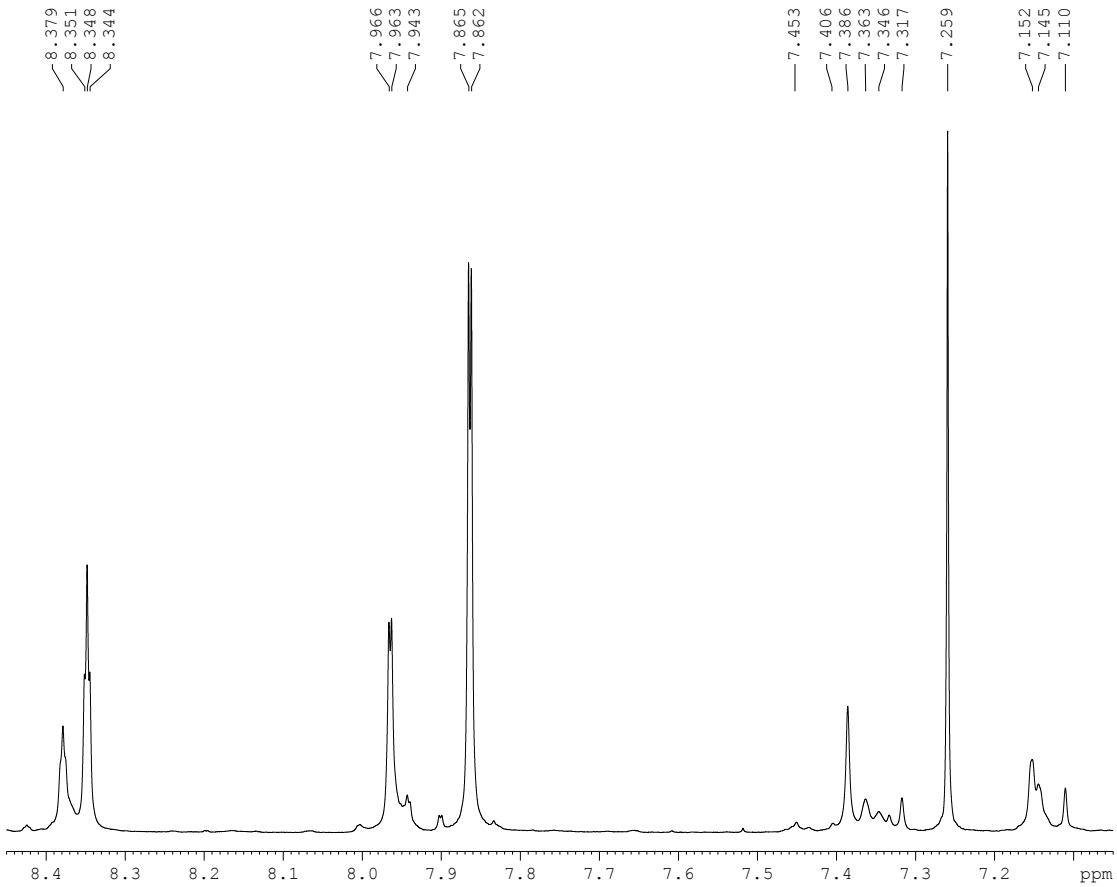


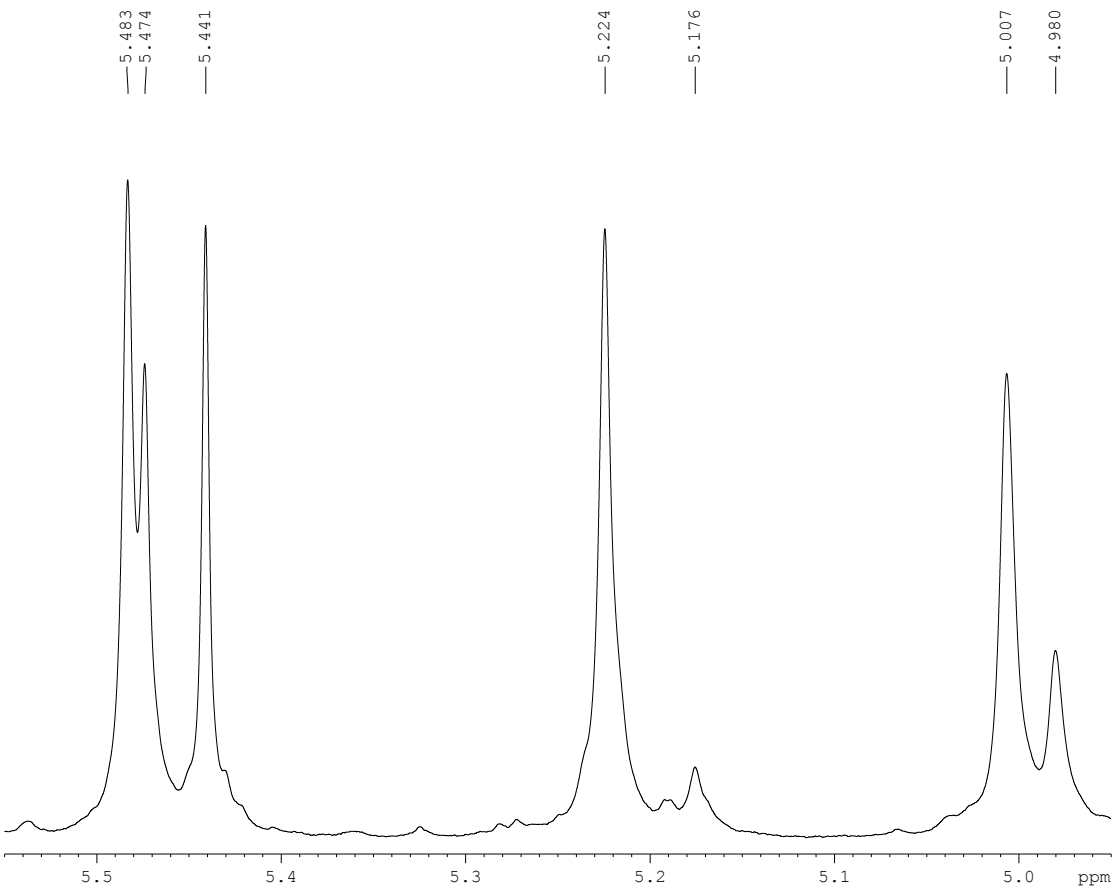



5.483
5.474
5.441
5.224
5.192
5.175
5.039
5.007
4.980
5.5
5.4
5.3
5.2
5.1
5.0
ppm

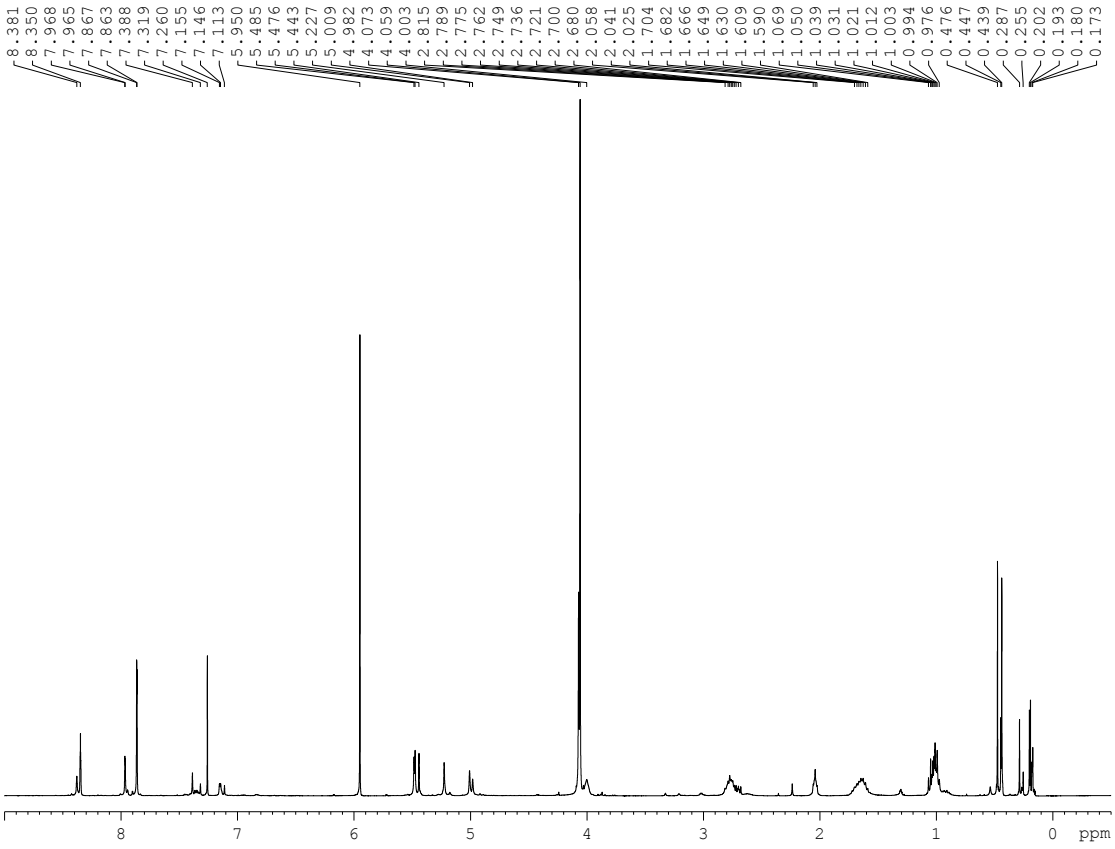
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 2 days.

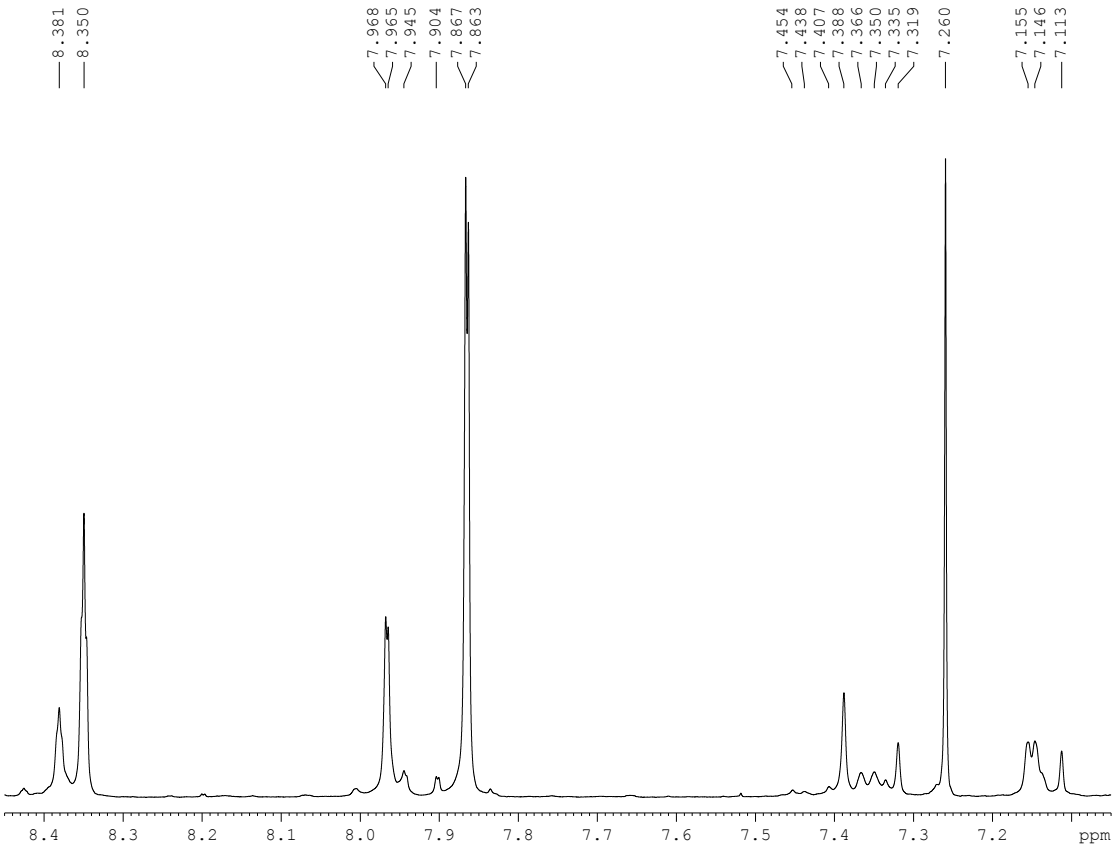


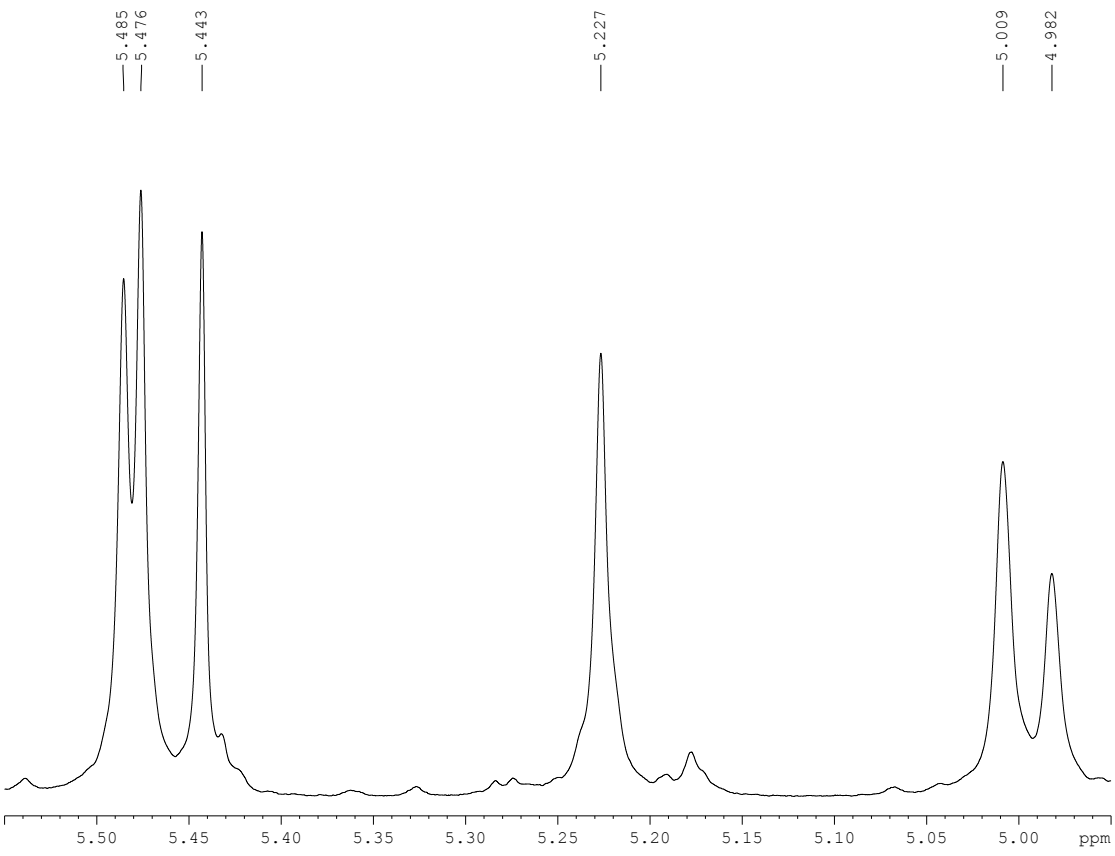



5.483
5.474
5.441
5.224
5.176
5.007
4.980
5.5
5.4
5.3
5.2
5.1
5.0
ppm

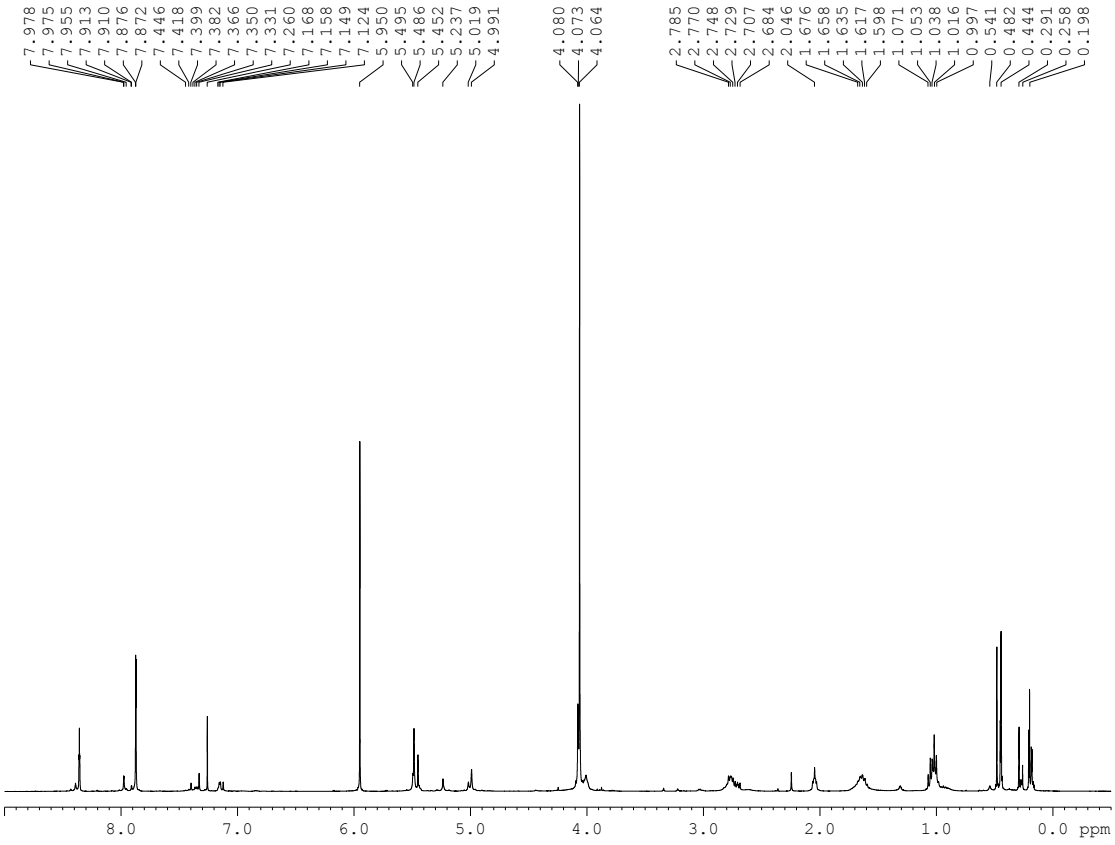
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 3 days.

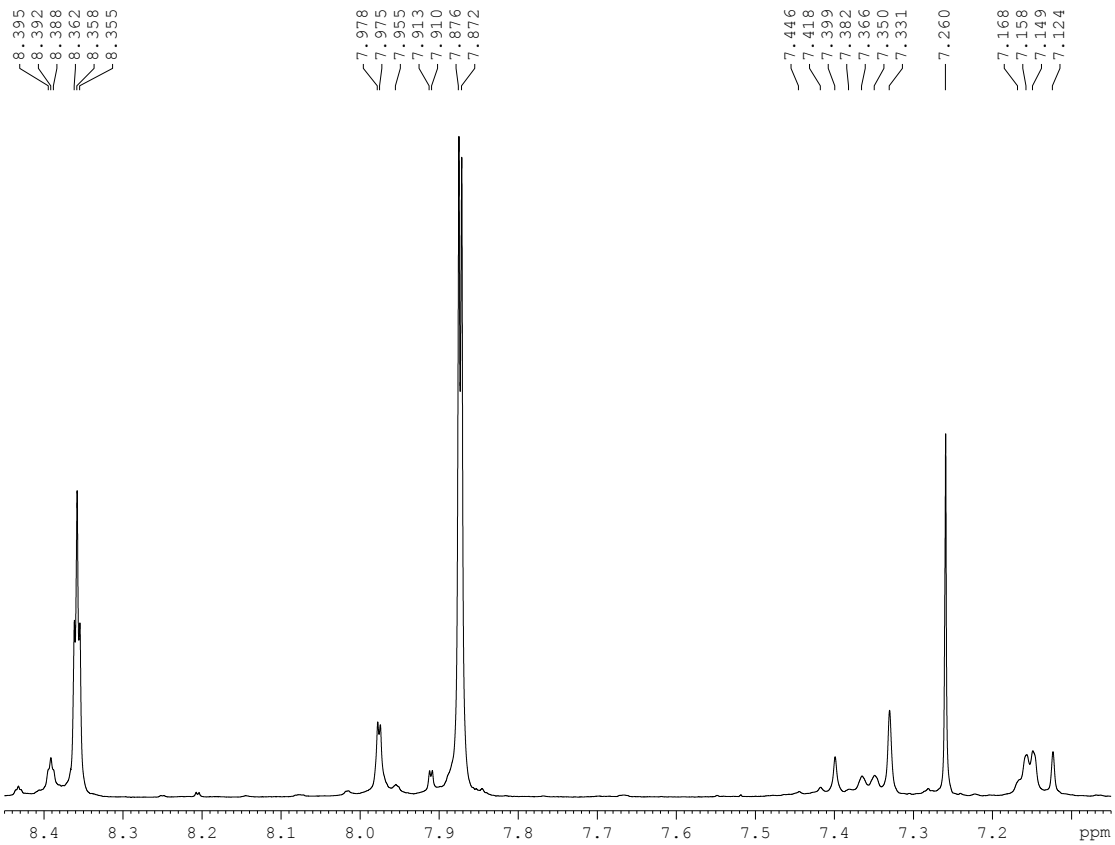


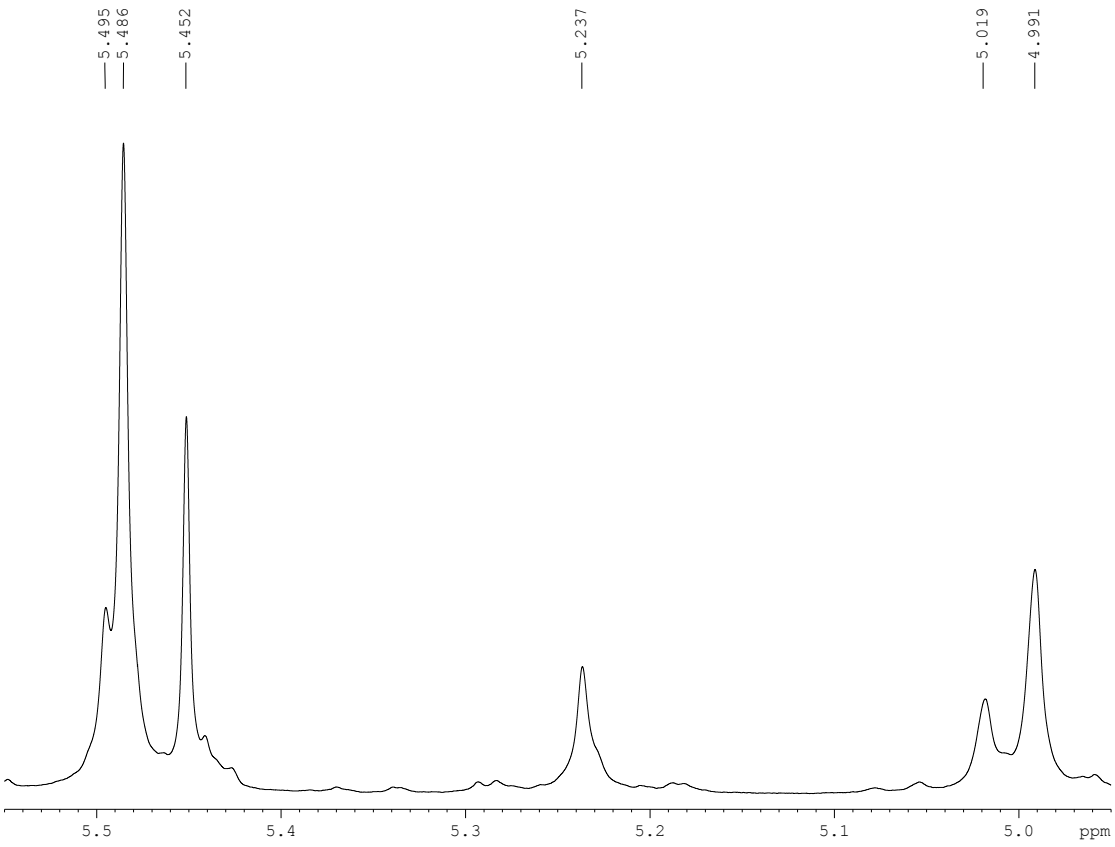



5.485
5.476
5.443
5.227
5.009
4.982
5.50
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
ppm

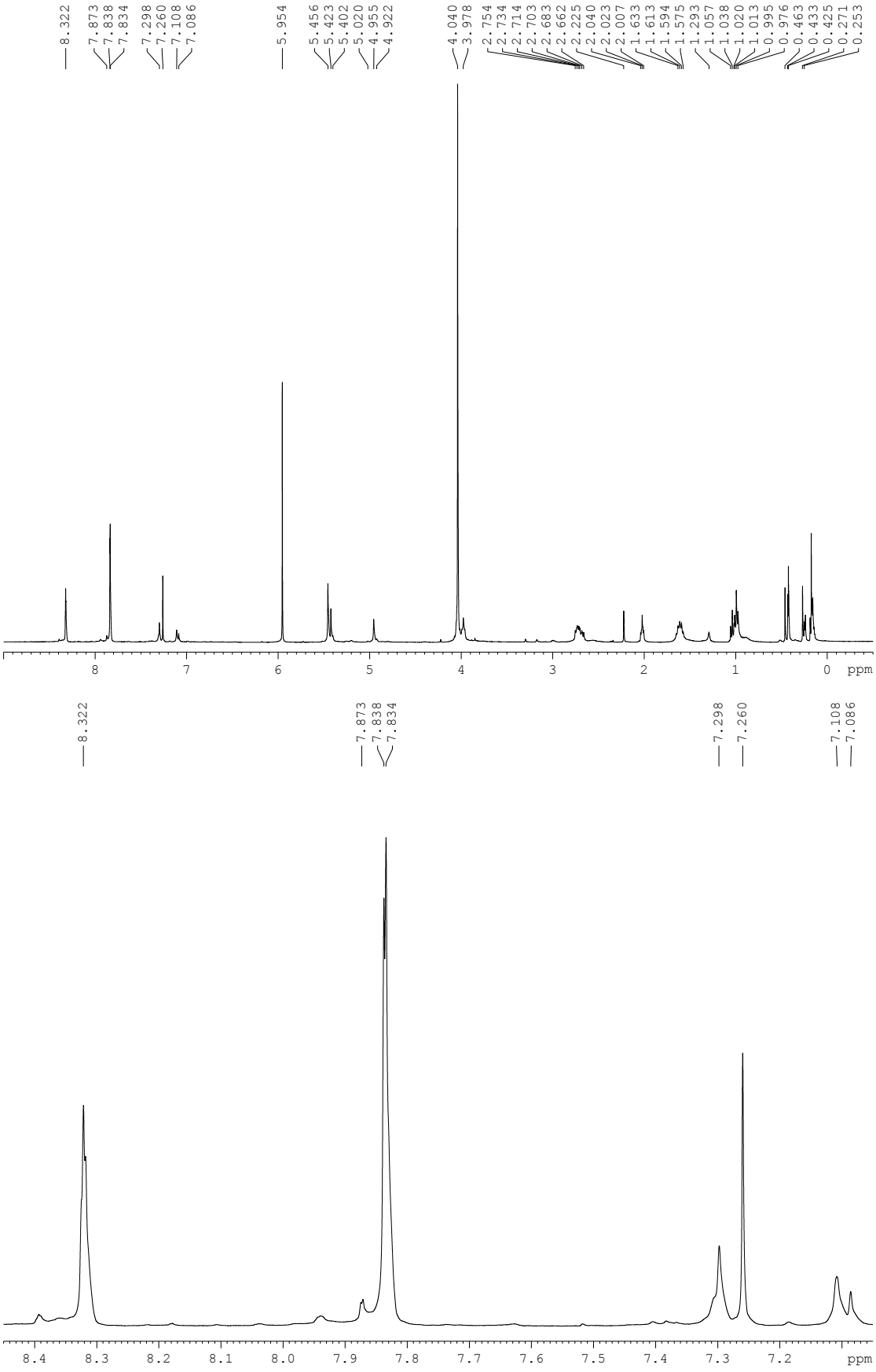
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 7 days.

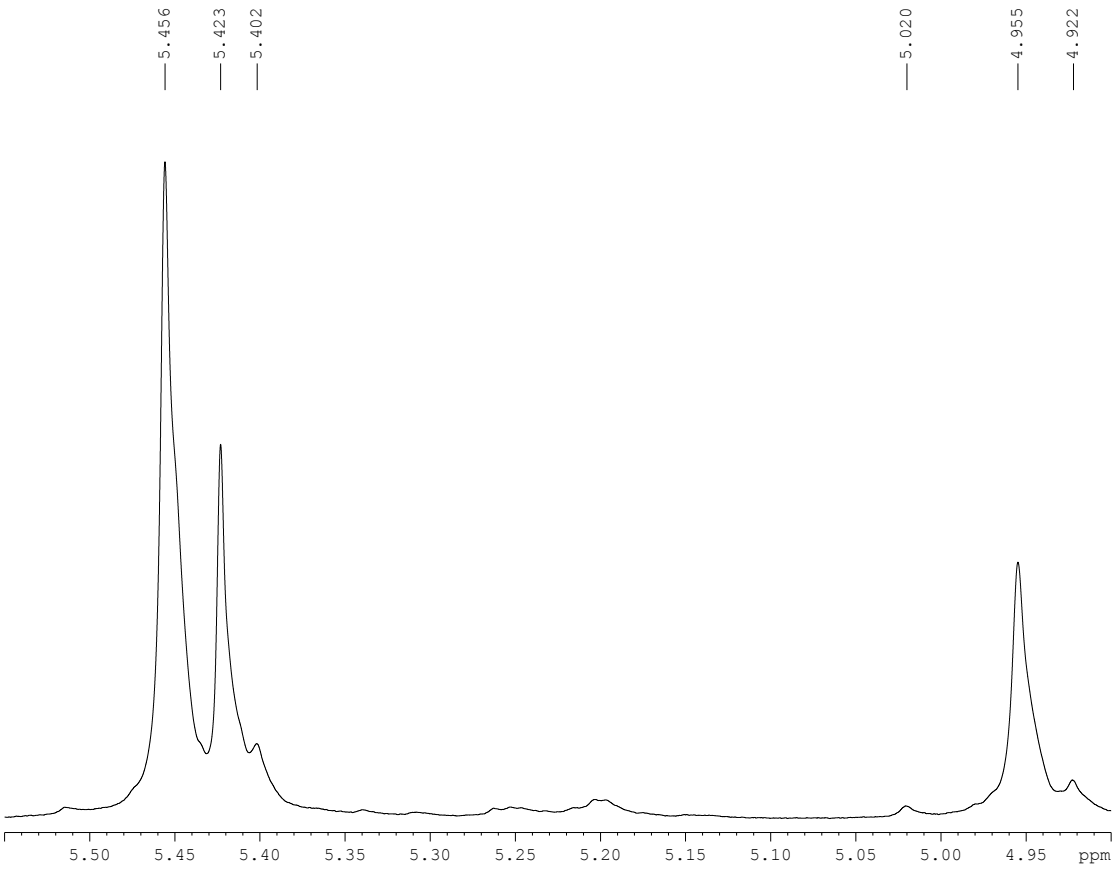





5.495
5.486
5.452
5.237
5.019
4.991
5.5
5.4
5.3
5.2
5.1
5.0
ppm

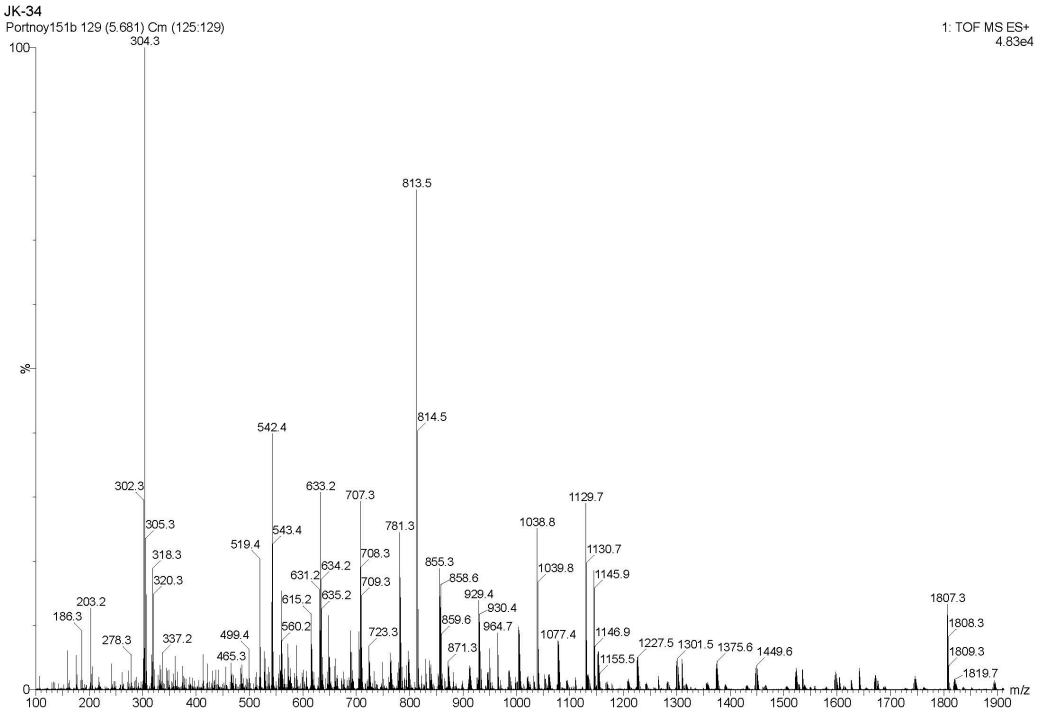
^{1}H-NMR of G3des$_{1,3}$(E) in 1:1 $CDCl_3$:TFA solution after 14 days.

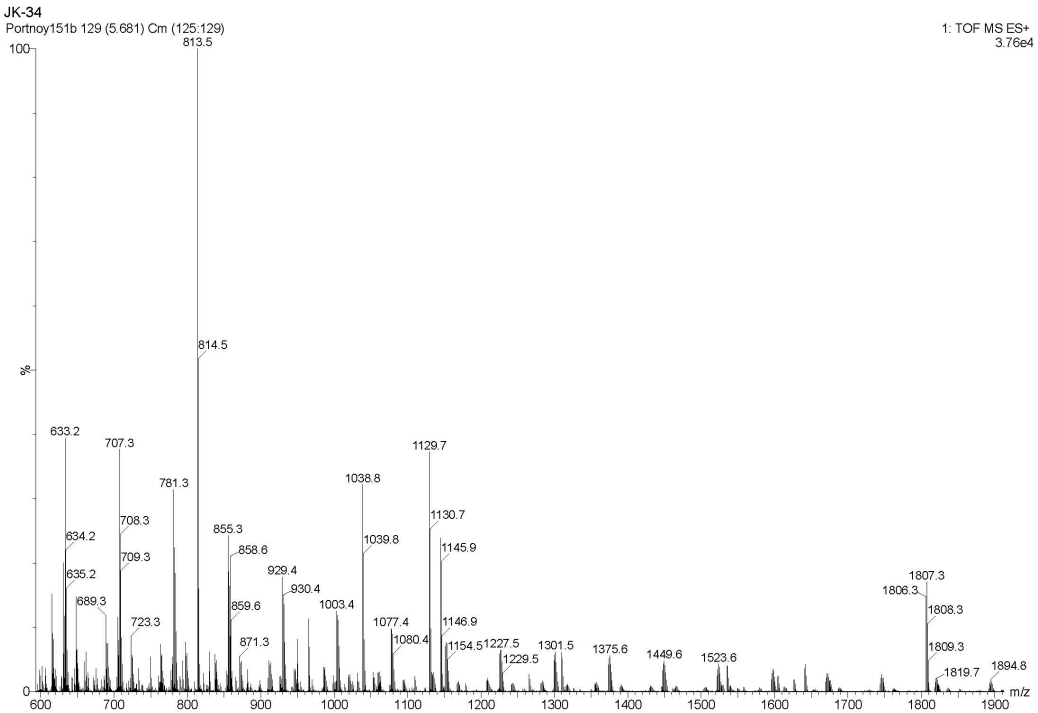



5.456
5.423
5.402
5.020
4.955
4.922
5.50
5.45
5.40
5.35
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
ppm

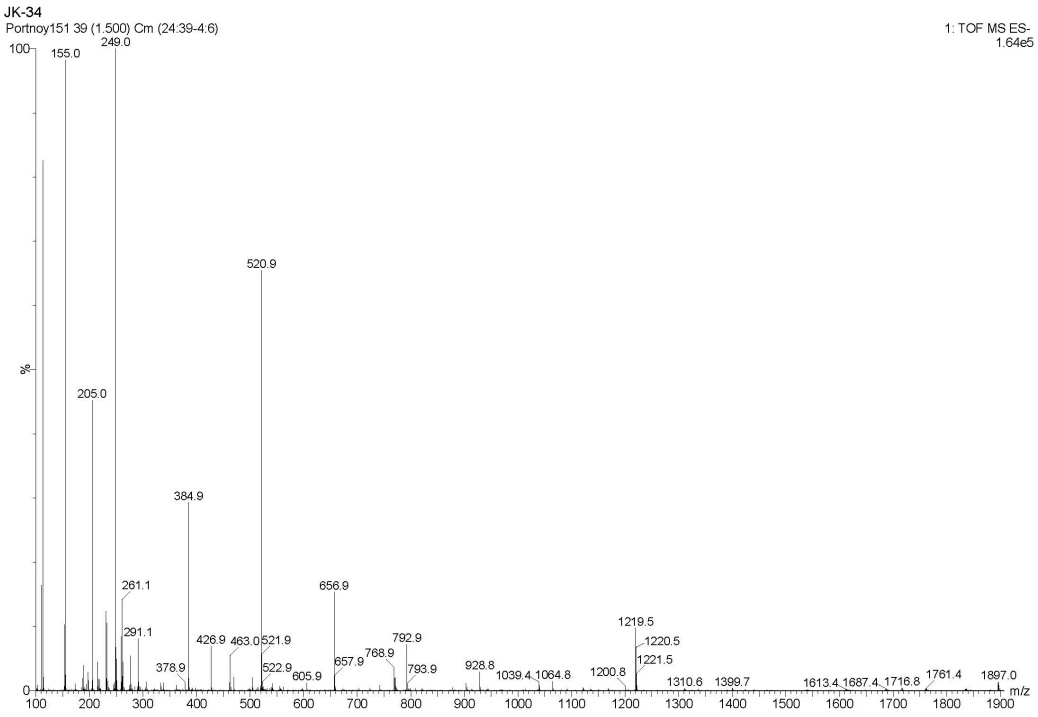
3. ES-MS of the disassembly mixture of G3(E), quenched after *ca.* 45 minutes.

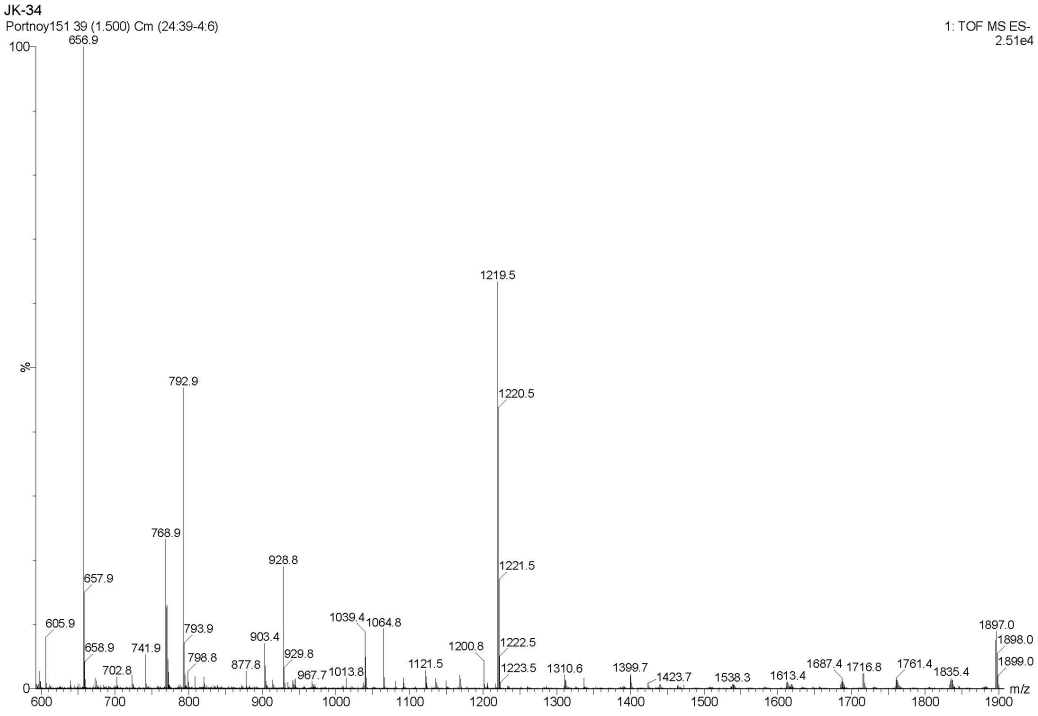
Positive ion detection mode





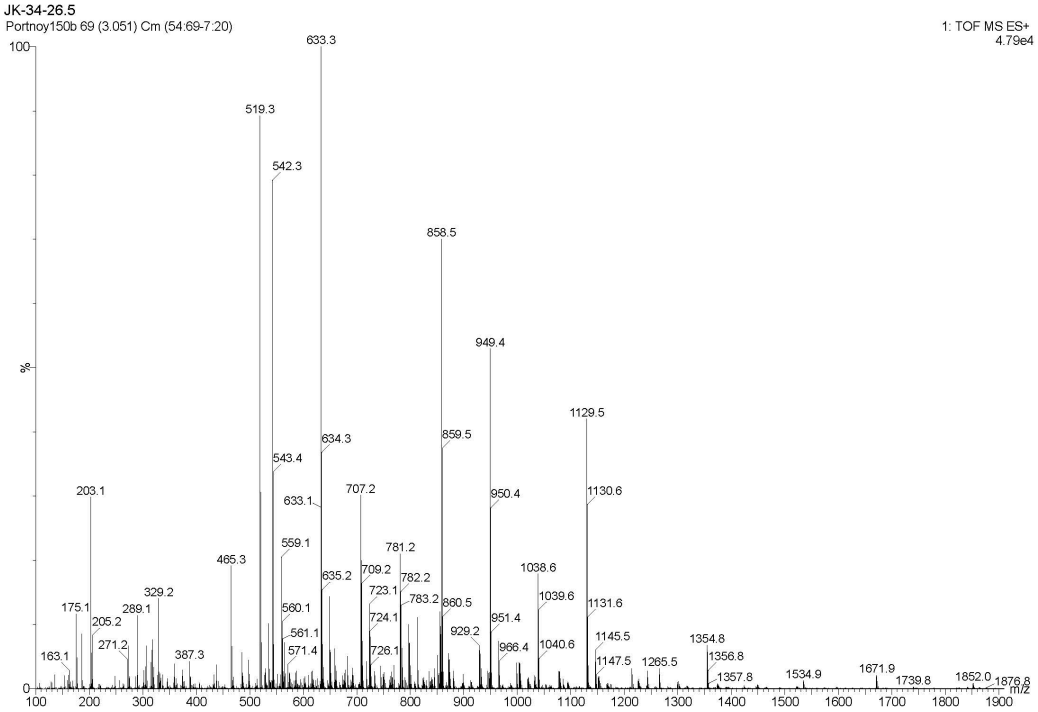
Negative ion detection mode

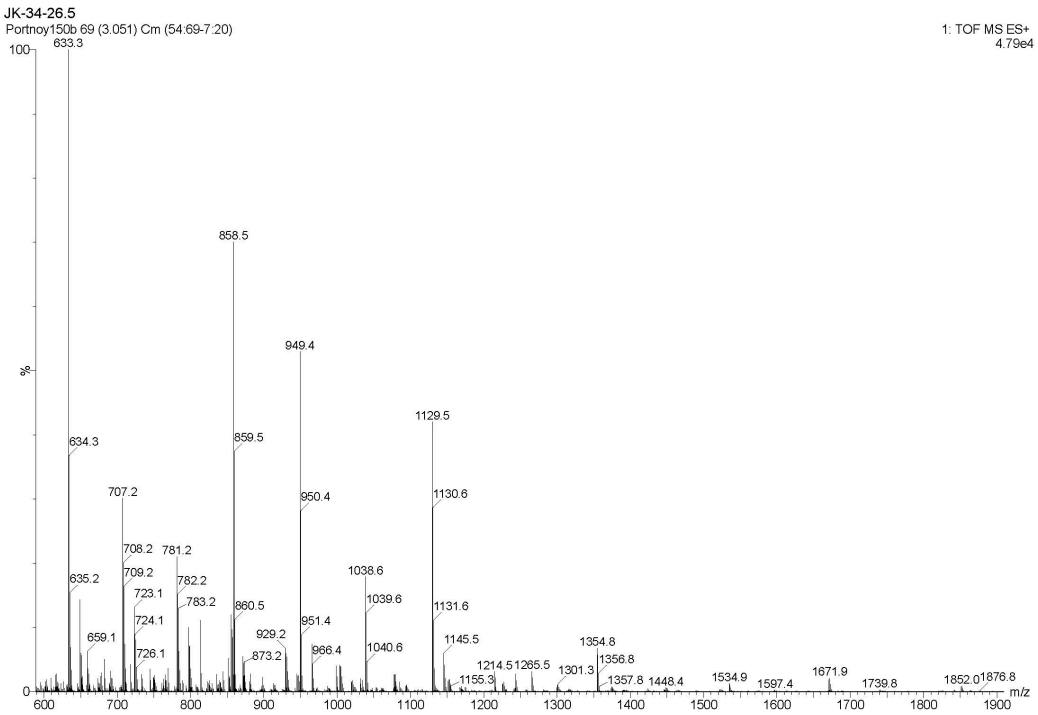




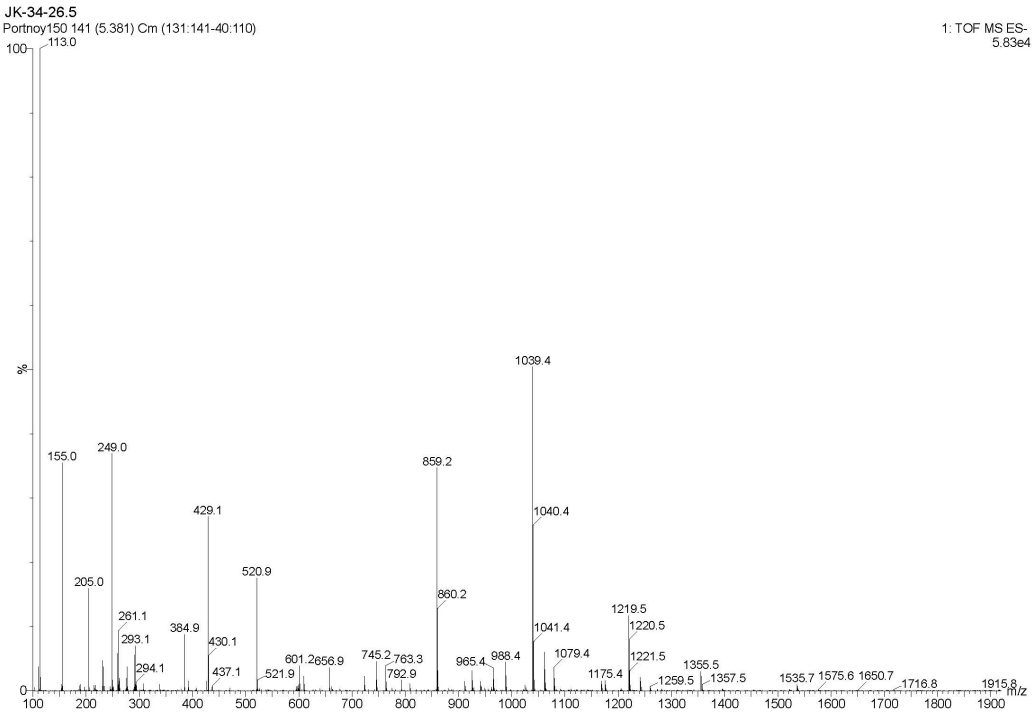
ES-MS of the disassembly mixture of G3(E), quenched after 27 hours.

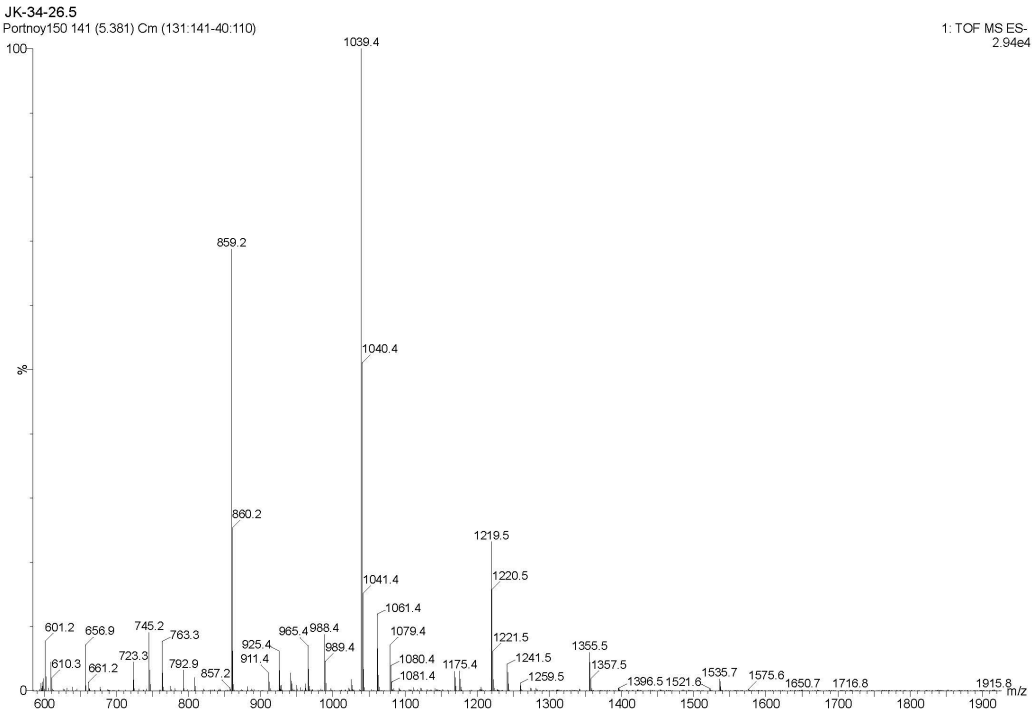
Positive ion detection mode





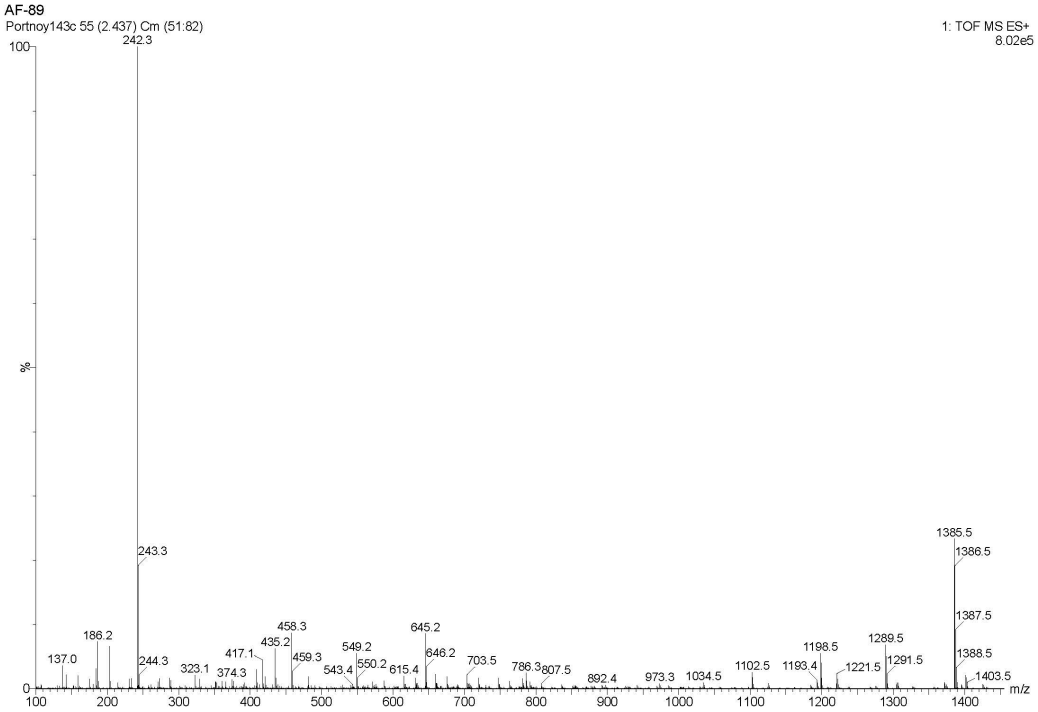
Negative ion detection mode

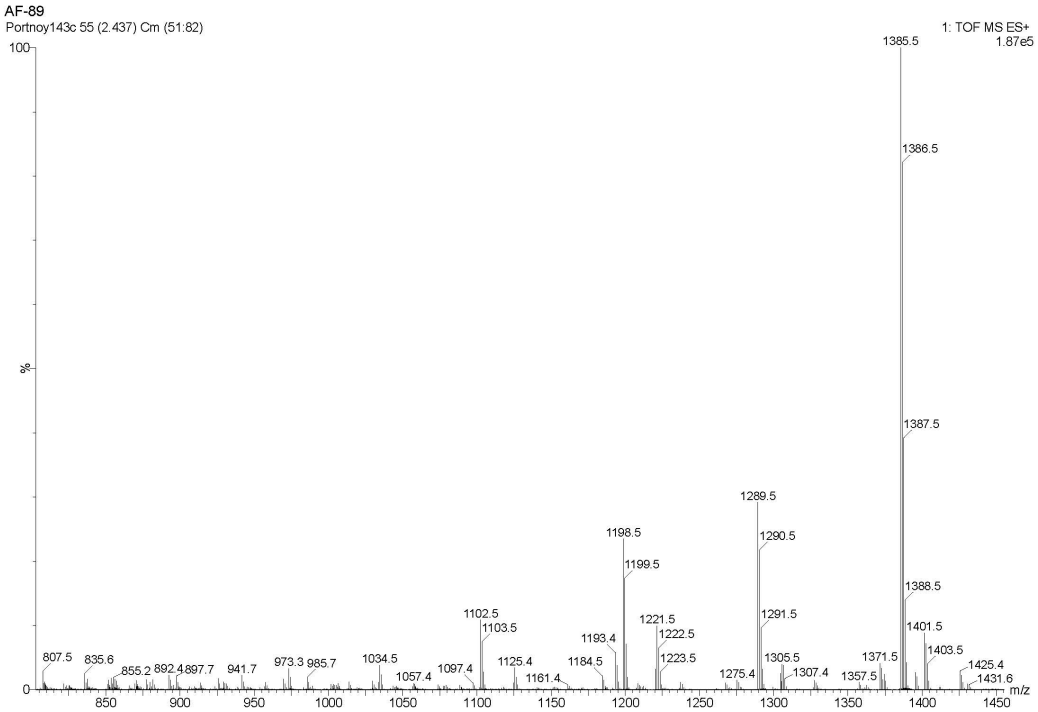




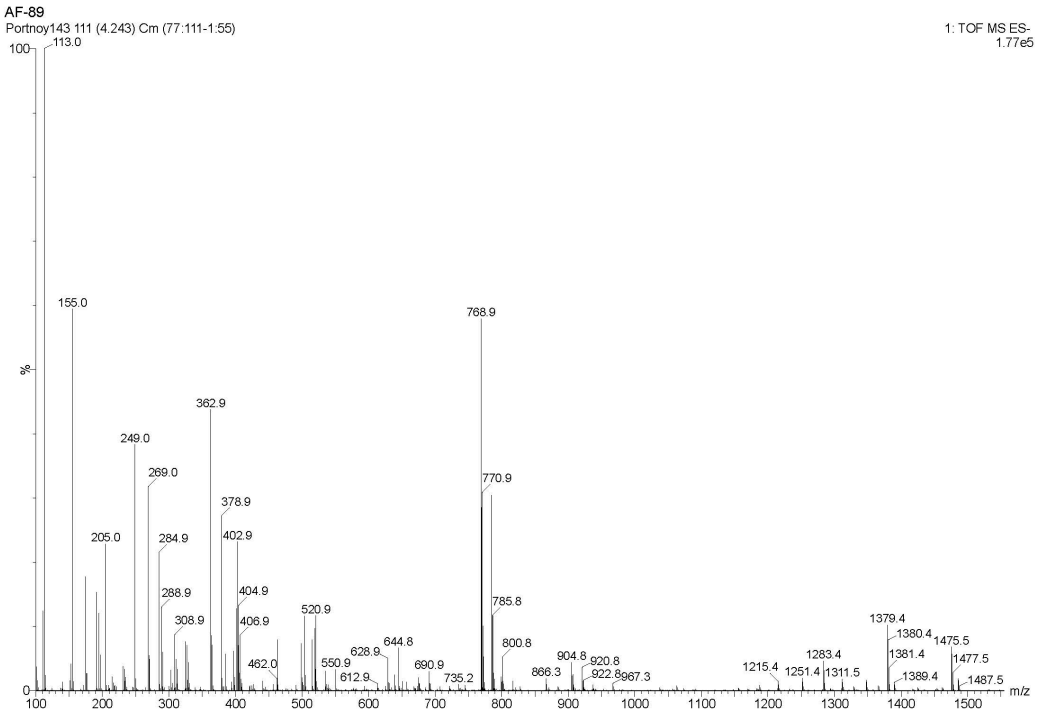
4. ES-MS of the disassembly mixture of G3des$_{1,3}$(E), quenched after *ca.* 45 minutes.

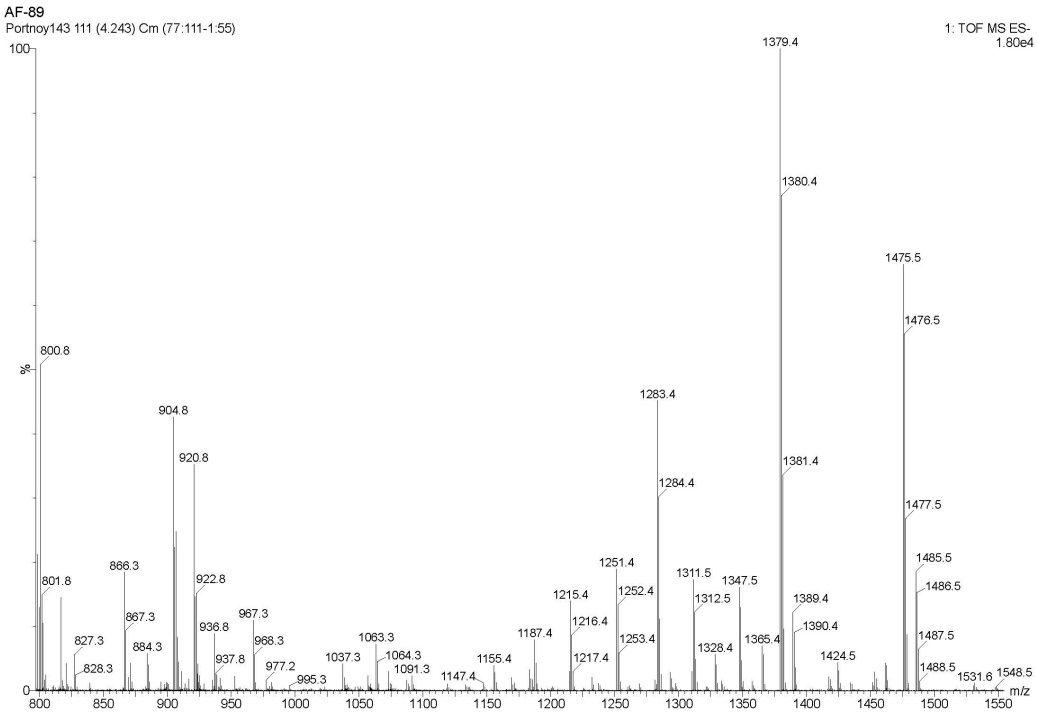
Positive ion detection mode





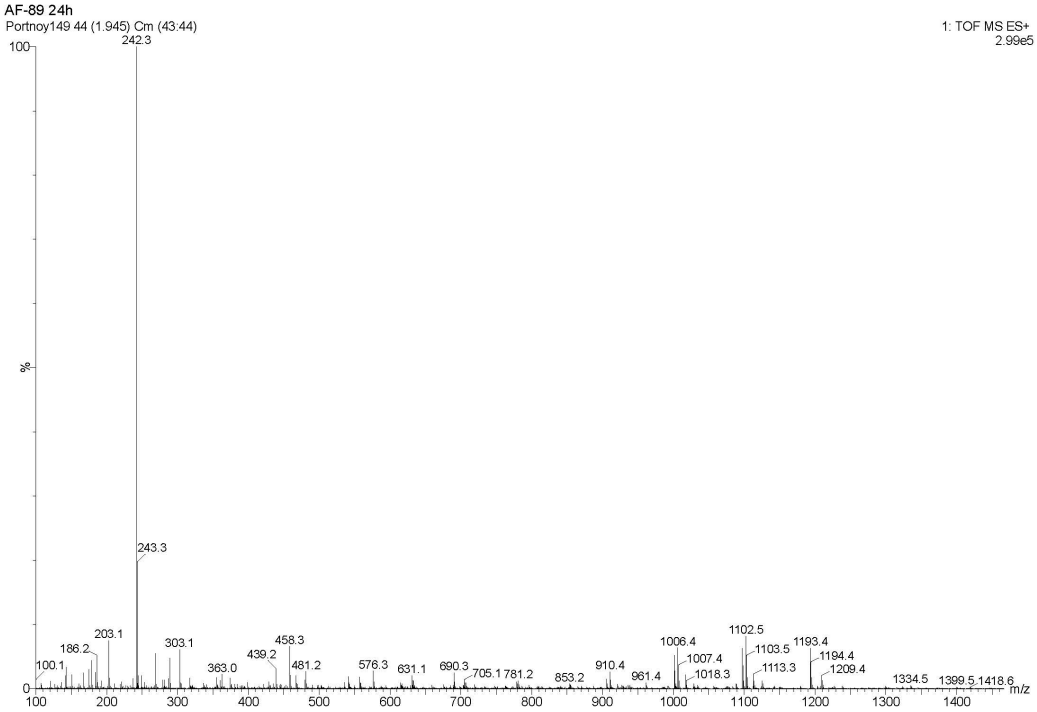
Negative ion detection mode

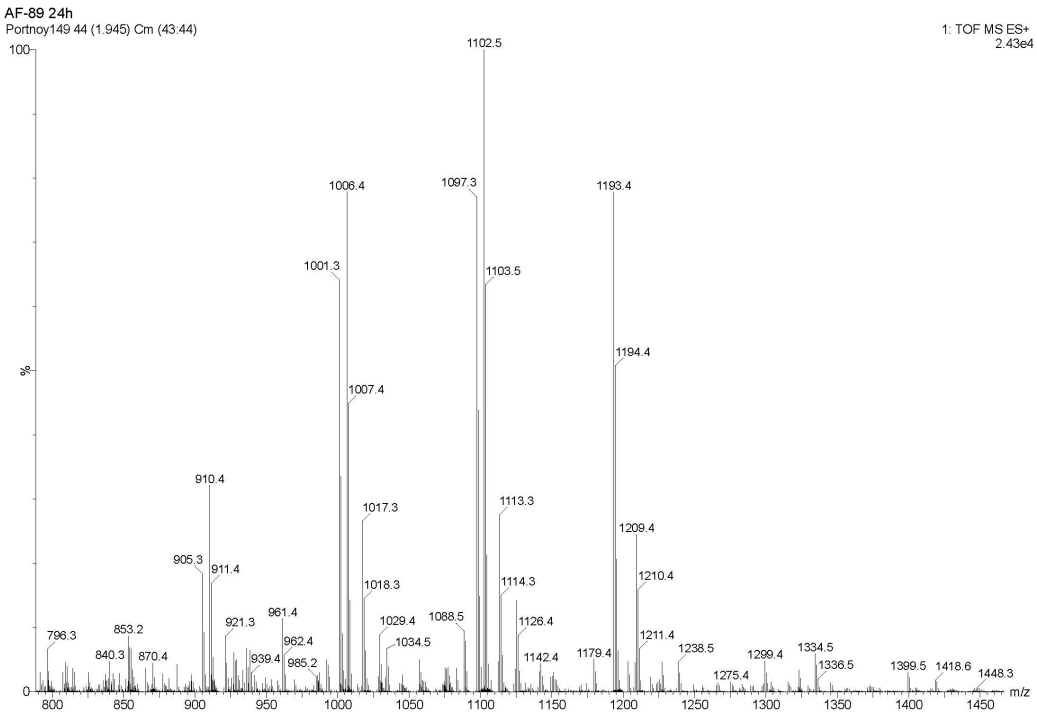




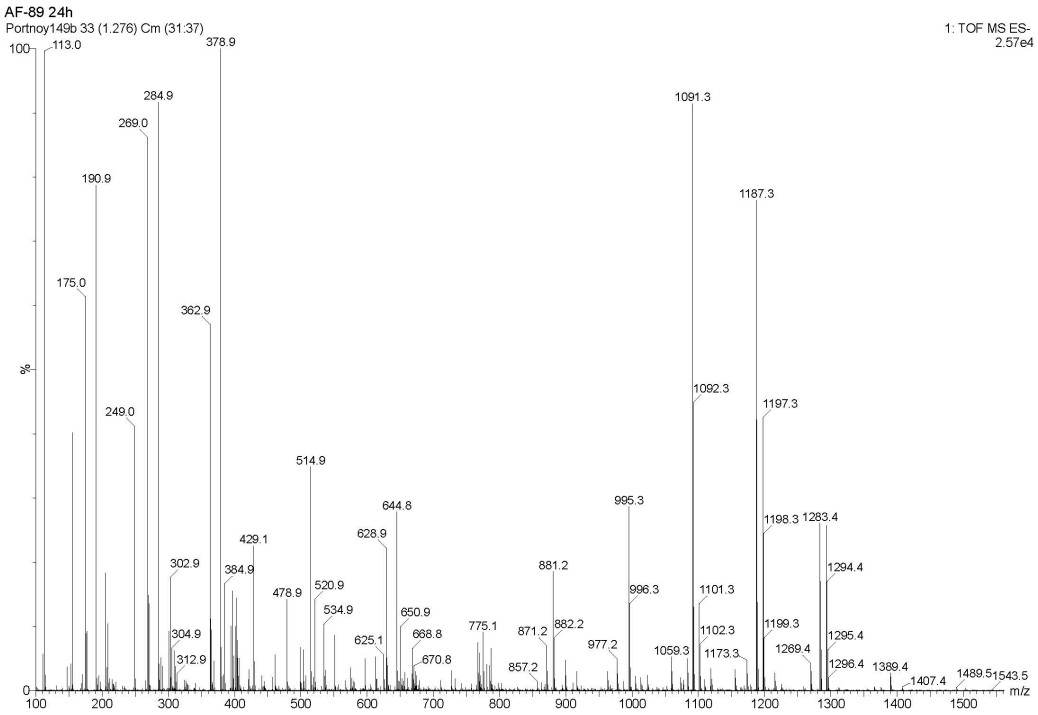
ES-MS of the disassembly mixture of G3des$_{1,3}$(E), quenched after *ca.* 24 hour.

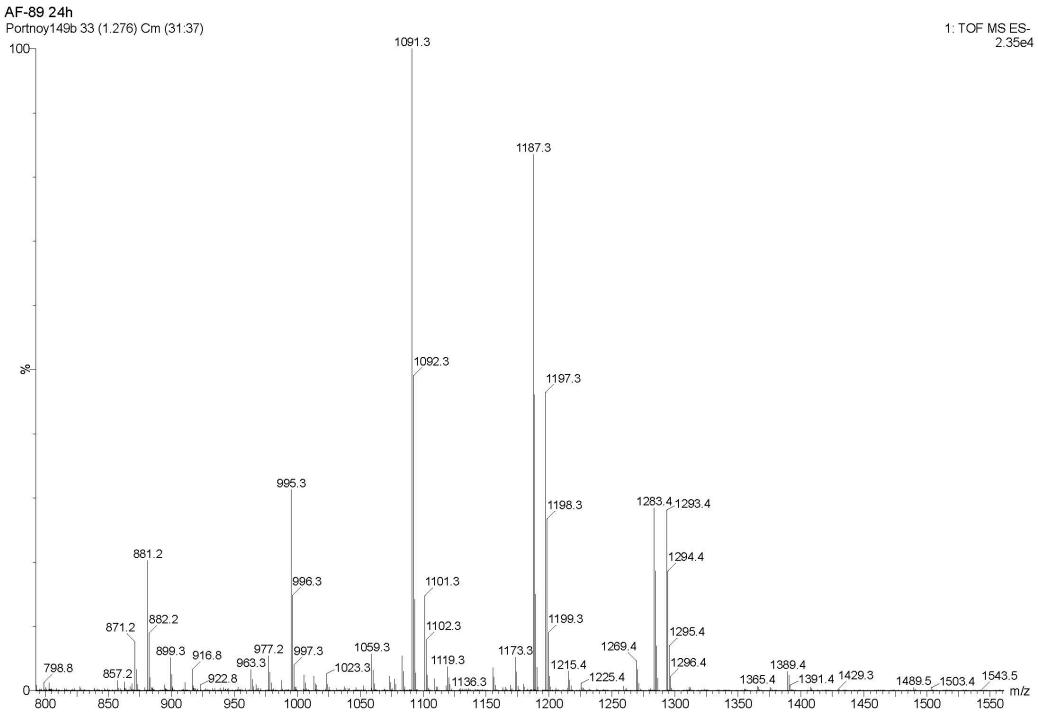
Positive ion detection mode





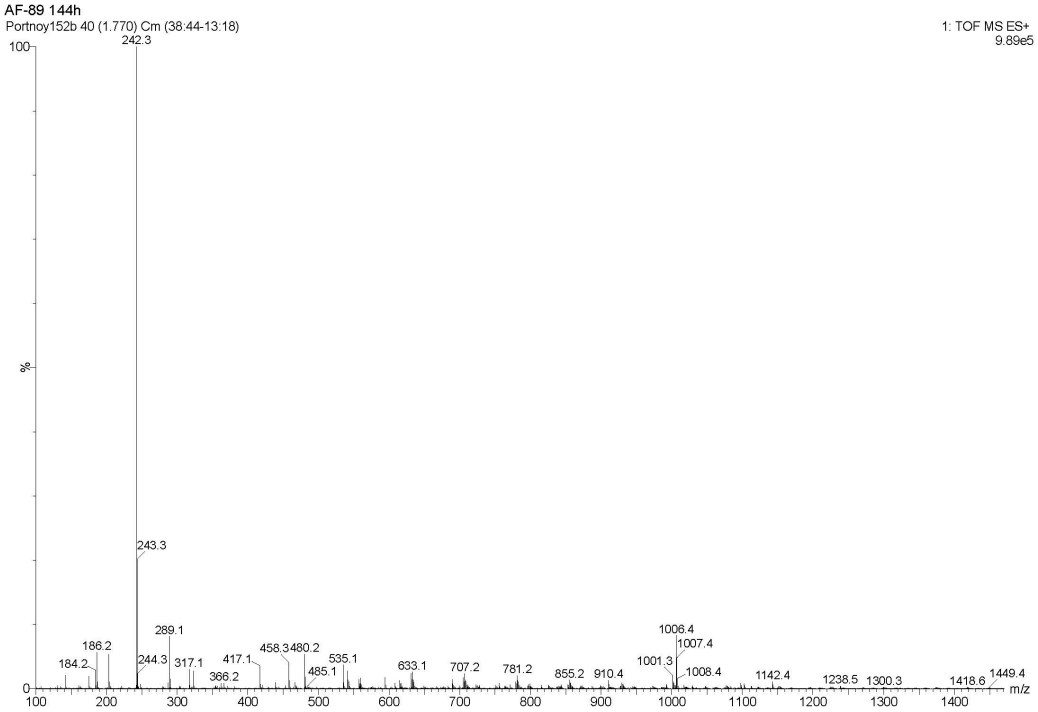
Negative ion detection mode

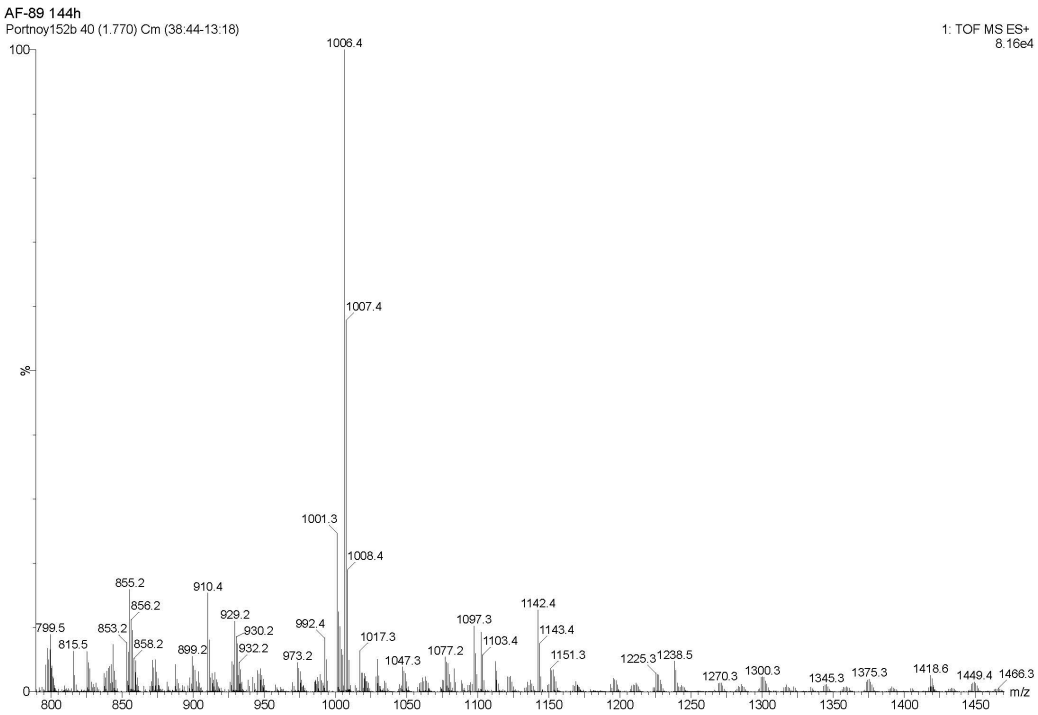




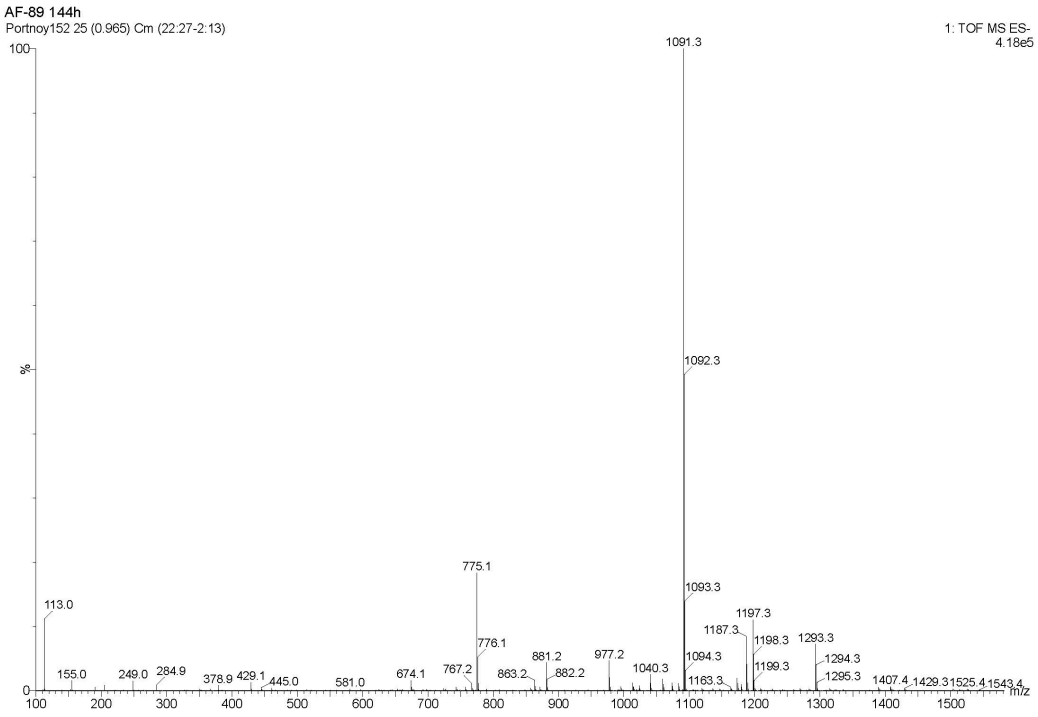
ES-MS of the disassembly mixture of G3des$_{1,3}$(E), quenched after one week.

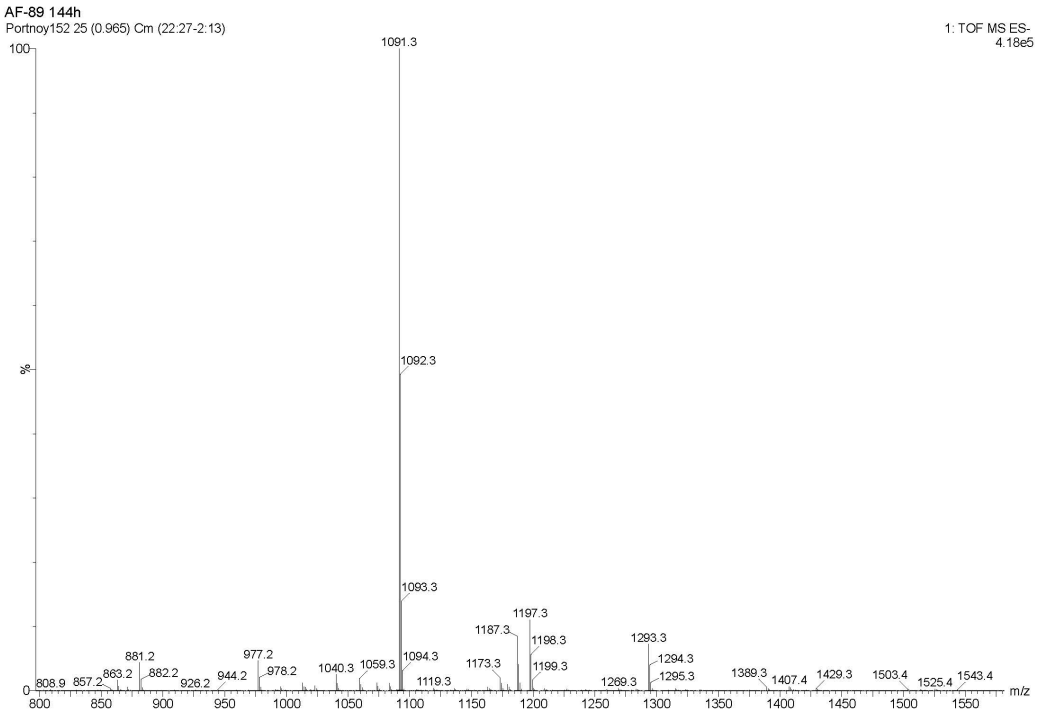
Positive ion detection mode





Negative ion detection mode





5. Synthesis of G3des$_{1,3}$(E)

G2des$_1$(CH$_2$OH):

$LiBH_4$ (4.71 mL, 9.43 mmol, 40 eq, 2M solution in THF) and $B(OMe)_3$ (0.05 ml, 0.47 mmol, 2 eq) were added to a suspension of the resin **G2des$_1$(E)** (0.93 g, 0.24 mmol, 0.24 mmol/g, 1 eq) in THF (8 mL).[1] The mixture was heated to 60 ^oC for 2 days. The resin was washed with aqueous ammonium chloride/THF, ethanolamine/THF, DMF/water, DMF, THF/water, THF, $CHCl_3$ and dried under vacuum. Yield 81%, loading 0.20 mmol/g.
Following TFA-induced cleavage: ^{1}H-NMR (400 MHz, $CDCl_3$/TFA 1:1): δ 7.34 (s, 2H); 7.15 (s, 3H); 5.49 (s, 8H); 5.00 (s, 4H); 2.78 (t, J = 8.0 Hz, 8H); 1.69-1.61 (m, 8H); 1.03 (t, J = 7.4 Hz, 12H).

G2des$_1$(CH$_2$Cl):

Hexachloroethane (0.70 g, 2.96 mmol, 20 eq) and triphenylphosphine (0.78 g, 2.96 mmol, 20 eq) were added to a suspension of the resin **G2des$_1$(CH$_2$OH)** (0.74 g, 0.15 mmol, 0.20 mmol/g, 1 eq) in THF (10 mL). The suspension was mixed at room temperature for 2 days. The resin was washed with THF, $CHCl_3$ and dried under vacuum. Yield 77%, loading 0.15 mmol/g.
Following TFA-induced cleavage: ^{1}H-NMR (400 MHz, $CDCl_3$/TFA 1:1): δ 7.31 (s, 2H); 7.15 (s, 3H); 4.98 (s, 4H); 4.66 (s, 8H); 2.79-2.72 (m, 8H); 1.69-1.61 (m, 8H); 1.03 (t, J = 7.4 Hz, 12H).

G3des$_{1,3}$(E):

K_2CO_3 (0.10 g, 0.76 mmol, 8 eq), dimethyl-5-hydroxyisophthalate (0.28 g, 1.33 mmol, 14 eq), TBAI (0.16 g, 0.43 mmol, 4.5 eq) and 18-crown-6 ether (0.02 g, 0.08 mmol, 0.85 eq) were added to a suspension of **G2des$_1$(CH$_2$Cl)** resin (0.63 g, 0.10 mmol, 0.15 mmol/g, 1 eq) in DMF (7 mL). The suspension was heated to 60 ^oC for 3 days. The resin was washed with DMF/water, DMF, THF/water, THF, $CHCl_3$ and dried under vacuum.
Following TFA-induced cleavage: ^{1}H-NMR (400 MHz, $CDCl_3$/TFA 1:1): δ 8.36 (s, 4H); 7.95 (s, 8H); 7.46 (s, 2H); 7.39 (s, 1H); 7.17 (s, 2H); 5.23 (s, 8H); 5.04 (s, 4H); 4.03 (s, 24H); 2.81 (t, J = 7.8 Hz, 8H); 1.71-1.68 (m, 8H); 1.00 (t, J = 7.3 Hz, 12H).

References

1. J. Karabline and M. Portnoy, *Org. Biomol. Chem.*, 2012, **10**, 4788-4794.