Supporting Information

Bis-rhodamines bridged with a diazoketone linker: synthesis, structure and photolysis

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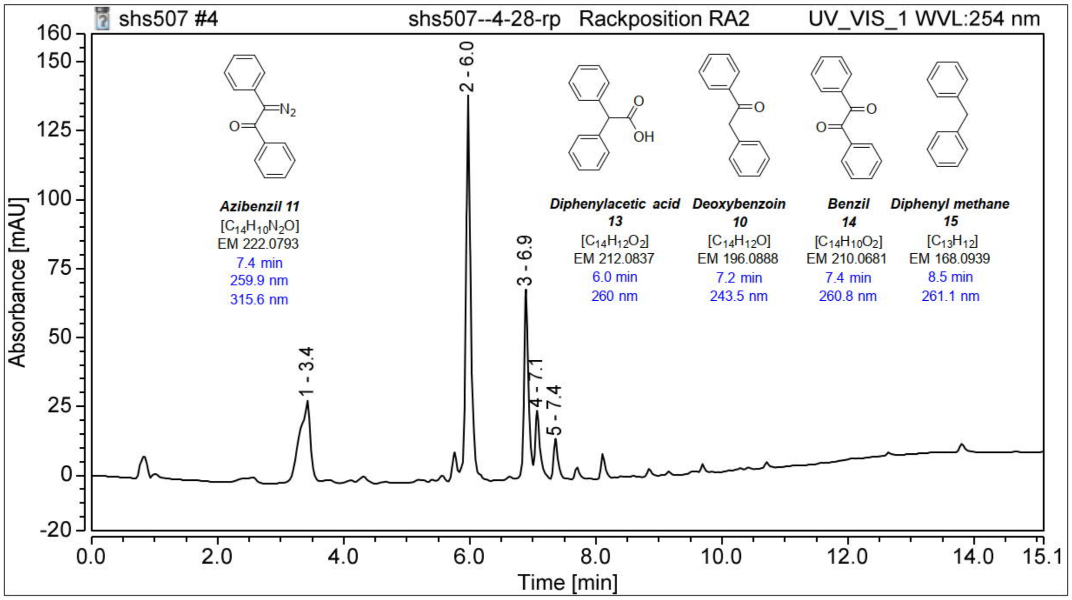
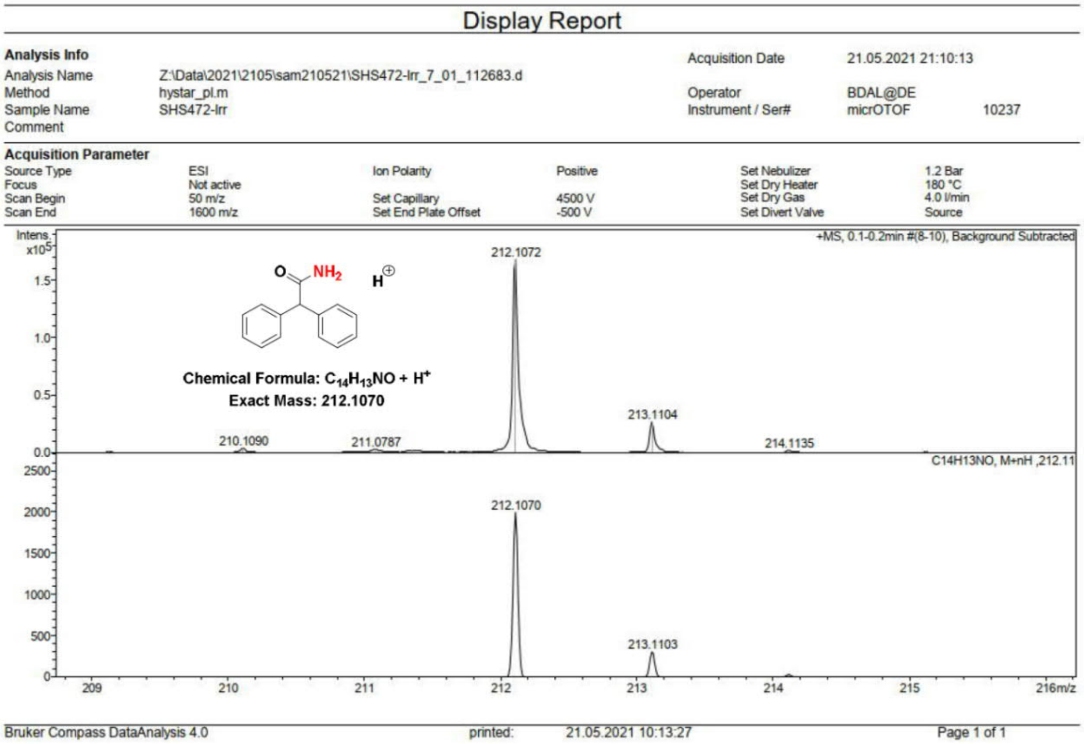


Figure S1. HPLC analysis of the reaction mixture: azibenzil (**11**) (0.1 mM) in acetonitrile (80% v/v) and aqueous HEPES buffer (20%, v/v) at pH 6.5 was irradiated with 365 nm light providing full conversion of the starting material.



Display Report

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Sample Name SHS472-Irr
Comment
Acquisition Date 21.05.2021 21:10:13
Operator BDAL@DE
Instrument / Ser# micrOTOF 10237

Acquisition Parameter
Source Type ESI
Focus Not active
Scan Begin 50 m/z
Scan End 1600 m/z
Ion Polarity Positive
Set Capillary 4500 V
Set End Plate Offset -500 V
Set Nebulizer 1.2 Bar
Set Dry Heater 180 °C
Set Dry Gas 4.0 l/min
Set Divert Valve Source

Bruker Compass DataAnalysis 4.0 printed: 21.05.2021 10:13:27 Page 1 of 1

Figure S2. HR-MS of the reaction solution obtained after photolysis of azibenzil (**11**, PhCOCN$_2$Ph) solutions in aqueous acetonitrile (80% acetonitrile, 20% water, v/v) with HCOONH$_4$ buffer (pH 7.3). The full conversion to a new substance with the same retention time, but without absorption maximum at 319 nm, was observed (see Figure 2 in the main text).

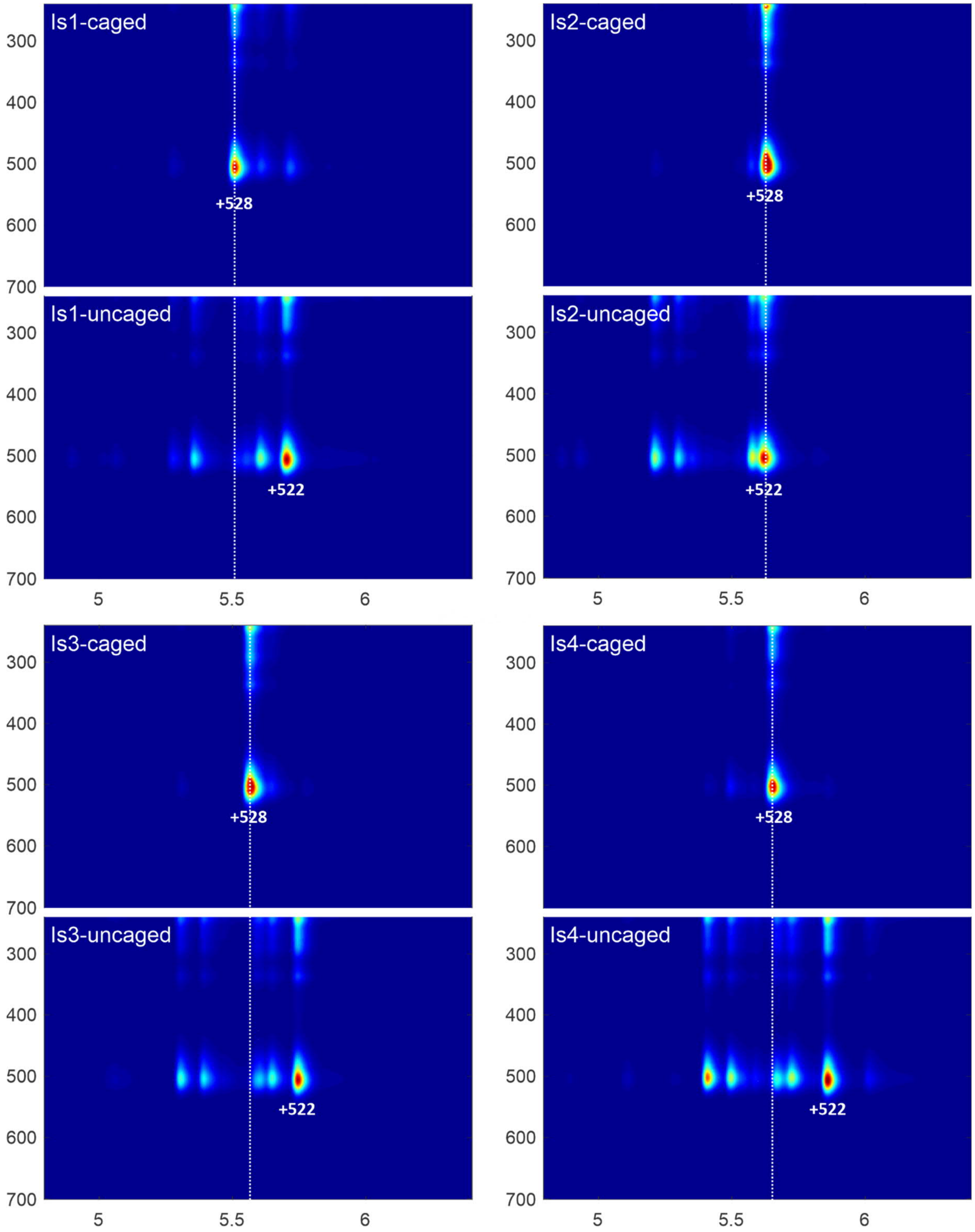
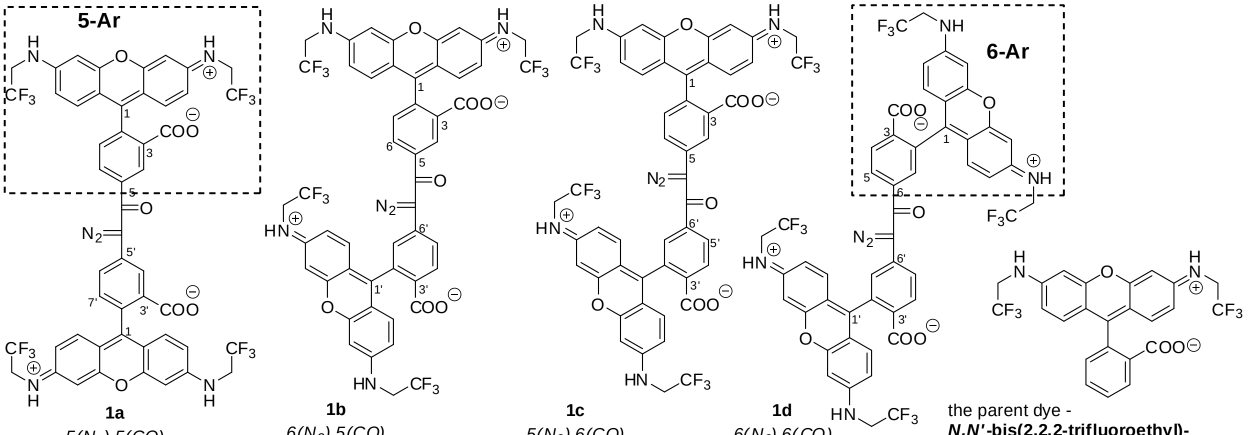


Figure S3a. 2D HPLC maps of the solutions of isomers 1-4 (for structures, see Figure **S3b**), before and after irradiation in MeCN (80% v/v) and aqueous 10 mM ammonium formate buffer (20% v/v; pH = 7.4), with 365 nm light, upon complete conversion. The *m/z* values of the main peaks $[M+2H]^{2+}$ are given for the starting materials (*m/z* 528) and the main reaction products (*m/z* 522).



1a
5(N₂),5(CO)
(Iso4)

1b
6(N₂),5(CO)
(Iso3)

1c
5(N₂),6(CO)
(Iso1)

1d
6(N₂),6(CO)
(Iso2)

Figure S3b. Structures of compounds **1a, 1b, 1c** and **1d** (isomers 4, 3, 1 and 2, respectively), and the parent rhodamine dye.

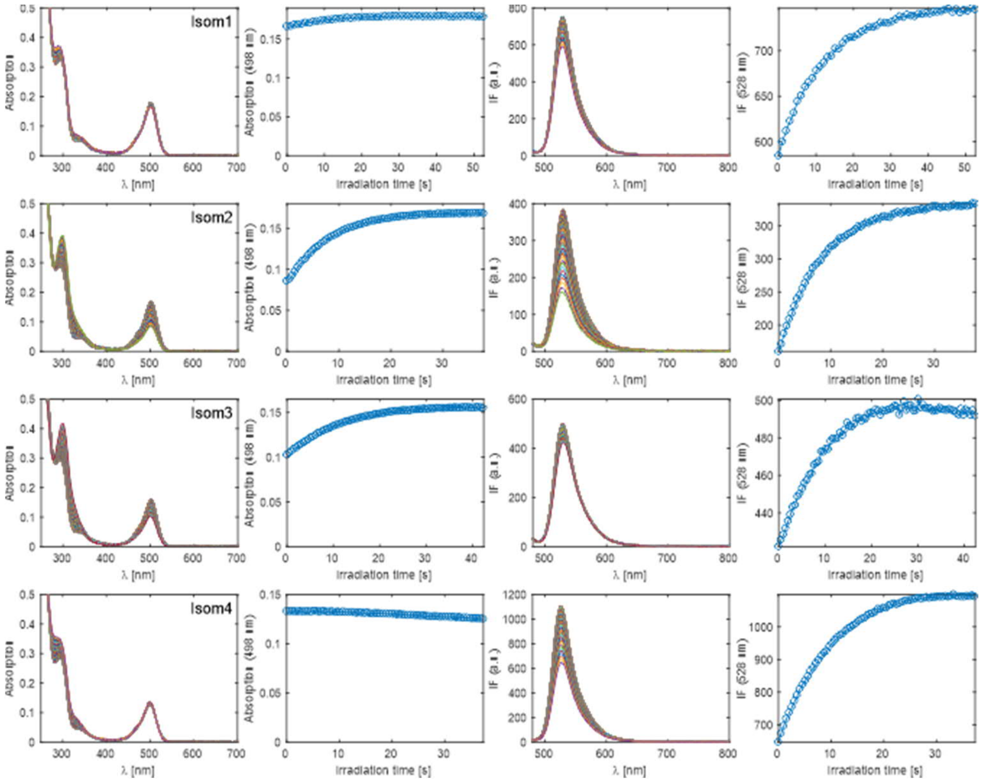


Figure S4a. Irradiation of isomers 1-4 (12 µM, for structures, see Figure S3b) in MeCN (80% v/v) and aqueous 10 mM ammonium formate buffer, pH = 7.4 (20% v/v). The samples were continuously stirred and kept at 20°C during irradiation with 365 nm light. Absorption at 498 nm and emission at 528 nm (λ_{EX} = 470 nm) were monitored and read out at fixed time intervals.

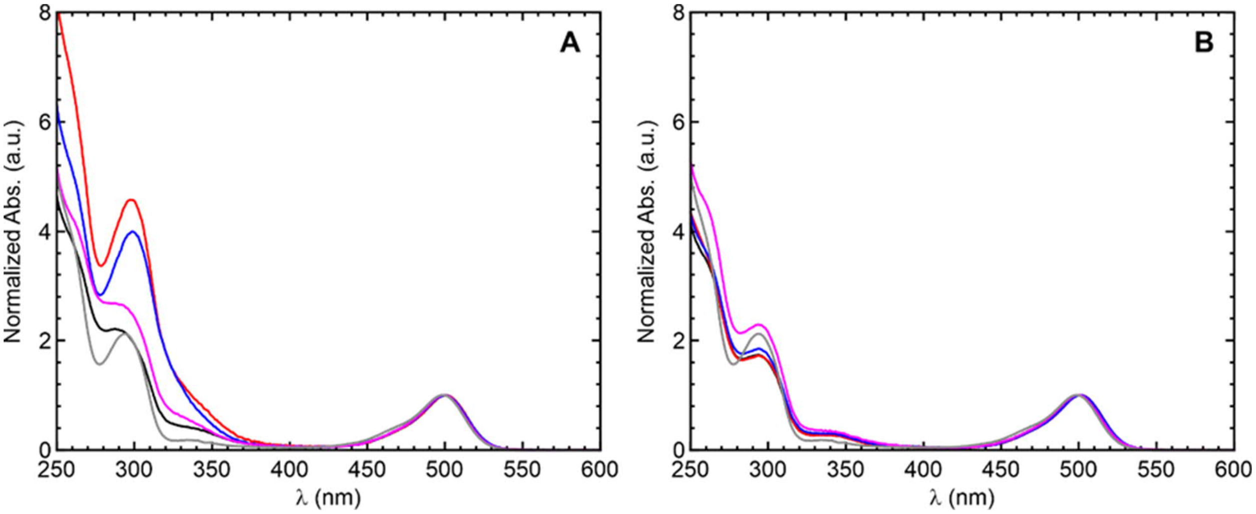


Figure S4b. Absorption spectra (normalized to the intensity of the band with the maximum at 498 nm) of compounds **1a** (purple), **1b** (blue), **1c** (black), **1d** (red) and the parent *N*,*N′*-bis(2,2,2-trifluoroethyl)rhodamine (grey) before (A) and after (B) photoconversion by irradiation with 365 nm source. For structures, see Figure S3b. Solvent: aqueous acetonitrile (80% acetonitrile, 20% water, v/v) with addition of $HCOONH_4$ buffer (pH 7.3).

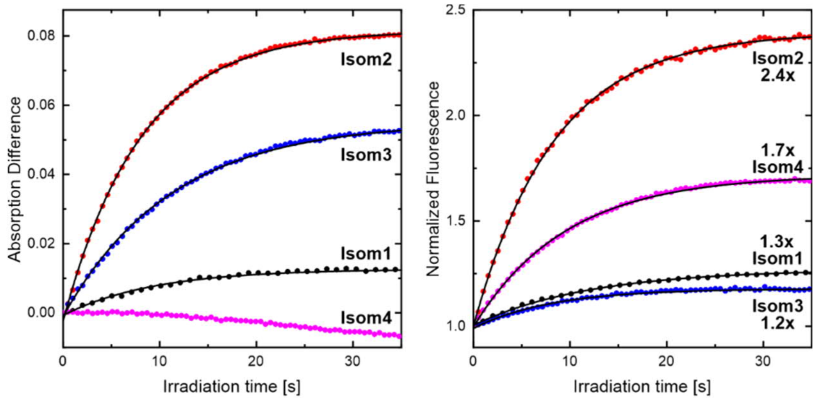
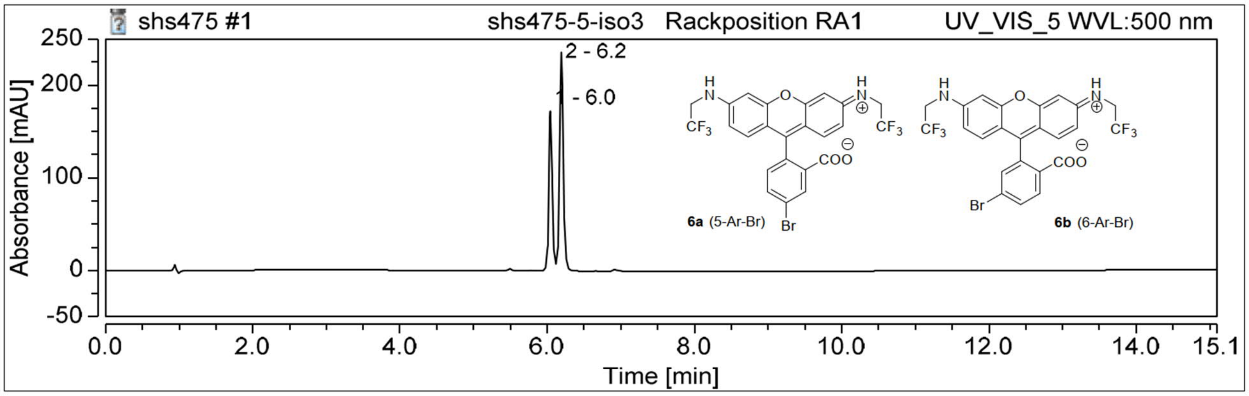
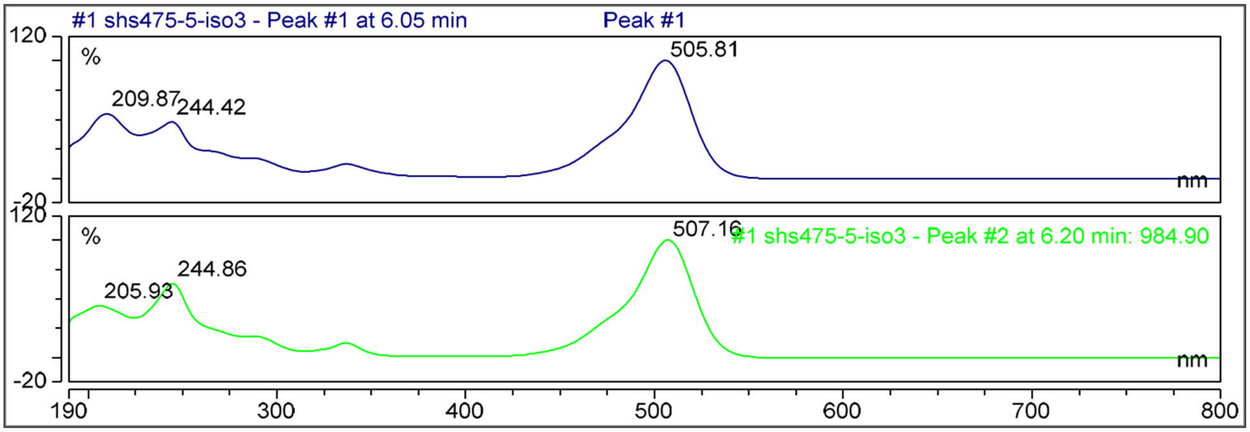


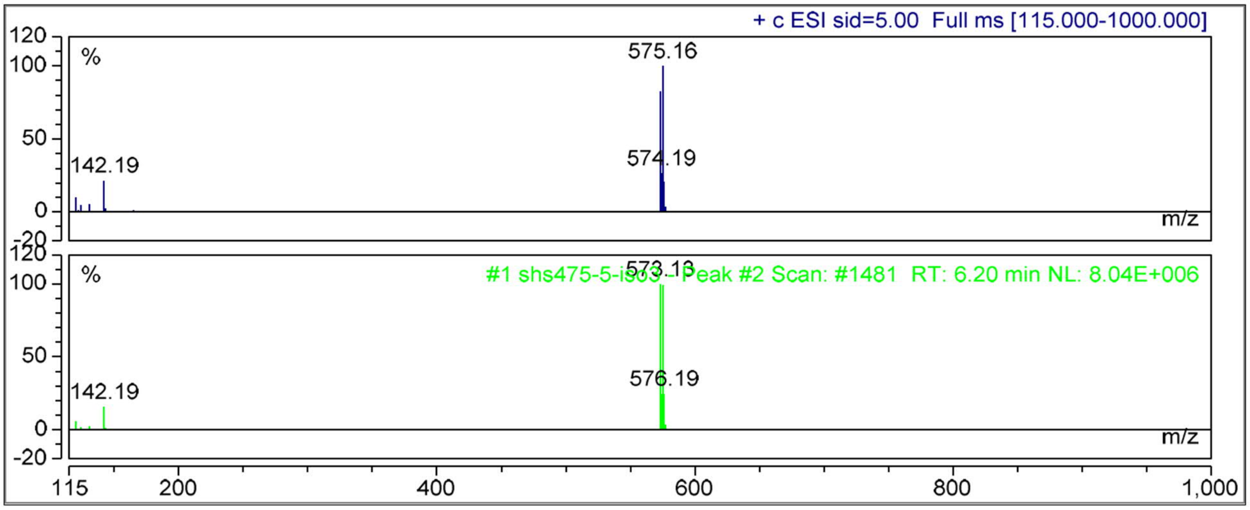
Figure S5. Normalized fluorescence (right) and absorption (left) transients during irradiation of isomers 1-4 (**1a-d**, 12 µM) with 365 nm light, as solutions in MeCN (80%) and aqueous 10 mM ammonium formate buffer; pH = 7.4 (20% v/v). Samples were continuously stirred and kept at 20°C during irradiation. Absorption at 498 nm and emissionat at 528 nm (λ_{EX} = 470 nm) were monitored at read out at fixed time intervals. The emission intensities were divided (normalized) by the corresponding initial value for each compound, and the initial absorbance was subtracted for each sample.

Bromorhodamines **6a** (5′-Br) and **6b** (6′-Br)

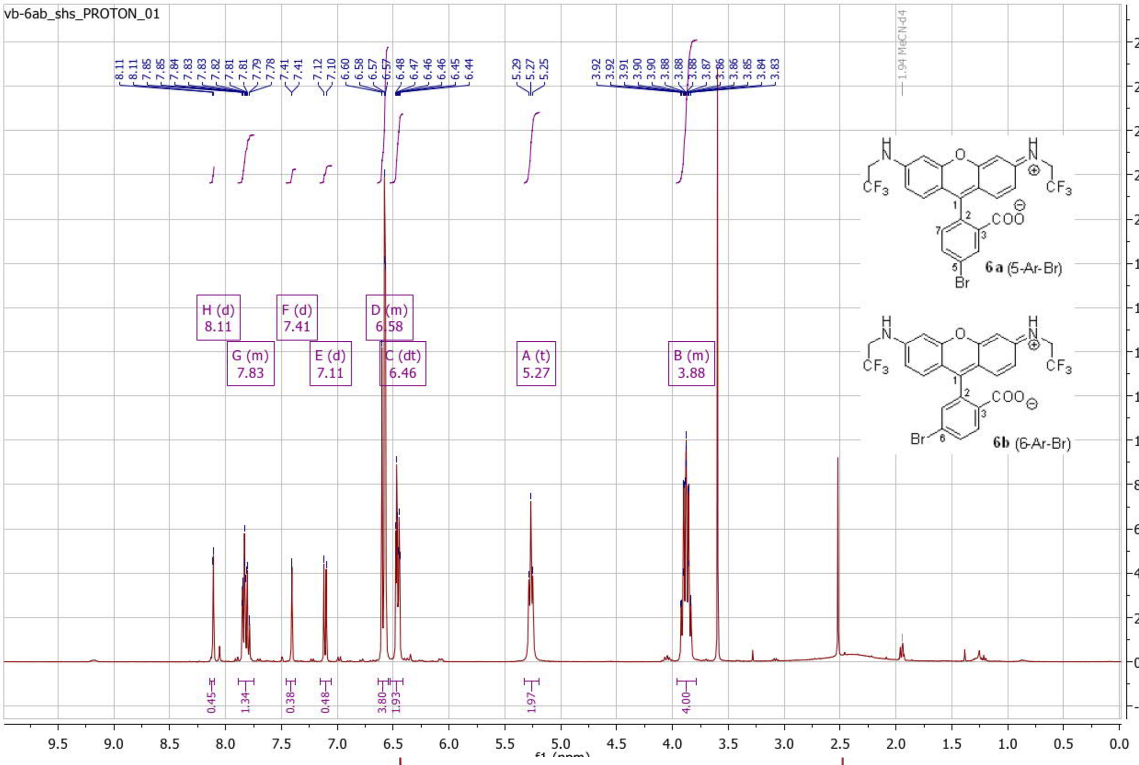
Probe : **shs475-5-iso3**
Lösungsmittel : **MeCN/H2O** **Aufgabemenge:** **3.0 µl**
Säule: Phenomenex Kinetex C18 2.6 µm **Länge:** 75 mm **iO :** 3.0 mm
Fluß (ml / Min) : **0.5** **Temperatur :** **25.0**
Detektor: DAD-3000 **Pumpe:** HPG-3200SD **Sampler:** WPS-3000
Laufmittel: **A = Acetonitril 0.1% FA** **B = Wasser 0.1% FA**
Gradient: A 20.0 % B 80.0 % **---->** A 100.0 % B 0.0 % T = 10 Min.

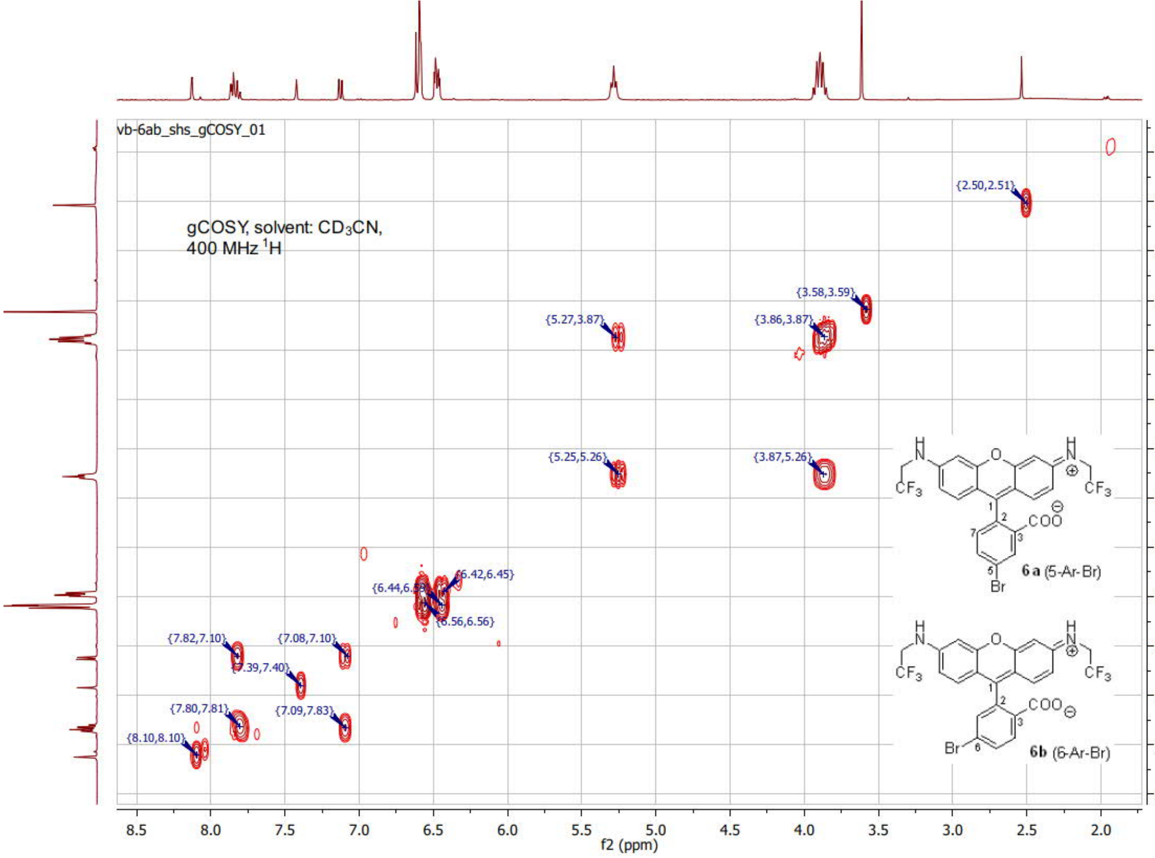


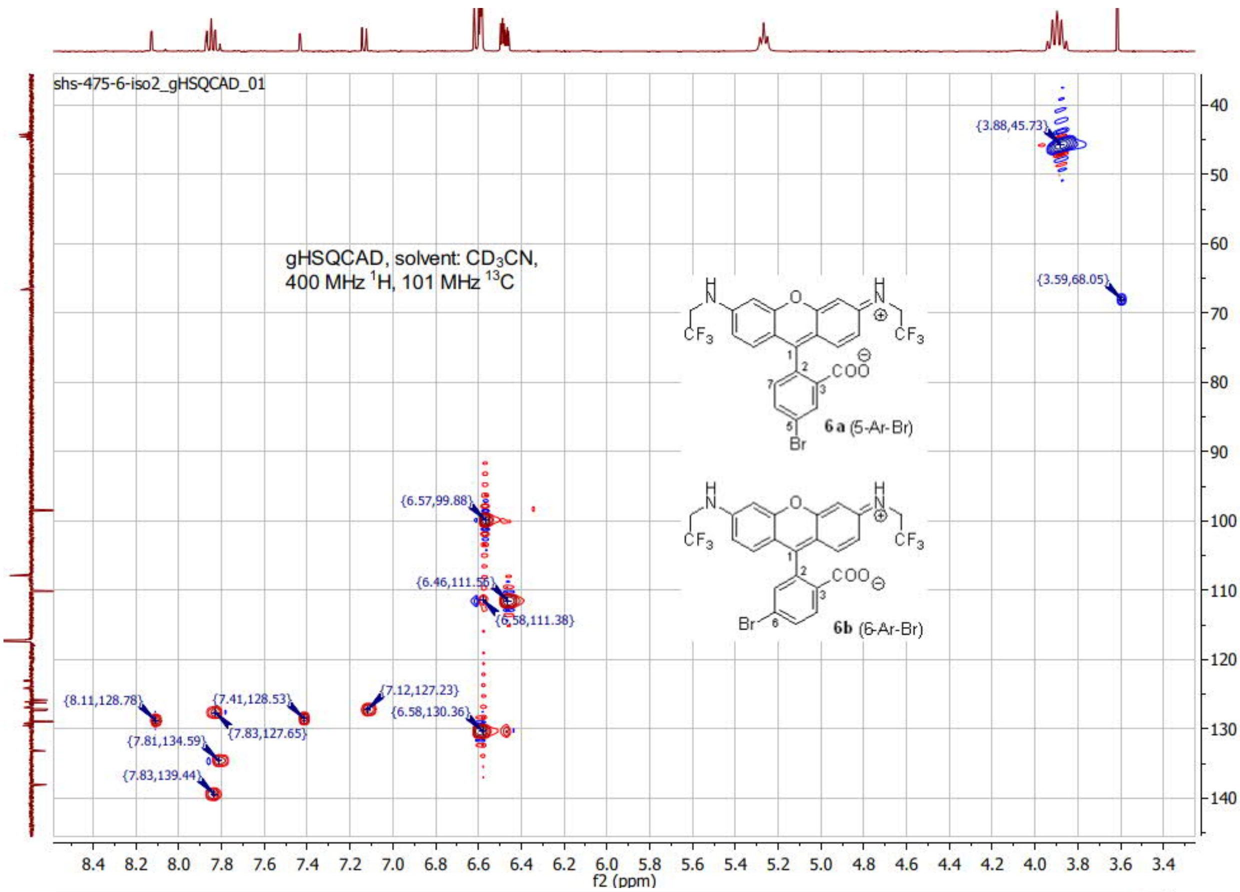


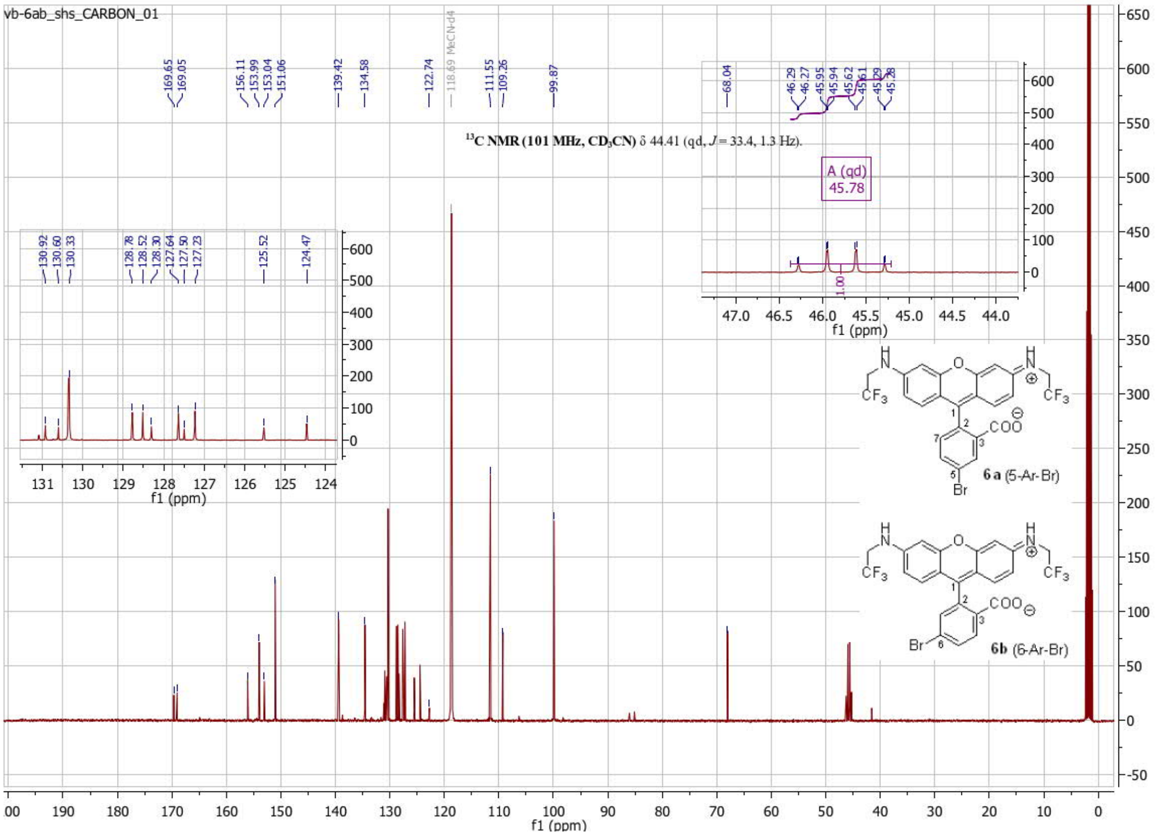


^{1}H NMR (400 MHz, CD_3CN) δ 8.11 (d, J = 1.8 Hz, 0H), 7.89 – 7.75 (m, 1H), 7.41 (d, J = 1.6 Hz, 0H), 7.11 (d, J = 8.2 Hz, 0H), 6.64 – 6.55 (m, 4H), 6.46 (dt, J = 8.7, 2.8 Hz, 2H), 5.27 (t, J = 6.9 Hz, 2H), 3.96 – 3.78 (m, 4H).

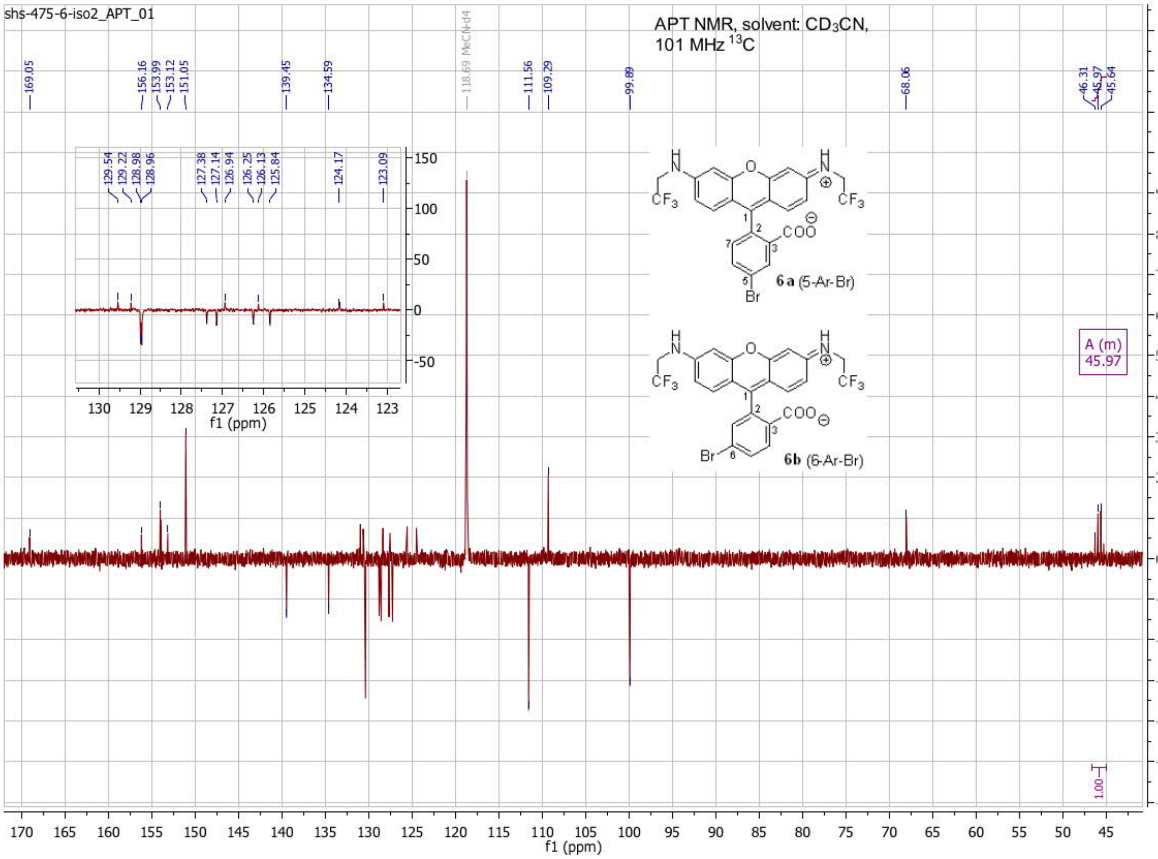








^{13}**C NMR (101 MHz, CD$_3$CN)** δ 44.41 (qd, *J* = 33.4, 1.3 Hz).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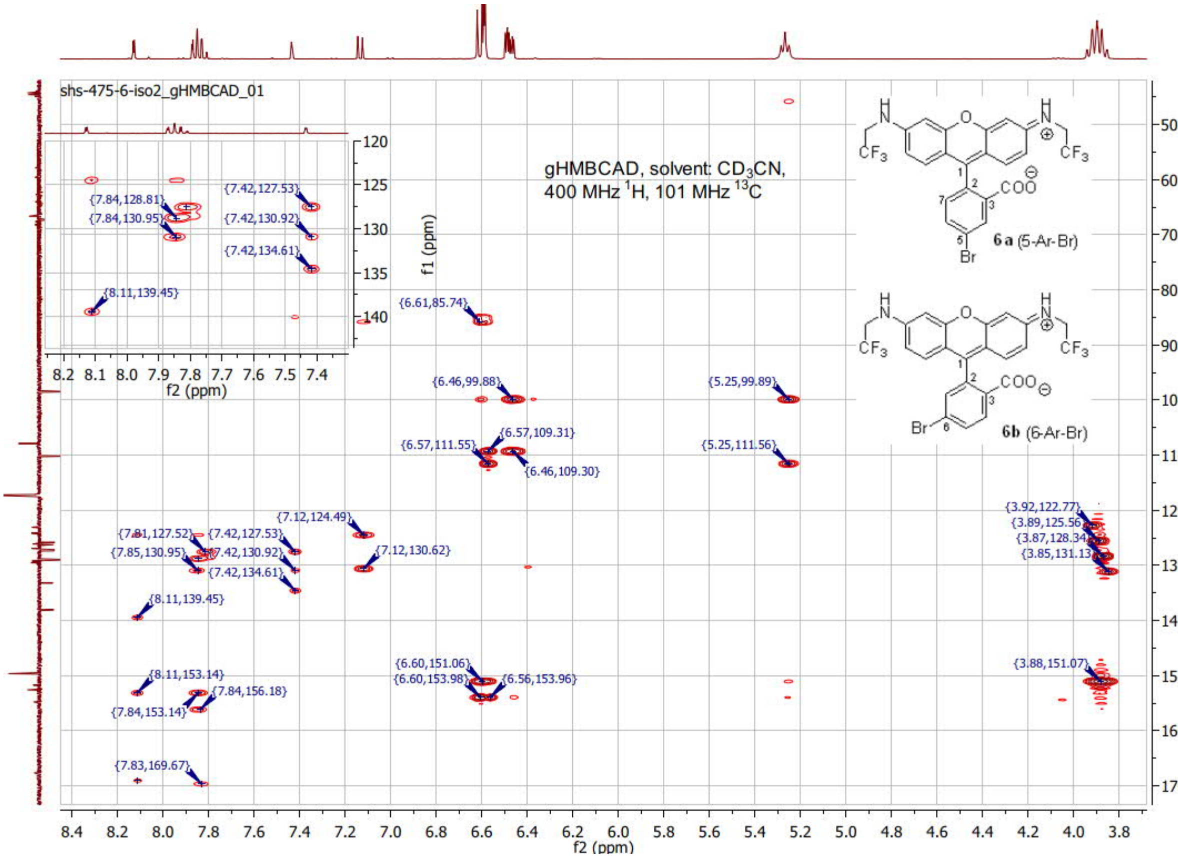
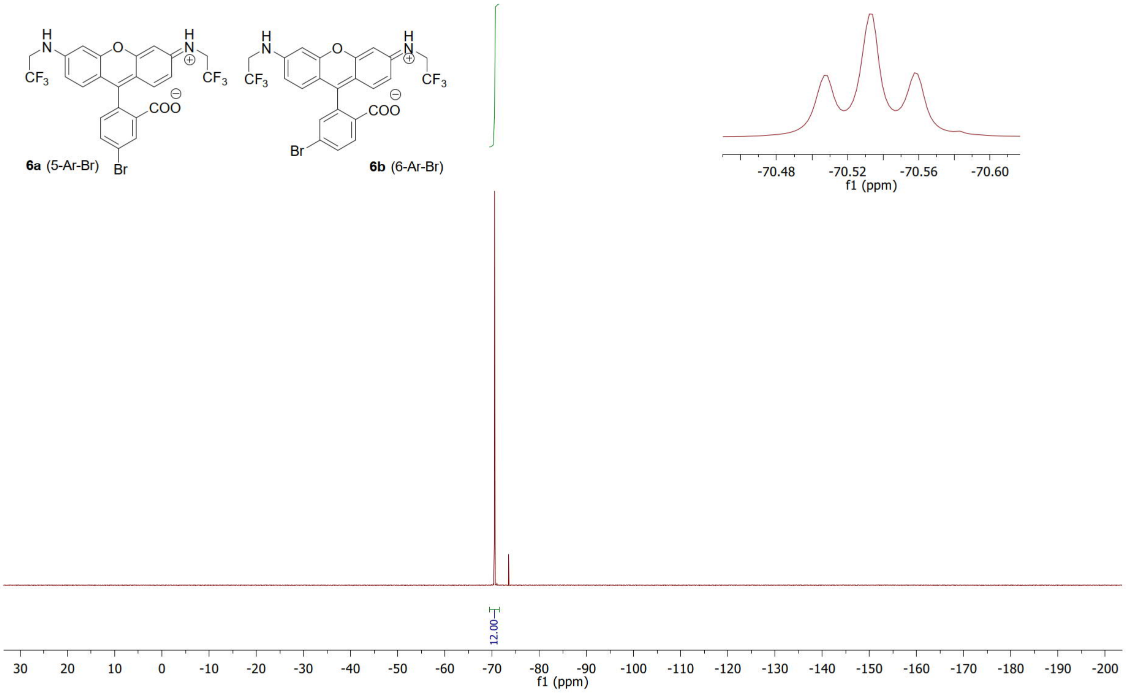
APT NMR, solvent: CD₃CN,
101 MHz ¹³C
169.05
156.16
153.99
153.12
151.05
139.45
134.59
118.69 MeCN-d4
111.56
109.29
99.89
68.06
46.31
45.97
45.64
129.54
129.22
128.98
128.96
127.38
127.14
126.94
126.25
126.13
125.84
124.17
123.09
150
100
50
0
-50
130 129 128 127 126 125 124 123
f1 (ppm)
6a (5-Ar-Br)
6b (6-Ar-Br)
Br
COO
A (m)
45.97
1.00
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45
f1 (ppm)


shs-475-6-iso2_gHMBCAD_01
gHMBCAD, solvent: CD₃CN,
400 MHz ¹H, 101 MHz ¹³C
{7.84,128.81}
{7.84,130.95}
{7.42,127.53}
{7.42,130.92}
{7.42,134.61}
{8.11,139.45}
120
125
130
135
140
8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4
f2 (ppm)
f1 (ppm)
{6.61,85.74}
{6.46,99.88}
{5.25,99.89}
{6.57,111.55}
{6.57,109.31}
{6.46,109.30}
{5.25,111.56}
{7.12,124.49}
{7.81,127.52}
{7.42,127.53}
{7.85,130.95}
{7.42,130.92}
{7.12,130.62}
{7.42,134.61}
{8.11,139.45}
{3.92,122.77}
{3.89,125.56}
{3.87,128.34}
{3.85,131.13}
{8.11,153.14}
{7.84,156.18}
{7.84,153.14}
{6.60,151.06}
{6.60,153.98}
{6.56,153.96}
{3.88,151.07}
{7.83,169.67}
6a (5-Ar-Br)
6b (6-Ar-Br)
Br
COO
50 60 70 80 90 100 110 120 130 140 150 160 170
8.4 8.2 8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8
f2 (ppm)

^{19}F NMR (376 MHz, DMSO-d_6) δ -70.53 (t, J = 9.6 Hz, 12F) ppm.

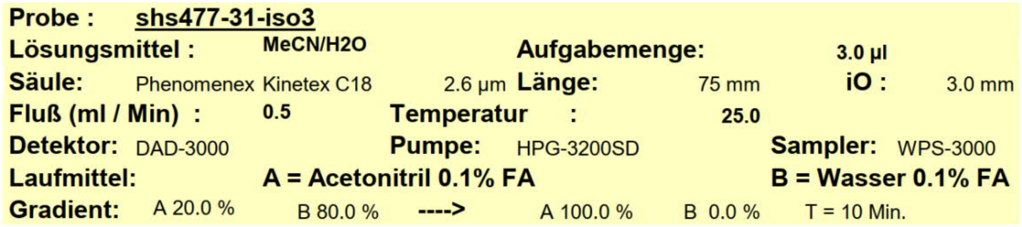
shs475-1-iso-2a_FLUORINE_01



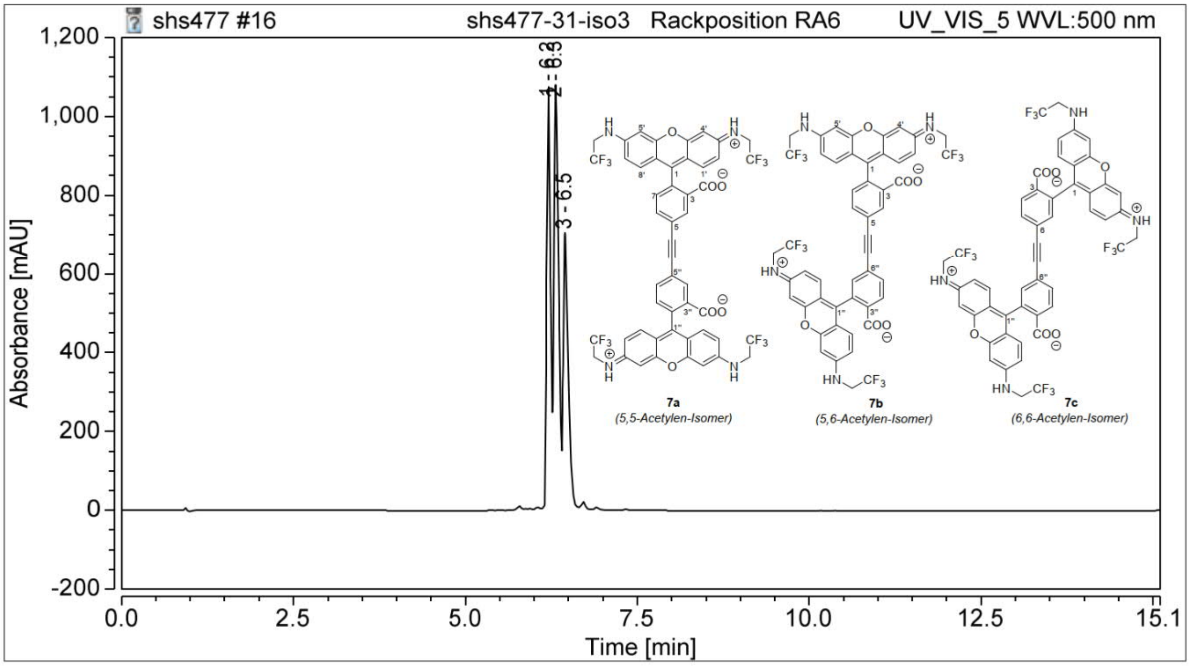
6a (5-Ar-Br)

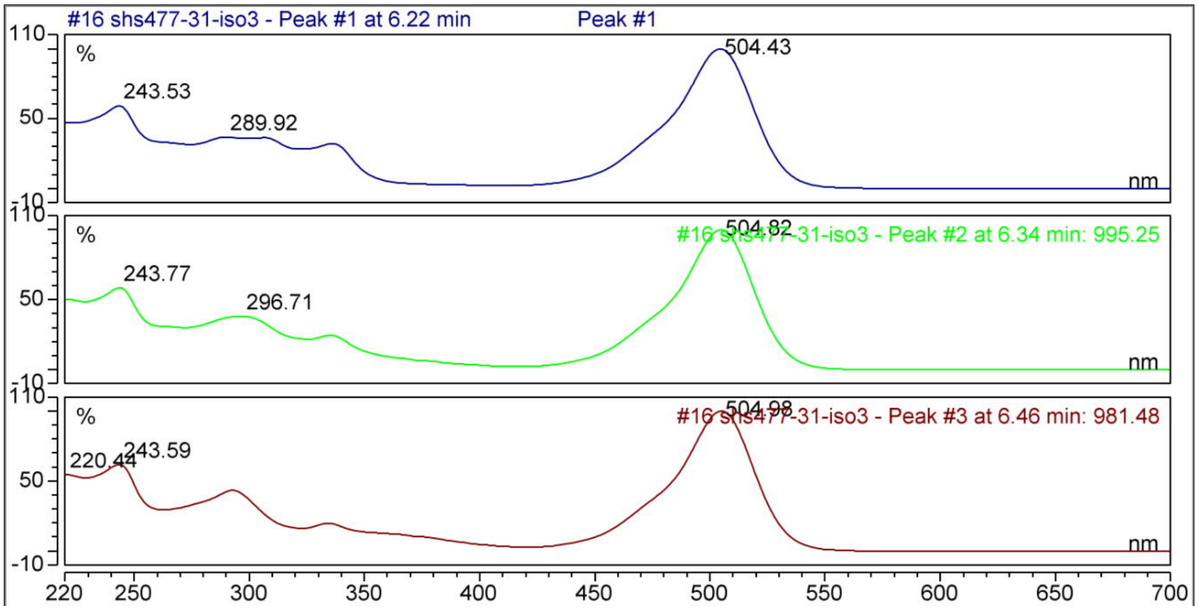
6b (6-Ar-Br)

Bis(rhodamine) acetylenes **7a** (peak 3), **7b** (peak 2), and **7c** (peak 3) are 5,5'-, 5,6′- and 6,6′-isomers, respectively.



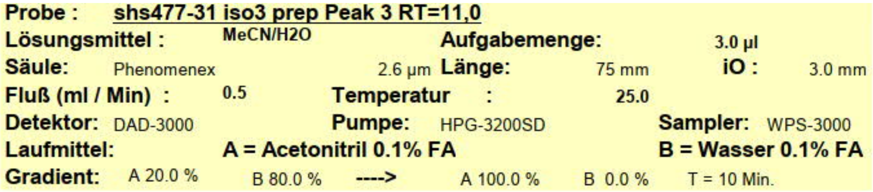
Probe : **shs477-31-iso3**
Lösungsmittel : MeCN/H2O **Aufgabemenge:** 3.0 µl
Säule: Phenomenex Kinetex C18 2.6 µm **Länge:** 75 mm **iO :** 3.0 mm
Fluß (ml / Min) : 0.5 **Temperatur :** 25.0
Detektor: DAD-3000 **Pumpe:** HPG-3200SD **Sampler:** WPS-3000
Laufmittel: **A = Acetonitril 0.1% FA** **B = Wasser 0.1% FA**
Gradient: A 20.0 % B 80.0 % ----> A 100.0 % B 0.0 % T = 10 Min.



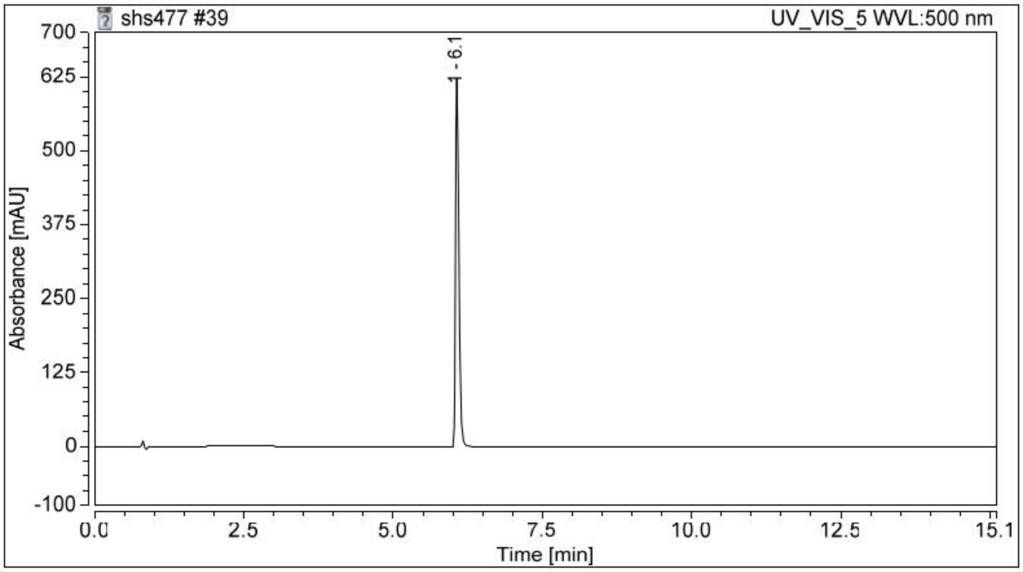


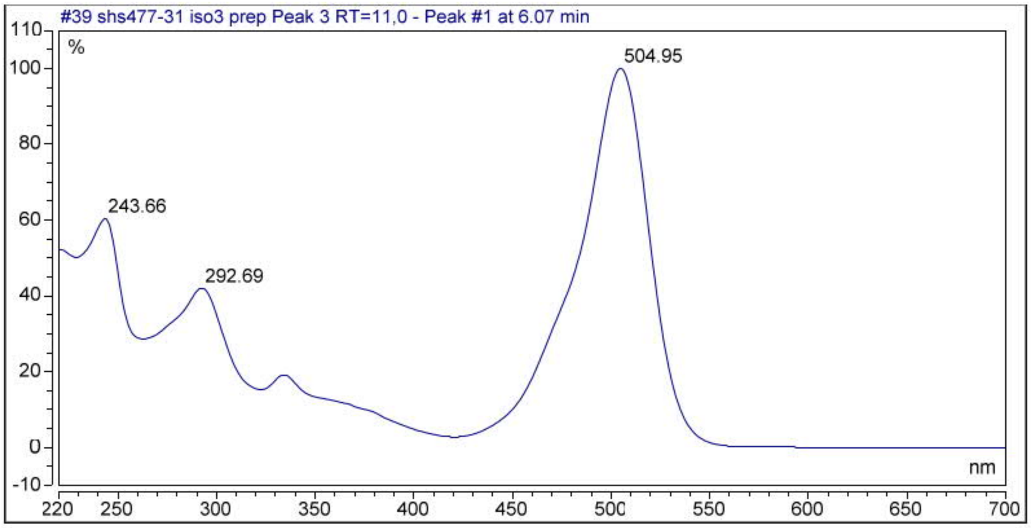
Analytical HPLC traces and NMR spectra of the individual regioisomers **7a** (peak 3), **7b** (peak 2) and **7c** (peak 1) isolated by means of preparative HPLC

Compound **7a**

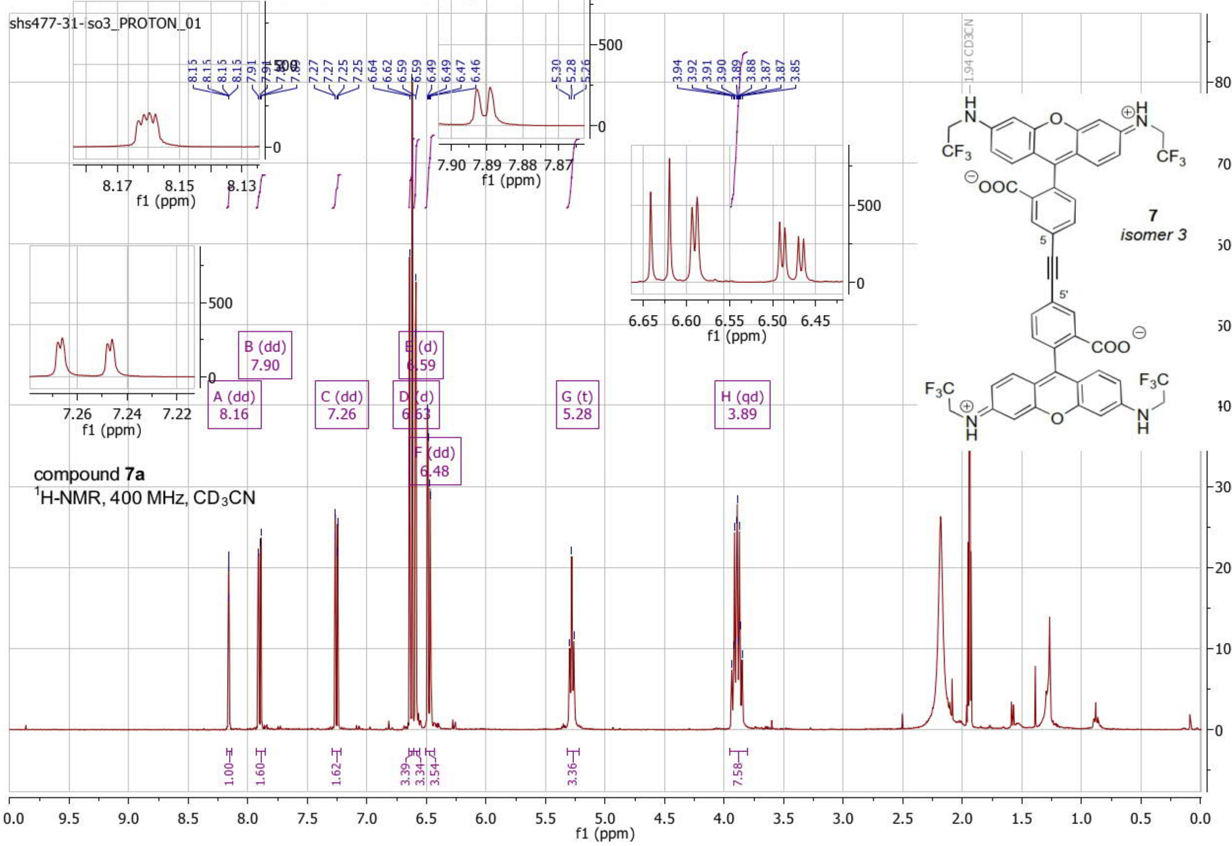


Probe : **shs477-31 iso3 prep Peak 3 RT=11,0**
Lösungsmittel : MeCN/H2O **Aufgabemenge:** 3.0 µl
Säule: Phenomenex 2.6 µm **Länge:** 75 mm **iO :** 3.0 mm
Fluß (ml / Min) : 0.5 **Temperatur :** 25.0
Detektor: DAD-3000 **Pumpe:** HPG-3200SD **Sampler:** WPS-3000
Laufmittel: **A = Acetonitril 0.1% FA** **B = Wasser 0.1% FA**
Gradient: A 20.0 % B 80.0 % ----> A 100.0 % B 0.0 % T = 10 Min.

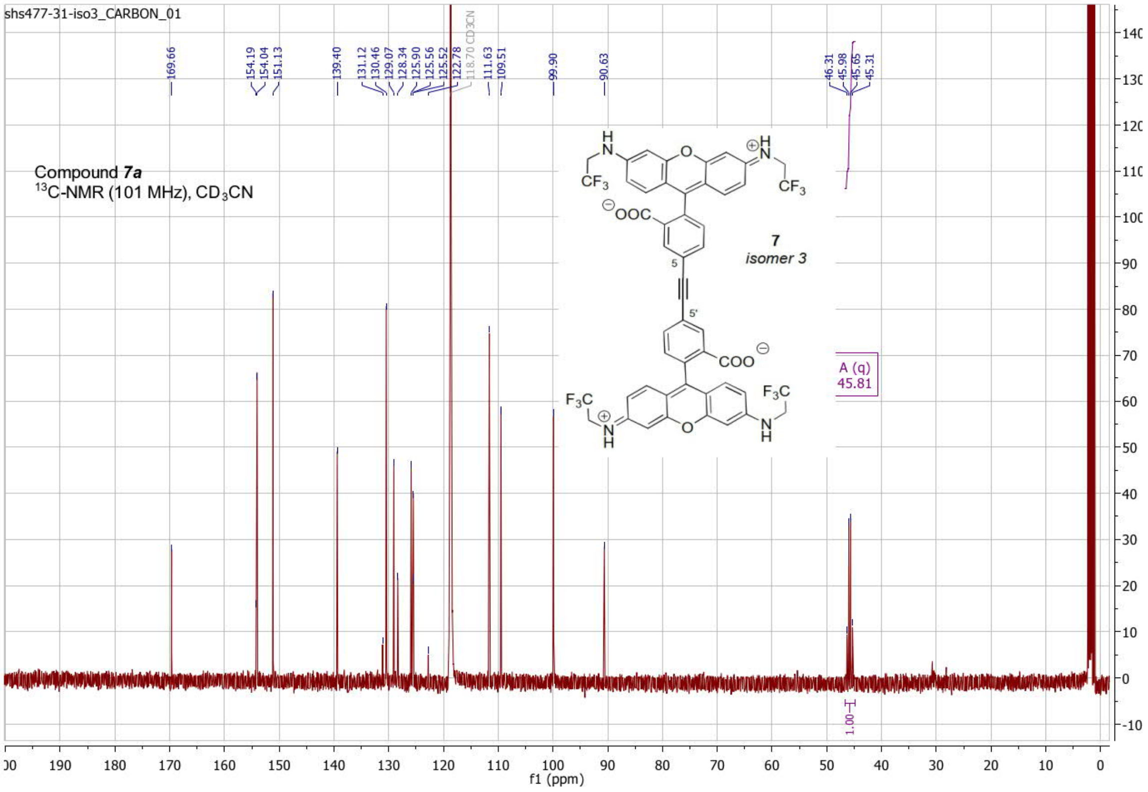




^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.16 (dd, J = 1.5, 0.8 Hz, 1H), 7.90 (dd, J = 8.0, 1.5 Hz, 2H), 7.26 (dd, J = 8.0, 0.9 Hz, 2H), 6.63 (d, J = 8.7 Hz, 3H), 6.59 (d, J = 2.4 Hz, 3H), 6.48 (dd, J = 8.7, 2.4 Hz, 4H), 5.28 (t, J = 7.0 Hz, 3H), 3.89 (qd, J = 9.3, 6.8 Hz, 8H).

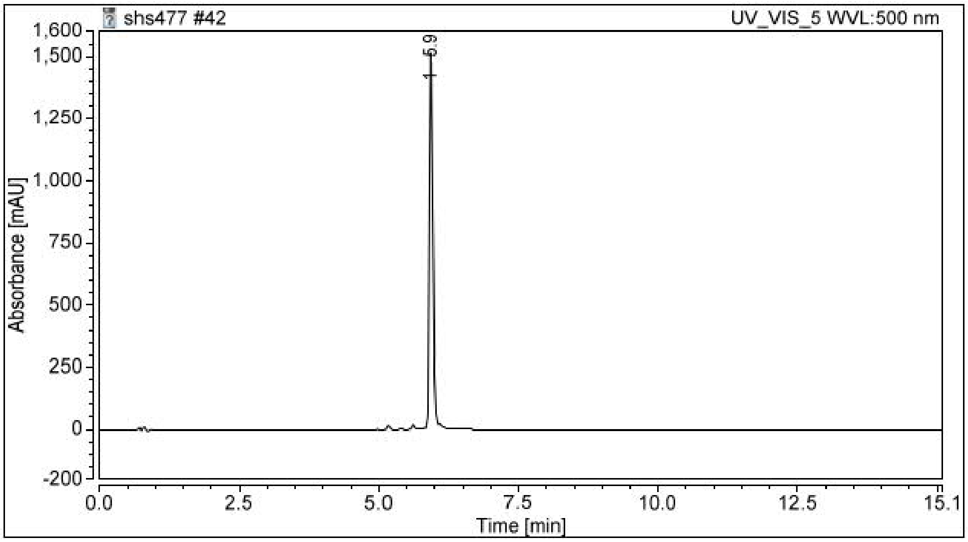


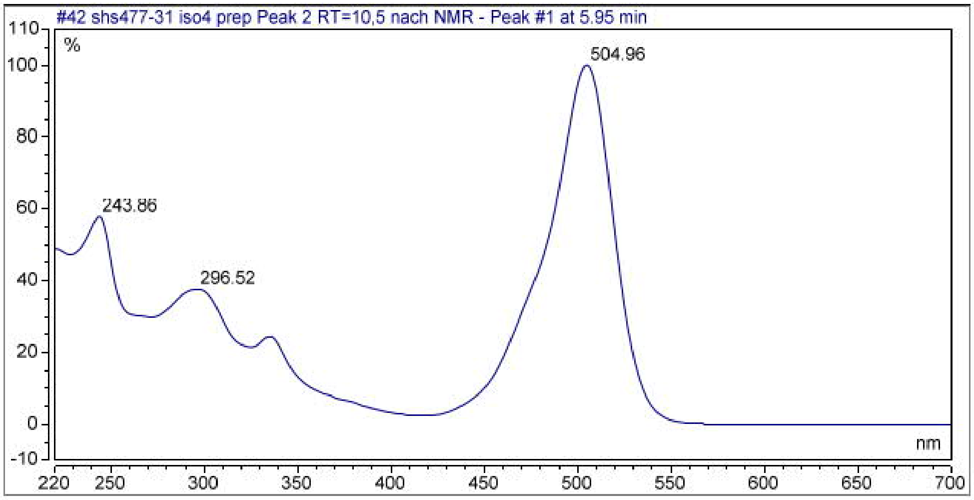
^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 45.81 (q, J = 33.4 Hz).



Compound **7b**

Probe : shs477-31 iso4 prep Peak 2 RT=10,5 nach
Lösungsmittel : MeCN/H2O **Aufgabemenge:** 3.0 µl
Säule: Phenomenex 2.6 µm **Länge:** 75 mm **iO :** 3.0 mm
Fluß (ml / Min) : 0.5 **Temperatur :** 25.0
Detektor: DAD-3000 **Pumpe:** HPG-3200SD **Sampler:** WPS-3000
Laufmittel: **A = Acetonitril 0.1% FA** **B = Wasser 0.1% FA**
Gradient: A 20.0 % B 80.0 % ----> A 100.0 % B 0.0 % T = 10 Min.

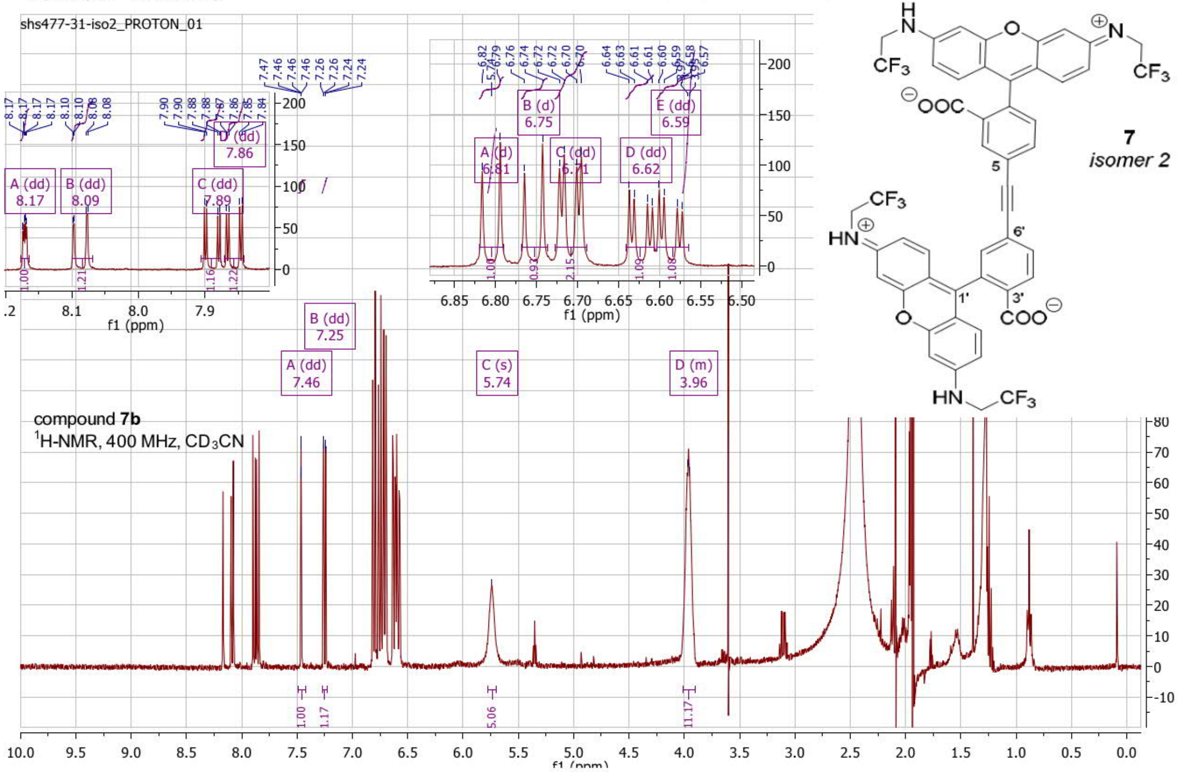


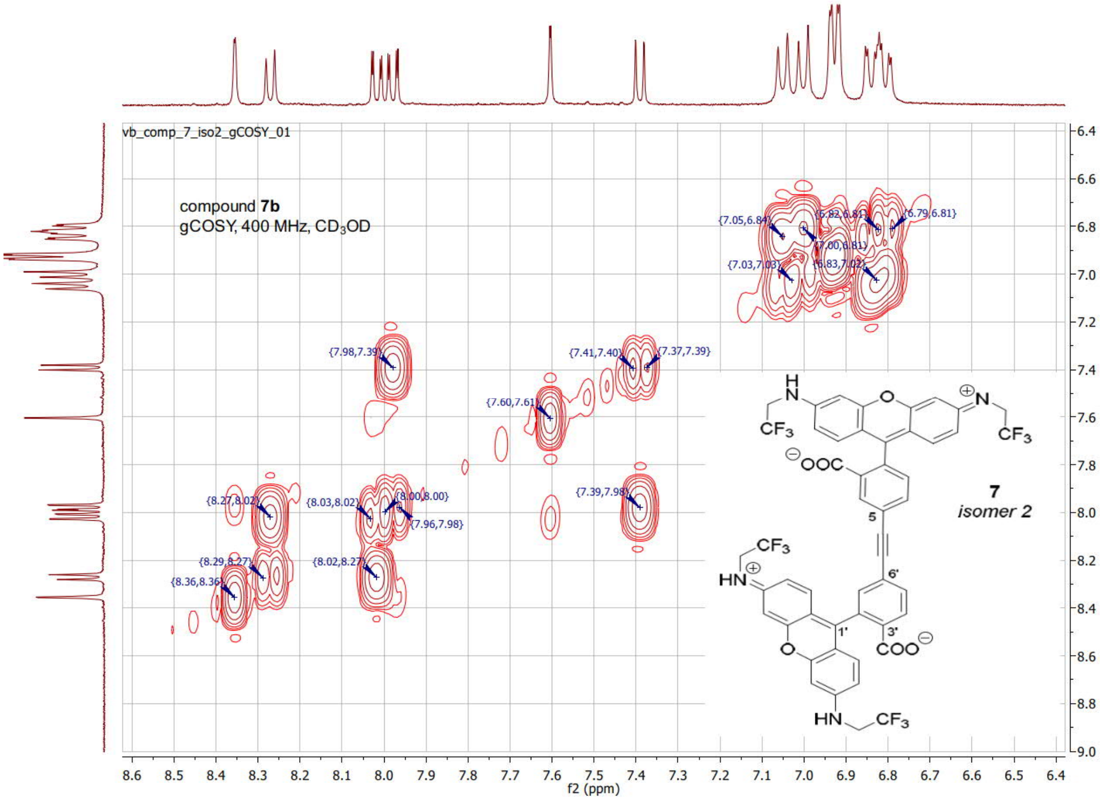


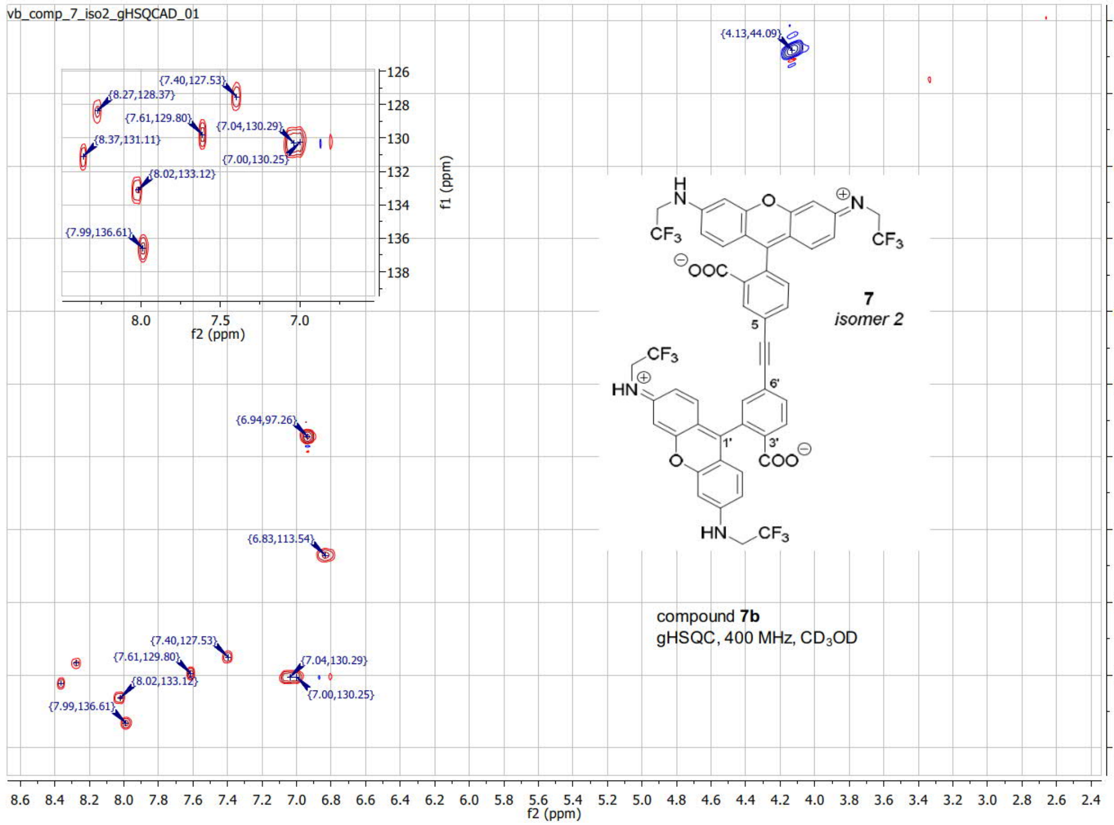
^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 7.46 (dd, J = 1.4, 0.7 Hz, 1H), 7.25 (dd, J = 8.0, 0.7 Hz, 1H), 5.74 (s, 5H), 4.01 – 3.91 (m, 11H).

δ 8.17 (dd, J = 1.6, 0.7 Hz, 1H), 8.09 (dd, J = 8.0, 0.7 Hz, 1H), 7.89 (dd, J = 8.0, 1.4 Hz, 1H), 7.86 (dd, J = 8.0, 1.5 Hz, 1H).

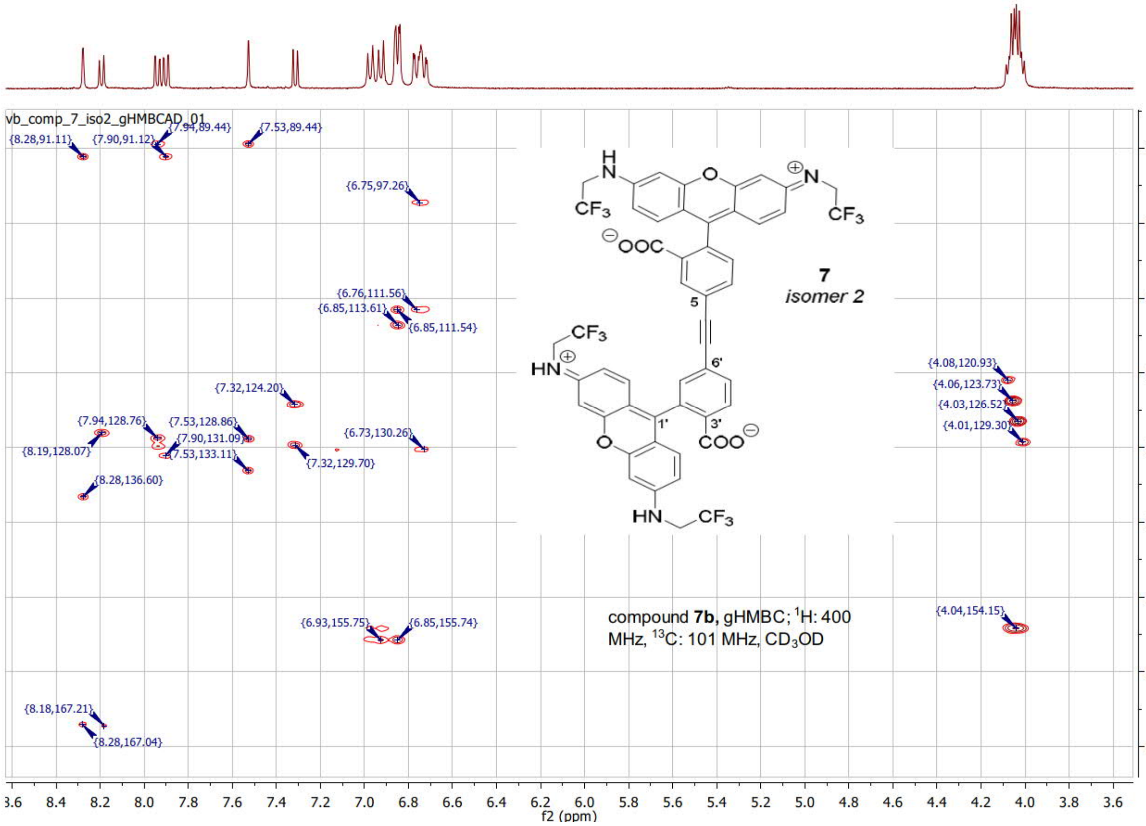
δ 6.81 (d, J = 8.8 Hz, 1H), 6.75 (d, J = 8.8 Hz, 1H), 6.71 (dd, J = 8.4, 2.4 Hz, 2H), 6.62 (dd, J = 8.8, 2.4 Hz, 1H), 6.59 (dd, J = 8.8, 2.4 Hz, 1H).





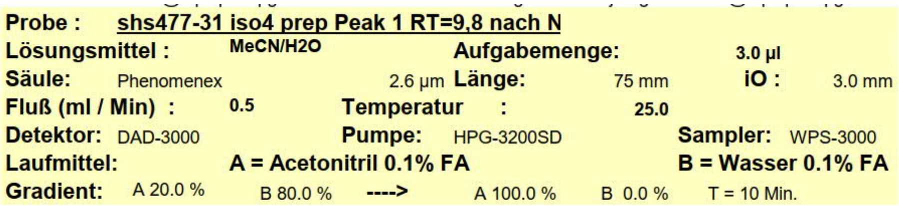


compound **7b**
gHSQC, 400 MHz, CD_3OD

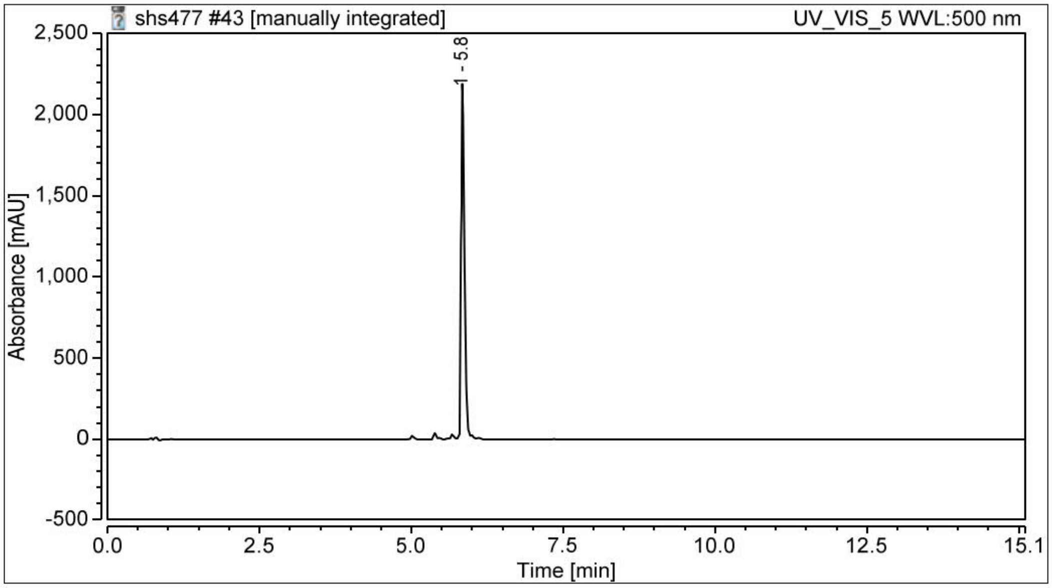


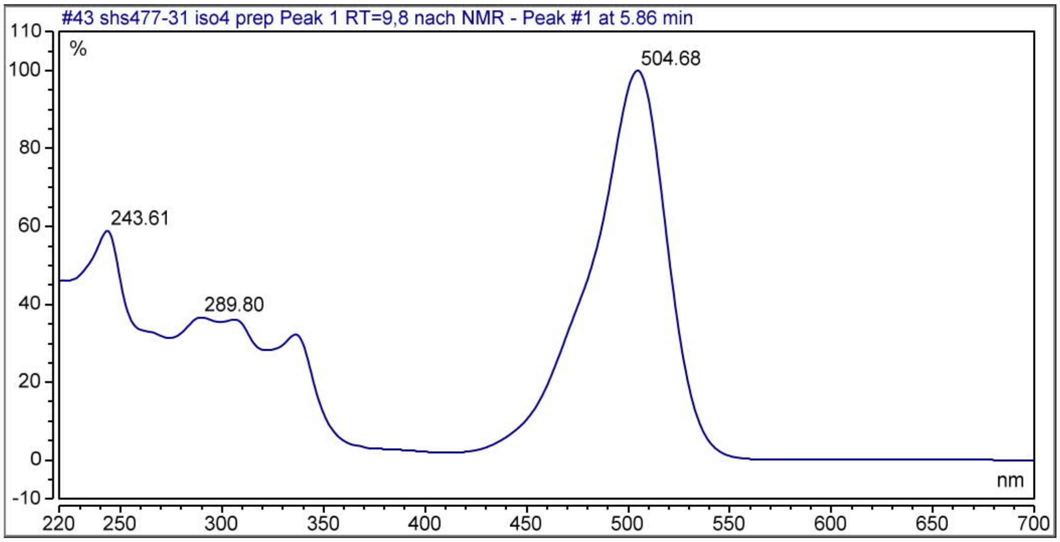
compound **7b,** gHMBC; ^{1}H: 400 MHz, ^{13}C: 101 MHz, CD_3OD

Compound **7c**

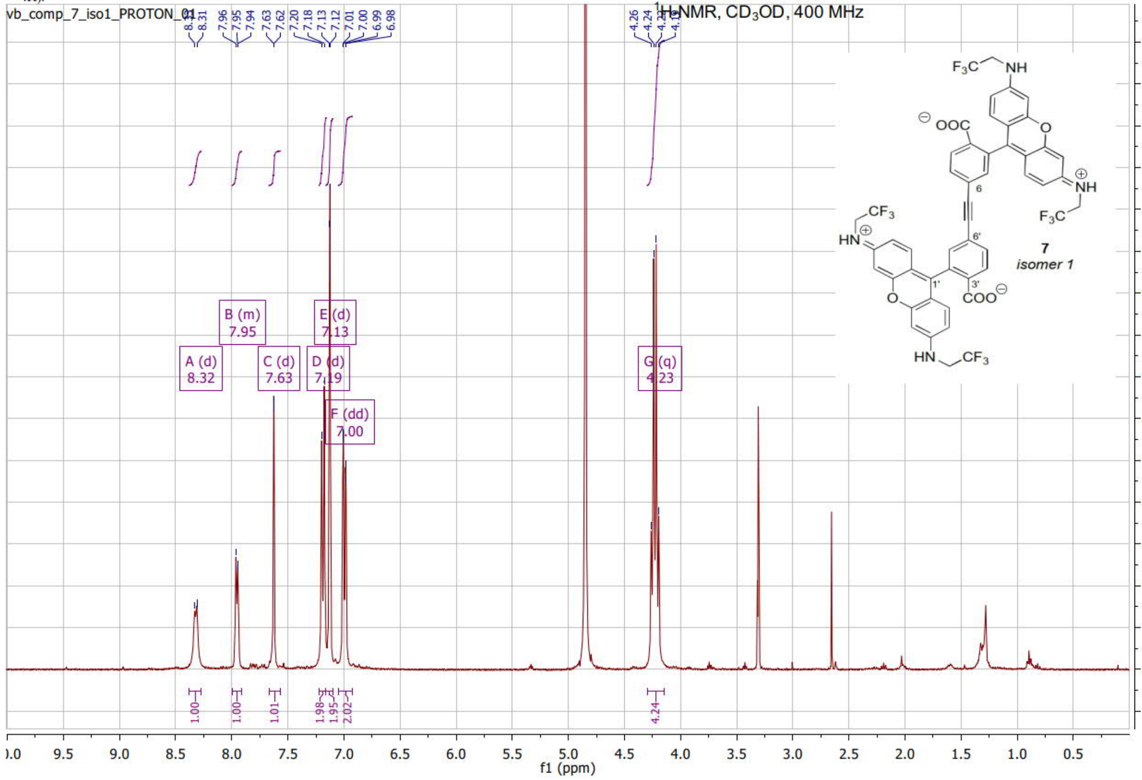


Probe : shs477-31 iso4 prep Peak 1 RT=9,8 nach N
Lösungsmittel : MeCN/H2O **Aufgabemenge:** 3.0 µl
Säule: Phenomenex 2.6 µm **Länge:** 75 mm **iO :** 3.0 mm
Fluß (ml / Min) : 0.5 **Temperatur :** 25.0
Detektor: DAD-3000 **Pumpe:** HPG-3200SD **Sampler:** WPS-3000
Laufmittel: A = Acetonitril 0.1% FA B = Wasser 0.1% FA
Gradient: A 20.0 % B 80.0 % ----> A 100.0 % B 0.0 % T = 10 Min.

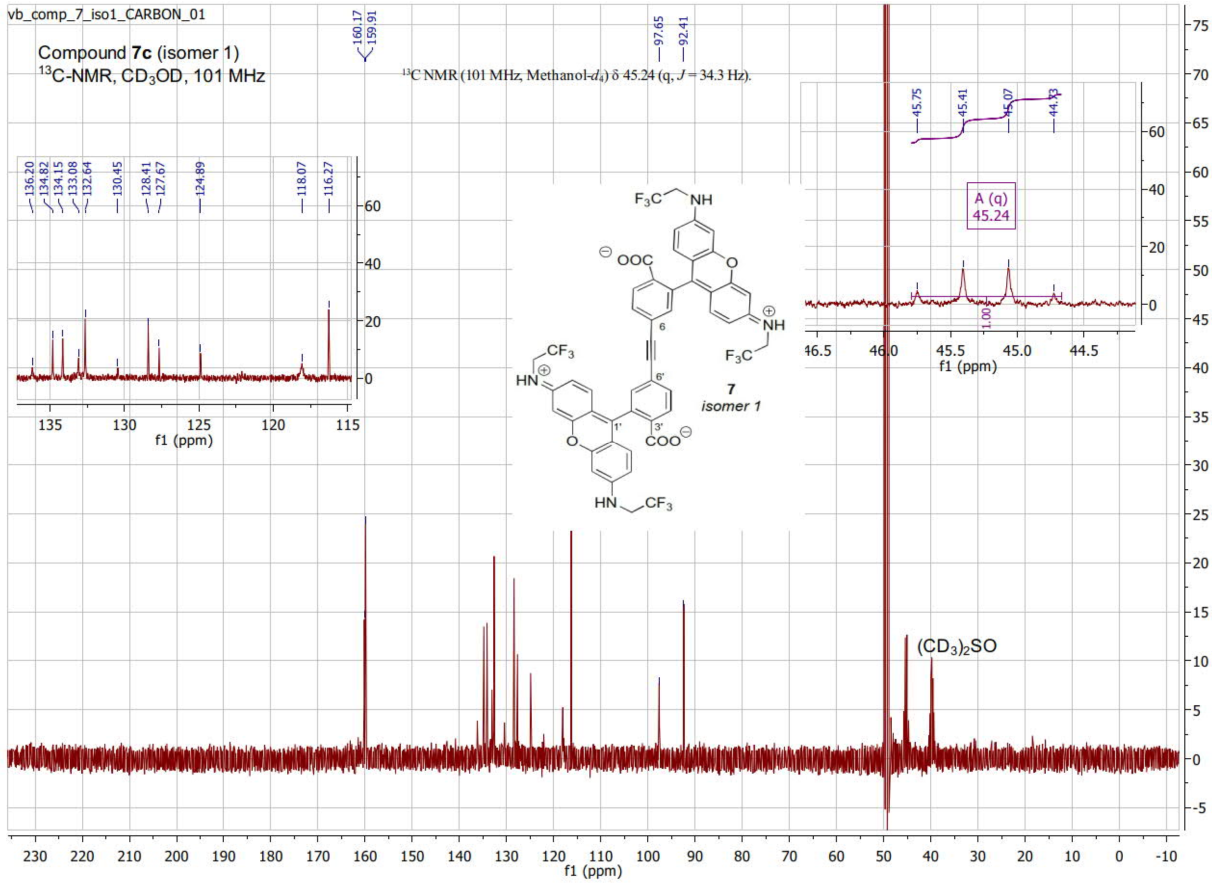




^{1}H NMR (400 MHz, Methanol-d_4) δ 8.32 (d, J = 7.9 Hz, 1H), 8.00 – 7.91 (m, 1H), 7.63 (d, J = 1.4 Hz, 1H), 7.19 (d, J = 9.2 Hz, 2H), 7.13 (d, J = 2.1 Hz, 2H), 7.00 (dd, J = 9.1, 2.2 Hz, 2H), 4.23 (q, J = 9.0 Hz, 4H).



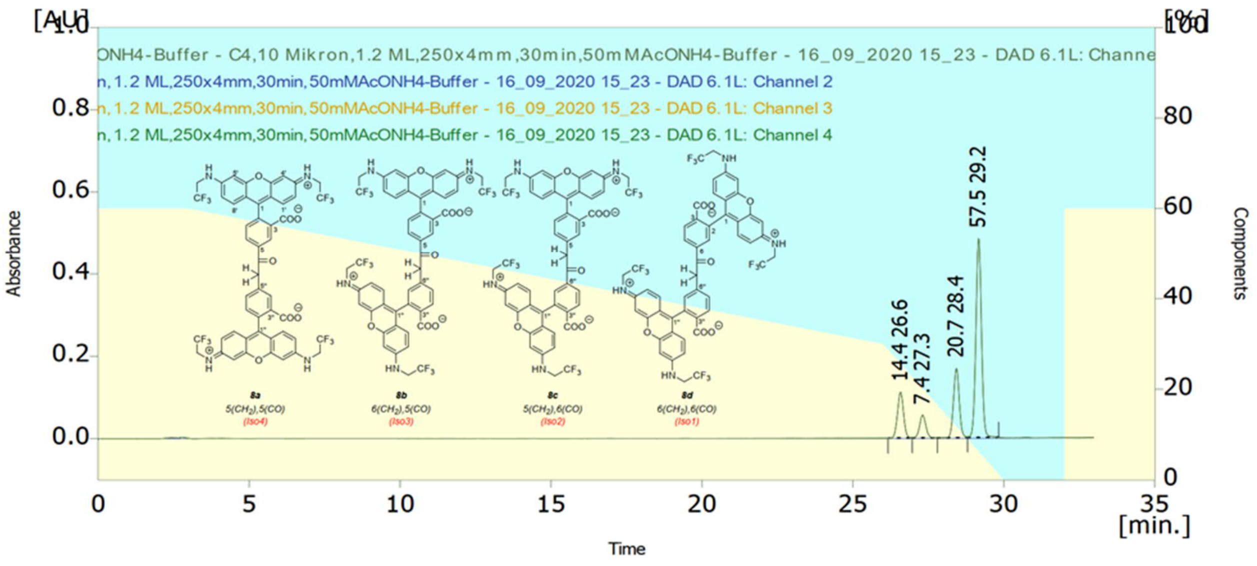
^{13}C NMR (101 MHz, Methanol-d_4) δ 45.24 (q, J = 34.3 Hz).



Bis-rhodamine ethanones **8a** [5(CH_2),5(CO)] (peak 4), **8b** [6(CH_2),5(CO)] (peak 3), **8c** [5(CH_2),6(CO)] (peak 2) and **8d** [6(CH_2),6(CO)] (peak 1)

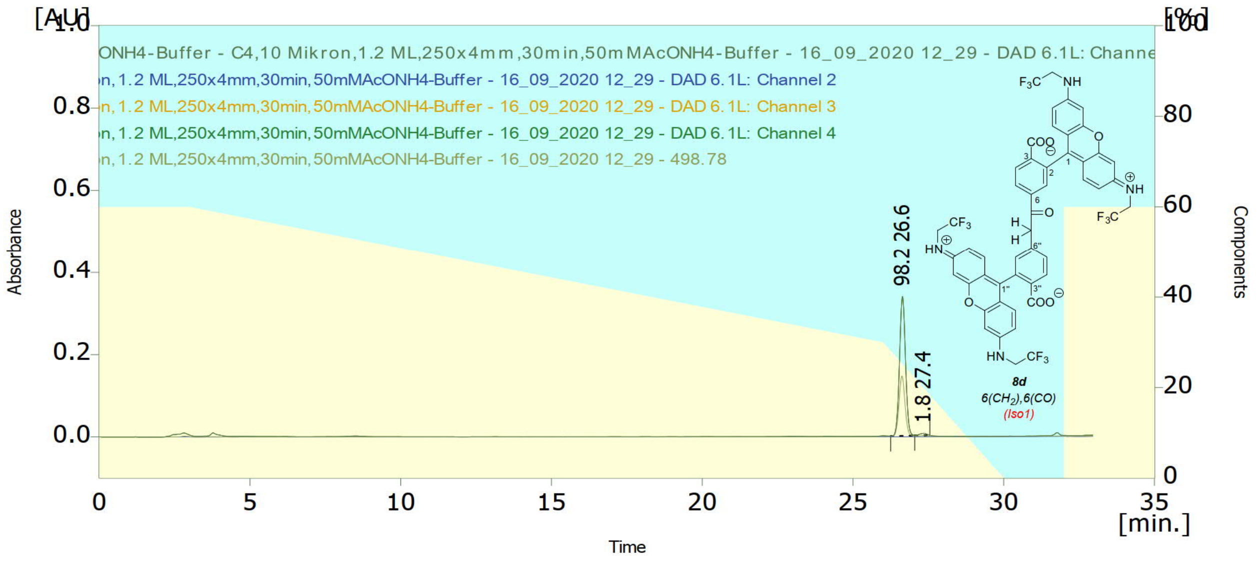
HPLC trace of the mixture of regioisomers

Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS479-31-Iso1234-ACN-H2O+50mM-AcONH4-Buff-40-60-70-30-254-630nm C4,10 Mikron,1.2 ML,250x4mm,30min,

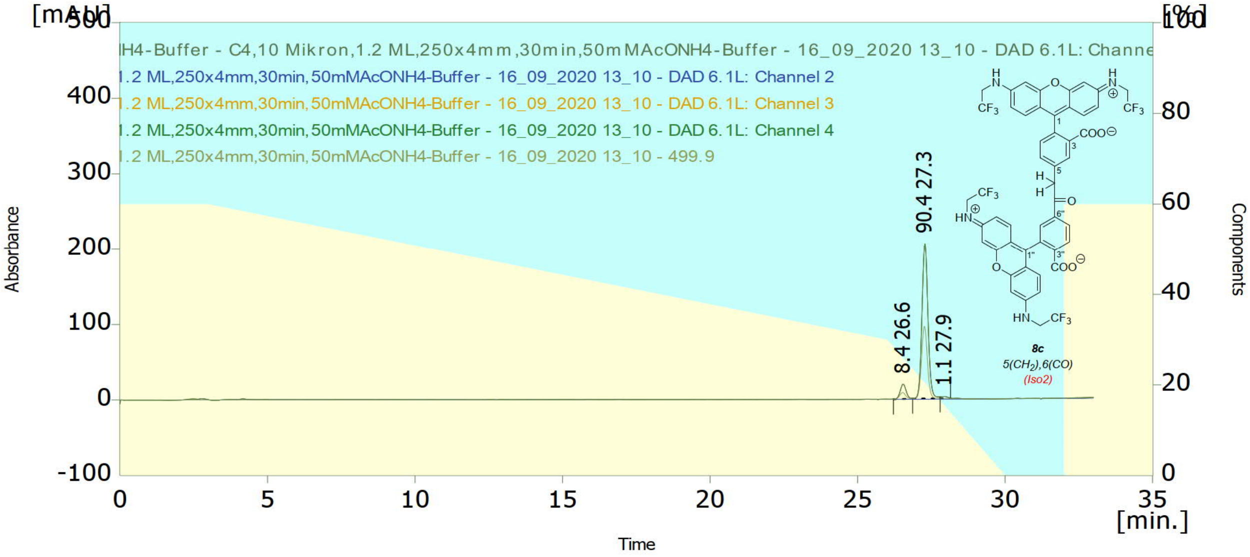


HPLC traces and NMR spectra of the isolated individual regioisomers **8a-d**

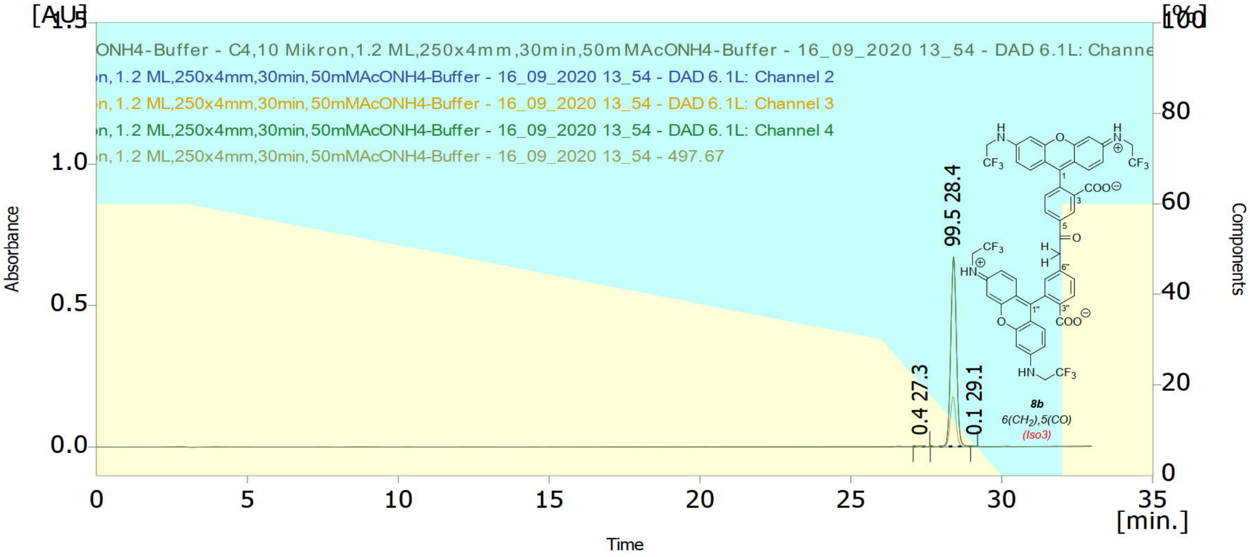
Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS479-31-Iso1-ACN-H2O+50mM-AcONH4-Buffer-40-60-70-30-254-630nm C4,10 Mikron,1.2 ML,250x4mm,30min,5



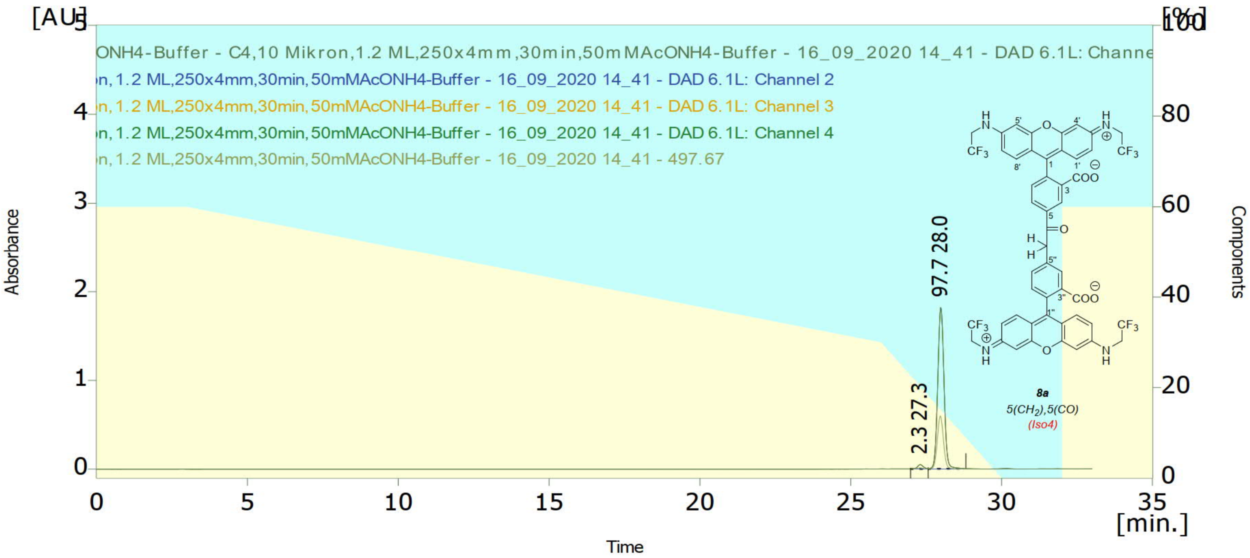
Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS479-31-Iso2-ACN-H2O+50mM-AcONH4-Buffer-40-60-70-30-254-630nm C4,10 Mikron,1.2 ML,250x4mm,30min,5



Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS479-31-Iso3-ACN-H2O+50mM-AcONH4-Buffer-40-60-70-30-254-630nm C4,10 Mikron,1.2 ML,250x4mm,30min,5

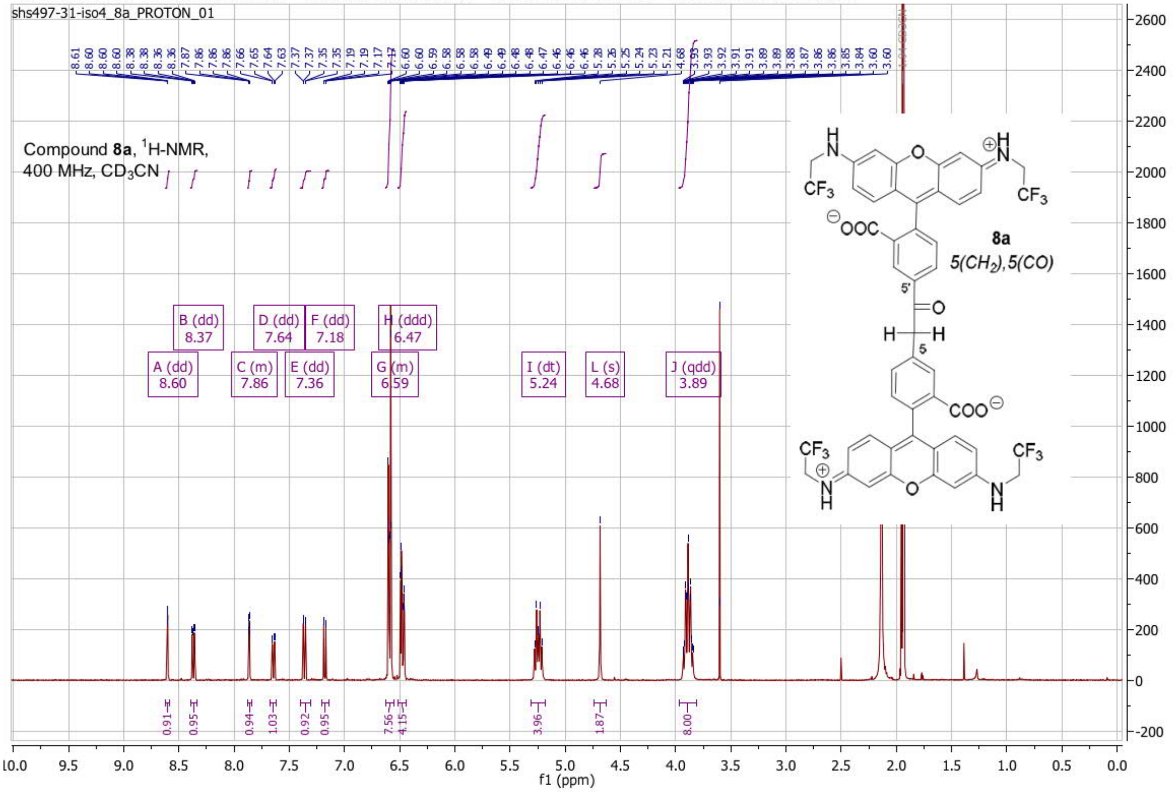


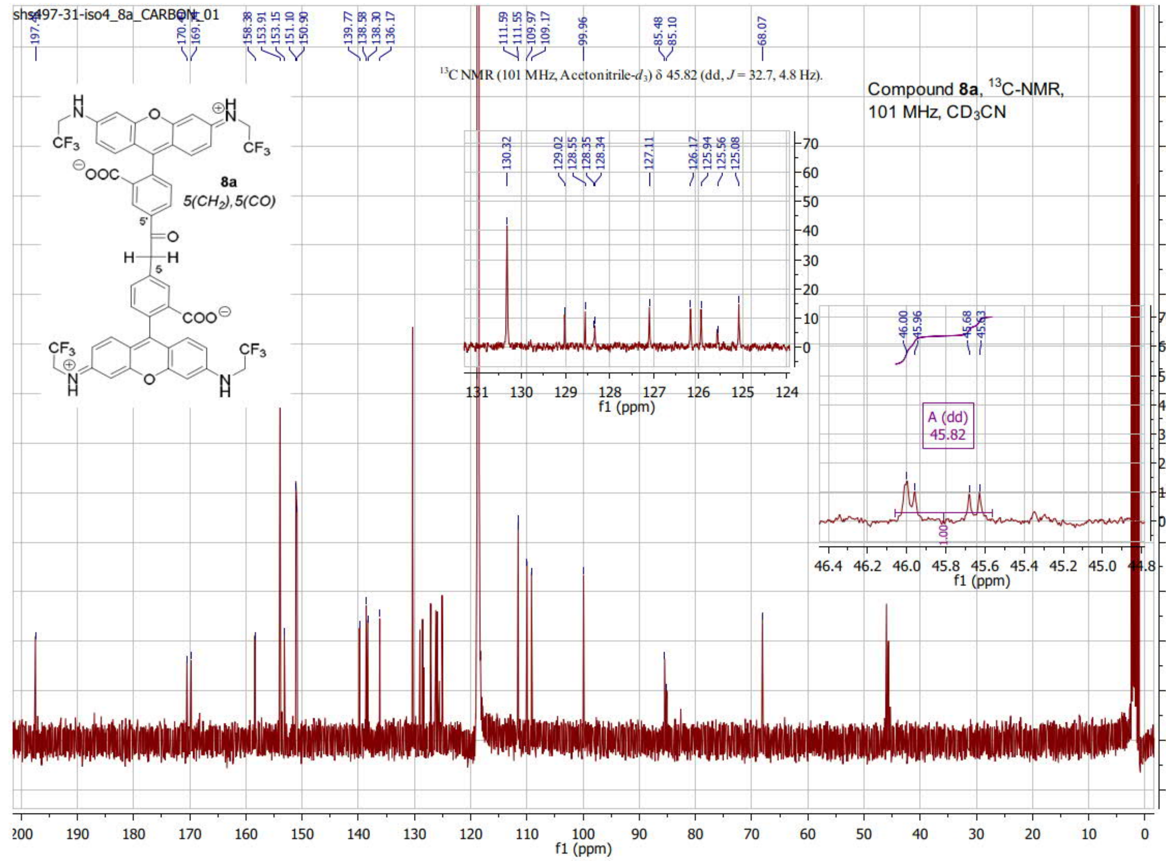
Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS479-31-Iso4-ACN-H2O+50mM-AcONH4-Buffer-40-60-70-30-254-630nm C4,10 Mikron,1.2 ML,250x4mm,30min,5



NMR spectra of compound **8a** [5(CH_2)-6(CO)]: ^{1}H (400 MHz) and ^{13}C{^{1}H} (101 MHz)

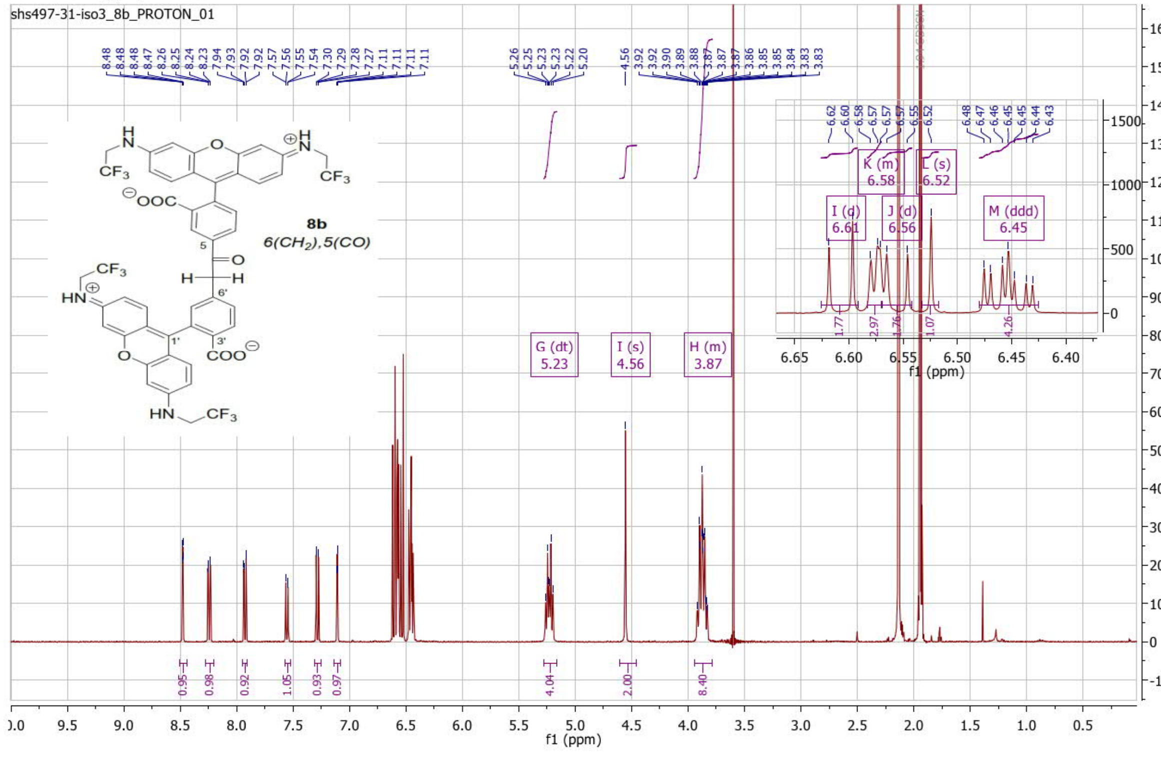
^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.60 (dd, J = 1.6, 0.7 Hz, 1H), 8.37 (dd, J = 8.1, 1.6 Hz, 1H), 7.87 – 7.84 (m, 1H), 7.64 (dd, J = 7.9, 1.6 Hz, 1H), 7.36 (dd, J = 8.0, 0.7 Hz, 1H), 7.18 (dd, J = 7.9, 0.7 Hz, 1H), 6.63 – 6.55 (m, 8H), 6.47 (ddd, J = 8.7, 3.2, 2.4 Hz, 4H), 5.24 (dt, J = 12.1, 7.0 Hz, 4H), 3.89 (qdd, J = 9.4, 7.0, 2.2 Hz, 8H), 4.68 (s, 2H).

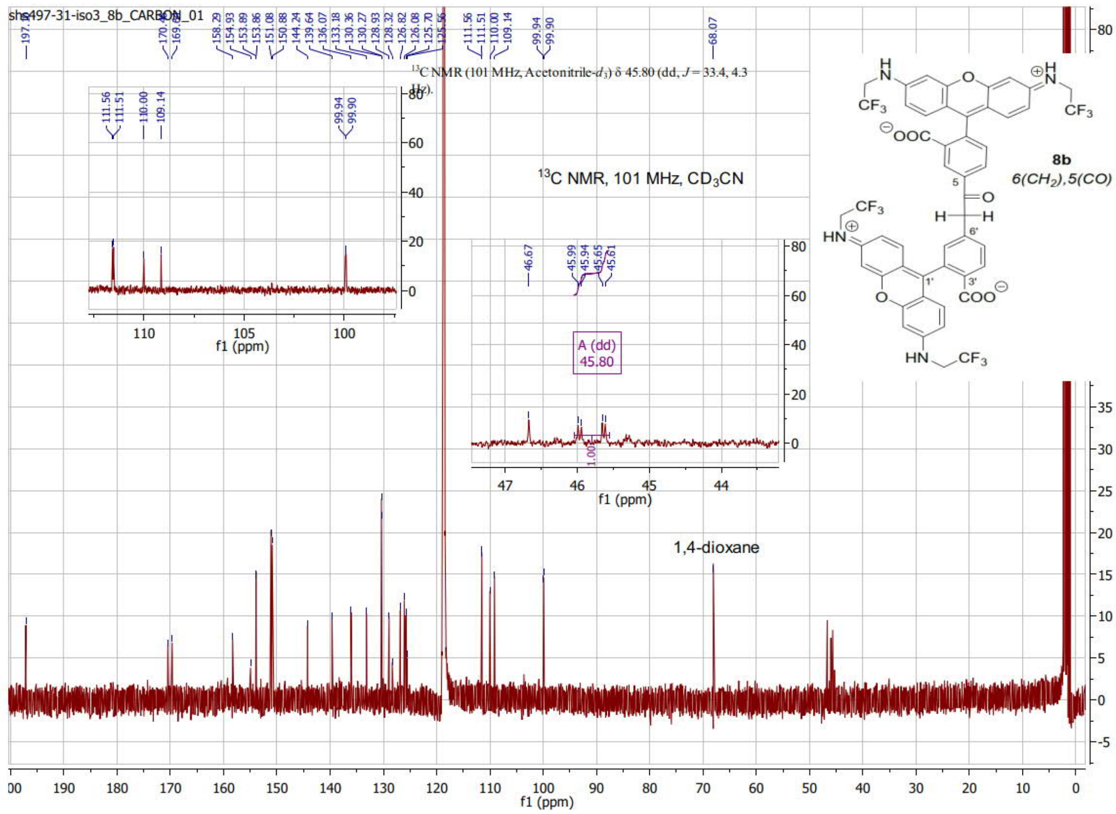




NMR spectra of compound **8b** [6(CH_2)-5(CO)]: ^{1}H (400 MHz) and ^{13}C{^{1}H} (101 MHz)

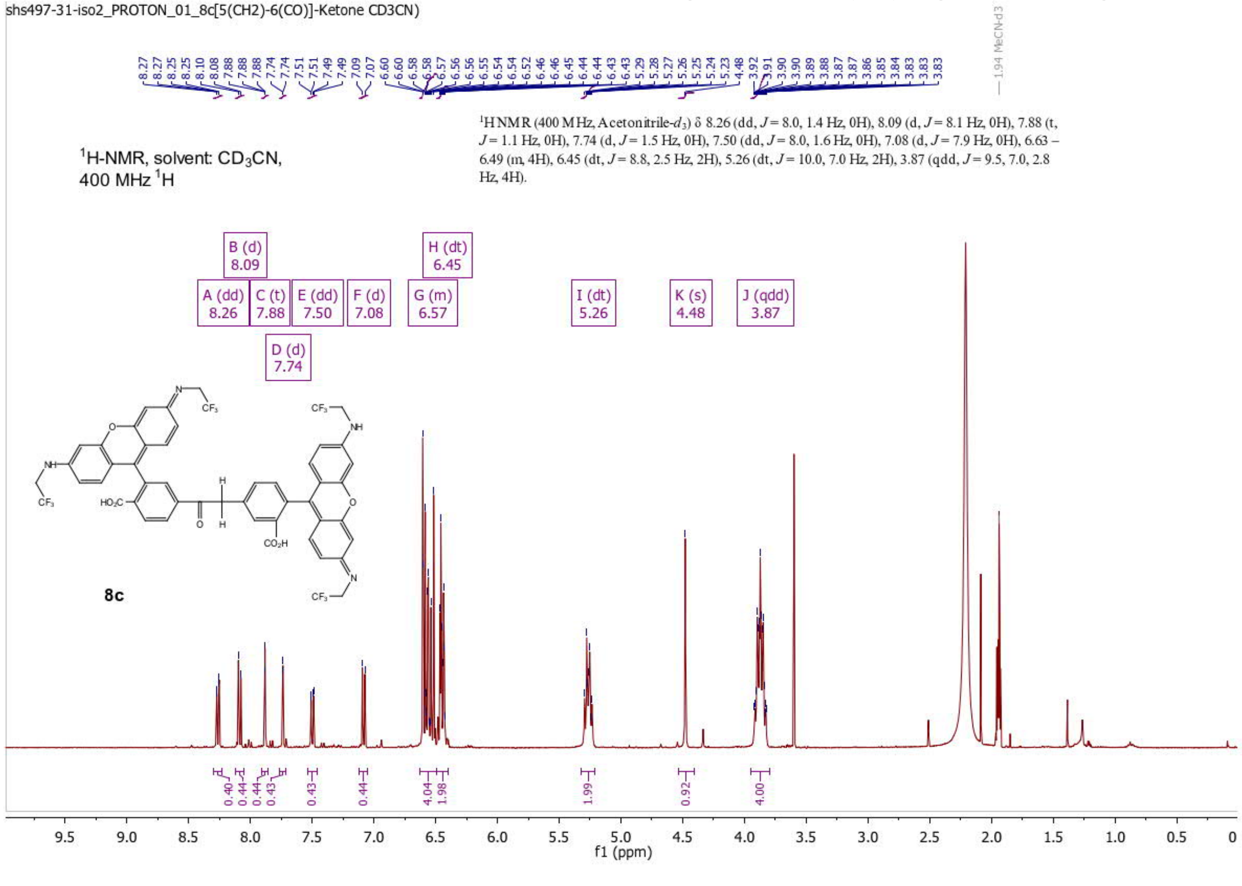
^{1}H NMR (400 MHz, CD_3CN) δ 8.48 (dd, *J* = 1.6, 0.8 Hz, 1H), 8.24 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.93 (dd, *J* = 7.9, 0.7 Hz, 1H), 7.56 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.28 (dd, *J* = 8.1, 0.7 Hz, 1H), 7.11 (dd, *J* = 1.4, 0.7 Hz, 1H), 6.61 (d, *J* = 8.7 Hz, 2H), 6.58 – 6.57 (m, 3H), 6.56 (d, *J* = 7.6 Hz, 2H), 6.52 (s, 1H), 6.45 (ddd, *J* = 8.9, 6.7, 2.4 Hz, 4H), 5.23 (dt, *J* = 11.7, 7.0 Hz, 4H), 3.95 – 3.79 (m, 8H) 4.56 (s, 2H).



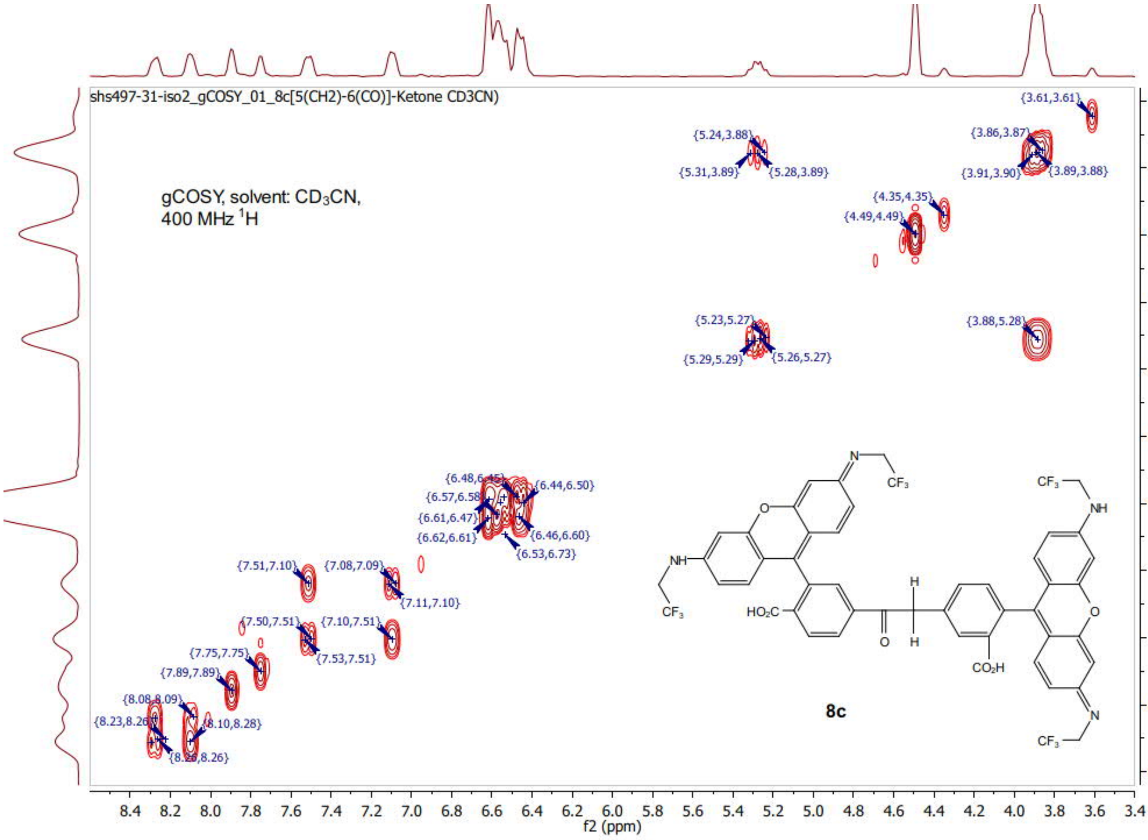


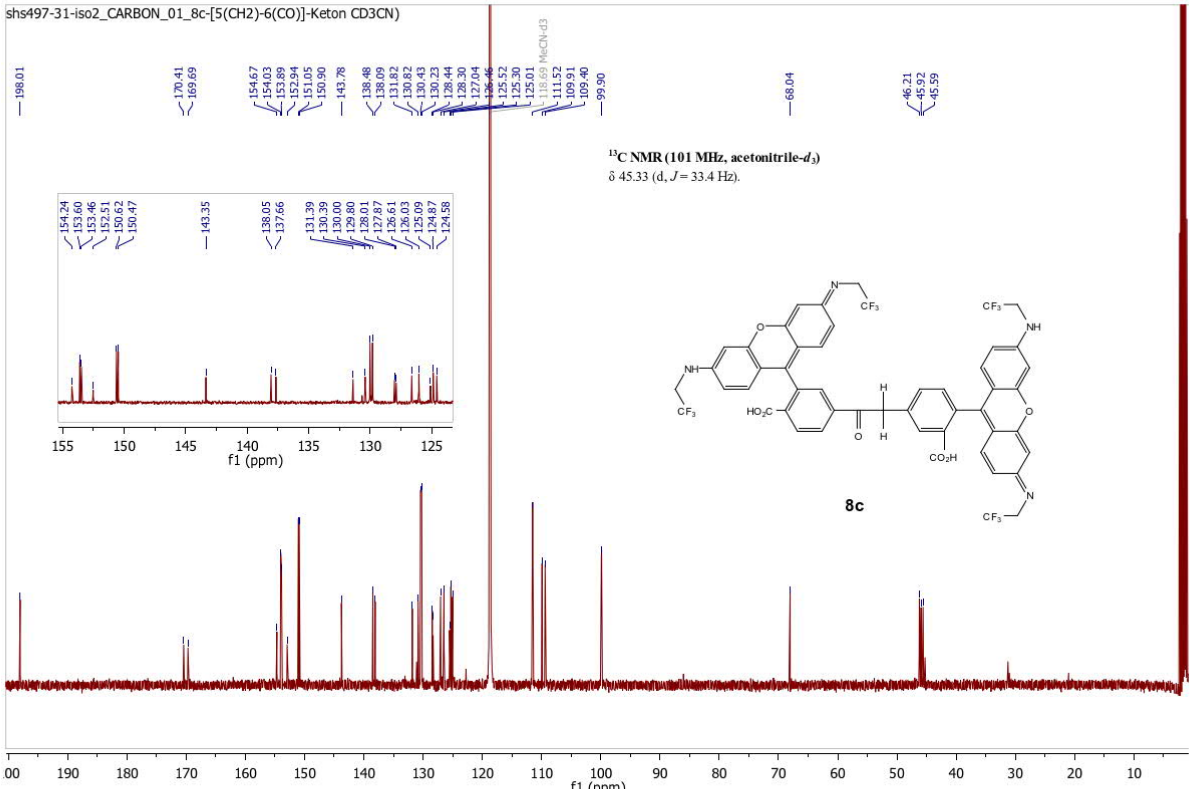
^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 45.80 (dd, J = 33.4, 4.3 Hz).

NMR spectra of compound **8c** [5(CH$_2$)-6(CO)]: ^{1}H-, gCOSY, ^{13}C{^{1}H}-, gHSQC and gHMBC.



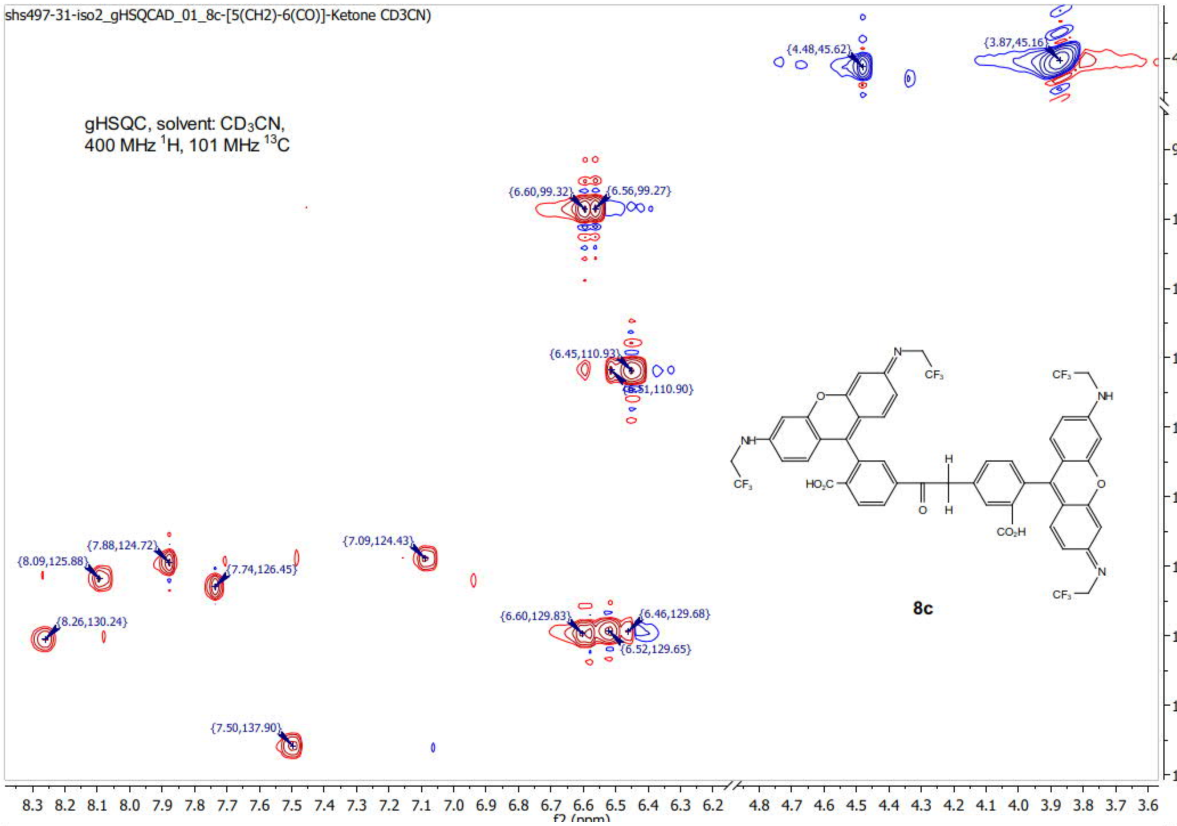
^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.26 (dd, J = 8.0, 1.4 Hz, 0H), 8.09 (d, J = 8.1 Hz, 0H), 7.88 (t, J = 1.1 Hz, 0H), 7.74 (d, J = 1.5 Hz, 0H), 7.50 (dd, J = 8.0, 1.6 Hz, 0H), 7.08 (d, J = 7.9 Hz, 0H), 6.63 – 6.49 (m, 4H), 6.45 (dt, J = 8.8, 2.5 Hz, 2H), 5.26 (dt, J = 10.0, 7.0 Hz, 2H), 3.87 (qdd, J = 9.5, 7.0, 2.8 Hz, 4H).

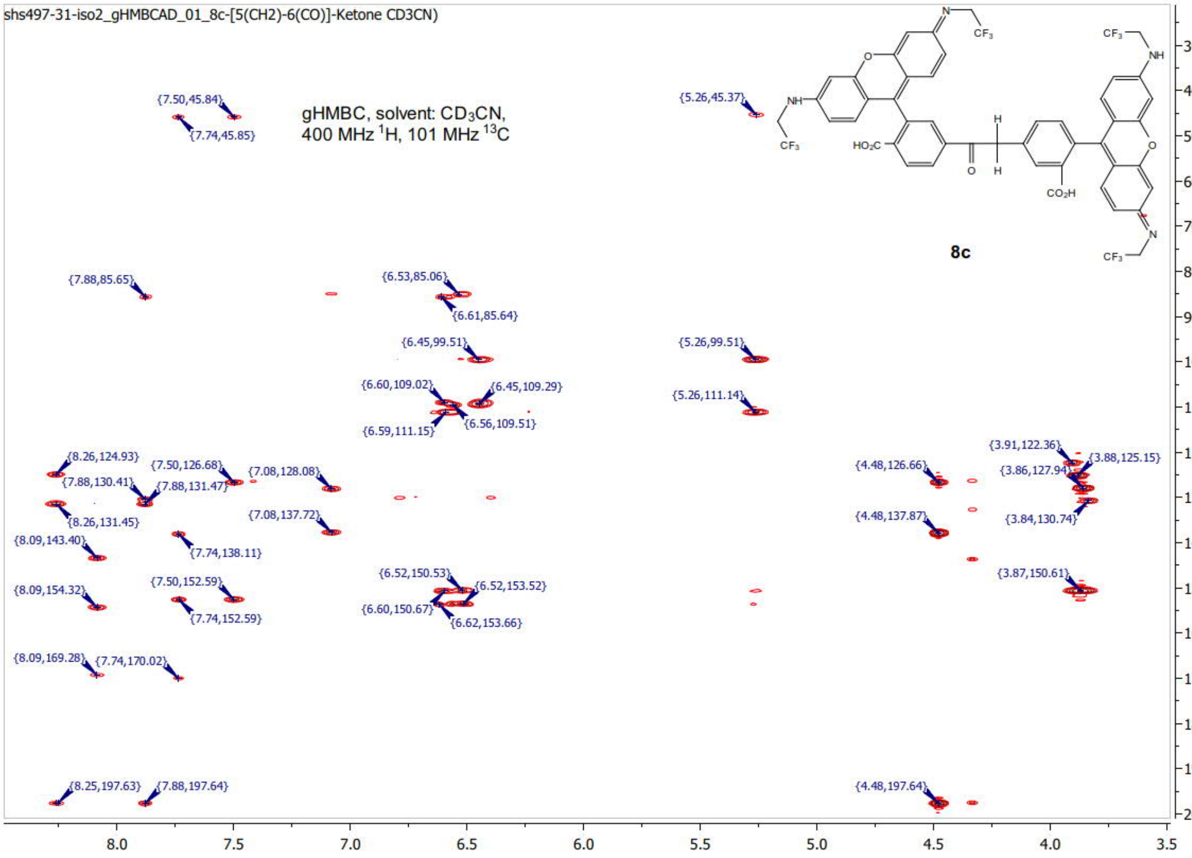


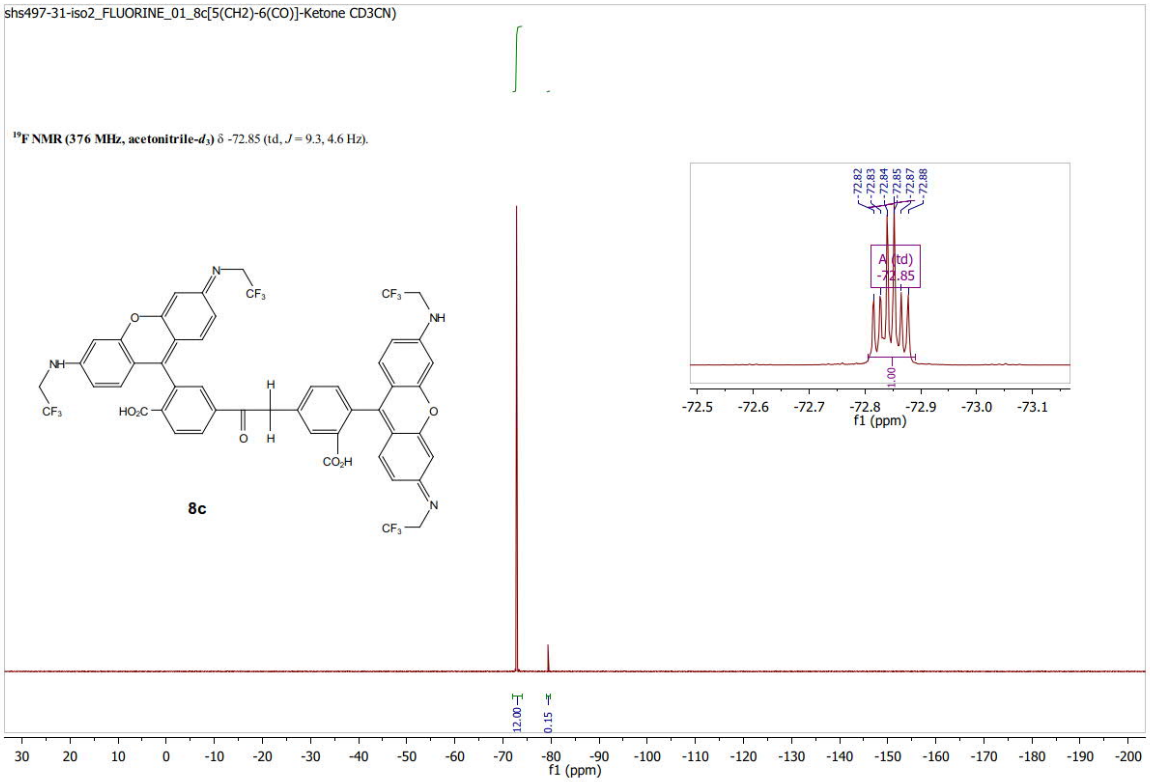


^{13}C NMR (101 MHz, acetonitrile-d_3)

δ 45.33 (d, J = 33.4 Hz).


shs497-31-iso2_gHSQCAD_01_8c-[5(CH2)-6(CO)]-Ketone CD3CN)
gHSQC, solvent: CD3CN, 400 MHz 1H, 101 MHz 13C
{4.48,45.62}
{3.87,45.16}
{6.60,99.32}
{6.56,99.27}
{6.45,110.93}
{6.51,110.90}
{7.88,124.72}
{8.09,125.88}
{7.74,126.45}
{7.09,124.43}
{8.26,130.24}
{6.60,129.83}
{6.46,129.68}
{6.52,129.65}
{7.50,137.90}
8c
f2 (ppm)

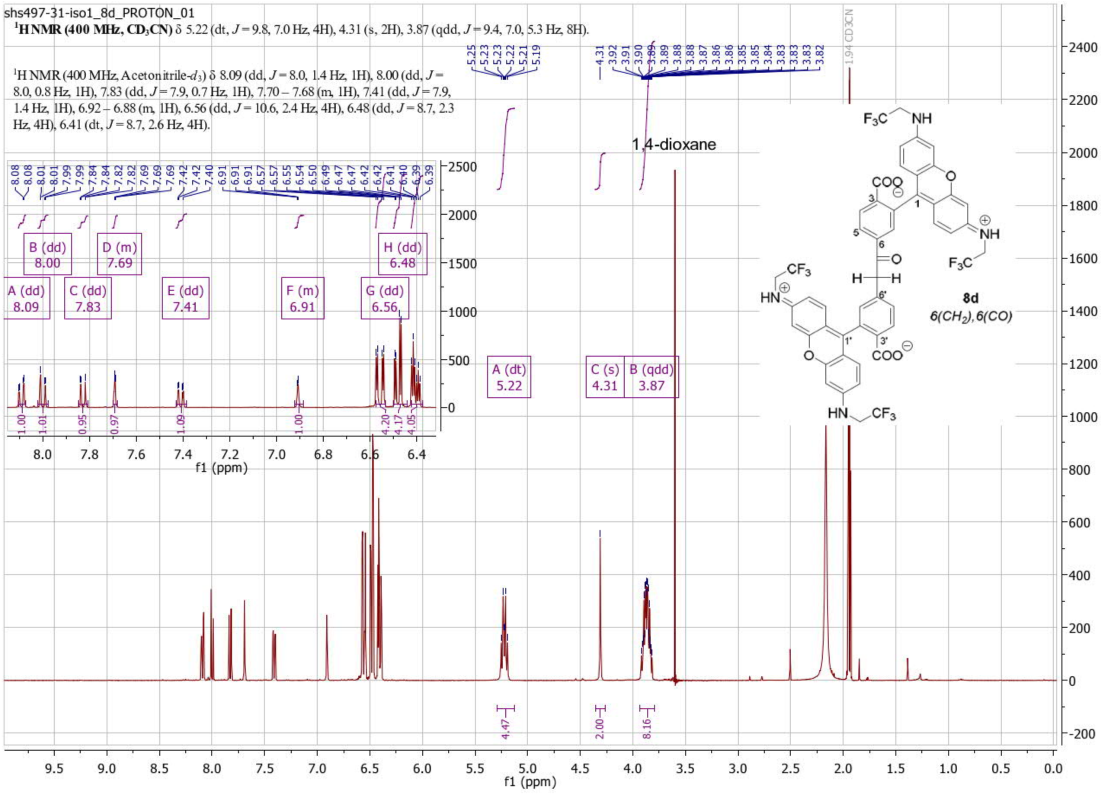

shs497-31-iso2_gHMBCAD_01_8c-[5(CH2)-6(CO)]-Ketone CD3CN)
gHMBC, solvent: CD3CN, 400 MHz 1H, 101 MHz 13C
{7.50,45.84}
{7.74,45.85}
{5.26,45.37}
8c
{7.88,85.65}
{6.53,85.06}
{6.61,85.64}
{6.45,99.51}
{5.26,99.51}
{6.60,109.02}
{6.45,109.29}
{6.59,111.15}
{6.56,109.51}
{5.26,111.14}
{8.26,124.93}
{7.50,126.68}
{7.88,130.41}
{7.88,131.47}
{7.08,128.08}
{8.26,131.45}
{7.08,137.72}
{8.09,143.40}
{7.74,138.11}
{8.09,154.32}
{7.50,152.59}
{7.74,152.59}
{6.52,150.53}
{6.52,153.52}
{6.60,150.67}
{6.62,153.66}
{8.09,169.28}
{7.74,170.02}
{8.25,197.63}
{7.88,197.64}
{4.48,126.66}
{4.48,137.87}
{4.48,197.64}
{3.91,122.36}
{3.88,125.15}
{3.86,127.94}
{3.84,130.74}
{3.87,150.61}


shs497-31-iso2_FLUORINE_01_8c[5(CH2)-6(CO)]-Ketone CD3CN)

^{19}F NMR (376 MHz, acetonitrile-d_3) δ -72.85 (td, J = 9.3, 4.6 Hz).

8c

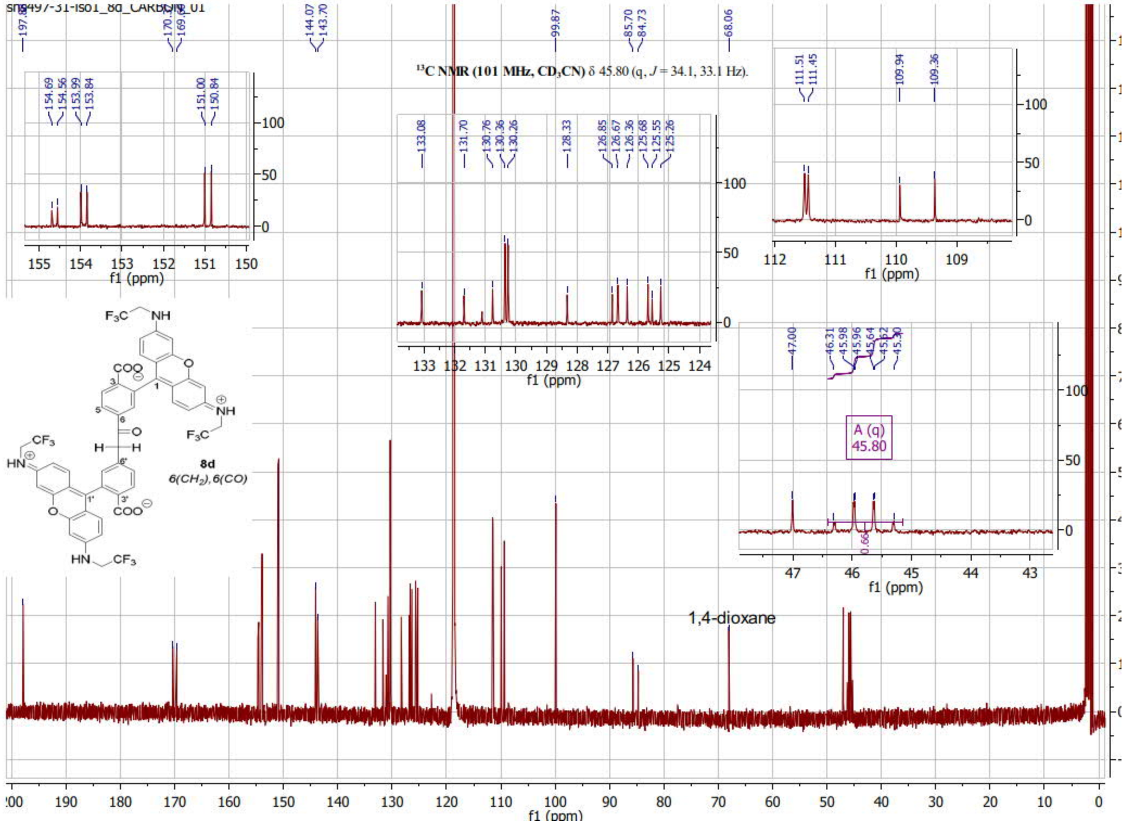
NMR spectra of compound **8d** [6(CH$_2$)-6(CO)]: ^{1}H (400 MHz) and ^{13}C{^{1}H} (101 MHz)


shs497-31-iso1_8d_PROTON_01

^{1}H NMR (400 MHz, CD$_3$CN) δ 5.22 (dt, J = 9.8, 7.0 Hz, 4H), 4.31 (s, 2H), 3.87 (qdd, J = 9.4, 7.0, 5.3 Hz, 8H).

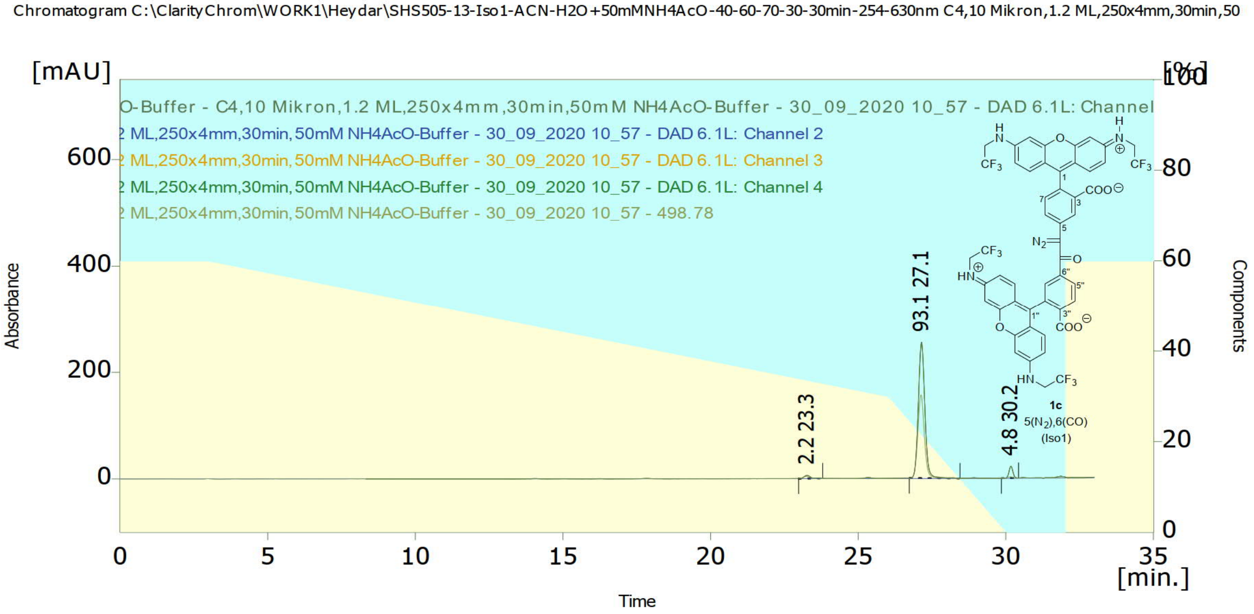
^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.09 (dd, J = 8.0, 1.4 Hz, 1H), 8.00 (dd, J = 8.0, 0.8 Hz, 1H), 7.83 (dd, J = 7.9, 0.7 Hz, 1H), 7.70 – 7.68 (m, 1H), 7.41 (dd, J = 7.9, 1.4 Hz, 1H), 6.92 – 6.88 (m, 1H), 6.56 (dd, J = 10.6, 2.4 Hz, 4H), 6.48 (dd, J = 8.7, 2.3 Hz, 4H), 6.41 (dt, J = 8.7, 2.6 Hz, 4H).

8d
6(CH$_2$),6(CO)



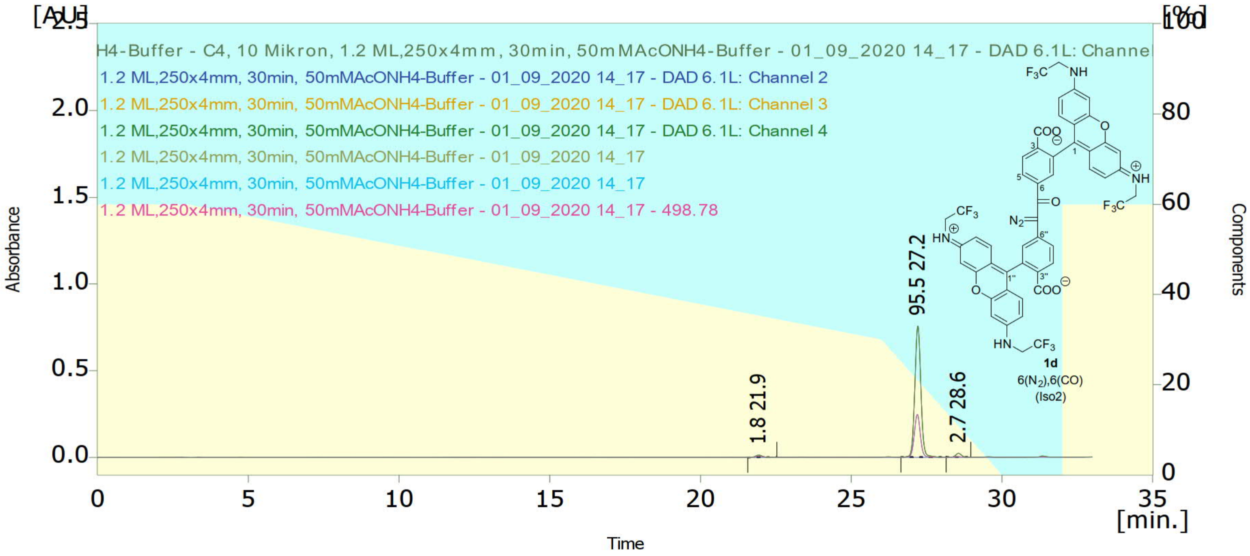
Bis-rhodamine diazoketones **1a** [5(N$_2$),5(CO)] (isomer 4), **1b** [6(N$_2$),5(CO)] (isomer 3), **1c** [5(N$_2$),6(CO)] (isomer 1) and **1d** [6(N$_2$),6(CO)] (isomer 2)

HPLC trace, isomer 1, **1c** [5(N$_2$),6(CO)]



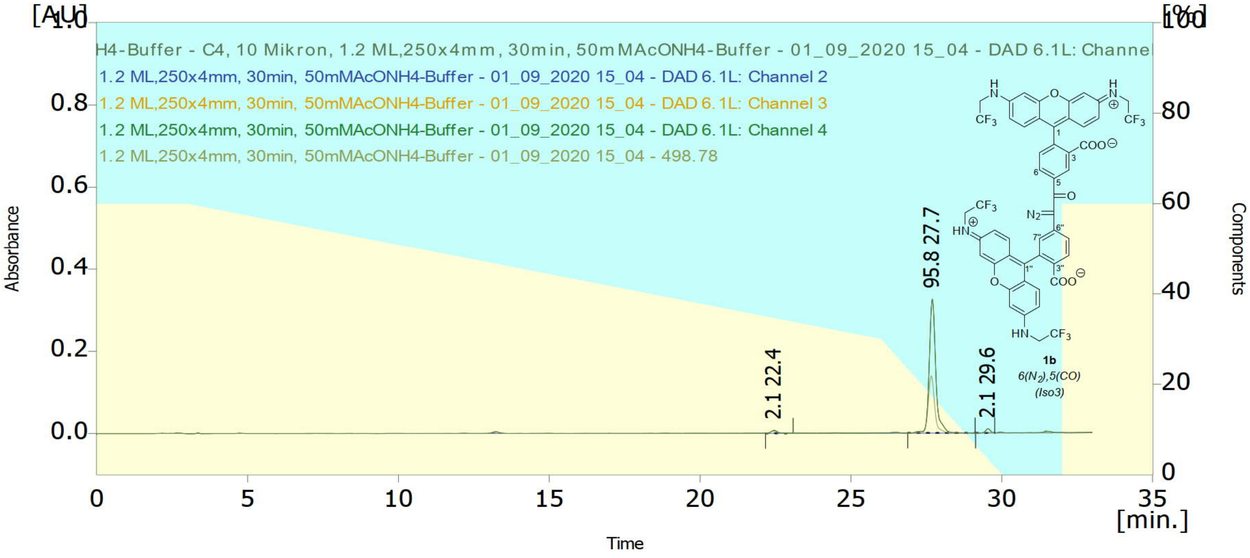
HPLC trace, isomer 2, **1d** [6(N_2),6(CO)]

Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS505-11-Iso2-ACN-ACN-H2O+50mM-AcONH4-Buf-40-60-70-30-254-630nm C4, 10 Mikron, 1.2 ML,250x4mm, 30



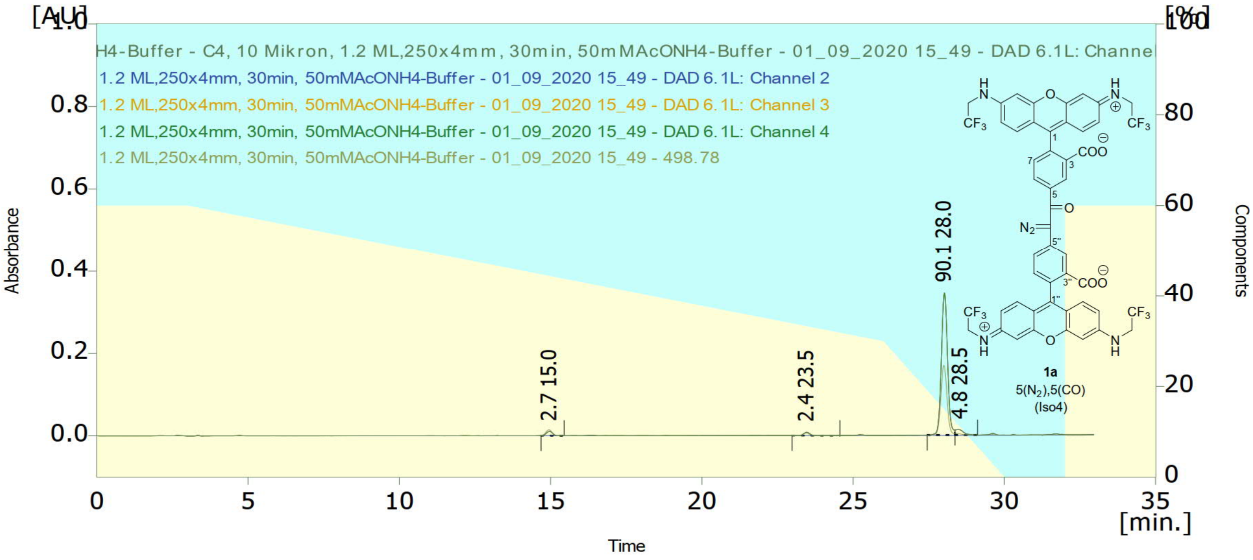
HPLC trace, isomer 3, **1b** [6(N_2),5(CO)]

Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS505-11-Iso3-ACN-ACN-H2O+50mM-AcONH4-Buf-40-60-70-30-254-630nm C4, 10 Mikron, 1.2 ML,250x4mm, 30

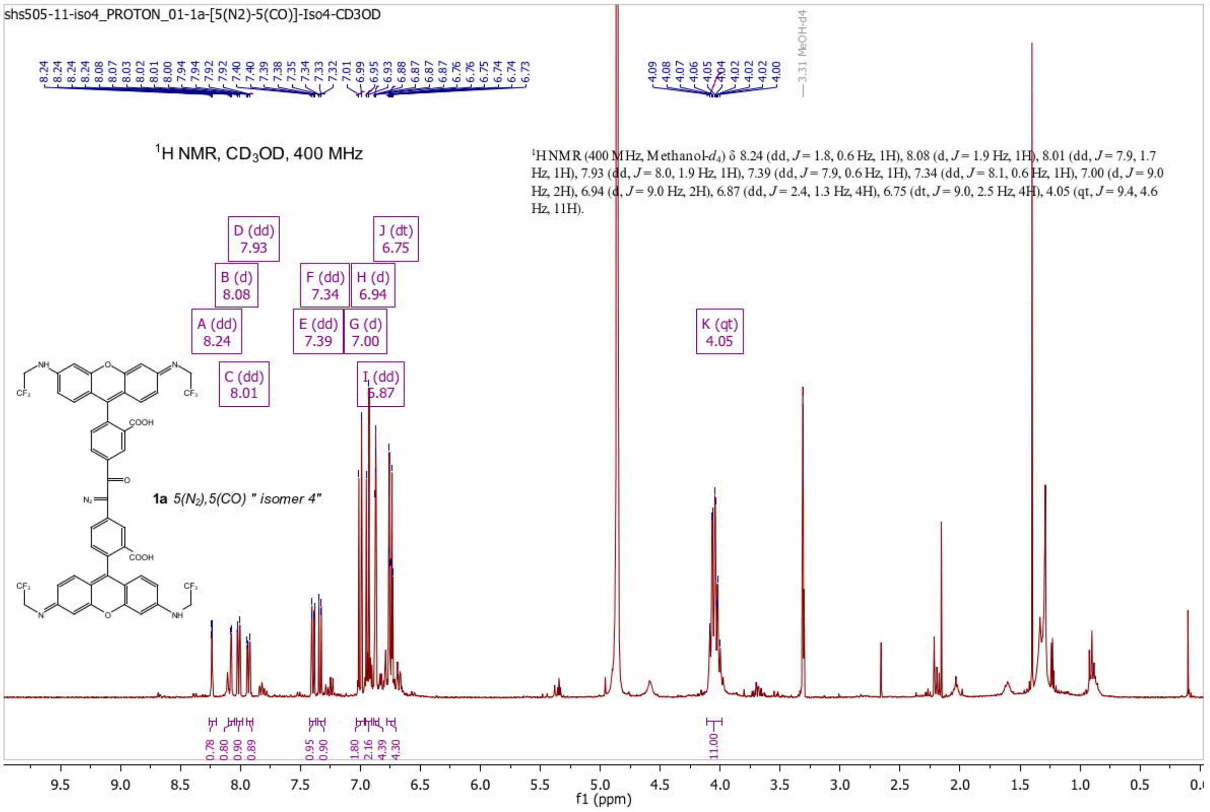


HPLC trace, isomer 4, **1a** [5(N_2),5(CO)]

Chromatogram C:\ClarityChrom\WORK1\Heydar\SHS505-11-Iso4-ACN-ACN-H2O+50mM-AcONH4-Buf-40-60-70-30-254-630nm C4, 10 Mikron, 1.2 ML,250x4mm, 30

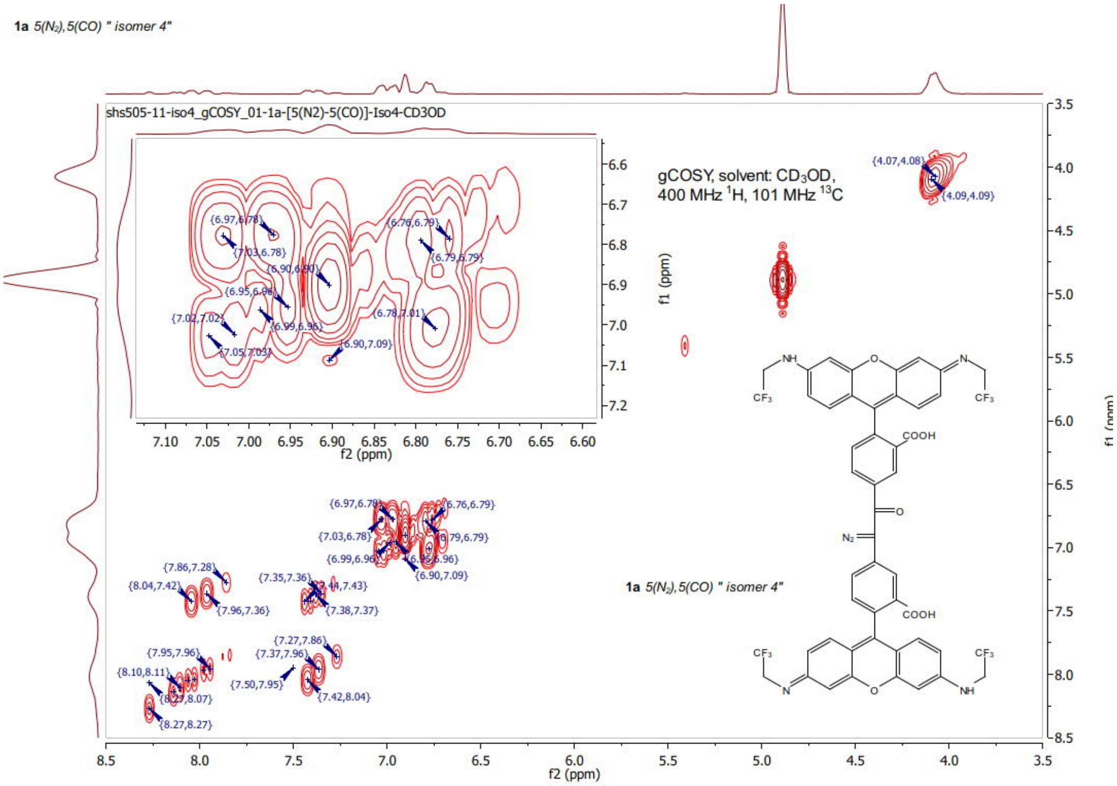


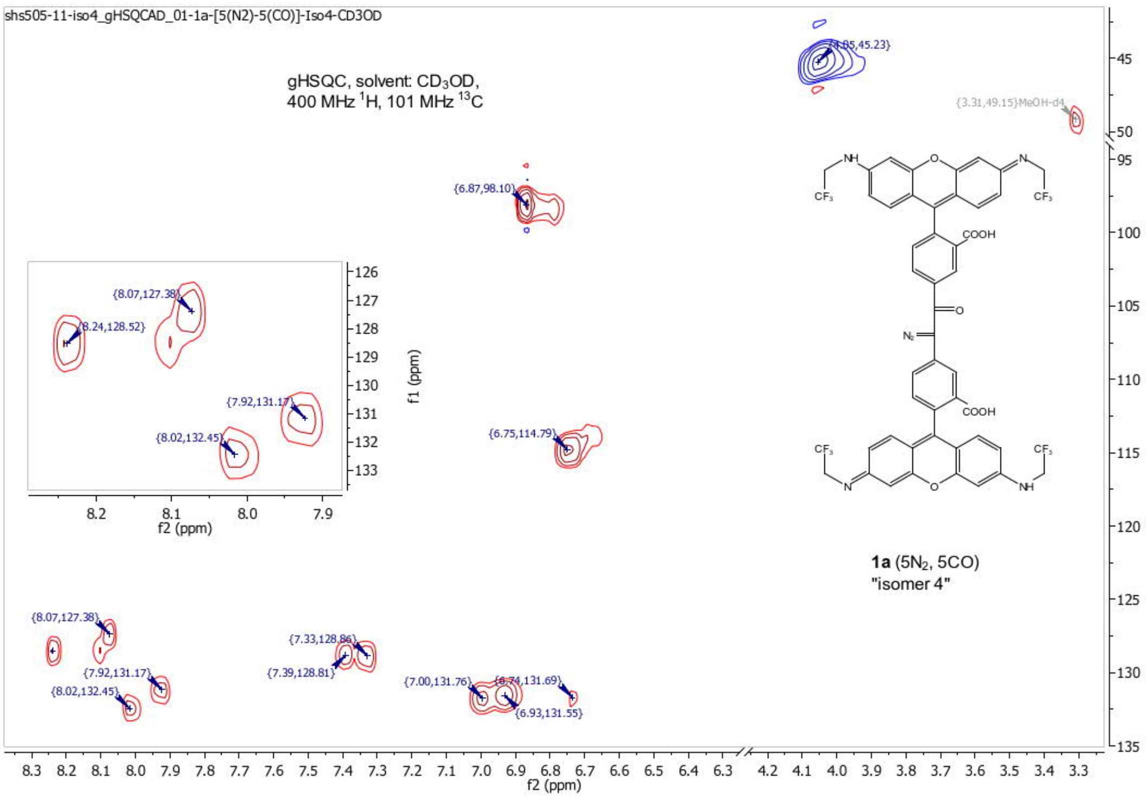
NMR spectra of compound **1a** [5(N_2), 5(CO)] (isomer 4)

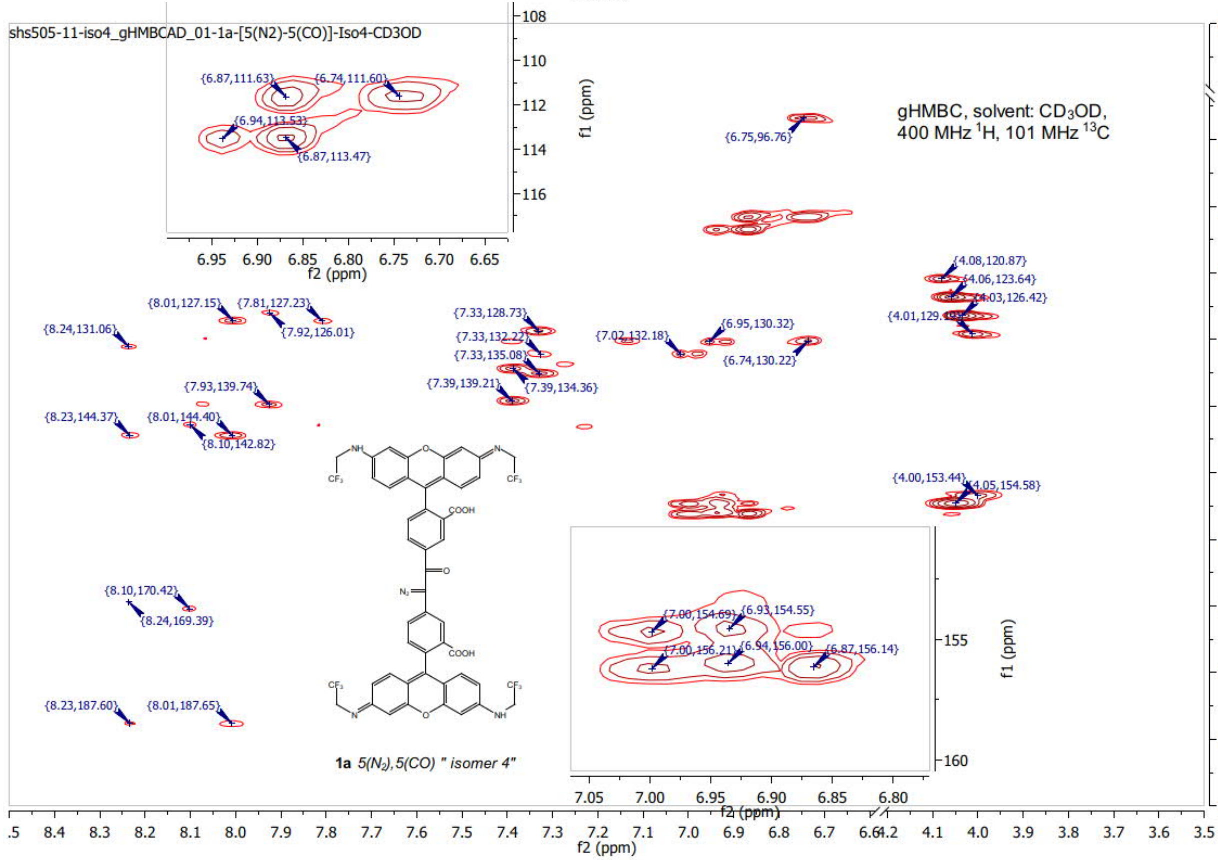


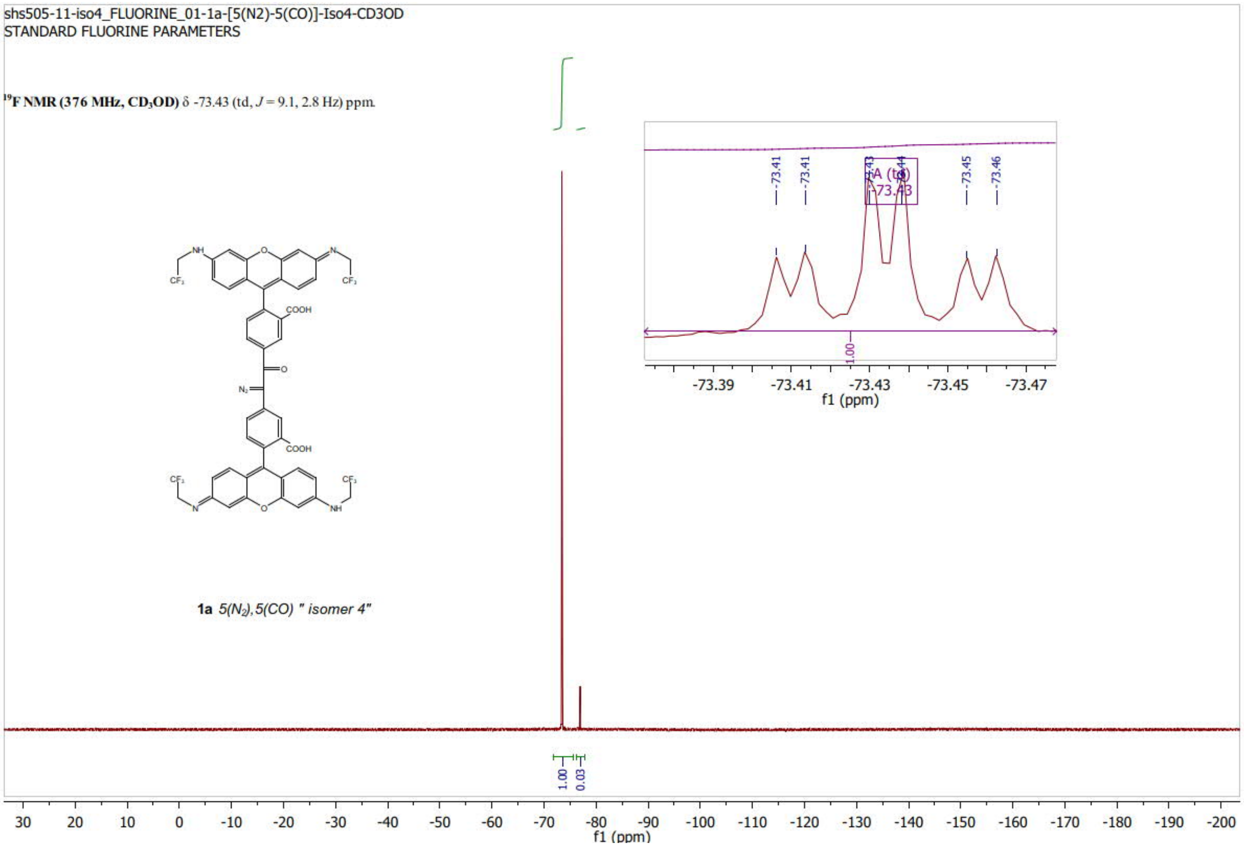
^{1}H NMR (400 MHz, Methanol-d_4) δ 8.24 (dd, J = 1.8, 0.6 Hz, 1H), 8.08 (d, J = 1.9 Hz, 1H), 8.01 (dd, J = 7.9, 1.7 Hz, 1H), 7.93 (dd, J = 8.0, 1.9 Hz, 1H), 7.39 (dd, J = 7.9, 0.6 Hz, 1H), 7.34 (dd, J = 8.1, 0.6 Hz, 1H), 7.00 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 6.87 (dd, J = 2.4, 1.3 Hz, 4H), 6.75 (dt, J = 9.0, 2.5 Hz, 4H), 4.05 (qt, J = 9.4, 4.6 Hz, 11H).

1a *5(N_2),5(CO) " isomer 4"*




shs505-11-iso4_gHSQCAD_01-1a-[5(N2)-5(CO)]-Iso4-CD3OD
gHSQC, solvent: CD3OD,
400 MHz 1H, 101 MHz 13C
1a (5N2, 5CO)
"isomer 4"
{4.05,45.23}
{3.31,49.15}MeOH-d4
{6.87,98.10}
{6.75,114.79}
{8.07,127.38}
{8.24,128.52}
{7.92,131.17}
{8.02,132.45}
{7.33,128.86}
{7.39,128.81}
{7.00,131.76}
{6.74,131.69}
{6.93,131.55}
COOH
N2
CF3
NH
N
O
f1 (ppm)
f2 (ppm)


shs505-11-iso4_gHMBCAD_01-1a-[5(N2)-5(CO)]-Iso4-CD3OD
gHMBC, solvent: CD3OD,
400 MHz 1H, 101 MHz 13C
1a 5(N2),5(CO) " isomer 4"
{6.87,111.63}
{6.74,111.60}
{6.94,113.53}
{6.87,113.47}
{6.75,96.76}
{4.08,120.87}
{4.06,123.64}
{4.03,126.42}
{4.01,129.40}
{8.01,127.15}
{7.81,127.23}
{7.92,126.01}
{8.24,131.06}
{7.33,128.73}
{7.33,132.22}
{7.33,135.08}
{7.39,139.21}
{7.39,134.36}
{7.02,132.18}
{6.95,130.32}
{6.74,130.22}
{7.93,139.74}
{8.23,144.37}
{8.01,144.40}
{8.10,142.82}
{4.00,153.44}
{4.05,154.58}
{7.00,154.69}
{6.93,154.55}
{7.00,156.21}
{6.94,156.00}
{6.87,156.14}
{8.10,170.42}
{8.24,169.39}
{8.23,187.60}
{8.01,187.65}
f1 (ppm)
f2 (ppm)

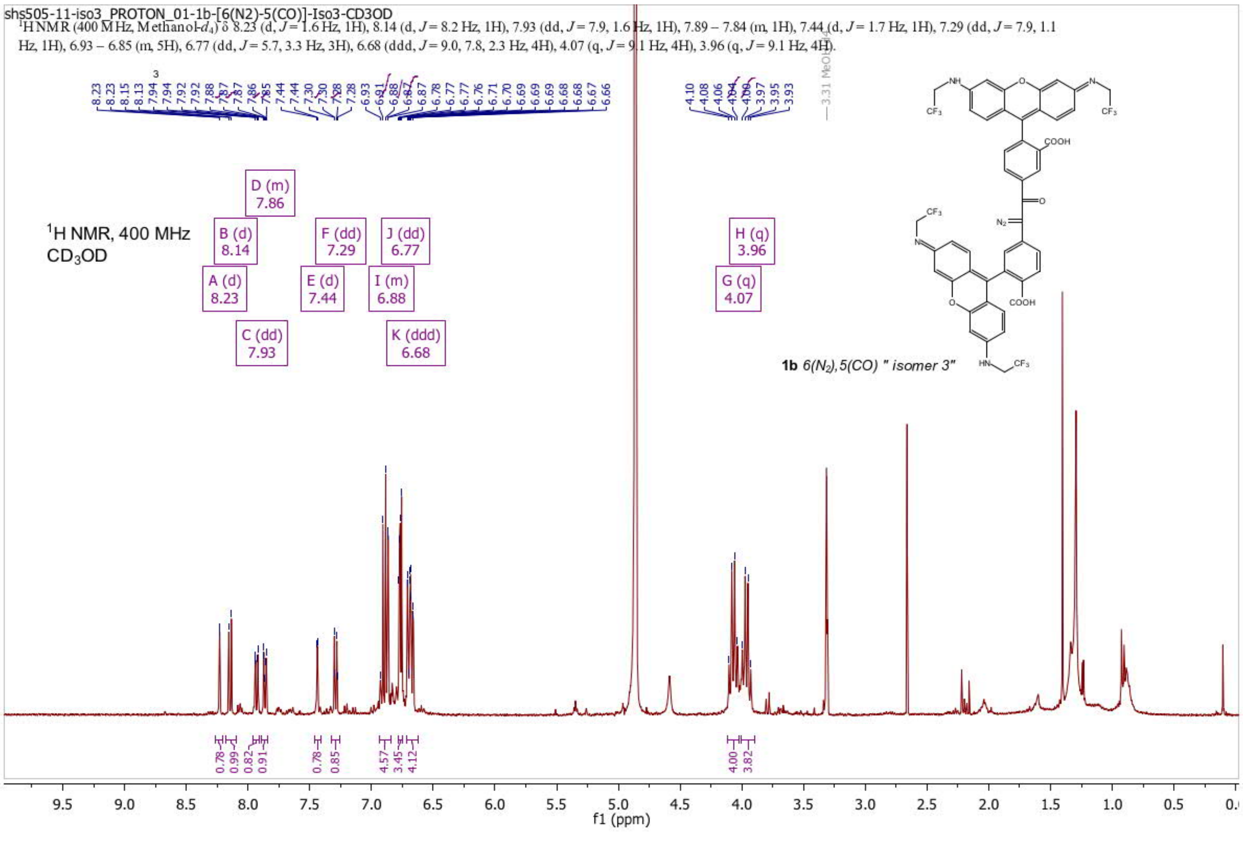


shs505-11-iso4_FLUORINE_01-1a-[5(N2)-5(CO)]-Iso4-CD3OD
STANDARD FLUORINE PARAMETERS

^{19}F NMR (376 MHz, CD_3OD) δ -73.43 (td, *J* = 9.1, 2.8 Hz) ppm.

1a *5(N_2),5(CO) " isomer 4"*

NMR spectra of compound **1b** [6(N_2),5(CO)] (isomer 3)

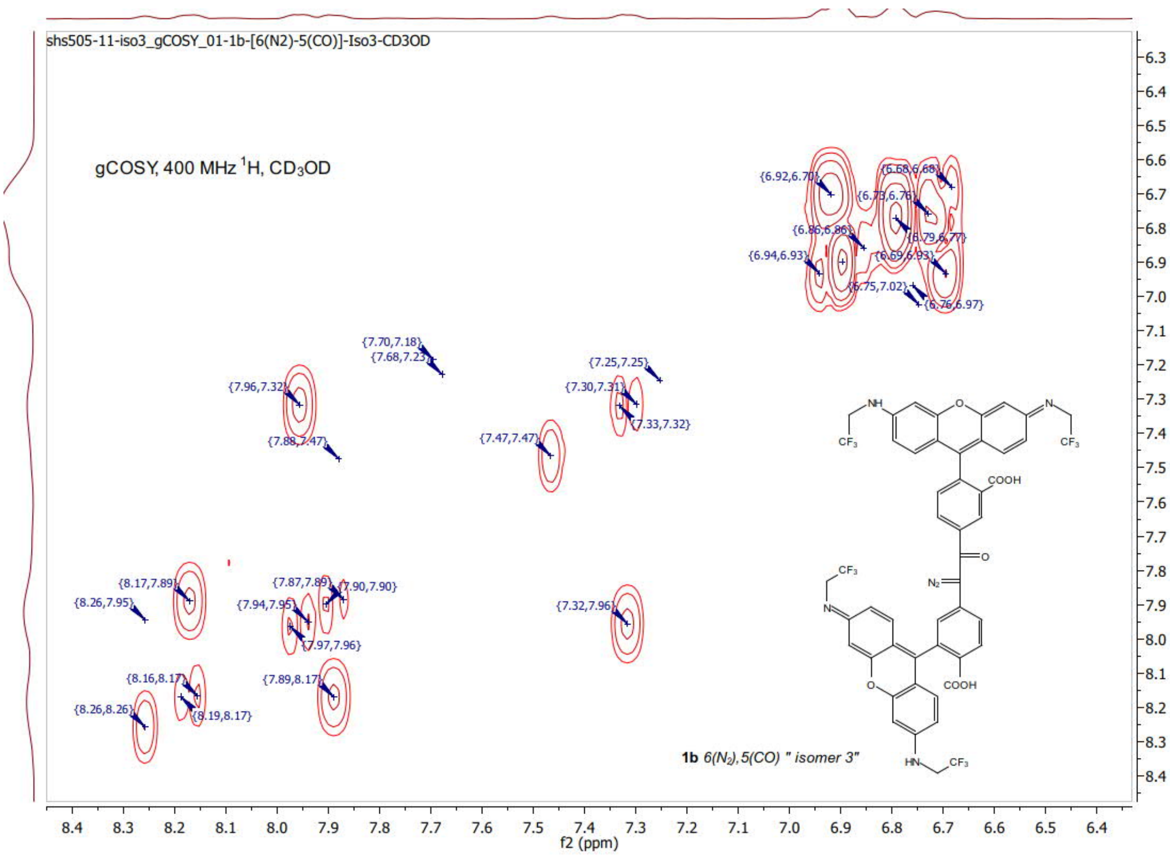


shs505-11-iso3_PROTON_01-1b-[6(N2)-5(CO)]-Iso3-CD3OD

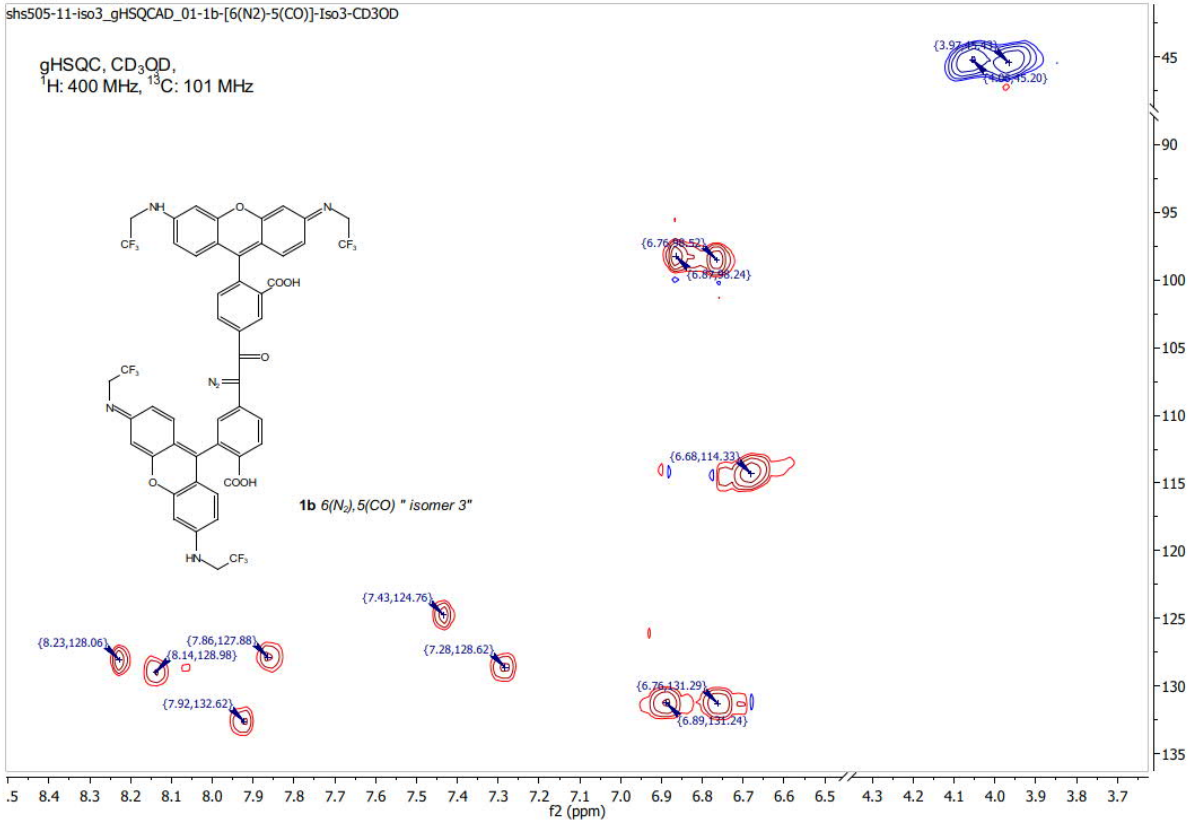
^1H NMR (400 MHz, Methanol-d_4) δ 8.23 (d, *J* = 1.6 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.93 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.44 (d, *J* = 1.7 Hz, 1H), 7.29 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.93 – 6.85 (m, 5H), 6.77 (dd, *J* = 5.7, 3.3 Hz, 3H), 6.68 (ddd, *J* = 9.0, 7.8, 2.3 Hz, 4H), 4.07 (q, *J* = 9.1 Hz, 4H), 3.96 (q, *J* = 9.1 Hz, 4H).

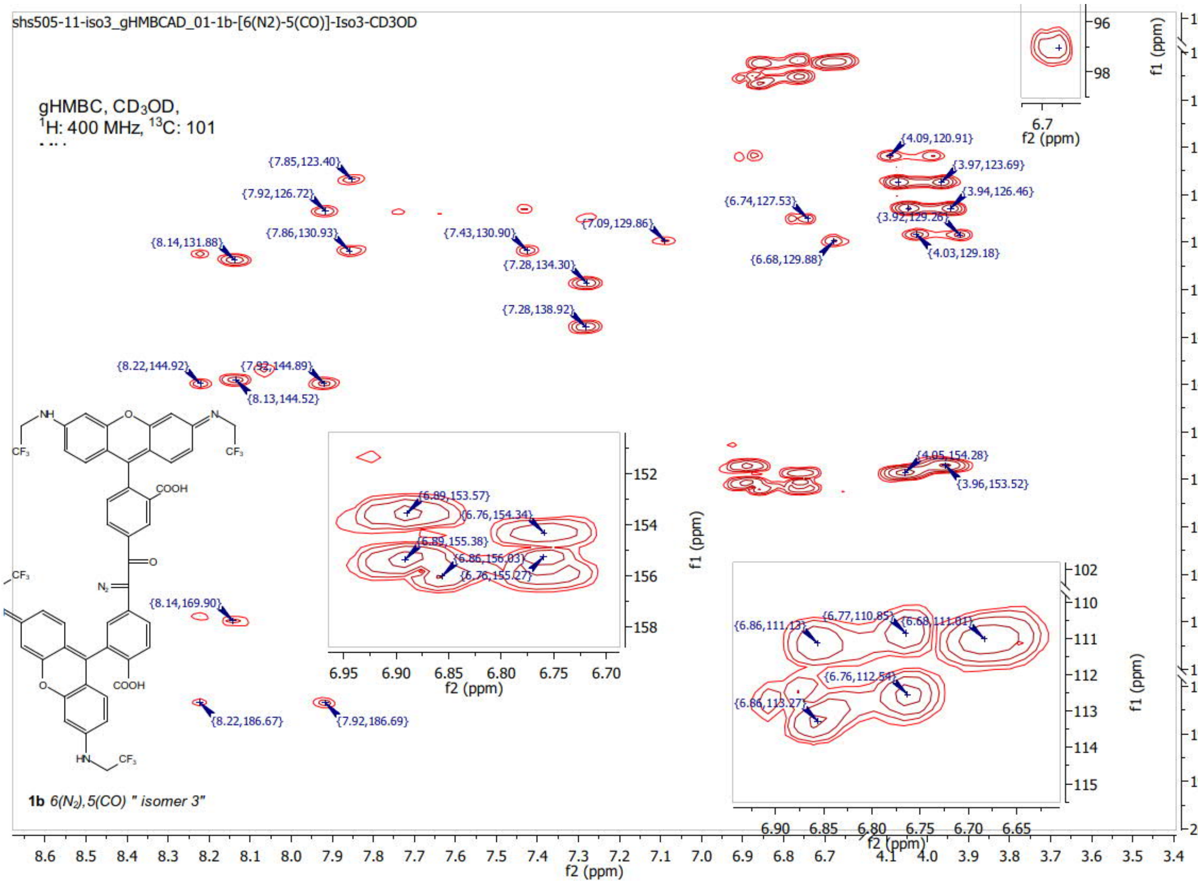
^1H NMR, 400 MHz
CD_3OD

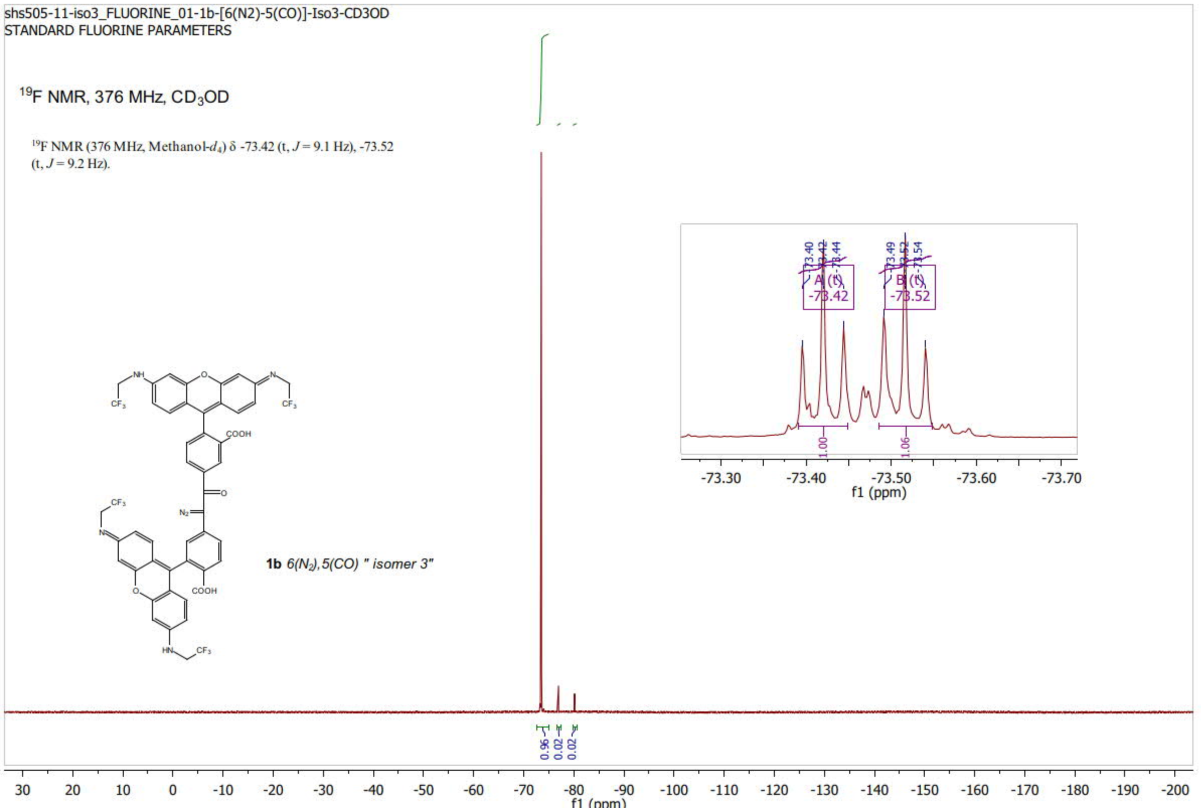
1b *6(N_2),5(CO) " isomer 3"*



^{1}H-^{13}C NMR ((400, 101) MHz, cd$_3$od) δ (8.26 126.72), (8.17 127.60), (7.95 131.24), (7.89 126.44), (7.46 123.38), (7.31 127.24), (6.92 129.86), (6.90 96.86), (6.79 97.13), (6.79 129.91), (6.71 112.85), (4.09 43.82), (4.00 44.05) ppm.

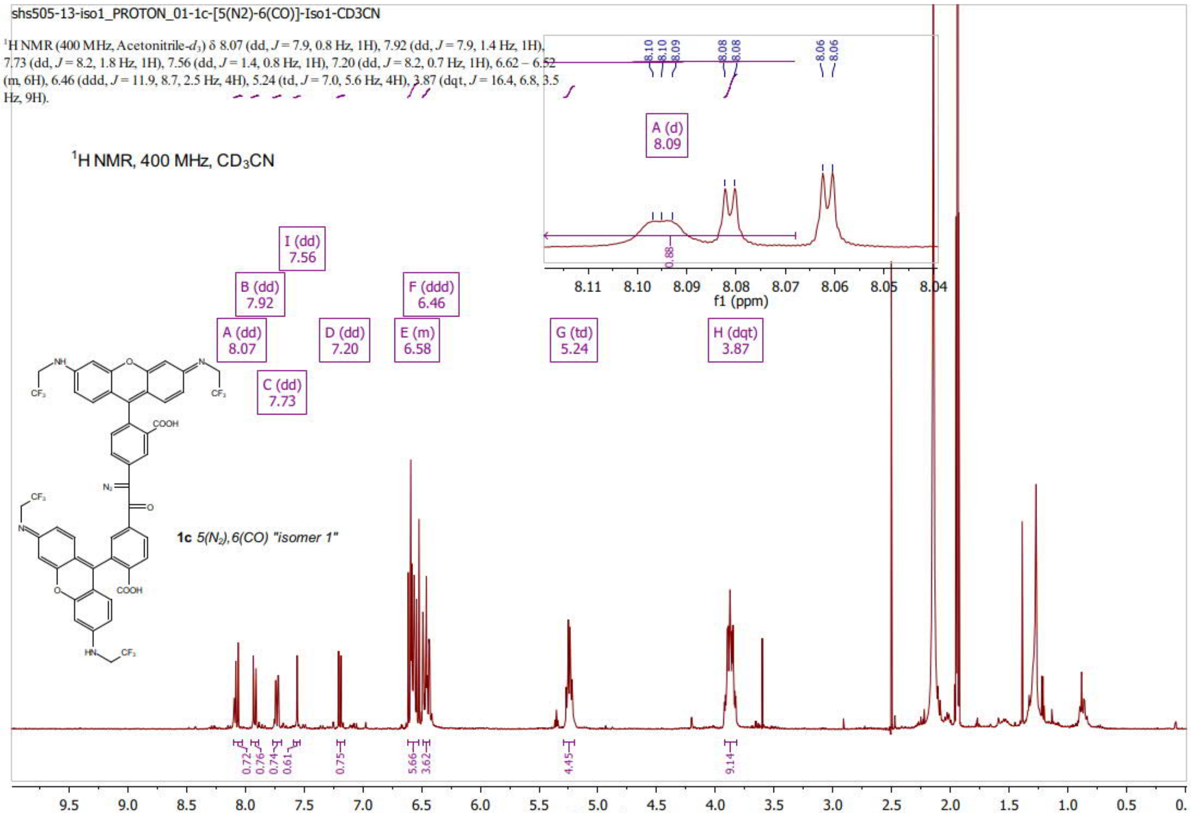






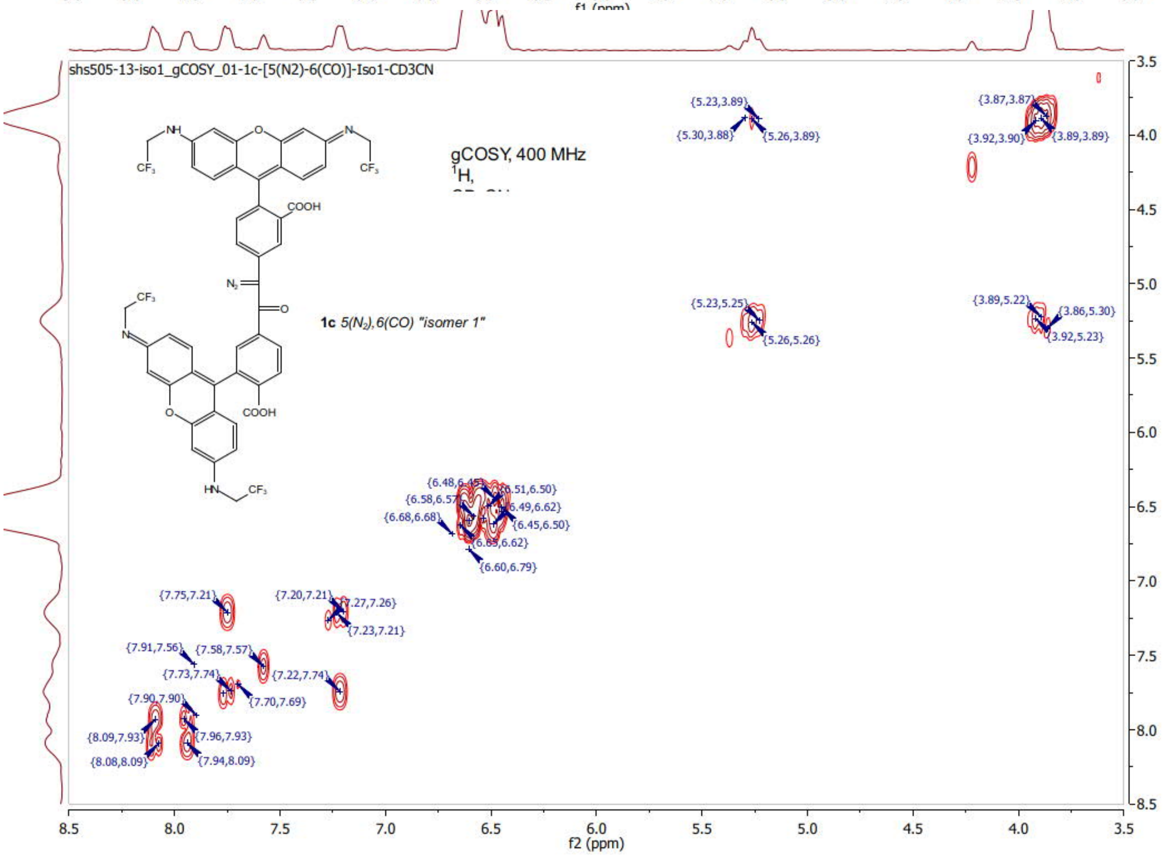
^{19}F NMR (376 MHz, Methanol-d_4) δ -73.42 (t, J = 9.1 Hz), -73.52 (t, J = 9.2 Hz).

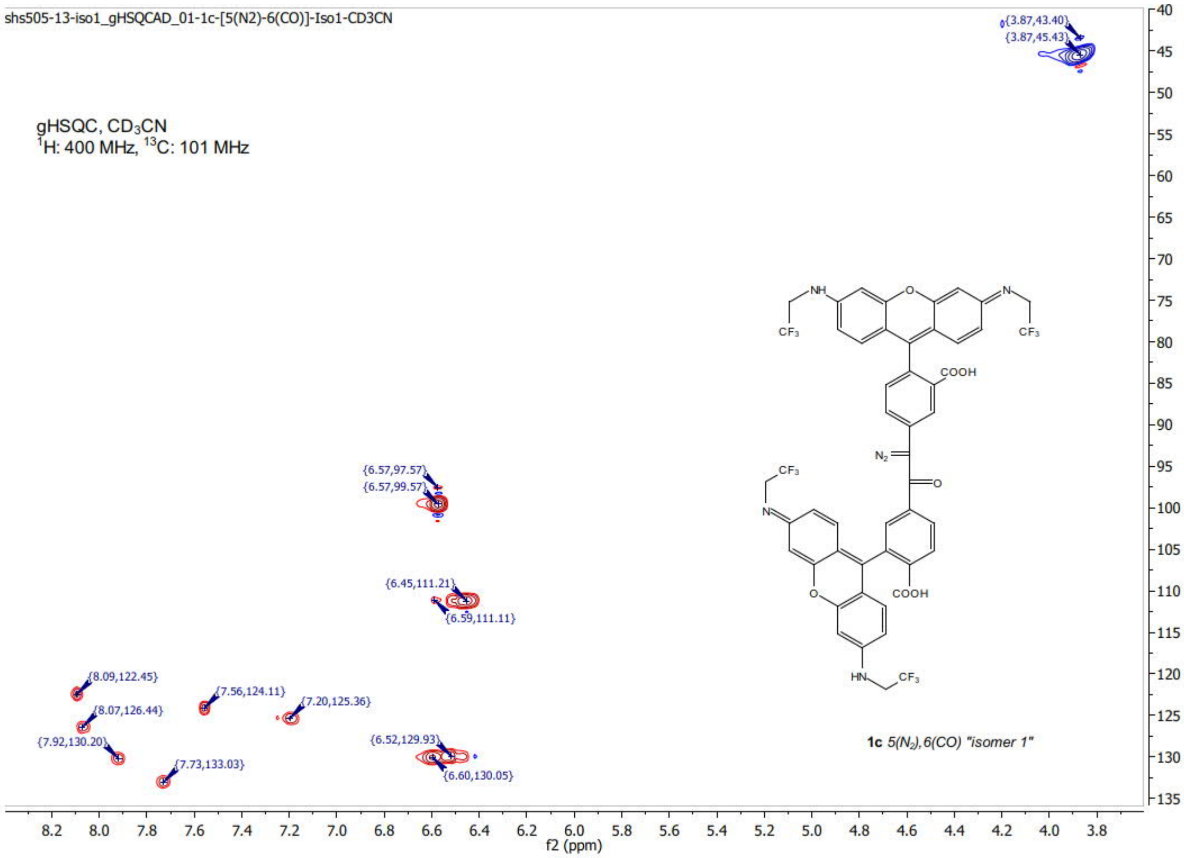
Compound **1c** [5(N_2),6(CO)] (isomer 1)

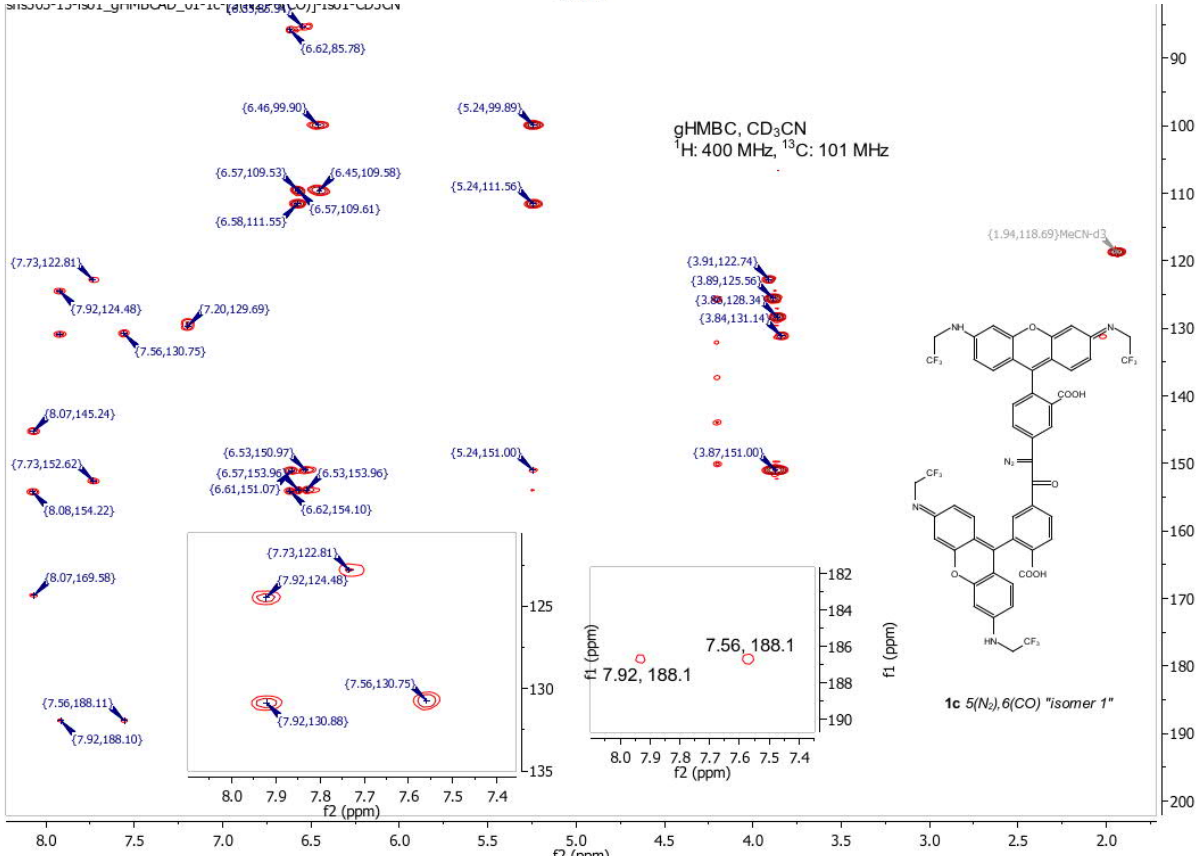


shs505-13-iso1_PROTON_01-1c-[5(N2)-6(CO)]-Iso1-CD3CN

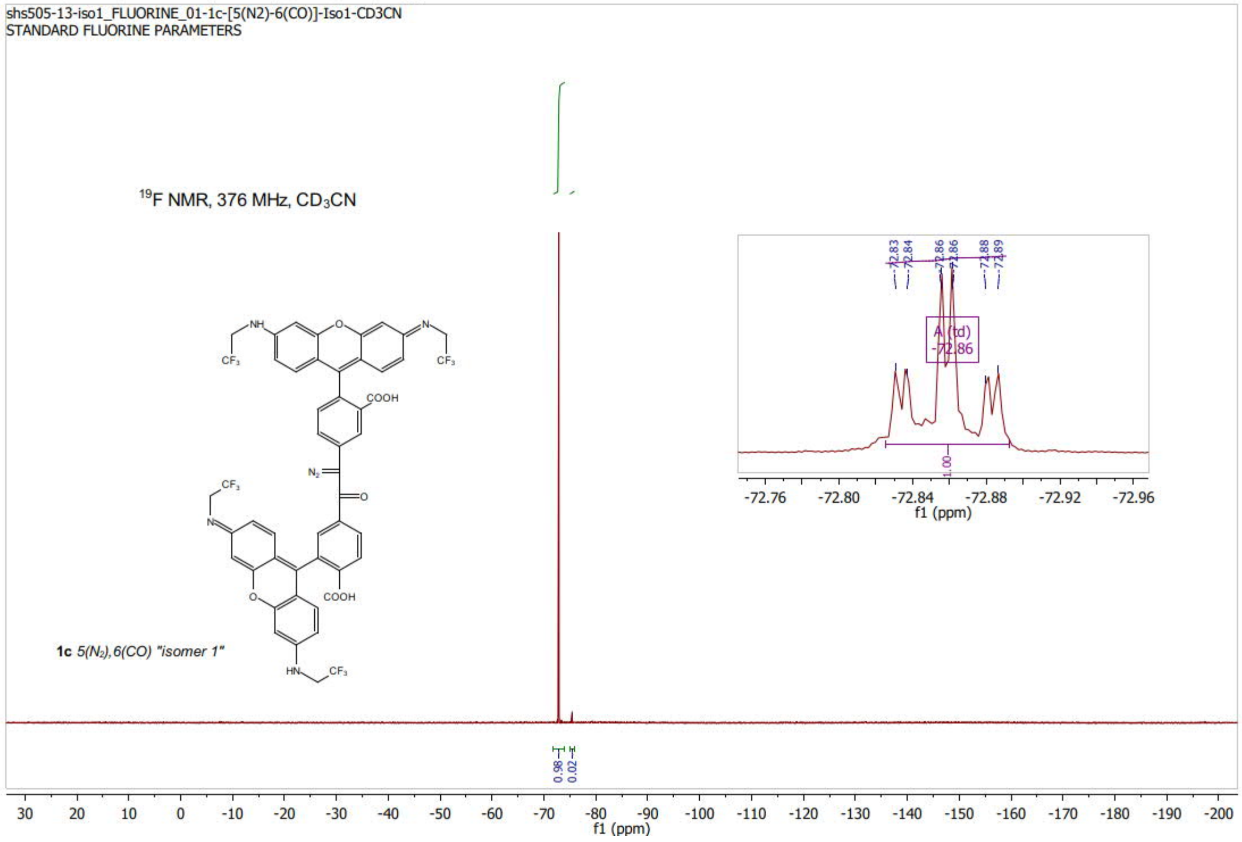
^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 8.07 (dd, J = 7.9, 0.8 Hz, 1H), 7.92 (dd, J = 7.9, 1.4 Hz, 1H), 7.73 (dd, J = 8.2, 1.8 Hz, 1H), 7.56 (dd, J = 1.4, 0.8 Hz, 1H), 7.20 (dd, J = 8.2, 0.7 Hz, 1H), 6.62 – 6.52 (m, 6H), 6.46 (ddd, J = 11.9, 8.7, 2.5 Hz, 4H), 5.24 (td, J = 7.0, 5.6 Hz, 4H), 3.87 (dqt, J = 16.4, 6.8, 3.5 Hz, 9H).



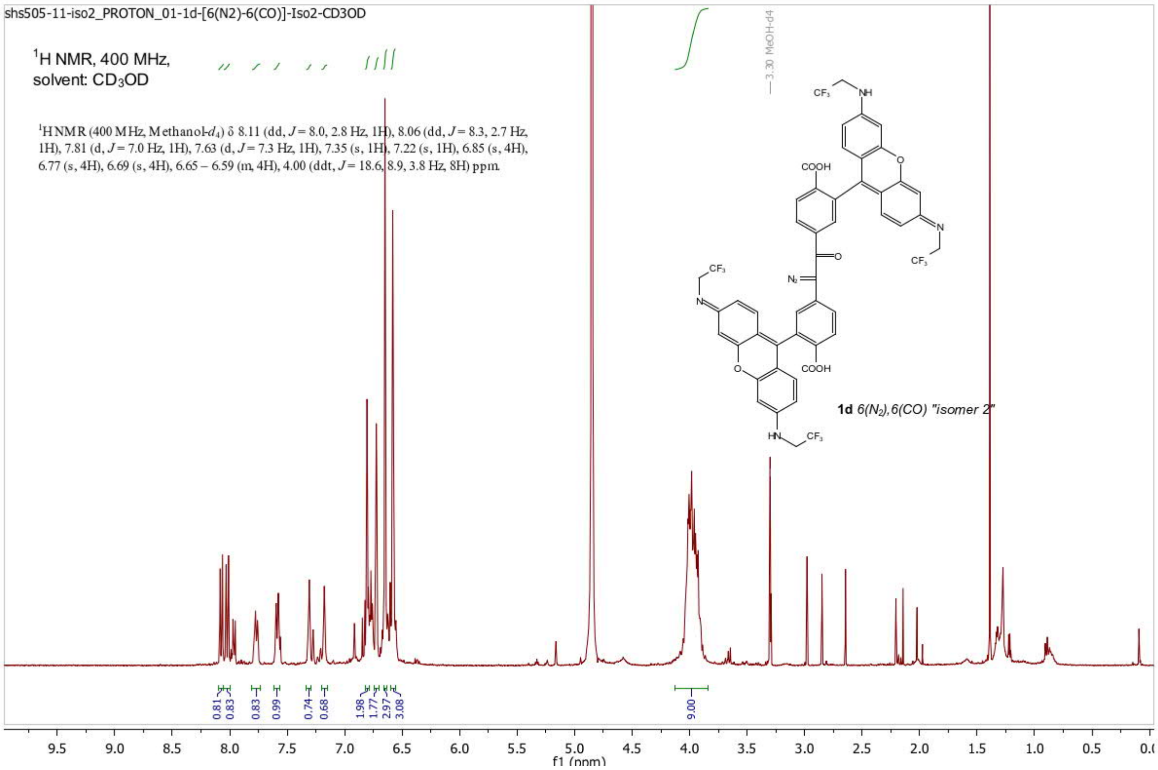

shs505-13-iso1_gHSQCAD_01-1c-[5(N2)-6(CO)]-Iso1-CD3CN
gHSQC, CD3CN
1H: 400 MHz, 13C: 101 MHz
{3.87,43.40}
{3.87,45.43}
{6.57,97.57}
{6.57,99.57}
{6.45,111.21}
{6.59,111.11}
{8.09,122.45}
{7.56,124.11}
{7.20,125.36}
{8.07,126.44}
{7.92,130.20}
{6.52,129.93}
{7.73,133.03}
{6.60,130.05}
NH
CF3
N
COOH
N2
O
HN
1c 5(N2),6(CO) "isomer 1"
f2 (ppm)


gHMBC, CD3CN
1H: 400 MHz, 13C: 101 MHz
{6.62,85.78}
{6.46,99.90}
{5.24,99.89}
{6.57,109.53}
{6.45,109.58}
{6.57,109.61}
{6.58,111.55}
{5.24,111.56}
{1.94,118.69}MeCN-d3
{7.73,122.81}
{7.92,124.48}
{7.20,129.69}
{7.56,130.75}
{3.91,122.74}
{3.89,125.56}
{3.86,128.34}
{3.84,131.14}
{8.07,145.24}
{7.73,152.62}
{6.53,150.97}
{6.57,153.96}
{6.53,153.96}
{6.61,151.07}
{6.62,154.10}
{5.24,151.00}
{3.87,151.00}
{8.08,154.22}
{8.07,169.58}
{7.56,188.11}
{7.92,188.10}
{7.92,130.88}
7.56, 188.1
7.92, 188.1
f1 (ppm)
f2 (ppm)
1c 5(N2),6(CO) "isomer 1"

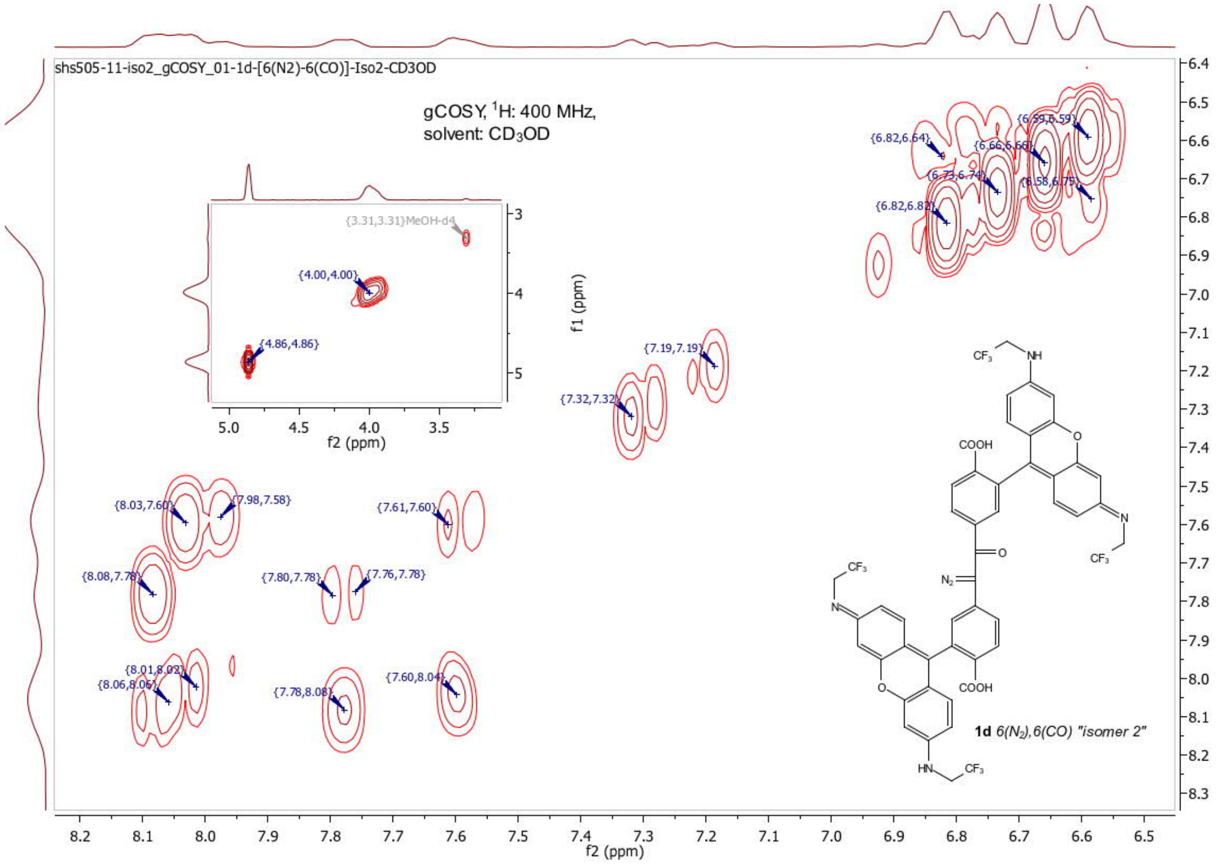
^{19}F NMR (376 MHz, Acetonitrile-d_3) δ -72.86 (td, J = 9.4, 2.1 Hz, 12F) ppm.



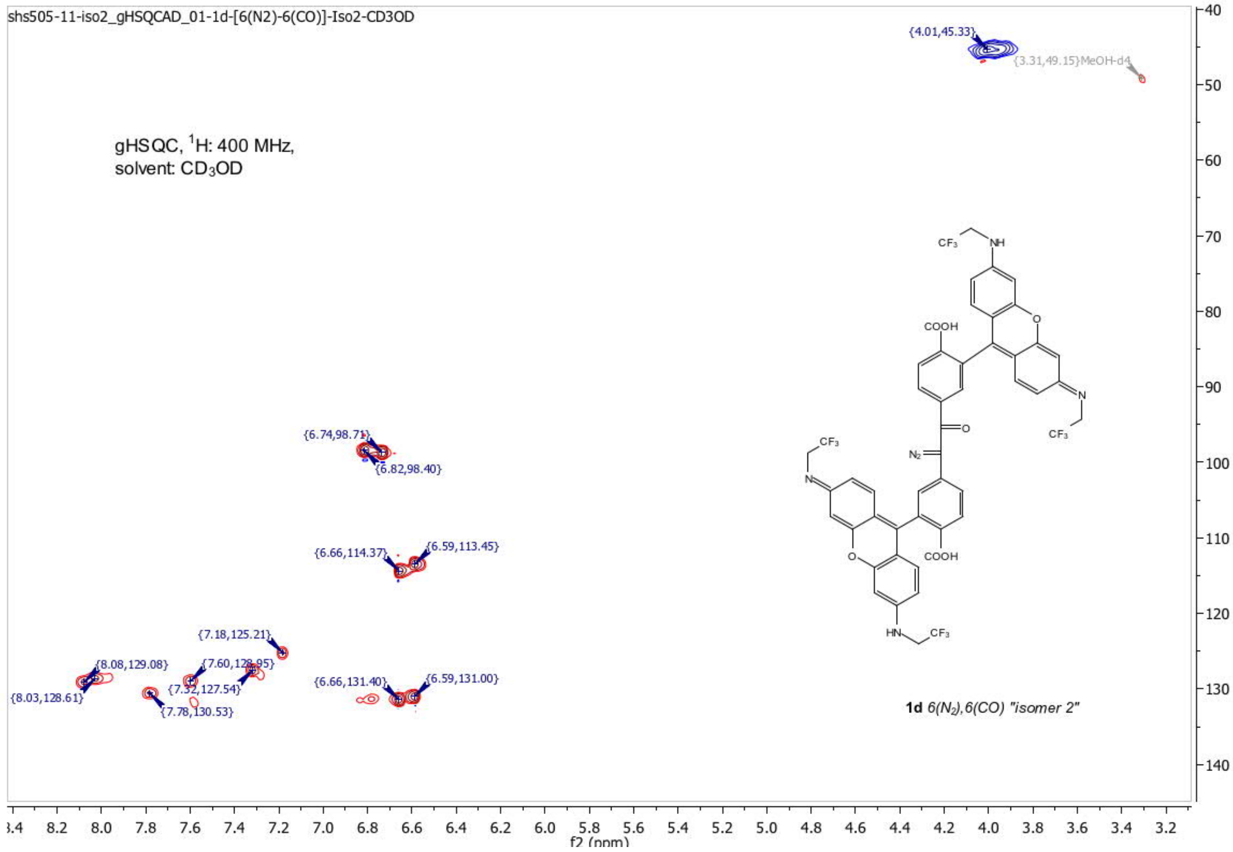
NMR spectra of compound **1d** [6(N$_2$),6(CO)] (isomer 2)



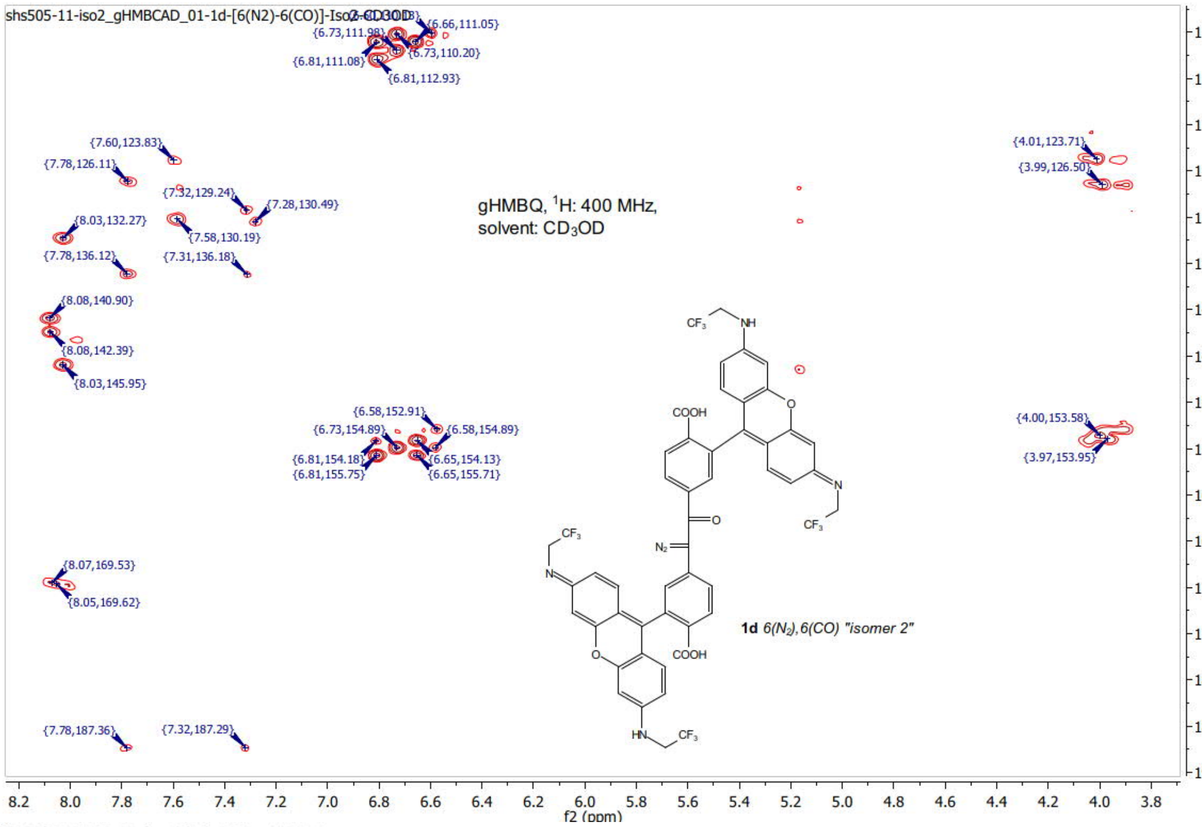
^{1}H NMR (400 MHz, Methanol-d_4) δ 8.11 (dd, J = 8.0, 2.8 Hz, 1H), 8.06 (dd, J = 8.3, 2.7 Hz, 1H), 7.81 (d, J = 7.0 Hz, 1H), 7.63 (d, J = 7.3 Hz, 1H), 7.35 (s, 1H), 7.22 (s, 1H), 6.85 (s, 4H), 6.77 (s, 4H), 6.69 (s, 4H), 6.65 – 6.59 (m, 4H), 4.00 (ddt, J = 18.6, 8.9, 3.8 Hz, 8H) ppm.



shs505-11-iso2_gCOSY_01-1d-[6(N2)-6(CO)]-Iso2-CD3OD
gCOSY, ^{1}H: 400 MHz,
solvent: CD$_3$OD
{3.31,3.31}MeOH-d4
{4.00,4.00}
{4.86,4.86}
{6.82,6.64}
{6.59,6.59}
{6.66,6.66}
{6.73,6.74}
{6.58,6.75}
{6.82,6.82}
{7.19,7.19}
{7.32,7.32}
{8.03,7.60}
{7.98,7.58}
{7.61,7.60}
{8.08,7.78}
{7.80,7.78}
{7.76,7.78}
{8.01,8.02}
{8.06,8.06}
{7.78,8.08}
{7.60,8.04}
f1 (ppm)
f2 (ppm)
CF₃
NH
COOH
O
N
N₂
HN
1d *6(N₂),6(CO) "isomer 2"*



shs505-11-iso2_gHSQCAD_01-1d-[6(N2)-6(CO)]-Iso2-CD3OD
gHSQC, ^{1}H: 400 MHz,
solvent: CD$_3$OD
{4.01,45.33}
{3.31,49.15}MeOH-d4
{6.74,98.71}
{6.82,98.40}
{6.66,114.37}
{6.59,113.45}
{7.18,125.21}
{8.08,129.08}
{7.60,128.95}
{7.32,127.54}
{8.03,128.61}
{7.78,130.53}
{6.66,131.40}
{6.59,131.00}
f2 (ppm)
CF₃
NH
COOH
O
N
N₂
HN
1d *6(N₂),6(CO) "isomer 2"*



^{19}F NMR (376 MHz, Methanol-d_4) δ -71.80 – -74.71 (m) ppm.