SUPPORTING INFORMATION

Synthesis of Bifunctional Amine-Squaramide Organocatalysts Derived from 3-((Dimethylamino)methylene)camphor

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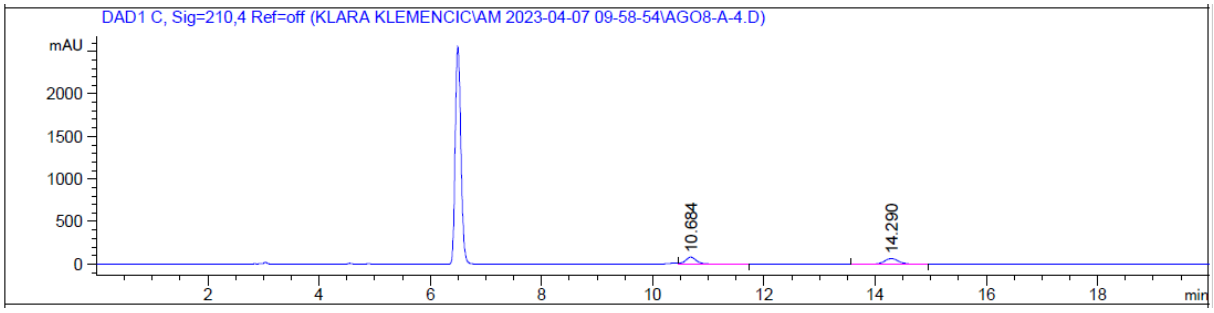
Table of contents

1. HPLC data

Evaluation of organocatalysts in O addition of acetylacetone to *trans*-β-nitrostyrene

HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm.
Enantiomers: *t*R = 10.684 minutes (*S*-isomer); 14.290 minutes (*R*-isomer).

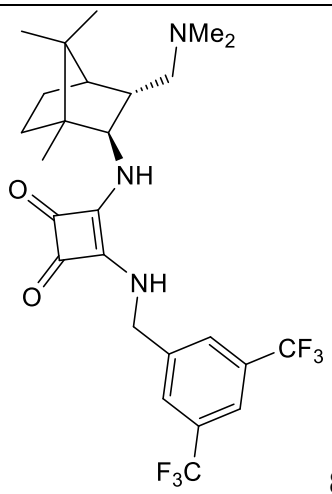
Racemate:



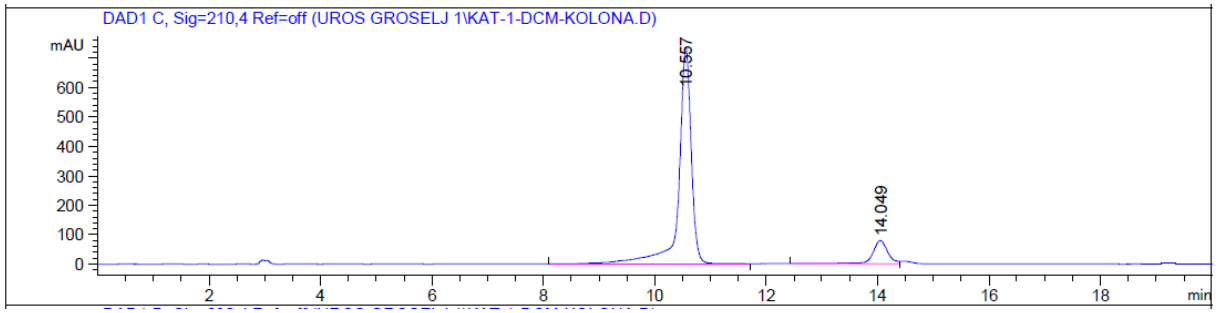
Signal 3: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.684	VB	0.2085	1140.34937	81.87765	50.0556
2	14.290	BB	0.2621	1137.81519	67.01278	49.9444
Totals :				2278.16455	148.89043	

Table S1, Entry 1

	Catalyst (in CH_2Cl_2)	Conversion (%)	*ee* (%)
1	 **8a**	100	77 (*S*)

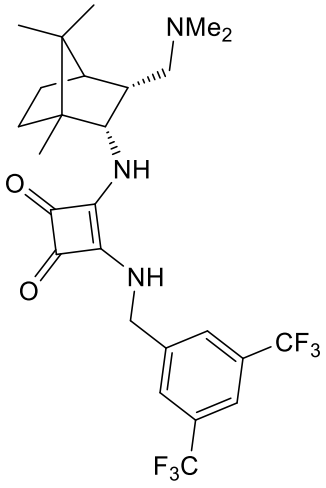
HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm. Enantiomers: *t*R = 10.628 minutes (major); 14.184 minutes (minor) – 77% *ee*.



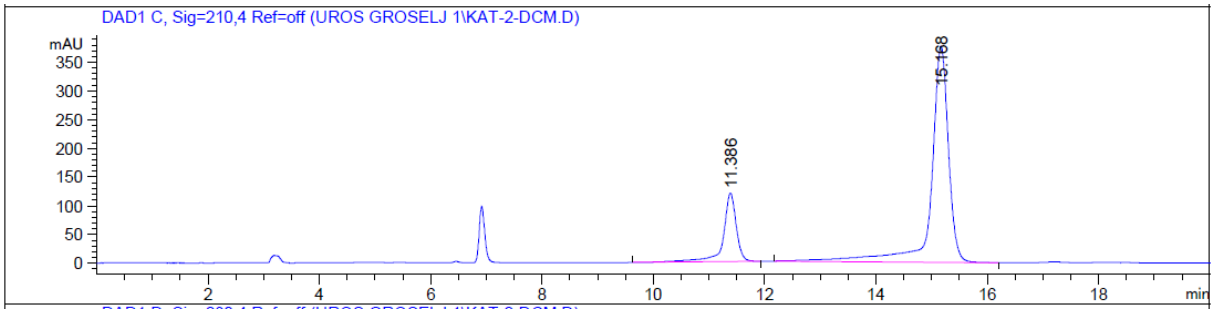
Signal 3: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.628	BB	0.2409	1.05530e4	644.94196	88.6412
2	14.184	BB	0.2937	1352.30310	68.69023	11.3588
Totals :				1.19053e4	713.63219	

Table S1, Entry 2

	Catalyst (in CH_2Cl_2)	Conversion (%)	*ee* (%)
2	 **8b**	94	62 (*R*)

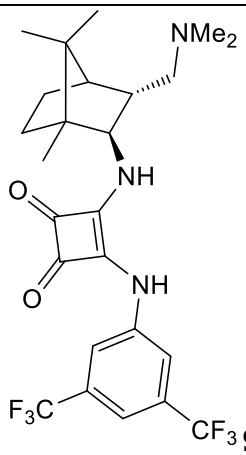
HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm. Enantiomers: *t*R = 11.386 minutes (minor); 15.168 minutes (major) – 62% *ee*.



Signal 3: DAD1 C, Sig=210,4 Ref=off

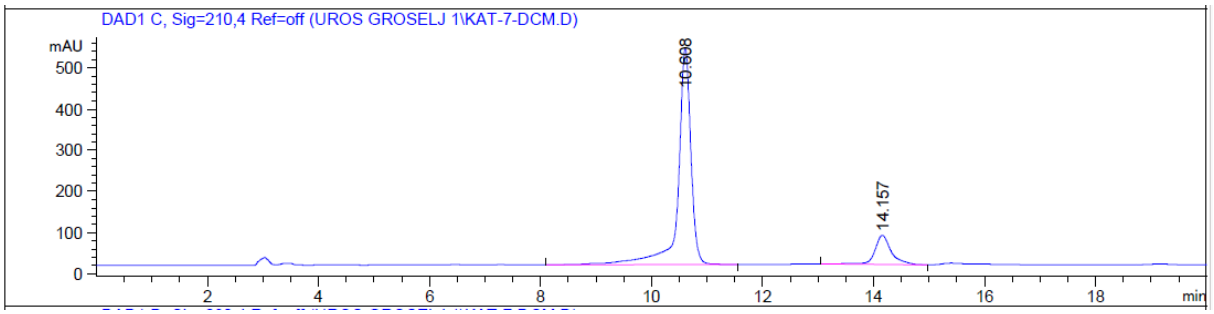
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.386	BB	0.2384	1924.68567	119.16663	19.0415
2	15.168	BB	0.3215	8183.18311	376.56961	80.9585
Totals :				1.01079e4	495.73624	

Table S1, Entry 3

	Catalyst (in CH_2Cl_2)	Conversion (%)	*ee* (%)
3	 **9a**	100	71 (*S*)

HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm.

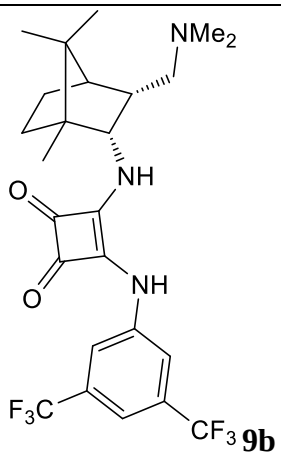
Enantiomers: *t*R = 10.608 minutes (major); 14.157 minutes (minor) – 71% *ee*.



Signal 3: DAD1 C, Sig=210,4 Ref=off

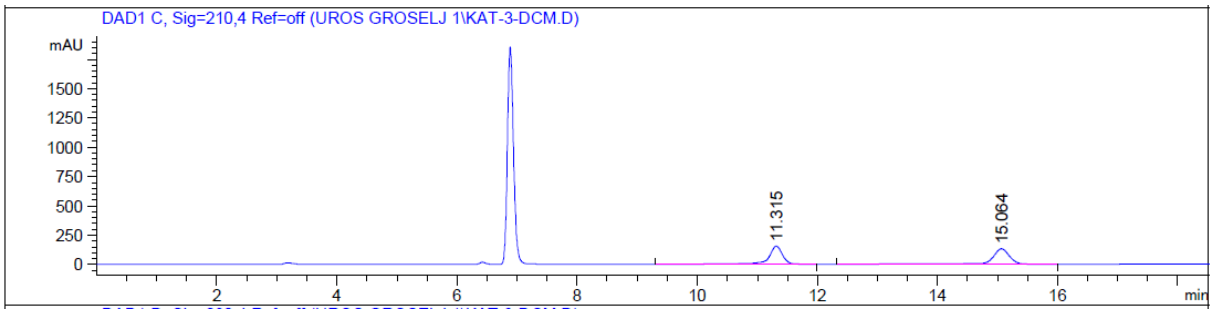
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.608	BB	0.2395	8585.89258	525.80615	85.4662
2	14.157	BB	0.3050	1460.06079	70.66812	14.5338
Totals :				1.00460e4	596.47427	

Table S1, Entry 4

	Catalyst (in CH_2Cl_2)	Conversion (%)	*ee* (%)
4	 **9b**	30	4 (*R*)

HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm.

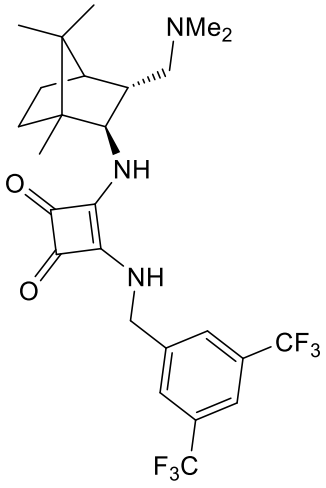
Enantiomers: *t*R = 11.315 minutes (minor); 15.064 minutes (major) – 4% *ee*.



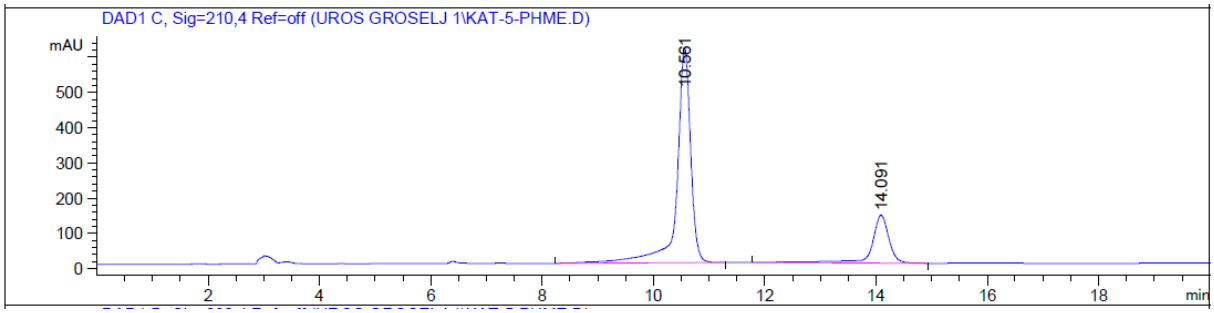
Signal 3: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.315	BB	0.2456	2608.80078	154.82761	47.7065
2	15.064	BB	0.3181	2859.63354	132.35744	52.2935
Totals :				5468.43433	287.18504	

Table S1, Entry 5

	Catalyst (in toluene)	Conversion (%)	*ee* (%)
5	 **8a**	40	57 (*S*)

HPLC: CHIRALPAK AD-H, *n*-hexane/*i*-PrOH = 90:10, flow rate: 1.0 mL/min; λ = 210 nm. Enantiomers: *t*R = 10.561 minutes (major); 14.091 minutes (minor) – 57% *ee*.

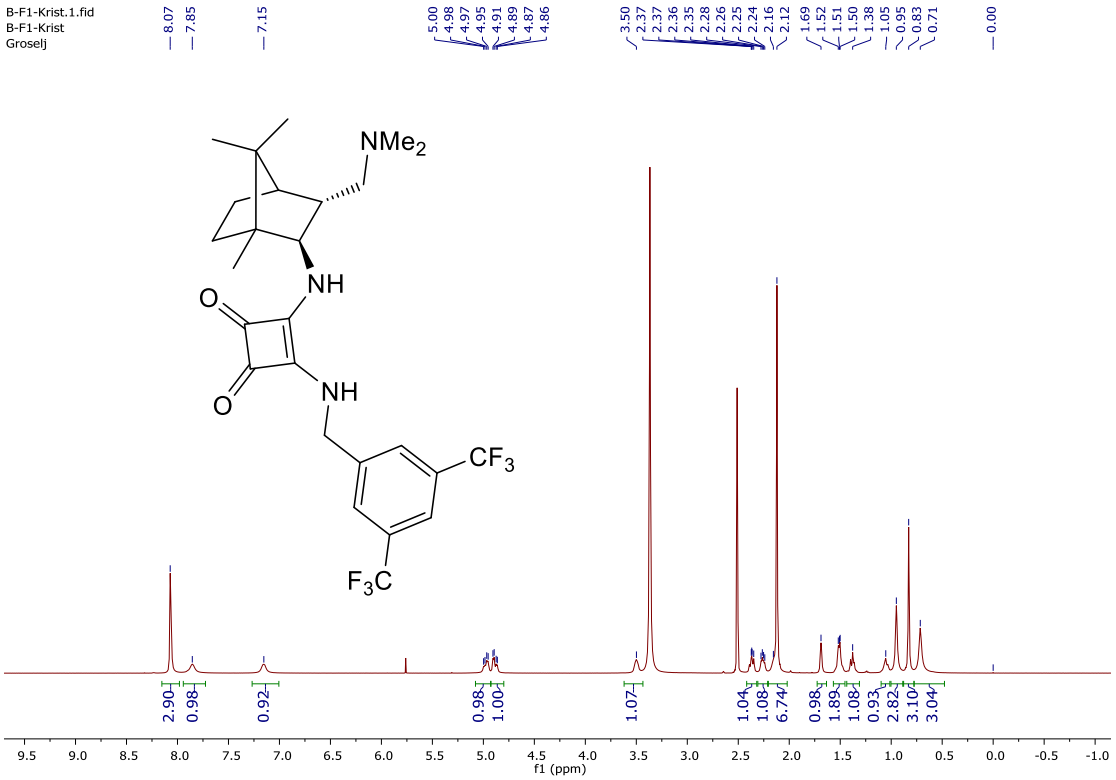


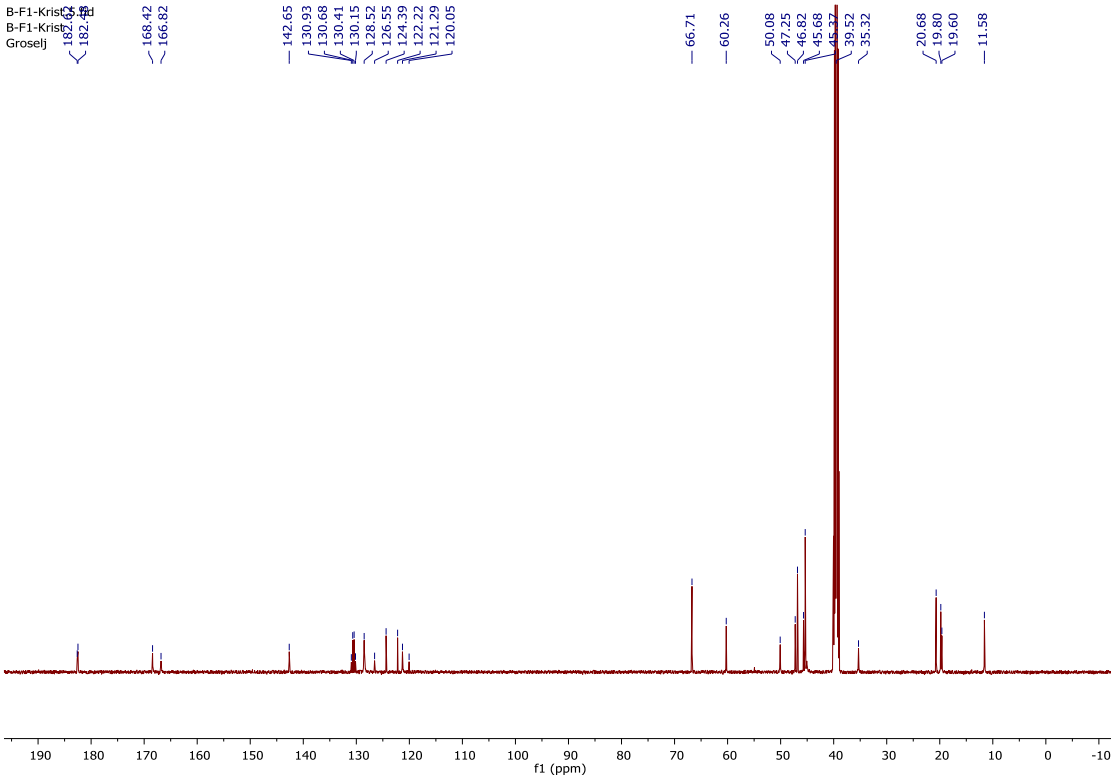
Signal 3: DAD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.561	BB	0.2573	1.06583e4	611.62604	78.6843
2	14.091	BB	0.3145	2887.36768	135.54224	21.3157
Totals :				1.35457e4	747.16827	

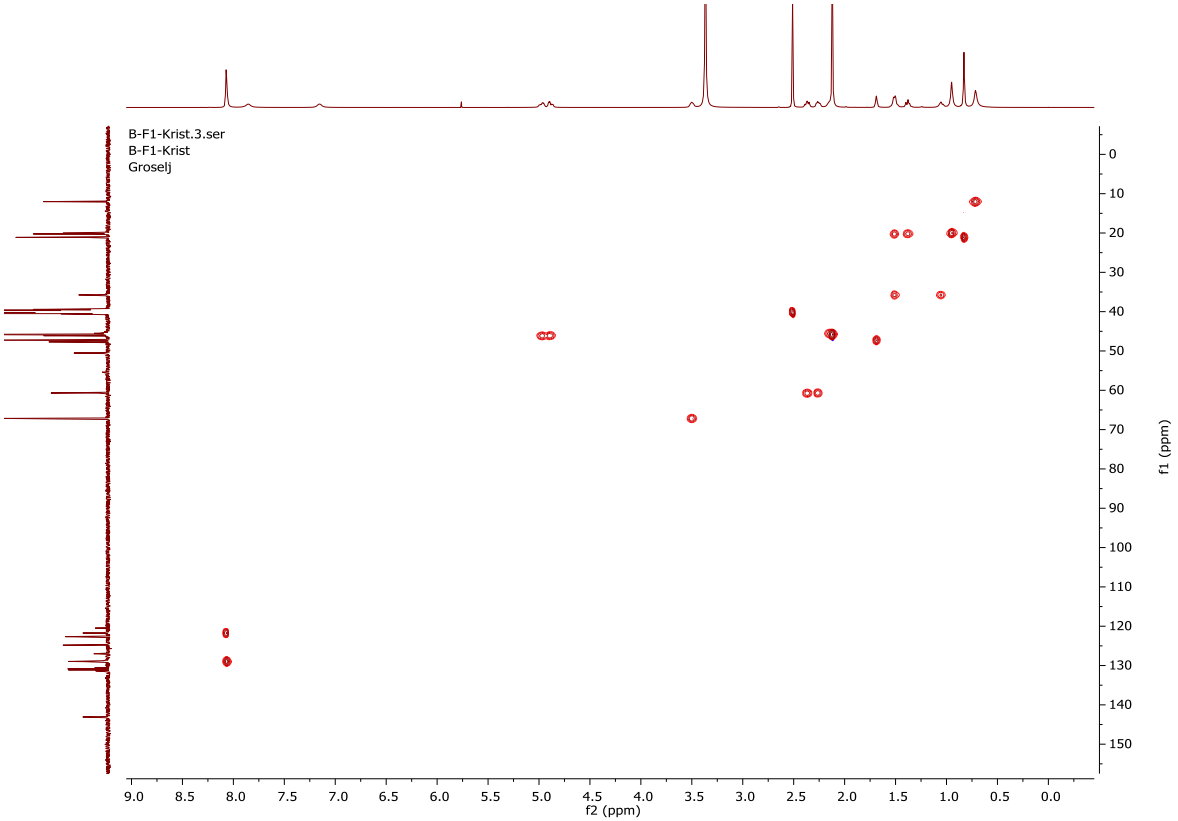
2. Copies of ^{1}H- and ^{13}C-NMR spectra

3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8a)

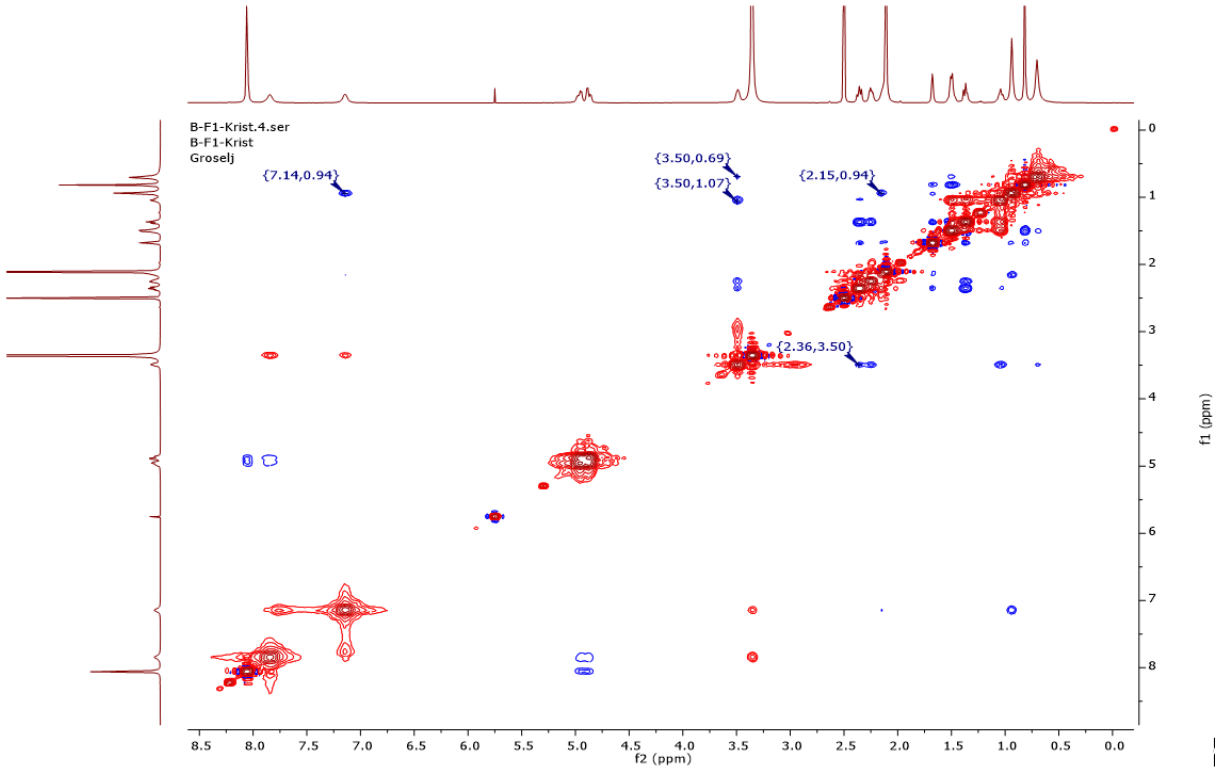




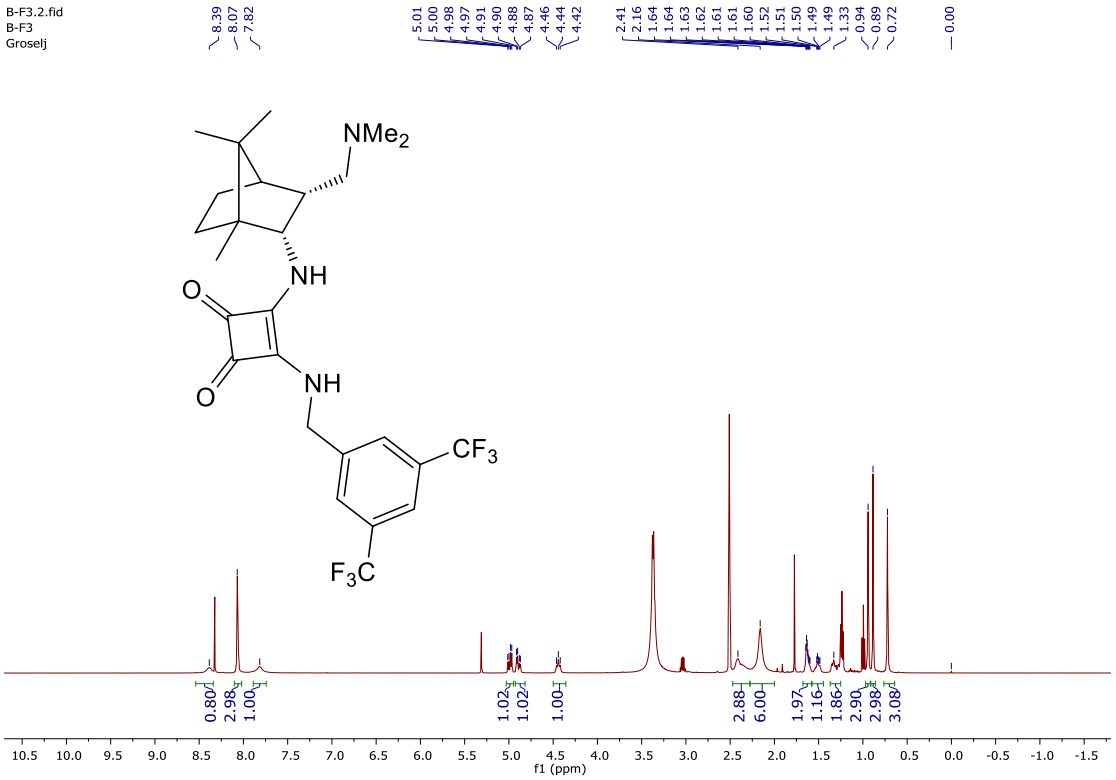
HSQC

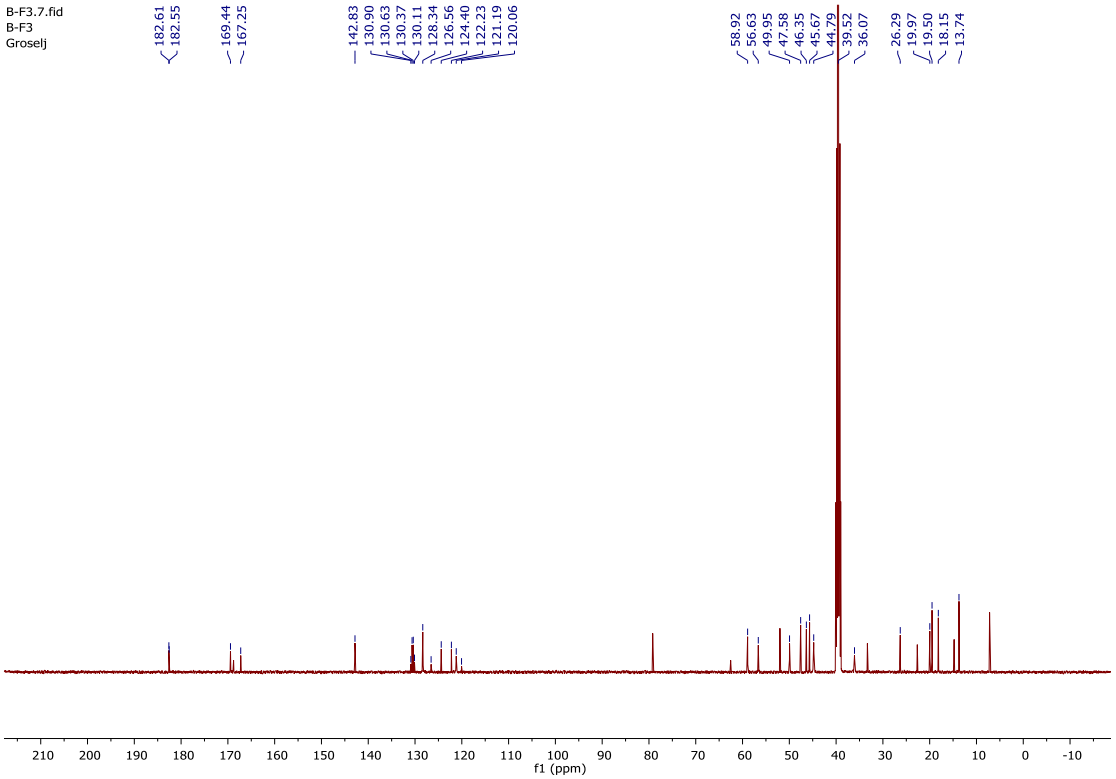

B-F1-Krist.3.ser
B-F1-Krist
Groselj
f2 (ppm)
f1 (ppm)

NOESY

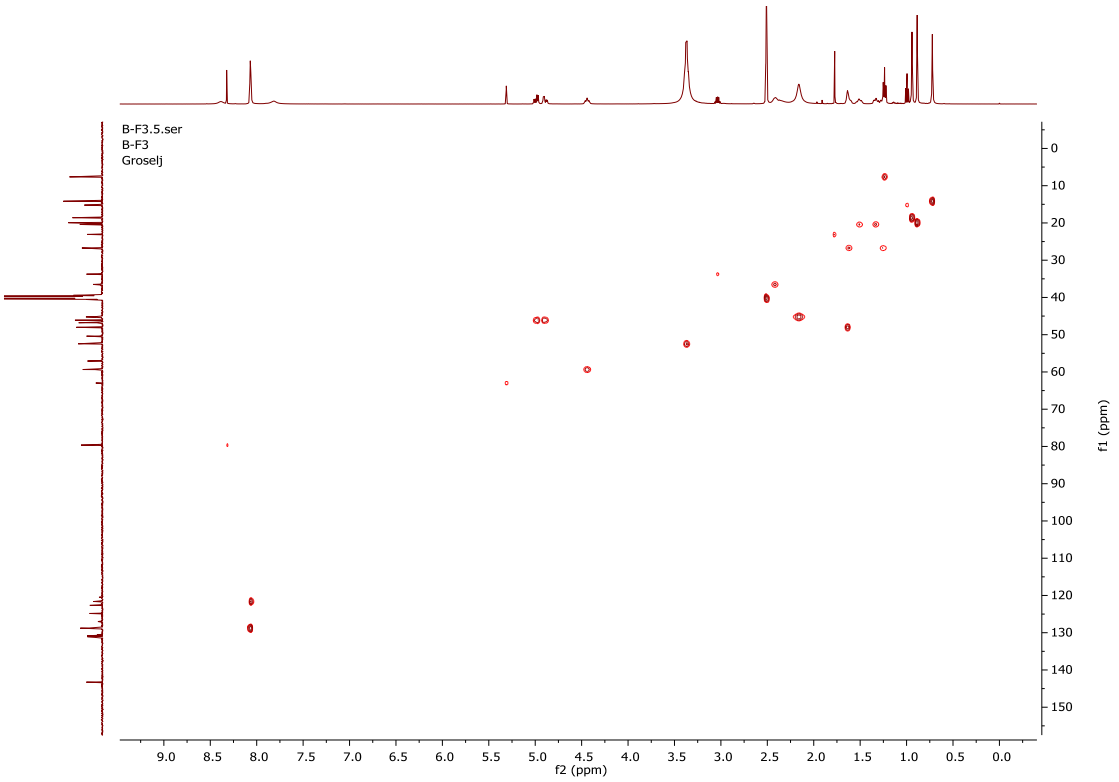

B-F1-Krist.4.ser
B-F1-Krist
Groselj
{7.14,0.94}
{3.50,0.69}
{3.50,1.07}
{2.15,0.94}
{2.36,3.50}
f2 (ppm)
f1 (ppm)

3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8b)

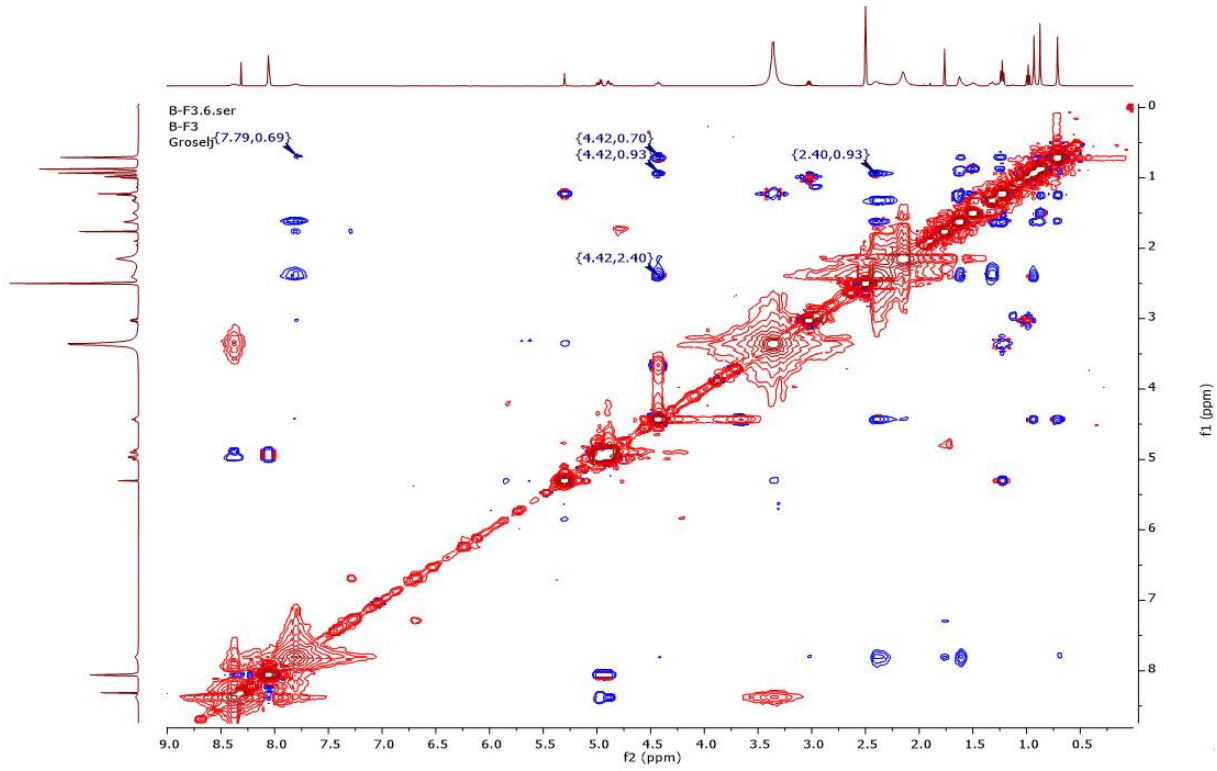




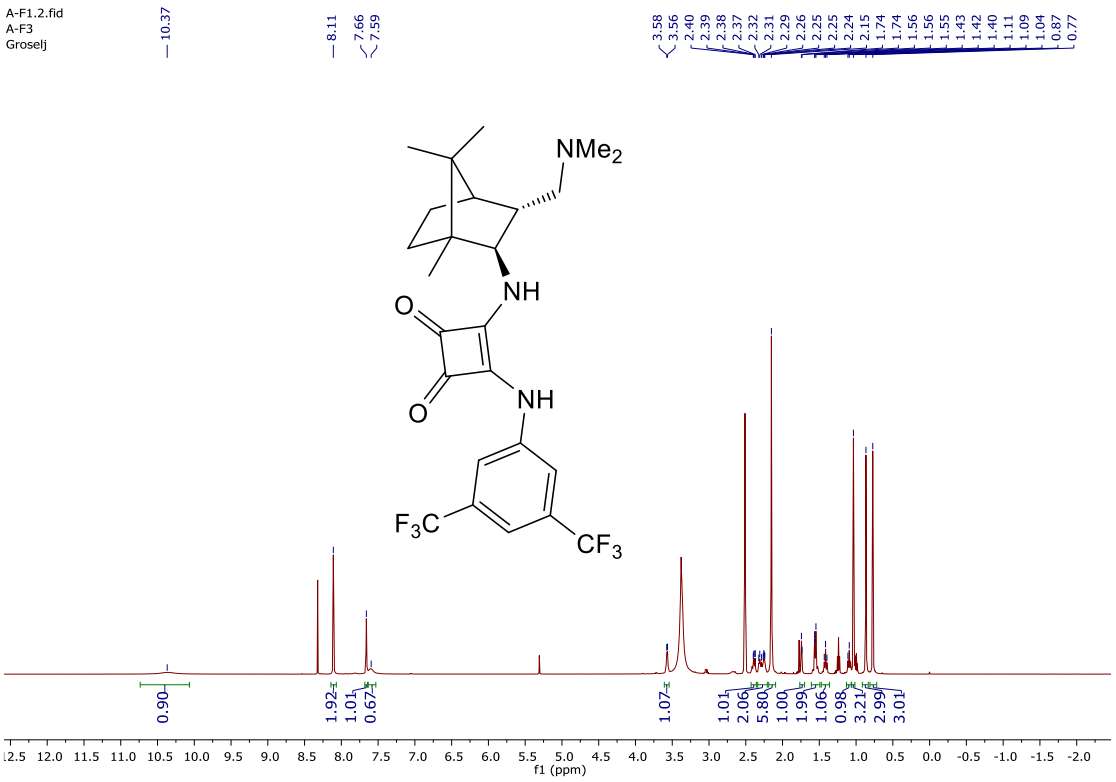
HSQC

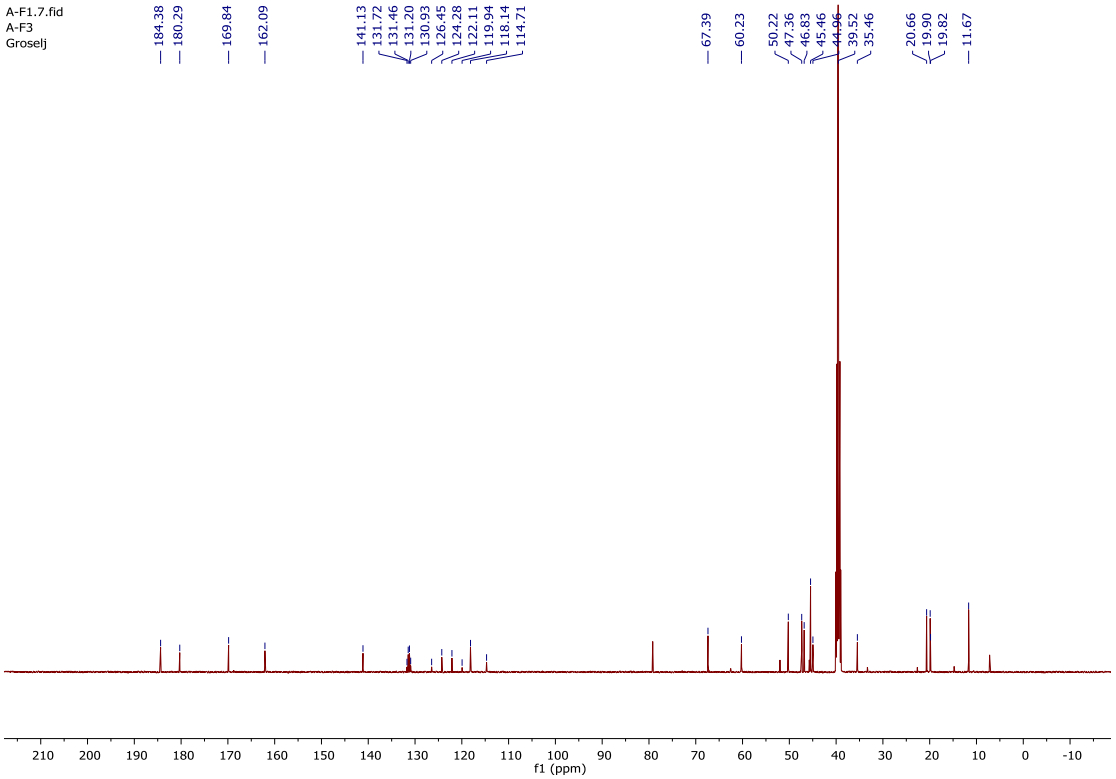

B-F3.5.ser
B-F3
Groselj
f2 (ppm)
f1 (ppm)

NOESY

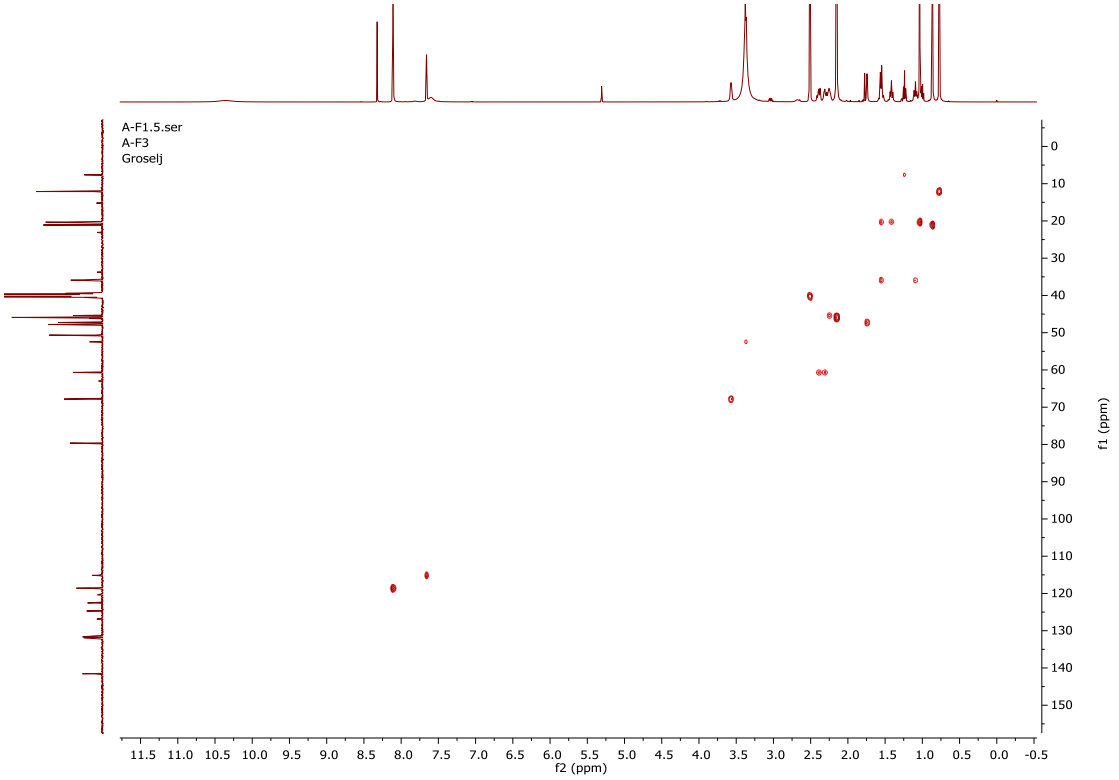

B-F3.6.ser
B-F3
Groselj
{7.79,0.69}
{4.42,0.70}
{4.42,0.93}
{2.40,0.93}
{4.42,2.40}
f2 (ppm)
f1 (ppm)

3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9a)





HSQC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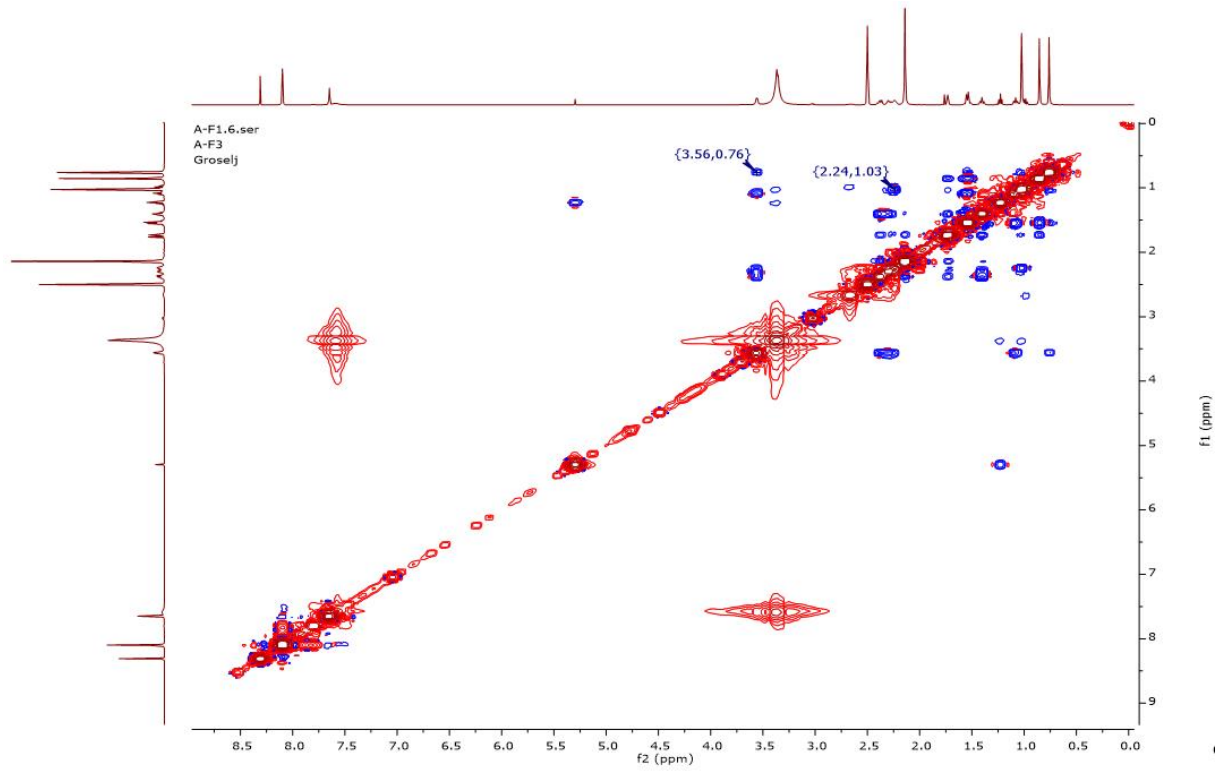
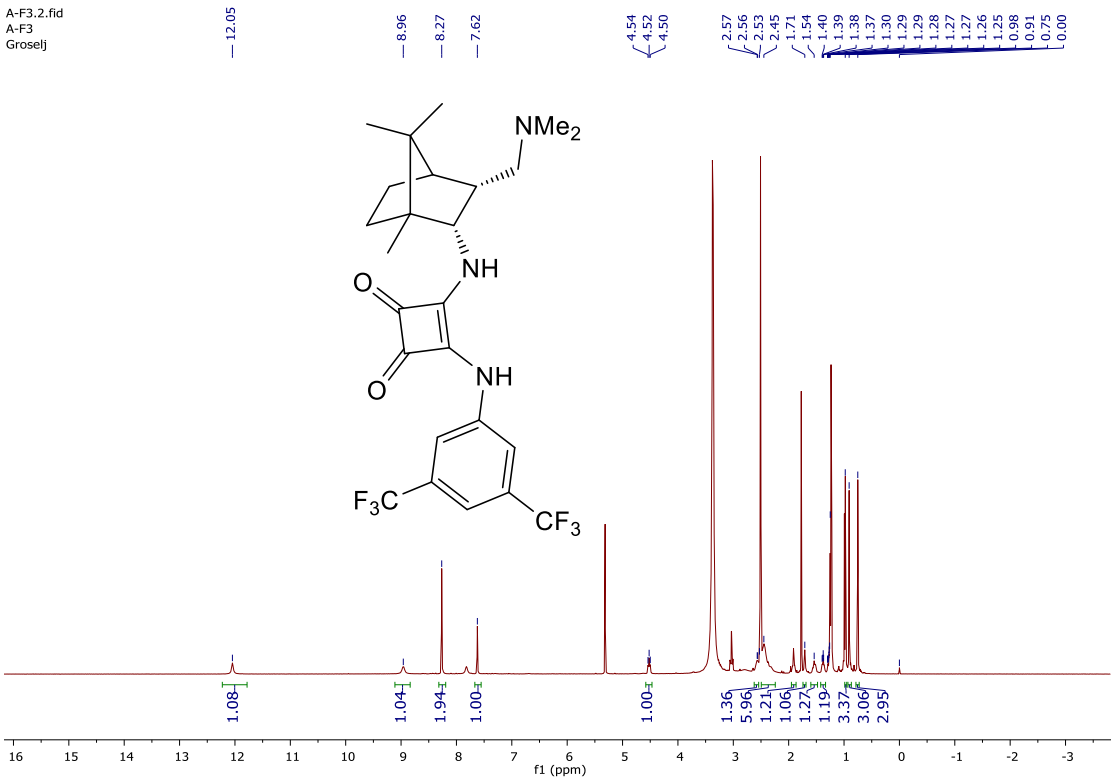
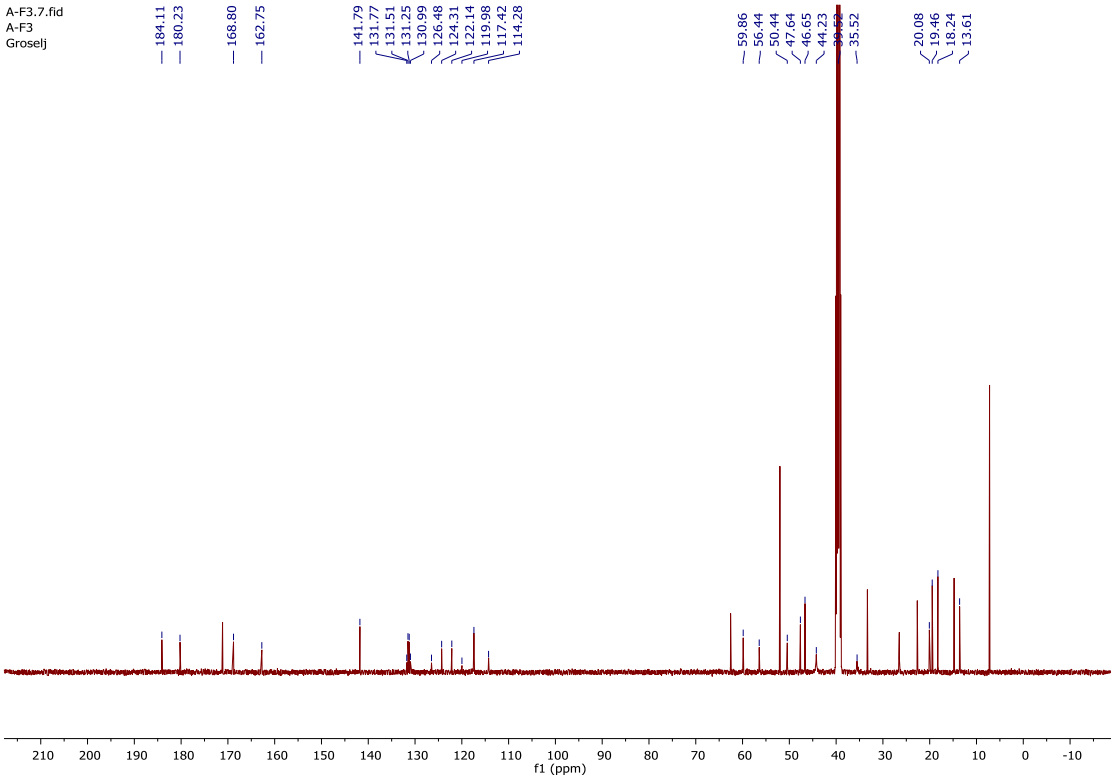
A-F3
Groselj
f2 (ppm)
f1 (ppm)

NOESY

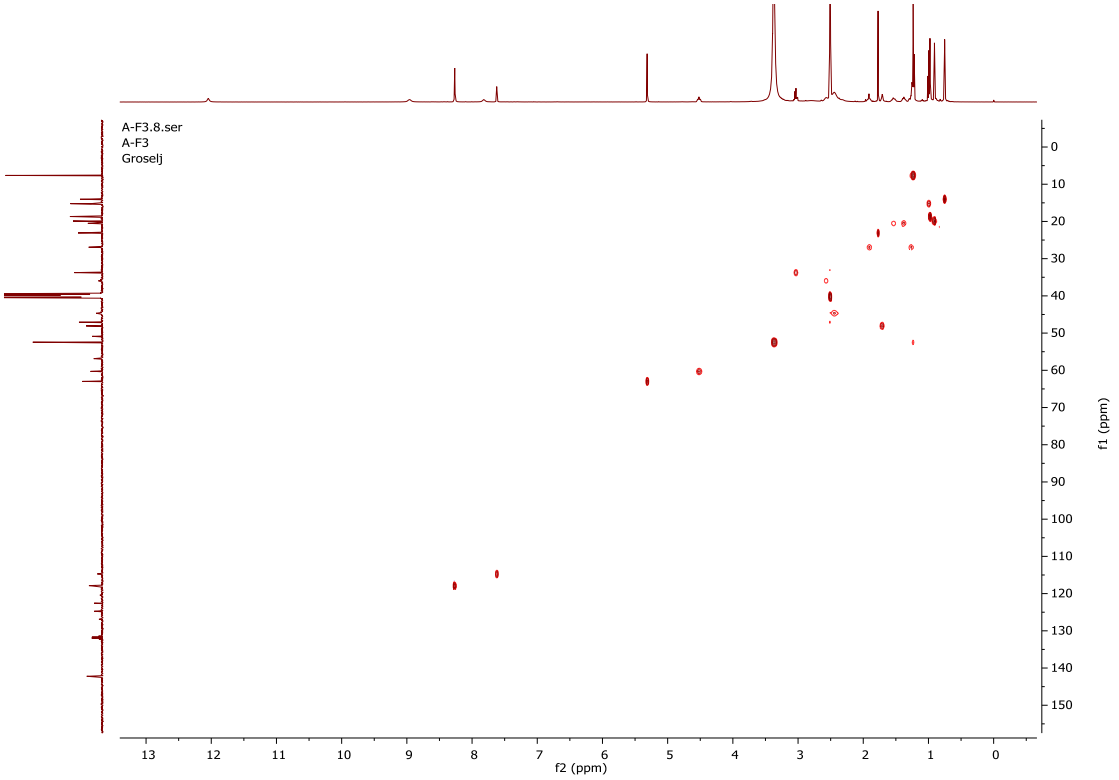

A-F1.6.ser
A-F3
Groselj
{3.56,0.76}
{2.24,1.03}
f2 (ppm)
f1 (ppm)

3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9b)





HSQC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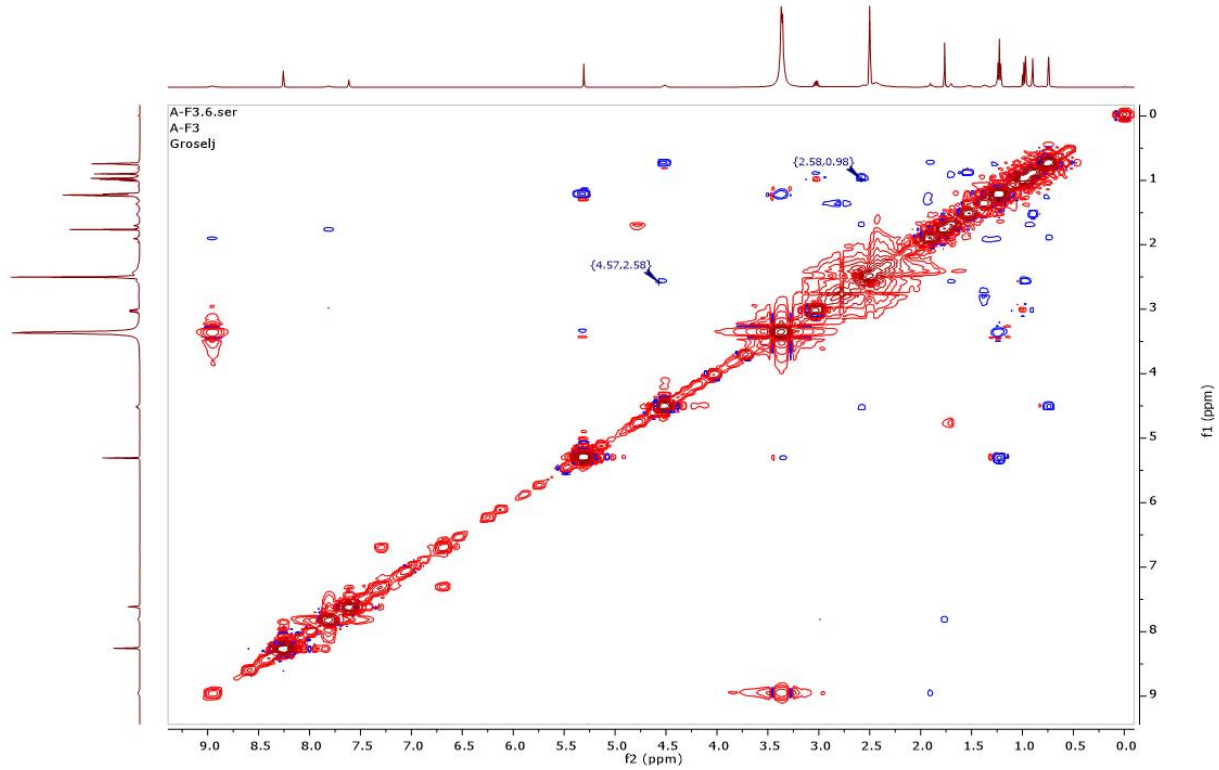
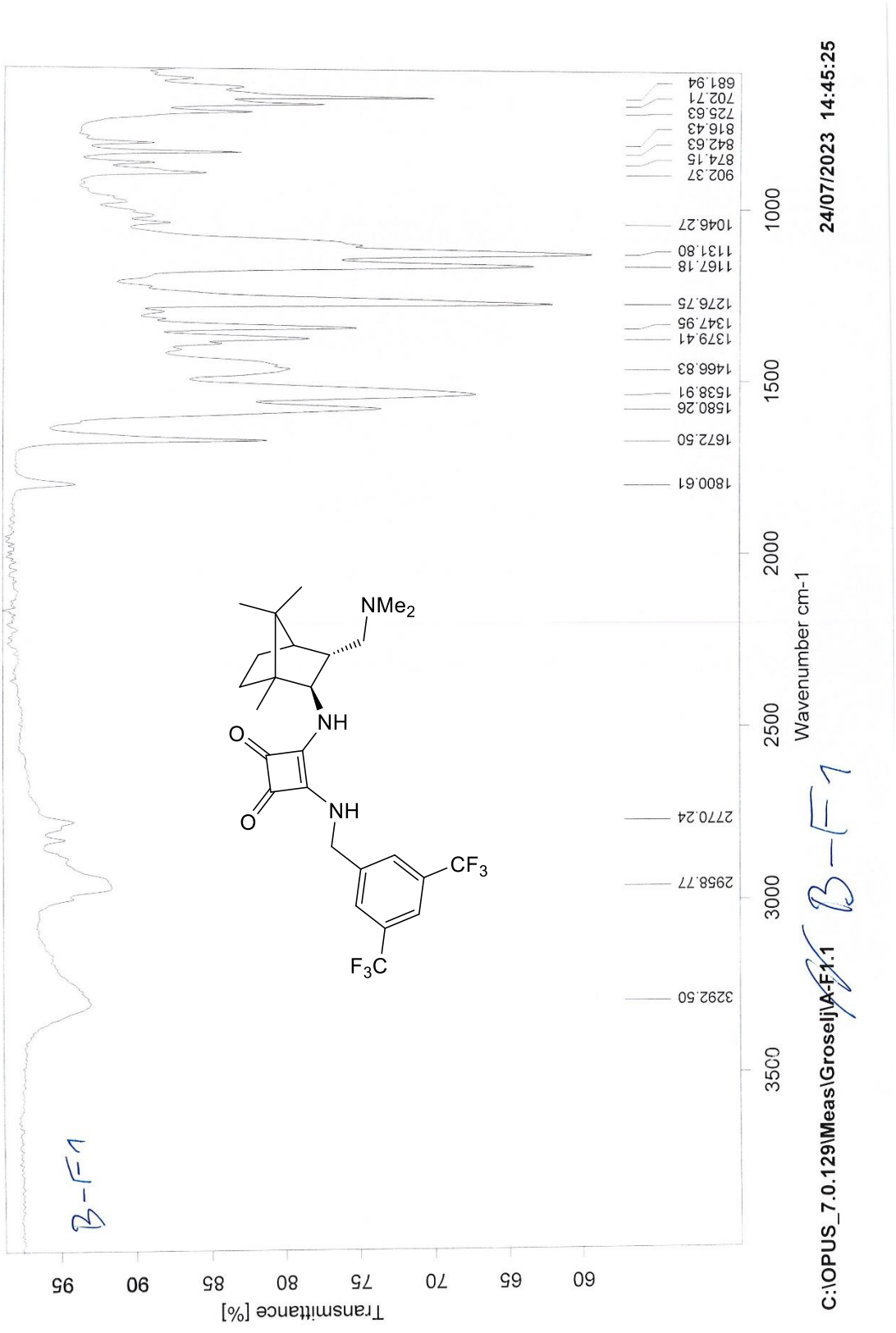
A-F3
Groselj
f2 (ppm)
f1 (ppm)

NOESY

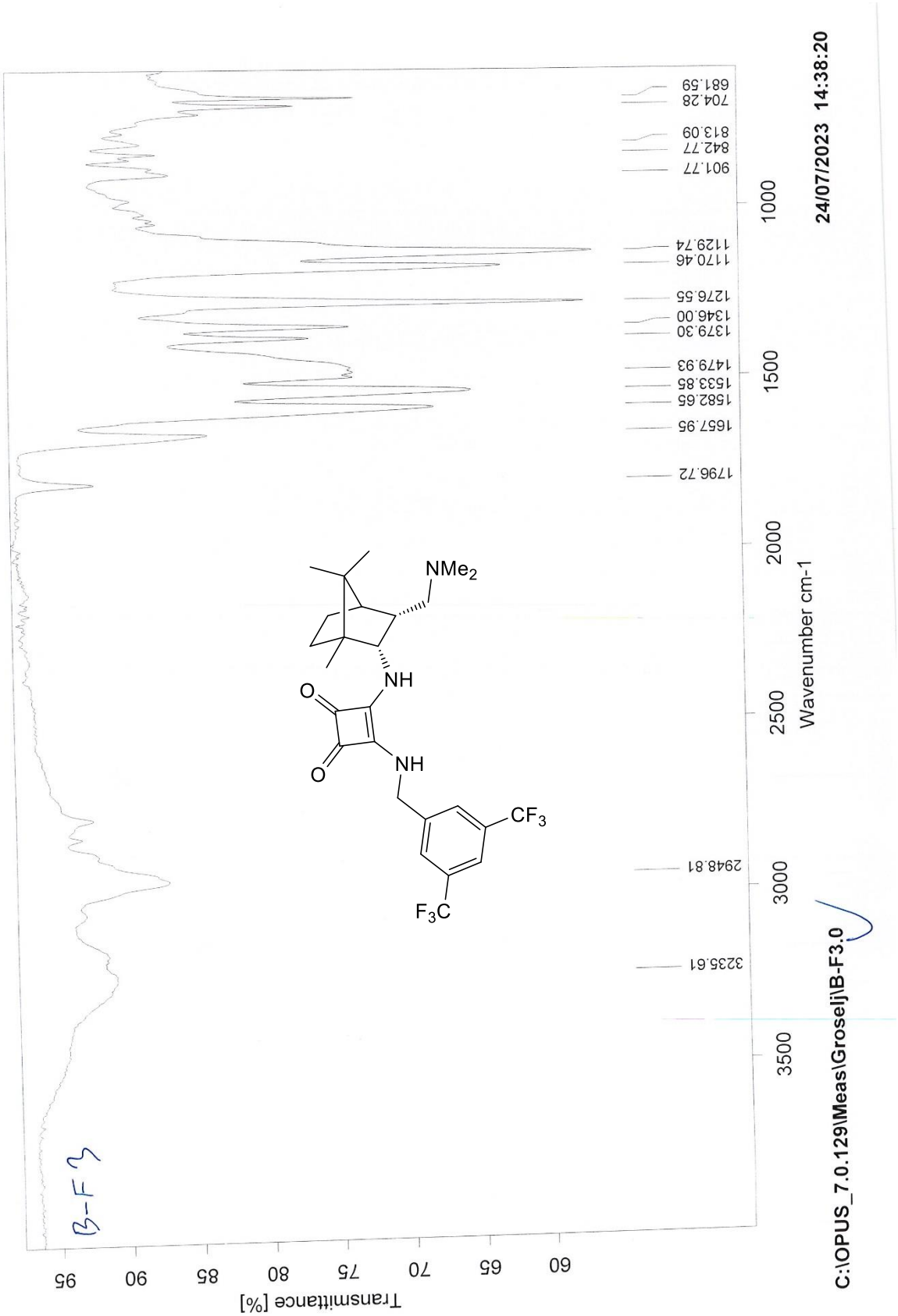

A-F3.6.ser
A-F3
Groselj
{2.58,0.98}
{4.57,2.58}
f2 (ppm)
f1 (ppm)

3. Copies of IR spectra

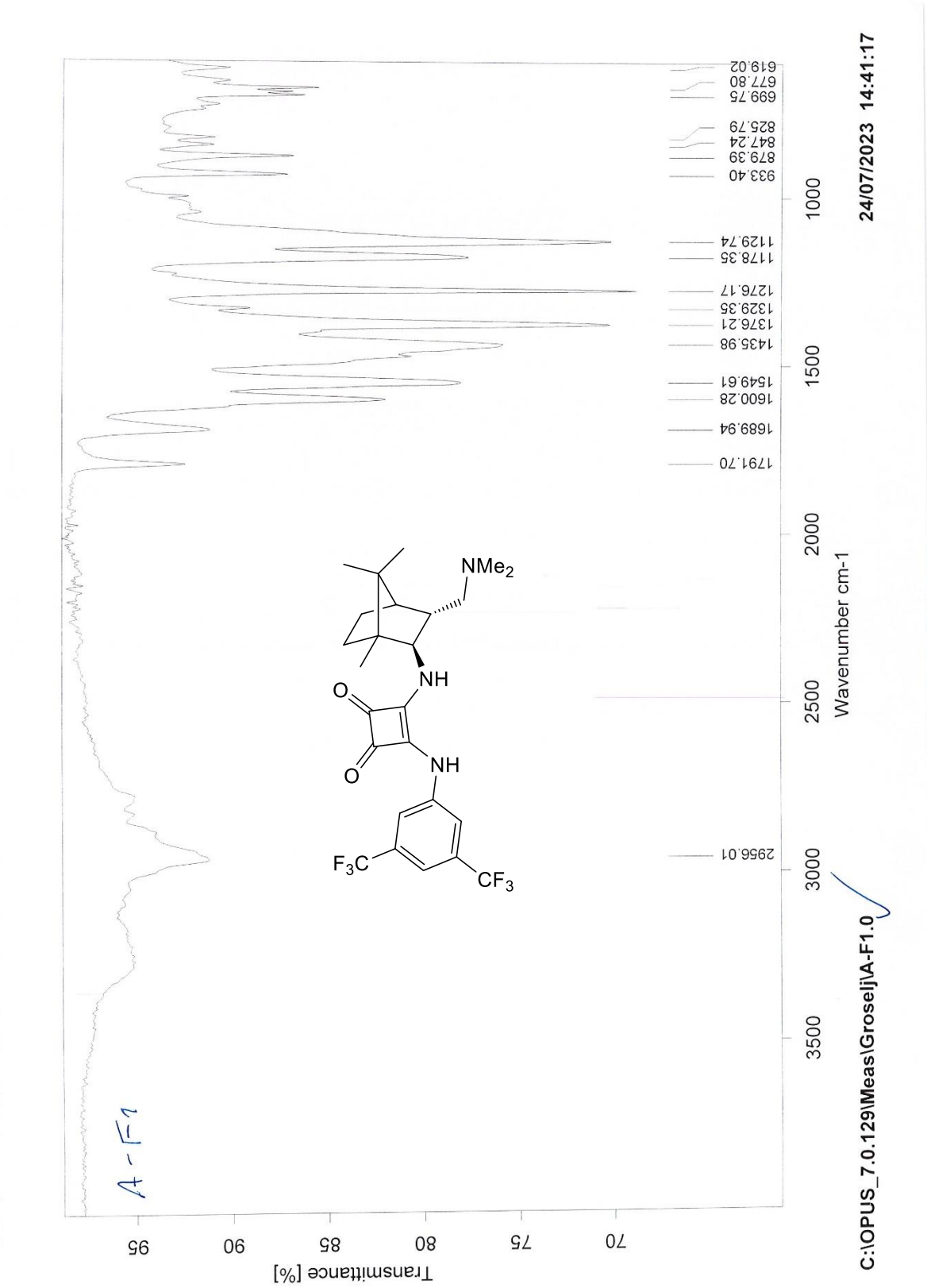
3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8a)



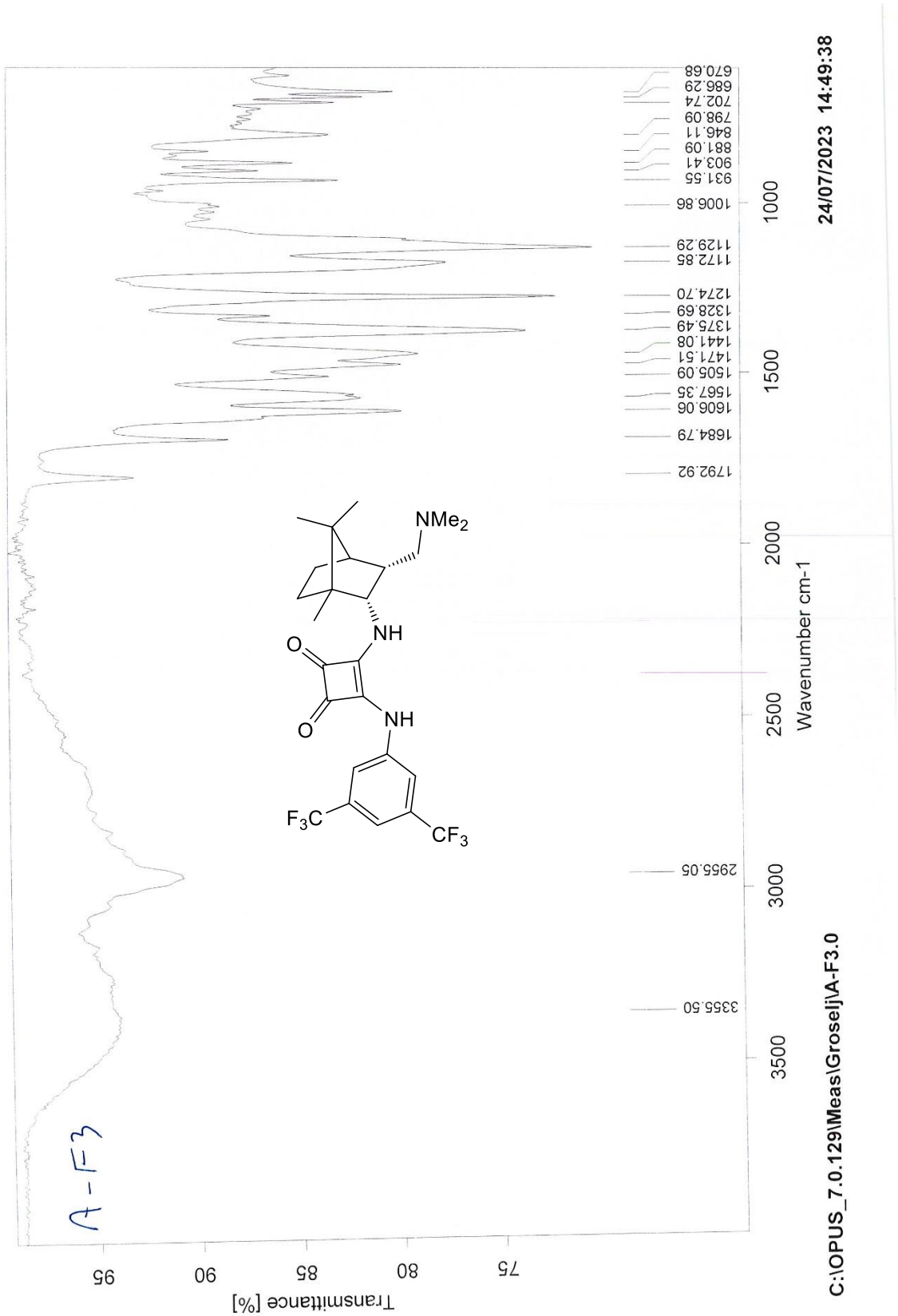
3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8b)



3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9a)

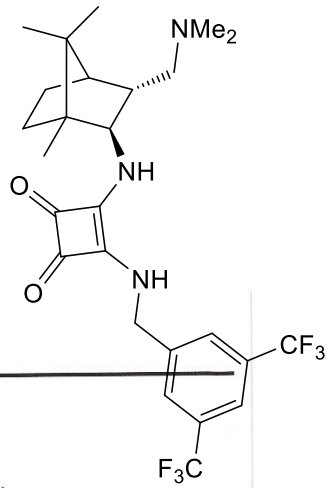


3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9b)



4. Copies of HRMS reports

3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8a)



Qualitative Compound Report

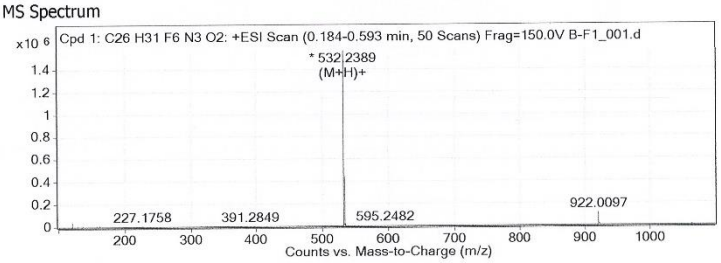
Data File	B-F1_001.d	**Sample Name**	B-F1
Sample Type	Sample	**Position**	Vial 5
Instrument Name	US10310002	**User Name**	TOF-PC\admin
Acq Method	Bypass.m	**Acquired Time**	7/25/2023 10:07:55 AM
IRM Calibration Status	Success	**DA Method**	Damijana.m
Comment			

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C26 H31 F6 N3 O2	532.239	0.252	Find by Molecular Feature	531.2317

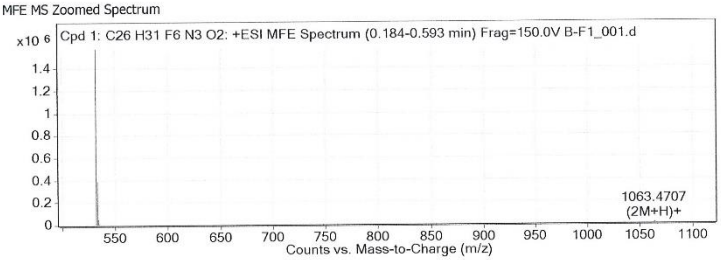
Compound Identification Results

Ion Mass	Calc Ion Mass	Difference	IonFormula	IonSpecies	Best
532.239	532.2393	0.3	C26 H32 F6 N3 O2	(M+H)+	✓
532.239	532.238	-1	C24 H30 F6 N6 O	(M+H)+	
532.239	532.2407	1.7	C28 H34 F6 O3	(M+H)+	
532.239	532.2412	2.2	C13 H30 F6 N12 O4	(M+H)+	
532.239	532.2366	-2.4	C23 H34 F6 N2 O5	(M+H)+	
532.239	532.2366	-2.4	C22 H28 F6 N9	(M+H)+	

MS Spectrum

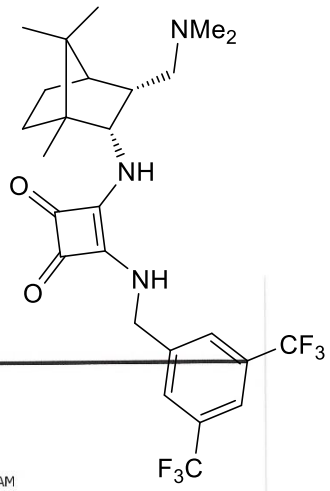


MFE MS Zoomed Spectrum



--- End Of Report ---

3-((3,5-Bis(trifluoromethyl)benzyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (8b)



Qualitative Compound Report

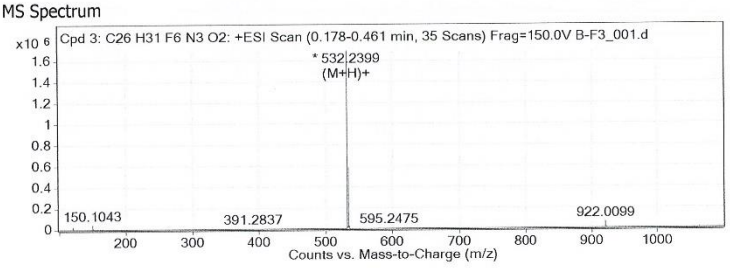
Data File	B-F3_001.d	**Sample Name**	B-F3
Sample Type	Sample	**Position**	Vial 6
Instrument Name	US10310002	**User Name**	TOF-PC\admin
Acq Method	Bypass.m	**Acquired Time**	7/25/2023 10:10:13 AM
IRM Calibration Status	Success	**DA Method**	Damijana.m
Comment			

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 3: C26 H31 F6 N3 O2	532.2391	0.254	Find by Molecular Feature	531.2319

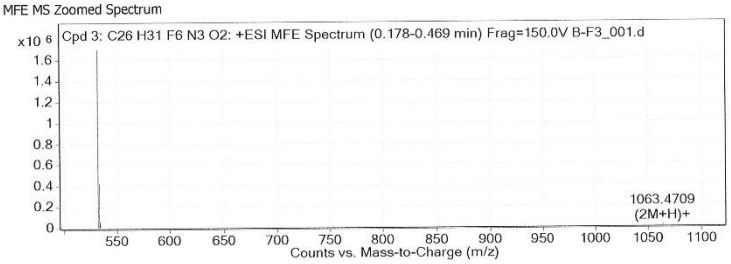
Compound Identification Results

Ion Mass	Calc Ion Mass	Difference	IonFormula	IonSpecies	Best
532.2391	532.2393	0.3	C26 H32 F6 N3 O2	(M+H)+	✓
570.1978	570.1984	0.6	C14 H25 F6 K N16	(M+K)+	
570.1978	570.1984	0.6	C15 H31 F6 K N9 O5	(M+K)+	
532.2391	532.238	-1.1	C24 H30 F6 N6 O	(M+H)+	
570.1978	570.1992	1.5	C31 H31 F6 K N	(M+K)+	
532.2391	532.2407	1.6	C28 H34 F6 O3	(M+H)+	
570.1978	570.1997	2	C16 H27 F6 K N13 O	(M+K)+	
532.2391	532.2412	2.1	C13 H30 F6 N12 O4	(M+H)+	
532.2391	532.2366	-2.4	C23 H34 F6 N2 O5	(M+H)+	
532.2391	532.2366	-2.4	C22 H28 F6 N9	(M+H)+	

MS Spectrum



MFE MS Zoomed Spectrum



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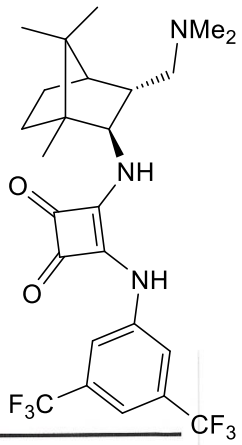
3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9a)



Qualitative Compound Report

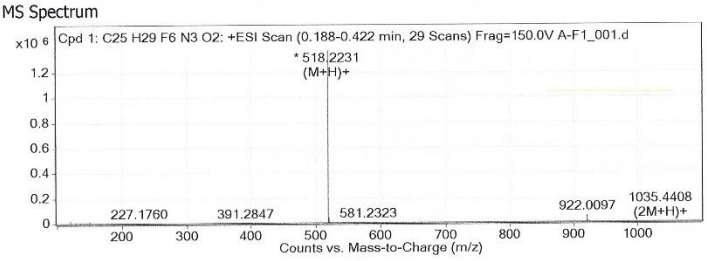
Data File	A-F1_001.d	**Sample Name**	A-F1
Sample Type	Sample	**Position**	Vial 3
Instrument Name	US10310002	**User Name**	TOF-PC\admin
Acq Method	Bypass.m	**Acquired Time**	7/25/2023 10:03:19 AM
IRM Calibration Status	Success	**DA Method**	Damijana.m
Comment			

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H29 F6 N3 O2	518.2237	0.251	Find by Molecular Feature	517.2164

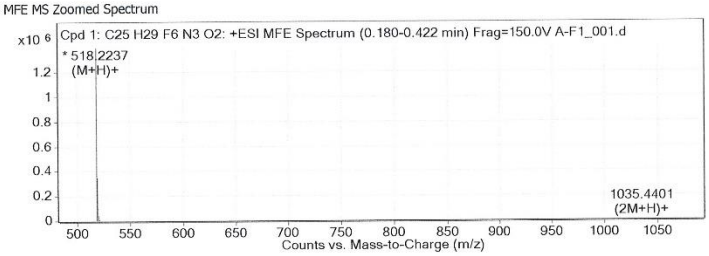
Compound Identification Results

Ion Mass	Calc Ion Mass	Difference	IonFormula	IonSpecies	Best
518.2237	518.2237	0	C25 H30 F6 N3 O2	(M+H)+	✓
518.2237	518.225	1.3	C27 H32 F6 O3	(M+H)+	
518.2237	518.2223	-1.4	C23 H28 F6 N6 O	(M+H)+	
518.2237	518.2255	1.8	C12 H28 F6 N12 O4	(M+H)+	
540.205	540.2029	-2	C21 H25 F6 N9 Na	(M+Na)+	
540.205	540.2029	-2	C22 H31 F6 N2 Na O5	(M+Na)+	

MS Spectrum



MFE MS Zoomed Spectrum



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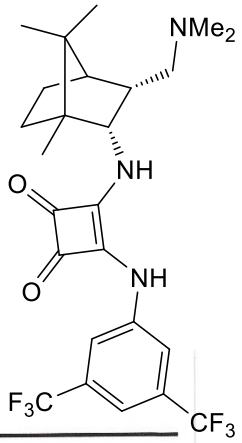
3-((3,5-Bis(trifluoromethyl)phenyl)amino)-4-(((1*S*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl)amino)cyclobut-3-ene-1,2-dione (9b)



Qualitative Compound Report

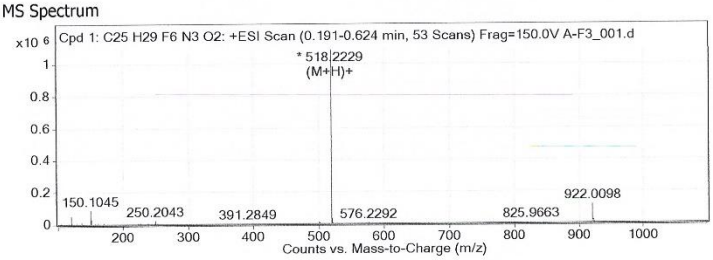
Data File	A-F3_001.d	**Sample Name**	A-F3
Sample Type	Sample	**Position**	Vial 4
Instrument Name	US10310002	**User Name**	TOF-PC\admin
Acq Method	Bypass.m	**Acquired Time**	7/25/2023 10:05:36 AM
IRM Calibration Status	Success	**DA Method**	Damijana.m
Comment			

Compound Label	*m/z*	RT	Algorithm	Mass
Cpd 1: C25 H29 F6 N3 O2	518.2235	0.253	Find by Molecular Feature	517.2162

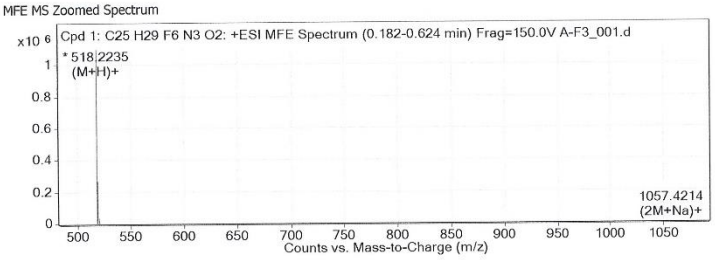
Compound Identification Results

Ion Mass	Calc Ion Mass	Difference	IonFormula	IonSpecies	Best
518.2235	518.2237	0.2	C25 H30 F6 N3 O2	(M+H)+	✓
518.2235	518.2223	-1.1	C23 H28 F6 N6 O	(M+H)+	
518.2235	518.225	1.5	C27 H32 F6 O3	(M+H)+	
540.2046	540.2029	-1.7	C21 H25 F6 N9 Na	(M+Na)+	
518.2235	518.2255	2	C12 H28 F6 N12 O4	(M+H)+	
518.2235	518.221	-2.5	C22 H32 F6 N2 O5	(M+H)+	

MS Spectrum



MFE MS Zoomed Spectrum



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6. X-Ray crystallography

Table S1. Crystal data and structure refinement for compound **8a**.

Empirical formula	$C_{28}H_{33}Cl_6F_6N_2O_2$
Formula weight	770.27
Temperature/K	150.00(14)
Crystal system	Monoclinic
Space group	$P2_1$
a [Å^3]	12.4392(4)
b [Å^3]	11.2805(3)
c [Å^3]	12.7042(4)
α [°]	90
β [°]	92.136(3)
γ [°]	90
V [Å^3]	1781.42(9)
Z	2
ρ_{calc} [g/cm^3]	1.436
μ [mm^{-1}]	0.544
F(000)	788.0
Crystal size/mm^3	0.5 × 0.3 × 0.2
Radiation	MoKα (λ = 0.71073)
Reflections collected	38098
Independent reflections	9803
R_{int}	0.0378
Data/restraints/parameters	9803/1/411
GOF	1.034
R_1, wR_2 [I>=2σ (I)]	0.0797, 0.2268
R_1, wR_2 (all data)	0.1009, 0.2495
$(\Delta\rho)_{max}$ [e Å^{-3}]	1.63
$(\Delta\rho)_{min}$ [e Å^{-3}]	–0.83
Flack parameter	0.034(18)

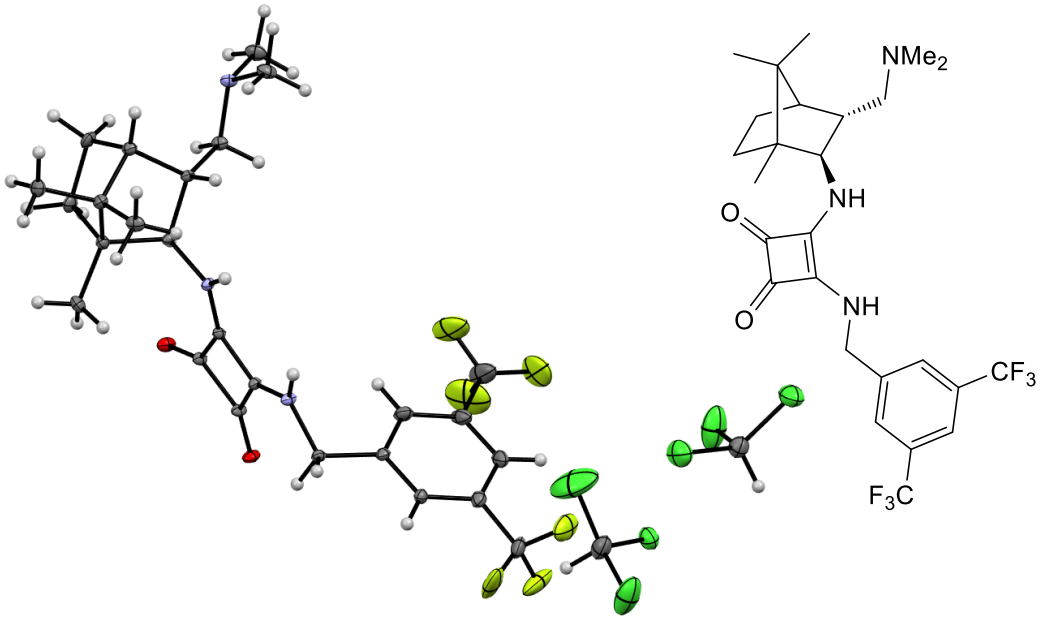

Figure S1. Molecular structure of product **8a**. Thermal ellipsoids are shown at 50% probability.