Electronic Supplementary Material (ESI) for RSC Advances.

Semi-synthesis, α-amylase inhibition, kinetic and molecular docking studies of arylidenes-based sesquiterpene coumarin isolated from *Ferula tunetana* POMEL ex BATT.

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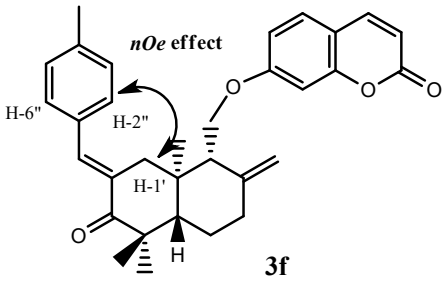
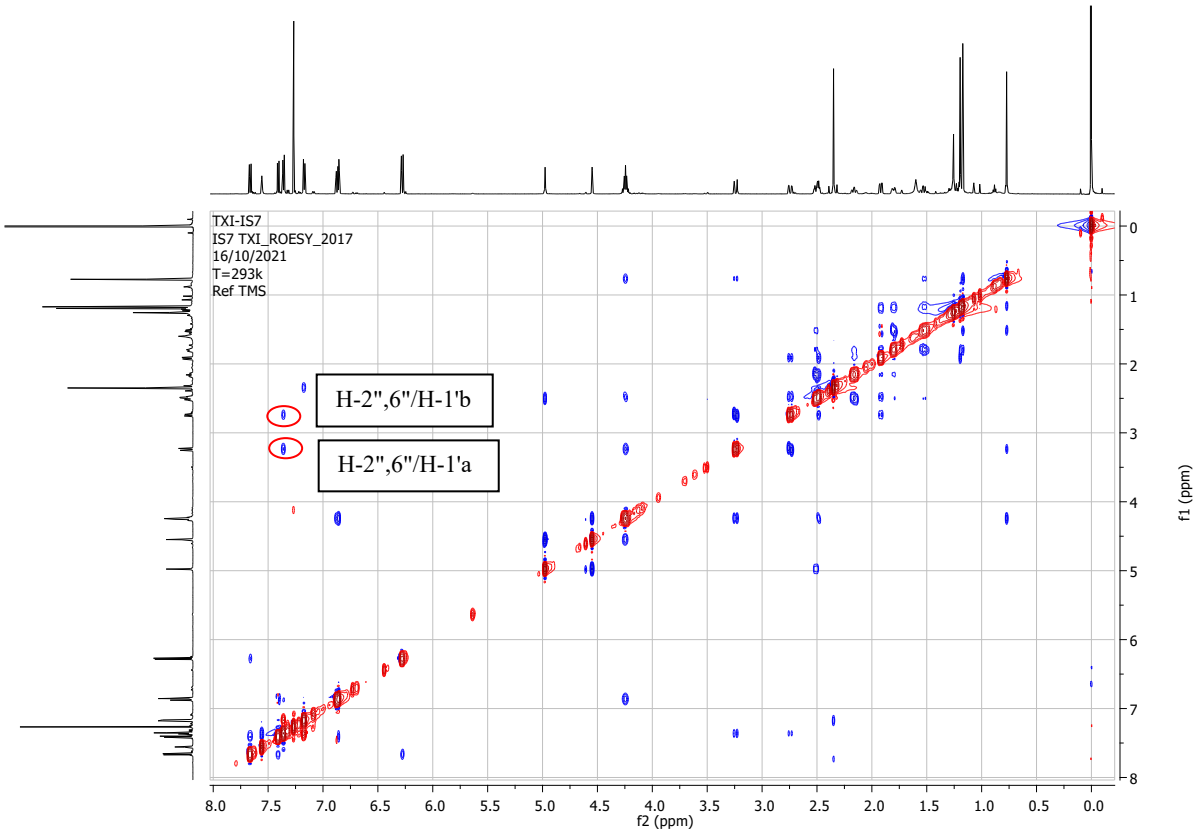
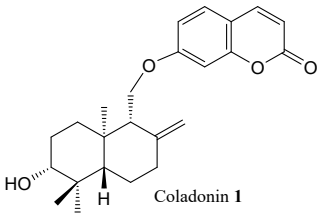


3f

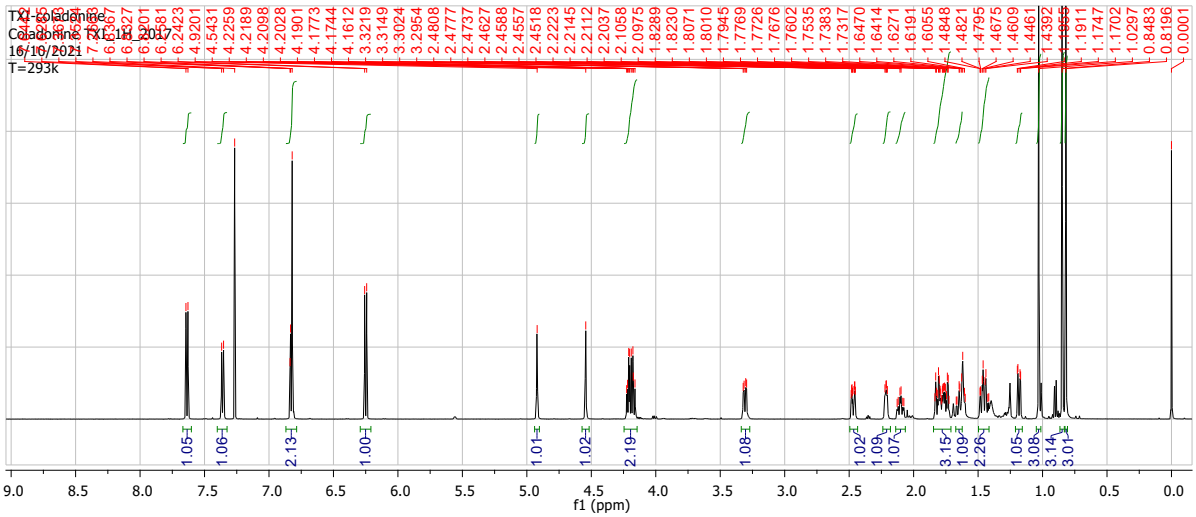


ROSY NMR spectrum of compound 3f

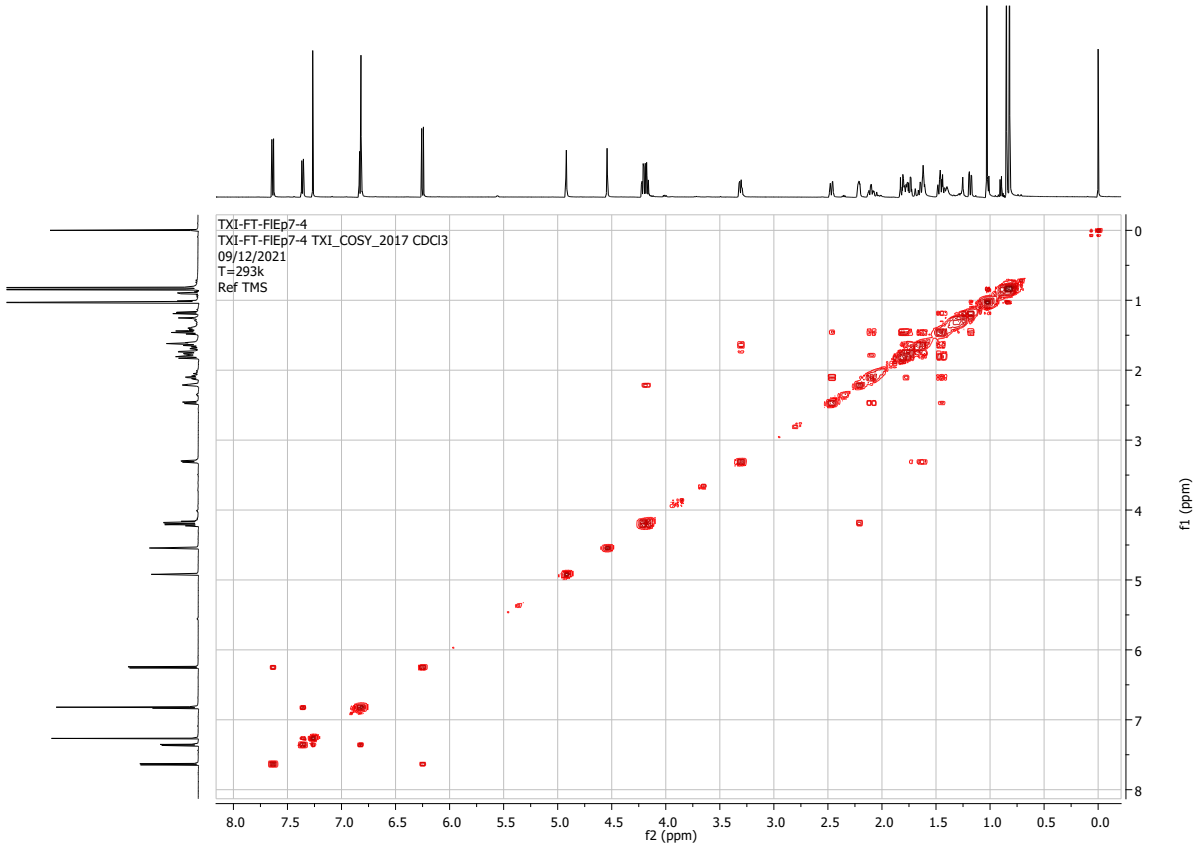
❖ S2: ^{1}H, HSQC and HMBC NMR spectra of compounds 1, 2 and 3a-m



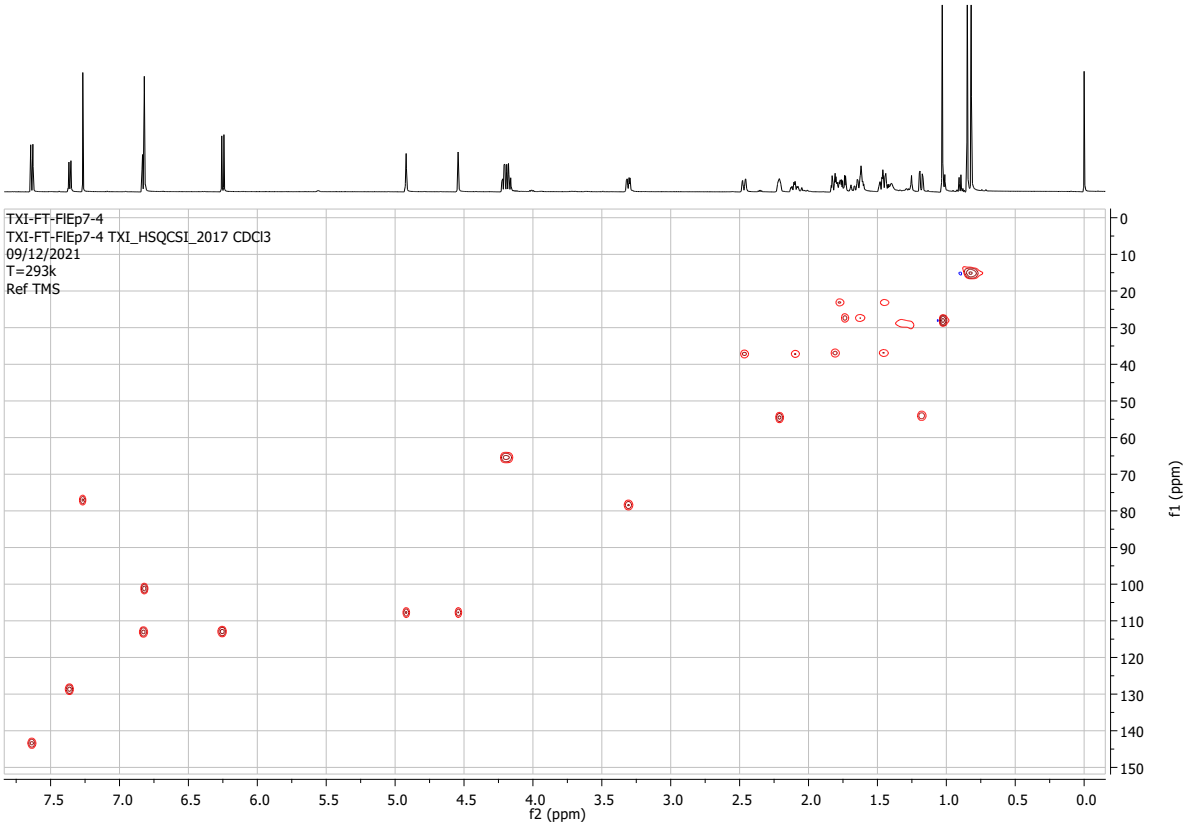
Coladonin **1**



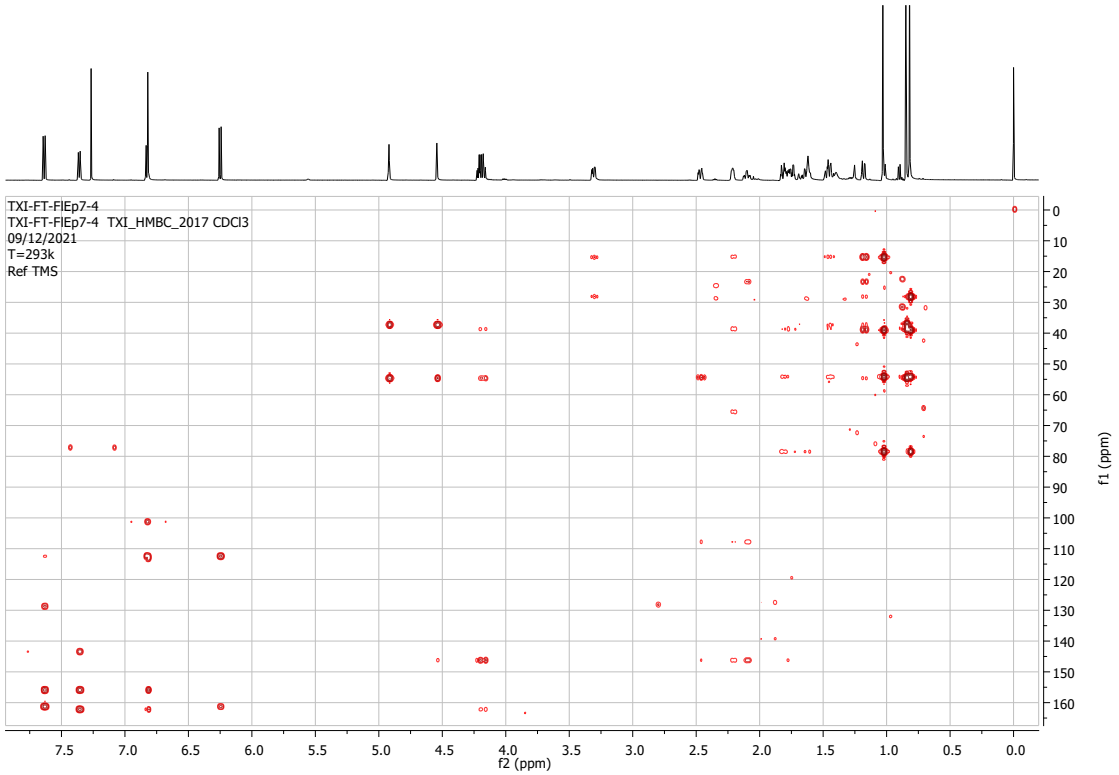
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 1



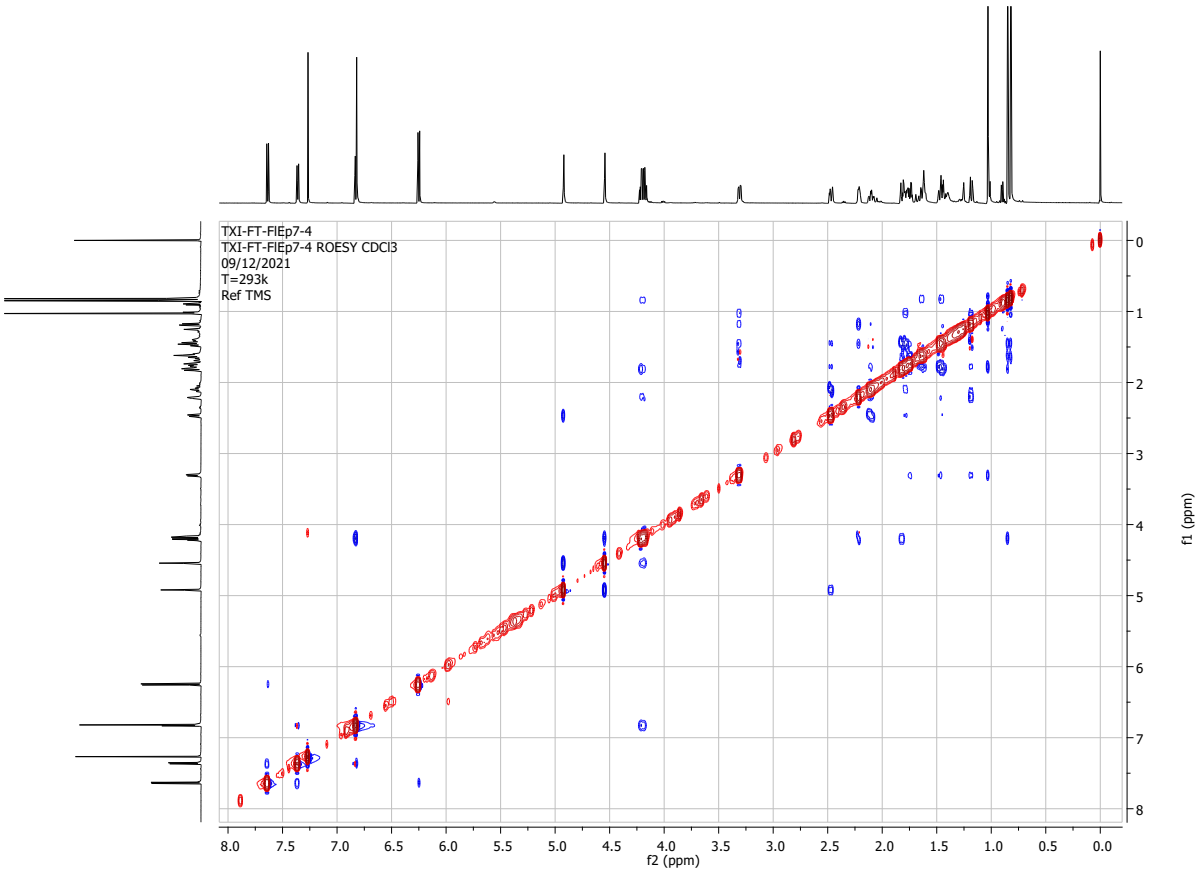
COSY spectrum of compound 1



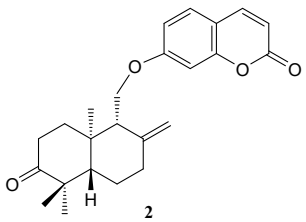
HSQC spectrum of compound 1



HMBC spectrum of compound 1



ROESY spectrum of compound 1



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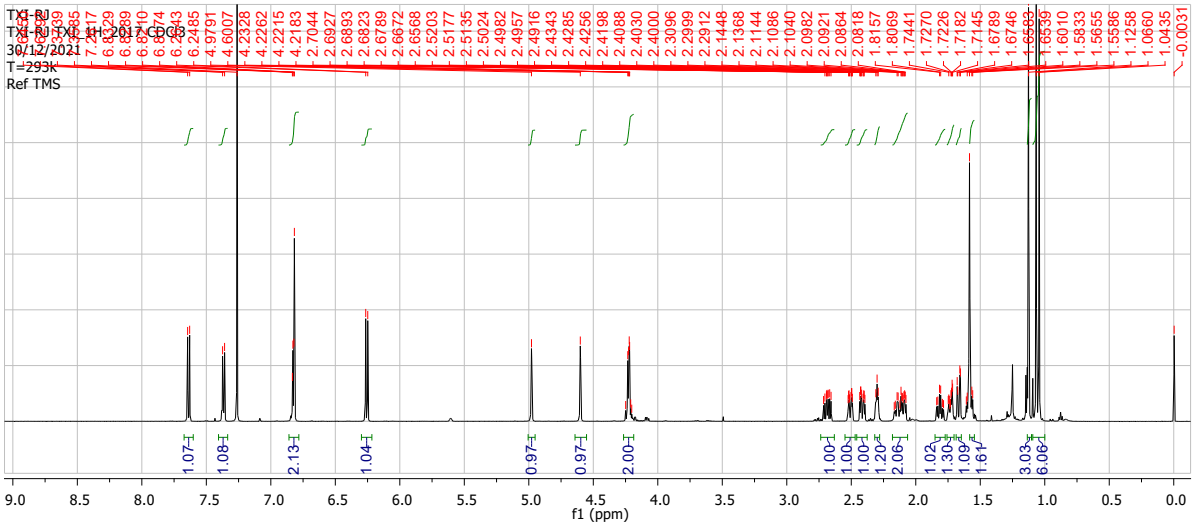
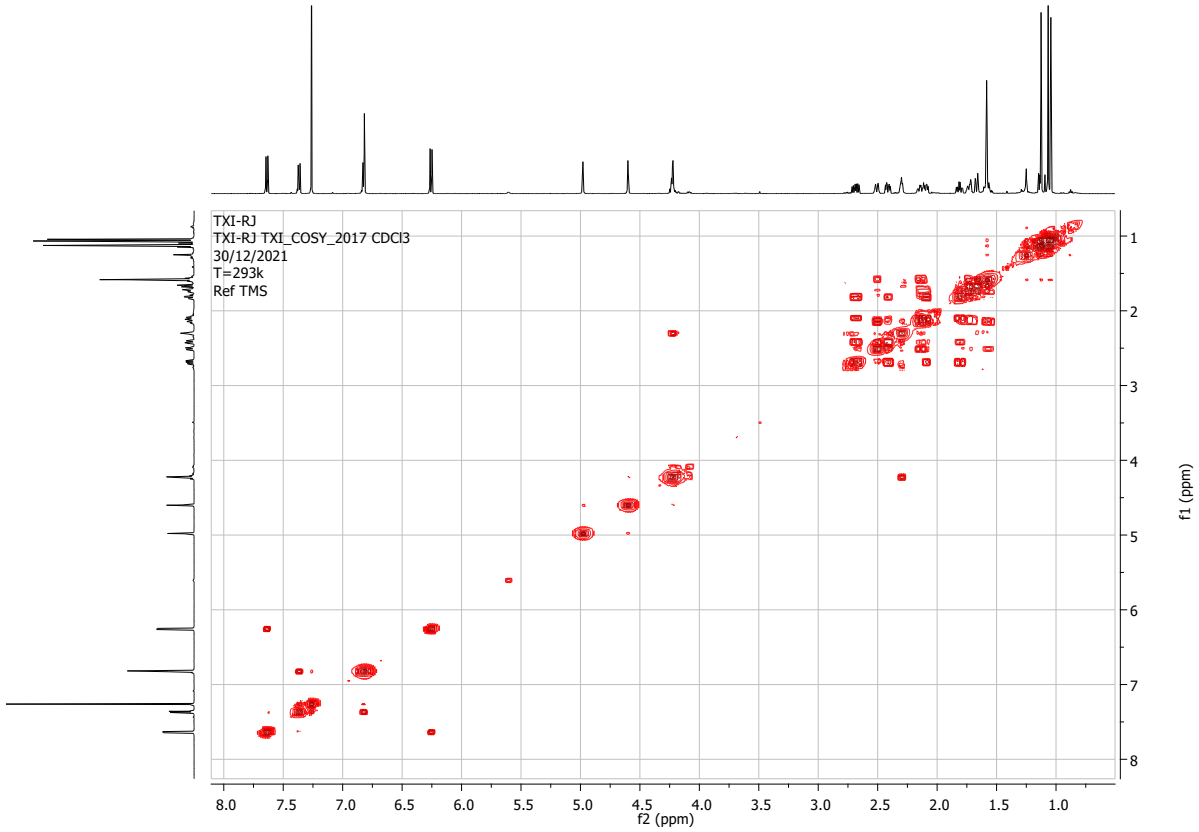
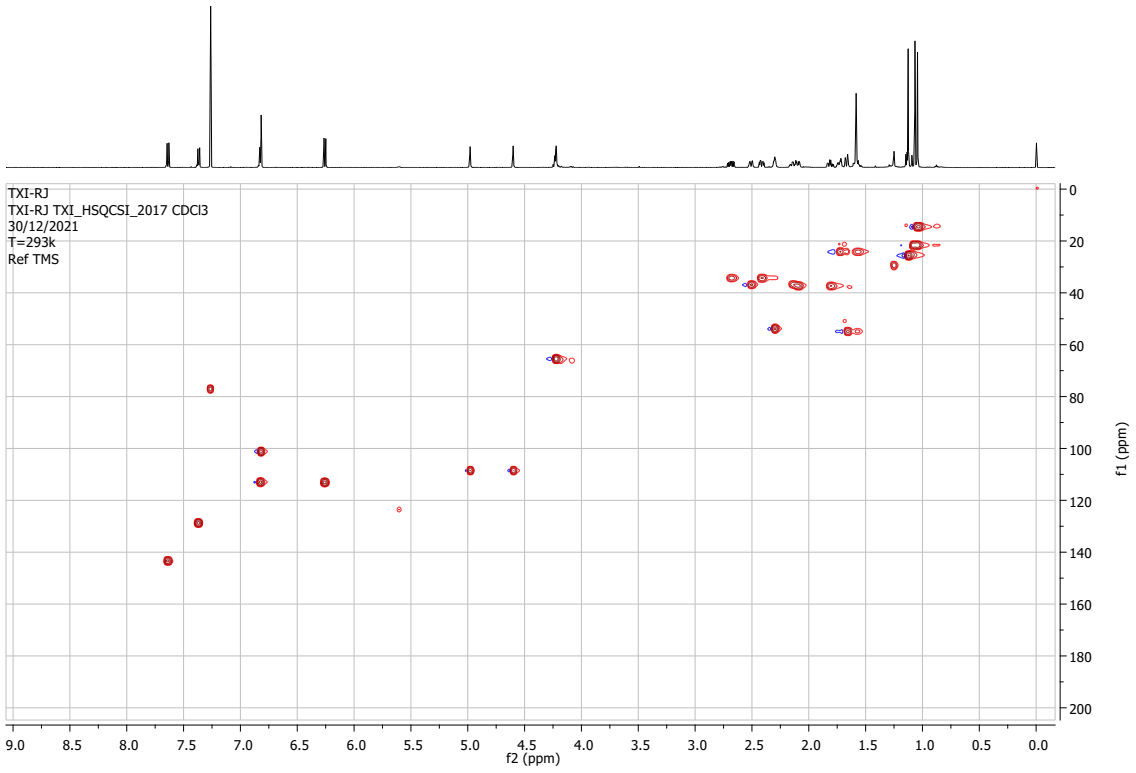


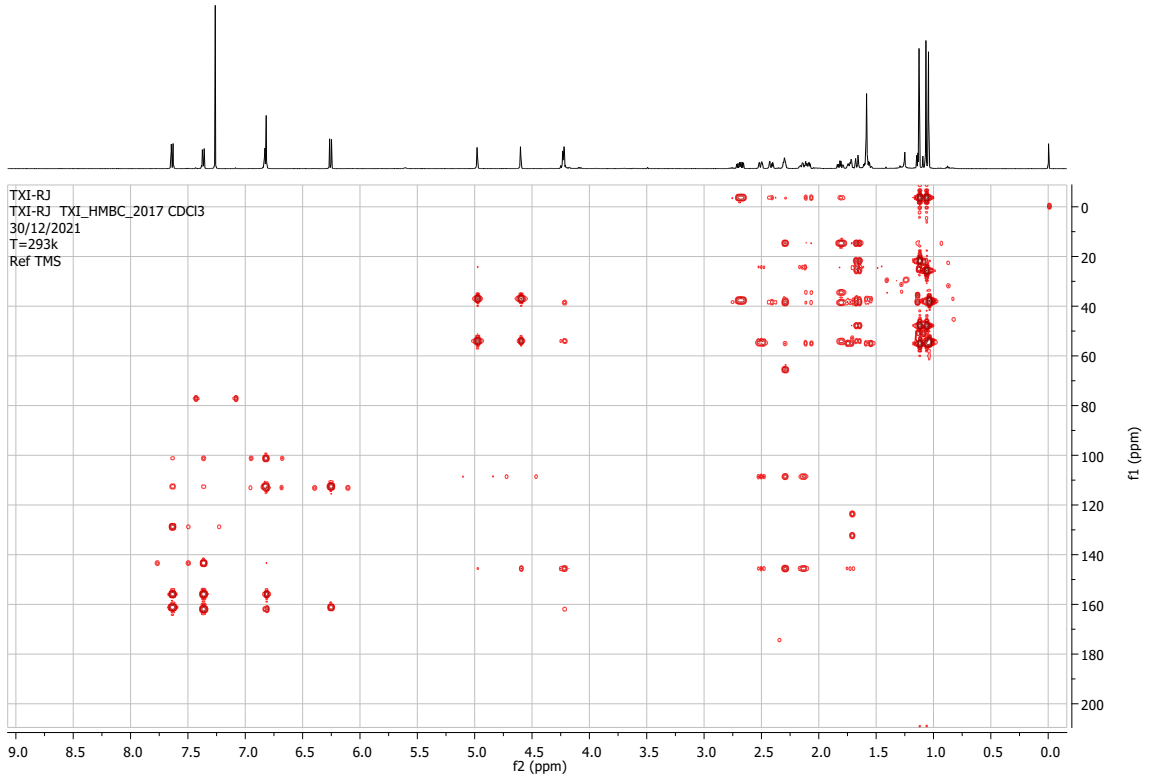
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 2



COSY spectrum of compound 2



HSQC spectrum of compound 2



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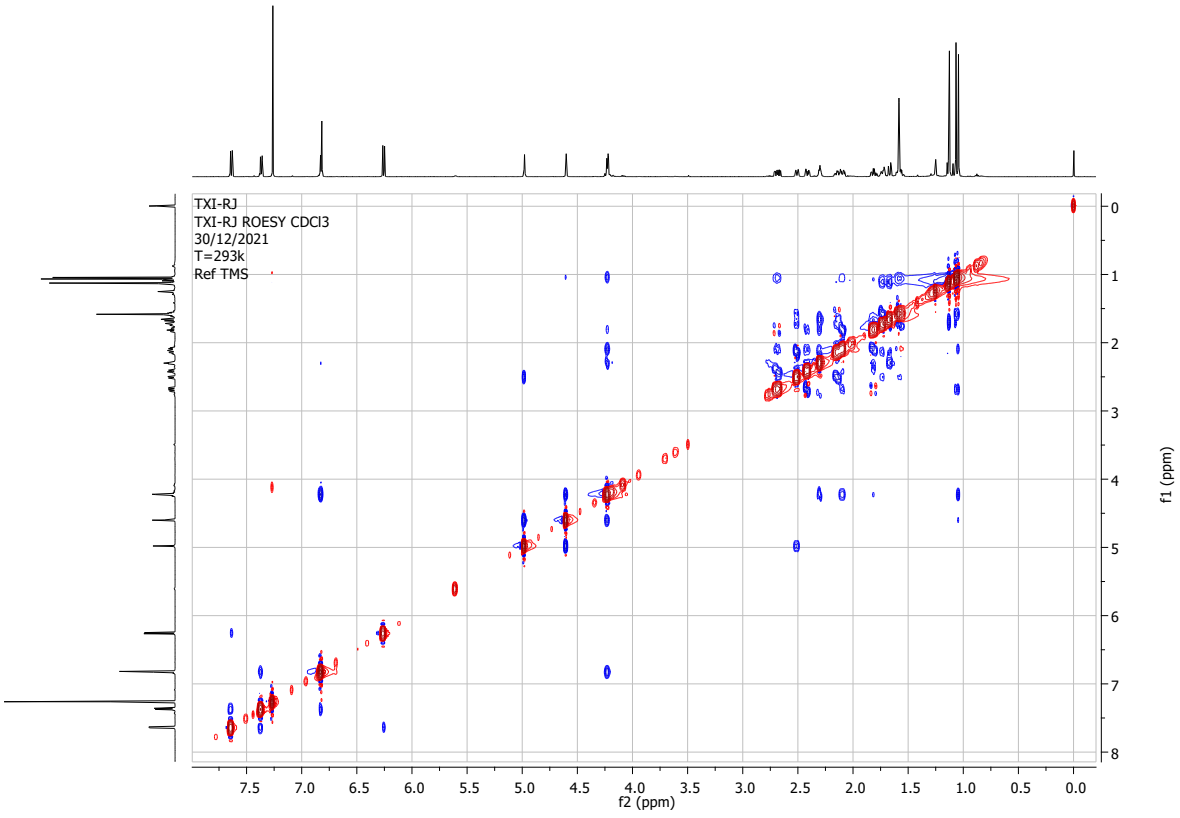
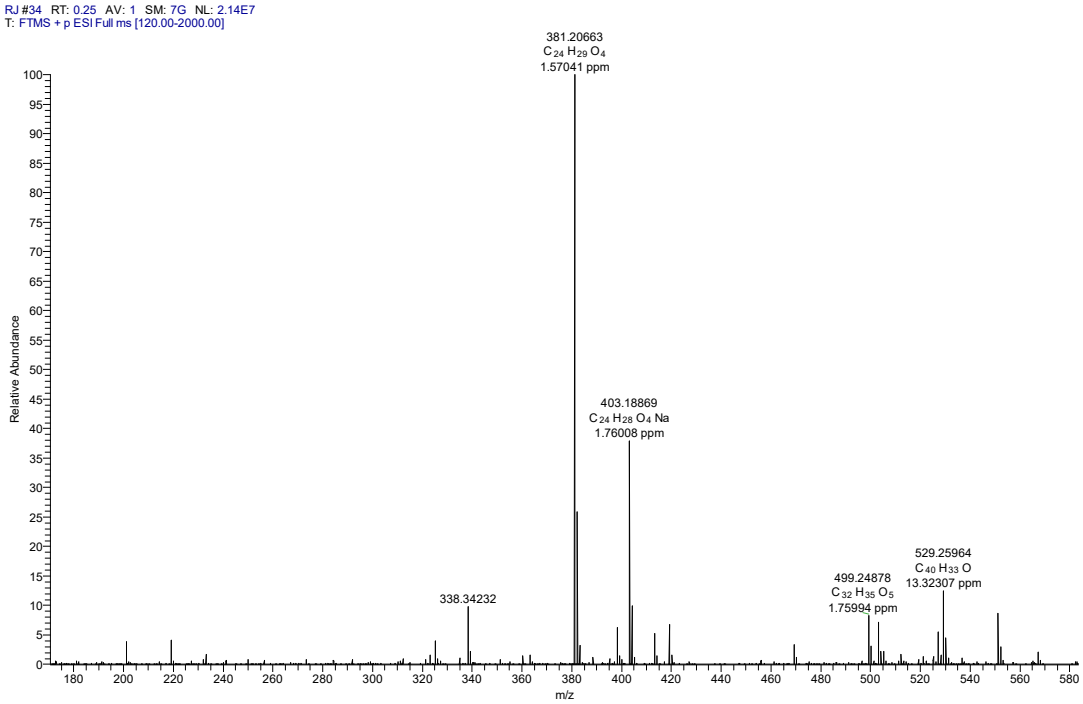
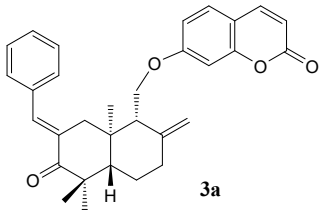


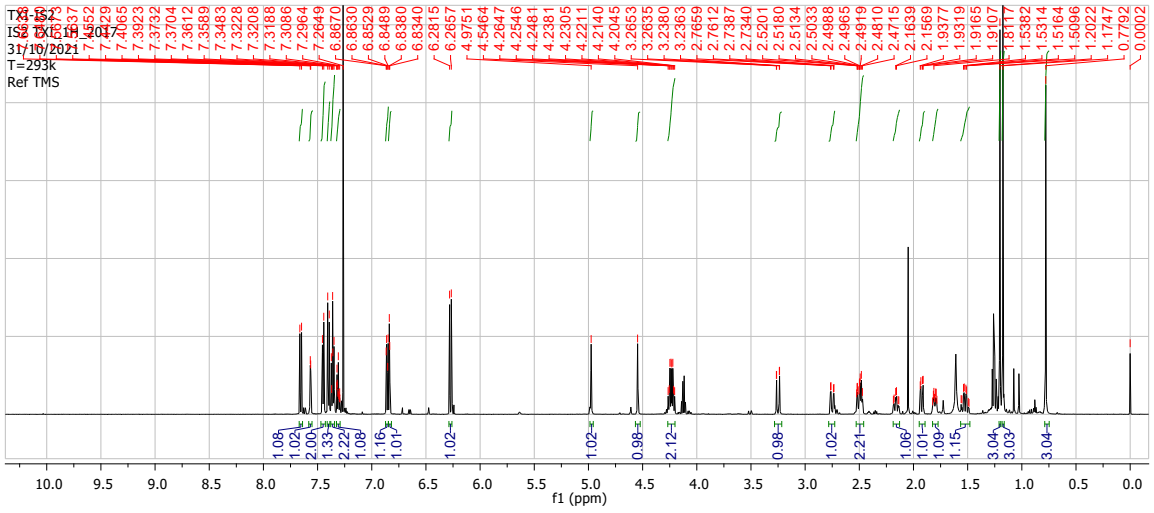
ROESY spectrum of compound 2



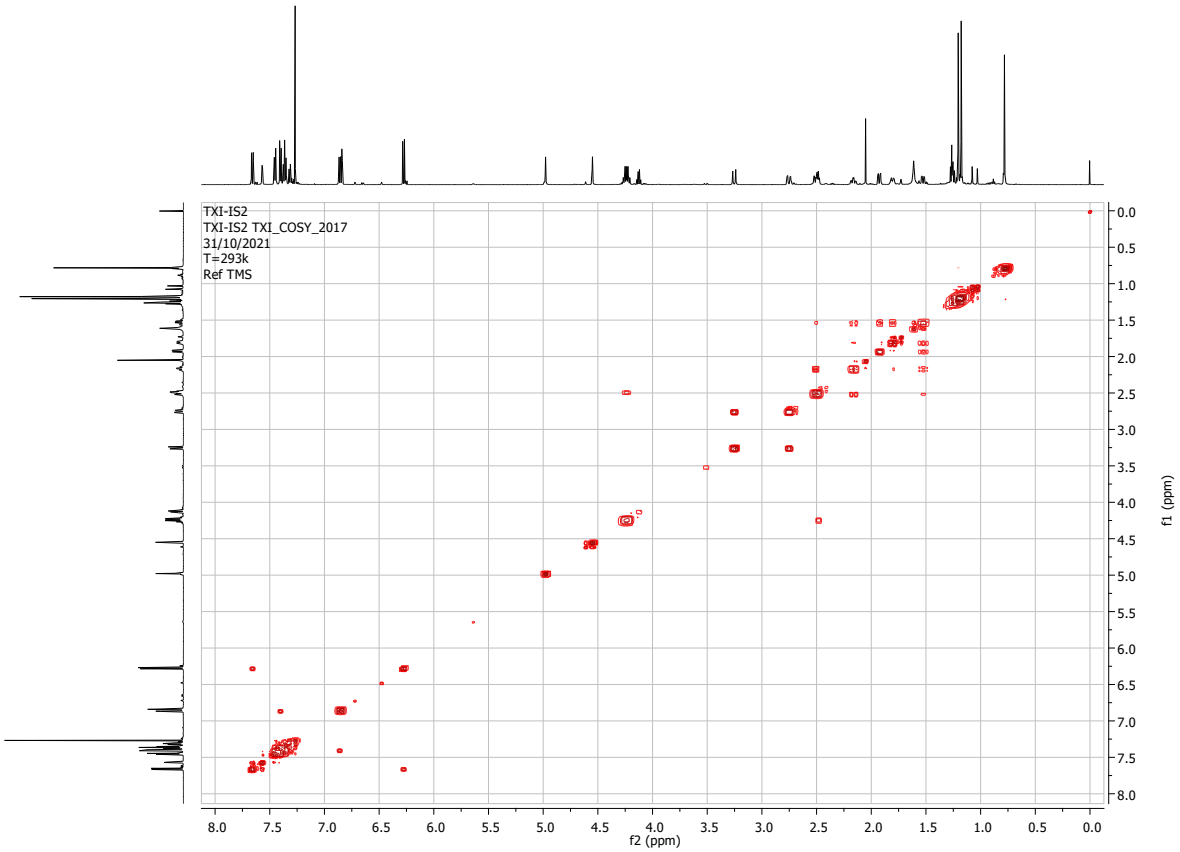
ESI-HRMS spectrum of compound 2



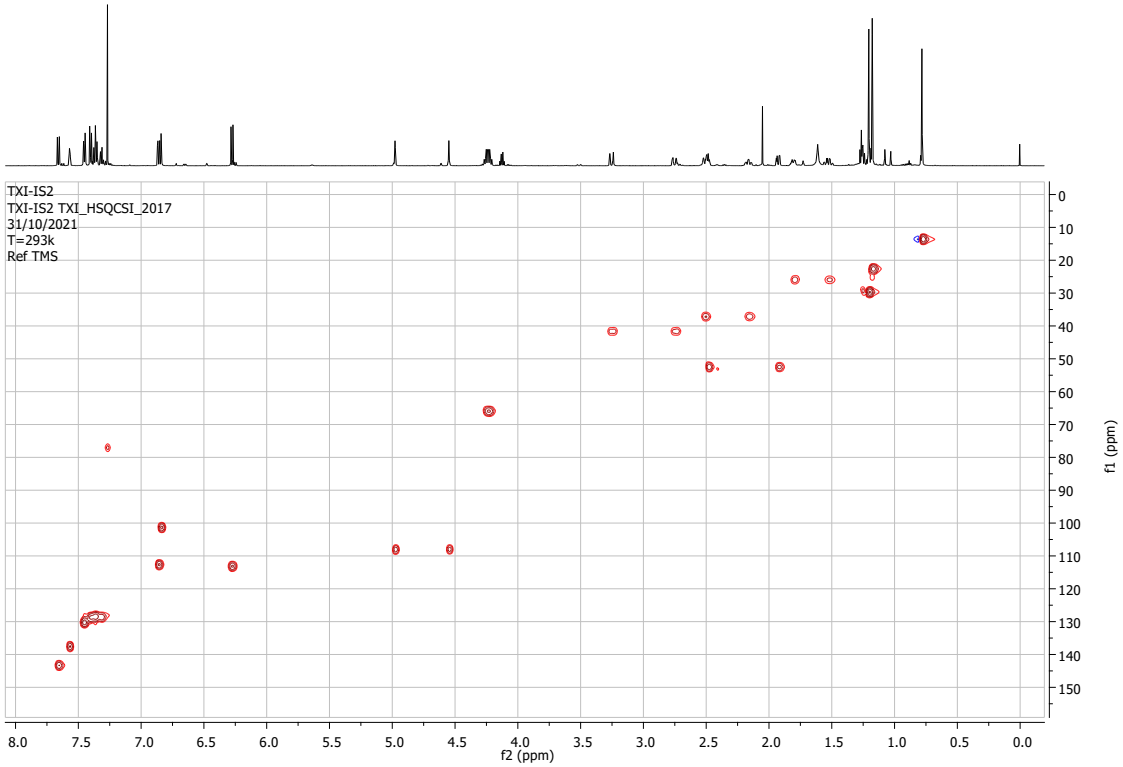
3a



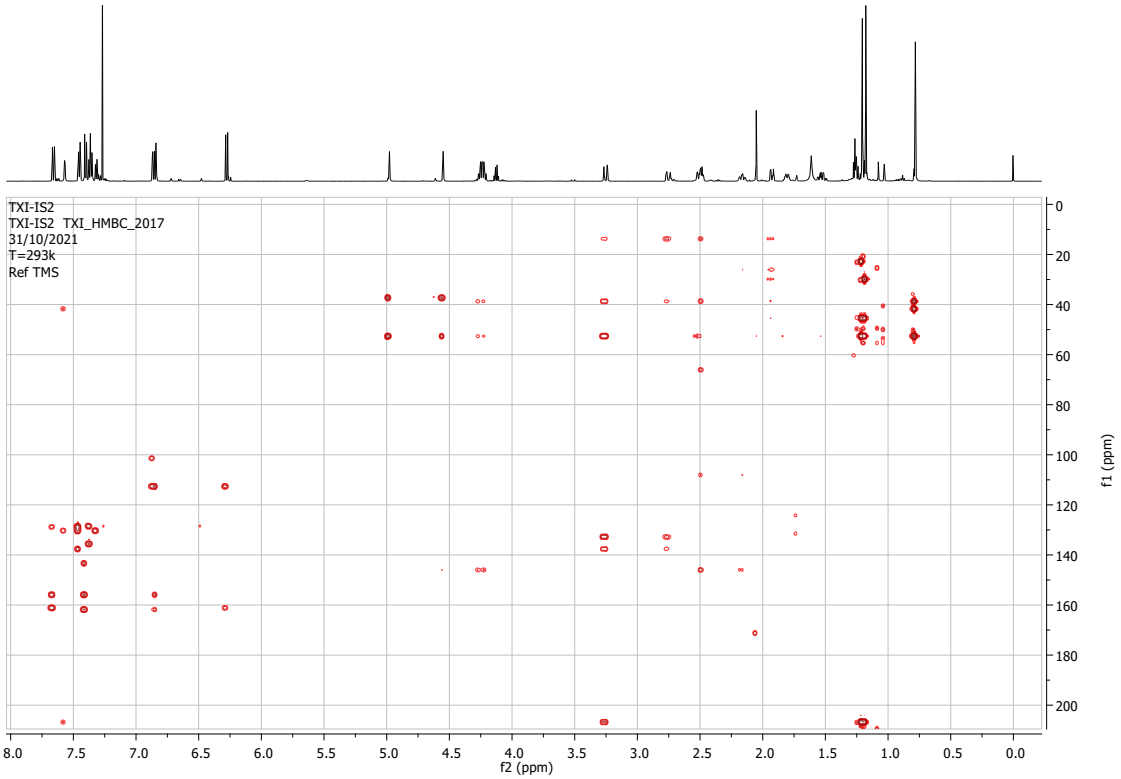
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3a



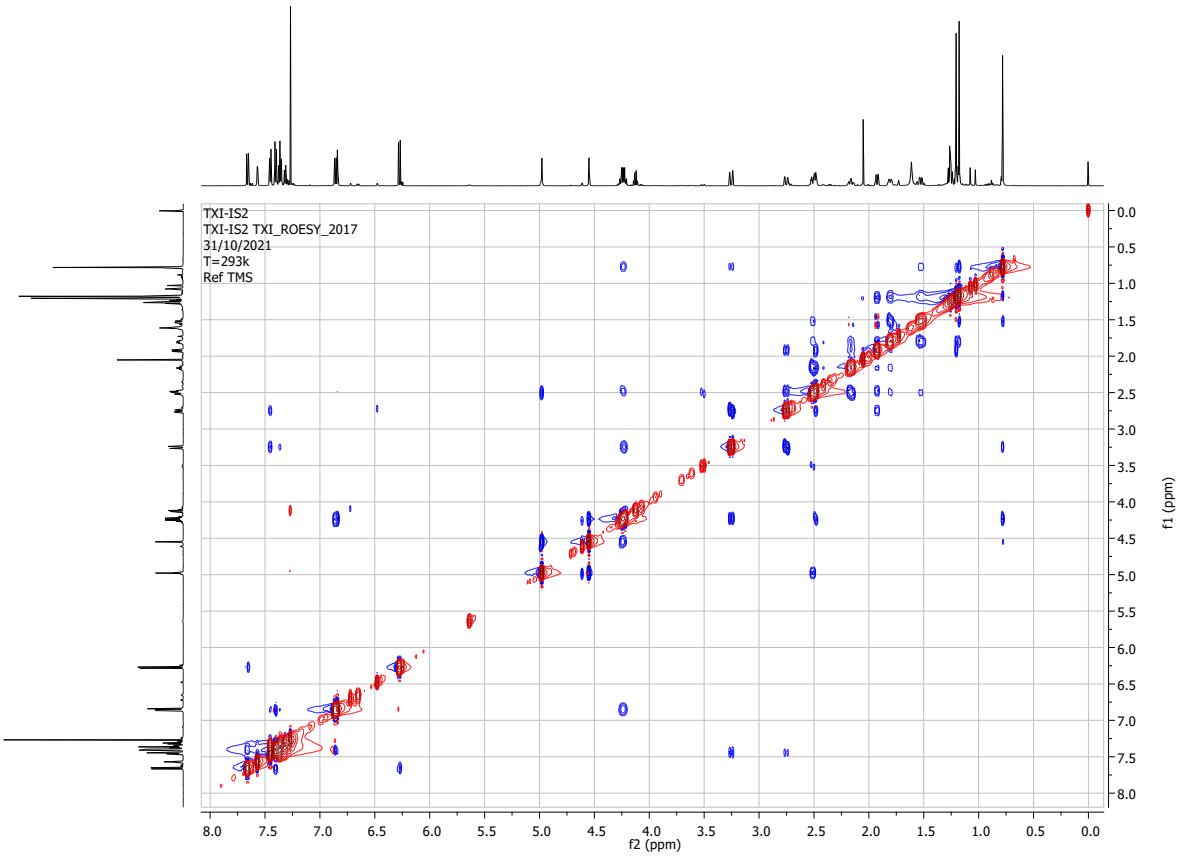
COSY spectrum of compound 3a



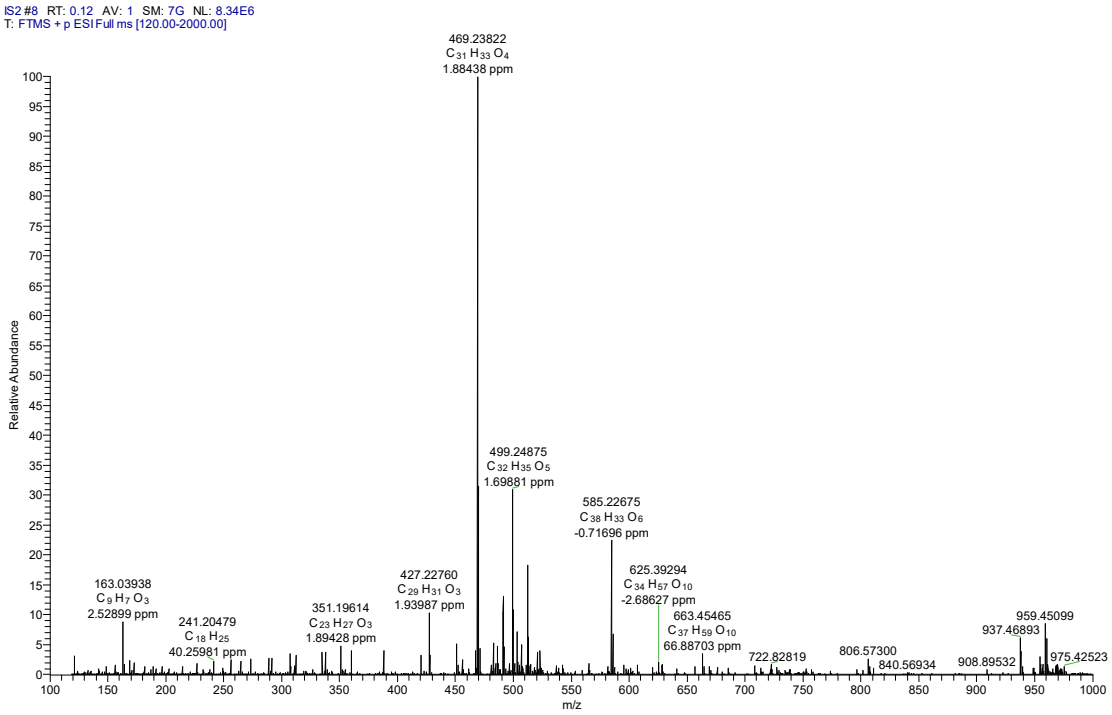
HSQC spectrum of compound 3a



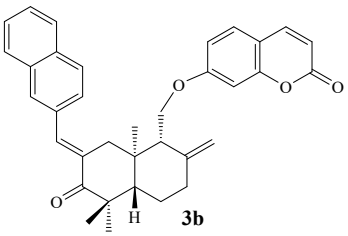
HMBC spectrum of compound 3a



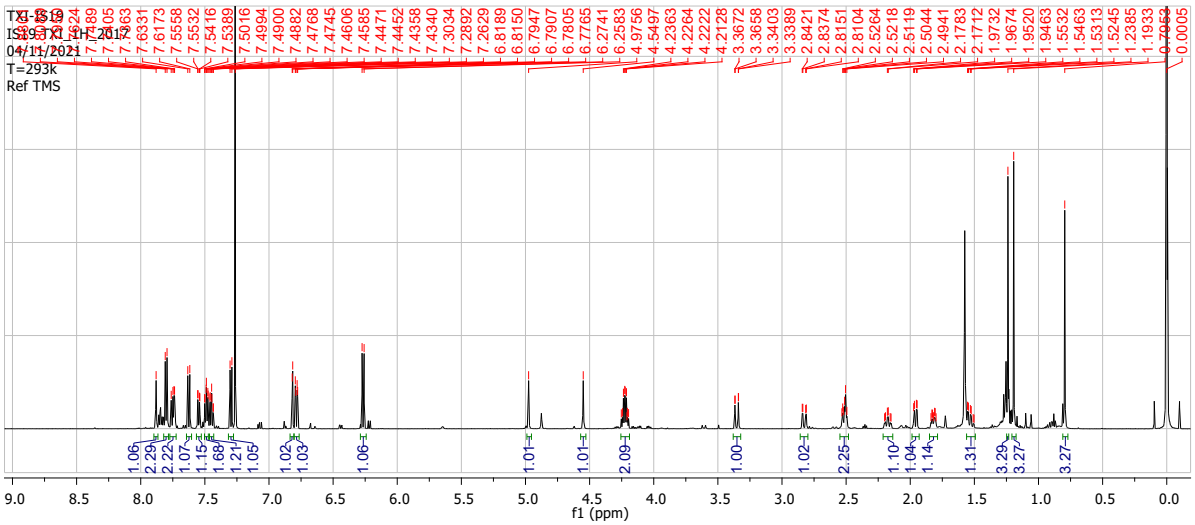
ROESY spectrum of compound 3a



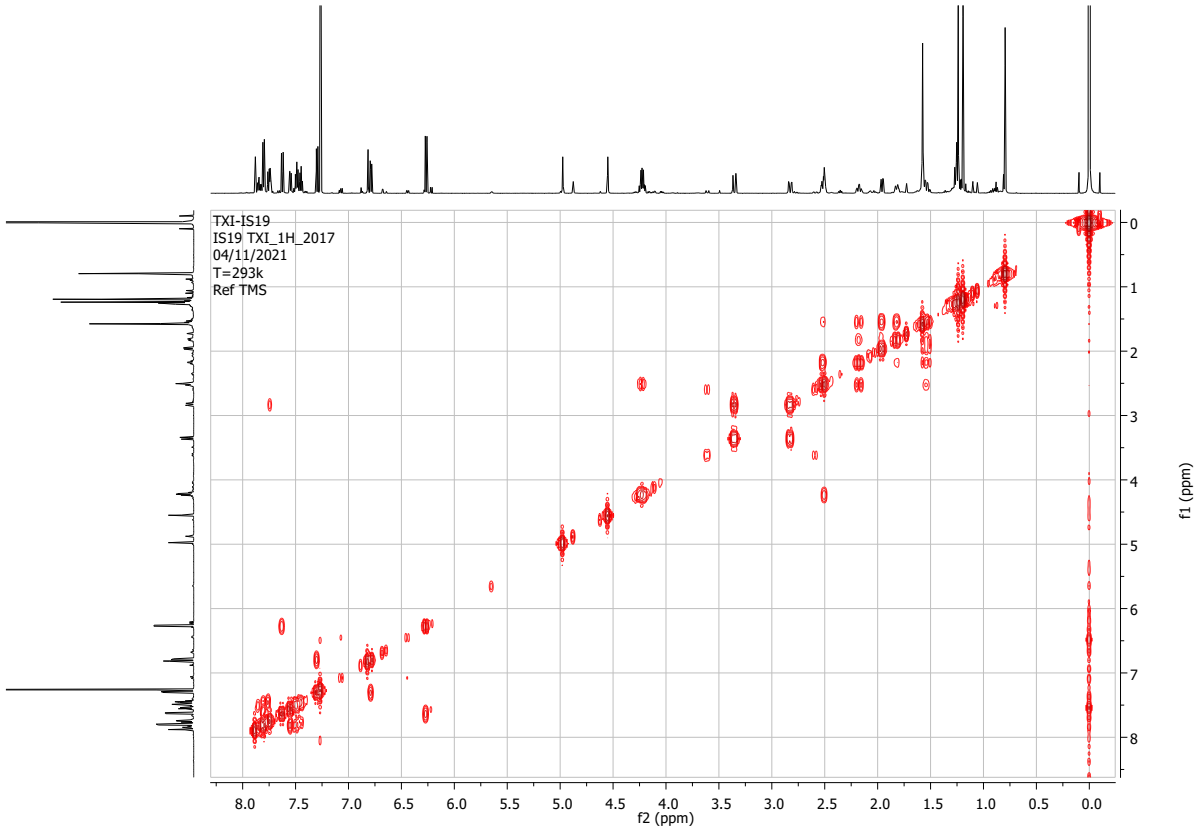
ESI-HRMS spectrum of compound 3a



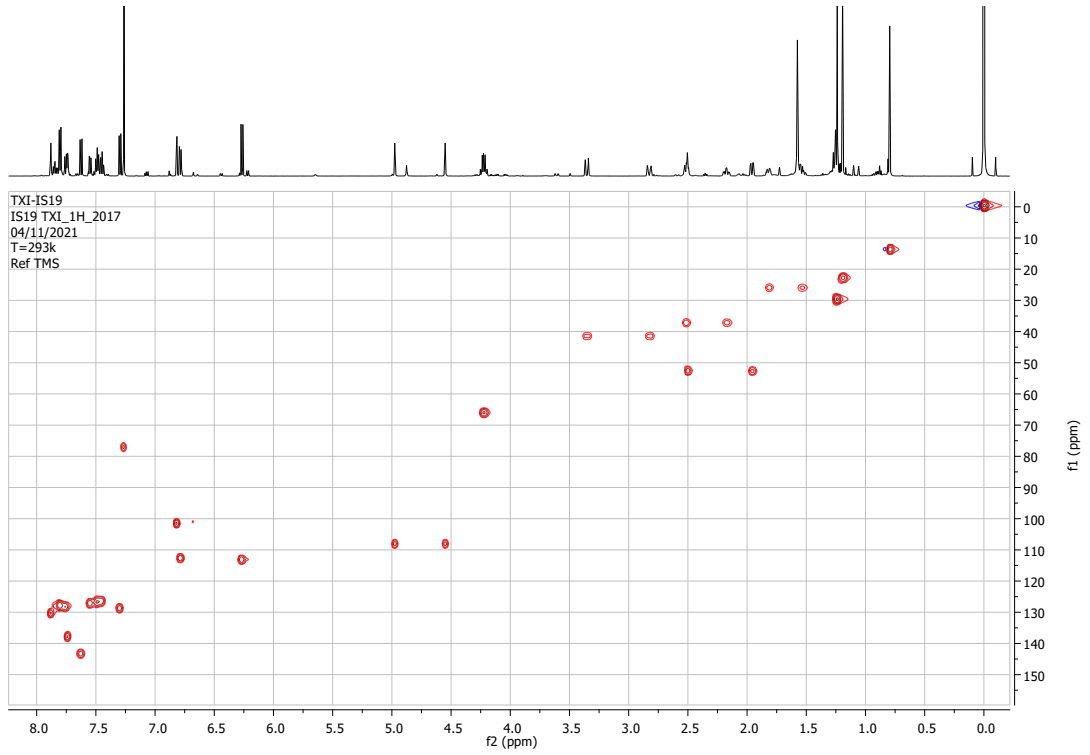
3b



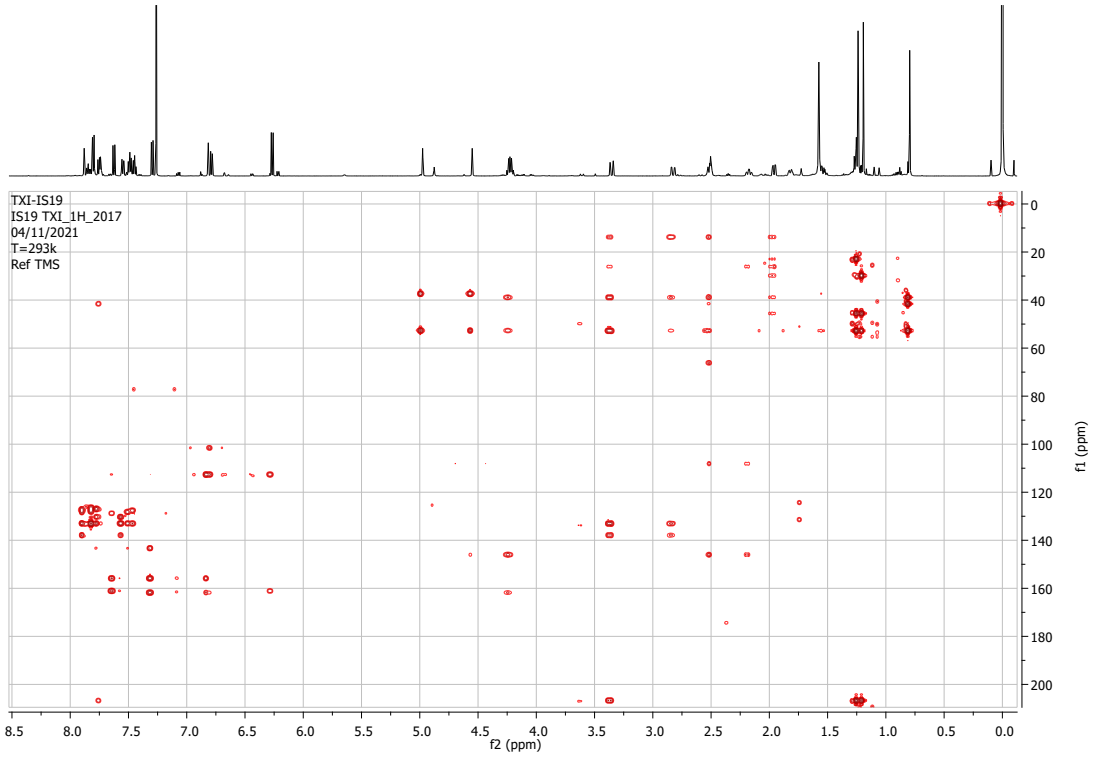
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3b



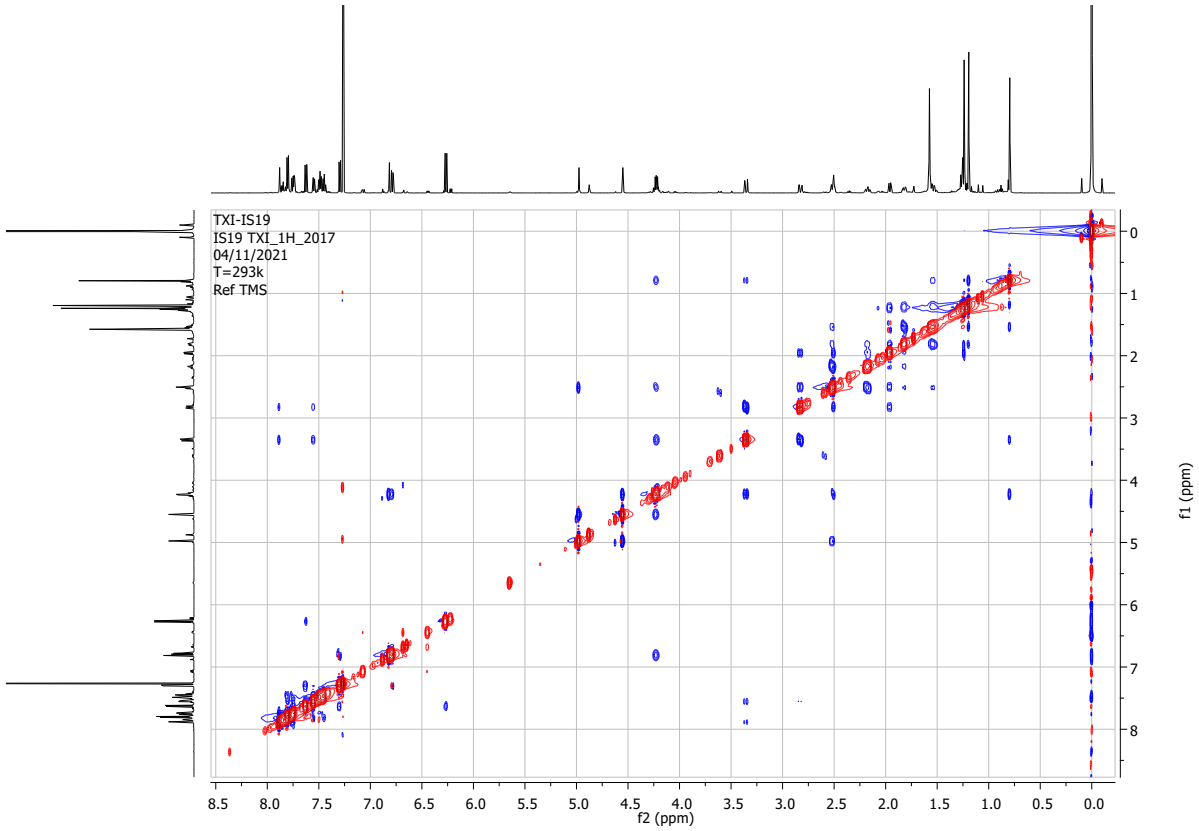
COSY spectrum of compound 3b



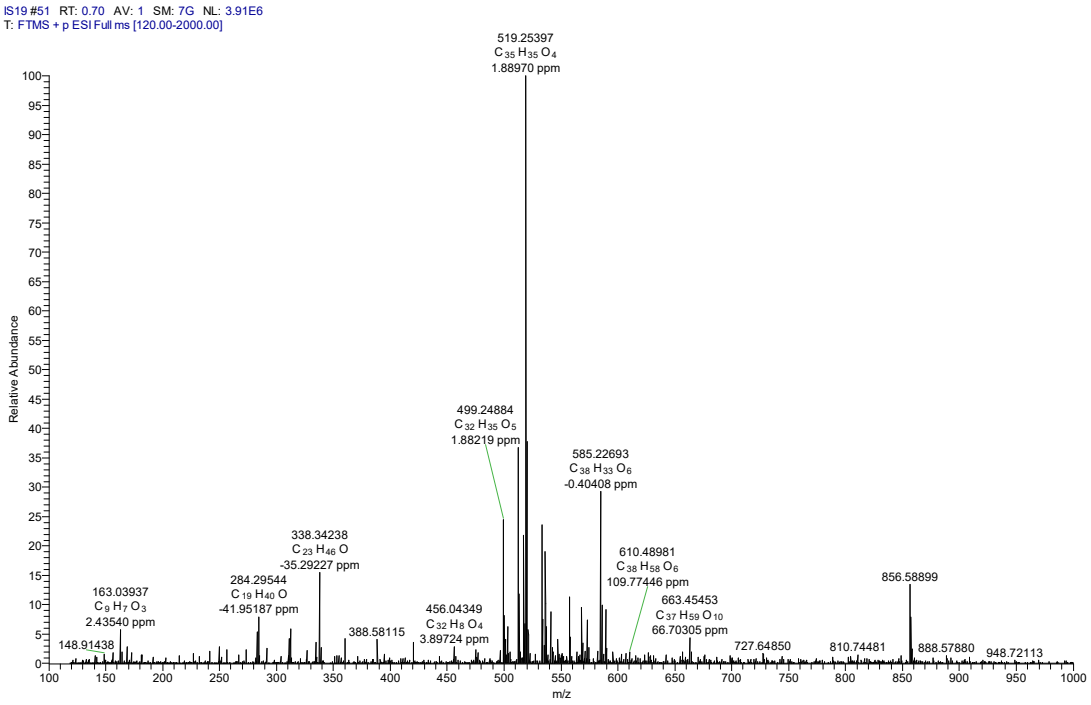
HSQC spectrum of compound 3b



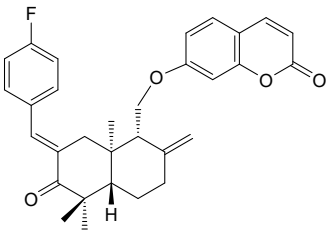
HMBC spectrum of compound 3b



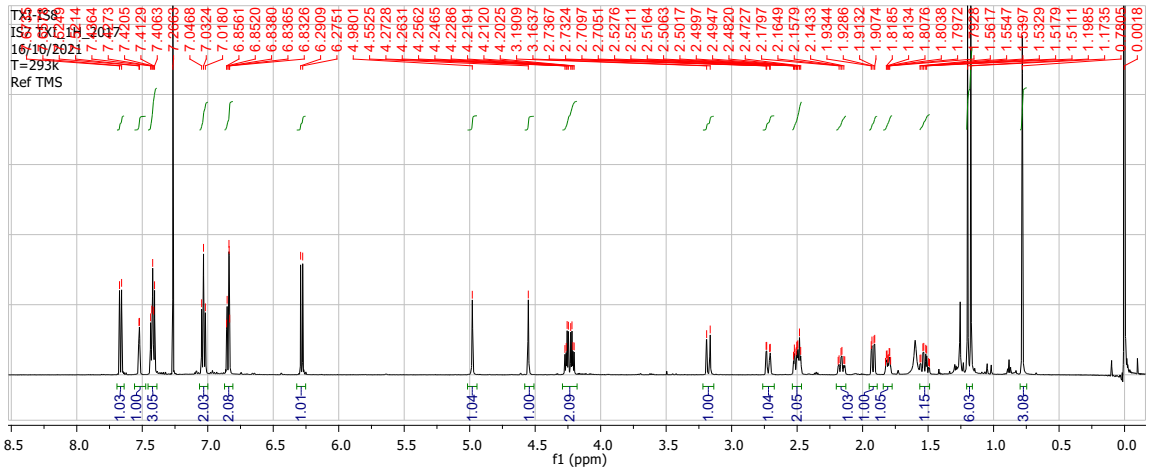
ROESY spectrum of compound 3b



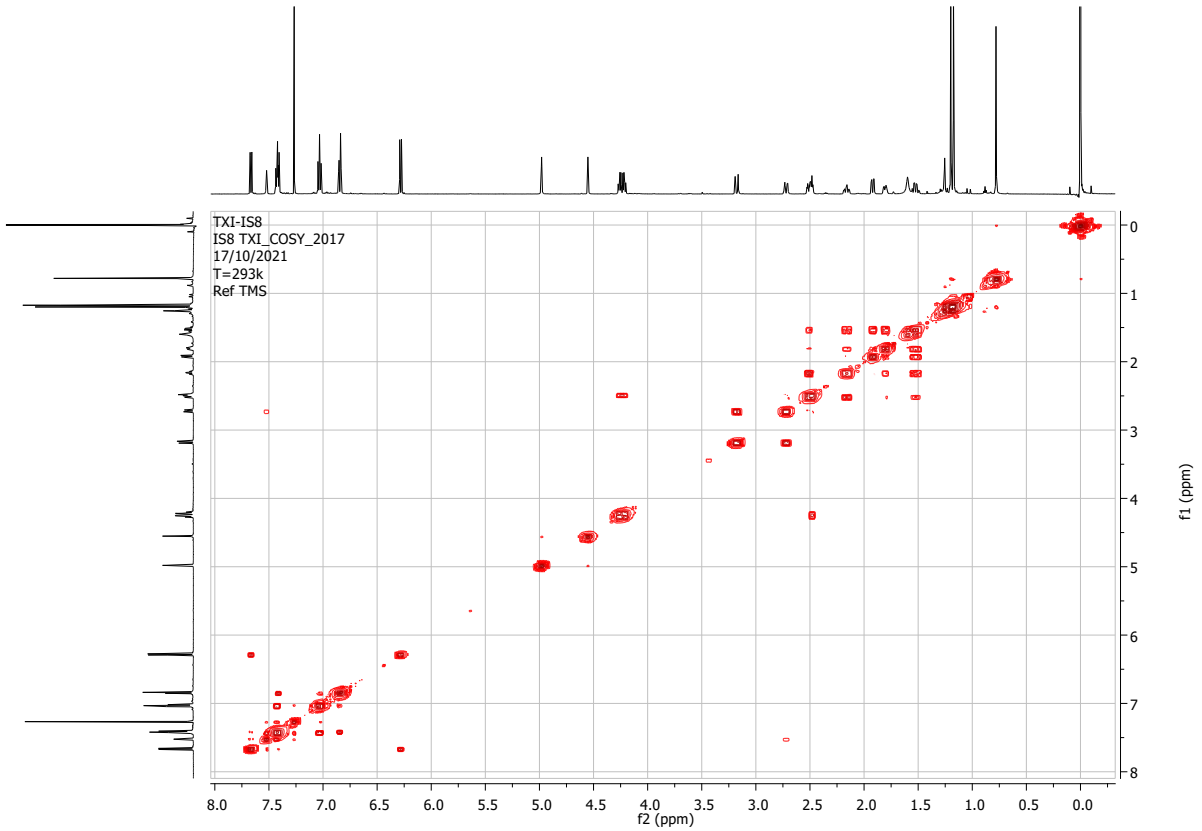
ESI-HRMS spectrum of compound 3b



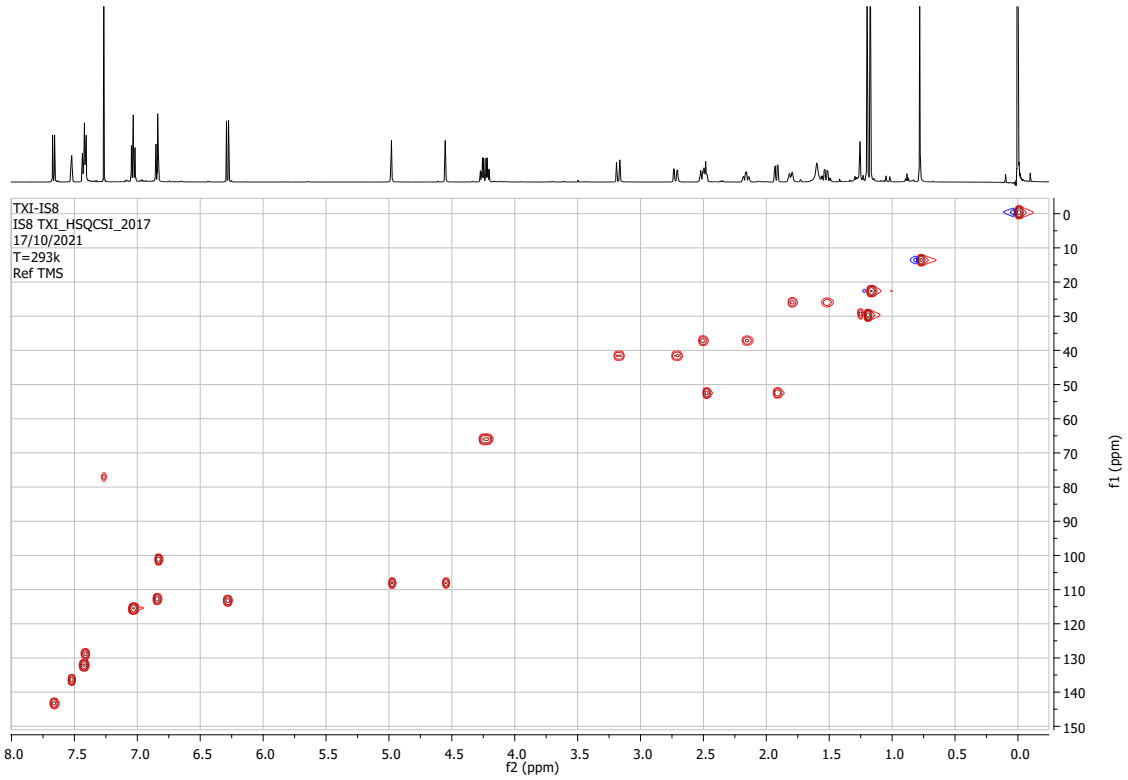
3c



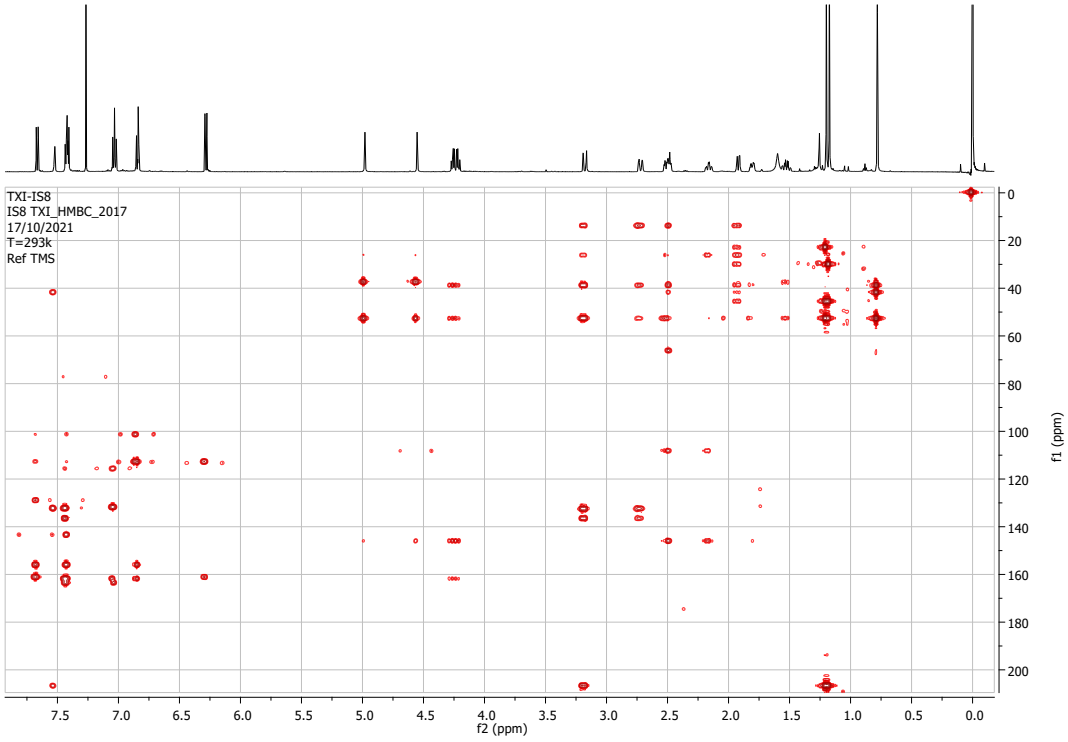
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3c



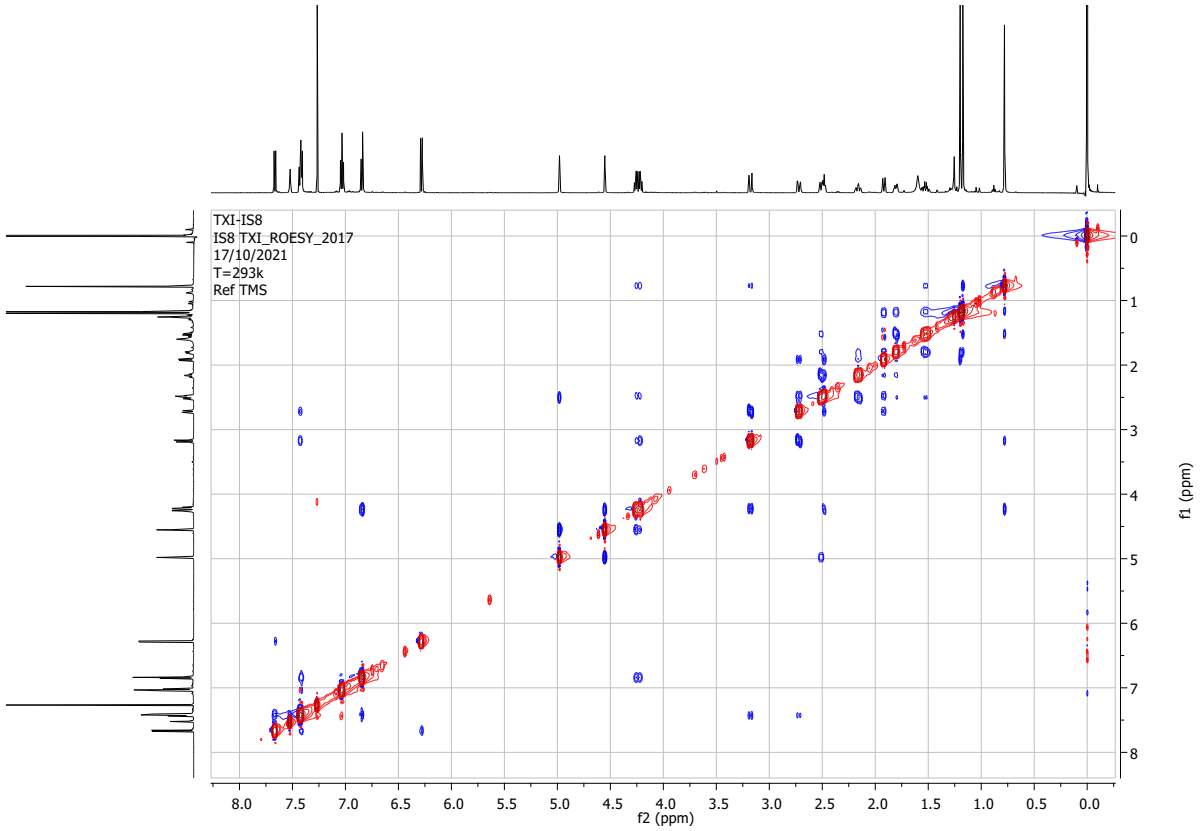
COSY spectrum of compound 3c



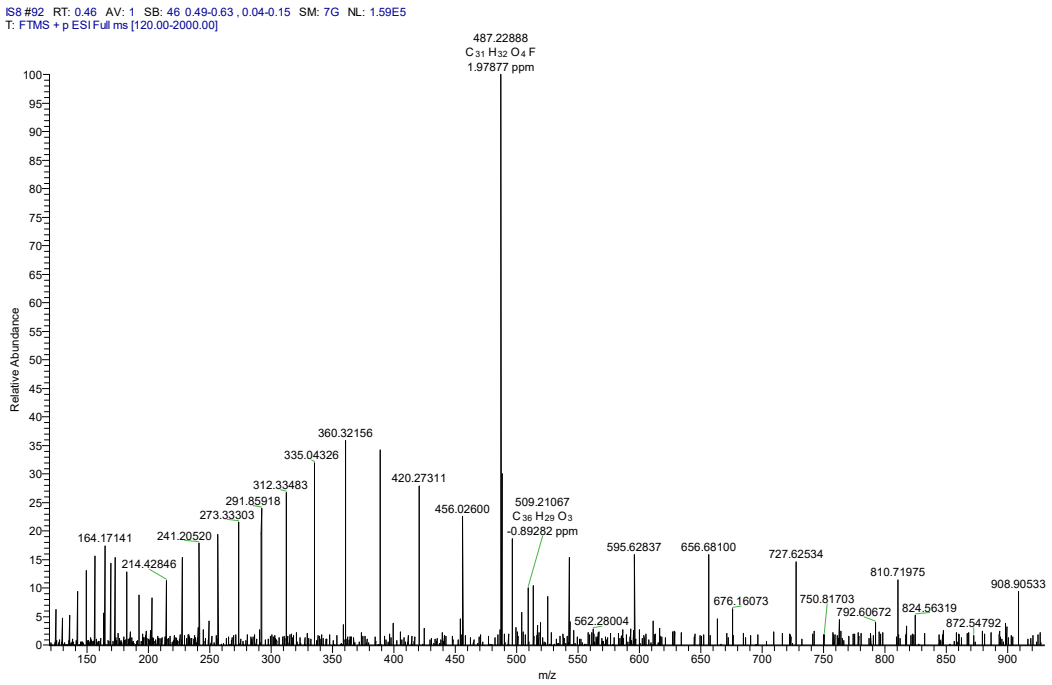
HSQC spectrum of compound 3c



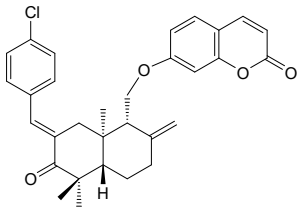
HMBC spectrum of compound 3c



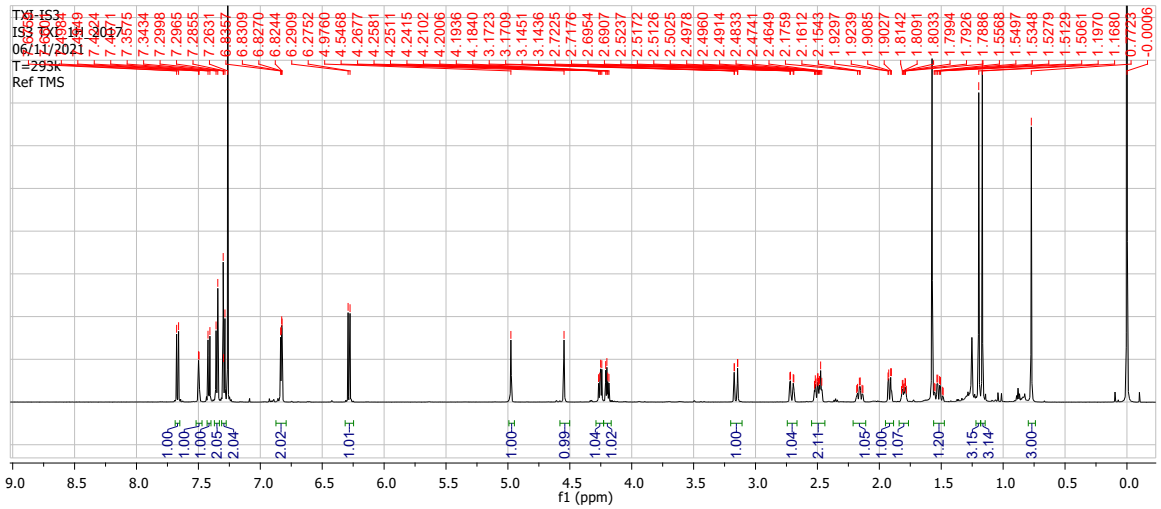
ROESY spectrum of compound 3c



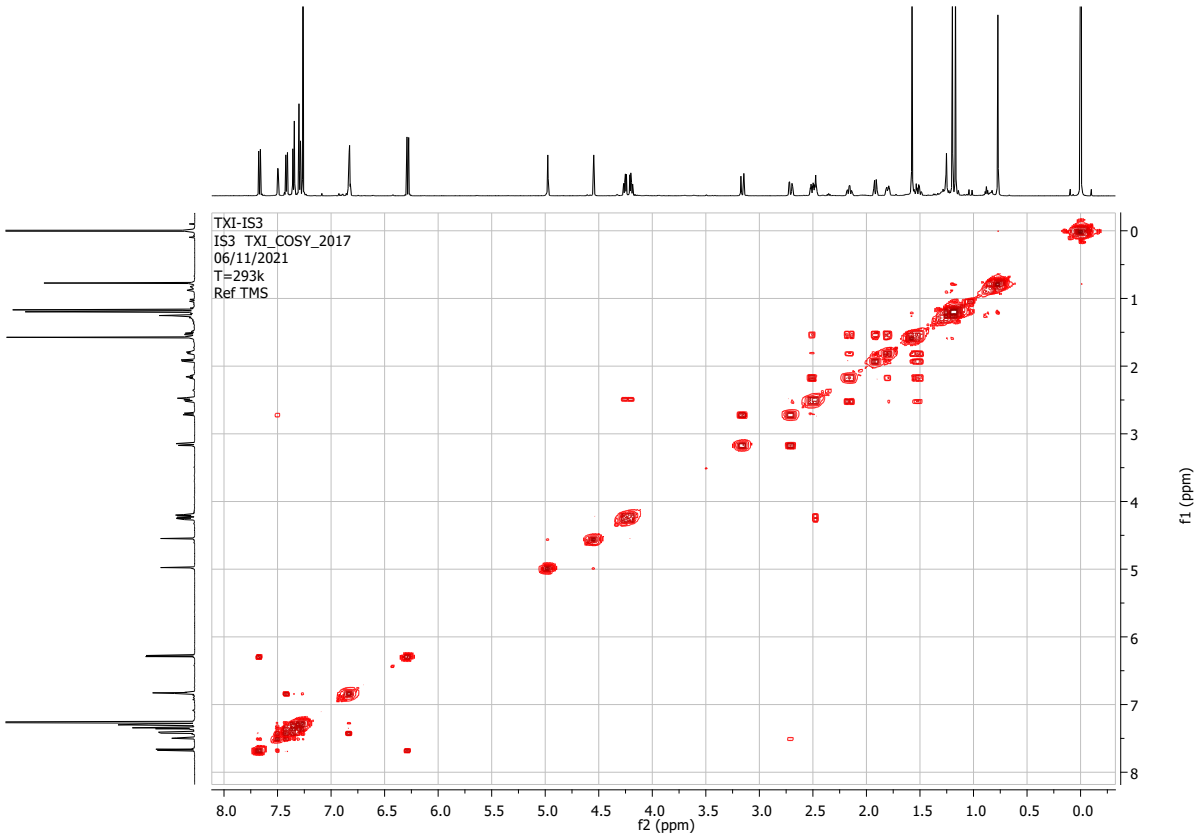
ESI-HRMS spectrum of compound 3c



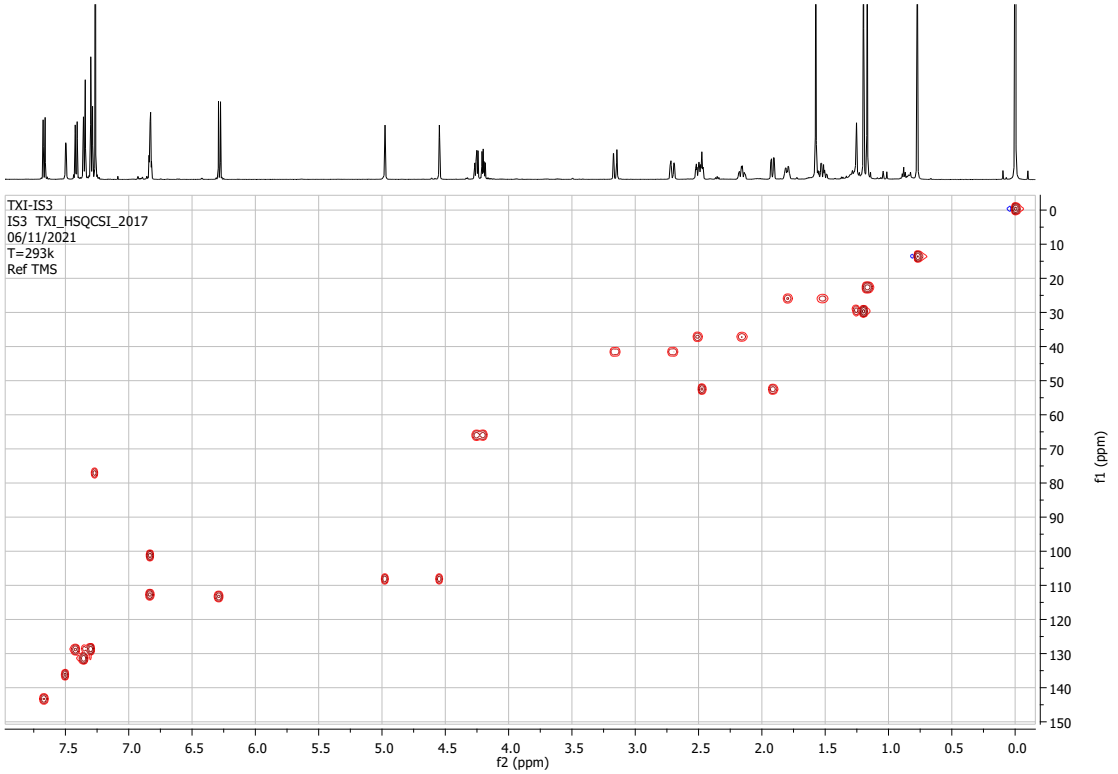
3d



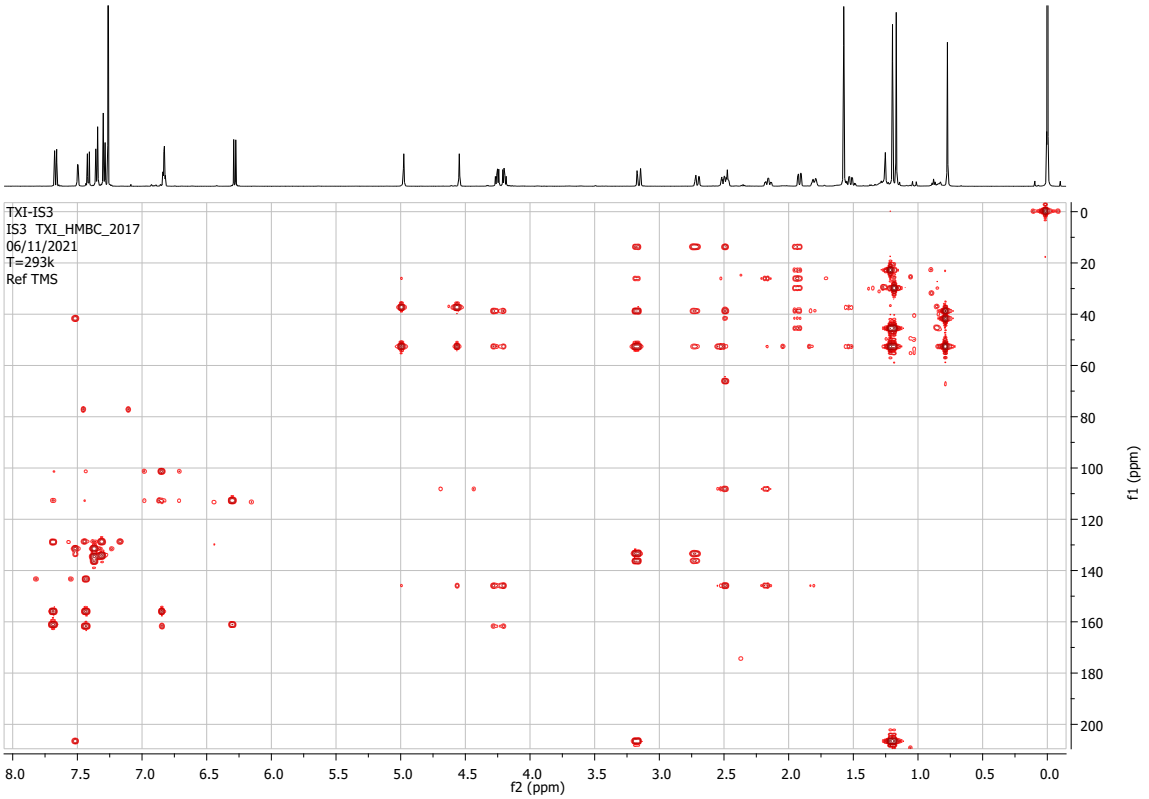
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3d



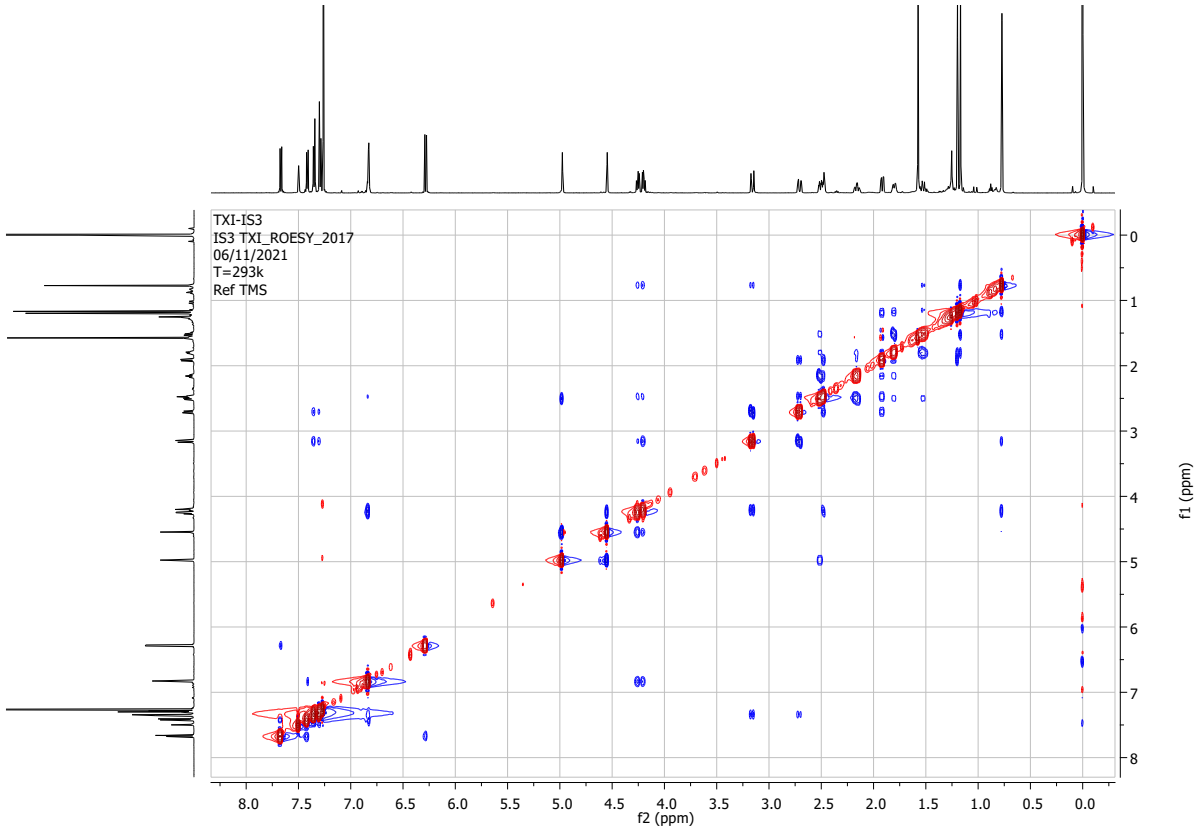
COSY spectrum of compound 3d



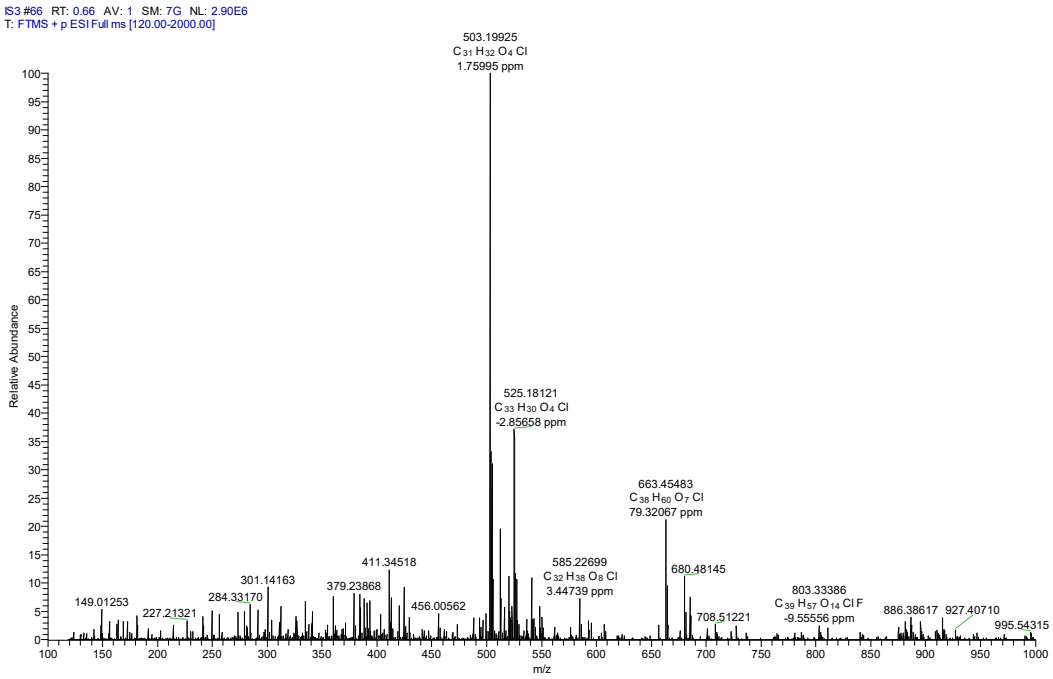
HSQC spectrum of compound 3d



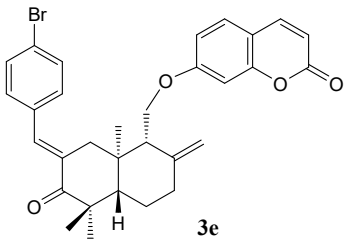
HMBC spectrum of compound 3d



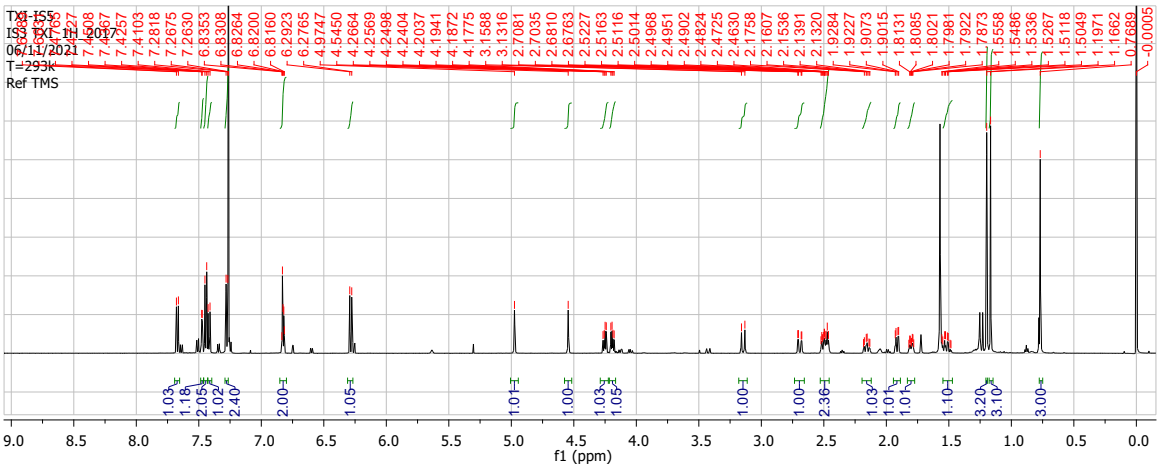
ROESY spectrum of compound 3d



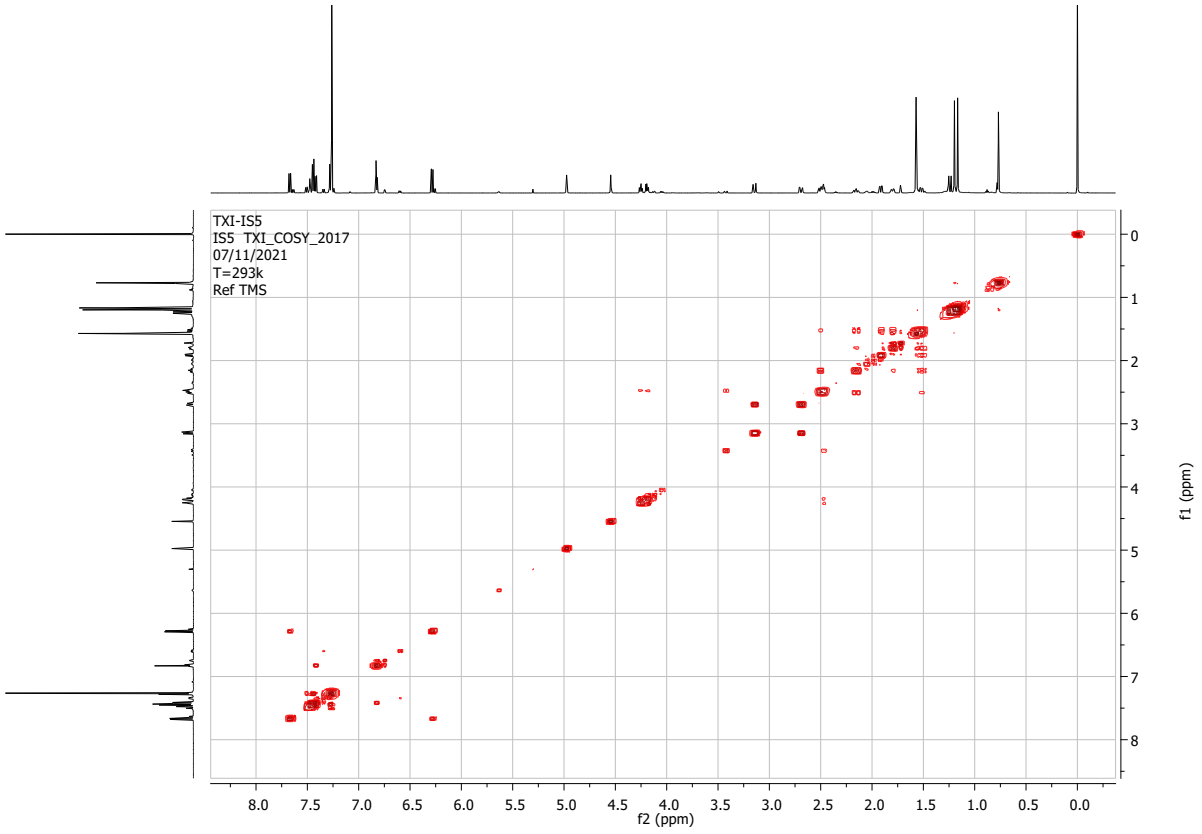
ESI-HRMS spectrum of compound 3d



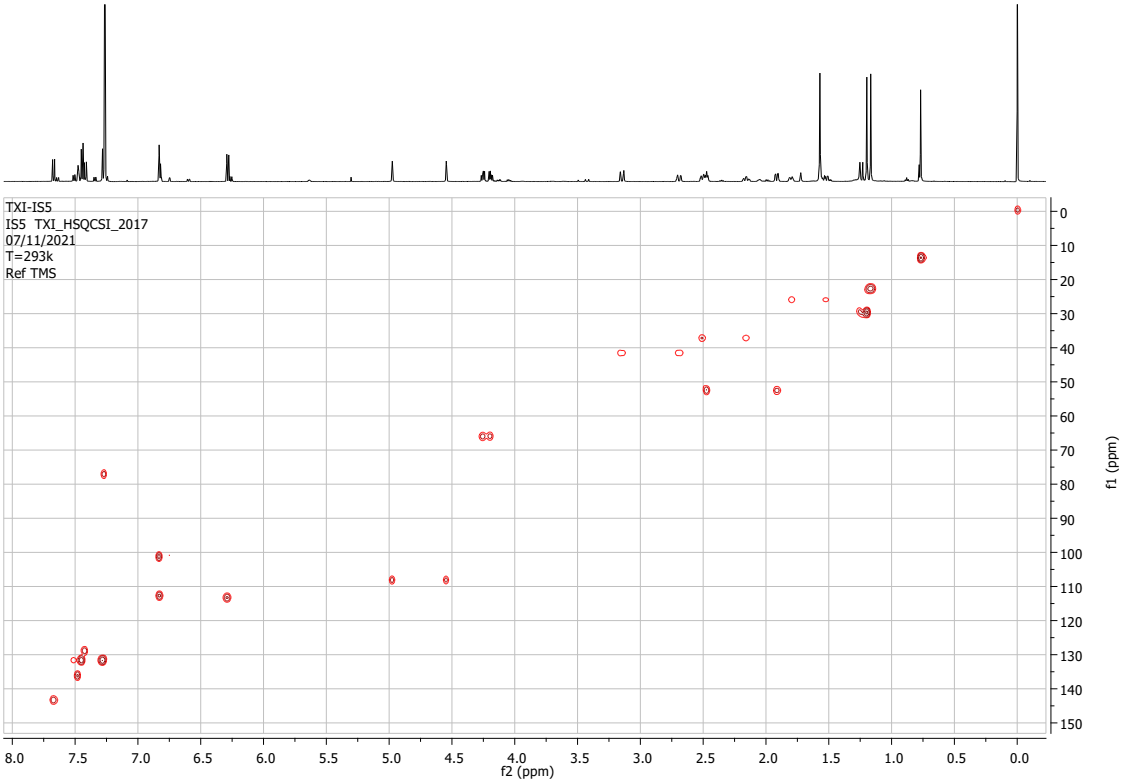
3e



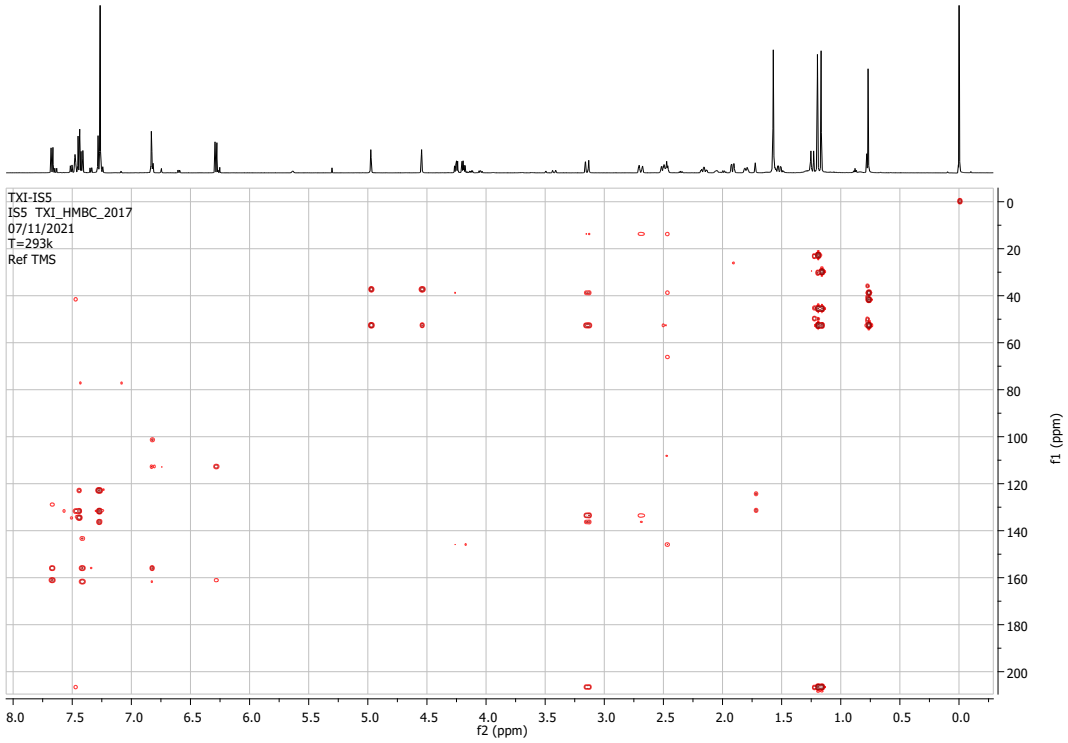
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3e



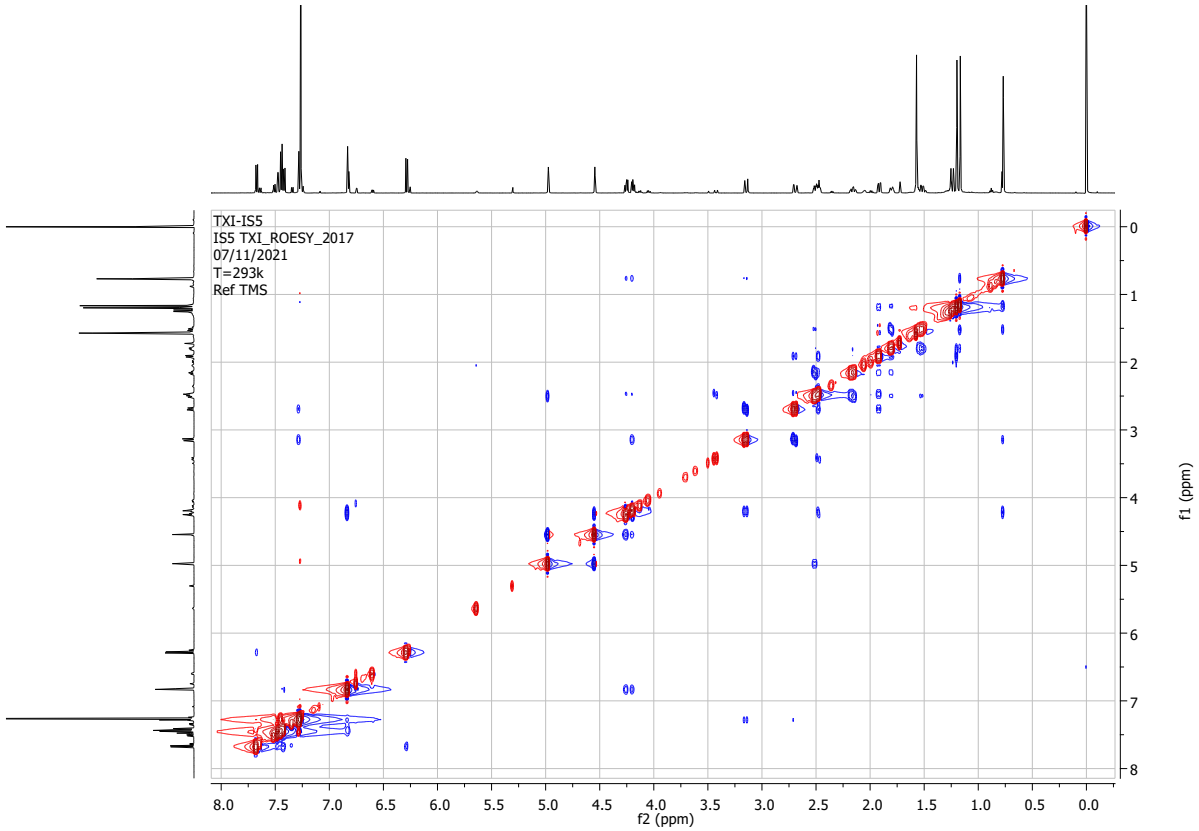
COSY spectrum of compound 3e



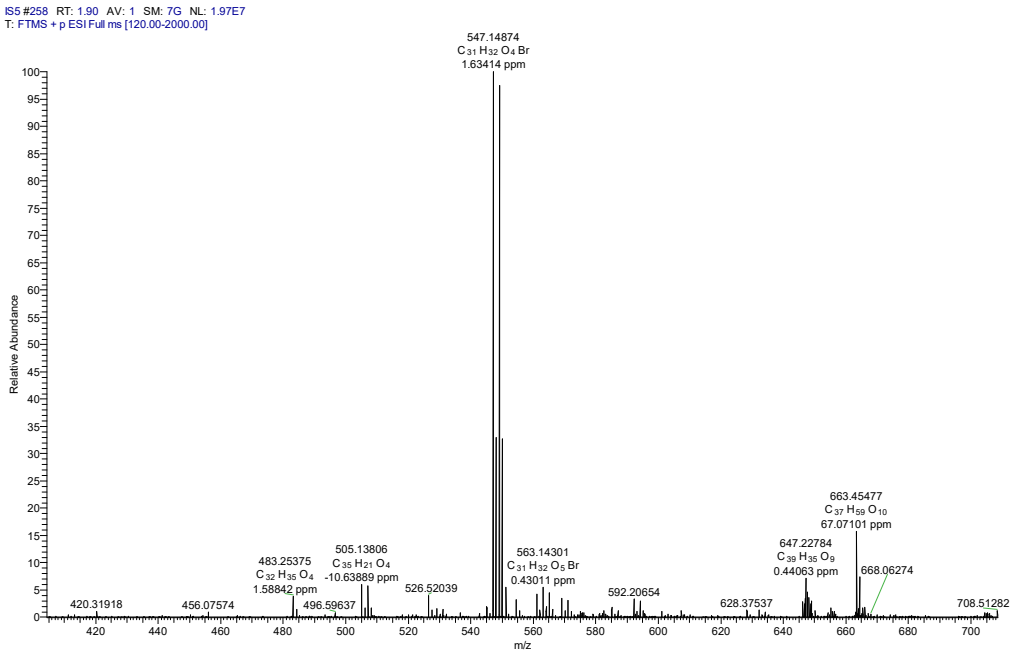
HSQC spectrum of compound 3e



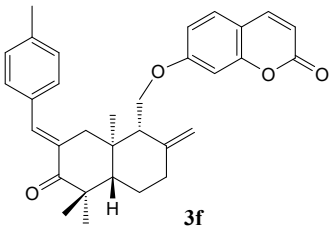
HMBC spectrum of compound 3e



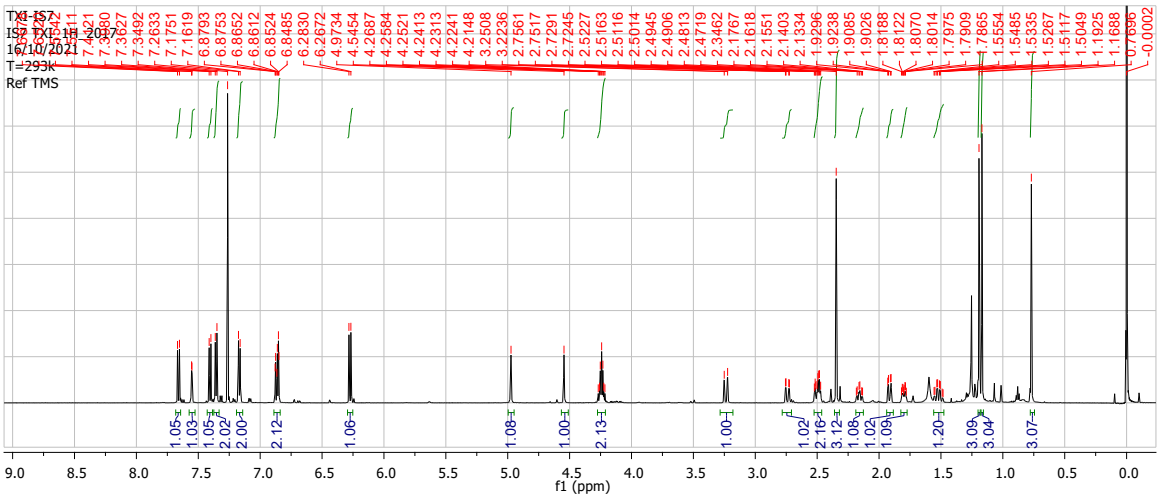
ROESY spectrum of compound 3e



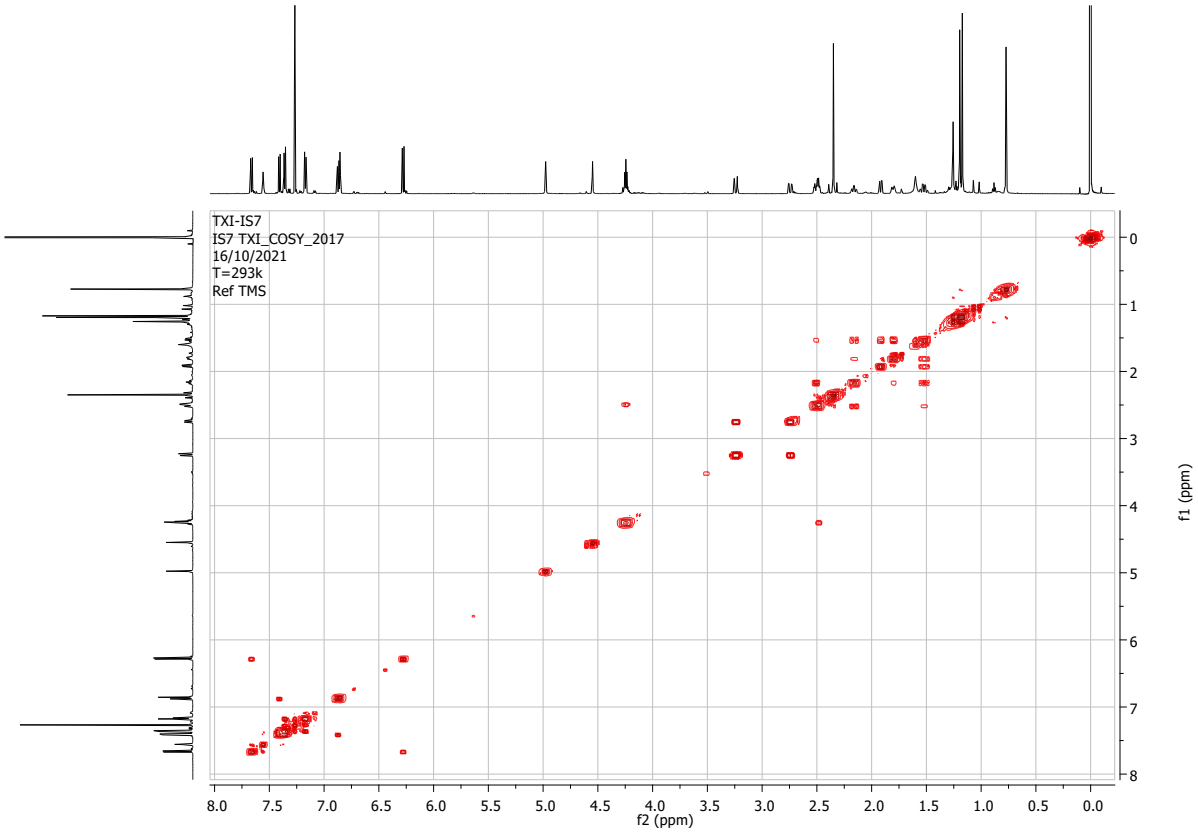
ESI-HRMS spectrum of compound 3e



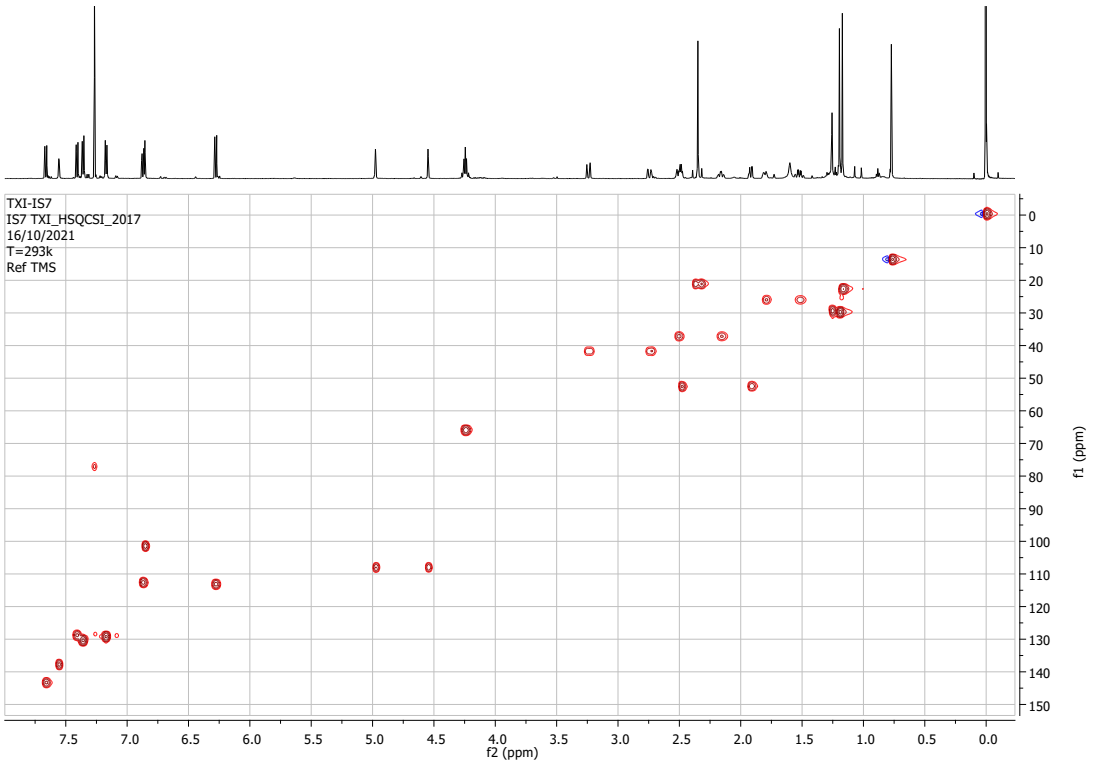
3f



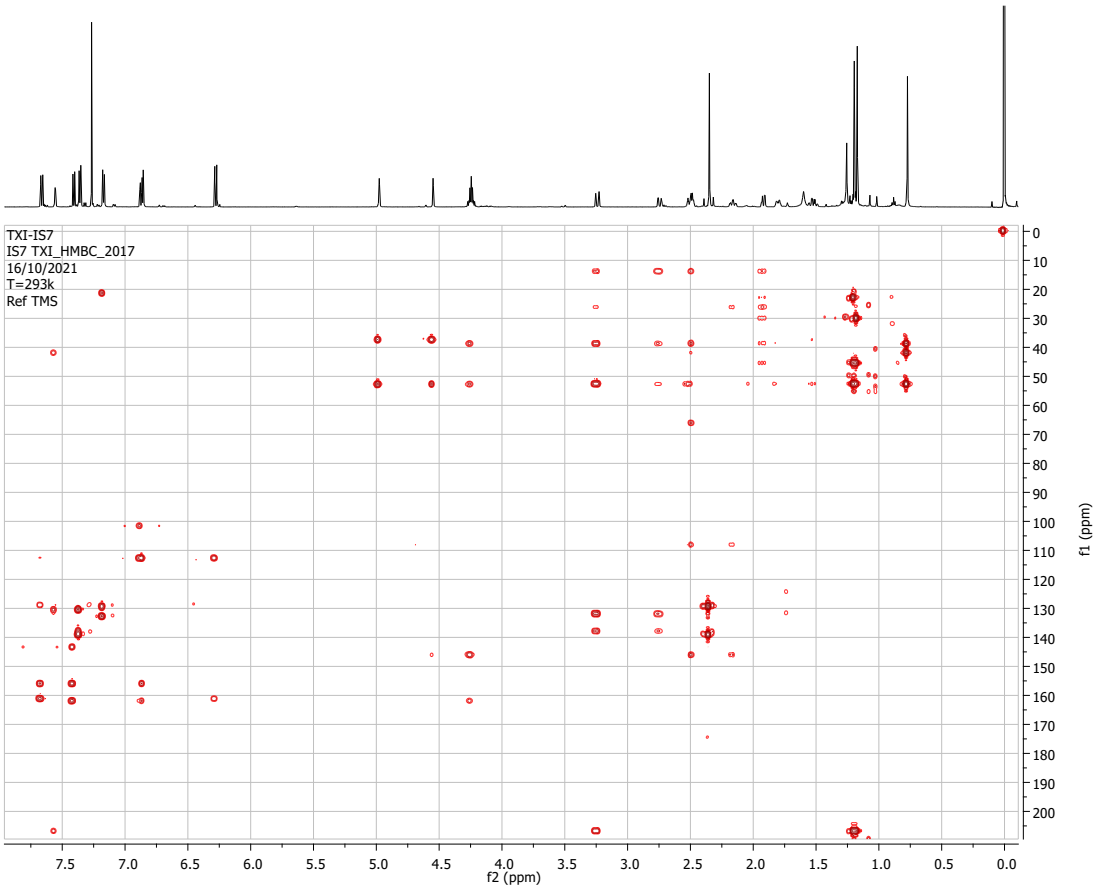
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3f



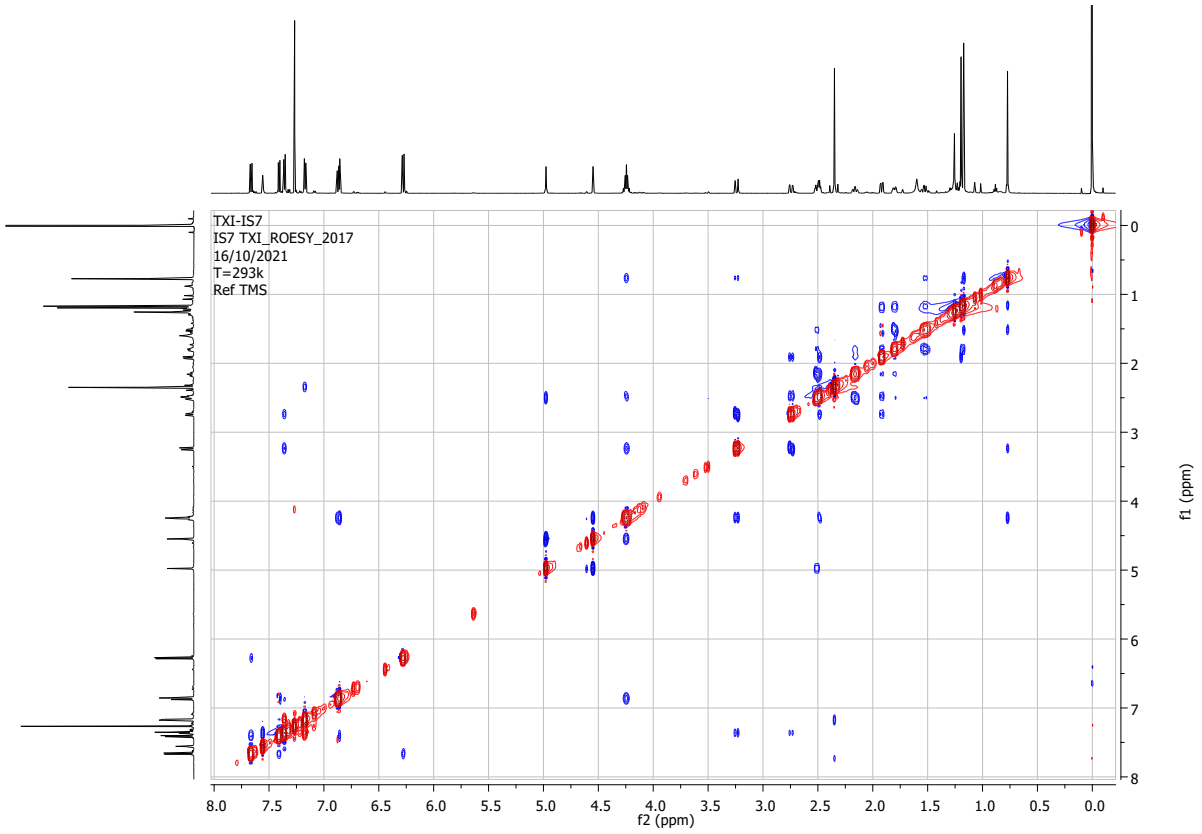
COSY spectrum of compound 3f



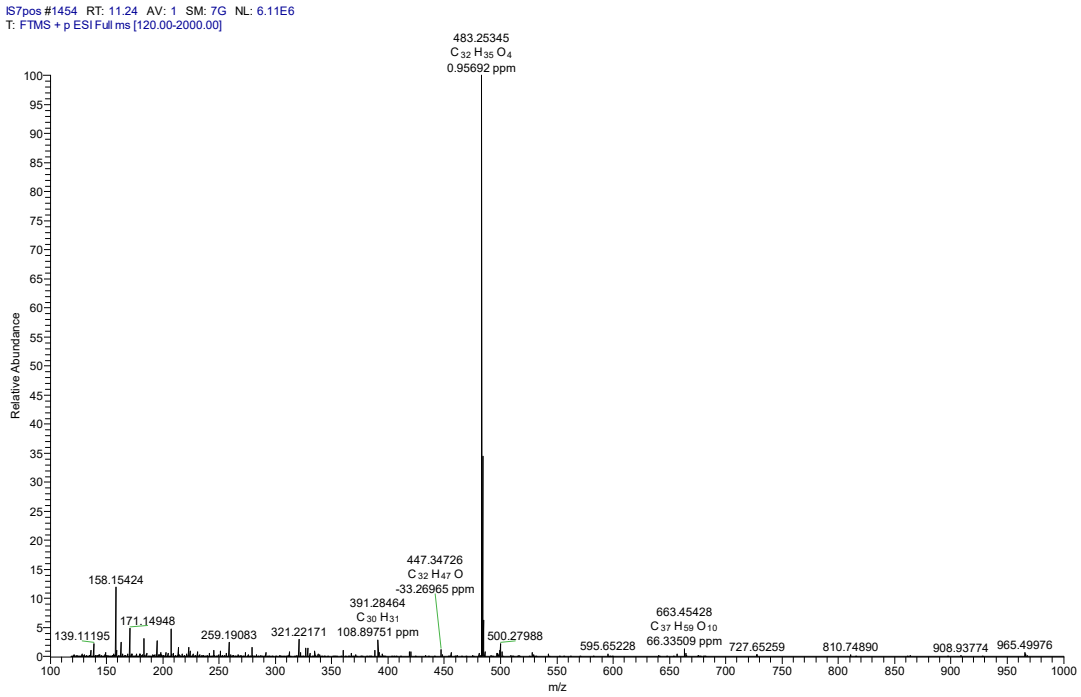
HSQC spectrum of compound 3f



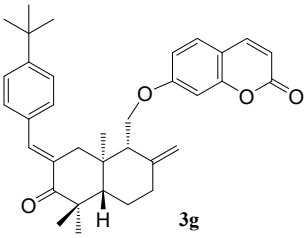
HMBC spectrum of compound 3f



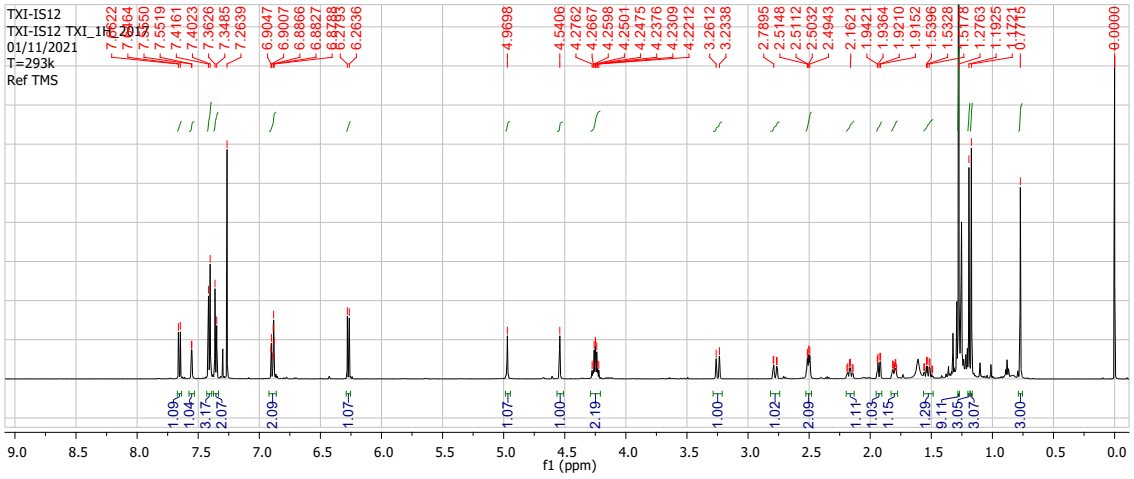
ROESY spectrum of compound 3f



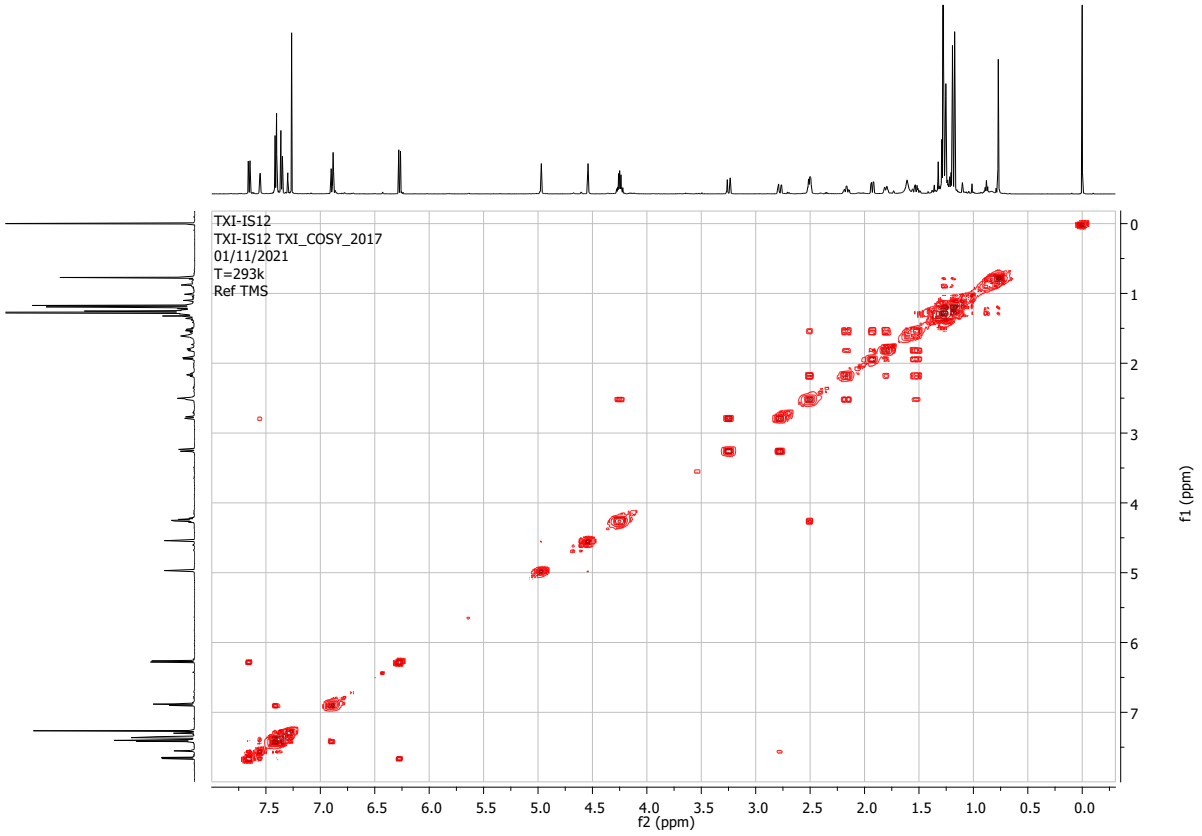
ESI-HRMS spectrum of compound 3f



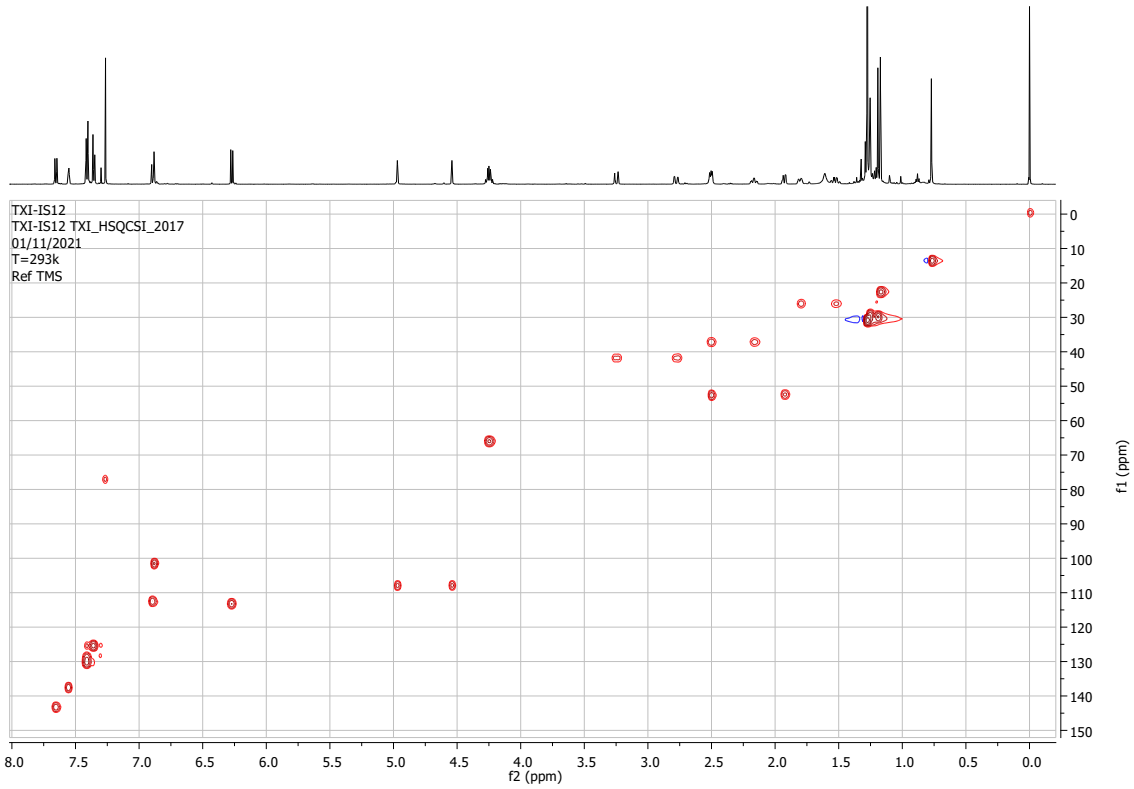
3g



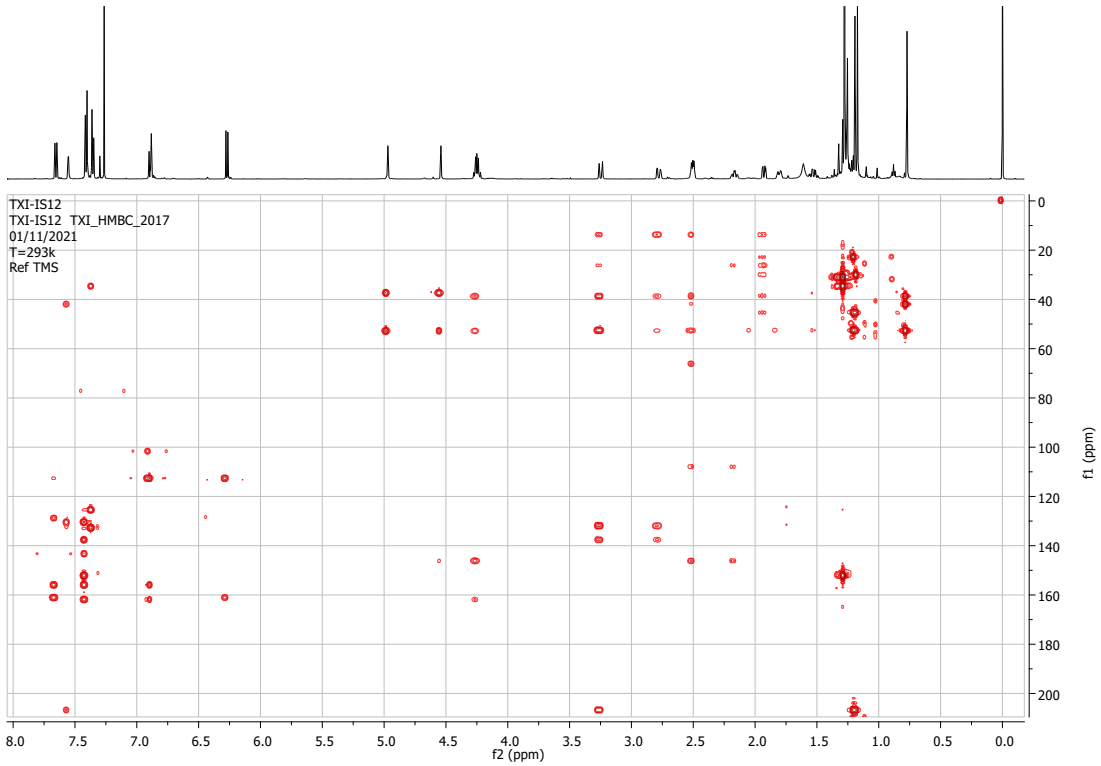
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3g



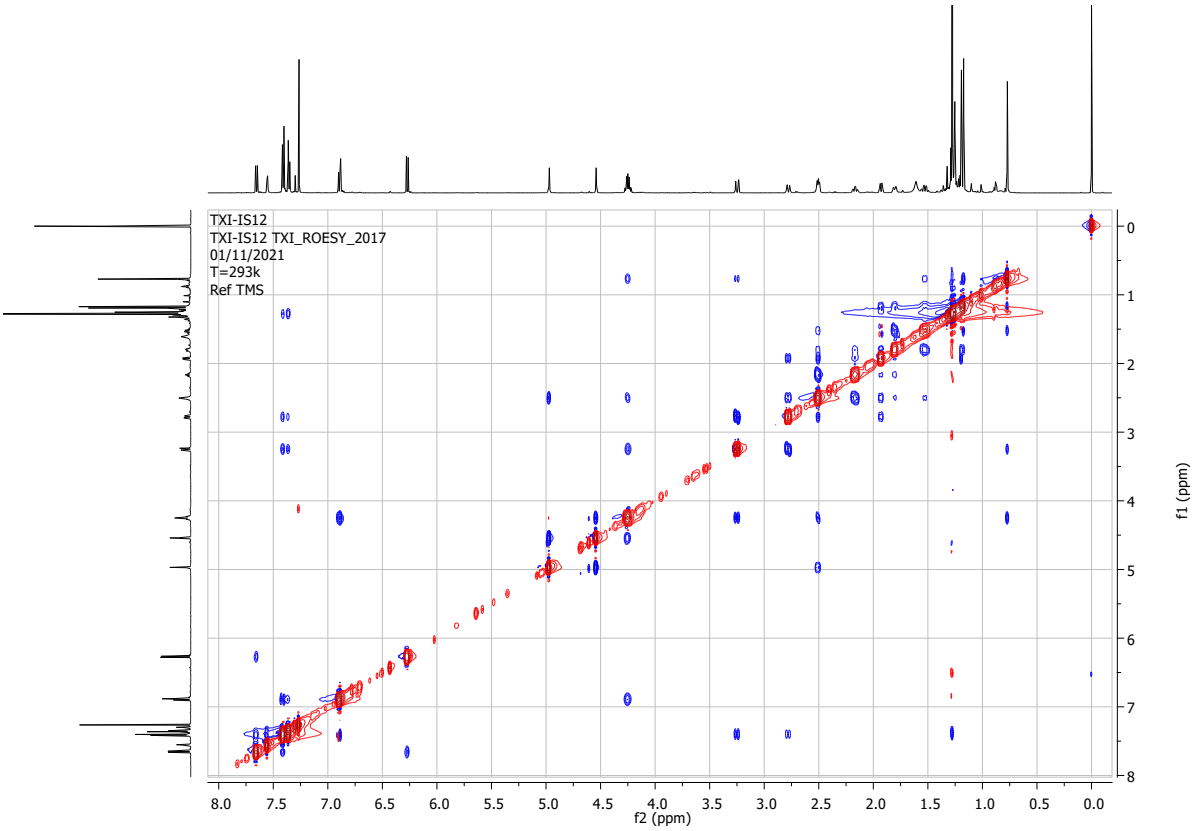
COSY spectrum of compound 3g



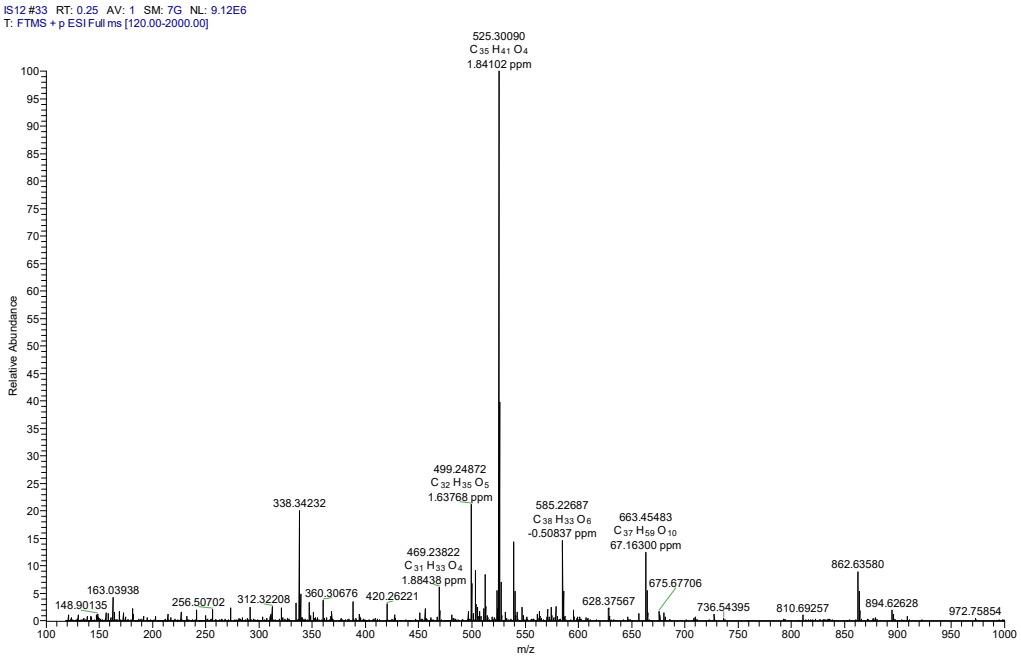
HSQC spectrum of compound 3g



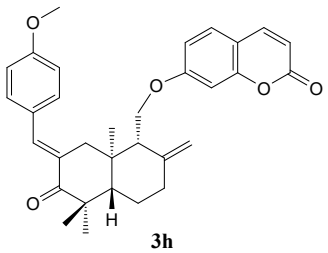
HMBC spectrum of compound 3g



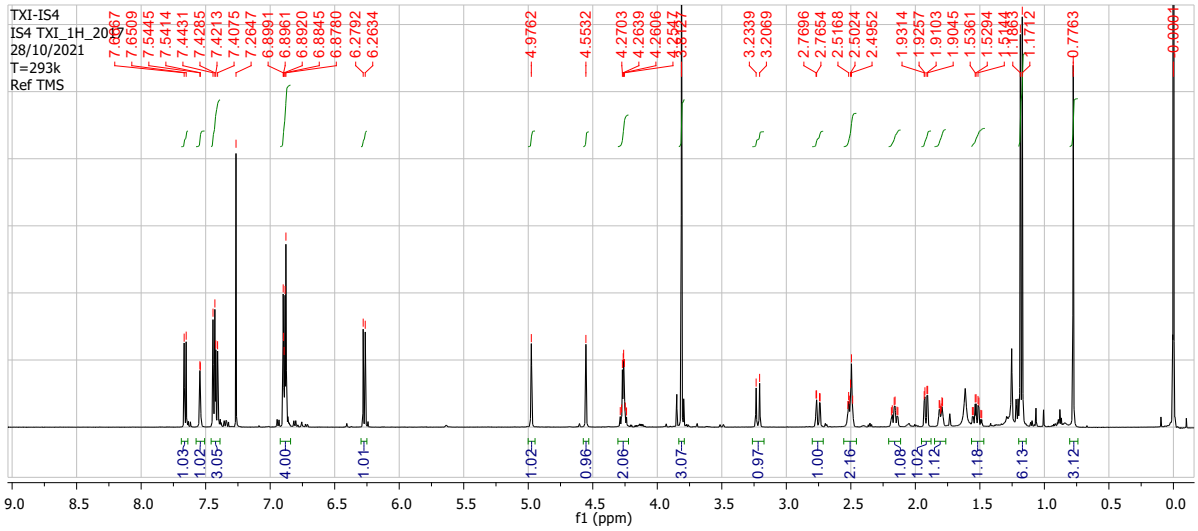
ROESY spectrum of compound 3g



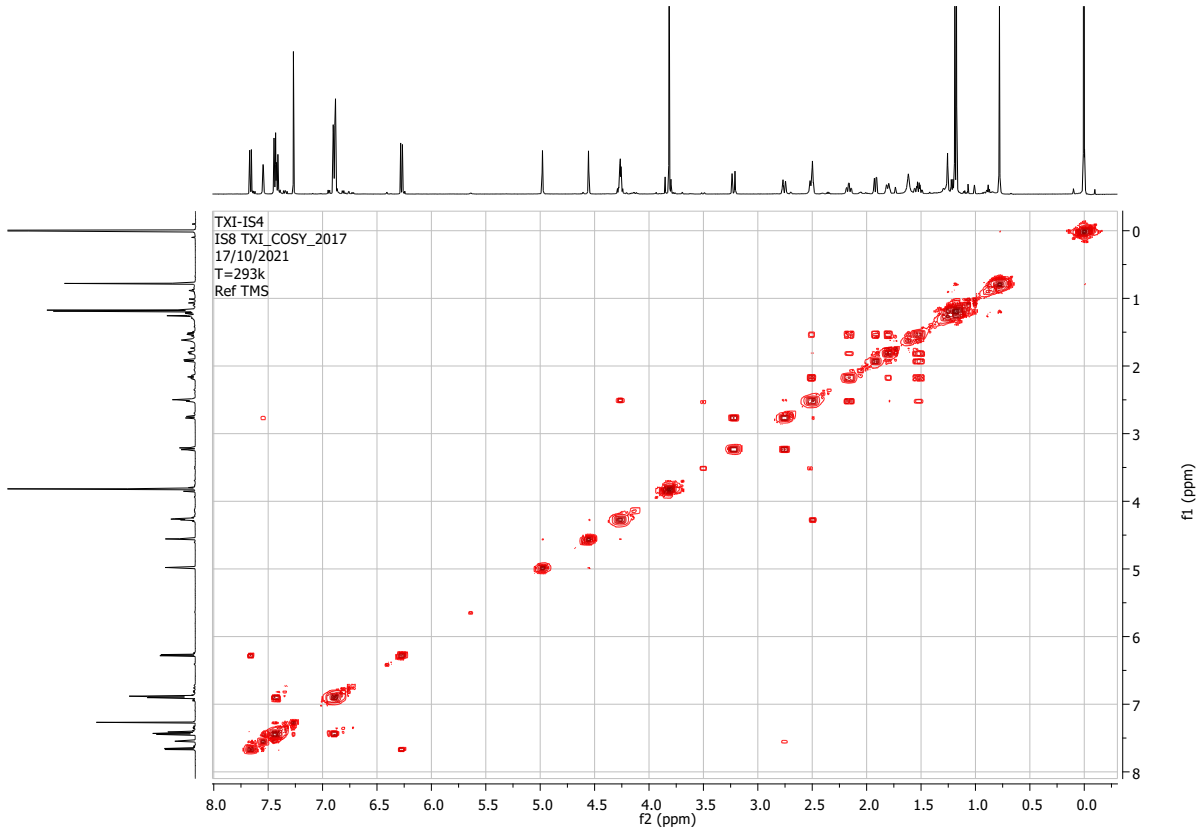
ESI-HRMS spectrum of compound 3g



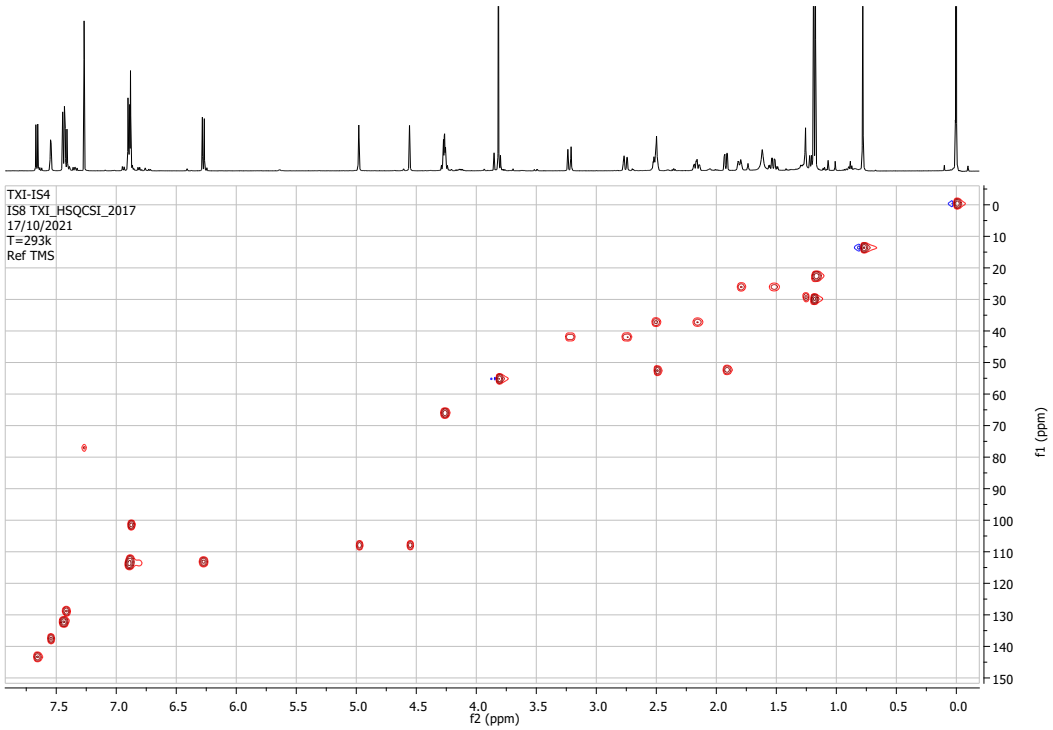
3h



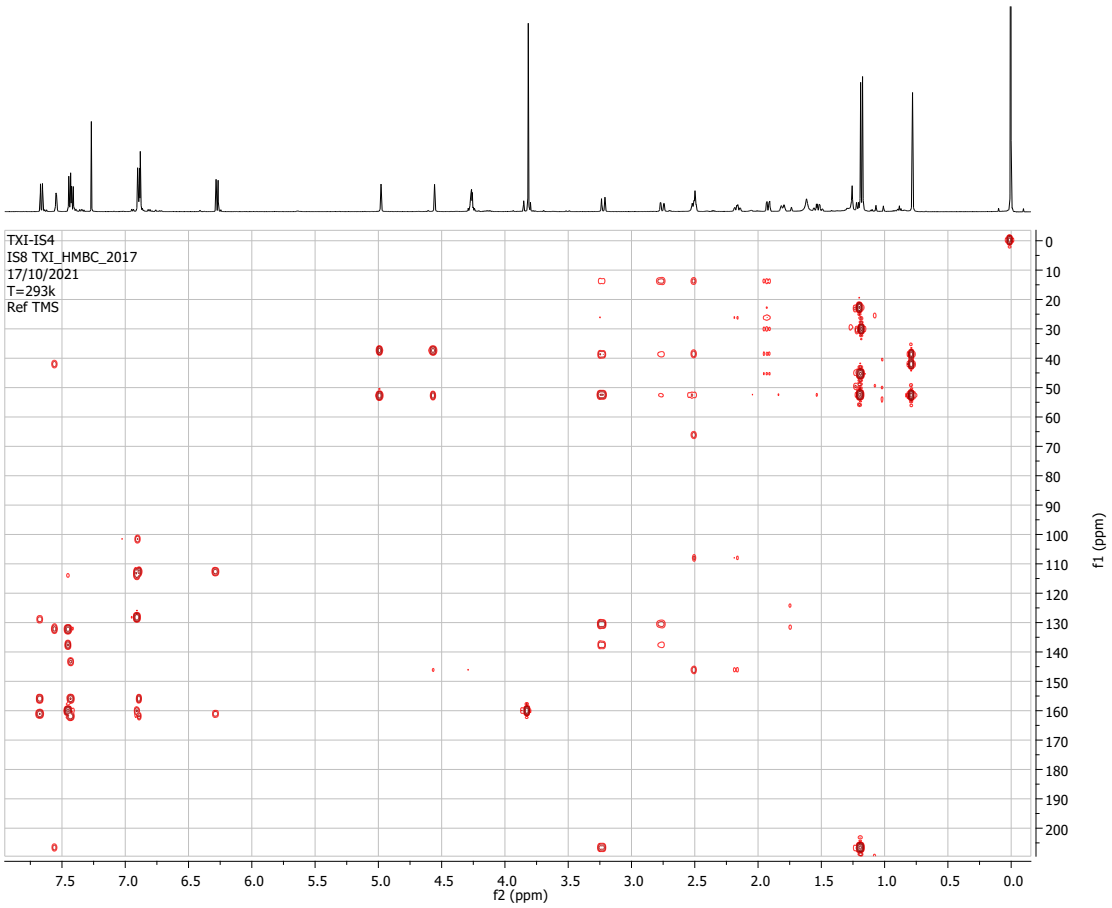
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3h



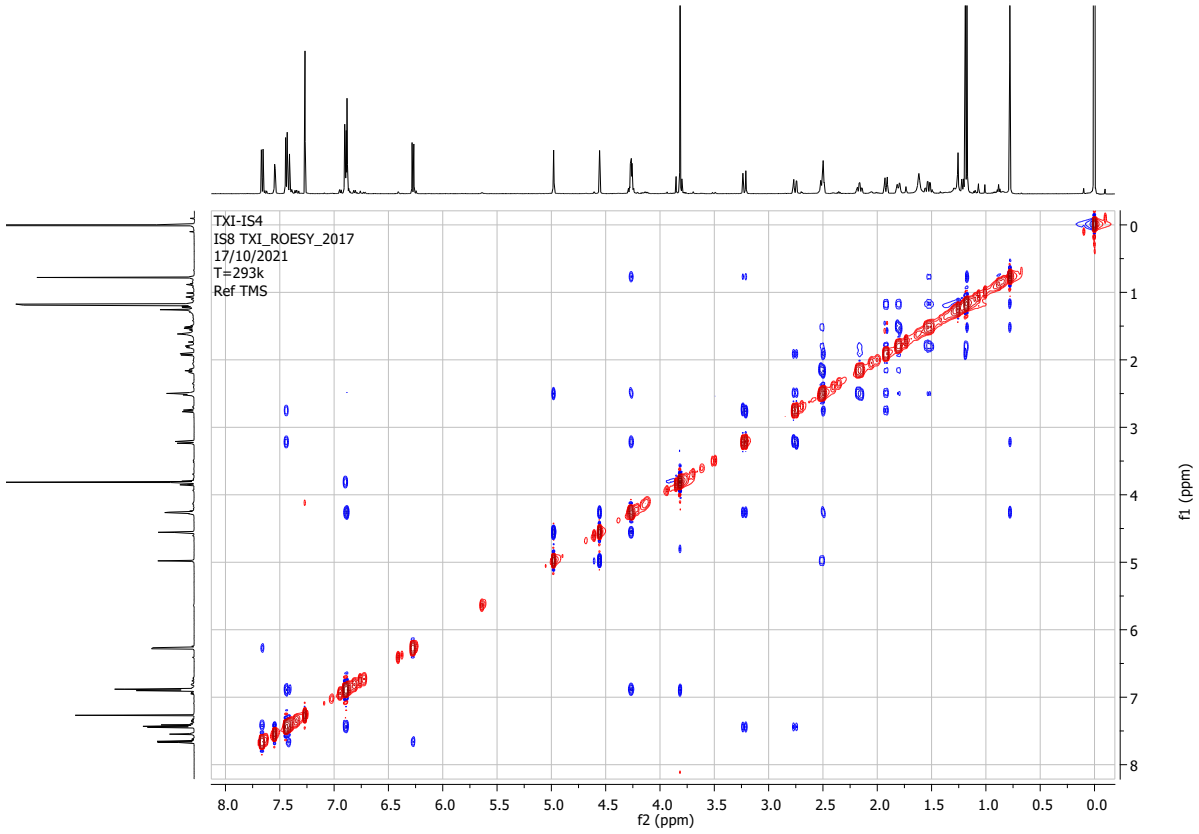
COSY spectrum of compound 3h



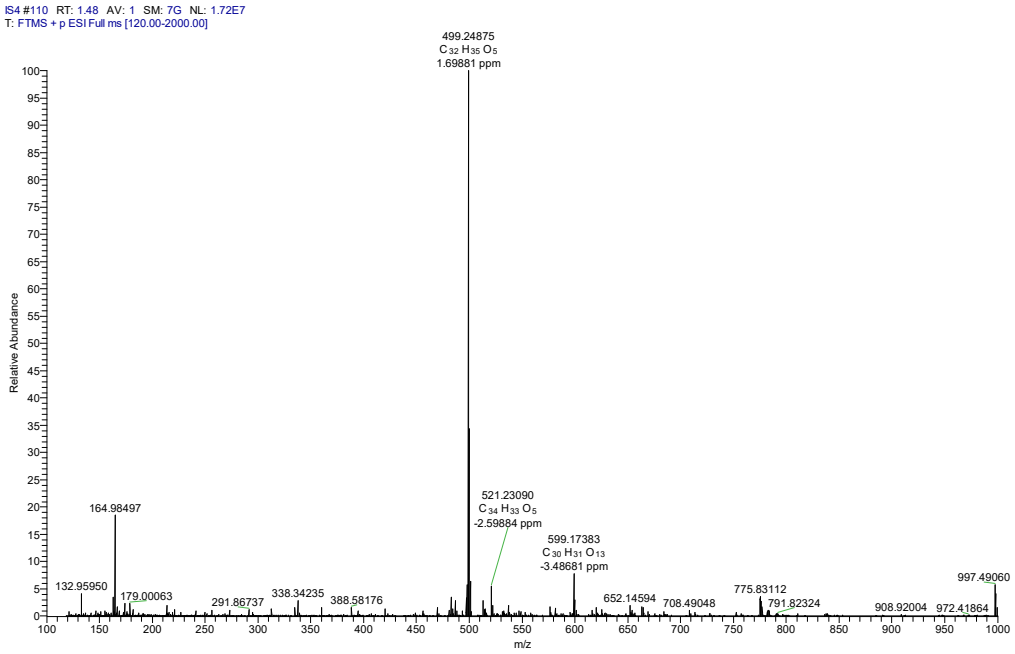
HSQC spectrum of compound 3h



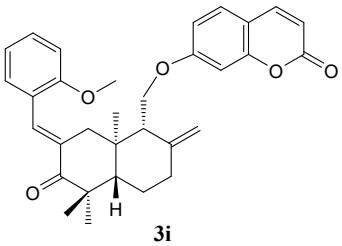
HMBC spectrum of compound 3h



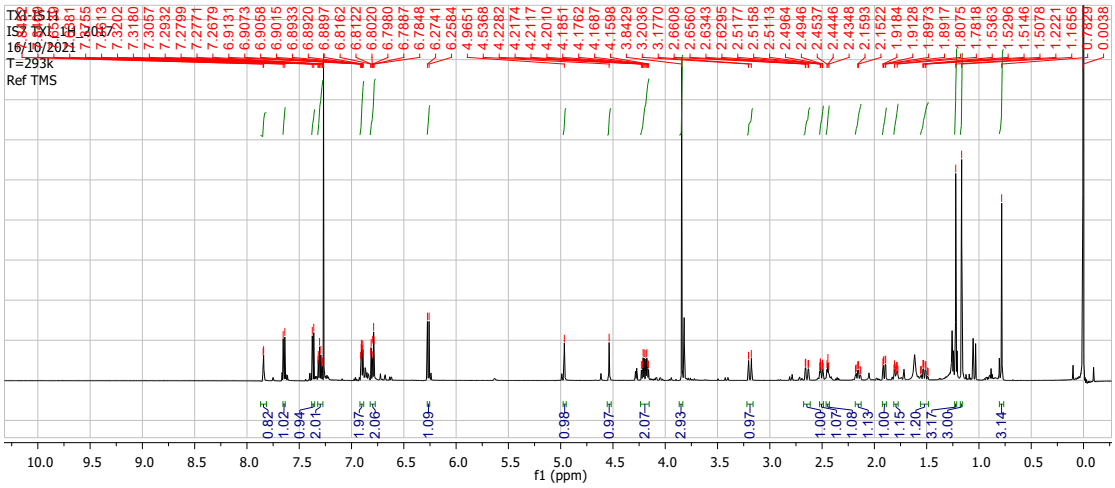
ROESY spectrum of compound 3h



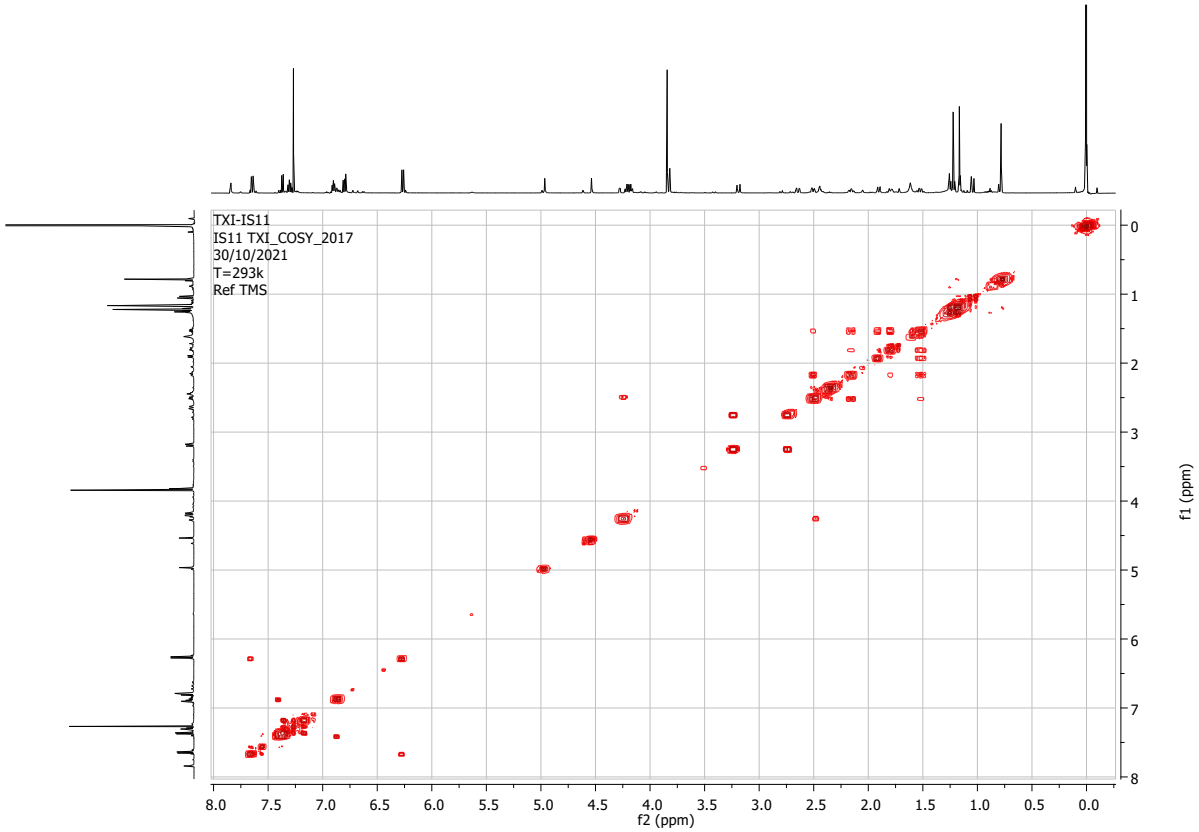
ESI-HRMS spectrum of compound 3h



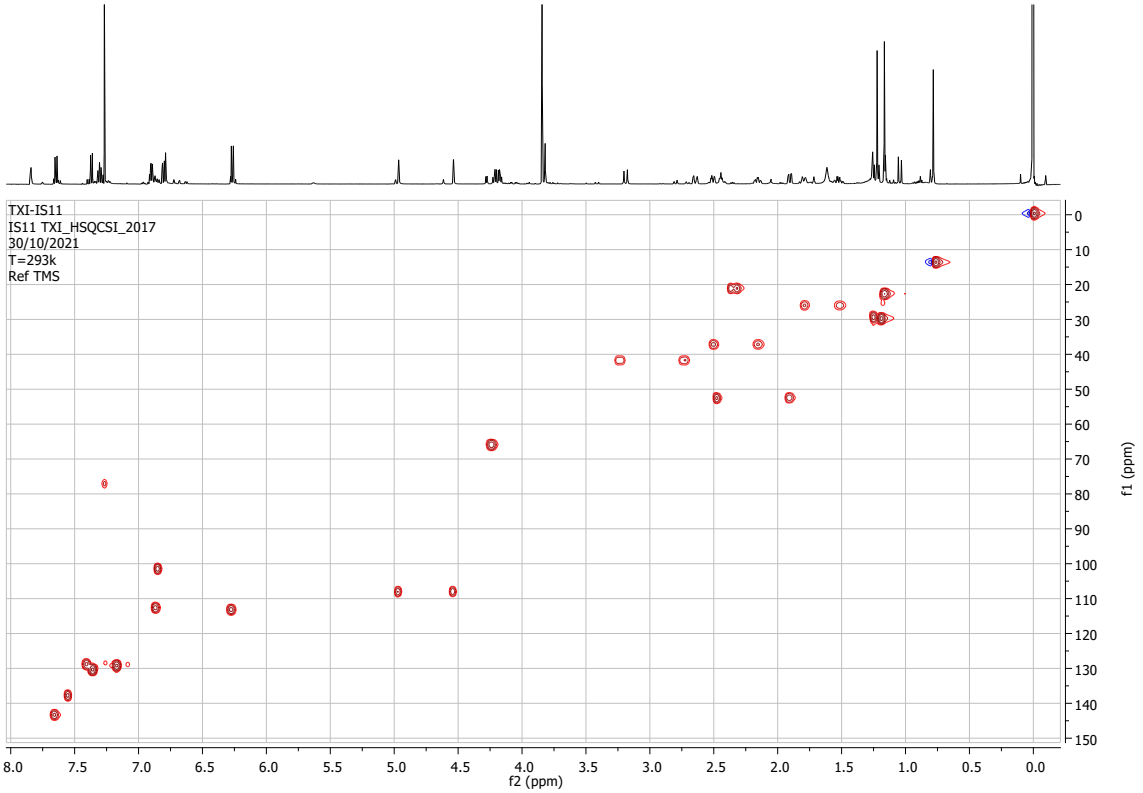
3i



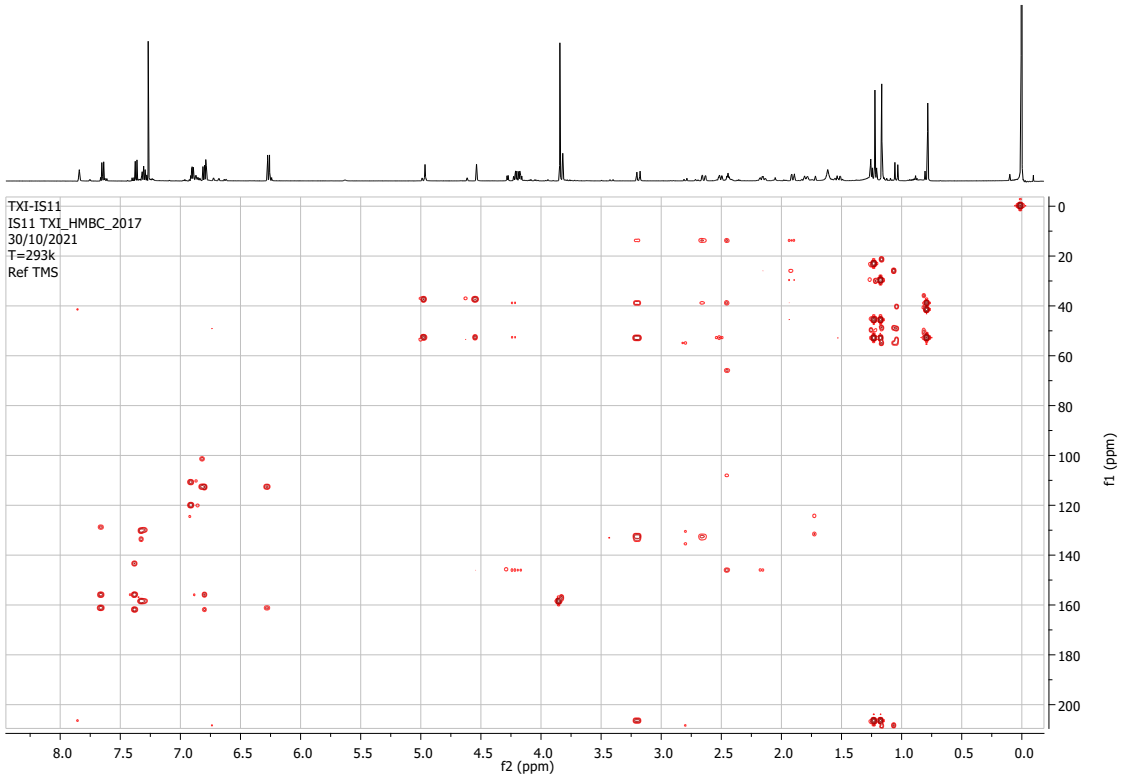
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3i



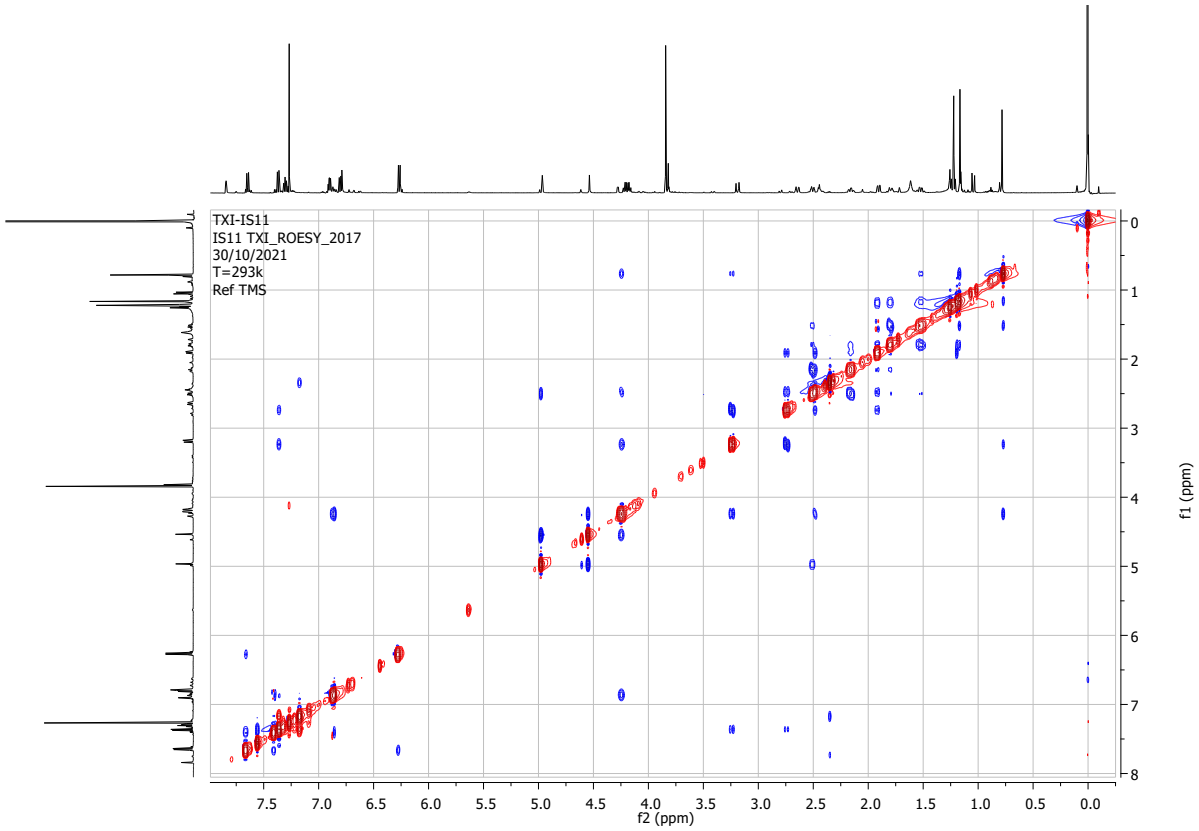
COSY spectrum of compound 3i



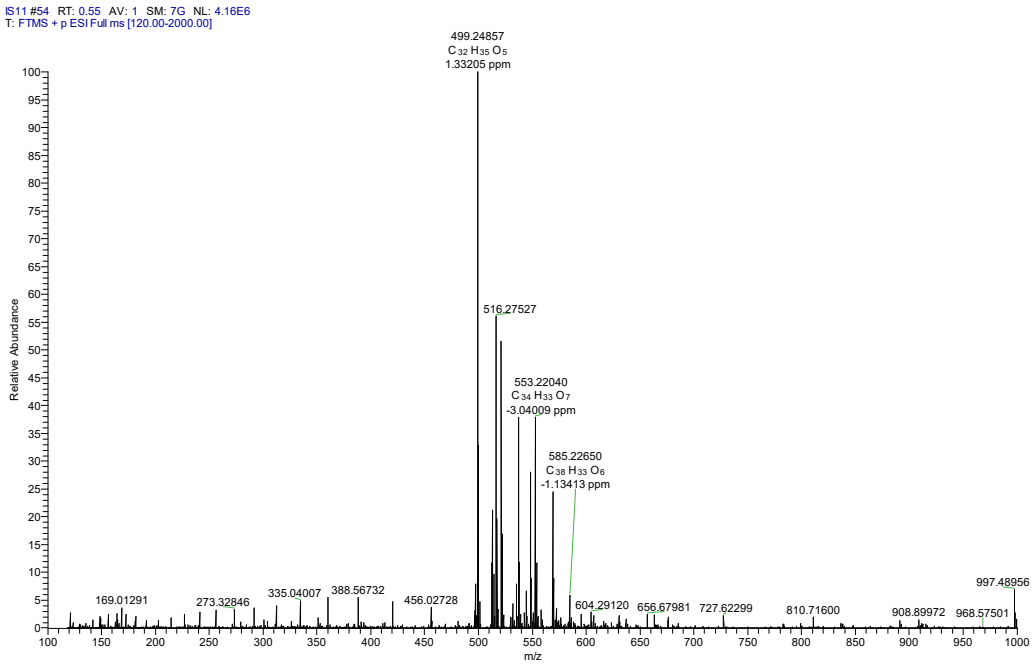
HSQC spectrum of compound 3i



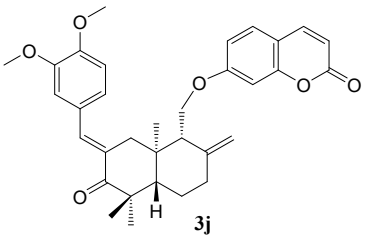
HMBC spectrum of compound 3i



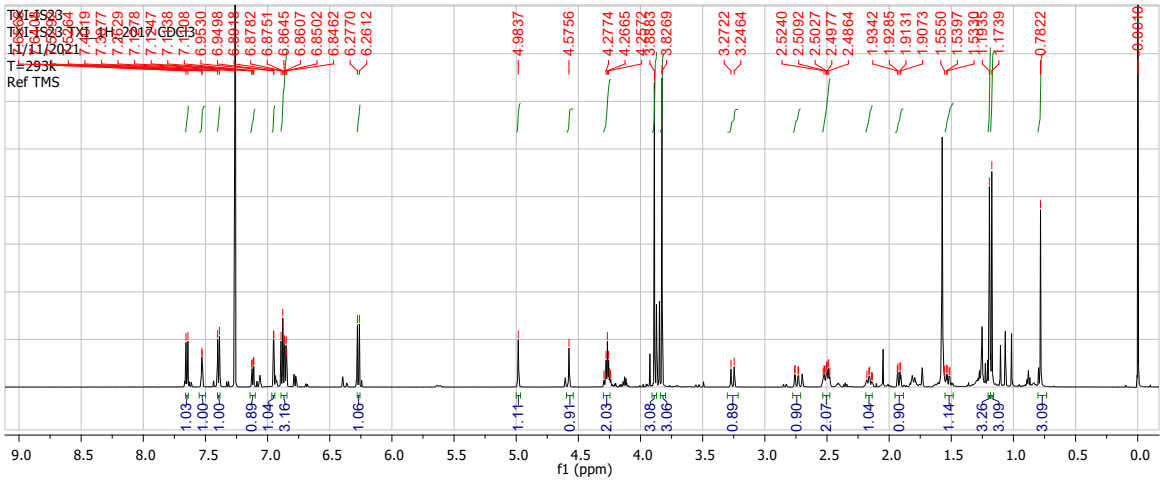
ROESY spectrum of compound 3i



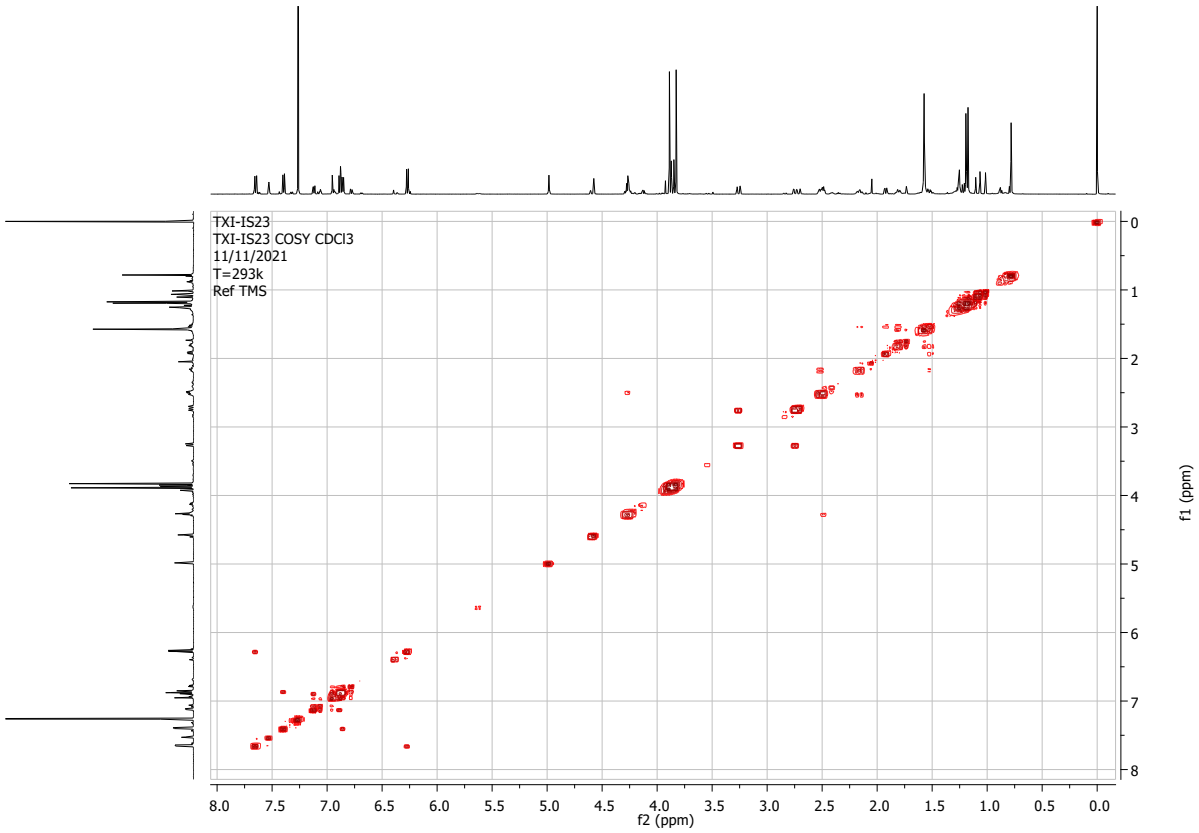
ESI-HRMS spectrum of compound 3i



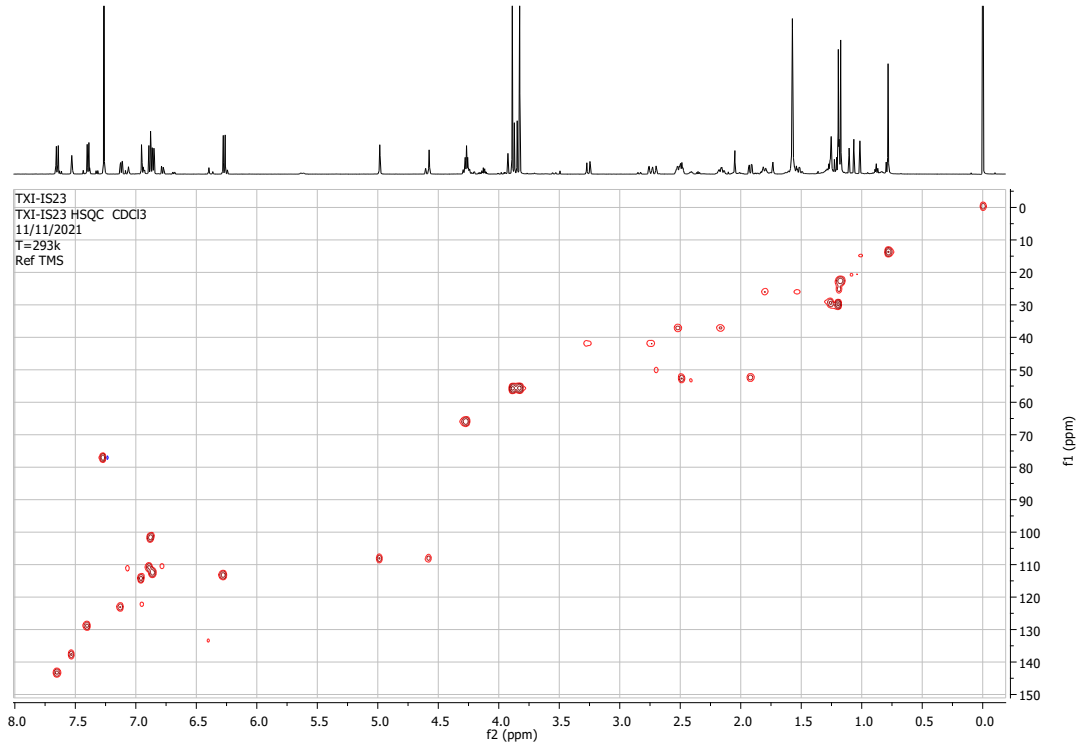
3j



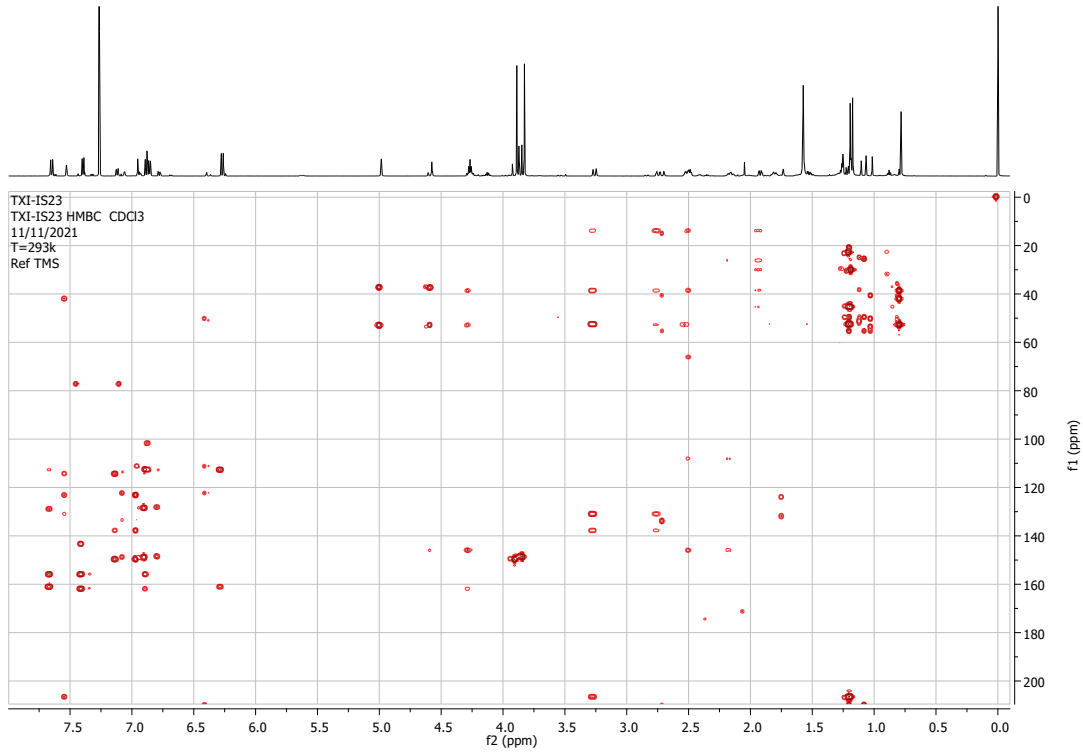
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3j



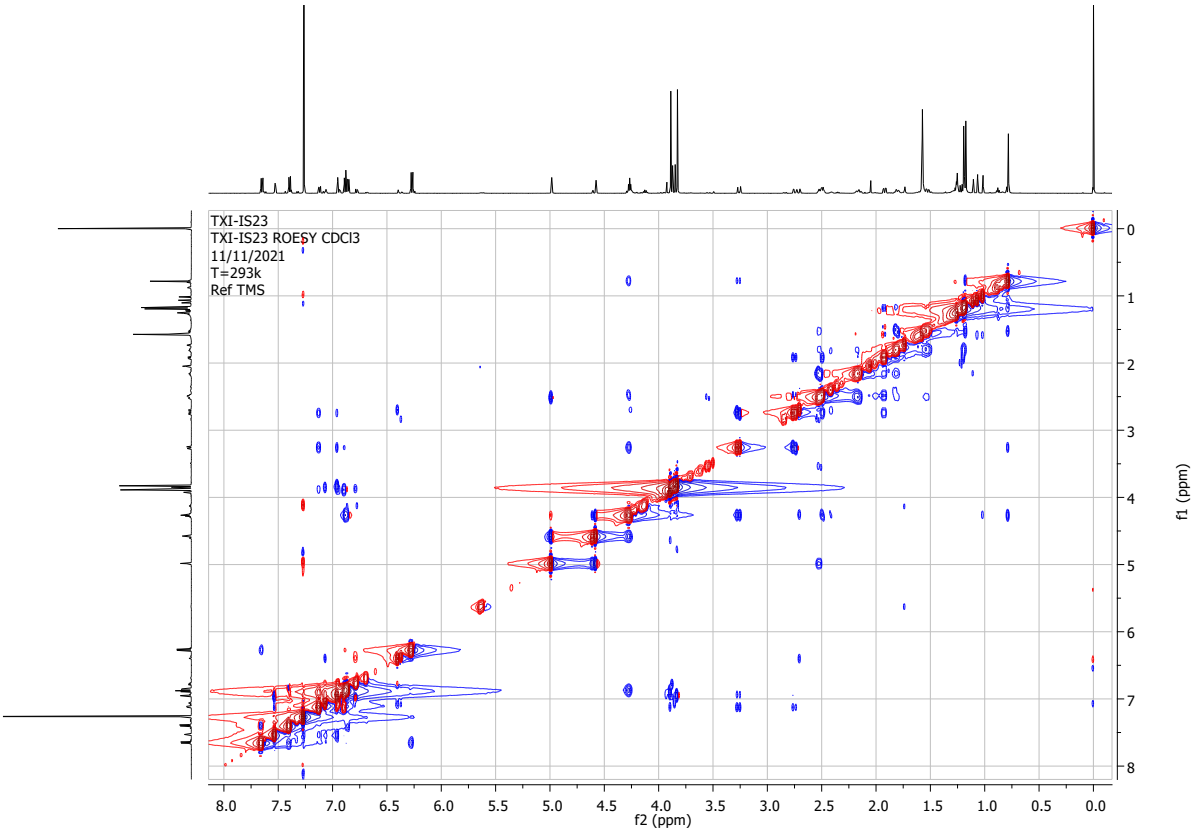
COSY spectrum of compound 3j



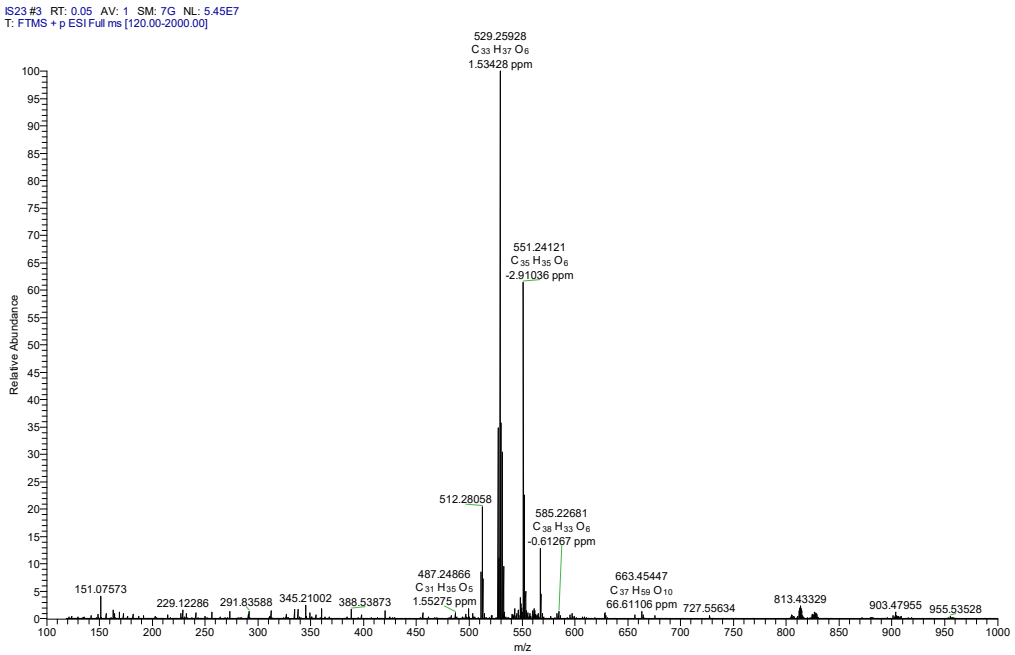
HSQC spectrum of compound 3j



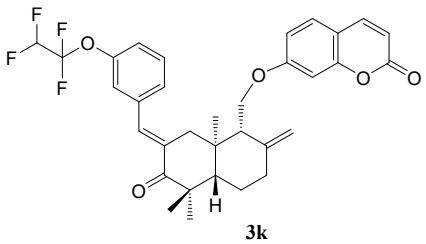
HMBC spectrum of compound 3j



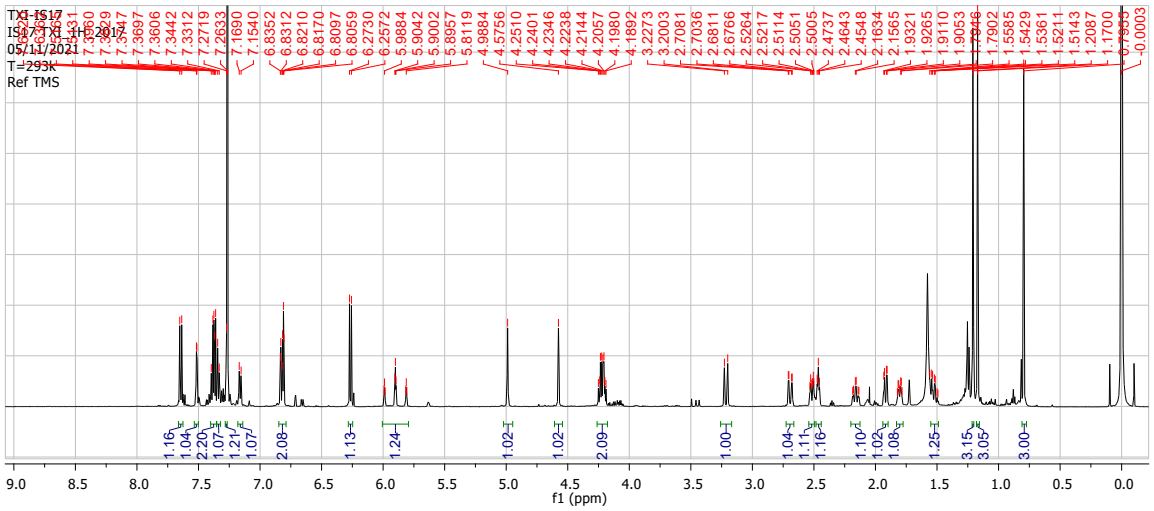
ROESY spectrum of compound 3j



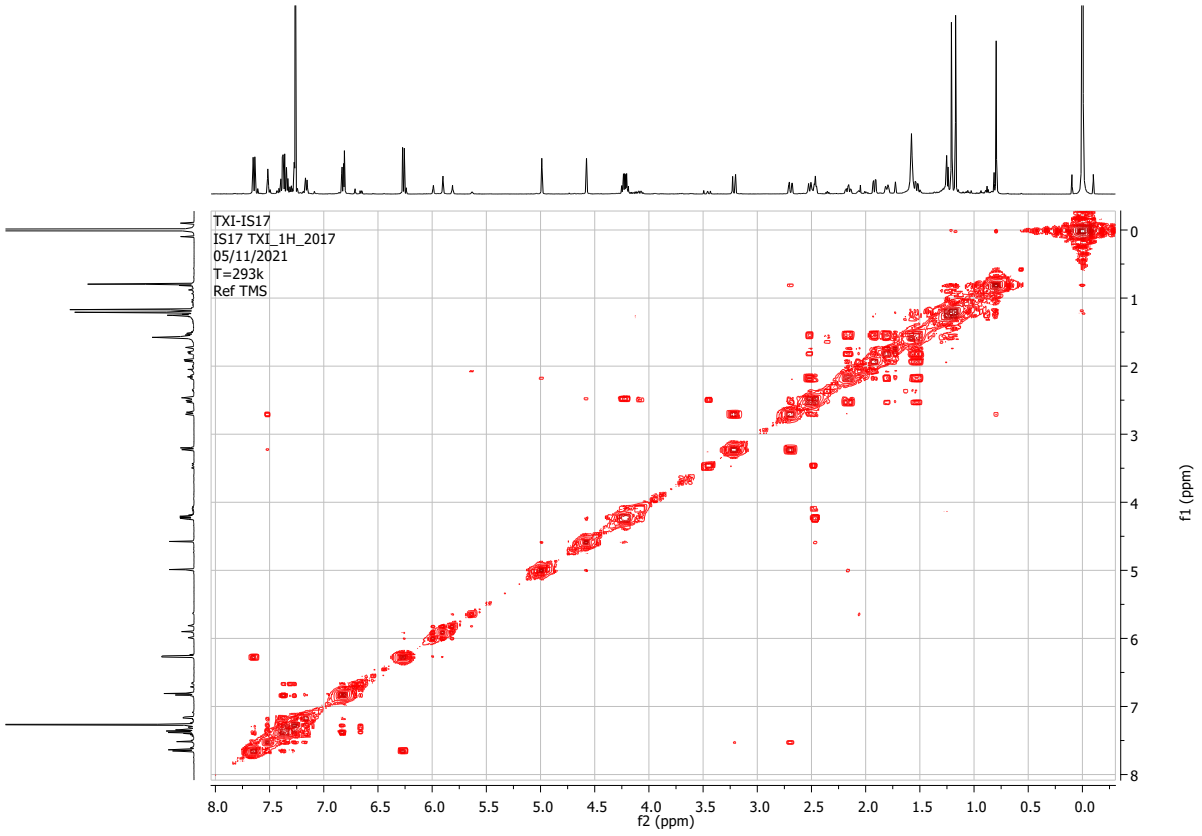
ESI-HRMS spectrum of compound 3j



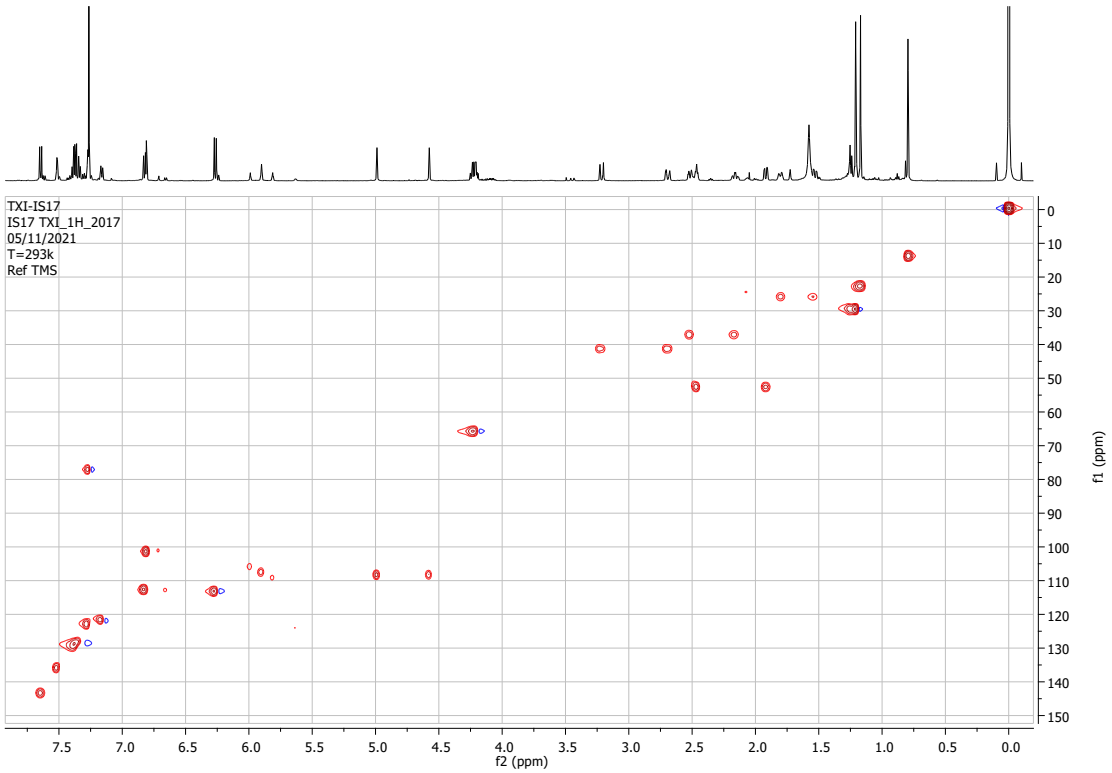
3k



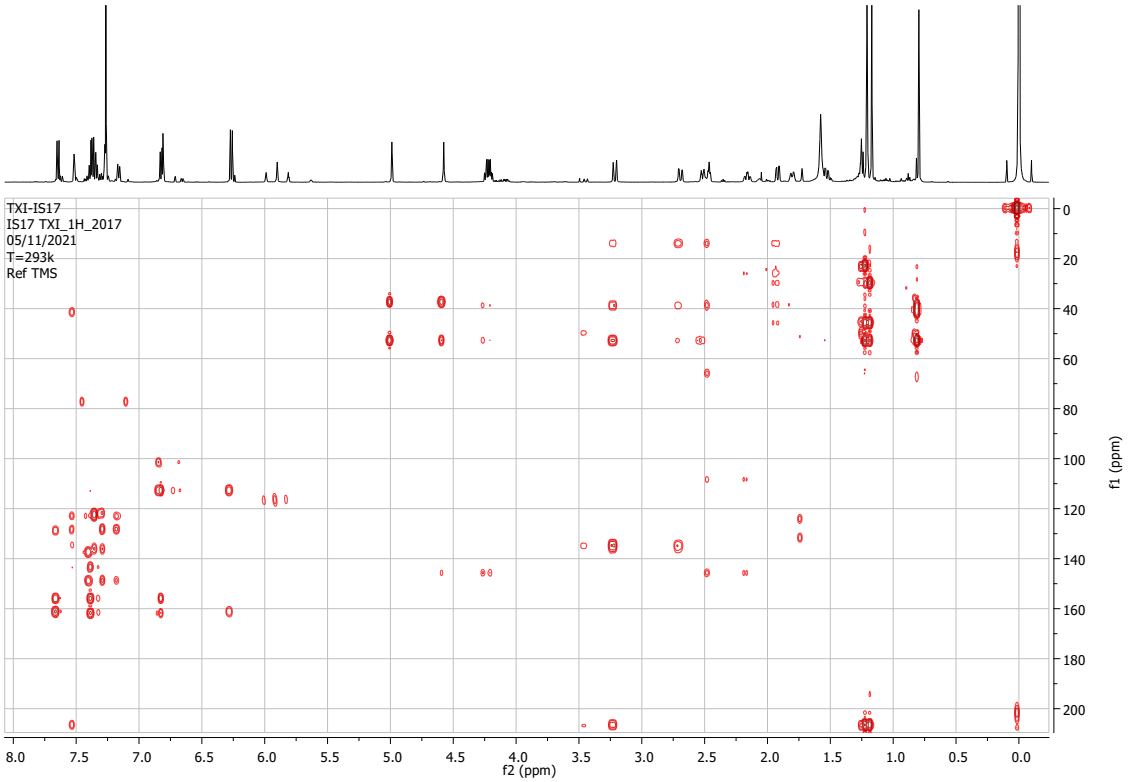
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3k



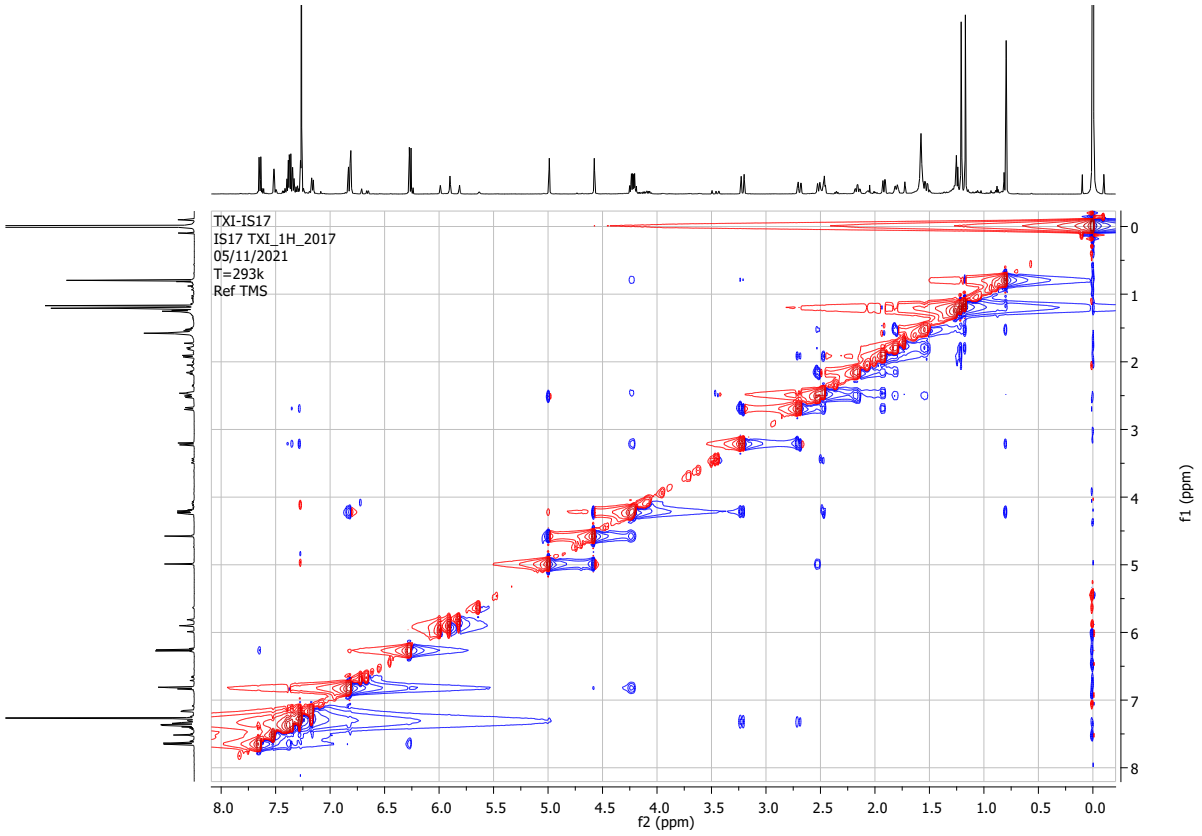
COSY spectrum of compound 3k



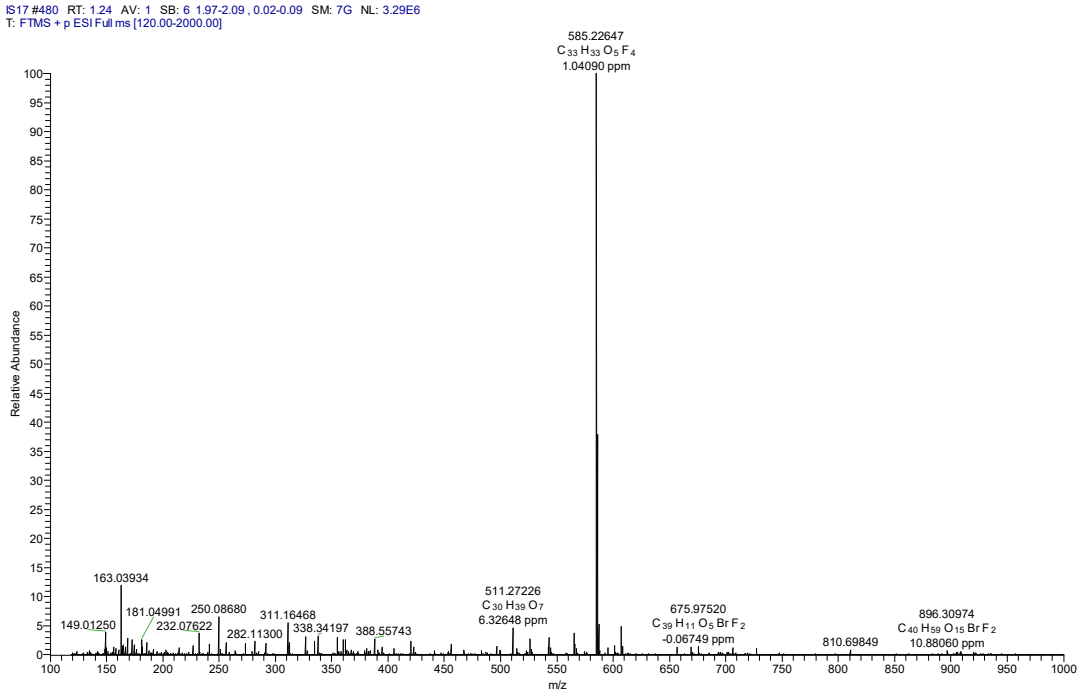
HSQC spectrum of compound 3k



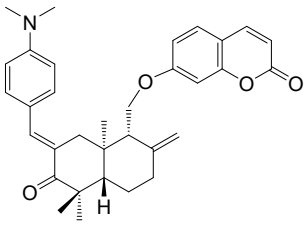
HMBC spectrum of compound 3k



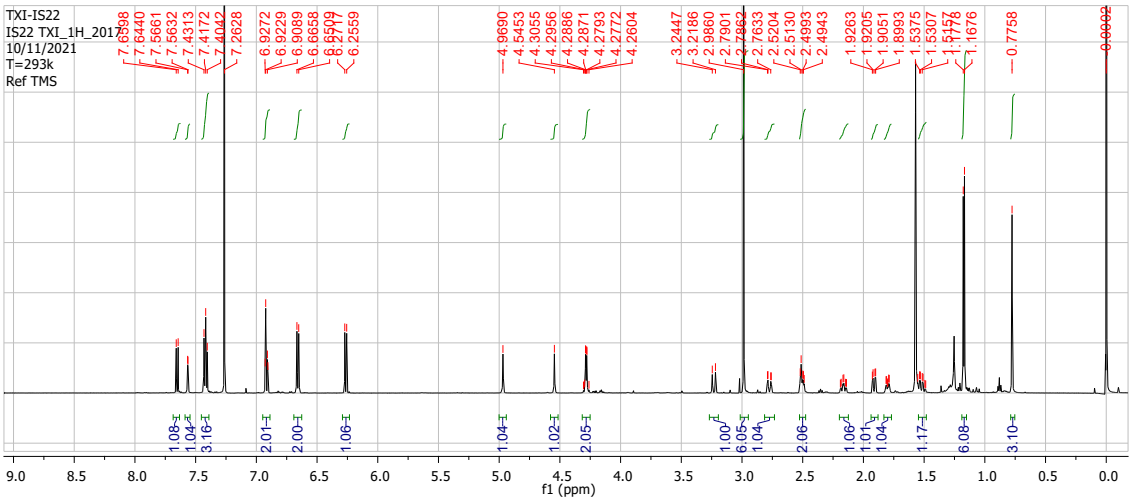
ROESY spectrum of compound 3k



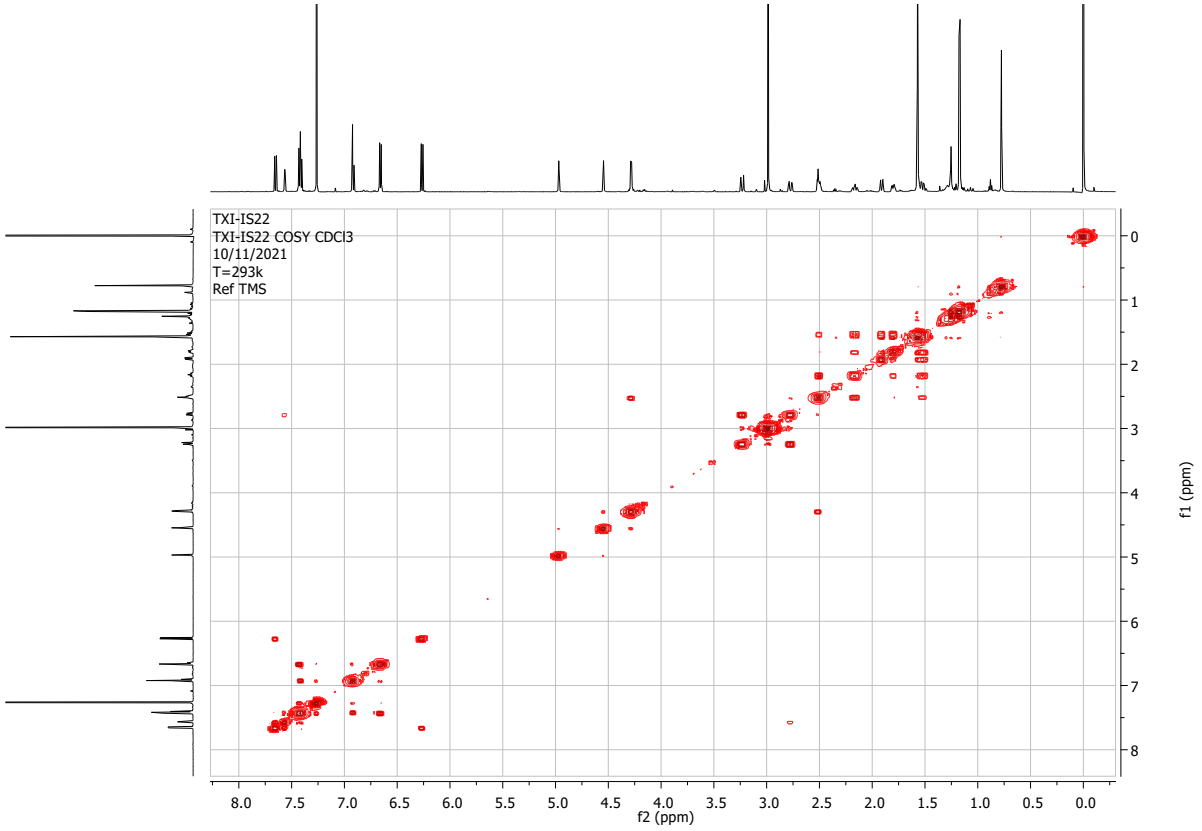
ESI-HRMS spectrum of compound 3k



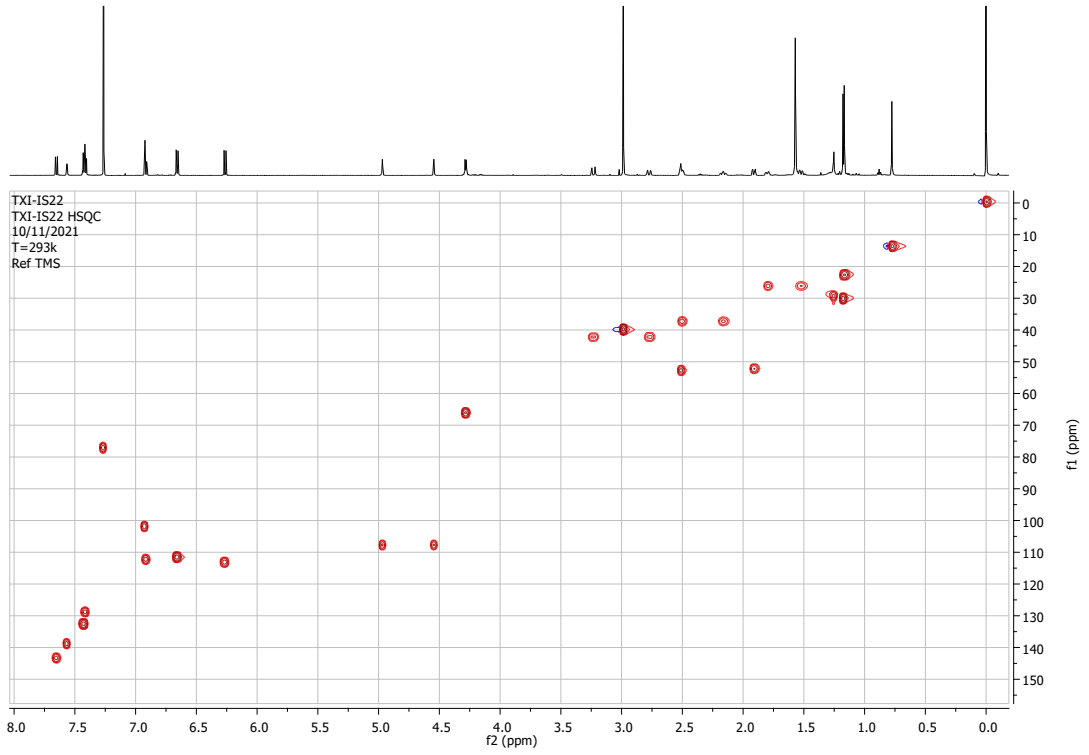
3l



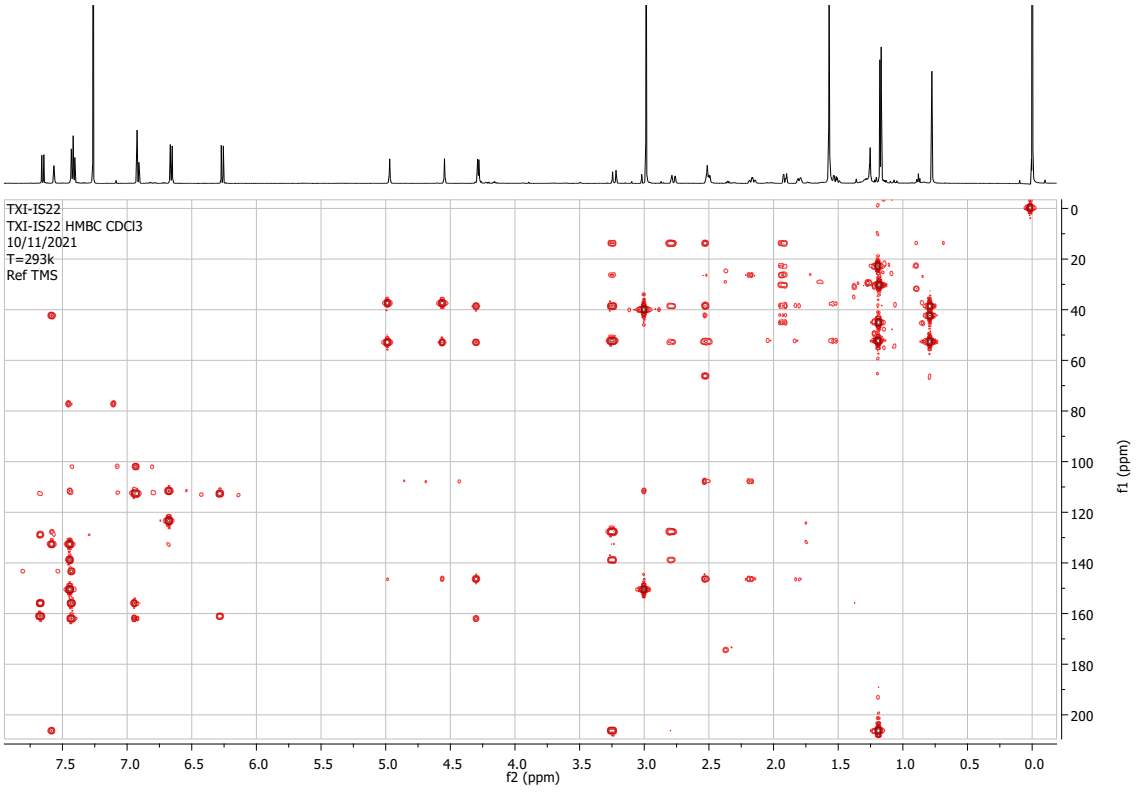
^{1}H NMR (600 MHz, $CDCl_3$) of compound 3l



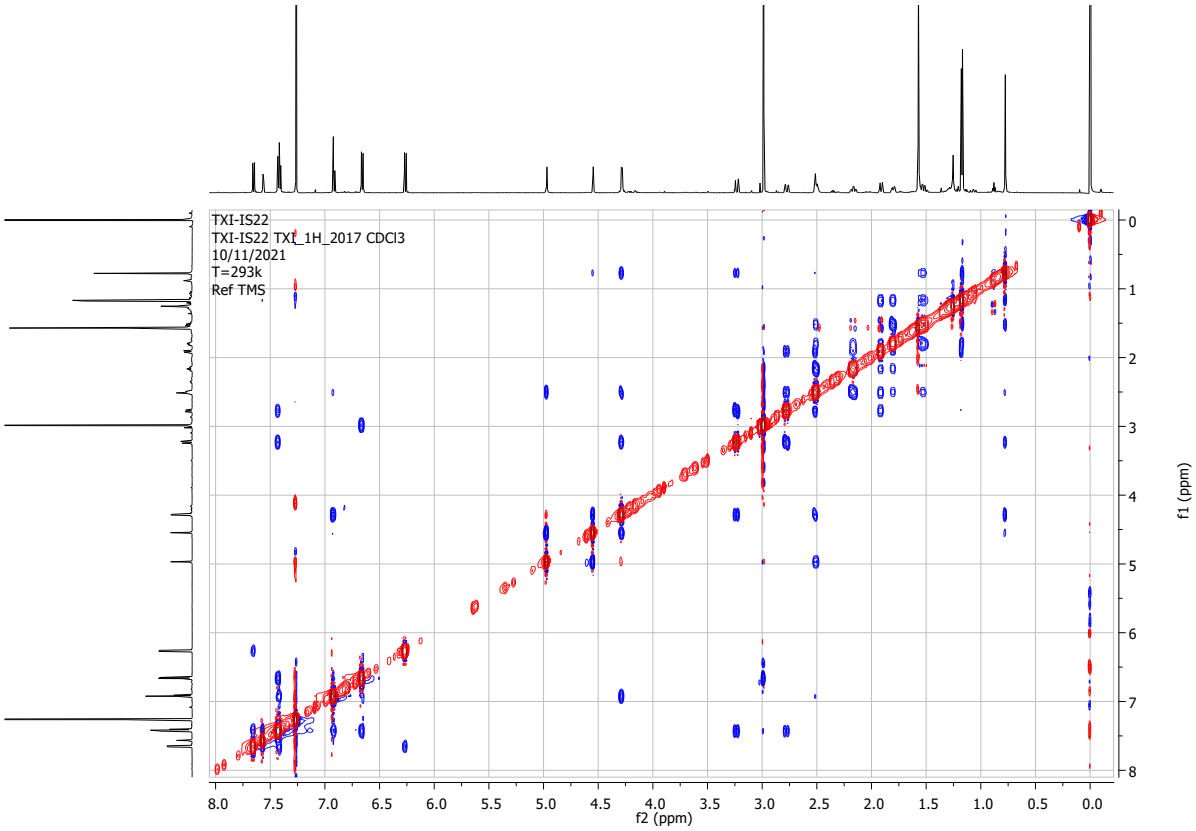
COSY spectrum of compound 3l



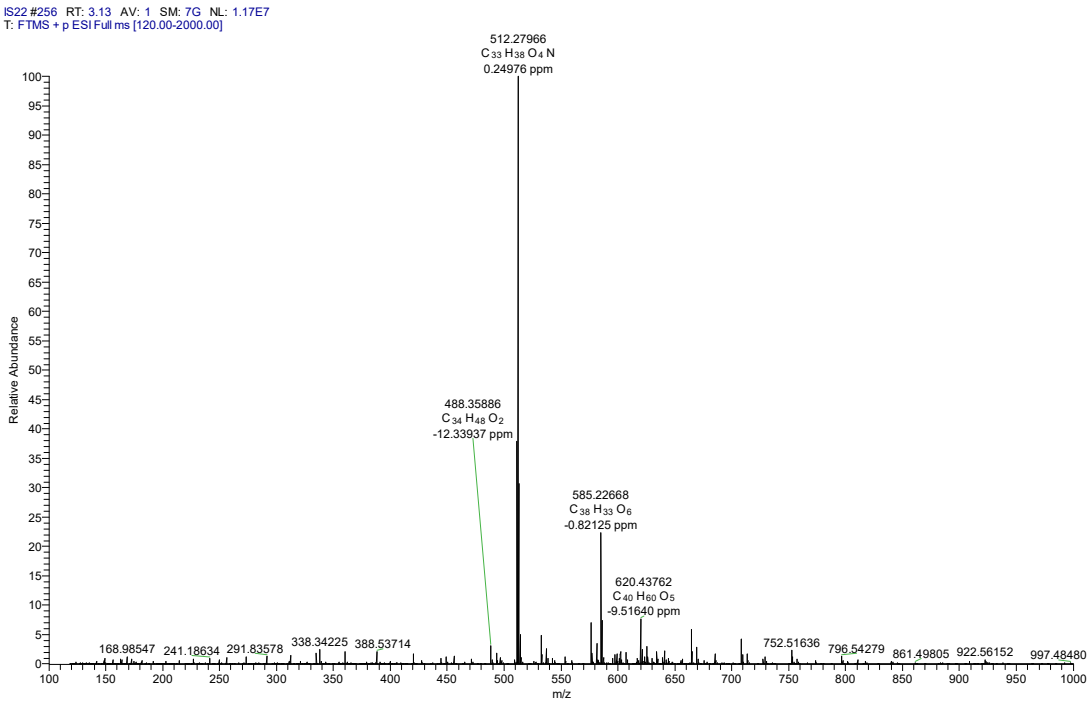
HSQC spectrum of compound 3l



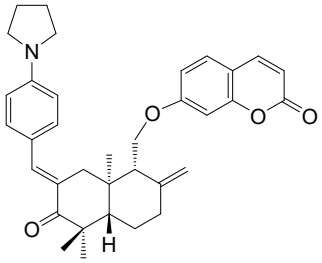
HMBC spectrum of compound 3l



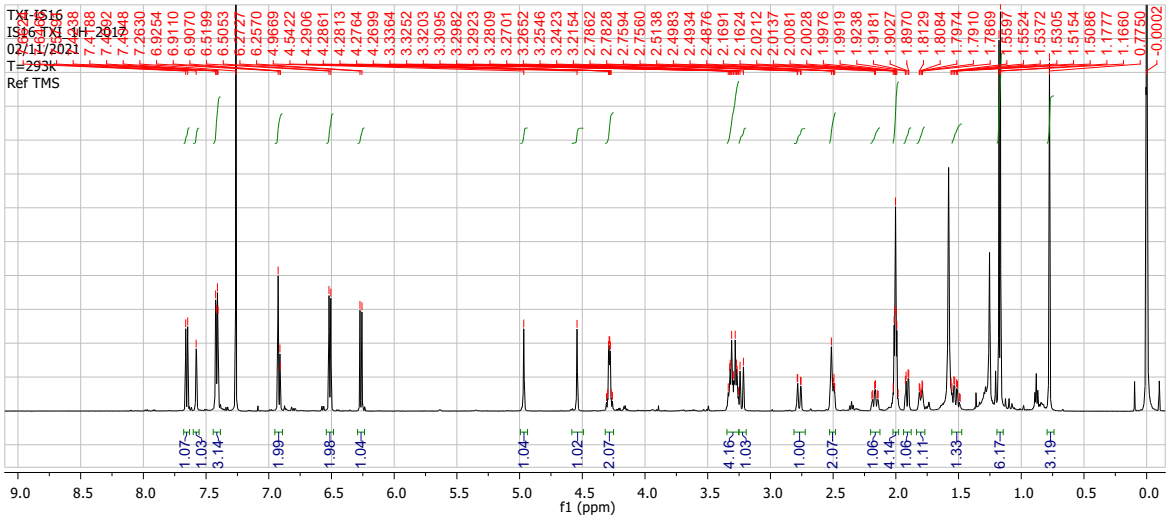
ROESY spectrum of compound 3l



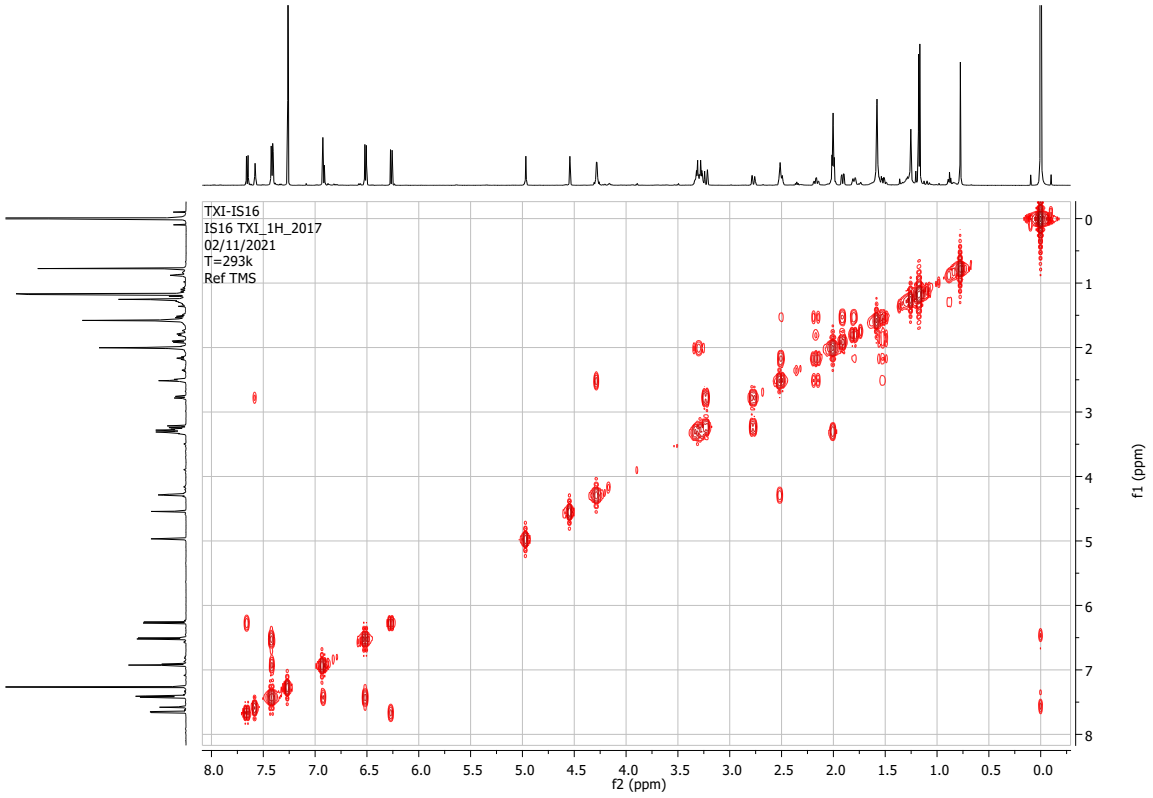
ESI-HRMS spectrum of compound 3l



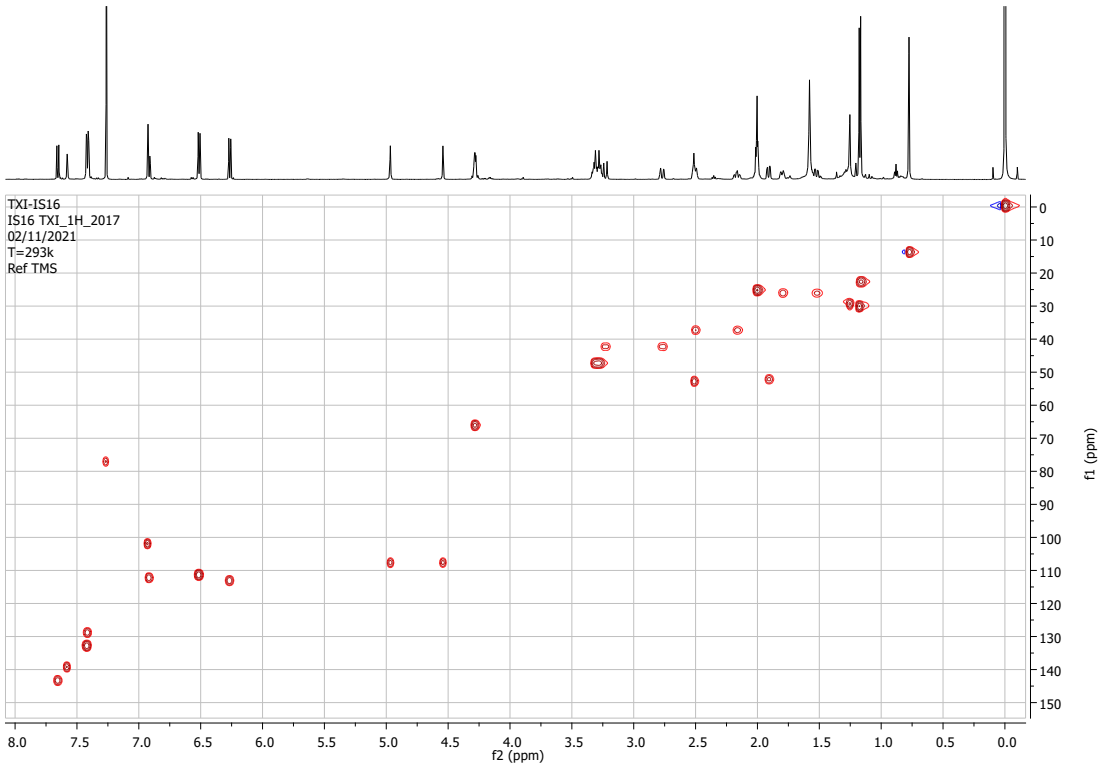
3m



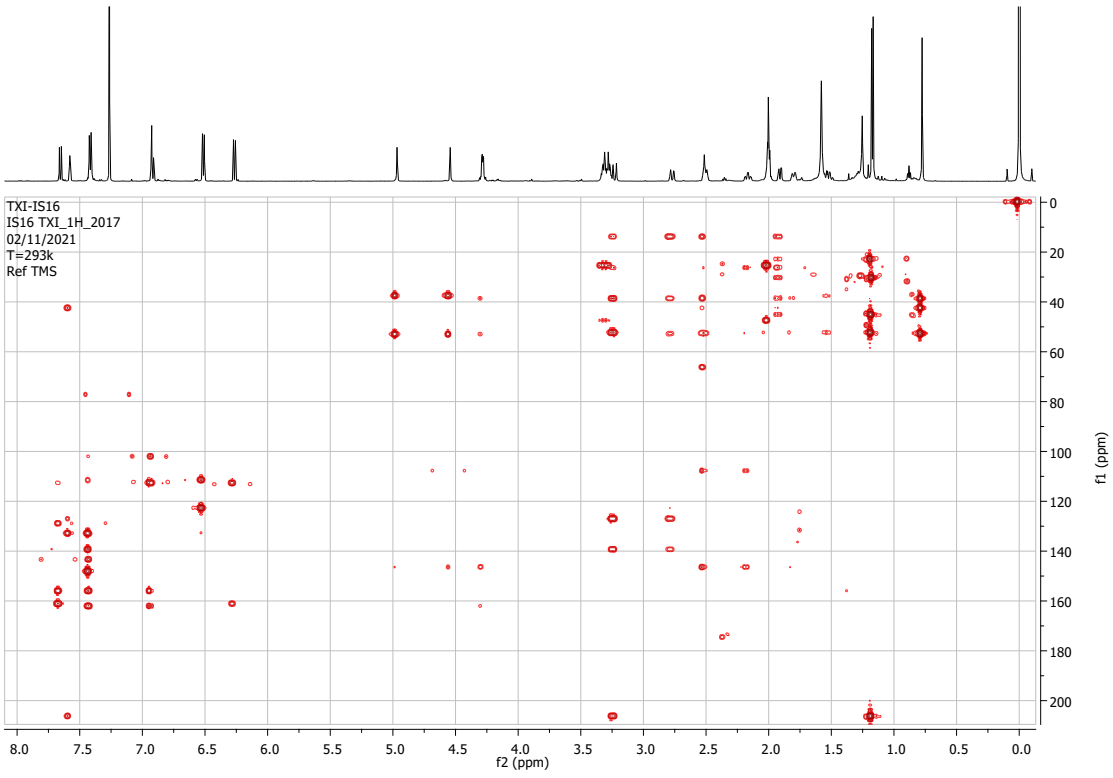
^{1}H NMR spectrum (600 MHz, $CDCl_3$) of compound 3m



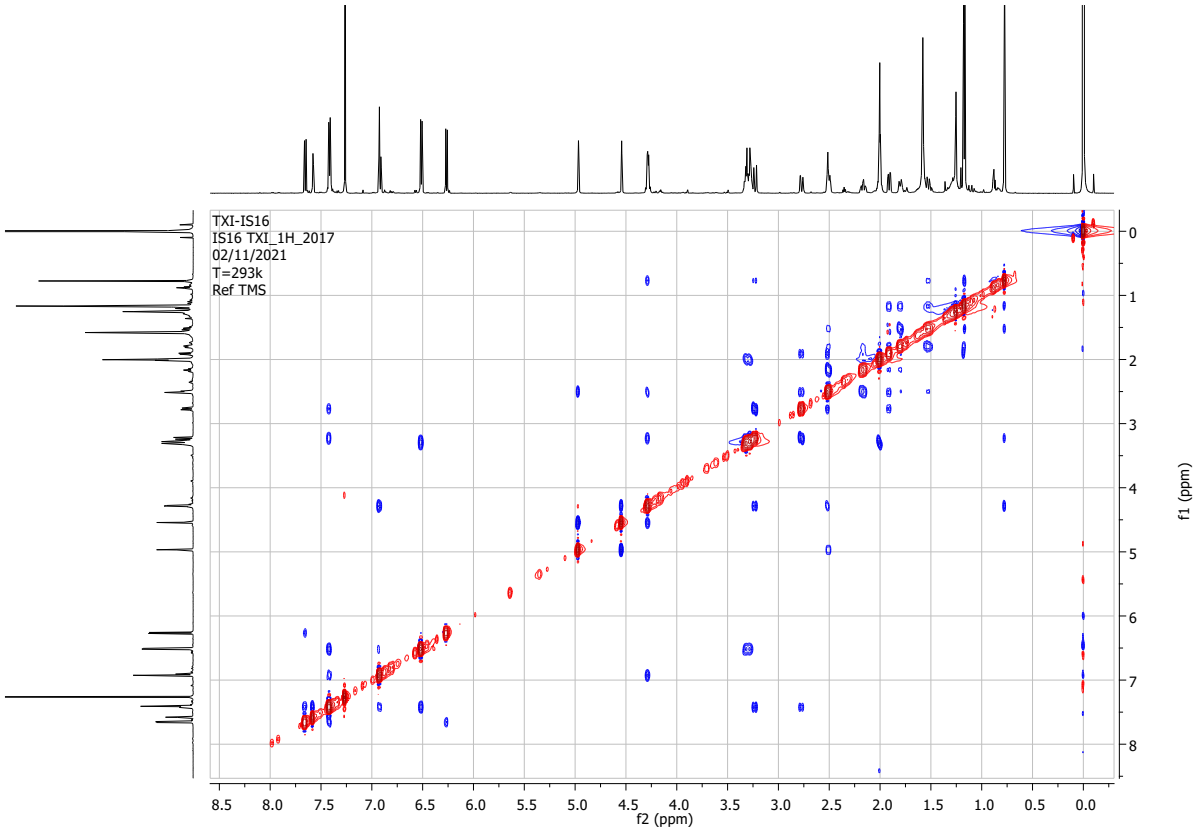
COSY spectrum of compound 3m



HSQC spectrum of compound 3m

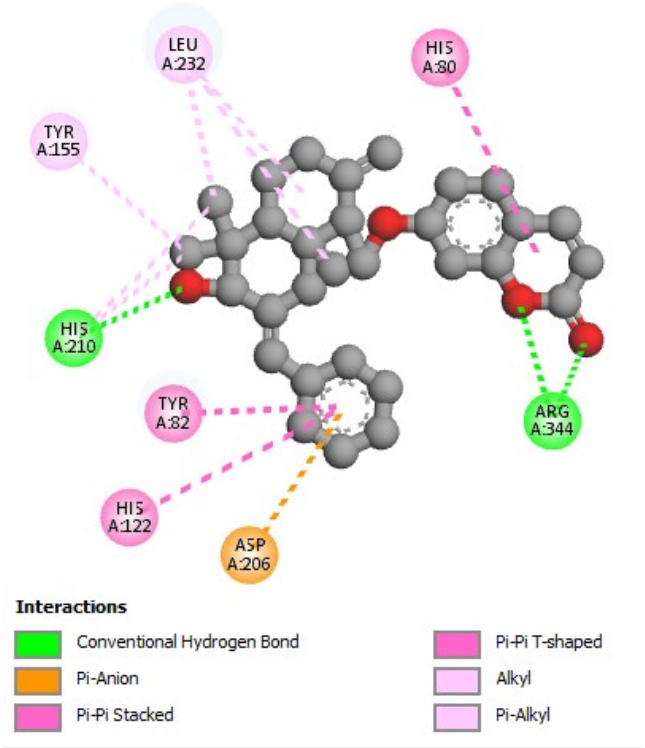


HMBC spectrum of compound 3m

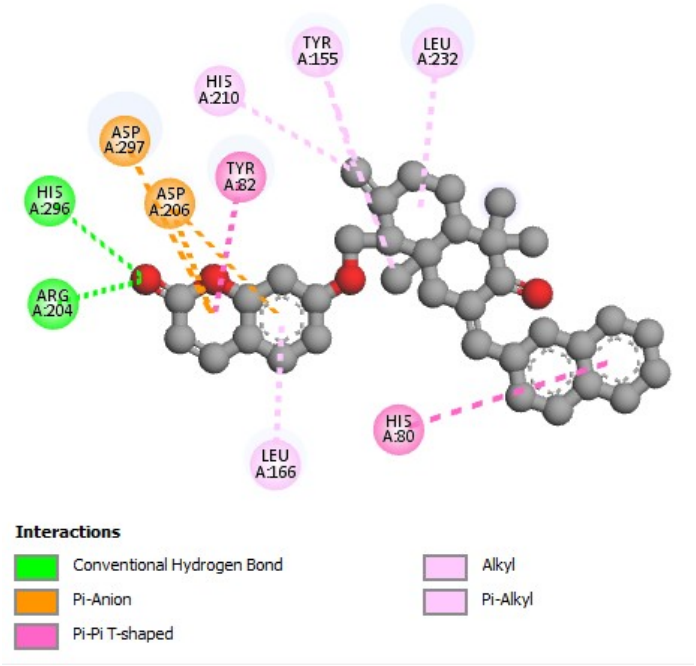


ROESY spectrum of compound 3m

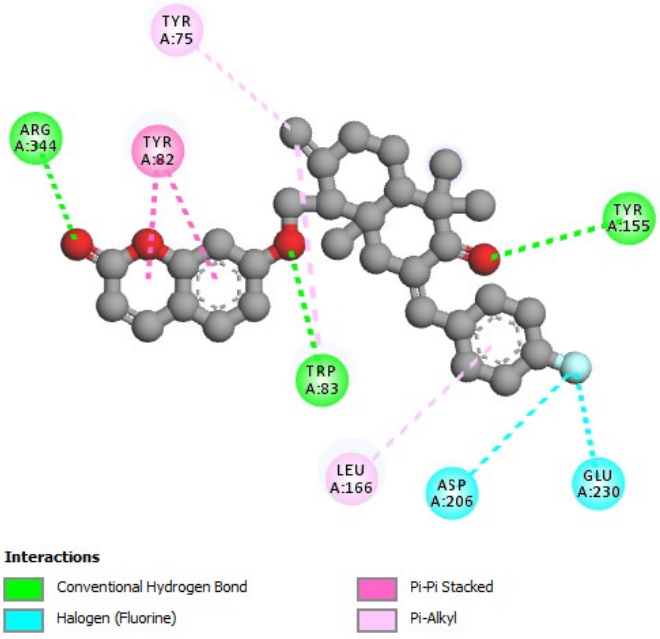
S3: Active site docking/blind docking poses of all compounds:



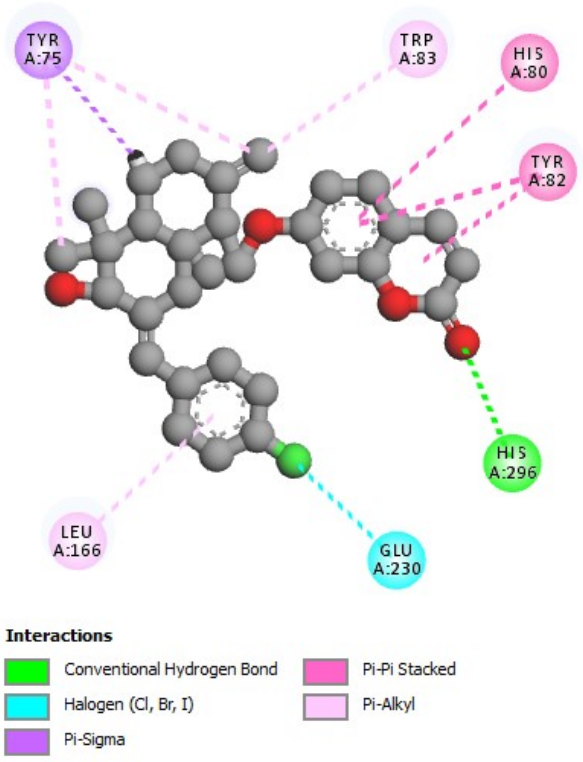
2D profile of compound 3a in the active site of α-amylase enzyme



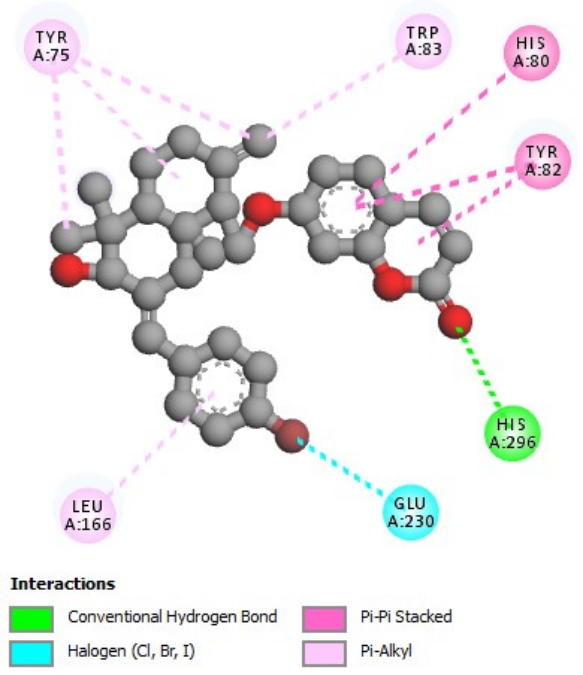
2D profile of compound 3b in the active site of α-amylase enzyme



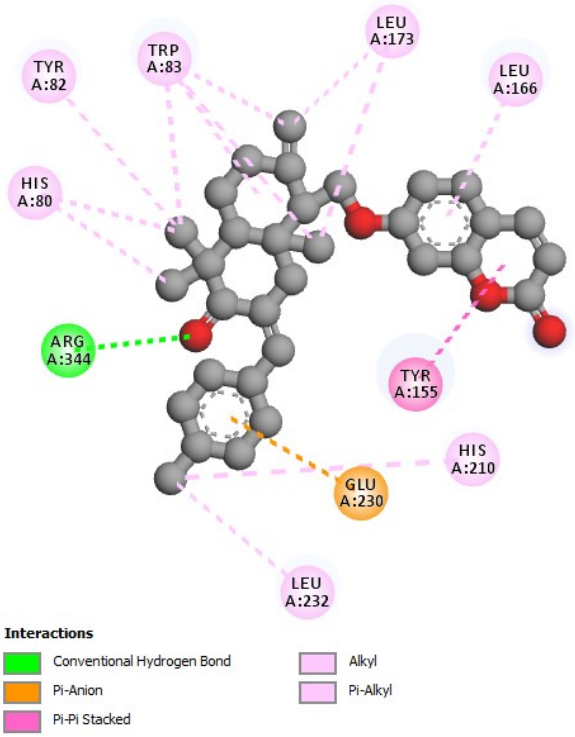
2D profile of compound 3c in the active site of α-amylase enzyme



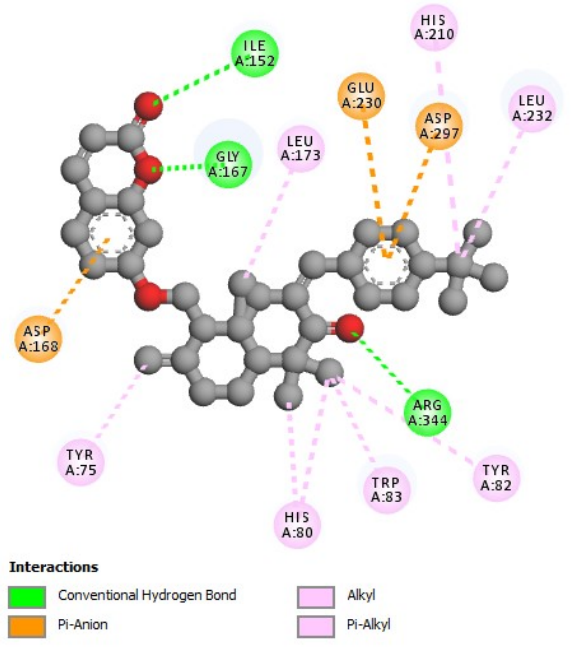
2D profile of compound 3d in the active site of α-amylase enzyme



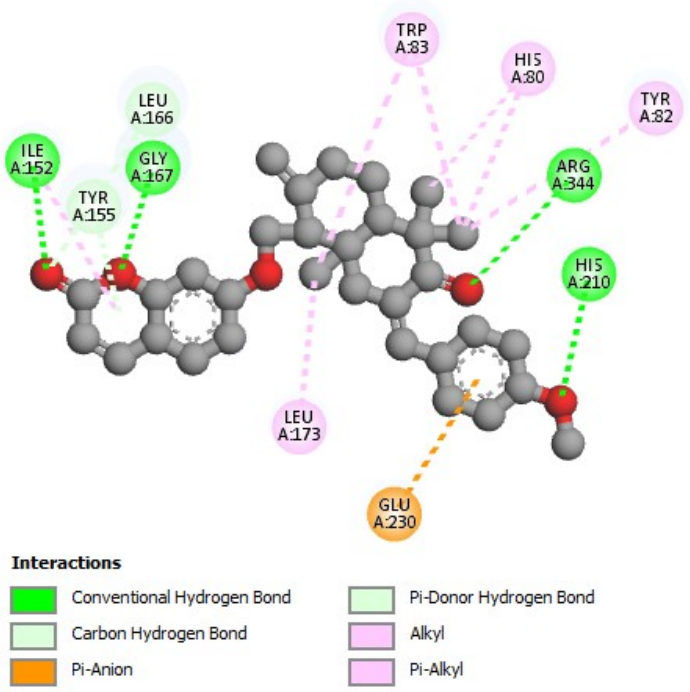
2D profile of compound 3e in the active site of α-amylase enzyme



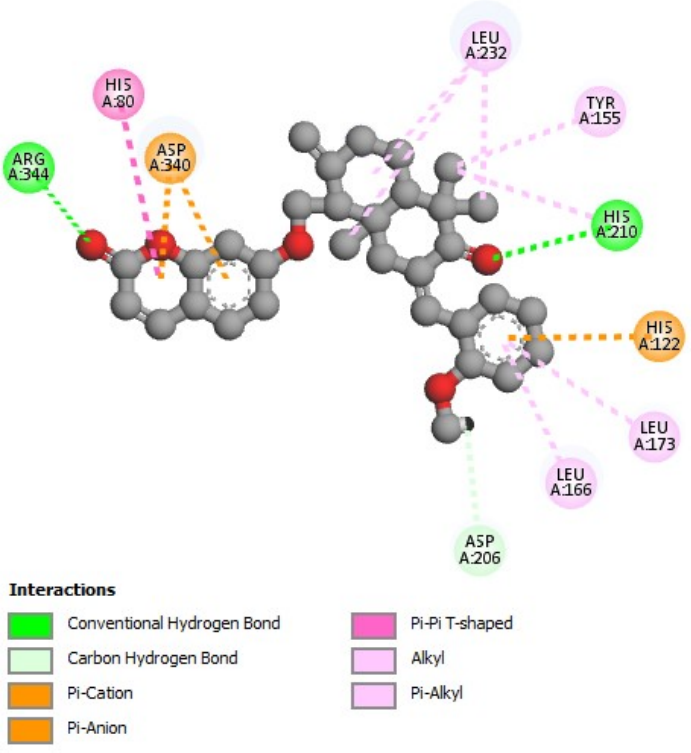
2D profile of compound 3f in the active site of α-amylase enzyme



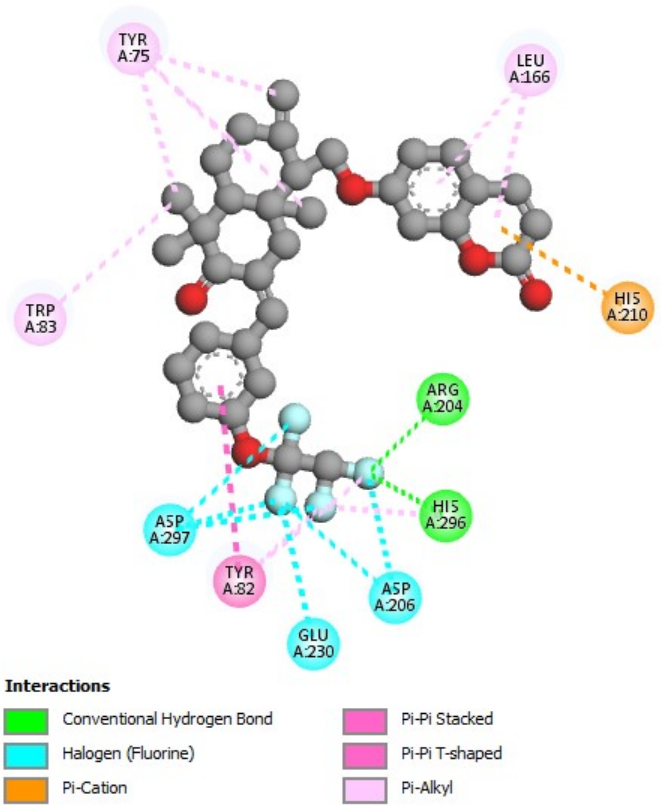
2D profile of compound 3g in the active site of α-amylase enzyme



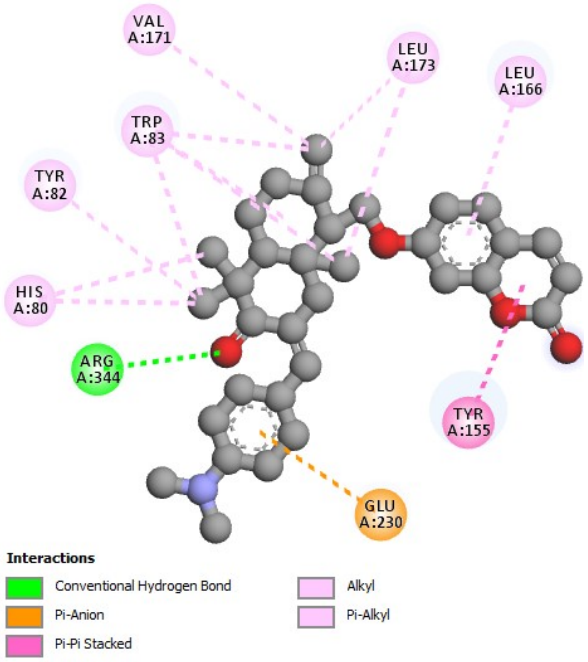
2D profile of compound 3h in the active site of α-amylase enzyme



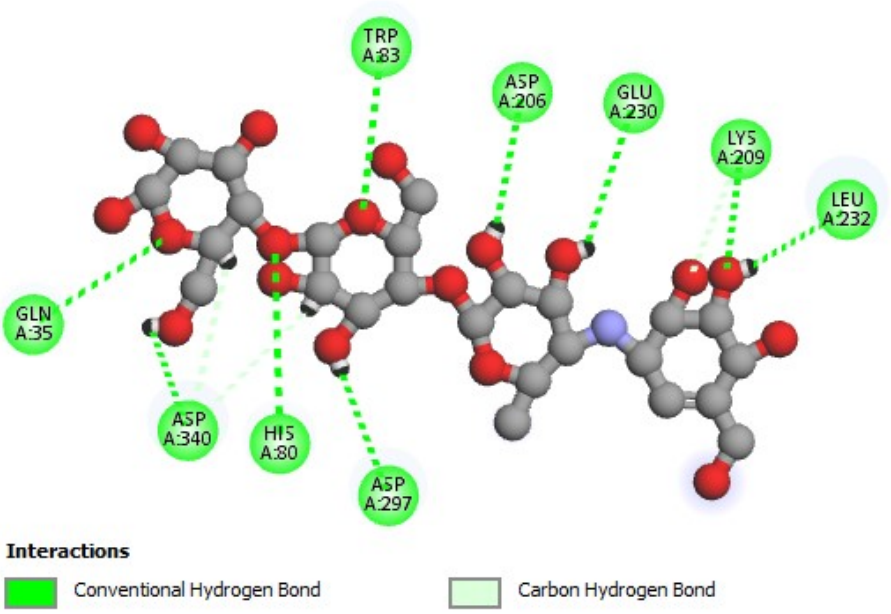
2D profile of compound 3i in the active site of α-amylase enzyme



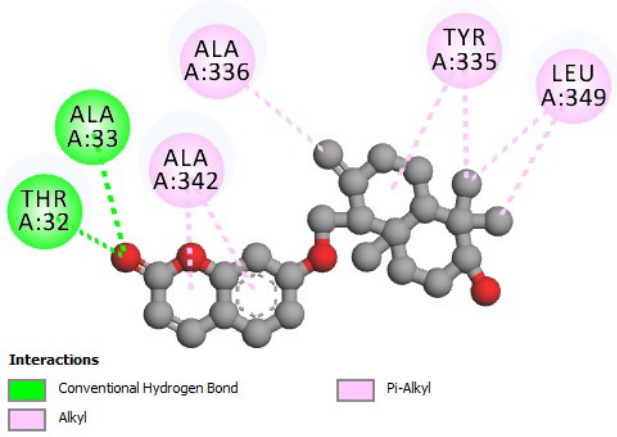
2D profile of compound 3k in the active site of α-amylase enzyme



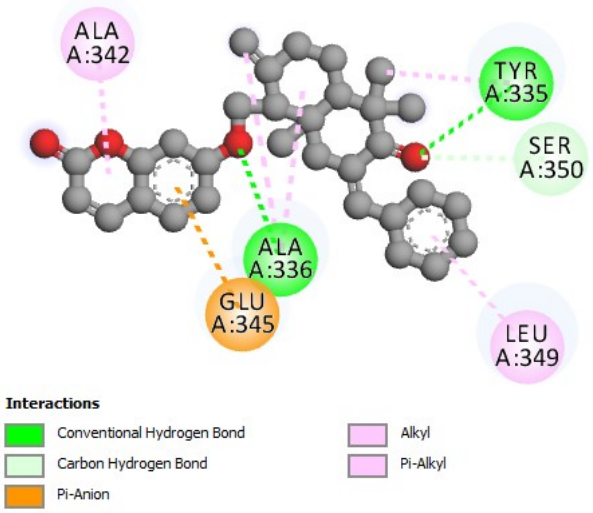
2D profile of compound 3l in the active site of α-amylase enzyme



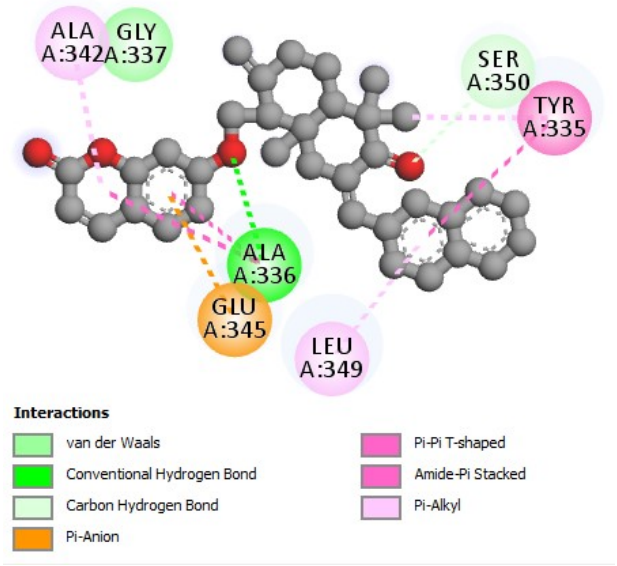
2D profile of acarbose in the active site of α-amylase enzyme



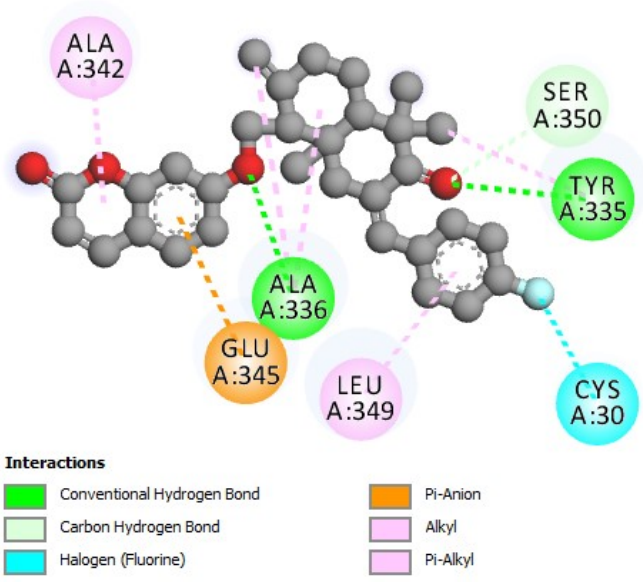
2D profile of compound 1 in the allosteric site of α-amylase enzyme



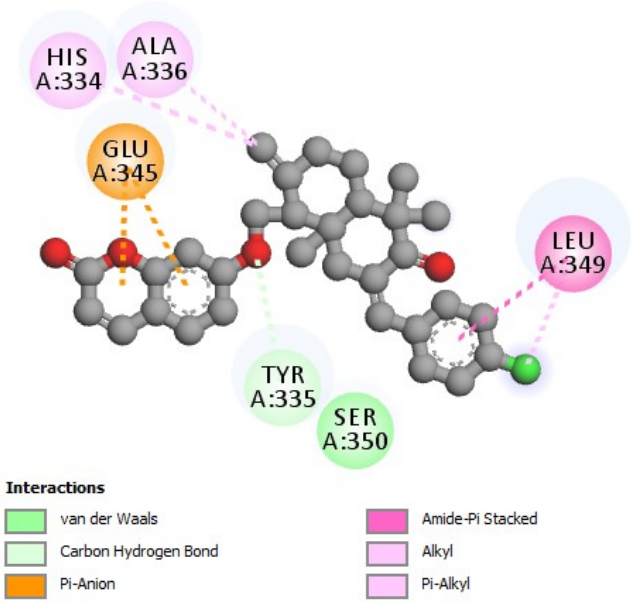
2D profile of compound 3a in the allosteric site of α-amylase enzyme



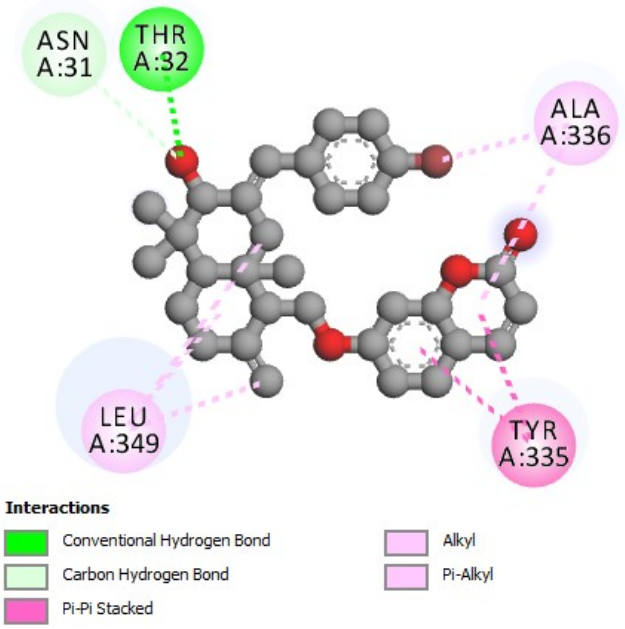
2D profile of compound 3b in the allosteric site of α-amylase enzyme



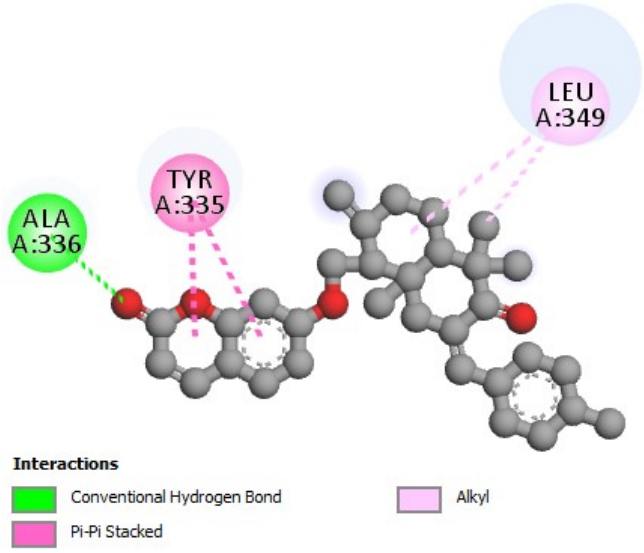
2D profile of compound 3c in the allosteric site of α-amylase enzyme



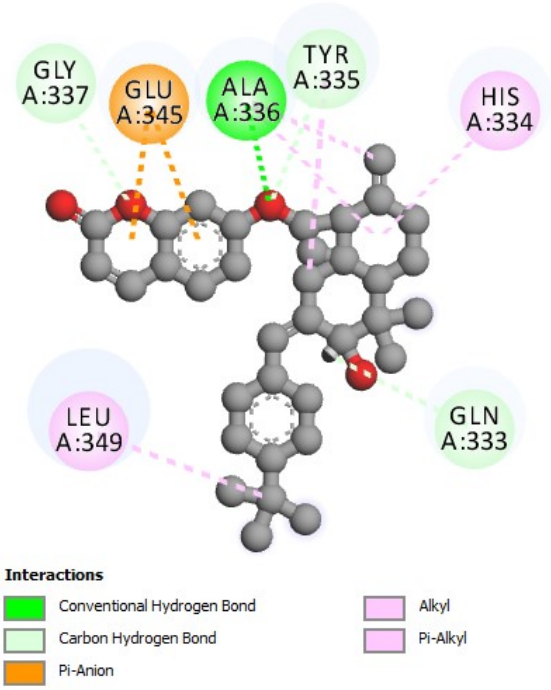
2D profile of compound 3d in the allosteric site of α-amylase enzyme



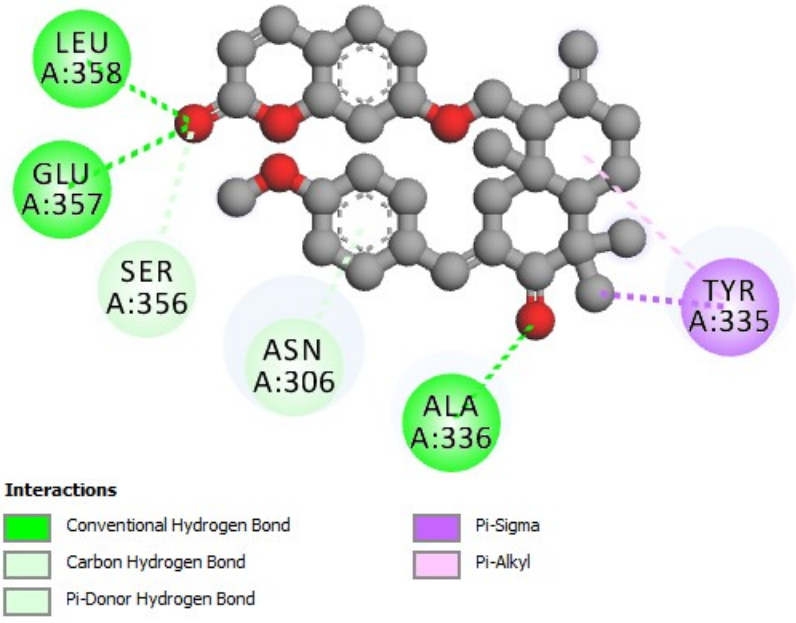
2D profile of compound 3e in the allosteric site of α-amylase enzyme



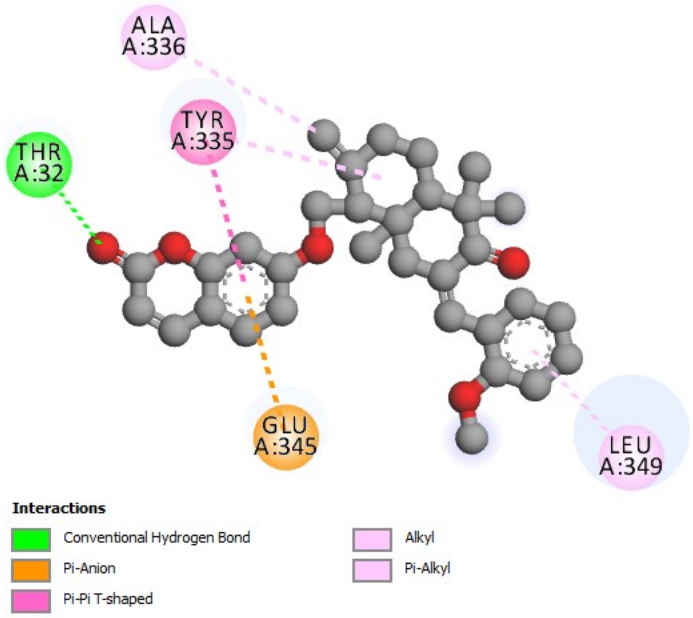
2D profile of compound 3f in the allosteric site of α-amylase enzyme



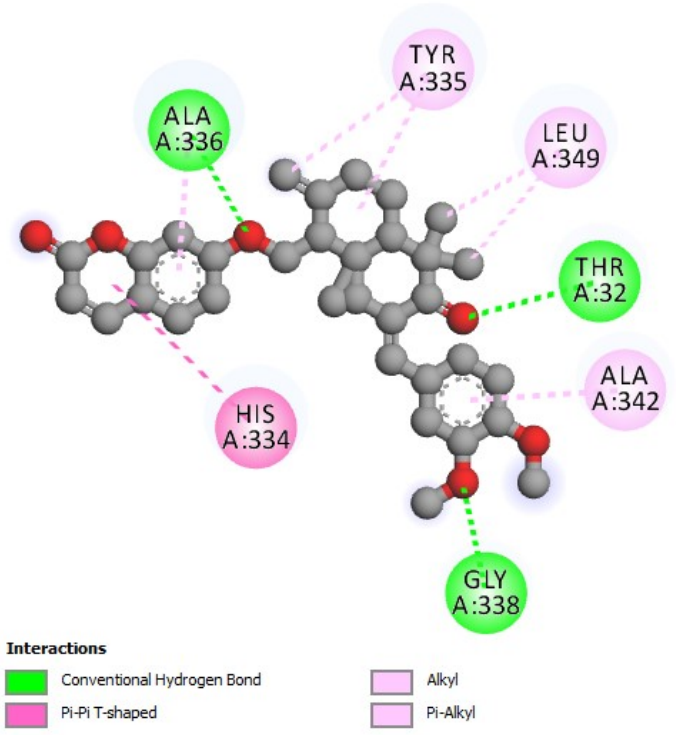
2D profile of compound 3g in the allosteric site of α-amylase enzyme



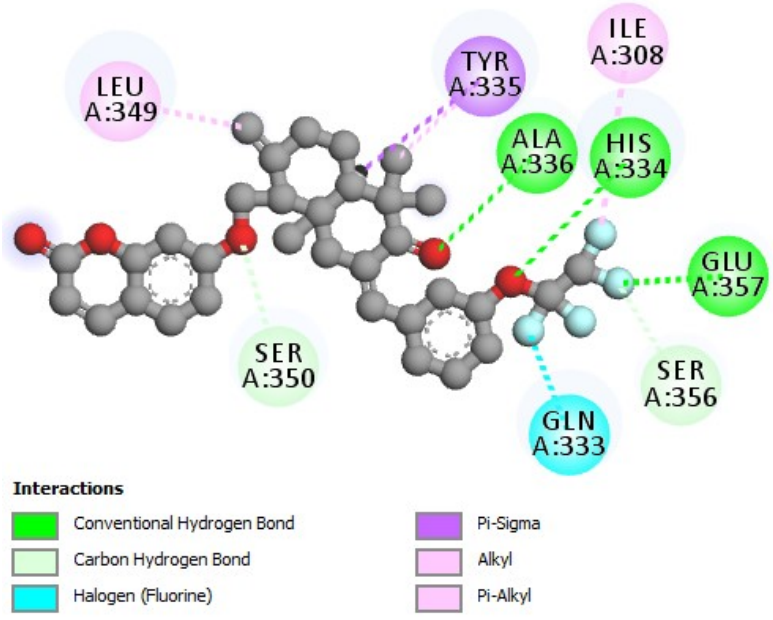
2D profile of compound 3h in the allosteric site of α-amylase enzyme



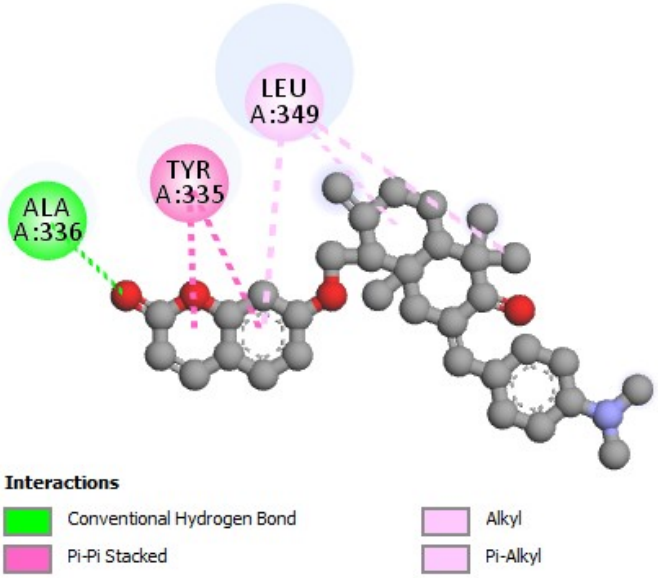
2D profile of compound 3i in the allosteric site of α-amylase enzyme



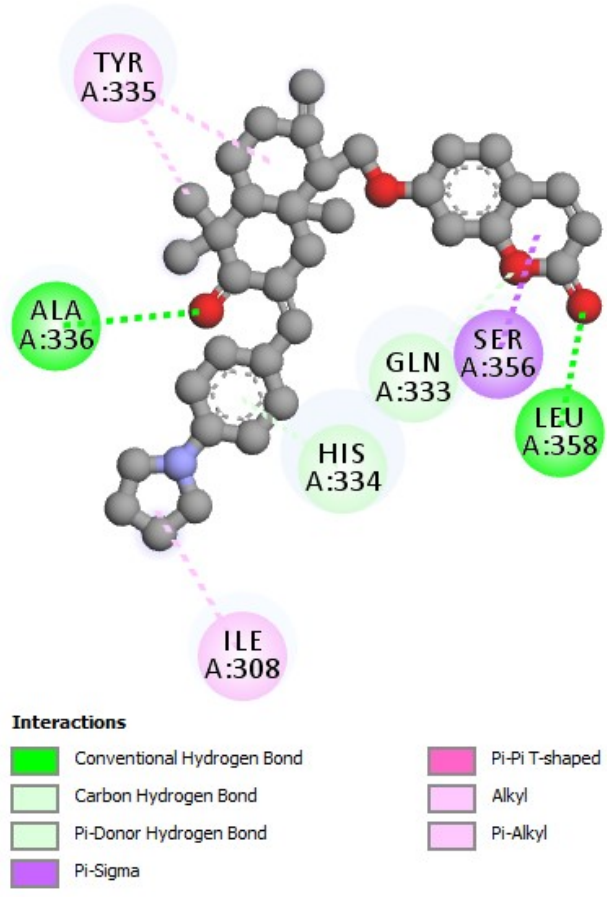
2D profile of compound 3j in the allosteric site of α-amylase enzyme



2D profile of compound 3k in the allosteric site of α-amylase enzyme



2D profile of compound 3l in the allosteric site of α-amylase enzyme



2D profile of compound 3m in the allosteric site of α-amylase enzyme

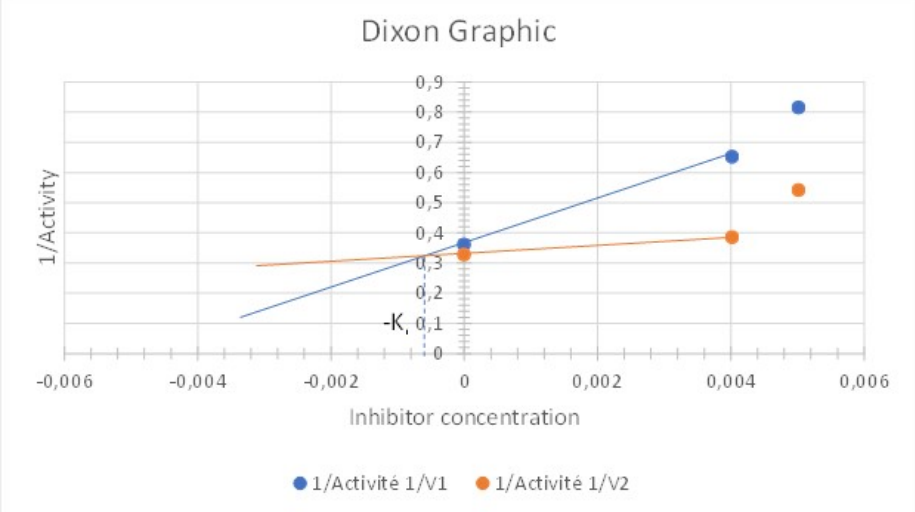
S4: Toxicity risk prediction for compounds 1 and 3a-m

Compound	Mutagenicity	Tumorigenicity	Irritation	Reproductive effect
1	🟢	🟢	🟢	🟢
3a	🟢	🟢	🟢	🟢
3b	🟢	🟢	🟢	🟢
3c	🟢	🟢	🟢	🟢
3d	🟢	🟢	🟢	🟢
3e	🟢	🟢	🟢	🟢
3f	🟢	🟢	🟢	🟢
3g	🟢	🟢	🟢	🟢
3h	🟢	🟢	🟢	🔴
3i	🟢	🟢	🟢	🟢
3j	🟢	🟢	🟢	🔴
3k	🟢	🟢	🟢	🟢
3l	🔴	🔴	🟢	🟢
3m	🔴	🟡	🟢	🟢

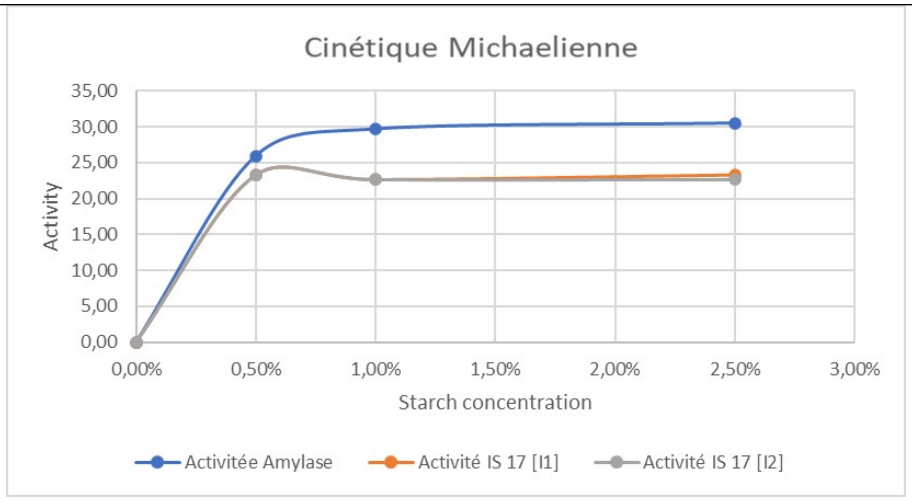
🟢 No risk
🟡 Medium risk
🔴 High risk

S5: Kinetic study of the three most active compounds

Kenitic study of 3K compound and detemination of Ki and Kmapp (form LB-plot previously done)

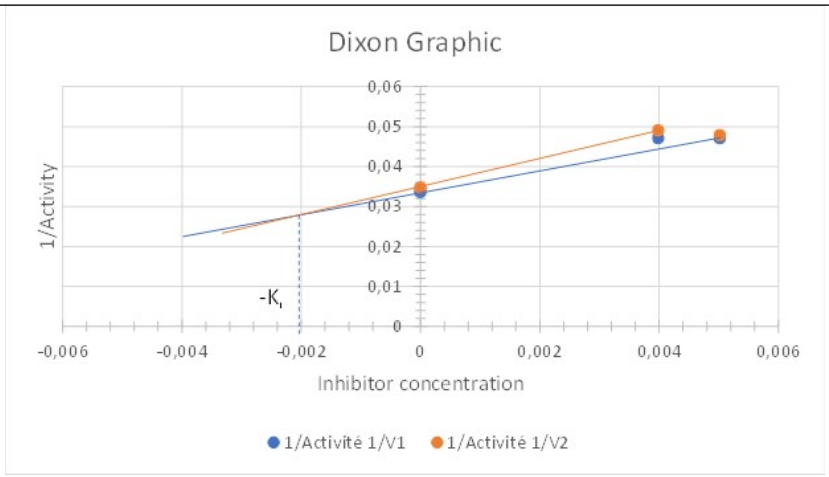


Dixon graphic and determination of Ki = 0.0006 mg/ml

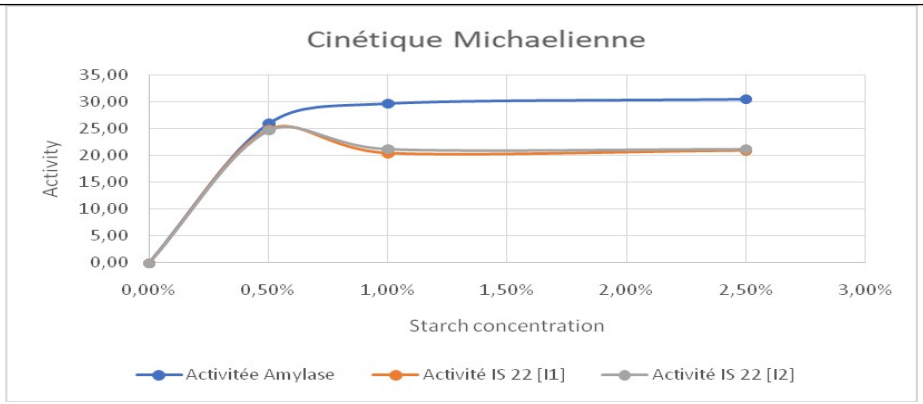


Graphical kinetec study section of 3K and Kmapp= 0.909mg/ml

Kenitic study of 3l compound and detemination of Ki and Kmapp (form LB-plot previously done)



Dixon graphic and determination of Ki = 0.002 mg/ml



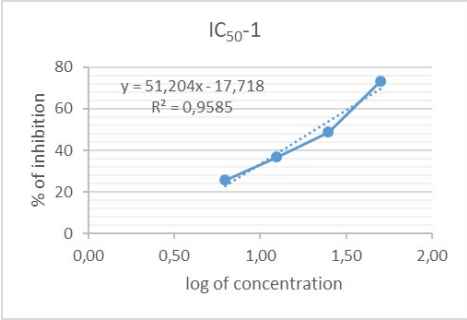
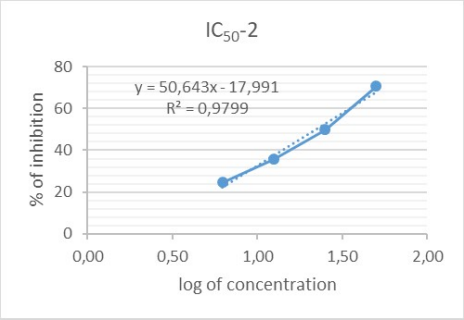
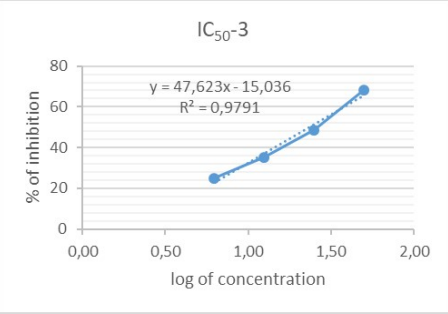
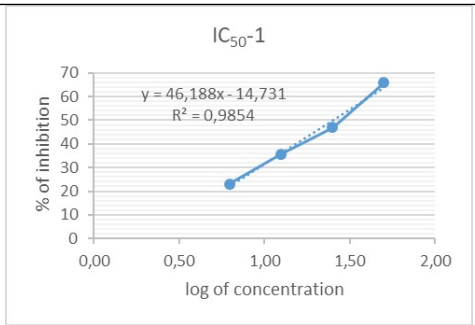
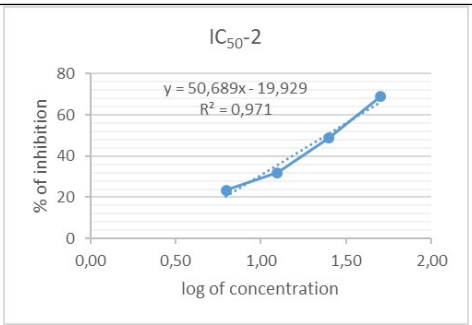
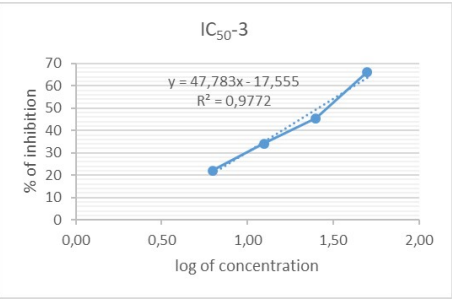
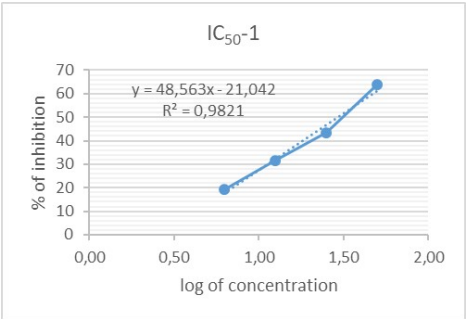
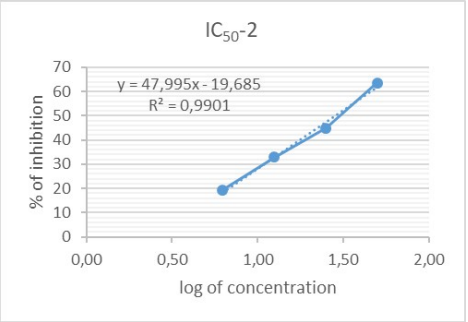
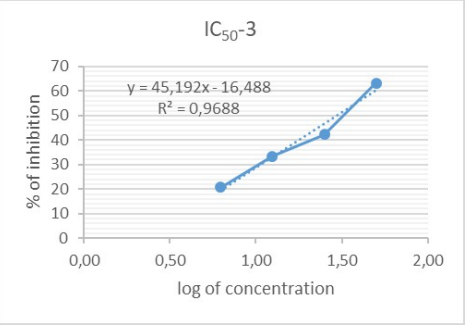
Graphical kinetec study section of 3l and Kmapp= 2 mg/ml

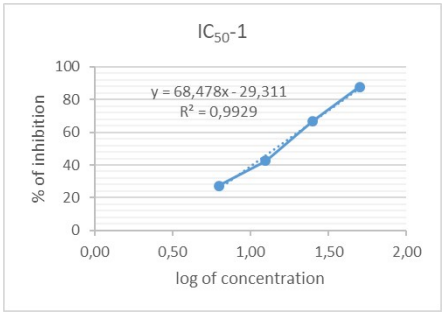
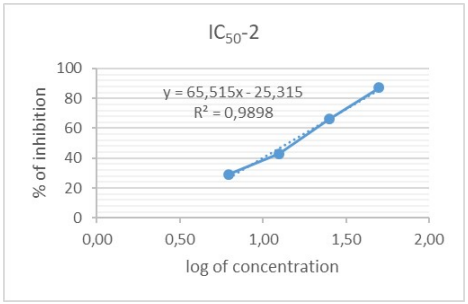
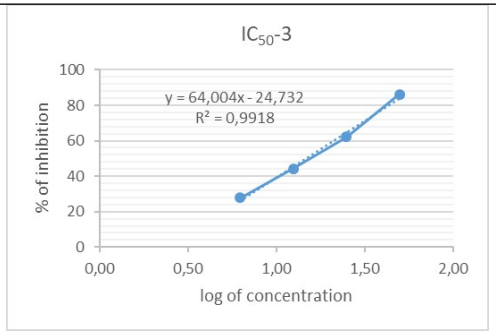
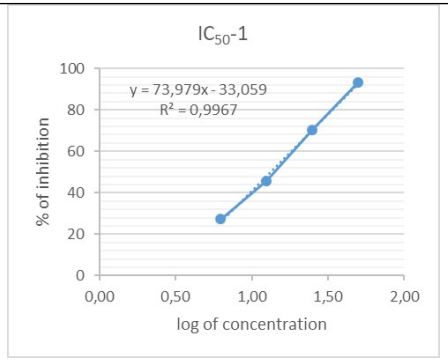
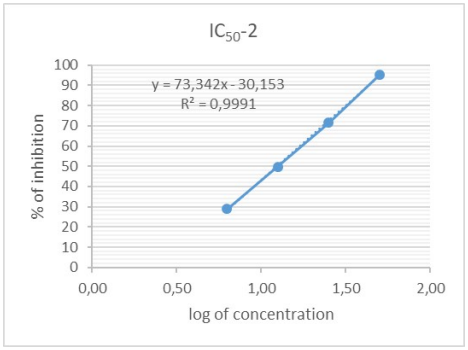
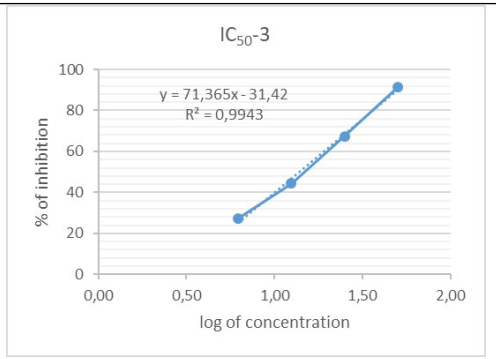
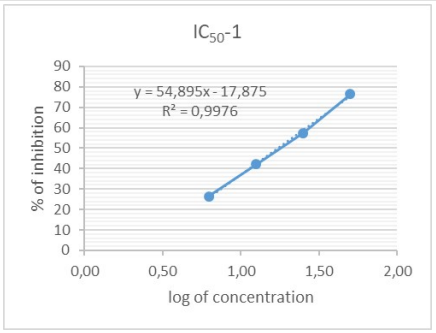
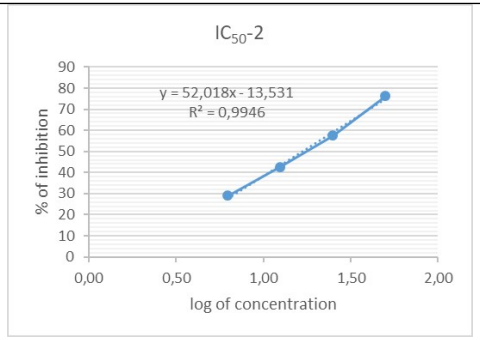
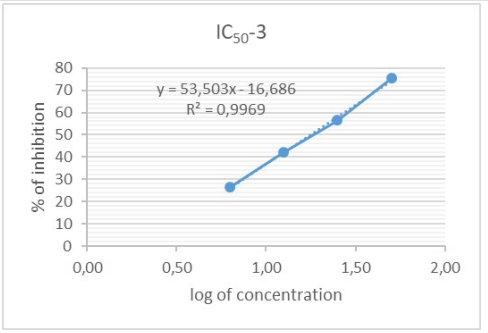
Kenitic study of 3K compound and detemination of Ki and Kmapp (form LB-plot previously done)

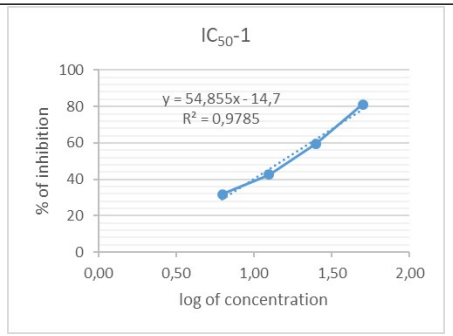
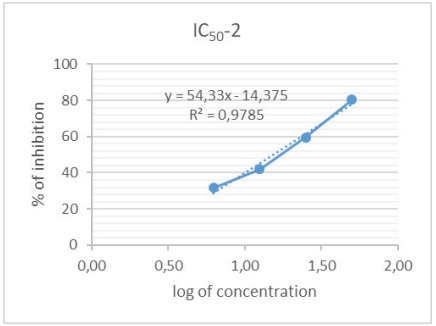
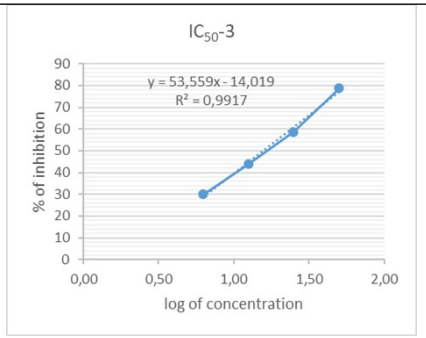
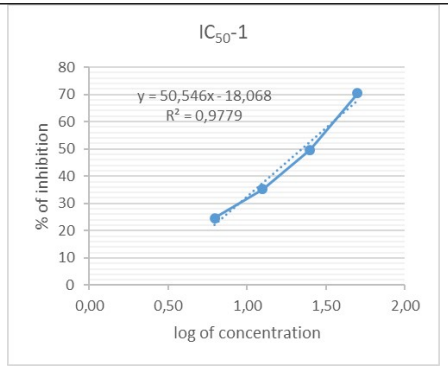
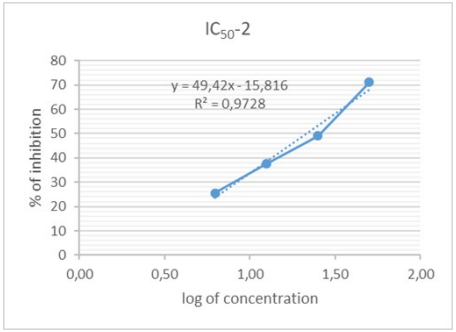
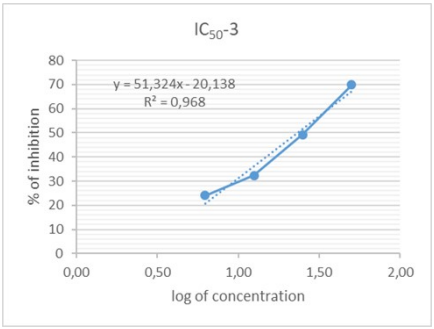
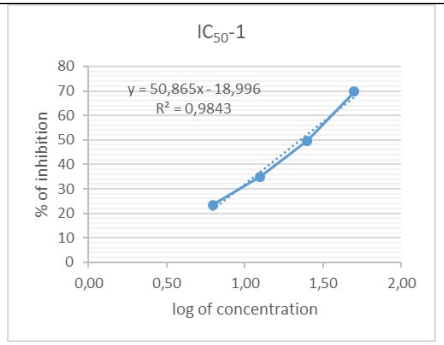
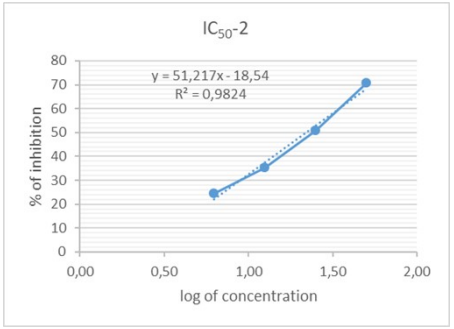
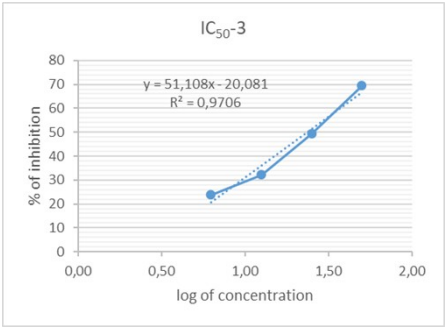
Dixon graphic and determination of Ki = 0.0006 mg/ml

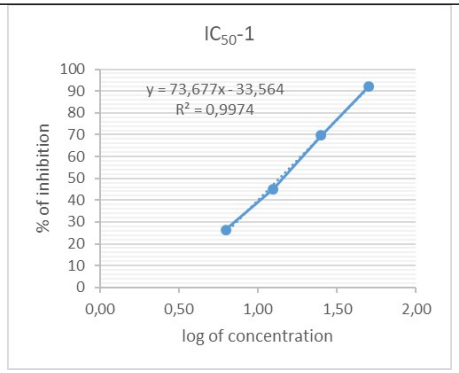
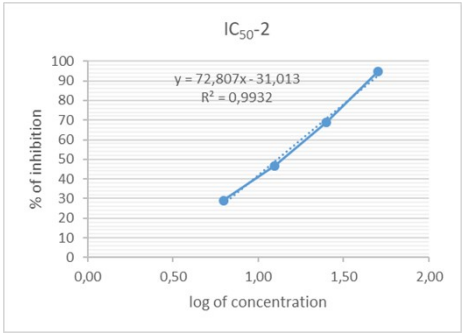
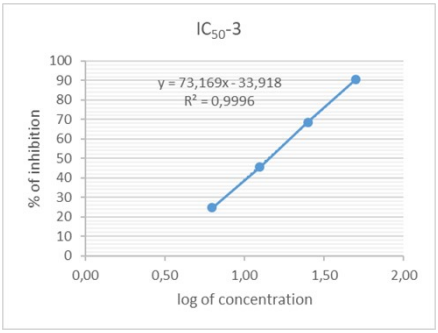
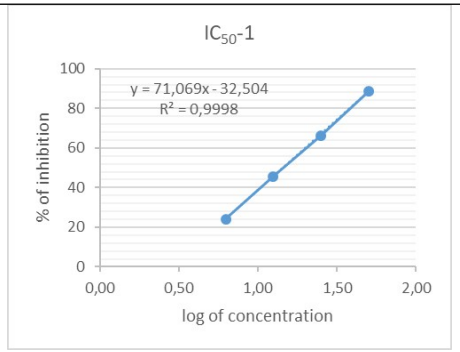
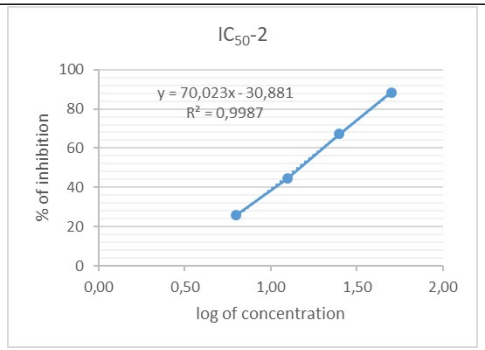
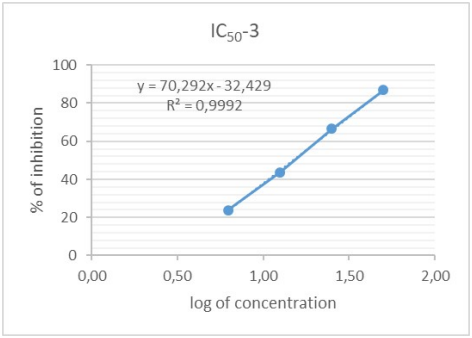
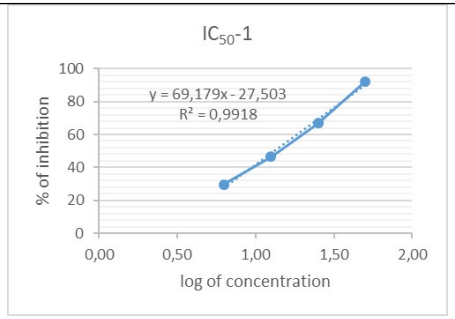
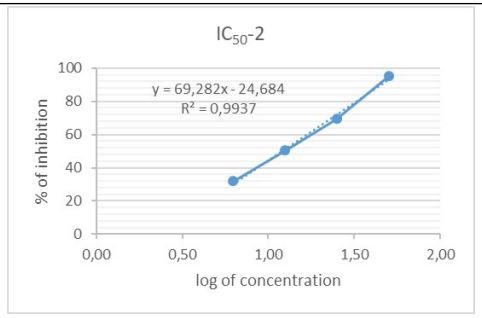
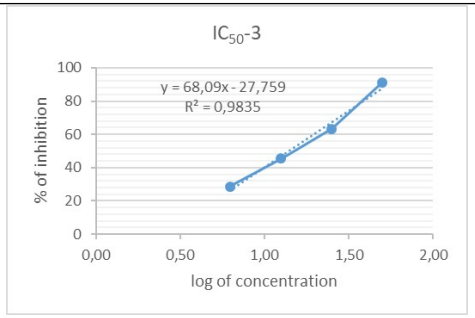
Graphical kinetec study section of 3m and Kmapp= 0.909 mg/ml

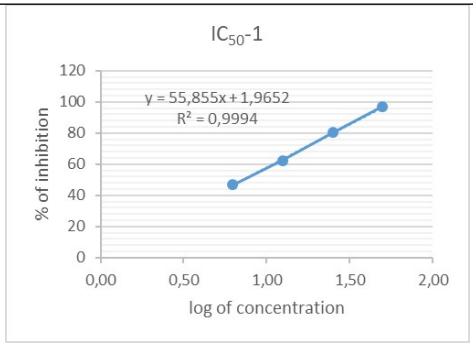
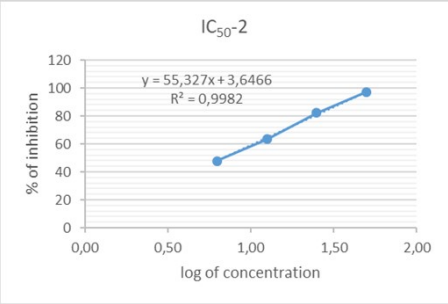
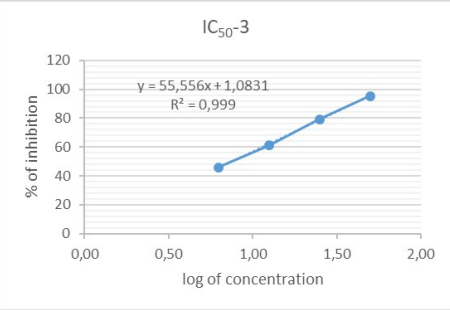
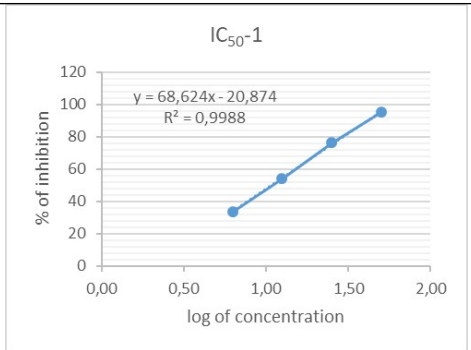
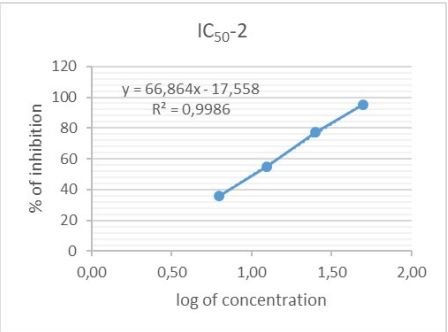
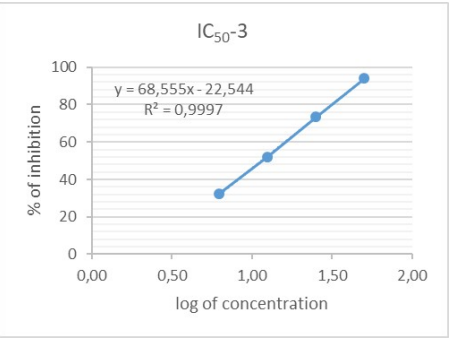
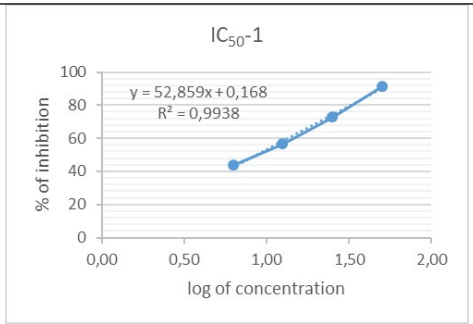
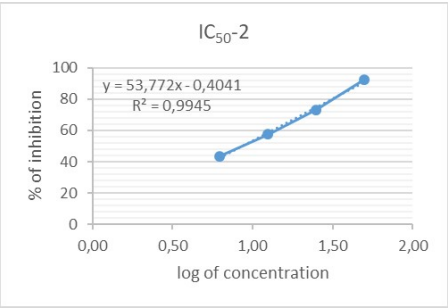
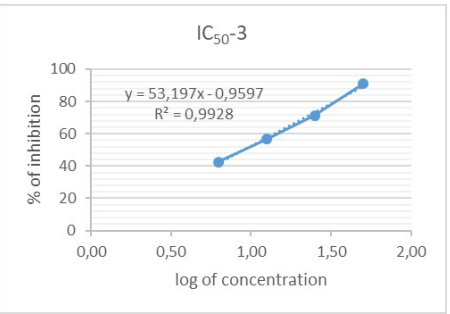
S6: IC_{50} graphs of all the tested compounds

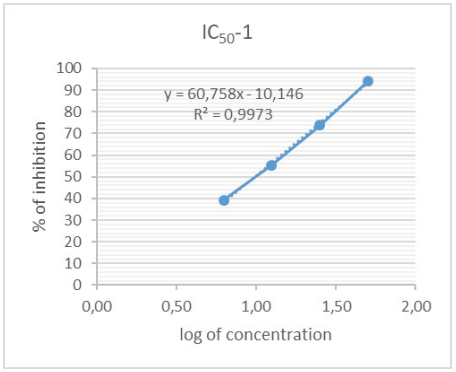
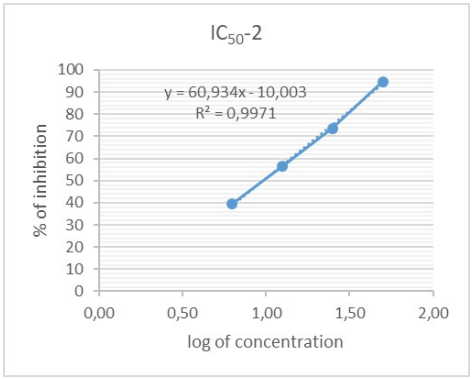
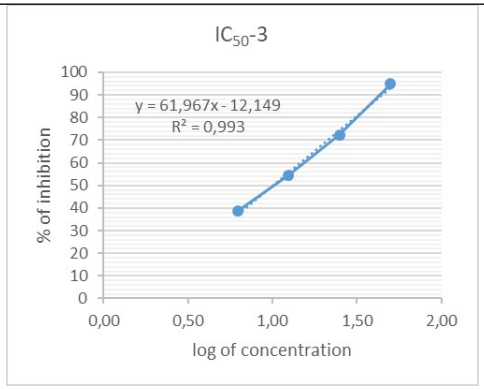
Compound	IC_{50} (1)	IC_{50} (2)	IC_{50} (3)	IC_{50} ± SD
1	 21.01	 22.01	 23.21	22.08 ± 1.10
2	 25.20	 23.96	 25.93	25.03 ± 0.99
3a	 29.03	 28.31	 29.60	28.98 ± 0.65

3b	 14.39	 14.11	 14.71	14.41 ± 0.30
3c	 13.27	 12.38	 13.83	13.16 ± 0.73
3d	 17.24	 16.65	 17.64	17.17 ± 0.50

3e	 15.12	 15.31	 15.68	15.37 ± 0.29
3f	 22.22	 21.47	 23.26	22.31 ± 0.90
3g	 22.72	 21.79	 23.51	22.67 ± 0.86

3h	 13.62	 12.96	 14.03	13.54 ± 0.54
3i	 14.48	 14.29	 14.88	14.55 ± 0.30
3j	 13.19	 11.97	 13.87	13.01 ± 0.96

3k	 7.24	 6.88	 7.59	7.24 ± 0.36
3l	 10.78	 10.24	 11.43	10.82 ± 0.60
3m	 8.76	 8.66	 9.08	8.83 ± 0.22

Acarbose (Positive control)	 9.77	 9.65	 10.07	9.83 ± 0.21