

Electronic Supplementary Information

Synthesis and biological evaluation of FJ-809, a compound originally described as MIM-1 and inhibitor of the anti-apoptotic protein Mcl-1.

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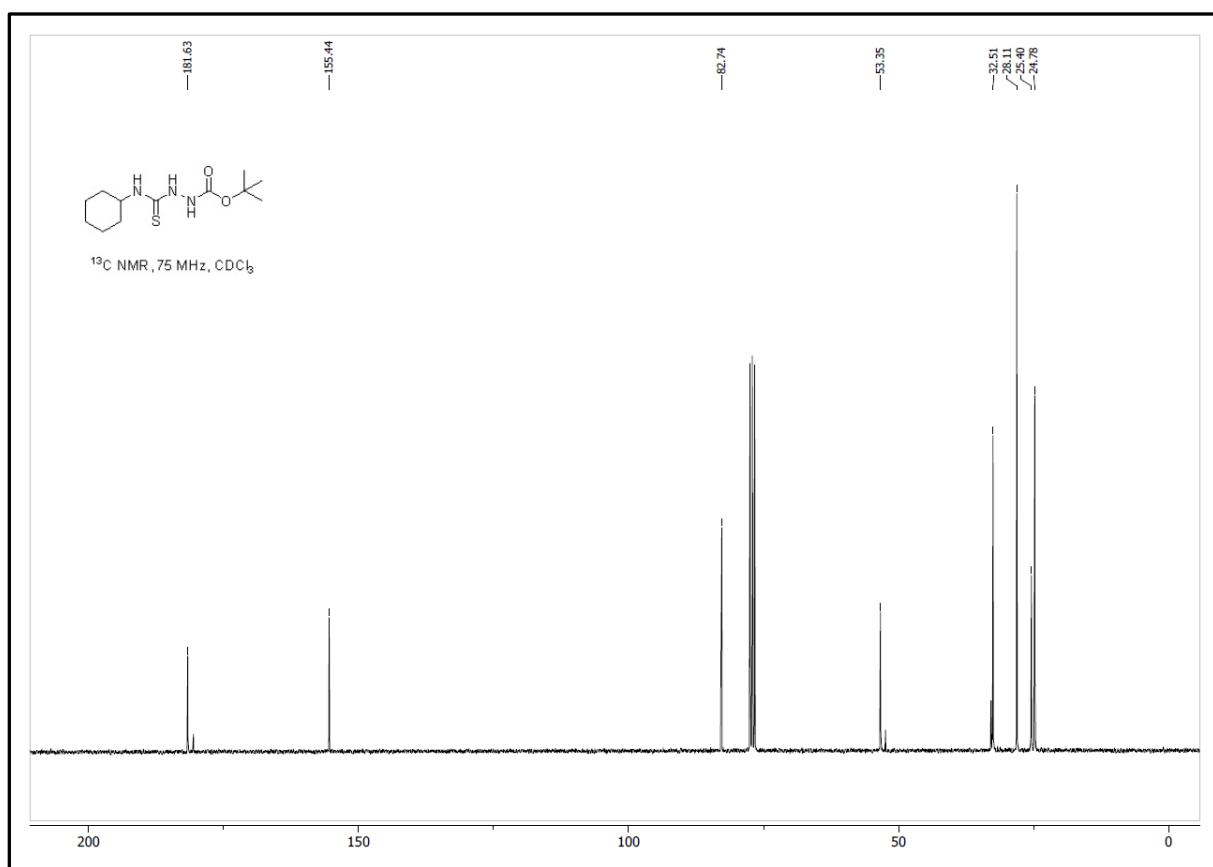
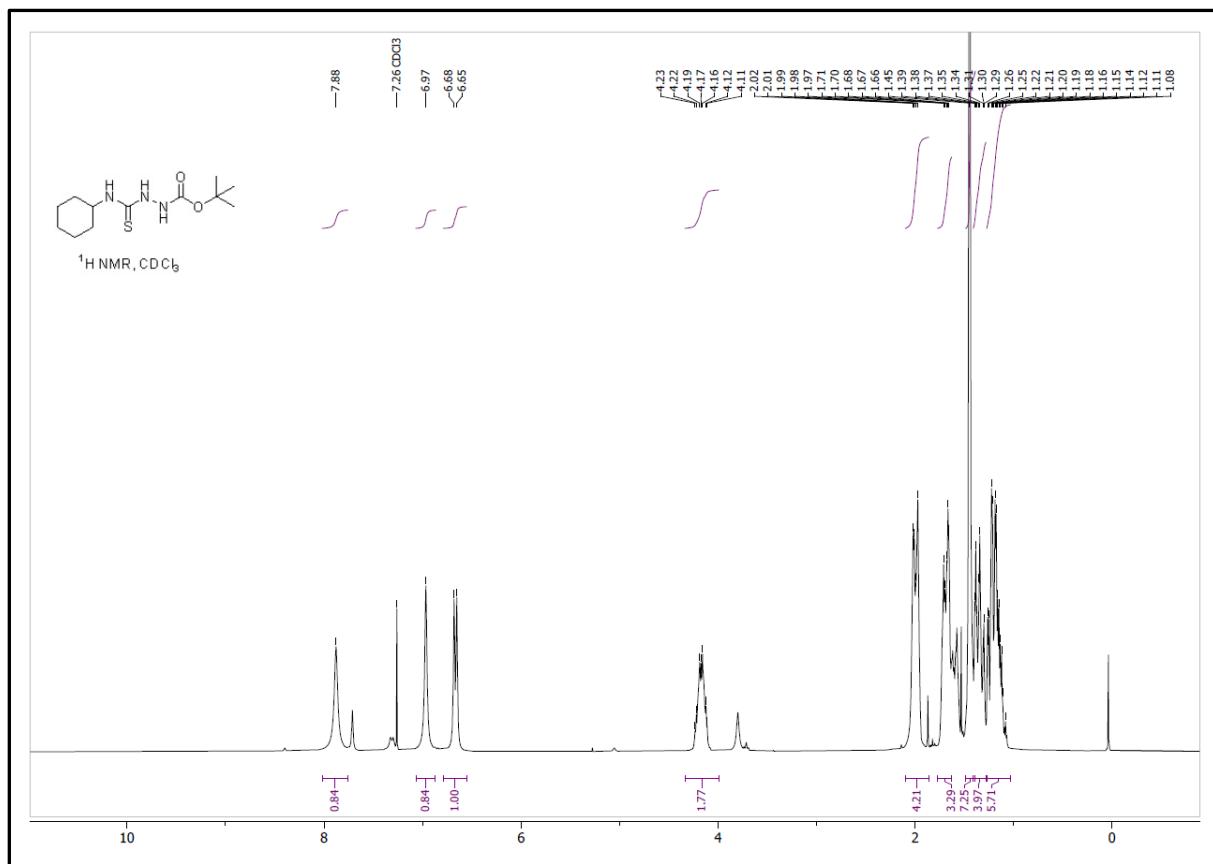
⁶Univ Rennes, CRMPO (Centre Régional de Mesures Physiques de l'Ouest), Avenue du Général Leclerc, 35042 Rennes Cedex, France.

⁷Bioprojet-Biotech, 4 rue du Chesnay Beauregard, BP 96205, 35762, Saint Grégoire, France.

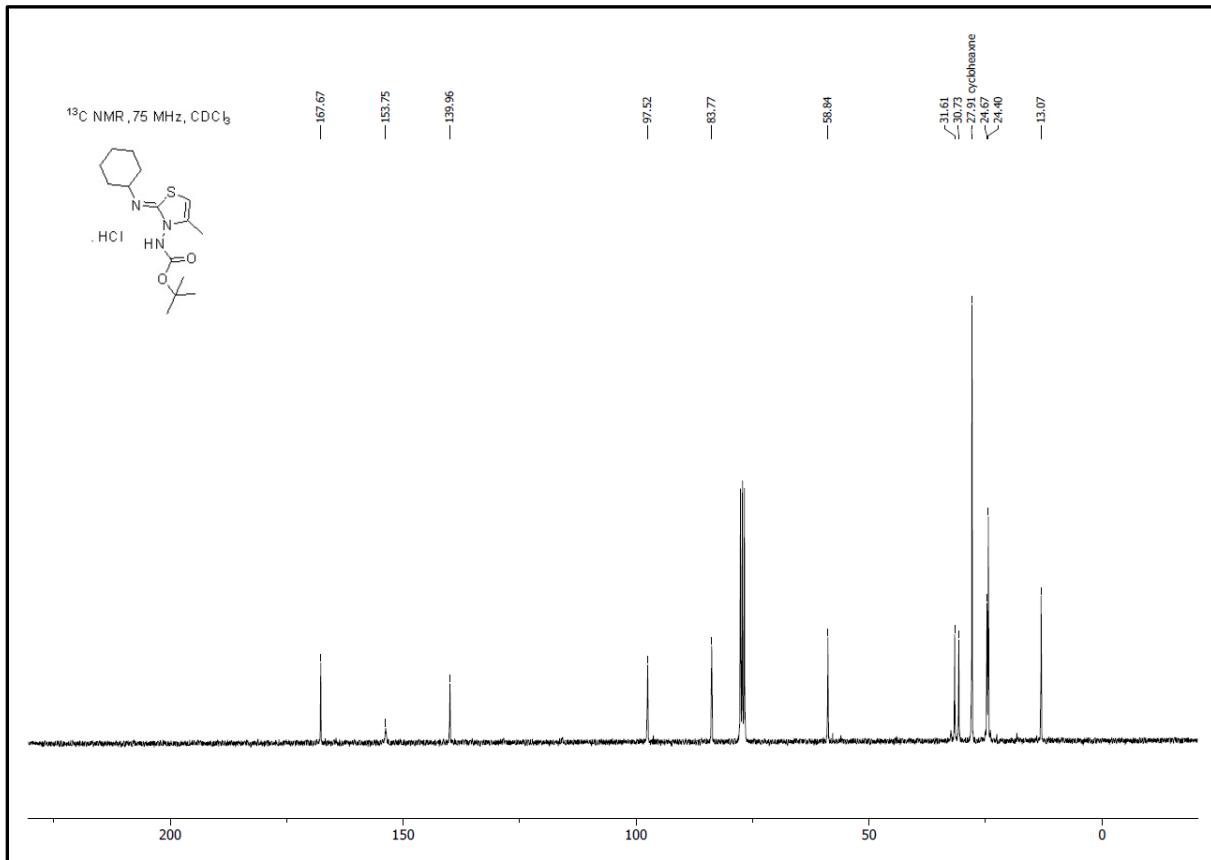
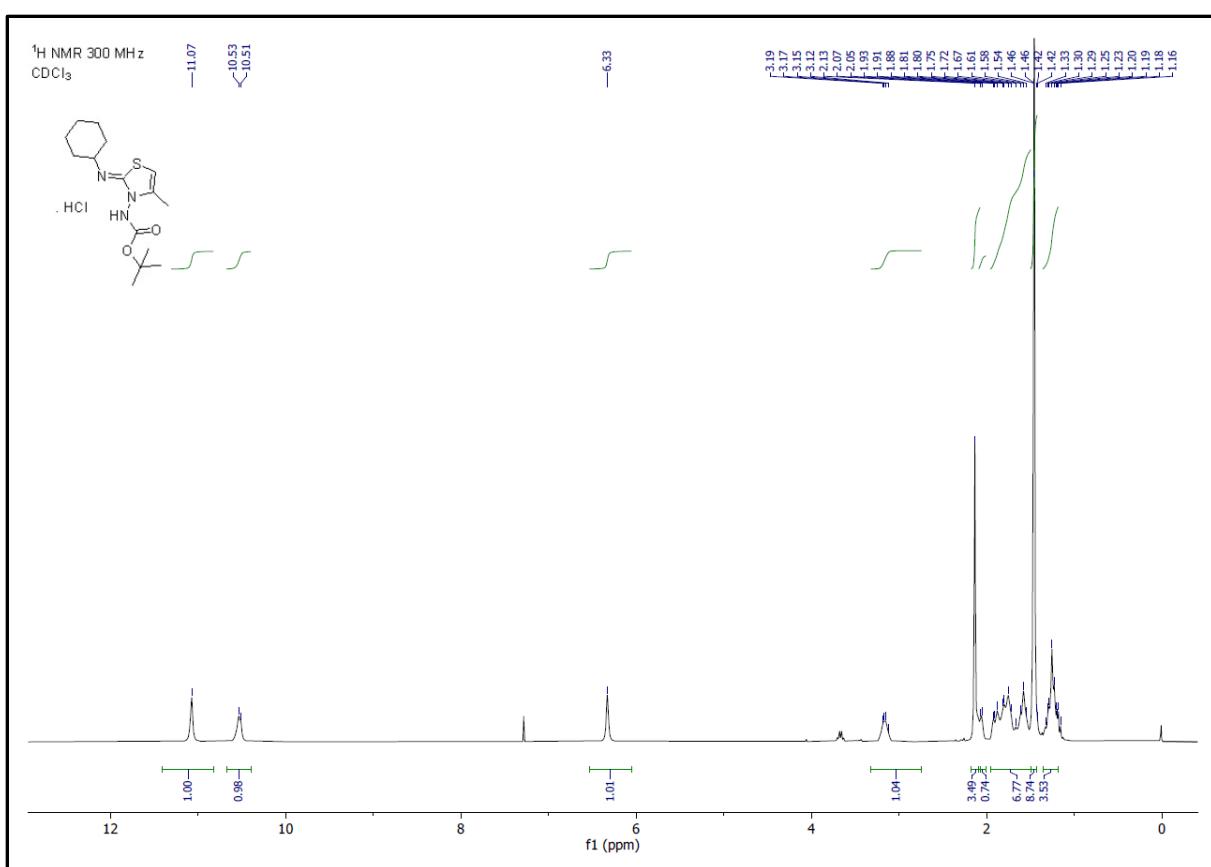
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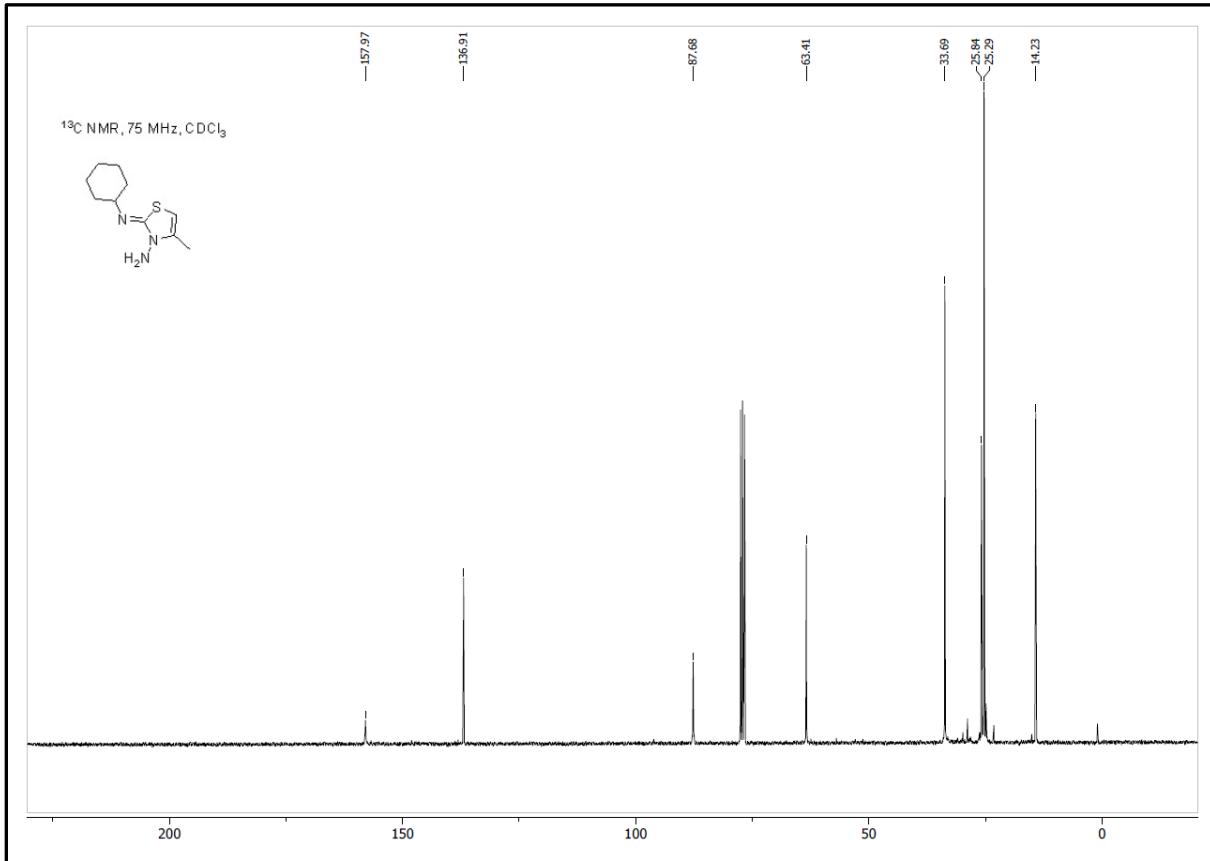
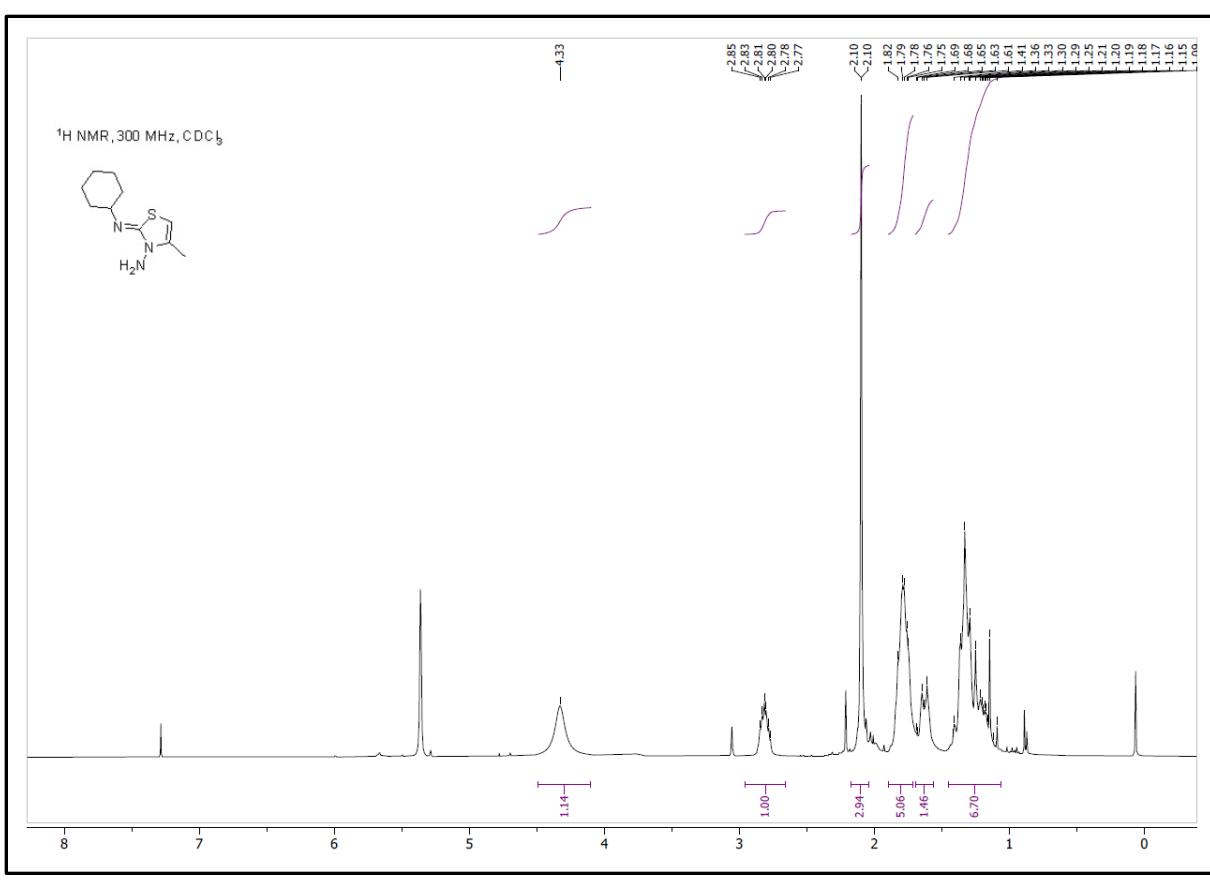
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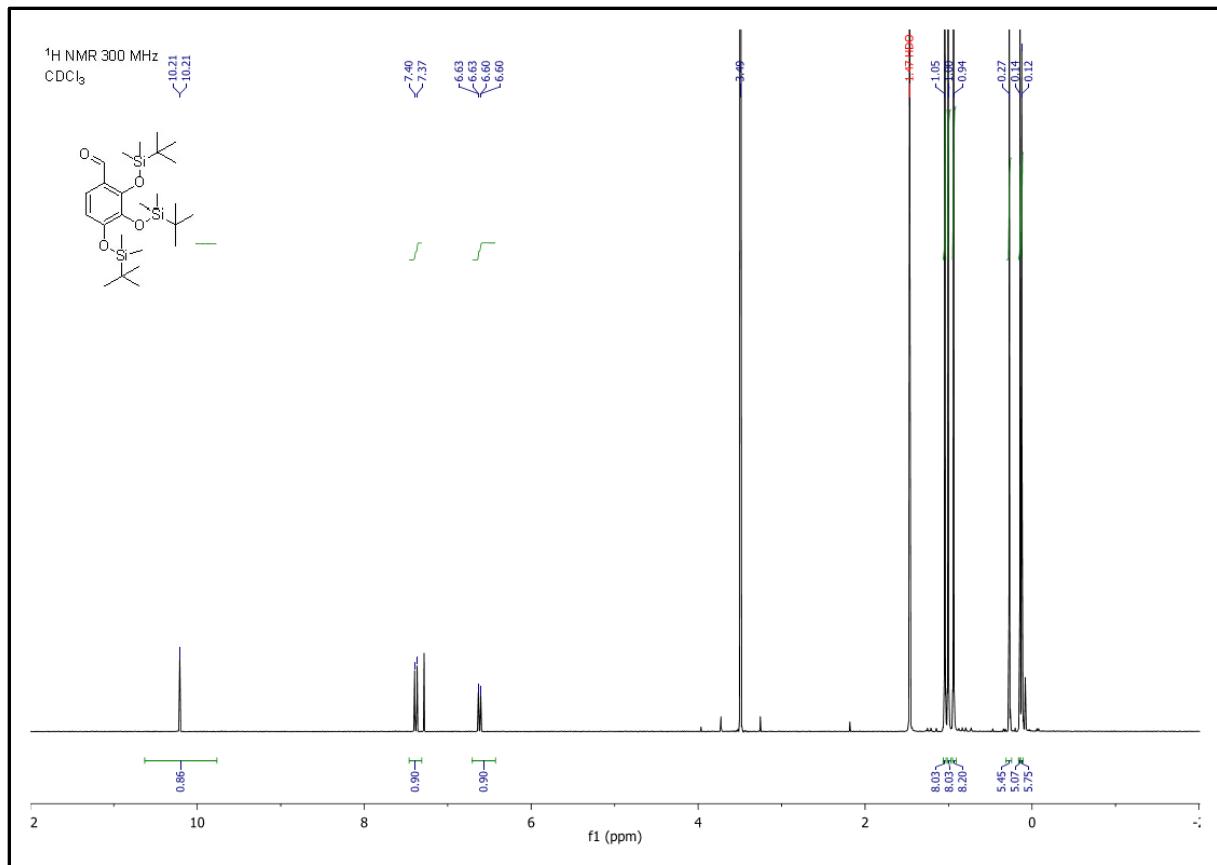
(Z)-tert-butyl (2-(cyclohexylimino)-4-methylthiazol-3(2H)-yl)carbamate hydrochloride (11)



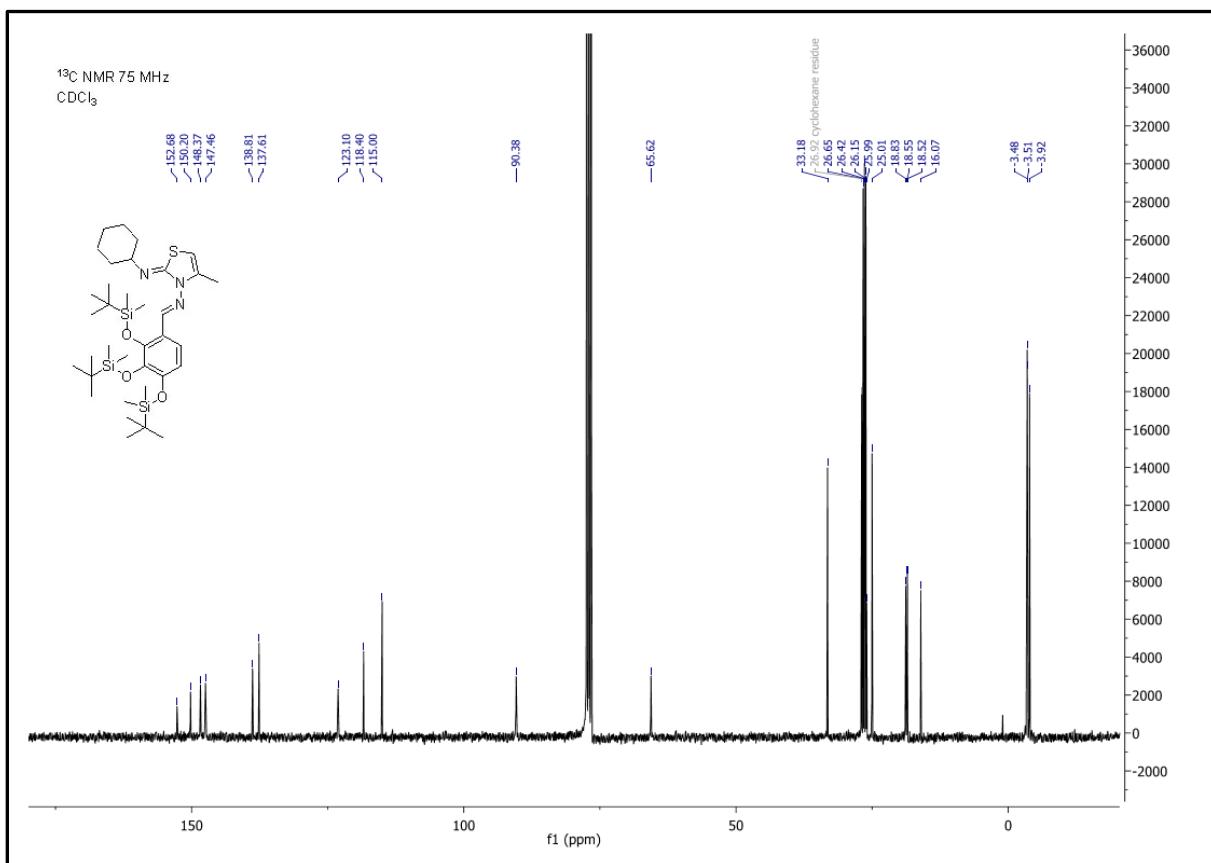
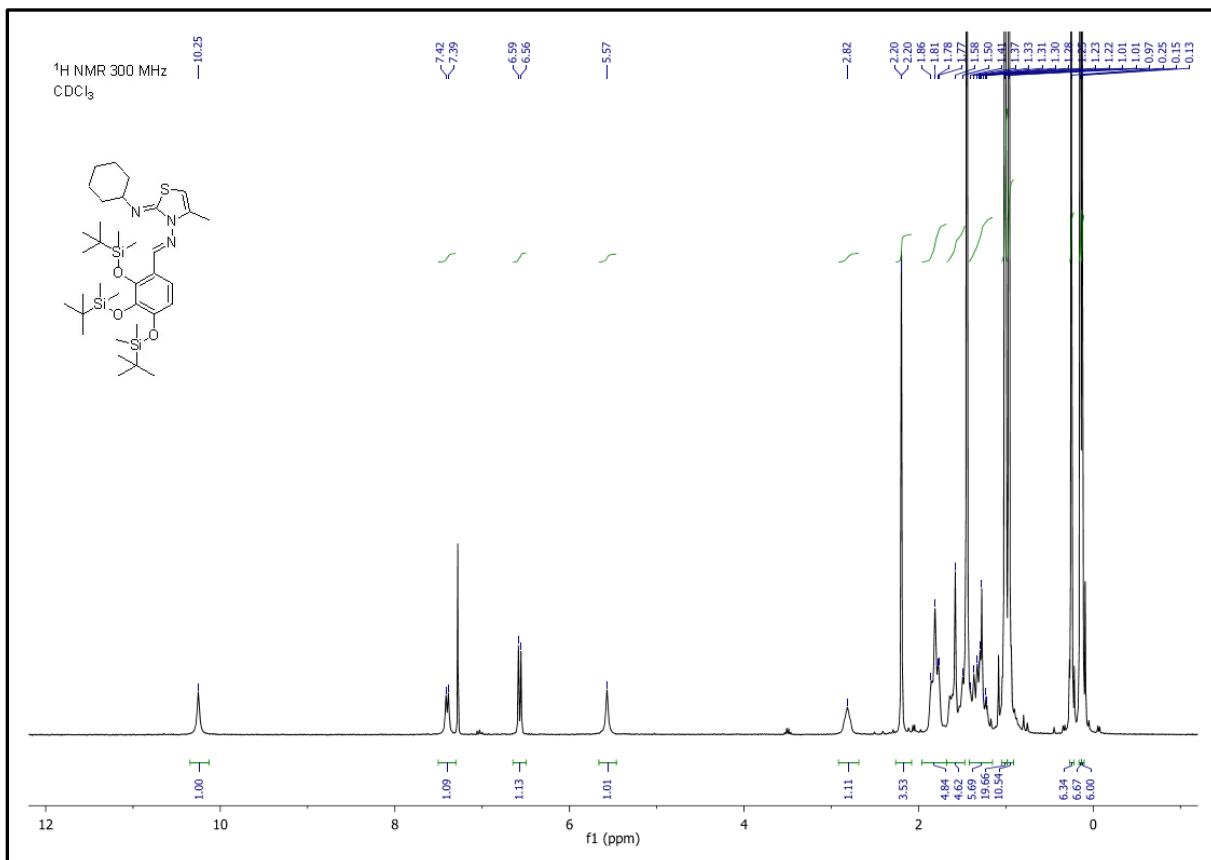
2-cyclohexylimino-4-methyl-2,3-dihydro-1,3-thiazol-3-amine (12)



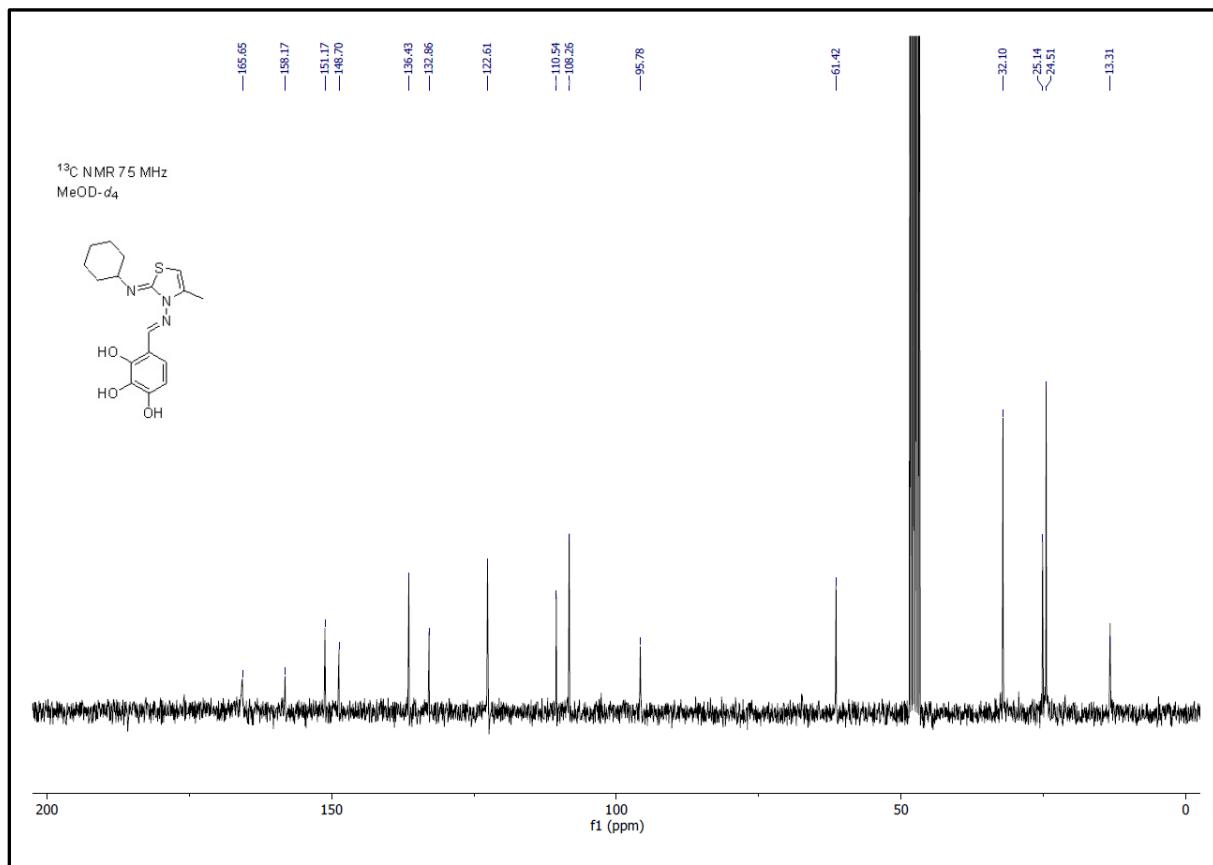
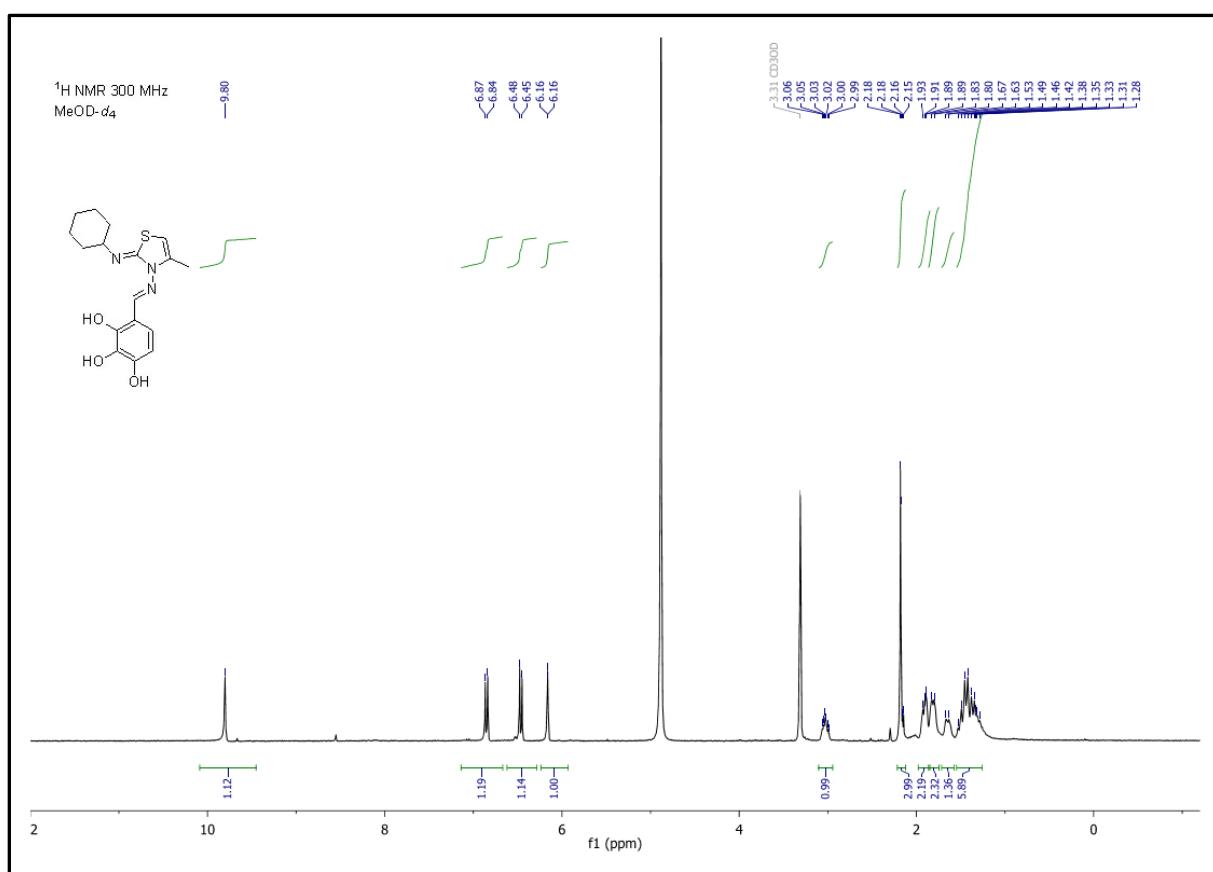
2,3,4-tris((tert-butyldimethylsilyl)oxy)benzaldehyde (13)



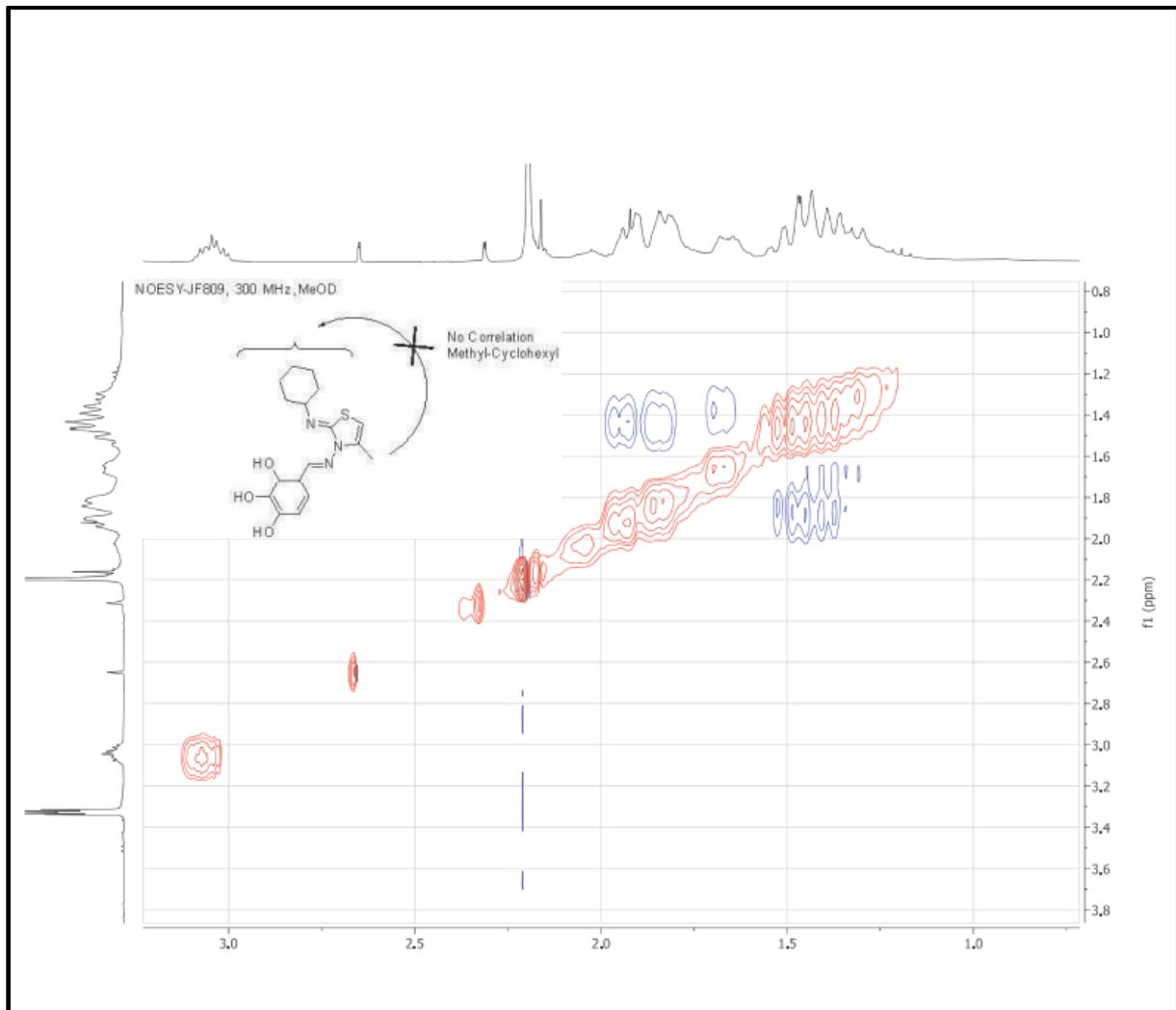
(2Z,NE)-2-(cyclohexylimino)-4-methyl-N-(2,3,4-tris((tert-butyldimethylsilyl)oxy)benzylidene)thiazol-3(2H)-amine (14)



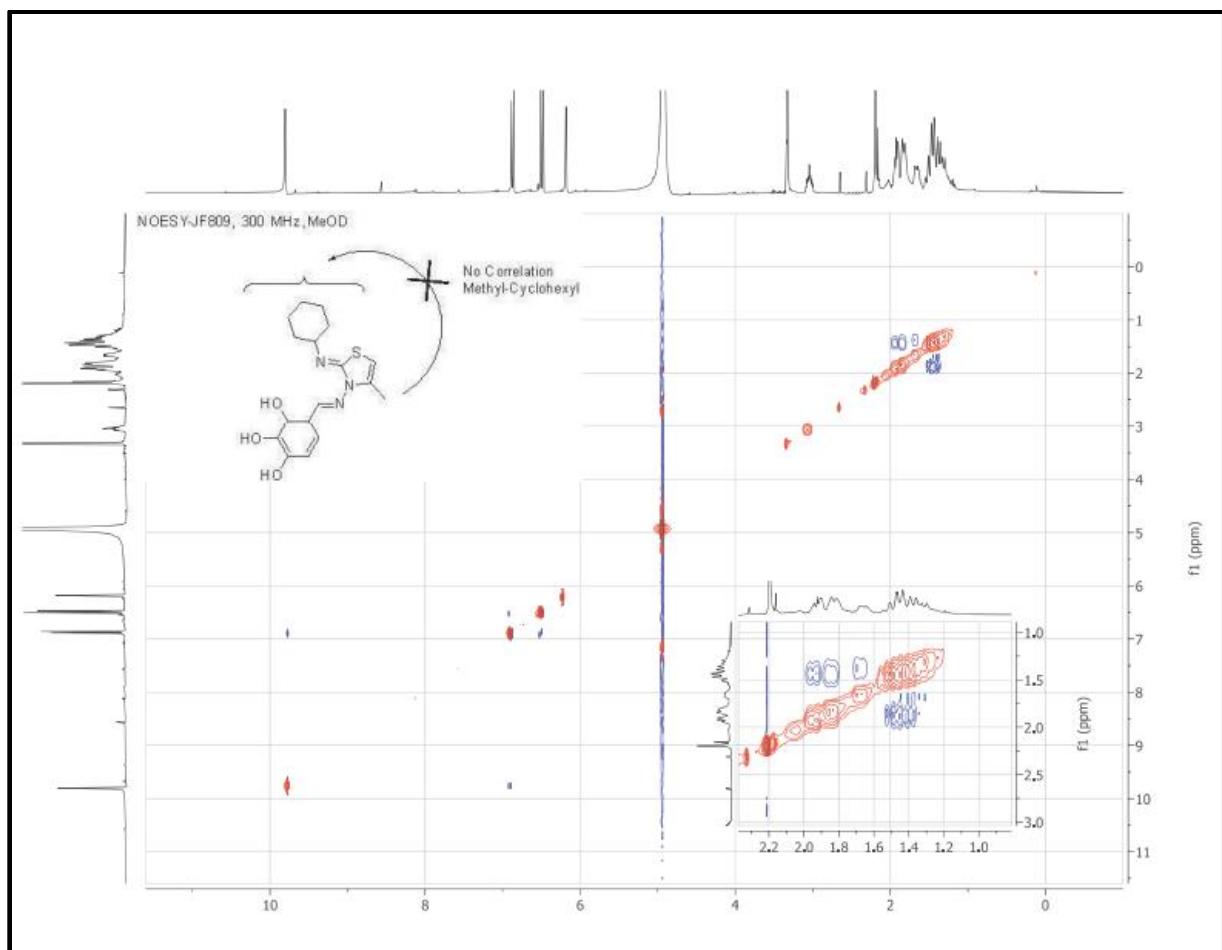
4-((E)-((Z)-2-(cyclohexylimino)-4-methylthiazol-3(2H)-yl)imino)methyl)benzene-1,2,3-triol (FJ-809)



NOESY spectrum (1) of compound FJ-809



NOESY spectrum (2) of compound FJ-809



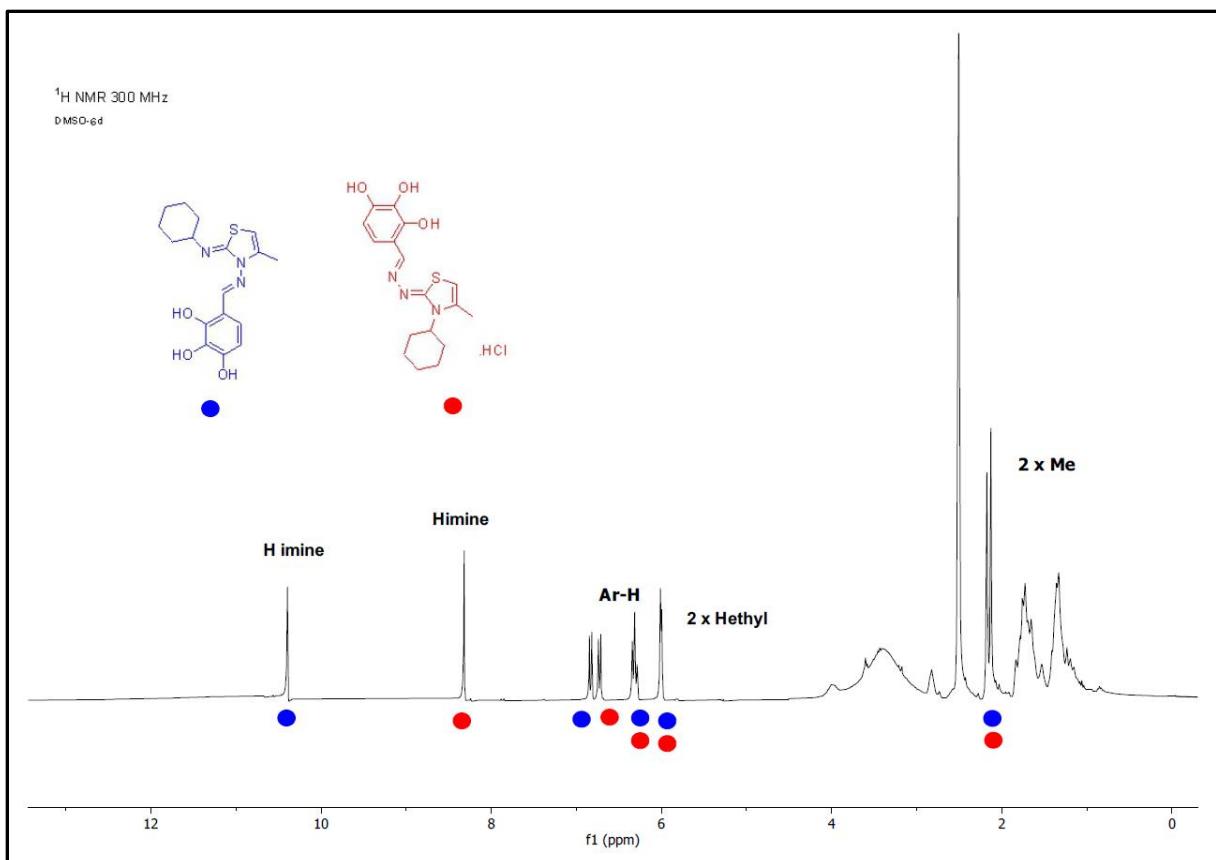
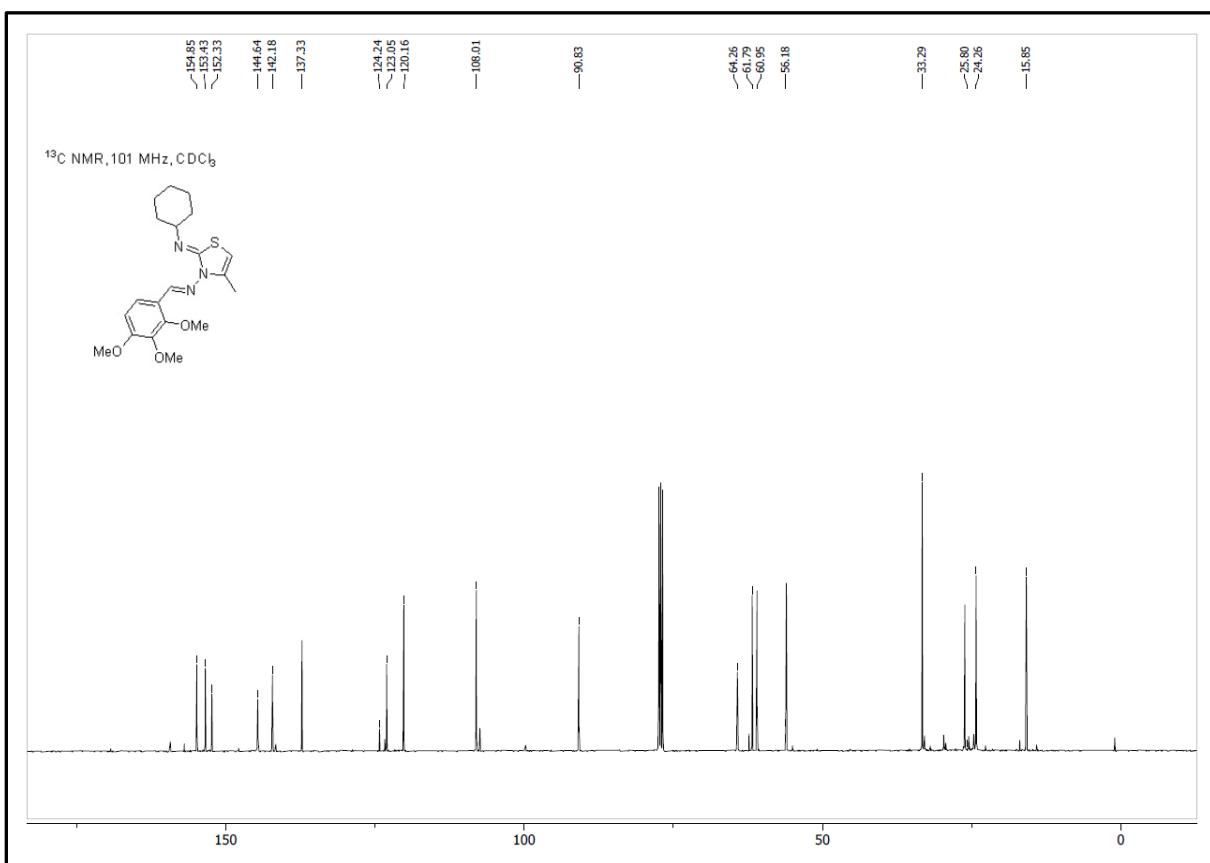
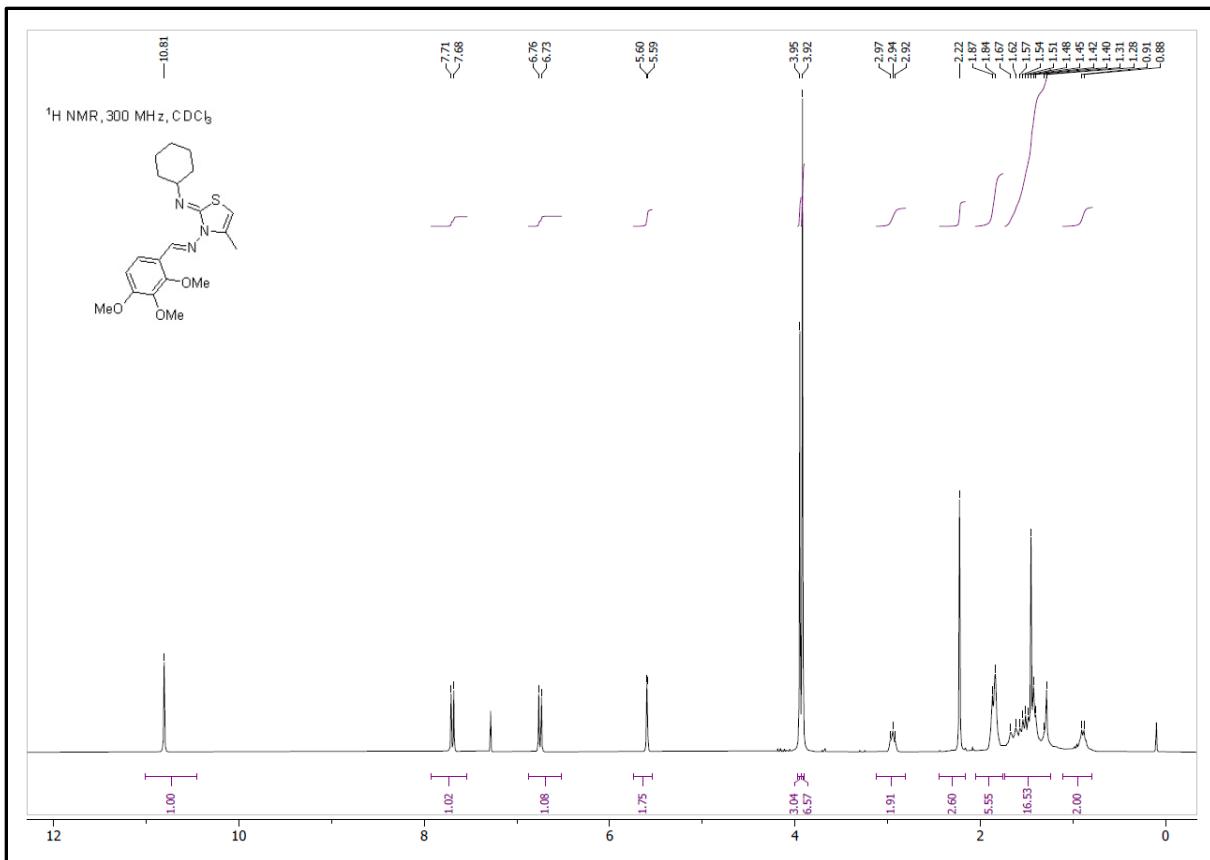


Figure S1: ¹H NMR spectrum of a 1:1 mixture of **FJ-809 (1)** and **MIM1 (2)**

(2Z,NE)-2-(cyclohexylimino)-4-methyl-N-(2,3,4-trimethoxybenzylidene)thiazol-3(2H)-amine (15)



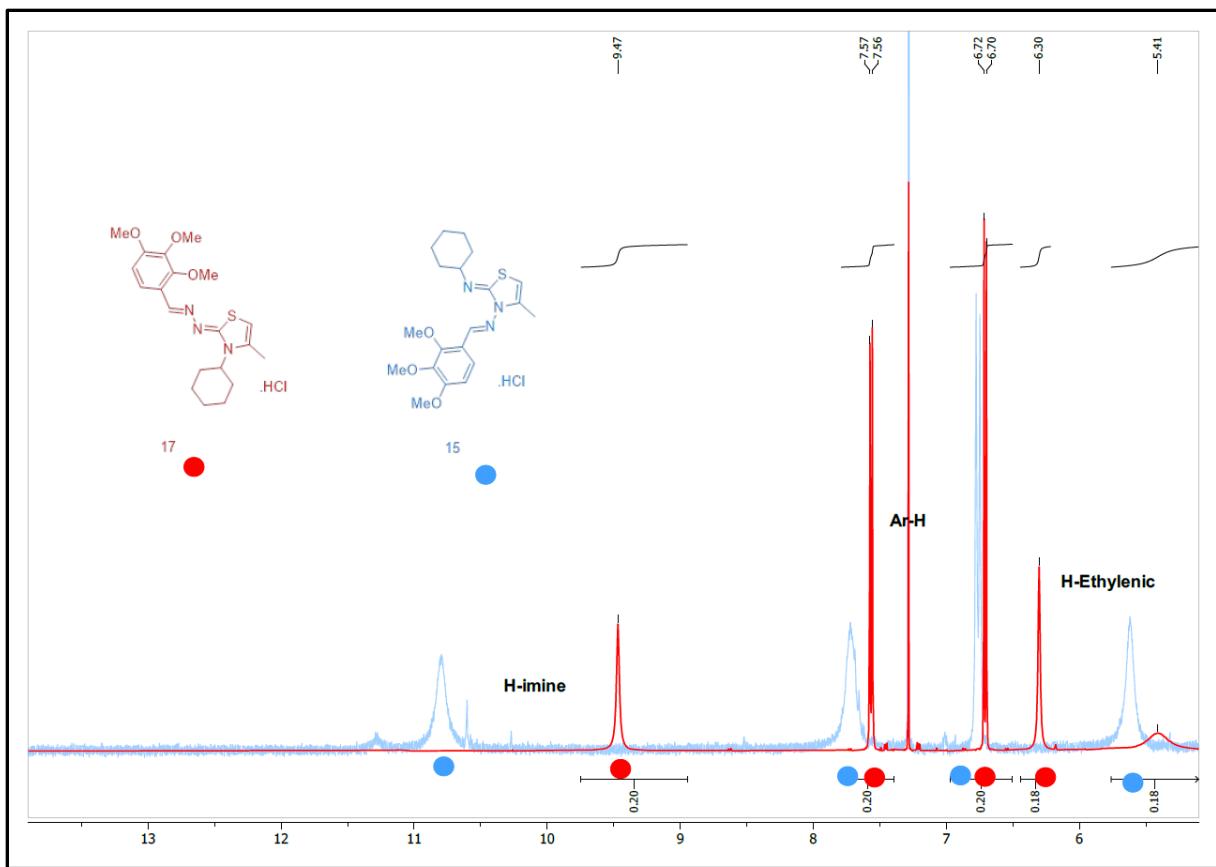
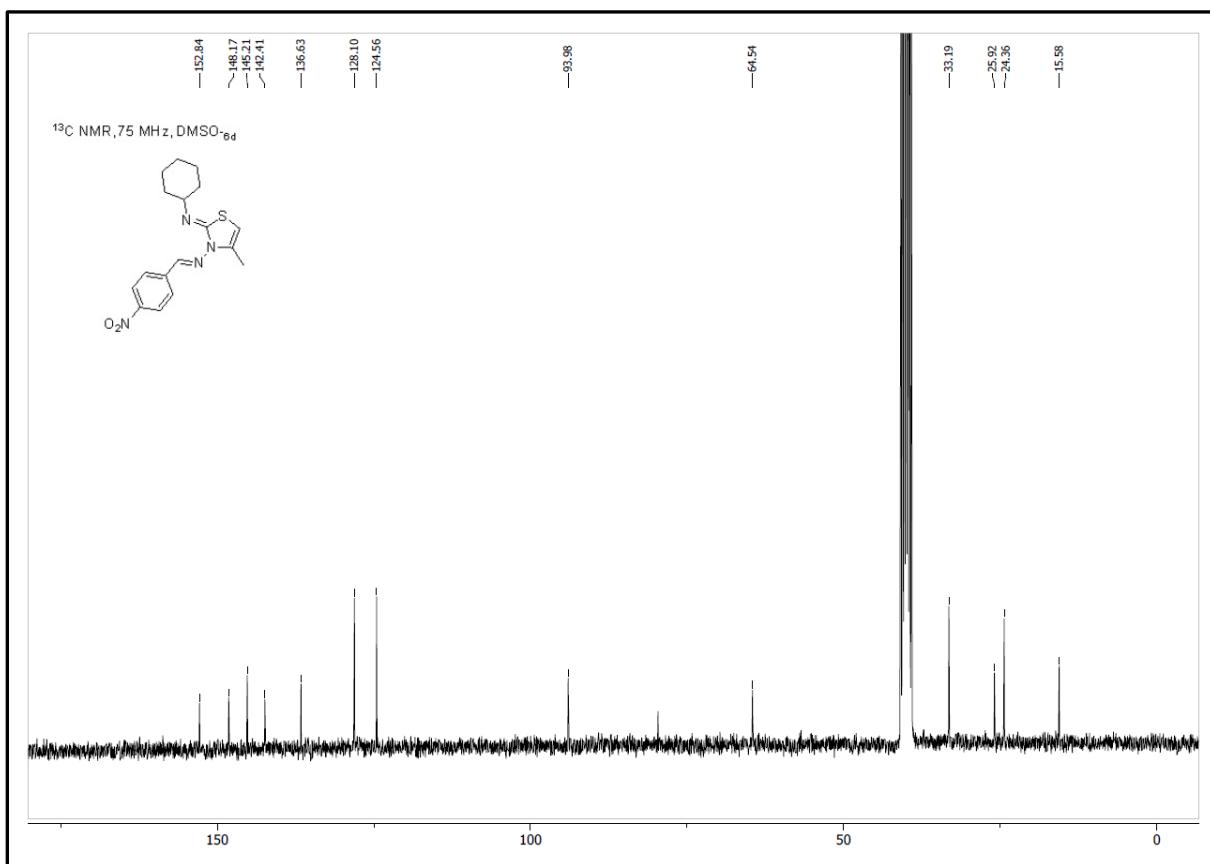
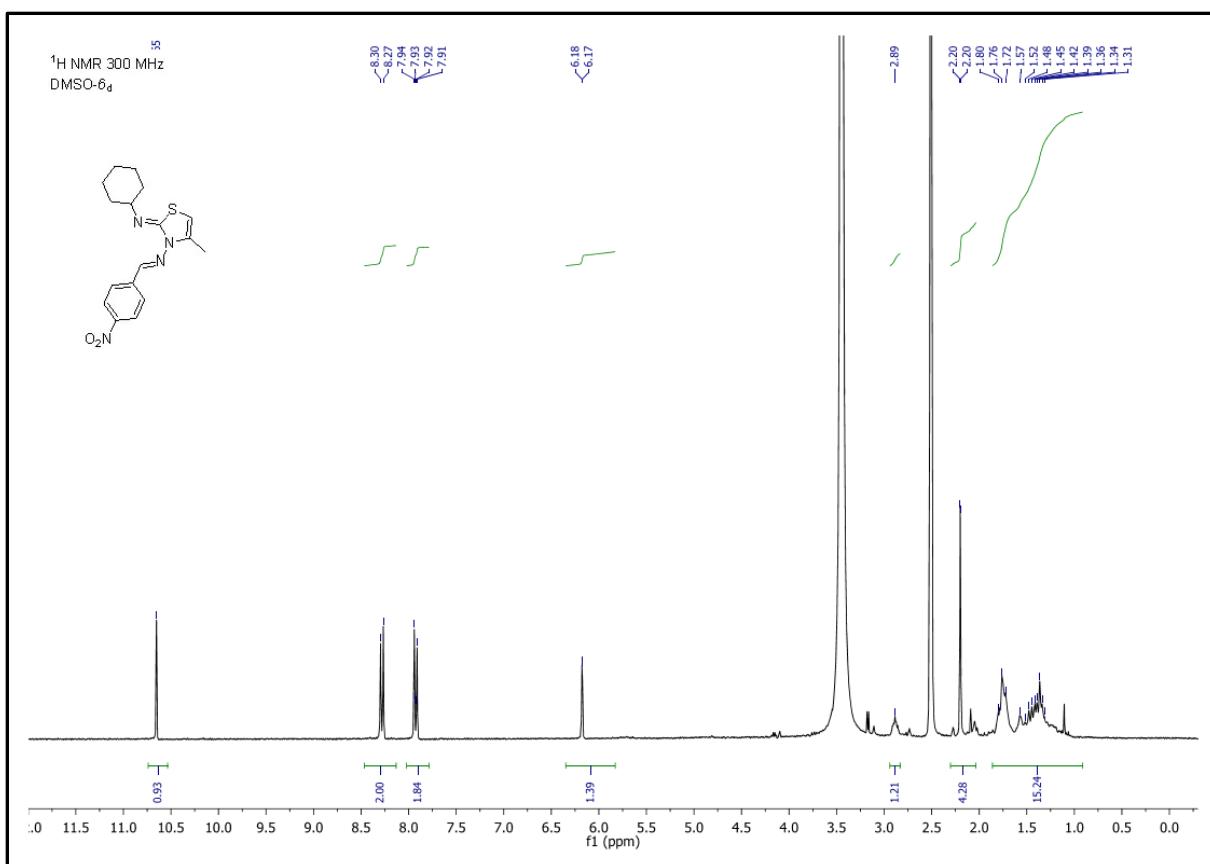


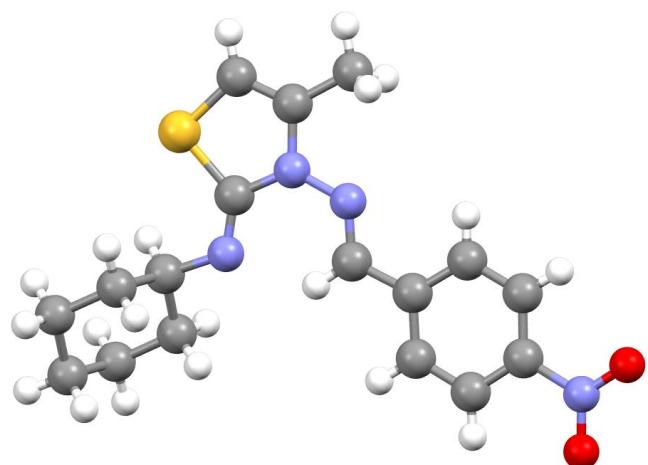
Figure S2: ^1H NMR spectrum of a 1:1 mixture of **15** and **17**

(2Z,NE)-2-(cyclohexylimino)-4-methyl-N-(4-nitrobenzylidene)thiazol-3(2H)-amine (16)



X-Ray data for **16**

CCDC 2123510 (for compound **16**), contain the supplementary crystallographical data for this paper.
These data can be obtained free of charge from the Cambridge Crystallographic Data Centre (CCDC),
12 Union Road, Cambridge CB2 1EZ, UK; fax, +44(0) 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk



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No syntax errors found. [CIF dictionary](#) [Interpreting this report](#)

Datablock: I

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	Calculated	Reported	
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Hall group	-P 2yn	-P 2yn	
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Sum formula	C17 H20 N4 O2 S	C17 H20 N4 O2 S	
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Dx, g cm ⁻³	1.343	1.343	
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F000'	728.76		
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Tmin'	0.887		
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test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

● Alert level G

PLAT072_ALERT_2_G SHELXL First Parameter in WGHT Unusually Large 0.14 Report

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0 ALERT level C = Check. Ensure it is not caused by an omission or oversight
1 ALERT level G = General information/check it is not something unexpected

0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
1 ALERT type 2 Indicator that the structure model may be wrong or deficient
0 ALERT type 3 Indicator that the structure quality may be low
0 ALERT type 4 Improvement, methodology, query or suggestion
0 ALERT type 5 Informative message, check

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● Alert level A

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At least one of these should be present.
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PUBL012_ALERT_1_A _publ_section_abstract is missing.
Abstract of paper in English.

● Alert level G

PUBL017_ALERT_1_G The _publ_section_references section is missing or
empty.

7 ALERT level A = Data missing that is essential or data in wrong format
1 ALERT level G = General alerts. Data that may be required is missing

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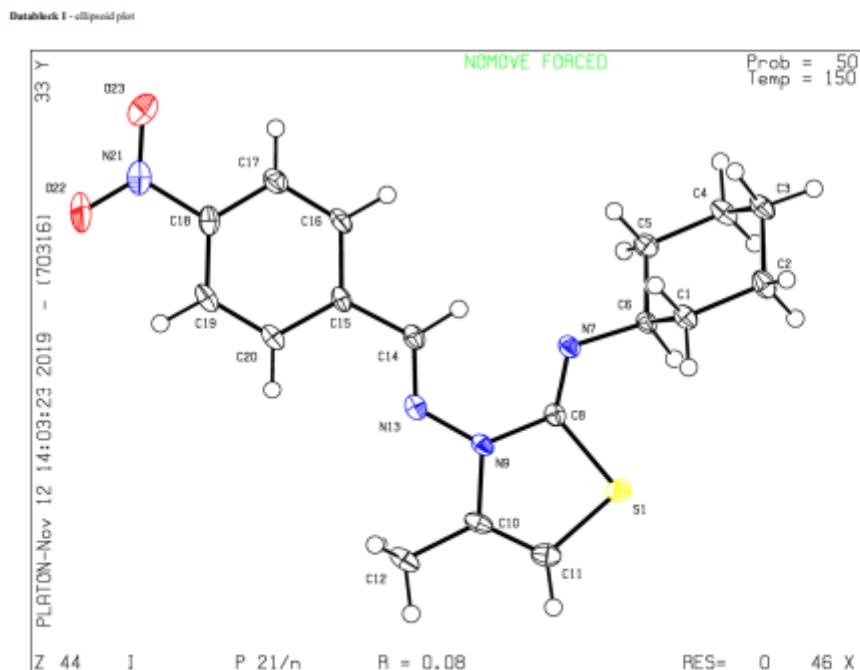
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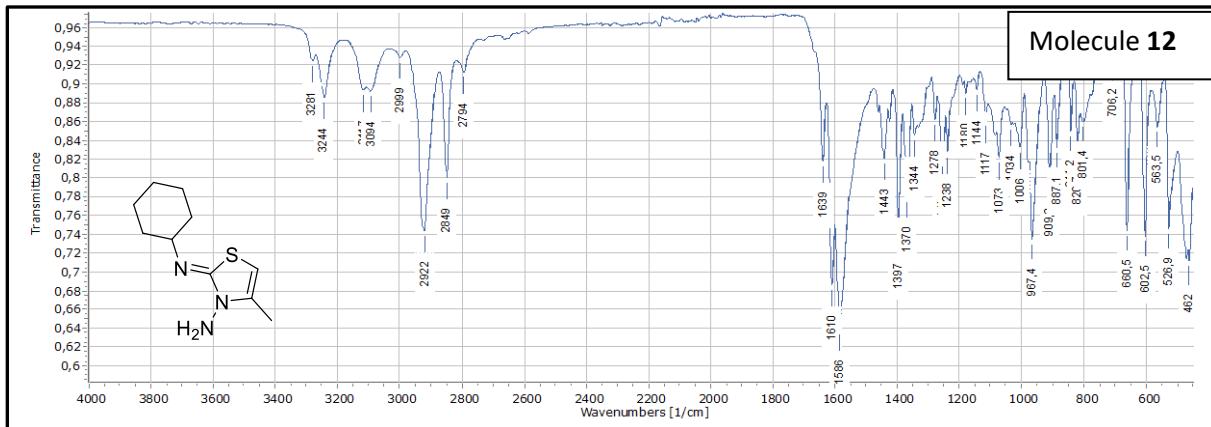
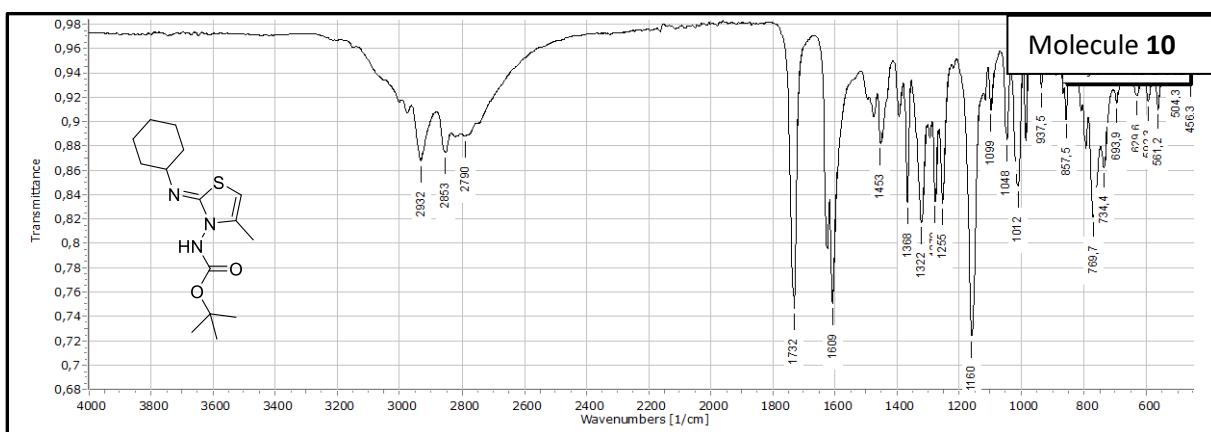
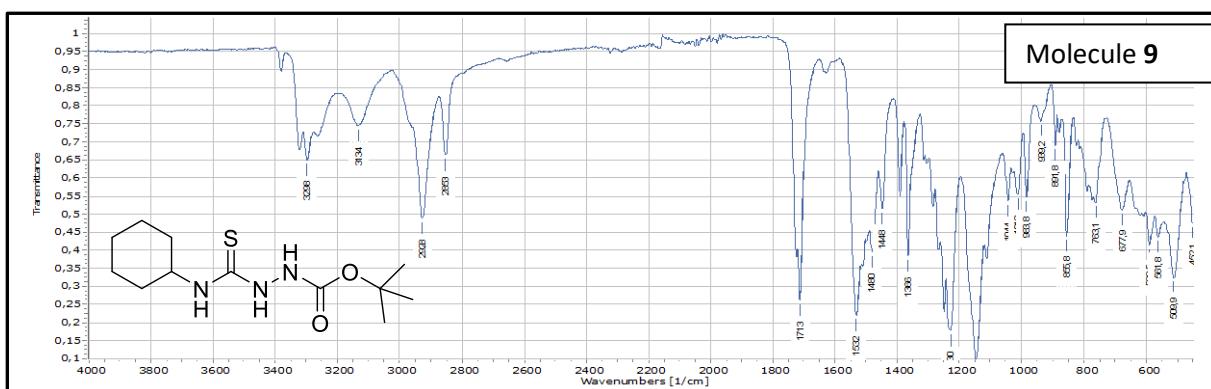
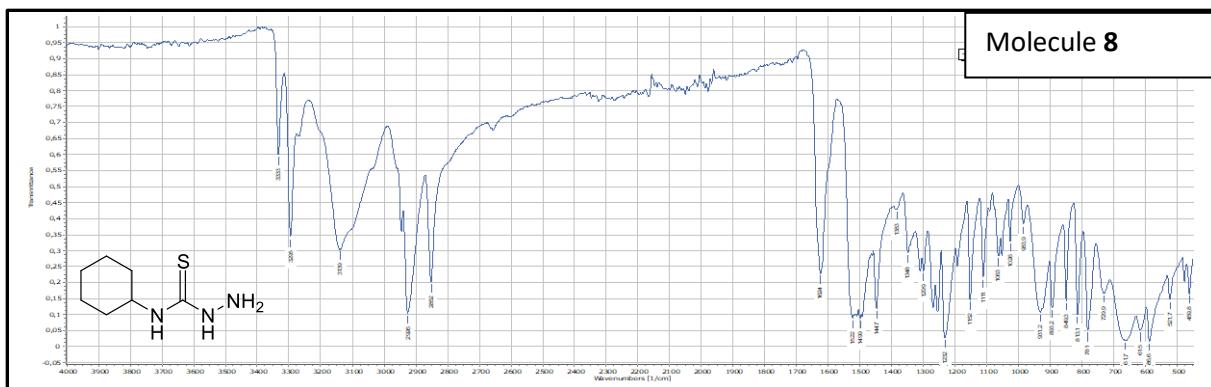
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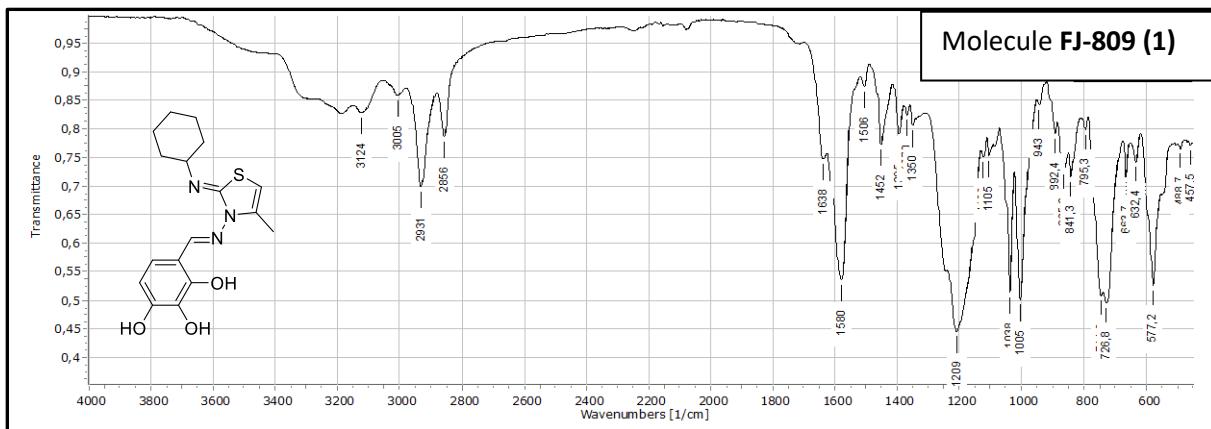
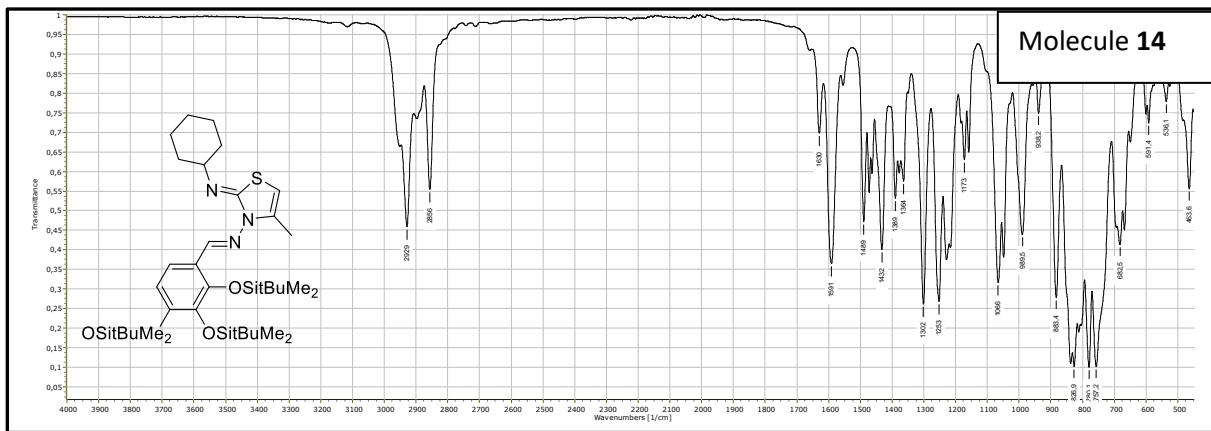
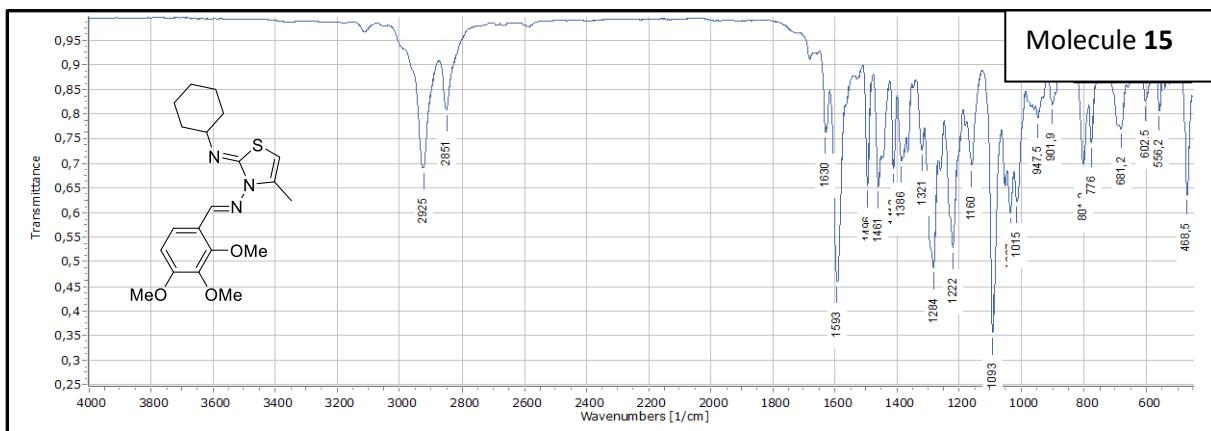
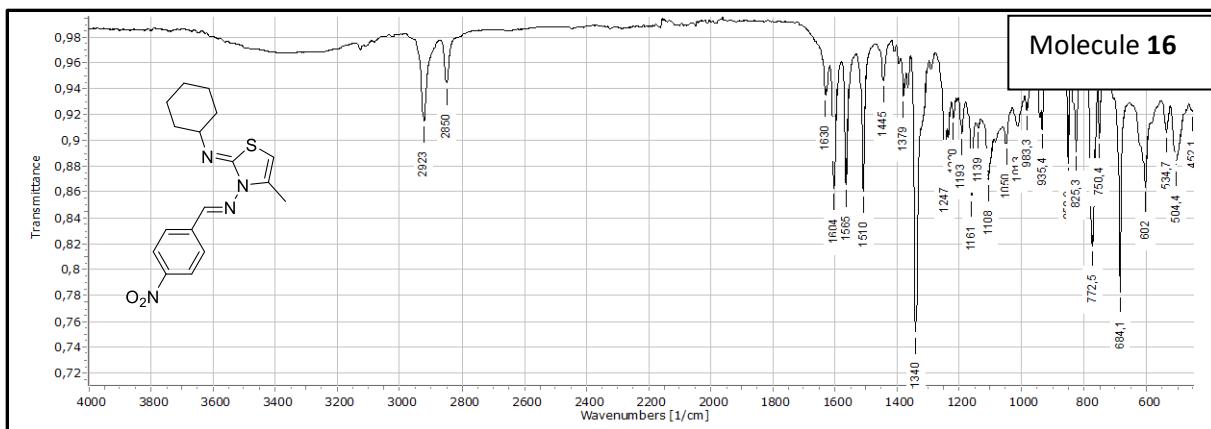
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SUPPLEMENTARY DATA Biology:

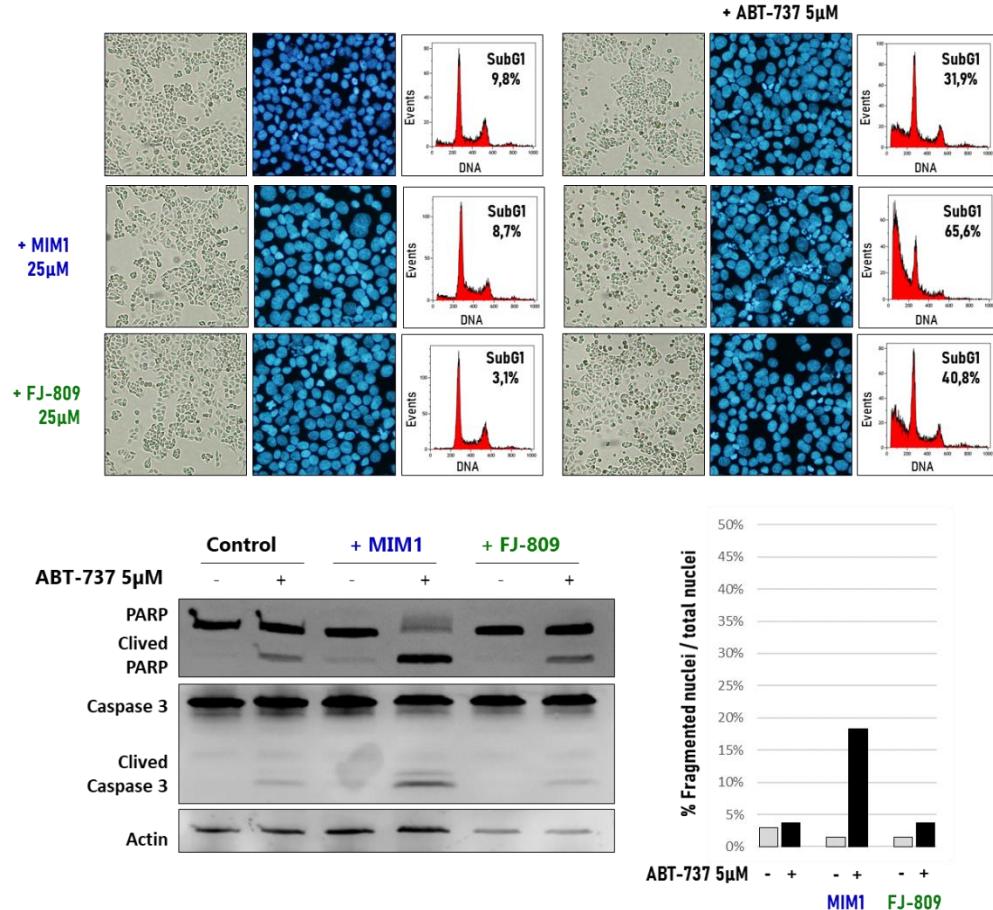
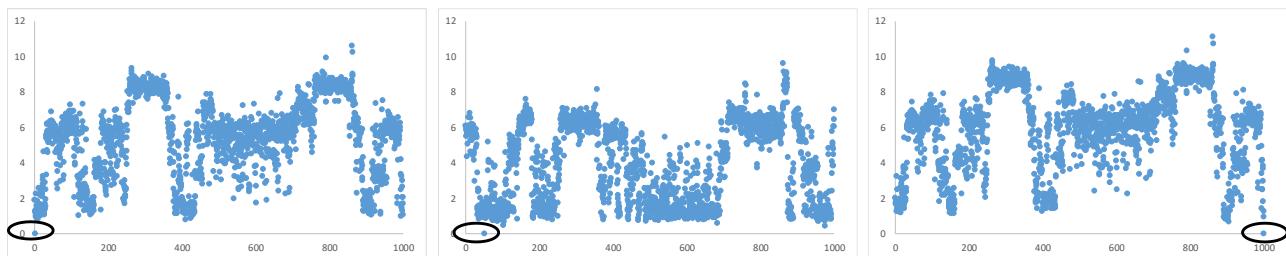


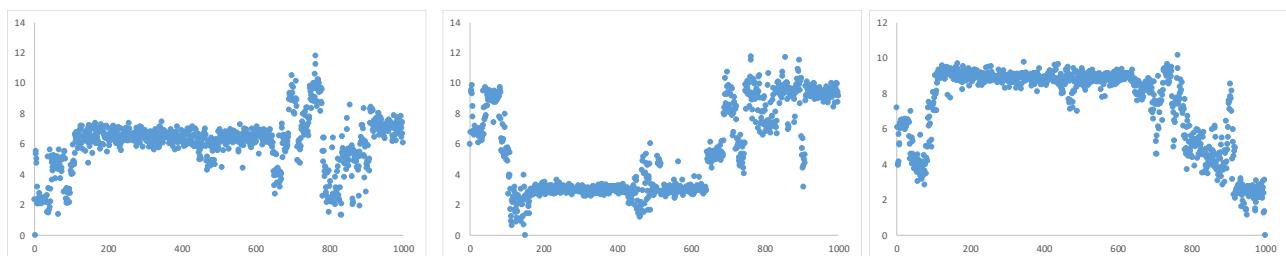
Figure S3: Evaluation of the biological effect of **MIM1** (2) and **FJ-809** (1) on IGROV1-R10 cell line
IGROV1-R10 chemoresistant ovarian cancer cell line was exposed either to **MIM1** or to **FJ809** (25µM) combined or not with ABT-737 (5µM). Effect on cellular and nuclear morphologies as well as cell cycle repartition is represented (A) and nuclei fragmentation is quantified (B). PARP and Caspase 3 cleavage is evaluated by western blot (C).

SUPPLEMENTARY DATA Molecular dynamics experiments

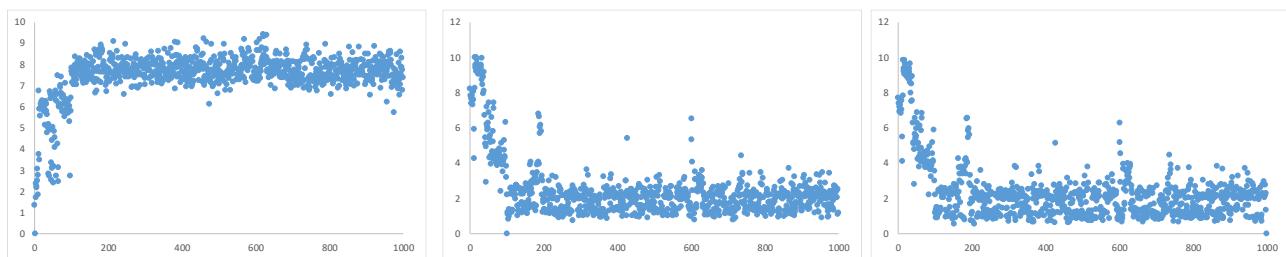
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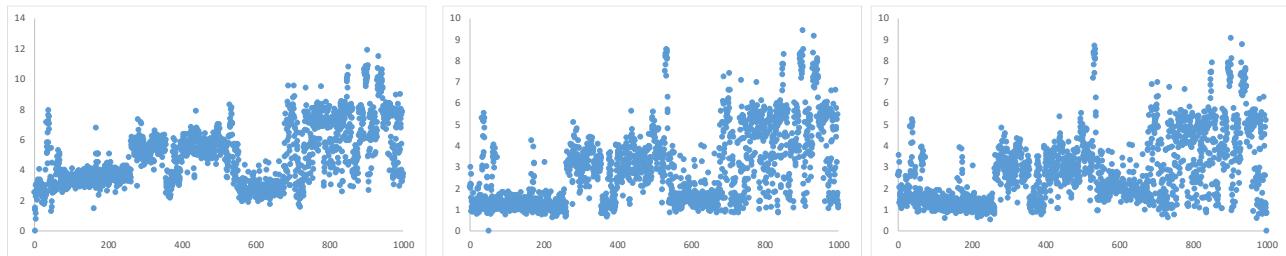
Molecular dynamics experiment n° 2



Molecular dynamics experiment n° 3



Molecular dynamics experiment n° 4



Molecular dynamics experiment n° 5

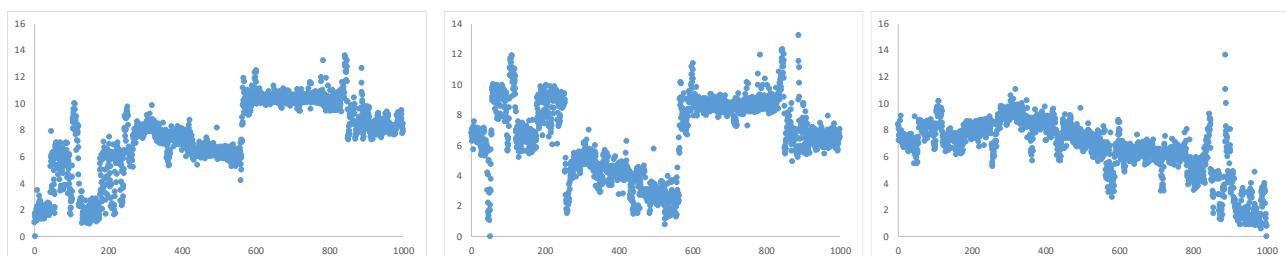
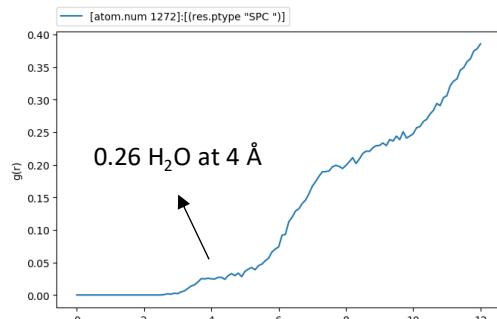


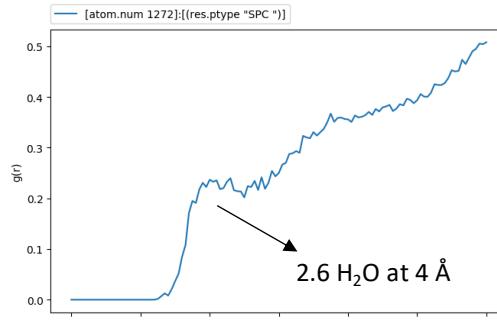
Figure S4

RMSD of **MIM1 (2)** in Mcl-1, as calculated from the initial state (left, see the ellipse), a early pseudo steady-state (middle), and final state (right). X-axis: time (ns), y-axis: RMSD (Å).

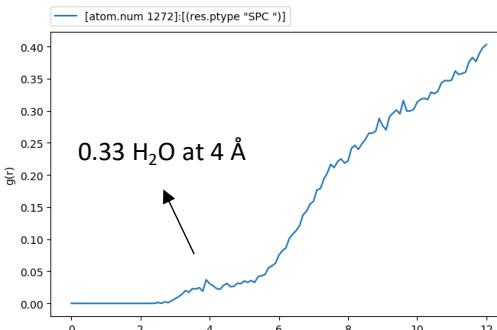
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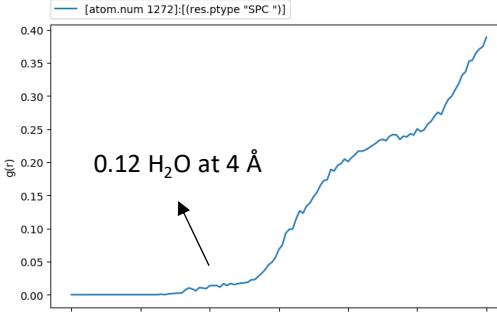
Molecular dynamics experiment n° 2



Molecular dynamics experiment n° 3



Molecular dynamics experiment n° 4



Molecular dynamics experiment n° 5

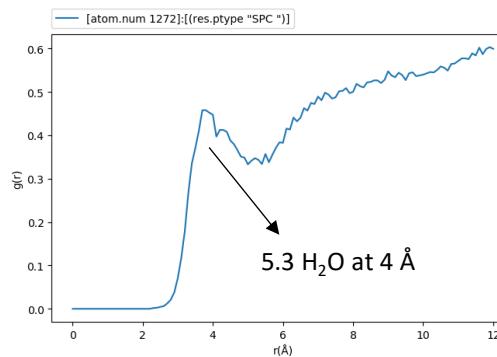
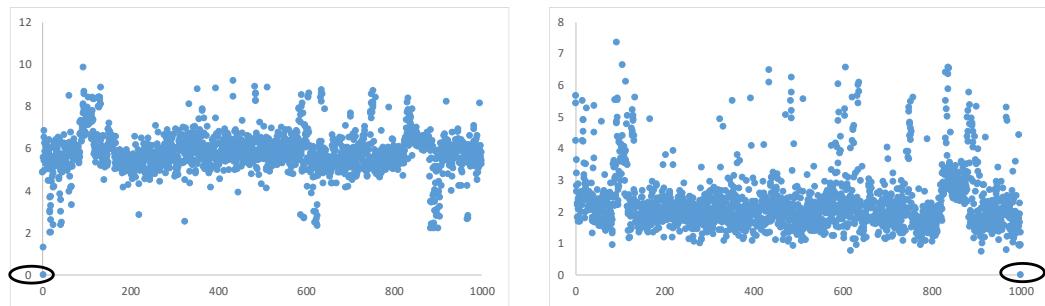


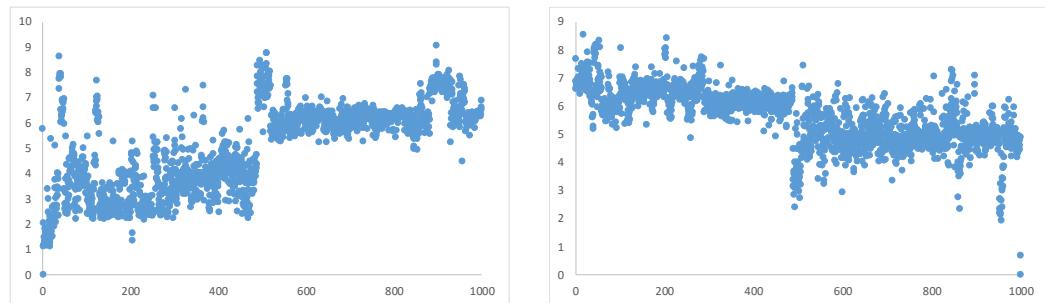
Figure S5

RDF of water molecules around the methyl group of **MIM1 (2)**. Integration of the RDF give an approximation of the average coordination number, here given at 4 \text{\AA}.

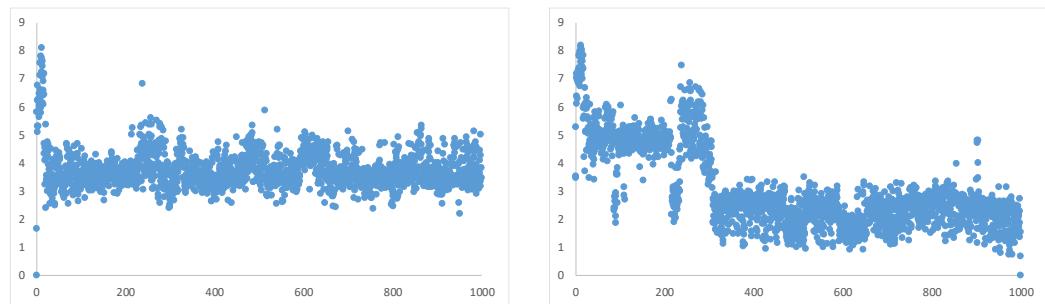
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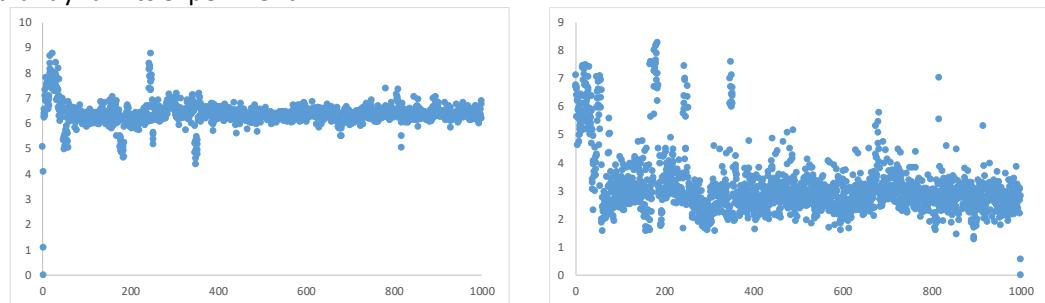
Molecular dynamics experiment n° 2



Molecular dynamics experiment n° 3



Molecular dynamics experiment n° 4



Molecular dynamics experiment n° 5

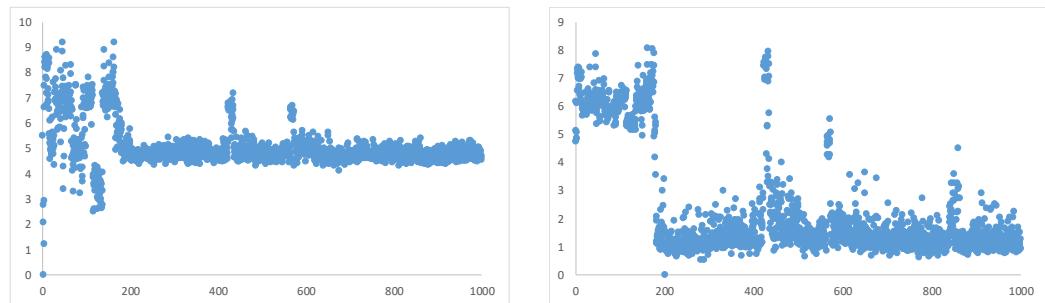
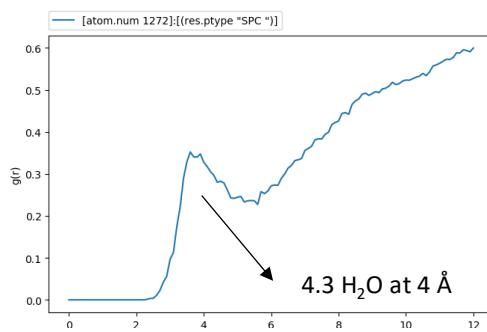


Figure S6

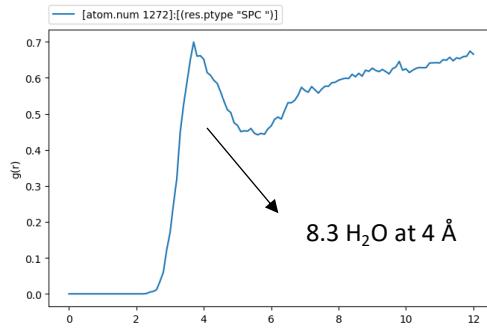
RMSD of **FJ-809 (1)** in Mcl-1, as calculated from the initial state (left, see the ellipse) and final state (right).

X-axis: time (ns), y-axis: RMSD (\AA).

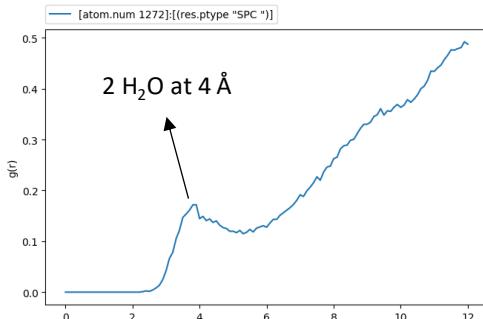
Molecular dynamics experiment n° 1



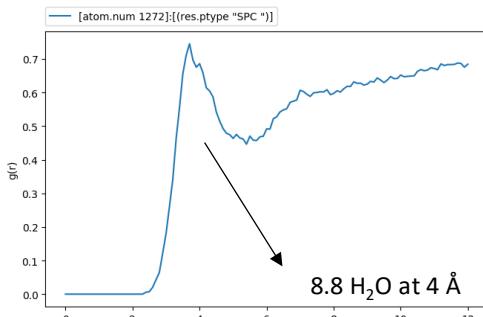
Molecular dynamics experiment n° 2



Molecular dynamics experiment n° 3



Molecular dynamics experiment n° 4



Molecular dynamics experiment n° 5

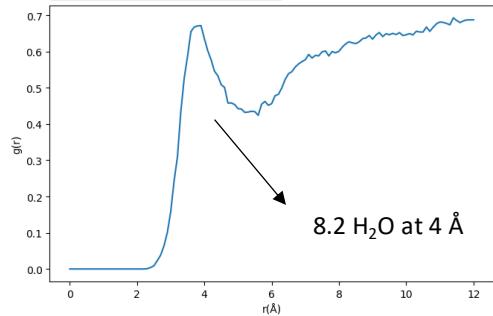


Figure S7

RDF of water molecules around the methyl group of **FJ-809 (1)**. Integration of the RDF give an approximation of the average coordination number, here given at 4 \AA .