

Cytotoxic Activity, Topoisomerase I Inhibition and In Silico Studies of New Sesquiterpene-aryl Ester Derivatives of (-) Drimenol

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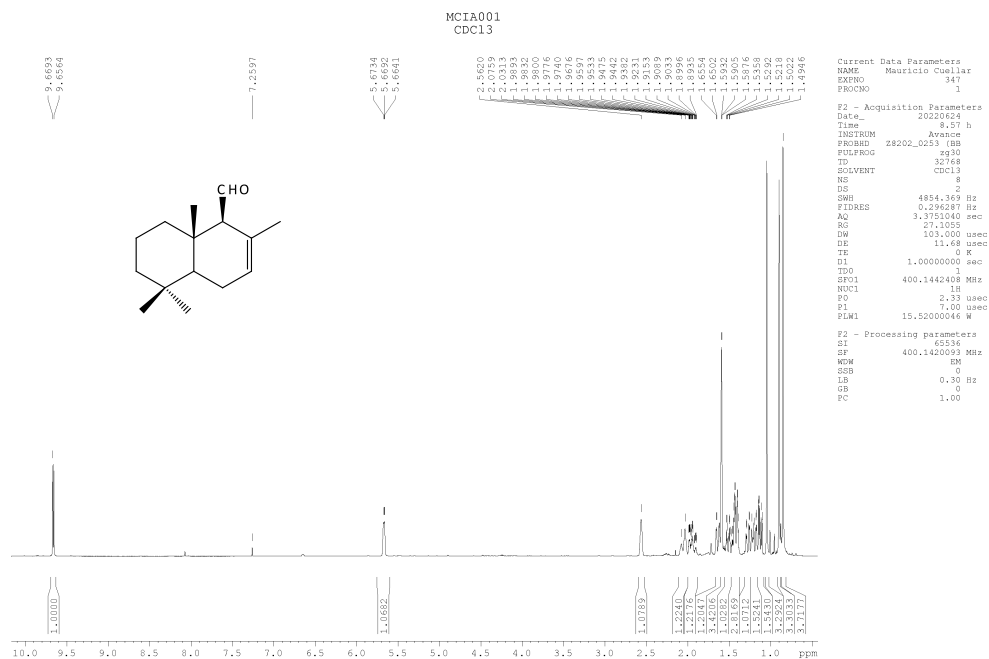
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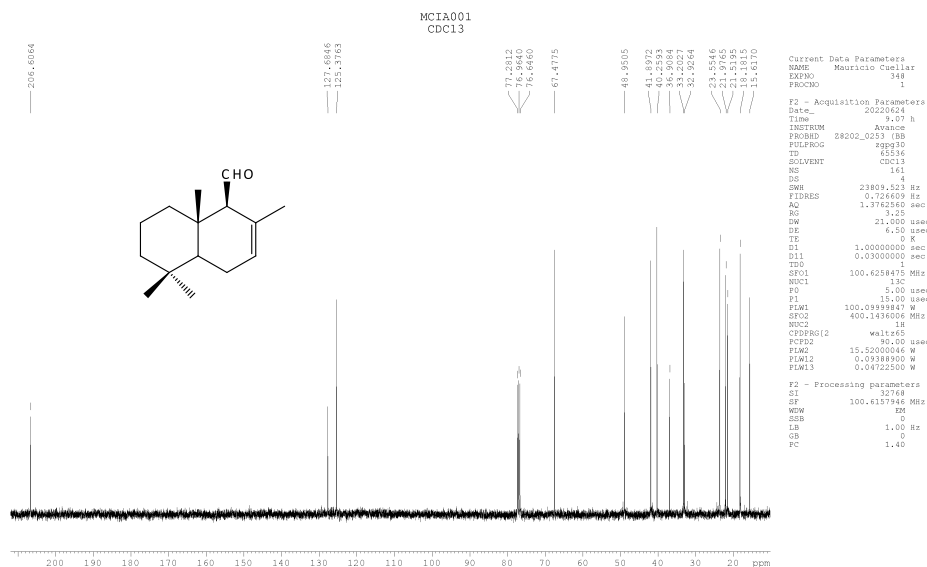
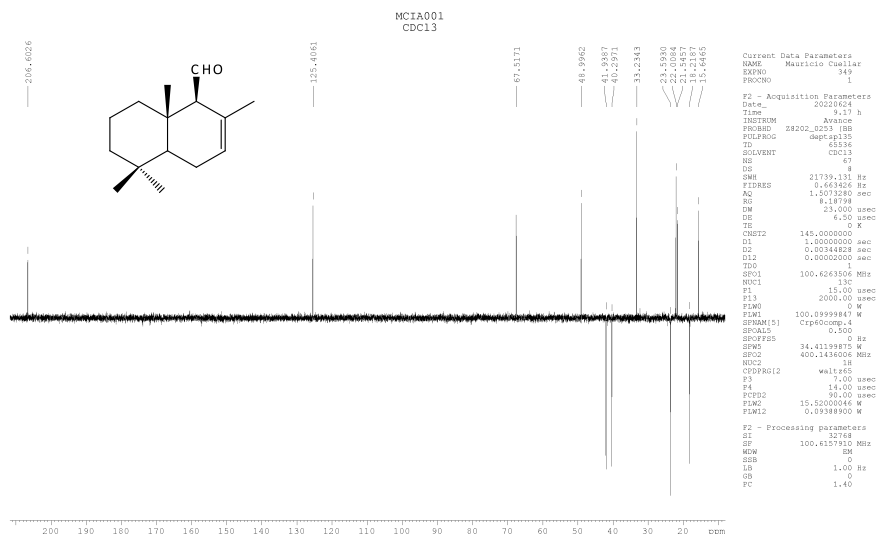
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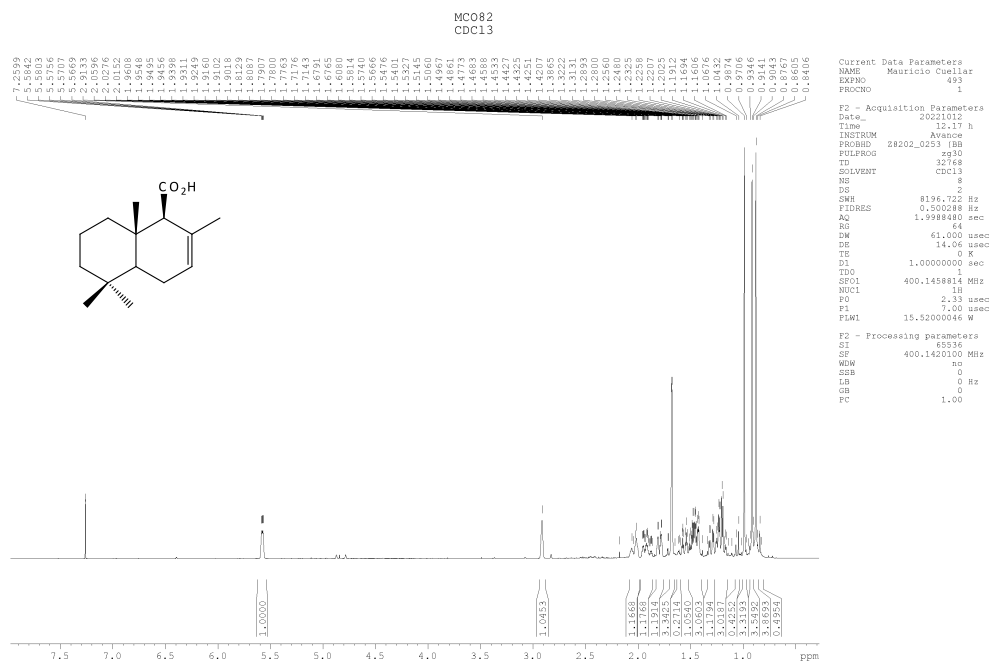
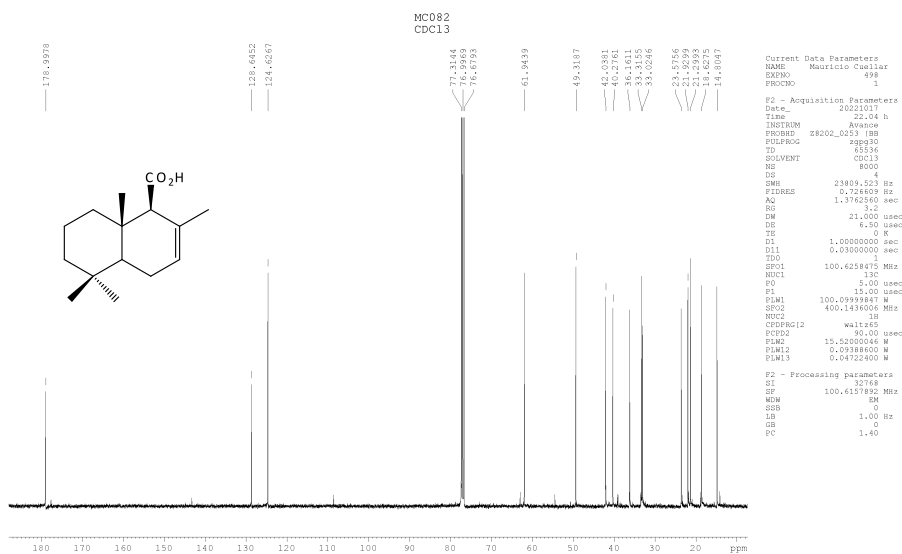
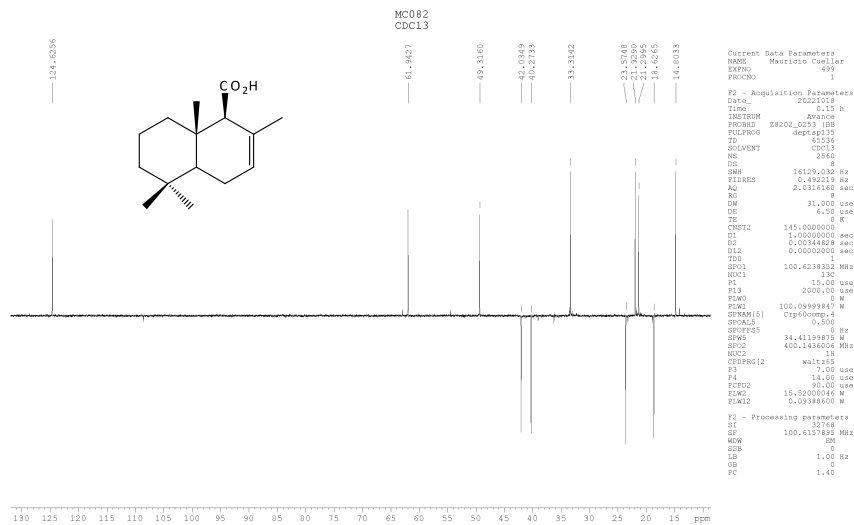
Index

¹ H, ¹³ C NMR and ¹³ C-DEPT 135 of selected compounds	page 02–17
HRMS of selected compounds.....	page 18–23
Molecular Docking and Molecular Dynamics results.....	page 24–26

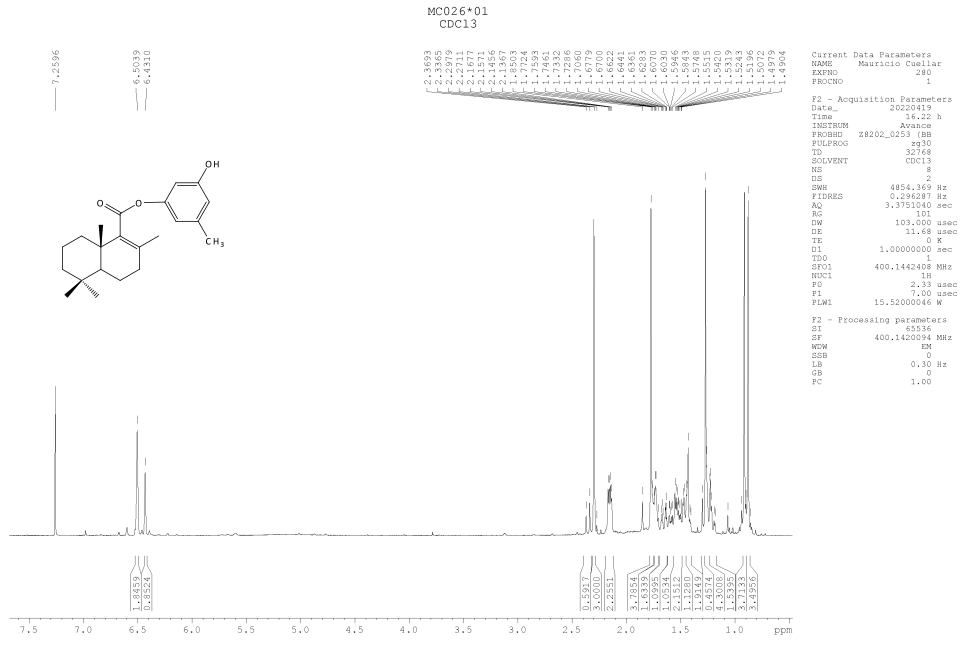
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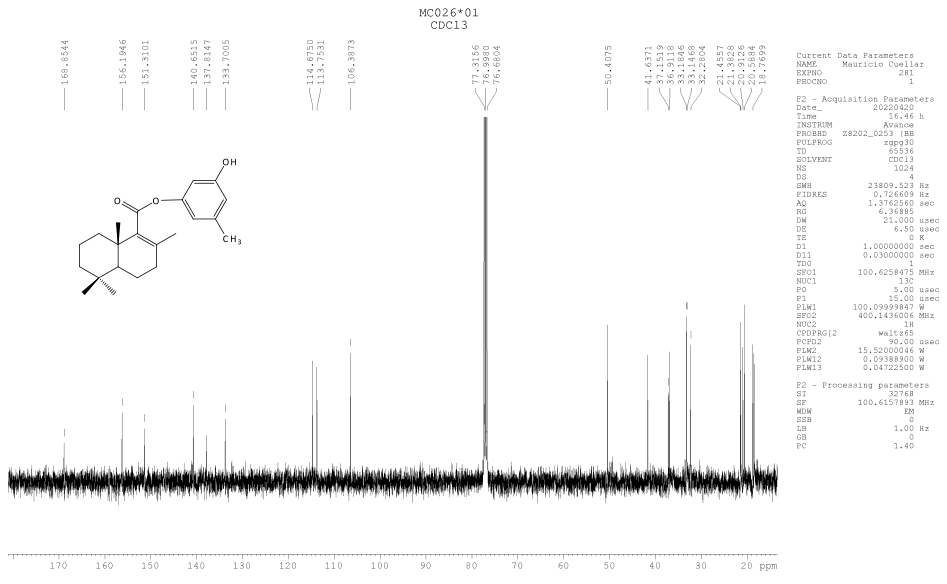
 ^{13}C -DEPT 135 NMR for drimenal

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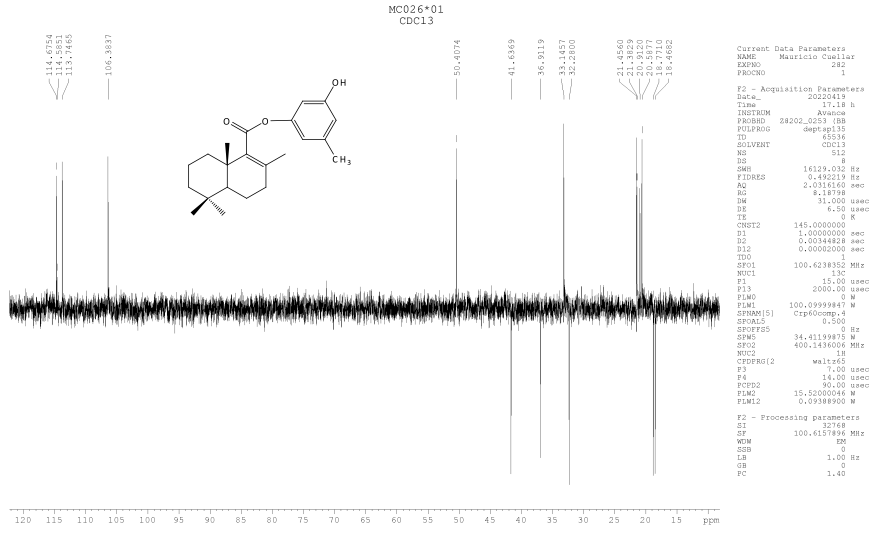
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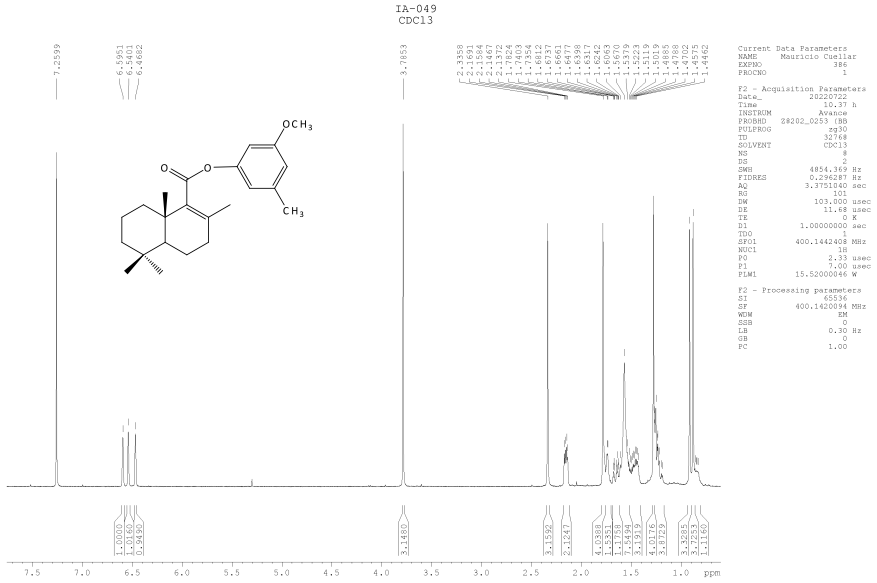
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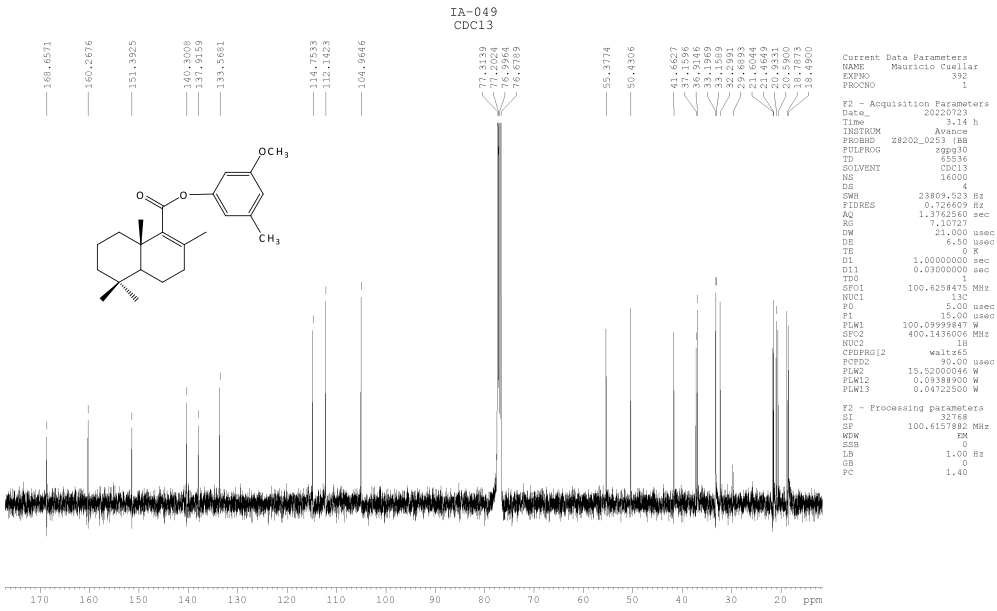
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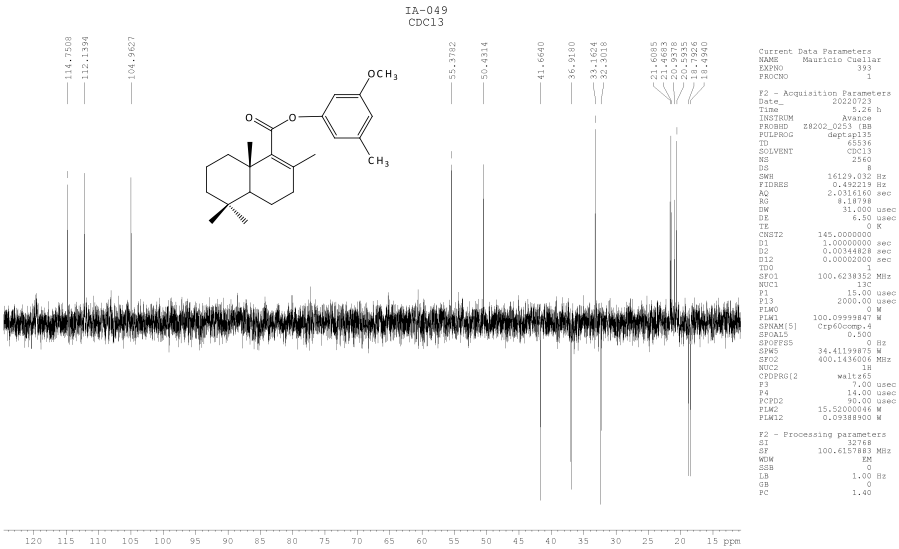
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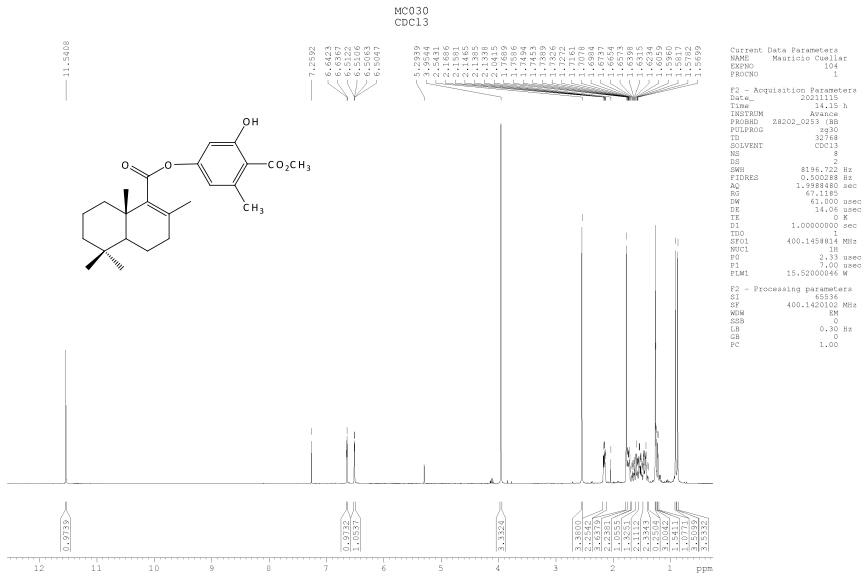
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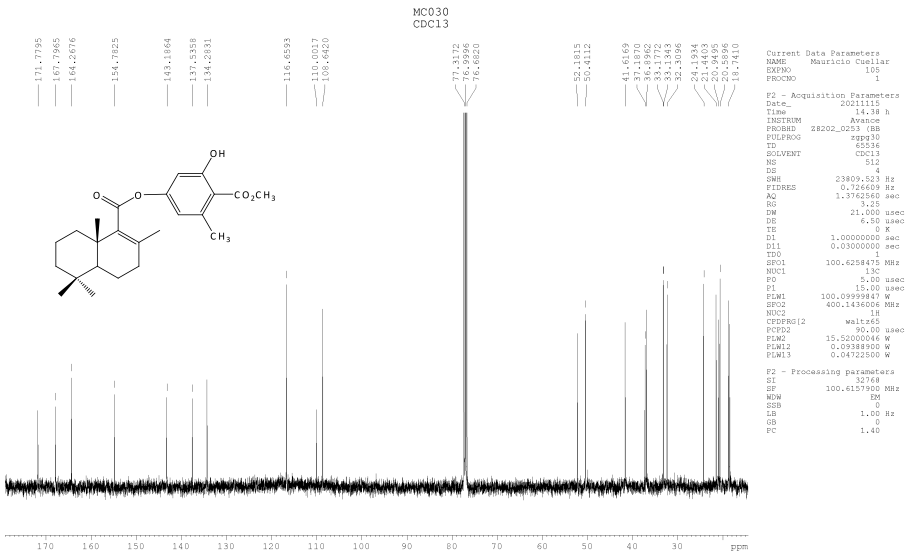
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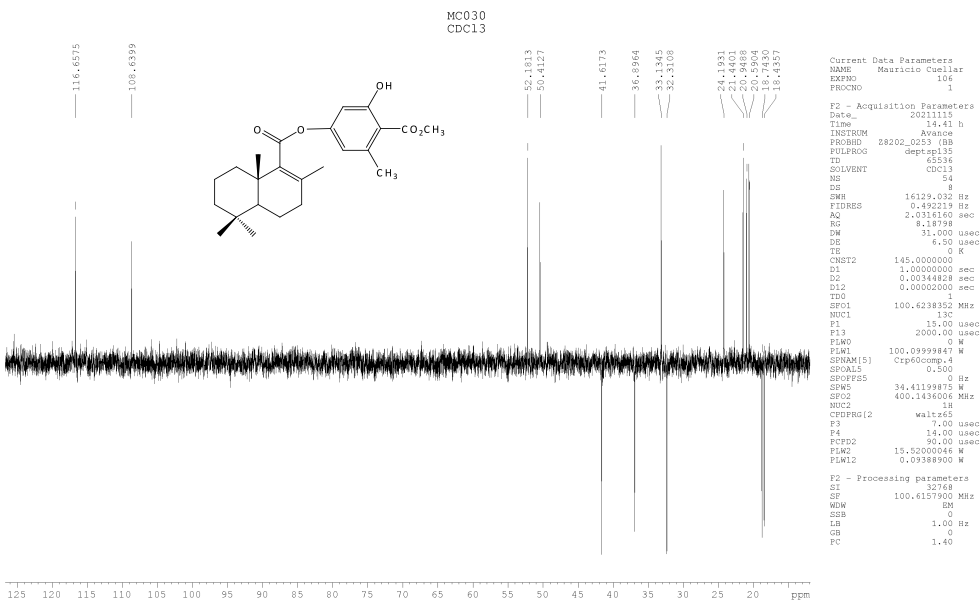
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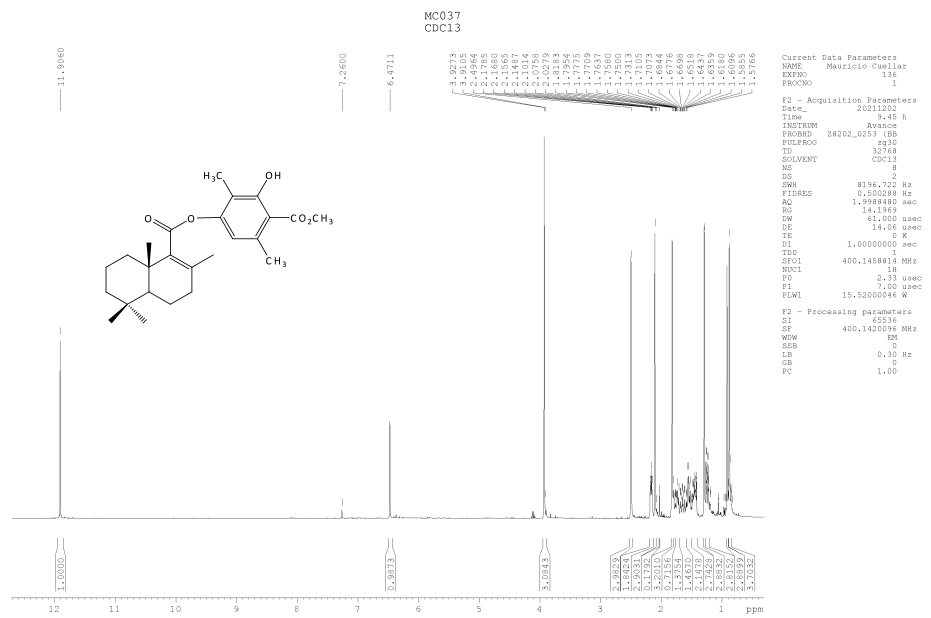
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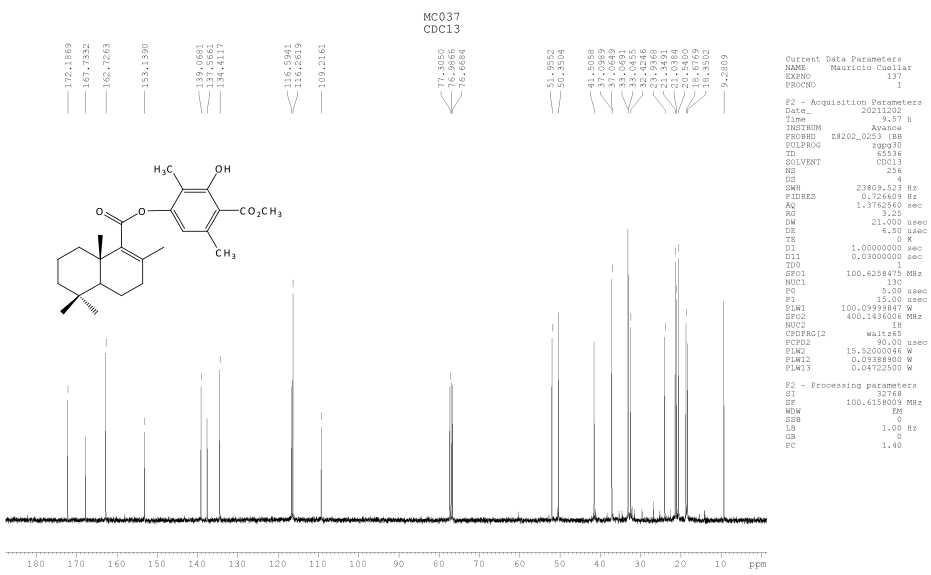
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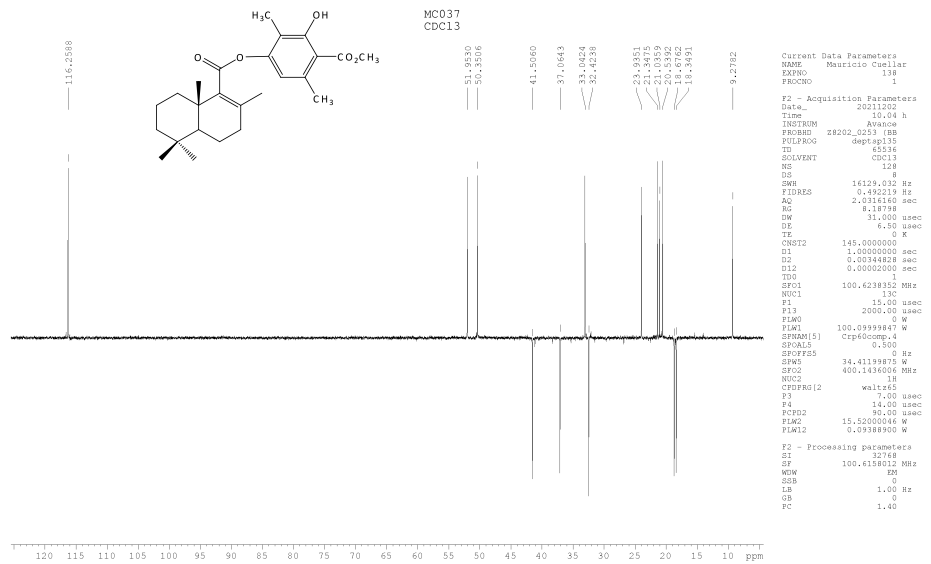
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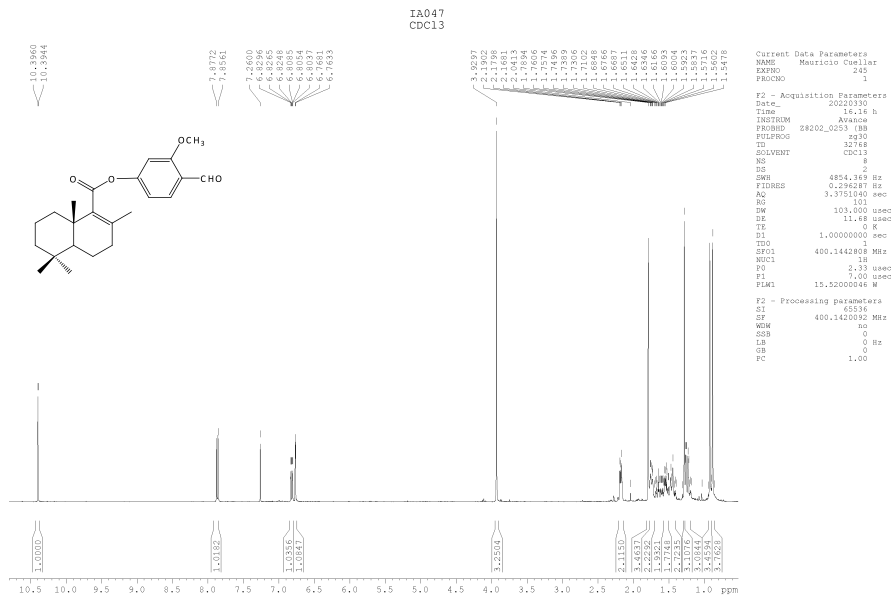
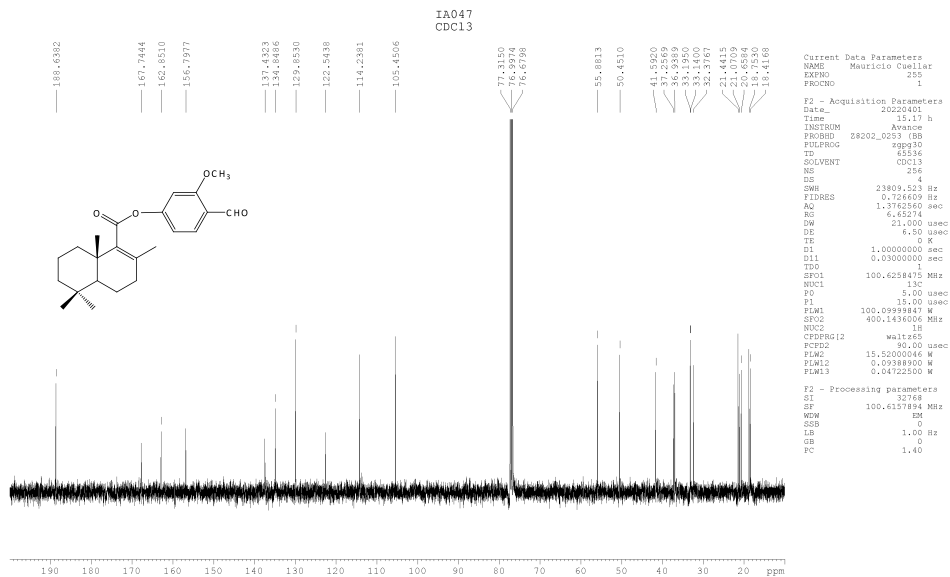
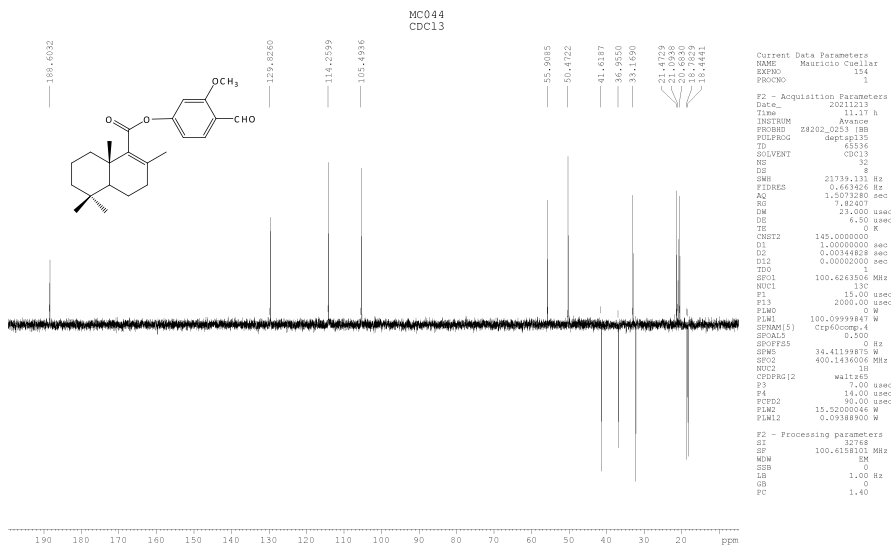


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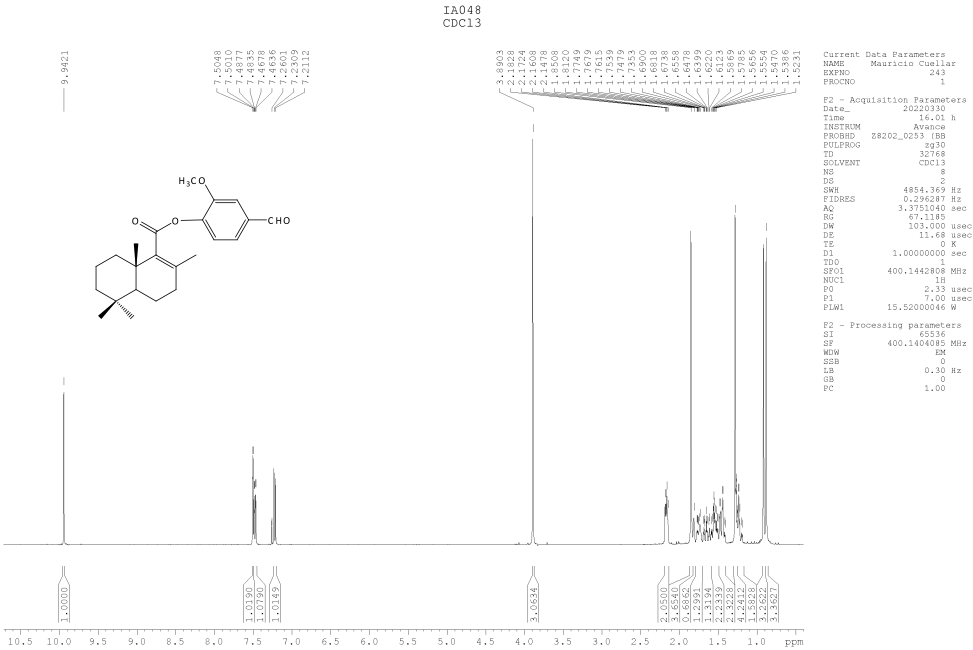


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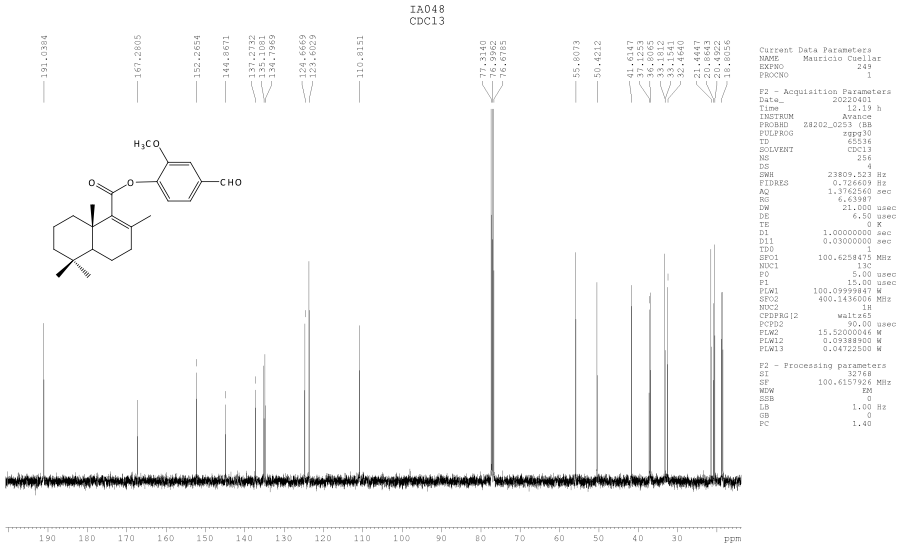


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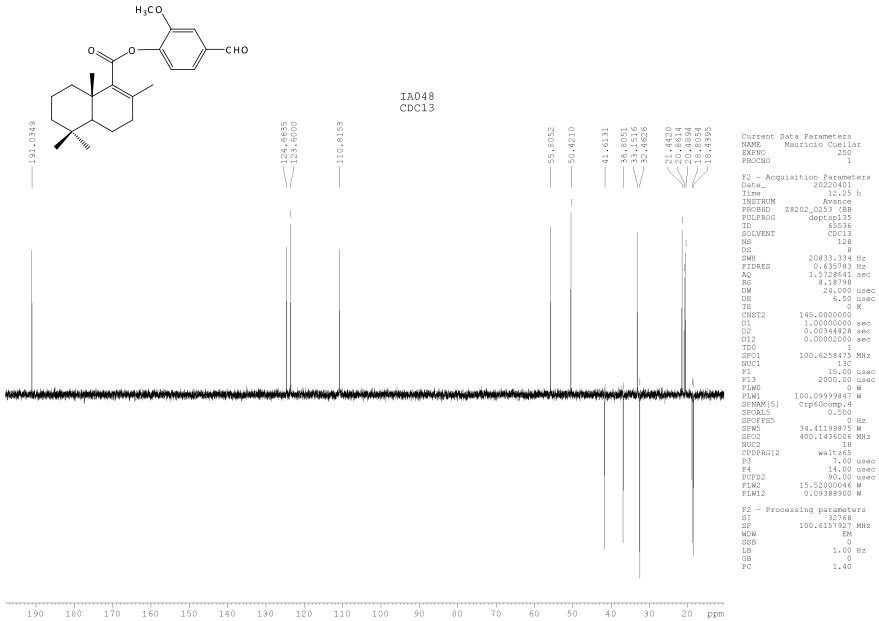
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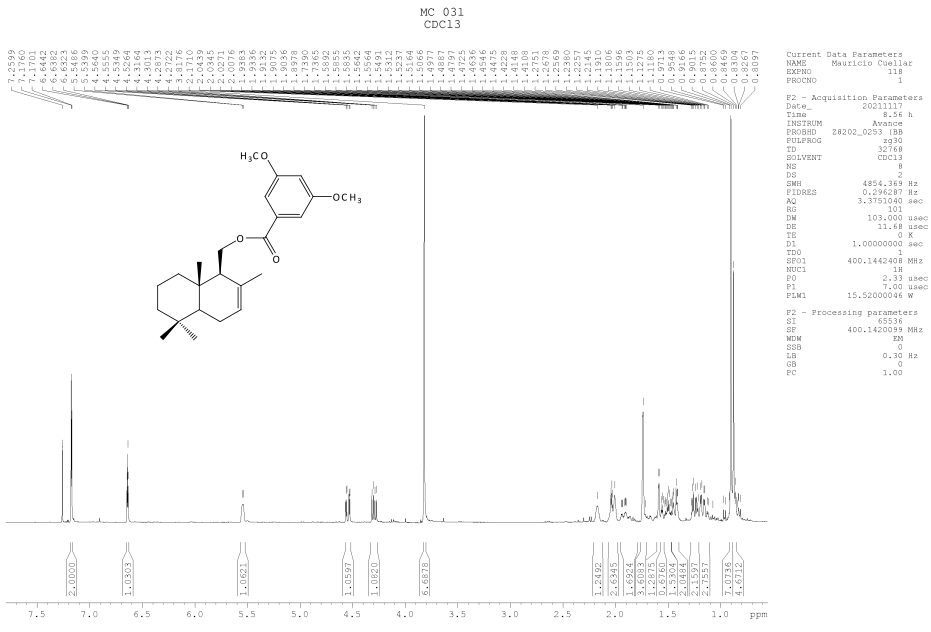
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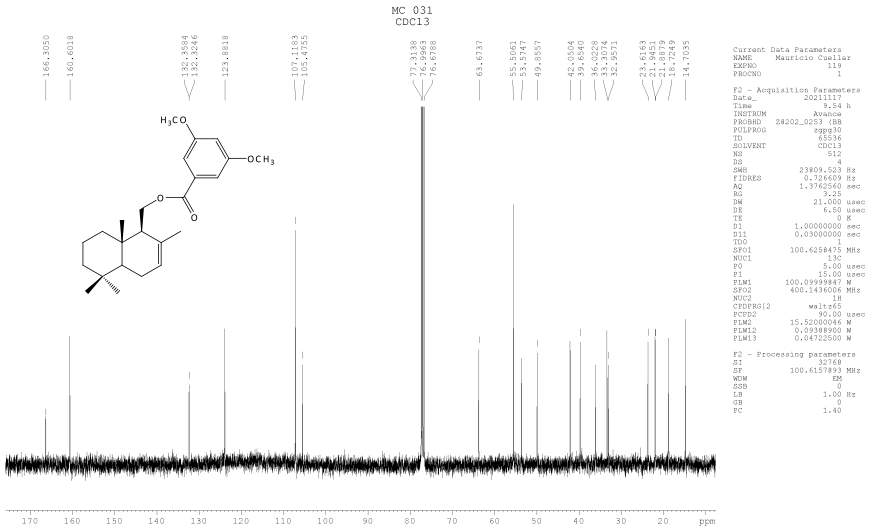
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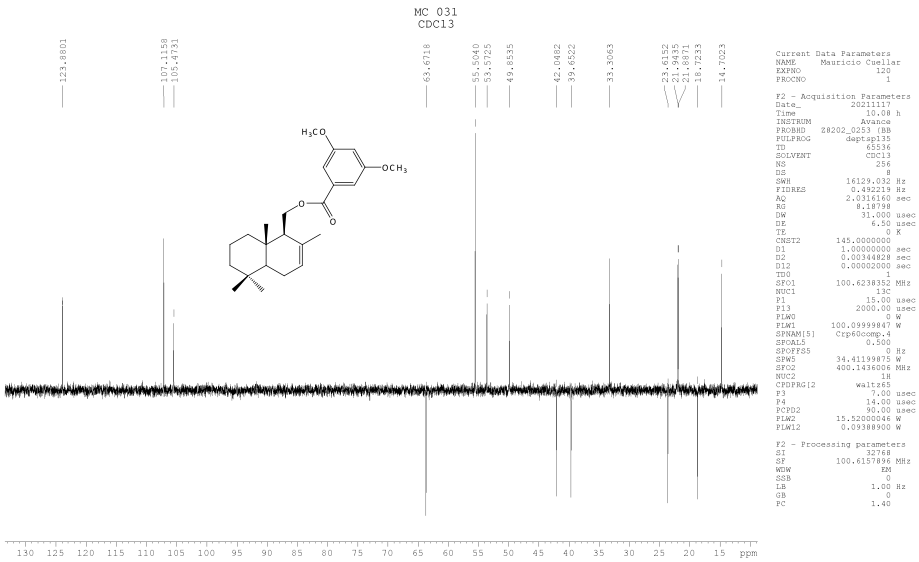
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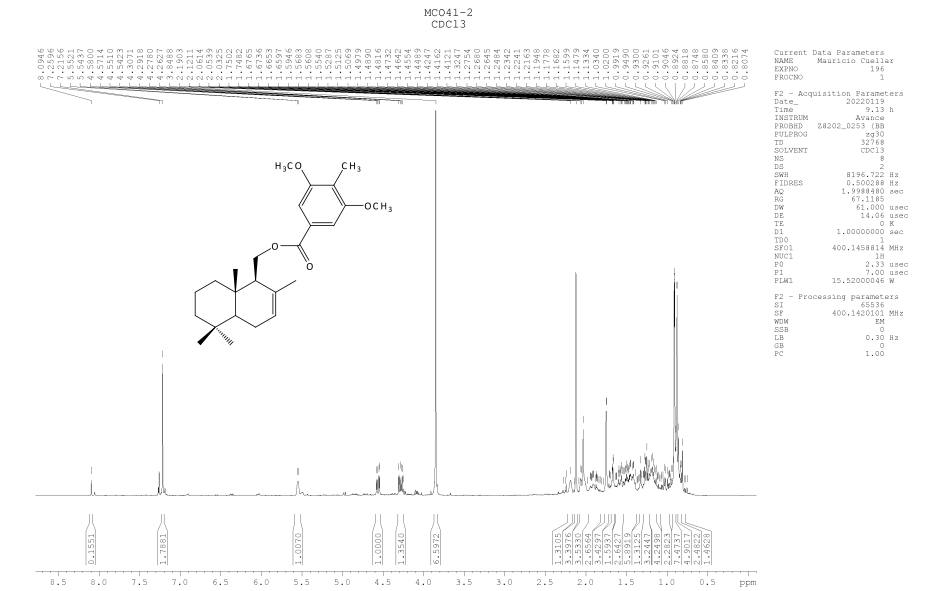
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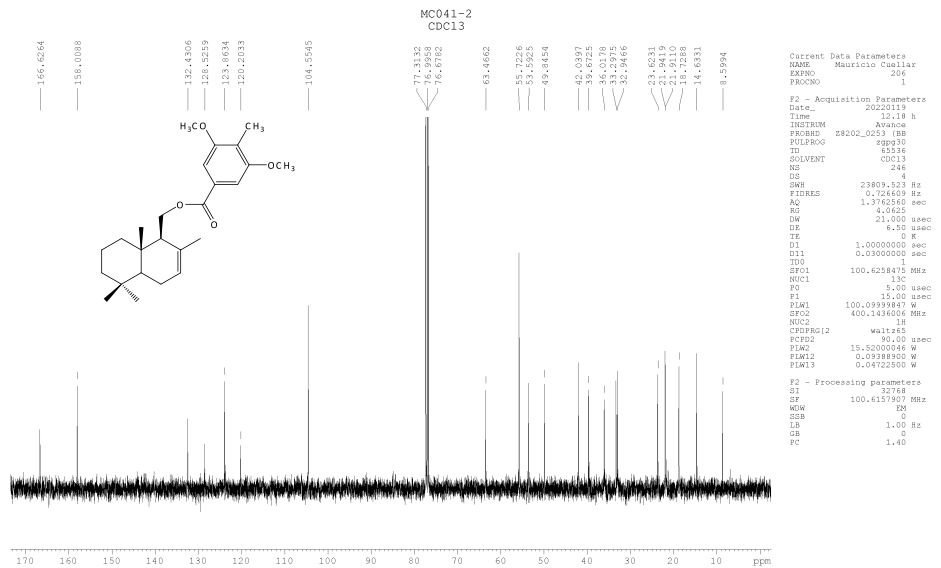
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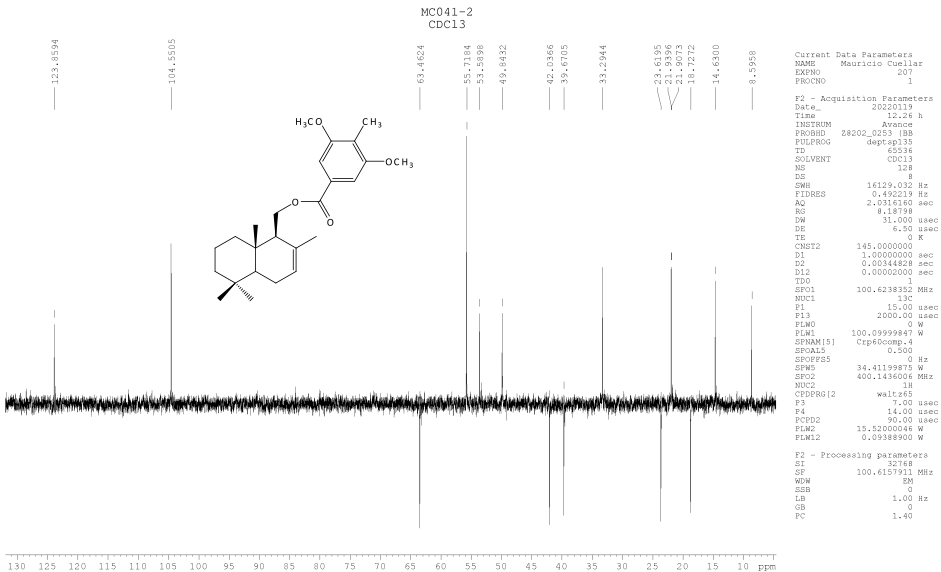
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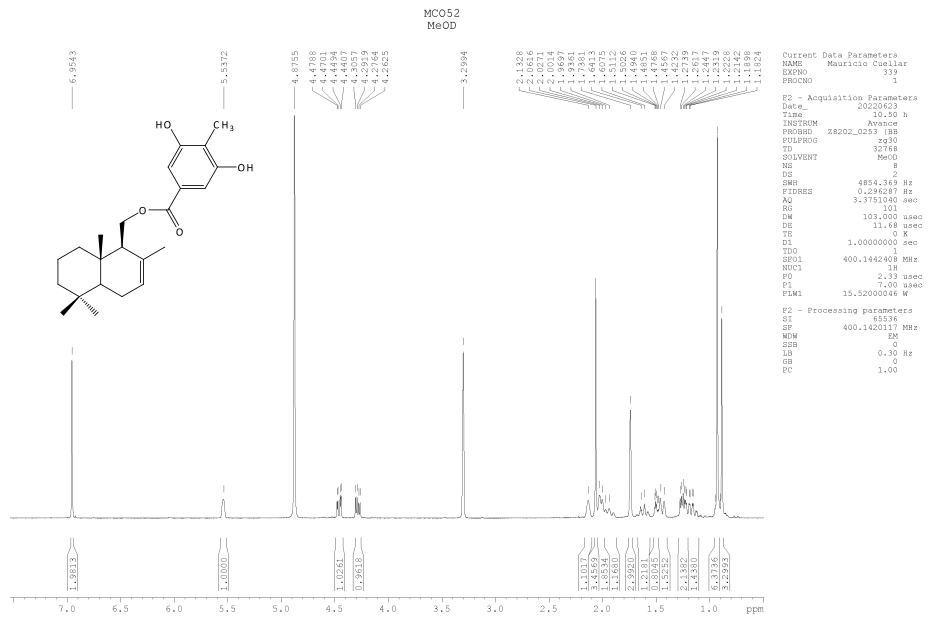
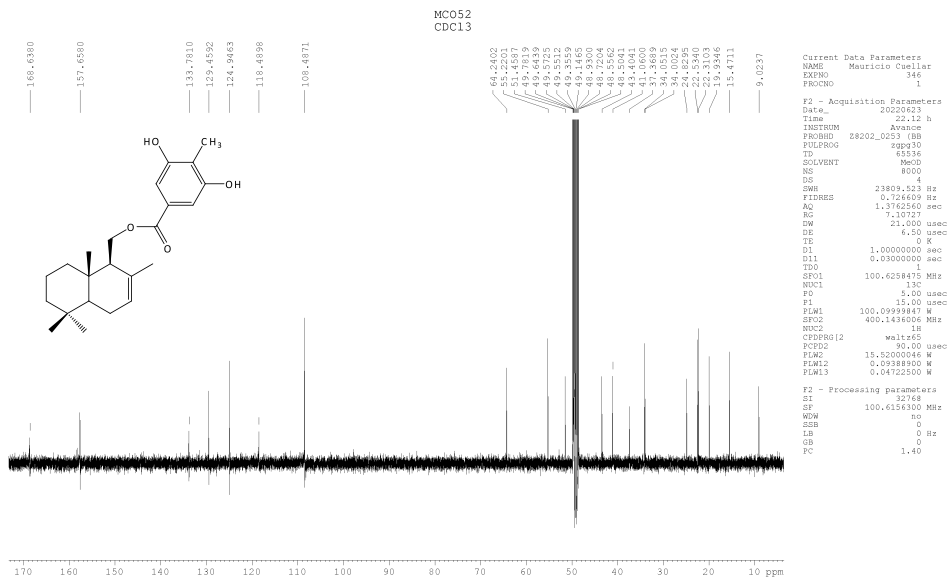
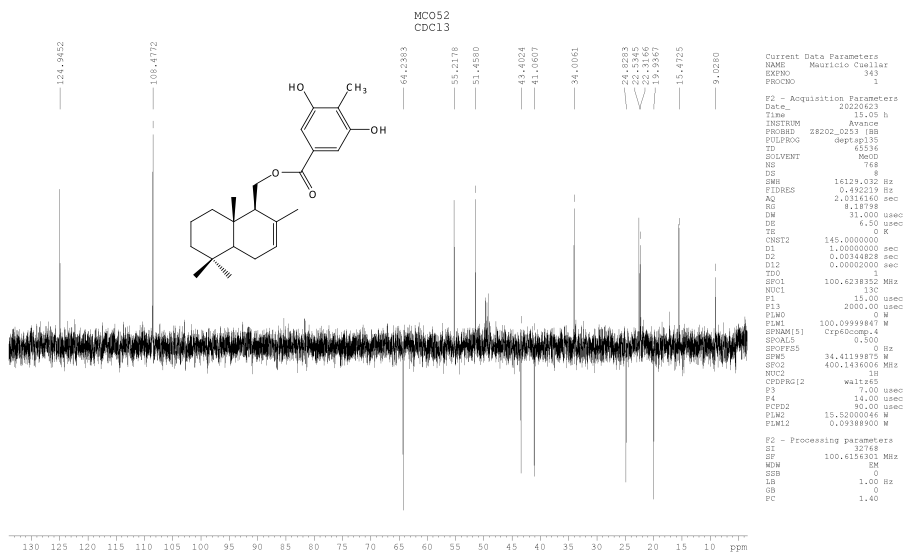


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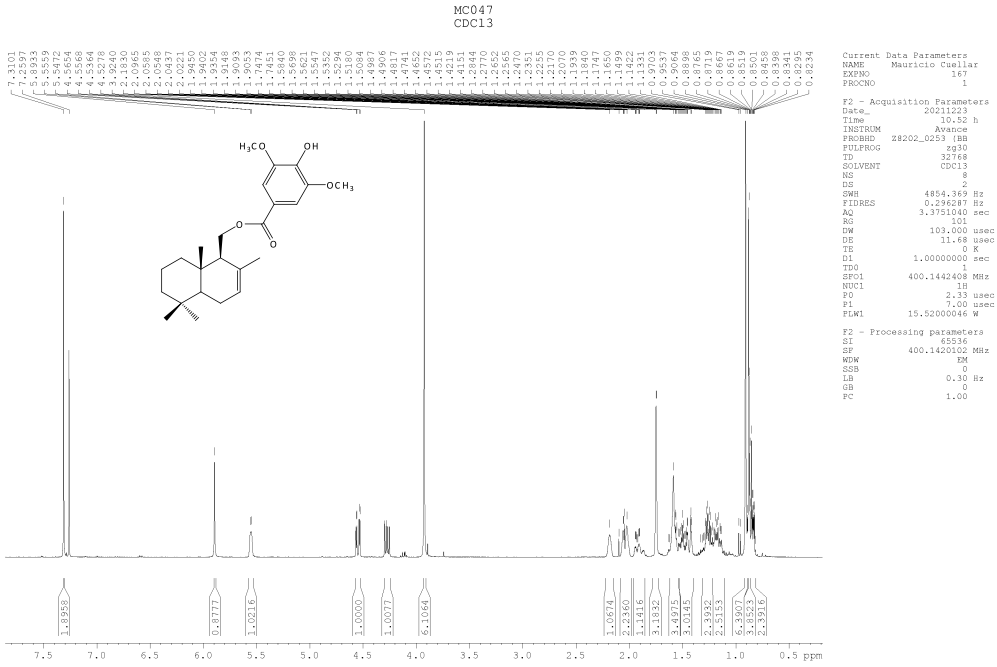


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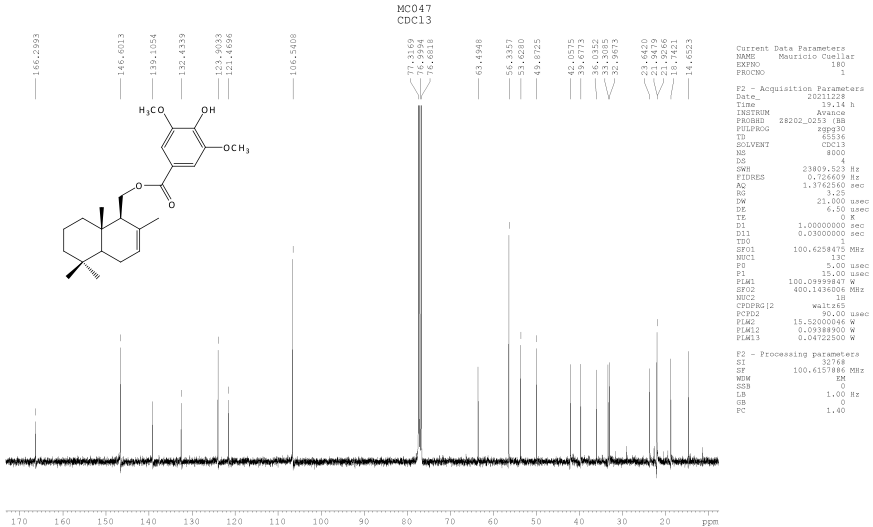


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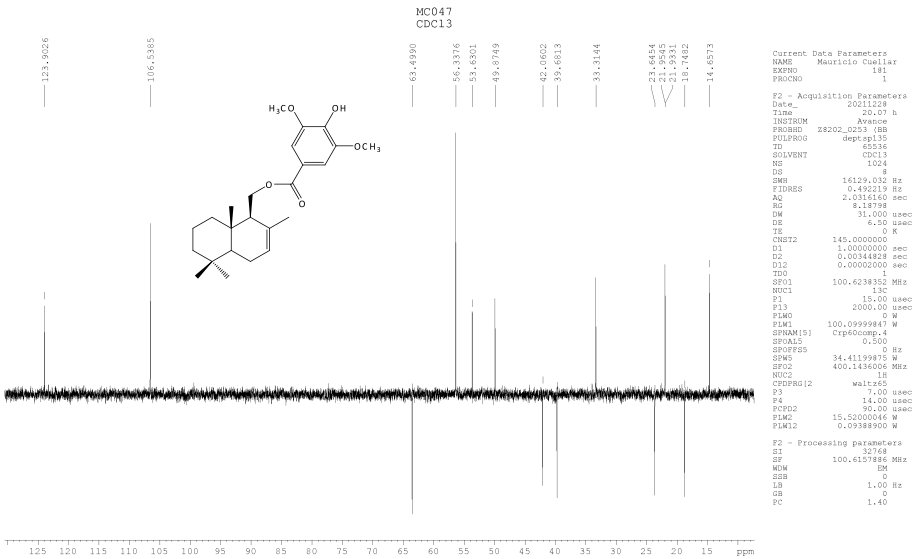
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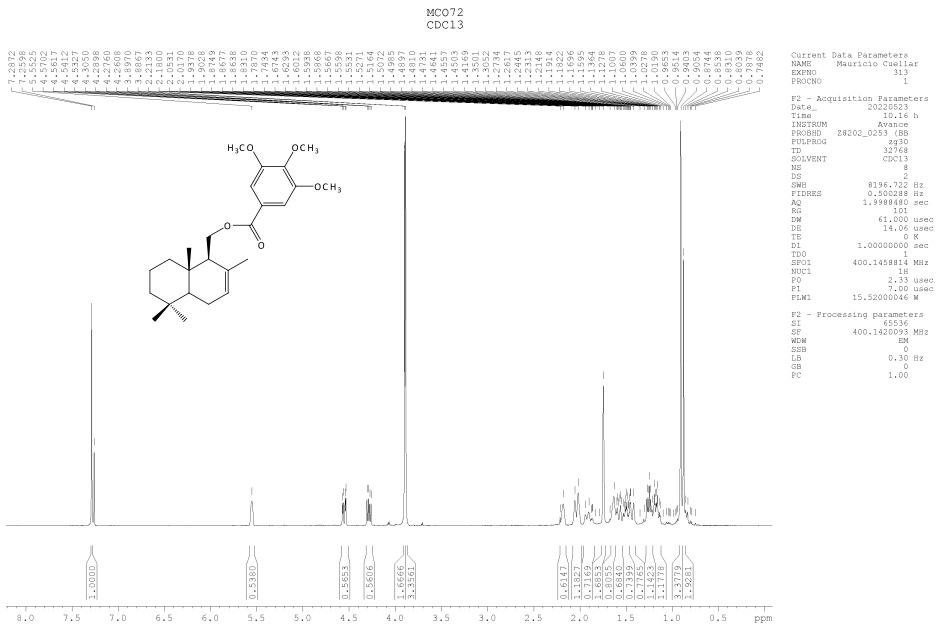
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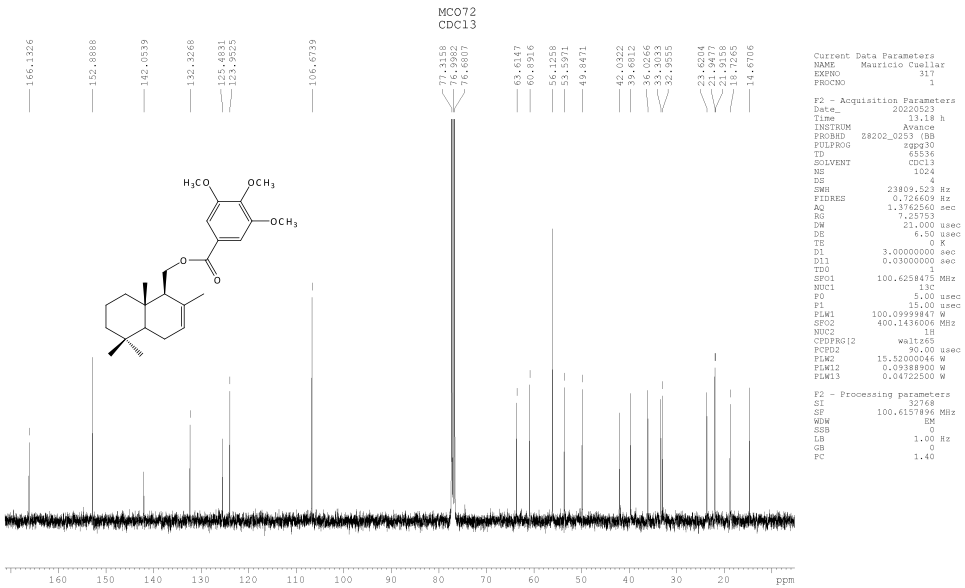
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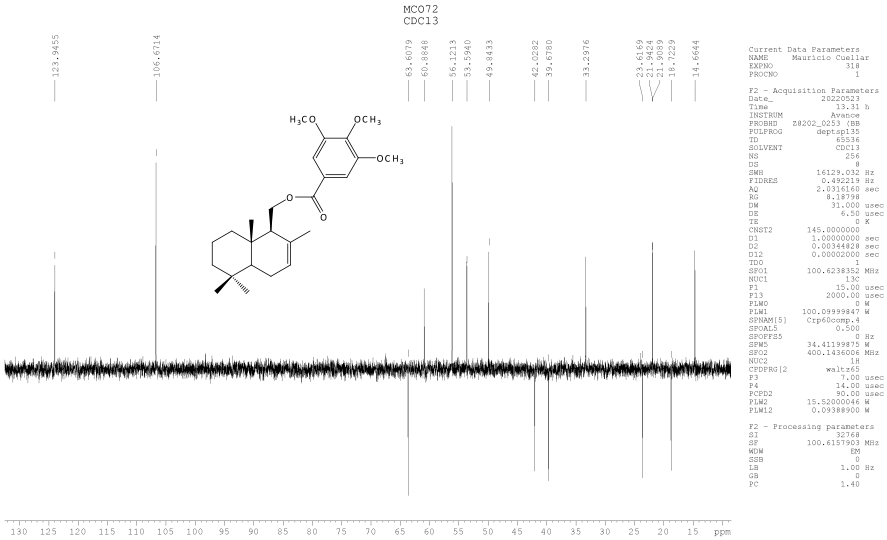
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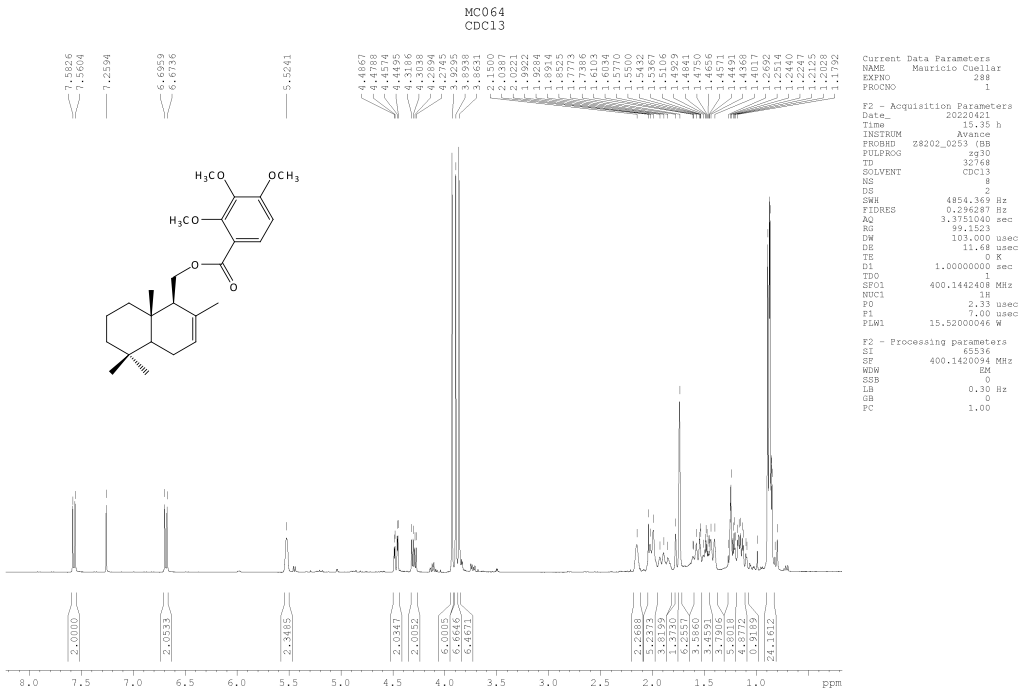
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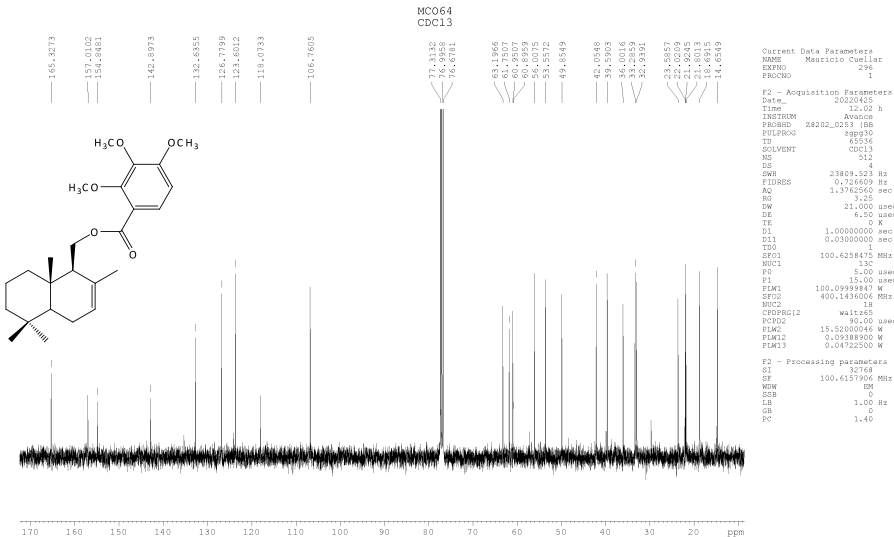
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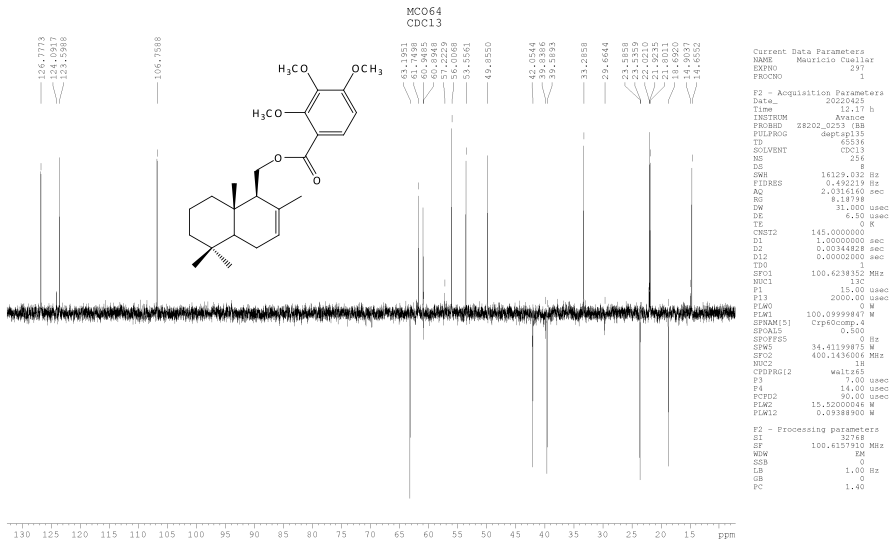
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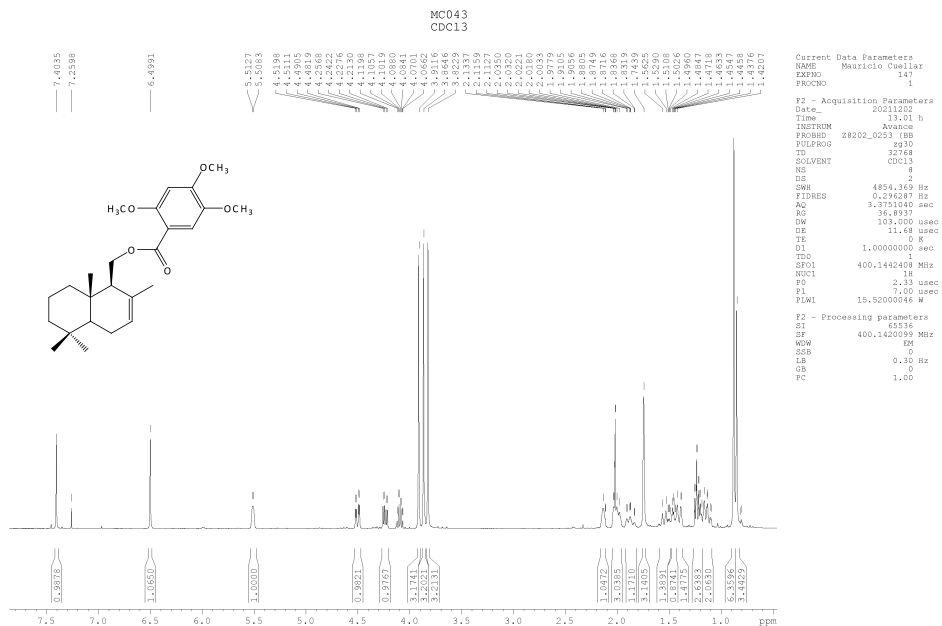
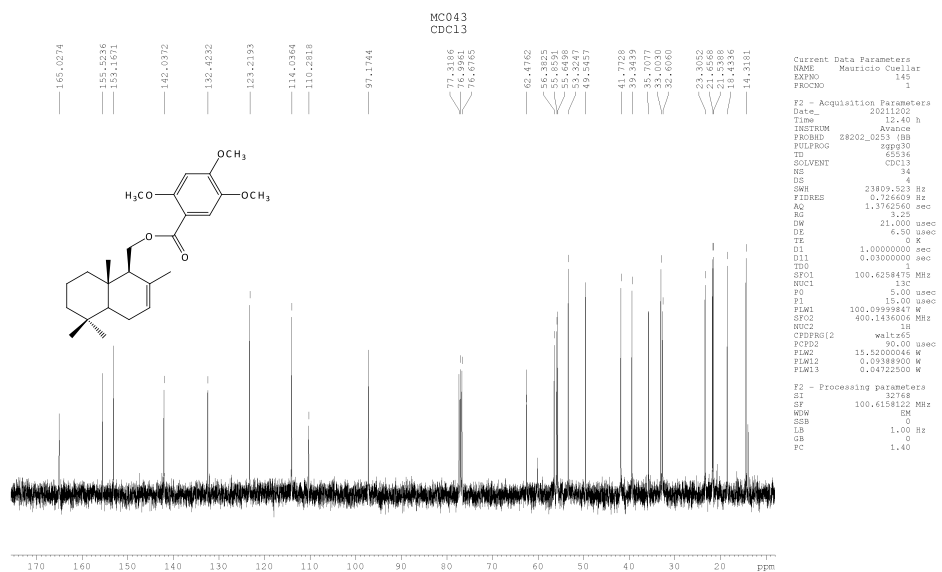
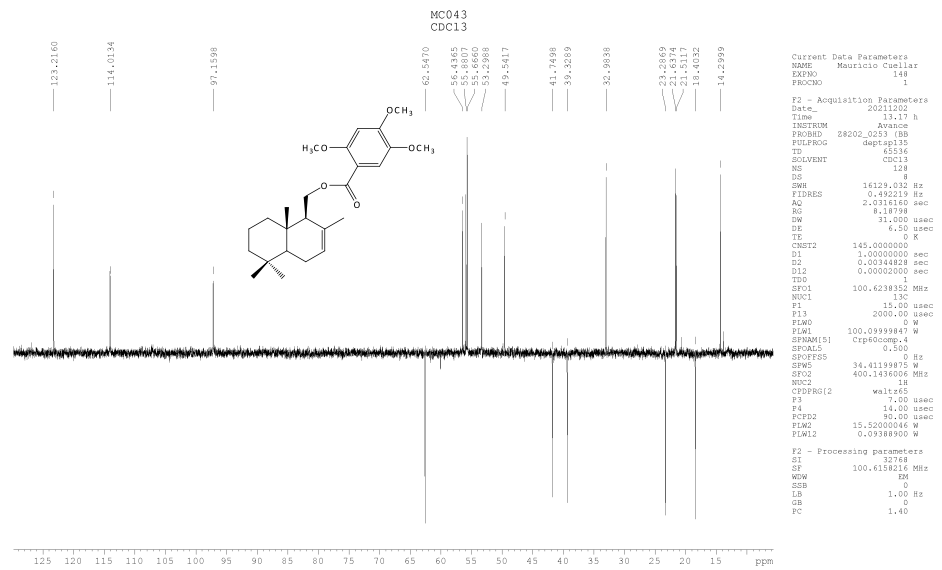


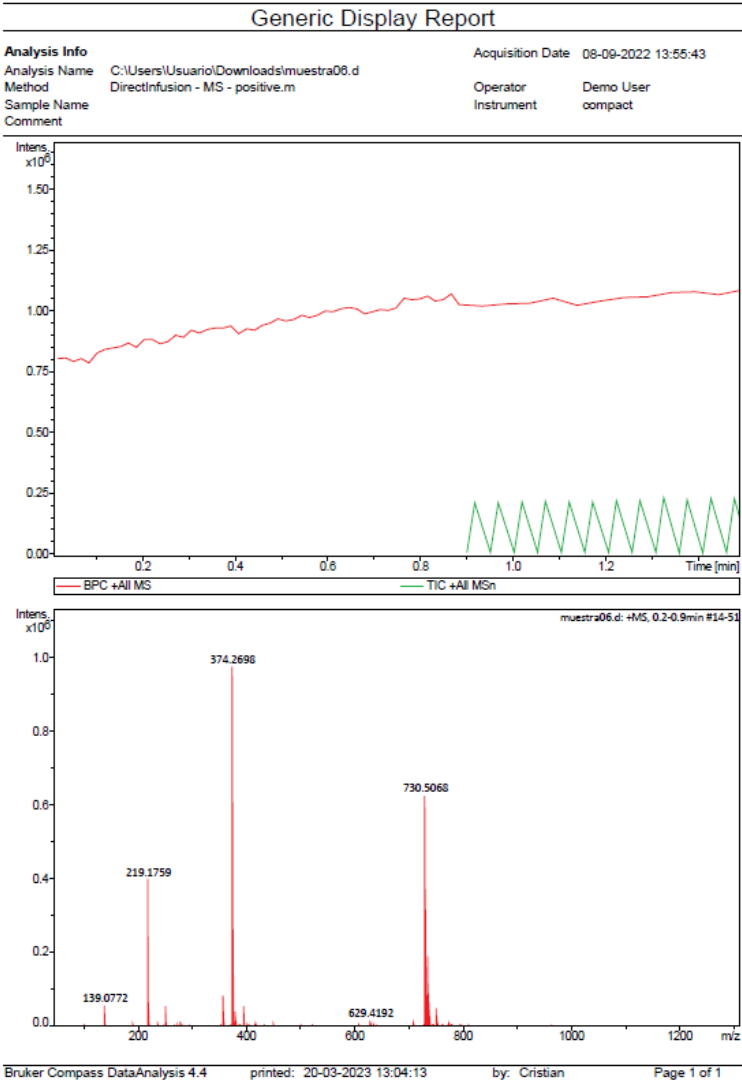
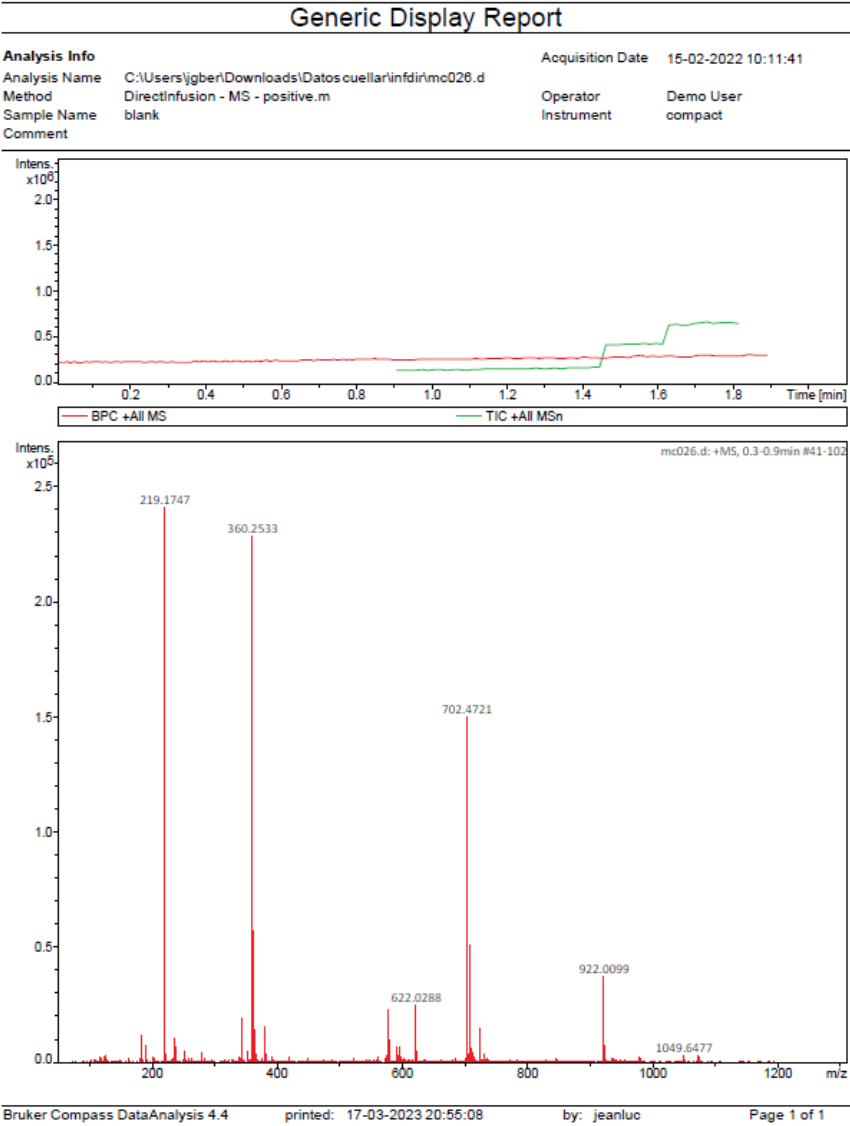
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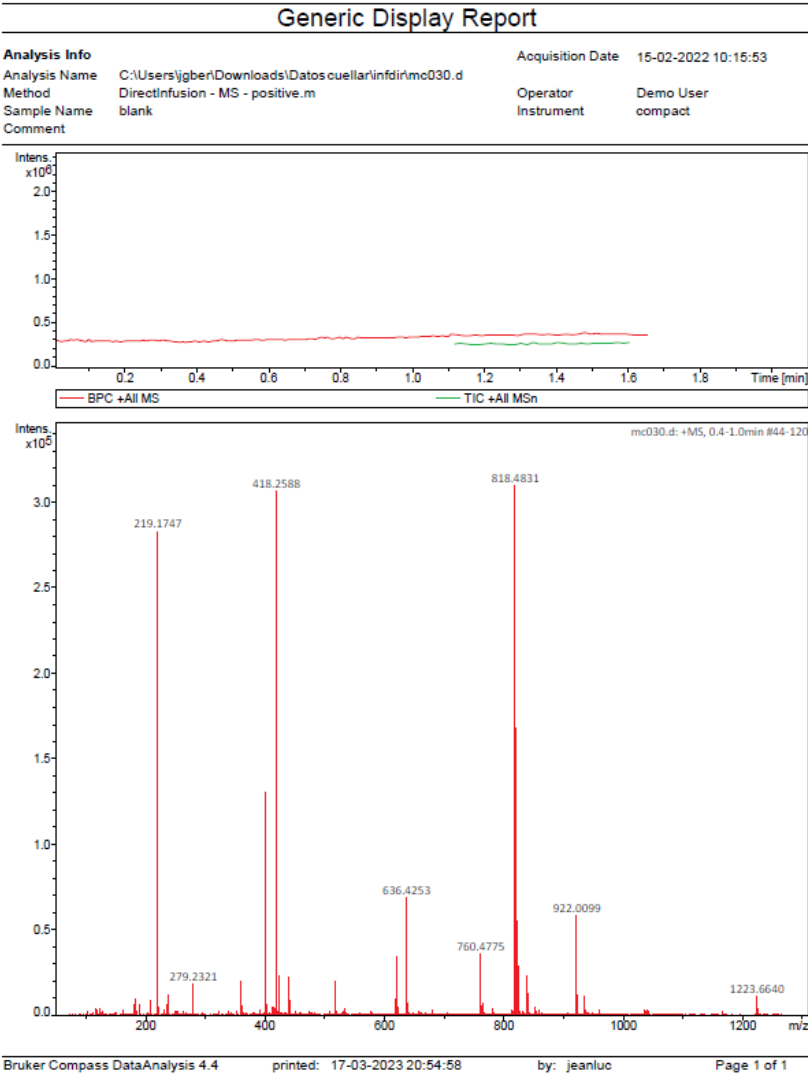


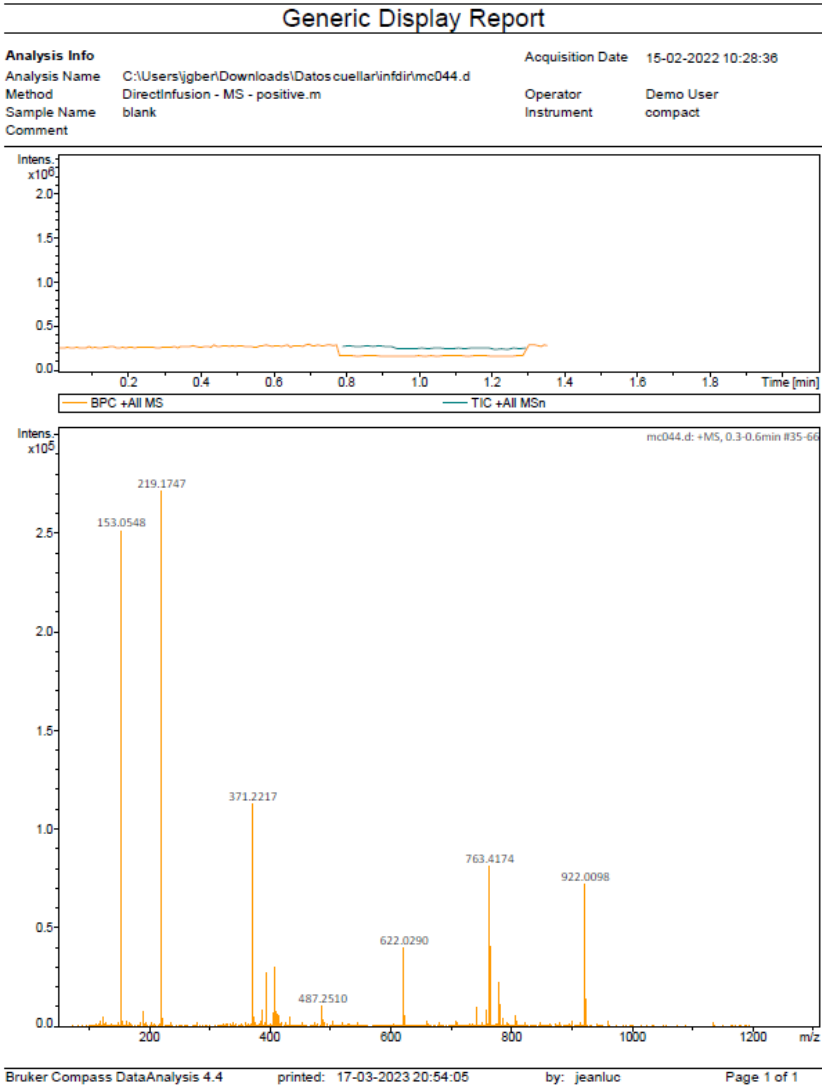
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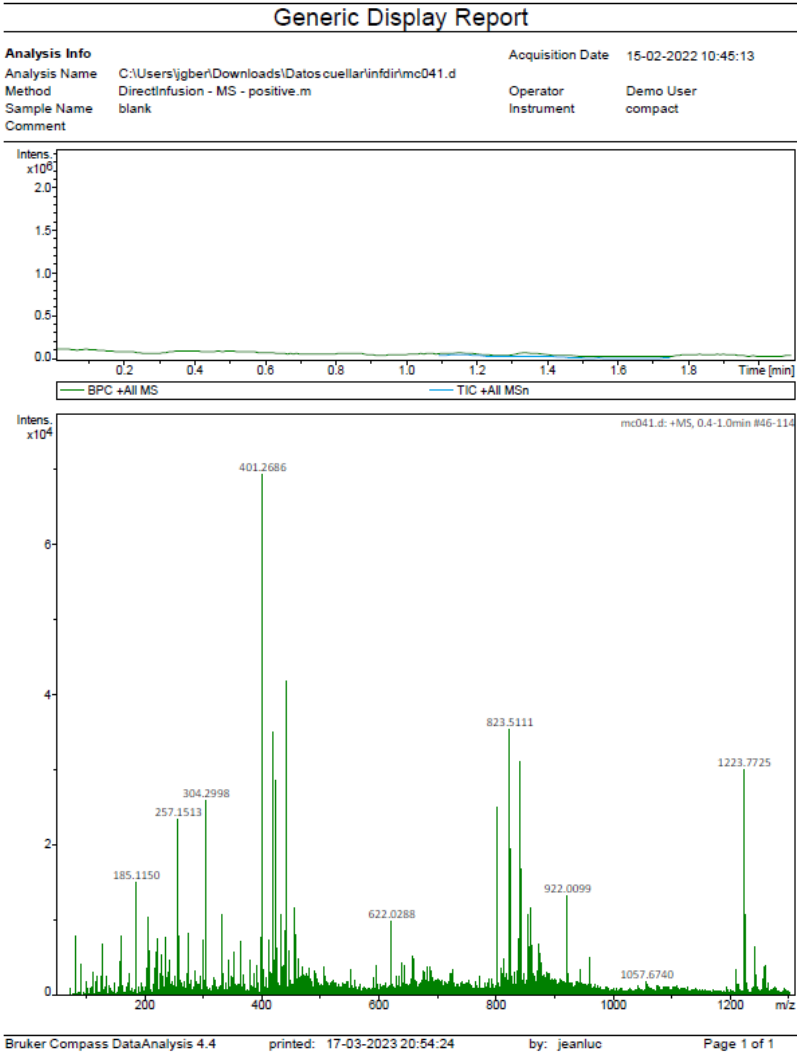
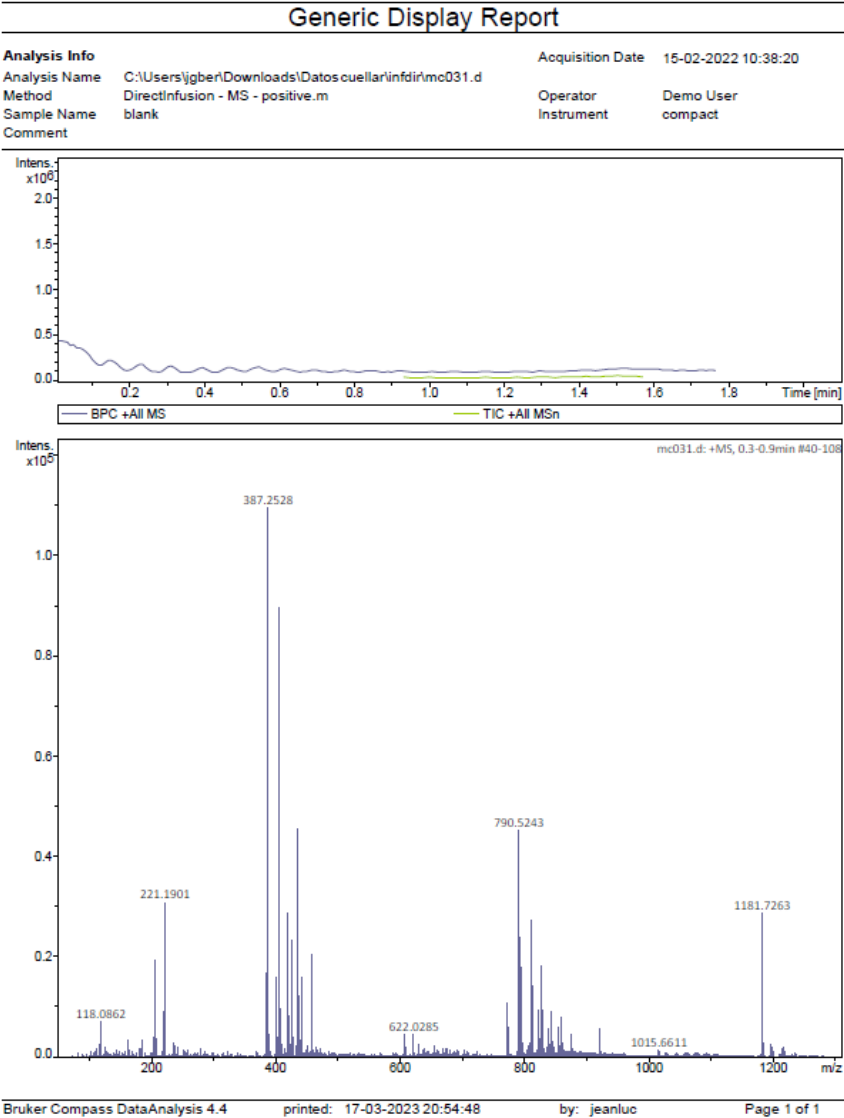


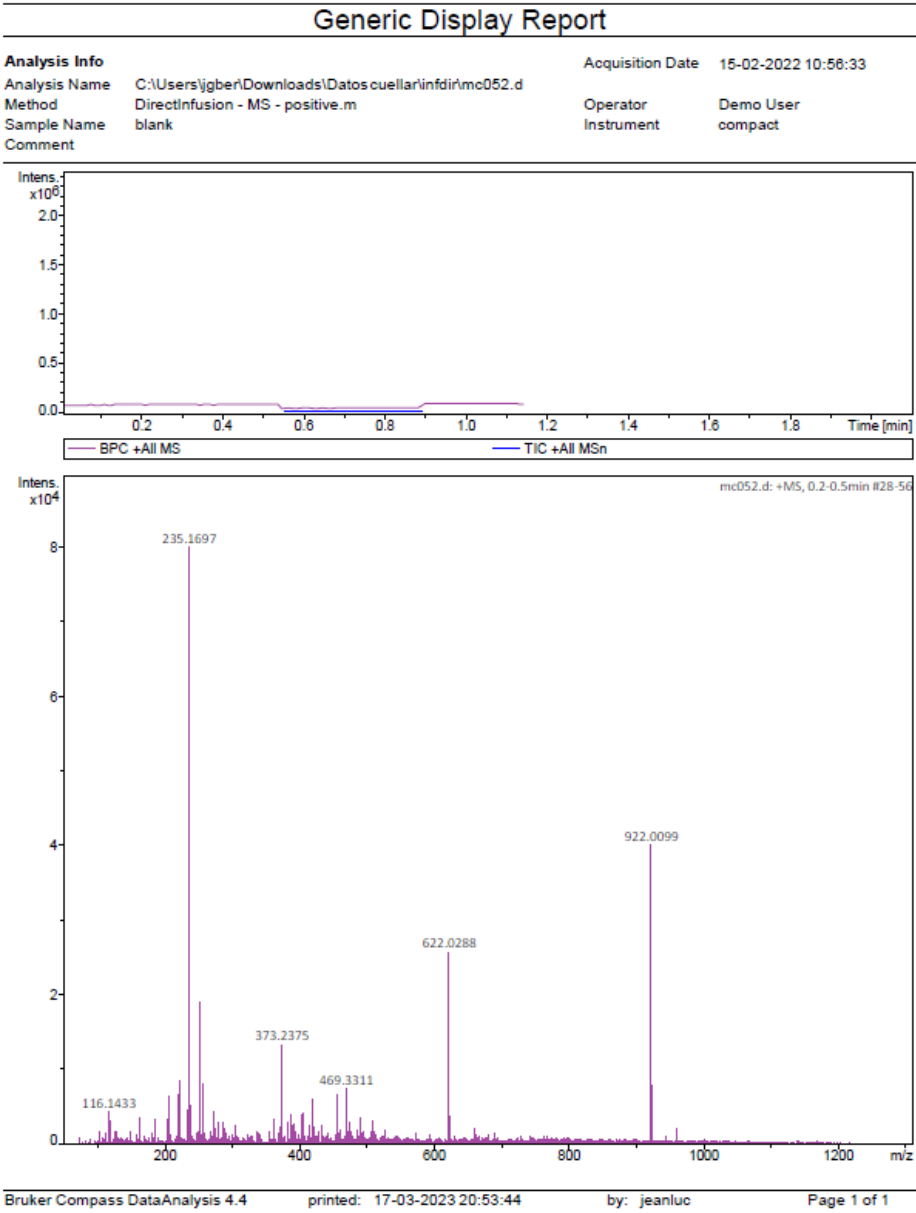
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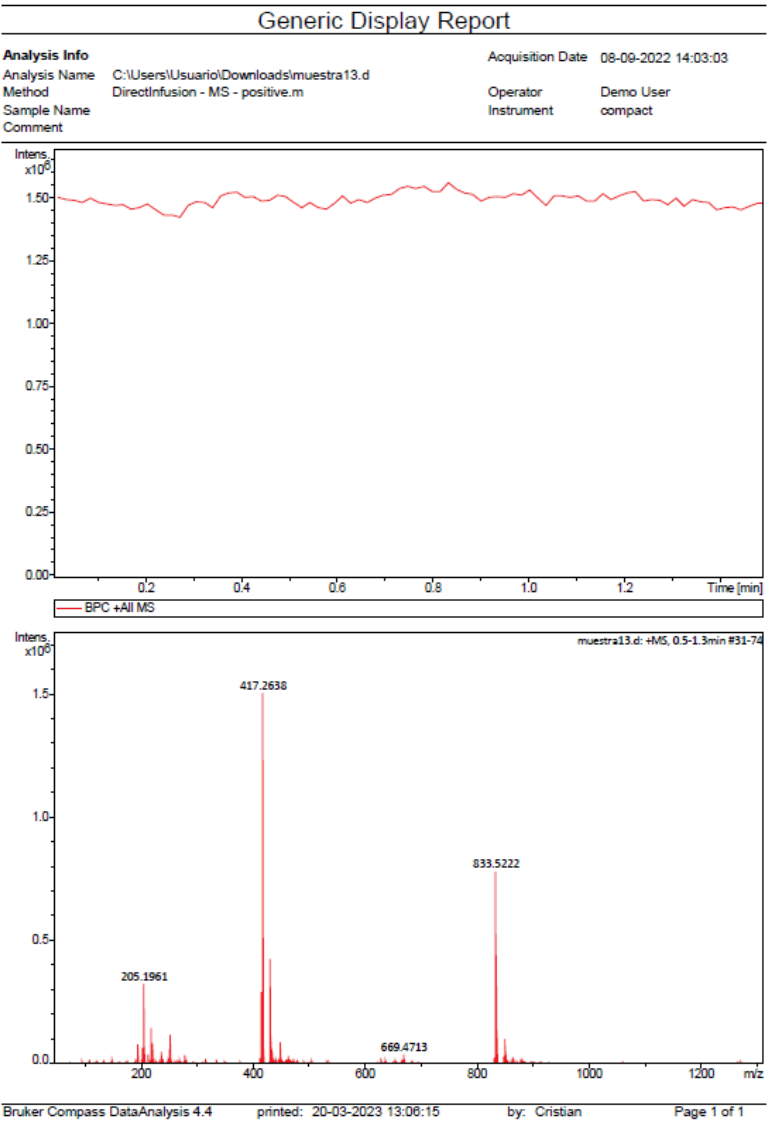


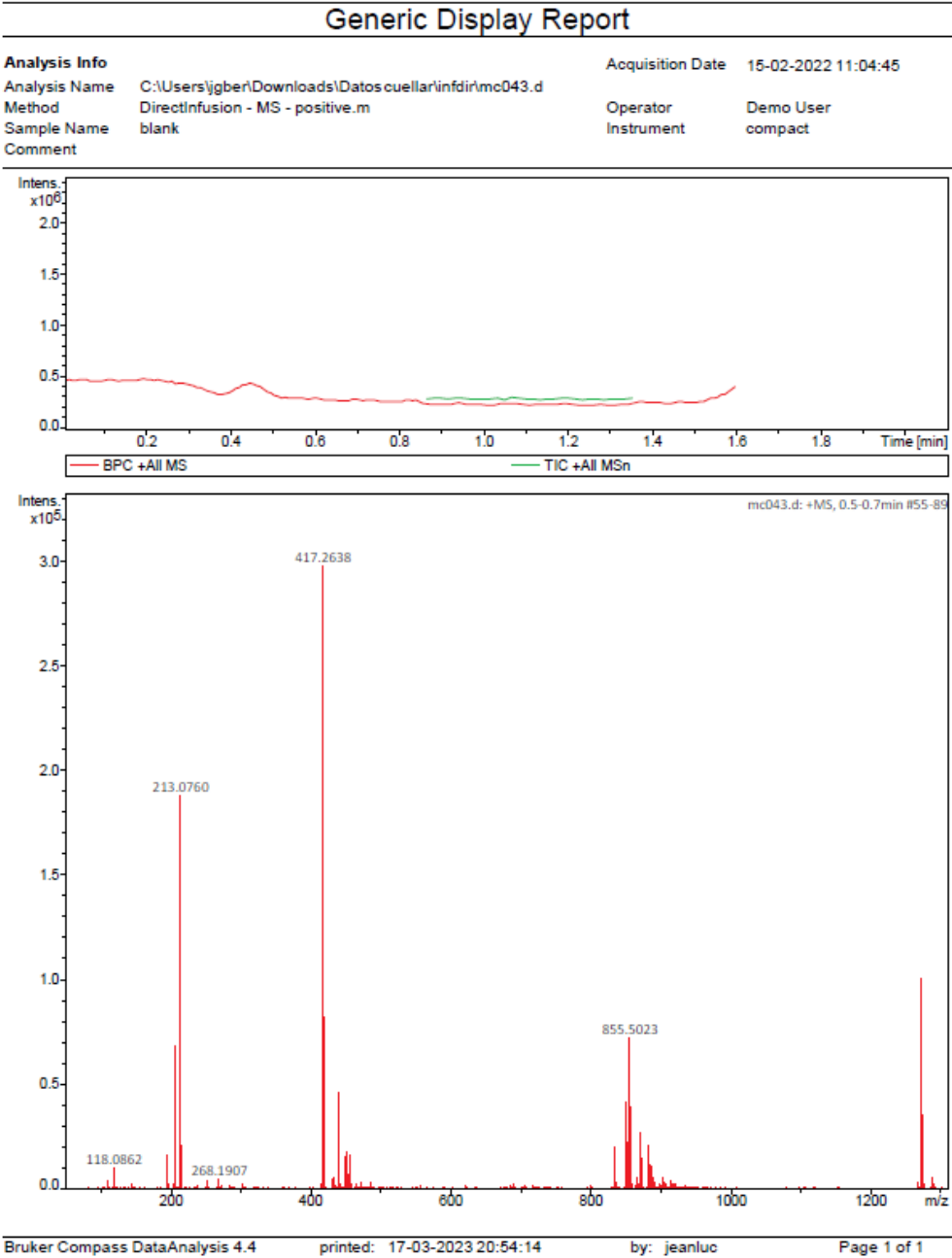












Protein-Ligand Contacts

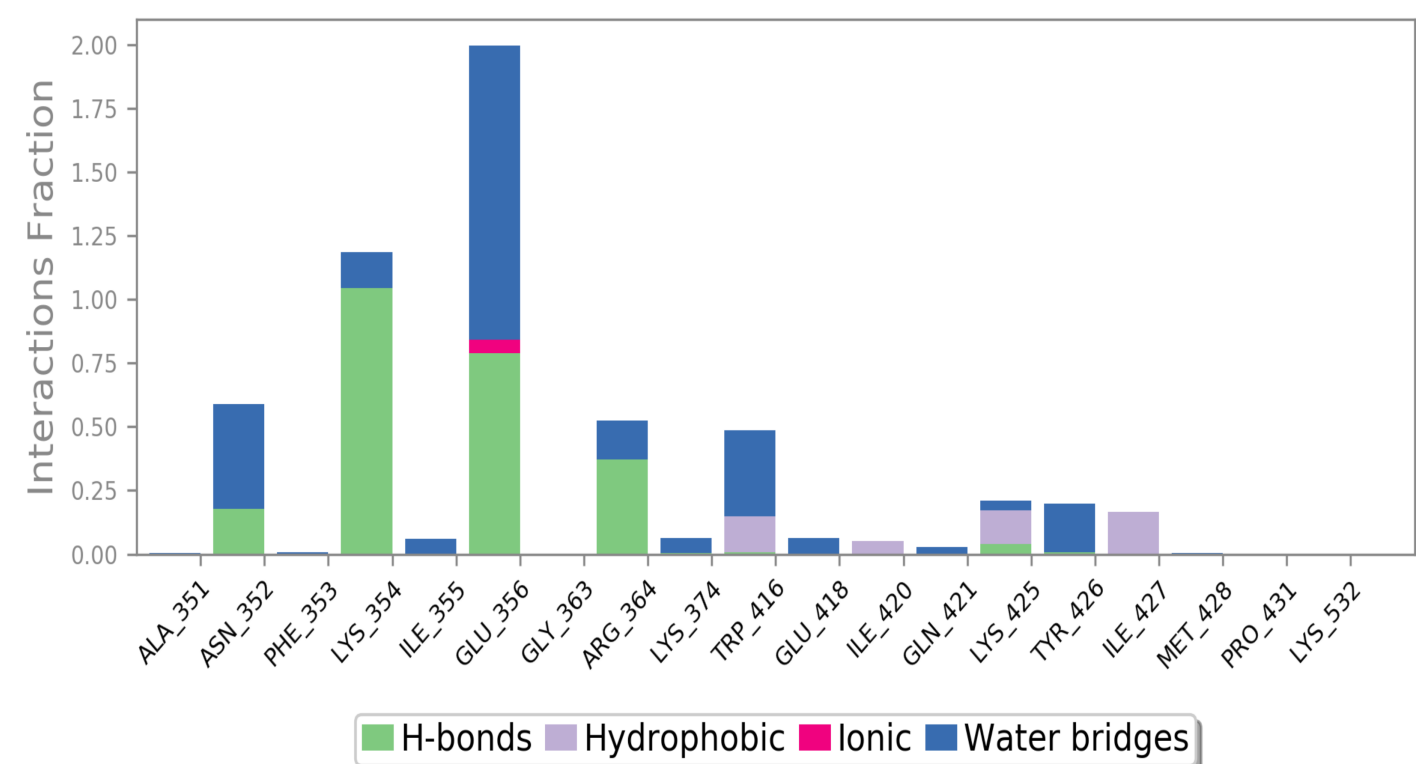


Figure S1. Protein-Daunorubicin contacts over time (100 ns).

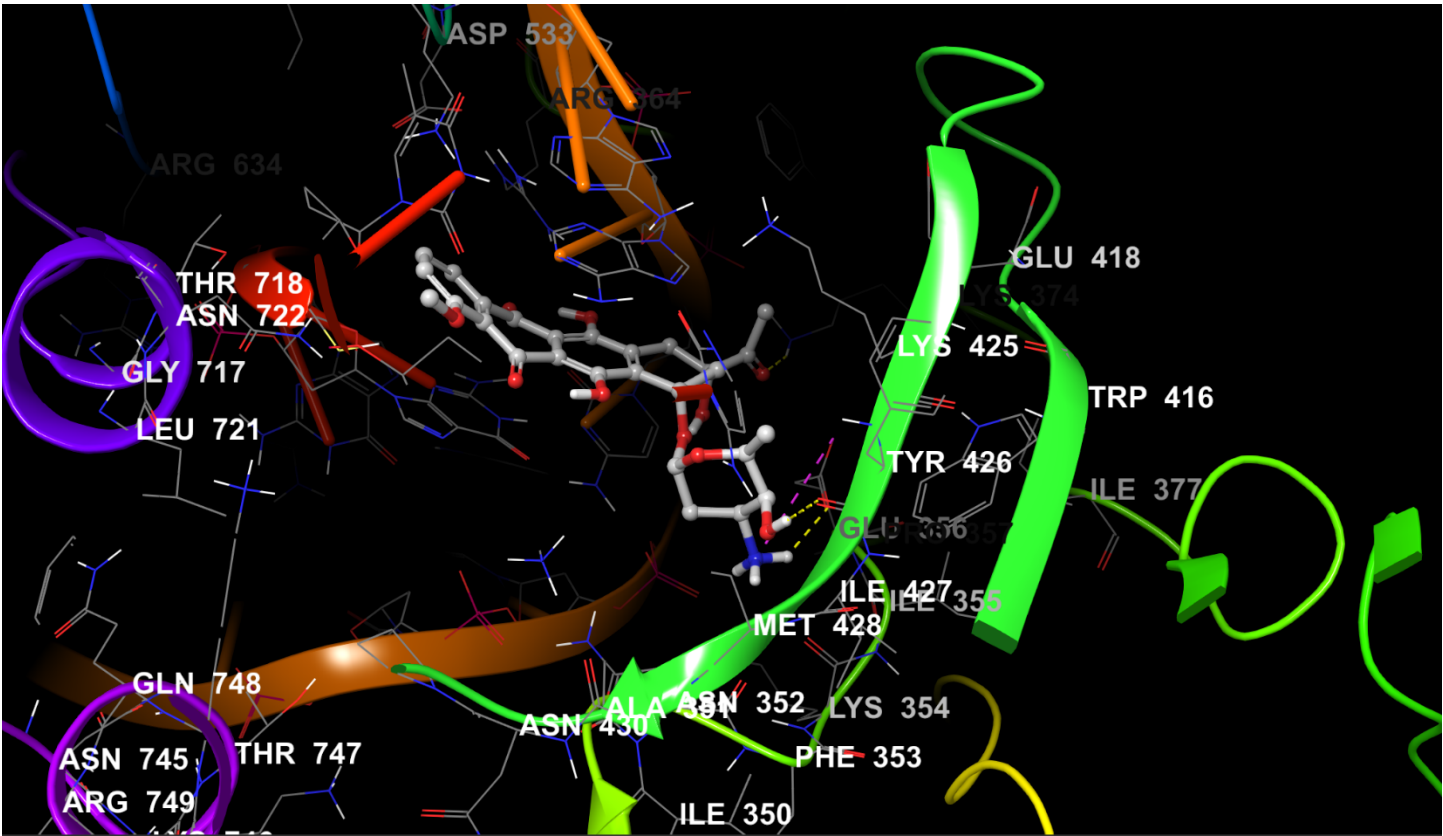


Figure S2. Daunorubicin first frame of molecular dynamics simulation (t =0 ns). Close-view capture. This view is the docking-output pose. The compound accommodates as and intercalating between the nitrogenated bases.



Figure S3. Daunorubicin last frame of molecular dynamics simulation (t = 100 ns). Far-view capture.

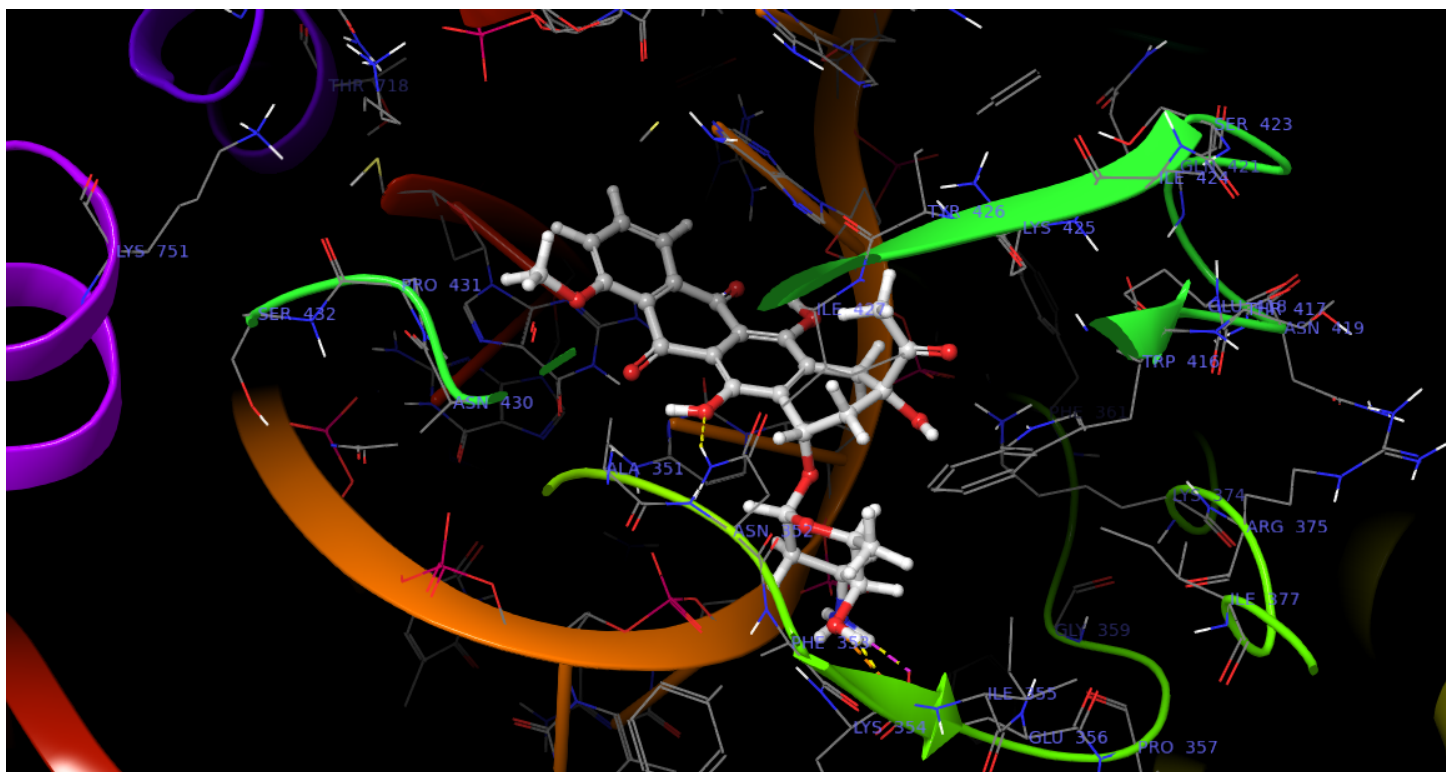


Figure S4. Daunorubicin last frame of molecular dynamics simulation (t= 100 ns). Close-view capture. The compound remains between the nitrogenated bases over time acting as an intercalating-drug.

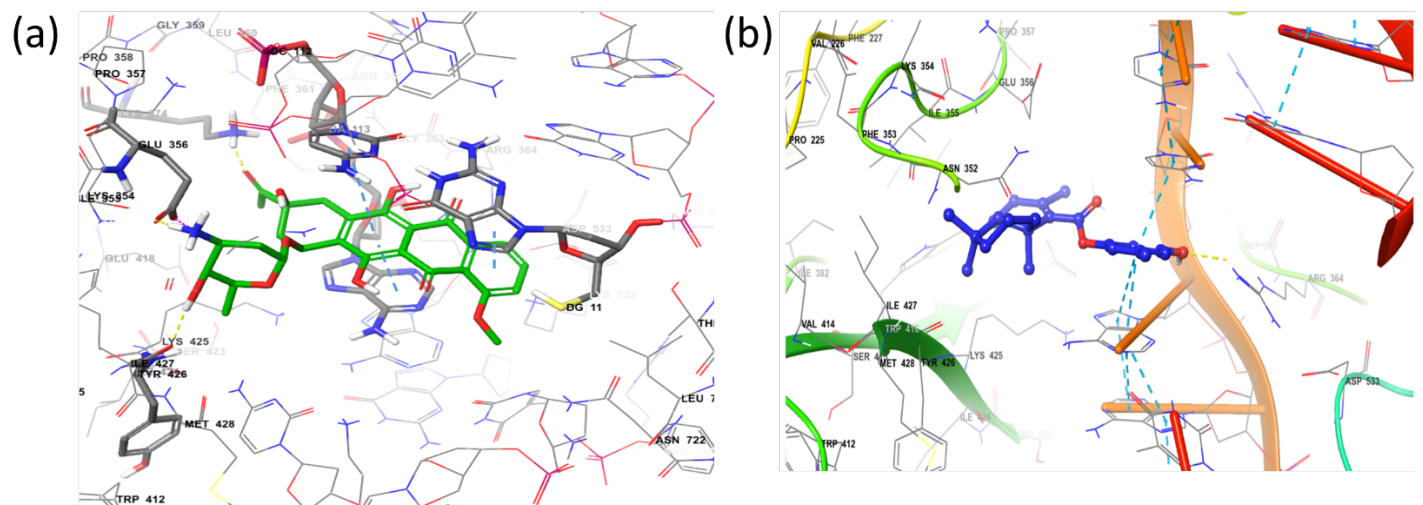


Figure S5. a) 3D pose obtained by docking for daunorubicin at the topotecan reference ligand site. Daunorubicin inserts as an intercalator between the DG11, DC112 and DA113 bases, establishing π -stacking interactions. **b)** 3D pose obtained by docking for compound **6a** at the topotecan reference ligand site. The benzene ring is oriented toward the DNA bases, while the drimanic fragment is oriented towards the enzyme.

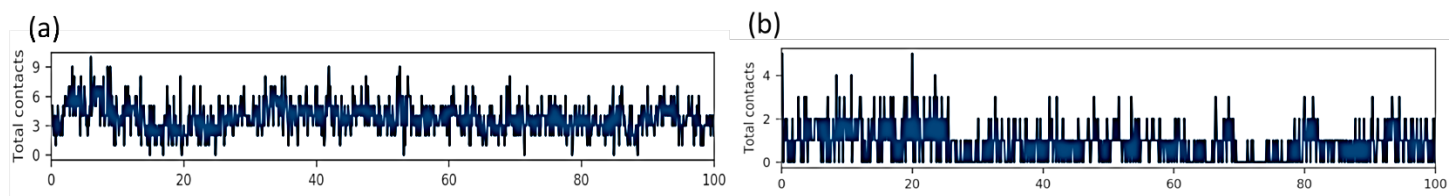


Figure S6. (a, b) Protein-ligand total contacts for daunorubicin, and compound **6a** respectively.