Supporting Information

Medicinal Chemistry Research

Macrocyclic Polyamine–Quinazoline Conjugates Show Mutant EGFR Inhibition and DNA-Damage-Associated Activity

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Supplementary comet-assay figure

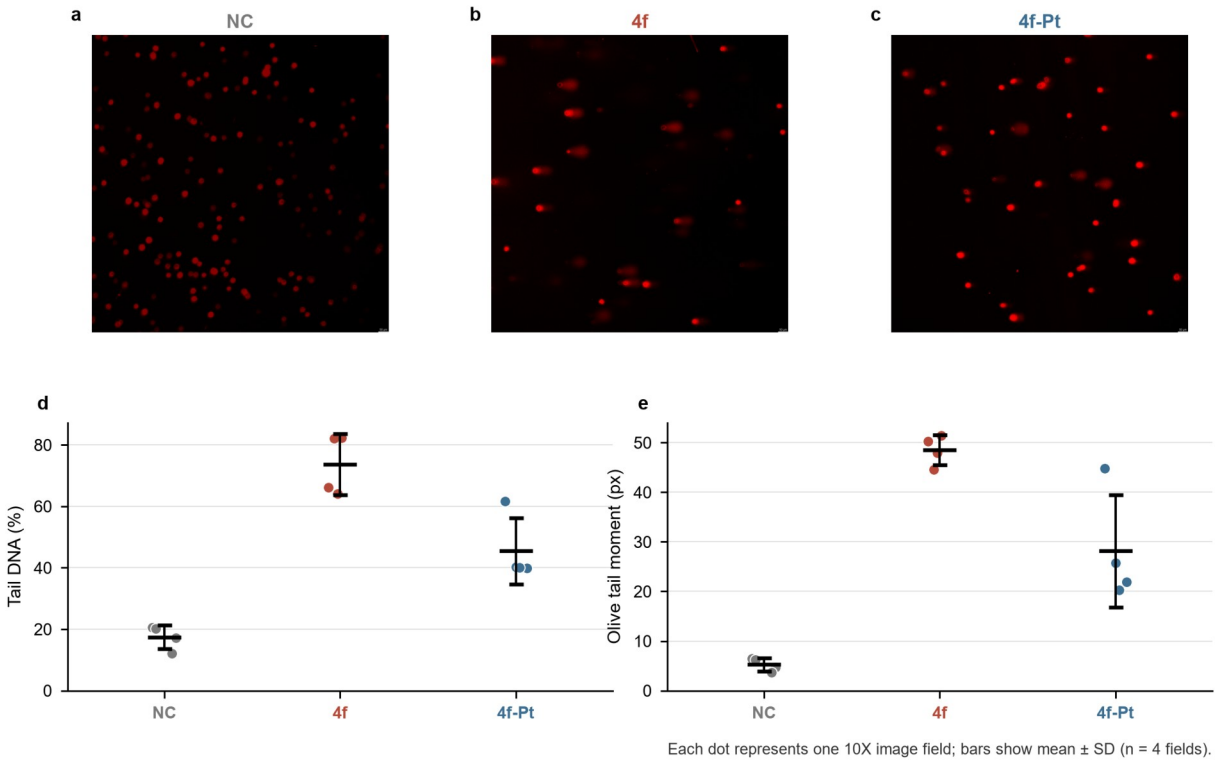


Figure S1. Representative comet images and quantitative analysis in NCI-H1975 cells. (a–c) Representative 10× fields from vehicle-treated cells and cells treated with 4f (40 μM) or 4f-Pt (154 μM). Scale bars, 50 μm. Fields were selected by proximity of their Tail DNA values to the corresponding group means. (d,e) Tail DNA and Olive tail moment measured with OpenComet v1.3.1 in ImageJ. Only objects classified as normal comets were included. Each point is the mean of one 10× field; bars show mean ± SD (n = 4 fields per condition).

Supplementary EGFR kinase inhibition curves

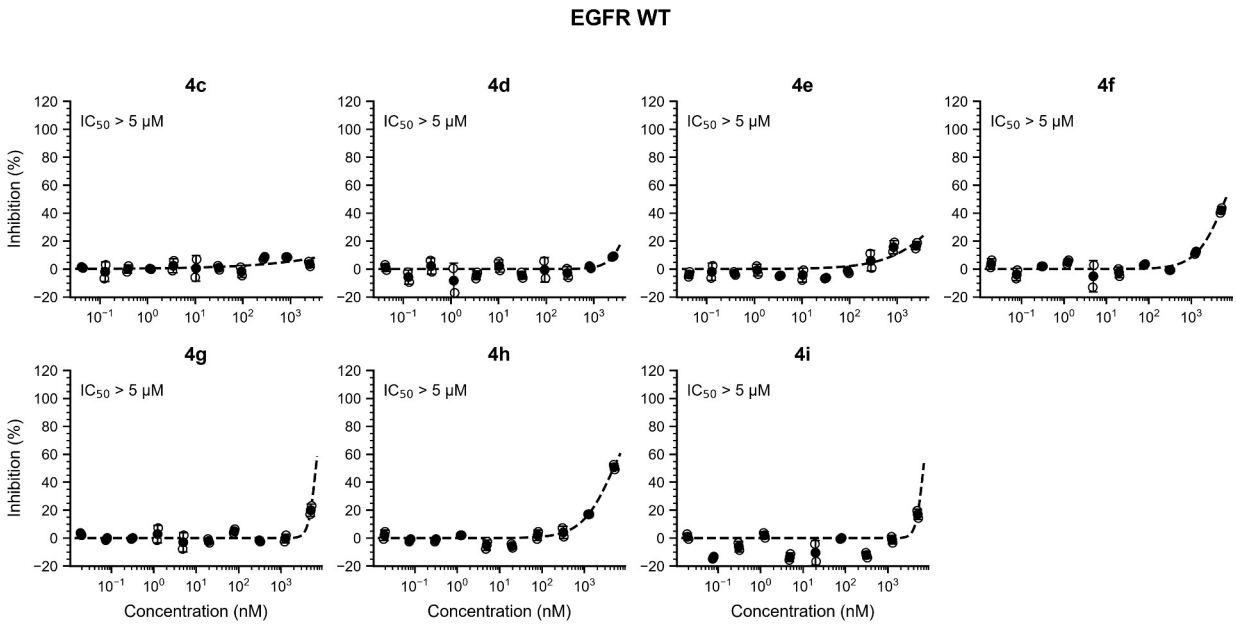


Figure S2. Concentration–response curves for inhibition of wild-type EGFR by the indicated compounds. Open circles show the two independent experiments, filled circles show the mean ± SD, and lines show variable-slope logistic fits (n = 2 independent experiments). IC_{50} values follow those reported in the main-text tables. Dashed curves denote IC_{50} values beyond the tested concentration range; an asterisk denotes an extrapolated value.

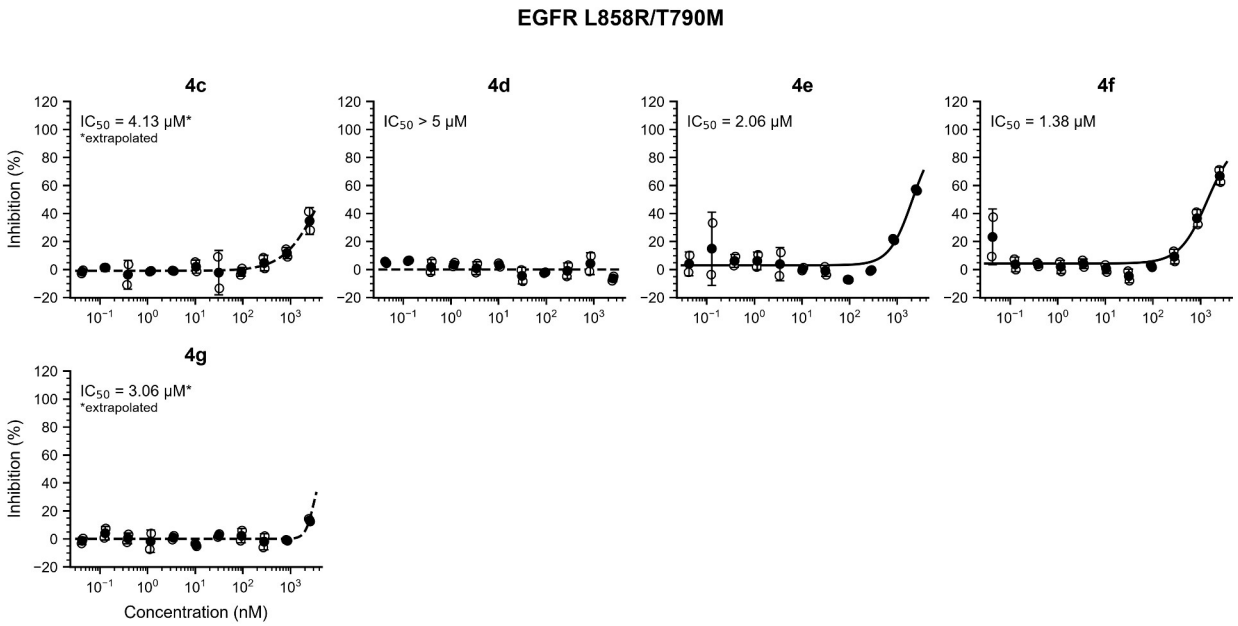


Figure S3. Concentration–response curves for inhibition of EGFR L858R/T790M by the indicated compounds. Open circles show the two independent experiments, filled circles show the mean ± SD, and lines show variable-slope logistic fits (n = 2 independent experiments). IC_{50} values follow those reported in the main-text tables. Dashed curves denote IC_{50} values beyond the tested concentration range; an asterisk denotes an extrapolated value.

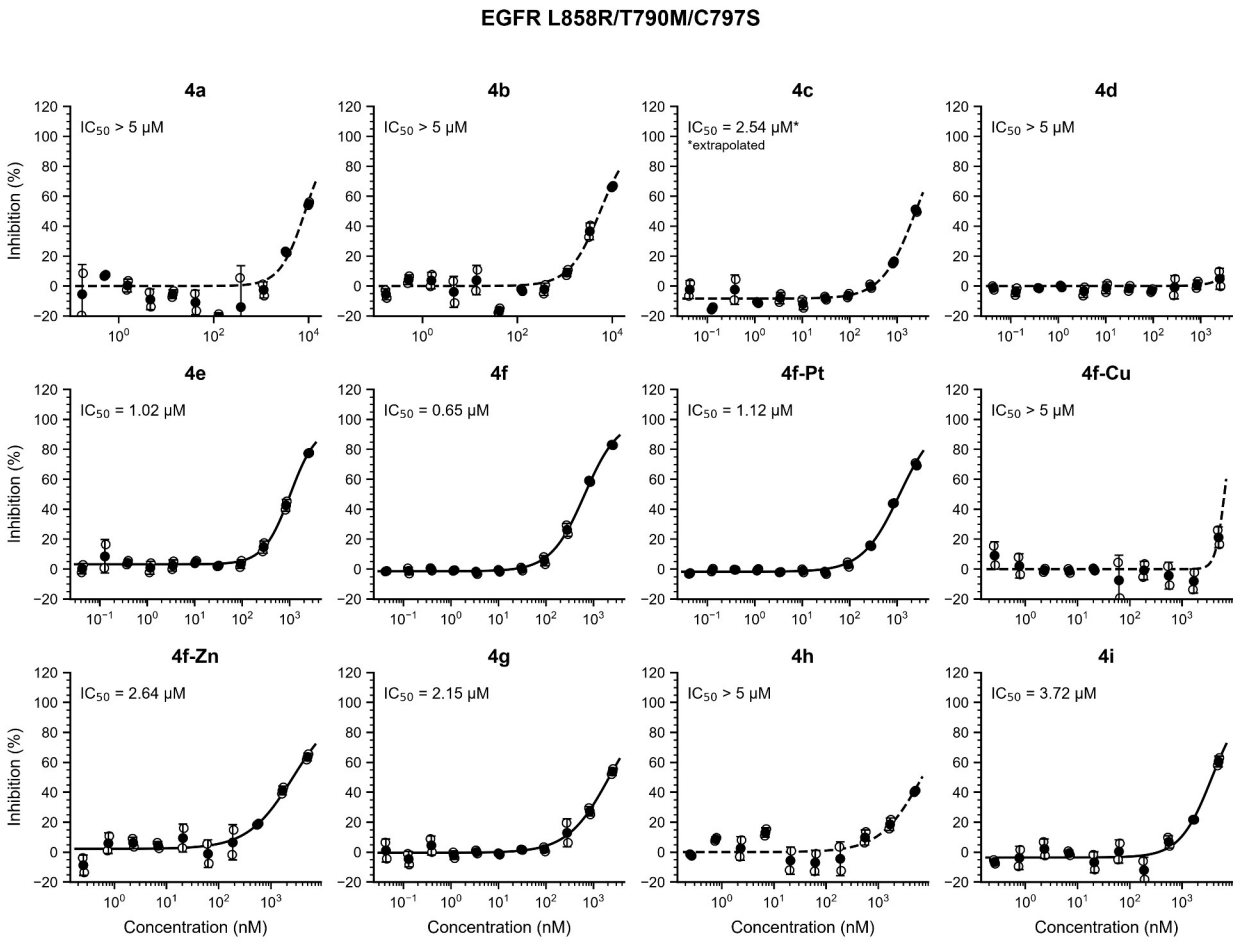


Figure S4. Concentration–response curves for inhibition of EGFR L858R/T790M/C797S by the indicated compounds. Open circles show the two independent experiments, filled circles show the mean ± SD, and lines show variable-slope logistic fits (n = 2 independent experiments). IC_{50} values follow those reported in the main-text tables. Dashed curves denote IC_{50} values beyond the tested concentration range; an asterisk denotes an extrapolated value.

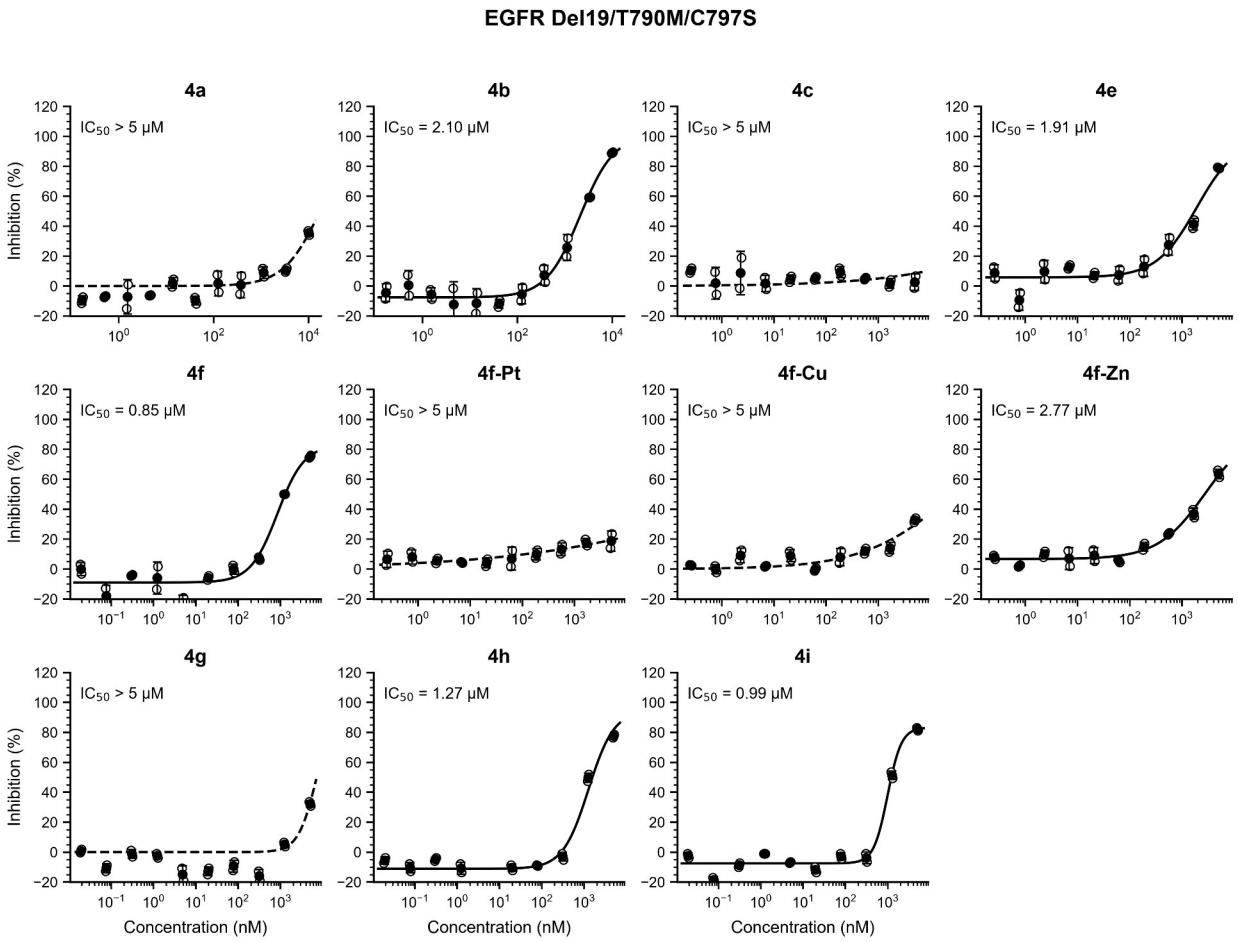
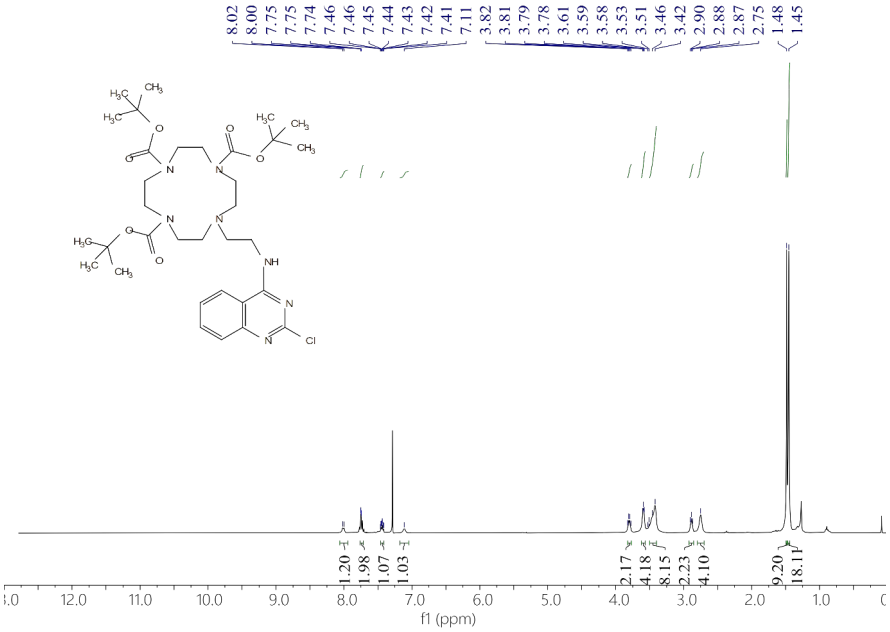


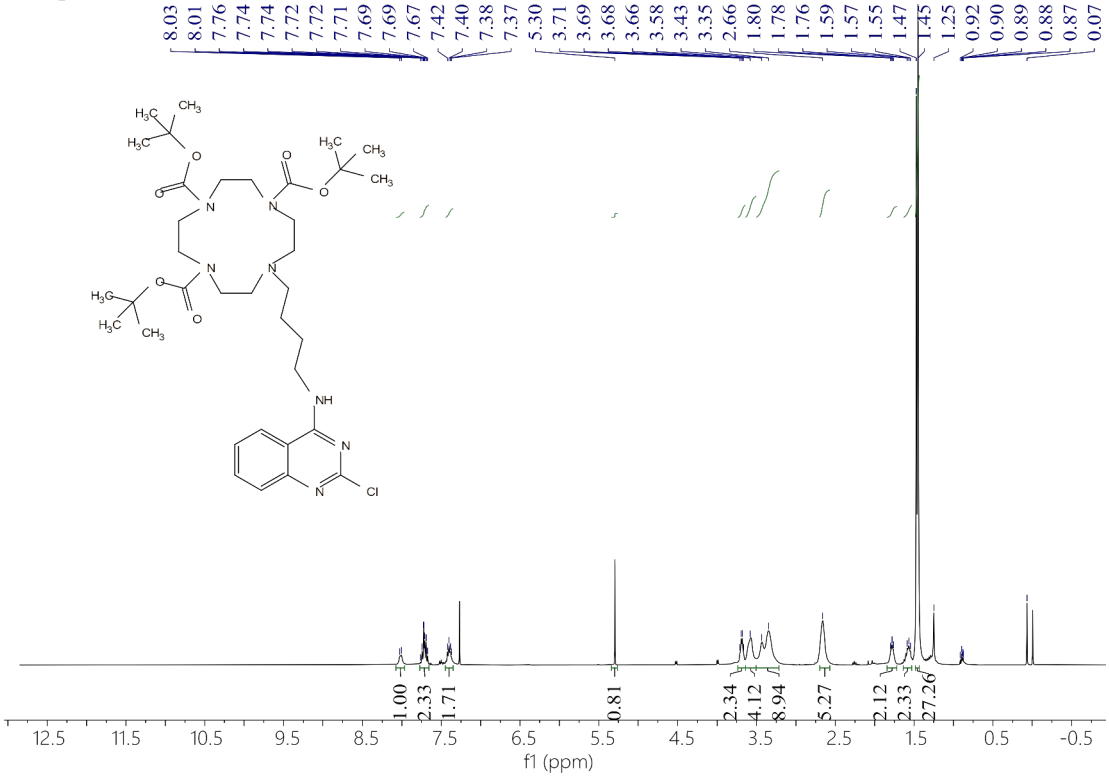
Figure S5. Concentration–response curves for inhibition of EGFR Del19/T790M/C797S by the indicated compounds. Open circles show the two independent experiments, filled circles show the mean ± SD, and lines show variable-slope logistic fits (n = 2 independent experiments). IC_{50} values follow those reported in the main-text tables. Dashed curves denote IC_{50} values beyond the tested concentration range; an asterisk denotes an extrapolated value.

NMR and HRMS spectra of synthesized compounds

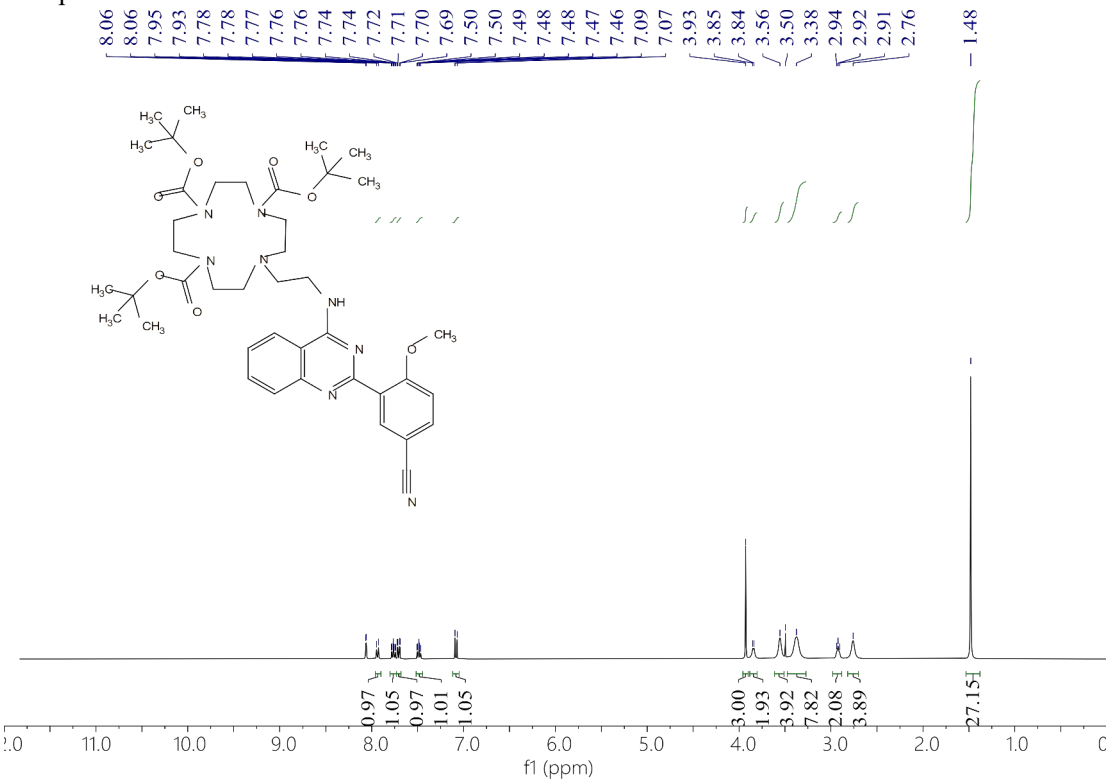
Compound **2a** ^{1}H NMR



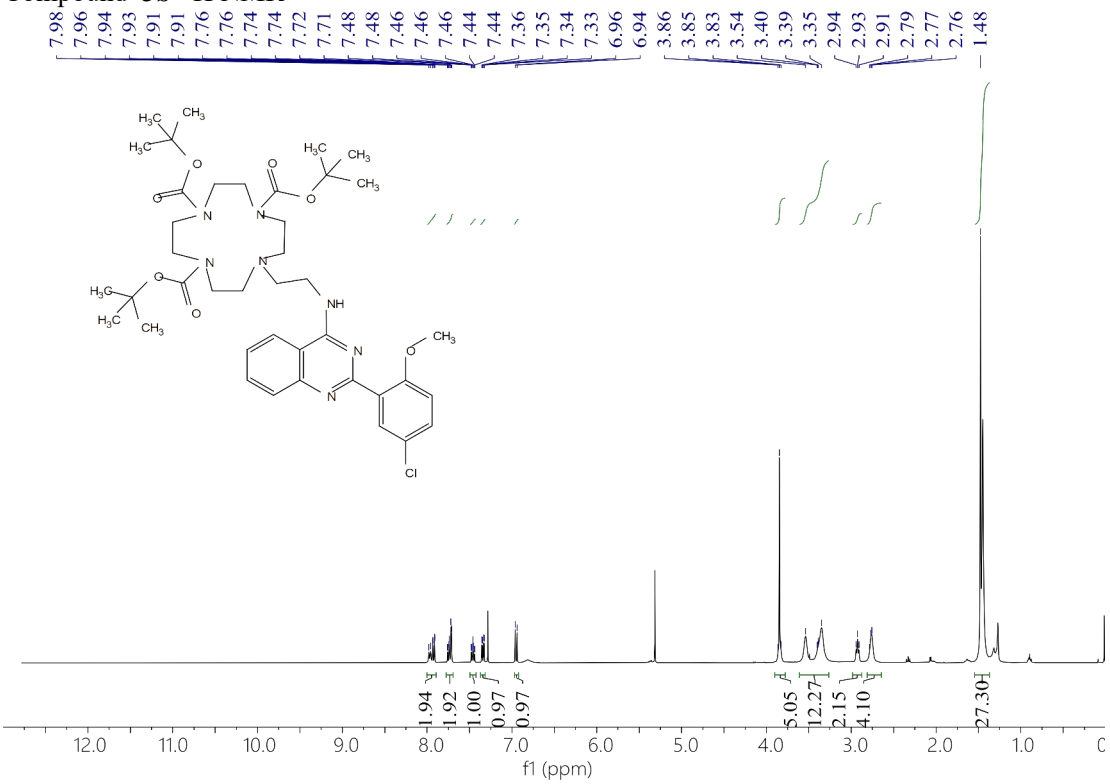
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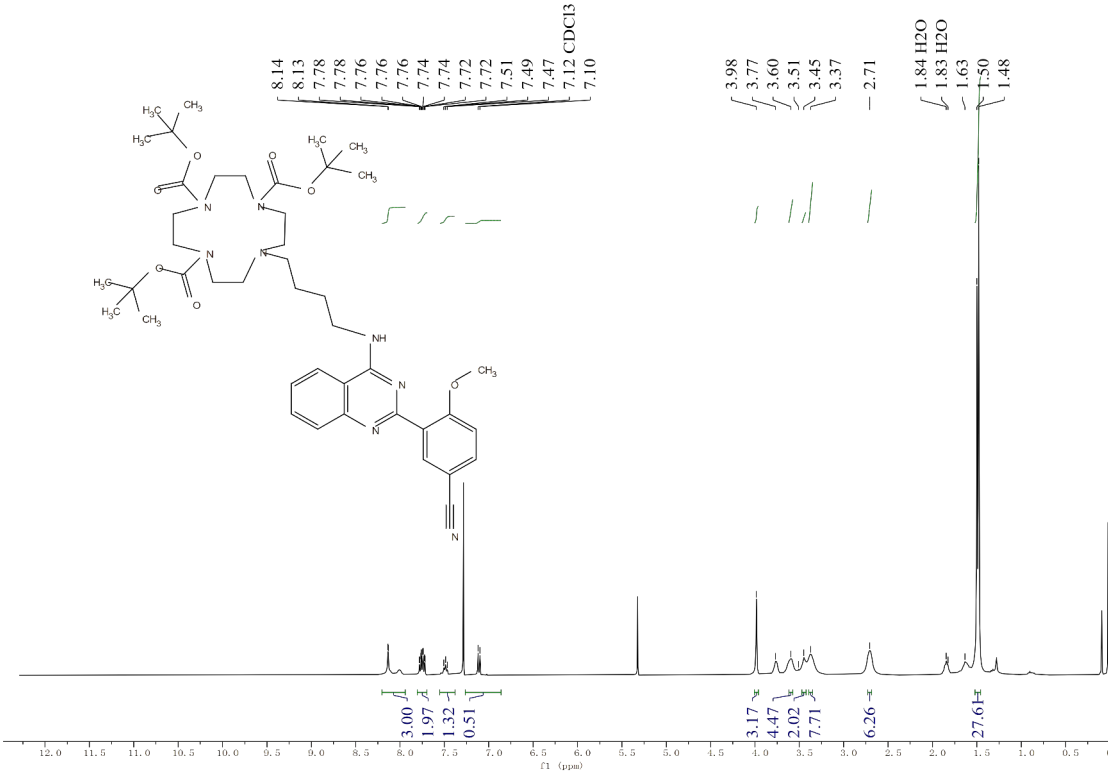
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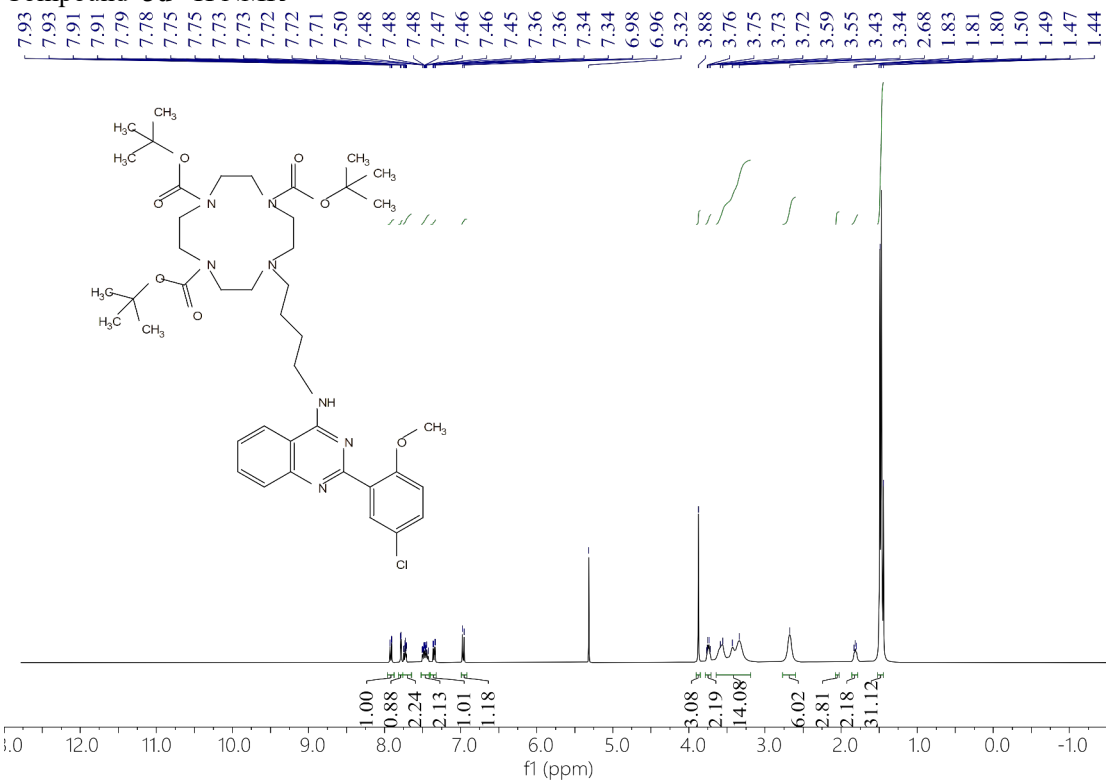
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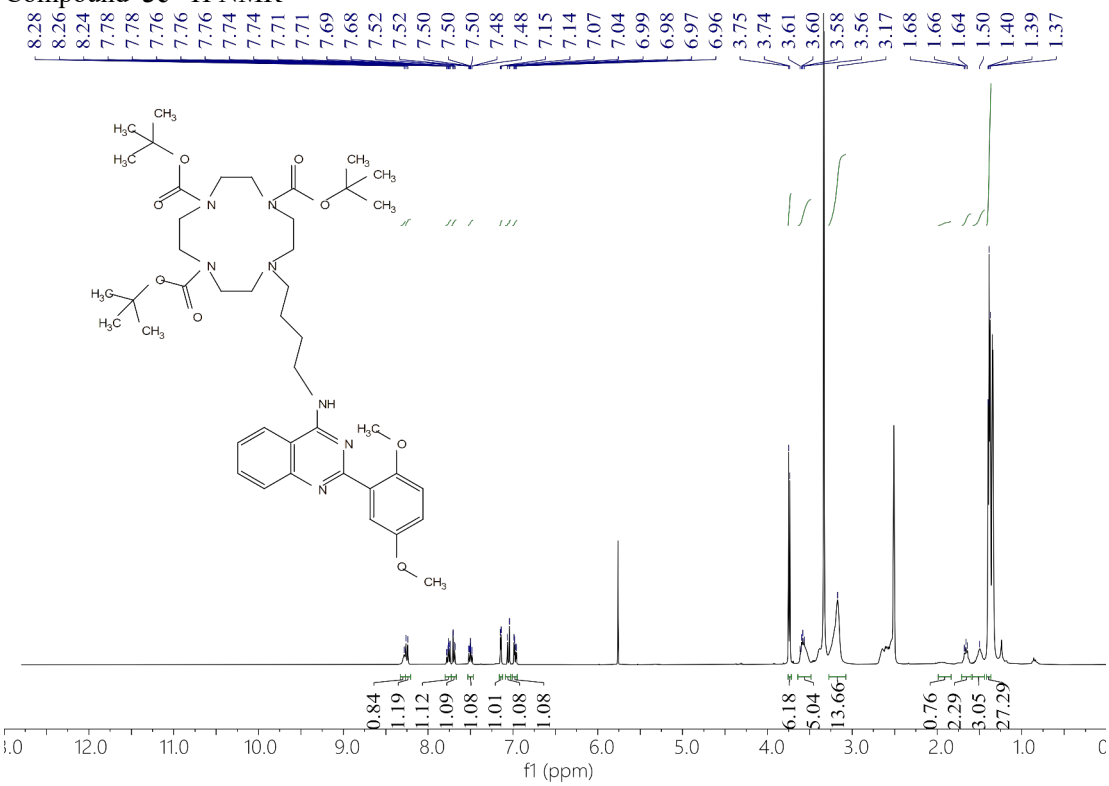
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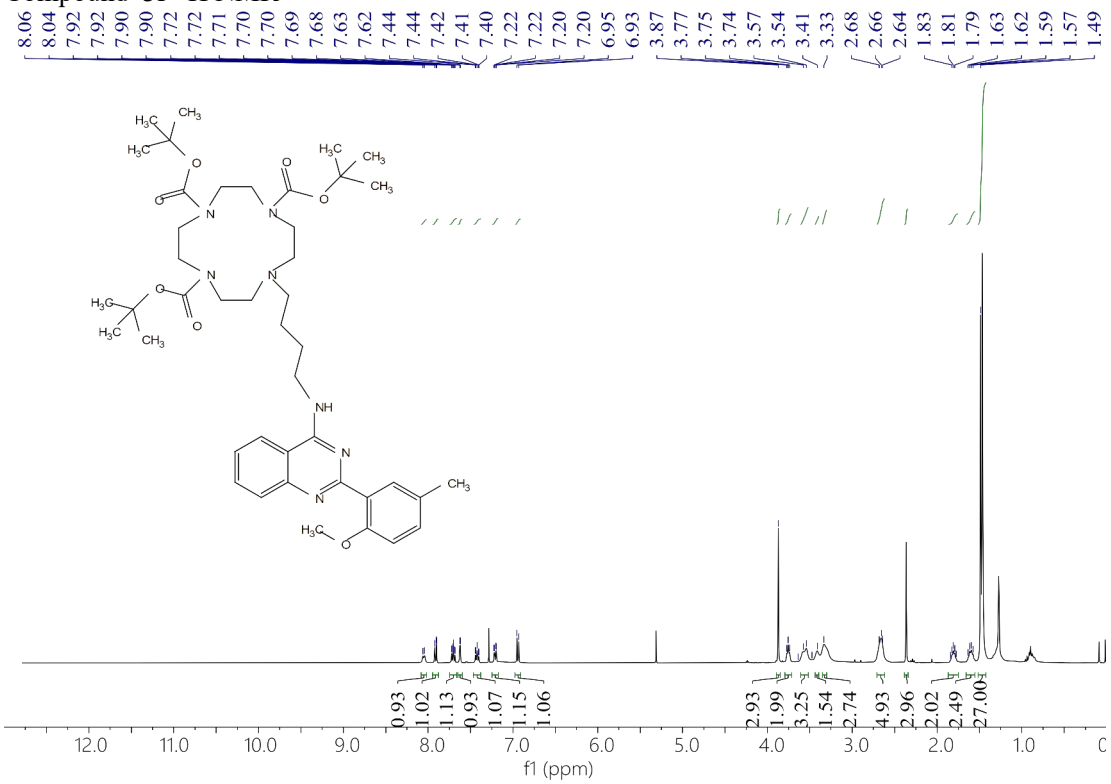
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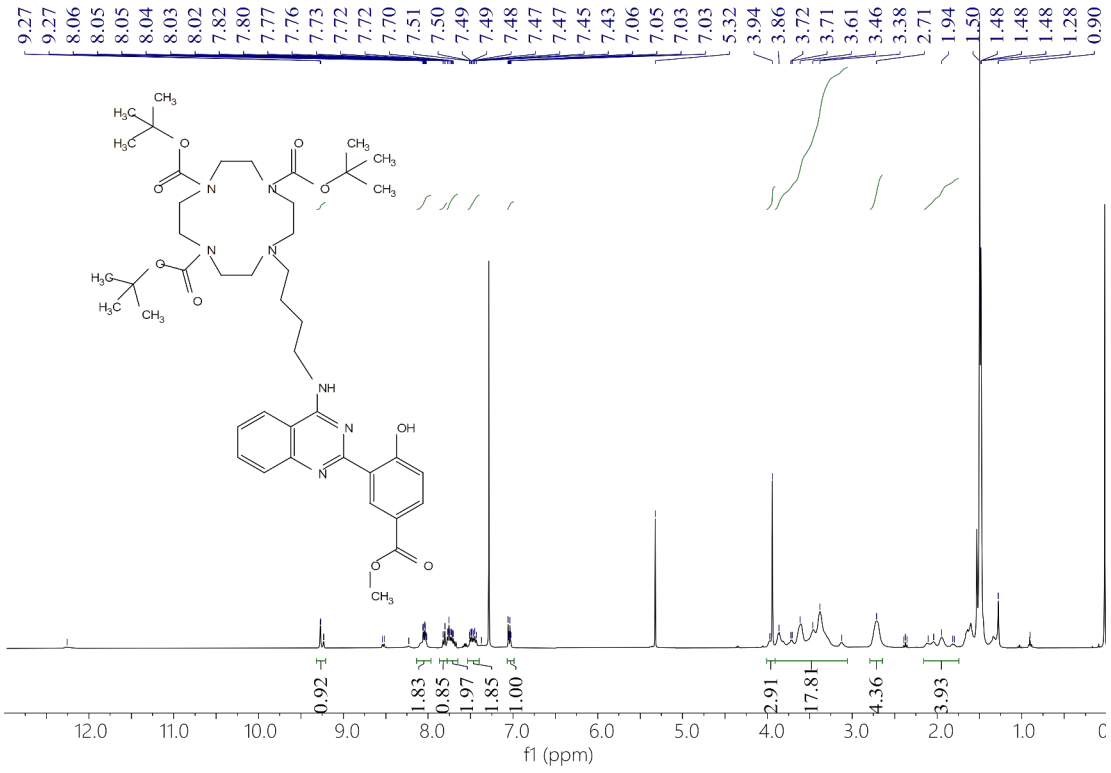
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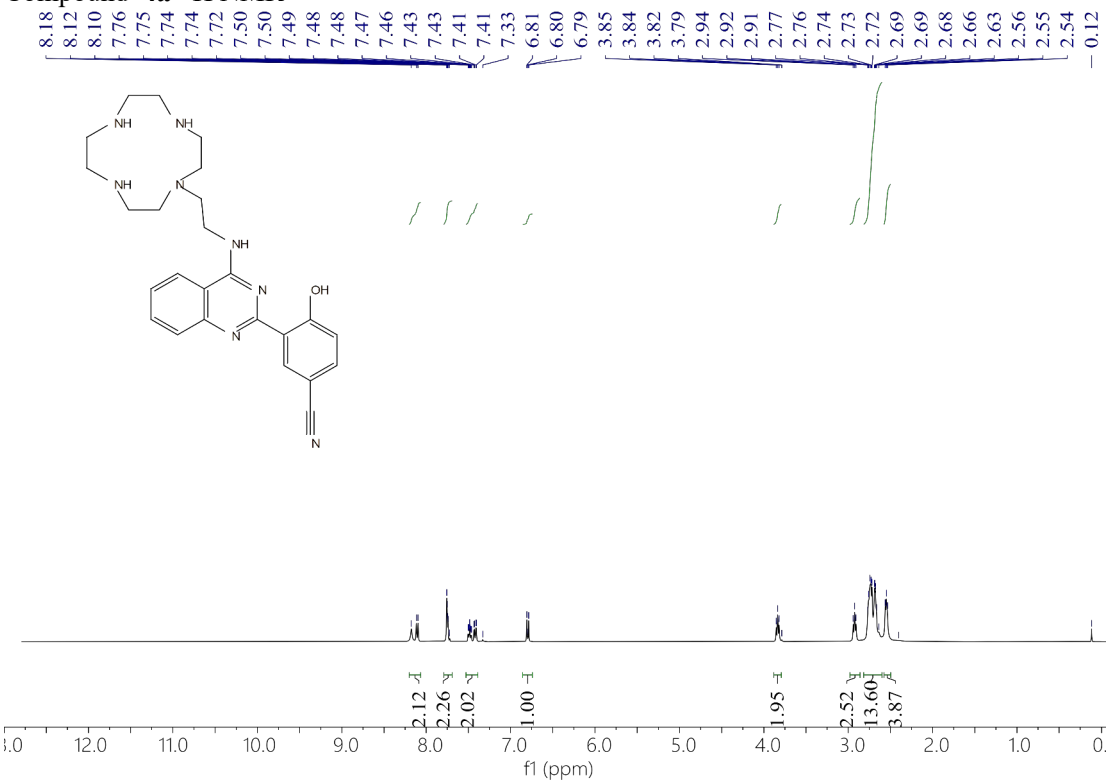
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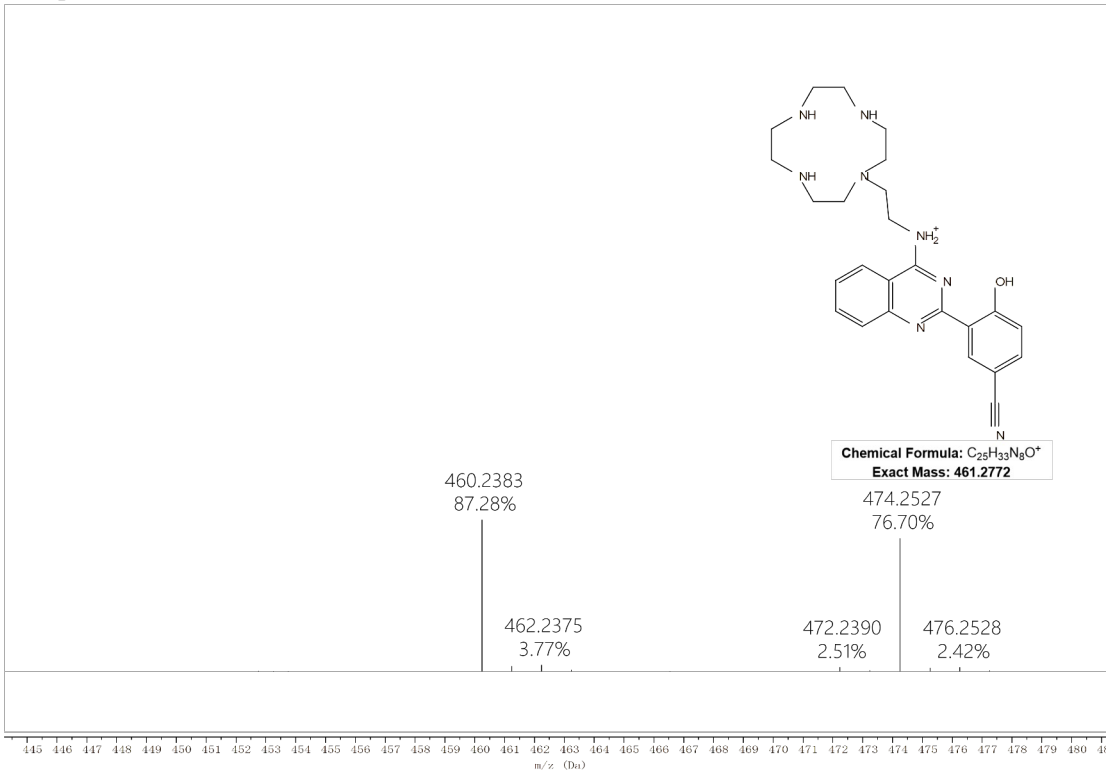
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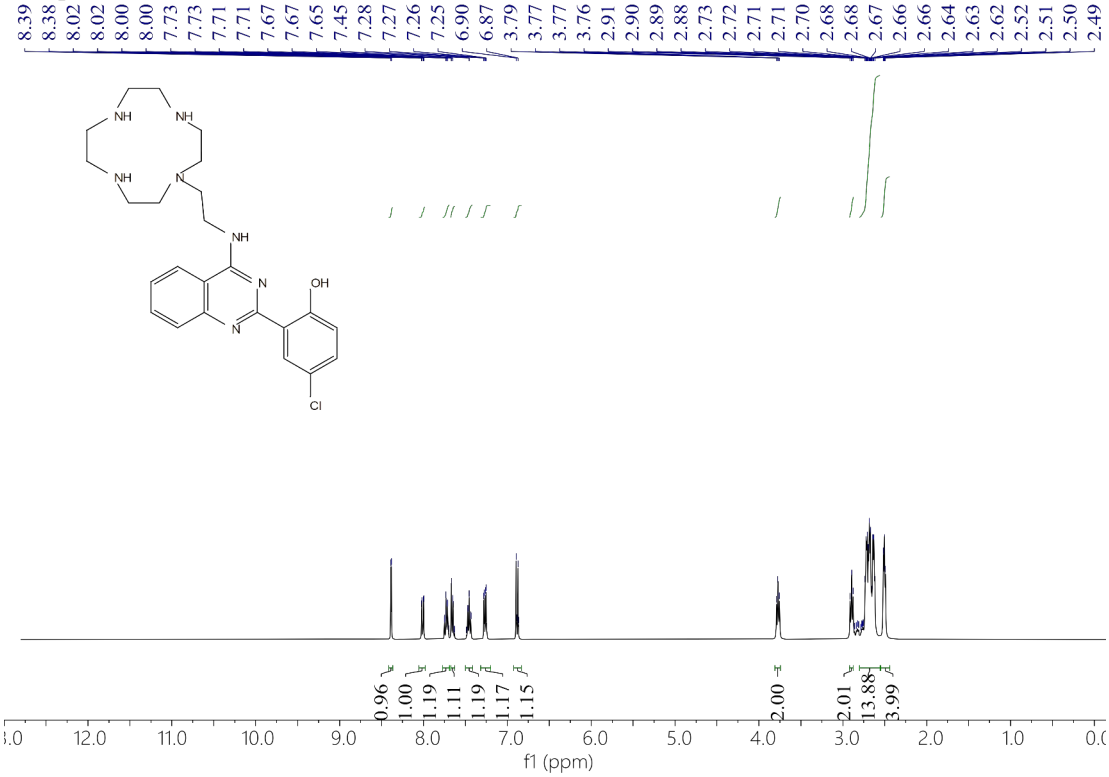
Compound **4a** ^{1}H NMR



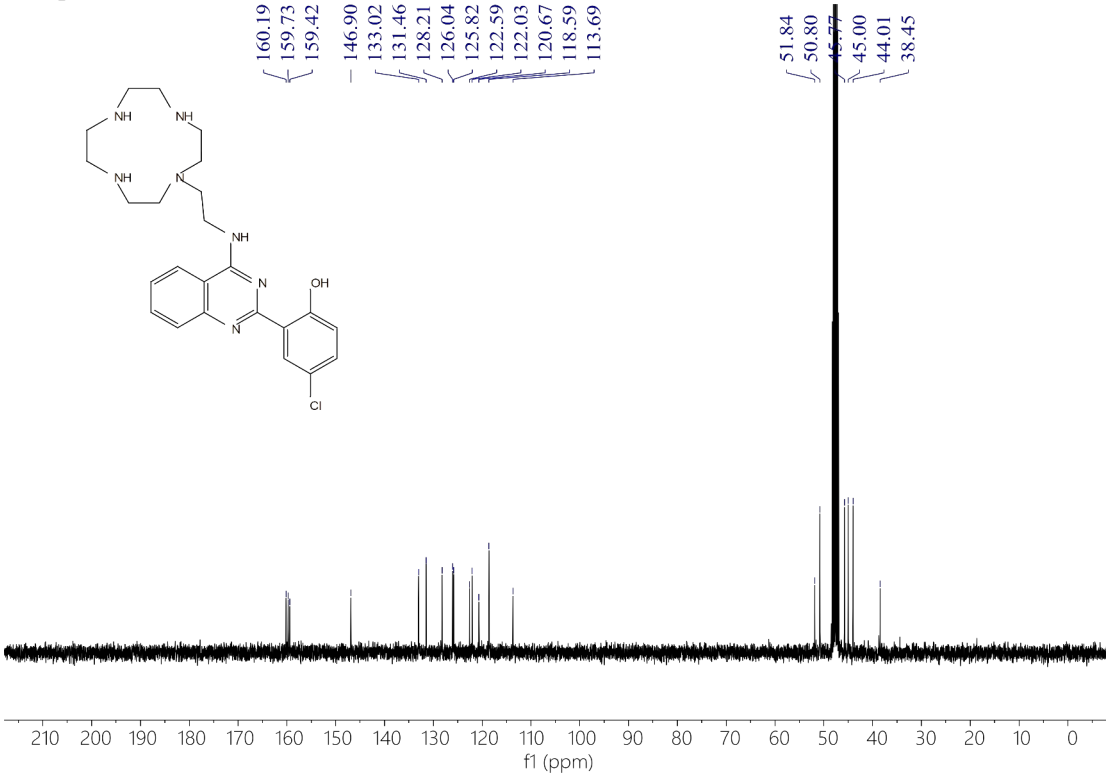
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Compound **4b** ^{1}H NMR



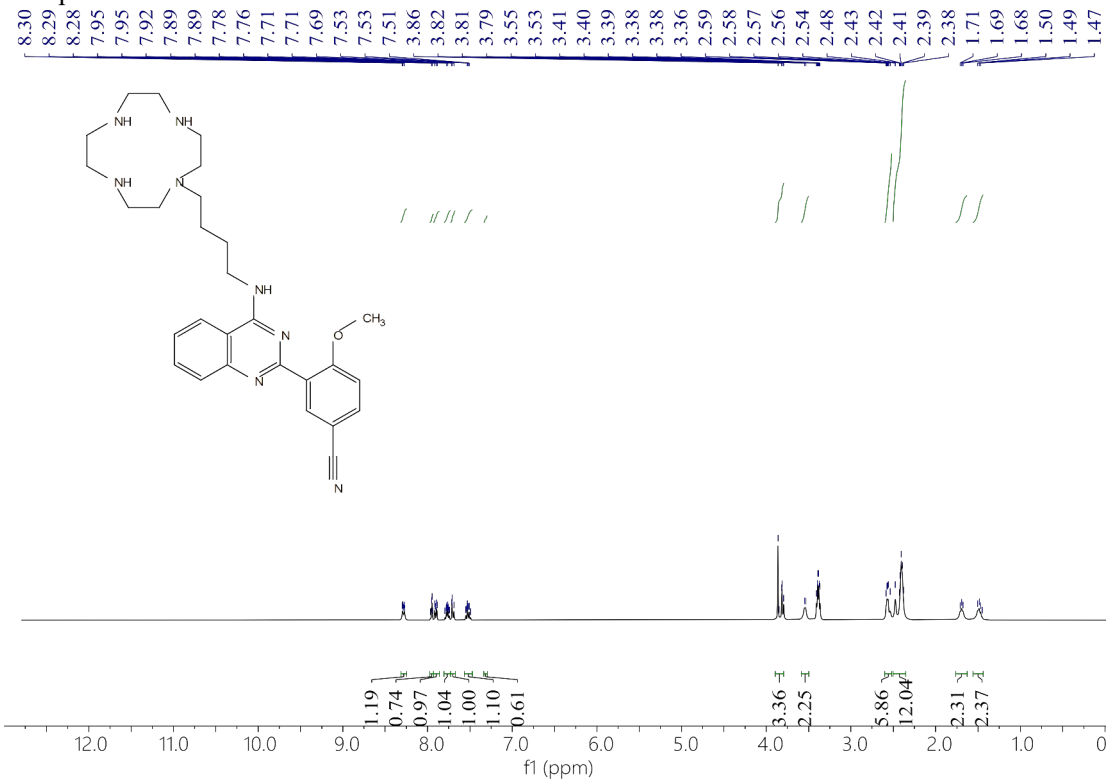
Compound **4b** ^{13}C NMR



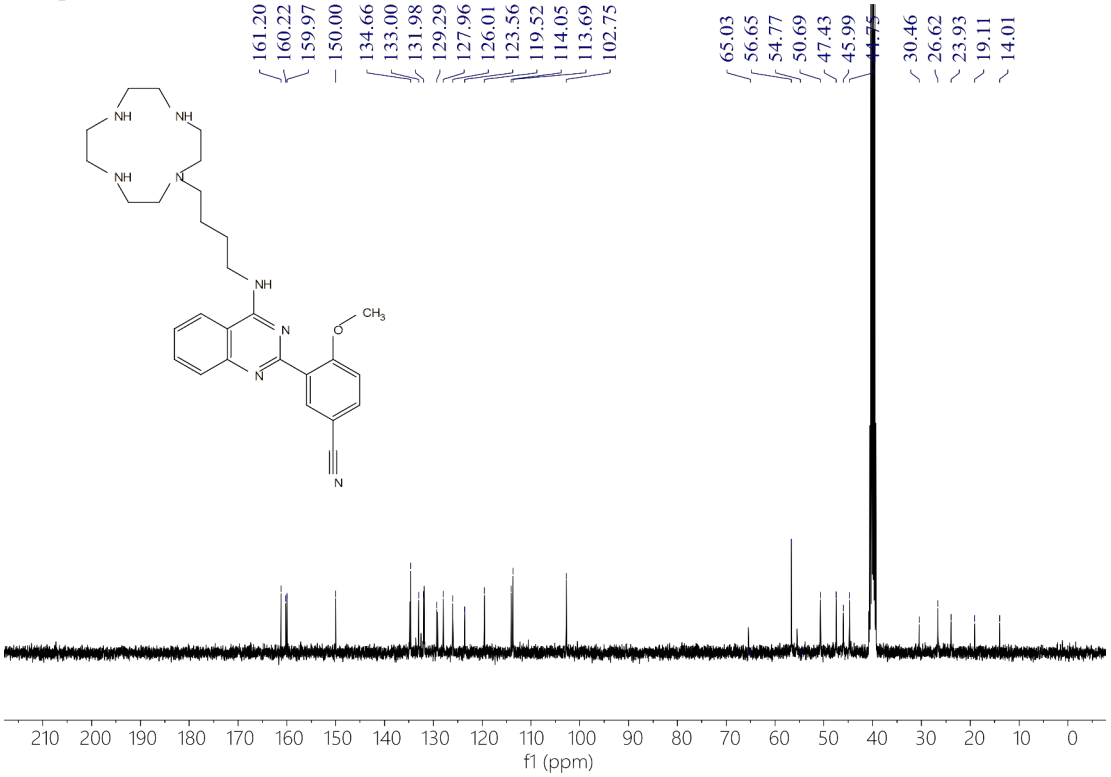
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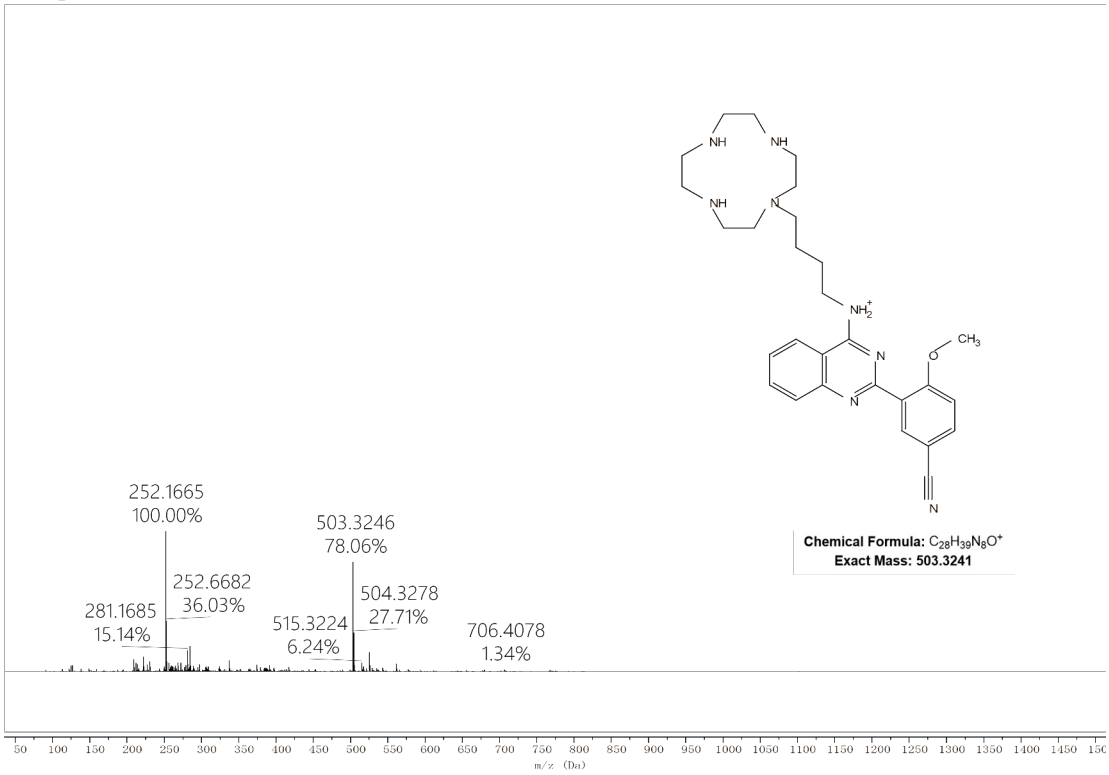
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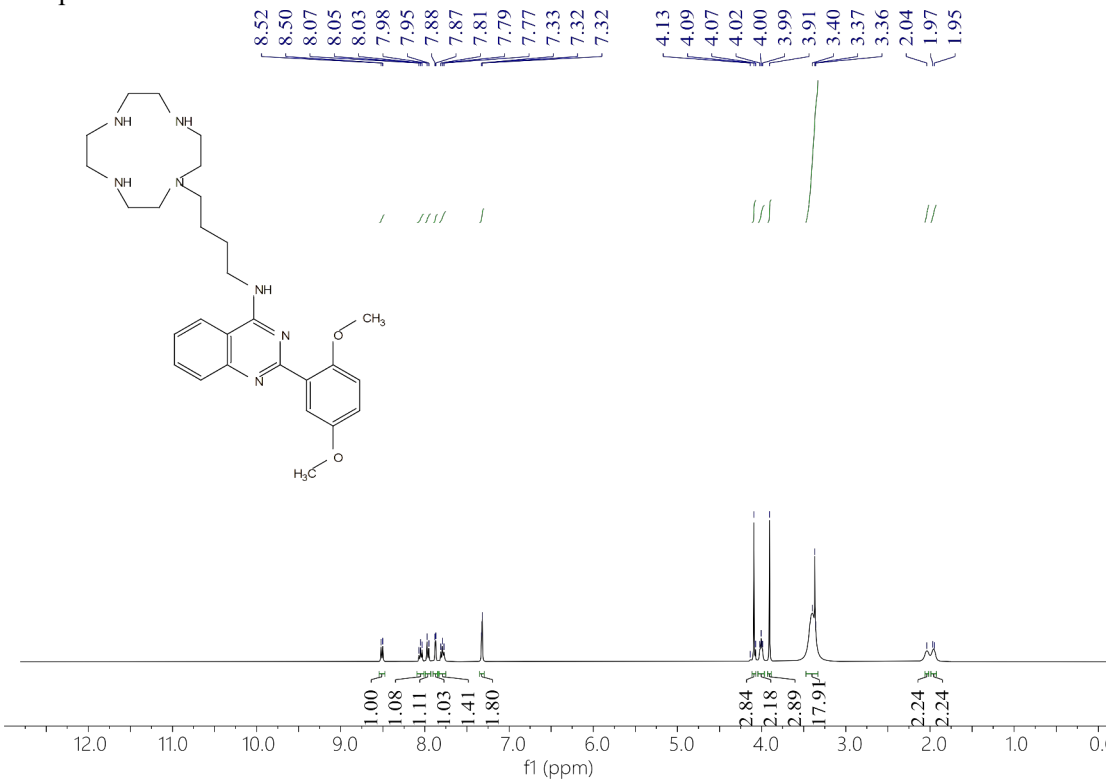
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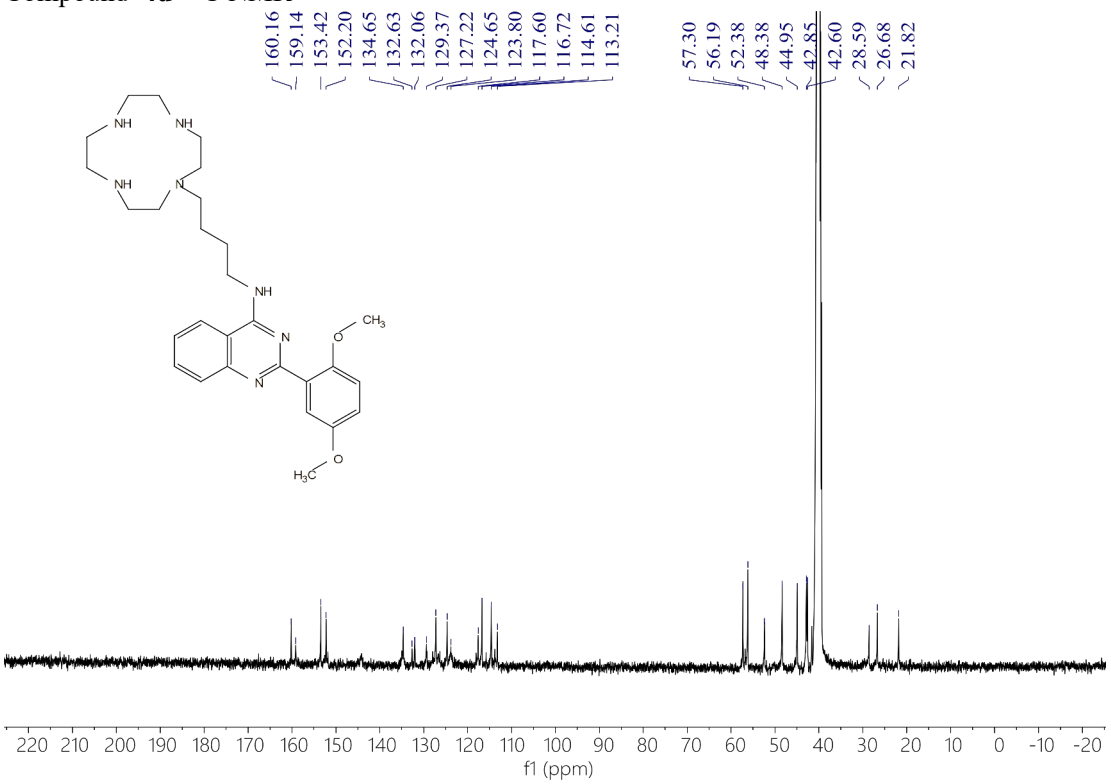
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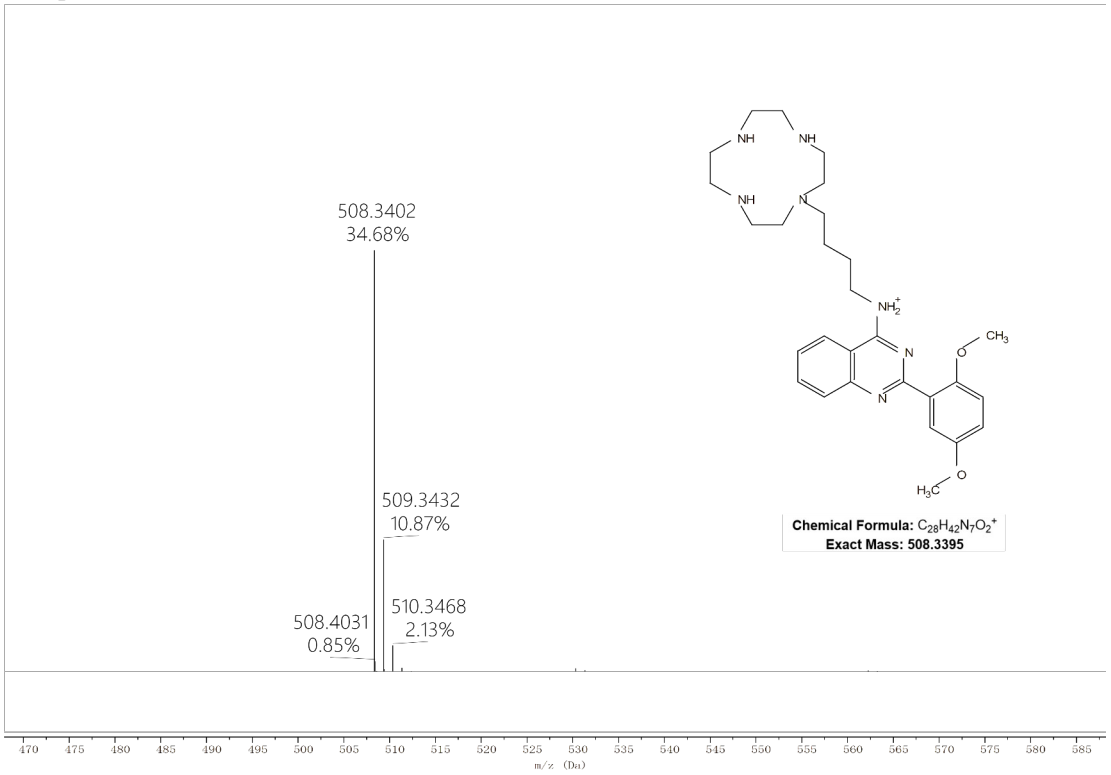
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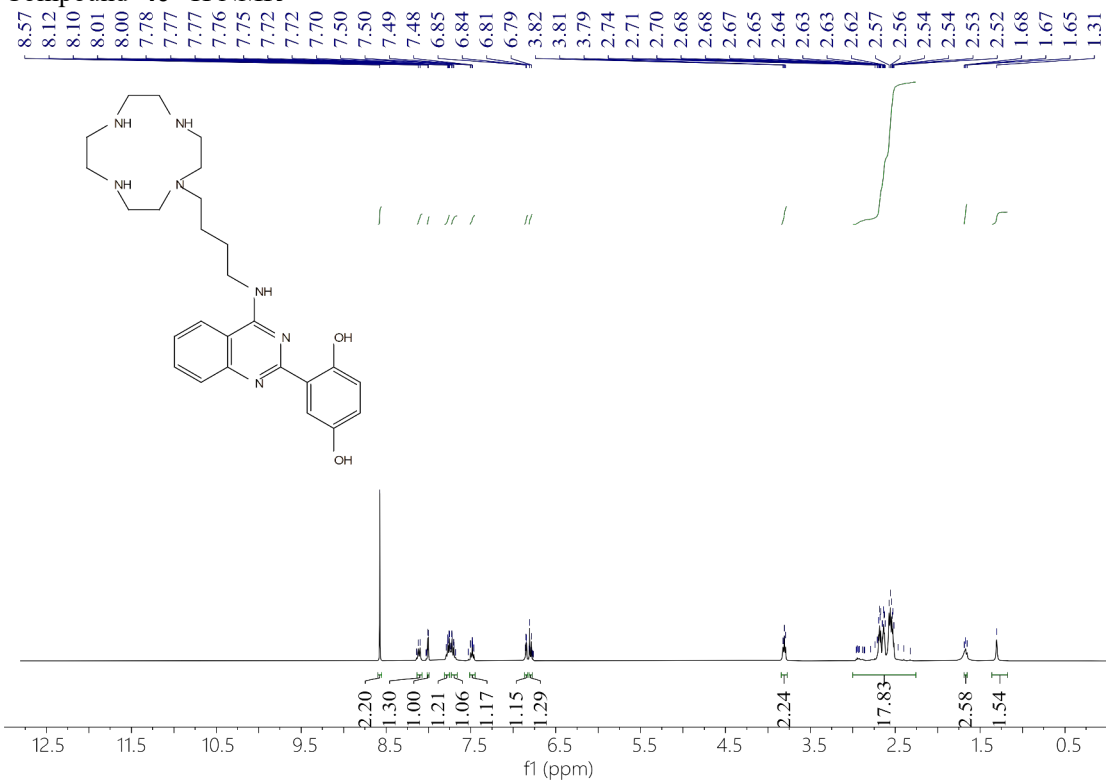
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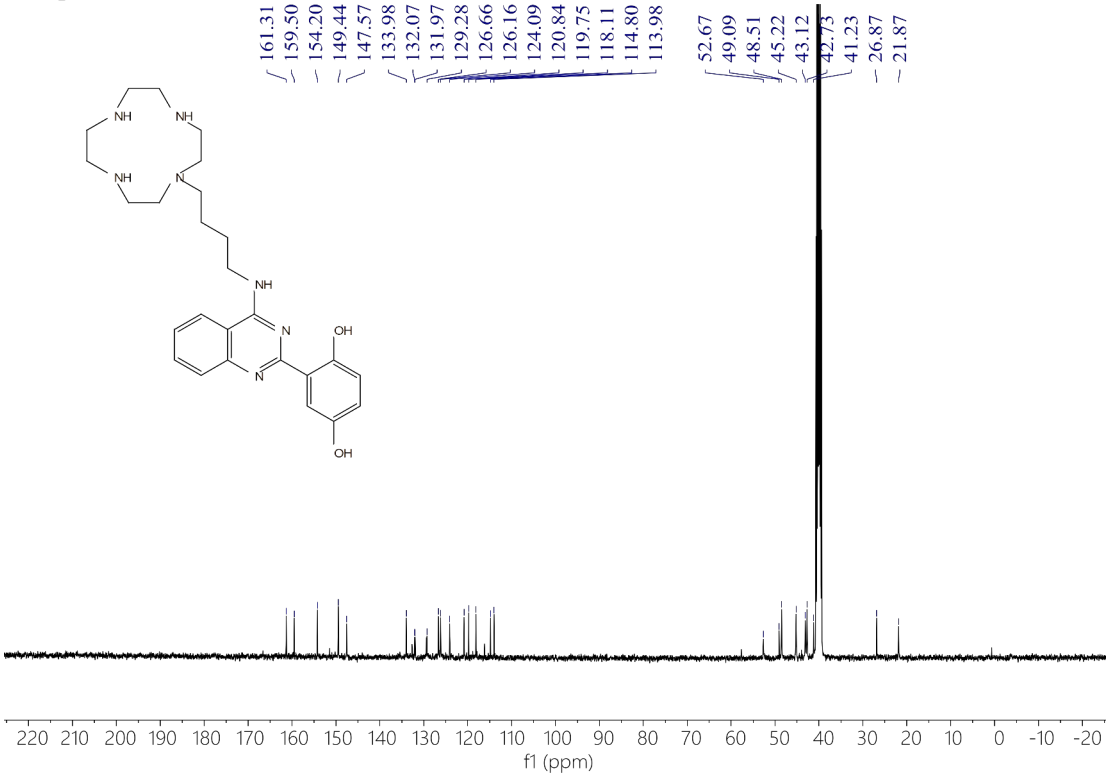
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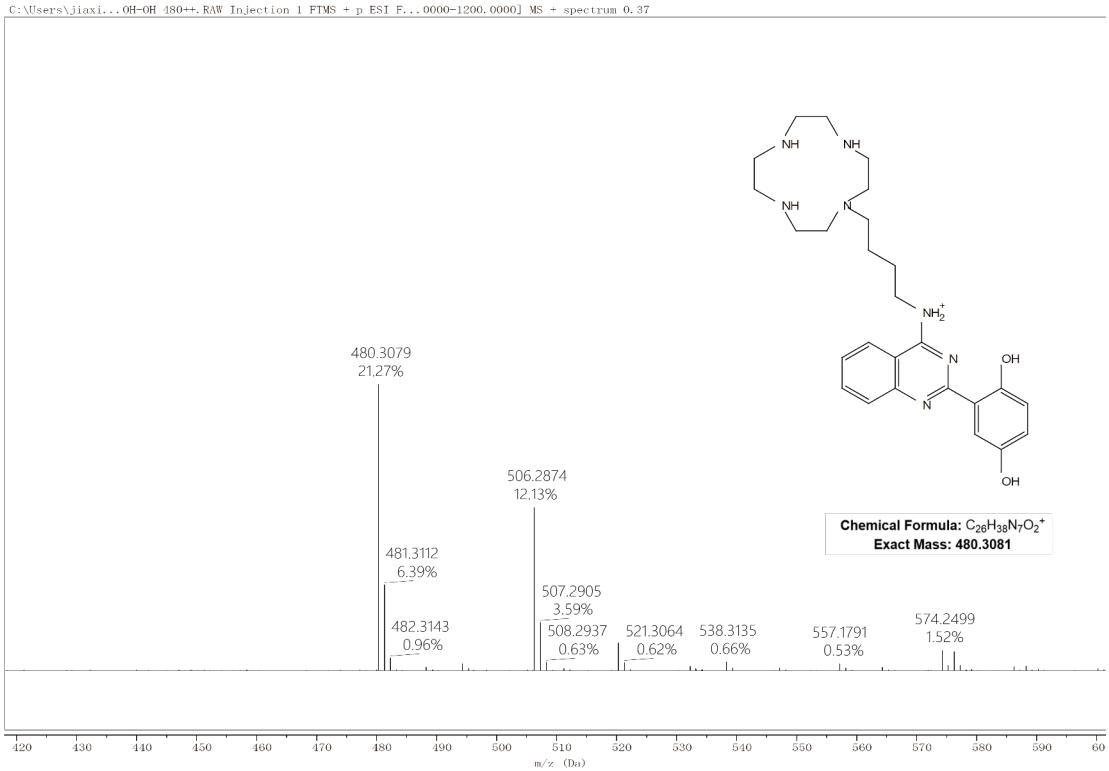
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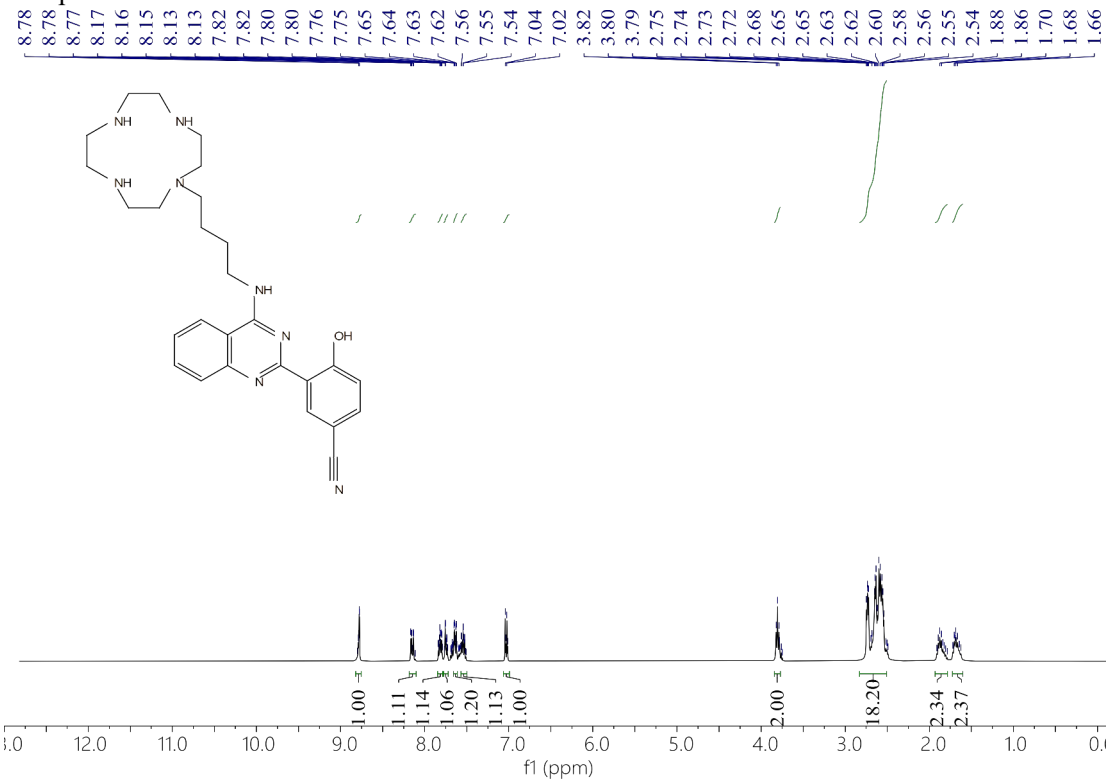
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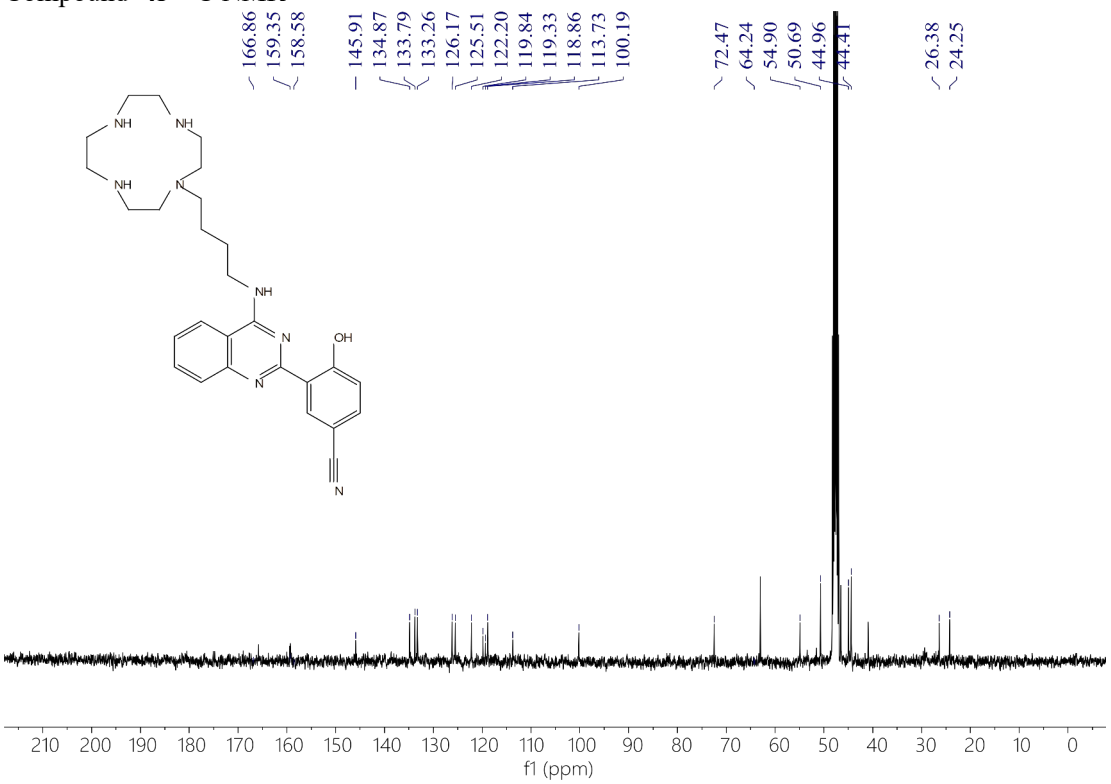
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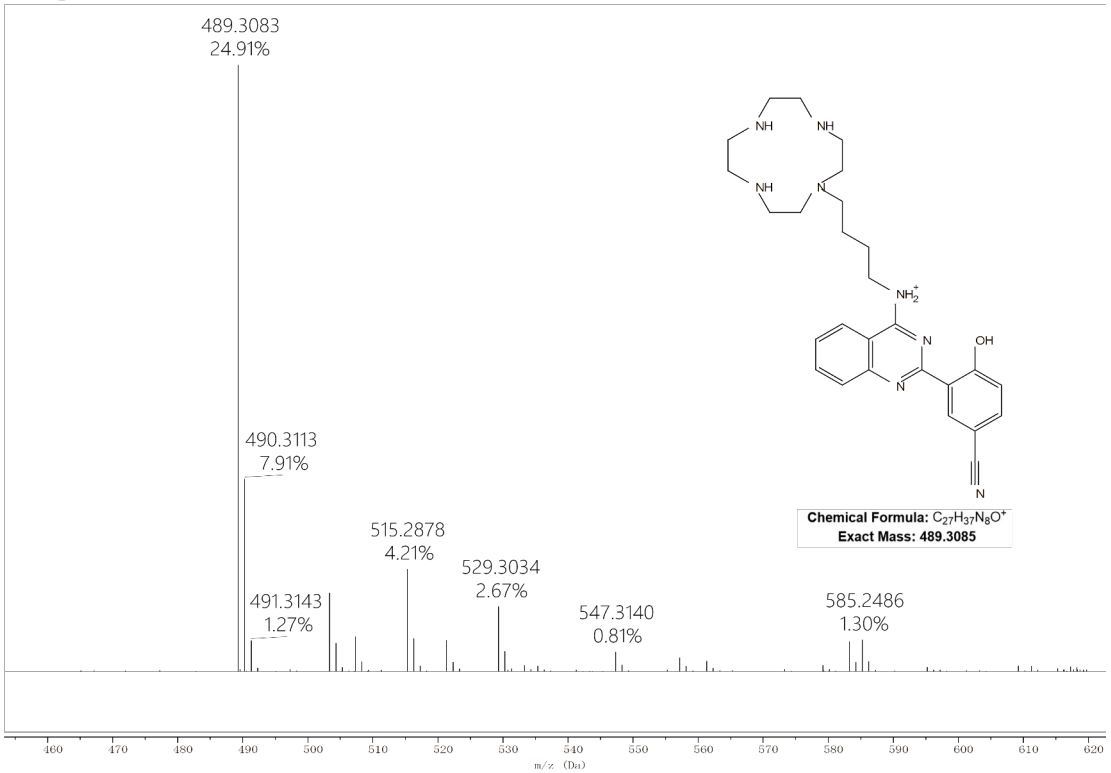
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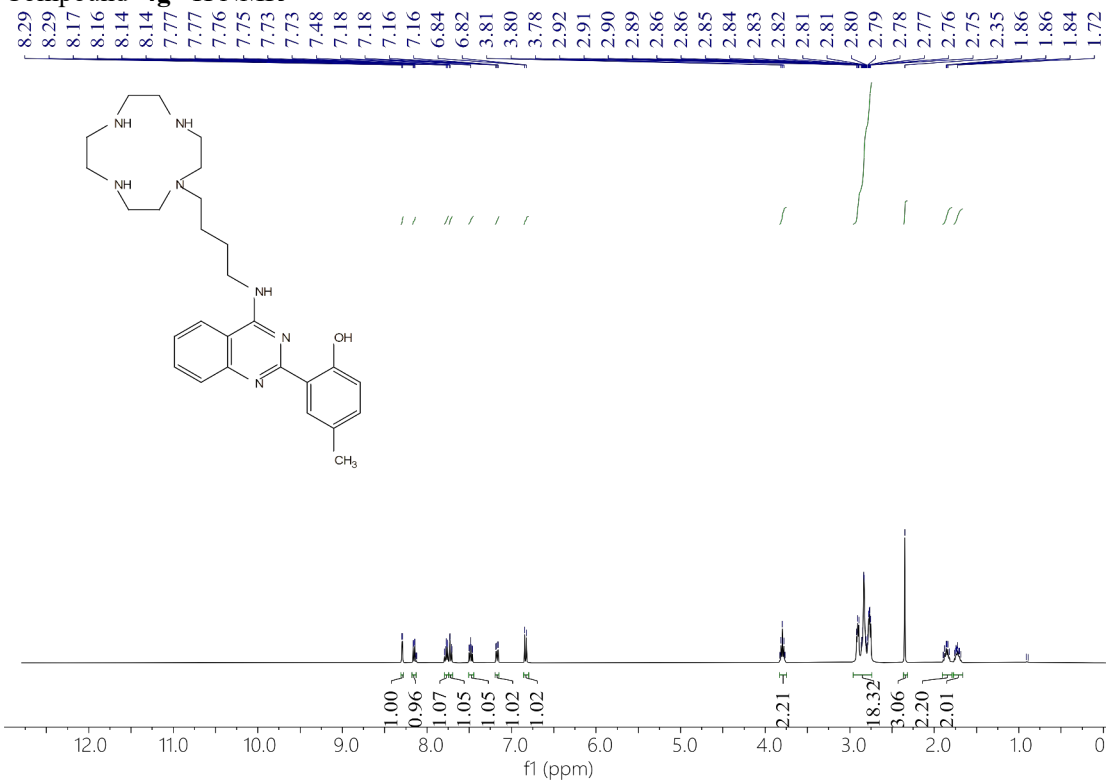
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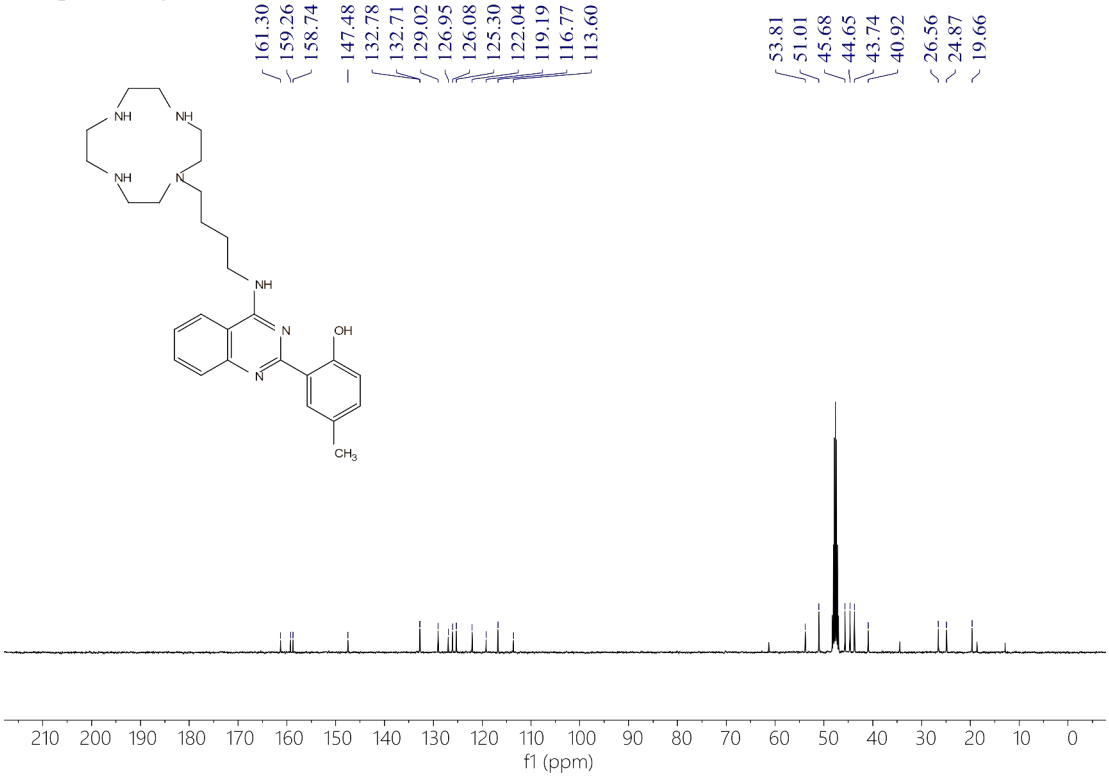
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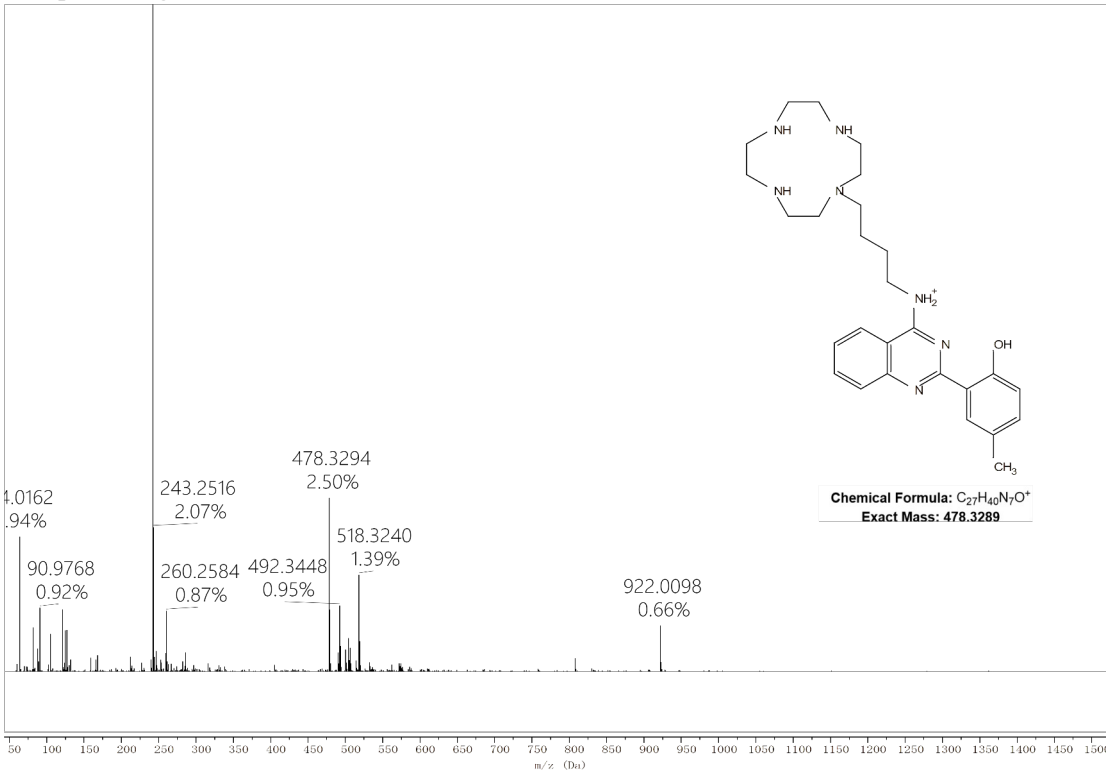
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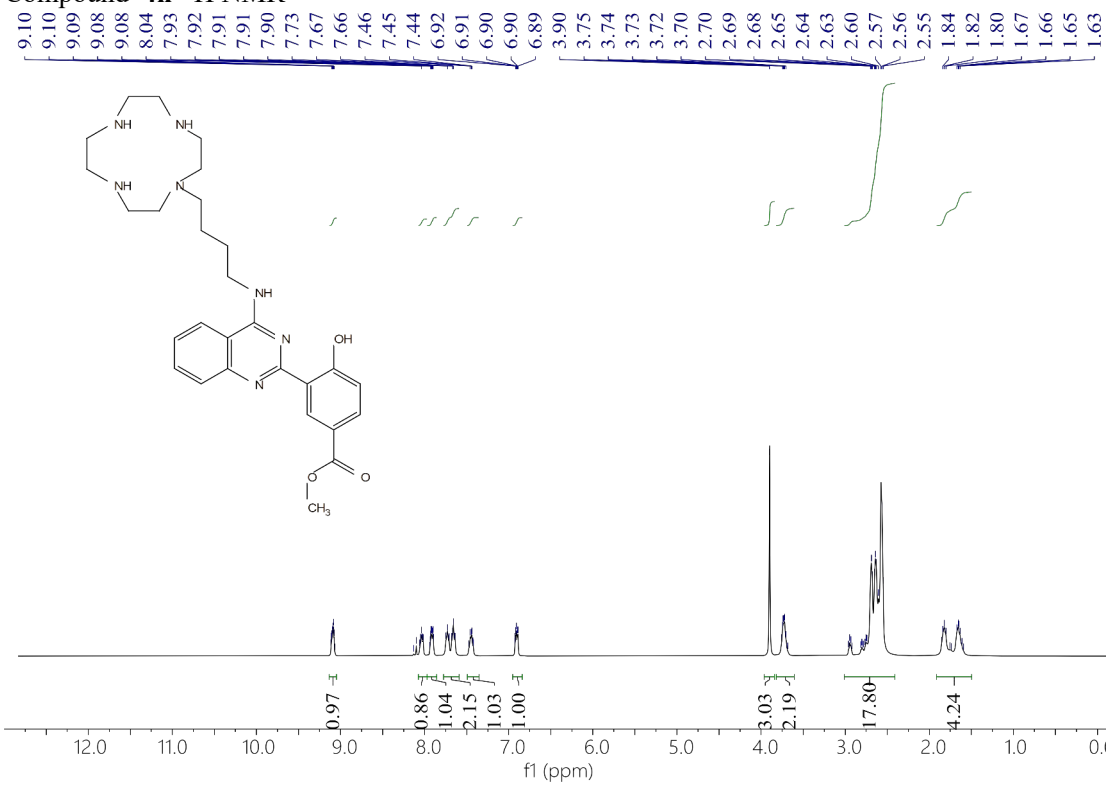
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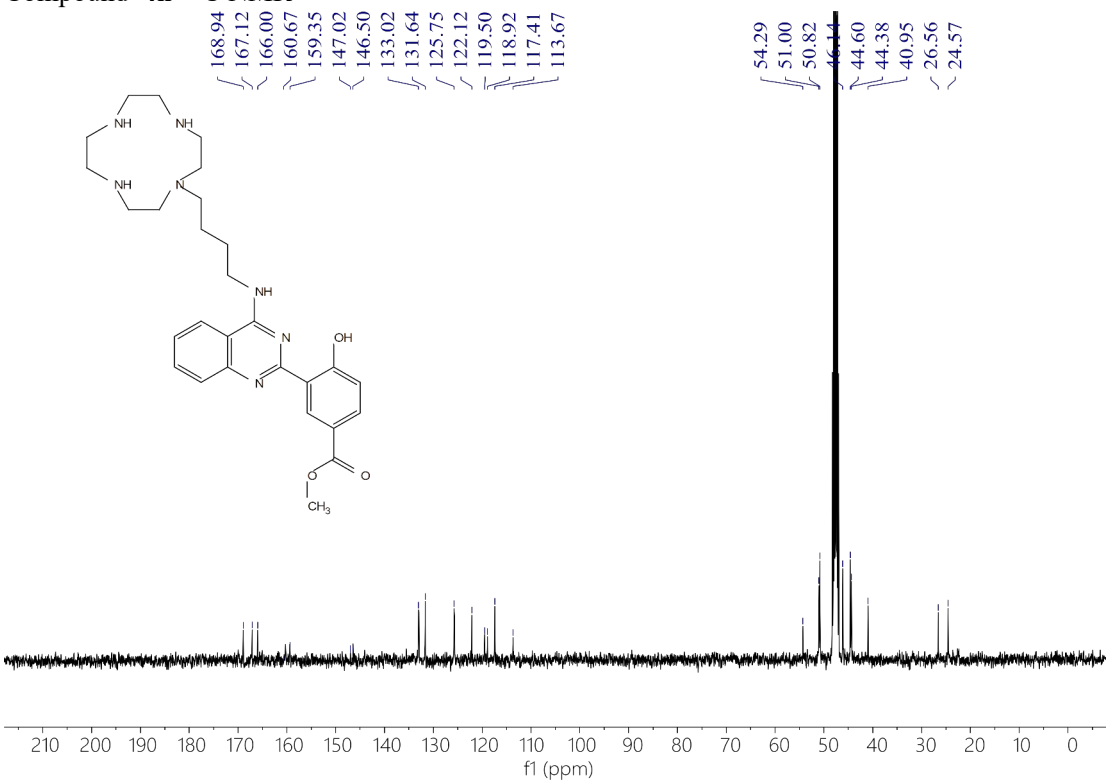
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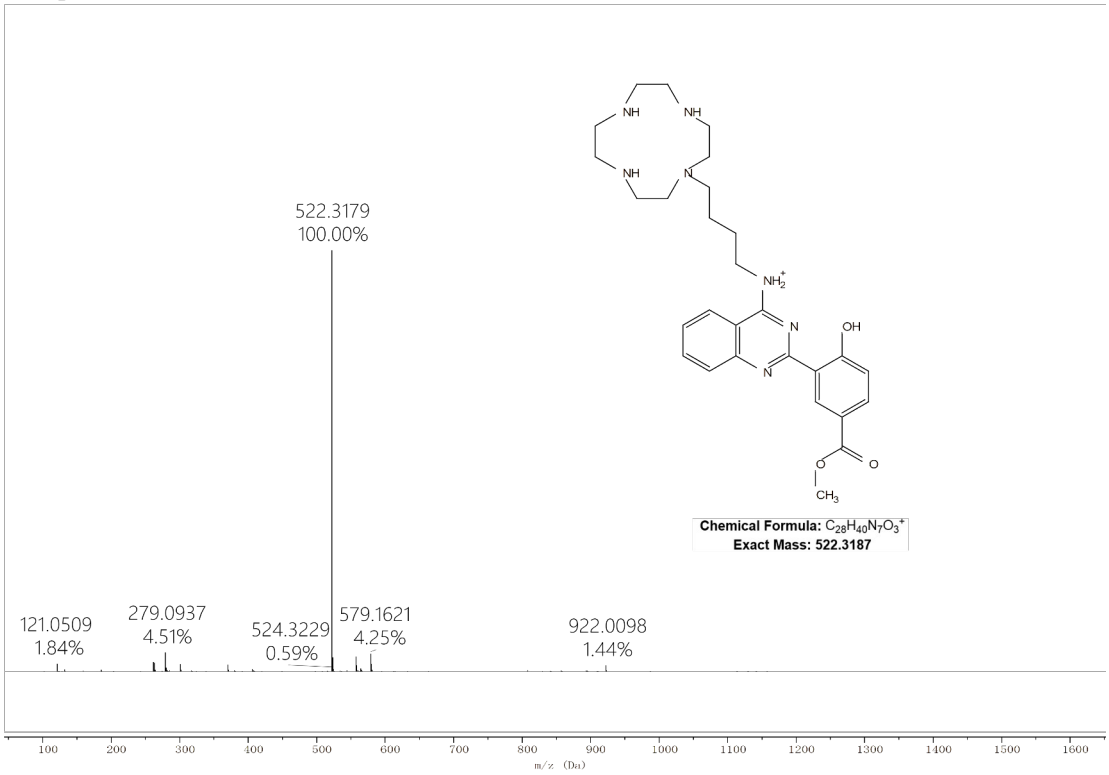
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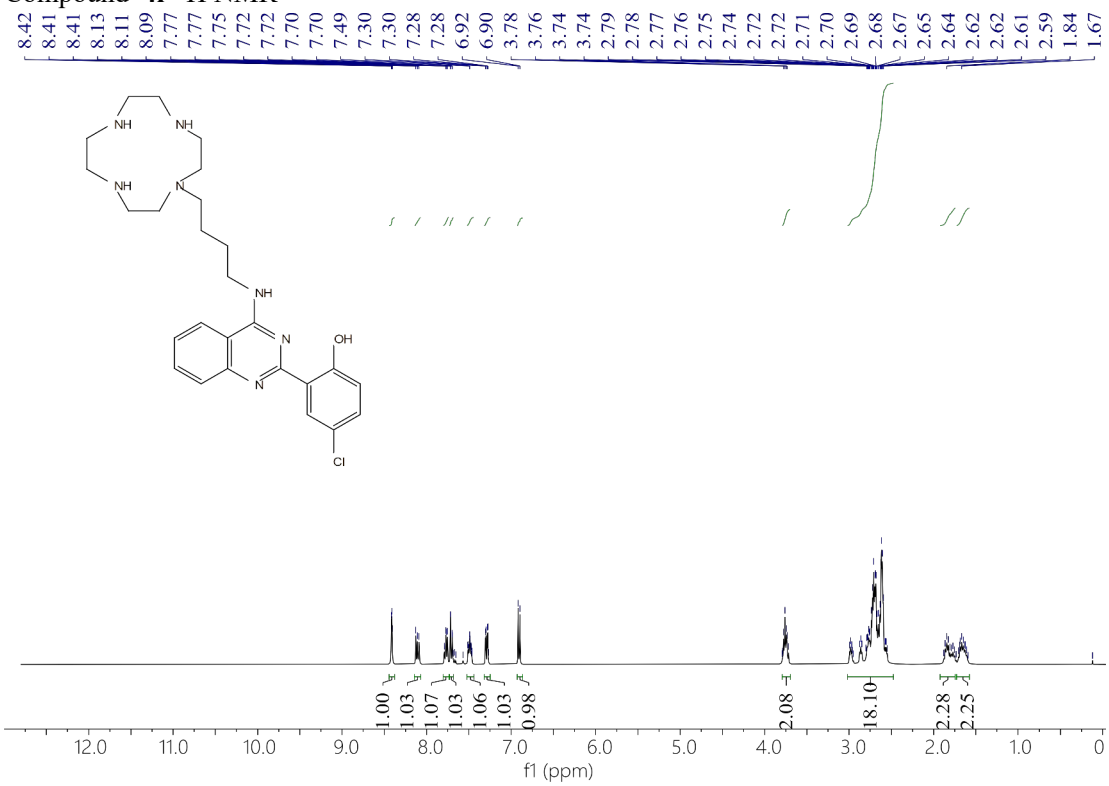
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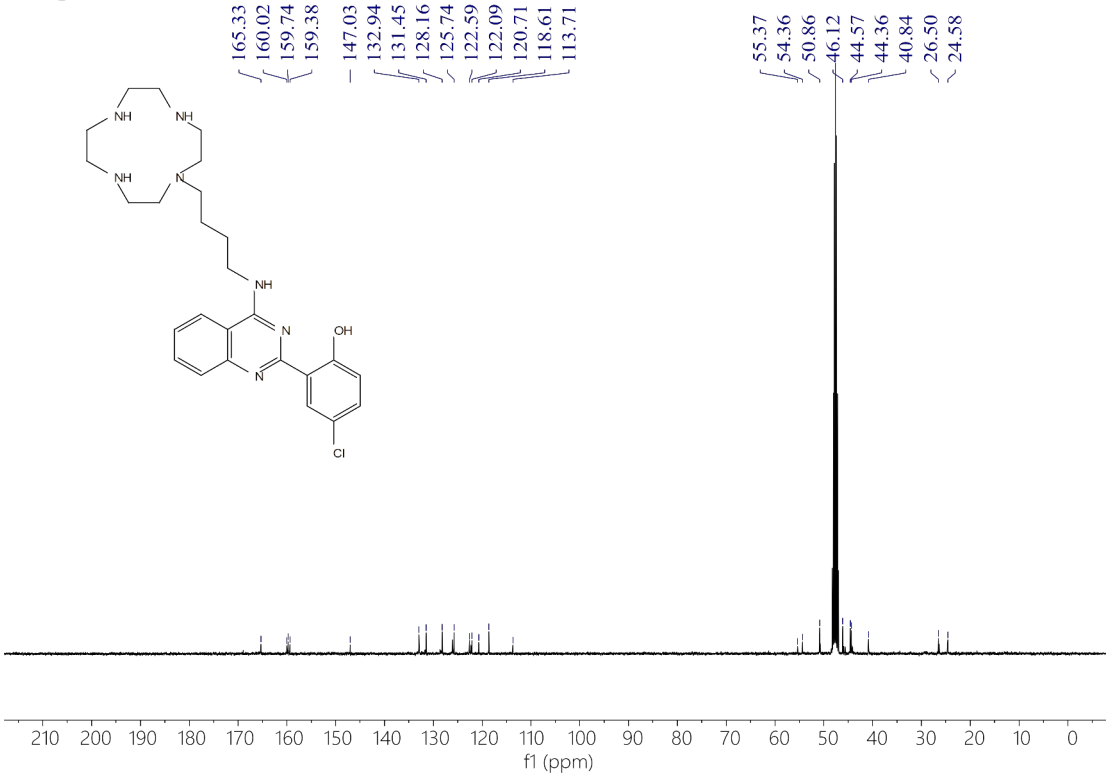
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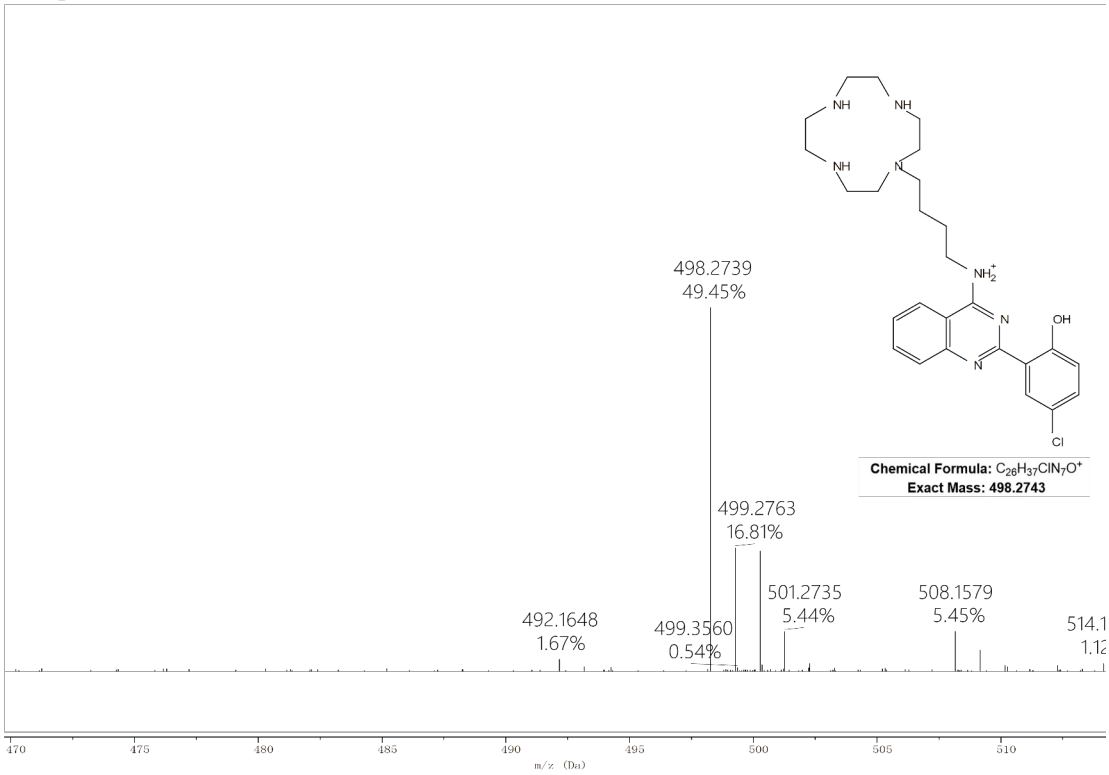
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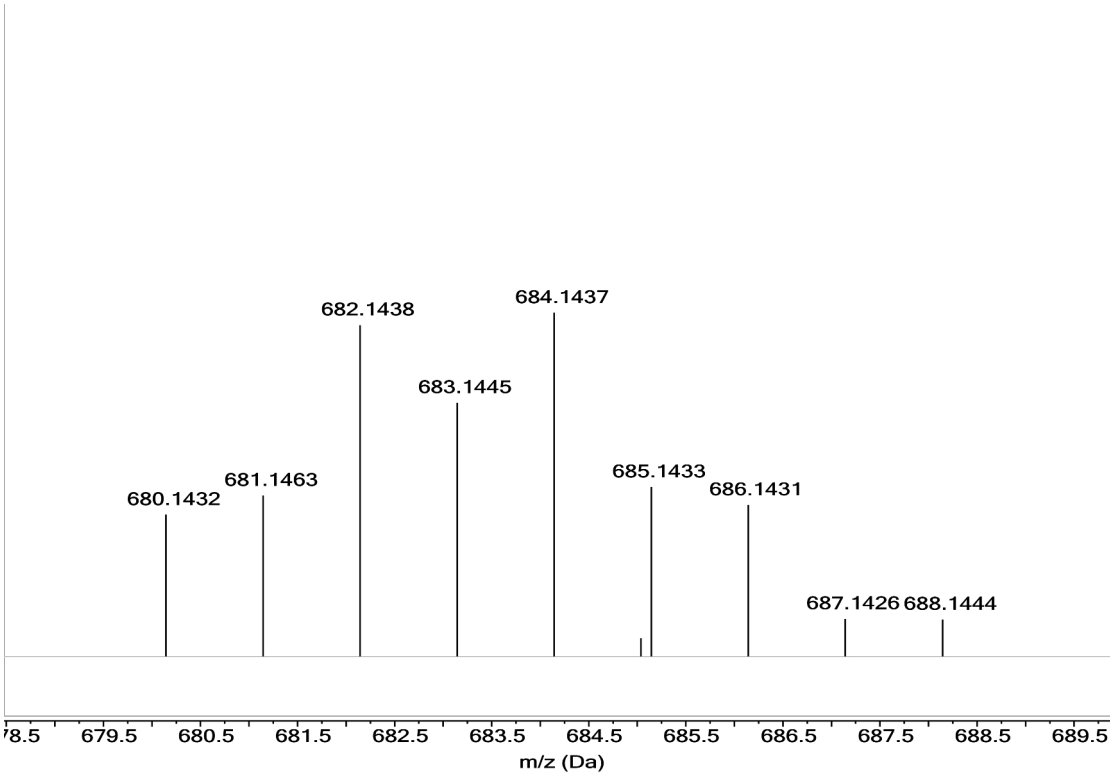
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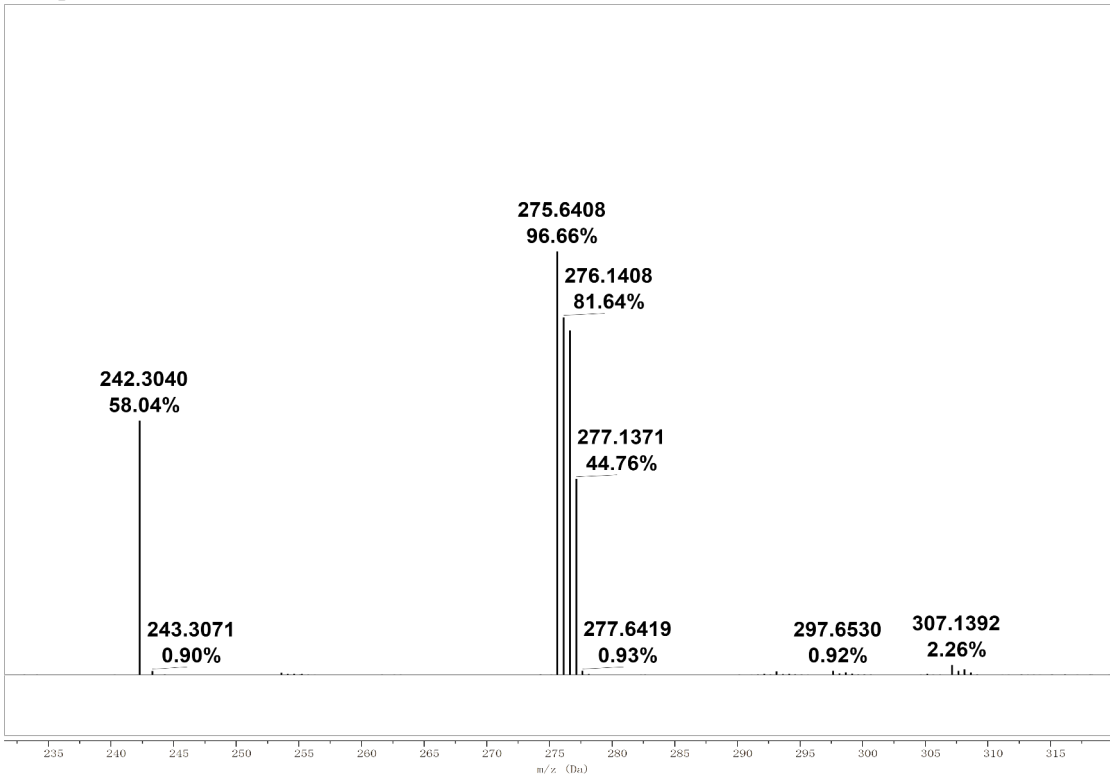
Compound **4i** HRMS



Compound **5a** HRMS



Compound **5b** HRMS



Compound **5c** HRMS

