

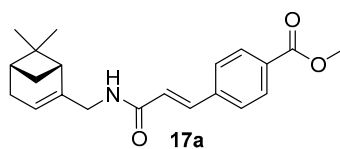
Hydroxamic Acids Containing a Bicyclic Pinane Backbone as Epigenetic and Metabolic Regulators: Synergizing Agents to Overcome Cisplatin Resistance

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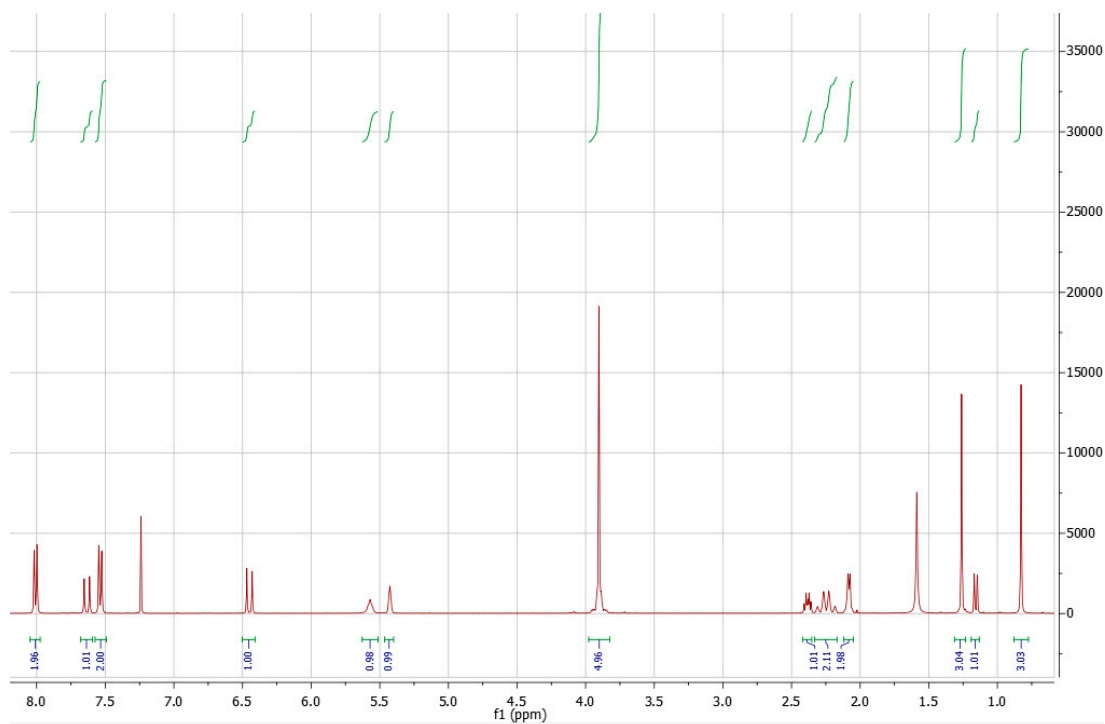
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² Department of Medicinal Chemistry, N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch, Russian Academy of Sciences, Lavrentiev Ave., 9, Novosibirsk 630090, Russia

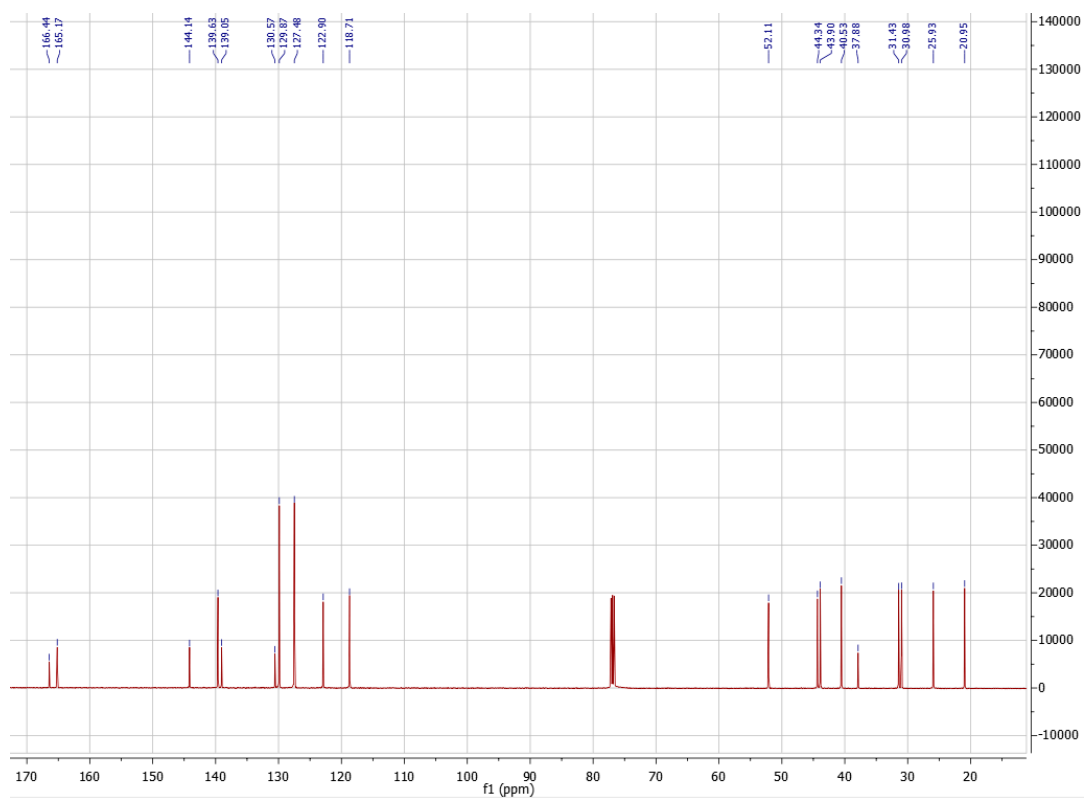
* Correspondence: neganovam@ipac.ac.ru; Tel.: +7-(962)-937-68-69



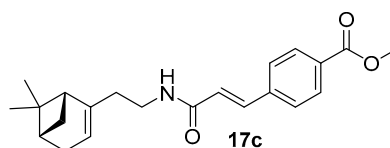
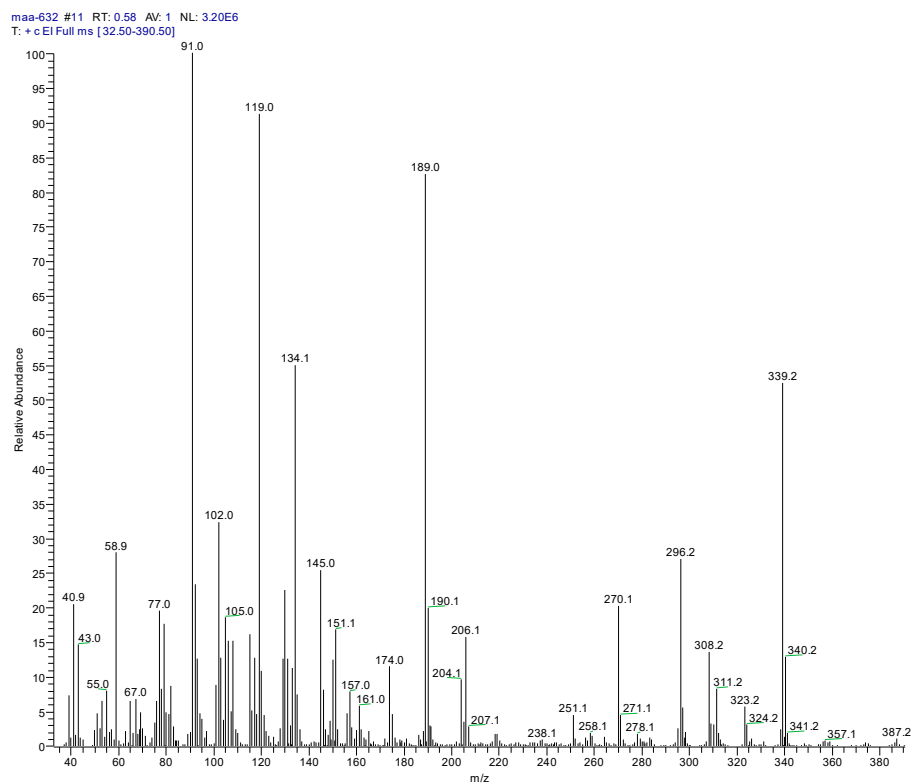
^1H NMR spectrum of compound **17a**



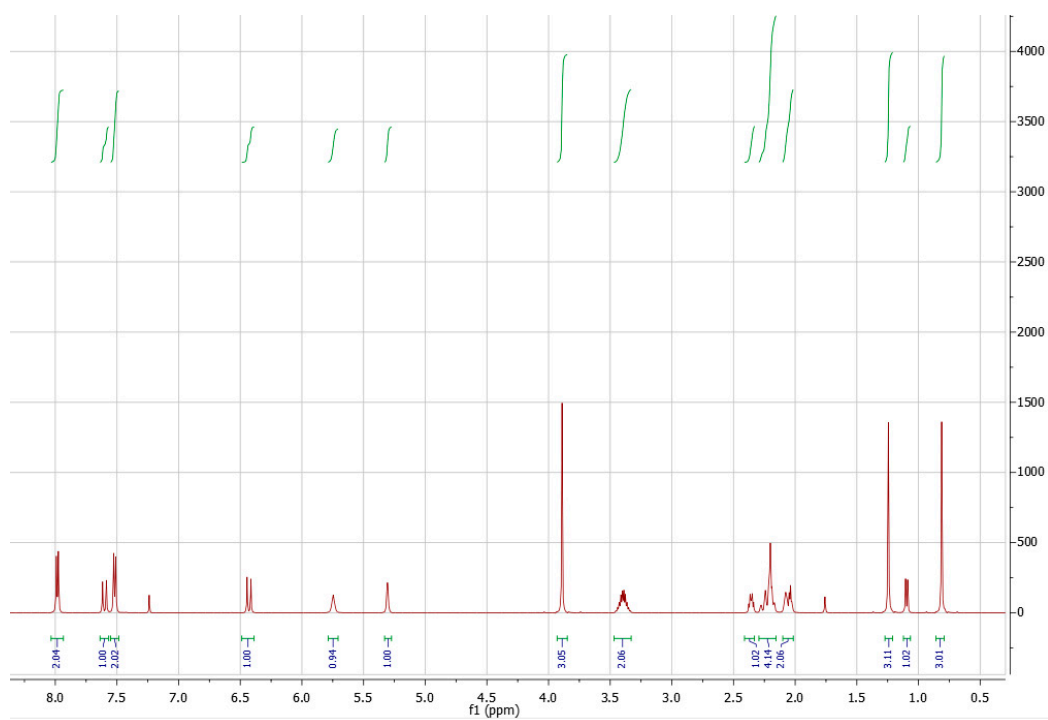
^{13}C NMR spectrum of compound **17a**



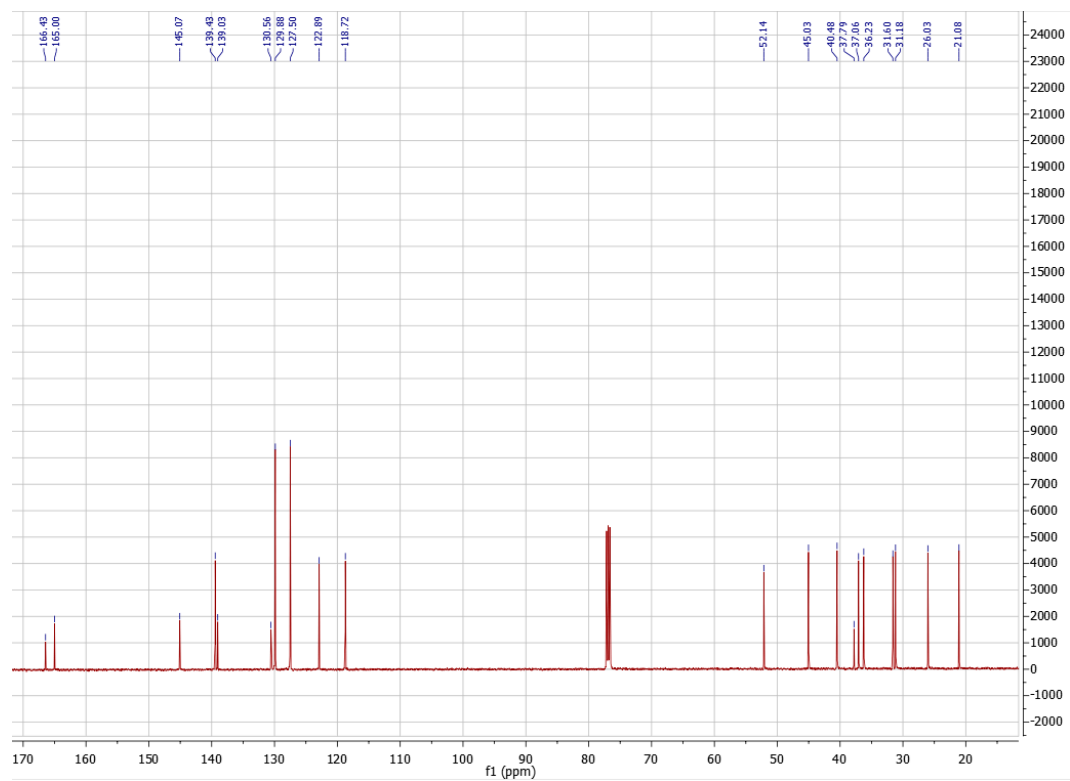
Mass-spectrum of compound **17a**



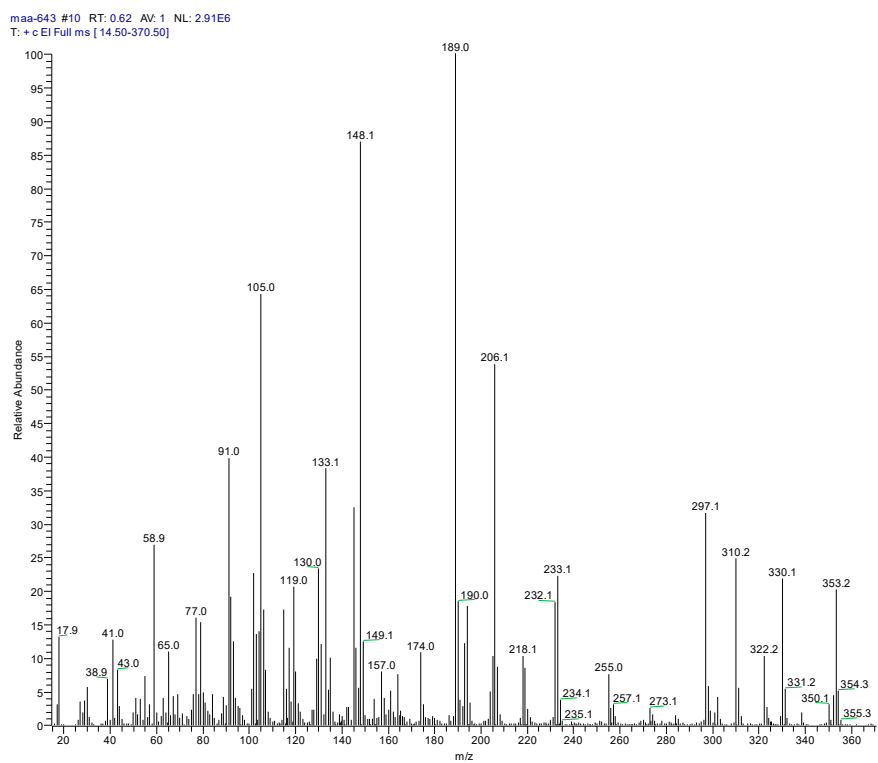
^1H NMR spectrum of compound **17c**

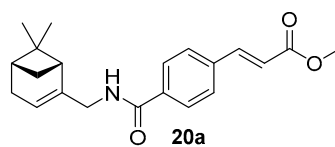


^{13}C NMR spectrum of compound **17c**



Mass-spectrum of compound **17c**

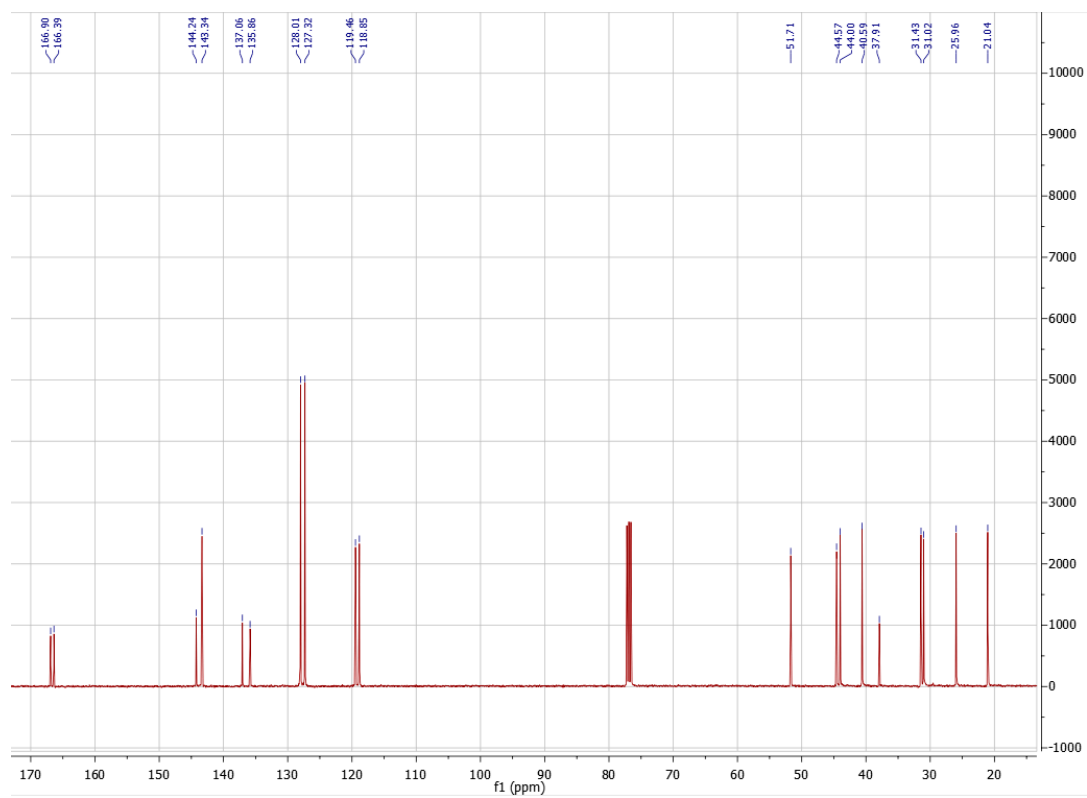




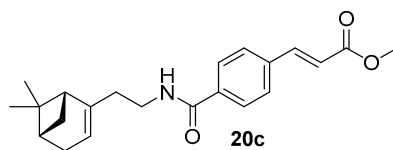
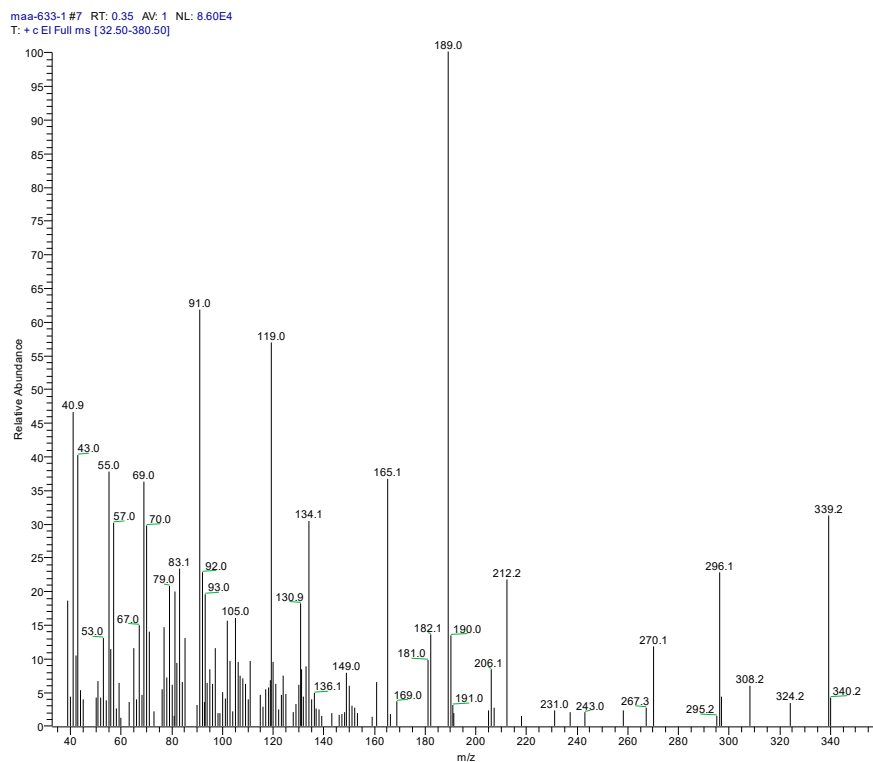
^1H NMR spectrum of compound **20a**



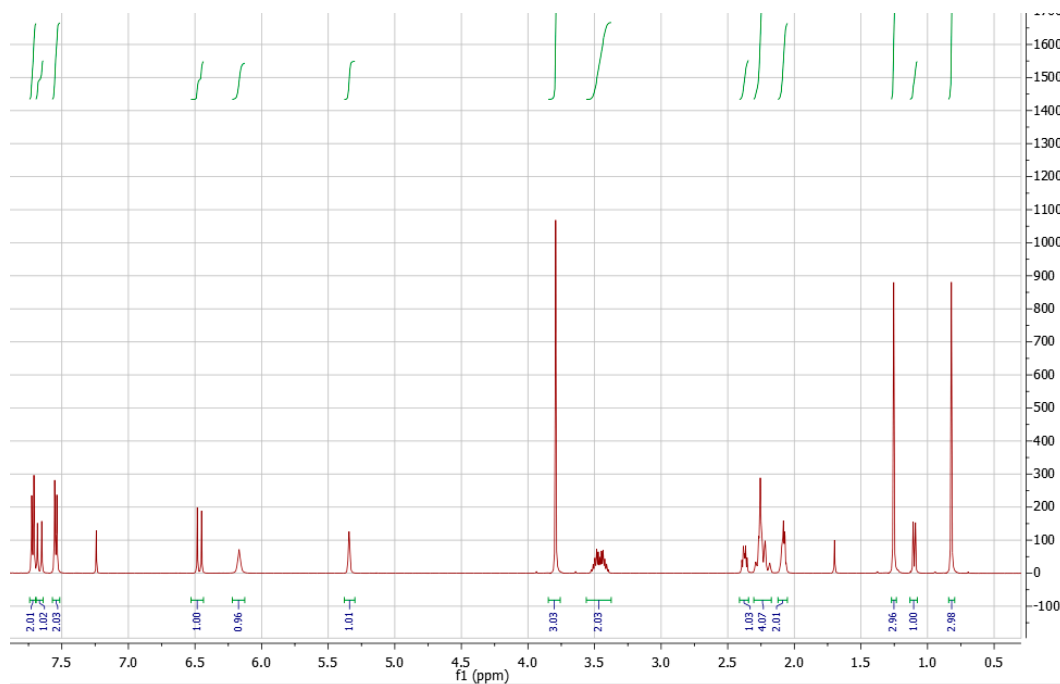
^{13}C NMR spectrum of compound **20a**



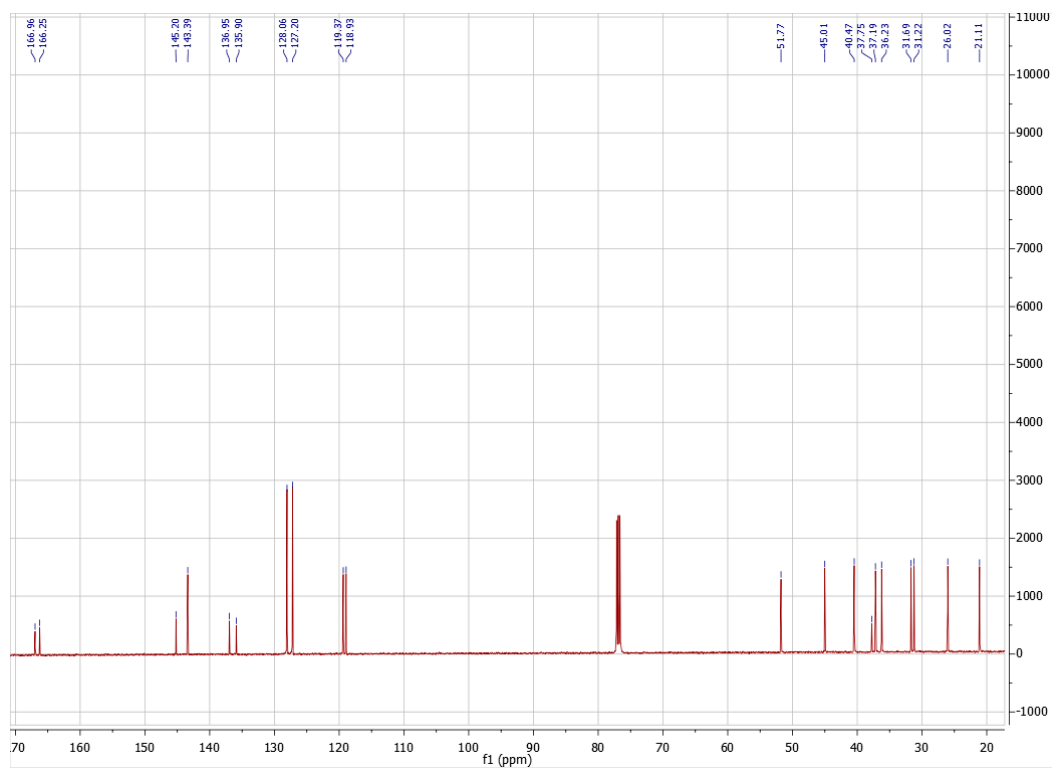
Mass-spectrum of compound 20a



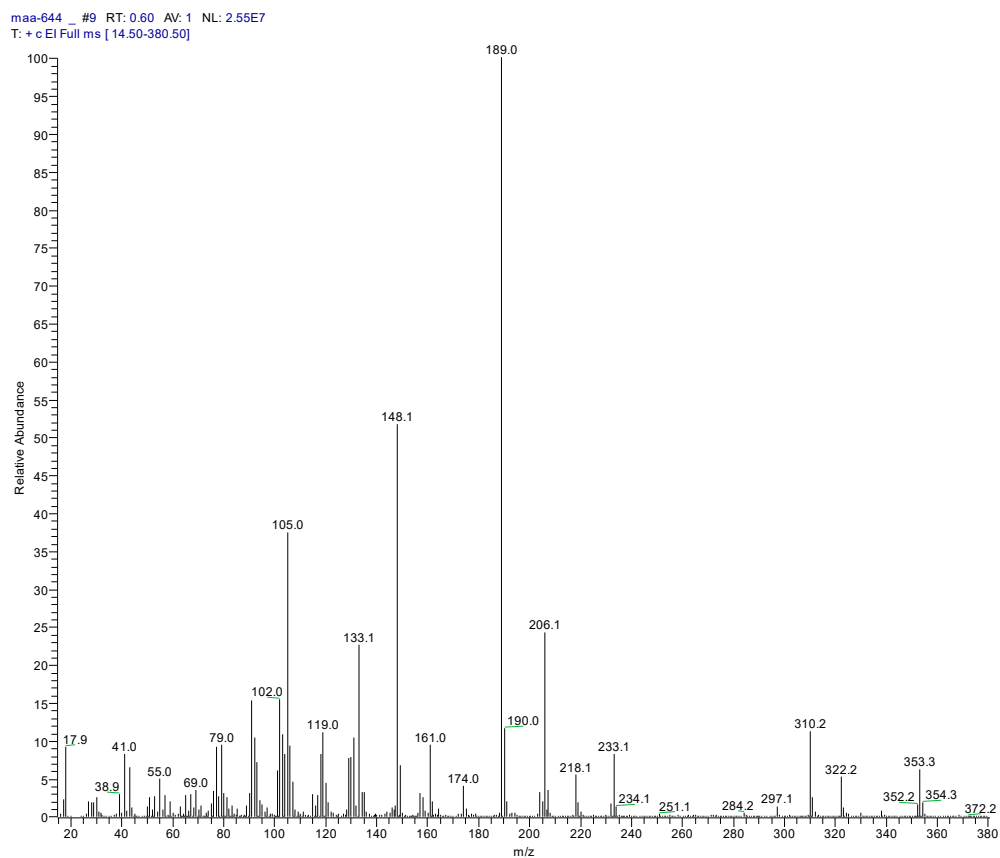
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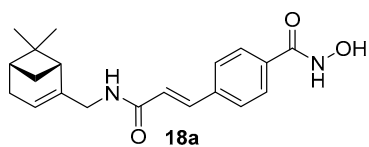


^{13}C NMR spectrum of compound **20c**

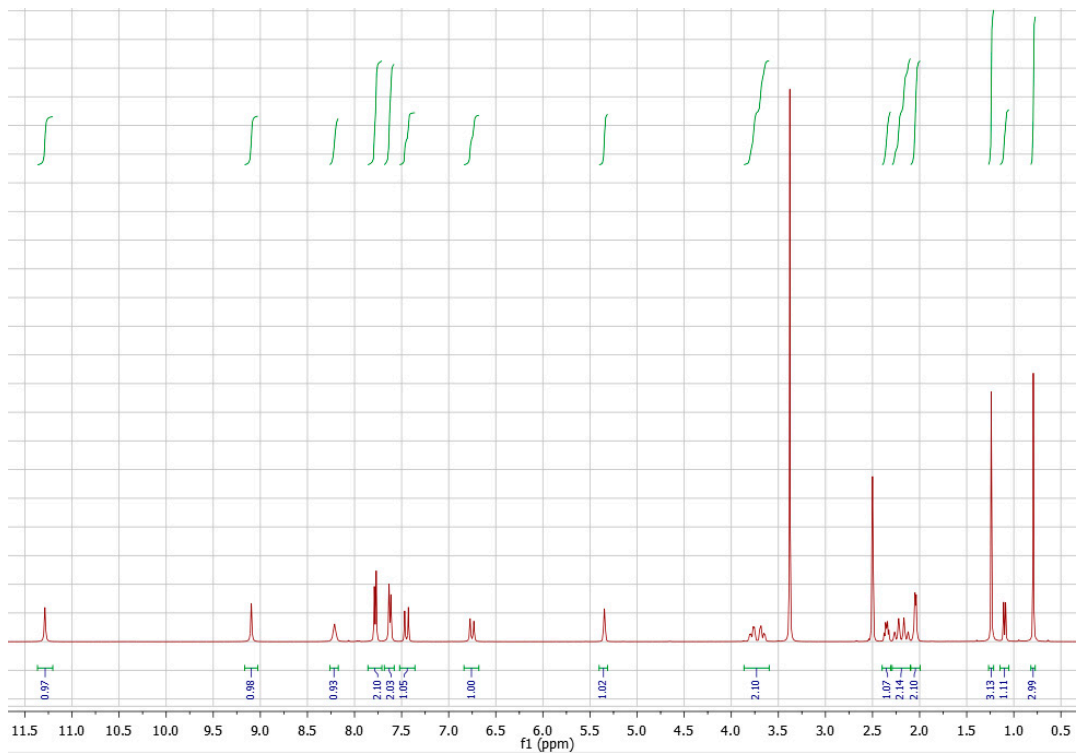


Mass-spectrum of compound **20c**

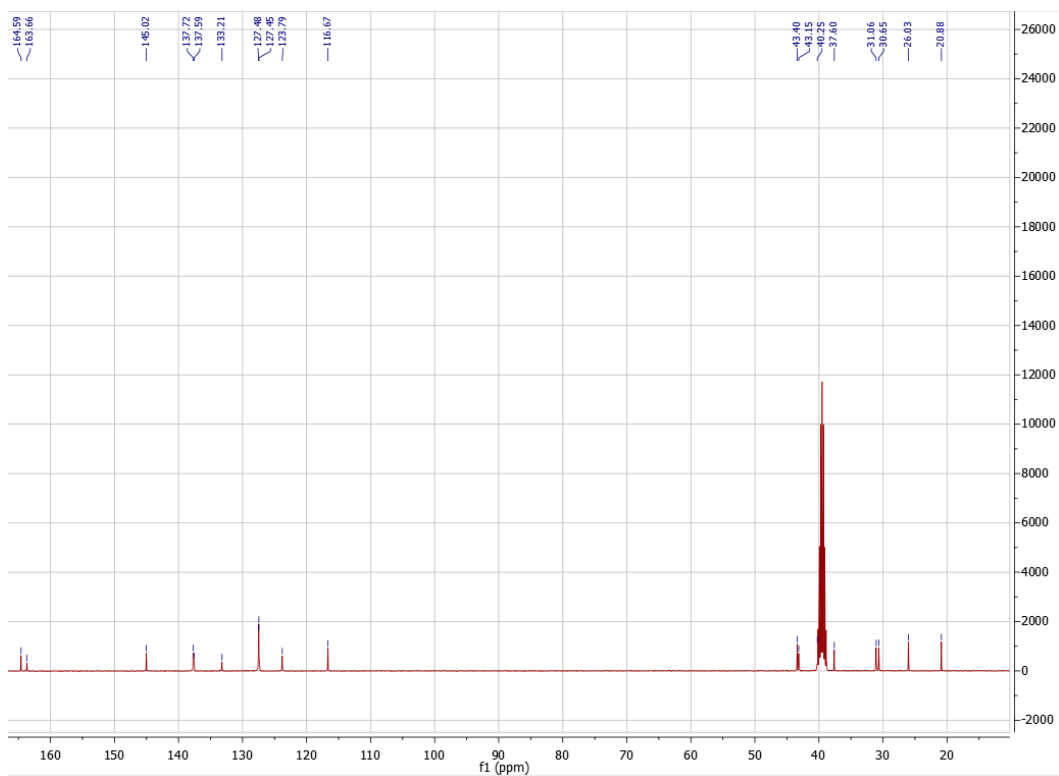




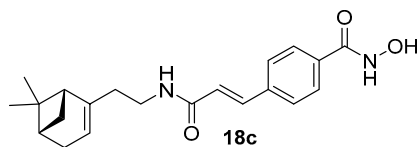
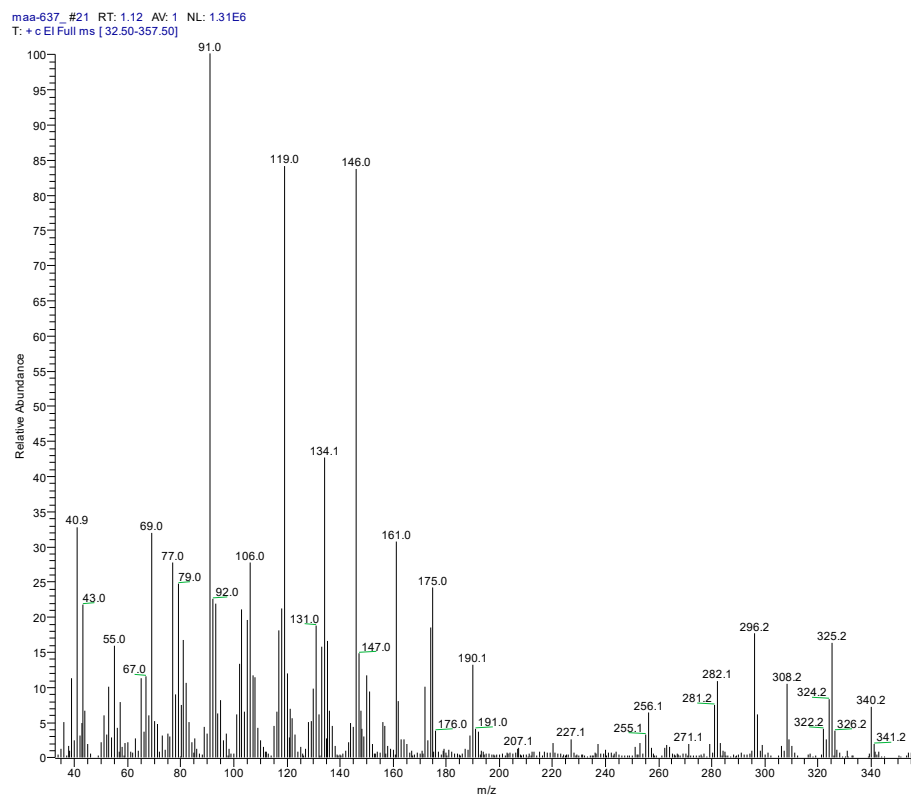
^1H NMR spectrum of compound **18a**



^{13}C NMR spectrum of compound **18a**



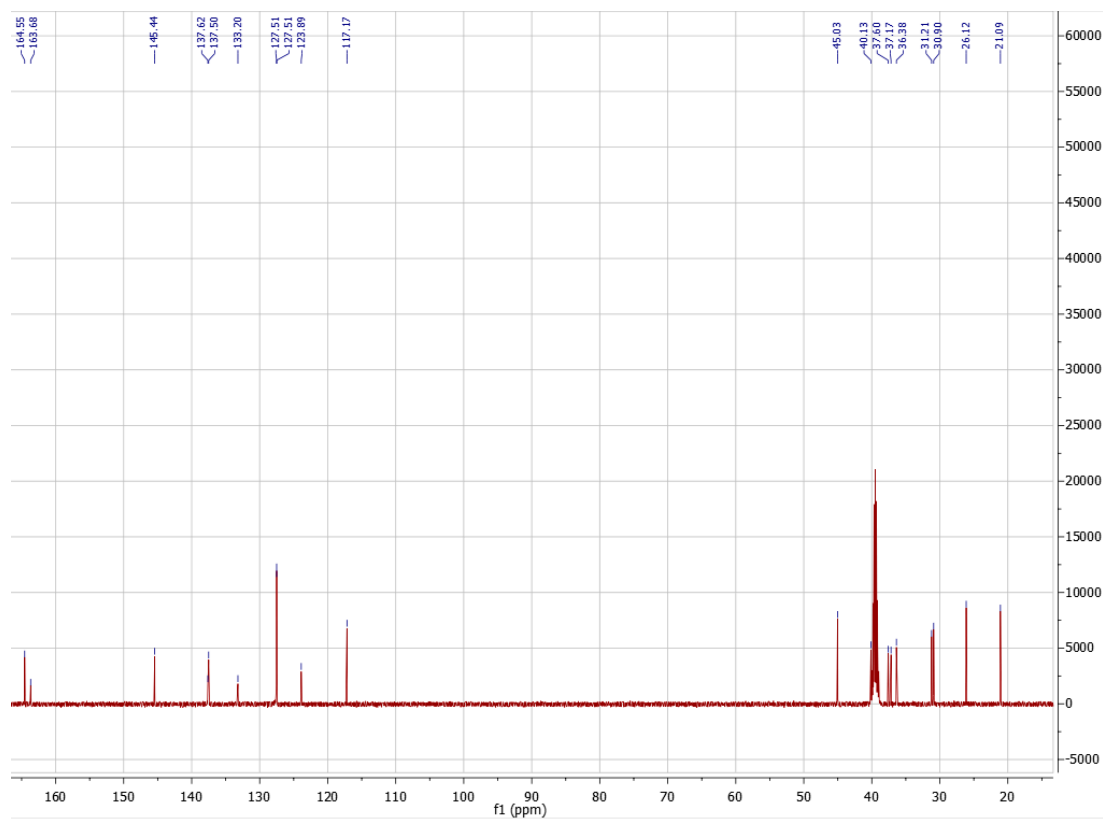
Mass-spectrum of compound **18a**



^1H NMR spectrum of compound **18c**

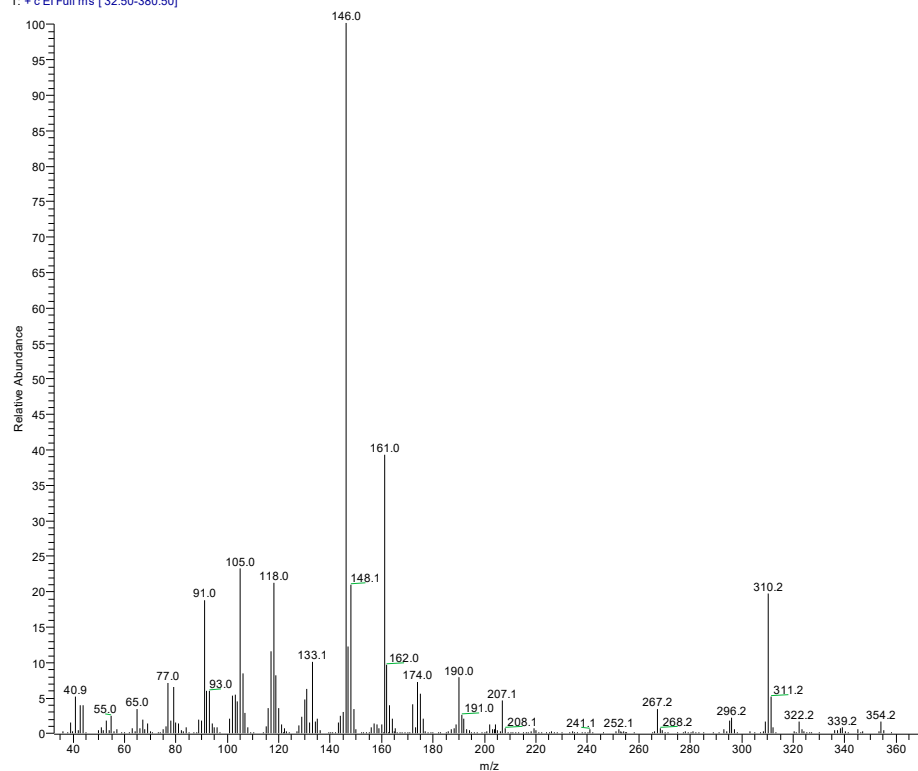


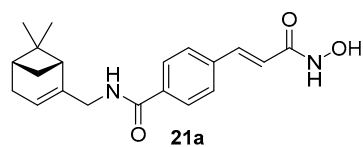
^{13}C NMR spectrum of compound **18c**



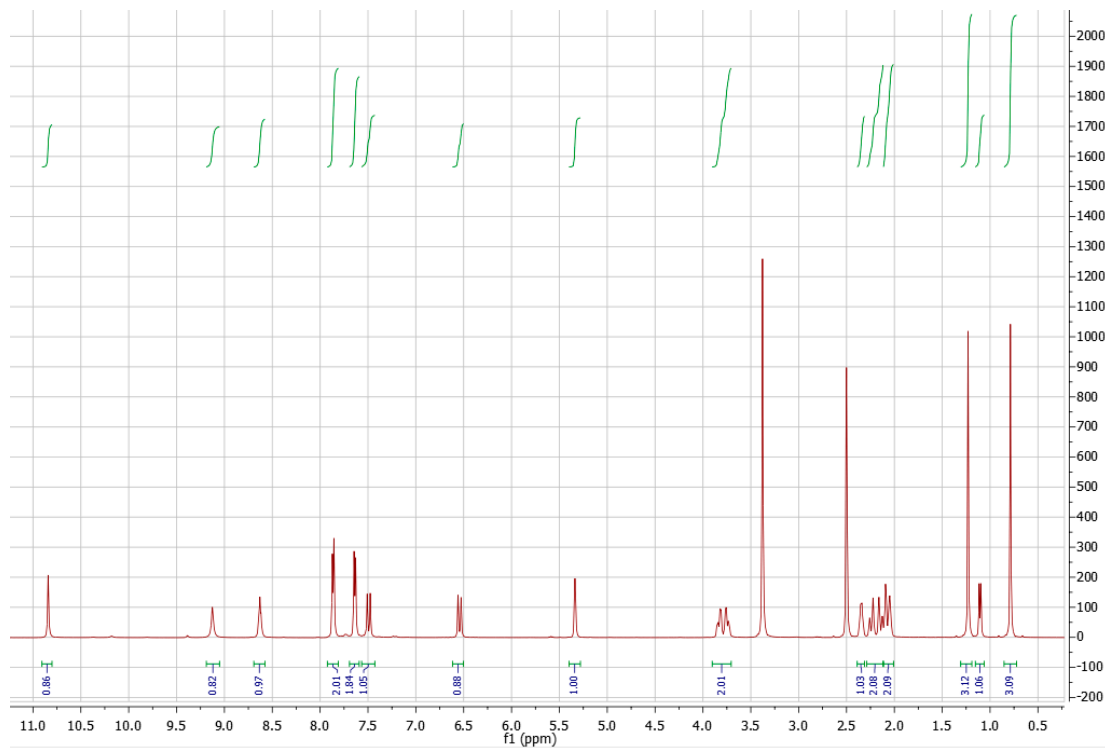
Mass-spectrum of compound **18c**

maa-645_#45 RT: 2.53 AV: 1 NL: 3.17E6
T: + c EI Full ms [32.50-380.50]

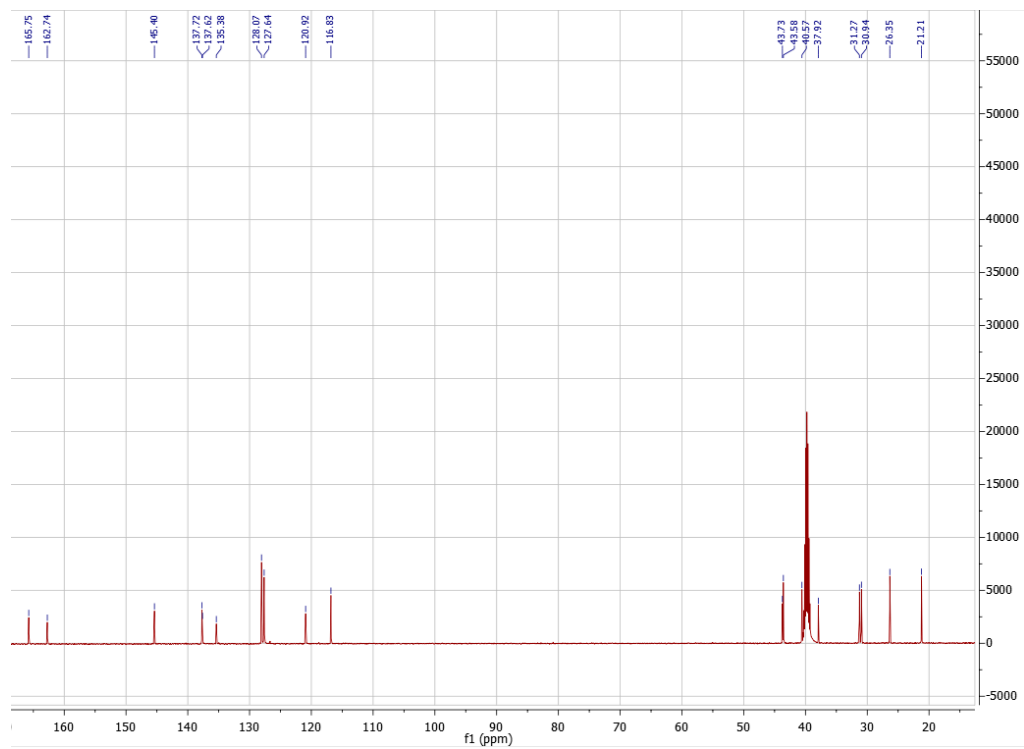




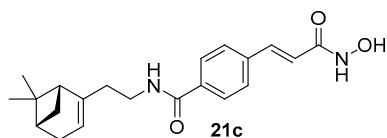
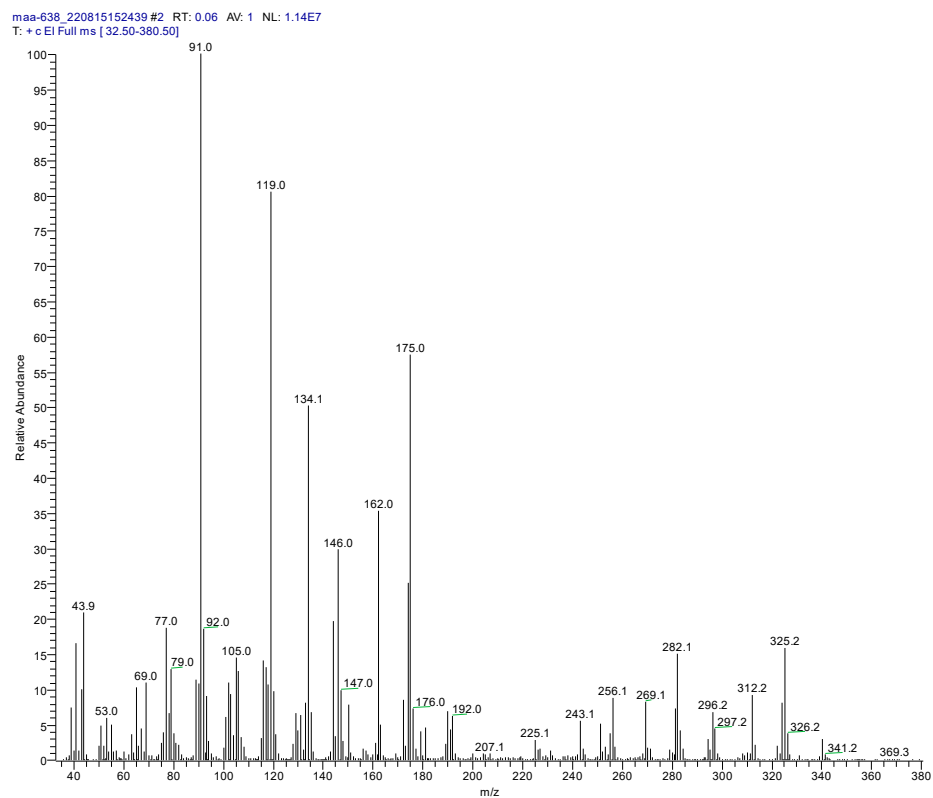
^1H NMR spectrum of compound **21a**



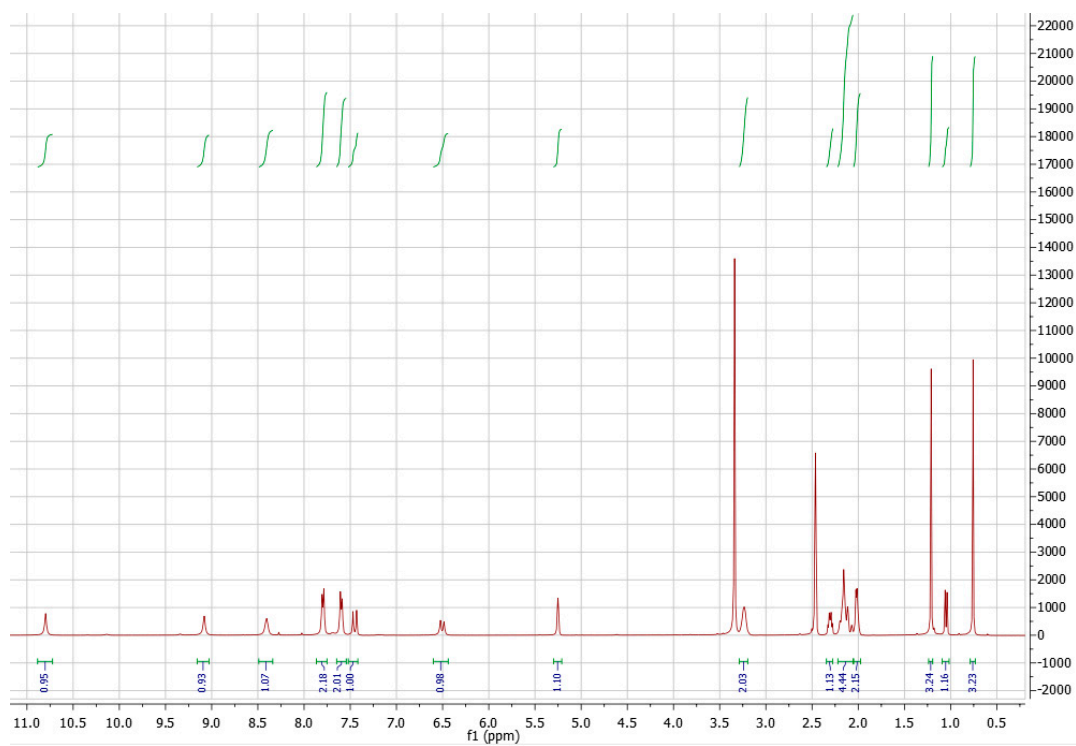
^{13}C NMR spectrum of compound **21a**



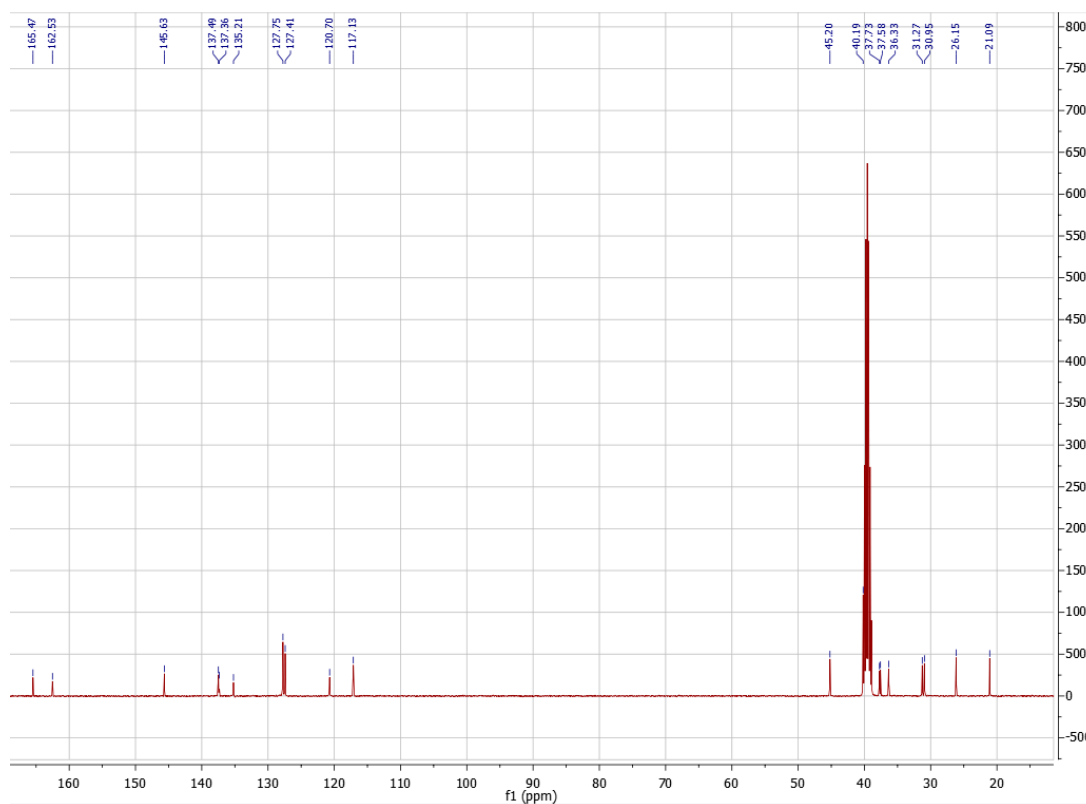
Mass-spectrum of compound **21a**



^1H NMR spectrum of compound **21c**



^{13}C NMR spectrum of compound **21c**



Mass-spectrum of compound **21c**

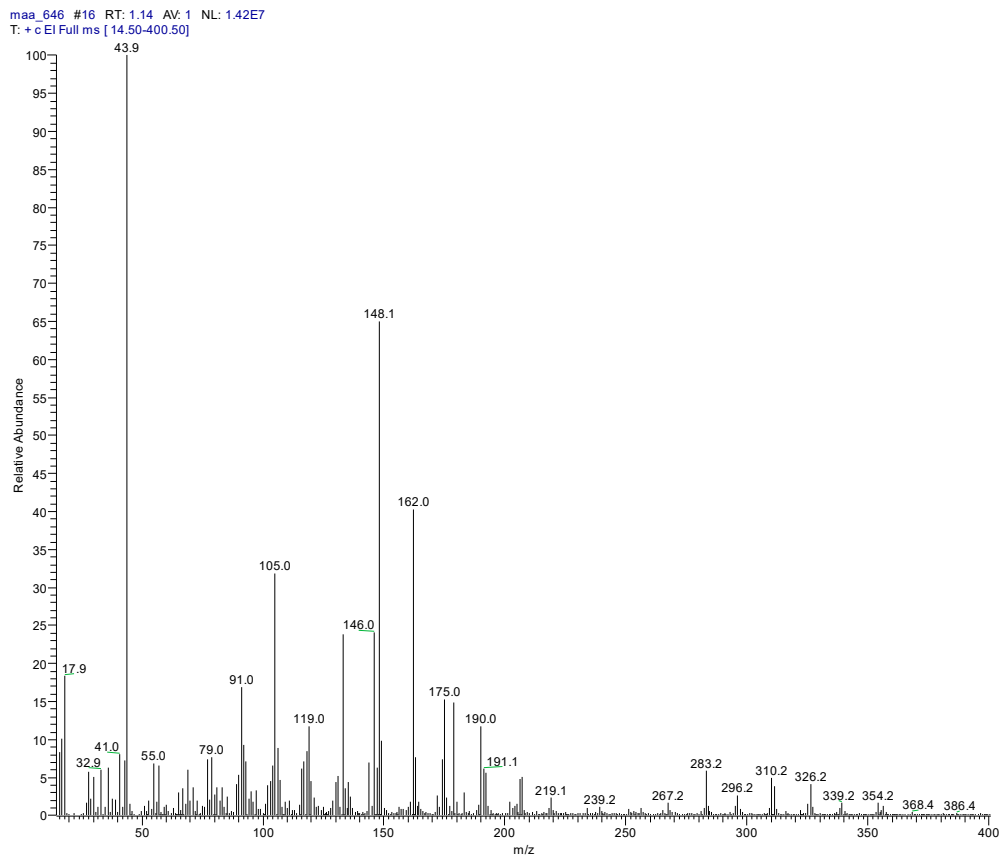


Figure S1. Molecular docking of ligands against Hexokinase 1 (PDB ID: 4F9O). Nitrogen and oxygen atoms are coloured in blue and red, respectively. Hydrogen bond (bright green dotted lines represents), van der Waals bond (light green dotted lines represents), other interactions (Alkyl are shown in light blue colour dotted lines; π -Alkyl - in light pink colour dotted lines; π -Anion - yellow colour dotted lines) Attractive charge are shown in beige colour dotted lines).

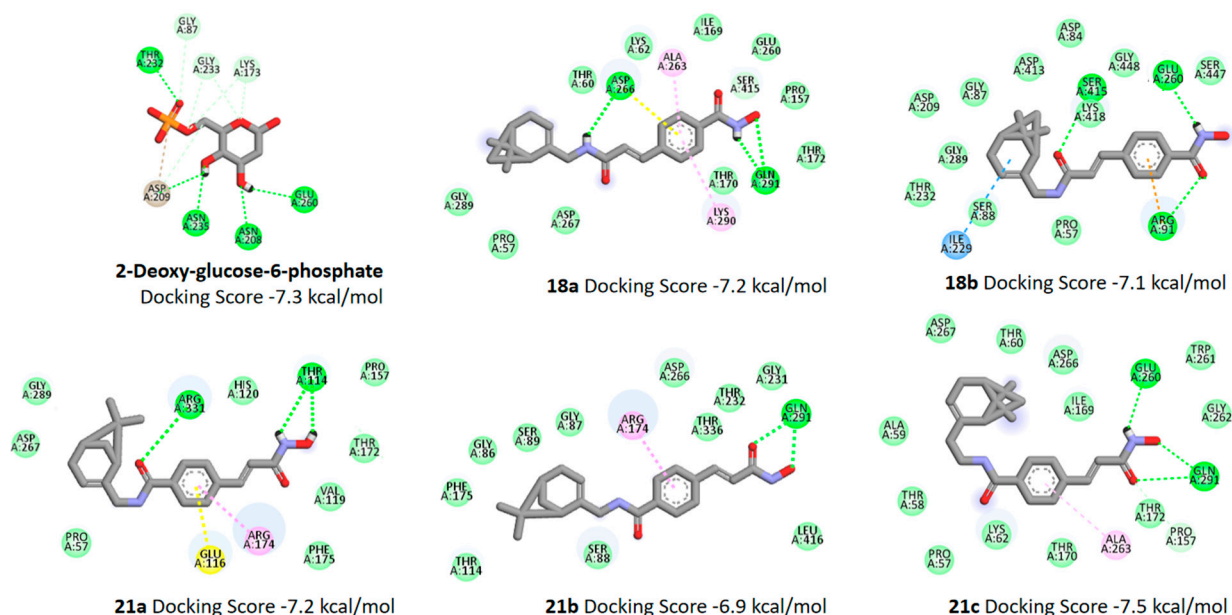


Figure S2. Molecular docking of ligands against 6-Phosphofructo-2-kinase (PDB ID: 1K6M). Nitrogen and oxygen atoms are coloured in blue and red, respectively. Hydrogen bond (bright green dotted lines represents), van der Waals bond (light green dotted lines represents), other interactions (Alkyl are shown in light blue colour dotted lines; π -Alkyl - in light pink colour dotted lines; π - π Stacked - in bright pink colour dotted lines, π -Cation - orange colour dotted lines).

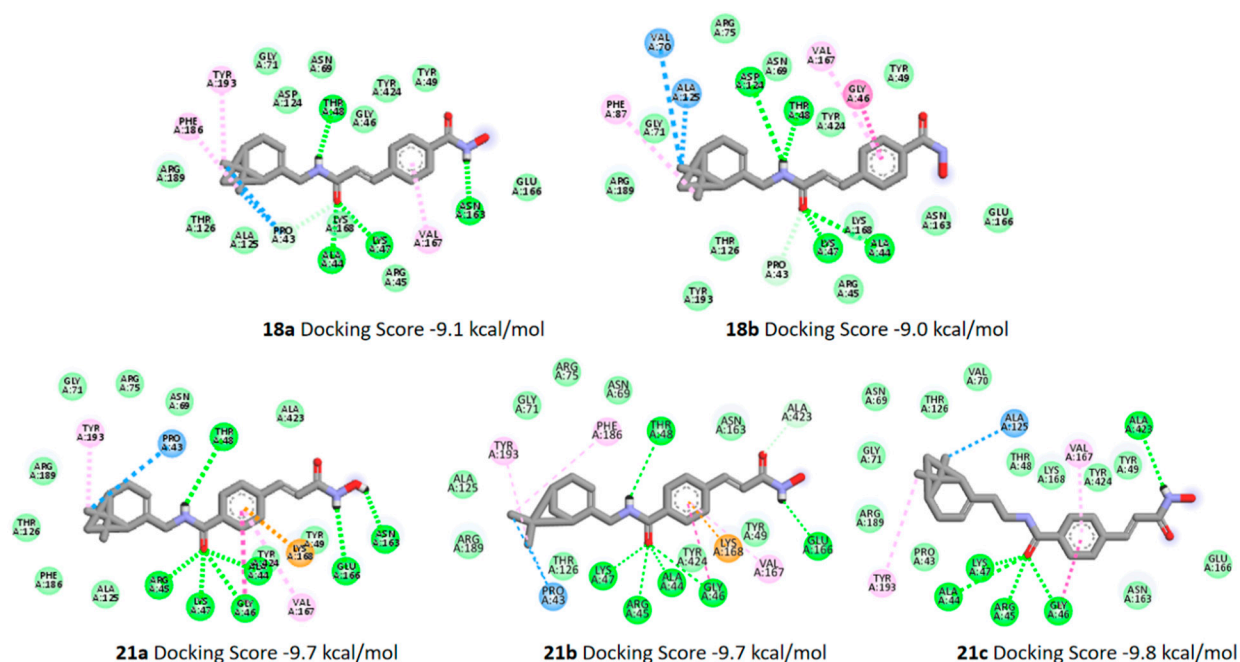
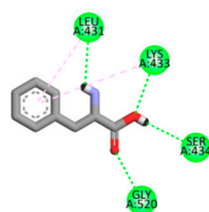
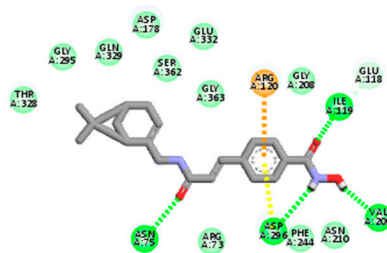


Figure S3. Molecular docking of ligands against Pyruvate kinase M2 (PDB ID: 1T5A). Nitrogen and oxygen atoms are coloured in blue and red, respectively. Hydrogen bond (bright green dotted lines represents),

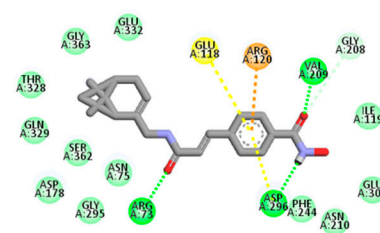
van der Waals bond (light green dotted lines represents), other interactions (π -Alkyl - in light pink colour dotted lines; π -Anion and π -Cation - yellow and orange colour dotted lines, respectively).



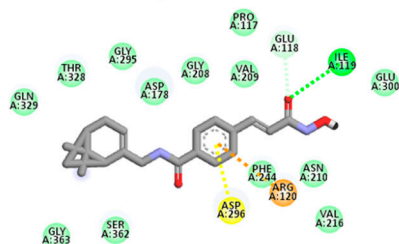
Phenylalanine
Docking Score -7.8 kcal/mol



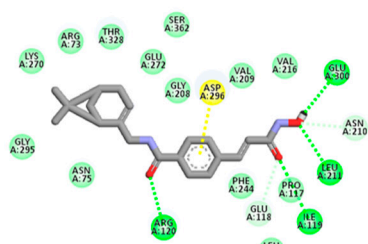
18a Docking Score -7.7 kcal/mol



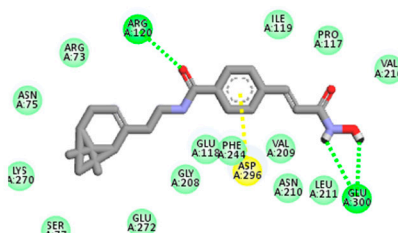
18b Docking Score -8.1 kcal/mol



21a Docking Score -8.6 kcal/mol



21b Docking Score -8.7 kcal/mol



21c Docking Score -8.0 kcal/mol