

Supplementary information

Possible neuroprotective effects of amide alkaloids from *Bassia indica* and *Agathophora alopecuroides* : *in vitro* and *in silico* investigations

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Abstract

In Alzheimer's disease (AD), the accumulation of amyloid- β plaques, overactivity of MAO-B, and phosphorylated tau protein in the central nervous system result in neuroinflammation and cognitive impairments. Therefore, the multi-targeting of these therapeutic targets has emerged as a promising strategy for the development of AD treatments. The current study reports the isolation and identification of seven amide alkaloids, namely, *N-trans*-feruloyl-3-methoxytyramine (**1**), *N-trans*-feruloyltyramine (**2**), *S*-(-)-*N-trans*-feruloylnormetanephrine (**3**), *S*-(-)-*N-trans*-feruloyloctopamine (**4**), *R*-(+)-*N-trans*-feruloyloctopamine (**5**), *N-trans*-caffeoyltyramine (**6**), and *S*-(-)-3-(4-hydroxy-3-methoxyphenyl)-*N*-[2-(4-hydroxyphenyl)-methoxyethyl]acrylamide (**7**), from *B. indica* and *A. alopecuroides*, which are halophytic plants that have been reported to contain diverse phytochemicals. Additionally, the study explores the potential inhibition effects of the isolates on β -secretase, monoamine oxidase enzymes, and phosphorylated tau protein, and their anti-aggregation effects on amyloid- β fibrils. Compounds **1**, **2**, and **7** showed potent inhibitory activity against BACE1, MAO-B, and phosphorylated tau protein, as well as anti-aggregation activity against A β -peptides. Additionally, compound **6** displayed a promising inhibition activity against MAO-B enzyme. Further in-depth *in silico* and modeling analyses (*i.e.*, docking, absolute binding free energy calculations, and molecular dynamics simulations) were carried out to reveal the binding mode of each active compound inside the corresponding enzyme (*i.e.*, MAO-B and BACE1). The results indicate that *B. indica*, *A. alopecuroides*, and the isolated amide alkaloids might be useful in the development of lead compounds for the prevention of neurodegenerative diseases, especially AD.

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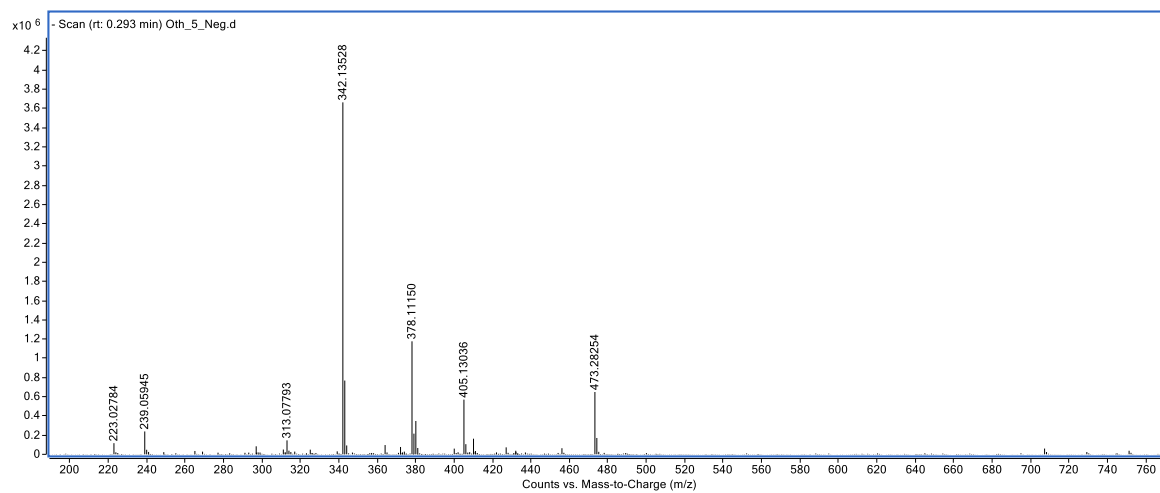


Figure S1: HR-MS of compound 1

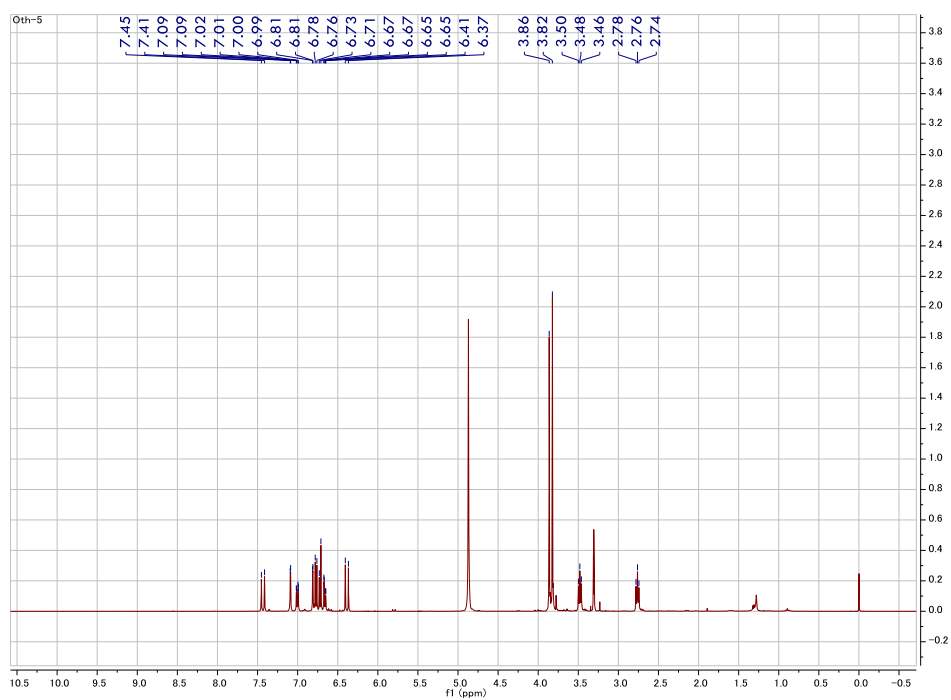


Figure S2: $^1\text{H-NMR}$ of compound 1

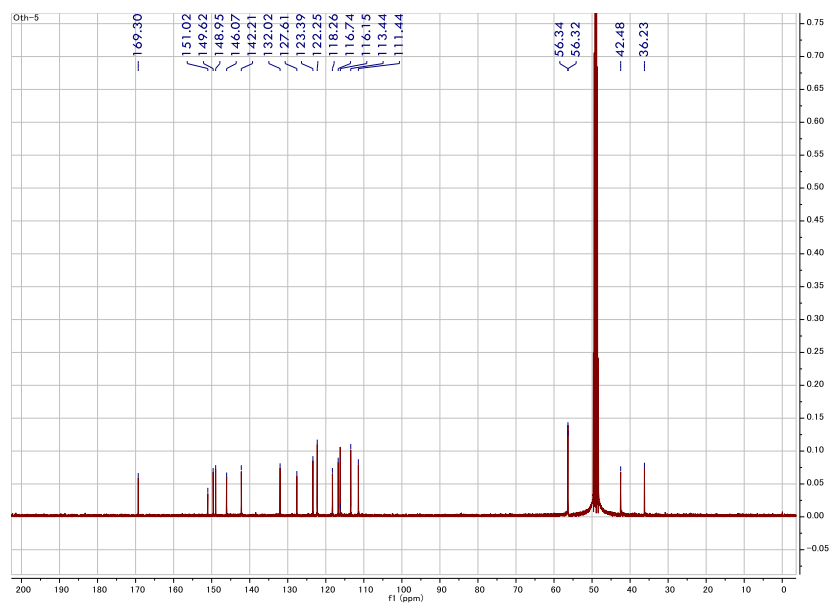


Figure S3: ^{13}C -NMR spectrum of compound 1

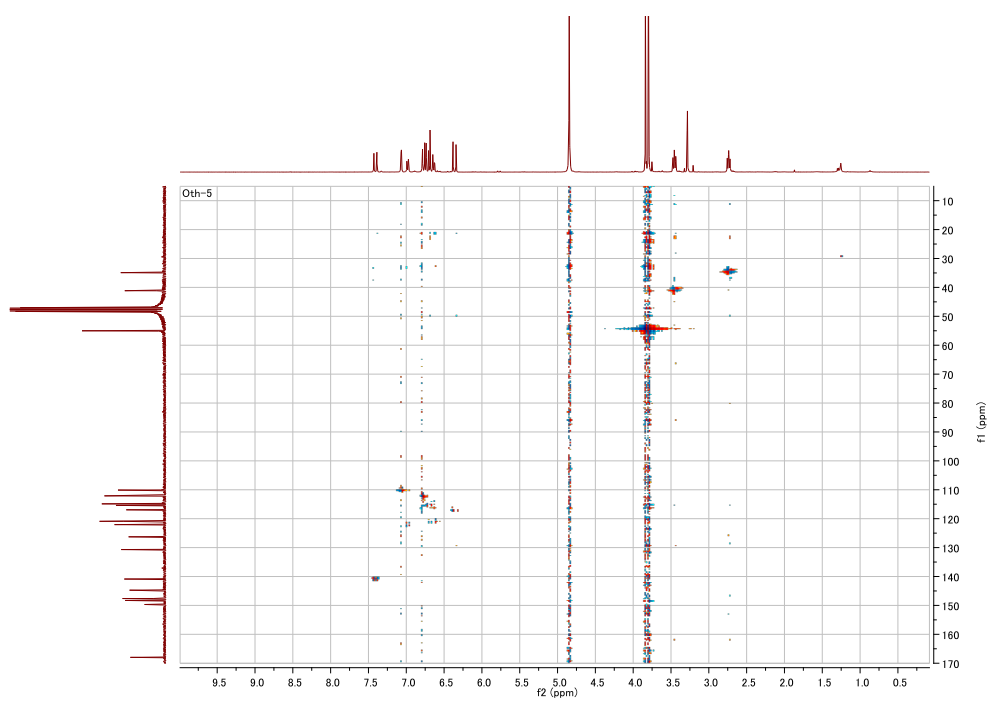


Figure S4: HSQC-NMR spectrum of compound 1

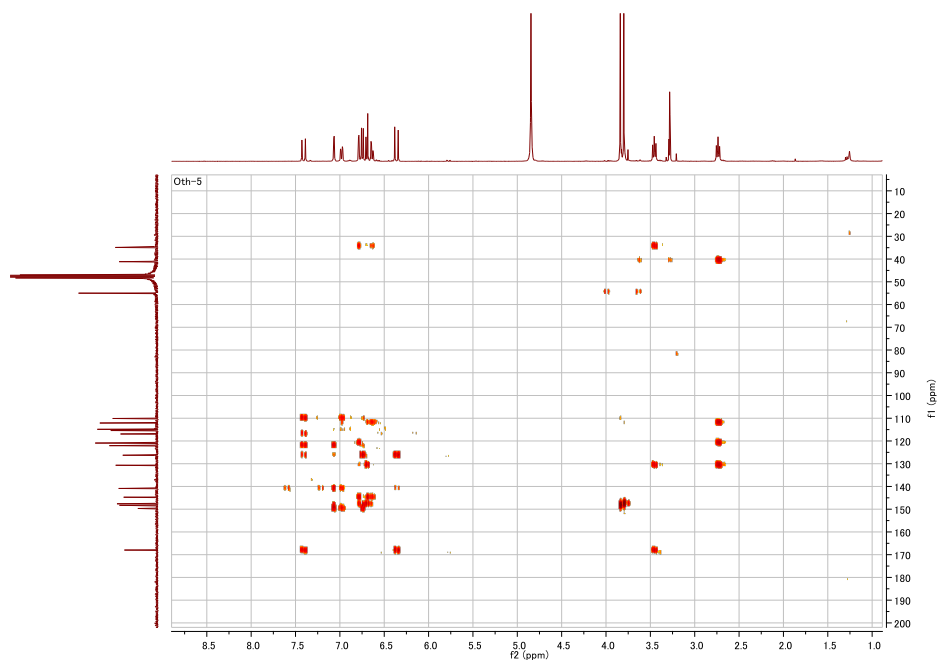


Figure S5: HMBC spectrum of compound 1

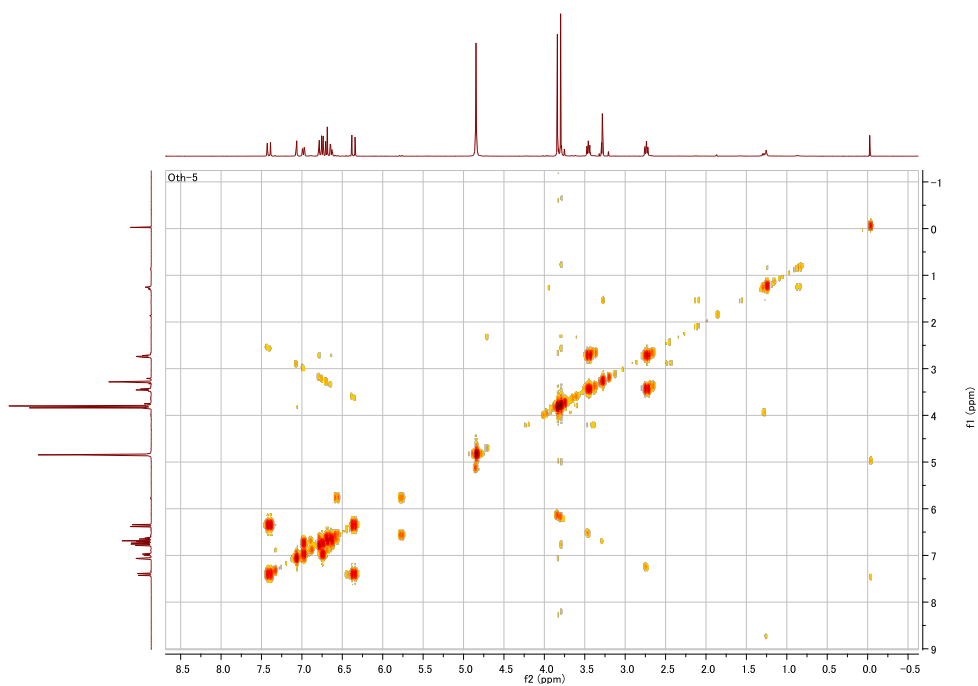


Figure S6: ^1H - ^1H COSY spectrum of compound 1

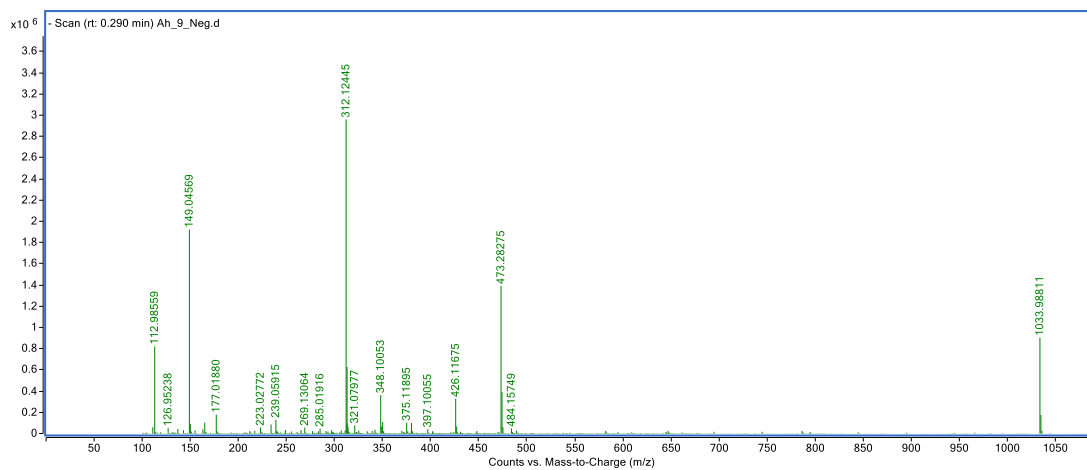


Figure S7: HR-MS of compound 2

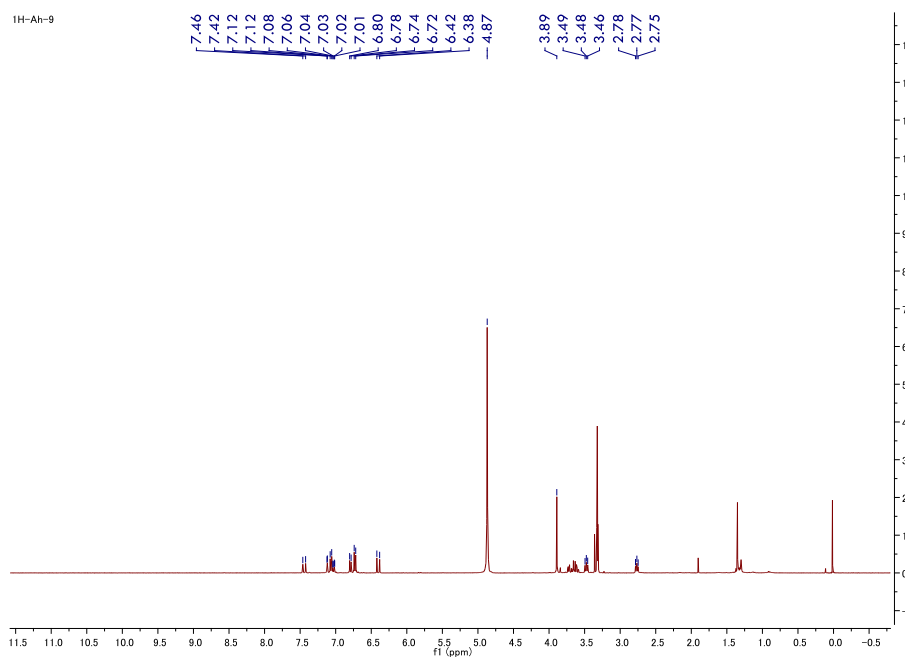


Figure S8: ¹H-NMR spectrum of compound 2

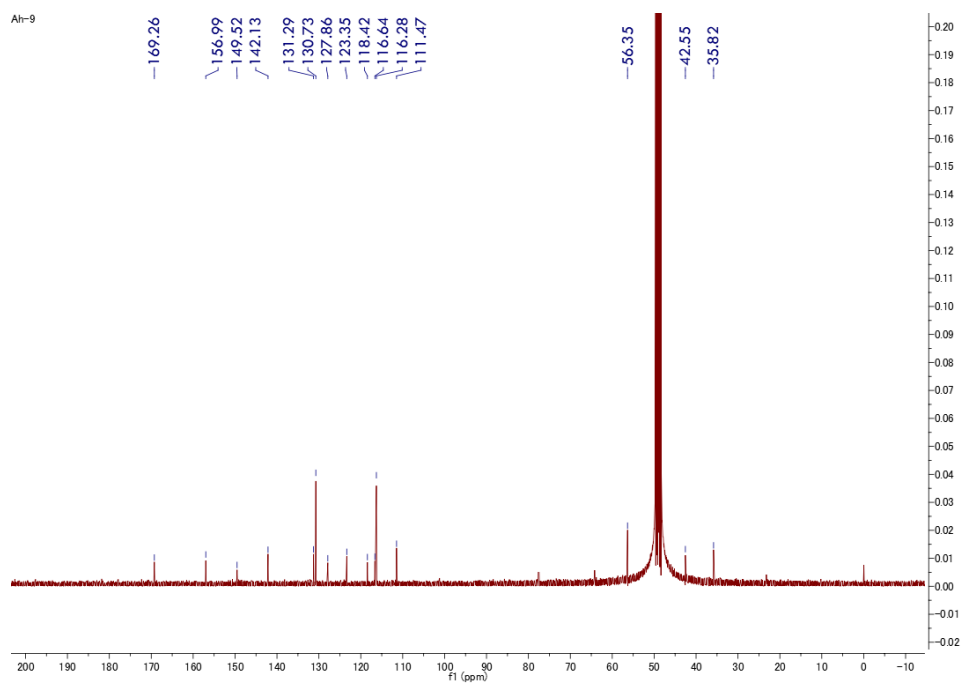


Figure S9: ^{13}C -NMR spectrum of compound 2

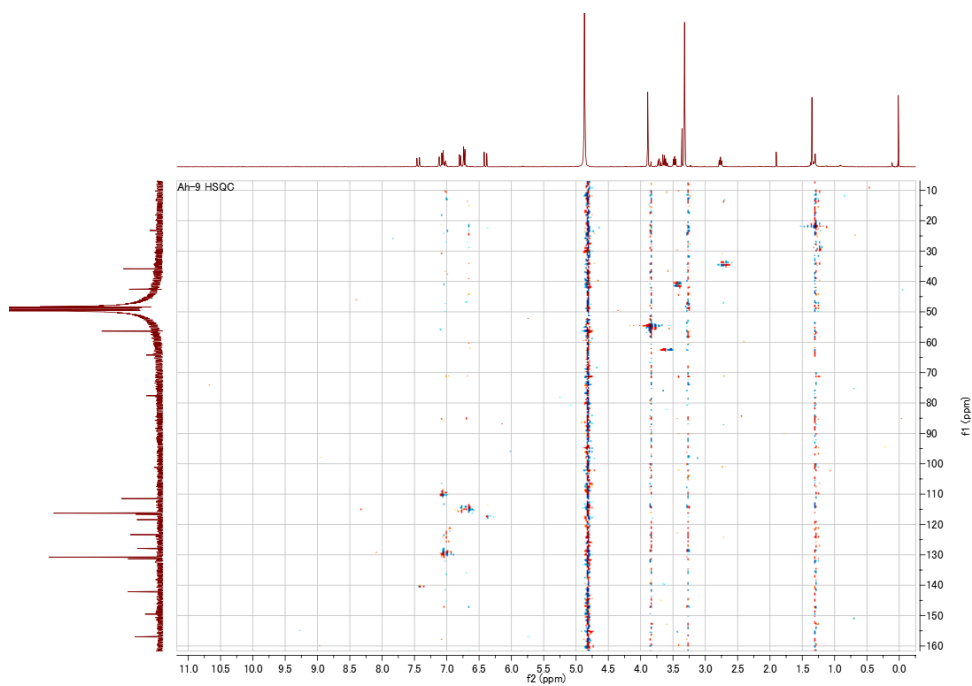


Figure S10: HSQC-NMR spectrum of compound 2

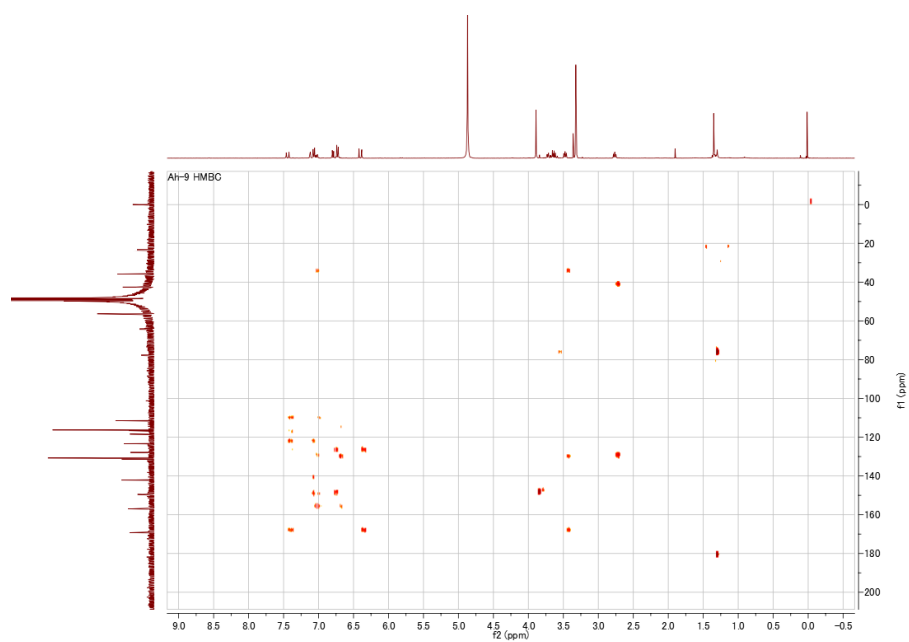


Figure S11: HMBC-NMR spectrum of compound 2

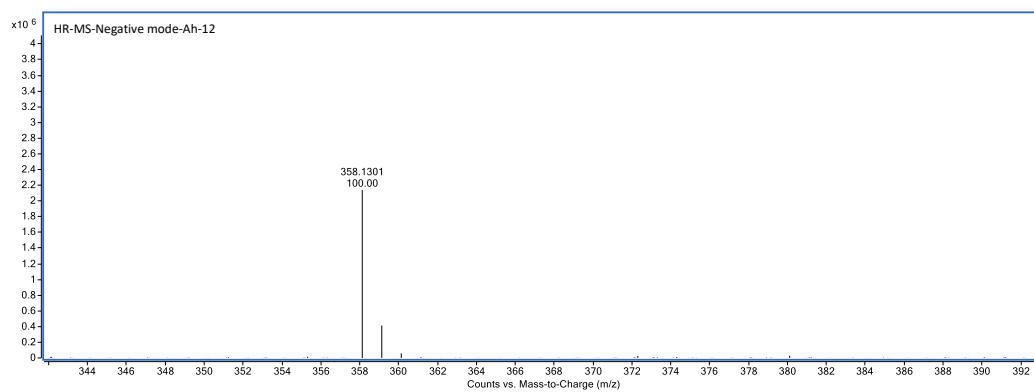


Figure S12: HR-MS spectrum of compound 3

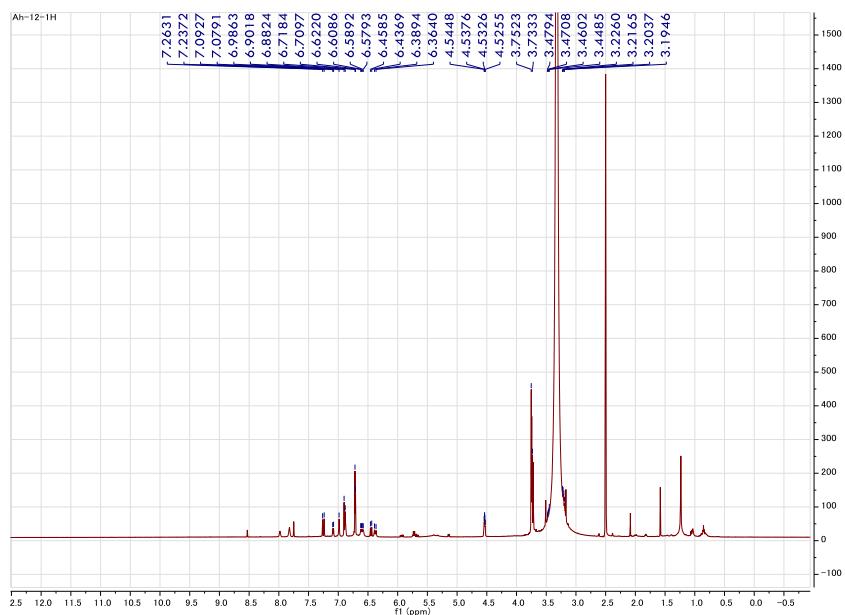


Figure S13: ¹H-NMR spectrum of compound 3

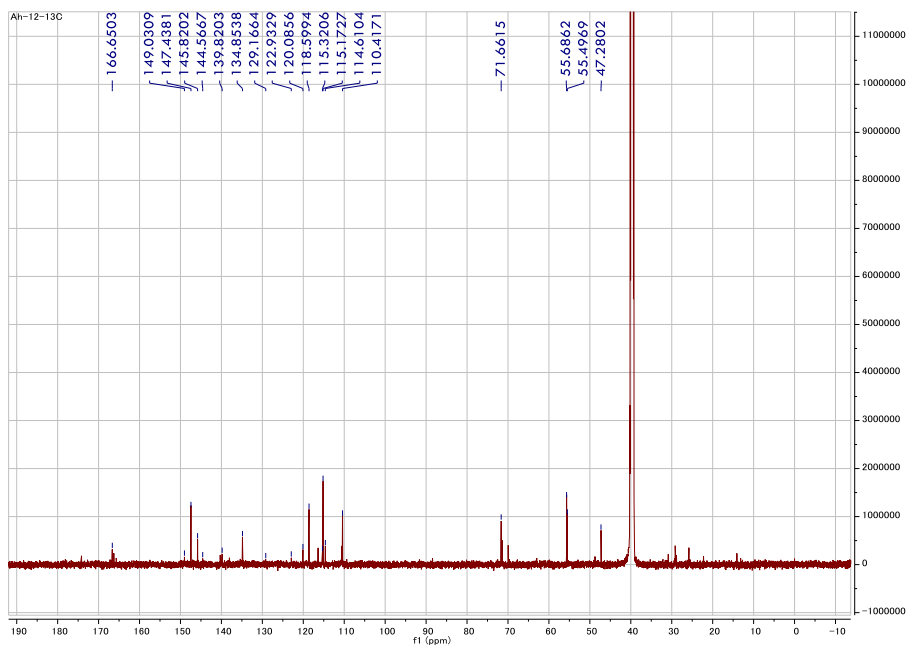


Figure S14: ¹³C-NMR spectrum of compound 3

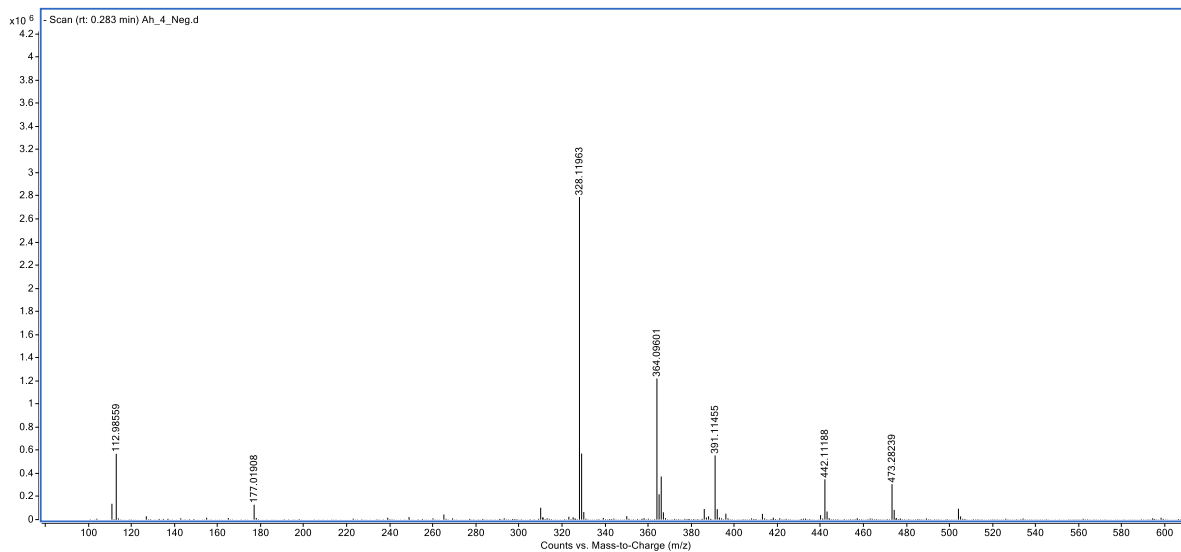


Figure S15: HR-MS spectrum of compound 4

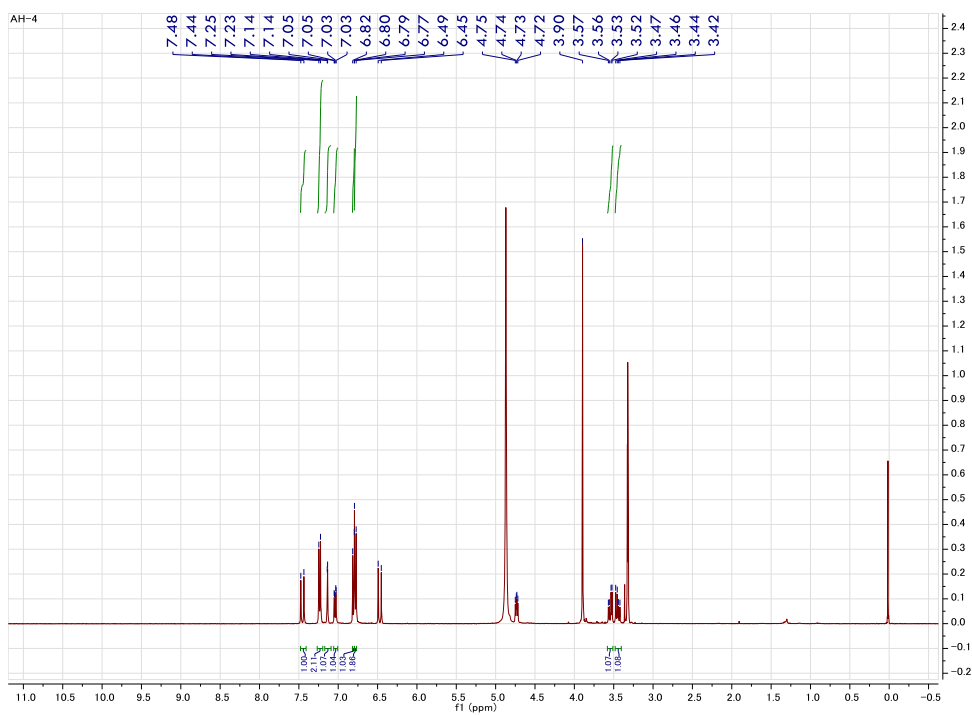


Figure S16: ¹H-NMR of compound 4

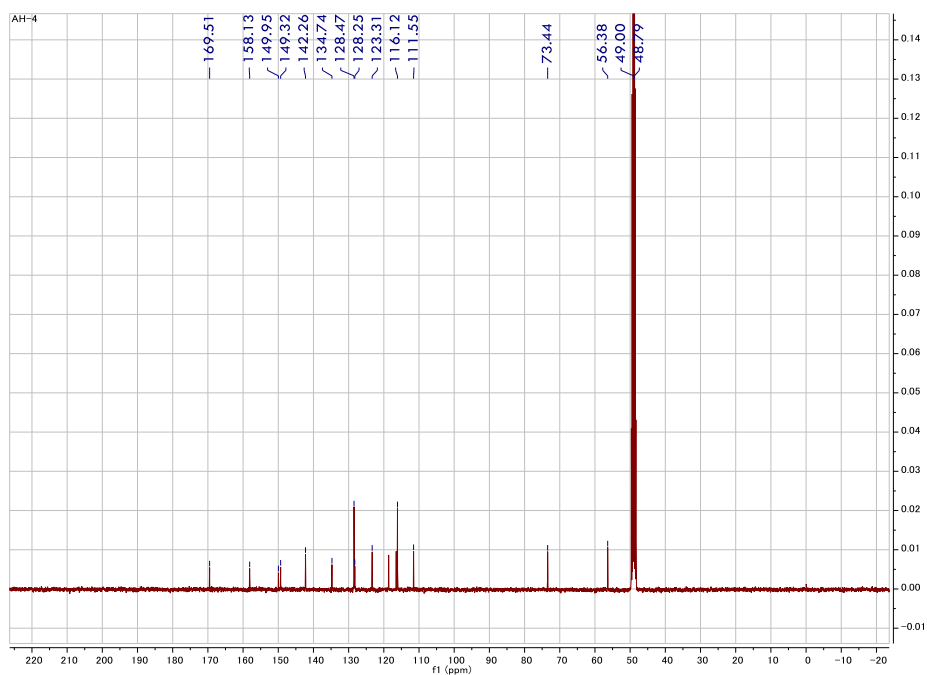


Figure S17: ^{13}C -NMR spectrum of compound 4

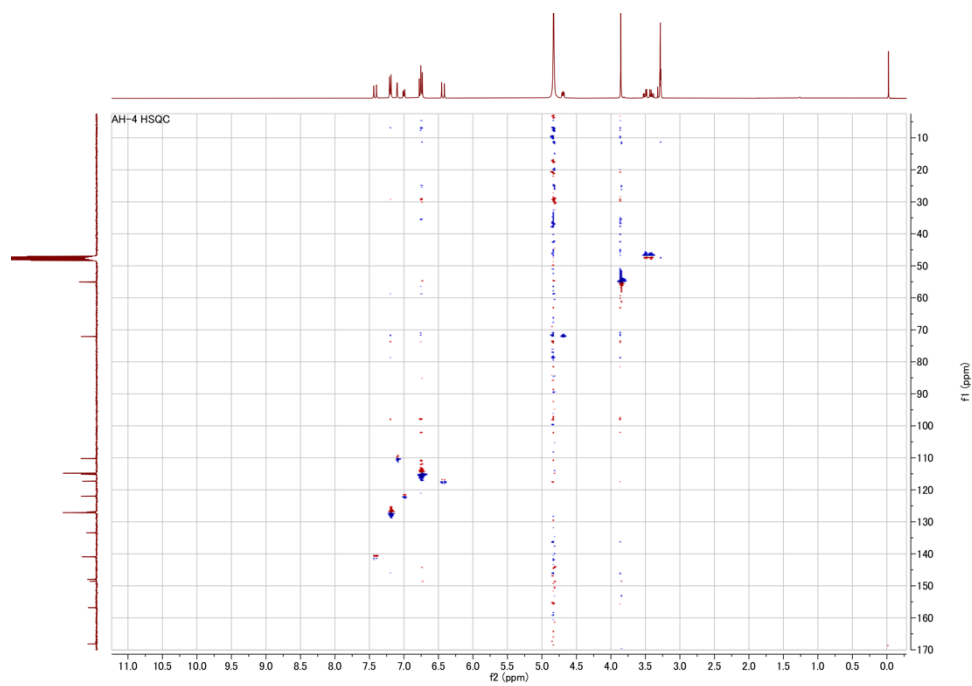


Figure S18: HSQC spectrum of compound 4

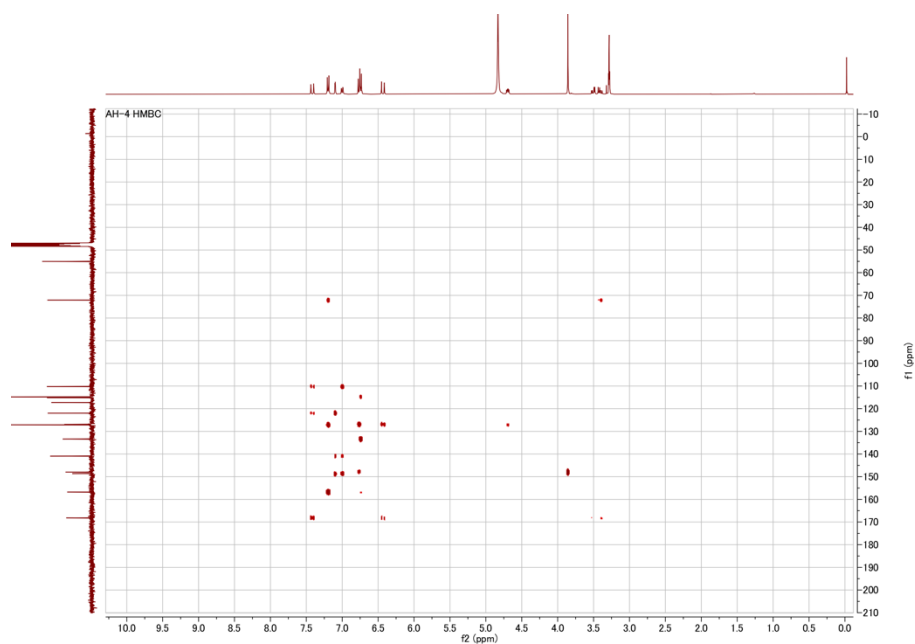


Figure S19: HMBC spectrum of compound 4

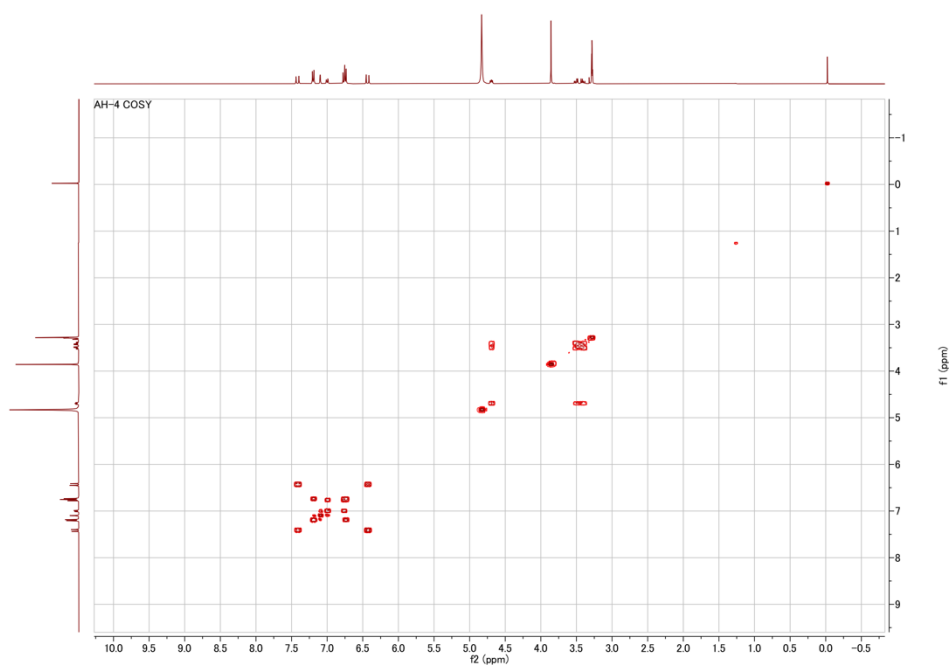


Figure S20: ¹H-¹H COSY spectrum of compound 4

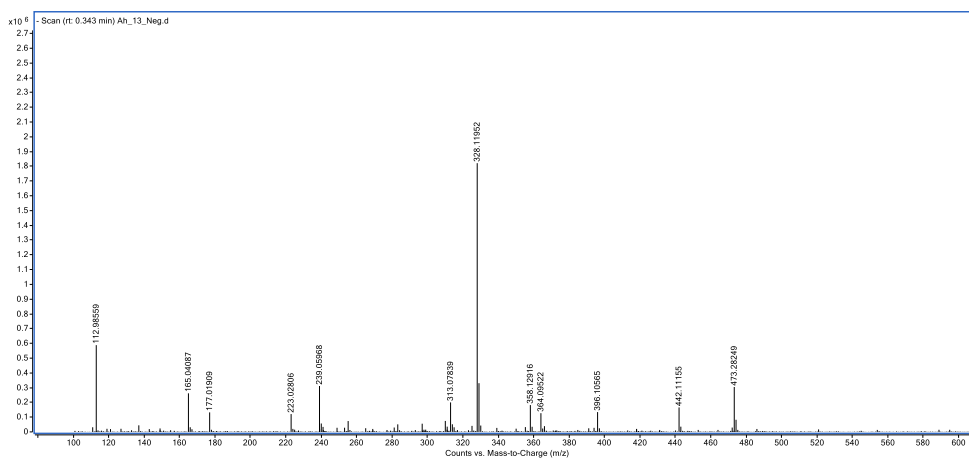


Figure S21: HR-MS of compound 5

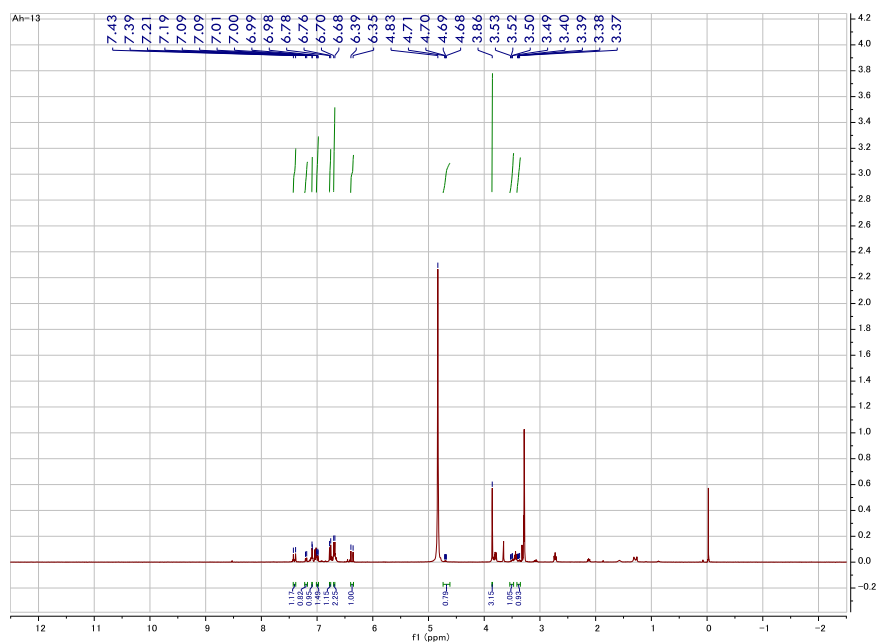


Figure S22: ¹H-NMR spectrum of compound 5

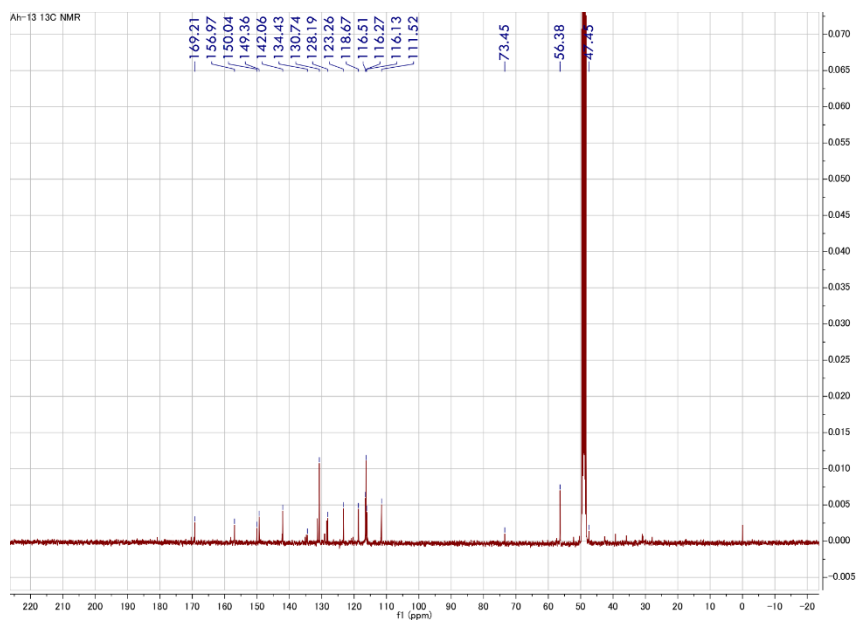


Figure S23: ¹³C-NMR spectrum of compound 5

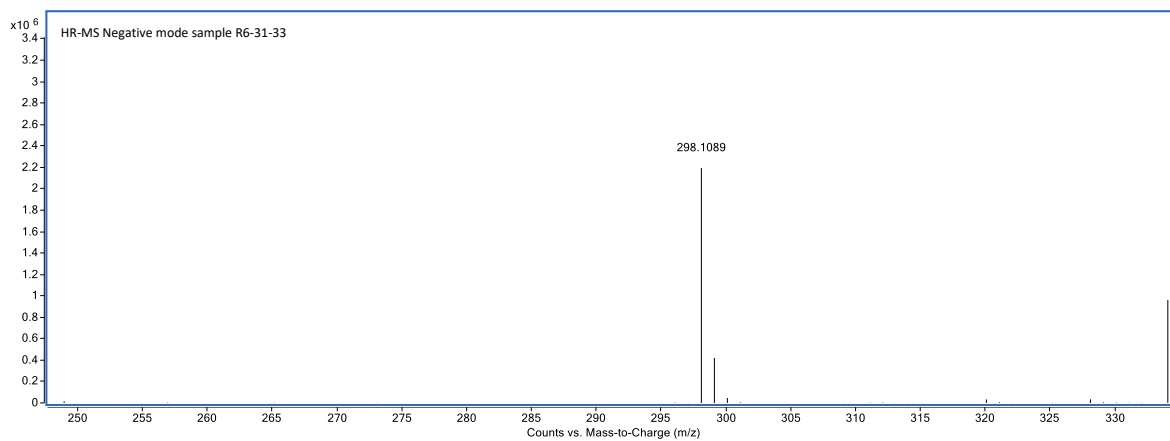


Figure S24: HR-MS of compound 6

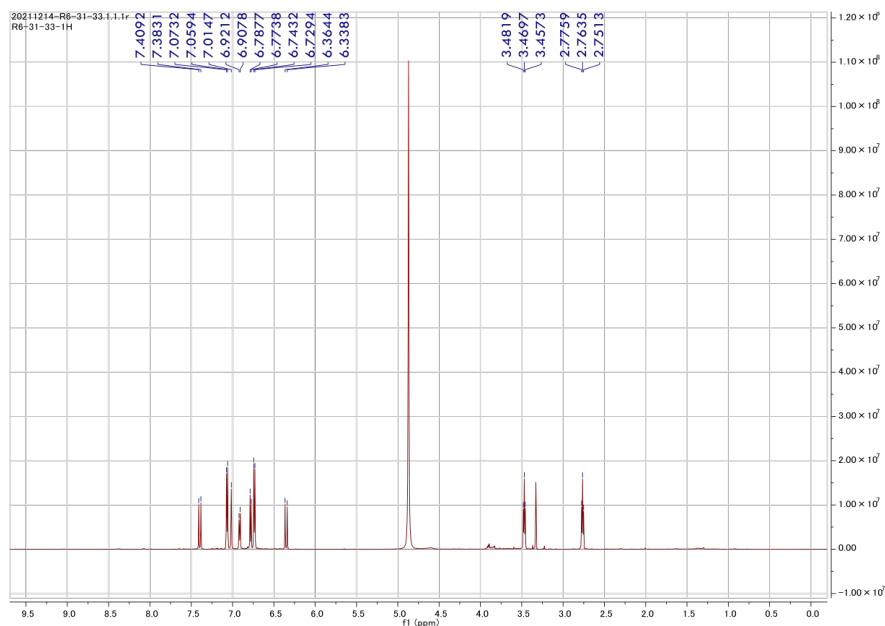


Figure S25: $^1\text{H-NMR}$ spectrum of compound 6

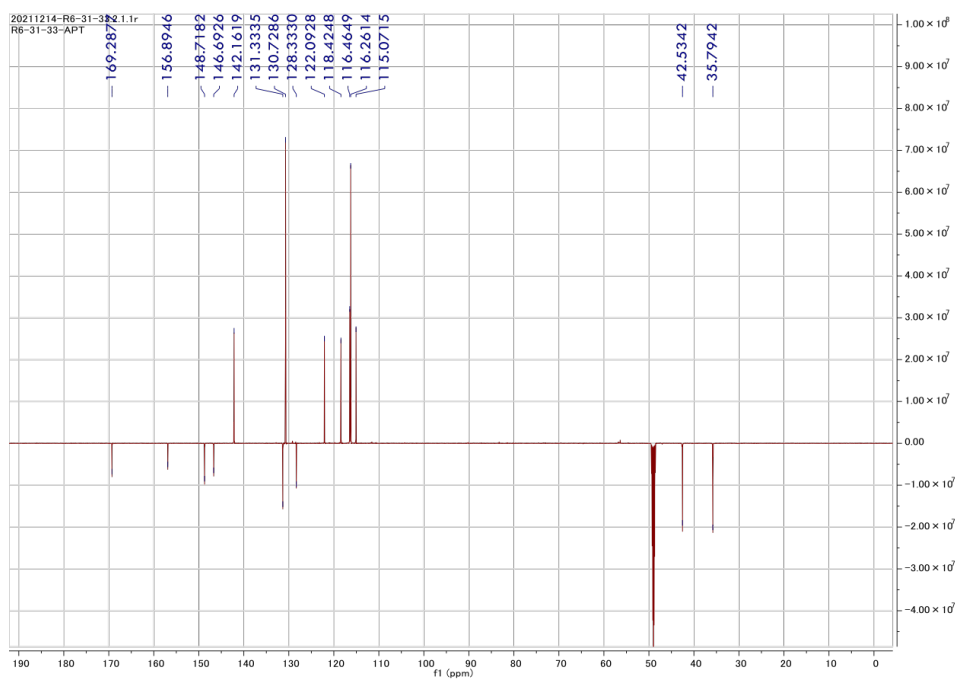


Figure S26: APT-NMR spectrum of compound 6

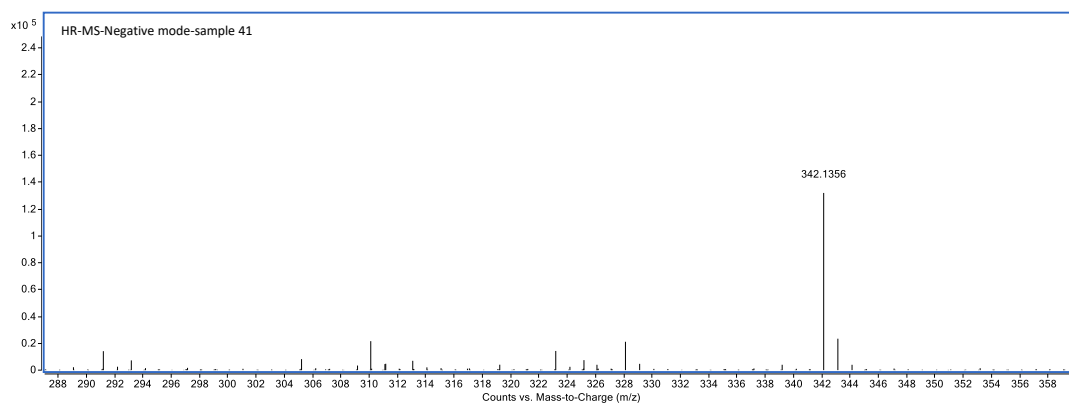


Figure S27: HR-MS spectrum of compound 7

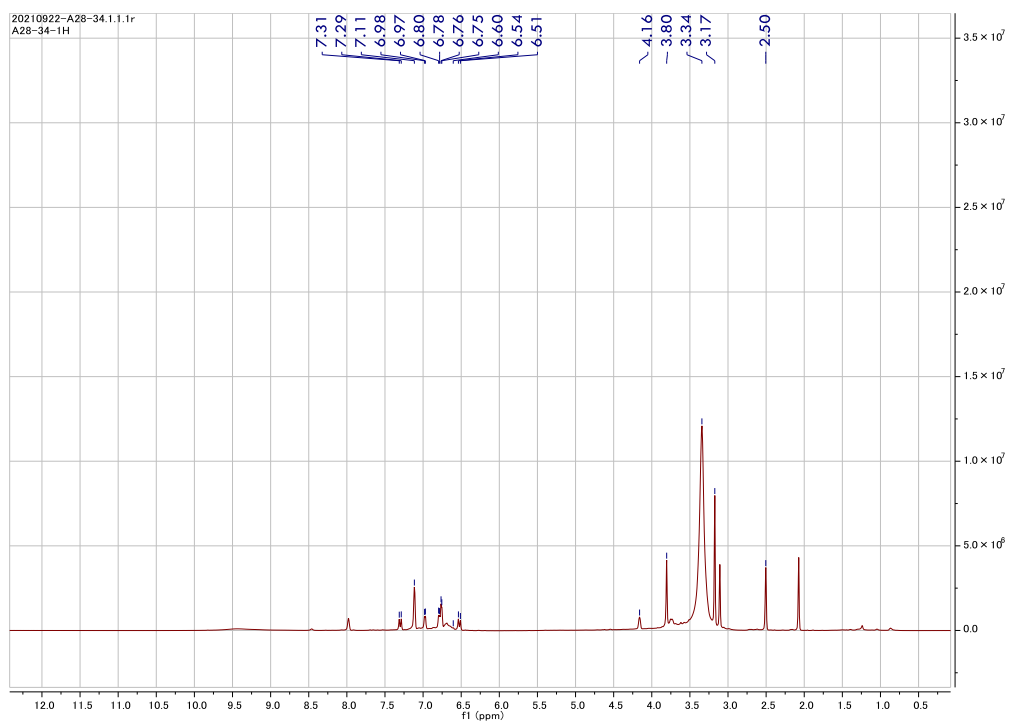


Figure S28: ¹H-NMR spectrum of compound 7

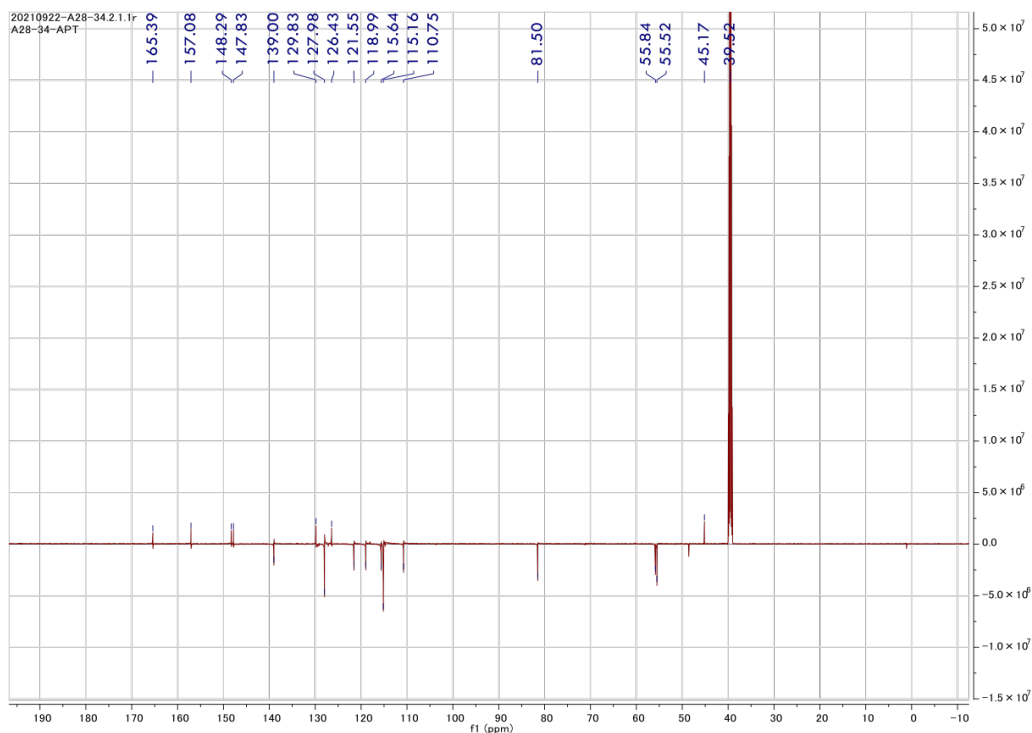


Figure S29: APT-NMR spectrum of compound 7

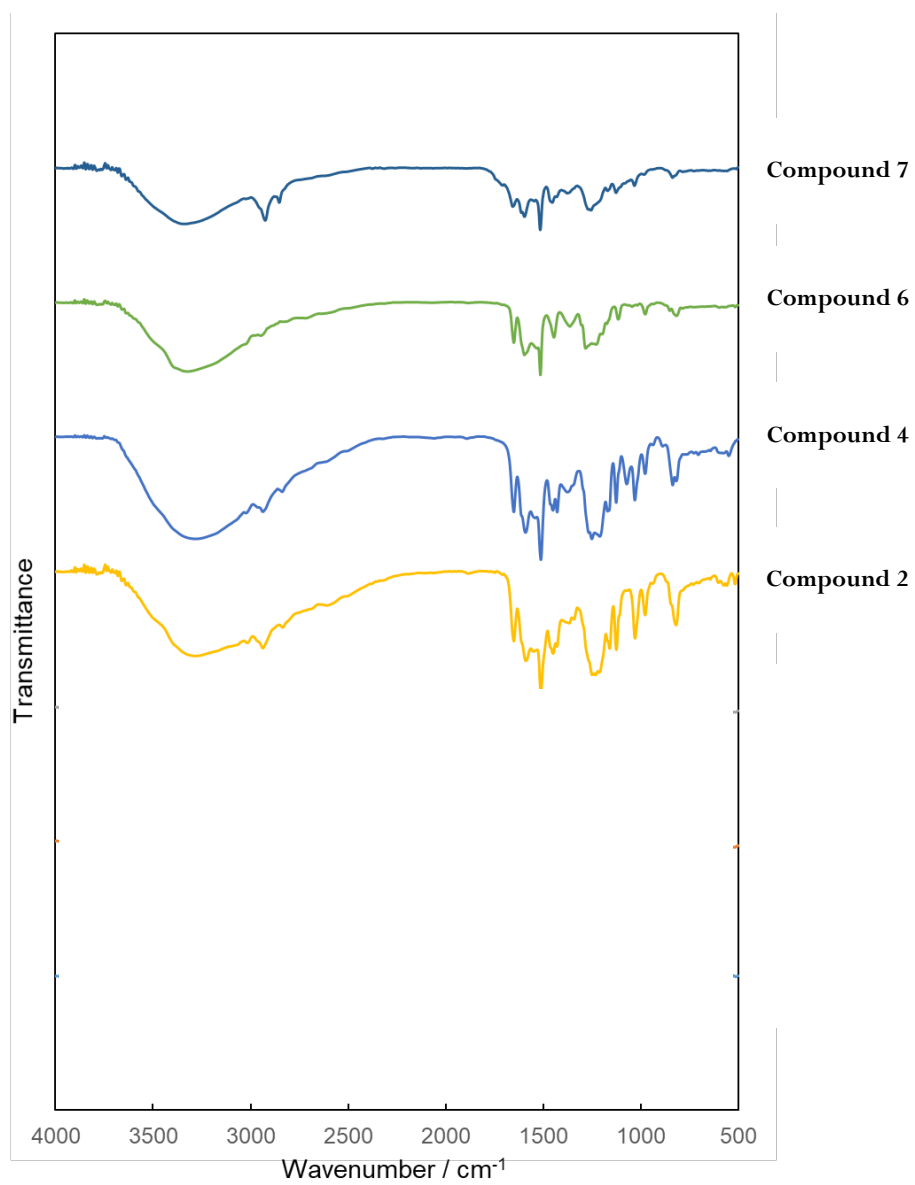


Figure S30: FT-IR spectrum of compounds 2, 4, 6, and 7