Library Screening, Divergent Evolution and Chemoenzymatic Relay Enabled Comprehensive Oxidation of *Labdane*

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SUPPLEMENTARY INFORMATION

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General Materials and Methods

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Solvents for chromatography were used as supplied by *GENERAL-REAGENT*®. Reactions were monitored by thin layer chromatography (TLC). TLC was performed with 0.25 mm Merck glass plates (silica gel 60 F_{254}) using shortwave UV light as the visualizing agent, $KMnO_4$, cerium ammonium molybdate (Hanessian's stain), phosphomolybdic acid and heat as developing agents. SiliaFlash® P60 silica gel (particle size: 40–63 μm, 230–400 mesh) was used for flash column chromatography. NMR spectra were recorded on a Bruker AVANCE NEO 400 MHz, Bruker AVANCE NEO 500 MHz and Bruker AVANCE III 600 MHz NMR spectrometer. The spectra were calibrated by using residual undeuterated solvents (for ^{1}H NMR) and deuterated solvents (for ^{13}C NMR) as internal references: undeuterated chloroform (δ_H = 7.26 ppm) and $CDCl_3$ (δ_C = 77.16 ppm); undeuterated methanol (δ_H = 3.31 ppm) and methanol-d_4 (δ_C = 49.00 ppm); undeuterated acetone (δ_H = 2.05 ppm) and acetone-d_6 (δ_C = 29.84 ppm). The following abbreviations areused to designate multiplicities: s = singlet, d = doublet, t = triplet, g= quartet, m = multiplet, br = broad. Melting points (m.p.) were recorded on an SGW X-4B apparatus. Specific rotations were recorded on Anton Paar MCP 5500. High-resolution mass spectra (HRMS) were recorded on a Waters G2-XS/APGC. Expression vectors were obtained via DNA synthesis from Universe Gene Technology (Tianjin) Co., Ltd. and were used directly to competent *E. coli* BL21(DE3). Competent *E. coli* BL21(DE3) strains were purchased from Sangon Biotech (Shanghai) Co., Ltd. All *E. coli* strains generated in this work are stored as glycerol stocks at −80 °C.

Protein and DNA Sequences

Protein sequence of Sth10:

MSNSTLVSFASLRTLLDTVVQPGGGSSSSDVLALAKTHSLELGLGAFAIVATRYMYQLLKRANALKELDGPSPISS
IWGDENLLSDFENGLSAHDELLNRYGSVCRIKGPLGEDRLWTADPRAINDIILKGFDHFHEPEGLLAWFDLSFGPT
LISQIGHKHKIQRKILNPVFTAAHMRKLTPIFHSITHYLEDVVASKVRASGGKTGIVDMYTWMSNVALEMIGQAGI
GHSFGVMEGKEPEYIDASRQLFILICRMWYIRPFLPILMKIGTTRFRQFVIERIPHGPTNEMKKVVDVMDKMATDI
YAQKKEALANGTLDSEIAAGNDIISMLLKQNEVVPPEDQMSEEEILAQVNGLIFAGHDTTSGGLTRTLHLLAQHPE
VQDQLRAEVREAHGLHGKELDYDQLNSLTYLDAVCRESLRLWSPAQTLERVAMKDWNLPLHYPVKSNDGKKMVTSL
NIPEGTHIYISLGSVNRDKQTWGDDADKFNPARWLSPPPASVTESRIPGVYSNMMTFSGGPRSCLGFKFSQLEMKV
VLSALVASFKFELGPEQHMWGAAGVLKPHVRHQDGTIDATPSLRMKVTLVEE

DNA sequence of Sth10:

GGATCCATGTCAAACTCAACATTAGTATCATTTGCATCATTACGTACATTGCTAGACACTGTTGTACAACCGGGTG
GAGGTTCTTCCTCATCCGACGTTCTGGCATTGGCCAAAACCCACAGTCTGGAGCTAGGTCTAGGGGCATTTGCTAT
TGTTGCAACAAGGTACATGTACCAGCTTTTAAAAAGGGCCAACGCCTTGAAAGAATTAGACGGACCATCTCCTATA
TCTTCAATCTGGGGGGATGAAAATCTTTTAAGTGACTTCGAAAACGGTCTAAGTGCCCATGACGAATTGTTGAATA
GGTATGGTTCTGTCTGCAGAATCAAAGGTCCATTGGGCGAAGATAGATTATGGACAGCTGATCCCAGAGCAATTAA
TGACATCATCTTAAAAGGATTCGACCATTTTCACGAACCAGAAGGTCTACTTGCTTGGTTCGACTTGAGCTTTGGT
CCAACTCTGATCTCACAGATTGGTCATAAGCATAAGATCCAAAGAAAGATTTTGAACCCGGTCTTCACAGCCGCCC
ACATGAGAAAGTTGACTCCGATCTTTCACTCCATAACACATTACCTAGAGGATGTAGTCGCCTCTAAAGTGAGAGC
TTCCGGCGGTAAAACCGGTATTGTTGACATGTACACGTGGATGTCAAATGTGGCTTTGGAGATGATAGGTCAAGCA
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GACATTTACGCTCAAAAAAAAGAAGCCCTGGCCAACGGGACGCTAGATAGTGAAATAGCAGCTGGTAACGATATCA
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AGTTAAATTCTCTAACATACCTAGATGCTGTATGTCGTGAGAGTCTTAGGTTATGGTCTCCTGCTCAAACTCTGGA
ACGTGTTGCTATGAAAGATTGGAACTTGCCACTGCATTACCCAGTTAAGTCCAACGACGGCAAGAAGATGGTAACT
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ACGACGCTGATAAATTCAATCCAGCCAGGTGGTTATCTCCACCACCCGCATCAGTGACCGAATCTAGAATCCCTGG
TGTTTATTCAAATATGATGACATTCAGTGGGGGTCCAAGAAGTTGCCTGGGGTTCAAATTCTCACAATTGGAGATG
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GTGTGCTAAAACCACATGTCAGGCATCAAGACGGCACTATAGATGCAACACCATCCTTGAGAATGAAAGTCACATT
GGTTGAAGAGTAA**AAGCTT**

Protein sequence of TnPOR:

MAPALSTNDLALIGVGVGLTTAFIFREQIFGDKKKSVPNAAKKAVADQGDPRDFVAKMIANKKRLAIFYGSQTGTA
EEYAIRIAKEAKSRFGLGSLVCDLEEYDFNKLDALPEGCAAIFVMATYGEGEPTDNAVEFMNNINEDDFEFSKGEH
RLEGLKYVVFGLGNKTYEHYNKVARDVDDKLTTLGAQRIGERGEGDDDKSMEEDYLEWKEKMWPEFARVMGVEEGA
GSDSPDFKVTEVDTHPPEKVYLGELSARALTKTRGIHDAKNPYPAPIQGIRELFAVGGERNCIHAEFNIEGSGITY
QHGDHVGLWPSNADVEVDRLLFSLGLGAPDRRTAVIDIESLDPQLAKVPFPVPTTYETVLRHYIDISSVASRQTLG
ALAKYAPTPEAGAALTALATDKAQYGSIVAGGCLKLGEVLQLVAGNSINSKPTGDNTTTWNIPFDVIVSAIPRLQP
RYYSISSSPKLHPTSIHVTCVVLKYESEASERAPSKWVFGVGSNYLLNLKMAAHGEQAPLLSEGGVESVTNPIYAI
SGPRSSYQGEAGYKAPIHVRRSTFRLPTNPKTPVIMIGPGTGVAPFRGFVQERVALARKAIEKNGEDALADWGQIS
LYYGCRDENEDFLYKDEWPEYQSELKGKFTMRNAFSRSGARKPDGSKIYVQDLLWEDRAAVSEAINEKRGYVYICG
DAKNMSKAVEDILIKIFNEAGKNGTEELKTMKERSRLLLDVWS

DNA sequence of TnPOR:

GAATTCATGGCCCCAGCTCTATCCACAAATGACTTAGCTTTAATCGGCGTAGGCGTAGGCTTAACGACGGCTTTTA
TTTTTAGGGAACAAATCTTTGGCGATAAAAAAAAAAGTGTTCCTAATGCCGCAAAAAAAGCCGTCGCAGATCAAGG
TGATCCCCGTGATTTCGTTGCTAAAATGATTGCTAATAAGAAGCGTTTGGCAATTTTTTATGGTTCTCAAACCGGT
ACAGCTGAGGAATATGCGATTCGTATAGCAAAAGAAGCTAAATCCAGATTCGGCTTGGGCTCTTTGGTTTGCGACC
TTGAAGAATACGATTTTAACAAGTTGGATGCTCTTCCAGAGGGTTGCGCTGCCATCTTCGTGATGGCAACGTATGG
TGAGGGTGAACCAACGGACAACGCTGTAGAGTTTATGAATAATATAAATGAAGATGACTTCGAGTTTAGTAAAGGT
GAACATCGTCTGGAGGGGCTAAAATATGTGGTGTTTGGTTTAGGTAACAAAACGTATGAGCATTACAACAAGGTGG
CTAGGGATGTTGATGATAAATTAACTACATTGGGTGCTCAGAGAATTGGTGAAAGAGGTGAGGGTGATGATGATAA
GTCTATGGAAGAAGATTACTTAGAATGGAAAGAAAAGATGTGGCCTGAGTTTGCAAGAGTGATGGGAGTTGAAGAA
GGTGCTGGTTCTGATTCTCCGGATTTTAAAGTGACGGAAGTCGATACGCACCCACCAGAAAAGGTATATCTTGGCG
AACTGAGCGCAAGAGCTCTTACCAAGACTCGTGGTATTCATGATGCAAAAAACCCTTACCCAGCCCCTATTCAAGG
GATTAGAGAGCTATTTGCCGTTGGTGGGGAAAGAAACTGTATCCATGCCGAGTTCAACATTGAAGGTTCAGGTATT
ACATATCAACATGGAGACCACGTTGGCCTTTGGCCATCTAACGCAGATGTAGAAGTCGATAGGTTACTGTTCTCTT
TAGGGTTGGGCGCACCAGACAGGAGGACCGCTGTTATTGATATAGAGTCTCTGGACCCACAACTTGCTAAAGTTCC
TTTTCCAGTCCCAACTACCTATGAAACAGTTTTGAGGCATTACATTGATATTAGCTCAGTTGCTTCAAGACAAACT
CTGGGTGCCTTAGCCAAATACGCTCCAACGCCTGAAGCCGGTGCTGCCTTAACAGCTCTGGCAACCGACAAAGCAC
AATACGGCAGCATTGTGGCTGGTGGTTGCTTGAAACTAGGTGAGGTTCTGCAATTGGTTGCTGGAAACTCAATTAA
TTCTAAACCTACAGGCGACAACACCACTACGTGGAACATTCCATTCGACGTGATTGTCTCAGCTATTCCTAGGTTA
CAACCTAGATACTATTCTATTTCCTCCAGCCCGAAGCTGCACCCCACATCTATTCATGTTACGTGTGTAGTGTTGA
AATACGAAAGTGAAGCCTCAGAAAGAGCACCGTCAAAGTGGGTTTTTGGGGTTGGATCTAATTATTTACTAAACCT
AAAGATGGCTGCACACGGTGAACAAGCACCACTGTTGTCTGAGGGTGGTGTCGAGTCAGTAACAAATCCTATCTAT
GCCATCTCTGGCCCAAGATCTTCTTACCAAGGTGAAGCTGGTTACAAAGCGCCTATTCATGTCAGAAGGAGTACGT
TCAGATTACCAACGAACCCGAAAACACCCGTTATTATGATCGGTCCAGGTACCGGTGTAGCACCTTTCAGAGGTTT
TGTGCAGGAGAGGGTCGCTTTGGCTAGAAAAGCTATTGAAAAAAATGGTGAAGACGCCTTAGCTGATTGGGGACAG

ATTTCTTTGTATTACGGATGCCGTGACGAAAATGAGGACTTCCTTTACAAAGATGAGTGGCCGGAATACCAGTCAG
AGTTGAAGGGAAAATTTACTATGAGAAATGCTTTTTCTAGATCAGGGGCGCGTAAGCCTGATGGTTCCAAGATATA
TGTTCAAGATCTATTGTGGGAAGATAGAGCAGCGGTTTCCGAAGCCATAAATGAAAAGAGAGGGTACGTCTATATT
TGCGGAGATGCTAAGAATATGTCTAAAGCTGTTGAGGATATATTGATAAAAATCTTCAATGAAGCGGGGAAAAACG
GTACAGAAGAGTTGAAAACGATGAAGGAAAGATCTAGACTGTTATTAGATGTGTGGTCATAA**ACTAGT**

Protein sequence of AndA:

MTIESKNYPPIRRVNASQGSDAAYQILQEDGCVIVEQVICPNIIAKISDDVNRVMDKATIGAKKGEQTHIINMHNR
TIHMGDLVLTSKTYRDELLNLPFAHEVLEKVFKKDSGDYWLNMGNILNMLPGAEAQRPHRDDYLYPVSQHMDPATS
PDLMINITFPLNEFRHDNGGTLLLPKSHTGPNADFYANAEDLPAAEMQVGDALIFTGKCVHGGGANRSDKPRIGLA
LAAQPGYLTPRESNVNVPRDIVETMTPLAQRMIGWGTVRTKDTYGLNMLQDKDFHEALGLKSKTA

DNA sequence of AndA:

ATGACCATTGAAAGCAAAAACTACCCGCCGATTCGTCGTGTGAATGCCAGTCAGGGTAGCGATGCAGCATATCAGA
TTCTGCAGGAAGATGGTTGCGTTATTGTTGAACAGGTTATTTGCCCGAATATTATTGCAAAAATCAGCGATGATGT
GAATCGTGTTATGGATAAAGCAACCATTGGCGCAAAAAAAGGTGAACAGACCCATATTATTAACATGCATAATCGT
ACCATCCATATGGGCGATCTGGTGCTGACCAGCAAAACCTATCGTGATGAACTGCTGAATCTGCCGTTTGCACATG
AAGTTCTGGAAAAAGTTTTTAAAAAGGACAGTGGCGATTATTGGCTGAATATGGGTAATATTCTGAATATGCTGCC
GGGTGCAGAAGCCCAGCGTCCGCATCGCGATGATTATCTGTATCCGGTTAGCCAGCATATGGATCCGGCAACCAGC
CCGGATCTGATGATTAATATTACCTTTCCGCTGAATGAATTCCGCCATGATAATGGCGGCACCCTGCTGCTGCCGA
AAAGCCATACCGGTCCGAATGCCGATTTTTATGCAAATGCCGAAGATCTGCCGGCAGCAGAAATGCAGGTTGGTGA
TGCACTGATTTTTACCGGTAAATGTGTTCATGGCGGCGGCGCCAATCGCAGCGATAAACCGCGTATTGGTCTGGCA
CTGGCCGCACAGCCGGGTTATCTGACCCCGCGTGAAAGCAATGTTAATGTGCCGCGCGATATTGTTGAAACCATGA
CCCCGCTGGCCCAGCGTATGATTGGCTGGGGTACCGTGCGCACCAAAGATACCTATGGTCTGAATATGTTACAGGA
TAAAGATTTTCACGAGGCACTGGGTCTGAAAAGCAAAACCGCC

Protein sequence of Trt7:

MTGQAEAIRRVHPTVSPKQAAQMLQEDGVIILKSFLAPDVMQRFQAEVDEDVEKTSTGARMKAYKLVNDKTKHMAD
LIVRSEVFRSDILTHPLYHAIADELFRADYGDHWLNASAVLQLMPGAPAQQLHRDEEIFAASKFRSPTDPQLSLSC
LVALTEFTEENGATRLIPGSHLWDSAHPAPSPDQTVPAIMQPGEAILFLGSLFHGGGENRTENVRRGLGMSLIPCQ
FTPYSSHMHVPRTIIETMTPLAQKLVGWRTVESHRQYPFWQGGDRRLEDVLGLASREA

DNA sequence of Trt7:

ATGACCGGCCAGGCAGAAGCAATTCGTCGTGTTCATCCGACCGTGAGCCCGAAACAGGCAGCACAGATGCTGCAGG
AAGATGGTGTGATTATTCTGAAAAGTTTTCTGGCACCGGATGTGATGCAGCGTTTTCAGGCCGAAGTTGATGAAGA
TGTTGAAAAAACCAGCACCGGTGCACGTATGAAAGCCTATAAACTGGTGAATGATAAAACCAAACACATGGCCGAT
CTGATTGTGCGTAGCGAAGTGTTTCGTAGCGATATTCTGACCCATCCGCTGTATCATGCAATTGCAGATGAACTGT
TTCGTGCAGATTATGGTGATCATTGGCTGAATGCCAGCGCCGTGCTGCAGCTGATGCCGGGTGCCCCTGCCCAGCA

GCTGCATCGTGATGAAGAAATTTTTGCAGCCAGTAAATTTCGCAGTCCGACCGATCCGCAGCTGAGTCTGAGTTGT
CTGGTGGCCCTGACCGAATTTACCGAAGAAAATGGTGCCACCCGCCTGATTCCGGGTAGTCATCTGTGGGATAGTG
CCCATCCGGCCCCGAGCCCGGATCAGACAGTTCCGGCCATTATGCAGCCGGGCGAAGCAATTCTGTTTCTGGGTAG
TCTGTTTCATGGTGGCGGTGAAAATCGCACCGAAAATGTGCGTCGCGGTCTGGGTATGAGTCTGATTCCGTGTCAG
TTTACCCCGTATAGCAGCCACATGCATGTTCCGCGCACCATTATTGAAACCATGACCCCGCTGGCACAGAAACTGG
TTGGCTGGCGCACCGTTGAAAGTCATCGTCAGTATCCGTTTTGGCAGGGCGGCGATCGTCGCCTGGAAGATGTGCT
GGGCCTGGCAAGTCGCGAAGCA

Protein sequence of MERO1:

MTIKEMPQPKTFGELKNLPLLNTDKPVQALMKIADELGEIFKFEAPGRVTRYLSSQRLIKEACDESRFDKNLSQAL
KFARDFGGDGLVTSWTHEKNWKKAHNILLPSFSQQAMKGYHAMMVDIAVQLVQKWERLNADEHIEVSEDMTRLTLD
TIGLCGFNYRFNSFYRDQPHPFIISMVRALDEVMNKLQRANPDDPAYDENKRQCQEDIKVMNDLVDKIIADRKARG
EQSDDLLTQMLNGKDPETGEPLDDGNISYQIITFLIAGHETTSGLLSFALYFLVKNPHVLQKVAEEAARVLVDPVP
SYKQVKQLKYVGMVLNEALRLWPTAPAFSLYAKEDTVLGGEYPLEKGDEVMVLIPQLHRDKTIWGDDVEEFRPERF
ENPSAIPQHAFKPFGNGQRACIGQQFALHEATLVLGMMLKHFDFEDHTNYELDIKETLTLKPEGFVVKAKSKKIPL
GGIPSPSTEQSAKKVRKKAENAHNTPLLVLYGSNMGTAEGTARDLADIAMSKGFAPQVATLDSHAGNLPREGAVLI
VTASYNGHPPDNAKQFVDWLDQASADEVKGVRYSVFGCGDKNWATTYQKVPAFIDETLAAKGAENIADRGEADASD
DFEGTYEEWREHMWSDVAAYFNLDIENSEDNKSTLSLQFVDSAADMPLAKMHGAFSTNVVASKELQQPGSARSTRH
LEIELPKEASYQEGDHLGVIPRNYEGIVNRVTARFGLDASQQIRLEAEEEKLAHLPLAKTVSVEELLQYVELQDPV
TRTQLRAMAAKTVCPPHKVELEALLEKQAYKEQVLAKRLTMLELLEKYPACEMKFSEFIALLPSIRPRYYSISSSP
RVDEKQASITVSVVSGEAWSGYGEYKGIASNYLAELQEGDTITCFISTPQSEFTLPKDPETPLIMVGPGTGVAPFR
GFVQARKQLKEQGQSLGEAHLYFGCRSPHEDYLYQEELENAQSEGIITLHTAFSRMPNQPKTYVQHVMEQDGKKLI
ELLDQGAHFYICGDGSQMAPAVEATLMKSYADVHQVSEADARLWLQQLEEKGRYAKDVWAG

DNA sequence of MERO1:

ATGACAATTAAAGAAATGCCTCAGCCAAAAACGTTTGGAGAGCTTAAAAATTTACCGTTATTAAACACAGATAAAC
CGGTTCAAGCTTTGATGAAAATTGCGGATGAATTAGGAGAAATCTTTAAATTCGAGGCGCCTGGTCGTGTAACGCG
CTACTTATCAAGTCAGCGTCTAATTAAAGAAGCATGCGATGAATCACGCTTTGATAAAAACTTAAGTCAAGCGCTT
AAATTCGCGCGTGATTTTGGCGGAGACGGGTTAGTTACAAGCTGGACGCATGAAAAAAATTGGAAAAAAGCGCATA
ATATCTTACTTCCAAGCTTTAGTCAGCAGGCAATGAAAGGCTATCATGCGATGATGGTCGATATCGCCGTGCAGCT
TGTTCAAAAGTGGGAGCGTCTAAATGCAGATGAGCATATTGAAGTATCGGAAGACATGACACGTTTAACGCTTGAT
ACAATTGGTCTTTGCGGCTTTAACTATCGCTTTAACAGCTTTTACCGAGATCAGCCTCATCCATTTATTATAAGTA
TGGTCCGTGCACTGGATGAAGTAATGAACAAGCTGCAGCGAGCAAATCCAGACGACCCAGCTTATGATGAAAACAA
GCGCCAGTGTCAAGAAGATATCAAGGTGATGAACGACCTAGTAGATAAAATTATTGCAGATCGCAAAGCAAGGGGT
GAACAAAGCGATGATTTATTAACGCAGATGCTAAACGGAAAAGATCCAGAAACGGGTGAGCCGCTTGATGACGGGA
ACATTAGCTATCAAATTATTACATTCTTAATTGCGGGACACGAAACAACAAGTGGTCTTTTATCATTTGCGCTGTA
TTTCTTAGTGAAAAATCCACATGTATTACAAAAAGTAGCAGAAGAAGCAGCACGAGTTCTAGTAGATCCTGTTCCA
AGCTACAAACAAGTCAAACAGCTTAAATATGTCGGCATGGTCTTAAACGAAGCGCTGCGCTTATGGCCAACTGCGC

CTGCGTTTTCCCTATATGCAAAAGAAGATACGGTGCTTGGAGGAGAATATCCTTTAGAAAAAGGCGACGAAGTAAT

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GGCTTTGTGCAGGCGCGCAAACAGCTAAAAGAACAAGGACAGTCACTTGGAGAAGCACATTTATACTTCGGCTGCC

GTTCACCTCATGAAGACTATCTGTATCAAGAAGAGCTTGAAAACGCCCAAAGCGAAGGCATCATTACGCTTCATAC

CGCTTTTTCTCGCATGCCAAATCAGCCGAAAACATACGTTCAGCACGTAATGGAACAAGACGGCAAGAAATTGATT

GAACTTCTTGATCAAGGAGCGCACTTCTATATTTGCGGAGACGGAAGCCAAATGGCACCTGCCGTTGAAGCAACGC

TTATGAAAAGCTATGCTGACGTTCACCAAGTGAGTGAAGCAGACGCTCGCTTATGGCTGCAGCAGCTAGAAGAAAA

AGGCCGATACGCAAAAGACGTGTGGGCTGGG

Protein sequence of KSA15 (heme domain):

MTIKEMPQPKTFGELKNLPLLNTDKPVQALMKIADELGEIFKFEAPGYVFRYLSSQRLIKEACDESRFDKNLSQAL

KFIRDFMGDGLATSWTHEKNWKKAHNILLPSFSQQAMKGYHAMMVDIAVQLVQKWERLNADEHIEVPEDMTRLTLD

TIGLCGFNYRFNSFYRDQPHPFITSMVRALDEAMNKLQRANPDDPAYDENKRQFQEDIKVMNDLVDKIIADRKASG

EQSDDLLTHMLNGKDPETGEPLDDENIRYQIITFLIAGHETTSGLLSFALYFLVKNPHVLQKAAEEAARVLVDPVP

SYKQVKQLKYVGMVLNEALRLWPTAPAFSLYAKEDTVLGGEYPLEKGDELMVLIPQLHRDKTIWGDDVEEFRPERF

ENPSAIPQHAFKPFGNGQRACIGQQFALHEATLVLGMMLKHFDFEDHTNYELDIKETLTLKPEGFVVKAKSKKIPL

GGIPSPSTEQSAKKVRKKAENAHNTP

DNA sequence of KSA15 (heme domain):

ATGACAATTAAAGAAATGCCTCAGCCAAAAACGTTTGGAGAGCTTAAAAATTTACCGTTATTAAACACAGATAAAC
CGGTTCAAGCTTTGATGAAAATTGCGGATGAGTTAGGTGAGATCTTTAAGTTCGAGGCCCCCGGGTATGTATTCCG
CTACCTGTCTAGTCAACGCTTAATCAAGGAAGCGTGTGACGAGTCTCGCTTCGACAAGAACTTAAGTCAGGCACTT
AAGTTCATTCGCGACTTCATGGGCGATGGCTTGGCGACATCGTGGACCCACGAGAAGAATTGGAAGAAGGCACACA
ATATTTTGCTTCCGAGCTTCTCACAACAAGCCATGAAGGGGTATCATGCAATGATGGTTGACATCGCAGTGCAGCT
CGTTCAGAAGTGGGAGCGCTTGAACGCTGATGAGCACATTGAAGTCCCAGAGGACATGACGCGTCTGACATTGGAC
ACGATTGGCTTATGTGGCTTTAATTATCGTTTTAACTCCTTCTATCGTGATCAACCGCACCCATTTATTACCTCTA
TGGTGCGCGCACTGGACGAAGCCATGAATAAGTTACAACGCGCAAACCCTGATGACCCCGCGTATGACGAGAACAA
GCGCCAATTTCAAGAGGACATCAAGGTTATGAACGACTTAGTAGACAAGATCATCGCGGACCGCAAGGCATCTGGT
GAACAGTCCGATGACCTGCTGACACACATGTTAAACGGGAAGGACCCAGAAACGGGCGAGCCACTGGACGATGAAA
ACATCCGTTATCAAATTATCACCTTCTTAATCGCAGGTCACGAGACCACGTCCGGCCTGCTTTCCTTCGCCCTCTA
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AGCTACAAGCAAGTTAAGCAATTGAAGTATGTCGGAATGGTTCTTAATGAGGCGCTGCGTCTCTGGCCAACTGCGC
CCGCCTTTAGCTTGTACGCGAAAGAGGACACTGTACTGGGCGGCGAGTACCCGTTAGAGAAGGGAGACGAACTGAT
GGTTTTGATTCCACAGTTACACCGTGACAAGACGATTTGGGGCGACGACGTTGAGGAGTTTCGCCCTGAACGCTTC
GAAAACCCGTCAGCGATTCCACAGCATGCCTTCAAGCCATTTGGTAATGGGCAACGCGCCTGCATCGGTCAGCAGT
TCGCTCTTCATGAAGCAACGCTGGTACTTGGTATGATGCTAAAACACTTTGACTTTGAAGATCATACAAACTACGA
GCTCGATATTAAAGAAACTTTAACGTTAAAACCTGAAGGCTTTGTGGTAAAAGCAAAATCGAAAAAAATTCCGCTT
GGCGGTATTCCTTCACCTAGCACTGAACAGTCTGCTAAAAAAGTACGCAAAAAGGCAGAAAACGCTCATAATACGC
CG

Protein sequence of Opt-13:

MLPKLVITHRVHEEILQLLAPHCELITNQTDSTLTREEILRRCRDAQAMMAFMPDRVDADFLQACPELRVIGCALK
GFDNFDVDACTARGVWLTFVPDLLTVPTAELAIGLAVGLGRHLRAADAFVRSGKFKGWQPHFYGTGLDNSTVGFLG
MGAIGLAMADRLQGWGATLQYHAAKALDTQTEQRLGLRQVACSELFASSDFILLALPLNADTLHLVNAELLALVRP
GALLVNPCRGSVVDEAAVLAALERGQLGGYAADVFEMEDWARADRPLCIDPALLAHPNTLFTPHIGSAVRAVRLEI
ERCAAQNILQALAGERPINAVNRLPKANPAAD

DNA sequence of Opt-13:

AGTCTGCGGCAGGATTGGCCTTGGGCAGACGGTTCACAGCGTTGATTGGGCGCTCACCTGCCAATGCCTGGAGGAT
GTTCTGCGCTGCACAACGTTCAATCTCCAGGCGCACCGCGCGCACTGCCGACCCTATGTGCGGAGTGAACAGCGTA
TTCGGATGCGCGAGCAGCGCAGGATCGATGCACAGCGGCCGGTCCGCGCGAGCCCAGTCTTCCATTTCGAATACAT
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TATAACGAGTTTCGGCAGCAT
```

Generation of pESC-URA-Sth10-TnPOR Expression Vector

Gene of Sth10 were excised with *BamHI* and *HindIII* and cloned into the same sites of the pESC-URA to yield the plasmid pESC-URA-Sth10. Gene of TnPOR were excised with *SpeI* and *EcoRI* and cloned into the same sites of the pESC-URA-Sth10 to yield the plasmid pESC-URA-Sth10-TnPOR. The resulting plasmid were further confirmed by DNA sequencing. Afterwards, they were transformed into *S. cerevisiae* YPH499 using the Frozen-EA Yeast Transformation IITM Kit (Zymo Research) and verified by PCR amplification.

Generation of pET22b(+)-MERO1and pRSF-Opt13 Co-expression Vector

The respective gene fragment of MERO1 was synthesized and assembled directly into pET22b(+) between *NdeI* and *XhoI* by Universe Gene Technology (Tianjin) Co to yield vector pET22b(+)-MERO1. Ltd. Opt-13 gene were inserted between *NcoI* and *XhoI* restriction sites of pRSF-1b to yield vector pRSF-Opt13. The resulting vectors pET22b(+)-MERO1 and pRSF-Opt13 were used to co-transform competent *E. coli* strain BL21(DE3).

Generation of pET22b(+)-KSA15 and pRSF-Opt13 Co-expression Expression Vector

The respective gene fragment of KSA15 heme domain was obtained via DNA synthesis from Universe Gene Technology (Tianjin) Co. A standard overlap extension PCR was performed on pET22b(+)-MERO1[1] to amplify its reductase domain and the rest of its backbone (minus its heme domain). Separately, a standard overlap extension PCR was performed on the respective heme domain gene fragments and the resulting linear fragments were ligated using NEBuilder HiFi DNA assembly to produce pET22b(+)-KSA15. The resulting vector pET22b(+)-KSA15 along with pRSF-Opt13 were used to co-transform competent *E. coli* strain BL21(DE3).

Generation of pET28a(+)-AndA and pET28a(+)-Trt7 expression Expression Vectors

The respective gene fragment of AndA and Trt7 was obtained via DNA synthesis from Universe Gene Technology (Tianjin) Co., Ltd. Both genes were inserted between NdeI and XhoI restriction sites of pET-

28a to yield vectors pET28a(+)-AndA and pET28a(+)-Trt7. The vectors were used directly to transform competent *E. coli* strain BL21(DE3).

Generation of Mutants of AndA

Site-saturated mutagenesis on pET28a(+)-AndA was performed by using standard QuikChange PCR method with primers containing the desired mutation at the appropriate position. The resulting PCR products were digested with DpnI, gel purified, and used directly to competent *E. coli* strain BL21(DE3).

General synthetic procedures

Method A: Sth10

S. cerevisiae strains hosting pESC-URA-Sth10-TnPOR were first inoculated into 4 mL uracil-free synthetic glucose medium (SD-URA, FunGenome Company) and cultured at 30 °C for 48 h at 220 rpm. Then cell culture was transfer into 50 mL uracil-free synthetic glucose medium (SD-URA, FunGenome Company) and cultured at 30 °C for 48 h at 220 rpm. 54 mL uracil-free culture was directly transfer 420 mL inducible medium which contained 1.8% (w/v) galactose and 0.2% (w/v) glucose and used directly for subsequent whole cell transformation.

Method B: Preparation of Clarified Lysate of *E. coli* Expressing AndA Mutants and Trt7

An overnight culture of recombinant *E. coli* BL21(DE3) cells harboring pET-28a(+)-based vector for expressing of AndA mutants or Trt7 plasmid was used to inoculate 500 mL TB media (in 2 L Erlenmeyer flasks) containing 50 µg/mL kanamycin. The cultures were shaken at 220 rpm at 37 °C for roughly 4 hours or until an optical density of $OD_{600} = 0.7 – 1.0$ was reached. The cultures were cooled to 20 °C (20 min) and then induced with IPTG to final concentrations of 0.5 mM. The cultures were allowed to continue for another 20 hours at 20 ºC and shaking at 220 rpm. Cell were harvested by centrifugation (4 °C, 15 min, 4,200 rpm), and the cell pellet was resuspended to 50 mM kPi (pH = 8.0) to required optical density of OD_{600}. Cells were disrupted by sonication (5 min, cycle = 1 s on/2 s off, 50% amplitude) and used directly for subsequent reactions.

Clarified lysates containing the desired enzyme variants were prepared from 50 mL expression cultures according to the procedure described above.

Method C: Preparation of Clarified Lysate of *E. coli* Expressing P450BM3 Variant and Opt13 in Co-transformed Cells

An overnight culture of recombinant *E. coli* BL21(DE3) cells harboring pET-22b(+)-based vector for expressing of $P450_{BM3}$ variant and pRSF-Opt13 plasmid was used to inoculate 500 mL TB media (in 2 L Erlenmeyer flasks) containing 50 µg/mL kanamycin, and 100 µg/mL ampicillin. The cultures were shaken at 220 rpm at 37 °C until an optical density of $OD_{600} = 0.7 – 1.0$ was reached. The cultures were cooled to 20 °C (20 min) and then induced with 5-aminolevulinic, IPTG and $FeSO_4{\cdot}7H_2O$ to final concentrations of 1.0 mM, 0.5 mM and 0.05 mM, respectively. The cultures were allowed to continue for another 20 hours at 20 ºC and shaking at 220 rpm. Cell were harvested by centrifugation (4 °C, 15 min, 4,200 rpm), and the cell pellet was resuspended to 50 mM kPi (pH = 8.0) to required optical density of OD_{600}. Cells were disrupted by sonication (5 min, cycle = 1 s on/2 s off, 50% amplitude) and pelleted by centrifugation (4 ℃, 15 min, 4200 rpm). The supernatant was used directly for subsequent reactions.

Clarified lysates containing the desired enzyme variants were prepared from 50 mL expression cultures according to the procedure described above.

Initial screen of enzyme variants

Method A: Sth10

Two 250 mL Erlenmeyer flasks were each charged with 47.5 mL of whole cell transformation expressing Sth10. A pre-dissolved solution of **12** (5 mg, 0.020 mmol, 0.40 mM final concentration) in 2.5 mL DMSO was added to the inducible medium, followed by 5-ALA to final concentration of 1.0 mM. The flasks were shaken at 220 rpm at 30 ºC under air for 72 h. The mixture was extracted with EtOAc (50 mL × 3) and combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Percentage conversion of the reaction was calculated based on ^1H NMR analysis of product: starting material ratio.

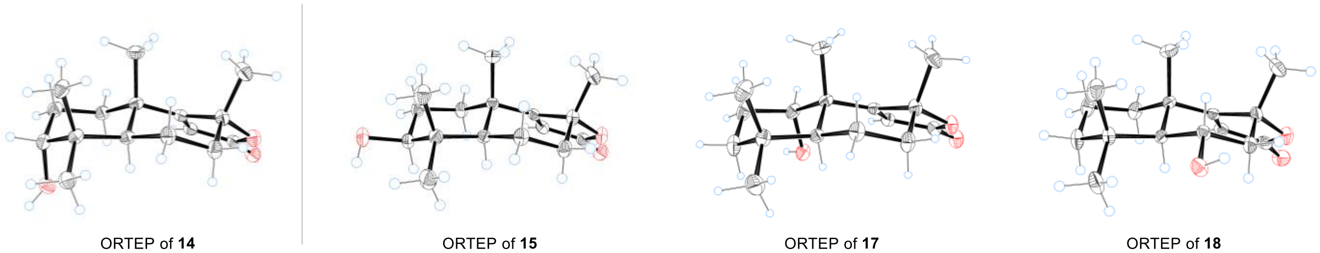
Method B: AndA Mutants and Trt7

A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* expressing AndA mutants and Trt7 (OD_{600} = 30/ 60). A pre-dissolved solution of **12** (12.5 mg, 0.050 mmol, 1.0 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (21.3 mg, 0.11 mmol, 2.1 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 125 mg, 0.66 mmol, 13.2 equiv.) and $FeSO_4{\cdot}7H_2O$ (7.0 mg, 0.025 mmol, 0.5 equiv.). The flask was shaken at 150 rpm at 30 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Percentage conversion of the reaction was calculated based on ^1H NMR analysis of product: starting material ratio.

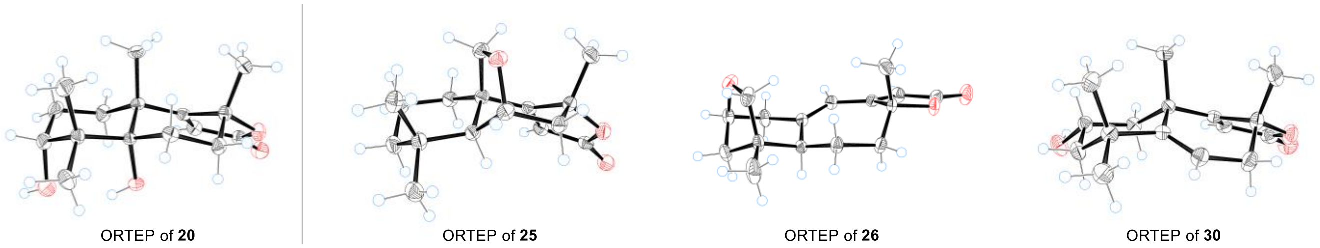
Method C: Bacterial P450

A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing bacterial P450 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **12** (25.0 mg, 0.10 mmol, 2 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by · NaNADP (25.0 mg, 0.032 mmol, 0.34 equiv.) and $Na_2HPO_3{\cdot}5H_2O$ (0.63 g, 2.89 mmol, 30.6 equiv.). The flask was shaken at 150 rpm at 23 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Percentage conversion of the reaction was calculated based on ^1H NMR analysis of product: starting material ratio.

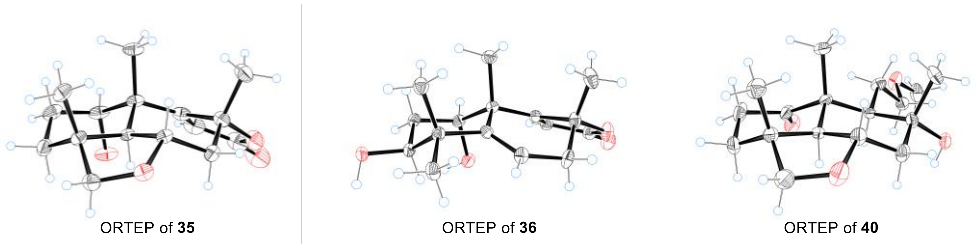
Figure S1. The ORTEP drawings of **14**, **15**, **17**, **18**, **20**, **25**, **26**, **30**, **35**, **36** and **40**.



ORTEP of **14** ORTEP of **15** ORTEP of **17** ORTEP of **18**



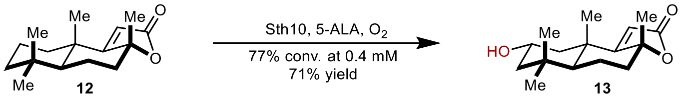
ORTEP of **20** ORTEP of **25** ORTEP of **26** ORTEP of **30**



ORTEP of **35** ORTEP of **36** ORTEP of **40**

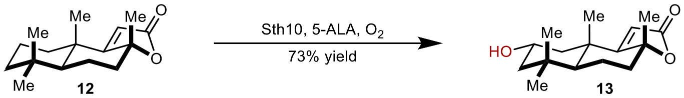
Crystallographic data for the structure reported in this article have been deposited at the Cambridge Crystallographic Data Centre, under deposition nos. CCDC 2348093 (**14**), CCDC 2348094 (**15**), CCDC 2348087 (**17**), CCDC 2348090 (**18**), CCDC 2348091 (**20**), CCDC 2348085 (**25**), CCDC 2348092 (**26**), CCDC 2348089 (**30**), CCDC 2348086 (**35**), CCDC 2348088 (**36**) and CCDC 2348161 (**40**). Copies of the data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures.

Synthetic procedures



Compound **13** was prepared according to the general procedure. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **13** (7.6 mg, 77% conversion, 71% yield) as a white powder.

Gram-scale synthesis of compound **13**:



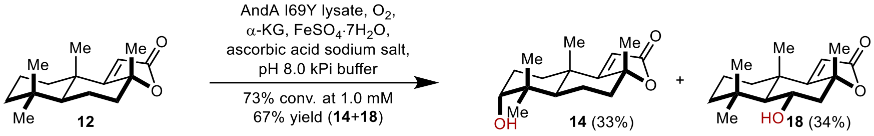
Thirty 2 L Erlenmeyer flasks were each charged with 474 mL of whole cell transformation expressing Sth10. A pre-dissolved solution of **12** (50 mg, 0.20 mmol, 0.40 mM final concentration) in 25 mL DMSO was added to the inducible medium, followed by 5-ALA to final concentration of 1.0 mM. The flasks were shaken at 220 rpm at 30 ºC under air for 72 h. The mixture was extracted with EtOAc (400 mL × 3) and combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **13** (1.17 g, 73% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.56 (s, 1H), 4.12 – 4.04 (m, 1H), 2.32 (dd, *J* = 9.1, 2.8 Hz, 1H), 2.18 (ddd, *J* = 12.0, 4.1, 2.3 Hz, 1H), 1.90 – 1.82 (m, 2H), 1.56 (s, 3H), 1.55 – 1.49 (m, 3H), 1.44 (dd, *J* = 11.6, 11.6 Hz, 1H), 1.23 (s, 3H), 1.17 (dd, *J* = 12.1, 12.1 Hz, 1H), 0.97 (s, 3H), 0.96 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 183.3, 172.2, 110.0, 87.1, 64.5, 55.4, 51.1, 46.2, 41.2, 40.8, 35.5, 33.6, 25.6, 22.6, 19.3, 19.2.

HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{16}H_{24}O_3Na^+$ 287.1618, found 287.1620.

$[\alpha]_D^{20}$ = −159.1 (*c* = 0.5, MeOH)



Compound **14** and **18** was prepared according to the general procedure (AndA I69Y, OD_{600} = 30). The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **14** (4.4 mg, 36% conversion, 33% yield) and **18** (4.5 mg, 37% conversion, 34% yield) as white solid.

(Compound **14**)**^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.55 (s, 1H), 3.50 – 3.47 (m, 1H), 2.30 (dd, *J* = 9.3, 2.8 Hz, 1H), 2.08 – 2.04 (m, 2H), 1.77 – 1.68 (m, 2H), 1.55 (s, 3H), 1.54 – 1.44 (m, 4H), 1.19 (s, 3H), 0.98 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 184.1, 172.5, 109.7, 87.3, 75.4, 48.6, 40.9, 39.6, 38.5, 30.3, 28.5, 25.5, 25.2, 22.0, 19.3, 18.1.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1801.

$[\alpha]_D^{20}$ = −188.8 (*c* = 0.5, MeOH)

[m.p.] = 185−187 °C

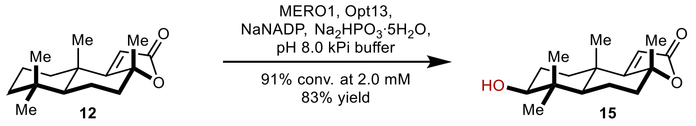
(Compound **18**)**^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.55 (s, 1H), 4.14 (ddd, *J* = 11.0, 11.0, 3.9 Hz, 1H), 2.55 (dd, *J* = 11.8, 3.8 Hz, 1H), 1.77 – 1.69 (m, 2H), 1.62 – 1.48 (m, 6H), 1.45 – 1.40 (m, 1H), 1.31 – 1.23 (m, 1H), 1.22 (s, 3H), 1.16 (s, 3H), 1.08 (s, 3H), 1.06 (d, *J* = 10.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 183.5, 172.3, 110.1, 86.0, 68.3, 59.8, 50.8, 43.6, 38.9, 37.5, 36.1, 34.7, 26.7, 22.0, 19.1, 18.1.

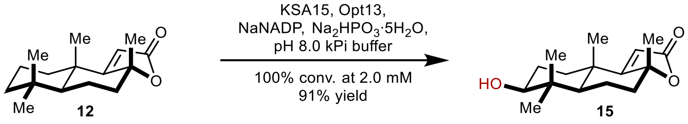
HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1802.

$[\alpha]_D^{20}$ = −103.7 (*c* = 0.5, MeOH)

[m.p.] = 110−112 °C

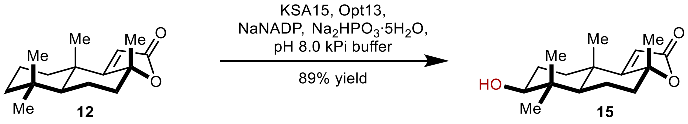


Compound **15** was prepared according to the general procedure (MERO1, $OD_{600} = 30$). The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **15** (22.1 mg, 91% conversion, 83% yield) as a white solid.



Compound **15** was prepared according to the general procedure (KSA15, $OD_{600} = 30$). The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **15** (24.3 mg, 91% conversion, 91% yield) as a white solid.

Gram-scale synthesis of compound **15**:



Six 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* co-expressing KSA15 and Opt13 ($OD_{600} = 30$). A pre-dissolved solution of **12** (250 mg, 1.0 mmol, 2.0 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by NaNADP (250 mg, 0.32 mmol, 0.32 equiv.) and $Na_2HPO_3·5H_2O$ (6.25 g, 28.9 mmol, 28.9 equiv.). The flasks were shaken at 150 rpm at 23 °C under air for 20 h. Then, 25 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **15** (1.42 g, 89% yield) as a white solid.

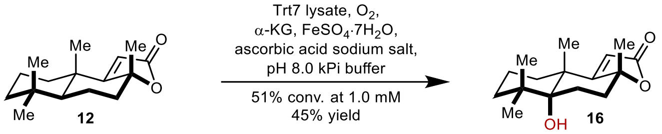
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.52 (s, 1H), 3.25 (dd, *J* = 11.1, 4.4 Hz, 1H), 2.30 (ddd, *J* = 12.3, 2.8, 2.8 Hz, 1H), 1.87 – 1.77 (m, 3H), 1.77 – 1.62 (m, 2H), 1.57 – 1.44 (m, 5H), 1.19 (s, 3H), 1.01 (s, 3H), 0.93 (dd, *J* = 12.0, 2.5 Hz, 1H), 0.88 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 184.0, 172.3, 109.9, 87.2, 78.2, 54.8, 40.6, 39.8, 39.5, 35.4, 28.3, 27.0, 25.4, 19.4, 18.3, 15.6.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1800.

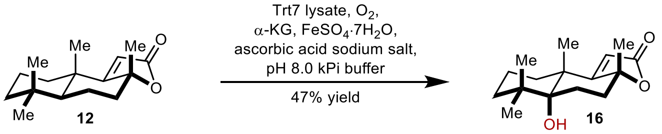
$[\alpha]_D^{20}$ = −152.8 (*c* = 0.5, MeOH)

[m.p.] = 155–157 °C



Compound **15** was prepared according to the general procedure (OD_{600} = 60). The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **15** (6.0 mg, 51% conversion, 45% yield) as white powder.

Gram-scale synthesis of compound **16**:



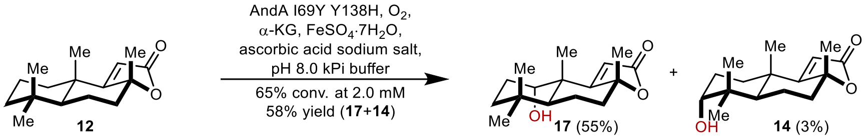
Twenty 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* expressing Trt7 (OD_{600} = 60). A pre-dissolved solution of **12** (125 mg, 0.50 mmol, 1.0 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (426 mg, 2.15 mmol, 4.3 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 2.50 g, 13.3 mmol, 26.6 equiv.) and $FeSO_4{\cdot}7H_2O$ (140 mg, 0.50 mmol, 1.0 equiv.). The flasks were shaken at 150 rpm at 30 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 7: 3 petroleum ether: EtOAc) to yield compound **16** (1.25 g, 47% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.57 (s, 1H), 2.09 – 1.94 (m, 3H), 1.91 (ddd, *J* = 14.4, 12.9, 4.8 Hz, 1H), 1.86 – 1.68 (m, 3H), 1.63 – 1.58 (m, 4H), 1.47 – 1.41 (m, 1H), 1.36 (s, 3H), 1.24 – 1.19 (m, 1H), 1.09 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 182.9, 172.5, 112.5, 86.6, 78.3, 44.2, 38.6, 35.9, 35.0, 30.5, 27.9, 26.5, 24.5, 23.6, 22.0, 17.6.

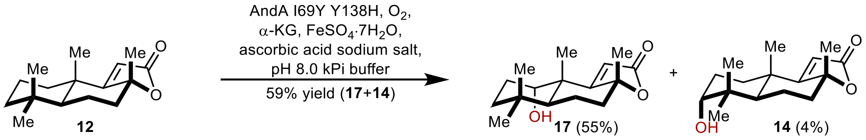
HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1799.

$[\alpha]_D^{25}$ = −153.0 (*c* = 0.05, MeOH)



Compound **17** was prepared according to the general procedure (OD$_{600}$ = 30). The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **17** (14.7 mg, 60% conversion, 55% yield) and compound **14** (0.8 mg, 5% conversion, 3% yield) as white solid.

Gram-scale synthesis of compound **17**:



Eight 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* expressing AndA-I69Y Y138H (OD$_{600}$ = 30). A pre-dissolved solution of **12** (250 mg, 1.0 mmol, 2.0 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (213 mg, 1.08 mmol, 1.1 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 1.25 g, 6.65 mmol, 6.6 equiv.) and $FeSO_4 \cdot 7H_2O$ (70 mg, 0.25 mmol, 0.25 equiv.). The flasks were shaken at 150 rpm at 30 ^{o}C under air for 20 h. Then, 25 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **15** (1.17 g, 55% yield) and **14** (89.3 mg, 4% yield) as white solid.

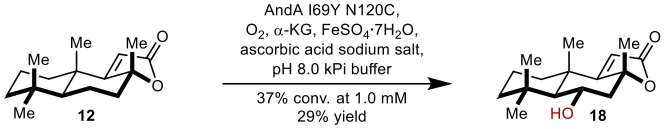
(Compound **17**)**^{1}H NMR (500 MHz, CDCl$_3$):** δ 5.88 (s, 1H), 4.05 – 4.01 (m, 1H), 2.25 – 2.20 (m, 1H), 2.16 (m, 1H), 1.90 – 1.82 (m, 1H), 1.72 (ddd, *J* = 14.4, 14.4, 4.7 Hz, 1H), 1.62 – 1.57 (m, 2H), 1.55 (s, 3H), 1.55 – 1.49 (m, 2H), 1.27 – 1.21 (m, 4H), 0.95 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 178.9, 172.9, 112.4, 87.8, 71.2, 47.0, 44.9, 39.3, 34.3, 34.1, 33.4, 26.5, 26.0, 21.9, 19.6, 19.2.

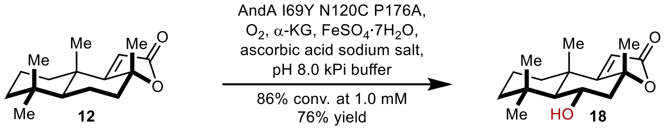
HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1800.

$[\alpha]_D^{20}$ = −72.2 (*c* = 0.5, MeOH)

[m.p.] = 171−173 °C

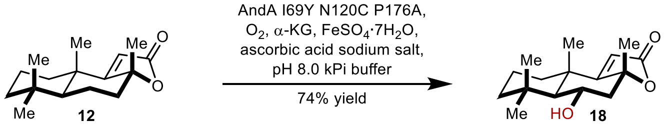


Compound **17** was prepared according to the general procedure (OD_{600} = 60). The crude material was purified by flash column chromatography (4: 1 to 2: 1 petroleum ether: EtOAc) to yield compound **18** (3.9 mg, 37% conversion, 29% yield) as a white solid.



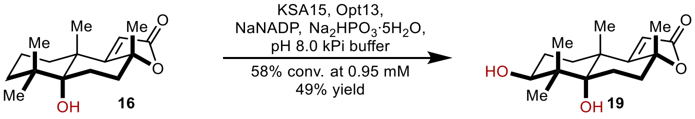
Compound **17** was prepared according to the general procedure (OD_{600} = 60). The crude material was purified by flash column chromatography (4: 1 to 2: 1 petroleum ether: EtOAc) to yield compound **18** (10.2 mg, 86% conversion, 76% yield) as a white solid.

Gram-scale synthesis of compound **18**:



Twelve 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* expressing AndA-I69Y N120C P176A (OD_{600} = 60). A pre-dissolved solution of **12** (125 mg, 0.50 mmol, 1.0 mM

final concentration) in 25 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (426 mg, 2.15 mmol, 4.3 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 2.5 g, 13.2 mmol, 26.4 equiv.) and $FeSO_4·7H_2O$ (140 mg, 0.50 mmol, 1.0 equiv.). The flasks were shaken at 150 rpm at 23 ºC under air for 20 h. Then, 25 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 2: 1 petroleum ether: EtOAc) to yield compound **18** (1.18 g, 74% yield) as white powder.



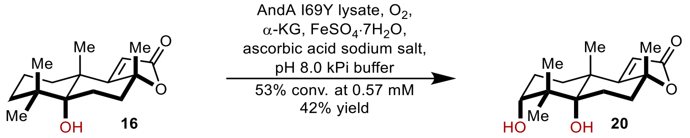
A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing KSA15 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **16** (12.5 mg, 0.047 mmol, 0.95 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by NaNADP (25 mg, 0.032 mmol, 0.67 equiv.) and $Na_2HPO_3·5H_2O$ (0.63 g, 2.89 mmol, 61.2 equiv.). The flask was shaken at 150 rpm at 23 ºC under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 to 1: 2 petroleum ether: EtOAc) to yield compound **19** (6.5 mg, 49% yield) as white powder.

^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.55 (s, 1H), 3.82 (dd, *J* = 11.2, 5.9 Hz, 1H), 2.23 (ddd, *J* = 12.9, 12.9, 5.3 Hz, 1H), 2.13 – 1.99 (m, 3H), 1.84 – 1.74 (m, 3H), 1.60 (s, 3H), 1.48 (ddd, *J* = 13.0, 3.5, 3.5 Hz, 1H), 1.37 (s, 3H), 1.03 (s, 3H), 0.99 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 186.3, 175.2, 112.3, 88.6, 80.7, 74.2, 45.3, 45.0, 35.2, 30.5, 27.5, 26.8, 25.7, 23.3, 22.3, 17.7.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_4H^+$ 281.1747, found 281.1751.

$[\alpha]_D^{20}$ = −108.6 (*c* = 0.5, MeOH)



Two 250 mL Erlenmeyer flasks were each charged with 47.5 mL of clarified lysate of *E. coli* expressing AndA-I69Y (OD_{600} = 60). A pre-dissolved solution of **16** (7.5 mg, 0.028 mmol, 0.57 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (42.6 mg, 0.22 mmol, 7.6 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 250 mg, 1.33 mmol, 46.8 equiv.) and $FeSO_4 \cdot 7H_2O$ (14.0 mg, 0.050 mmol, 1.8 equiv.). The flasks were shaken at 150 rpm at 30 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (2: 1 to 2: 3 petroleum ether: EtOAc) to yield compound **20** (6.7 mg, 42% yield) as a white solid.

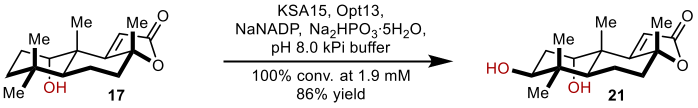
^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.59 (s, 1H), 3.54 (dd, *J* = 2.7, 2.7 Hz, 1H), 2.34 (ddd, *J* = 13.4, 13.4, 3.2 Hz, 1H), 2.28 – 2.20 (m, 1H), 2.04 (dd, *J* = 13.0, 4.7 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.81 – 1.73 (m, 2H), 1.61 (s, 3H), 1.41 – 1.36 (m, 4H), 1.11 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 186.6, 175.3, 112.1, 88.7, 81.1, 77.8, 45.7, 42.0, 34.9, 26.9, 26.5, 26.0, 25.7, 24.5, 23.4, 22.9.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_4H^+$ 281.1747, found 281.1749.

$[\alpha]_D^{20}$ = −166.0 (*c* = 0.5, MeOH)

[m.p.] = 264–266 °C



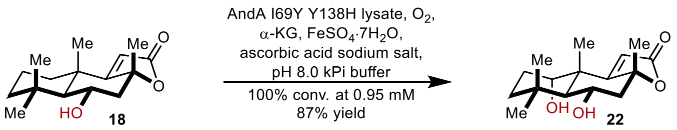
A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing KSA15 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **17** (25.0 mg, 0.095 mmol, 1.9 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by NaNADP (25.0 mg, 0.032 mmol, 0.34 equiv.) and $Na_2HPO_3·5H_2O$ (0.63 g, 2.89 mmol, 30.6 equiv.). The flask was shaken at 150 rpm at 23 ºC under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (2: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **21** (22.9 mg, 86% yield) as white powder.

^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.84 (s, 1H), 4.06 (s, 1H), 3.72 (dd, *J* = 12.1, 4.7 Hz, 1H), 2.24 (ddd, *J* = 12.3, 2.9, 2.9 Hz, 1H), 2.10 (m, 1H), 1.94 – 1.88 (m, 1H), 1.85 (ddd, *J* = 14.0, 4.2, 4.2 Hz, 1H), 1.75 – 1.65 (m, 1H), 1.60 (d, *J* = 19.2 Hz, 4H), 1.47 (ddd, *J* = 12.8, 12.8, 3.9 Hz, 1H), 1.25 (s, 3H), 1.04 (s, 3H), 0.89 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 181.4, 175.3, 113.3, 89.7, 73.4, 72.6, 47.6, 45.7, 40.9, 40.1, 35.4, 28.8, 26.6, 20.1, 19.9, 16.1.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_4H^+$ 281.1747, found 281.1751.

$[\alpha]_D^{20}$ = –69.4 (*c* = 0.5, MeOH)



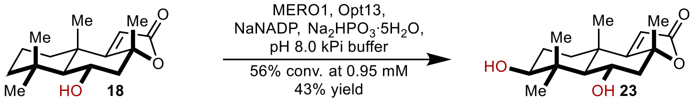
A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* expressing AndA-L69Y Y138H (OD_{600} = 30). A pre-dissolved solution of **16** (12.5 mg, 0.047 mmol, 0.95 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (21.3 mg, 0.11 mmol, 2.3 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 125 mg, 0.66 mmol, 14.1 equiv.) and $FeSO_4·7H_2O$ (7.0 mg, 0.025 mmol, 0.53 equiv.). The flask was shaken at 150 rpm at 30 ºC under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (2: 1 to 2: 3 petroleum ether: EtOAc) to yield compound **20** (11.5 mg, 87% yield) as white powder.

^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.93 (s, 1H), 4.14 (ddd, *J* = 11.0, 11.0, 3.6 Hz, 1H), 3.94 – 3.90 (m, 1H), 2.42 (dd, *J* = 11.8, 3.6 Hz, 1H), 2.23 – 2.13 (m, 1H), 1.87 (ddd, *J* = 14.1, 14.1, 4.6 Hz, 1H), 1.69 (d, *J* = 11.0 Hz, 1H), 1.62 (m, 4H), 1.58 – 1.50 (m, 1H), 1.29 (s, 3H), 1.20 (s, 3H), 1.17 – 1.10 (m, 4H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 180.9, 175.2, 113.6, 88.3, 71.9, 68.2, 52.5, 50.2, 45.0, 37.4, 36.8, 35.3, 27.8, 26.5, 22.7, 20.6.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_4H^+$ 281.1747, found 281.1750.

$[\alpha]_D^{20}$ = –27.0 (*c* = 0.2, MeOH)



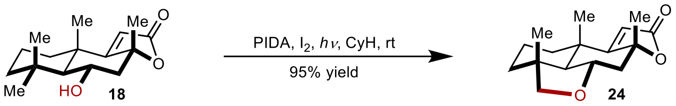
A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing Mero1 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **18** (12.5 mg, 0.047 mmol, 0.95 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by NaNADP (25 mg, 0.032 mmol, 0.67 equiv.) and $Na_2HPO_3·5H_2O$ (0.63 g, 2.89 mmol, 61.2 equiv.). The flask was shaken at 150 rpm at 23 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (2: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **21** (5.7 mg, 43% yield) as white powder.

^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.64 (s, 1H), 4.20 (ddd, *J* = 11.0, 11.0, 3.7 Hz, 1H), 3.17 (dd, *J* = 10.0, 5.6 Hz, 1H), 2.48 (dd, *J* = 11.9, 3.7 Hz, 1H), 1.82 – 1.69 (m, 4H), 1.64 – 1.55 (m, 4H), 1.29 (s, 3H), 1.27 (s, 3H), 1.07 (d, *J* = 10.7 Hz, 1H), 1.03 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 185.6, 174.4, 110.8, 88.1, 79.0, 68.2, 59.8, 51.4, 41.4, 39.9, 36.5, 30.8, 27.3, 26.7, 19.4, 16.2.

HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{16}H_{24}O_4Na^+$ 303.1567, found 303.1572.

$[\alpha]_D^{20}$ = −76.3 (*c* = 0.5, MeOH)



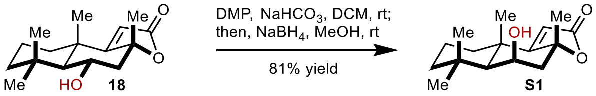
Compound **18** (1.50 g, 5.67 mmol, 1.0 equiv.), PIDA (2.56 g, 7.94 mmol, 1.4 equiv.) and I_2 (1.73 g, 6.81 mmol, 1.2 equiv.) was dissolved in CyH (100 mL). The solution was irradiated with a flood lamp (200 W) at room temperature for 30 min. The reaction was quenched by sat. aq. $Na_2S_2O_3$ (20 mL) and extracted with EtOAc (100 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **24** (1.42 g, 95% yield) as white powder.

^{1}H NMR (500 MHz, Acetone-*d*$_6$): δ 5.67 (s, 1H), 4.08 (ddd, *J* = 11.1, 11.1, 4.4 Hz, 1H), 3.62 (d, *J* = 7.3 Hz, 1H), 3.46 (d, *J* = 7.4 Hz, 1H), 2.60 (dd, *J* = 11.1, 4.4 Hz, 1H), 1.94 – 1.83 (m, 2H), 1.75 – 1.69 (m, 2H), 1.55 (s, 4H), 1.47 (dd, *J* = 10.8, 10.8 Hz, 1H), 1.30 – 1.24 (m, 5H), 1.18 (s, 3H).

^{13}C NMR (126 MHz, Acetone-*d*$_6$): δ 184.0, 171.7, 111.5, 87.9, 84.7, 72.0, 61.4, 47.0, 40.6, 38.1, 37.8, 36.3, 26.9, 19.9, 19.3, 17.8.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_3H^+$ 263.1642, found 263.1645.

$[\alpha]_D^{20}$ = −82.5 (*c* = 0.5, MeOH)



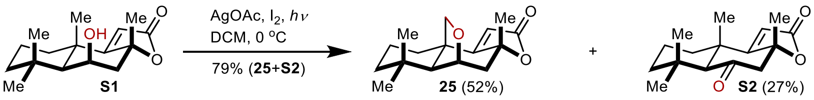
To a stirred solution of compound **13** (185 mg, 0.70 mmol, 1.0 equiv.) and $NaHCO_3$ (147 mg, 1.75 mmol, 2.5 equiv.) in DCM (8 mL) was added DMP (594 mg, 0.73 mmol, 2 equiv.) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (10 mL) and $Na_2S_2O_3$ (10 mL). Then, the mixture was extracted with DCM (20 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was re-dissolved in MeOH (10 mL), $NaBH_4$ (29.1 mg, 0.77 mmol, 1.1 equiv.) was added at 0 °C. After stirring at room temperature for 30 min, the reaction was quenched by brine and extracted with DCM (20 mL × 3). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **S1** (150 mg, 81% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.56 (s, 1H), 4.61 – 4.55 (m, 1H), 2.46 (dd, *J* = 13.8, 2.7 Hz, 1H), 1.84 (ddd, *J* = 13.8, 3.4, 3.4 Hz, 4H), 1.78 – 1.69 (m, 2H), 1.60 (ddd, *J* = 14.2, 3.4, 3.4 Hz, 1H), 1.56 (s, 3H), 1.51 (ddd, *J* = 13.2, 13.2, 3.7 Hz, 1H), 1.44 (d, *J* = 13.2 Hz, 1H), 1.27 (s, 3H), 1.20 (ddd, *J* = 13.4, 13.4, 3.9 Hz, 1H), 1.00 (s, 3H), 0.97 (d, *J* = 2.1 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.4, 172.6, 110.1, 86.9, 67.3, 56.9, 48.4, 43.9, 39.8, 39.7, 35.1, 33.3, 27.5, 24.0, 20.2, 18.5.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1801.

$[\alpha]_D^{20}$ = –162.8 (*c* = 0.5, MeOH)



Compound **S1** (10 mg, 0.038 mmol, 1.0 equiv.), AgOAc (31.6 mg, 0.19 mmol, 5 equiv.) and I_2 (48.0 mg, 0.19 mmol, 5 equiv.) was dissolved in DCM (1 mL). The solution was irradiated with a flood lamp (150 W) at 0 °C for 1 h. The reaction was quenched by sat. aq. $Na_2S_2O_3$ (2 mL) and extracted with DCM (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (3: 1 to 3: 2 petroleum: EtOAc) to yield **25** (5.2 mg, 52% yield) and **S2** (2.7 mg, 27% yield) as white powder.

(Compound **25**)**^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.69 (s, 1H), 4.41 (d, *J* = 4.1 Hz, 1H), 3.88 (q, *J* = 9.0 Hz, 2H), 2.58 (dd, *J* = 13.3, 4.2 Hz, 1H), 1.90 – 1.83 (m, 2H), 1.78 (d, *J* = 13.4 Hz, 1H), 1.70 (s, 3H), 1.67 – 1.61 (m, 2H), 1.51 (ddd, *J* = 13.6, 3.1, 3.1 Hz, 1H), 1.30 (s, 1H), 1.22 – 1.14 (m, 1H), 1.04 (s, 3H), 0.94 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 182.5, 172.1, 109.5, 87.3, 76.9, 69.5, 62.2, 48.5, 46.4, 39.5, 34.0, 32.1, 28.6, 25.2, 22.9, 17.8.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_3H^+$ 263.1642, found 263.1649.

$[\alpha]_D^{20}$ = −171.7 (*c* = 0.2, MeOH)

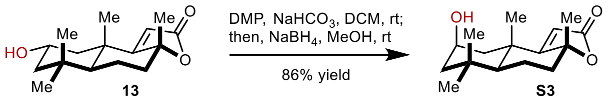
[m.p.] = 140−142 °C

(Compound **S2**)**^{1}H NMR (500 MHz, $CDCl_3$):** δ 5.79 (s, 1H), 2.87 (d, *J* = 12.2 Hz, 1H), 2.74 (d, *J* = 12.2 Hz, 1H), 2.19 (s, 1H), 1.94 – 1.88 (m, 1H), 1.78 – 1.62 (m, 3H), 1.57 (s, 3H), 1.45 – 1.40 (m, 1H), 1.26 (s, 3H), 1.22 (s, 3H), 1.13 (ddd, *J* = 13.2, 13.2, 3.6 Hz, 1H), 0.95 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 205.3, 180.7, 171.4, 111.6, 87.0, 63.4, 56.7, 42.4, 40.3, 37.3, 33.4, 32.3, 26.9, 21.6, 19.9, 18.0.

HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{16}H_{22}O_3Na^+$ 285.1461, found 285.1463.

$[\alpha]_D^{20}$ = −126.9 (*c* = 0.5, MeOH)



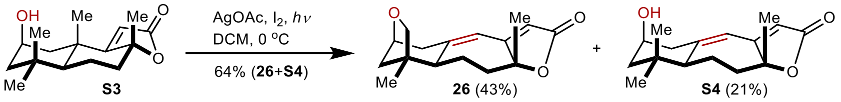
To a stirred solution of compound **13** (200 mg, 0.76 mmol, 1.0 equiv.) and $NaHCO_3$ (159 mg, 1.89 mmol, 2.5 equiv.) in DCM (10 mL) was added DMP (642 mg, 1.51 mmol, 2 equiv.) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (10 mL) and $Na_2S_2O_3$ (10 mL). Then, the mixture was extracted with DCM (20 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was re-dissolved in MeOH (10 mL), $NaBH_4$ (31.5 mg, 0.83 mmol, 1.1 equiv.) was added at 0 °C. After stirring at room temperature for 30 min, the reaction was quenched by brine and extracted with DCM (20 mL × 3). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **S3** (173 mg, 86% yield) as white powder.

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.51 (s, 1H), 4.38 – 4.31 (m, 1H), 2.35 – 2.27 (m, 1H), 2.10 (d, *J* = 14.0 Hz, 1H), 1.90 – 1.84 (m, 1H), 1.76 (ddd, *J* = 14.9, 3.7, 3.7 Hz, 2H), 1.67 – 1.55 (m, 4H), 1.55 – 1.44 (m, 5H), 1.16 (s, 3H), 1.02 (dd, *J* = 12.2, 2.2 Hz, 1H), 0.93 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 184.6, 172.4, 109.6, 87.4, 67.9, 55.5, 47.3, 42.3, 40.8, 39.8, 34.2, 33.6, 25.7, 23.5, 19.6, 19.5.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{24}O_3H^+$ 265.1798, found 265.1797.

$[\alpha]_D^{20}$ = −135.9 (*c* = 0.5, MeOH)



Compound **S3** (10 mg, 0.038 mmol, 1.0 equiv.), AgOAc (31.6 mg, 0.19 mmol, 5 equiv.) and I_2 (48.0 mg, 0.19 mmol, 5 equiv.) was dissolved in DCM (1 mL). The solution was irradiated with a flood lamp (200 W) at 0 °C for 1 h. The reaction was quenched by sat. aq. $Na_2S_2O_3$ (2 mL) and extracted with DCM (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (3: 1 to 3: 2 petroleum: EtOAc) to yield **26** (4.3 mg, 43% yield) and **S4** (2.1 mg, 21% yield) as white powder.

(Compound **26**)**^{1}H NMR (500 MHz, CDCl$_3$):** δ 6.22 – 6.19 (m, 1H), 5.57 (s, 1H), 4.36 – 4.32 (m, 1H), 3.90 (d, *J* = 8.4 Hz, 1H), 3.35 (dd, *J* = 8.4, 1.5 Hz, 1H), 2.74 (d, *J* = 17.7 Hz, 1H), 2.59 – 2.50 (m, 1H), 2.39 – 2.32 (m, 2H), 2.05 – 1.97 (m, 1H), 1.93 (ddd, *J* = 11.6, 6.3, 2.5 Hz, 1H), 1.81 (ddd, *J* = 13.3, 13.3, 1.8 Hz, 1H), 1.72 – 1.65 (m, 2H), 1.52 (s, 3H), 1.17 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.6, 171.6, 149.5, 119.9, 113.8, 87.1, 74.5, 74.1, 52.0, 45.0, 44.5, 43.6, 38.3, 26.0, 25.3, 22.3.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{20}O_3H^+$ 261.1485, found 261.1489.

$[\alpha]_D^{20}$ = +267.5 (*c* = 0.2, MeOH)

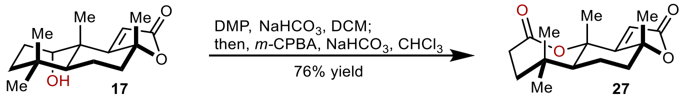
[m.p.] = 94–97 °C

(Compound **S4**)**^{1}H NMR (500 MHz, CDCl$_3$):** δ 6.25 (s, 1H), 5.60 (s, 1H), 4.21 – 4.16 (m, 1H), 2.65 – 2.54 (m, 2H), 2.29 (ddd, *J* = 13.2, 6.1, 1.8 Hz, 1H), 2.15 (dd, *J* = 9.3, 5.3 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.81 (ddd, *J* = 13.3, 13.3, 1.9 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.51 (s, 3H), 1.13 (s, 3H), 0.99 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 172.7, 171.5, 150.2, 118.3, 113.8, 87.9, 67.5, 51.3, 47.5, 46.0, 36.8, 36.3, 30.8, 25.3, 24.3, 23.8.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_3H^+$ 263.1642, found 263.1645.

$[\alpha]_D^{20}$ = +254.0 (*c* = 0.5, MeOH)



To a stirred solution of compound **17** (26.4 mg, 0.1 mmol, 1.0 equiv.) and $NaHCO_3$ (16.8 mg, 0.2 mmol, 2.0 equiv.) in DCM (2 mL) was added DMP (63.6 mg, 0.15 mmol, 1.5 equiv.) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (2 mL) and $Na_2S_2O_3$ (2 mL). Then, the mixture was extracted with DCM (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was re-dissolved in $CHCl_3$ (2 mL), $NaHCO_3$ (16.8 mg, 0.20 mmol, 2.0 equiv.) was added followed by *m*-CPBA (36.5 mg, 0.18 mmol, 1.8 equiv., 85%) at room temperature. After stirring at same temperature for 12 h, the reaction mixture was filtered through a Celite pad and washed with DCM (2 mL × 2). The resulting filtrate was washed sat. aq. $Na_2S_2O_3$ (2 mL), sat. aq. $NaHCO_3$ (2 mL) and brine, dried over anhydrous

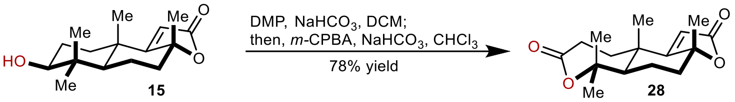
Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **27** (21.3 mg, 76% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.18 (s, 1H), 2.84 – 2.75 (m, 1H), 2.70 (dd, *J* = 17.5, 9.4 Hz, 1H), 2.27 (dd, *J* = 9.2, 3.0 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.86 (dd, *J* = 13.9, 10.4 Hz, 1H), 1.73 (s, 3H), 1.65 – 1.58 (m, 2H), 1.56 – 1.47 (m, 5H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 177.5, 173.0, 170.8, 114.4, 86.1, 85.3, 54.7, 39.2, 36.5, 36.3, 32.1, 31.8, 23.8, 22.9, 22.6, 21.7.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_4H^+$ 279.1591, found 279.1590.

$[\alpha]_D^{20}$ = −122.2 (*c* = 0.5, MeOH)



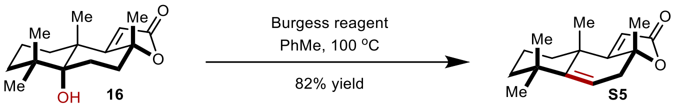
To a stirred solution of compound **15** (26.4 mg, 0.1 mmol, 1.0 equiv.) and $NaHCO_3$ (16.8 mg, 0.2 mmol, 2.0 equiv.) in DCM (2 mL) was added DMP (63.6 mg, 0.15 mmol, 1.5 equiv.) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (2 mL) and $Na_2S_2O_3$ (2 mL). Then, the mixture was extracted with DCM (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was re-dissolved in $CHCl_3$ (2 mL), $NaHCO_3$ (16.8 mg, 0.20 mmol, 2.0 equiv.) was added followed by *m*-CPBA (36.5 mg, 0.18 mmol, 1.8 equiv., 85%) at room temperature. After stirring at same temperature for 12 h, the reaction mixture was filtered through a Celite pad and washed with DCM (2 mL × 2). The resulting filtrate was washed sat. aq. $Na_2S_2O_3$ (2 mL), sat. aq. $NaHCO_3$ (2 mL) and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (3: 2 petroleum: EtOAc) to yield **28** (21.8 mg, 78% yield) as white powder.

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.62 (s, 1H), 2.90 – 2.82 (m, 1H), 2.78 (ddd, *J* = 16.4, 7.6, 2.8 Hz, 1H), 2.34 – 2.29 (m, 1H), 2.10 – 2.03 (m, 1H), 1.97 (ddd, *J* = 14.3, 7.6, 2.7 Hz, 1H), 1.93 – 1.89 (m, 1H), 1.72 – 1.62 (m, 2H), 1.59 (s, 3H), 1.58 – 1.52 (m, 1H), 1.50 (s, 3H), 1.47 (s, 3H), 1.37 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 181.5, 173.8, 171.2, 112.0, 86.6, 85.4, 55.8, 42.0, 39.7, 34.3, 33.8, 31.5, 25.2, 24.7, 23.3, 18.4.

HRMS (*m/z*): [M+ H]$^+$ calcd for $C_{16}H_{22}O_4H^+$ 279.1591, found 279.1589.

$[\alpha]_D^{20}$ = −191.7 (*c* = 0.5, MeOH)



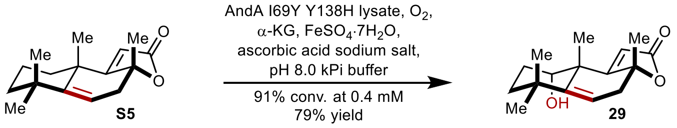
To a solution of compound **16** (1.70 g, 6.43 mmol, 1.0 equiv.) in toluene (50 mL) was added burgess reagent (3.05 g, 12.8 mmol, 2.0 equiv.) at room temperature. After stirring at 100 °C for 4 h, the reaction was cooled down to room temperature and concentrated *in vacuo*. The crude material was purified by flash column chromatography (8: 1 petroleum: EtOAc) to yield **S5** (1.30 g, 82% yield) as white powder.

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.58 (s, 1H), 5.48 (dd, *J* = 5.5, 2.2 Hz, 1H), 2.65 (dd, *J* = 16.9, 5.5 Hz, 1H), 2.34 (d, *J* = 16.9 Hz, 1H), 1.98 – 1.86 (m, 2H), 1.67 – 1.61 (m, 1H), 1.59 (s, 3H), 1.56 – 1.50 (m, 1H), 1.50 – 1.45 (m, 4H), 1.24 (ddd, *J* = 13.4, 13.4, 4.0 Hz, 1H), 1.19 (s, 3H), 1.11 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 183.8, 172.9, 147.2, 116.3, 109.6, 84.6, 41.5, 40.9, 40.0, 38.6, 37.0, 32.9, 28.7, 25.8, 25.4, 18.2.

HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{22}O_2H^+$ 247.1693, found 247.1693.

$[\alpha]_D^{20}$ = −215.0 (*c* = 0.5, MeOH)



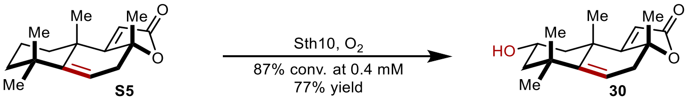
Two 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* expressing AndA-I69Y Y138H (OD_{600} = 30). A pre-dissolved solution of **12** (50 mg, 0.2 mmol, 0.4 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (213 mg, 1.08 mmol, 5.3 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 1.25 g, 6.6 mmol, 32.7 equiv.) and $FeSO_4 \cdot 7H_2O$ (70 mg, 0.25 mmol, 1.2 equiv.). The flasks were shaken at 150 rpm at 30 ºC under air for 20 h. Then, 25 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 2: 1 petroleum ether: EtOAc) to yield compound **29** (42.1 mg, 79% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.74 (dd, *J* = 6.0, 2.0 Hz, 1H), 5.73 (s, 1H), 4.08 (dd, *J* = 2.6, 2.6 Hz, 1H), 2.63 (dd, *J* = 16.7, 6.0 Hz, 1H), 2.36 – 2.30 (m, 1H), 2.28 – 2.19 (m, 1H), 1.78 – 1.67 (m, 2H), 1.57 (s, 3H), 1.52 (s, 3H), 1.40 – 1.34 (m, 1H), 1.21 (s, 3H), 1.16 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 179.0, 172.7, 143.7, 120.4, 110.9, 84.9, 72.7, 46.7, 39.3, 36.7, 34.5, 32.8, 29.2, 25.7, 25.4, 24.7.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_3H^+$ 263.1642, found 263.1642.

$[\alpha]_D^{20}$ = −155.4 (*c* = 0.5, MeOH)



A 2 L Erlenmeyer flask was charged with 474 mL of whole cell transformation expressing Sth10. A pre-dissolved solution of **12** (50 mg, 0.2 mmol, 0.4 mM final concentration) in 25 mL DMSO was added to the inducible medium, followed by 5-ALA to final concentration of 1.0 mM. The flask was shaken at 220 rpm at 30 ºC under air for 72 h. The mixture was extracted with EtOAc (400 mL × 3) and combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **13** (41.0 mg, 77% yield) as a white solid.

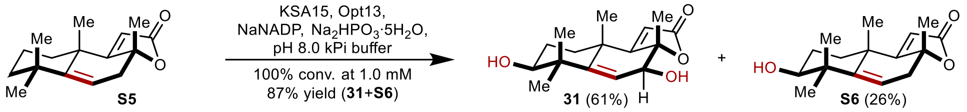
^{1}H NMR (500 MHz, Methanol-d_4): δ 5.72 (s, 1H), 5.64 (dd, J = 5.4, 2.1 Hz, 1H), 4.27 – 4.18 (m, 1H), 2.73 (dd, J = 17.0, 5.5 Hz, 1H), 2.36 – 2.27 (m, 2H), 1.90 – 1.84 (m, 1H), 1.60 (s, 3H), 1.56 (s, 3H), 1.36 (dd, J = 11.7, 11.7 Hz, 1H), 1.27 (s, 3H), 1.21 – 1.13 (m, 4H).

^{13}C NMR (126 MHz, Methanol-d_4): δ 184.9, 174.7, 146.8, 118.5, 110.5, 86.3, 64.4, 51.1, 47.8, 42.1, 41.7, 38.6, 33.4, 29.8, 27.0, 25.7.

HRMS (m/z): [M+Na]$^+$ calcd for $C_{16}H_{22}O_3Na^+$ 285.1461, found 285.1463.

$[\alpha]_D^{20}$ = −196.4 (c = 0.5, MeOH)

[m.p.] = 197−198 °C



A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing KSA15 and Opt13 (OD$_{600}$ = 30). A pre-dissolved solution of **S5** (12.5 mg, 0.05 mmol, 1 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by NaNADP (25 mg, 0.032 mmol, 0.63 equiv.) and $Na_2HPO_3 \cdot 5H_2O$ (0.63 g, 2.89 mmol, 57.0 equiv.). The flask was shaken at 150 rpm at 23 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 2: 3 petroleum ether: EtOAc) to yield compound **31** (8.7 mg, 61% yield) and **S6** (3.5 mg, 26% yield) as white powder.

(Compound **31**)**^{1}H NMR (500 MHz, Methanol-d_4):** δ 5.75 (s, 1H), 5.50 (d, J = 1.8 Hz, 1H), 4.10 (d, J = 1.8 Hz, 1H), 3.15 (dd, J = 11.7, 4.6 Hz, 1H), 2.04 (ddd, J = 13.2, 3.3, 3.3 Hz, 1H), 2.01 – 1.91 (m, 1H), 1.85 – 1.78 (m, 1H), 1.57 – 1.48 (m, 7H), 1.20 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 183.7, 174.9, 148.3, 125.7, 112.1, 90.3, 78.1, 76.7, 43.7, 40.8, 36.7, 28.3, 27.6, 26.4, 22.4, 19.1.

HRMS (*m/z*): [M+Na]$^+$ calcd for $C_{16}H_{22}O_4Na^+$ 301.1410, found 301.1413.

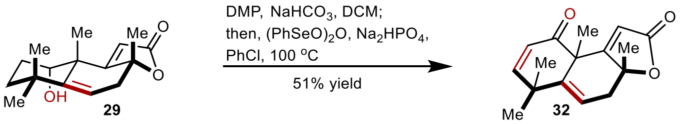
[α]$^{20}_{D}$ = −128.5 (*c* = 0.2, MeOH)

(Compound **S6**)**^{1}H NMR (500 MHz, Methanol-*d*$_4$):** δ 5.69 (s, 1H), 5.68 (dd, *J* = 5.6, 2.2 Hz, 1H), 3.15 (dd, *J* = 11.7, 4.6 Hz, 1H), 2.72 (dd, *J* = 16.9, 5.6 Hz, 1H), 2.30 – 2.24 (m, 1H), 2.04 (ddd, *J* = 13.0, 3.4, 3.4 Hz, 1H), 2.02 – 1.91 (m, 1H), 1.85 – 1.78 (m, 1H), 1.60 (s, 3H), 1.58 – 1.51 (m, 4H), 1.19 (s, 3H), 1.14 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 185.8, 175.0, 147.5, 119.3, 110.5, 86.3, 78.1, 43.9, 41.5, 40.9, 36.9, 28.3, 27.6, 26.1, 25.3, 22.7.

HRMS (*m/z*): [M+ Na]$^+$ calcd for $C_{16}H_{22}O_3Na^+$ 285.1461, found 285.1462.

[α]$^{20}_{D}$ = −145.5 (*c* = 0.2, MeOH)



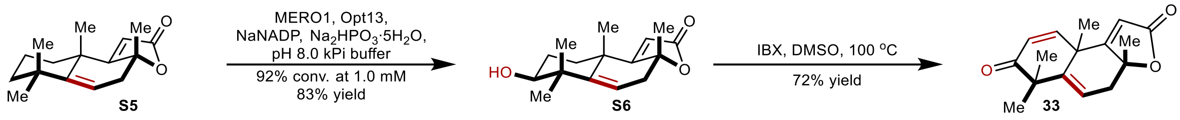
To a stirred solution of compound **29** (10.0 mg, 0.038 mmol, 1.0 equiv.) and $NaHCO_3$ (8 mg, 0.095 mmol, 2.5 equiv.) in DCM (1 mL) was added DMP (32.3 mg, 0.076 mmol, 2 equiv.) at 0 °C. After stirring at room temperature for 2 h, the reaction was quenched by sat. aq. $NaHCO_3$ (1 mL) and $Na_2S_2O_3$ (1 mL). Then, the mixture was extracted with DCM (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material re-dissolved in PhCl (1 mL), Na_2HPO_4 (21.6 mg, 0.15 mmol, 4 equiv.) was added followed by $(PhSeO)_2O$[1] (54.9 mg, 0.15mmol, 4 equiv.). After stirring at 100 °C for 4 h, the reaction mixture was concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **32** (5.1 mg, 51% yield) as pale yellow powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.76 (s, 1H), 6.59 (d, *J* = 10.2 Hz, 1H), 5.90 (d, *J* = 10.1 Hz, 1H), 5.84 (dd, *J* = 6.1, 2.2 Hz, 1H), 2.69 (dd, *J* = 17.0, 6.1 Hz, 1H), 2.38 (d, *J* = 16.9 Hz, 1H), 1.73 (s, 3H), 1.61 (s, 3H), 1.45 (s, 3H), 1.36 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 197.4, 172.7, 171.0, 156.2, 141.7, 123.8, 121.8, 115.2, 84.8, 50.7, 39.2, 39.0, 30.8, 29.8, 29.0, 25.6.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{18}O_3H^+$ 259.1329, found 259.1329.

$[\alpha]_D^{20}$ = −156.9 (*c* = 0.2, MeOH)



A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing Mero1 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **S5** (12.5 mg, 0.05 mmol, 1 mM final concentration) in 2.5 mL DMSO was added to the lysaste, followed by NaNADP (25 mg, 0.032 mmol, 0.63 equiv.) and $Na_2HPO_3{\cdot}5H_2O$ (0.63 g, 2.89 mmol, 57.0 equiv.). The flask was shaken at 150 rpm at 23 ºC under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (4: 1 to 3: 2 petroleum ether: EtOAc) to yield compound **S6** (11.1 mg, 83% yield) as white powder.

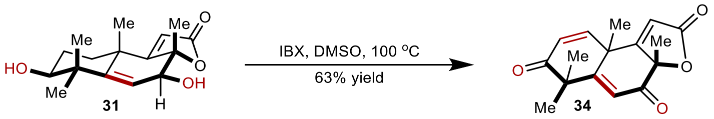
Compound **S6** (11.1 mg, 0.042 mmol, 1.0 equiv.) and IBX (71.1 mg, 0.25 mmol, 6 equiv.) was dissolved in DMSO (1 mL) at room temperature. After stirring at 100 °C for 72 h, the reaction was quenched by sat. aq. $NaHCO_3$ (1 mL) and extracted with EtOAc (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (7: 3 petroleum: EtOAc) to yield **33** (7.9 mg, 72% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08 (d, *J* = 10.1 Hz, 1H), 6.04 (d, *J* = 10.1 Hz, 1H), 5.79 (s, 1H), 5.74 – 5.69 (m, 1H), 2.80 (dd, *J* = 17.6, 5.1 Hz, 1H), 2.43 (d, *J* = 17.6 Hz, 1H), 1.71 (s, 3H), 1.69 (s, 3H), 1.43 (s, 3H), 1.35 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 201.4, 175.9, 171.3, 149.4, 141.6, 126.3, 120.1, 111.2, 84.2, 48.8, 41.2, 40.6, 29.4, 28.4, 26.0, 25.3.

HRMS (*m/z*): $[M+ Na]^+$ calcd for $C_{16}H_{18}O_3Na^+$ 281.1148, found 281.1151.

$[\alpha]_D^{20}$ = –81.0 (*c* = 0.5, MeOH)



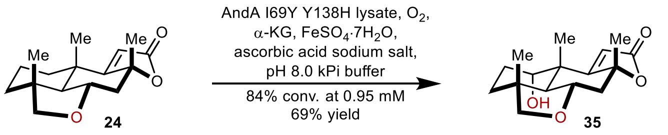
Compound **31** (10.0 mg, 0.036 mmol, 1.0 equiv.) and IBX (60.4 mg, 0.22 mmol, 6 equiv.) was dissolved in DMSO (1 mL) at room temperature. After stirring at 100 °C for 96 h, the reaction was quenched by sat. aq. $NaHCO_3$ (1 mL) and extracted with EtOAc (2 mL × 3). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (3: 2 petroleum: EtOAc) to yield **34** (6.2 mg, 63% yield) as pale yellow powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.10 (d, *J* = 10.1 Hz, 1H), 6.23 – 6.18 (m, 2H), 5.86 (s, 1H), 1.91 (s, 3H), 1.84 (s, 3H), 1.55 (s, 3H), 1.44 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 198.2, 191.2, 171.2, 169.4, 167.2, 146.9, 126.8, 124.6, 113.7, 87.6, 50.3, 42.3, 29.5, 27.9, 24.8, 24.7.

HRMS (*m/z*): $[M+ Na]^+$ calcd for $C_{16}H_{16}O_4Na^+$ 295.0941, found 295.0943.

$[\alpha]_D^{20}$ = –49.6 (*c* = 0.5, MeOH)



Twelve 2 L Erlenmeyer flasks were each charged with 475 mL of clarified lysate of *E. coli* expressing AndA-I69Y Y138H (OD_{600} = 30). A pre-dissolved solution of **24** (125 mg, 0.48 mmol, 0.95 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by ascorbic acid sodium salt (213 mg, 1.08 mmol, 2.3 equiv.), α-ketoglutaric acid (disodium salt dihydrate, 1.25 g, 6.65 mmol, 13.9 equiv.) and $FeSO_4 \cdot 7H_2O$ (70 mg, 0.25 mmol, 0.53 equiv.). The flasks were shaken at 150 rpm at 30 °C under air for 20 h. Then, 25 g NaCl was added to flask and the mixture was extracted with EtOAc (400 mL × 3). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (400 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (3: 2 to 1: 2 petroleum ether: EtOAc) to yield compound **35** (1.10 g, 69% yield) as a white solid.

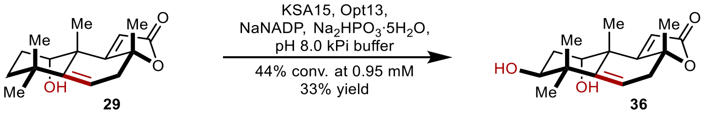
^{1}H NMR (500 MHz, Acetone-*d*$_6$): δ 5.83 (s, 1H), 4.13 – 4.03 (m, 2H), 3.61 (d, *J* = 7.3 Hz, 1H), 3.48 (d, *J* = 7.3 Hz, 1H), 2.55 (dd, *J* = 11.0, 4.3 Hz, 1H), 2.23 – 2.15 (m, 1H), 1.89 (d, *J* = 11.9 Hz, 1H), 1.79 – 1.66 (m, 2H), 1.55 (s, 3H), 1.51 – 1.42 (m, 2H), 1.29 (s, 3H), 1.18 (s, 3H).

^{13}C NMR (126 MHz, Acetone-*d*$_6$): δ 177.5, 172.1, 114.4, 88.2, 84.5, 72.0, 70.7, 52.9, 45.6, 42.9, 40.7, 30.3, 28.0, 27.8, 19.2, 19.2.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_4H^+$ 279.1591, found 279.1590.

$[\alpha]_D^{20}$ = −8.1 (*c* = 0.5, MeOH)

[m.p.] = 243–244 °C



A 2L Erlenmeyer flask was charged with 475 mL of clarified lysate of *E. coli* co-expressing KSA15 and Opt13 (OD_{600} = 30). A pre-dissolved solution of **29** (125 mg, 0.48 mmol, 0.95 mM final concentration) in 25 mL DMSO was added to the lysaste, followed by NaNADP (250 mg, 0.32 mmol, 0.67 equiv.) and $Na_2HPO_3 \cdot 5H_2O$ (625 mg, 28.9 mmol, 60.7 equiv.). The flask was shaken at 150 rpm at 23 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 5). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by flash column chromatography (2: 1 to 1: 2 petroleum ether: EtOAc) to yield compound **36** (43.8 mg, 33% yield) as a white solid.

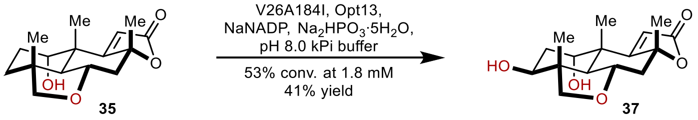
^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 5.84 (d, *J* = 5.4 Hz, 1H), 5.72 (s, 1H), 4.16 (s, 1H), 3.67 (dd, *J* = 12.1, 4.7 Hz, 1H), 2.63 (dd, *J* = 16.5, 6.1 Hz, 1H), 2.31 (d, *J* = 16.4 Hz, 1H), 2.21 (dd, *J* = 13.0, 13.0 Hz, 1H), 1.94 (ddd, *J* = 14.0, 4.2, 4.2 Hz, 1H), 1.58 (s, 3H), 1.52 (s, 3H), 1.22 (s, 3H), 1.14 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 181.2, 175.3, 144.4, 122.3, 111.9, 86.8, 73.2, 73.0, 47.1, 43.7, 39.8, 34.8, 28.4, 26.4, 25.7, 23.3.

HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{22}O_4H^+$ 279.1591, found 279.1593.

$[\alpha]_D^{20}$ = −122.7 (*c* = 0.5, MeOH)

[m.p.] = 226–228 °C



A 250 mL Erlenmeyer flask was charged with 47.5 mL of clarified lysate of *E. coli* co-expressing V26A184I and Opt13 (OD_{600} = 30). A pre-dissolved solution of **35** (25 mg, 0.090 mmol, 1.8 mM final concentration) in 2.5 mL MeOH was added to the lysaste, followed by NaNADP (25 mg, 0.032 mmol, 0.35 equiv.) and $Na_2HPO_3 \cdot 5H_2O$ (0.63 g, 2.89 mmol, 32.2 equiv.). The flask was shaken at 150 rpm at 23 °C under air for 20 h. Then, 5 g NaCl was added to flask and the mixture was extracted with EtOAc (50 mL × 5). The combined organic extracts were washed with sat. aq. $NaHCO_3$ (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude material was purified by PTLC (10: 1 DCM:MeOH) to yield compound **37** (10.9 mg, 41% yield) as white powder.

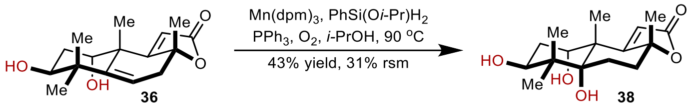
^{1}H NMR (500 MHz, Methanol-*d*$_4$: $CDCl_3$ = 3: 2): δ 5.86 (s, 1H), 4.15 (ddd, *J* = 11.2, 11.2, 4.3 Hz, 1H), 4.07 (dd, *J* = 2.7, 2.7 Hz, 1H), 3.88 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.82 (d, *J* = 7.7 Hz, 1H), 3.69 (d, *J* = 7.7

Hz, 1H), 2.62 (dd, *J* = 11.1, 4.2 Hz, 1H), 2.09 – 2.02 (m, 1H), 1.88 (ddd, *J* = 14.3, 3.8, 3.8 Hz, 1H), 1.79 (d, *J* = 11.8 Hz, 1H), 1.61 – 1.54 (m, 4H), 1.25 (s, 3H), 1.16 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$: CDCl$_3$ = 3: 2): δ 177.9, 174.2, 114.6, 89.6, 84.6, 72.9, 72.4, 72.3, 51.8, 46.3, 44.6, 42.4, 36.6, 27.8, 19.3, 14.1.

HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{22}O_5H^+$ 295.1540, found 295.1540.

$[\alpha]_D^{20}$ = –15.1 (*c* = 0.5, MeOH: CHCl$_3$ = 1:1)



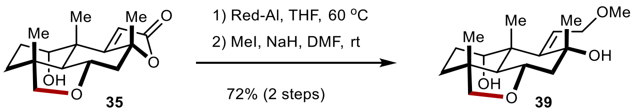
To a stirred solution of compound **36** (10.0 mg, 0.036 mmol, 1.0 equiv.), Mn(dpm)$_3$ (26.1 mg, 0.043 mmol, 1.2 equiv.) and PPh$_3$ (14.1 mg, 0.054 mmol, 1.5 equiv.) in *i*-PrOH (1 mL), PhSi(O*i*-Pr)H$_3$ (32 uL, 0.18 mmol, 5 equiv.) was added slowly at room temperature under O$_2$ atmosphere. After stirring at 90 °C for 24 h, the mixture was concentrated *in vacuo*. The crude material was purified by PTLC (EtOAc) to yield **38** (4.6 mg, 43% yield) and **36** (3.1 mg, 31% yield) as white powder.

^{1}H NMR (500 MHz, Methanol-*d*$_4$): δ 6.06 (s, 1H), 4.18 (dd, *J* = 2.8, 2.8 Hz, 1H), 4.06 (dd, *J* = 12.2, 4.9 Hz, 1H), 2.20 (ddd, *J* = 14.5, 12.3, 2.5 Hz, 1H), 2.13 – 2.06 (m, 1H), 1.99 (ddd, *J* = 14.3, 9.8, 5.1 Hz, 3H), 1.86 – 1.80 (m, 1H), 1.61 (s, 3H), 1.35 (s, 3H), 1.09 (s, 3H), 0.99 (s, 3H).

^{13}C NMR (126 MHz, Methanol-*d*$_4$): δ 180.9, 175.3, 114.9, 89.1, 83.2, 74.9, 70.1, 47.7, 45.6, 35.6, 34.7, 27.5, 26.1, 23.2, 23.1, 18.1.

HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{24}O_5H^+$ 297.1697, found 297.1695.

$[\alpha]_D^{20}$ = –78.4 (*c* = 0.2, MeOH)



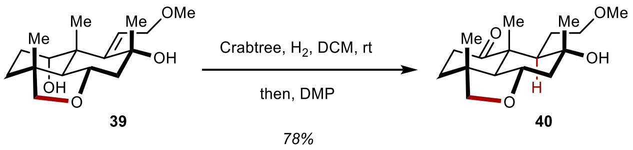
To a stirred solution of compound **35** (400 mg, 1.44 mmol, 1.0 equiv.) in THF (15 mL) was added Red-Al (60% in toluene, 2.0 mL, 5.76 mmol, 4.0 equiv.) dropwise via syringe at room temperature. After stirring at 60 ºC for 4 h, the reaction mixture was quenched with saturated Rochelle´s salt (50 mL). After 12 h, the mixture was extracted with EtOAc (3 × 100 mL). The combined organic extracts was washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The colorless oil as crude product was directly used in next step without further purification. The colorless oil was redissolved in DMF (10 mL). To the stirred solution was added CH$_3$I (0.11 ml, 1.73 mmol, 1.2 equiv.) followed by NaH (172 mg, 4.32 mmol, 3.0 equiv.). The mixture was stirred at room temperature. After 1 h, the reaction mixture was quenched with saturated aq. NH$_4$Cl (20 mL) and extracted with EtOAc (3 × 50 mL). The combined organic extract was washed with brine, dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (100% EtOAc) to afford **39** (290 mg, 72% yield) as white powder.

^{1}H NMR (500 MHz, CDCl$_3$): δ 5.43 (dd, *J* = 5.5, 5.5 Hz, 1H), 4.43 (dd, *J* = 13.2, 5.2 Hz, 1H), 4.27 (dd, *J* = 13.2, 6.0 Hz, 1H), 3.95 (dd, *J* = 2.9, 2.9 Hz, 1H), 3.83 (ddd, *J* = 11.3, 11.3, 4.2 Hz, 1H), 3.66 (d, *J* = 7.3 Hz, 1H), 3.49 (d, *J* = 7.3 Hz, 1H), 3.37 (s, 3H), 2.37 (dd, *J* = 11.5, 4.2 Hz, 1H), 2.00 – 1.92 (m, 1H) 1.79 (d, *J* = 11.9 Hz, 1H), 1.65 – 1.56 (m, 2H), 1.48 (d, *J* = 2.6 Hz, 1H), 1.41 (s, 3H), 1.12 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 152.0, 123.9, 83.8, 75.3, 71.0, 71.0, 69.9, 58.4, 51.0, 50.5, 44.9, 40.3, 31.2, 29.6, 25.5, 24.4, 19.3.

HRMS (*m/z*): [M+Na]$^+$ calcd for C$_{17}$H$_{28}$O$_4$Na$^+$ 319.1885, found 319.1878.

$[\alpha]_D^{25}$ = + 54.5 (*c* = 0.25, MeOH).



39

40

To a stirred solution of compound **39** (290 mg, 0.98 mmol, 1.0 equiv.) in degassed DCM (15 mL) was added Crabtree's catalyst (40 mg, 0.05 mmol, 0.05 equiv.). The reaction mixture was allowed to stir under H_2 (balloon pressure) at room temperature for 12 h. Then, Dess-Martin periodinane (64 mg, 1.50 mmol, 1.5 equiv.) was added to the mixture. The reaction mixture was stirred for 1 h before it was quenched with saturated aq. $Na_2S_2O_3$ (10 mL) and $NaHCO_3$ (10 mL). Then, it was extracted with EtOAc (3 × 100 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1:1 petroleum ether: EtOAc) to yield compound **40** (226 mg, 78% yield) as a white solid.

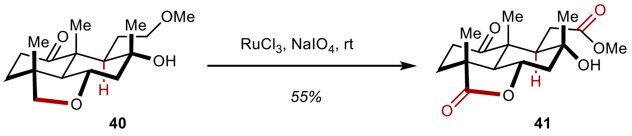
^{1}H NMR (500 MHz, Chloroform-*d*): δ 3.87 (ddd, *J* = 11.2, 11.2, 4.3 Hz, 1H), 3.71 (d, *J* = 7.6 Hz, 1H), 3.66 (dd, *J* = 5.6, 3.3 Hz, 2H), 3.50 (d, *J* = 7.6 Hz, 1H), 3.38 (s, 3H), 2.93 (ddd, *J* = 14.2, 14.2, 6.1 Hz, 1H), 2.32 (dd, *J* = 11.6, 4.3 Hz, 1H), 2.17 (ddd, *J* = 15.0, 4.6, 2.1 Hz, 1H), 1.95 (ddd, *J* = 12.8, 6.2, 2.2 Hz, 1H), 1.90 – 1.82 (m, 2H), 1.78 – 1.71 (m, 2H), 1.53 (d, *J* = 11.4 Hz, 1H), 1.44 (dd, *J* = 11.4, 11.4 Hz, 1H), 1.38 (s, 3H), 1.18 (s, 3H), 1.18 (s, 3H).

^{13}C NMR (126 MHz, Chloroform-*d*): δ 214.0, 82.8, 73.9, 73.0, 71.8, 62.8, 58.8, 53.0, 51.7, 48.4, 39.7, 37.4, 35.1, 27.6, 26.4, 19.7, 14.4.

HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{28}O_4Na^+$ 319.1885, found 319.1877.

$[\alpha]_D^{25}$ = +28.9 (*c* = 0.25, MeOH).

[m.p.] = 133–135 °C



Ether **40** (200 mg, 0.68 mmol, 1.0 equiv.) was dissolved in CH_3CN (10 mL) and CCl_4 (10 mL). Then, potassium phosphate buffer (1 M, pH = 7, 10 mL) was added followed by $RuCl_3$ (153 mg, 0.68 mmol, 1.0 equiv.) and $NaIO_4$ (292 mg, 1.36 mmol, 2.0 equiv.). The mixture was stirred vigorously at room temperature. After 4 h, another portion of $NaIO_4$ (0.5 equiv.) was added and the mixture was stirred for

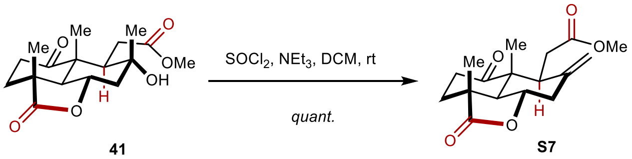
12 h. This was repeated once, then another portion of $NaIO_4$ (0.5 equiv.) was added and stirred for another 12 h. The reaction was quenched with saturated aq. $Na_2S_2O_3$ (50 mL) and extracted with EtOAc (3 × 100 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (1:1 petroleum ether:EtOAc) to yield compound **41** (123 mg, 55% yield) as white powder.

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.29 (ddd, J = 11.2, 11.2, 4.5 Hz, 1H), 3.67 (s, 3H), 2.84 – 2.75 (m, 1H), 2.74 (d, J = 13.1 Hz, 1H), 2.48 – 2.38 (m, 3H), 2.25 (ddd, J = 15.6, 4.8, 2.0 Hz, 1H), 1.90 (d, J = 11.4 Hz, 1H), 1.60 (dd, J = 11.3, 11.3 Hz, 1H), 1.41 (s, 3H), 1.16 (s, 3H), 1.15 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 210.3, 178.7, 175.2, 73.4, 72.5, 59.5, 52.1, 49.2, 49.0, 46.9, 40.9, 34.2, 33.9, 31.2, 23.9, 15.6, 14.9.

HRMS (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{24}O_6Na^+$ 347.1471, found 347.1463.

$[\alpha]_D^{25}$ = –5.4 (c = 0.25, MeOH).



To a stirred solution of compound **41** (100 mg, 0.31 mmol, 1.0 equiv.) in DCM (10 mL) was added Et_3N (0.26 ml, 1.86 mmol, 6.0 equiv.) followed by $SOCl_2$ (50 μl, 0.68 mmol, 2.0 equiv.). The reaction mixture was allowed to stir at –90 °C for 1 h. Then, the reaction mixture was quenched with saturated aq. NH_4Cl (10 mL) and extracted with EtOAc (3 × 30 mL). The combined organic extract was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (2:1 petroleum ether: EtOAc) to yield compound **S7** (90 mg, 95% yield) as white powder.

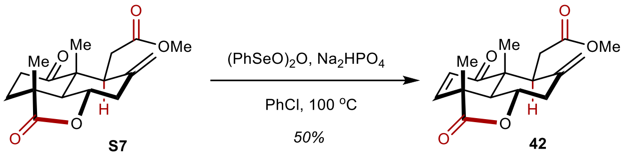
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.15 (s, 1H), 4.89 (s, 1H), 4.29 (ddd, J = 11.0, 11.0, 5.1 Hz, 1H), 3.67 (s, 3H), 3.33 (dd, J = 16.3, 2.8 Hz, 1H), 3.02 – 2.91 (m, 2H), 2.79 (ddd, J = 15.6, 13.3, 6.5 Hz, 1H), 2.46 (dd,

J = 16.3, 11.4 Hz, 1H), 2.40 (ddd, J = 15.6, 4.7, 2.1 Hz, 1H), 2.28 (dd, J = 11.2, 11.2 Hz, 1H), 2.15 – 2.11 (m, 1H), 2.13 – 2.10 (m,1H), 2.09 – 2.02 (m, 1H), 1.47 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 211.6, 178.7, 172.8, 141.8, 115.8, 74.0, 59.8, 51.9, 50.0, 45.4, 42.5, 41.3, 35.9, 33.8, 32.2, 15.7, 13.4.

HRMS (*m/z*): [M+Na]$^+$ calcd for $C_{17}H_{22}O_5Na^+$ 329.1365, found 347.1358.

$[\alpha]_D^{25}$ = +33.7 (c = 0.25, MeOH).



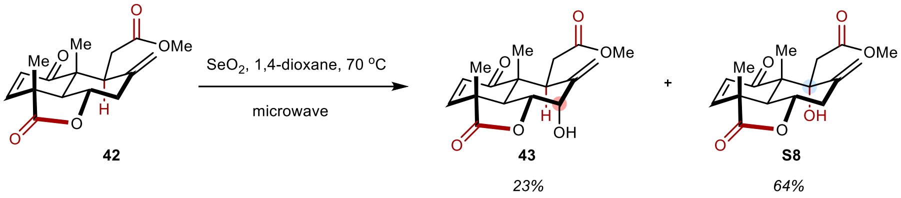
To a stirred solution of compound **S7** (20.0 mg, 0.07 mmol, 1.0 equiv.) in PhCl (10 mL) was added Na_2HPO_4 (49.3 mg, 0.35 mol, 5.0 equiv.) and benzeneseleninic acid anhydride[1] (75.6 mg, 0.21 mol, 3.0 equiv.). The reaction mixture was stirred at 100 ºC for 4 h after which time TLC analysis indicated that all starting material was consumed. The reaction was cooled to room temperature before it was purified by flash column chromatography (3:1 petroleum ether: EtOAc) to yield compound **42** (10.0 mg, 50% yield) as white powder.

^{1}H NMR (500 MHz, CDCl$_3$): δ 7.27 (d, J = 9.7 Hz, 1H), 5.97 (d, J = 9.7 Hz, 1H), 5.20 (dd J = 1.5, 1.5 Hz, 1H), 4.96 (dd, J = 1.4, 1.4 Hz, 1H), 4.36 (ddd, J = 11.7, 10.3, 5.3 Hz, 1H), 3.67 (s, 3H), 3.62 (dd, J = 16.6, 3.0 Hz, 1H), 3.05 (dd, J = 11.9, 5.3 Hz, 1H), 2.67 (d, J = 11.7 Hz, 1H), 2.60 (dd, J = 16.6, 11.4 Hz, 1H), 2.39 (dd, J = 11.1, 11.1 Hz, 1H), 1.43 (s, 3H), 1.04 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 201.8, 175.9, 172.9, 149.8, 141.5, 131.7, 116.6, 74.6, 57.2, 52.0, 46.4, 46.2, 44.2, 42.8, 31.8, 18.5, 13.8.

HRMS (*m/z*): [M+H]$^+$ calcd for $C_{17}H_{20}O_5H^+$ 305.1389, found 305.1385.

$[\alpha]_D^{25}$ = +81.1 (c = 0.25, MeOH).



To a stirred solution of compound **42** (10.0 mg, 0.03 mmol, 1.0 equiv.) in 1,4-dioxane (2.0 mL) was added SeO_2 (10.0 mg, 0.09 mol, 3.0 equiv.). The reaction mixture was stirred at 70 ºC for 2 h under microwave condition before it was concentrated *in vacuo*. The residue was purified by flash column chromatography (1:1 petroleum ether: EtOAc) to yield compound **43** (2.40 mg, 23% yield) and compound **S8** (6.70 mg, 64% yield) as white powder.

(Compound **43**) **^{1}H NMR (600 MHz, CDCl$_3$):** δ 7.24 (d, *J* = 9.7 Hz, 1H), 5.97 (d, *J* = 9.7 Hz, 1H), 5.21 (s, 1H), 5.18 (s, 1H), 4.92 (s, 1H), 4.38 – 4.31 (m, 1H), 3.87 (d, *J* = 17.1 Hz, 1H), 3.75 (s, 1H), 3.74 (s, 3H), 3.72 (s, 1H), 2.97 – 2.89 (m, 2H), 2.80 (dd, *J* = 11.5, 5.4 Hz, 1H), 1.40 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (151 MHz, CDCl$_3$): δ 201.1, 176.2, 174.9, 149.5, 144.7, 132.4, 116.6, 78.1, 74.7, 52.3, 50.9, 48.3, 43.7, 38.5, 35.2, 18.4, 15.0.

HRMS (*m/z*): [M+Na]$^+$ calcd for $C_{17}H_{20}O_6Na^+$ 343.1158, found 343.1151.

$[\alpha]_D^{25}$ = +26.2 (*c* = 0.1, CHCl$_3$).

(Compound **S8**) **^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.28 (d, *J* = 9.7 Hz, 1H), 5.98 (d, *J* = 9.7 Hz, 1H), 5.40 (s, 1H), 5.08 (s, 1H), 4.76 (d, *J* = 3.4 Hz, 1H), 4.38 (dd, *J* = 12.3, 3.5 Hz, 1H), 3.61 (dd, *J* = 16.6, 3.2 Hz, 1H), 3.43 (d, *J* = 11.5 Hz, 1H), 3.40 (d, *J* = 12.3 Hz, 1H), 2.59 (dd, *J* = 16.5, 11.7 Hz, 1H), 1.44 (s, 3H), 1.03 (s, 3H).

^{13}C NMR (126 MHz, CDCl$_3$): δ 201.6, 175.5, 172.7, 149.6, 144.6, 131.9, 118.2, 76.3, 72.5, 52.0, 47.2, 46.1, 44.1, 40.8, 31.3, 18.4, 13.0.

HRMS (*m/z*): [M+Na]$^+$ calcd for $C_{17}H_{20}O_6Na^+$ 343.1158, found 343.1150.

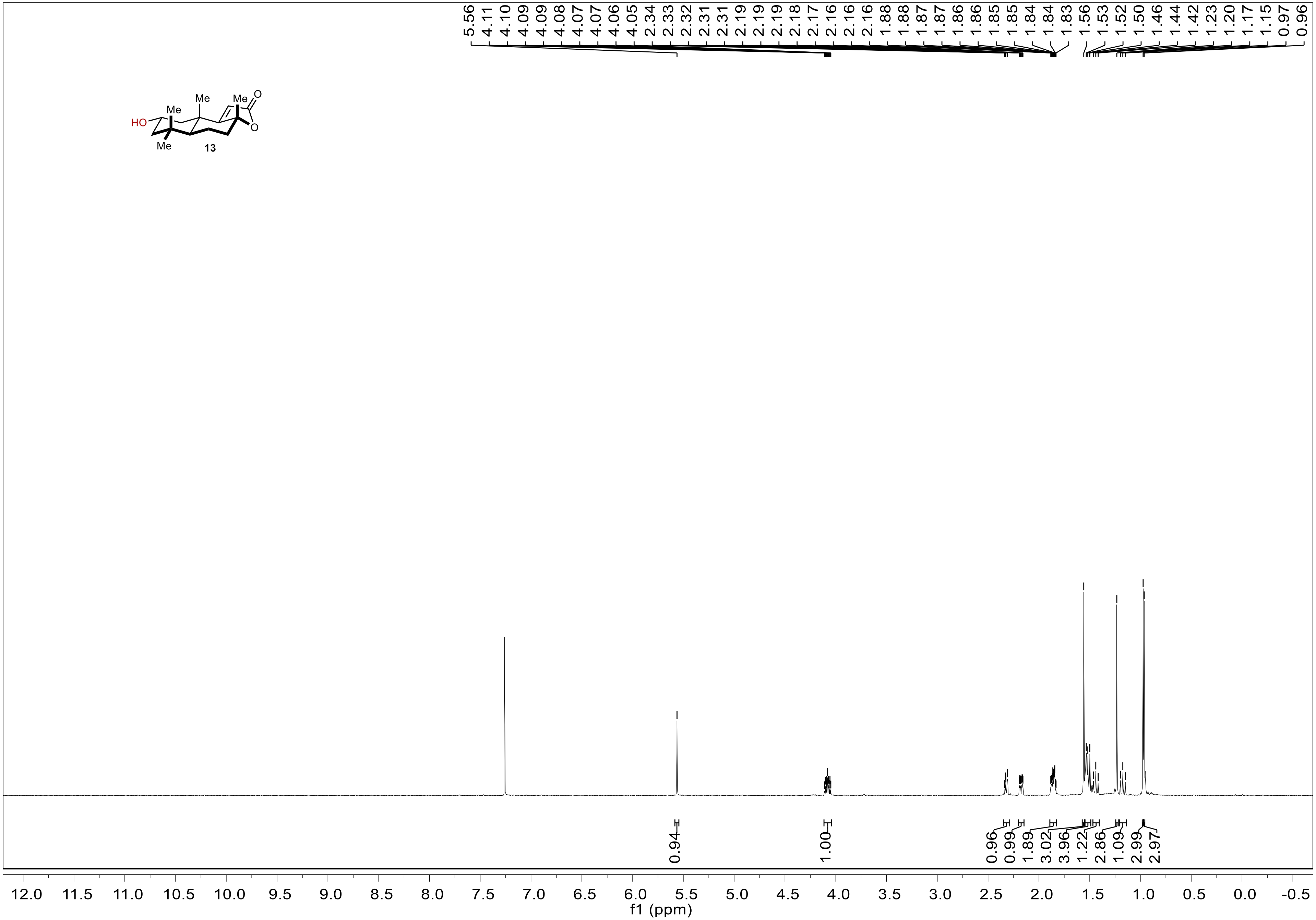
$[\alpha]_D^{25}$ = +68.2 (*c* = 0.25, MeOH).

References

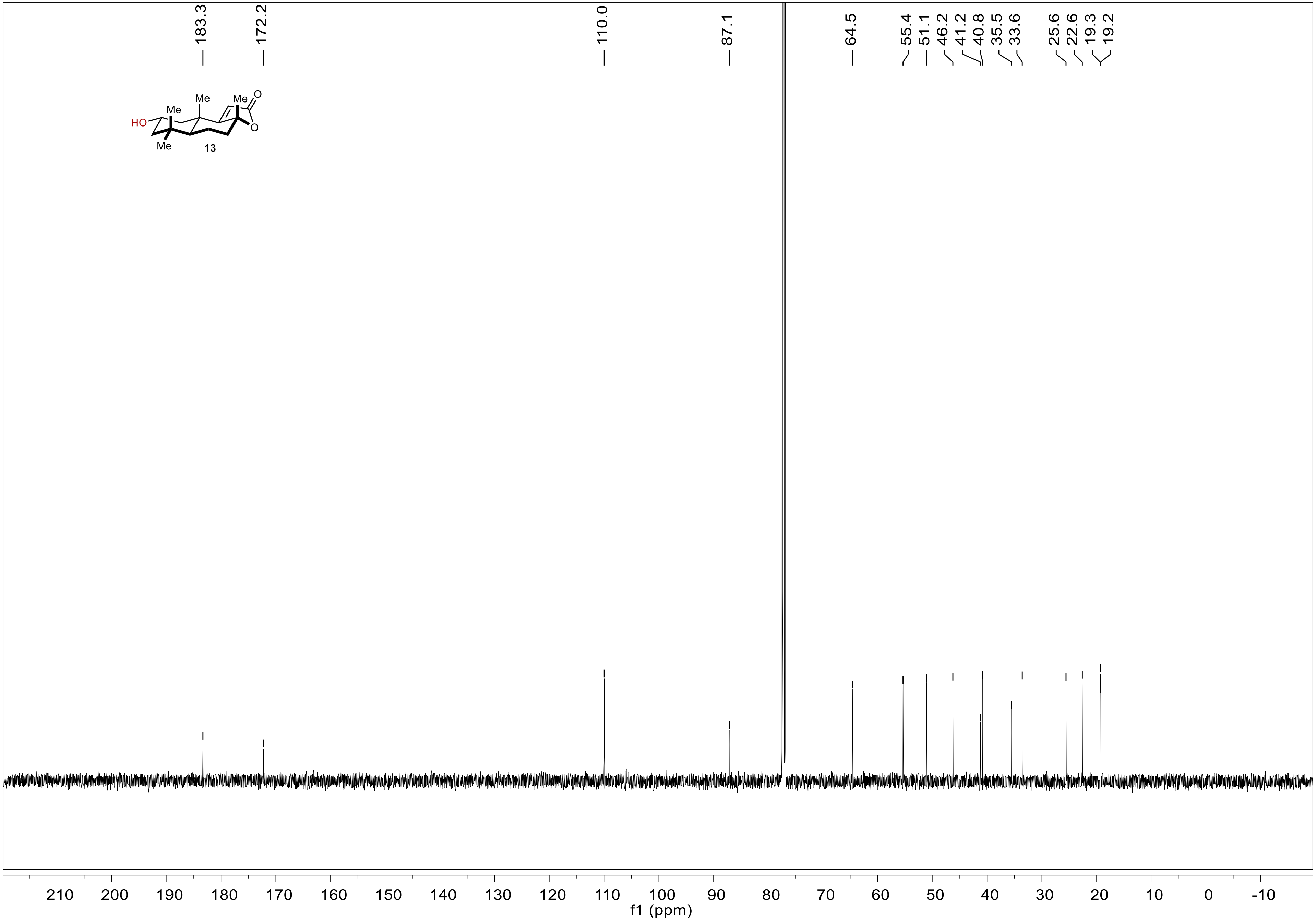
1. Yang, F. & Porco, J. A., Jr. Unified, asymmetric Total Synthesis of the Asnovolins and Related Spiromeroterpenoids: A Fragment Coupling Approach. *J. Am. Chem. Soc.* **144**, 12970–12978 (2022).

NMR Spectra of Compounds

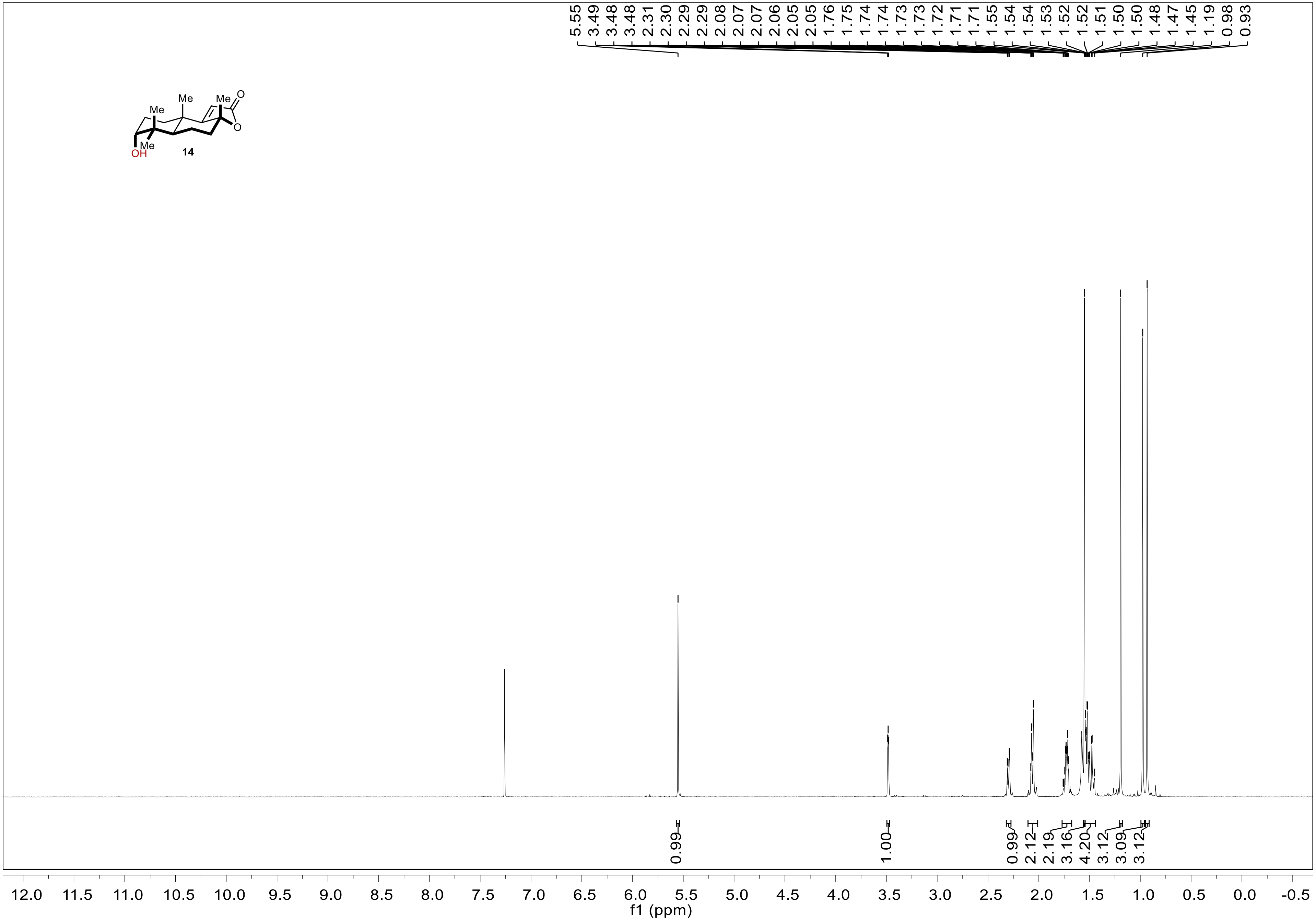
^{1}H NMR Spectrum of compound 13 (500 MHz, $CDCl_3$)



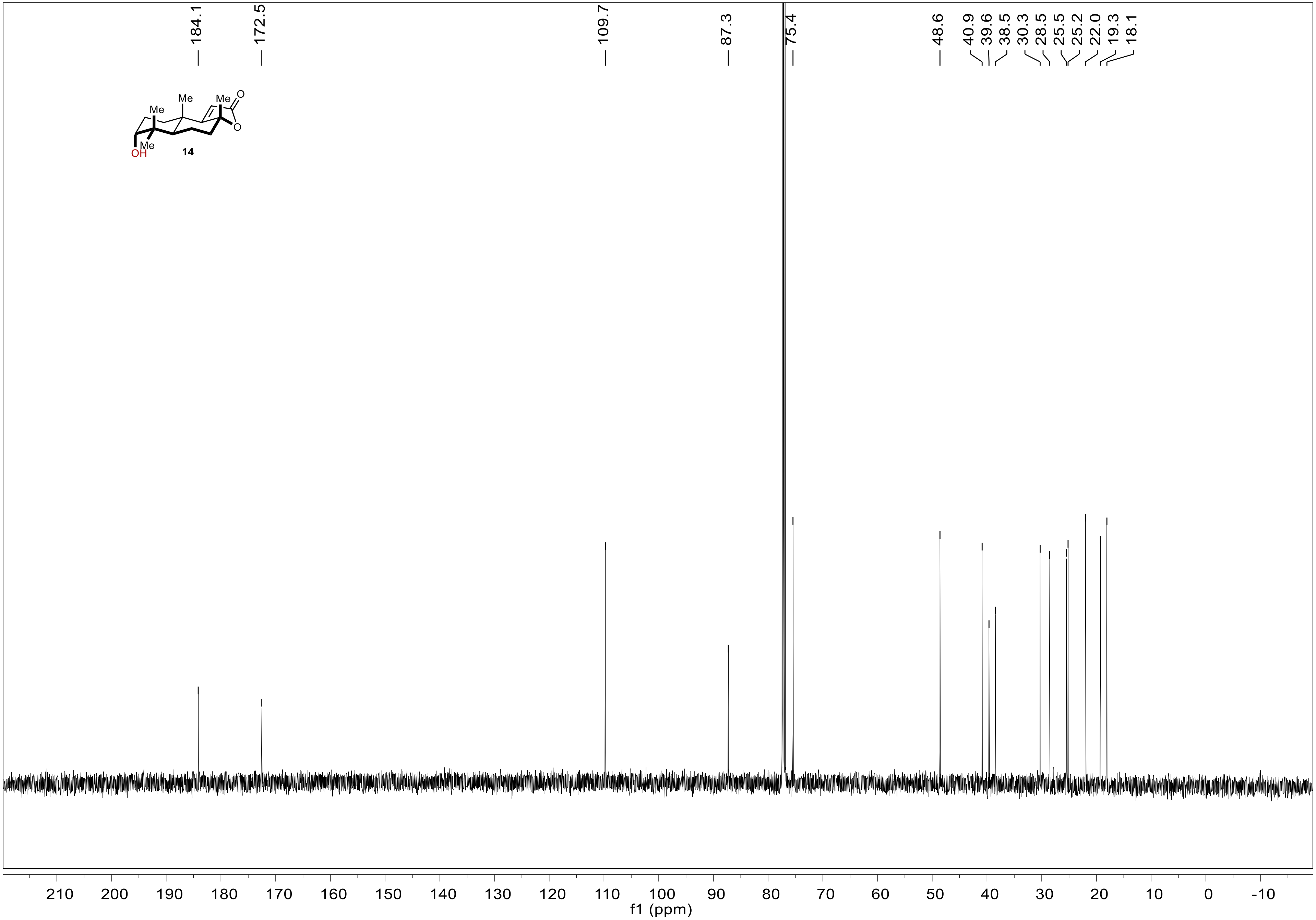
^{13}C NMR Spectrum of compound 13 (126 MHz, $CDCl_3$)



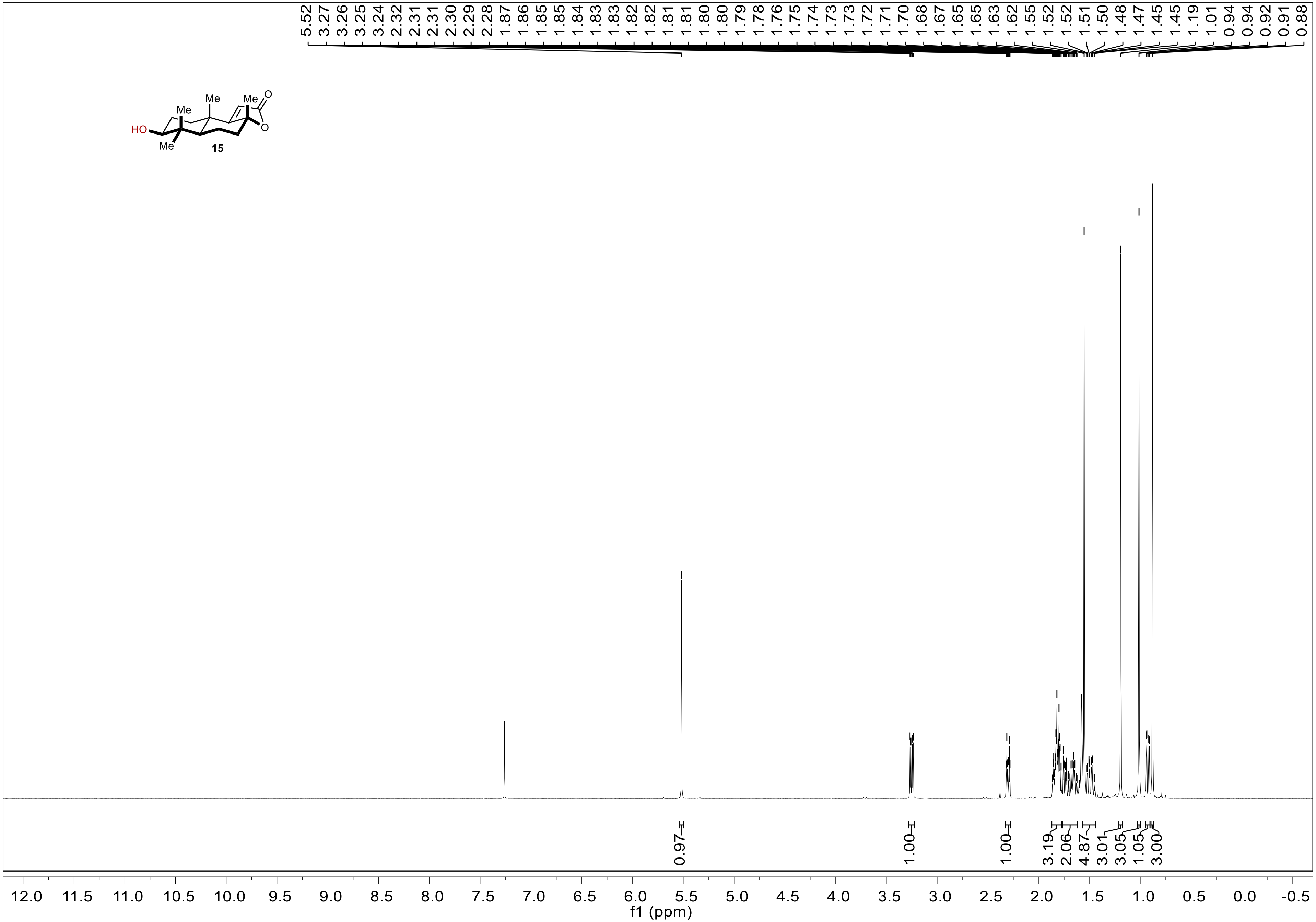
^{1}H NMR Spectrum of compound 14 (500 MHz, CDCl$_3$)



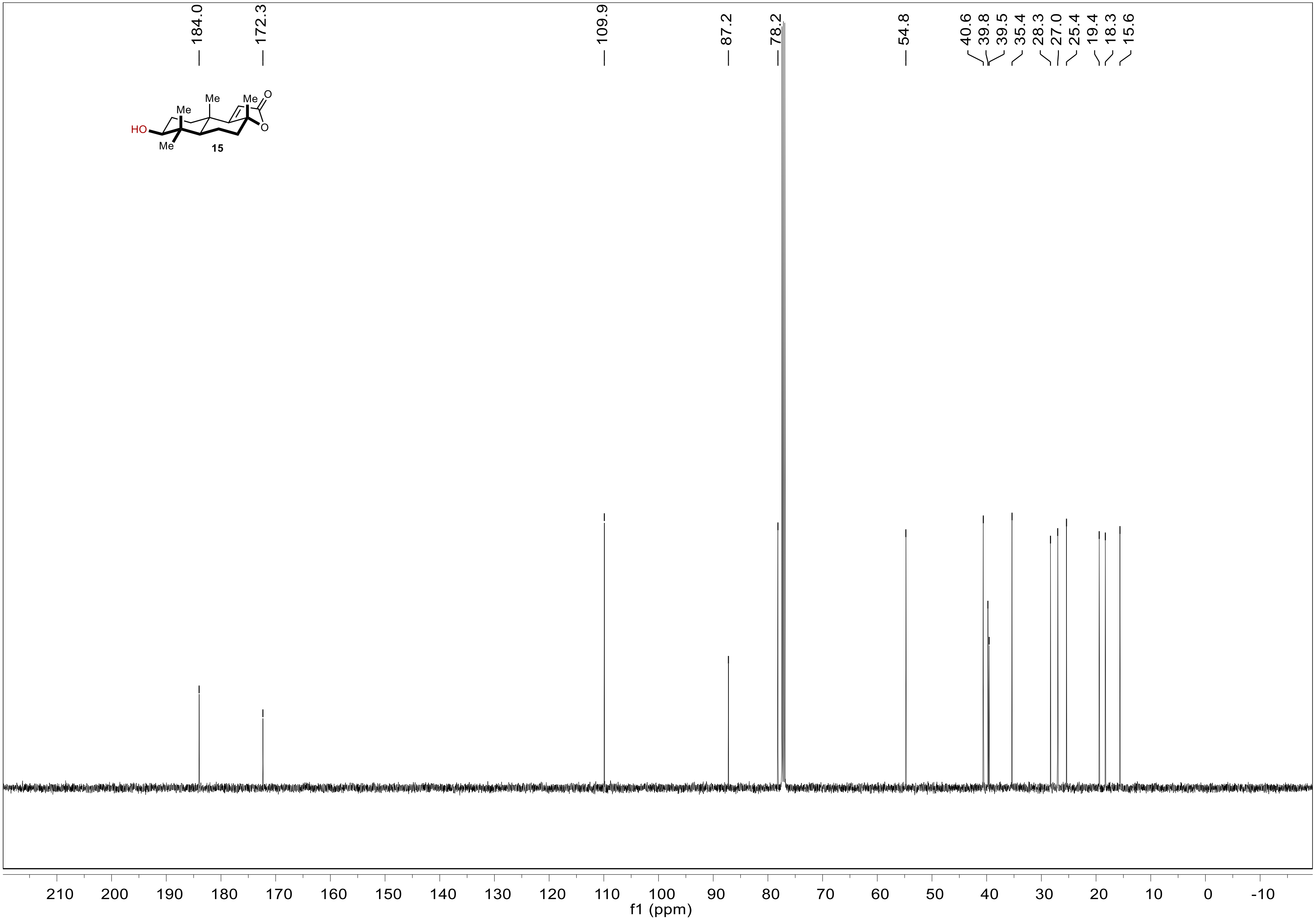
^{13}C NMR Spectrum of compound 14 (126 MHz, CDCl$_3$)



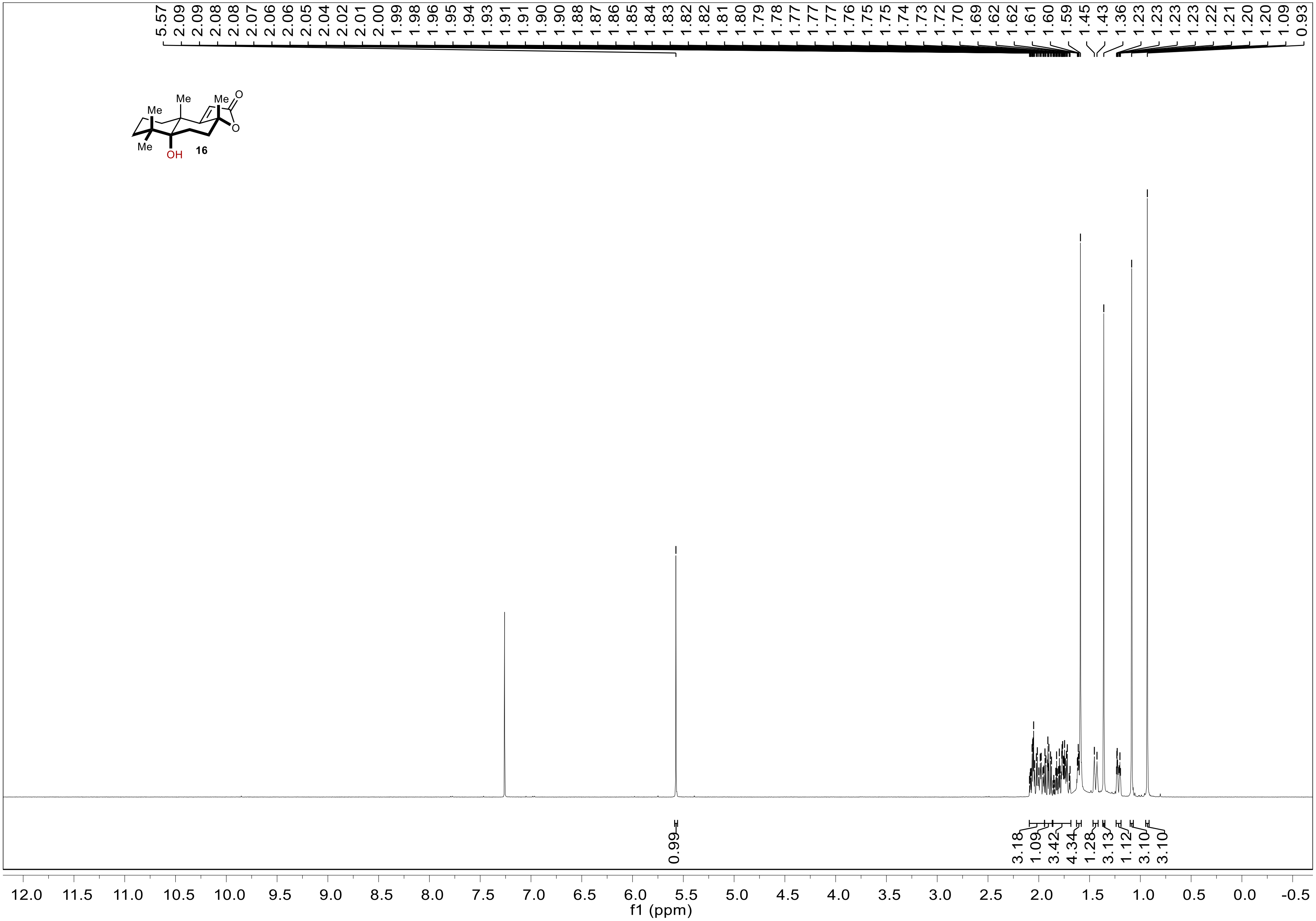
^{1}H NMR Spectrum of compound 15 (500 MHz, $CDCl_3$)



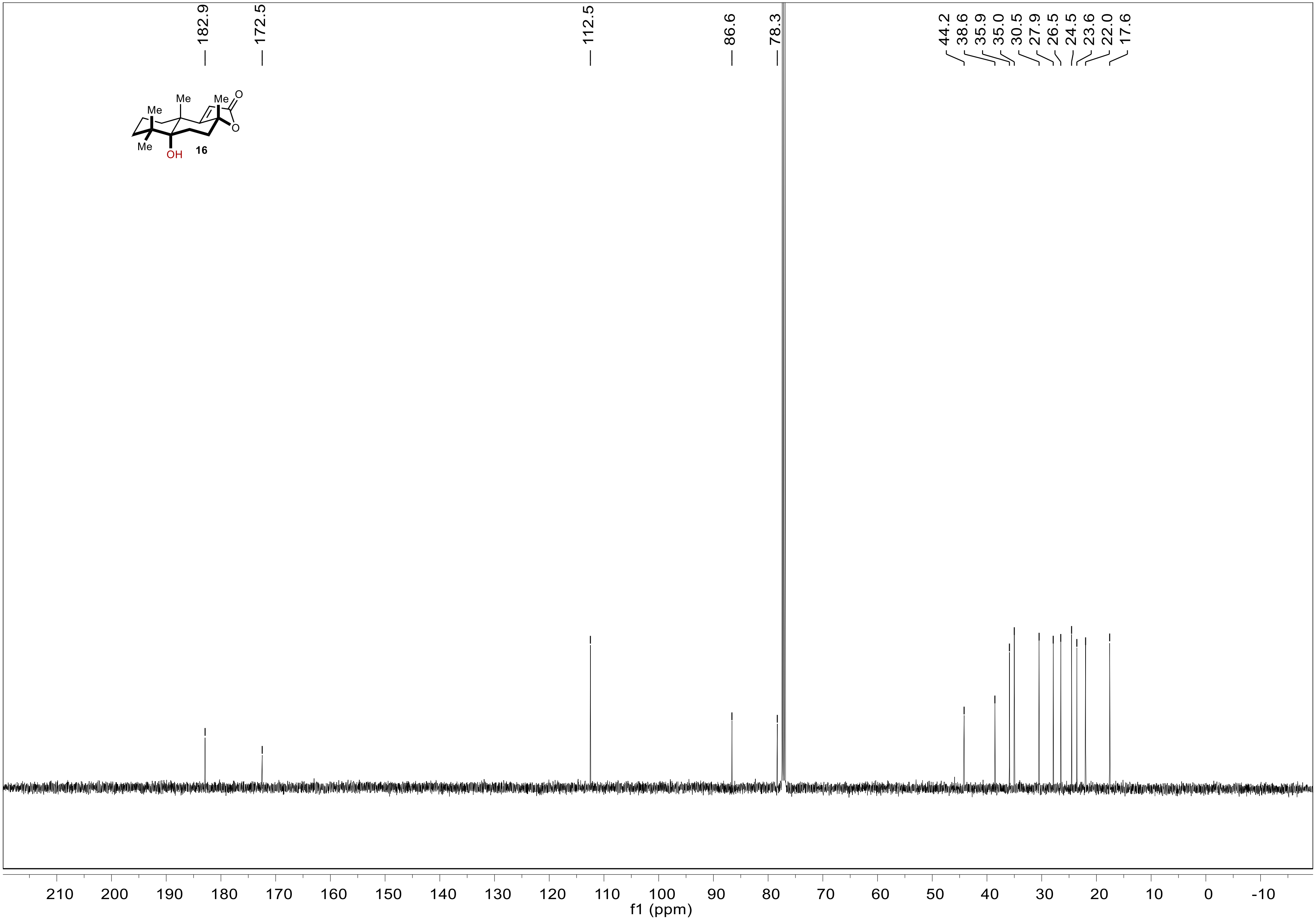
^{1}H NMR Spectrum of compound 15 (500 MHz, $CDCl_3$)



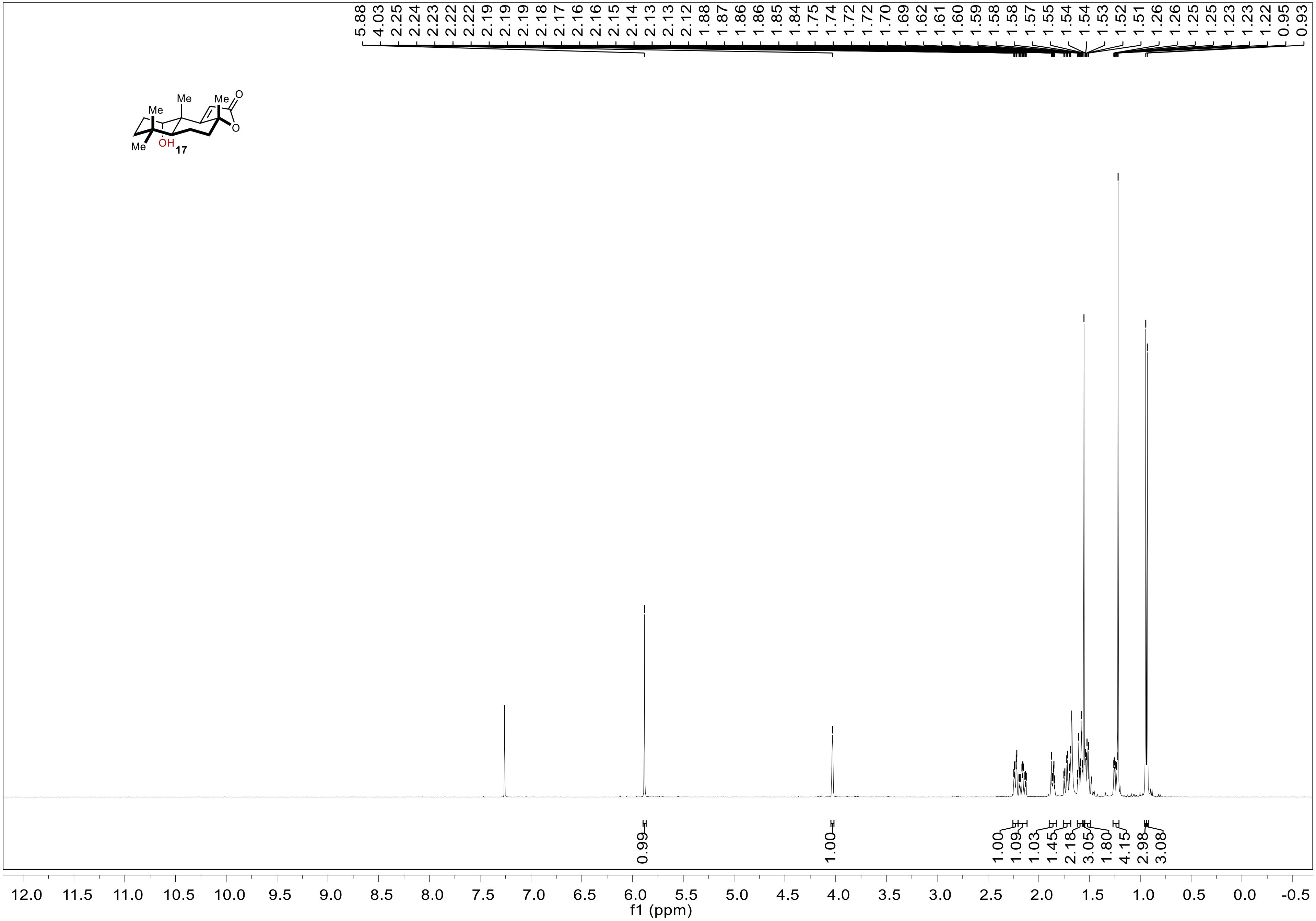
^1H NMR Spectrum of compound 16 (500 MHz, $CDCl_3$)



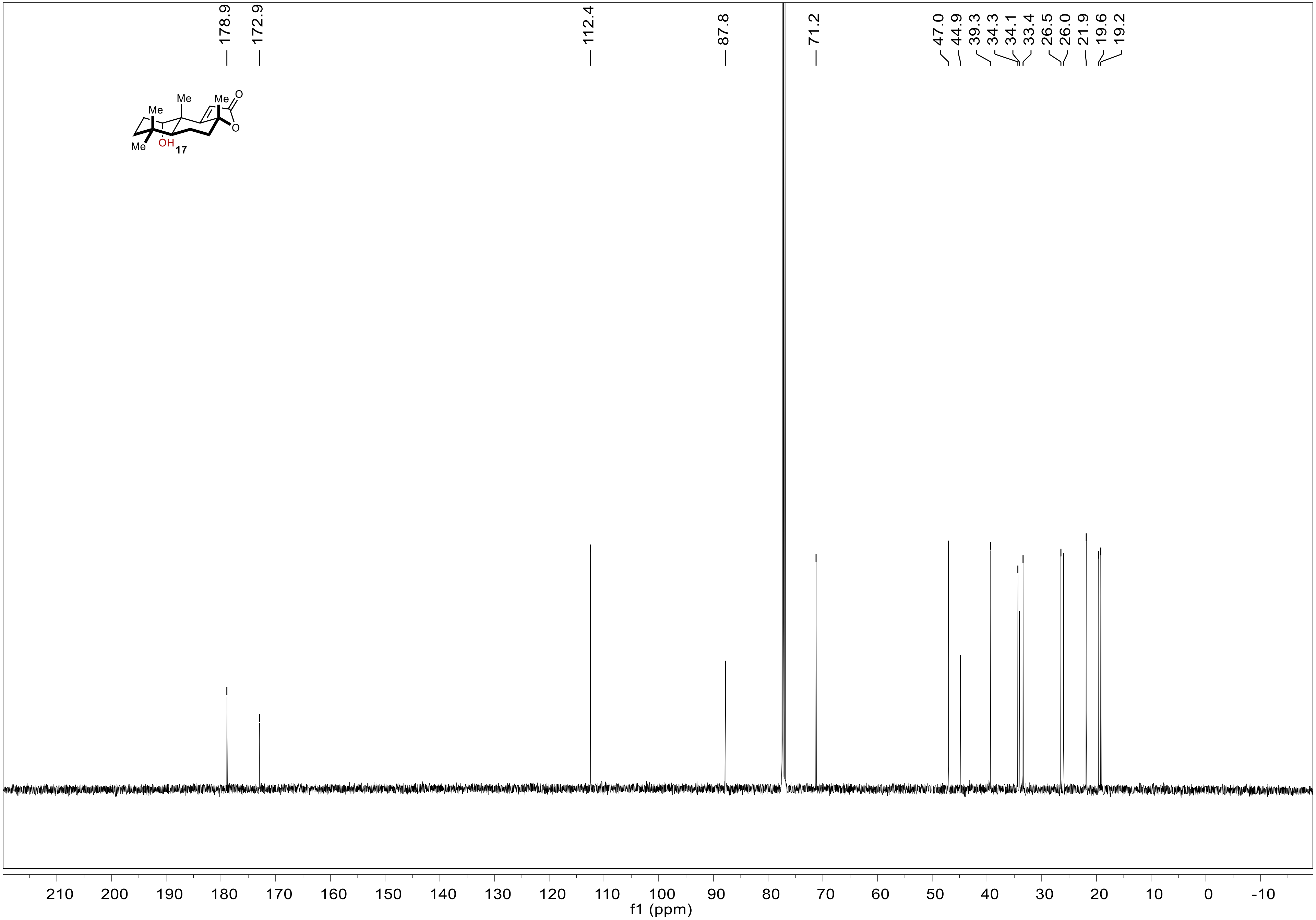
^{13}C NMR Spectrum of compound 16 (126 MHz, $CDCl_3$)



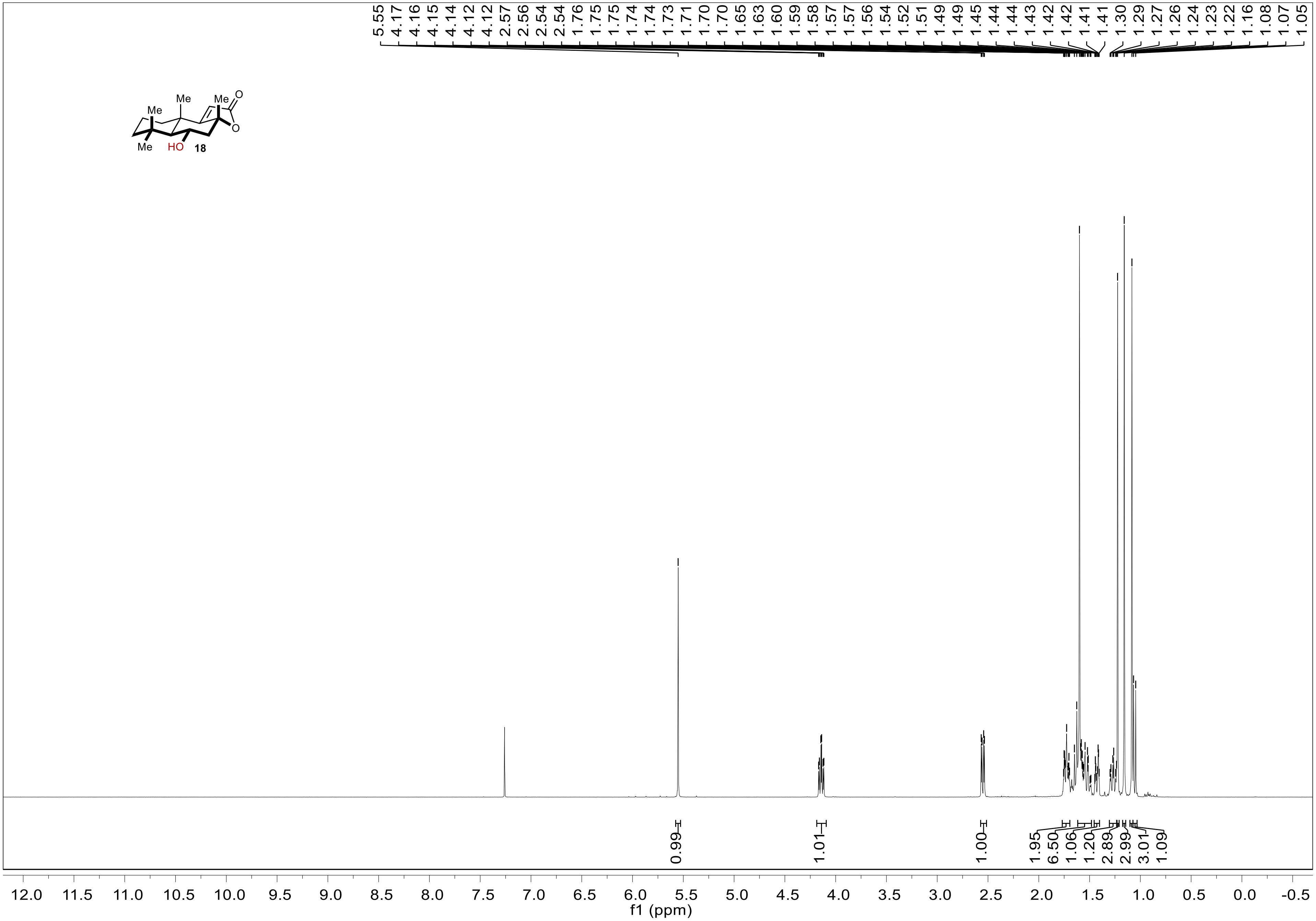
^{1}H NMR Spectrum of compound 17 (500 MHz, $CDCl_3$)



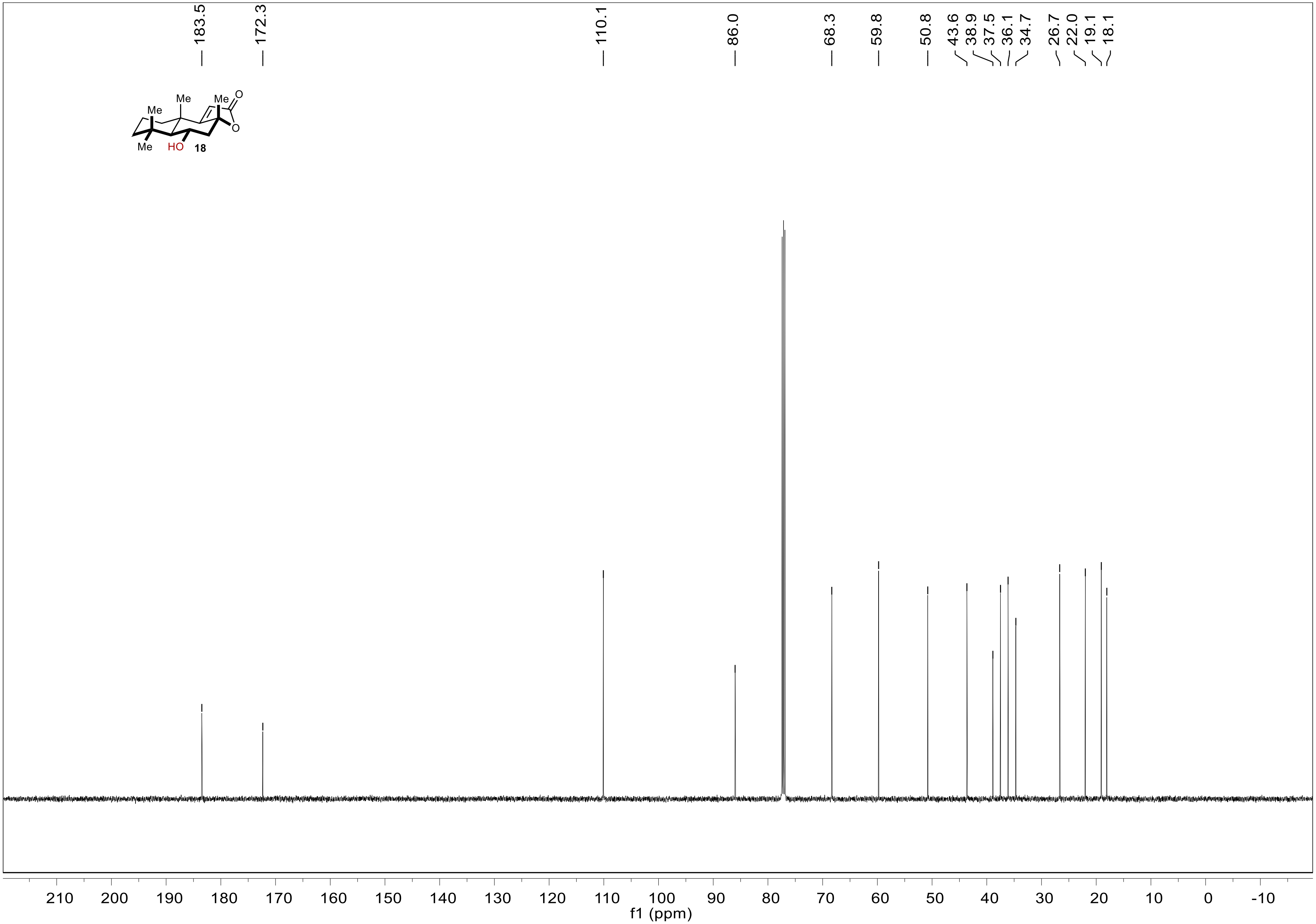
^{13}C NMR Spectrum of compound 17 (126 MHz, $CDCl_3$)



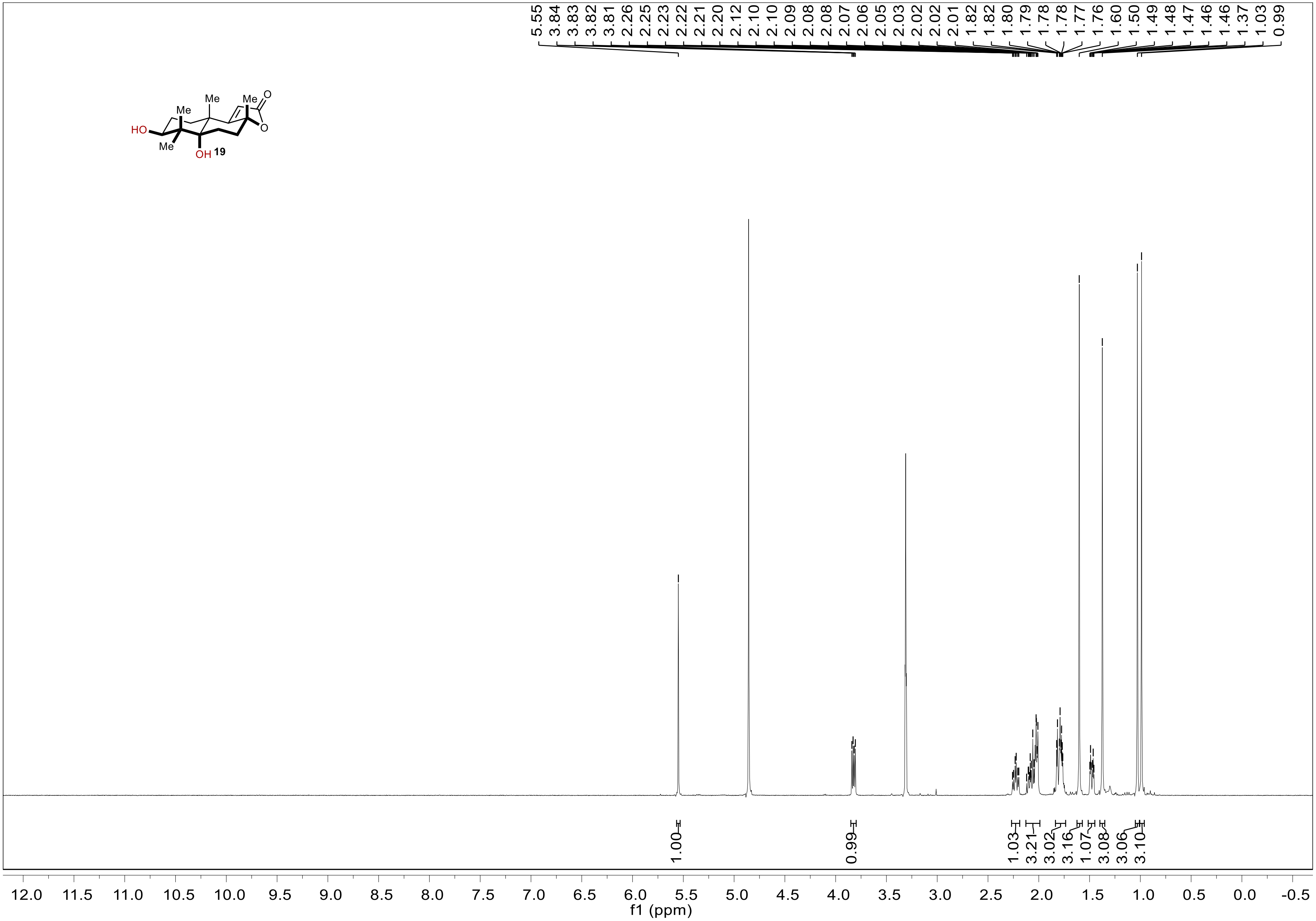
^{1}H NMR Spectrum of compound 18 (500 MHz, $CDCl_3$)



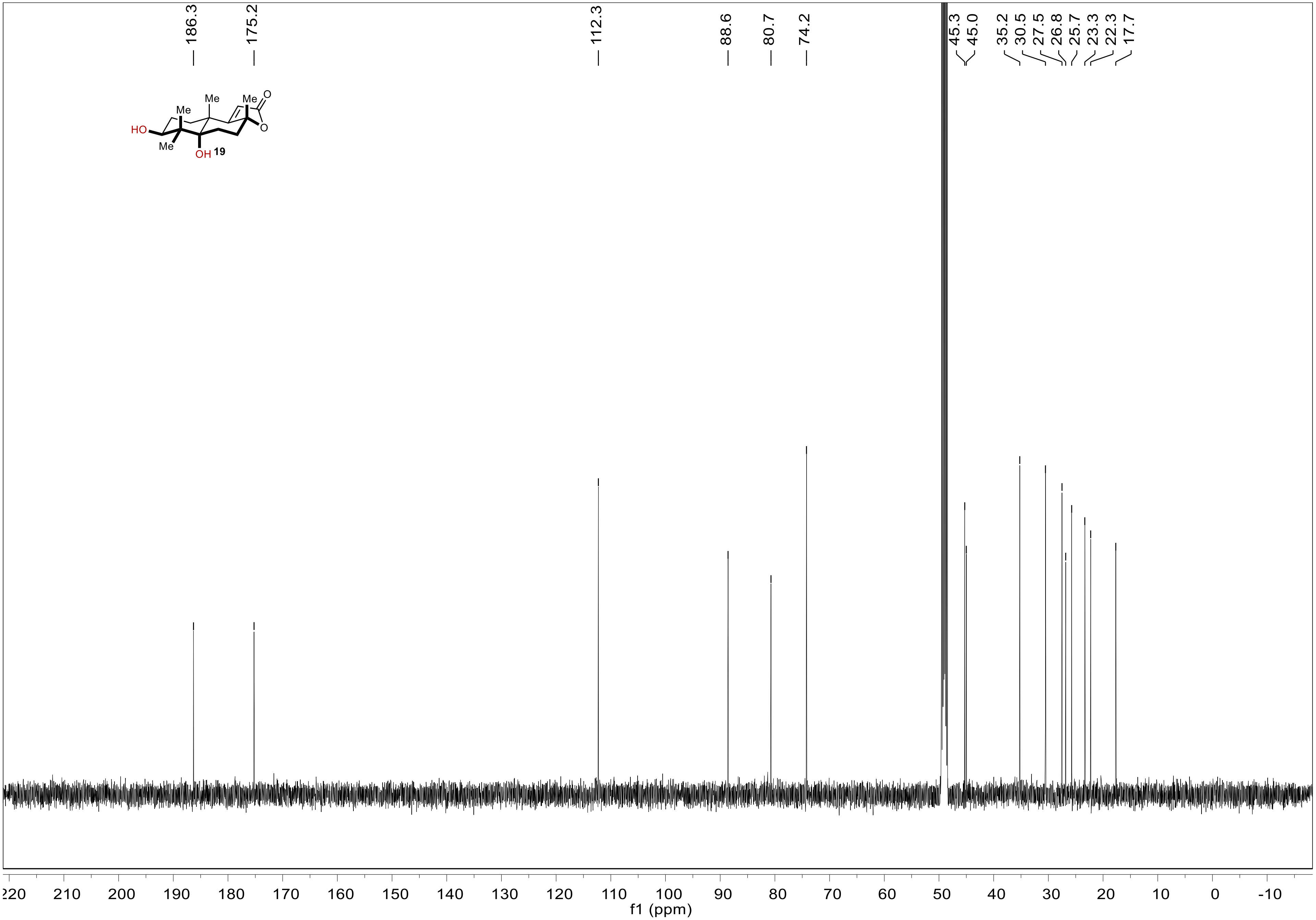
^{13}C NMR Spectrum of compound 18 (126 MHz, $CDCl_3$)



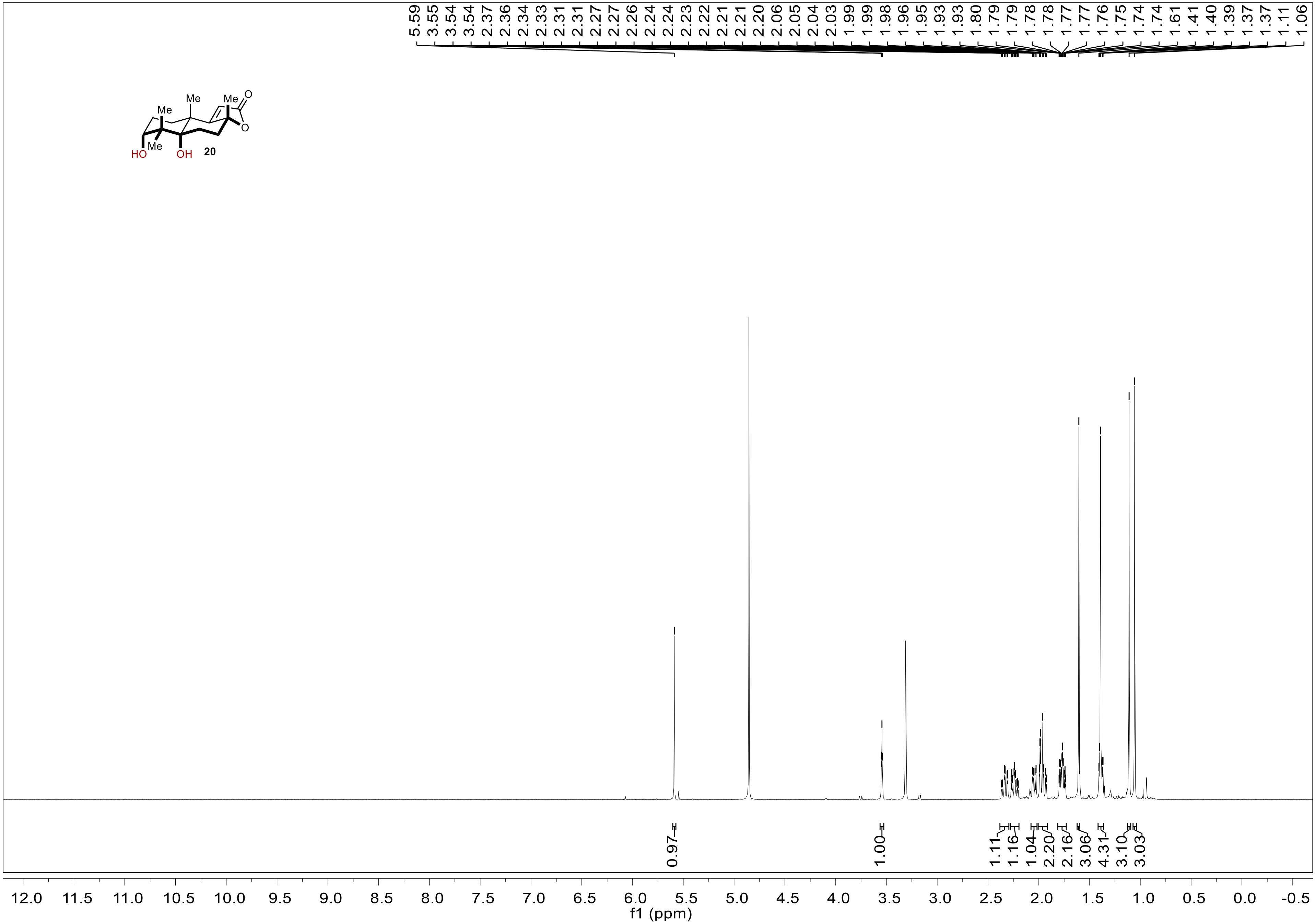
^{1}H NMR Spectrum of compound 19 (500 MHz, Methanol-d_4)



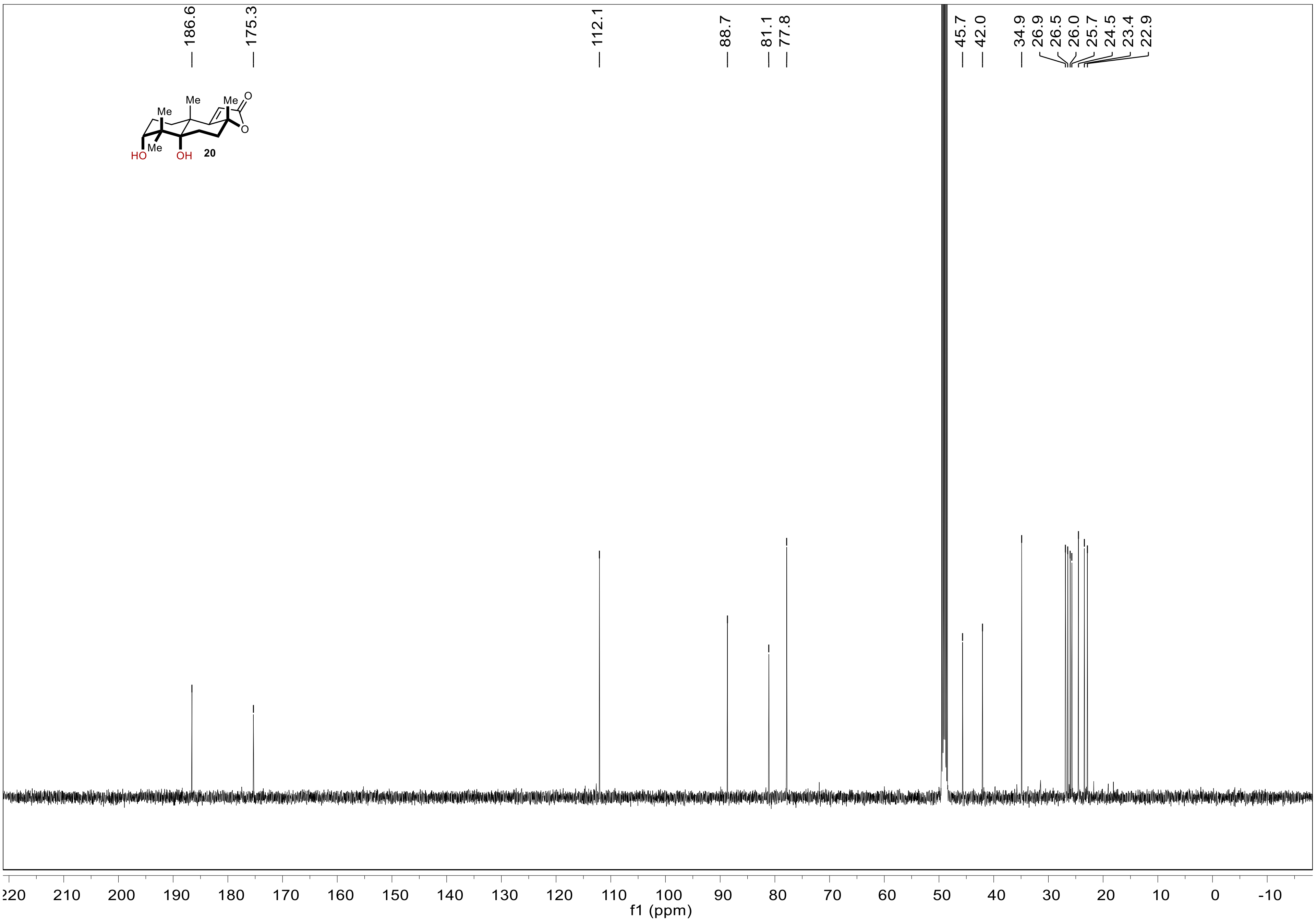
^{1}H NMR Spectrum of compound 19 (126 MHz, Methanol-d_4)



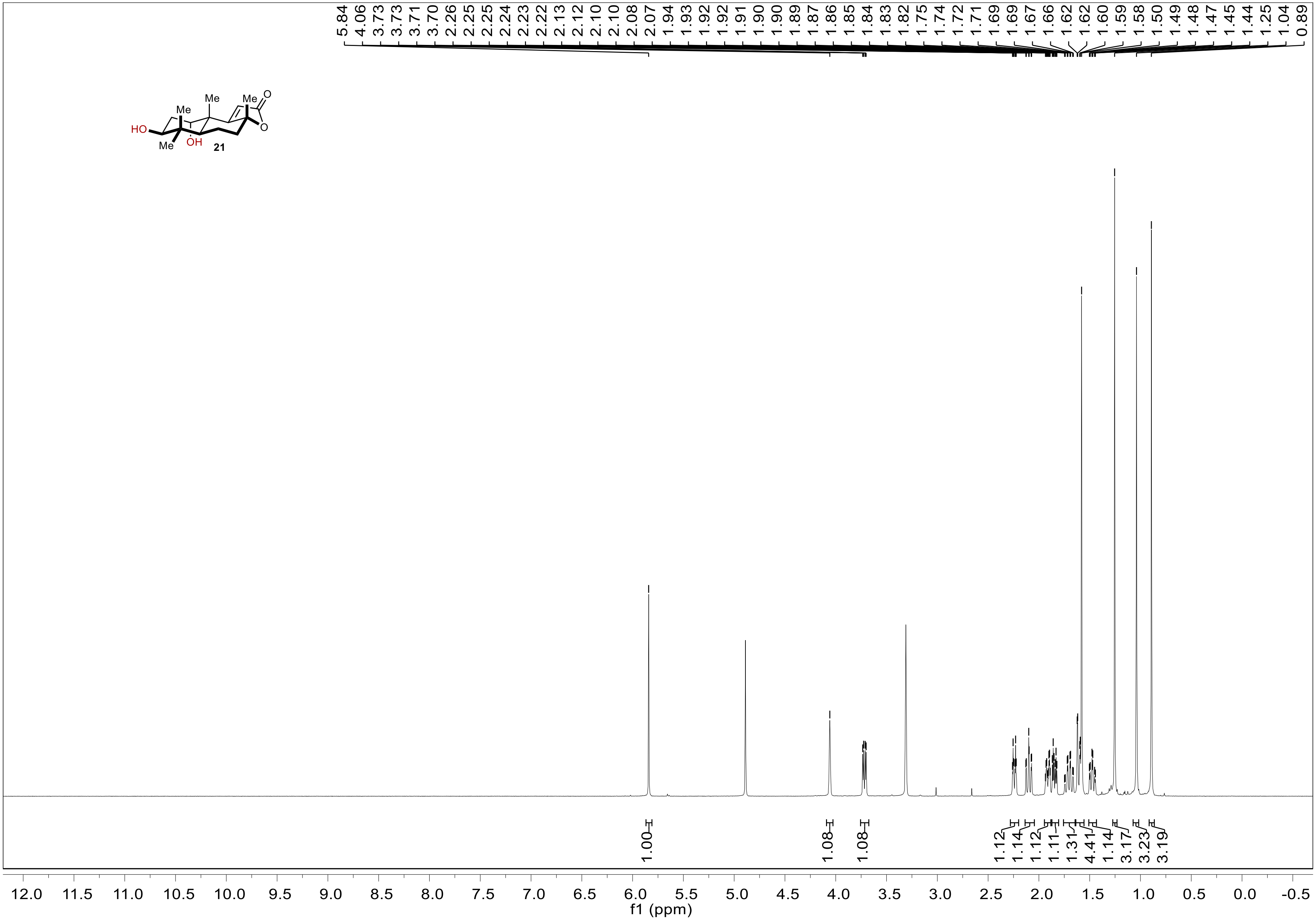
^{1}H NMR Spectrum of compound 20 (500 MHz, Methanol-d_4)



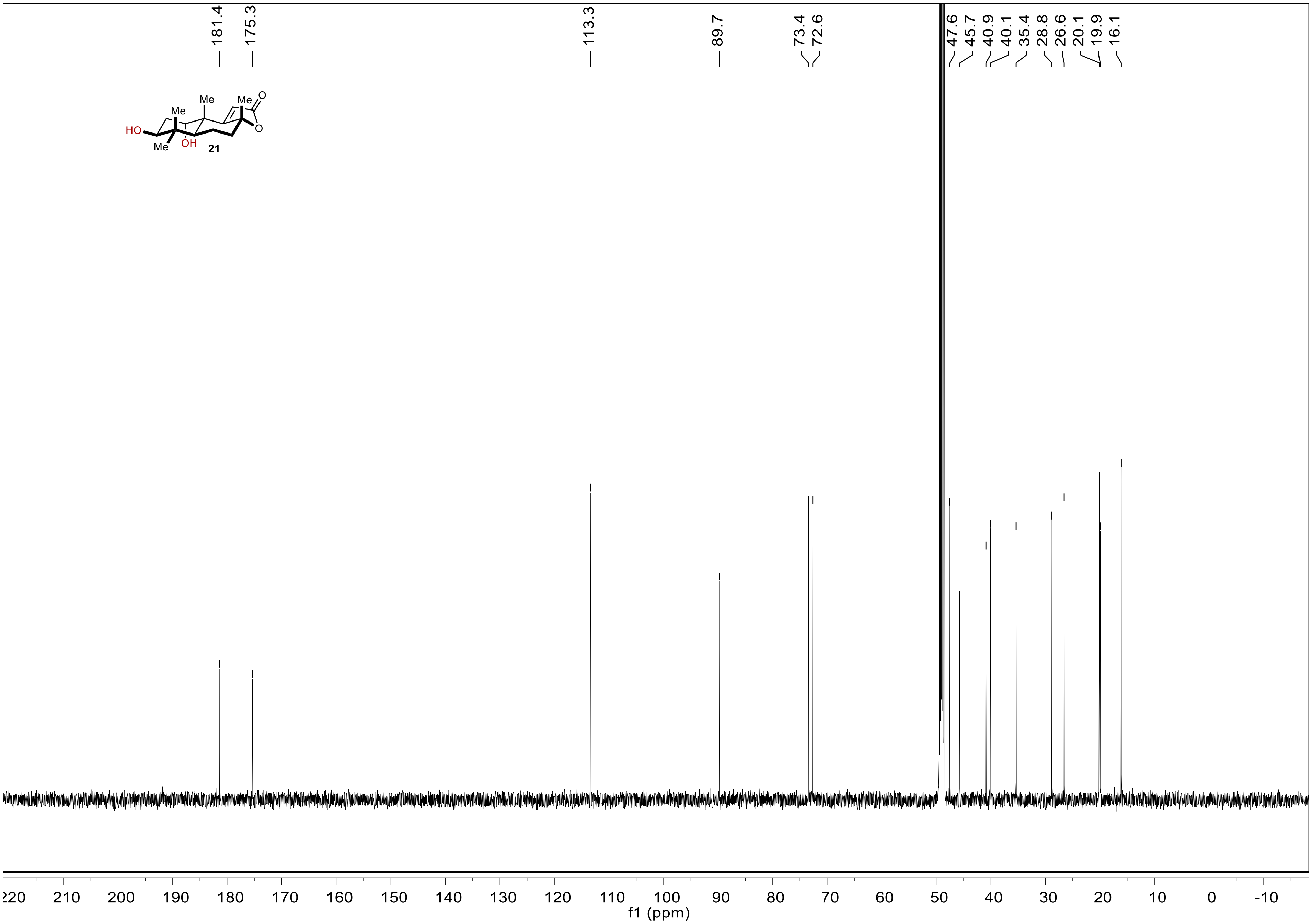
^{13}C NMR Spectrum of compound 20 (126 MHz, Methanol-d_4)



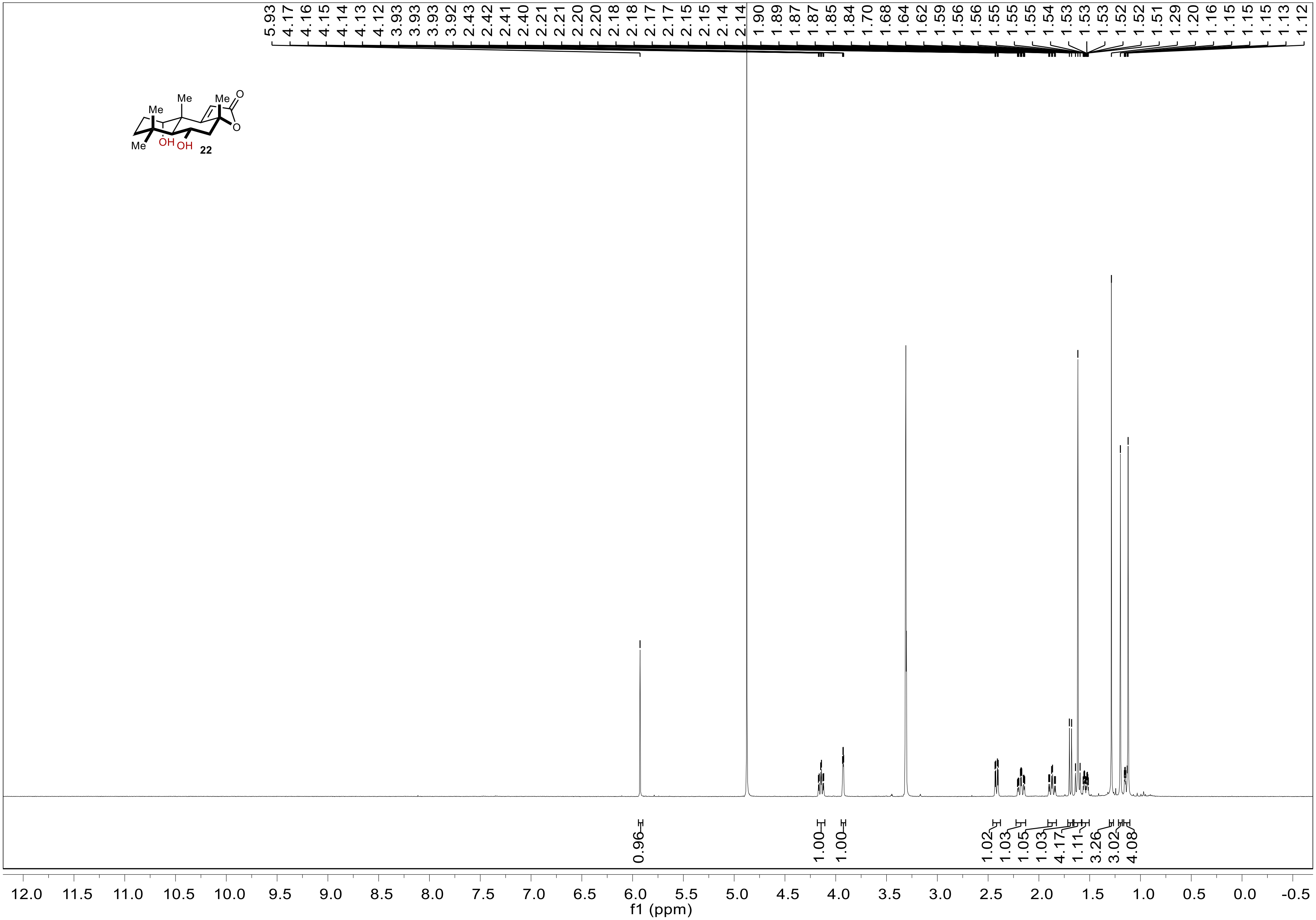
^{1}H NMR Spectrum of compound 21 (500 MHz, Methanol-d_4)



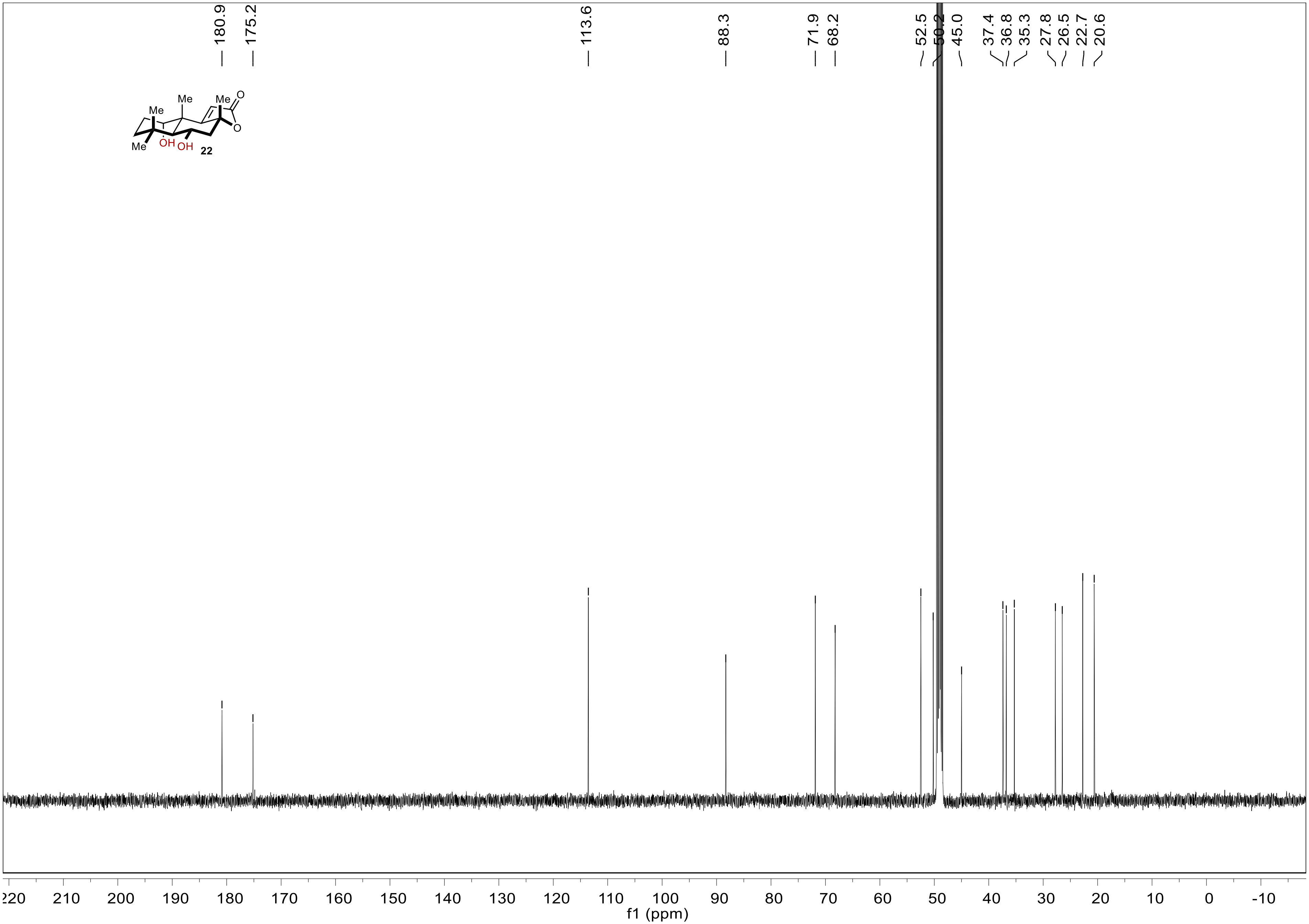
^{13}C NMR Spectrum of compound 21 (126 MHz, Methanol-*d*$_4$)



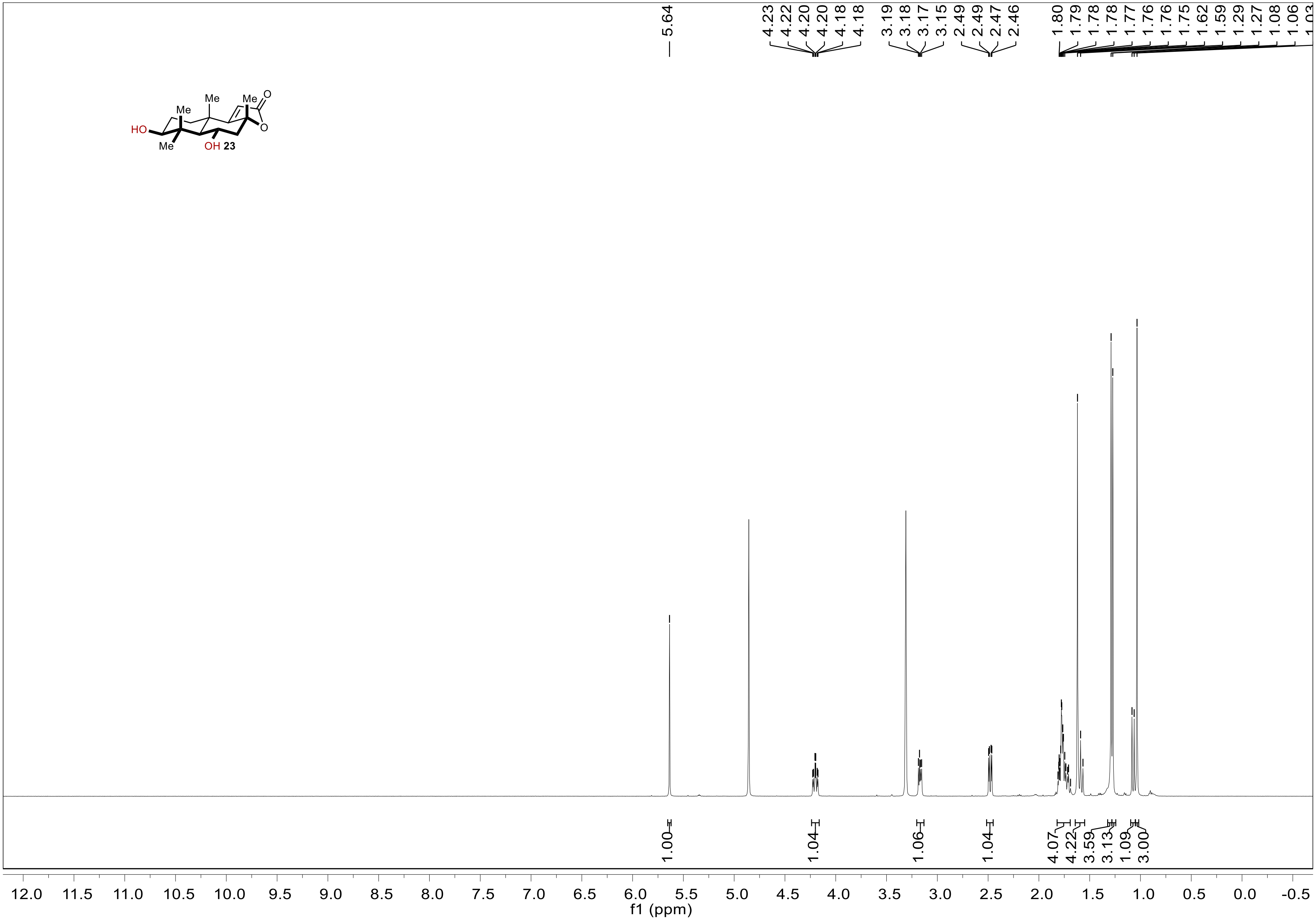
^{1}H NMR Spectrum of compound 22 (500 MHz, Methanol-d_4)



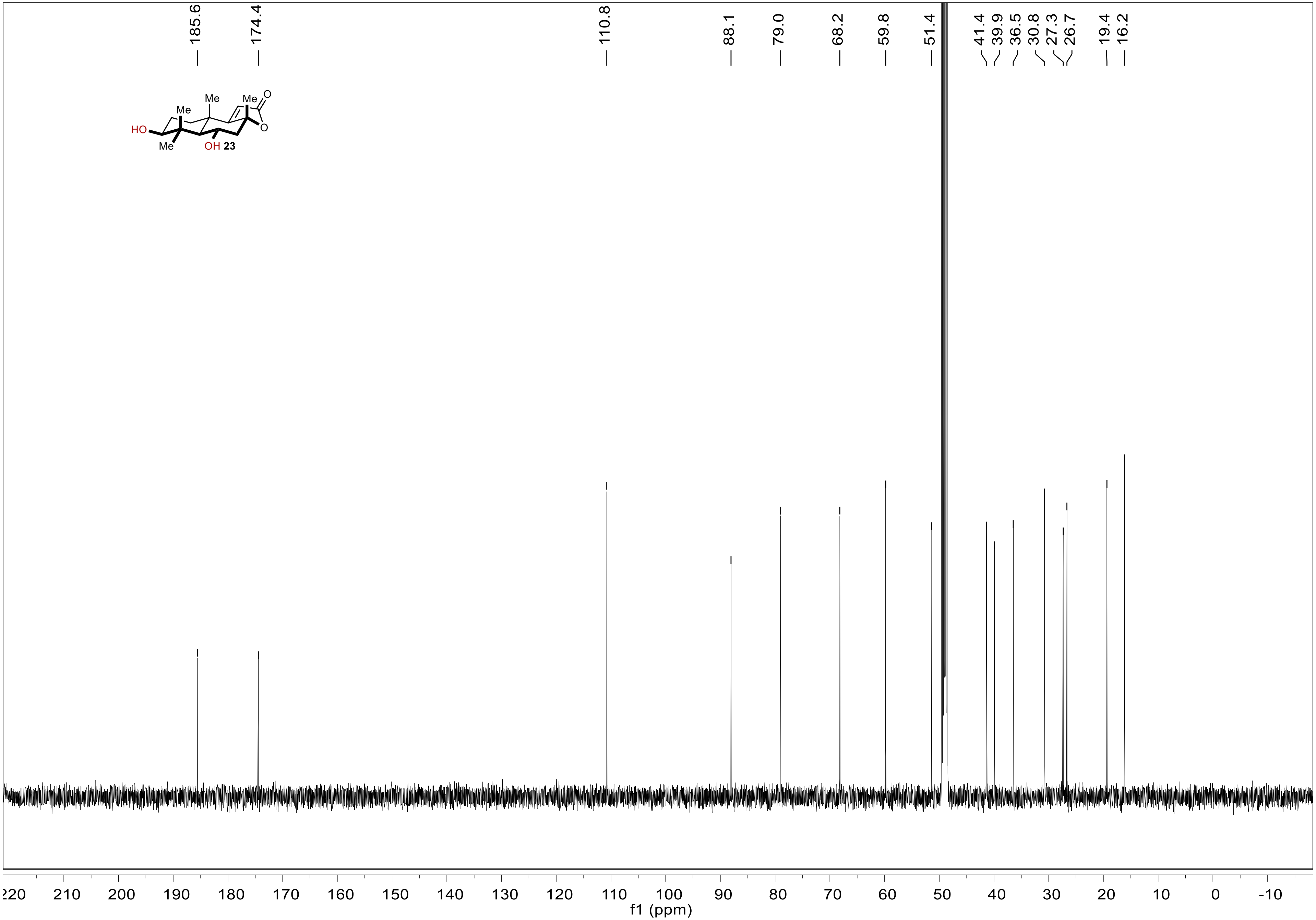
^{13}C NMR Spectrum of compound 22 (126 MHz, Methanol-d_4)



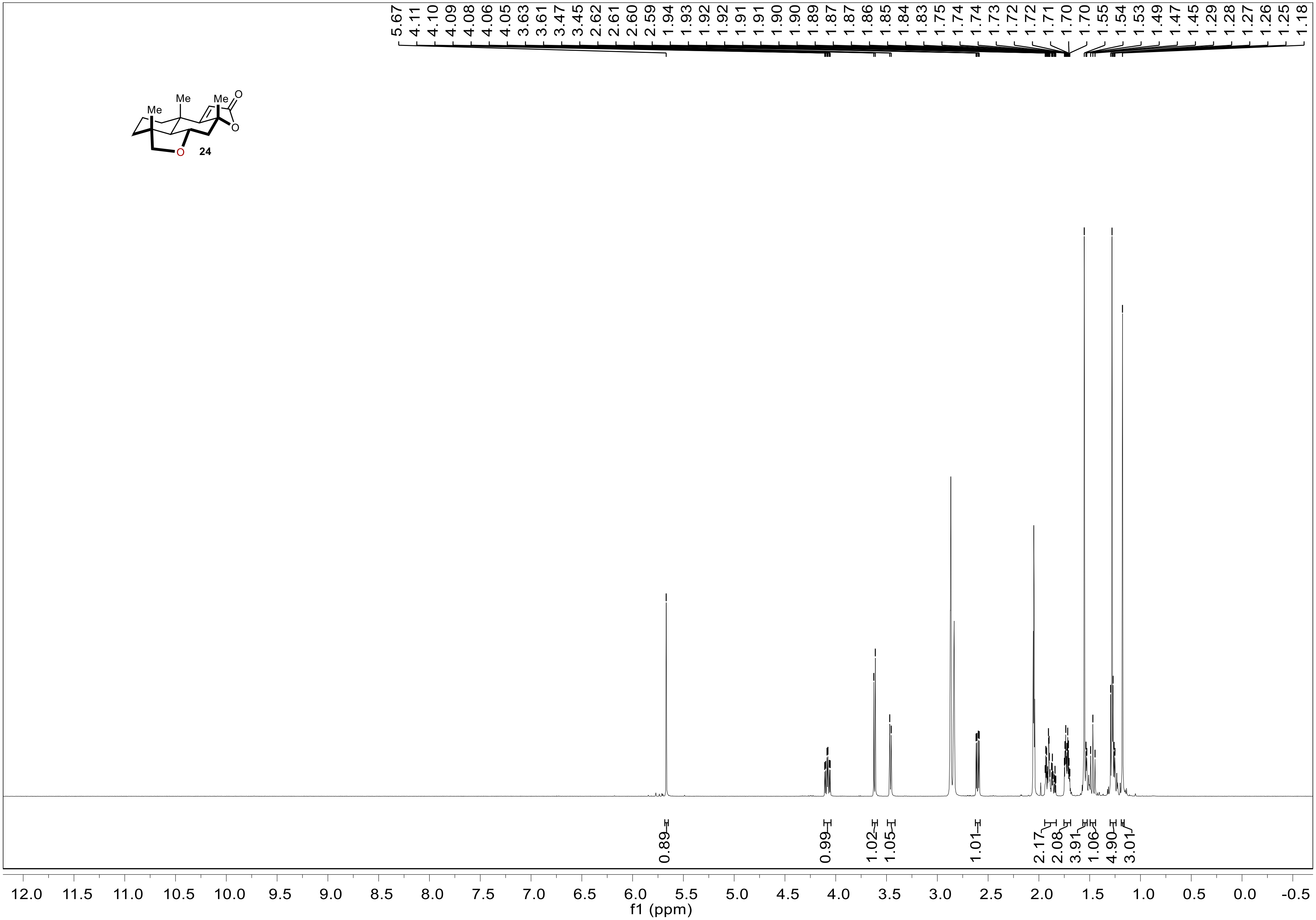
^{1}H NMR Spectrum of compound 23 (500 MHz, Methanol-*d*$_4$)



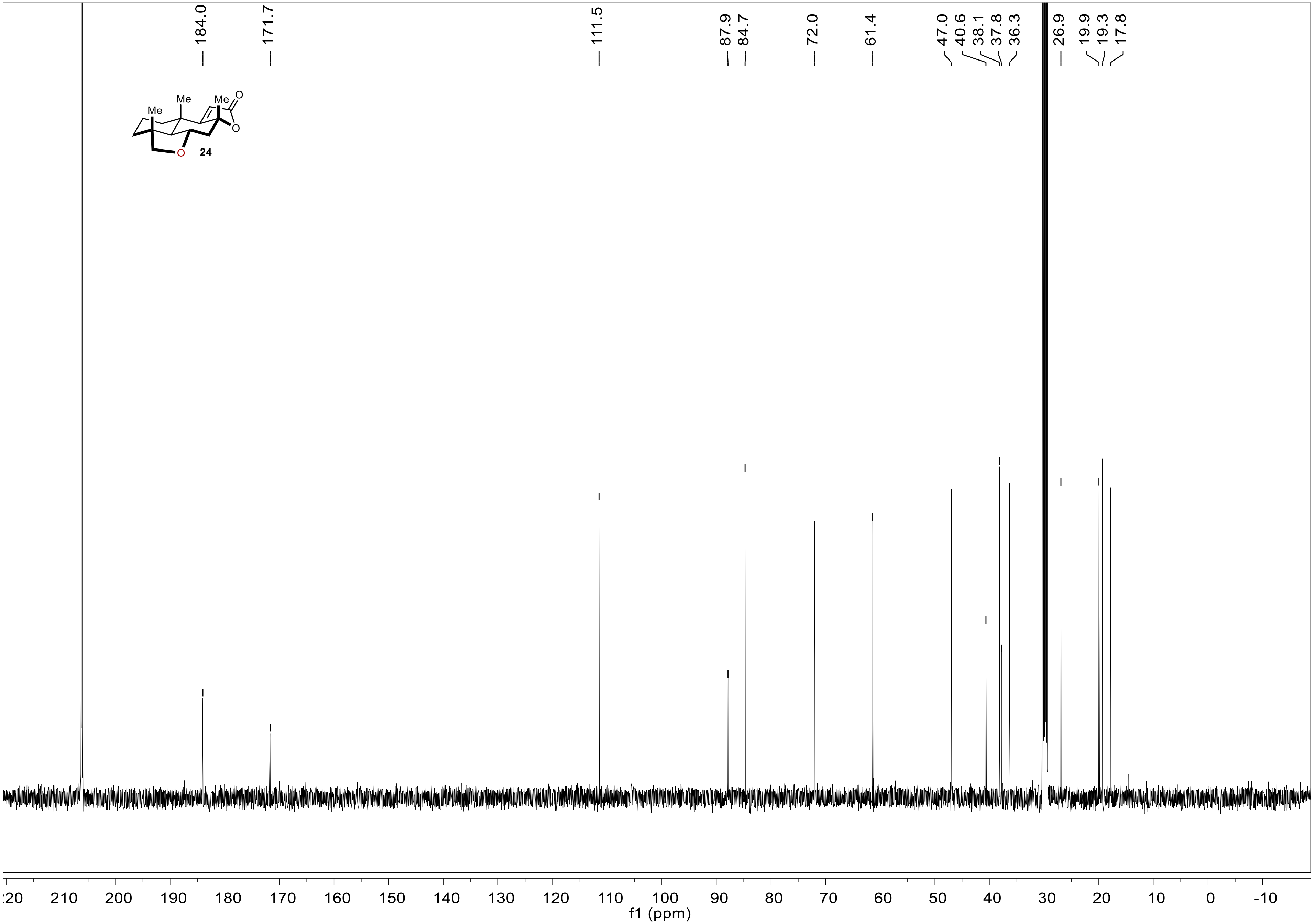
^{13}C NMR Spectrum of compound 23 (126 MHz, Methanol-d_4)



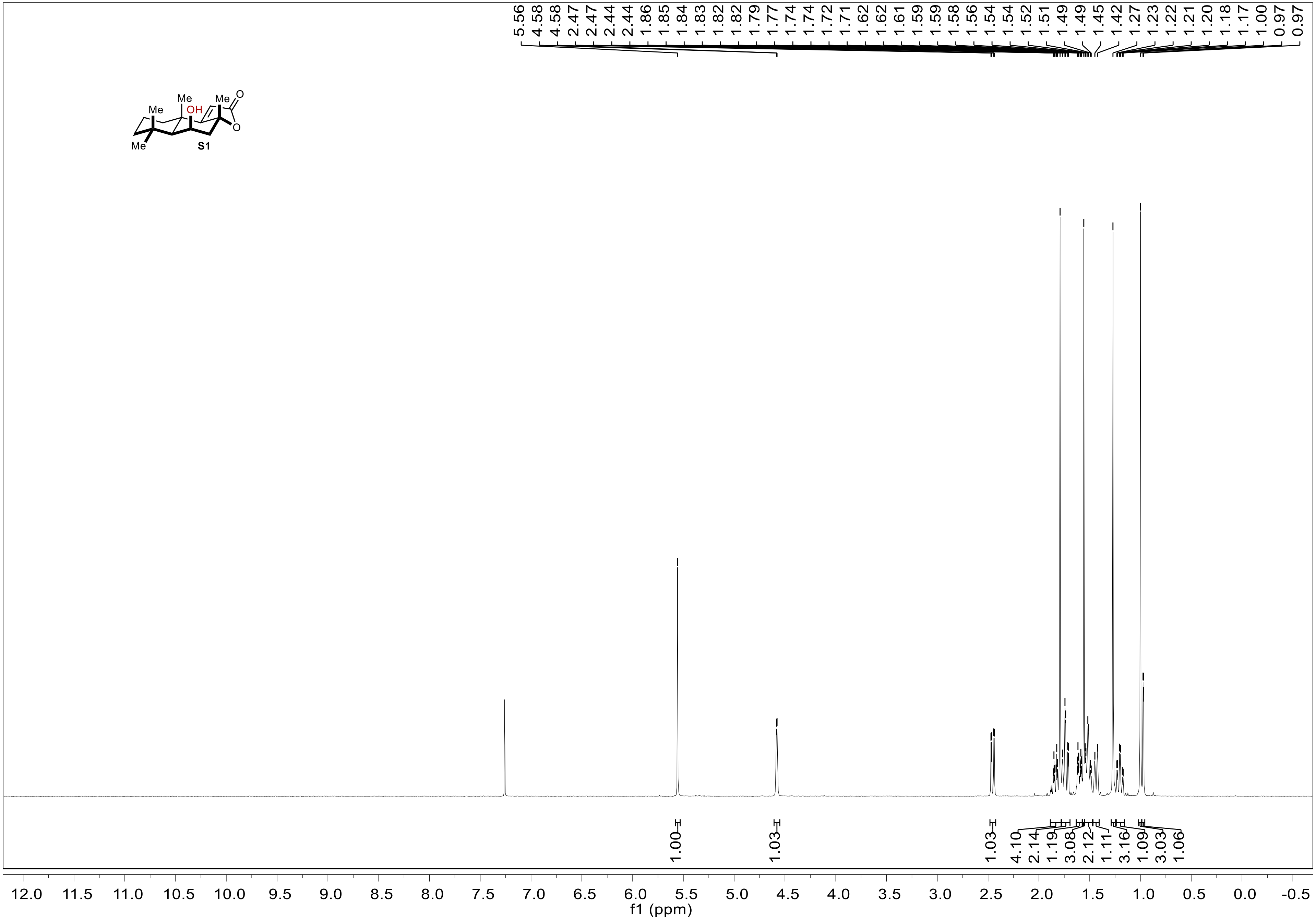
^{1}H NMR Spectrum of compound 24 (500 MHz, Acetone-d_6)



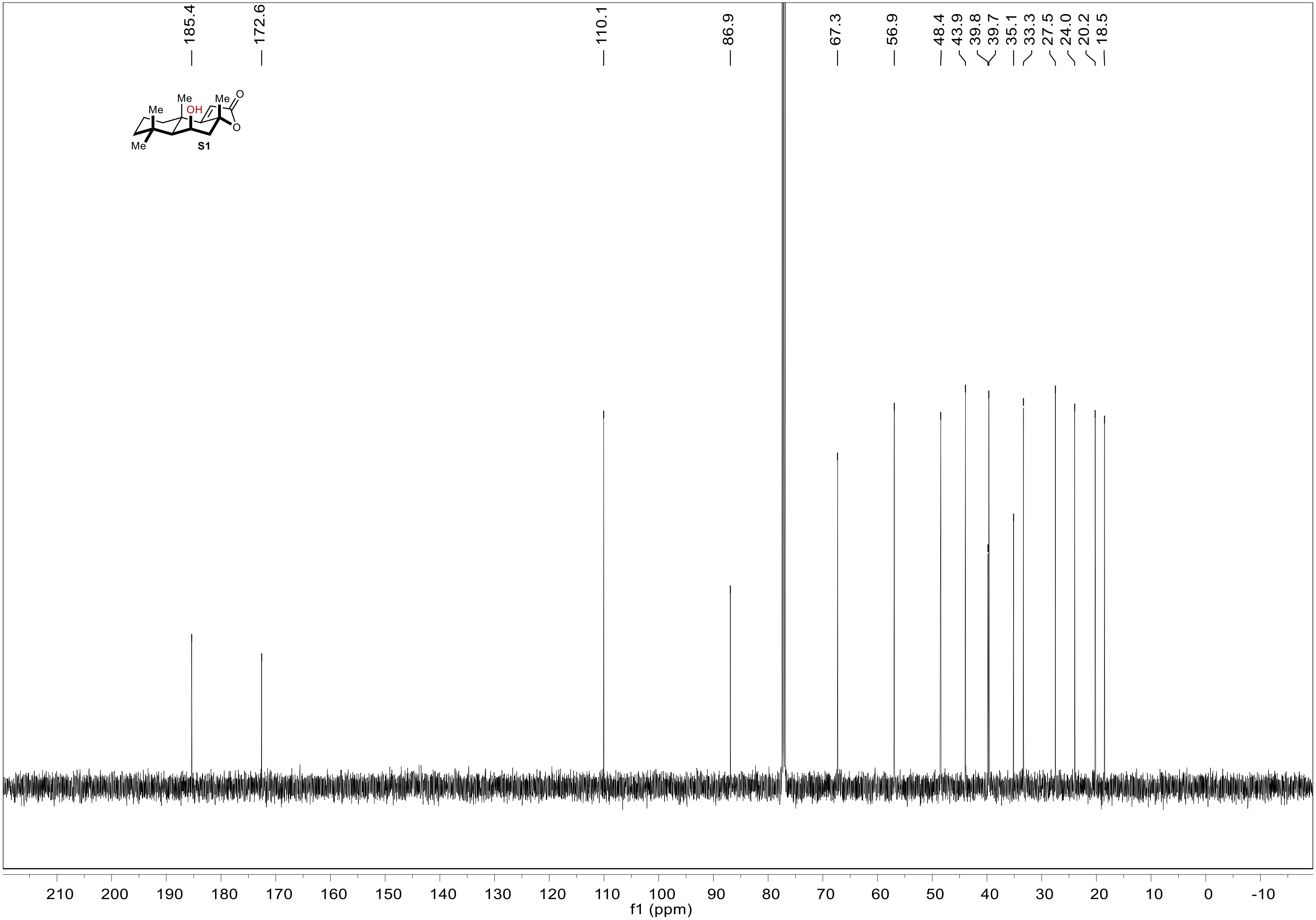
^{13}C NMR Spectrum of compound 24 (126 MHz, Acetone-d_6)



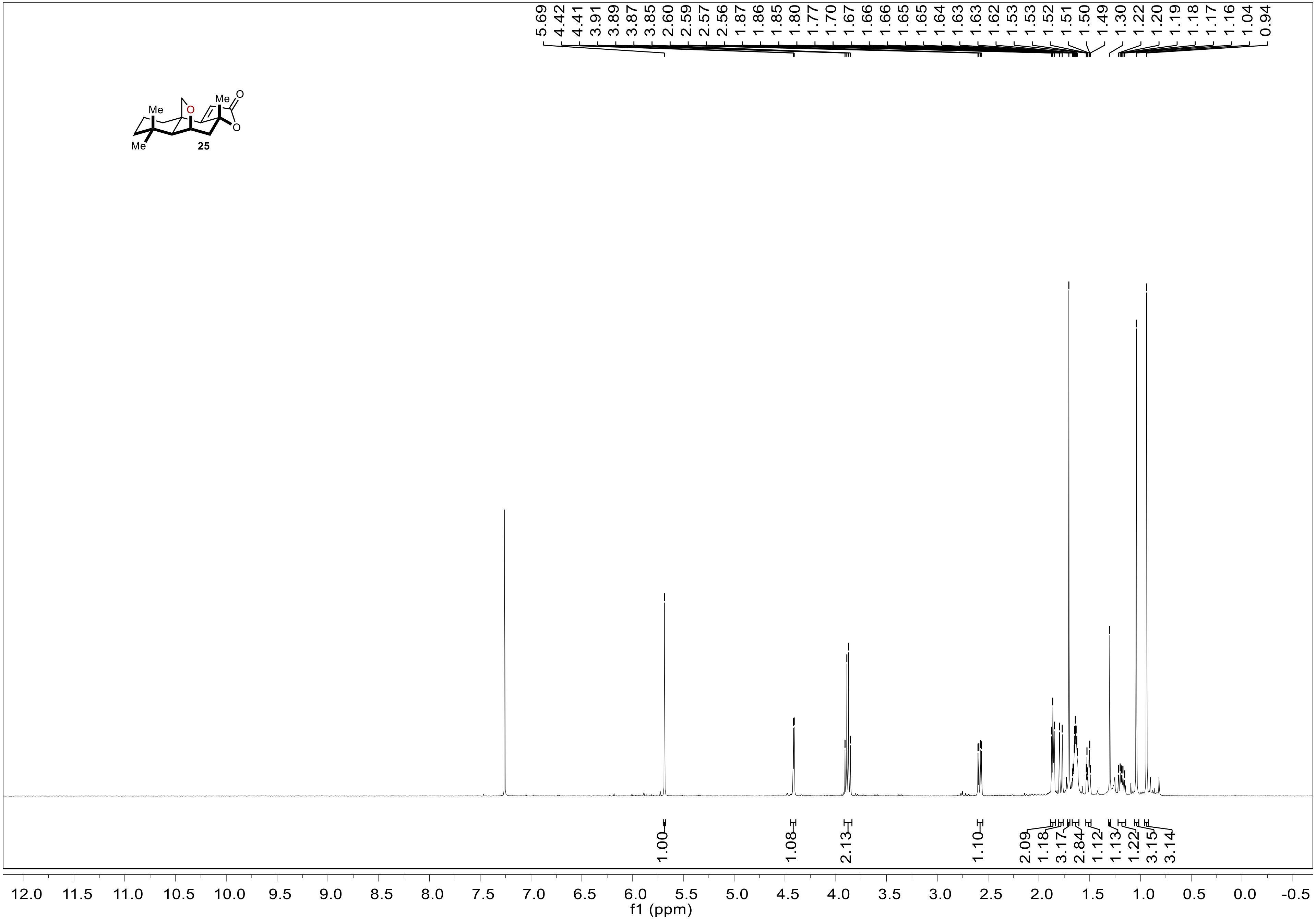
^{1}H NMR Spectrum of compound S1 (500 MHz, $CDCl_3$)



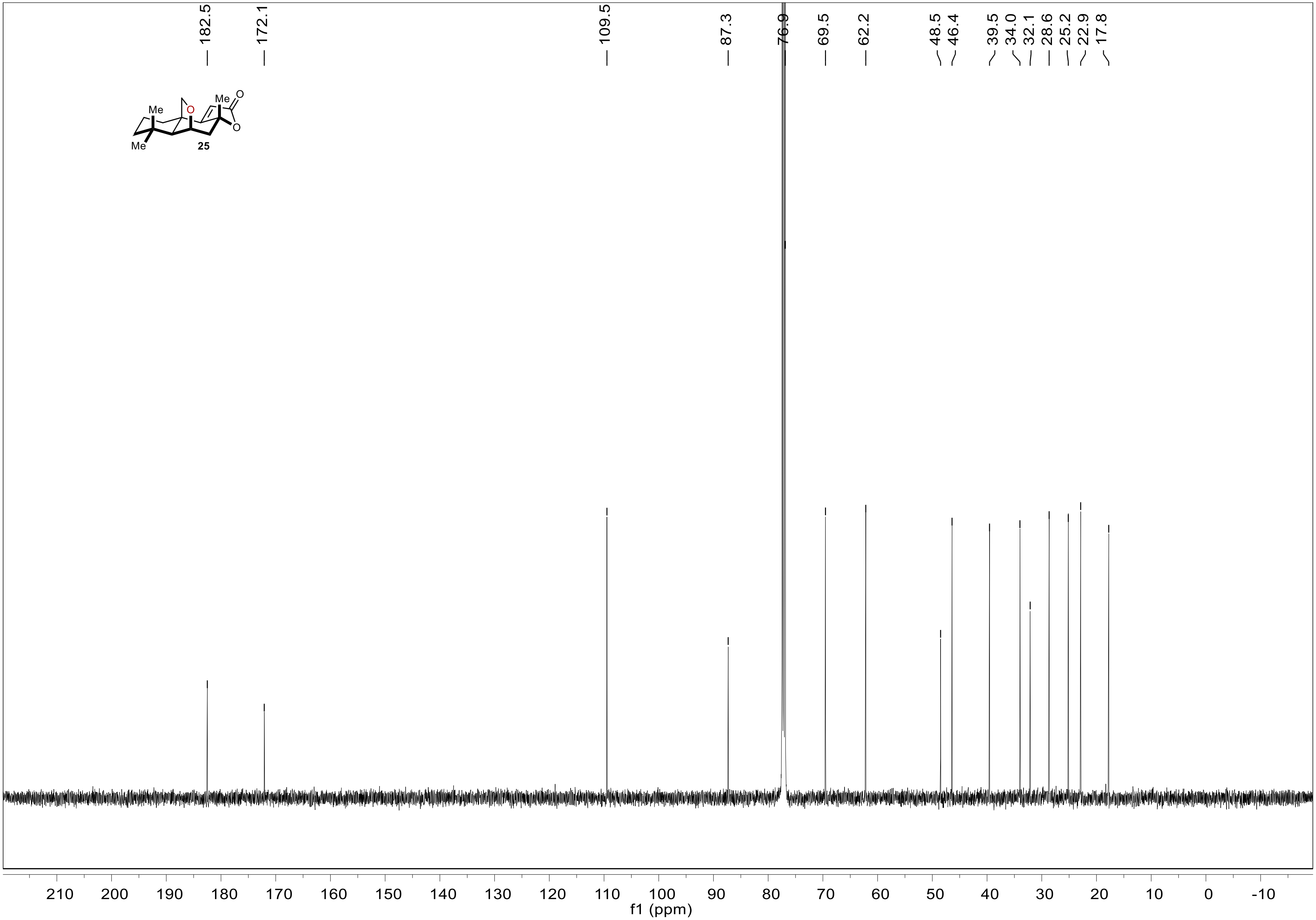
^{13}C NMR Spectrum of compound S1 (126 MHz, $CDCl_3$)



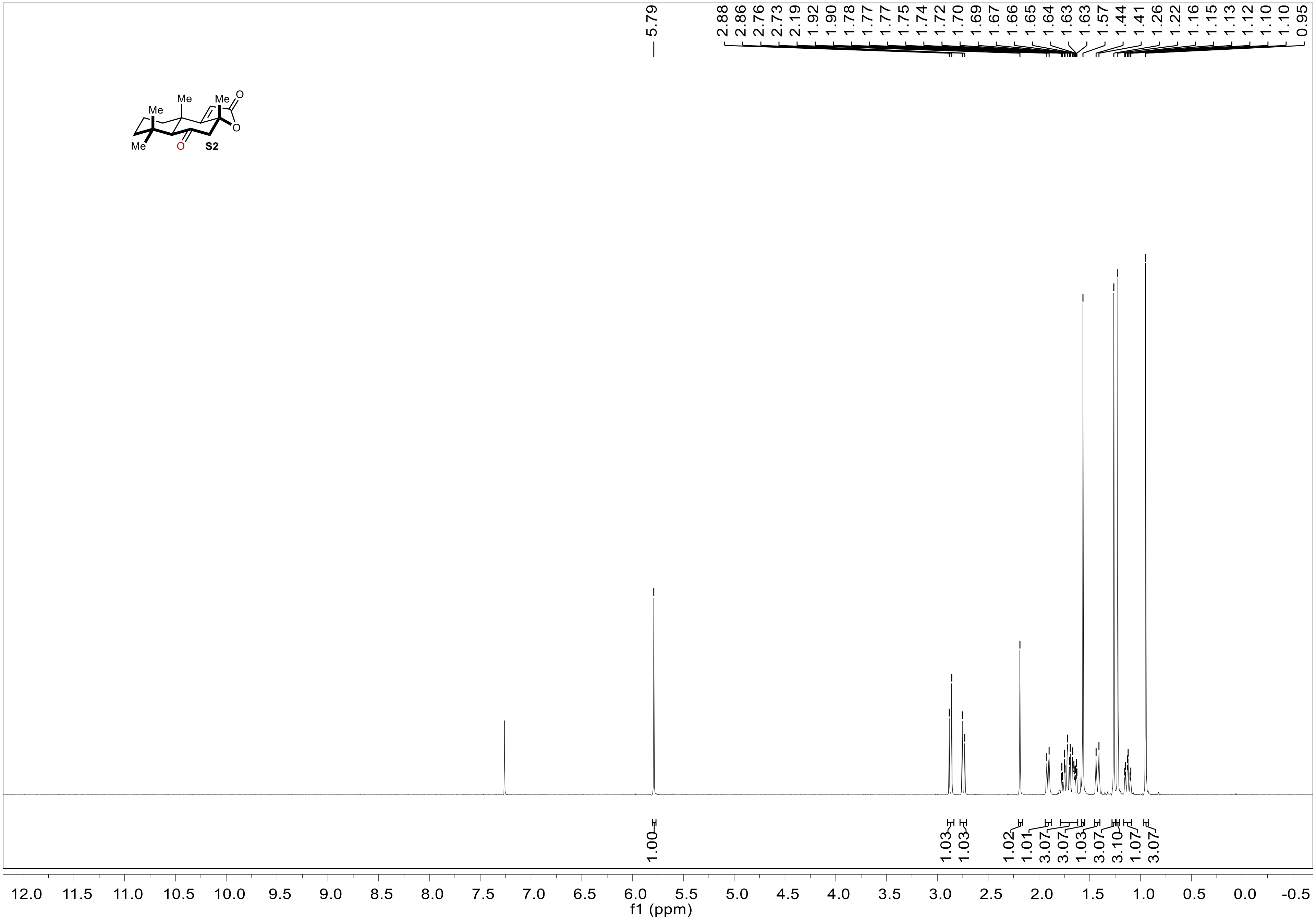
^{1}H NMR Spectrum of compound 25 (500 MHz, CDCl$_3$)



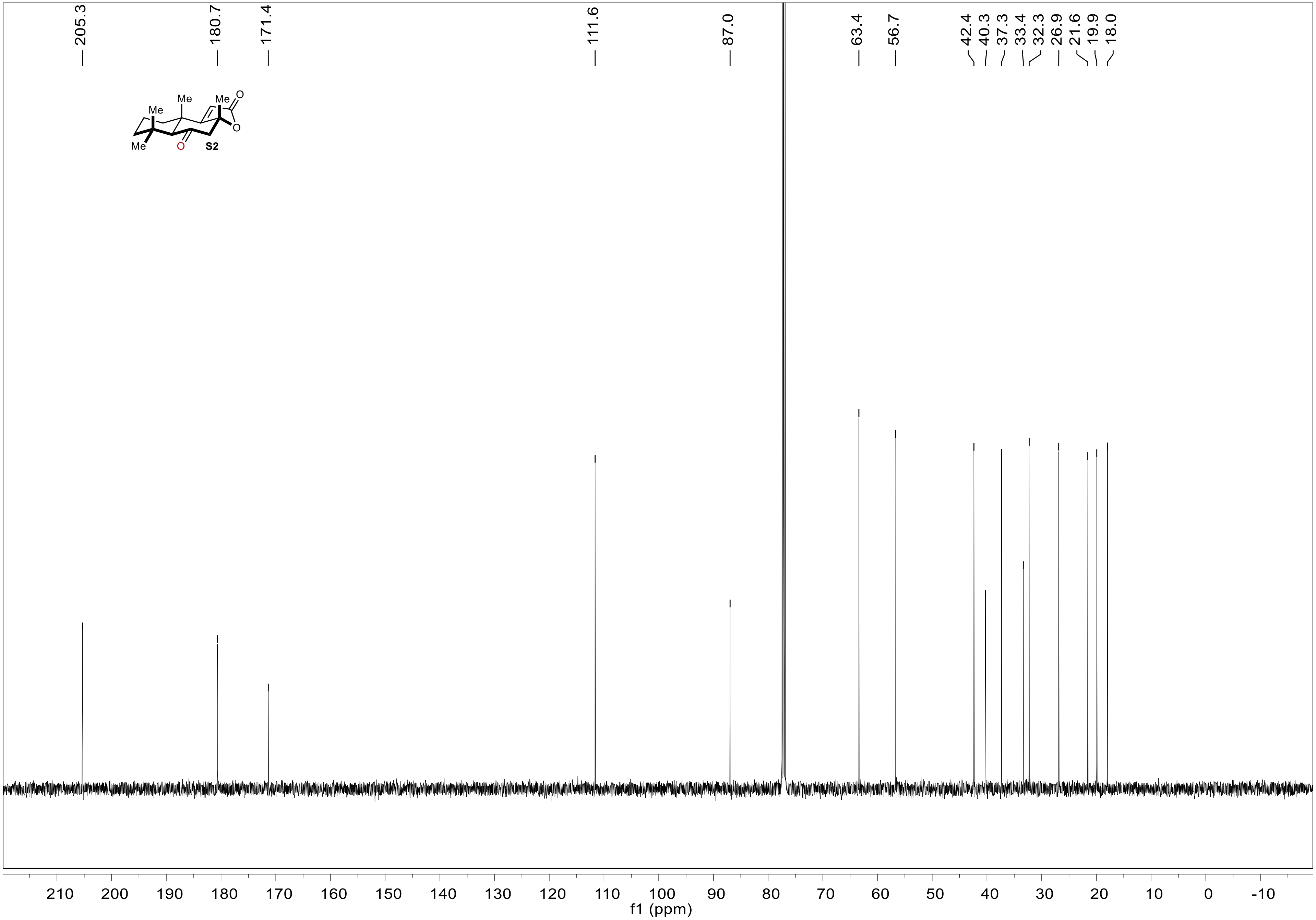
^{13}C NMR Spectrum of compound 25 (126 MHz, CDCl$_3$)



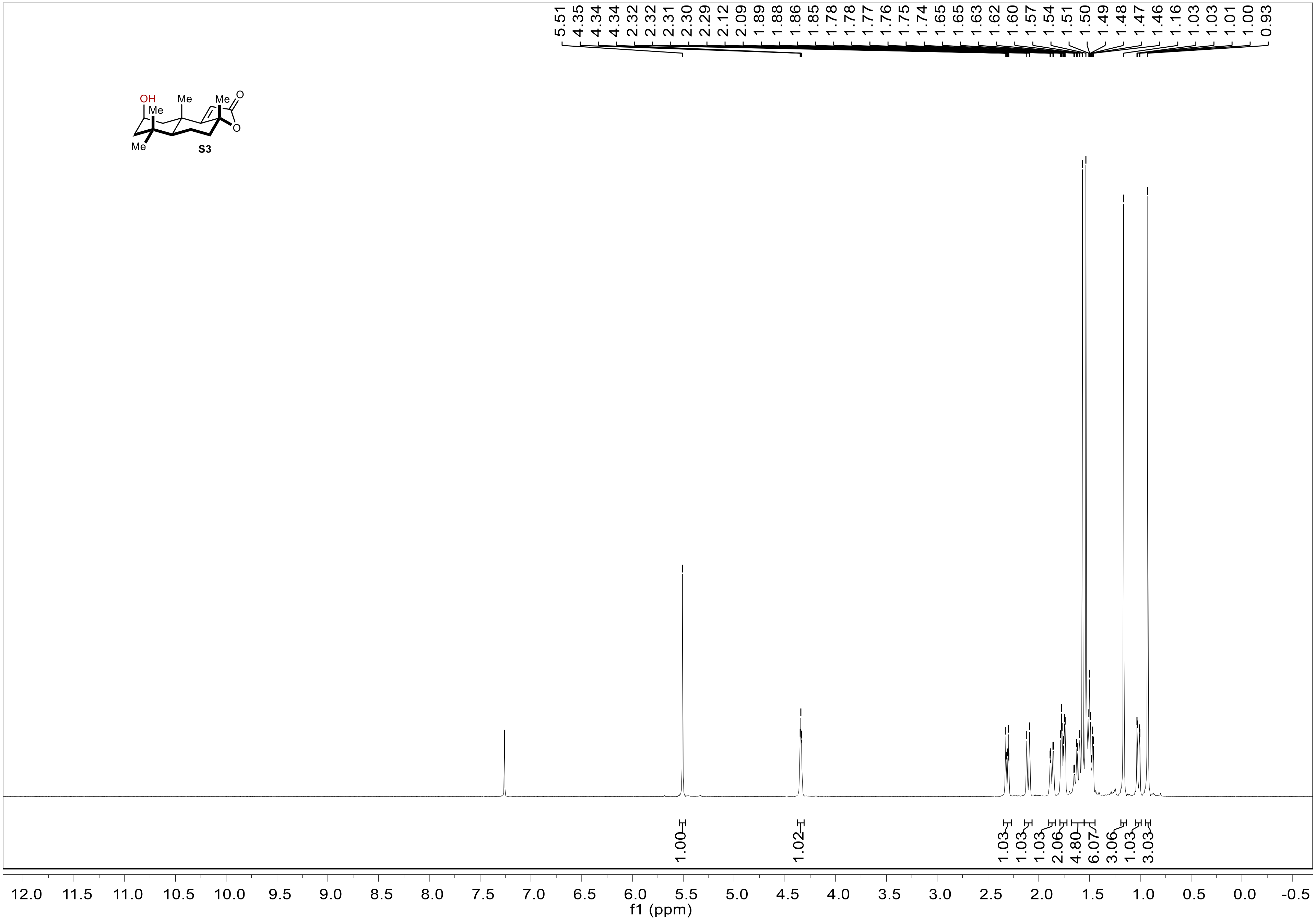
^{1}H NMR Spectrum of S2 (500 MHz, CDCl$_3$)



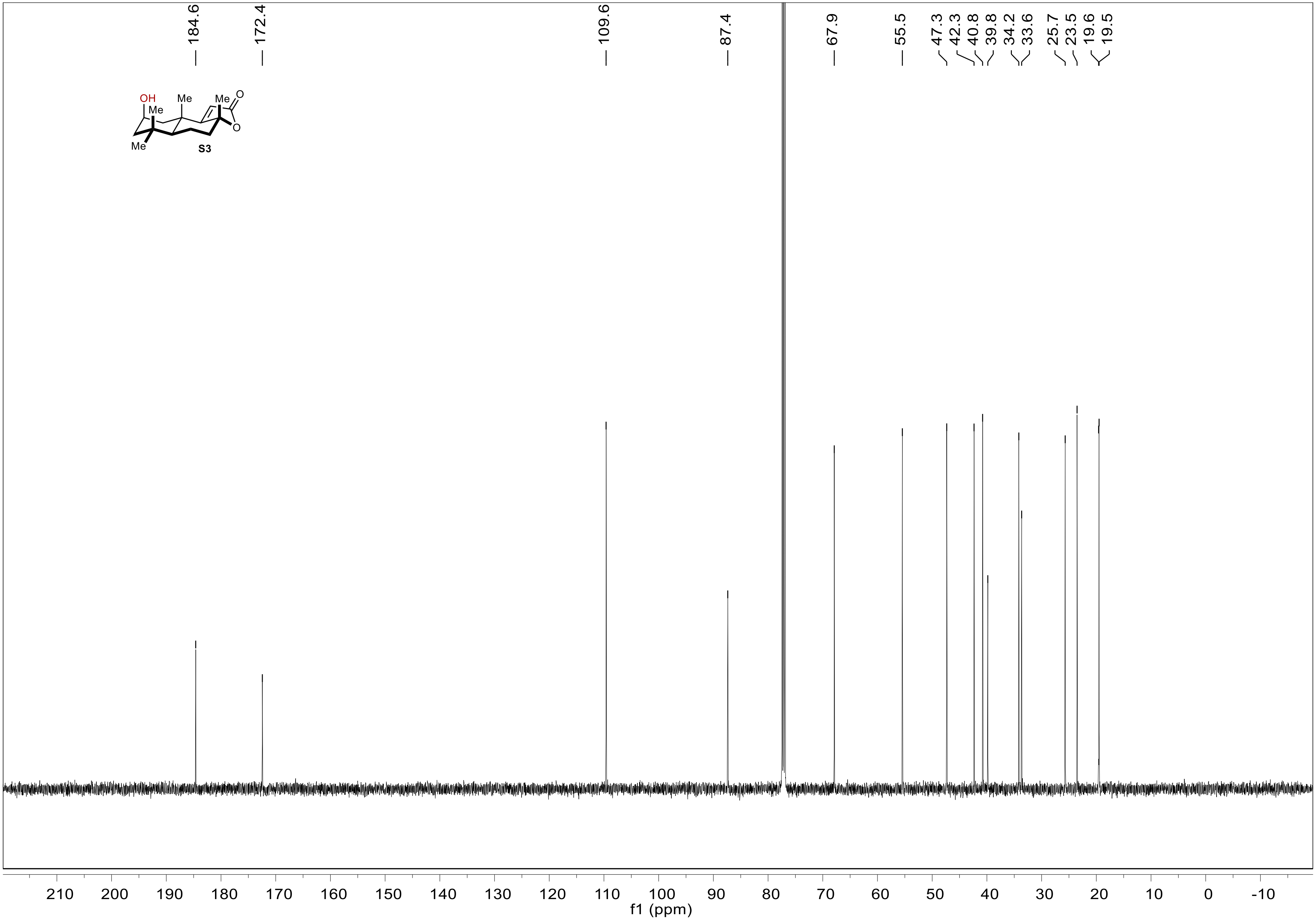
^{13}C NMR Spectrum of S2 (126 MHz, $CDCl_3$)



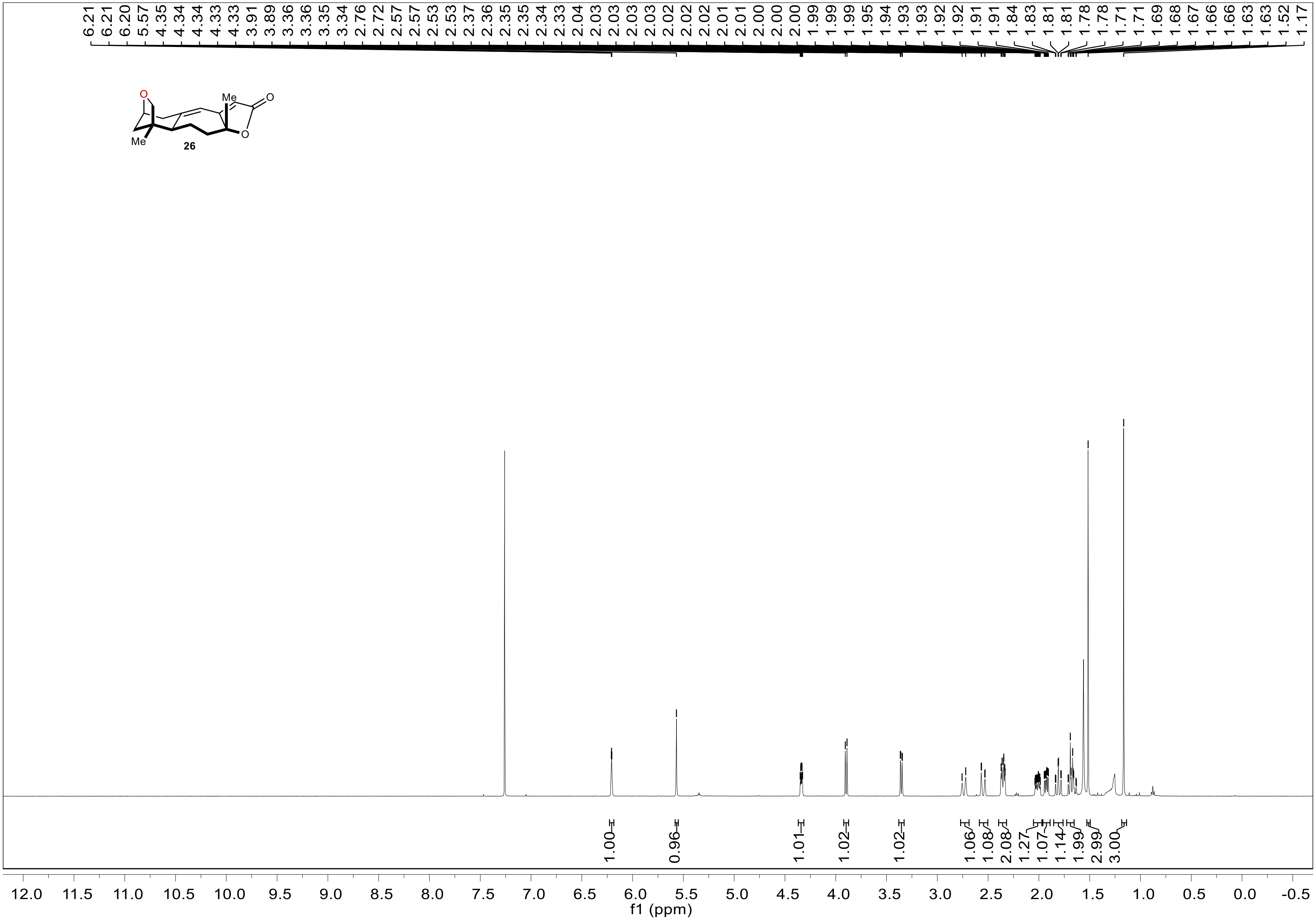
^{1}H NMR Spectrum of compound S3 (500 MHz, CDCl$_3$)



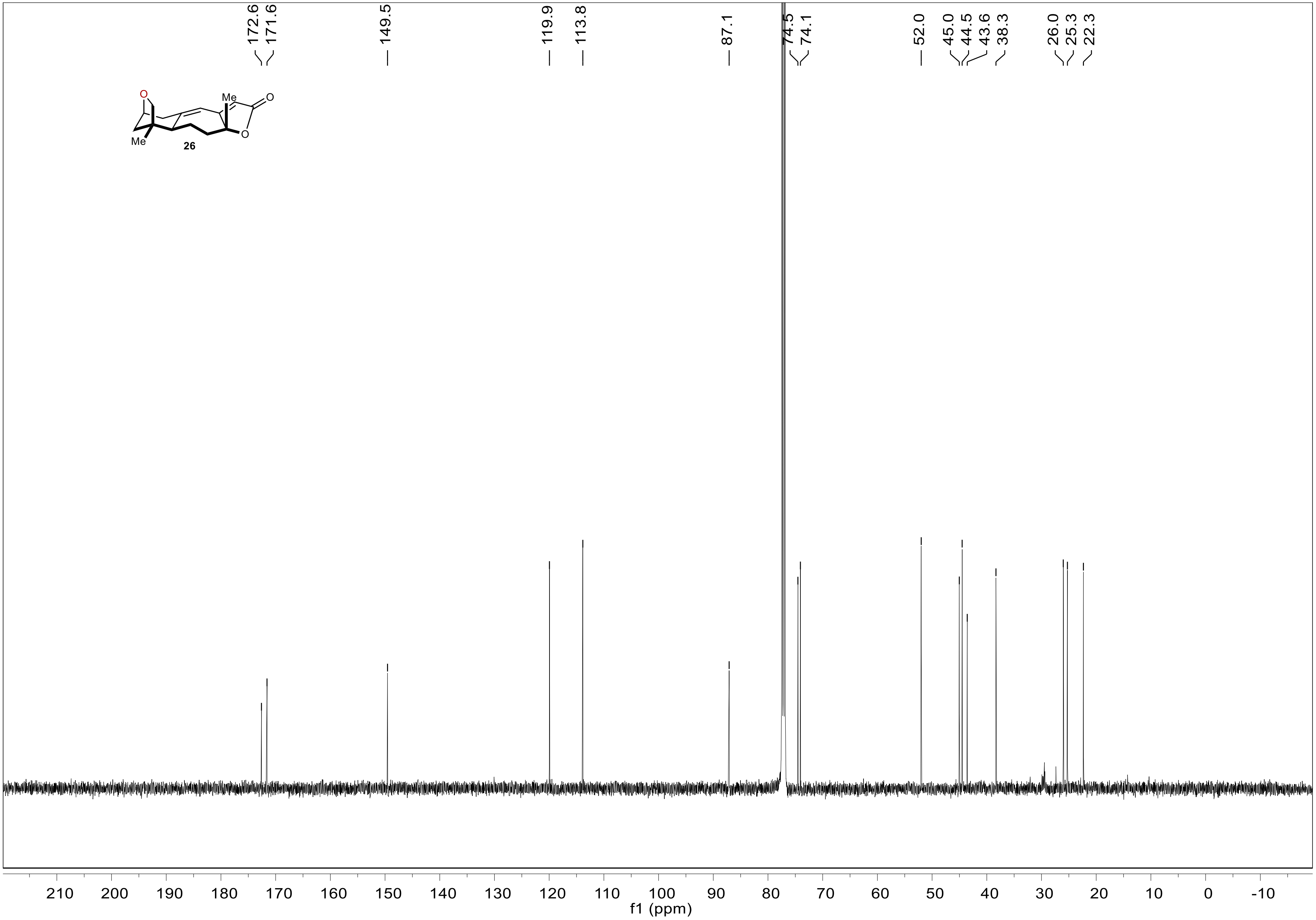
^{13}C NMR Spectrum of compound S3 (126 MHz, CDCl$_3$)



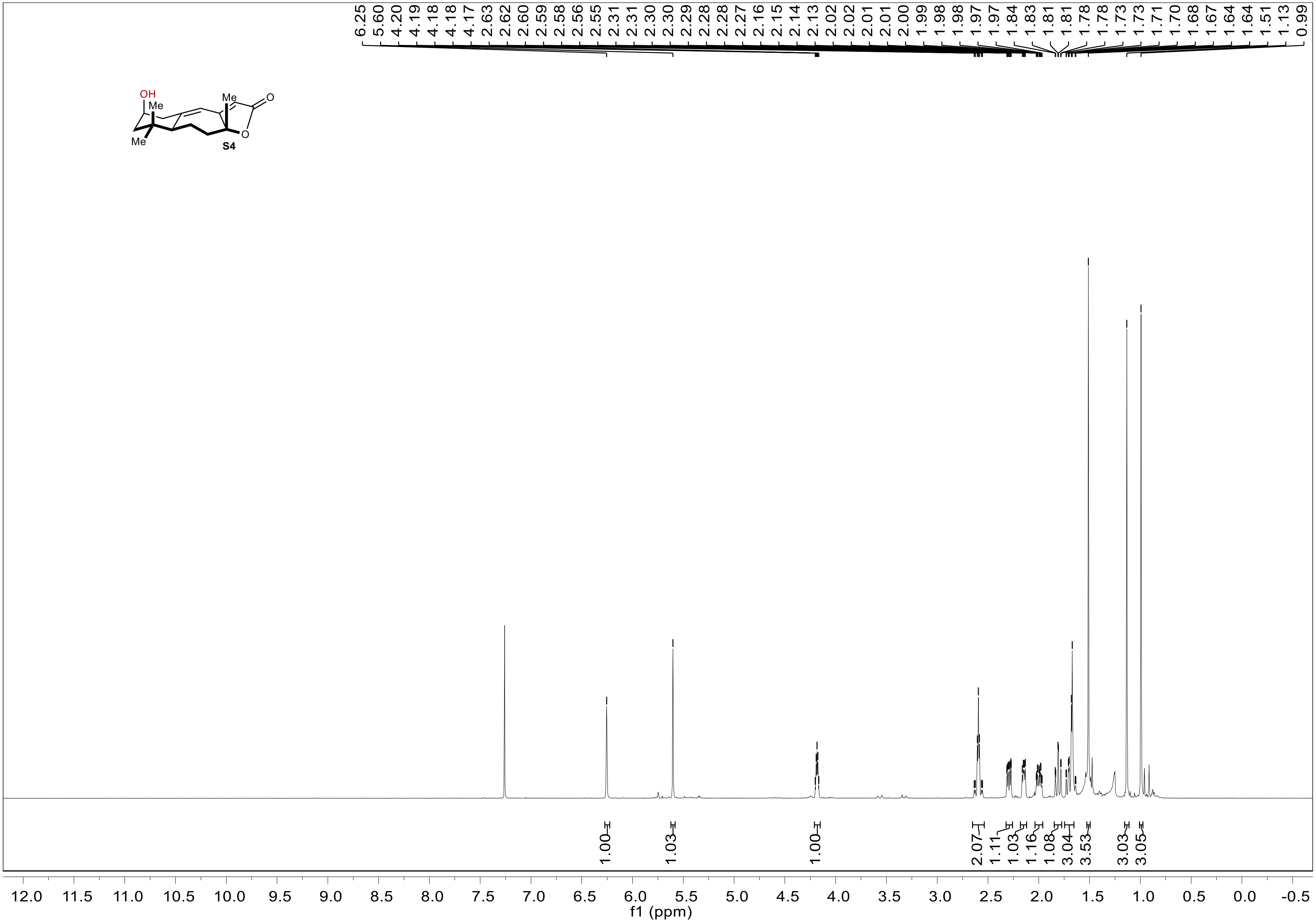
^{13}C NMR Spectrum of compound 26 (126 MHz, $CDCl_3$)



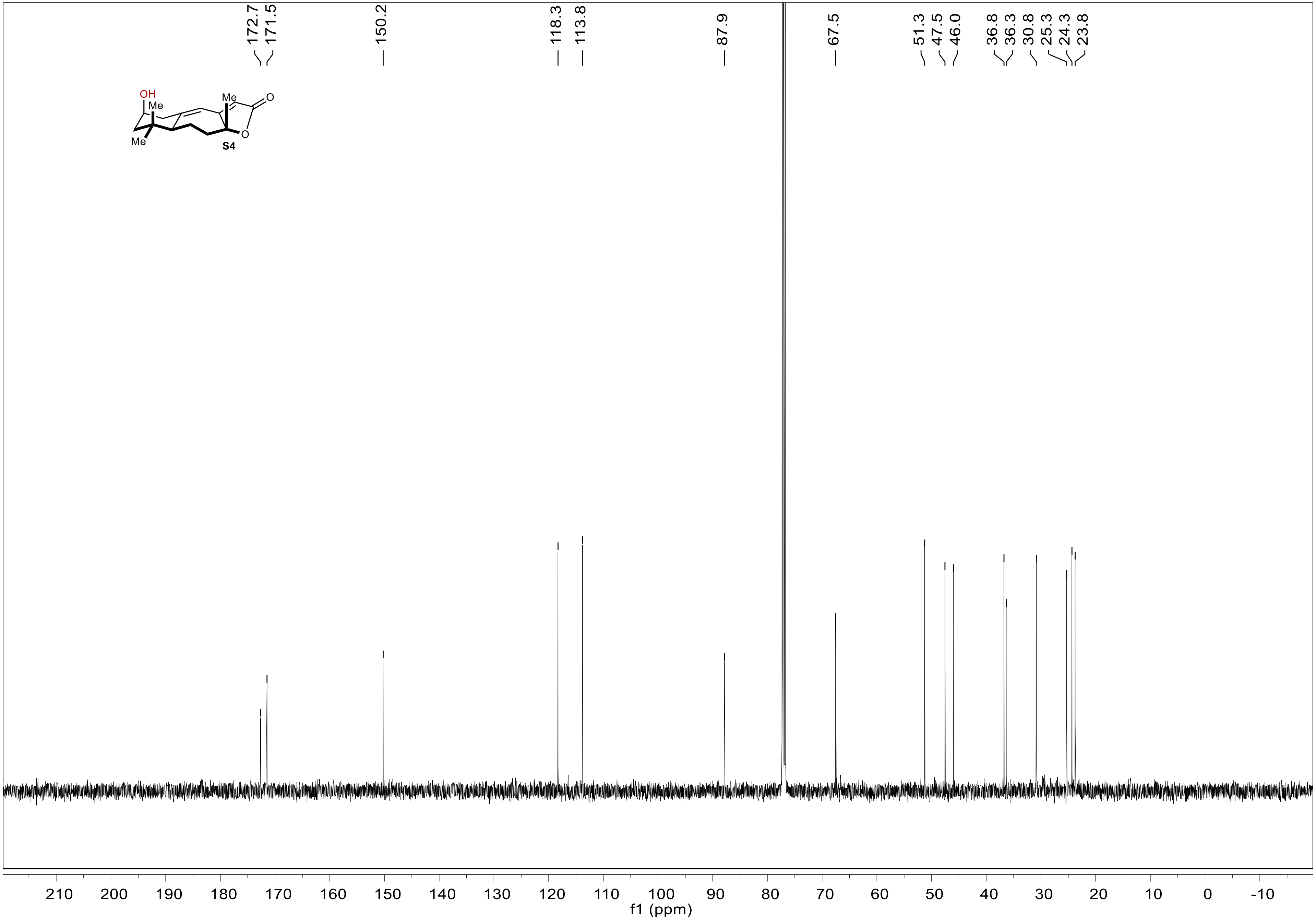
^{13}C NMR Spectrum of compound 26 (126 MHz, CDCl$_3$)



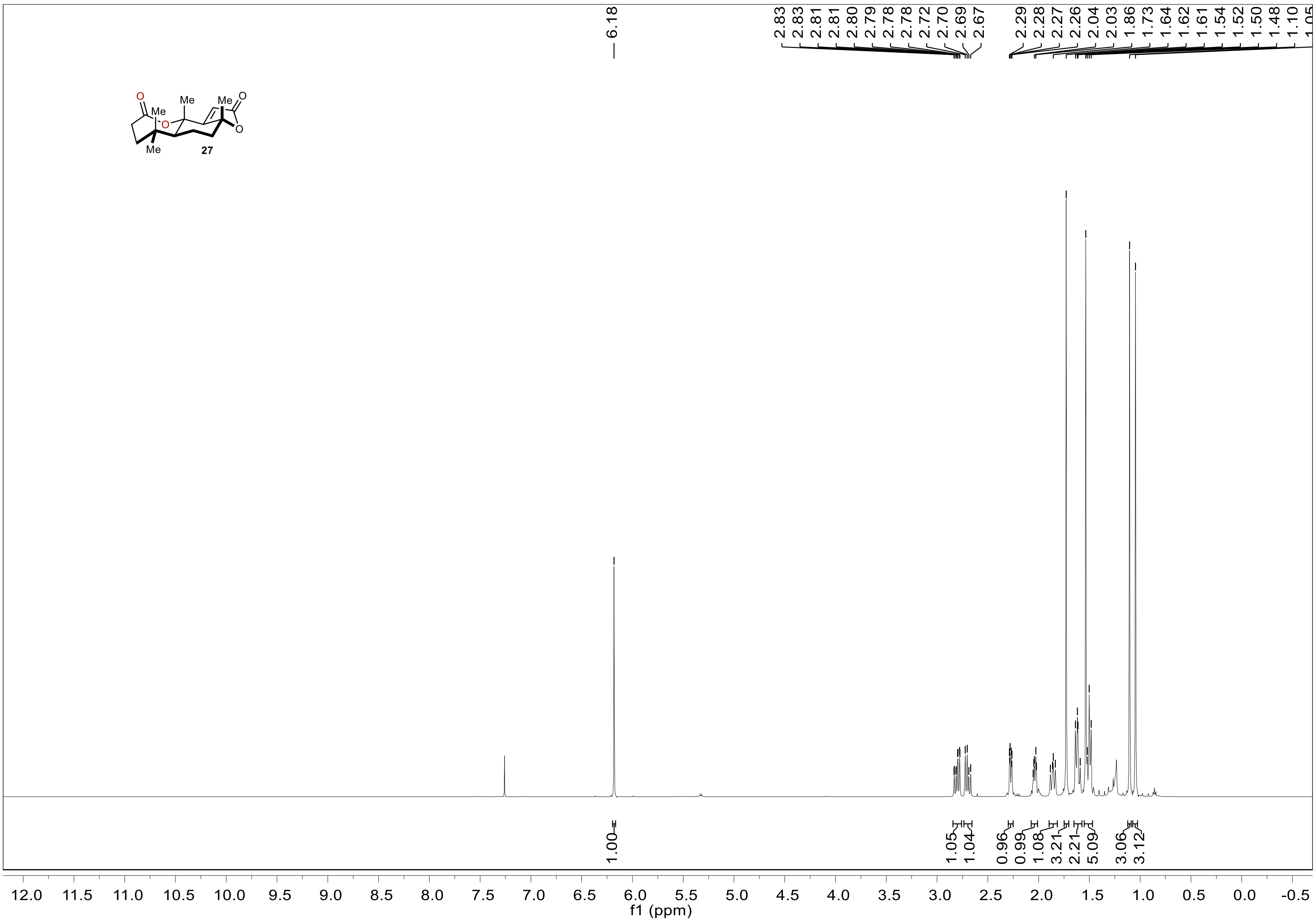
^{1}H NMR Spectrum of S4 (500 MHz, $CDCl_3$)



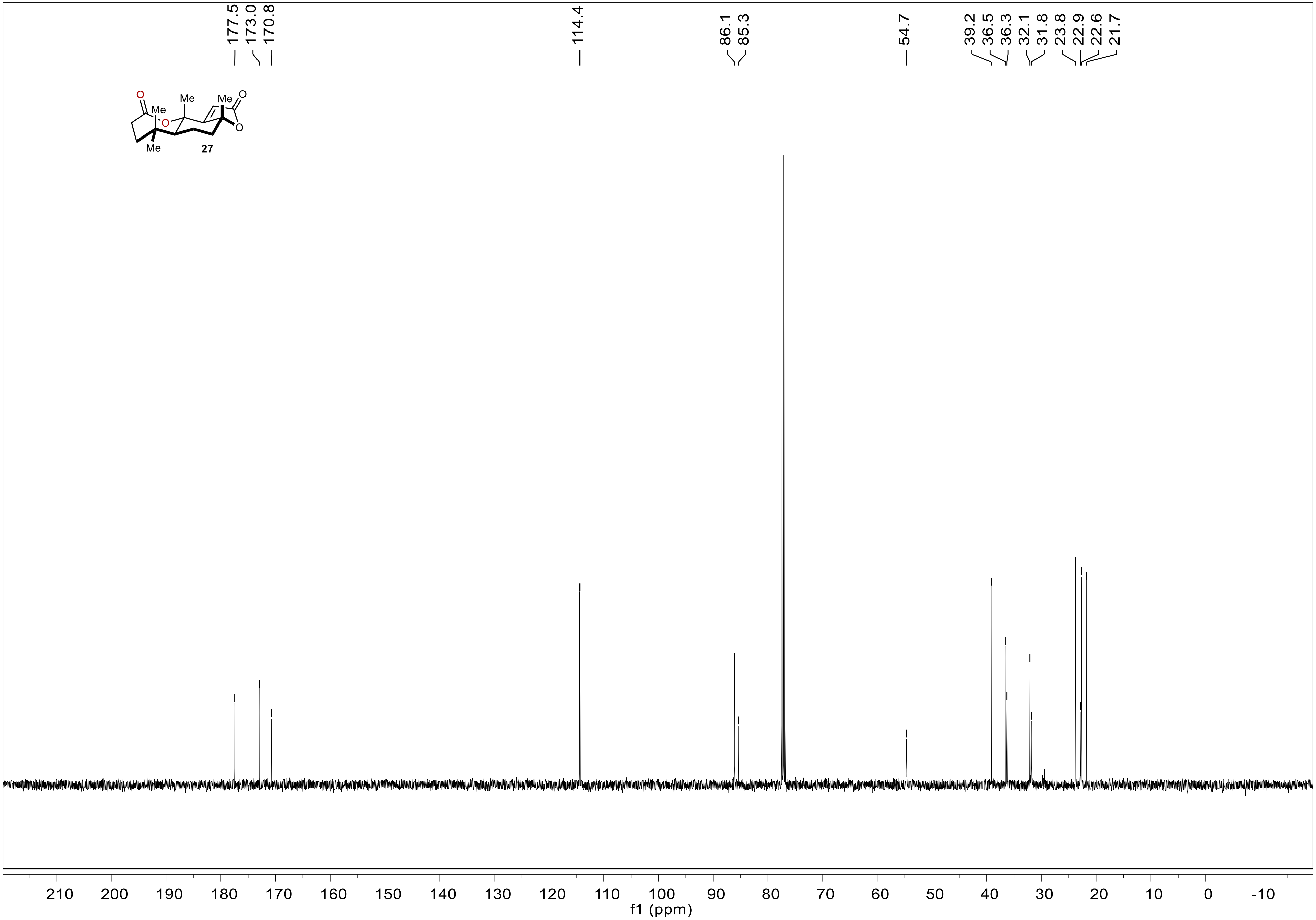
^{13}C NMR Spectrum of S4 (126 MHz, $CDCl_3$)



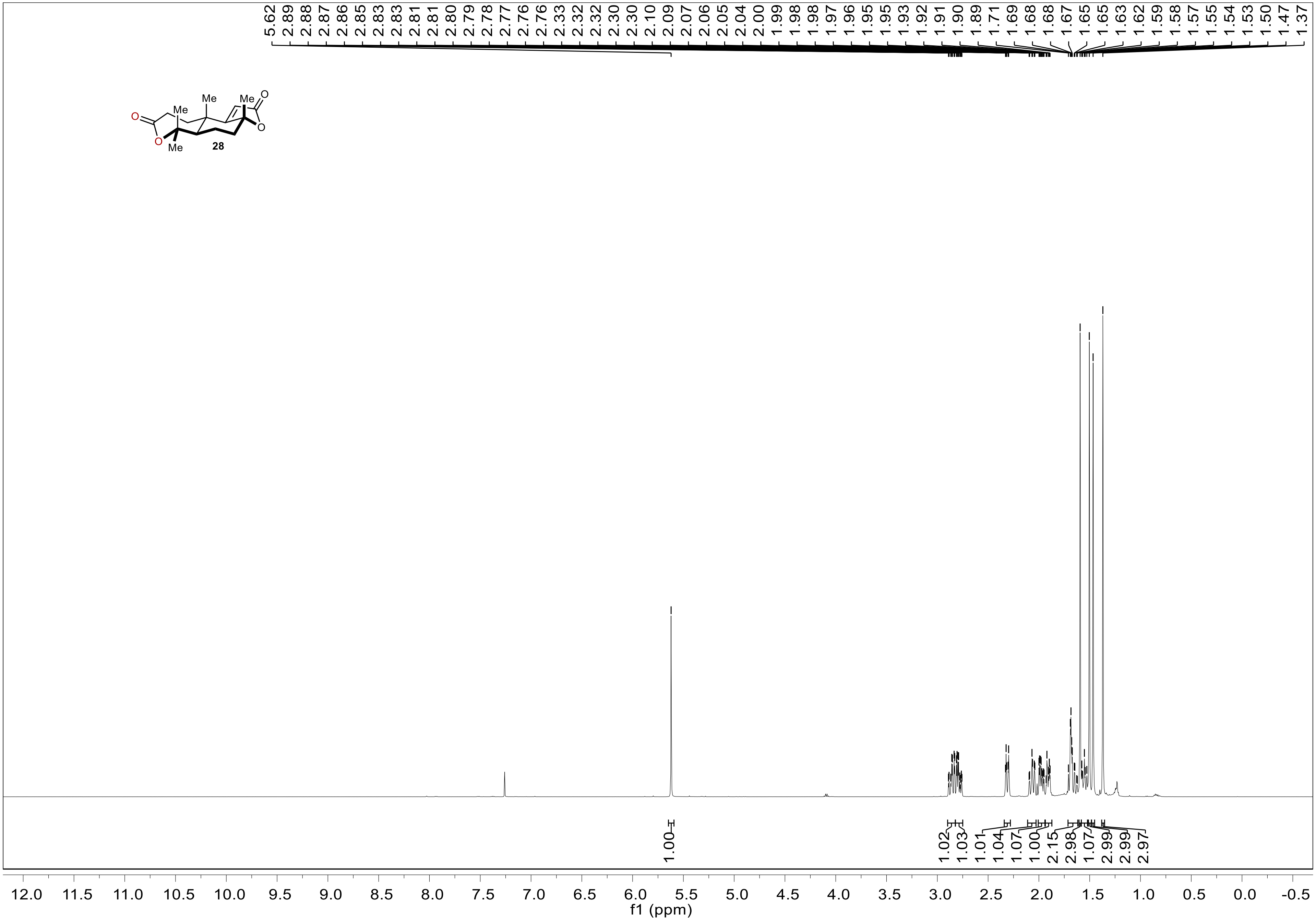
^{1}H NMR Spectrum of compound 27 (500 MHz, $CDCl_3$)



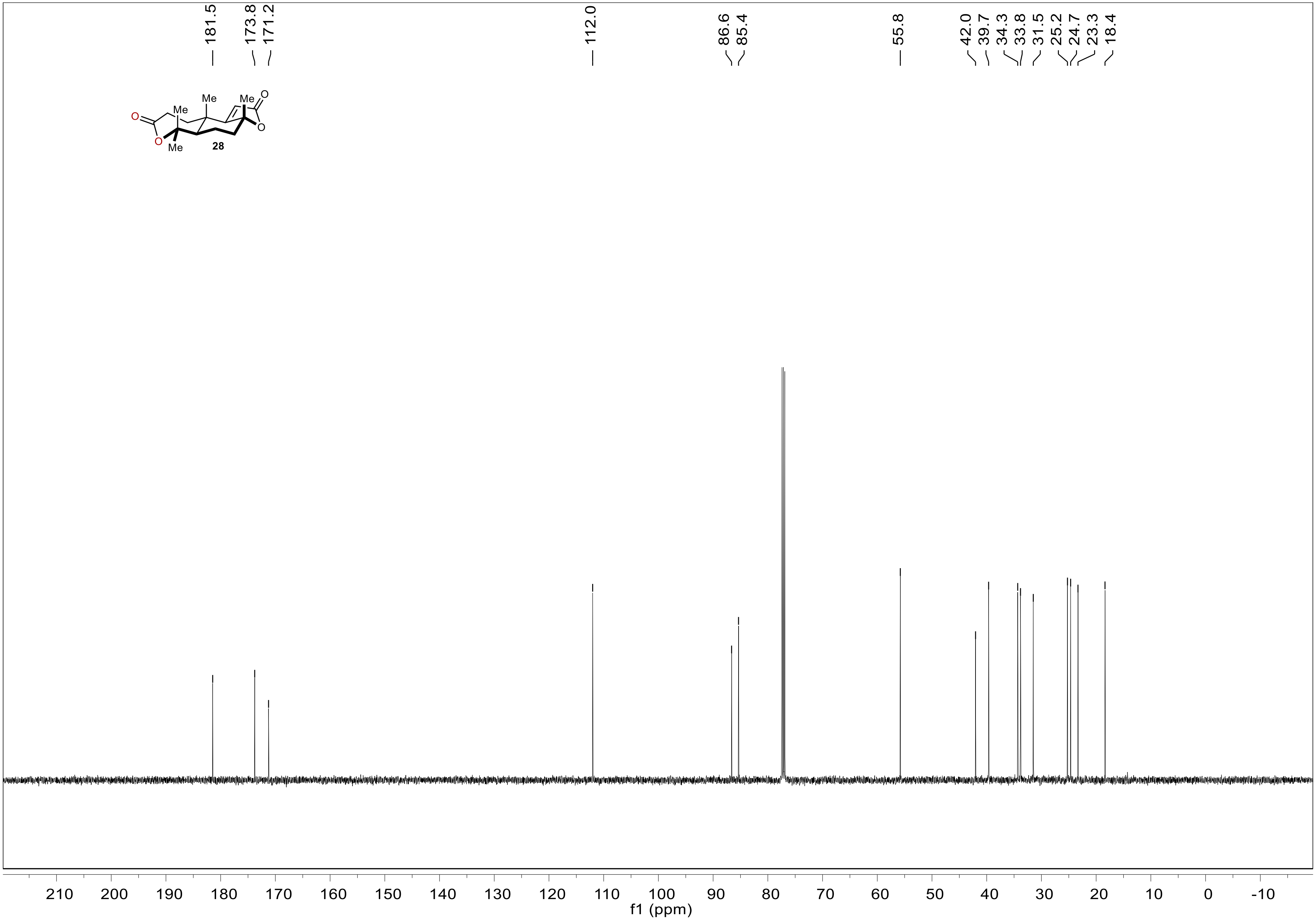
^{13}C NMR Spectrum of compound 27 (126 MHz, CDCl$_3$)



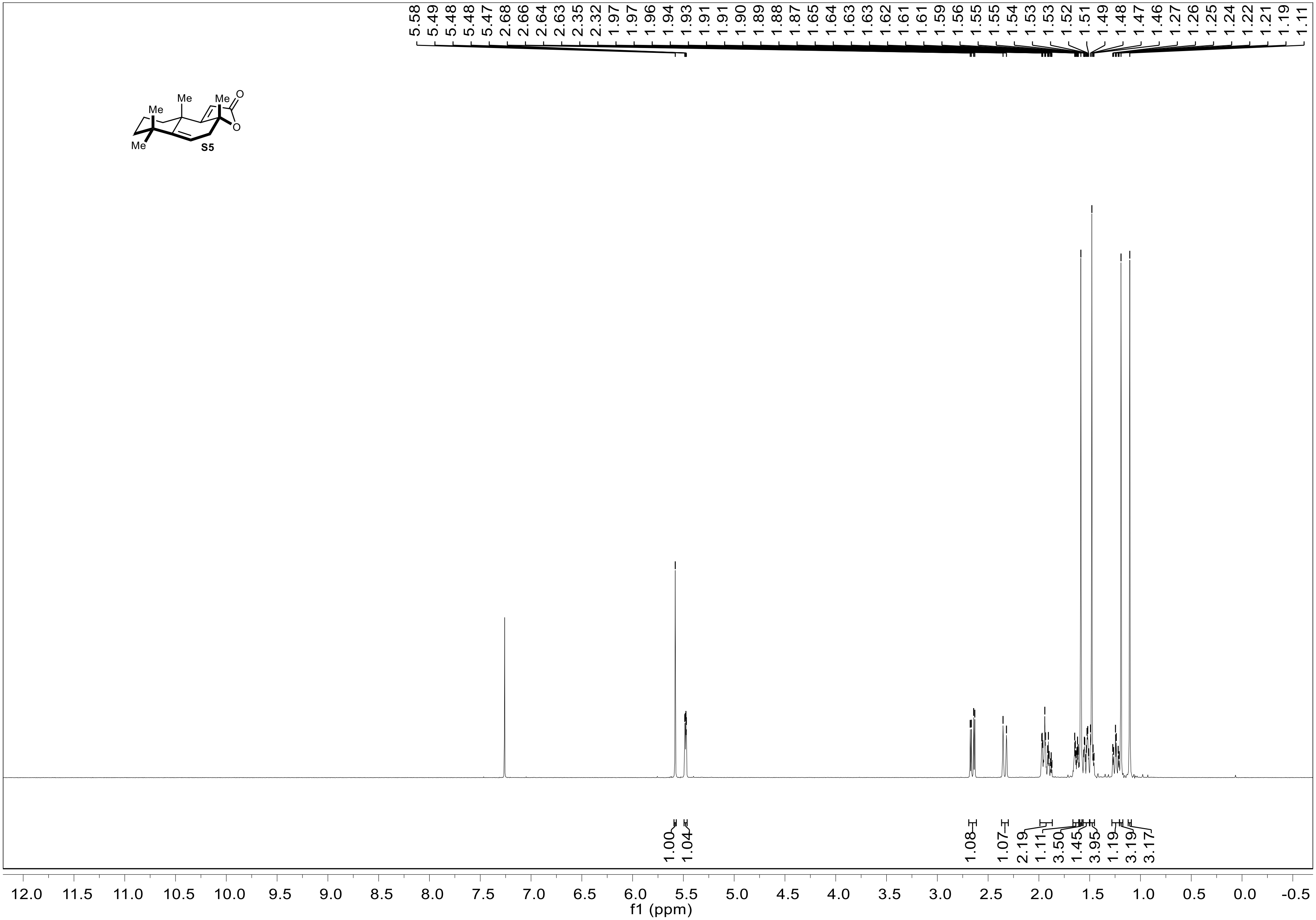
^{1}H NMR Spectrum of compound 28 (500 MHz, $CDCl_3$)



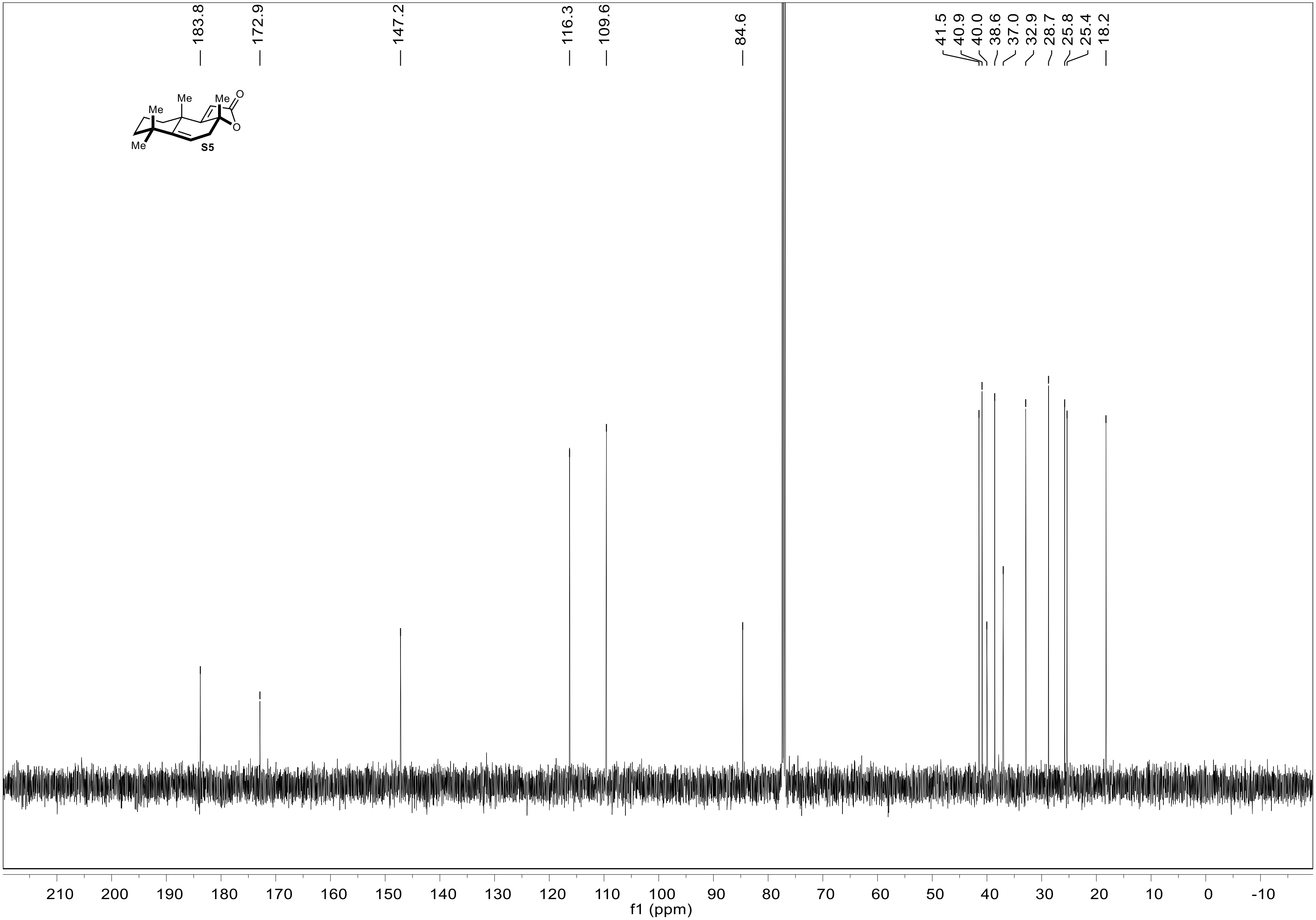
^{13}C NMR Spectrum of compound 28 (126 MHz, $CDCl_3$)



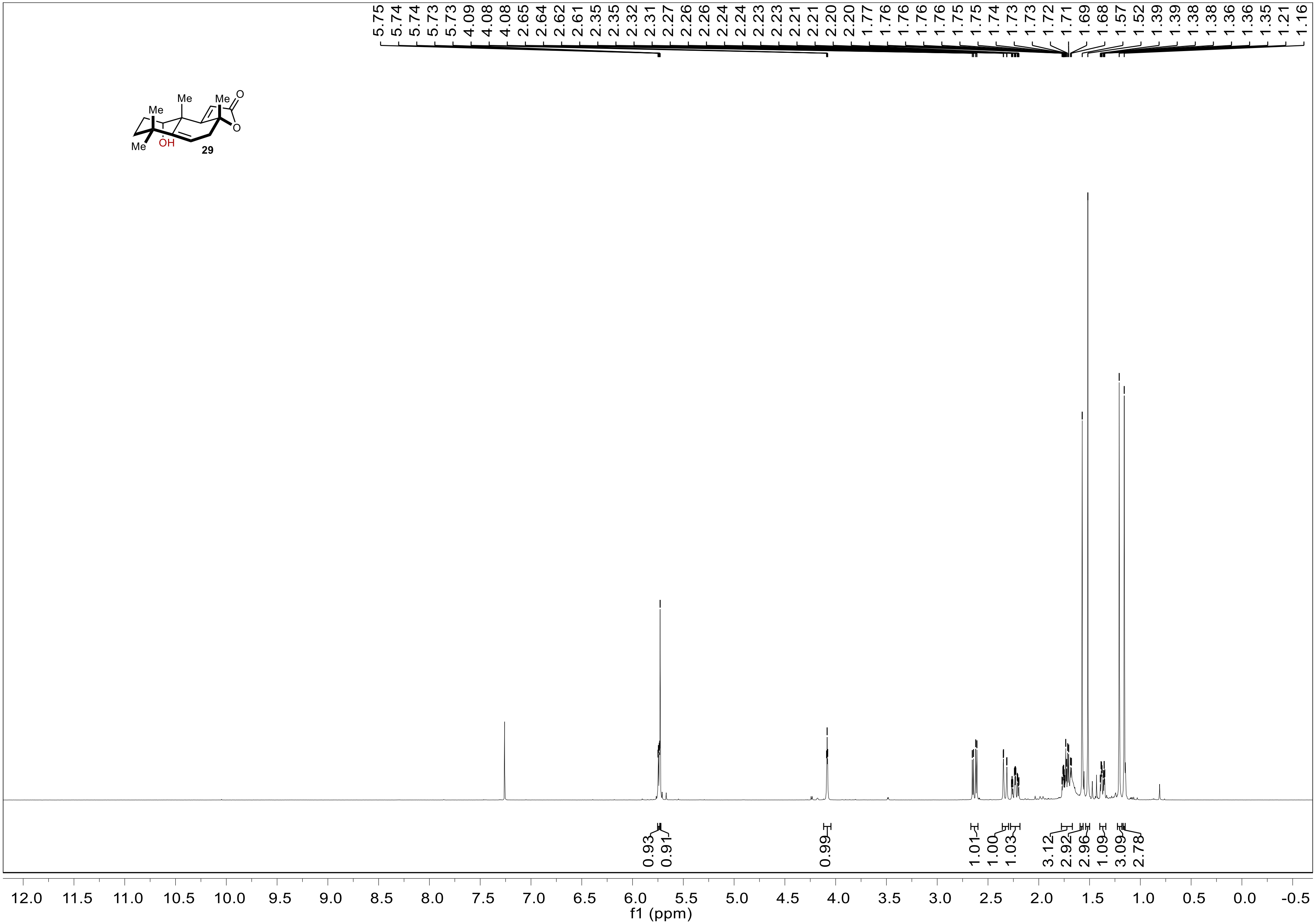
^{1}H NMR Spectrum of compound S5 (500 MHz, CDCl$_3$)



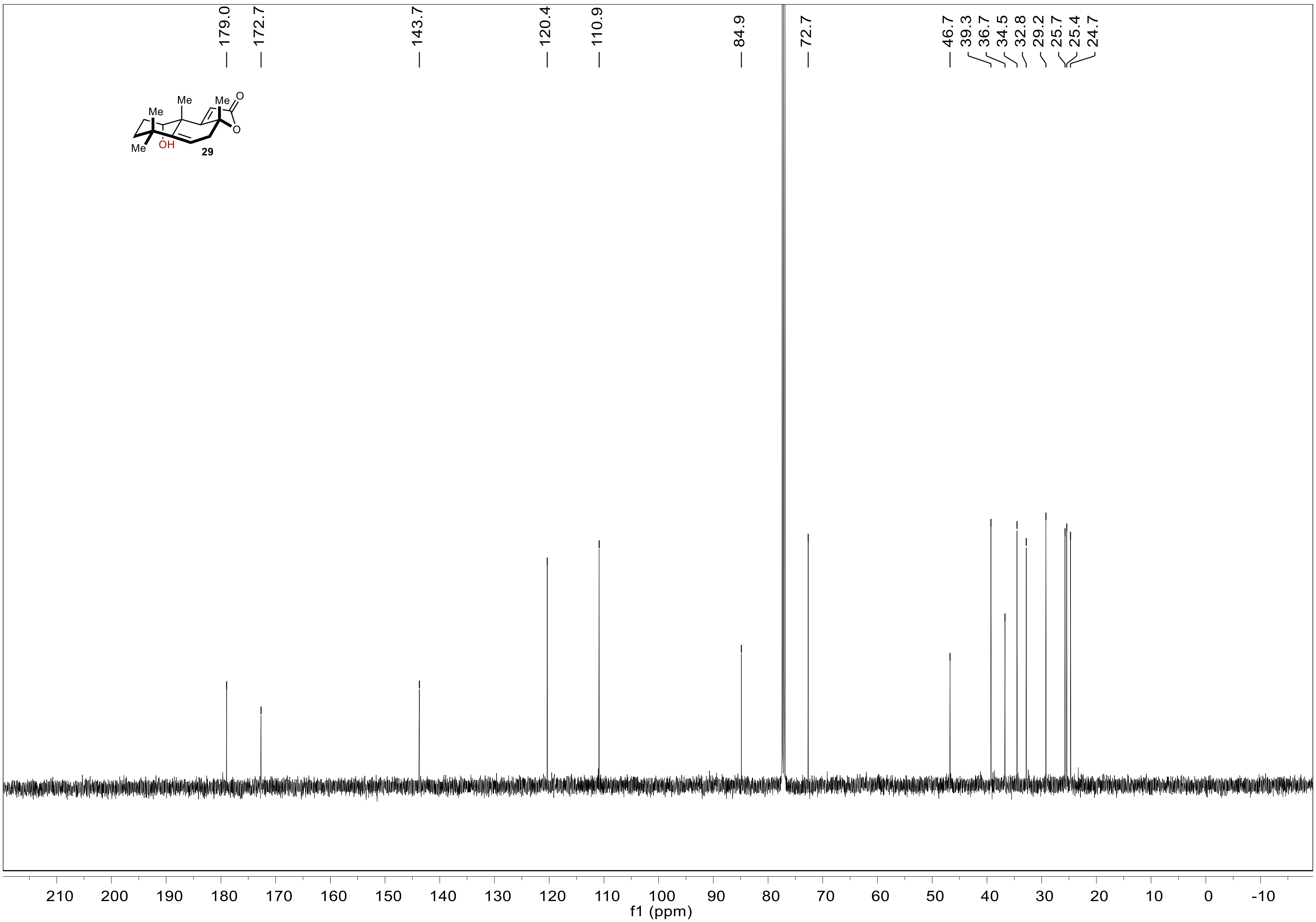
^{13}C NMR Spectrum of compound S5 (126 MHz, $CDCl_3$)



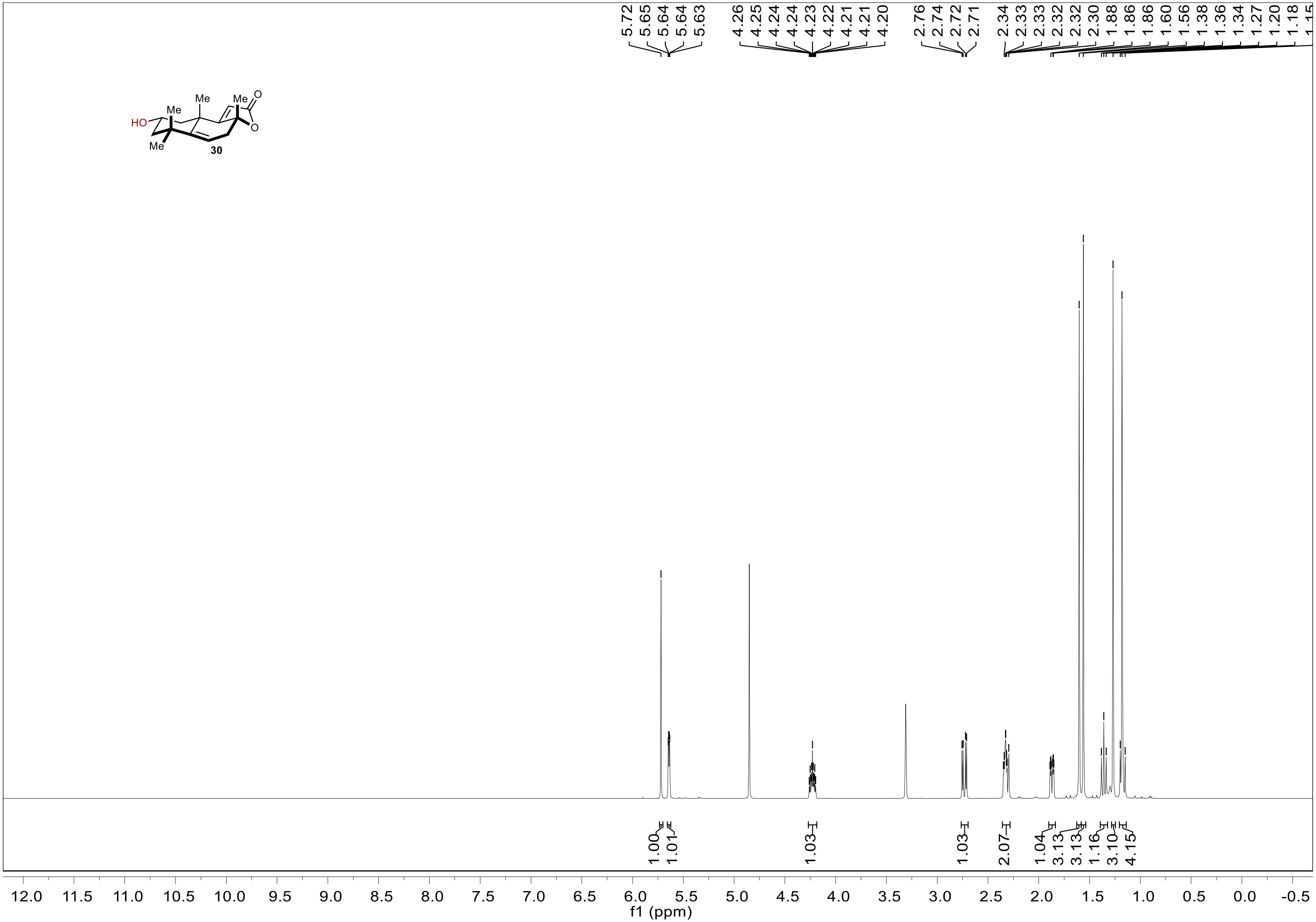
^1H NMR Spectrum of compound 29 (500 MHz, $CDCl_3$)



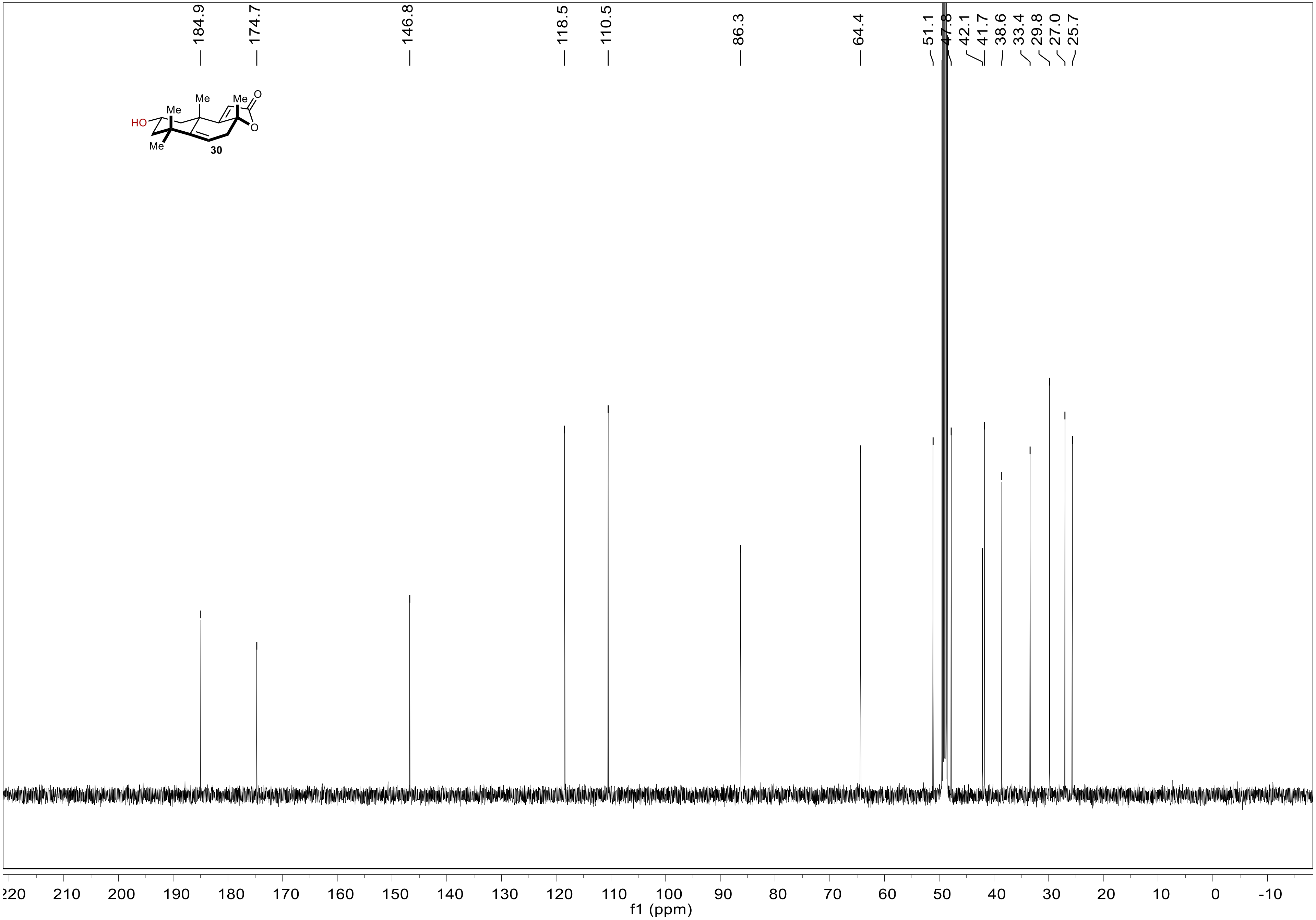
^{13}C NMR Spectrum of compound 29 (126 MHz, CDCl$_3$)



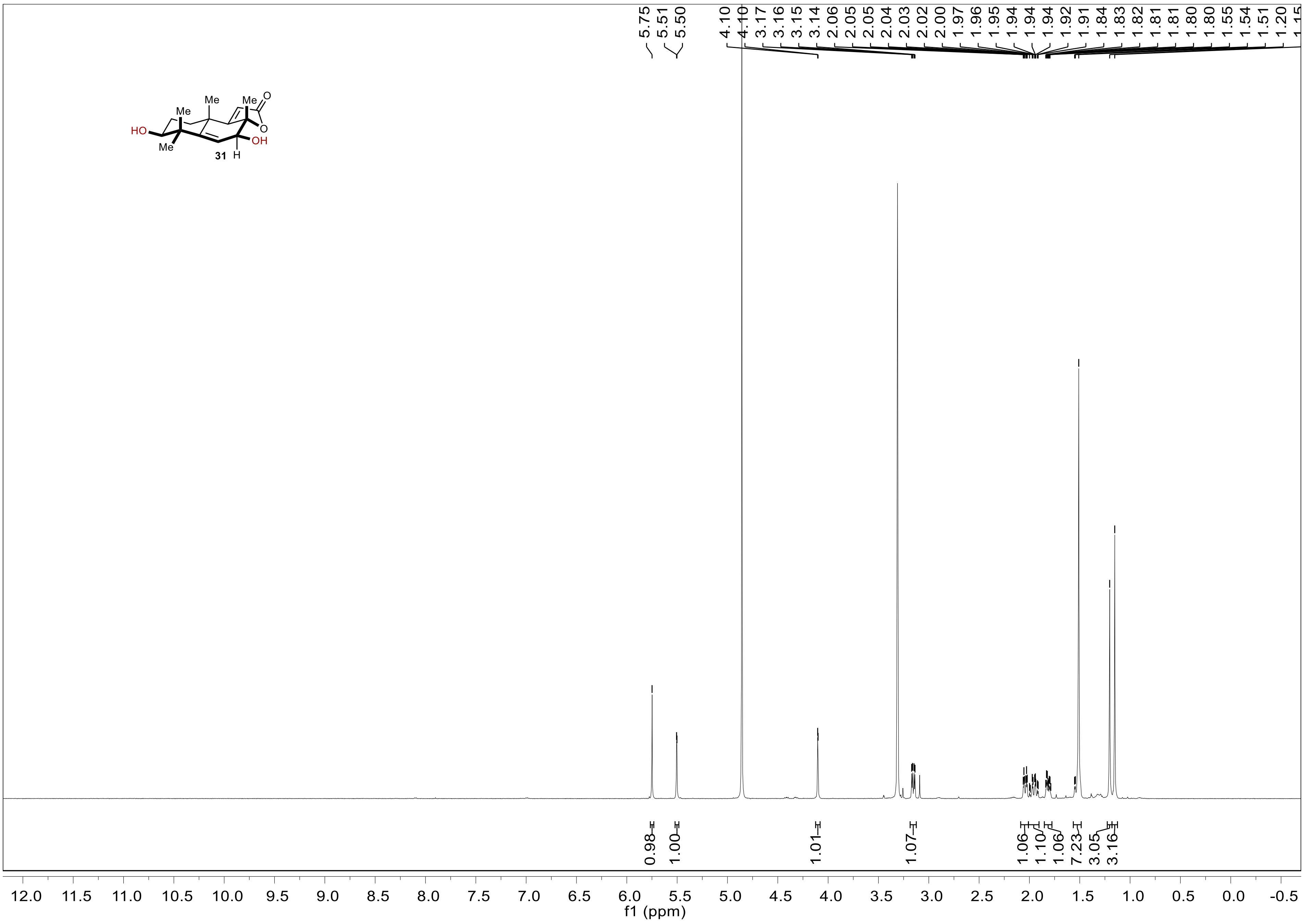
^{1}H NMR Spectrum of compound 30 (500 MHz, Methanol-d_4)



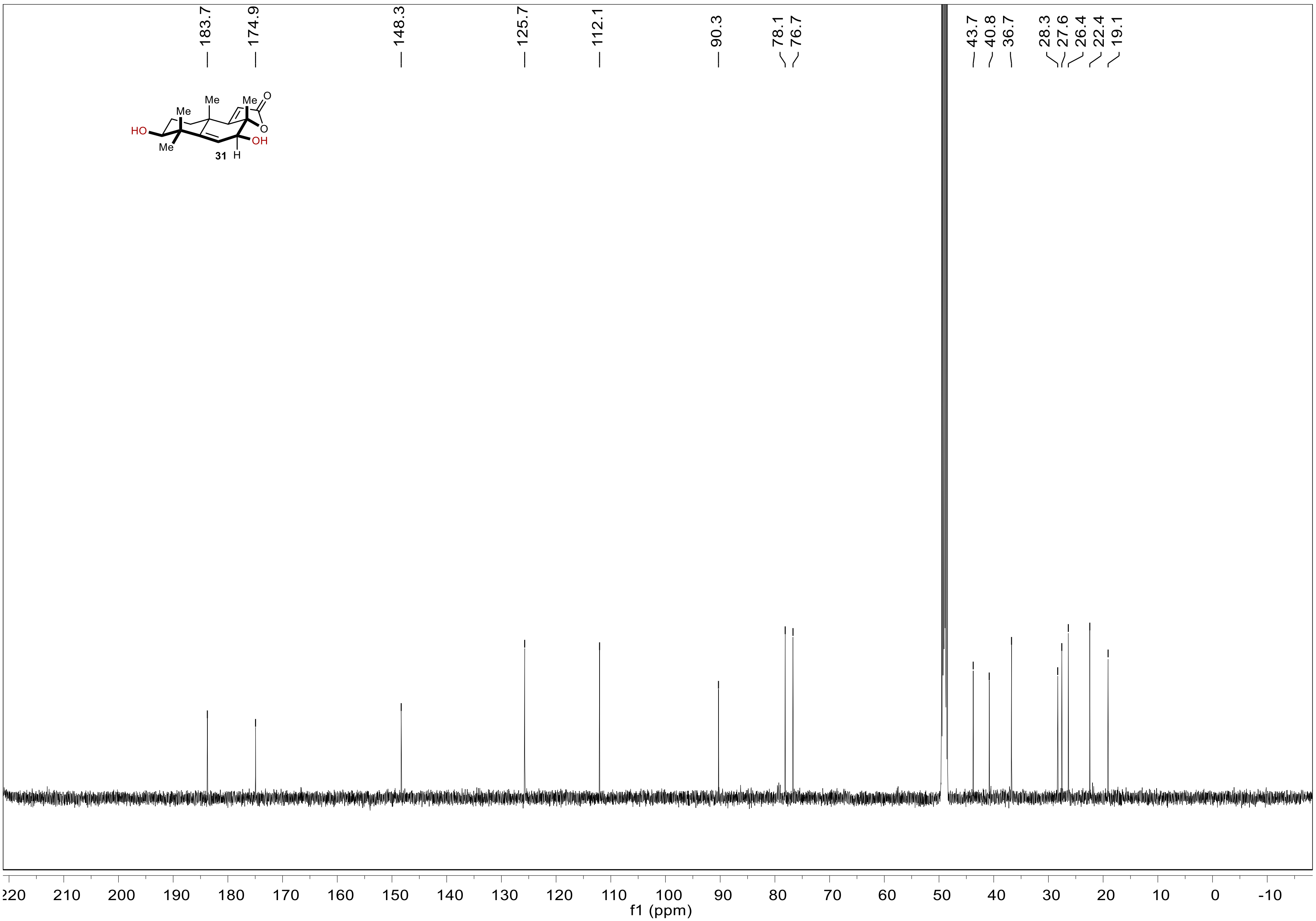
^{13}C NMR Spectrum of compound 30 (126 MHz, Methanol-d_4)



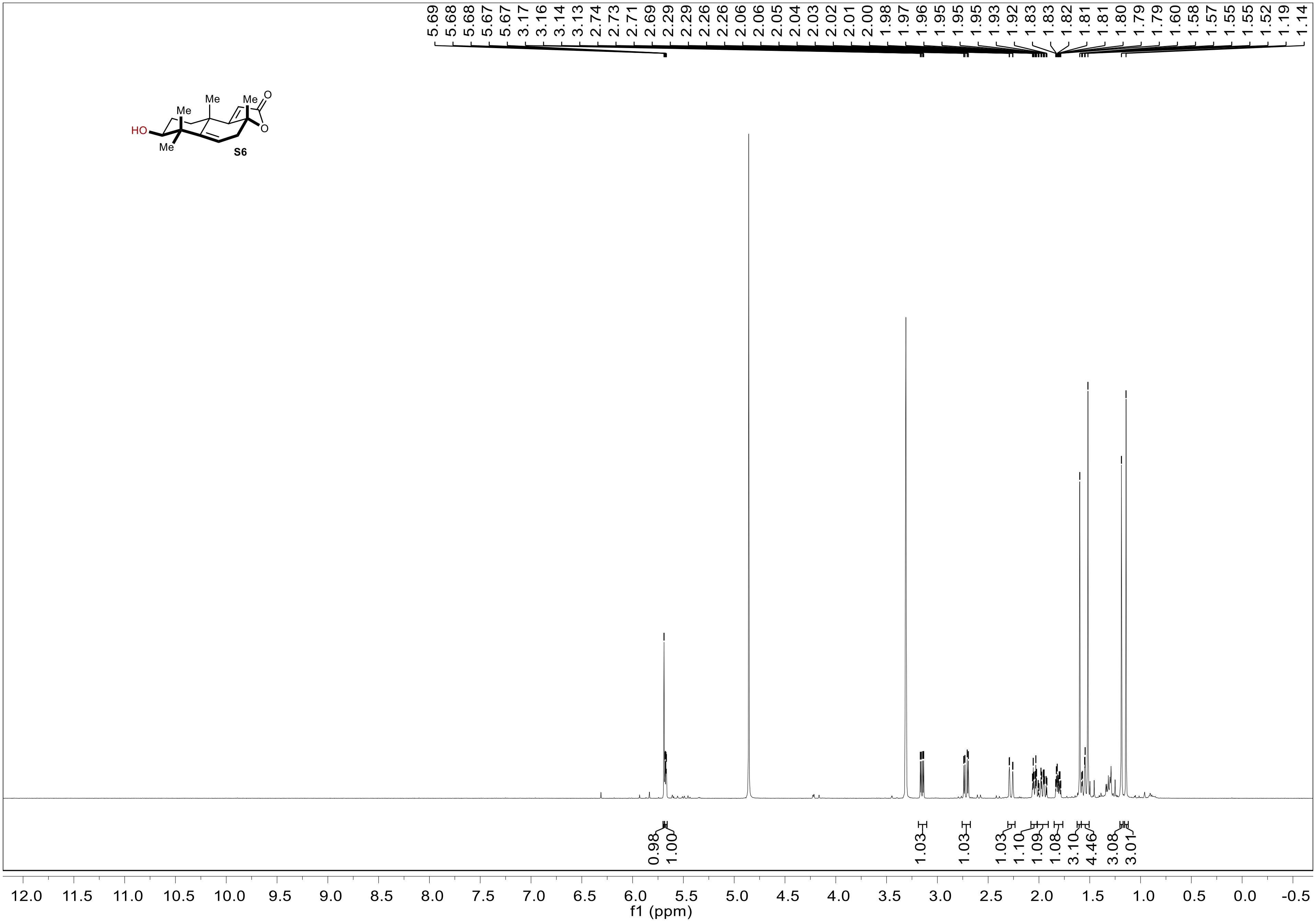
^{1}H NMR Spectrum of compound 31 (500 MHz, Methanol-d_4)



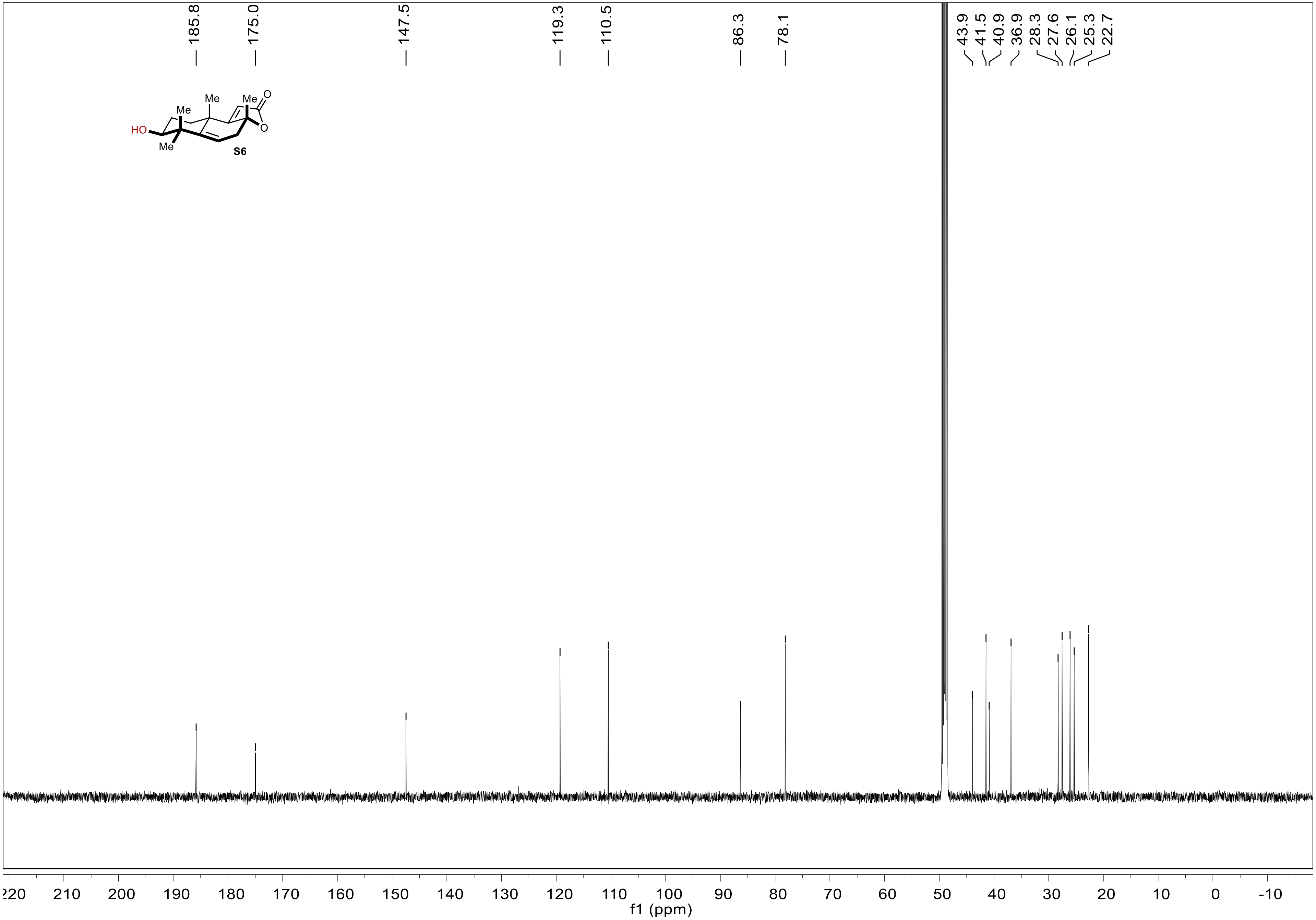
^{13}C NMR Spectrum of compound 31 (126 MHz, Methanol-*d*$_4$)



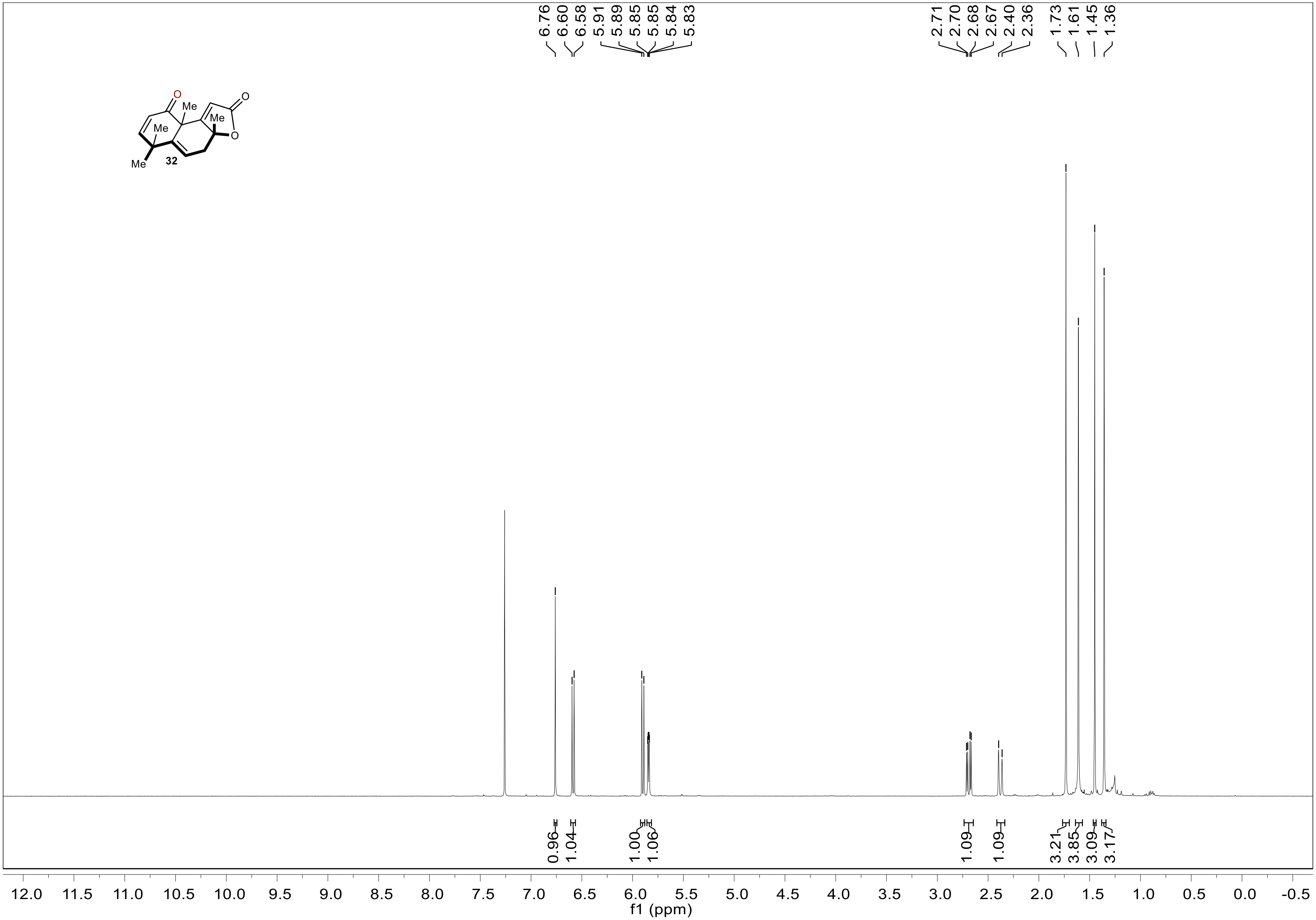
^{1}H NMR Spectrum of compound S6 (500 MHz, Methanol-d_4)



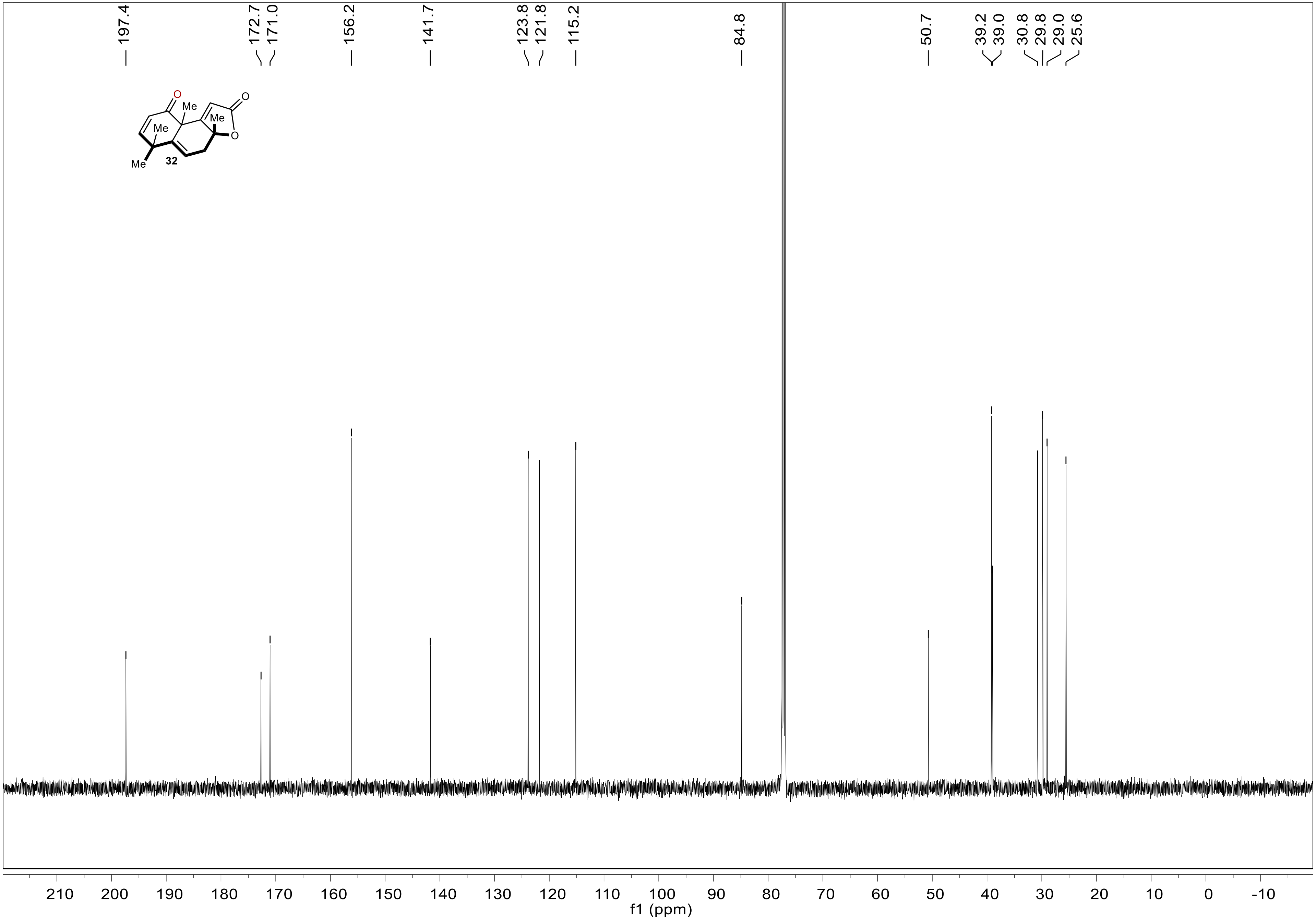
^{13}C NMR Spectrum of compound S6 (126 MHz, Methanol-*d*$_4$)



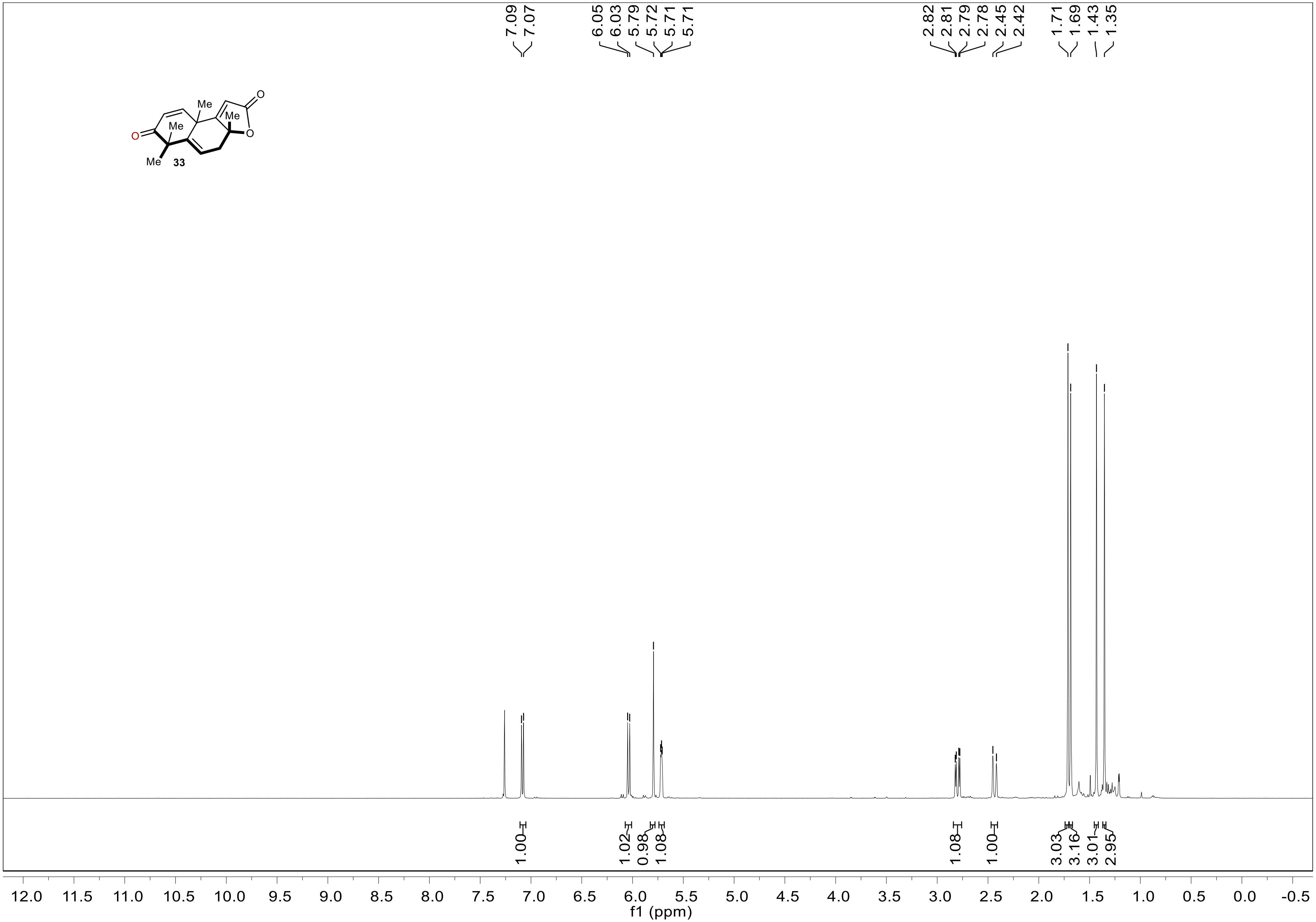
^{1}H NMR Spectrum of compound 32 (500 MHz, $CDCl_3$)



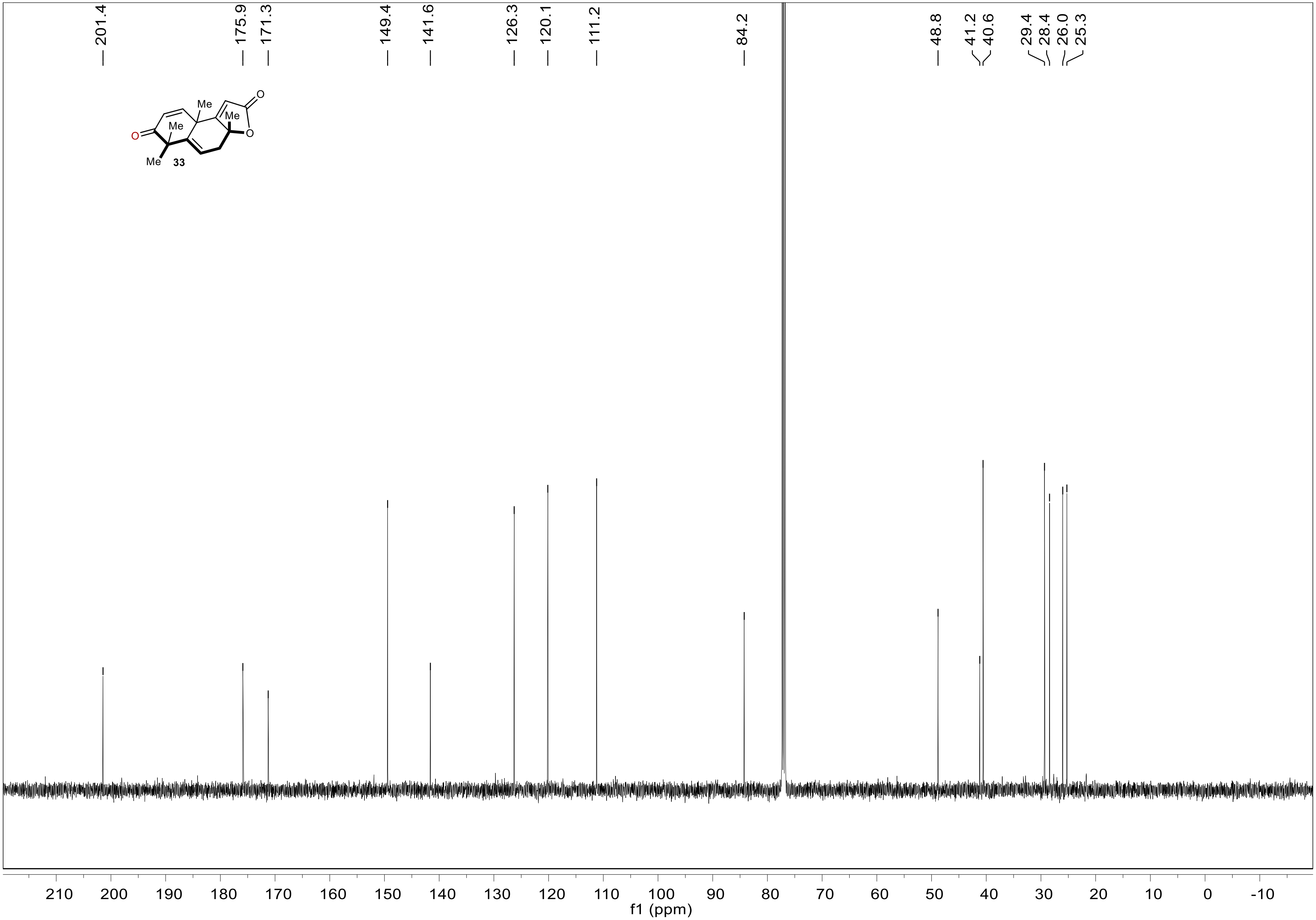
^{13}C NMR Spectrum of compound 32 (126 MHz, CDCl$_3$)



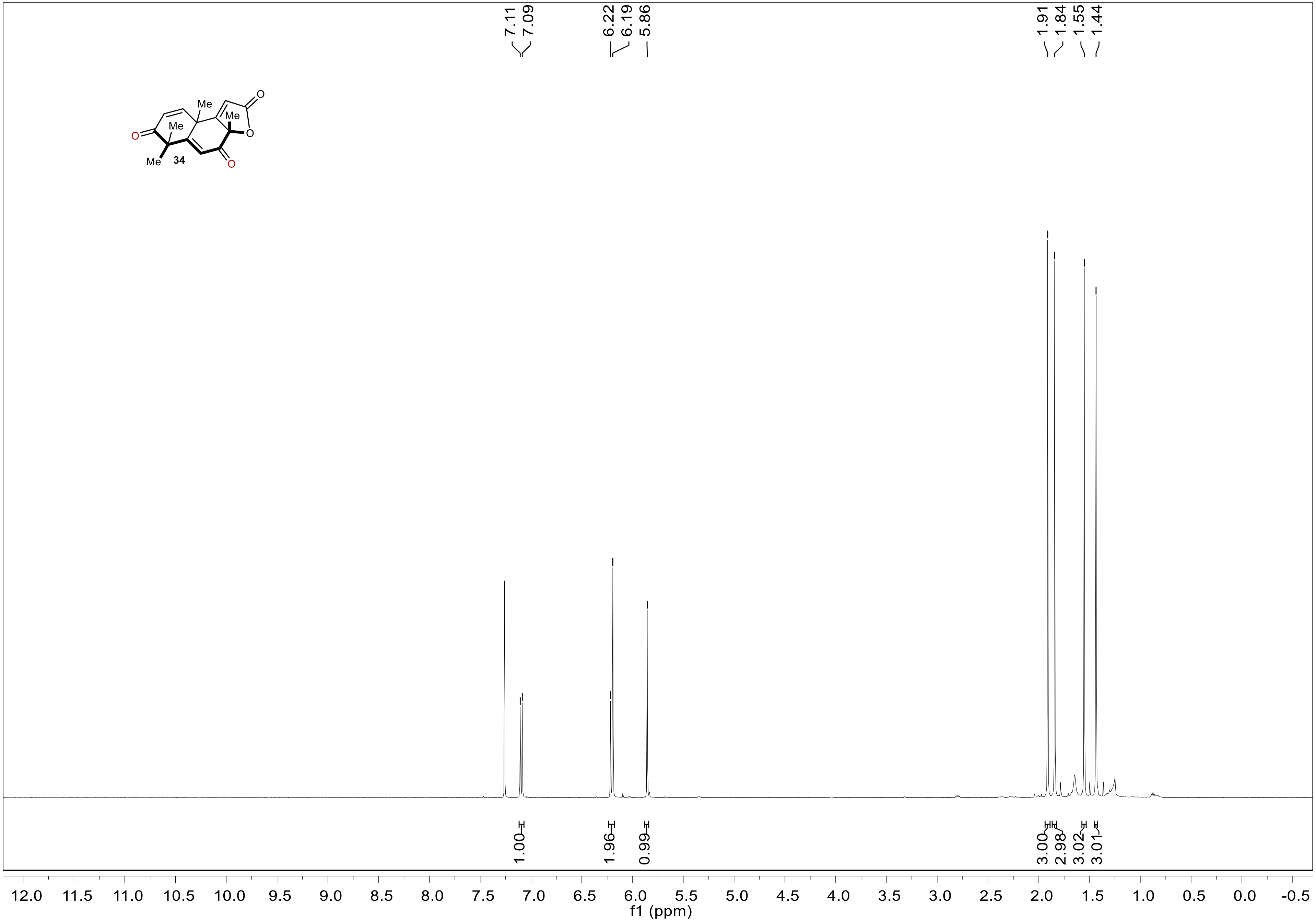
^{1}H NMR Spectrum of compound 33 (500 MHz, CDCl$_3$)



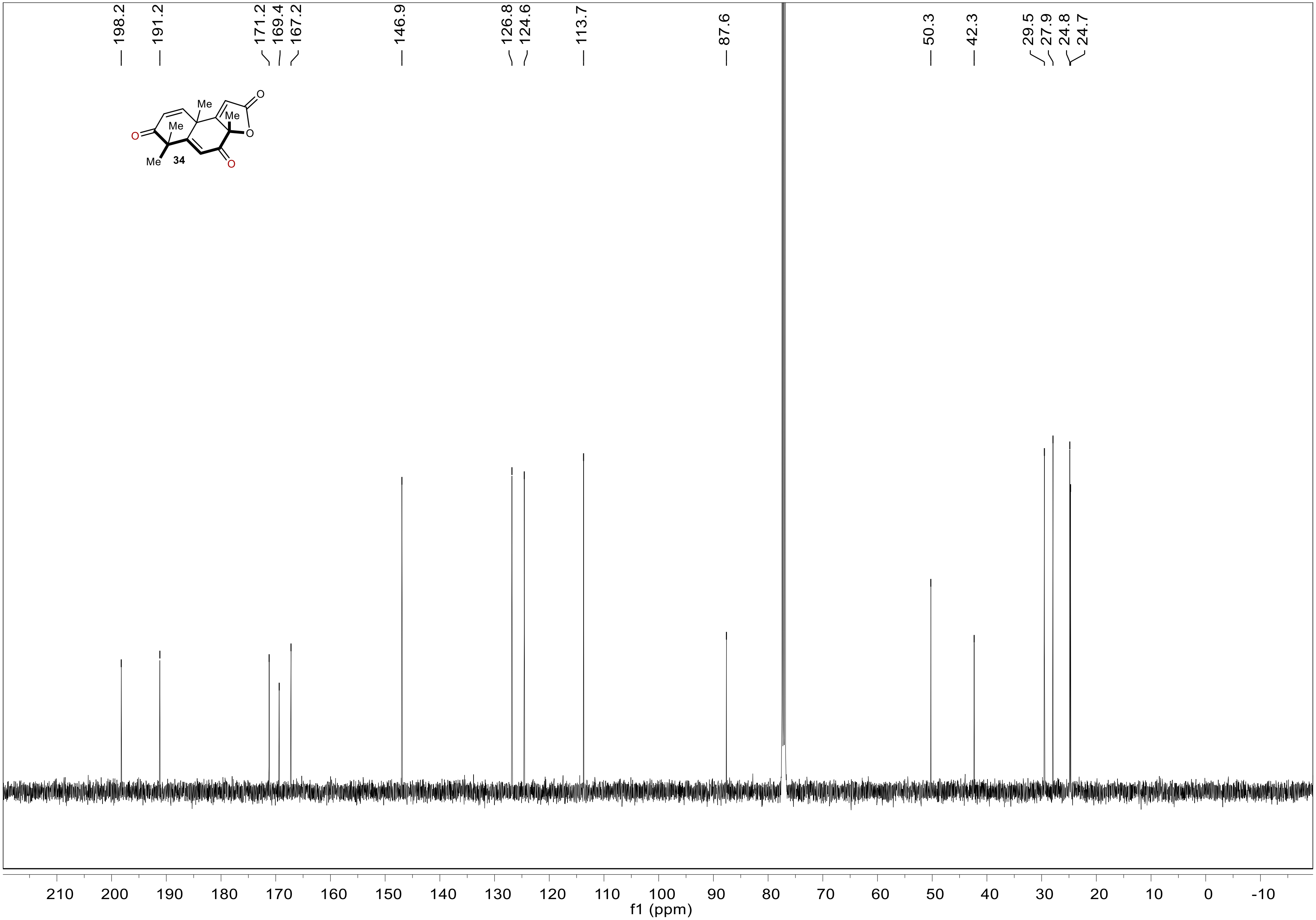
^{13}C NMR Spectrum of compound 33 (126 MHz, $CDCl_3$)



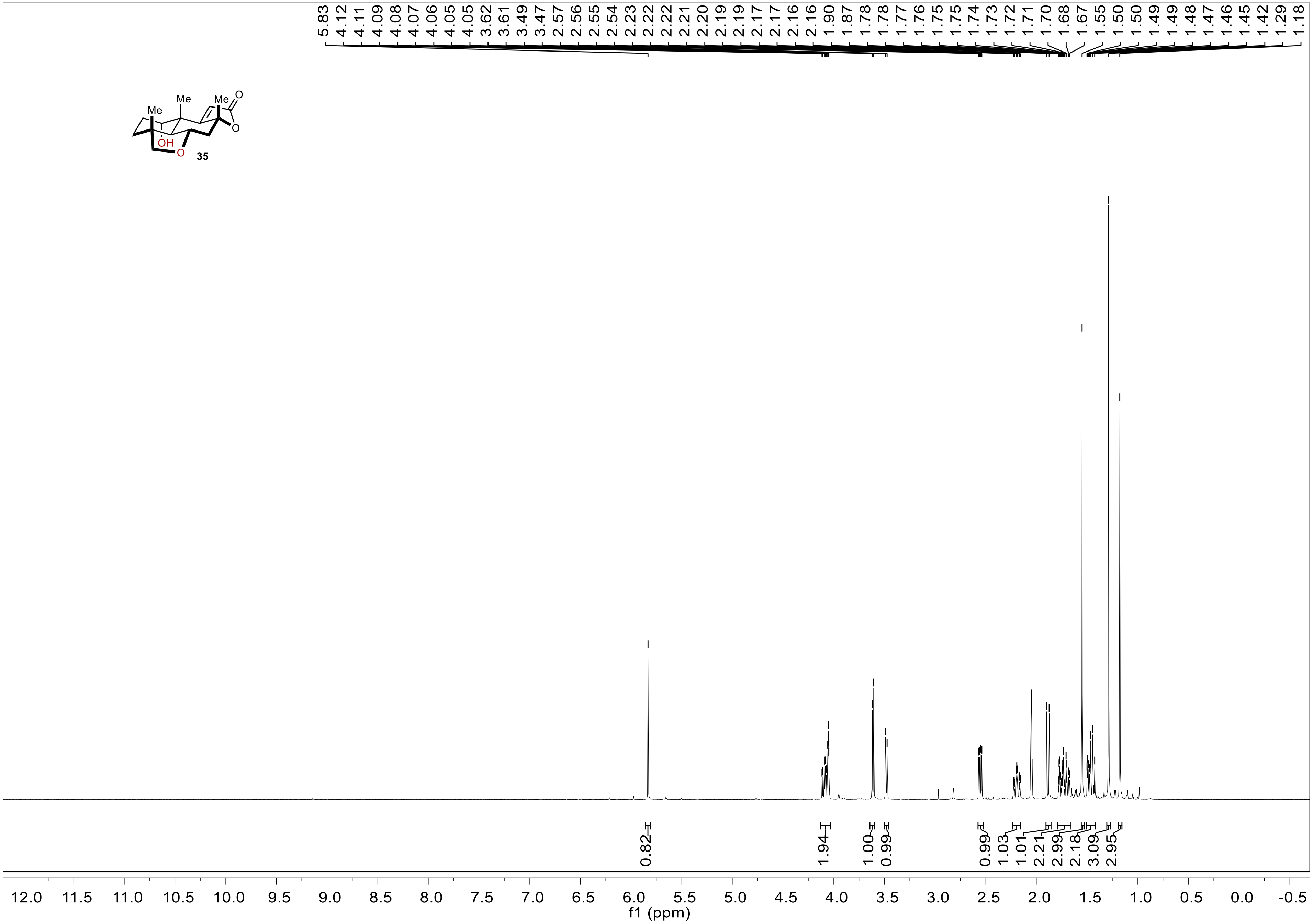
^{1}H NMR Spectrum of compound 34 (500 MHz, $CDCl_3$)



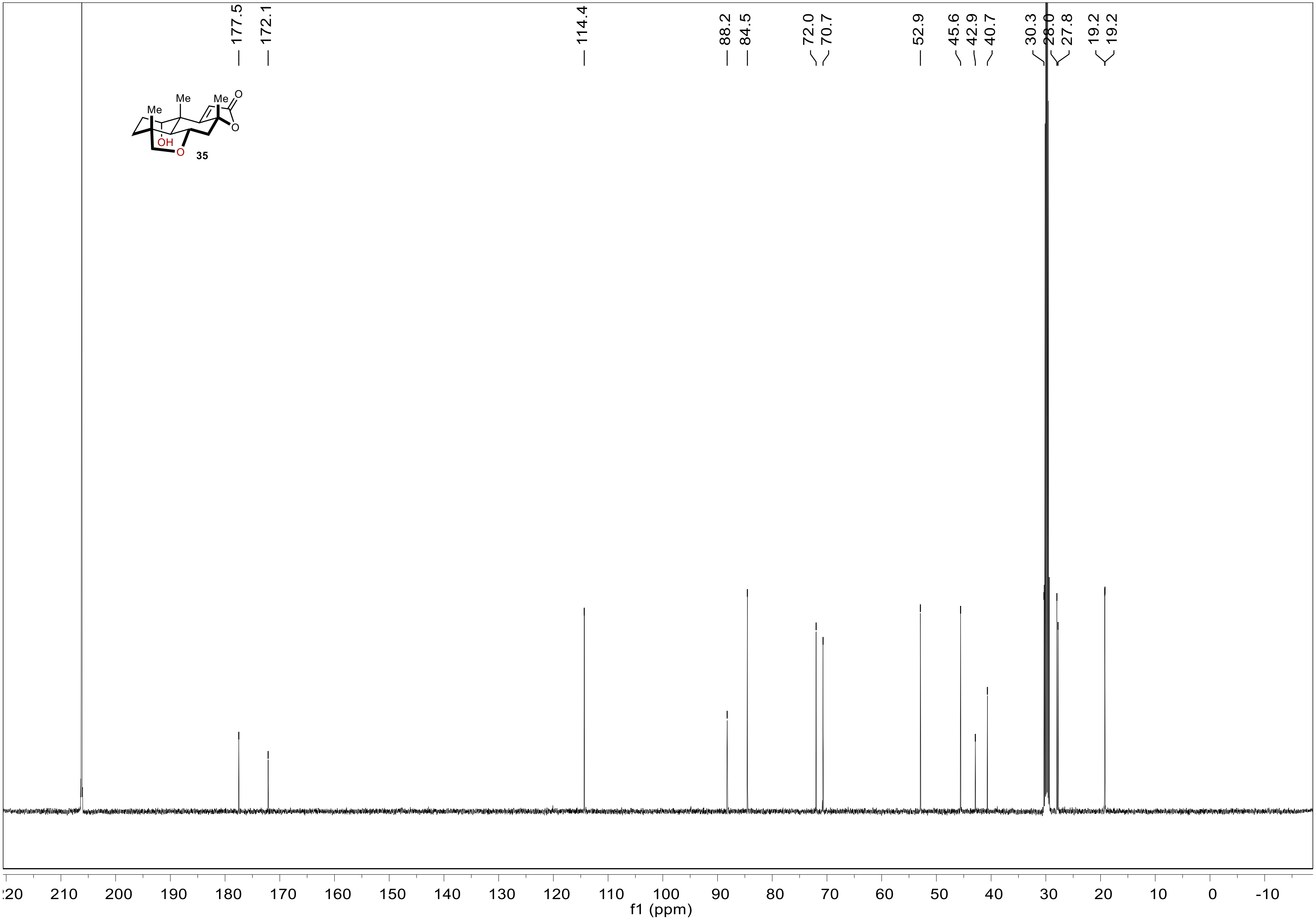
^{13}C NMR Spectrum of compound 34 (126 MHz, $CDCl_3$)



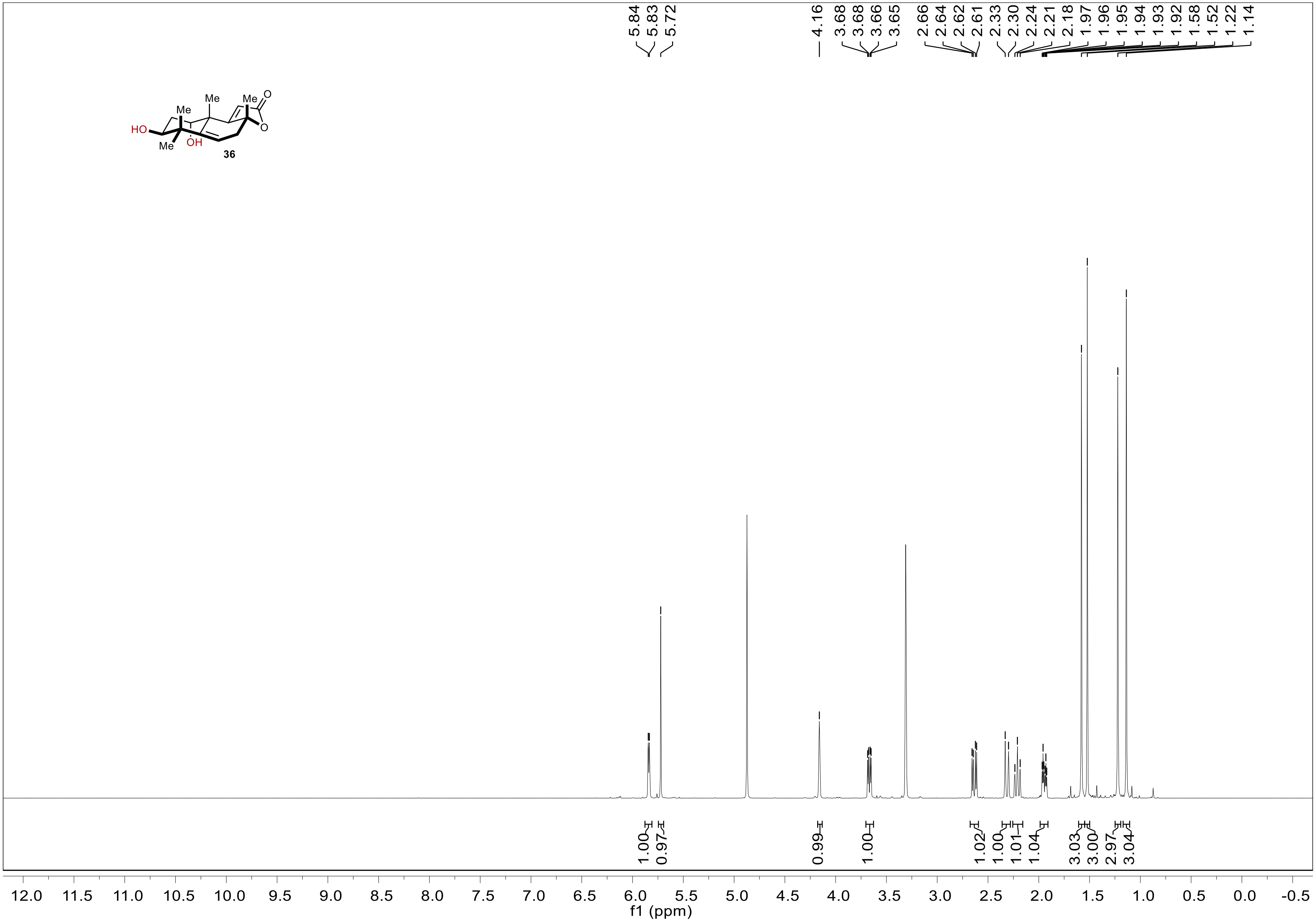
^{1}H NMR Spectrum of 35 (500 MHz, Acetone-d_6)



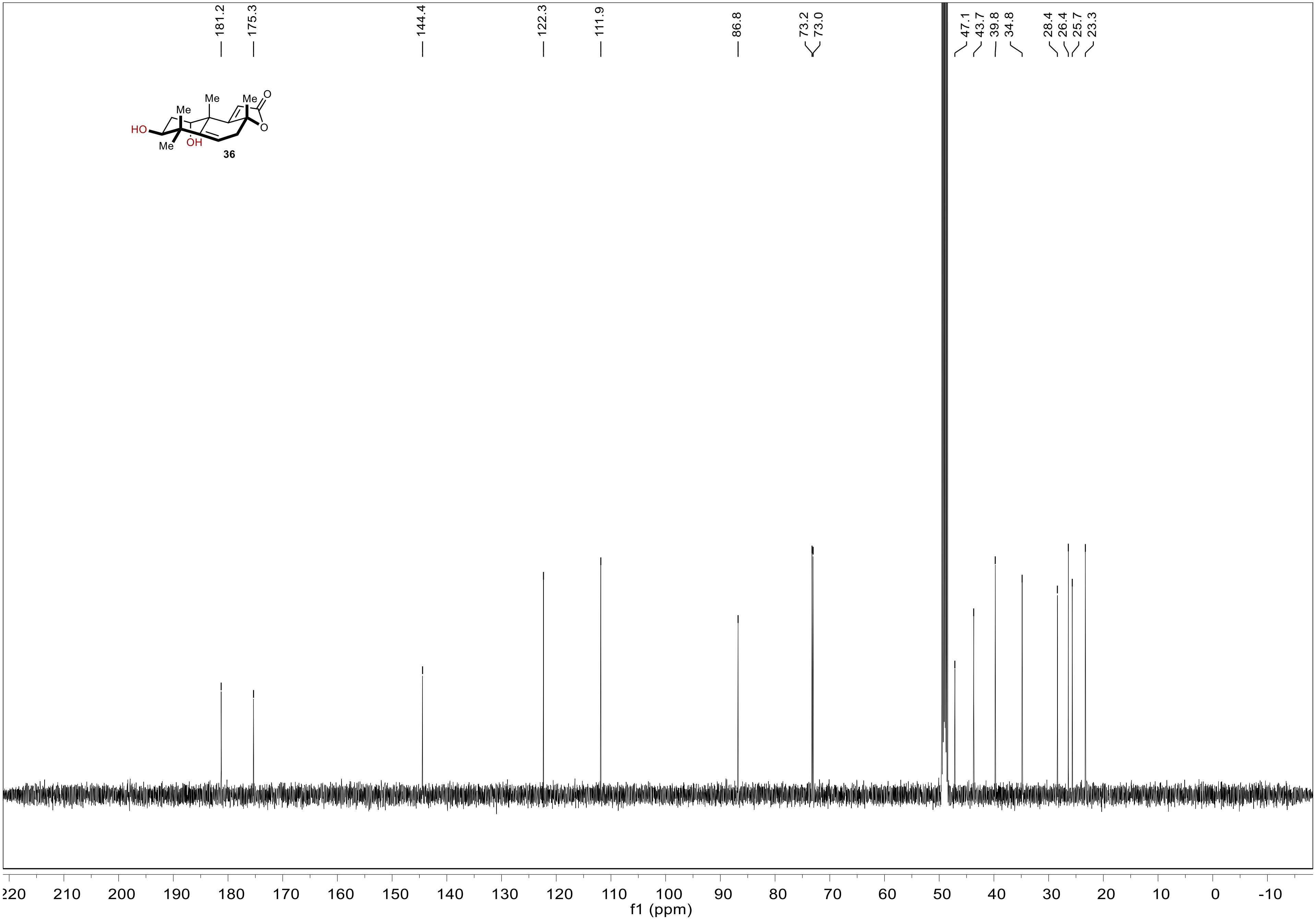
^{13}C NMR Spectrum of 35 (126 MHz, Acetone-*d*$_6$)



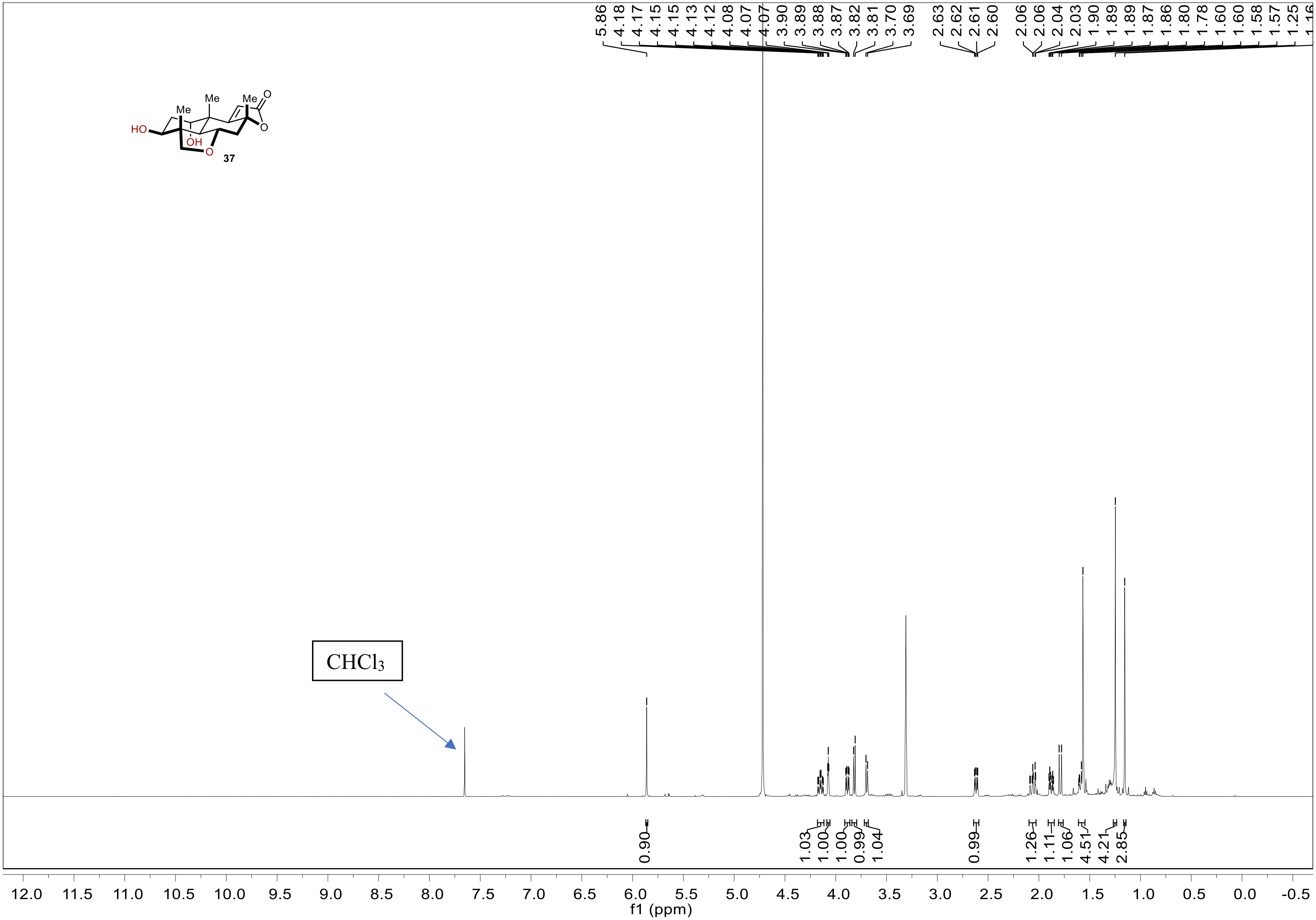
^{1}H NMR Spectrum of compound 36 (500 MHz, Methanol-d_4)



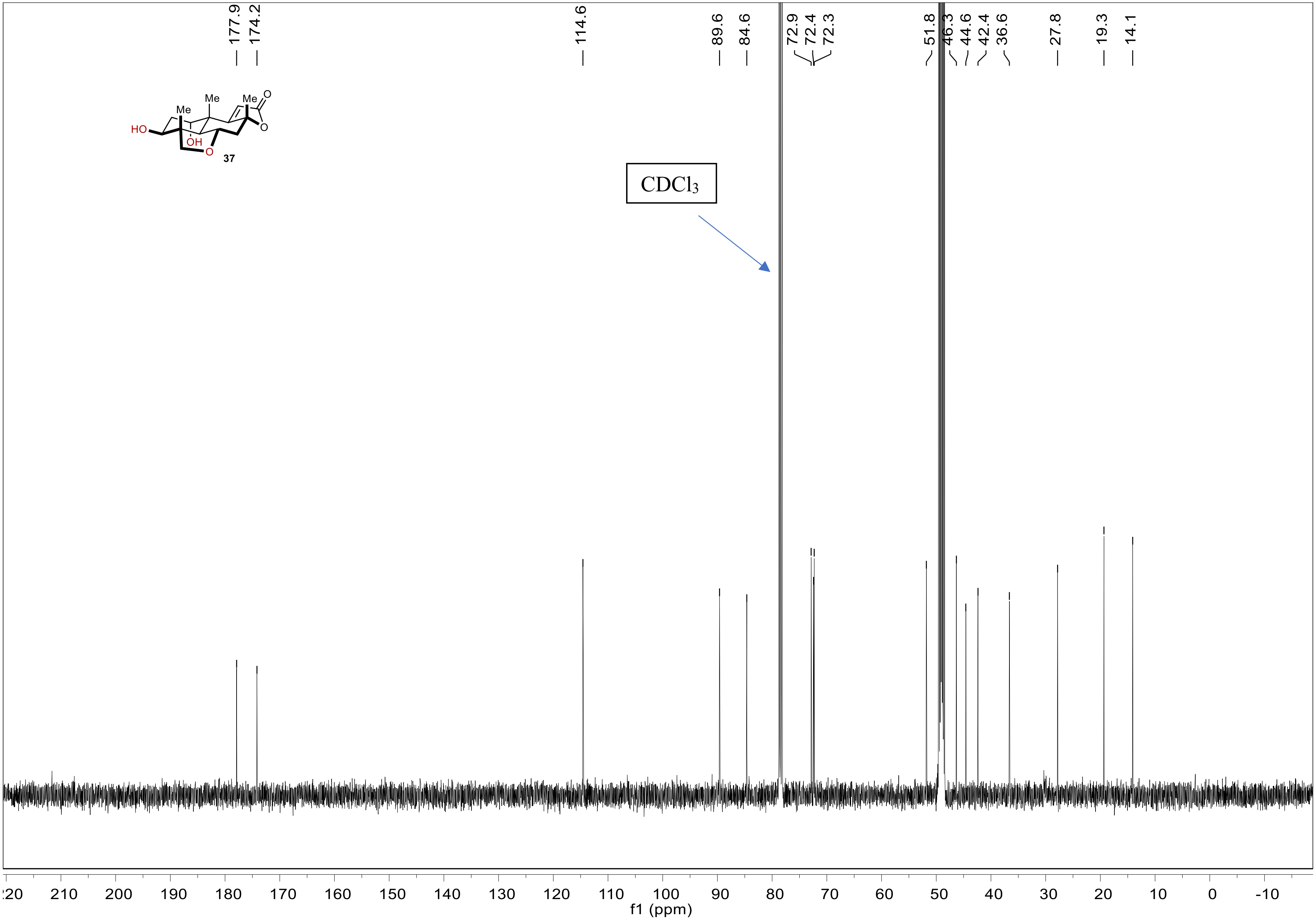
^{13}C NMR Spectrum of compound 36 (126 MHz, Methanol-*d*$_4$)



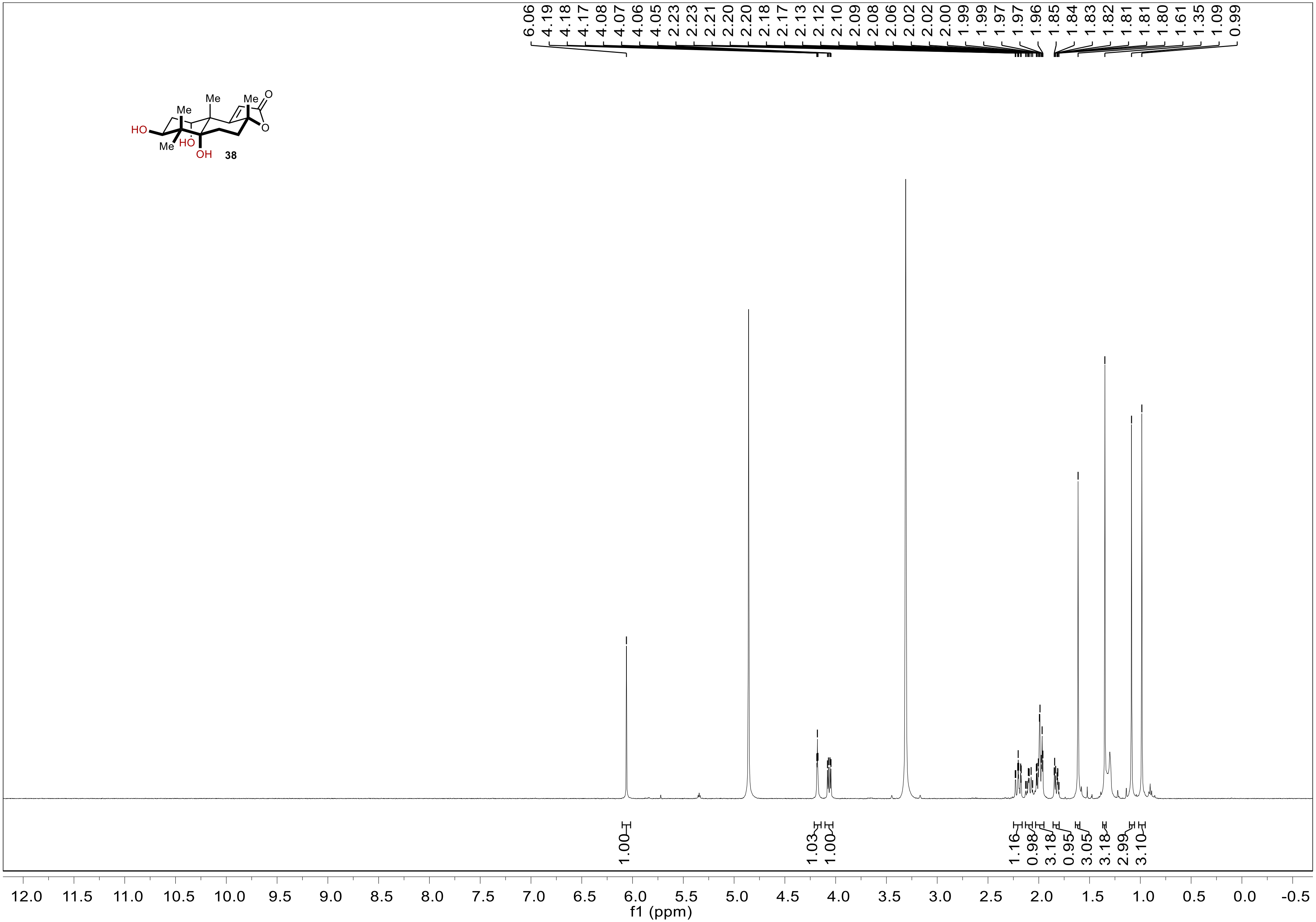
^{1}H NMR Spectrum of compound 37 (500 MHz, Methanol-d_4: $CDCl_3$ = 3: 2)



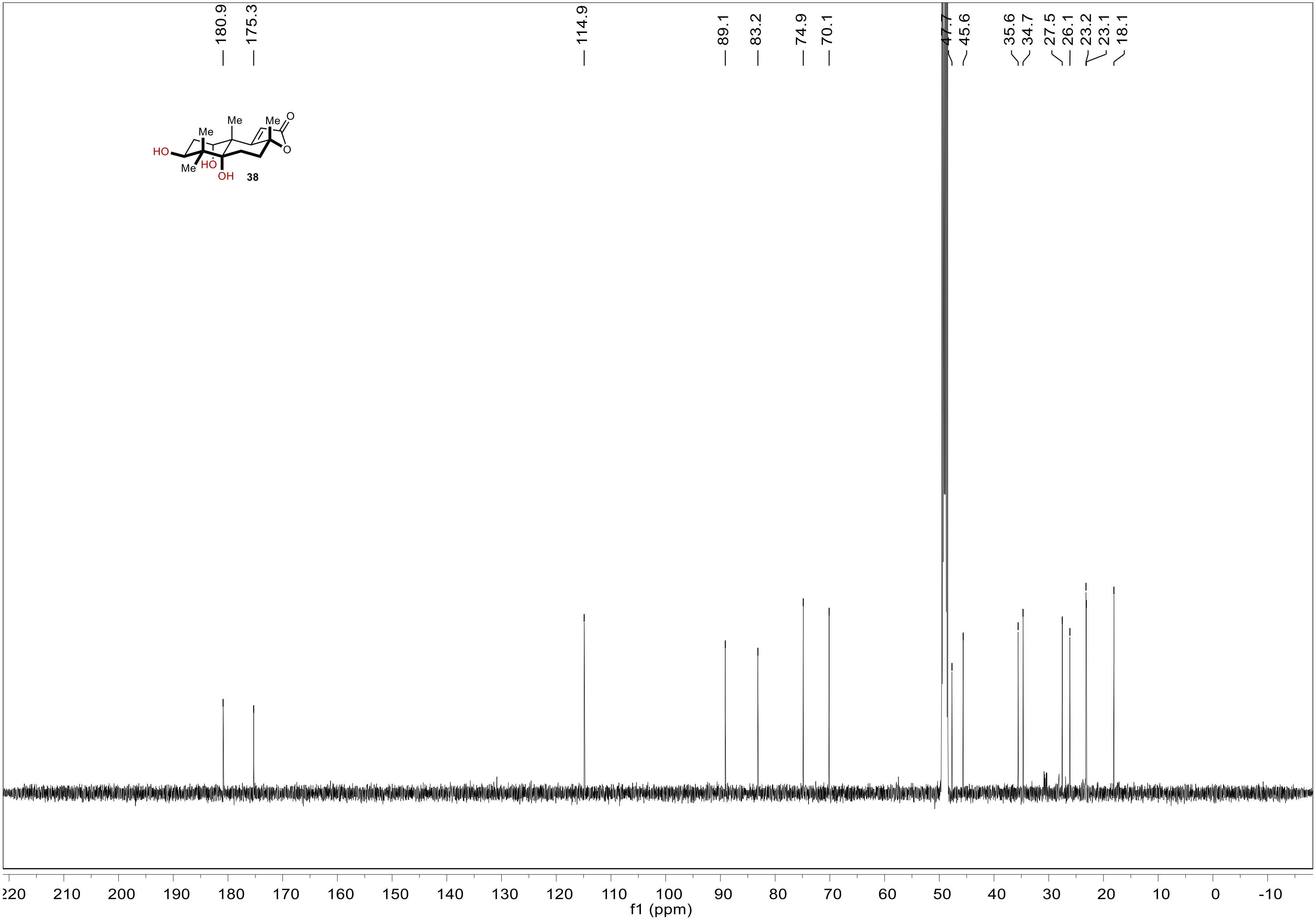
^{13}C NMR Spectrum of compound 37 (126 MHz, Methanol-d_4: $CDCl_3$ = 3: 2)



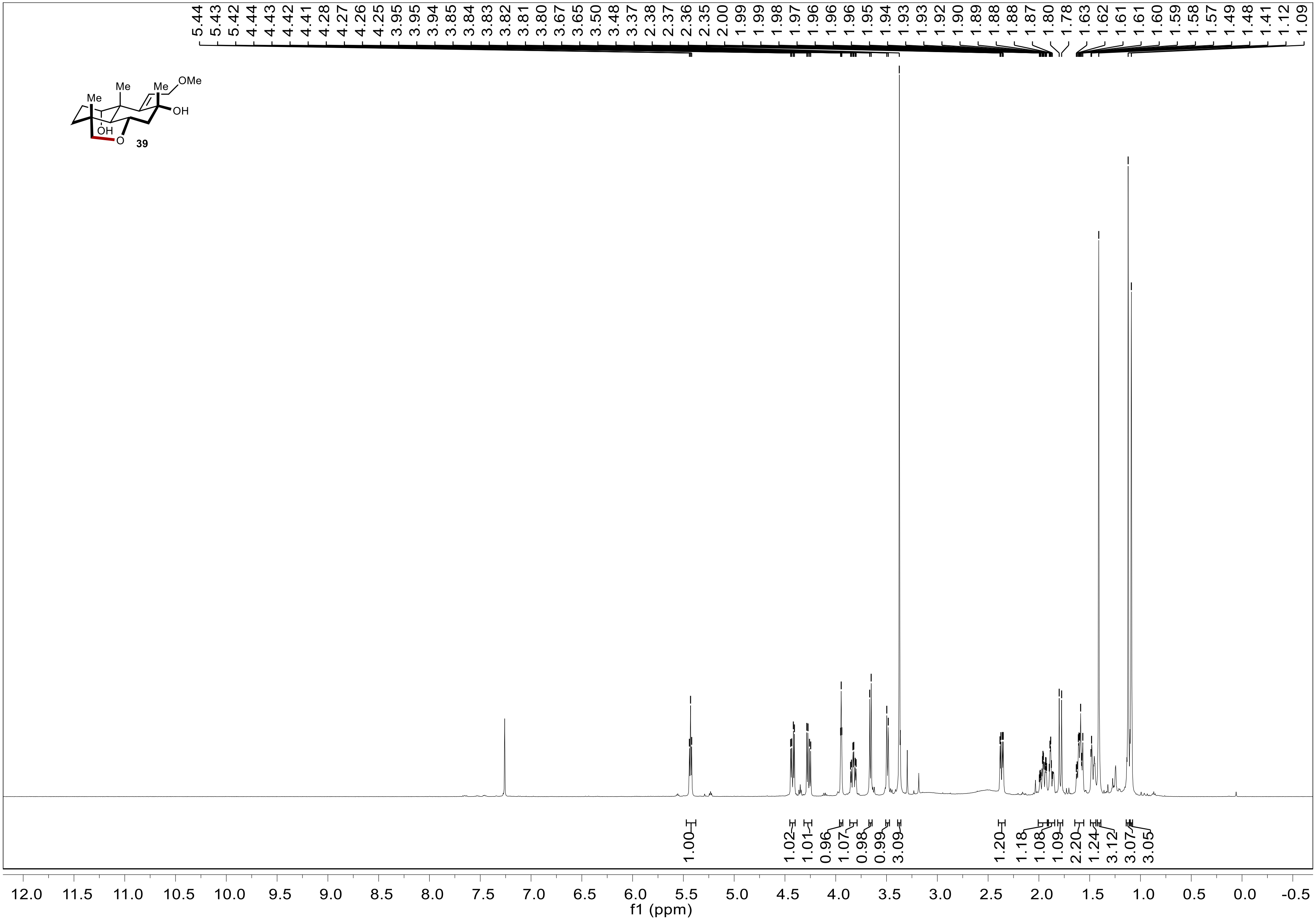
^{1}H NMR Spectrum of compound 38 (500 MHz, Methanol-d_4)



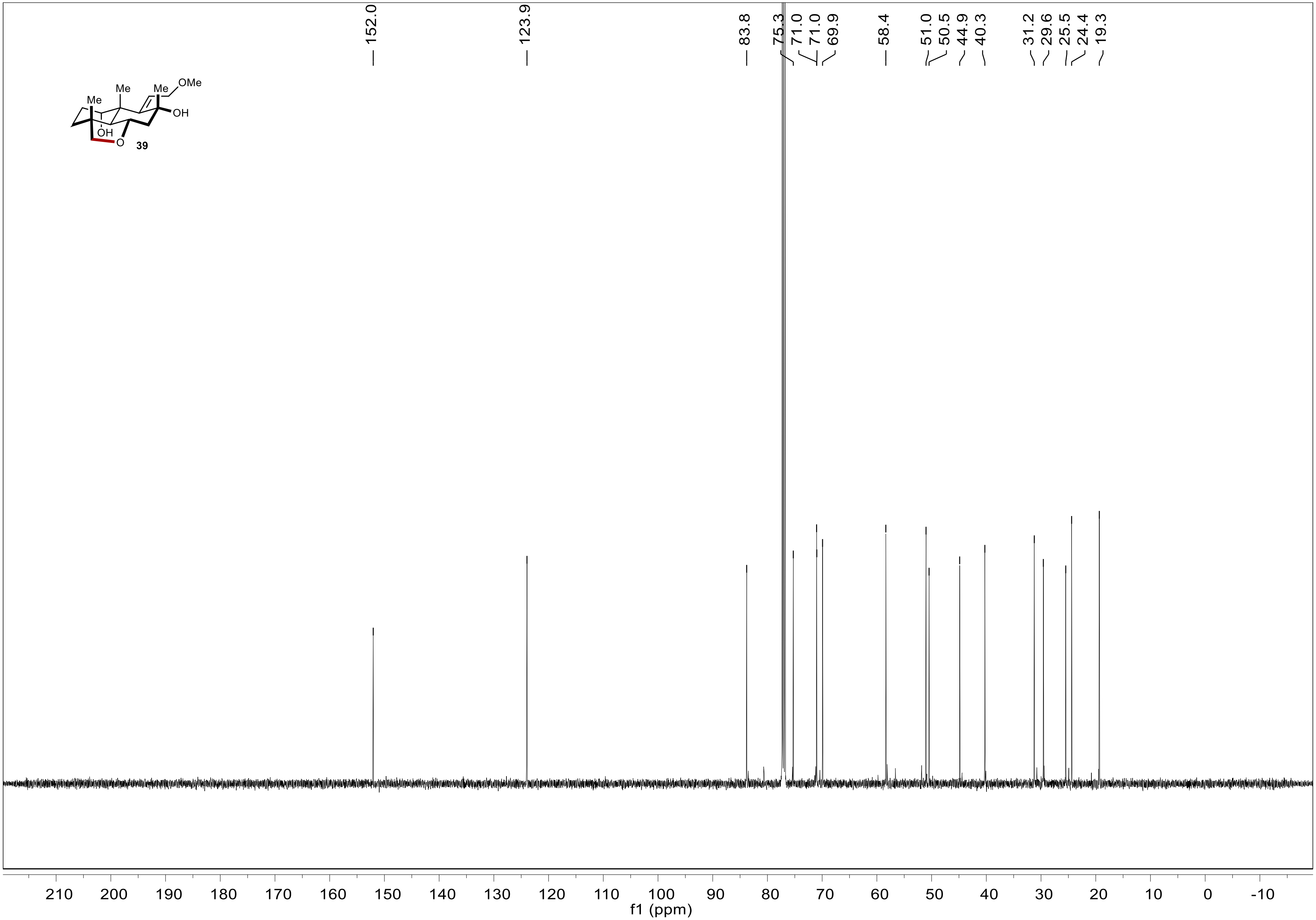
^{13}C NMR Spectrum of compound 38 (126 MHz, Methanol-d_4)



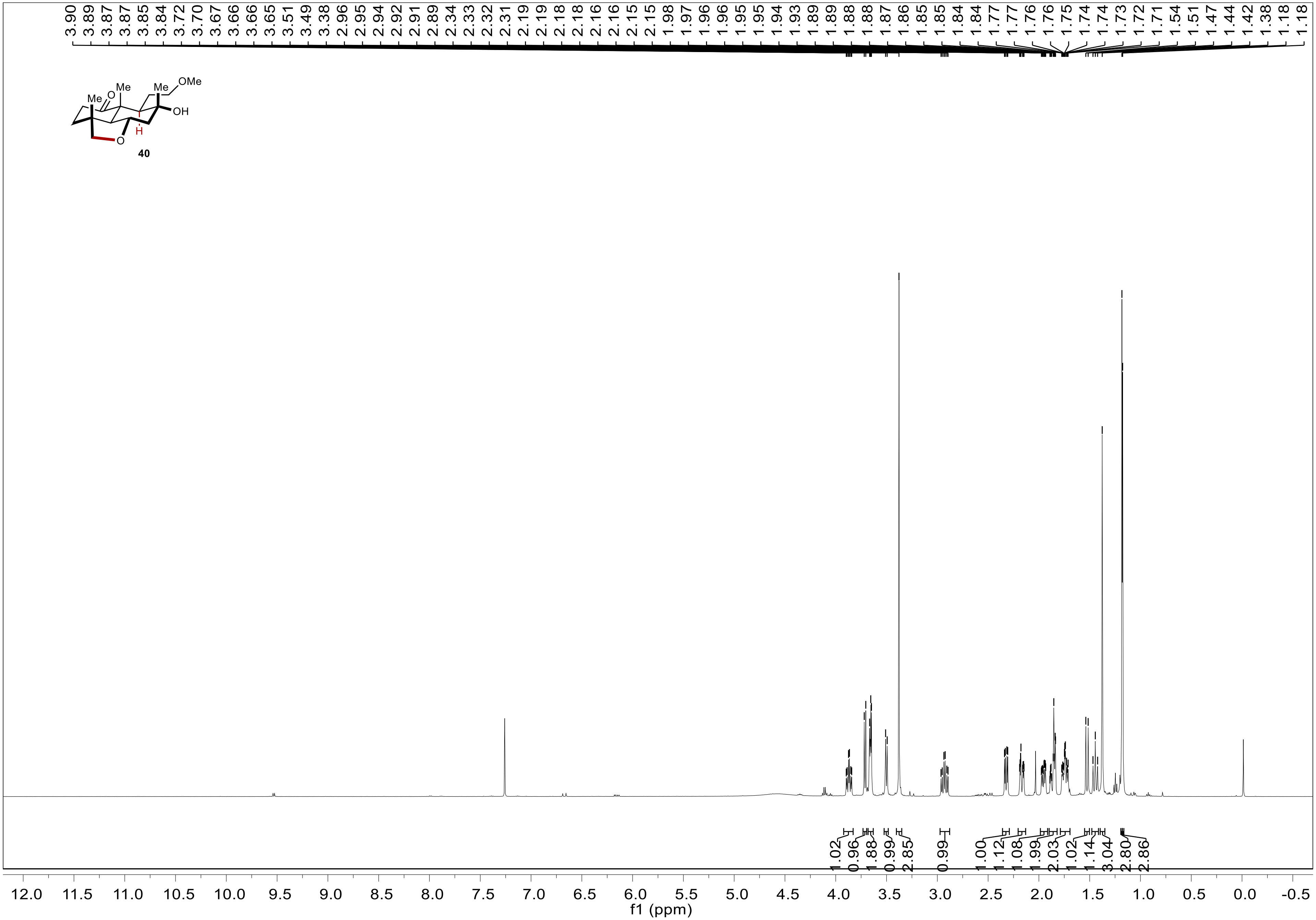
^{1}H NMR Spectrum of compound 39 (500 MHz, $CDCl_3$)



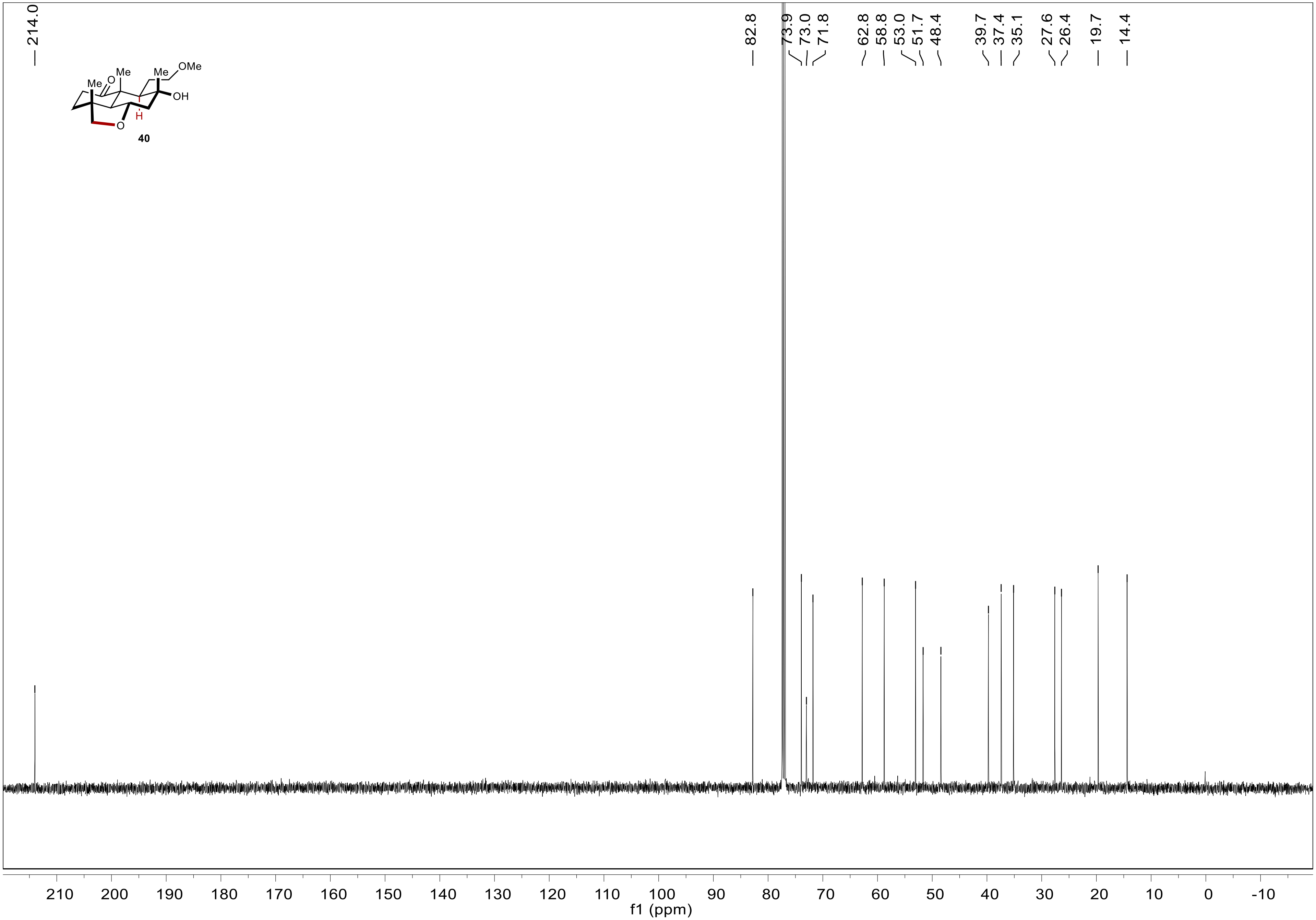
^{13}C NMR Spectrum of compound 39 (126 MHz, CDCl$_3$)



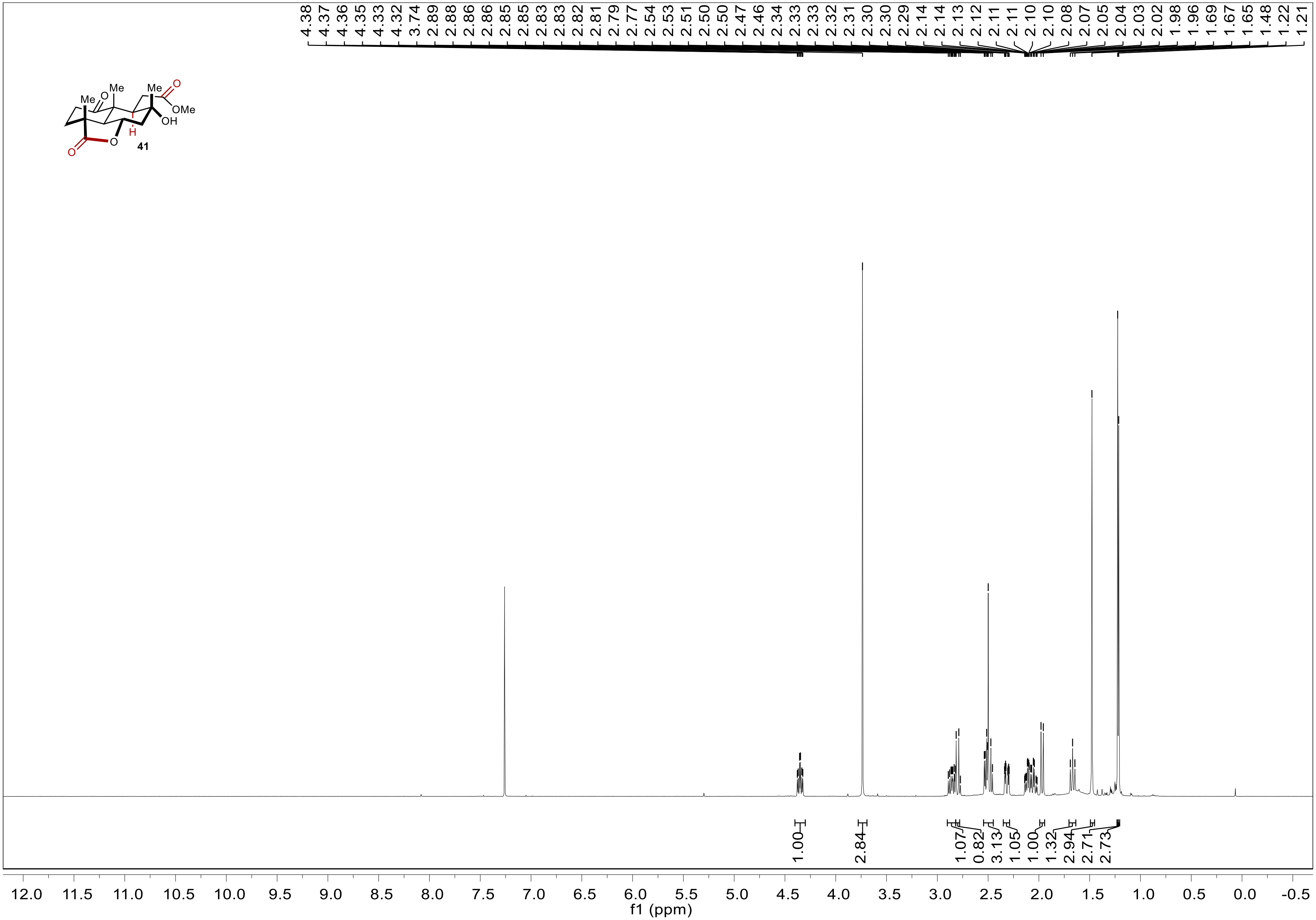
^{1}H NMR Spectrum of compound 40 (500 MHz, CDCl$_3$)



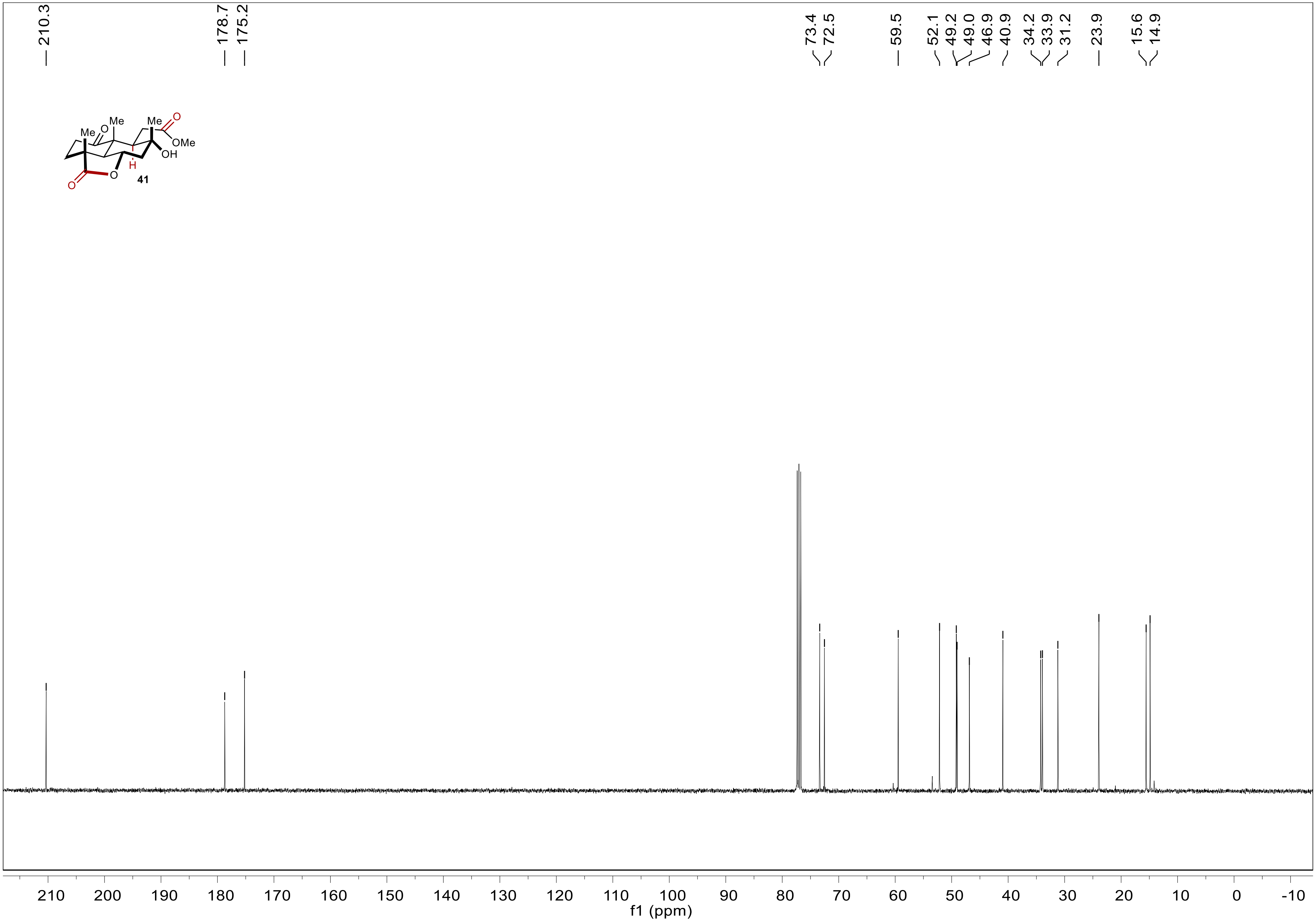
^{13}C NMR Spectrum of compound 40 (126 MHz, CDCl$_3$)



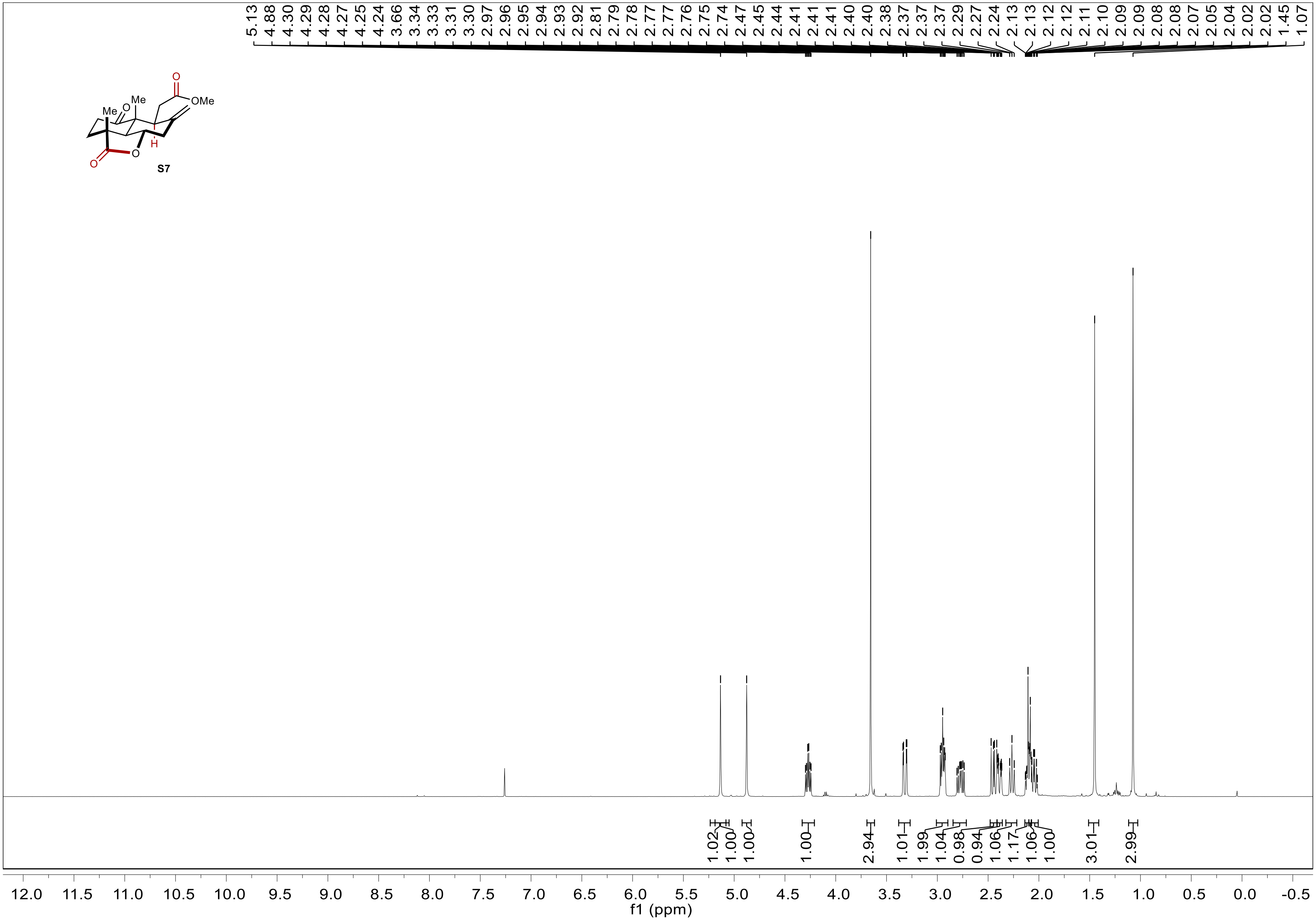
^{1}H NMR Spectrum of compound 41 (500 MHz, CDCl$_3$)



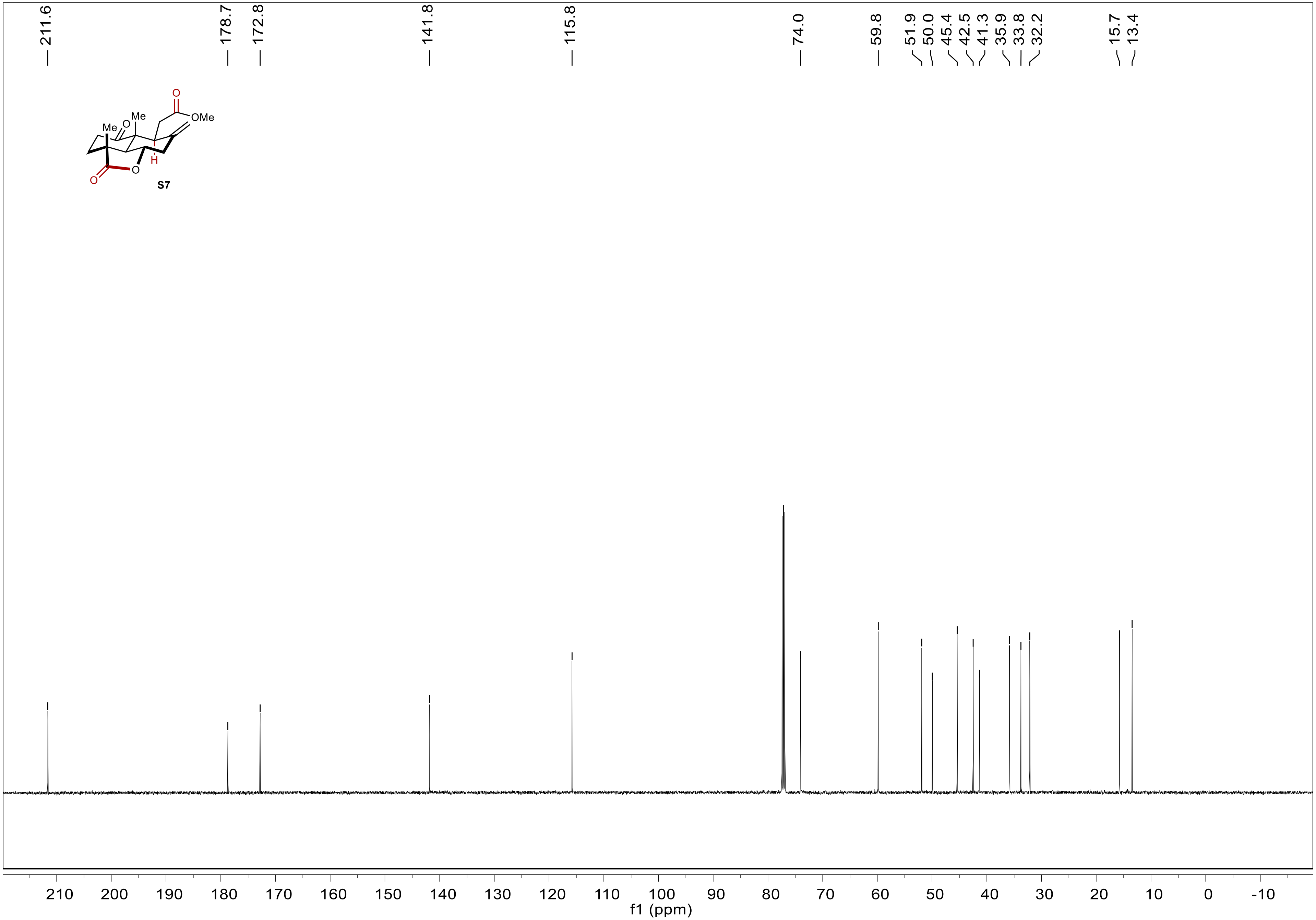
^{13}C NMR Spectrum of compound 41 (126 MHz, $CDCl_3$)



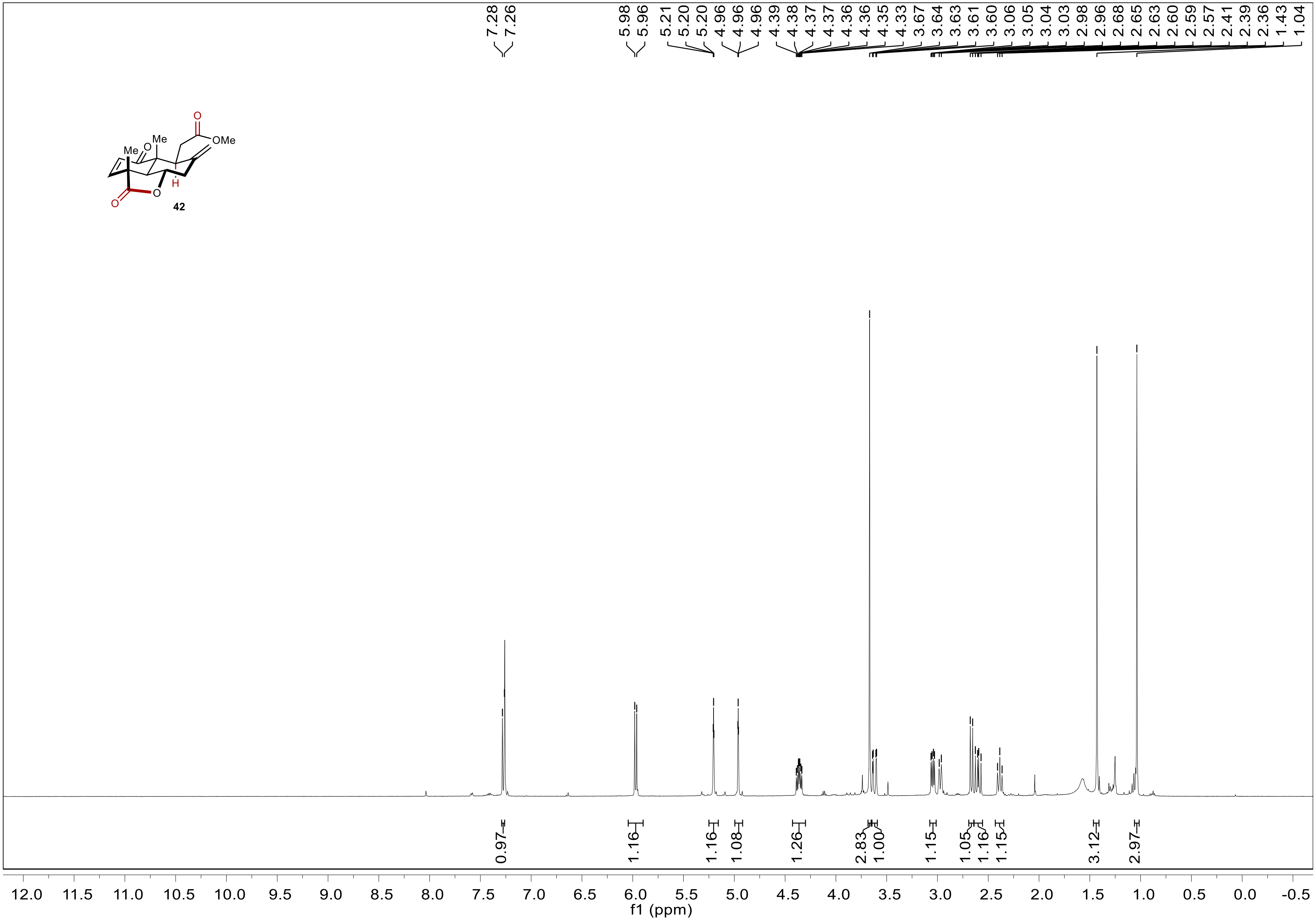
^{1}H NMR Spectrum of compound S7 (500 MHz, $CDCl_3$)



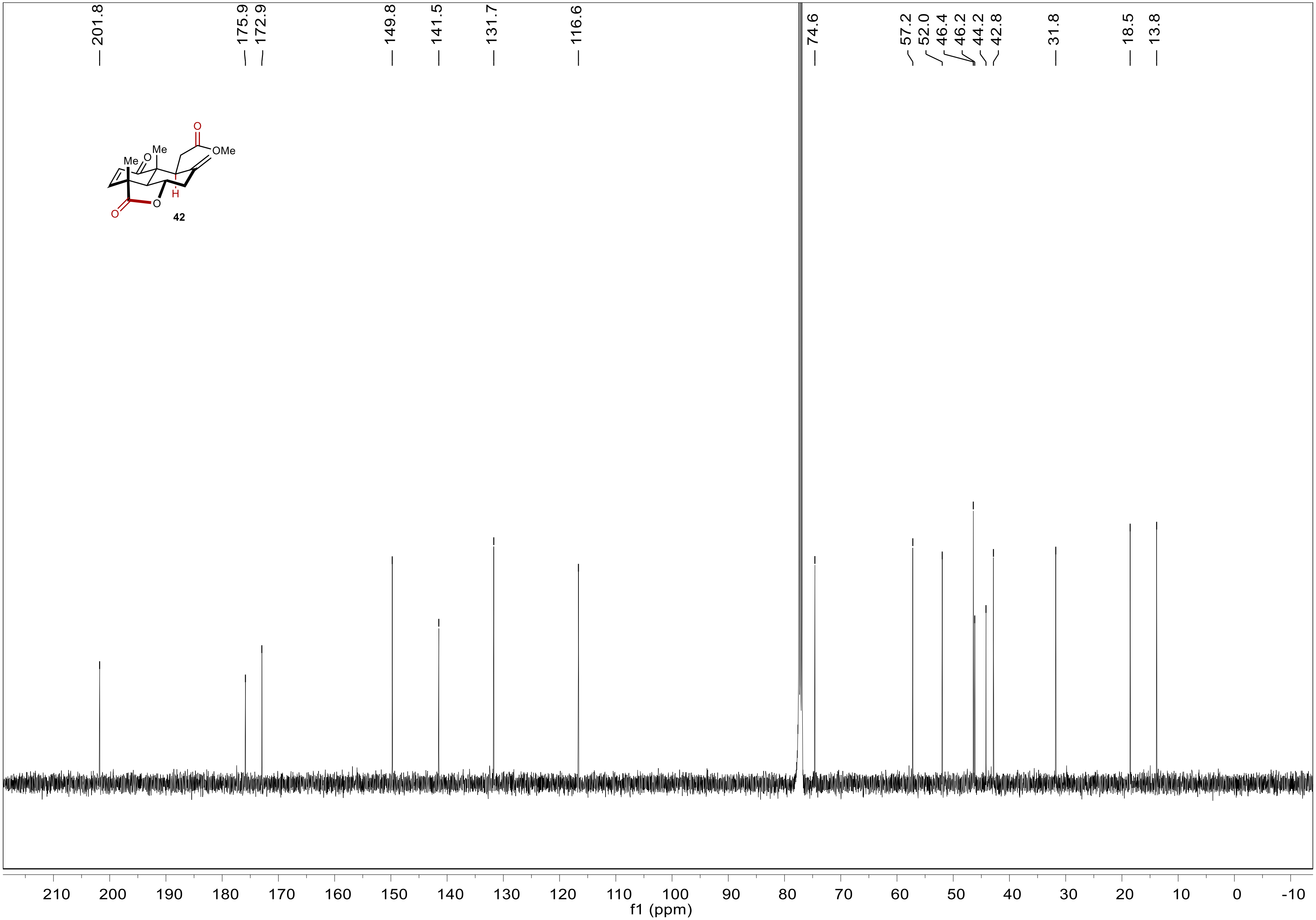
^{13}C NMR Spectrum of compound S7 (126 MHz, $CDCl_3$)



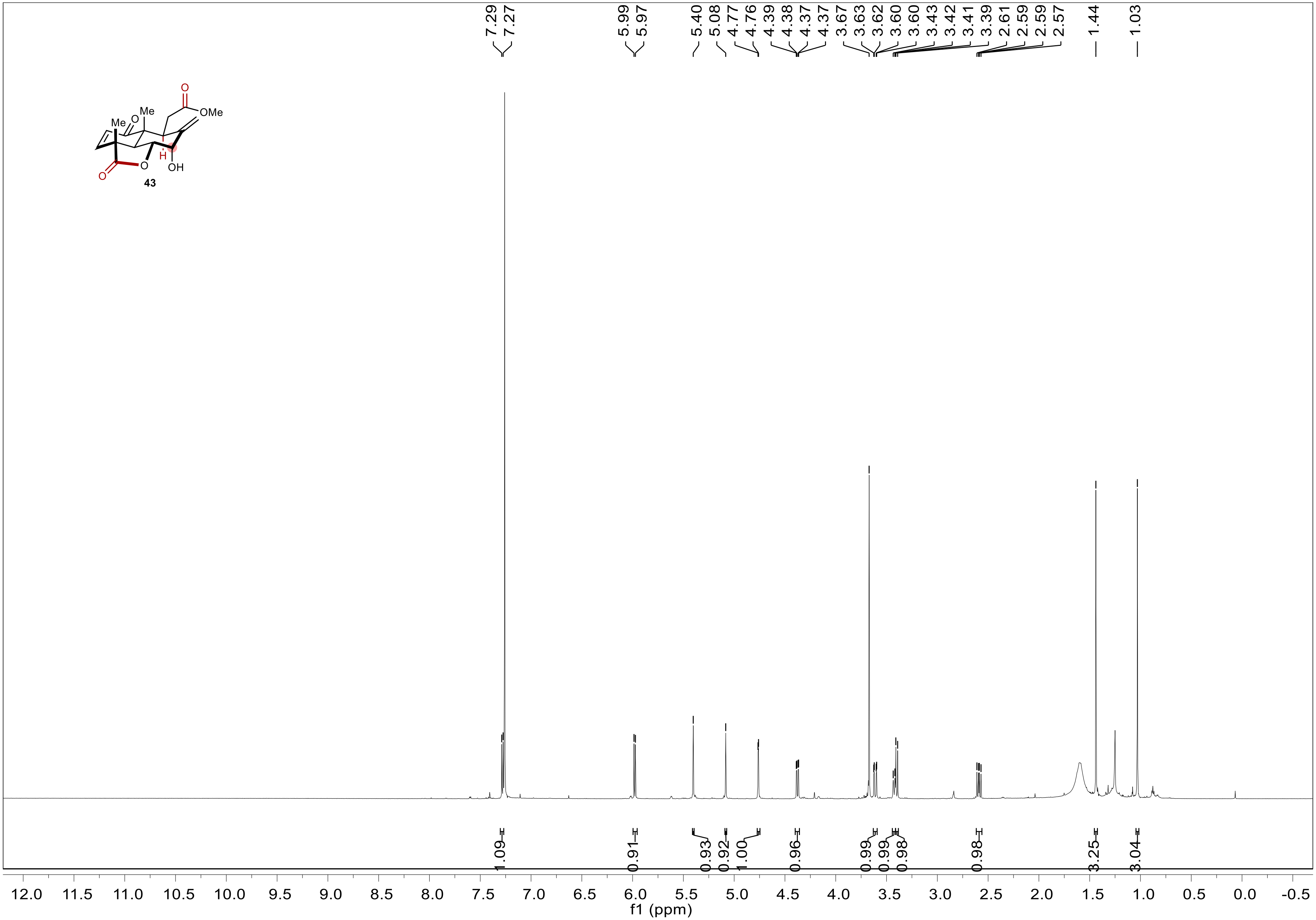
^{1}H NMR Spectrum of compound 42 (500 MHz, $CDCl_3$)



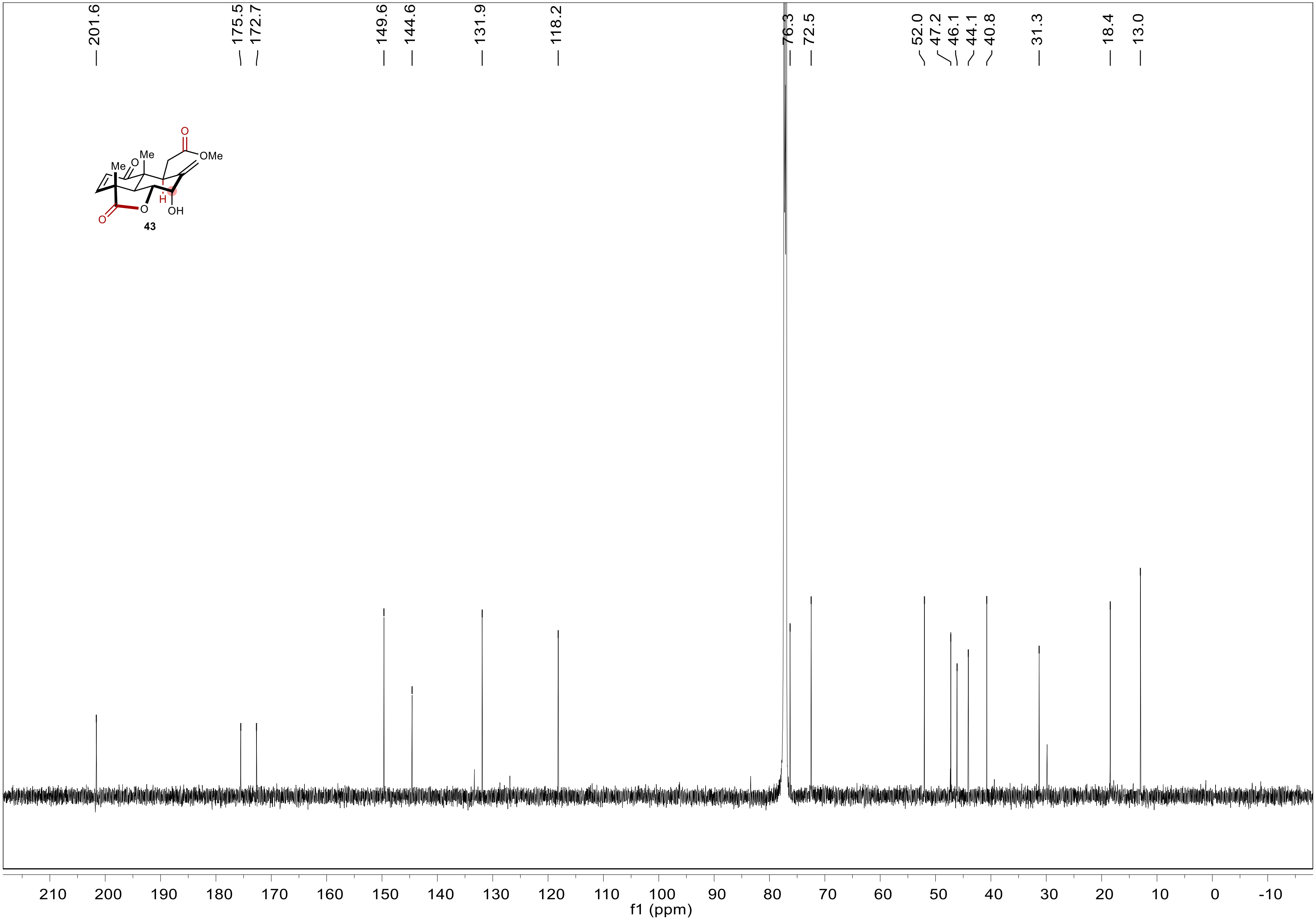
^{13}C NMR Spectrum of compound 42 (126 MHz, $CDCl_3$)



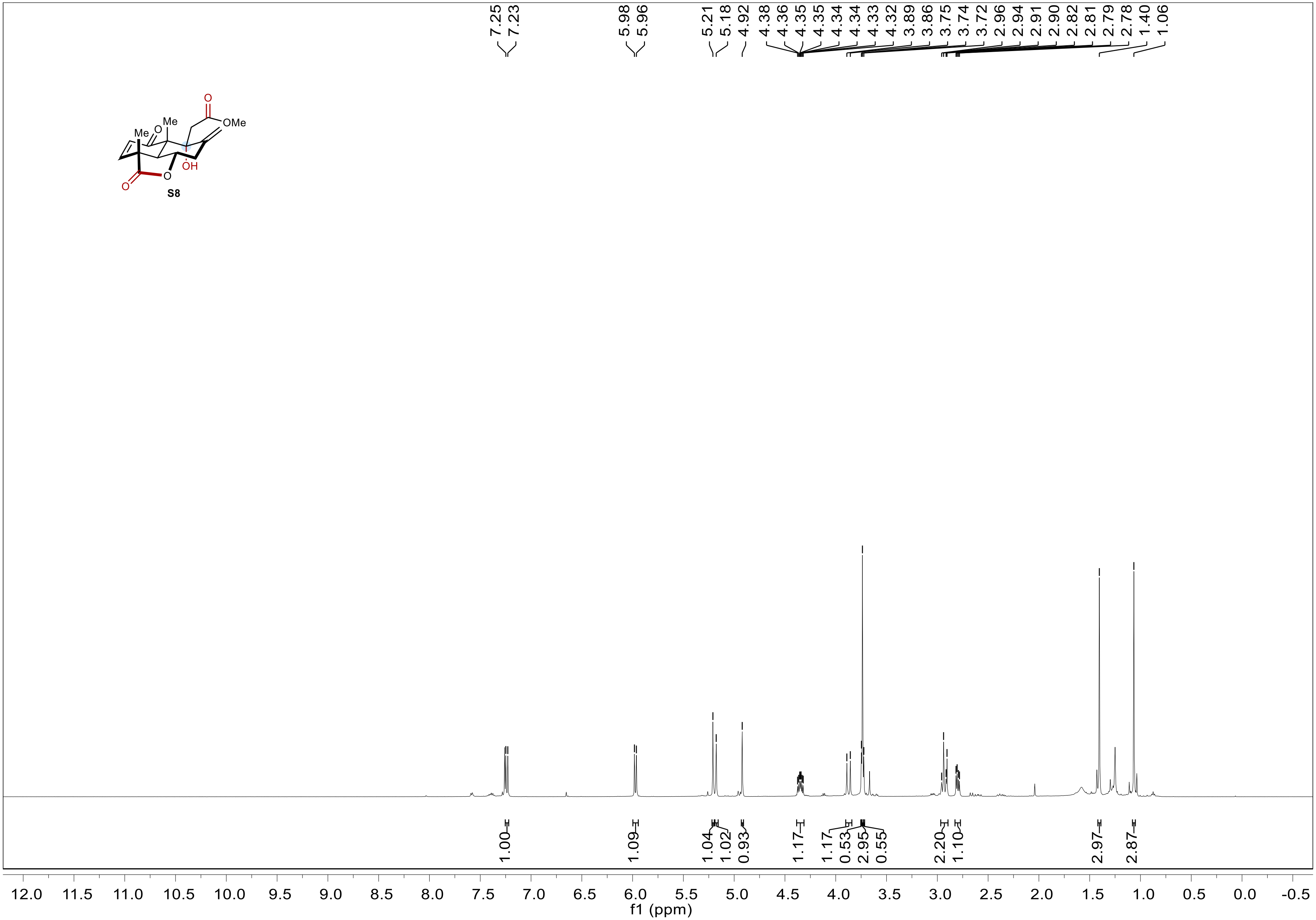
^{1}H NMR Spectrum of compound 43 (600 MHz, CDCl$_3$)



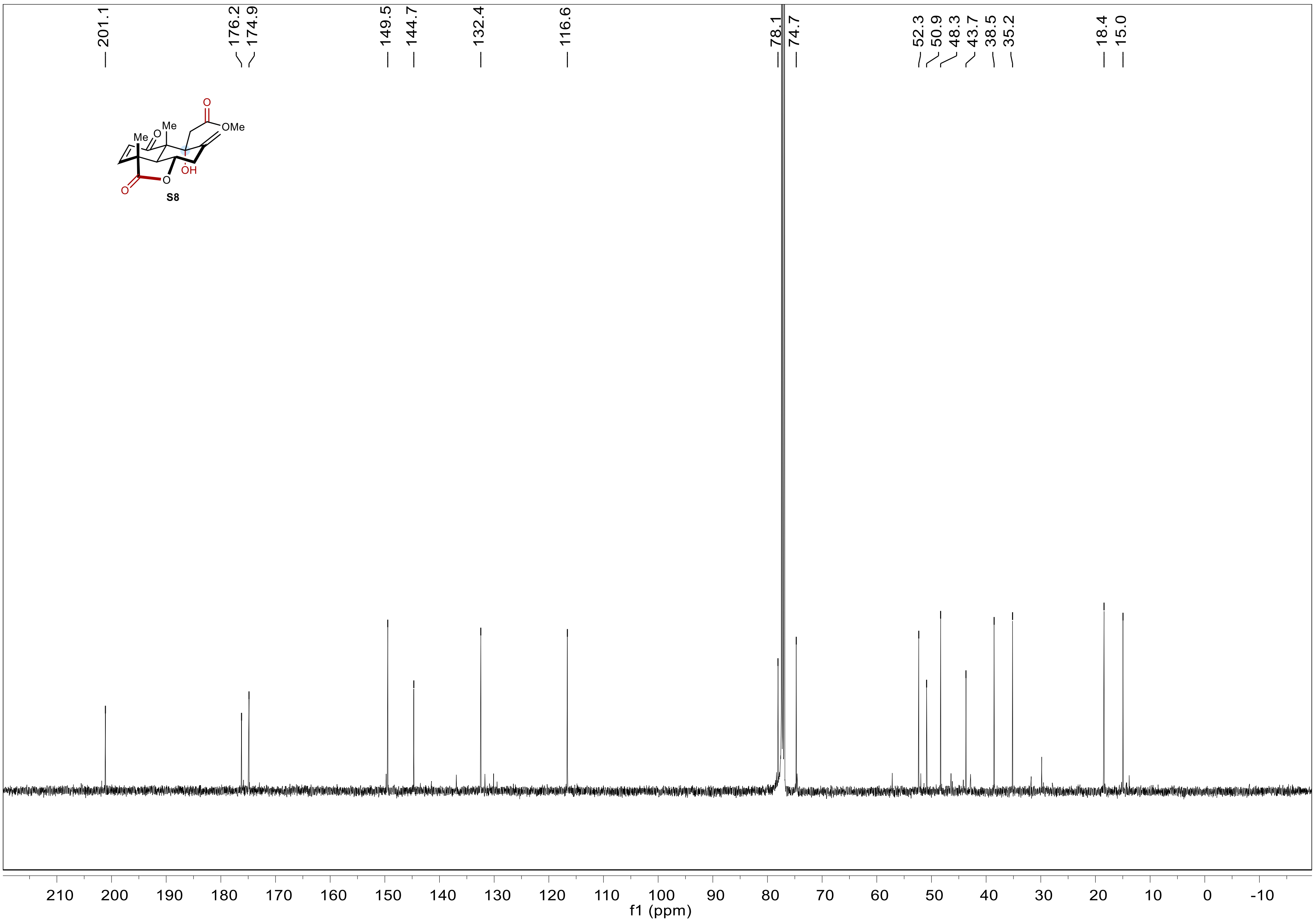
^{13}C NMR Spectrum of compound 43 (151 MHz, $CDCl_3$)



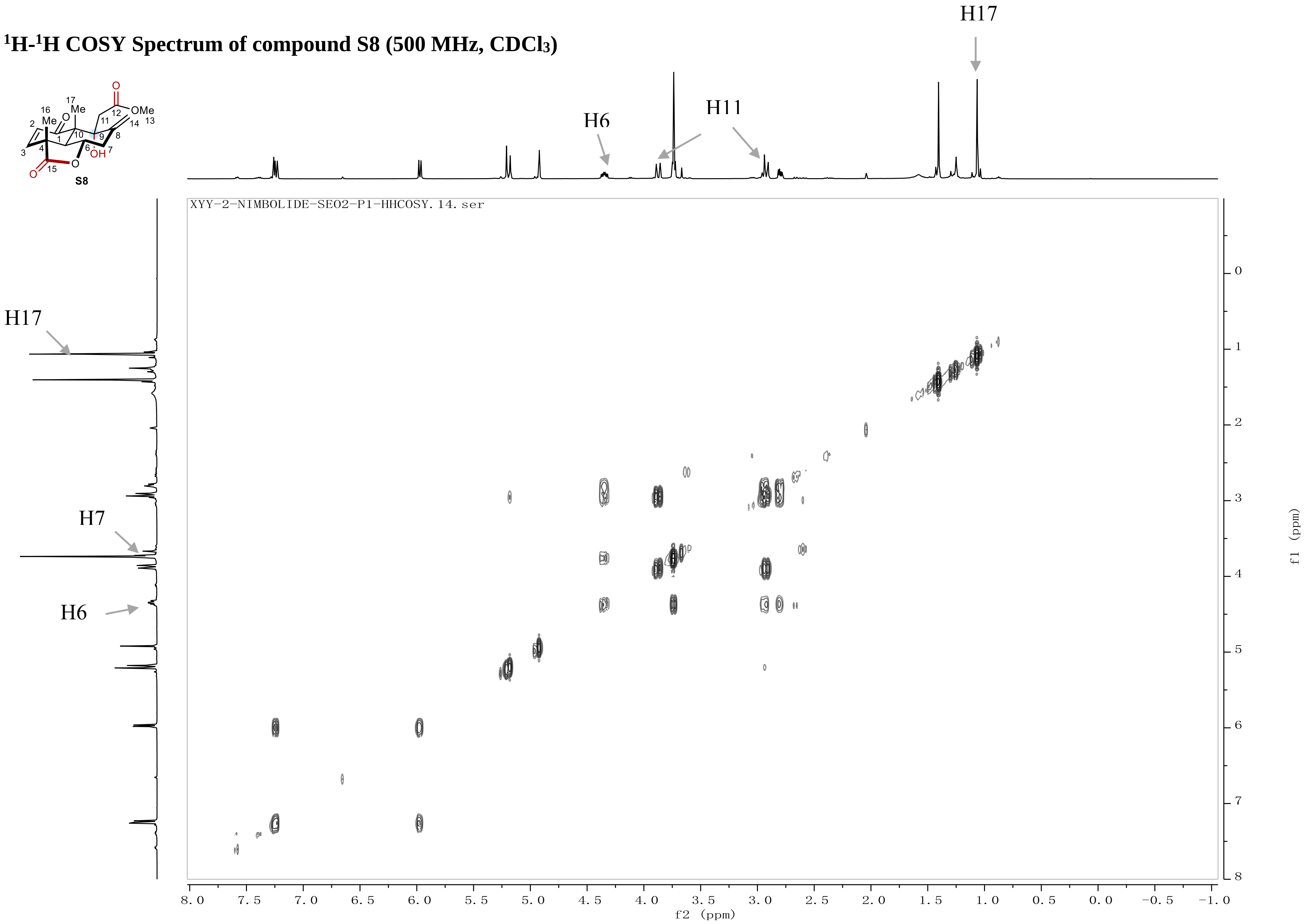
^{1}H NMR Spectrum of compound S8 (500 MHz, $CDCl_3$)



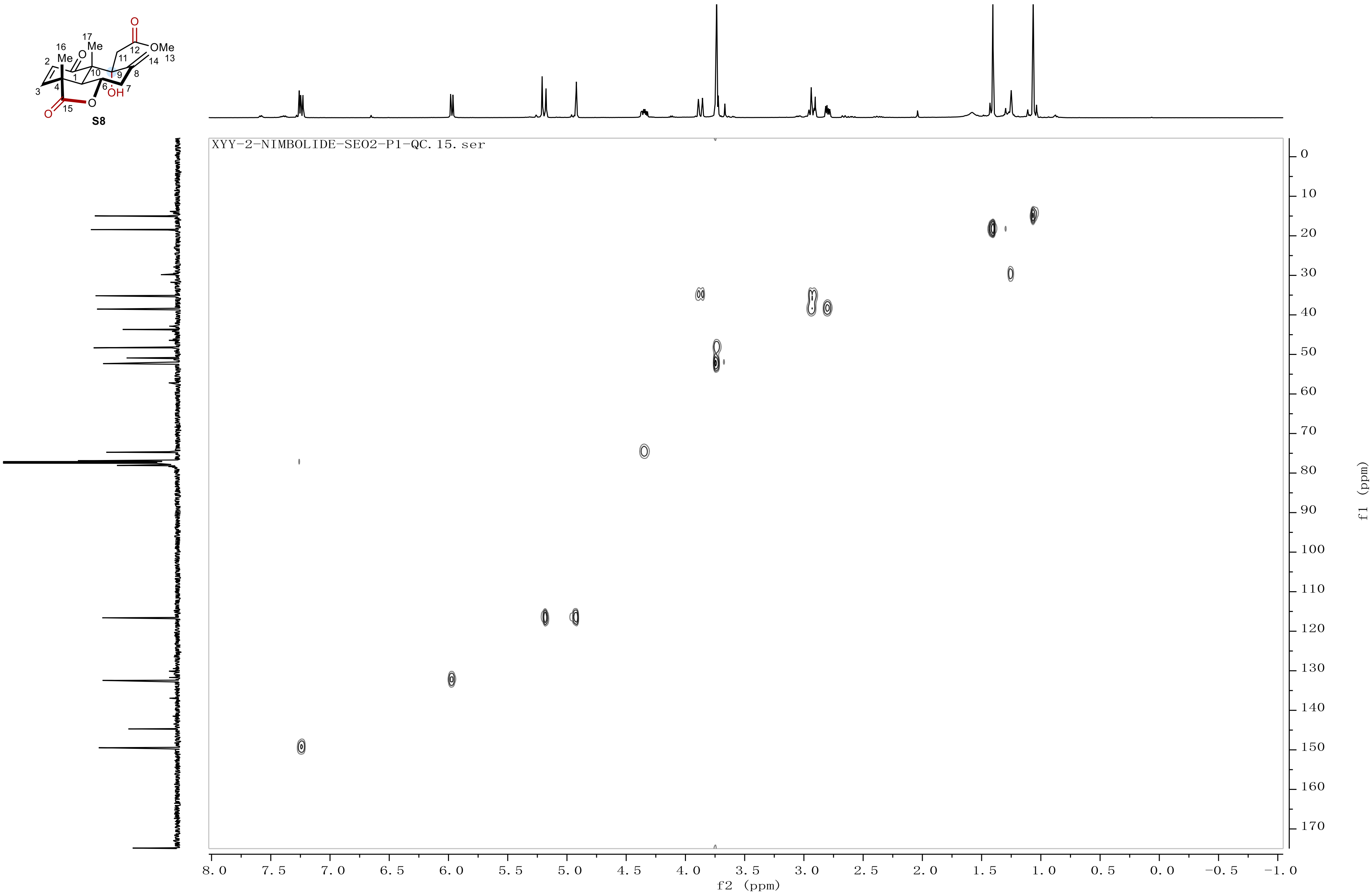
^{13}C NMR Spectrum of compound S8 (126 MHz, $CDCl_3$)



^1H-^1H COSY Spectrum of compound S8 (500 MHz, $CDCl_3$)

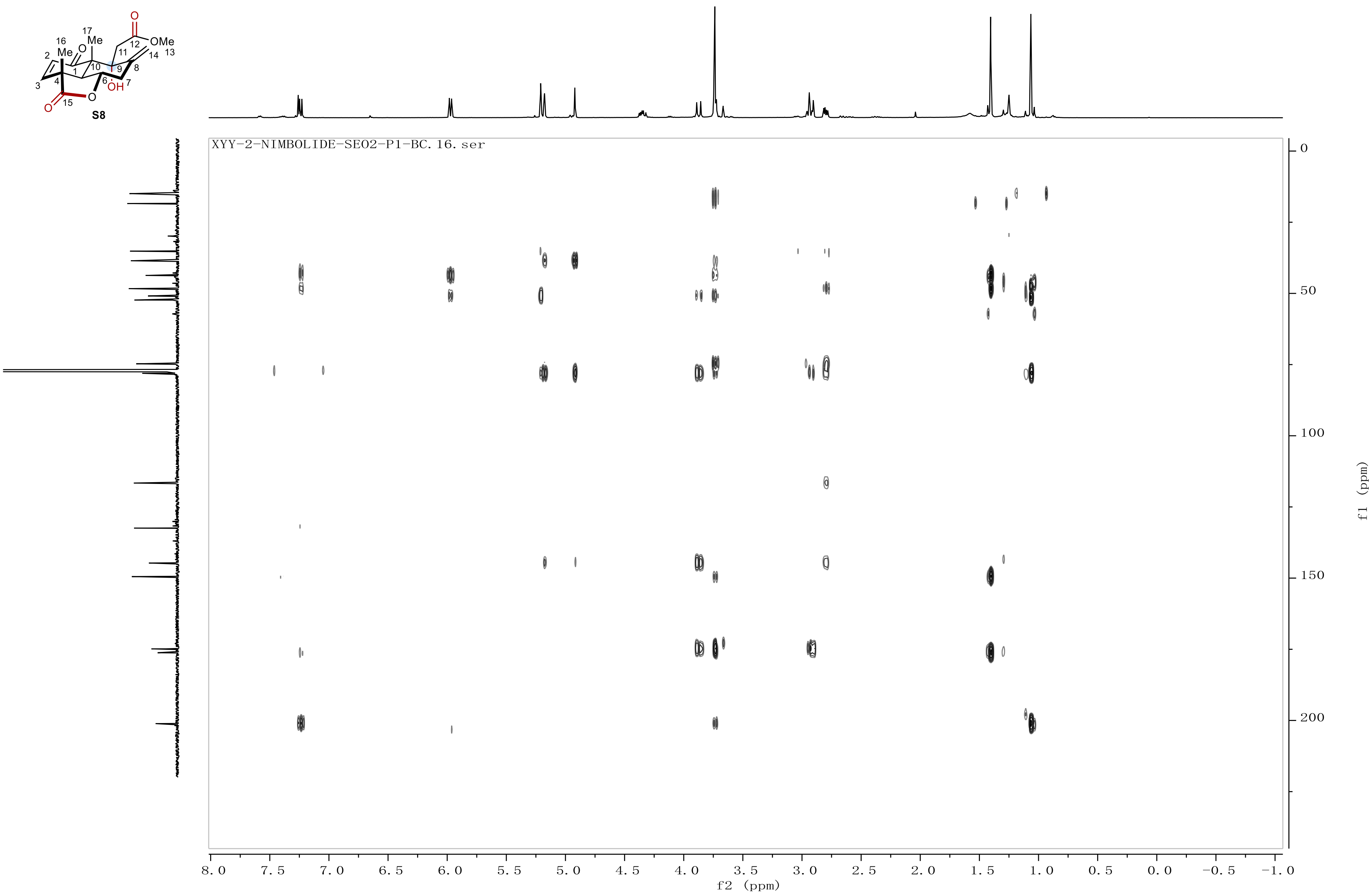


HSQC Spectrum of compound S8 (500 MHz, $CDCl_3$)



S8

HMBC Spectrum of compound S8 (500 MHz, $CDCl_3$)



NOESY Spectrum of compound S8 (500 MHz, CDCl$_3$)