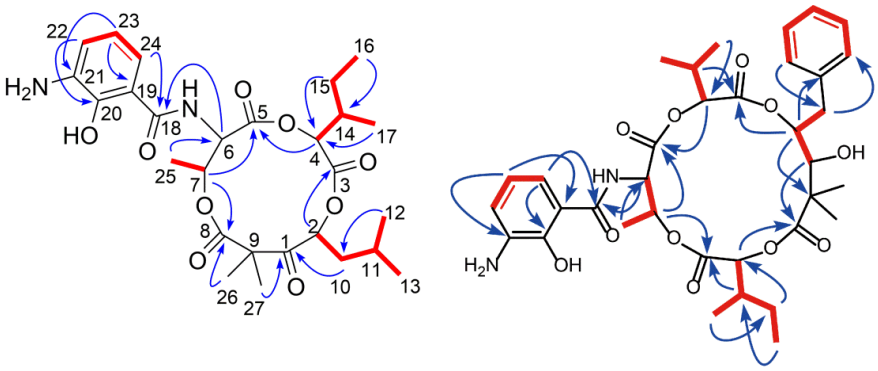
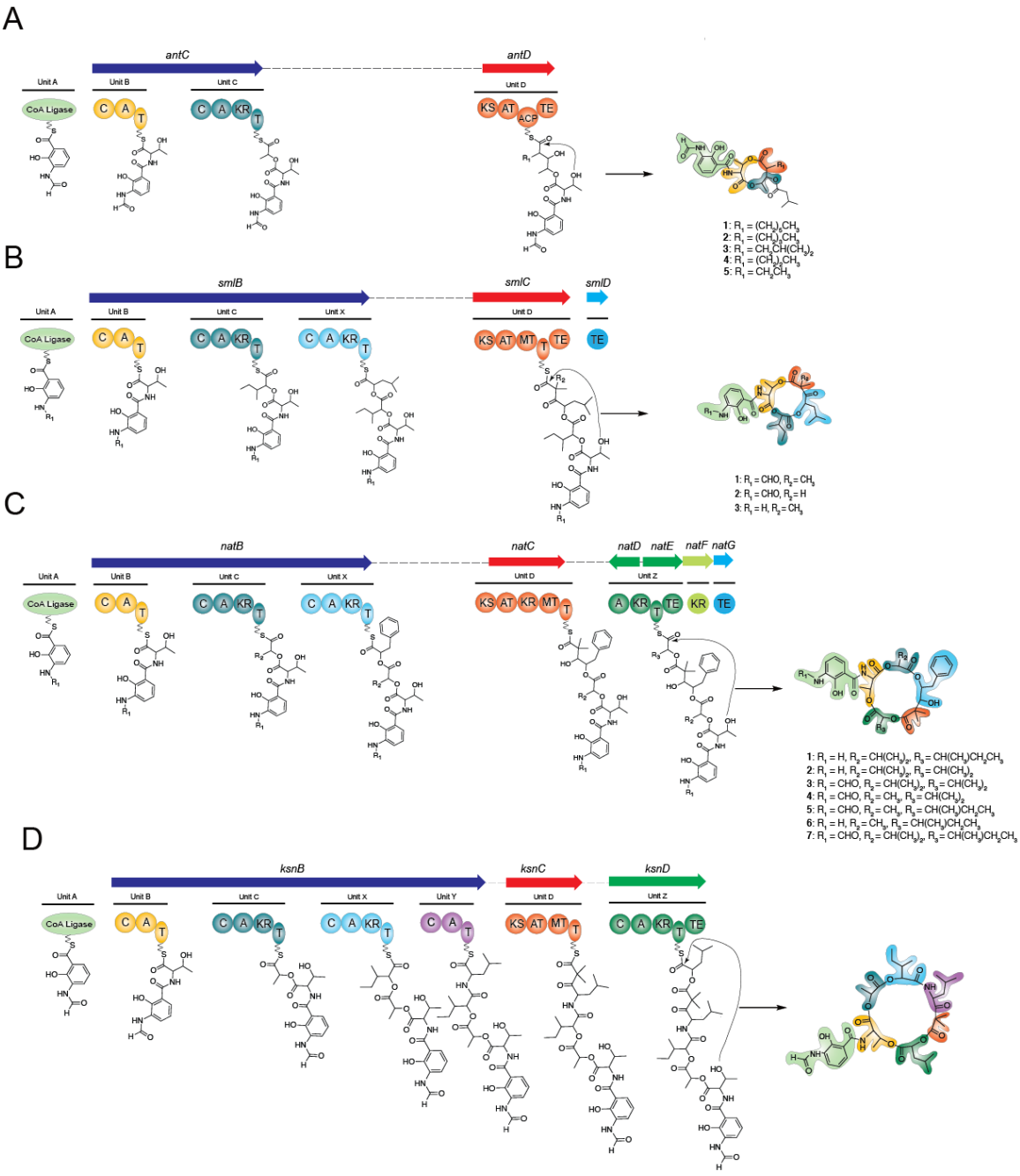
Supplemental Table 1 Primers used in this study.

Primer Names	Forward	Reverse
ADM21-GAP-1	5'-GCGCGGTCGGTCAGATCGT-3'	5'-GAATTCCCCTACAGCGCG-3'
ADM21-GAP-2	5'-TCTCCATGGCCGACTTCTT-3'	5'-CCGTCCAGCTGGTTGAGG-3'
ADM21-GAP-3	5'-GCAGCTCAACGCGCACTTC-3'	5'-GCTCCCCGGCCGCGAGCA-3'
ML55- GAP-1	5'-CAACGCCCATGTGATCCT-3'	5'-AGGACATCGGGGAGTTCTG-3'
ML55-GAP-2	5'-CCTCGGACAGCACGAGAC-3'	5'-TGCTTCTTGAGGATCTTCCC-3'
ORINO-GAP-1	5'-GCTATGGCTACACCCTGGTC-3'	5'-GCCTATCTGTACCGGGTCAC-3'
ORINO -GAP-2	5'-GTGGGGCCCGCTGCTGT-3'	5'-TGACCCGCTCCTCGCGC-3'
ORINO -GAP-3	5'-CGGTGTGCCCGCGCCCGGGG-3'	5'-TCATCACATGGTGCGCGCCC-3'
ORINO -GAP-4	5'-CTCGGCGACGGTTCGCTGG-3'	5'-TCCTCATGCGCCGCCACC-3'

Supplemental Figure 1 Representitive ^{1}H-^{1}H COSY and ^{1}H-^{13}C HMBC correlations of isolated compounds.

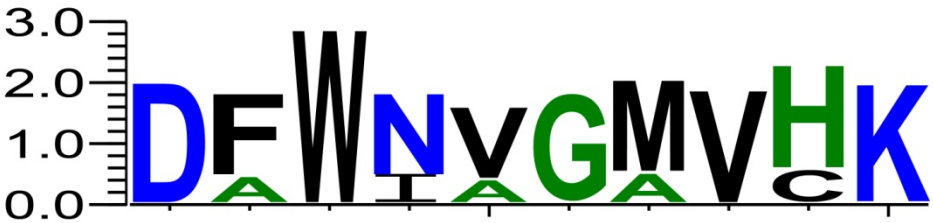


Supplemental Figure 2 Representation of the PKS-NRPS biosynthetic pathway for the 9-, 12-, 15-, and 18-membered antimycin-type depsipeptide subclasses, highlighting the flexibility of the biosynthetic units, X, Y, and Z.

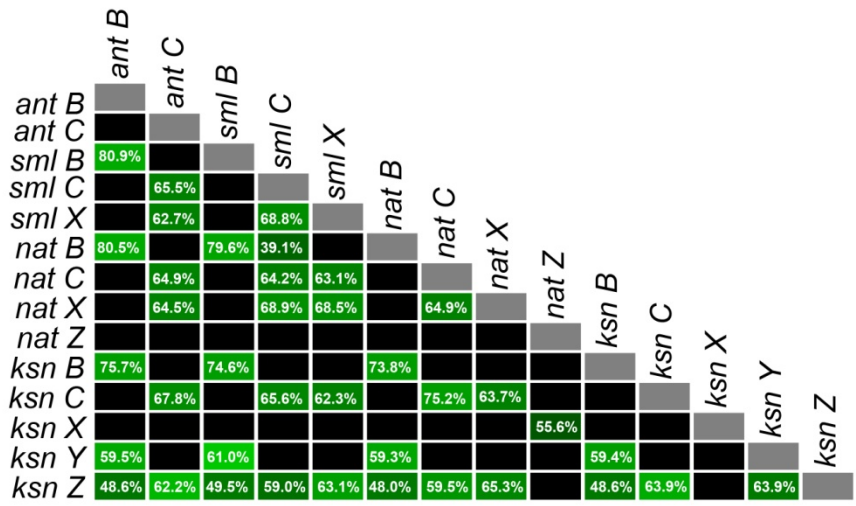


Supplemental Figure 3 (A) Predicted adenylation domains loading amino acid codes. **(B)** Heatmap of the Geneious nucleotide alignment of the adenylation domains of the antimycin (*ant*), JBIR-06 (*sml*), neoantimycin (*nat*) and respirantin (*ksn*) NRPS clusters, demonstrating the genetic similarity in colour and percentage.

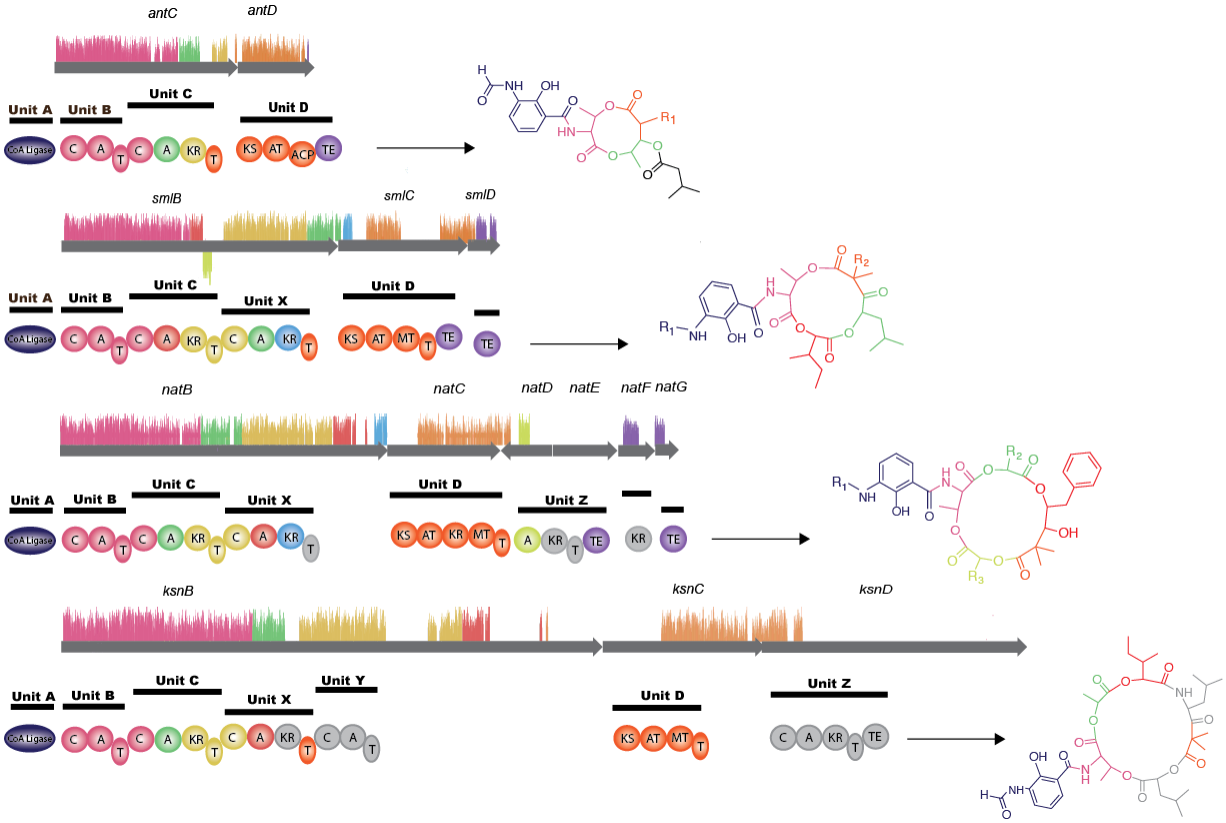
A



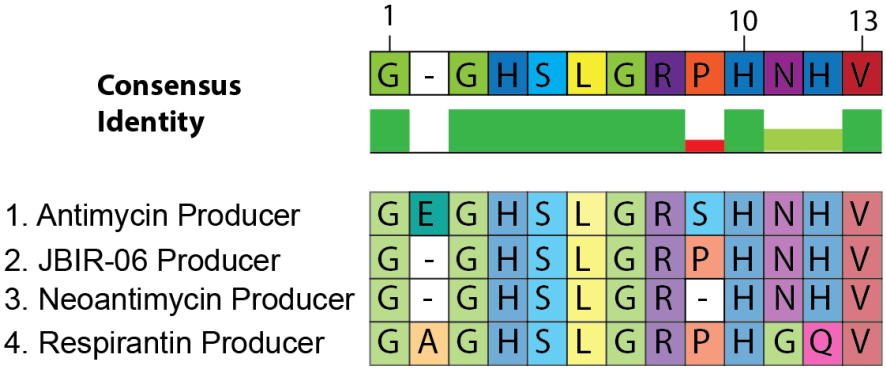
B



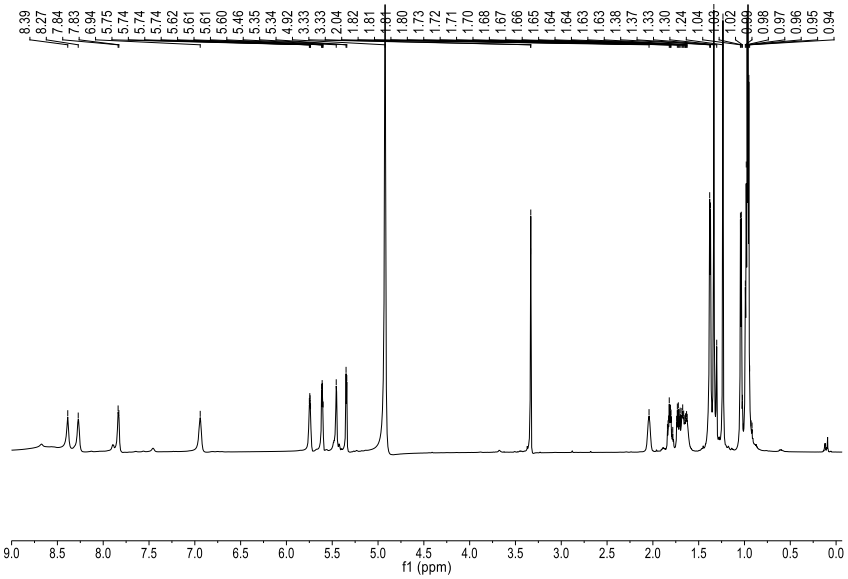
Supplemental Figure 4 Mauve analysis of the nucleotide sequences encoding the antimycin-type PKS-NRPS enzymology from *Streptomyces* sp. ADM21 (*ant*), *Streptomyces* sp. ML55 (*sml*), *Streptoverticillium orinoci* (*nat)* and Alaskan *Kitasataspora* sp. (*ksn)*. Nucleotide sequences were pairwise aligned using the program Geneious. Colour indicates genetic similarity, and the height and frequency of the coloured lines depicts the degree of similarity.



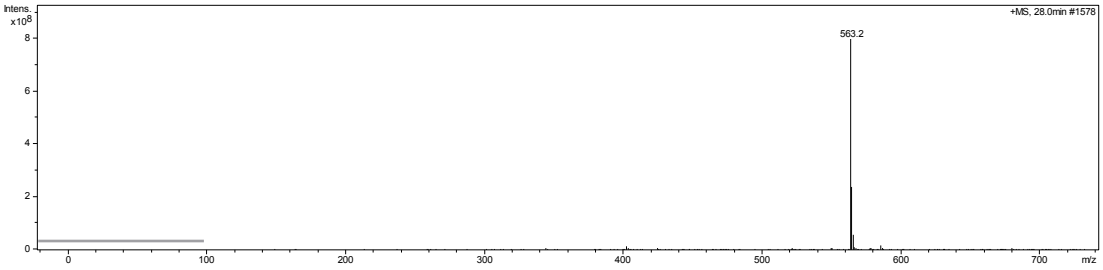
Supplemental Figure 5 Predicted conserved amino acid sequence of acyltransferases.



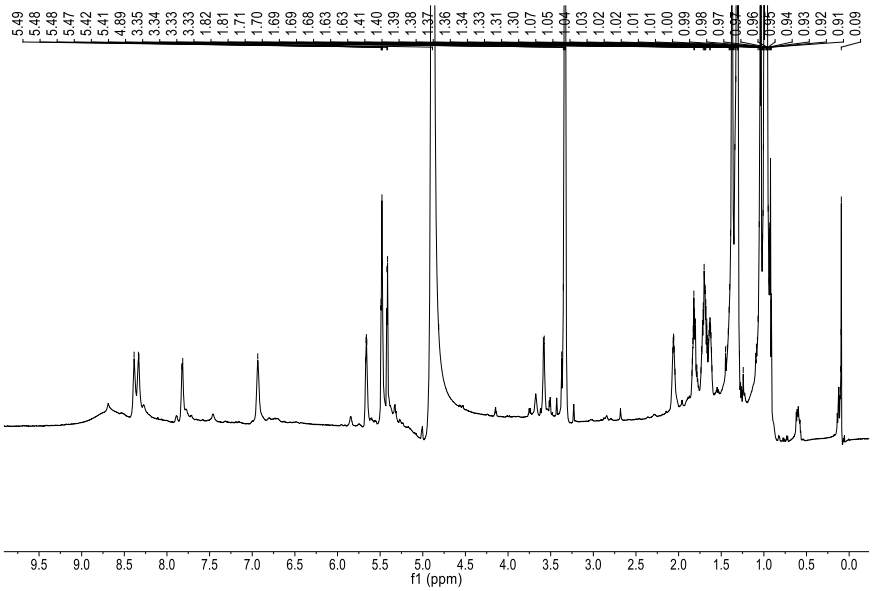
Supplemental Figure 6 ^{1}H NMR spectrum of JBIR-06.



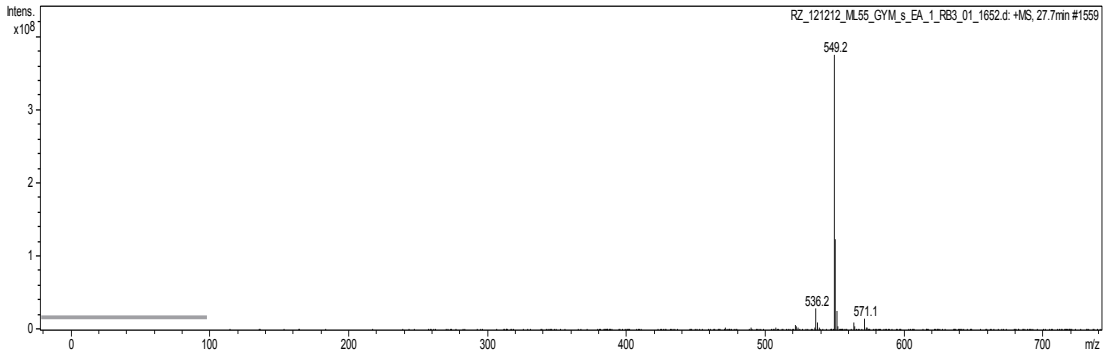
Supplemental Figure 7 MS spectrum of JBIR-06.



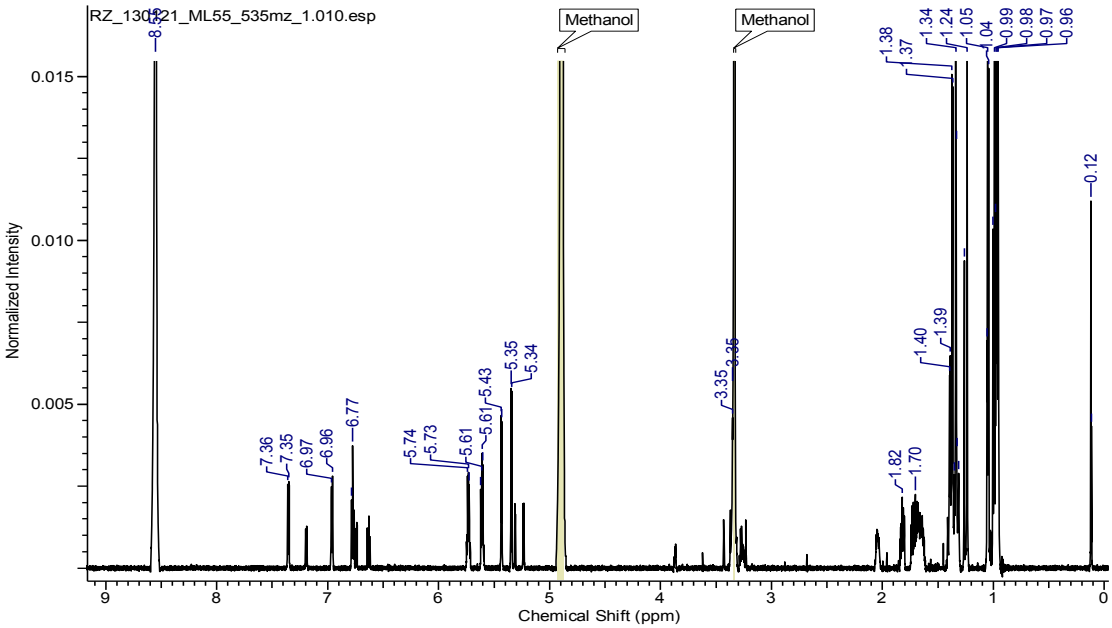
Supplemental Figure 8 ^{1}H NMR spectrum of JBIR-52.



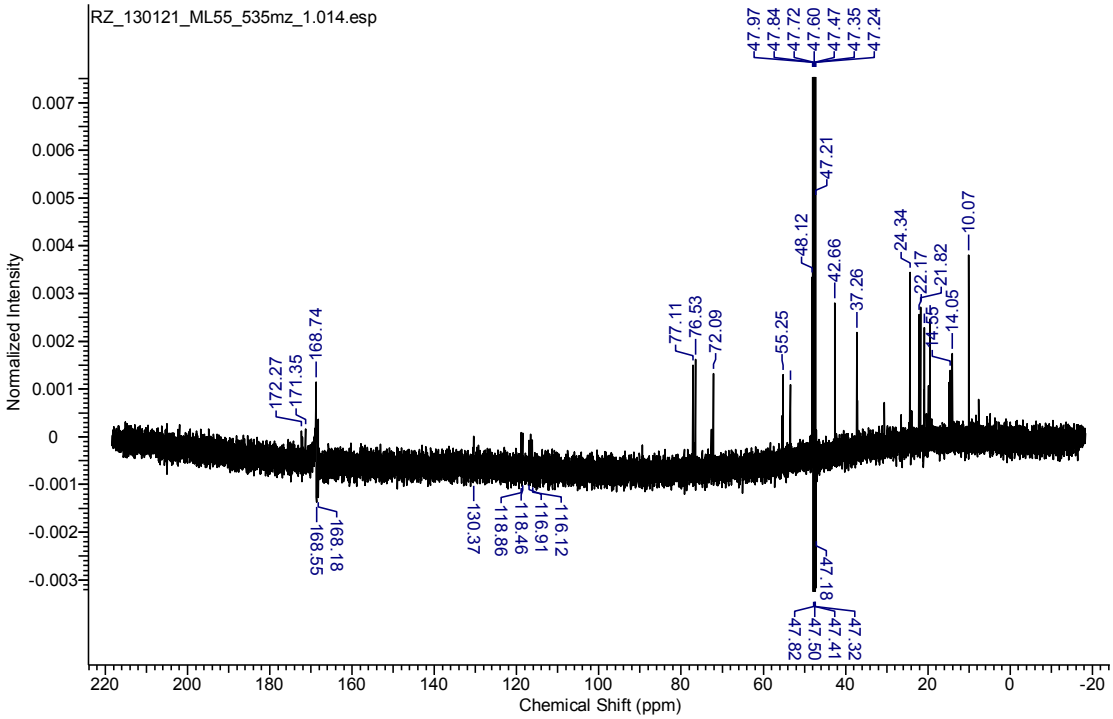
Supplemental Figure 9 MS spectrum of JBIR-52.



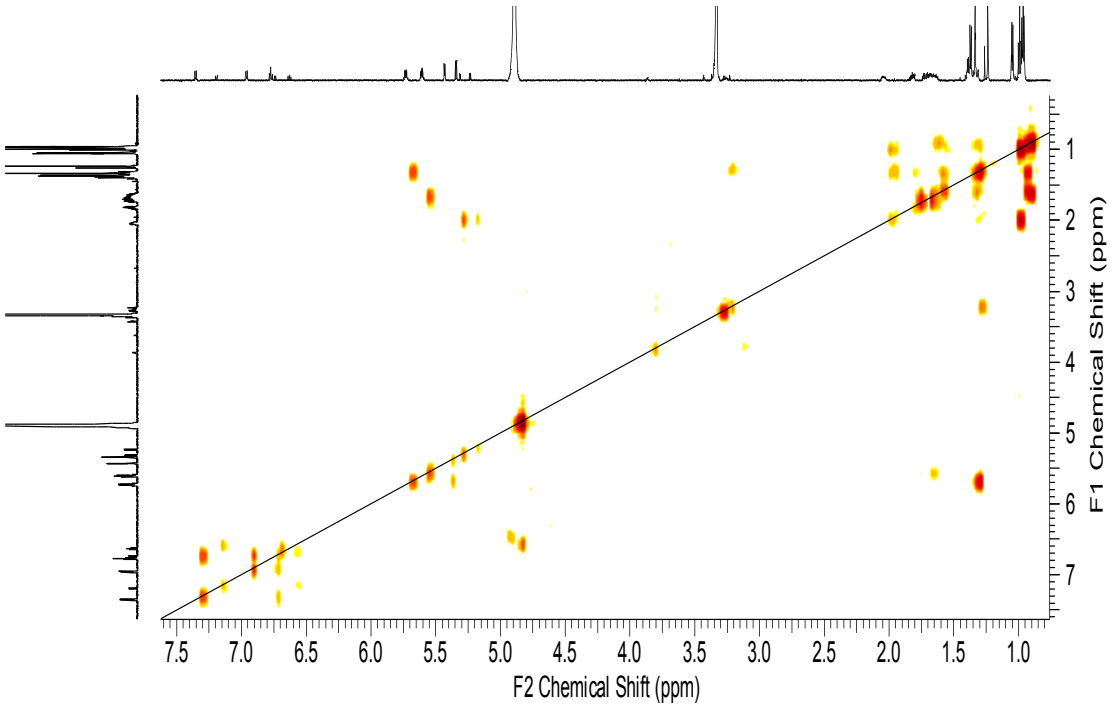
Supplementary Figure 10 ^{1}H NMR spectrum of compound JBIR-06-1.



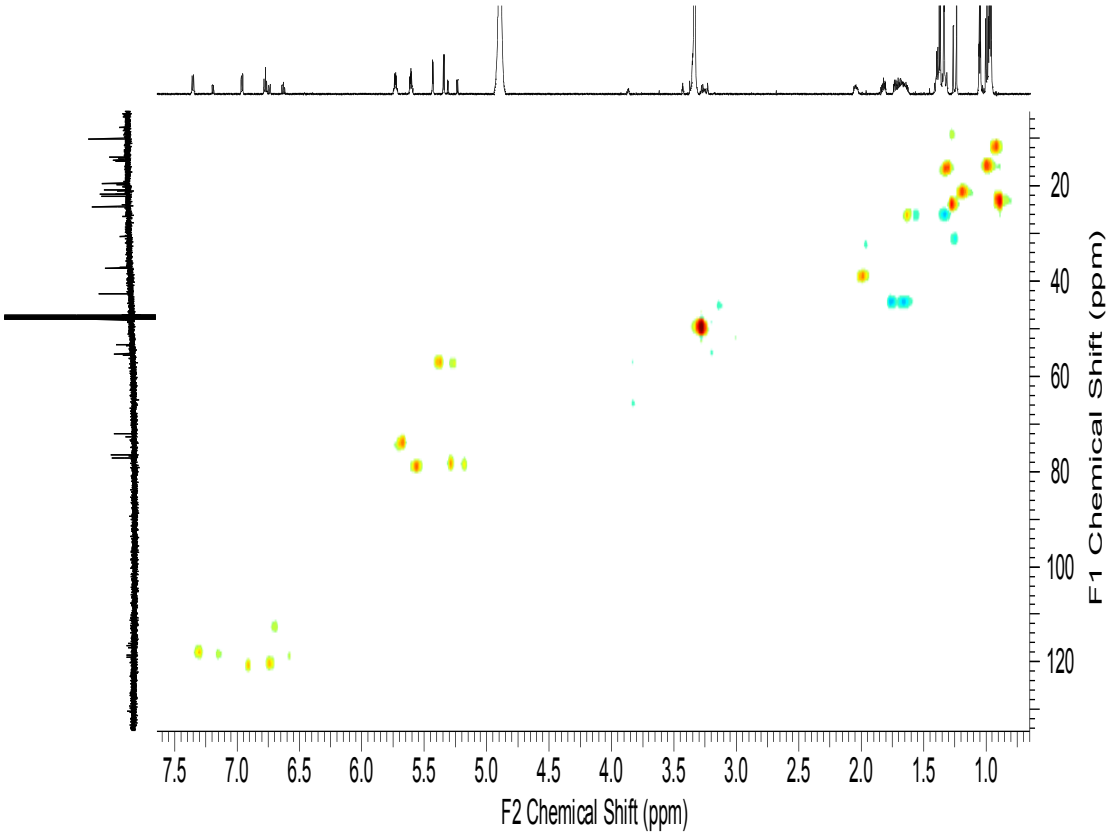
Supplementary Figure 11 ^{13}C NMR spectrum of compound JBIR-06-1.



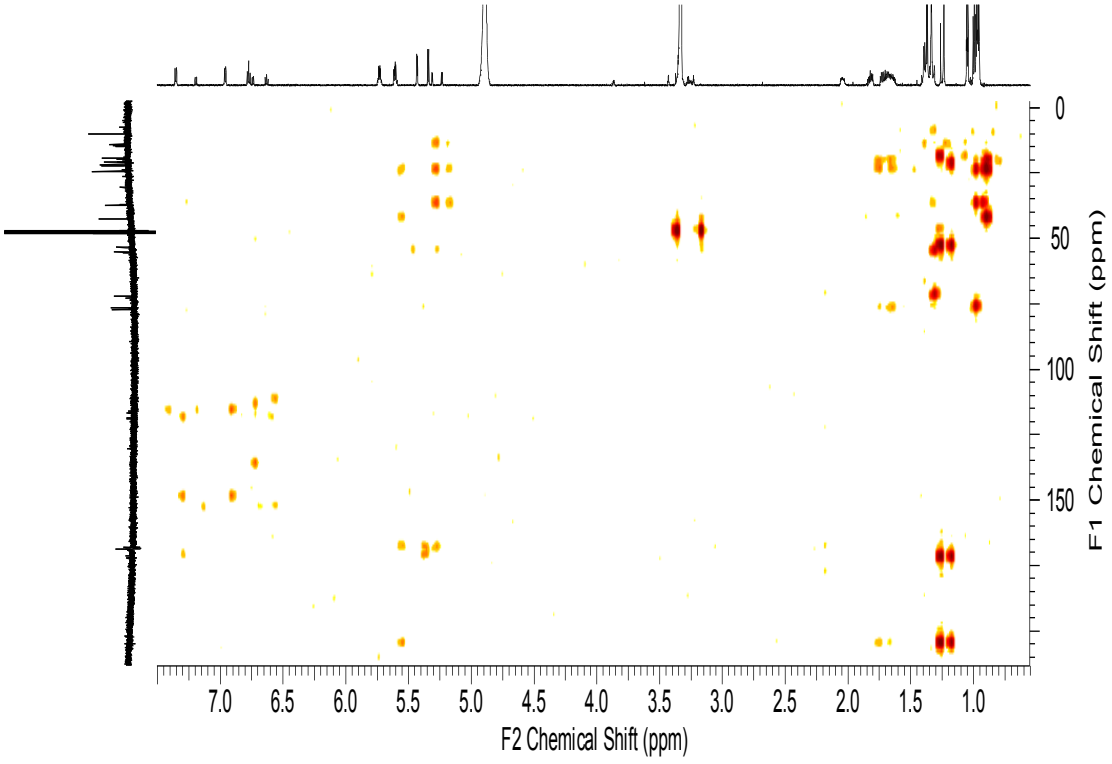
Supplementary Figure 12 ^{1}H-^{1}H COSY spectrum of compound JBIR-06-1.



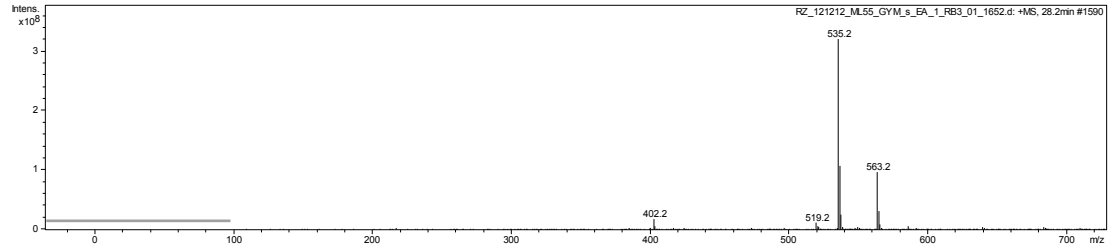
Supplementary Figure 13 HMQC spectrum of compound JBIR-06-1.



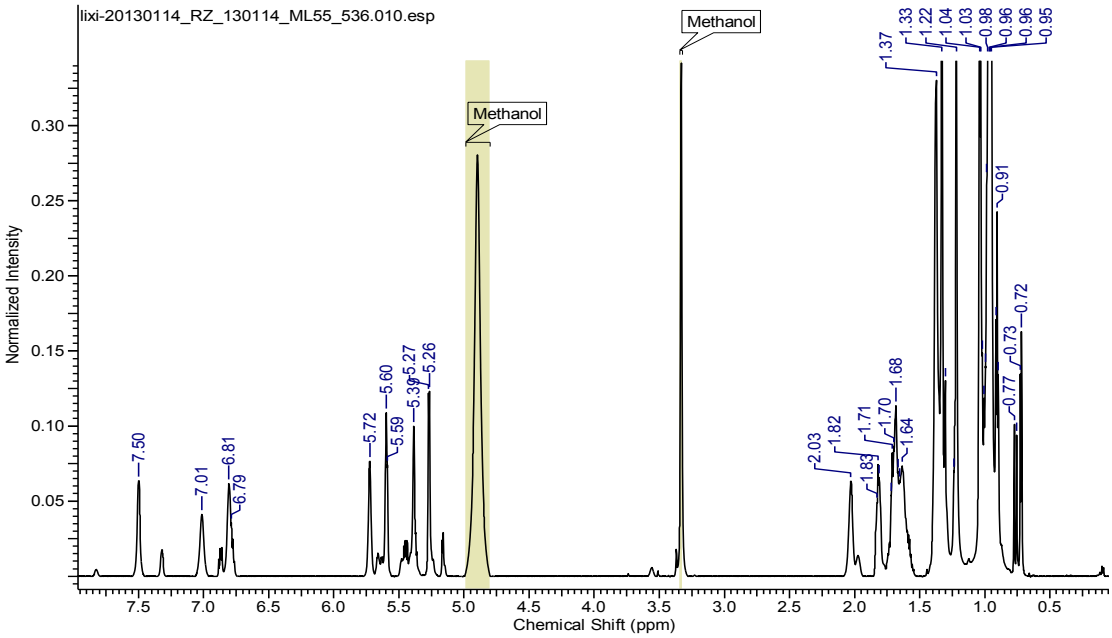
Supplementary Figure 14 HMBC spectrum of compound JBIR-06-1.



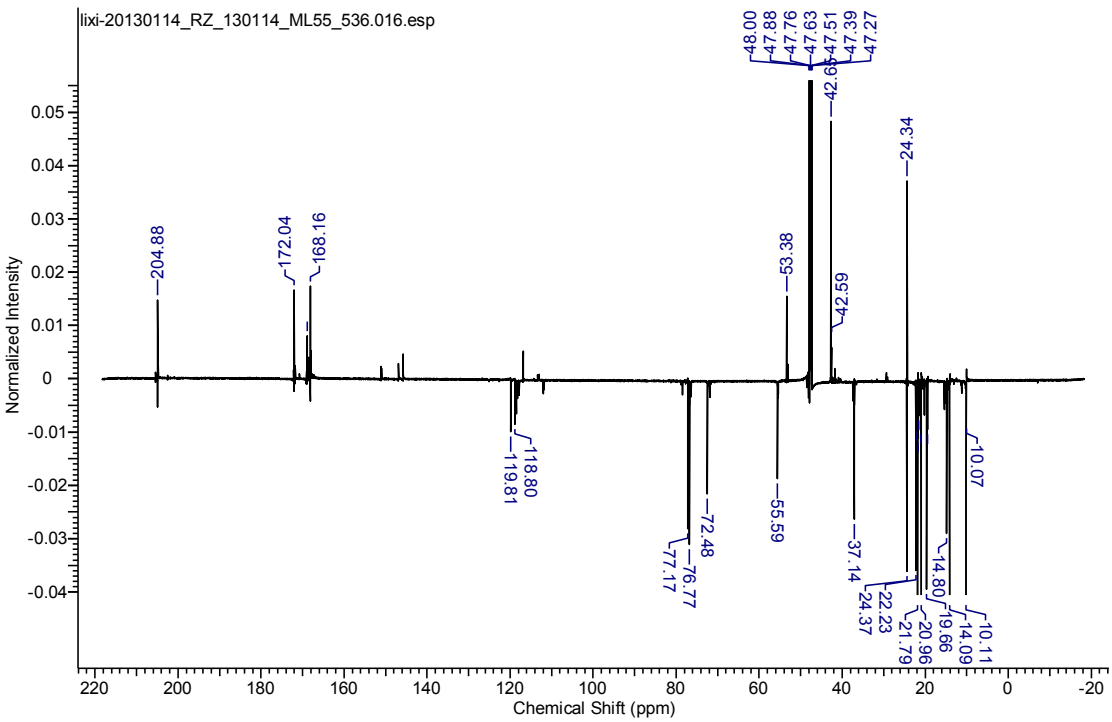
Supplemental Figure 15 MS spectrum of JBIR-06-01.



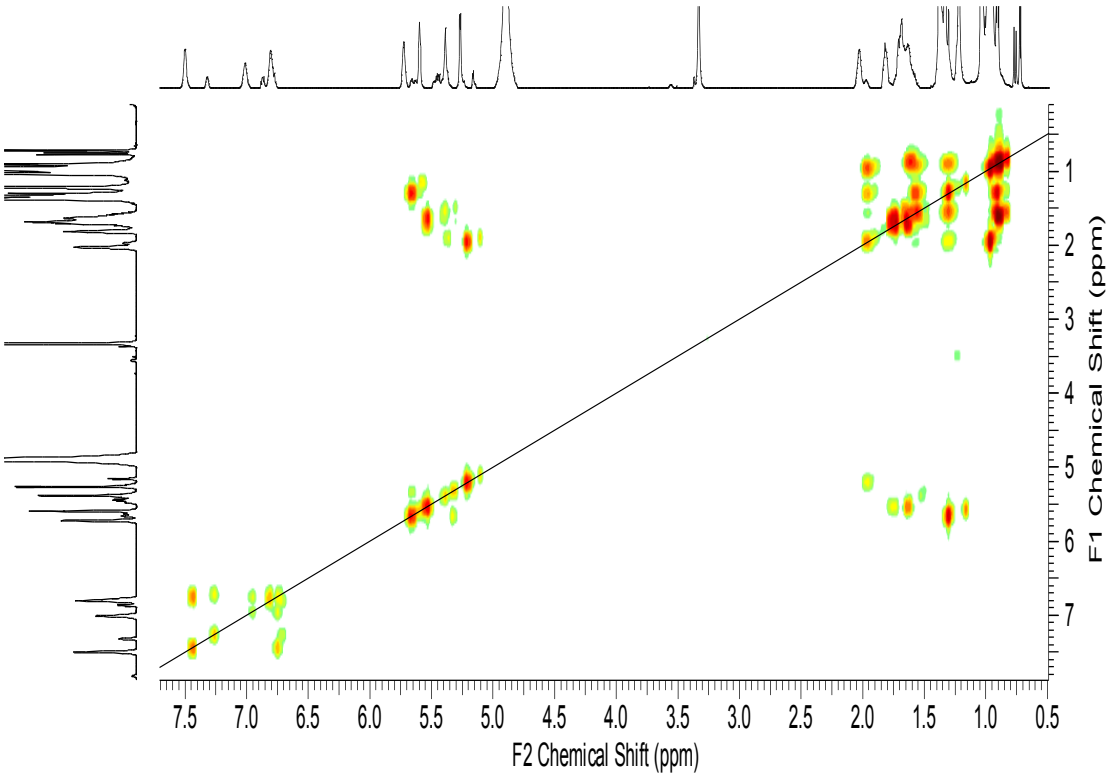
Supplementary Figure 16 ^{1}H NMR spectrum of compound JBIR-06-2.



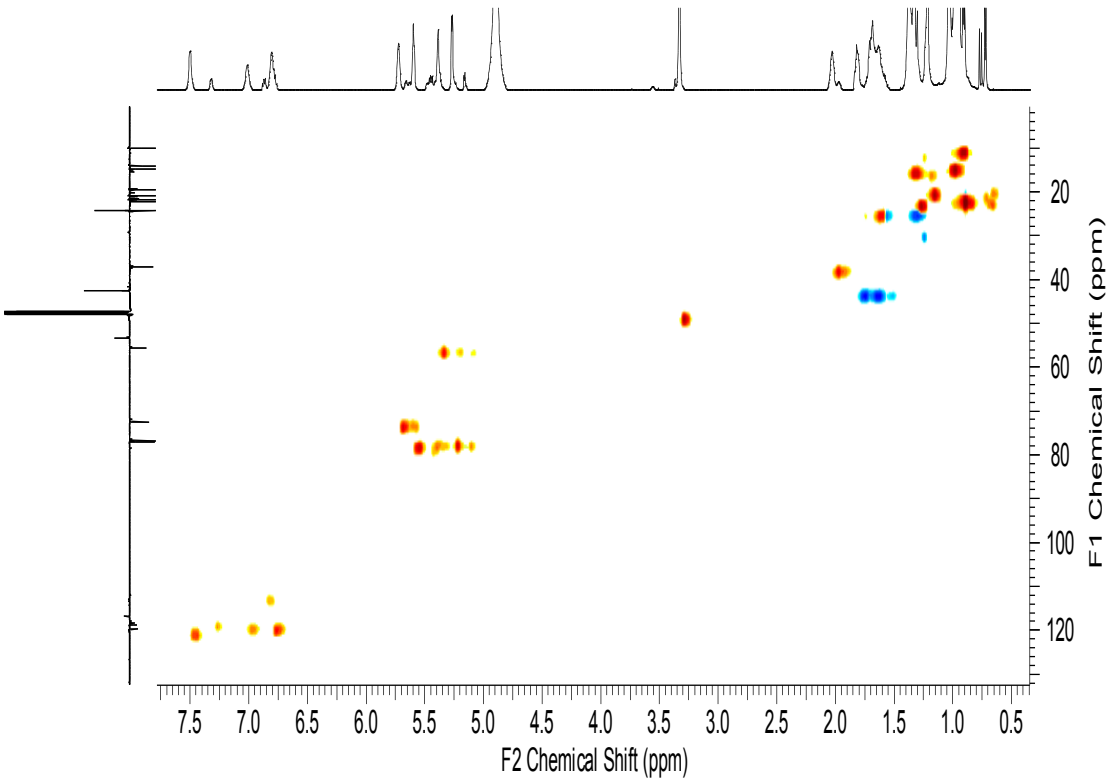
Supplementary Figure 17 ^{13}C NMR spectrum of compound JBIR-06-2.



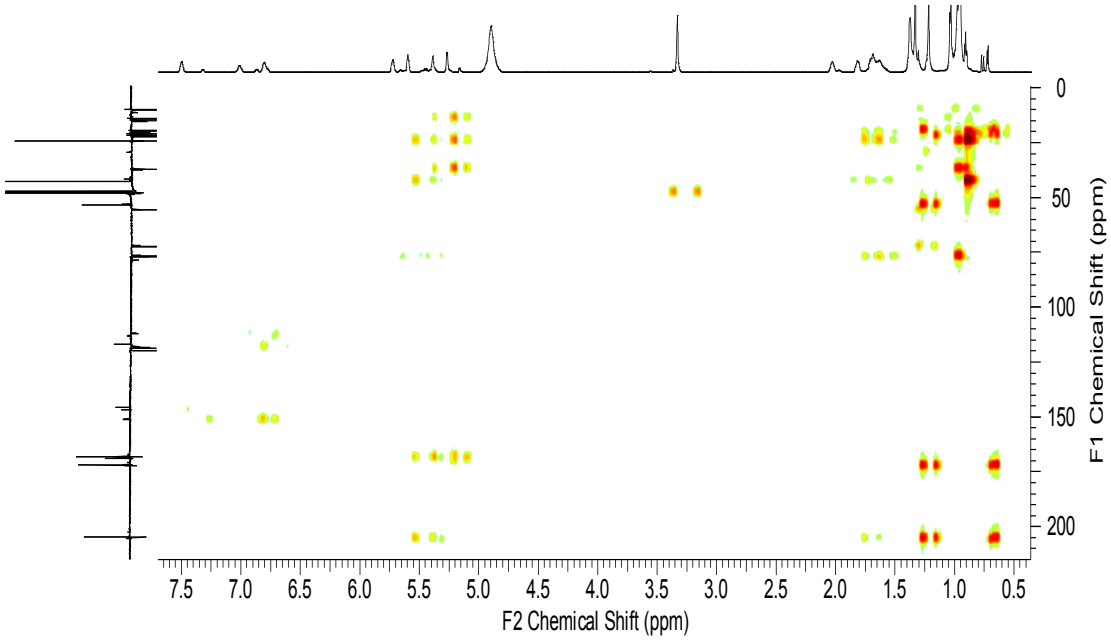
Supplementary Figure 18 ^{1}H-^{1}H COSY spectrum of compound JBIR-06-2.



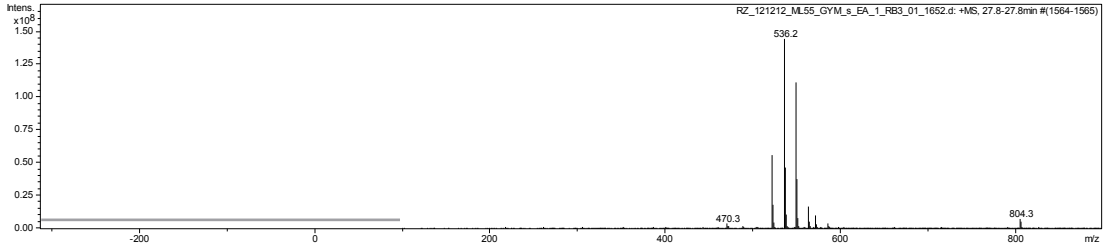
Supplementary Figure 19 HMQC spectrum of compound JBIR-06-2.



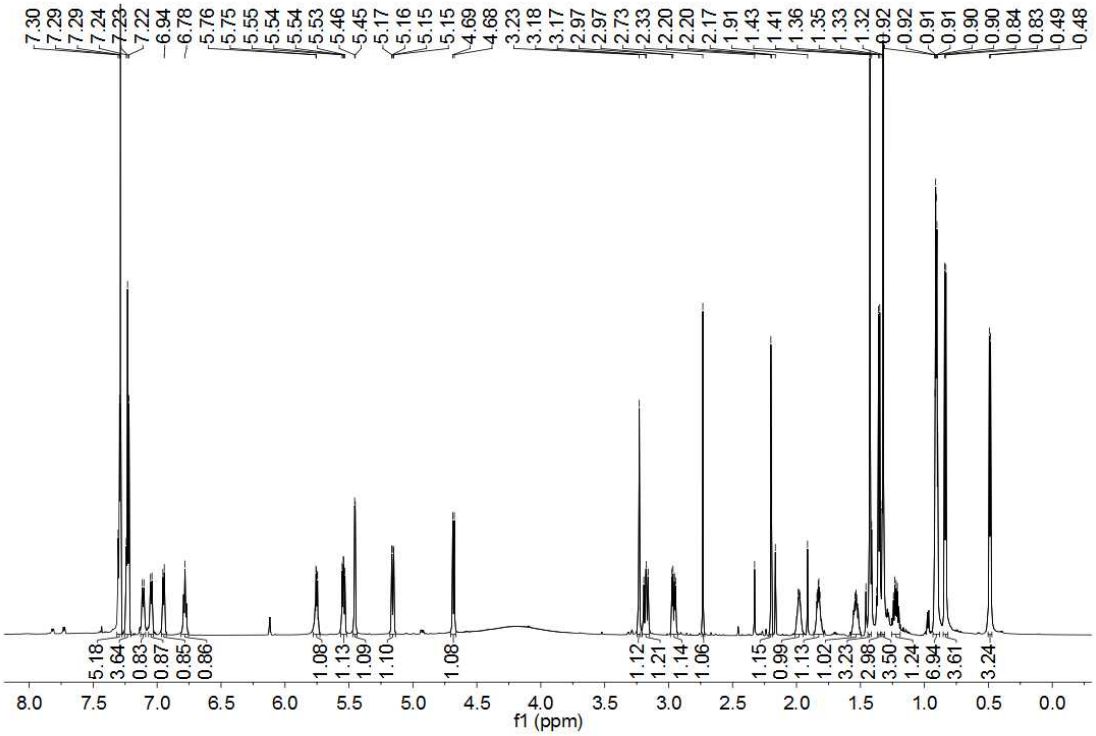
Supplementary Figure 20 HMBC spectrum of compound JBIR-06-2.



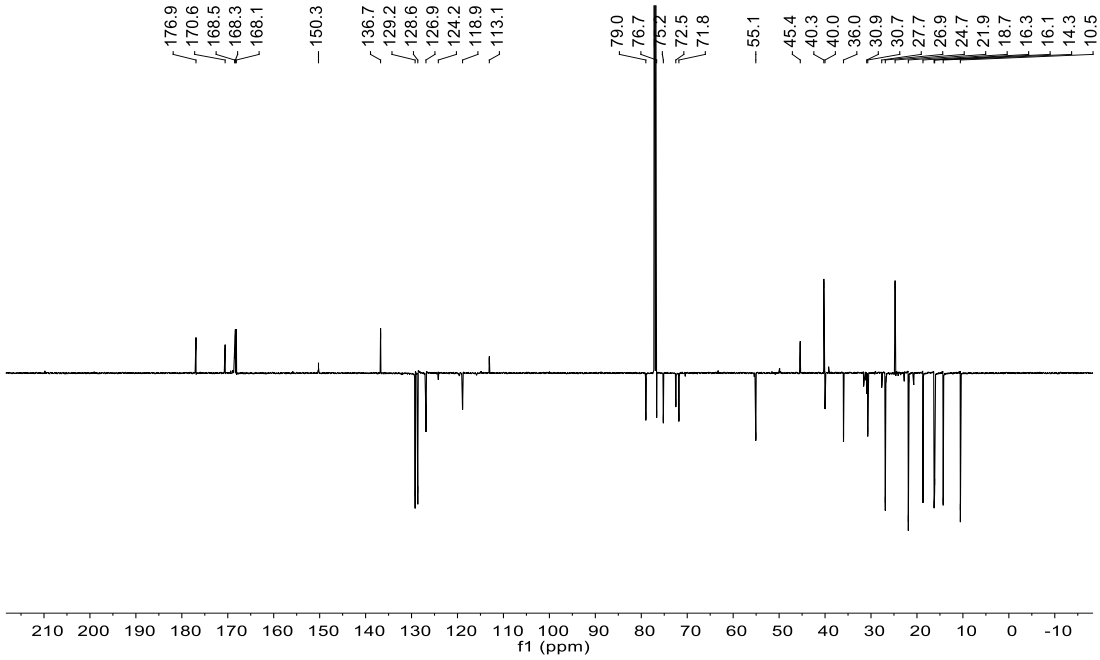
Supplemental Figure 21 MS spectrum of JBIR-06.



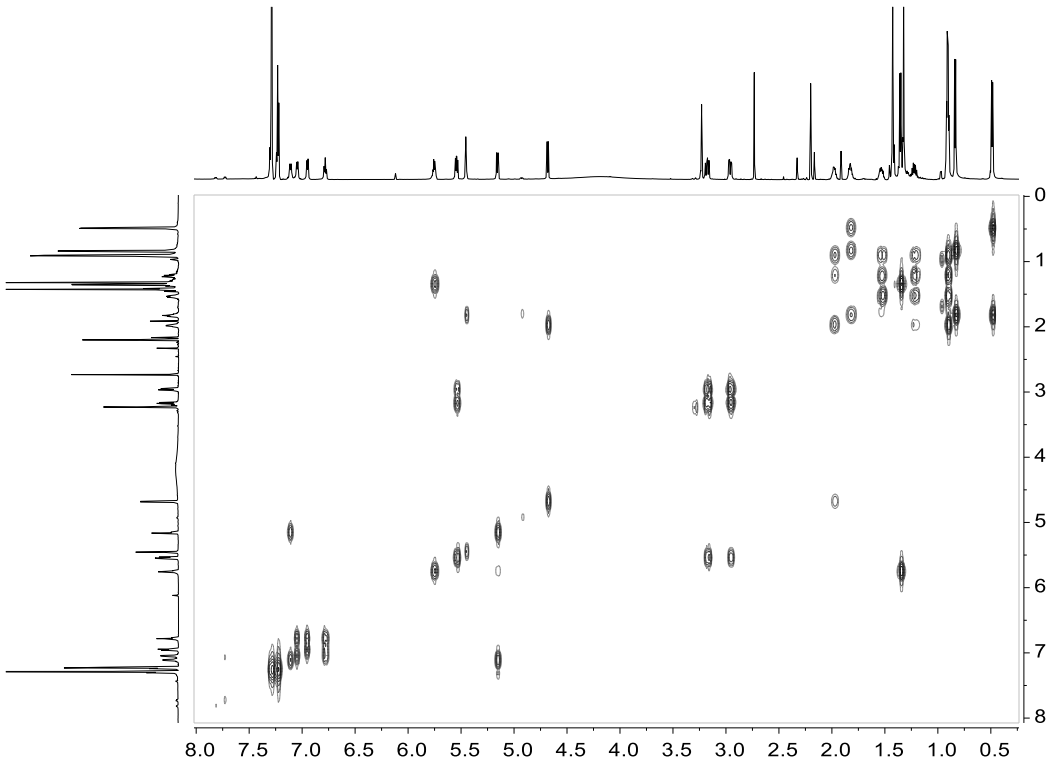
Supplemental Figure 22 ^{1}H NMR spectrum of Neo-1



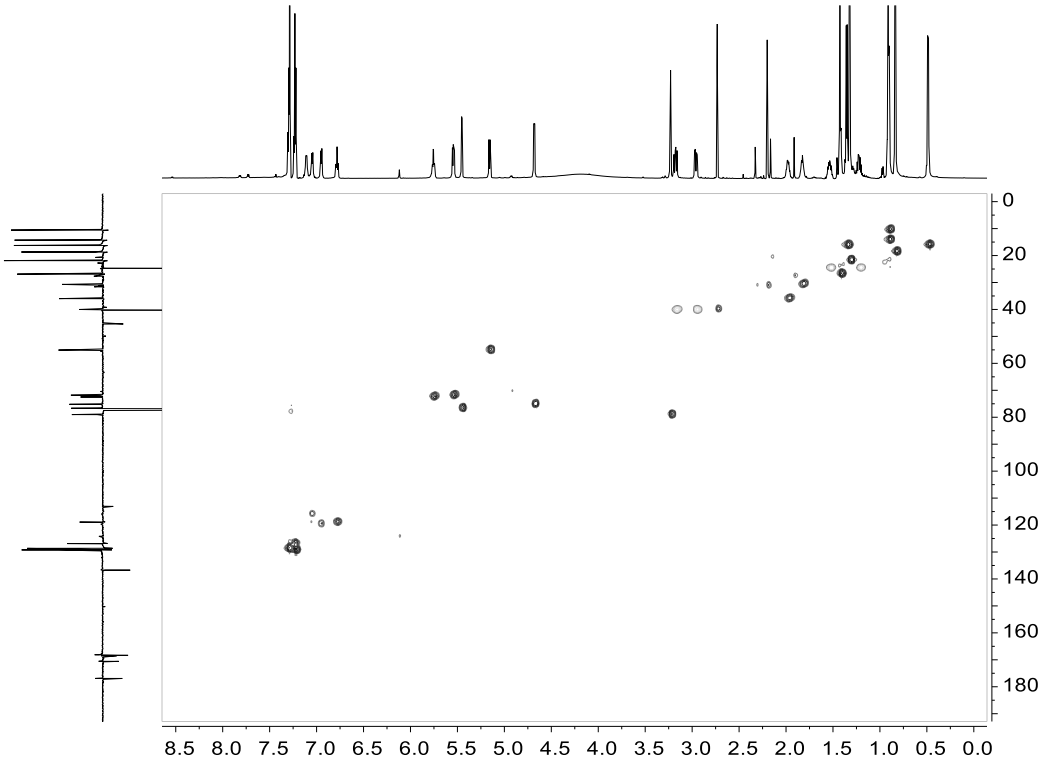
Supplemental Figure 23 ^{13}C NMR spectrum of Neo-1.



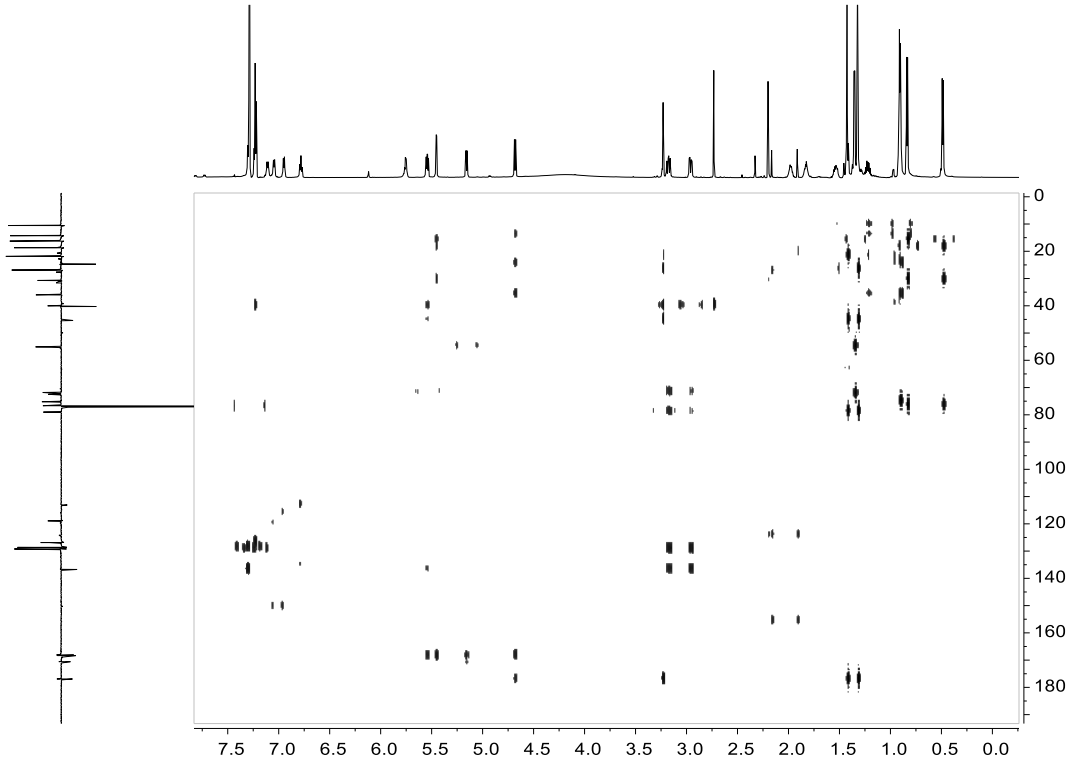
Supplemental Figure 24 ^{1}H-^{1}H COSY spectrum of Neo-1.



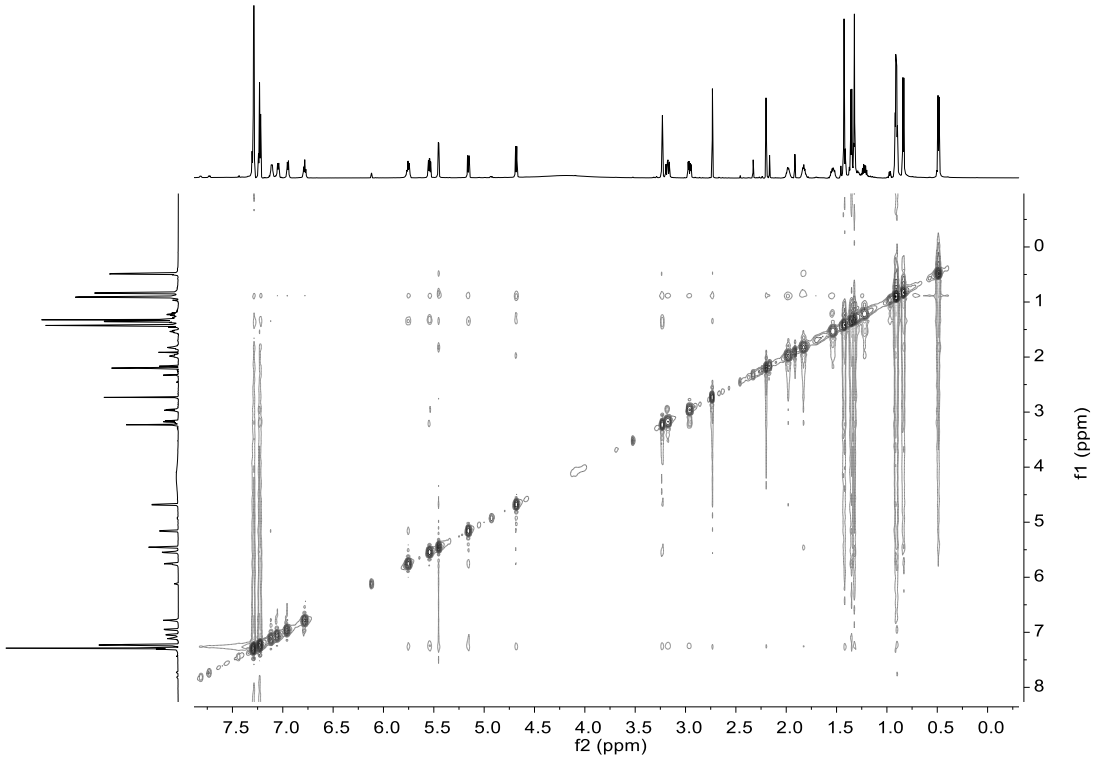
Supplemental Figure 25 ^{1}H-^{13}C HMQC spectrum of Neo-1.



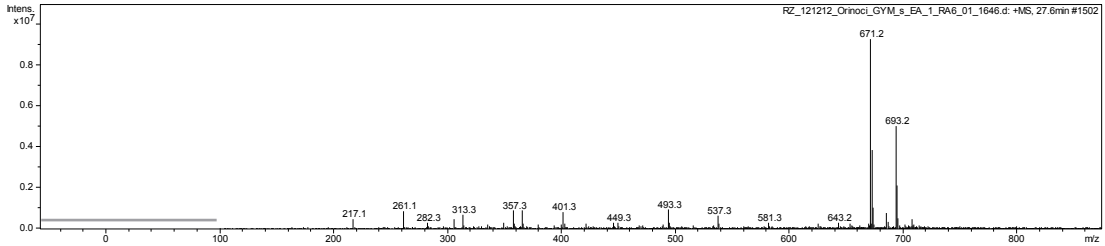
Supplemental Figure 26 ^{1}H-^{13}C HMBC spectrum of Neo-1.



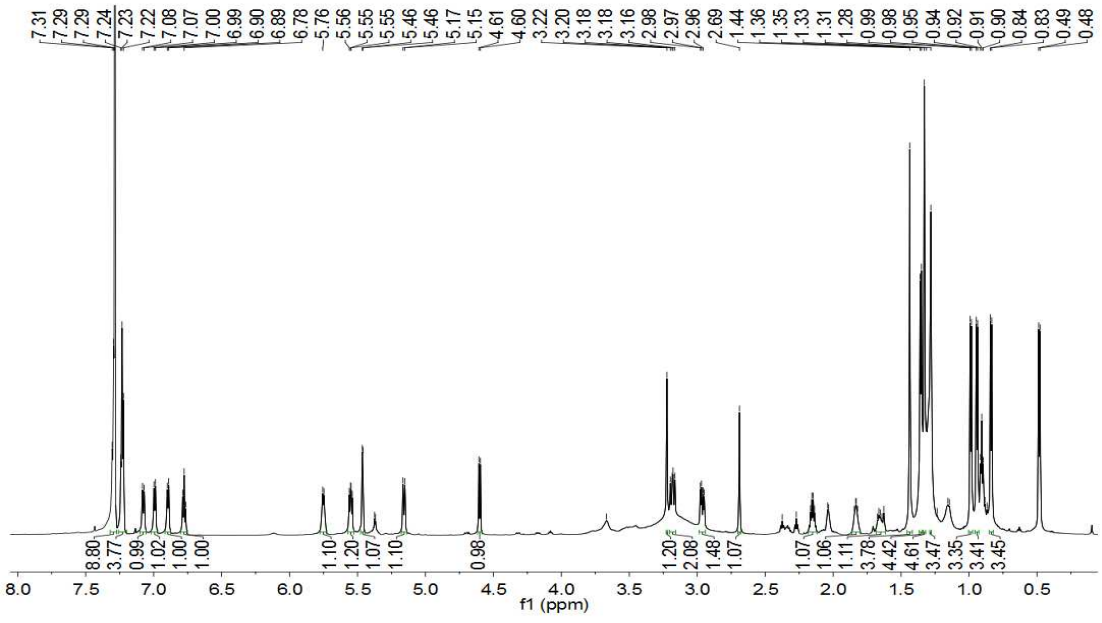
Supplemental Figure 27 ^{1}H-^{1}H NOESY spectrum of Neo-1.



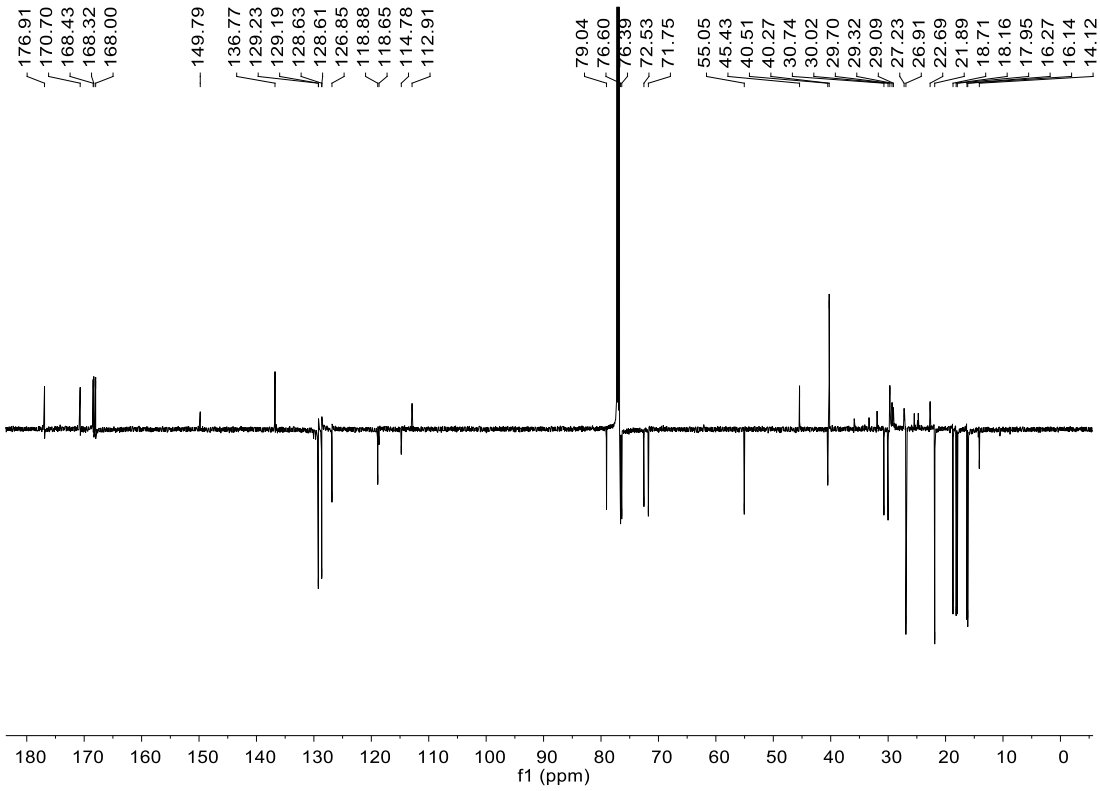
Supplemental Figure 28 MS spectrum of Neo-1.



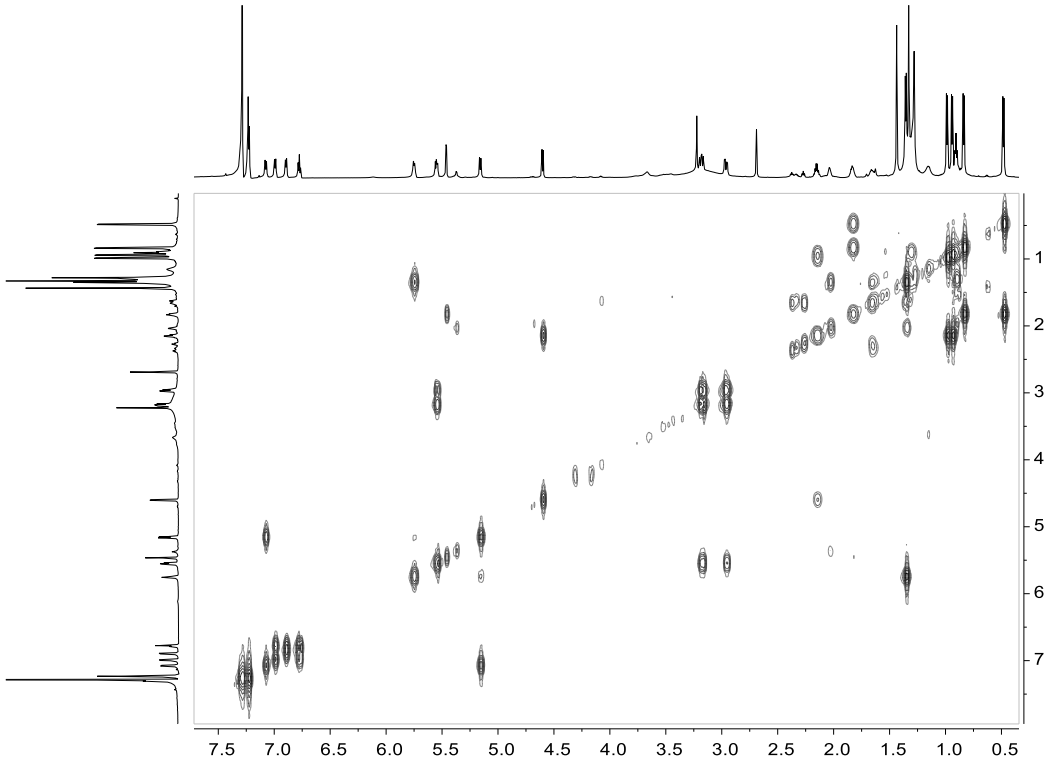
Supplemental Figure 29 ^{1}H NMR spectrum of Neo-2.



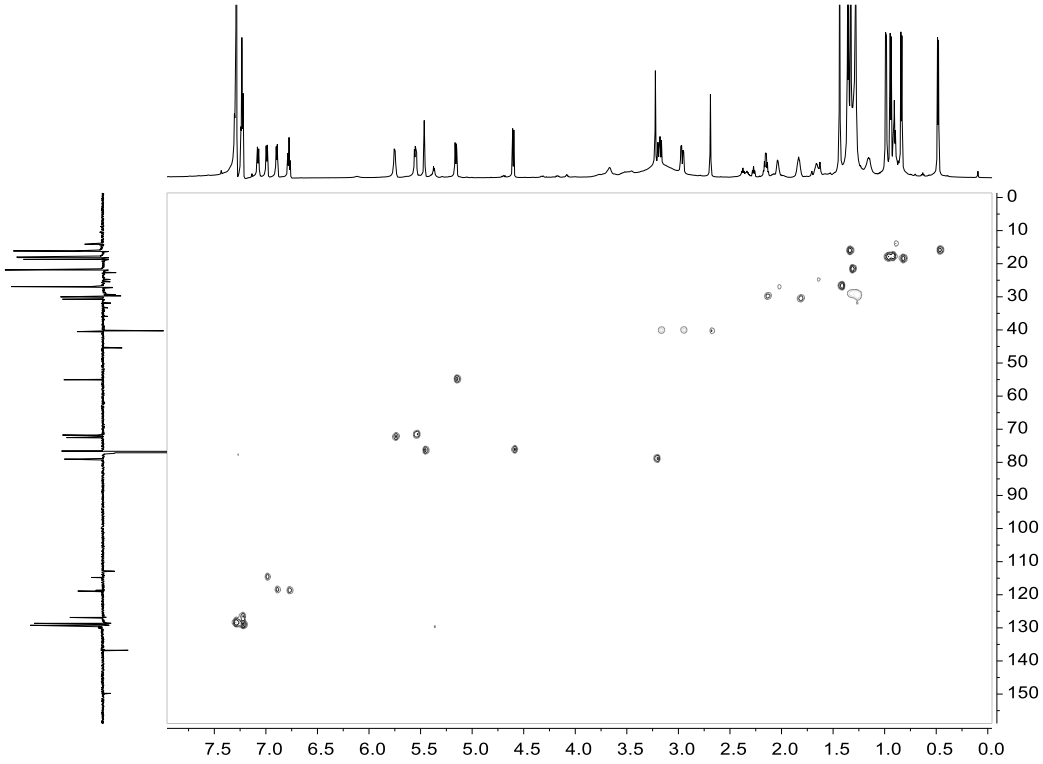
Supplemental Figure 30 ^{13}C NMR spectrum of Neo-2.



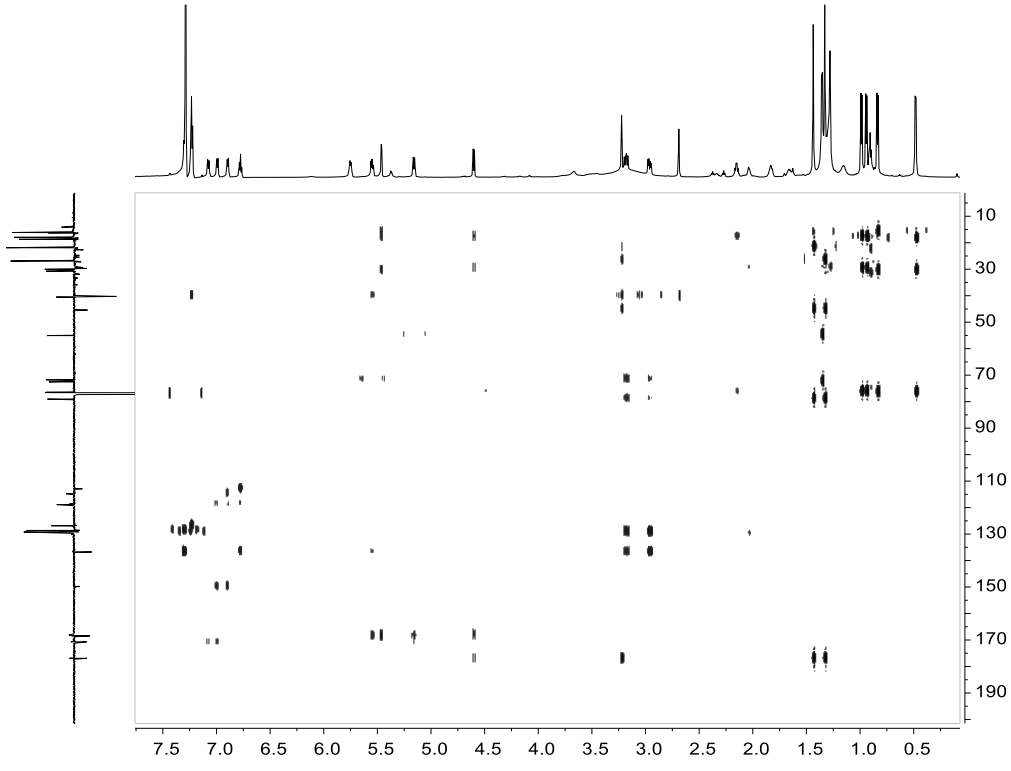
Supplemental Figure 31 ^{1}H-^{1}H COSY spectrum of Neo-2.



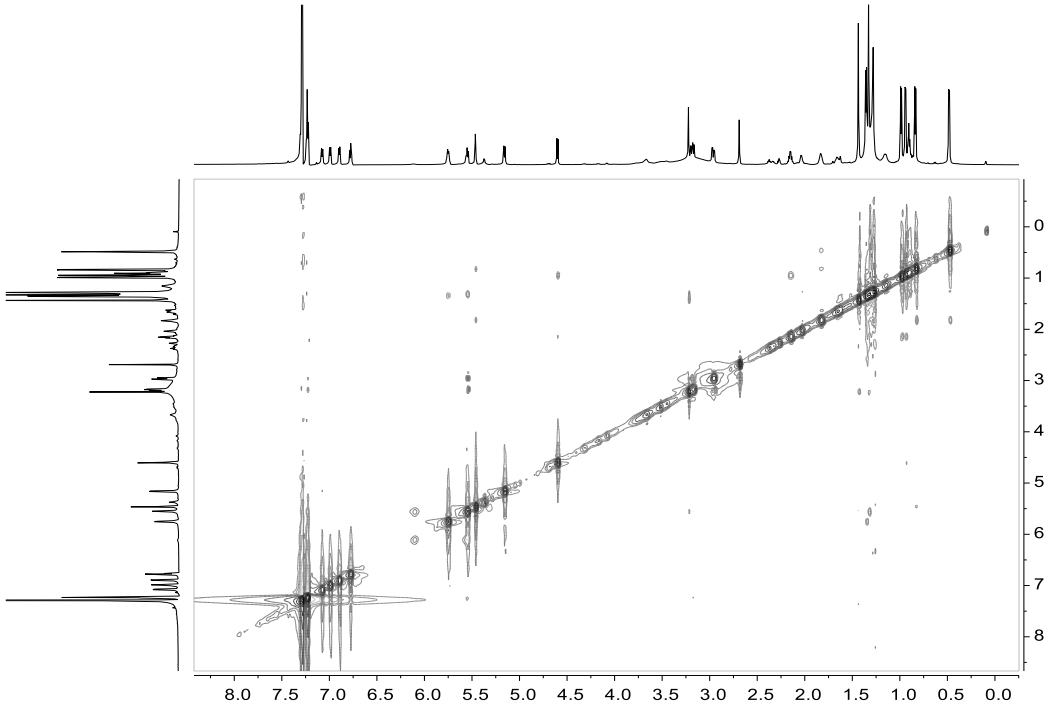
Supplemental Figure 32 ^{1}H-^{13}C HMQC spectrum of Neo-2.



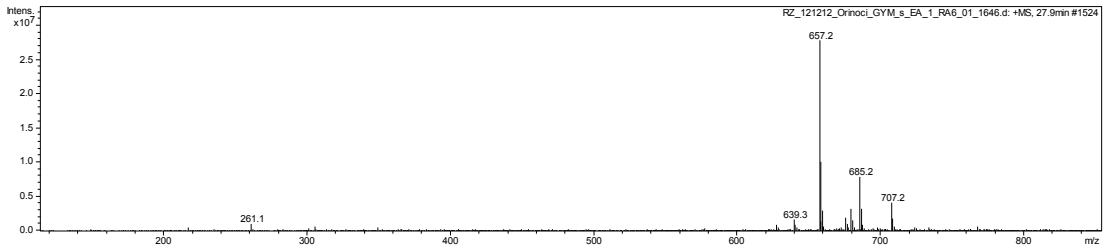
Supplemental Figure 33 ^{1}H-^{13}C HMBC spectrum of Neo-2.



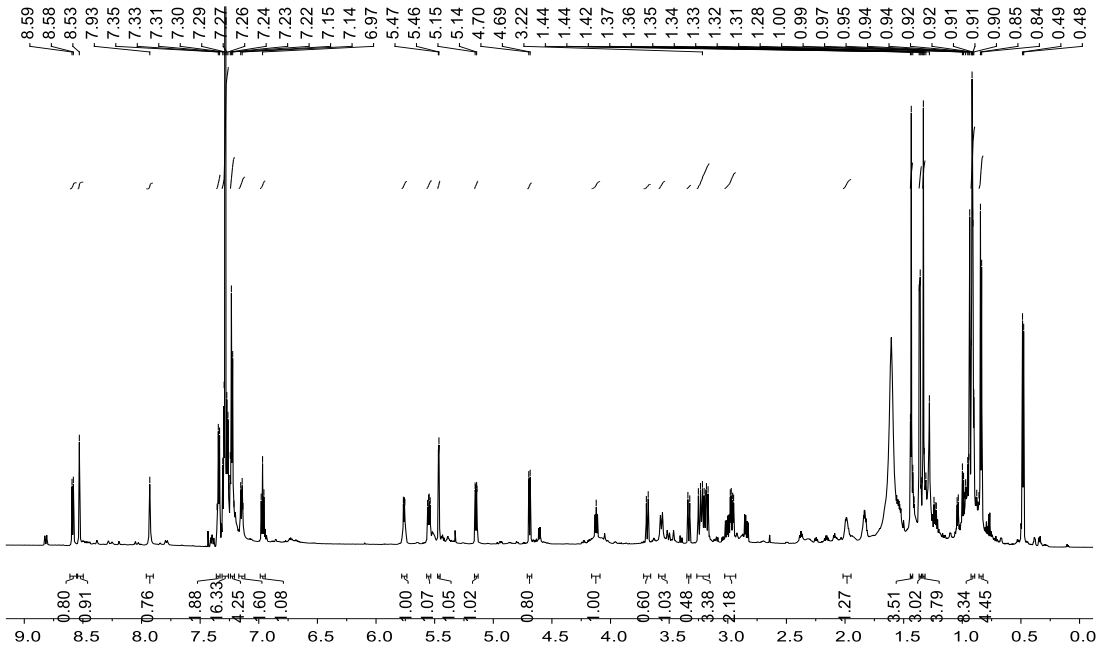
Supplemental Figure 34 ^{1}H-^{1}H NOESY spectrum of Neo-2.



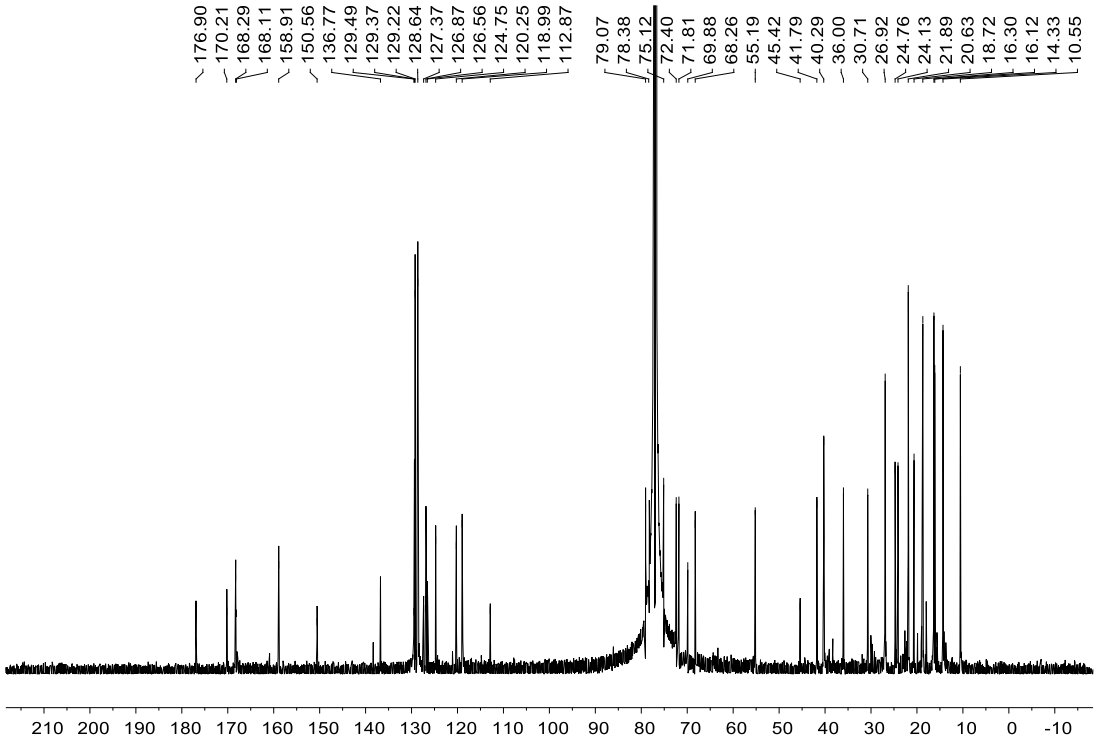
Supplemental Figure 35 MS spectrum of Neo-2.



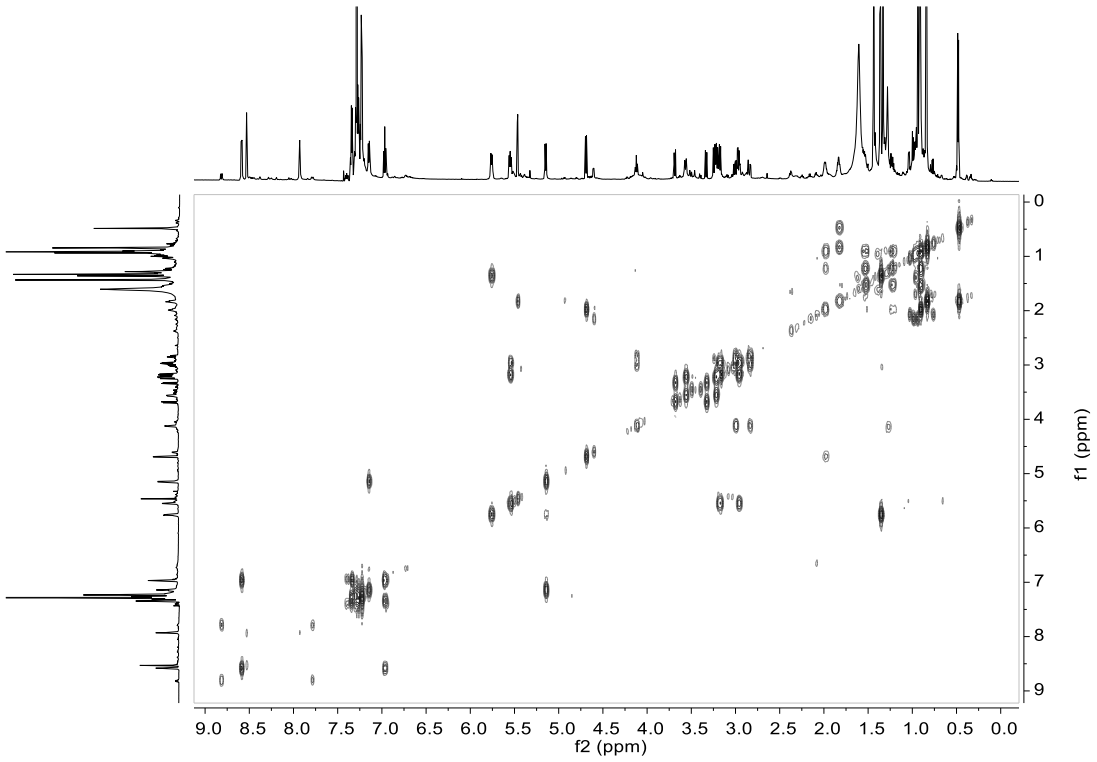
Supplemental Figure 36 ^{1}H NMR spectrum of Neo-3.



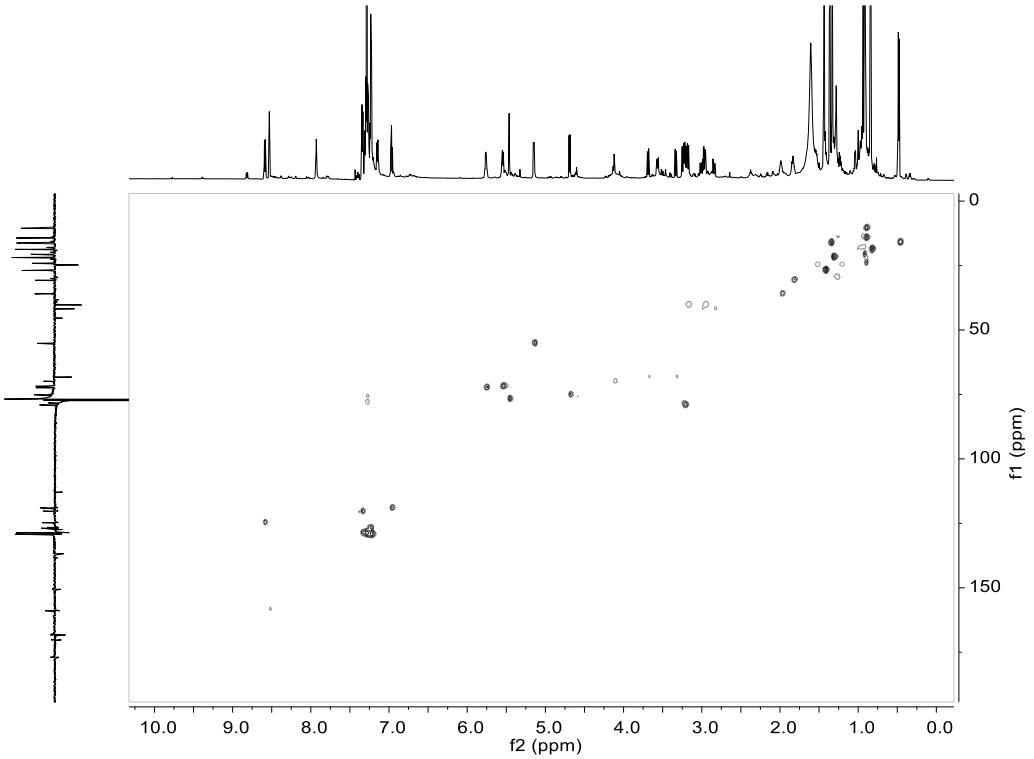
Supplemental Figure 37 ^{13}C NMR spectrum of Neo-3.



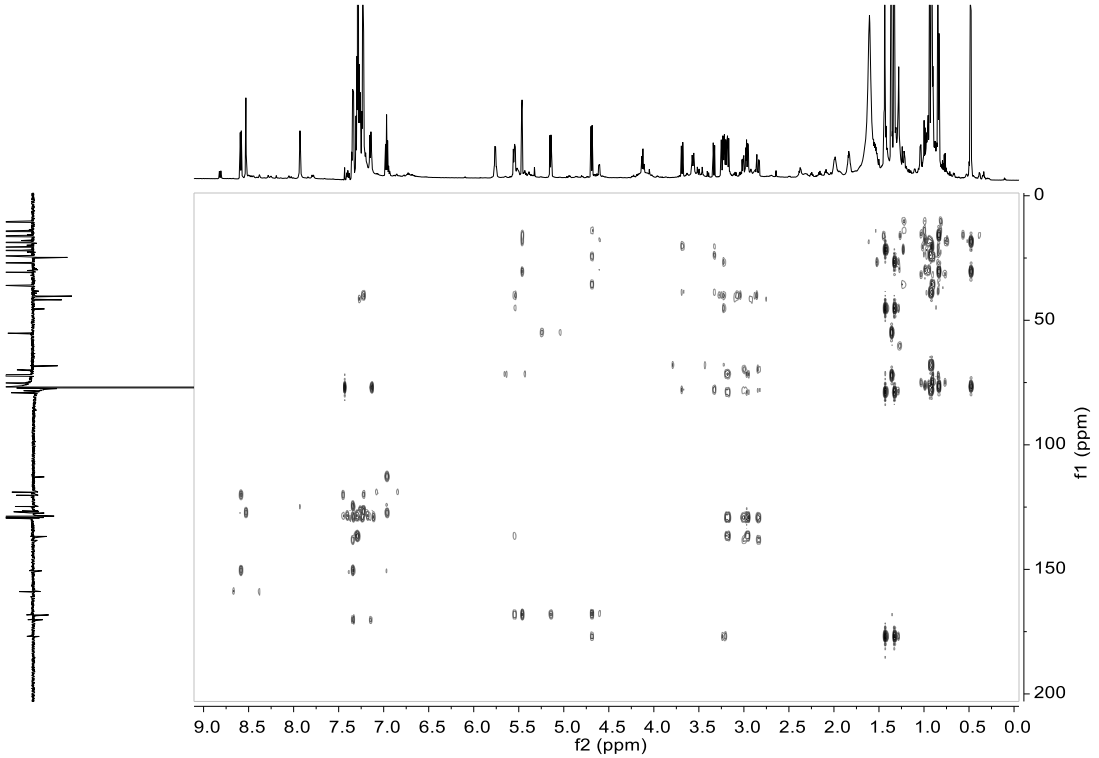
Supplemental Figure 38 ^{1}H-^{1}H COSY spectrum of Neo-3.



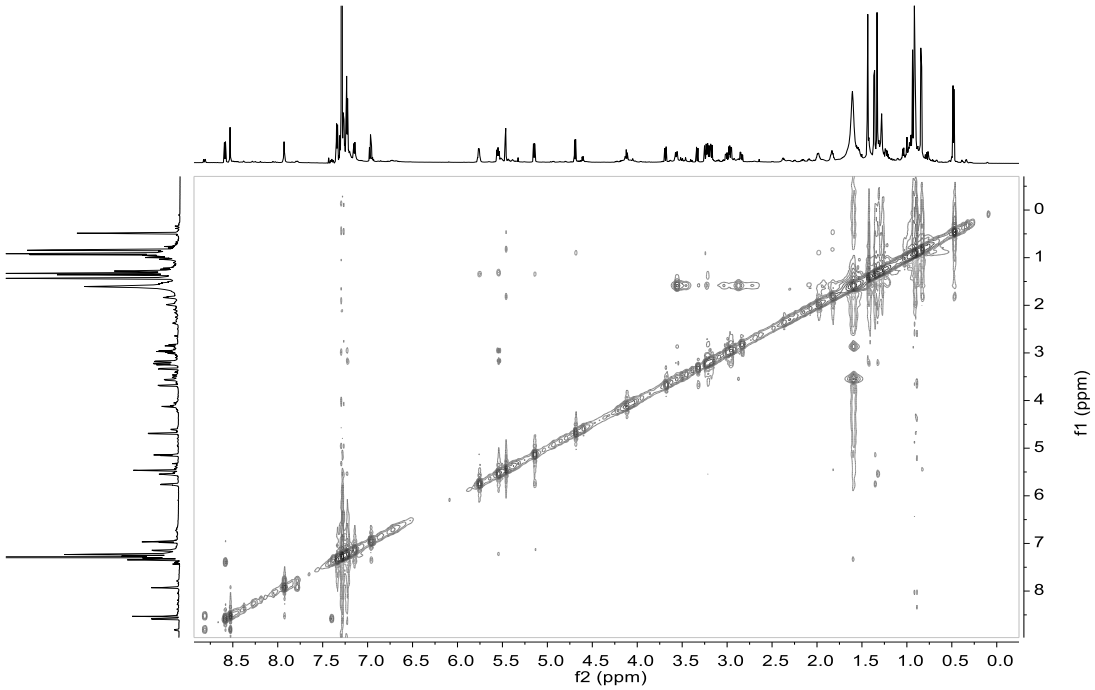
Supplemental Figure 39 ^{1}H-^{13}C HMQC spectrum of Neo-3.



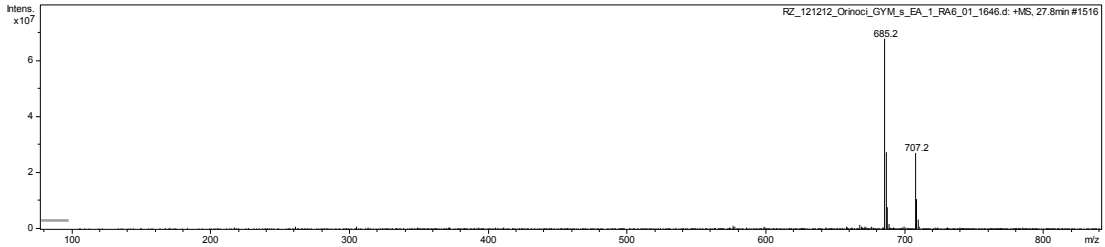
Supplemental Figure 40 ^{1}H-^{13}C HMBC spectrum of Neo-3.



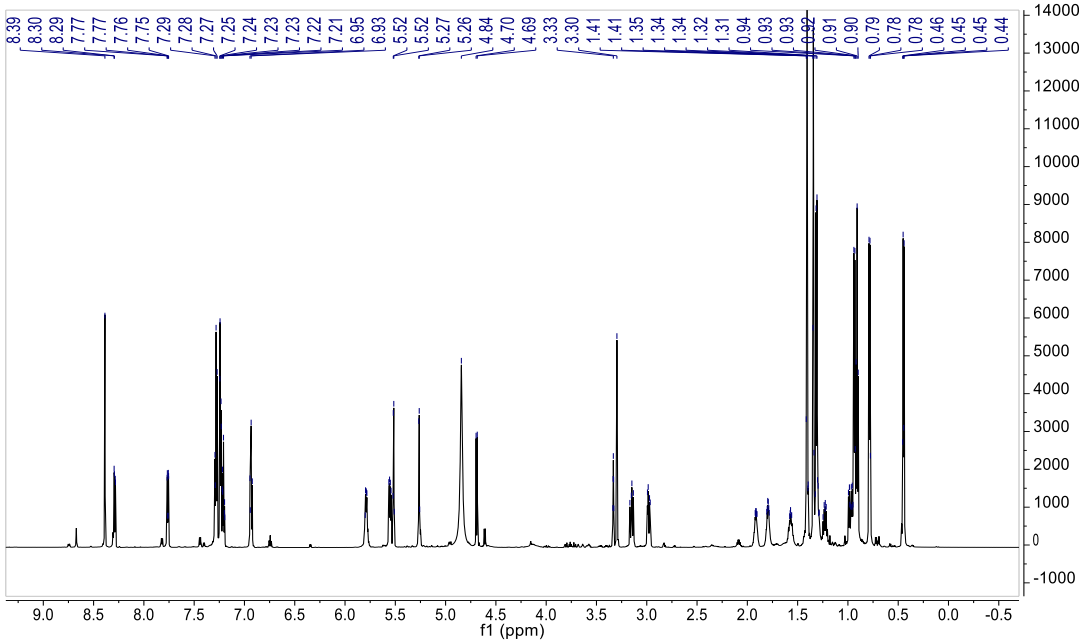
Supplemental Figure 41 ^{1}H-^{1}H NOESY spectrum of Neo-3.



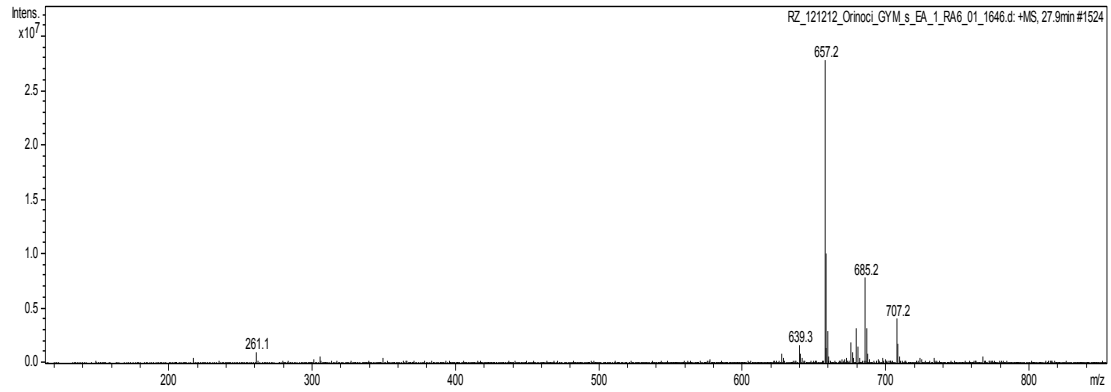
Supplemental Figure 42 MS spectrum of Neo-3.



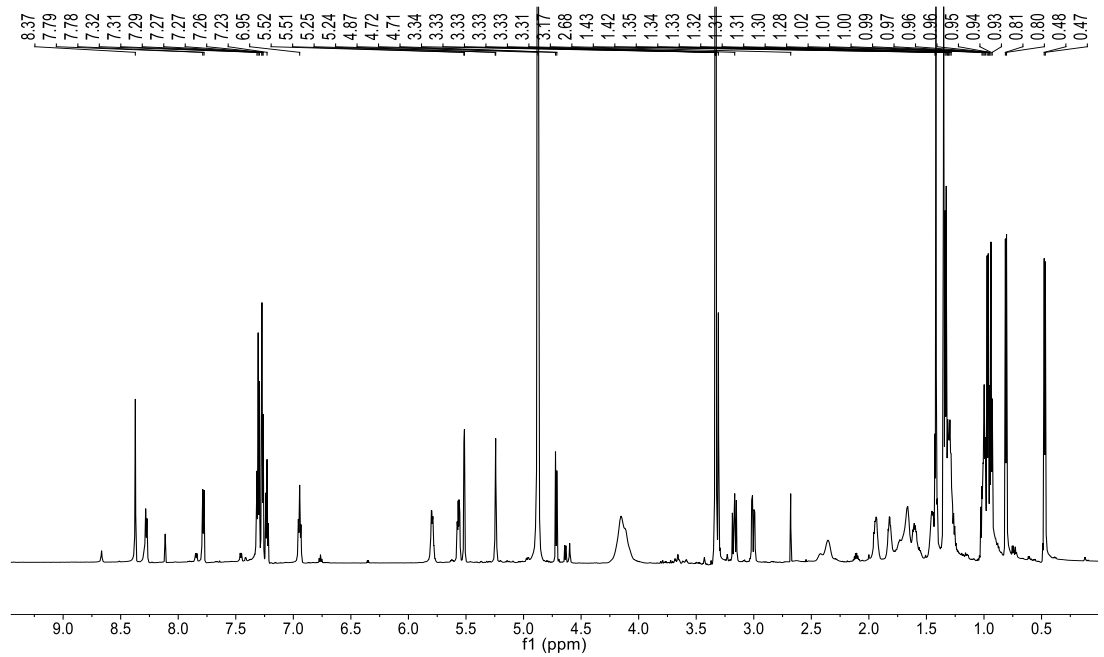
Supplemental Figure 43 ^{1}H NMR spectrum of Neo-4.



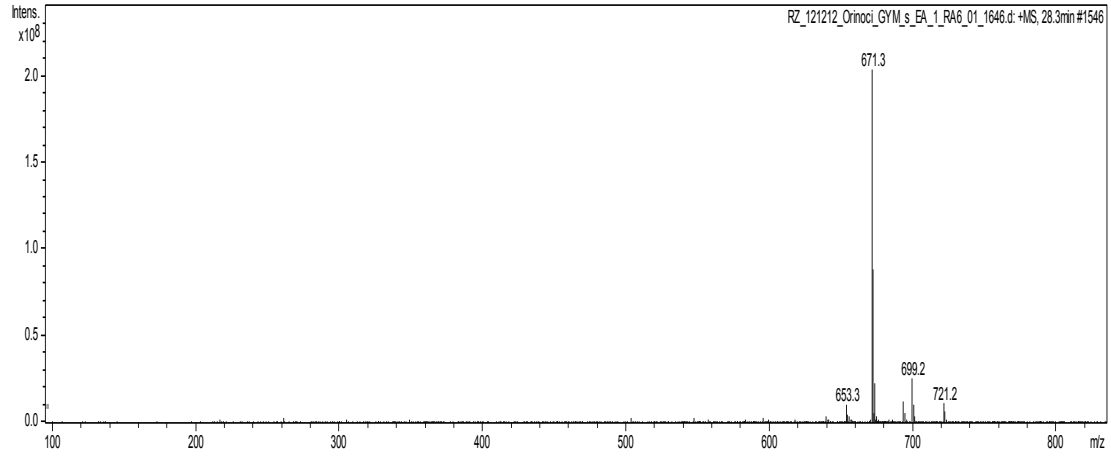
Supplemental Figure 44 MS spectrum of Neo-4.



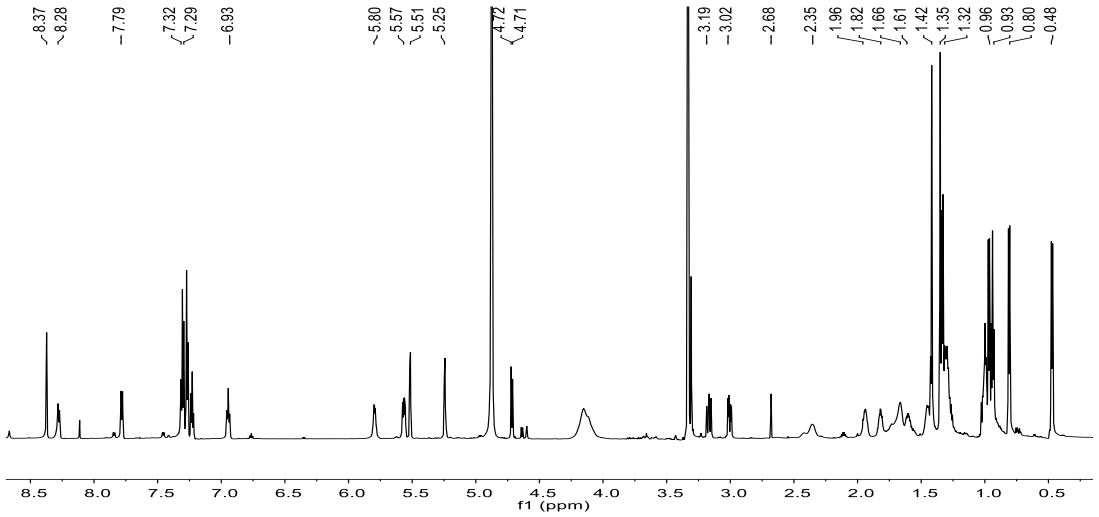
Supplemental Figure 45 ^{1}H NMR spectrum of Neo-5.



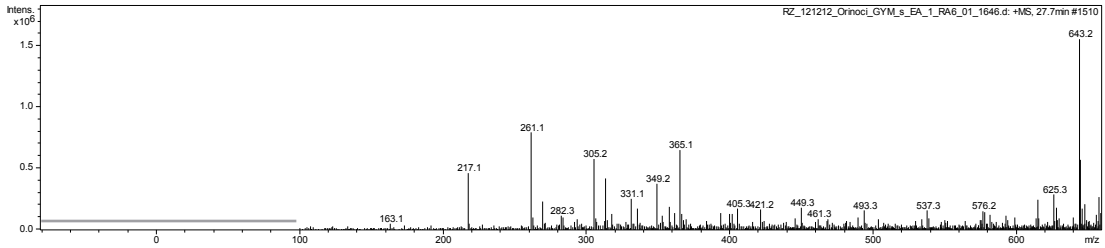
Supplemental Figure 46 MS spectrum of Neo-05.



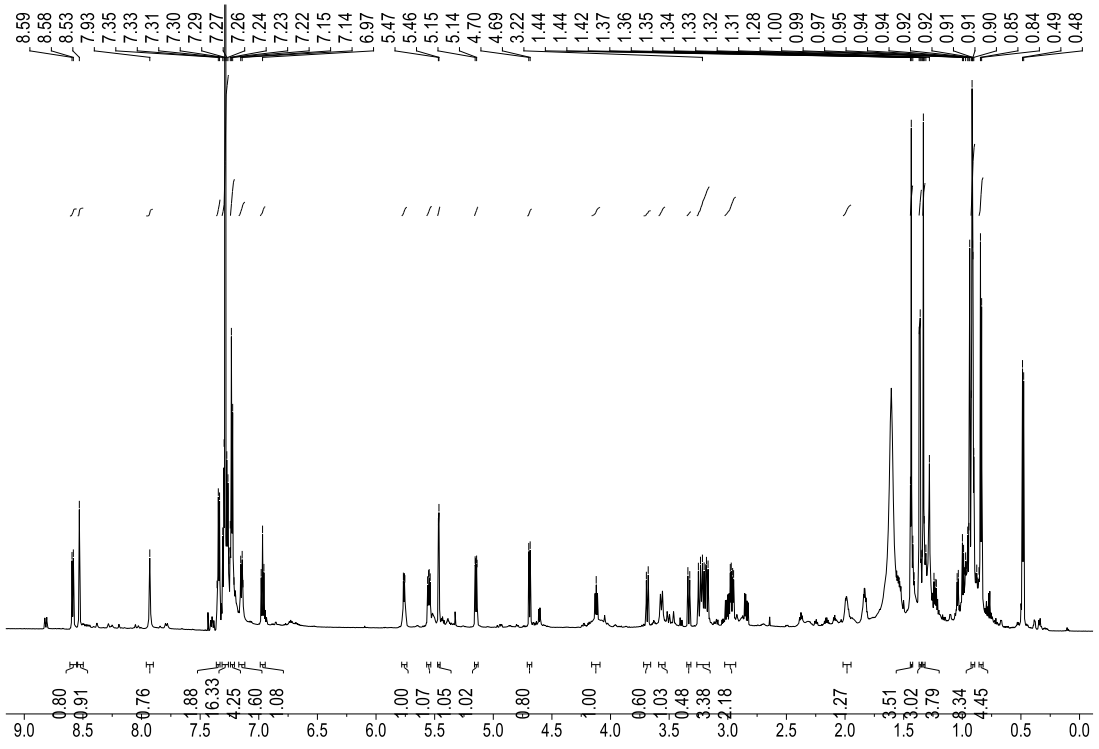
Supplemental Figure 47 ^{1}H NMR spectrum of Neo-6.



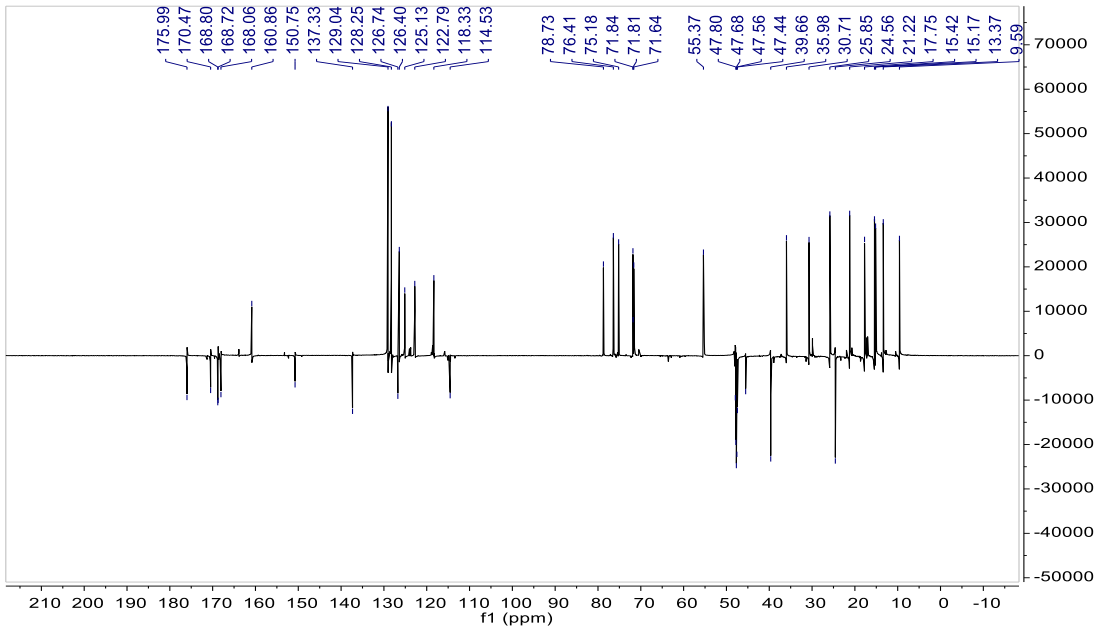
Supplemental Figure 48 MS spectrum of Neo-6.



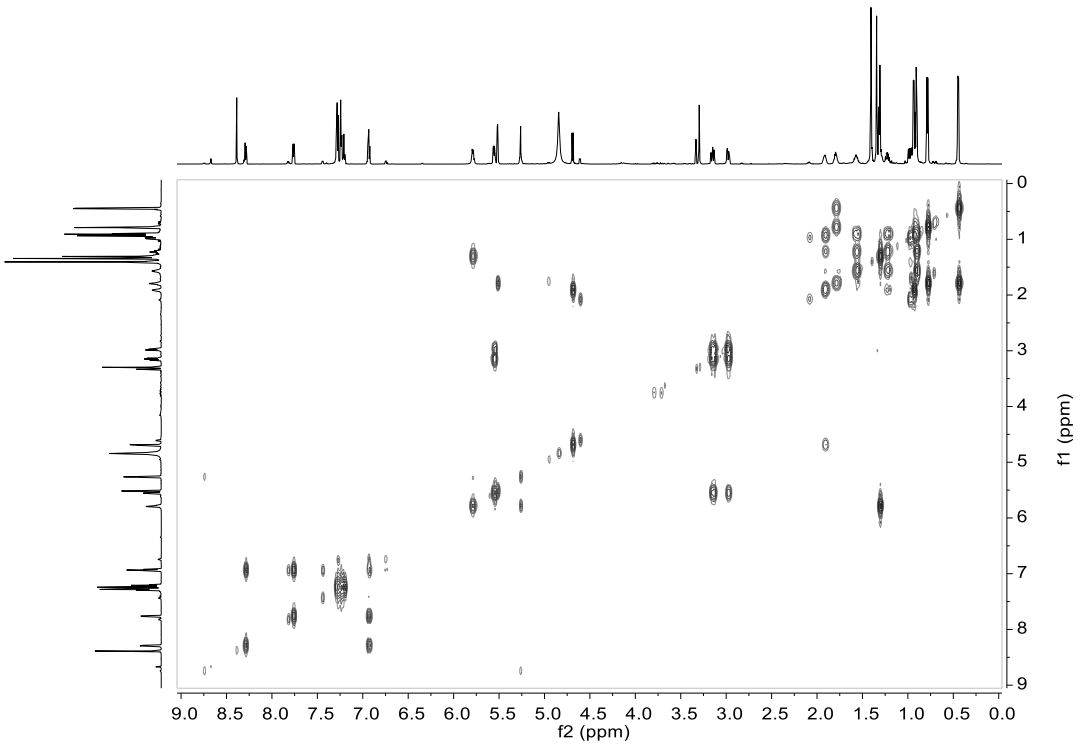
Supplemental Figure 49 ^{1}H NMR spectrum of Neo-7.



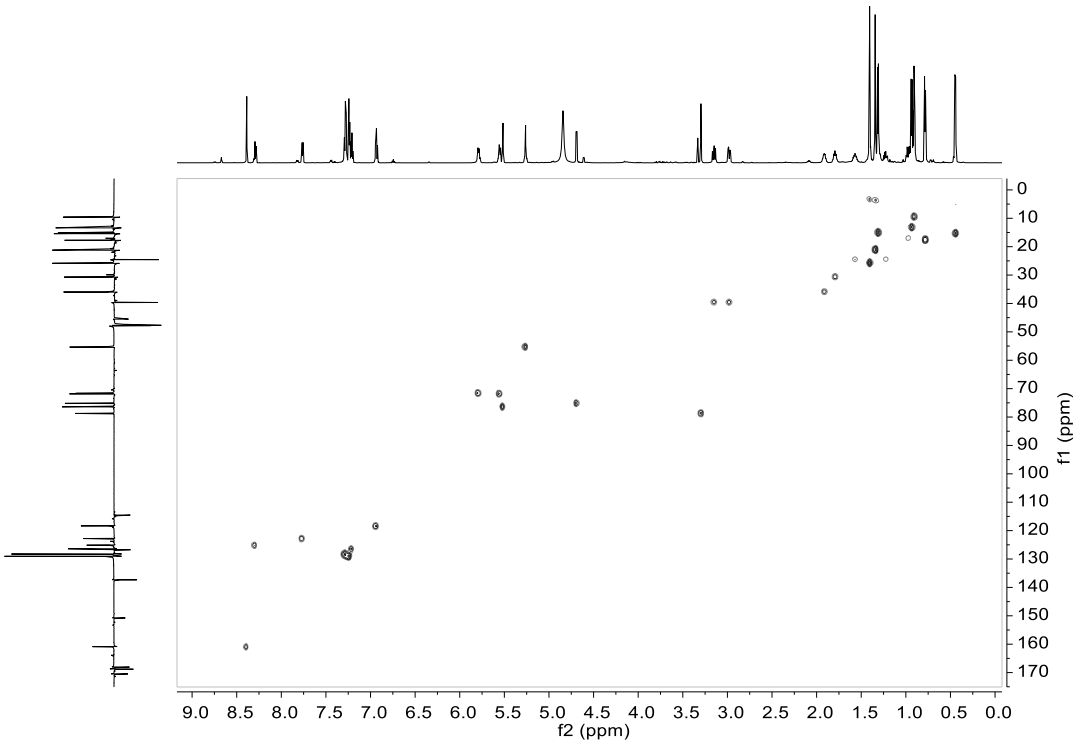
Supplemental Figure 50 ^{13}C NMR spectrum of Neo-7.



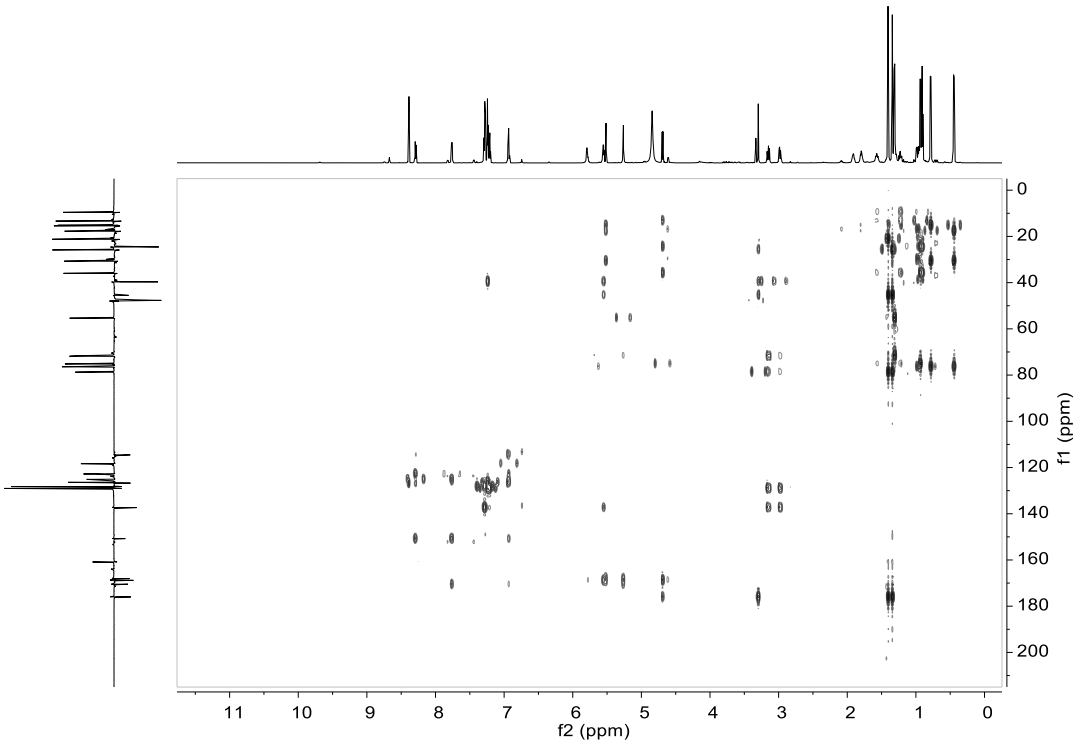
Supplemental Figure 51 ^{1}H-^{1}H COSY spectrum of Neo-7.



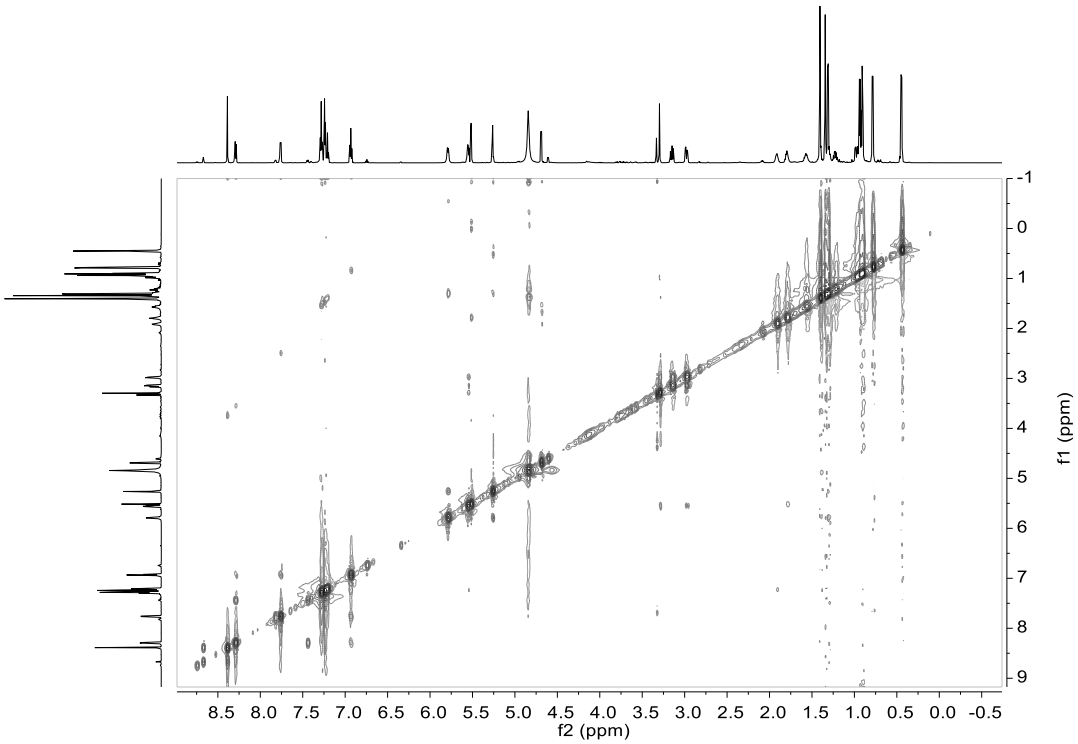
Supplemental Figure 52 ^{1}H-^{13}C HMQC spectrum of Neo-7.



Supplemental Figure 53 ^{1}H-^{13}C HMBC spectrum of Neo-7.



Supplemental Figure 54 ^{1}H-^{1}H NOESY spectrum of Neo-7.



Supplemental Figure 55 MS spectrum of Neo-7.