SUPPORTING INFORMATION:
Small molecule anticancer agents kill cancer cells by harnessing reactive oxygen species in an iron-dependent manner

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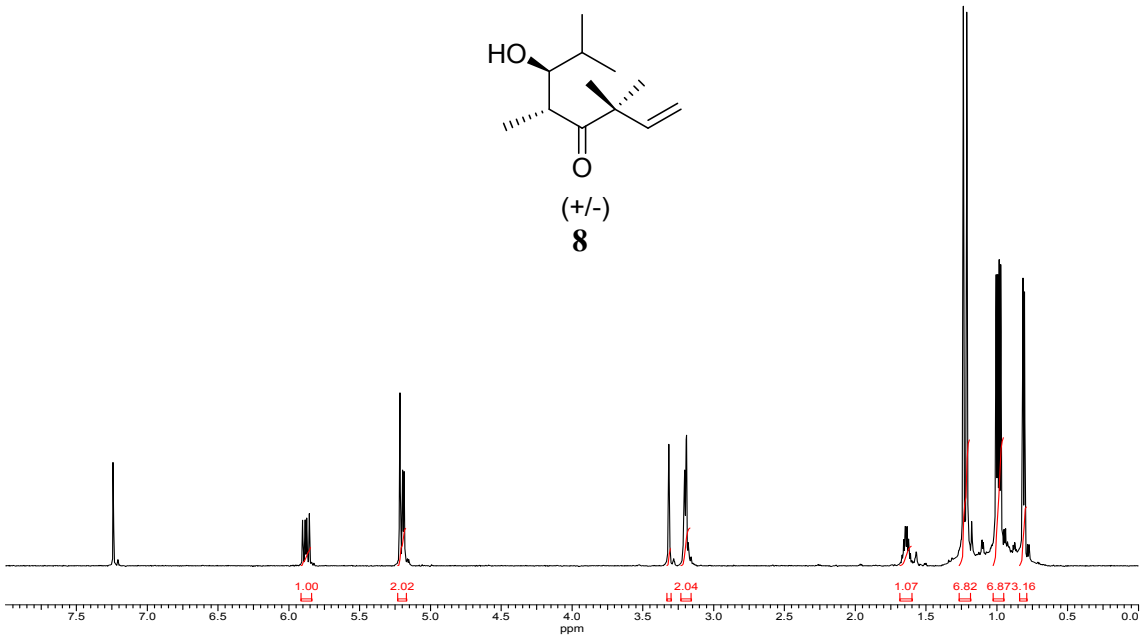
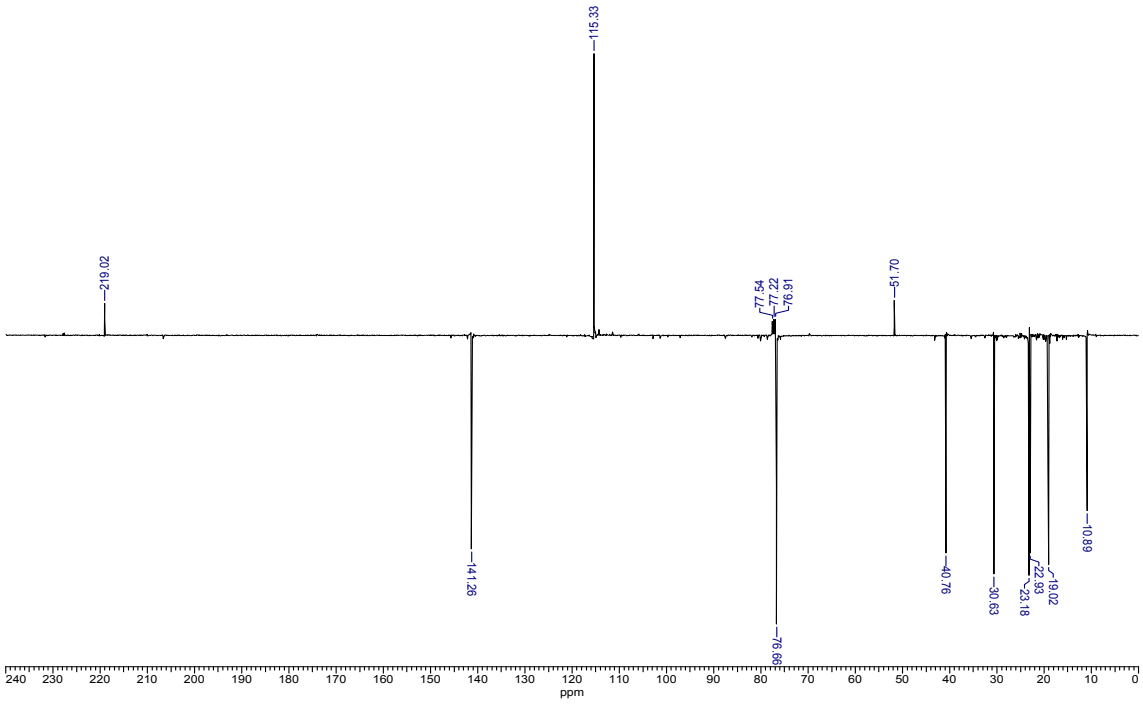
^{1}H NMR of (*5R*, *6S*) and (*5S*, *6R*)-6-hydroxy-3,3,5,7-tetramethyl-oct-1-en-4-one ((+/-) 8)



^{13}C NMR of (*5R*, *6S*) and (*5S*, *6R*)-6-hydroxy-3,3,5,7-tetramethyl-oct-1-en-4-one ((+/-) 8)



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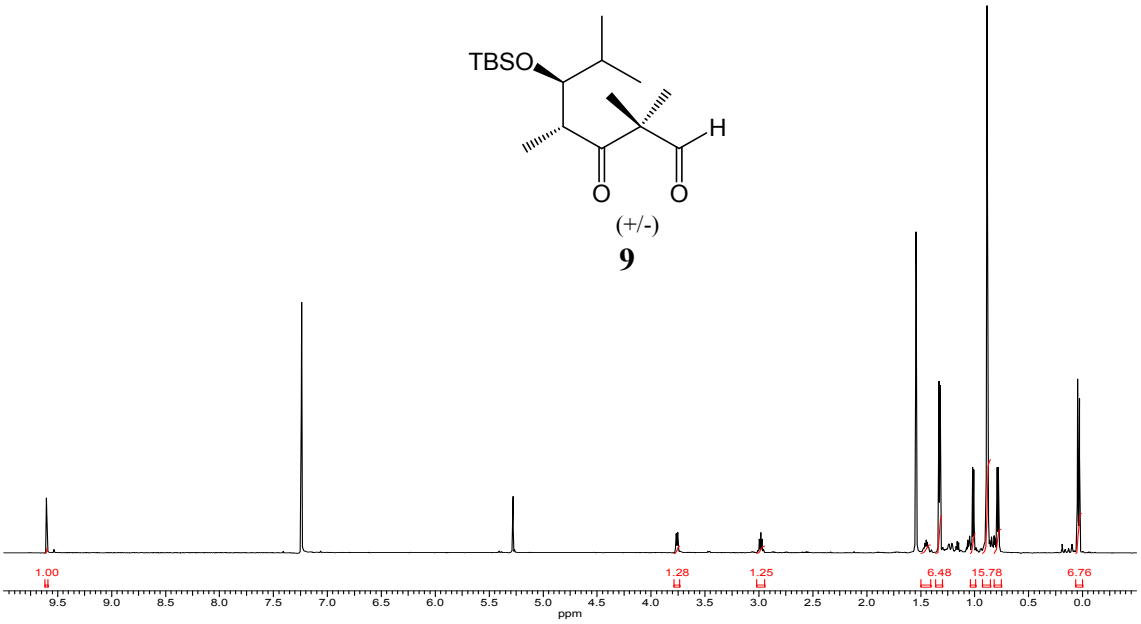

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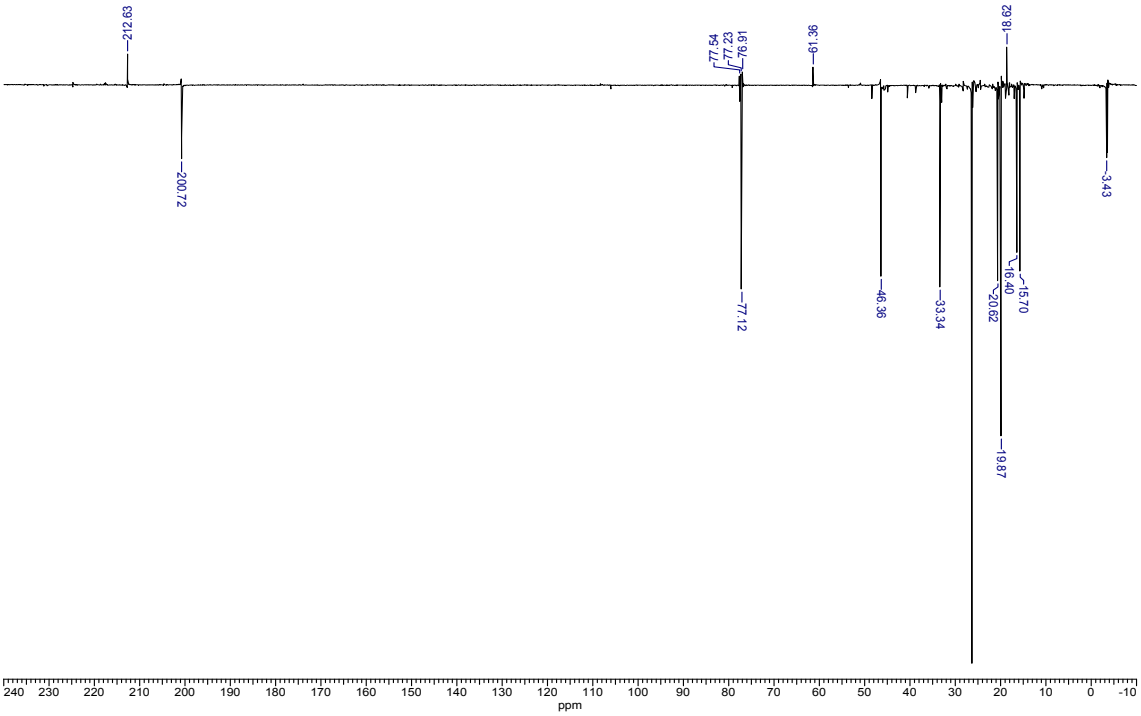
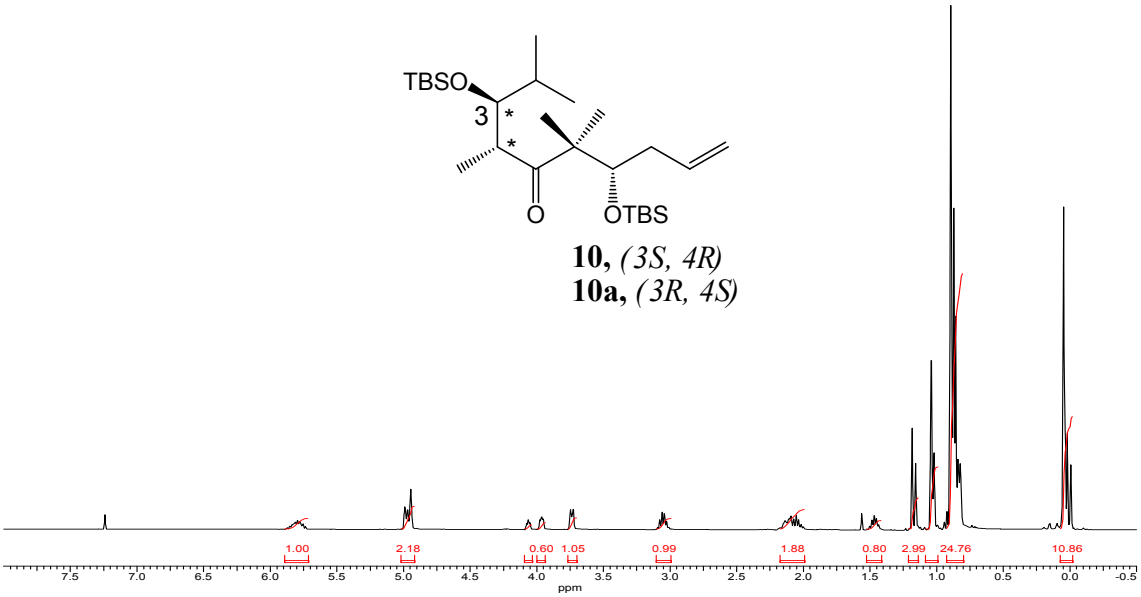
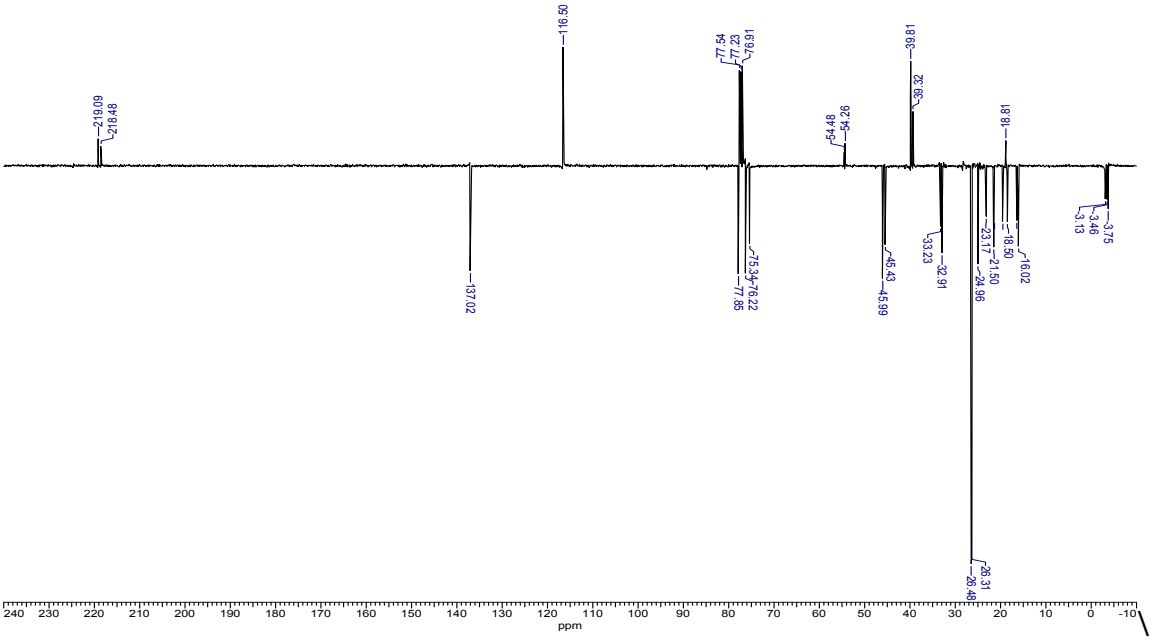


^{1}H NMR of (*3S,4R,7S*)-3,7-bis-(*tert*-butyldimethylsilyloxy)-2,4,6,6-tetramethyldec-9-en-5-one and (*3R,4S,7S*)- 3,7-bis-(*tert*-butyldimethylsilyloxy)-2,4,6,6-tetramethyldec-9-en-5-one (10 and 10a)

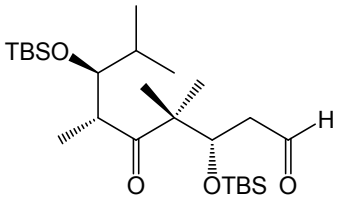


10, *(3S, 4R)*
10a, *(3R, 4S)*

^{13}C NMR of (*3S,4R,7S*)-3,7-bis-(*tert*-butyldimethylsilyloxy)-2,4,6,6-tetramethyldec-9-en-5-one and (*3R,4S,7S*)- 3,7-bis-(*tert*-butyldimethylsilyloxy)-2,4,6,6-tetramethyldec-9-en-5-one (10 and 10a)

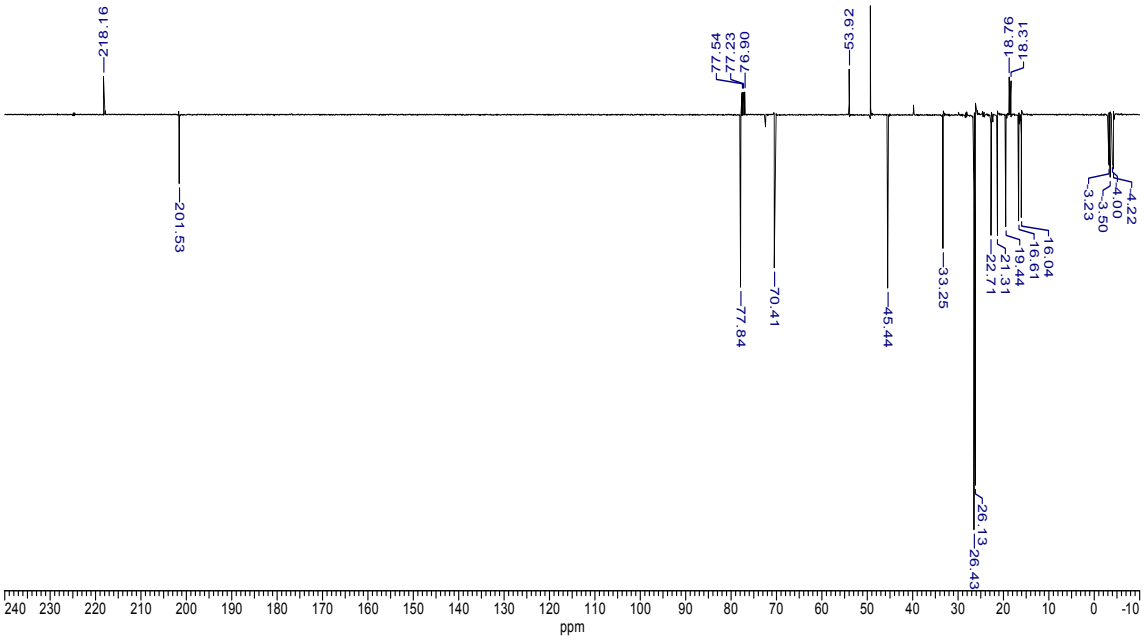


^{1}H NMR of (*3S,6R,7S*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanal (11)

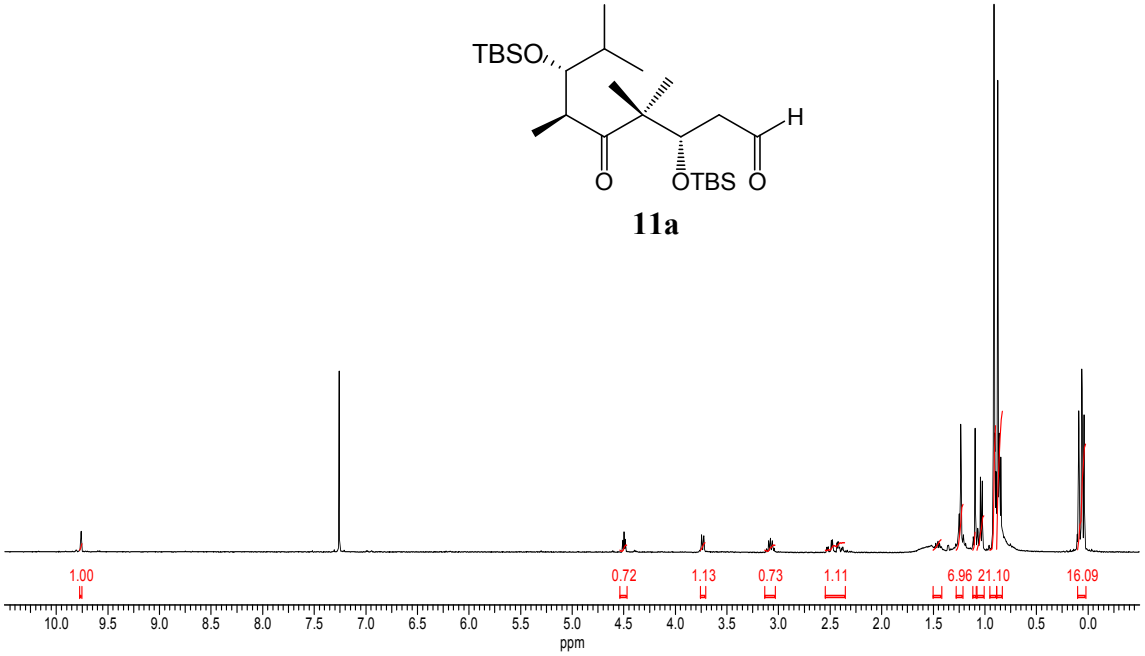


11

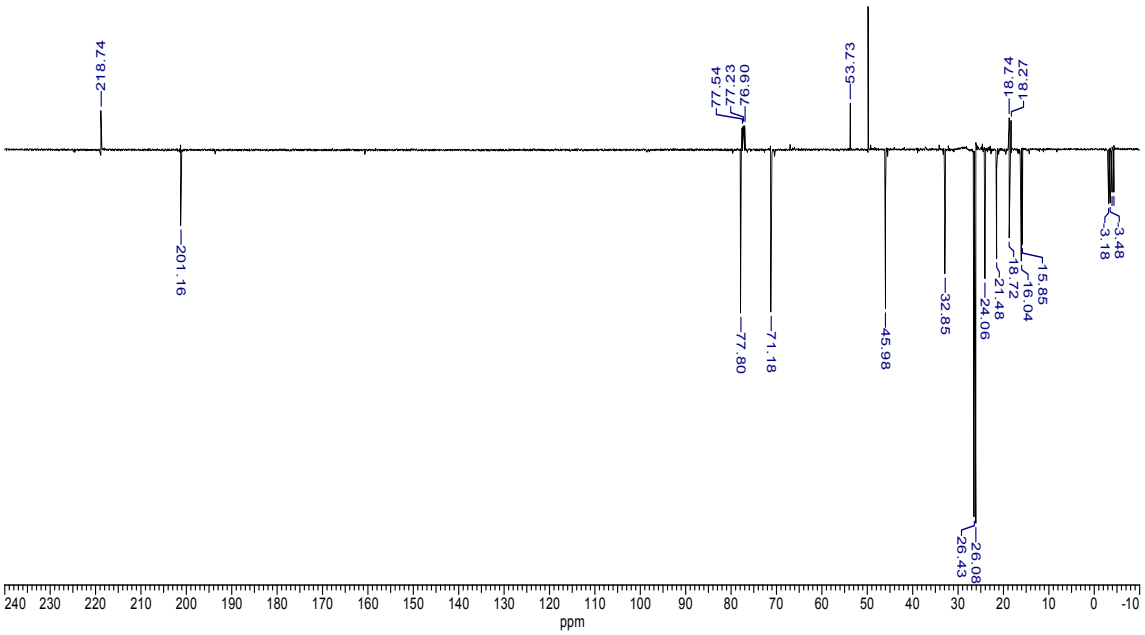
^{13}C NMR of (*3S,6R,7S*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanal (11)



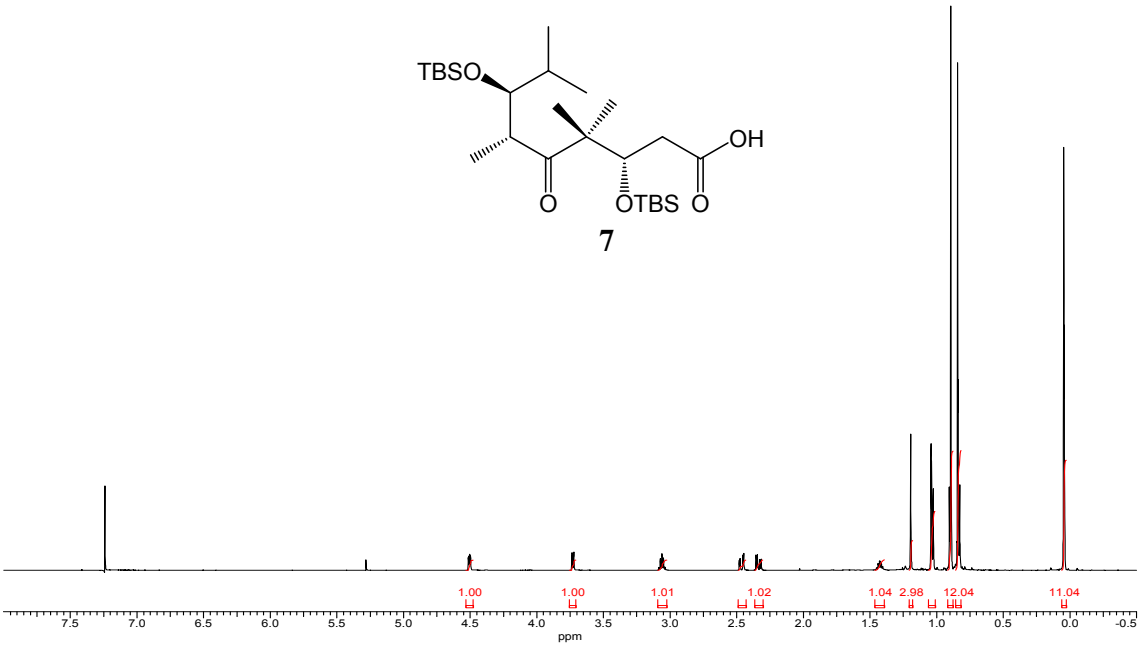
^{1}H NMR of (*3S,6S,7R*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanal (11a)



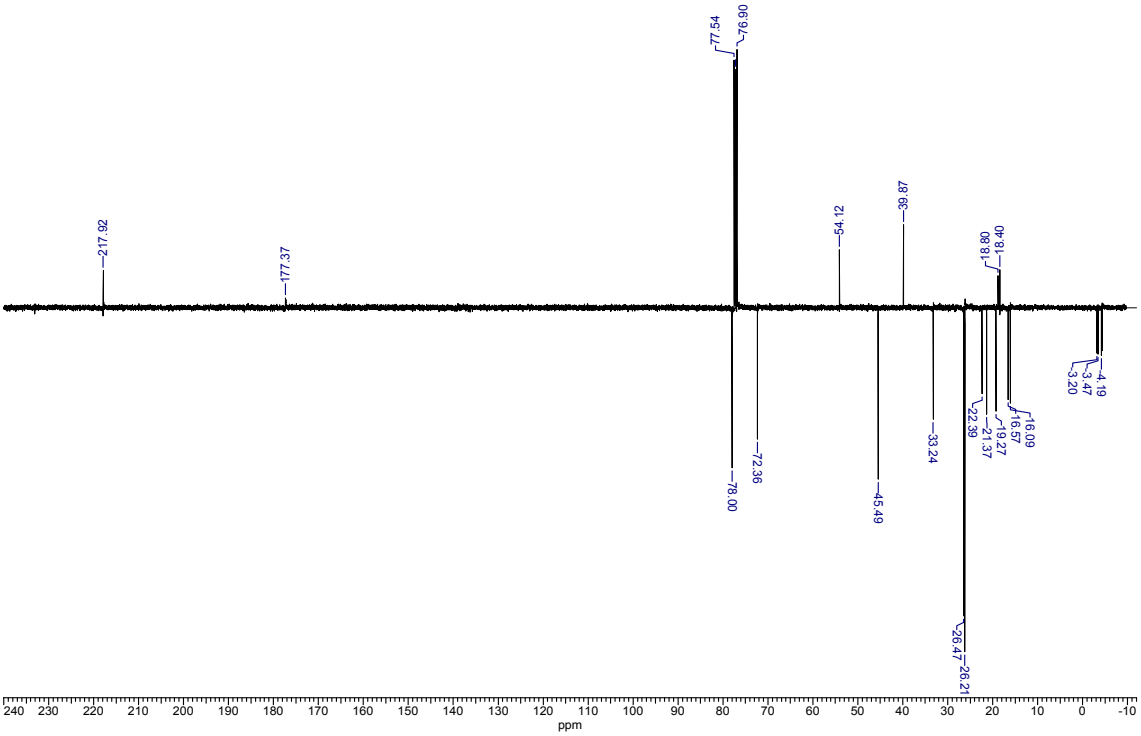
^{13}C NMR of (*3S,6S,7R*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanal (11a)



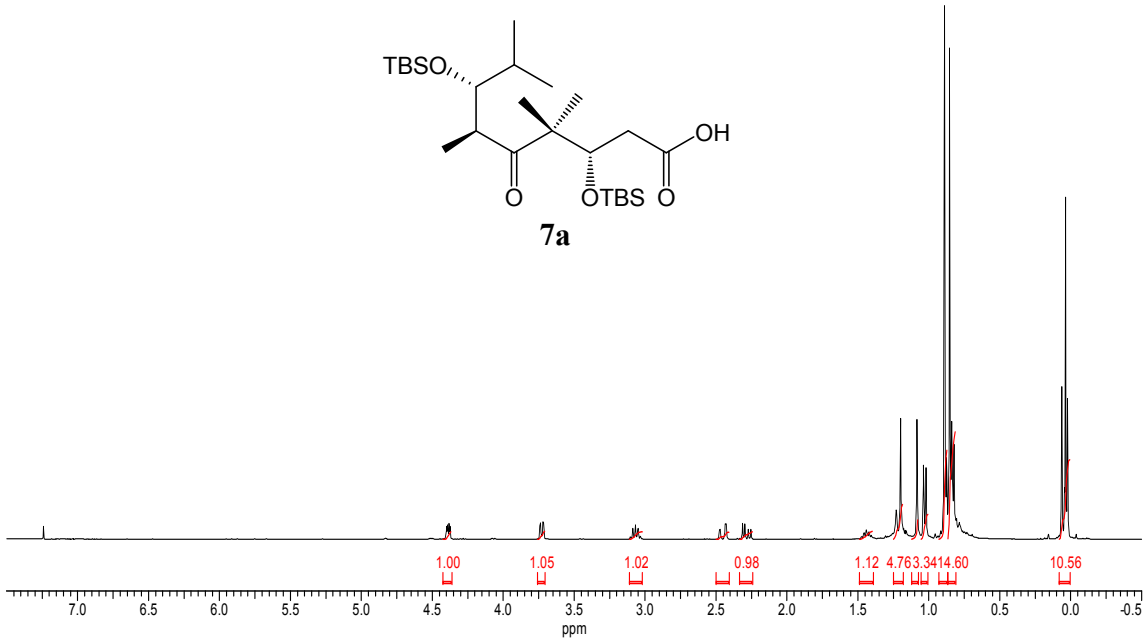
^{1}H NMR of (*3S,6R,7S*)-3,7-bis(*tert*-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanoic acid (7)



^{13}C NMR of (*3S,6R,7S*)-3,7-bis(*tert*-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanoic acid (7)

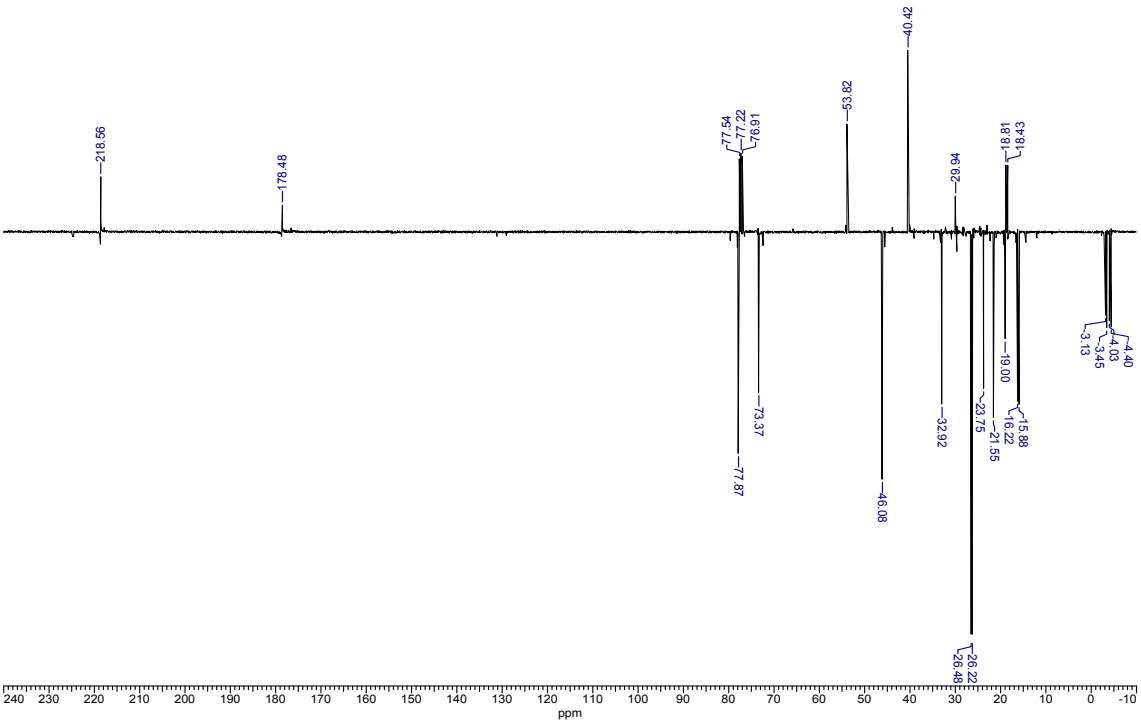


^{1}H NMR of (*3S,6S,7R*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanoic acid (7a)

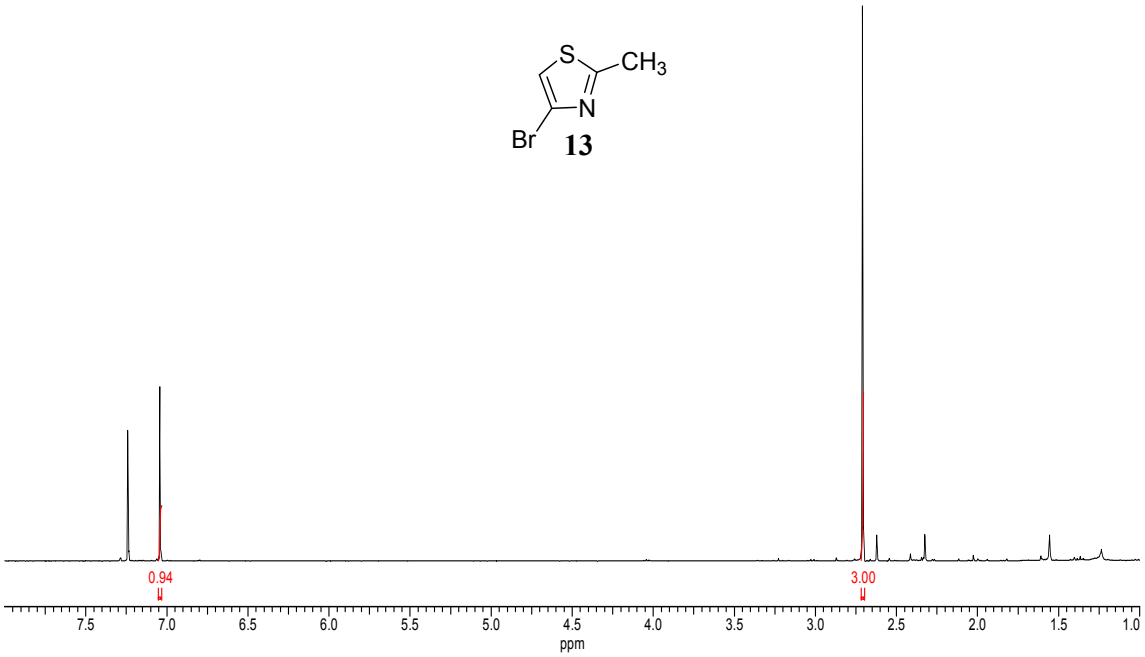


7a

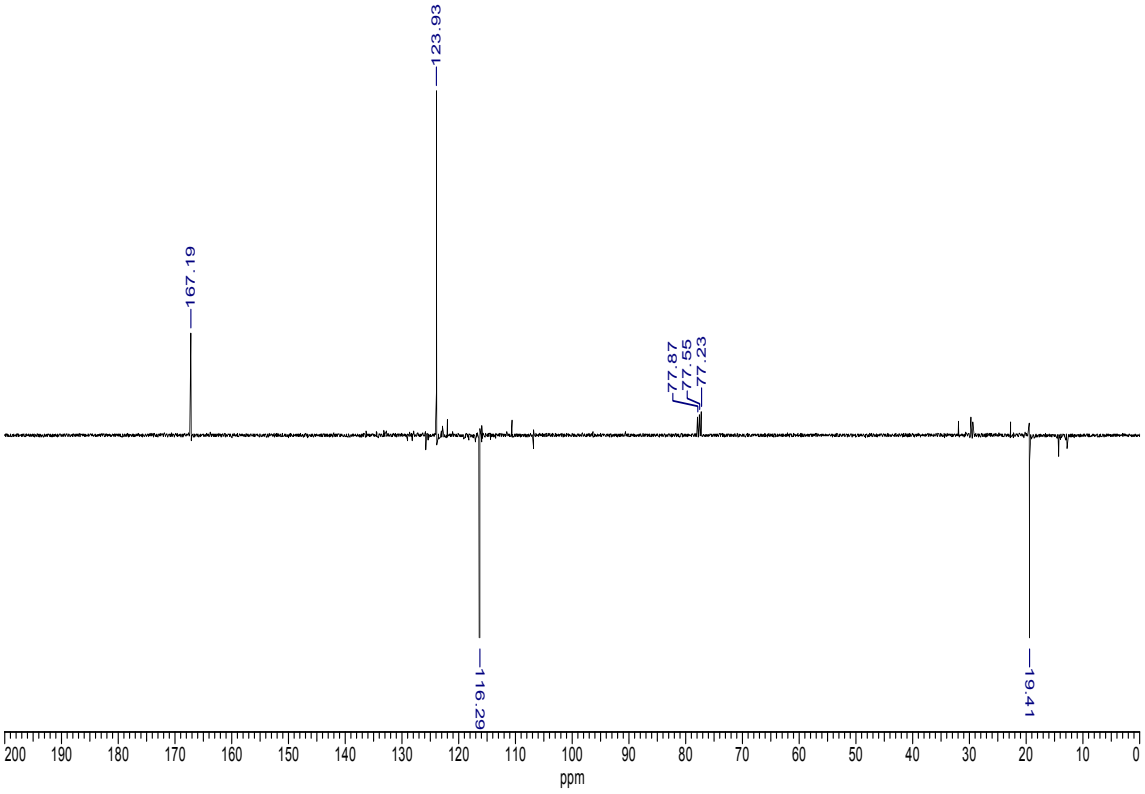
^{13}C NMR of (*3S,6S,7R*)-3,7-bis(tert-butyldimethylsilyloxy)-4,4,6,8-tetramethyl-5-oxononanoic acid (7a)



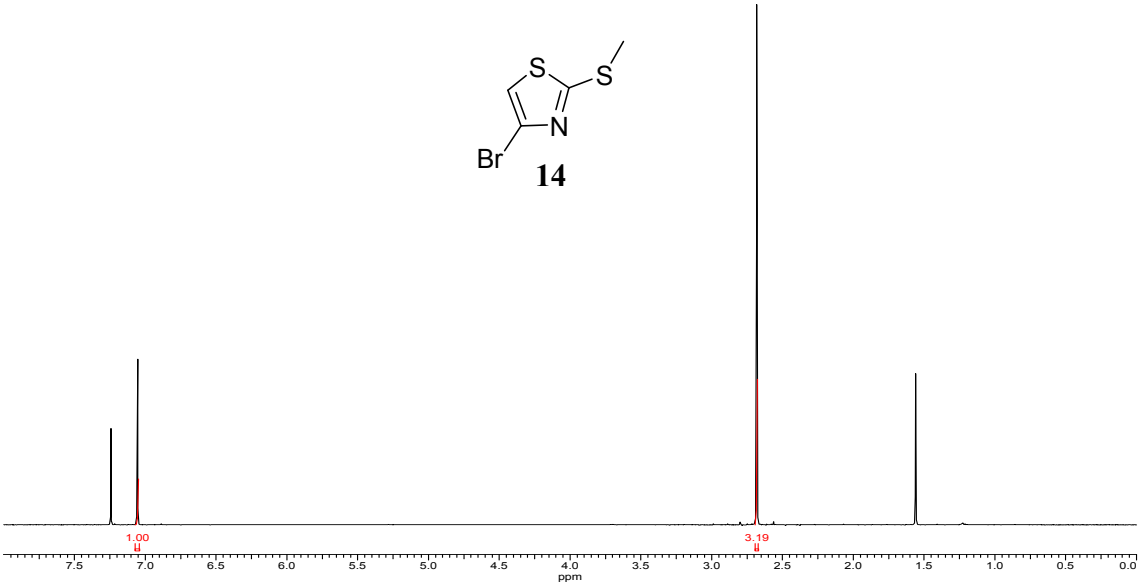
^{1}H NMR of 2-methyl-4-bromothiazole (13)



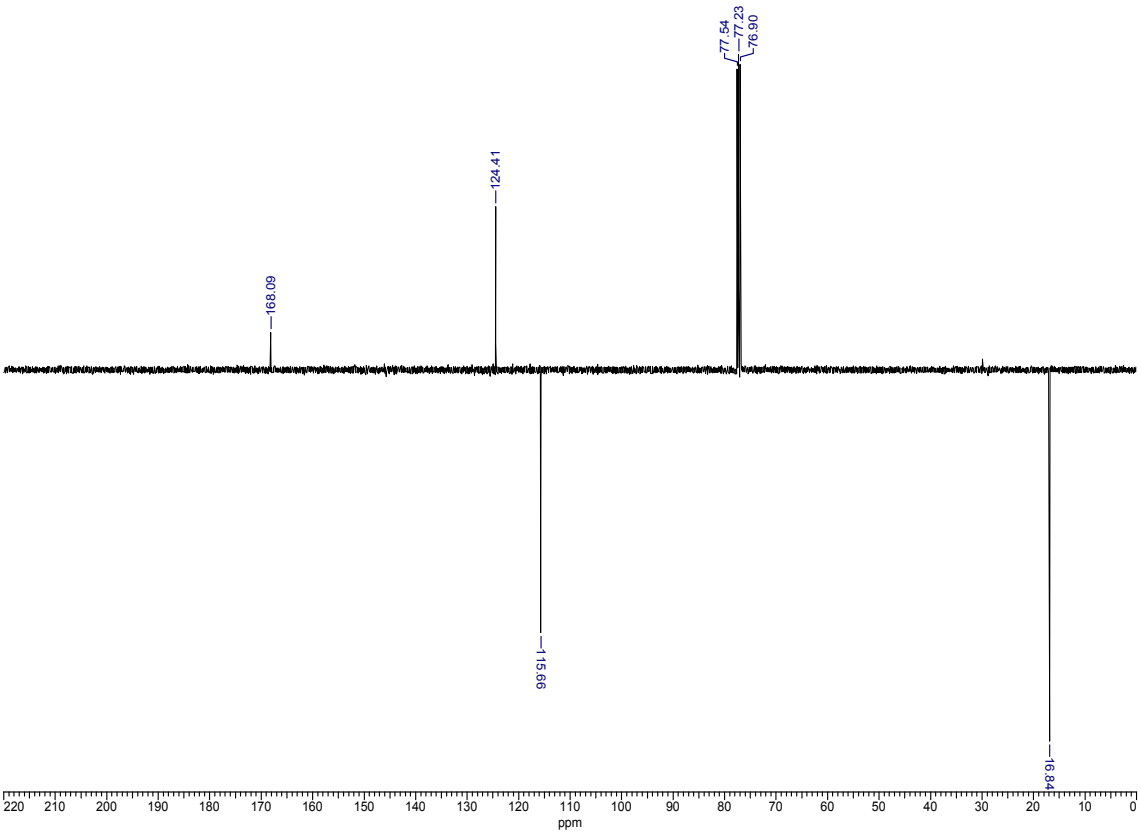
^{13}C NMR of 2-methyl-4-bromothiazole (13)



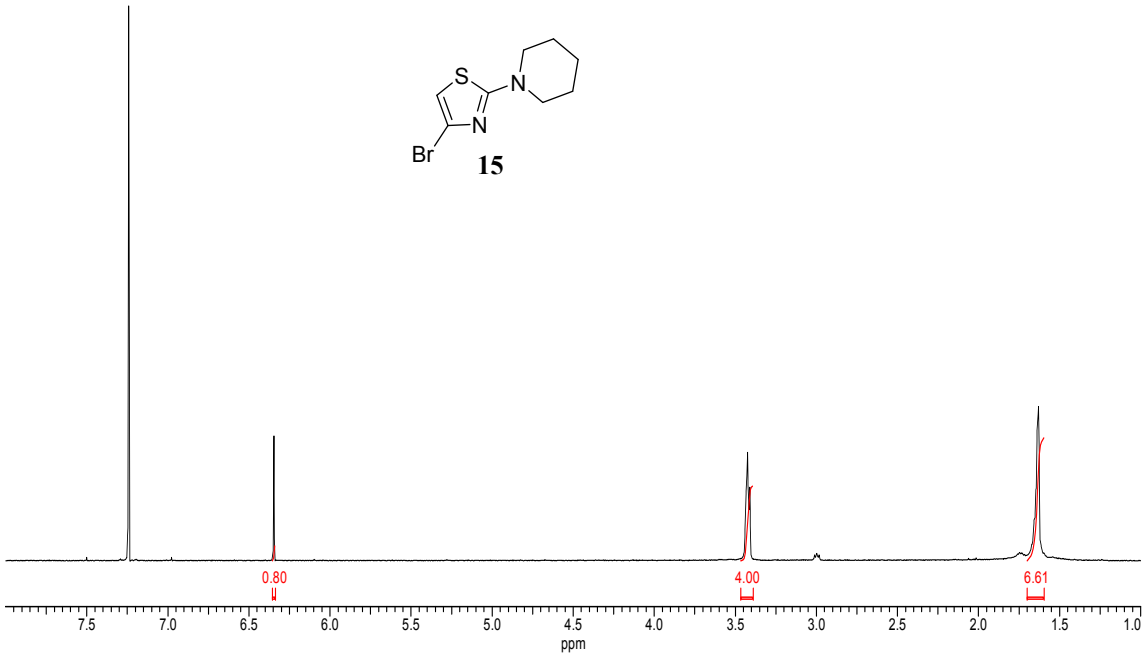
^{1}H NMR of 2-(methylthio)-4-bromothiazole (14)



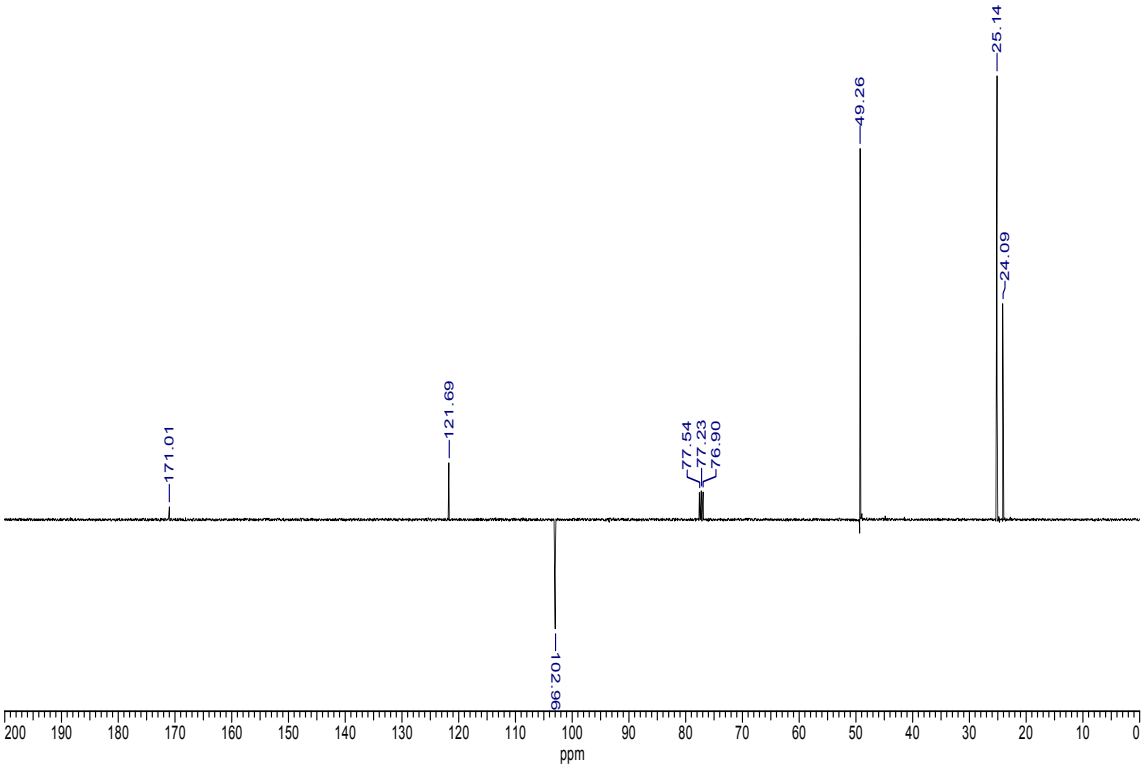
^{13}C NMR of 2-(methylthio)-4-bromothiazole (14)



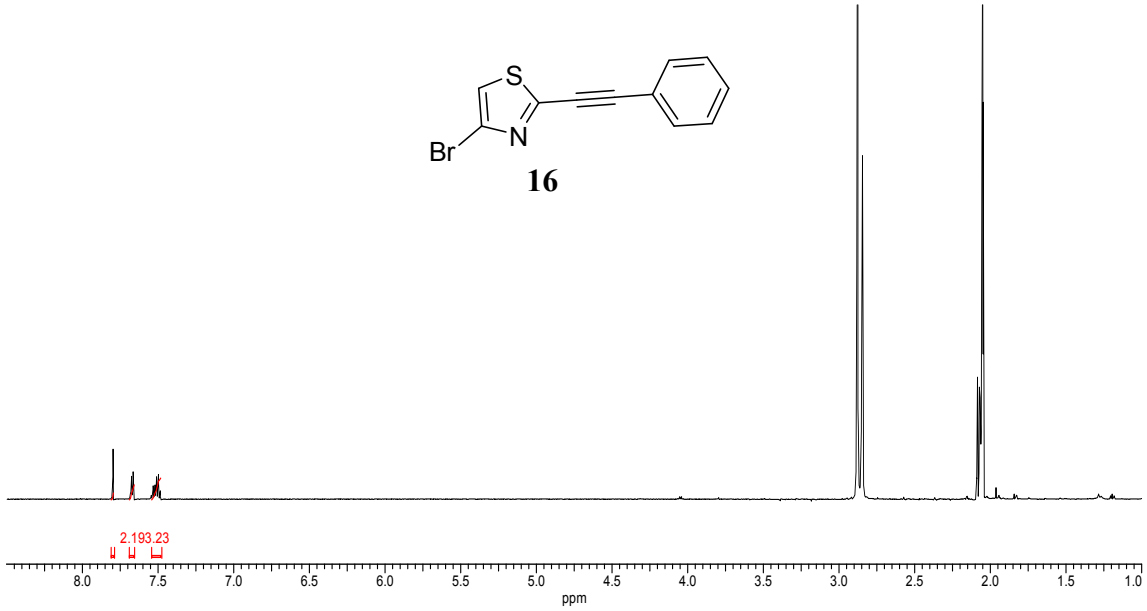
^{1}H NMR of 2-(piperidin-1-yl)-4-bromothiazole (15)



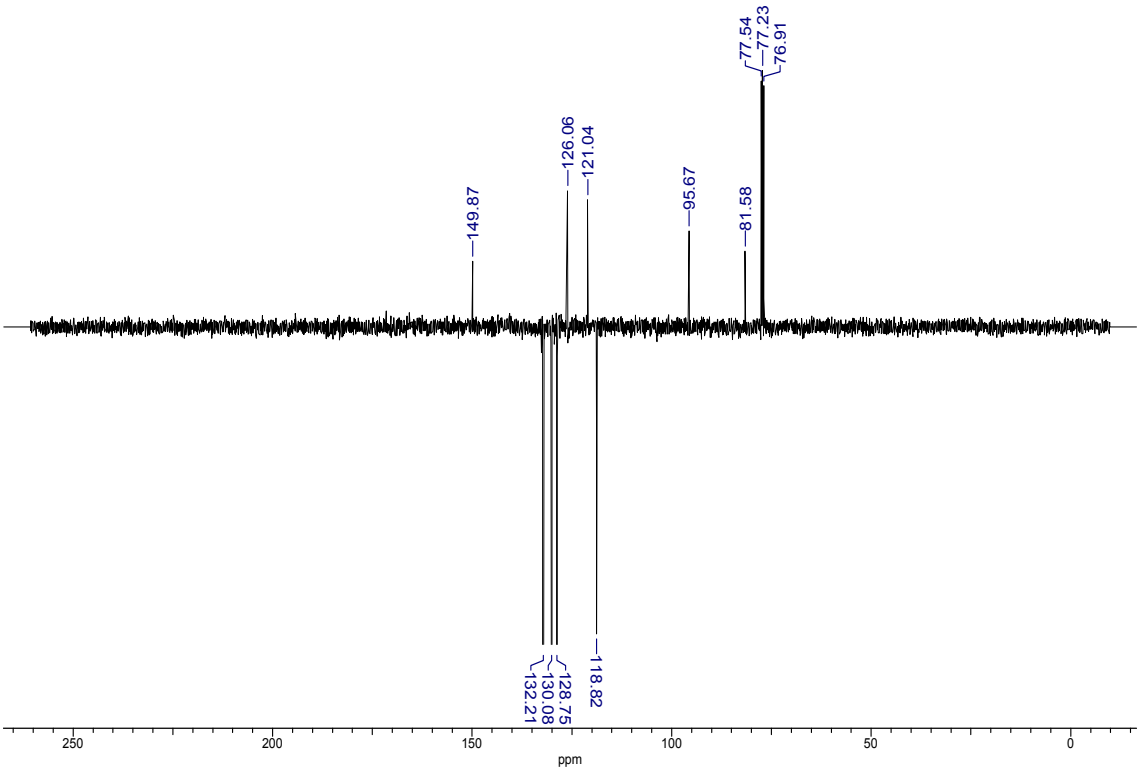
^{13}C NMR of 2-(piperidin-1-yl)-4-bromothiazole (15)



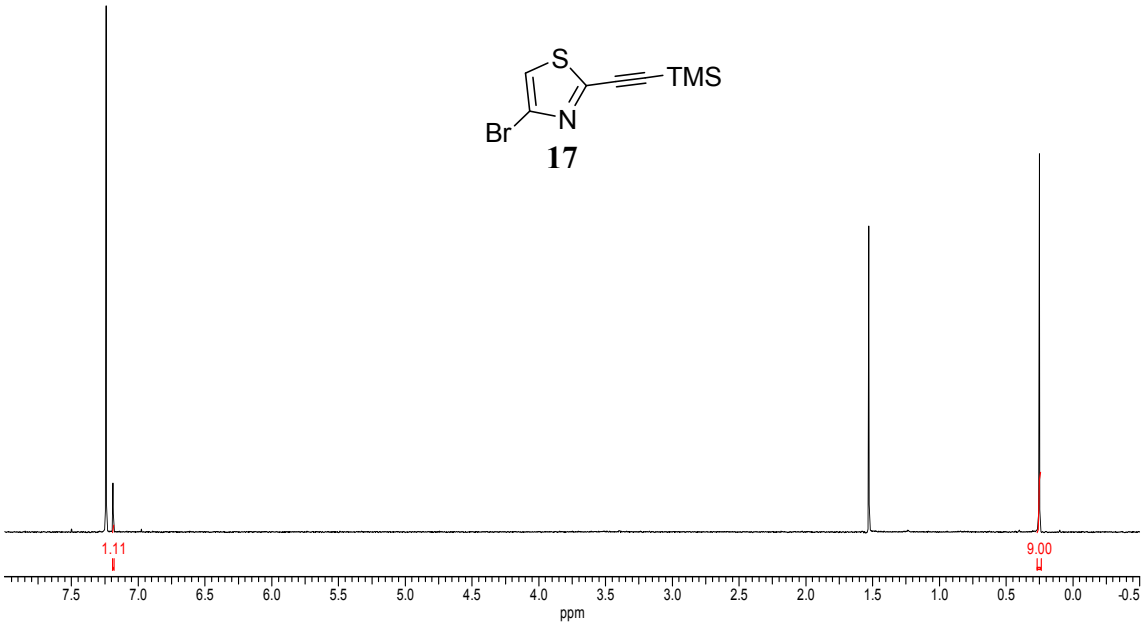
^{1}H NMR of 2-(phenylethynyl)-4-bromothiazole (16)



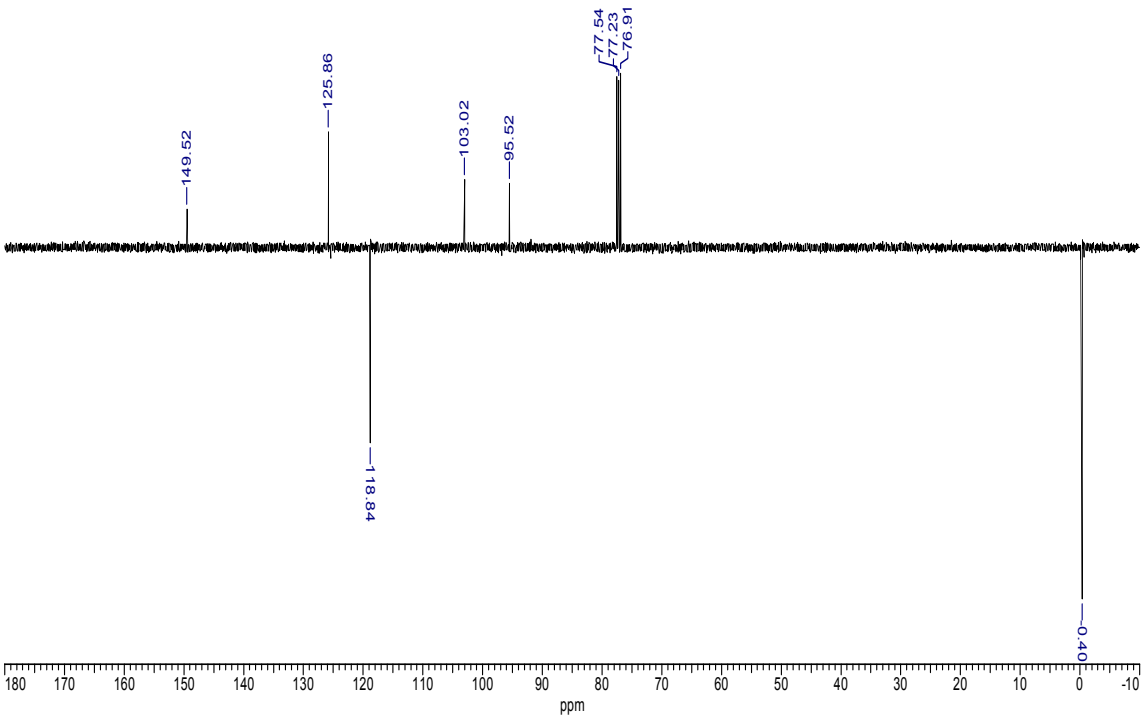
^{13}C NMR of 2-(phenylethynyl)-4-bromothiazole (16)



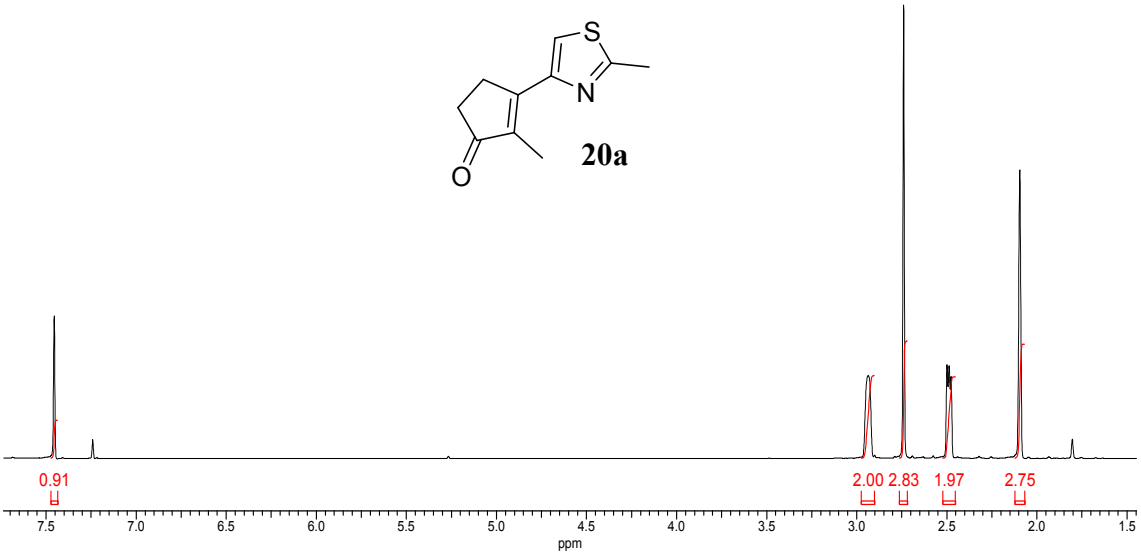
^{1}H NMR of 2–((trimethylsilyl)ethynyl)-4-bromothiazole (17)



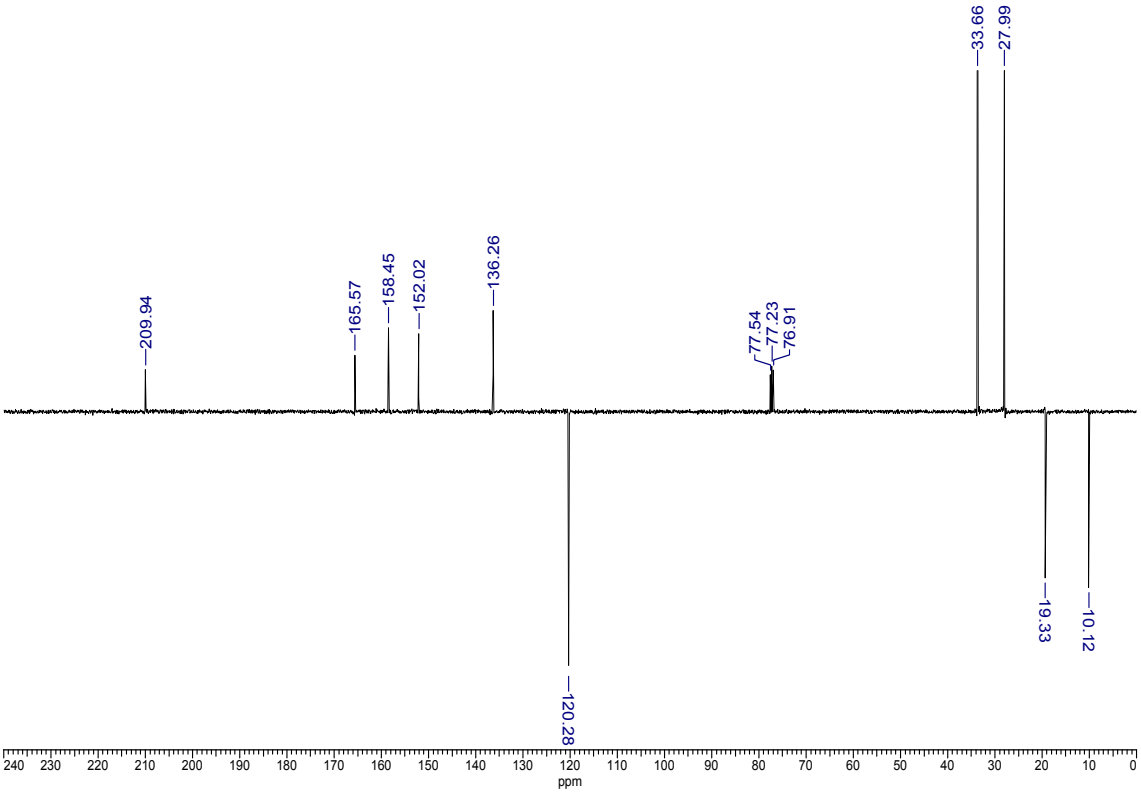
^{13}C NMR of 2–((trimethylsilyl)ethynyl)-4-bromothiazole (17)



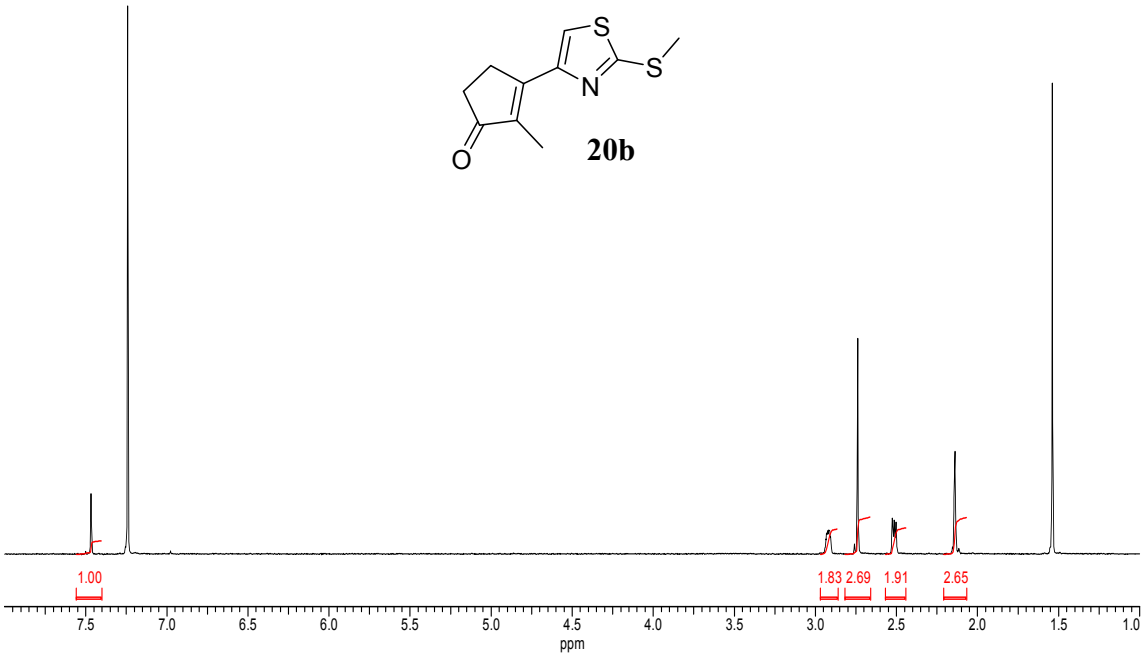
^{1}H NMR of 2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enone (20a)



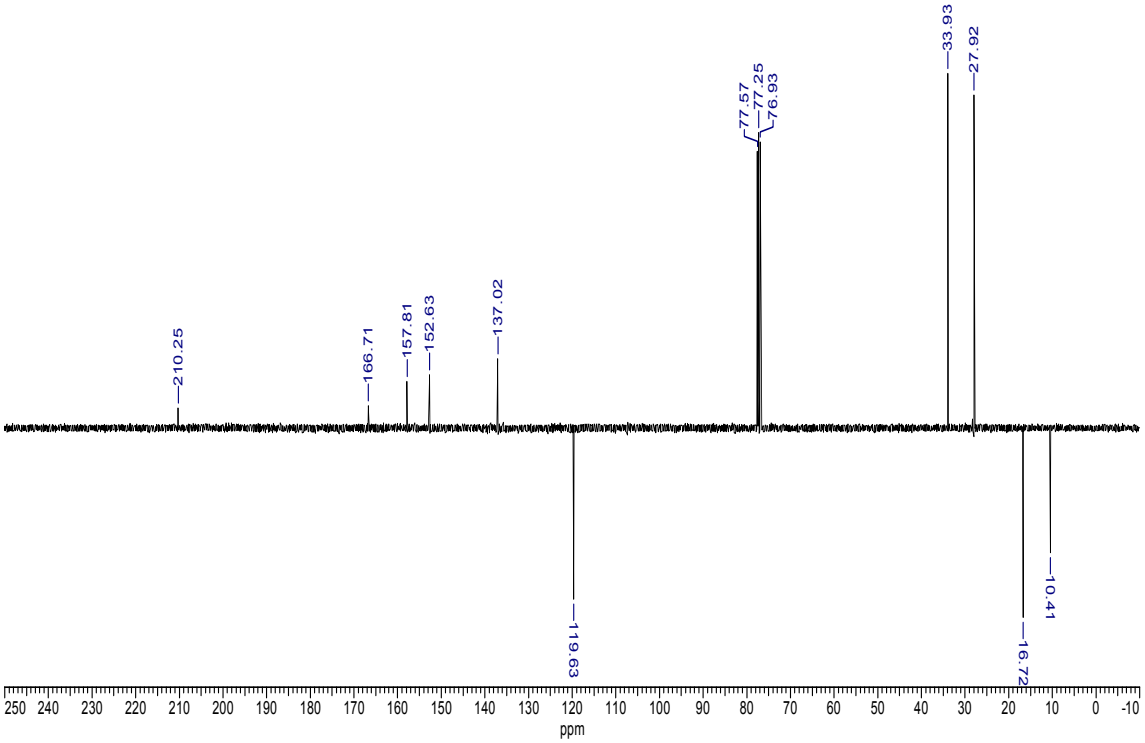
^{13}C NMR of 2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enone (20a)



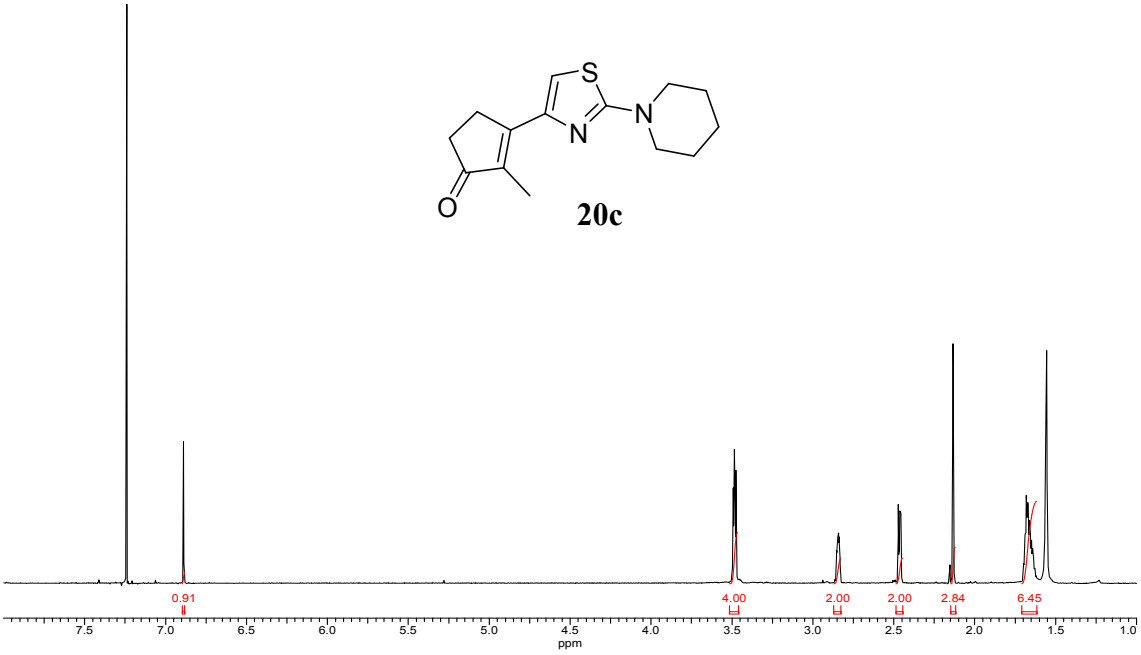
^{1}H NMR of 2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enone (20b)



^{13}C NMR of 2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enone (20b)

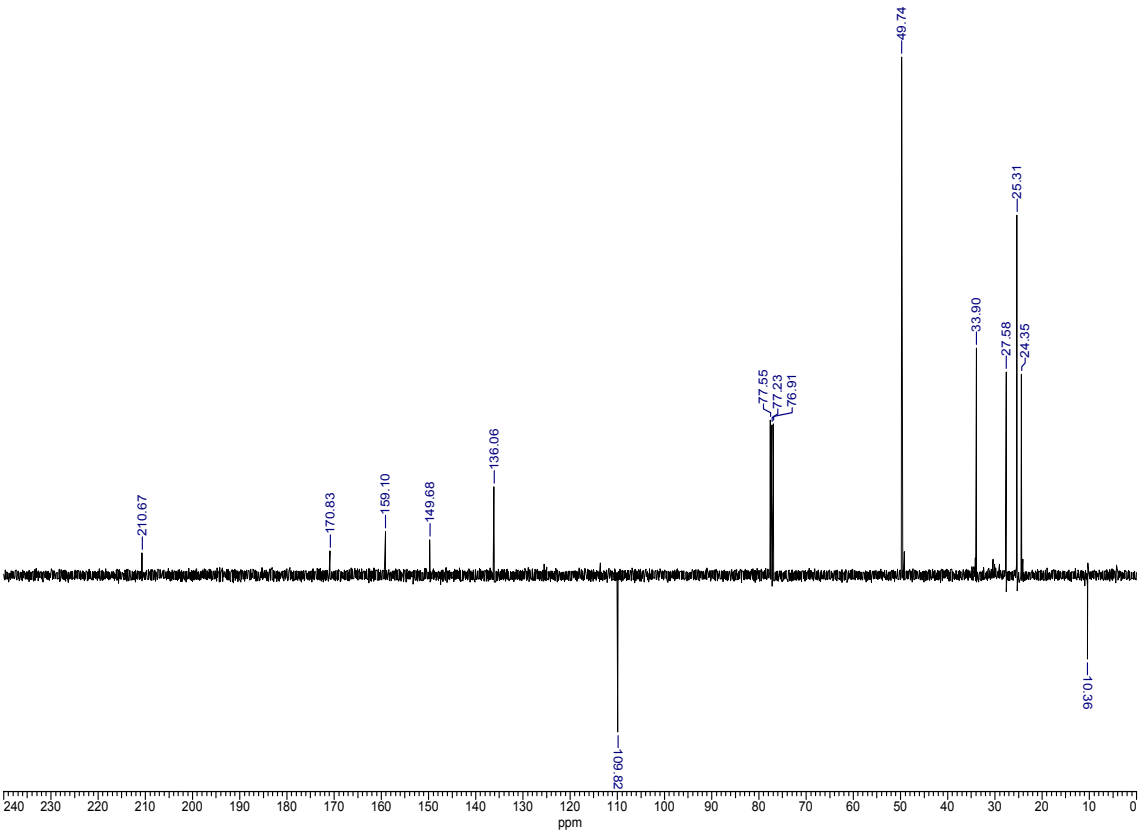


^{1}H NMR of 2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enone (20c)



20c

^{13}C NMR of 2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enone (20c)



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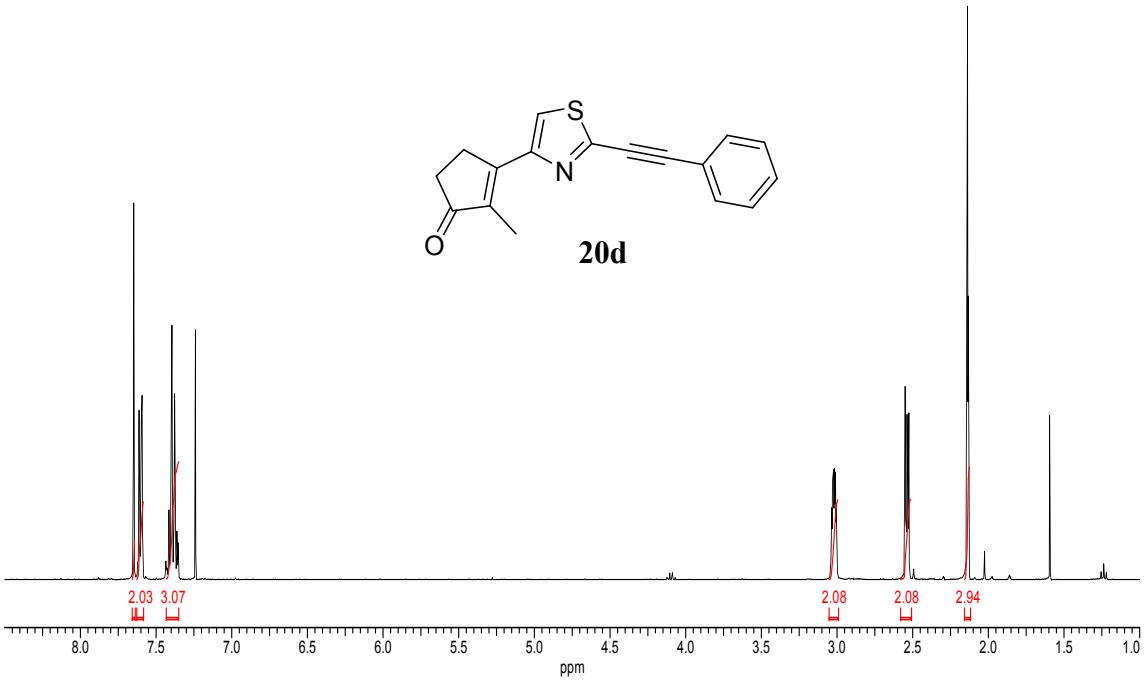
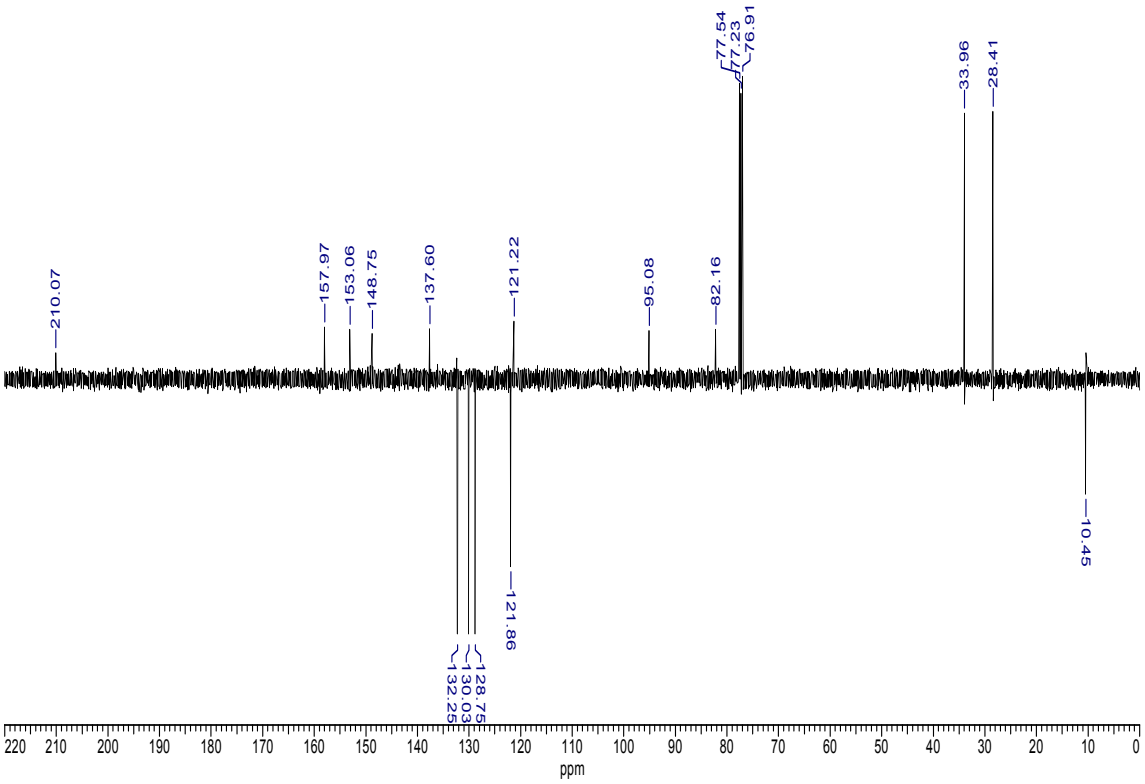
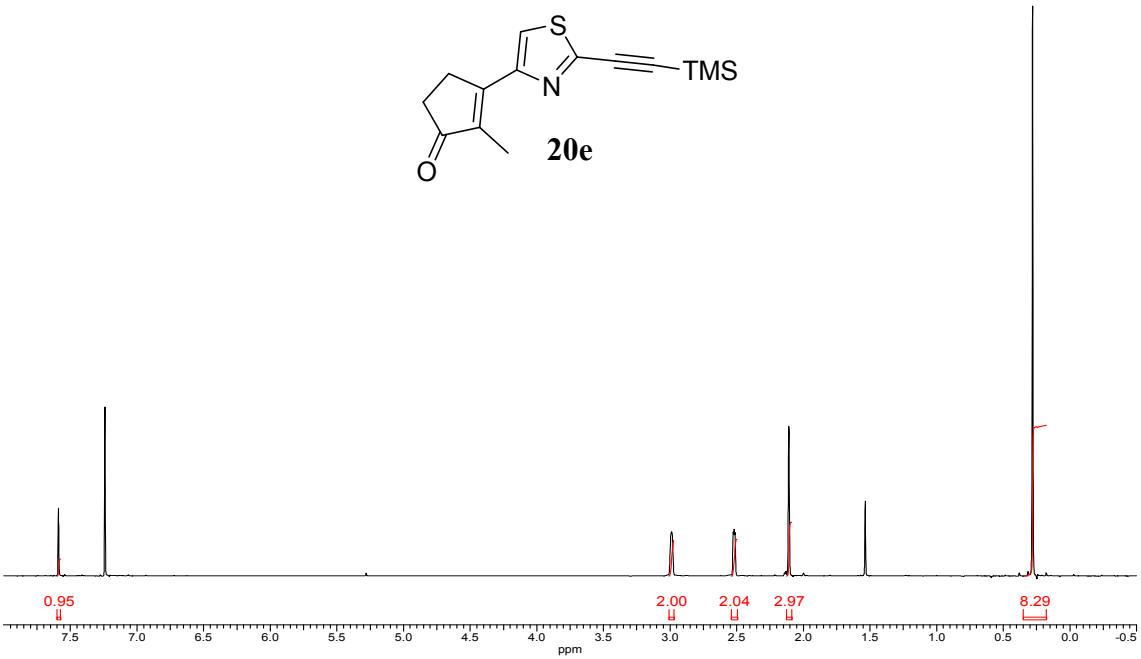


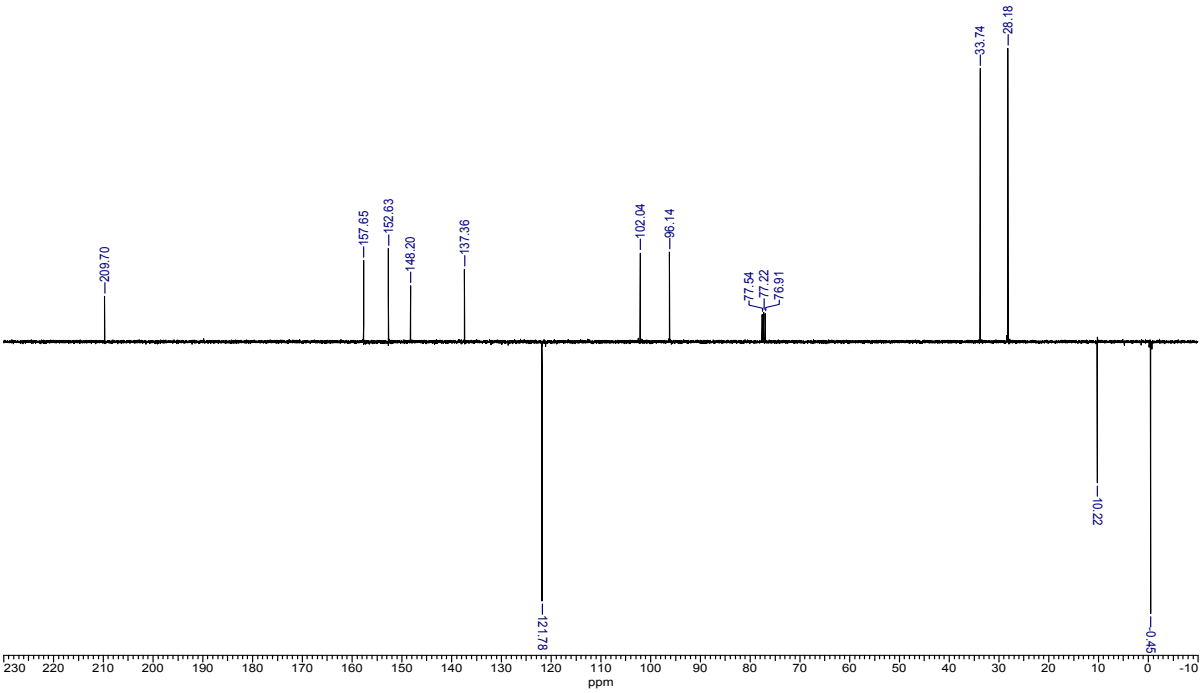
[13]C NMR of 2-methyl-3-(2-(phenylethynyl)thiazol-4-yl)cyclopent-2-enone (20d)



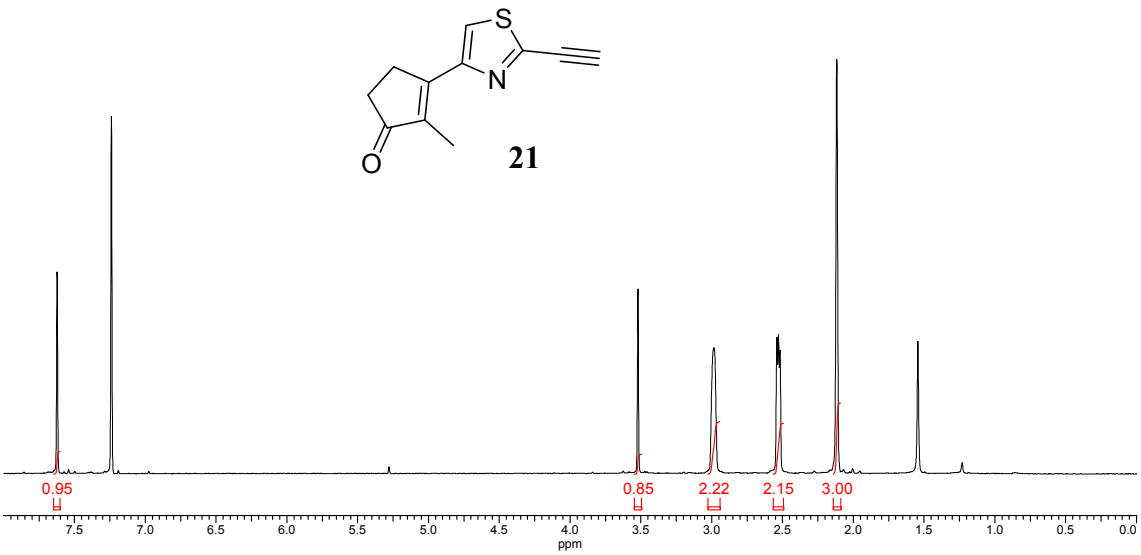
^{1}H NMR of 2-methyl-3-(2-((trimethylsilyl)ethynyl)thiazol-4-yl)cyclopent-2-enone (20e)



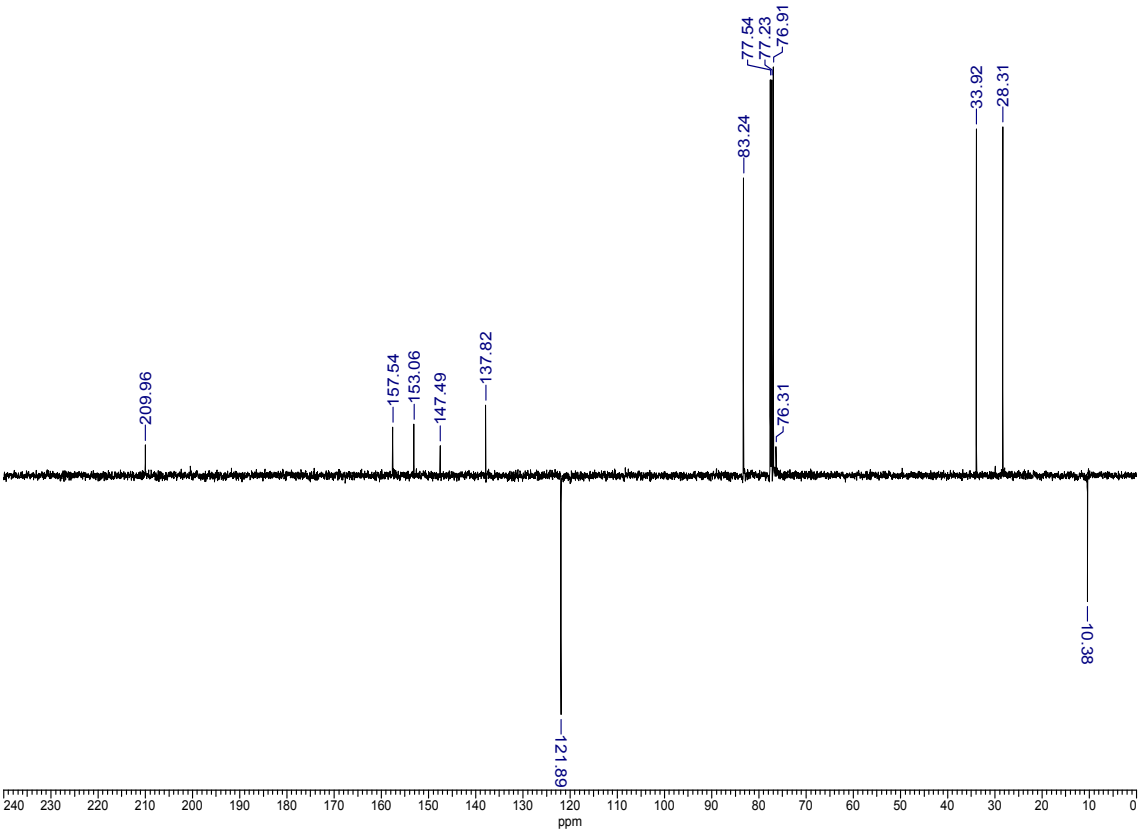
^{13}C NMR of 2-methyl-3-(2-((trimethylsilyl)ethynyl)thiazol-4-yl)cyclopent-2-enone (20e)



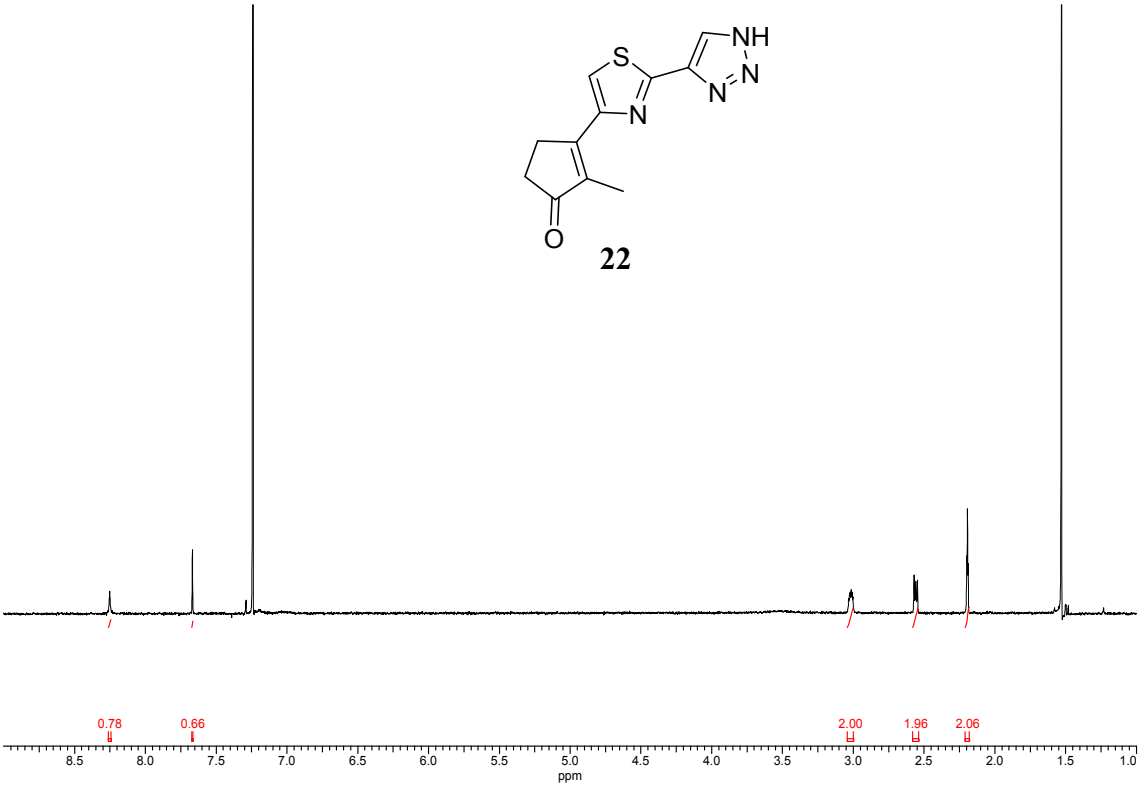
^{1}H NMR of 3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enone (21)



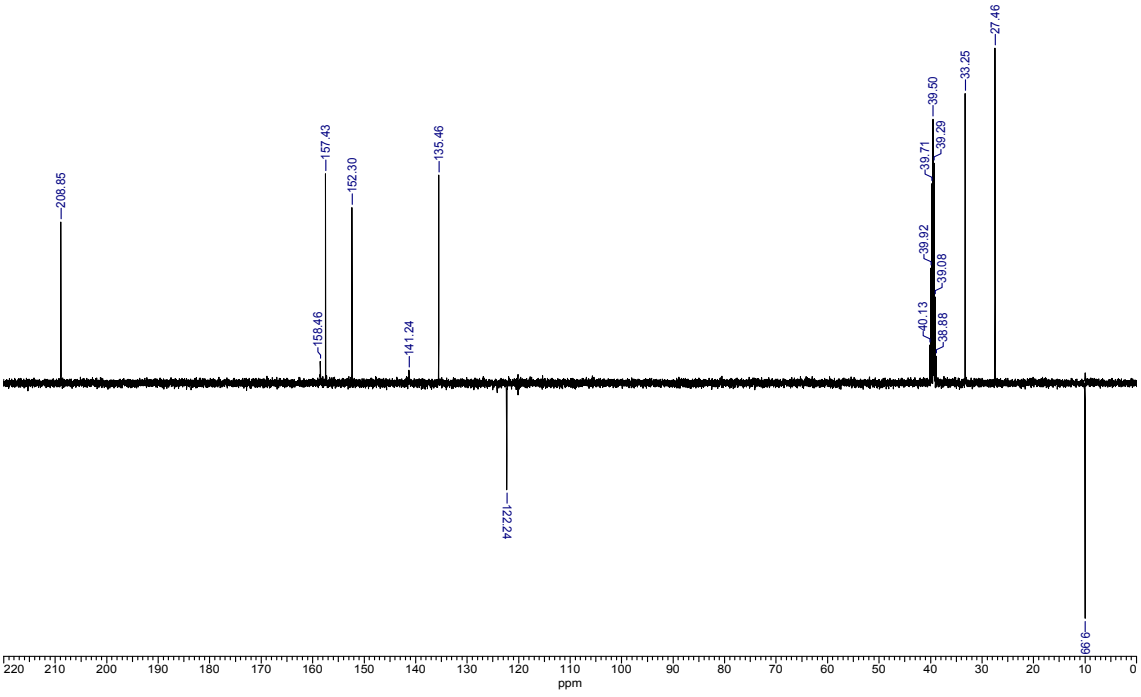
13C NMR of 3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enone (21)



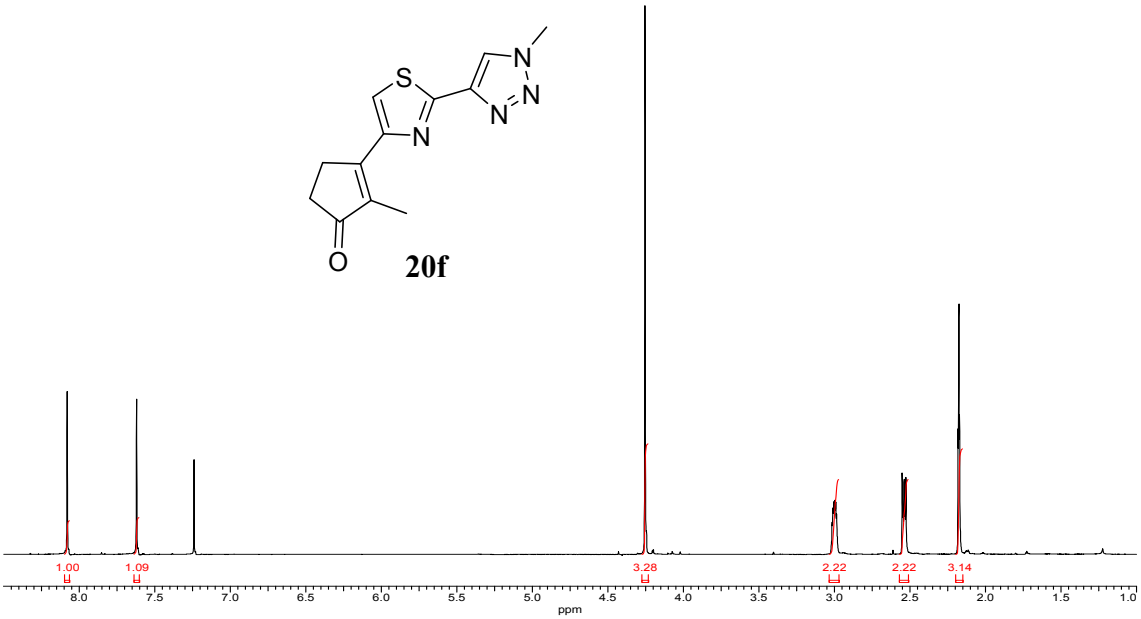
^{1}H NMR of 3-(2-(1H-1,2,3-triazol-4-yl)thiazol-4-yl)-2-methylcyclopent-2-enone (22)



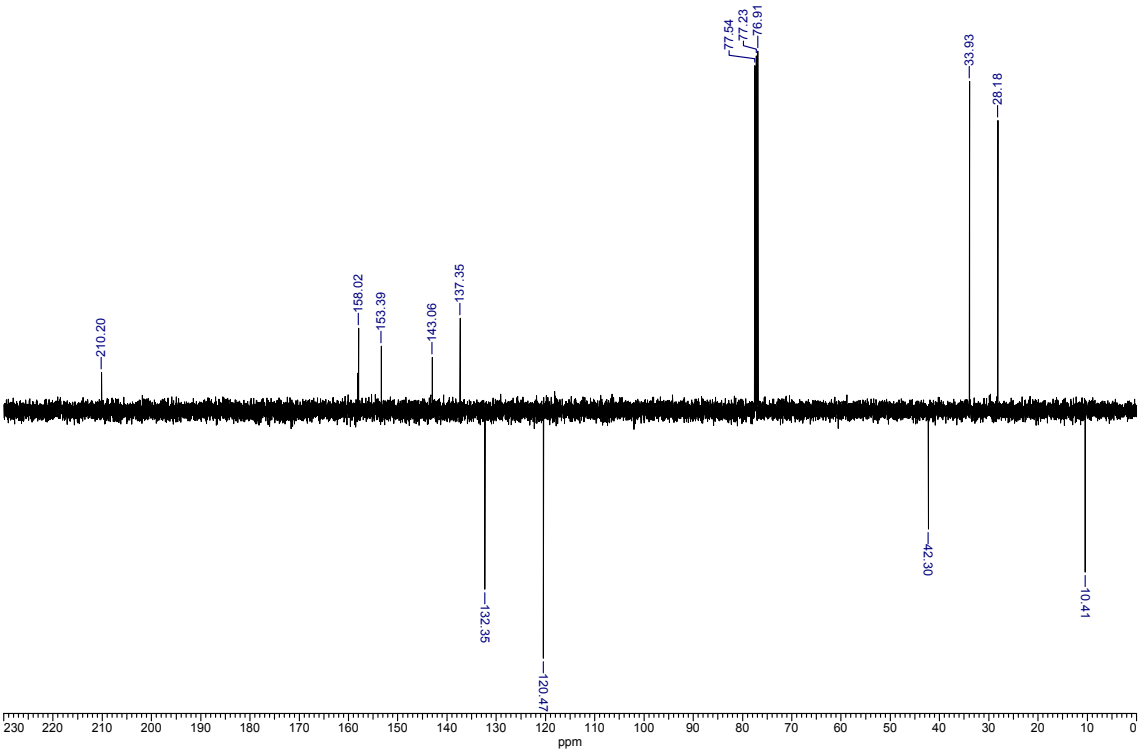
^{13}C NMR of 3-(2-(1H-1,2,3-triazol-4-yl)thiazol-4-yl)-2-methylcyclopent-2-enone (22)



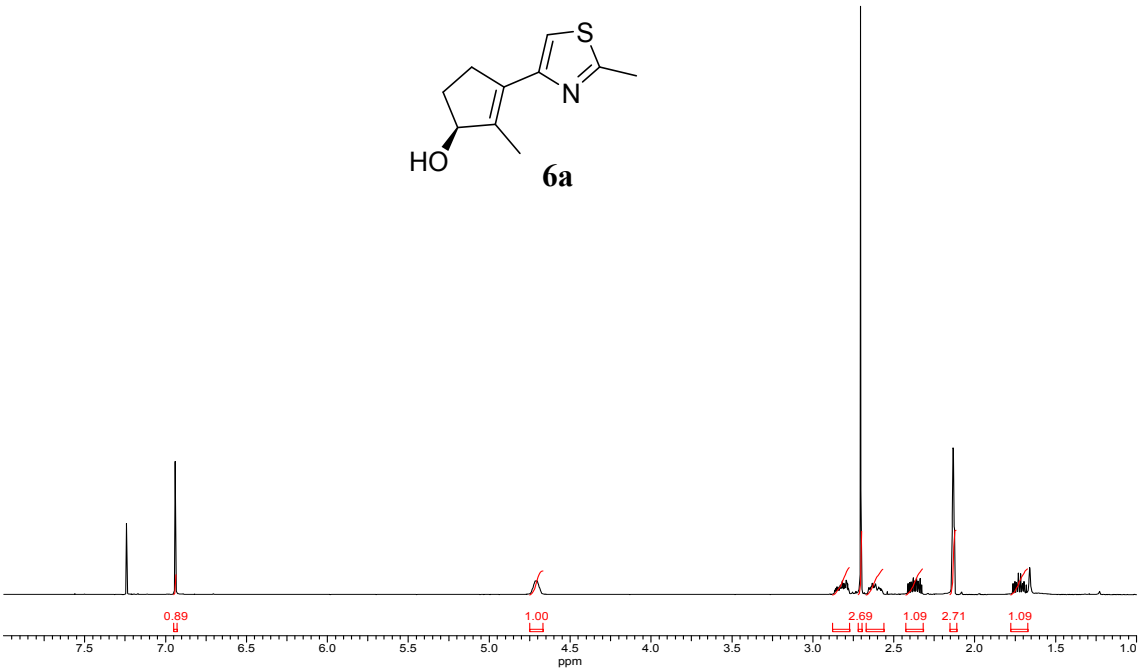
^{1}H NMR of 2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enone (20f)



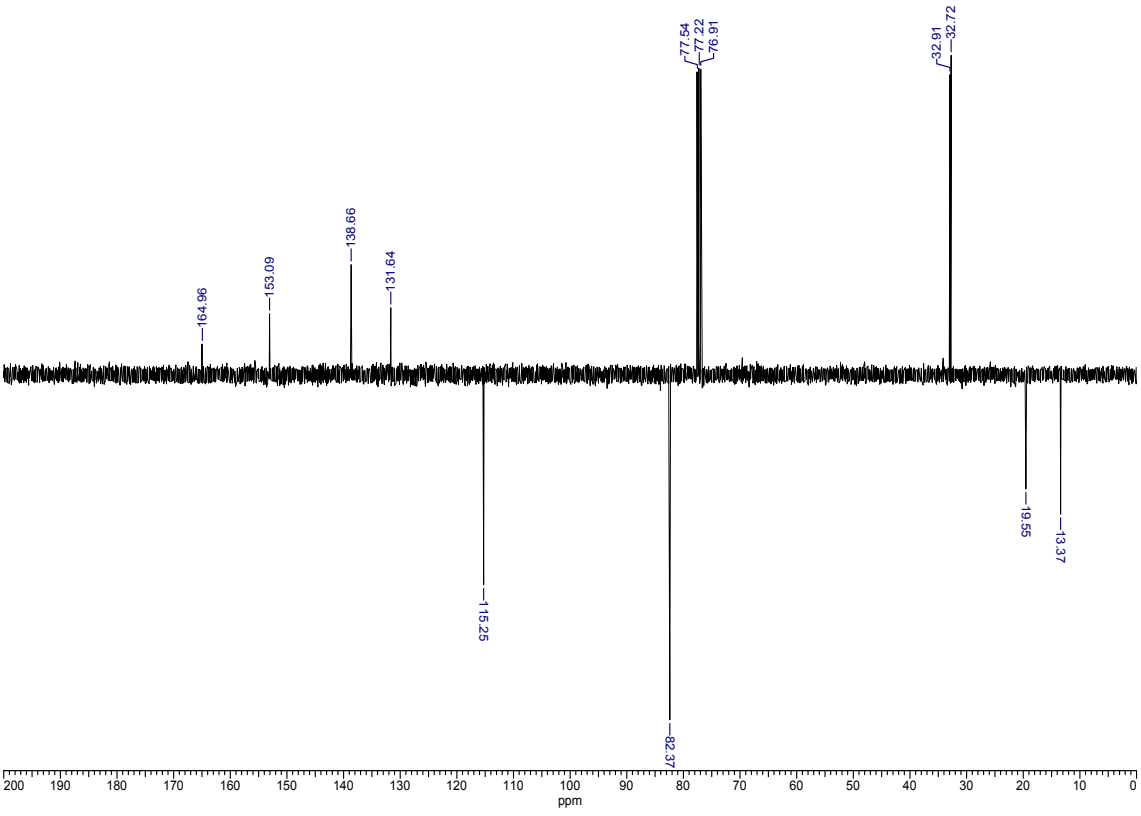
^{13}C NMR of 2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enone (20f)



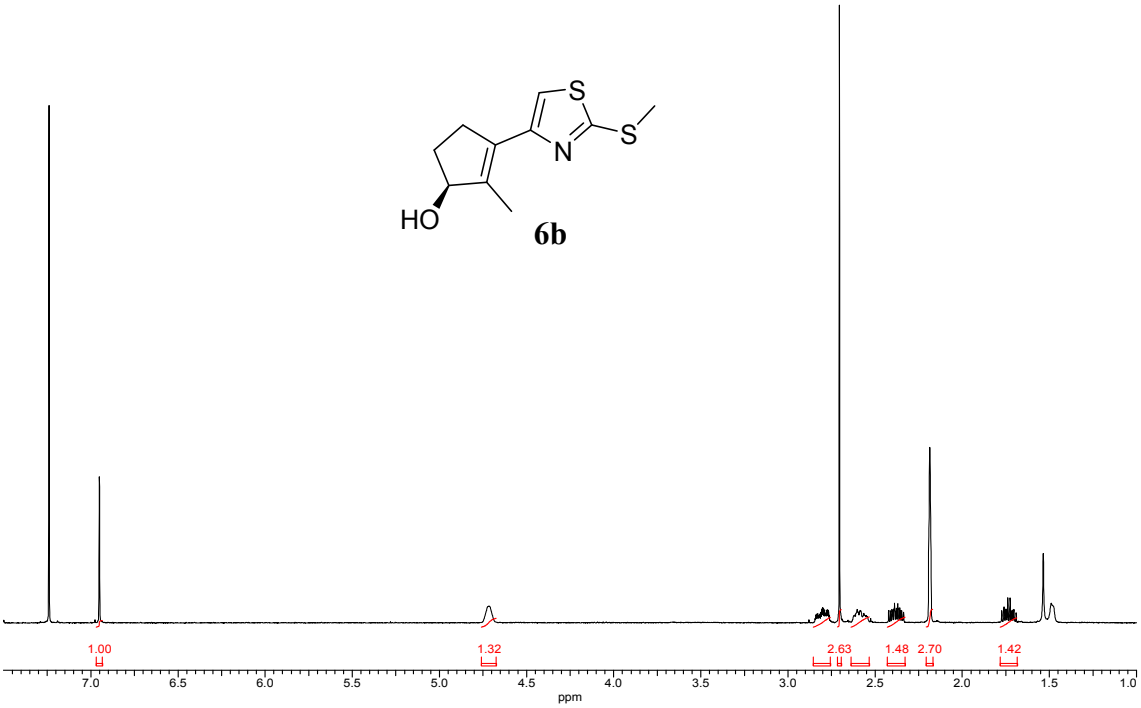
^{1}H NMR of (*S*)-2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enol (6a)



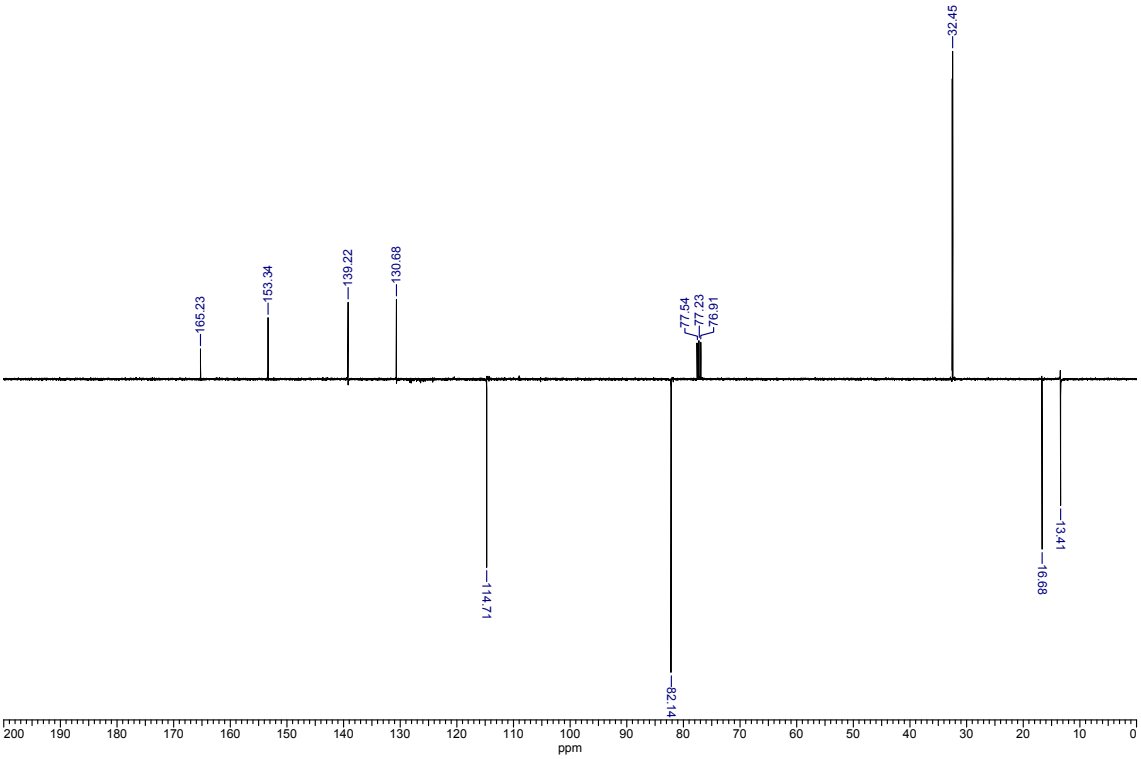
^{13}C NMR of (*S*)-2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enol (6a)



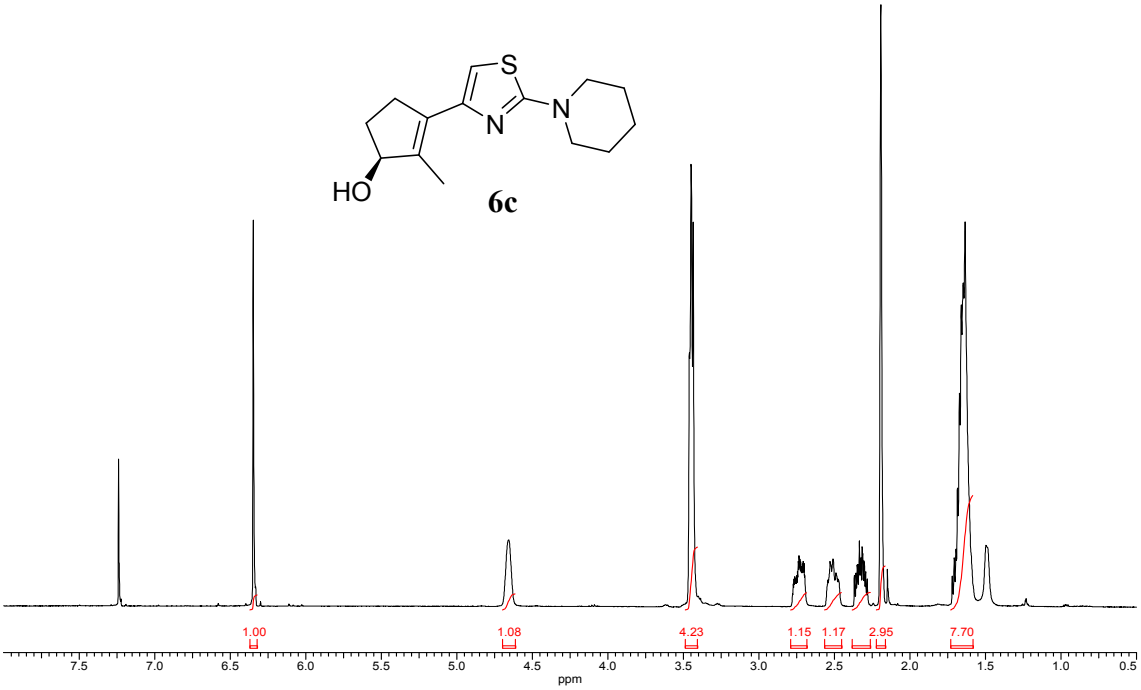
^{1}H NMR of (*S*)-2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enol (6b)



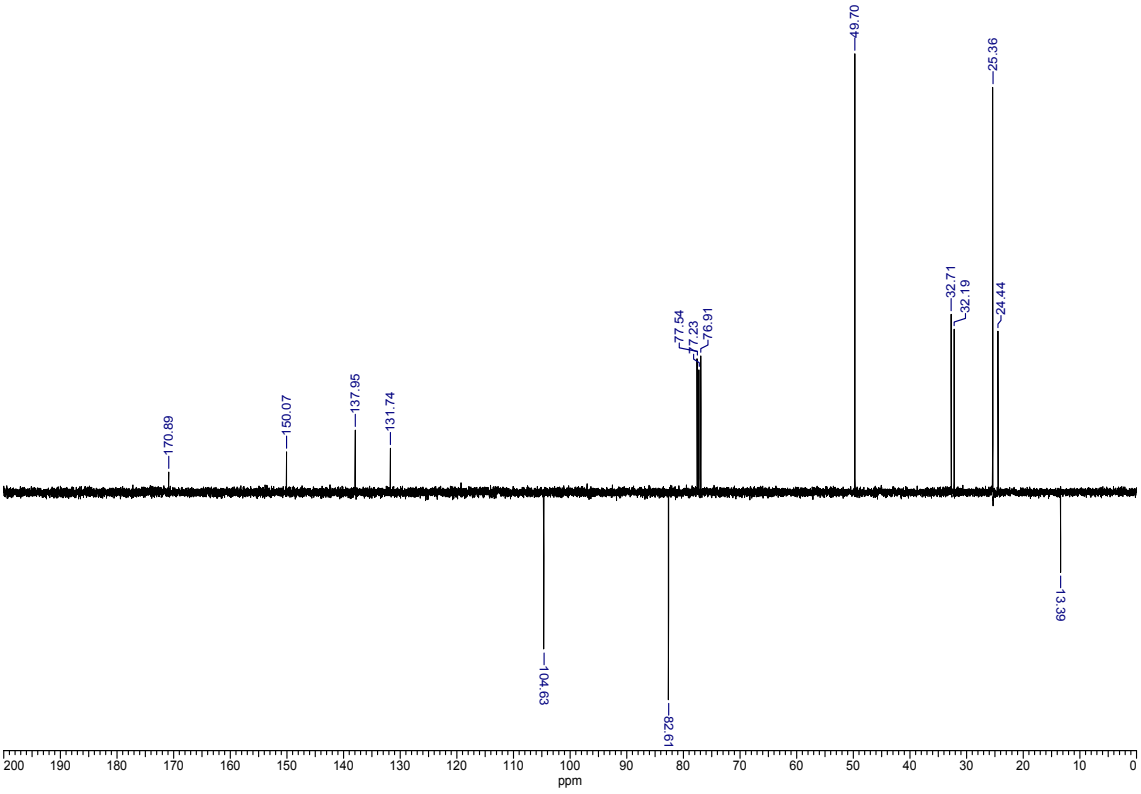
^{13}C NMR of (*S*)-2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enol (6b)



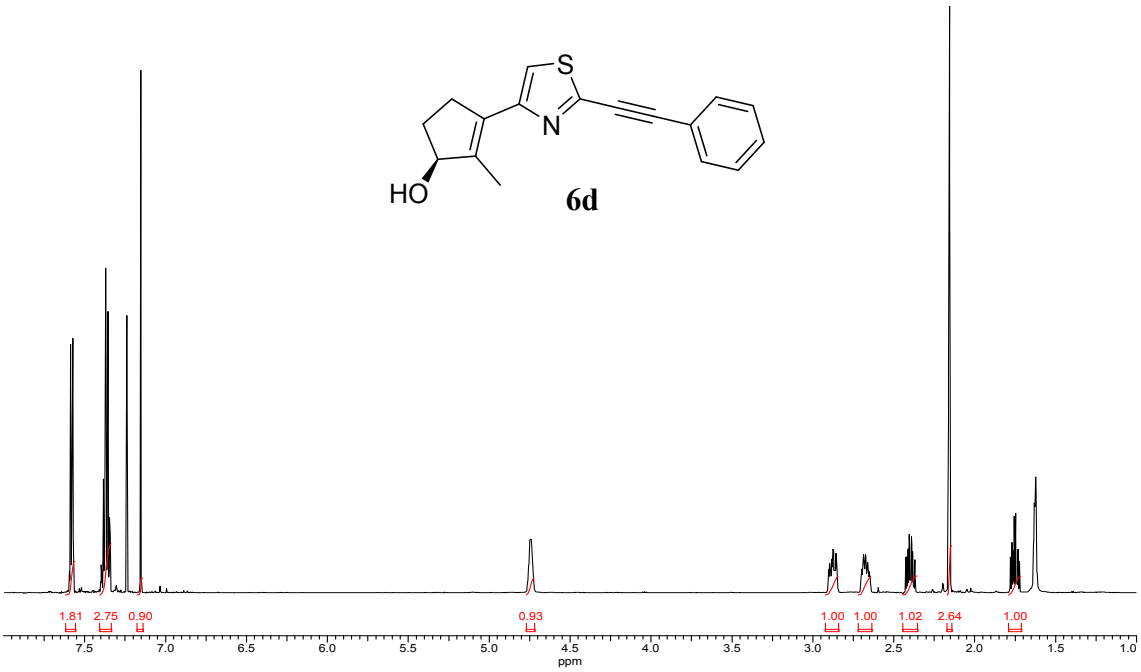
^{1}H NMR of 2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enol (6c)



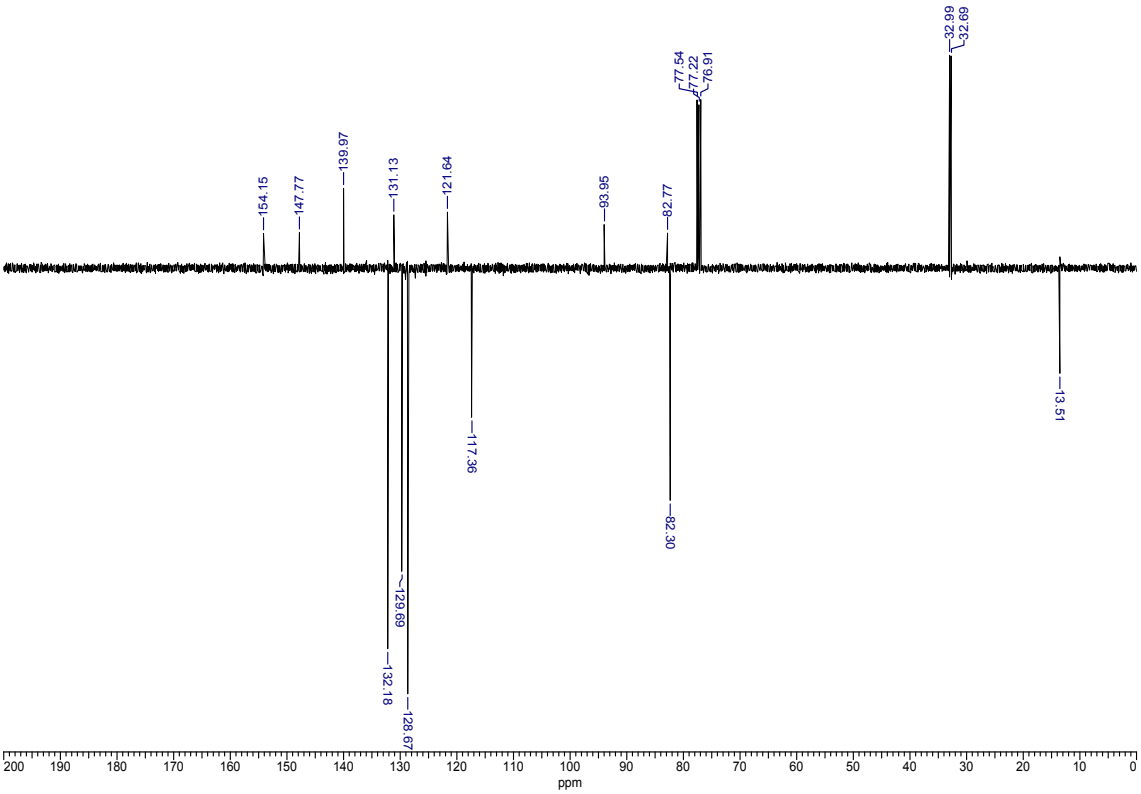
^{13}C NMR of 2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enol (6c)



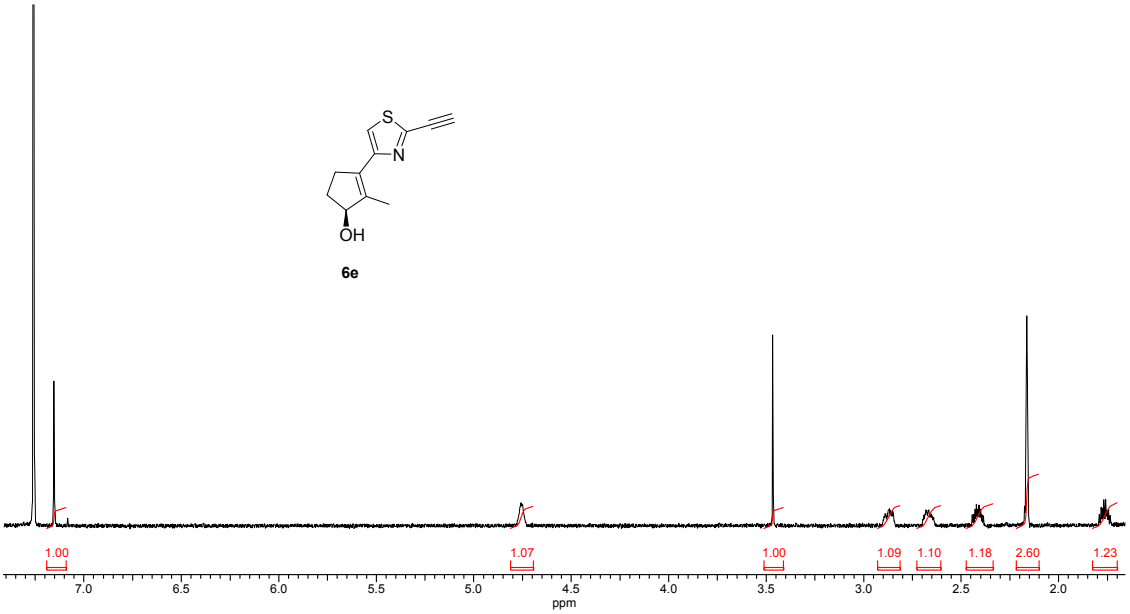
^{1}H NMR of (*S*)-2-methyl-3-(2-(phenylethynyl)thiazol-4-yl)cyclopent-2-enol (6d)



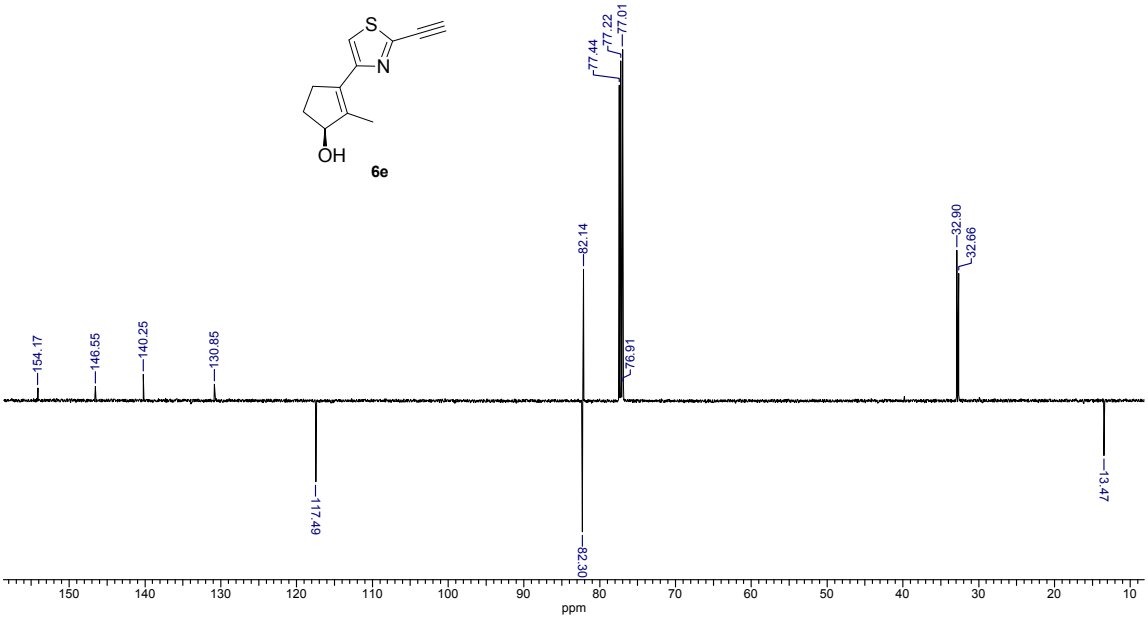
^{13}C NMR of (*S*)-2-methyl-3-(2-(phenylethynyl)thiazol-4-yl)cyclopent-2-enol (6d)



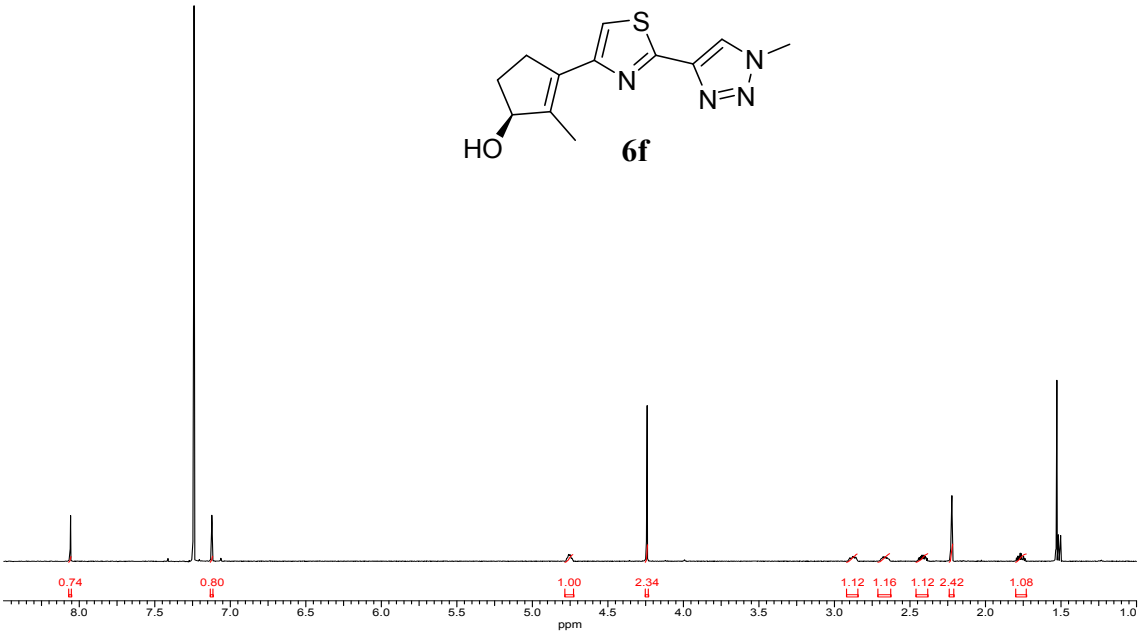
^{1}H NMR of (*S*)-3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enol (6e)



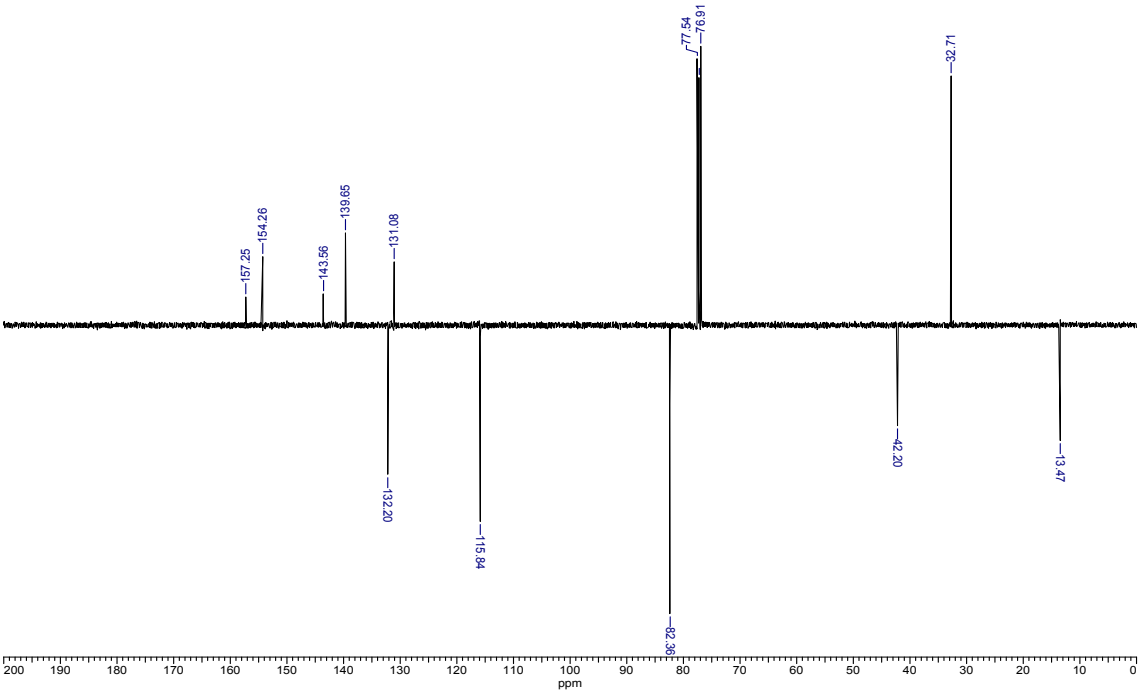
^{13}C NMR of (*S*)-3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enol (6e)



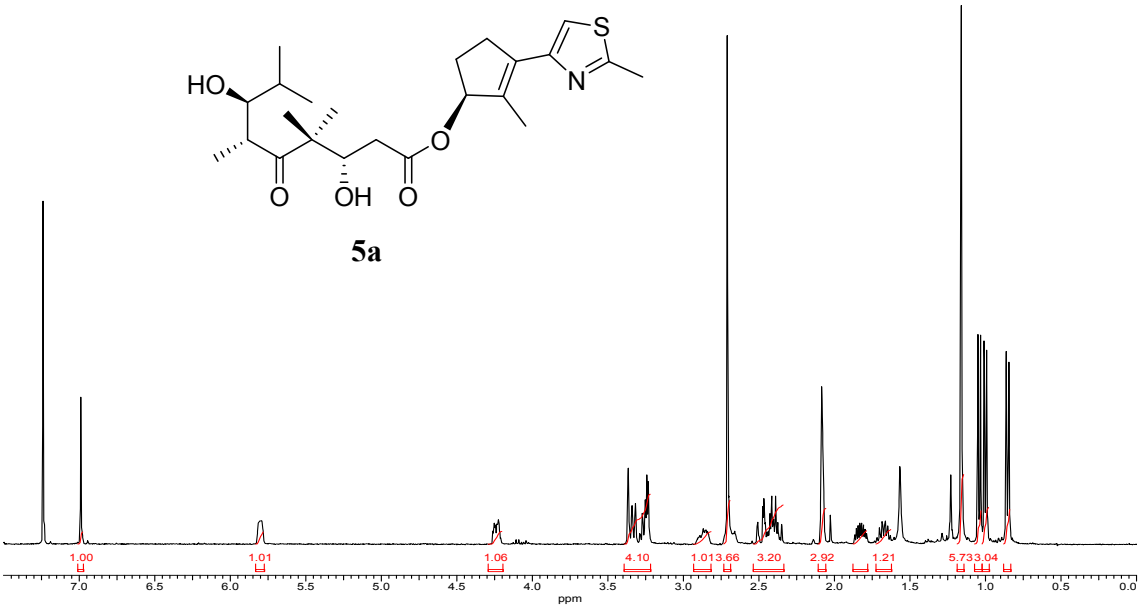
^{1}H NMR of (*S*)-2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enol (6f)



^{13}C NMR of (*S*)-2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enol (6f)

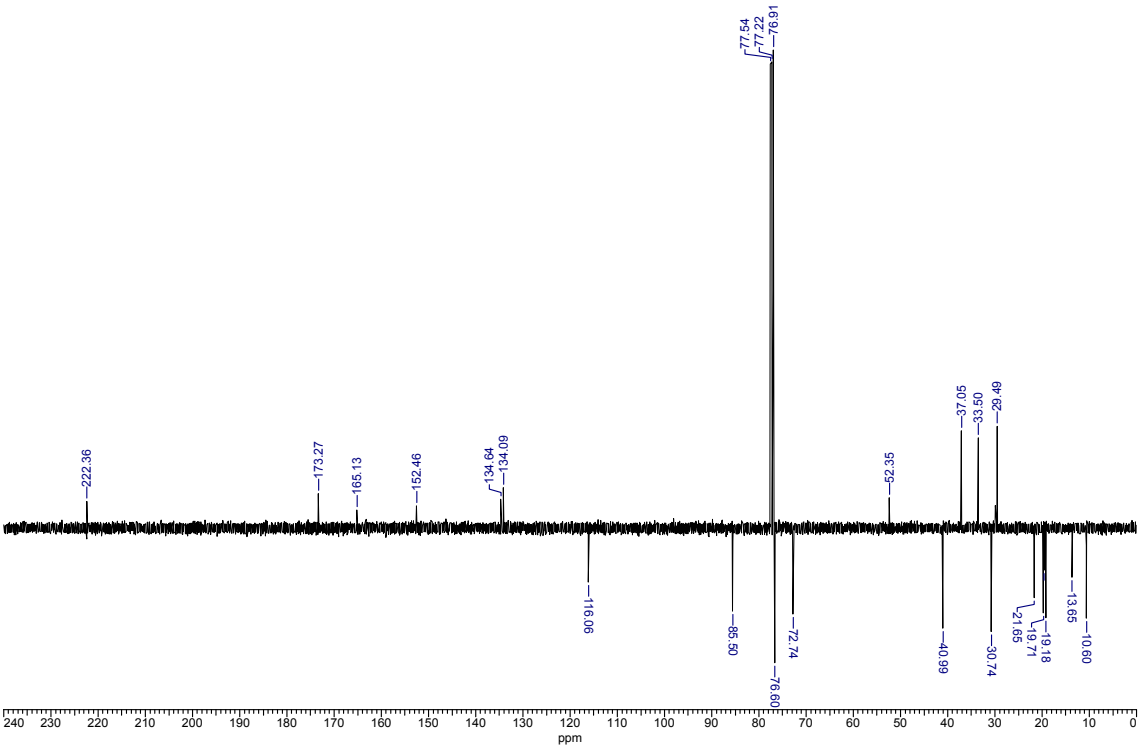


^{1}H NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5a)

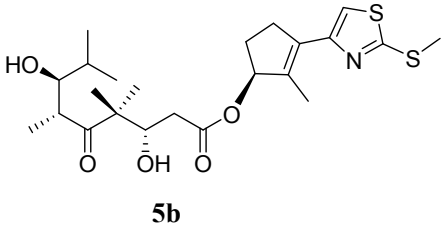


5a

^{13}C NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-methylthiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5a)

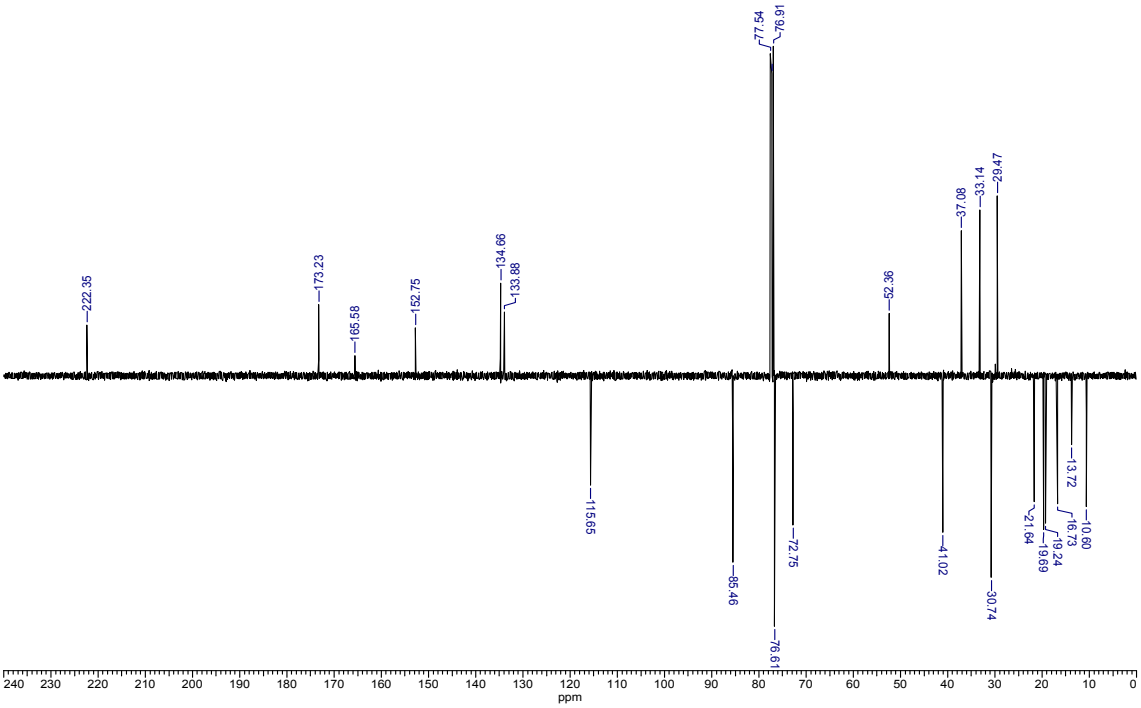


^{1}H NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5b)

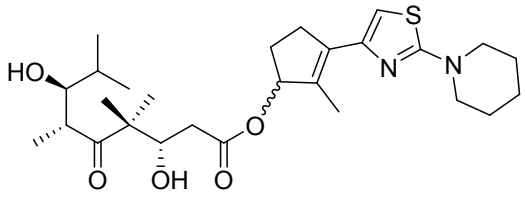


5b

^{13}C NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(methylthio)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5b)

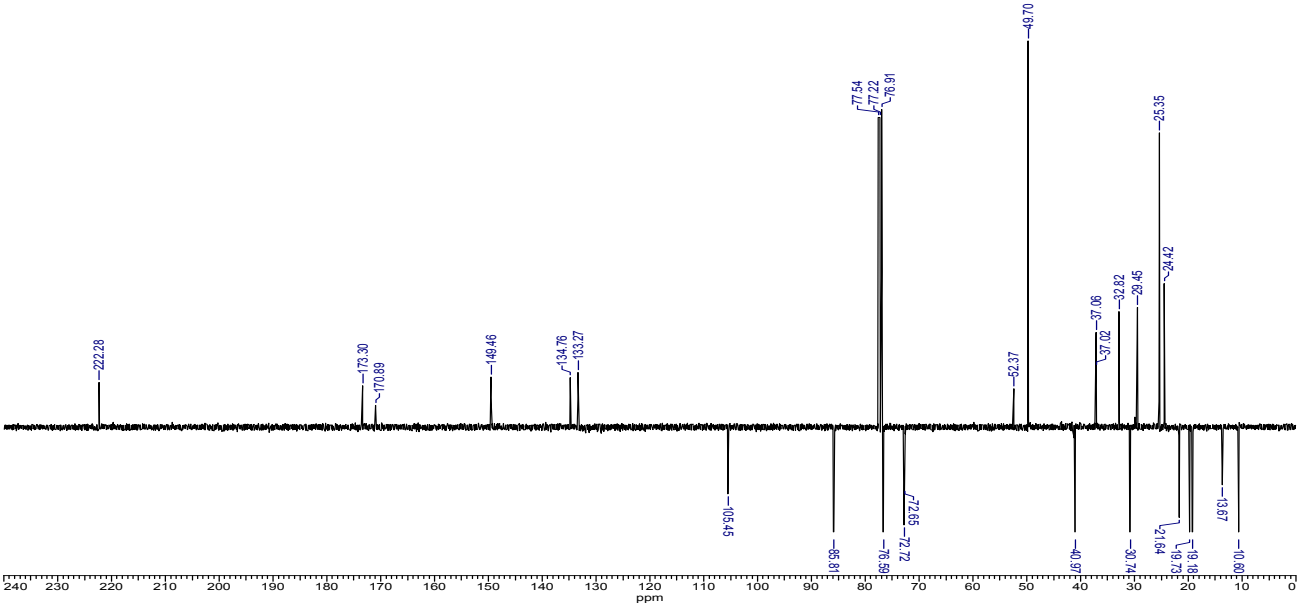


^{1}H NMR of (*3S,6R,7S*)-((*R*)-2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate and (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5c)

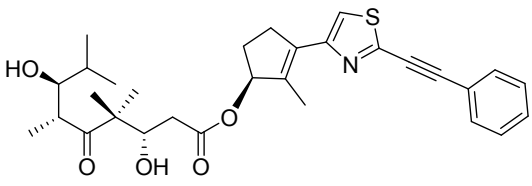


5c

^{13}C NMR of (*3S,6R,7S*)-((*R*)-2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate and (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(piperidin-1-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5c)

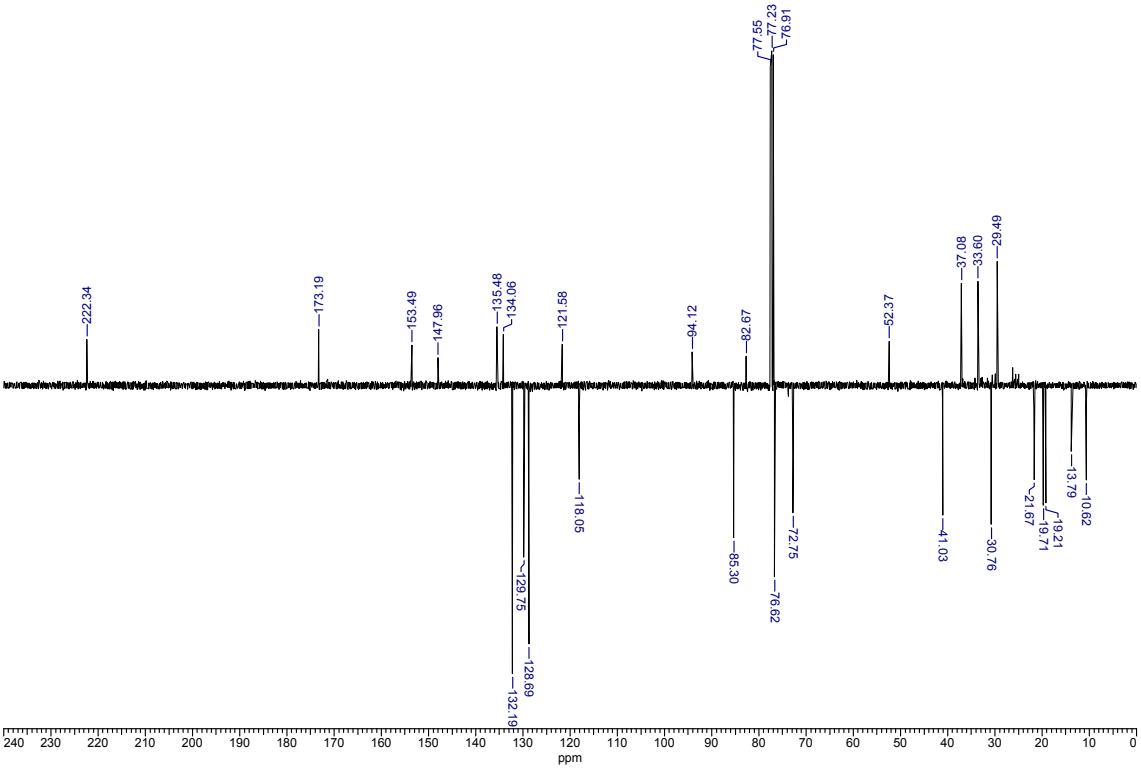


^{1}H NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(phenylethynyl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5d)

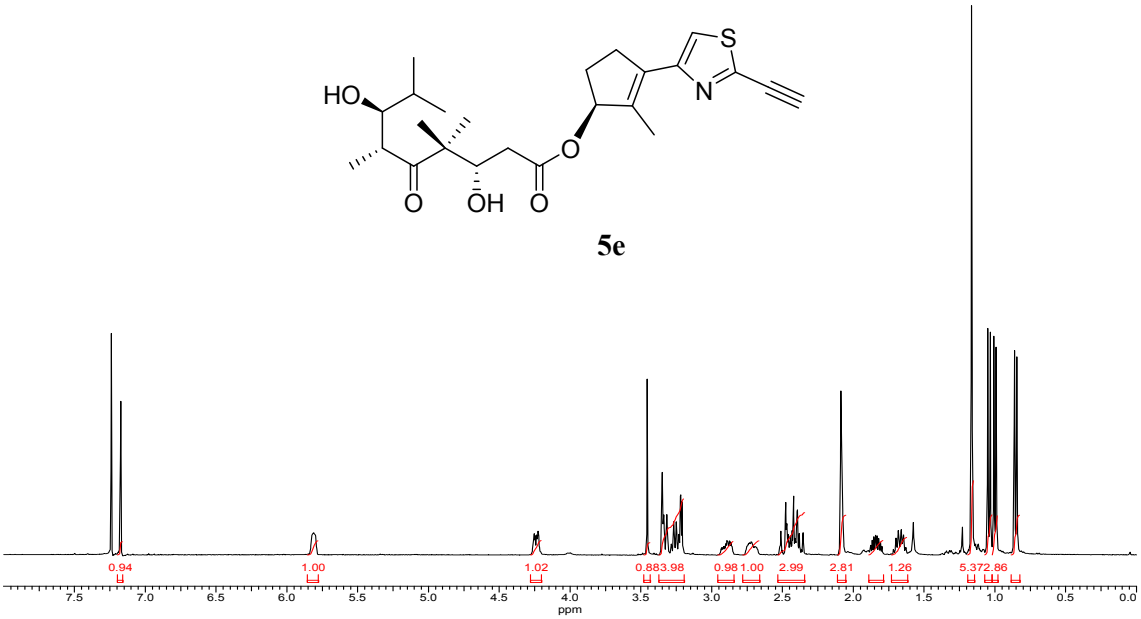


5d

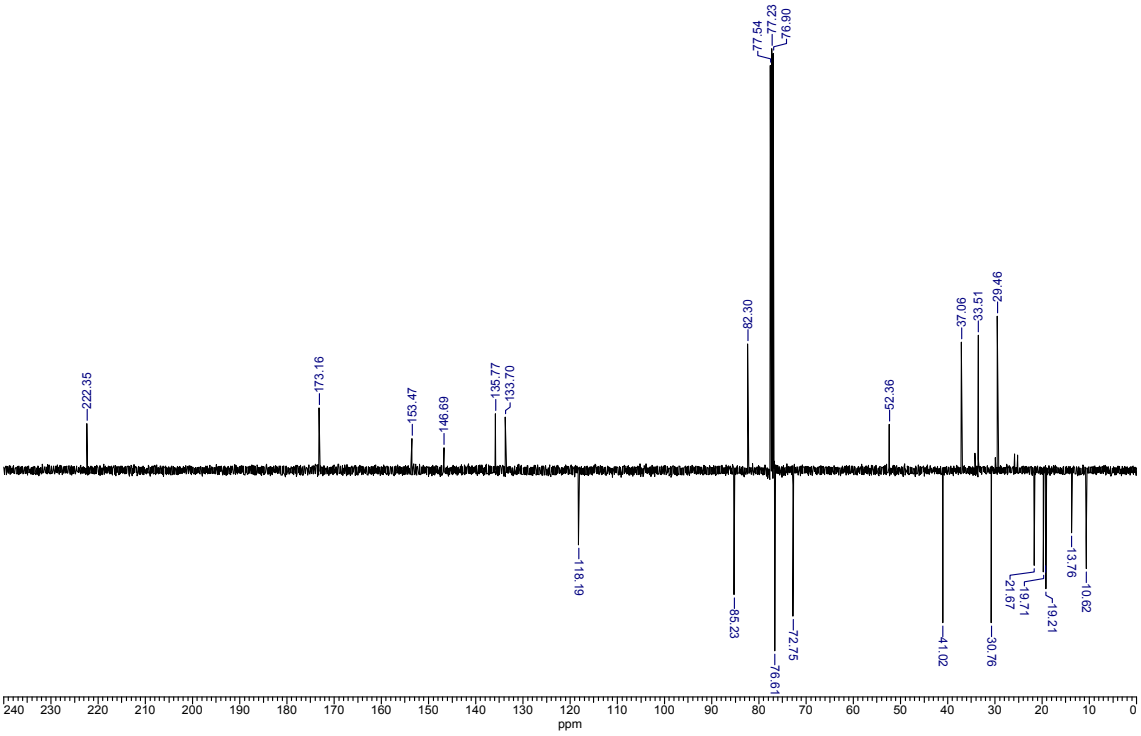
^{13}C NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(phenylethynyl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5d)



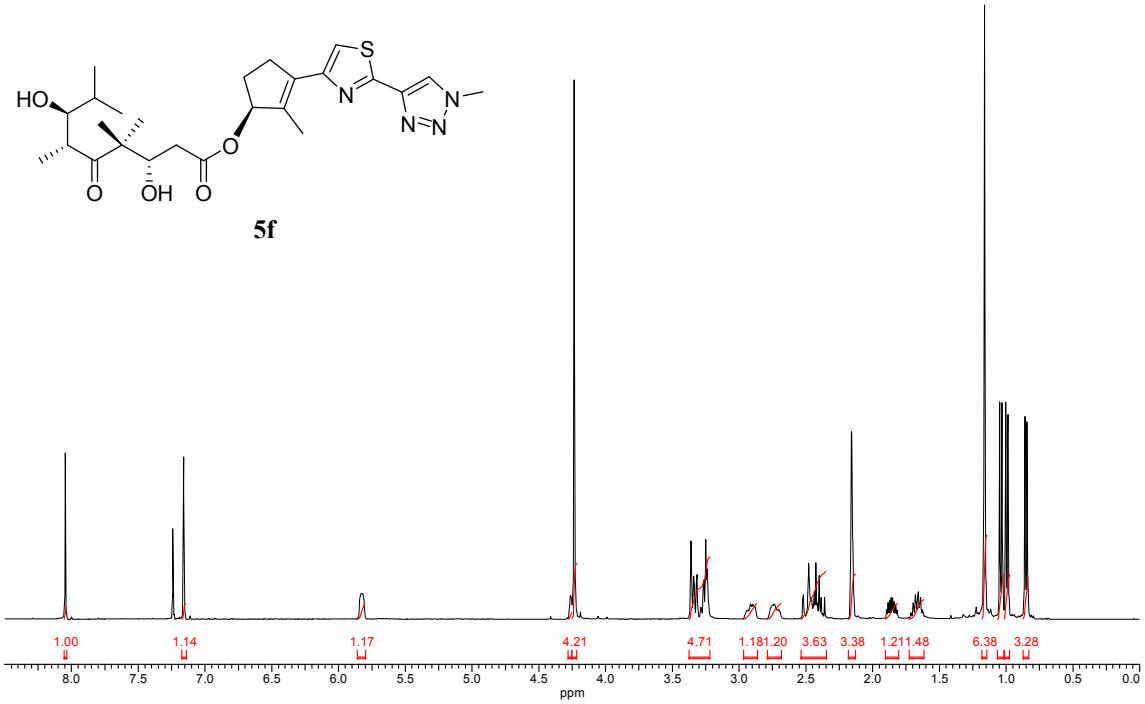
^{1}H NMR of (*3S,6R,7S*)-((*S*)-3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5e)



^{13}C NMR of (*3S,6R,7S*)-((*S*)-3-(2-ethynylthiazol-4-yl)-2-methylcyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5e)

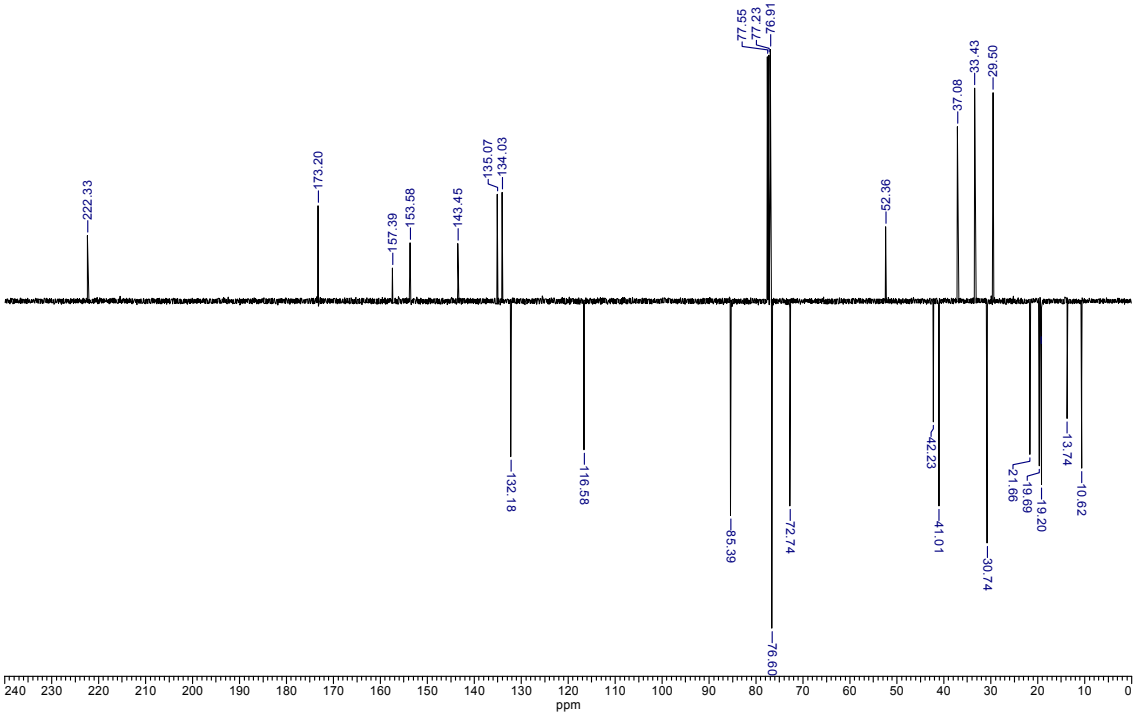


^{1}H NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5f)

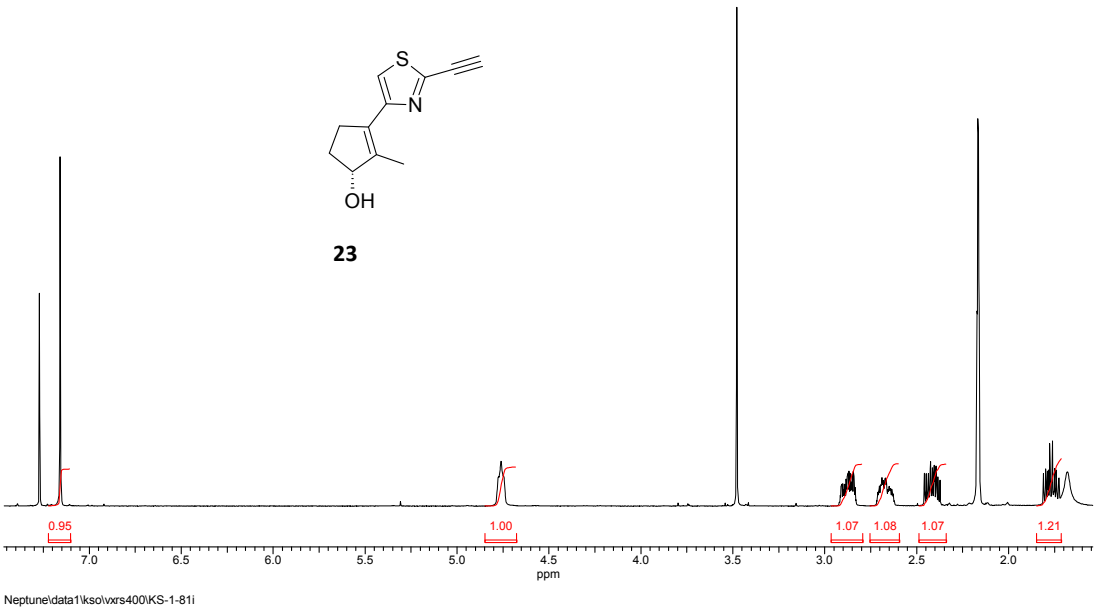


5f

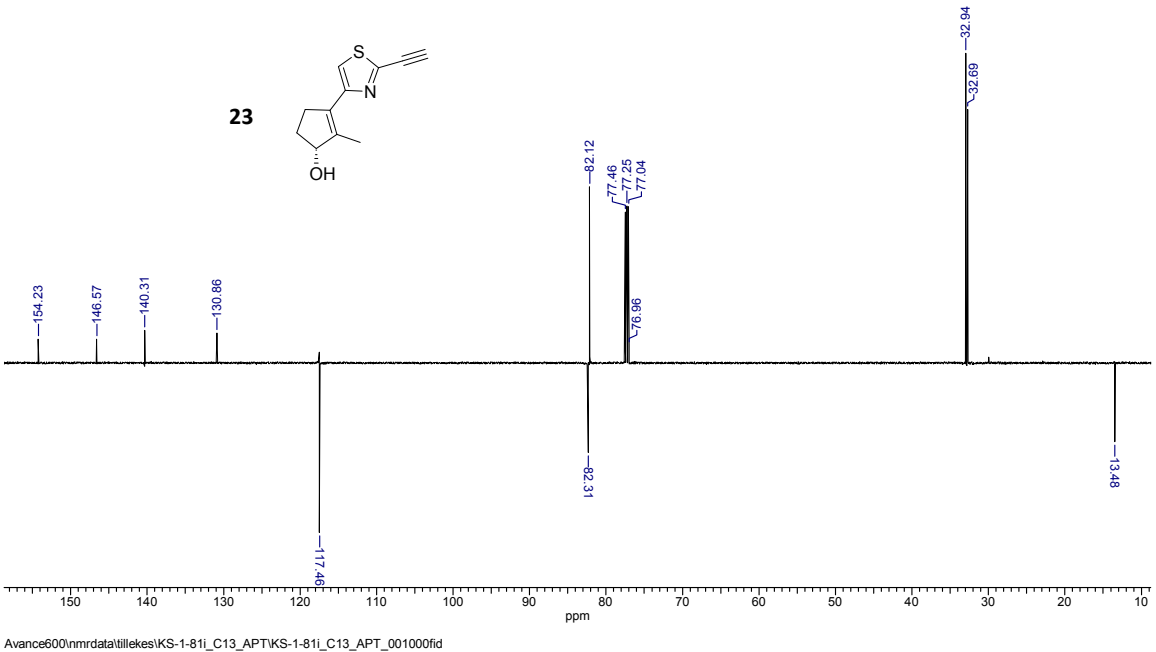
^{13}C NMR of (*3S,6R,7S*)-((*S*)-2-methyl-3-(2-(1-methyl-1H-1,2,3-triazol-4-yl)thiazol-4-yl)cyclopent-2-enyl) 3,7-dihydroxy-4,4,6,8-tetramethyl-5-oxononanoate (5f)



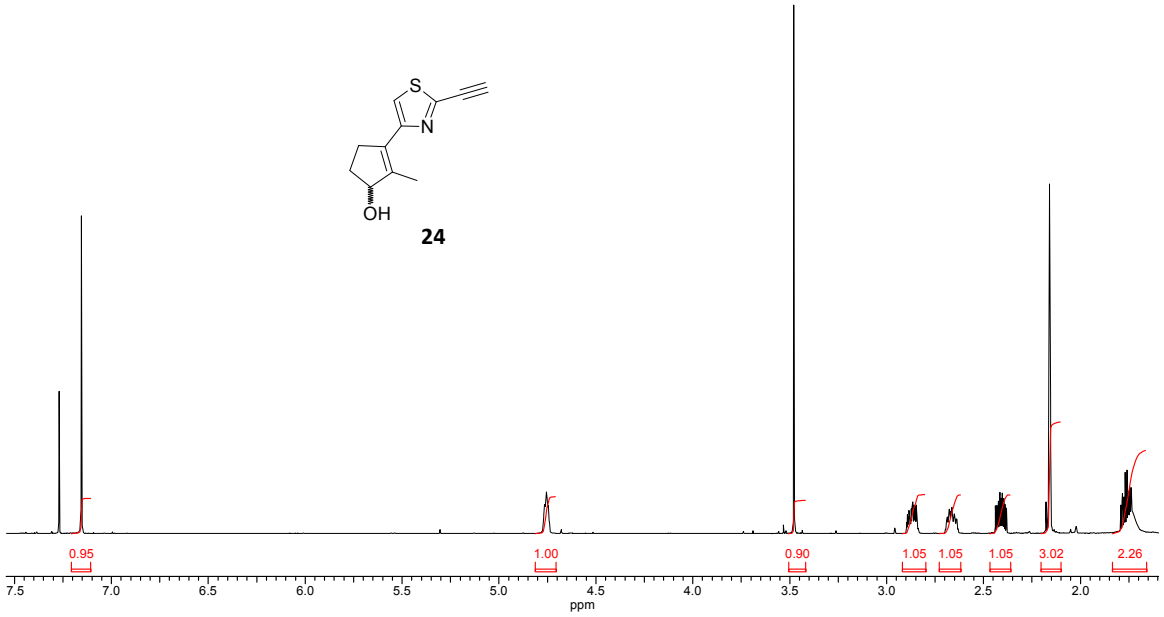
^{1}H NMR of *(R)*-3-(2-Ethynylthiazol-4-yl)-2-methylcyclopent-2-enol (23)



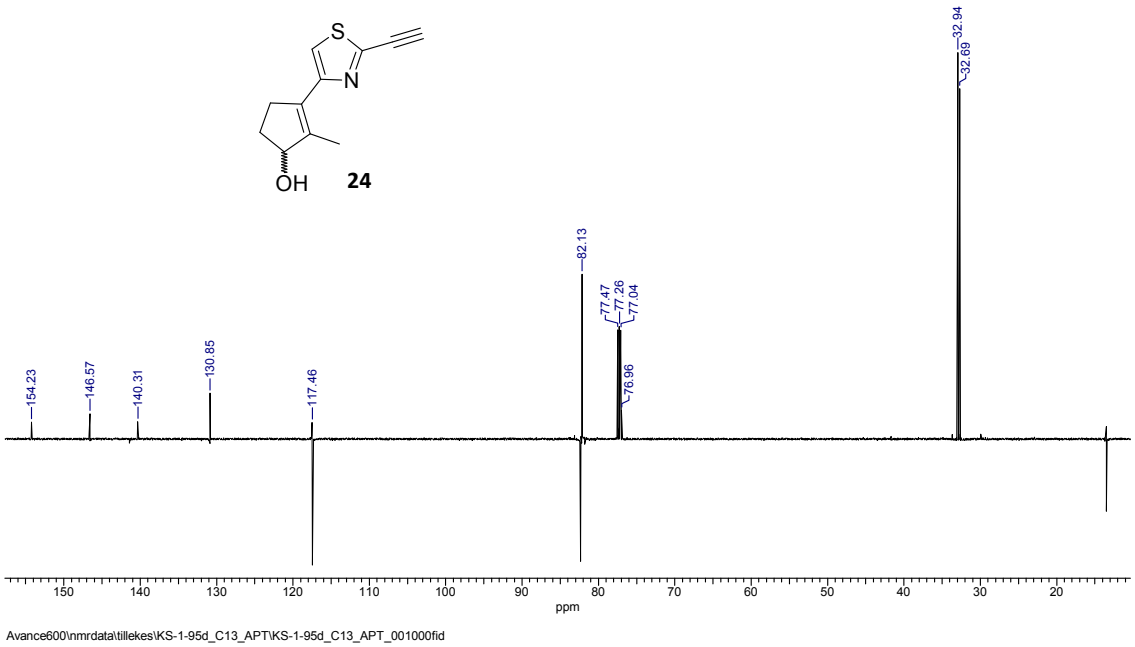
^{13}C NMR of *(R)*-3-(2-Ethynylthiazol-4-yl)-2-methylcyclopent-2-enol (23)



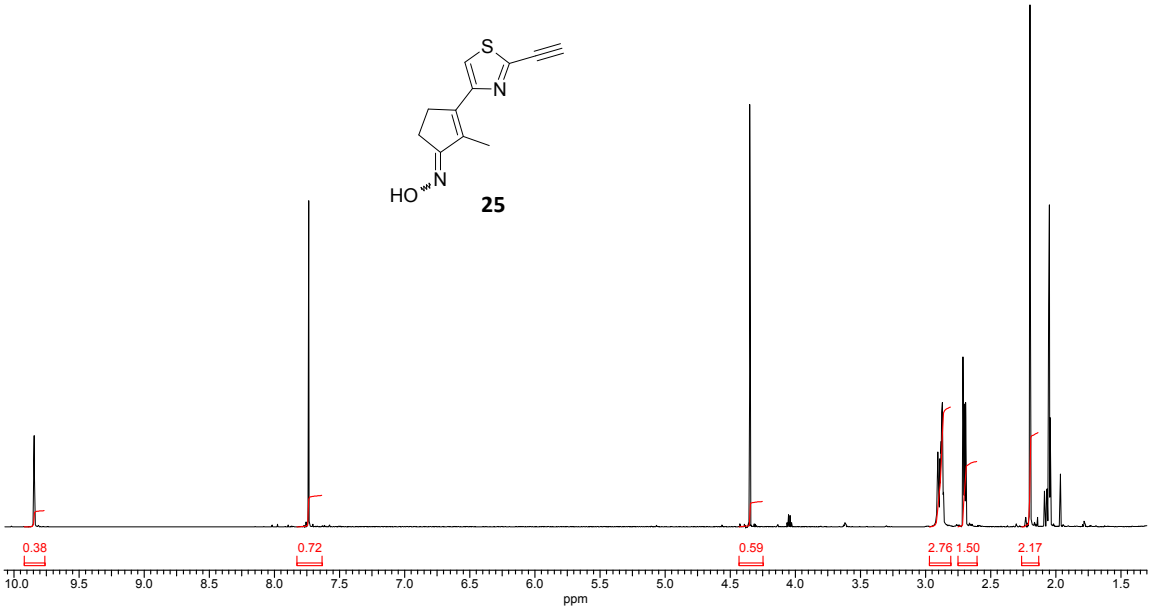
^{1}H NMR of 2-Methyl-3-(2-((trimethylsilyl)ethynyl)thiazole-4-yl)cyclopent-2-enol (24)



^{13}C NMR of 2-Methyl-3-(2-((trimethylsilyl)ethynyl)thiazole-4-yl)cyclopent-2-enol (24)



^{1}H NMR of 3-(2-Ethynylthiazol-4-yl)-2-methylcyclopent-2-enone oxime (25)



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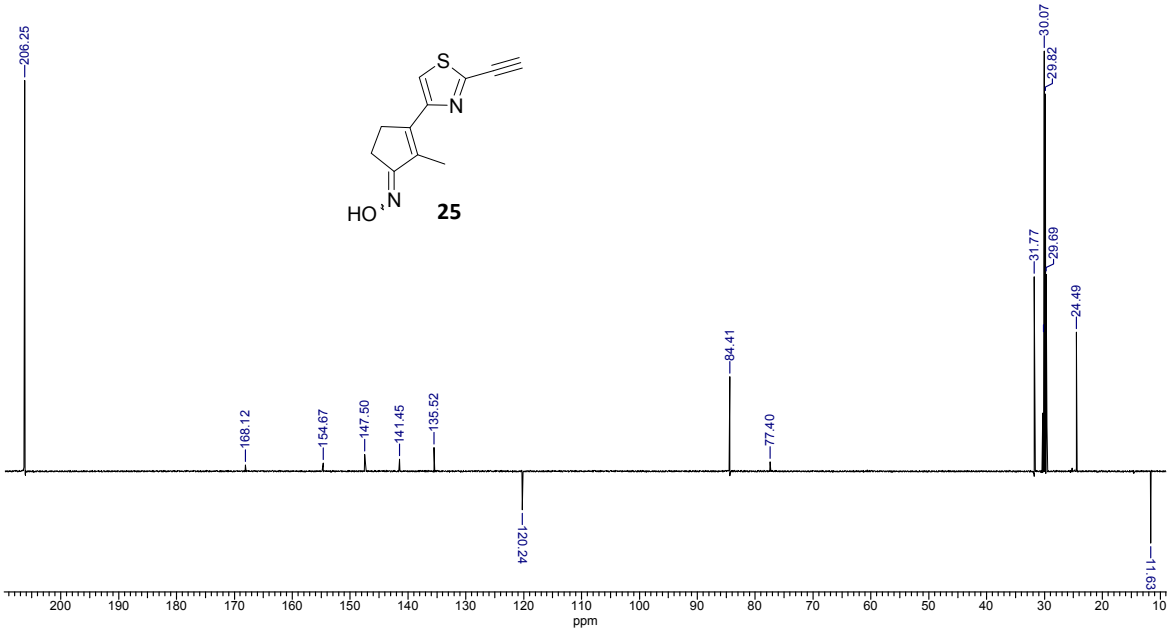
^{13}C NMR of 3-(2-Ethynylthiazol-4-yl)-2-methylcyclopent-2-enone oxime (25)



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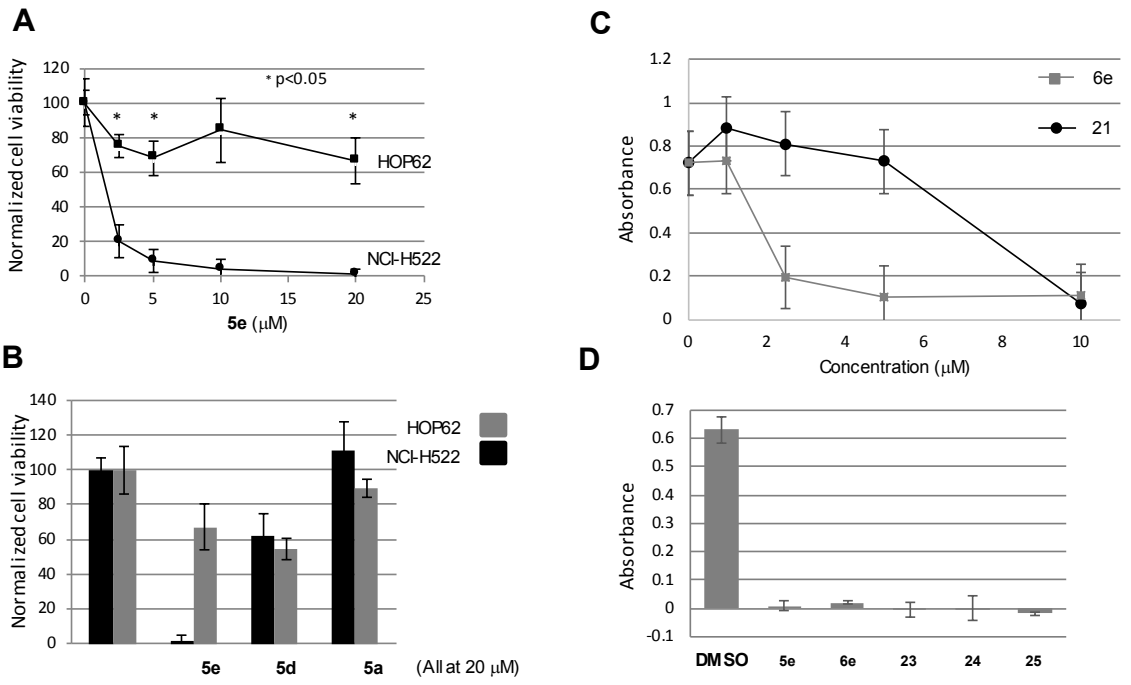
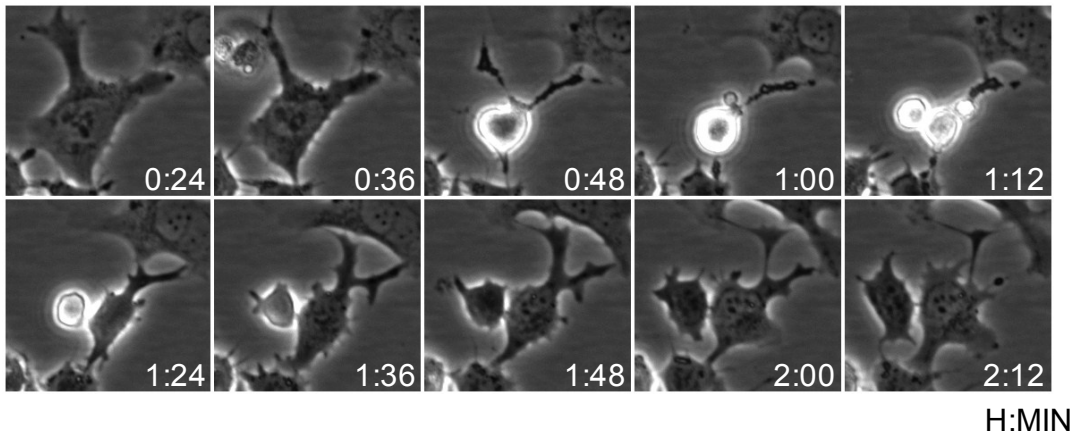
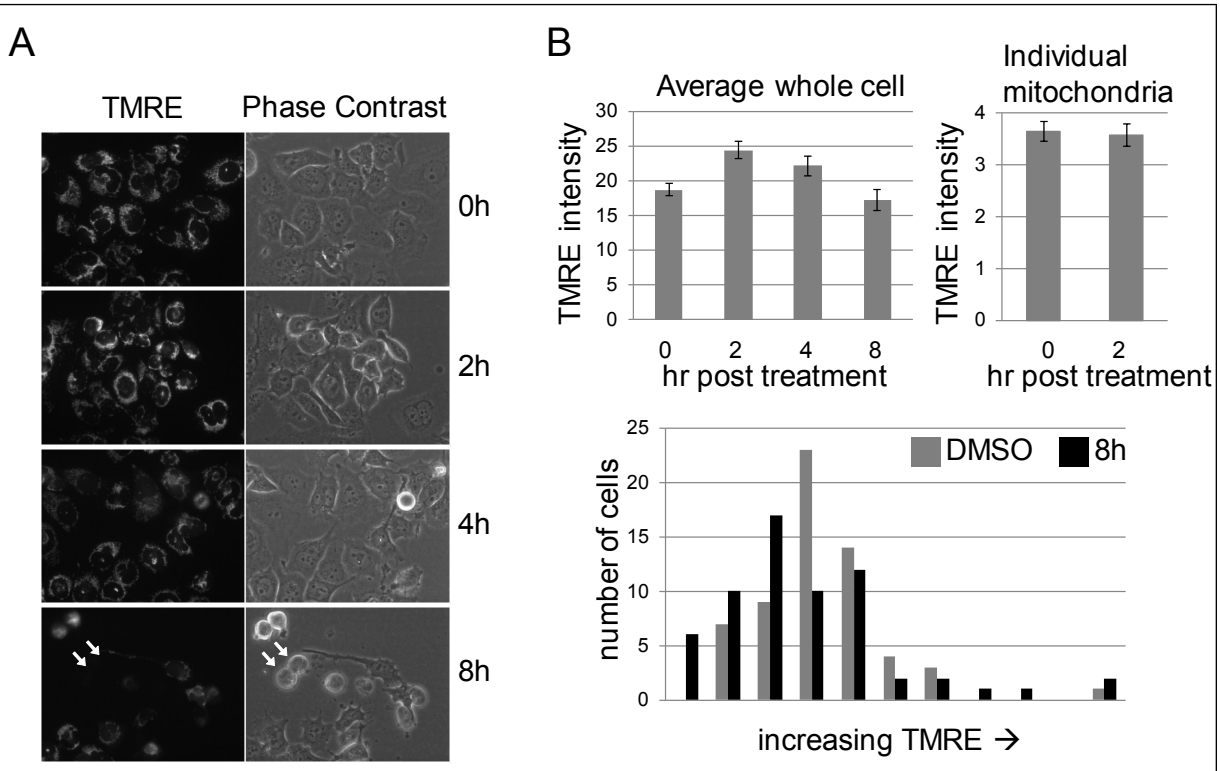


Supplemental Figure S1. Initial assessment toxicity induced by compound **5e** and analogues. (A and B) NCI-H522 or HOP-62 cells were plated and exposed to the indicated compounds at the doses specified. Cells treated for 5 days were analyzed by methylene blue staining to determine viable cells. Average values are shown with bars to represent standard deviation. *p<0.05. (C and D) NCI-H522 were exposed to the compounds indicated. Three days later, viability was determined either by measuring absorbance after methylene blue staining (in C) or using the MTS assay (in D) as described in materials and methods. In "C", significantly lower absorbance was observed after either 2.5μM or 5μM of **6e** compared to compound **21** (p<0.02). In "D" all compounds resulted in significantly lower absorbance compared to DMSO (p<0.005, students t-test).



Supplemental Figure S2. Time lapse microscopy of NCI-H522 cells exposed to **6e**. Images were captured every 12 min. In the example shown, mitosis begins 48 min after drug addition. Two other cells in the same field completed mitosis, and by the end of the movie (19 h post drug addition) all cells were dead.



Supplemental Figure S3. Effect of compound **6e** (10μM) on mitochondrial function. NCI H522 cells treated for times indicated with compound **6e** and stained with TMRE to indicate mitochondrial potential. (A) Representative microscopic fields of stained cells. Arrowheads: two cells that have lost mitochondrial membrane potential; phase contrast indicates that these are dead cells. (B) Quantitation of TMRE staining from microscopic images in whole cells or individual mitochondria.