

Design, Synthesis and Preliminary Biological Evaluation of Rivastigmine-INDY Hybrids as Multitarget Ligands Against Alzheimer's Disease by Targeting Butyrylcholinesterase and DYRK1A/CLK1 Kinases

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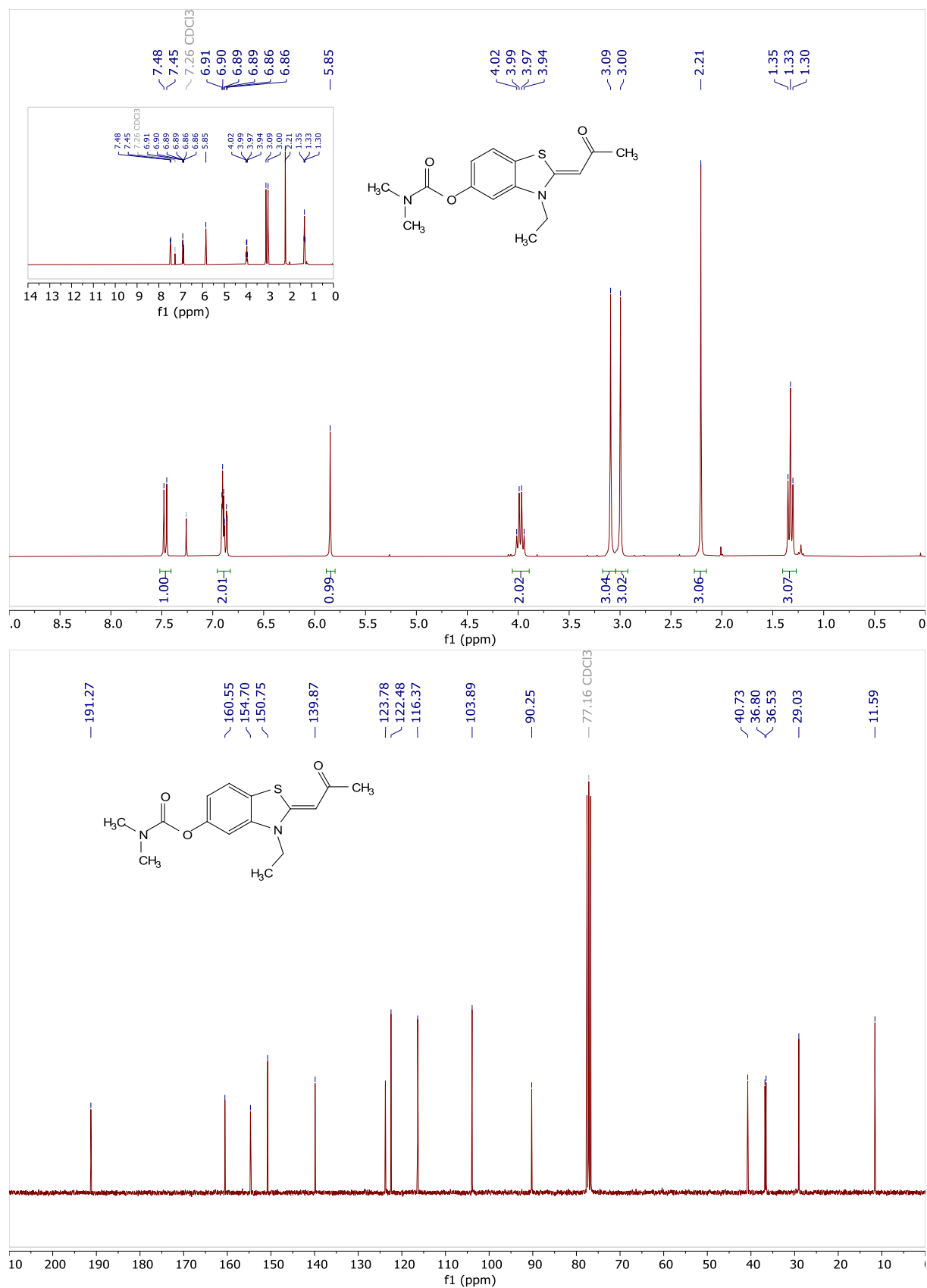
[§]UNICAEN, CERMN (Centre d'Etudes et de Recherche sur le Médicament de Normandie), Normandie Univ., Bd Becquerel, F-14032 Caen, France

Contents

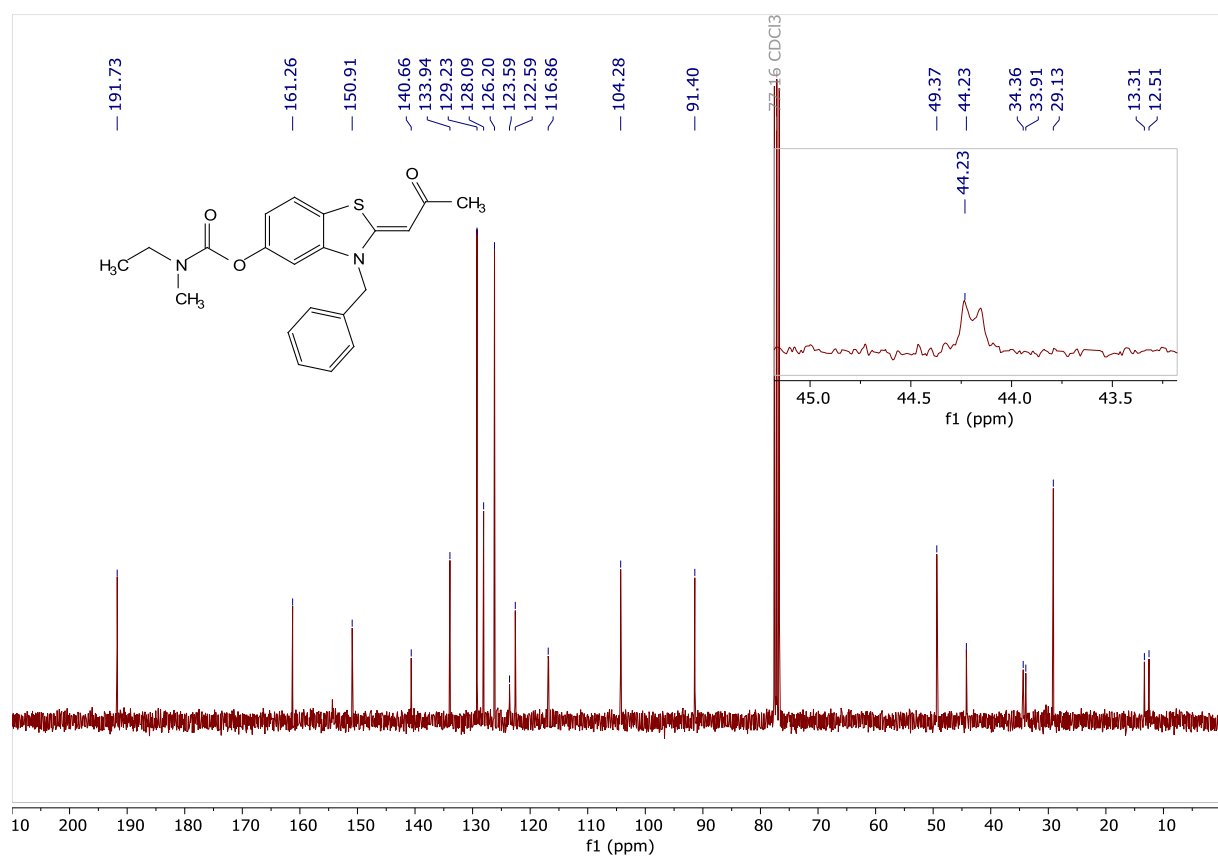
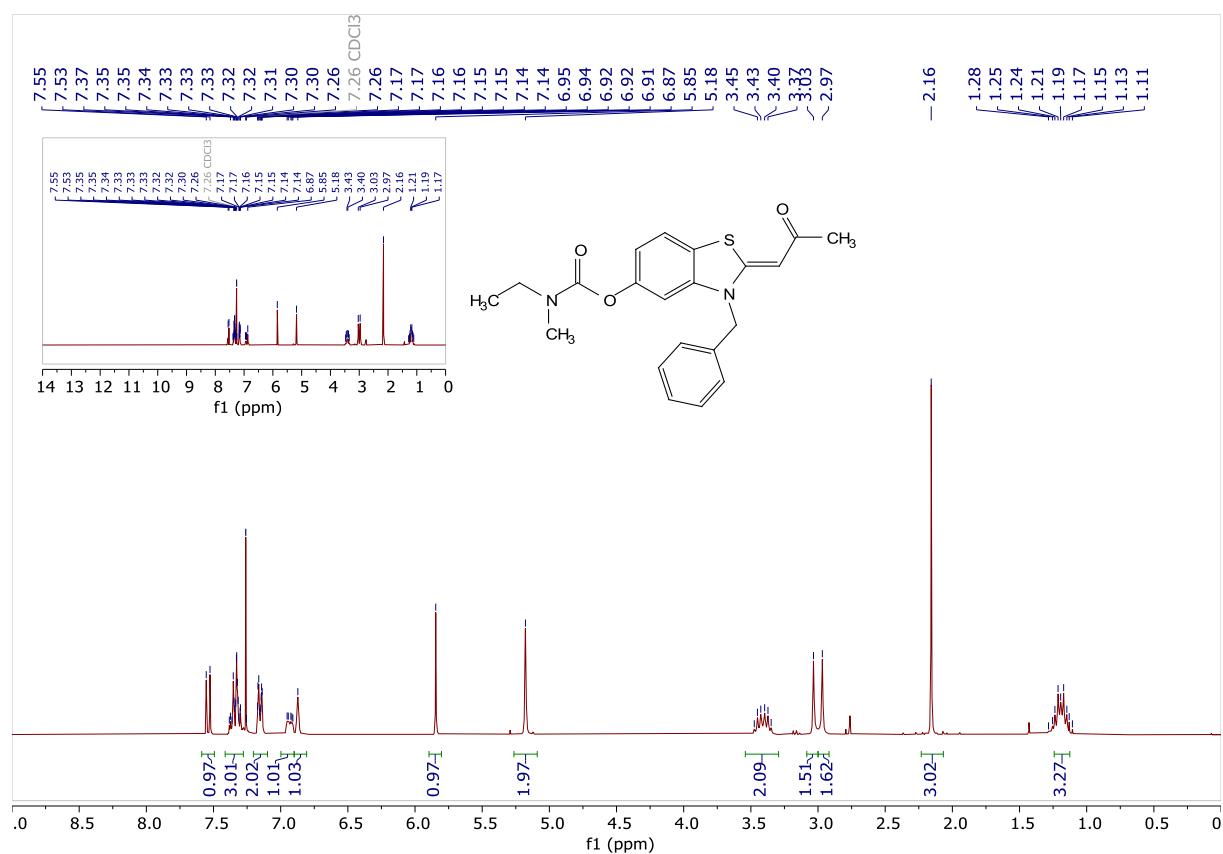
I - NMR spectra.....	2
II – High-resolution mass spectrometry spectra 1b-p	41
III – Amino-acid sequences alignment of <i>eq</i> BuChE and <i>h</i> BuChE.....	49

I - NMR spectra

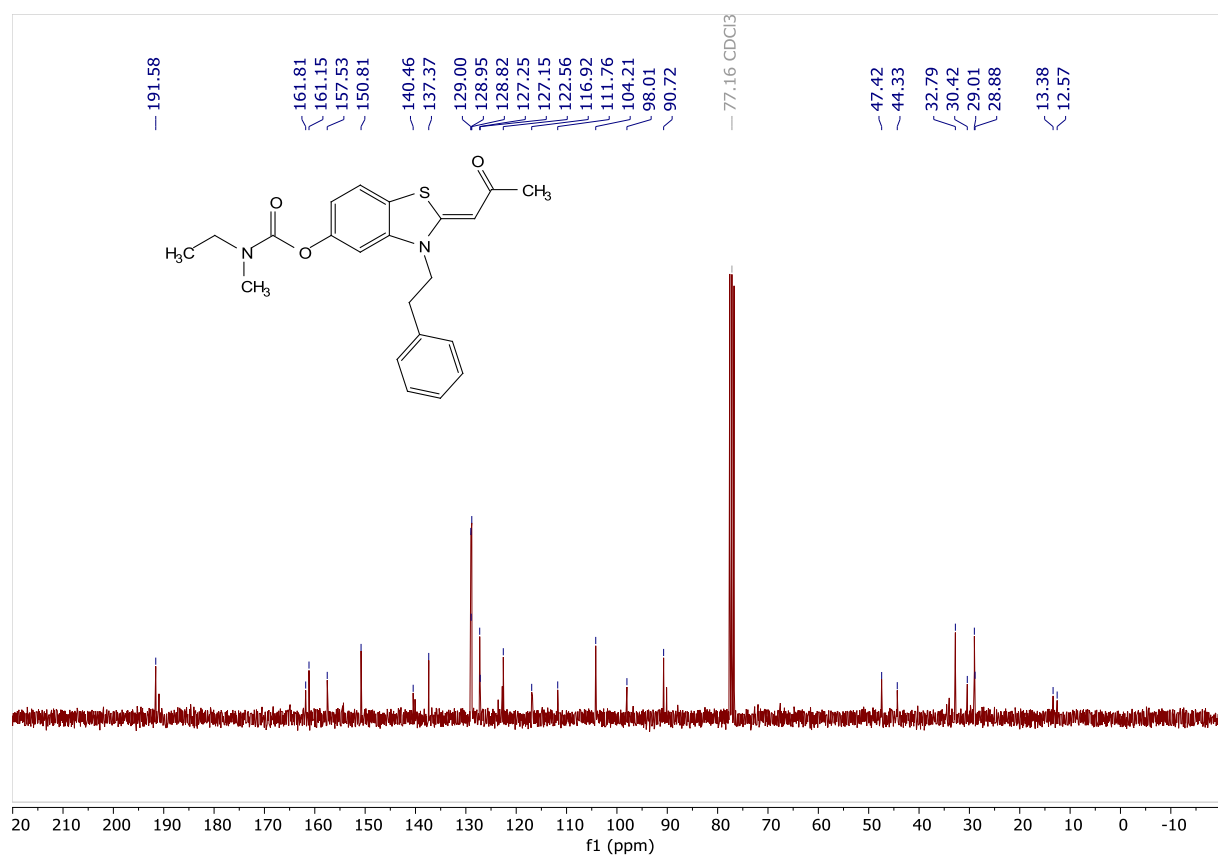
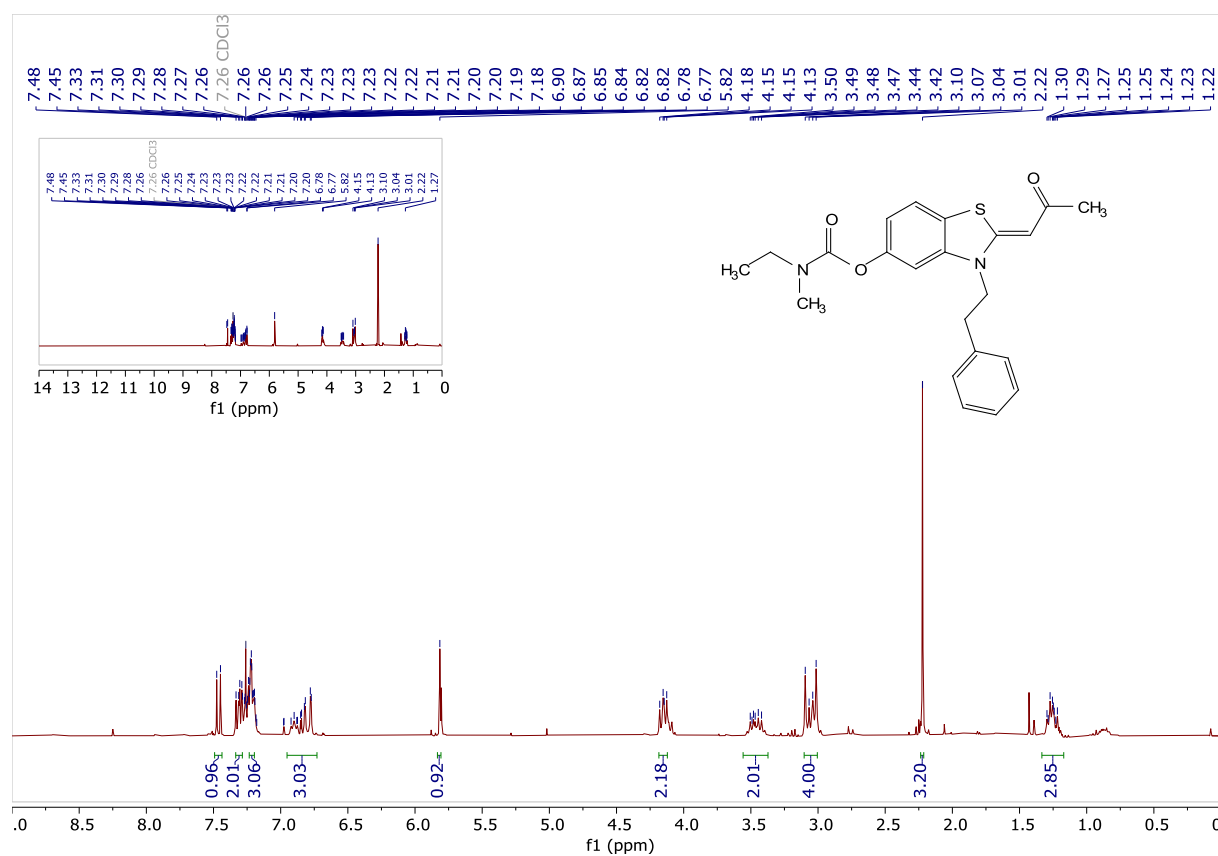
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl dimethylcarbamate (**1a**)



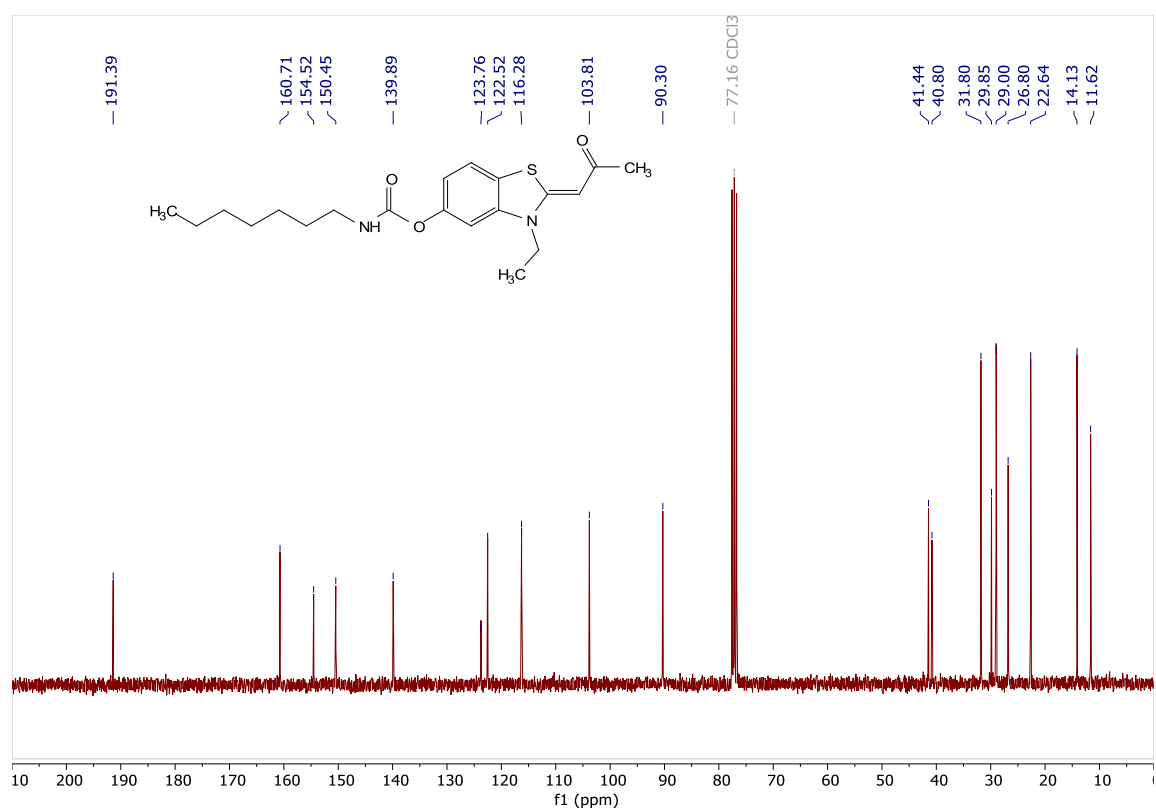
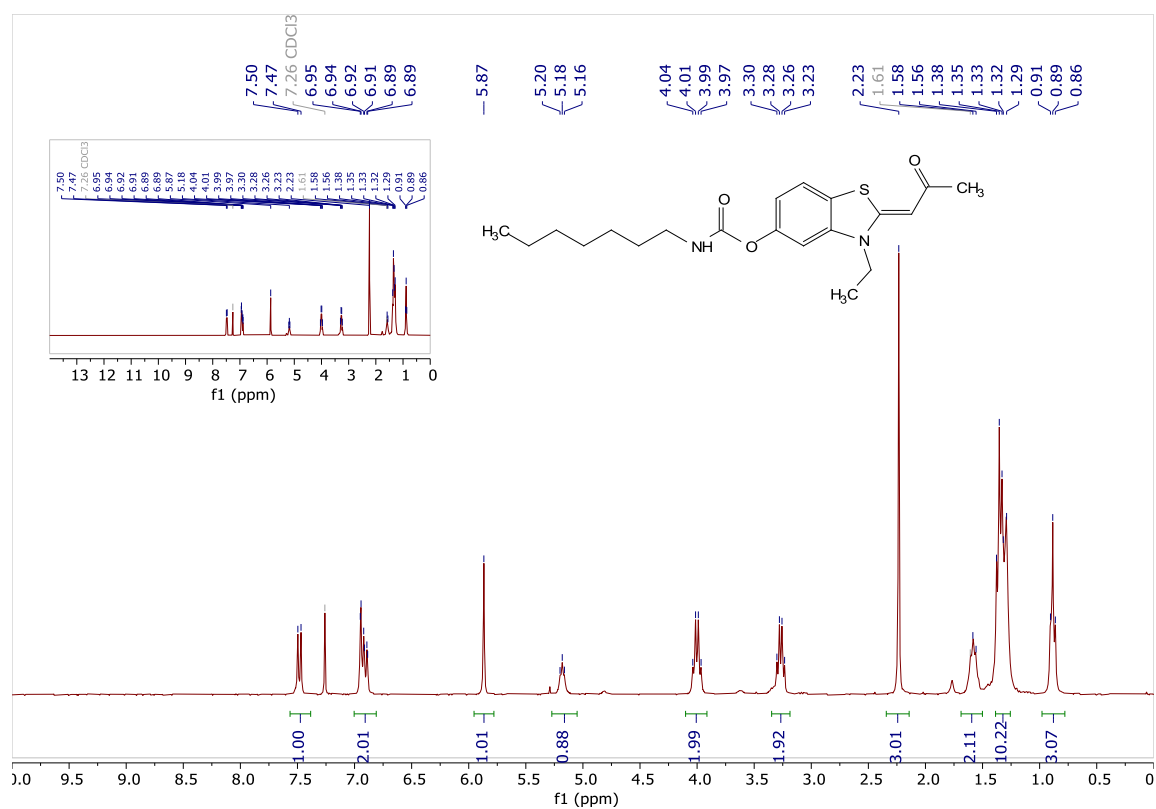
(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl ethyl(methyl) carbamate (**1b**)



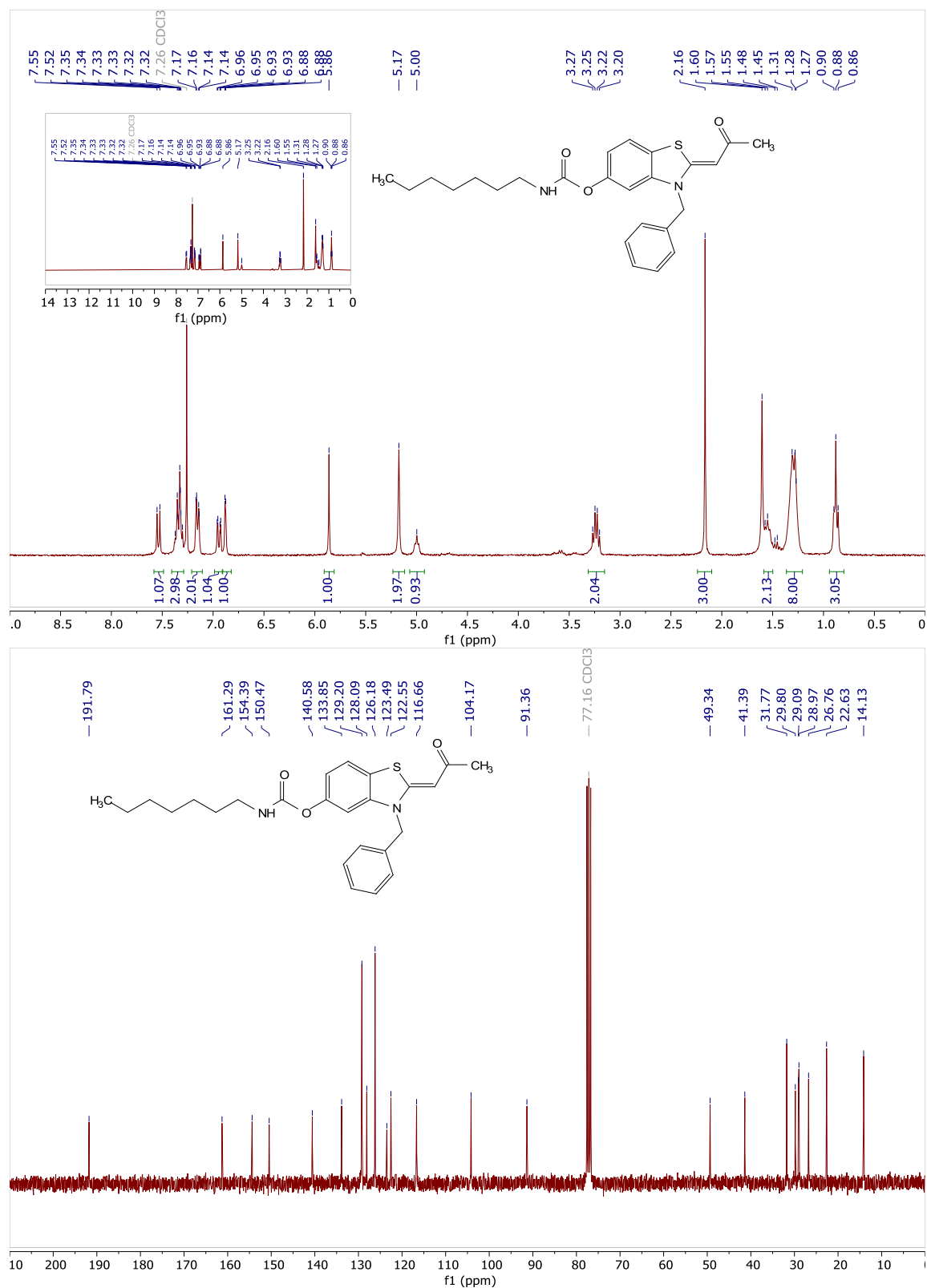
(Z)-3-Phenethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl ethyl(methyl) carbamate (1c)



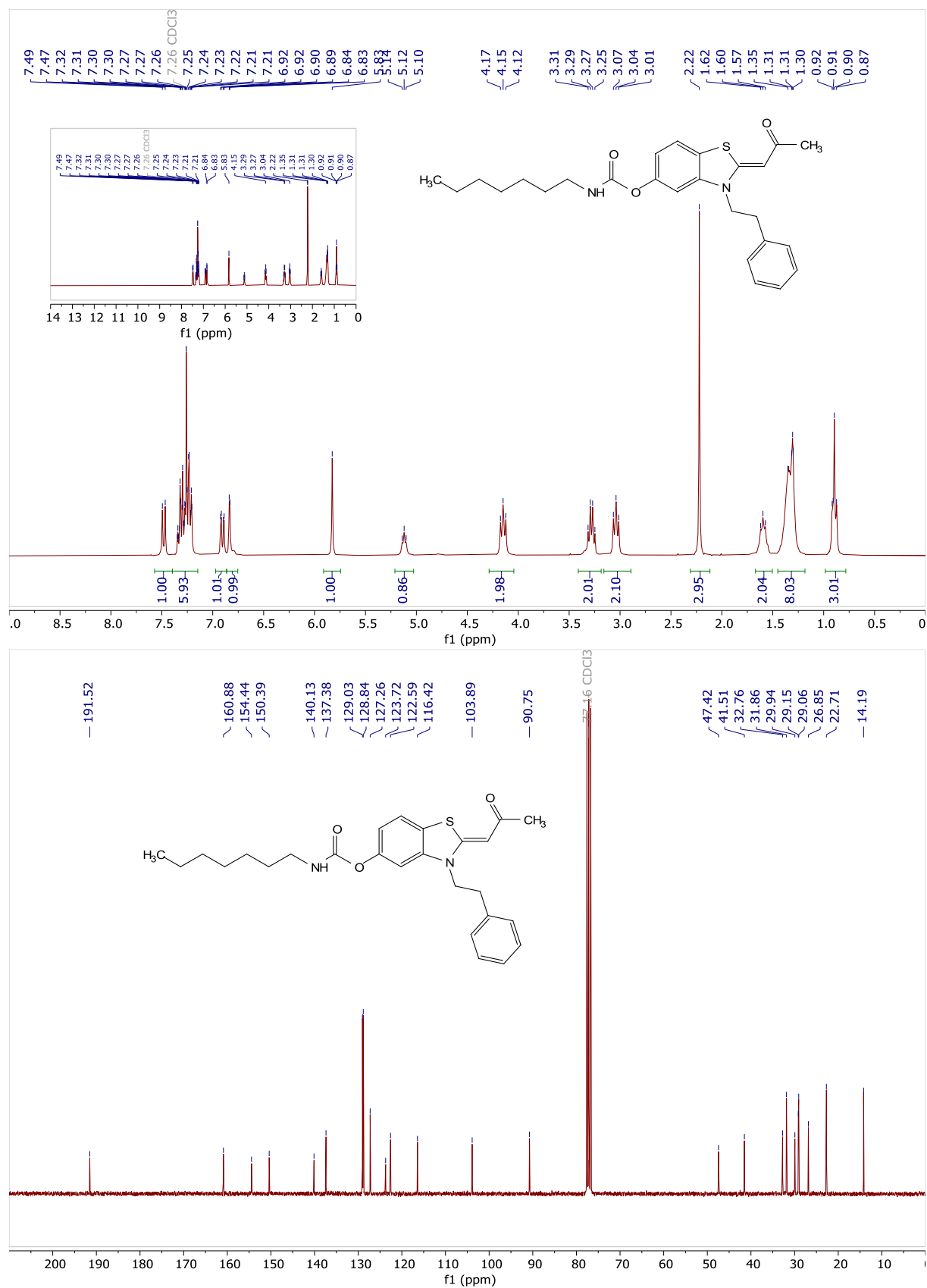
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzo[d]thiazol-5-yl heptylcarbamate (**1d**)



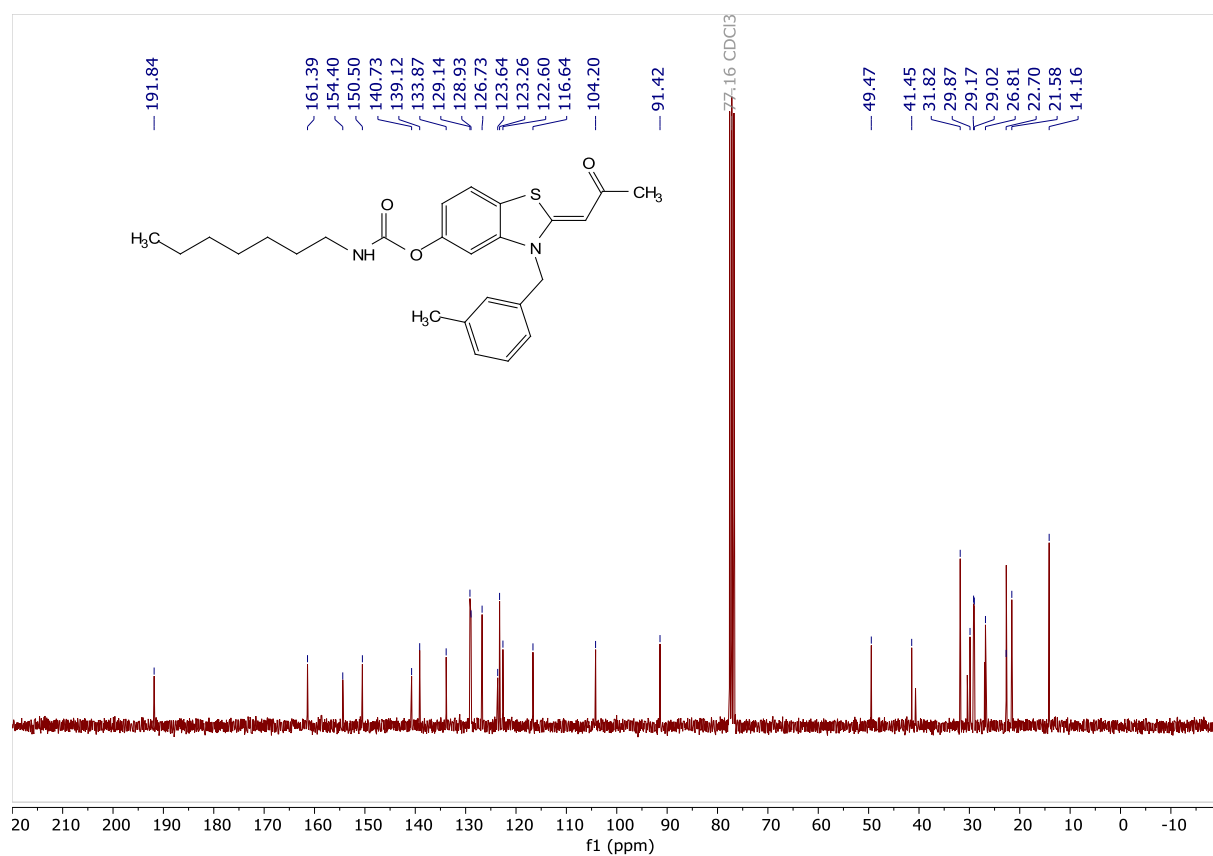
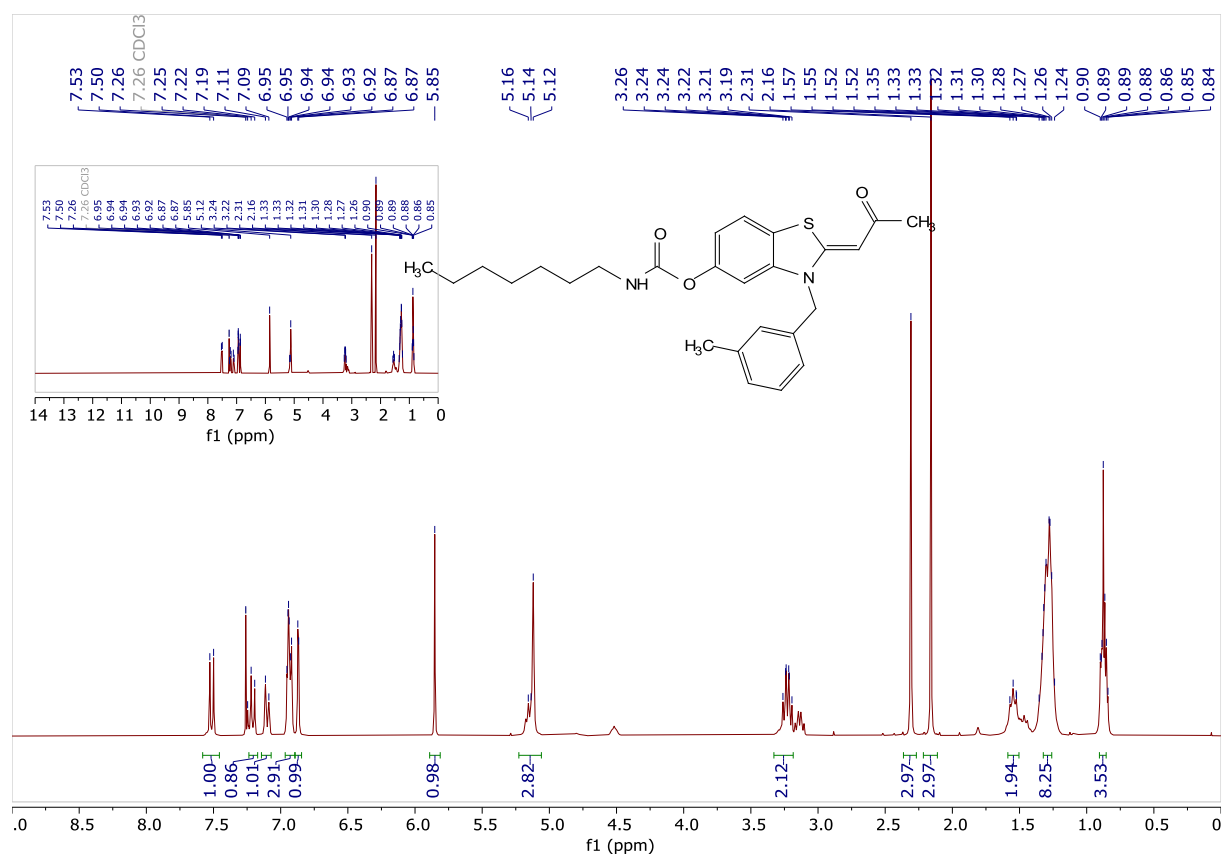
(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1e**)



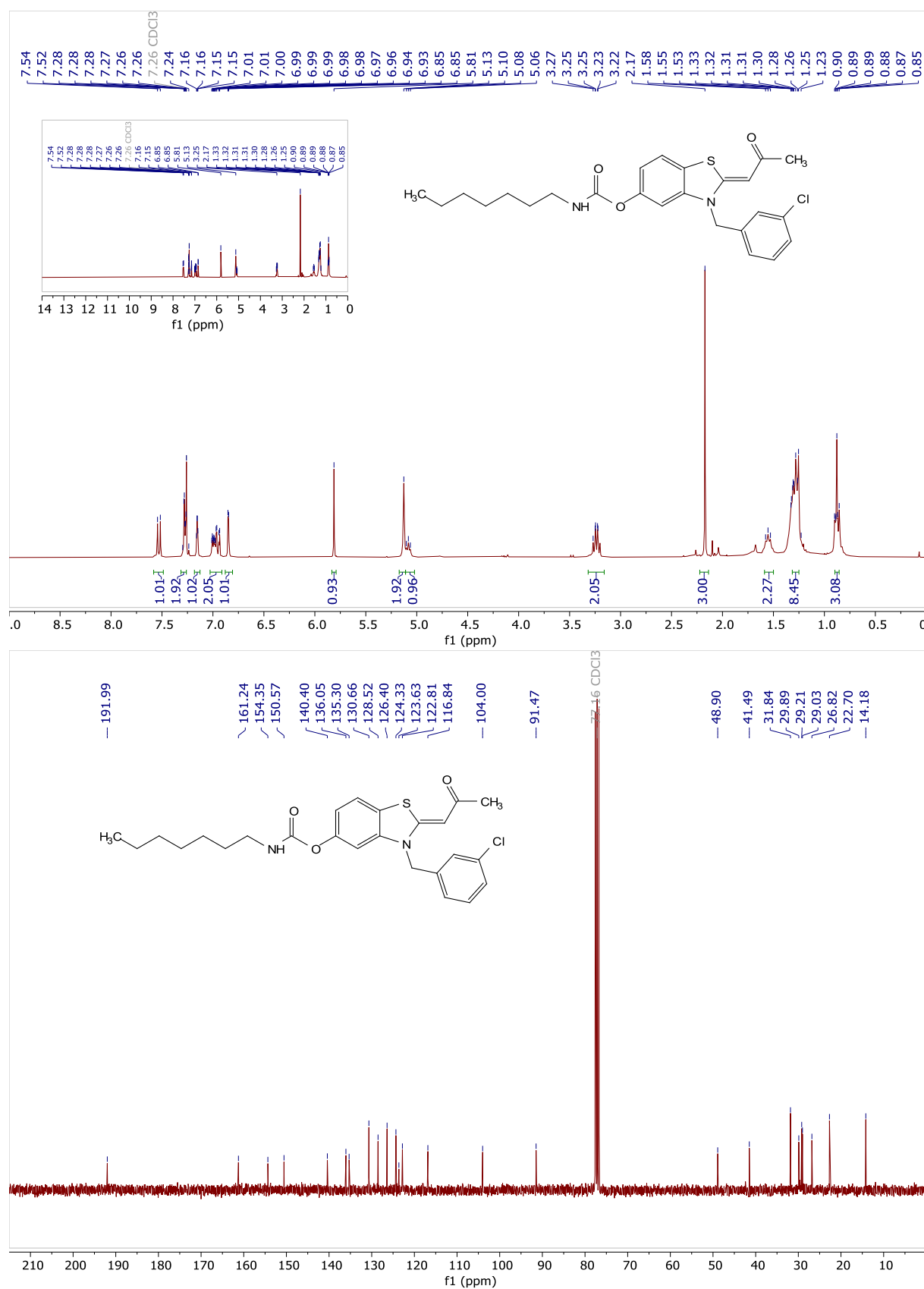
(Z)-2-(2-Oxopropylidene)-3-phenethyl-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (1f)



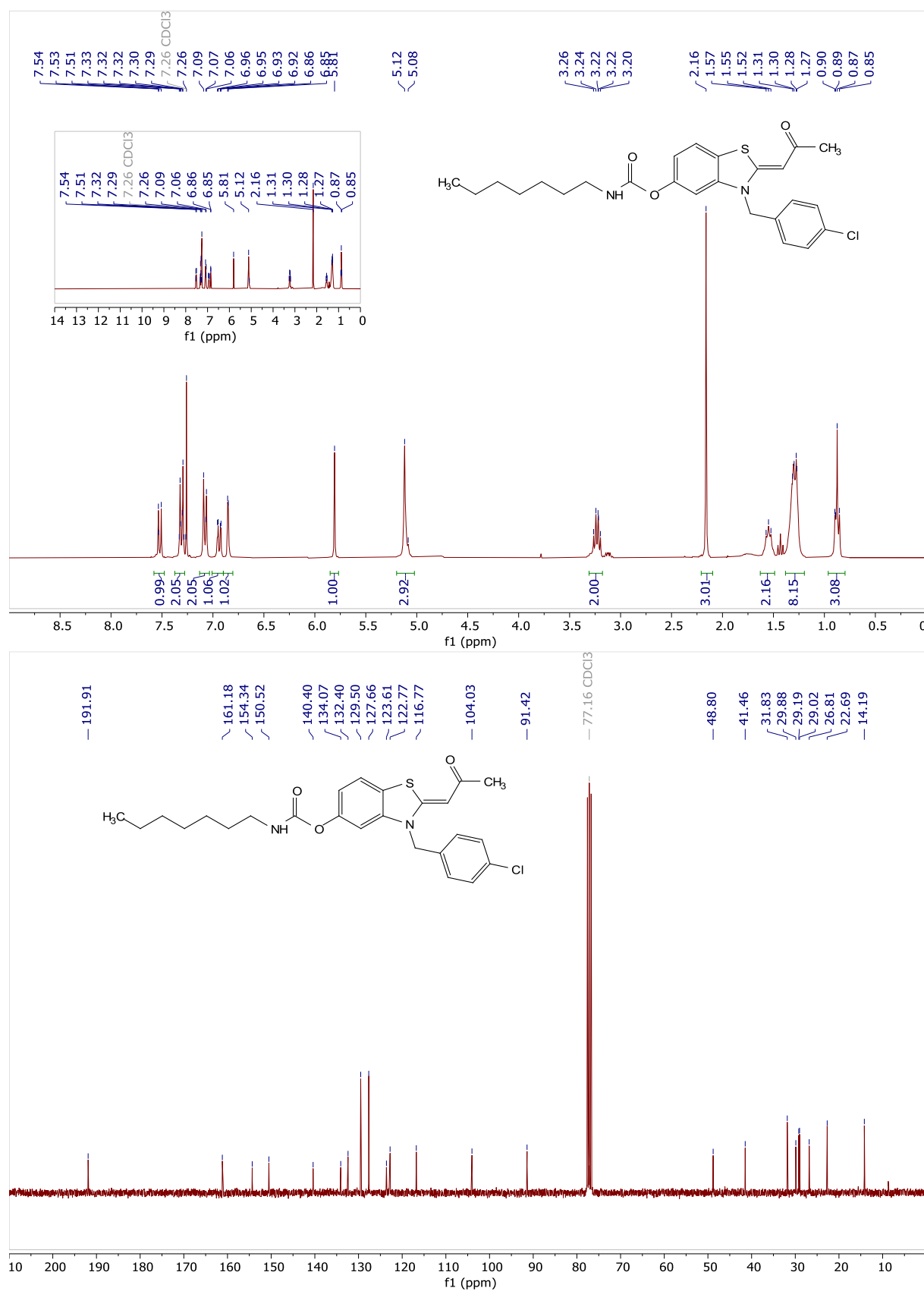
(Z)-3-(3-Methylbenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1g**)



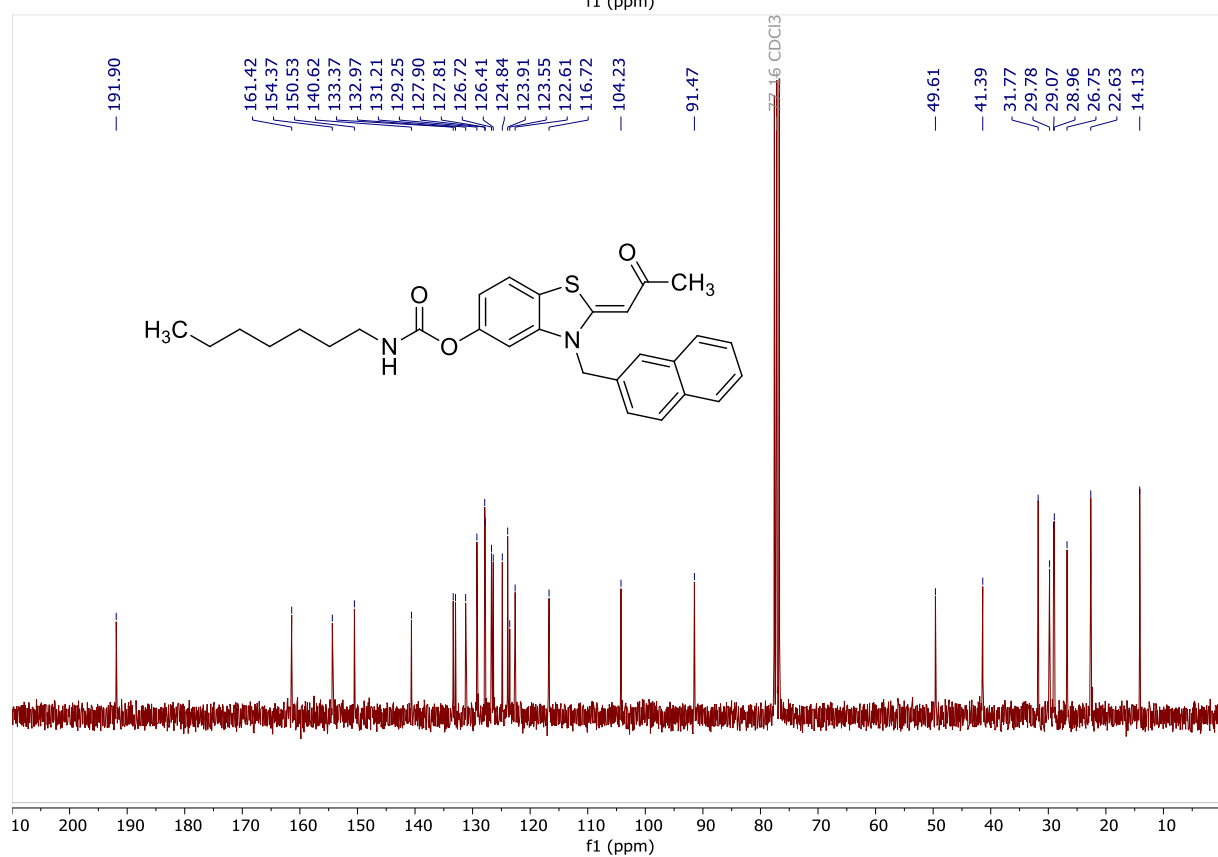
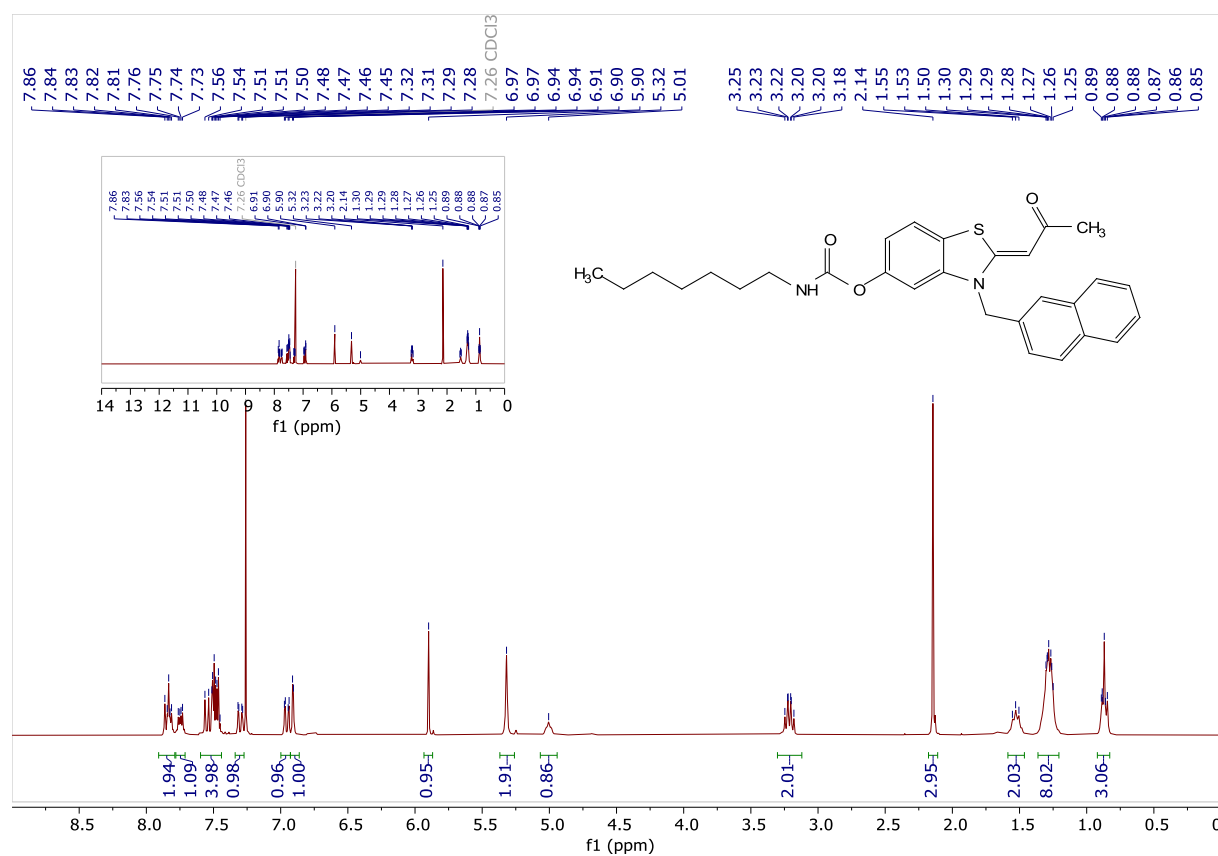
(Z)-3-(3-Chlorobenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1h**)



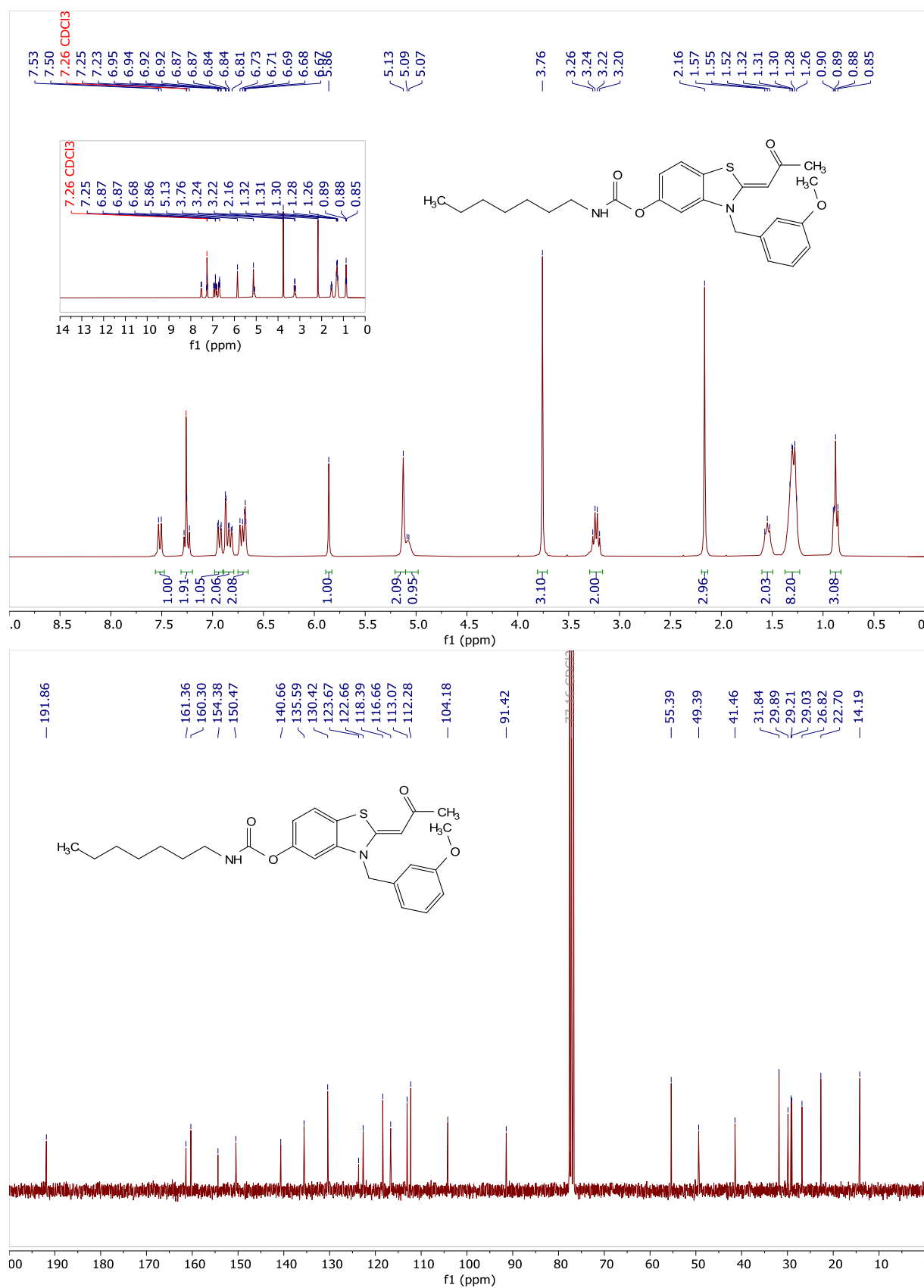
(Z)-3-(4-Chlorobenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1i**)



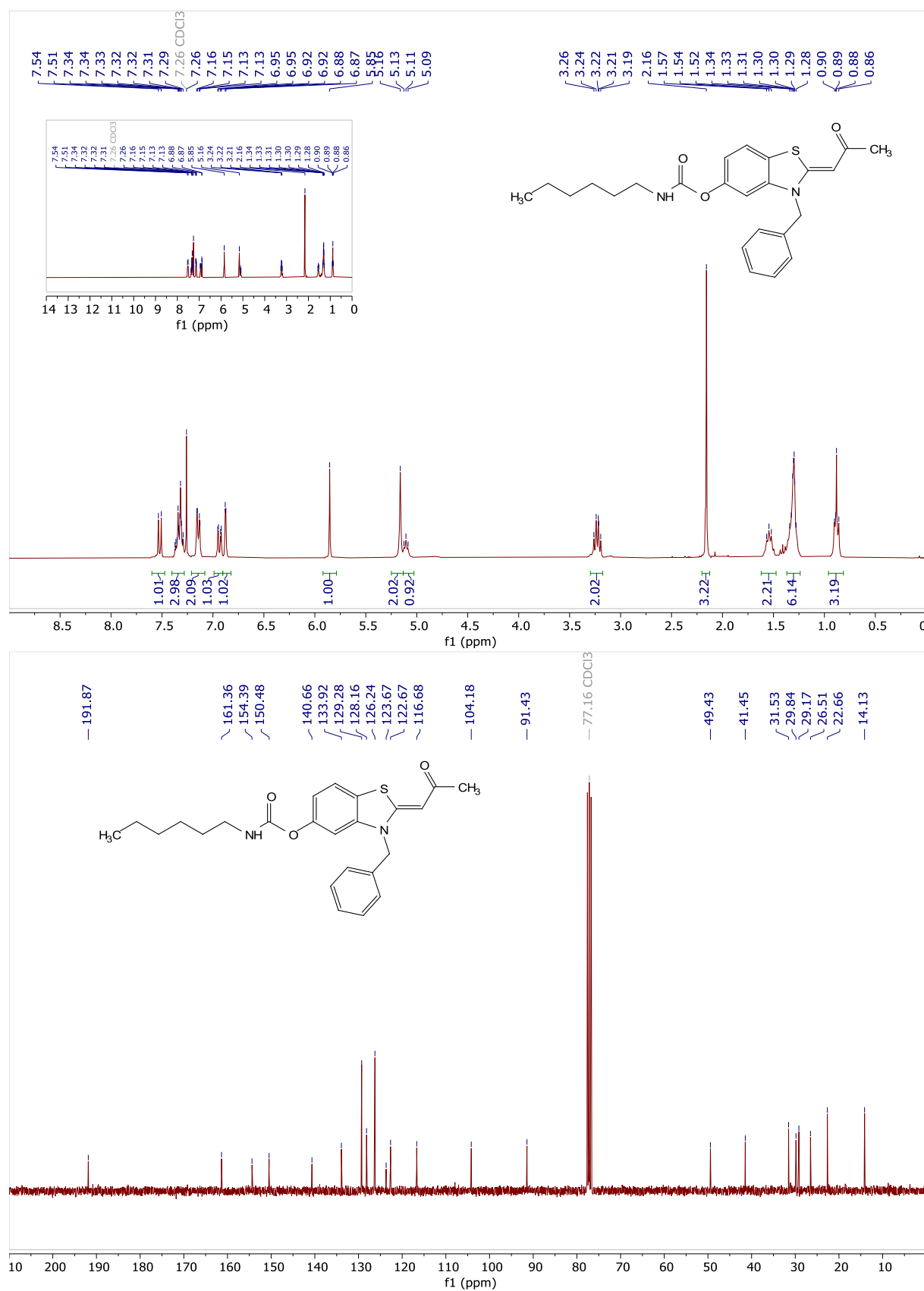
(Z)-3-(2-Naphtyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1j**)



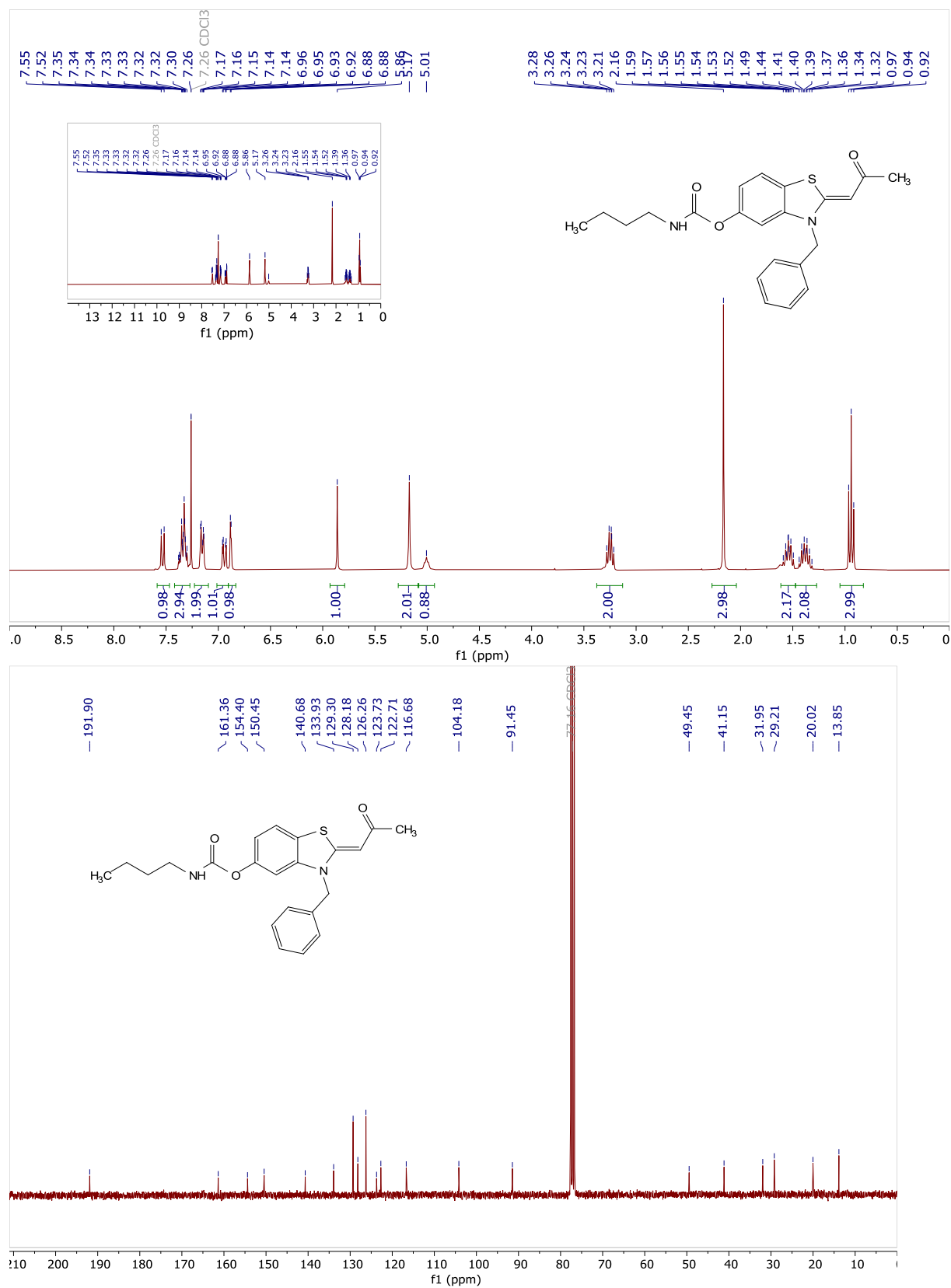
(Z)-3-(3-Methoxybenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1k**)



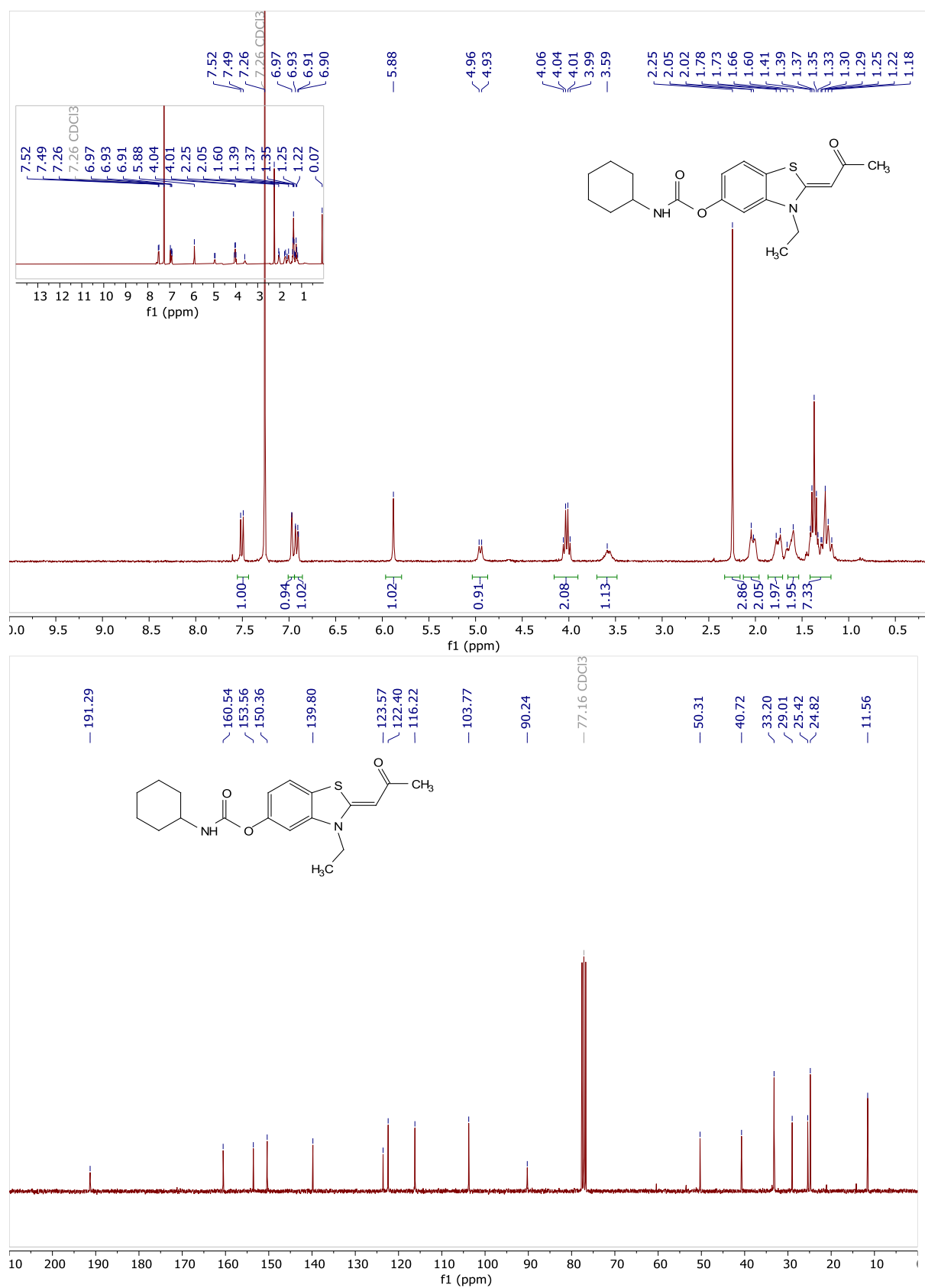
(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl hexylcarbamate (**1l**)



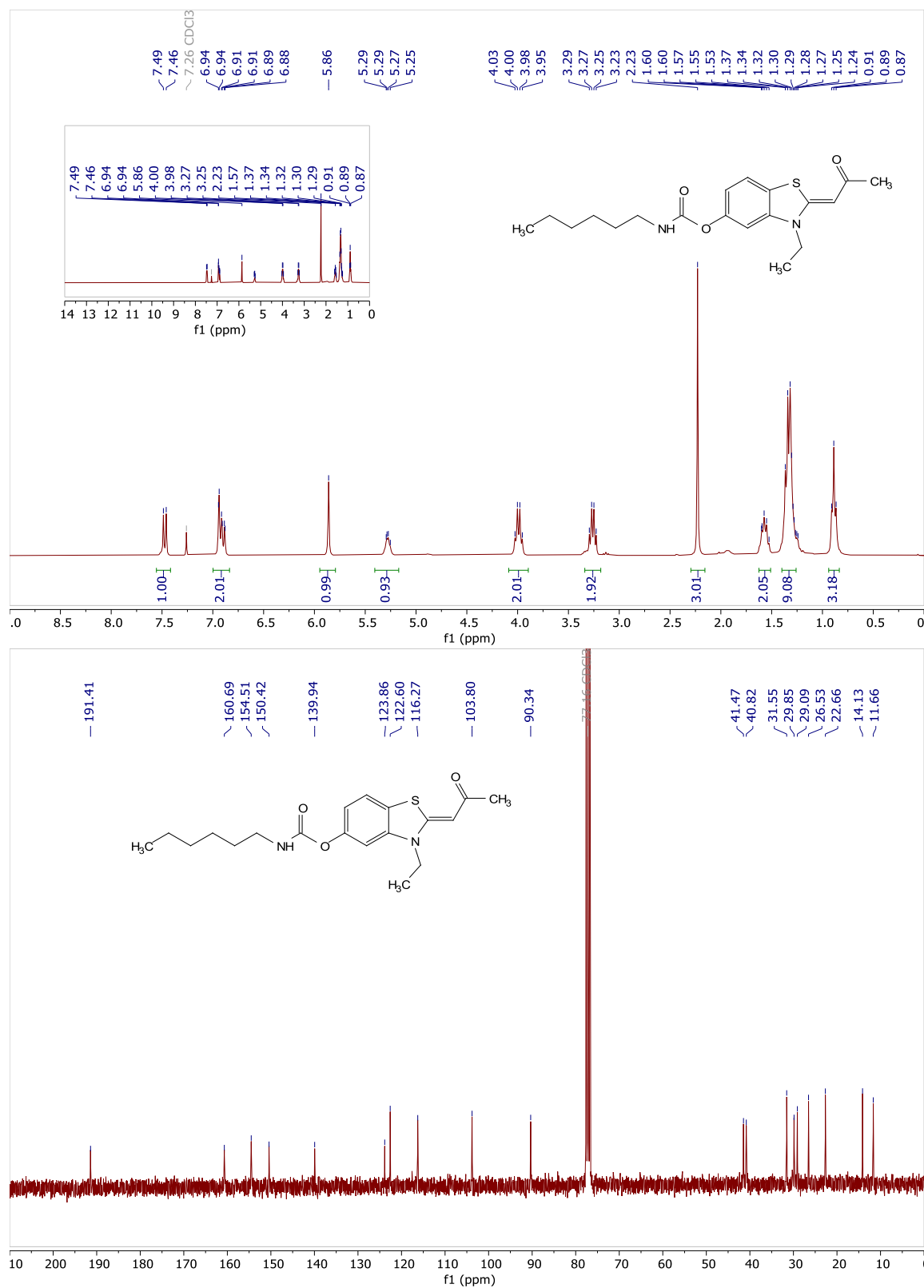
(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl butylcarbamate (**1m**)



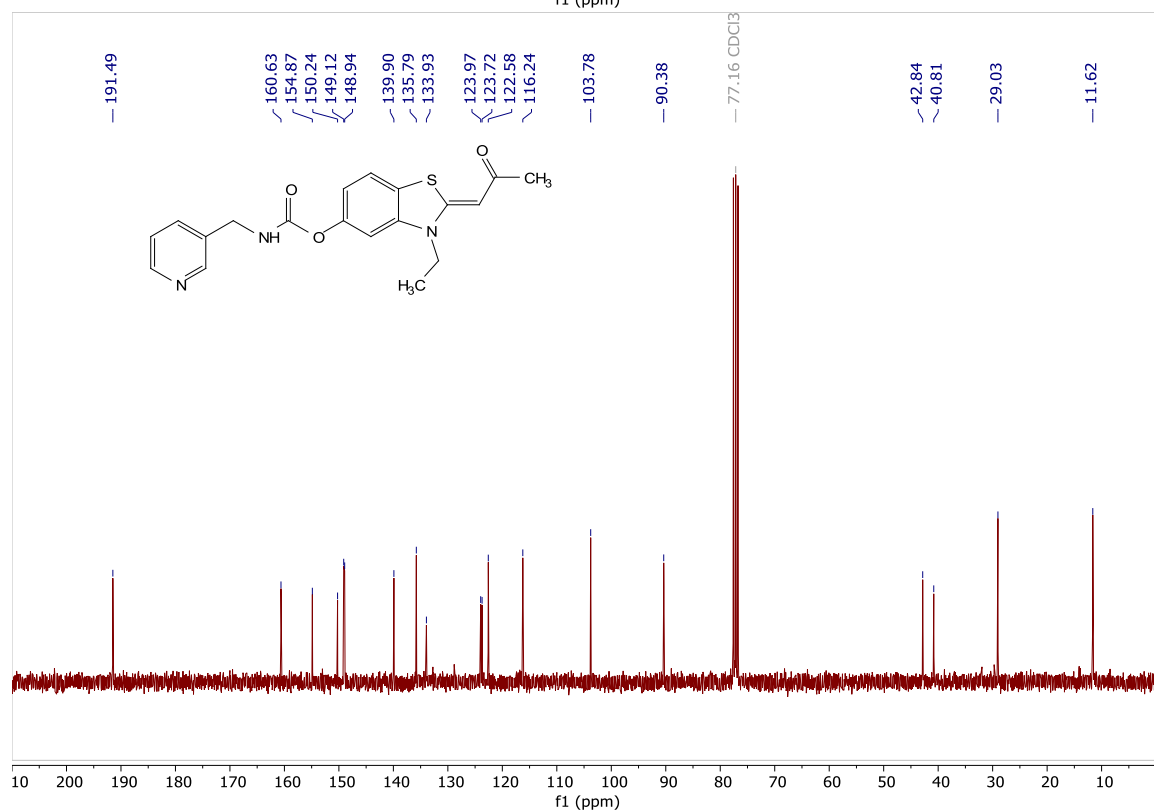
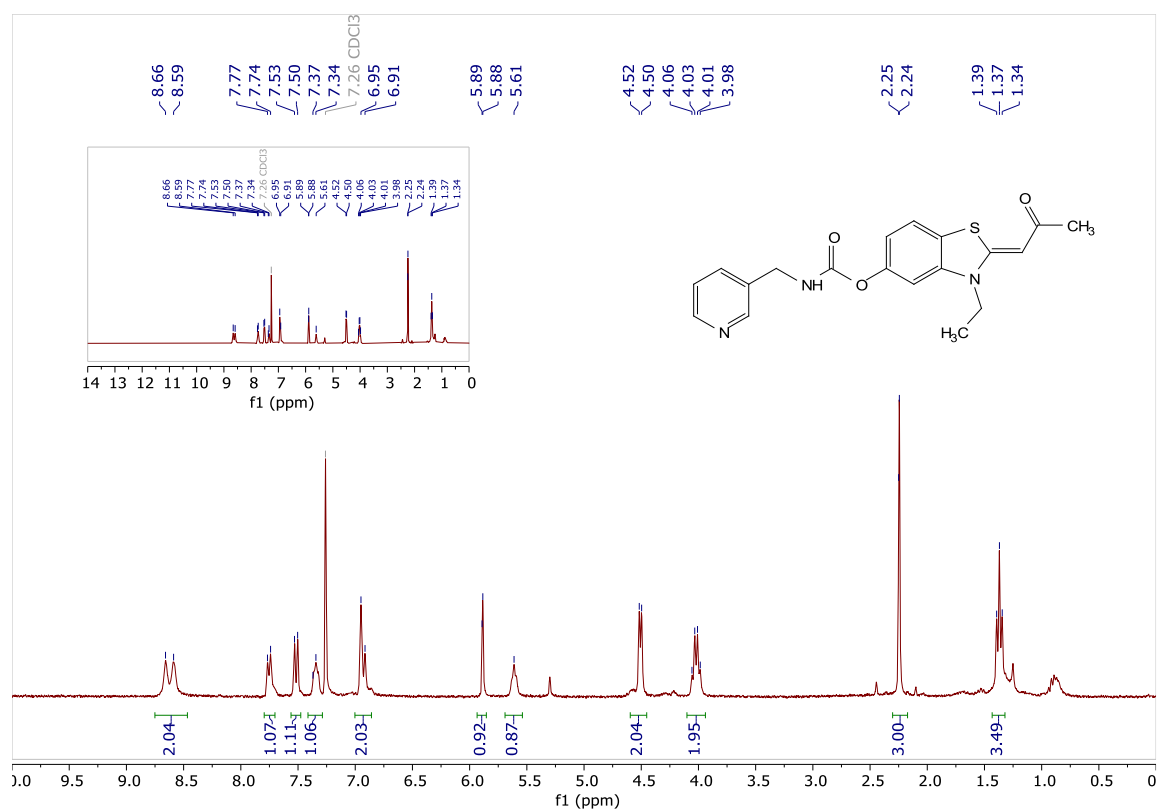
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl cyclohexylcarbamate (**1n**)



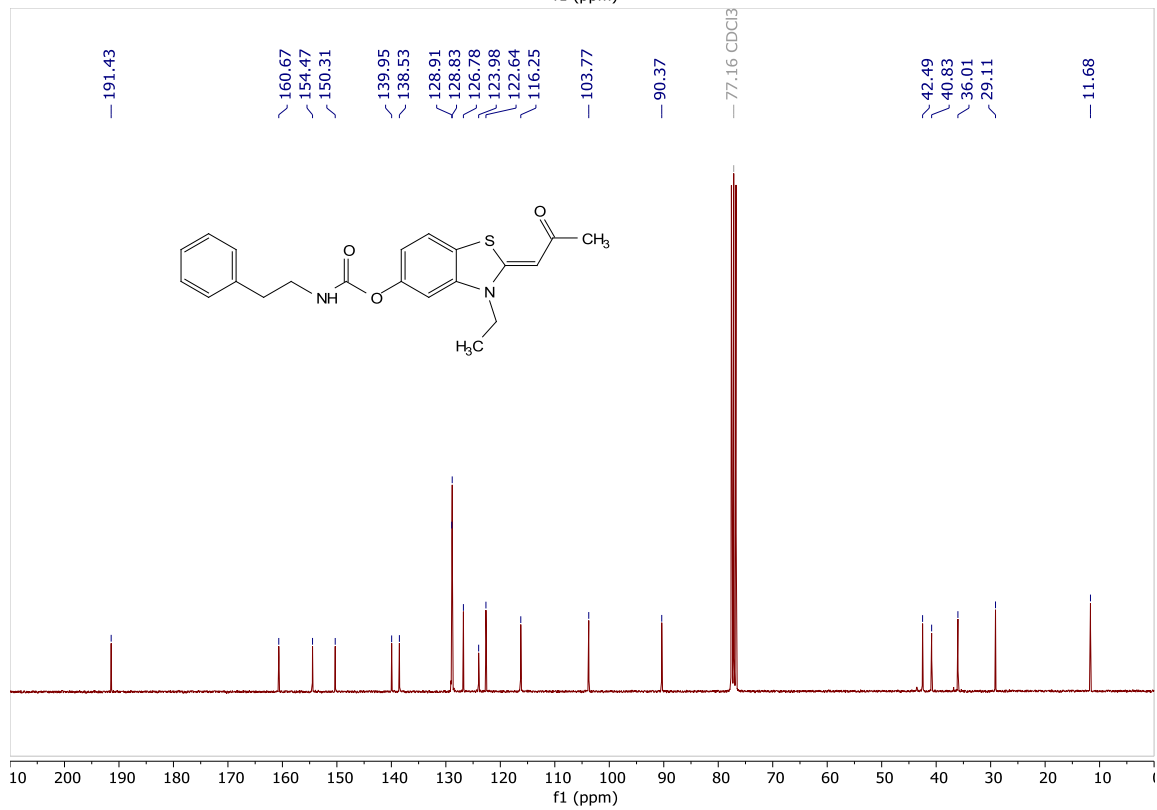
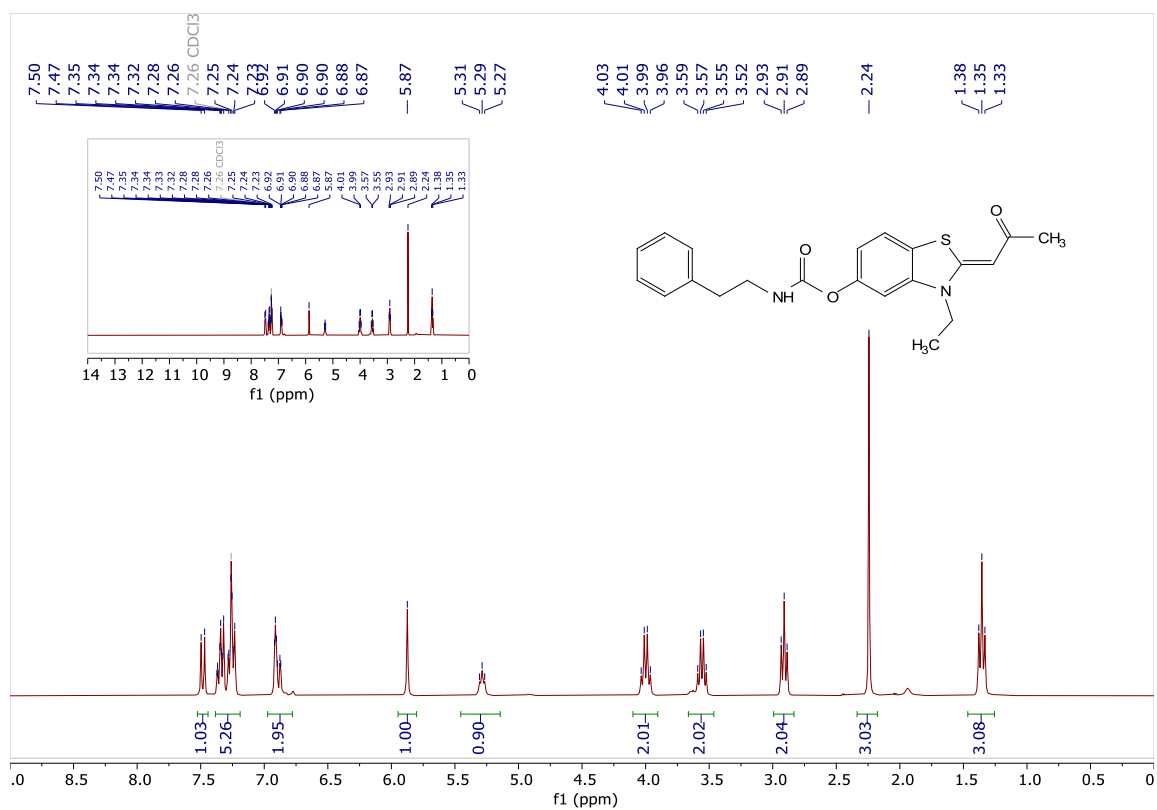
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl hexylcarbamate (10)



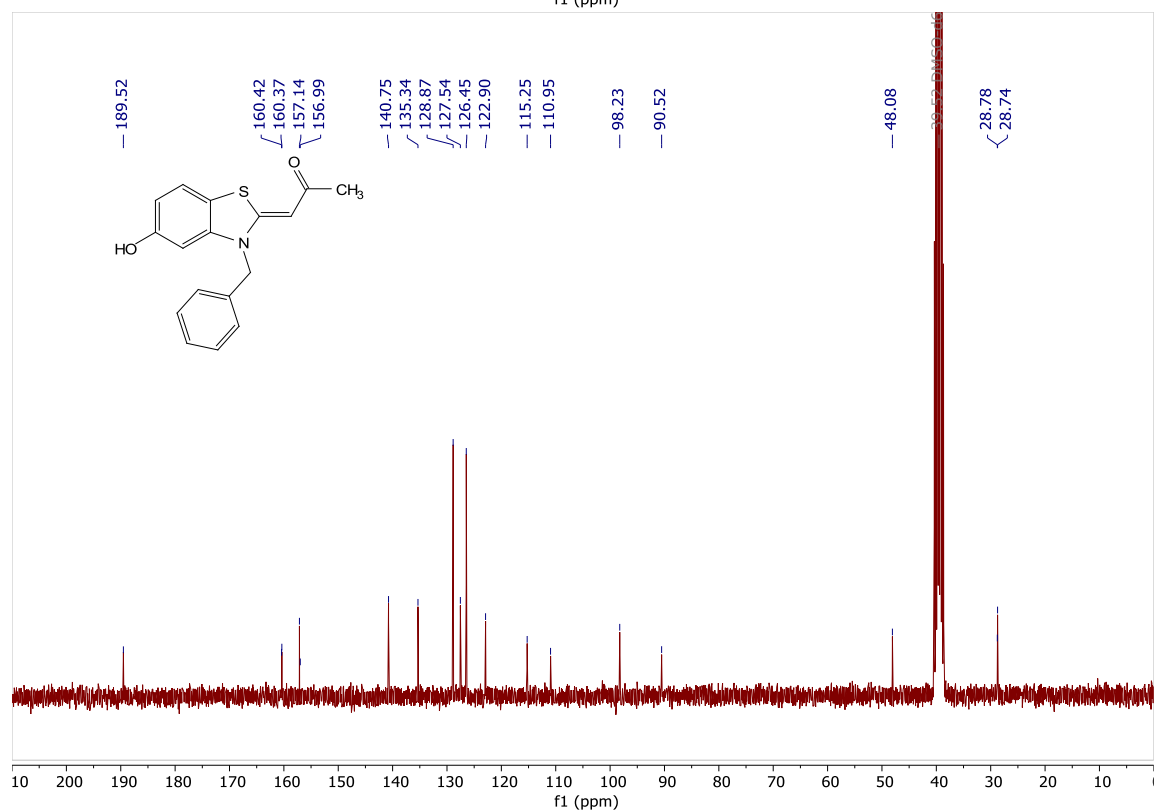
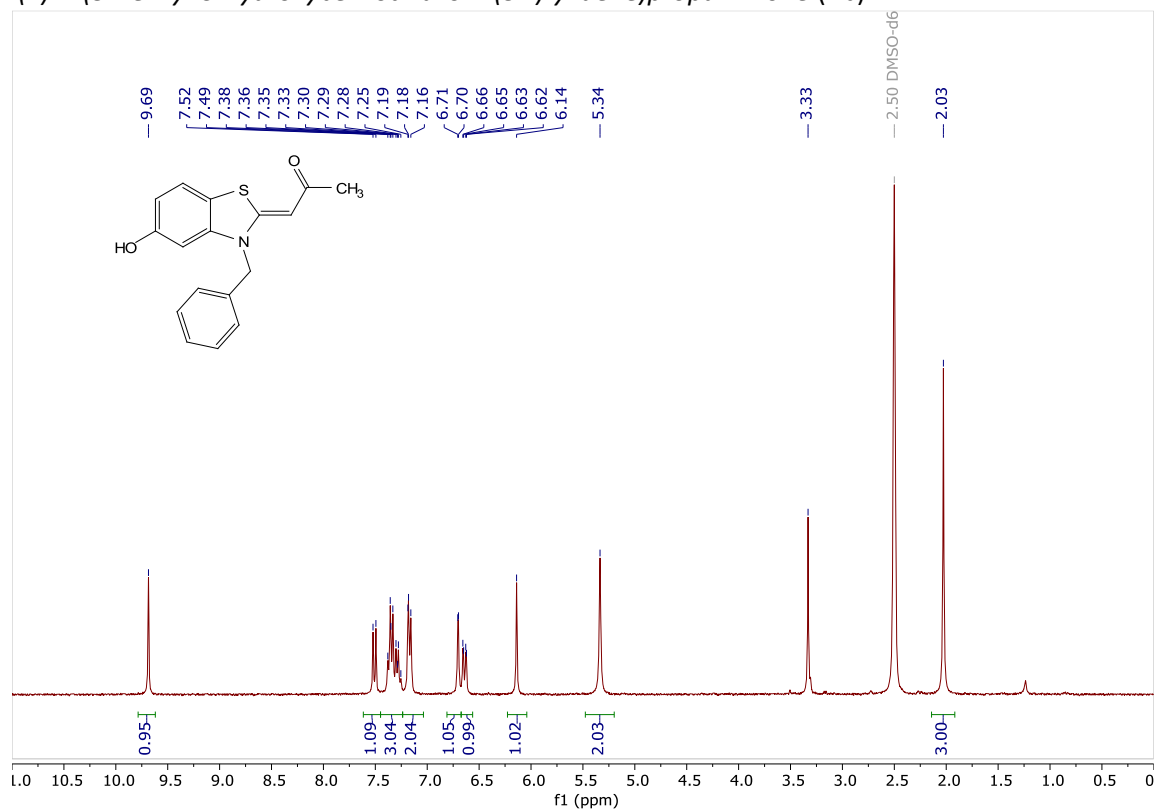
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl (pyridin-3-ylmethyl) carbamate (1p)



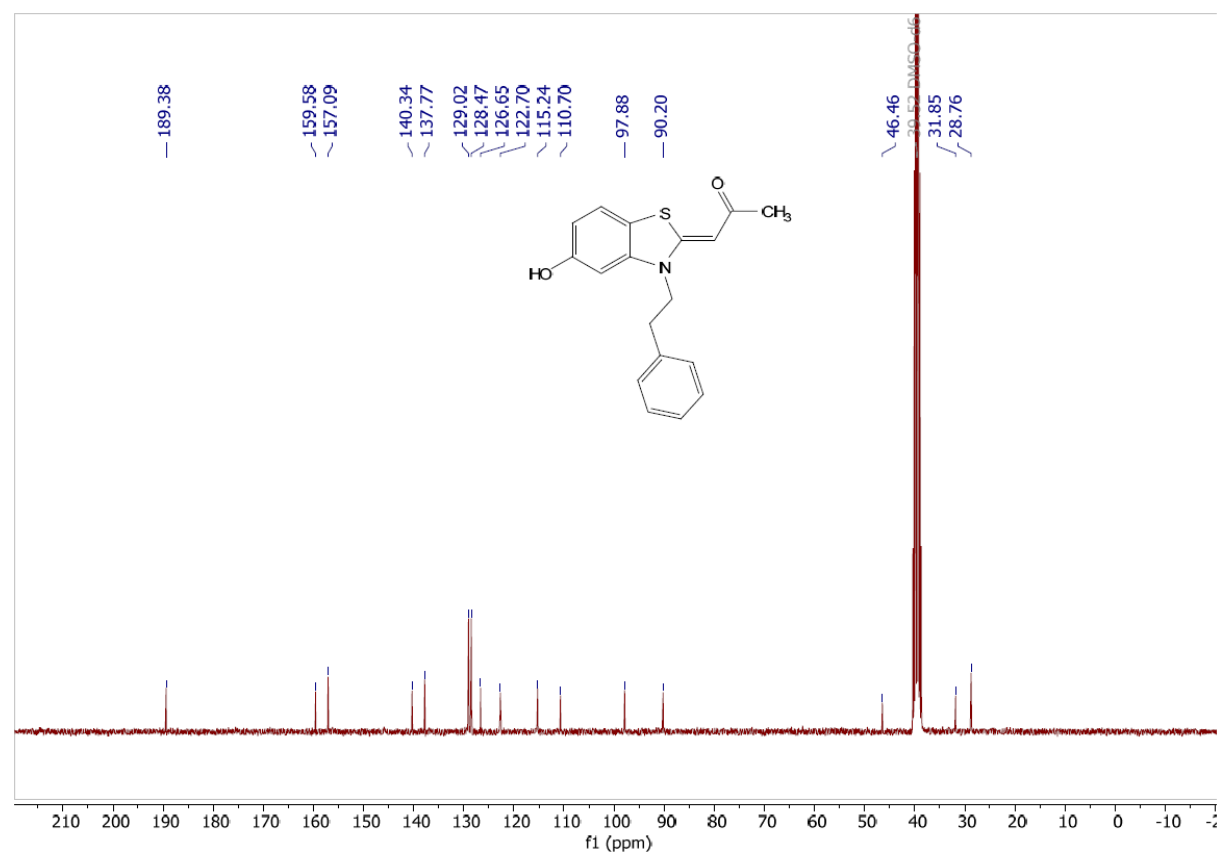
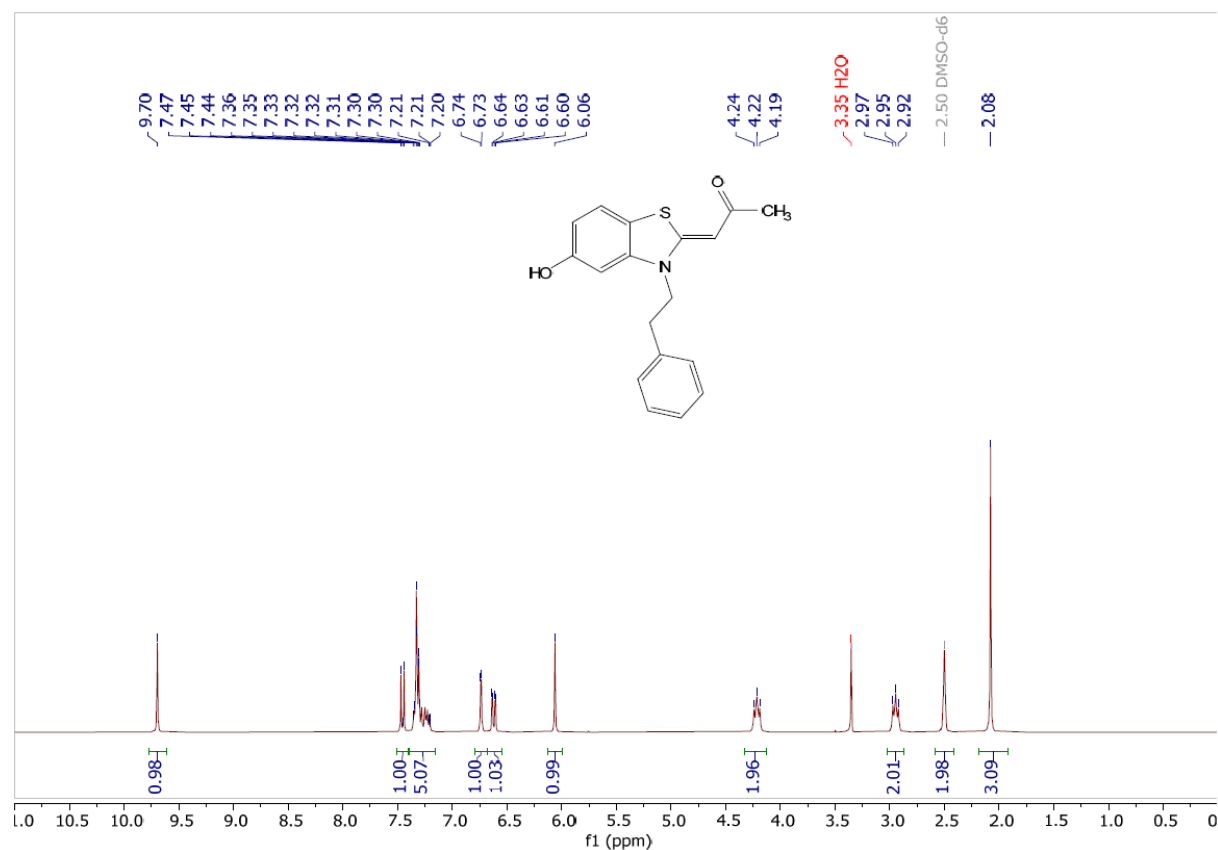
(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl phenethylcarbamate (1q)



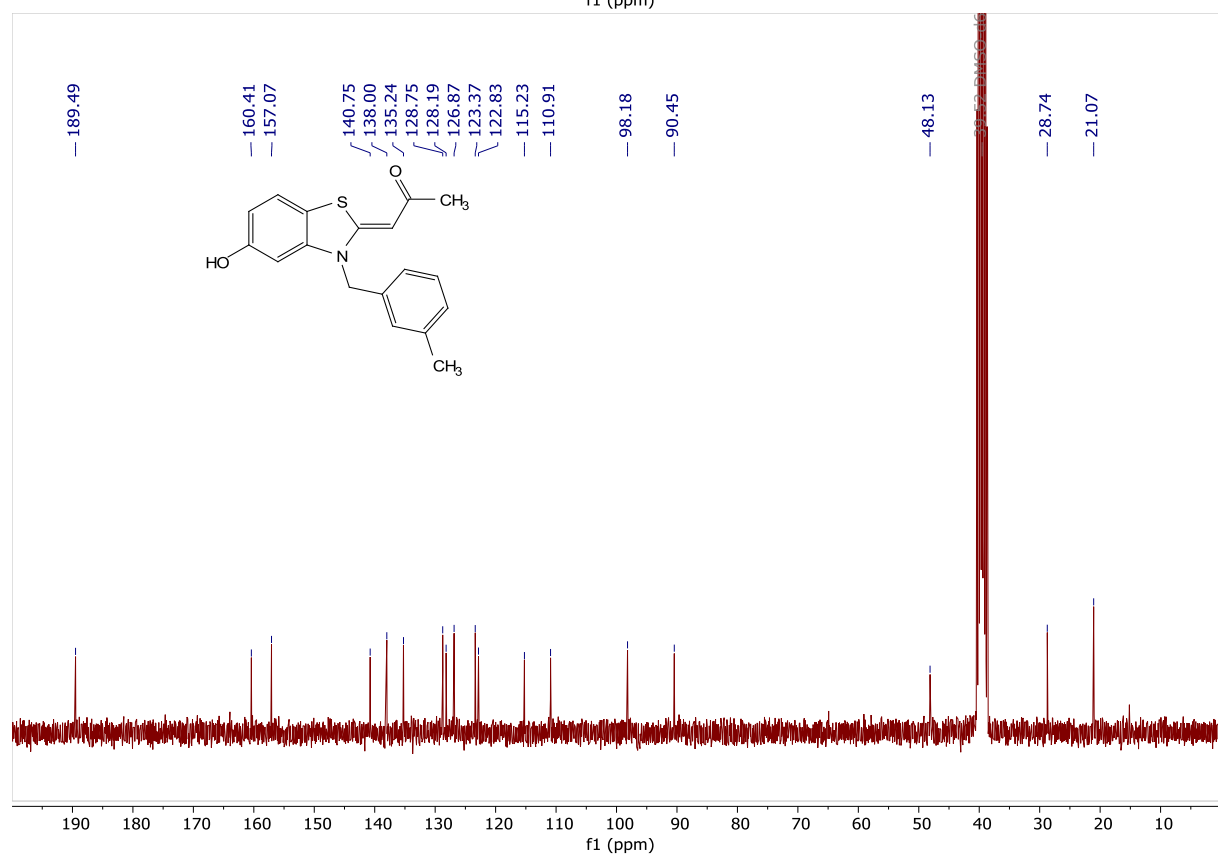
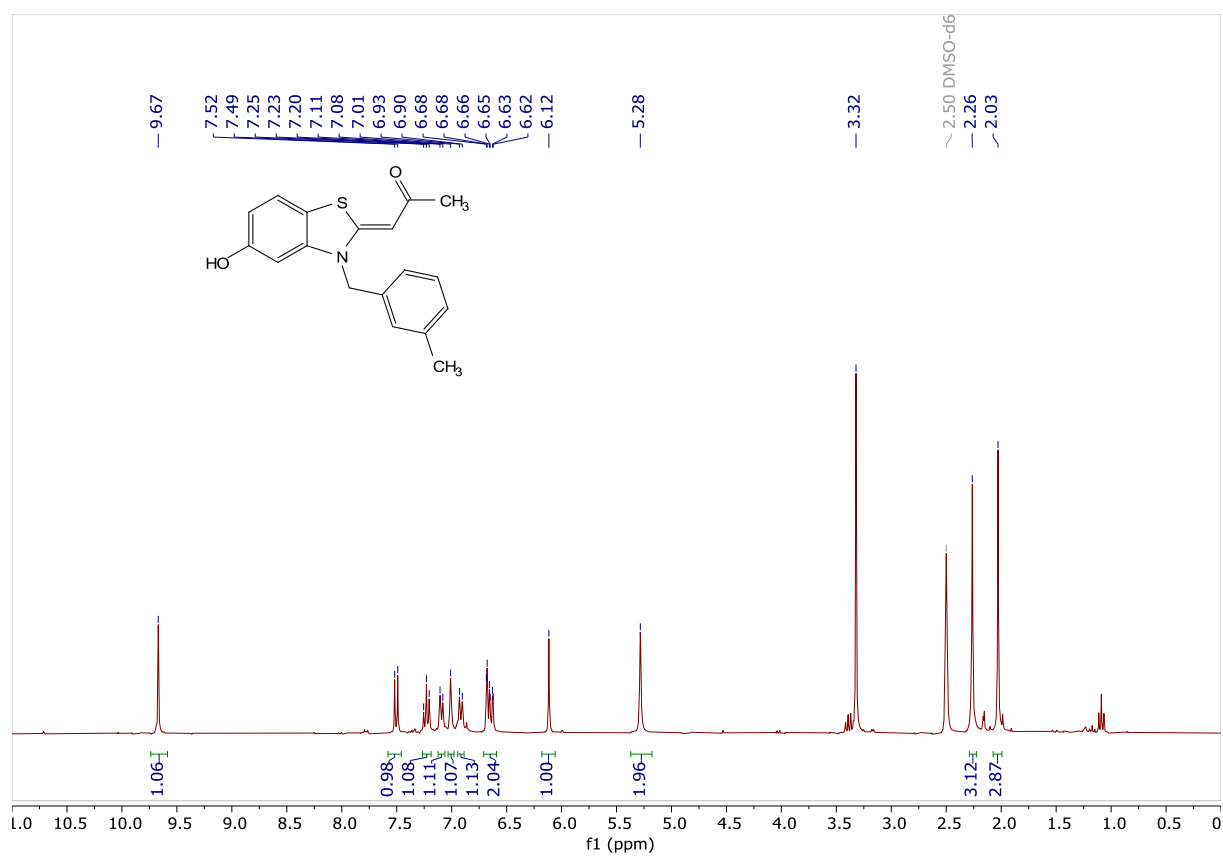
(Z)-1-(3-Benzyl-5-hydroxybenzothiazol-2(3H)-ylidene)propan-2-one (2b)



(Z)-1-(5-Hydroxy-3-phenethylbenzo[d]thiazol-2(3H)-ylidene)propan-2-one (**2c**)



(Z)-1-(5-Hydroxy-3-(3-methylbenzyl)benzothiazol-2(3H)-ylidene)propan-2-one (**2d**)



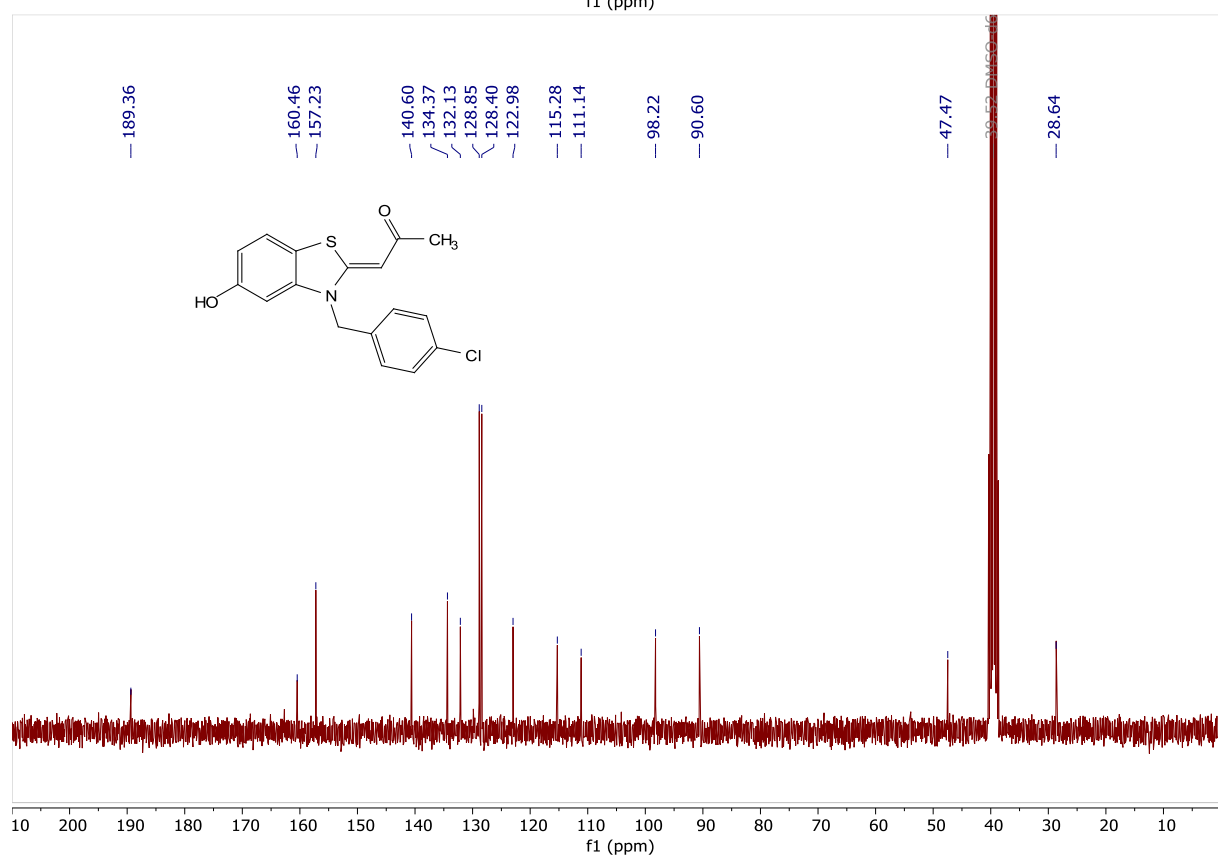
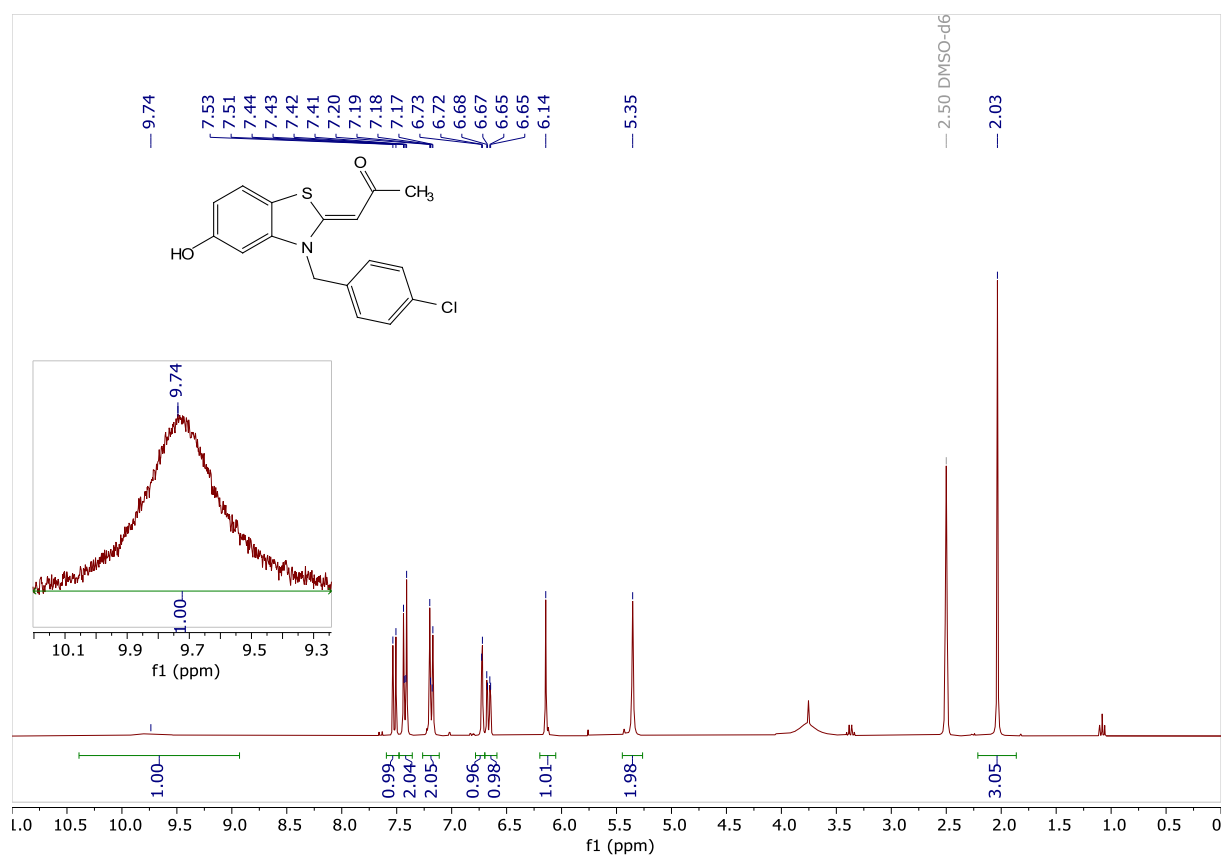
Chemical structure: CC(=O)N1C(Sc2ccc(O)cc2)N(Cc3ccc(Cl)cc3)C1

¹H NMR spectrum (DMSO-d₆) showing peaks and integrations:

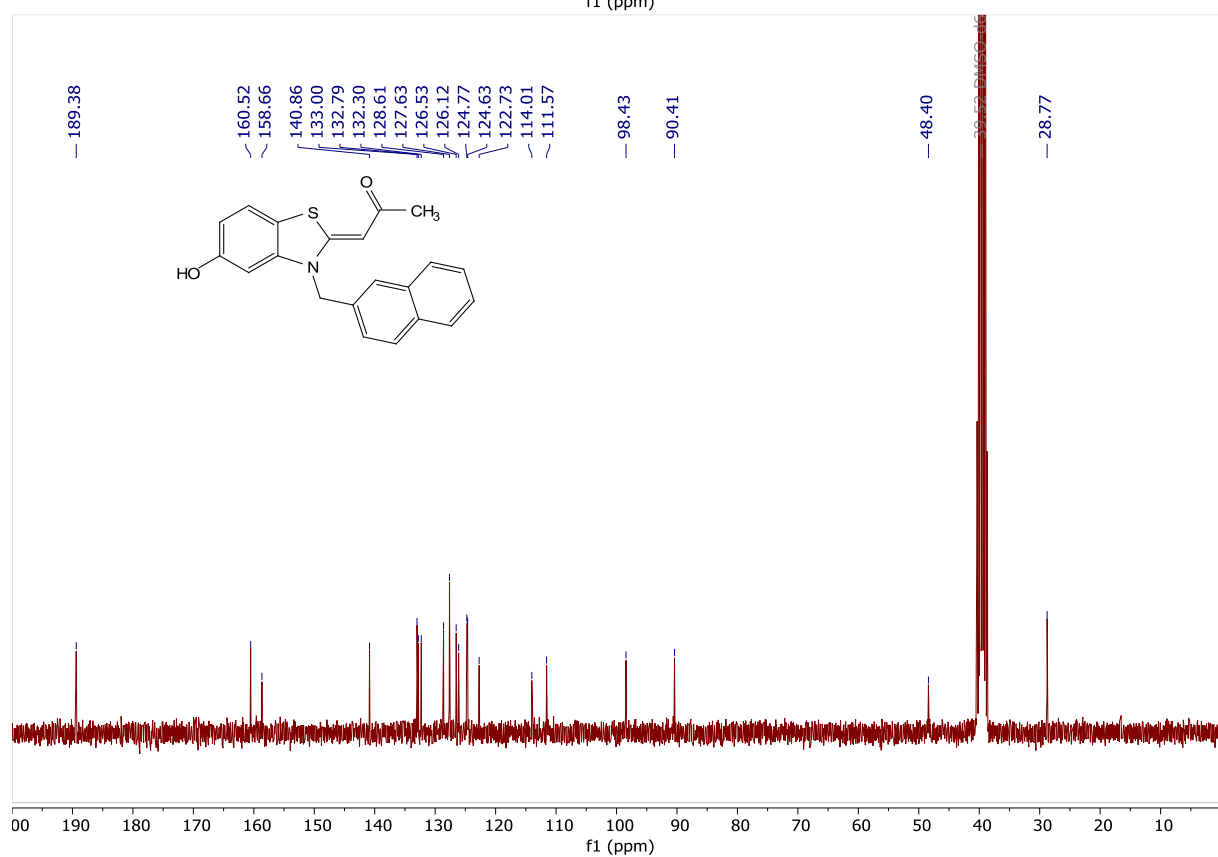
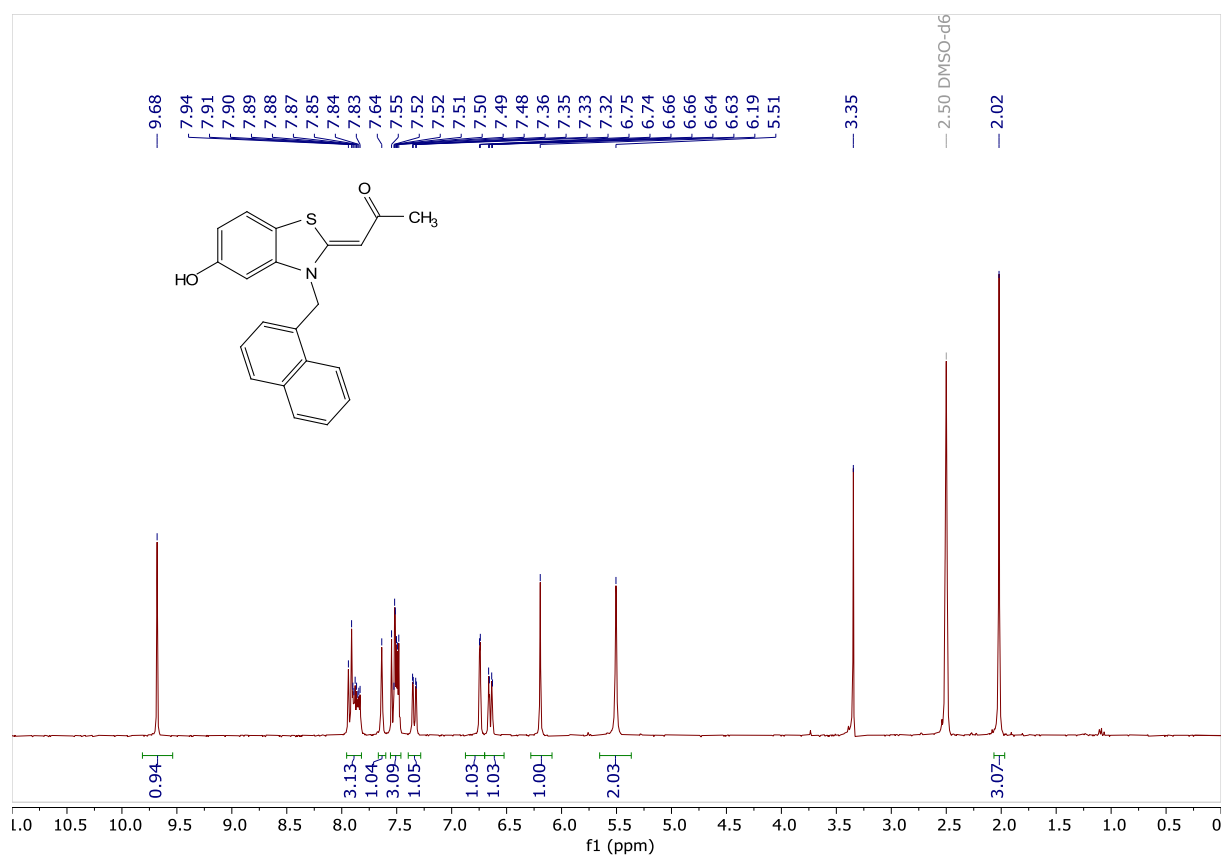
Chemical Shift (ppm)	Integration
9.66	0.96
7.53, 7.50, 7.39, 7.38, 7.37, 7.36, 7.27, 7.26, 7.26, 7.08, 7.07, 7.06, 7.05, 6.71, 6.71, 6.67, 6.67, 6.64, 6.15	1.03, 2.08, 1.01, 1.03, 1.02, 1.02, 1.00
5.37	1.98
3.42	
2.50 (DMSO-d ₆)	
2.04	2.99



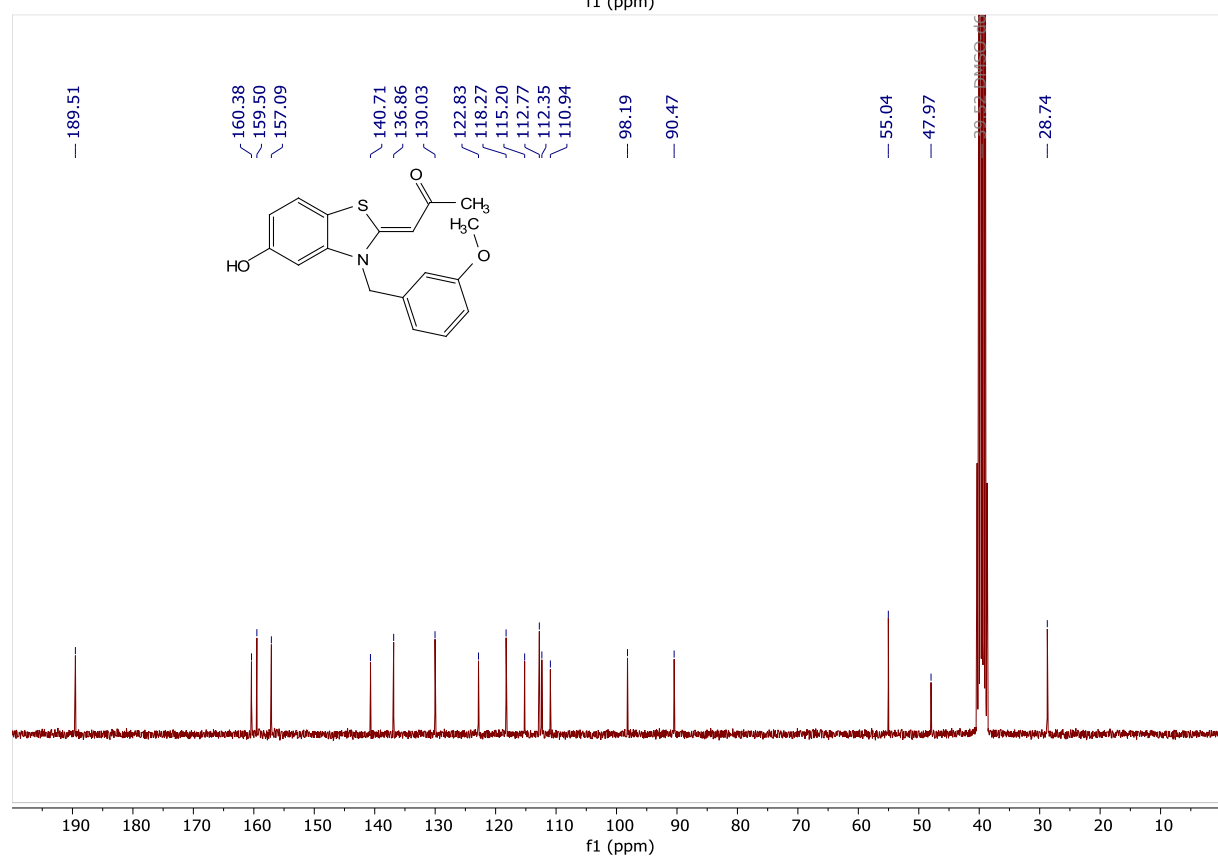
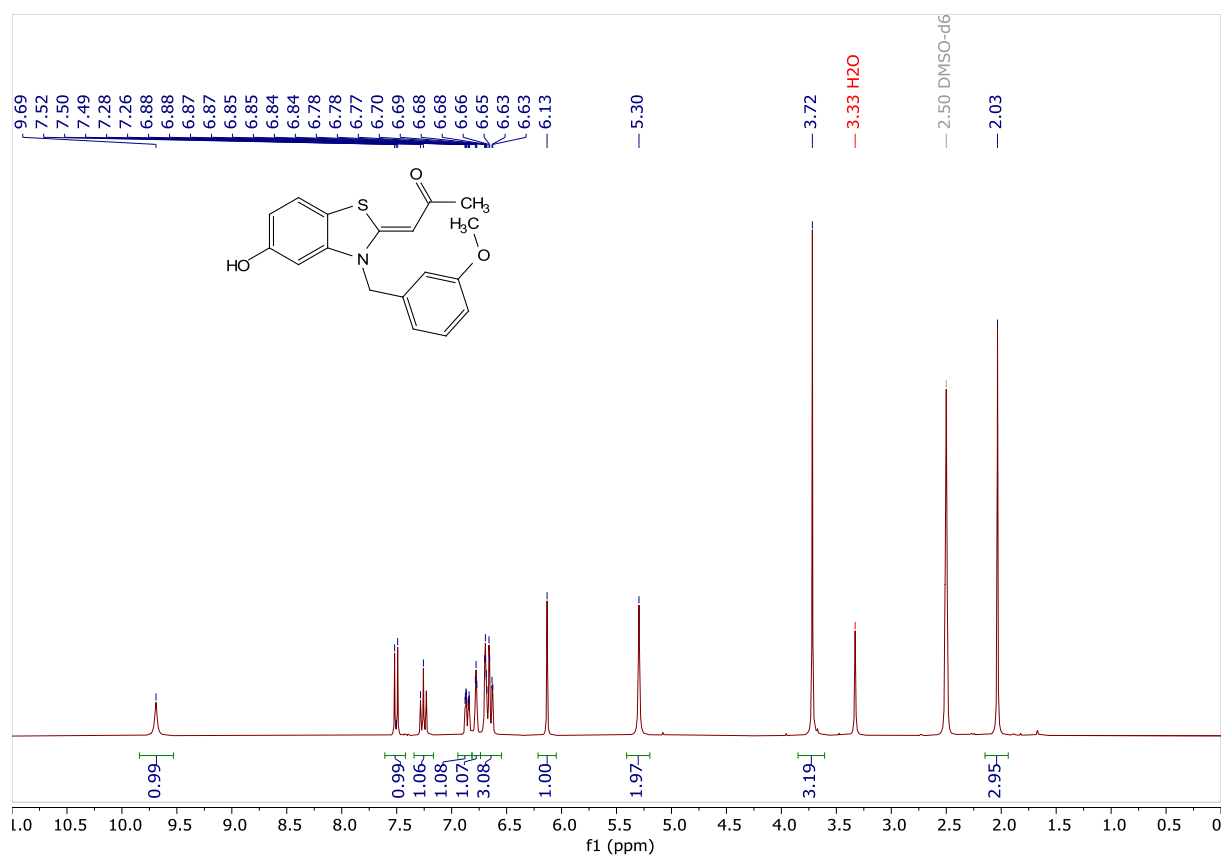
(Z)-1-(5-Hydroxy-3-(4-chlorobenzyl)benzothiazol-2(3H)-ylidene)propan-2-one (2f)



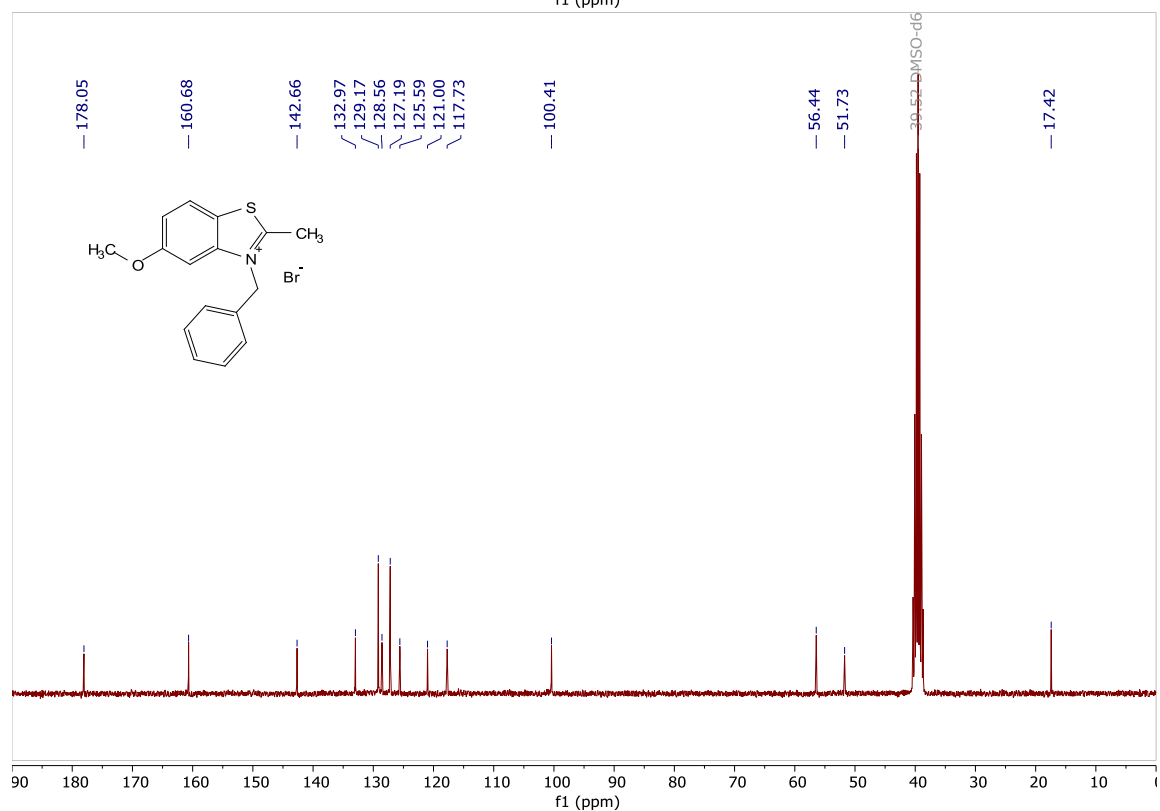
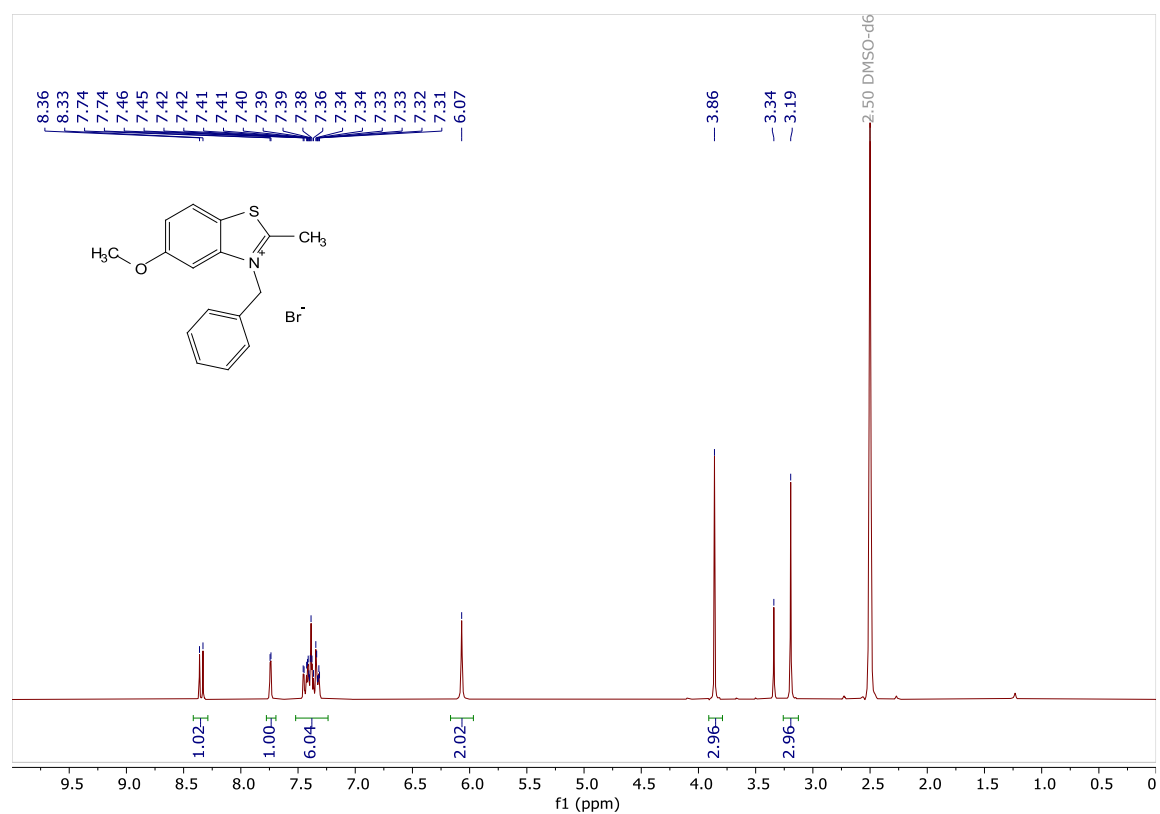
(Z)-1-(5-Hydroxy-3-(naphthalen-2-ylmethyl)benzothiazol-2(3H)-ylidene)propan-2-one (**2g**)



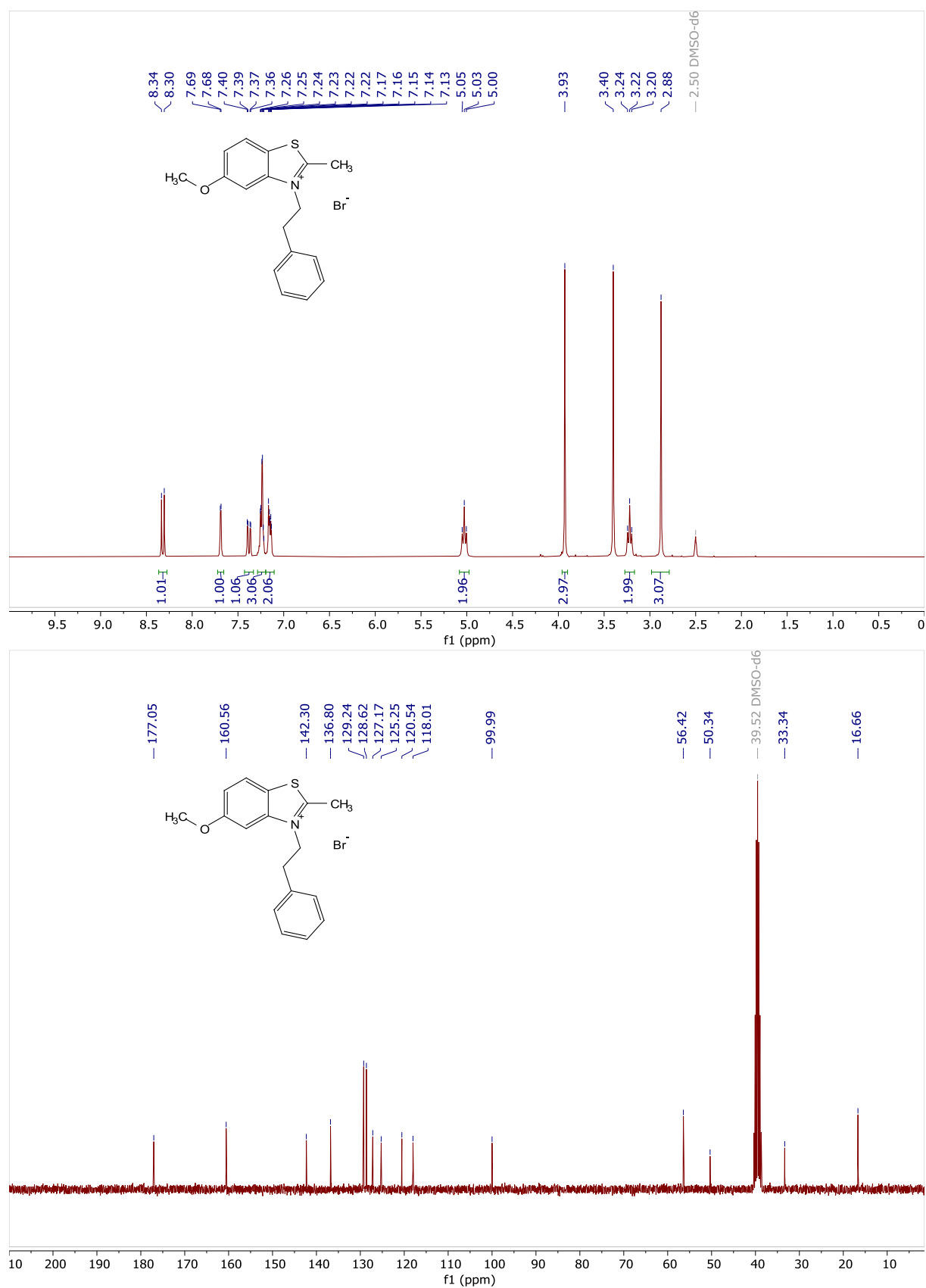
(Z)-1-(5-Hydroxy-3-(3-methoxybenzyl)benzothiazol-2(3H)-ylidene)propan-2-one (2h)



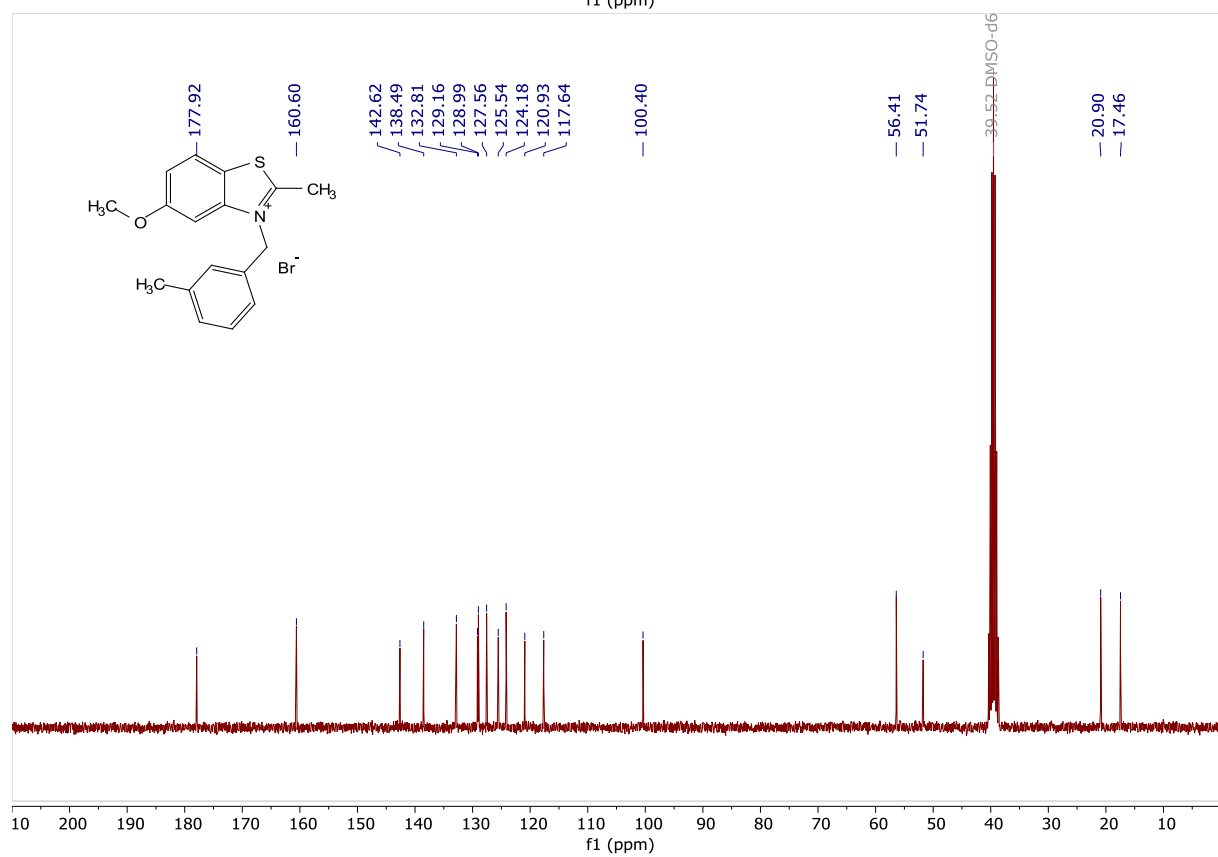
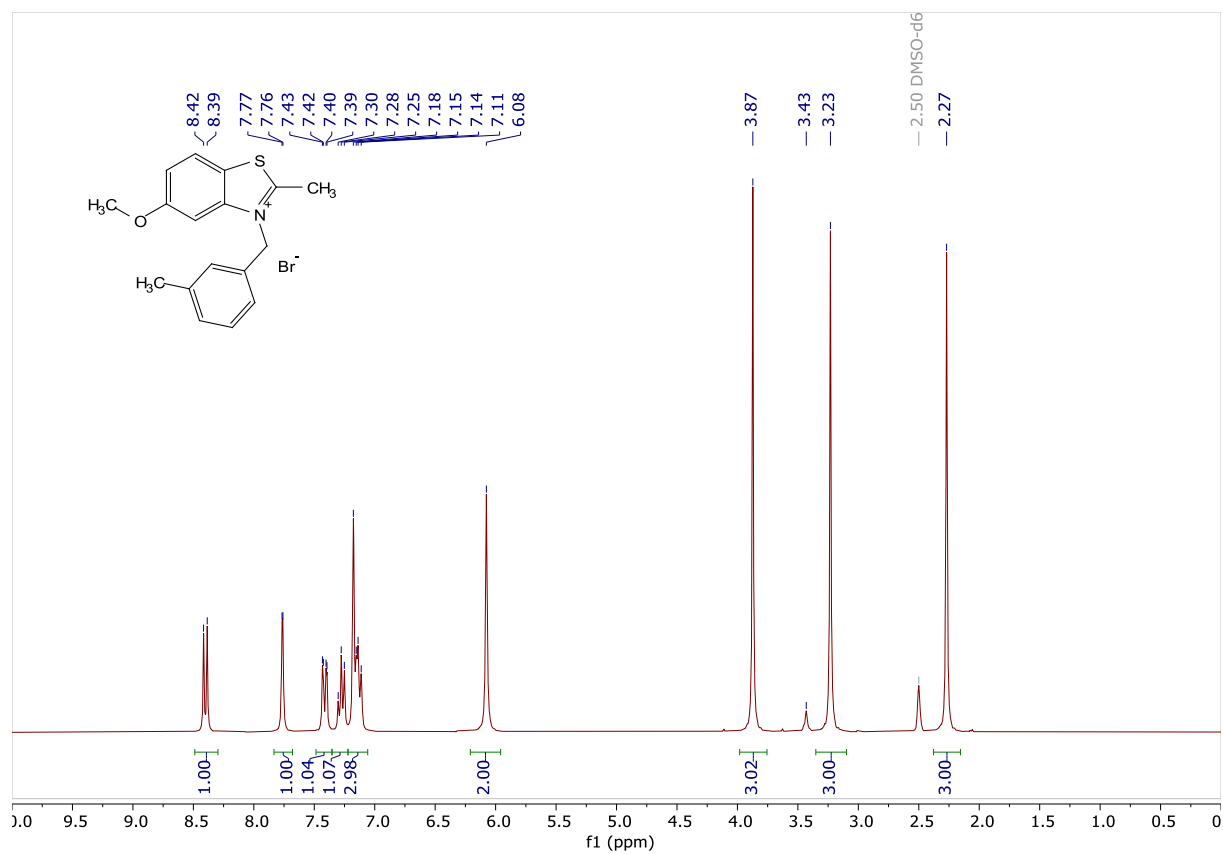
3-Benzyl-5-methoxy-2-methylbenzothiazol-3-ium bromide (3b)



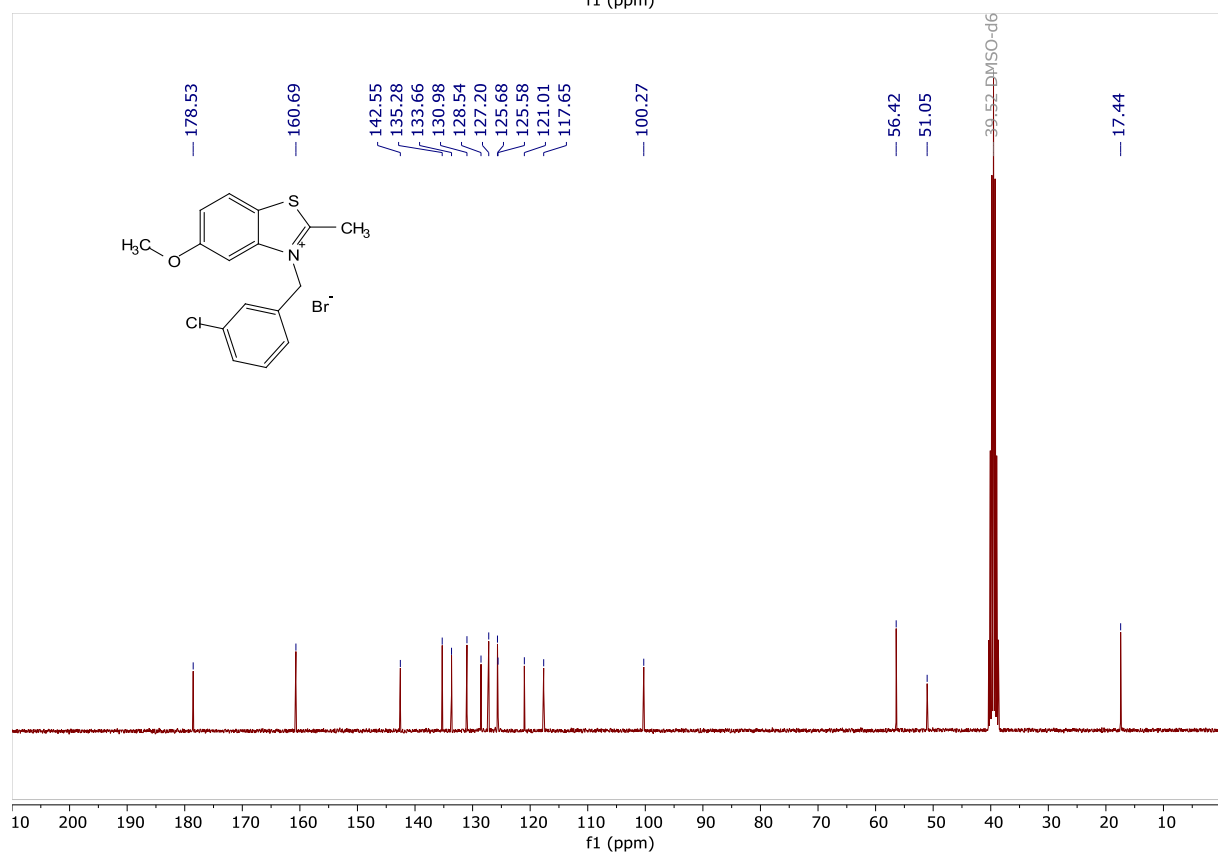
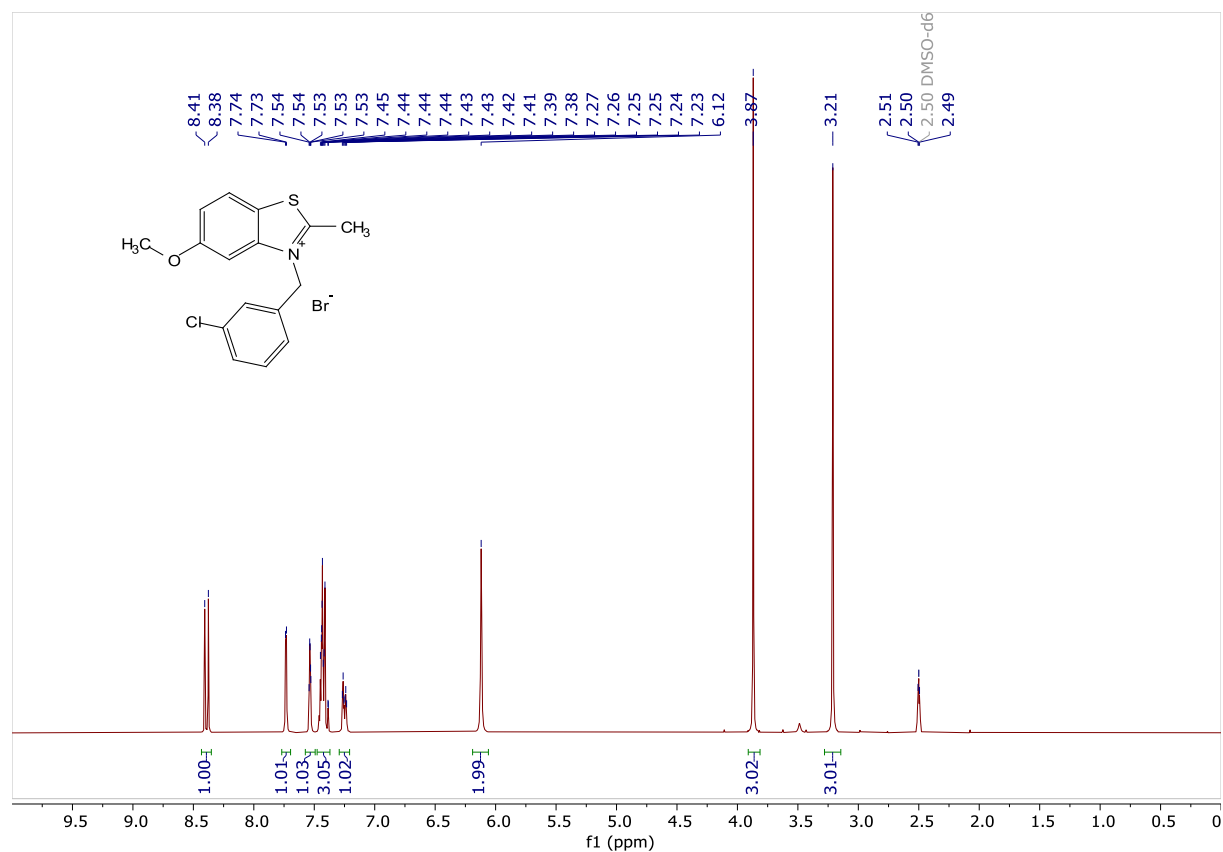
5-Methoxy-2-methyl-3-phenethylbenzothiazol-3-ium bromide (**3c**)



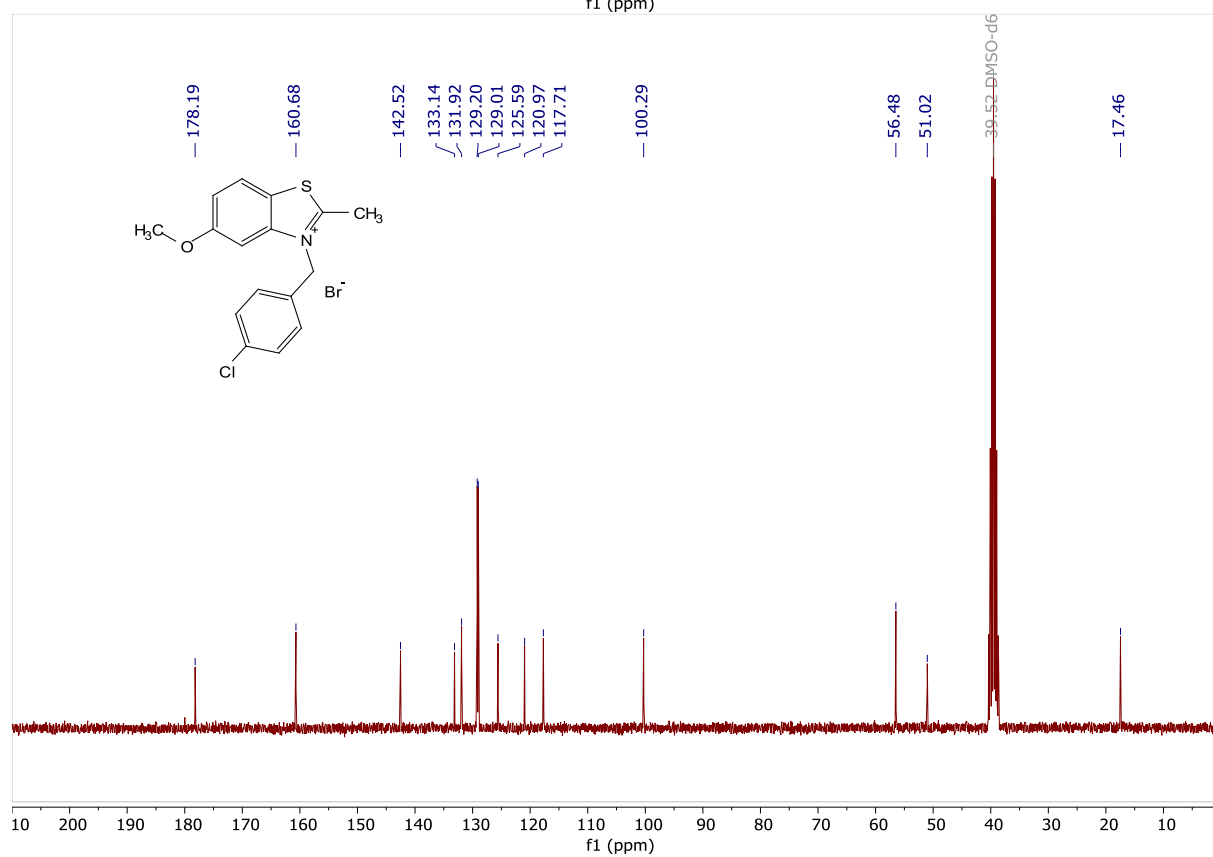
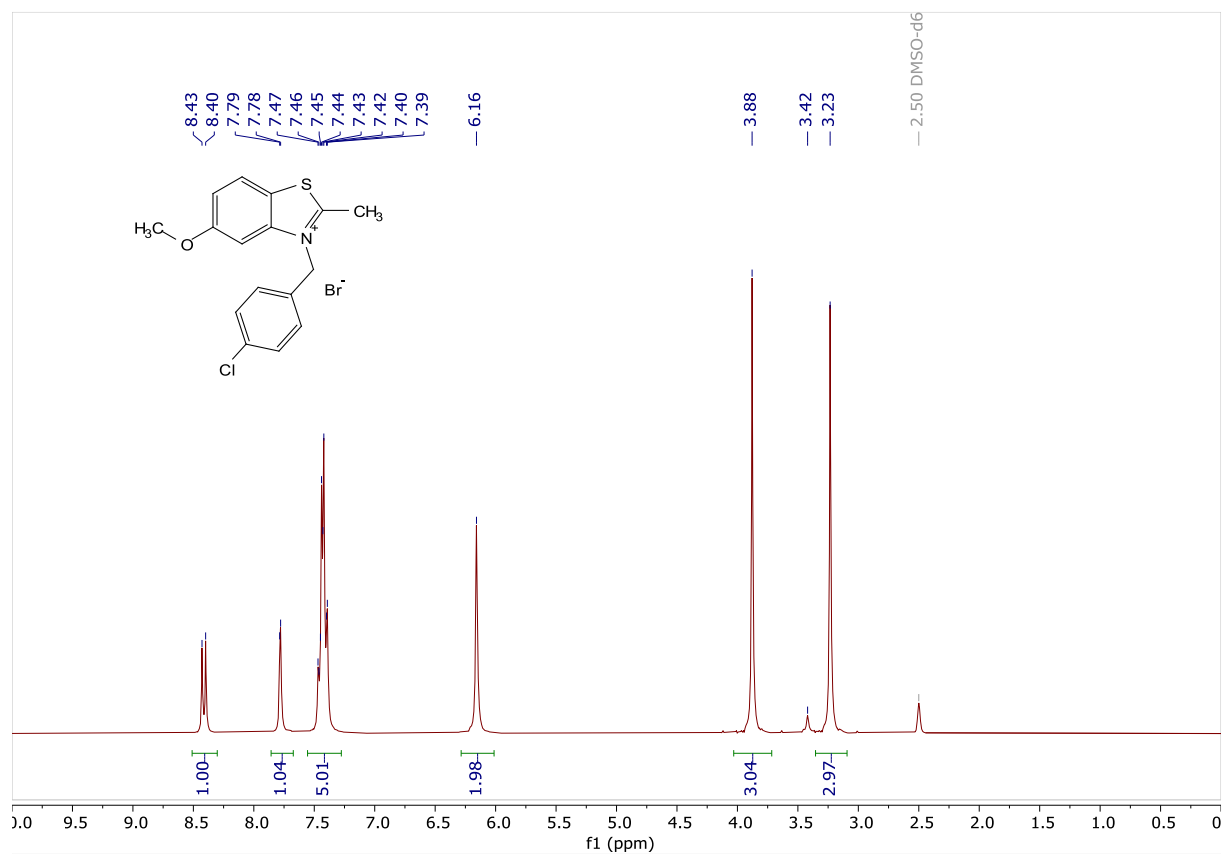
5-Methoxy-3-(3-methylbenzyl)-2-methylbenzothiazol-3-ium bromide (**3d**)



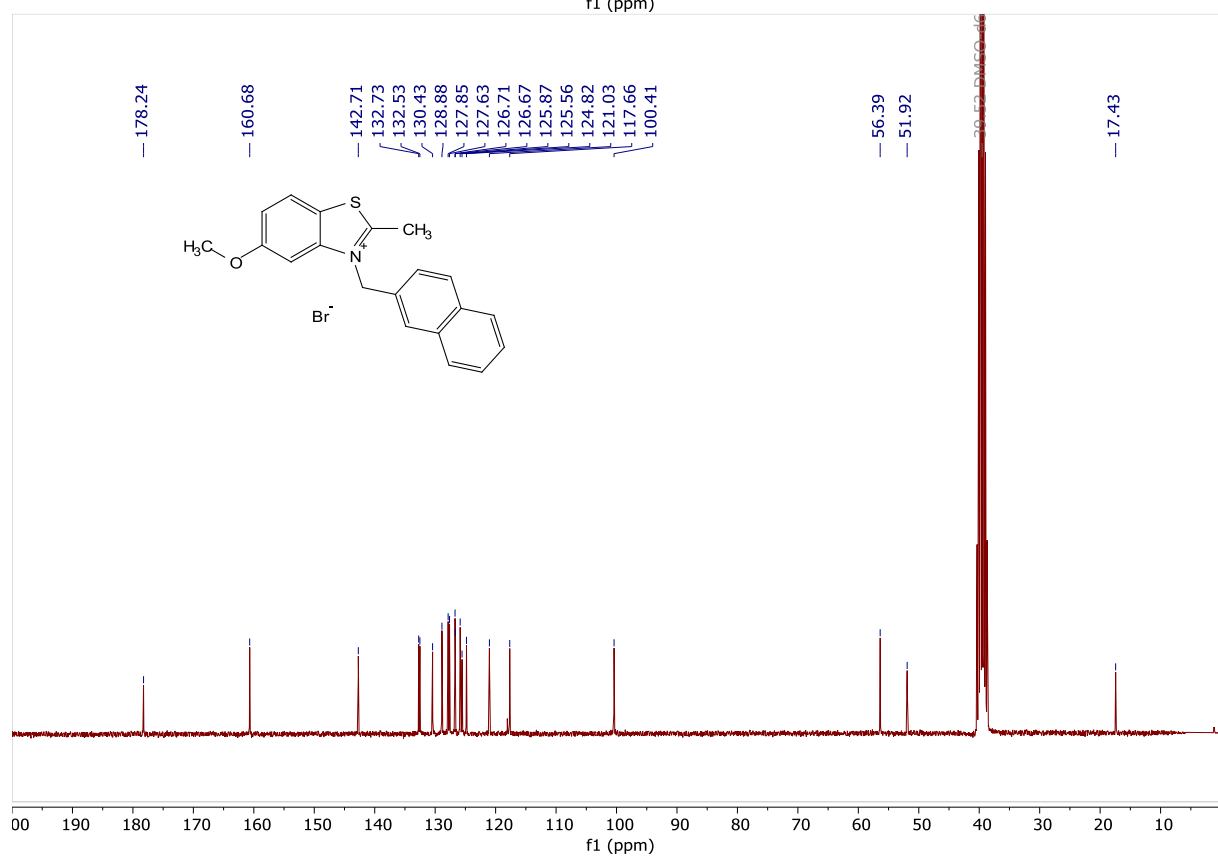
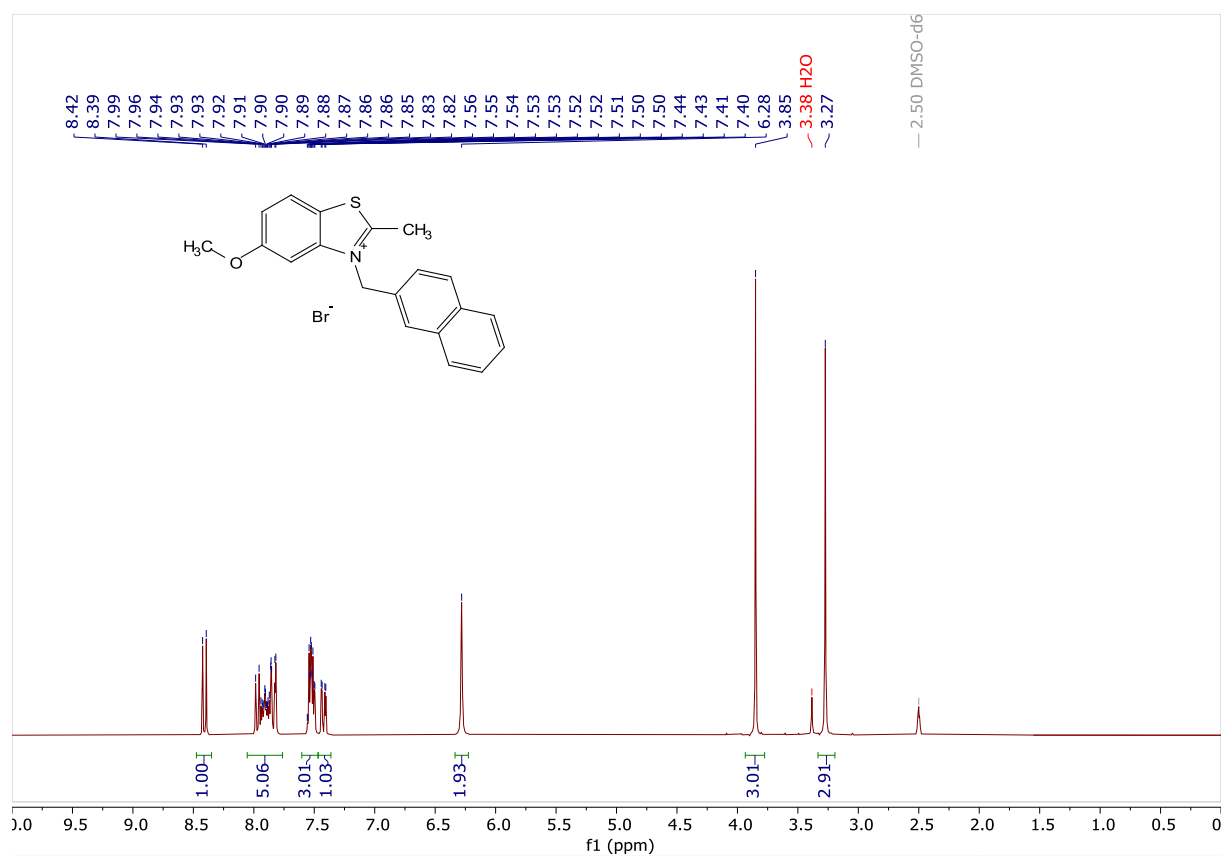
5-Methoxy-3-(3-chlorobenzyl)-2-methylbenzothiazol-3-ium bromide (**3e**)



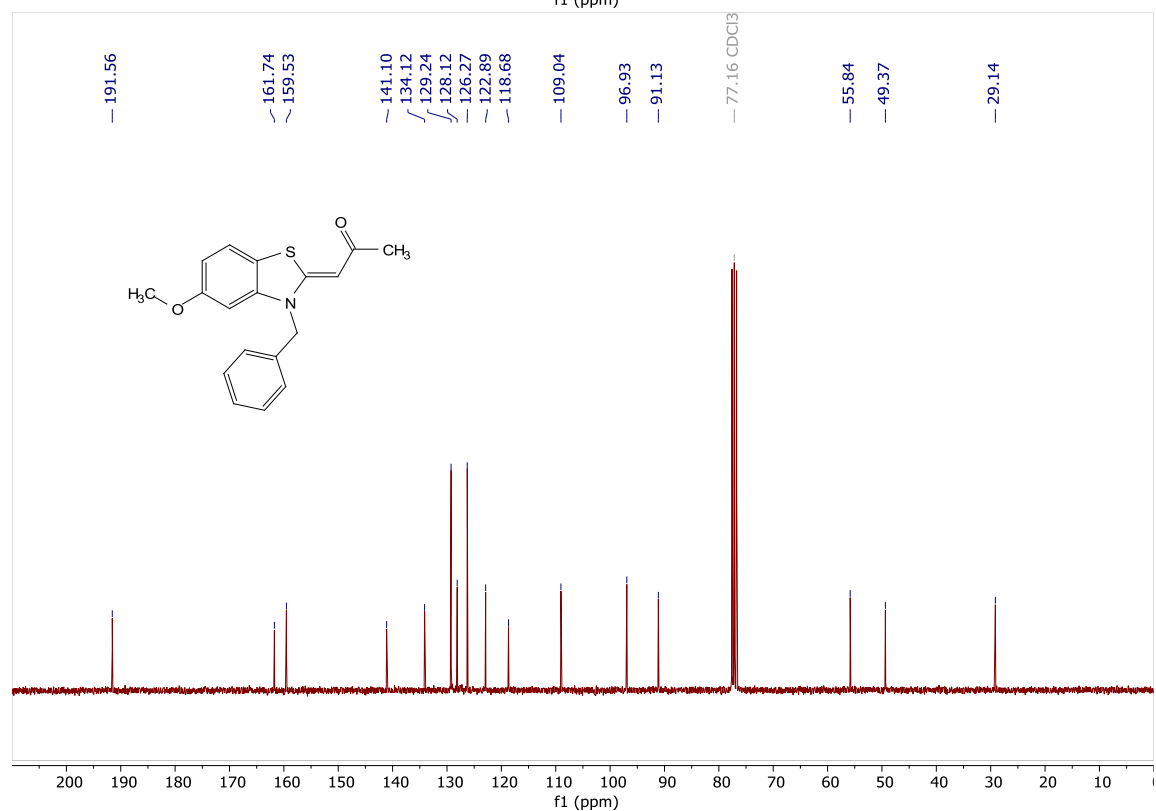
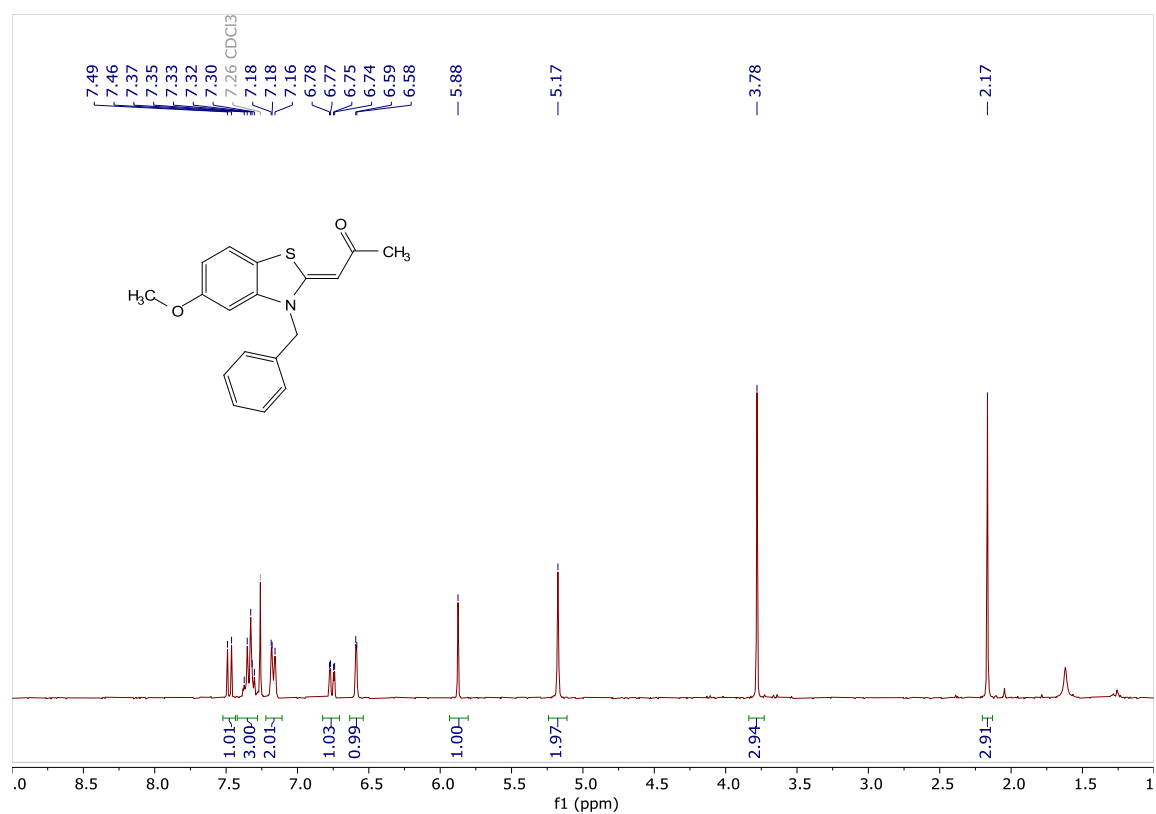
5-Methoxy-3-(4-chlorobenzyl)-2-methylbenzothiazol-3-ium bromide (**3f**)



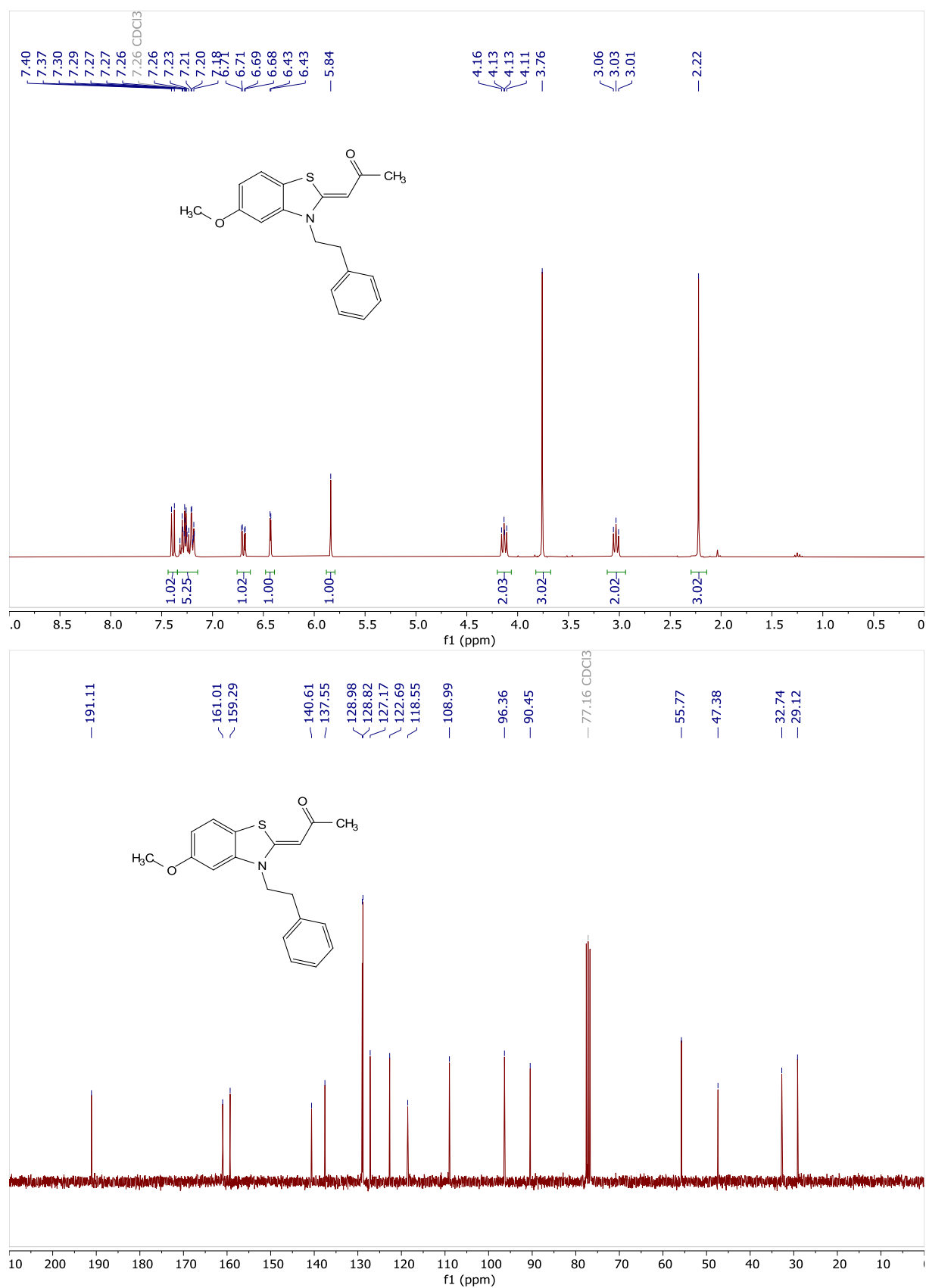
5-Methoxy-2-methyl-3-(naphthalen-2-ylmethyl)benzothiazol-3-ium bromide (**3g**)



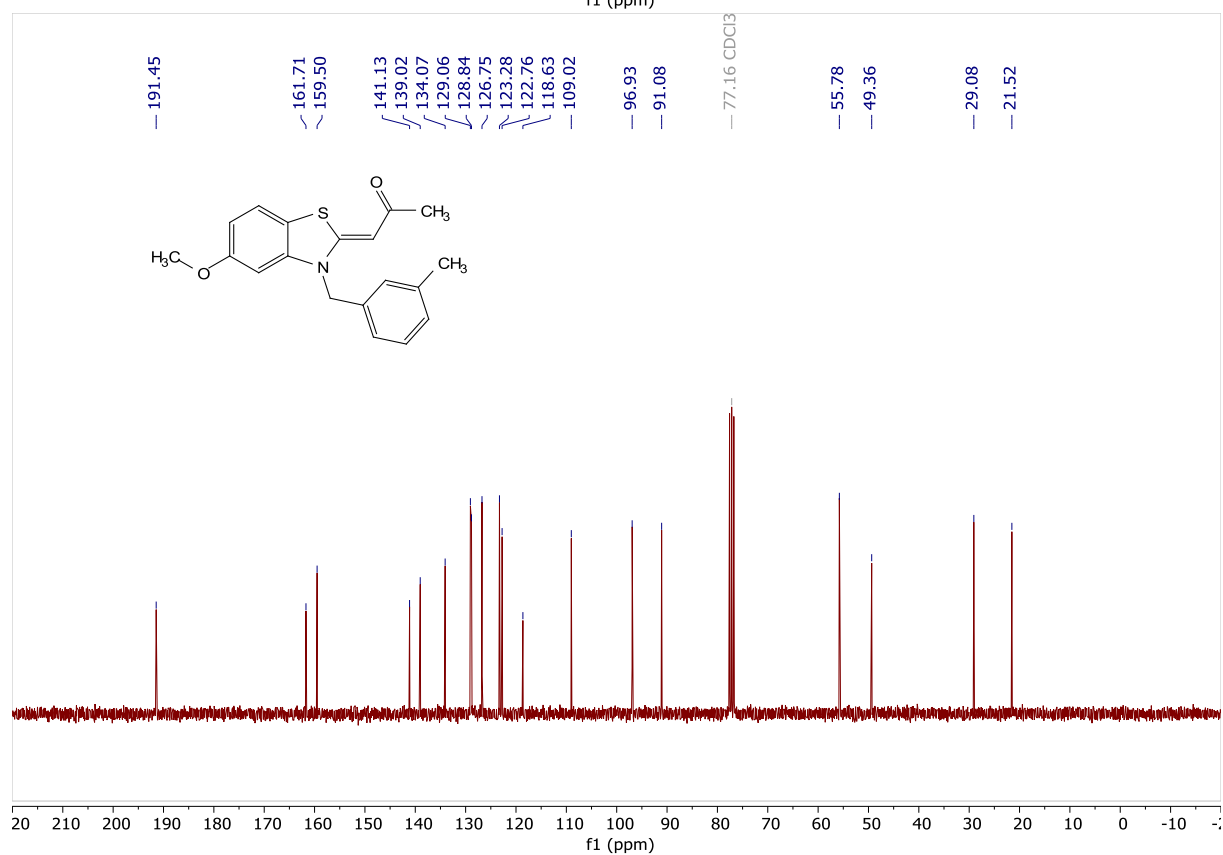
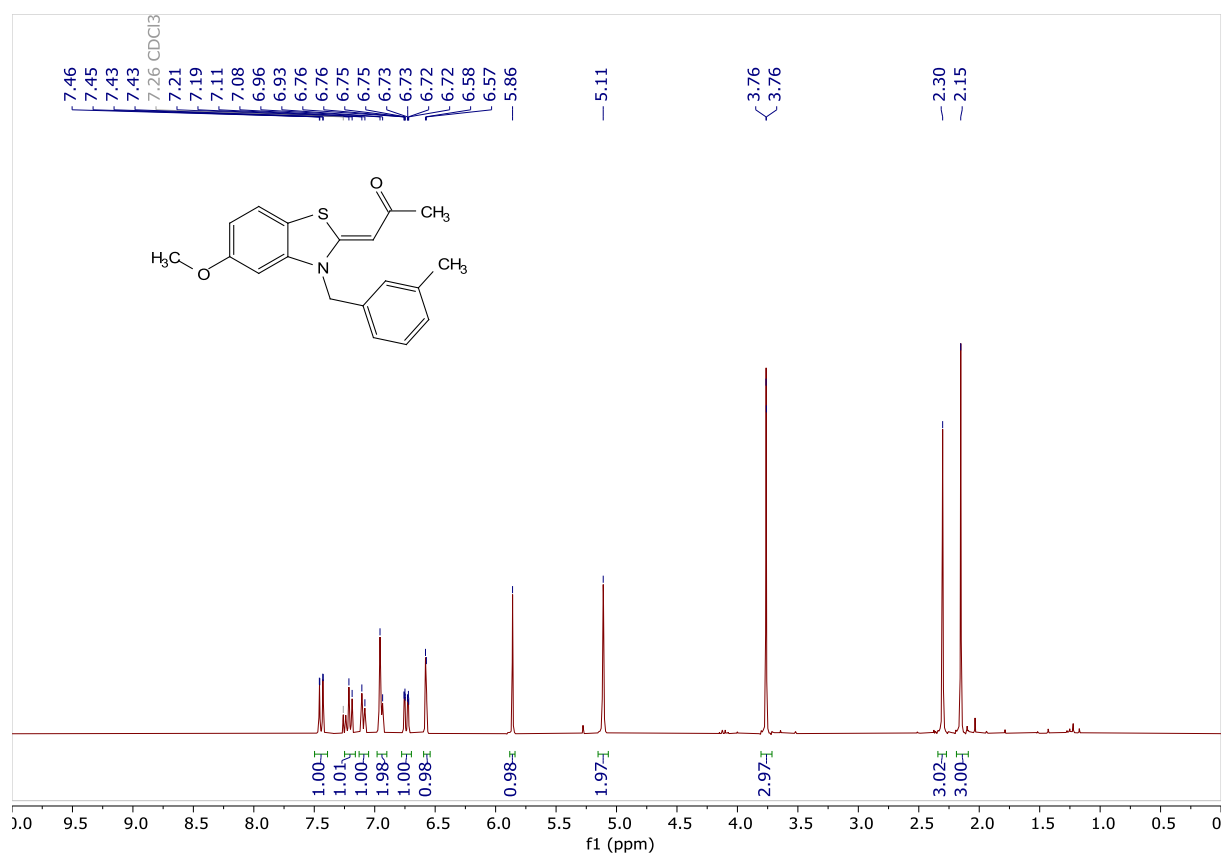
(Z)-1-(3-Benzyl-5-methoxybenzothiazol-2(3*H*)-ylidene)propan-2-one (**4b**)



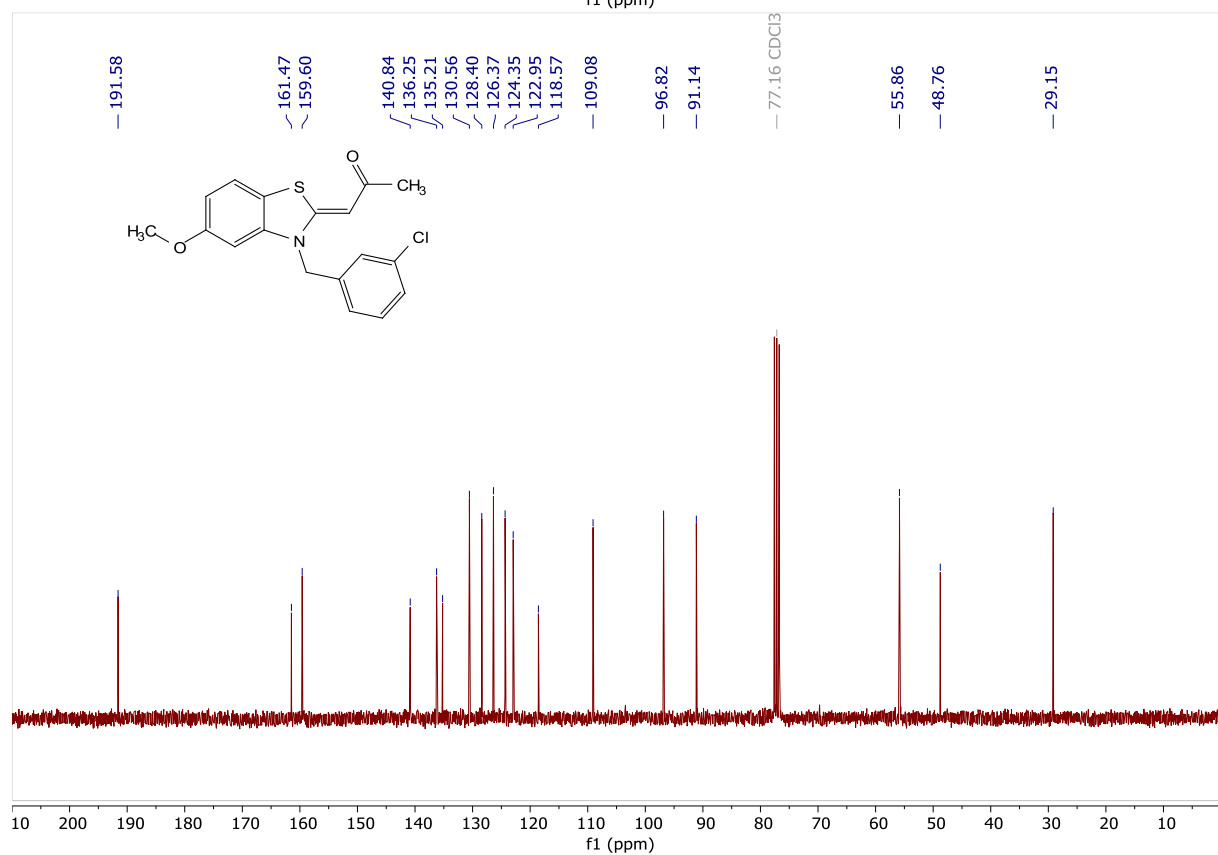
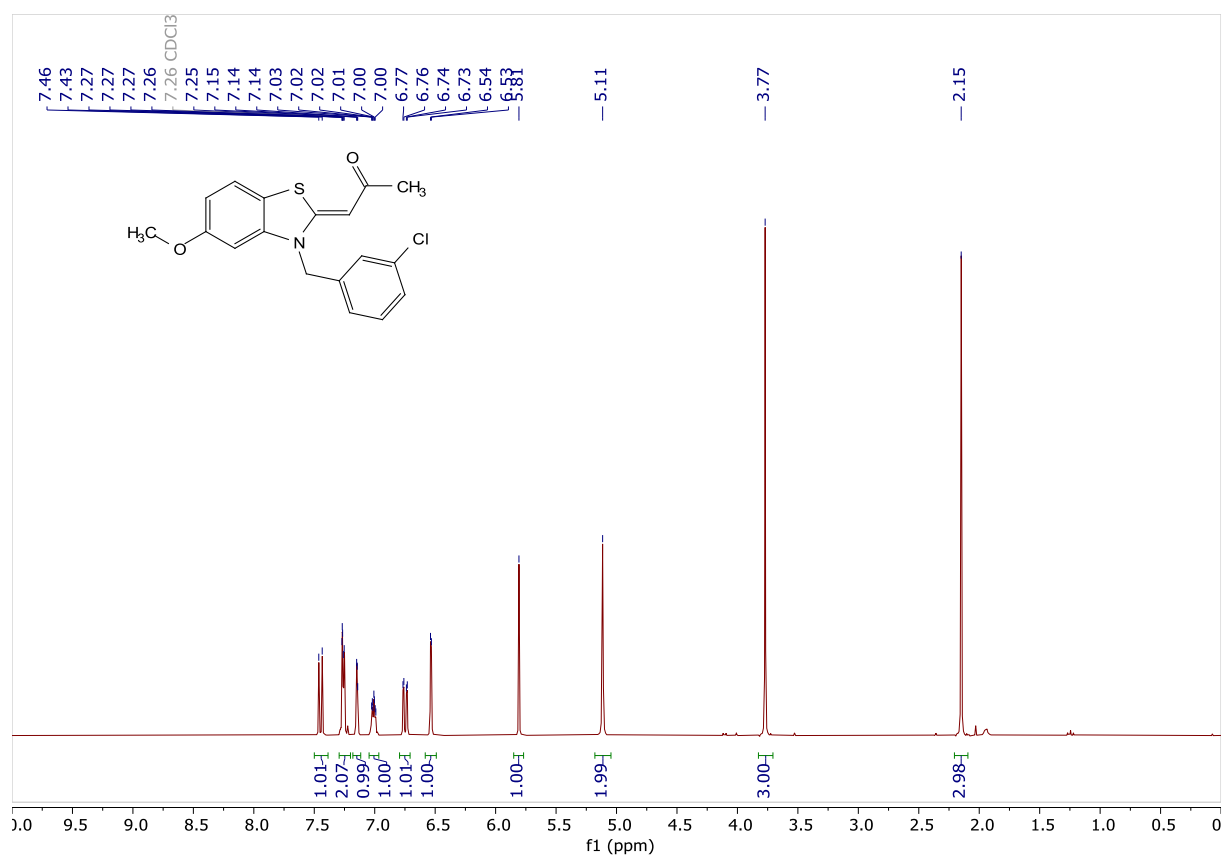
(Z)-1-(5-Methoxy-3-phenethylbenzothiazol-2(3H)-ylidene)propan-2-one (4c)



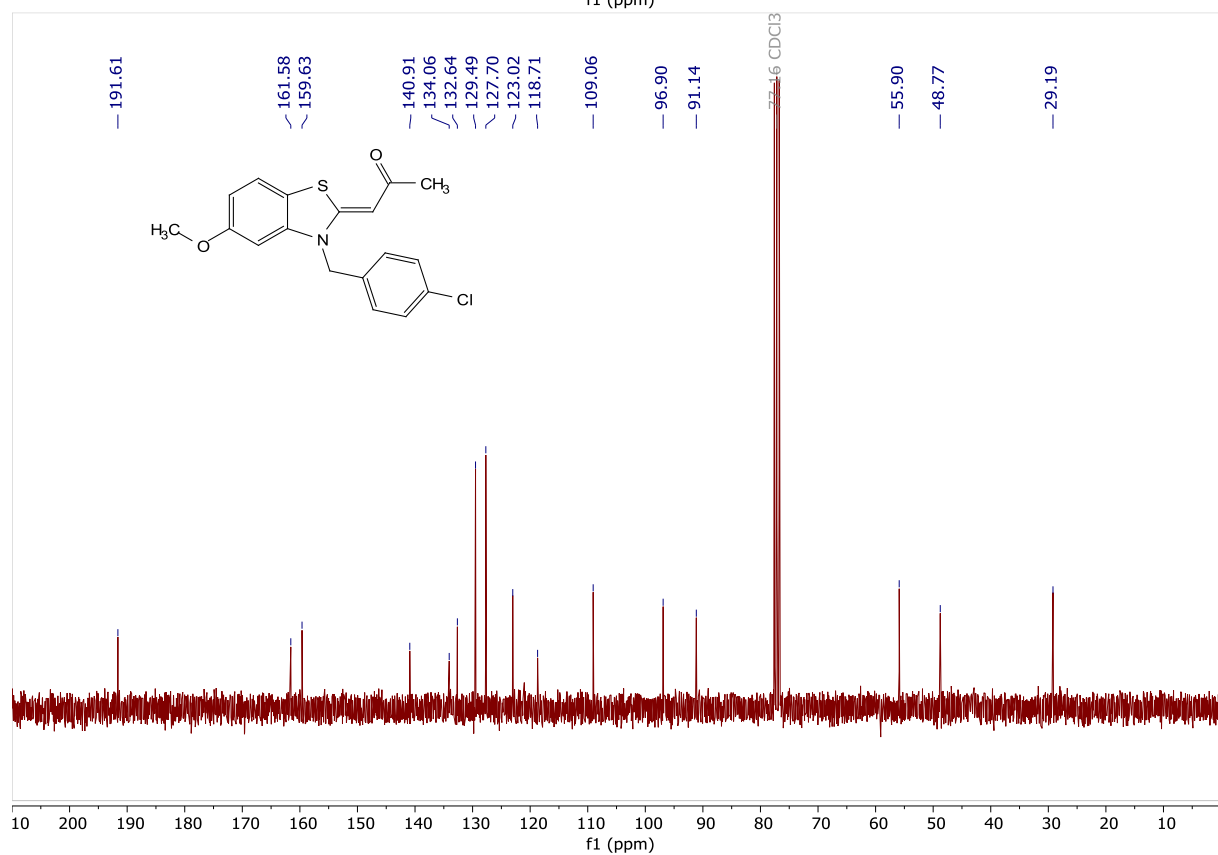
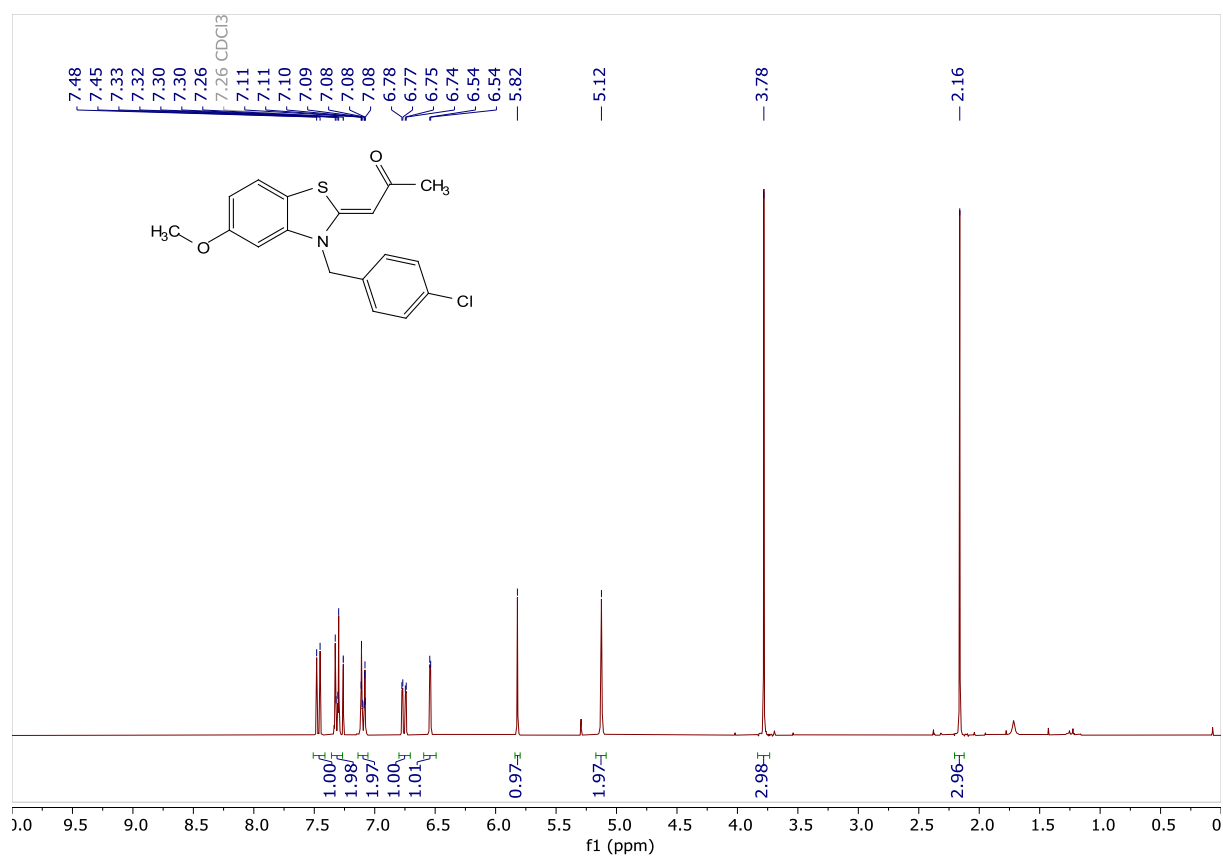
(Z)-1-(5-Methoxy-3-(3-methylbenzyl)benzothiazol-2(3*H*)-ylidene)propan-2-one (**4d**)



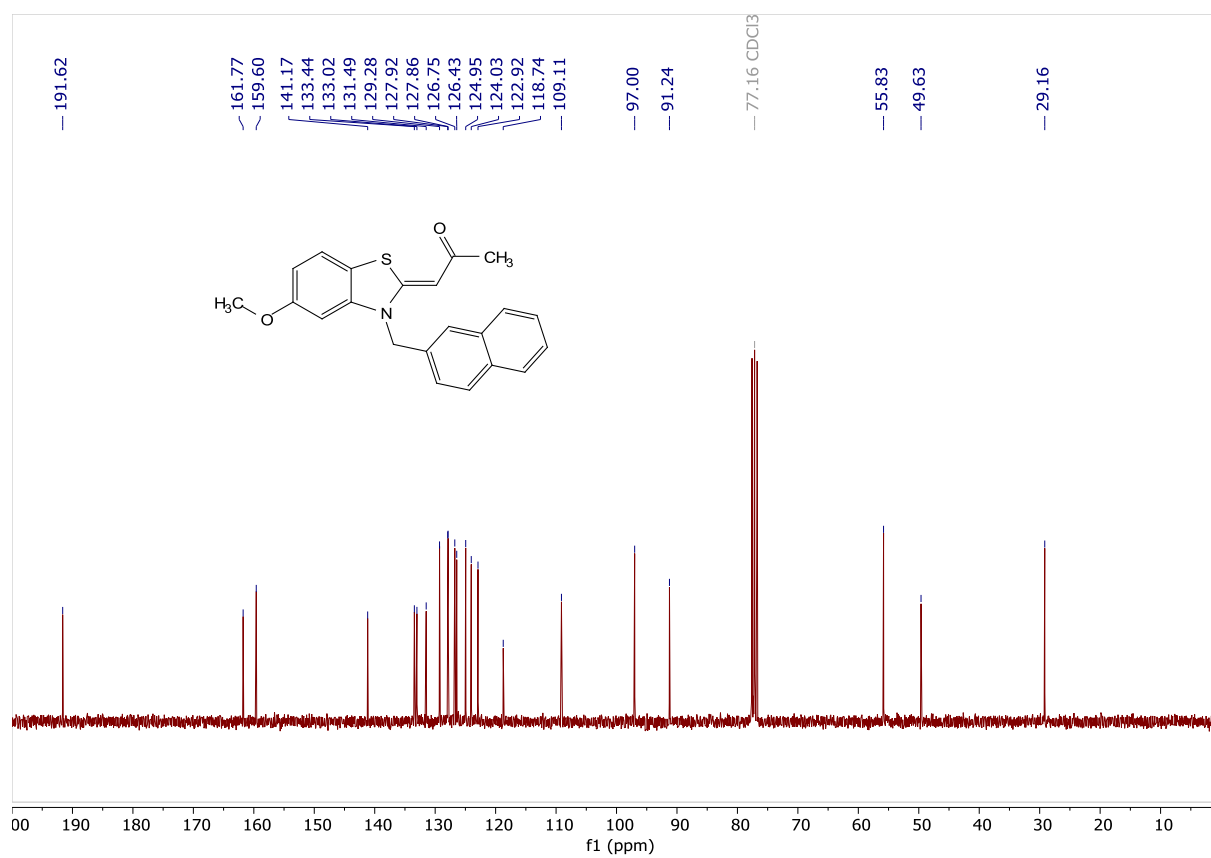
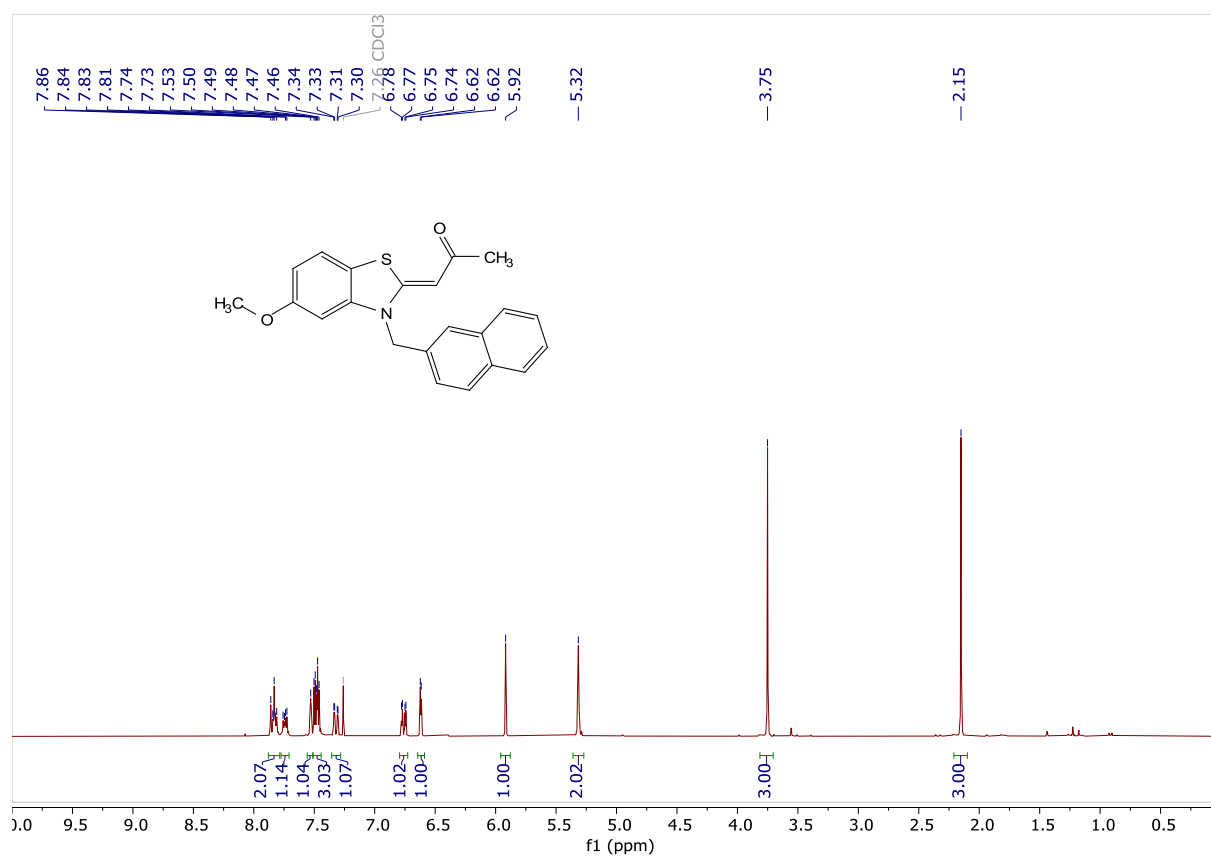
(Z)-1-(5-Methoxy-3-(3-chlorobenzyl)benzothiazol-2(3H)-ylidene)propan-2-one (4e)



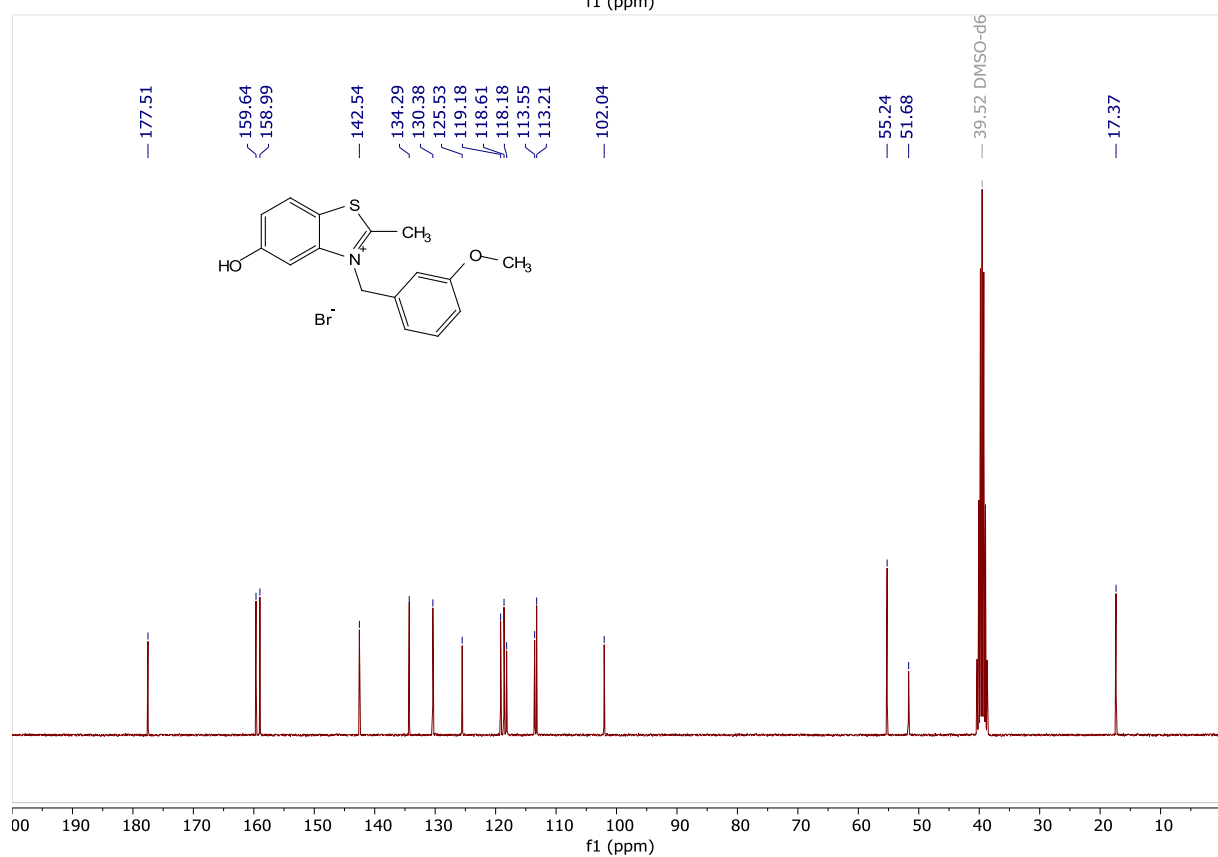
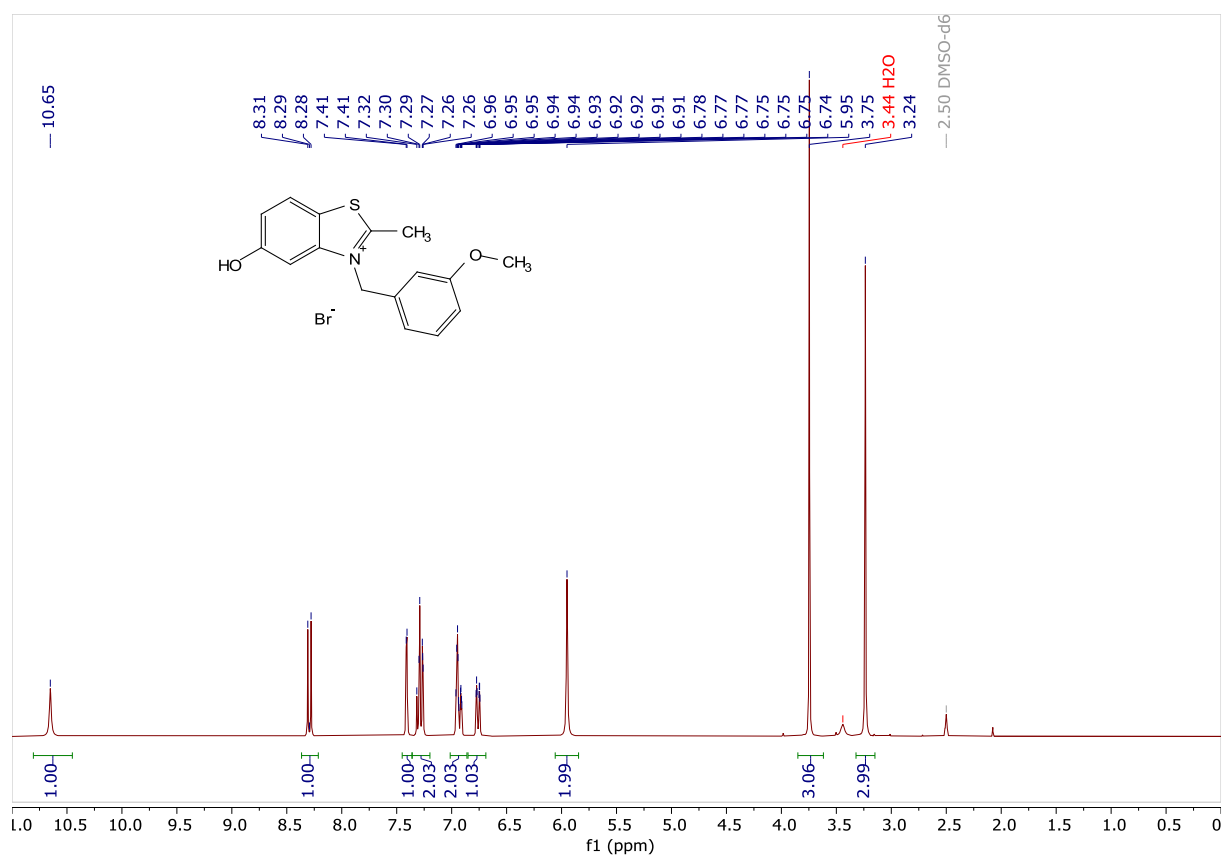
(Z)-1-(5-Methoxy-3-(4-chlorobenzyl)benzothiazol-2(3H)-ylidene)propan-2-one (**4f**)



(Z)-1-(5-Methoxy-3-(naphthalen-2-ylmethyl)benzothiazol-2(3H)-ylidene)propan-2-one (4g)



5-Hydroxy-3-(3-methoxybenzyl)-2-methylbenzothiazol-3-ium bromide (**5**)

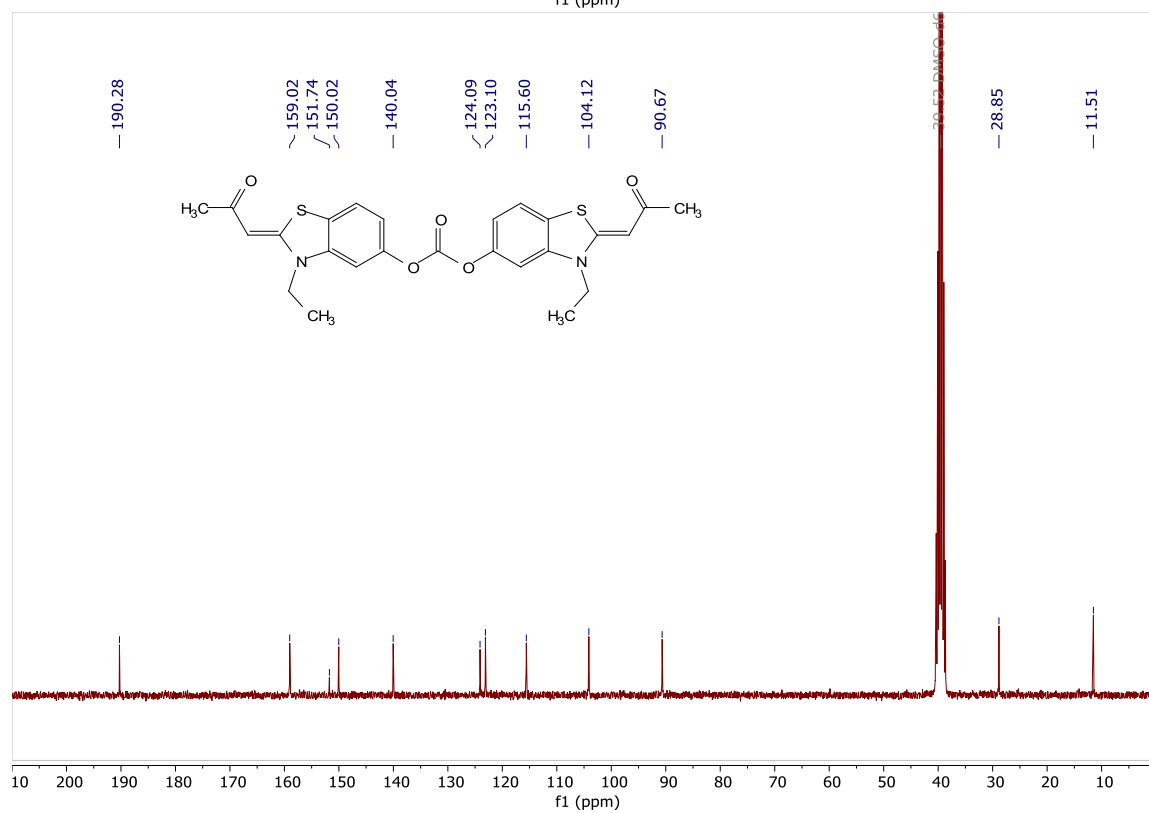
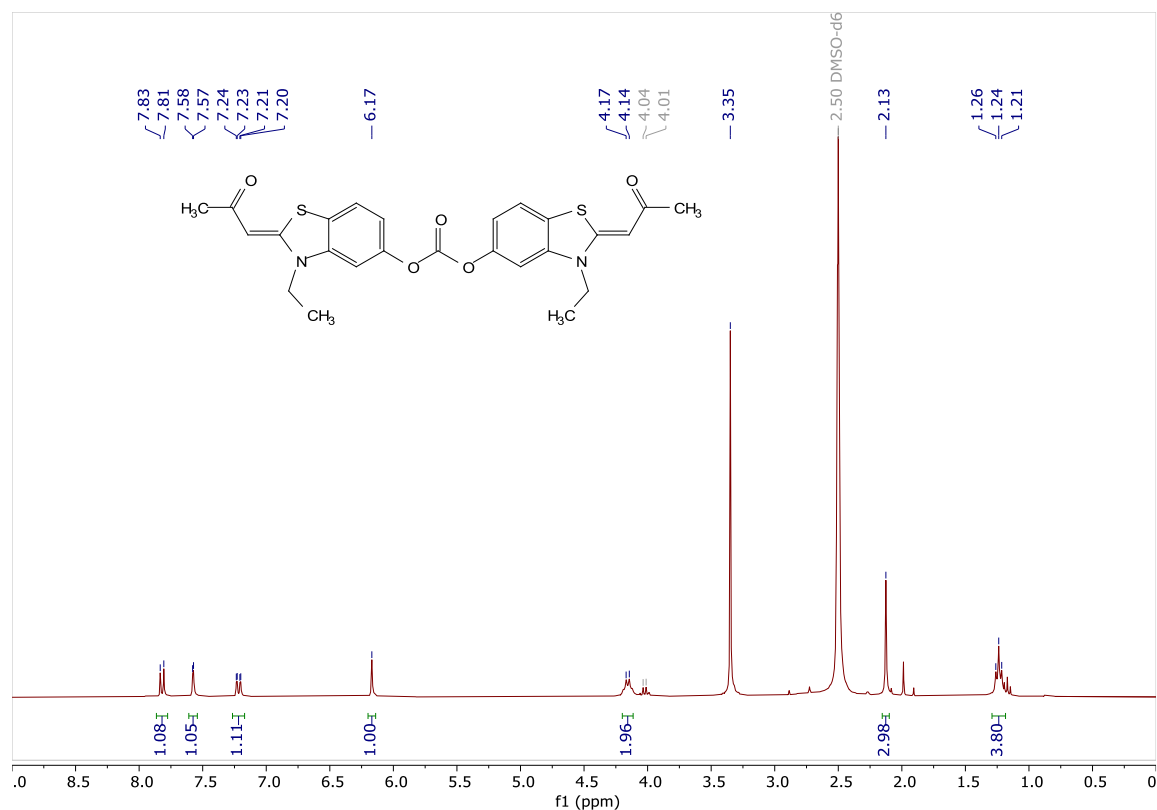


Chemical structure of compound 10: CC(=O)OC1=CC=C(C=C1)N(Cc2ccccc2OC(=O)C)C3=CC=CC=C3S3

¹H NMR spectrum (DMSO-d₆) of compound 10. The x-axis represents the chemical shift in ppm (f1), ranging from 0 to 10. The spectrum shows several peaks with corresponding integration values and chemical shift labels.

Chemical Shift (ppm)	Integration
7.79, 7.76, 7.28, 7.25, 7.24, 7.22, 6.98, 6.97, 6.95, 6.95, 6.88, 6.87, 6.86, 6.85, 6.84, 6.84, 6.78, 6.78, 6.77, 6.69, 6.69, 6.67, 6.66, 6.15, 5.34	0.97, 1.98, 1.01, 1.01, 0.99, 1.00, 0.98, 2.00
3.71	2.97
3.33	
2.50 (DMSO-d ₆)	3.07
2.25	2.92
2.06	

Bis((Z)-3-ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl) carbonate (7)



II – High-resolution mass spectrometry spectra 1b-p

(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl ethyl(methyl) carbamate (1b)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 7.0 PPM / DBE: min = 0.0, max = 15.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

220 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-5 S: 0-1

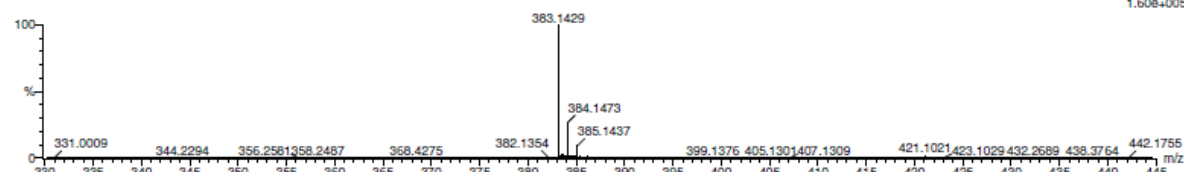
06-Oct-2021

2110056 387 (2.373) Cm (385:390)

MTK-100

2:26

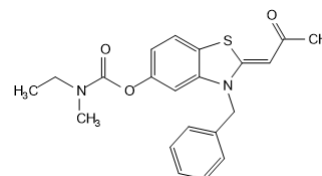
1: TOF MS ES+
1.60e+005



Minimum:

Maximum: 10.0 7.0 0.0 15.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
383.1429	383.1429	0.0	0.0	11.5	910.3	0.0	C21 H23 N2 O3 S



(Z)-3-Phenethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl ethyl(methyl) carbamate (1c)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 2.0, max = 20.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

266 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-4 S: 0-2

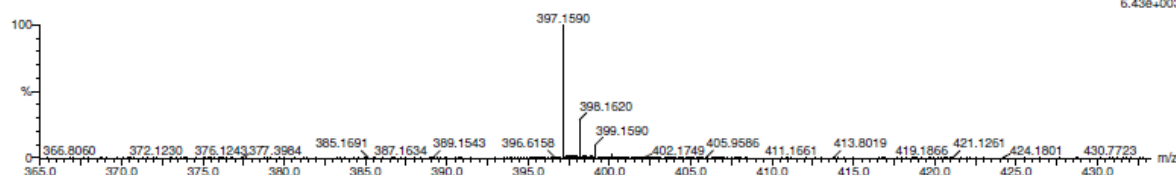
23-Feb-2022

2202153 422 (2.594) Cm (419:429-(355:362+602:619))

MTK-158

1:6

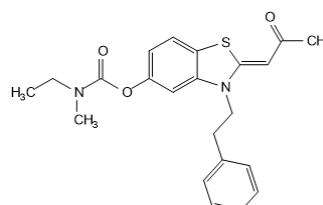
1: TOF MS ES+
6.43e+003



Minimum:

Maximum: 10.0 5.0 2.0 20.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
397.1590	397.1586	0.4	1.0	11.5	495.0	0.0	C22 H25 N2 O3 S



Elemental Composition Report

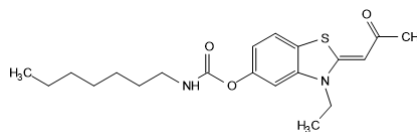
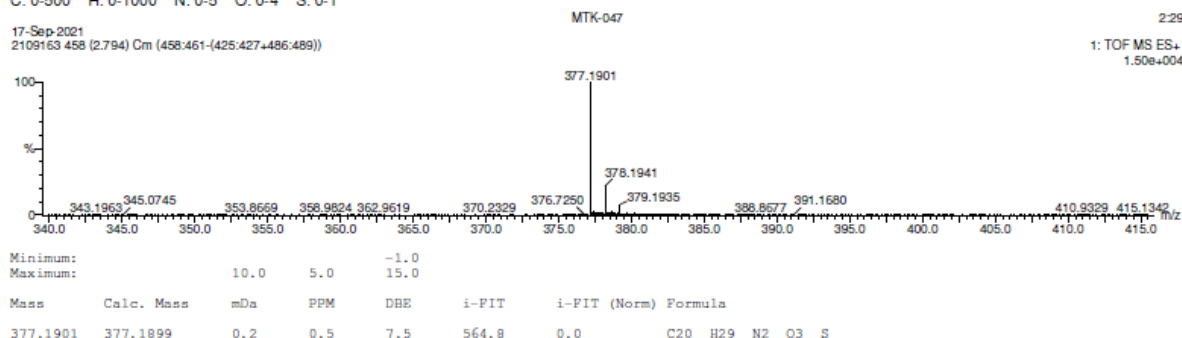
Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.0, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
 280 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
 Elements Used:
 C: 0-500 H: 0-1000 N: 0-5 O: 0-4 S: 0-1

17-Sep-2021
2109163 458 (2.794) Cm (458:461-(425:427+486:489))



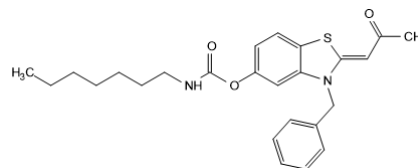
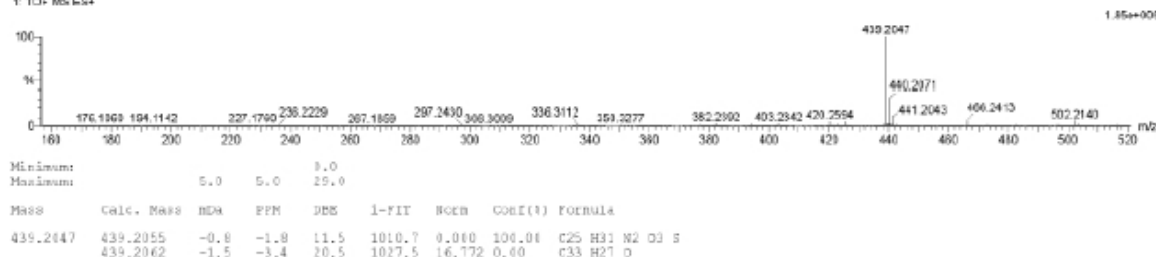
Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 0.0, max = 29.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions
494 formula(s) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 0-1000 H: 0-1000 N: 0-5 O: 0-5 S: 0-1
20-Apr-2017 1704073.1554 (11.865) Cm (1641:1966-2110.2157)
V1541
1. TOF MS ES+



(Z)-2-(2-Oxopropylidene)-3-phenethyl-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1f**)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 0.0, max = 14.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

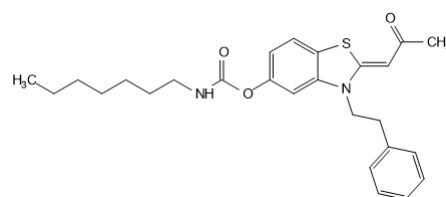
700 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

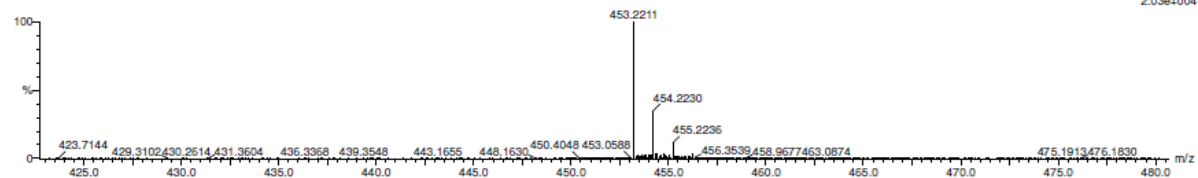
C: 0-500 H: 0-1000 10B: 0-1 11B: 0-1 N: 0-3 O: 0-3 S: 0-1

MTK-148

2201145 515 (3.127) Cm (512:517:457:454)



1: TOF MS ES+
2.03e+004



Minimum: 0.0
Maximum: 5.0 5.0 14.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
453.2211	453.2212	-0.1	-0.2	11.5	387.5	n/a	n/a	C26 H33 N2 O3 S

(Z)-3-(3-Methylbenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1g**)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 0.0, max = 18.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

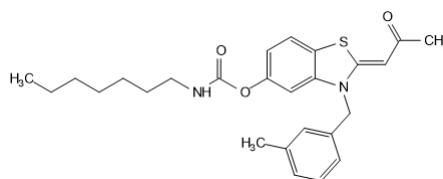
176 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

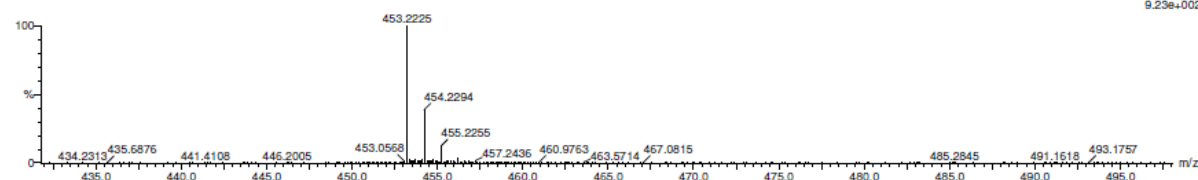
C: 0-500 H: 0-1000 N: 0-3 O: 0-3 S: 0-1

MTK-159

2201149 531 (3.190) Cm (531:444:624))



1: TOF MS ES+
9.23e+002



Minimum: 0.0
Maximum: 5.0 5.0 18.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
453.2225	453.2212	1.3	2.9	11.5	141.2	n/a	n/a	C26 H33 N2 O3 S

(Z)-3-(3-Chlorobenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1h**)

Elemental Composition Report

Page 1

Multiple Mass Analysis: 2 mass(es) processed

Tolerance = 7.0 PPM / DBE: min = 0.0, max = 15.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

1972 formula(e) evaluated with 7 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-5 S: 0-1 ³⁵Cl: 0-1 ³⁷Cl: 0-1

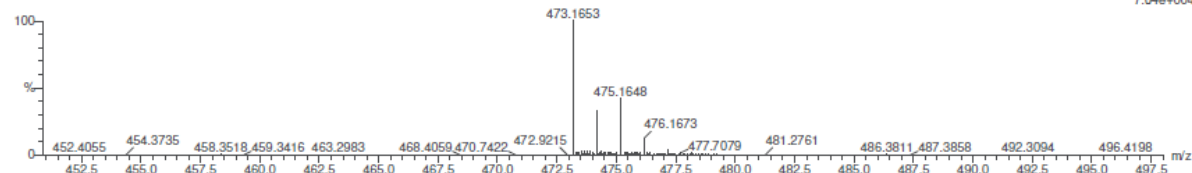
06-Oct-2021

2110058 523 (3.201) Cm (523:526)

MTK-108

2:31

1: TOF MS ES+
7.04e+004



Minimum:	35.00					0.0			
Maximum:	100.00		10.0	7.0	15.0				
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
473.1653	100.00	473.1666	-1.3	-2.7	11.5	702.0	0.6	C25 H30 N2 O3 S 35Cl	
		473.1651	0.2	0.4	11.5	702.3	0.9	C28 H33 S 35Cl 37Cl	
		473.1657	-0.4	-0.8	12.5	708.9	7.5	C25 H28 N2 O5 37Cl	
		473.1676	-2.3	-4.9	7.5	709.2	7.8	C24 H33 O5 35Cl 37Cl	
475.1648	41.81	475.1636	1.2	2.5	11.5	667.3	0.5	C25 H30 N2 O3 S 37Cl	
		475.1654	-0.6	-1.3	6.5	667.7	0.9	C24 H35 O3 S 35Cl 37Cl	
		475.1621	2.7	5.7	11.5	674.5	7.8	C27 H31 O3 35Cl 37Cl	

(Z)-3-(4-Chlorobenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1i**)

Elemental Composition Report

Page 1

Multiple Mass Analysis: 2 mass(es) processed

Tolerance = 7.0 PPM / DBE: min = 0.0, max = 15.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

1972 formula(e) evaluated with 7 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-5 S: 0-1 ³⁵Cl: 0-1 ³⁷Cl: 0-1

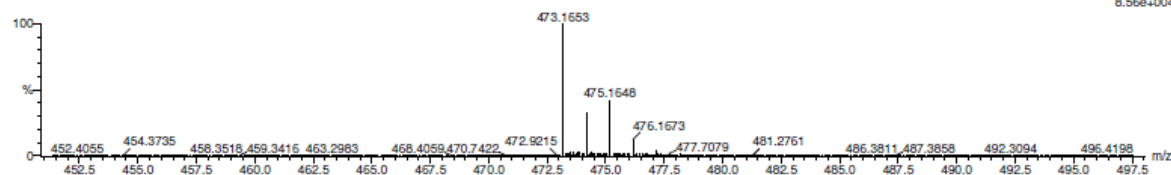
06-Oct-2021

2110058 523 (3.201) Cm (523:526)

MTK-110

2:28

1: TOF MS ES+
8.56e+004



Minimum:	35.00					0.0			
Maximum:	100.00		10.0	7.0	15.0				
Mass	RA	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula	
473.1653	100.00	473.1666	-1.3	-2.7	11.5	702.0	0.6	C25 H30 N2 O3 S 35Cl	
		473.1651	0.2	0.4	11.5	702.3	0.9	C28 H33 S 35Cl 37Cl	
		473.1657	-0.4	-0.8	12.5	708.9	7.5	C25 H28 N2 O5 37Cl	
		473.1676	-2.3	-4.9	7.5	709.2	7.8	C24 H33 O5 35Cl 37Cl	
475.1648	41.81	475.1636	1.2	2.5	11.5	667.3	0.5	C25 H30 N2 O3 S 37Cl	
		475.1654	-0.6	-1.3	6.5	667.7	0.9	C24 H35 O3 S 35Cl 37Cl	
		475.1621	2.7	5.7	11.5	674.5	7.8	C27 H31 O3 35Cl 37Cl	

(Z)-3-(2-Naphtyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1j**)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 0.0, max = 18.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

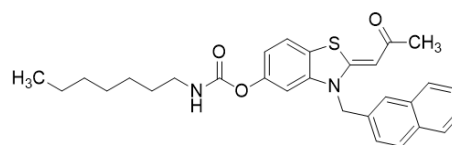
195 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

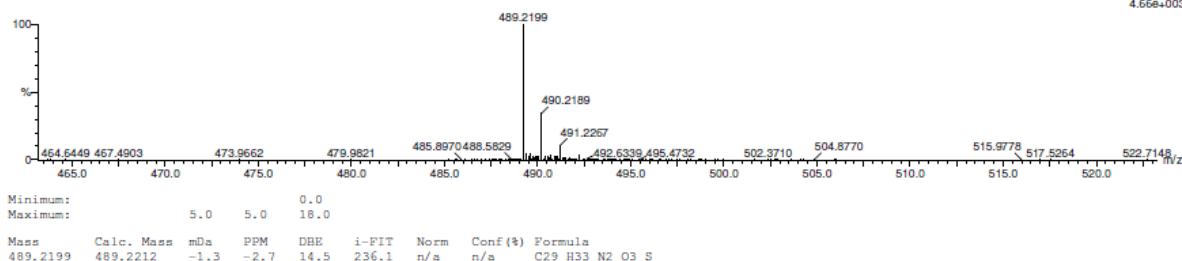
C: 0-500 H: 0-1000 N: 0-3 O: 0-3 S: 0-1

MTK-149

2201148 537 (3.261) Cm (537:539-(435:466+680:693))



1: TOF MS ES+
4.66e+003



(Z)-3-(3-Methoxybenzyl)-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl heptylcarbamate (**1k**)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 7.0 PPM / DBE: min = 0.0, max = 15.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

268 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

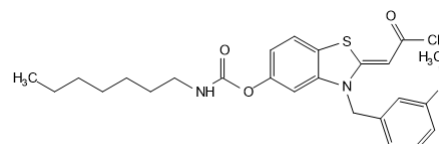
Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-5 S: 0-1

06-Oct-2021

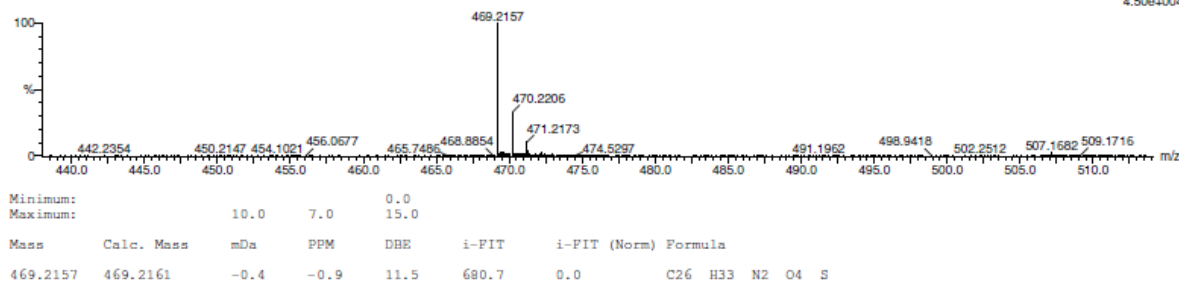
2110057 495 (3.037) Cm (495:497-(461:463+562:565))

MTK-104



2:27

1: TOF MS ES+
4.50e+004



(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl hexylcarbamate (1l)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 7.0 PPM / DBE: min = 0.0, max = 15.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

244 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-5 S: 0-1

06-Oct-2021

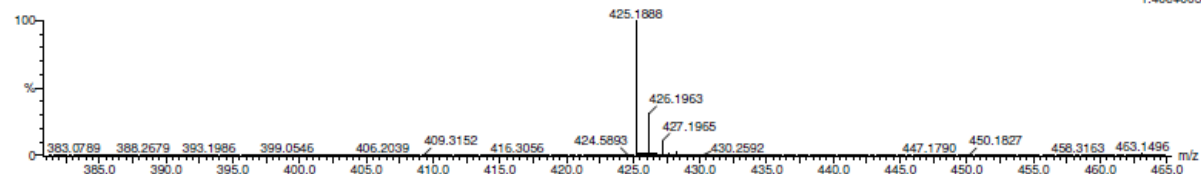
2110055 464 (2.838) Cm (463/464)

MTK-80

2.25

1: TOF MS ES+

1.40e+005



Minimum:

Maximum: 10.0 7.0 0.0 15.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula
425.1888	425.1899	-1.1	-2.6	11.5	670.3	0.0	C24 H29 N2 O3 S

(Z)-3-Benzyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl butylcarbamate (1m)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = 0.0, max = 15.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 6

Monoisotopic Mass, Even Electron Ions

320 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 0-1000 H: 0-1000 N: 0-3 O: 0-8 S: 0-1

23-Mar-2017

V1531

1: TOF MS ES+

1703072 1857 (11.217) Cm (1856/1857/1858/1859/1860/1861/1862/1863/1864/1865/1866/1867/1868/1869/1870/1871/1872/1873/1874/1875/1876/1877/1878/1879/1880/1881/1882/1883/1884/1885/1886/1887/1888/1889/1890/1891/1892/1893/1894/1895/1896/1897/1898/1899/1900/1901/1902/1903/1904/1905/1906/1907/1908/1909/1910/1911/1912/1913/1914/1915/1916/1917/1918/1919/1920/1921/1922/1923/1924/1925/1926/1927/1928/1929/1930/1931/1932/1933/1934/1935/1936/1937/1938/1939/1940/1941/1942/1943/1944/1945/1946/1947/1948/1949/1950/1951/1952/1953/1954/1955/1956/1957/1958/1959/1960/1961/1962/1963/1964/1965/1966/1967/1968/1969/1970/1971/1972/1973/1974/1975/1976/1977/1978/1979/1980/1981/1982/1983/1984/1985/1986/1987/1988/1989/1990/1991/1992/1993/1994/1995/1996/1997/1998/1999/2000/2001/2002/2003/2004/2005/2006/2007/2008/2009/2010/2011/2012/2013/2014/2015/2016/2017/2018/2019/2020/2021/2022/2023/2024/2025/2026/2027/2028/2029/2030/2031/2032/2033/2034/2035/2036/2037/2038/2039/2040/2041/2042/2043/2044/2045/2046/2047/2048/2049/2050/2051/2052/2053/2054/2055/2056/2057/2058/2059/2060/2061/2062/2063/2064/2065/2066/2067/2068/2069/2070/2071/2072/2073/2074/2075/2076/2077/2078/2079/2080/2081/2082/2083/2084/2085/2086/2087/2088/2089/2090/2091/2092/2093/2094/2095/2096/2097/2098/2099/2100/2101/2102/2103/2104/2105/2106/2107/2108/2109/2110/2111/2112/2113/2114/2115/2116/2117/2118/2119/2120/2121/2122/2123/2124/2125/2126/2127/2128/2129/2130/2131/2132/2133/2134/2135/2136/2137/2138/2139/2140/2141/2142/2143/2144/2145/2146/2147/2148/2149/2150/2151/2152/2153/2154/2155/2156/2157/2158/2159/2160/2161/2162/2163/2164/2165/2166/2167/2168/2169/2170/2171/2172/2173/2174/2175/2176/2177/2178/2179/2180/2181/2182/2183/2184/2185/2186/2187/2188/2189/2190/2191/2192/2193/2194/2195/2196/2197/2198/2199/2200/2201/2202/2203/2204/2205/2206/2207/2208/2209/2210/2211/2212/2213/2214/2215/2216/2217/2218/2219/2220/2221/2222/2223/2224/2225/2226/2227/2228/2229/2230/2231/2232/2233/2234/2235/2236/2237/2238/2239/2240/2241/2242/2243/2244/2245/2246/2247/2248/2249/2250/2251/2252/2253/2254/2255/2256/2257/2258/2259/2260/2261/2262/2263/2264/2265/2266/2267/2268/2269/2270/2271/2272/2273/2274/2275/2276/2277/2278/2279/2280/2281/2282/2283/2284/2285/2286/2287/2288/2289/2290/2291/2292/2293/2294/2295/2296/2297/2298/2299/2300/2301/2302/2303/2304/2305/2306/2307/2308/2309/2310/2311/2312/2313/2314/2315/2316/2317/2318/2319/2320/2321/2322/2323/2324/2325/2326/2327/2328/2329/2330/2331/2332/2333/2334/2335/2336/2337/2338/2339/2340/2341/2342/2343/2344/2345/2346/2347/2348/2349/2350/2351/2352/2353/2354/2355/2356/2357/2358/2359/2360/2361/2362/2363/2364/2365/2366/2367/2368/2369/2370/2371/2372/2373/2374/2375/2376/2377/2378/2379/2380/2381/2382/2383/2384/2385/2386/2387/2388/2389/2390/2391/2392/2393/2394/2395/2396/2397/2398/2399/2400/2401/2402/2403/2404/2405/2406/2407/2408/2409/2410/2411/2412/2413/2414/2415/2416/2417/2418/2419/2420/2421/2422/2423/2424/2425/2426/2427/2428/2429/2430/2431/2432/2433/2434/2435/2436/2437/2438/2439/2440/2441/2442/2443/2444/2445/2446/2447/2448/2449/2450/2451/2452/2453/2454/2455/2456/2457/2458/2459/2460/2461/2462/2463/2464/2465/2466/2467/2468/2469/2470/2471/2472/2473/2474/2475/2476/2477/2478/2479/2480/2481/2482/2483/2484/2485/2486/2487/2488/2489/2490/2491/2492/2493/2494/2495/2496/2497/2498/2499/2500/2501/2502/2503/2504/2505/2506/2507/2508/2509/2510/2511/2512/2513/2514/2515/2516/2517/2518/2519/2520/2521/2522/2523/2524/2525/2526/2527/2528/2529/2530/2531/2532/2533/2534/2535/2536/2537/2538/2539/2540/2541/2542/2543/2544/2545/2546/2547/2548/2549/2550/2551/2552/2553/2554/2555/2556/2557/2558/2559/2560/2561/2562/2563/2564/2565/2566/2567/2568/2569/2570/2571/2572/2573/2574/2575/2576/2577/2578/2579/2580/2581/2582/2583/2584/2585/2586/2587/2588/2589/2590/2591/2592/2593/2594/2595/2596/2597/2598/2599/2600/2601/2602/2603/2604/2605/2606/2607/2608/2609/2610/2611/2612/2613/2614/2615/2616/2617/2618/2619/2620/2621/2622/2623/2624/2625/2626/2627/2628/2629/2630/2631/2632/2633/2634/2635/2636/2637/2638/2639/2640/2641/2642/2643/2644/2645/2646/2647/2648/2649/2650/2651/2652/2653/2654/2655/2656/2657/2658/2659/2660/2661/2662/2663/2664/2665/2666/2667/2668/2669/2670/2671/2672/2673/2674/2675/2676/2677/2678/2679/2680/2681/2682/2683/2684/2685/2686/2687/2688/2689/2690/2691/2692/2693/2694/2695/2696/2697/2698/2699/2700/2701/2702/2703/2704/2705/2706/2707/2708/2709/2710/2711/2712/2713/2714/2715/2716/2717/2718/2719/2720/2721/2722/2723/2724/2725/2726/2727/2728/2729/2730/2731/2732/2733/2734/2735/2736/2737/2738/2739/2740/2741/2742/2743/2744/2745/2746/2747/2748/2749/2750/2751/2752/2753/2754/2755/2756/2757/2758/2759/2760/2761/2762/2763/2764/2765/2766/2767/2768/2769/2770/2771/2772/2773/2774/2775/2776/2777/2778/2779/2780/2781/2782/2783/2784/2785/2786/2787/2788/2789/2790/2791/2792/2793/2794/2795/2796/2797/2798/2799/2800/2801/2802/2803/2804/2805/2806/2807/2808/2809/2810/2811/2812/2813/2814/2815/2816/2817/2818/2819/2820/2821/2822/2823/2824/2825/2826/2827/2828/2829/2830/2831/2832/2833/2834/2835/2836/2837/2838/2839/2840/2841/2842/2843/2844/2845/2846/2847/2848/2849/2850/2851/2852/2853/2854/2855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(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl cyclohexylcarbamate (1n)

Elemental Composition Report

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -3.0, max = 100.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

429 formula(e) evaluated with 2 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 0-500 H: 1-1000 N: 0-6 O: 0-6 S: 0-1

Minimum:

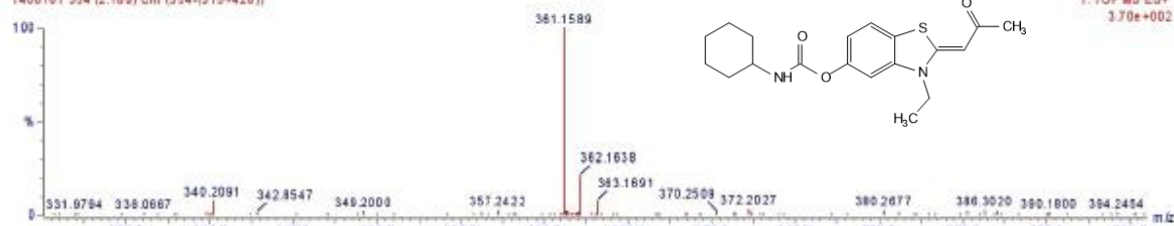
Maximum: 5.0 5.0 -3.0

Mass Calc. Mass mDa PPM DBE i-FIT i-FIT (Norm) Formula

361.1589 361.1592 -0.3 -0.8 17.5 42.6 0.7 C27 H21 O

361.1586 361.1586 0.3 0.8 8.5 42.7 0.7 C19 H25 N2 O3 S

24-Jun-2014
1406161 354 (2.189) Cm (354-(315+428))



(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl hexylcarbamate (1o)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

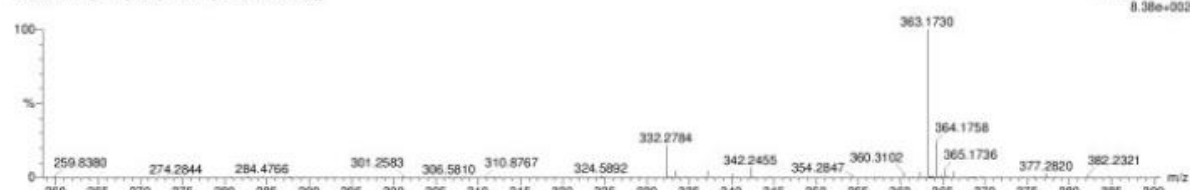
251 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-6 S: 0-1

AB391

1609024 447 (2.701) Cm (446/451-(562/570+293/309))



Minimum:

Maximum: 15.0 5.0 -1.5

Mass Calc. Mass mDa PPM DBE i-FIT i-FIT (Norm) Formula

363.1730 363.1742 -1.2 -3.3 7.5 79.0 0.0 C19 H27 N2 O3 S

(Z)-3-Ethyl-2-(2-oxopropylidene)-2,3-dihydrobenzothiazol-5-yl (pyridin-3-ylmethyl) carbamate (**1p**)

Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 4

Monoisotopic Mass, Even Electron Ions

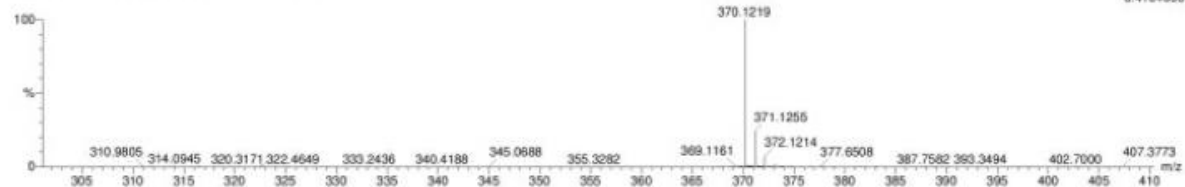
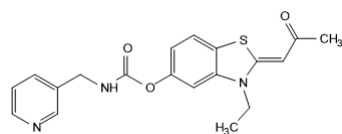
250 formula(e) evaluated with 2 results within limits (all results (up to 1000) for each mass)

Elements Used:

C: 0-500 H: 0-1000 N: 0-3 O: 0-6 S: 0-1

AB298

1609925 298 (1.795) Cm (298.305-(187.202+464.475))

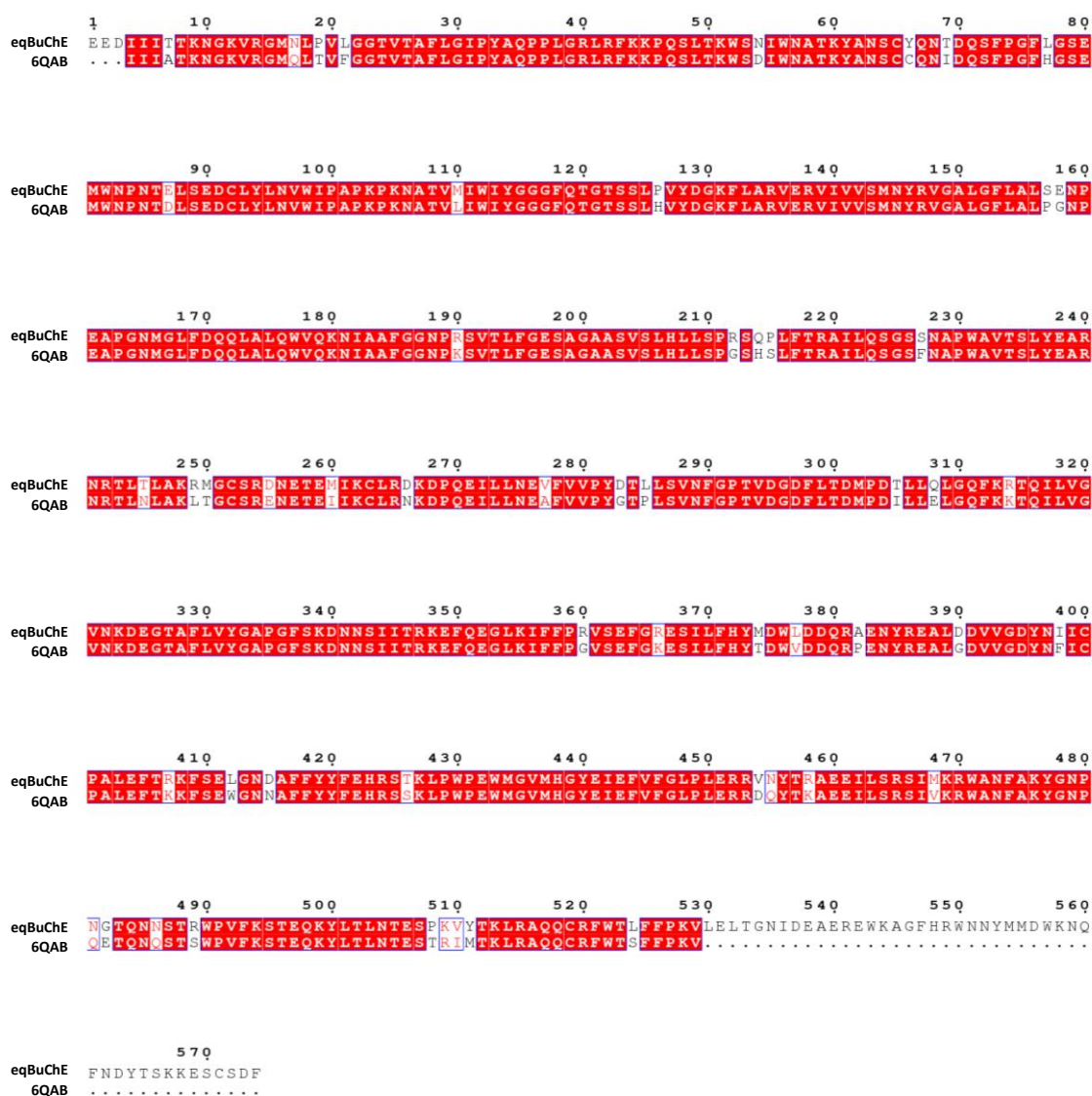


2:11
1: TOF MS ES+
8.41e+003

Minimum:										
Maximum:			15.0	-5.0	-1.5					
					50.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	i-FIT (Norm)	Formula			
370.1219	370.1225	-0.6	-1.6	11.5	278.2	0.0	C19	H20	N3	O3
	370.1232	-1.3	-3.5	20.5	294.8	16.7	C27	H16	N	O

III – Amino-acid sequences alignment of *eqBuChE* and *hBuChE*

Amino-acid sequences alignment of equineBuChE and humanBuChE (6QAB). The figure of alignment was made with ESPript (ESPript - <https://esprict.ibcp.fr>)¹.



¹ X. Robert, P. Gouet. *Nucl. Acids Res.* **2014**, 42(W1), W320-W324.