2,2,2-Trifluoroacetophenone: An Organocatalyst for an Environmentally-friendly Epoxidation of Alkenes

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Supporting Information

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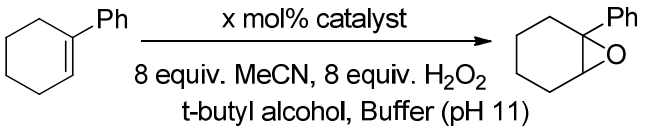
General Remarks

Chromatographic purification of products was accomplished using forced-flow chromatography. Thin-layer chromatography (TLC) was performed on aluminum backed silica plates (0.2 mm, 60 F_{254}). Visualization of the developed chromatogram was performed by fluorescence quenching using phosphomolybdic acid, anisaldehyde or ninhydrin stains. Melting points were determined on a hot stage apparatus. IR spectra were recorded on a FT-IR spectrometer and are reported in terms of frequency of absorption (cm^{-1}). Mass spectra (ESI) were recorded on a LC-MS spectrometer. HRMS spectra were recorded on HRMS spectrometer. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on 200 MHz, 188 MHz and 50 MHz respectively, and are internally referenced to residual solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, bs = broad signal, bs m = broad multiplet), coupling constant and assignment. Data for ^{19}F NMR are internally referenced to trifluoroacetic acid. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). Mass spectra and conversions of the reactions were recorded on a GC-MS spectrometer utilizing a column (F.T : 0.25μm, I.D. : 0.25mm, L : 30m, T_{max} : 350 ^{o}C).

Catalyst Optimization of the Reaction Conditions of the Epoxidation of 1-Phenyl-cyclohexene



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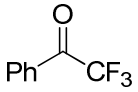
2		5	1	>99
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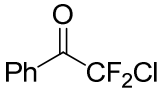
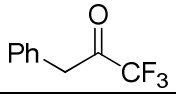
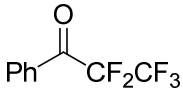
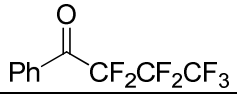
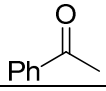
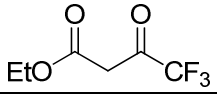
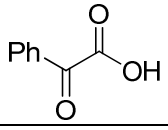
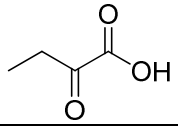
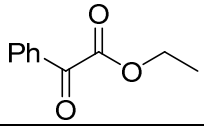
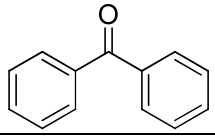
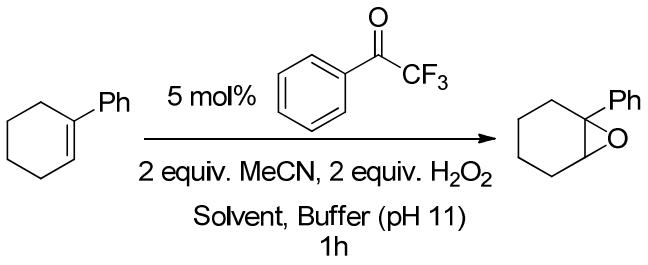
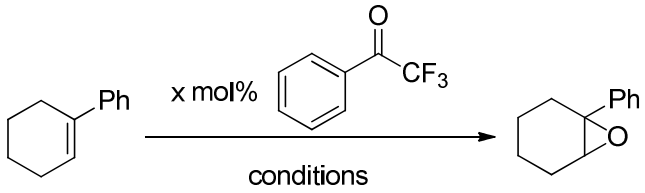
		1	24	58
3		5	1	92
4		5	1	59
5		5	1	98
6		5	1	98
7		5	1	12
8		5	1	43
9		5	1	11
10		5	1	12
11		5	1	9
12		5	1	traces

Solvent Optimization of the Reaction Conditions of the Epoxidation of 1-Phenyl-cyclohexene



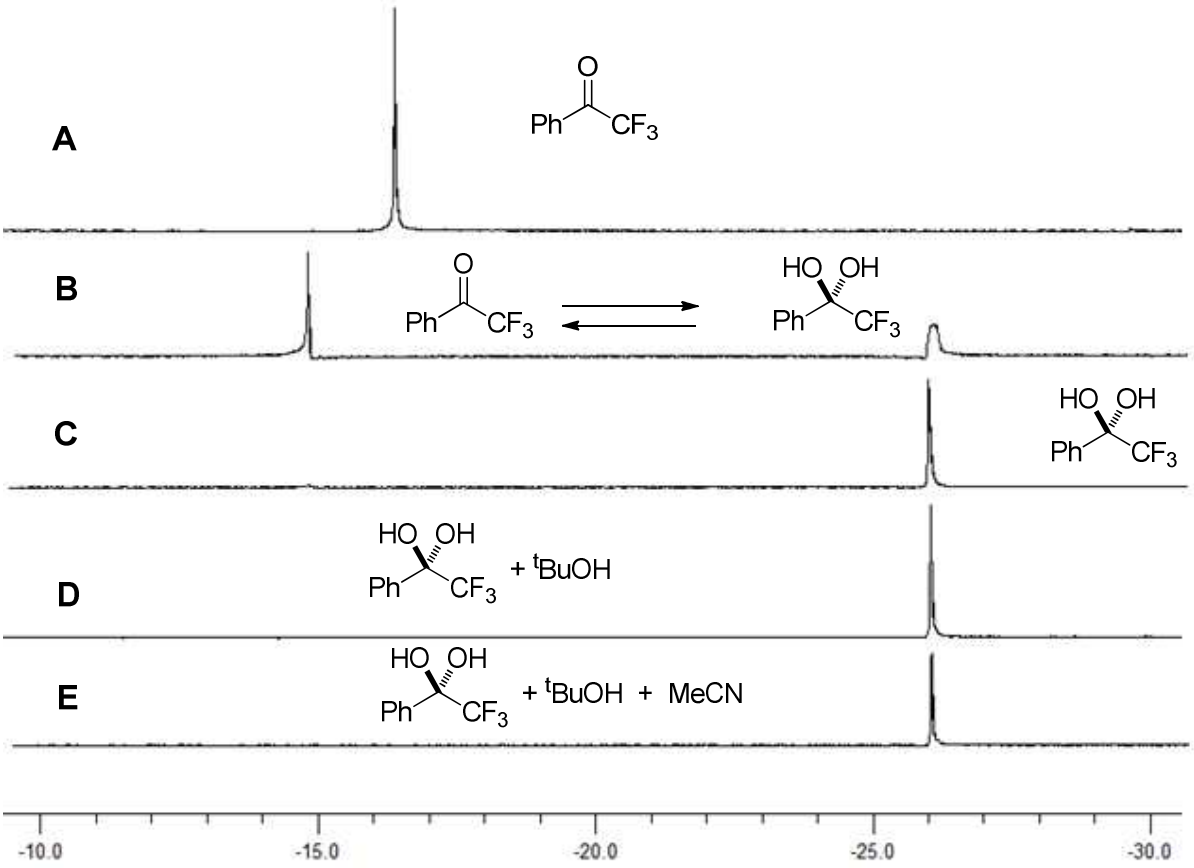
Solvent	Yield (%)
t-Butanol	>99
t-Amyl alcohol	99
Et_2O	60
MeOH	traces
i-PrOH	82
EtOAc	95
CH_2Cl_2	33
$CHCl_3$	40
DMSO	35
DMF	49

Optimization of the Reaction Conditions of the Epoxidation of 1-Phenyl-cyclohexene



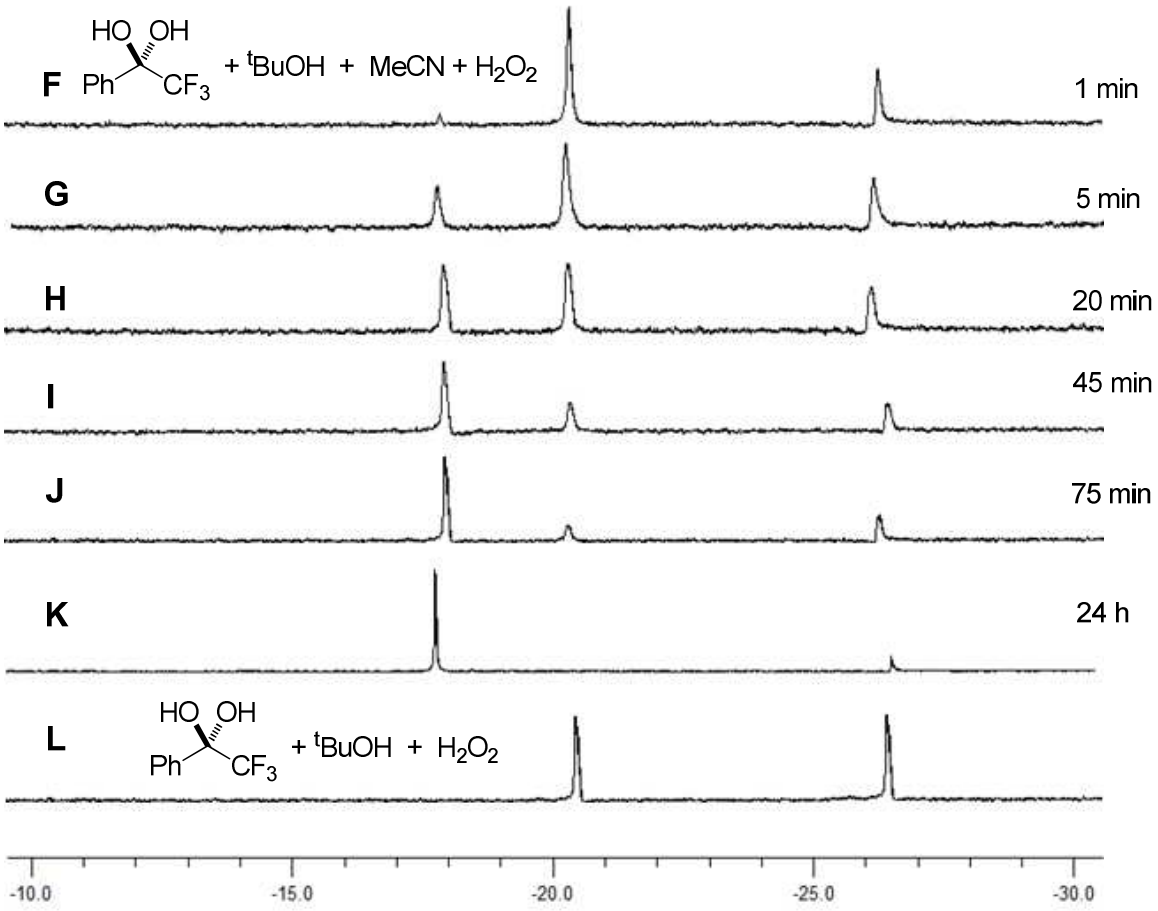
Cat. (%)	MeCN (equiv)	H_2O_2 (equiv)	Solvent	Buffer *(measured pH)*	GC-Yield (%)	Time (h)
10	8	8	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	0.5
10	4	4	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	0.5
10	2	2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	1
10	1.5	1.2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	1
10	0	8	t-BuOH	K_2CO_3/EDTA (pH 11.11)	traces	1
5	2	2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	1
5	1.5	1.2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	24
2	8	8	t-BuOH	K_2CO_3/EDTA (pH 11.11)	>99	1
2	2	2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	70	24
2	1.5	1.2	t-BuOH	K_2CO_3/EDTA (pH 11.11)	14	24
pH						
5	2	2	t-BuOH	K_2CO_3 (pH 10.99)	>99	24
5	2	2	t-BuOH	Buffer (pH 7.50)	12	24
5	2	2	t-BuOH	Buffer (pH 8.35)	17	24
5	2	2	t-BuOH	Water (pH 7.00)	traces	24
5	2	2	t-BuOH	Na_2CO_3 (pH 10.47)	73	24

^{19}F-NMR Experiments for the Study of the Reaction Mechanism



In order to shed more light to the reaction mechanism, the reaction was monitored by ^{19}F-NMR (internally referenced to trifluoroacetic acid). For 2,2,2-trifluoroacetophenone in $CDCl_3$, a singlet at -16.4 ppm was observed by ^{19}F-NMR (**A**). Once the same compound was diluted in D_2O (buffer solution of the reaction in D_2O), two signals appeared immediately. The peak at -14.8 ppm is assigned to the keto form, while the singlet peak at -25.9 ppm is assigned to the hydrate form (**B**). After 5 min, the equilibrium lay exclusively to the hydrate form (**C**). Upon addition of *tert*-butanol (**D**) or MeCN (**E**), no change was observed.

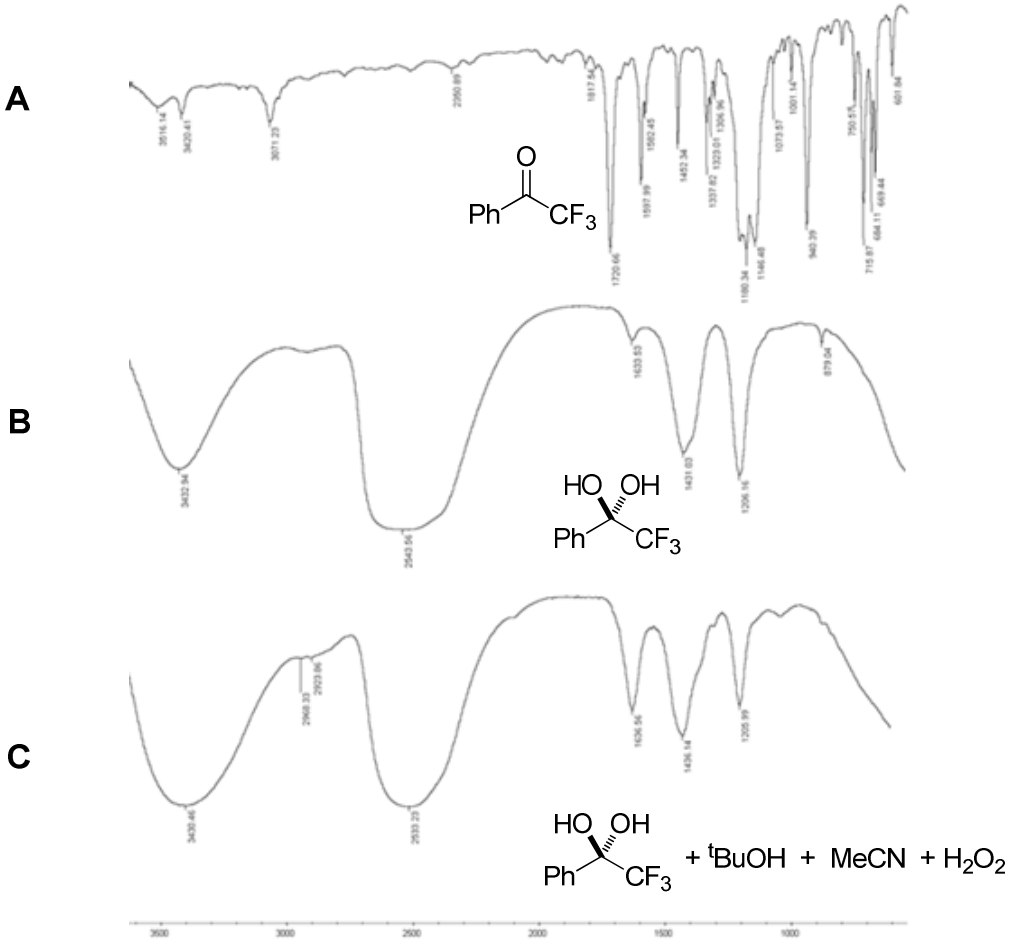
Upon addition of H_2O_2 to the mixture, immediately a new peak at -20.3 ppm appeared (**F**). It is clear, a new compound bearing fluorine was formed *in situ*. This is believed to be a perhydrate (compound **IV**, Scheme 2 of the manuscript), since the same compound was obtained when no MeCN was added in the reaction mixture (**L**). As the time goes by



and if no olefin is added, the peak that corresponds to the perhydrate was decreasing and a new peak at -17.8 ppm was appearing. This new peak at -17.8 ppm is believed to be the dihydroperoxide. This species (-17.8 ppm) is not capable of promoting the oxidation when used as the catalyst of the reaction (15% yield, 24 h). Monitoring the reaction mixture, the decrease of the concentration of the perhydrate is followed by an increase of the new peak at -17.8 ppm (**G**: 5 min after addition of the H_2O_2, **H**: 20 min after addition of the H_2O_2, **I**: 45 min after addition of the H_2O_2, **J**: 75 min after addition of the H_2O_2). After 24 h, the perhydrate is not present in the reaction mixture (**K**). At this period a slight amount of the hydrate of the ketone was present but the main product observed was the dihydroperoxide (**K**). Perhydrate **IV** is also formed when MeCN is not added to the reaction mixture. Perhydrate **IV** by itself is not capable of promoting the oxidation (see Scheme 1 of the manuscript where in the absence of MeCN, low yield is observed). Thus, MeCN has a dual role in the reaction via the formation of the peroxycarboximidic acid:

firstly, to promote the completion of the oxidation of **I** to **IV** and secondly, to contribute to the formation of the active oxidant species.

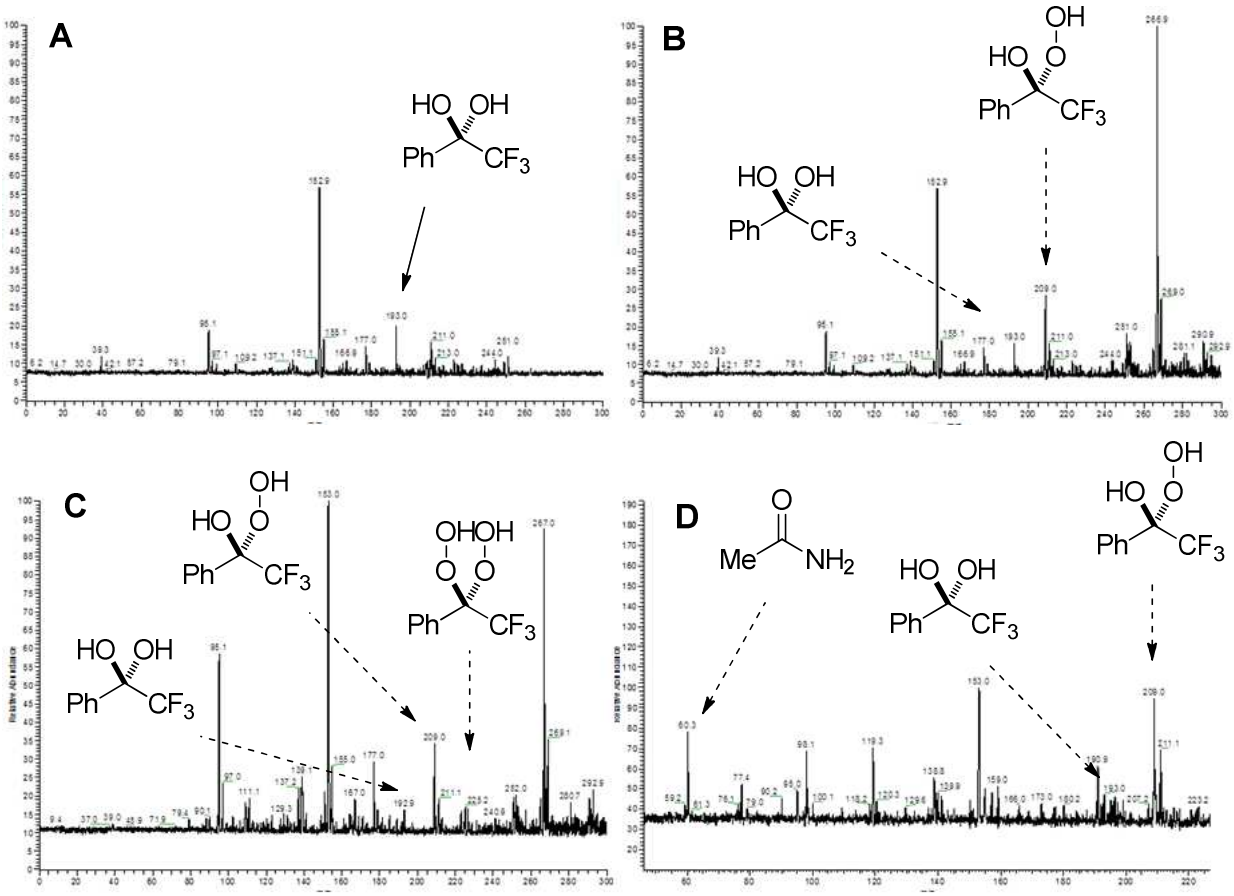
IR Experiments for the Study of the Reaction Mechanism



Initially, in the IR spectrum of the 2,2,2-trifluoroacetophenone (in $CHCl_3$), a peak assigned to the carbonyl was observed at 1720 cm^{-1} (**A**). Once the same compound was diluted in the buffer solution of the reaction in H_2O, that peak disappeared indicating the formation of the corresponding hydrate form (**B**). The addition of ^tBuOH, MeCN and H_2O_2 led to IR spectrum **C**. Similar peaks were identified as in **B**. In addition, a peak at 1636 cm^{-1} can be identified, and could be assigned to the acetamide C=O bond stretch.

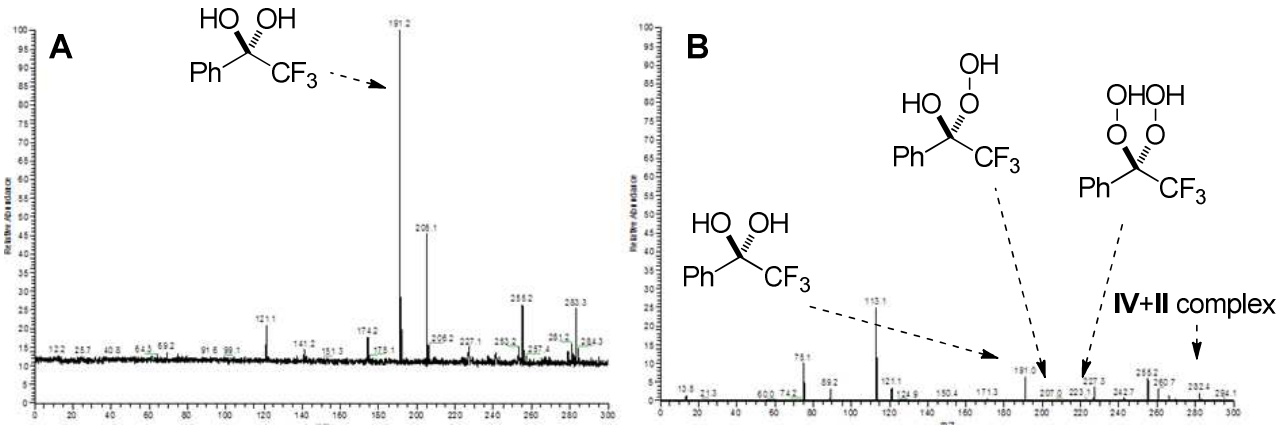
MS Mechanistic Experiments

Positive mode

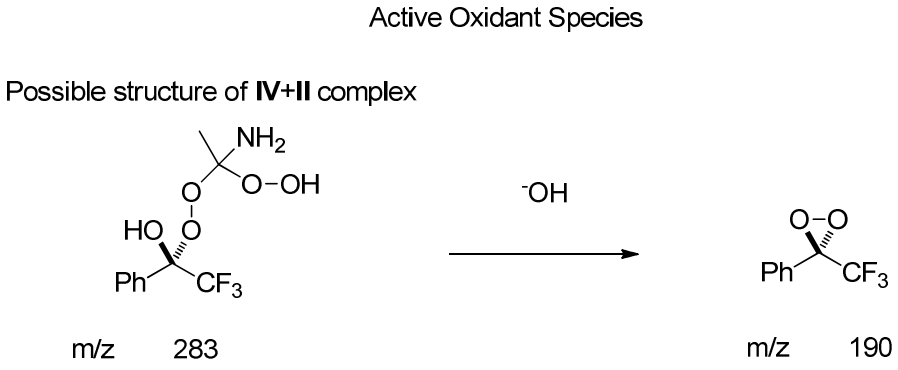


MS spectra under positive ion mode were recorded. 2,2,2-Trifluoroacetophenone in H_2O-buffer existed in the hydrate form and gave a molecular ion that can be observed at *m/z* 193 ($M+H^+$) (**A**). ^{t}BuOH, MeCN and H_2O_2 were added to the reaction mixture, aliquots were taken and injected. Immediately, an ion with *m/z* 209 was observed which may be assigned to the molecular ion of the perhydrate intermediate ($M+H^+$) (**B**). After 20 min, in addition to the perhydrate intermediate with *m/z* 209, another peak was observed at *m/z* 225 ($M+H^+$), which could be assigned to the dihydroperoxide of the 2,2,2-trifluoroacetophenone (**C**). As the reaction time is passing by, along with the 2,2,2-trifluoroacetophenone hydrate (*m/z* 193) and perhydrate intermediate (*m/z* 209), a new peak at (*m/z* 60) appeared, which corresponds to the acetamide, the by-product of the oxidation (**D**).

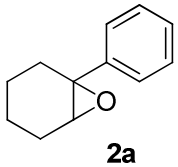
Negative mode



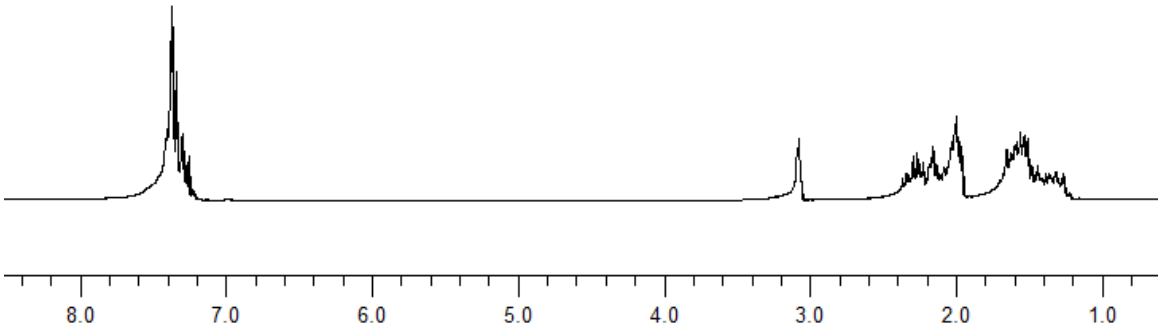
MS spectra under negative ion mode were recorded. 2,2,2-Trifluoroacetophenone in H_2O-buffer existed in the hydrate form and gave a molecular ion that can be observed at *m/z* 191 ($M\text{-}H^-$) (**A**). ^{t}BuOH, MeCN and H_2O_2 were added to the reaction mixture, aliquots were taken and injected. Immediately, an ion with *m/z* 207 was observed which can be assigned to the molecular ion of the perhydrate intermediate ($M\text{-}H^-$) (**B**). Also, an ion with *m/z* 223 was observed which corresponds to the molecular ion of the dihydroperoxide ($M\text{-}H^-$). An ion with *m/z* 282 was also observed, which can be attributed to **IV**+**II** complex. A proposed structure of this complex is shown below. This could be the active oxidant species of the reaction. However, under the basic pH of the reaction mixture, the possibility of this complex collapsing in order to form a dioxirane cannot be ruled out at this moment.

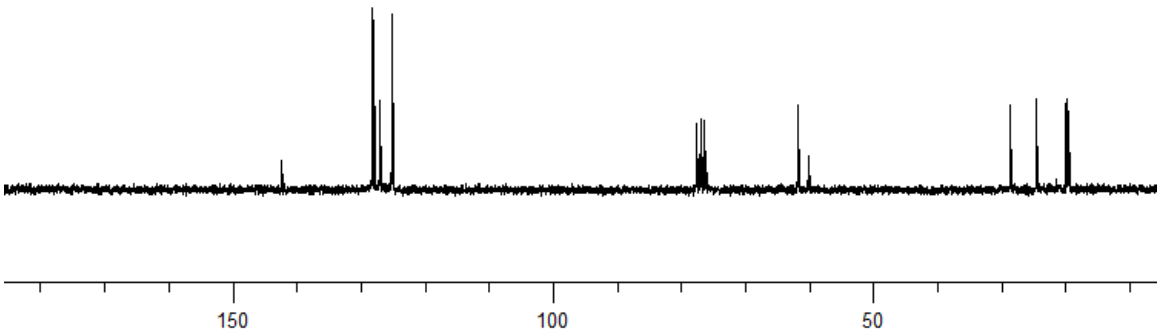


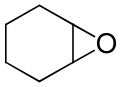
NMR SPECTRA



2a







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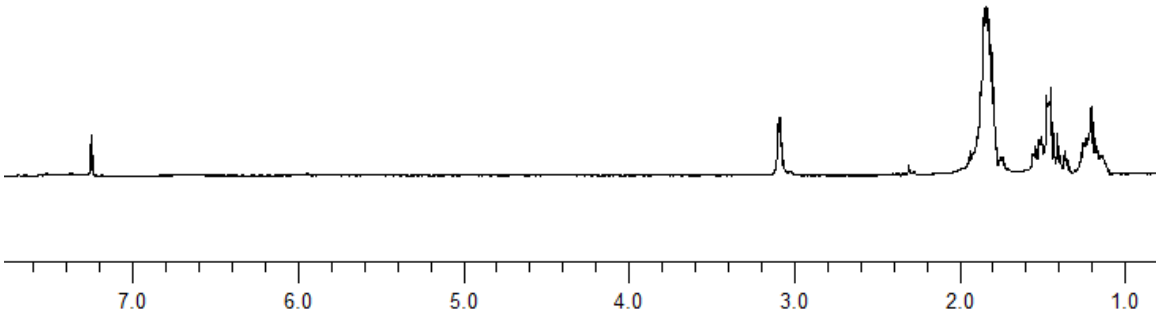

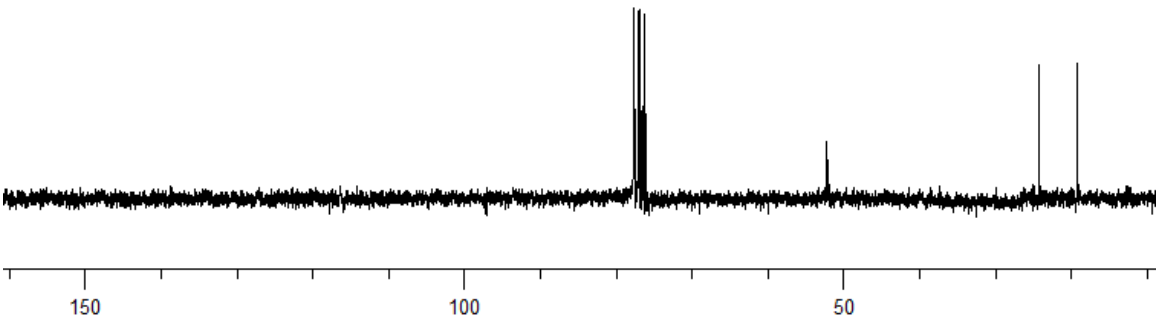

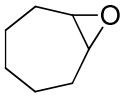

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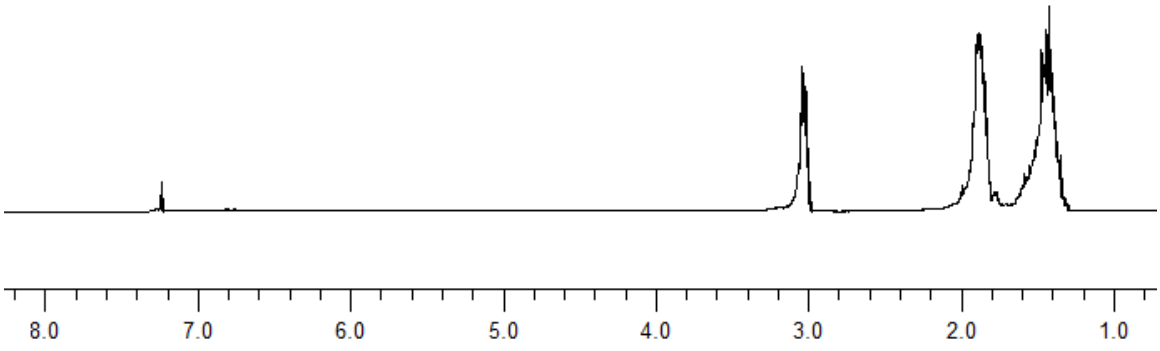

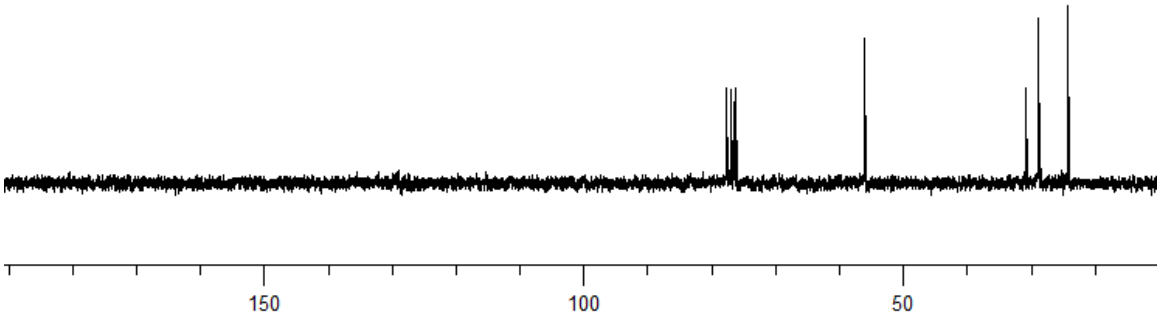

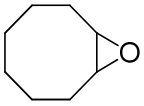

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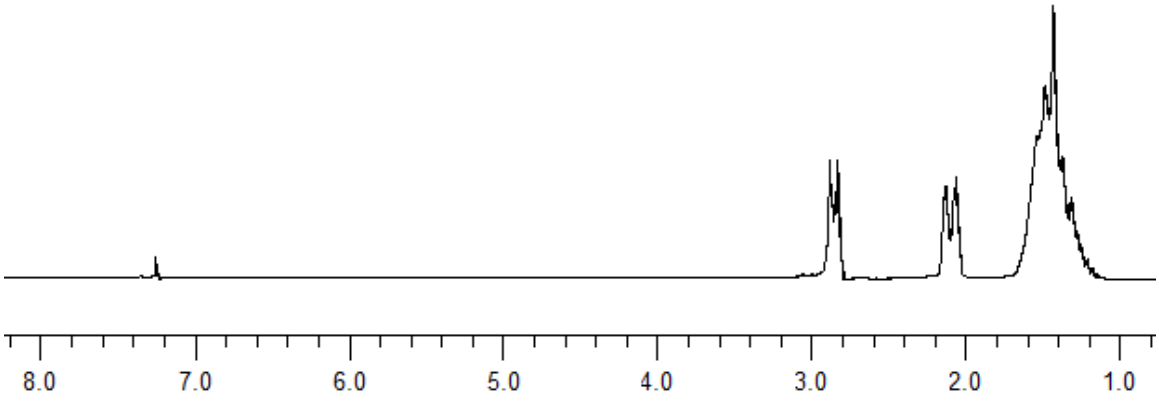

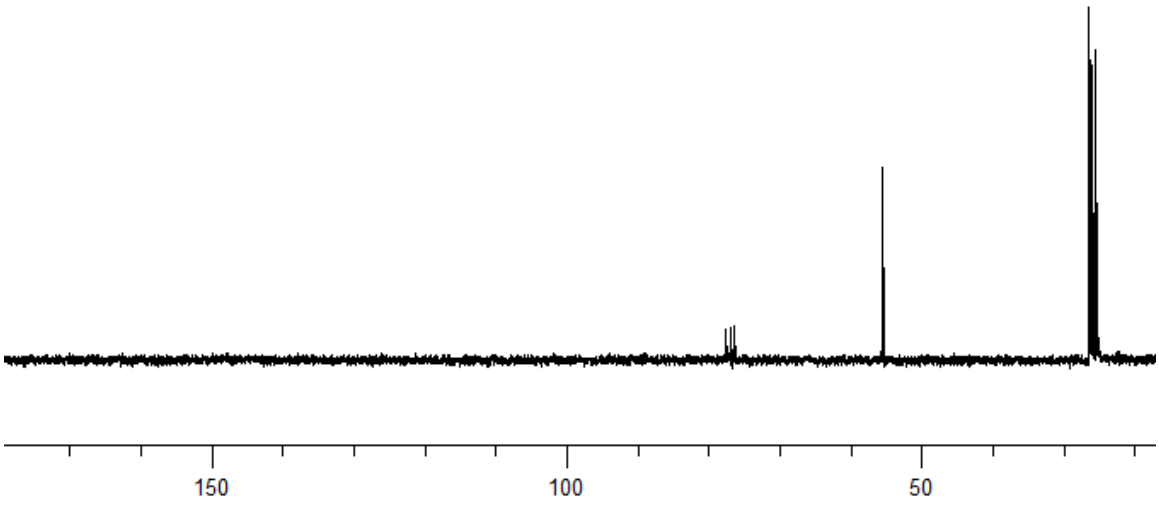

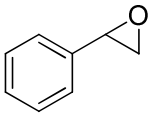

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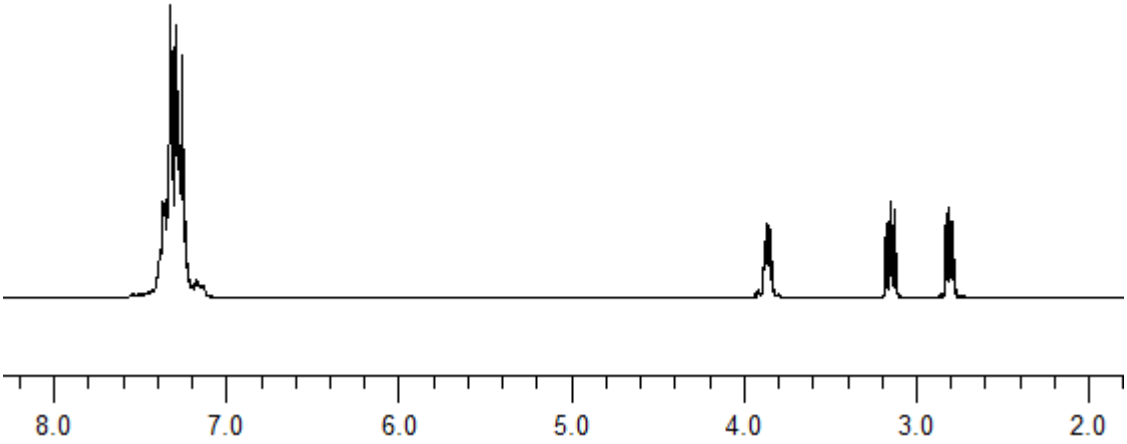

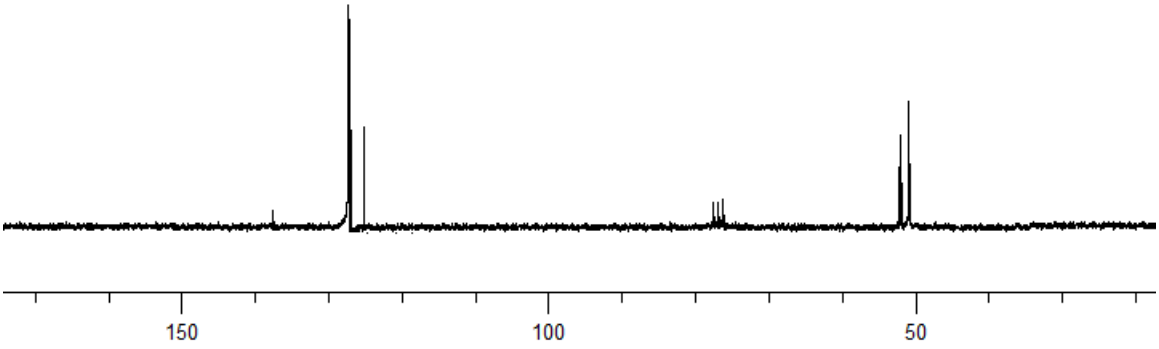

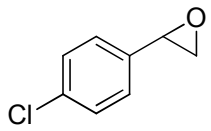

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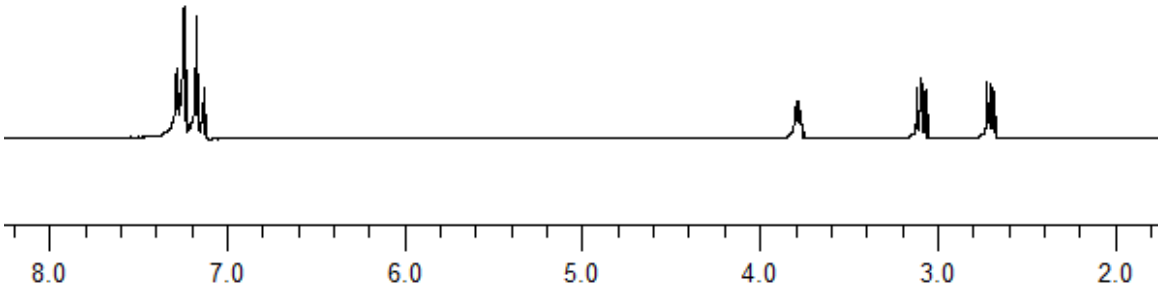

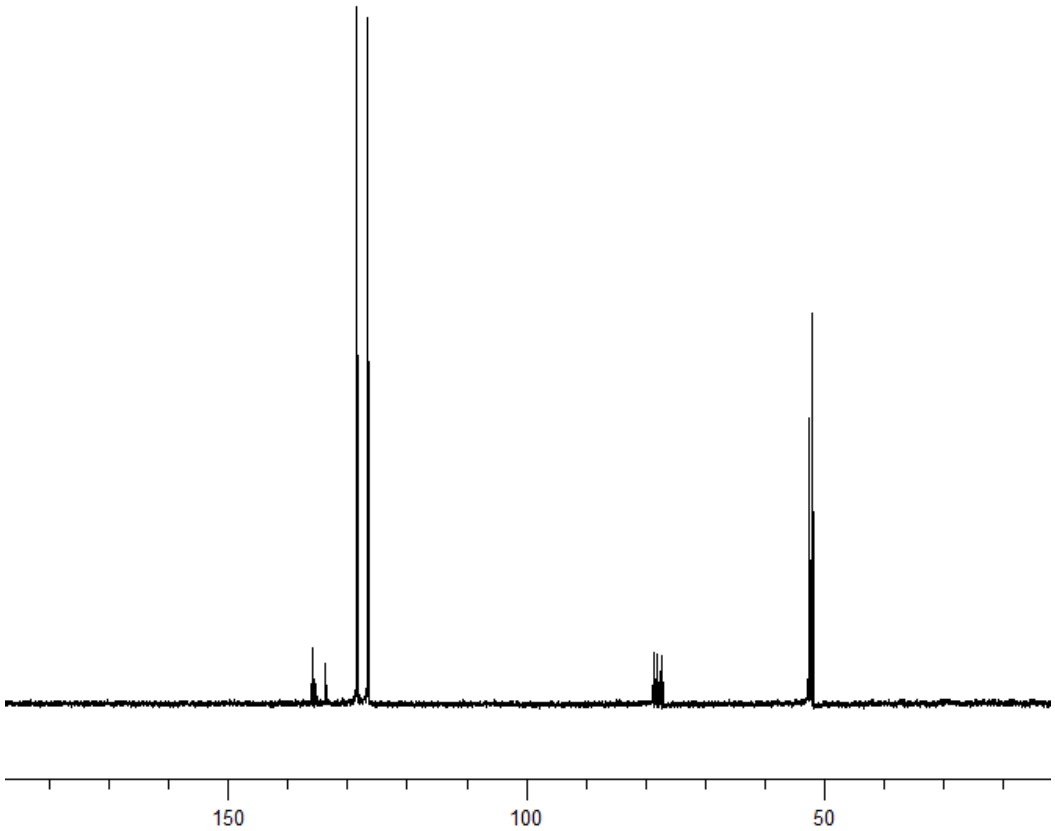

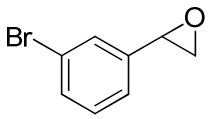

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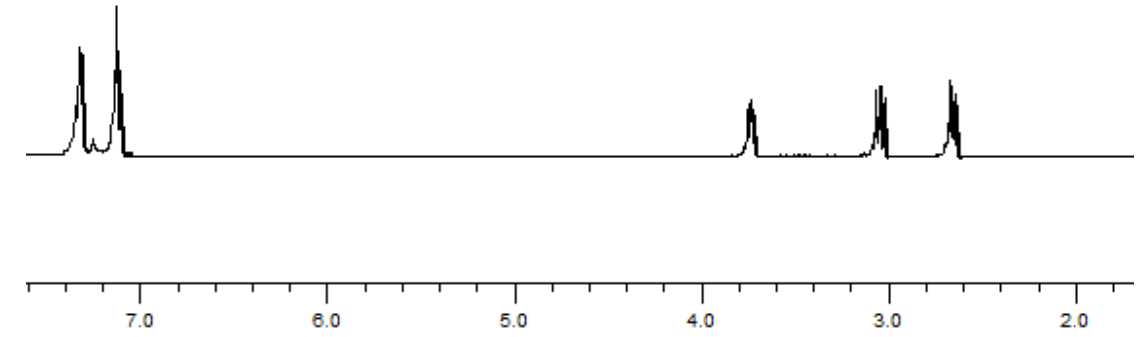

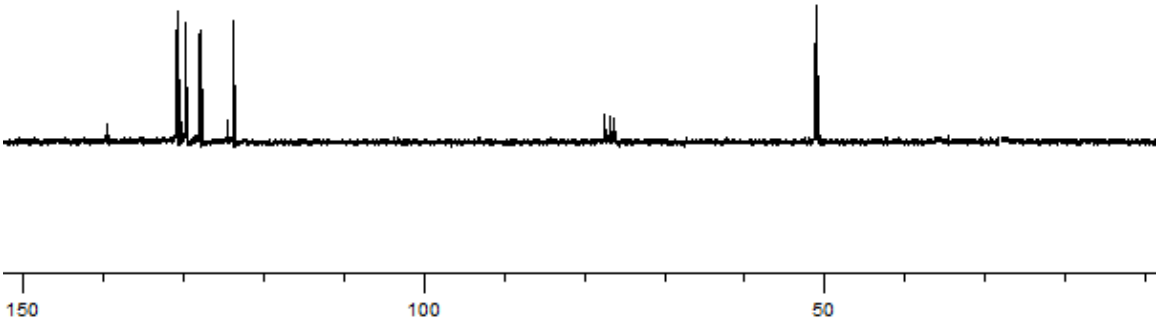

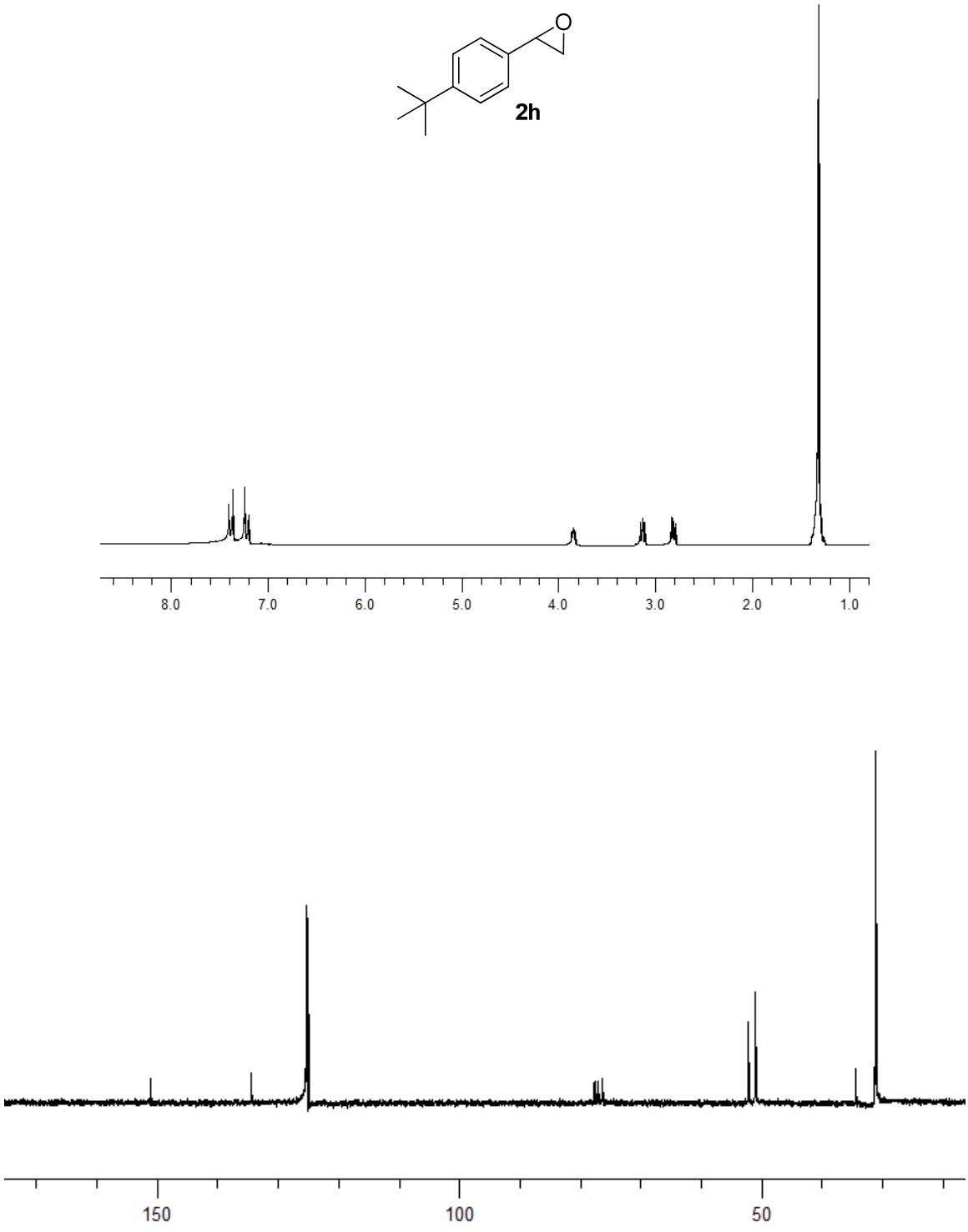
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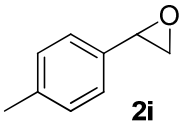

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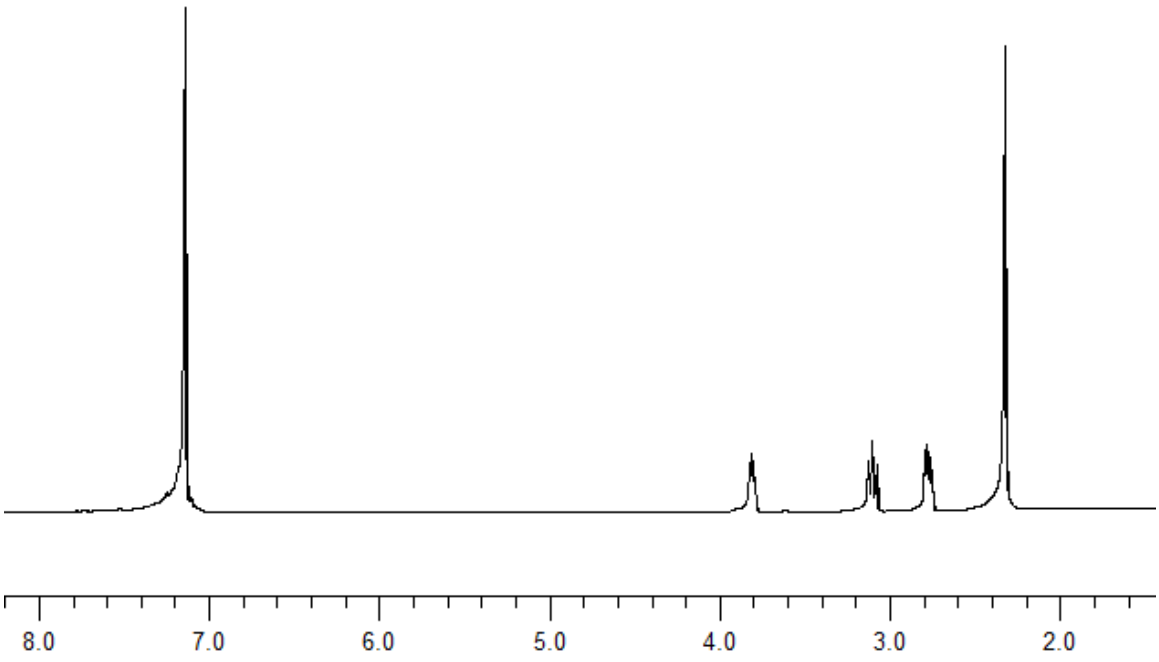

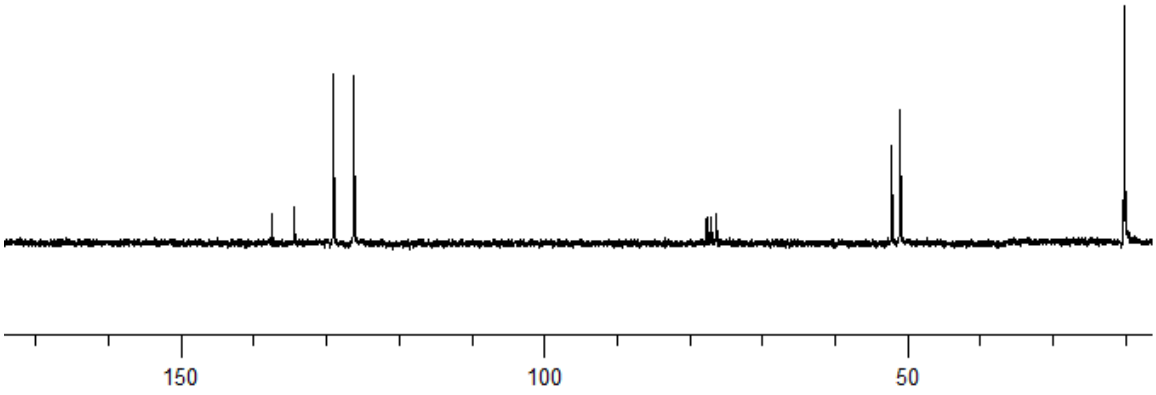

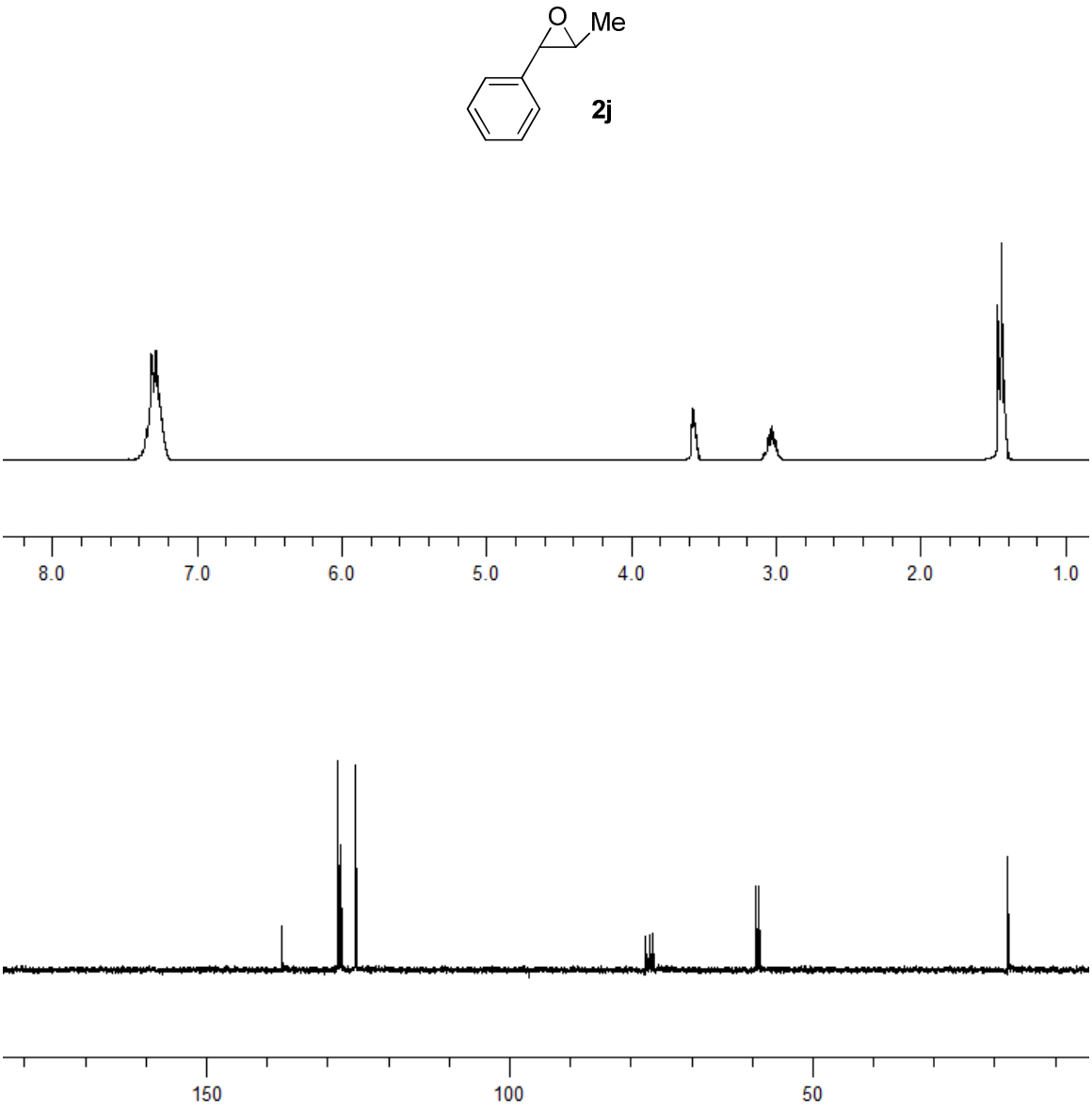
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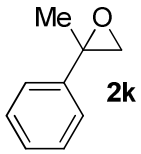

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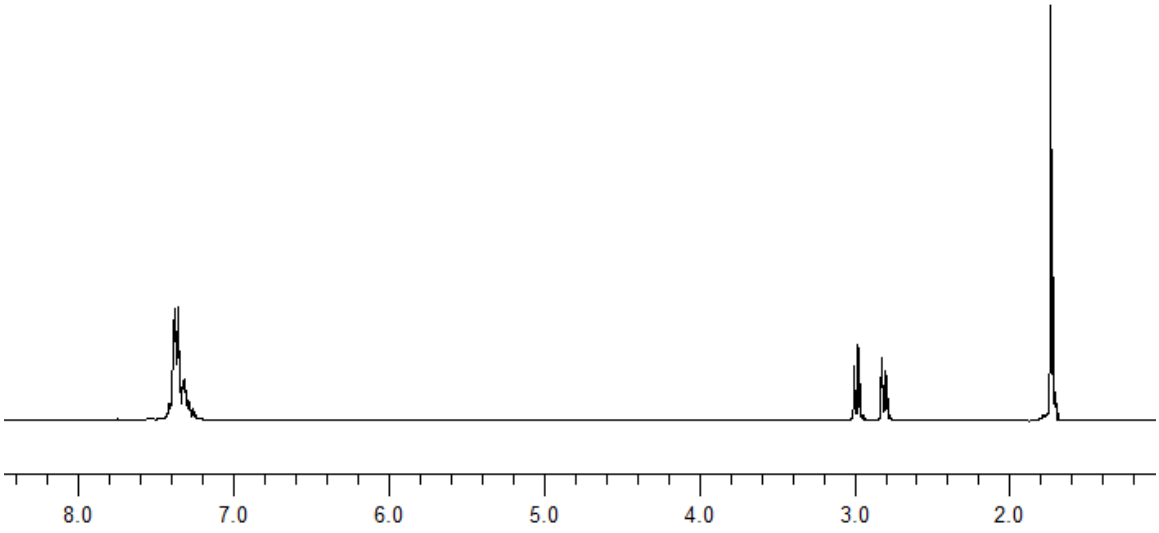

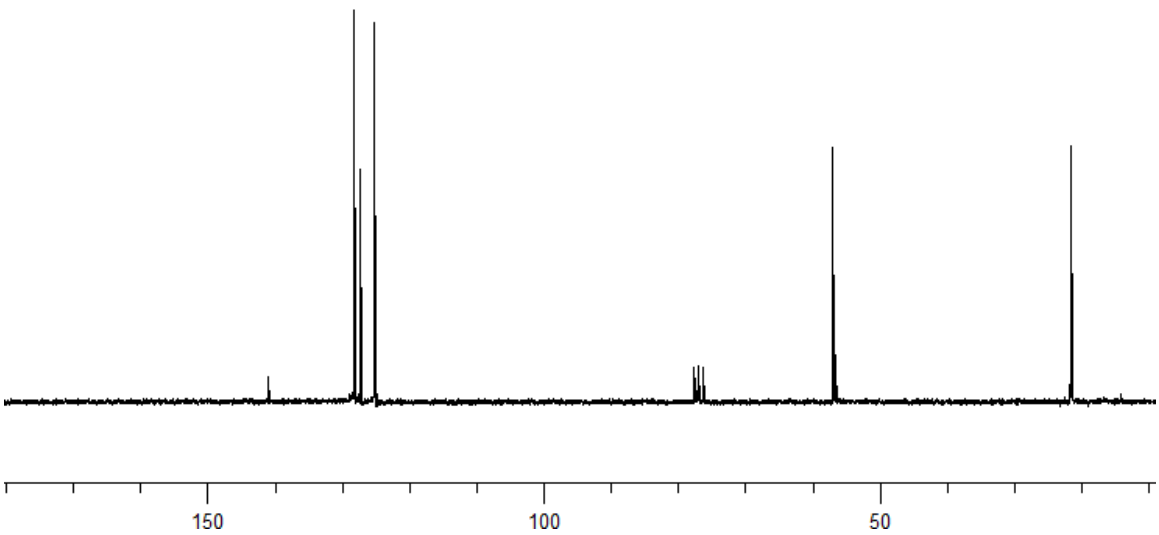

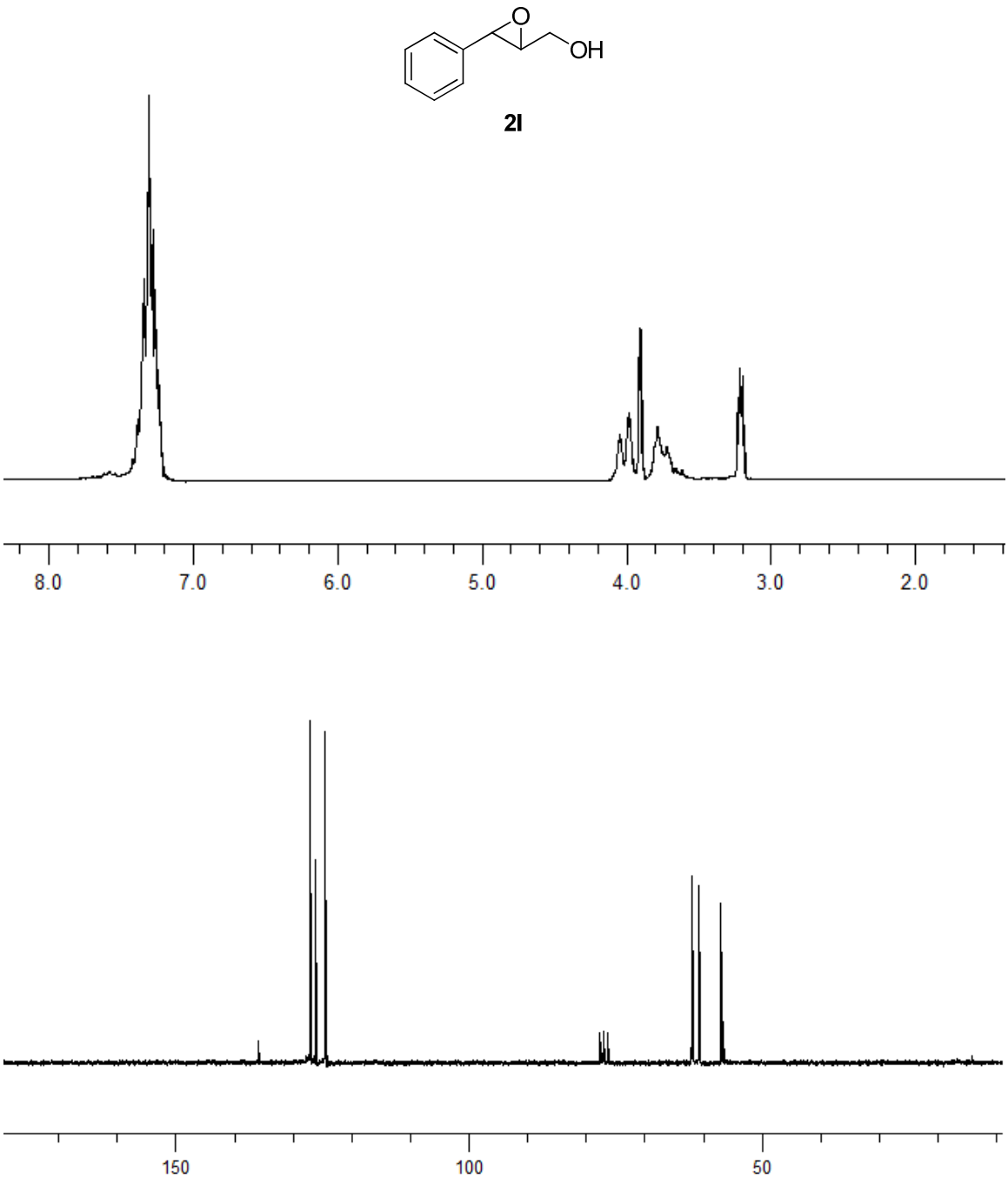

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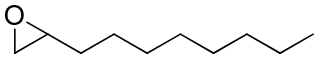

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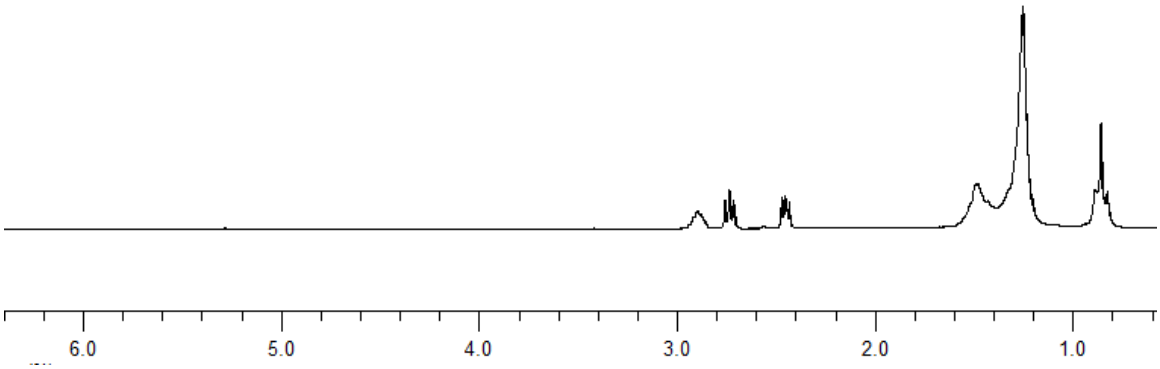

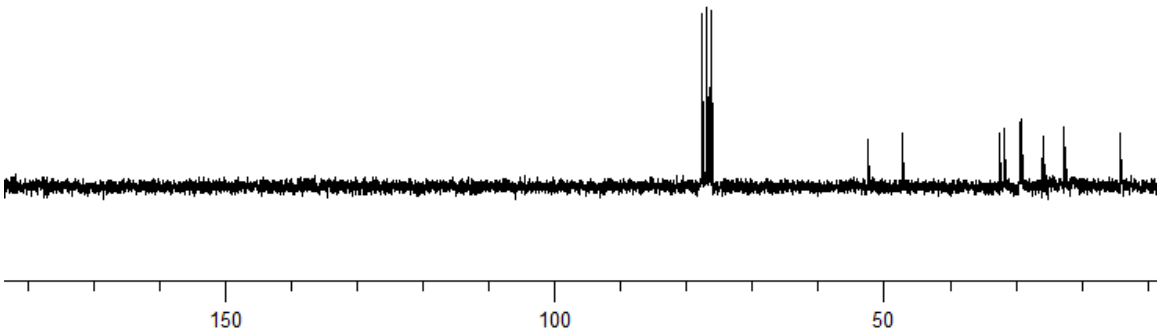

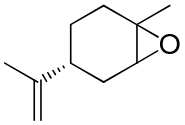

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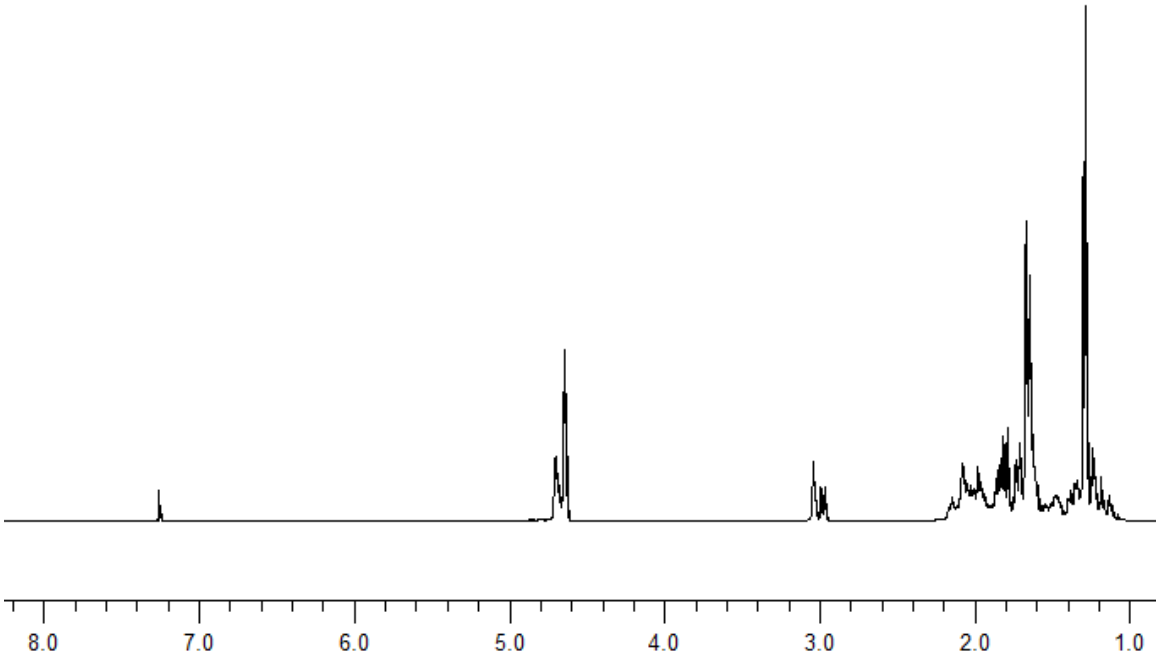

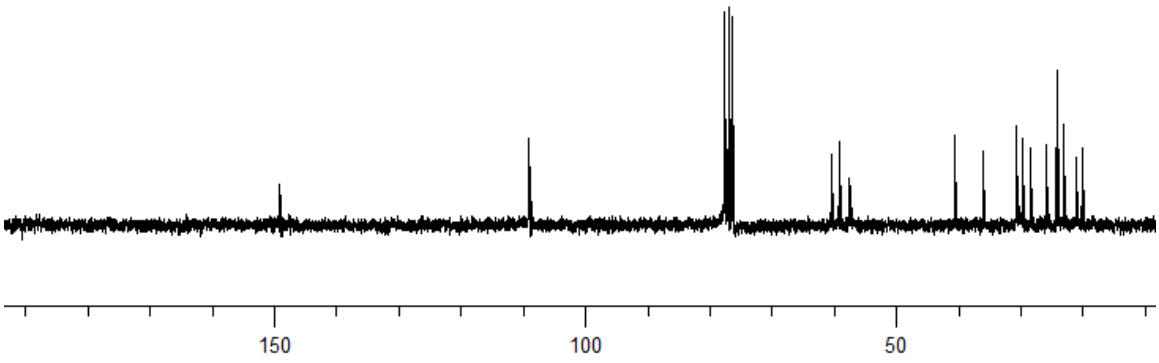

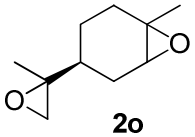

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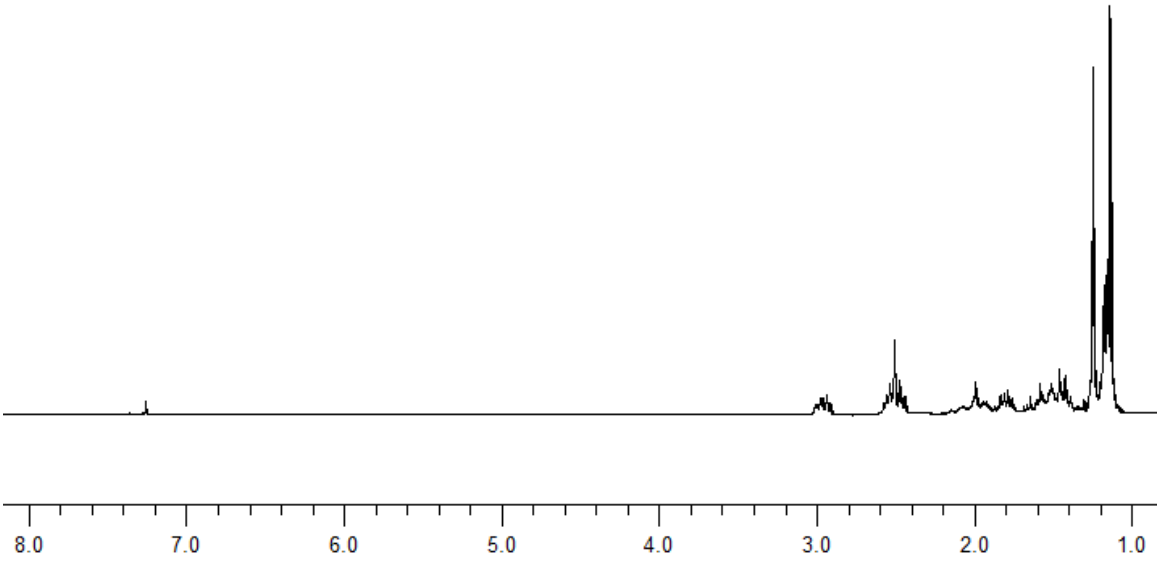

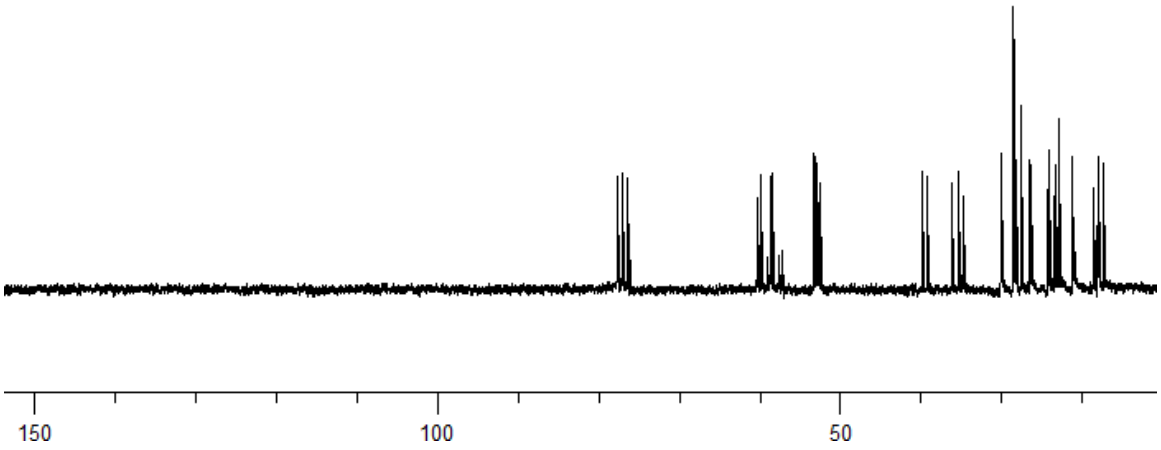

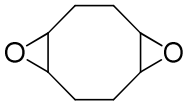

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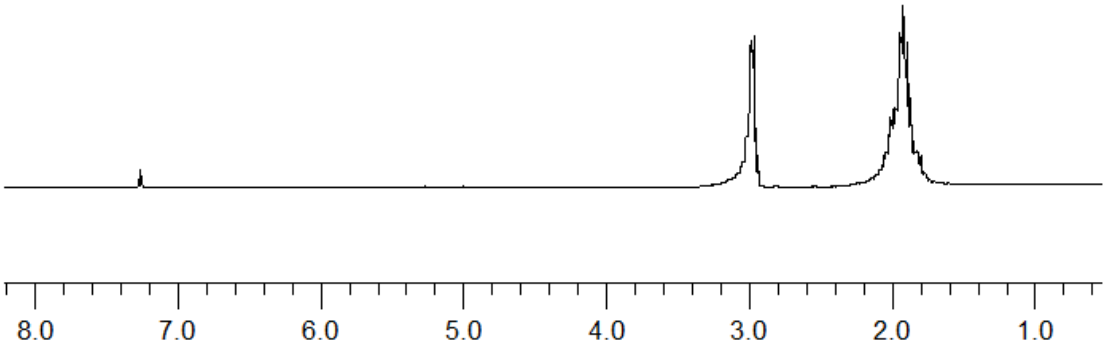

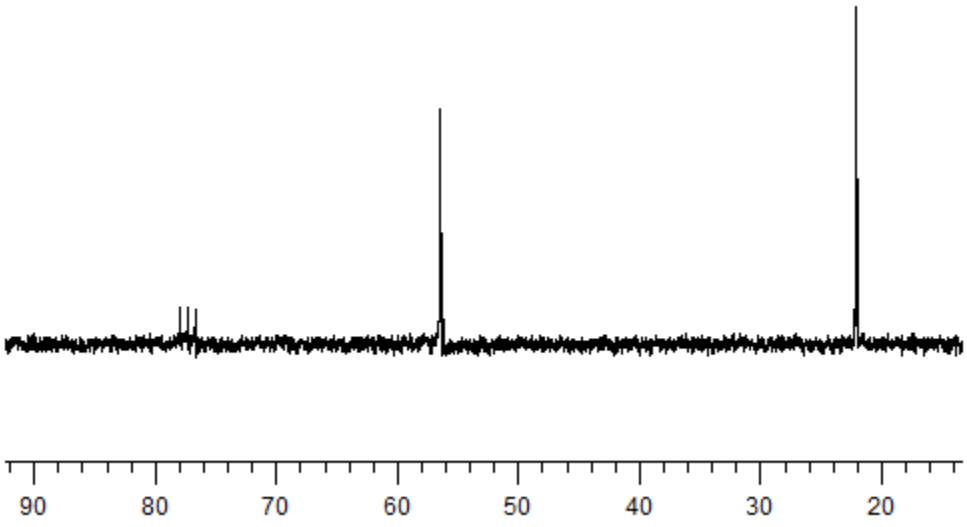

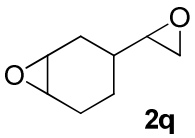

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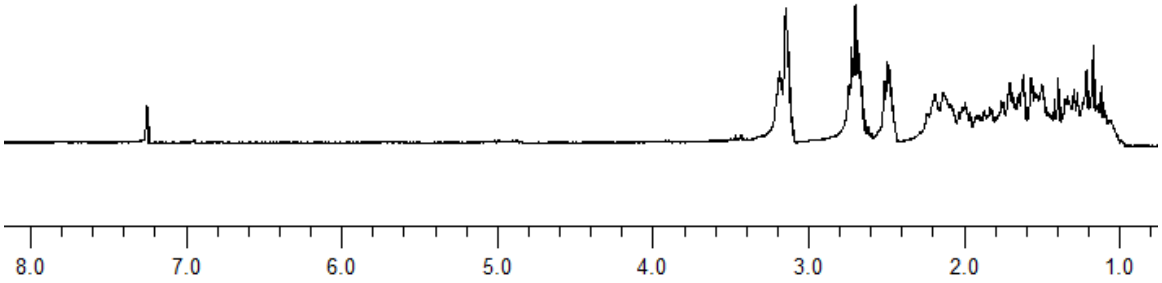

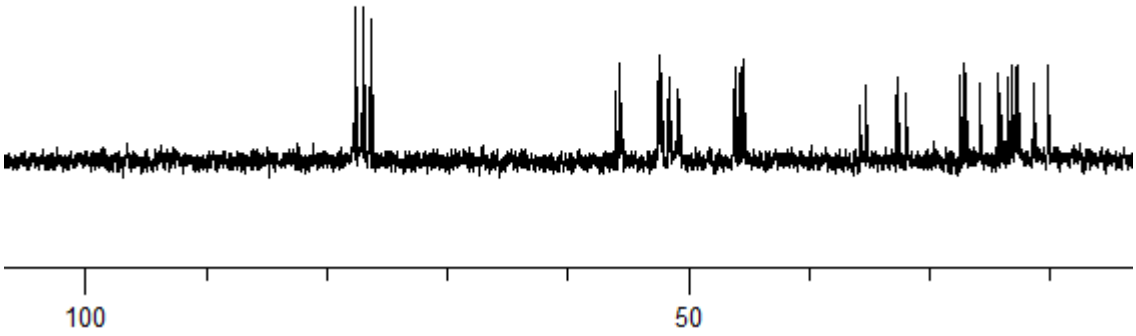

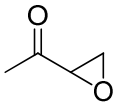

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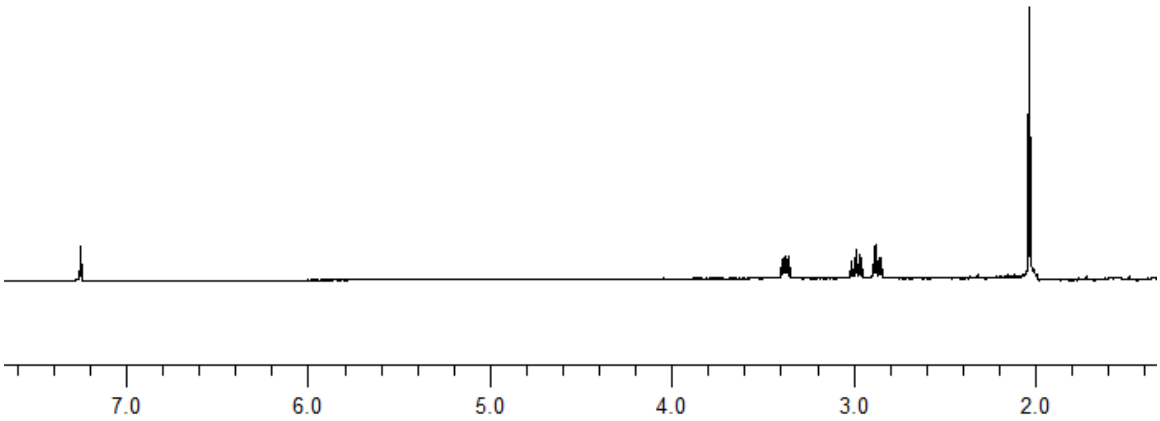

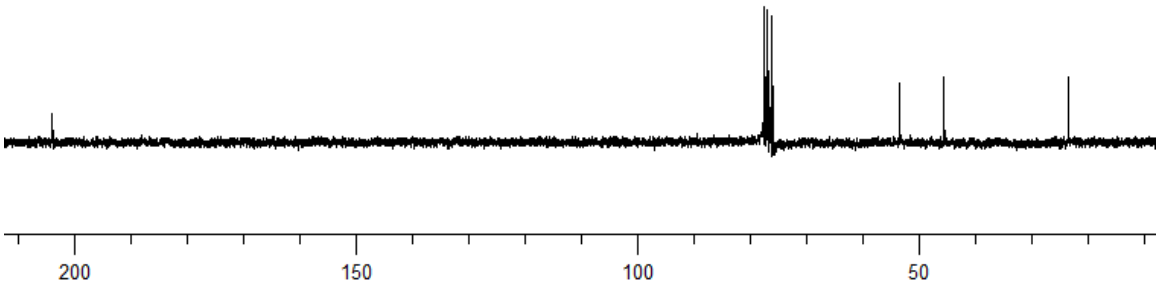

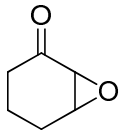

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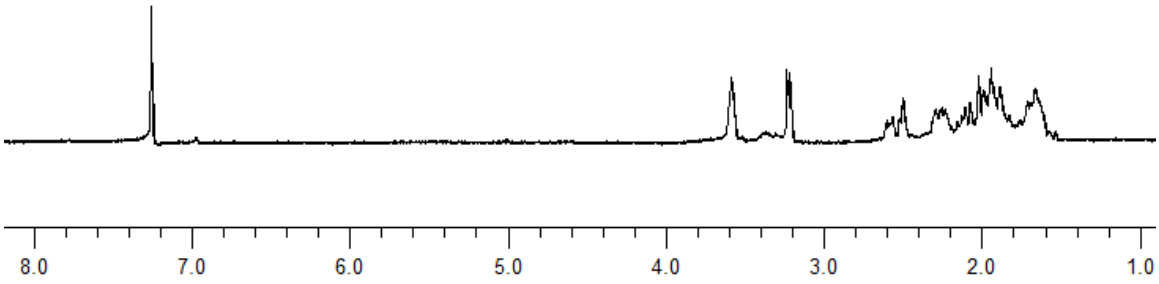

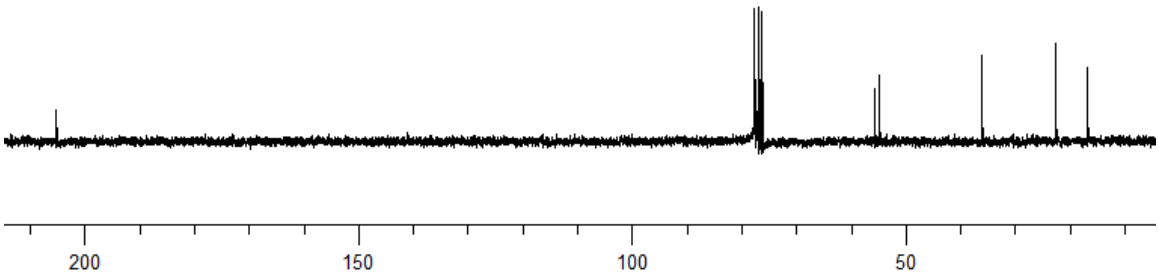

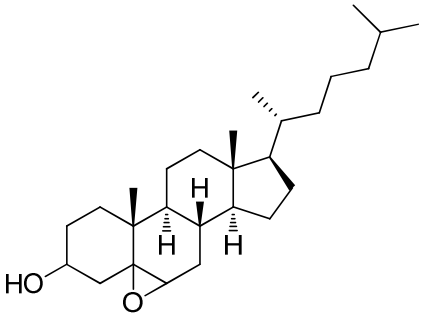

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