Aliphatic C–H Activation with Aluminium Trichloride–Acetyl Chloride: Expanding the Scope of the Baddeley Reaction for the Functionalisation of Saturated Hydrocarbons

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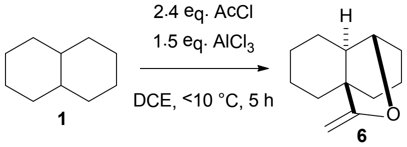
ELECTRONIC SUPPORTING INFORMATION

EXPERIMENTAL PROCEDURES

Large-Scale Synthesis of Baddeley's enol ether **6**

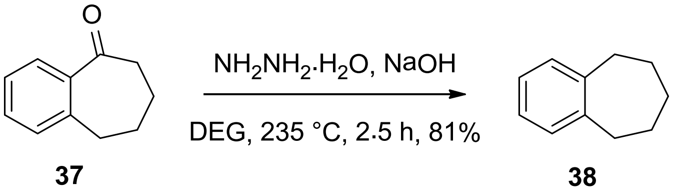


This reaction was performed in accordance with Baddeley's literature procedure.[5b-f] Acetyl chloride (85.45 mL, 1.197 mol, 2.40 equiv) was gradually added with stirring to a cooled (<25 °C) mixture of aluminium chloride (100.0 g, 0.75 mol, 1.50 equiv) in DCM (225 mL). The resulting yellow-brown solution was decanted into a flask, cooled to <10 °C, and decalin **1** (80.9 mL, 0.51 mol, 1.00 equiv) was gradually added over 30 min with stirring and cooling to keep the temperature of the reaction mixture below 10 °C. After a further 2 h at 10-15°C, the mixture was gradually added to a vigorously stirred slurry of crushed ice (1 kg) and water. The lower organic layer was separated and, together with DCM extracts of the aqueous layer, washed several times with ice-cold water and dried over $MgSO_4$, then filtered. The filtrate was concentrated under reduced pressure. Fractional distillation of the residual brown oil gave (1*S**,4a*R**,8a*R**)-9-methyleneoctahydro-1H-1,4a-(epoxymethano)naphthalene **6** (b.p. 82-85 °C / 5.8 Torr) which was then further purified by refluxing with $LiAlH_4$ (0.5 g) in dry diethyl ether (30 mL) for 30 min. Excess of hydride was destroyed by cautious addition of ethyl acetate (5 mL), and ice-cold dilute sulphuric acid (50 mL, 0.5 N) was gradually added to the cooled mixture. The ethereal layer was rapidly separated and, with further ethereal extracts of aqueous layer, was washed with water (2 × 50 mL) and dried over $MgSO_4$, then filtered. The filtrate was concentrated under reduced pressure. Further distillation afforded pure (1*S**,4a*R**,8a*R**)-9-methyleneoctahydro-1H-1,4a-(epoxymethano)naphthalene **6** (22.81 g, 25%) as a pale yellow oil; b.pt. 65 °C / 1.5 Torr; δ_H (250 MHz, $CDCl_3$) 4.22 (1H, dt, *J* 1.0, 0.5 Hz, >CH-O-), 4.03 (1H, d, *J* 4.5 Hz, $=CH_2$), 3.66 (1H, d, *J* 1.5 Hz, $=CH_2$), 1.88-1.07 (15H, m, cy-CH); δ_C (75 MHz, $CDCl_3$) 166.0 (>*C*=CH_2), 80.4 (>CH-O-), 76.9 ($=CH_2$), 50.0 (3°), 46.2 (4°), 39.5 (2°), 31.3 (2°), 30.2 (2°), 26.5 (2°), 24.9 (2°), 22.1 (2°), 18.9 (2°); ν_{max} (film) 2927, 2860, 1679, 1455, 1369, 1198, 1106, cm^{-1}; TOF-ESI+ *m/z* calculated for $(C_{12}H_{18}O + H)^+$, 179.1435, found, 179.1422.

Use of different Lewis acids

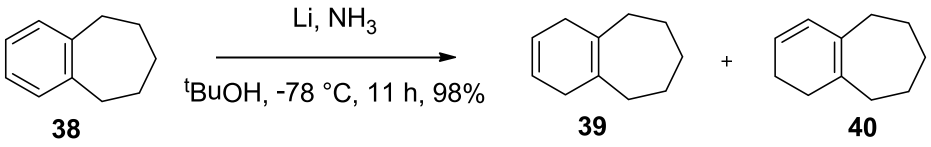
Lewis acid	Reaction with **1** and AcCl under Baddeley conditions
$FeCl_3$	9% yield of **6**
$ZnCl_2$	No reaction
$BF_3.Et_2O$	No reaction

*6,7,8,9-tetrahydro-5H-benzo[7]annulene, **38***



Reaction performed in accordance with a literature procedure[24a].

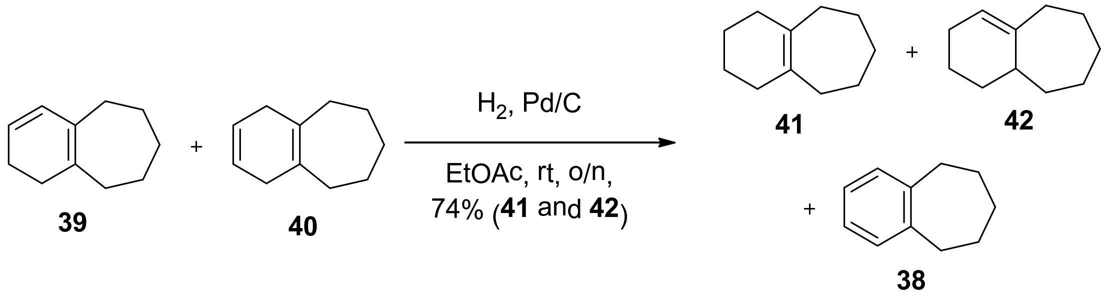
*4,5,6,7,8,9-hexahydro-1H-benzo[7]annulene, **40** and 2,5,6,7,8,9-hexahydro-1H-benzo[7]annulene, **39***



This reaction was adapted from a literature procedure[24b].

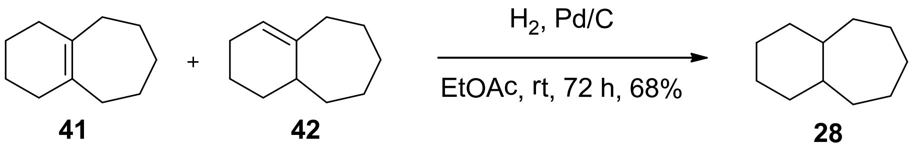
2-necked 1 L flask and cold finger were oven dried and flushed with Ar, then cooled to -78 °C in a dry ice/acetone bath. Ammonia (200 mL) was condensed into the flask, then a mixture of ^{t}BuOH (78 mL), Et_2O (14 mL) and 6,7,8,9-tetrahydro-5H-benzo[7]annulene (10.8 g, 0.074 mol, 1.0 eq.) was added slowly, with stirring. Over 6 h, Li (3.85 g, 0.555 mol, 7.5 eq.) was added piecewise to the RM, turning a distinctive blue colour. After addition of Li, RM stirred at -78 °C for a further 5 h, then ice bath removed and NH_3 was allowed to evaporate overnight. The solid residue was quenched by gradual addition of ^{i}PrOH, MeOH and then H_2O over 2 h, then cooled to rt, transferred to separating funnel and extracted with petrol (3 x 100 mL). Organic layers combined and washed with brine, dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure. The crude product was flushed through a silica pad with hexanes to give a mixture of dialkenes (**39** and **40**, 10.71 g, 98%) as a colourless oil. The mixture was taken forward to hydrogenation without further purification.

*2,3,4,5,6,7,8,9-octahydro-1H-benzo[7]annulene, **41** and 2,3,5,6,7,8,9,9a-octahydro-1H-benzo[7]annulene, **42***



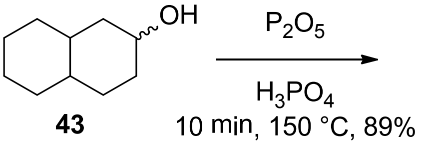
To a mixture of dienes **39** and **40** (5.42 g) dissolved in EtOAc (100 mL) was added Pd/C (100 mg). The reaction was allowed to stir at room temperature overnight under 1 atmosphere of H_2. Gas was removed under vacuum and reaction vessel flushed with N_2. Pd/C removed by filtering through a celite pad and filtrate concentrated under reduced pressure. Column chromatography (100% petrol) gave a mixture of alkenes **41** and **42** (colourless oil, visualised by $KMnO_4$ stain, R_f 0.98, 4.08 g, 74%) and 6,7,8,9-tetrahydro-5H-benzo[7]annulene (colourless oil, visualised by UV, R_f 0.83, 0.25 g, 5%). The mixture of alkenes was taken forward to further hydrogenation without separation.

*Bicyclo[5,4,0]undecane, **28***



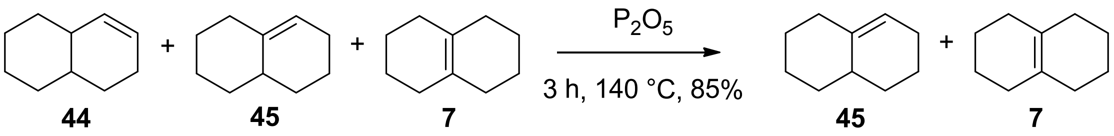
To a mixture of alkenes **41** and **42** (3.51 g, 0.023 mol, 1.0 eq) dissolved in EtOAc (100 mL) was added Pd/C (80 mg). The reaction was allowed to stir at room temperature for 3 days under 1 atmosphere of H_2. Gas was removed under vacuum and reaction vessel flushed with N_2. Pd/C removed by filtering through a celite pad and filtrate concentrated under reduced pressure. A mixture of *cis* and *trans* decahydro-1H-benzo[7]annulene **28** was obtained as a colourless oil (3.03 g, 85%). δ_H (250 MHz, $CDCl_3$) 0.82 – 1.79 (40H, m); δ_C (75 MHz, $CDCl_3$) 46.1, 38.6, 36.1, 36.0, 32.7, 32.4, 31.2, 27.5, 26.8, 26.5, 25.8, 24.4; ν_{max} 2917, 2850, 1446, 1260, 1099, 1018, 805 cm^{-1}

*$\Delta^{1,2}$ octalin, **44**, $\Delta^{1,9}$ octalin, **45** and $\Delta^{9,10}$ octalin, **7***



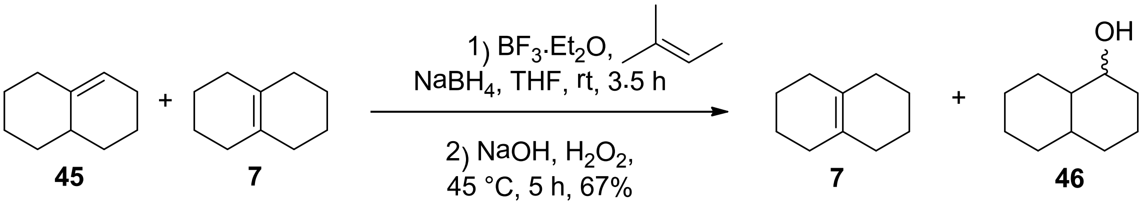
Reaction performed in accordance with a literature procedure[26a].

*$\Delta^{1,9}$ octalin, **45** and $\Delta^{9,10}$ octalin, **7***



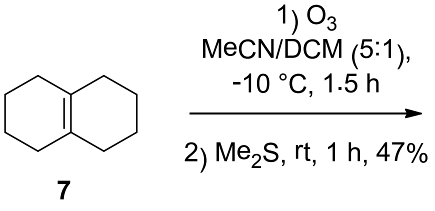
Reaction performed in accordance with a literature procedure[26a].

*$\Delta^{9,10}$ octalin, **7***



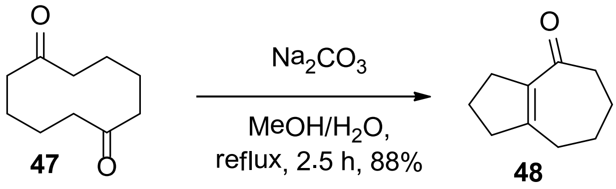
Reaction performed in accordance with a literature procedure[26b].

*Cyclodecane-1,6-dione,**47***



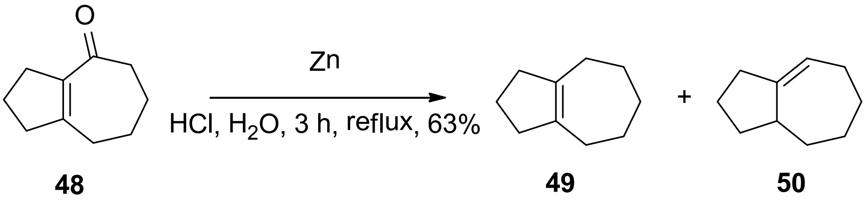
This reaction was performed in accordance with a literature procedure[26c].

2,3,5,6,7,8-hexahydroazulen-4(1H)-one, ***48***



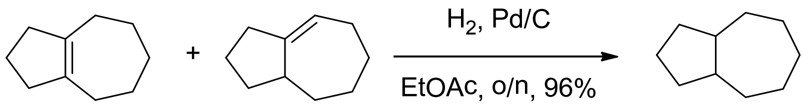
This reaction was performed in accordance with a literature procedure[26c].

1,2,3,4,5,6,7,8-octahydroazulene, ***49*** *and 1,2,3,3a,5,6,7,8-octahydroazulene,* ***50***



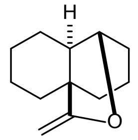
To a mixture of 2,3,5,6,7,8-hexahydroazulen-4(1H)-one **48** (4.50 g, 0.03 mol, 1.0 eq.) and zinc powder (45 g, 0.69 mol, 23.0 eq.) was gradually added an HCl solution (9 M in H_2O, 187mL). Reaction mixture heated to reflux at 100 °C for 3 h. After cooling to rt, reaction mixture was *carefully* diluted by addition to 300 mL of water and transferred to a separating funnel. Organic layer extracted with pentane (3 x 100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The mixture of alkenes, **49** and **50** (2.58g, 63%, colourless oil) were taken forward to hydrogenation without further purification.

*Bicyclo[5.3.0]undecane, **30***

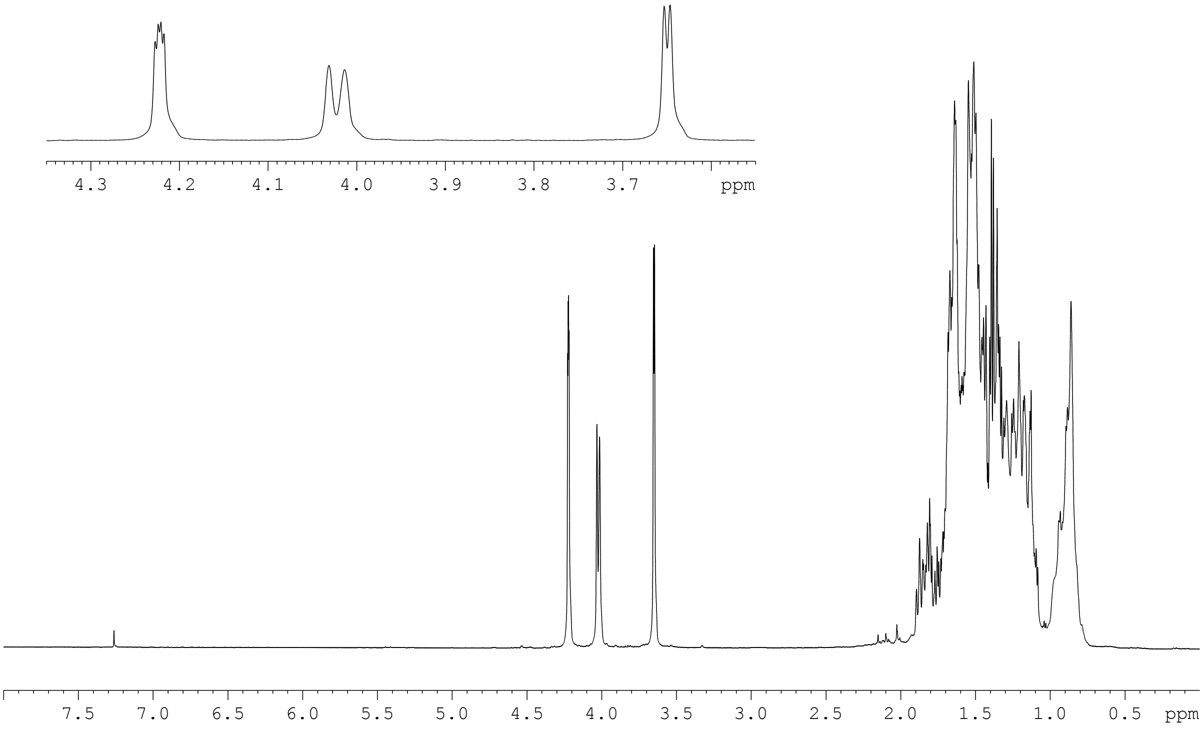


49 **50** **30**

A mixture of alkenes, **49** and **50**, (2.80 g, 0.021 mol, 1.0 eq.) were dissolved in EtOAc (80 mL) to which Pd/C (230 mg) The reaction was allowed to stir at room temperature overnight under 1 atmosphere of H_2. Gas was then removed under vacuum, Pd/C removed by flushing reaction mixture through a celite pad and EtOAc removed under reduced pressure. A mixture of *cis* and *trans* bicyclo[5.3.0]undecane **30** was identified as a colourless oil (2.74 g, 96%). δ_H (300 MHz, $CDCl_3$) 2.49 – 1.02 (36H, m); δ_C (75 MHz, $CDCl_3$) 46.3, 43.4, 35.8, 35.1, 34.3, 32.9, 31.7, 29.7, 28.0, 26.6, 26.5, 24.0; ν_{max} 2917, 2850, 1449, 1358, 1156, 949 cm^{-1}


H
O

6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3.8
3.7
ppm
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6.5
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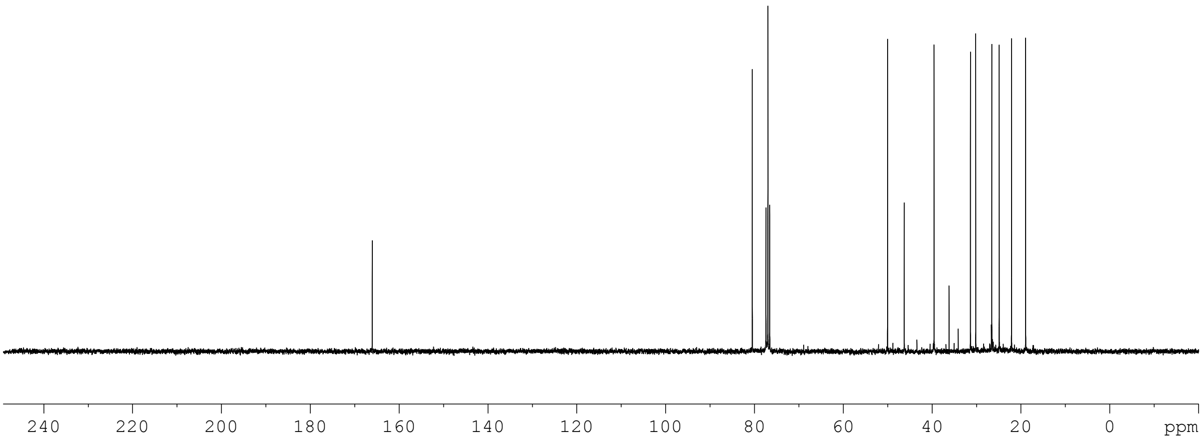
0.5
ppm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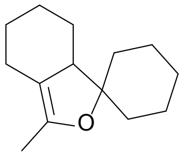
ppm



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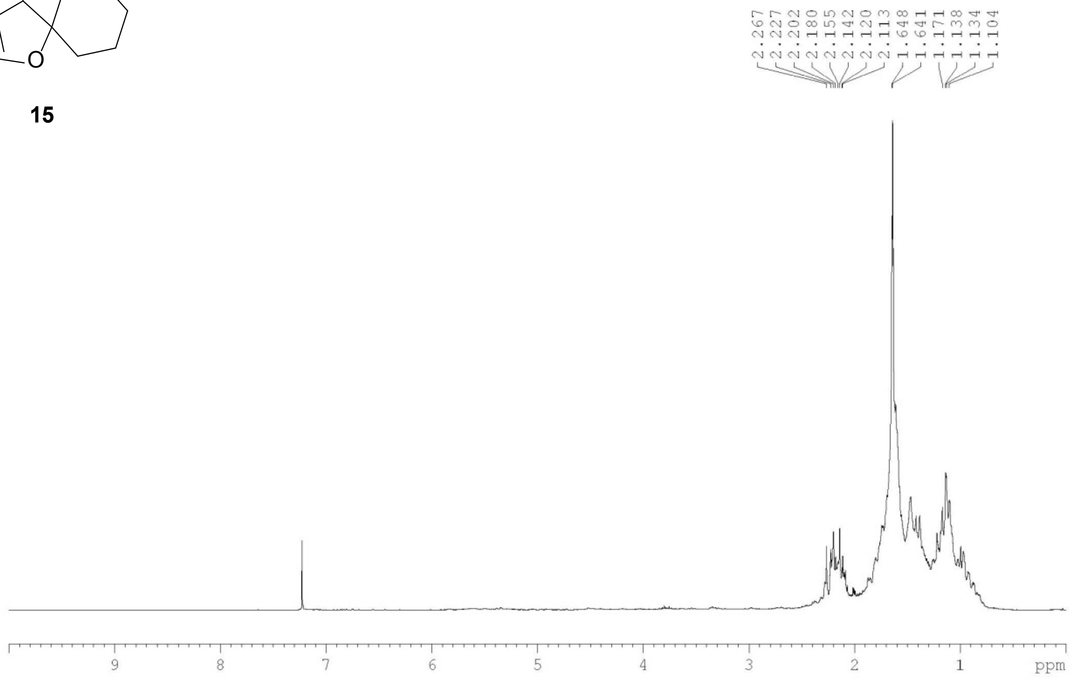
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7
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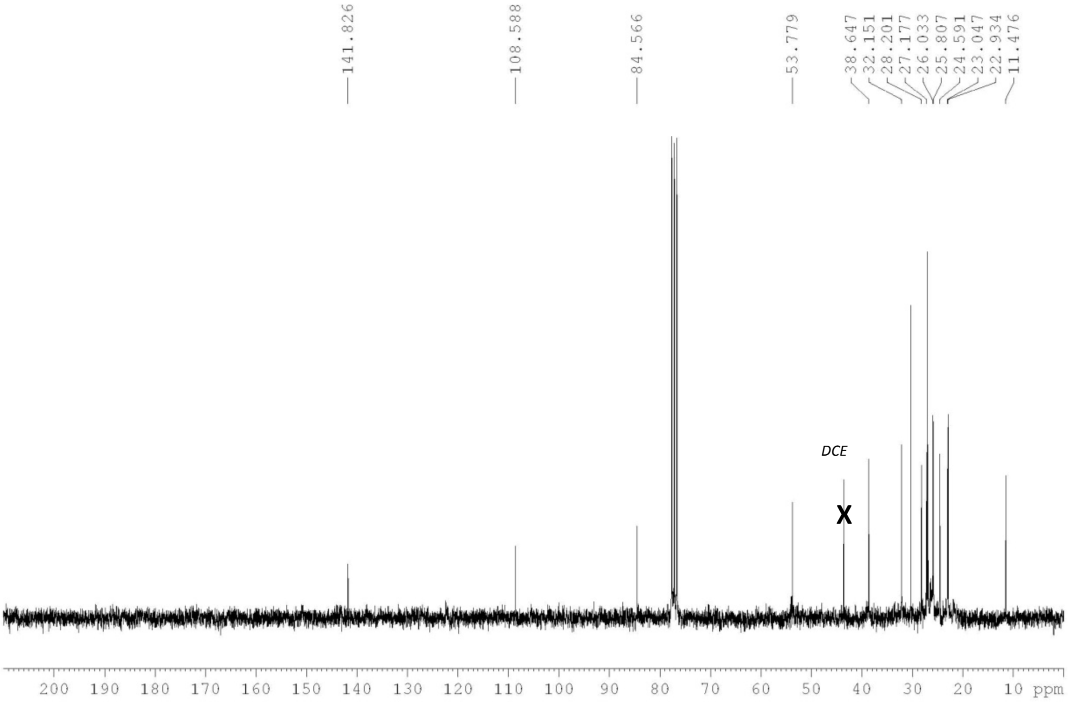
1
ppm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32.151
28.201
27.177
26.033
25.807
24.591
23.047
22.934
11.476
DCE
X
200
190
180
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160
150
140
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120
110
100
90
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70
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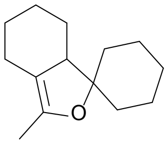
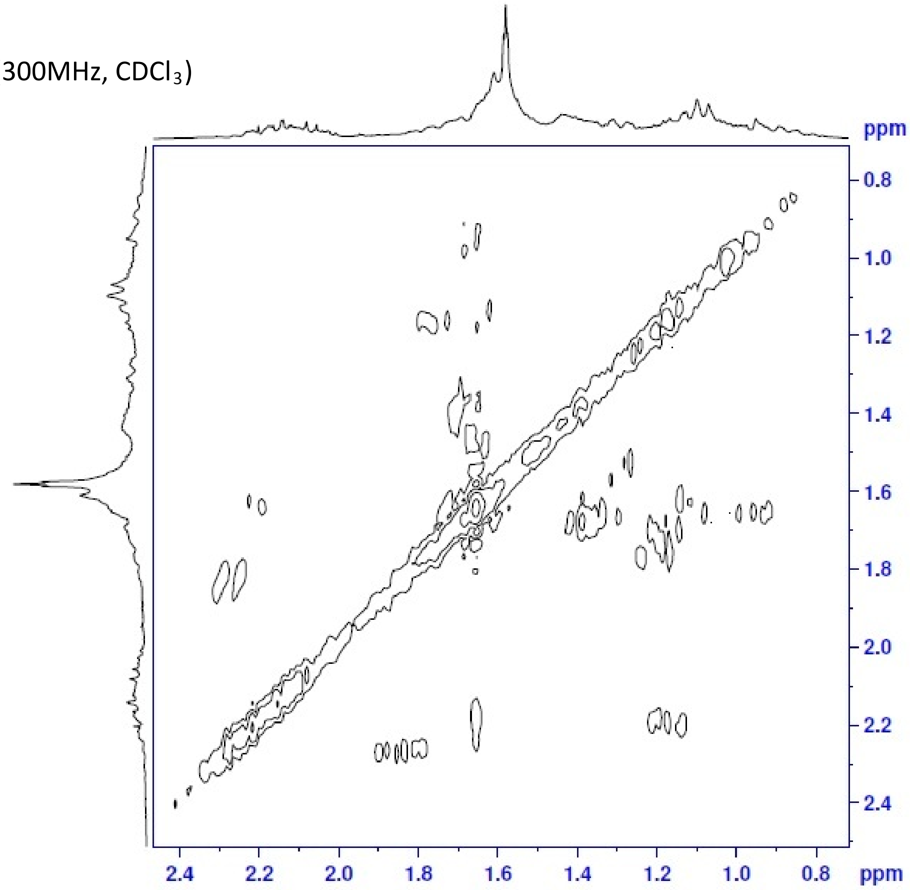
40
30
20
10
ppm

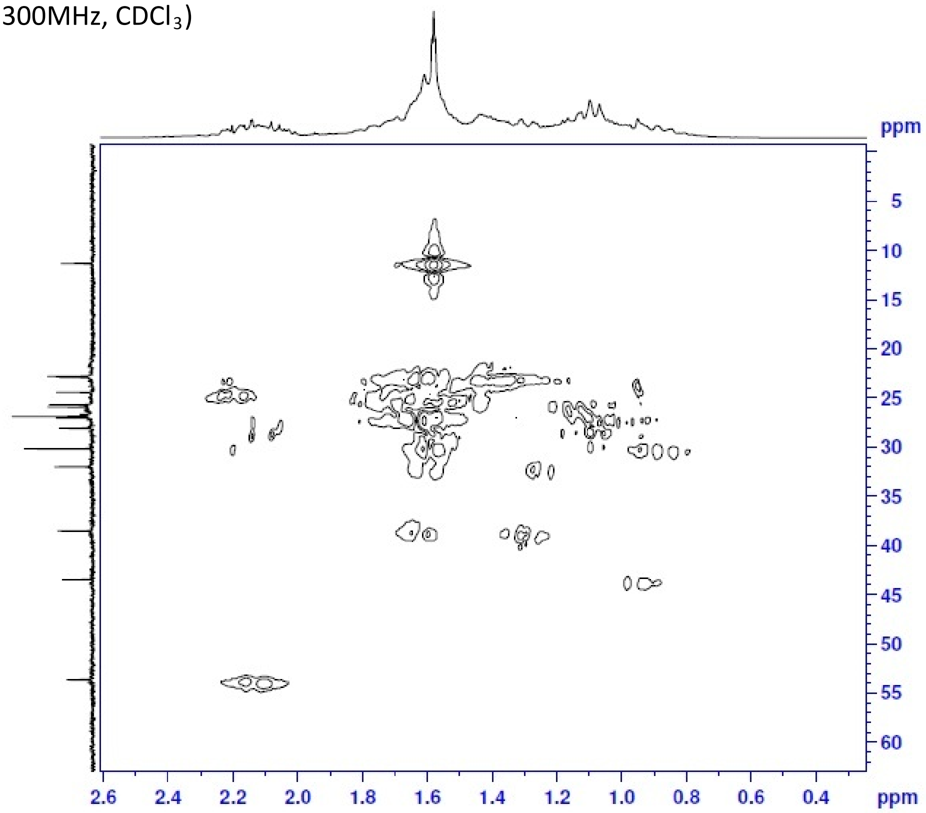


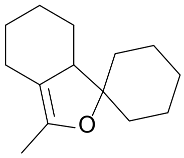
15

COSY (300MHz, $CDCl_3$)



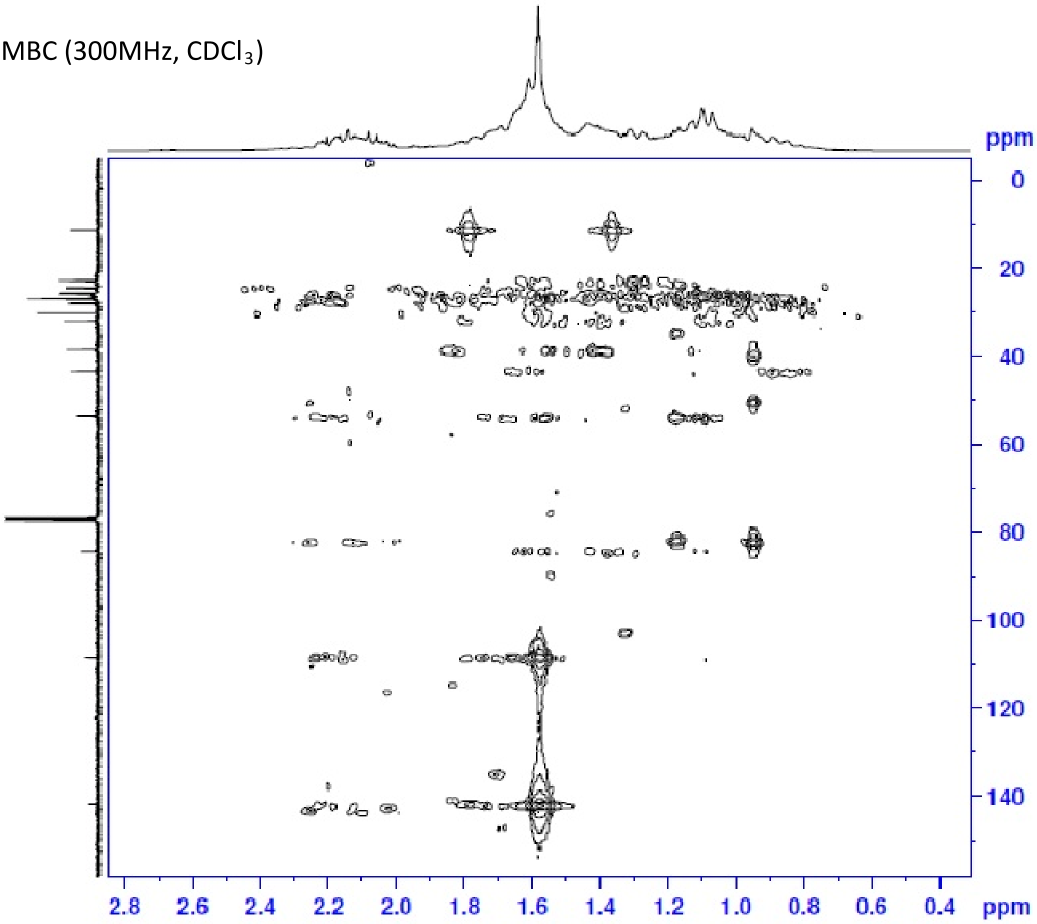
HMQC (300MHz, $CDCl_3$)



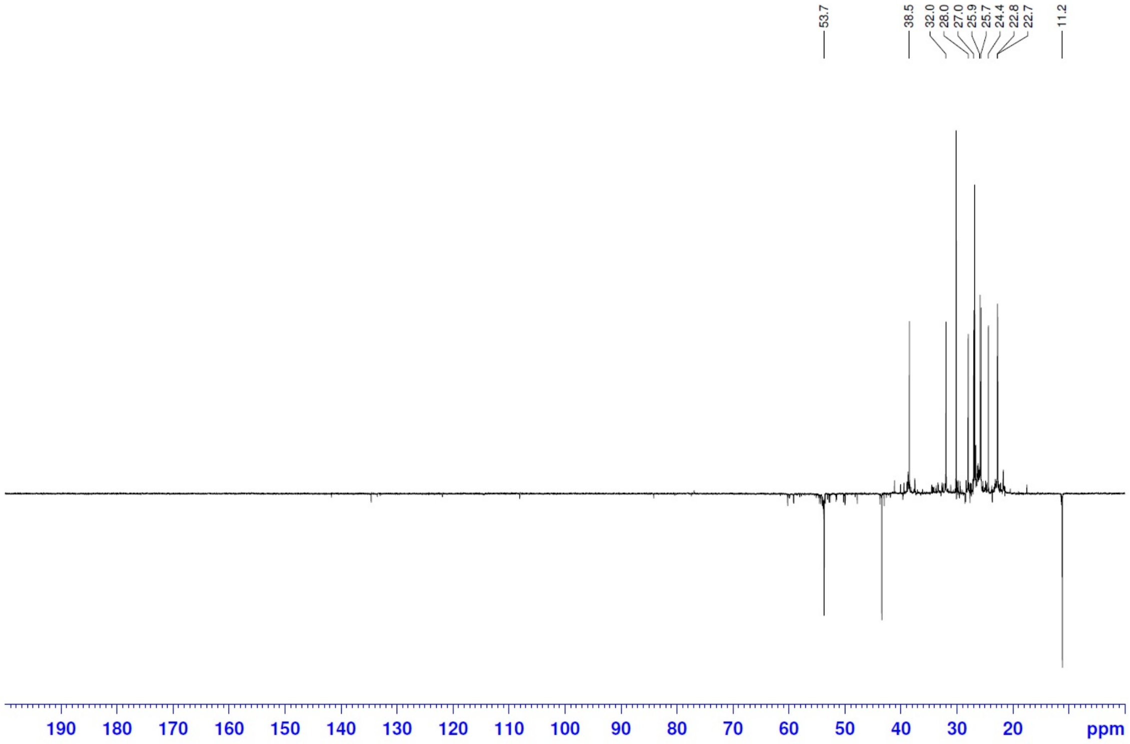


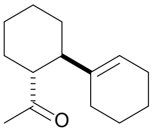
15

HMBC (300MHz, $CDCl_3$)



DEPT-135 (100MHz, $CDCl_3$)





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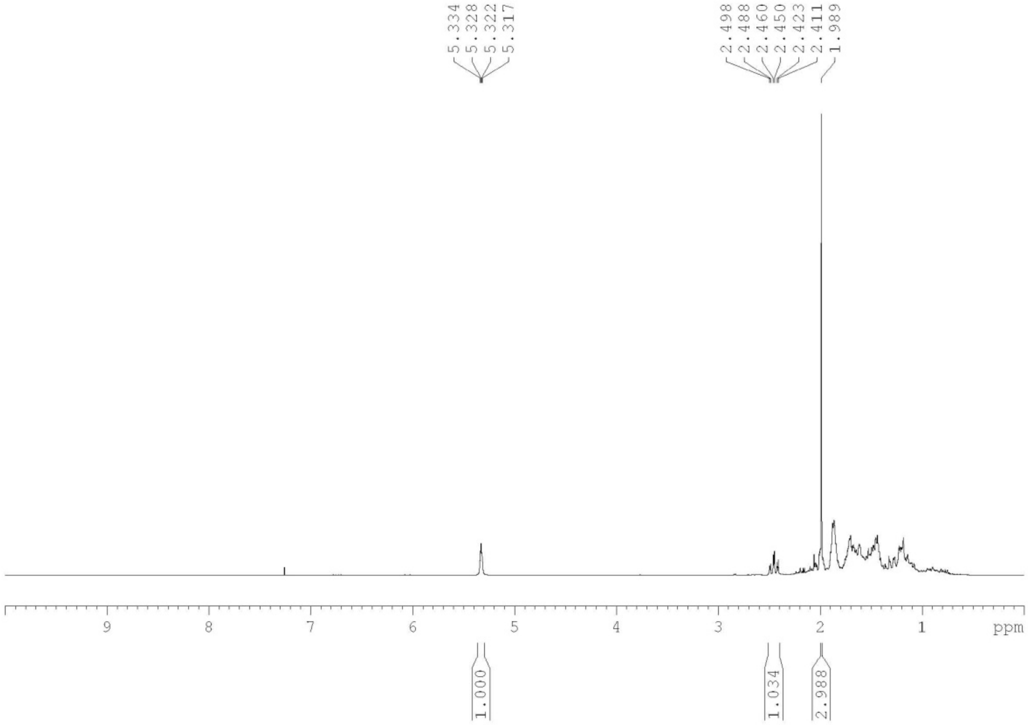
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4
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2
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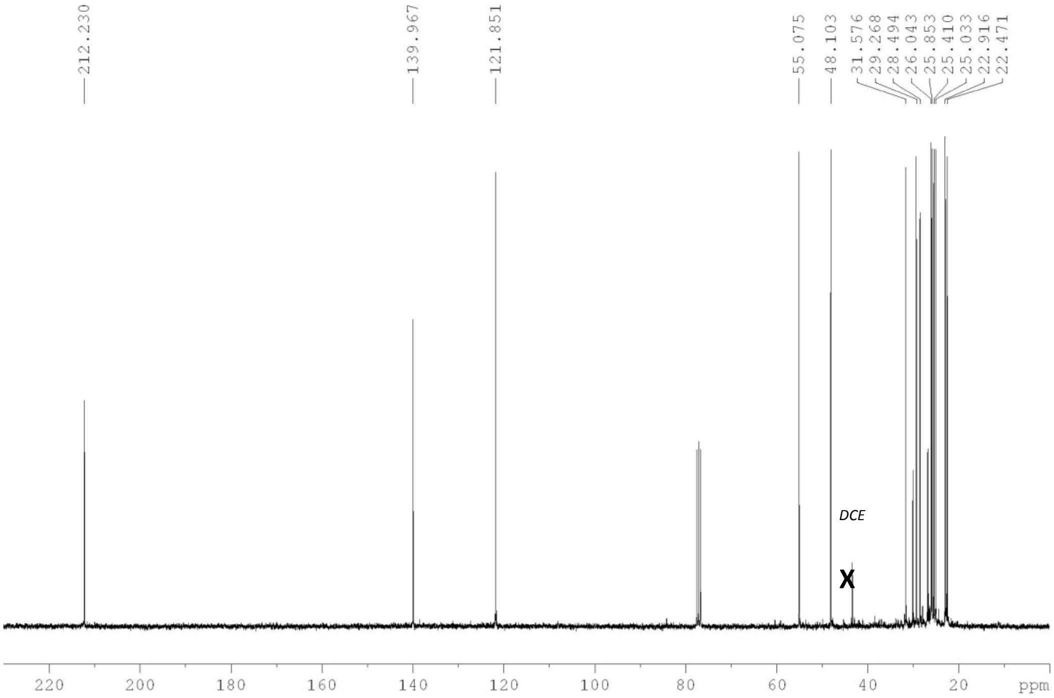
2.988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25.853
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22.471
DCE
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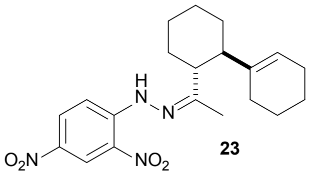
20
ppm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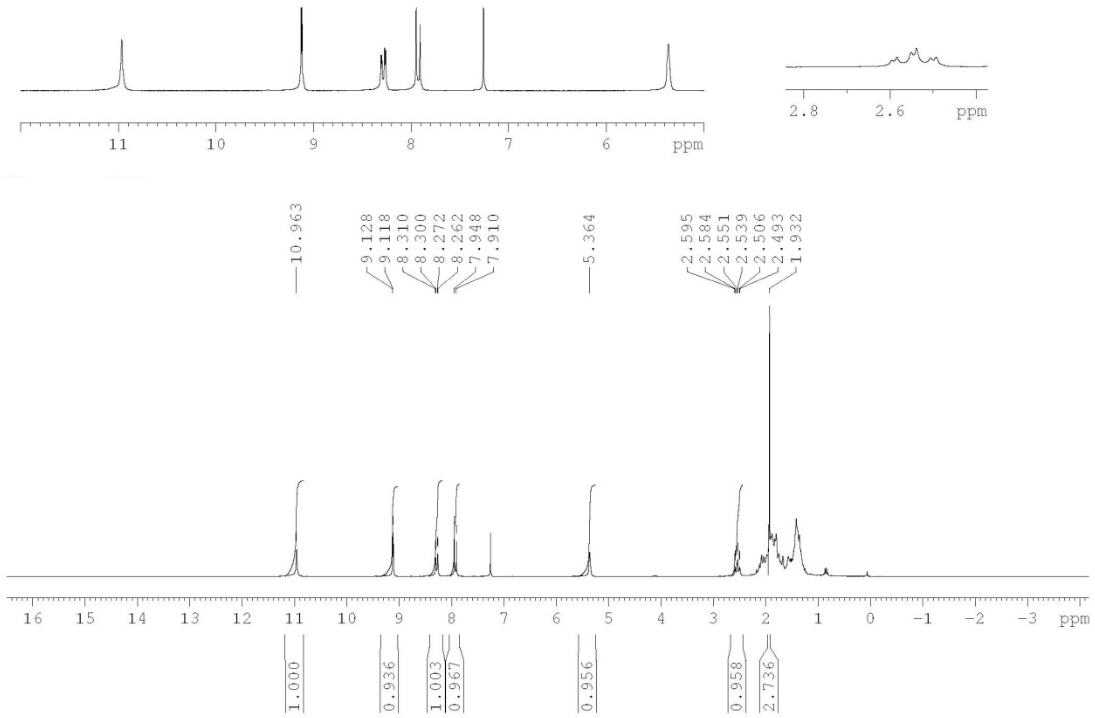
N
N
O2N
NO2

23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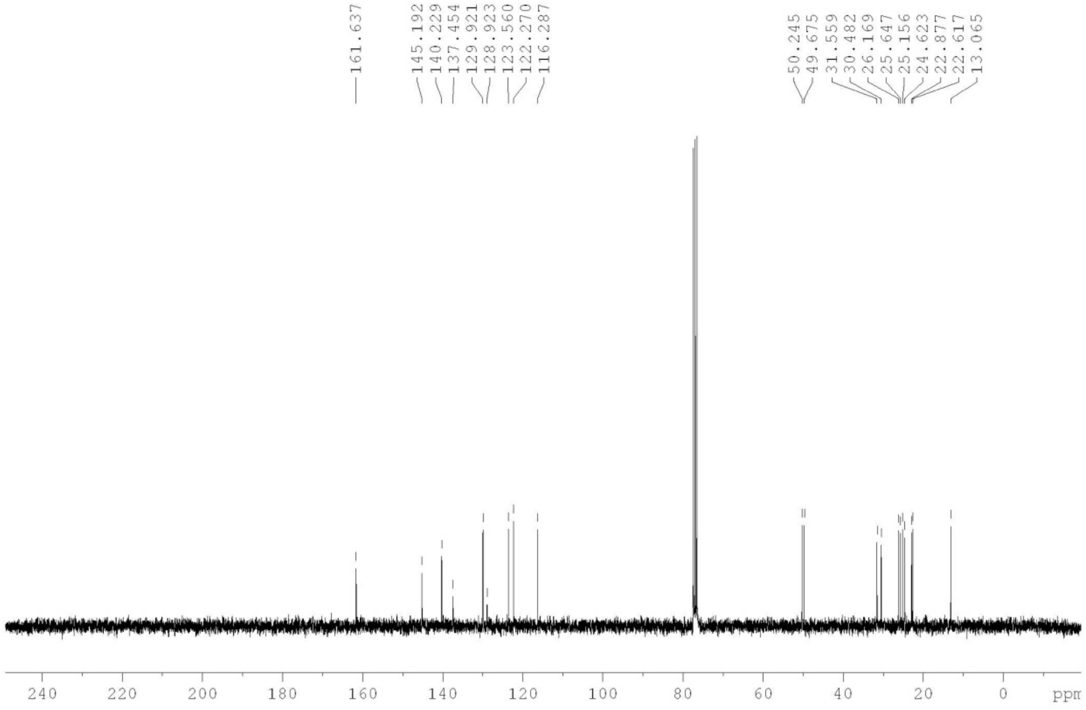
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30.482
26.169
25.647
25.156
24.623
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40
20
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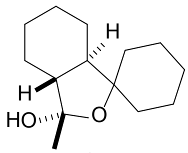
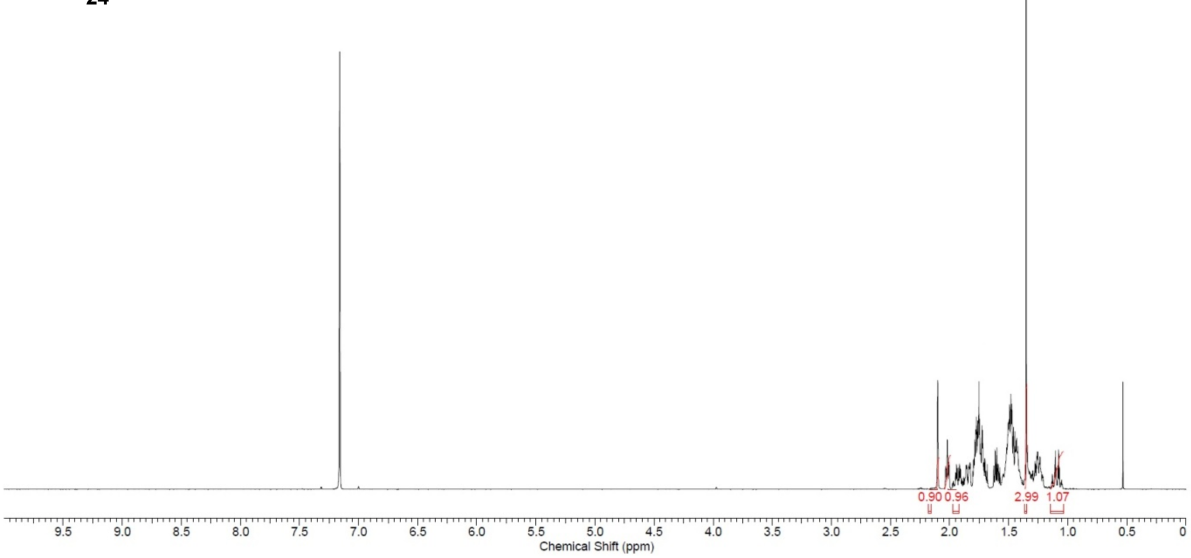
pp


H
H
HO
O

24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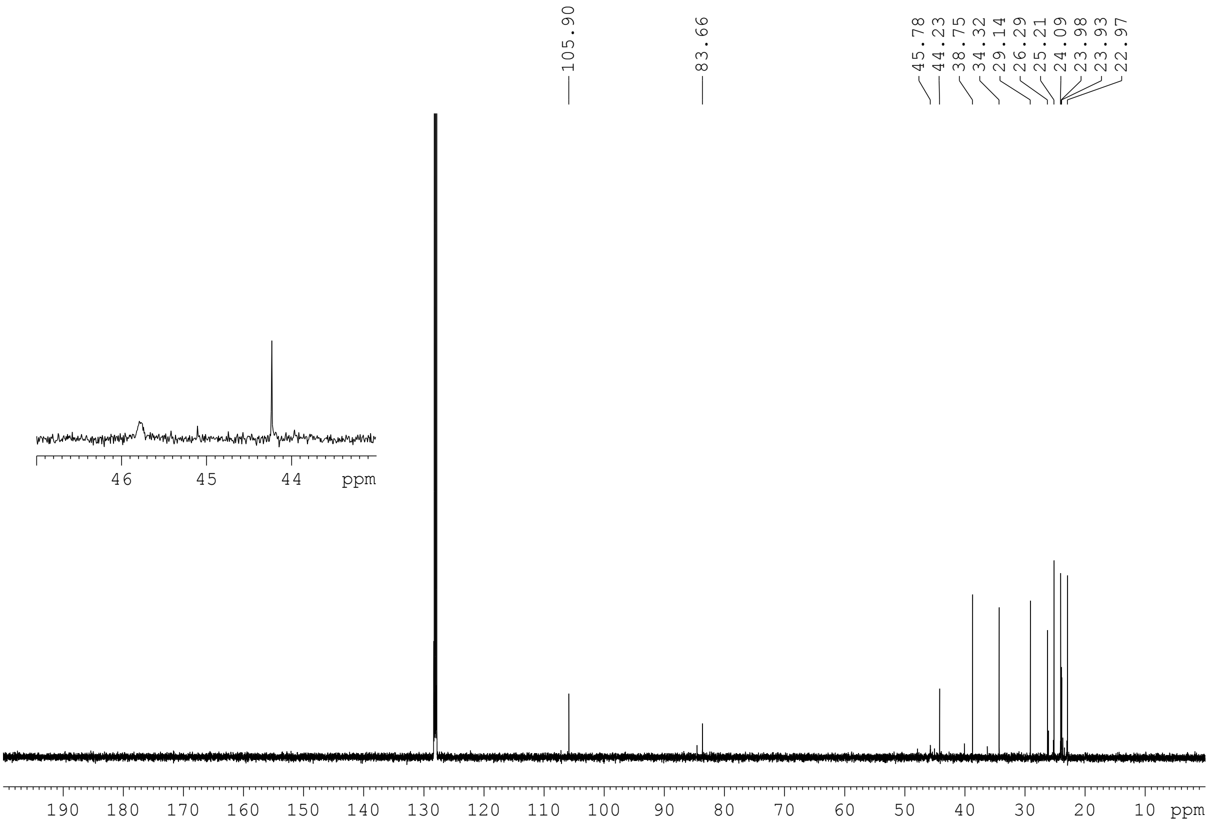
Chemical Shift (ppm)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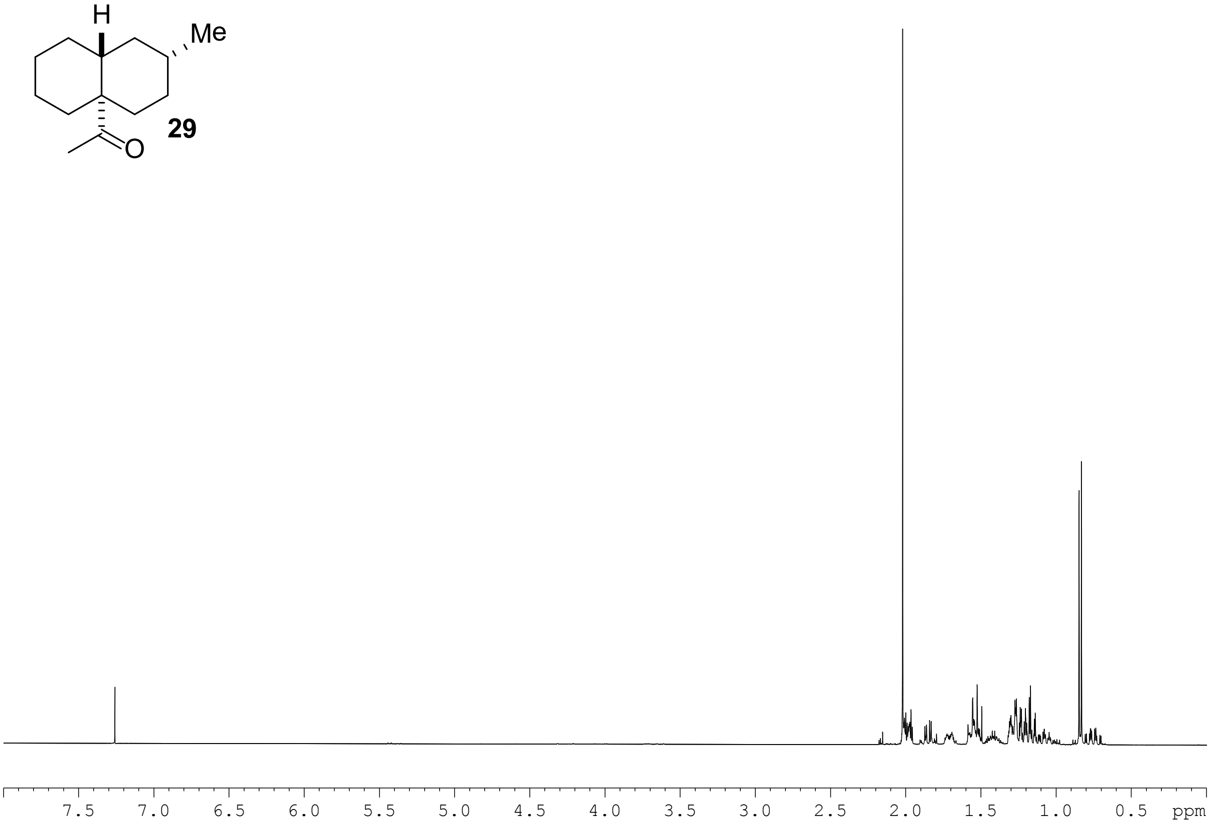
H
Me
O

29

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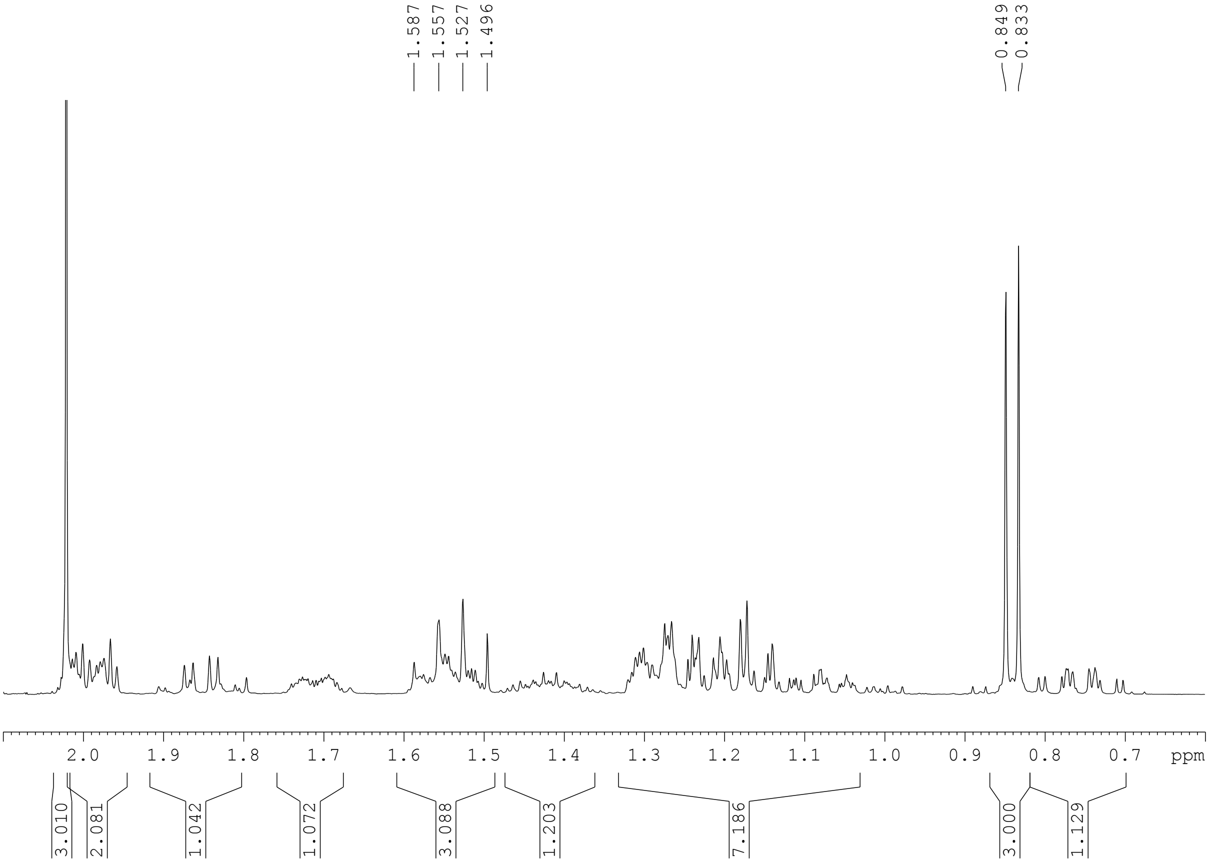
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1.3
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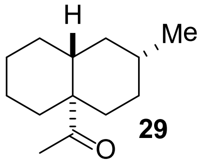
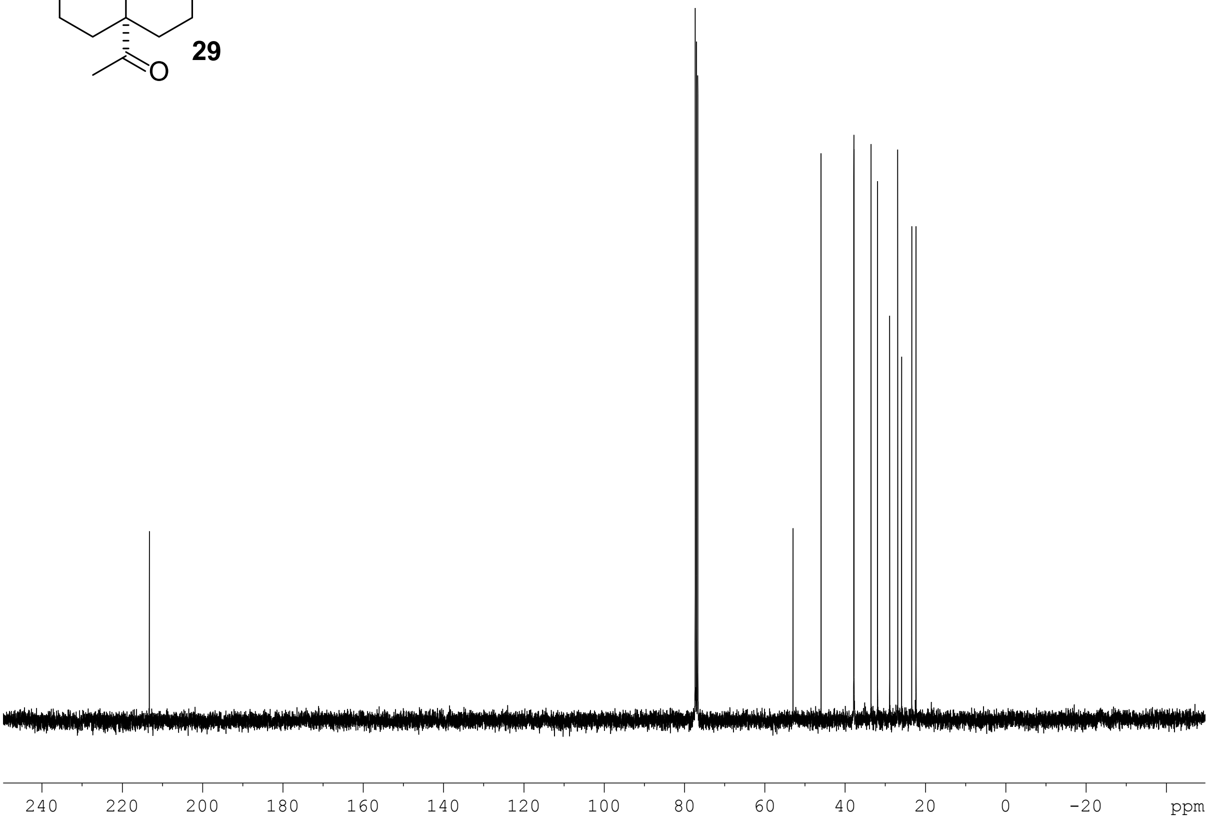
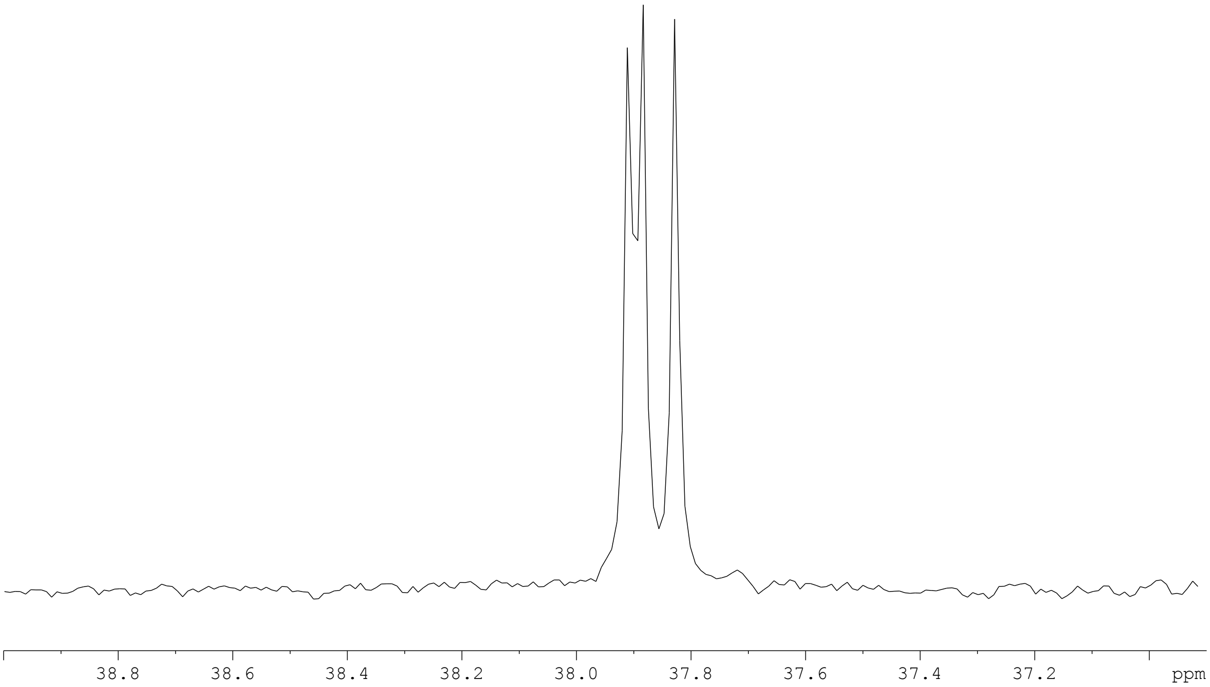
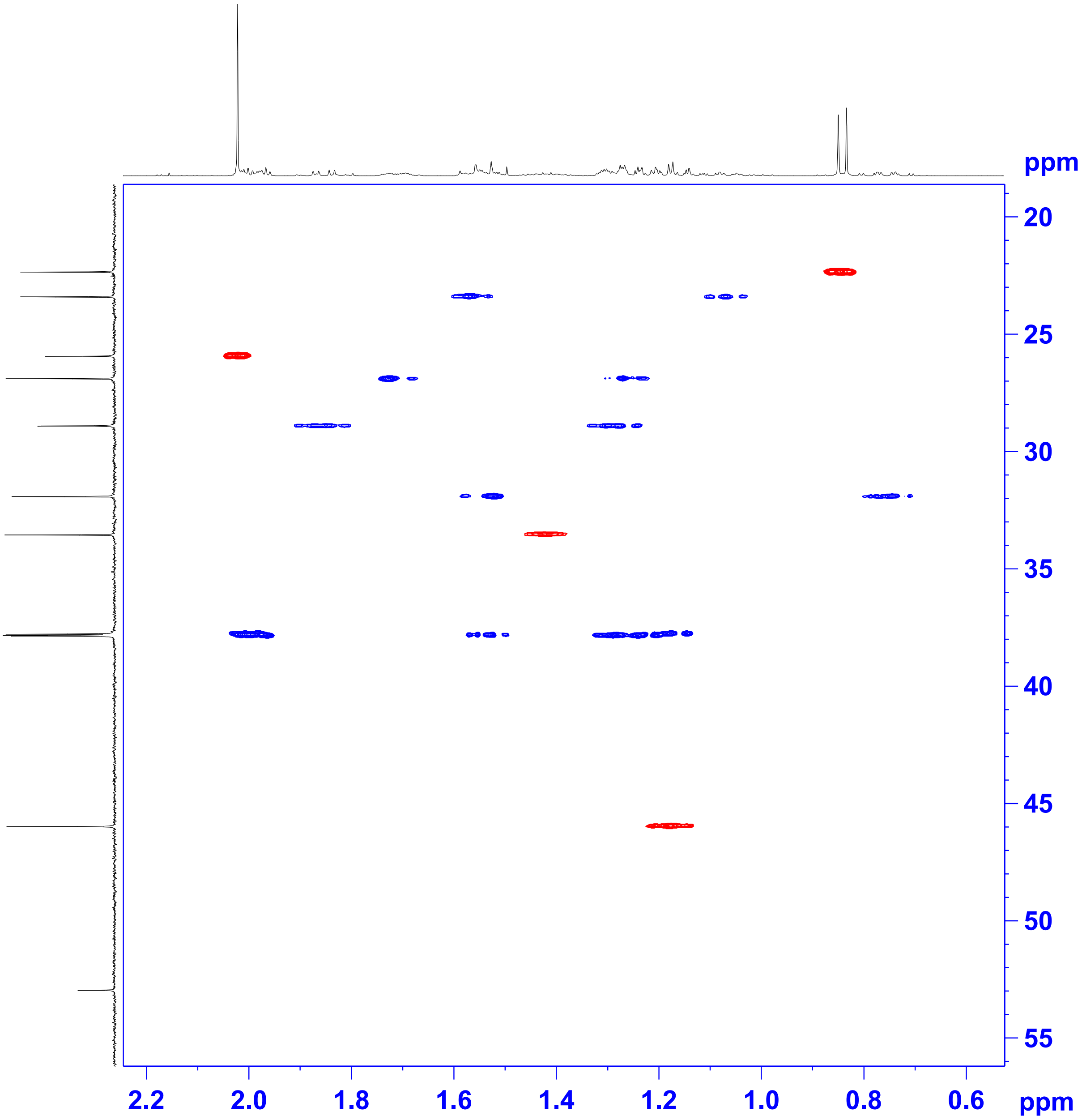

H
Me
O

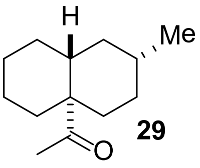
29


240
220
200
180
160
140
120
100
80
60
40
20
0
-20
ppm


38.8
38.6
38.4
38.2
38.0
37.8
37.6
37.4
37.2
ppm

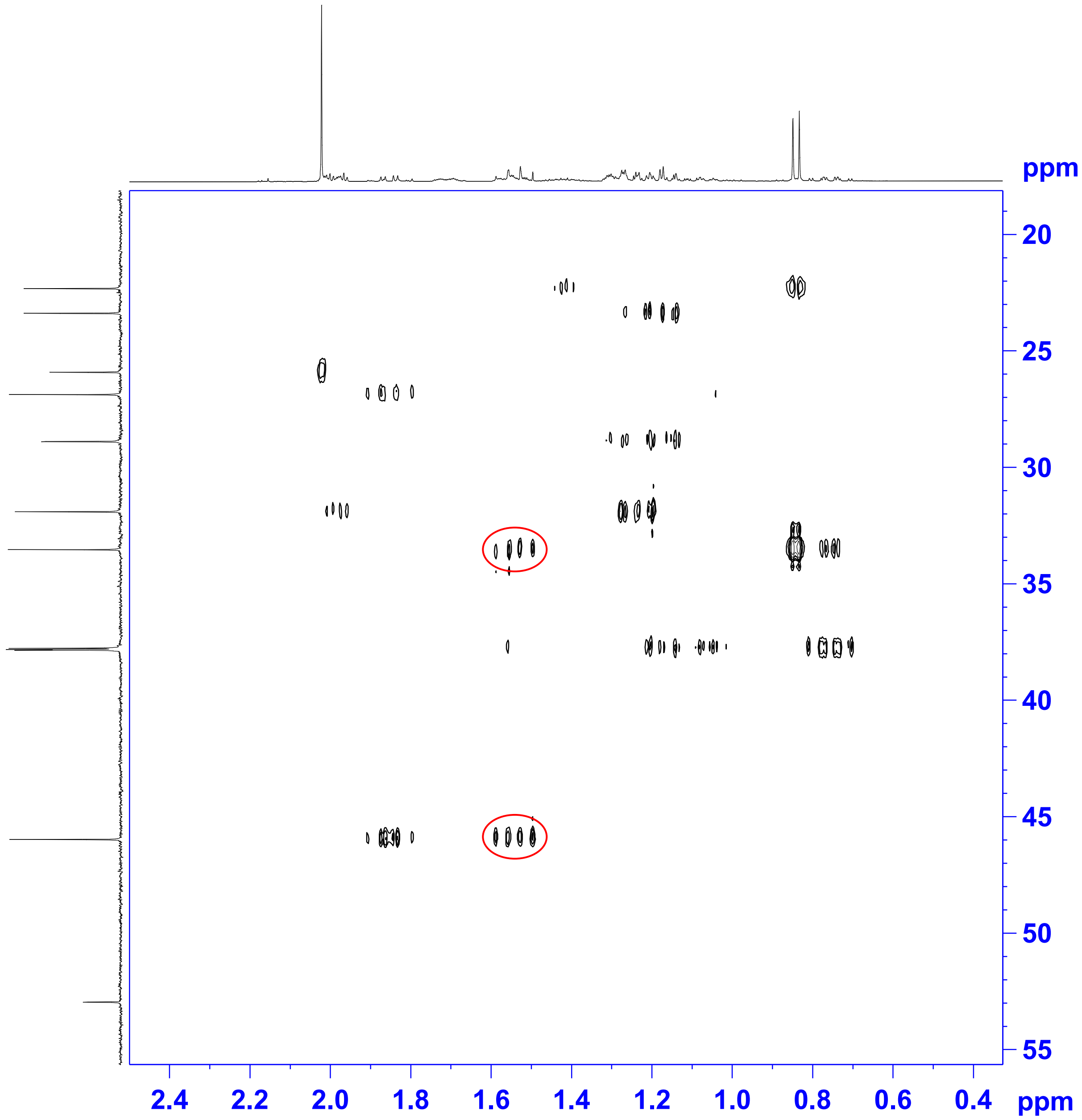
Multiplicity edited HSQC (400 MHz, $CDCl_3$): red = CH/CH_3; blue = CH_2

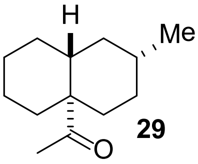




29

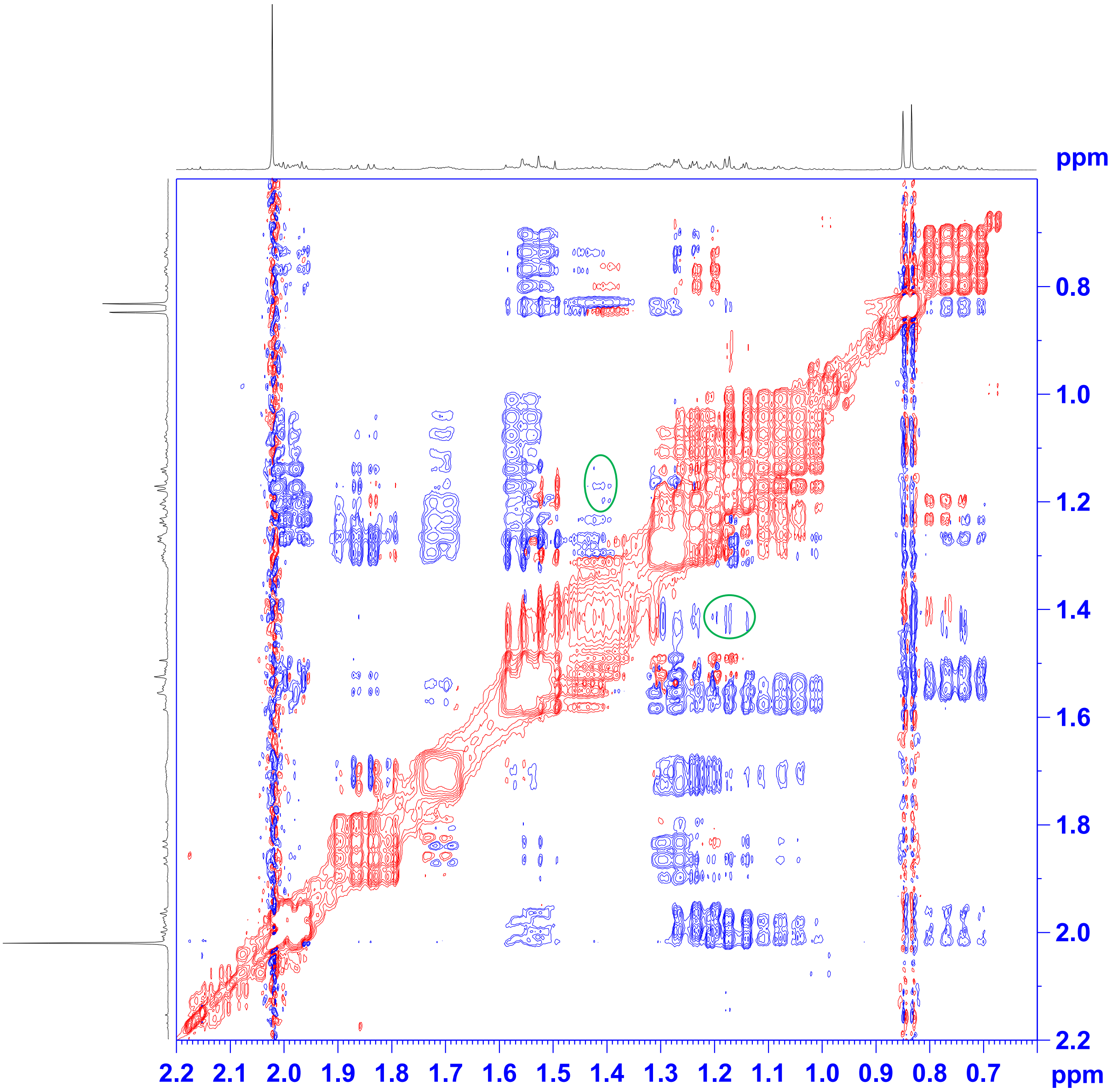
H2BC ($CDCl_3$, 400 MHz)

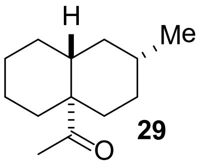




29

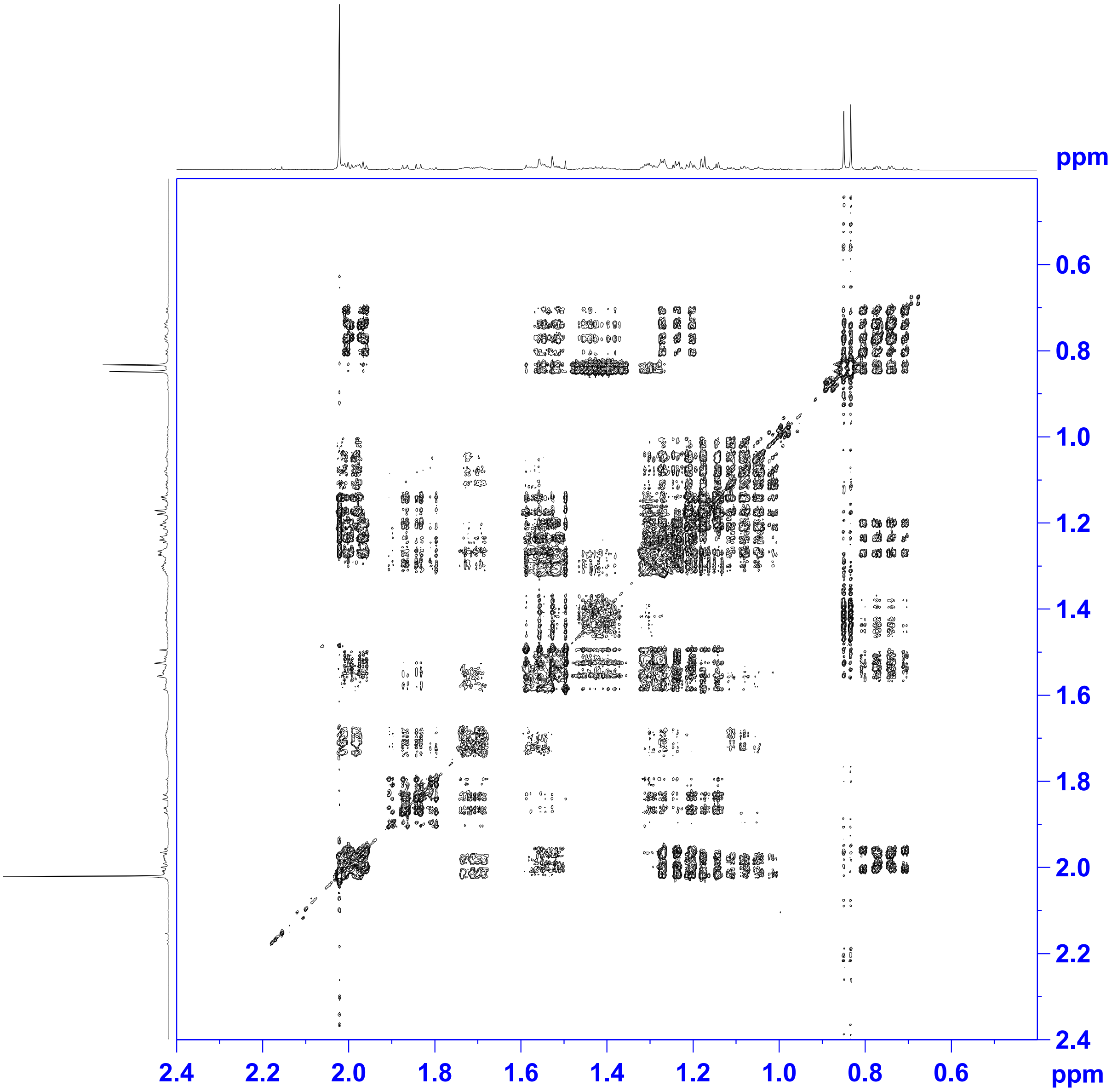
NOESY (400 MHz, $CDCl_3$)

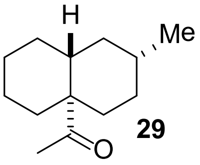




29

COSY (400 MHz, $CDCl_3$)





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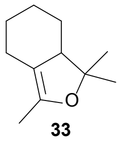
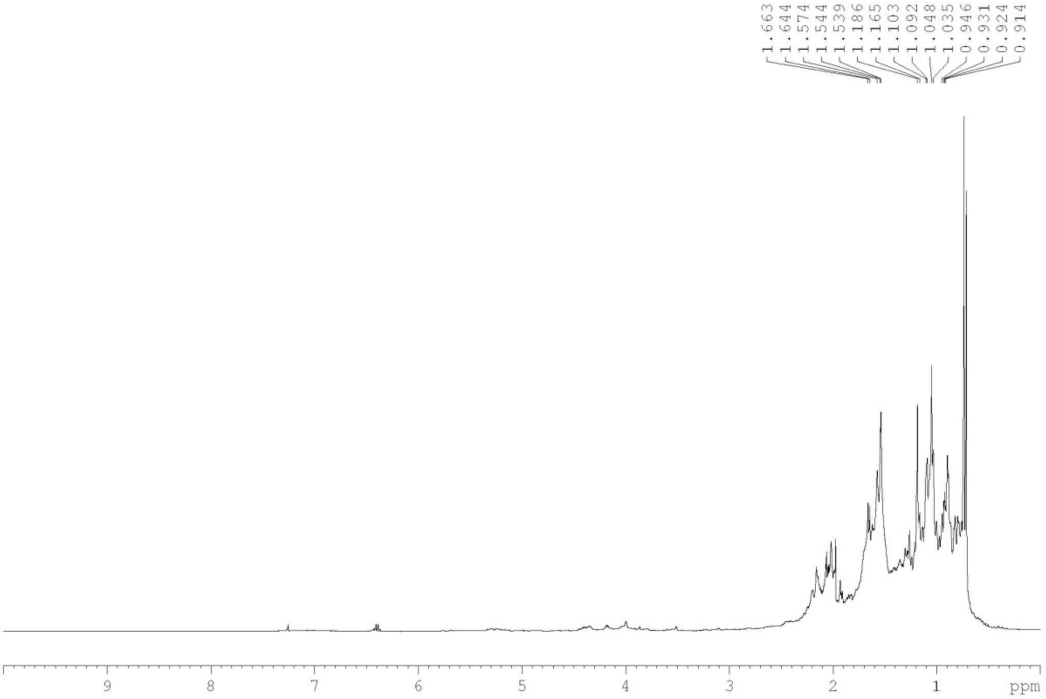
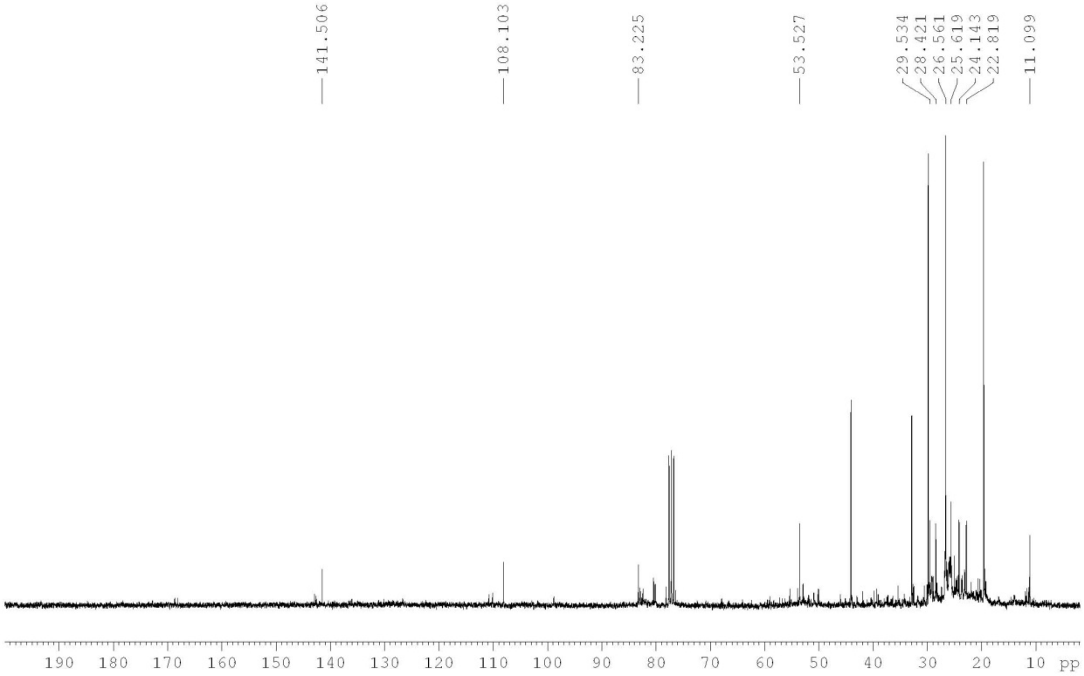
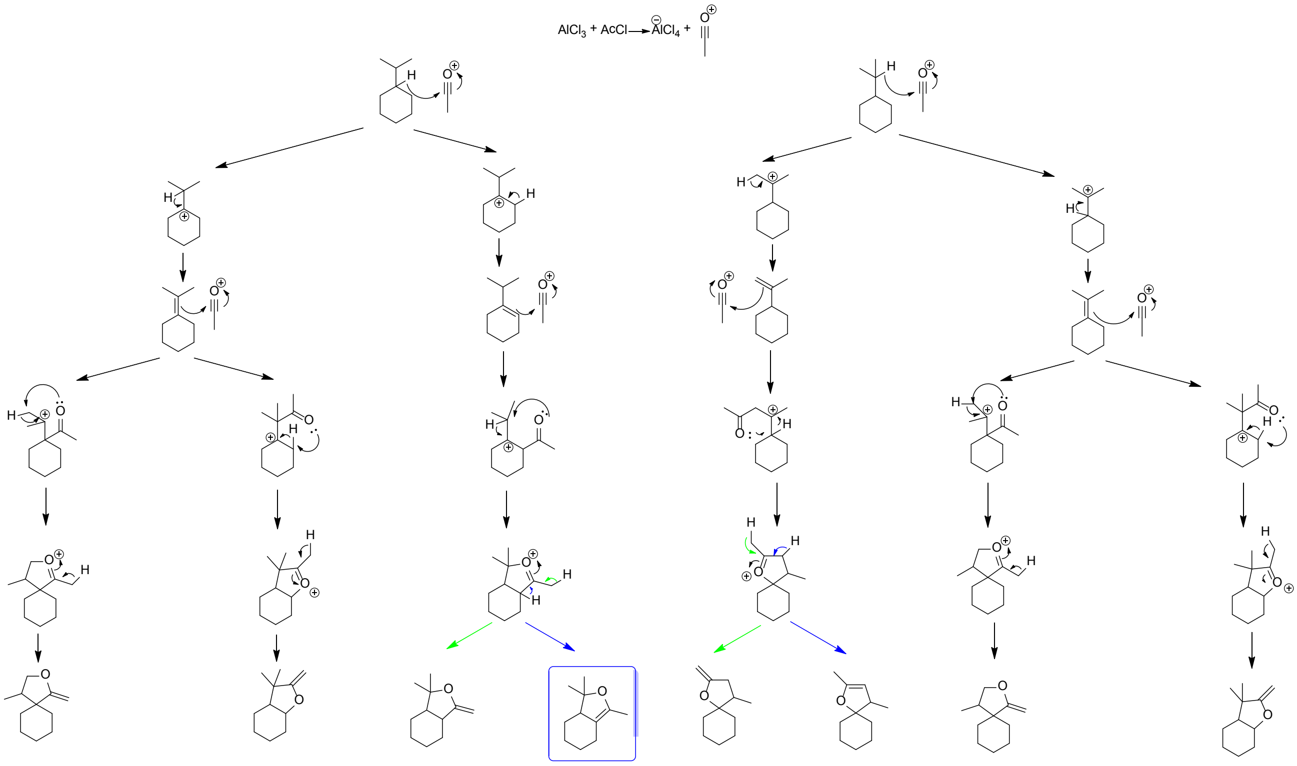


33

CRUDE
SPECTRA







Note: Only those pathways that involved tertiary carbocations were considered, both at the point of initial hydride abstraction and attack on the 2nd equivalent of acylium ion by the alkene.