An Efficient Construction of Polycyclic Derivatives *via* a High Selective Cu^{I} –Catalyzed Domino Reductive-Aldol Cyclization.

Julia Deschamp, Olivier Riant*

Unité de chimie organique et médicinale, Université catholique de Louvain

Place Louis Pasteur 1, B-1348 Louvain-la-Neuve (Belgium)

Supporting Information

A] General.

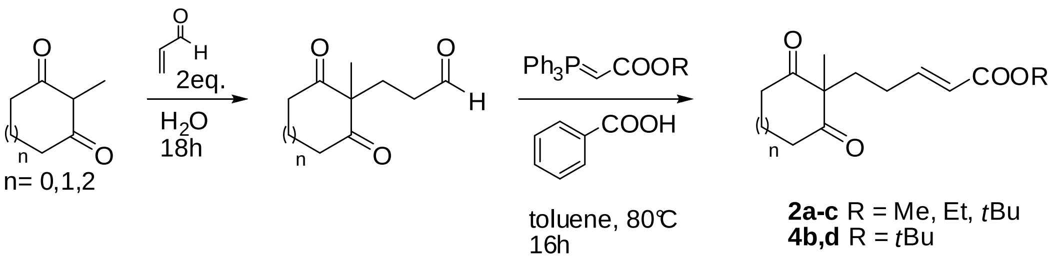
NMR spectra were recorded on Brucker spectrometers (300 MHz and 500 MHz for ^{1}H, 75 MHz and 125 MHz for ^{13}C). Chemical shifts are reported in δ ppm from tetramethylsilane with the solvent resonance as the internal standard for ^{1}H NMR and chloroform-*d* (δ 77.0 ppm) for ^{13}C NMR. Coupling constants (*J*) are given in hertz. Following abbreviations classify the multiplicity: s = singulet, d = doublet, t = triplet, q = quartet, m = mutiplet, br = broad signal. The attribution of the different protons was realized thanks to Jmod spectra, COSY and HMBC correlations. The mass spectra and the high-resolution mass spectra (HRMS) were obtained respectively from the mass-service at Université catholique de Louvain (Varian MAT-44 or FINNIGAN MAT TSQ 70 spectrometers) and at Université de Mons (Autospec 6F spectrometer). IR spectra were recorded on Shimadzu FTIR-8400S spectrometer. $[\alpha]_{\mathrm{D}}^{20}$ values were measured on a Perkin-Elmer 241 MC Polarimeter (concentration *c* are given in g/100mL). Analytical gas-chromatography was performed on a ThermoFinningan Trace GC using a CHIRALSIL-DEX CB (25 m, 0.25 mm, 25 µm).

B] Materials.

All reactions were carried out in a flame dried glassware under an inert atmosphere of argon. Toluene was distilled under argon over sodium. $CuF(PPh_3)_3.2MeOH$ was prepared according to the reported procedure (D. J. Gulliver, W. Levason, M. Webster, *Inorg. Chim. Acta* **1981**, *52*, 153. The following ligands were generously provided by Hoffmann-La Roche (BIPHEP) and Solvias (JosiPhos, WalPhos, MandyPhos, TaniaPhos).

C] Syntheses and characterizations of the precursors 2a-c and 4a-e.

The precursors **2a-c** and **4b,d**,[1, 2] the ylides[3] and the 2-methyl-1,3-cycloheptanedione[4, 5] were synthesized according to the reported literature procedure.

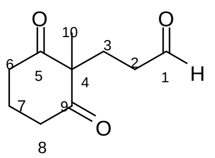


To a suspension of the 2-methyl-1,3-cycloalkanedione (50mmol) in water (125mL) was added acrolein (75mmol, 1.5eq). The mixture was stirred at room temperature for 18 hours. Then, water and the excess of acrolein were evaporated under reduced pressure. The wet solid obtained was stirred with dichloromethane (50mL). After 15 minutes, the slight suspension was filtered and the filtrate is dried on $MgSO_4$. After filtration, the solution was concentrated in vacuo to afford the corresponding 2-

methyl-2-propionaldehyde-1,3-cycloalcanedione (quantitative yields) of a sufficient purity for the next step.

The aldehyde (50mmol) and the appropriate Wittig reagent (75mmol) were warmed at 80°C in toluene (150mL) in presence of benzoic acid (50mmol) for 18 hours. The solution was successively washed with bicarbonate aqueous solution and brine. The organic solution was then dried on $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified via column chromatography (CH_2Cl_2/AcOEt: 98/2) and gave a colourless oil (75-96%).

3-(1-methyl-2,6-dioxocyclohexyl)propanal



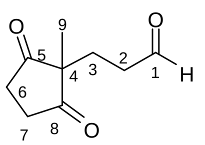
$C_{10}H_{14}O_3$
M = 182.22 g.mol^{-1}
RN = 552855-46-6
yellow oil
quantitative yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.30 (s, 3H, H_{10}) ; 1.97 (m, 2H, H_7) ; 2.12 (m, 2H, H_3) ; 2.36 (m, 2H, H_2) ; 2.69 (m, 4H, H_6 and H_8) ; 9.70 (s, 1H, H_1).

RMN ^{13}C (75MHz, $CDCl_3$) δ 17.5 (C_7) ; 21.5 (C_{10}) ; 27.2 (C_3) ; 37.8 (C_6 and C_8) ; 39.3 (C_2) ; 65.0 (C_4) ; 201.0 (C_1) ; 209.8 (C_5 and C_9).

MS (+CI) : $[M+H]^+$ = 183.0.

3-(1-methyl-2,5-dioxocyclopentyl)propanal



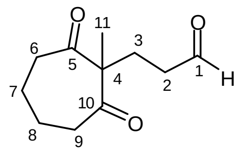
$C_9H_{12}O_3$
M = 168.19 g.mol^{-1}
RN = 66976-99-6
yellow oil
quantitative yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.12 (s, 3H, H_9) ; 1.92 (t, ^3J = *7.3Hz*, 2H, H_2) ; 2.47 (t, ^3J = *7.3 Hz*, 2H, H_3) ; 2.79 (m, 4H, H_6 and H_7) ; 9.66 (s, 1H, H_1).

RMN ^{13}C (75MHz, $CDCl_3$) δ 19.3 (C_9) ; 25.9 (C_3) ; 34.7 (C_6 and C_7) ; 39.3 (C_2) ; 55.1 (C_4) ; 200.7 (C_1) ; 215.6 (C=O).

MS (+CI) : $[M+H]^+$ = 169.0.

3-(1-methyl-2,7-dioxocycloheptyl)propanal



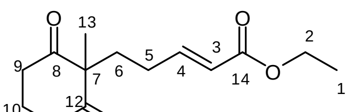
$C_{11}H_{16}O_3$
M = 196.24 g.mol^{-1}
yellow oil
quantitative yield

RMN ^{1}H (500MHz, CDCl$_3$) δ 1.18 (s, 3H, H_{11}) ; 1.86 (m, 4H, H_7 and H_8) ; 2.07 (t, $^3J_{H3-H2}$ = *7.1 Hz*, 2H, H_3) ; 2.36 (t, $^3J_{H2-H3}$ = *7.2 Hz*, 2H, H_2) ; 9.70 (s, 1H, H_1).

RMN ^{13}C (75MHz, CDCl$_3$) δ 17.7 (C_{11}) ; 25.2 (C_3) ; 27.9 (C_7 and C_8) ; 38.3 (C_2) ; 41.3 (C_6 and C_9) ; 63.3 (C_4) ; 200.6 (C_1) ; 212.6 (C_5 and C_{10}).

MS (+CI) : $[M+H]^+$ = 197.3.

Ethyl (*E*)-5-(1-methyl-2,6-dioxocyclohexyl)pent-2-enoate 2a



2a

$C_{14}H_{20}O_4$
M = 252.31 g.mol^{-1}
RN = 915285-97-1
pale yellow oil
90% yield

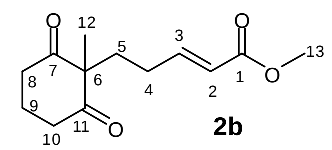
RMN ^{1}H (250MHz, CDCl$_3$) δ 1.28 (s, 3H, H_{13}) ; 1.28 (t, ^3J = *7.1 Hz*, 3H, H_1) ; 2.03 (m, 6H, H_5, H_6 and H_{10}) ; 2.66 (m, 4H, H_9 and H_{11}) ; 4.16 (q, ^3J = *7.1 Hz*, 2H, H_2) ; 5.80 (dt, $^3J_{H3-H4}$ = *15.8$_5$ Hz* and $^4J_{H3-H5}$ = *1.5 Hz*, 1H, H_3) ; 6.85 (dt, $^3J_{H4-H3}$ = *15.8$_5$ Hz* and $^3J_{H4-H5}$ = *6.3$_5$ Hz*, 1H, H_4).

RMN ^{13}C (62.5MHz, CDCl$_3$) δ 14.1 (C_{13}) ; 15.2 (C_9) ; 21.1 (C_1) ; 27.4 and 34.0 (C_4 and C_5) ; 37.9 (C_9 and C_{11}) ; 60.1 (C_2) ; 64.8 (C_7) ; 121.9 (C_3) ; 147.3 (C_4) ; 166.3 (C_{14}) ; 209.8 (C_8 and C_{12}).

MS (+CI) : $[M+H]^+$ = 253.0. HRMS (CI+) calcd for $C_{14}H_{21}O_4$: 253.1440 found 253.1442.

IR (film, cm^{-1}) ν 2925, 2854, 1706, 1460, 1256, 1134, 1099.

methyl (*E*)-5-(1-methyl-2,6-dioxocyclohexyl)pent-2-enoate 2b[6]



2b

$C_{13}H_{18}O_4$
M = 238.12 g.mol^{-1}
pale yellow oil
90% yield

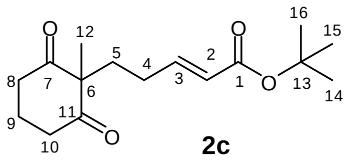
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.28 (s, 3H, H_{12}) ; 1.96 (m, 6H, H_4, H_5) ; 2.68 (m, 4H, H_8 and H_{10}) ; 3.72 (s, 3H, H_{13}) ; 5.82 (dt, $^3J_{H2-H3}$ = *15.6 Hz* and $^4J_{H2-H4}$ = *1.5 Hz*, 1H, H_2) ; 6.87 (dt, $^3J_{H3-H2}$ = *15.6$_5$ Hz* and $^3J_{H3-H4}$ = *6.5 Hz*, 1H, H_3).

RMN ^{13}C (75MHz, CDCl$_3$) δ 17.5 (C_9); 21.3 (C_{12}); 27.5 (C_4) ; 34.0 (C_5) ; 37.9 (C_8 and C_{10}) ; 51.5 (C_{13}) ; 64.8 (C_6) ; 121.5 (C_2) ; 147.7 (C_3) ; 166.8 (C_1) ; 209.9 (C_7 and C_{11}).

MS (+CI) : $[M+H]^+$ = 239.2.

IR (film, cm^{-1}) ν 2925, 2854, 1706, 1460, 1256, 1134, 1099.

***tert*butyl (*E*)-5-(1-méthyl-2,6-dioxocyclohexyl)pent-2-enoate 2c**



2c

$C_{16}H_{24}O_4$
M = 280.36 g.mol^{-1}
pale yellow oil
96% yield

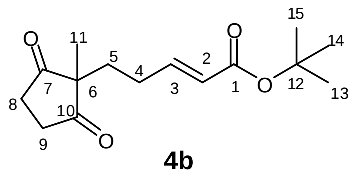
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.27 (s, 3H, H_{12}) ; 1.46 (s, 9H, H_{14}, H_{15} and H_{16}) ; 1.95 (m, 6H, H_4, H_5 and H_9) ; 2.67 (m, 4H, H_8 and H_{10}) ; 5.68 (dt, $^3J_{H2\text{-}H3}$ = *15.6 Hz* and $^4J_{H2\text{-}H4}$ = *1.5 Hz*, 1H, H_2) ; 6.75 (dt, , $^3J_{H3\text{-}H2}$ = *15.6 Hz* et $^3J_{H3\text{-}H4}$ = *6.4 Hz*, 1H, H_3).

RMN ^{13}C (75 MHz, CDCl$_3$) δ 17.5 (C_9) ; 20.8 (C_{12}) ; 27.3 et 34.4 (C_4 et C_5) ; 28.1 (C_{14}. C_{15} et C_{16}) ; 37.9 (C_8 et C_{10}) ; 64.9 (C_6) ; 80.3 (C_{13}) ; 123.7 (C_2) ; 146.0 (C_3) ; 165.7 (C_1) ; 209.8 (C_7 et C_{11}).

MS (+CI) : $[M+H]^+$ = 281.4. HRMS (CI+) calcd for $C_{16}H_{25}O_4$: 281.1753 found 281.1746.

IR (film, cm^{-1}) ν 2975, 2933, 1726, 1650, 1319, 1284, 1255, 1155.

***tert*butyl (*E*)-5-(1-methyl-2,5-dioxocyclopentyl)pent-2-enoate 4b**



4b

$C_{15}H_{22}O_4$
M = 266.34 g.mol^{-1}
pale yellow oil
93% yield

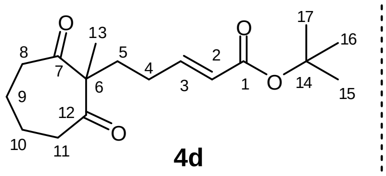
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.12 (s, 3H, H_{11}) ; 1.45 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.78 and 2.03 (2 × m, 2 × 2H, H_4 and H_5) ; 2.76 (m, 4H, H_8 and H_9) ; 5,67 (dt, $^3J_{H2\text{-}H3}$ = *15.6Hz* and $^4J_{H2\text{-}H4}$ = *1.5Hz*, 1H, H_2) ; 6.67 (dt, $^3J_{H3\text{-}H2}$ = *15,6Hz* and $^3J_{H3\text{-}H4}$ = *6.9Hz*, 1H, H_3).

RMN ^{13}C (75 MHz, CDCl$_3$) δ 19.8 (C_{11}) ; 27.1 and 32.9 (C_4 and C_5) ; 28.1 (C_{13}. C_{14} and C_{15}) ; 35.0 (C_8 and C_9) ; 56.1 (C_6) ; 80.3 (C_{12}) ; 124.1 (C_2) ; 145.6 (C_3) ; 165.5 (C_1) ; 215.8 (C_7 and C_{10}).

MS (+CI) : $[M+H]^+$ = 267.4. HRMS (CI+) calcd for $C_{15}H_{23}O_4$: 267.1596 found 267.1593.

IR (film, cm^{-1}) ν 2977, 2931, 1766, 1716, 1652, 1454, 1367, 1288, 1255, 1157.

_tert_butyl _(E)_-5-(1-methyl-2,7-dioxocycloheptyl)pent-2-enoate 4d



$C_{17}H_{26}O_4$
M = 294.39 g.mol^{-1}
pale yellow oil
80% yield

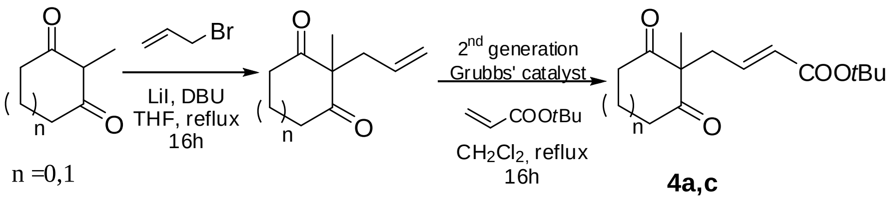
RMN ^{1}H (300 MHz, $CDCl_3$) δ 1.22 (s, 3H, H_{13}) ; 1.48 (s, 9H, H_{15}, H_{16} and H_{17}) ; 1.89 (m, 8H, H_4, H_5, H_9 and H_{10}) ; 2.45 (m, 4H, H_8 and H_{11}) ; 5.77 (dt, $^{3}J_{H2\text{-}H3} = 15.6Hz$ and $^{4}J_{H2\text{-}H4} = 1.5Hz$, 1H, H_2) ; 6.77 (dt, $^{3}J_{H3\text{-}H2} = 15.6Hz$ and $^{3}J_{H3\text{-}H4} = 6.4Hz$, 1H, H_3).

RMN ^{13}C (75 MHz. $CDCl_3$) δ 17.9 (C_{13}) ; 26.4 (C_9 and C_{10}) ; 28.0 (C_5) ; 28.3 (C_{15}. C_{16} and C_{17}); 32.0 (C_4); 41.4 (C_8 and C_{11}); 64.1 (C_6); 80.3 (C_{14}); 123.8 (C_2); 146.3 (C_3); 165.9 (C_1); 212.4 (C_7 and C_{12}).

MS (+CI) : $[M+H]^+$ = 281.4. HRMS (CI+) calcd for $C_{17}H_{27}O_4$: 295.1909 found 295.1909.

IR (film, cm^{-1}) ν 2978, 2930, 1765, 1715, 1653, 1454, 1367, 1289, 1255, 1157.

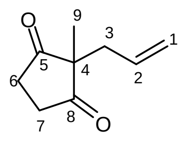
The precursors **4a,c** were synthesized according to the literature procedure.[7-9]



To a solution of 2-methyl-1,3-cycloalkanedione (10mmol) in THF (30mL) were successively added lithium iodide (11mmol, 1.1eq.) and DBU (11mmol, 1.1eq.). After several minutes, a white precipitate was formed. After stirring for 30 minutes, allyl bromide (20mmol, 2eq.) was added to the suspension, and then the mixture was refluxed for 11 hours. After cooling at room temperature, the mixture was poured on ice-water and was extracted with ethyl acetate (4×5mL). The combined organic phase were successively washed with water, a aqueous sodium thiosulfate solution (5%) and brine, then was dried on $MgSO_4$ and evaporated under reduced pressure. The residue was purified by column chromatography (cyclohexane/AcOEt: 70/30) and led to a colourless oil.

To a solution of Grubbs' second generation metathesis catalyst (0.01mmol, 1mol%) in distilled dichloromethane (2mL) was added under argon a solution of the pure 2-allyl-2-methyl-1,3-cycloalkanedione (1mmol) and tertbutyl acrylate (4mmol, 4eq.) in distilled dichloromethane (4mL). the solution was refluxed under argon for 16 hours. After reducing the solution to 1mL, the residue was purified by column chromatography (CH_2Cl_2/MeOH: 98/2) and afforded a pale yellow oil in good yields.

2-allyl-2-methyl-cyclopentane-1,3-dione



$C_9H_{12}O_2$
M = 152.19 g.mol^{-1}
RN =26828-48-8
colourless oil
65% yield

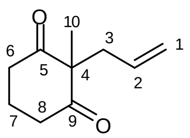
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.27 (s, 3H, H_9) ; 2.35 (t, ^3J = *7.5Hz*, 2H, H_3) ; 2.72 (m, 4H, H_6 and H_7) ; 5.06 (m, 2H, H_1) ; 5.58 (ddt, $^3J_{transH2\text{-}H1a}$ = *15.6Hz*, $^3J_{cisH2\text{-}H1b}$ = *9.0Hz*, $^3J_{H2\text{-}H3}$ = *7.5Hz*, 1H, H_2).

RMN ^{13}C (75MHz, CDCl$_3$) δ 18.8 (C_9) ; 35.4 (C_6 and C_7) ; 40.0 (C_3) ; 56.7 (C_4) ; 119.8 (C_1) ; 131.4 (C_2) ; 216.2 (C_5 and C_8).

MS (+CI) : [M+H]$^+$ = 153.4.

IR (film, cm^{-1}) ν 3078, 2975, 1718, 1685, 1450.

2-allyl-2-methyl-cyclohexane-1,3-dione



$C_{10}H_{14}O_2$
M = 166.22 g.mol^{-1}
RN = 31929-07-4
colourless oil
75% yield

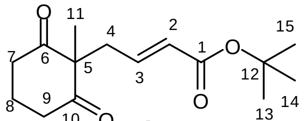
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.24 (s, 3H, H_{10}) ; 1.96 (m, 2H, H_7) ; 2.53 (d, $^3J_{H3\text{-}H2}$ = *7.3Hz*, 2H, H_3); 2.64 (m, 4H, H_6 et H_8) ; 5.03 (m, 2H, H_1) ; 5.56 (ddt, $^3J_{transH2\text{-}H1a}$ = *17.3Hz*, $^3J_{cisH2\text{-}H1b}$ = *9.7Hz*, $^3J_{H2\text{-}H3}$ = *7.3Hz*, 1H, H_2).

RMN ^{13}C (62.5MHz, CDCl$_3$) δ 14.3 (C_7) ; 19.6 (C_{10}) ; 27. 2 (CH_2) ; 38.0 (C_6 and C_8) ; 41.3 (C_3) ; 65.3 (C_4) ; 119.2 (C_1) ; 132.3 (C_2) ; 209.9 (C_5 and C_9).

MS (APCI) : [M+H]$^+$ = 167.4.

IR (film, cm^{-1}) ν 3082, 2973, 1722, 1695, 1460.

*tert*butyl (*E*) 4-(1-methyl-2,6-dioxycyclohexyl)but-2-enoate 4a



4a

$C_{15}H_{22}O_4$
M = 266.33 g.mol^{-1}
pale yellow oil
97% yield

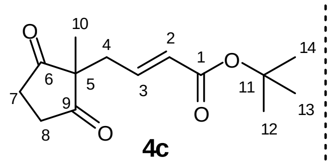
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.30 (s, 3H, H_{11}) ; 1.44 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.94 (m, 2H, H_8) ; 2.64 (m, 6H, H_4, H_7 and H_9) ; 5.73 (dt, $^3J_{H2\text{-}H3}$ = *15.5Hz* and $^4J_{H2\text{-}H4}$ = *1.3Hz*, 1H, H_2) ; 6.56 (dt, $^3J_{H3\text{-}H2}$ = *15.5Hz* and $^3J_{H3\text{-}H4}$ = *7.7Hz*, 1H, H_3).

RMN ^{13}C (75MHz, CDCl$_3$) δ 17.3 (C$_8$) ; 22.2 (C$_{11}$) ; 28.1 (C$_{13}$. C$_{14}$ and C$_{15}$) ; 37.4 (C$_4$) ; 38.0 (C$_7$ and C$_9$); 64.5 (C$_6$) ; 80.4 (C$_{12}$) ; 126.8 (C$_2$) ; 141.4 (C$_3$) ; 165.3 (C$_1$) ; 209.2 (C$_6$ and C$_{10}$).

MS (+CI) : [M+H]$^+$ = 267.3. HRMS (CI+) calcd for $C_{15}H_{23}O_4$: 267.1596 found 267.1597.

IR (film, cm^{-1}) ν 2975, 2935, 1708, 1652, 1367, 1367, 1255, 1155.

***tert*butyl (*E*) 4-(1-methyl-2,5-dioxycyclopentyl)but-2-enoate 4c**



$C_{14}H_{20}O_4$
M = 252.21 g.mol^{-1}
pale yellow oil
93% yield

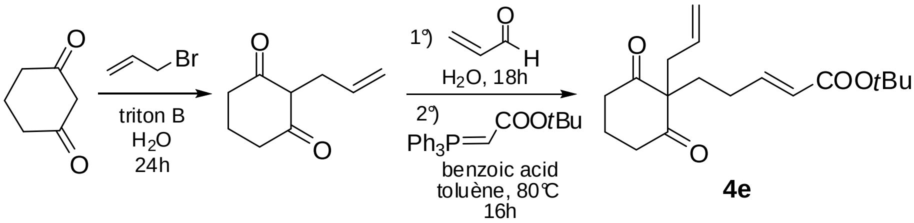
RMN ^{1}H (300MHz, CDCl$_3$) δ 1.15 (s, 3H, H$_{10}$) ; 1.44 (s, 9H, H$_{12}$, H$_{13}$ and H$_{14}$) ; 2.45 (dd, $^3J_{H4\text{-}H3}$ = *.7Hz* and $^4J_{H4\text{-}H2}$ = *1.3Hz*, 2H, H$_4$) ; 2.78 (m, 4H, H$_7$ and H$_8$) ; 5.72 (dt, $^3J_{H2\text{-}H3}$ = *15,5Hz* and $^4J_{H2\text{-}H4}$ = *1.3Hz*, 1H, H$_2$) ; 6.56 (dt, $^3J_{H3\text{-}H2}$ = *15.5Hz* and $^3J_{H3\text{-}H4}$ = *7.8Hz*, 1H, H$_3$).

RMN ^{13}C (75MHz, CDCl$_3$) δ 19.8 (C$_{10}$) ; 28.1 (C$_{13}$. C$_{14}$ and C$_{15}$) ; 35.1 (C$_7$ and C$_8$) ; 36.9 (C$_4$) ; 56.1 (C$_5$) ; 80.6 (C$_{11}$) ; 127.5 (C$_2$) ; 139.7 (C$_3$) ; 165.6 (C$_1$) ; 215.2 (C$_6$ and C$_9$).

MS (+CI) : [M+H]$^+$ = 253.3. HRMS (CI+) calcd for $C_{14}H_{20}O_4$: 253.1017 found 253.1099.

IR (film, cm^{-1}) ν 2970, 2931, 1716, 1655, 1365, 1218, 1159.

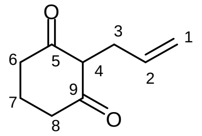
The precursor **4e** was prepared according to the literature procedure.[1, 2, 10]



To a solution of 1,3-cyclohexanedione (50mmol) in water (25mL) were added at room temperature a solution of benzyltriethylammonium hydroxide in methanol (Triton B, 40% w/w, 50mmol, 1eq.) followed by allyl bromide (60mmol, 1.2eq.). After stirring for 16 hours at room temperature, the mixture was filtrated and the filtrate was extracted with dichloromethane (3×20mL). the combined organic phases were washed with brine (2×20mL), dried on $MgSO_4$ and concentrated in vacuo. The residue was treated by an aqueous sodium hydroxide (0.5M, 10mL) and then washed with diethyl ether (3×10mL). An aqueous chlorhydric acid (0.5M, 10mL) was added until a neutral pH, the solution was then extracted with diethyl ether (3×10mL). The combined organic phases were dried on $MgSO_4$, filtrated and evaporated under reduced pressure to afford a yellow oil.

The metathesis between 2-allyl-1,3-cyclohexanedione and *tert*butyl acrylate gave the expected precursor **4e** according to the previous above procedures.

2-allylcyclohexane-1,3-dione



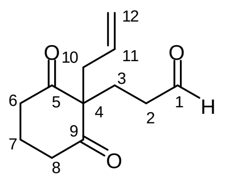
$C_9H_{12}O_2$
M = 152.19 g.mol^{-1}
RN = 42738-68-1
yellow oil
58% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.97 (m, 2H, H_7) ; 2.44 (m, 4H, H_6 and H_8) ; 2.64 (m, 1H, H_4) ; 3.14 (m, 2H, H_3); 5.15 (m, 2H, H_1) ; 5.85 (m, 1H, H_2).

RMN ^{13}C (75MHz, CDCl$_3$) δ 20.6 (C_7) ; 26.2 (C_3) ; 40.0 (C_6 and C_8) ; 65.3 (C_4) ; 116.7 (C_1) ; 136.1 (C_2) ; 204.1 (C_5 and C_9).

MS (+CI) : $[M+H]^+$ = 153.2.

3-(1-allyl-2,6-dioxocyclohexyl)propanal



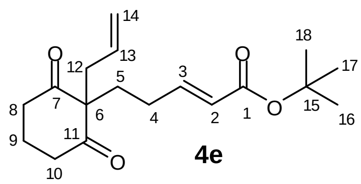
$C_{12}H_{16}O_3$
M = 208.25 g.mol^{-1}
yellow oil
92% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 2.11 (m, 2H, H_7) ; 2.32 (m, 4H, H_3 and H_{10}) ; 2.51 (m, 2H, H_2) ; 2.63 (m, 4H, H_6 and H_8) ; 5.00 (m, 2H, H_{12}) ; 5.68 (m, 1H, H_{11}) ; 9.67 (s, 1H, H_1).

RMN ^{13}C (75MHz, CDCl$_3$) δ 17.5 (C_7) ; 27.2 (C_3) ; 37.8 (C_6 and C_8) ; 39.3 (C_2) ; 41.5 (C_{10}) ; 65.0 (C_4) ; 120.0 (C_{12}) ; 132.0 (C_{13}) ; 201.0 (C_1) ; 209.8 (C_5 and C_9).

MS (+CI) : $[M+H]^+$ = 209.3.

***tert*butyl (*E*) 5-(1-allyl-2,6-dioxocyclohexyl)pent-2-enoate 4e**



4e

$C_{18}H_{26}O_4$
M = 306.4 g.mol^{-1}
pale yellow oil
51% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.46 (s, 9H, H_{16}, H_{17} and H_{18}) ; 1.93 (m, 6H, H_4, H_5 and H_9) ; 2.47 (d, $^3J_{H12\text{-}H13}$ = *7.4Hz*, 2H, H_{12}) ; 2.60 (t, ^3J = *7.2 Hz*, 4H, H_8 and H_{10}) ; 5.06 (m, 2H, H_{14}) ; 5.55 (ddt, $^3J_{transH13\text{-}H14a}$ = *16.7Hz*, $^3J_{cisH13\text{-}H14b}$ = *10.3Hz* and $^3J_{H13\text{-}H12}$ = *7.4Hz*, 1H, H_{13}) ; 5.70 (dt, $^3J_{H2\text{-}H3}$ = *15.6. Hz*, $^4J_{H2\text{-}H4}$ = *1.4Hz*, 1H, H_2) ; 6.70 (dt, $^3J_{H3\text{-}H2}$ = *15.6 Hz*, $^3J_{H3\text{-}H4}$ = *6.1Hz*, 1H, H_3).

RMN ^{13}C (75MHz, CDCl$_3$) δ 16.8 (C_9) ; 27.4 (C_4) ; 28.1 (C_{16}. C_{17} and C_{18}) ; 32.9 (C_5) ; 39.3 (C_8 and C_{10}) ; 41.5 (C_{12}) ; 68.2 (C_6) ; 80.2 (C_{16}) ; 119.6 (C_{14}) ; 123.6 (C_2) ; 131.9 (C_{13}) ; 146.1 (C_3) ; 165.7 (C_1) ; 209.9 (C_7 and C_{11}).

MS (ESI) : $[M+Na]^+$ = 329.2. **HRMS (ESI)** calcd for $C_{18}H_{26}O_4Na$: 329.1729 found 329.1729.

IR (film, cm^{-1}) ν 3025, 2935, 1708, 1652, 1367, 1367, 1255, 1155.

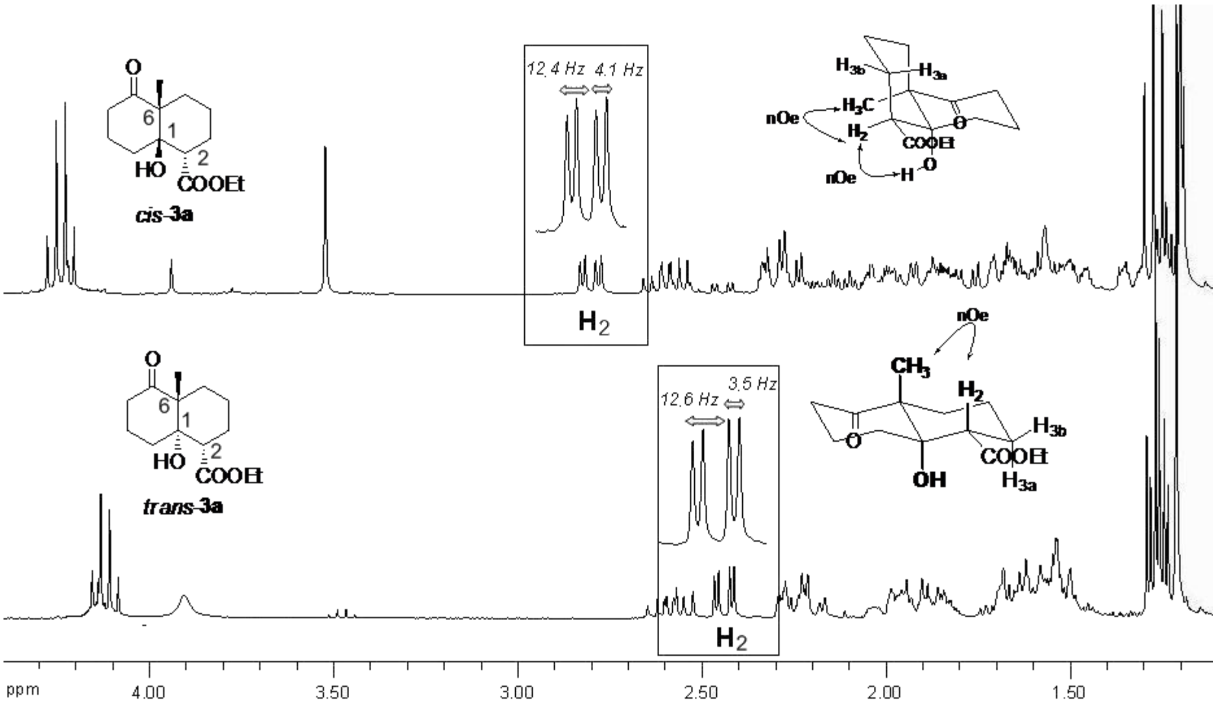
C] General procedure for the catalytic reductive aldol reaction.

A 25 mL flame-dried round bottom flask equipped with a magnetic stirrer, was charged with $CuF(PPh_3)_3.2MeOH$ (9.0mg, 0.01mmol), ligand (0.01mmol) and toluene (10mL). The catalyst solution was stirred for 30 minutes at room temperature and phenylsilane (180 μL, 1.40mmol) was added at the same temperature. After cooling the solution at –50 °C, the appropriate substrate in toluene (2mL) was added to the solution. The mixture was stirred for 2 hour at –50 °C under argon. Conversion, d.r. and e.e. were followed by gas chromatography on an aliquot sample (hydrolysis by 1 mL of aqueous HCl 3M solution and filtered through a plug of silica). The reaction mixture was quenched by adding an aqueous HCl solution (3M, 10mL). The aqueous layer was extracted by diethyl ether (3×5 mL). Then, the combined organic layers were washed with brine (20 mL), dried over anhydre $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography to yield the corresponding cyclized adduct.

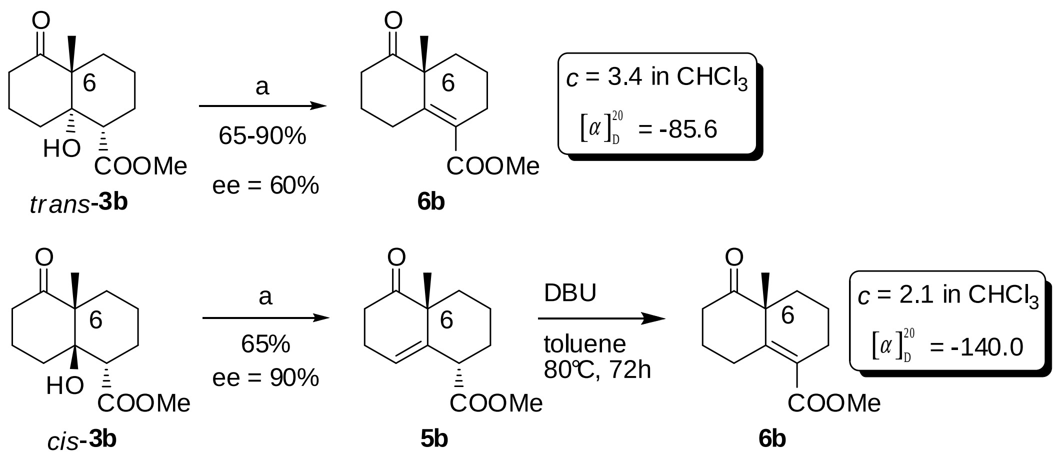
E] Determination of the relative configuration of adducts 3a-c and 5a-e.

Diastereoisomer ratio was determined by Chiral GC analysis. The relative configurations were determined by NMR analysis and nOe experiments.

In each pure isomer, the hydrogen H_2 has a large coupling constant (J = 12.4 and 12.6Hz) which is an axial/axial coupling. This infers that the hydrogen H_2 is in axial position. Furthermore, the nOe correlations (δ_H 1.22 ↔2.79 ↔3.49ppm) on the *cis*-**3a** show that the CH_3 group, the OH group and the hydrogen H_2 are *Syn*. These different observations have been shown on each pure isomers **3a-c** and **5a-e**.



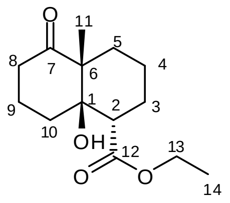
E] Determination of the absolute configuration of the adduct 3.



The absolute configuration at C_6 was determined by conversion into the olefin **6** (T. Katoh, S. Mizumoto, M. Fudesaka, M. Takeo, T. Kajimoto, M. Node, *Tetrahedron Asymmetry* **2006,** *17*, 1655-1662.) and comparison of the optical rotation value of the latter with the reported value (J. Yamazaki, A. V. Bedekar, T. Watanabe, K. Tanaka, J. Watanabe, K. Fuji, *Tetrahedron Asymmetry* **2002,** *13*, 729-734.). $[\alpha]_D^{20}$ -85.6 (c = 3.4 in $CHCl_3$) and –140 (c = 2.1 in $CHCl_3$) the configuration is *S.*

F] Characterization of compounds.

2-ethoxycarbonyl-1-hydroxy-6-methylbicyclo[4,4,0]-decan-7-one 3a



cis-**3a**

$C_{14}H_{22}O_4$

M = 254.32 g.mol^{-1}

pale yellow oil

cis/trans : 82/18

ee$_{cis}$: 82%

80% yield

RMN ^{1}H (500MHz, CDCl$_3$) δ 1.22 (s, 3H, H_{11}) ; 1.29 (t, $^3J_{H14-H13} = 7.1Hz$, 3H, H_{14}) ; 1.51 (m, 2H, H_{5a} and H_{10a}) ; 1.59 (m, 3H, H_{3a}, H_{4a} and H_{9a}) ; 1.88 (m, 2H, H_{3b}, H_{10b}) ; 2.10 (m, 2H, H_{4b} and H_{9b}) ; 2.29 (m, 2H, H_{5b} and H_{8a}) ; 2.58 (ddd, $^2JH_{8a-H8b} = 15.0Hz$, $^3J_{ax-ax} = 14.1Hz$ *and* $^3J_{ax-éq} = 6.7Hz$, 1H, H_{8b}); 2.79 (dd, $^3J_{ax-ax} = 12.4Hz$ *and* $^3J_{ax-éq} = 4.1Hz$, 1H, H_2) ; 3.49 (sl, 1H, OH) ; 4.20 (q, $^3J_{H13-H14} = 7.1Hz$, 2H, H_{13}).

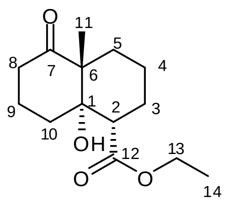
RMN ^{13}C (75MHz, CDCl$_3$) δ 14.2 (C_{14}) ; 14.7 (C_{11}) ; 19.9 (C_9) ; 20.2 and 25.0 (C_3 and C_4) ; 28.3 (C_5); 34.1 (C_{10}) ; 36.9 (C_8) ; 48.5 (C_2) ; 54.4 (C_6) ; 61.1 (C_{13}) ; 73.3 (C_1) ; 174.3 (C_{12}) ; 214.3 (C_7).

MS (+CI) : $[M+H]^+$ = 255.1. **HRMS (CI +)** calcd for $C_{14}H_{23}O_4$: 255.1596 found 255.1584.

IR (film, cm^{-1}) ν 3487, 2950, 2939, 2873, 1728, 1703, 1465, 1450, 1392, 1313, 1257, 1135.

Chiral GC: oven 160°C, flow = 1.2 mL/min tr = 34.89 min et 35.30 min.

$[\alpha]_D^{20}$ -18.5 (c=0.27 in CH_2Cl_2)



trans-**3a**

$C_{14}H_{22}O_4$

M = 254.32 g.mol^{-1}

pale yellow oil

trans/cis : 18/82

ee$_{trans}$: 33 %

80% yield

RMN ^{1}H (500MHz, CDCl$_3$) δ 1.21 (s, 3H, H_{11}) ; 1.25 (t, $^3J_{H14-H13} = 7.1Hz$, 3H, H_{14}) ; 1.54 (m, 3H, H_4 and H_{10a}) ; 1.62 (m, 3H, H_{3a}, H_{5a} and H_{9a}) ; 1.90 (m, 3H, H_{3b}, H_{5b} and H_{9b}) ; 2.24 (m, 2H, H_{8a} and H_{10b}); 2.45 (dd, $^3J_{ax-ax} = 12.6Hz$ *and* $^3J_{ax-éq} = 3.5Hz$, 1H, H_2) ; 2.57 (ddd, $^2JH_{8a-H8b} = 15.5Hz$, $^3J_{ax-ax} = 13.5Hz$ and $^3J_{ax-éq} = 7.8Hz$, 1H, H_{8b}) ; 3.90 (sl, 1H, OH) ; 4.16 (q, $^3J_{H13-H14} = 7.1Hz$, 2H, H_{13}).

RMN ^{13}C (75MHz, CDCl$_3$) δ 14.1 (C_{14}) ; 19.2 (C_9) ; 21.6 (C_{11}) ; 22.5, 25.5 and 28.9 (C_3, C_4 and C_5) ; 32.4 (C_{10}) ; 36.4 (C_8) ; 47.2 (C_2) ; 54.1 (C_6) ; 60.9 (C_{13}) ; 74.0 (C_1) ; 176.2 (C_{12}) ; 213.3 (C_7).

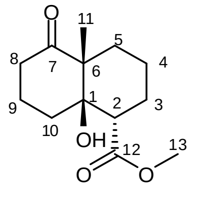
MS (+CI) : $[M+H]^+$ = 255.1.

IR (film, cm^{-1}) ν 3498, 2974, 2937, 2873, 1704, 1463, 1392, 1311, 1230, 1110.

Chiral GC : oven 160°C, flow = 1.2 mL/min tr = 16.41 min et 16.80 min.

$[\alpha]_D^{20}$ -5.5 (c=0.37 in CH_2Cl_2)

2-methoxycarbonyl-1-hydroxy-6-methylbicyclo[4,4,0]-decan-7-one 3a



cis-**3b**

$C_{13}H_{20}O_4$

M = 240.30 g.mol^{-1}

pale yellow oil

trans/cis : 28/72

ee$_{trans}$: 84%

80% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.22 (s, 3H, H_{11}) ; 1.37 (m, 1H, H_{9a}) ; 1.51 (m, 1H, H_{10a}) ; 1.52-2.20 (m, 7H, H_3, H_4, H_5, H_{9b}) ; 2.27 (m, 2H, H_{8a} and H_{10a}) ; 2.68 (ddd, *$^2JH_{8a\text{-}H8b}$ = 14.8Hz, $^3J_{ax\text{-}ax}$ = 13.6Hz and $^3J_{ax\text{-}éq}$ =6.6Hz*, 1H, H_{8b}); 2.79 (dd, *$^3J_{ax\text{-}ax}$ = 12.5Hz and $^3J_{ax\text{-}éq}$ = 4.1Hz*, 1H, H_2) ; 3.41 (sl, 1H, OH); 3.74 (s, 3H, H_{13}).

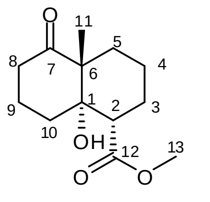
RMN ^{13}C (75MHz, CDCl$_3$) δ 14.7 (C_{11}) ; 19.9 and 20.1 (C_4 and C_5); 20.1 (C_3); 25.1 (C_{10}); 34.1 (C_9) ; 36.9 (C_8) ; 49.6 (C_2) ; 52.1 (C_{13}) ; 54.4 (C_6) ; 76.3 (C_1) ; 174.8 (C_{12}) ; 214.2 (C_7).

MS (+CI) : $[M+H]^+$ = 241.1. **HRMS (CI +)** calcd for $C_{13}H_{20}O_4$: 241.1596 found 241.1590.

IR (film, cm^{-1}) ν 3487, 2950, 2939, 2873, 1728, 1703, 1465, 1450, 1392, 1313, 1257, 1135.

Chiral GC: oven 160°C, flow = 1.2 mL/min tr = 47.92 min and 48.79 min.

$[\alpha]_D^{20}$ -37.8 (c=2.14 in CH_2Cl_2)



trans-**3b**

$C_{13}H_{20}O_4$

M = 240.30 g.mol^{-1}

pale yellow oil

trans/cis : 28/72

ee$_{trans}$: 60%

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.22 (s, 3H, H_{11}) ; 1.50-1.68 (m, 6H, H_{3a}, H_{4a}, H_5 H_{9a}, H_{10a}) ; 1.89-1.99 (m, 3H, H_{3b}, H_{4b} and H_{10b}) ; 2.17-2.23 (m, 2H, H_{8a}, H_{9b}) ; 2.46 (dd, *$^3J_{ax\text{-}ax}$ = 12.5Hz and $^3J_{ax\text{-}éq}$ = 4.1Hz*, 1H, H_2) ; 2.57 (ddd, *$^2JH_{8a\text{-}H8b}$ = 15.5Hz, $^3J_{ax\text{-}ax}$ = 13.6Hz* and *$^3J_{ax\text{-}éq}$ = 7.7Hz*, 1H, H_{8b}) ; 3.71 (s, 3H, H_{13}) ; 3.85 (sl, 1H, OH).

RMN ^{13}C (75MHz, CDCl$_3$) δ 19.3 (C_4) ; 21.5 (C_5) ; 22.5 (C_{11}) ; 25.5 (C_{10}) ; 28.9 (C_3) ; 32.5 (C_9) ; 36.4 (C_8) ; 47.1 (C_2) ; 52.0 (C_{13}) ; 54.1 (C_6) ; 74.0 (C_1) ; 176.7 (C_{12}) ; 213.3 (C_7).

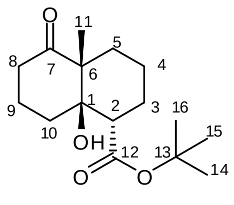
MS (+CI) : $[M+H]^+$ = 241.2.

IR (film, cm^{-1}) ν 3498, 2974, 2937, 2873, 1704, 1463, 1392, 1311, 1230, 1110.

Chiral GC : oven 160°C, flow = 1.2 mL/min tr = 20.13 min et 21.30 min.

$[\alpha]_D^{20}$ -13.2 (c=0.38 in CH_2Cl_2)

2-*tert*butoxycarbonyl-1-hydroxy-6-methylbicyclo-[4,4,0]-decan-7-one 3c



cis-**3c**

$C_{16}H_{24}O_4$
M = 282.38 g.mol^{-1}
pale yellow oil
cis/trans : 100/0
ee$_{trans}$: 95%
80% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.21 (s, 3H, H_{11}) ; 1.35 (m, 1H, H_{10a}) ; 1.49 (m, 9H, H_{14}, H_{15} and H_{16}) ; 1.60-1.75 (m, 2H, H_{3a} and H_{9a}) ; 1.84-1.95 (m, 5H, H_{3b}, H_{4a}, H_{5a}, H_{9b}, H_{10a}) ; 2.17-2.33 (m, 3H, H_{4b}, H_{5b}, H_{8a}) ; 2.57 (ddd → td, $^2JH_{8a\text{-}H8b}$ = $^3J_{ax\text{-}ax}$ = *13.9Hz and* $^3J_{ax\text{-}éq}$ =*6.8Hz*, 1H, H_{8b}) ; 2.71 (dd, $^3J_{ax\text{-}ax}$ = *12.3Hz and* $^3J_{ax\text{-}éq}$ = *4.0Hz*, 1H, H_2) ; 3.72 (sl, 1H, OH).

RMN ^{13}C (75MHz, CDCl$_3$) δ 14.8 (C_{11}) ; 20.0 and 20.1 (C_4 and C_9) ; 25.1 (C_3) ; 28.1 (C_{14}, C_{15} and C_{16}) ; 28.2 (C_5) ; 34.1 (C_{10}) ; 36.9 (C_8) ; 48.8 (C_2) ; 54.5 (C_6) ; 82.2 (C_{13}) ; 73.3 (C_1 and C_6) ; 173.6 (C_{12}) ; 214.5 (C_7).

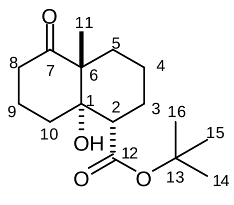
MS (+CI) : $[M+H]^+$ = 283.3. **HRMS (CI +)** calcd for $C_{16}H_{27}O_4$: 283.1909 found 283.1899.

IR (film, cm^{-1}) ν 3487, 2958, 2929, 1707, 1429, 1367, 1151, 1058.

Chiral GC: oven 170°C, flow = 1.2 mL/min tr = 25.15 min et 26.01 min.

$[\alpha]_D^{20}$ -15.7 (c=10.1 in CH_2Cl_2)

The minor product *trans*-**3c** was isolated when the racemic adducts **3c** was prepared.



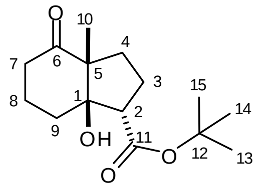
trans-**3c**

$C_{16}H_{26}O_4$
M = 282.38 g.mol^{-1}
pale yellow oil

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.20 (s, 3H, H_{11}) ; 1.32-1.39 (m, 2H) ; 1.46 (s, 9H, H_{14}, H_{15} and H_{16}) ; 1.46-1.56 (m, 2H) ; 1.62-1.73 (m, 2H) ; 1.83-1.97 (m, 2H) ; 2.16-2.29 (m, 2H, H_{8a} +) ; 2.29-2.35 (dd, $^3J_{ax\text{-}ax}$ = *12.5Hz and* $^3J_{ax\text{-}éq}$ = *3.5Hz*, 1H, H_2) ; 2.52-2.65 (ddd, $^2JH_{8a\text{-}H8b}$ = *15.7Hz*, $^3J_{ax\text{-}ax}$ = *13.3Hz* and $^3J_{ax\text{-}éq}$ = *7.8Hz*, 1H, H_{8b}) ; 4.03 (sl, 1H, OH).

RMN ^{13}C (75MHz, CDCl$_3$) δ 21.6 (C_{11}) ; 19.2, 22.5, 25.5 and 28.6 (4×CH_2) ; 28.8 (C_{14}, C_{15} and C_{16}); 32.4 (CH_2) ; 36.5 (C_8) ; 48.2 (C_2) ; 55.1 (C_6) ; 74.0 (C_1) ; 72.3 (C_{13}) ; 174.2 (C_{12}) ; 210.3 (C_7).

2-*tert*butoxycarbonyl-1-hydroxy-5-methylbicyclo-[4,3,0]-nonane-6-one 5a



cis-**5a**

$C_{15}H_{24}O_4$
M = 268.35 g.mol^{-1}
colourless
cis/trans : 94/6
80% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.13 (s, 3H, H_{10}) ; 1.43 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.55 (m, 2H, H_{4a} and H_{9a}) ; 1.75-1.85 (m, 3H, H_{4a}, H_{8a} and H_{9b}) ; 1.90-2.13 (m, 3H, H_3 and H_{8a}) ; 2.24-2.31 (m, 1H, H_{7a}) ; 2.36 (sl, 1H, OH) ; 2.46 (ddd, $^2JH_{7a\text{-}H7b} = 15.3Hz$, $^3J_{ax\text{-}ax} = 13.5Hz$ *et* $^3J_{ax\text{-}eq} = 6.1Hz$, 1H, H_{7a}) ; 3.01 (dd, $^3J_{trans} = 10.0Hz$ and $^3J_{cis} = 9.4Hz$, 1H, H_{2a}).

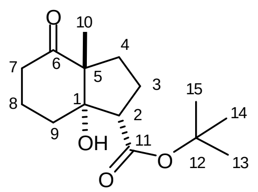
RMN ^{13}C (75MHz, CDCl$_3$) δ 17.1 (C_{10}) ; 20.7 (C_3) ; 21.2 (C_8) ; 28.2 (C_{13}, C_{14} and C_{15}) ; 30.7 (C_9) ; 33.4 (C_4) ; 36.9 (C_7) ; 53.8 (C_2) ; 58.3 (C_5) ; 81.7 (C_{11}) ; 85.1 (C_1) ; 172.0 (C_{11}) ; 213.1 (C_6).

MS (+CI) : $[M+H]^+$ = 269.4 . **HRMS (CI +)** calcd for $C_{15}H_{26}O_4$: 269.1909 found 269.1916.

IR (film, cm^{-1}) ν 3519, 2972, 2941, 1724, 1704, 1456, 1429, 1367, 1147.

Chiral GC: oven 160°C, flow = 1.2 mL/min tr = 26.03 min et 26.84 min.

$[\alpha]_D^{20}$ +25.0 (c = 1.2 in CH_2Cl_2).



trans-**5a**

$C_{15}H_{24}O_4$
M = 268.35 g.mol^{-1}
colourless oil
trans/cis : 6/94
ee$_{trans}$: 85%

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.21 (s, 3H, H_{10}) ; 1.45 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.50-1.60 (m, 4H, H_4, H_9) ; 1.84-1.93 (m, 2H, H_{3a} and H_{8a}) ; 1.94-2.04 (m, 2H, H_{3b} and H_{8b}) ; 2.22-2.29 (m, 1H, H_{7a}) ; 2.36 (sl, 1H, OH) ; 2.49-2.56 (dd→t, $^3J_{trans} = {}^3J_{cis} = 9.9Hz$, 1H, H_{2a}); 2.54-2.66 (ddd, $^2JH_{7a\text{-}H7b} = 13.2Hz$, $^3J_{ax\text{-}ax} = 7.8Hz$ *et* $^3J_{ax\text{-}eq} = 5.7Hz$, 1H, H_{7a}) ;

RMN ^{13}C (75MHz, CDCl$_3$) δ 171 (C_{10}) ; 21.7, 22.3, (C_3 and C_8) ; 28.1 (C_{13}, C_{14} and C_{15}) ; 31.7 (C_9) ; 32.4 (C_4) ; 35.6 (C_7) ; 51.8 (C_2) ; 57.3 (C_5) ; 80.7 (C_{11}) ; 82.1 (C_1) ; 171.0 (C_{11}) ; 214.1 (C_6).

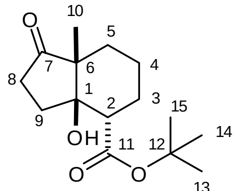
MS (+CI) : $[M+H]^+$ = 269.4.

IR (film, cm^{-1}) ν 3519, 2972, 2941, 1724, 1704, 1456, 1429, 1367, 1147.

Chiral GC: oven 160°C, flow = 1.2 mL/min tr = 14.68 min et 15.29 min.

$[\alpha]_D^{20}$ +22.5 (c = 2.0 in CH_2Cl_2).

2-*tert*butoxycarbonyl-1-hydroxy-6-methylbicyclo-[4,3,0]-nonane-7-one 5b



cis-**5b**

$C_{15}H_{24}O_4$
M = 268.35 g.mol^{-1}
colourless oil
cis/trans : 89/11
ee$_{cis}$: 97%
80% yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.09 (s, 3H, H_{10}) ; 1.30 (m, 2H, H_5) ; 1.40-1.52 (m, 2H, H_{3a} and H_{4a}) ; 1.49 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.64-1.68 (m, 1H, H_{4b}) ; 1.82-1.91 (ddd, $^2JH_{8a\text{-}H8b}$ = *13.3Hz*, $^3J_{trans}$ = *8.6Hz and* $^3J_{cis}$ =*2.1Hz,* 1H, H_{9a}) ; 1.97-2.04 (m, 1H, H_{3b}) ; 2.17-2.26 (m, 1H, H_{9b}) ; 2.41-2.49 (m, 2H, H_8) ; 2.58 (dd, $^3J_{ax\text{-}ax}$ = *12.4Hz* and $^3J_{ax\text{-}éq}$ = *4.5Hz,* 1H, H_2) ; 3.59 (sl, 1H, OH).

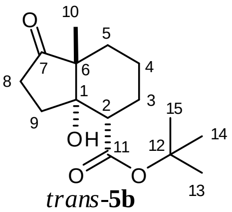
RMN ^{13}C (75MHz, $CDCl_3$) δ 12.9 (C_{10}) ; 20.1 (C_4) ; 25.9 (C_3) ; 27.7 (C_9) ; 28.1 (C_{13}, C_{14} and C_{15}) ; 32.0 (C_5) ; 32.8 (C_8) ; 48.0 (C_2) ; 53.5 (C_6) ; 79.4 (C_{12}) ; 82.2 (C_1) ; 173.3 (C_{11}) ; 220.1 (C_7).

MS (+CI) : $[M+H]^+$ = 269.4. **HRMS (CI +)** calcd for $C_{15}H_{26}O_4$: 269.1753 found 269.1744.

IR (film, cm^{-1}) ν 3460, 2972, 2930,1724, 1705, 1456, 1431, 1367, 1247.

Chiral GC: oven 170°C, flow = 1.2 mL/min tr = 15.85 min et 16.82 min.

$[\alpha]_D^{20}$ +111,3 (c = 8.0 in CH_2Cl_2).



trans-**5b**

$C_{15}H_{24}O_4$
M = 268,35 g.mol^{-1}
colourless oil
trans/cis : 11/89
ee$_{trans}$: 72 %

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.02 (s, 3H, H_{10}) ; 1.25-1.42 (m, 2H, H_{3a} and H_{4a}) ; 1.43 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.55-1.80 (m, 2H, H_{4b} and H_{5a}) ; 1.80-2.00 (m, 3H, H_{3b}, H_{5b} and H_{9a}) ; 2.05-2.28 (m, 3H, H_{8a}, H_{9b} and H_2) ; 2.57 (m, 1H, H_{8b}) ; 4.00 (sl, 1H, OH).

RMN ^{13}C (75MHz, $CDCl_3$) δ 17.1 (C_{10}) ; 20.7 (C_4) ; 25.1 (C_5) ; 28.1 (C_{13}, C_{14} and C_{15}) ; 28.7 (C_3) ; 31.2 (C_9) ; 34.3 (C_8) ; 48.3 (C_2) ; 53.6 (C_6) ; 80.2 (C_1) ; 82.2 (C_{12}) ; 175.6 (C_{11}) ; 218.3 (C_7).

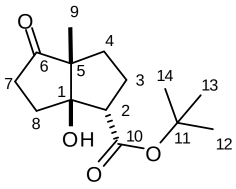
MS (+CI) : $[M+H]^+$ = 269.4.

IR (film, cm^{-1}) ν 3460, 2972, 2930,1724, 1705, 1456, 1431, 1367, 1247.

Chiral GC: oven 160°C, flow = 1.2 mL/min tr = 14.10 min et 14.33 min.

$[\alpha]_D^{20}$ +8.7 (c = 2.3 dans CH_2Cl_2).

2-*tert*butoxycarbonyl-1-hydroxy-5-methylbicyclo-[3,3,0]-octane-6-one 5d



cis-**5c**

$C_{14}H_{22}O_4$
M = 254,32 g.mol^{-1}
colorless oil
ee$_{cis}$: 66%
85% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.09 (s, 3H, H_9) ; 1.50 (s, 9H, H_{12}, H_{13} and H_{14}) ; 1.53-1.59 (m, 1H, H_{3a}) ; 1.76-1.99 (m, 5H, H_{3b}, H_4, and H_8) ; 2.35-2.44 (m, 1H, H_{7a}) ; 2.41-2.61 (m, 1H, H_{7b}) ; 2.73 (sl, 1H, OH) ; 2.95 (dd, $^3J_{trans}$ = *9.7Hz* and $^3J_{cis}$ =*9.4Hz*, 1H, H_2).

RMN ^{13}C (75MHz, CDCl$_3$) δ 16.7 (C_9) ; 23.2 (C_3) ; 28.2 (C_{12}, C_{13} and C_{14}) ; 30.7 (C_8) ; 33.2 (C_4) ; 35.5 (C_7) ; 54.0 (C_2) ; 58.4 (C_5) ; 81.8 (C_{11}) ; 87.6 (C_1) ; 171.9 (C_{11}) ; 220.6 (C_6).

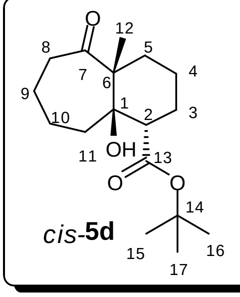
MS (+CI) : $[M+H]^+$ = 255.3. **HRMS (CI +)** calcd for $C_{14}H_{23}O_4$: 255.1596 found 255.1591.

IR (film, cm^{-1}) ν 3519, 2972, 2941, 1724, 1704, 1456, 1429, 1367, 1147.

Chiral GC: oven 170°C, flow = 1.2 mL/min tr = 9.64 min et 10.05 min.

$[\alpha]_D^{20}$ +62.5 (c = 2.0 in CH_2Cl_2).

2-*tert*butoxycarbonyl-1-hydroxy-6-methylbicyclo-[4,3,0]-octane-7-one 5d



cis-**5d**

$C_{17}H_{28}O_4$
M = 296.20 g.mol^{-1}
pale yellow oil
cis/trans : 100/0
ee$_{cis}$: 95%
80% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.48 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.48-1.66 (m, 5H, H_{3a}, H_7 and H_8) ; 1.70-2.00 (m, 3H, H_{2a}, H_{3b} and H_{9a}) ; 2.03-2.10 (m, 2H, H_{2b} and H_{9b}) ; 2.10-2.20 (m, 2H, H_{4a} and H_{16a}); 2.65 (ddd → td, $^2JH_{4b-H4a}$ = $^3J_{ax-ax}$ = *13.9Hz* and $^3J_{ax-éq}$ = *6.7Hz*, 1H, H_{4b}) ; 2.79 (dd, $^3J_{ax-ax}$ = *13.0Hz* and $^3J_{ax-éq}$ = *4.3Hz*, 1H, H_{10}) ; 2.89 (m, 1H, H_{16b}) ; 3.70 (sl, 1H, OH) ; 5.02 (m, 2H, H_{18}) ; 5.98 (dtd, $^3J_{transH17-H18a}$ = *17.2 Hz*, $^3J_{H17-H16}$ = *9.9 Hz et* $^3J_{cisH17-H18b}$ = *4.5 Hz*, 1H, H_{17}).

RMN ^{13}C (75MHz, CDCl$_3$) δ 19.5, 20.8 et 24.9 (C_3, C_8 and C_9) ; 28.1 (C_{13}, C_{14} and C_{15}) ; 28.7 and 29.7 (C_2 and C_7) ; 33.1 (C_{16}) ; 37.5 (C_4) ; 48.7 (C_{10}) ; 56.8 (C_6) ; 78.3 (C_1) ; 82.3 (C_{12}) ; 116.2 (C_{18}) ; 136.9 (C_{17}) ; 173.5 (C_{11}) ; 213.8 (C_5).

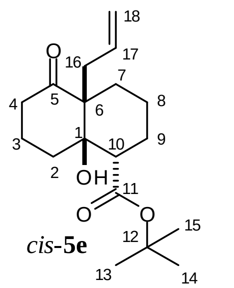
MS (+CI) : $[M+H]^+$ =297.1. **HRMS (ESI)** calcd for $C_{17}H_{28}O_4Na$: 319.1885 found 319.1883.

IR (film, cm^{-1}) ν 3533, 2974, 2937, 2864, 1734, 1689, 1448, 1369, 1257, 1155, 1103.

Chiral GC: oven 160°C, flow = 1.2 mL/min, tr = 48.65 min et 49.84 min.

$[\alpha]_D^{20}$ +8.5 (c =2.0 in CH_2Cl_2).

6-allyl-2-*tert*-butoxycarbonyl-1-hydroxybicyclo[4,4,0]-decan-7-one 5e



cis-**5e**

$C_{18}H_{28}O_4$

M = 308.41 g.mol^{-1}

colourless oil

cis/trans : 100/0

ee = 94%

70% yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.48 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.48-1.66 (m, 5H, H_{3a}, H_7 and H_8) ; 1.70-2.00 (m, 3H, H_{2a}, H_{3b} and H_{9a}) ; 2.03-2.10 (m, 2H, H_{2b} and H_{9b}) ; 2.10-2.20 (m, 2H, H_{4a} and H_{16a}); 2.65 (ddd → td, $^2JH_{4b\text{-}H4a}$ = $^3J_{ax\text{-}ax}$ = *13.9Hz* and $^3J_{ax\text{-}éq}$ = *6.7Hz*, 1H, H_{4b}) ; 2.79 (dd, $^3J_{ax\text{-}ax}$ = *13.0Hz* and $^3J_{ax\text{-}éq}$ = *4.3Hz*, 1H, H_{10}) ; 2.89 (m, 1H, H_{16b}) ; 3.70 (sl, 1H, OH) ; 5.02 (m, 2H, H_{18}) ; 5.98 (dtd, $^3J_{transH17\text{-}H18a}$ = *17.2 Hz*, $^3J_{H17\text{-}H16}$ = *9.9 Hz et* $^3J_{cisH17\text{-}H18b}$ = *4.5 Hz*, 1H, H_{17}).

RMN ^{13}C (75MHz, CDCl$_3$) δ 19.5, 20.8 et 24.9 (C_3, C_8 and C_9) ; 28.1 (C_{13}, C_{14} and C_{15}) ; 28.7 and 29.7 (C_2 and C_7) ; 33.1 (C_{16}) ; 37.5 (C_4) ; 48.7 (C_{10}) ; 56.8 (C_6) ; 78.3 (C_1) ; 82.3 (C_{12}) ; 116.2 (C_{18}) ; 136.9 (C_{17}) ; 173.5 (C_{11}) ; 213.8 (C_5).

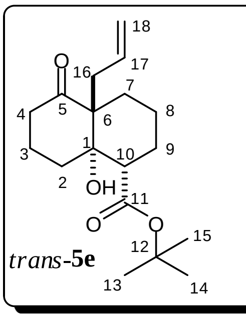
MS (+CI) : $[M+H]^+$ =309.2. **HRMS (CI +)** calcd for $C_{18}H_{29}O_4$: 309.2066 found 309.2061.

IR (film, cm^{-1}) ν 3456, 2974, 2962, 2935, 1703,1647, 1458, 1367, 1257, 1147.

Chiral GC: oven 160°C, flow = 1.2 mL/min, tr = 48.65 min et 49.84 min.

$[\alpha]_D^{20}$ -17.6 (c =0.73 in CH_2Cl_2).

The adduct *trans*-**5e** was isolated when the racemic mixture **5e** was synthesized.



trans-**5e**

$C_{18}H_{28}O_4$

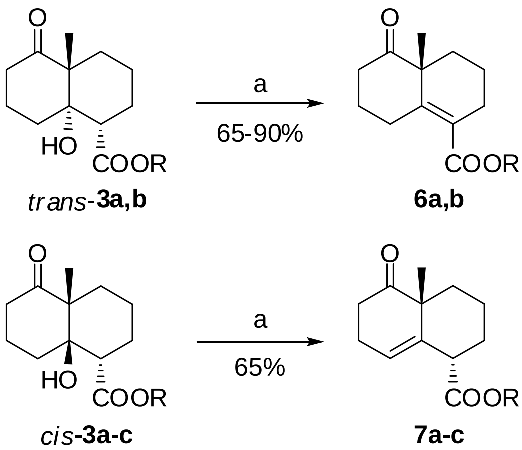
M = 308.41 g.mol^{-1}

colourless oil

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.45 (s, 9H, H_{13}, H_{14} and H_{15}) ; 1.44-1.66 (m, 5H, H_{3a}, H_{2a}, H_{9a} and H_8); 1.85-2.00 (m, 2H, H_{3b} and H_{9b}) ; 2.10 (m, 2H, H_7) ; 2.24-2.31 (m, 3H, H_{2b}, H_{4a} and H_{10}) ; 2.45-2.52 (m, 2H, H_{4b} and H_{16a}) ; 2.67 (dd, $^3J_{ax\text{-}ax}$ = *14.4Hz* and $^3J_{ax\text{-}éq}$ = *7.4Hz*, 1H, H_{16b}) ; 4.07 (sl, 1H, OH); 5.00 (m, 2H, H_{18}) ; 5.98 (ddt, $^3J_{transH13\text{-}H14a}$ = *16.7Hz*, $^3J_{cisH13\text{-}H14b}$ = *10.3Hz and* $^3J_{H13\text{-}H12}$ = *7.4 Hz*, 1H, H_{17}).

RMN ^{13}C (75MHz, CDCl$_3$) δ 19.4 (C_3) ; 21.3 (C_8) ; 25.1 (C_9) ; 26.1 (C_7) ; 28.0 (C_{13}, C_{14} and C_{15}) ; 32.4 (C_2) ; 37.6 (C_4) ; 38.9 (C_{16}) ; 48.0 (C_{10}) ; 57.7 (C_6) ; 74.6 (C_1) ; 81.9 (C_{12}) ; 117.9 (C_{18}) ; 132.7 (C_{17}) ; 175.7 (C_{11}) ; 211.5 (C_5).

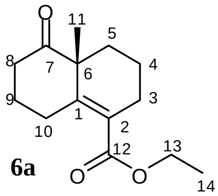
G] Elimination of bicyclic adducts 3a-c



To a solution of adduct **3a-c** (1mmol) and distilled triethylamine (25mmol, 25eq.) in distilled dichloromethane (10mL) were added at -20°C (5eq.) methanesulfonyl chloride (5mmol×5, 5eq×5.) each hour for 5 hours. After stirring -20°C for 12 hours, an aqueous HCl (3M) solution was added dropwise to the mixture at -20°C and the biphasic solution was slowly warmed to ambient temperature. After extraction of the aqueous layer with dichloromethane (3×5mL), the combined organic phases were successively washed with aqueous $NaHCO_3$ and brine, dried on MgSO4, filtered and evaporated in vacuo. The residue was purified by column chromatography (CH_2Cl_2/AcOEt: 99/1) to afford a pale yellow oil.

The coumpounds **7a-c** were isomerizated upon the literature procedure.[6]

2-ethoxycarbonyl-6-methylbicyclo[4,4,0]dec-1-en-7-one 6b.



6a

$C_{14}H_{20}O_3$
M = 236.31g.mol^{-1}
pale yellow oil
80% yield

RMN ^{1}H (500MHz, $CDCl_3$) δ 1.29 (t, $^3J_{H14-H13}$ = *7.2Hz*, 3H, H_{14}) ; 1.34 (s, 3H, H_{11}) ; 1.55-1.70 (m, 4H, H_4, H_{5a} and H_{9a}) ; 1.85-1.92 (m, 1H, H_{5b}) ; 1.95-2.04 (m, 1H, H_{9b}) ; 2.20-2.30 (m, 2H, H_3) ; 3.35-2.45 (m, 2H, H_{8a} and H_{10a}) ; 2.59-2.66 (ddd, $^2JH_{8a-H8b}$ = *15.2Hz*, $^3J_{ax-ax}$ = *12.0Hz* and $^3J_{ax-éq}$ = *6.5Hz*, 1H, H_{8b}) ; 3.04-3.13 (m, 1H, H_{10b}) ; 4.18 (q, $^3J_{H13-H14}$ = *7.2Hz*, 2H, H_{13}).

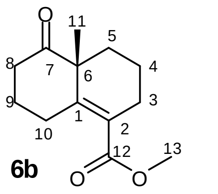
RMN ^{13}C (75MHz, $CDCl_3$) δ 14.2 (C_{11}) ; 18.3 (C_4) ; 23.5 (C_9) ; 25.8 (C_{14}) ; 26.6 (C_{10}) ; 27.3 (C_3) ; 37.3 (C_8) ; 51.3 (C_6) ; 60.4 (C_{13}) ; 127.4 (C_2) ; 145.7 (C_1) ; 169.7 (C_{12}) ; 213.5 (C_7).

MS (+CI) : $[M+H]^+$ = 237.1. **HRMS (CI +)** calcd for $C_{14}H_{20}O_3$: 236.1412 found 436.1425.

IR (film, cm^{-1}) ν 2977, 2927, 2854, 1722, 1710, 1315, 1261, 1188, 1143.

$[\alpha]_D^{20}$ -118.5 (c=1.3 in CH_2Cl_2)

2-methoxycarbonyl-6-methylbicyclo[4,4,0]dec-1-en-7-one 6a.



6b

$C_{13}H_{18}O_3$
M = 222.28g.mol^{-1}
pale yellow oil
95% yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.34 (s, 3H, H_{11}) ; 1.55-1.64 (m, 4H, H_4, H_{5a} and H_{9a}) ; 1.85-1.92 (m, 1H, H_{5b}) ; 1.94-2.05 (m, 1H, H_{9b}) ; 2.25 (m, 2H, H_3) ; 3.35-2.41 (m, 2H, H_{8a} and H_{10a}) ; 2.59-2.66 (ddd, $^2JH_{8a-H8b}$ = *15.3Hz*, $^3J_{ax-ax}$ = *12.0Hz* and $^3J_{ax-éq}$ = *6.5Hz*, 1H, H_{8b}) ; 3.06-3.14 (m, 1H, H_{10b}) ; 3.74 (s, 3H, H_{13}).

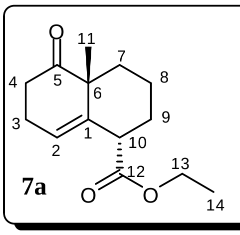
RMN ^{13}C (75MHz, $CDCl_3$) δ 18.3 (C_4) ; 23.5 (C_9); 25.8 (C_{11}); 26.6 (C_{10}) ; 27.3 (C_3) ; 30.9 (C_5) ; 37.7 (C_8) ; 51.3 (C_6) ; 51.6 (C_{13}) ; 127.4 (C_2) ; 145.7 (C_1) ; 169.7 (C_{12}) ; 213.5 (C_7).

MS (+CI) : $[M+H]^+$ = 223.4.

IR (film, cm^{-1}) ν 2959, 2927, 2854, 1716, 1693, 1454, 1369, 1317, 1269, 1178.

$[\alpha]_D^{20}$ -140.0 (c=2.1 in $CHCl_3$)

10-ethoxycarbonyl-6-methylbicyclo[4,4,0]dec-1-en-5-one 7b.



7a

$C_{14}H_{20}O_3$
M = 236.31g.mol^{-1}
pale yellow oil
85% yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.21 (s and t, $^3J_{H14\text{-}H13}$ = *7.2Hz*, 6H, H_{11} and H_{14}) ; 1.54-1.95 (m, 6H, H_7, H_8 and H_9) ; 2.38-2.45 (m, 2H, H_3) ; 2.45-2.55 (m, 1H, H_{4a}) ; 2.20-2.30 (ddd, $^2JH_{8a\text{-}H8b}$ = *15.2Hz,* $^3J_{ax\text{-}ax}$ = *12.0Hz and* $^3J_{ax\text{-}éq}$ = *6.5Hz*, 1H, H_{4b}) ; 3.11 (m, 1H, H_{10}) ; 5.40 (m, 1H, H_2).

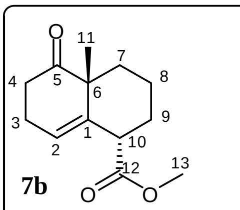
RMN ^{13}C (75MHz, $CDCl_3$) δ 20.4 (C_8) ; 21.9 (C_{11}) ; 24.8 (C_3) ; 28.1 (C_{14}, C_{15} and C_{16}) ; 30.5 (C_9) ; 34.6 (C_7) ; 35.5 (C_4) ; 47.0 (C_{10}) ; 48.1 (C_6) ; 80.7 (C_{13}) ; 118.3 (C_2) ; 141.1 (C_1) ; 173.3 (C_{12}) ; 214.6 (C_5).

MS (+CI) : $[M+H]^+$ = 237.4. **HRMS (CI +)** calcd for $C_{14}H_{20}O_3$: 236.1412 found 436.1431.

IR (film, cm^{-1}) ν 2977, 2933, 2866, 1772, 1730, 1706, 1456, 1313, 1259, 1170.

$[\alpha]_D^{20}$ -117.5 (c=1.3 in CH_2Cl_2)

10-methoxycarbonyl-6-methylbicyclo[4,4,0]dec-1-en-5-one 7a



7b

$C_{13}H_{18}O_3$
M = 222.28g.mol^{-1}
pale yellow oil
95% yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.29 (s, 3H, H_{11}) ; 1.41-1.53 (m, 1H, H_{7a}) 1.60-1.70 (m, 2H, H_{8a} and H_{9a}) ; 1.75-1.85 (m, 2H, H_{7b}, H_{8b}) ; 1.90-1.96 (m, 1H, H_{9b}) ; 2.35-2.42 (m, 2H, H_3) ; 2.43-2.50 (m, 1H, H_{4a}) ; 2.57-2.66 (ddd, $^2JH_{8a\text{-}H8b}$ = *15.2Hz,* $^3J_{ax\text{-}ax}$ = *12.0Hz* and $^3J_{ax\text{-}éq}$ = *6.5Hz*, 1H, H_{4b}) ; 3.29 (m, 1H, H_{10}) ; 3.75 (s, 3H, H_{13}) ; 5.36 (m, 1H, H_2).

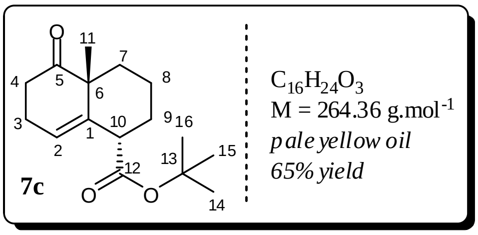
RMN ^{13}C (75MHz, $CDCl_3$) δ 20.4 (C_8) ; 21,9 (C_{11}) ; 24,7 (C_3) ; 30,4 (C_9) ; 34,6 (C_7) ; 35,4 (C_4) ; 46,3 (C_{10}) ; 48,0 (C_6) ; 51.7 (C_{13}) ; 118,8 (C_2) ; 140,6 (C_1) ; 174,3 (C_{12}) ; 214,3 (C_5).

MS (+CI) : $[M+H]^+$ = 223.4. **HRMS (CI +)** calcd for $C_{13}H_{18}O_3$: 222.1256 found 222.1272.

IR (film, cm^{-1}) ν 2945, 2867, 1736, 1708, 1633, 1433, 1365, 1218, 1147.

$[\alpha]_D^{20}$ -108.8 (c=1.6 in $CHCl_3$)

10-*tert*butoxycarbonyl-6-methylbicyclo[4,4,0]dec-1-en-5-one 7c.



RMN ^{1}H (300MHz, CDCl$_3$) δ 1.29 (s, 3H, H_{11}) ; 1.49 (s, 9H, H_{14}, H_{15} and H_{16}) ; 1.40-1.95 (m, 6H, H_7, H_8 and H_9) ; 2.38-2.45 (m, 2H, H_3) ; 2.45-2.55 (m, 1H, H_{4a}) ; 2.20-2.30 (ddd, $^2JH_{8a\text{-}H8b} = 15.2Hz$, $^3J_{ax\text{-}ax} = 12.0Hz$ and $^3J_{ax\text{-}éq} = 6.5Hz$, 1H, H_{4b}) ; 3.11 (m, 1H, H_{10}) ; 5.47 (m, 1H, H_2).

RMN ^{13}C (75MHz, CDCl$_3$) δ 20.4 (C_8) ; 21.9 (C_{11}) ; 24.8 (C_3) ; 28.1 (C_{14}, C_{15} and C_{16}) ; 30.5 (C_9) ; 34.6 (C_7) ; 35.5 (C_4) ; 47.0 (C_{10}) ; 48.1 (C_6) ; 80.7 (C13) ; 118.3 (C_2) ; 141.1 (C_1) ; 173.3 (C_{12}) ; 214.6 (C_5).

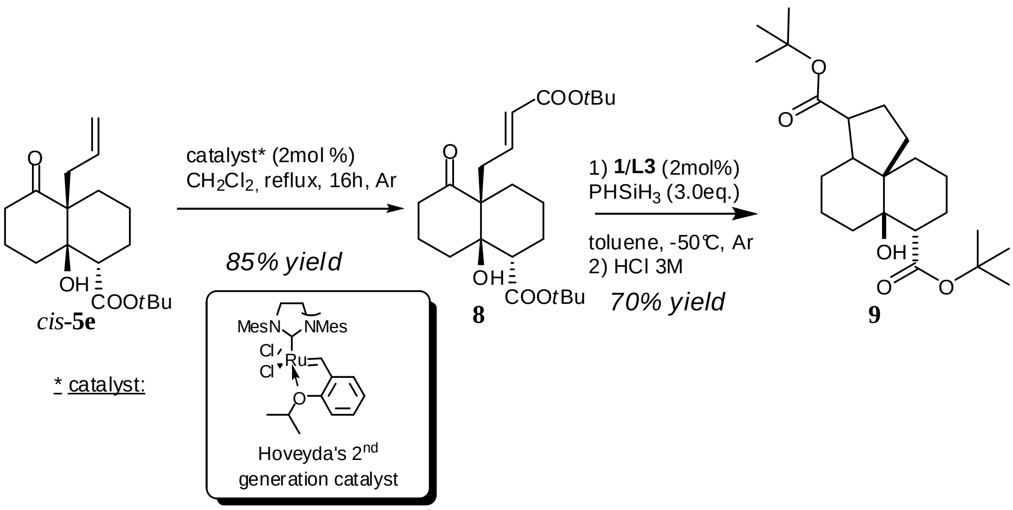
MS (+CI) : $[M+H]^+$ = 265.4. **HRMS (CI +)** calcd for $C_{16}H_{24}O_3$: 464.1725 found 464.1740.

IR (film, cm^{-1}) ν 2927, 2854, 1716, 1693, 1454, 1369, 1317, 1269, 1178.

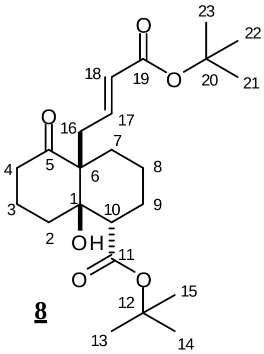
$[\alpha]_D^{20}$ -105.2 (c=1.6 in $CHCl_3$)

H] Synthesis of the tricyclic adduct 8

The α,β-unsaturated ester **7** was obtained by a cross metathesis in presence of the Hoveyda's second generation catalyst according to the reported procedure.[11-14]



2-*tert*butoxycarbonyl-6-[(*E*)-4-*tert*butoxy-4-oxobut-2- enyl]- 1-hydroxybicyclo[4,4,0]-decan-7-one <u>8</u>



<u>8</u>

$C_{23}H_{36}O_6$

M = 408.43 g.mol^{-1}

huile incolore

85 % yield

RMN ^{1}H (300MHz, CDCl$_3$) δ 1.39 et 1.48 (2 $\times$ s, 2 $\times$ 9H, H_{13}, H_{14}, H_{15}, H_{21}, H_{22} and H_{23}) ; 1.50-1.60 (m, 3H, H_{3a}, H_8) ; 1.70-1.80 (m, 3H, H_{2a}, H_{7a} and H_{9a}) ; 1.95-2.10 (m, 3H, H_{3b}, H_{7b} and H_{9b}) ; 2.15-2.25 (m, 3H, H_{2b}, H_{4a} and H_{16a}) ; 2.65 (ddd → td, $^2J_{H4b\text{-}H4a}$ = $^3J_{ax\text{-}ax}$ = *14.0Hz*, and $^3J_{ax\text{-}éq}$ = *6.6Hz*, 1H, H_{4b}) ; 2,70 (dd, $^3J_{ax\text{-}ax}$ = *12.7Hz* and $^3J_{ax\text{-}éq}$ = *4.2Hz*, 1H, H_{10}) ; 2,95 (dd, $^2J_{H16b\text{-}16^a}$ = *14.7Hz*, $^3J_{H16b\text{-}H17}$ = *4.2Hz*, 1H, H_{16b}) ; 3.75 (sl, 1H, OH) ; 5.70 (d, $^3J_{transH18\text{-}H17}$ = *16.0Hz*, 1H, H_{18}) ; 6.91 (ddd, $^3J_{transH17\text{-}H18a}$ = *16.0Hz*, $^3J_{H17\text{-}H16a}$ = *5.6Hz* and $^3J_{H17\text{-}H16b}$ = *4.4Hz*, 1H, H_{17}).

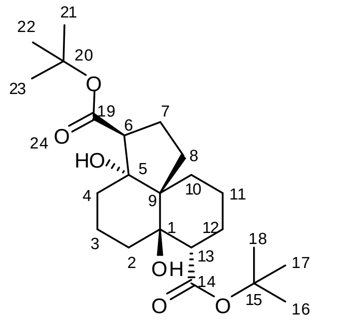
RMN ^{13}C (75MHz, CDCl$_3$) δ 19.7 and 20.7 (C_3 and C_8) ; 24.7 (C_9) ; 28.2 and 28.1 (C_{13}, C_{14}, C_{15}, C_{21}, C_{22} and C_{23}) ; 28.6 and 29.8 (C_2 and C_7) ; 31.2 (C_4) ; 37.4 (C_{16}) ; 48.6 (C_{10}) ; 57.1 (C_6) ; 78.2 (C_1) ; 79.9 (C_{20}) ; 82.5 (C_{12}) ; 124.7 (C_{18}) ; 146.5 (C_{17}) ; 165.9 (C_{19}) ; 173.4 (C_{11}) ; 213.0 (C_5).

MS (+CI): $[M+H]^+$ = 409.5. **HRMS (CI +)** calcd for $C_{23}H_{37}O_6$: 409.2590 found 409.2580.

IR (film, cm^{-1}) ν 3458, 2974, 2935, 2873, 1704, 1647, 1456, 1367, 1257, 1149.

$[\alpha]_D^{20}$ -119.4 (c =2.1 in CH_2Cl_2).

tricyclic adduct 9



9

$C_{23}H_{38}O_6$

M = 410.54 g.mol^{-1}

colourless oil

70% yield

RMN ^{1}H (300MHz, $CDCl_3$) δ 1.19-1.25 (m, 2H, CH_2) ; 1.45 et 1.47 (2 × s, 2 × 9H, H_{16}, H_{17}, H_{18}, H_{21}, H_{22} and H_{23}) ; 1.35-1.50 (m, 3H, CH_2 which H_{3a}) ; 1.54-1.69 (m, 4H, CH_2 which H_4) ; 1.73-1.90 (m, 5H, CH_2 which H_{3b} and H_{8a}) ; 1.95-2.16 (m, 2H, CH_2 which H_{8b}) ; 2.55 (dd, $^3J_{ax\text{-}ax} = 12.9Hz$ and $^3J_{ax\text{-}éq} = 3.9Hz$, 1H, H_2) ; 3.62 (dd → t, $^3J = 9.8Hz$, 1H, H_9) ; 3.89 (sl, 2H, 2×OH).

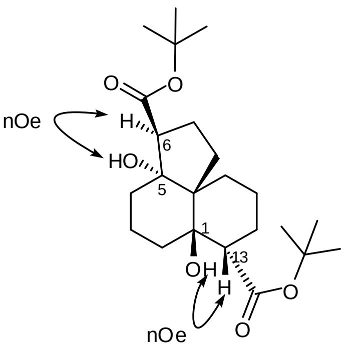
RMN ^{13}C (75MHz, $CDCl_3$) δ 18.1 and 21.9 (C_4 and C_{12}) ; 25.8 and 27.2 (C_5 and C_7) ; 28.1 and 28.2 (C_{16}, C_{17}, C_{18}, C_{21}, C_{22} and C_{23}) ; 29.1 and 29.8 (C_3 and C_8) ; 31.2 and 31.6 (C_{11} and C_{13}) ; 49.9 (C_9) ; 51.2 (C_2) ; 54.3 (C_6) ; 75.4 (C_{10}) ; 80.8 (C_1) ; 81.9 and 82.9 (C_{15} and C_{20}) ; 174.4 and 176.3 (C_{14} and C_{19}).

MS (+CI) : $[M+H]^+$ = 411.2. **HRMS (CI +)** calcd for $C_{23}H_{39}O_6$: 411.2747 found 411.2741.

IR (film, cm^{-1}) ν 3535, 3452, 2970, 2935, 2869, 1735, 1712, 1450, 1365, 1217, 1153.

$[\alpha]_D^{20}$ -115.4 (c = 0.8 in CH_2Cl_2).

The relative configurations at C_6 and C_{13} were determined by nOe experiments.



I] Spectra

table 1, entries 1-6

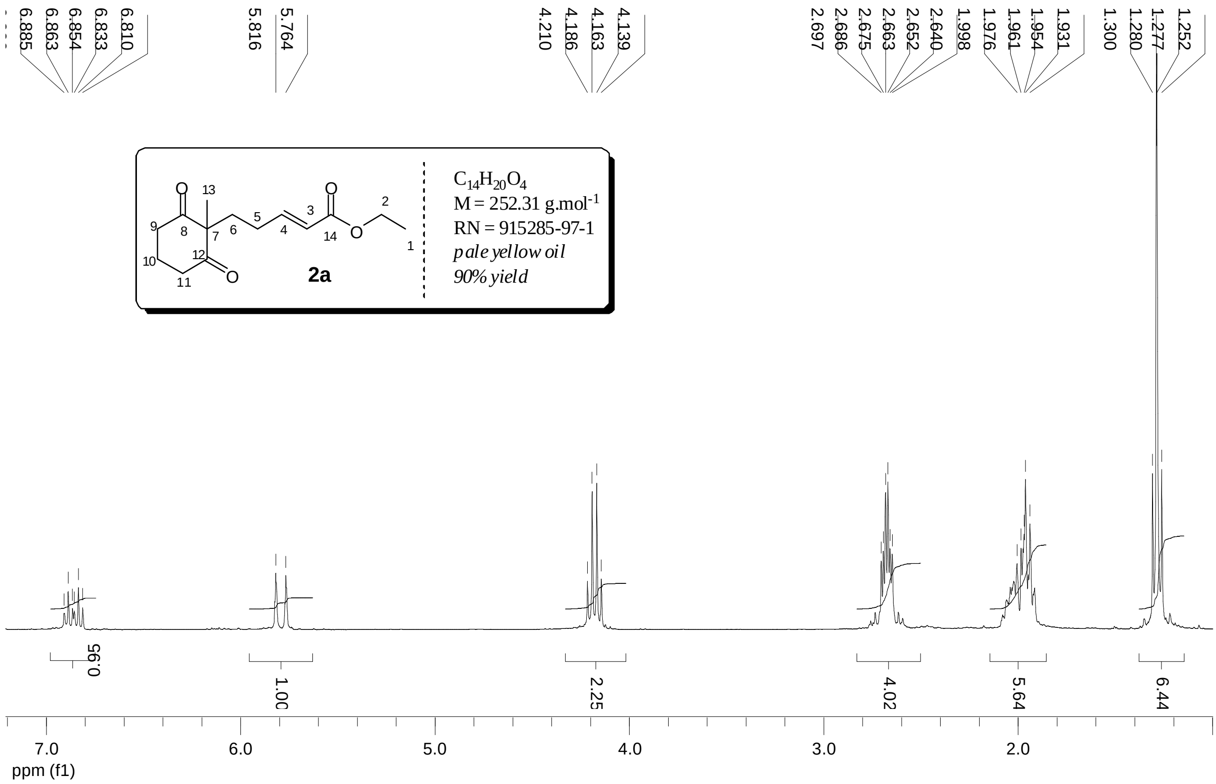
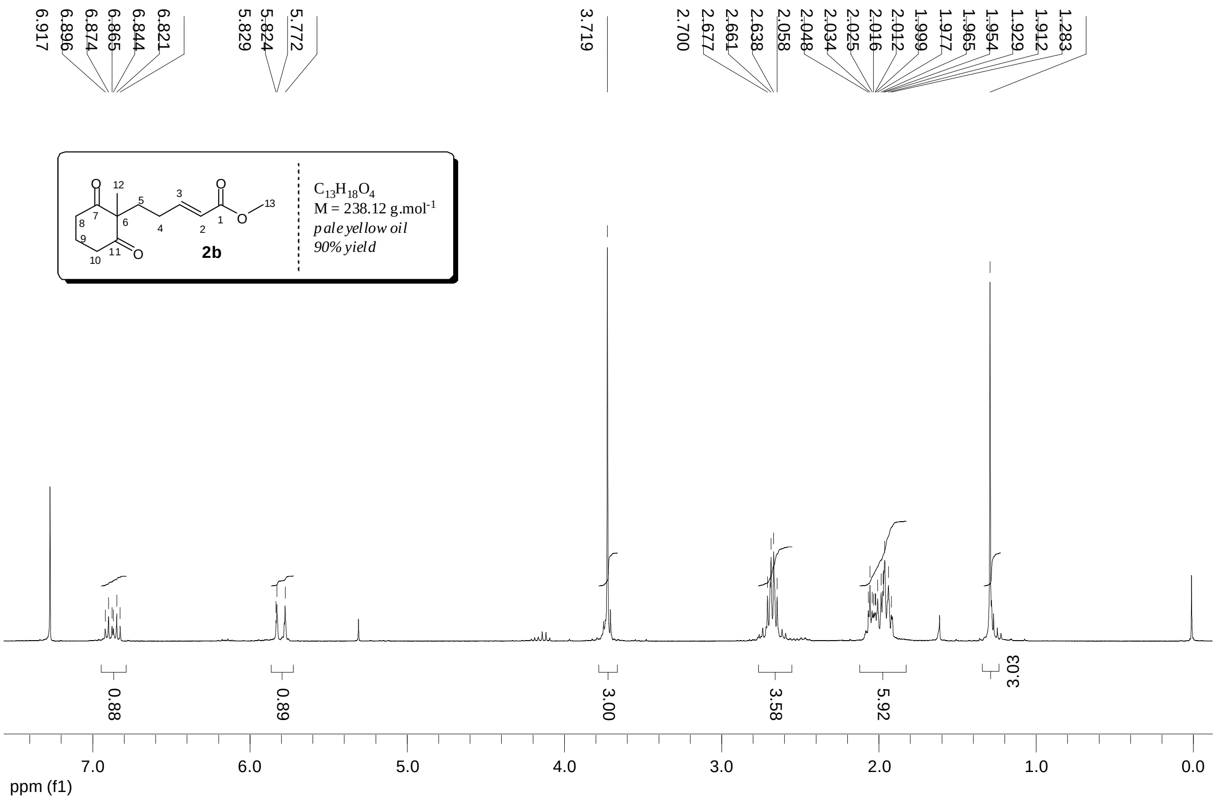


table 1, entry 7



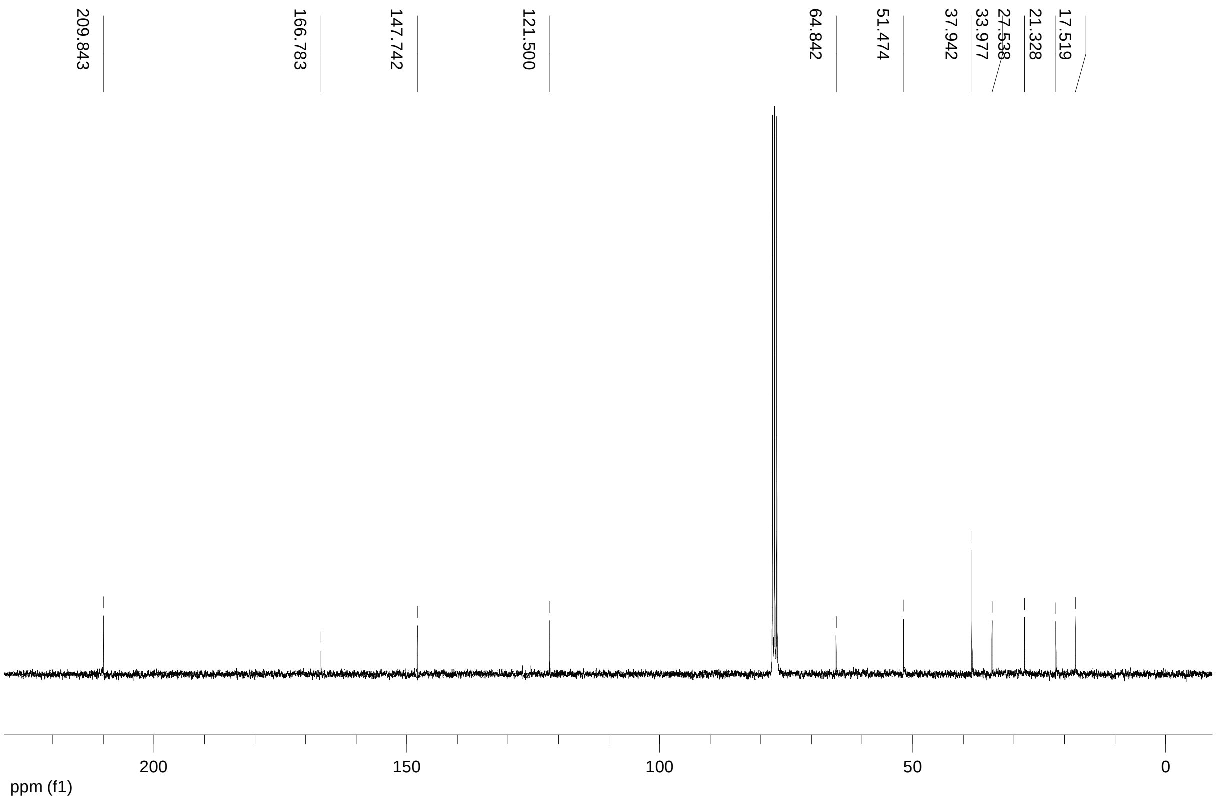
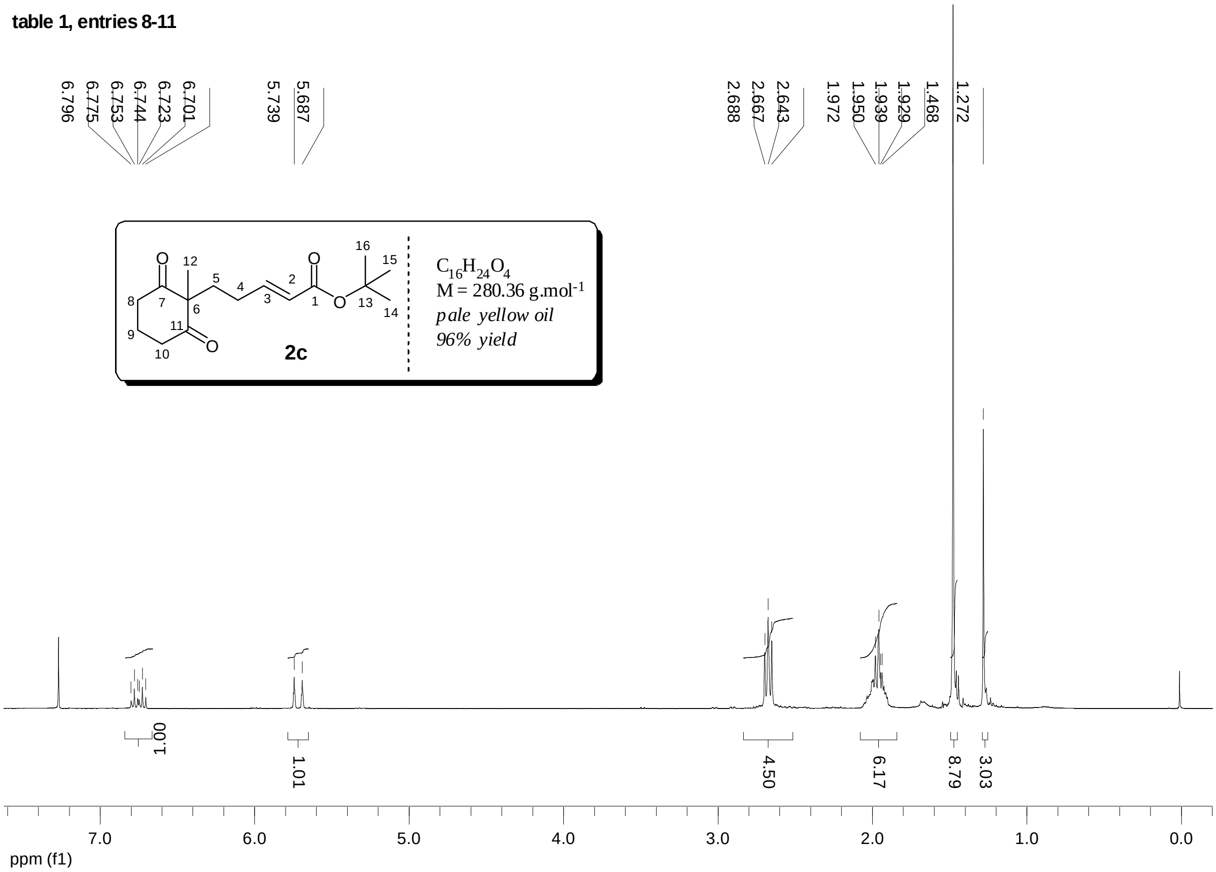


table 1, entries 8-11



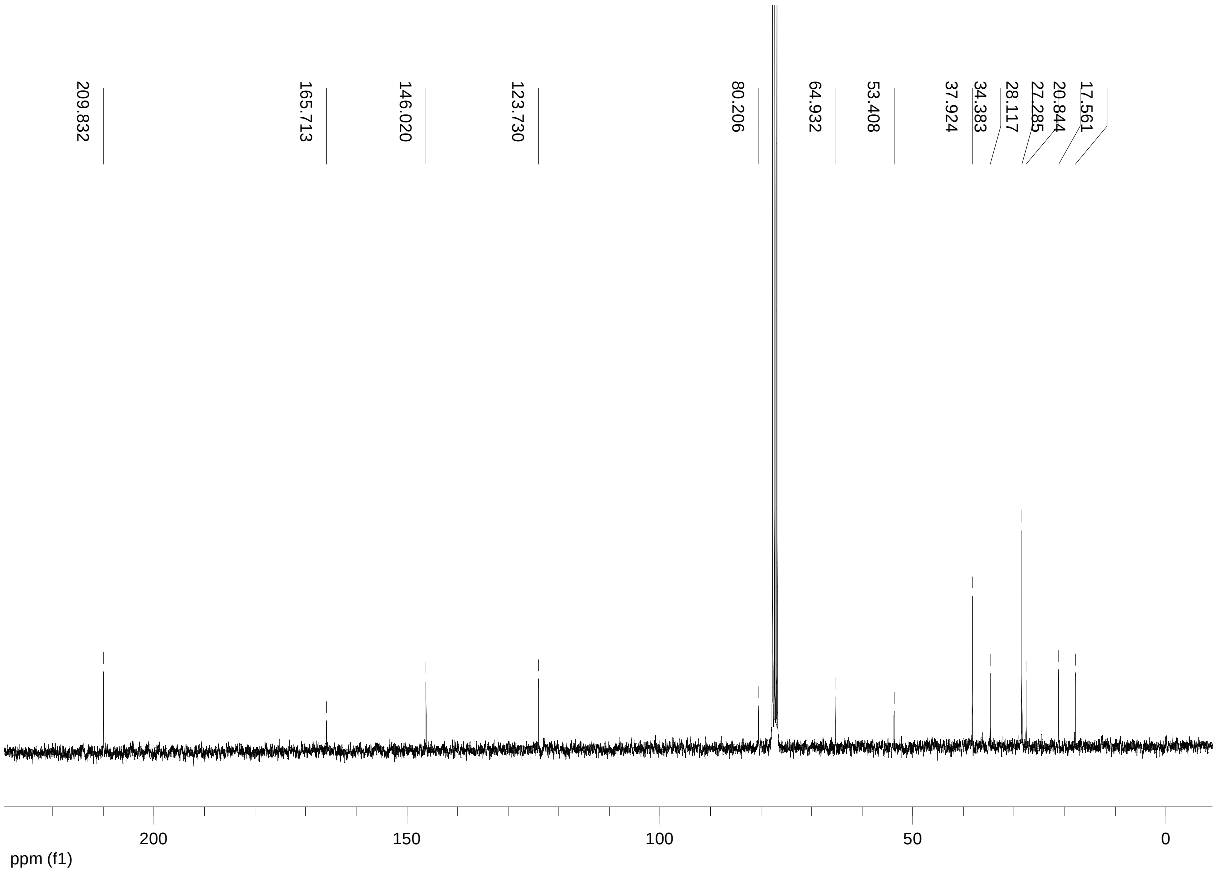
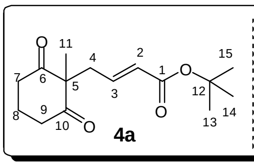
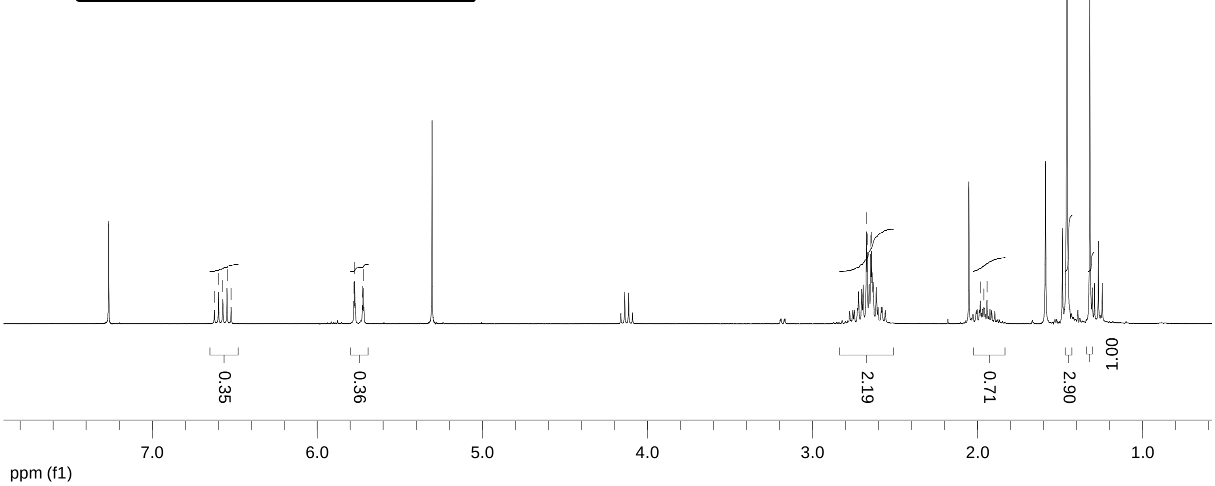


table 2, entry 2



$C_{15}H_{22}O_4$
M = 266.33 g.mol^{-1}
pale yellow oil
97% yield



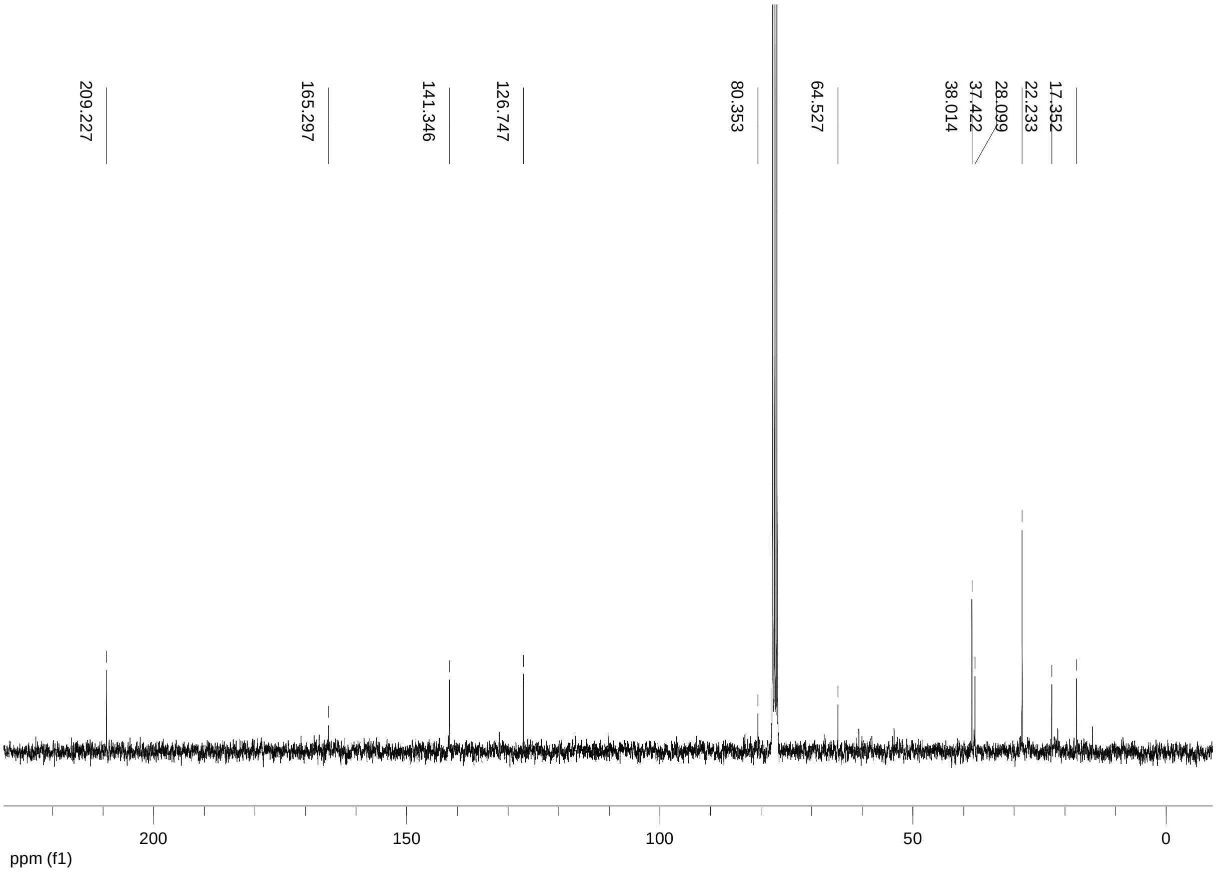
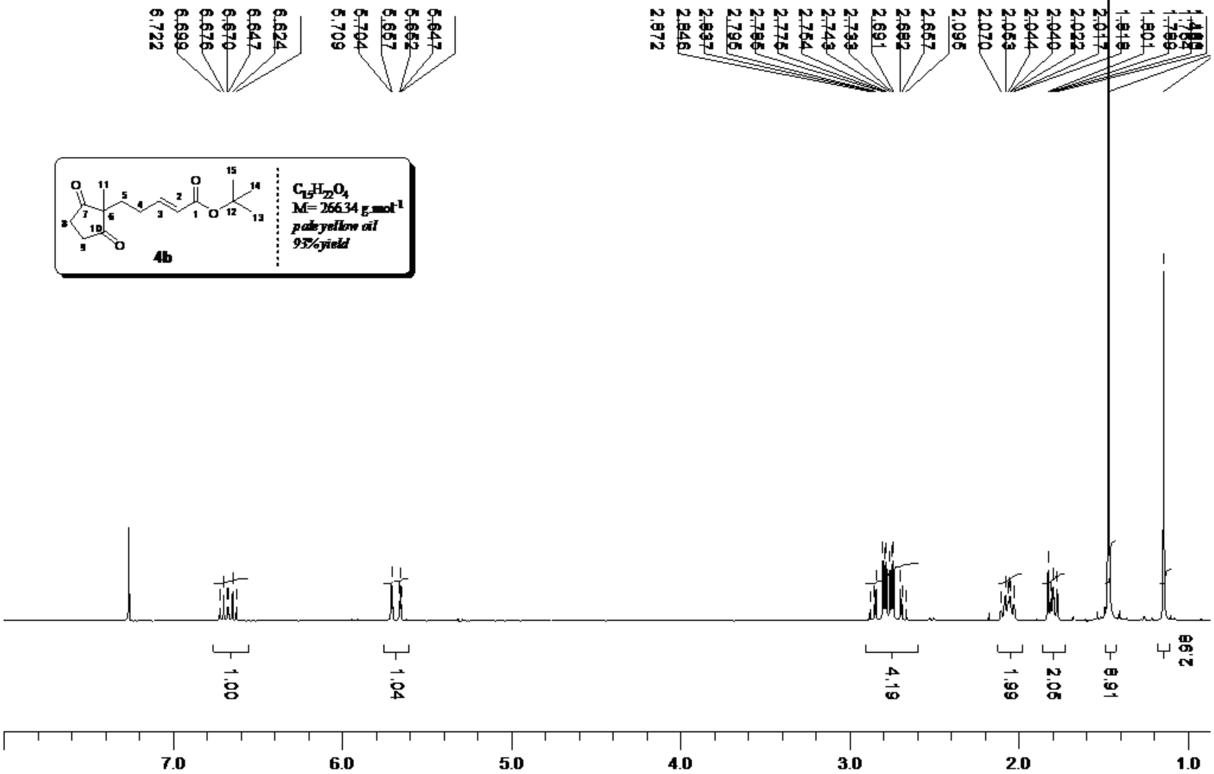


table 2, entry 3



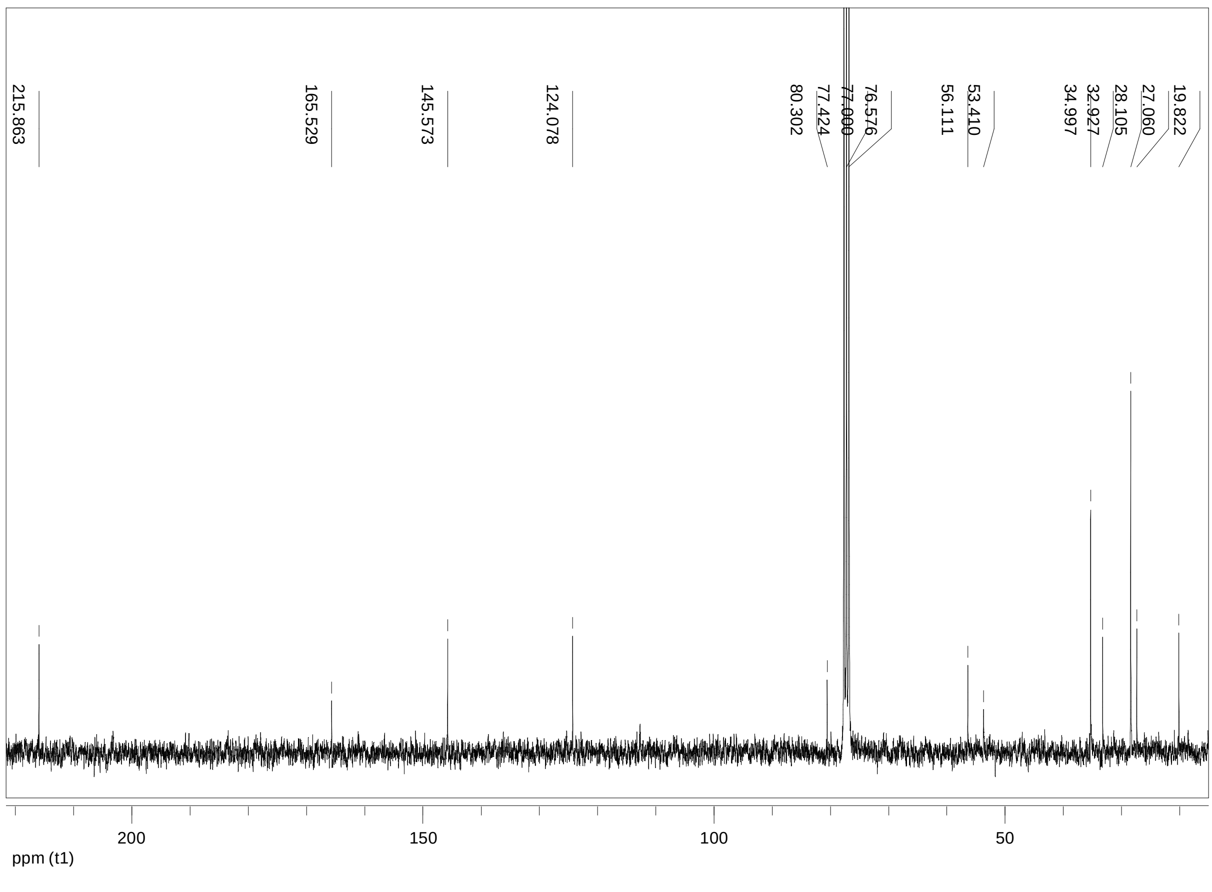
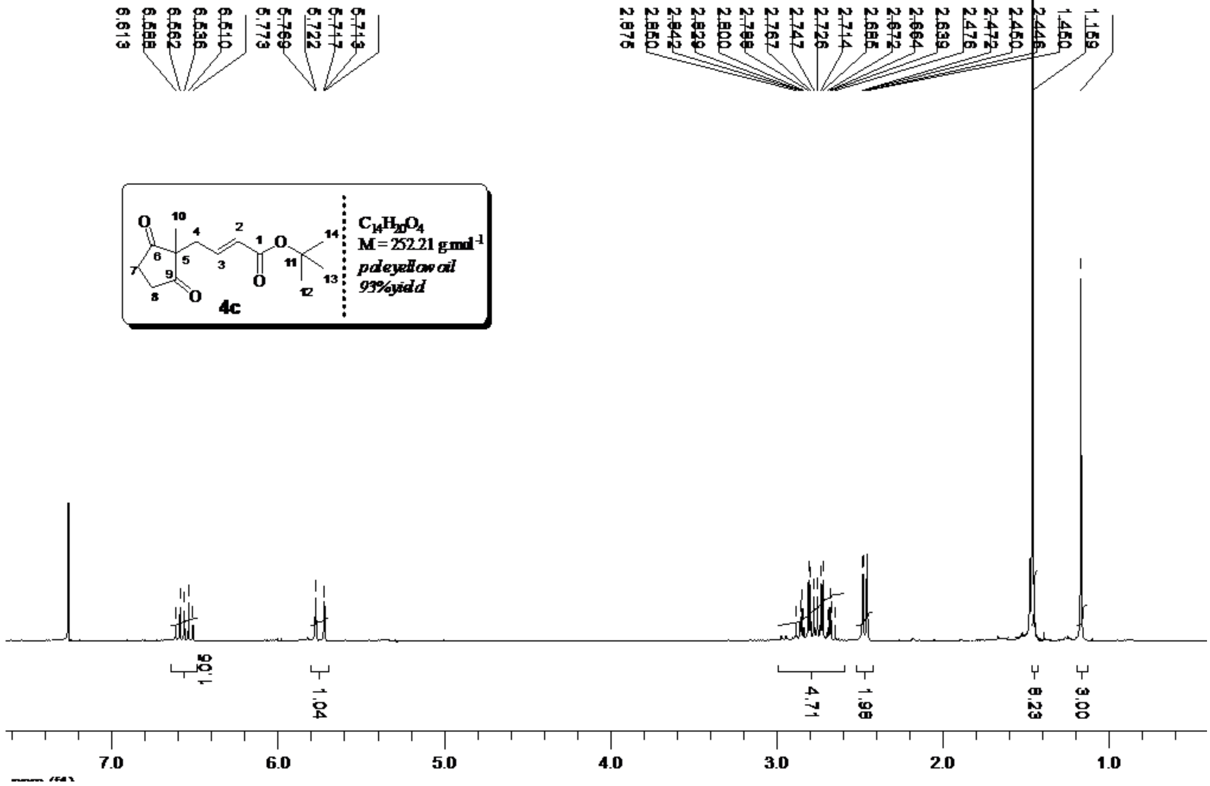


table 2, entry 4



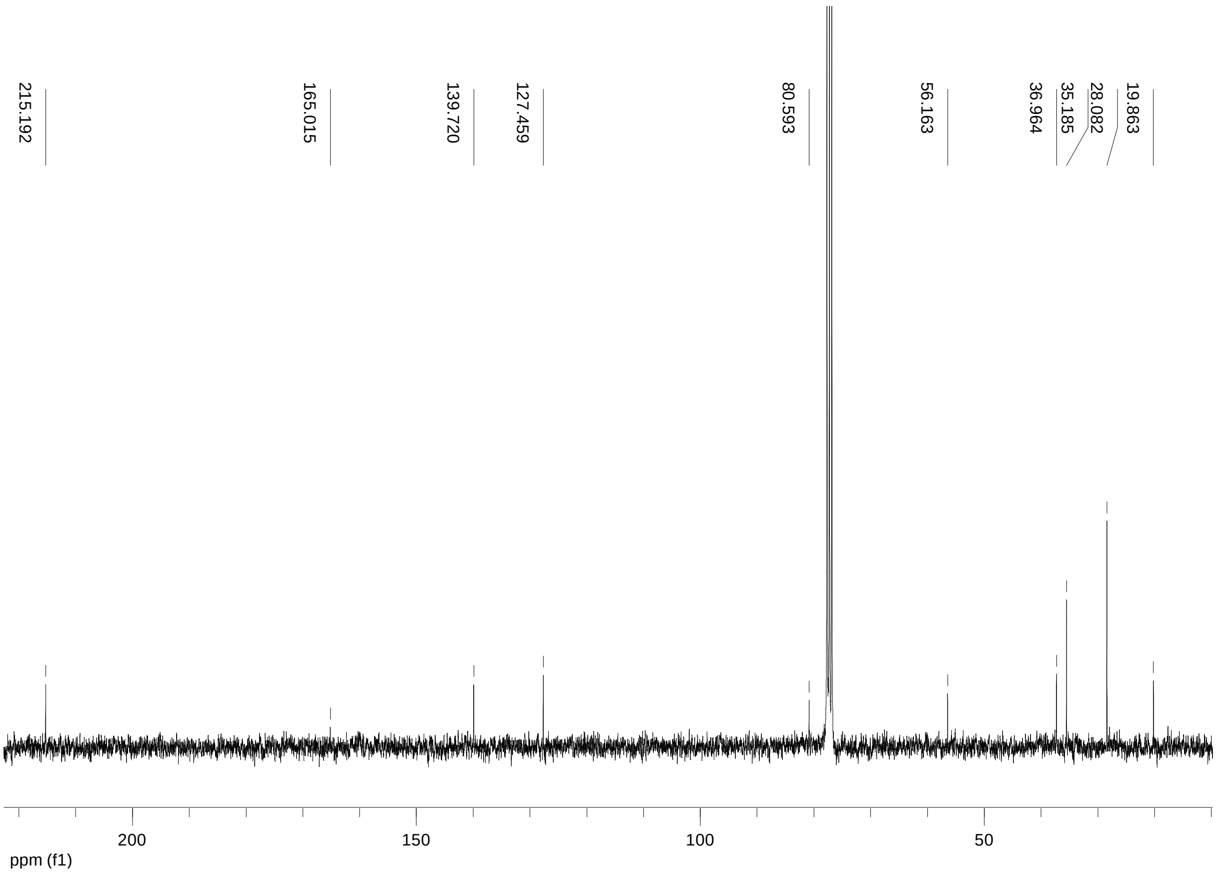
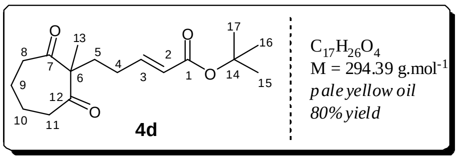
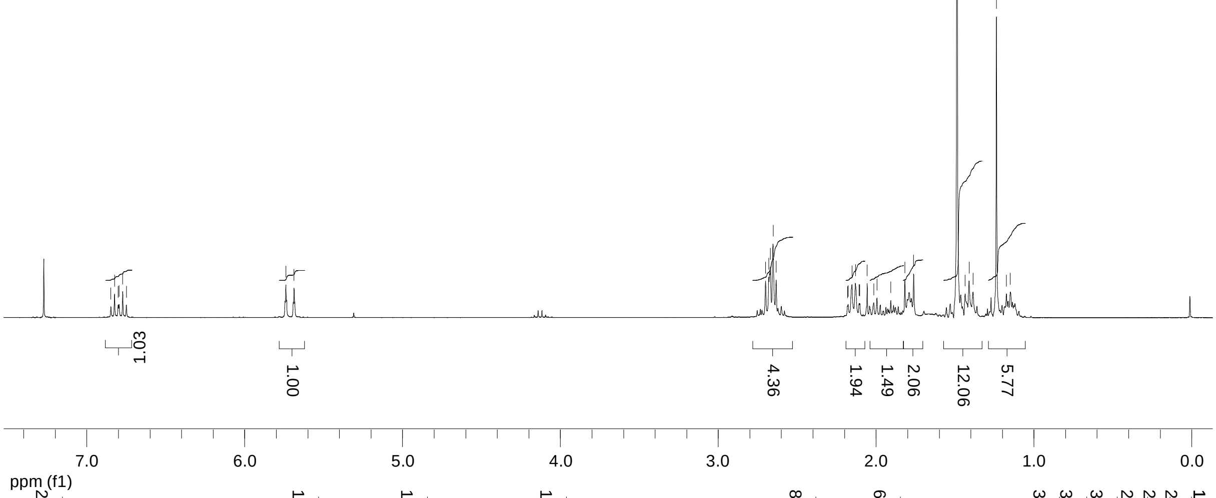


table 2, entry 5





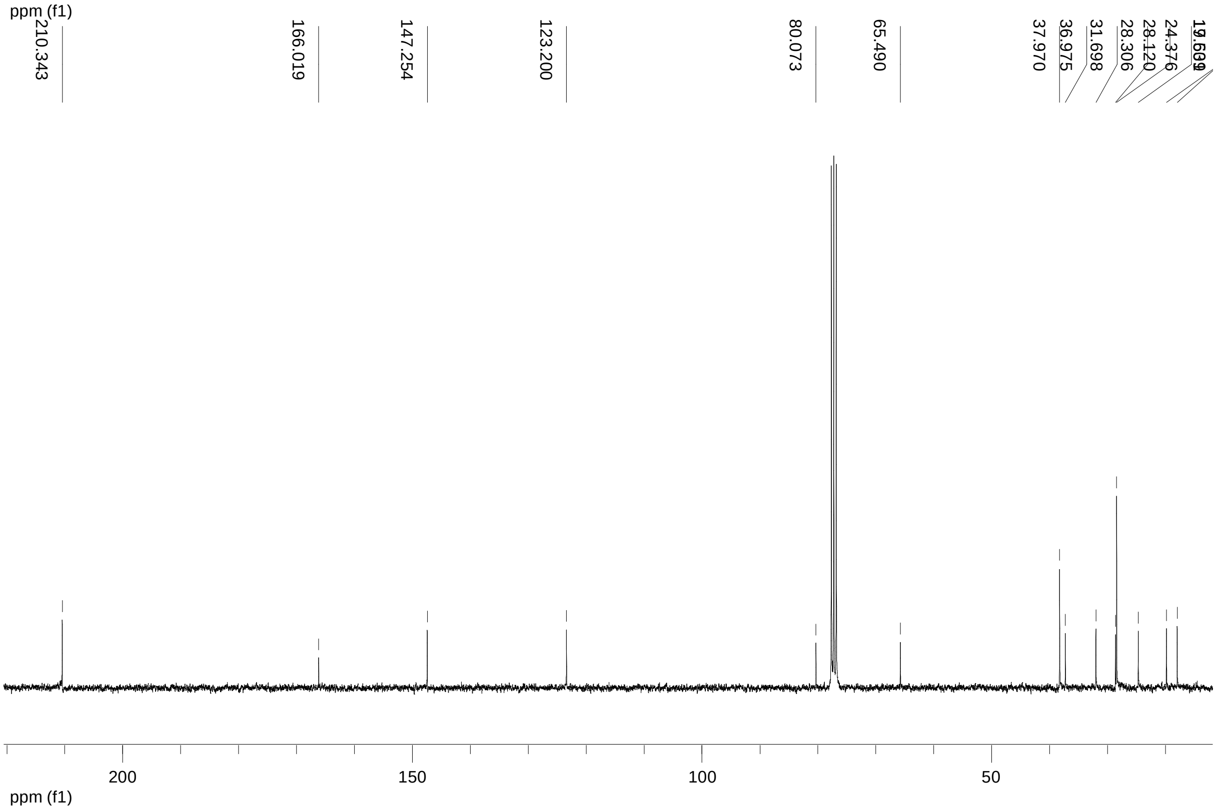
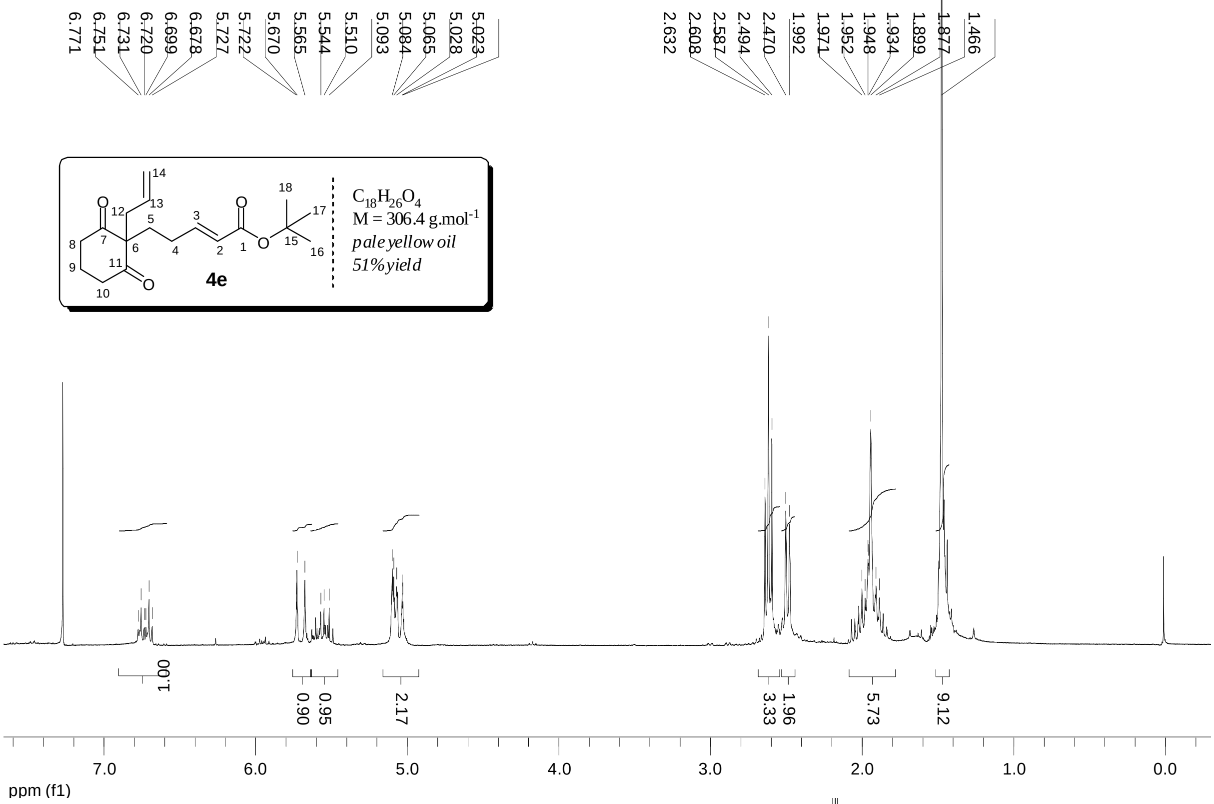


table 2, entry 6



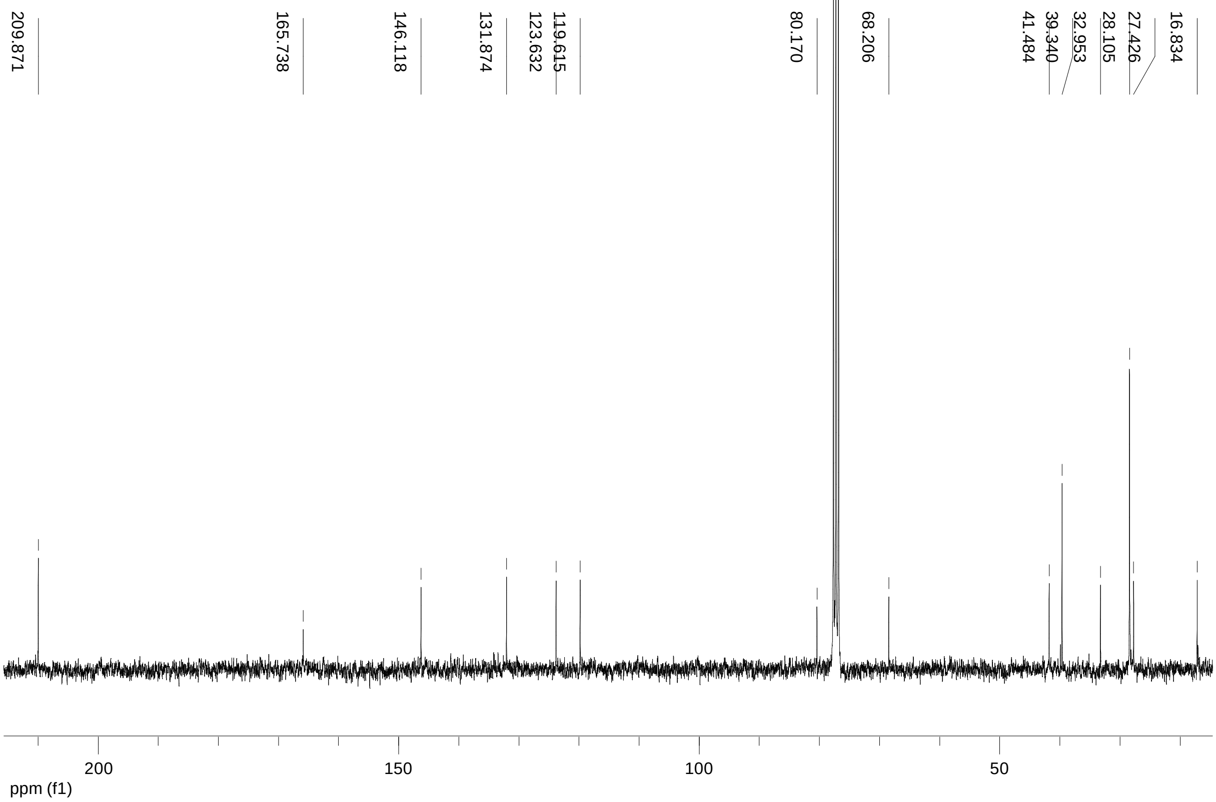
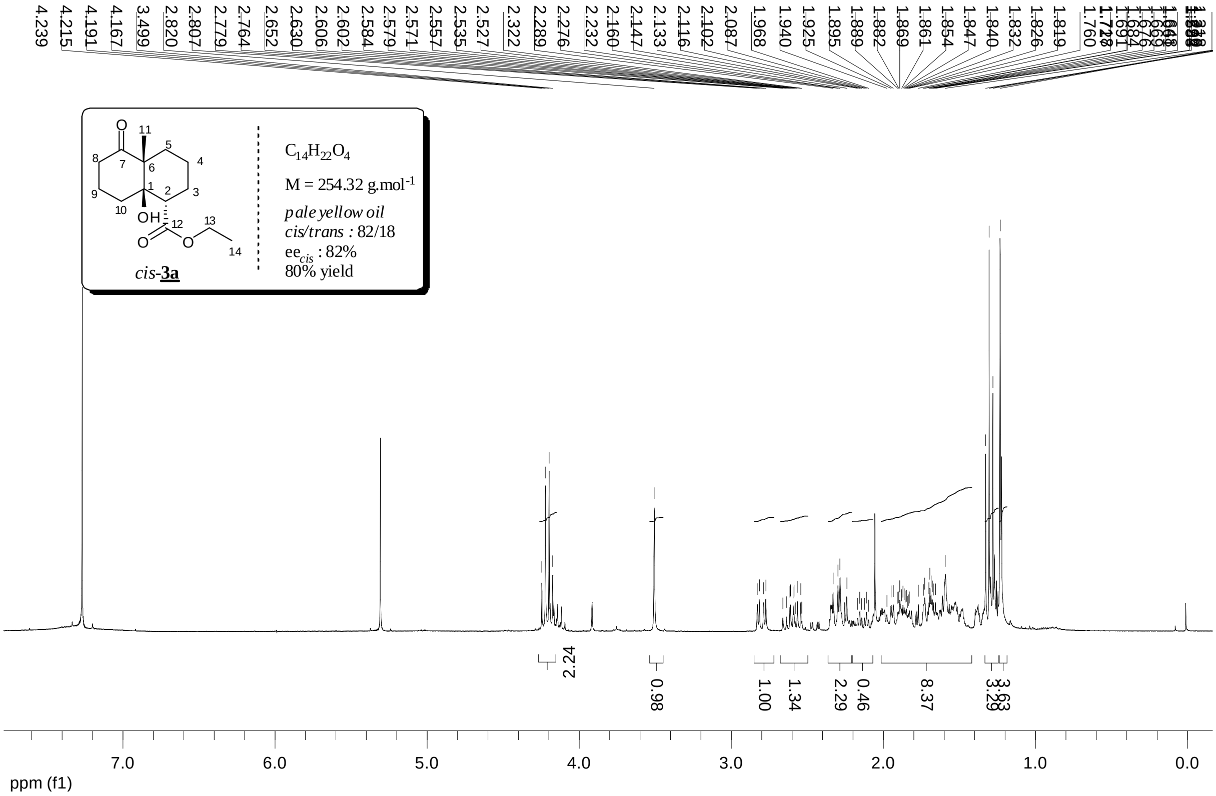


table1, entries 1-6



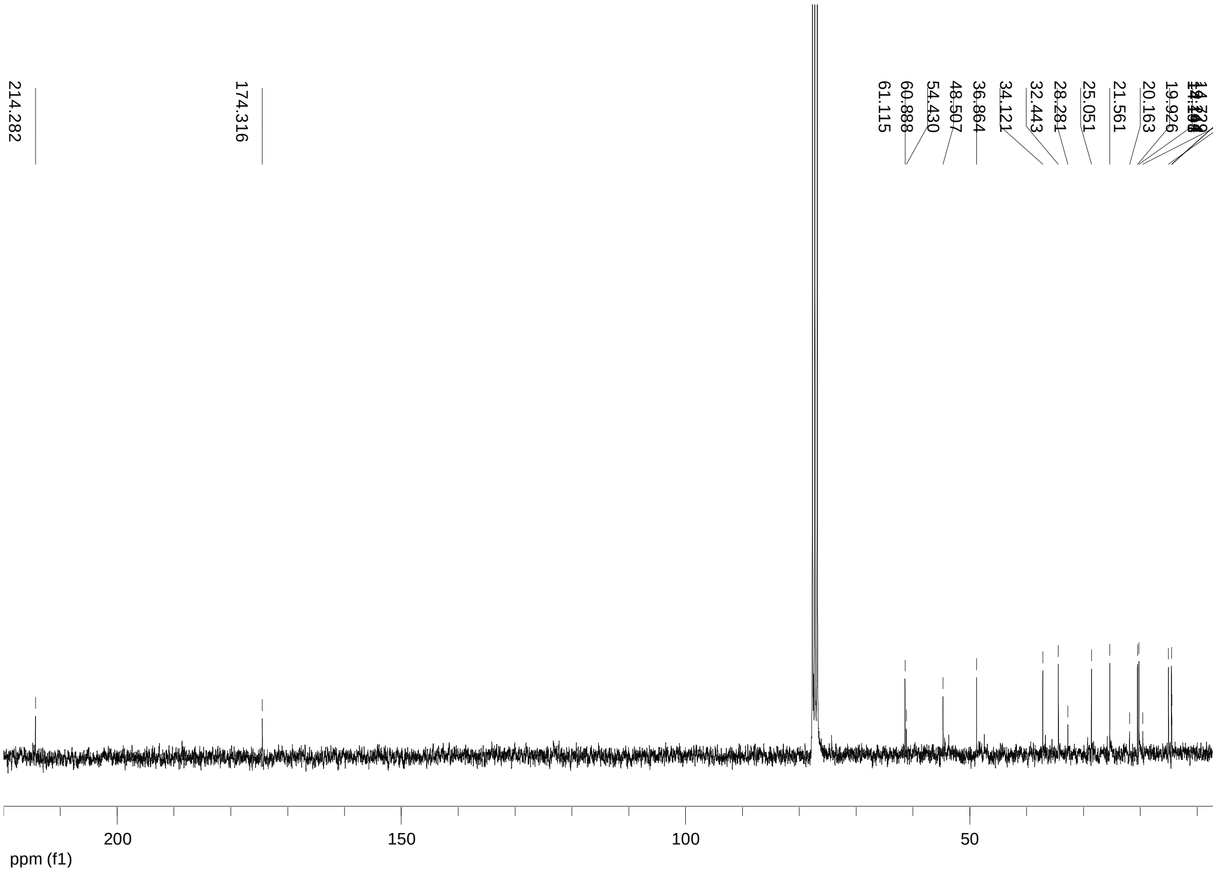
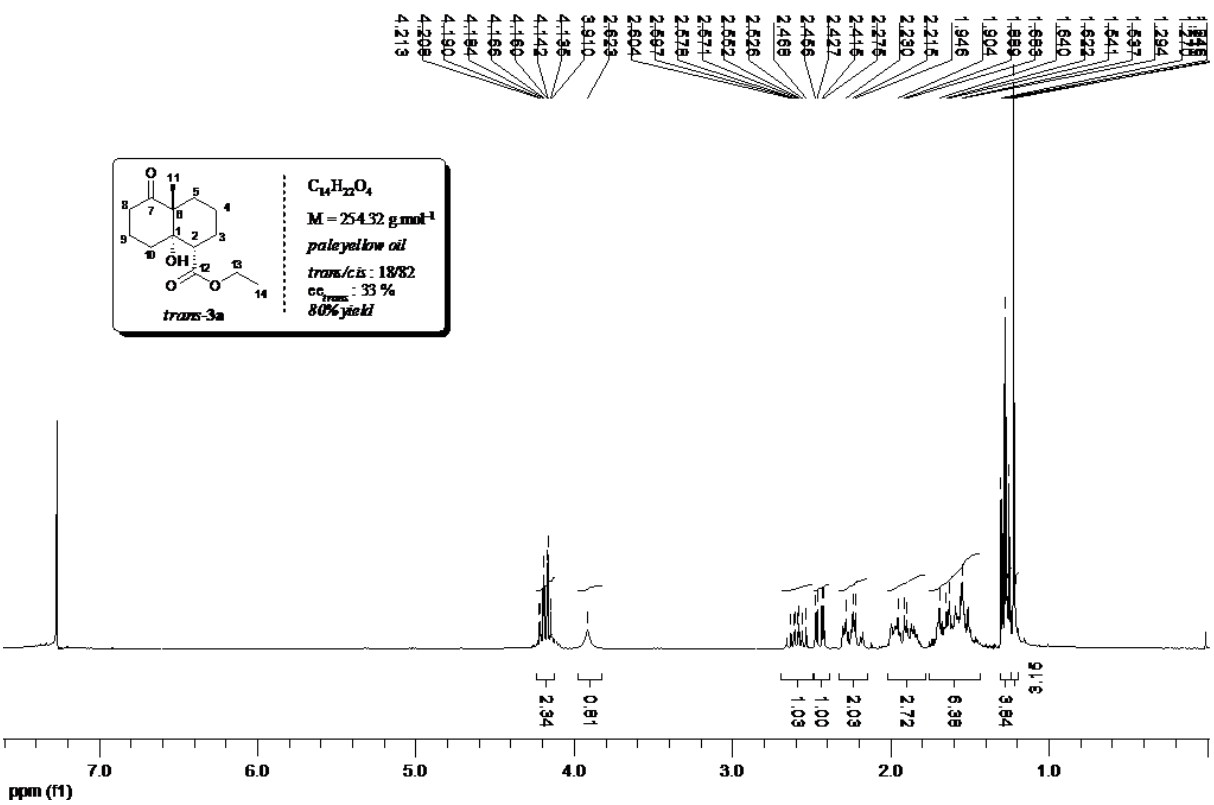
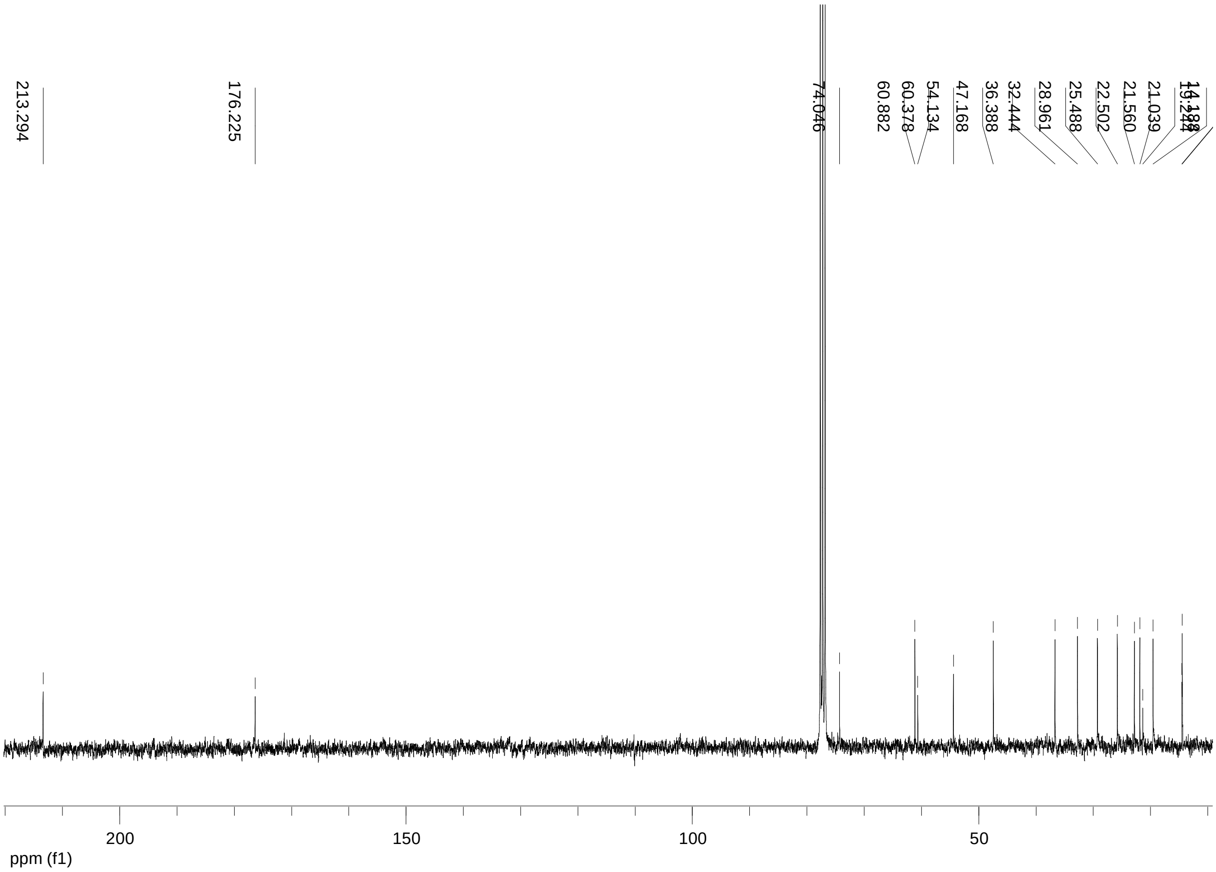


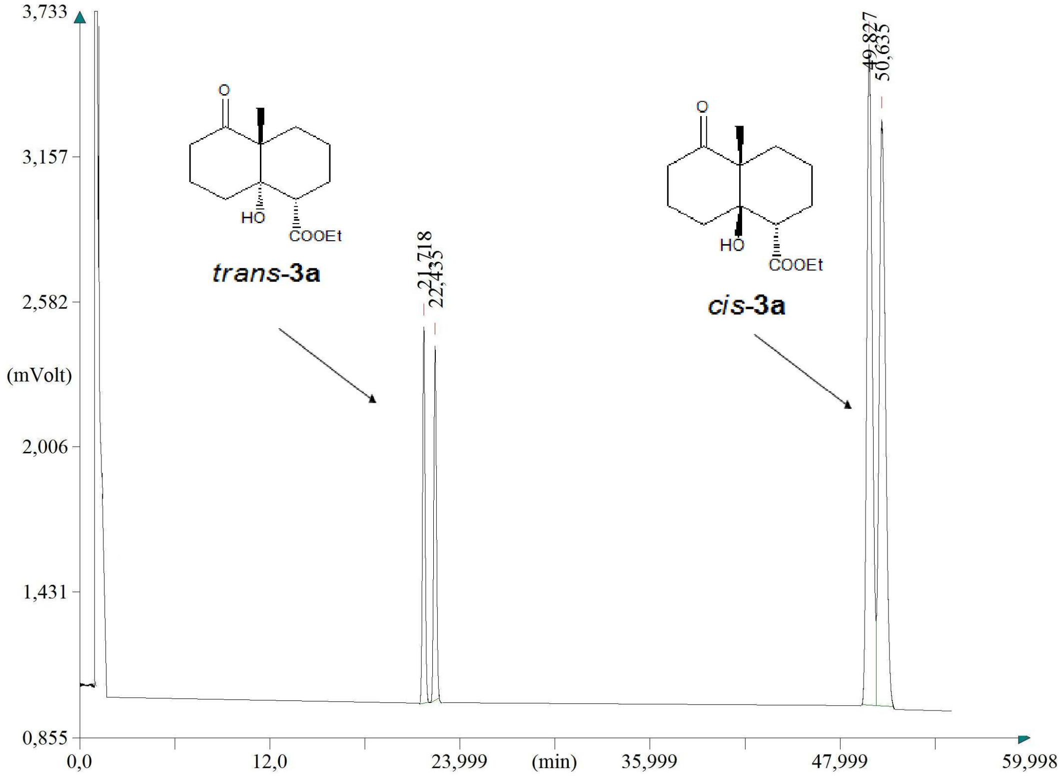
table 1, entries 1-6





Title Racemic mixture

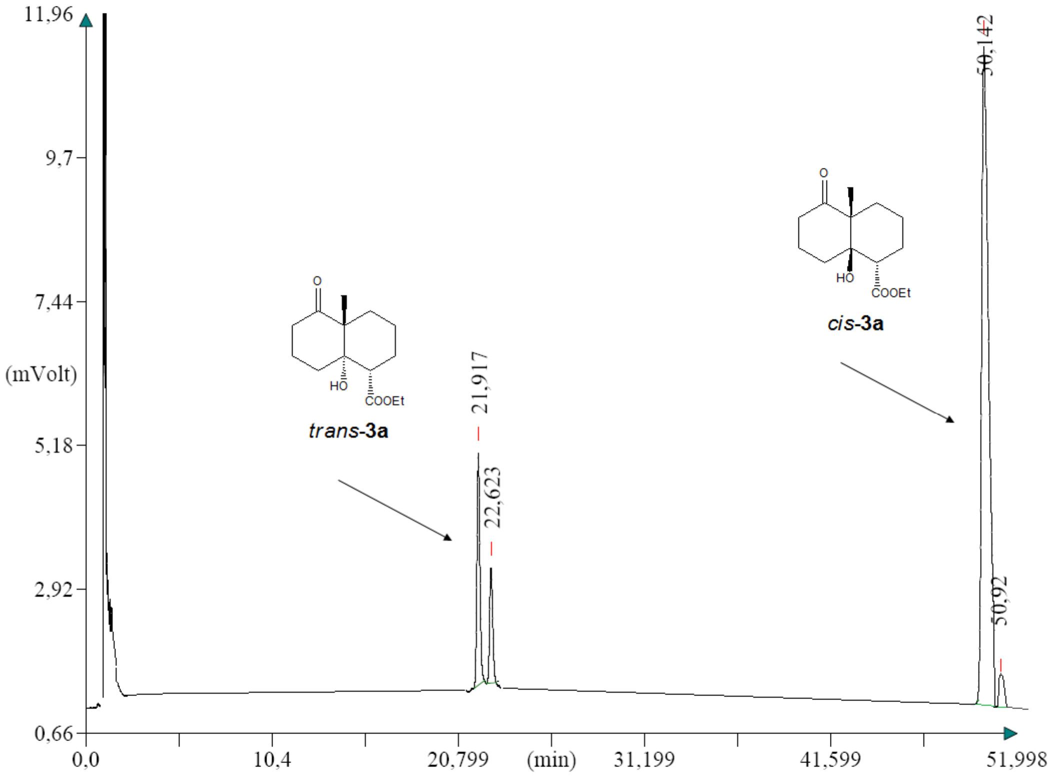
Method filename: G:\Julia\cyclisations\03072006\Rntandem.mth
Method name: Rn tandem
GC method:
Sample ID: jd519f2
Chromatogram filename: G:\Julia\cyclisations\03072006\jd519f2-3.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	21.718	168014	10.406	Manual integ.	
2	22.435	165788	10.268	Manual integ.	
3	49.827	636612	39.429	Manual integ.	
4	50.635	644176	39.897	Manual integ.	
		1614589			

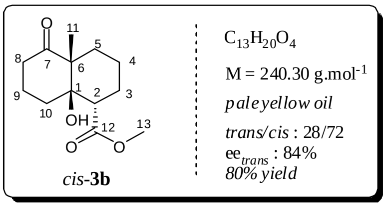
Title

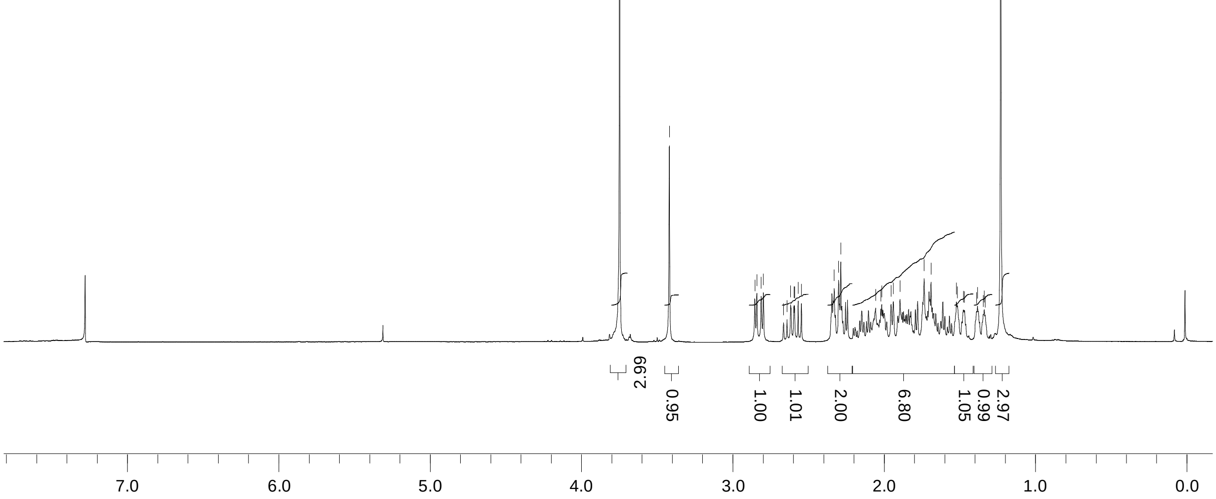
Method filename: G:\Julia\cyclisations\12072006\Rntandem.mth
Method name: Rn tandem
GC method:
Sample ID: JD570
Chromatogram filename: JD570-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type
1	21.917	435586	12.101	Manual inte
2	22.623	218861	6.080	Manual inte
3	50.142	2831143	78.651	Manual inte
4	50.920	114022	3.168	Manual inte
		3599612		

table 1, entry 7





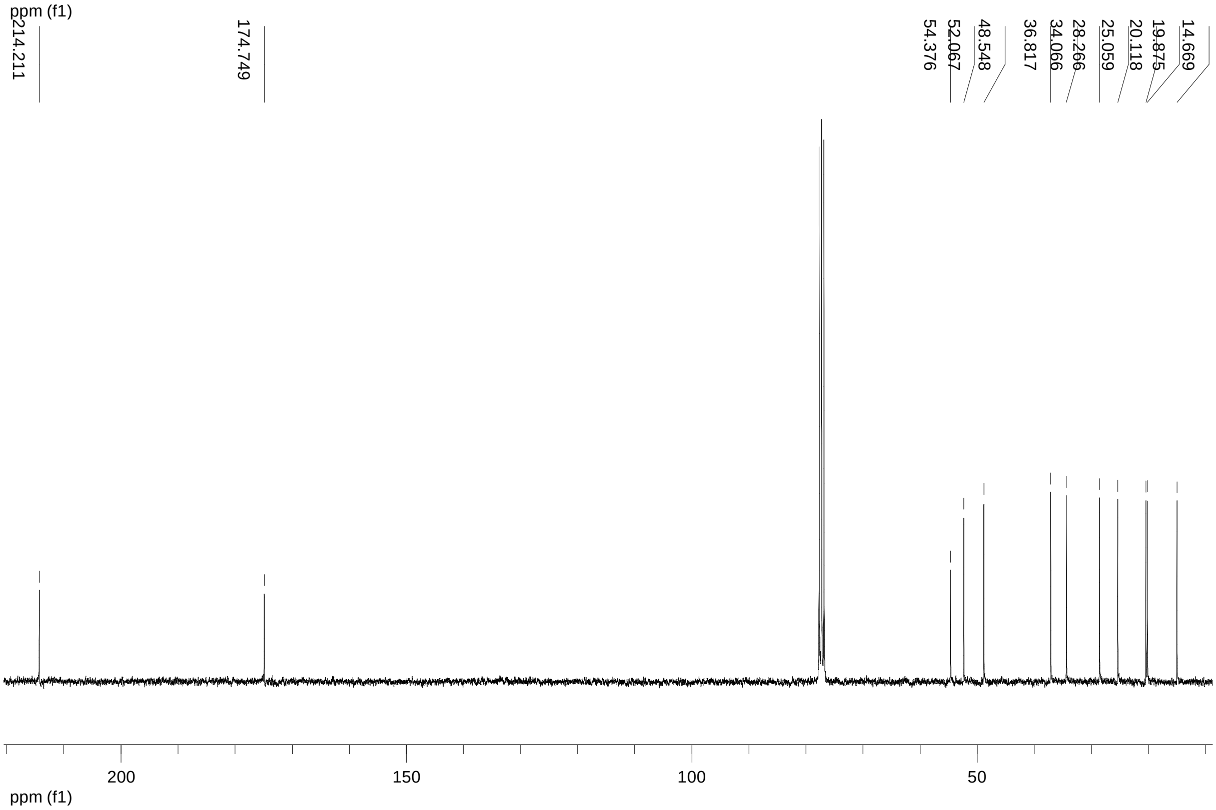
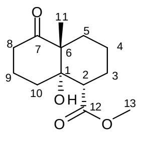


table 1, entry 7



trans-**3b**

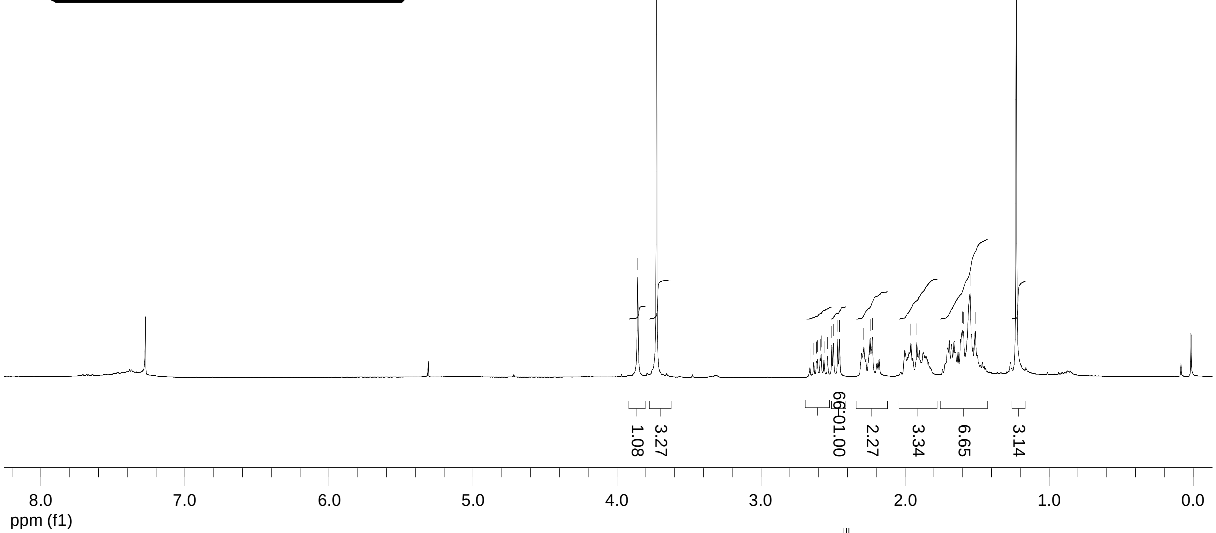
$C_{13}H_{20}O_4$

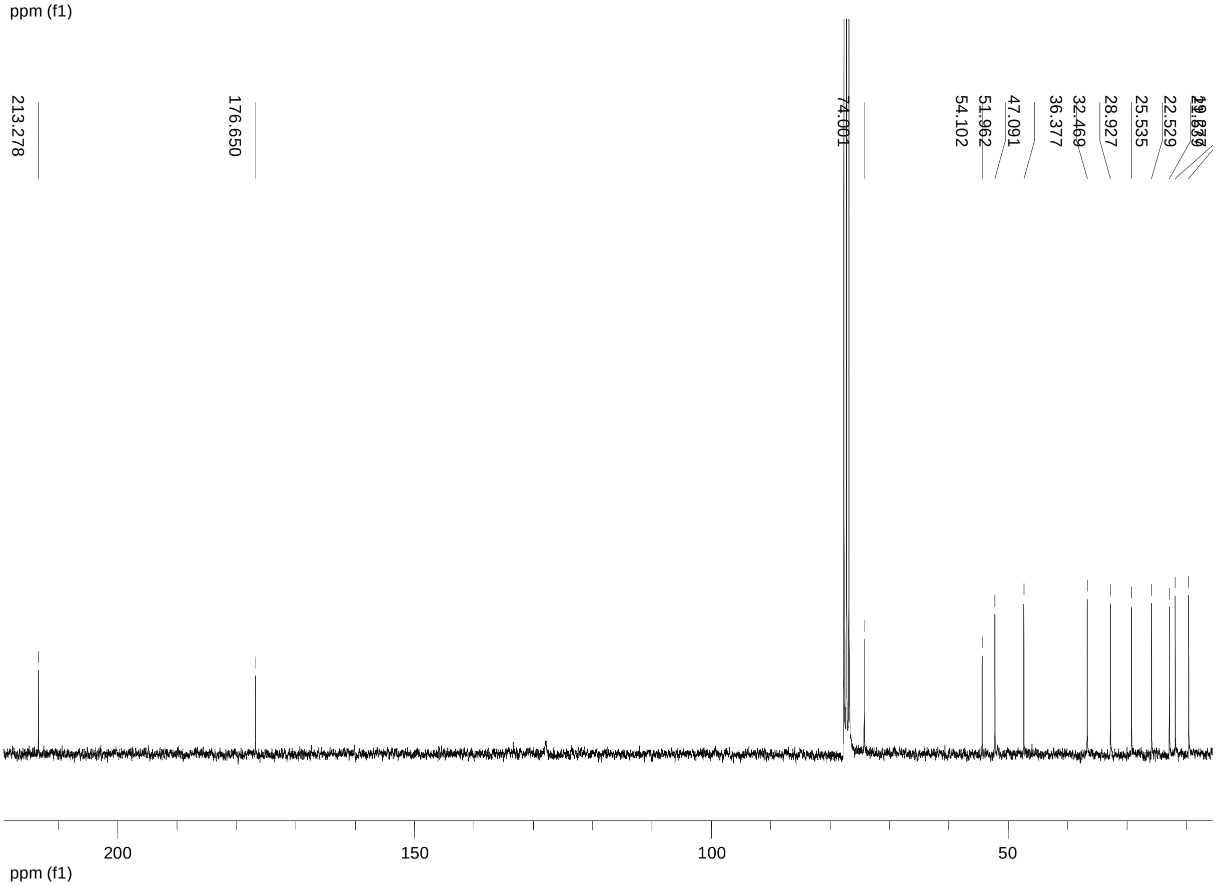
M = 240.30 g.mol^{-1}

pale yellow oil

trans/cis : 28/72

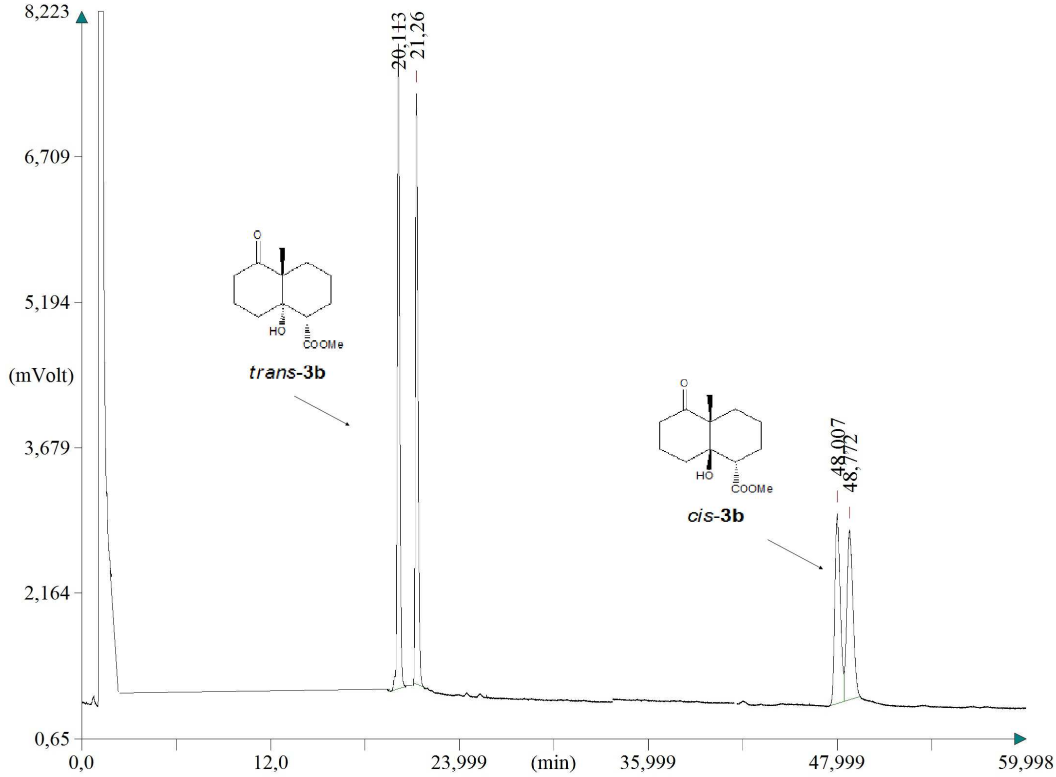
ee_{trans} : 60%





Title Racemic mixture

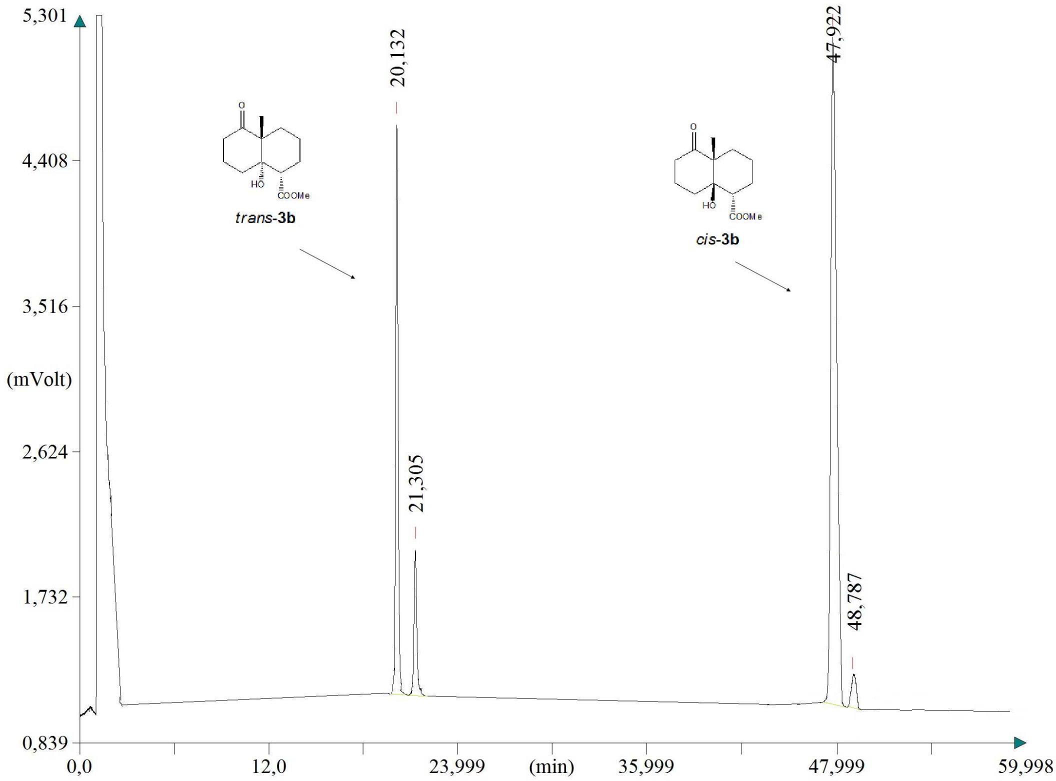
Method filename:	G:\Julia\cyclisations\16032008\Rntandem.mth
Method name:	Rn tandem
GC method:	iso150
Sample ID:	jd765rac (# 22)
Chromatogram filename:	jd765rac-2.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	20.113	735691	30.690	Manual integ.	
2	21.260	709174	29.584	Manual integ.	
3	48.007	473934	19.771	Manual integ.	
4	48.772	478380	19.956	Manual integ.	
		2397179			

Title

Method filename: G:\Julia\cyclisations\16032008\Rntandem.mth
Method name: Rn tandem
GC method: iso150
Sample ID: jd765 (# 23)
Chromatogram filename: jd765-2.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	20.132	348444	22.367	Manual integ.	
2	21.305	92904	5.963	Manual integ.	
3	47.922	1025832	65.848	Manual integ.	
4	48.787	90700	5.822	Manual integ.	
		1557880			

table 1, entries 8-11

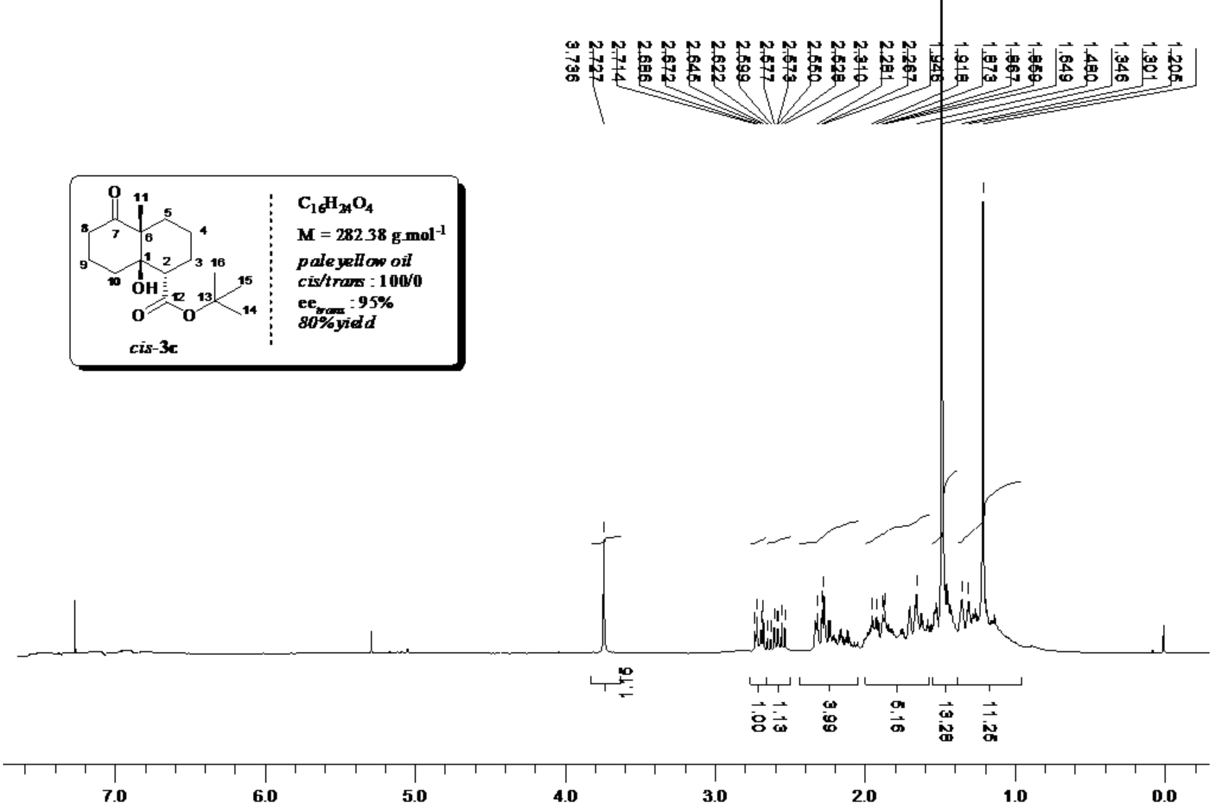
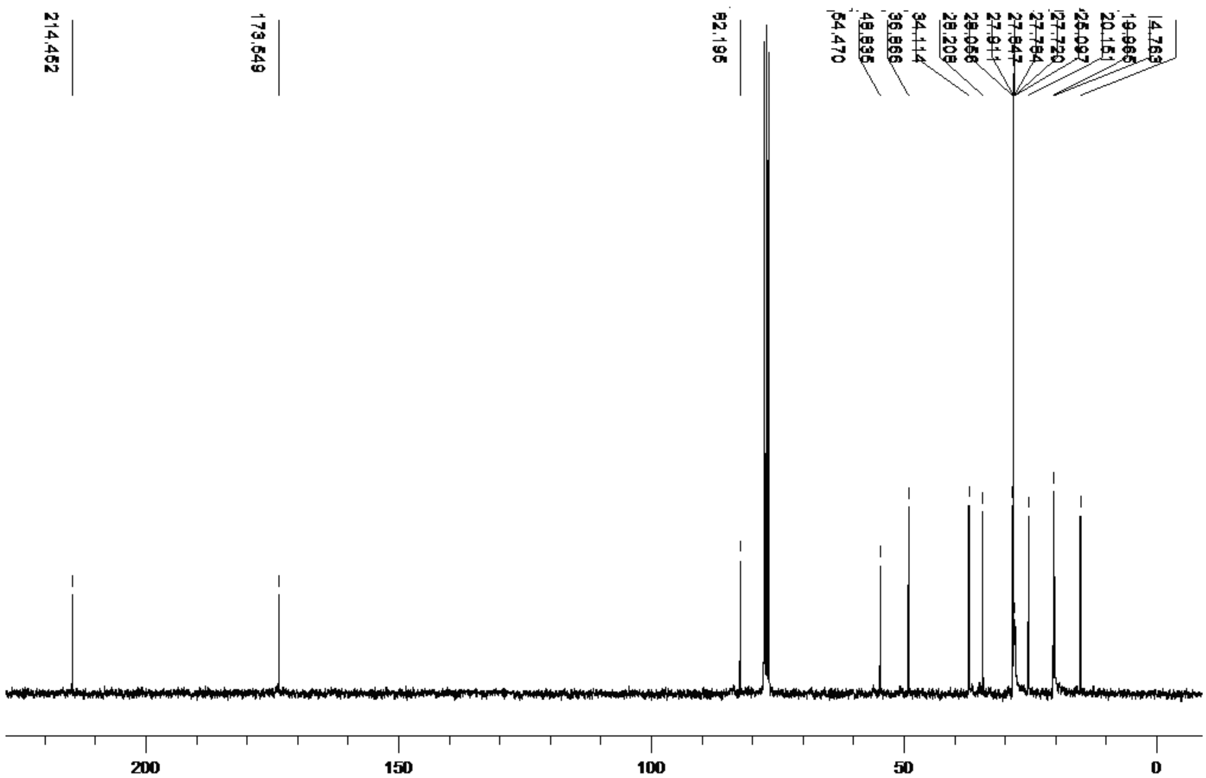
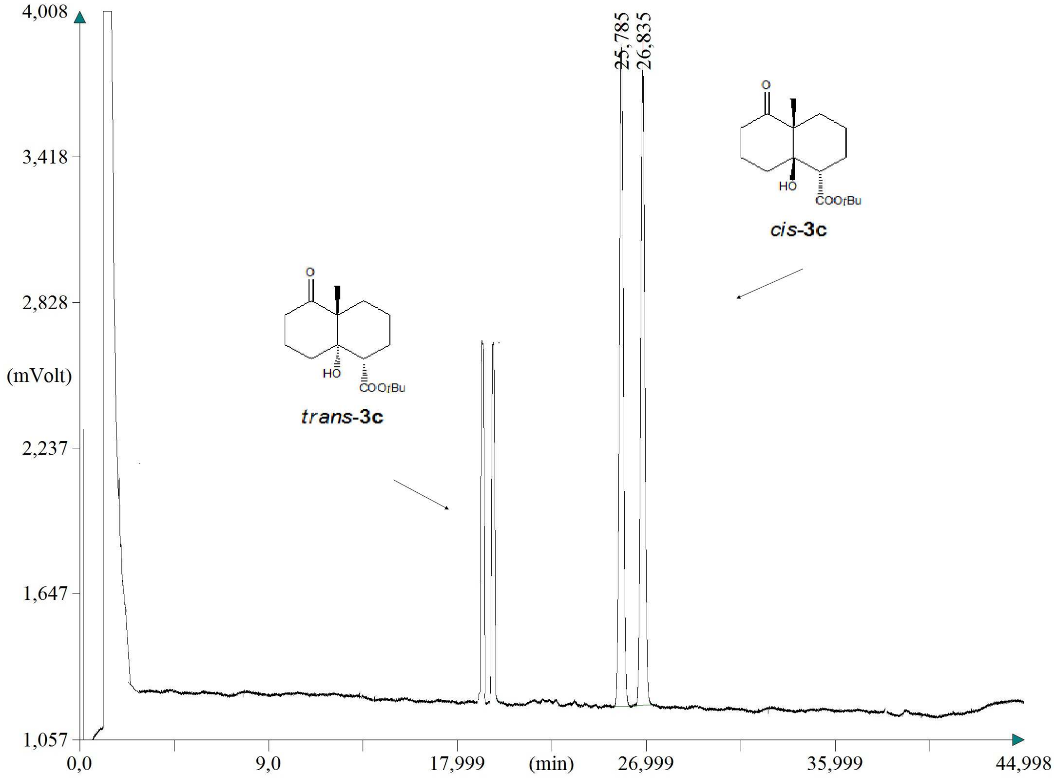


table 1, entries 8-11



Title Racemic mixture

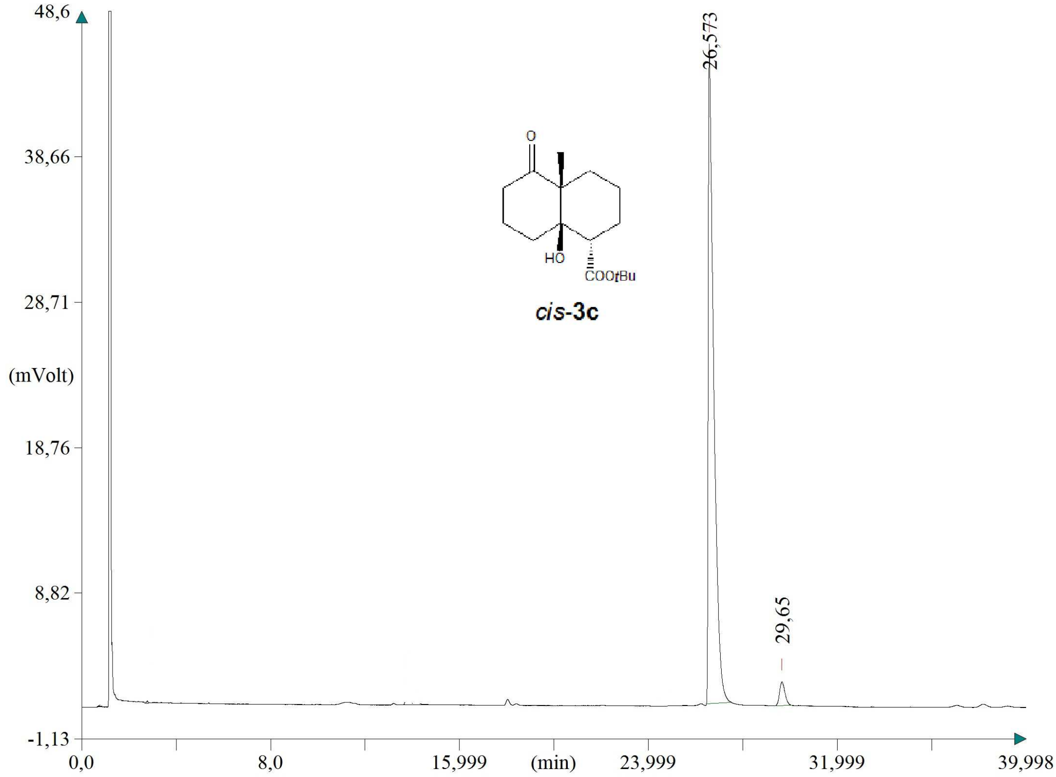
Method filename: G:\Julia\cyclisations\01082007\Rntandem.mth
Method name: Rn tandem
GC method: iso 160
Sample ID: jd666
Chromatogram filename: G:\Julia\cyclisations\01082007\1§jd666f1-2.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	25.785	364067	50.241	Manual integ.	
2	26.835	360575	49.759	Manual integ.	
		724642			

Title

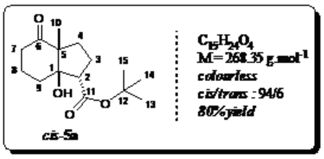
Method filename: G:\Julia\cyclisations\12102006\Rntandem.mth
Method name: Rn tandem
GC method:
Sample ID: jd583f3
Chromatogram filename: G:\Julia\cyclisations\12102006\jd583f3.dat

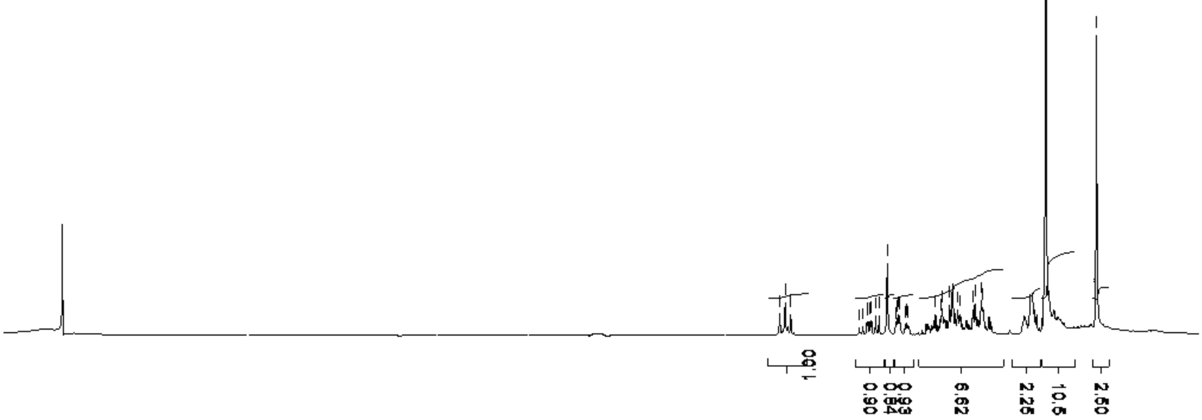


Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	26.573	7231031	96.528	Manual integ.	
2	29.650	260056	3.472	Manual integ.	
		7491087			

Warning Chromatogram has been subjected to manual integration.

table 2, entry 2





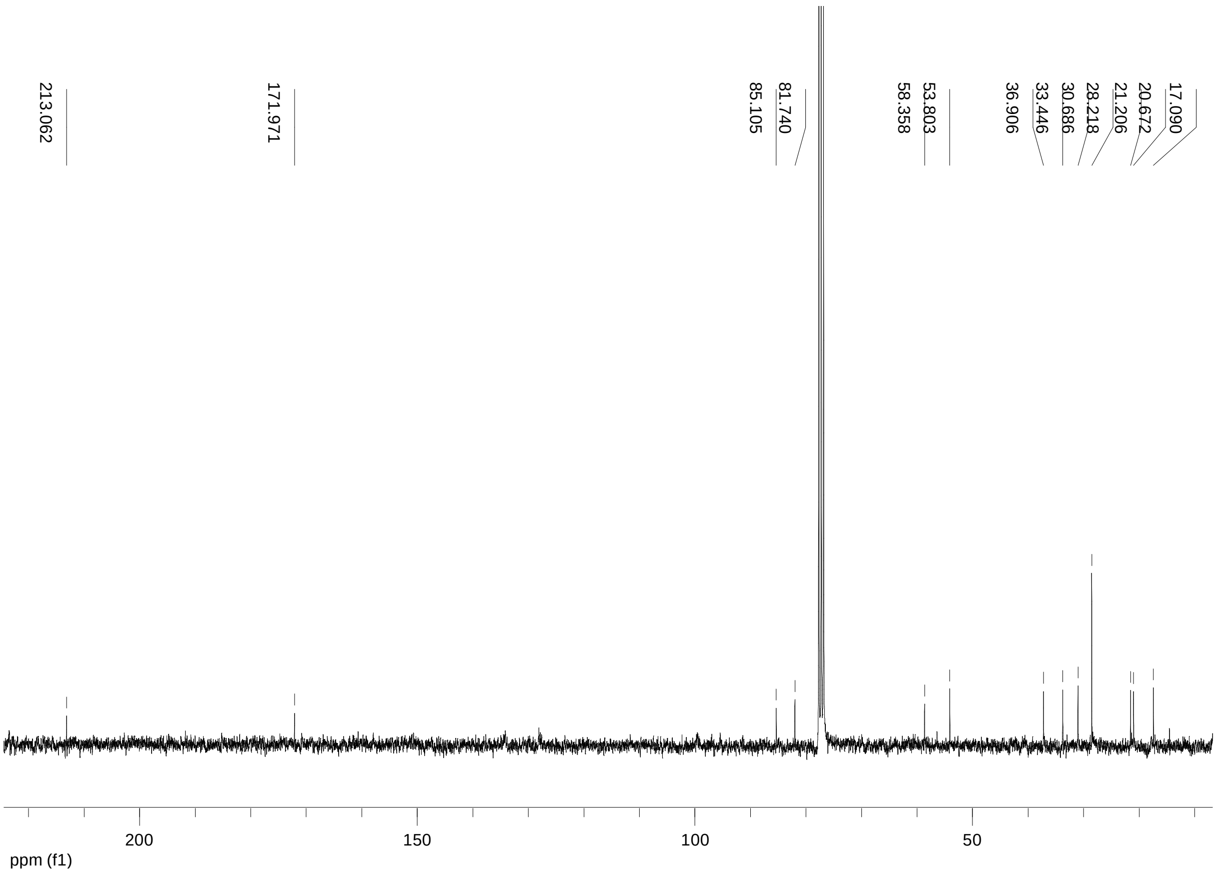
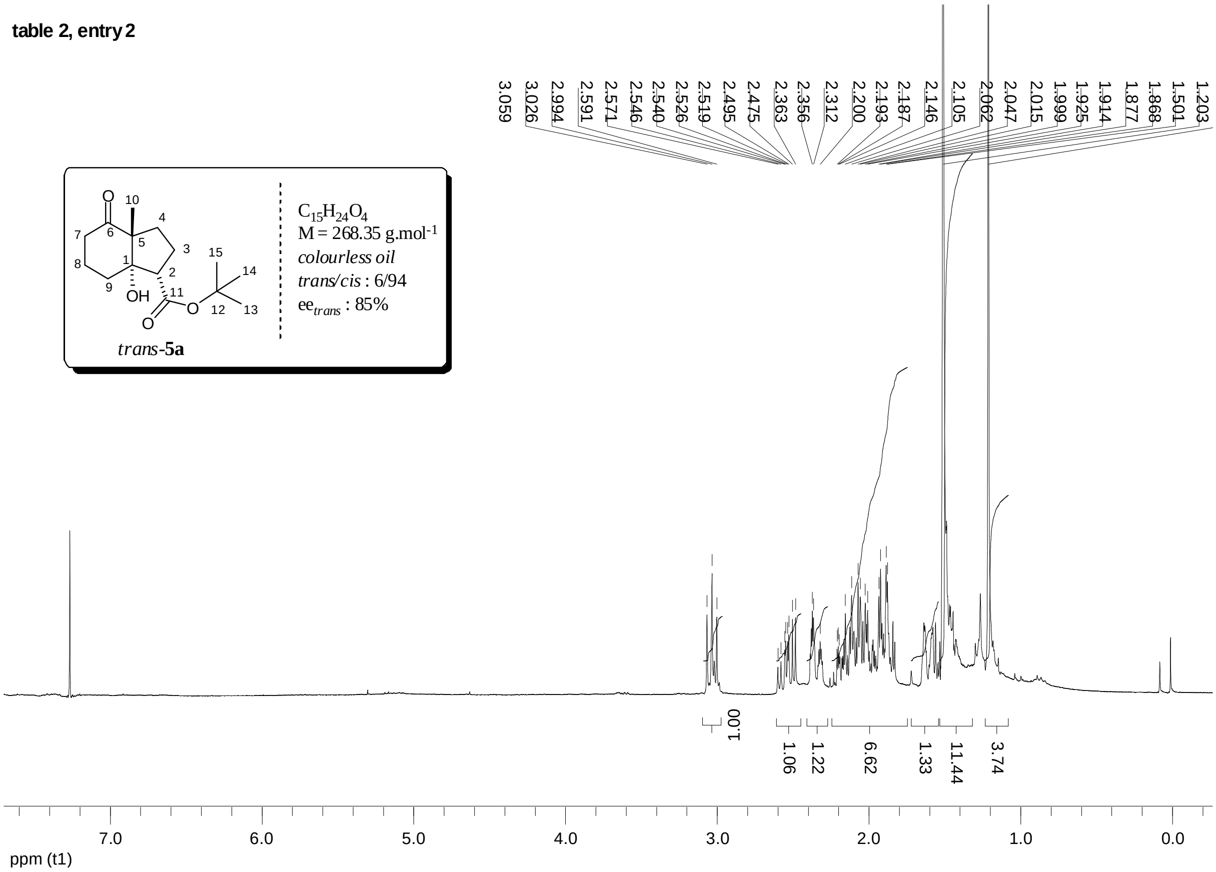
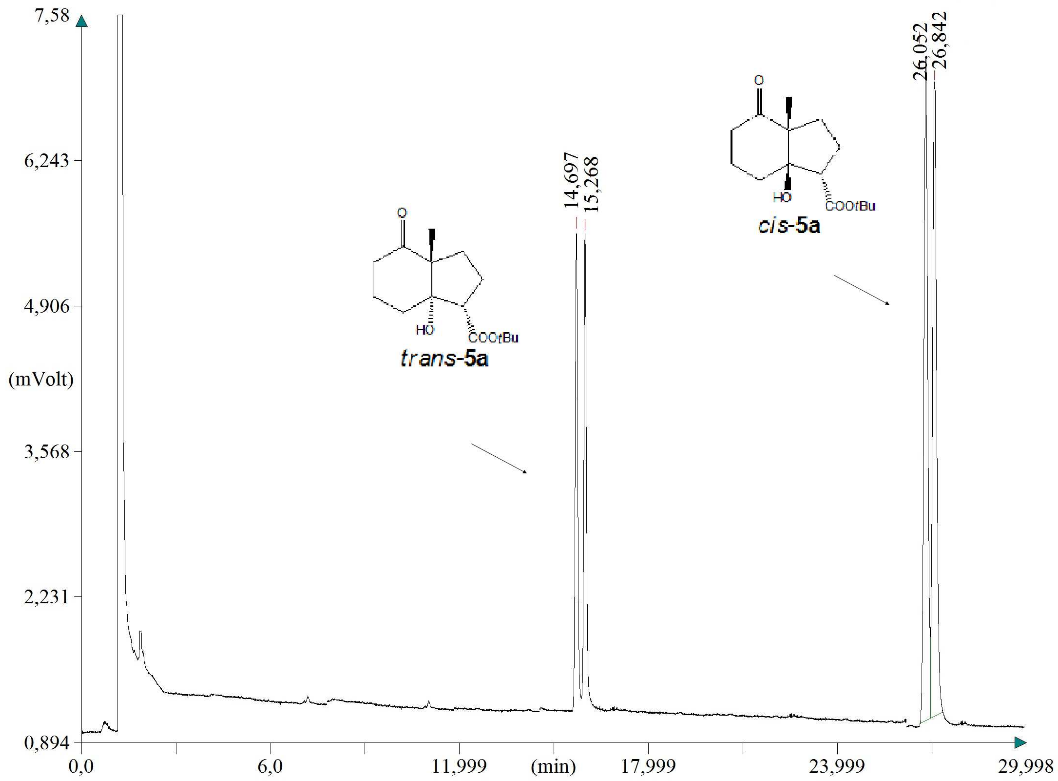


table 2, entry 2



Title Racemic mixture

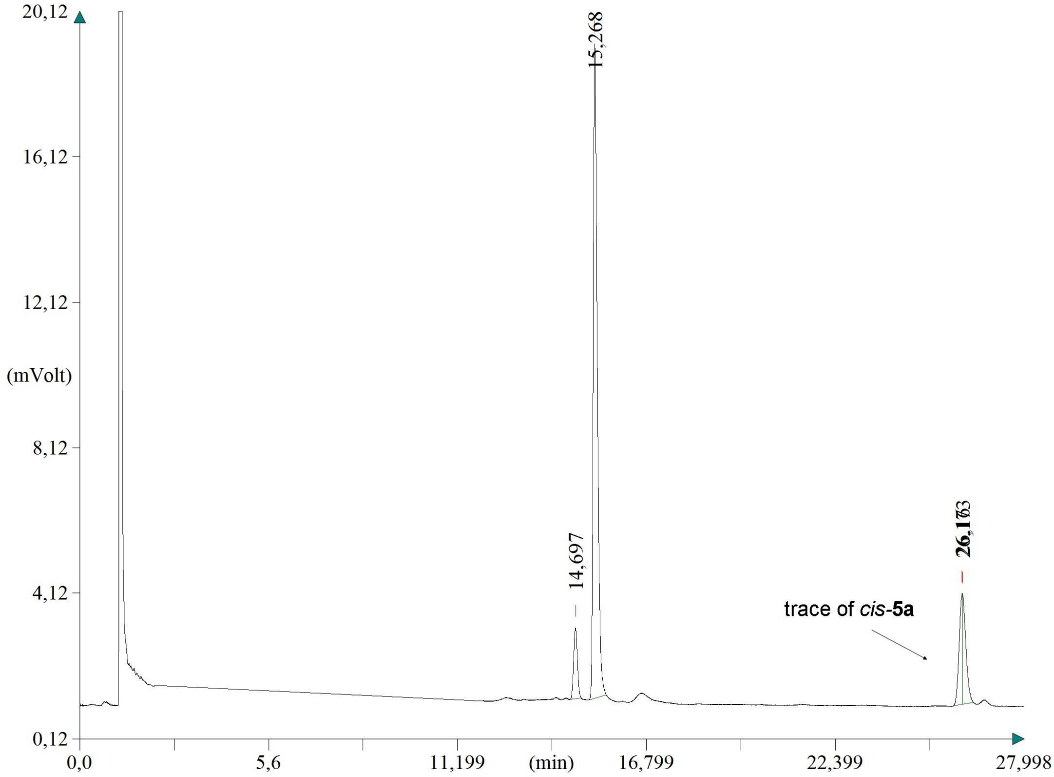
Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	JD606RAC
Chromatogram filename:	G:\Julia\cyclisations\14112006\JD606RAC-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	26.052	513639	49.034	Fused	
2	26.842	533868	50.966	Fused	
		1047507			

Title   Purified *trans*-**5a**

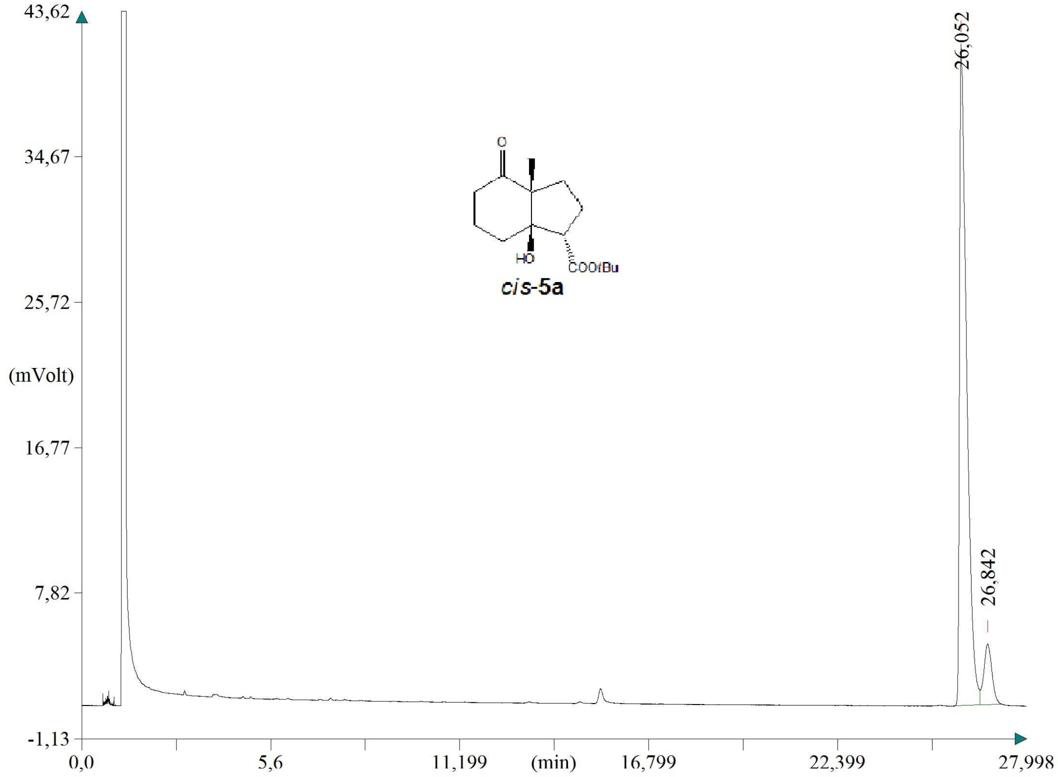
Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd606f0
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd606f0-2.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	14.697	147844	7.158	Resolved	
2	15.268	1504662	72.850	Resolved	
3	26.160	199836	9.675	Fused	
4	26.173	213089	10.317	Fused	
		2065431			

Title Purified *cis*-**5a**

Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd606f1
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd606f1-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	26.052	5986406	90.521	Manual integ.	
2	26.842	626894	9.479	Manual integ.	
		6613300			

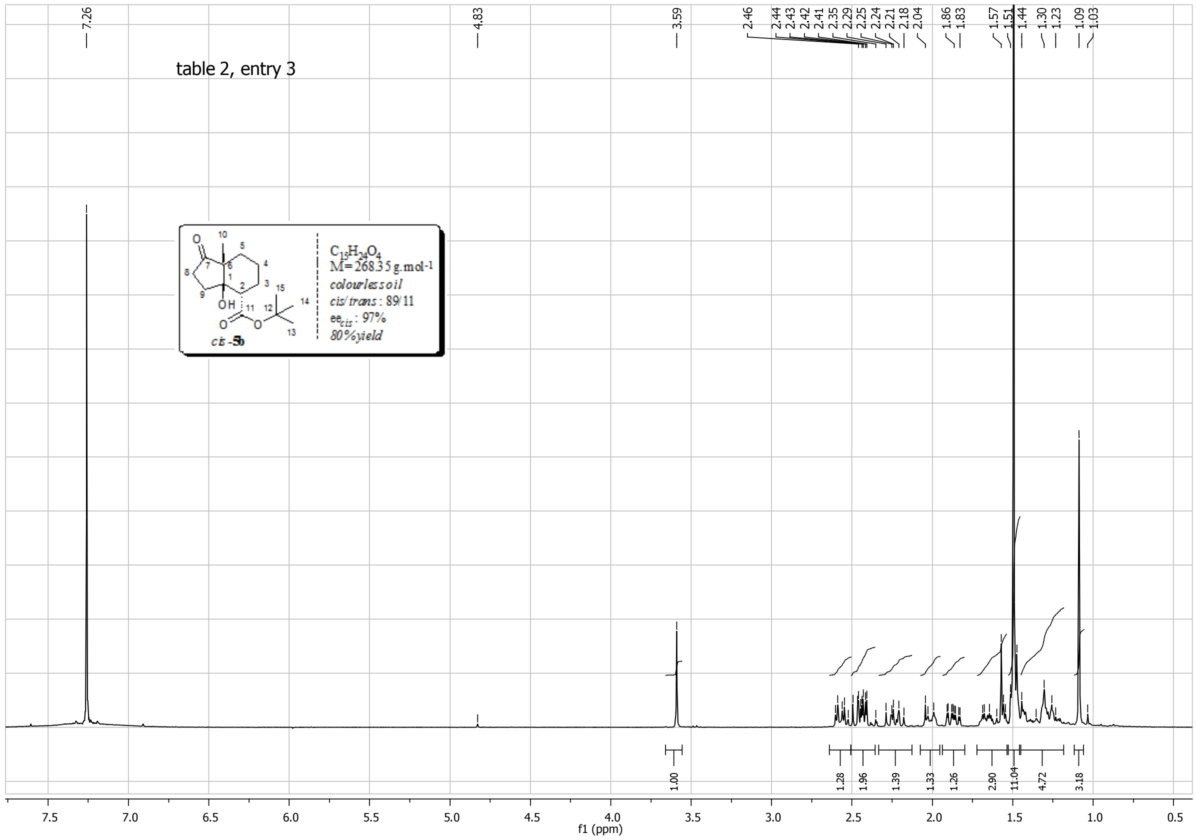
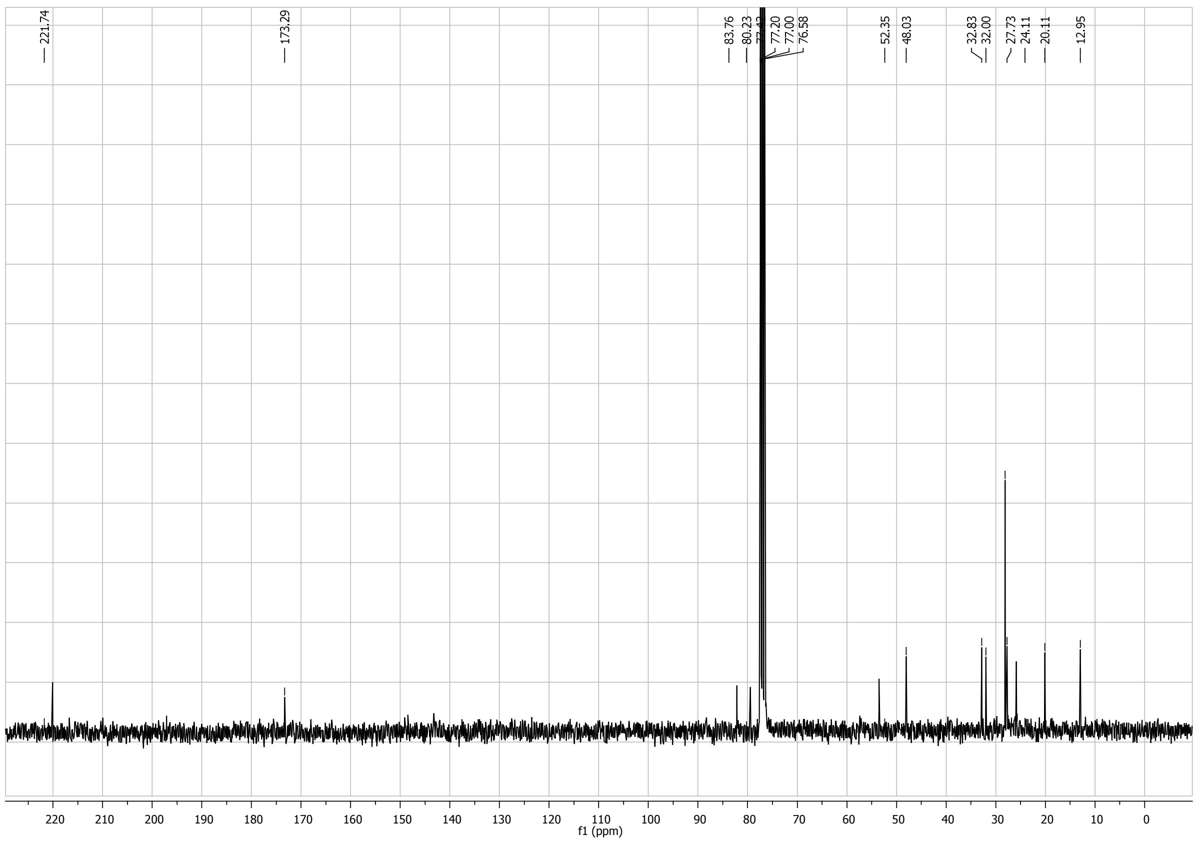
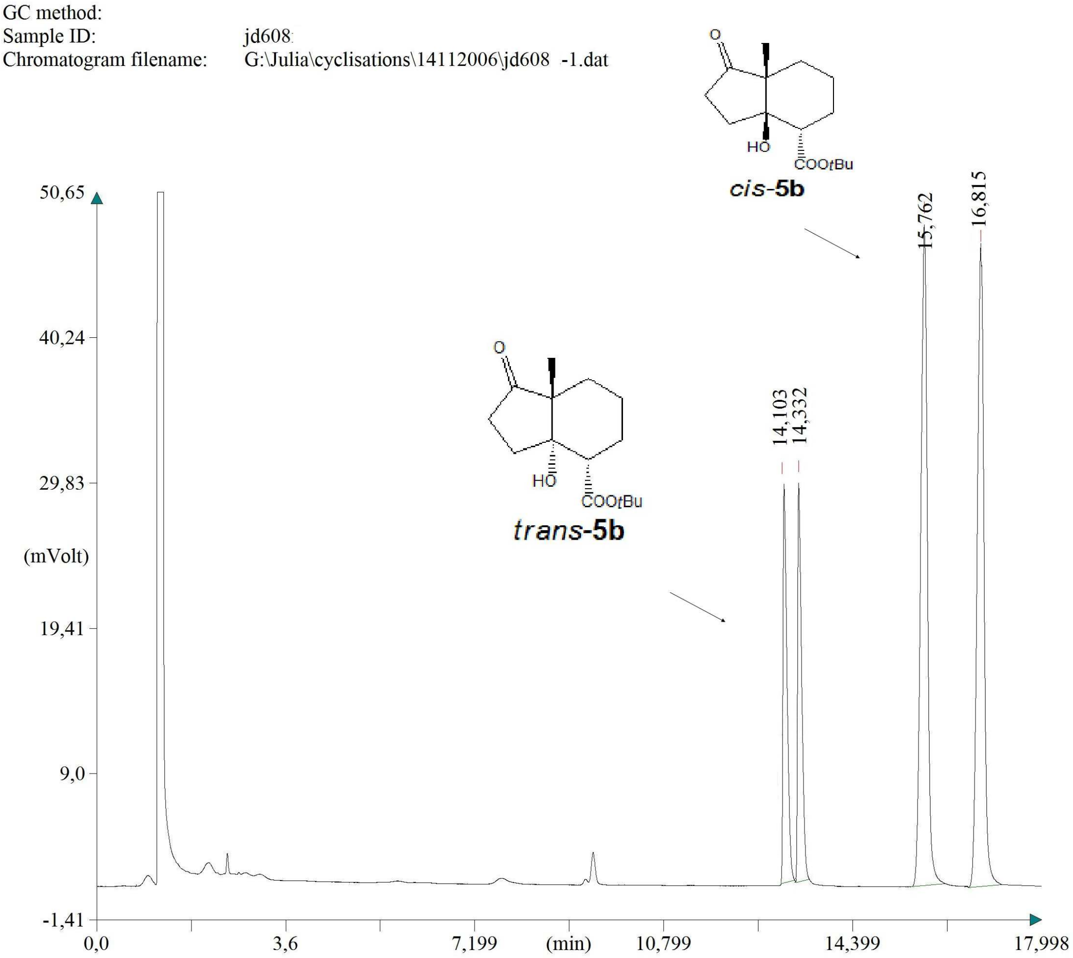


table 2, entry 3
$C_{15}H_{24}O_4$
M = 268.35 g.mol-1
colourless oil
cis/trans : 89/11
ee_{cis} : 97%
80% yield
cis-5b
f1 (ppm)


f1 (ppm)

Title Racemic mixture

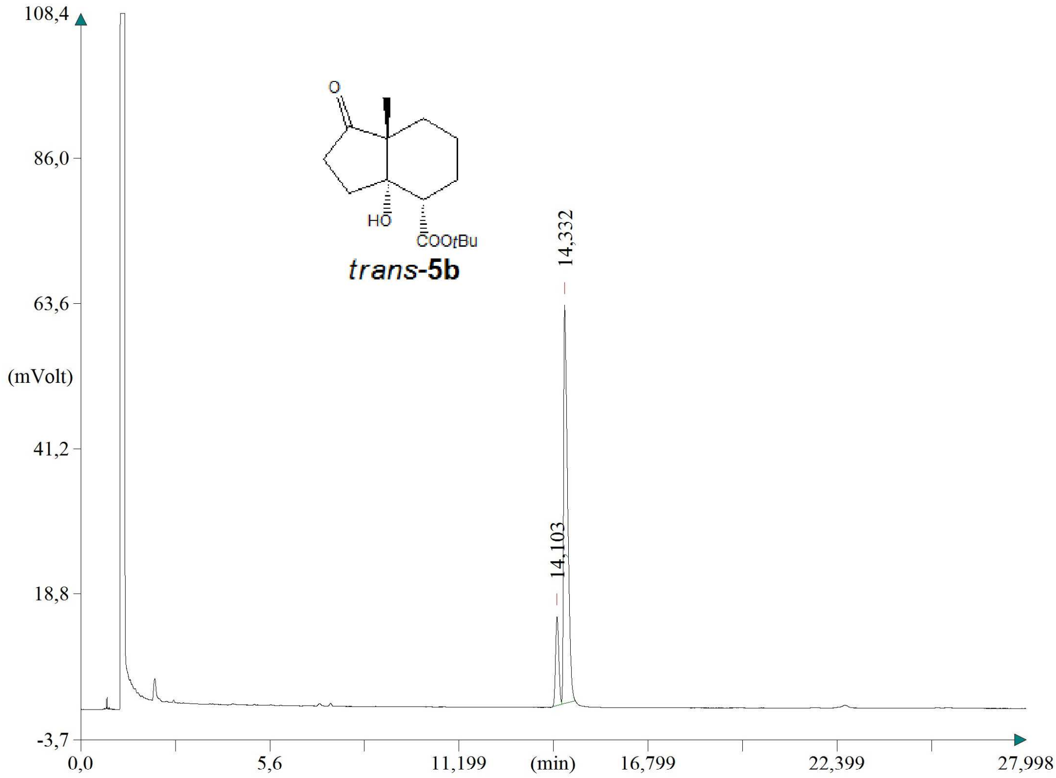
Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd608
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd608 -1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)

Title Purified *trans*-**5b**

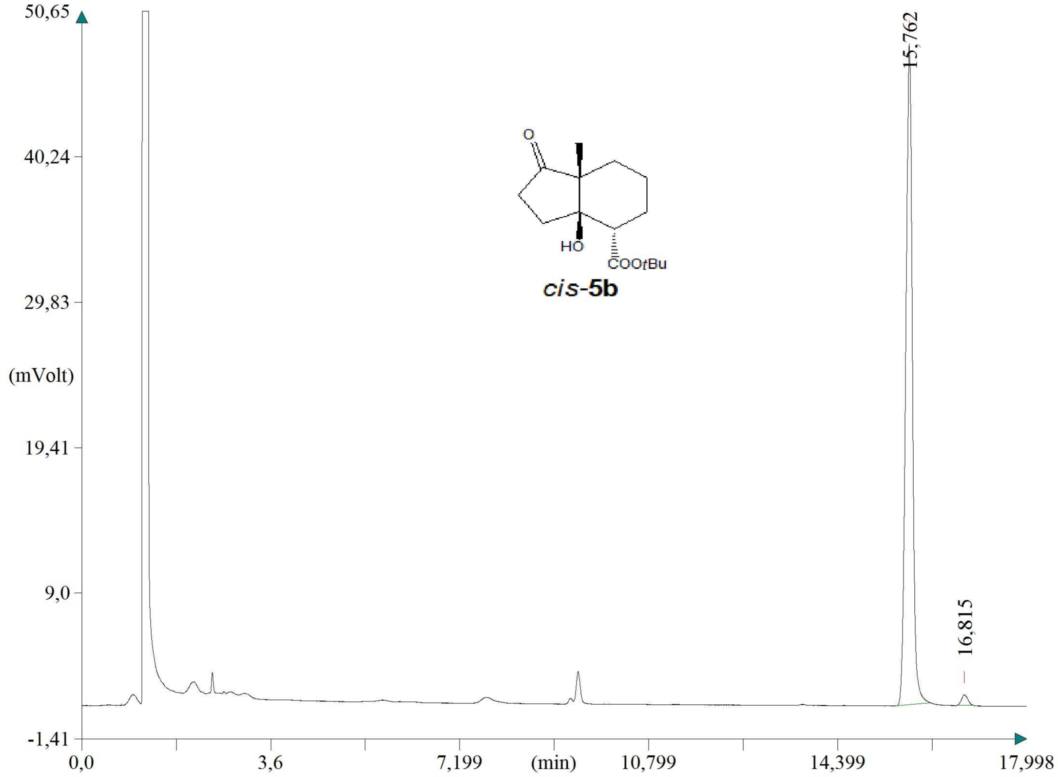
Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd608f1
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd608f1-2.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	U (
1	14.103	903609	7.979	Resolved	
2	14.332	5087830	44.925	Resolved	

Title Purified *cis*-**5b**

Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd608f2
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd608f2-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	15.762	4121798	98.475	Resolved	
2	16.815	63836	1.525	Manual integ.	
		4185633			

Warning Chromatogram has been subjected to manual integration.

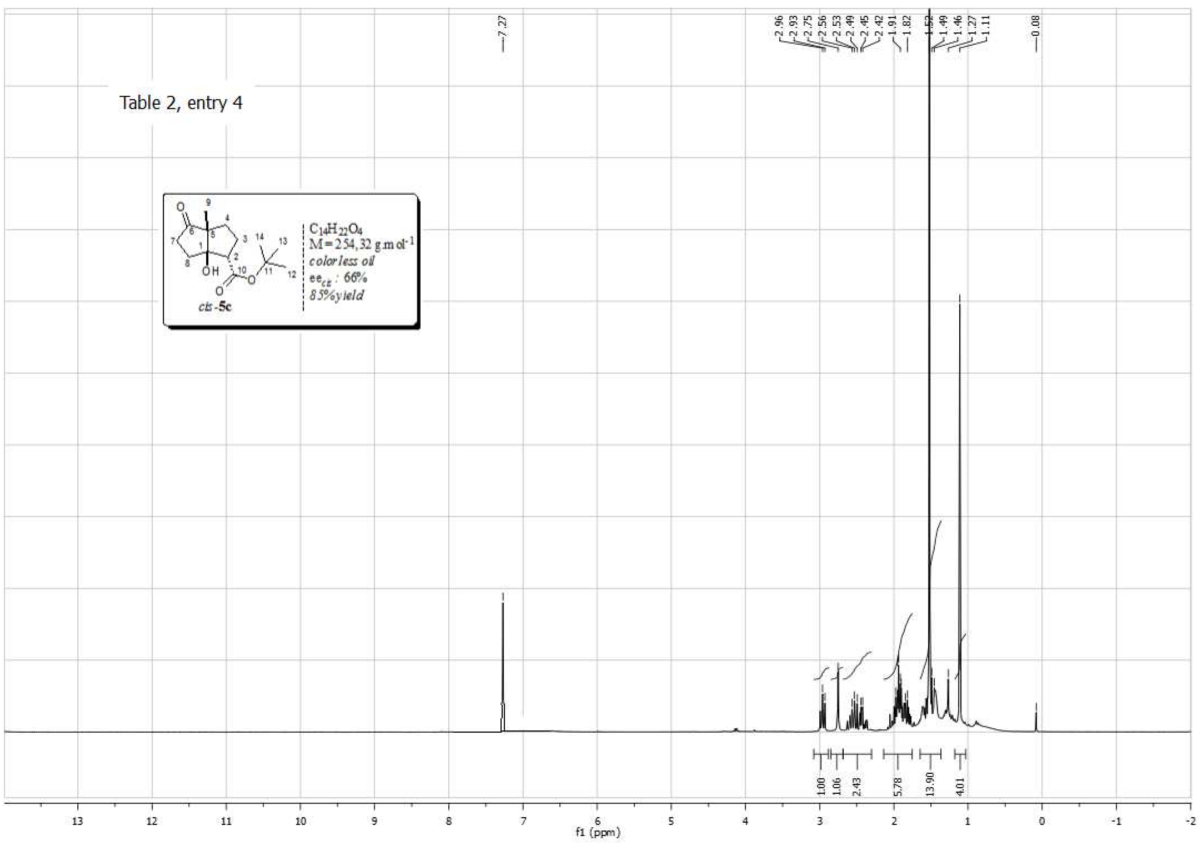
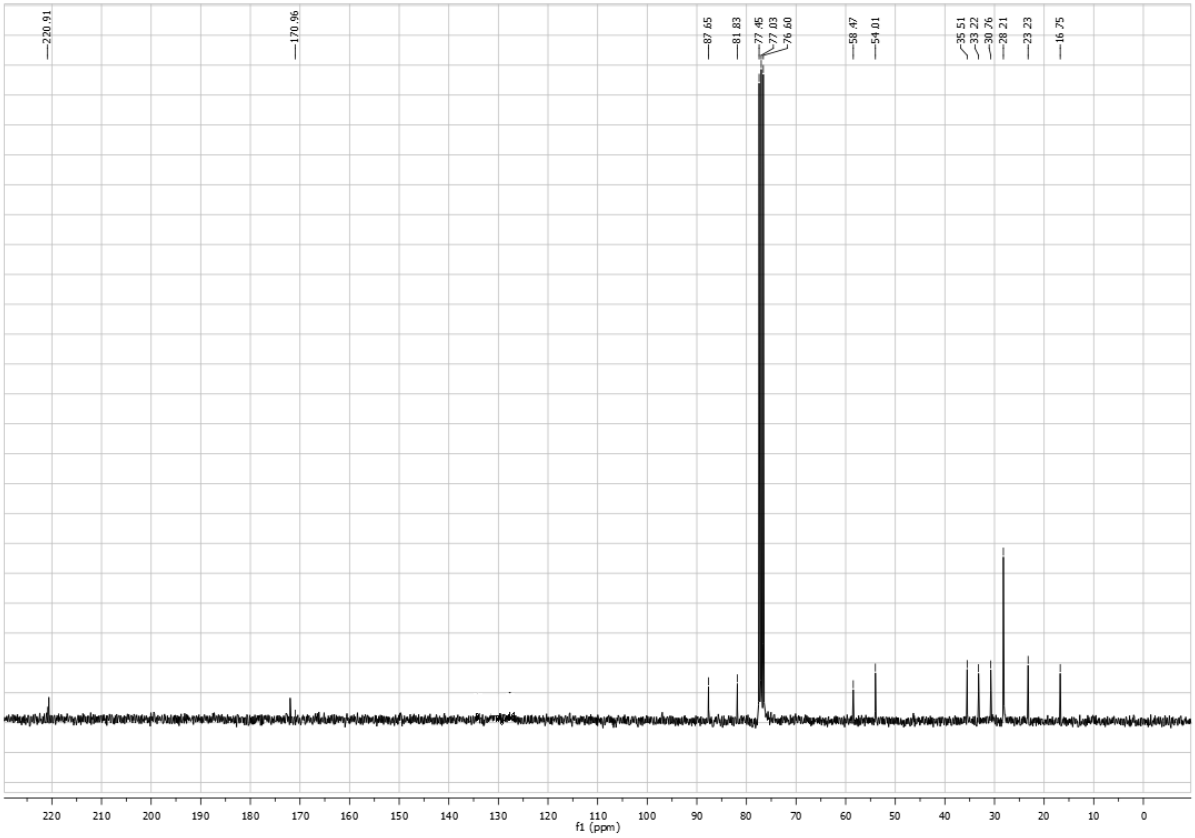
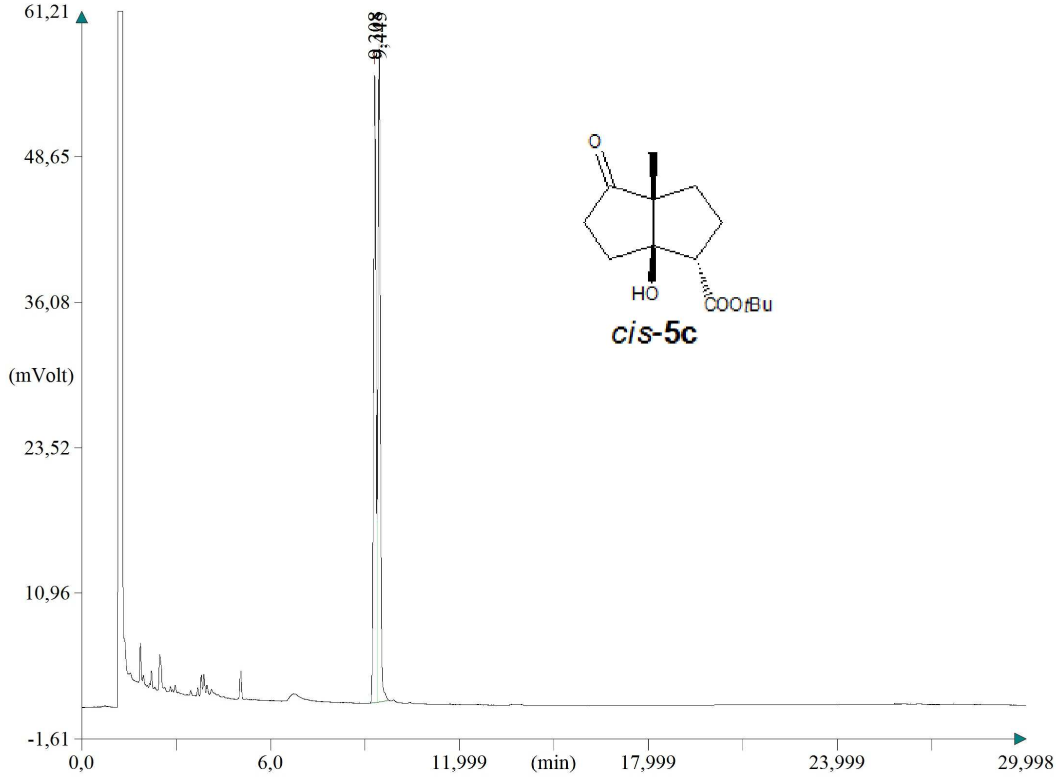


Table 2, entry 4
$C_{14}H_{22}O_4$
M = 254,32 g.mol-1
colorless oil
cis-5c
85% yield
f1 (ppm)


f1 (ppm)

Title Racemic mixture

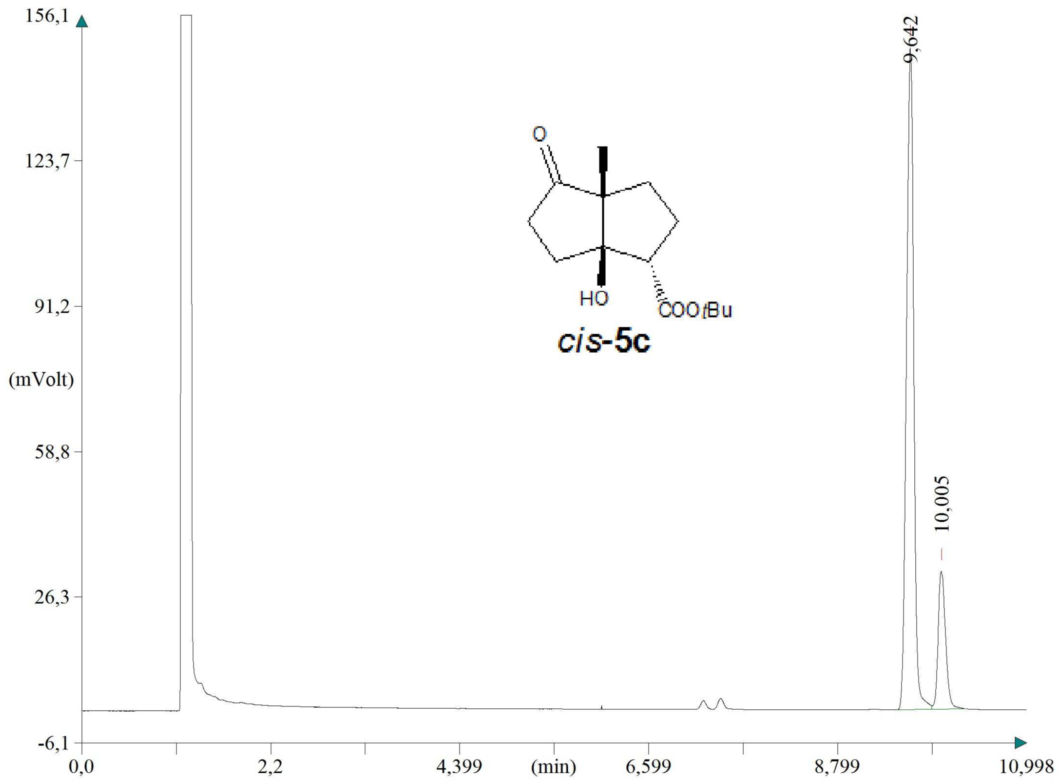
Method filename: G:\Julia\cyclisations\14112006\Rntandem.mth
Method name: Rn tandem
GC method:
Sample ID: JD607RAC
Chromatogram filename: G:\Julia\cyclisations\14112006\JD607RAC-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	9.308	2957573	34.285	Fused	
2	9.445	3098481	35.919	Fused	

Title Purified *cis*-**5c**

Method filename:	G:\Julia\cyclisations\14112006\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd607f1
Chromatogram filename:	G:\Julia\cyclisations\14112006\jd607f1-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	9.642	8674176	82.344	Fused	
2	10.005	1859950	17.656	Fused	
		10534130			

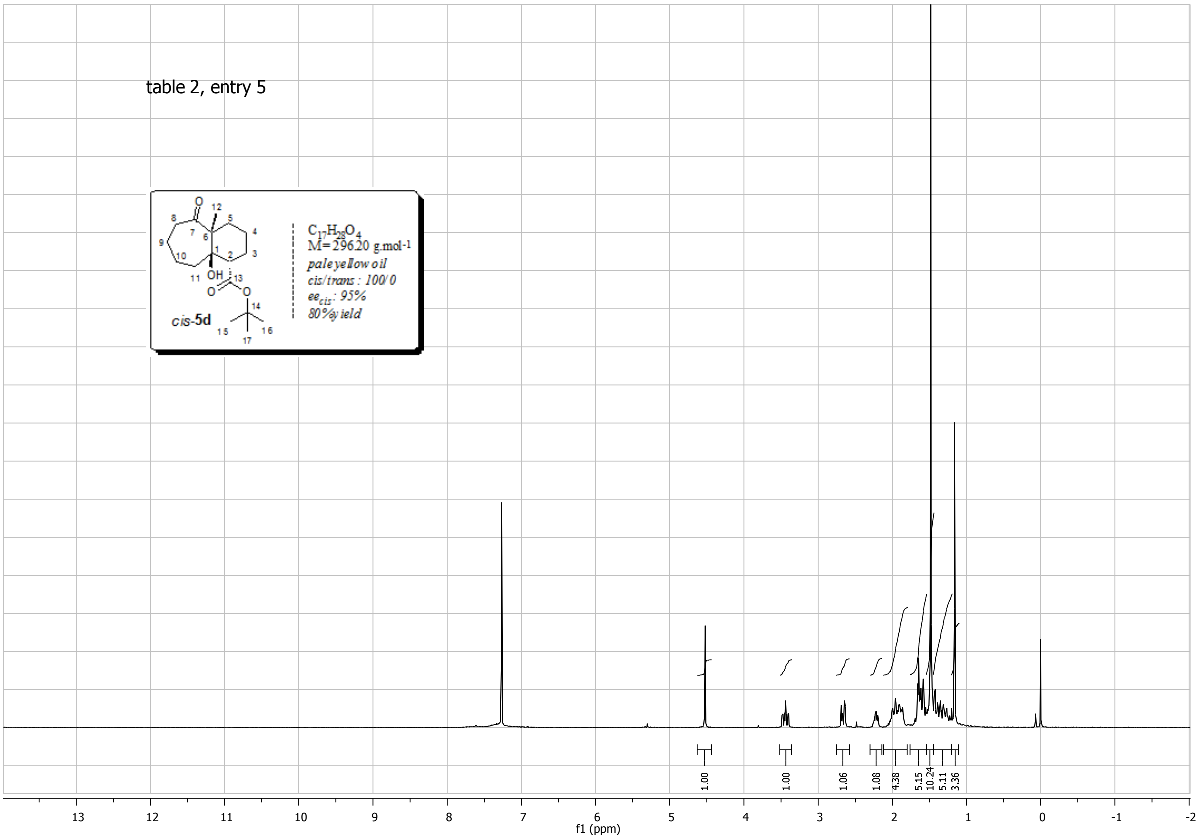
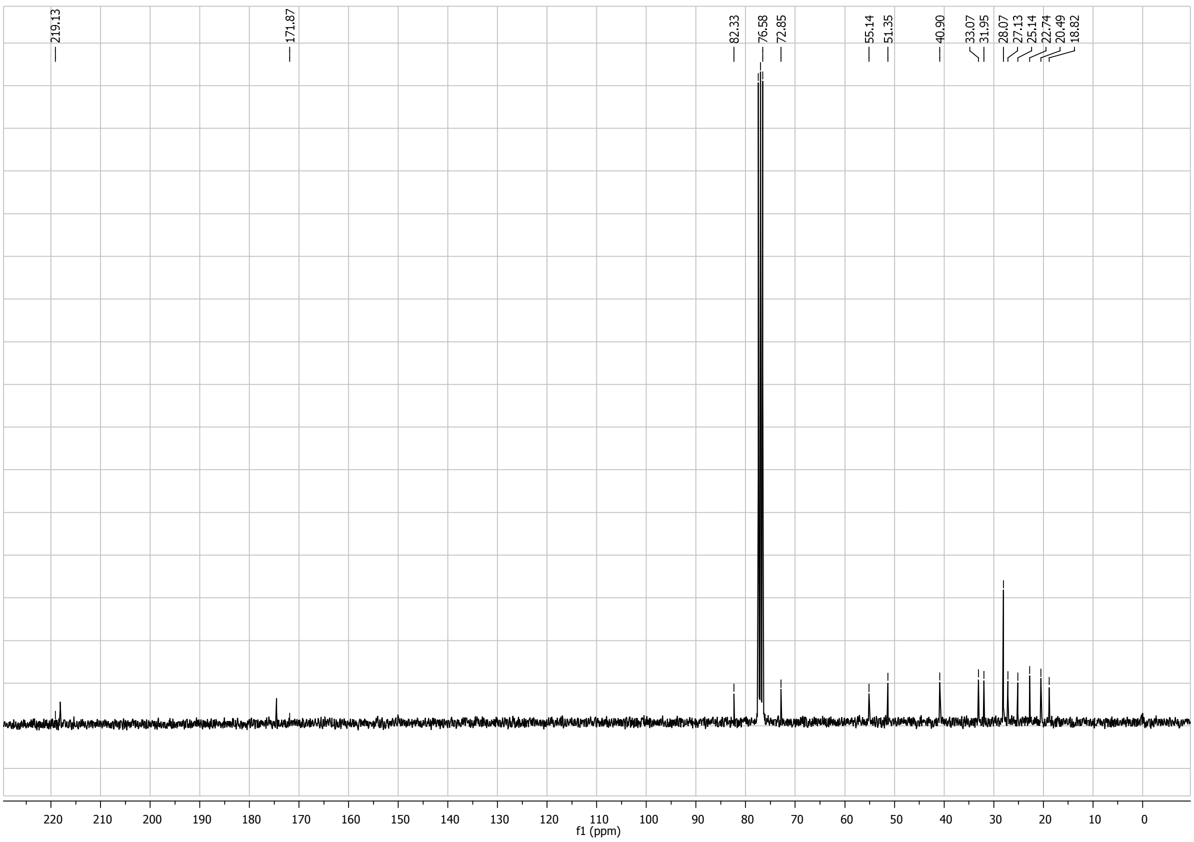
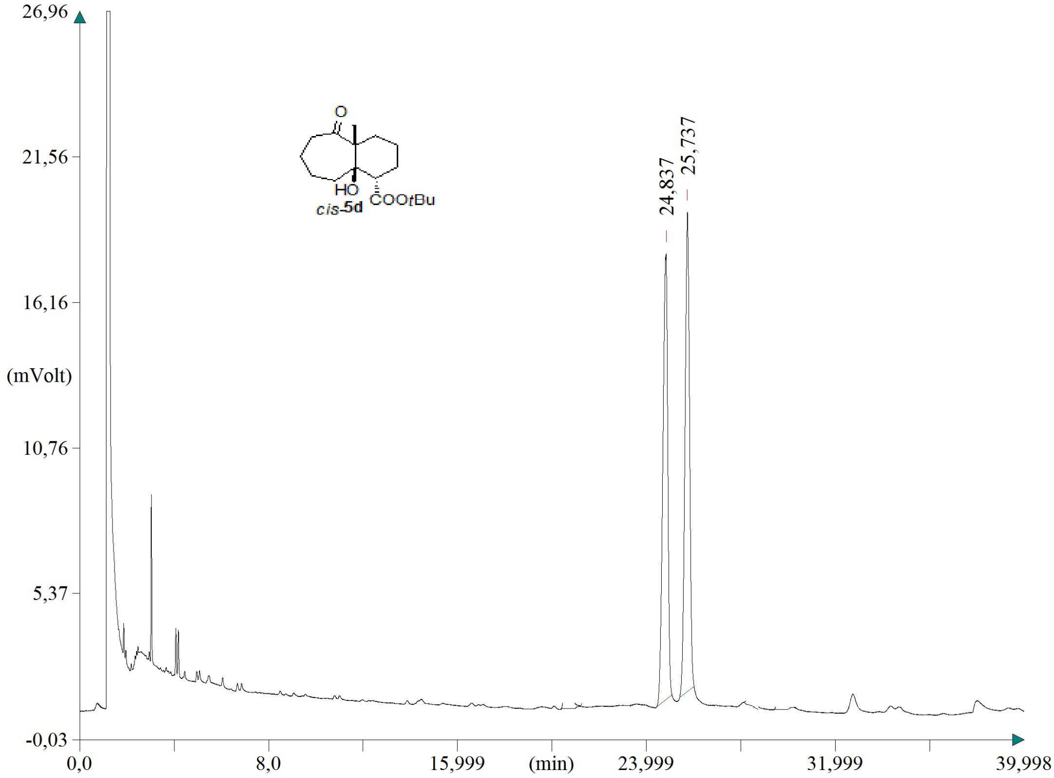


table 2, entry 5
cis-5d
$C_{17}H_{28}O_4$
M= 296.20 g.mol-1
pale yellow oil
cis/trans : 100/0
ee_{cis}: 95%
80% yield
1.00
1.00
1.06
1.08
4.38
5.15
10.24
5.11
3.36
f1 (ppm)


219.13
171.87
82.33
76.58
72.85
55.14
51.35
40.90
33.07
31.95
28.07
27.13
25.14
22.74
20.49
18.82
f1 (ppm)

Title Racemic mixture

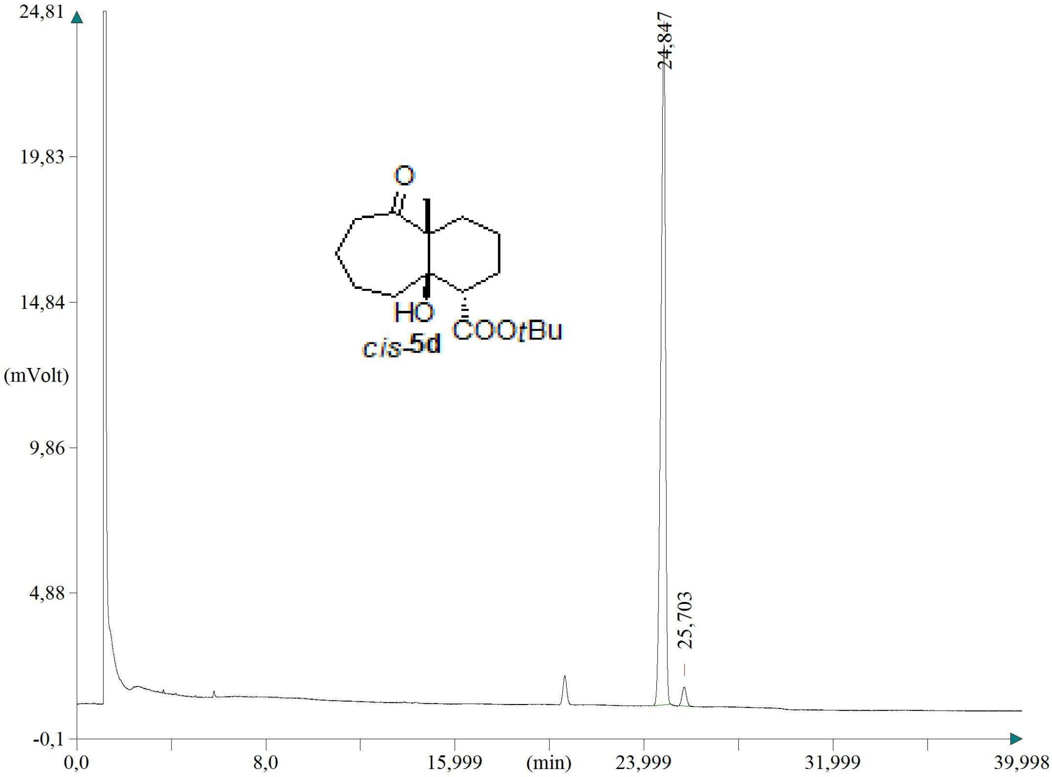
Method filename:	G:\Julia\cyclisations\16032008\Rntandem.mth
Method name:	Rn tandem
GC method:	iso170
Sample ID:	gsjd107-1rac (# 8)
Chromatogram filename:	gsjd107-1rac-3.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	24.837	2460514	49.639	Manual integ.	
2	25.737	2496293	50.361	Manual integ.	
		4956807			

Title Purified *cis*-**5d**

Method filename: G:\Julia\cyclisations\16032008\Rntandem.mth
Method name: Rn tandem
GC method: iso170
Sample ID: gsjd107-2p2 (# 15)
Chromatogram filename: gsjd107-2p2-1.dat



Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	24.847	3103676	97.383	Manual integ.	
2	25.703	83410	2.617	Manual integ.	
		3187086			

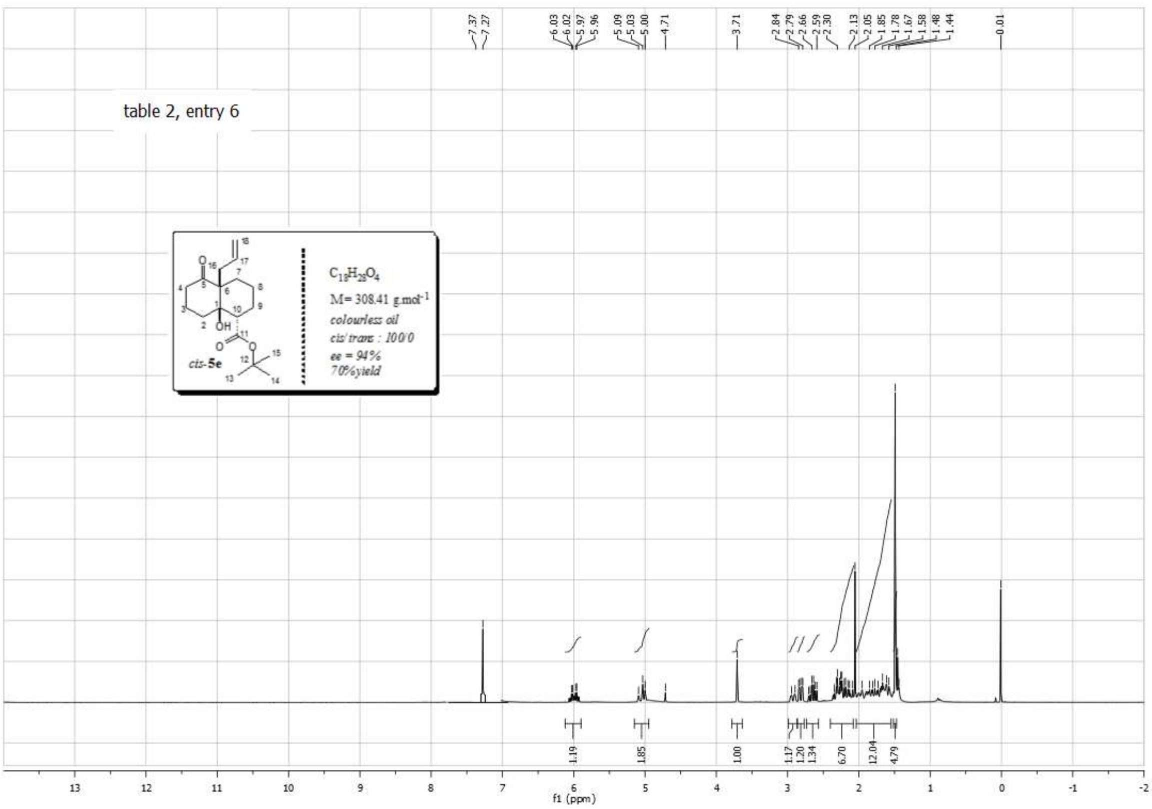
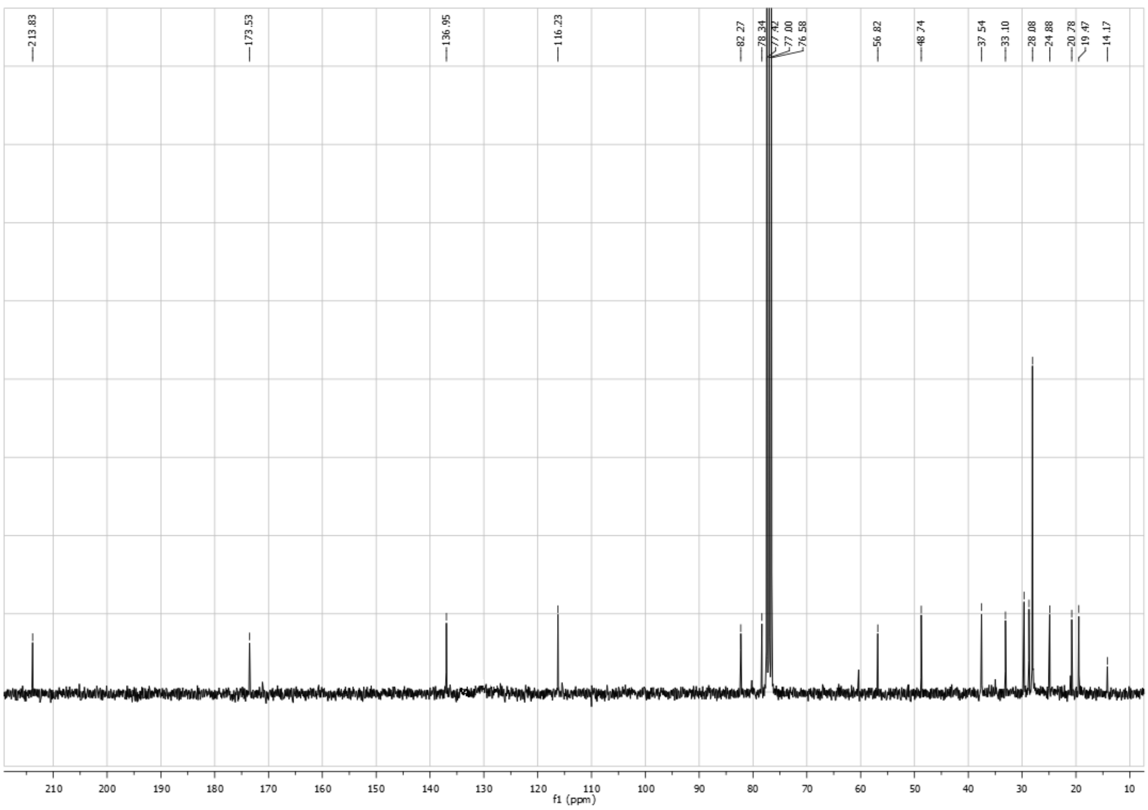
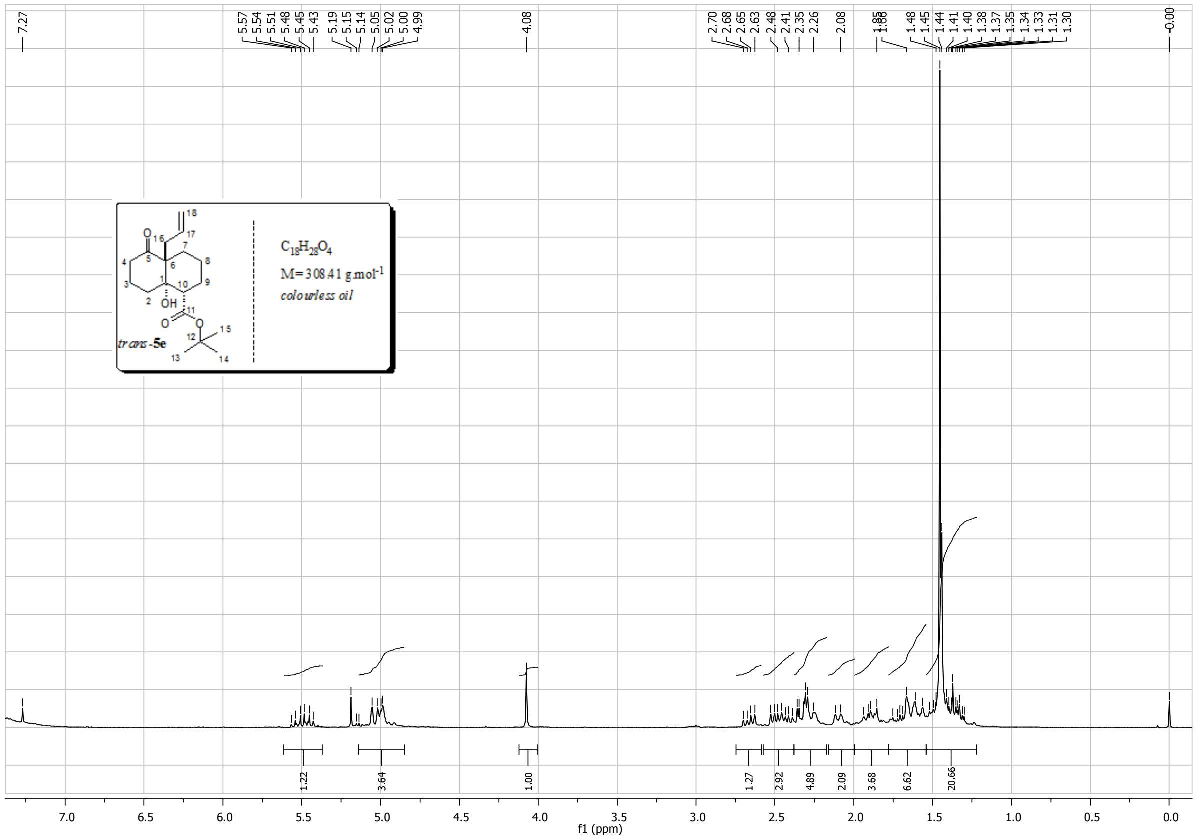
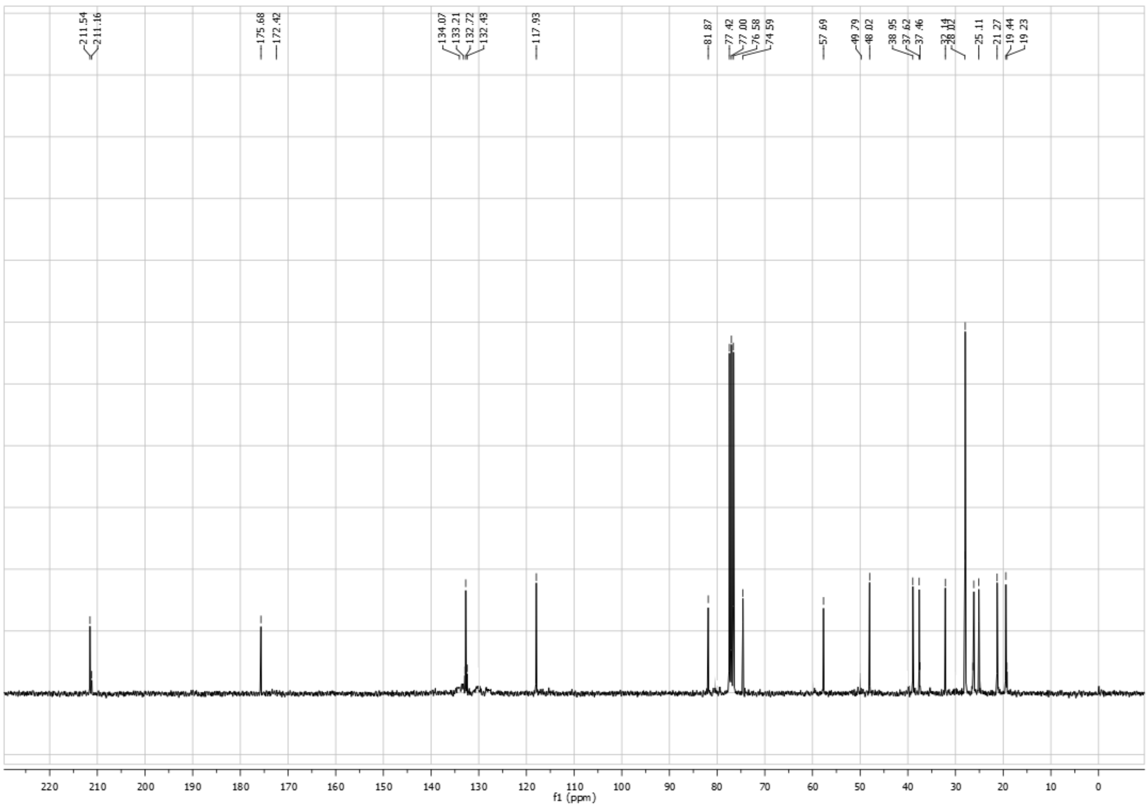


table 2, entry 6
cis-5e
$C_{18}H_{28}O_4$
M= 308.41 g.mol^{-1}
colourless oil
cis/trans : 100/0
ee = 94%
70% yield
f1 (ppm)


f1 (ppm)



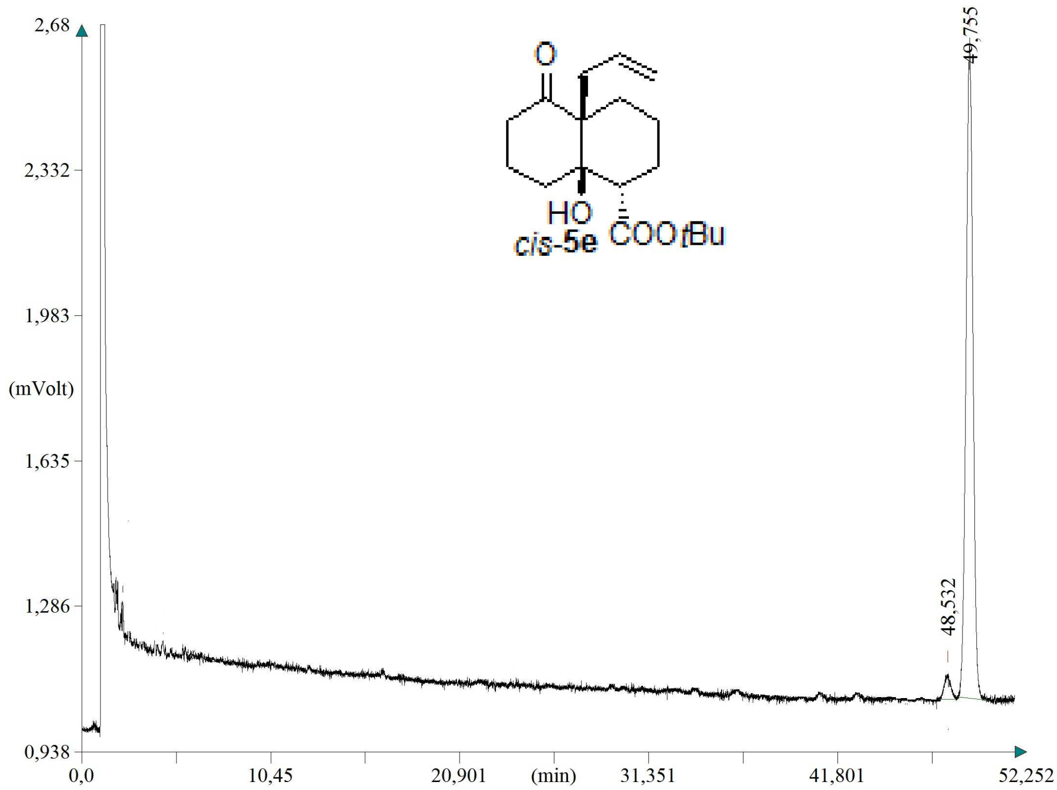
7.27
5.57 5.54 5.51 5.48 5.45 5.43 5.19 5.15 5.14 5.05 5.02 5.00 4.99
4.08
2.70 2.68 2.65 2.63 2.48 2.41 2.35 2.26 2.08
1.48 1.45 1.44 1.41 1.40 1.38 1.37 1.35 1.34 1.33 1.31 1.30
-0.00
trans-5e
$C_{18}H_{28}O_4$
M=308.41 g.mol^{-1}
colourless oil
1.22
3.64
1.00
1.27
2.92
4.89
2.09
3.68
6.62
20.66
f1 (ppm)



211.54 211.16
175.68 172.42
134.07 133.21 132.72 132.43
117.93
81.87 77.42 77.00 76.58 74.59
57.69 49.79 48.02 38.95 37.62 37.46
25.11 21.27 19.44 19.23
f1 (ppm)

Title Purified *cis*-**5e**

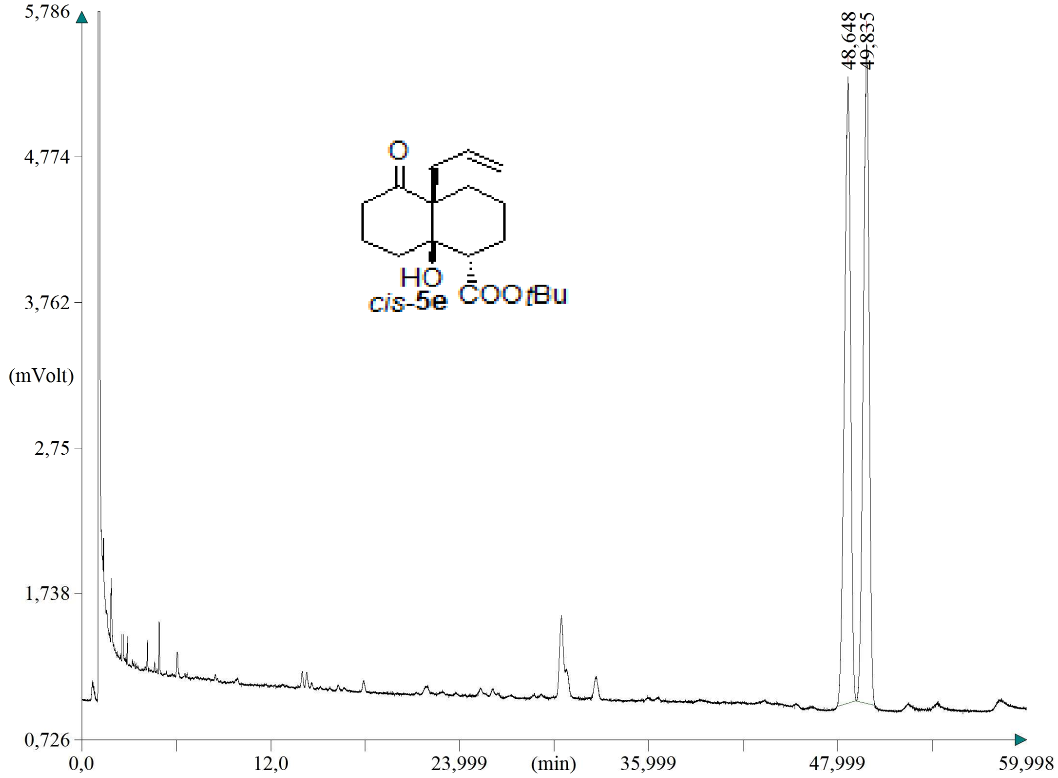
Method filename:	G:\Julia\cyclisations\01082007\Rntandem.mth
Method name:	Rn tandem
GC method:	
Sample ID:	jd721
Chromatogram filename:	G:\Julia\cyclisations\01082007\jd721-1.dat



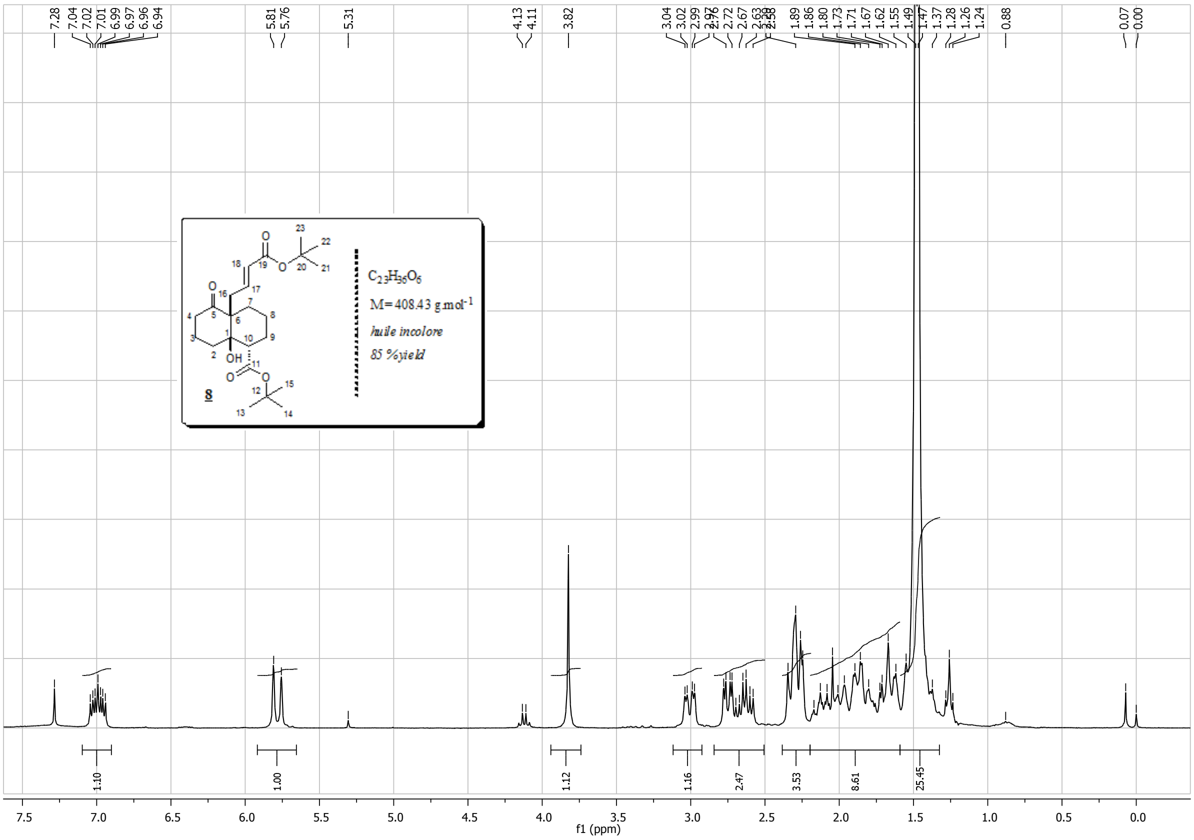
Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	48.532	14291	3.333	Manual integ.	
2	49.755	414513	96.667	Manual integ.	
		428804			

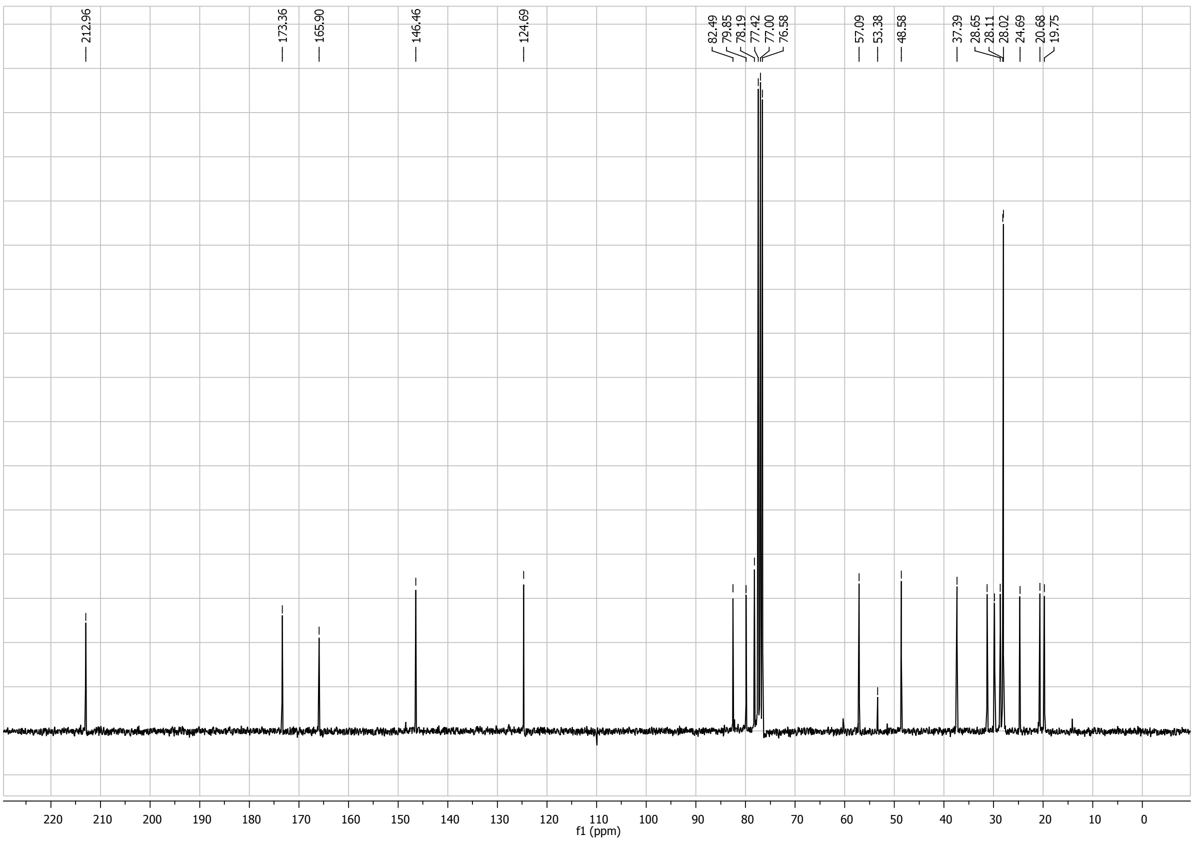
Title Racemic mixture

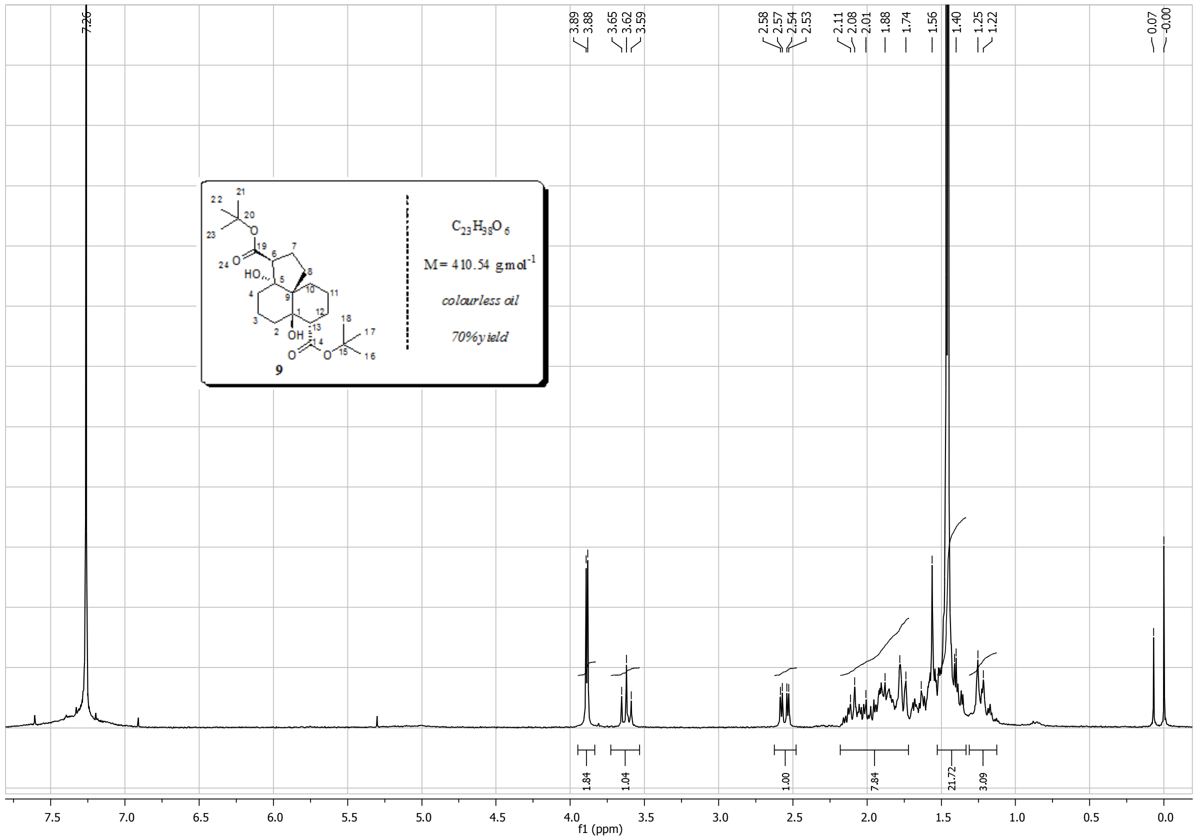
Method filename:	G:\Julia\cyclisations\01082007\Rntandem.mth
Method name:	Rn tandem
GC method:	iso165
Sample ID:	jdsc04f2 (# 30)
Chromatogram filename:	jdsc04f2-7.dat

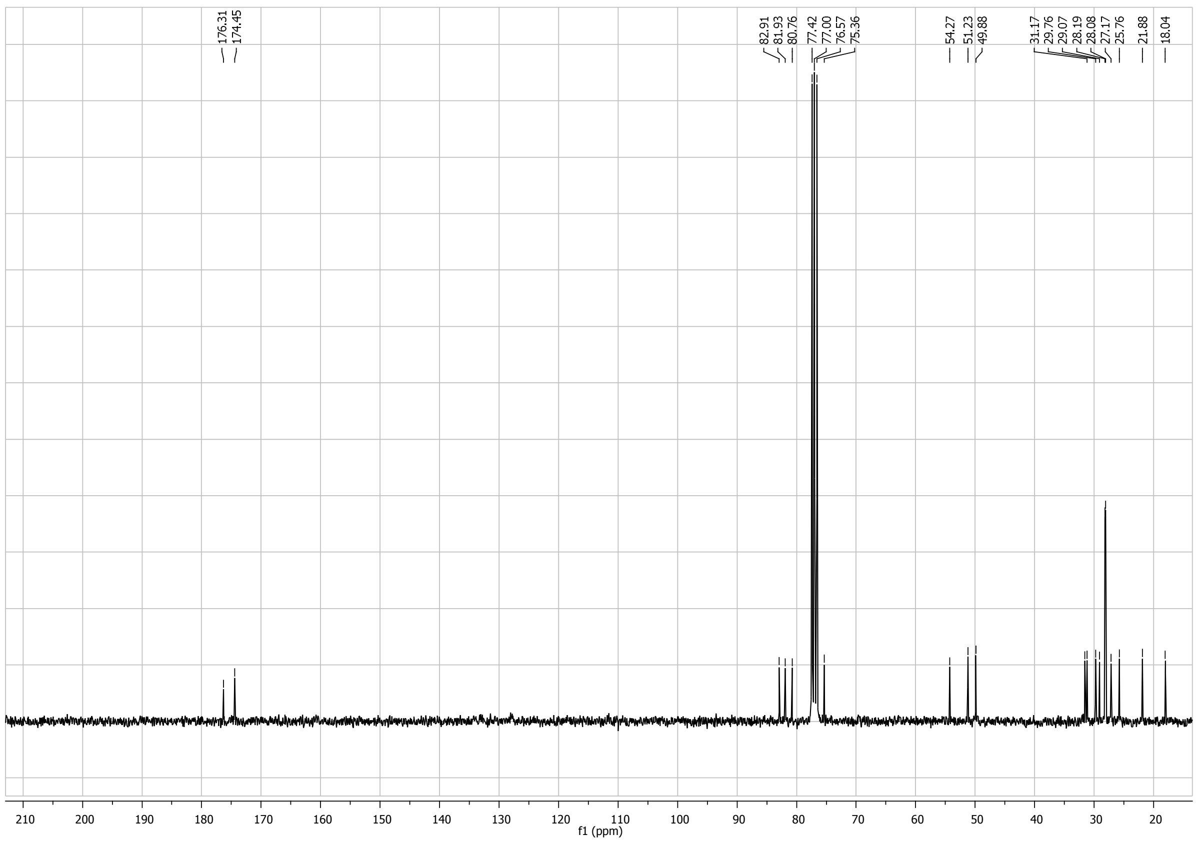


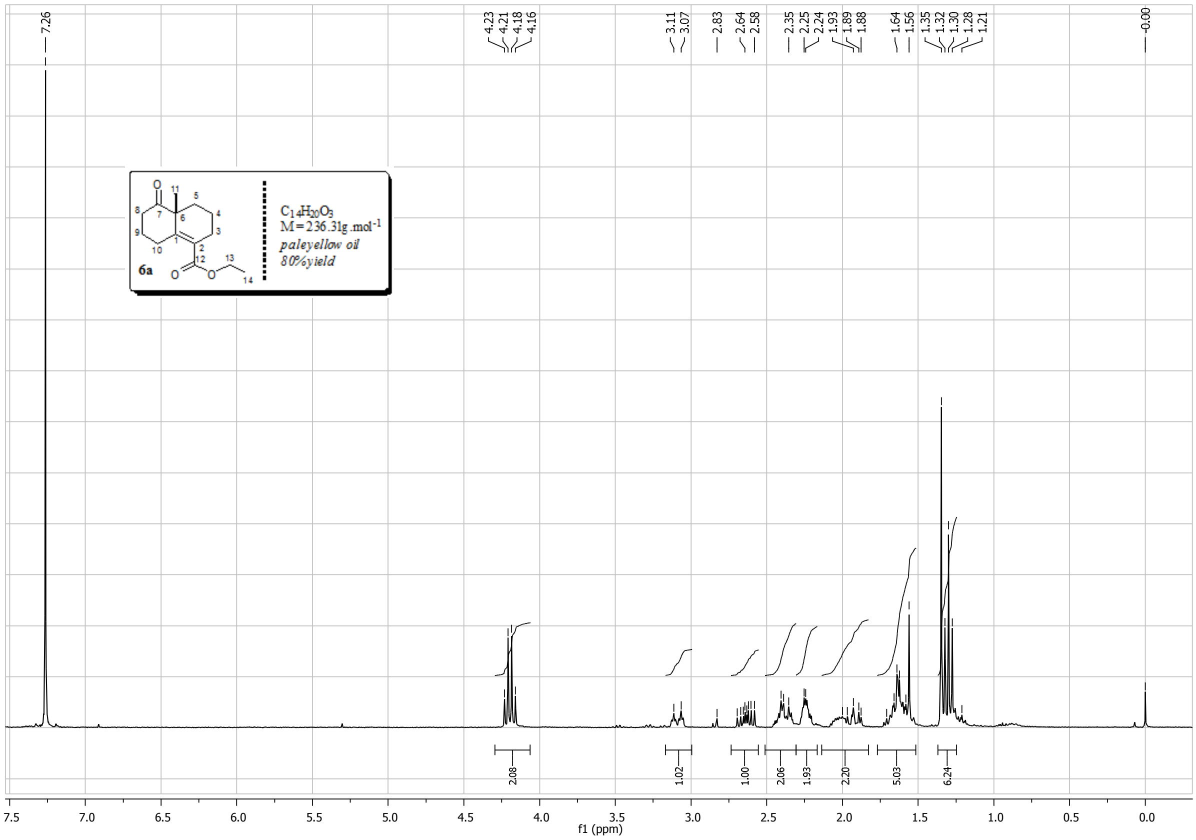
Peak Number (#)	Retention Time (min)	Area (.1*uV*sec)	Area % (%)	Peak Type	USP R (R)
1	48.648	1174794	50.014	Manual integ.	
2	49.835	1174132	49.986	Manual integ.	
		2348926			

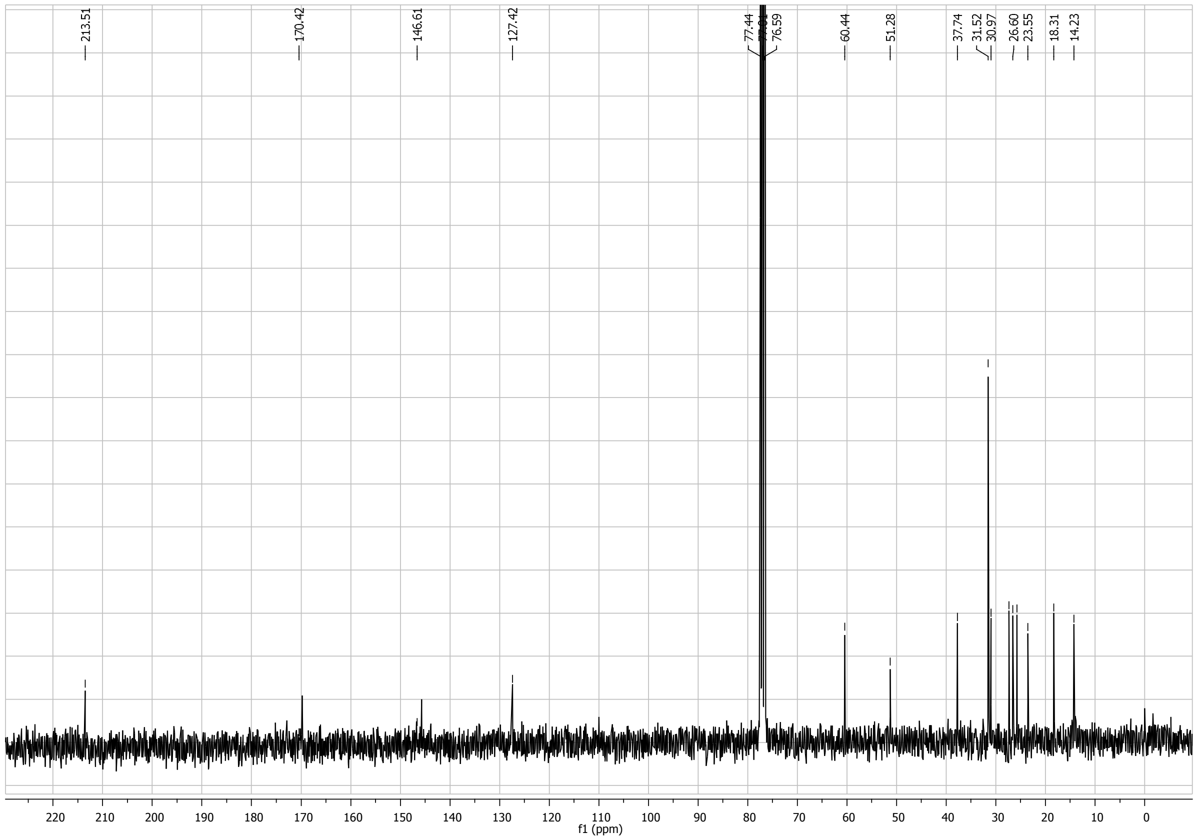

7.28 7.04 7.02 7.01 6.99 6.97 6.96 6.94 5.81 5.76 5.31 4.13 4.11 3.82 3.04 3.02 2.99 2.72 2.67 2.63 1.89 1.86 1.80 1.73 1.71 1.67 1.62 1.55 1.49 1.47 1.37 1.28 1.26 1.24 0.88 0.07 0.00
$C_{23}H_{36}O_6$
M= 408.43 g.mol-1
huile incolore
85 % yield
8
1.10 1.00 1.12 1.16 2.47 3.53 8.61 25.45
f1 (ppm)

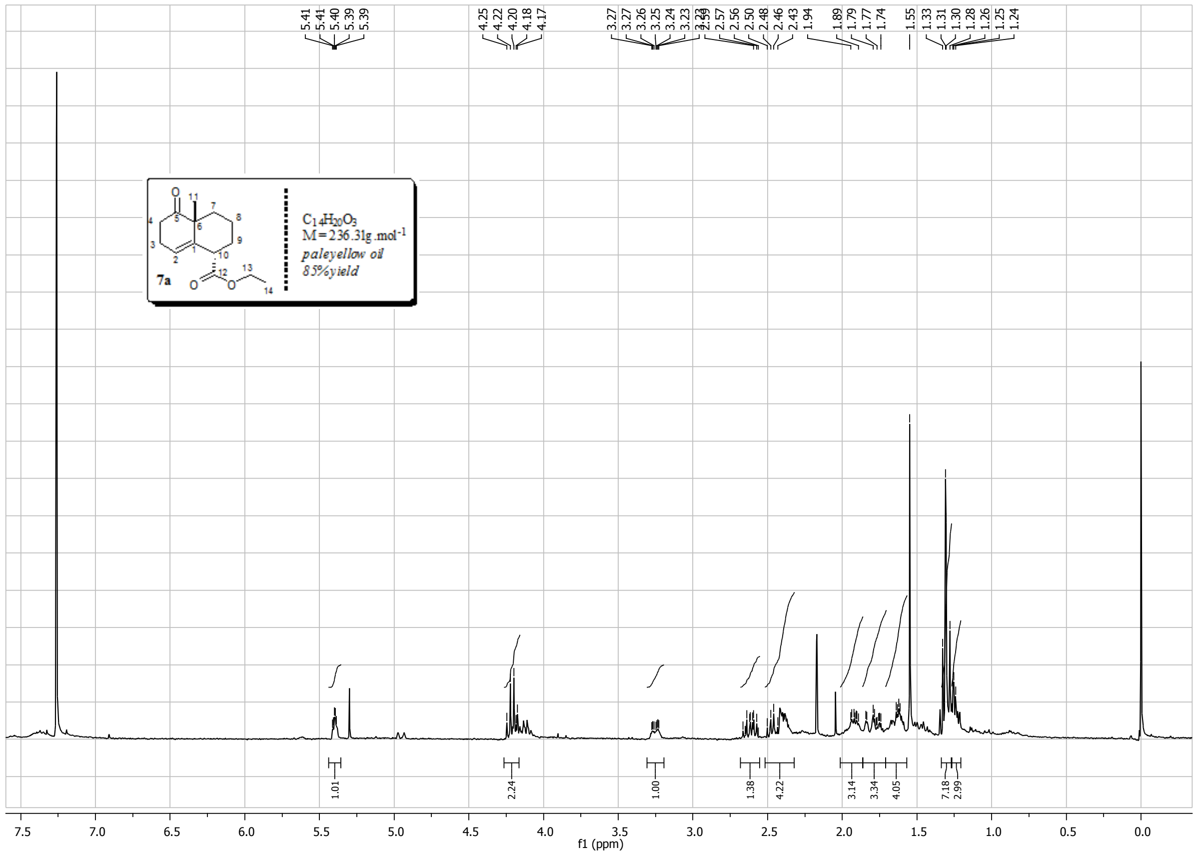

212.96 173.36 165.90 146.46 124.69 82.49 79.85 78.19 77.42 77.00 76.58 57.09 53.38 48.58 37.39 28.65 28.11 28.02 24.69 20.68 19.75
f1 (ppm)

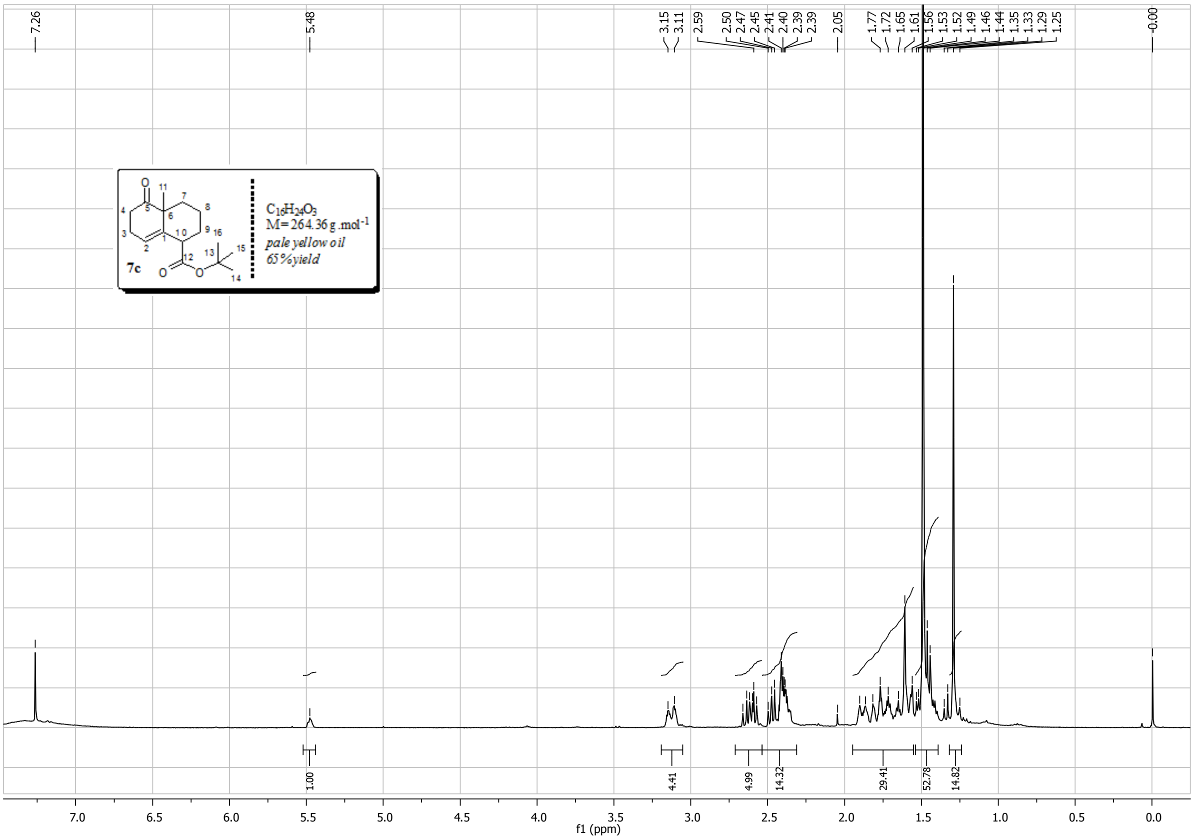

C23H38O6
M= 410.54 gmol-1
colourless oil
70% yield
f1 (ppm)

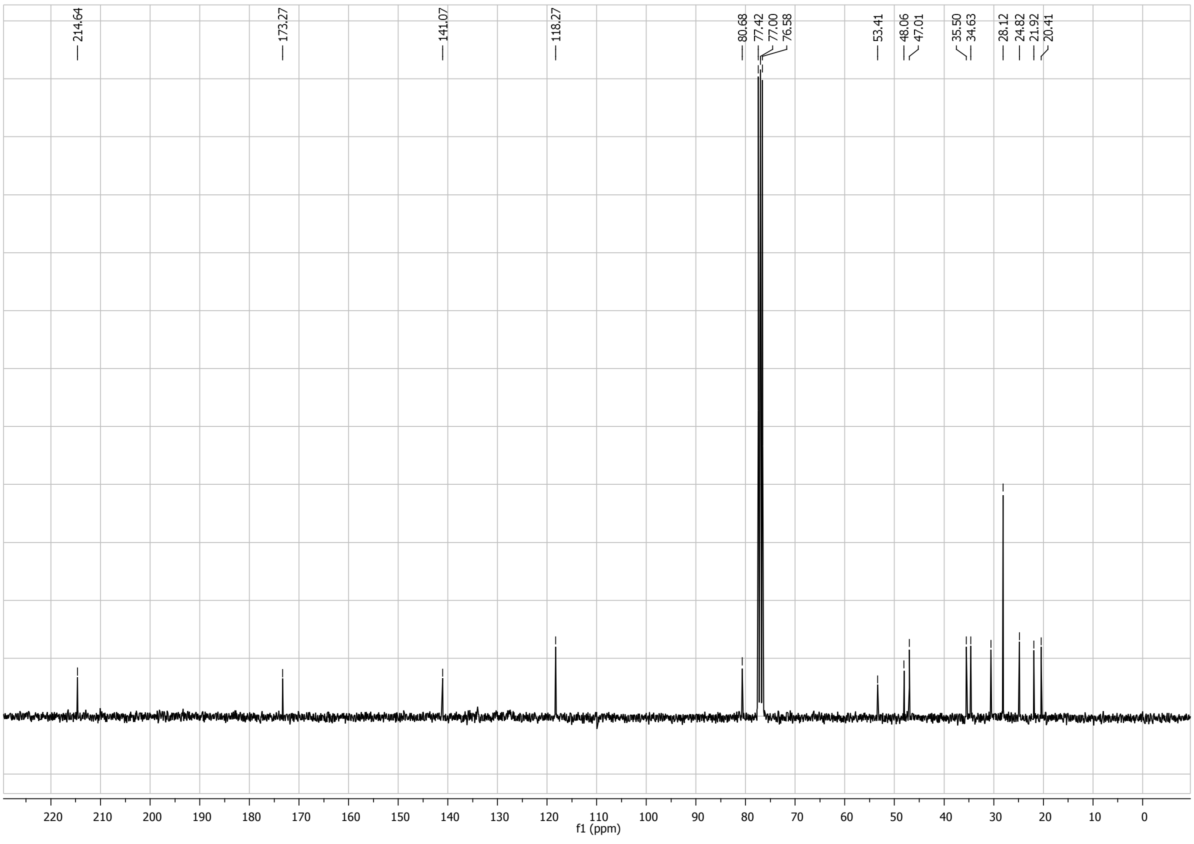

f1 (ppm)

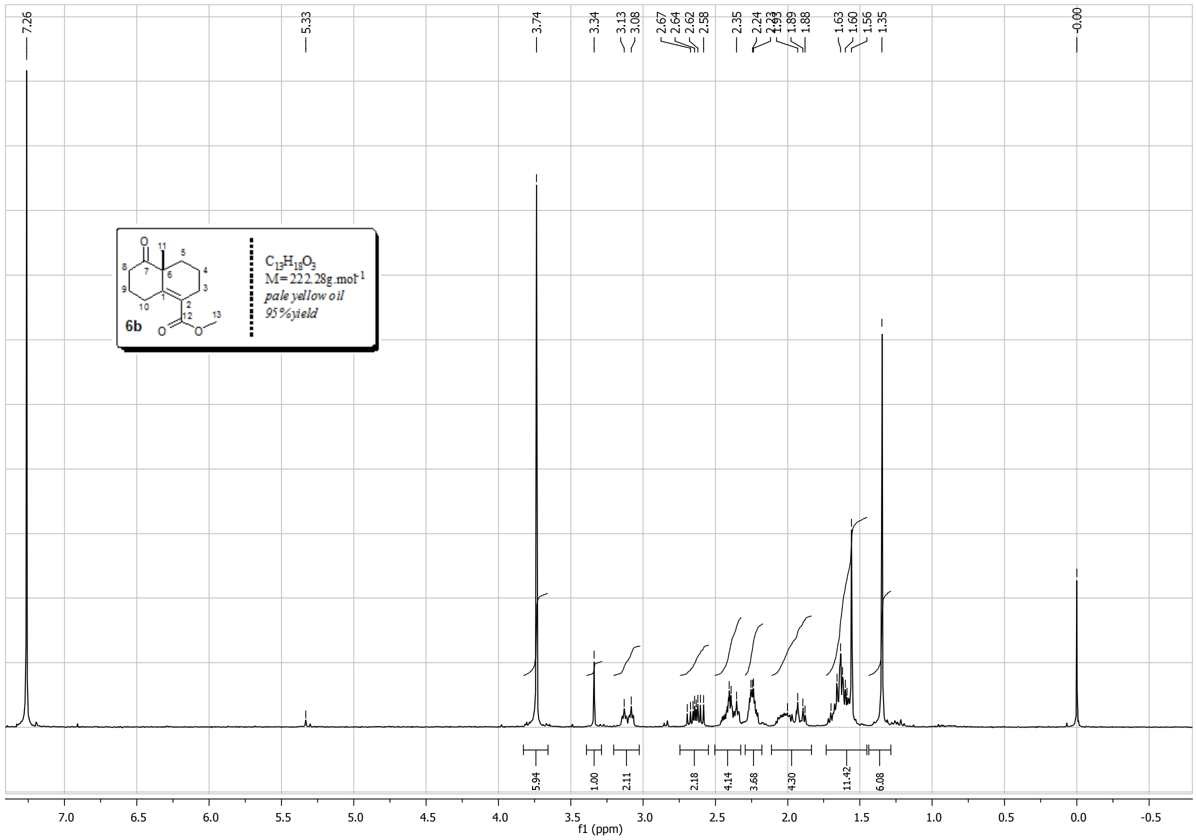

6a
$C_{14}H_{20}O_3$
M = 236.31g.mol-1
paleyellow oil
80%yield
7.26
4.23 4.21 4.18 4.16
3.11 3.07
2.83 2.64 2.58
2.35 2.25 2.24 1.93 1.89 1.88
1.64 1.56 1.35 1.32 1.30 1.28 1.21
-0.00
2.08 1.02 1.00 2.06 1.93 2.20 5.03 6.24
f1 (ppm)

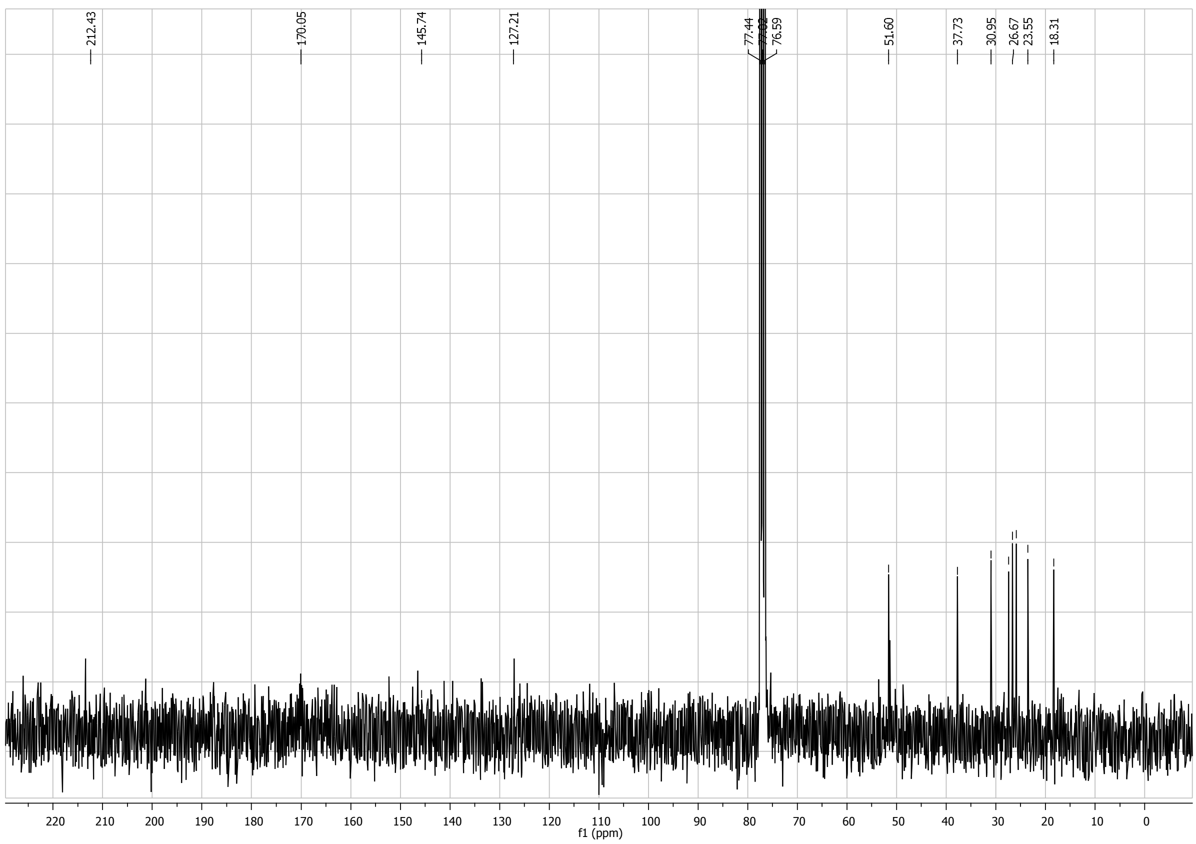

213.51
170.42
146.61
127.42
77.44 76.59
60.44
51.28
37.74 31.52 30.97 26.60 23.55 18.31 14.23
f1 (ppm)

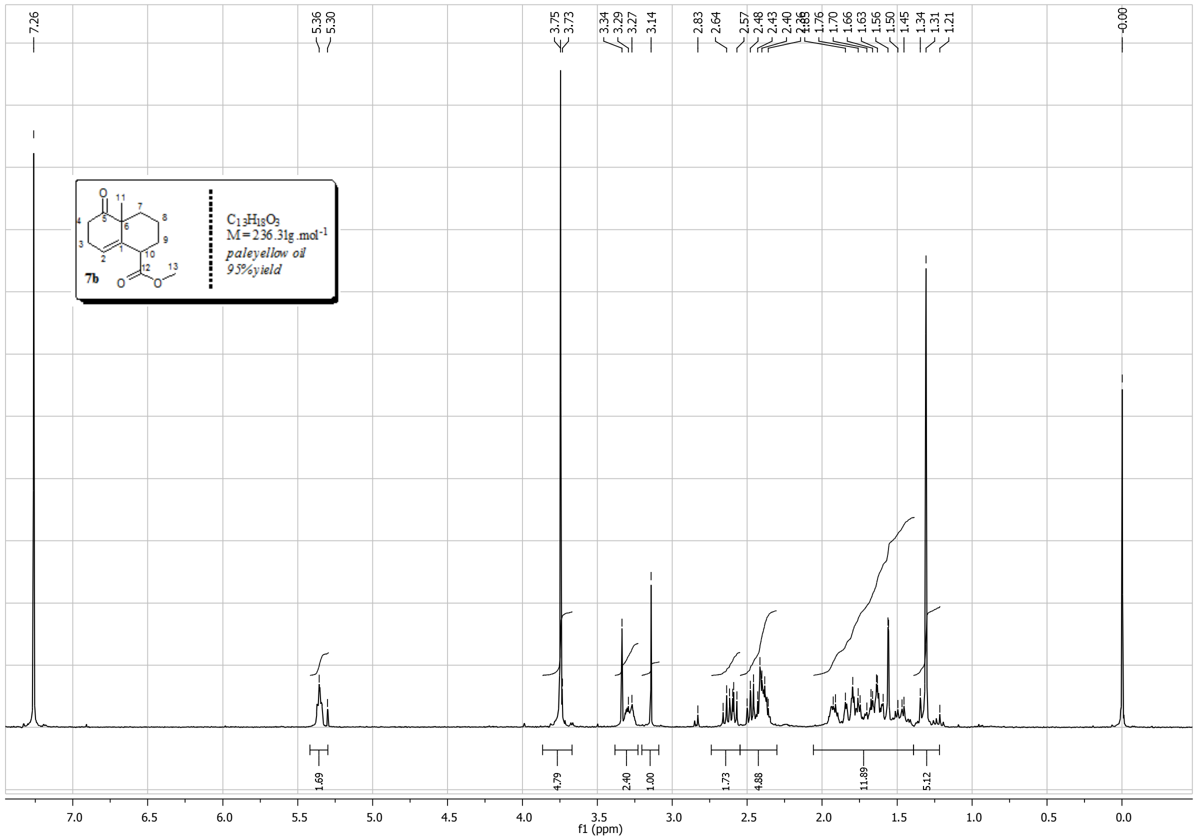

7a
$C_{14}H_{20}O_3$
M = 236.31g.mol-1
paleyellow oil
85%yield
f1 (ppm)


7c
C16H24O3
M= 264.36 g .mol-1
pale yellow oil
65% yield
7.26
5.48
3.15
3.11
2.59
2.50
2.47
2.45
2.41
2.40
2.39
2.39
2.05
1.77
1.72
1.65
1.61
1.56
1.53
1.52
1.49
1.46
1.44
1.35
1.33
1.29
1.25
-0.00
1.00
4.41
4.99
14.32
29.41
52.78
14.82
f1 (ppm)

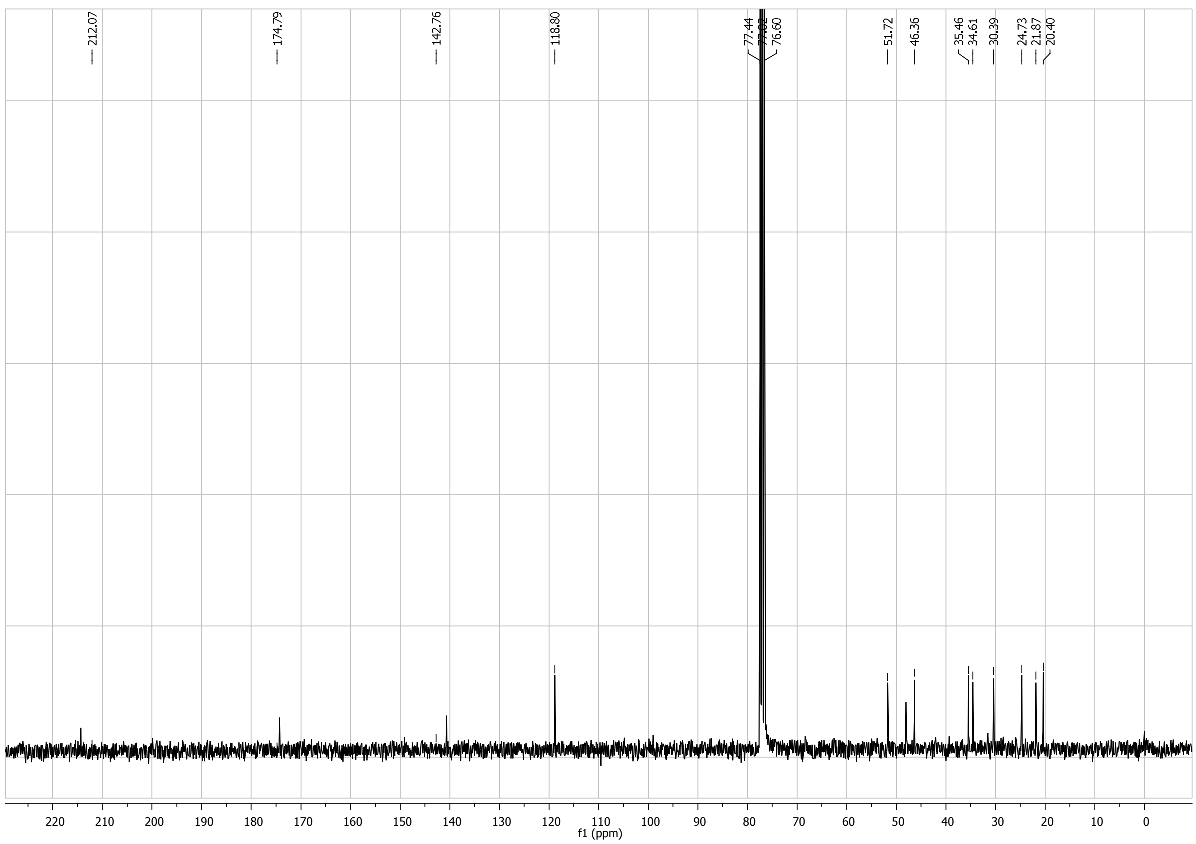

214.64
173.27
141.07
118.27
80.68
77.42
77.00
76.58
53.41
48.06
47.01
35.50
34.63
28.12
24.82
21.92
20.41
f1 (ppm)


7.26
5.33
3.74
3.34
3.13
3.08
2.67
2.64
2.62
2.58
2.35
2.24
1.89
1.88
1.63
1.60
1.56
1.35
-0.00
6b
C13H18O3
M=222.28g.mol-1
pale yellow oil
95%yield
5.94
1.00
2.11
2.18
4.14
3.68
4.30
11.42
6.08
f1 (ppm)


212.43
170.05
145.74
127.21
77.44
76.59
51.60
37.73
30.95
26.67
23.55
18.31
f1 (ppm)



7.26
5.36
5.30
3.75
3.73
3.34
3.29
3.27
3.14
2.83
2.64
2.57
2.48
2.43
2.40
1.76
1.70
1.66
1.63
1.56
1.50
1.45
1.34
1.31
1.21
-0.00
7b
$C_{13}H_{18}O_3$
M = 236.31g.mol-1
paleyellow oil
95%yield
1.69
4.79
2.40
1.00
1.73
4.88
11.89
5.12
f1 (ppm)



212.07
174.79
142.76
118.80
77.44
76.60
51.72
46.36
35.46
34.61
30.39
24.73
21.87
20.40
f1 (ppm)

J] REFERENCES

1. R. R. Huddleston, M. J. Krische, *Org. Lett.* **2003,** *5*, 1143-1146.
2. T. Thiemann, K. Umeno, J. Wang, Y. Tabuchi, K. Arima, M. Watanabe, Y. Tanaka, H. Gorohmaru, S. Mataka, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2090-2110.
3. T. M. Werkhoven, R. van Nispen, J. Lugtenburg, *Eur. J. Org. Chem.* **1999**, 2909-2914.
4. J. A. Ragan, T. W. Makowski, D. J. A. Ende, P. J. Clifford, G. R. Young, A. K. Conrad, S. A. Eisenbeis, *Org. Process Res. Dev.* **1998,** *2*, 379-381.
5. S. A. Barrack, W. H. Okamura, *J. Org. Chem.* **1986,** *51*, 3201-3206.
6. T. Katoh, S. Mizumoto, M. Fudesaka, M. Takeo, T. Kajimoto, M. Node, *Tetrahedron Asymmetry* **2006,** *17*, 1655-1662.
7. A. V. Bedekar, T. Watanabe, K. Tanaka, K. Fuji, *Synthesis* **1995**, 1069-1070.
8. P. K. Koesh, M. J. Krische, *Org. Lett.* **2004,** *6*, 691-694.
9. A. K. Chatterjee, J. P. Morgan, M. Scholl, R. H. Grubbs, *J. Am. Chem. Soc.* **2000,** *122*, 3783-3784.
10. P. Renouf, J. M. Poirier, P. Duhamel, *J. Chem. Soc. Perkin Trans. 1* **1997**, 1739-1745.
11. J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus, A. H. Hoveyda, *J. Am. Chem. Soc.* **1999,** *121*, 791-799.
12. S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, *J. Am. Chem. Soc.* **2000,** *122*, 8168-8179.
13. J. Cossy, S. BouzBouz, A. H. Hoveyda, *J. Organomet. Chem.* **2001,** *634*, 215-221.
14. J. Cossy, S. BouzBouz, A. H. Hoveyda, *J. Organomet. Chem.* **2001,** *624*, 327-332.

All references on reductive-aldol reactions catalyzed by various metal transition states:

15. For initial works on reductive-aldol reaction catalyzed by different metals see: [Rh] (a) Revis, A.; Hilty, T. K. *Tetrahedron Lett.* **1987,** *28*, 4809-4812. (b) Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990,** *31*, 5331-5334. [Co] (c) Isayama, S.; Mukaiyama, T. *Chem. Lett.* **1989**, 2005-2008. [Pd] (d) Kiyooka, S.; Shimizu, A.; Torii, S. *Tetrahedron Lett.* **1998,** *39*, 5237-5238. [Cu] (e) Ooi, T.; Doda, K.; Sakai, D.; Maruoka, K. *Tetrahedron Lett.* **1999,** *40*, 2133-2136. [Ni] (f) Chrovian, C. C.; Montgomery, J. *Org. Lett.* **2007,** *9*, 537-540.

16. For intermolecular reductive-aldol mediated by rhodium complexes in presence of organosilane see: (a) Taylor, S. J.; Morken, J. P. *J. Am. Chem. Soc.* **1999,** *121*, 12202-12203. (b) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000,** *122*, 4528-4529. (c) Zhao, C. X.; Bass, J.; Morken, J. P. *Org. Lett.* **2001,** *3*, 2839-2842. (d) Russell, A. E.; Fuller, N. O.; Taylor, S. J.; Aurriset, P.; Morken, J. P. *Org. Lett.* **2004,** *6*, 2309-2312. (e) Fuller, N. O.; Morken, J. P. *Synlett* **2005**, 1459-1461. (f) Nishiyama, H.; Shiomi, T.; Tsuchiya, Y.; Matsuda, I. *J. Am. Chem. Soc.* **2005,** *127*, 6972-6973. (g) Shiomi, T.; Ito, J.-i.; Yamamoto, Y.; Nishiyama, H. *Eur. J. Org. Chem.* **2006**, 5594-5600. (h) Shiomi, T.; Nishiyama, H. *Org. Lett.* **2007,** *9*, 1651-1654. (i) Nishiyama, H.; Ishikawa, J.; Shiomi, T. *Tetrahedron Lett.* **2007,** *48*, 7841-7844.

17. For intermolecular reductive-aldol reactions catalyzed by rhodium complexes in presence of hydrogen see: (a) Jang, H.-Y.; Huddleston, R. R.; Krische, M. J. *J. Am. Chem. Soc.* **2002,** *124*, 15156-15157. (b) Jung, C. K.; Garner, S. A.; Krische, M. J. *Org. Lett.* **2006,** *8*, 519-522. (c) Han, S. B.; Krische, M. J. *Org. Lett.* **2006,** *8*, 5657-5660. (d) Jung, C. K.; Krische, M. J. *J. Am. Chem. Soc.* **2006,** *128*, 17051-17056. (e) Garner, S. A.; Krische, M. J. *J. Org. Chem.* **2007,** *72*, 5843-5846. (f) Bee, C.; Han, S. B.; Hassan, A.; Lida, H.; Krische, M. J. *J. Am. Chem. Soc.* **2008,** *130*, 2746-2747.

18. For intermolecular reductive-aldol mediated by other metals in presence of organosilane see: [Ir] (a) Zhao, C. X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2001,** *3*, 1829-1831. (b) Townes, J. A.; Evans, M. A.; Queffelec, J.; Taylor, S. J.; Morken, J. P. *Org. Lett.* **2002,** *4*, 2537-2540. [Co] (c) Lumby, R. J. R.; Joensuu, P. M.; Lam, H. W. *Org. Lett.* **2007,** *9*, 4367-4370. [In] (d) Inoue, K.; Ishida, T.; Shibata, I.; Baba, A. *Adv. Synth. Catal.* **2002,** *344*, 283-287. (b) Shibata, I.; Kato, H.; Ishida, T. ; Yasuda, M.; Baba, A. *Angew. Chem. Int. Ed.* **2004,** *43*, 711-714. (c) Miura, K.; Yamada, Y.; Tomita, M.; Hosomi, A. *Synlett* **2004**, 1985-1989.

19. For diastereoselective intramolecular reductive aldol cyclizations catalyzed by rhodium complexes in presence of organosilane see: (a) Emiabata-Smith, D.; McKillop, A.; Mills, C.; Motherwell, W. B.; whitehead, A. J. *Synlett* **2001,** *8*, 1302-1304. (b) Freiria, M.; whitehead, A. J.; Tocher, D. A.; Motherwell, W. B. *Tetrahedron* **2004,** *60*, 2673-2692. For diastereoselective intramolecular reductive aldol cyclizations catalyzed by rhodium complexes in presence of hydrogen see: (c) Huddleston, R. R.; Krische, M. J. *Org. Lett.* **2003,** *5*, 1143-1146. (d) Koesh, P. K.; Krische, M. J. *Org. Lett.* **2004,** *6*, 691-694. (e) Jang, H.-Y.; Krische, M. J. *Eur. J. Org. Chem.* **2004**, 3953-3958. (f) Jang, H. Y.; rische, M. J. *Acc. Chem. Res.* **2004,** *37*, 653-661. (g) Bocknack, B. M.; Wang, L.-C.; Krische, M. J. *Proc. Natl. Acad. Sci. USA* **2004,** *101*, 5421-5424. For diastereoselective cobalt-catalyzed reductive-aldol and Michael cycloreductions see: (h) Baik, T.-G.; Luis, A. L.; Wang, L.-C.; Krische, M. J. *J. Am. Chem. Soc.* **2001,** *123*, 5112-5113. (i) Baik, T.-G.; Luis, A. L.; Wang, L.-C.; Krische, M. J. *J. Am. Chem. Soc.* **2001,** *123*, 6716-6717. (j) Wang, L.-C.; Jang, H.-Y.; Roh, Y.; Lynch, V.; Schultz, A. J.; Wang, X.; Krische, M. J. *J. Am. Chem. Soc.* **2002,** *124*, 9448-9453. (k) Lam, H. W.; Joensuu, P. M.; Murray, G. J.; Fordyce, E. A. F.; Prieto, O.; Luebbers, T. *Org. Lett.* **2006,** *8*, 3729-3732. For diastereoselective reductive-aldol reactions catalyzed by nickel see : (l) Joensuu, P.M.; Murray, G.J.; Fordyce, E.A.F.; Luebbers, T.; Lam, H.W. *J. Am. Chem. Soc.* **2008**, *130*, 7328-7338. For diastereoselective reductive-aldol reactions mediated by the stryker's reagent see: (m) Chiu, P.; Chen, B.; Cheng, K. F. *Tetrahedron Lett.* **1998,** *39*, 9229-9232. (n) Chiu, P.; Szeto, C. P.; Geng, Z.; Cheng, K. F. *Org. Lett.* **2001,** *3*, 1901-1903. (o) Chiu, P.; Szeto, C. P.; Geng, Z.; Cheng, K. F. *Tetrahedron Lett.* **2001,** *42*, 4091-4093. (p) Chiu, P.; Leung, S. K. *Chem. Comm.* **2004**, 2308-2309. (q) Chung, W. K.; Chiu, P. *Synlett* **2005**, 55-58.

20. For tandem conjugated addition-electrophilic trapping catalyzed by copper see (a) Agapiou, K.; Cauble, D. F.; Krische, M. J. *J. Am. Chem. Soc.* **2004,** *126*, 4528-4529. For enantioselective reductive-aldol cyclization catalyzed by copper complexes see (b) Lam, H. W.; Joensuu, P. M. *Org. Lett.* **2005,** *7*, 4225-4228. For non-enantioselective reductive-aldol cyclization catalyzed by copper complexes see (c) Lam, H. W.; Murray, G. J.; Firth, J. D. *Org. Lett.* **2005,** *7*, 5743-5746.