

Supplementary Information for:

**Highly stereoselective construction of the C2 stereocentre of α -tocopherol (vitamin E) by
asymmetric addition of Grignard reagents to ketones**

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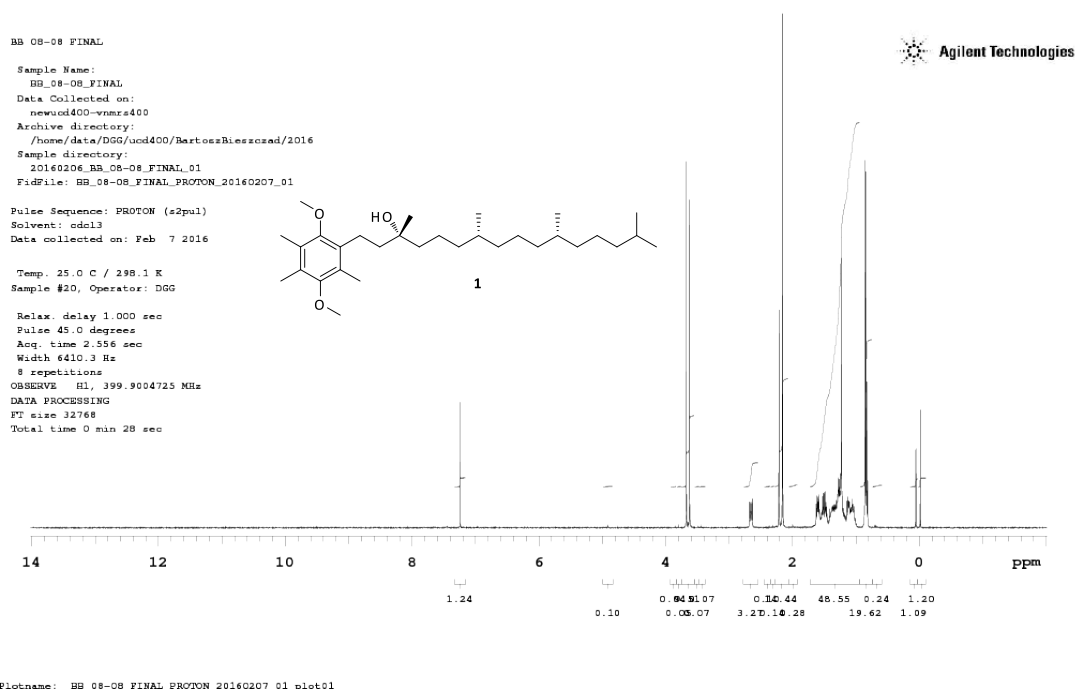
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1. General Experimental

All chemicals were supplied by Aldrich apart from natural phytol, which was supplied by Wuhan ChemFaces Biochemical Co. Microwave assisted reactions were performed using CEM Discover microwave instrument (S-series). Supercritical Fluid Chromatography (SFC) analysis was made using ACQUITY UPC2 system with auto-sampler, combined with PDA Detector Type UPLC eLambda 800 nm. Chiral column Chiralpak® IA-3 of internal diameter of 4.6 mm, 100 mm with particles size of 3 μm was used to separate diastereoisomers in a single case with methanol as a co-solvent. Samples were prepared in heptanes in approximately 1 mg/mL. All NMR analysis was performed using 300, 400 or 500 MHz Varian spectrometers. NMR samples were made in CDCl_3 . ^1H and ^{13}C NMR chemical shifts are given relative to tetramethylsilane.

2. NMR spectra of products and intermediates



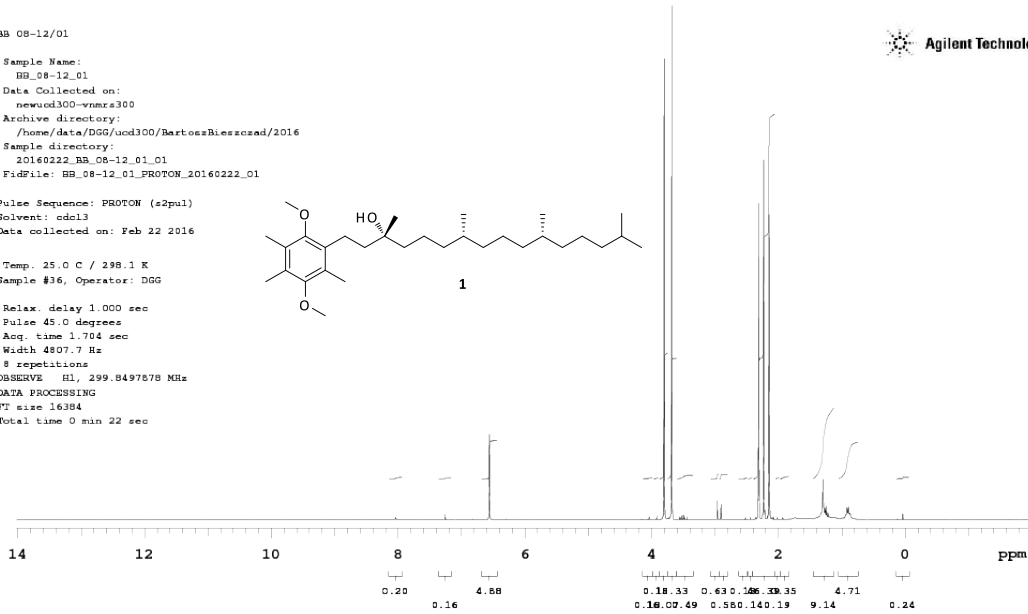
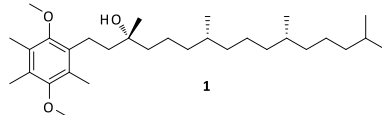
BB 08-12/01

Sample Name:
BB_08-12_01
Data Collected on:
newucd300-vnmr300
Archive directory:
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Sample directory:
20160222_BB_08-12_01_01
FidFile: BB_08-12_01_PROTON_20160222_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 22 2016

Temp. 25.0 C / 298.1 K
Sample #36, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497678 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_08-12_01_PROTON_20160222_01_plot01

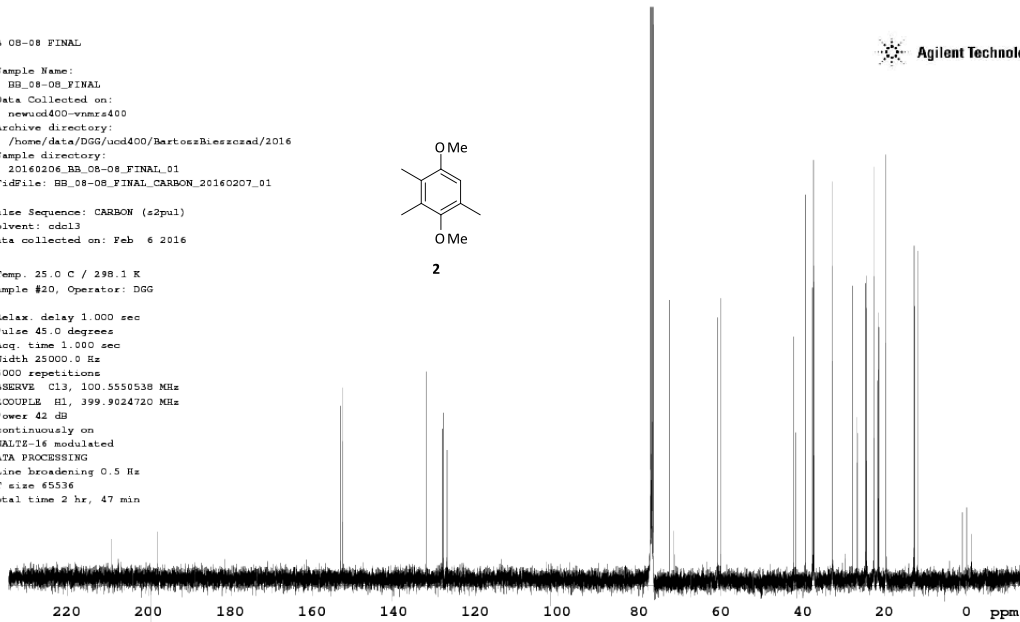
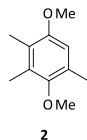
BB 08-08 FINAL

Sample Name:
BB_08-08_FINAL
Data Collected on:
newucd400-vnmr400
Archive directory:
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Sample directory:
20160206_BB_08-08_FINAL_01
FidFile: BB_08-08_FINAL_CARBON_20160207_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: Feb 6 2016

Temp. 25.0 C / 298.1 K
Sample #20, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.000 sec
Width 25000.0 Hz
5000 repetitions
OBSERVE C13, 100.5550538 MHz
DECOUPLE H1, 399.9024720 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 2 hr, 47 min



Plotname: BB_08-08_FINAL_CARBON_20160207_01_plot01

BB 08-11/02 F2

Sample Name:
BB_08-11_02_F2

Data Collected on:
newud400-wmrs400

Archive directory:
/home/data/DGG/ucd400/BartoszBieszczad/2016

Sample directory:
20160212_BB_08-11_02_F2_01

FidFile: BB_08-11_02_F2_PROTON_20160212_01

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Feb 12 2016

Temp. 25.0 C / 298.1 K

Sample #14, Operator: DGG

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 2.556 sec

Width 6410.3 Hz

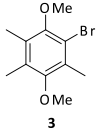
8 repetitions

OBSERVE H1, 399.9004725 MHz

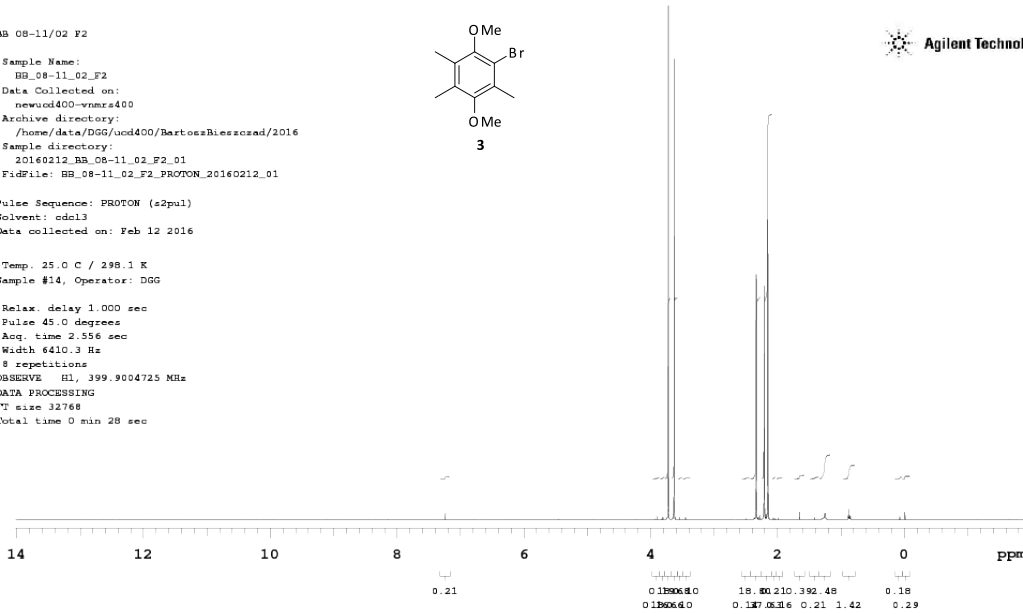
DATA PROCESSING

FT size 32768

Total time 0 min 28 sec



Agilent Technologies



Plotname: BB_08-11_02_F2_PROTON_20160212_01_plot01

BB 08-51/01

Sample Name:
BB_08-51_01

Data Collected on:
newud400-wmrs400

Archive directory:
/home/data/DGG/ucd400/BartoszBieszczad/2016

Sample directory:
20160712_BB_08-51_01_01

FidFile: BB_08-51_01_PROTON_20160712_01

Pulse Sequence: PROTON (s2pul)

Solvent: cdcl3

Data collected on: Jul 12 2016

Temp. 25.0 C / 298.1 K

Sample #34, Operator: DGG

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 2.556 sec

Width 6410.3 Hz

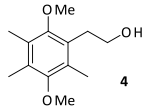
8 repetitions

OBSERVE H1, 399.9004725 MHz

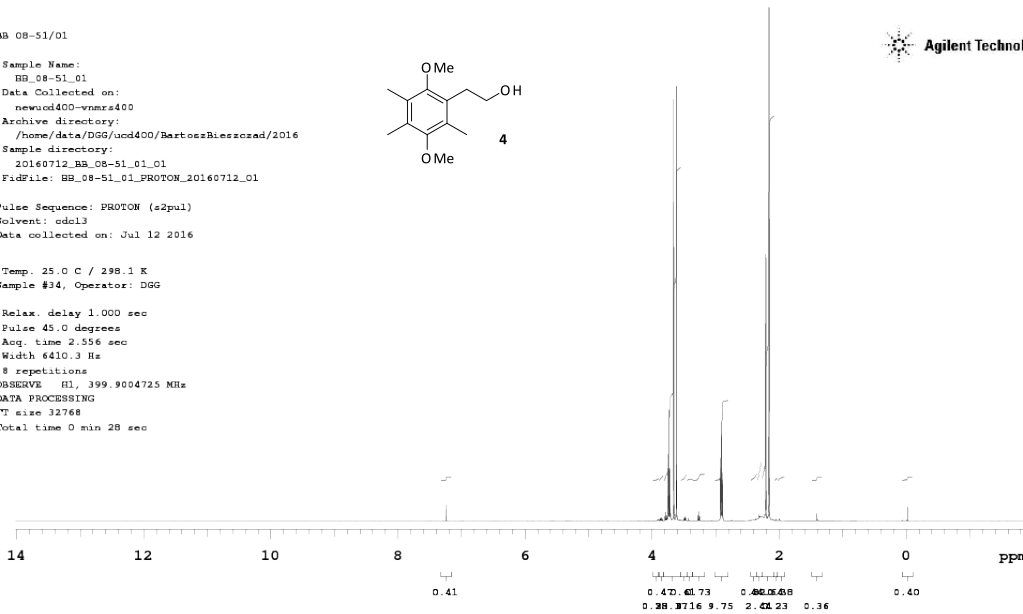
DATA PROCESSING

FT size 32768

Total time 0 min 28 sec



Agilent Technologies



Plotname: BB_08-51_01_PROTON_20160712_01_plot01

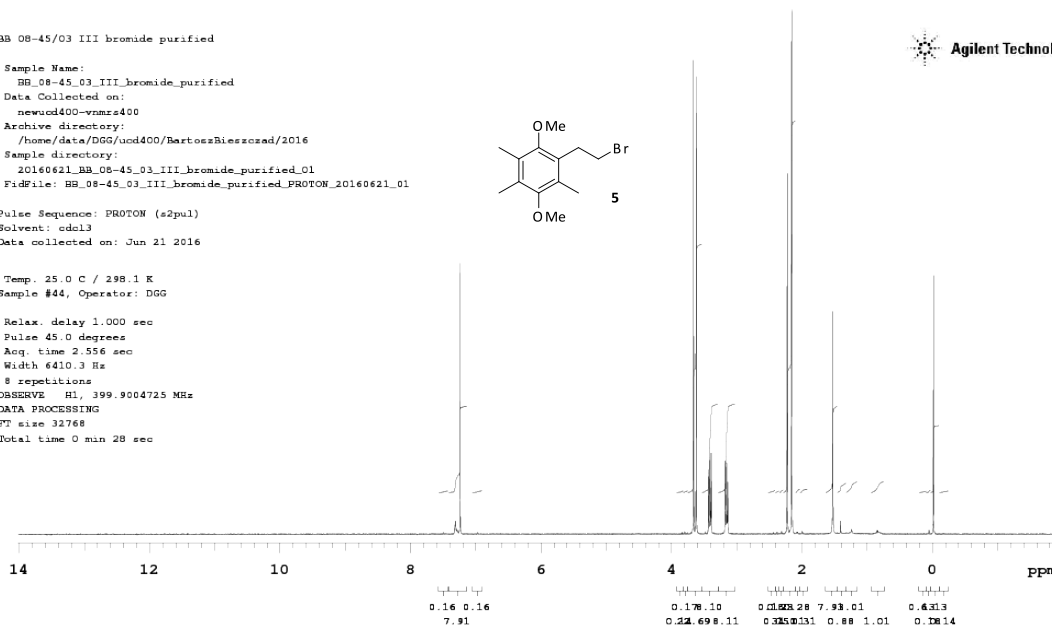
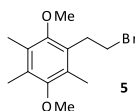
BB 08-45/03 III bromide purified

Sample Name:
BB_08-45_03_III_bromide_purified
Data Collected on:
newucd400-vnmrs400
Archive directory:
/home/data/DGG/ucd400/BartoszBieszczad/2016
Sample directory:
20160621_BB_08-45_03_III_bromide_purified_01
FidFile: BB_08-45_03_III_bromide_purified_PROTON_20160621_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jun 21 2016

Temp. 25.0 C / 298.1 K
Sample #44, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9004725 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec



Plotname: BB_08-45_03_III_bromide_purified_PROTON_20160621_01_plot01

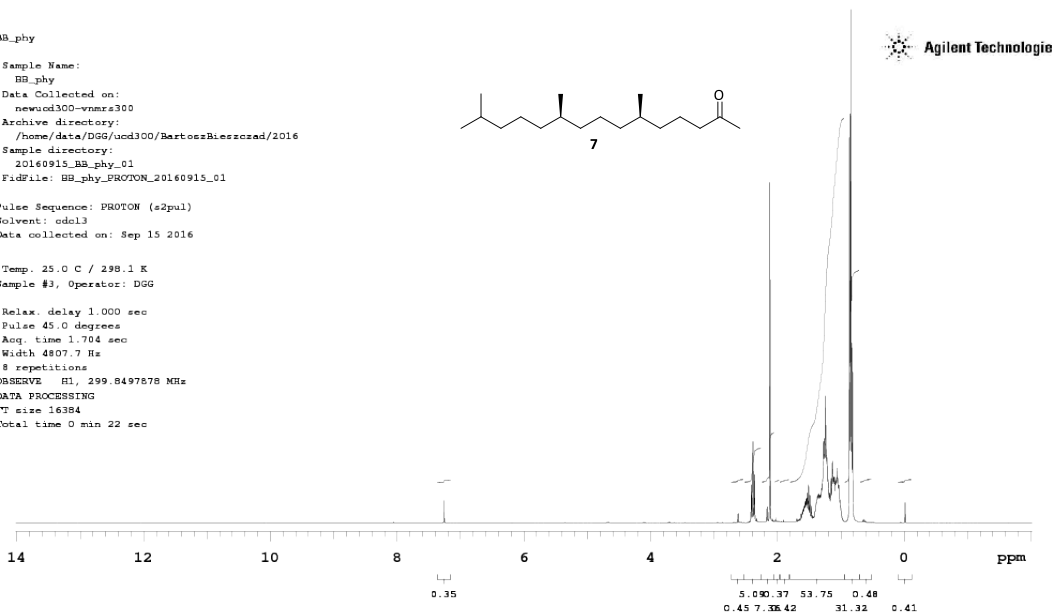
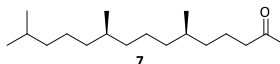
BB_phy

Sample Name:
BB_phy
Data Collected on:
newucd300-vnmrs300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2016
Sample directory:
20160915_BB_phy_01
FidFile: BB_phy_PROTON_20160915_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Sep 15 2016

Temp. 25.0 C / 298.1 K
Sample #3, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_phy_PROTON_20160915_01_plot01

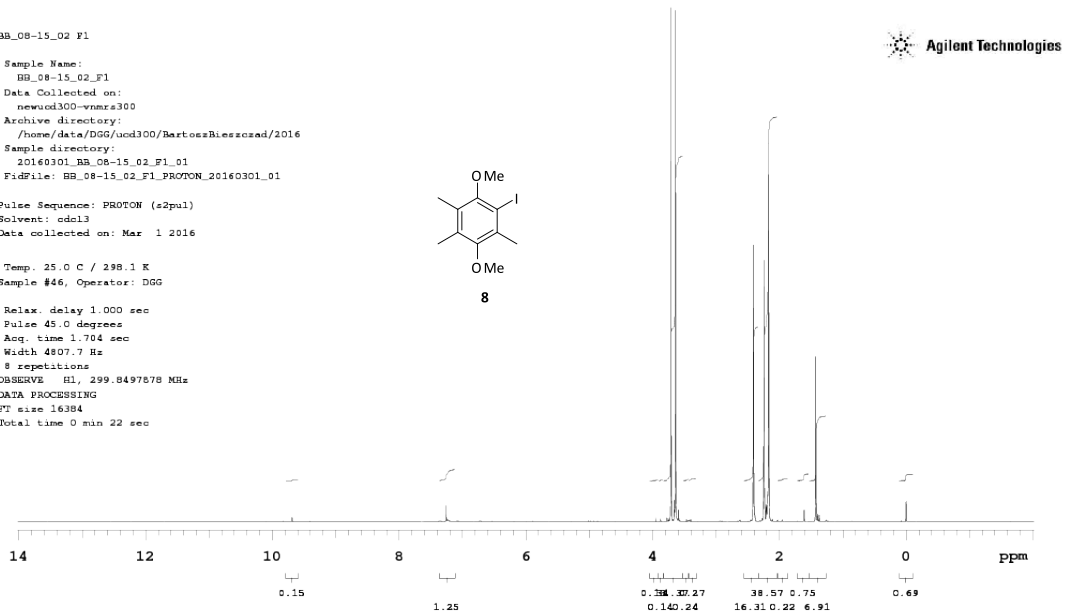
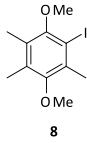
BB_08-15_02_F1

Sample Name:
BB_08-15_02_F1
Data Collected on:
newud300-wmrs300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2016
Sample directory:
20160301_BB_08-15_02_F1_01
FidFile: BB_08-15_02_F1_PROTON_20160301_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Mar 1 2016

Temp. 25.0 C / 298.1 K
Sample #46, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_08-15_02_F1_PROTON_20160301_01_plot01

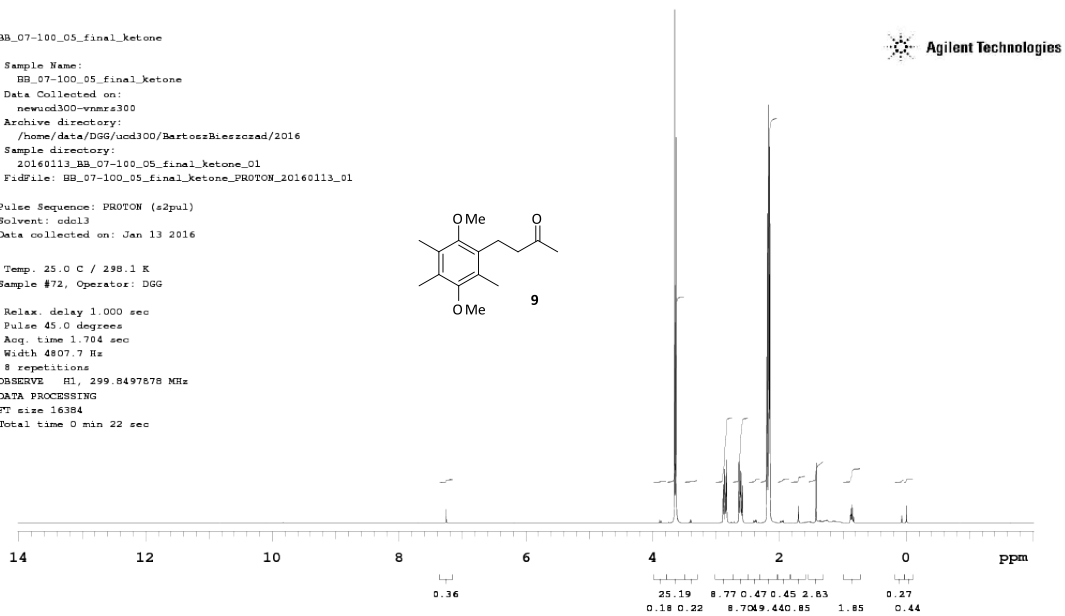
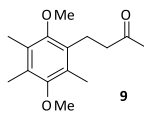
BB_07-100_05_final_ketone

Sample Name:
BB_07-100_05_final_ketone
Data Collected on:
newud300-wmrs300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2016
Sample directory:
20160113_BB_07-100_05_final_ketone_01
FidFile: BB_07-100_05_final_ketone_PROTON_20160113_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 13 2016

Temp. 25.0 C / 298.1 K
Sample #72, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_07-100_05_final_ketone_PROTON_20160113_01_plot01

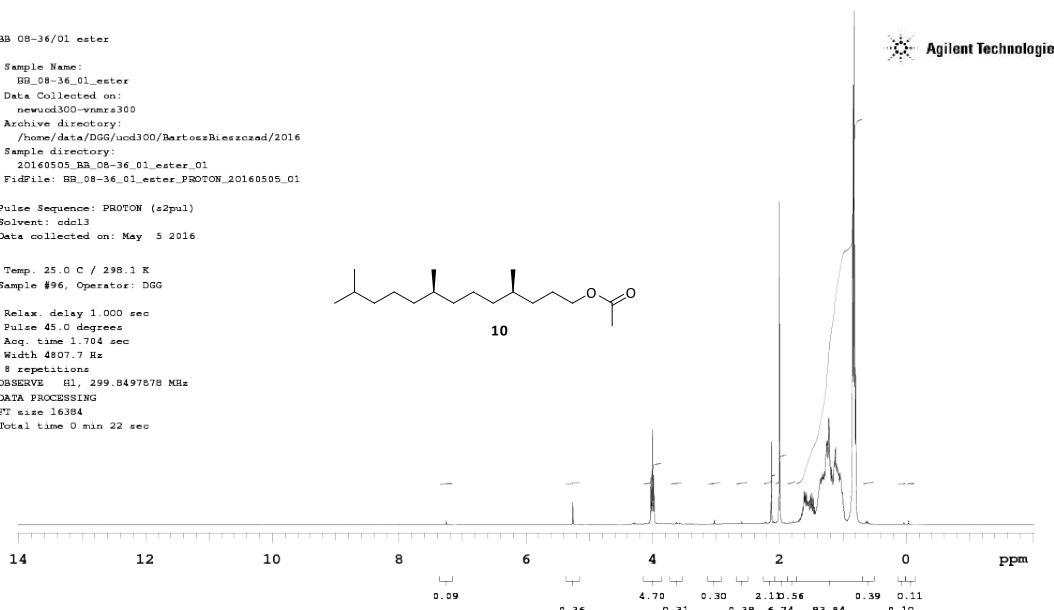
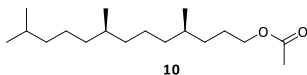
BB 08-36/01 ester

Sample Name:
BB_08-36_01_ester
Data Collected on:
newuod300-wmra300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2016
Sample directory:
20160505_BB_08-36_01_ester_01
FidFile: BB_08-36_01_ester_PROTON_20160505_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 5 2016

Temp. 25.0 C / 298.1 K
Sample #96, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_08-36_01_ester_PROTON_20160505_01_plot01

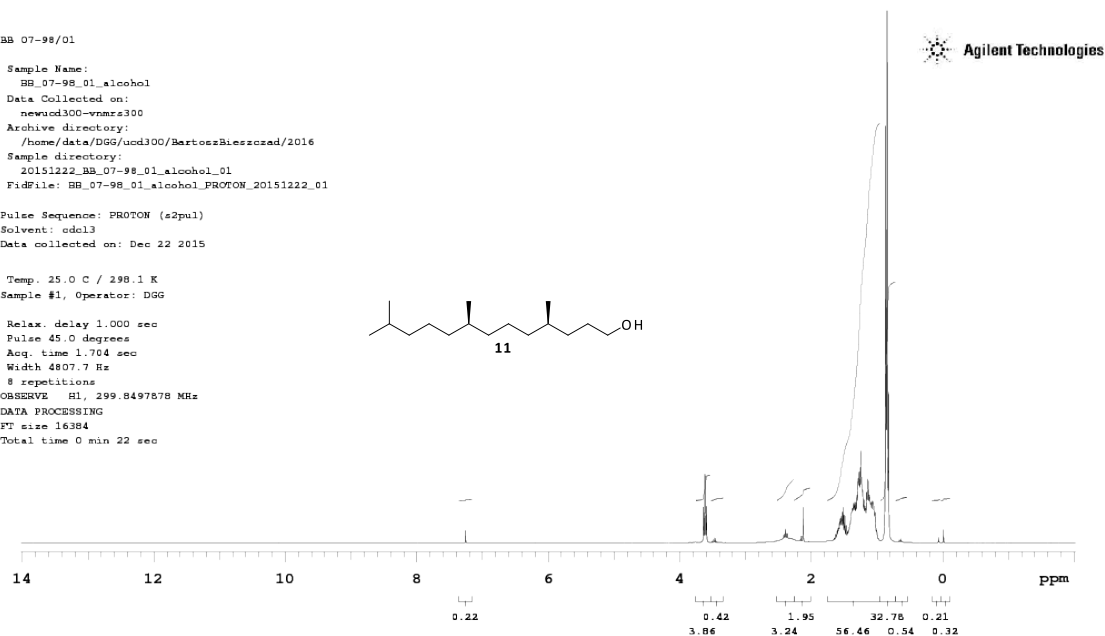
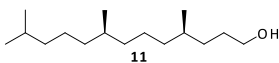
BB 07-98/01

Sample Name:
BB_07-98_01_alcohol
Data Collected on:
newuod300-wmra300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2016
Sample directory:
20151222_BB_07-98_01_alcohol_01
FidFile: BB_07-98_01_alcohol_PROTON_20151222_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Dec 22 2015

Temp. 25.0 C / 298.1 K
Sample #1, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_07-98_01_alcohol_PROTON_20151222_01_plot01

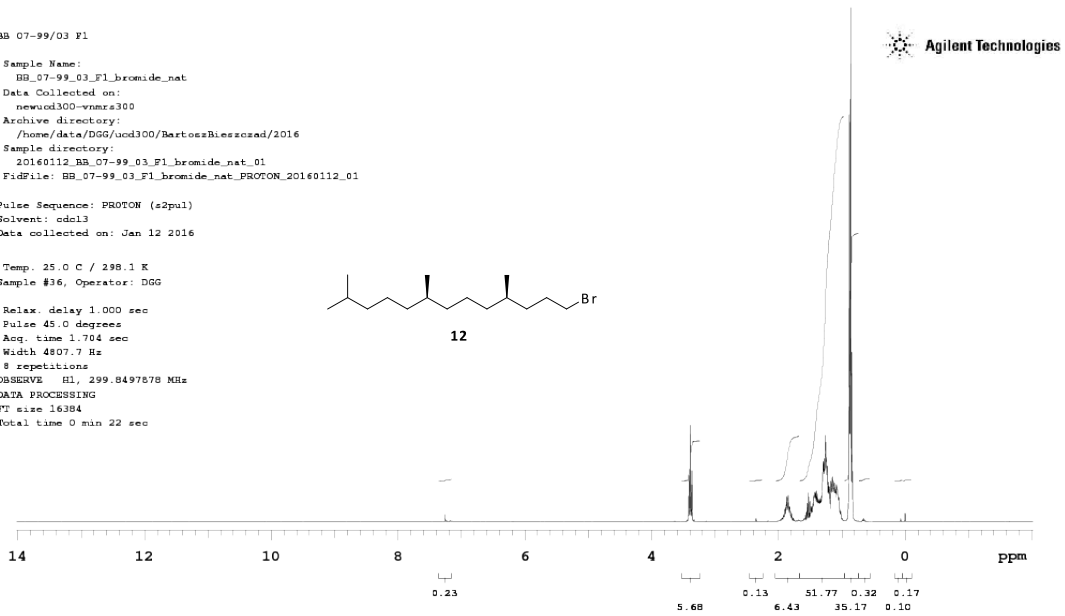
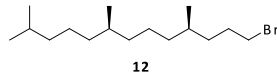
BB 07-99/03 F1

Sample Name:
BB_07-99_03_F1_bromide_nat
Data Collected on:
newud300-vnmr300
Archive directory:
/home/data/DGG/ucd300/BertossBlesszed/2016
Sample directory:
20160112_BB_07-99_03_F1_bromide_nat_01
FidFile: BB_07-99_03_F1_bromide_nat_PROTON_20160112_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 12 2016

Temp. 25.0 C / 298.1 K
Sample #36, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_07-99_03_F1_bromide_nat_PROTON_20160112_01_plot01

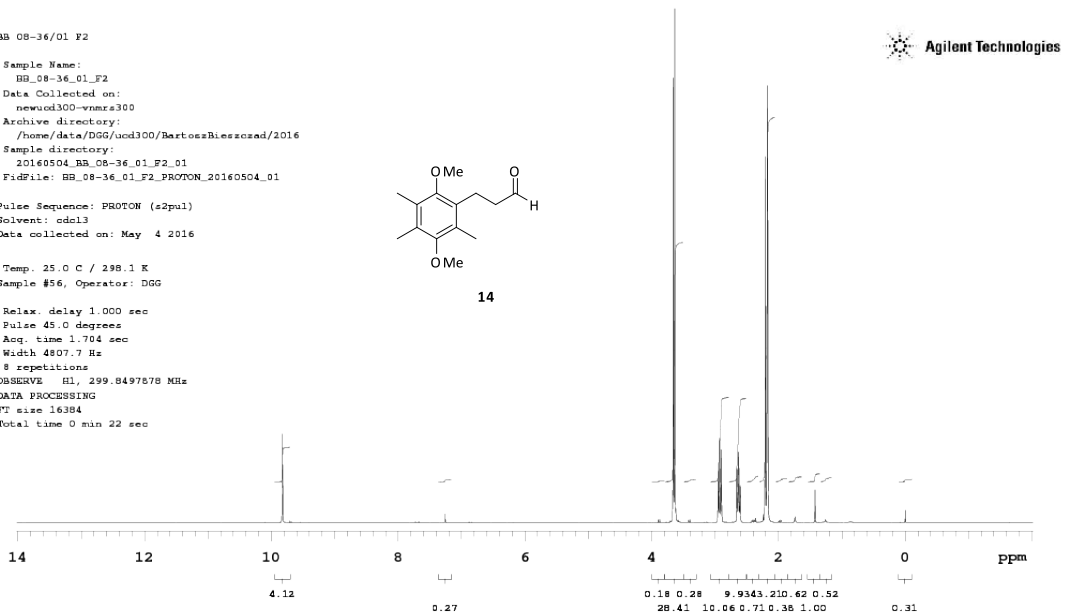
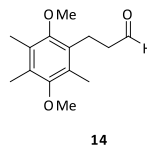
BB 08-36/01 F2

Sample Name:
BB_08-36_01_F2
Data Collected on:
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Archive directory:
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Sample directory:
20160504_BB_08-36_01_F2_01
FidFile: BB_08-36_01_F2_PROTON_20160504_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 4 2016

Temp. 25.0 C / 298.1 K
Sample #56, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec



Plotname: BB_08-36_01_F2_PROTON_20160504_01_plot01

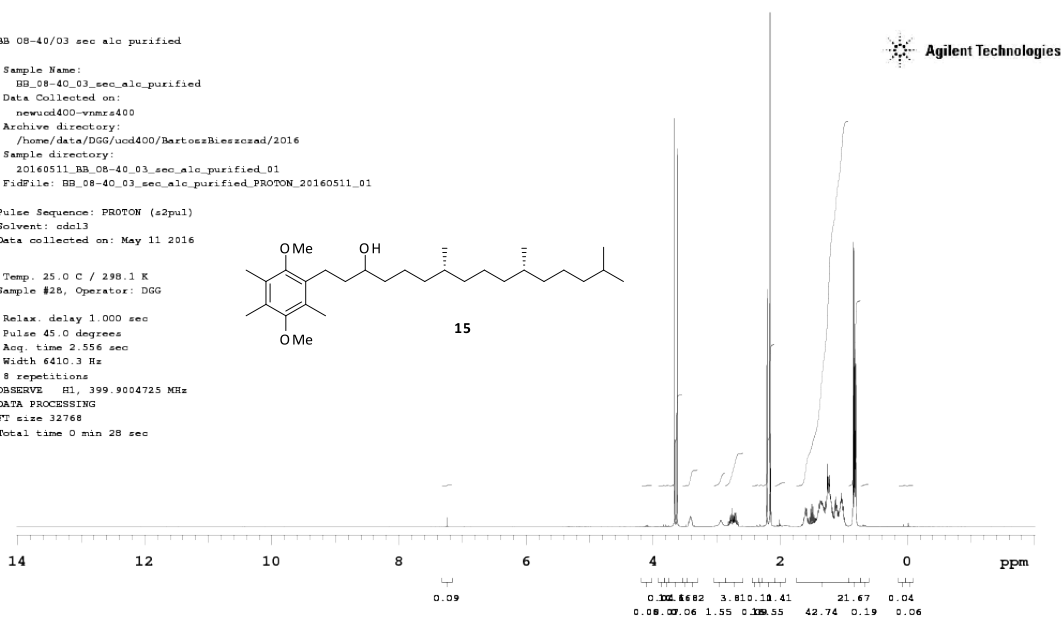
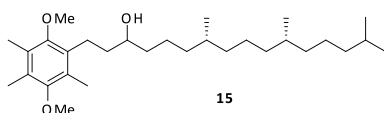
BB 08-40/03 sec alc purified

Sample Name: BB_08-40_03_sec_alc_purified
Data Collected on: newud400-vnmr400
Archive directory: /home/data/DGG/ucd400/BartoszBieszczad/2016
Sample directory: 20160511_BB_08-40_03_sec_alc_purified_01
FidFile: BB_08-40_03_sec_alc_purified_PROTON_20160511_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2016

Temp. 25.0 C / 298.1 K
Sample #28, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9004725 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec



Plotname: BB_08-40_03_sec_alc_purified_PROTON_20160511_01_plot01

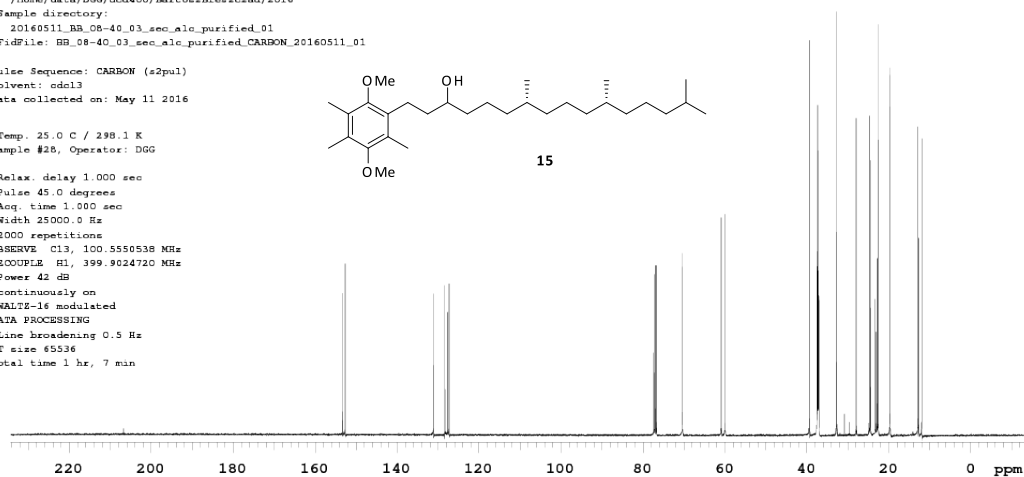
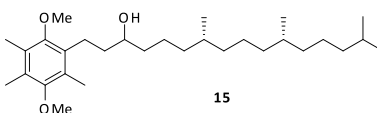
BB 08-40/03 sec alc purified

Sample Name: BB_08-40_03_sec_alc_purified
Data Collected on: newud400-vnmr400
Archive directory: /home/data/DGG/ucd400/BartoszBieszczad/2016
Sample directory: 20160511_BB_08-40_03_sec_alc_purified_01
FidFile: BB_08-40_03_sec_alc_purified_CARBON_20160511_01

Pulse Sequence: CARBON (s2pul)
Solvent: cdcl3
Data collected on: May 11 2016

Temp. 25.0 C / 298.1 K
Sample #28, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.000 sec
Width 25000.0 Hz
2000 repetitions
OBSERVE C13, 100.5550538 MHz
DECOUPLE H1, 399.9024720 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 7 min



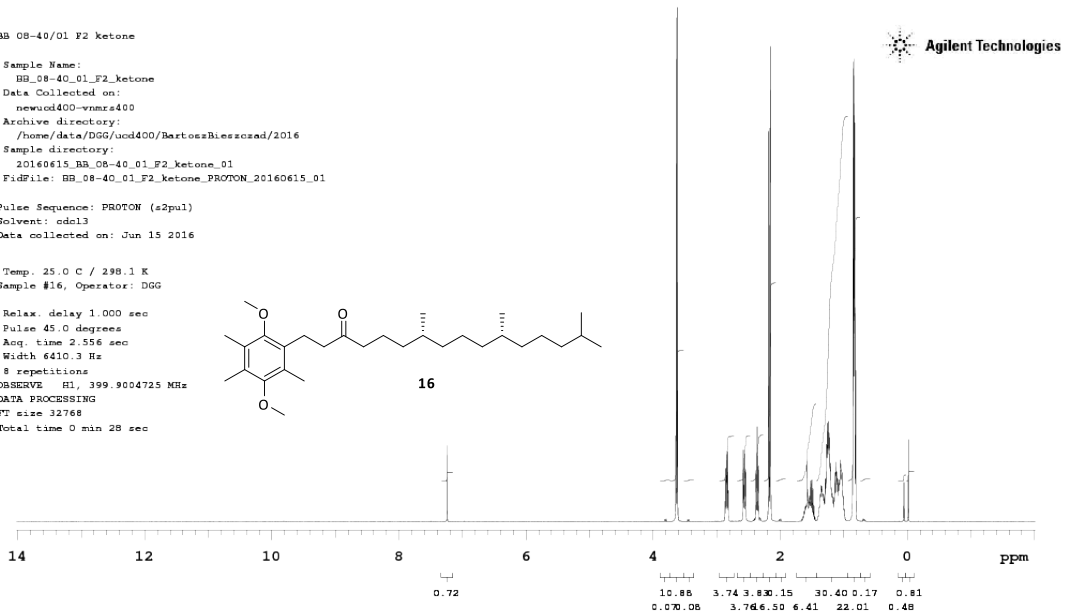
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BB 08-40/01 F2 ketone

Sample Name:
BB_08-40_01_F2_ketone
Data Collected on:
newud400-vnmr400
Archive directory:
/home/data/DGG/ucd400/BartoszBieszczad/2016
Sample directory:
20160615_BB_08-40_01_F2_ketone_01
FidFile: BB_08-40_01_F2_ketone_PROTON_20160615_01
Pulse Sequence: PROTON (s2pu1)
Solvent: cdcl3
Data collected on: Jun 15 2016

Temp. 25.0 C / 298.1 K
Sample #16, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.556 sec
Width 6410.3 Hz
8 repetitions
OBSERVE H1, 399.9004725 MHz
DATA PROCESSING
FT size 32768
Total time 0 min 28 sec



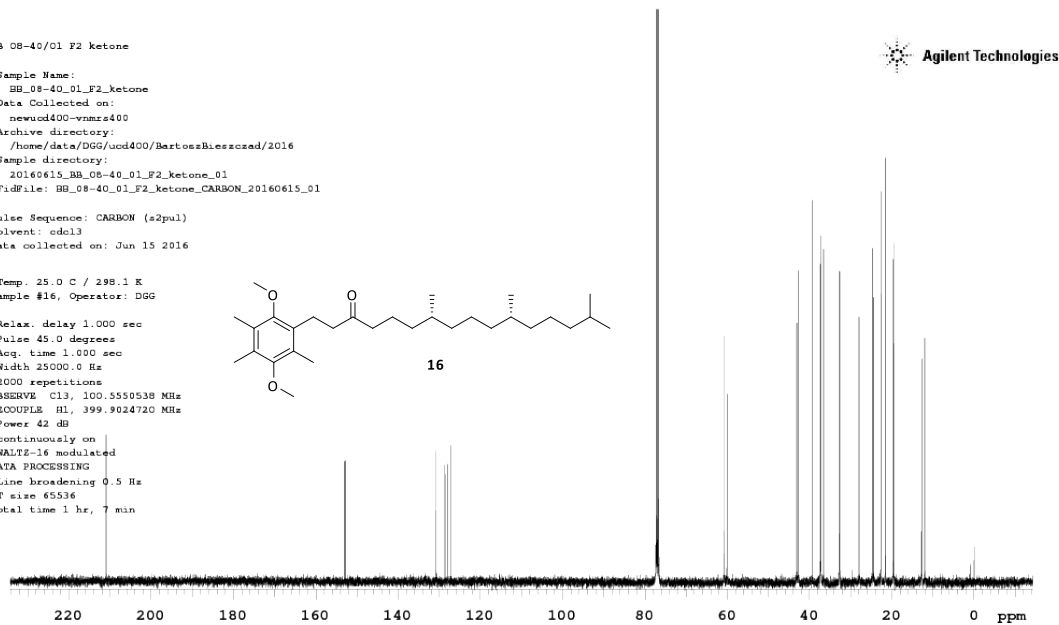
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BB 08-40/01 F2 ketone

Sample Name:
BB_08-40_01_F2_ketone
Data Collected on:
newud400-vnmr400
Archive directory:
/home/data/DGG/ucd400/BartoszBieszczad/2016
Sample directory:
20160615_BB_08-40_01_F2_ketone_01
FidFile: BB_08-40_01_F2_ketone_CARBON_20160615_01
Pulse Sequence: CARBON (s2pu1)
Solvent: cdcl3
Data collected on: Jun 15 2016

Temp. 25.0 C / 298.1 K
Sample #16, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.000 sec
Width 25000.0 Hz
2000 repetitions
OBSERVE C13, 100.5550538 MHz
DECOUPLE H1, 399.9024720 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 7 min



Plotname: BB_08-40_01_F2_ketone_CARBON_20160615_01_plot01

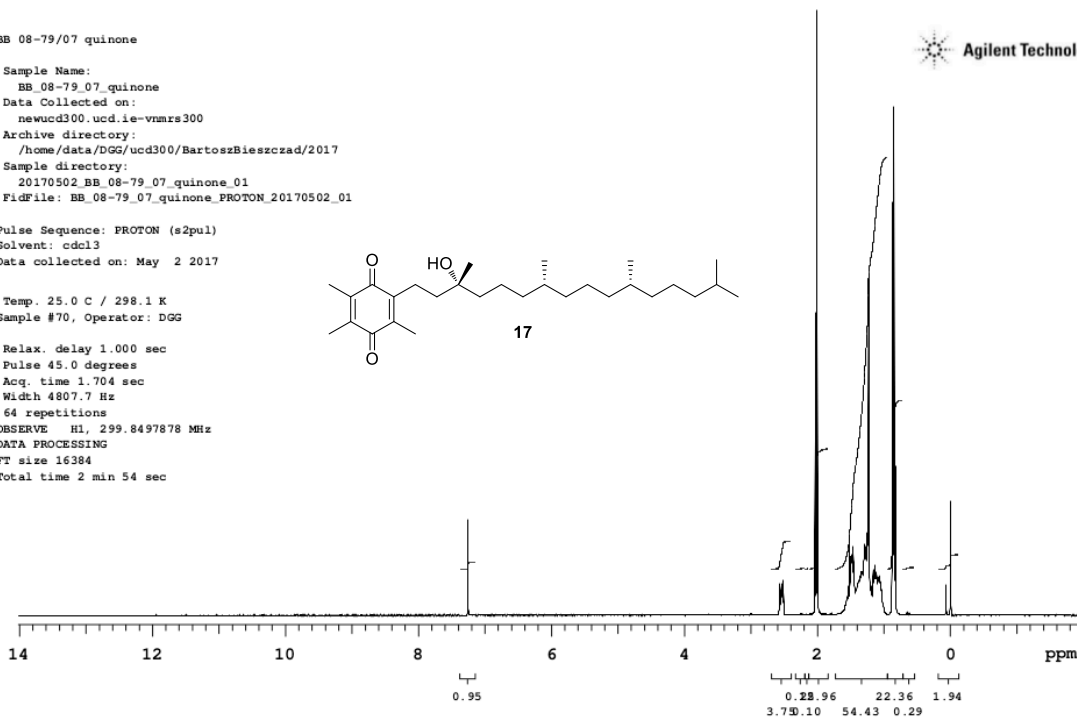
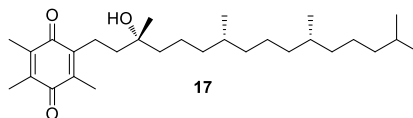
BB 08-79/07 quinone

Sample Name:
BB_08-79_07_quinone
Data Collected on:
newucd300.ucd.ie-vmrs300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2017
Sample directory:
20170502_BB_08-79_07_quinone_01
Fidfile: BB_08-79_07_quinone_PROTON_20170502_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: May 2 2017

Temp. 25.0 C / 298.1 K
Sample #70, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
64 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 2 min 54 sec



Plotname: BB_08-79_07_quinone_PROTON_20170502_01_plot01

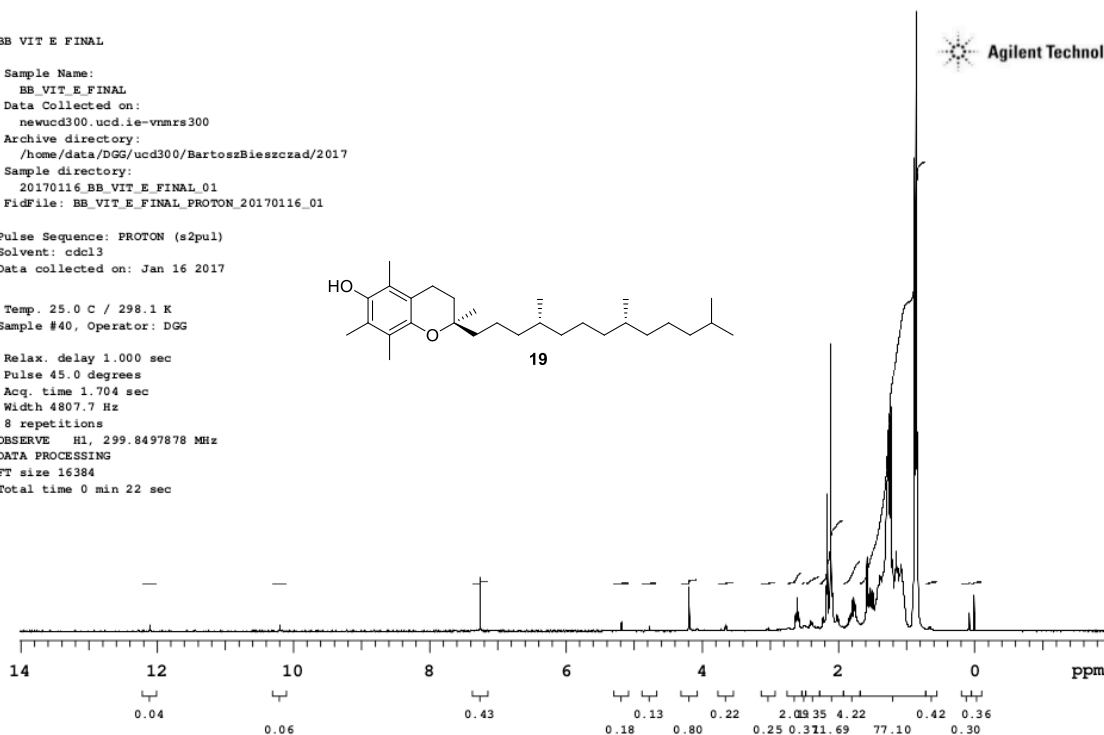
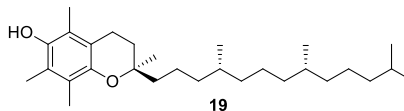
BB VIT E FINAL

Sample Name:
BB_VIT_E_FINAL
Data Collected on:
newucd300.ucd.ie-vmrs300
Archive directory:
/home/data/DGG/ucd300/BartoszBieszczad/2017
Sample directory:
20170116_BB_VIT_E_FINAL_01
Fidfile: BB_VIT_E_FINAL_PROTON_20170116_01

Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Jan 16 2017

Temp. 25.0 C / 298.1 K
Sample #40, Operator: DGG

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.704 sec
Width 4807.7 Hz
8 repetitions
OBSERVE H1, 299.8497878 MHz
DATA PROCESSING
FT size 16384
Total time 0 min 22 sec

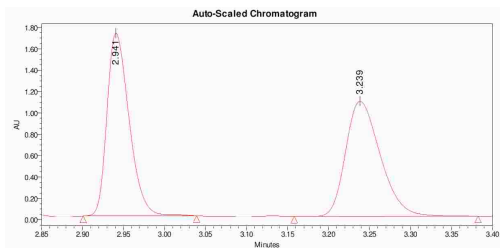


Plotname: BB_VIT_E_FINAL_PROTON_20170116_01_plot01

3. Chromatograms of 1-(2,5-dimethoxy-3,4,6-trimethylphenyl)-3,7,11,15-tetramethylhexadecan-3-ol (1)

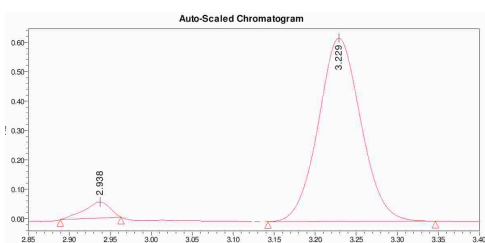
(i) SCF Chromatograms of high dr materials from Route 3

a) (R,R,R) and (S,R,R) – (50 : 50 dr)



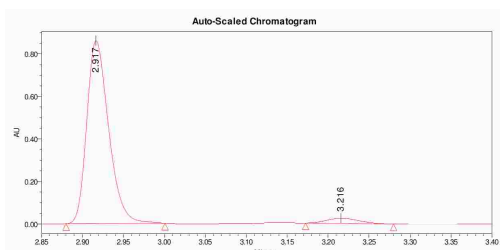
Peak Results						
Name	RT	Area	Height	Amount	Units	% Area
1	2.941	3220436	1713660			50.46
2	3.239	3161196	1077738			49.54

b) (S,R,R) – diastereoisomer – 95 : 5 dr



Peak Results						
Name	RT	Area	Height	Amount	Units	% Area
1	2.938	119150	54303			5.03
2	3.229	2250052	623906			94.97

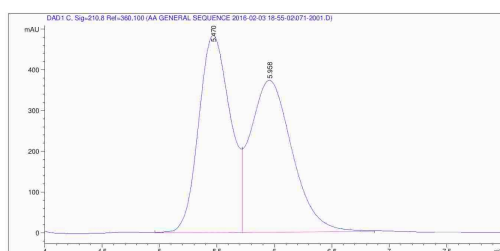
c) (R,R,R) – diastereoisomer – 96 : 4 dr



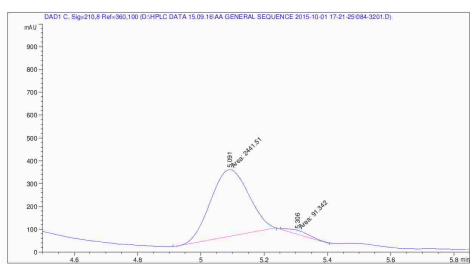
Peak Results						
Name	RT	Area	Height	Amount	Units	% Area
1	2.917	1600452	860266			95.91
2	3.216	68277	24903			4.09

(ii) Best HPLC Chromatograms (OJH column, resolution = 0.4)

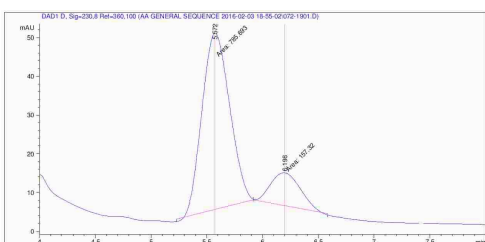
a) (R,R,R) and (S,R,R) – (50 : 50 dr) :



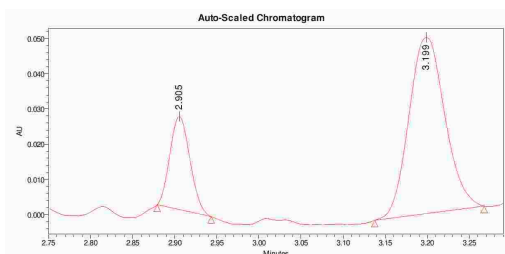
b) **(R,R,R)** – diastereoisomer of high dr from Route 3



c) **(R,R,R)** – diastereoisomer of moderate dr from Route 2



(iii) **SCF Chromatogram: (S,R,R)** – diastereoisomer of moderate dr from Route 1



Peak Results						
Name	RT	Area	Height	Amount	Units	% Area
1	2.905	43838	26471			22.74
2	3.199	148906	50069			77.26