Site-Selective Oxidation, Amination and Epimerization Reactions of Complex Polyols Enabled by Transfer Hydrogenation

Christopher K. Hill, John F. Hartwig*

University of California, Berkeley, California 94720, United States
Email: jhartwig@berkeley.edu

Supporting Information

Table of Contents

1. General Experimental Details

1.1 List of Abbreviations

DCE, dichloroethane
DCM, dichloromethane
DMAP, p-dimethylamino-pyridine
DMP, Dess Martin's Periodinane
DMSO, dimethylsulfoxide
DPPB, 1,4-bis(diphenylphosphino)butane
HFIP, hexafluoroisopropanol
Ir-1, Cp*IrCl(N-(4-dimethylaminophenyl)-2-pyridylcarboxamide)
MeOH, methanol
MTBE, methyl tert-butyl ether
Mupirocin M.E., Mupirocin methyl ester
NBS, N-bromo succinimide
NMM, N-methyl-morpholine
Pt-1, $[Pt(DPPB)(OH)]_2[BF4]_2$
TFE, trifluoroethanol
THF, tetrahydrofuran
TLC, thin layer chromatography

1.2 Equipment and Methods

All air-sensitive manipulations were conducted in a nitrogen-filled glovebox or by standard Schlenk techniques under nitrogen. All glassware were heated in an oven and cooled under an inert atmosphere prior to use. NMR spectra were acquired on 400 MHz, 500 MHz, 600 MHz, 700 MHz, or 900 MHz Bruker instruments operated by the College of Chemistry or QB3/Department of Molecular Biology at the University of California, Berkeley. NMR spectra were processed with MestReNova 9.0 (Mestrelab Research SL). Chemical shifts are reported in ppm and referenced to residual solvent peaks ($CHCl_3$ in $CDCl_3$: 7.26 ppm for ^1H and 77.36 ppm for ^{13}C). Coupling constants are reported in hertz. GC analyses were obtained on an Agilent 6890 GC equipped with an HP-5 column (25 m x 0.20 mm ID x 0.33 m film) and an FID detector. GC yields were calculated using dodecane as the internal standard. High resolution mass spectra were obtained at

the QB3/Chemistry Mass Spectrometry Facility operated by the Department of Molecular Biology and the College of Chemistry, University of California, Berkeley. Elemental analyses were obtained via the Microanalytical Facility operated by the College of Chemistry, University of California, Berkeley. X-ray crystal structures were obtained via X-ray Crystallography Facility operated by the College of Chemistry, University of California, Berkeley.

1.3 Chemicals

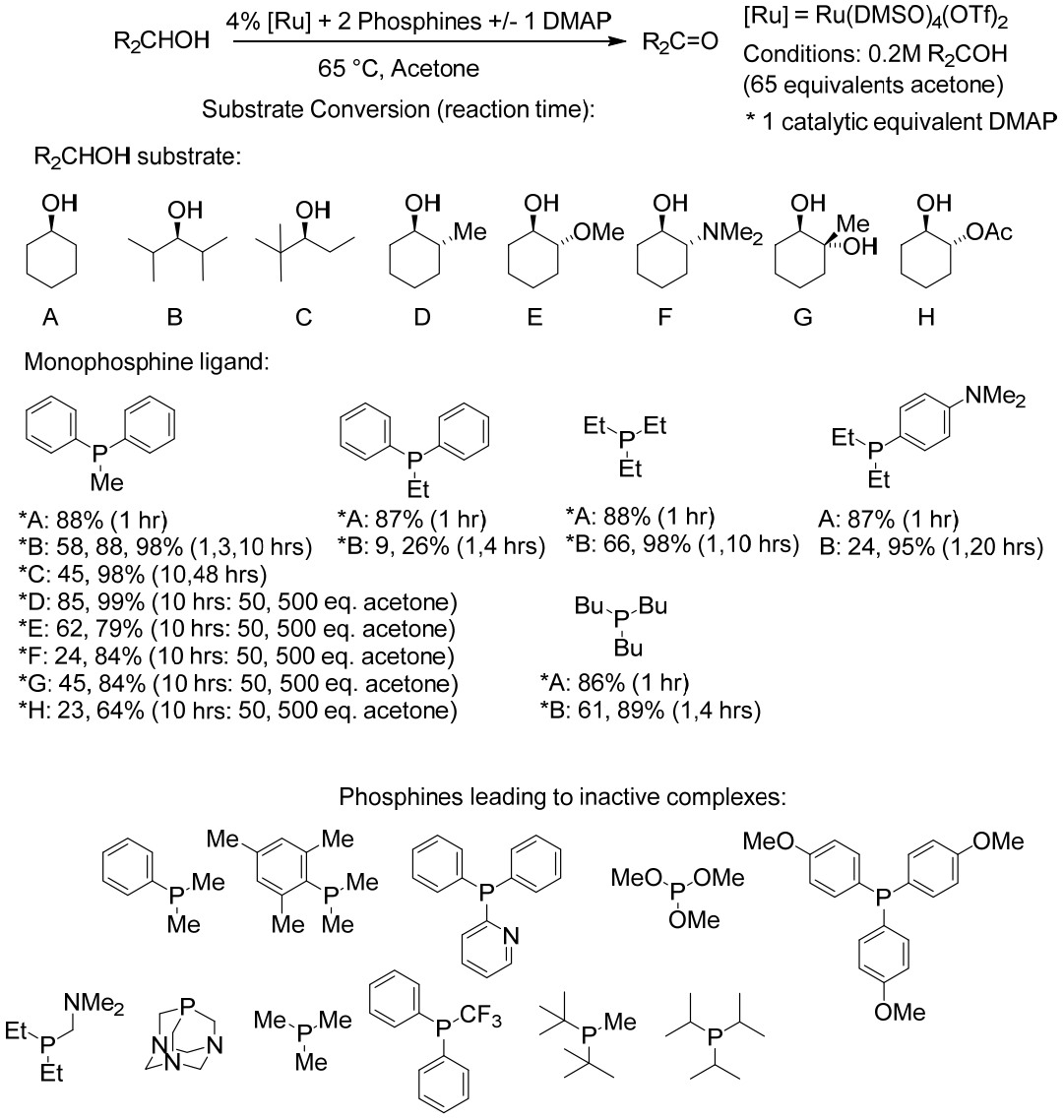
Substrates were purchased from Sigma-Aldrich and used without further purification unless mentioned otherwise. Ruthenium trichloride hydrate was purchased from Strem Chemicals. Dry acetone and trifluoroethanol were purchased from Acros Organics, Inc. Deacetylbaccatin III, aucubin, kirenol, fusidic acid, ivermectin, and genipin were purchased from AvaChem Scientific, Inc. Brefeldin A, forskolin, and phorbol were purchased from LC Laboratories. Digoxigenin was purchased from Santa Cruz Biotechnology, Inc. Lagochiline was purchased from Cayman Chemical. Andrographolide, estriol, ivermectin, and d-glucal were purchased from AK Scientific. Mupirocin methyl ester prepared following the published procedure.[1] $[Pt(dppb)(OH)]_2[BF_4]_2$ (**Pt-1**) was prepared following published procedures.[2,3] Cp*IrCl(N-(4-dimethylaminophenyl)-2-pyridylcarboxamide) (**Ir-1**) was prepared following published procedures.[4,5] Waymouth's catalyst $[Pd(neocuproine)(OAc)]_2[OTf]_2$, was prepared according to literature procedures.[6,7]

2. Catalyst Development

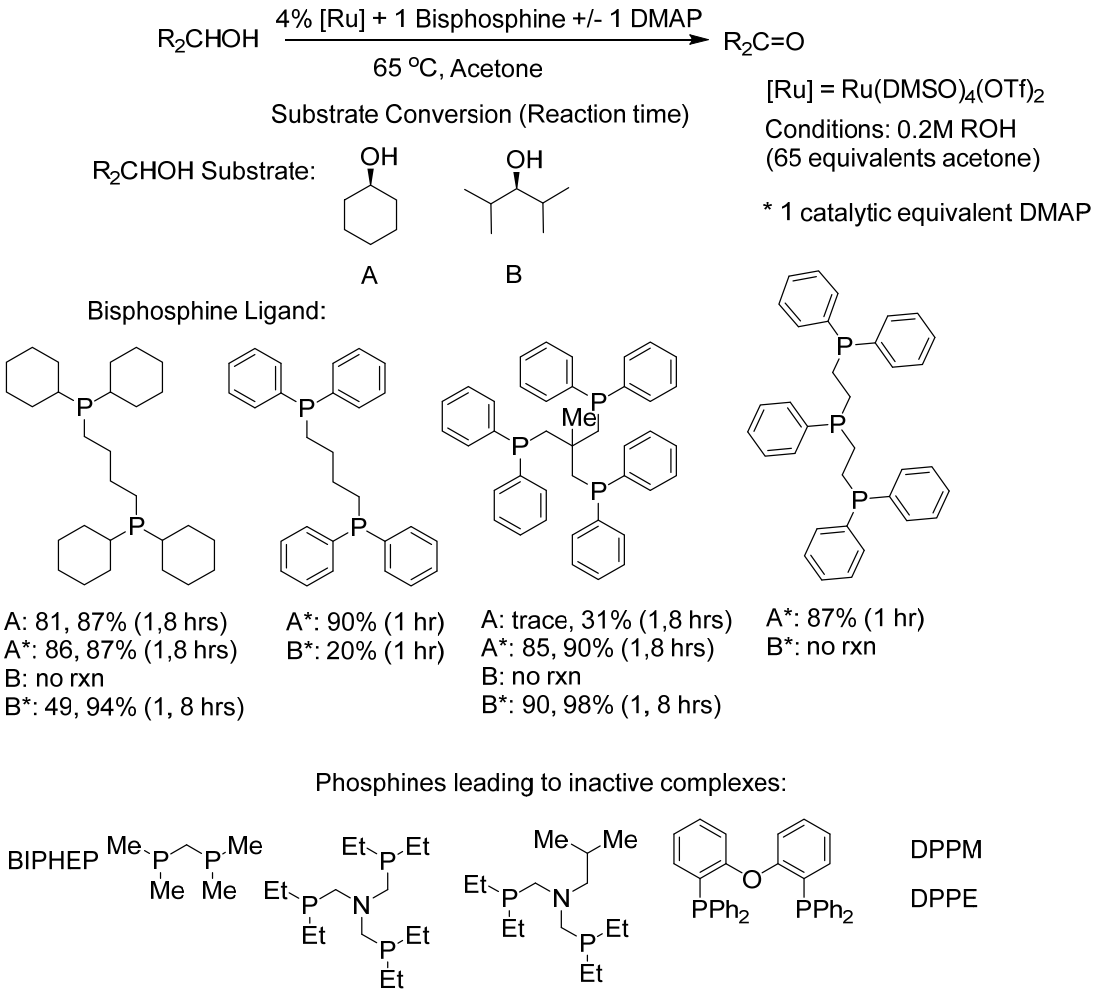
2.1 1st generation catalyst:

$[Ru(DMSO)_4Cl_2]$ (48 mg, 0.10 mmol) and AgOTf (51 mg, 0.20 mmol, 2 equiv) were weighed into a 1 dram vial, and acetone (1 mL) was added. The mixture was stirred at 65 ˚C for 90 minutes and then filtered to give a solution of $[Ru(DMSO)_4(OTf)_2]$ (0.1 M). To this solution, phosphine (0.2 mmol for monophosphines or 0.1 mmol for bisphosphines) (e.g. for PEt_3, 30 μL, 0.20 mmol, 2 equiv) and DMAP (12 mg, 0.10 mmol, 1 equiv) were added, and the mixture was briefly stirred to generate a solution of active catalyst. For reactions run without amine, the same procedure was used to generate a stock catalyst solution, but DMAP was omitted. Alcohol oxidation reactions were conducted by dissolving the substrate alcohol (0.1 mmol) and dodecane internal standard (0.05 mmol) in acetone solvent (0.46 mL) and then adding measured aliquots of the catalyst solution (0.0040 mmol, 40 μL of 0.10 M solution, 4% catalyst) to generate reaction solutions (0.2 M). The reactions were then heated at 65 ˚C until completion. A series of monophosphine and bisphosphine ligands were investigated using this system, and the results for oxidation of a series of model alcohols is shown in Tables S1 and S2. This catalyst system enables oxidation of hindered secondary alcohols but is less active than later generations of the catalyst.

2.2 Figure 1: Model alcohol oxidations with 1st generation catalysts containing monophosphine ligands

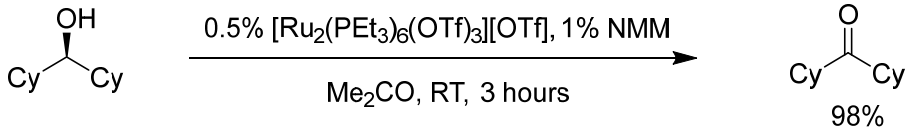


2.3 Figure 2: Model alcohol oxidations with 1st generation catalysts containing bisphosphine ligand



2.4 2nd generation catalyst:

The DMSO-free precursor $[Ru_2(PEt_3)_6(OTf)_3][OTf]$ (**Ru-2**) was developed. Alcohol oxidations in pure acetone catalyzed by this species were much faster than those catalyzed by the 1st generation catalyst. To generate a stock solution of the active catalyst, equimolar [Ru] precursor and NMM are combined in acetone solvent. For example to make a 0.01 M stock solution of active catalyst, **Ru-2** (7.5 mg, 0.0050 mmol) and NMM (1.1 μL, 0.010 mmol) were combined in acetone (1 mL). To conduct a model alcohol oxidation, dicyclohexylcarbinol (7.9 mg, 0.040 mmol), dodecane internal standard (4.5 μL, 0.020 mmol, 0.5 equiv), and acetone (110 μL) were combined in a one-dram vial. Then, an aliquot of active catalyst stock solution (0.010 M, 40 μL, 1% [Ru], NMM) was added. The vial was capped, and the mixture was allowed to stand at room temperature for 3 hours and then exposed to air to halt the reaction. GC analysis showed 98% conversion to of the starting alcohol to dicyclohexylketone.



The reactions of many (non-basic) simple and complex alcohols conducted in 1:1 TFE:acetone solvent were much faster than those in neat acetone, and this change to the medium enabled many oxidations to be conducted with lower catalyst loadings. See, for example, the oxidation of dicyclohexylcarbinol by **Ru-2** in 1:1 acetone:TFE solvent (main text figure 2B, left side).

2.5 Procedures for the alcohol oxidation and ketone reduction reactions reported in main text Figure 2:

Oxidation of secondary alcohols (main text Figure 2B):

With acetone acceptor: To generate a stock solution of the active catalyst, equimolar [Ru] precursor and NMM were combined in TFE:acetone solvent. To make a 0.01 M stock solution of active catalyst, **Ru-2** (7.5 mg, 0.0050 mmol) and NMM (1.1 μL, 0.010 mmol) were combined in 1:1 TFE:acetone (1 mL). To conduct a model alcohol oxidation, dicyclohexylcarbinol (7.9 mg, 0.040 mmol), dodecane internal standard (4.5 μL, 0.020 mmol, 0.5 equiv), and 1:1 TFE:acetone (192 μL) were combined in a one-dram vial. Then, an aliquot of active catalyst stock solution (0.01 M, 9 μL, 0.2% [Ru], NMM) was added, and the vial was capped. The mixture was allowed to stand at room temperature for 3 hours and then exposed to air to halt the reaction. GC analysis showed 99% conversion to of the starting alcohol to dicyclohexylketone.

With stoichiometric acceptors: To generate a stock solution of the active catalyst, equimolar [Ru] precursor and NMM were combined in TFE solvent. To make a 0.01 M stock solution of active catalyst, **Ru-2** (7.5 mg, 0.0050 mmol) and NMM (1.1 μL, 0.010 mmol) TFE (1 mL). To conduct a model alcohol oxidation, dicyclohexylcarbinol (19 mg, 0.10 mmol), 3,5-dimethylanisole internal standard (7 μL, 0.05 mmol, 0.5 equiv), acceptor (trifluoroacetophenone: 16 μL, 0.11 mmol, 1.1 equiv or 1,4-dicyclohexylketone: 12 mg, 0.11 mmol, 1.1 equiv) and TFE (40 μL) were combined in a one-dram vial. Then, an aliquot of active catalyst stock solution (20 μL, 0.01 M [Ru], 0.1% **Ru-2**, 0.2% NMM) was added, and the vial was capped. The mixture was allowed to stand at room temperature for 4 hours and then exposed to air to halt the reaction. GC analysis showed 99.5% conversion of the starting alcohol to dicyclohexylketone.

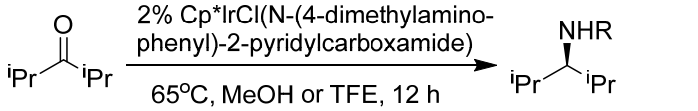
Relative rates for oxidation of primary versus secondary alcohols (main text Figure 2C):

For reactions involving a single alcohol undergoing oxidation, 0.1 mmol alcohol and 0.05 mmol dodecane internal standard were combined in acetone to form a 0.2 M solution upon addition of an acetone solution of equimolar **Ru-2** and NMM (0.001 mmol [Ru], 0.001 mmol NMM). For reactions involving two alcohols undergoing oxidation competitively in the same vessel, 0.05 mmol of each alcohol was used, while the rest of the procedure was the same as that for reactions of the single alcohols, except as noted in the main text diagram. The amount of remaining substrate alcohol and product aldehyde or ketone was determined via GCMS, by comparison to the dodecane internal standard.

Reduction of hindered ketone (main text Figure 2D):

To generate a stock solution of the active catalyst, equimolar [Ru] precursor and NMM were combined in TFE. To make a 0.01 M stock solution of active catalyst, **Ru-2** (7.5 mg, 0.0050 mmol) and NMM (1.1 μL, 0.010 mmol) were combined in TFE (1 mL). Pinocolone (13 μL, 0.1 mmol) and 3,5-dimethylanisole internal standard (14 μL, 0.1 mmol) were dissolved in 1:1 TFE:isopropanol (380 μL) and then an aliquot of catalyst solution (20 μL, 0.01M [Ru], 0.2% **Ru-2**, 0.4% NMM) in TFE was added. The reaction was then heated at 45 ˚C for 3 hours, and then allowed to cool to room temperature. GC analysis showed 99% conversion to of the starting ketone to methy-tert-butyl carbinol.

2.6 Procedure for a model hindered ketone reductive amination reaction with Ir-1:



R = H, 85%

R = $(CH_2)_5CH_3$, 80%

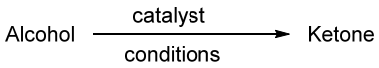
Hindered ketone amination:

R = H: Diisopropylketone (4.3 μL, 0.030 mmol), ammonium formate (3.8 mg, 0.060 mmol, 2 equiv), formic acid (1.1 μL, 0.030 mmol, 1 equiv), **Ir-1** (0.4 mg, 0.0006 mmol, 2%), and dodecane internal standard (3.4 μL, 0.015 mmol, 0.5 equiv) were weighed into a vial, and a magnetic stir bar was added. MeOH (150 μL) was then added, the vial was capped, and the reaction was heated at 65 ˚C for 15 hours.

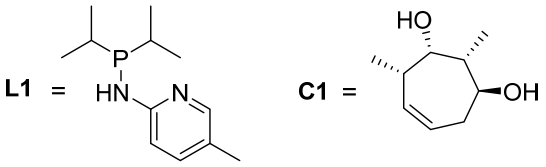
For R = $(CH_2)_5CH_3$: Diisopropylketone (4.3 μL, 0.03 mmol), n-hexylamine (5.1 μL, 0.060 mmol, 1.3 equiv), formic acid (2.8 μL, 0.075 mmol, 2.5 equiv), and **Ir-1** (0.4 mg, 0.0006 mmol, 2%), and dodecane internal standard (3.4 μL, 0.015 mmol, 0.5 equiv) were weighed into a vial, and a magnetic stir bar was added. TFE (150 μL) was then added, the vial was capped, and the reaction was heated at 65 ˚C for 15 hours.

After allowing the reactions to cool to room temperature, ethyl acetate, KOH solution (1M), and brine were added. The organic and aqueous phases were allowed to separate. GC analysis of the organic phase showed an 85% yield for R = H and 80% yield for R = $(CH_2)_5CH_3$.

3. Model catalytic oxidation comparisons



Reaction	Catalyst	Substrate	Solvent	Temperature, Time	Ketone Yield
1	2% $[Ru(COD)Cl_2]_2$, 1 KO^{t}Bu	cyclohexanol	acetone	30 °C, 4 h	72%
2	2% $[Ru(COD)Cl_2]_2$, 1 KO^{t}Bu	trans-2-methyl-cyclohexanol	acetone	30 °C, 4 h	25%
3	2% $[Ru(COD)Cl_2]_2$, 1 KO^{t}Bu	diisopropylcarbinol	acetone	30 °C, 4 h	none
4	4% Ru(p-cymene)(Ts-DPEN)Cl, 1 KO^{t}Bu	cyclohexanol	acetone	30 °C, 4 h	13%
5	4% Ru(p-cymene)(Ts-DPEN)Cl, 1 KO^{t}Bu	trans-2-methyl-cyclohexanol	acetone	30 °C, 4 h	18%
6	4% Ru(p-cymene)(Ts-DPEN)Cl, 1 KO^{t}Bu	diisopropylcarbinol	acetone	30 °C, 4 h	0%
7	4% Ru(p-cymene)(DM-SEGphos)$(DPEN)Cl_2$, 1 KO^{t}Bu	cyclohexanol	acetone	30 °C, 4 h	40%
8	4% Ru(p-cymene)(DM-SEGphos)$(DPEN)Cl_2$, 1 KO^{t}Bu	trans-2-methyl-cyclohexanol	acetone	30 °C, 4 h	18%
9	4% Ru(p-cymene)(DM-SEGphos)$(DPEN)Cl_2$, 1 KO^{t}Bu	diisopropylcarbinol	acetone	30 °C, 4 h	none
10	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	benzyl alcohol	acetone/toluene	25 °C, 16 h	99%
11	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	butanol	acetone/toluene	25 °C, 16 h	77%
12	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	3-pentanol	acetone/toluene	25 °C, 16 h	99%
13	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	cyclohexanol	acetone/toluene	25 °C, 16 h	91%
14	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	2-methyl-cyclohexanol	acetone/toluene	25 °C, 16 h	66%
15	5% Ru(COD)Cl, 5% **L1**, 1 KO^{t}Bu	diisopropylcarbinol	acetone/toluene	25 °C, 16 h	28%
16	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	cyclohexanol	acetone	30 °C, 8 h	23%
17	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	trans-2-methyl- cyclohexanol	acetone	50 °C, 8 h	28%
18	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	trans-2-methyl- cyclohexanol	acetone	70 °C, 8 h	32%
19	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	trans-2-methyl- cyclohexanol	acetone	90 °C, 8 h	67%
20	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	cyclohexanol	acetone	80 °C, 4 h	40%
21	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	trans-2-methyl- cyclohexanol	acetone	80 °C, 4 h	33%
22	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	diisobutylcarbinol	acetone	80 °C, 4 h	11%
23	2.5 % Ru(p-cymene)(Ts-DPEN)Cl, 2.75% KOH	diisopropylcarbinol	acetone	80 °C, 4 h	trace
24	5 % Ru(p-cymene)(Ts-DPEN)Cl, 5.5% KOH	**C1**	acetone	50 °C, 16 h	none
25	5 % Ru(p-cymene)(Ts-DPEN)Cl, 5.5% KOH	**C1**	acetone	80 °C, 16 h	none
26	2.5% Ru(p-cymene)Cl_2, 2.75% **L1**, 2.75% KOH	cyclohexanol	acetone	80 °C, 4 h	78%
27	2.5% Ru(p-cymene)Cl_2, 2.75% **L1**, 2.75% KOH	trans-2-methyl- cyclohexanol	acetone	80 °C, 4 h	95%
28	2.5% Ru(p-cymene)Cl_2, 2.75% **L1**, 2.75% KOH	diisopropylcarbinol	acetone	80 °C, 4 h	39%
29	4% Ru-MACHO, 4% KOH	cyclohexanol	acetone/toluene	50 °C, 5 h	75%
30	4% Ru-MACHO, 4% KOH	trans-2-methyl- cyclohexanol	acetone/toluene	50 °C, 5 h	86%
31	4% Ru-MACHO, 4% KOH	diisopropylcarbinol	acetone/toluene	50 °C, 5 h	11%
32	4% Ru-MACHO, 4% KOH	cyclohexanol	acetone/toluene	80 °C, 5 h	81%
33	4% Ru-MACHO, 4% KOH	trans-2-methyl- cyclohexanol	acetone/toluene	80 °C, 5 h	88%
34	4% Ru-MACHO, 4% KOH	diisopropylcarbinol	acetone/toluene	80 °C, 5 h	65%
35	4% $Ru(PPh_3)Cl_2$, 8% KOH	cyclohexanol	acetone/toluene	50 °C, 5 h	8%
36	4% $Ru(PPh_3)Cl_2$, 8% KOH	trans-2-methyl- cyclohexanol	acetone/toluene	50 °C, 5 h	4%
37	4% $Ru(PPh_3)Cl_2$, 8% KOH	diisopropylcarbinol	acetone/toluene	50 °C, 5 h	none
38	4% $Ru(PPh_3)Cl_2$, 8% KOH	cyclohexanol	acetone/toluene	80 °C, 5 h	6%
39	4% $Ru(PPh_3)Cl_2$, 8% KOH	trans-2-methyl- cyclohexanol	acetone/toluene	80 °C, 5 h	4%
40	4% $Ru(PPh_3)Cl_2$, 8% KOH	diisopropylcarbinol	acetone/toluene	80 °C, 5 h	0%
41	2% Shvo's catalyst	cyclohexanol	acetone/toluene	50 °C, 5 h	74%
42	2% Shvo's catalyst	trans-2-methyl- cyclohexanol	acetone/toluene	50 °C, 5 h	70%
43	2% Shvo's catalyst	diisopropylcarbinol	acetone/toluene	50 °C, 5 h	30%
44	2% Shvo's catalyst	cyclohexanol	acetone/toluene	80 °C, 5 h	78%
45	2% Shvo's catalyst	trans-2-methyl- cyclohexanol	acetone/toluene	80 °C, 5 h	86%
46	2% Shvo's catalyst	diisopropylcarbinol	acetone/toluene	80 °C, 5 h	95%



Notes:

1) The use of strong bases such as KOH and KO^{t}Bu in acetone solvent invariably leads to aldol side products derived from the acetone.

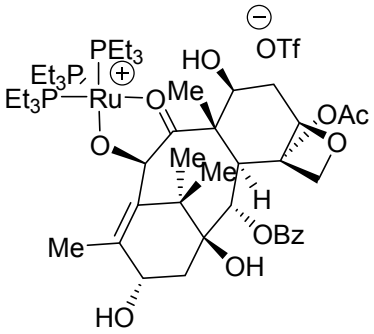
2) The reactions were run at 0.2M concentration.

3) The catalysts were preformed.

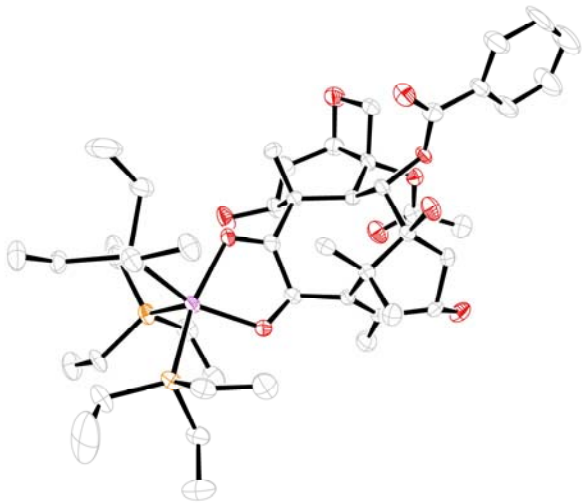
4) Racemic trans-2-methyl-cyclohexanol was employed along with racemic mixtures of chiral catalysts.

4. Isolation of [Ru]-alkoxide

Deacetylbaccatin III (11 mg, 0.02 mmol) was combined with acetone (0.3 mL) and a magnetic stir bar in a one dram vial. Then a solution of **Ru-2** (15 mg, 0.01 mmol) and triethylamine (4.2 µL, 0.03 mmol, 1.5 equiv) in acetone (0.3 mL) was added and the mixture was stirred to form a solution. The vial was capped and heated at 50 ºC for 30 minutes, and turned to a deep purple color. The reaction was allowed to cool to room temperature and then diluted with 1 mL of diethyl ether. The solution was then filtered, layered with diethyl ether, and placed at -30 ºC. Large deep-purple crystals formed over several weeks. X-ray crystallography revealed the purple complex to be [Ru(PEt$_3$)$_3$(DAB III alkoxide)][OTf].



[Ru(PEt$_3$)$_3$(DAB III alkoxide)][OTf]



5. Complex Epimerization Reactions

Fusidic acid methyl ester epimerization:

*With **Ru-2** (Figure 5B):* See procedure for this reaction and isolated yield in Section 6. ^{1}H NMR Yield = 84% epi-fusidic acid methyl ester.

With Shvo's catalyst (main text): Fusidic acid methyl ester (20 mg, 0.04 mmol) was combined with Shvo's catalyst (1.7 mg, 1.5 μmol, 4 mol %), toluene (150 μL), and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. The vial was capped, and the reaction was heated at 70 ˚C for 3 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was NMR spectroscopy with chloroform-*d*. ^{1}H NMR result (70 ˚C): 84% epi-fusidic acid methyl ester obtained.

With $(Ph_5Cp)Ru(CO)_2Cl/KO^tBu$ (main text): Fusidic acid methyl ester (20 mg, 0.04 mmol) was combined with THF (50 μL) and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of $(Ph_5Cp)Ru(CO)_2Cl$ (2 mg, 3.2 μmol, 8.0 mol %) and KO^tBu (0.35 mg, 3.1 μmol, 7.8 mol %) in THF (50 μL) was added as an aliquot from a stock solution. The vial was capped, and the reaction was heated at 50 ˚C or at 70 ˚C for 3 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was NMR spectroscopy with chloroform-*d*. ^{1}H NMR result (50 ˚C or 70 ˚C): No conversion.

Ouabain epimerization:

*With **Ru-2** (Figure 5B):* Ouabain octahydrate (30 mg, 0.06 mmol) was combined with TFE (60 μL) and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (5 mg, 6.6 μmol, 8.0 mol %) and NMM (0.75 μL, 13 μmol, 16 mol %) in TFE (40 μL) was added from a stock solution. The vial was capped, and the reaction was heated at 70 ˚C for 11 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was analyzed NMR spectroscopy in methanol-d_4. ^{1}H NMR Yield = 60% epi-ouabain.

With Shvo's catalyst (main text): Ouabain octahydrate (15 mg, 0.03 mmol) was combined with Shvo's catalyst (1.8 mg, 1.7 μmol, 8 mol %), THF (100 μL) and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. The vial was capped, and the reaction was heated at 70 ˚C or at 100 ˚C for 11 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was NMR spectroscopy in methanol-d_4. ^{1}H NMR result (70 ˚C or 100 ˚C) : No conversion.

With $(Ph_5Cp)Ru(CO)_2Cl/KO^tBu$ (main text): Ouabain octahydrate (15 mg, 0.03 mmol) was combined with THF (50 μL) and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of $(Ph_5Cp)Ru(CO)_2Cl$ (1.05 mg, 1.7 μmol, 8.0 mol %) and KO^tBu (0.18 mg, 1.6 μmol, 7.8 mol %) in THF (50 μL) was added as an aliquot from a stock solution. The vial was capped, and the reaction was heated at 50 ˚C or at 70 ˚C for 11 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was NMR spectroscopy in methanol-d_4. ^{1}H NMR result (50 ˚C or 70 ˚C): No conversion.

6. Complex Molecule Oxidation Comparisons

Table 1: Classical Oxidation Reactions:[a]

Molecule	Oxidant	Result
Andrographolide	DMP[b]	49% aldehyde, 35% keto-aldehyde, 8% 3-ketone product.
Andrographolide	Waymouth's catalyst[c]	65% aldehyde, 30% keto-aldehyde, no 3-ketone.
Andrographolide	NBS/Acetone[d]	Complex mixture of many products.
Andrographolide	Jones Reagent[8]	1.5% aldehyde, 2% keto-aldehyde, 5% 3-ketone.
Andrographolide	Swern Reagent[e]	65% conversion to an unknown. No 3-ketone or aldehyde product.
Andrographolide	$AlEt_2OEt$/trifluoroacetone[f]	No conversion to 3-ketone or aldehyde.
Andrographolide	Ru-MACHO/KOH[g]	Low conversion of starting material.
Andrographolide	Shvo's catalyst[h]	43% 3-ketone, 32% of aldehyde with an additional side reaction generating a new olefin, 19% of a product that underwent loss of the hydroxy-enoate functionality in addition to alcohol oxidation, and 4% of a product that has lost the 1,1 disubstituted olefin.
Mupirocin M.E.	DMP[i]	Complex mixture of many (5-6) products, no 13-ketone.
Mupirocin M.E.	TEMPO/NaOCl/KBr[9]	11%, 11%, and 31% of the 7,13-diketone, 7-ketone, and 13-ketone
Mupirocin M.E.	Swern Reagent[j]	Mixture of many products. No 13-ketone.
Mupirocin M.E.	$AlEt_2OEt$/trifluoroacetone[k]	Mixture of many products. No 13-ketone.
Mupirocin M.E.	Ru-MACHO/KOH[l]	90% conversion. Decomposition to 4 or more products. No 13-ketone.
Mupirocin M.E.	Shvo's catalyst[m]	94% conversion into a mixture of 2 products which result from 13-oxidation in addition to undiagnosed side reactions. 13-keto-mupirocin methyl ester was not obtained. The remaining 6% was starting material (2%) or converted into another compound without 13-oxidation.

Ouabain	DMP[n]	73% conversion. Multiple products, no 1-ketone.
Ouabain	Waymouth's catalyst[o]	Low conversion to multiple products. No 1-ketone.
Ouabain	Swern Reagent[p]	Full conversion to multiple products. New olefin peaks are present. No 1-ketone or aldehyde product.
Ouabain	$AlEt_2OEt$/trifluoroacetone[q]	Full conversion to multiple products. New olefin peaks are present. No 1-ketone or aldehyde product.
Ouabain	Ru-MACHO/KOH[r]	45% conversion to a modified structure without oxidation. Likely an isomer of ouabain.
Ouabain	Shvo's catalyst[s]	Low conversion of starting material. No oxidation.
Kirenol	DMP[t]	75% conversion to multiple products, no 15-ketone.
Kirenol	$AlEt_2OEt$/trifluoroacetone[u]	Full conversion to mixture of several products, no 15-ketone.
D-glucal	$AlEt_2OEt$/trifluoroacetone[v]	No conversion to vinylogous ester

Conditions and Procedures for classical alcohol oxidation reactions. (a) Standard procedures from previous reports were used (DMP,[10] Waymouth's catalyst,[7] NBS/acetone,[11] Swern reagent,[12] $AlEt_2OEt$/trifluoroacetone[13]). In several cases, the oxidation procedures were adapted to the use of THF, dioxane, or CH_3CN solvent to dissolve the substrate. For all of the reactions applied to complex substrates, the literature results were first reproduced in the original solvent or the substitute solvent. The reactions of complex molecules were monitored by thin layer chromatography. After completion, the reactions were analyzed by NMR spectroscopy of the crude reaction. Trimethoxybenzene (0.5 equiv) was added after the reaction prior to the workup as an internal standard. (b) CH_3CN, 1.25 equiv DMP, RT, 1 h (c) 9:1 CH_3CN:H_2O, 2.5% [Pd(neocuproine)(OAc)]2[OTf]$_2$, 1 equiv benzoquinone, 50 ˚C, 2 h (d) 2.5:1 acetone:H_2O, 1.1 NBS, 40 ˚C (e) THF, 1.5 equiv DMSO/$(COCl)_2$ (-78 ˚C, 20 min), then NEt_3 (-78 ˚C to RT) (f) dioxane, 0.3 equiv $AlEt_2OEt$, 5 equiv trifluoroacetone, RT, 21 h (g) Me_2CO, 4% Ru-MACHO, 4% KOH ([Ru] premixed at RT for 15 min with KOH), 80 ˚C, 4 h (h) Me_2CO, 4% Shvo dimer (8% [Ru]), 65 ˚C, 3.5 h (i) DCM, 1.25 equiv DMP, 0 ˚C to RT, 3 h (j) DCM, 1.5 equiv DMSO/$(COCl)_2$ (-78 ˚C, 20 min), then NEt_3 (-78 ˚C to RT) (k) DCM, 0.3 equiv $AlEt_2OEt$, 5 equiv trifluoroacetone, RT, 24 h (l) 1:1 Me_2CO:toluene, 4% Ru-MACHO, 4% KOH ([Ru] premixed at RT for 15 min with KOH), 65 ˚C, 4 h (m) 1:1 Me_2CO:toluene, 2% Shvo dimer (4% [Ru]), 65 ˚C, 4 h (n) THF, 1.25 equiv DMP, 0 ˚C to RT, 3 h (o) 9:1 CH_3CN:H_2O, 2.5% [Pd(neocuproine)(OAc)]$_2$[OTf]$_2$, 1 equiv benzoquinone, 50 ˚C, 5 h (p) THF, 1.5 equiv DMSO/$(COCl)_2$ (-78 ˚C, 20 min), then NEt_3 (-78 ˚C to RT) (q) dioxane, 0.3 equiv $AlEt_2OEt$, 5 equiv trifluoroacetone, RT, 21 h (r) Me_2CO, 4% Ru-MACHO, 4% KOH ([Ru] premixed at RT for 15 min with KOH), 80 ˚C, 3 h (s) Me_2CO, 2%

Shvo dimer (4% [Ru]), 80 ˚C, 3 h (t) THF, 1.25 equiv DMP, RT, 2 h (u) dioxane, 0.3 equiv $AlEt_2OEt$, 5 equiv trifluoroacetone, RT, 30 h (v) dioxane, 0.3 equiv $AlEt_2OEt$, 5 equiv trifluoroacetone, RT, 21 h.

7. Deuterium Incorporation Tests

Complex substrates (main text): To make a 0.01 M stock solution of active catalyst, **Ru-2** (7.5 mg, 0.0050 mmol) and NMM (1.1 µL, 0.010 mmol) were combined in acetone-d_6 (1 mL). Andrographolide (5.0 mg, 0.014 mmol) was combined with acetone-d_6 (250 µL), isopropanol-d_8 (5.5 µL, 0.072 mmol, 5 equiv), and a magnetic stir bar in a 1 dram vial. Then catalyst solution (5.7 µL, 0.1 M [Ru]) was added, the vial was capped, and the reaction was heated at 65 ˚C for 3 hours with stirring and then cooled to RT. The solvent was fully evaporated. Both ^1H and ^2H NMR were then conducted on the product in methanol solvent with chloroform internal standard. Analogous procedures were used to test for deuterium incorporation during the dehydrogenation of estriol (5 mg, 1.3% [Ru], 200 µL acetone-d_6, 65 ˚C, 3h), ouabain (5 mg, 3.5% [Ru], 250 µL acetone-d_6, 65 ˚C, 3h), and fusidic acid methyl ester (5 mg, 3% [Ru], 140 µL acetone-d_6, 65 ˚C, 2h).

Deuterium incorporation into a combination of 2-methyl-1-pentanol and cyclohexanol (main text):

2-methyl-1-pentanol (5 µL, 0.05 mmol), cyclohexanol (5 µL, 0.05 mmol), isopropanol-d_8 (5 µL, 0.05 mmol), and dodecane internal standard (5 µL, 0.05 mmol) and were combined acetone-d_6 (400 uL). Then an aliquot of acetone-d_6 solution of equimolar **Ru-2** and NMM (10 µL, 0.1M, 0.001 mmol [Ru], 0.001 mmol NMM, 2 mole % [Ru] versus each alcohol) was added. The vial was capped and reacted at room temperature for 10 minutes, then exposed to air and analyzed by GCMS. No conversion of 2-methyl-1-pentanol to aldehyde occurred under these conditions and no deuterium was incorporated into the remaining starting alcohol. 60% conversion of cyclohexanol to cyclohexanone occurred, and the remaining cyclohexanol showed 1.5% incorporation of deuterium.

8. Procedures and spectral data for isolated products

Procedures for the synthesis of metal complexes and spectral data:

cis-[Ru(DMSO)$_4$Cl$_2$]. A modification of the known procedure reported by Wilkinson[14] yields this compound with improved convenience, purity, and reproducibility at multi-gram scale. In a 500 mL flask, 2.50 g of $RuCl_3$-xH2O was combined with DMSO (12 mL) and NPr_3 (2.25 mL) along with a magnetic stir bar. The system was placed under a reflux condenser and flushed with N_2 for 5 minutes at room temperature with stirring. Then, the solution was heated with stirring at 145 ˚C for 6-7 minutes in an oil bath. During this time, a mild reflux occurred, and the color changed from black to green to dark red/yellow. The flask was removed from the bath, and the solution was allowed to cool to room temperature, at which point the product crystallized from solution. Acetone (40 mL) was added under nitrogen, and the solution was allowed to stand for 20 minutes to allow precipitation to be complete. Under air, the product was collected by filtration and rinsed with acetone and ether and dried under vacuum. Larger crystals were obtained by recrystallization from minimal hot DMSO. To do so, the material was dissolved in ~7 mL DMSO at 165 ˚C in a 20 mL vial and then removed from the heat. The product crystallized at room temperature in the dark. The supernatant was removed, the crystals were rinsed with acetone, and then ether, and then the

crystals were dried under high vacuum. Yield = 3.30 g (71%). Analytical data matched those in the literature. The combined supernatants from this synthesis were saved in an open flask under air, and more product formed over a couple days. Addition of acetone to the supernatant and recrystallization of the precipitate from DMSO yielded additional pure product (12%). Combined yield = 3.69 g (83%).

Note: the addition of alkylamine is hypothesized to prevent decomposition of the target product by removing acidic by-products (increasingly problematic at >1g scale for the Wilkinson synthesis) from the reaction and serving as a mild reductant of Ru(III) to Ru(II).

$[Ru_2Cl_3(PPh_2Me)_6][Cl]$ (Ru-1-Cl)

cis-$[Ru(DMSO)_4Cl_2]$ (630 mg, 1.30 mmol), PPh_2Me (0.798 mL, 4.29 mmol, 3.3 equiv), and MeOH (16 mL) were combined and stirred at room temperature for 90 minutes. Over this period, the supernatant turned orange brown and then yellow. The solid was removed by filtration, rinsed with ether, and dried under vacuum. The supernatant was placed in the freezer (-30 ˚C) overnight, after which time additional crystalline product was collected by filtration. Yield = 831 mg (83%). ^{1}H NMR (600 MHz, chloroform-d_1) δ 7.27 (t, J = 7.5 Hz, 6H), 7.07 (m, 12H), 7.02 (m, 12H), 1.82 (m, 9H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 136.70 (m), 132.93, 129.58, 127.95, 19.88 (m). Anal. Calc'd C:60.63 H:5.09 Found C:60.34 H:5.18.

$[Ru_2Cl_3(PEt_3)_6][Cl]$ (Ru-2-Cl)

cis-$[Ru(DMSO)_4Cl_2]$ (1.00 g, 2.06 mmol), PEt_3 (1.0 mL, 6.8 mmol, 3.3 equiv), and MeOH (4 mL) were combined and heated at 65 ˚C for 90 minutes with stirring. Over this period, all the material dissolved, and the supernatant turned green and then bright yellow/orange. The reaction solution was allowed to cool to RT and then was transferred to a larger flask under N_2 and slowly diluted with 250 mL 5:1 ether: pentane to crystallize the product. The yellow needles thus formed were collected by filtration (the filtration can be done under air) and rinsed once with ether, then pentane, and then dried under high vacuum. Yield = 885 mg (81%). ^{1}H NMR (400 MHz, chloroform-*d*) δ 1.92 (m, 36H), 1.21 (m, 54H). ^{13}C NMR (151 MHz, methylene chloride-d_2) δ 20.44, 10.35. Anal. Calc'd C:41.07 H:8.62 Found C:41.13 H:8.46.

$[Ru_2Cl_3(PEt_2(p\text{-}Me_2N\text{-}Ph))_6][Cl]$ (Ru-3-Cl)

cis-$[Ru(DMSO)_4Cl_2]$ (1.00 g, 2.06 mmol), PEt_2(p-Me_2N-Ph) (1.4 mL, 6.8 mmol, 3.3 equiv) and MeOH (4 mL) were combined and stirred at 65 ˚C for 90 minutes. The solution was then allowed to return to RT, and then kept to -30 ˚C overnight. During this time yellow crystalline product formed. The supernatant was transferred to another vial, along with an ether rinse (2 mL). The supernatant was placed back into the freezer, and more crystals formed over 24 hours, which were rinsed with ether. The combined product was dried by high vacuum. Combined yield = 1.37 g (83%) ^{1}H NMR (600 MHz, methanol-d_4) δ 7.00 – 6.83 (m, 12H), 6.62 (d, J = 8.3 Hz, 12H), 3.00 (s, 36H), 2.41 – 2.12 (m, 24H), 1.04 – 0.71 (m, 36H). ^{13}C NMR (151 MHz, methanol-d_4) δ 152.10, 135.34, 120.72 (m), 112.63, 40.48, 24.39 (m), 10.13. Anal. Calc'd C:54.06 H:7.56 N:5.25 Found C:53.81 H:7.79 N:5.10. The product structure was confirmed by x-ray crystallography.

Figure 3: X-ray crystal structure of **Ru-3-Cl**

$[Ru_2(OTf)_3(PPh_2Me)_6][OTf]$ (Ru-1)

$[Ru_2Cl_3(PPh_2Me)_6][Cl]$ (**Ru-1-Cl**) (170 mg, 0.110 mmol) and AgOTf (113 mg, 0.440 mmol, 4 equiv) were combined in TFE (2 mL) and stirred at RT overnight (or 65 ˚C for 2 hours). The solution was then filtered and the solvent was evaporated to form a residue. The residue was triturated with isopropyl ether (2 x 0.8 ml), and dried under high vacuum. Yield = 210 mg (95%) red powder. ^{1}H NMR (500 MHz, chloroform-*d*) δ 7.55 (t, J = 7.3 Hz, 6H), 7.45 (m, 12H), 7.36 (t, J = 7.3 Hz, 12H), 2.09 (m, 9H). ^{13}C NMR (126 MHz, acetone-d6) δ 133.59 (m), 133.10 (m), 132.01 (s), 130.01 (m), 15.54 (m). The intensity of the triflate CF_3 signal in the ^{13}C NMR spectrum was too low to observe. Anal. Calc'd C:49.25 H:3.93 Found C:49.12 H:4.18.

$[Ru_2(OTf)_3(PEt_3)_6][OTf]$ (Ru-2)

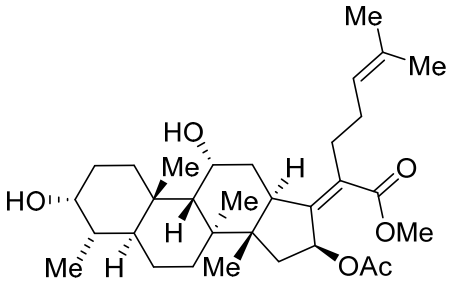
$[Ru_2Cl_3(PEt_3)_6][Cl]$ (**Ru-2-Cl**) (1.0 g, 0.95 mmol) and AgOTf (976 mg, 3.80 mmol, 4 equiv) were combined in TFE (5 mL) and stirred at RT overnight (or 65 ˚C for 2 hours). The reaction solution was then filtered and concentrated to ~1.5 mL. Isopropyl ether (10 mL) was added, and the product was allowed to crystallize overnight. The supernatant was removed, and the crystalline product was rinsed with isopropyl ether (1 mL) and then dried by high vacuum. Yield = 1.32 g (92%) yellow-orange crystals. ^{1}H NMR (600 MHz, methylene chloride-d_2) δ 1.97 (s, 18H), 1.23 (m, 27H). ^{13}C NMR (151 MHz, methylene Chloride-d_2) δ 20.44, 10.35. The intensity of the triflate CF_3 signal in the ^{13}C NMR spectrum was too low to observe. Anal. Calc'd C:31.87 H:6.02 S:8.51 Found C:31.76 H:6.16 S:8.18. The identity of the product was confirmed by x-ray crystallography (see main text Figure 2 for structure).

$[Ru_2(OTf)_3(PEt_2(p\text{-}Me_2N\text{-}Ph))_6][OTf]$ (Ru-3)

$[Ru_2Cl_3(PEt_2(p\text{-}Me_2N\text{-}Ph))_6][Cl]$ (**Ru-3-Cl**) (102 mg, 0.0640 mmol) and AgOTf (66 mg, 0.26 mmol, 4 equiv) were combined in acetone (1.5 mL) and stirred at RT overnight. The solution was then filtered and concentrated to ~0.75 mL, layered with pentane, and allowed to precipitate overnight. Then the supernatant was removed, and the product was dried under high vacuum. Yield = 114 mg (87%) yellow-orange powder. ^{1}H NMR (600 MHz, acetone-d6) δ 7.24 (m, 12H), 6.78

(m, 12H), 3.04 (s, 36H), 2.31 (m, 12H), 2.15 (m, 12H), 0.98 (m, 36H). ^{13}C NMR (151 MHz, acetone-d_6) δ 152.54, 135.33 (m), 133.99 (q), 120.37 (q, CF_3), 113.29, 40.13, 20.43 (m), 9.68 (q). Anal. Calc'd C:44.44 H:5.89 N:4.09 Found C:44.25 H:6.03 N:4.16.

Procedures for Substrate Preparation and Spectral Data:

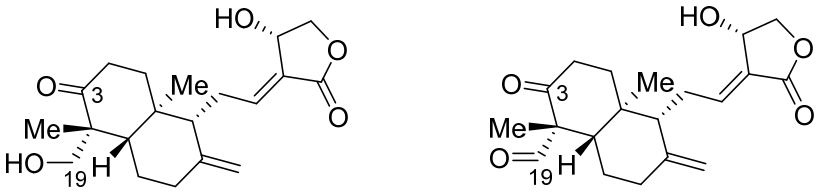


Fusidic acid methyl ester. Fusidic acid (1.655 mmol, 878 mg) was dissolved in 54 mL of a 2:1 mixture of toluene:methanol. TMS diazomethane was added dropwise until a yellow color persisted (2.5 mmol, 1.25 mL, 2 M in ether). The resulting mixture was stirred for 2 hours at room temperature. The reaction was then quenched with acetic acid (30 μL) and neutralized with 5% bicarbonate solution. The mixture was diluted with dichloromethane, and the bicarbonate layer was removed. The dichloromethane layer was washed two times with brine and dried over Na_2SO_4. Removal of volatile materials yielded pure methyl fusidate. Yield = 886 mg (98%). ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.84 (d, J = 8.5 Hz, 1H), 5.08 (t, J = 7.2 Hz, 1H), 4.34 (m, 1H), 3.75 (m, 1H), 3.64 (s, 3H), 3.03 (d, J = 11.6 Hz, 1H), 2.48 (m, 1H), 2.41 (m, 1H), 2.31 (dt, J = 13.1, 3.2 Hz, 1H), 2.22 – 2.07 (m, 4H), 2.03 (m, 1H), 1.97 (s, 3H), 1.91 – 1.80 (m, 2H), 1.80 – 1.71 (m, 2H), 1.67 (s, 3H), 1.62 – 1.47 (m, 7H), 1.41 (d, J = 3.5 Hz, 1H), 1.37 (s, 3H), 1.32 (d, J = 3.5 Hz, 1H), 1.27 (d, J = 14.3 Hz, 1H), 1.18 – 1.04 (m, 2H), 0.97 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.90 (s, 3H). ^{13}C NMR (151 MHz, chloroform-d) δ 170.65, 170.29, 148.04, 132.51, 130.42, 123.01, 74.36, 71.29, 68.27, 51.33, 49.15, 48.67, 43.84, 39.40, 39.03, 37.10, 36.27, 36.09, 35.53, 32.55, 30.30, 29.97, 28.89, 28.24, 25.67, 24.22, 22.57, 20.93, 20.67, 17.80, 17.71, 15.87. HRMS (ESI+) calc'd for [$C_{32}H_{50}O_6Na^+$]: 553.3500, found: 553.3497.

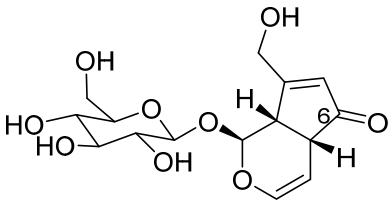
Procedures for Alcohol Dehydrogenation and Product Spectral Data:

General procedure (II) for alcohol oxidation: The procedure was conducted under an N_2 atmosphere. The catalyst precursor (**Ru-1**, **Ru-2**, or **Ru-3**) was dissolved in acetone or the specified reaction solvent, and an equimolar amount of NMM was added. The resulting solution was quickly mixed to generate the active catalyst. This solution of the catalyst was then added to a solution or slurry of the substrate alcohol in the specified reaction solvent in a vial or flask containing a magnetic stir bar. For the reactions in which a homogeneous solution did not form at room temperature (estriol, kirenol, ouabain, brefeldin), the starting materials composed of large crystals were crushed, sonicated in the reaction solvent, or pre-stirred in the reaction solvent to improve the rate of dissolution and reaction. The reactions were all heated at the indicated temperature for the indicated time. For reactions that were homogeneous upon mixing, stirring was not necessary. Reactions that began as slurries were stirred vigorously with one or more magnetic

stir bars. Small-scale reactions were conducted in Teflon capped one, two, or five dram glass vials, while larger-scale reactions were conducted in a sealed Schlenk flask or a round bottom flask fit with a reflux condenser. All of the reported reactions became fully homogeneous before completion. Upon completion, the solvent was evaporated by rotary evaporation, and the product was purified by recrystallization or column chromatography. Care was taken to premix the ruthenium precursor and the base in the reaction solvent before addition of the solution of catalyst to the solution or slurry of the substrate alcohol. The selectivity of the oxidation reactions was lower if the substrate was mixed with the catalyst precursor prior to mixing the catalyst precursor and amine.



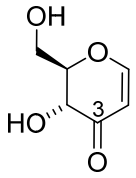
3-keto-andrographolide (1a) and 3,19-keto-aldehyde-andrographolide. Andrographolide (1.10 g, 3.14 mmol) was combined with acetone (50 mL), TFE (11 mL), THF (11 mL), and a magnetic stir bar in a 250 mL Schlenk flask, and the resulting mixture was stirred to form a slurry. Then, a solution of **Ru-2** (90 mg, 1.9 mol %, 0.06 mmol) and NMM (13 μL, 3.8 mol %, 0.12 mmol) premixed in acetone (5 mL) was added. The flask was sealed. The reaction was heated at 65 ˚C for 3 hours and then cooled to RT. The solvent was fully evaporated. Then the residue was dissolved in 15 mL THF and silica gel (10 g) was added. The solvent was fully evaporated by rotary evaporation to deposit the crude product on the silica gel. The product was then purified by silica gel chromatography with 2% MeOH in $CHCl_3$ (until 3,19-keto-aldehyde-andrographolide and trace 19-aldehyde-andrographolide elute) and then with 2% to 3.5% MeOH in $CHCl_3$ (3-keto-andrographolide elutes). Yields: **3-keto-andrographolide (1a)** (720 mg, 65%) and **3,19-keto-aldehyde-andrographolide** (220 mg, 20%). Spectral data of this product match those published previously (*28,44*). Highly crystalline 3-keto-andrographolide was obtained by dissolving the product in minimal ethyl acetate at 80 ˚C, layering with hot hexane, and allowing the mixture to cool and crystallize for several hours. The supernatant was concentrated to obtain a second crop. Yield = 642 mg (58%) of transparent crystals.



6-keto-aucubin (1b)

Aucubin (9.4 mg, 0.027 mmol) was combined with acetone (2 mL) and a magnetic stir bar in a one dram vial, and the resulting mixture was stirred to form a slurry. Then, a solution of **Ru-2** (1.02 mg, 0.7 μmol, 2.5%) and NMM (0.15 μL, 1.4 μmol, 5%) in 0.7 mL of acetone was added. The vial was capped, and the reaction was heated at 65 ˚C for 1 hour. The reaction was allowed to cool, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with 0 to 15% MeOH in $CHCl_3$. Yield = 8.2 mg (87%). ^{1}H NMR (600

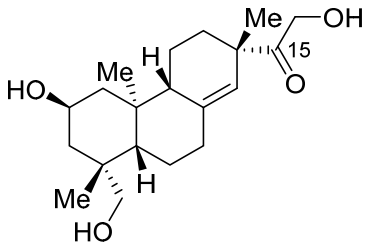
MHz, methanol-d_4) δ 6.39 (dd, J = 6.0, 2.4 Hz, 1H), 6.22 (s, 1H), 5.16 (dd, J = 6.0, 3.7 Hz, 1H), 4.88 (d, J = 6.7 Hz, 1H), 4.79 (d, J = 18.9 Hz, 1H), 4.68 (d, J = 7.9 Hz, 1H), 4.40 (d, J = 18.7 Hz, 1H), 3.86 (d, J = 12.1 Hz, 1H), 3.65 (dd, J = 12.0, 5.4 Hz, 1H), 3.37 (dd, J = 9.0, 9.0 Hz, 1H), 3.29 – 3.16 (m, 5H). ^{13}C NMR (151 MHz, methanol-d_4) δ 207.92, 182.58, 142.33, 128.50, 102.47, 100.22, 98.27, 78.36, 77.92, 74.90, 71.52, 62.70, 62.61, 47.04, 45.62. HRMS (ESI+) calcd for [$C_{15}H_{20}O_9Na^+$]: 367.1000, found: 367.0998. IR (neat) (cm^{-1}) 1700.1, 1648.0, 1618.8.



3-keto-D-glucal (1c)

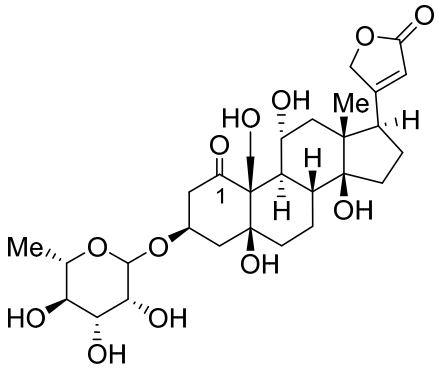
D-glucal (150 mg, 1.03 mmol) was combined with 1:1 acetone:TFE (13 mL) in a 20 mL vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a solution. Then, a solution of **Ru-2** (12 mg, 0.0080 mmol, 0.75 mol %) and NMM (1.7 µL, 0.015 mmol, 1.5 mol %) in 1:1 acetone:TFE (2 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 4 hours with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with 25 to 45% ethyl acetate in hexanes. Yield = 130 mg (88%) white solid.

Alternative procedure: D-glucal (150 mg, 1.03 mmol) was combined with 1 acetone (13 mL) in a 20 mL vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a solution. Then, a solution of **Ru-3** (34 mg, 0.016 mmol, 1.6 mol %) and NMM (3.4 µL, 0.030 mmol, 3 mol %) in 1 acetone (2 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 3 hours with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with 25 to 45% ethyl acetate in hexanes. Yield = 127 mg (86%). Spectral data match a previous report.[16]



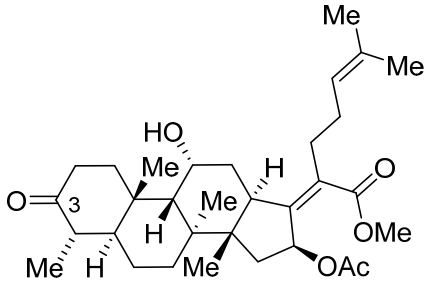
15-keto-kirenol (1d)

Kirenol (50 mg, 0.148 mmol) was combined with acetone (2.7 mL) and a magnetic stir bar in a two-dram vial, and the resulting mixture was stirred to form a slurry. Then, a solution of **Ru-1** (7.4 mg, 3.7 µmol, 2.5%) and NMM (0.80 µL, 7.4 µmol, 5%) in acetone (1 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 1 hour with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with a gradient of 10% MeOH in $CHCl_3$ to 20% MeOH in $CHCl_3$. Yield = 27 mg (54%). Analytical data match the reported natural product.[17]



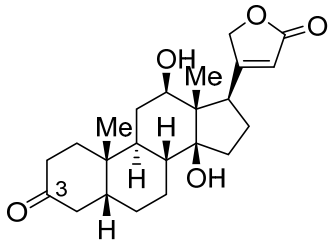
1-keto-ouabain (1e)

Ouabain octahydrate (1.00 g, 1.37 mmol) was combined with acetone (30 mL) in a 150 mL Schlenk flask, along with a magnetic stir bar, and the resulting mixture was stirred to form a fine slurry. A solution of **Ru-2** (36.2 mg, 0.024 mmol, 1.75%) and NMM (5.3 µL, 0.048 mmol, 3.5%) in acetone (7 mL) was then added. The flask was sealed, and the reaction was heated at 65 ˚C for 3.5 hours and then cooled to RT. The solvent was concentrated to ~12-13 mL under reduced pressure and then transferred to a 20 mL vial along with a THF rinse of the reaction flask. The solution was then dried down to a residue by rotary evaporation. The residue was recrystallized by dissolving it in minimal CH_3CN (10-12 mL) at 85 ˚C and then immediately removing the reaction from heat and allowing the solution to cool to RT overnight during which time white microcrystalline solid formed (700 mg). The supernatant was transferred into a second vial and then concentrated (to ~4 mL), and additional microcrystalline product formed (36 mg). The supernatant was removed and the product dried under high vacuum. Combined yield = 736 mg (92%). ^{1}H NMR (600 MHz, methanol-*d*$_4$) δ 5.92 (s, 1H), 5.02 (d, J = 18.4 Hz, 1H), 4.92 (d, J = 18.4 Hz, 1H), 4.81 (s, 1H), 4.48 (s, 1H), 4.40 (d, J = 12.1 Hz, 1H), 4.18 (d, J = 12.2 Hz, 1H), 4.16 (td, J = 13.5, 4.3, 1H), 3.72 (bs, 1H), 3.69 (dq, J = 12.4, 6.2 Hz, 2H), 3.56 (dd, J = 9.5, 3.2 Hz, 1H), 3.44 (dd, J = 13.8, 4.4 Hz, 1H), 3.37 (t, J = 9.5 Hz, 1H), 2.87 (dd, J = 9.2, 5.4 Hz, 1H), 2.65 (dd, J = 15.5, 3.0 Hz, 1H), 2.52 (d, J = 13.9 Hz, 1H), 2.32 – 2.17 (m, 3H), 2.06 (d, J = 13.7 Hz, 1H), 1.97 (td, J = 12.6, 4.2 Hz, 1H), 1.91 (dp, J = 14.7, 5.8, 4.7 Hz, 1H), 1.80 (dd, J = 12.6, 9.6 Hz, 1H), 1.77 – 1.71 (m, 2H), 1.68 (dd, J = 13.1, 4.3 Hz, 1H), 1.60 (d, J = 13.7 Hz, 1H), 1.53 – 1.40 (m, 2H), 1.28 (d, J = 6.2 Hz, 3H), 0.93 (s, 3H). ^{13}C NMR (151 MHz, methanol-*d*$_4$) δ215.47, 177.61, 177.04, 118.14, 101.27, 85.55, 82.03, 78.33, 75.28, 73.77, 72.32, 72.27, 70.48, 67.27, 61.76, 59.75, 51.72, 51.35, 51.13, 49.97, 45.13, 40.25, 36.06, 35.75, 33.25, 27.89, 24.93, 17.97, 17.33.. HRMS (ESI+) calcd for [$C_{29}H_{42}O_{12}Na^+$]: 605.2568, found: 605.2578. IR (neat) (cm^{-1}) 1726.3, 1687.0 (shoulder), 1621.8.



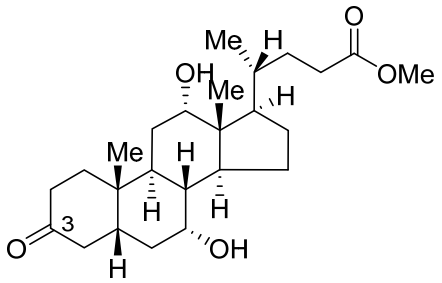
3-keto-fusidic acid methyl ester (1f)

Fusidic acid methyl ester (244 mg, 0.460 mmol) was combined with 1:1 acetone:TFE (6 mL) and a magnetic stir bar in a 20 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (5.2 mg, 3.5 μmol, 0.75 mol %) and NMM (0.76 μL, 6.9 μmol, 1.5 mol %) in 1:1 acetone:TFE (1 mL) was added. The vial was capped, and the reaction was heated at 60 ˚C for 4 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was purified by silica gel chromatography, eluting with 1:1 hexanes:ethyl acetate. Yield = 237 mg (97%) of a transparent solid. *Alternative procedure:* Fusidic acid methyl ester (530 mg, 1 mmol) was combined with acetone (9 mL) and a magnetic stir bar in a 20 mL vial, and the resulting mixture was stirred to form a solution. A solution of **Ru-3** (30.8 mg, 0.75 mol %, 0.015 mmol [Ru]) and NMM (3.3 μL, 3 mol %, 0.03 mmol) in acetone (1 mL) was then added. The vial was capped. The reaction was heated at 50 ˚C for 4 hours and then cooled to RT. The solvent was removed under reduced pressure, and the residue was purified by silica gel column, eluting with 1:1 hexanes: ethyl acetate. Yield = 501 mg (94.8%) of transparent solid. Spectral data match the reported product.[15]



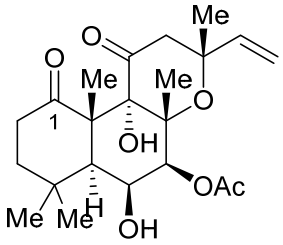
3-keto-digoxigenin (1g)

Digoxigenin (8 mg, 0.02 mmol) was combined with acetone (0.2 mL) in a one dram vial, along with a magnetic stir bar. The resulting mixture and was stirred to form a solution. Then, a solution of **Ru-2** (0.15 mg, 0.11 μmol, 0.5 %) and NMM (0.023 μL, 0.21 μmol, 1%) in acetone (0.1 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 70 minutes with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were evaporated. Addition of several drops of ethyl acetate led to crystallization, yielding pure product. Yield = 7 mg (87.5%) transparent crystals. Analytical data match those of the reported compound.[18]



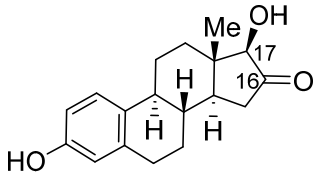
3-keto-cholic acid methyl ester (1h)

Cholic acid methyl ester (250 mg, 0.590 mmol) was combined with acetone (5.5 mL) in a one dram vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a solution. Then, a solution of **Ru-2** (3.3 mg, 2.2 μmol, 0.38%) and NMM (0.5 μL, 4 μmol, 0.8%) in acetone (1 mL) was added. The vial was capped, and the reaction was heated at 35 ˚C for 4 hours with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were removed. The crude product was purified by silica gel chromatography with EA/hexanes. Yield = 234 mg (94%). Analytical data for the product matches those reported previously.[19]



1-keto-forskolin (1i)

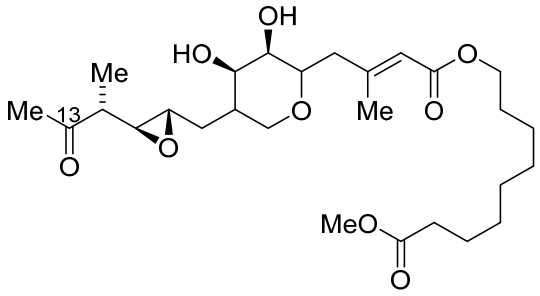
Forskolin (12 mg, 0.030 mmol) was combined with 1:1 acetone:TFE acetone (0.41 mL) and a magnetic stir bar in a one dram vial. The resulting mixture was stirred to form a solution. Then, an aliquot of 0.01 M active catalyst stock solution was added (0.88 μmol, 90 μL, 1.5% **Ru-2**, 3% NMM). The 0.01 M stock solution of active catalyst was made by combining **Ru-2** (8 mg, 0.005 mmol) and NMM (1.1 μL, 0.010 mmol) in 1:1 acetone:TFE (1 mL). The vial was capped, and the reaction was heated at 65 ˚C for 2.5 hours with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with 85:15 DCM:MTBE. Yield = 10.5 mg (88%). Analytical data for the product match those reported previously.[20]



16-keto-estriol (1j)

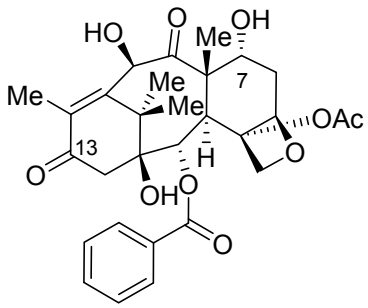
Estriol (288 mg, 1 mmol) was combined with acetone (12 mL) in a 20 mL vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a slurry. Then, a solution of **Ru-2**

(9.4 mg, 0.0065 mmol, 0.63%) and NMM (1.4 µL, 0.013 mmol, 1.3%) in acetone (2 mL) were added. The vial was capped, and the reaction was heated at 65 ˚C for 5 hours with stirring. During this period, the reaction mixture becomes fully homogeneous. The reaction was allowed to cool to RT, and all of the volatile materials were removed. Then CH_3CN (4 mL) was added to the residue and the mixture was stirred at RT for 1 hour. The white powder precipitate was collected by filtration, and rinsed with CH_3CN, and dried under vacuum. The supernatant was evaporated and triturated with CH_3CN (2 x 300 µL), and then dried under vacuum. Combined yield = 277 mg (97%) of a white powder. ^{1}H NMR (600 MHz, methanol-d_4) δ 7.08 (d, J = 8.4 Hz, 1H), 6.55 (dd, J = 8.4, 2.5 Hz, 1H), 6.48 (d, J = 2.3 Hz, 1H), 3.82 (s, 1H), 2.86 – 2.73 (m, 2H), 2.42 – 2.22 (m, 3H), 2.01 (dt, J = 12.3, 3.0 Hz, 1H), 1.92 – 1.77 (m, 2H), 1.67 (m, 1H), 1.59 (td, J = 12.9, 3.6 Hz, 1H), 1.55 – 1.44 (m, 2H), 1.38 (tq, J = 12.0, 6.5 Hz, 1H), 0.76 (s, 3H). ^{13}C NMR (151 MHz, methanol-d_4) δ 217.06, 154.65, 137.21, 130.73, 125.56, 114.68, 112.43, 85.94, 43.75, 43.72, 42.42, 37.81, 36.12, 35.15, 29.11, 27.38, 25.79, 10.55. HRMS (ESI-) calcd for [$C_{18}H_{21}O_3^-$]:285.1496, found: 285.1492. IR (neat) (cm^{-1}) 1740.8.



13-keto-mupirocin methyl ester (1k)

Mupirocin methyl ester (100 mg, 0.190 mmol) was combined with acetone (1.5 mL) in a one dram vial, forming a solution. Then, a solution of **Ru-2** (15 mg, 9.5 µmol, 5%) and NMM (2.1 µL, 19 µmol, 10%) in acetone (0.5 mL) was added. The vial was capped and the reaction was heated at 50 ˚C for 3.5 hours. The reaction was cooled to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography, eluting with 50 to 55% ethyl acetate in hexanes. Yield = 70 mg (70%). Analytical data match those of the reported compound.[9]

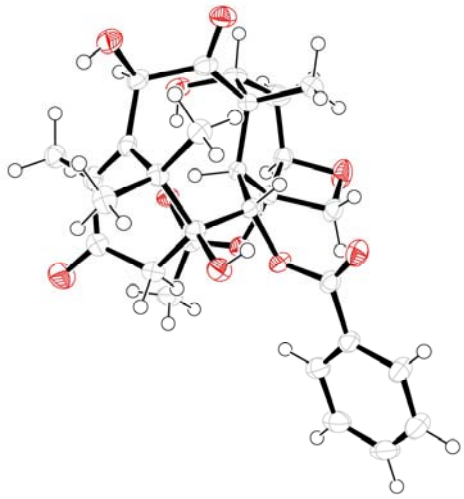


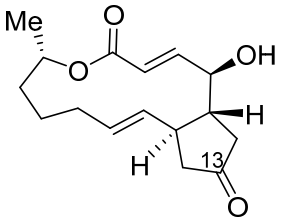
7-epi-13-keto-deacetylbaccatin III (1l)

Deacetylbaccatin III (100 mg, 0.184 mmol) was combined with TFE (2 mL), $MgOTf_2$ (105 mg, 0.322 mmol, 1.75 equiv), and trifluoroacetophenone (516 µL, 3.67 mmol, 20 equiv) in a two dram

vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a slurry. Then, a solution of **Ru-2** (49 mg, 0.032 mmol, 17.5%) and NMM (7 µL, 0.64 mmol, 35%) in 0.5 mL TFE was added. The vial was capped, and the reaction was heated at 85 ˚C for 6 hours with stirring. The reaction was allowed to cool to RT, and the vial contents were transferred to a separatory funnel, along with ethyl acetate (30 mL). The mixture was extracted with saturated bicarbonate (3 mL) and then brine (3 mL). The organic layer was collected, and a second extraction with ethyl acetate (30 mL) was conducted. The combined organic phases were dried with Na_2SO_4, filtered through a glass-fritted funnel, and the organic solvent was evaporated. The crude product was then purified by silica gel chromatography with 10 to 22% ethyl acetate in hexanes. Yield 71 mg (71%) of a white solid. ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.08 (d, J = 7.8 Hz, 2H), 7.65 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 5.79 (d, J = 7.2 Hz, 1H), 5.62 (s, 1H), 4.91 (dd, J = 9.3, 3.3 Hz, 1H), 4.59 (d, J = 11.8 Hz, 1H), 4.42 (d, J = 8.9 Hz, 1H), 4.37 (d, J = 8.9 Hz, 1H), 4.19 (s, 1H), 4.03 (d, J = 7.2 Hz, 1H), 3.67 (dd, J = 11.0, 3.4 Hz, 1H), 3.03 (d, J = 19.8 Hz, 1H), 2.68 (d, J = 19.8 Hz, 1H), 2.39 (dd, J = 15.9, 9.4 Hz, 1H), 2.29 (m, 1H), 2.27 (s, 3H), 1.99 (s, 3H), 1.84 (s, 1H), 1.69 (s, 3H), 1.24 (s, 3H), 1.15 (s, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 213.27, 198.07, 172.34, 167.04, 157.36, 139.42, 134.22, 130.18, 129.08, 129.00, 82.26, 81.88, 79.74, 79.33, 77.72, 75.45, 73.59, 58.36, 43.16, 42.69, 40.12, 35.55, 32.43, 22.04, 18.08, 16.54, 13.88. HRMS (ESI+) calcd for [$C_{29}H_{34}O_{10}Na^+$]: 565.2044, found: 565.2049. IR (neat) (cm^{-1}) 1718.8, 1691.2, 1663.8, 1605.8. Product confirmed by x-ray crystallography.

Figure 4: X-ray crystal structure of 7-epi-10-keto-DAB III (**2d**)

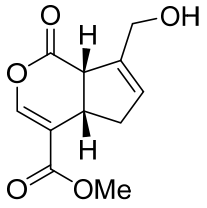




13-keto-brefeldin A (1m)

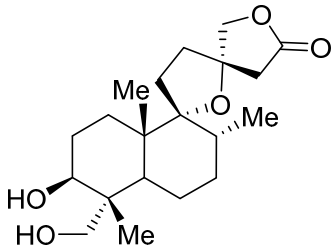
Brefeldin (25 mg, 0.089 mmol) was combined with 1:1 acetone:TFE (2.5 mL) in a one dram vial, along with a magnetic stir bar, and the resulting mixture was stirred to form a slurry. Then, a

solution of **Ru-1** (3.6 mg, 1.8 umol, 2%) and NMM (0.4 µL, 3.6 µmol, 4%) in 1:1 acetone:TFE (0.5 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 2.5 hours with stirring. The reaction was allowed to cool to RT, and all of the volatile materials were removed. The crude product was purified by silica gel chromatography, eluting with 3.5% MeOH in $CHCl_3$. Yield = 21.4 mg (87%). ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.38 (dd, J = 15.7, 3.5 Hz, 1H), 5.96 (dd, J = 15.7, 1.9 Hz, 1H), 5.81 (ddd, J = 15.0, 9.6, 5.1 Hz, 1H), 5.20 (dd, J = 15.3, 9.2 Hz, 1H), 4.91 (dtd, J = 11.6, 7.2, 5.3 Hz, 1H), 4.23 (d, J = 9.4 Hz, 1H), 2.83 (dd, J = 19.1, 8.5 Hz, 1H), 2.69 (p, J = 9.6 Hz, 1H), 2.53 (dd, J = 18.9, 8.4 Hz, 1H), 2.19 (ddd, J = 19.2, 10.5, 1.8 Hz, 1H),1.99-2.14 (m, 3H), 1.94 – 1.80 (m, 3H), 1.74 (dt, J = 16.1, 8.1 Hz, 1H), 1.54 (dtt, J = 10.4, 7.5, 3.8 Hz, 1H), 1.27 (d, J = 6.3 Hz, 3H), 1.04 (tdd, J = 13.2, 6.8, 3.5 Hz, 1H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 216.00, 166.10, 150.50, 135.29, 132.48, 118.63, 76.83, 71.83, 50.06, 46.70, 45.00, 42.64, 34.48, 31.74, 26.57, 20.86. HRMS (ESI-) calcd for [$C_{16}H_{21}O_4^-$]: 277.1445, found: 277.1445.



Genipin lactone (1n)

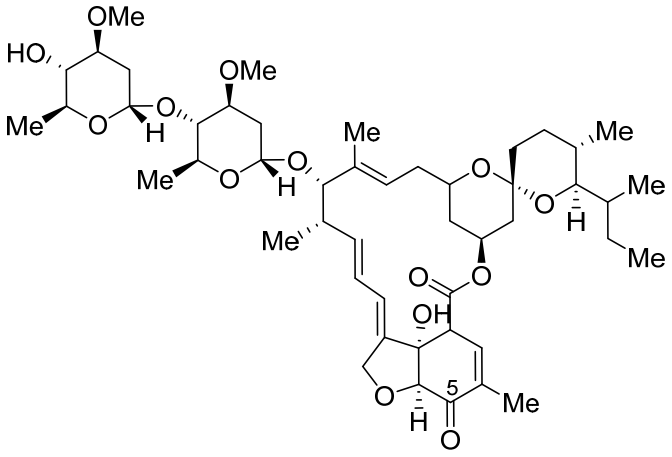
Genipin (100 mg, 0.44 mmol) was combined with acetone (10 mL) and a magnetic stir bar in a one-dram vial, and the resulting mixture was stirred to form a solution. Then, a solution of **Ru-2** (18 mg, 12 µmol, 2.8%) and NMM (2.7 µL, 24 µmol, 5.5%) in acetone (1 mL) was added. The vial was capped, and the reaction was heated at 65 ˚C for 3 hours with stirring. The reaction was cooled to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography with 95:5 $CHCl_3$:CH_3CN. Yield = 69 mg (69%). Analytical data match those of the reported compound.[21]



Lagochirsine (lagochiline spirolactone) (1o)

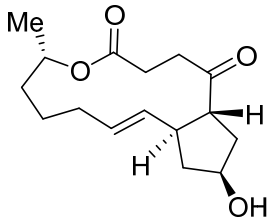
Lagochilin (10 mg, 0.028 mmol) was combined with trifluoroacetophenone (7.86 µL, 0.056 mmol, 2 equiv), dioxane (0.2 mL), and a magnetic stir bar in a one dram vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (1.2 mg, 0.7 µmol, 2.5%) and NMM (0.15 µL, 1.4 µmol, 5%) in dioxane (0.1 mL) was added. The vial was capped and the reaction was heated at 100 ˚C for 4 hours with stirring. The reaction was cooled to RT and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography with 20:1 EA:MeOH. Yield = 4 mg (40%). 1H NMR (600 MHz, chloroform-*d*) δ 4.31 (d, J = 8.7 Hz, 1H), 4.09 (d, J = 8.7 Hz, 1H), 3.70 (dd, J = 9.6, 3.0 Hz, 1H), 3.60 (dd, J = 11.2, 4.2 Hz, 1H), 3.45 (d, J = 10.1 Hz, 1H), 2.95 (d, J = 17.1 Hz, 1H), 2.83 (s, 1H), 2.51 (d, J = 17.1 Hz, 1H), 2.28 (s, 1H), 2.14 – 2.01 (m, 3H), 1.79 – 1.63 (m, 4H), 1.63 – 1.61 (m, 2H), 1.49 (dd, J = 11.8, 3.2 Hz, 1H),

1.42 (d, J = 11.2 Hz, 3H), 1.38 – 1.21 (m, 4H), 0.94 (s, 3H), 0.90 (s, 3H), 0.81 (d, J = 6.6 Hz, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 174.85, 94.12, 86.09, 78.51, 76.84, 72.53, 42.43, 42.15, 42.10, 41.51, 37.85, 36.10, 31.39, 30.43, 29.75, 26.87, 21.68, 17.79, 17.54, 11.34. HRMS (ESI-) calcd for [$C_{16}H_{21}O_4^-$]: 277.1445, found: 277.1445. IR (neat) (cm^{-1}) 1774.1.



5-keto-ivermectin (1p)

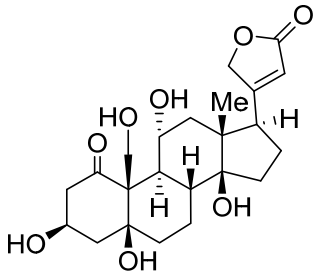
Ivermectin (35 mg, 0.04 mmol) was combined with dioxane (0.1 mL) and a magnetic stir bar, and the resulting mixture was stirred to form a solution. Then, a solution of **Ru-2** (3.3 mg, 2.2 μmol, 5.5%), NMM (0.49 μL, 4.4 μmol, 11%), and trifluoroacetophenone (112 μL, 0.800 mmol, 20 equiv) in dioxane (0.1 mL) was added. The vial was capped, and the reaction was heated at 100 ˚C for 2.5 hours with stirring. The reaction was cooled to RT, and all of the volatile materials were evaporated. The trifluoroacetophenone was evaporated under high vacuum at 80 ˚C. The crude product was purified by silica gel chromatography with 2.5:1 hexanes:ethyl acetate. Yield = 19 mg (54%). ^{1}H NMR (900 MHz, chloroform-*d*) δ 6.57 (m, 1H), 5.93 (dt, J = 11.1, 2.2, 1H), 5.79 (dd, J = 15.1, 9.9 Hz, 1H), 5.72 (dd, J = 15.1, 11.2 Hz, 1H), 5.45 – 5.37 (m, 2H), 4.99 (d, J = 11.5 Hz, 1H), 4.78 (d, J = 3.4 Hz, 1H), 4.76 (dd, J = 14.4, 2.2 Hz, 1H), 4.73 (dd, J = 14.4, 2.2 Hz, 1H), 4.07 (s, 1H), 3.95 (s, 1H), 3.86 (s, 1H), 3.83 (dq, J = 11.1, 6.3 Hz, 1H), 3.77 (dq, J = 11.1, 6.1 Hz, 1H), 3.68 (dddd, J = 11.5, 11.5, 4.1, 2.0 Hz, 1H), 3.62 (ddd, J = 11.4, 8.6, 4.9 Hz, 1H), 3.58 (m, 1H), 3.48 (ddd, J = 11.5, 8.9, 4.8 Hz, 1H), 3.43 (s, 3H), 3.42 (s, 3H), 3.25 (dd, J = 9.1, 9.1 Hz, 1H), 3.22 (dd, J = 9.0, 1.6 Hz, 1H), 3.19 – 3.15 (ddd, J = 9.1, 9.1, 1.5, 1H), 2.53 (dqd, J = 13.9, 7.0, 2.9 Hz, 1H), 2.48 (d, J = 1.7 Hz, 1H), 2.37 – 2.31 (m, 2H), 2.31 – 2.20 (m, 3H), 2.00 (ddd, J = 12.1, 4.7, 1.7 Hz, 1H), 1.90 (m, 3H), 1.78 (d, J = 11.1 Hz, 1H), 1.67 (d, J = 13.1 Hz, 1H), 1.59 – 1.56 (m, 2H), 1.55 – 1.48 (m, 6H), 1.49 – 1.37 (m, 4H), 1.28 (d, J = 6.2 Hz, 3H), 1.26 (d, J = 6.3 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H), 0.94 (t, J = 7.4 Hz, 3H), 0.86 (d, J = 6.8 Hz, 3H), 0.85 (m, 1H), 0.79 (d, J = 5.9 Hz, 3H).^{13}C NMR (151 MHz, chloroform-*d*) δ 192.22, 172.54, 139.27, 138.09, 138.00, 137.04, 135.27, 124.82, 121.99, 118.54, 98.69, 97.68, 94.98, 82.10, 81.83, 81.01, 80.62, 79.54, 78.37, 76.93, 76.33, 70.03, 69.56, 68.32, 67.46, 67.44, 56.65, 56.55, 46.83, 41.40, 40.08, 37.09, 35.93, 35.66, 34.69, 34.39, 34.24, 31.41, 28.23, 27.51, 20.24, 18.59, 17.84, 17.60, 15.60, 15.32, 12.59, 12.28. HRMS (ESI-) calcd for [$C_{48}H_{71}O_{14}^-$]: 871.4849, found: 871.4840. IR (neat) (cm^{-1}) 1719.0, 1679.9.



2,3-dihydro-1-keto-brefeldin A (1q)

$[Ru(DMSO)_4Cl_2]$ (24 mg, 0.050 mmol) and AgOTf (25 mg, 0.10 mmol, 2 equivalents) were weighed into a one-dram vial, and acetone (1 mL) was added. The mixture was stirred at 65 ˚C for 90 minutes and then filtered to give a solution of $[Ru(DMSO)_4(OTf)_2]$ (0.05 M). To this solution. 1,4-bis-(dicyclohexylphosphino)butane (23 mg, 0.050 mmol, 1 equiv) was added, and the mixture was stirred for 5 minutes to generate a solution of active catalyst. An aliquot (36 µL, 0.050 M, 1.8 µmol [Ru], 5%) of this catalyst solution was then added to a slurry of Brefeldin A (10 mg, 0.036 mmol) in 1:1 acetone:DCE (1 mL) with a magnetic stir bar in a one dram vial. The vial was then capped, and the mixture was heated at 65 ˚C for 25 min. The reaction was then cooled to RT, and all of the volatile materials were evaporated. The crude product was purified by silica gel chromatography with 4% MeOH in $CHCl_3$. Yield = 9 mg (90%). ^{1}H NMR (500 MHz, chloroform-*d*) δ 5.55 (ddd, J = 15.1, 10.0, 4.9 Hz, 1H), 5.33 (dd, J = 15.3, 8.9 Hz, 1H), 4.78 (m, 1H), 4.42 (m, 1H), 3.08 – 2.93 (m, 2H), 2.80 (ddd, J = 14.9, 8.0, 4.0 Hz, 1H), 2.67 (p, J = 9.3 Hz, 1H), 2.58 (ddd, J = 17.2, 9.0, 3.6 Hz, 1H), 2.35 (ddd, J = 15.7, 8.5, 4.4 Hz, 2H), 1.98 (m, 2H), 1.86 (m, 2H), 1.58 – 1.39 (m, 5H), 1.28 (m, 1H), 1.19 (d, J = 6.4 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 210.86, 172.79, 133.21, 132.06, 72.45, 71.69, 56.41, 47.02, 42.66, 39.44, 38.80, 32.52, 31.02, 29.40, 24.08, 19.50. HRMS (ESI+) calcd for $[C_{16}H_{25}O_4^+]$: 281.1747, found: 281.1749.

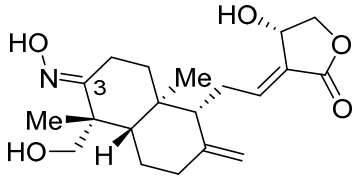
Procedures for the Synthesis of Derivatives and Spectral Data



1-keto-oubagenin (2a)

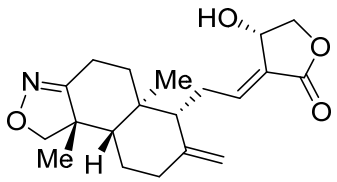
Keto-ouabain (125 mg, 0.215 mmol), hydroxylamine-o-sulfonic acid (56.0 mg, 0.490 mmol, 2.3 equiv), and 10:1 TFE:H_2O (2.5 mL) were combined in a one dram vial, along with a magnetic stir bar. The vial was capped, and the reaction was heated at 50 ˚C for 12 hours. After this time, the volatile materials were evaporated under vacuum at 65 ˚C. Then the residue was dissolved in 1:10:89 28% NH_4OH:MeOH:THF, and filtered through a plug of Na_2SO_4. The solvents were then fully evaporated. The residue was taken up in THF and silica gel was added (~1.5 g), and the product was deposited onto the silica gel by rotary evaporation. Silica gel chromatography, eluting with 3.5 to 7% MeOH in $CHCl_3$ yielded deglycosyl-keto-ouabain. Yield = 75 mg (80%) white

powder. ^{1}H NMR (500 MHz, chloroform-*d*) δ 5.92 (s, 1H), 5.02 (d, J = 18.4 Hz, 1H), 4.91 (d, J = 18.4 Hz, 1H), 4.43 – 4.39 (m, 1H), 4.37 (d, J = 11.8 Hz, 1H), 4.31 (d, J = 11.8 Hz, 1H), 3.88 (td, J = 11.1, 4.3 Hz, 1H), 3.44 – 3.29 (m, 2H), 2.90 – 2.83 (m, 1H), 2.70 (dd, J = 15.1, 3.3 Hz, 1H), 2.44 (dt, J = 13.7, 4.5 Hz, 2H), 2.31 – 2.18 (m, 3H), 2.10 – 2.03 (m, 1H), 1.95 – 1.84 (m, 2H), 1.83 – 1.74 (m, 2H), 1.72 – 1.61 (m, 3H), 1.54 – 1.40 (m, 2H), 0.91 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 215.32, 177.56, 177.06, 118.19, 85.47, 84.13, 75.28, 71.99, 67.00, 61.87, 58.90, 51.70, 51.33, 51.00, 50.00, 47.51, 40.33, 37.75, 36.69, 33.18, 27.90, 24.94, 17.31. HRMS (ESI+) calcd for [$C_{23}H_{32}O_8Na^+$]: 459.1989, found: 459.1985. IR (neat) (cm^{-1}) 1722.7, 1684.2, 1620.0.



Andrographolide-3-oxime (2b)

3-keto-andrographolide (mmol) and 1.05 NH_2OH-HCl (1.05 equiv) were weighed into a 20 mL vial. Pyridine (2.8 mL) was added, followed by a magnetic stir bar. The vial was capped and heated at 40 ˚C for 2.5 hours, and then cooled to room temperature. The reaction mixture was fully dried down and then the resulting residue was recrystallized from hot 49:49:2 benzene:MeOH:benzene:NEt_3 (65 ˚C). The supernatant was removed, and the product was rinsed with cold 1:1 MeOH/benzene mixture, and then dried under high vacuum to obtain a white solid (75 mg). The combined supernatant was concentrated, and more product crystallized from solution (12 mg), which was rinsed with cold MeOH/benzene mixture and then dried by high vacuum. Combined yield = 87 mg (73%). ^{1}H NMR (600 MHz, methanol-d_4) 6.85 (td, *J* = 6.8, 1.8 Hz, 1H), 5.02 (d, *J* = 6.0 Hz, 1H), 4.92 (s, 1H), 4.71 (s, 1H), 4.47 (dd, *J* = 10.2, 6.1 Hz, 1H), 4.16 (dd, *J* = 10.3, 2.1 Hz, 1H), 3.85 (d, *J* = 11.1 Hz, 1H), 3.41 (d, *J* = 11.2 Hz, 1H), 3.24 (ddd, *J* = 15.3, 5.1, 3.5 Hz, 1H), 2.68 – 2.57 (m, 2H), 2.45 (ddd, *J* = 13.0, 4.2, 2.5 Hz, 1H), 2.13 (ddd, *J* = 15.3, 13.1, 5.3 Hz, 1H), 2.04 (td, *J* = 13.0, 4.9 Hz, 1H), 1.99 – 1.87 (m, 3H), 1.59 (dd, *J* = 13.0, 2.6 Hz, 1H), 1.48 (qd, *J* = 13.0, 4.2 Hz, 1H), 1.36 (td, *J* = 13.1, 5.0 Hz, 1H), 1.22 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (151 MHz, methanol-d_4) δ 172.60, 164.13, 149.13, 148.66, 129.90, 109.44, 76.13, 66.66, 66.12, 57.58, 57.03, 47.33, 40.35, 38.92, 38.30, 25.82, 25.70, 22.36, 18.78, 15.21. HRMS (ESI+) calcd for [C20H30NO5$^+$]: 364.2118, found: 364.2119. IR (neat) (cm^{-1}) 1740.2, 1722.6, 1673.7, 1643.9.



Andrographolide isoxazole (2c)

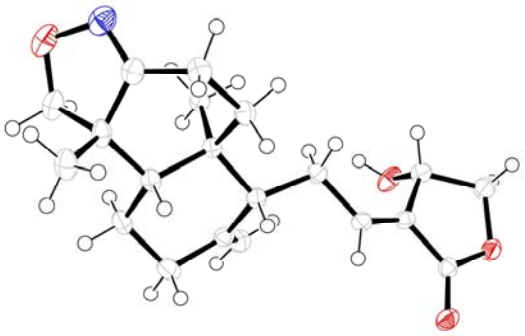
Method A (main text figure 2, reaction): Andrographolide-3-oxime (45 mg, 0.13 mmol) was dissolved in THF, and NEt_3 (35 µL) was added, followed by TsCl (31 mg, 0.163 mmol, 1.3 equiv). The reaction was stirred for 36 hours at 40 ºC, after which time a second portion of NEt_3 and TsCl were added. The reaction was heated at 40 ˚C for another 36 hours. Then, the reaction was allowed

to cool to RT and filtered, and the solvent was evaporated. Chromatography on silica gel, eluting with a gradient of 0 to 5% MeOH in DCM gave 3,19-andrographolide isoxazole (25 mg, 55%).

Method B (main text figure 2, reaction): 3-keto-andrographolide (50 mg, 0.144 mmol) was combined with NH_2OSO_3H (33 mg, 0.288 mmol, 2 equiv) in 1:1 TFE:0.01% TFA(aq) (2.5 mL) and stirred at 50 ˚C for 24 hours. The reaction was then allowed to cool to RT, and saturated $NaHCO_3$ (2 mL) was added. The mixture was then extracted with 4:1 EA:THF (3 x 10 mL). The organic extracts were combined, dried over Na_2SO_4, and filtered, and the solvent was evaporated. The resulting residue was purified by silica gel chromatography with 0 to 5% MeOH in $CHCl_3$. Yield = 24.5 mg (49%).

Method C: The product was isolated as a side product from the synthesis of andrographolide lactam (main text figure 2, reaction). ^{1}H NMR (600 MHz, methanol-d_4) δ 6.84 (td, J = 6.7, 1.8 Hz, 1H), 5.03 (m, 1H), 4.97 (q, J = 1.3 Hz, 1H), 4.74 (q, J = 1.3 Hz, 1H), 4.47 (dd, J = 10.2, 6.1 Hz, 1H), 4.16 (dd, J = 10.2, 2.1 Hz, 1H), 4.01 (d, J = 7.8 Hz, 1H), 3.96 (d, J = 7.8 Hz, 1H), 2.70 – 2.56 (m, 4H), 2.43 (ddd, J = 12.9, 4.3, 2.4 Hz, 1H), 2.14-1.99 (m, 3H), 1.81 – 1.74 (m, 2H), 1.69 (ddt, J = 12.8, 5.6, 2.9 Hz, 1H), 1.42 (qd, J = 13.1, 4.3 Hz, 1H), 1.25 (s, 3H), 0.76 (s, 3H).^{13}C NMR (151 MHz, methanol-d_4) δ 172.56, 167.52, 148.74, 148.00, 130.07, 110.50, 78.83, 76.12, 66.66, 55.66, 54.29, 53.13, 41.18, 38.34, 35.20, 26.21, 26.11, 24.94, 18.11, 13.96. HRMS (ESI+) calcd for [$C_{20}H_{28}NO_4^+$]: 346.2013, found: 346.2013. IR (neat) (cm^{-1}) 1721.8, 1675.8, 1647.7. Product confirmed by x-ray crystallography.

Figure 5: X-ray crystal structure of Andrographolide-isoxazole (**2c**)

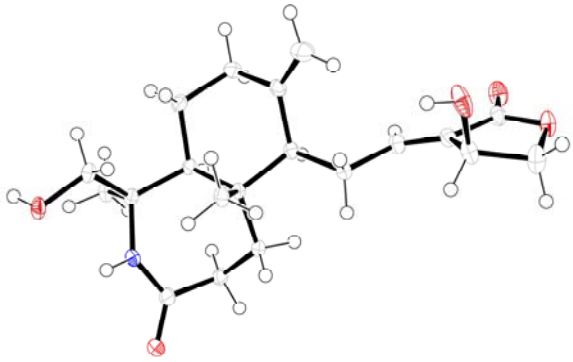


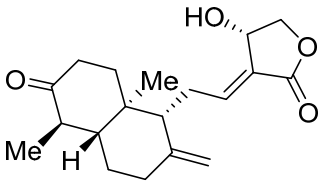
Andrographolide lactam (2d)

3-keto-andrographolide (108 mg, 0.310 mmol) was combined with hydroxylamine-o-sulfonic acid (70 mg, 0.62 mmol, 2 equiv) and 1:1 TFE:2.5% $NaHCO_3$(aq) in a 20 mL vial along with a magnetic stir bar. The vial was flushed with N_2, capped, and stirred at 50 ˚C for 40 minutes then at 80 ˚C for 1 hour. The reaction was then allowed to cool to RT and was concentrated with a rotary evaporation under vacuum to a volume of 1.5 mL. Saturated $NaHCO_3$ (2 mL) and brine (5 mL) were then added, and the mixture was extracted with 3:1 EA:THF three times (50 mL each). The organic extracts were combined, dried over Na_2SO_4 and filtered, and the solvent was evaporated. The

resulting residue was purified by silica gel chromatography, eluting with 0 to 5% MeOH in $CHCl_3$ (with 0.2% NH_4OH added to the $CHCl_3$) to elute andrographolide isoxazole (38 mg, 35% yield) and then with 5 to 8% MeOH in $CHCl_3$ to elute the target lactam. Yield = 36 mg (32%). The product elutes in a fairly broad band with a yield lower than is expected by NMR spectroscopy (NMR yield = 45%). ^{1}H NMR (600 MHz, methanol-*d*$_4$) δ 6.84 (td, J = 6.6, 1.7 Hz, 1H), 5.03 (d, J = 6.1 Hz, 1H), 4.95 (s, 1H), 4.72 (s, 1H), 4.47 (dd, J = 10.2, 6.2 Hz, 1H), 4.16 (dd, J = 10.2, 2.1 Hz, 1H), 3.73 (d, J = 10.9 Hz, 1H), 3.50 (d, J = 10.9 Hz, 1H), 2.70 – 2.61 (m, 3H), 2.45 – 2.38 (m, 2H), 2.20 (dd, J = 8.2, 5.7 Hz, 1H), 2.12 – 2.05 (m, 2H), 1.96 – 1.90 (m, 2H), 1.83 (ddd, J = 14.6, 7.8, 2.9 Hz, 1H), 1.53 (qd, J = 13.1, 4.3 Hz, 1H), 1.35 (s, 3H), 0.95 (s, 3H). ^{13}C NMR (151 MHz, methanol-*d*$_4$) δ 178.90, 172.57, 148.94, 148.63, 129.89, 109.71, 76.11, 66.70, 66.69, 61.27, 55.89, 53.67, 43.01, 38.55, 36.87, 32.20, 27.89, 27.79, 26.28, 17.76.HRMS (ESI+) calcd for [$C_{20}H_{29}NO_5Na^+$]: 386.1938, found: 386.1934. IR (neat) (cm^{-1}) 1738, 1671, 1632, 1570 (shoulder). The product structure was confirmed by x-ray crystallography.

Figure 6: X-ray crystal structure of Andrographolide lactam (**2d**)



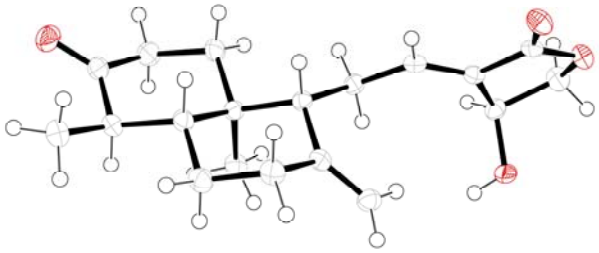


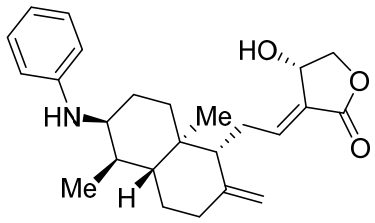
Dehydroxymethyl-andrographolide (2e)

3-keto-andrographolide (100 mg, 0.287 mmol) was combined with methyl acrylate (200 µL, 2.21 mmol, 8 equiv), TFE (2 mL), and a magnetic stir bar in a 20 mL vial and stirred to form a solution. SmI_2 in THF (0.1 M, 6 mL, 2 equiv) was then added, the vial was capped, and the mixture was heated at 65 ˚C with stirring for 25 minutes. The reaction was then allowed to cool to room temperature, and saturated bicarbonate solution (5 mL) was added. The mixture was extracted with ethyl acetate (3 x 15 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and the solvent was concentrated to ~8 mL. Silica gel (~2 g) was added and the solvent was removed by rotary evaporation to deposit the product onto the silica gel. Chromatography on silica gel, eluting with 0 to 3% MeOH in $CHCl_3$ yielded the dehydroxymethyl ketone (38 mg, 40% yield) as a white solid. ^{1}H NMR (500 MHz, methanol-*d*$_4$) δ 6.87 (td, J = 6.7, 1.7 Hz, 1H), 5.03 (d, J = 6.1 Hz, 1H), 4.99 (s, 1H), 4.77 (s, 1H), 4.47 (dd, J = 10.2, 6.1 Hz, 1H), 4.16 (dd, J = 10.2, 2.1 Hz, 1H),

2.76 – 2.66 (m, 2H), 2.58 (td, J = 14.7, 14.3, 6.0 Hz, 1H), 2.44 (ddd, J = 13.2, 4.2, 2.4 Hz, 1H), 2.40 (dq, J = 6.1, 12.2, 1H), 2.30 (ddd, J = 14.5, 4.7, 2.5 Hz, 1H), 2.16 (ddd, J = 12.9, 6.3, 2.4 Hz, 1H), 2.13 – 2.05 (m, 2H), 1.85 (ddt, J = 13.0, 5.3, 3.0 Hz, 1H), 1.61 (td, J = 13.6, 4.7 Hz, 1H), 1.50 (ddd, J = 12.2, 12.2, 3.4 Hz, 1H), 1.32 (qd, J = 13.1, 4.3 Hz, 1H), 1.01 (s, 3H), 0.98 (d, J = 6.5 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 213.89, 171.19, 147.66, 147.05, 128.52, 108.71, 74.76, 65.25, 53.64, 53.05, 44.62, 38.75, 38.47, 37.43, 36.64, 27.79, 24.68, 11.33, 10.57. HRMS (ESI-) calcd for [$C_{19}H_{25}O_4^-$]: 317.1758, found: 317.1754. IR (neat) (cm^{-1}) 1725.9, 1708.3, 1678.0. The product structure was confirmed by x-ray crystallography.

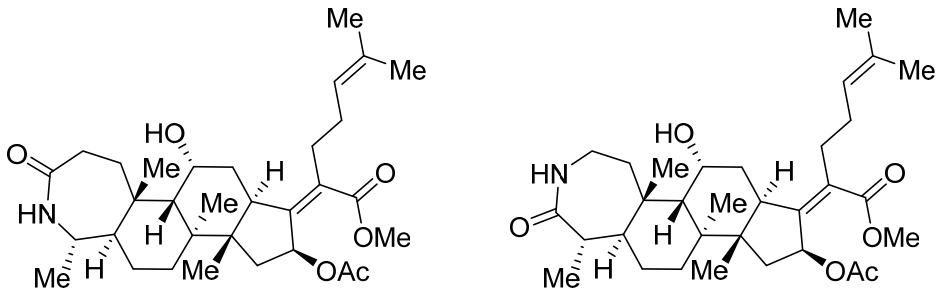
Figure 7: X-ray crystal structure of De-hydroxymethyl-andrographolide (**2e**)





3-(N-phenyl)amino-dehydroxymethyl-andrographolide (2f)

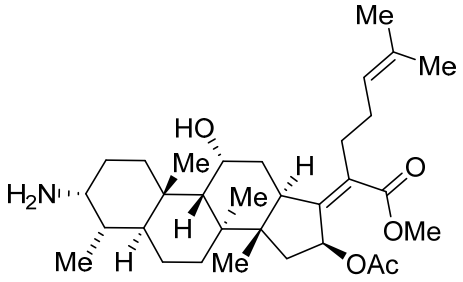
1e (19 mg, 0.060 mmol) was combined with aniline (16 µL, 0.18 mmol 3 equiv), formic acid (9 µL, 0.24 mmol, 4 equiv), **Ir-1** (1.7 mg, 0.0028 mmol, 4.5 %), and TFE (0.5 mL) in a small Schlenk flask, along with a magnetic stir bar. The flask was sealed and heated at 65 ˚C with stirring for 19 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide pressure buildup ceased (after 5 minutes, 10 minutes, 30 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). The reaction was then cooled to room temperature and saturated $NaHCO_3$ solution (1 mL) was added. The mixture was extracted with 3:1 ethyl acetate:THF (4 x 4 mL). The organic extracts were dried over Na_2SO_4, filtered and dried down to a residue. The residue was purified by silica gel chromatography, eluting with $CHCl_3$ followed by a gradient of 0% to 0.5% CH_3OH in $CHCl_3$. Yield = 10.6 mg (45%). ^{1}H NMR (900 MHz, methanol-*d*$_4$) δ 7.05 (t, J = 7.8 Hz, 2H), 6.93 – 6.88 (m, 1H), 6.65 (d, J = 7.9 Hz, 2H), 6.52 (t, J = 7.2 Hz, 1H), 5.01 (d, J = 5.9 Hz, 1H), 4.93 (s, 1H), 4.70 (s, 1H), 4.45 (dd, J = 10.2, 6.1 Hz, 1H), 4.16 (dd, J = 10.2, 1.9 Hz, 1H), 3.56 – 3.52 (m, 1H), 2.72 (ddd, J = 16.7, 6.9, 2.9 Hz, 1H), 2.59 (ddd, J = 17.2, 11.4, 6.7 Hz, 1H), 2.46 – 2.41 (m, 1H), 2.15 (td, J = 13.2, 5.1 Hz, 1H), 2.12 (d, J = 10.9 Hz, 1H), 1.85 (dq, J = 13.6, 2.8 Hz, 1H), 1.83 – 1.77 (m, 2H), 1.67 (tt, J = 13.9, 3.7 Hz, 1H), 1.61 (td, J = 12.1, 3.2 Hz, 1H), 1.56 (dt, J = 12.7, 3.2 Hz, 1H), 1.51 (td, J = 13.6, 3.5 Hz, 1H), 1.14 (qd, J = 12.9, 4.3 Hz, 1H), 0.94 (d, J = 6.8 Hz, 3H), 0.78 (s, 3H). ^{13}C NMR (226 MHz, methanol-*d*$_4$) δ 172.74, 150.20, 149.88, 149.50, 129.98, 129.64, 116.95, 113.96, 109.19, 76.20, 66.63, 55.75, 54.70, 46.61, 40.29, 38.44, 35.93, 33.78, 27.93, 27.16, 25.74, 17.33, 12.72. HRMS (ESI+) calcd for [$C_{25}H_{34}NO_3^+$]: 396.2533, found: 396.2528.



Fusidic lactam (2h, 2i)

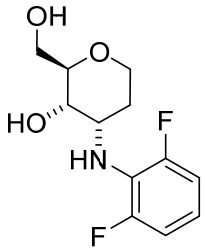
3-keto-methyl fusidate (80 mg, 0.15 mmol) was combined with hydroxylamine-o-sulfonic acid (26 mg, 0.23 mmol, 1.5 equiv) in 1:1 HFIP:H_2O (1.9 mL) along with a magnetic stir bar. The resulting solution was heated at 50 ˚C with stirring for 20 minutes and then at 80 ˚C for 30 minutes. The reaction was then cooled to room temperature, and saturated bicarbonate (3 mL) was added. The mixture was extracted with 1.5:1 ethyl acetate:THF (4 x 8 mL). The organic layers were filtered through Na_2SO_4 in a glass fritted filter, collected, and dried down into a 25 mL round bottom schlenk flask. To the residue 1:1 acetone:H_2O (10 mL) was added, the flask was sealed and heated at 80 ˚C for 10 minutes with stirring, and then cooled to room temperature. Brine (3 mL) was added to the mixture and then it was extracted with 1.5:1 ethyl acetate:THF (4 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated to 10 mL. Silica gel (~1.5 g) was added and then the solvent was fully evaporated by rotary evaporation to deposit the product onto the silica gel. Silica gel chromatography, eluting with 2.25% MeOH in DCM yielded purified fusidic lactam. **1h** eluted first. Yield = 38 mg (46%). ^{1}H NMR (900 MHz, chloroform-*d*) δ 5.86 (d, J = 8.3 Hz, 1H), 5.42 (d, J = 4.6 Hz, 1H), 5.08 (t, J = 6.9 Hz, 1H), 4.40 (s, 1H), 3.64 (s, 3H), 3.41 (h, J = 6.5 Hz, 1H), 3.03 (d, J = 11.9 Hz, 1H), 2.56 (ddd, J = 14.0, 10.4, 2.6 Hz, 1H), 2.52 – 2.37 (m, 4H), 2.29 (dt, J = 13.1, 2.7 Hz, 1H), 2.15 (dd, J = 14.4, 8.7 Hz, 1H), 2.12 (dt, J = 14.8, 7.4 Hz, 1H), 2.04 (dt, J = 14.8, 7.4 Hz, 1H), 1.97 (s, 3H), 1.94 (m, 1H), 1.92 – 1.82 (m, 3H), 1.67 (s, 3H), 1.60 (s, 3H), 1.52 (s, 1H), 1.49 (m, 1H), 1.33 – 1.28 (m, 4H), 1.26 (d, J = 3.6 Hz, 1H), 1.18 (d, J = 6.6 Hz, 3H), 1.16 – 1.06 (m, 2H), 1.13 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (226 MHz, chloroform-*d*) δ 176.41, 170.66, 170.48, 148.27, 132.80, 130.97, 123.14, 77.36, 74.42, 67.98, 51.58, 49.15, 48.67, 48.62, 48.08, 44.09, 39.80, 39.31, 39.25, 36.58, 35.56, 33.77, 32.64, 29.10, 28.36, 25.88, 25.74, 22.79, 22.56, 21.11, 20.93, 18.18, 17.91. HRMS (ESI+) calcd for [$C_{32}H_{49}NO_5Na^+$]: 566.3452 found: 566.3443. IR (neat) (cm^{-1}) 1715.6, 1650.5. Next an impurity eluted, followed by **1i**. **1i** partially overlapped with the impurity and the impure fractions were purified by a second column, eluting with 2% MeOH in DCM. Combined yield = 11 mg (13%). ^{1}H NMR (900 MHz, chloroform-*d*) δ 5.87 (d, J = 8.2 Hz, 1H), 5.59 (t, J = 6.2 Hz, 1H), 5.08 (t, J = 6.6 Hz, 1H), 4.44 (s, 1H), 3.65 (s, 3H), 3.50 (m, 1H), 3.21 (m, 1H), 3.01 (d, J = 12.1 Hz, 1H), 2.49 – 2.41 (m, 3H), 2.32 (p, J = 7.4 Hz, 1H), 2.27 (d, J = 13.2 Hz, 1H), 2.17 – 2.11 (m, 2H), 2.04 (dt, J = 14.5, 7.8 Hz, 1H), 1.99 (d, J = 4.9 Hz, 1H), 1.98 (s, 3H), 1.92 (td, J = 13.0, 2.2 Hz, 2H), 1.84 (t, J = 10.6 Hz, 1H), 1.71 – 1.66 (m, 4H), 1.60 (s, 3H), 1.46 – 1.40 (m, 2H), 1.33 (d, J = 14.2 Hz, 1H), 1.28 (s, 3H), 1.24 (d, J = 7.2 Hz, 3H), 1.19 (m, 1H), 1.13 (s, 3H), 1.12 (m, 1H), 1.03 (td, J = 13.8, 5.8 Hz, 1H), 0.94 (s, 3H). ^{13}C NMR (226 MHz, chloroform-*d*) δ 180.56, 170.60, 170.50, 148.44, 132.78, 131.07, 123.17, 74.36, 68.40, 51.60, 49.25, 48.11, 44.16, 43.80, 42.99, 39.48, 39.35, 39.23, 38.66, 37.99, 36.86, 36.35, 29.13, 28.35, 26.04, 25.89, 24.21, 23.60, 21.12, 18.27,

17.92, 16.92. HRMS (ESI+) calcd for [$C_{32}H_{49}NO_5Na^+$]: 566.3452 found: 566.3447. IR (neat) (cm^{-1}) 1716.8, 1641.2.



3-amino-fusidic acid methyl ester (2j)

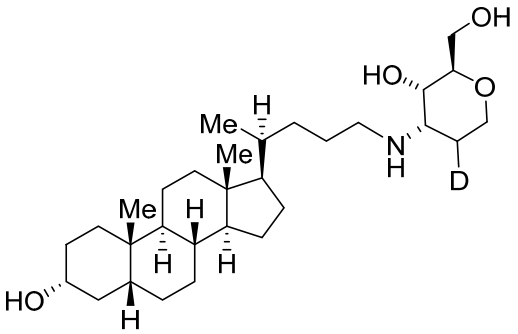
3-keto-methyl fusidate (50 mg, 0.094 mmol), ammonium formate (18 mg, 0.29 mmol, 3 equiv), and **Ir-1** (1.4 mg, 0.0024 mmol, 2.5%) were weighed into a small Schlenk flask, along with a magnetic stir bar. MeOH (300 µL) and acetic acid (5.4 µL, 0.094 mmol, 1 equiv) were then added. The mixture was heated at 60 ˚C with stirring for 4 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide pressure buildup ceased (after 5 minutes, 10 minutes, 30 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). After the reaction, 5% Na_2CO_3 (1 mL) was added, and the mixture was extracted with ethyl acetate (3 x 2.5 mL each). The organic fractions were combined, dried over Na_2SO_4, and filtered, and the solvent was evaporated. Preparative reverse phase HPLC with a C18 column , eluting with a gradient of 0 to 95% CH_3CN in H_2O yielded pure 3-amino-fusidic acid methyl ester (39 mg, 73%). ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.83 (d, *J* = 8.4 Hz, 1H), 5.07 (m, 1H), 4.32 (s, 1H), 3.62 (s, 3H), 3.02 (d, J = 11.6 Hz, 1H), 2.92 (s, 1H), 2.46 (m, 1H), 2.40 (m, 1H), 2.27 (d, J = 13 Hz, 1H), 2.21-2.07 (m, 3H), 2.06-1.98 (m, 2H), 1.96 (s, 3H), 1.90 (m, 1H), 1.82 (m, 1H), 1.73 – 1.51 (m, 13H), 1.45 (d, J = 12.4 Hz, 2H), 1.36 (s, 3H), 1.25 (d, J = 14.0 Hz, 1H), 1.15-1.04 (m, 2H), 0.96 (s, 3H), 0.88 (s, 3H), 0.84 (d, J = 7 Hz, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 170.90, 170.51, 148.30, 132.69, 130.39, 123.15, 74.52, 68.18, 51.55, 51.54, 49.35, 48.77, 44.02, 39.56, 39.12, 37.30, 35.88, 35.78, 35.70, 32.14, 30.20, 30.12, 29.02, 28.44, 25.88, 24.14, 23.38, 21.12, 20.99, 17.89, 17.80, 16.57. HRMS (ESI+) calcd for [$C_{32}H_{52}NO_5^+$]: 530.3840, found: 530.3830.



1,2-dihydro-3-(N-2,6-difluorophenyl)amino-D-glucal (2l)

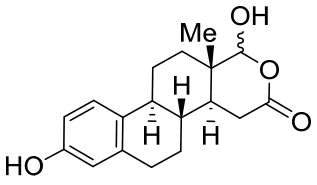
Keto-d-glucal (20 mg, 0.14 mmol) was combined with 2,6-difluoro aniline (31 uL, 0.29 mmol, 2 equiv), formic acid (16 µL, 0.42 mmol, 3 equiv), **Ir-1** (2.6 mg, 0.0042 mmol, 3%), MeOH (0.20 mL), and a magnetic stir bar in a 5 mL Schlenk flask. The reaction was heated at 65 ˚C under nitrogen for 16 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide

pressure buildup ceased (after 5 minutes, 10 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). After the reaction, the mixture was neutralized by the addition of NEt_3 (30 µL) in 1:1 THF:ethyl acetate, filtered through a plug of basic alumina, and the solvent was evaporated. The product was isolated by silica gel chromatography, eluting with 25 to 50% ethyl acetate in hexanes. Yield = 29 mg (80%) oil. ^{1}H NMR (600 MHz, chloroform-*d*) δ 6.91 – 6.77 (m, 3H), 3.96 – 3.88 (m, 2H), 3.86 – 3.69 (m, 5H), 3.50 (ddd, J = 9.5, 5.8, 3.8 Hz, 1H), 2.88 (d, J = 8.0 Hz, 1H), 2.12 (t, J = 6.1 Hz, 1H), 1.92 – 1.83 (m, 1H), 1.78 (dq, J = 14.4, 2.8 Hz, 1H).^{13}C NMR (151 MHz, chloroform-*d*) δ 155.24, 124.51, 120.76, 111.87, 76.76, 68.00, 63.55, 61.46, 54.38, 30.10. HRMS (ESI+) calcd for [$C_{12}H_{16}F_2NO_3^+$]: 260.1093, found: 260.1091.



1,2-dihydro-3-(N-lithocholic)amino-D-glucal (2m)

Keto-d-glucal (8.2 mg, 0.057 mmol) was combined with lithocholic amine (25 mg, 0.068 mmol, 1.2 equiv), formic acid (5.4 µL, 0.14 mmol, 2.5 equiv), Ir-1 (1 mg, 0.0017 mmol, 3%), and methanol-d4 (500 µL) in a small shlenk flask. The flask was sealed and heated at 60 ˚C under nitrogen for 20 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide pressure buildup ceased (after 10 minutes, 30 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). Then the reaction was cooled to room temperature and saturated bicarbonate was added (0.8 mL). The mixture was extracted (3 x 3 mL) with $CHCl_3$. The organic phases were combined, dried over Na_2SO_4, and dried down. The product was isolated by silica gel chromatography with 0 to 15% MeOH in 1:4 benzene:$CHCl_3$. Yield = 12 mg (43%) plus recovered d-glucal (3 mg, 35%). ^{1}H NMR (500 MHz, chloroform-d) δ 3.83 – 3.51 (m, 6H), 3.00 (s, 1H), 2.67 (s, 1H), 2.51 (s, 1H), 2.04 (d, J = 11.2 Hz, 1H), 1.97 – 1.73 (m, 5H), 166 - 1.63 (m, 2H), 1.55 – 1.24 (m, 14H), 1.24 – 1.06 (m, 7H), 1.05 – 0.91 (m, 7H), 0.71 (s, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ 76.90, 71.01, 66.76, 61.80, 60.93, 56.55, 56.25, 55.15, 48.05, 47.88, 42.48, 42.13, 40.49, 40.16, 35.84, 35.76, 35.62, 35.07, 34.28, 33.26, 29.78, 28.02, 26.96, 26.27, 25.79, 23.88, 22.54, 20.55, 17.78, 11.08. HRMS (ESI+) calcd for [$C_{30}H_{53}DNO_5^+$]: 493.4110, found: 493.4100.

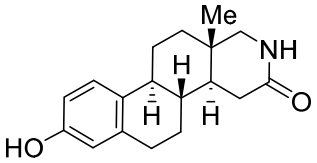


Estriol lactol (2o)

Keto-estriol (50 mg, 0.17 mmol) was combined with THF (0.5 mL), **[Pt(dppb)(OH)]$_2$[BF4]$_2$** (8 mg, 5.5 μmol, 3 %), 30% H_2O_2(aq) (35 μL, 0.35 mmol, 2 equiv) , and a magnetic stir bar in a one dram vial. The mixture was stirred at room temperature with monitoring by TLC. During the first 20 minutes, the vial was kept with a loose cap to allow for gas evolution. After 20 minutes gas evolution ceased and the vial was capped. After one day a second aliquot of H_2O_2 (aq) (35 μL, 0.35 mmol, 2 equiv) was added. After 2 days the reaction was determined to be complete. Additional THF was then added (1 mL) and the reaction mixture was eluted through a plug of Na_2SO_4 followed by a rinse of THF (1 mL). To the solution silica gel (~1 g) was added and the product was deposited onto the silica gel by rotary evaporation. Chromatography on silica gel with 5% MeOH in DCM yielded the acid-lactol (46.5 mg, 84%).

Alternative procedure: Keto-estriol (100 mg, 0.35 mmol) was combined with THF (1 mL), **[Pt(dppb)(OH)]$_2$[BF4]$_2$** (16 mg, 11 μmol, 3 %), 30% H_2O_2(aq) (140 μL, 2.8 mmol, 4 equiv), and a magnetic stir bar in a one dram vial. The mixture was stirred at room temperature for 20 minutes until gas evolution ceased. Then the vial was capped and heated at 45 ˚C with monitoring by TLC. After 6 hours the reaction was determined to be complete and cooled to room temperature. Additional THF was then added (1 mL) and the reaction mixture was eluted through a plug of Na_2SO_4 followed by a rinse of THF (1 mL). To the solution silica gel (~1 g) was added and the product was deposited onto the silica gel by rotary evaporation. Chromatography on silica gel with 5% MeOH in DCM yielded the acid-lactol (86 mg, 77%).

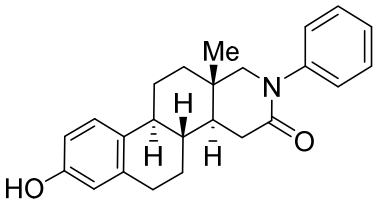
Note regarding isomeric forms and NMR characterization: At room temperature in solution, the product is in rapid equilibrium between 3 different isomeric forms: an acid-aldehyde and both possible hemiacetal epimers. NMR studies were conducted at -40 ˚C in order to observe all three species (in a 1.4:1:1 ratio, respectively). In addition to the study of ^{1}H and ^{13}C NMR spectra for the product, ^{1}H-^{13}C HSQC and comparison of the product ^{13}C spectrum to the ^{13}C spectra of other estriol derivatives enabled all of the ^{13}C peaks to be located. 5 out of the 6 aromatic ^{13}C peaks for the hemiacetal epimers are superposed, and the aromatic phenol ^{13}C peak is superposed for all 3 isomeric forms. 3 of the aliphatic ^{13}C peaks are superposed for the hemiacetal epimers. 3 distinct ^{13}C peaks in the 9 to 16 ppm range correspond to the –CH_3 group in the three different isomeric forms. ^{1}H NMR (500 MHz, tetrahydrofuran-d_8) δ 11.82 – 11.39 (m, 1H), 9.34 (s, 1H), 8.79 – 8.59 (m, 3H), 7.37 (s, 1H), 7.08 (s, 4H), 6.55 – 6.47 (m, 3H), 6.42 (s, 3H), 5.19 – 5.04 (m, 2H), 2.81 – 2.60 (m, 8H), 2.48 – 2.27 (m, 6H), 2.26 – 2.05 (m, 6H), 1.97 – 1.83 (m, 6H), 1.57 – 1.50 (m, 1H), 1.48 – 1.16 (m, 12H), 1.04 – 0.81 (m, 9H). ^{13}C NMR (126 MHz, , tetrahydrofuran-d_8) δ 206.35, 174.97, 170.77, 170.03, 156.66, 156.66, 156.64, 137.95, 137.94, 137.86, 130.72, 130.62, 130.34, 127.32, 127.06, 127.06, 115.60, 115.59, 115.55, 113.80, 113.70, 113.68, 105.23, 103.37, 51.33, 43.96, 43.89, 43.77, 41.73, 41.67, 40.43, 39.94, 39.88, 37.63, 37.17, 36.38, 35.60, 35.31, 33.77, 32.85, 32.37, 31.97, 31.13, 30.87, 30.83, 27.75, 26.98, 26.79, 26.71, 26.49, 26.48, 15.81, 13.31, 9.94. HRMS (ESI-) calcd for [$C_{18}H_{21}O_4^-$]: 301.1445, found: 301.1444. IR (neat, RT) (cm^{-1}) 1695.4, 1672.5, 1606.2. Additional confirmation of the structure of this product was obtained by transforming it into lactam derivatives **2p** and **2q** in high yield under reductive amination conditions.



Estriol-N-H-lactam (2p)

Method A (main test figure 3 reaction xviii): Keto-estriol (25 mg, 0.087 mmol) was combined with ammonium formate (17 mg, 0.26 mmol, 3 equiv), acetic acid (5 μL, 0.087, 1 equiv), **Ir-1** (1.32 mg, 2.2 μmol, 2.5%), MeOH (200 μL), and a magnetic stir bar in a small Schlenk flask. The reaction was heated at 60 ˚C under nitrogen for 4 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide pressure buildup ceased (after 5 minutes, 10 minutes, 30 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). Upon completion, the reaction was cooled to room temperature and saturated bicarbonate was added (2 mL). The mixture was extracted with ethyl acetate (3 x 10 mL). The organic phases were combined, dried over Na_2SO_4, and dried down. The product was isolated by silica gel chromatography with 0 to 5% MeOH in $CHCl_3$. Yield = 13.5 (54%).

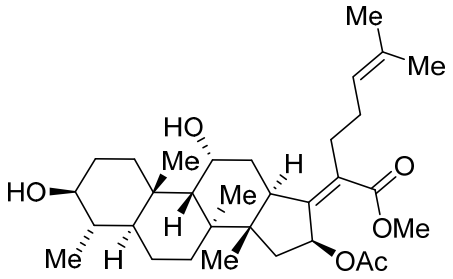
Method B (main text figure 3 reaction xvi): Estriol-acid-lactol (11 mg, 0.036 mmol) was combined with ammonium formate (7 mg, mmol, 3 equiv), formic acid (1.4 μL, 1 equiv), **Ir-1** (0.6 mg, mmol, 2.5%), MeOH (700 μL), and a magnetic stir bar in a 5 mL Schlenk flask. The reaction was heated at 60 ˚C under nitrogen for 4 hours. The flask was periodically exposed to Schlenk line N_2 until carbon dioxide pressure buildup ceased (after 10 minutes, 30 minutes, and 1 hour the flask was briefly opened to N_2 and then resealed). Yield = 8.5 mg (78%). ^{1}H NMR (600 MHz, methanol-d_4) δ 7.10 (d, J = 8.5 Hz, 1H), 6.55 (d, J = 8.5 Hz, 1H), 6.49 (s, 1H), 3.04 (d, J = 12.0 Hz, 1H), 2.95 (d, J = 12.0 Hz, 1H), 2.81 – 2.75 (m, 2H), 2.56 (dd, J = 18.1, 5.8 Hz, 1H), 2.38 – 2.32 (m, 1H), 2.27 (t, J = 9.6 Hz, 1H), 2.01 – 1.91 (m, 2H), 1.74 – 1.67 (m, 1H), 1.57 (td, J = 11.9, 11.2, 5.8 Hz, 1H), 1.51 – 1.39 (m, 2H), 1.32 – 1.19 (m, 2H), 0.99 (s, 3H). ^{13}C NMR (151 MHz, methanol-d_4) δ 174.99, 156.13, 138.62, 132.03, 127.20, 115.87, 113.93, 56.57, 44.42, 44.12, 41.50, 38.17, 33.38, 33.29, 30.78, 27.05, 26.98, 16.25. HRMS (ESI+) calcd for [$C_{18}H_{24}NO_2^+$]: 286.1702, found: 286.1797. IR (neat) (cm^{-1}) 1740.6, 1673.1, 1644.5.



Estriol-N-phenyl-lactam (2q)

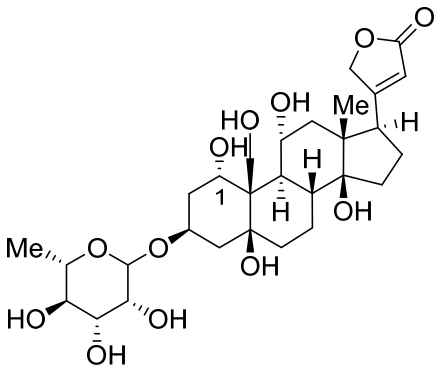
Estriol-acid-lactol (19 mg, 0.063 mmol) was combined with aniline (12 μL, 2 equiv), formic acid (7 μL, 3 equiv), **Ir-1** (mg, mmol, 2.5%), MeOH (1 mL), and a magnetic stir bar in a 5 mL Schlenk flask. The reaction was heated at 60 ˚C under nitrogen for 12 hours. During the first 4 hours the flask was left open to the Schlenk line via a reflux condenser to allow for the release of carbon dioxide. During the reaction, a white precipitate formed. After the reaction, the mixture was neutralized by the addition of 30 μL triethylamine. The resulting mixture was then filtered to collect the white solid product in a glass-fritted funnel. The product was rinsed with methanol

twice and then dried under high vacuum. Yield = 18.5 mg (77%) white powder. ^{1}H NMR (600 MHz, dimethylformamide-d_7) δ 9.19 (s, 1H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.33 (d, *J* = 7.7 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 6.67 – 6.62 (m, 1H), 6.59 – 6.55 (m, 1H), 3.63 (d, *J* = 11.5 Hz, 1H), 3.20 (d, *J* = 11.4 Hz, 1H), 2.79 (dd, *J* = 10.1, 5.5 Hz, 2H), 2.64 (dd, *J* = 17.8, 5.9 Hz, 1H), 2.35 (d, *J* = 10.1 Hz, 1H), 2.28 (d, *J* = 10.2 Hz, 1H), 2.13 (dd, *J* = 17.8, 12.7 Hz, 1H), 1.99 (dt, *J* = 11.7, 5.9 Hz, 1H), 1.76 – 1.68 (m, 2H), 1.52 – 1.37 (m, 2H), 1.28 (dt, *J* = 10.8, 6.2 Hz, 2H), 1.12 (s, 3H). ^{13}C NMR (151 MHz, dimethylformamide-d_7) δ 169.51, 156.81, 145.45, 138.55, 131.55, 129.84, 127.47, 127.23, 127.14, 116.04, 114.06, 65.68, 44.88, 43.74, 41.10, 37.66, 34.90, 34.34, 30.66, 26.90, 26.87, 16.60. HRMS (ESI+) calcd for [$C_{24}H_{28}NO_2^+$]: 362.2115, found: 362.2115.



3-epi-fusidic acid methyl ester (3a)

Method A: 3-keto-fusidic acid methyl ester (83 mg, 0.16 mmol) was combined with 1:3 ^{i}PrOH:TFE (3.1 mL) and a magnetic stir bar in a 20 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (4.8 mg, 3.2 μmol, 2.0 mol %) and NMM (0.76 μL, 6.4 μmol, 4.0 mol %) in TFE (0.2 mL) was added from a stock solution. The vial was capped, and the reaction was heated at 65 ˚C for 1 hour with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was purified by silica gel chromatography, eluting with 15% to 18% ethyl acetate in hexanes. Yield = 67 mg (82%) of a transparent solid. *Method B:* Fusidic acid methyl ester (40 mg, 0.08 mmol) was combined with TFE (80 μL) and a magnetic stir bar in a 20 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (4.6 mg, 3.0 μmol, 4.0 mol %) and NMM (0.75 μL, 6.1 μmol, 8.0 mol %) in TFE (80 μL) was added from a stock solution. The vial was capped, and the reaction was heated at 70 ˚C for 11 hours with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was purified by silica gel chromatography, eluting with 15% to 18% ethyl acetate in hexanes. Yield = 32 mg (80%) of a transparent solid. ^{1}H NMR (700 MHz, chloroform-*d*) δ 5.83 (d, J = 8.4 Hz, 1H), 5.07 (t, J = 6.8 Hz, 1H), 4.33 (s, 1H), 3.63 (s, 3H), 3.12 (td, J = 10.5, 5.3 Hz, 1H), 3.00 (d, J = 12.0 Hz, 1H), 2.50 – 2.37 (m, 2H), 2.27 (d, J = 13.2 Hz, 1H), 2.17 – 2.08 (m, 2H), 2.01 (dq, J = 15.1, 7.4 Hz, 1H), 1.97 (s, 3H), 1.94 – 1.82 (m, 3H), 1.77 – 1.72 (m, 2H), 1.70 – 1.67 (m, 1H), 1.66 (s, 3H), 1.62 (td, J = 12.9, 12.4, 4.2 Hz, 1H), 1.58 (s, 3H), 1.54 (s, 1H), 1.53 – 1.48 (m, 1H), 1.38 (ddt, J = 16.7, 12.6, 6.5 Hz, 1H), 1.32 (s, 1H), 1.31 (s, 3H), 1.29 – 1.22 (m, 2H), 1.11 (tq, J = 13.6, 6.7 Hz, 2H), 0.99 (s, 3H), 0.95 (d, J = 6.2 Hz, 3H), 0.89 (s, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 170.80, 170.52, 148.18, 132.72, 130.62, 123.15, 76.64, 74.48, 68.43, 51.55, 49.13, 48.82, 44.01, 43.02, 39.75, 39.53, 39.19, 36.86, 36.01, 34.41, 32.91, 31.73, 29.04, 28.40, 25.87, 24.32, 23.83, 21.10, 21.10, 17.89, 17.87, 15.49. HRMS (ESI+) calcd for [$C_{32}H_{50}O_6Na^+$]: 553.3500, found: 553.3497.



1-epi-ouabain (3b)

1-keto-ouabain (45 mg, 0.77 mmol) was combined with 1:3 ^{i}PrOH:TFE (1.7 mL) and a magnetic stir bar in a 4 mL vial, and the resulting mixture was stirred to form a solution. Then a solution of **Ru-2** (2 mg, 2.8 μmol, 1.8 mol %) and NMM (0.30 μL, 6.4 μmol, 3.6 mol %) in TFE (100 μL) was added from a stock solution. The vial was capped, and the reaction was heated at 65 ˚C for 1 hour with stirring. The reaction was then allowed to cool to RT, and all of the volatile materials were evaporated by rotary evaporation. The crude product was purified by silica gel chromatography, eluting with 15% to 25% methanol in dichloromethane. Yield = 41 mg (90%) of a transparent solid. ^{1}H NMR (700 MHz, methanol-d_4) δ 5.93 (s, 1H), 5.02 (d, J = 18.0 Hz, 1H), 4.92 (d, J = 18.0 Hz, 1H), 4.87 – 4.83 (m, 2H), 4.34 (d, J = 11.4 Hz, 1H), 4.21 (s, 1H), 4.14 (d, J = 11.4 Hz, 1H), 3.90 (td, J = 10.8, 4.9 Hz, 1H), 3.79 (dd, J = 3.2, 1.7 Hz, 1H), 3.69 – 3.63 (m, 2H), 3.40 (t, J = 9.4 Hz, 1H), 2.88 (dd, J = 8.4, 5.3 Hz, 1H), 2.30 (td, J = 13.4, 3.2 Hz, 1H), 2.19 (ddt, J = 19.0, 12.8, 6.2 Hz, 3H), 2.04 (d, J = 12.8 Hz, 1H), 1.98 (m, 1H), 1.94 (td, J = 14.1, 4.9 Hz, 1H), 1.89 (dd, J = 9.7, 12.0 Hz, 1H), 1.83 (m, 1H), 1.74 (tt, J = 13.0, 7.4 Hz, 3H), 1.60 – 1.47 (m, 3H), 1.29 (m, 1H), 1.28 (d, *J* = 6.3 Hz, 3H), 0.90 (s, 3H). ^{13}C NMR (151 MHz, methanol-d_4) δ 176.11, 175.63, 116.73, 99.24, 83.96, 78.41, 73.82, 73.69, 72.46, 71.02, 71.00, 69.17, 64.51, 63.97, 60.96, 50.24, 48.97, 48.82, 45.72, 39.12, 35.45, 34.36, 34.09, 31.83, 28.97, 26.20, 23.86, 16.56, 15.47. HRMS (ESI+) calcd for [$C_{29}H_{44}O_{12}Na^{+}$]: 607.2725, found: 607.2726.

9. References

1. Sun, X., Lee, H., Lee, S. & Tan, K. L. Catalyst recognition of cis-1,2-diols enables site-selective functionalization of complex molecules. *Nat. Chem.* **5,** 790–5 (2013).
2. Melorose, J., Perroy, R. & Careas, S. Dimeric Complexes of Platinum(I) containing a Platinum-Platinum Bond. *J. Chem. Soc. Dalt. Trans.* 951–955 (1977).
3. Li, J.-J., Li, W. & Sharp, P. R. Phosphine-Based Platinum(II) Hydroxo and Oxo Complexes. *Inorg. Chem.* **35,** 604–613 (1996).
4. Martínez, A. M., Rodríguez, N., Arrayás, R. G. & Carretero, J. C. Copper-catalyzed ortho-C-H amination of protected anilines with secondary amines. *Chem. Commun. (Camb).* **2,** 2801–2803 (2014).
5. Watanabe, M., Tanaka, K., Miki, T. & Murata, K. Process for Preparing Amine Compound. (2012). doi:US 2012/0065426 A1
6. Ten Brink, G. J., Arends, I. W. C. E., Hoogenraad, M., Verspui, G. & Sheldon, R. A. Catalytic Conversions in Water. Part 23: Steric Effects and Increased Substrate Scope in

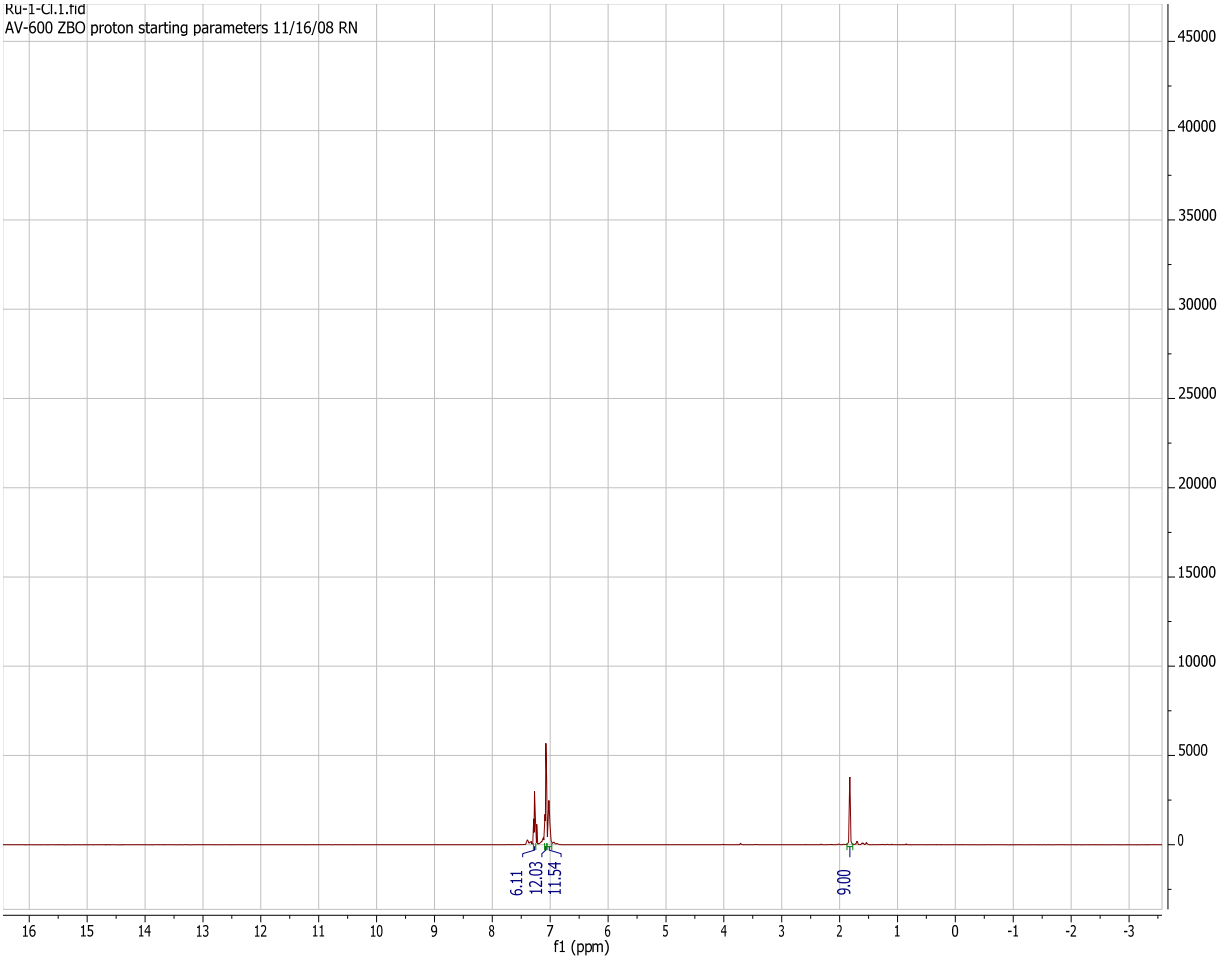
the Palladium-Neocuproine Catalyzed Aerobic Oxidation of Alcohols in Aqueous Solvents. *Adv. Synth. Catal.* **345,** 1341–1352 (2003).

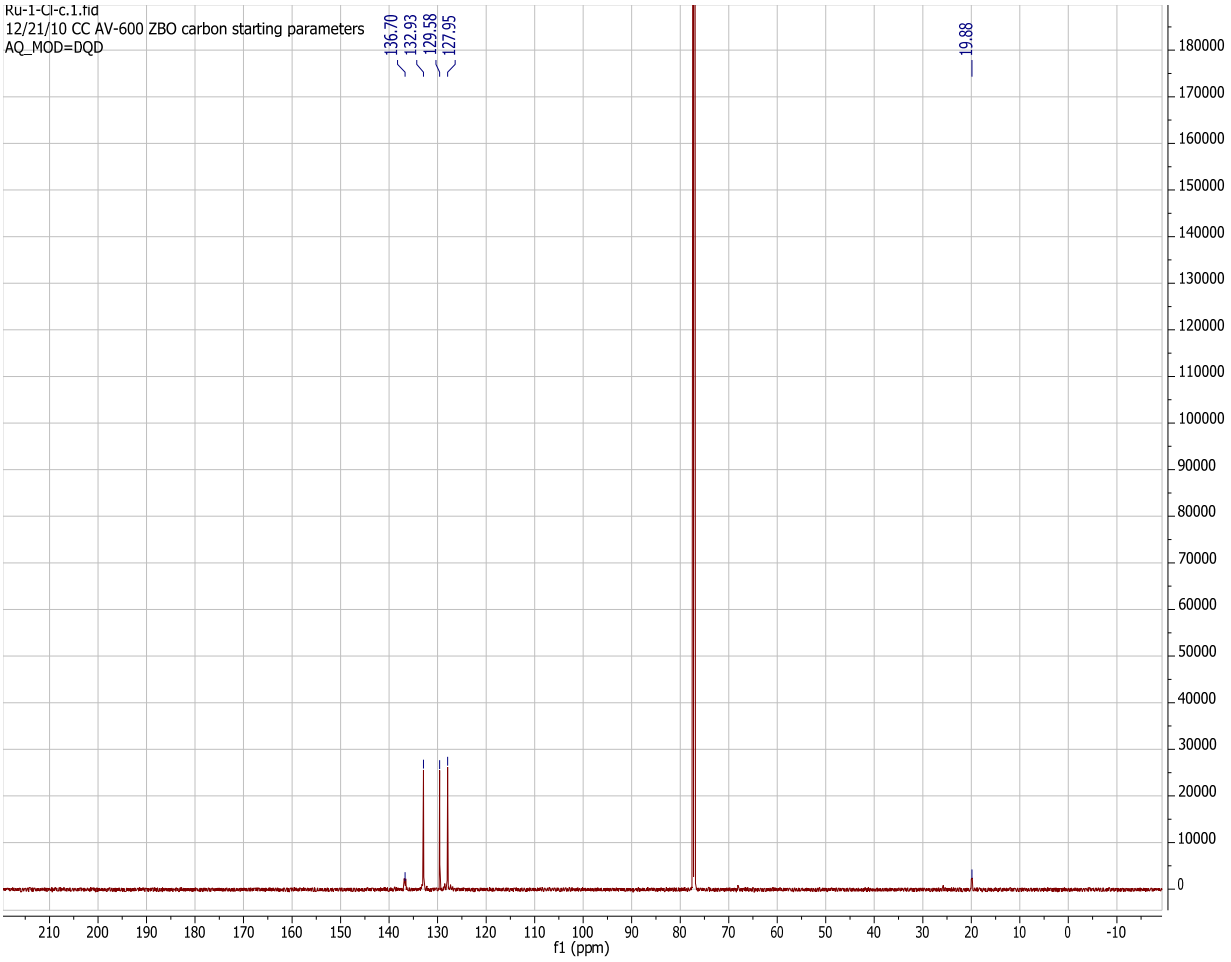
7. Conley, N. R., Labios, L. A., Pearson, D. M., McCrory, C. C. L. & Waymouth, R. M. Aerobic alcohol oxidation with cationic palladium complexes: Insights into catalyst design and decomposition. *Organometallics* **26,** 5447–5453 (2007).
8. Mathad, V. T., Kumar, S. & Raj, K. Oxidation studies on Andrographolide. *Nat. Prod. Res.* **20,** 1053–1058 (2006).
9. Scott, R. W. *et al.* Mupirocin F: Structure elucidation, synthesis and rearrangements. *Tetrahedron* **67,** 5098–5106 (2011).
10. Dess, D. B. & Martin, J. C. Readily accessible 12-I-5 oxidant for the conversion of primary and secondary alcohols to aldehydes and ketones. *J. Org. Chem.* **48,** 4155–4156 (1983).
11. Fieser, L. F. & Rajagopalan, S. Selective Oxidation with N-Bromosuccinimide. I. Cholic Acid. *J. Am. Chem. Soc.* **71,** 3935–3938 (1949).
12. Omura, K. & Swern, D. Oxidation of alcohols by 'activated' dimethyl sulfoxide. a preparative, steric and mechanistic study. *Tetrahedron* **34,** 1651–1660 (1978).
13. Mello, R., Martínez-Ferrer, J., Asensio, G. & González-Núñez, M. E. Oppenauer oxidation of secondary alcohols with 1,1,1-trifluoroacetone as hydride acceptor. *J. Org. Chem.* **72,** 9376–9378 (2007).
14. Spencer, A., Evans, I. P. & Wilkinson, G. Dichlorotetrakis(dimethyl sulphoxide)ruthenium(II) and its Use as a Source Material for Some New Ruthenium(II) Complexes. *J. Chem. Soc. Dalt. Trans.* 204–209 (1973).
15. Welankiwar, S. S. & Murphy, W. S. Stereoselective Oxidation of Fusidic Acid Derivatives. *J. Chem. Soc. Perkin Trans. 1* 710–712 (1976).
16. Hayashi, M., Yamada, K. & Nakayama, S. Dehydrogenation of D-Glycals by Palladium Supported on Activated Charcoal under Ethylene Atmosphere: Synthesis of 1,5-Anhydrohex-1-en-3-uloses. *Synthesis (Stuttg).* 1869–1871 (1999).
17. Xiang, Y., Zhang, H., Fan, C. Q. & Yue, J. M. Novel diterpenoids and diterpenoid glycosides from Siegesbeckia orientalis. *J. Nat. Prod.* **67,** 1517–1521 (2004).
18. Habermehl, G. G. & Hammann, P. E. Rearrangement of 14 / 3-Hydroxy-12ß-sulfoxy-steroids to 13 , 17-Seco-12 , 17-cyclo-steroids ; a 2D-NMR Analysis. *Z. Naturforsch* 656–660 (1985).
19. Aher, N. G., Pore, V. S., Mishra, N. N., Shukla, P. K. & Gonnade, R. G. Design and synthesis of bile acid-based amino sterols as antimicrobial agents. *Bioorganic Med. Chem. Lett.* **19,** 5411–5414 (2009).
20. Bhat, S. V, Bajwa, B. S., Dornauer, H. & de Souza, N. J. Reactions of Forskolin, a Biologically Active Diterpenoid from Coleus forskohlii. *J. Chem. Soc. Perkin Trans. 1* 767–771 (1982).
21. Luo, J. *et al.* Synthesis of Stable Genipin Derivatives and Studies of Their Neuroprotective Activity in PC12 Cells. *ChemMedChem* **7,** 1661–1668 (2012).

10. NMR spectra of isolated compounds

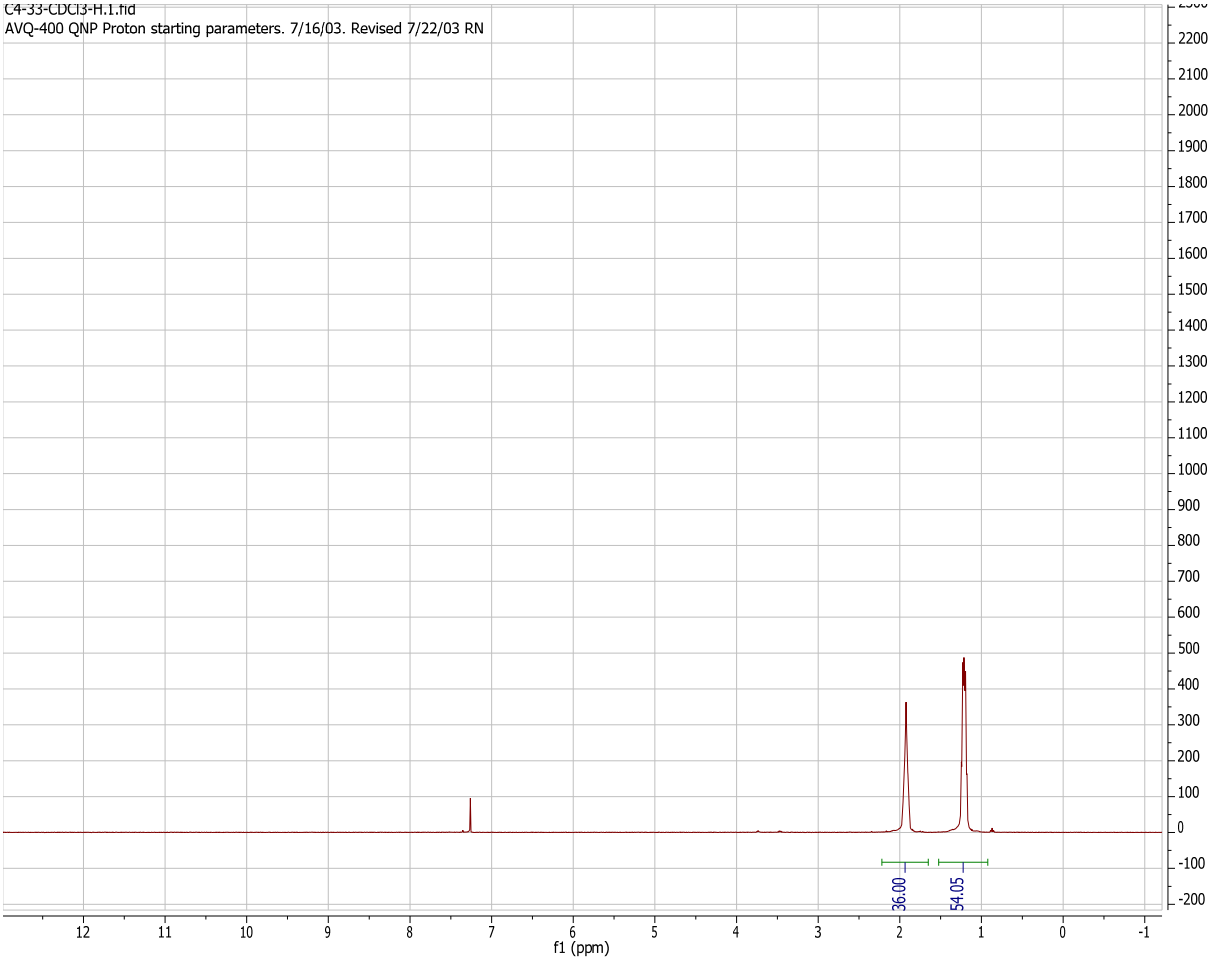
Ruthenium complex NMR data:

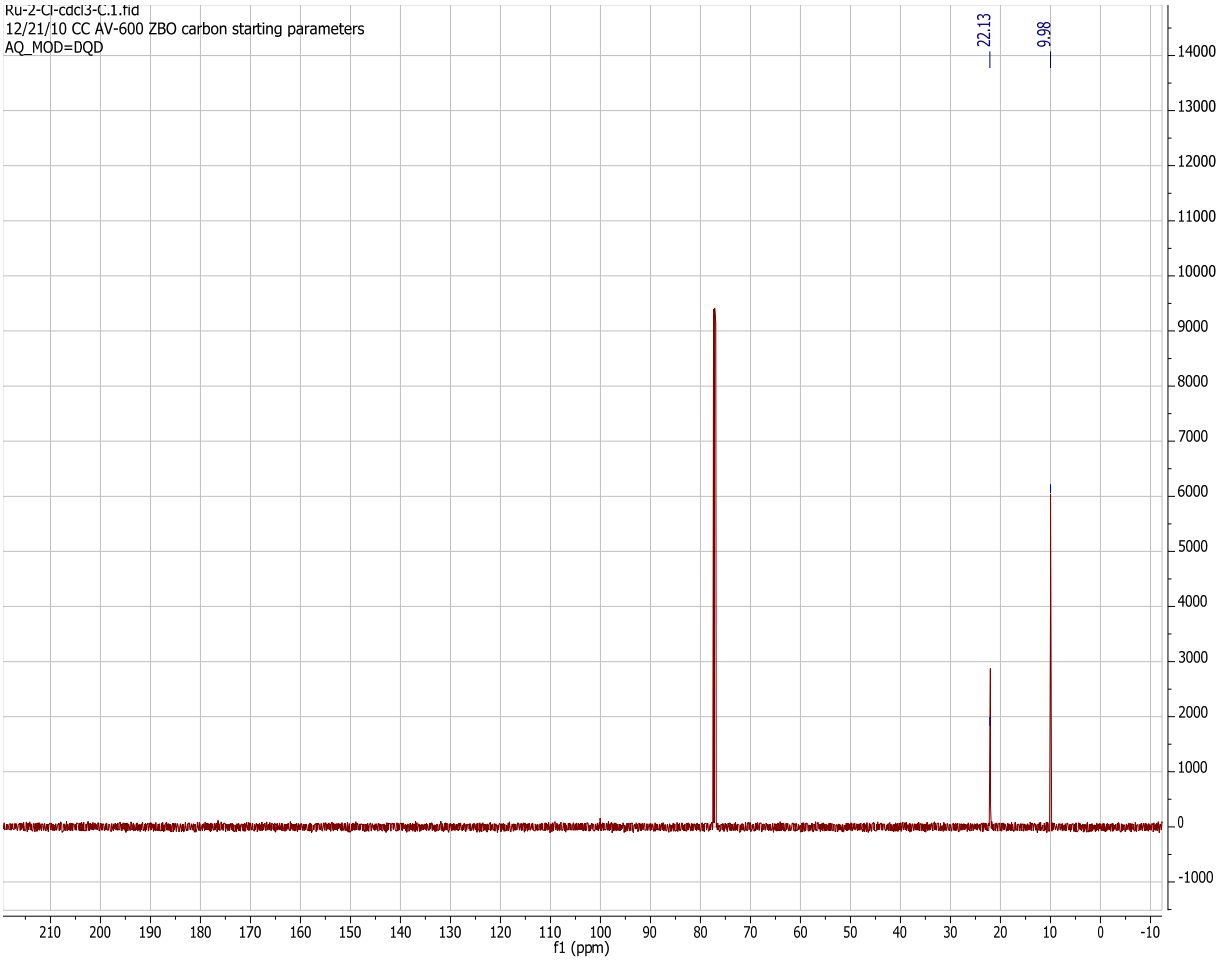
Ru-1-Cl:



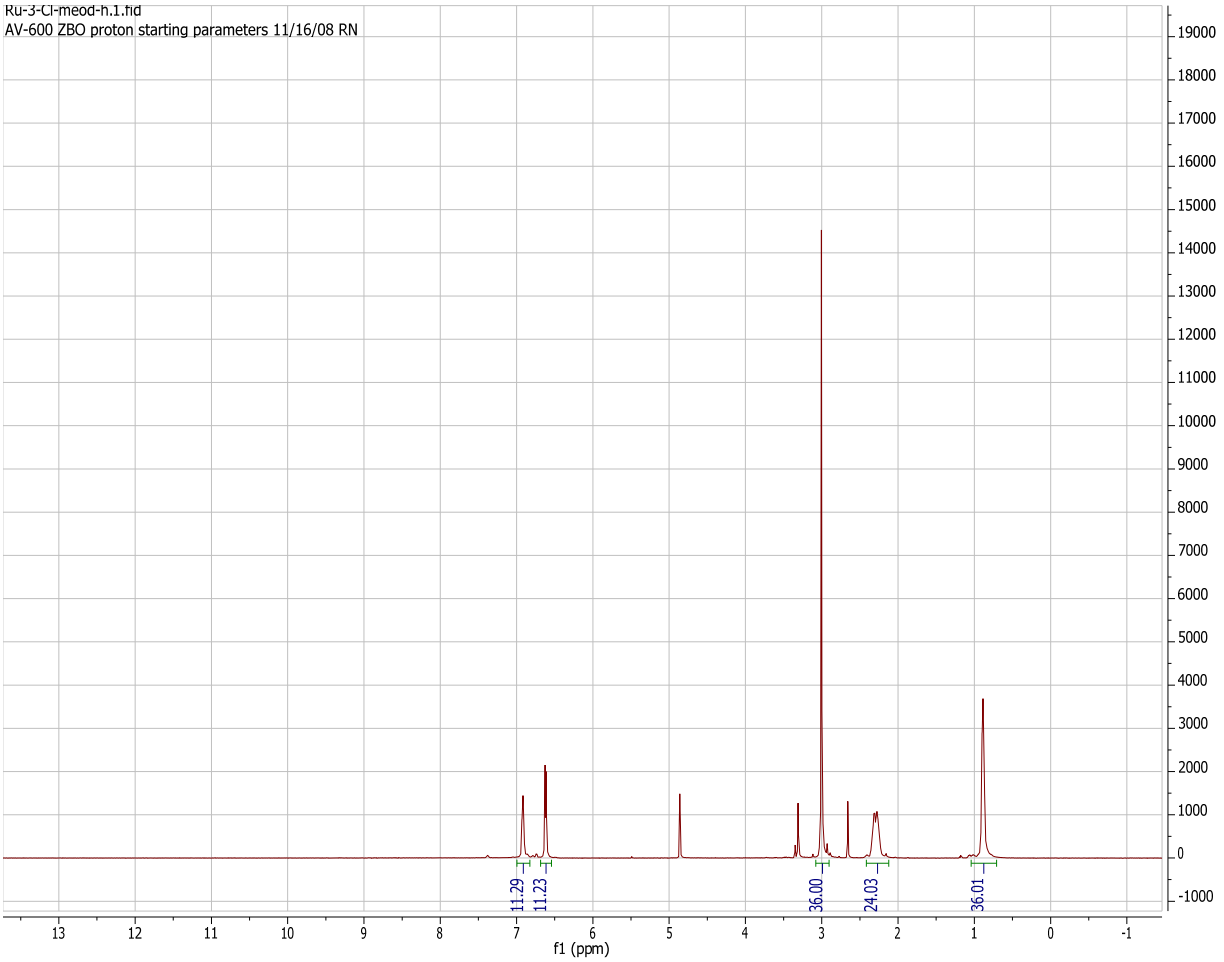

Ru-1-Cl-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
136.70
132.93
129.58
127.95
19.88
f1 (ppm)

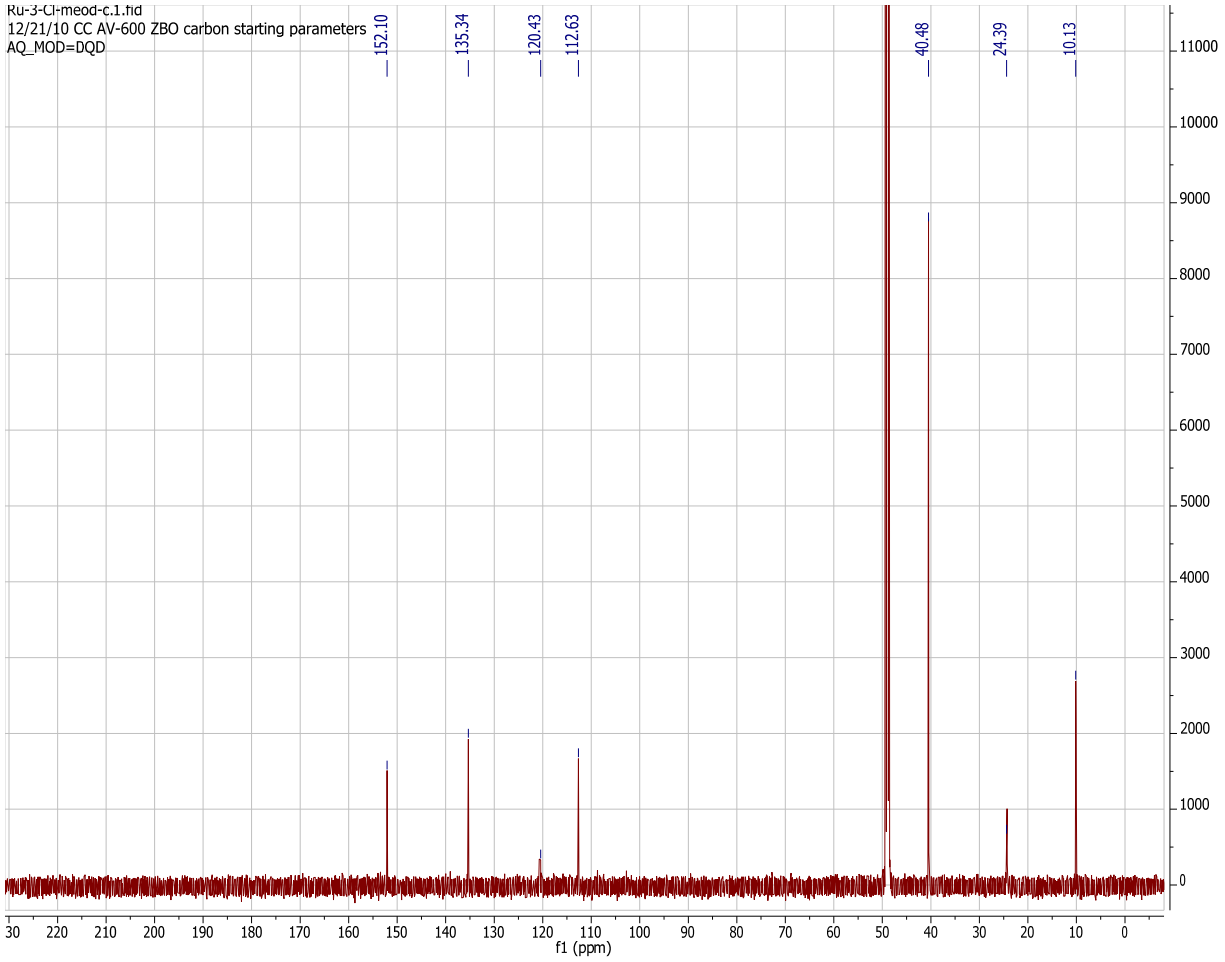
Ru-2-Cl:


C4-33-CDCl3-H.1.fid
AVQ-400 QNP Proton starting parameters. 7/16/03. Revised 7/22/03 RN
36.00
54.05
f1 (ppm)

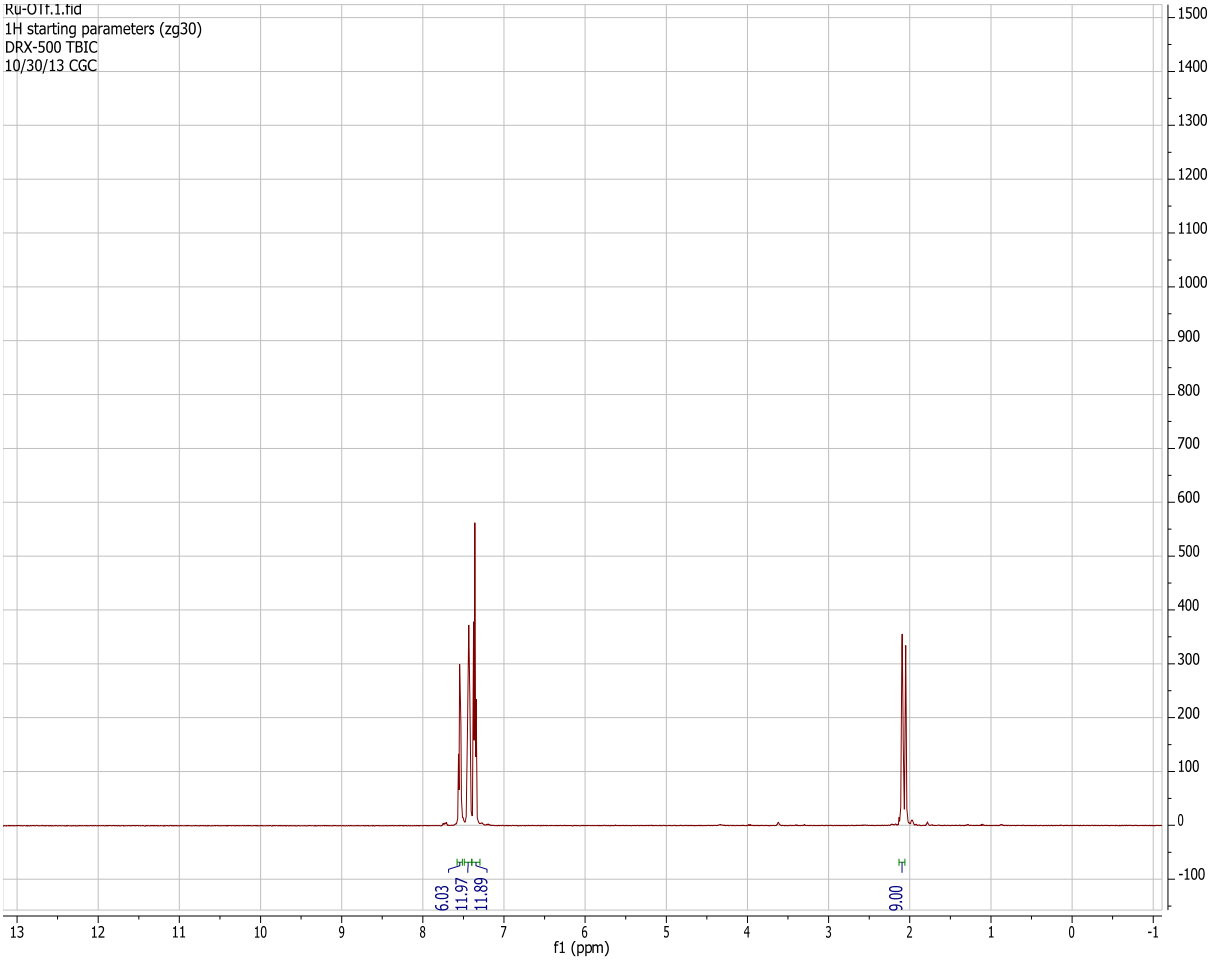

Ru-2-Cl-cdcl3-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
22.13
9.98
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

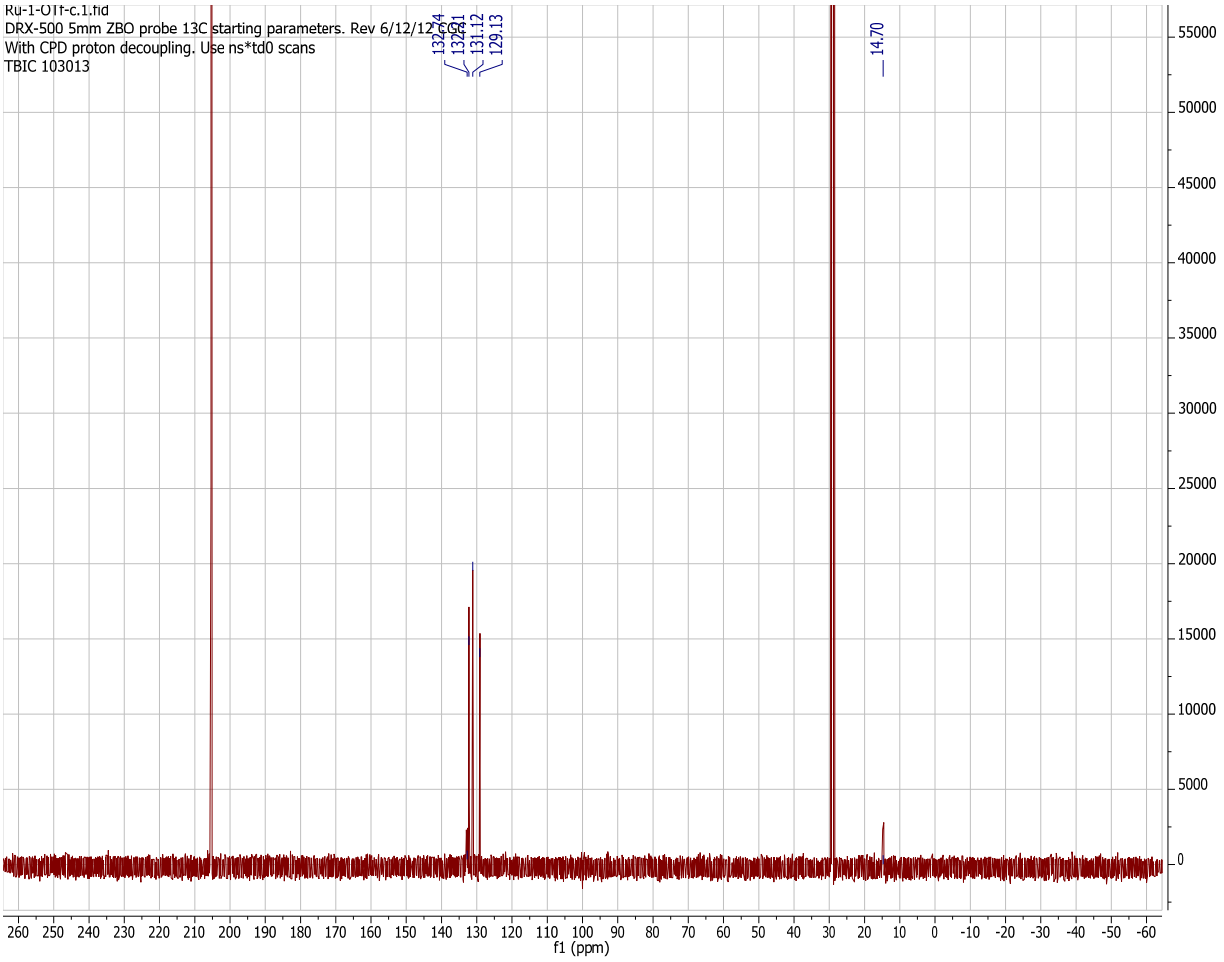
Ru-3-Cl:


Ru-3-Cl-meod-h.1.fid
AV-600 ZBO proton starting parameters 11/16/08 RN
11.29
11.23
36.00
24.03
36.01
f1 (ppm)

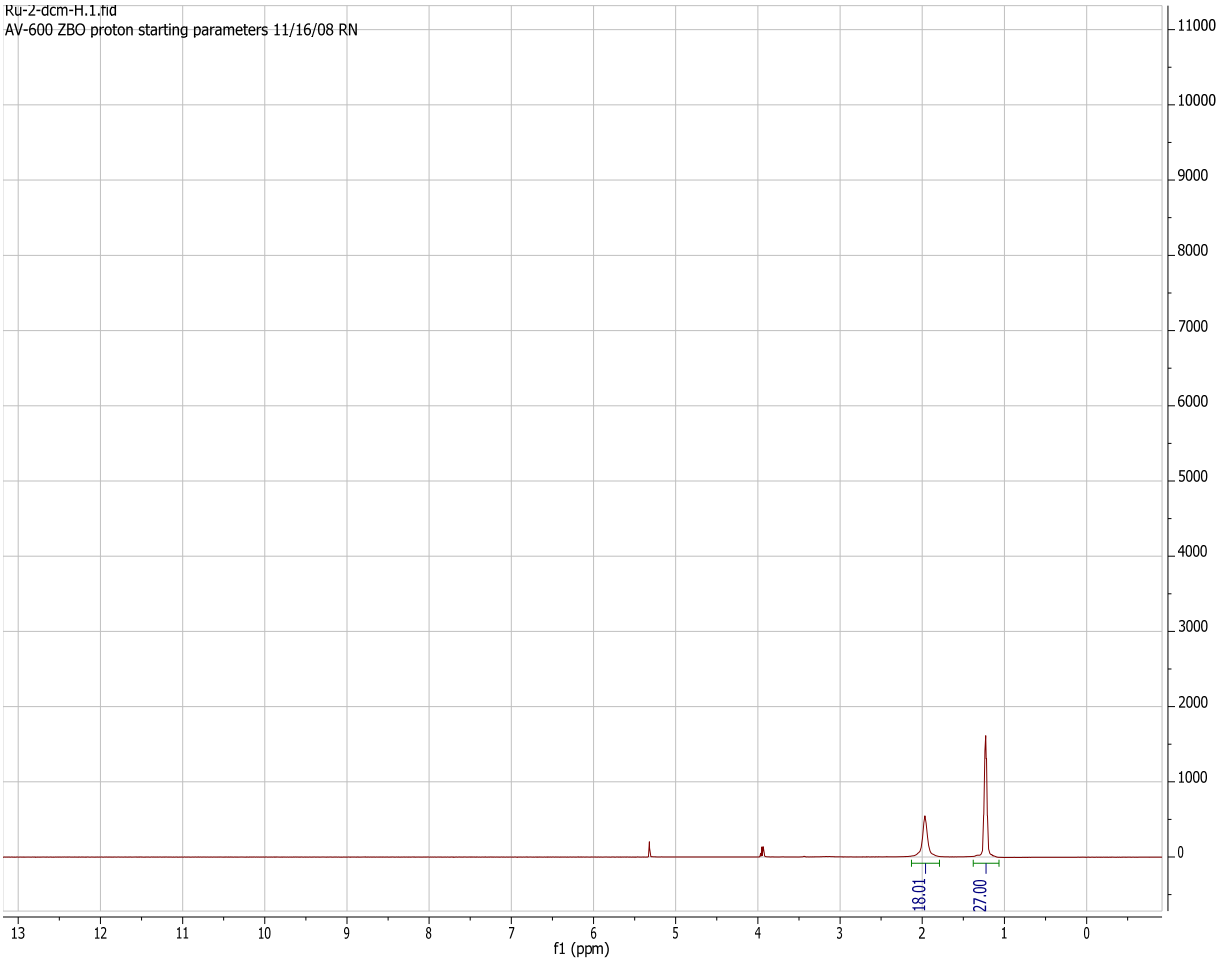

Ru-3-Cl-meod-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
152.10
135.34
120.43
112.63
40.48
24.39
10.13
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Ru-1:

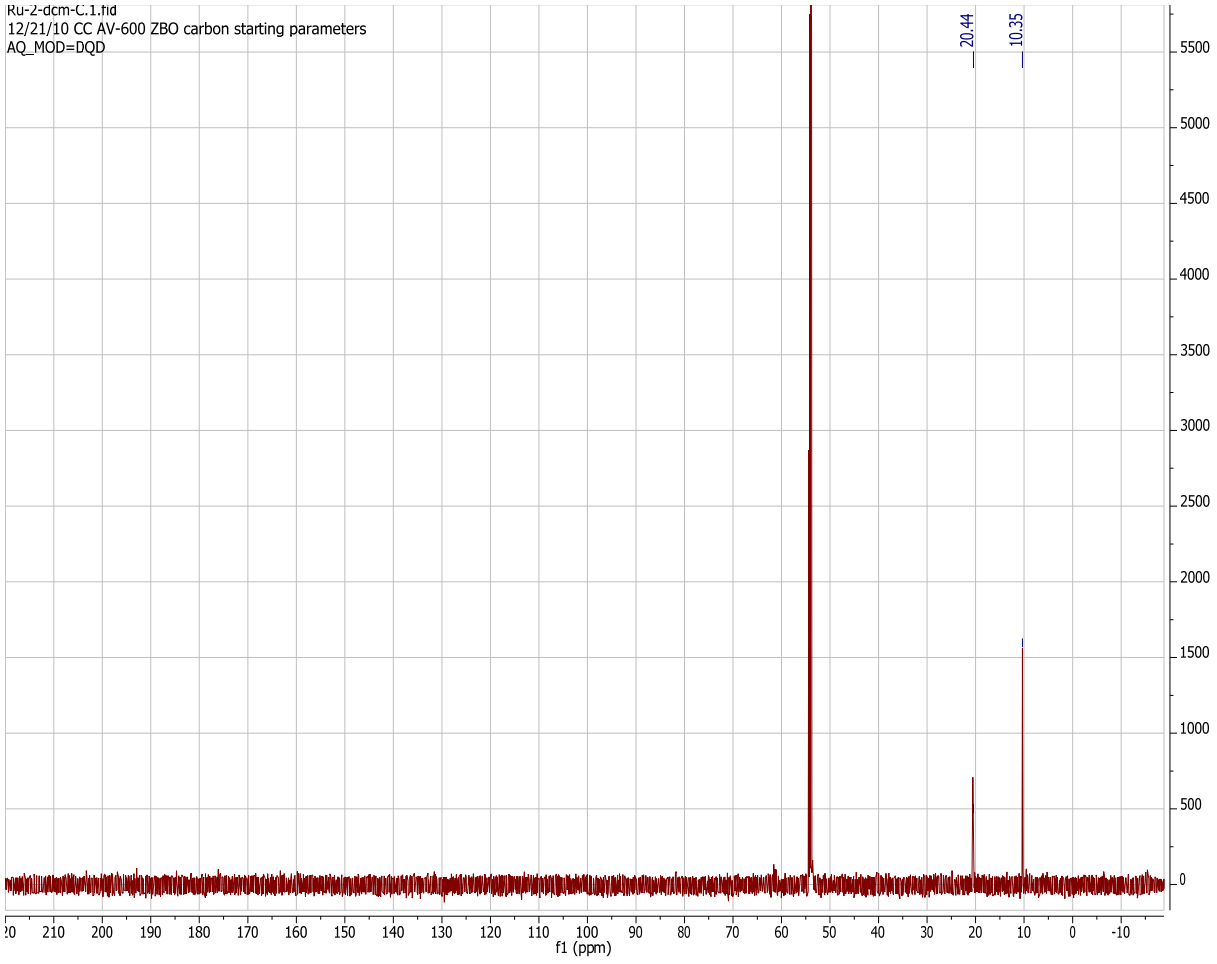

Ru-OTf.1.fid
1H starting parameters (zg30)
DRX-500 TBIC
10/30/13 CGC
6.03
11.97
11.89
9.00
f1 (ppm)


Ru-1-OTf-c.1.fid
DRX-500 5mm ZBO probe 13C starting parameters. Rev 6/12/12 CG
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
132.24
132.01
131.12
129.13
14.70
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
260 250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60
f1 (ppm)

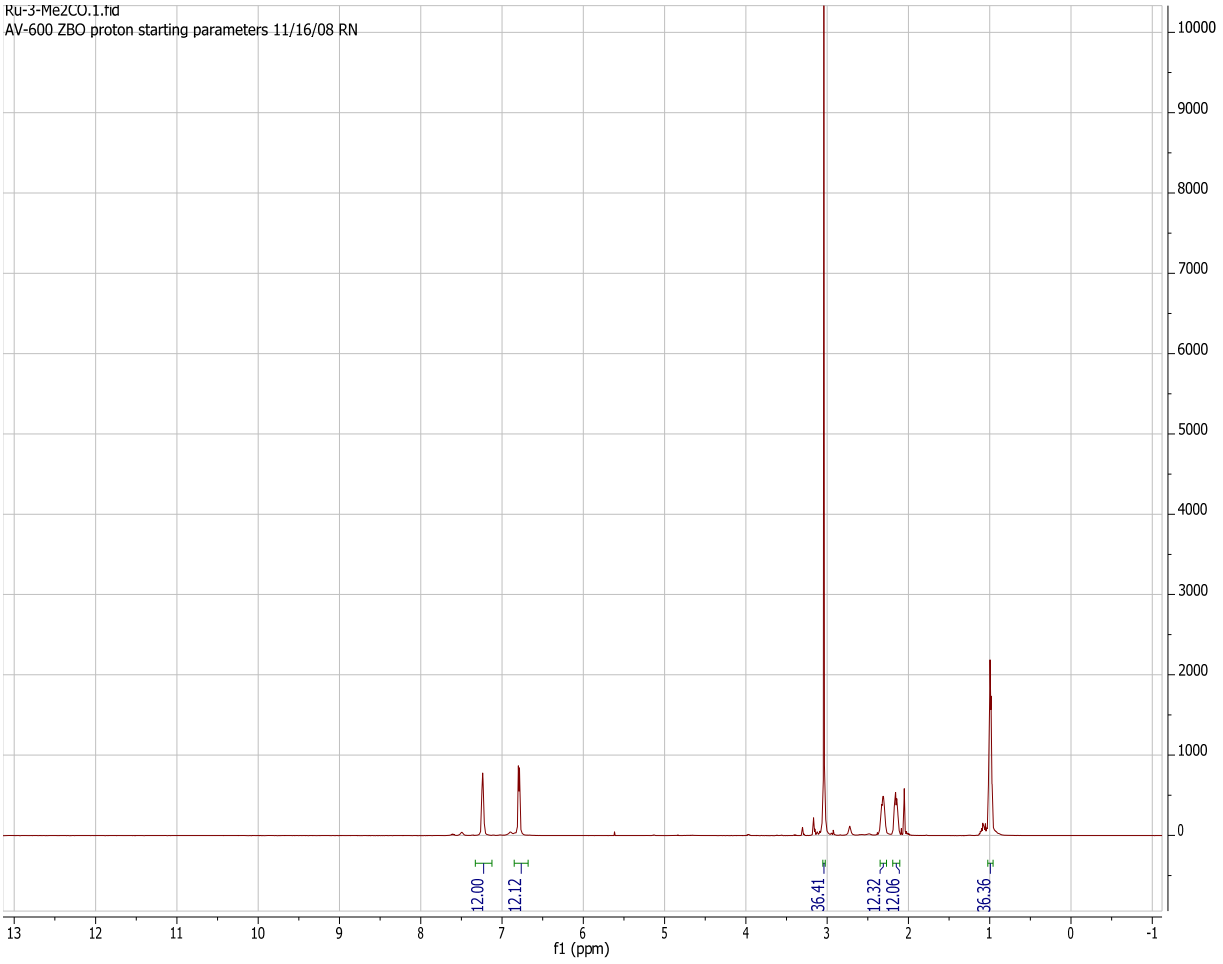
Ru-2:

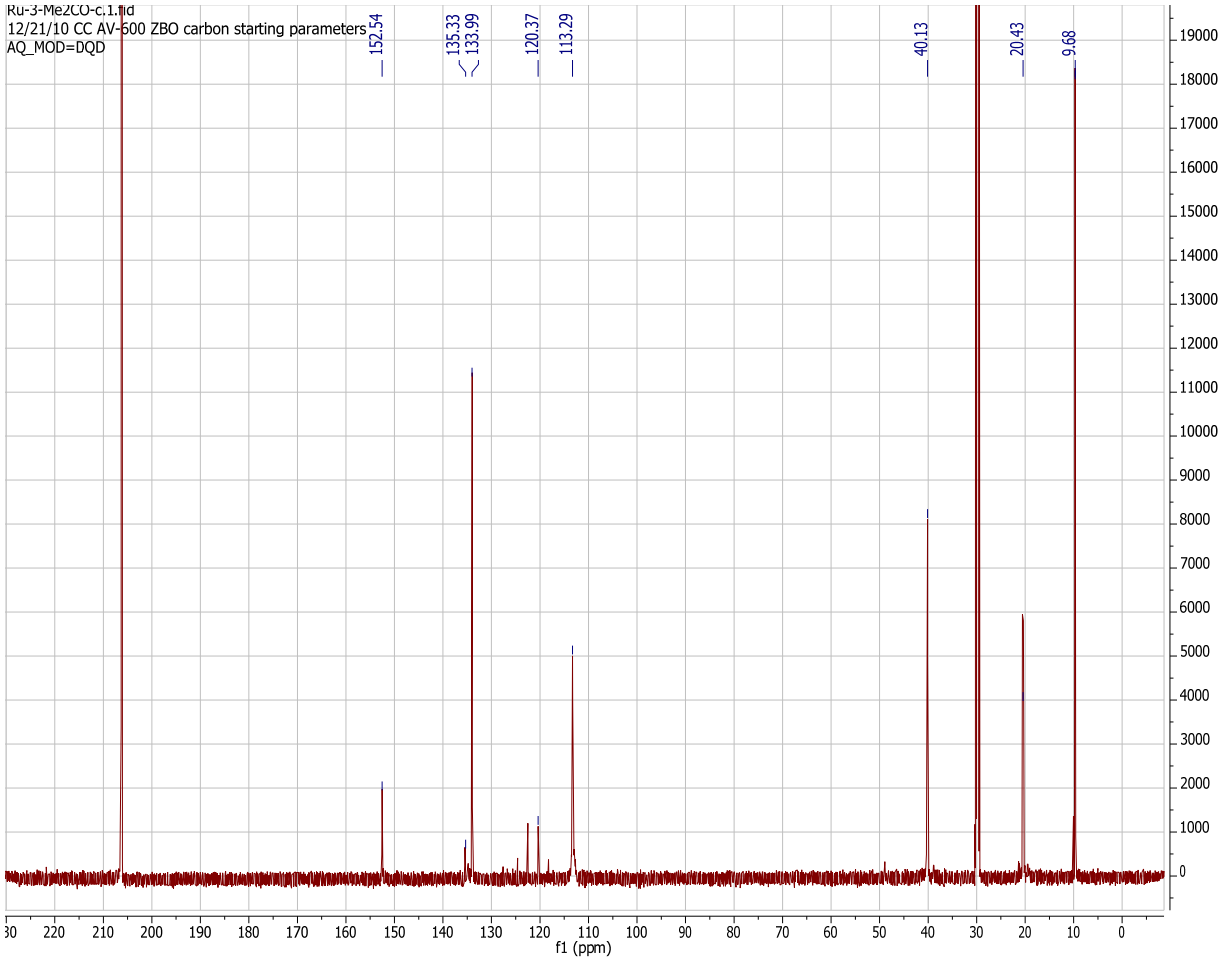


*the peak at 3.9 is trace trifluoroethanol


Ru-2-dcm-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
20.44
10.35
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

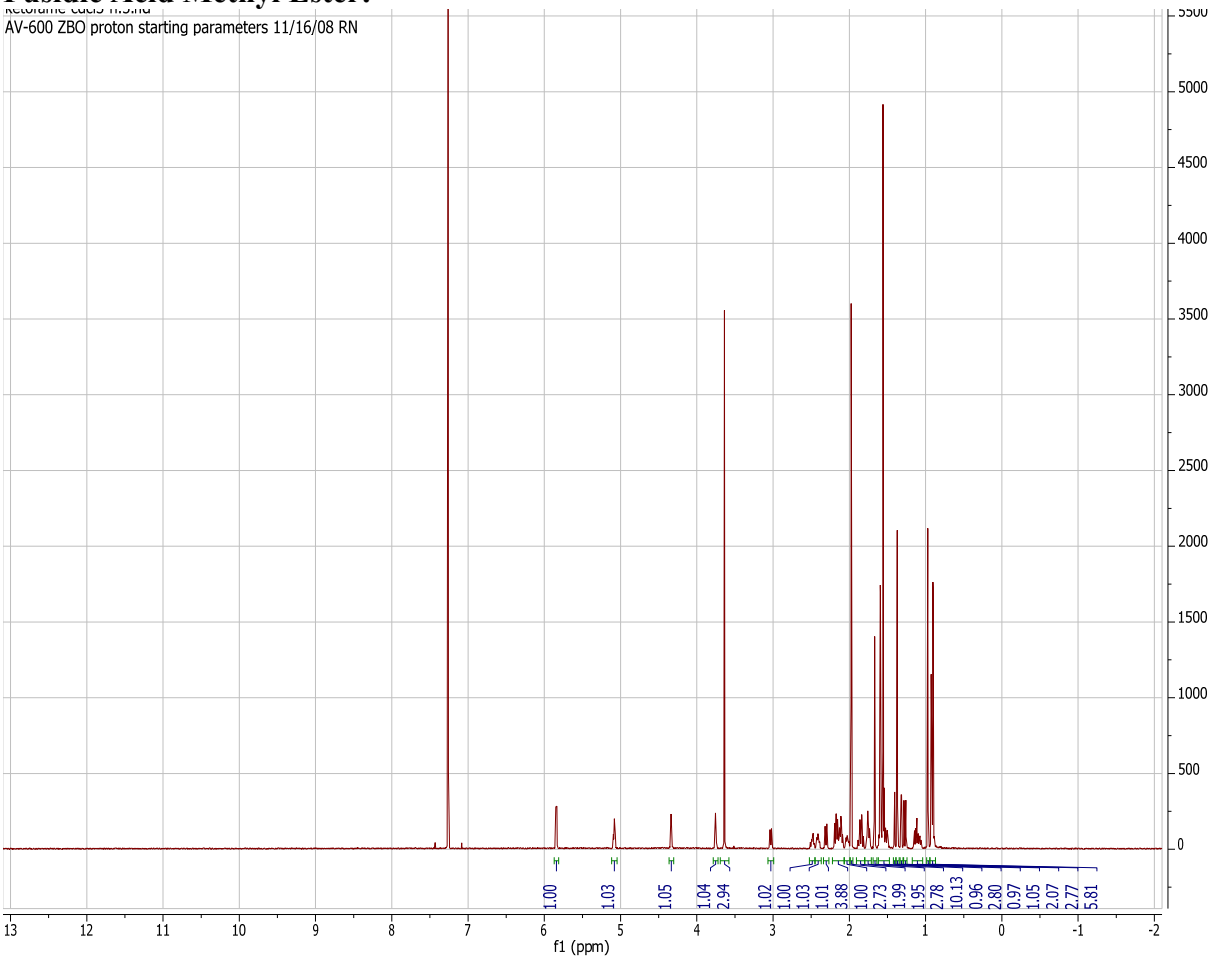
Ru-3:

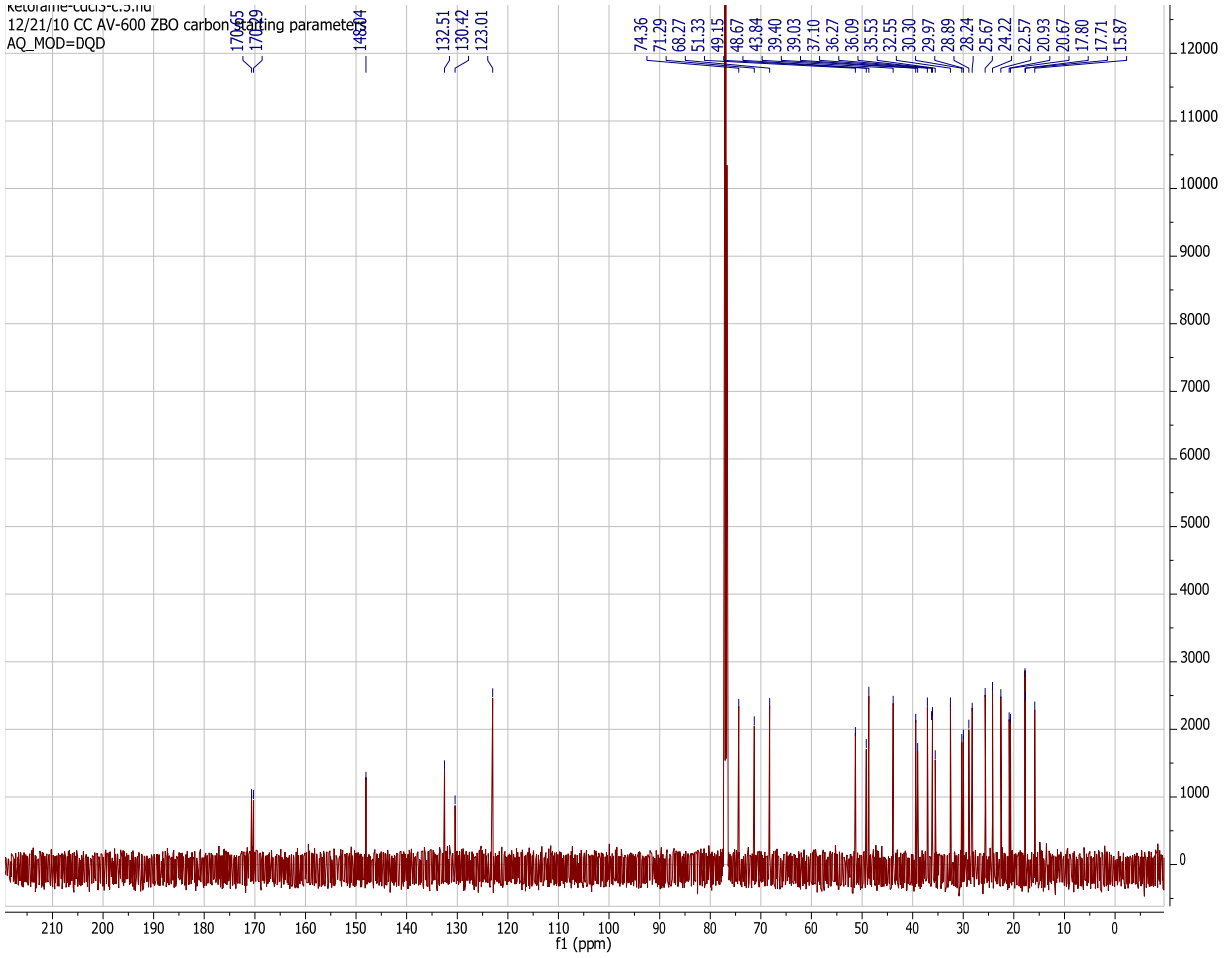

Ru-3-Me2CO.1.fid
AV-600 ZBO proton starting parameters 11/16/08 RN
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
12.00
12.12
36.41
12.32
12.06
36.36
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


Ru-3-Me2CO-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
152.54
135.33
133.99
120.37
113.29
40.13
20.43
9.68
f1 (ppm)

Substrate NMR data:

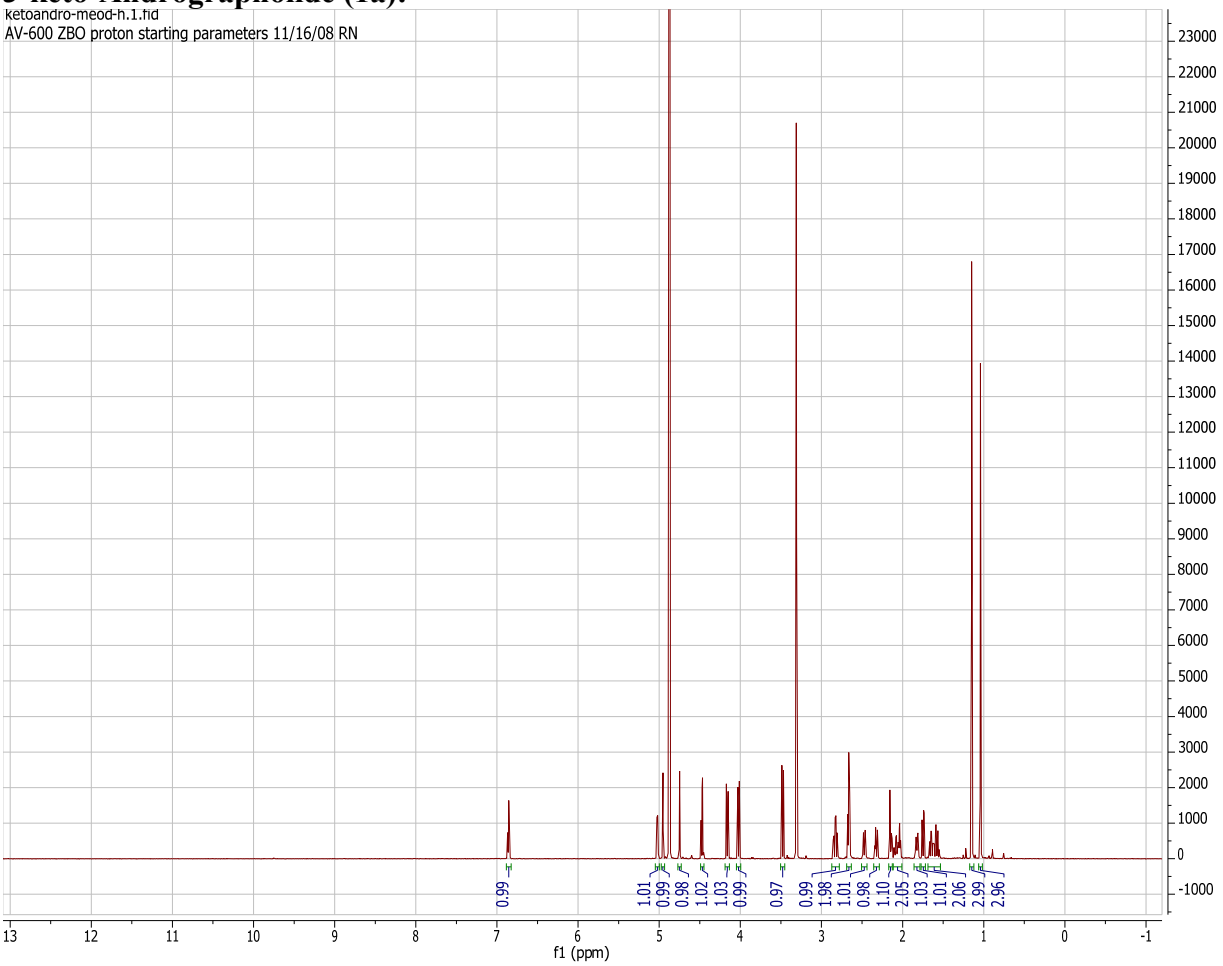
Fusidic Acid Methyl Ester:

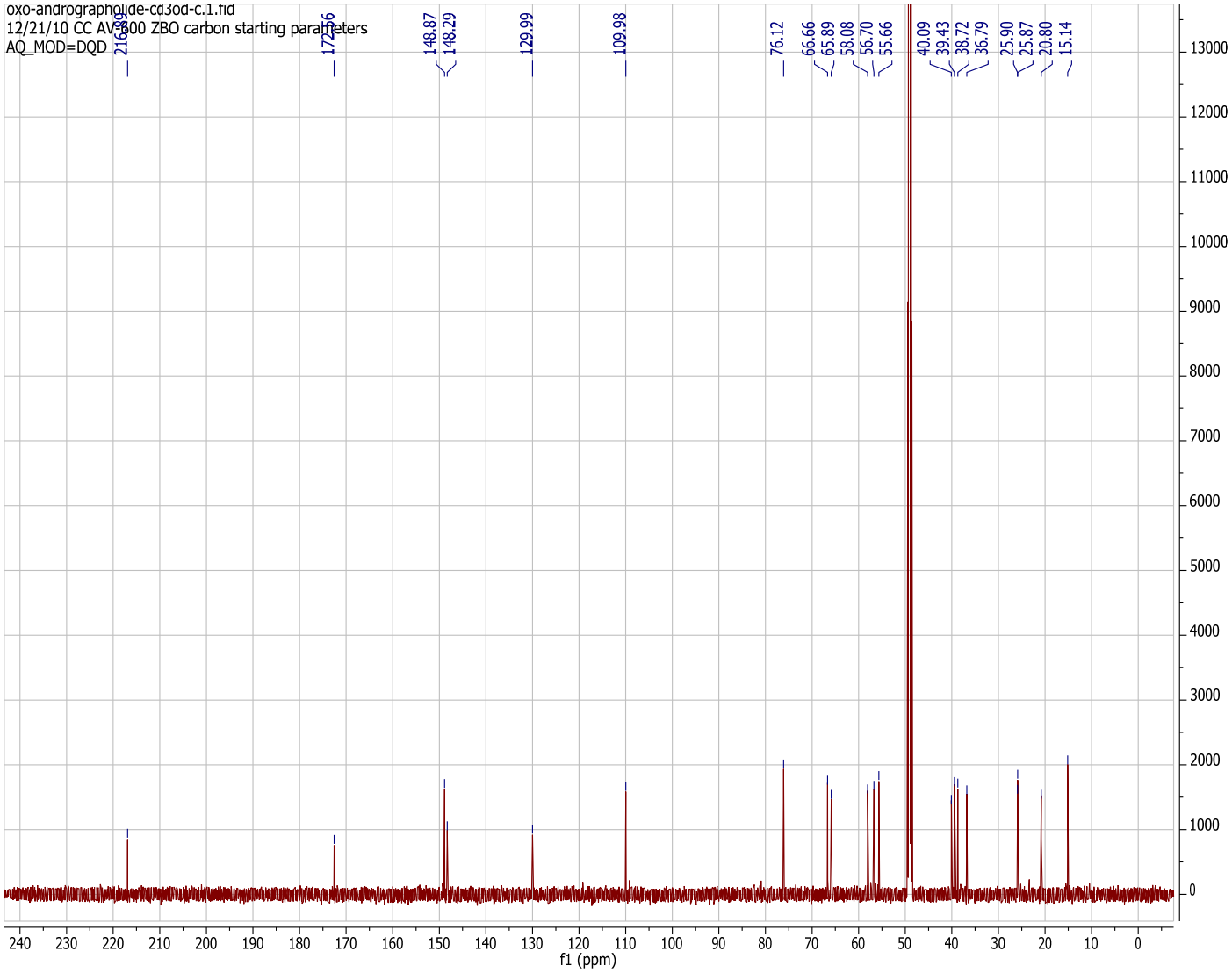



12/21/10 CC AV-600 ZBO carbon setting parameter
AQ_MOD=DQD
170.55
170.29
146.04
132.51
130.42
123.01
74.36
71.29
68.27
51.33
49.15
48.67
43.84
39.40
39.03
37.10
36.27
36.09
35.53
32.55
30.30
29.97
28.89
28.24
25.67
24.22
22.57
20.93
20.67
17.80
17.71
15.87
f1 (ppm)

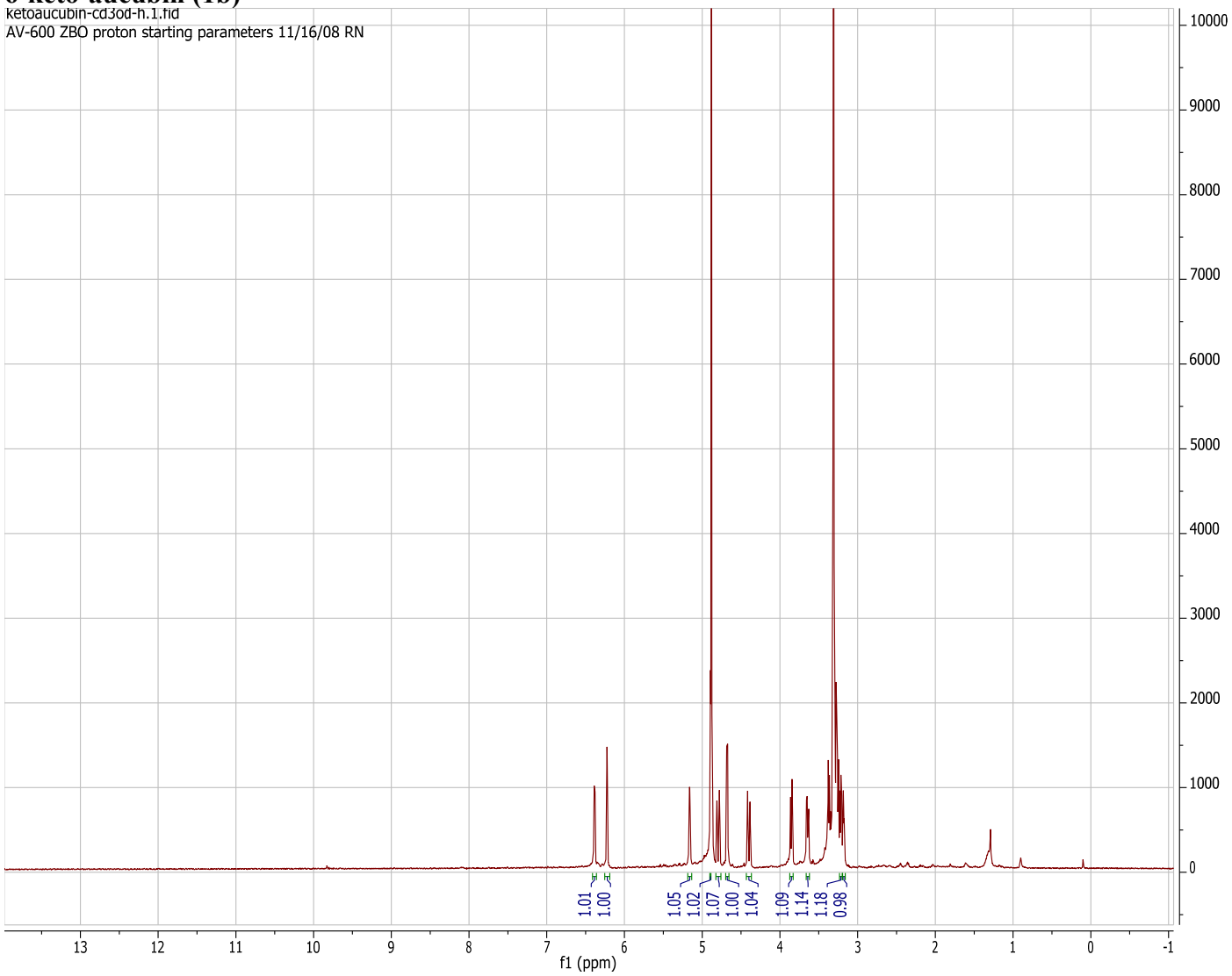
Oxidation product NMR data:

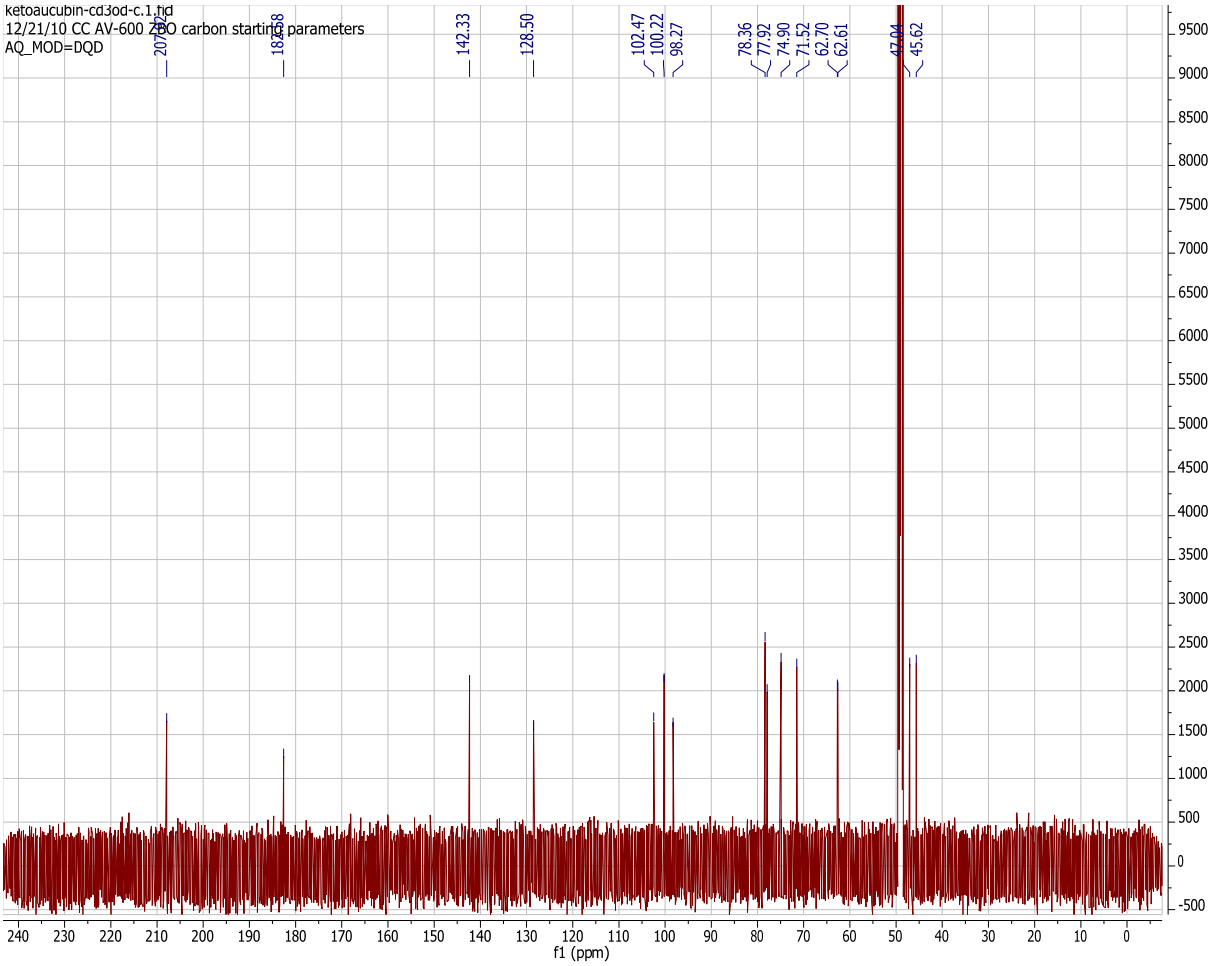
3-keto-Andrographolide (1a):



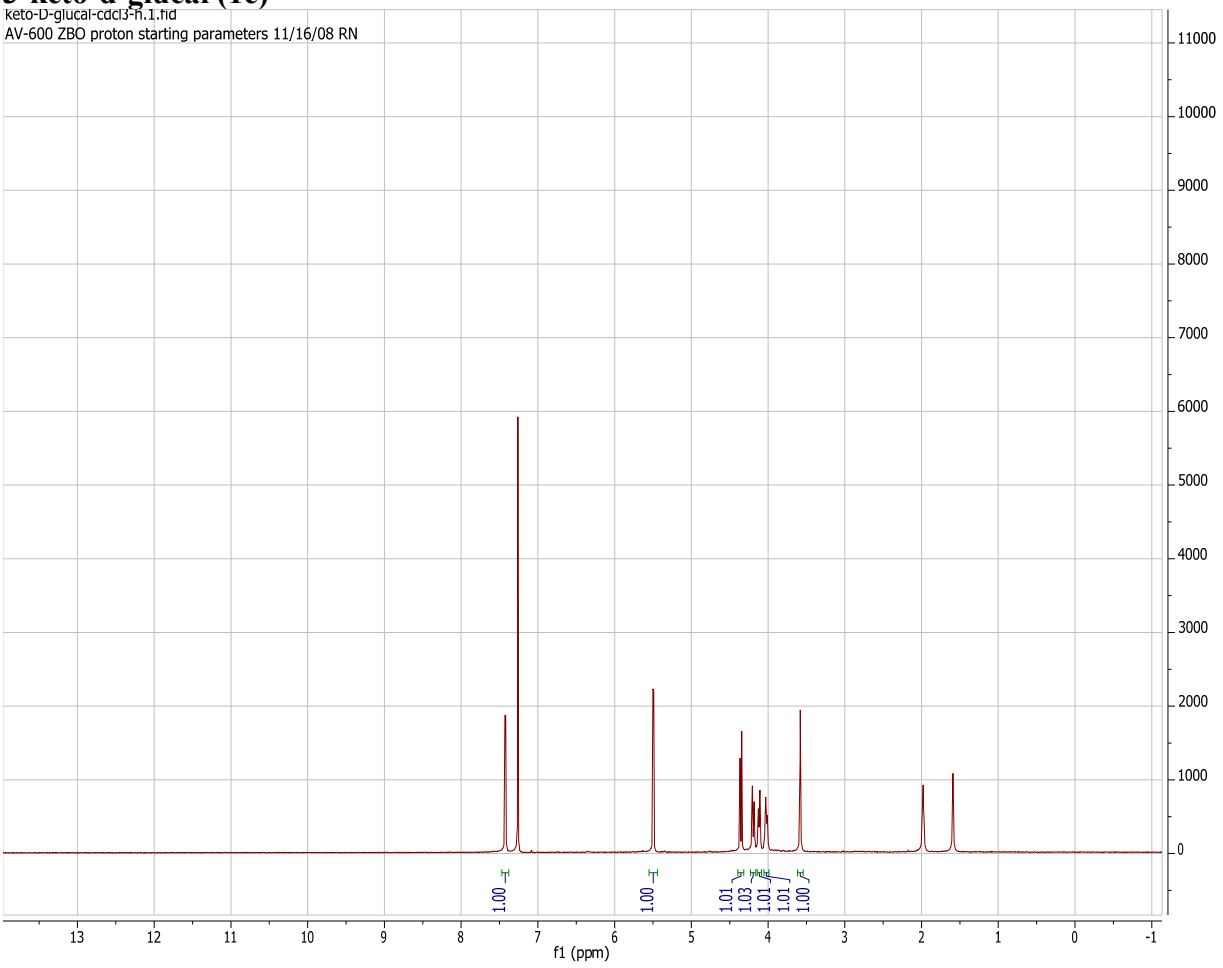

oxo-andrographolide-cd3od-c.1.fid
12/21/10 CC AV600 ZBO carbon starting parameters
AQ_MOD=DQD
216.99
172.66
148.87
148.29
129.99
109.98
76.12
66.66
65.89
58.08
56.70
55.66
40.09
39.43
38.72
36.79
25.90
25.87
20.80
15.14
f1 (ppm)

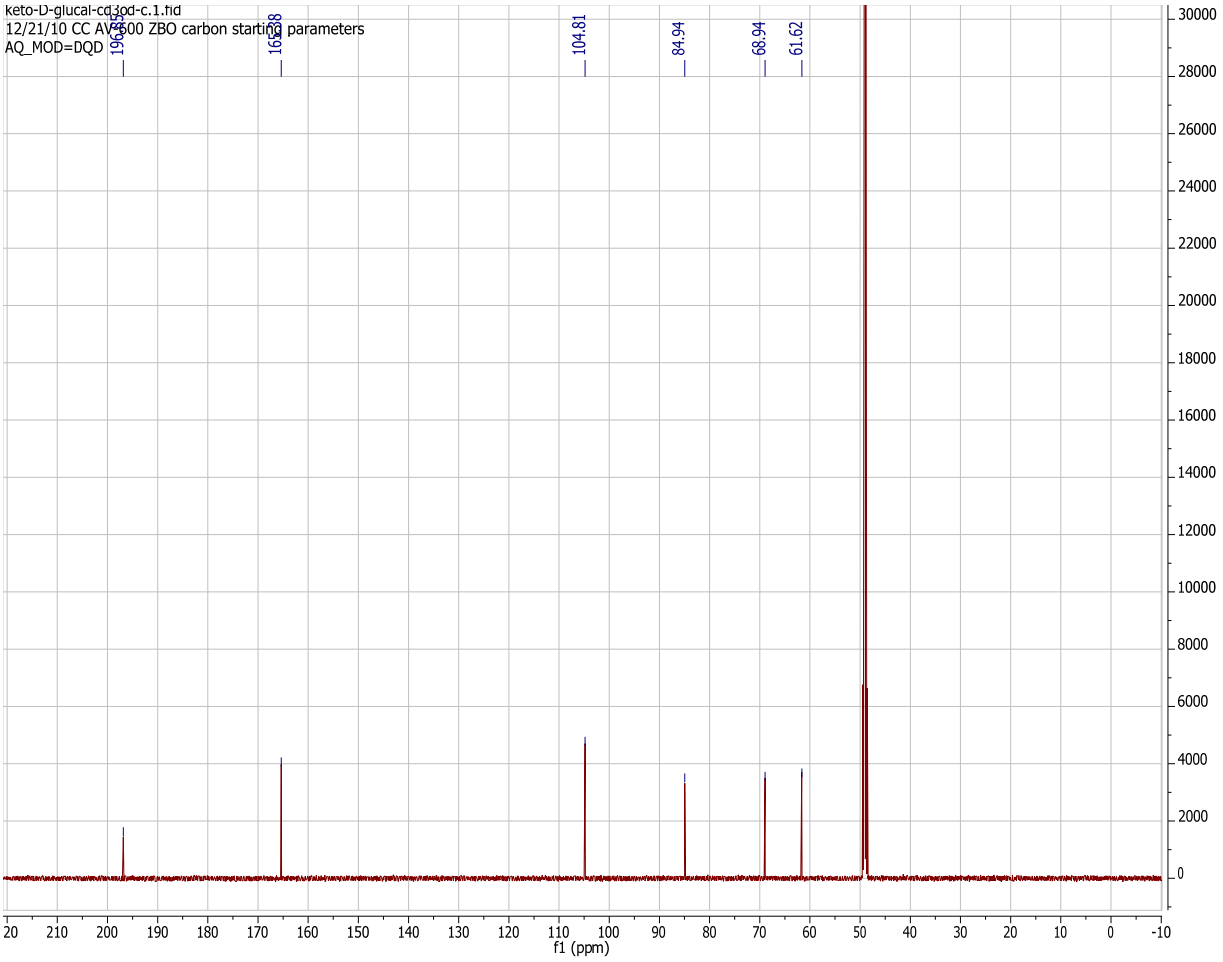
6-keto-aucubin (1b)



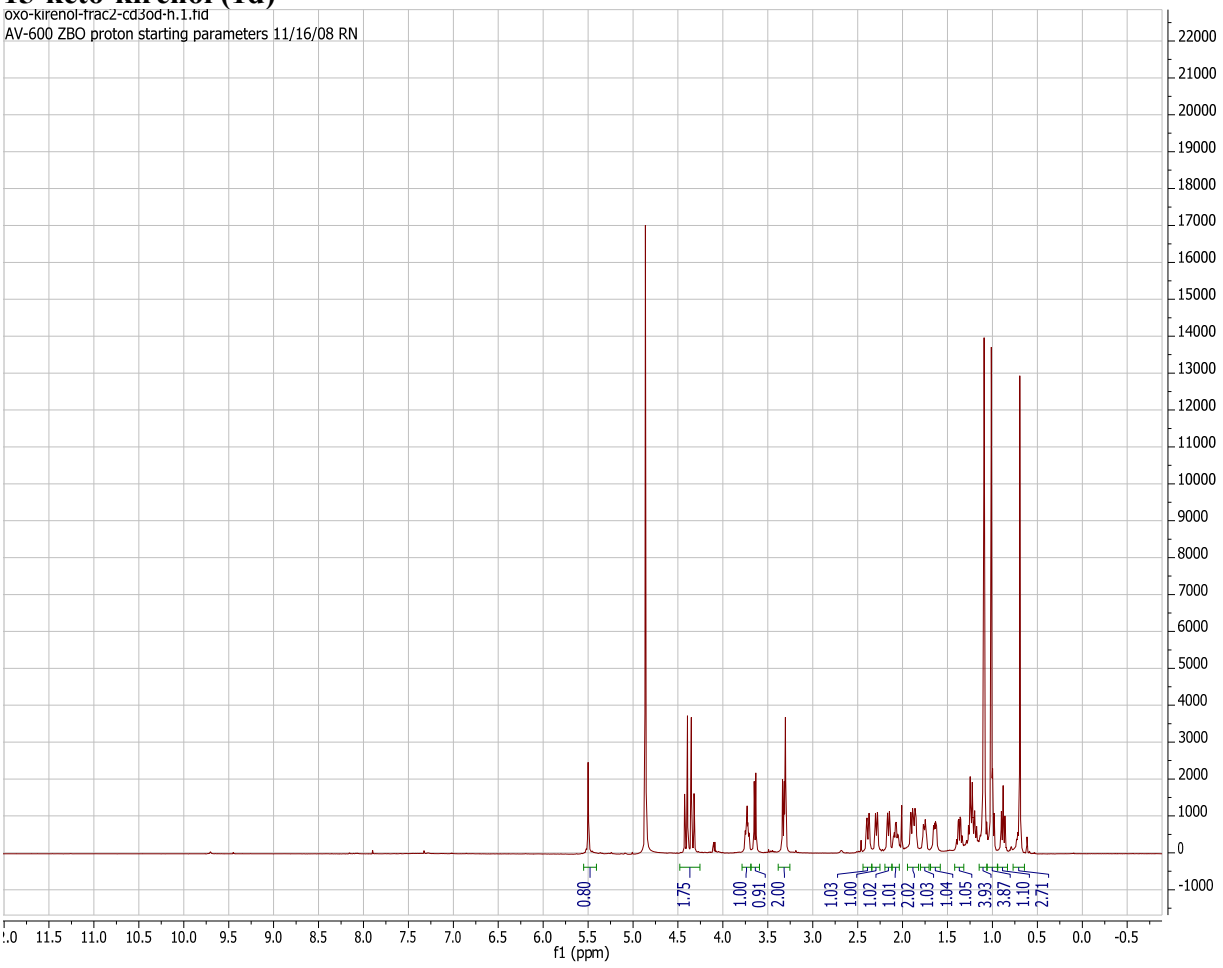

ketoaucubin-cd3od-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
207.72
184.38
142.33
128.50
102.47
100.22
98.27
78.36
77.92
74.90
71.52
62.70
62.61
47.04
45.62
f1 (ppm)

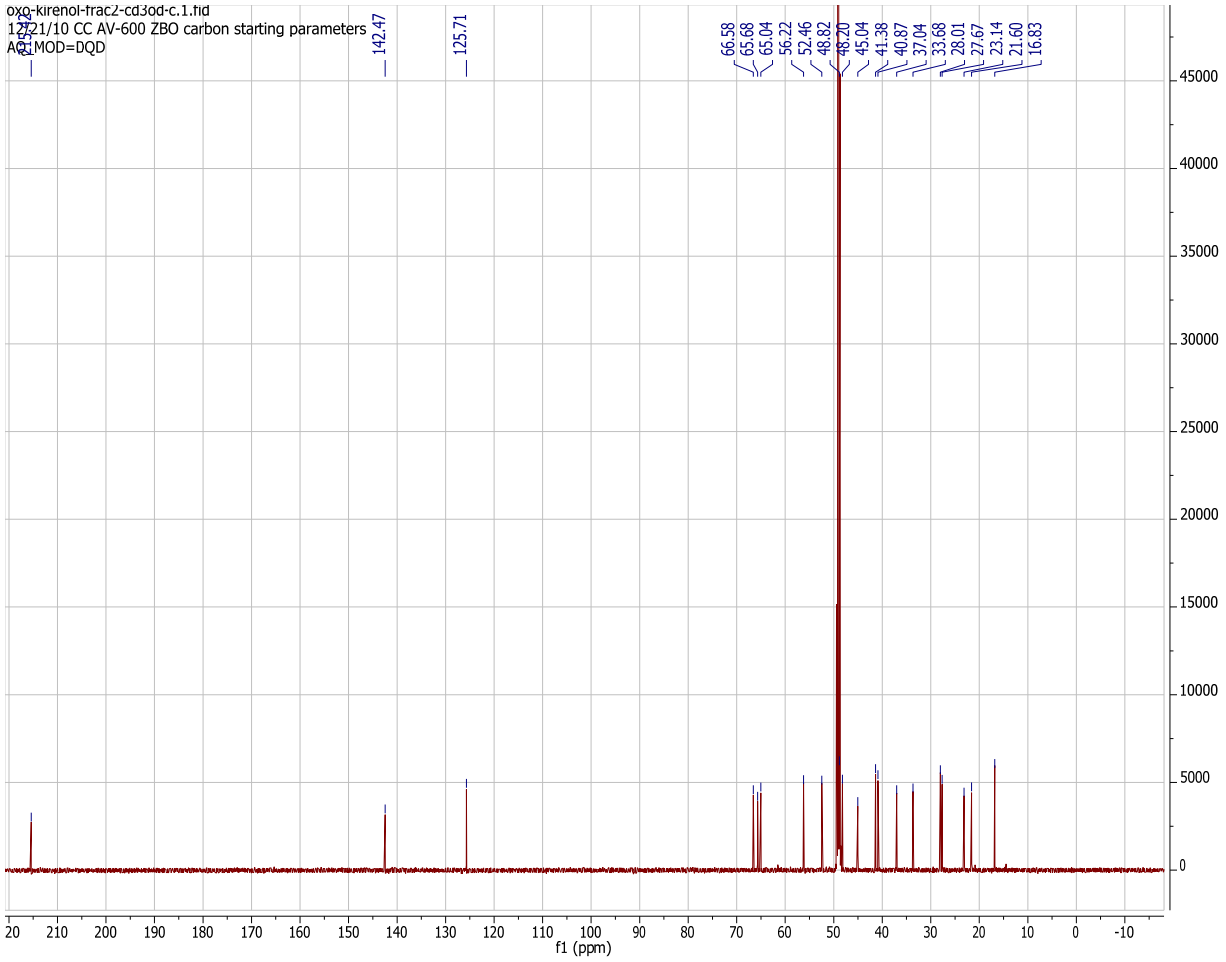
3-keto-d-glucal (1c)



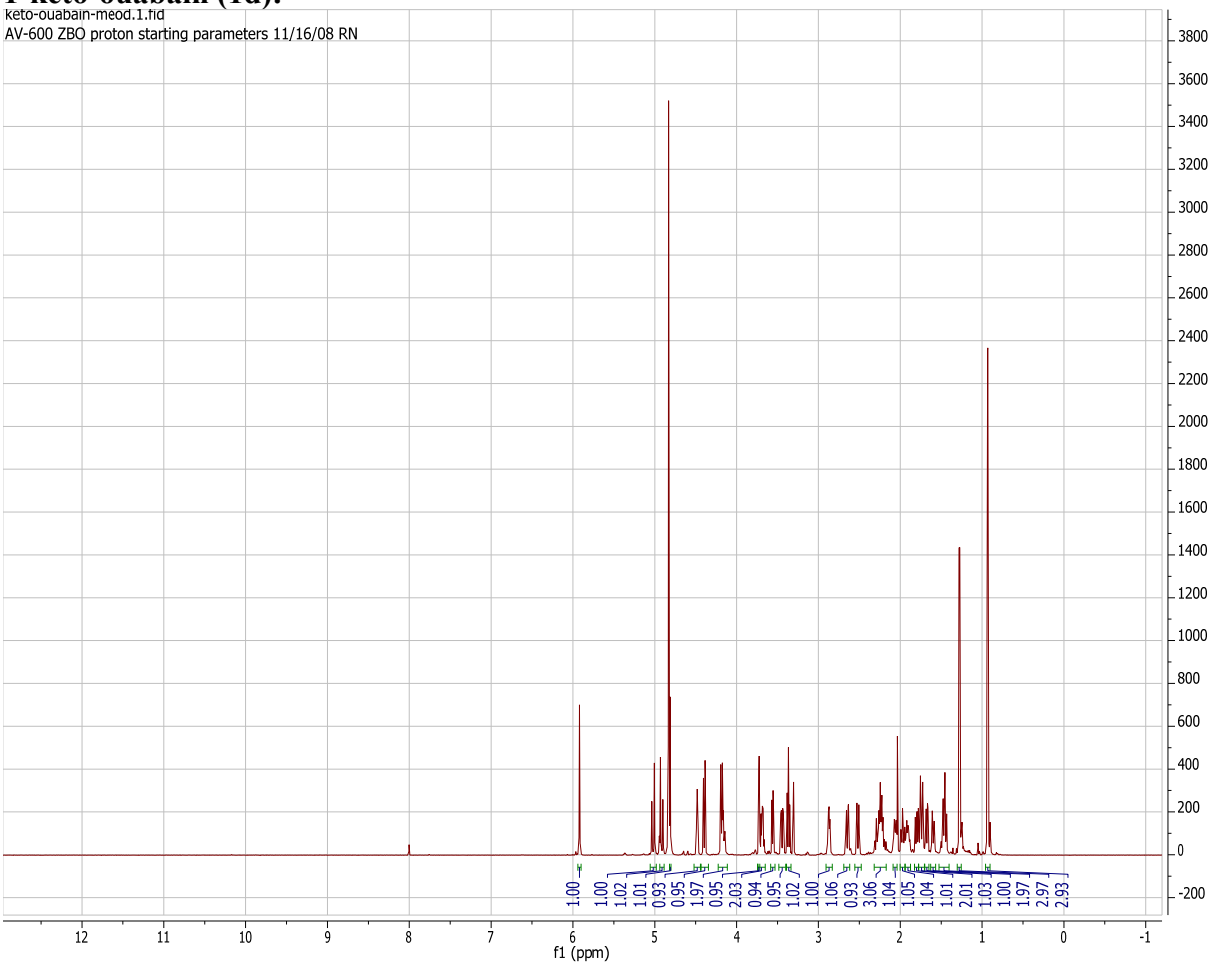

keto-D-glucal-cd3od-c.1.fid
12/21/10 CC AV600 ZBO carbon starting parameters
AQ_MOD=DQD
196.53
165.08
104.81
84.94
68.94
61.62
f1 (ppm)

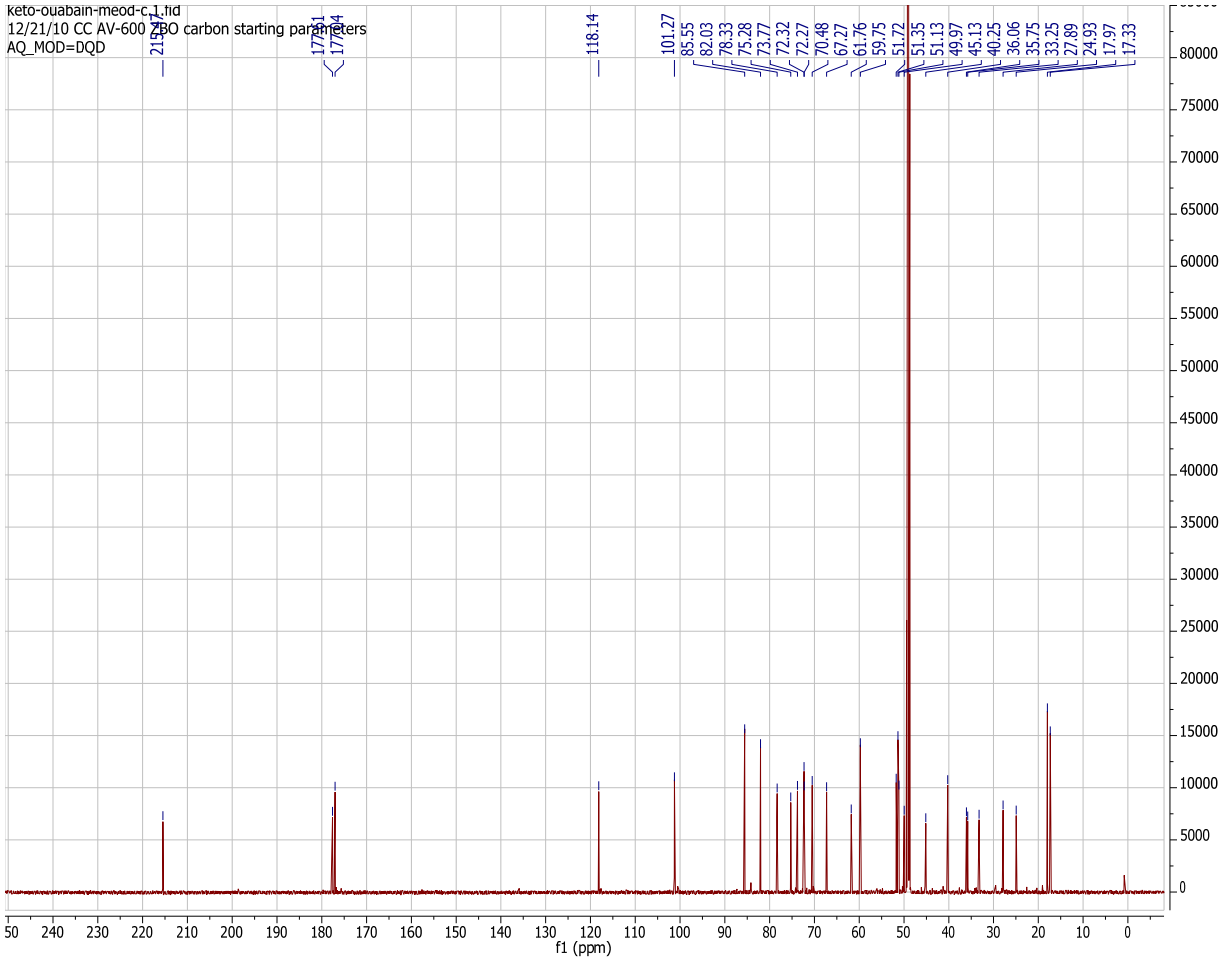
15-keto-kirenol (1d)



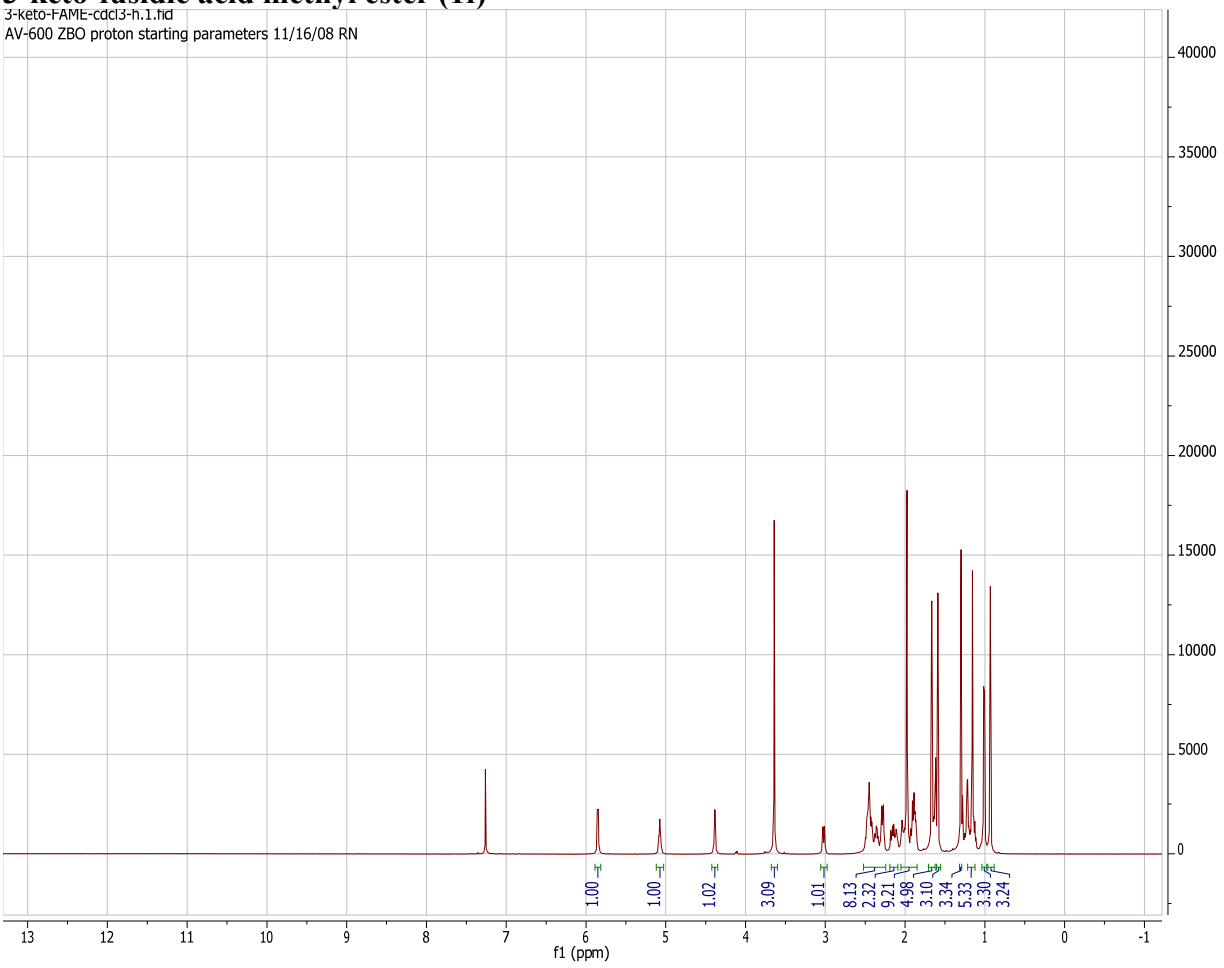

oxo-kirenol-frac2-cd3od-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
212.52
142.47
125.71
66.58
65.68
65.04
56.22
52.46
48.82
48.20
45.04
41.38
40.87
37.04
33.68
28.01
27.67
23.14
21.60
16.83
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

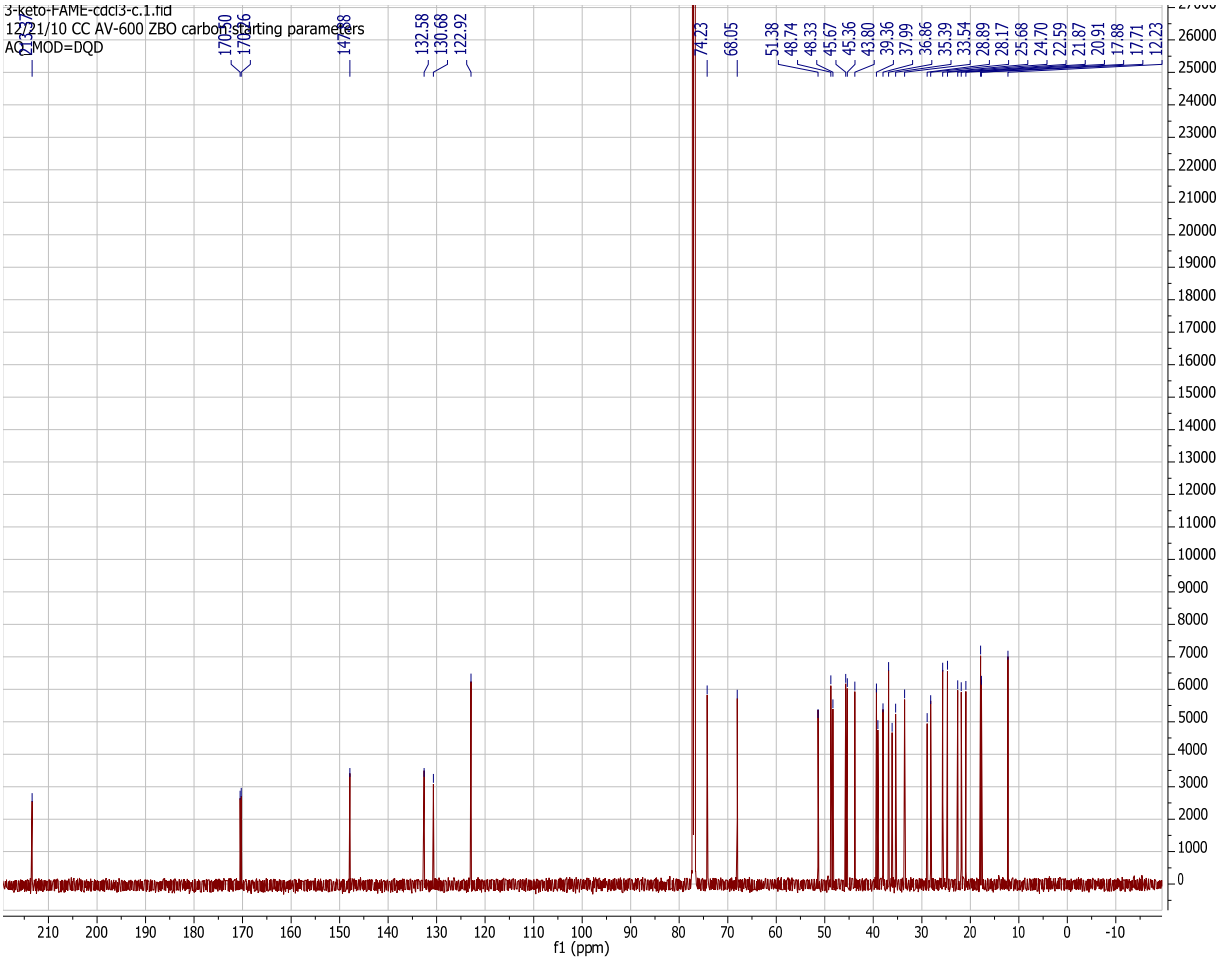
1-keto-ouabain (1d):



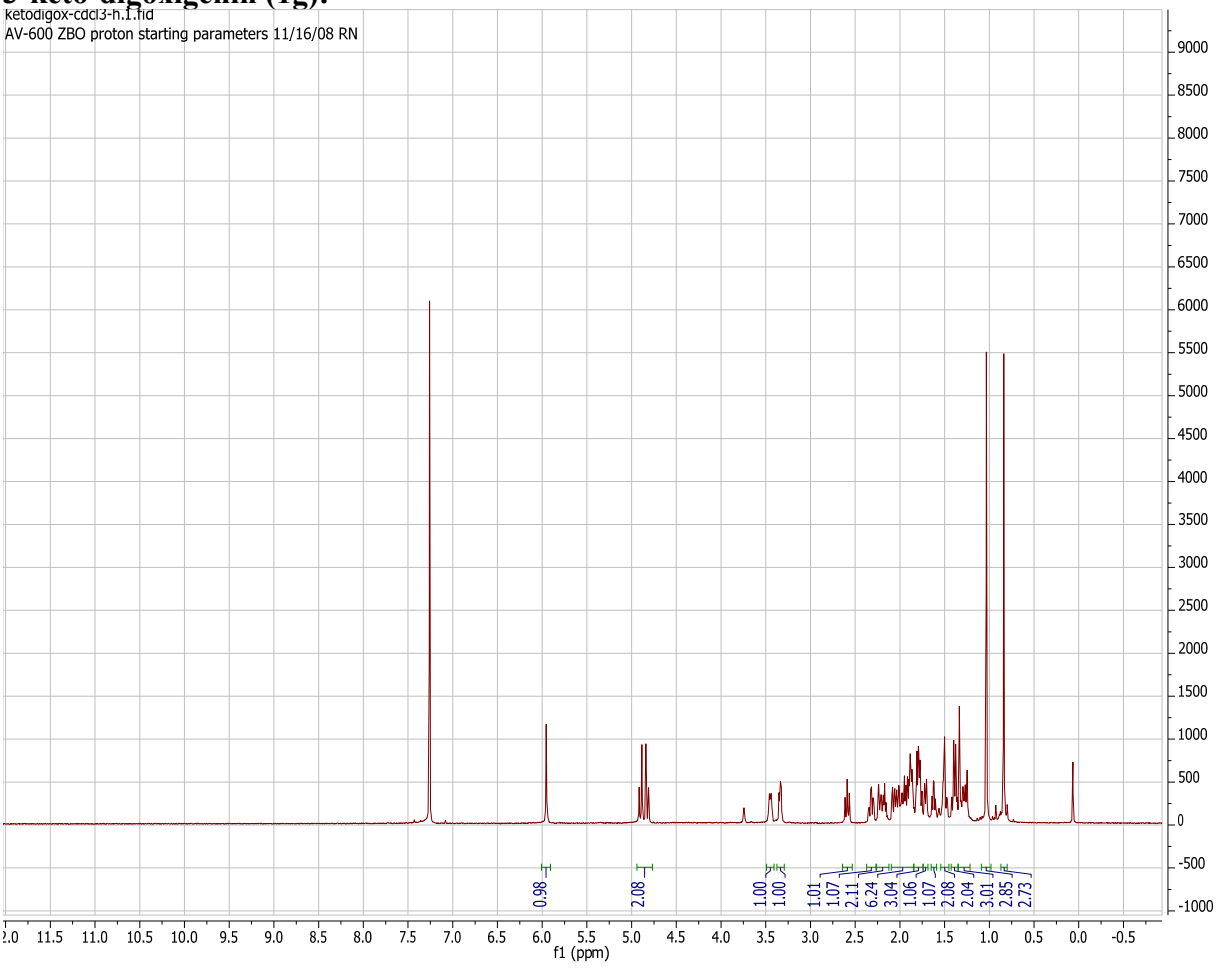

keto-ouabain-meod-c_1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
218.17
177.41
177.04
118.14
101.27
85.55
82.03
78.33
75.28
73.77
72.32
72.27
70.48
67.27
61.76
59.75
51.72
51.35
51.13
49.97
45.13
40.25
36.06
35.75
33.25
27.89
24.93
17.97
17.33
f1 (ppm)

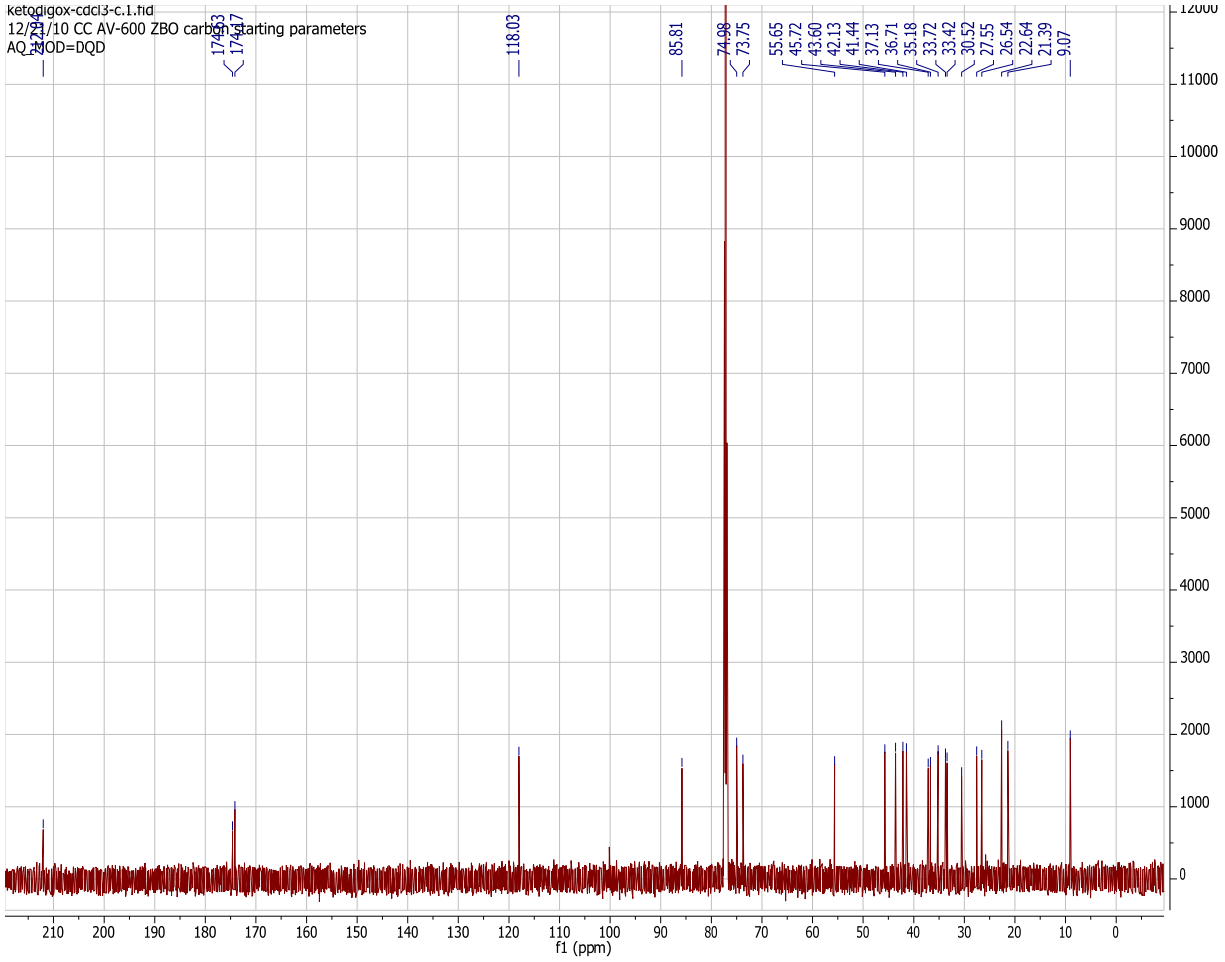
3-keto-fusidic acid methyl ester (1f)



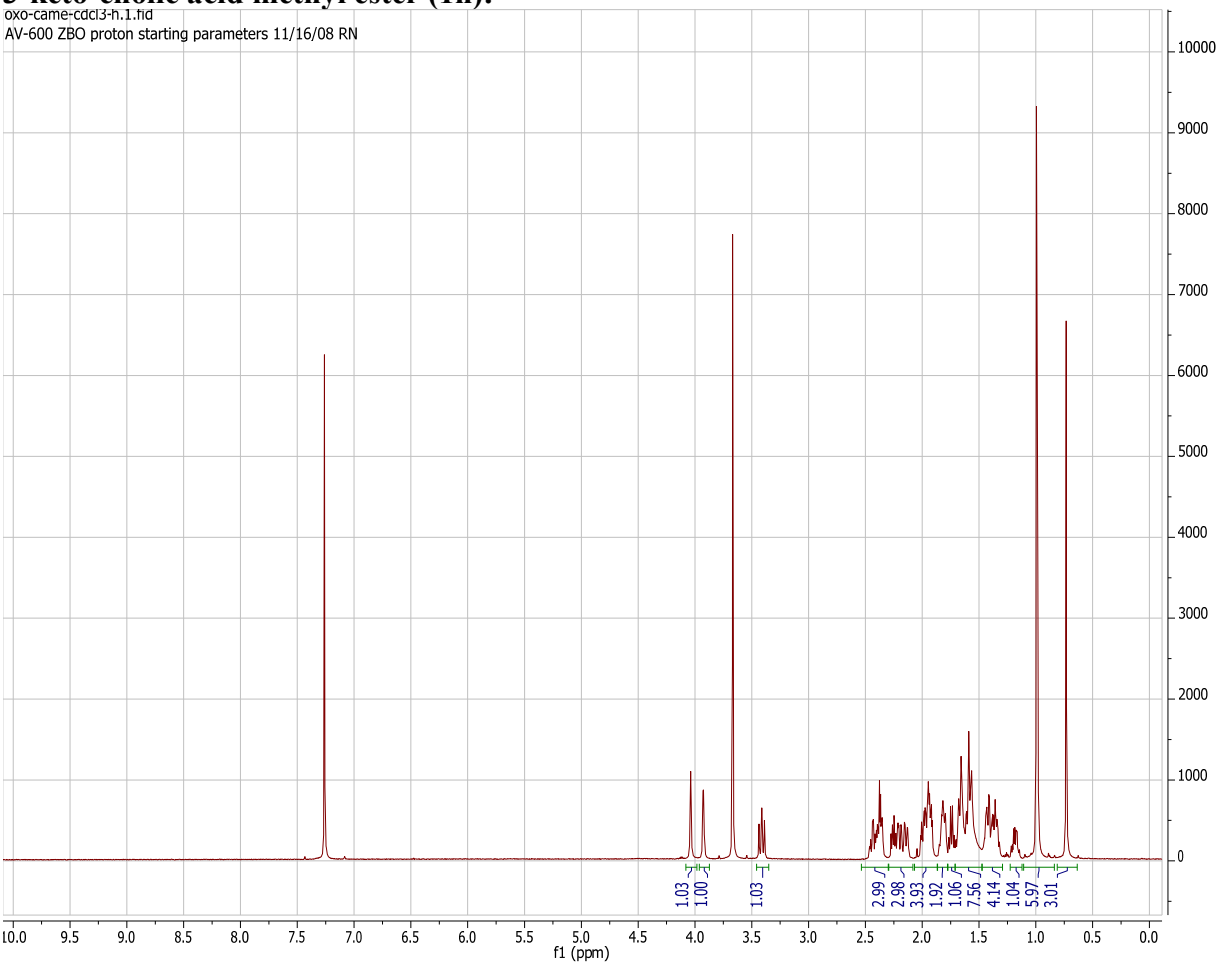

3-keto-FAME-cdcl3-c.1.fid
12721/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
14.23
170.10
170.36
147.88
132.58
130.68
122.92
74.23
68.05
51.38
48.74
48.33
45.67
45.36
43.80
39.36
37.99
36.86
35.39
33.54
28.89
28.17
25.68
24.70
22.59
21.87
20.91
17.88
17.71
12.23
f1 (ppm)

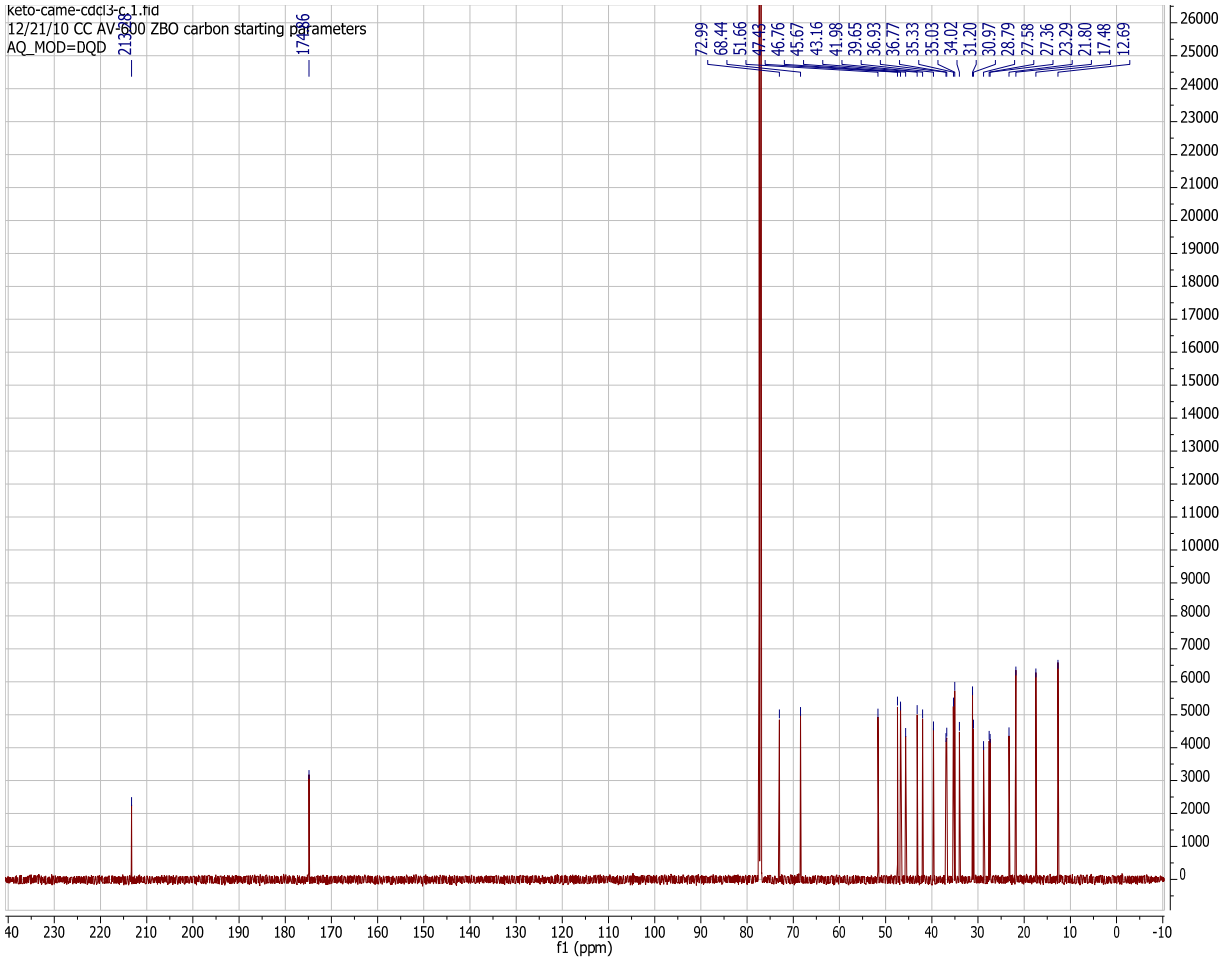
3-keto-digoxigenin (1g):



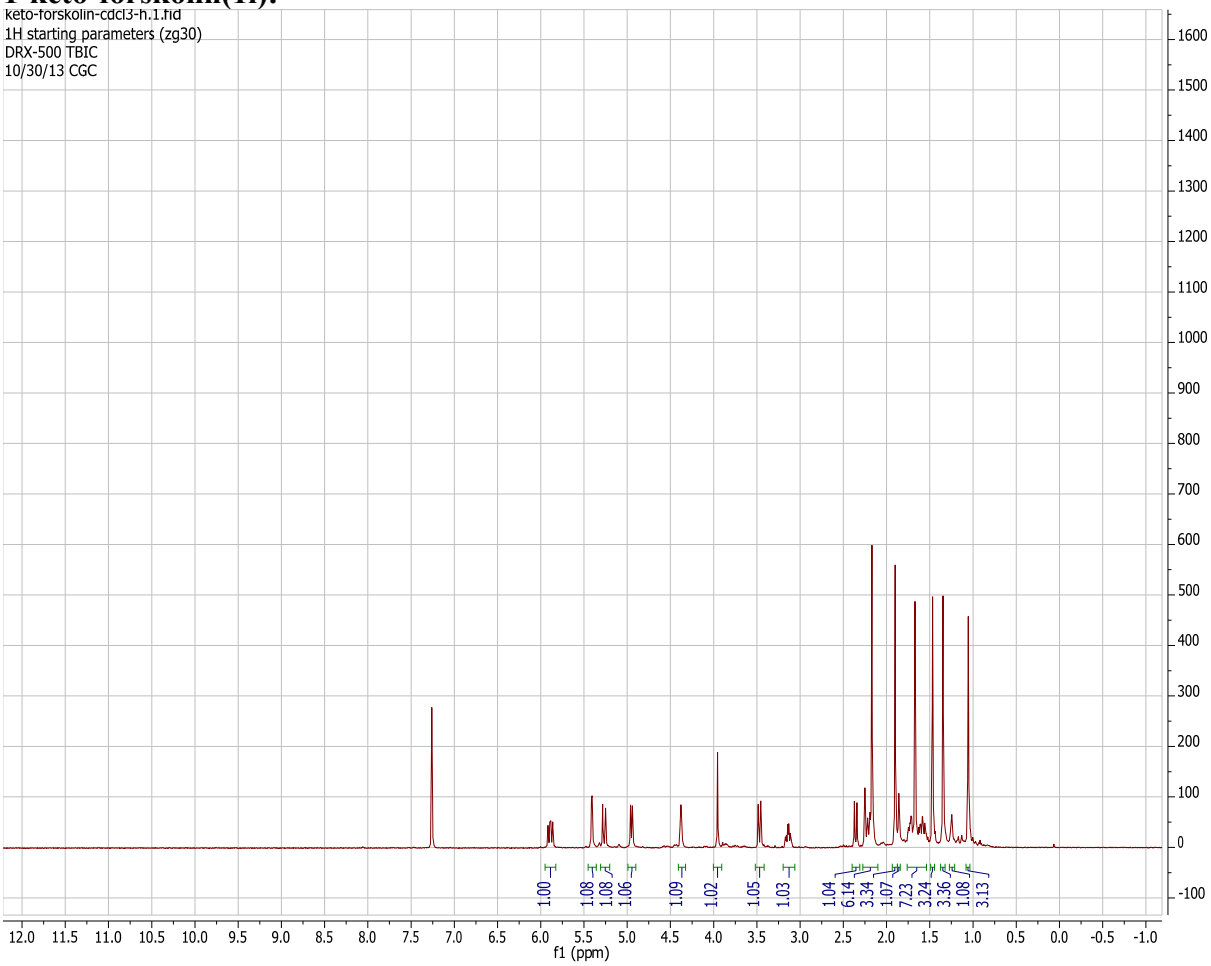

ketodigox-cdcl3-c.1.fid
12/23/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
208.94
174.33
174.17
118.03
85.81
74.98
73.75
55.65
45.72
43.60
42.13
41.44
37.13
36.71
35.18
33.72
33.42
30.52
27.55
26.54
22.64
21.39
9.07
f1 (ppm)

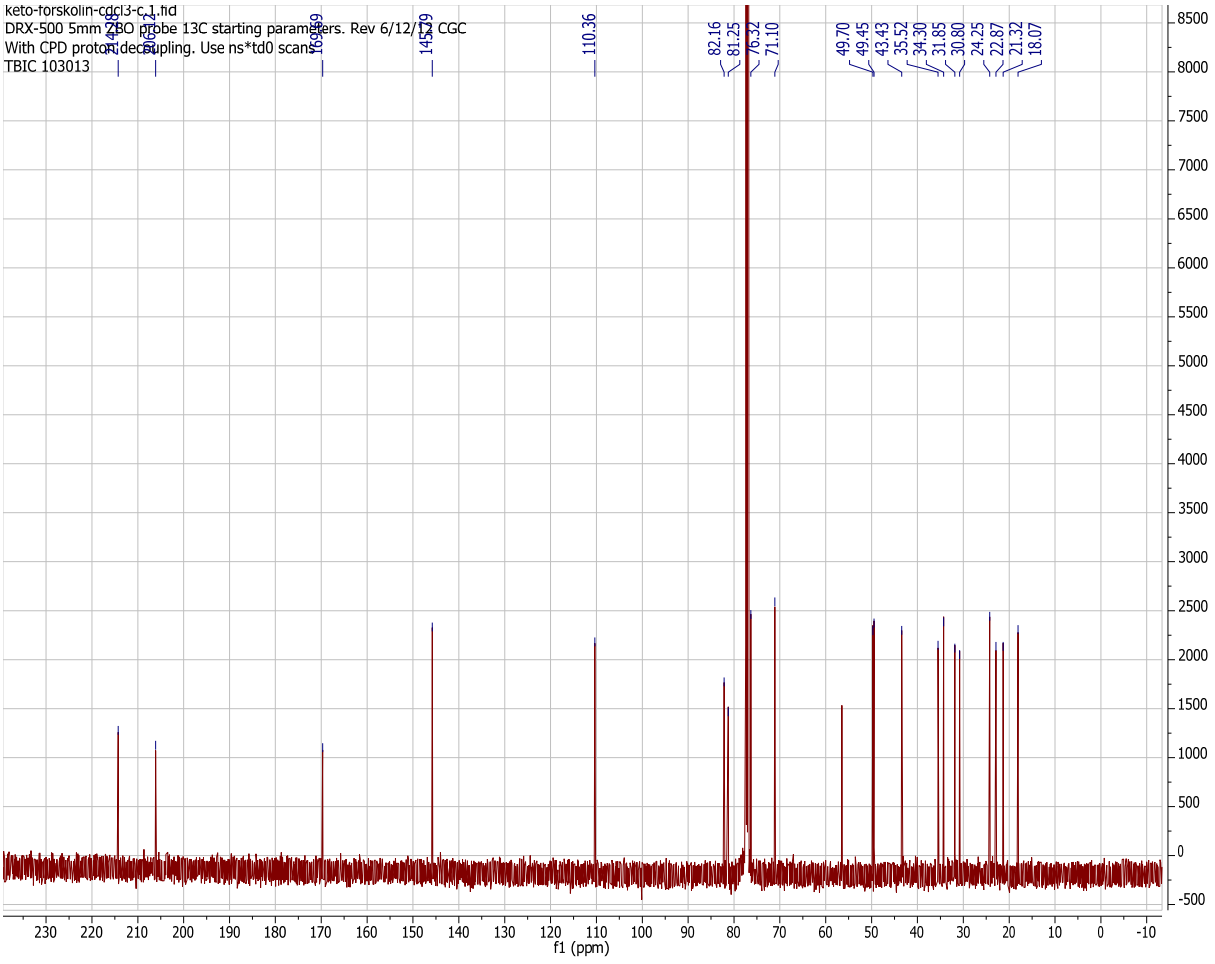
3-keto-cholic acid methyl ester (1h):



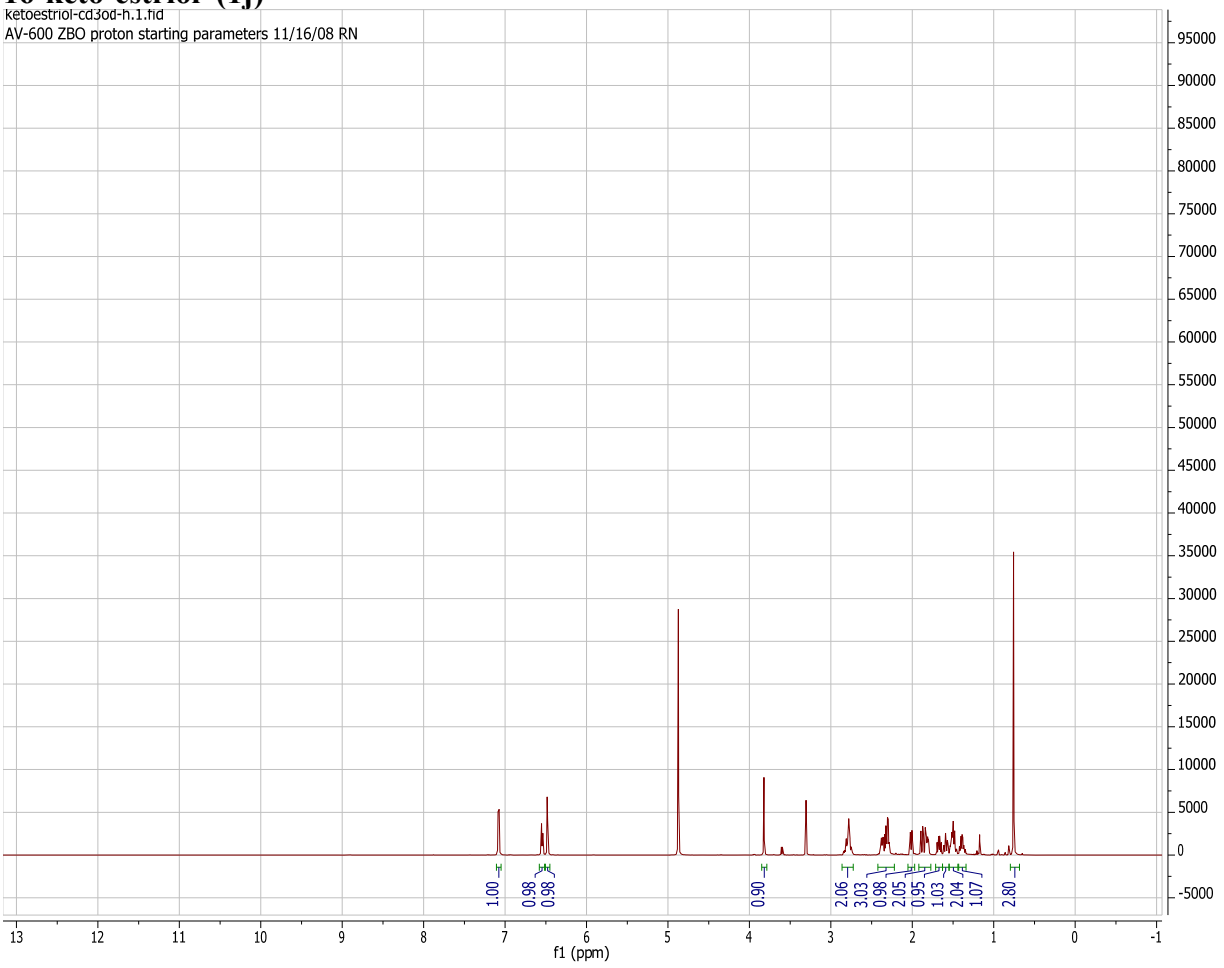

keto-came-cdcl3-c_1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
213.88
174.96
72.99
68.44
51.66
47.43
46.76
45.67
43.16
41.98
39.65
36.93
36.77
35.33
35.03
34.02
31.20
30.97
28.79
27.58
27.36
23.29
21.80
17.48
12.69
f1 (ppm)

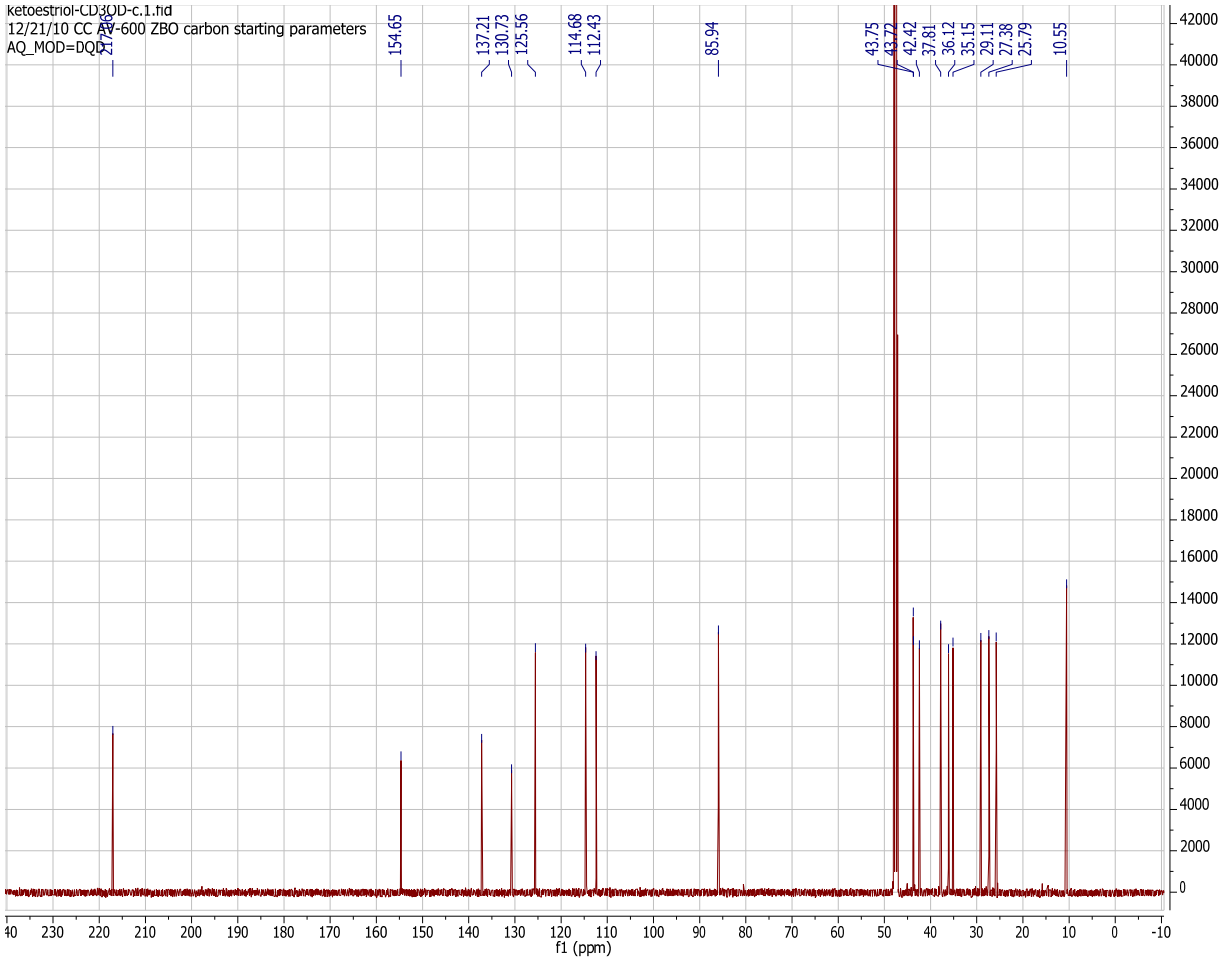
1-keto-forskolin(1i):



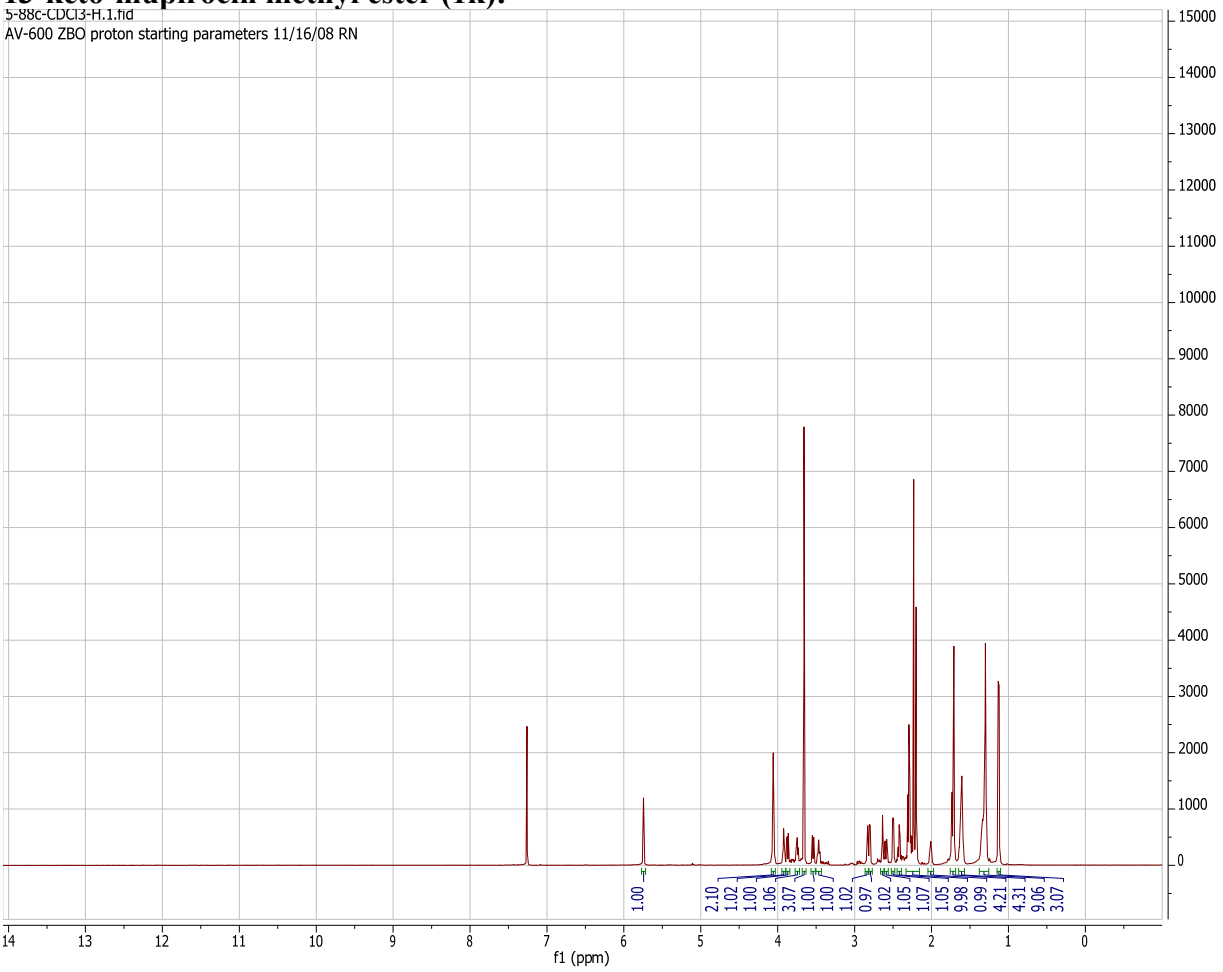

keto-forskolin-cdcl3-c_1.fid
DRX-500 5mm ZBO probe 13C starting parameters. Rev 6/12/12 CGC
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
208.99
204.22
169.99
145.29
110.36
82.16
81.25
76.32
71.10
49.70
49.45
43.43
35.52
34.30
31.85
30.80
24.25
22.87
21.32
18.07
f1 (ppm)

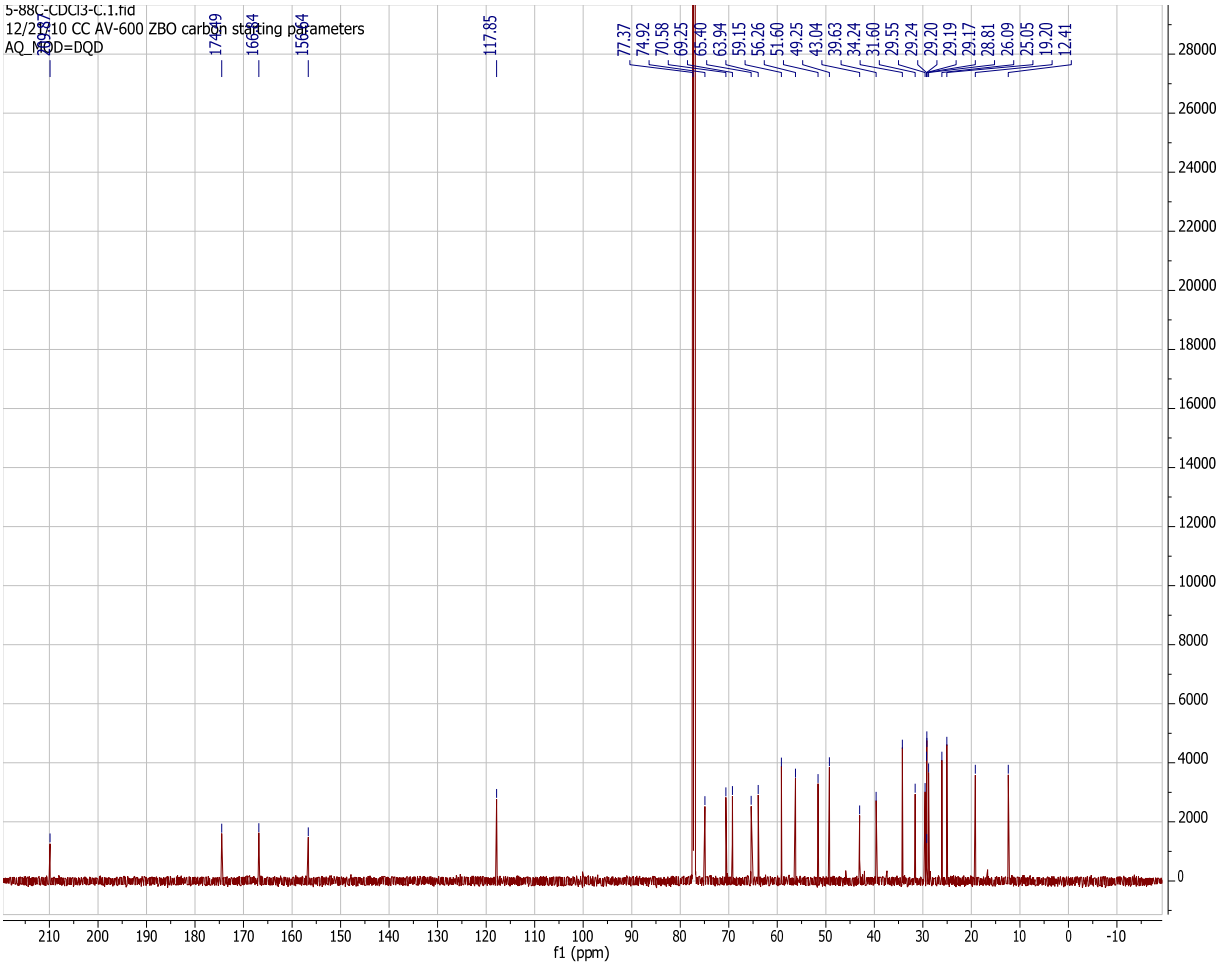
16-keto-estriol (1j)



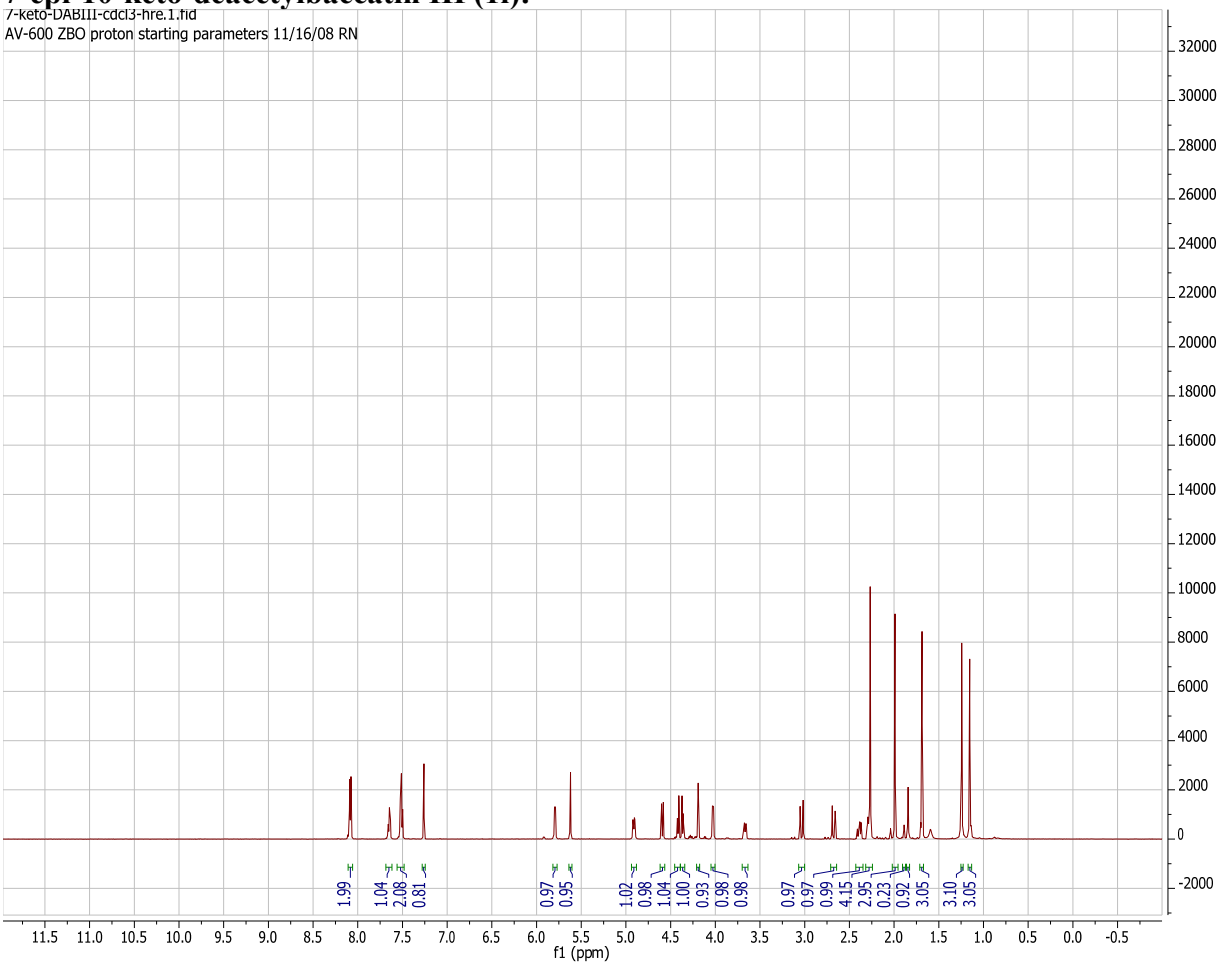

ketoestriol-CD3OD-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
217.96
154.65
137.21
130.73
125.56
114.68
112.43
85.94
43.75
43.72
42.42
37.81
36.12
35.15
29.11
27.38
25.79
10.55
f1 (ppm)

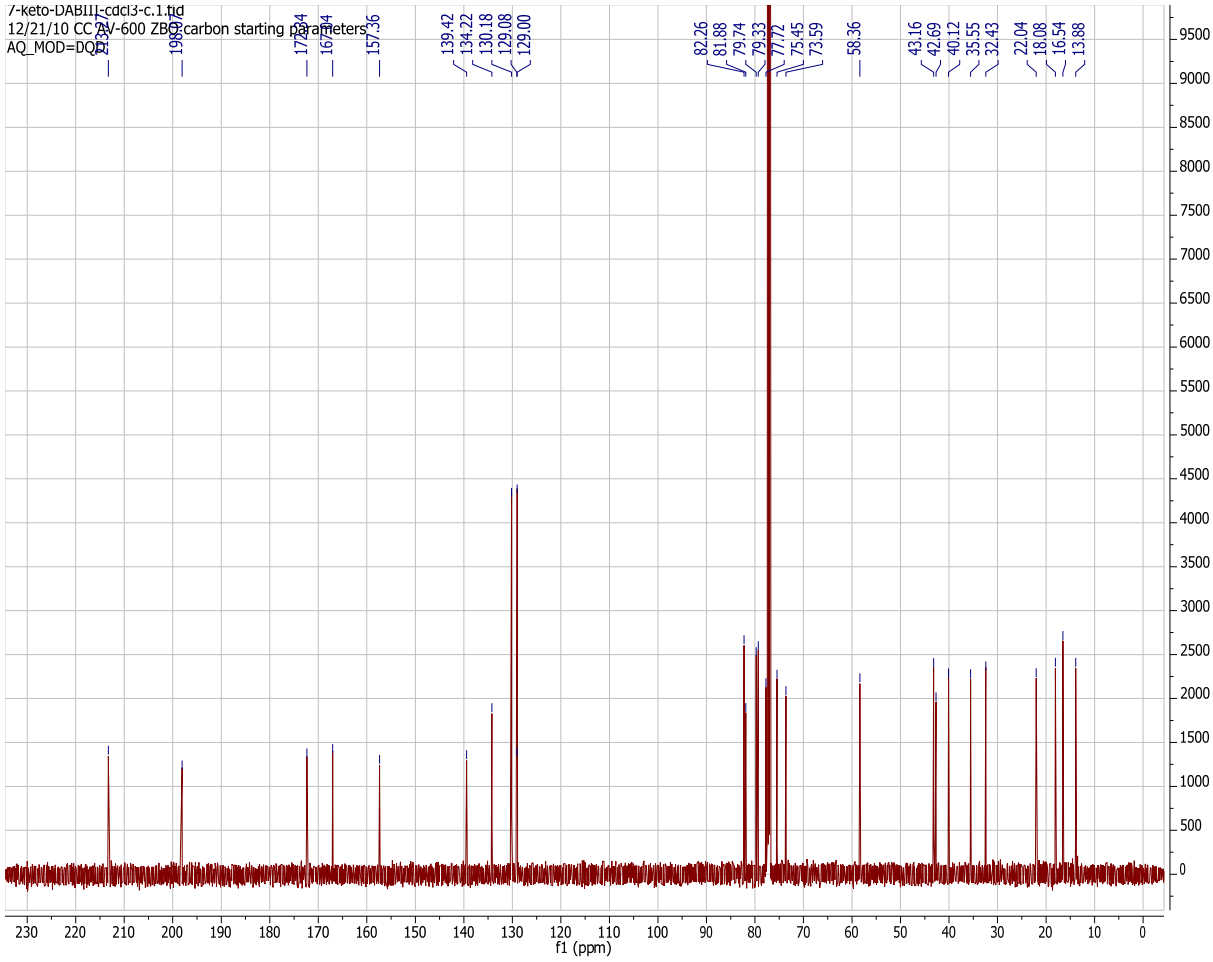
13-keto-mupirocin methyl ester (1k):



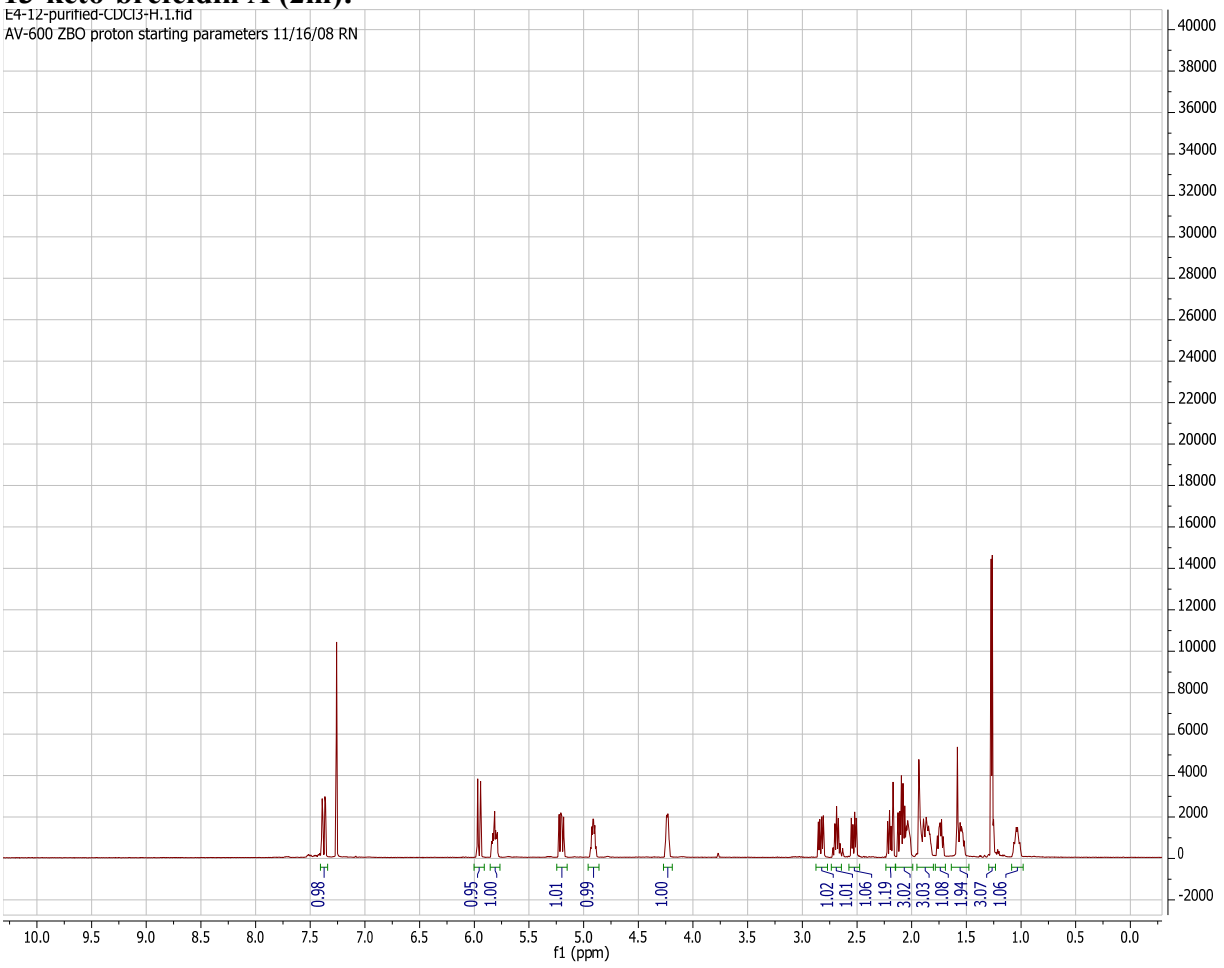

5-88C-CDCl3-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
174.99
166.24
156.64
117.85
77.37
74.92
70.58
69.25
65.40
63.94
59.15
56.26
51.60
49.25
43.04
39.63
34.24
31.60
29.55
29.24
29.20
29.19
29.17
28.81
26.09
25.05
19.20
12.41
f1 (ppm)

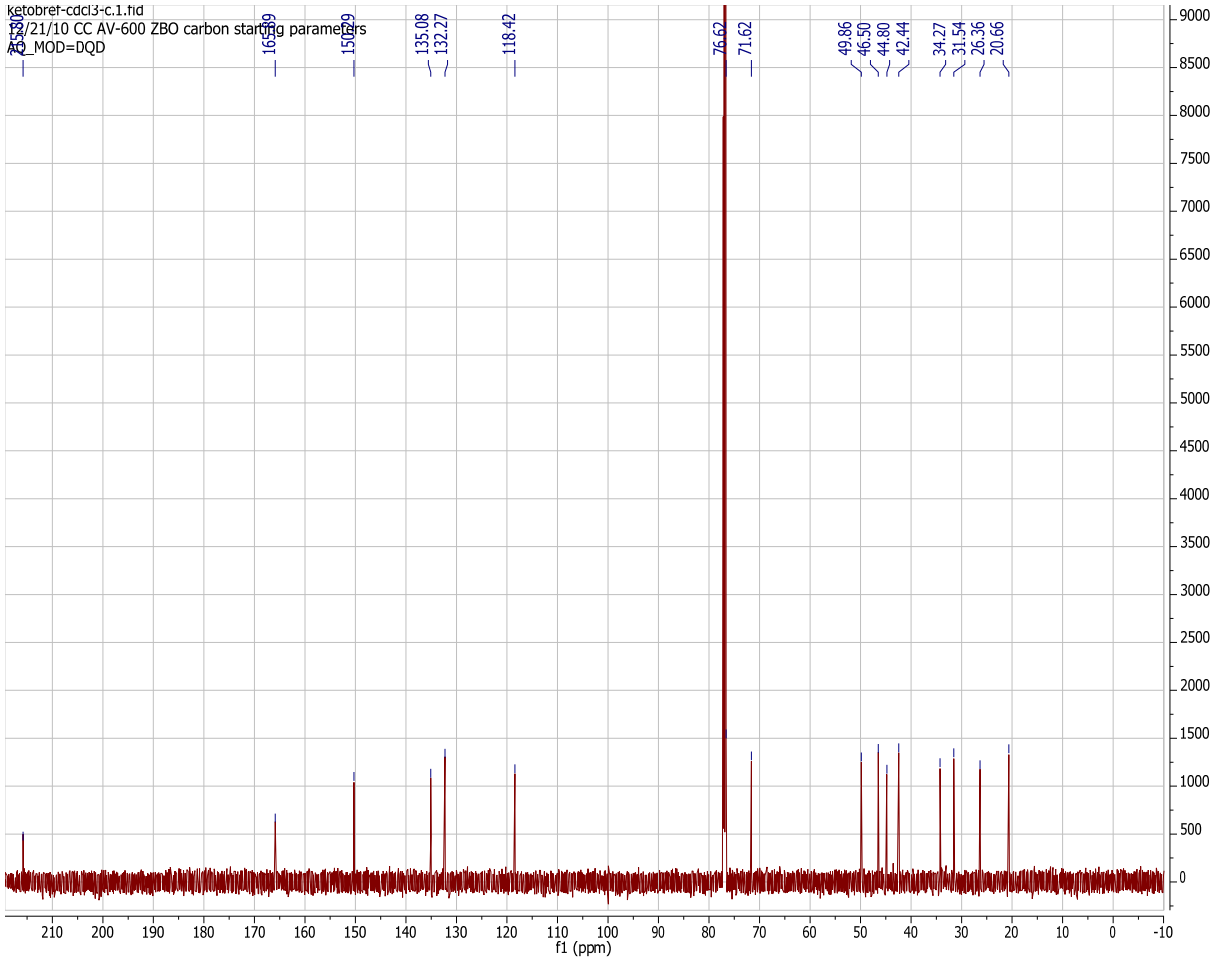
7-epi-10-keto-deacetylbaccatin III (1l):



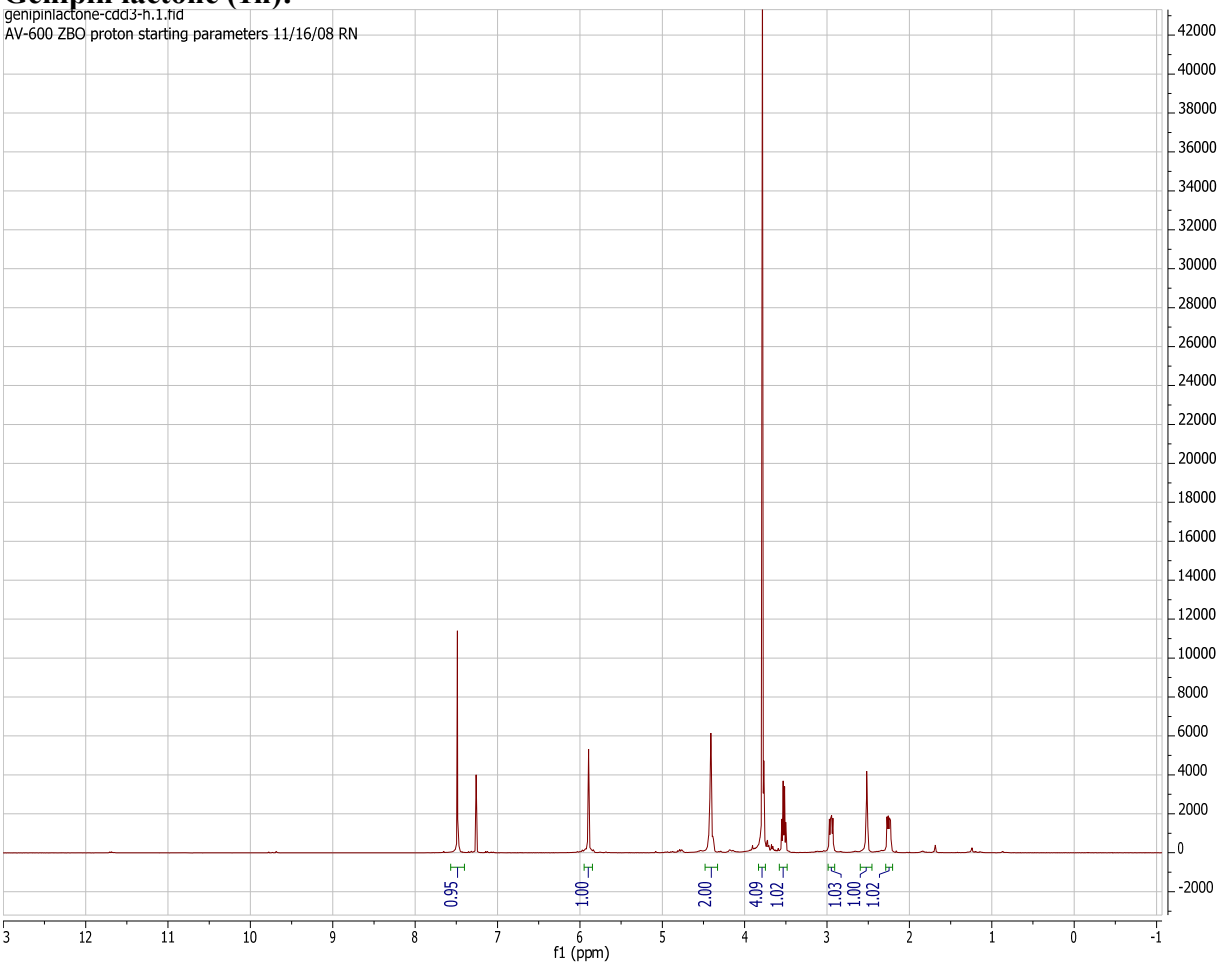

7-keto-DABIII-cdcl3-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
207.77
198.75
172.44
167.74
157.36
139.42
134.22
130.18
129.08
129.00
82.26
81.88
79.74
79.33
77.72
75.45
73.59
58.36
43.16
42.69
40.12
35.55
32.43
22.04
18.08
16.54
13.88
f1 (ppm)

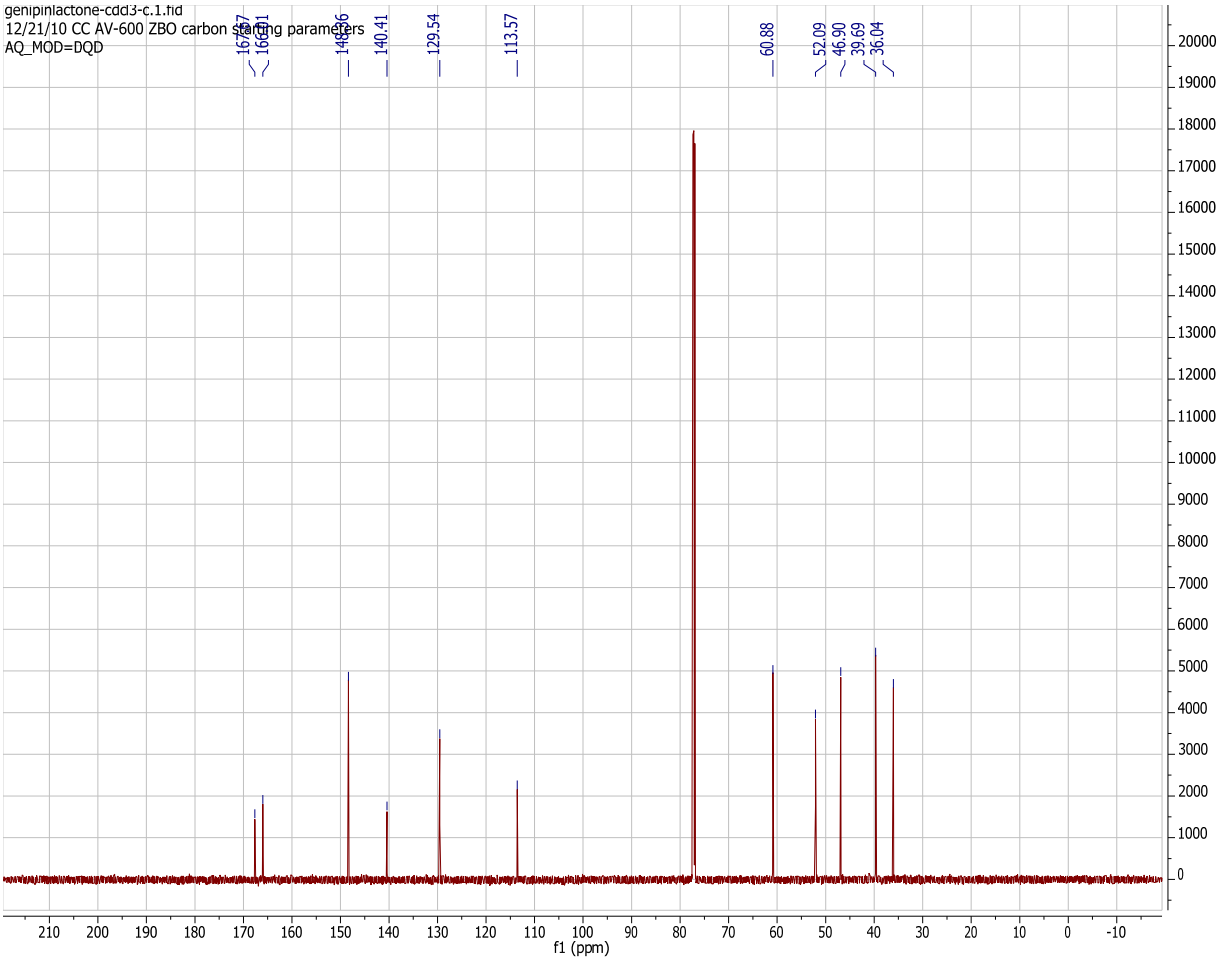
13-keto-brefeldin A (2m):



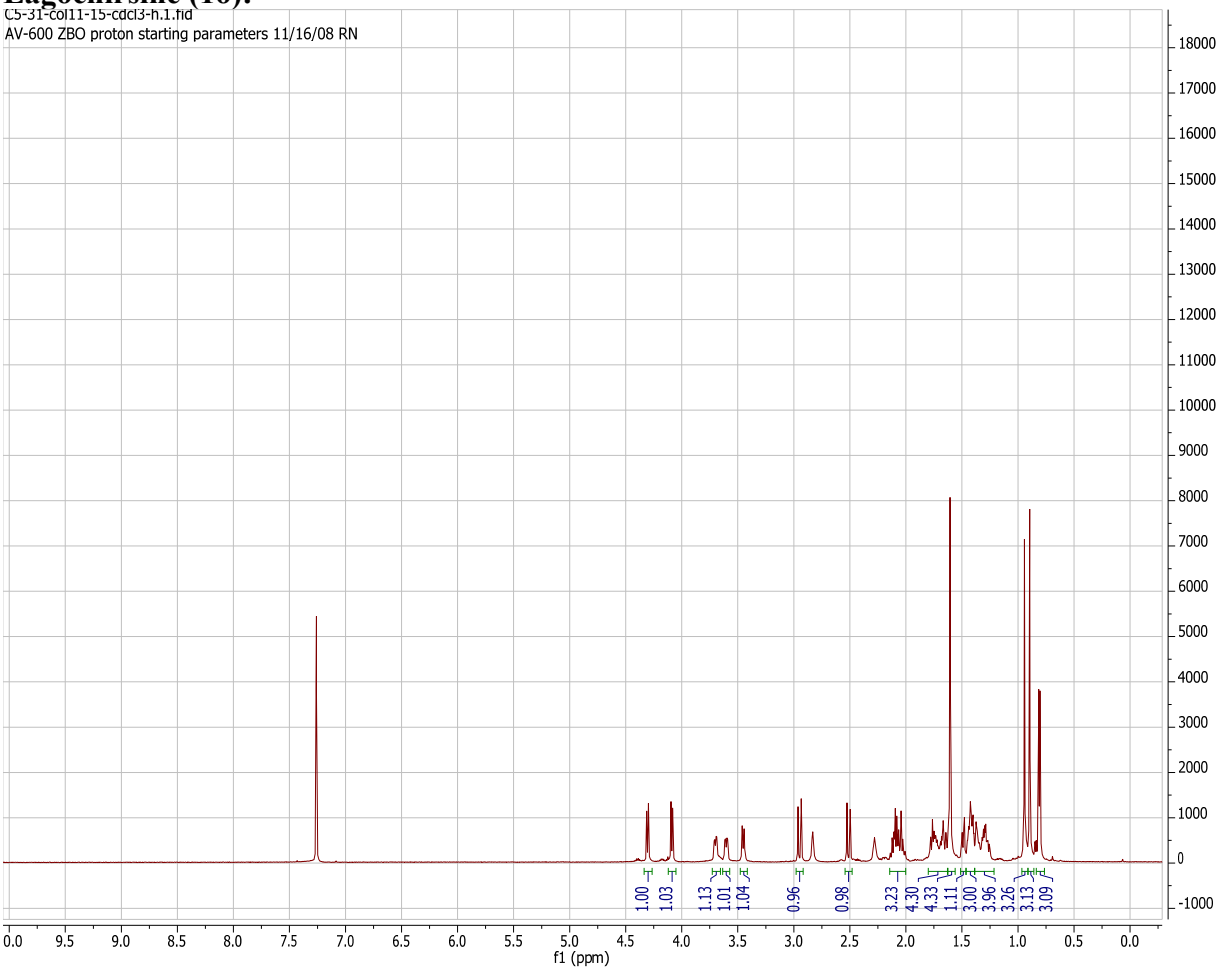

ketobref-cdcl3-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
165.39
150.29
135.08
132.27
118.42
76.62
71.62
49.86
46.50
44.80
42.44
34.27
31.54
26.36
20.66
f1 (ppm)

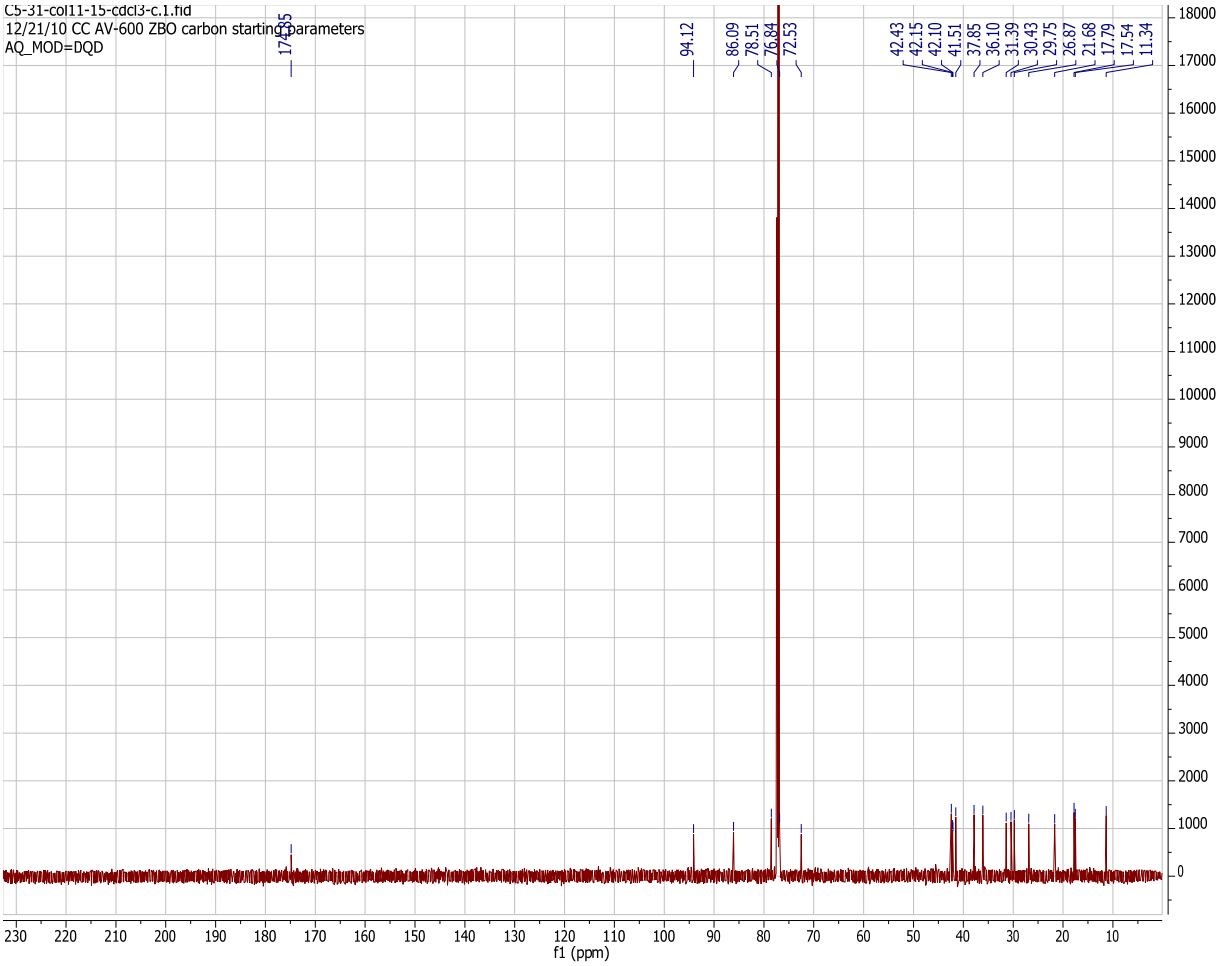
Genipin lactone (1n):



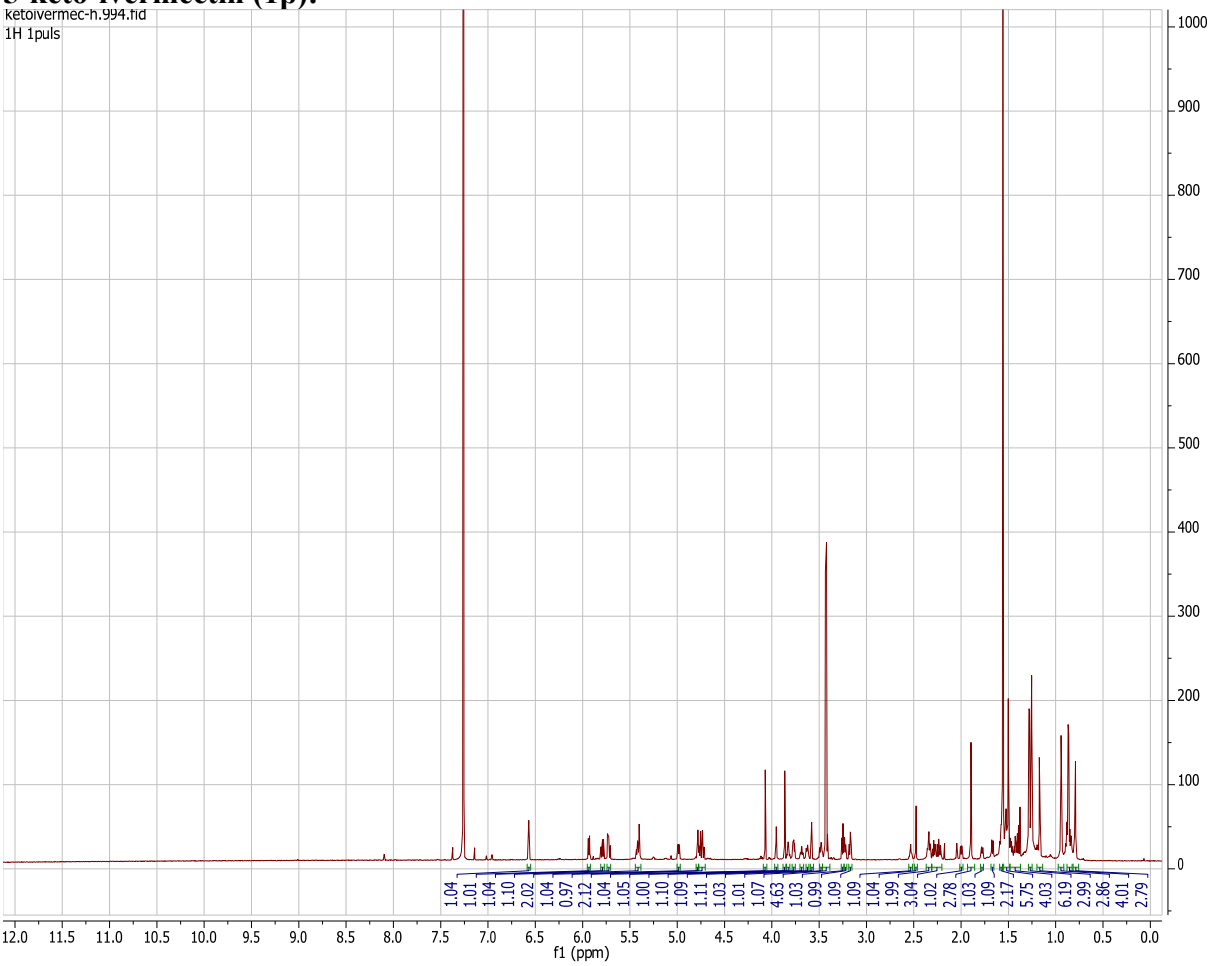

genipinlactone-cdd3-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
167.27
166.91
148.36
140.41
129.54
113.57
60.88
52.09
46.90
39.69
36.04
f1 (ppm)

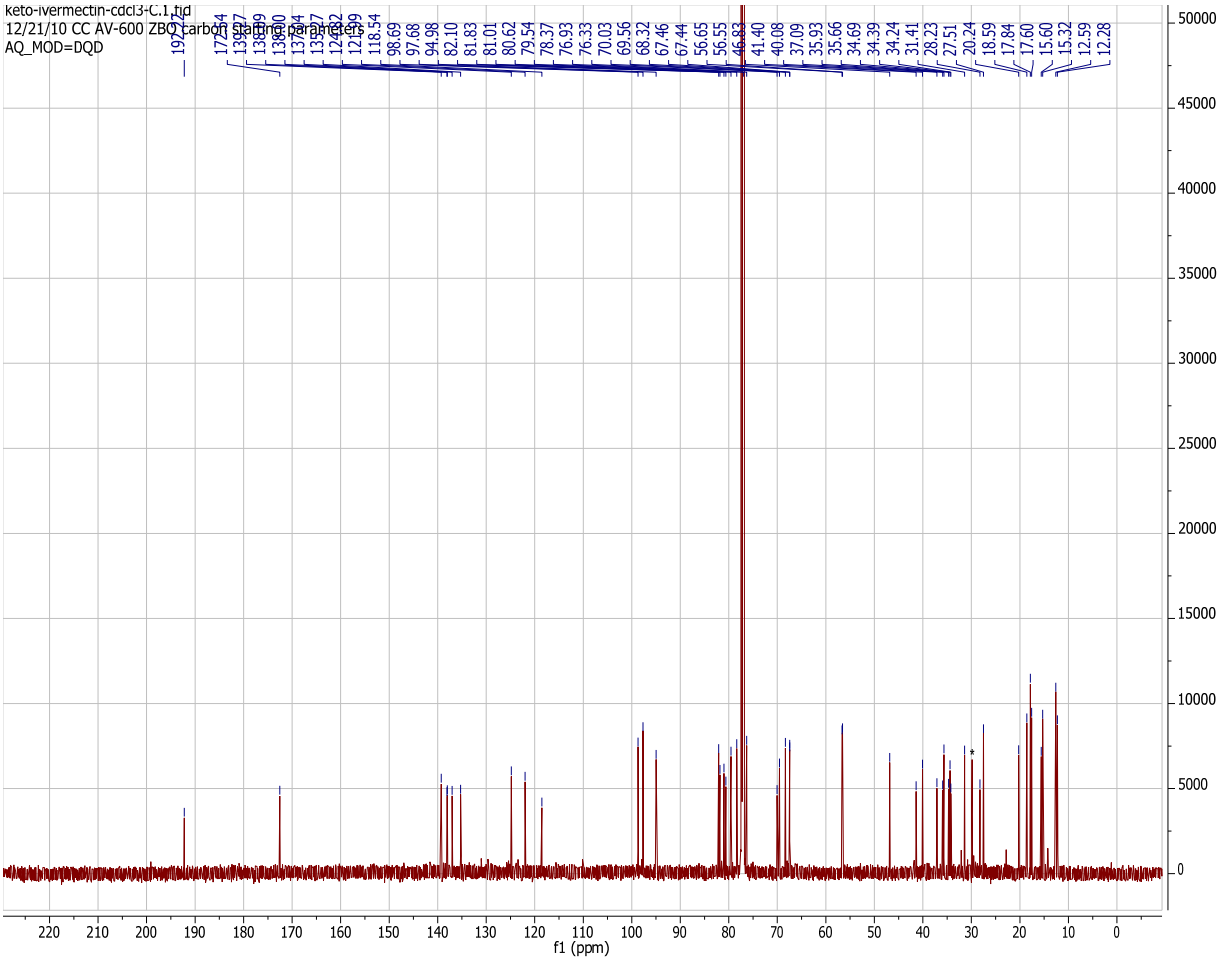
Lagochirsine (1o):




C5-31-col11-15-cdcl3-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
174.35
94.12
86.09
78.51
76.84
72.53
42.43
42.15
42.10
41.51
37.85
36.10
31.39
30.43
29.75
26.87
21.68
17.79
17.54
11.34
f1 (ppm)

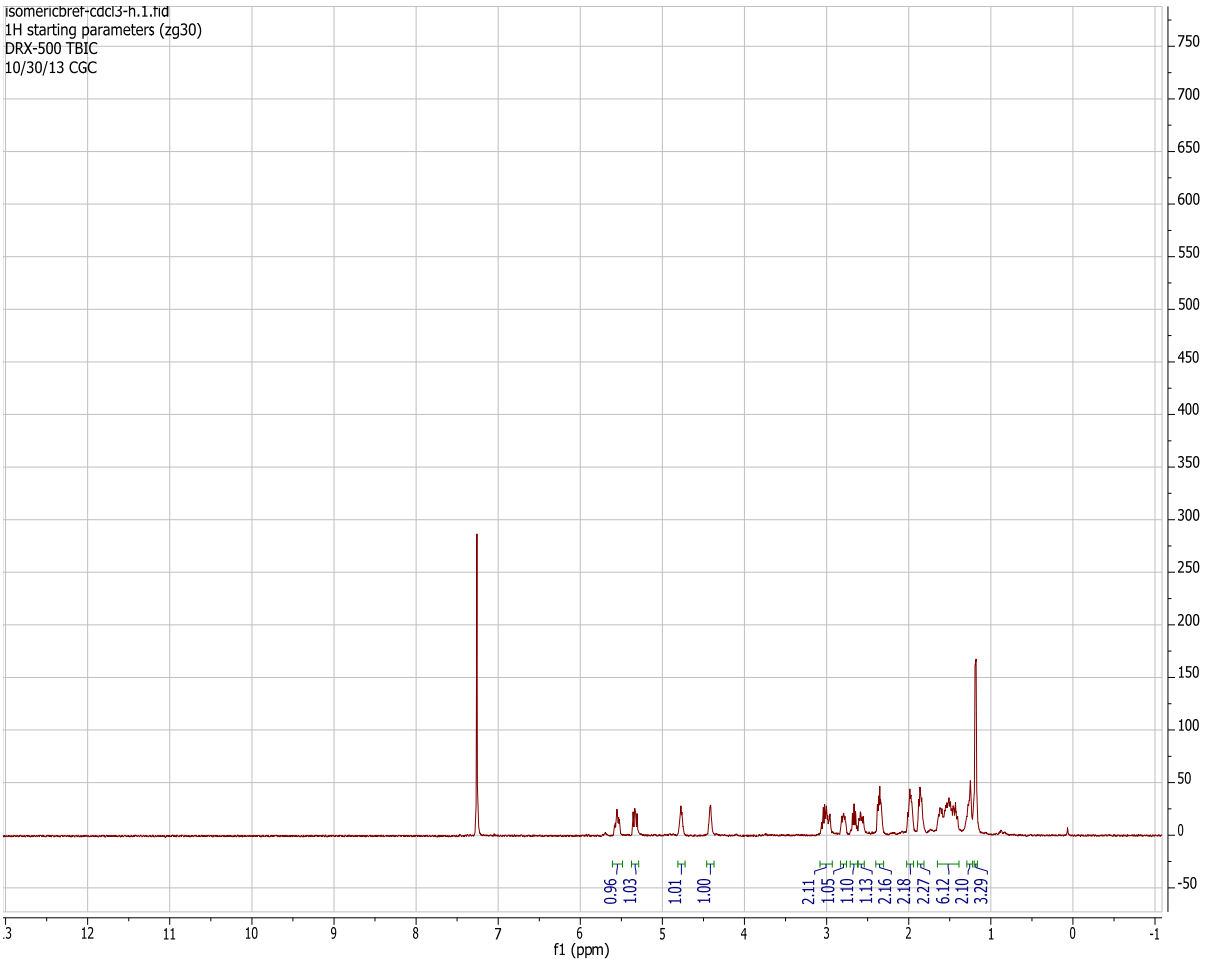
5-keto-ivermectin (1p):

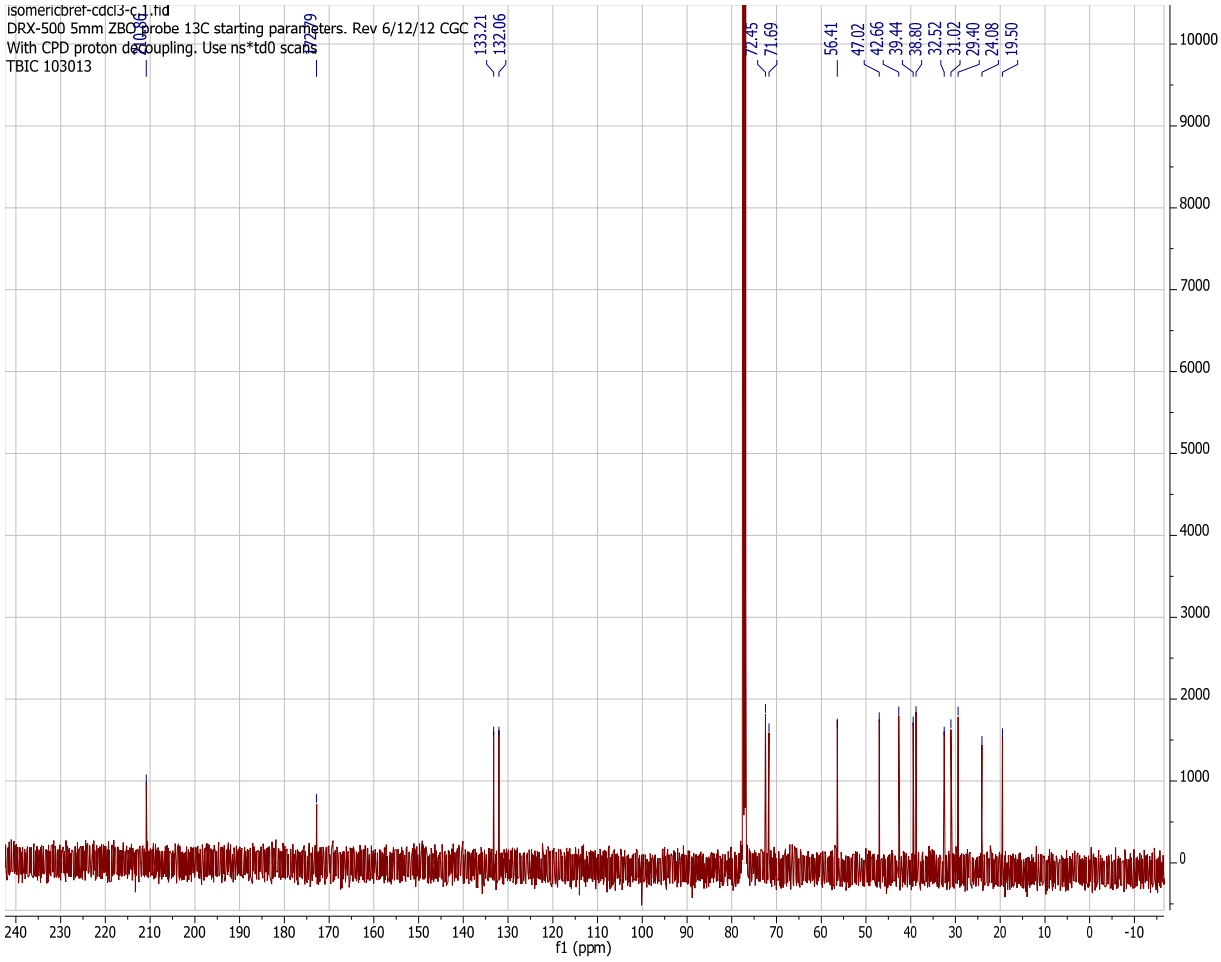




*petroleum-grease

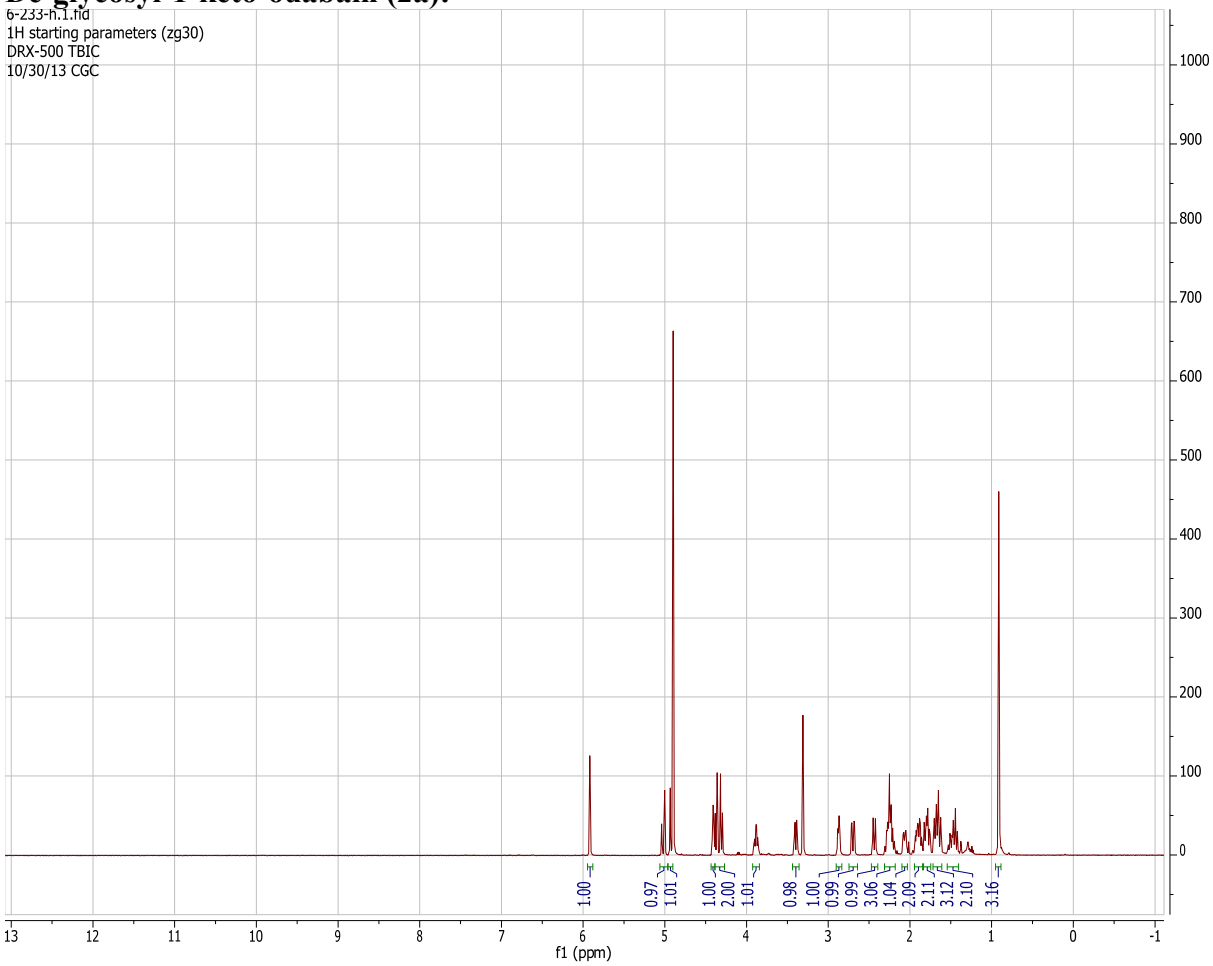
2,3-dihydro-1-keto-brefeldin A (1q)

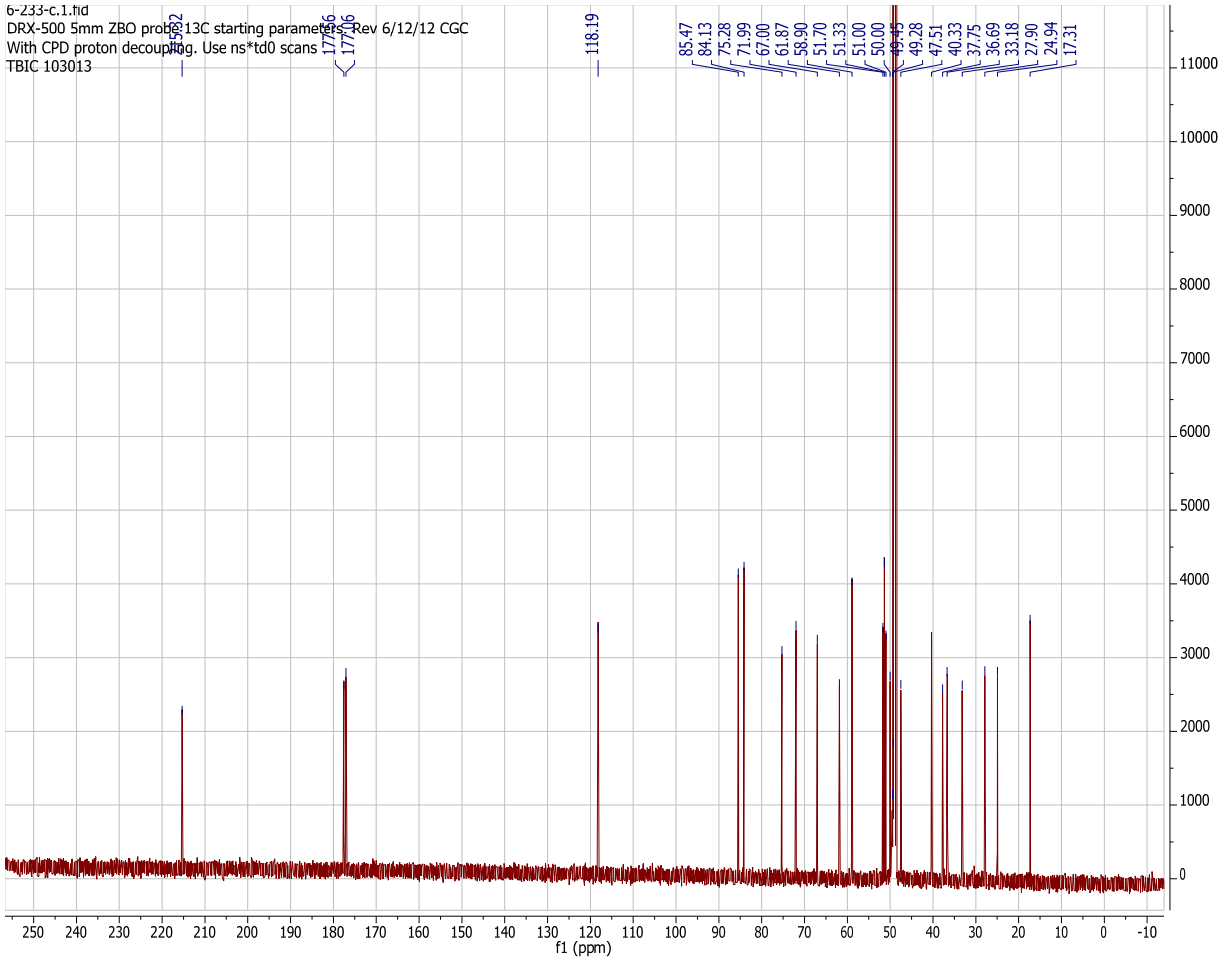



isomericbref-cdcl3-c-1.fid
DRX-500 5mm ZBO probe 13C starting parameters. Rev 6/12/12 CGC
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
208.06
167.79
133.21
132.06
72.45
71.69
56.41
47.02
42.66
39.44
38.80
32.52
31.02
29.40
24.08
19.50
f1 (ppm)

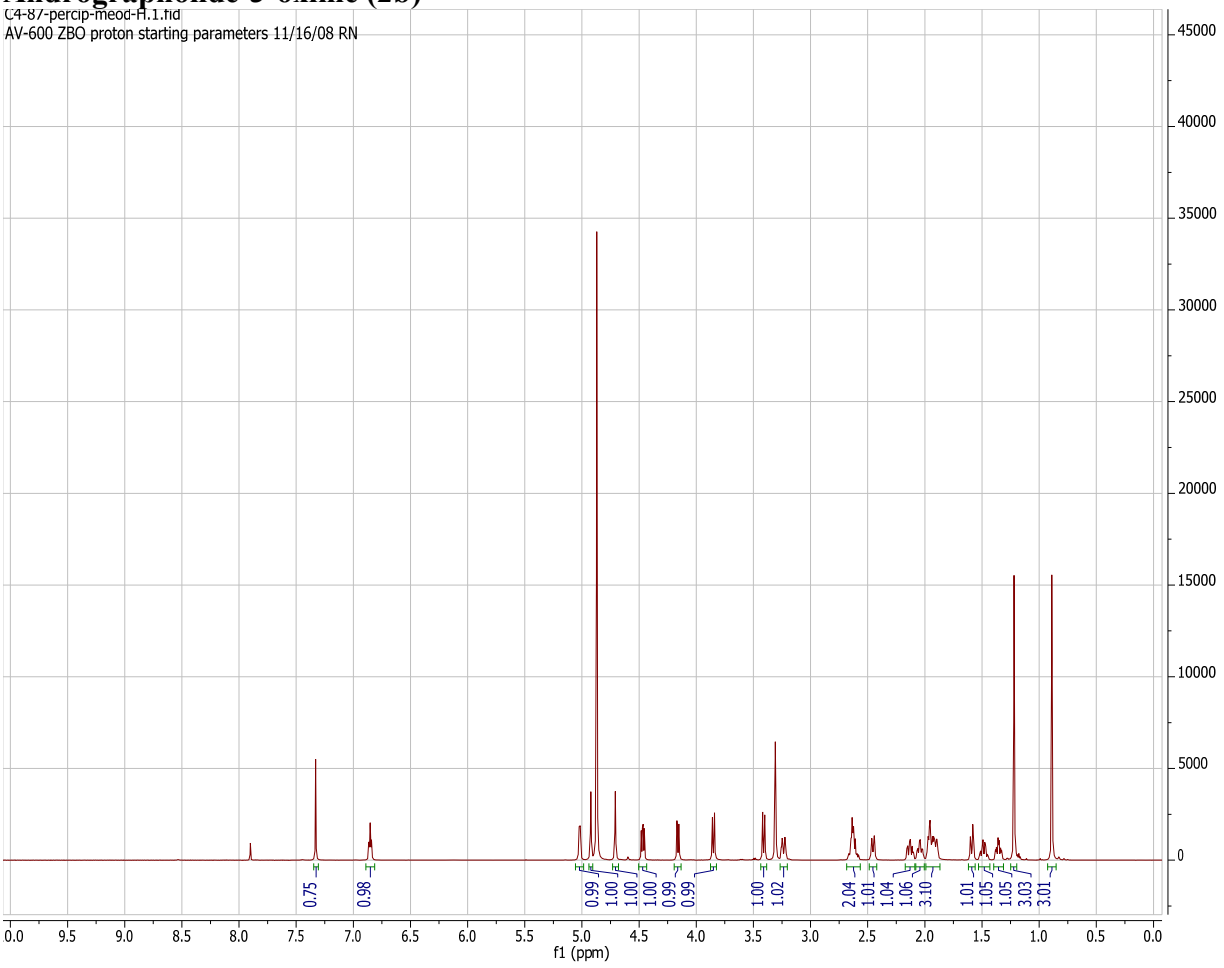
Derivative NMR data:

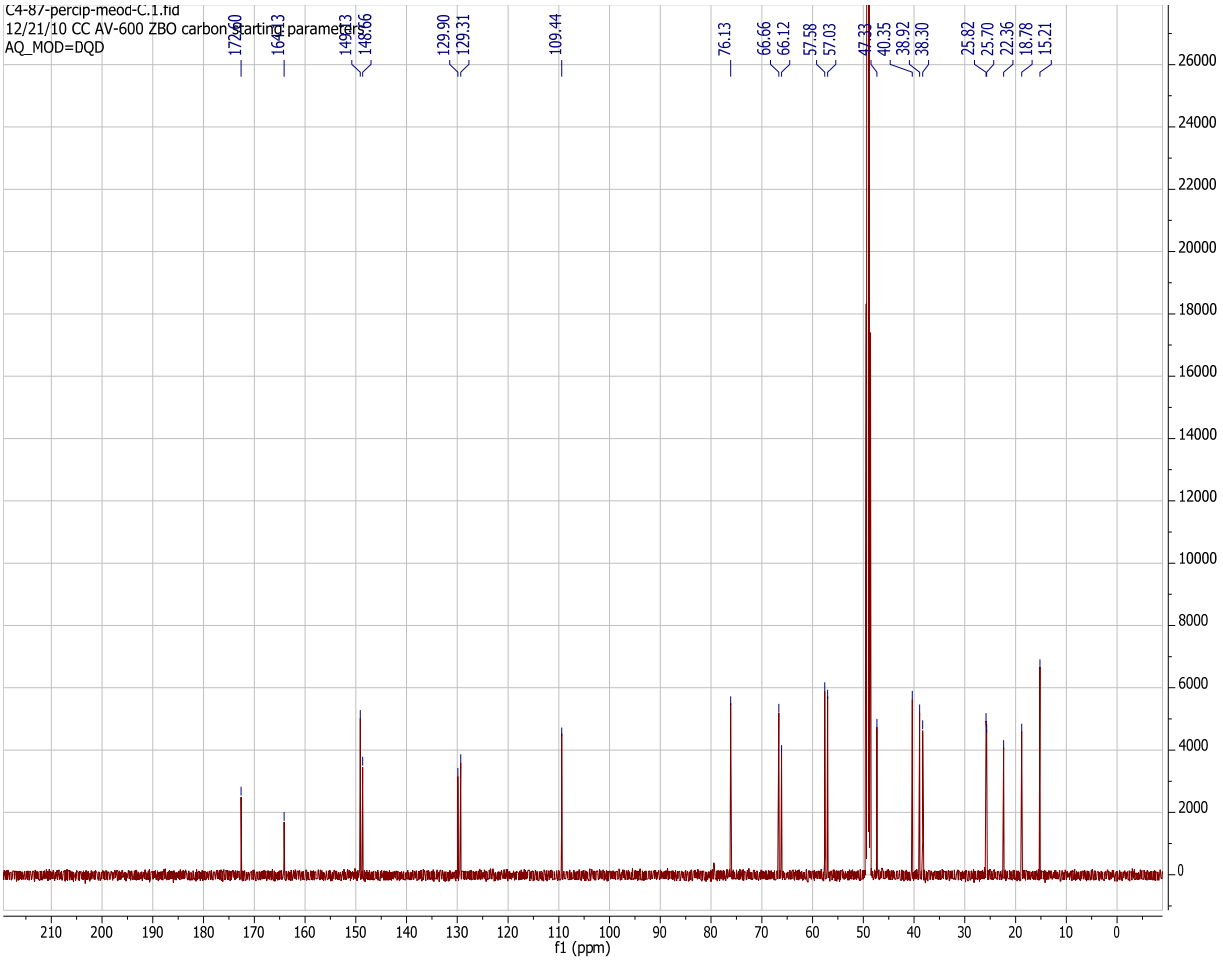
De-glycosyl-1-keto-ouabain (2a):



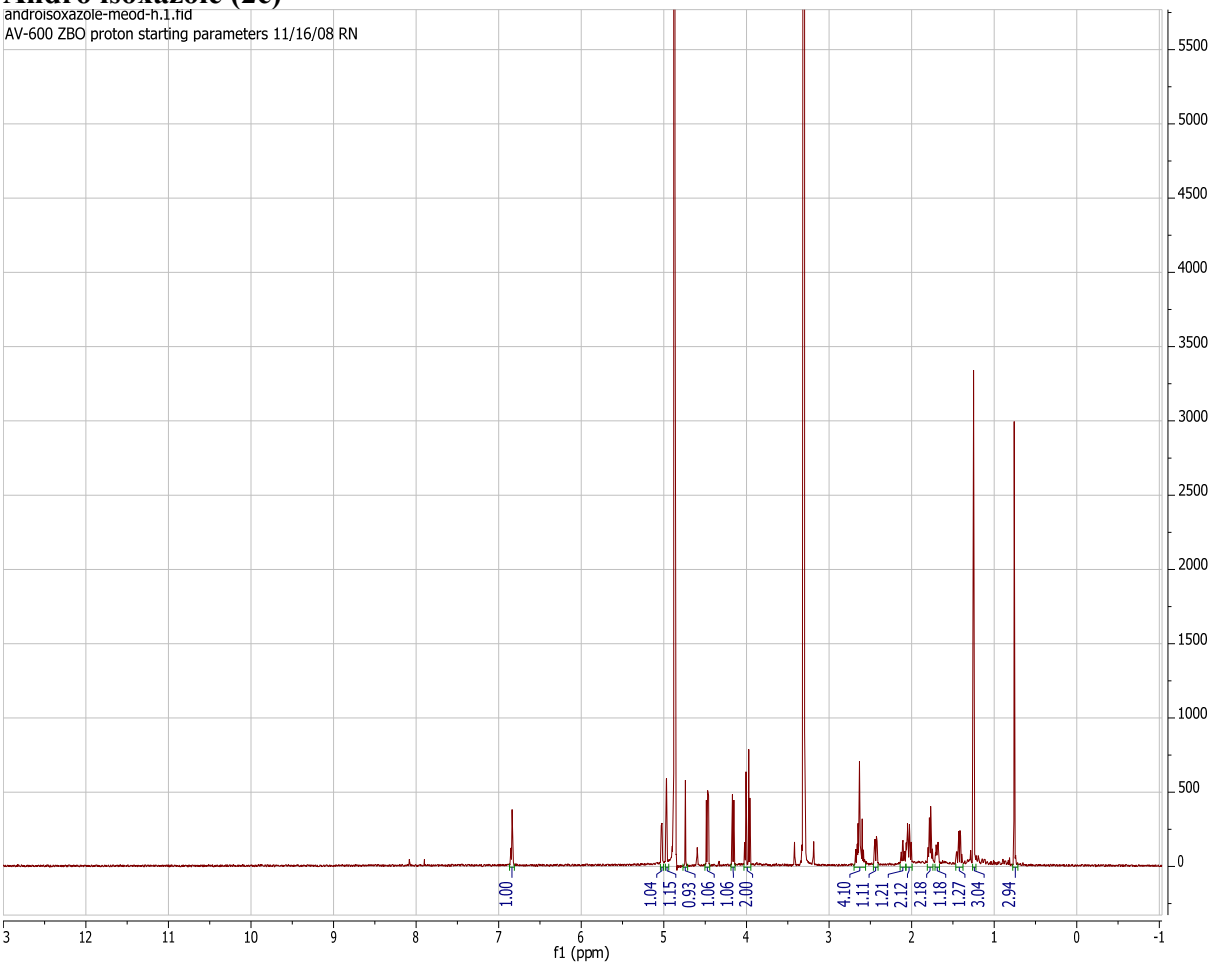

6-233-c.1.fid
DRX-500 5mm ZBO proton/13C starting parameters, Rev 6/12/12 CGC
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
214.92
177.66
177.46
118.19
85.47
84.13
75.28
71.99
67.00
61.87
58.90
51.70
51.33
51.00
50.00
49.45
49.28
47.51
40.33
37.75
36.69
33.18
27.90
24.94
17.31
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
250 240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

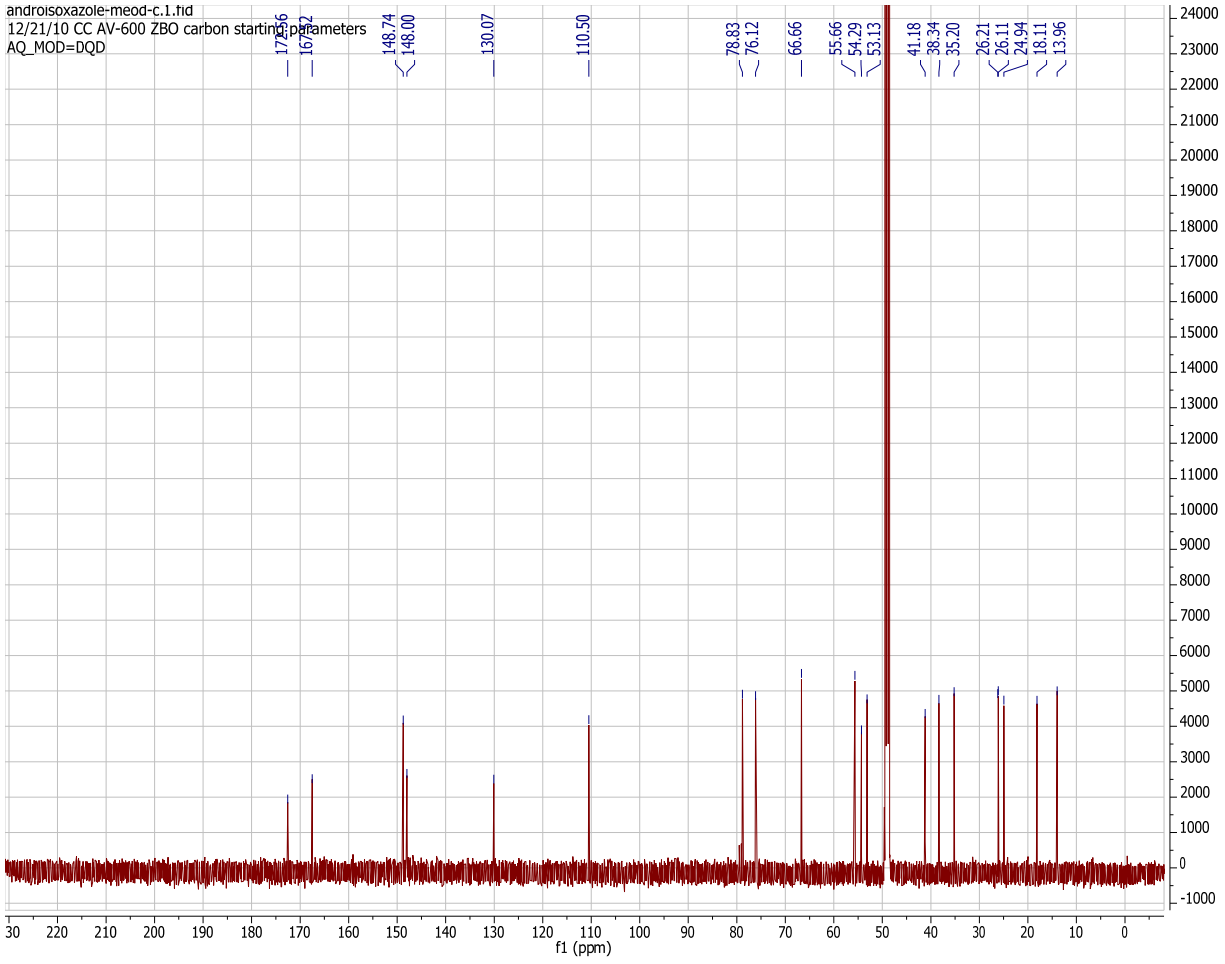
Andrographolide-3-oxime (2b)



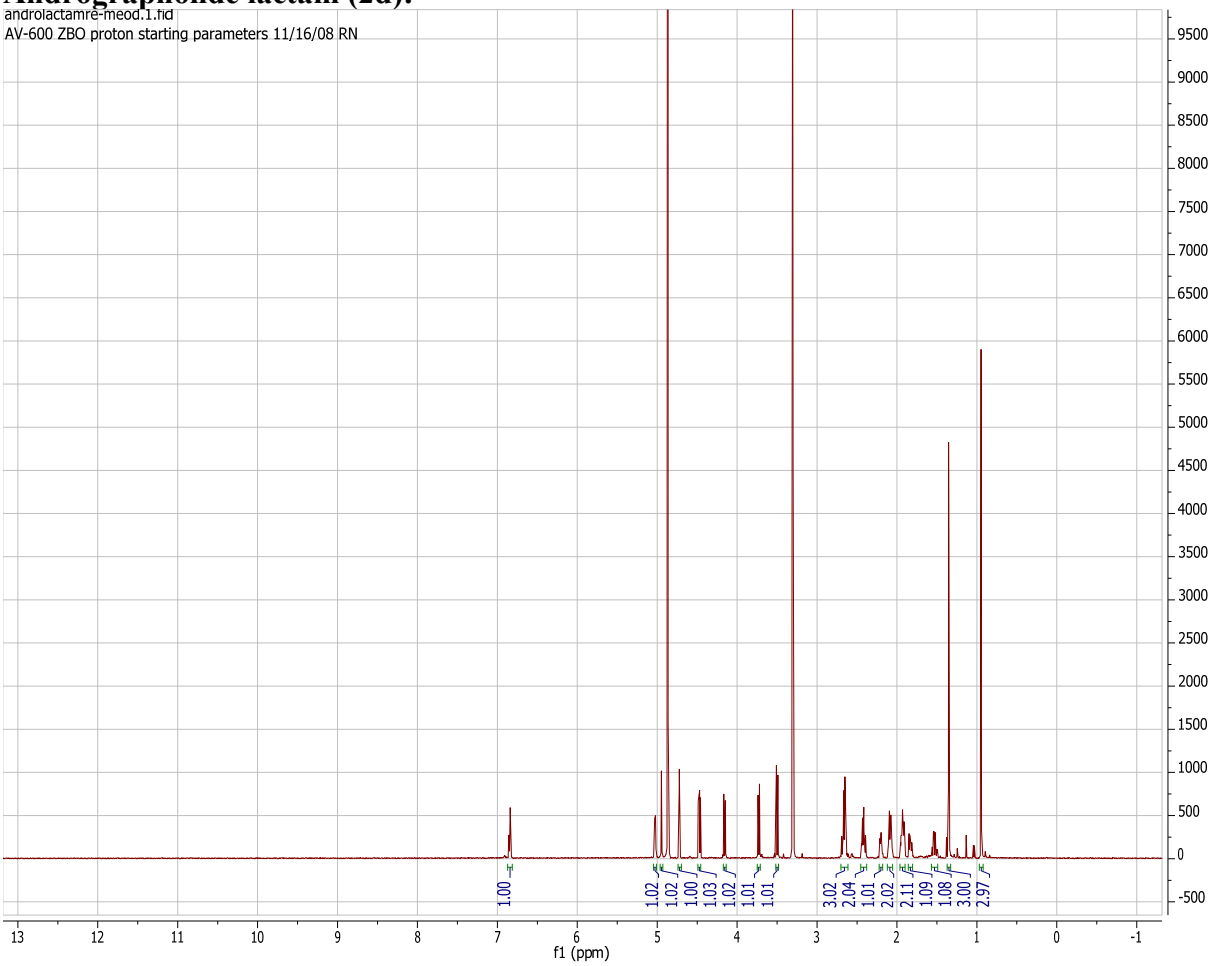

C4-87-percip-meod-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
172.00
164.13
149.53
148.66
129.90
129.31
109.44
76.13
66.66
66.12
57.58
57.03
47.33
40.35
38.92
38.30
25.82
25.70
22.36
18.78
15.21
f1 (ppm)

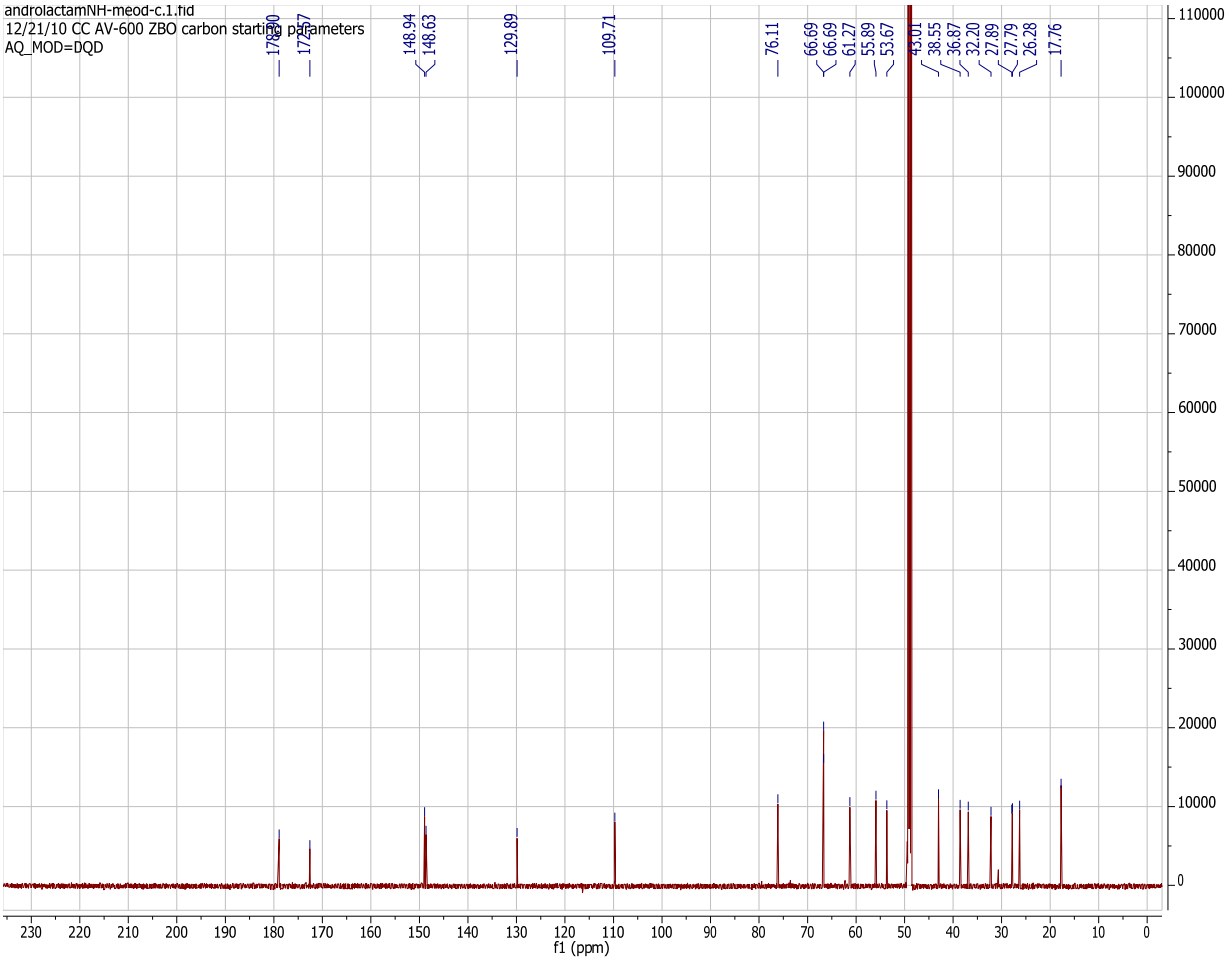
Andro isoxazole (2c)



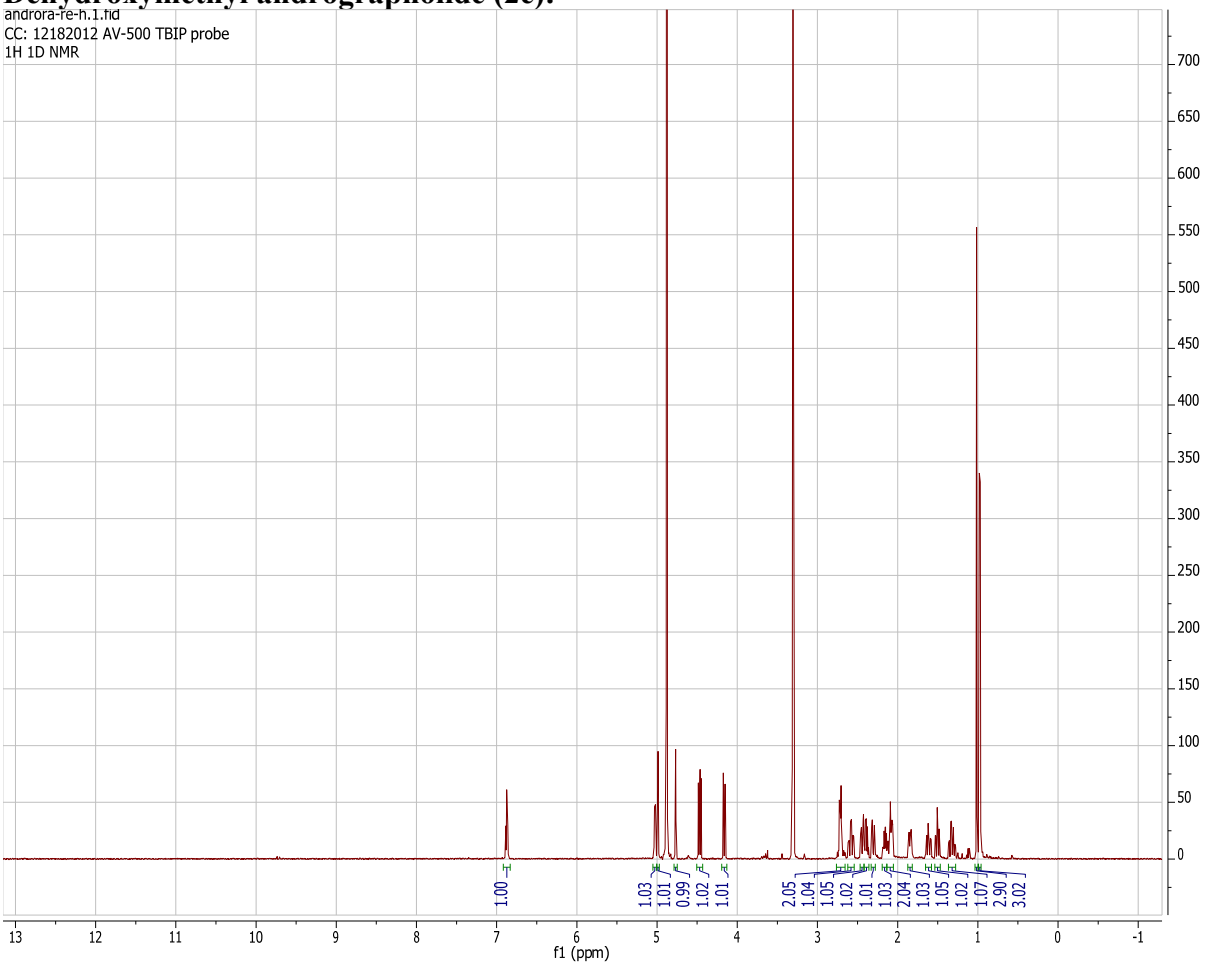

androisoxazole-meod-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
174.56
167.92
148.74
148.00
130.07
110.50
78.83
76.12
66.66
55.66
54.29
53.13
41.18
38.34
35.20
26.21
26.11
24.94
18.11
13.96
f1 (ppm)

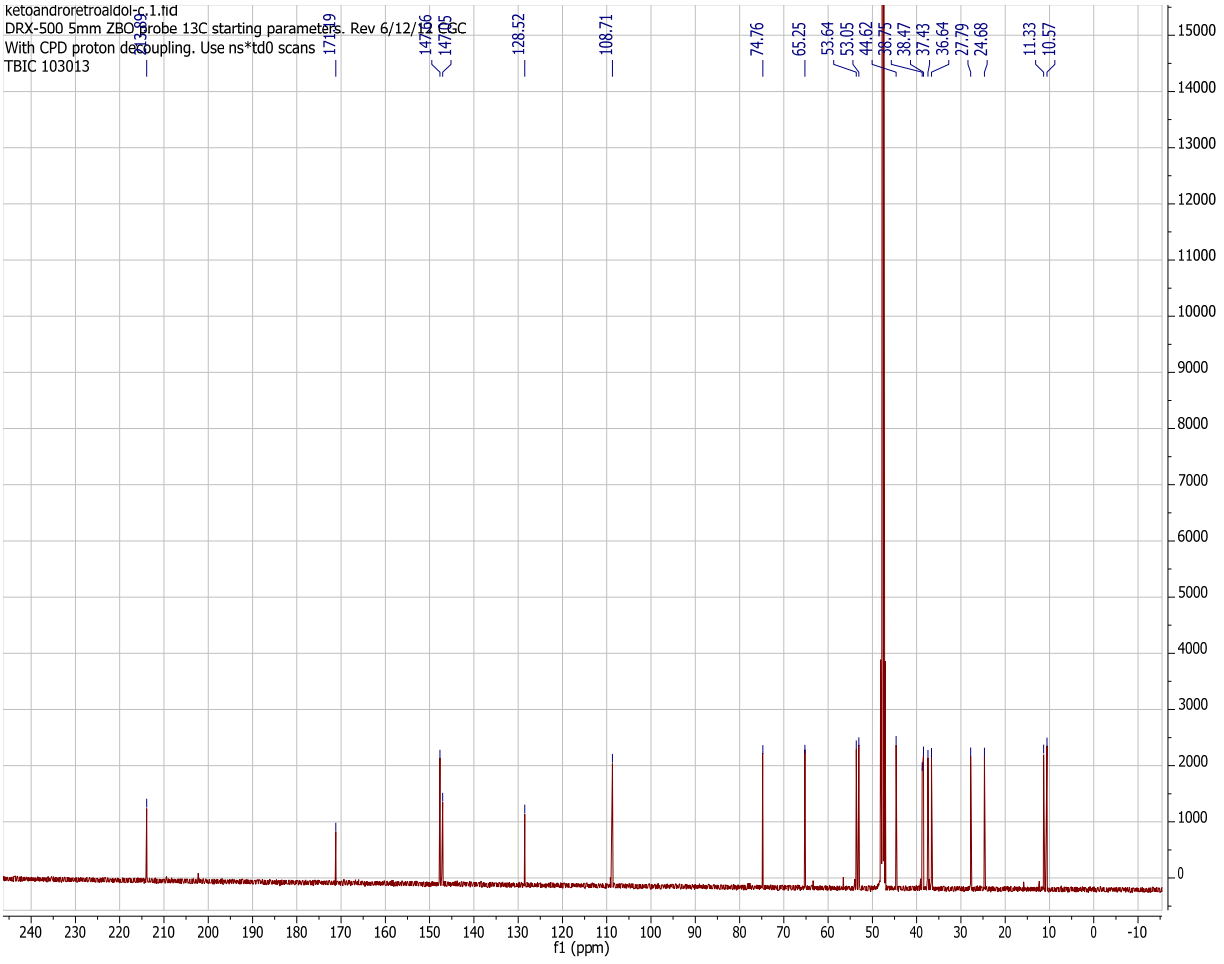
Andrographolide lactam (2d):



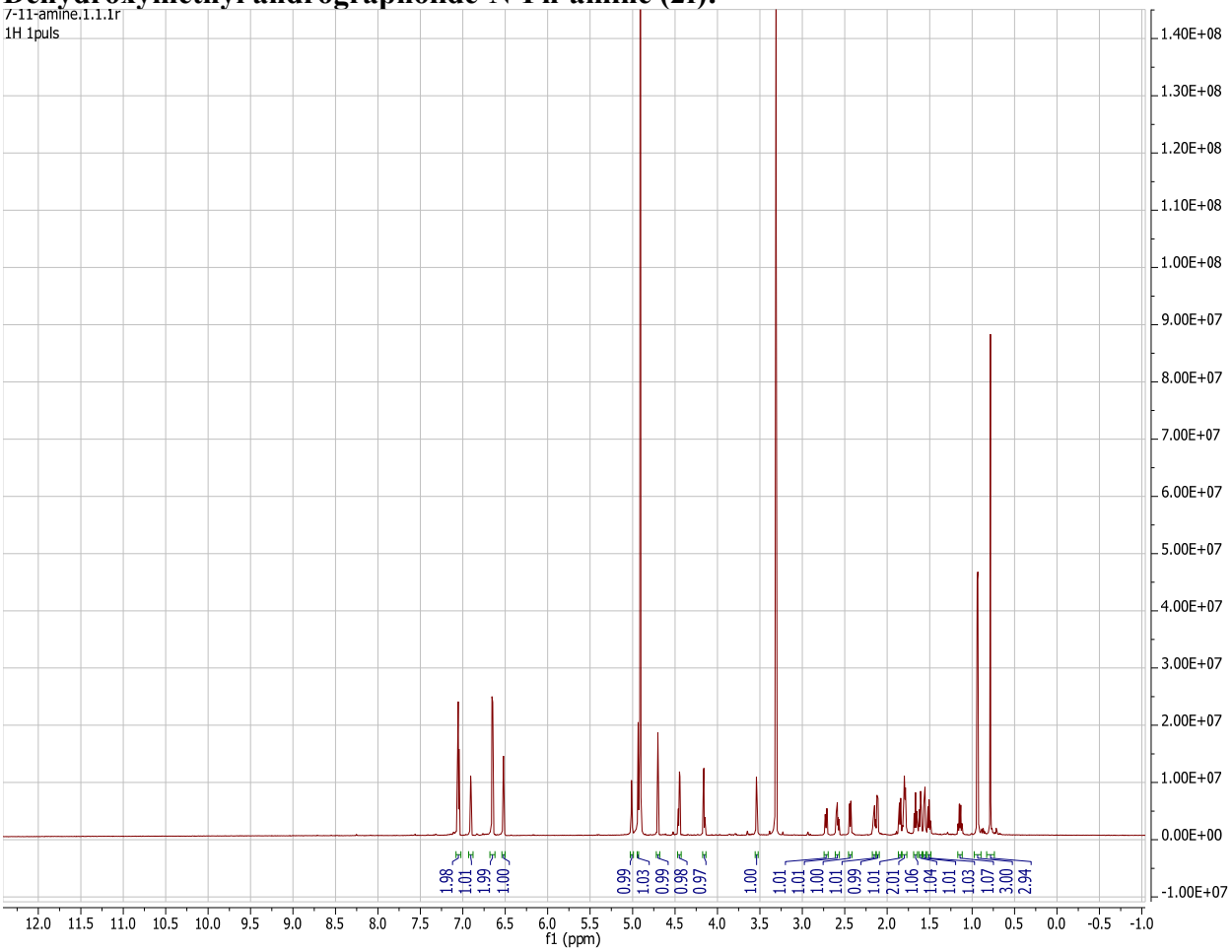

androlactamNH-meod-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
148.94
146.63
129.89
109.71
76.11
66.69
66.69
61.27
55.89
53.67
43.01
38.55
36.87
32.20
27.89
27.79
26.28
17.76
f1 (ppm)

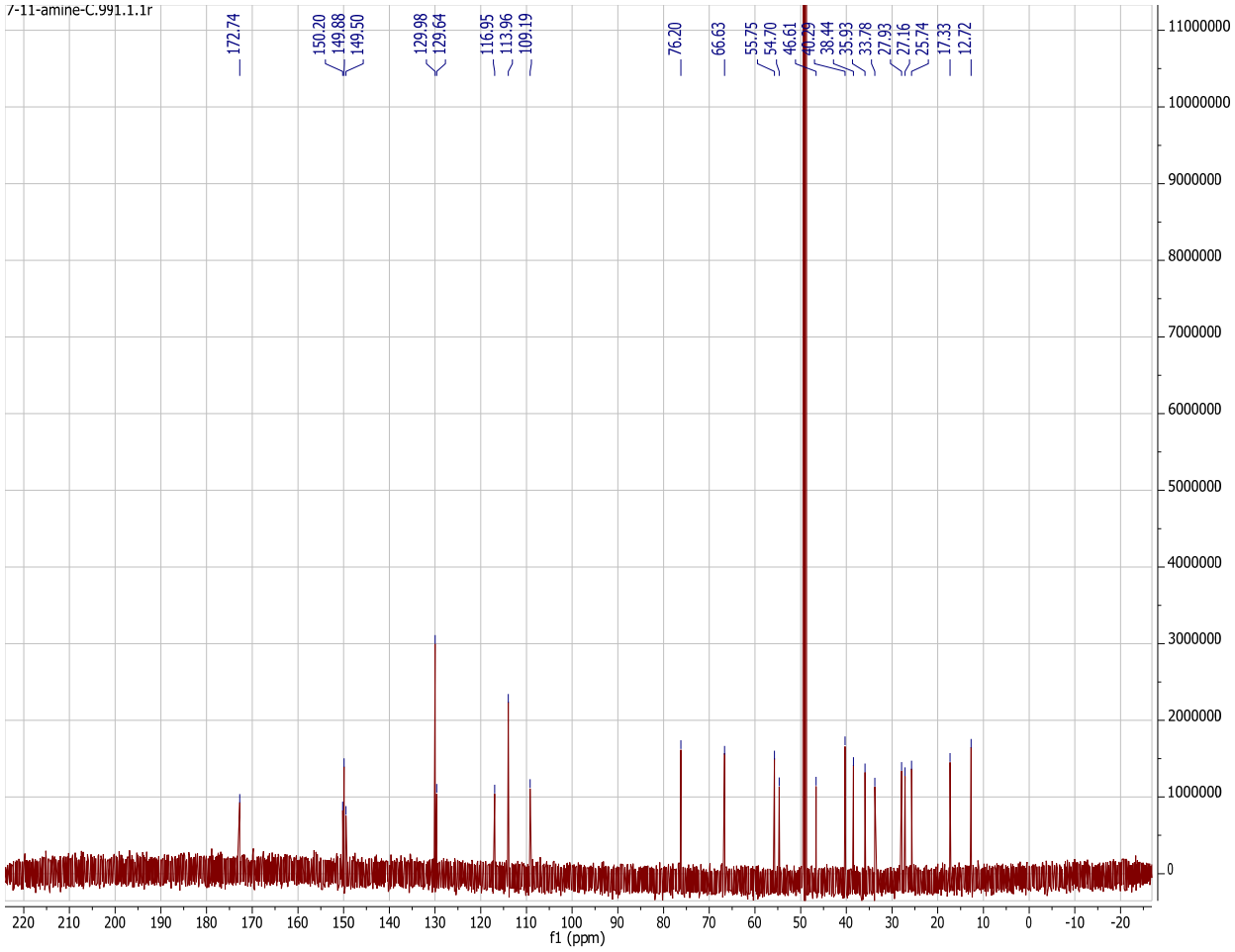
Dehydroxymethyl andrographolide (2e):



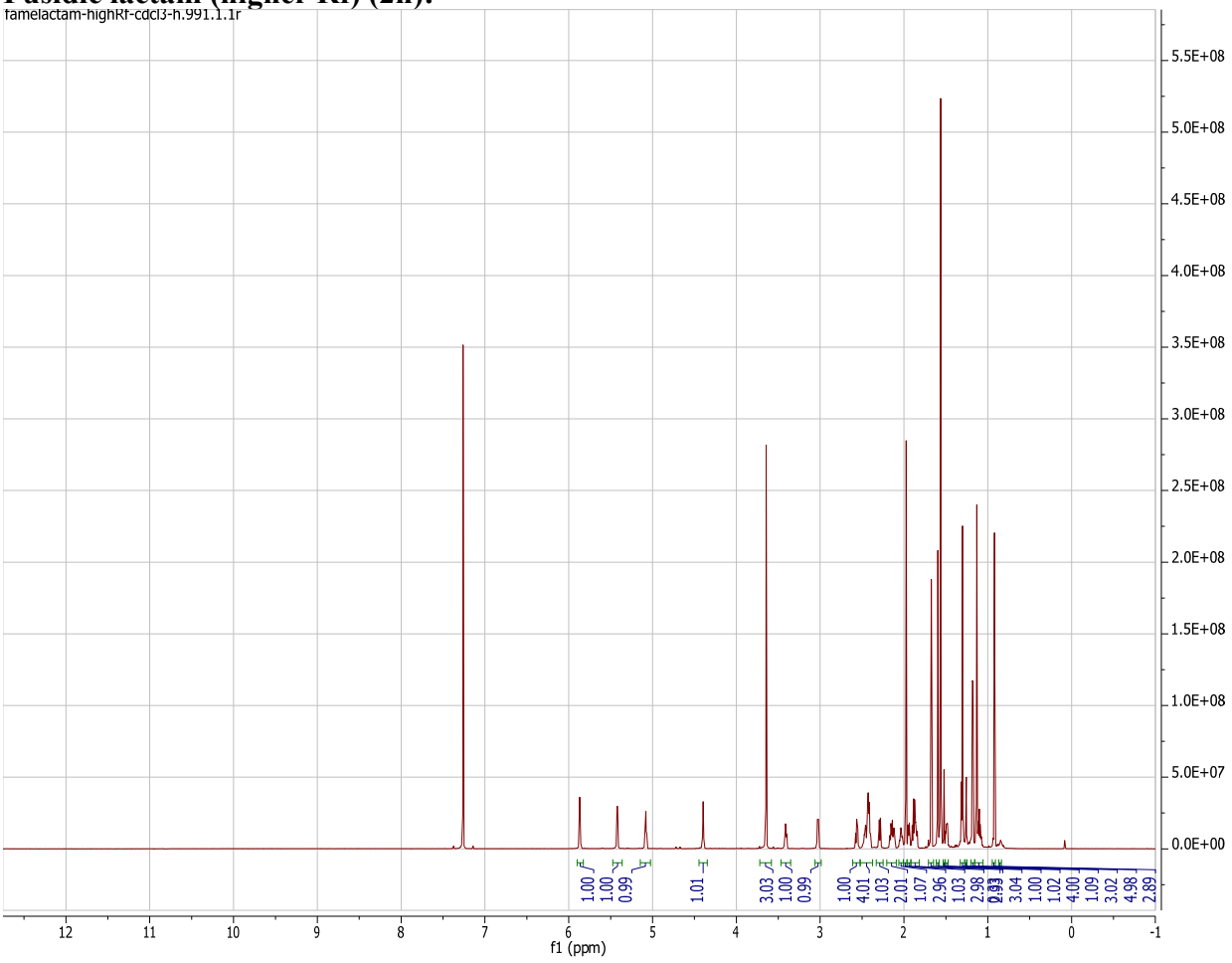

ketoandroretroaldol-c 1.fid
DRX-500 5mm ZBO Probe 13C starting parameters. Rev 6/12/12 CGC
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
208.39
171.19
147.36
147.05
128.52
108.71
74.76
65.25
53.64
53.05
44.62
38.75
38.47
37.43
36.64
27.79
24.68
11.33
10.57
f1 (ppm)

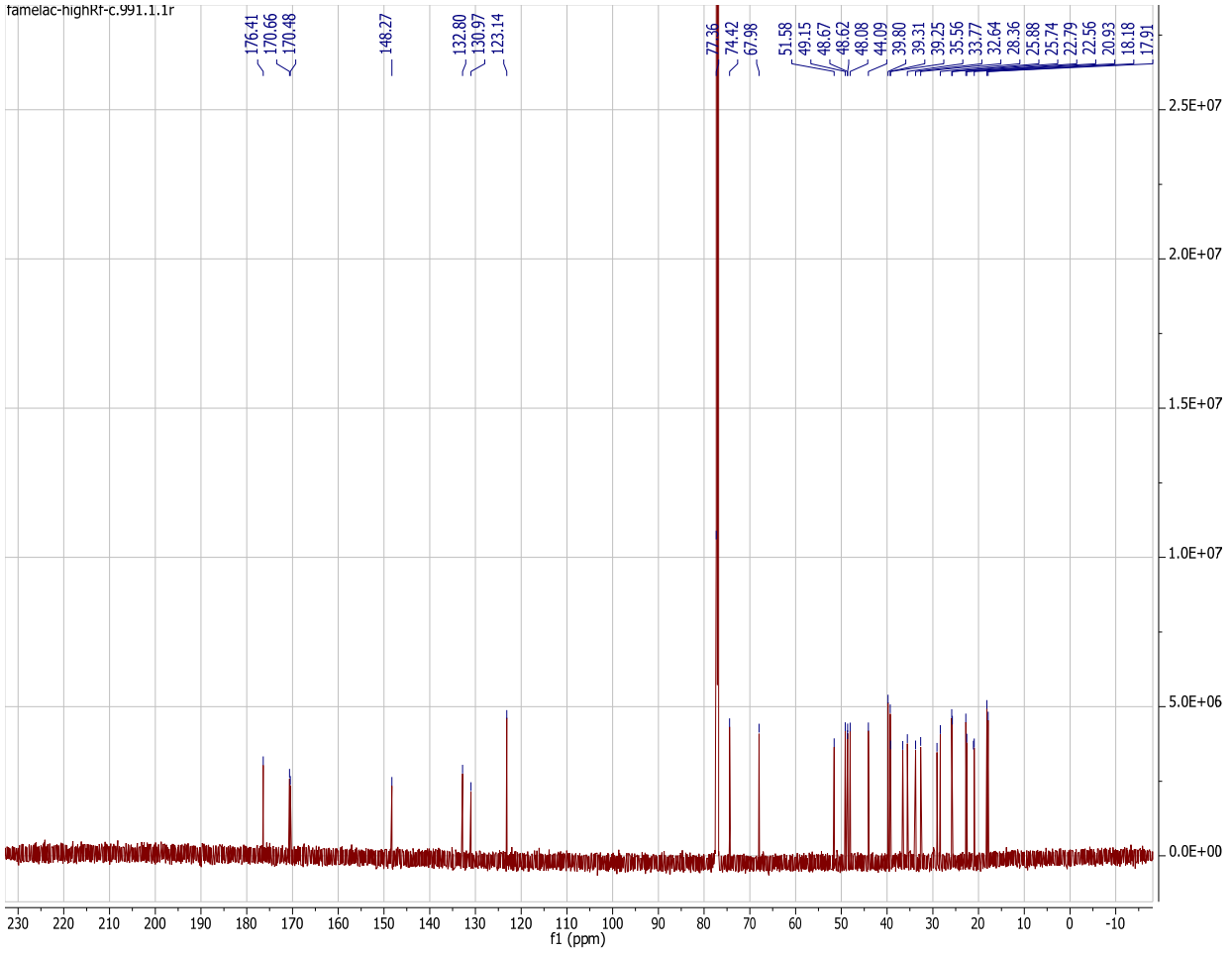
Dehydroxymethyl andrographolide-N-Ph-amine (2f):



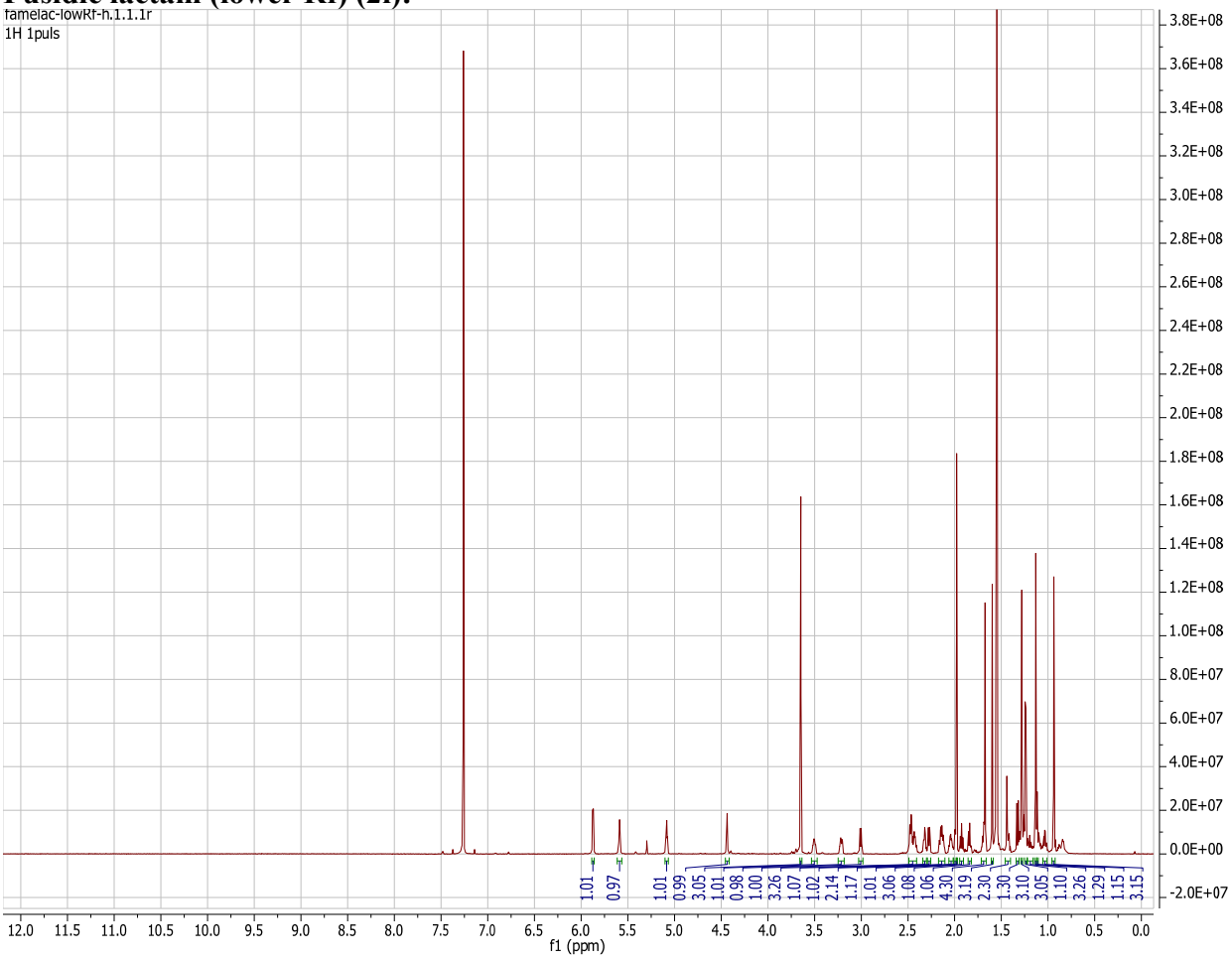

7-11-amine-C.991.1.1r
172.74
150.20
149.88
149.50
129.98
129.64
116.95
113.96
109.19
76.20
66.63
55.75
54.70
46.61
40.29
38.44
35.93
33.78
27.93
27.16
25.74
17.33
12.72
11000000
10000000
9000000
8000000
7000000
6000000
5000000
4000000
3000000
2000000
1000000
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

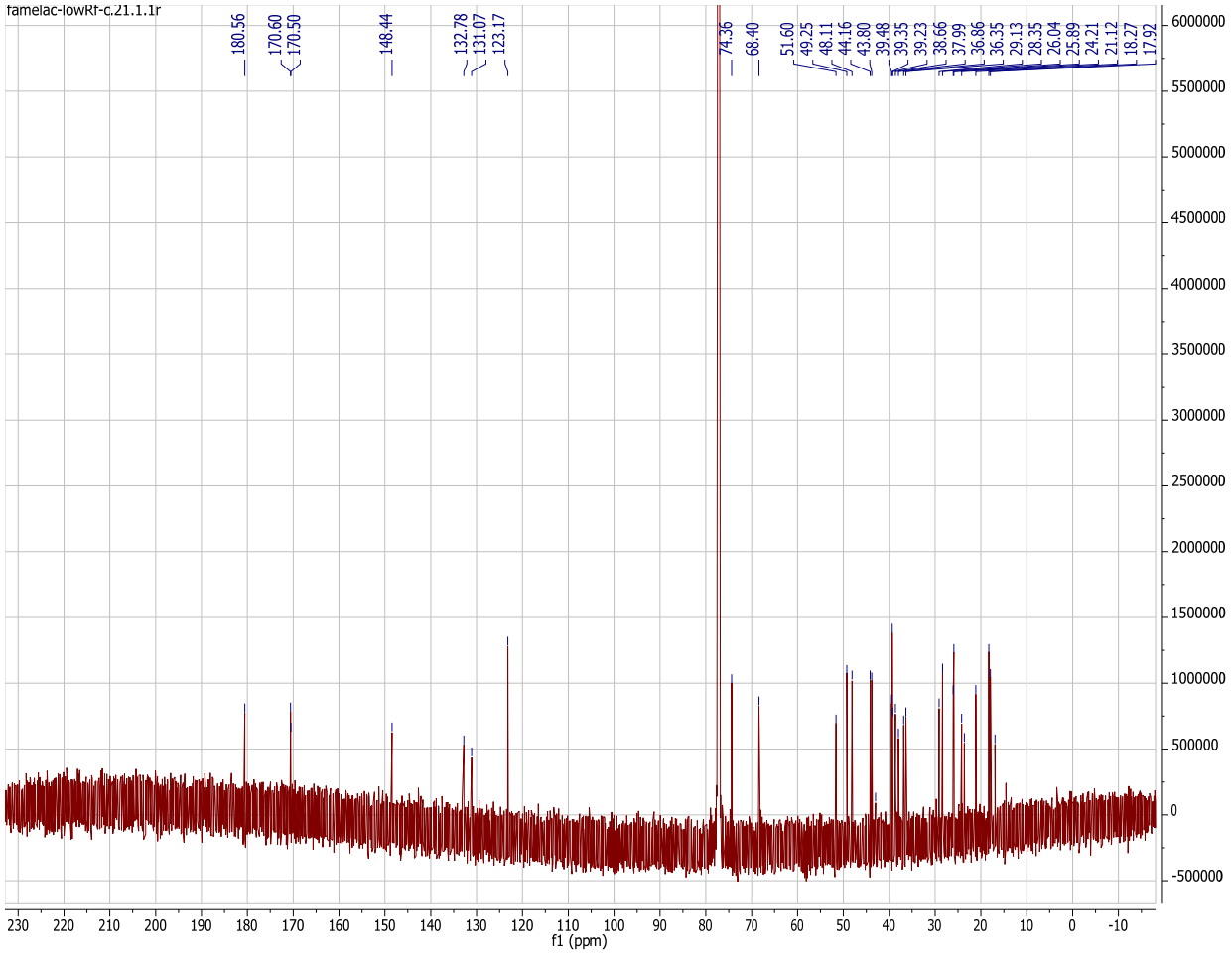
Fusidic lactam (higher Rf) (2h):



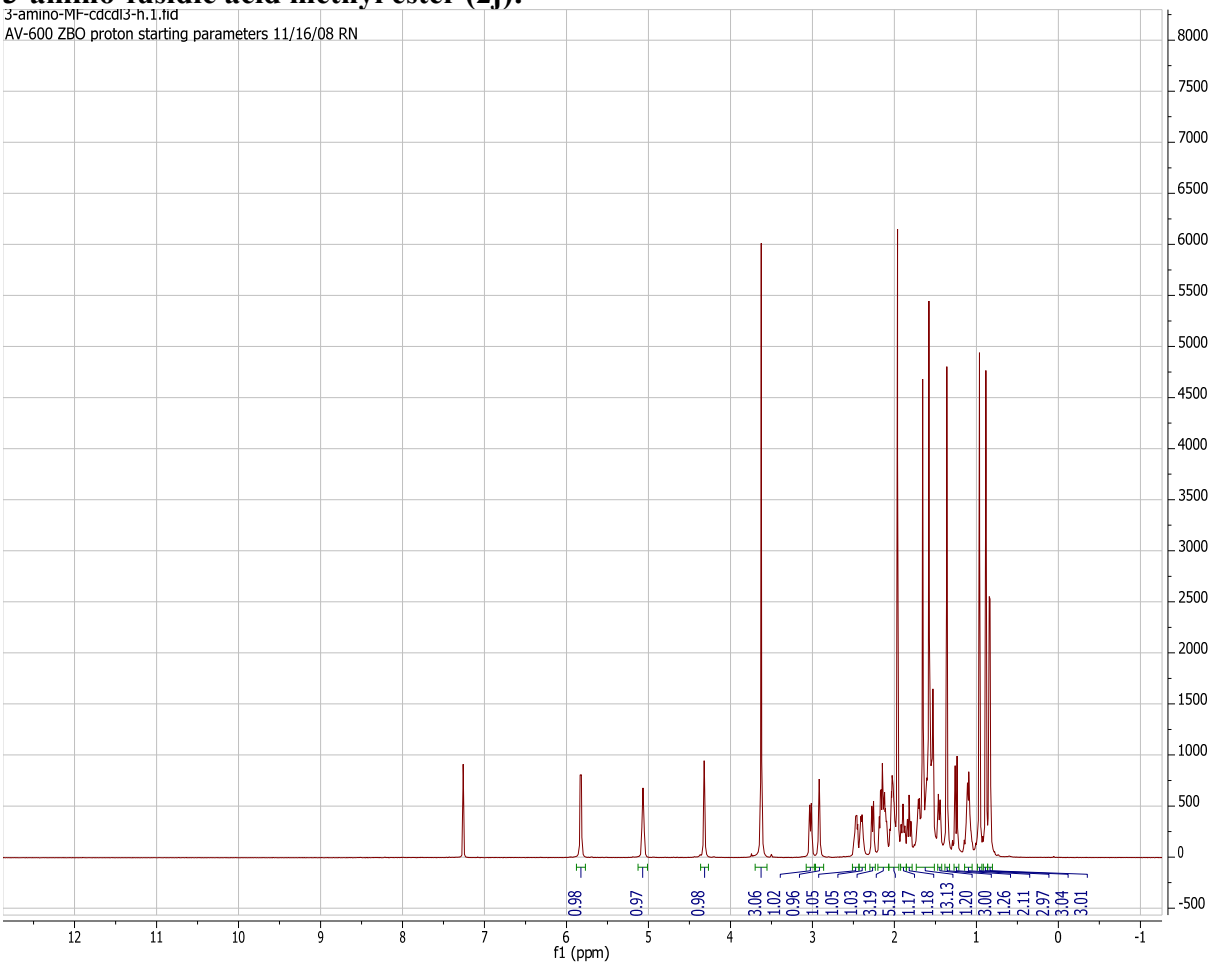

famelac-highRf-c.991.1.1r
176.41
170.66
170.48
148.27
132.80
130.97
123.14
77.36
74.42
67.98
51.58
49.15
48.67
48.62
48.08
44.09
39.80
39.31
39.25
35.56
33.77
32.64
28.36
25.88
25.74
22.79
22.56
20.93
18.18
17.91
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

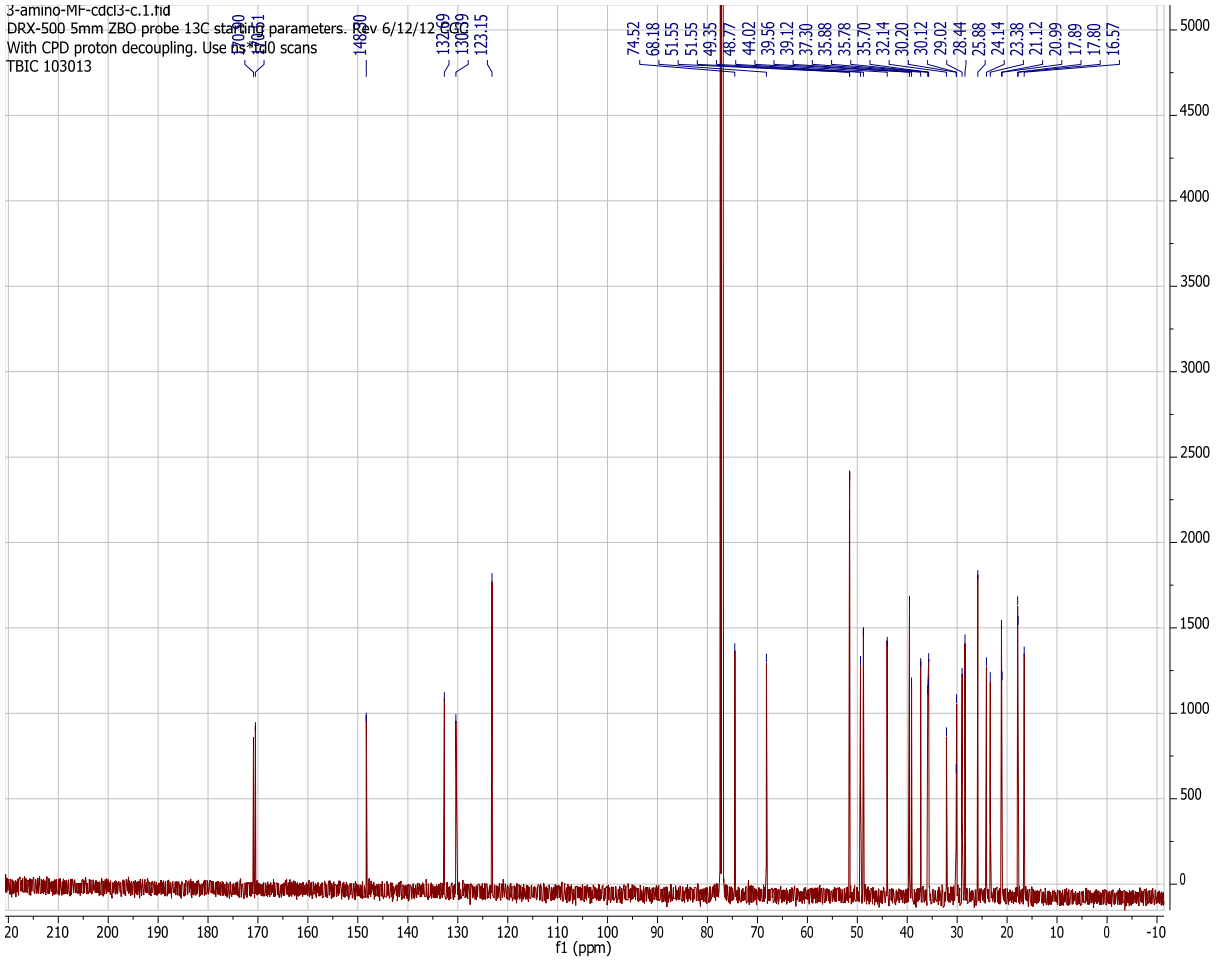
Fusidic lactam (lower Rf) (2i):



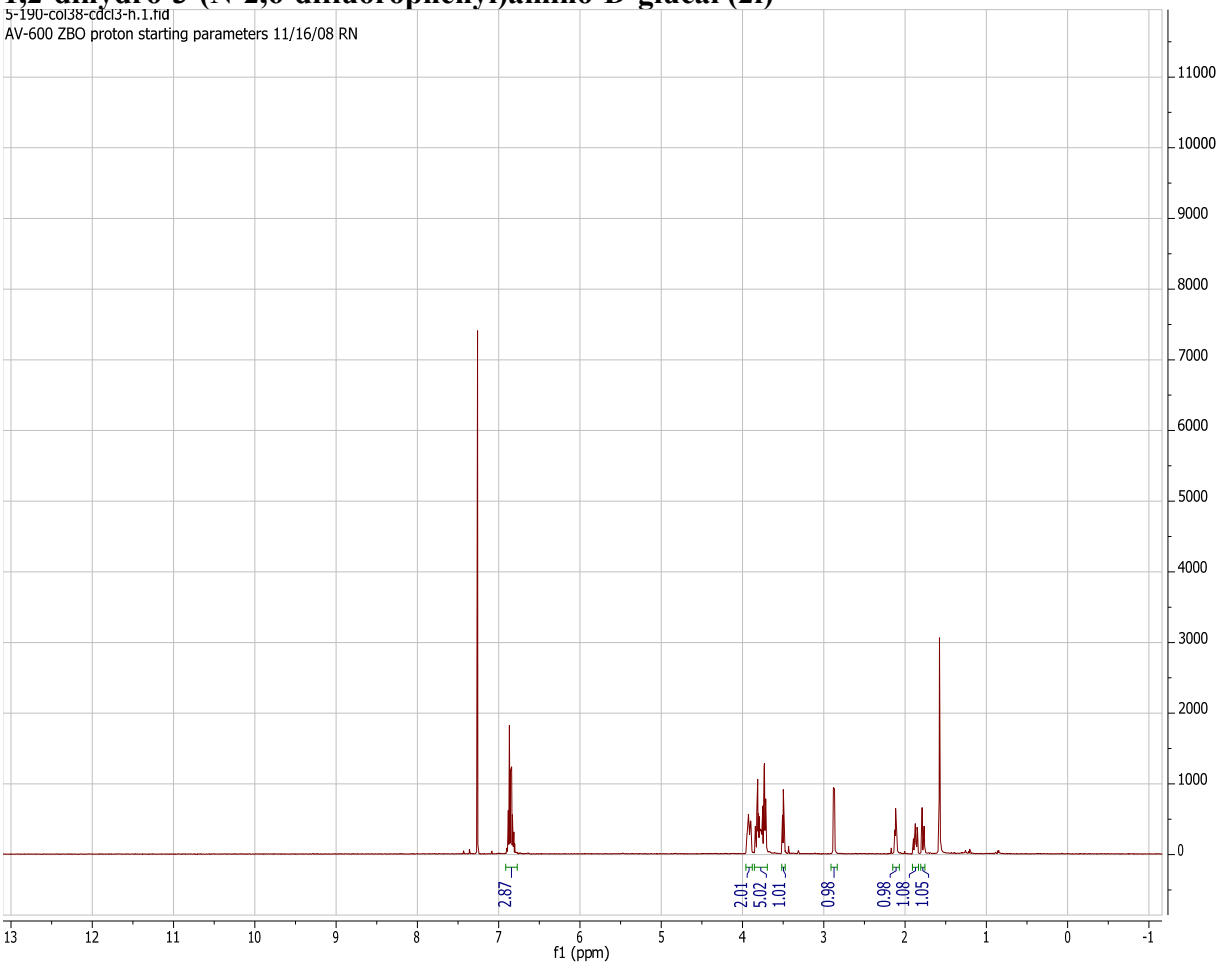

famelac-lowRf-c.21.1.1r
180.56
170.60
170.50
148.44
132.78
131.07
123.17
74.36
68.40
51.60
49.25
48.11
44.16
43.80
39.48
39.35
39.23
38.66
37.99
36.86
36.35
29.13
28.35
26.04
25.89
24.21
21.12
18.27
17.92
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

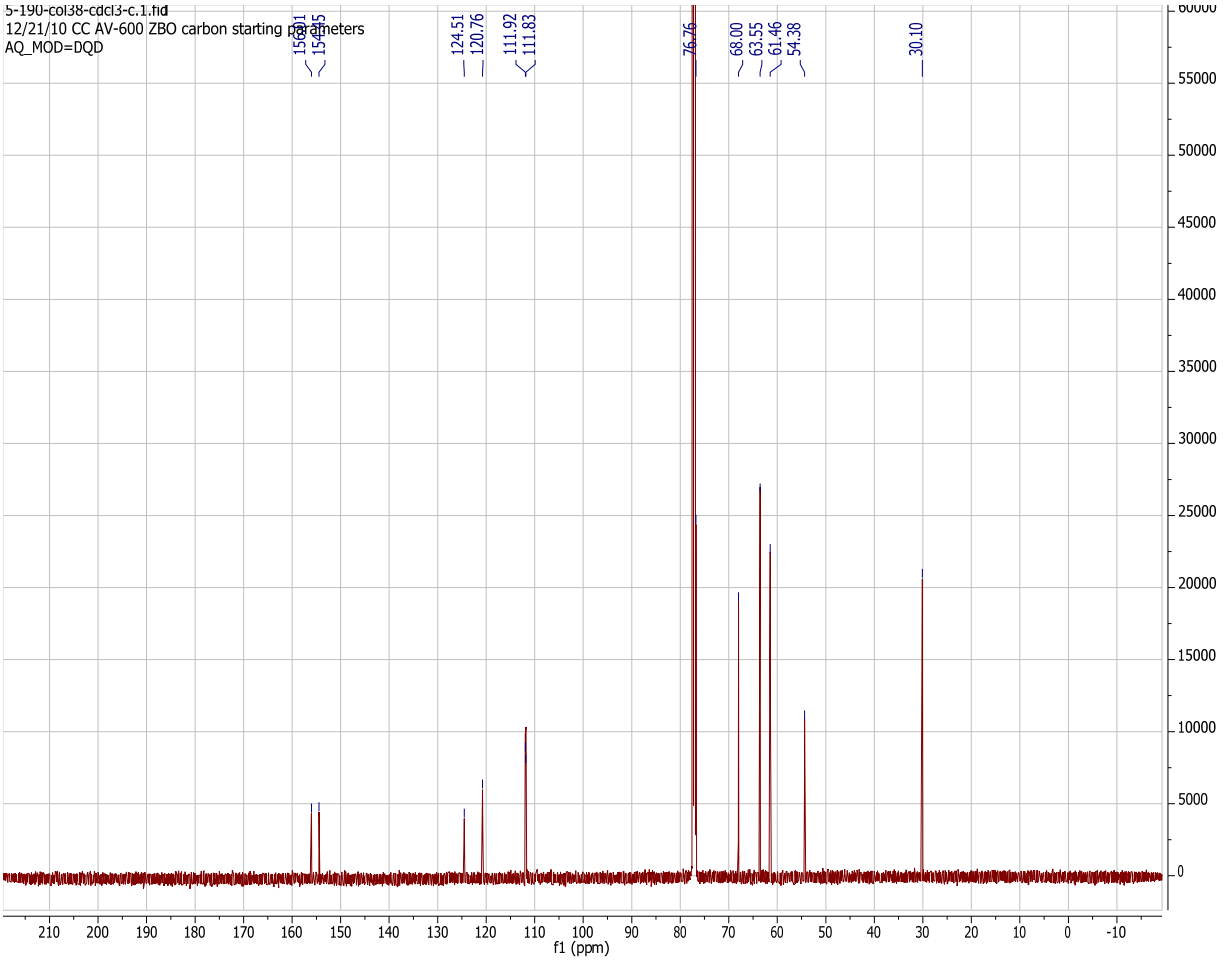
3-amino-fusidic acid methyl ester (2j):



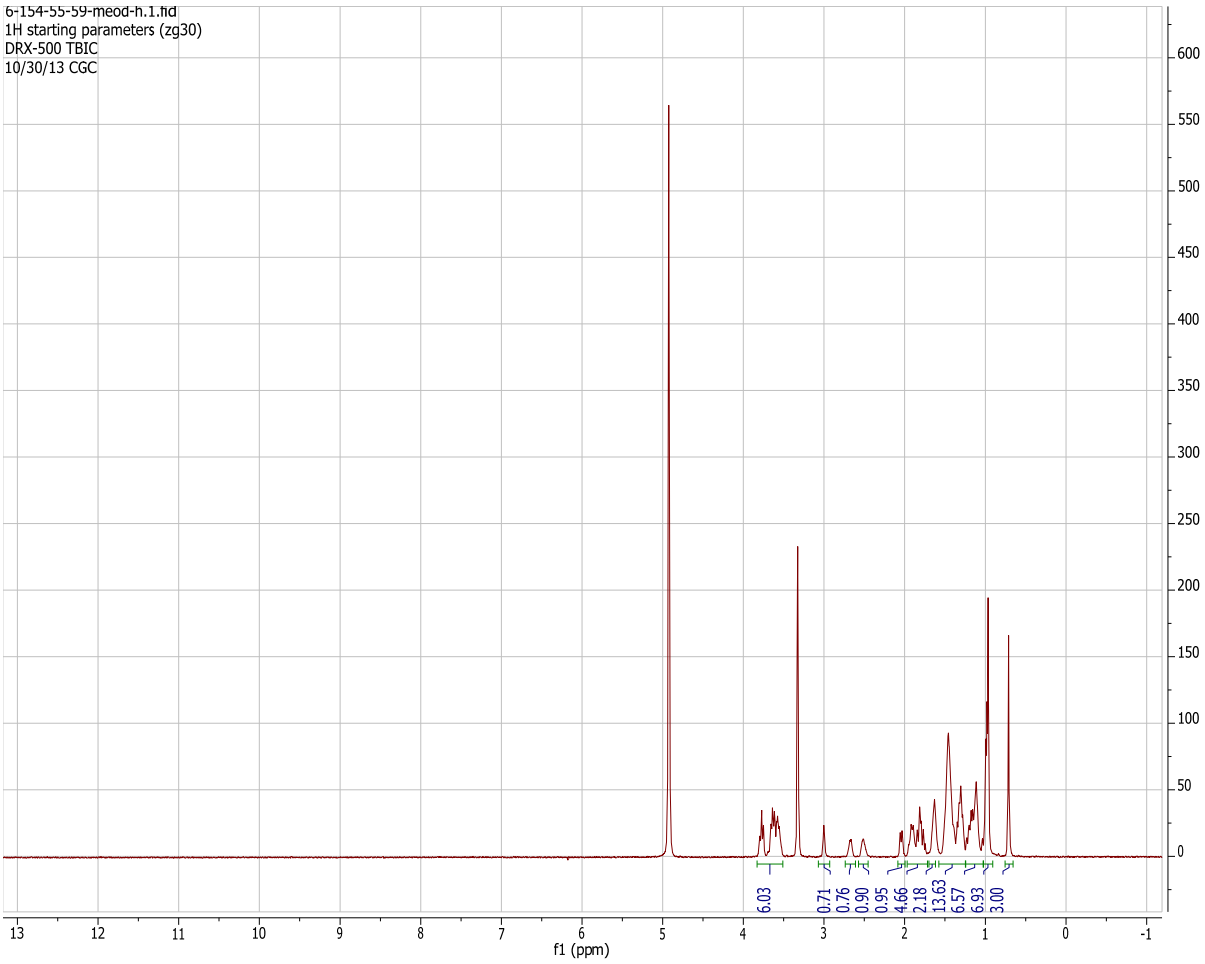

3-amino-MF-cdcl3-c.1.fid
DRX-500 5mm ZBO probe 13C standard parameters. Rev 6/12/12 EGM
With CPD proton decoupling. Use ns = 1000 scans
TBIC 103013
169.90
169.51
148.00
132.99
130.09
123.15
74.52
68.18
51.55
51.55
49.35
48.77
44.02
39.56
39.12
37.30
35.88
35.78
35.70
32.14
30.20
30.12
29.02
28.44
25.88
24.14
23.38
21.12
20.99
17.89
17.80
16.57
f1 (ppm)

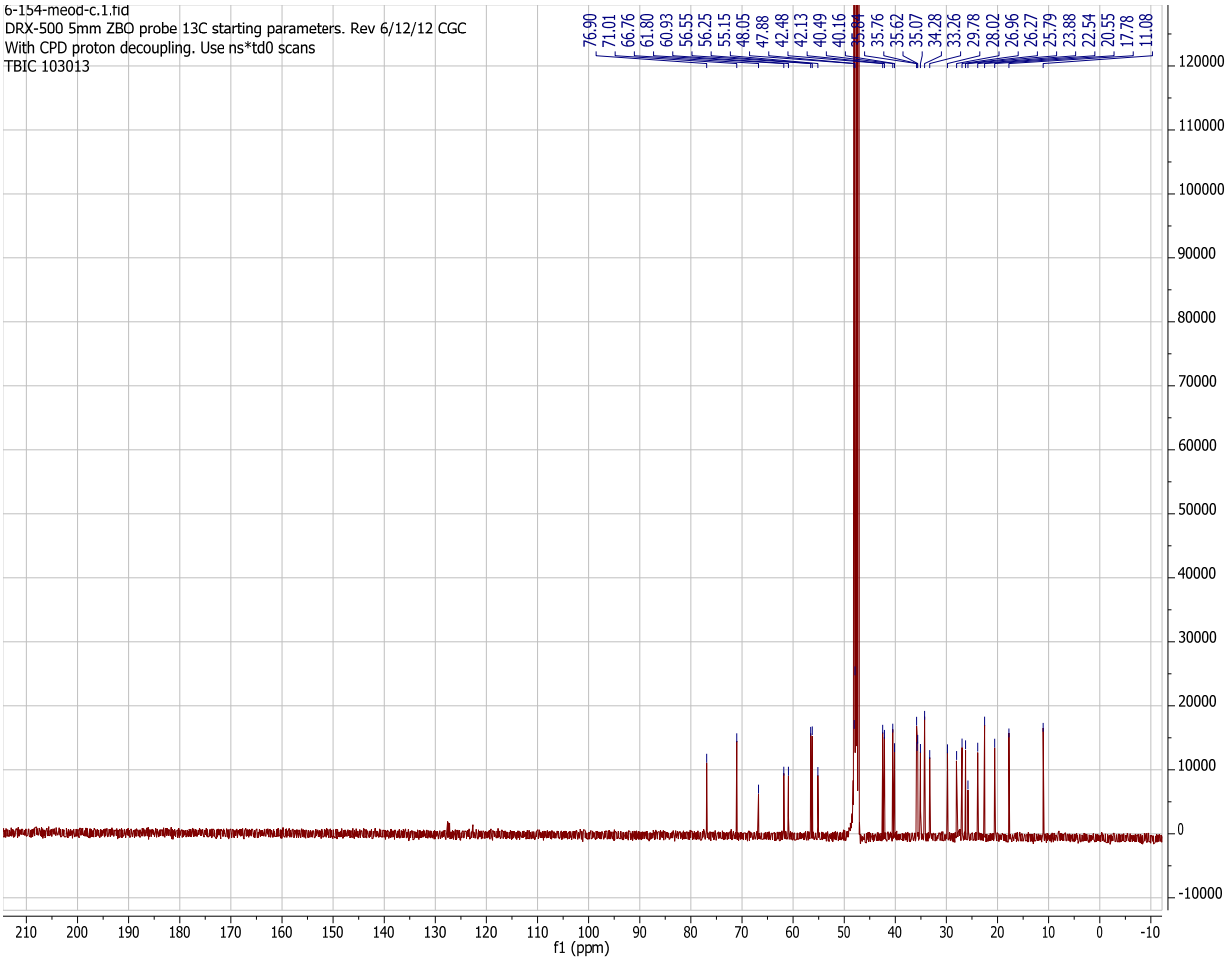
1,2-dihydro-3-(N-2,6-difluorophenyl)amino-D-glucal (2l)



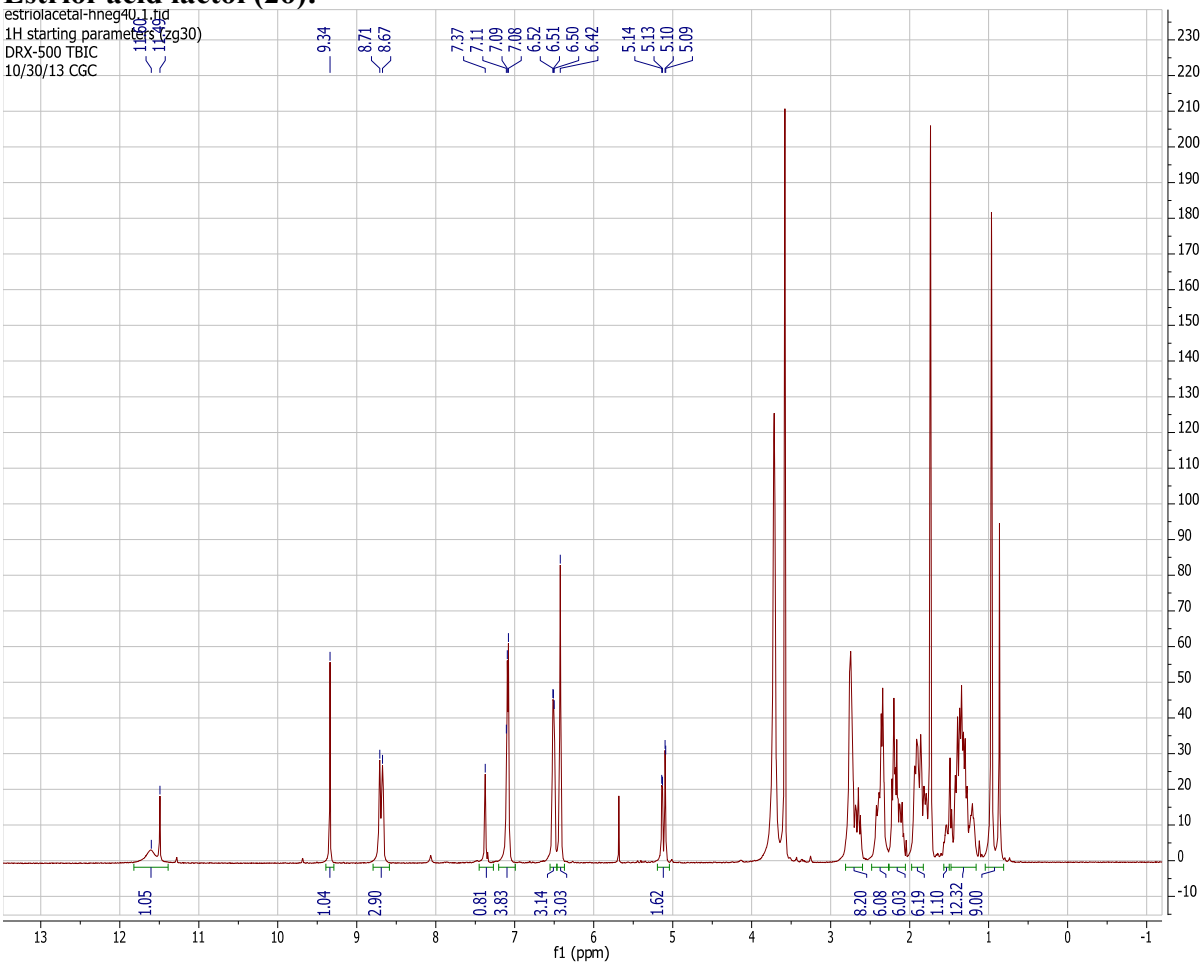

5-190-col38-cdcl3-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
156.01
154.55
124.51
120.76
111.92
111.83
76.76
68.00
63.55
61.46
54.38
30.10
f1 (ppm)

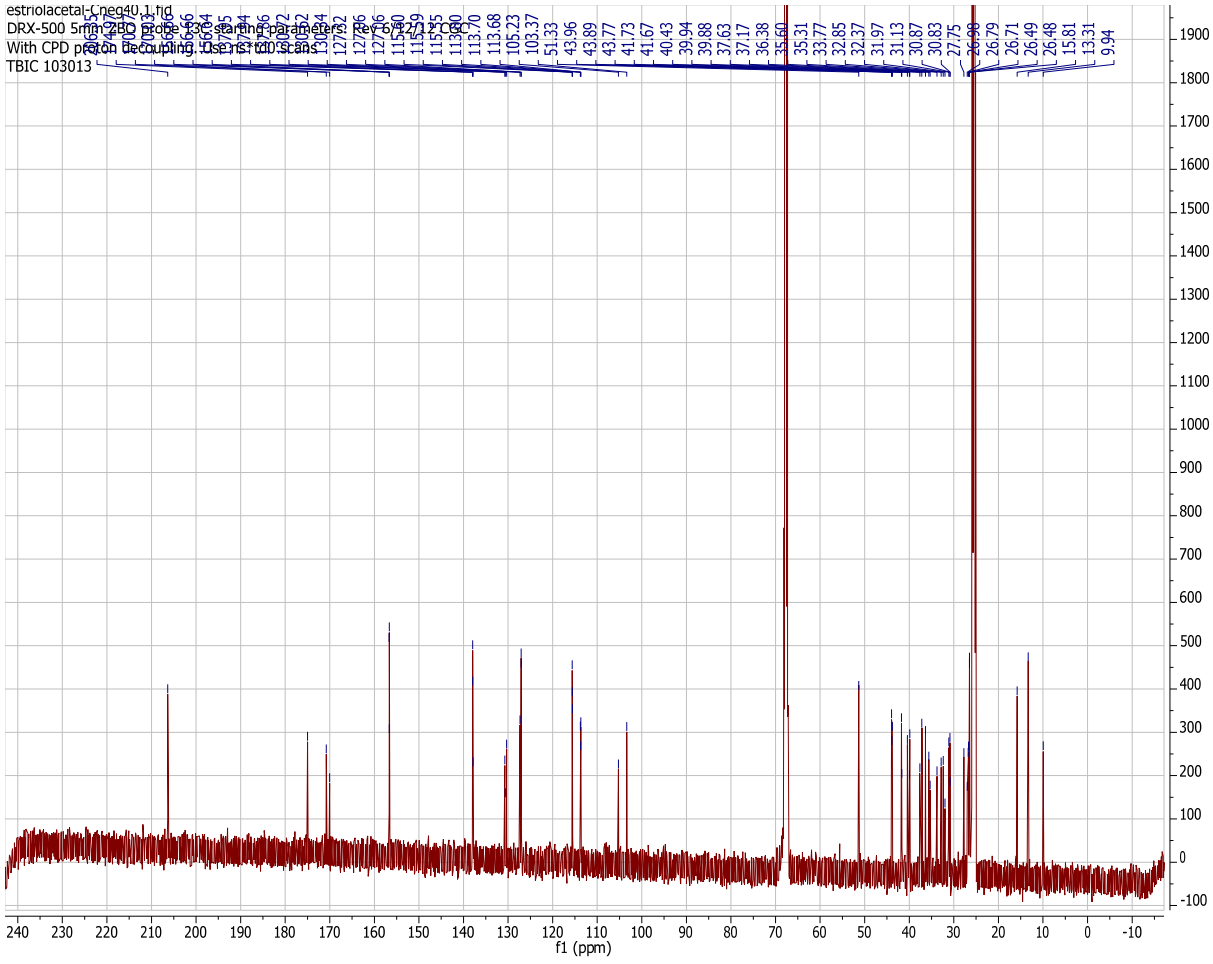
1,2-dihydro-3-(N-lithocholic)amino-D-glucal (2m)



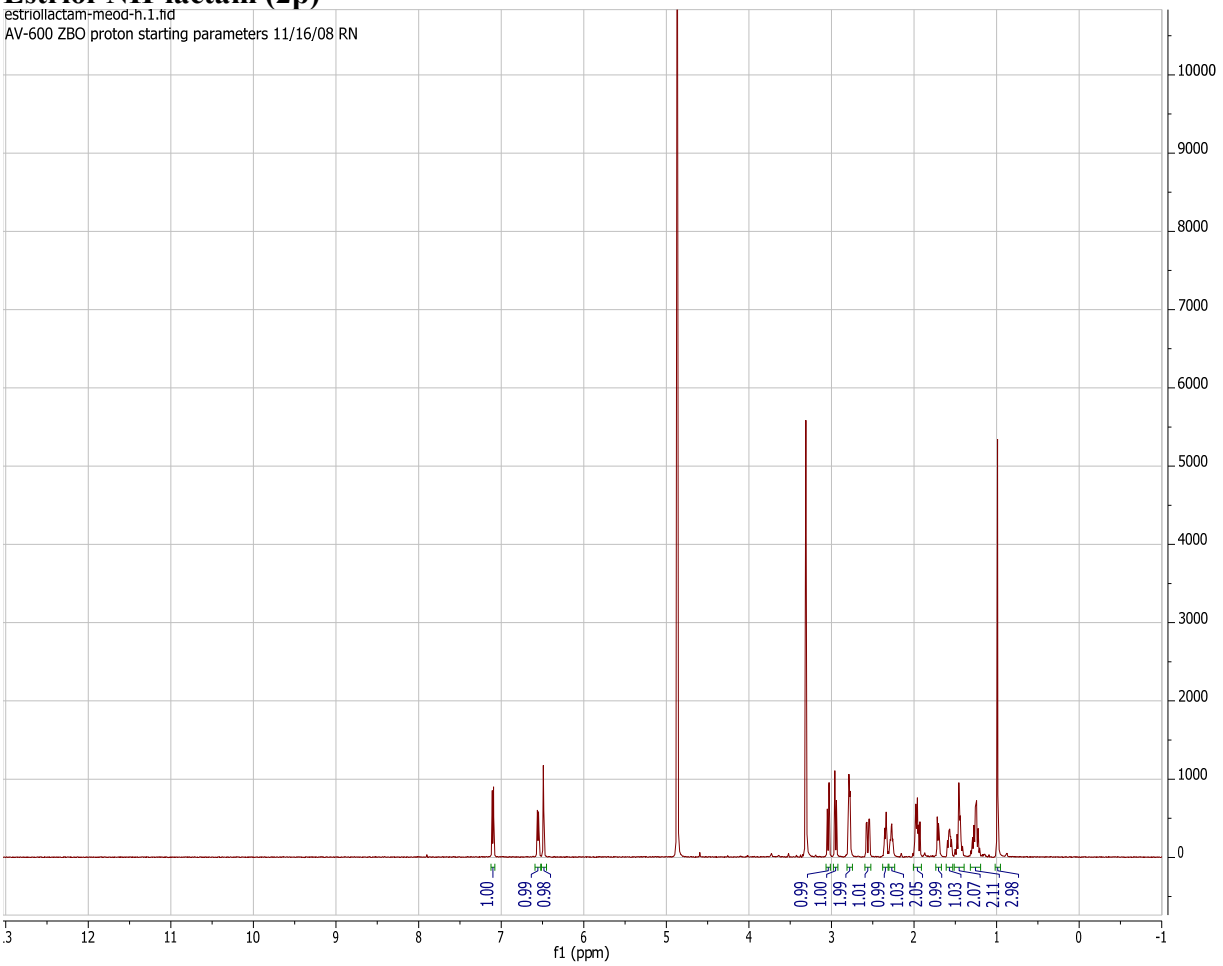

6-154-meod-c.1.fid
DRX-500 5mm ZBO probe 13C starting parameters. Rev 6/12/12 CGC
With CPD proton decoupling. Use ns*td0 scans
TBIC 103013
76.90
71.01
66.76
61.80
60.93
56.55
56.25
55.15
48.05
47.88
42.48
42.13
40.49
40.16
35.76
35.62
35.07
34.28
33.26
29.78
28.02
26.96
26.27
25.79
23.88
22.54
20.55
17.78
11.08
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

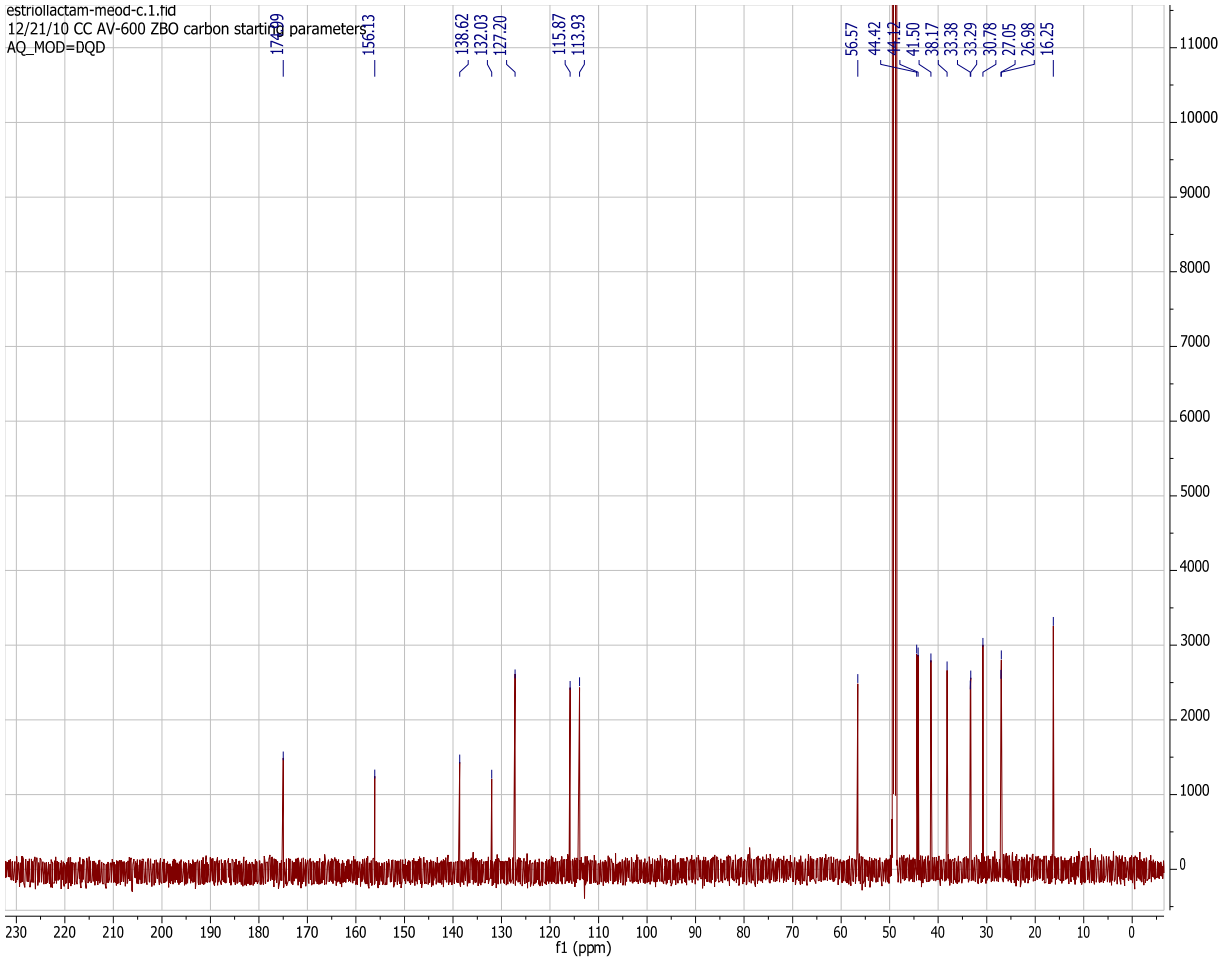
Estriol-acid lactol (2o):



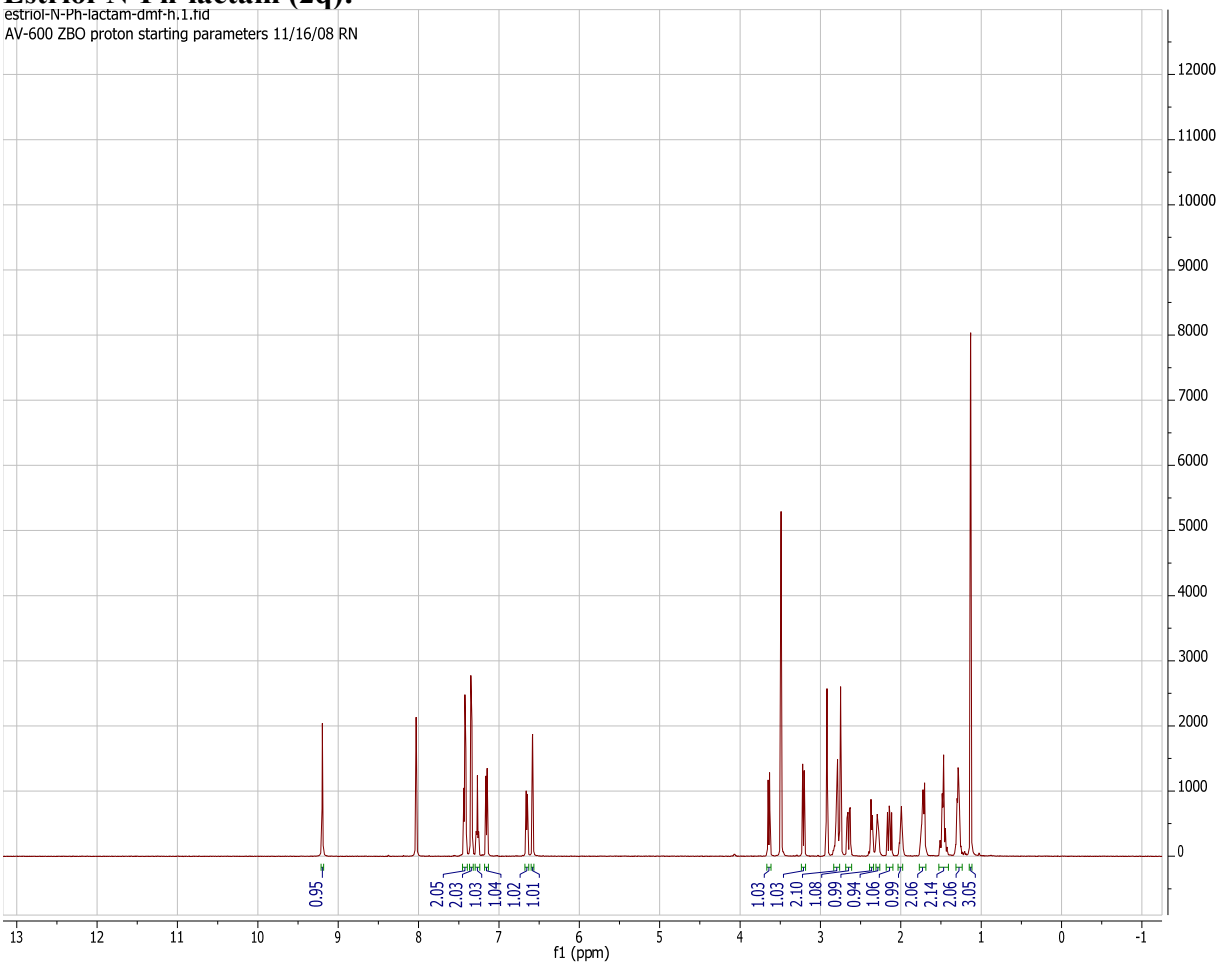

estriolacetal-Cneq40.1.fid
DRX-500 5mm ZBO probe 13C starting parameters: Rev 6/27/12 CDC
With CPD proton decoupling - Use ns for 1D scans
TBIC 103013
f1 (ppm)

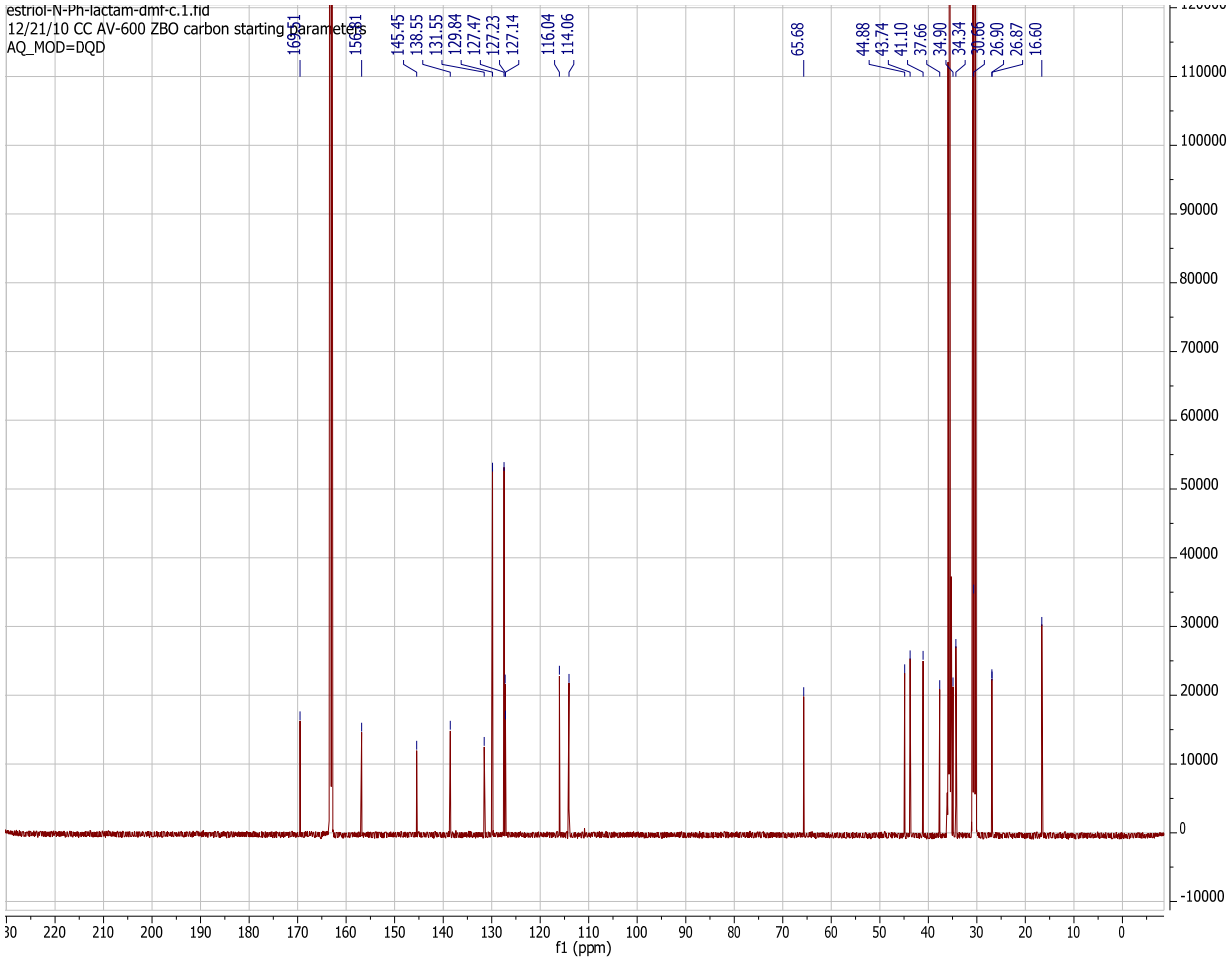
Estriol-NH-lactam (2p)



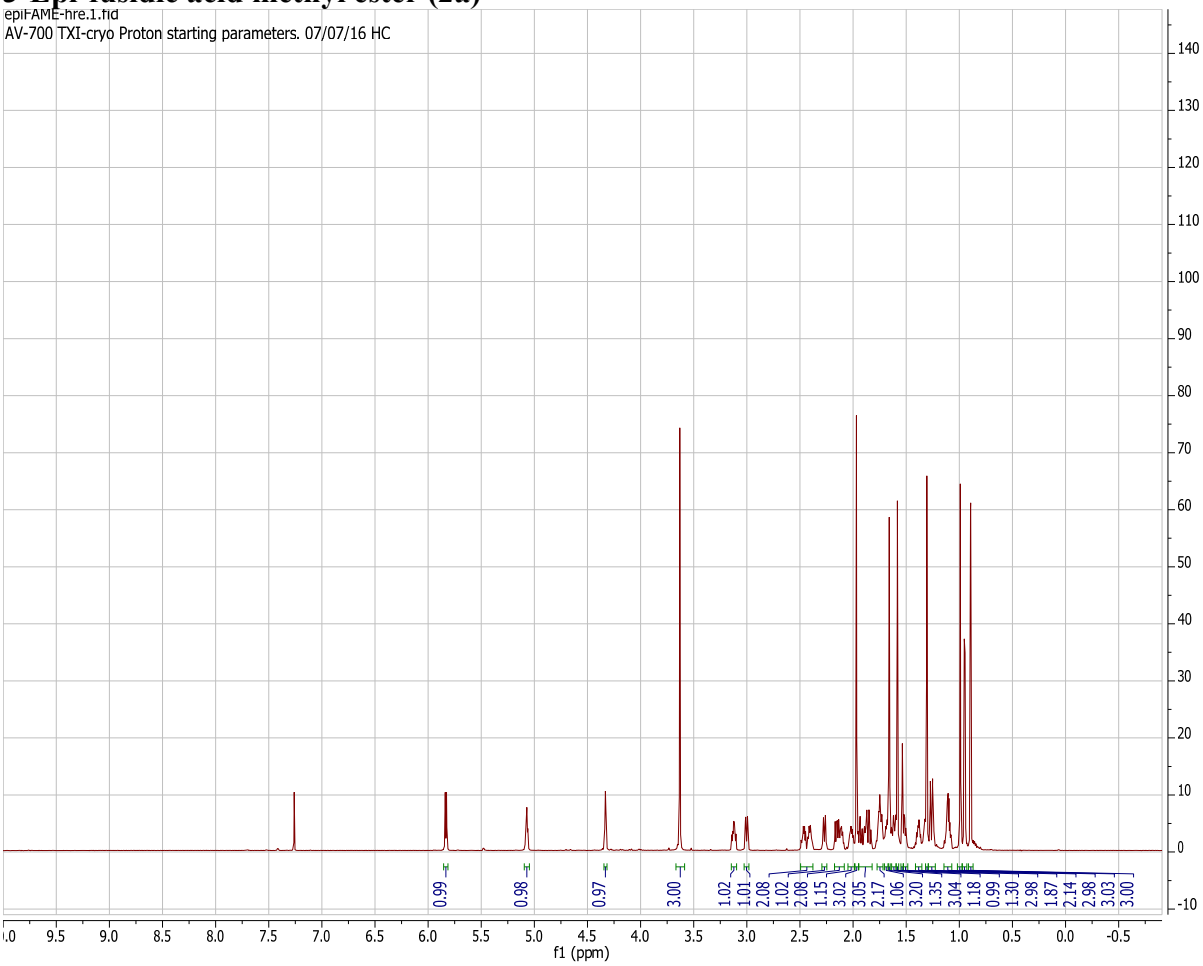

estriollactam-meod-c.1.fid
12/21/10 CC AV-600 ZBO carbon startup parameters
AQ_MOD=DQD
174.99
156.13
138.62
132.03
127.20
115.87
113.93
56.57
44.42
44.12
41.50
38.17
33.38
33.29
30.78
27.05
26.98
16.25
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

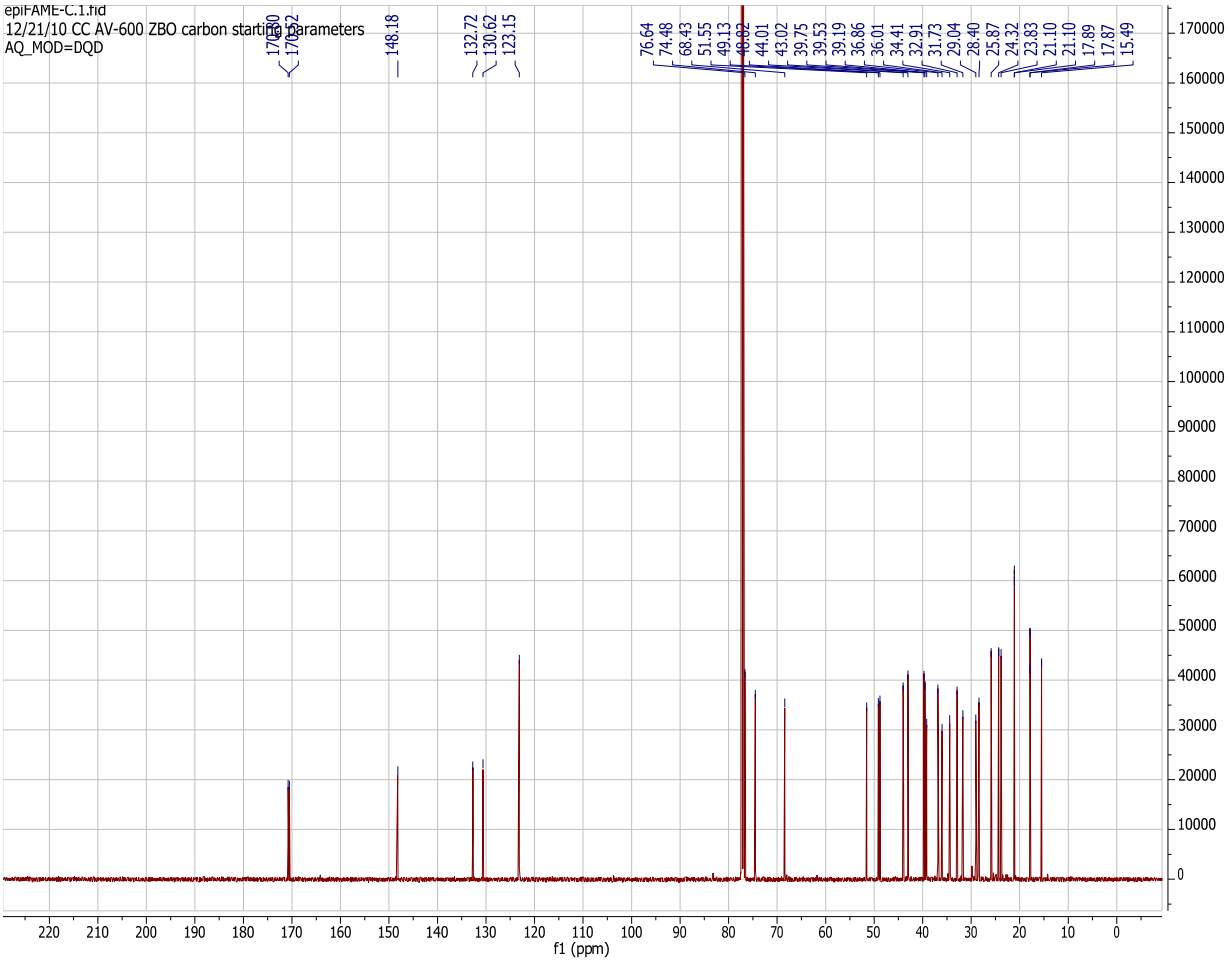
Estriol-N-Ph-lactam (2q):



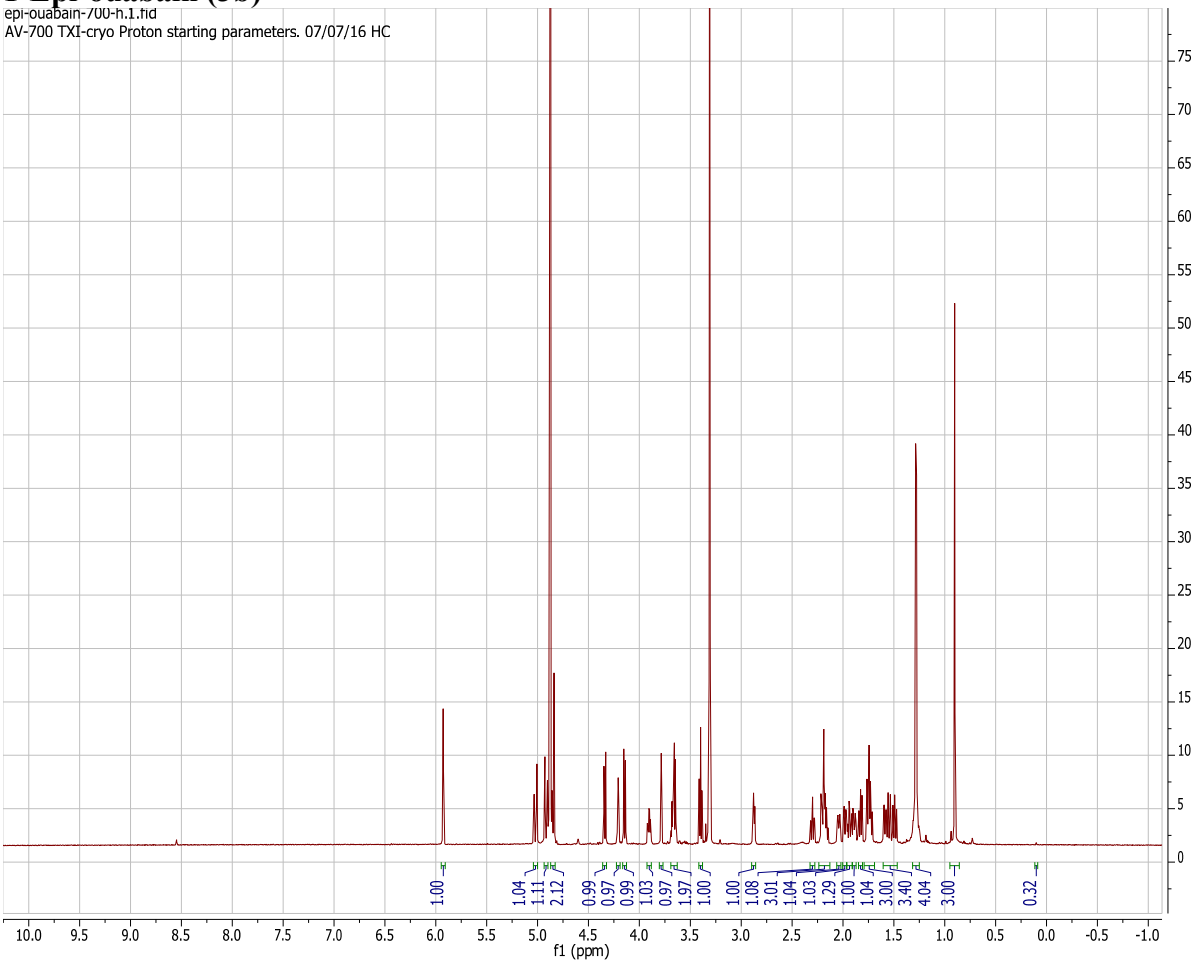

estriol-N-Ph-lactam-dmf-c.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
169.21
156.31
145.45
138.55
131.55
129.84
127.47
127.23
127.14
116.04
114.06
65.68
44.88
43.74
41.10
37.66
34.90
34.34
30.66
26.90
26.87
16.60
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

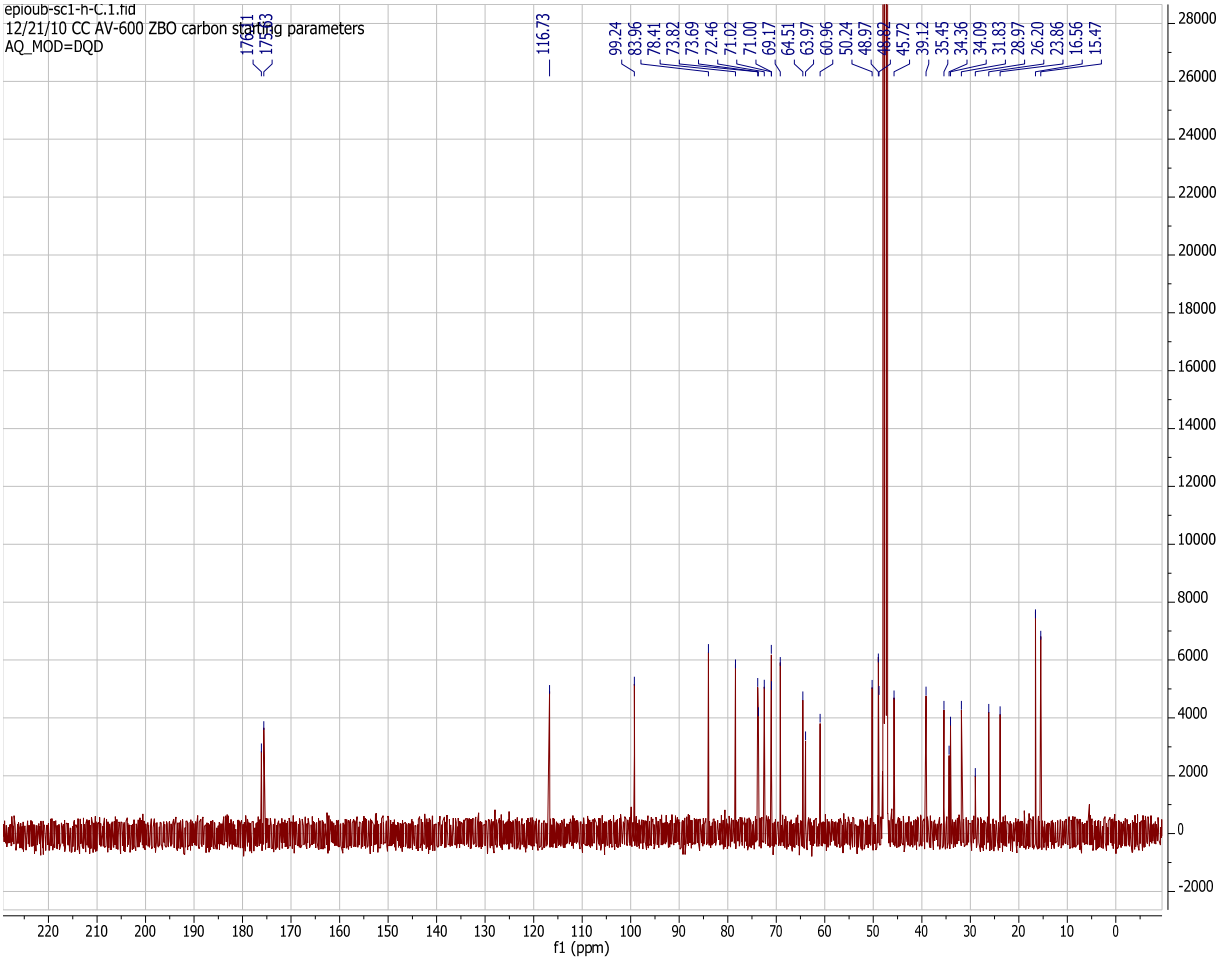
3-Epi-fusidic acid methyl ester (2a)




epiFAME-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
170.80
170.62
148.18
132.72
130.62
123.15
76.64
74.48
68.43
51.55
49.13
48.82
44.01
43.02
39.75
39.53
39.19
36.86
36.01
34.41
32.91
31.73
29.04
28.40
25.87
24.32
23.83
21.10
21.10
17.89
17.87
15.49
f1 (ppm)

1-Epi-ouabain (3b)




epioub-sc1-h-C.1.fid
12/21/10 CC AV-600 ZBO carbon starting parameters
AQ_MOD=DQD
176.11
175.83
116.73
99.24
83.96
78.41
73.82
73.69
72.46
71.02
71.00
69.17
64.51
63.97
60.96
50.24
48.97
48.83
45.72
39.12
35.45
34.36
34.09
31.83
28.97
26.20
23.86
16.56
15.47
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

11. X-ray structure collection conditions, crystal data, and selected bond lengths and angles

$[Ru(PEt_3)_6(OTf)_3][OTf]$ (Ru-2)

Collection conditions and crystal data:

A yellow prism 0.120 x 0.100 x 0.100 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 50 mm and exposure time was 10 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 25.000° in θ. A total of 72674 reflections were collected covering the indices, -16<=*h*<=16, -17<=*k*<=17, -21<=*l*<=21. 12686 reflections were found to be symmetry independent, with an R_{int} of 0.0435. Indexing and unit cell refinement indicated a primitive, triclinic lattice. The space group was found to be P -1 (No. 2). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 13.5505(6) Å	□= 87.2530(10)°.
	b = 14.5882(7) Å	□= 89.5790(10)°.
	c = 17.5957(8) Å	□ = 85.8470(10)°.
Volume	3465.1(3) $Å^3$	
Z	2	
Density (calculated)	1.445 Mg/m^3	
Absorption coefficient	0.773 mm^{-1}	
F(000)	1552	
Crystal size	0.120 x 0.100 x 0.100 mm^3	
Theta range for data collection	1.159 to 25.373°.	
Index ranges	-16<=h<=16, -17<=k<=17, -21<=l<=21	
Reflections collected	72674	
Independent reflections	12686 [R(int) = 0.0435]	
Completeness to theta = 25.000°	99.9 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.928 and 0.837
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	12686 / 0 / 663
Goodness-of-fit on F^2	1.058
Final R indices [I>2sigma(I)]	R1 = 0.0716, wR2 = 0.1933
R indices (all data)	R1 = 0.0856, wR2 = 0.2090
Extinction coefficient	n/a
Largest diff. peak and hole	3.096 and -3.176 e.$Å^{-3}$

Bond lengths (angstroms)

O(1)-Ru(1)	2.237(4)
O(3)-Ru(2)	2.275(4)
O(4)-Ru(1)	2.277(4)
O(6)-Ru(2)	2.221(4)
O(7)-Ru(1)	2.284(4)
O(9)-Ru(2)	2.268(4)
P(1)-Ru(1)	2.2826(16)
P(2)-Ru(1)	2.2770(16)
P(3)-Ru(1)	2.2870(16)
P(4)-Ru(2)	2.2853(17)
P(5)-Ru(2)	2.2798(18)
P(6)-Ru(2)	2.2813(17)

Bond angles (degrees)

O(1)-Ru(1)-P(2)	92.88(12)
O(1)-Ru(1)-O(4)	82.29(15)
P(2)-Ru(1)-O(4)	88.41(12)
O(1)-Ru(1)-P(1)	171.31(12)
P(2)-Ru(1)-P(1)	94.77(6)
O(4)-Ru(1)-P(1)	93.81(12)
O(1)-Ru(1)-O(7)	79.45(16)
P(2)-Ru(1)-O(7)	169.11(12)
O(4)-Ru(1)-O(7)	82.93(16)
P(1)-Ru(1)-O(7)	92.40(12)
O(1)-Ru(1)-P(3)	86.69(12)
P(2)-Ru(1)-P(3)	94.16(6)
O(4)-Ru(1)-P(3)	168.80(12)
P(1)-Ru(1)-P(3)	96.84(6)
O(7)-Ru(1)-P(3)	93.12(12)
O(6)-Ru(2)-O(9)	79.50(16)
O(6)-Ru(2)-O(3)	82.73(17)
O(9)-Ru(2)-O(3)	81.88(16)
O(6)-Ru(2)-P(5)	169.04(13)
O(9)-Ru(2)-P(5)	91.83(12)
O(3)-Ru(2)-P(5)	89.46(13)
O(6)-Ru(2)-P(6)	89.94(13)
O(9)-Ru(2)-P(6)	92.77(12)
O(3)-Ru(2)-P(6)	171.60(12)
P(5)-Ru(2)-P(6)	97.21(6)
O(6)-Ru(2)-P(4)	92.43(13)
O(9)-Ru(2)-P(4)	169.84(12)
O(3)-Ru(2)-P(4)	91.04(12)
P(5)-Ru(2)-P(4)	95.41(7)
P(6)-Ru(2)-P(4)	93.39(6)

$[Ru_2Cl_3(PEt_2(p\text{-}Me_2N\text{-}Ph))_6][Cl]$

Collection conditions and crystal data:

A yellow prism 0.060 x 0.050 x 0.040 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 20 seconds per frame using a scan width of 1.0°. Data collection was 100.0% complete to 25.000° in □. A total of 21926 reflections were collected covering the indices, -22<=*h*<=23, -22<=*k*<=22, -34<=*l*<=53. 2934 reflections were found to be symmetry independent, with an R_{int} of 0.0229. Indexing and unit cell refinement indicated a obverse, trigonal lattice. The space group was found to be R -3 c :H (No. 167). The

data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2016). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2016.

Wavelength	0.71073 Å	
Crystal system	Trigonal	
Space group	R -3 c :H	
Unit cell dimensions	a = 19.1308(14) Å	□= 90°.
	b = 19.1308(14) Å	□= 90°.
	c = 45.364(3) Å	□ = 120°.
Volume	14378(2) $Å^3$	
Z	6	
Density (calculated)	1.304 Mg/m^3	
Absorption coefficient	0.553 mm^{-1}	
F(000)	6011	
Crystal size	0.060 x 0.050 x 0.040 mm^3	
Theta range for data collection	1.522 to 25.342°.	
Index ranges	-22<=h<=23, -22<=k<=22, -34<=l<=53	
Reflections collected	21926	
Independent reflections	2934 [R(int) = 0.0229]	
Completeness to theta = 25.000°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.928 and 0.863	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2934 / 0 / 172	
Goodness-of-fit on F^2	1.082	
Final R indices [I>2sigma(I)]	R1 = 0.0596, wR2 = 0.1480	
R indices (all data)	R1 = 0.0654, wR2 = 0.1543	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.375 and -0.956 e.$Å^{-3}$	

Bond lengths (angstroms)

P(1)-Ru(1)	2.3147(10)
Cl(1)-Ru(1)	2.4717(10)

Bond angles (degrees)

C(2)-C(1)-P(1)	117.5(3)
Ru(1)-Cl-Ru(1)	87.57(4)
P(1)-Ru(1)-P(1)	97.58(4)
P(1)-Ru(1)-Cl(1)	165.35(4)
P(1)#2-Ru(1)-Cl(1)	88.99(3)
P(1)#3-Ru(1)-Cl(1)	94.51(3)
Cl(1)-Ru(1)-Cl(1)	77.40(3)

[Ru(PEt$_3$)$_3$(DAB III alkoxide)][OTf]

Collection conditions and crystal data:

A purple plate 0.060 x 0.060 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 50 mm and exposure time was 20 seconds per frame using a scan width of 2.0°. Data collection was 100.0% complete to 25.000° in θ. A total of 62451 reflections were collected covering the indices, -20<=*h*<=21, -27<=*k*<=28, -17<=*l*<=16. 10935 reflections were found to be symmetry independent, with an R_{int} of 0.0572. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 2 (No. 18). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 2	
Unit cell dimensions	a = 18.0432(12) Å	□= 90°.
	b = 23.4251(15) Å	□= 90°.
	c = 14.1114(9) Å	□ = 90°.
Volume	5964.4(7) Å^3	
Z	4	
Density (calculated)	1.361 Mg/m^3	
Absorption coefficient	0.447 mm^{-1}	

F(000)	2584
Crystal size	0.060 x 0.060 x 0.030 mm^3
Theta range for data collection	1.425 to 25.385°.
Index ranges	-20<=h<=21, -27<=k<=28, -17<=l<=16
Reflections collected	62451
Independent reflections	10935 [R(int) = 0.0572]
Completeness to theta = 25.000°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.928 and 0.835
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10935 / 0 / 659
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0530, wR2 = 0.1272
R indices (all data)	R1 = 0.0604, wR2 = 0.1319
Absolute structure parameter	-0.049(11)
Extinction coefficient	n/a
Largest diff. peak and hole	1.168 and -0.686 e.$Å^{-3}$

Bond lengths (angstroms)

O(1)-Ru(1)	2.019(5)
O(2)-Ru(1)	2.146(4)
P(1)-Ru(1)	2.2894(19)
P(2)-Ru(1)	2.2274(19)
P(3)-Ru(1)	2.2932(18)

Bond angles (degrees)

O(1)-Ru(1)-O(2)	77.73(17)
O(1)-Ru(1)-P(2)	109.00(15)
O(2)-Ru(1)-P(2)	93.62(14)
O(1)-Ru(1)-P(1)	91.27(14)
O(2)-Ru(1)-P(1)	166.03(13)
P(2)-Ru(1)-P(1)	98.15(7)
O(1)-Ru(1)-P(3)	155.43(14)
O(2)-Ru(1)-P(3)	91.46(13)
P(2)-Ru(1)-P(3)	93.48(7)
P(1)-Ru(1)-P(3)	95.30(7)

7-epi-13-keto-deacetylbaccatin III (1l)

Collection conditions and crystal data:

A colorless blade 0.060 x 0.050 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 10 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 67.000° in θ. A total of 58052 reflections were collected covering the indices, -37<=*h*<=37, -9<=*k*<=9, -14<=*l*<=14. 5502 reflections were found to be symmetry independent, with an R_{int} of 0.0357. Indexing and unit cell refinement indicated a C-centered, monoclinic lattice. The space group was found to be C 2 (No. 5). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	C 2	
Unit cell dimensions	a = 31.069(5) Å	□= 90°.
	b = 8.3615(14) Å	□= 108.006(6)°.
	c = 12.387(2) Å	□ = 90°.
Volume	3060.3(9) $Å^3$	
Z	4	
Density (calculated)	1.178 Mg/m^3	
Absorption coefficient	0.741 mm^{-1}	
F(000)	1152	
Crystal size	0.060 x 0.050 x 0.030 mm^3	
Theta range for data collection	2.991 to 68.393°.	
Index ranges	-37<=h<=37, -9<=k<=9, -14<=l<=14	
Reflections collected	58052	
Independent reflections	5502 [R(int) = 0.0357]	
Completeness to theta = 67.000°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.929 and 0.802	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5502 / 1 / 360	
Goodness-of-fit on F^2	1.079	
Final R indices [I>2sigma(I)]	R1 = 0.0284, wR2 = 0.0756	

R indices (all data)	R1 = 0.0285, wR2 = 0.0757
Absolute structure parameter	0.08(2)
Extinction coefficient	n/a
Largest diff. peak and hole	0.328 and -0.219 e.Å^{-3}

Bond lengths (angstroms):

C13 carbonyl	1.213(3)

Andrographolide-isoxazole (2c)

Collection conditions and crystal data:

A colorless rod 0.060 x 0.050 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 1 seconds per frame using a scan width of 2.0°. Data collection was 99.9% complete to 67.000° in θ. A total of 11847 reflections were collected covering the indices, -7<=*h*<=7, -10<=*k*<=10, -20<=*l*<=20. 3291 reflections were found to be symmetry independent, with an R_{int} of 0.0294. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014. Absolute stereochemistry was unambiguously determined to be *R* at C11 and *S* at C1, C6, C7, and C20, respectively.

Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 6.4097(3) Å	□= 90°.
	b = 8.4981(5) Å	□= 99.264(2)°.
	c = 16.8156(9) Å	□ = 90°.
Volume	904.00(8) Å^3	
Z	2	
Density (calculated)	1.269 Mg/m^3	
Absorption coefficient	0.709 mm^{-1}	
F(000)	372	
Crystal size	0.060 x 0.050 x 0.030 mm^3	

Theta range for data collection	2.662 to 68.471°.
Index ranges	-7<=h<=7, -10<=k<=10, -20<=l<=20
Reflections collected	11847
Independent reflections	3291 [R(int) = 0.0294]
Completeness to theta = 67.000°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.850
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3291 / 1 / 229
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0279, wR2 = 0.0753
R indices (all data)	R1 = 0.0285, wR2 = 0.0758
Absolute structure parameter	0.10(6)
Extinction coefficient	n/a
Largest diff. peak and hole	0.205 and -0.118 e.Å^{-3}

Bond lengths (angstroms):

Isoxazole C=N	1.273(3)
Isoxazole N-O	1.435(3)
Isoxazole C-O	1.447(3)

Bond angles (degrees)

Isoxazole C-N-O	107.43(18)
Isoxazole N-O-C	107.53(14)

Andrographolide lactam (2d)

Collection conditions and crystal data:

A colorless prism 0.080 x 0.050 x 0.050 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 1 seconds per frame using a scan width of 2.0°. Data collection was 98.0% complete to 67.000° in □. A total of 12578 reflections were collected covering the indices, -7<=*h*<=6, -10<=*k*<=10, -20<=*l*<=20. 3362 reflections were found to be symmetry independent, with an R_{int} of 0.0274. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21 (No. 4). The data were

integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2016). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2016. Absolute stereochemistry was unambiguously determined to be *R* at C1 and C6, and *S* at C5, C10, and C18, respectively.

Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 6.3381(3) Å	□= 90°.
	b = 9.0722(5) Å	□= 97.521(2)°.
	c = 16.6745(9) Å	□ = 90°.
Volume	950.54(9) $Å^3$	
Z	2	
Density (calculated)	1.270 Mg/m^3	
Absorption coefficient	0.739 mm^{-1}	
F(000)	392	
Crystal size	0.080 x 0.050 x 0.050 mm^3	
Theta range for data collection	5.352 to 68.207°.	
Index ranges	-7<=h<=6, -10<=k<=10, -20<=l<=20	
Reflections collected	12578	
Independent reflections	3362 [R(int) = 0.0274]	
Completeness to theta = 67.000°	98.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.929 and 0.839	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3362 / 1 / 239	
Goodness-of-fit on F^2	1.052	
Final R indices [I>2sigma(I)]	R1 = 0.0270, wR2 = 0.0701	
R indices (all data)	R1 = 0.0271, wR2 = 0.0703	
Absolute structure parameter	0.01(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.192 and -0.202 e.$Å^{-3}$	

Bond lengths (angstroms):

Lactam N-C	1.334(3)

Lactam C=O 1.244(2)

Bond angles (degrees)

Lactam N-C-O 120.61(18)

Dehydroxymethyl-andrographolide (2e)

Collection conditions and crystal data:

A colorless prism 0.060 x 0.030 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 60 mm and exposure time was 2 seconds per frame using a scan width of 2.0°. Data collection was 99.0% complete to 67.000° in θ. A total of 16979 reflections were collected covering the indices, -7<=*h*<=7, -9<=*k*<=9, -38<=*l*<=38. 3071 reflections were found to be symmetry independent, with an R_{int} of 0.0404. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be P 21 21 21 (No. 19). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT-2014) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2016). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2016. Absolute stereochemistry was unambiguously determined to be *R* at C1, C6, and C7, and *S* at C2 and C17, respectively.

Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 6.4884(2) Å	□= 90°.
	b = 8.2721(2) Å	□= 90°.
	c = 32.1550(9) Å	□ = 90°.
Volume	1725.85(8) $Å^3$	
Z	4	
Density (calculated)	1.225 Mg/m^3	
Absorption coefficient	0.682 mm^{-1}	
F(000)	688	
Crystal size	0.060 x 0.030 x 0.030 mm^3	
Theta range for data collection	2.748 to 68.403°.	
Index ranges	-7<=h<=7, -9<=k<=9, -38<=l<=38	
Reflections collected	16979	

Independent reflections	3071 [R(int) = 0.0404]
Completeness to theta = 67.000°	99.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.929 and 0.841
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3071 / 0 / 211
Goodness-of-fit on F^2	1.105
Final R indices [I>2sigma(I)]	R1 = 0.0351, wR2 = 0.0851
R indices (all data)	R1 = 0.0381, wR2 = 0.0868
Absolute structure parameter	0.01(9)
Extinction coefficient	n/a
Largest diff. peak and hole	0.155 and -0.192 e.$Å^{-3}$

Bond lengths (angstroms):

C3 carbonyl	1.213(3)