



BDG SYNTHESIS

Certificate of Analysis

BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

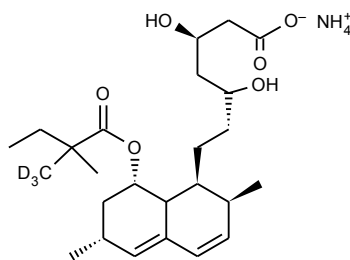
Neil Beare

Neil Beare, PhD, Director
4 December 2014

Name: Simvastatin Acid-d₃ Ammonium Salt

CAS Number: 139893-43-9 (unlabelled)

Structure:



Molecular Weight: C₂₅H₃₆D₃O₆·NH₄ = 456.63

Lot Number: BDG 10749.3

Appearance: White powder

Purity By HPLC: 98.4 %

Isotopic Purity: Under 0.5 % d₀

Re-test Date: 4 December 2019

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
Light:	protect from strong sunlight.
Caution:	only experienced laboratory personnel should handle the material.

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic Labelling: signals at the site of deuteration are greatly diminished, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: no residual solvents are observed.

Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic Labelling: signals at the site of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found m/z 462.2912. $C_{25}H_{37}D_3NaO_6$ $[M+Na]^+$ requires m/z 462.2905. The deviation of 1.5 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for d_0 material was seen (detection limit about 0.5 %).

HPLC

A sharp, symmetrical peak is observed (98.4 %). Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis

	Found:	C 65.72, H 9.01, D 1.35, N 3.03 %
$C_{25}H_{36}D_3O_6 \cdot NH_4$	Requires:	C 65.76, H 8.83, D 1.32, N 3.07 %

The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

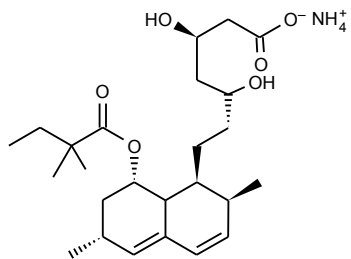
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.



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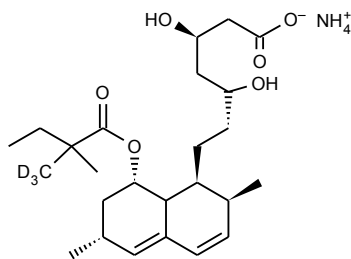
Proton NMR Spectrum of Simvastatin Acid Ammonium Salt (top) and Simvastatin Acid-d₃ Ammonium Salt (bottom) in Methanol-d₄



HOD

4xCH
4.0 H

3xCH₃+6xCH₂
+4xCH
25.1 H



Lot Number: BDG 10749.3

NMR
Solvent

4xCH
3.9 H

2xCH
2.0 H

2xCH₃+6xCH₂
+4xCH
22.1 H

2xCH₃
6.0 H

9

8

7

6

5

4

3

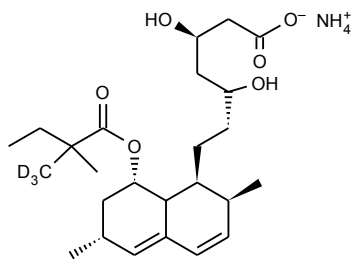
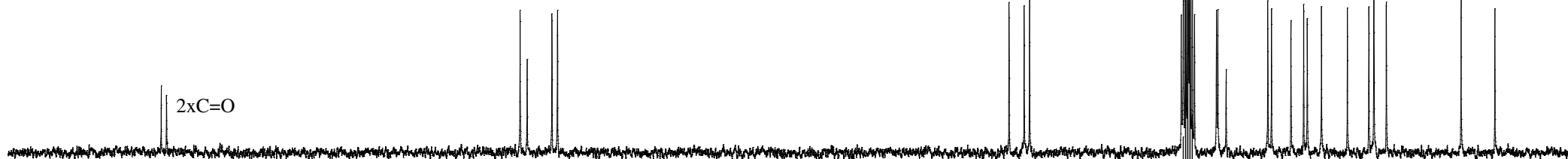
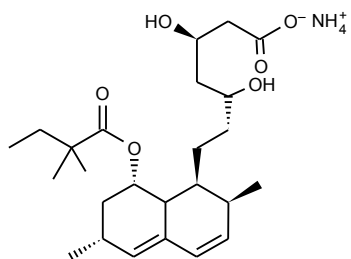
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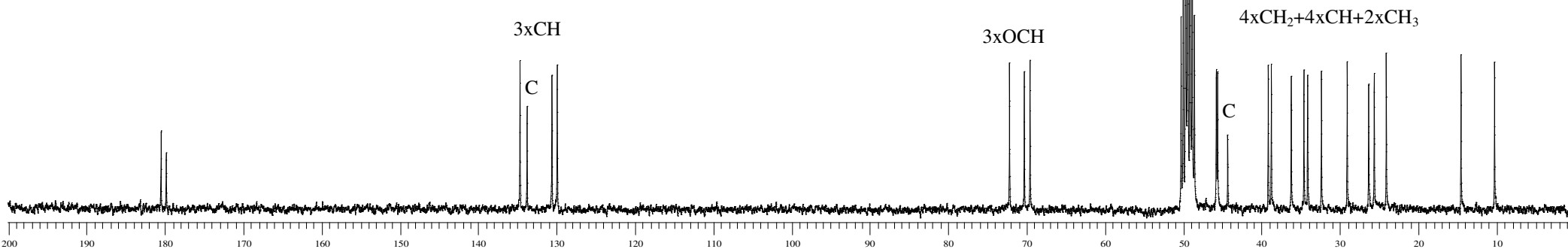


BDG SYNTHESIS

Carbon-13 NMR Spectrum of Simvastatin Acid Ammonium Salt (top) and Simvastatin Acid-d₃ Ammonium Salt (bottom) in Methanol-d₄



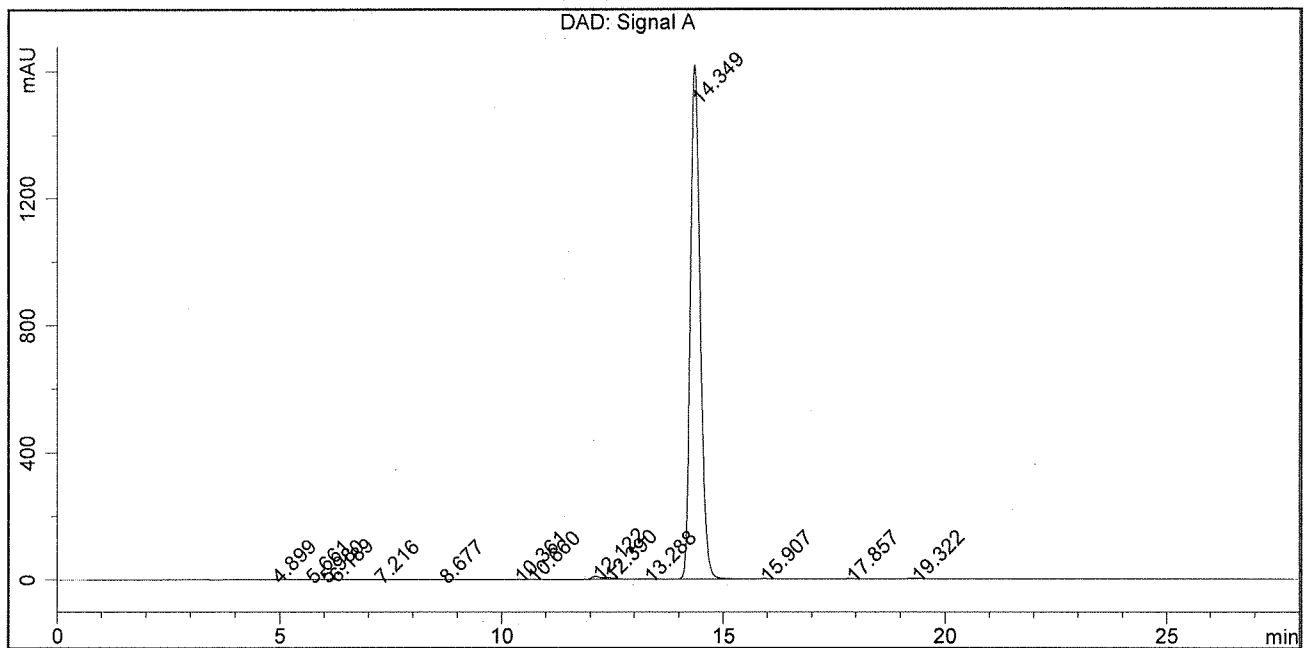
Lot Number: BDG 10749.3



BDG - Analysis of Simvastatin Acid-d3 Ammonium Salt

Column : Phenomenex Luna C18 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase A : 50:50 10 mM Potassium diHydrogen Phosphate pH=4.0 : Acetonitrile
 Mobile Phase B : 25:75 10 mM Potassium diHydrogen Phosphate pH=4.0 : Acetonitrile
 Gradient : T0=100:0, T15=0:100, T25=0:100, T27=100:0, T30=100:0
 Flow Rate : 1.0 mL/min Column Temperature : 20C Run time : 30 mins
 Sample Solvent : 40:60 10 mM KH2PO4 pH=4.0 : Acetonitrile Detection : UV 238 nm

Sample Name	BDG 10749.3	Instrument	AnalyticalLC01
Acquisition	04/12/2014, 14:31:56	Method (rev.)	LC10170d (4)
Sequence	BDG_04Dec2014b - Reprocessed	Vial Position	11
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	4.90 min	1.5052	15.4817	0.1500 min	0.061 %
2	5.66 min	0.6754	5.0229	0.1128 min	0.020 %
3	5.98 min	1.0816	7.9945	0.1162 min	0.032 %
4	6.19 min	4.7368	41.6607	0.1346 min	0.164 %
5	7.22 min	0.3755	4.5572	0.1556 min	0.018 %
6	8.68 min	0.3975	4.7483	0.1574 min	0.019 %
7	10.36 min	0.4565	5.8457	0.1754 min	0.023 %
8	10.66 min	0.6443	8.1737	0.1760 min	0.032 %
9	12.12 min	9.7530	133.3593	0.2015 min	0.526 %
10	12.39 min	5.8624	93.9126	0.2229 min	0.370 %
11	13.29 min	1.1604	21.3403	0.2586 min	0.084 %
12	14.35 min	1618.4574	24951.2575	0.2379 min	98.366 %
13	15.91 min	0.9449	13.5382	0.2072 min	0.053 %
14	17.86 min	0.8381	25.5432	0.3836 min	0.101 %
15	19.32 min	2.3744	33.3651	0.2139 min	0.132 %