BDG SYNTHESIS

Certificate of Analysis

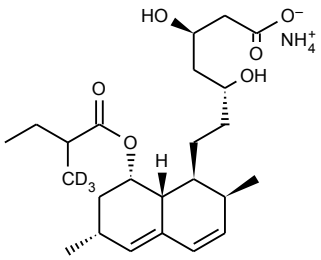
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
28 October 2016

Name: **Lovastatin Acid-d_3 Ammonium Salt**

CAS Number: 77550-67-5 (unlabelled)

Structure:



Molecular Weight: $C_{24}H_{34}D_3O_6 \cdot NH_4 = 442.60$

Lot Number: BDG 5906

Appearance: White, crystalline solid

Purity By HPLC: 96.3 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 28 October 2017

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. Avoid warming solutions - the material may revert to the lactone form.

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: a trace of an unidentified impurity is seen in the baseline.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. Some of the peaks are duplicated indicating that the product is a mixture of two diastereoisomers which is expected and is a consequence of the synthetic route used to generate the product. The relative intensities of these duplicated peaks are close to that seen for the two main peaks in the HPLC trace.
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* 448.2730. $C_{24}H_{35}D_3NaO_6$ $[M+Na]^+$ requires *m/z* 448.2749. The deviation of 4.1 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

Two sharp, overlapping peaks are observed (total integration = 96.3 area %). 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 65.15, H 8.91, D 1.41, N 3.02 %
$C_{24}H_{34}D_3O_6{\cdot}NH_4$	Requires:	C 65.13, H 8.65, D 1.37, N 3.16 %

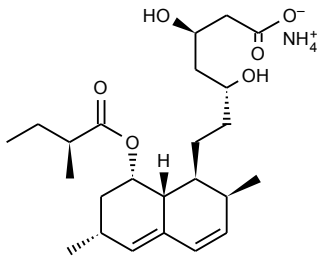
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

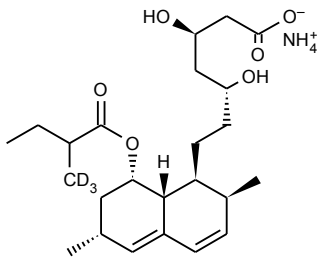
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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.

BDG SYNTHESIS

Proton NMR Spectrum of Lovastatin Acid Ammonium Salt (top) and Lovastatin Acid-d_3 Ammonium Salt (bottom) in DMSO-d_6





Lot Number: BDG 5906

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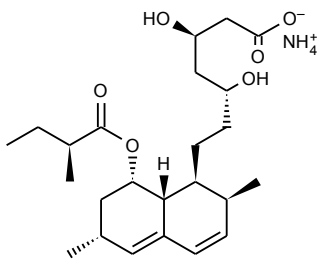
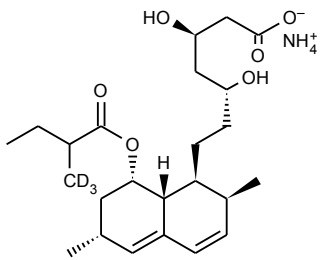
Carbon-13 NMR Spectrum of Lovastatin Acid Ammonium Salt (top) and Lovastatin Acid-d_3 Ammonium Salt (bottom) in DMSO-d_6





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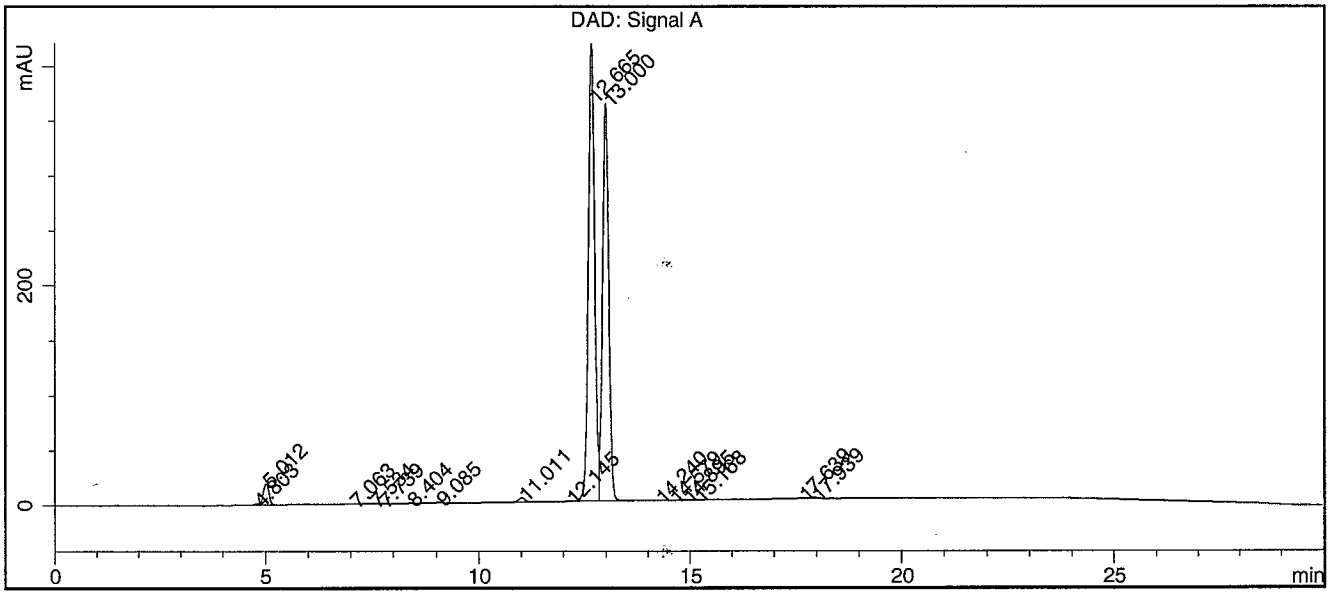
BDG - Analysis of Lovastatin Acid-d3 Ammonium Salt

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18(2) RP 4 x 3 mm
Mobile Phase A : 50:50:0.1 Water : Acetonitrile : Phosphoric Acid
Mobile Phase B : 25:75:0.1 Water : Acetonitrile : Phosphoric Acid
Gradient : T0=100:0, T15=0:100, T20=0:100, T25=100:0, T30=100:0
Flow Rate : 1.0 mL/min . . . . . Column Temperature : 20 C . . . . . Detection : UV 238 nm
Sample Solvent : 40:60 10 mM KH2PO4 pH=4.0 : Acetonitrile

Sample Name	BDG 5906	**Instrument**	AnalyticalLC01
Acquisition	28/10/2016, 13:52:27	**Method (rev.)**	LC10120a (22)
Sequence	BDG_28Oct2016b - Reprocessed	**Vial Position**	12
Operator	solvation010\cerityadmin	**Injection**	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	4.80 min	1.0390	6.6402	0.0926 min	0.080 %
2	5.01 min	19.0018	183.2024	0.1545 min	2.206 %
3	7.06 min	0.2528	4.2908	0.2120 min	0.052 %
4	7.53 min	0.2033	4.3030	0.2569 min	0.052 %
5	7.74 min	0.2722	3.2560	0.1536 min	0.039 %
6	8.40 min	0.2732	2.2123	0.1165 min	0.027 %
7	9.09 min	0.9800	11.6594	0.1748 min	0.140 %
8	11.01 min	3.9440	42.8599	0.1628 min	0.516 %
9	12.14 min	0.2038	2.1419	0.1386 min	0.026 %
10	12.67 min	417.2157	4282.7978	0.1598 min	51.565 %
11	13.00 min	362.0312	3719.1262	0.1599 min	44.779 %
12	14.24 min	0.3165	3.9804	0.1607 min	0.048 %
13	14.58 min	0.2438	2.3815	0.1440 min	0.029 %
14	14.89 min	0.2720	3.3976	0.1637 min	0.041 %
15	15.17 min	0.3131	4.3971	0.1778 min	0.053 %
16	17.64 min	0.9475	12.7658	0.2012 min	0.154 %
17	17.94 min	1.2415	16.1878	0.1881 min	0.195 %