

BDG SYNTHESIS

Certificate of Analysis

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

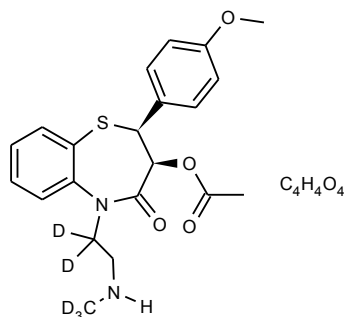
Neil Beare

Neil Beare, PhD, Director
15 April 2016

Name: *N*-Desmethyldiltiazem-*d*₅ Maleate

CAS Number: 86408-45-9 (unlabelled free base)

Structure:



Molecular Weight: $C_{21}H_{19}D_5N_2O_4S \cdot C_4H_4O_4 = 521.59$

Lot Number: BDG 15316

Appearance: White, crystalline solid

Purity By HPLC: 98.4 %

Isotopic Purity: Under 0.5 % *d*₀

Re-test Date: 15 April 2021

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. The complexity of the spectrum indicates two rotamers of the product are present in solution.

Isotopic Labelling: signals at the sites 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. Most signals are duplicated indicating that two rotamers of the product are present in solution.

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

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 406.1853. $C_{21}H_{20}D_5N_2O_4S$ $[M+H]^+$ requires m/z 406.1849. The deviation of 1.0 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 somewhat broadened, slightly tailing peak is observed (98.4 %). The peak on the solvent front is from maleic acid, confirmed by a spiking experiment. 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 57.59, H 4.52, D 1.96, N 5.42 %
$C_{21}H_{19}D_5N_2O_4S \cdot C_4H_4O_4$	Requires:	C 57.57, H 4.44, D 1.93, N 5.37 %

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).

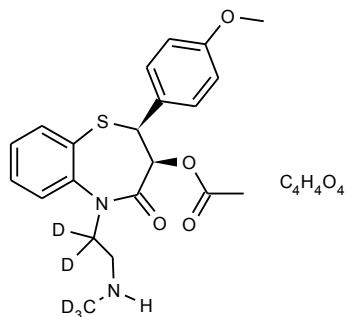
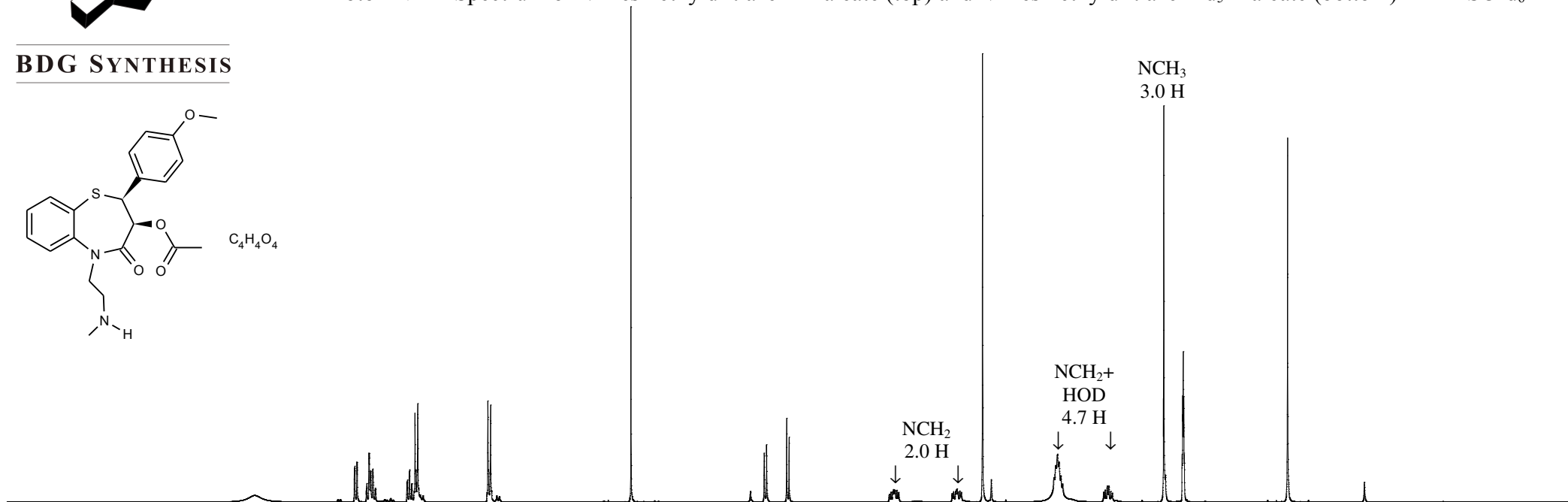
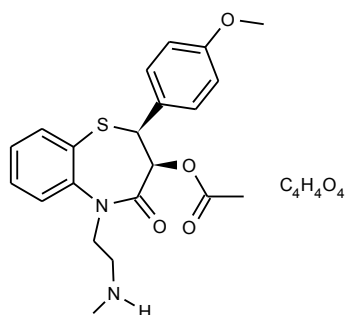
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

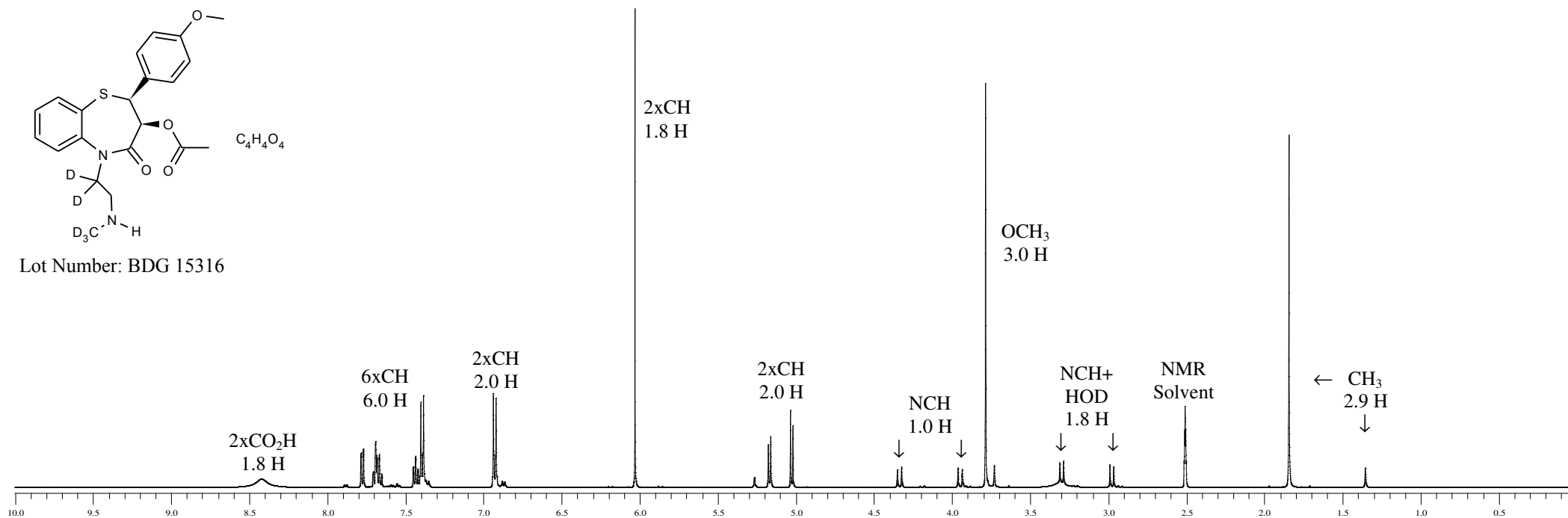


Proton NMR Spectrum of *N*-Desmethyldiltiazem Maleate (top) and *N*-Desmethyldiltiazem-*d*₅ Maleate (bottom) in DMSO-*d*₆

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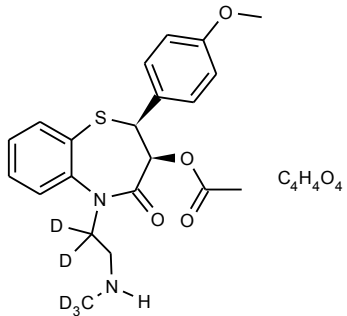
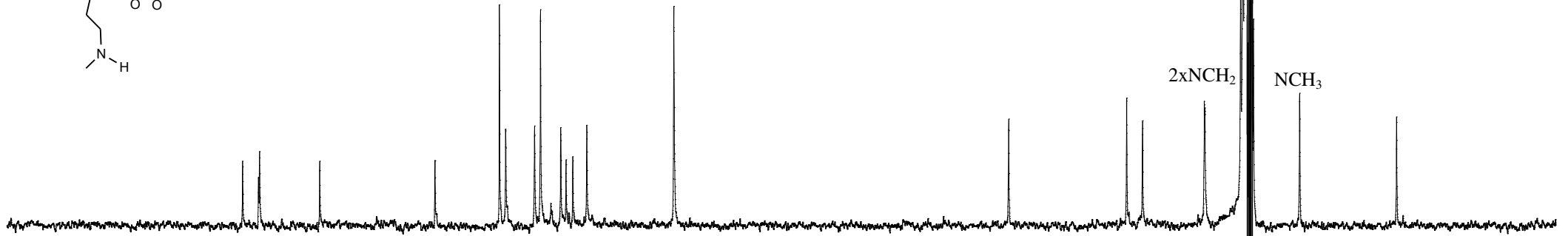
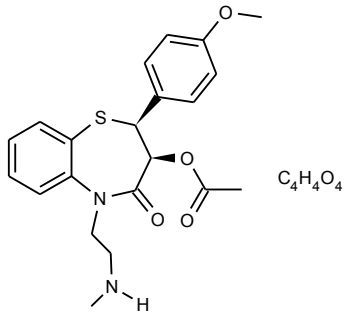
Lot Number: BDG 15316



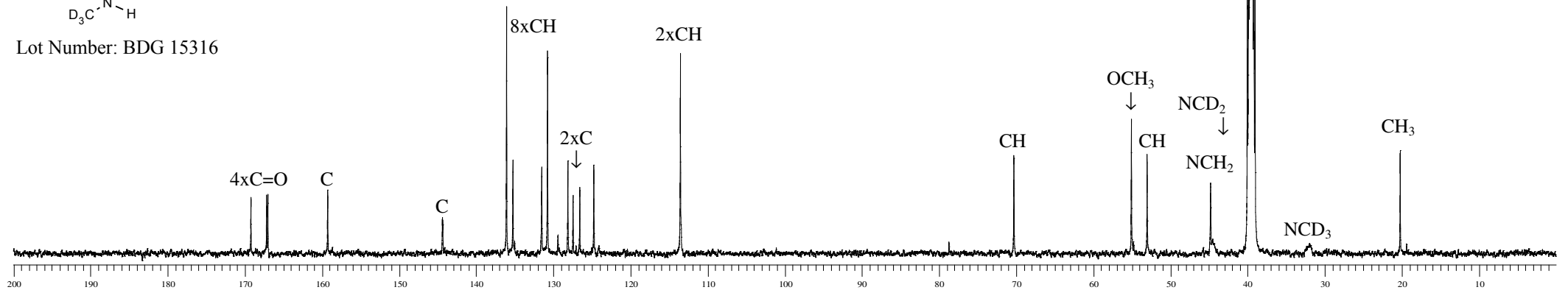


Carbon-13 NMR Spectrum of *N*-Desmethyldiltiazem Maleate (top) and *N*-Desmethyldiltiazem- d_5 Maleate (bottom) in DMSO- d_6

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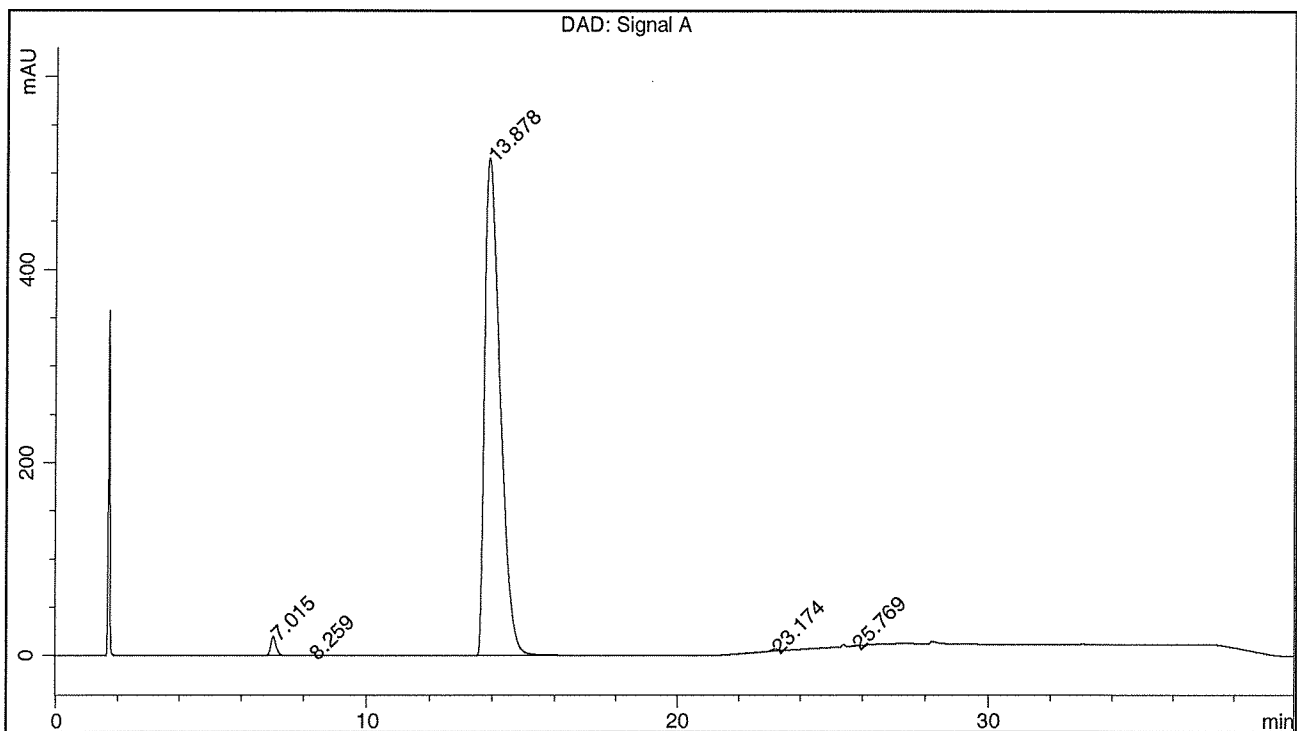
Lot Number: BDG 15316



BDG - Analysis of N-Desmethyldiltiazem-d5 Maleate

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase A : 70:25:5 50mM KH₂PO₄ + 0.02% Triethylamine pH=4.5 (H₃PO₄) : Acetonitrile : Ethanol
 Mobile Phase B : Acetonitrile
 Gradient (A:B) : T0=100:0, T18=100:0, T25=50:50, T35=50:50, T36=100:0, T40=100:0
 Flow Rate : 1.5 mL/min
 Sample Solvent : 70:30 Water : Acetonitrile
 Column Temperature : 20 C
 Injection Volume : 10 uL
 Detection : UV at 240 nm

Sample Name	BDG 15316	Instrument	AnalyticalLC01
Acquisition	15/04/2016, 13:51:53	Method (rev.)	LC10355c (15)
Sequence	BDG_15Apr2016b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.02 min	19.9832	245.3134	0.1872 min	1.350 %
2	8.26 min	0.3522	8.6817	0.2996 min	0.048 %
3	13.88 min	516.0127	17879.9470	0.5263 min	98.369 %
4	23.17 min	2.0945	36.1497	0.2694 min	0.199 %
5	25.77 min	0.9782	6.3164	0.0993 min	0.035 %