BDG SYNTHESIS

Certificate of Analysis

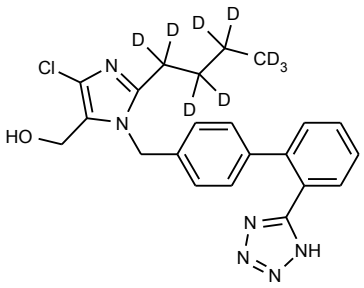
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
11 January 2016

Name: **Losartan-d_9**

CAS Number: 114798-26-4 (unlabelled)

Structure:



Molecular Weight: $C_{22}H_{14}D_9ClN_6O$ = 431.97

Lot Number: BDG 5147.9

Appearance: White, crystalline solid

Corrected Purity: 99.3 % (HPLC) - 0.2 % (acetonitrile) = 99.1 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 11 January 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.

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Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Isotopic Labelling: the broadened signal at 2.5 ppm is assigned to the methylene protons in the side chain next to the imidazole ring; this signal indicates incomplete deuteration at this position. Remaining signals for the side chain are absent, indicating clean deuteration at these positions.
Residual Solvents: a small amount of acetonitrile (0.2 % *w/w*) is 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 sites 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* 432.2267. $C_{22}H_{15}D_9ClN_6O$ $[M+H]^+$ requires *m/z* 432.2265. The deviation of 0.4 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 %). Although the predominant peak is for d_9 material, significant d_7-d_8 species are probably present.

HPLC

A sharp, slightly tailing peak is observed (99.3 %). 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 61.46, H 3.23, D 4.15, N 19.69 %
$C_{22}H_{14}D_9ClN_6O$	Requires:	C 61.17, H 3.27, D 4.20, N 19.46 %

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).

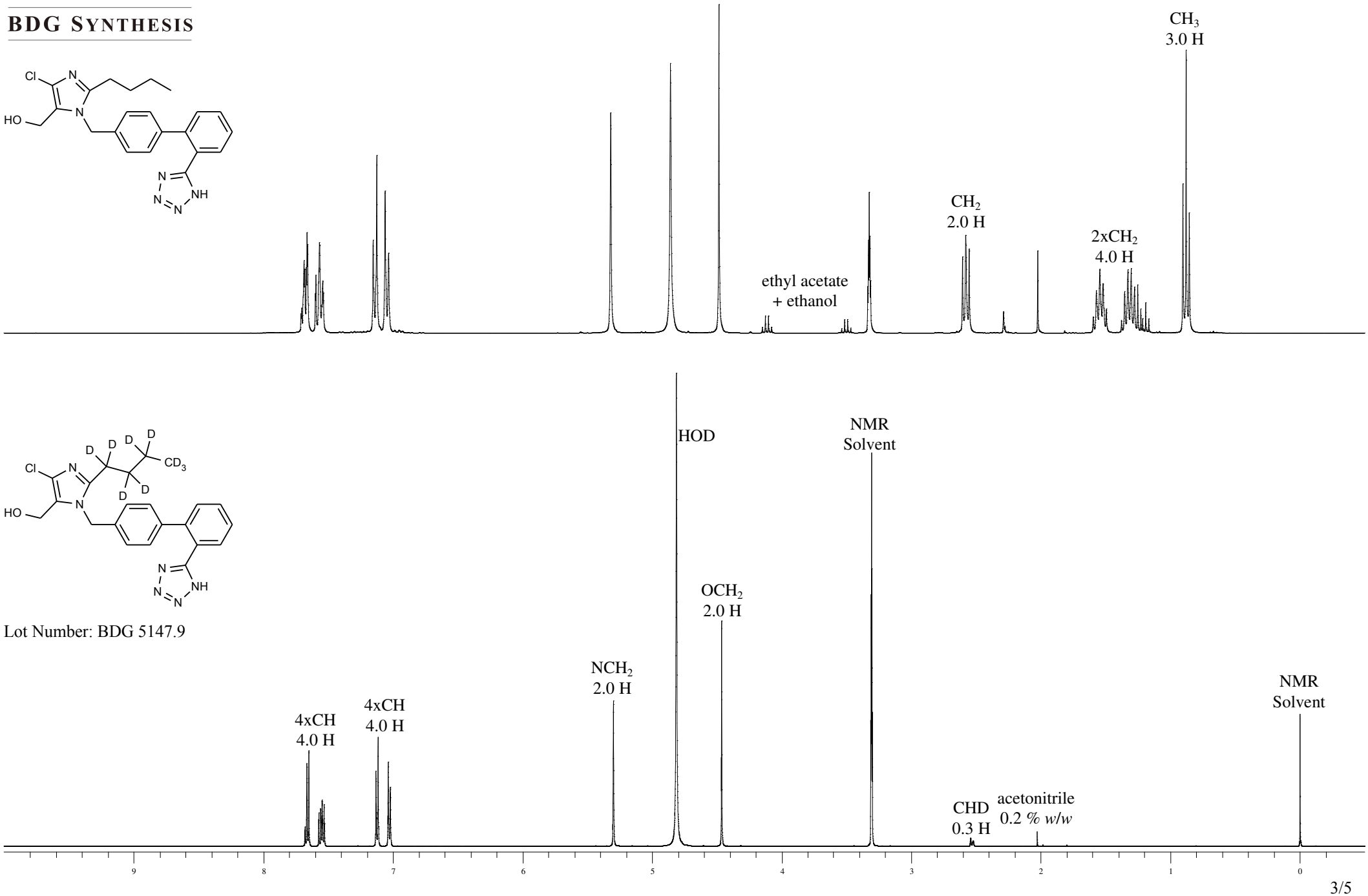
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

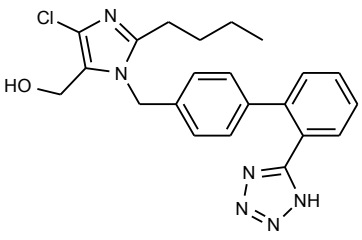
Proton NMR Spectrum of Losartan (top) and Losartan-d_9 (bottom) in Methanol-d_4

Lot Number: BDG 5147.9



BDG SYNTHESIS

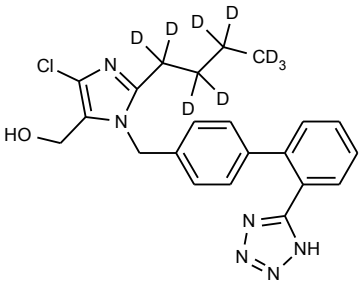
Carbon-13 NMR Spectrum of Losartan (top) and Losartan-d_9 (bottom) in Methanol-d_4



NMR Solvent +NCH_2

3xCH_2

CH_3



4xCH

Lot Number: BDG 5147.9

3xCH

CH

OCH_2

3xC

3xC

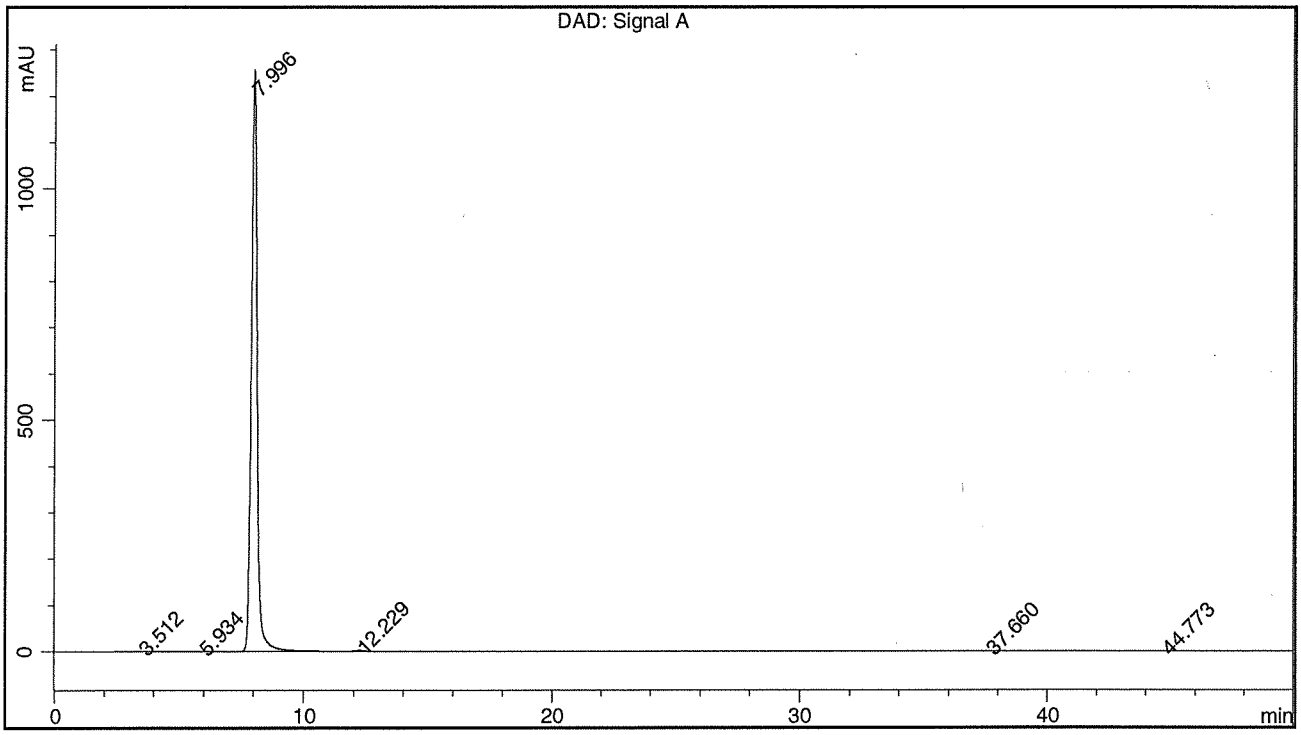
2xC

170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

BDG - Analysis of Losartan-d9

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 4 x 3 mm
Mobile Phase : 65:35:0.25 Water : Acetonitrile : Phosphoric Acid
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Injection Volume : 10 uL
Column Temperature : 20C
Detection : UV at 210 nm

Sample Name	BDG 5147.9	Instrument	AnalyticalLC01
Acquisition	11/01/2016, 19:51:02	Method (rev.)	LC10397a (8)
Sequence	BDG_11Jan2015c - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.51 min	0.2156	2.7337	0.1679 min	0.013 %
2	5.93 min	0.2063	3.9938	0.2458 min	0.019 %
3	8.00 min	1257.3452	20868.4664	0.2536 min	99.294 %
4	12.23 min	2.1597	60.6034	0.4234 min	0.288 %
5	37.66 min	0.2213	16.0387	0.8656 min	0.076 %
6	44.77 min	0.6818	65.0905	1.1338 min	0.310 %