BDG SYNTHESIS

Certificate of Analysis

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

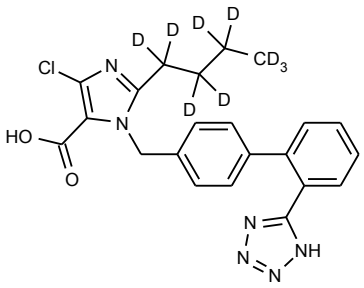
Barry Dent

Barry R. Dent, PhD, Director
10 August 2005

Name: **Losartan Carboxylic Acid-d_9**

CAS Number: 124750-92-1 (unlabelled)

Structure:



Molecular Weight: $C_{22}H_{12}D_9ClN_6O_2$ = 445.95

Lot Number: BDG 5148.2

Appearance: White, crystalline solid

Corrected Purity: 98.4 % (HPLC) - 0.5 % (acetonitrile) - 2.4 % (water) = 95.5 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 10 August 2010

Storage and Handling:

Temperature:	ambient laboratory temperature; may be refrigerated.
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: the broadened signal at 2.6 ppm is assignted to the methylene protons in the side chain next to the imidazole ring; this signal indicates incomplete deuteration at the position. Remaining signals for the side chain are absent, indicating clean deuteration at these positions.
Residual Solvents: a small amount of acetonitrile (0.5 % *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* 446.2057. $C_{22}H_{13}D_9ClN_6O_2$ $[M+H]^+$ requires *m/z* 446.2058. The deviation of 0.3 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, 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 57.50, H 2.70, D 4.05, N 18.48 %
$C_{22}H_{12}D_9ClN_6O_2 \cdot 0.6H_2O$	Requires:	C 57.85, H 2.91, D 3.97, N 18.40 %, H_2O 2.37 %
$C_{22}H_{12}D_9ClN_6O_2$	Requires:	C 59.25, H 2.71, D 4.06, N 18.85 %

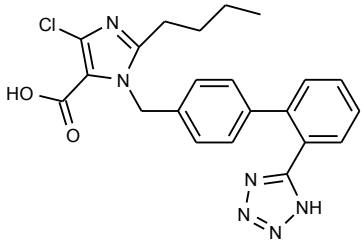
The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend that the “best-fit” water content be used when determining corrected purity.

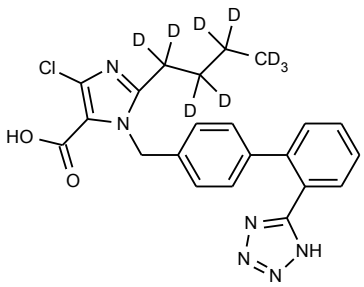
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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 Carboxylic Acid (top) and Losartan Carboxylic Acid-d_9 (bottom) in Methanol-d_4

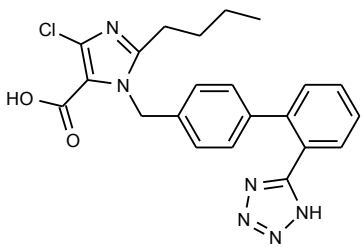


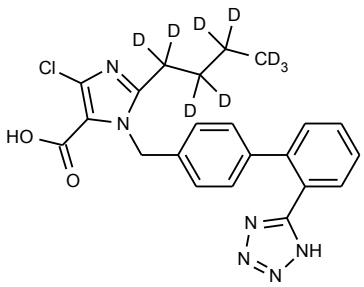


Lot Number: BDG 5148.2

BDG SYNTHESIS

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





Lot Number: BDG 5148.2

)ata File D:\HPCHEM\1\DATA\2005\AUG05\BDG08A\002-0501.D Sample Name: BDG 5148.2

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==========================================================================
Injection Date  : 8/1/05 5:19:07 PM              Seq. Line :   5
Sample Name     : BDG 5148.2                      Location : Vial 2
Acq. Operator   : YRLman                             Inj :   1
                                                 Inj Volume : 10 µl
Acq. Method     : N:\LC1100\1\METHODS\LC10175A.M
Last changed    : 8/1/05 3:44:41 PM by YRLman
Analysis Method : N:\LC1100\1\METHODS\LC10175A.M
Last changed    : 8/2/05 9:12:23 AM by YRLman
                  (modified after loading)

BDG - isocratic analysis of losartan carboxylic acid on Luna C18, 5um, 250 x 4.6mm ID.  #
LC10175
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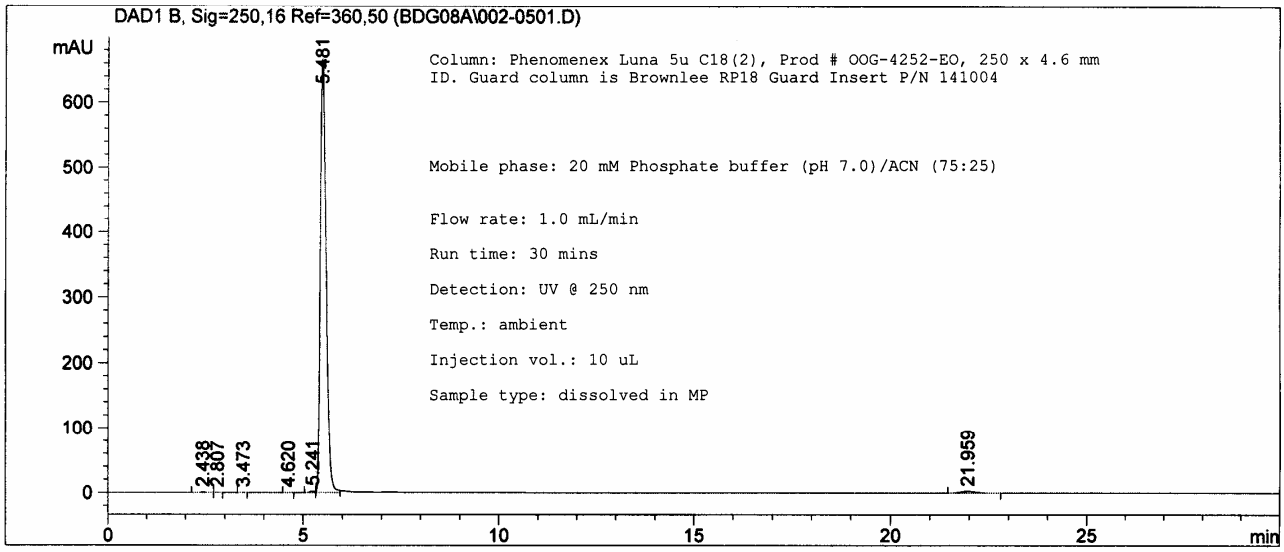


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==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000

Signal 1: DAD1 B, Sig=250,16 Ref=360,50
```

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.438	MF	0.1951	11.22267	9.58772e-1	0.1609
2	2.807	FM	0.1268	2.99431	3.93563e-1	0.0429
3	3.473	MM	0.1149	2.69145	3.90369e-1	0.0386
4	4.620	MM	0.1590	2.75808	2.89104e-1	0.0395
5	5.241	MF	0.1333	19.56549	2.44542	0.2805
6	5.481	MF	0.1715	6860.24219	666.61505	98.3665
7	21.959	MM	0.4709	74.68980	2.64355	1.0709

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Totals :                   6974.16399  673.73582

 Results obtained with enhanced integrator!
==========================================================================
                          *** End of Report ***
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