



BDG SYNTHESIS

Certificate of Analysis

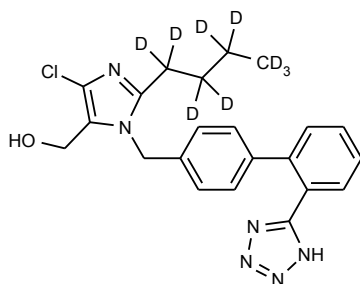
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
10 August 2005

Name: Losartan-d₉
CAS Number: 114798-26-4 (unlabelled)

Structure:



Molecular Weight: C₂₂H₁₄D₉ClN₆O = 431.97
Lot Number: BDG 5147.9
Appearance: White, crystalline solid
Corrected Purity: 99.8 % (HPLC) - 0.3 % (acetonitrile) = 99.5 %
Isotopic Purity: Under 0.5 % d₀
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 2.5 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 (0.3 % 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. $C_{22}H_{15}D_9CIN_6O$ $[M+H]^+$ 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 somewhat broadened, slightly tailing peak is observed (99.8 %). 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 % |
| $C_{22}H_{14}D_9CIN_6O$ | 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).

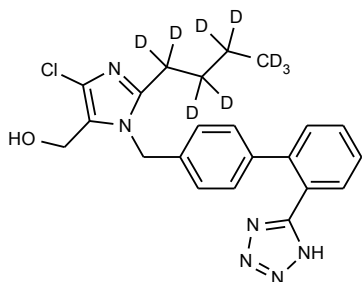
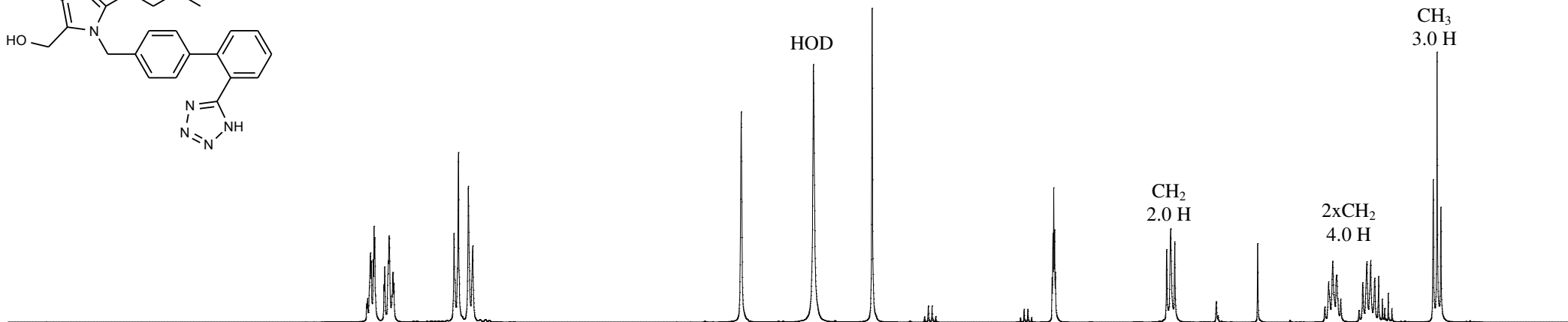
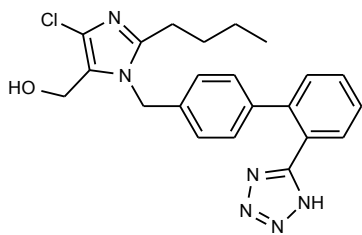
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

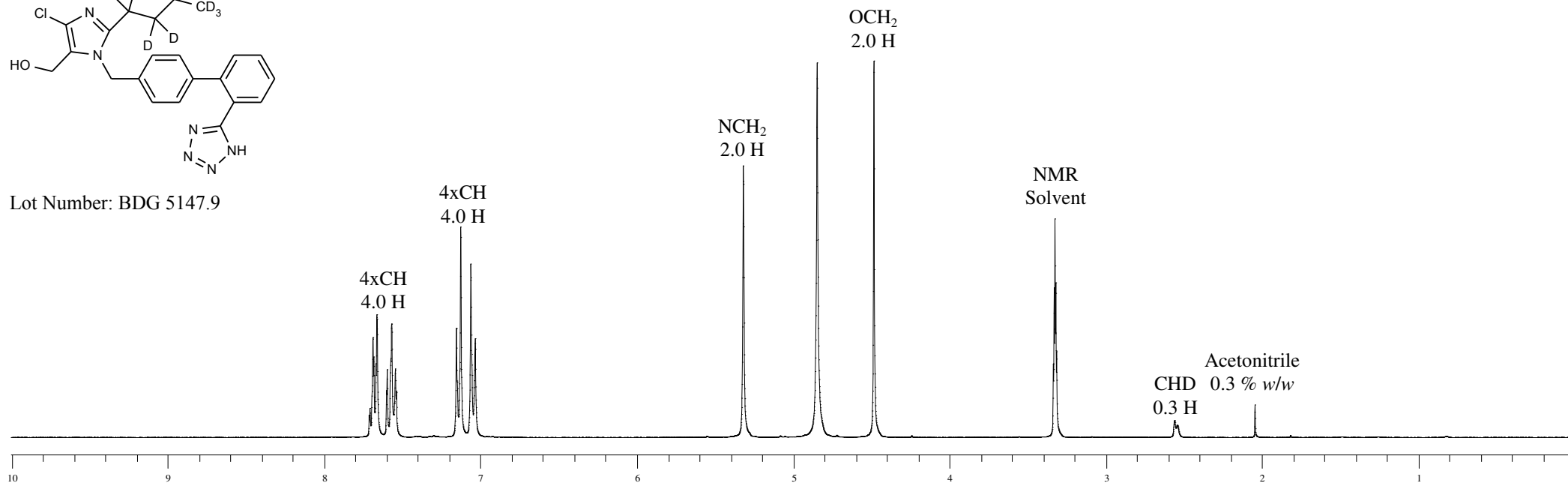


Proton NMR Spectrum of Losartan (top) and Losartan-d₉ (bottom) in Methanol-d₄

BDG SYNTHESIS



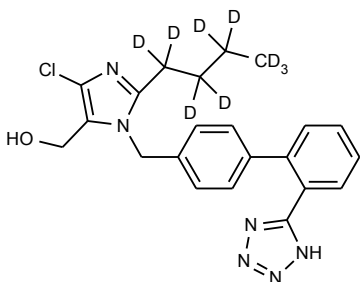
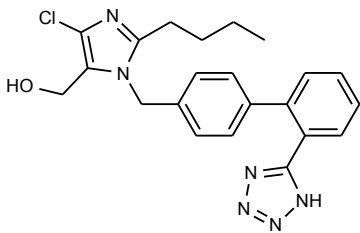
Lot Number: BDG 5147.9



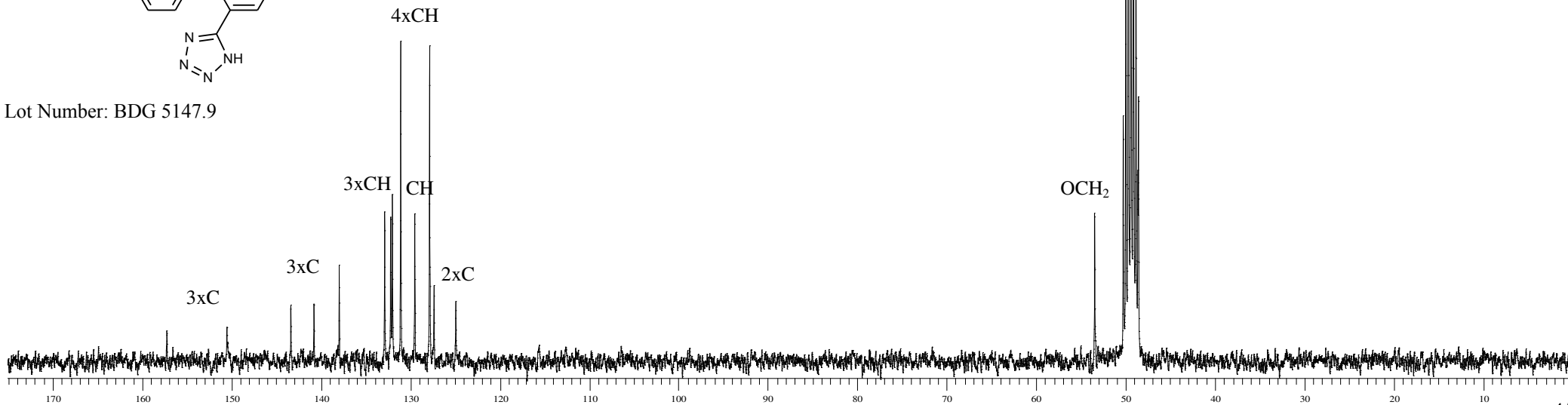


Carbon-13 NMR Spectrum of Losartan (top) and Losartan-d₉ (bottom) in Methanol-d₄

BDG SYNTHESIS



Lot Number: BDG 5147.9



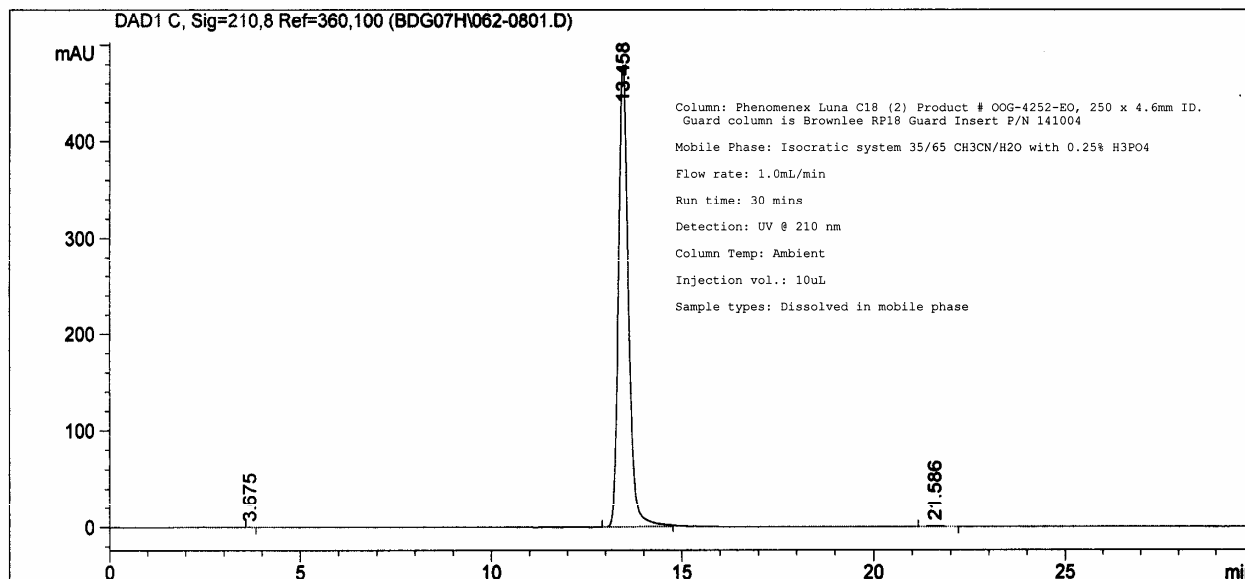
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Injection Date   : 7/29/05 2:19:13 PM           Seq. Line   :    8
Sample Name     : BDG 5147.9                   Location    : Vial 62
Acq. Operator   : YRLman                       Inj         :    1
                                           Inj Volume  : 10 µl

Acq. Method     : N:\LC1100_2\1\METHODS\LC40074A.M
Last changed    : 7/29/05 2:18:02 PM by YRLman
                  (modified after loading)

Analysis Method : N:\LC1100_2\1\METHODS\LC40074A.M
Last changed    : 7/29/05 4:34:36 PM by YRLman
                  (modified after loading)
    
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Isocratic analysis of BDG samples 250mm x 4.6mm 5µm Luna C18(2) with Brownlee RP18 guard and 35/65 CH3CN/H2O with 0.25% H3PO4, #LC40074



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 Area Percent Report
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Sorted By       : Signal
Multiplier     : 1.0000
Dilution       : 1.0000
    
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Signal 1: DAD1 C, Sig=210,8 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|--------|---------------|------|-------------|--------------|--------------|---------|
| 1 | 3.675 | BB | 0.0898 | 2.05286 | 3.43188e-1 | 0.0234 |
| 2 | 13.458 | MM | 0.3047 | 8765.82129 | 479.53488 | 99.7569 |
| 3 | 21.586 | BB | 0.3170 | 19.31029 | 7.68947e-1 | 0.2198 |

Totals : 8787.18444 480.64702

Results obtained with enhanced integrator!

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 *** End of Report ***