



BDG SYNTHESIS

Certificate of Analysis

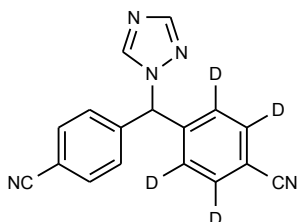
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
12 July 2005

Name: Letrozole-d₄
CAS Number: 112809-51-5 (unlabelled)

Structure:



Molecular Weight: C₁₇H₇D₄N₅ = 289.33
Lot Number: BDG 6153.3
Appearance: White, crystalline solid
Purity By HPLC: 99.5 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 12 July 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: signals at the sites of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: a trace (under 0.1 % w/w) of ethanol 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 290.1342. $C_{17}H_8D_4N_5$ $[M+H]^+$ requires m/z 290.1340. The deviation of 0.9 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 sharp, symmetrical peak is observed (99.5 %). 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 70.39, H 2.44, D 2.79, N 24.23 %
$C_{17}H_7D_4N_5$	Requires:	C 70.57, H 2.44, D 2.78, N 24.21 %

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).

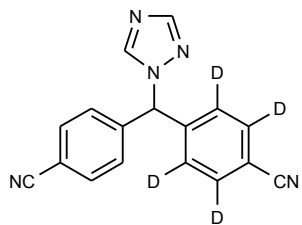
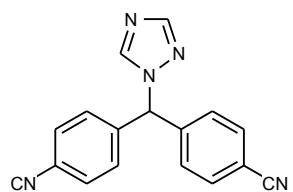
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

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.

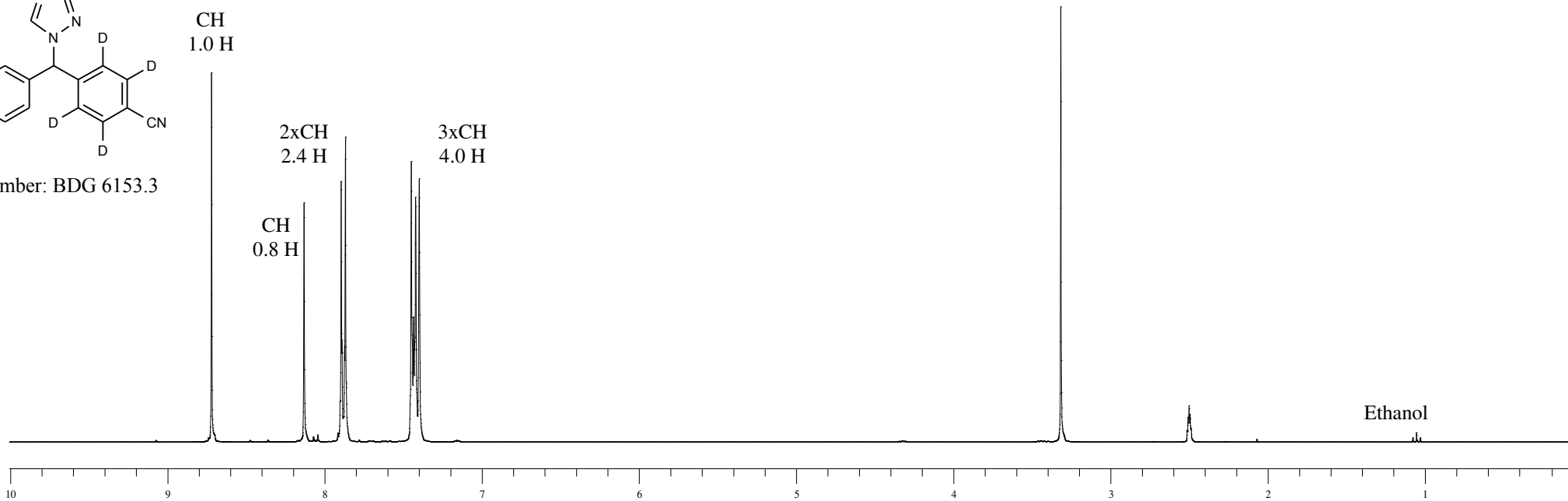


Proton NMR Spectrum of Letrozole (top) and Letrozole-d₄ (bottom) in DMSO-d₆

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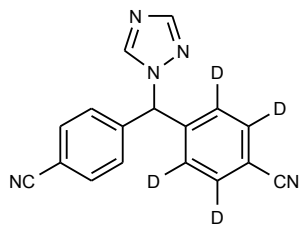
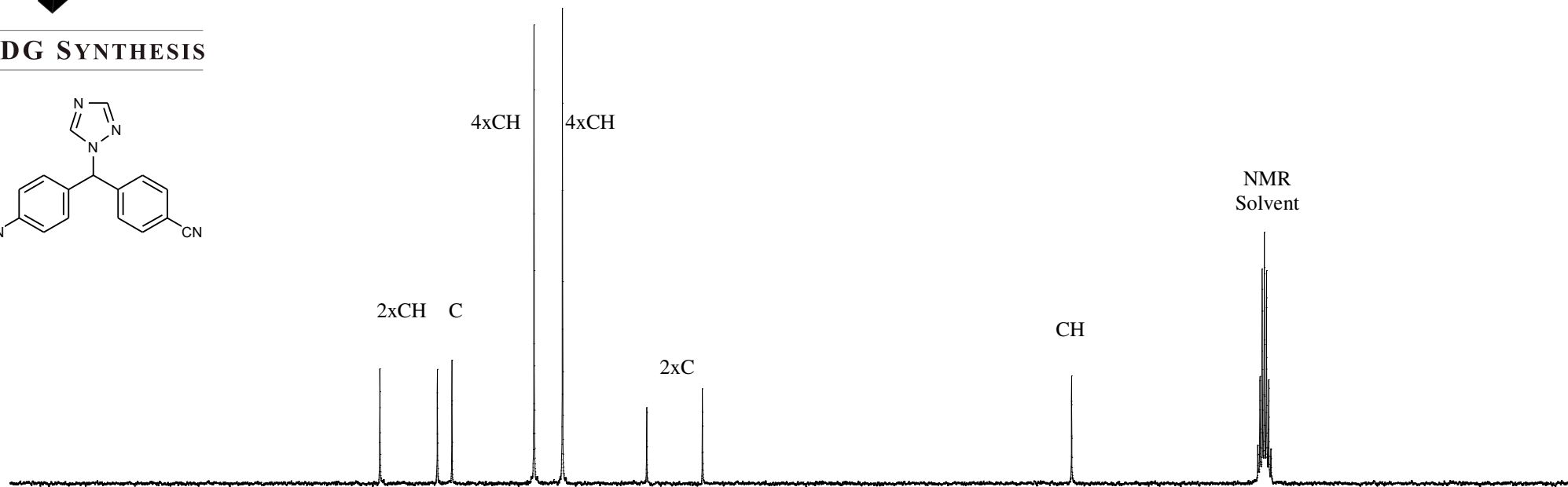
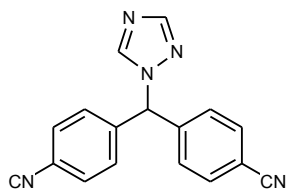
Lot Number: BDG 6153.3



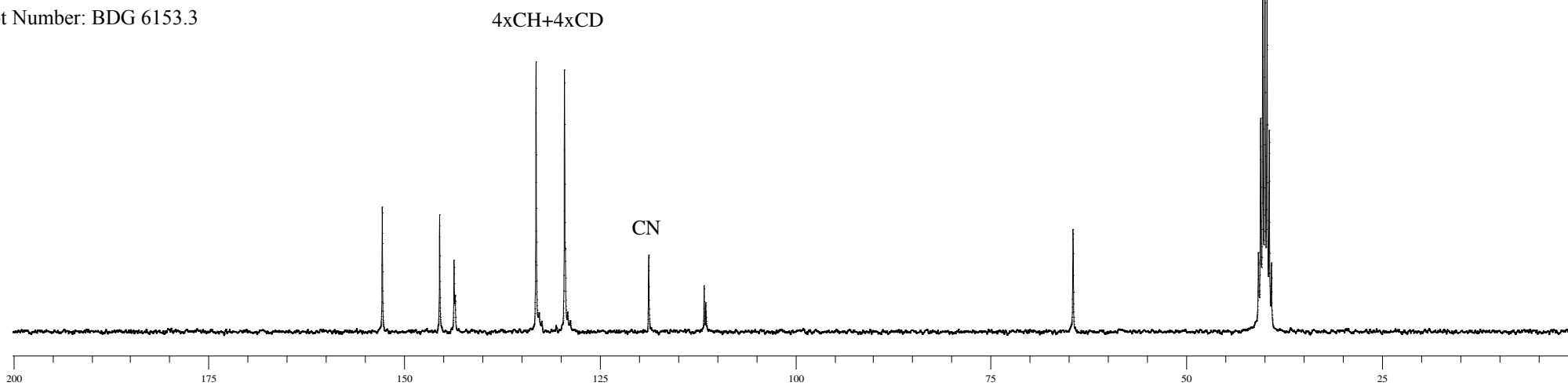


Carbon-13 NMR Spectrum of Letrozole (top) and Letrozole-d₄ (bottom) in DMSO-d₆

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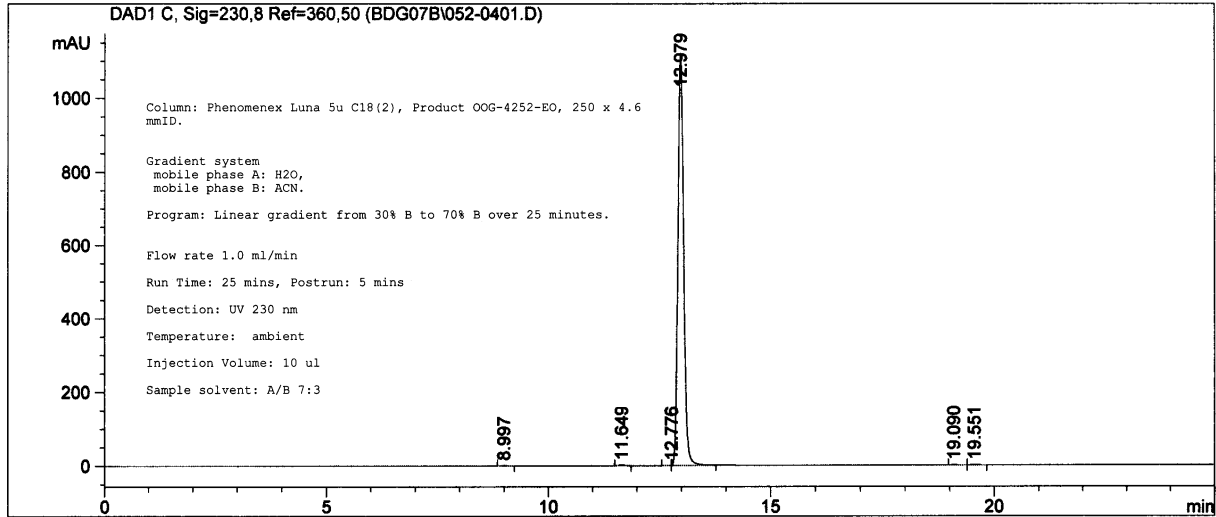
Lot Number: BDG 6153.3



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Injection Date   : 7/6/05 3:42:10 PM           Seq. Line :    4
Sample Name     : BDG6153.3                   Location  : Vial 52
Acq. Operator   : YRLman                       Inj       :    1
                                           Inj Volume: 10 µl
Acq. Method     : N:\LC1100_2\1\METHODS\LC40233A.M
Last changed    : 7/6/05 2:06:14 PM by YRLman
Analysis Method : N:\LC1100_2\1\METHODS\LC40233A.M
Last changed    : 7/6/05 4:35:52 PM by YRLman
                  (modified after loading)
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BDG - Gradient analysis of letrozole on Luna C18, 5µm, 250 x 4.6mm, #LC40233



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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=230,8 Ref=360,50

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.997	MM	0.1379	8.25124	9.97154e-1	0.0816
2	11.649	BB	0.1274	17.89770	2.14286	0.1769
3	12.776	MM	0.0788	3.88040	8.20753e-1	0.0384
4	12.979	MF	0.1494	1.00638e4	1122.44641	99.4755
5	19.090	MF	0.1919	9.83115	8.54000e-1	0.0972
6	19.551	FM	0.2190	13.19825	1.00442	0.1305

Totals : 1.01168e4 1128.26560

Results obtained with enhanced integrator!

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 *** End of Report ***