

BDG SYNTHESIS

Certificate of Analysis

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

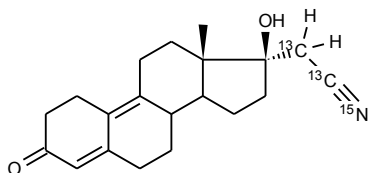
Barry Dent

Barry R. Dent, PhD, Director
9 March 2010

Name: Dienogest-¹³C₂, ¹⁵N

CAS Number: 65928-58-7 (unlabelled)

Structure:



Molecular Weight: C₁₈¹³C₂H₂₅¹⁵NO₂ = 314.40

Lot Number: BDG 8983.5

Appearance: White, crystalline solid

Corrected Purity: 100.0 % (HPLC) - 0.2 % (benzene) - 0.4 % (ethyl acetate) = 99.4 %

Isotopic Purity: Under 0.5% M-3

Re-test Date: 9 March 2015

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 spectrum is of little value in determining isotopic purity. The CH₂ signals are split by ¹³C-¹H coupling as expected.

Residual Solvents: small amounts of benzene (0.2 % w/w) and ethyl acetate (0.4 % w/w) 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.

Isotopic Labelling: the spectrum is of little value in determining isotopic purity, although the signals at the labelling sites are massively enhanced as expected. ¹³C-¹³C and ¹³C-¹⁵N coupling are also observed.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 337.1819. C₁₈¹³C₂H₂₅¹⁵NNaO₂ [M+Na]⁺ requires *m/z* 337.1815. The deviation of 1.2 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for M-3 material was seen (detection limit about 0.5 %).

HPLC

A sharp, symmetrical peak is observed (100.0 %). 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 77.23, H 8.26, N 4.83 %
C ₁₈ ¹³ C ₂ H ₂₅ ¹⁵ NO ₂	Requires:	C 77.03, H 8.01, N 4.77 %

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).

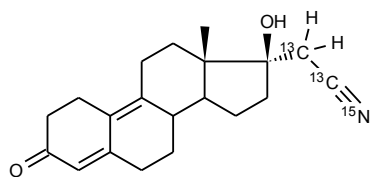
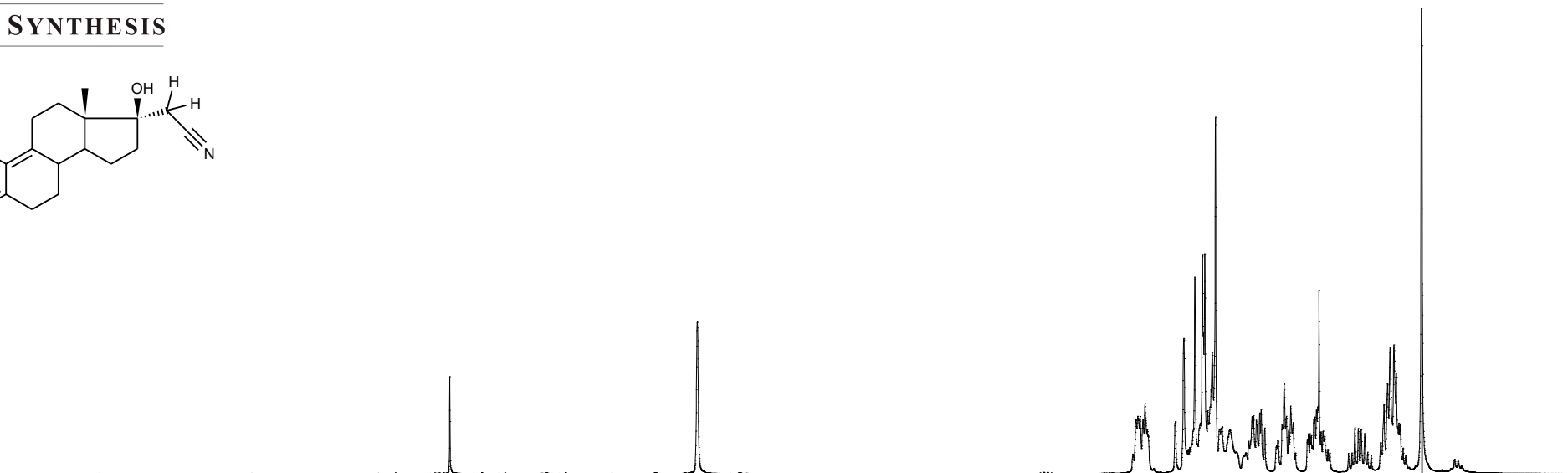
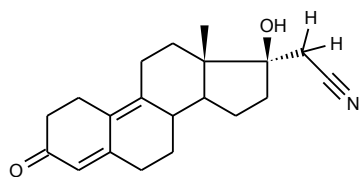
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

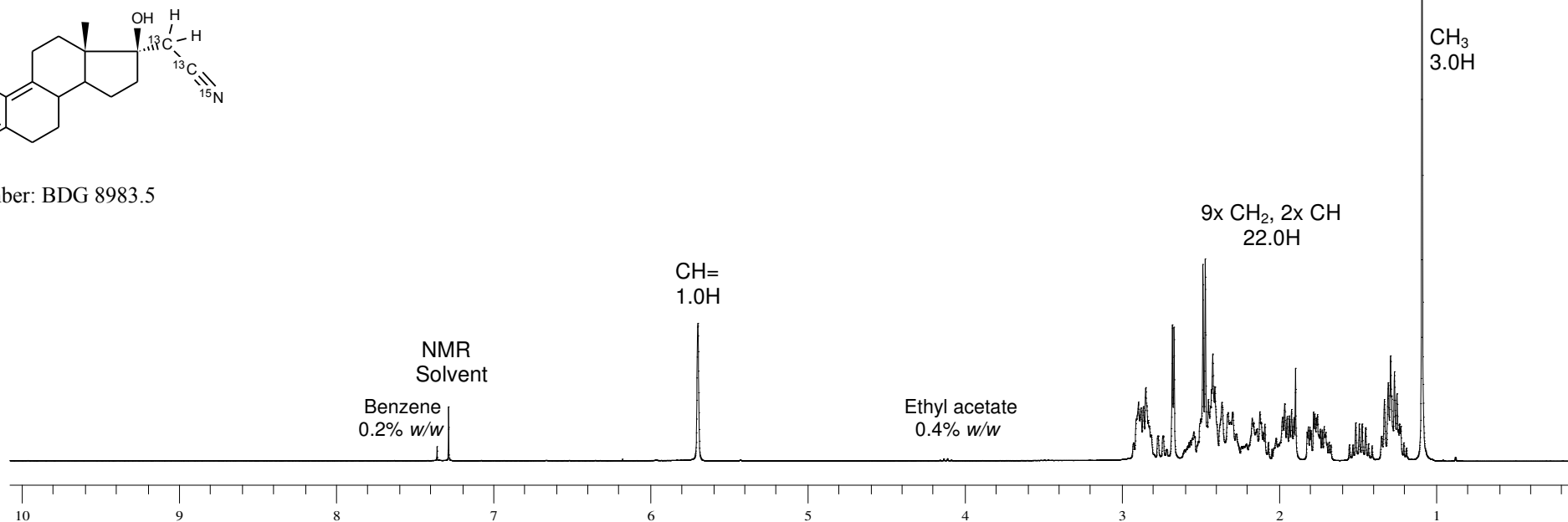


Proton NMR Spectrum of Dienogest (top) and Dienogest-¹³C₂,¹⁵N (bottom) in CDCl₃

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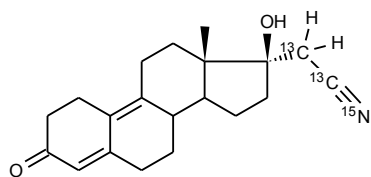
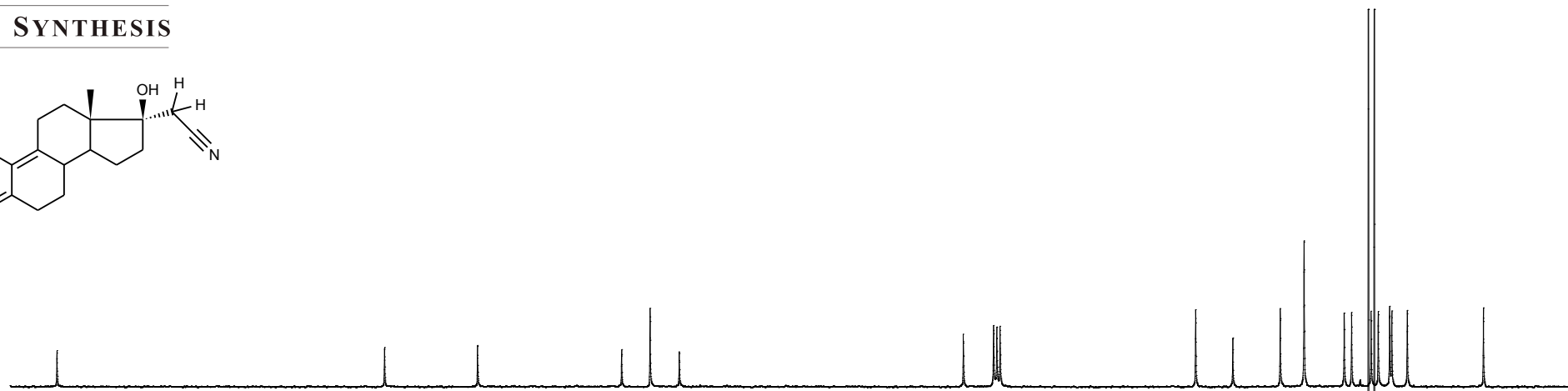
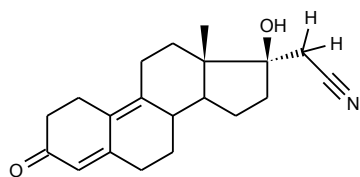
Lot Number: BDG 8983.5



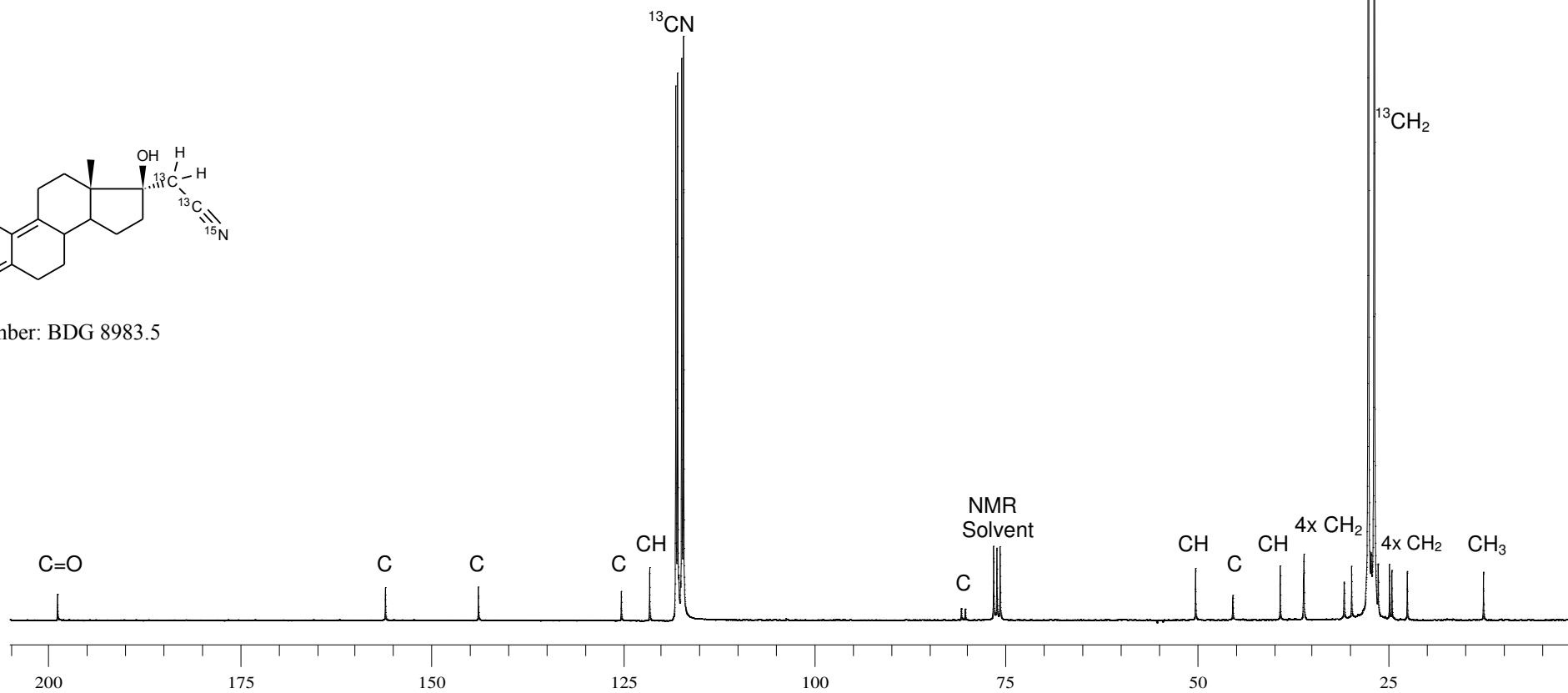


Carbon-13 NMR Spectrum of Dienogest (top) and Dienogest-¹³C₂, ¹⁵N (bottom) in CDCl₃

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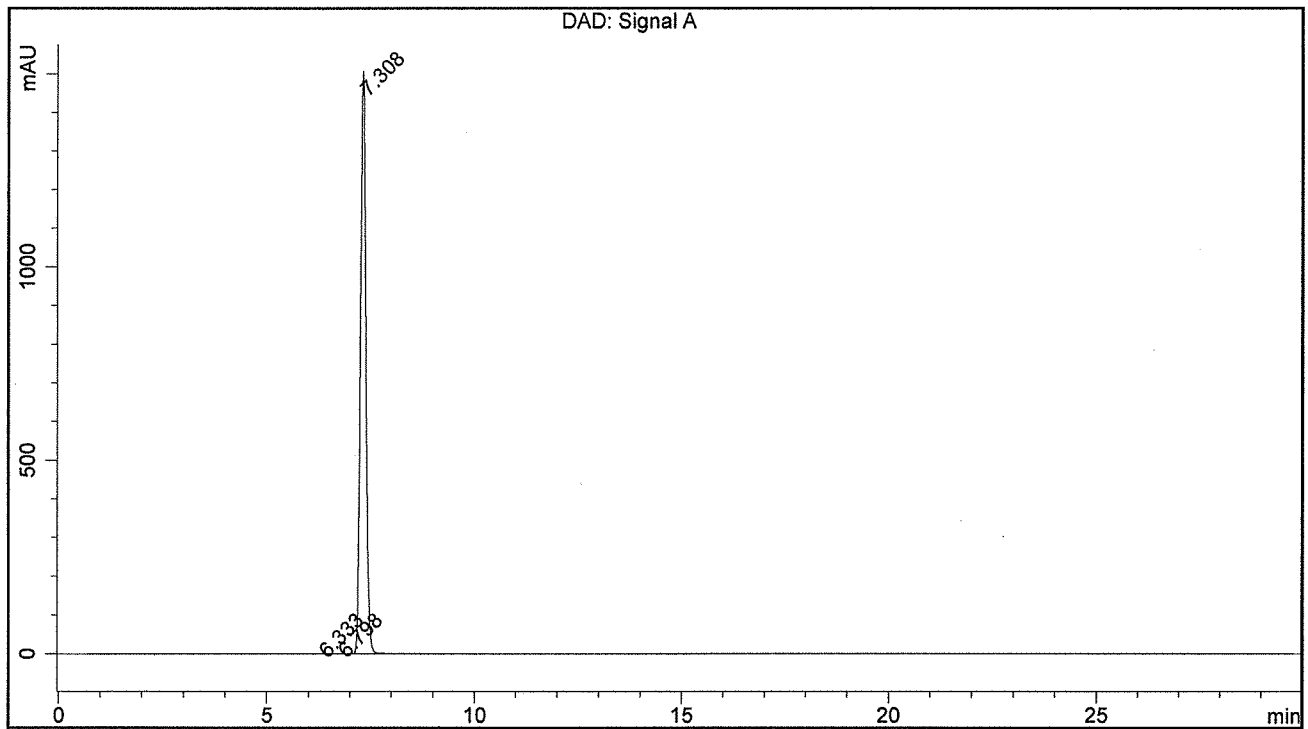
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BDG - Analysis of Dienogest-13C2,15N

Column : Phenomenex Luna C18 (2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 55:45 Water : Acetonitrile
 Flow Rate : 1 mL/min
 Column Temperature : 20C
 Sample Solvent : 1:1 Water : Acetonitrile
 Injection Volume : 10 uL
 Detection : UV at 308 nm

Sample Name	BDG 8983.5	Instrument	AnalyticalLC01
Acquisition	09/03/2010, 10:26:47	Method (rev.)	LC10370ae (7)
Sequence	BDG_09Mar2010c - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	6.33 min	0.1763	4.7492	0.3383 min	0.034 %
2	6.80 min	0.1655	1.3994	0.1267 min	0.010 %
3	7.31 min	1506.3193	13803.9780	0.1409 min	99.955 %