BDG SYNTHESIS

Certificate of Analysis

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

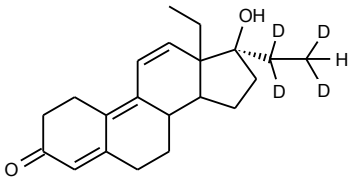
Barry Dent

Barry R. Dent, PhD, Director
20 March 2009

Name: **Tetrahydrogestrinone-d_4**

CAS Number: 618903-56-3 (unlabelled)

Structure:



Molecular Weight: $C_{21}H_{24}D_4O_2$ = 316.47

Lot Number: BDG 8760.4

Appearance: Pale yellow, crystalline solid

Corrected Purity: 97.6 % (HPLC) - 2.4 % (hexanes) - 1.7 % (water) = 93.5 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 20 March 2014

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	may be hygroscopic; store desiccated; recommended to determine water content periodically.
Light:	store in an amber vial and protect from bright light.
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: signals at the sites of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of hexanes (2.4 % *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 what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 339.2226. $C_{21}H_{24}D_4NaO_2$ $[M+Na]^+$ requires *m/z* 339.2233. The deviation of 2.0 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 %), however there was a range of isotopomers from d_2 to d_6.

HPLC

A sharp, symmetrical peak is observed (97.6 %). 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 78.42, H 8.23, D 2.74 %
$C_{21}H_{24}D_4O_2 \cdot 0.3H_2O$	Requires:	C 78.36, H 7.70, D 2.50 %, H_2O 1.68 %
$C_{21}H_{24}D_4O_2$	Requires:	C 79.70, H 7.64, D 2.55 %

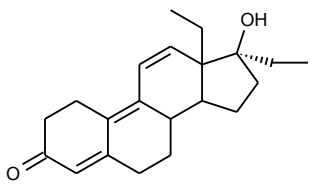
The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the "best-fit" hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend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

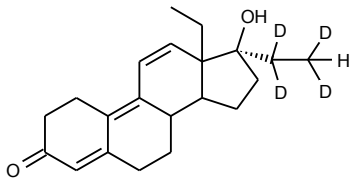
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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 Tetrahydrogestrinone (top) and Tetrahydrogestrinone-d_4 (bottom) in $CDCl_3$

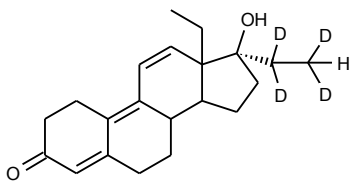




Lot Number: BDG 8760.4

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Tetrahydrogestrinone-d_4 in $CDCl_3$

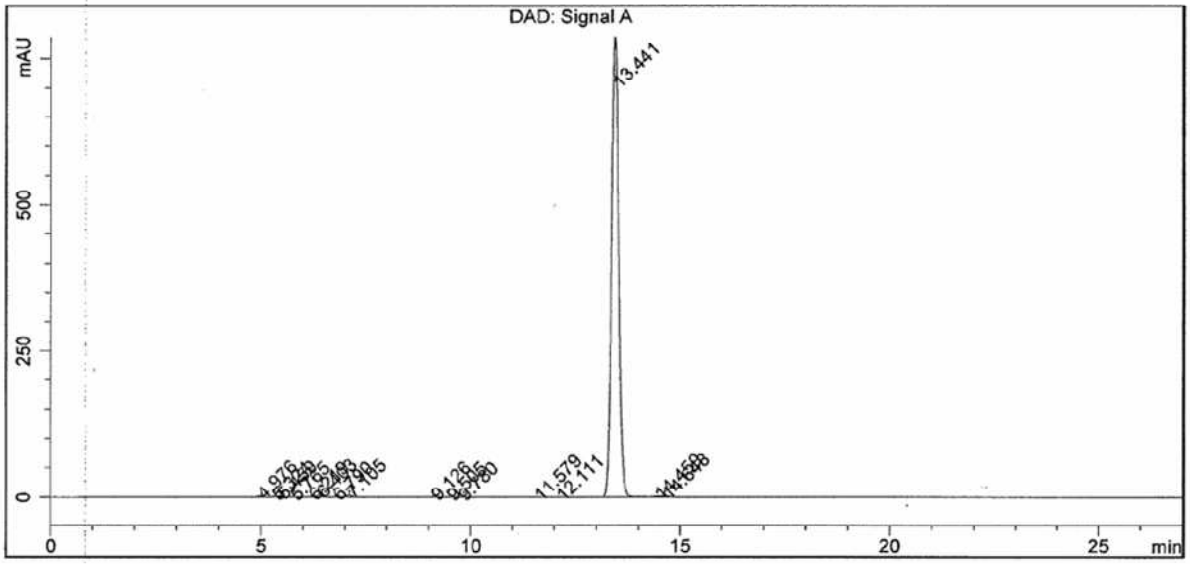


Lot Number: BDG 8760.4

BDG - Analysis of Tetrahydrogestrinone-d4.

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : Water . . . . . Mobile Phase B : Acetonitrile
Gradient (A:B) : T0=50:50, T20=30:70, T25=30:70, T28=50:50, T30=50:50
Flow Rate : 1.0 mL/min . . . . . Column Temperature : 20C
Sample Solvent : Mobile Phase . . . . . Injection Volume : 10 uL . . . . . Detection : UV at 342 nm

Sample Name	BDG 8760.4	Instrument	AnalyticalLC01
Acquisition	20/03/2009, 09:38:53	Method (rev.)	LC10314a (12)
Sequence	BDG_20Mar2009b - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	4.98 min	2.8888	19.9557	0.1026 min	0.209 %
2	5.32 min	1.0454	6.2372	0.0916 min	0.065 %
3	5.46 min	2.5388	18.1821	0.1076 min	0.191 %
4	5.77 min	0.4309	2.9952	0.1051 min	0.031 %
5	6.22 min	1.2271	11.7950	0.1341 min	0.124 %
6	6.40 min	5.8468	45.6497	0.1171 min	0.478 %
7	6.79 min	1.0828	8.6958	0.1237 min	0.091 %
8	7.11 min	4.5944	35.3931	0.1199 min	0.371 %
9	9.13 min	1.2070	14.0783	0.1721 min	0.148 %
10	9.50 min	0.3163	2.7492	0.1274 min	0.029 %
11	9.78 min	0.3304	3.1919	0.1427 min	0.033 %
12	11.58 min	0.8310	8.6170	0.1590 min	0.090 %
13	12.11 min	0.3266	3.8176	0.1684 min	0.040 %
14	13.44 min	791.7492	9319.2968	0.1833 min	97.644 %
15	14.46 min	1.6422	16.9141	0.1562 min	0.177 %
16	14.65 min	2.0771	26.5638	0.1932 min	0.278 %