BDG SYNTHESIS

Certificate of Analysis

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

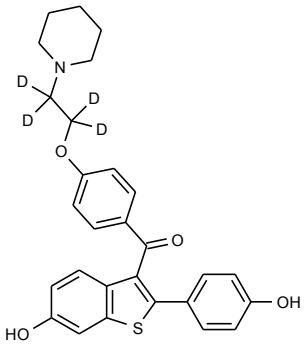
Barry Dent

Barry R. Dent, PhD, Director
4 May 2012

Name: **Raloxifene-d_4**

CAS Number: none (unlabelled 84449-90-1)

Structure:



Molecular Weight: $C_{28}H_{23}D_4NO_4S$ = 477.61

Lot Number: BDG 12493.3

Appearance: Yellow, crystalline solid

Corrected Purity: 99.9 % (HPLC) - 4.9 % (diethyl ether) - 1.9 % (water) = 93.2 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 4 May 2017

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
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 diethyl ether (4.9 % *w/w*) and a trace (under 0.1 % *w/w*) of acetone 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: 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* 478.1984. $C_{28}H_{24}D_4NO_4S$ $[M+H]^+$ requires *m/z* 478.1990. The deviation of 1.3 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 %).

HPLC

A somewhat broadened, symmetrical peak is observed (99.9 %). 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 69.14, H 5.26, D 1.76, N 2.71 %
$C_{28}H_{23}D_4NO_4S{\cdot}0.5H_2O$	Requires:	C 69.11, H 4.97, D 1.66, N 2.88 %, H_2O 1.85 %
$C_{28}H_{23}D_4NO_4S$	Requires:	C 70.41, H 4.85, D 1.69, N 2.93 %

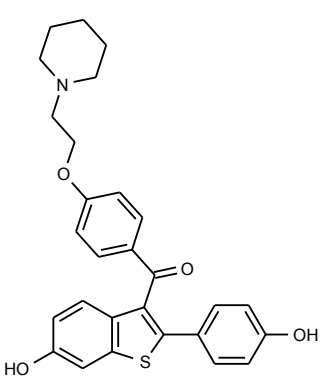
The elemental analyses fall slightly outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend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

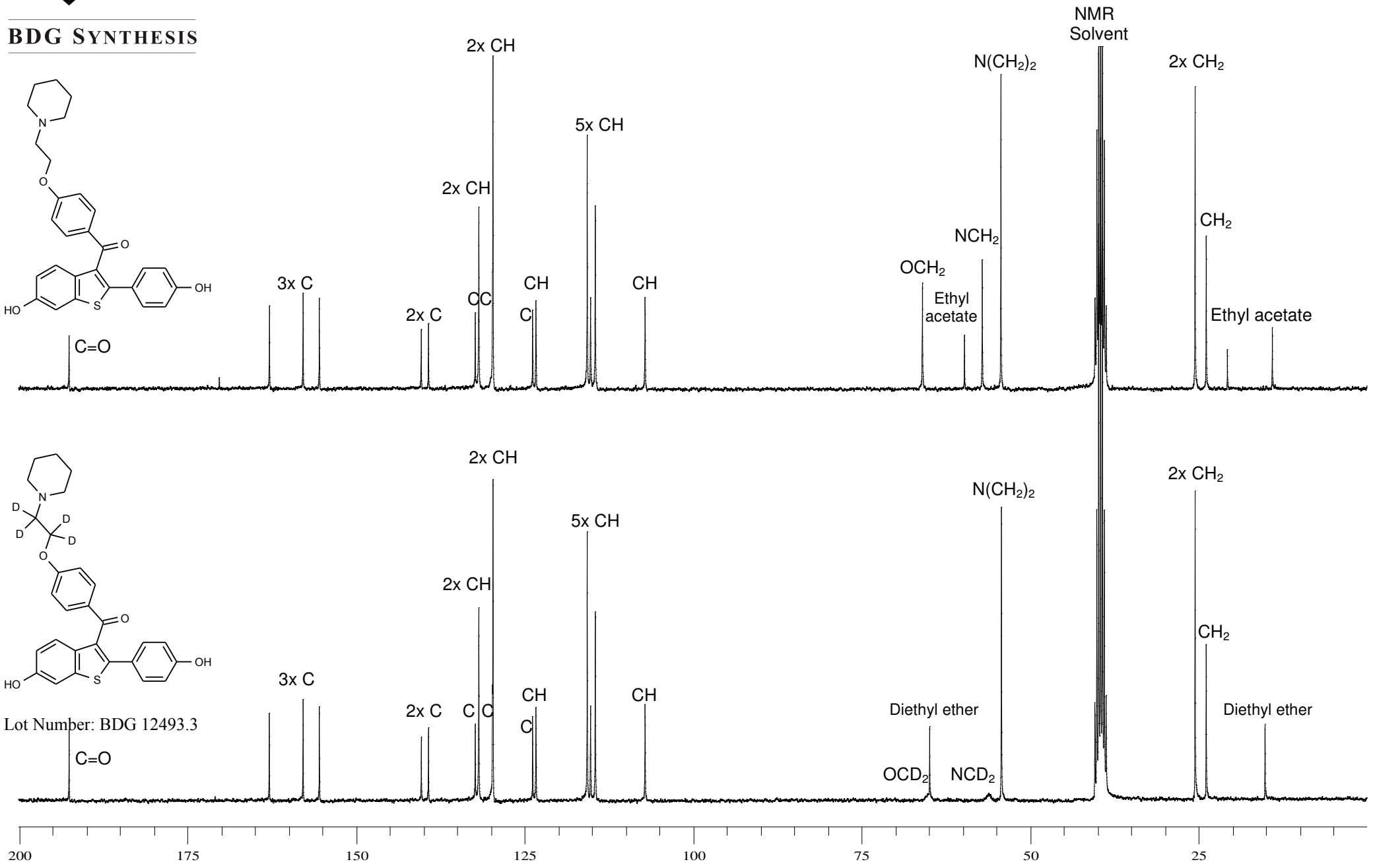
Proton NMR Spectrum of Raloxifene (top) and Raloxifene-d_4 (bottom) in DMSO-d_6



Lot Number: BDG 12493.3

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Raloxifene (top) and Raloxifene-d_4 (bottom) in DMSO-d_6



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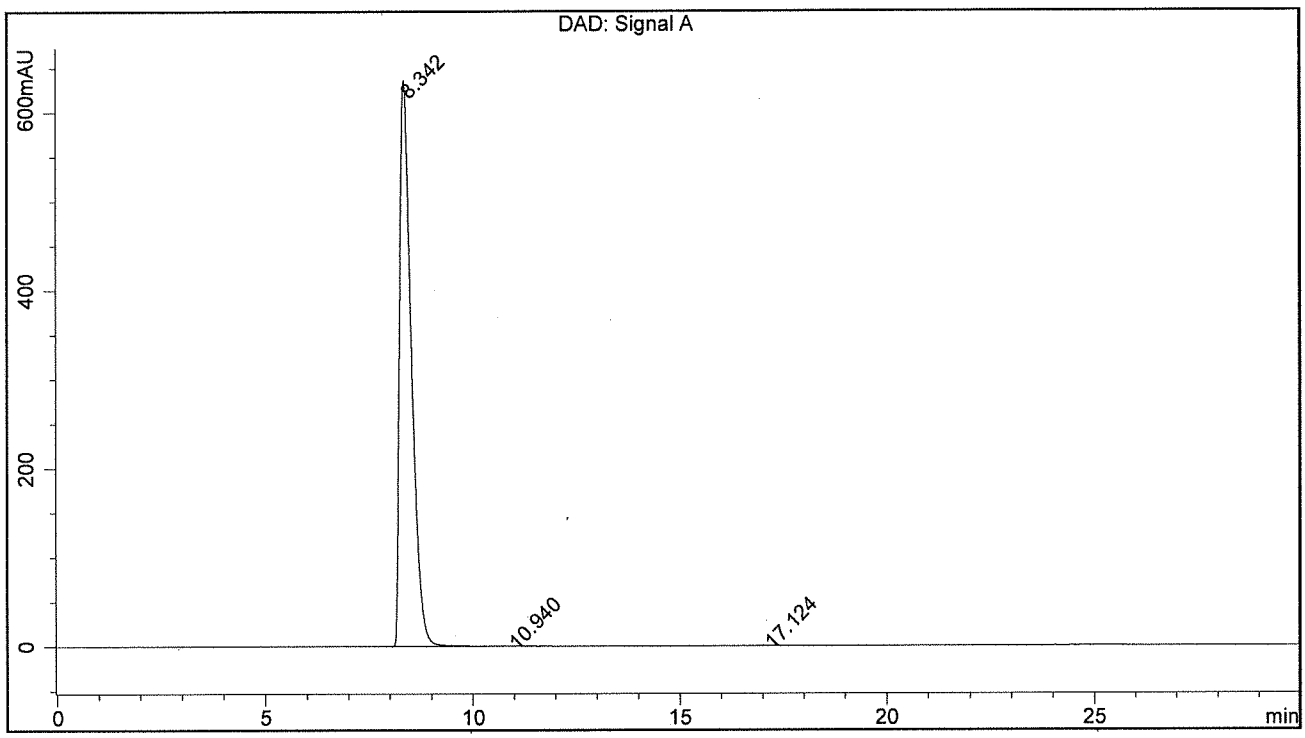
BDG - Analysis of Raloxifene-d4

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex SecurityGuard C18 4 x 3mm
Mobile Phase : 70:30 20 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 287 nm

Sample Name	BDG 12493.3	Instrument	AnalyticalLC01
Acquisition	04/05/2012, 13:44:12	Method (rev.)	LC10505a (5)
Sequence	BDG_04May2012c - Reprocessed	Vial Position	61
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	8.34 min	636.2480	12553.0725	0.3022 min	99.885 %
2	10.94 min	0.2490	5.7460	0.3413 min	0.046 %
3	17.12 min	0.2252	8.7092	0.4751 min	0.069 %