



## BDG SYNTHESIS

### Certificate of Analysis

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

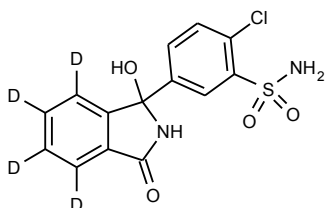
*Neil Beare*

Neil Beare, PhD, Director  
25 February 2012

**Name:** Chlorthalidone-d<sub>4</sub>

**CAS Number:** 77-36-1 (unlabelled)

**Structure:**



**Molecular Weight:** C<sub>14</sub>H<sub>7</sub>D<sub>4</sub>ClN<sub>2</sub>O<sub>4</sub>S = 342.79

**Lot Number:** BDG 5400.2

**Appearance:** White, crystalline solid

**Corrected Purity:** 99.1 % (HPLC) - 0.7 % (diethyl ether) - 0.5 % (benzene) = 97.9 %

**Isotopic Purity:** Under 0.5 % d<sub>0</sub>

**Re-test Date:** 25 February 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:	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 greatly diminished, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: small amounts of benzene (0.5 % w/w) and diethyl ether (0.7 % 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: 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  $m/z$  343.0452.  $C_{14}H_8D_4ClN_2O_4S$   $[M+H]^+$  requires  $m/z$  343.0457. The deviation of 1.5 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 (99.1 %). 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 49.68, H 2.10, D 2.40, Cl 10.60, N 7.85 %
$C_{14}H_7D_4ClN_2O_4S$	Requires:	C 49.05, H 2.06, D 2.35, Cl 10.34, N 8.17 %

The elemental analyses fall within generally accepted limits for establishing the molecular formula given, except the result for carbon. 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).

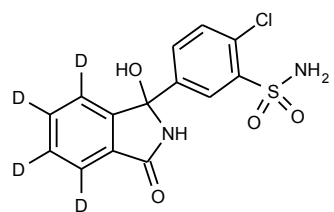
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

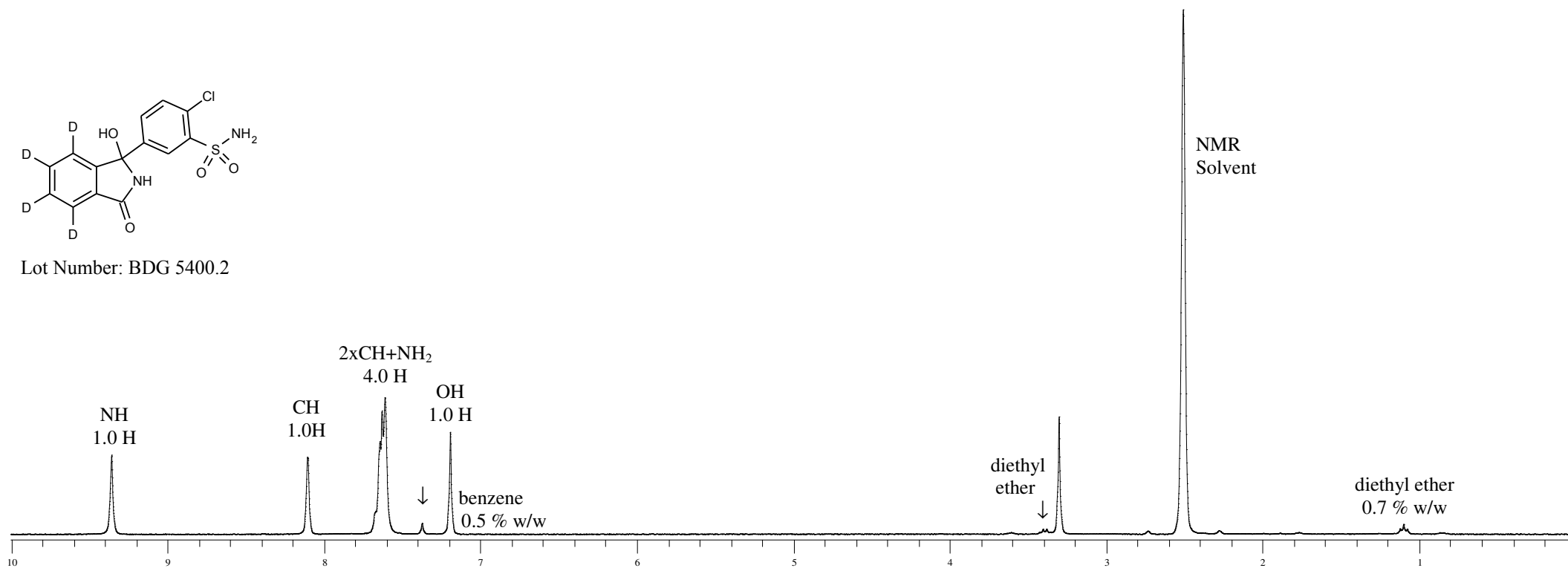


Proton NMR Spectrum of Chlorthalidone (top) and Chlorthalidone-d<sub>4</sub> (bottom) in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



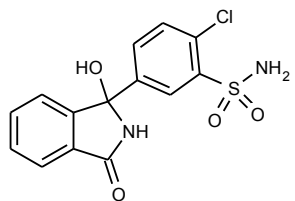
Lot Number: BDG 5400.2



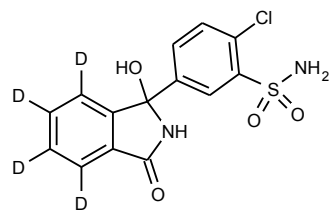
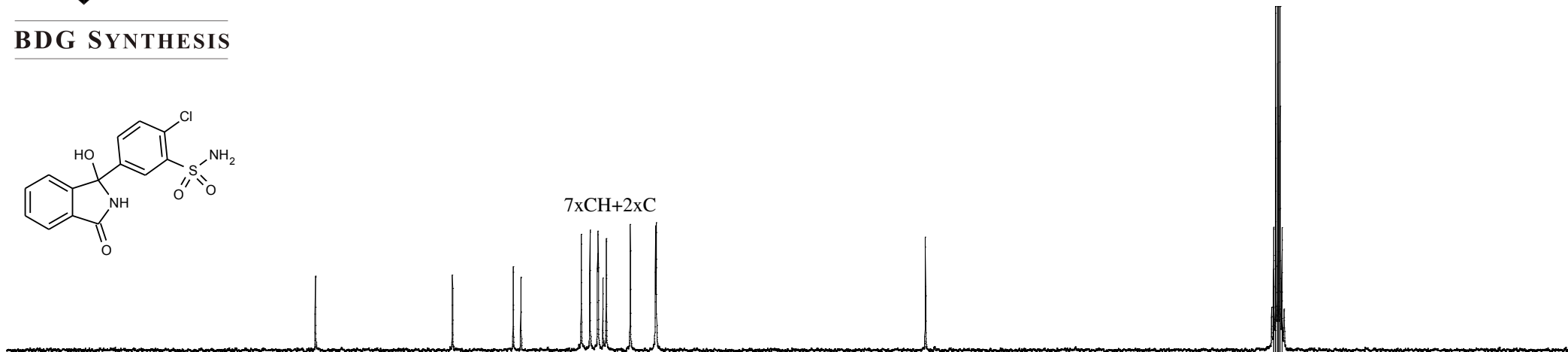


Carbon-13 NMR Spectrum of Chlorthalidone (top) and Chlorthalidone-d<sub>4</sub> (bottom) in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



7xCH+2xC



Lot Number: BDG 5400.2

2xCH+C

CH

C

2xC

CD

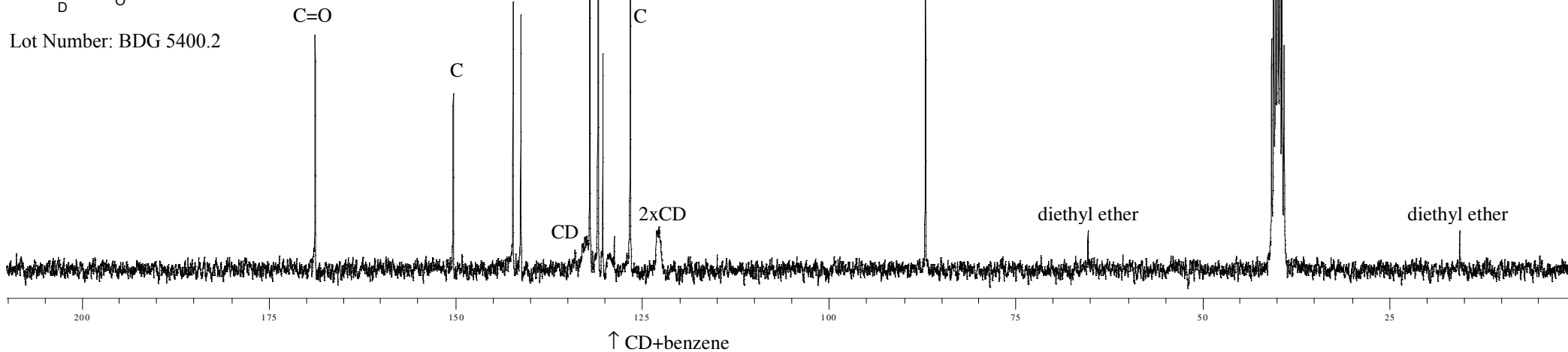
2xCD

C-O

NMR Solvent

diethyl ether

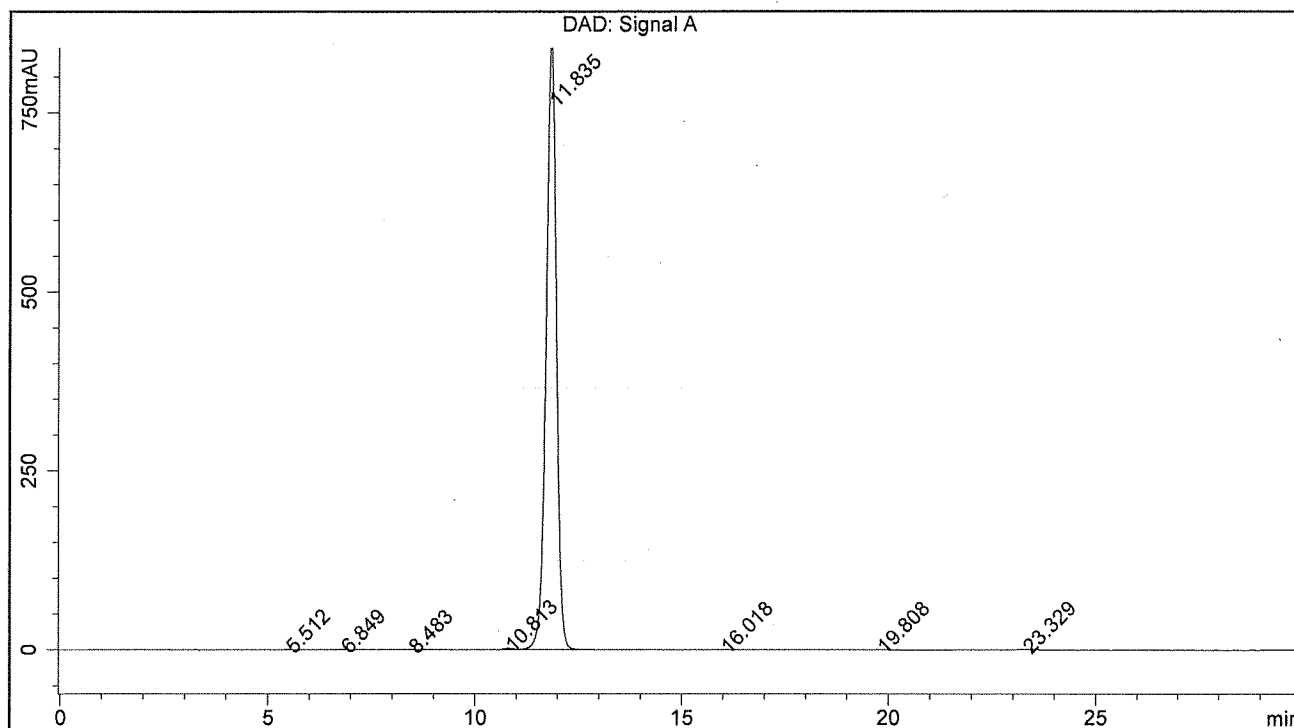
diethyl ether



BDG - Analysis of Chlorthalidone-d4

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm  
 Guard : Phenomenex SecurityGuard C18 4 x 3mm  
 Mobile Phase : 63:27:10 50 mM Potassium diHydrogen Phosphate pH=3.0 : Methanol : Acetonitrile  
 Flow Rate : 1.0 mL/min  
 Sample Solvent : Mobile Phase  
 Column Temperature : 20C  
 Injection Volume : 10 uL  
 Detection : UV at 225 nm

<b>Sample Name</b>	BDG 5400.2	<b>Instrument</b>	AnalyticalLC01
<b>Acquisition</b>	25/02/2012, 16:31:41	<b>Method (rev.)</b>	LC10492a ( 8)
<b>Sequence</b>	BDG_25Feb2012c - Reprocessed	<b>Vial Position</b>	1
<b>Operator</b>	solvation010\cerityadmin	<b>Injection</b>	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.51 min	0.7191	6.8367	0.1469 min	0.046 %
2	6.85 min	0.4332	11.1971	0.3335 min	0.075 %
3	8.48 min	0.2524	14.5992	0.6988 min	0.098 %
4	10.81 min	2.2025	42.8677	0.2911 min	0.286 %
5	11.83 min	850.6633	14821.9200	0.2673 min	99.055 %
6	16.02 min	0.2960	6.9302	0.2971 min	0.046 %
7	19.81 min	0.3954	30.1727	0.9062 min	0.202 %
8	23.33 min	0.8162	28.7678	0.4632 min	0.192 %