



## BDG SYNTHESIS

### Certificate of Analysis

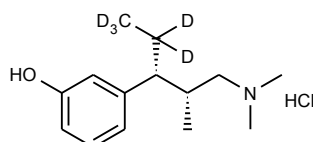
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

*Barry Dent*

Barry R. Dent, PhD, Director  
15 February 2012

**Name:** Tapentadol-d<sub>5</sub> HCl  
**CAS Number:** 175591-23-8 (unlabelled free base)

**Structure:**



**Molecular Weight:** C<sub>14</sub>H<sub>18</sub>D<sub>5</sub>NO·HCl = 262.83

**Lot Number:** BDG 12457.3

**Appearance:** White, crystalline solid

**Purity By HPLC:** 98.9 %

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

**Re-test Date:** 15 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 what would be expected for unlabelled material.

Residual Solvents: traces (under 0.1 % w/w) of ethyl acetate and methanol are observed.

Impurities: traces of unidentified impurities are seen in the baseline.

### Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

Isotopic Labelling: the signal at one site of deuteration indicates slight label loss.

### High-resolution Mass Spectrum (ESI+)

Found  $m/z$  227.2171.  $C_{14}H_{19}D_5NO$   $[M+H]^+$  requires  $m/z$  227.2172. The deviation of 0.4 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 %). The sample contains approximately 9%  $d_4$  material.

### HPLC

A sharp, symmetrical peak is observed (98.9 %). 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.

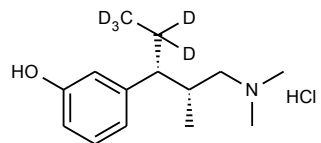
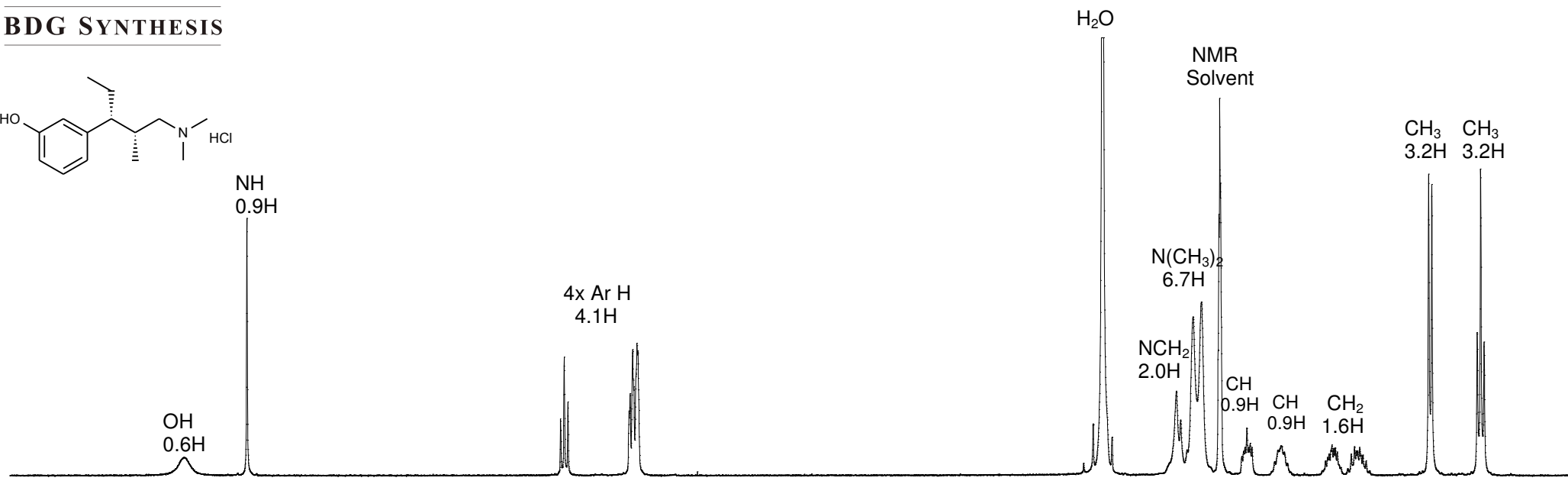
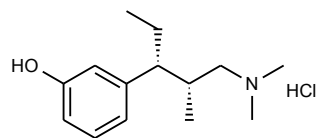
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

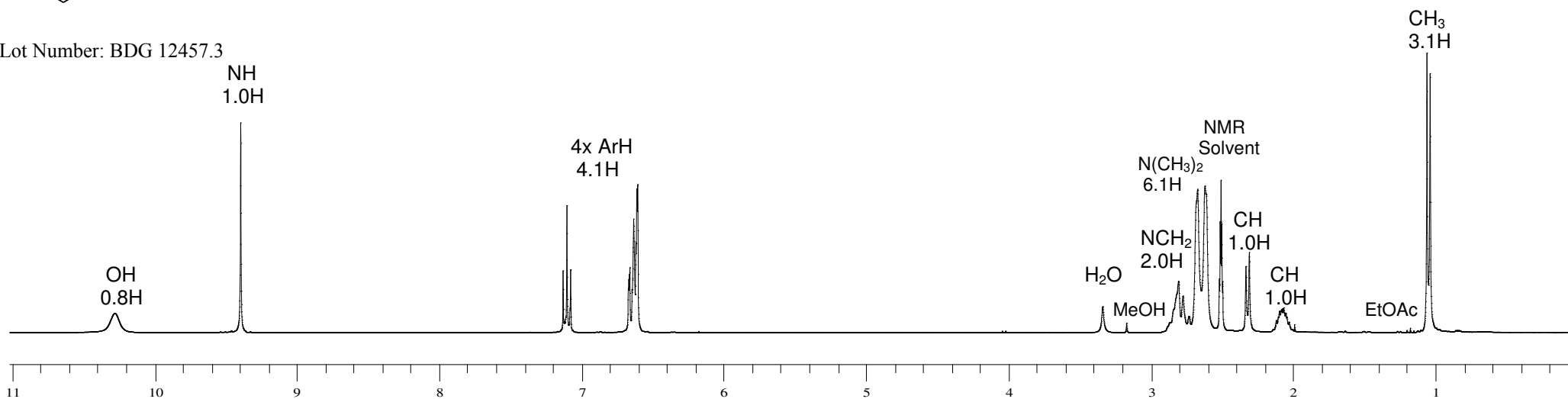


Proton NMR Spectrum of Tapentadol HCl (top) and Tapentadol-d<sub>5</sub> HCl (bottom) in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



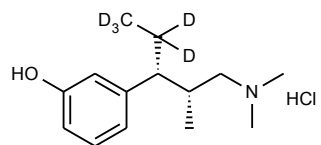
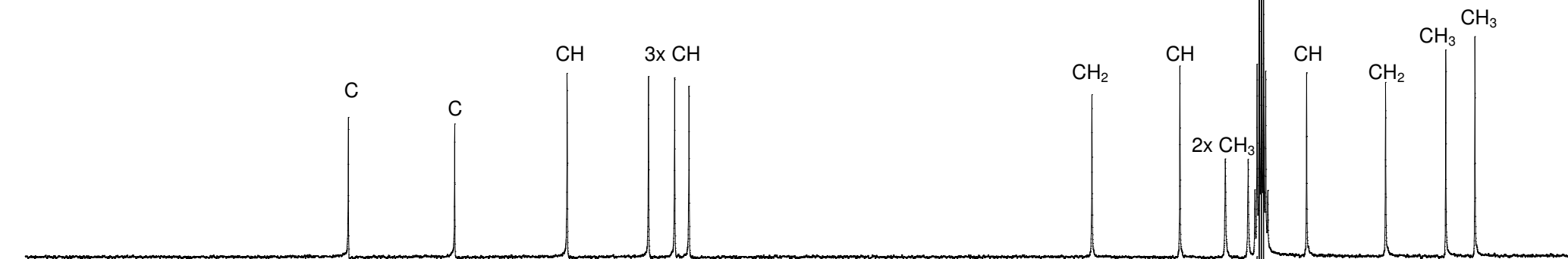
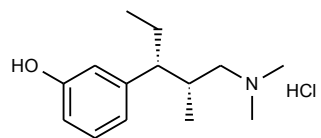
Lot Number: BDG 12457.3



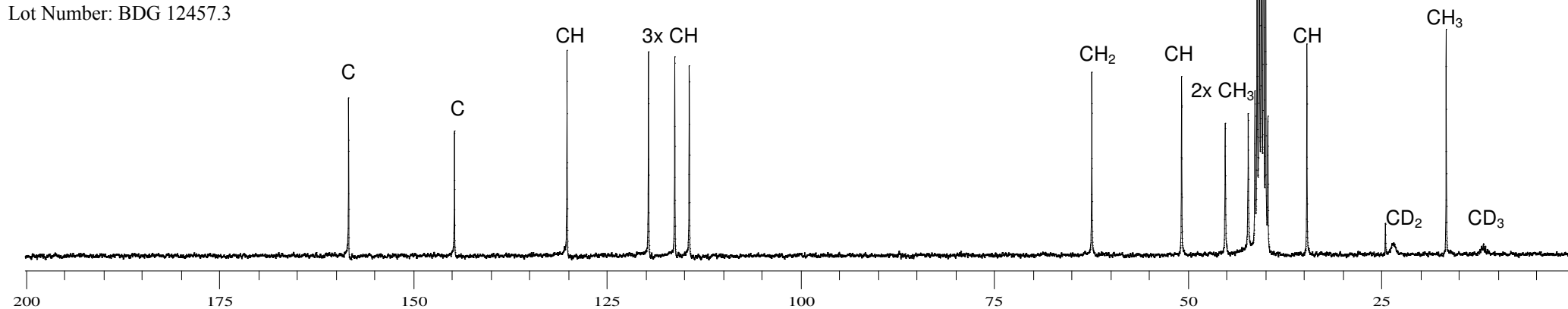


Carbon-13 NMR Spectrum of Tapentadol HCl (top) and Tapentadol-d<sub>5</sub> HCl (bottom) in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



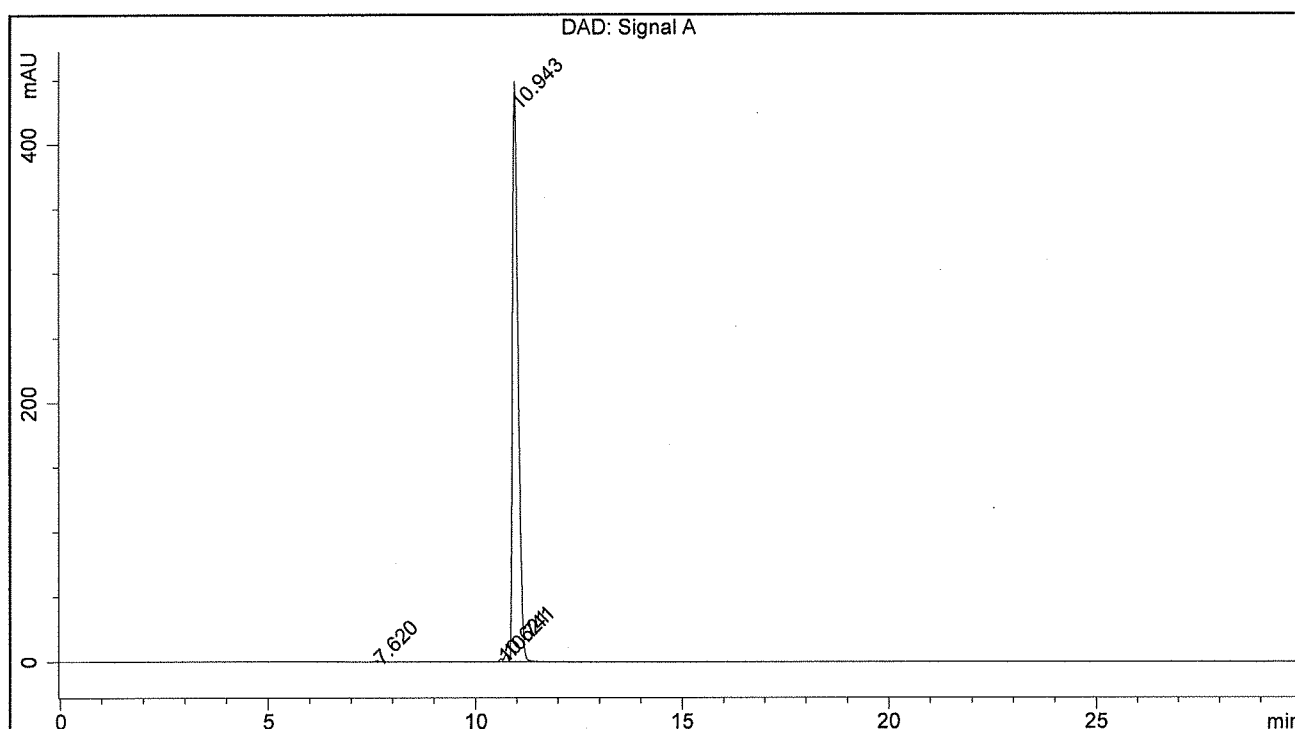
Lot Number: BDG 12457.3



BDG - Analysis of Tapentadol-d5 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm  
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm  
 Mobile Phase A : 90:10:0.01 Water : Acetonitrile : Trifluoroacetic Acid  
 Mobile Phase B : 50:50:0.01 Water : Acetonitrile : Trifluoroacetic Acid  
 Gradient (A:B) : T0=100:0, T20=0:100, T24=0:100, T36=100:0, T30=100:0  
 Flow Rate : 1.0 mL/min  
 Sample Solvent : 85:15 Water : Acetonitrile  
 Column Temperature : 20C  
 Injection Volume : 10 uL  
 Detection : UV at 274 nm

Sample Name	BDG 12457.3	Instrument	AnalyticalLC01
Acquisition	15/02/2012, 20:27:06	Method (rev.)	LC10488b ( 8)
Sequence	BDG_15Feb2012b	Vial Position	5
Operator	solvation010\cerityadmin	Injection	3 of 3



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.62 min	0.8544	4.7752	0.0852 min	0.112 %
2	10.62 min	2.4363	11.6847	0.0720 min	0.273 %
3	10.74 min	5.4935	31.5856	0.0891 min	0.739 %
4	10.94 min	448.8191	4228.6138	0.1419 min	98.877 %