BDG SYNTHESIS

Certificate of Analysis

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

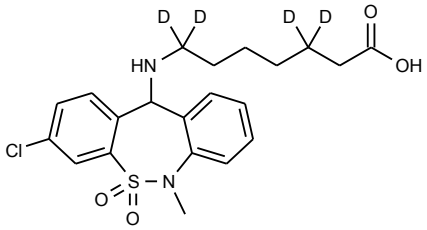
Barry Dent

Barry R. Dent, PhD, Director
14 June 2012

Name: **Tianeptine-d_4**

CAS Number: 66981-73-5 (unlabelled)

Structure:



Molecular Weight: $C_{21}H_{21}D_4ClN_2O_4S$ = 440.98

Lot Number: BDG 13481.3

Appearance: White, crystalline solid

Corrected Purity: 98.7 % (HPLC) - 0.6 % (hexanes) - 1.0 % (toluene) = 97.1 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 14 June 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.

Mailing:
BDG Synthesis Limited
PO Box 38627, Wellington Mail Centre,
Wellington 5045, New Zealand.

Shipping:
BDG Synthesis Limited
Gracefield Research Centre, Building F,
69 Gracefield Rd, Lower Hutt 5010, New Zealand.

Phone: + 64 4 569 0520
Fax: + 64 4 569 0521

info@bdg.co.nz
www.bdg.co.nz

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 what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: small amounts of hexanes (0.6 % *w/w*) and toluene (1 % *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 what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 441.1549. $C_{21}H_{22}D_4ClN_2O_4S$ $[M+H]^+$ requires *m/z* 441.1553. The deviation of 0.9 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 (98.7 %). 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 58.00, H 4.94, D 1.88, N 6.20 %
$C_{21}H_{21}D_4ClN_2O_4S$	Requires:	C 57.20, H 4.80, D 1.83, N 6.35 %

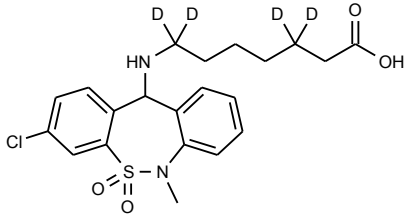
The elemental analyses fall within generally accepted limits (+/- 0.4 %) for establishing the molecular formula given, except the result for carbon. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because 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.

BDG SYNTHESIS

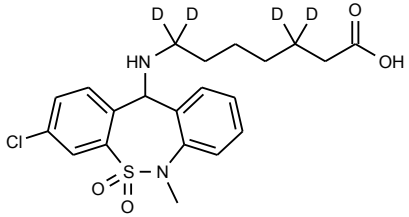
Proton NMR Spectrum of Tianeptine-d_4 in DMSO-d_6



Lot Number: BDG 13481.3

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Tianeptine-d_4 in DMSO-d_6



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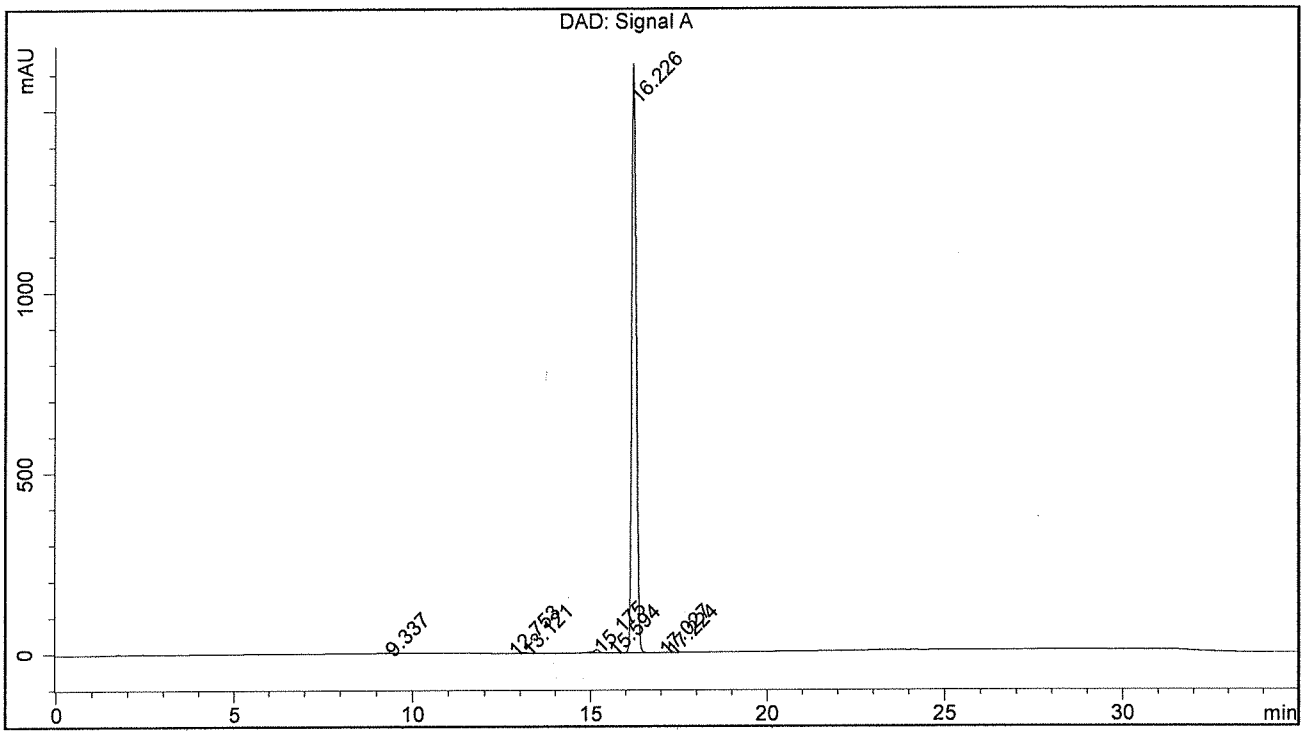
BDG - Analysis of Tianeptine-d4

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 47.5:31.5:21 Ion pair solution : Acetonitrile : Methanol
Mobile Phase B : 20:60:20 Ion pair solution : Acetonitrile : Methanol
Ion pair solution = 2 g/L Sodium Dodecylsulphate pH 2.5 (H3PO4)
Gradient (A:B) : T0=100:0, T20=0:100, T28=0:100, T30=100:0, T35=100:0
Flow Rate : 1.0 mL/min . . . . . Sample Solvent : 50:50 Water : Methanol
Column Temperature : 30C . . . . . Injection Volume : 10 uL . . . . . Detection : UV at 220 nm

Sample Name	BDG 13481.3	Instrument	AnalyticalLC01
Acquisition	14/06/2012, 14:51:35	Method (rev.)	LC10521a (6)
Sequence	BDG_14Jun2012b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	9.34 min	0.9306	10.3682	0.1640 min	0.071 %
2	12.75 min	0.3882	3.5299	0.1421 min	0.024 %
3	13.12 min	2.6225	23.5903	0.1429 min	0.161 %
4	15.17 min	9.4252	139.9969	0.2053 min	0.957 %
5	15.59 min	0.3589	3.3210	0.1300 min	0.023 %
6	16.23 min	1624.9257	14434.2183	0.1416 min	98.688 %
7	17.03 min	0.9357	7.2868	0.1209 min	0.050 %
8	17.22 min	0.3754	3.8690	0.1363 min	0.026 %