



BDG SYNTHESIS

Certificate of Analysis

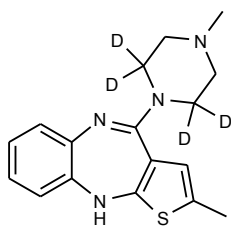
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare

Neil Beare, PhD, Director
24 January 2017

Name: Olanzapine-d₄
CAS Number: 132539-06-1 (unlabelled)

Structure:



Molecular Weight: C₁₇H₁₆D₄N₄S = 316.46
Lot Number: BDG 14074.3
Appearance: Yellow, crystalline powder
Corrected Purity: 99.9 % (HPLC) - 2.8 % (acetonitrile) - 5.4 % (water) = 91.7 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 24 January 2022
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.

Identity and Purity

Proton NMR Spectrum

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

Isotopic Labelling: due to the masking of one set of piperazine signals by those of HOD from the NMR solvent, the spectrum is of little value in determining isotopic purity.

Residual Solvents: a small amount of acetonitrile (2.8 % w/w) is 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 the site of deuteration is absent compared with the spectrum for unlabelled material, indicating complete deuterium incorporation.

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 317.1739. $C_{17}H_{17}D_4N_4S$ $[M+H]^+$ requires m/z 317.1738. The deviation of 0.3 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 sharp, slightly tailing 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 61.04, H 5.30, D 2.65, N 17.42 %
$C_{17}H_{16}D_4N_4S \cdot 1.0H_2O$	Requires:	C 61.05, H 5.42, D 2.41, N 16.75 %, H_2O 5.39 %
$C_{17}H_{16}D_4N_4S$	Requires:	C 64.52, H 5.10, D 2.55, N 17.70 %

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.

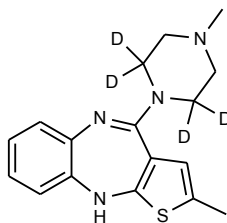
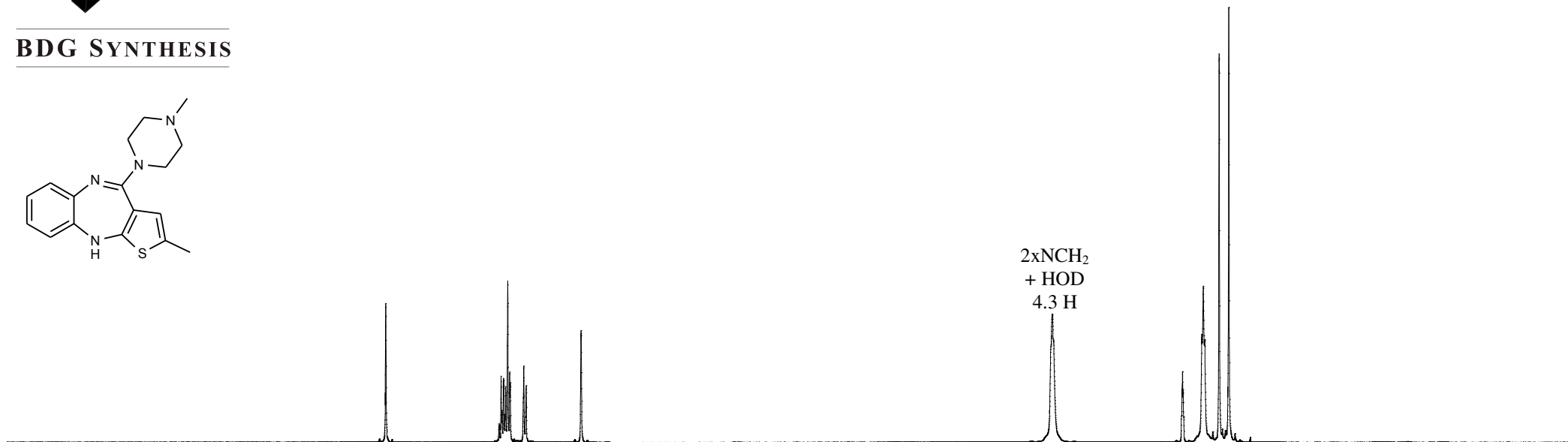
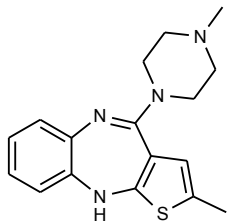
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

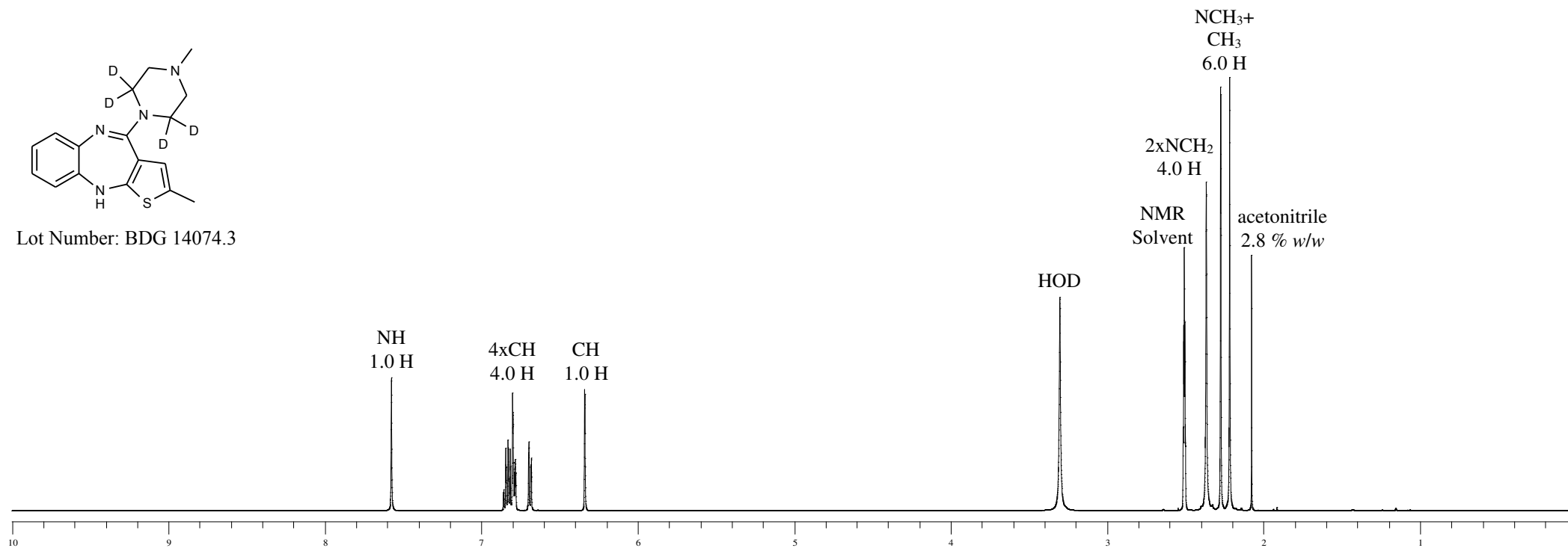


Proton NMR Spectrum of Olanzapine (top) and Olanzapine-d₄ (bottom) in DMSO-d₆

BDG SYNTHESIS



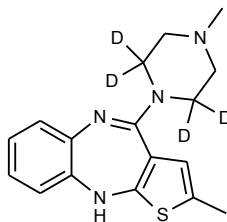
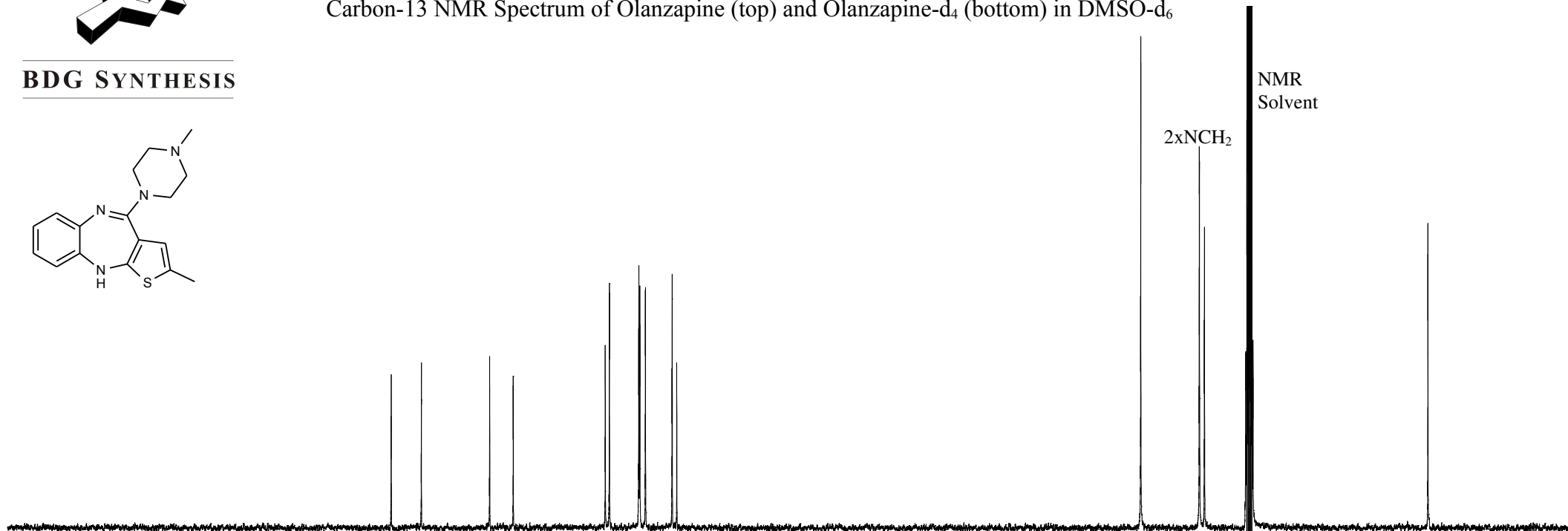
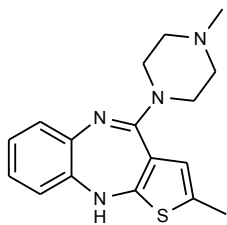
Lot Number: BDG 14074.3



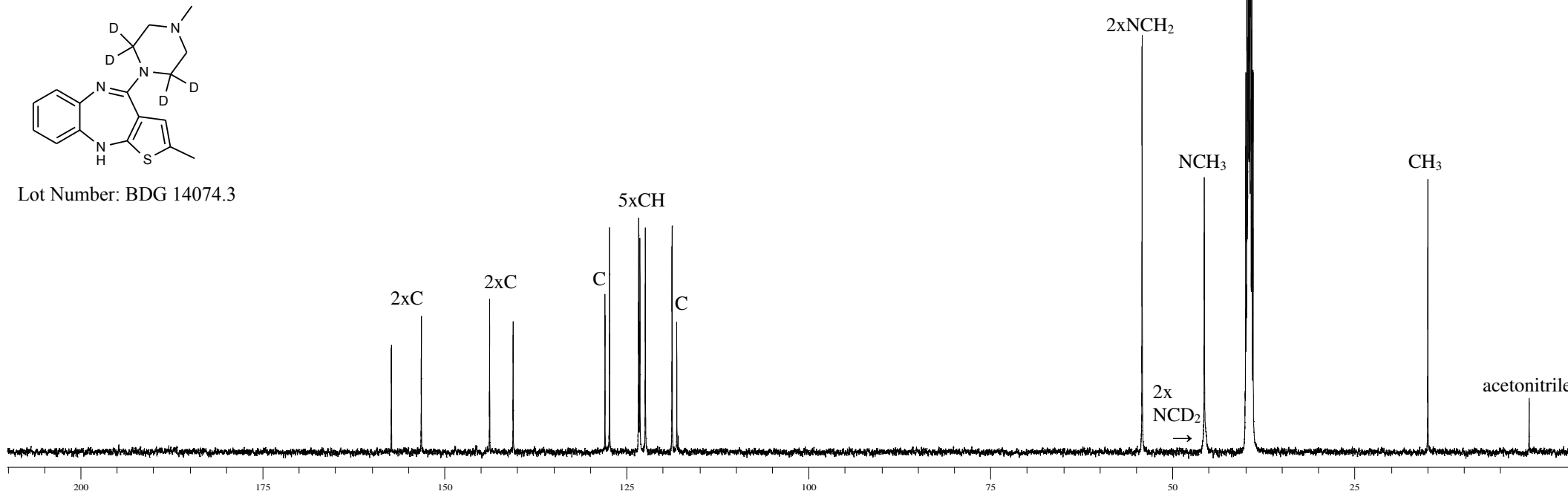


Carbon-13 NMR Spectrum of Olanzapine (top) and Olanzapine-d₄ (bottom) in DMSO-d₆

BDG SYNTHESIS



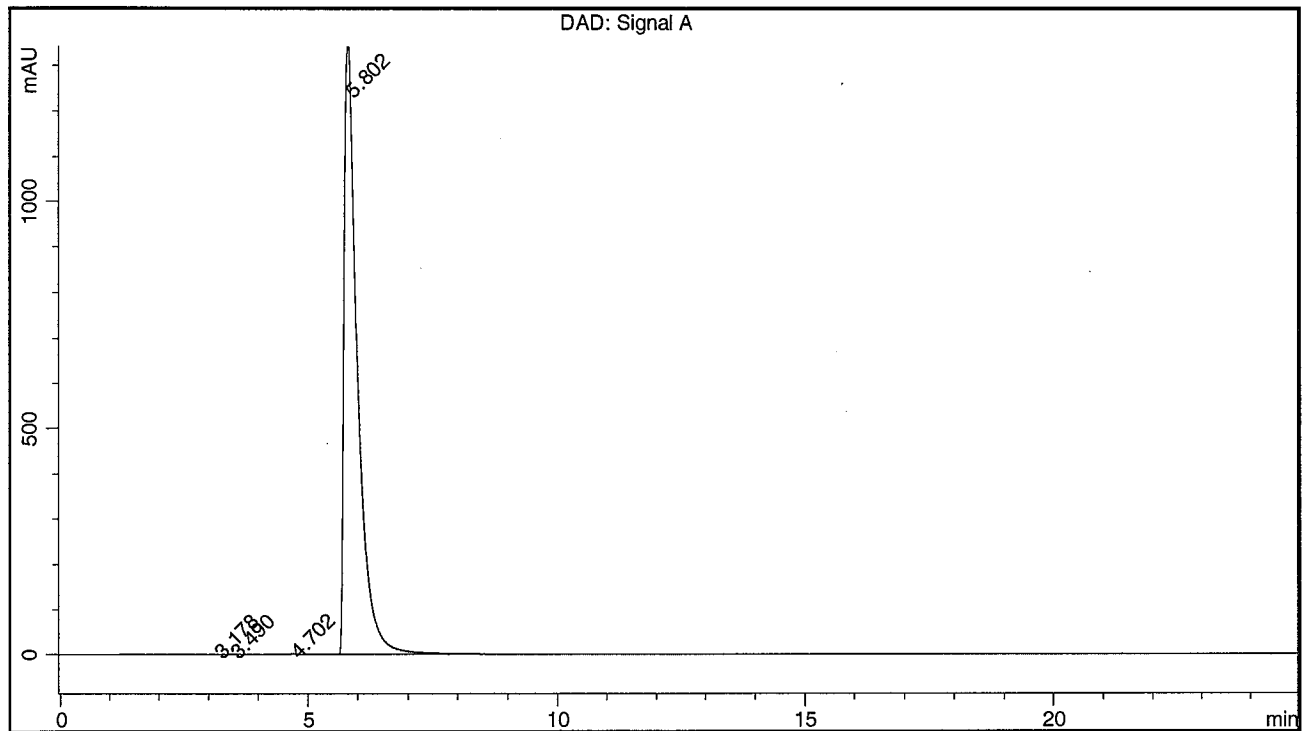
Lot Number: BDG 14074.3



BDG - Analysis of Olanzapine-d4

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex SecurityGuard C18 4 x 3mm
 Mobile Phase : 65:35 50 mM Ammonium Acetate pH=5.5 : Acetonitrile
 Flow Rate : 1.0 mL/min
 Sample Solvent : Mobile Phase
 Column Temperature : 20 C
 Injection Volume : 10 uL
 Detection : UV at 254 nm

Sample Name	BDG 14074.3	Instrument	AnalyticalLC01
Acquisition	24/01/2017, 19:26:04	Method (rev.)	LC10482a (5)
Sequence	BDG_24Jan2017c - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.18 min	0.7131	6.0468	0.1309 min	0.024 %
2	3.49 min	0.2260	2.4585	0.1489 min	0.010 %
3	4.70 min	2.1536	28.4209	0.1840 min	0.113 %
4	5.80 min	1362.8573	25186.0320	0.2696 min	99.854 %