

BDG SYNTHESIS

Certificate of Analysis

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

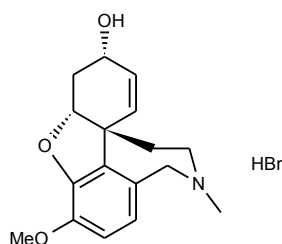
Barry Dent

Barry R. Dent, PhD, Director
27 November 2010

Name: (+)-Galanthamine HBr

CAS Number: 60384-53-4 (free base)

Structure:



Molecular Weight: $C_{17}H_{21}NO_3 \cdot HBr = 368.27$

Lot Number: BDG 5402.2

Appearance: Off-white, crystalline solid

Corrected Purity: 97.8 % (HPLC) - 1.0 % (methanol) - 1.0 % (water) = 95.8 %

Re-test Date: 27 November 2011

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	may be hygroscopic; store desiccated; recommended to determine water content periodically.
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. The signal for the N-methyl group is split (2:1) indicating the presence of different conformers in solution.

Residual Solvents: a small amount of methanol (1.0 % w/w) and a trace (under 0.1 % w/w) of diethyl ether are observed.

Impurities: an unidentified impurity is also observed as a small signal at 3.3 ppm.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. Some signals are observed as collapsed multiplets, which is sometimes observed for nitrogen-containing compounds that can adopt several conformations in solution.

High-resolution Mass Spectrum (ESI+)

Found m/z 288.1618. $C_{17}H_{22}NO_3$ $[M+H]^+$ requires m/z 288.1594. The deviation of 8.2 ppm is somewhat outside normally accepted limits for the establishment of identity by HRMS, and the mass spectral data should be considered in conjunction with other identity criteria.

HPLC

A somewhat broadened, slightly tailing peak is observed (97.8 %). 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 54.64, H 6.25, N 3.67 %
$C_{17}H_{21}NO_3 \cdot HBr \cdot 0.2H_2O$	Requires:	C 54.91, H 6.07, N 3.77 %
$C_{17}H_{21}NO_3 \cdot HBr$	Requires:	C 55.44, H 6.02, N 3.80 %

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.

Karl-Fischer Analysis

	Found:	H ₂ O 1.0 %
$C_{17}H_{21}NO_3 \cdot HBr \cdot 0.2H_2O$	Requires:	H ₂ O 1.0 %

Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

Specific Rotation

Found: $[\alpha]_D = +86.4^\circ$ (c = 1.012, H₂O).

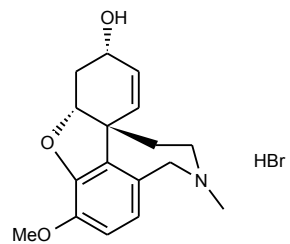
Lit. (Merck Index) $[\alpha]_D = -93.1^\circ$ (c = 0.1015, H₂O) for HBr salt of natural product.

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.

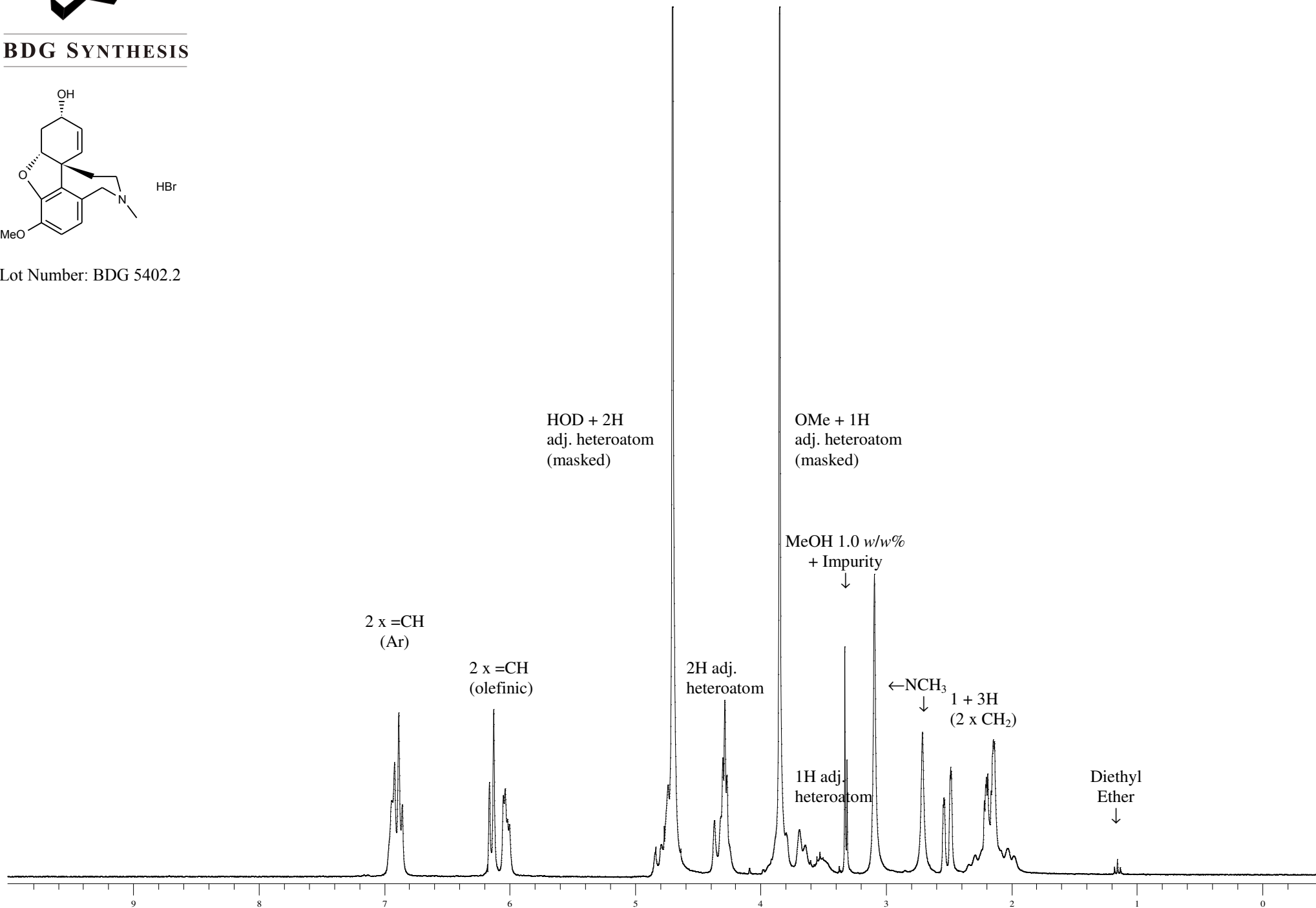


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Lot Number: BDG 5402.2

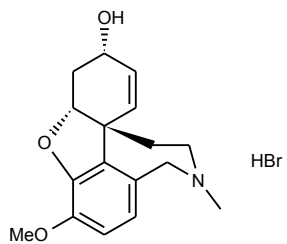
Proton NMR Spectrum of (+)-Galanthamine HBr in D₂O



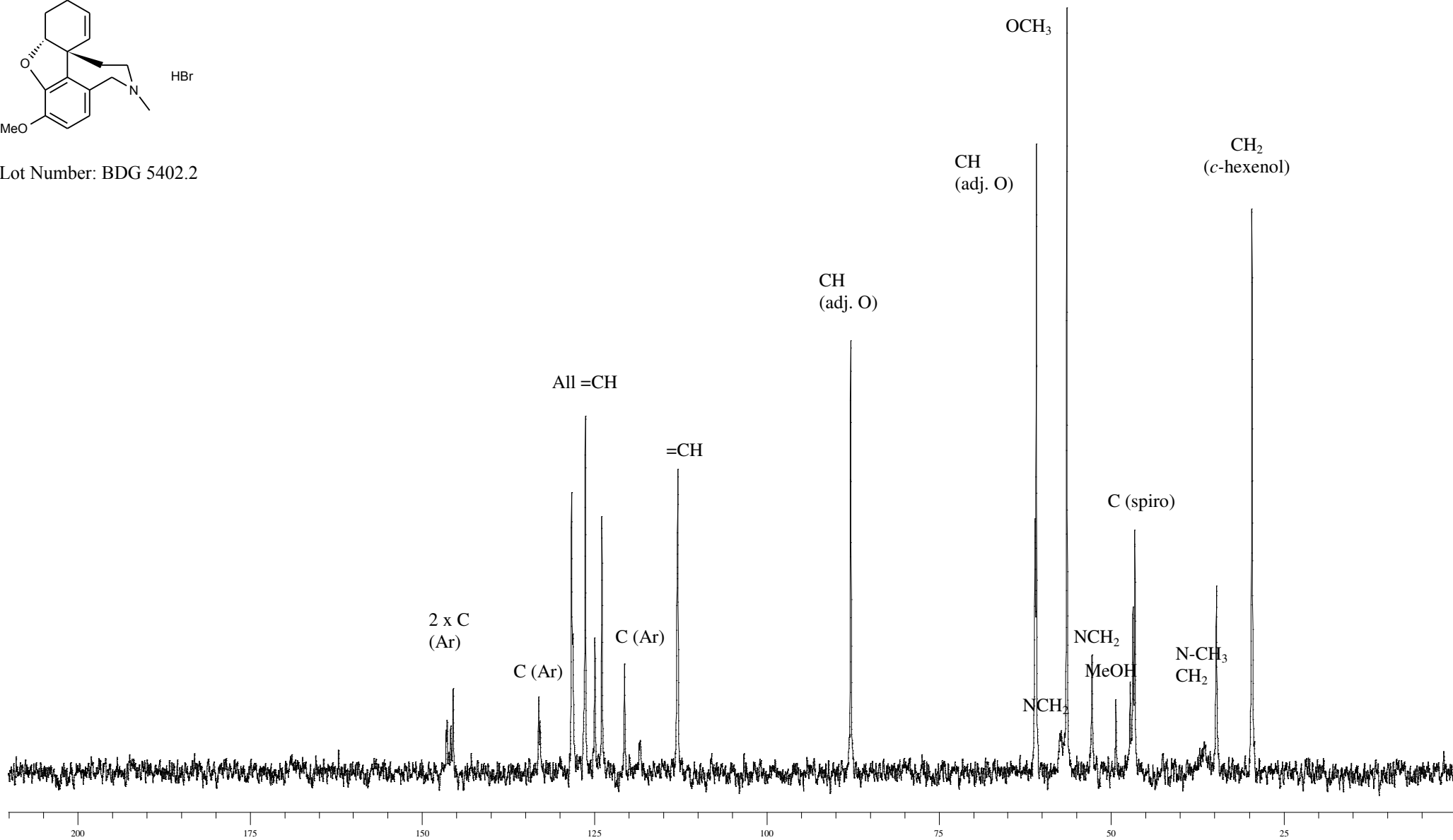


Carbon-13 NMR Spectrum of (+)-Galanthamine HBr in D₂O

BDG SYNTHESIS



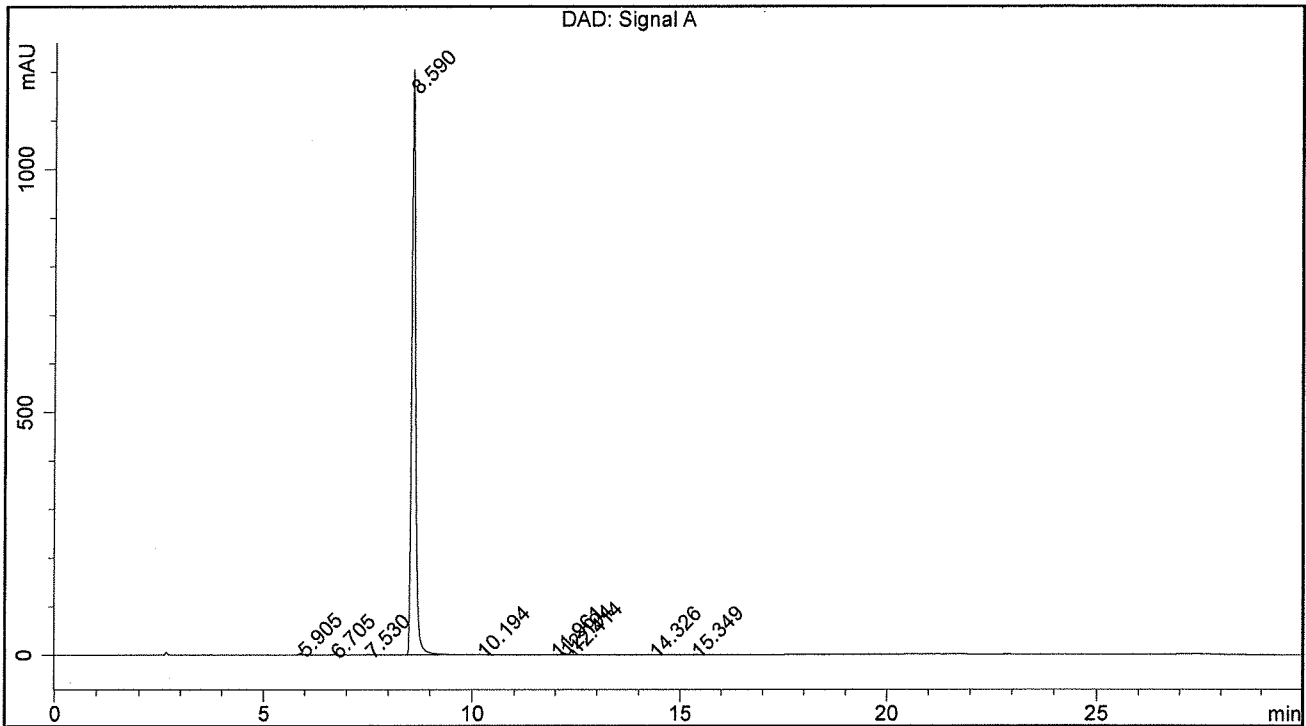
Lot Number: BDG 5402.2



BDG - Analysis of (+)-Galanthamine-HBr

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 20 mM Potassium diHydrogen Phosphate pH = 6.0 : Acetonitrile
 Mobile Phase B: 50:50 20 mM Potassium diHydrogen Phosphate pH = 6.0 : Acetonitrile
 Gradient (A:B) : T0=100:0, T20=0:100, T24=0:100, T27=100:0, T30=100:0
 Flow Rate : 1.0 mL/min
 Sample Solvent : 90:10 Water : Acetonitrile
 Column Temperature : 40C
 Injection Volume : 10 uL
 Detection : UV at 230 nm

Sample Name	BDG 5402.2	Instrument	AnalyticalLC01
Acquisition	27/11/2010, 15:37:55	Method (rev.)	LC10005c (5)
Sequence	BDG_27Nov2010d - Reprocessed	Vial Position	12
Operator	solvation010\lcerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.91 min	3.2203	25.1518	0.1171 min	0.313 %
2	6.70 min	0.6216	10.7584	0.2099 min	0.134 %
3	7.53 min	1.2181	8.6871	0.1052 min	0.108 %
4	8.59 min	1204.2811	7861.1051	0.0982 min	97.794 %
5	10.19 min	0.6136	6.2535	0.1429 min	0.078 %
6	11.96 min	0.5799	3.3776	0.0860 min	0.042 %
7	12.19 min	3.9730	29.6807	0.1112 min	0.369 %
8	12.41 min	10.2698	81.2096	0.1183 min	1.010 %
9	14.33 min	0.4872	5.4635	0.1588 min	0.068 %
10	15.35 min	0.5718	6.7415	0.1436 min	0.084 %