BDG SYNTHESIS

Certificate of Analysis

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

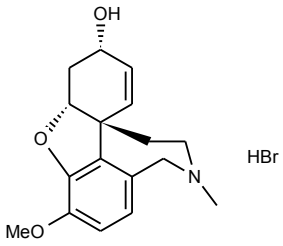
Barry Dent

Barry R. Dent, PhD, Director
19 February 2013

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) - 0.9 % (methanol) - 0.2 % (diethyl ether) - 1.0 % (water) = 95.7 %

Re-test Date: 19 February 2018

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.

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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: small amounts of diethyl ether (0.2 % *w/w*) and methanol (0.9 % *w/w*) are observed.
Impurities: an unidentified impurtiy 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 sharp, symmetrical 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_2O 1.0 %
$C_{17}H_{21}NO_3 \cdot HBr \cdot 0.2H_2O$	Requires:	H_2O 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

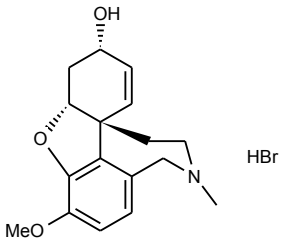
Found: $[\alpha]_D = +86.4^o$ (c = 1.012, H_2O).
Lit. (Merck Index) $[\alpha]_D = -93.1^o$ (c = 0.1015, H_2O) for HBr salt of natural product.

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.

BDG SYNTHESIS

Proton NMR Spectrum of (+)-Galanthamine HBr in D_2O



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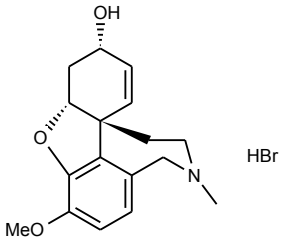
BDG SYNTHESIS

Carbon-13 NMR Spectrum of (+)-Galanthamine HBr in D_2O

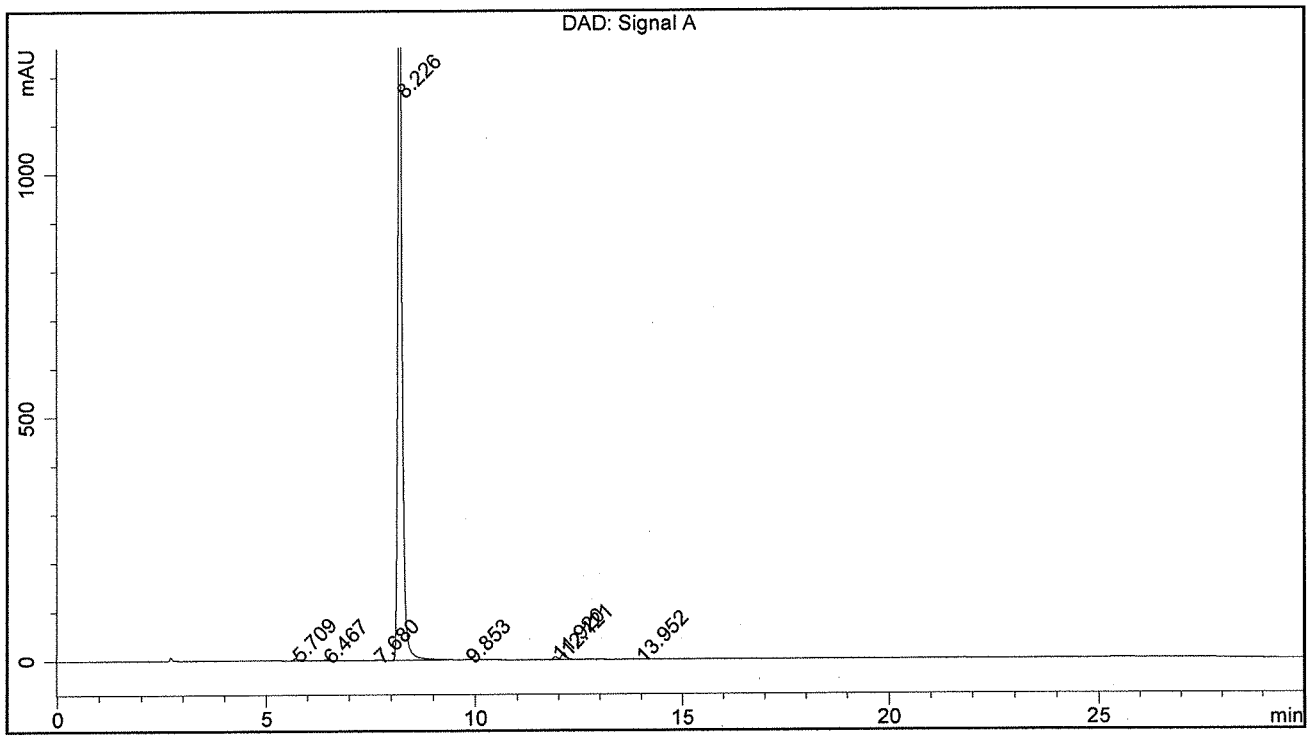


Lot Number: BDG 5402.2

BDG - Analysis of (+)-Galanthamine-HBr

Column : Phenomenex Luna C8(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	19/02/2013, 20:22:59	**Method (rev.)**	LC10005c (6)
Sequence	BDG_19Feb2013a	**Vial Position**	1
Operator	solvation010\cerityadmin	**Injection**	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.71 min	4.1487	31.0045	0.1112 min	0.287 %
2	6.47 min	2.0891	23.1405	0.1552 min	0.214 %
3	7.68 min	1.5705	11.8814	0.1103 min	0.110 %
4	8.23 min	1519.8905	10553.8989	0.1030 min	97.789 %
5	9.85 min	1.0143	11.8272	0.1460 min	0.110 %
6	11.92 min	5.5522	39.5381	0.1071 min	0.366 %
7	12.12 min	14.2249	115.0235	0.1203 min	1.066 %
8	13.95 min	0.5467	6.1703	0.1397 min	0.057 %