



BDG SYNTHESIS

Certificate of Analysis

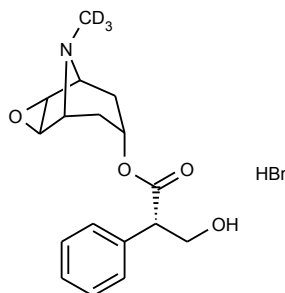
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
18 October 2009

Name: Scopolamine-d₃ HBr
CAS Number: 114-49-8 (unlabelled trihydrate)

Structure:



Molecular Weight: C₁₇H₁₈D₃NO₄·HBr = 387.28
Lot Number: BDG 2750.1
Appearance: White, crystalline solid
Corrected Purity: 95.5 % (HPLC) - 2.8 % (methanol) - 4.4 % (water) = 88.3 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 18 October 2014
Storage and Handling: Temperature: ambient laboratory temperature; may be refrigerated.
Humidity: may be hygroscopic; store desiccated; recommended to determine water content periodically.
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. Some signals have smaller, downfield, counterparts and these may arise as a result of two unequal conformational populations within the molecule. The presence of a structurally similar impurity as the source of these smaller signals was dismissed because the duplication of signals disappears when a small sample of the material is converted into its free base and re-examined by ¹H NMR. The spectrum for the unlabelled material only shows one set of peaks. We presume that minor pH or water content differences account for the disparity.

Isotopic Labelling: signals at the site of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: a small amount of methanol (2.8 % w/w) is 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. Small signals for some peaks are thought to arise from the presence of different conformational populations (see comments for the proton NMR above).

Isotopic Labelling: the signal for the N-Methyl carbon is masked by a methylene carbon and therefore cannot be used to ascertain the extent of deuterium incorporation.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 307.1736. C₁₇H₉D₃NO₄ [M+H]⁺ requires *m/z* 307.1734. The deviation of 0.7 ppm is within normally accepted limits for the establishment of identity by HRMS. No signal for d₀ material was seen (detection limit about 0.5 %).

HPLC

A sharp, symmetrical peak is observed (95.5 %). 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 50.44, H 5.16, D 1.72, N 3.39 %
C ₁₇ H ₁₈ D ₃ NO ₄ ·HBr·1.0H ₂ O	Requires:	C 50.38, H 5.22, D 1.49, N 3.46 %, H ₂ O 4.44 %
C ₁₇ H ₁₈ D ₃ NO ₄ ·HBr	Requires:	C 52.72, H 4.94, D 1.56, N 3.62 %

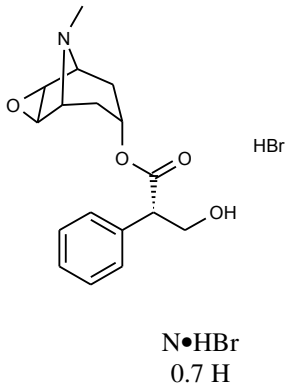
The elemental analyses fall somewhat outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given. In the absence of a Karl-Fischer water analysis, we recommend 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.

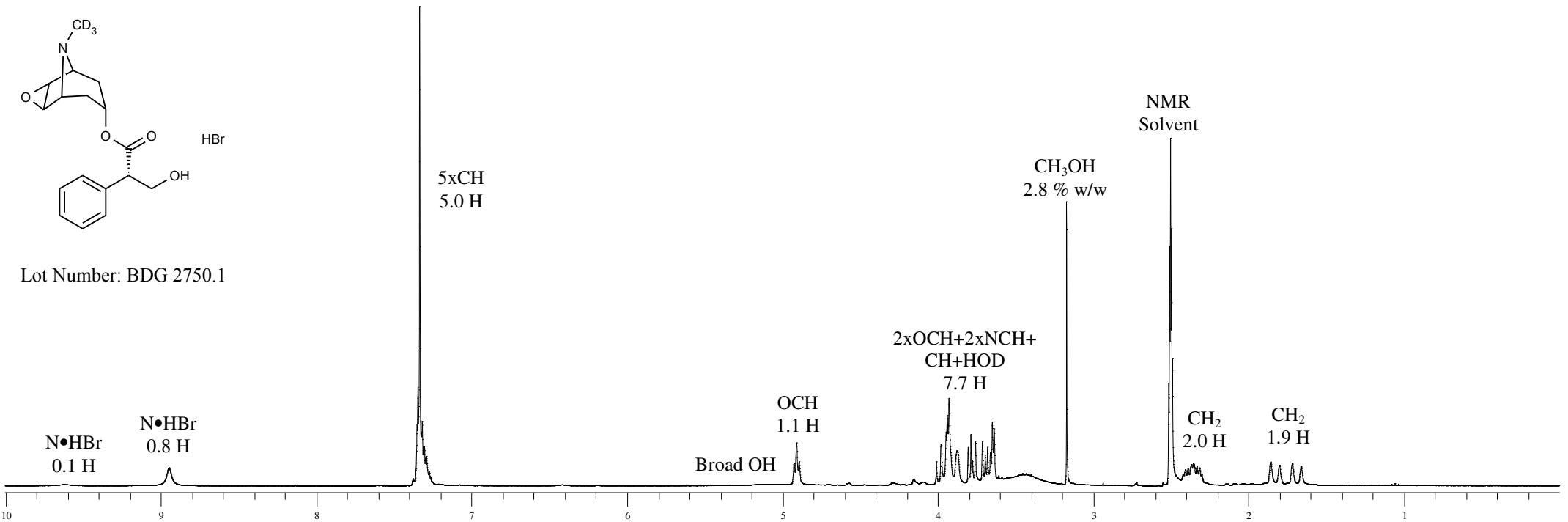
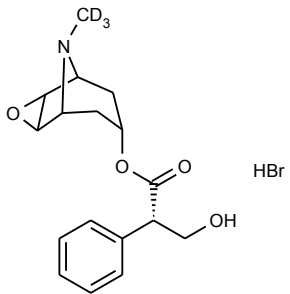
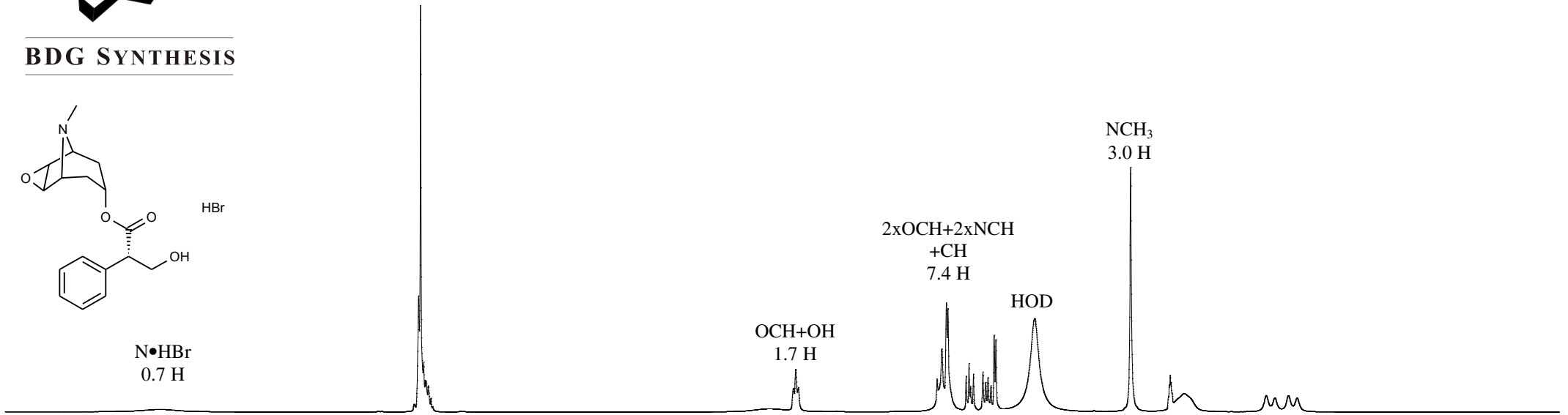
The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.



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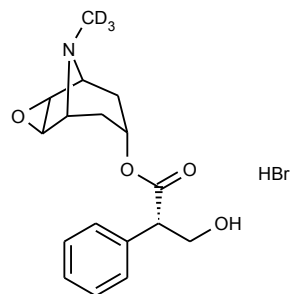
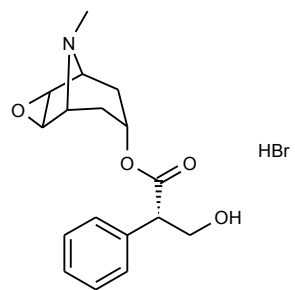
Proton NMR Spectrum of Scopolamine HBr (top) and Scopolamine-d₃ HBr (bottom) in DMSO-d₆



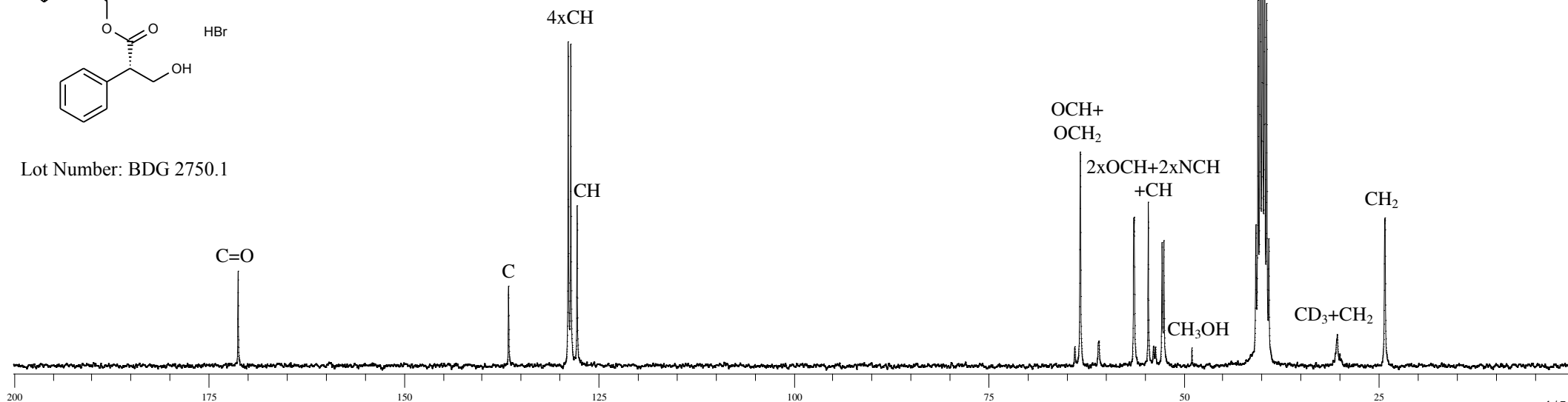


Carbon-13 NMR Spectrum of Scopolamine HBr (top) and Scopolamine-d₃ HBr (bottom) in DMSO-d₆

BDG SYNTHESIS



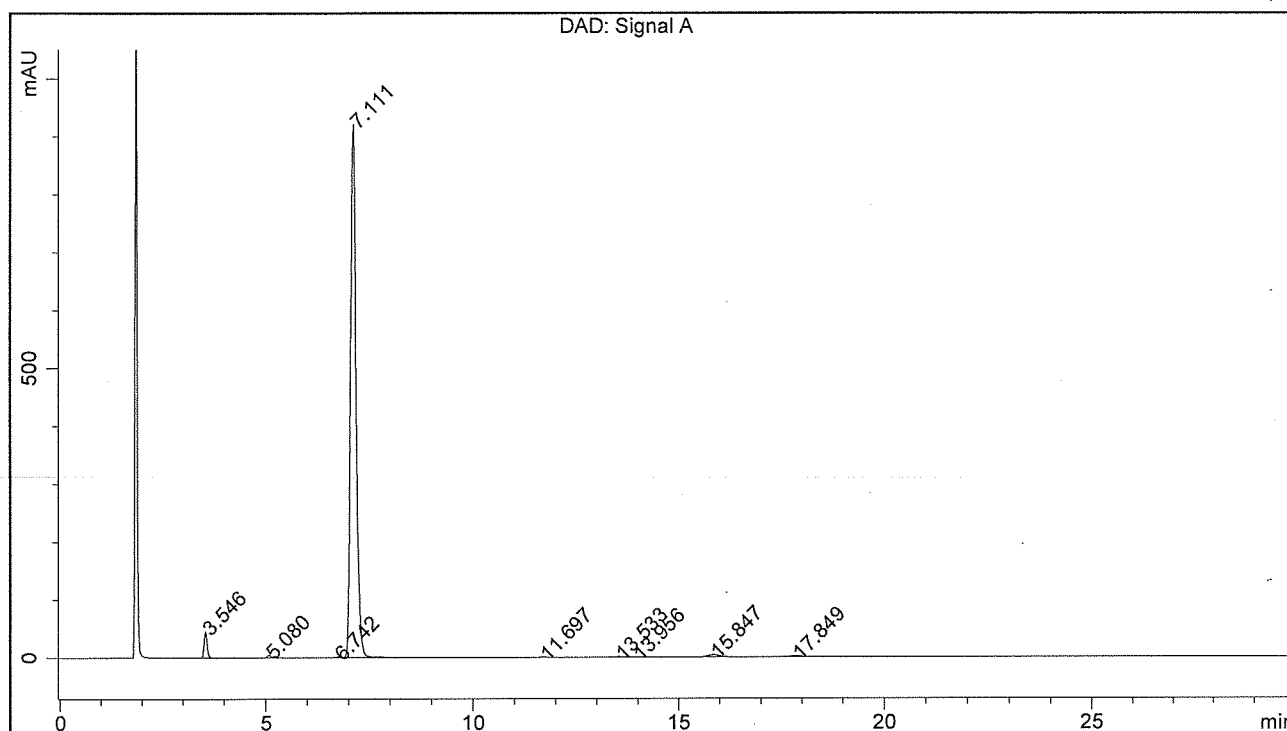
Lot Number: BDG 2750.1



BDG - Analysis of Scopolamine-d3 HBr

Column : Phenomenex Luna C8(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C8 RP 4 x 3 mm
 Mobile Phase : 55:45 8.7 mM Sodium Dodecylsulphate pH=2.5 (H3PO4) : Acetonitrile
 Flow Rate : 1.0 mL/min
 Sample Solvent : Mobile Phase
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV 210 nm

Sample Name	BDG 2750.1	Instrument	AnalyticalLC01
Acquisition	18/10/2009, 21:57:41	Method (rev.)	LC10344a (3)
Sequence	BDG_18Oct2009e - Reprocessed	Vial Position	2
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.55 min	45.1163	224.1499	0.0760 min	2.476 %
2	5.08 min	4.0142	26.5333	0.1011 min	0.293 %
3	6.74 min	1.3475	11.5802	0.1343 min	0.128 %
4	7.11 min	921.2191	8643.3608	0.1435 min	95.492 %
5	11.70 min	0.4262	6.1630	0.2007 min	0.068 %
6	13.53 min	0.9239	18.1692	0.2874 min	0.201 %
7	13.96 min	0.2484	7.6664	0.3721 min	0.085 %
8	15.85 min	3.7500	75.1667	0.3059 min	0.830 %
9	17.85 min	1.6274	38.5681	0.3485 min	0.426 %