



BDG SYNTHESIS

Certificate of Analysis

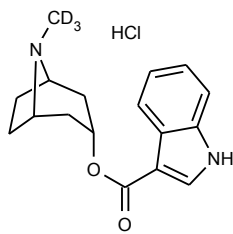
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
6 November 2013

Name: Tropisetron-d₃ HCl
CAS Number: 105826-92-4 (unlabelled)

Structure:



Molecular Weight: C₁₇H₁₇D₃N₂O₂·HCl = 323.83
Lot Number: BDG 12897.2
Appearance: Off-white, crystalline solid
Corrected Purity: 100.0 % (HPLC) - 2.0 % (ethanol) - 0.7 % (diethyl ether) - 1.6 % (water) = 95.7 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 6 November 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.

Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. Some signals are duplicated indicating two conformers of the product exist in solution.

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

Residual Solvents: small amounts of diethyl ether (0.7 % w/w) and ethanol (2.0 % 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. Some signals are duplicated indicating two conformers of the product exist in solution.

Isotopic Labelling: signals at the site of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found m/z 288.1788. $C_{17}H_{18}D_3N_2O_2$ $[M+H]^+$ requires m/z 288.1791. The deviation of 1.0 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 (100.0 %). 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 62.17, H 5.74, D 1.91, N 8.32 %
$C_{17}H_{17}D_3N_2O_2 \cdot HCl \cdot 0.3H_2O$	Requires:	C 62.02, H 5.69, D 1.84, N 8.51 %, H_2O 1.64 %
$C_{17}H_{17}D_3N_2O_2 \cdot HCl$	Requires:	C 63.05, H 5.60, D 1.87, N 8.65 %

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. In the absence of a Karl-Fischer water analysis, we recommend that the "best-fit" water content be used when determining corrected purity.

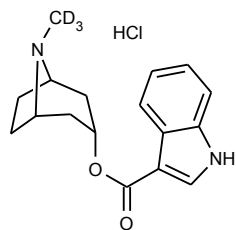
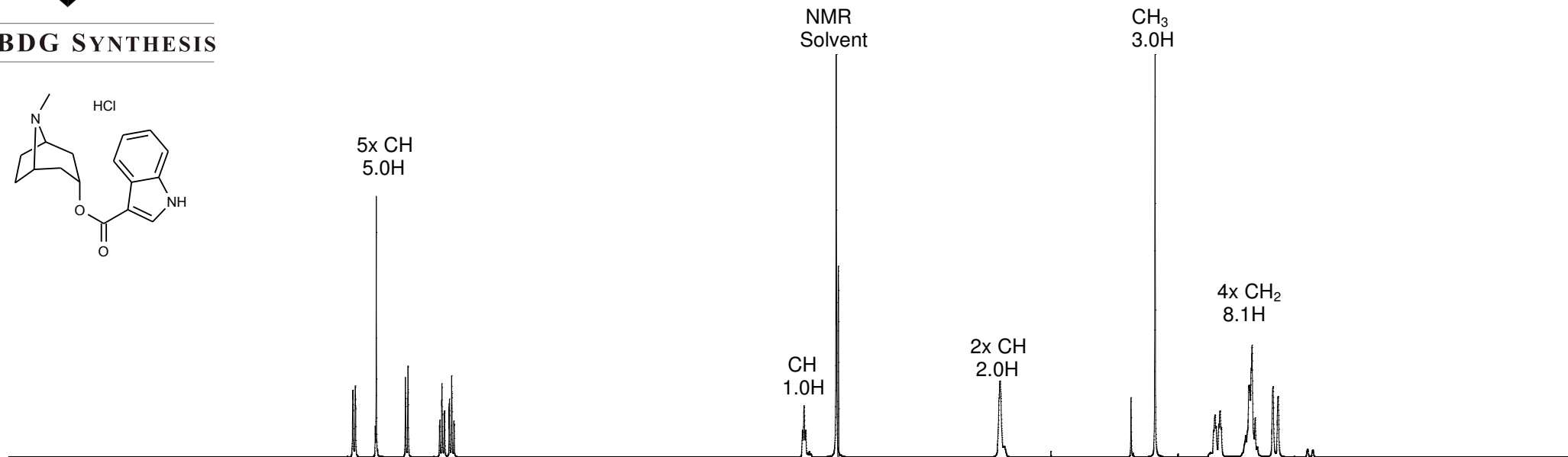
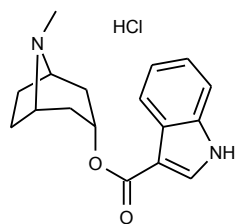
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

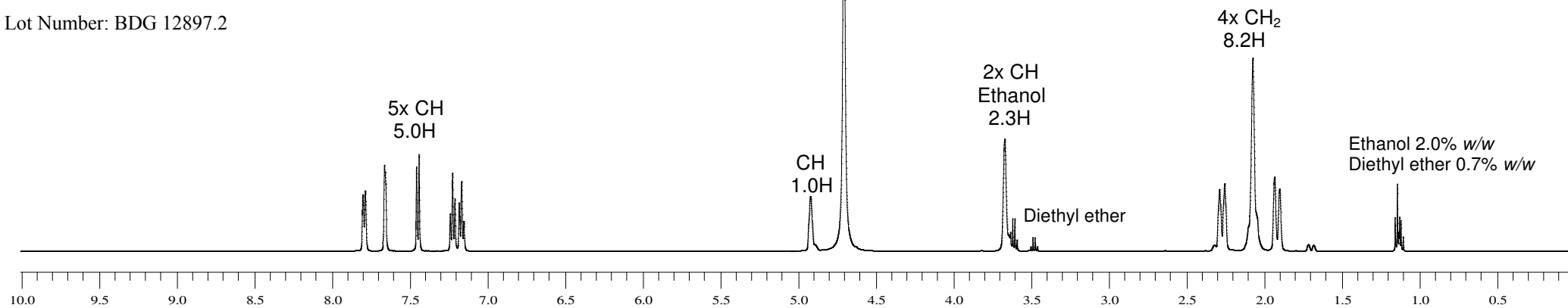


Proton NMR Spectrum of Tropisetron HCl (top) and Tropisetron-d₃ HCl (bottom) in D₂O

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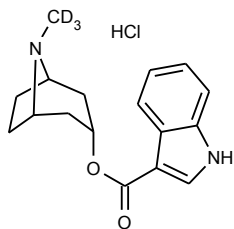
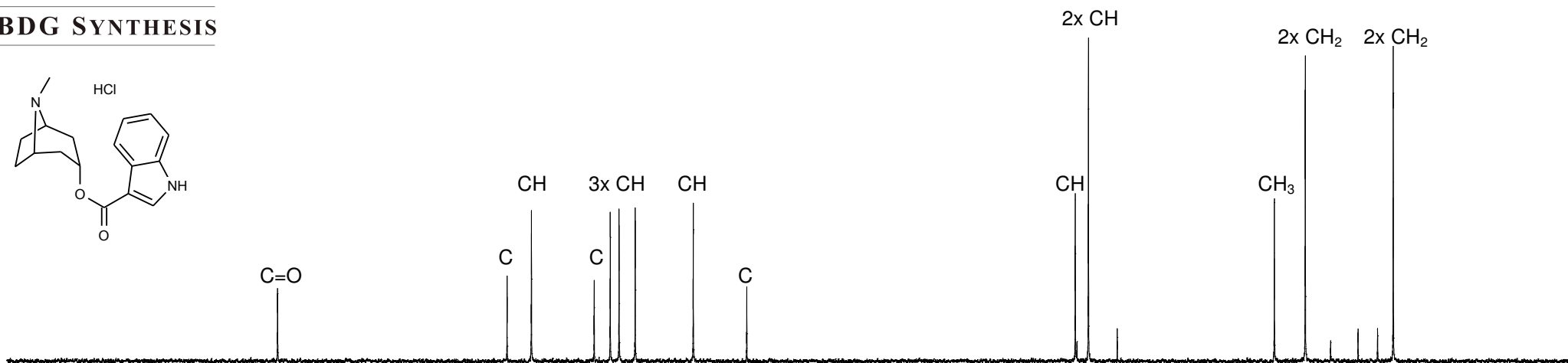
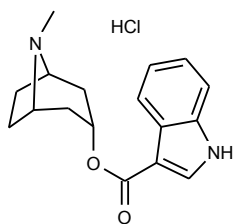
Lot Number: BDG 12897.2



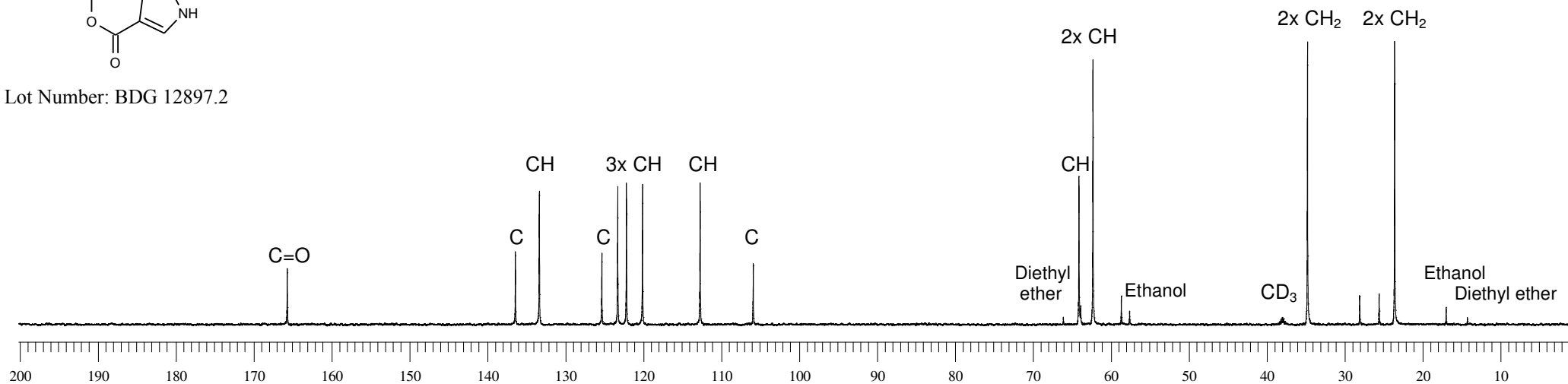


Carbon-13 NMR Spectrum of Tropisetron HCl (top) and Tropisetron-d₃ HCl (bottom) in D₂O

BDG SYNTHESIS



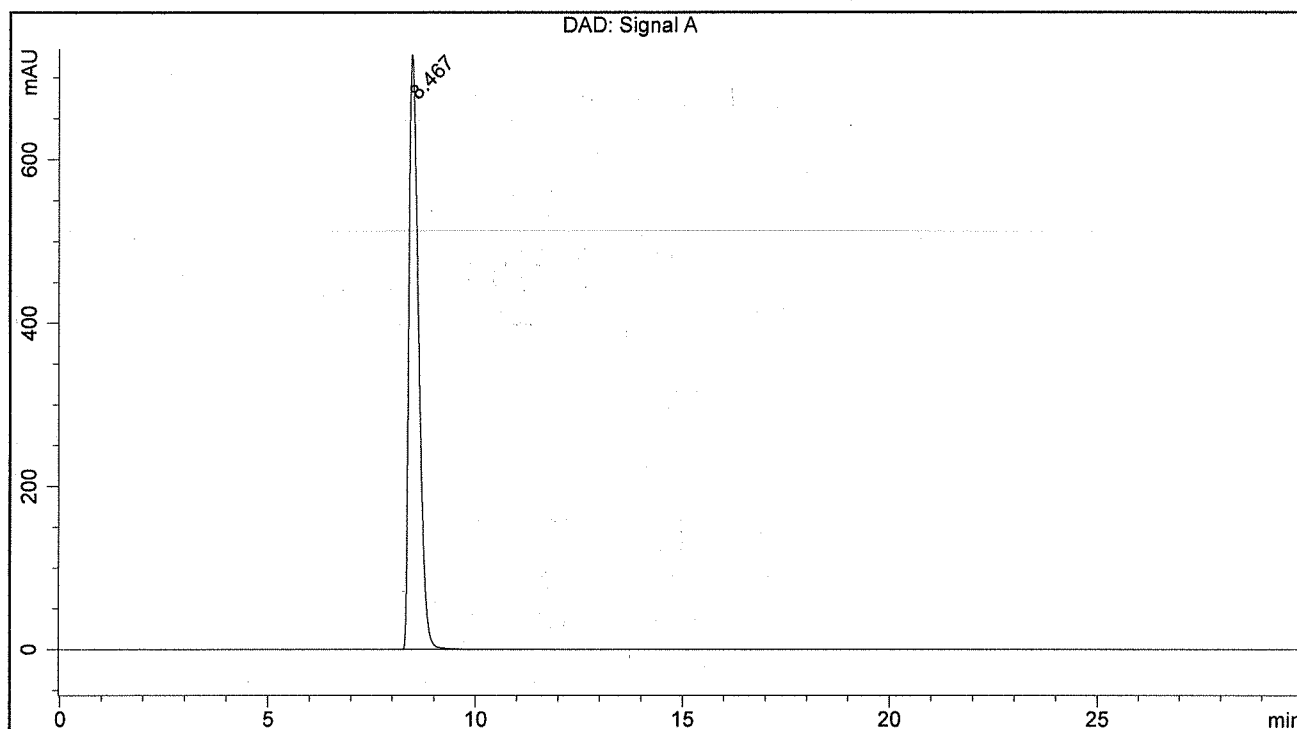
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BDG - Analysis of Tropisetron-d3 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 75:25 50mM Ammonium Acetate pH=4.5 : Acetonitrile
 Flow Rate : 1.0 mL/min
 Sample Solvent : 80:20 Water : Acetonitrile
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 285 nm

Sample Name	BDG 12897.2	Instrument	AnalyticalLC01
Acquisition	06/11/2013, 13:43:10	Method (rev.)	LC10589a (5)
Sequence	BDG_06Nov2013b - Reprocessed	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	8.47 min	726.4109	11876.7851	0.2547 min	100.000 %