

BDG SYNTHESIS

Certificate of Analysis

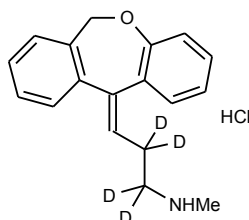
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
29 April 2011

Name: Nordoxepin-d₄ HCl
CAS Number: 2887-91-4 (unlabelled)

Structure:



Molecular Weight: C₁₈H₁₅D₄NO·HCl = 305.84

Lot Number: BDG 6179.1

Appearance: White, crystalline solid

Purity By HPLC: 100.0 %

Isotopic Purity: Under 0.5 % d₀

Re-test Date: 29 April 2016

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.

Analysis of the spectrum indicates a *Z* : *E* isomeric ratio of approximately 3.8 : 1. In the spectrum of the unlabelled material this ratio is 1 : 9, *Z* : *E*.

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

Residual Solvents: traces (under 0.1 % w/w) of ethyl acetate and dioxane 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.

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

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 270.1796. $C_{18}H_{16}D_4NO$ $[M+H]^+$ requires m/z 270.1795. The deviation of 0.4 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

Two, nearly resolved peaks are observed (100.0 % combined area, approximately 1.0 : 3.7 ratio of *E* and *Z* isomers). 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 70.47, H 5.28, D 2.64, N 4.59 %
$C_{18}H_{15}D_4NO \cdot HCl$	Requires:	C 70.69, H 5.27, D 2.63, N 4.58 %

The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

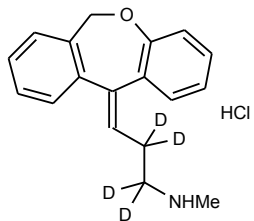
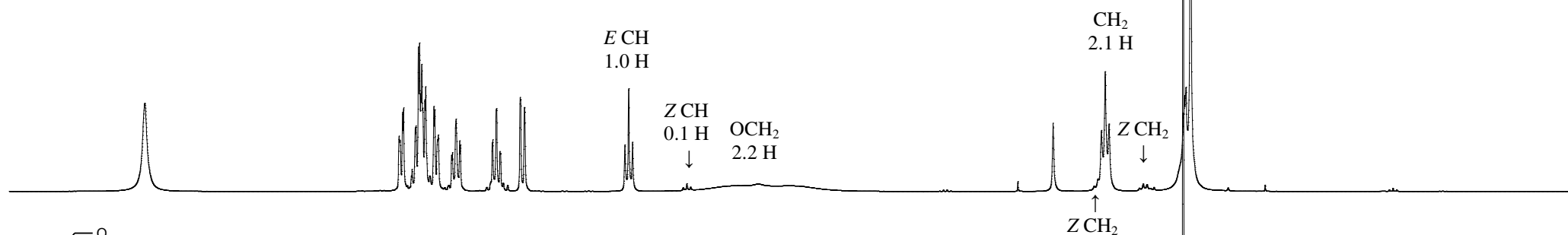
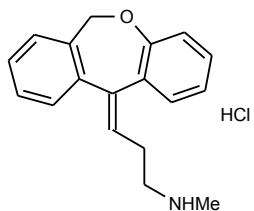
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

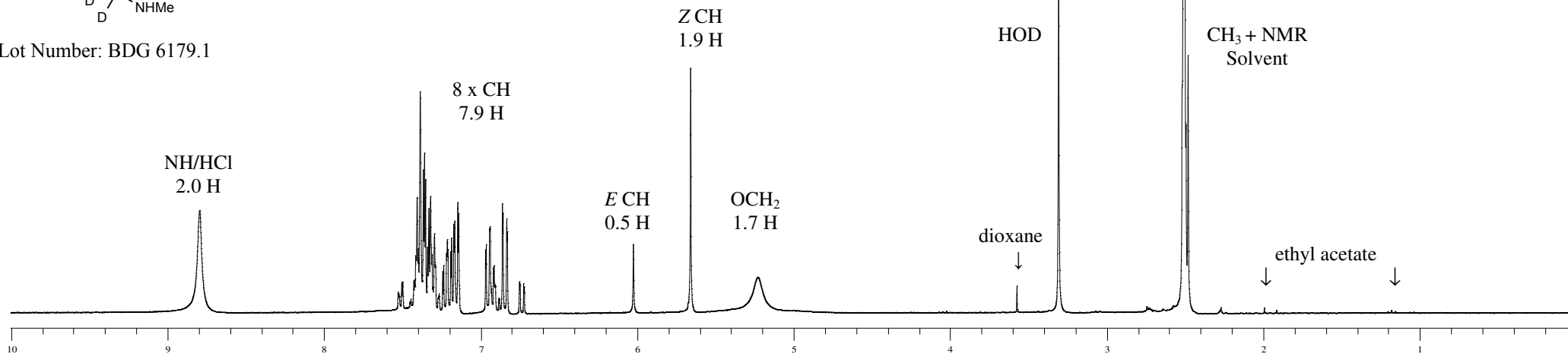


Proton NMR Spectrum of Nordoxepin HCl (top) and Nordoxepin-d₄ HCl (bottom) in DMSO-d₆

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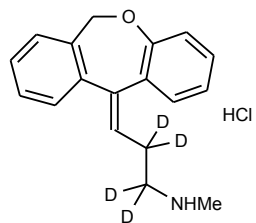
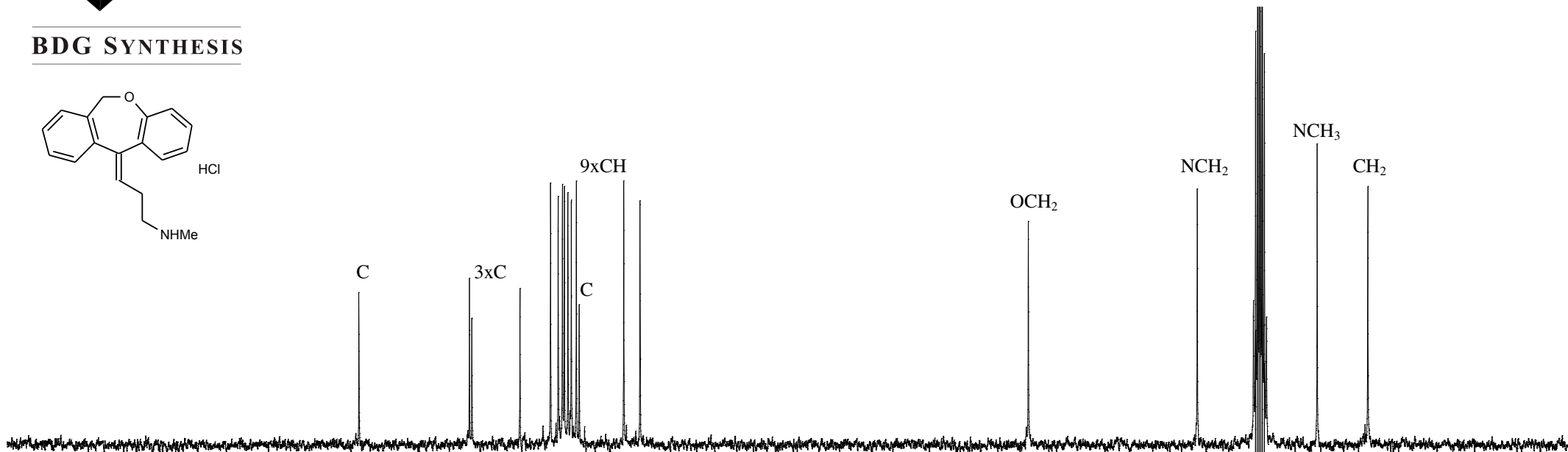
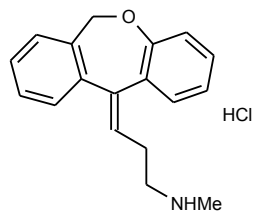
Lot Number: BDG 6179.1



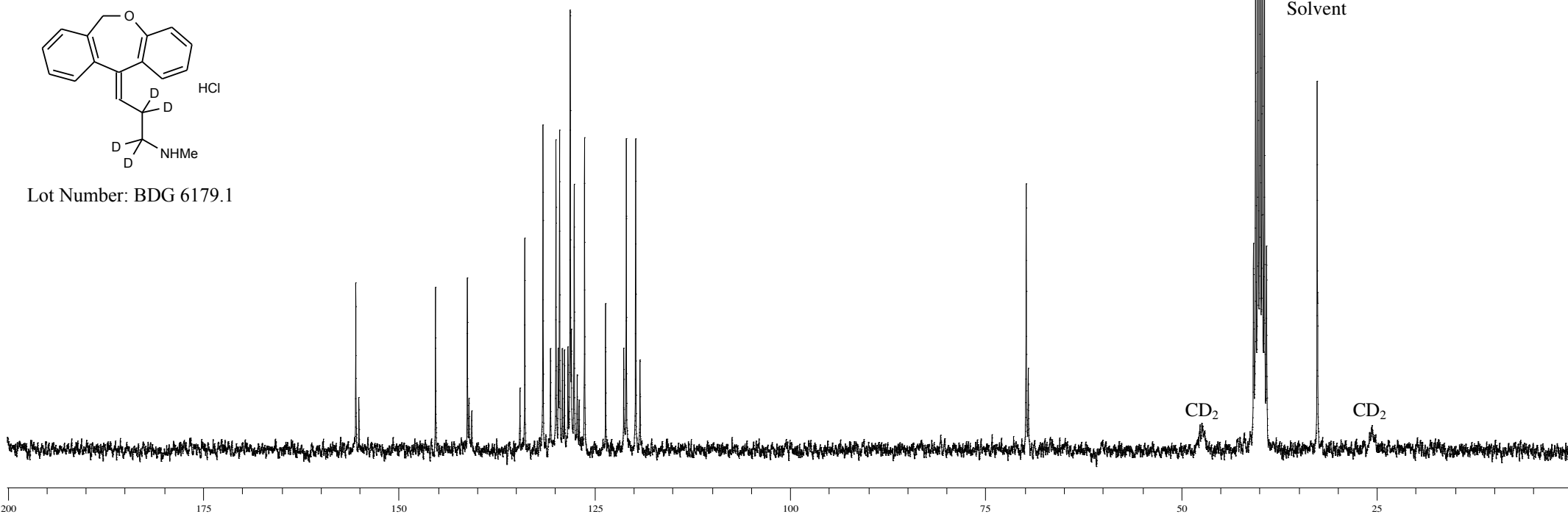


Carbon-13 NMR Spectrum of Nordoxepin HCl (top) and Nordoxepin-d₄ HCl (bottom) in DMSO-d₆

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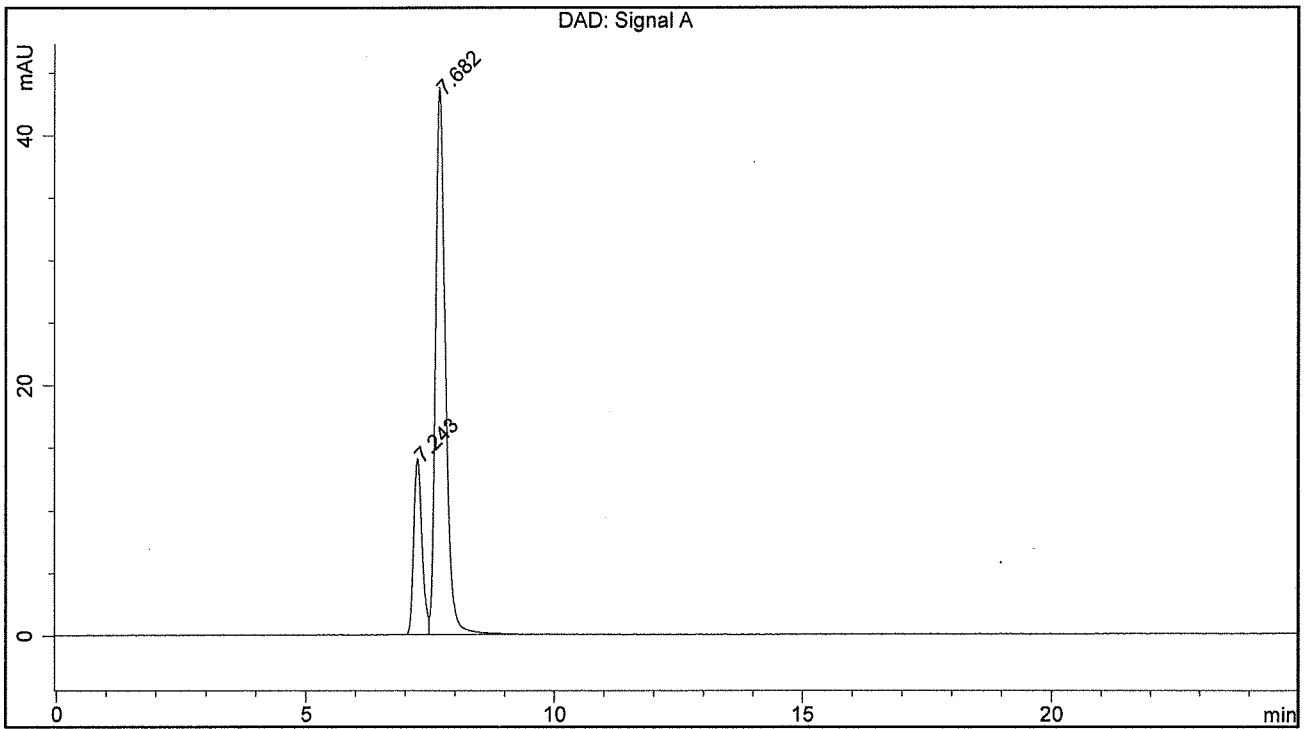
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BDG - Analysis of Nordoxepin-d4 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 40:60:2.0 Water : Methanol : Acetic Acid
 Flow Rate : 1.0 mL/min
 Sample Solvent : Mobile Phase
 Injection Volume : 10 uL
 Column Temperature : 50C
 Detection : UV at 254 nm

Sample Name	BDG 6179.1	Instrument	AnalyticalLC01
Acquisition	29/04/2011, 09:55:19	Method (rev.)	LC10438a (7)
Sequence	BDG_29Apr2011a - Reprocessed	Vial Position	31
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.24 min	14.0757	162.3585	0.1786 min	21.072 %
2	7.68 min	43.7029	608.1423	0.2123 min	78.928 %