



BDG SYNTHESIS

Certificate of Analysis

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

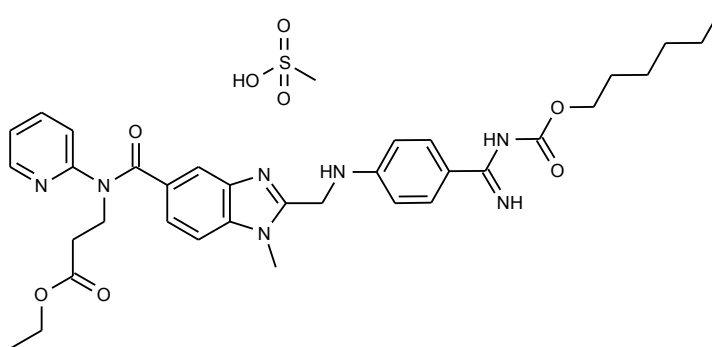
Neil Beare

Neil Beare, PhD, Director
8 December 2014

Name: Dabigatran Etexilate Mesylate

CAS Number: 872728-81-9

Structure:



Molecular Weight: $C_{34}H_{41}N_7O_5 \cdot CH_4O_3S = 723.84$

Lot Number: BDG 14180.1

Appearance: White, crystalline solid

Corrected Purity: 99.4 % (HPLC) - 2.0 % (water) = 97.4 %

Re-test Date: 8 December 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.

Residual Solvents: no residual solvents are observed.

Impurities: traces of unidentified impurities are seen in the baseline.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

High-resolution Mass Spectrum (TOF MS ES+)

Found m/z 628.3239. $C_{34}H_{42}N_7O_5$ $[M+H]^+$ (free base) requires m/z 628.3247. The deviation of 1.3 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A somewhat broadened, slightly tailing peak is observed (99.4 %). 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 57.42, H 6.46, N 13.39, S 3.68 %
$C_{34}H_{41}N_7O_5 \cdot CH_4O_3S \cdot 0.5H_2O$	Requires:	C 57.36, H 6.33, N 13.38, S 4.38 %
$C_{34}H_{41}N_7O_5 \cdot CH_4O_3S$	Requires:	C 58.08, H 6.27, N 13.55, S 4.43 %

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. A difference between the measured and calculated result for sulfur, even when allowing for the presence of water, is noted. However, a deviation from a 1:1 ratio of free base versus mesylate components is not supported by the observed proton NMR data. We conclude that the material is a 1:1 mesylate salt that also comprises some water of crystallization.

Karl-Fischer Analysis

	Found:	H ₂ O 2.0 %
$C_{34}H_{41}N_7O_5 \cdot CH_4O_3S \cdot 0.5H_2O$	Requires:	H ₂ O 1.2 %

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.

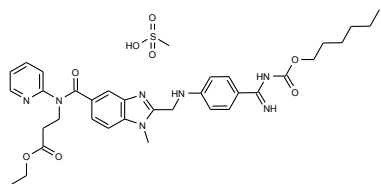
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

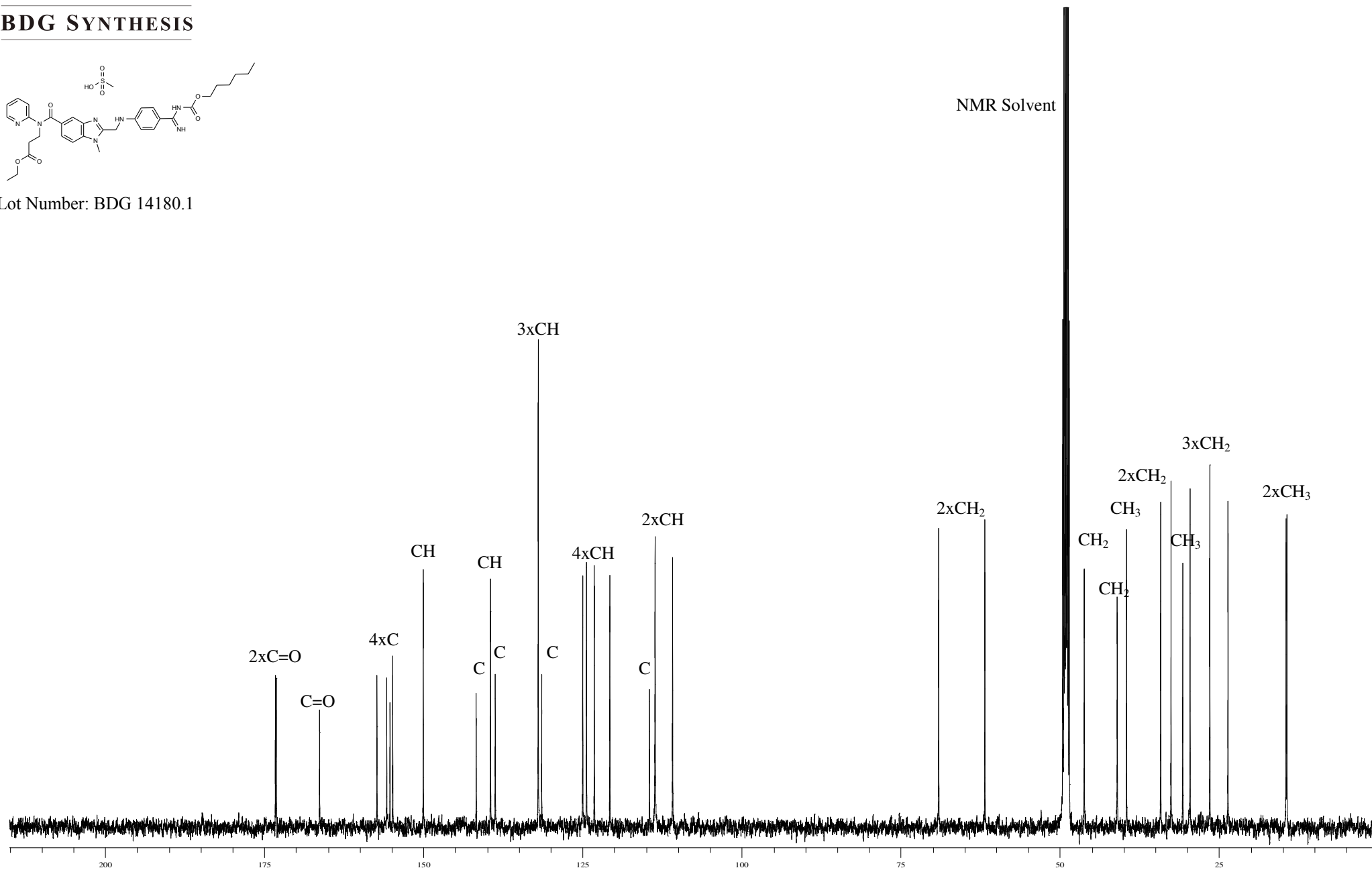


Carbon-13 NMR Spectrum of Dabigatran Etexilate Mesylate in Methanol-d₄

BDG SYNTHESIS



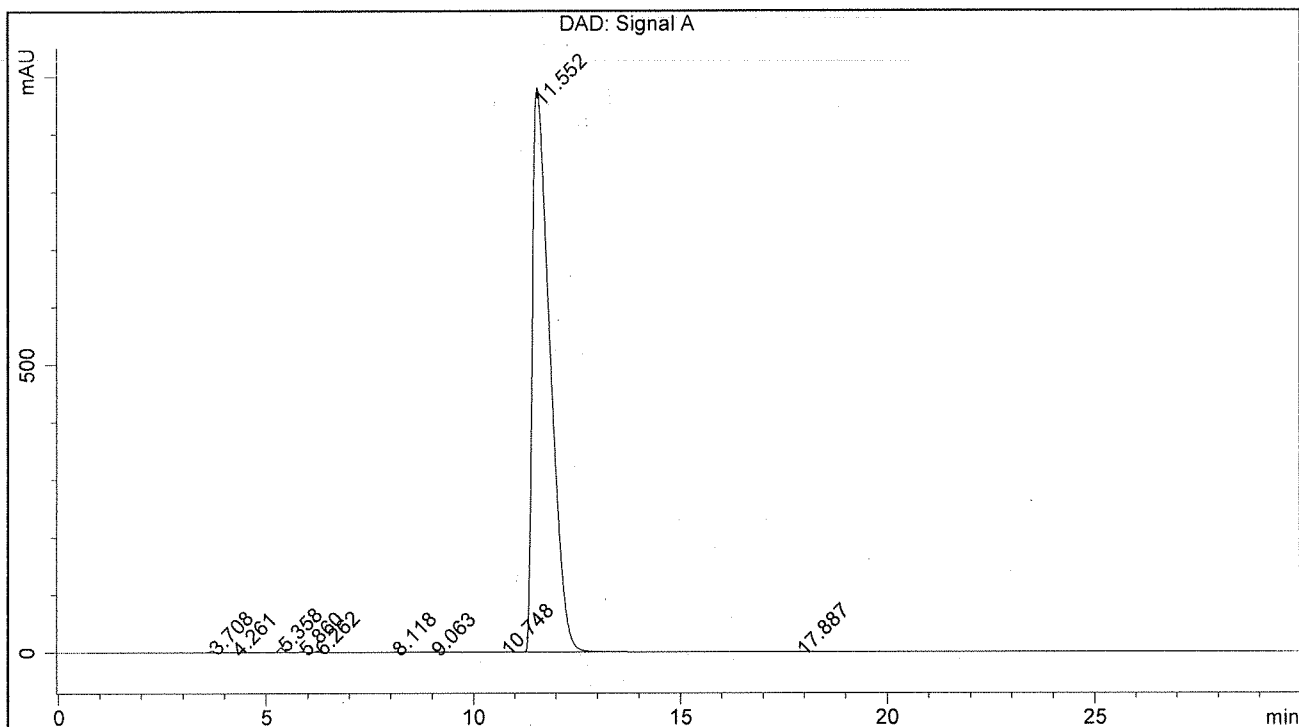
Lot Number: BDG 14180.1



BDG - Analysis of Dabigatran Etexilate Mesylate

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 58:42 50 mM Formic Acid pH=3.8 (Ammonium Hydroxide) : Acetonitrile
 Flow Rate : 1.0 mL/min Sample Solvent : Mobile Phase
 Column Temperature : 20C Injection Volume : 10 uL Detection : UV at 342 nm

Sample Name	BDG 14180.1	Instrument	AnalyticalLC01
Acquisition	08/12/2014, 18:07:42	Method (rev.)	LC10546a (9)
Sequence	BDG_08Dec2014a	Vial Position	14
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.71 min	3.1301	21.5172	0.1082 min	0.074 %
2	4.26 min	0.2639	2.7748	0.1667 min	0.010 %
3	5.36 min	8.2029	77.2122	0.1458 min	0.267 %
4	5.86 min	1.3060	13.3258	0.1550 min	0.046 %
5	6.26 min	2.5613	28.2515	0.1647 min	0.098 %
6	8.12 min	0.4525	8.7050	0.2684 min	0.030 %
7	9.06 min	0.1039	3.0822	0.3740 min	0.011 %
8	10.75 min	0.7255	17.3126	0.3304 min	0.060 %
9	11.55 min	979.8481	28768.7100	0.4345 min	99.385 %
10	17.89 min	0.1945	5.9695	0.3741 min	0.021 %