

BDG SYNTHESIS

Certificate of Analysis

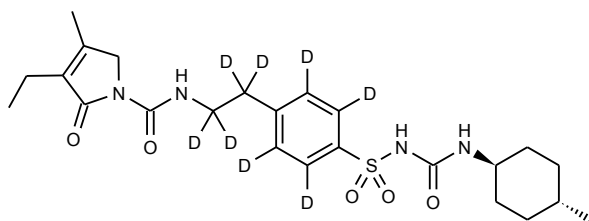
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
21 October 2008

Name: Glimepiride-d₈
CAS Number: 93479-97-1 (unlabelled)

Structure:



Molecular Weight: C₂₄H₂₆D₈N₄O₅S = 498.67
Lot Number: BDG 7655.1
Appearance: White powder
Corrected Purity: 97.6 % (HPLC) - 0.7 % (water) = 96.9 %
Isotopic Purity: Under 0.5 % d₀
Re-test Date: 21 October 2013
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.

Isotopic Labelling: a small amount of aromatic H/D exchange is observed. Signals at the other sites of deuteration are absent, compared with the spectrum of unlabelled material, indicating clean deuteration in these positions.

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.

Isotopic Labelling: a small amount of aromatic H/D exchange is observed. Signals at the other sites of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration in these positions.

High-resolution Mass Spectrum (ESI-)

Found m/z 497.2697. $C_{24}H_{25}D_8N_4O_5S$ $[M-H]^-$ requires m/z 497.2697. The deviation of 0.2 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 (97.6 %). 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 57.06, H 5.27, D 3.25, N 11.18 %
$C_{24}H_{26}D_8N_4O_5S \cdot 0.2H_2O$	Requires:	C 57.39, H 5.30, D 3.21, N 11.15 %, H_2O 0.72 %
$C_{24}H_{26}D_8N_4O_5S$	Requires:	C 57.81, H 5.26, D 3.23, N 11.24 %

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.

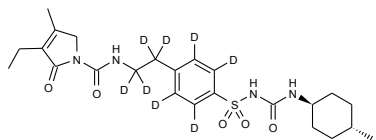
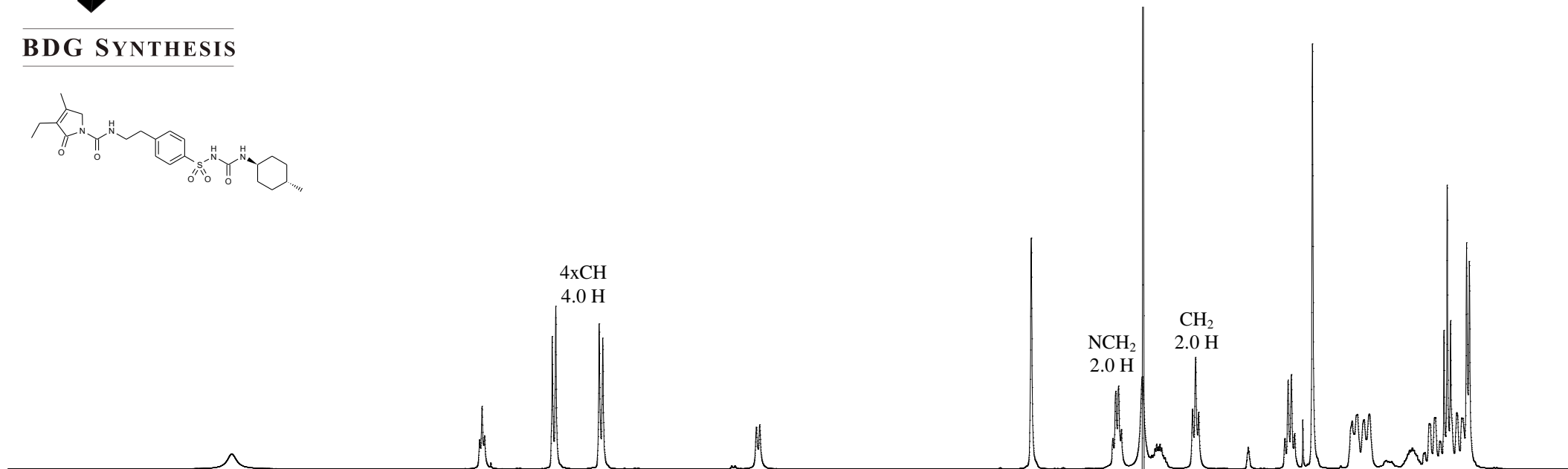
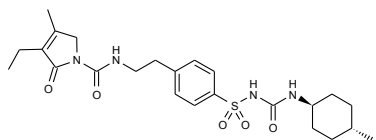
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

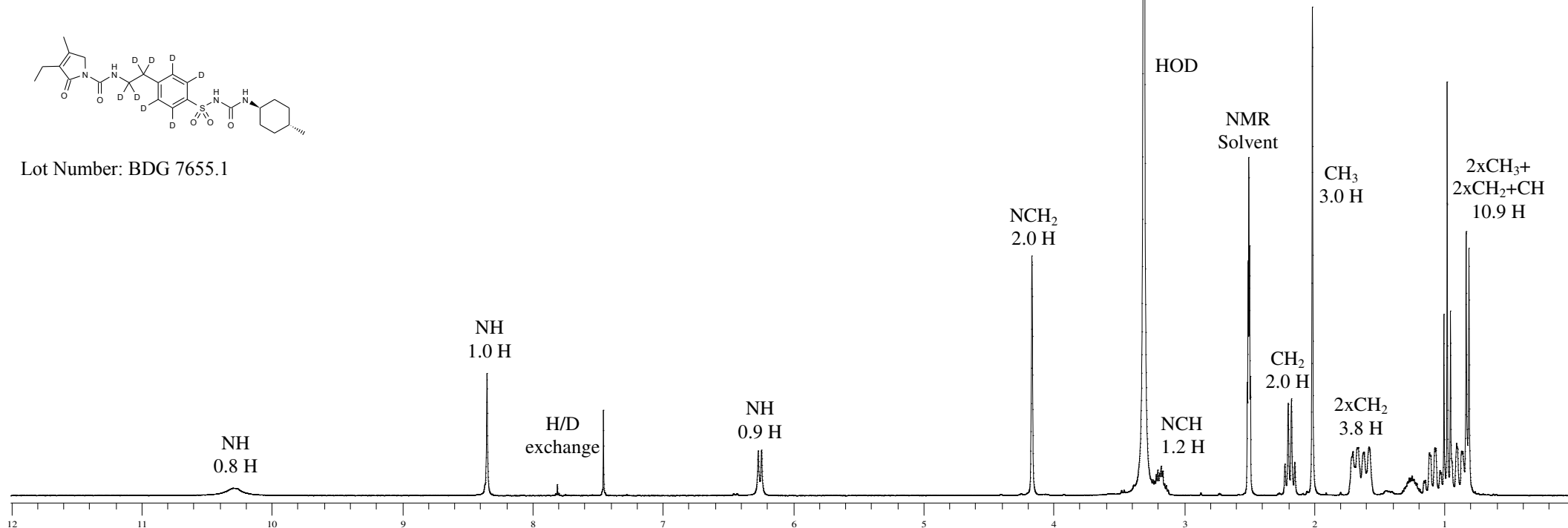


Proton NMR Spectrum of Glimepiride (top) and Glimepiride-d₈ (bottom) in DMSO-d₆

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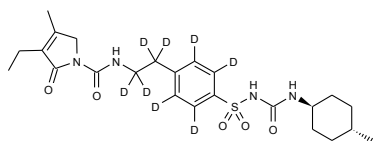
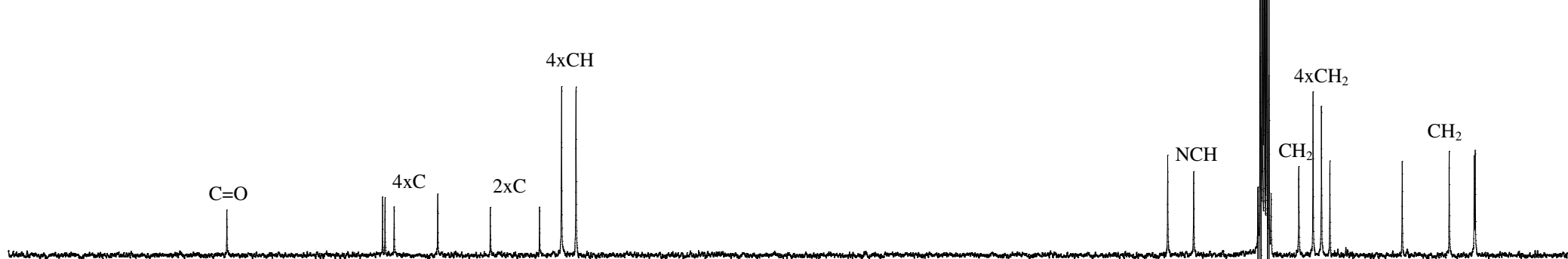
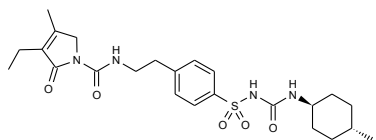
Lot Number: BDG 7655.1



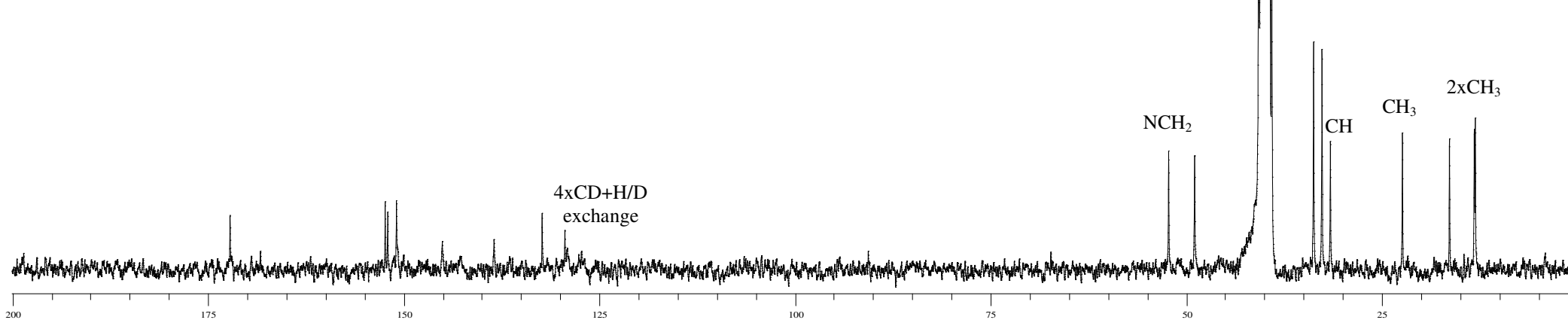


Carbon-13 NMR Spectrum of Glimepiride (top) and Glimepiride-d₈ (bottom) in DMSO-d₆

BDG SYNTHESIS



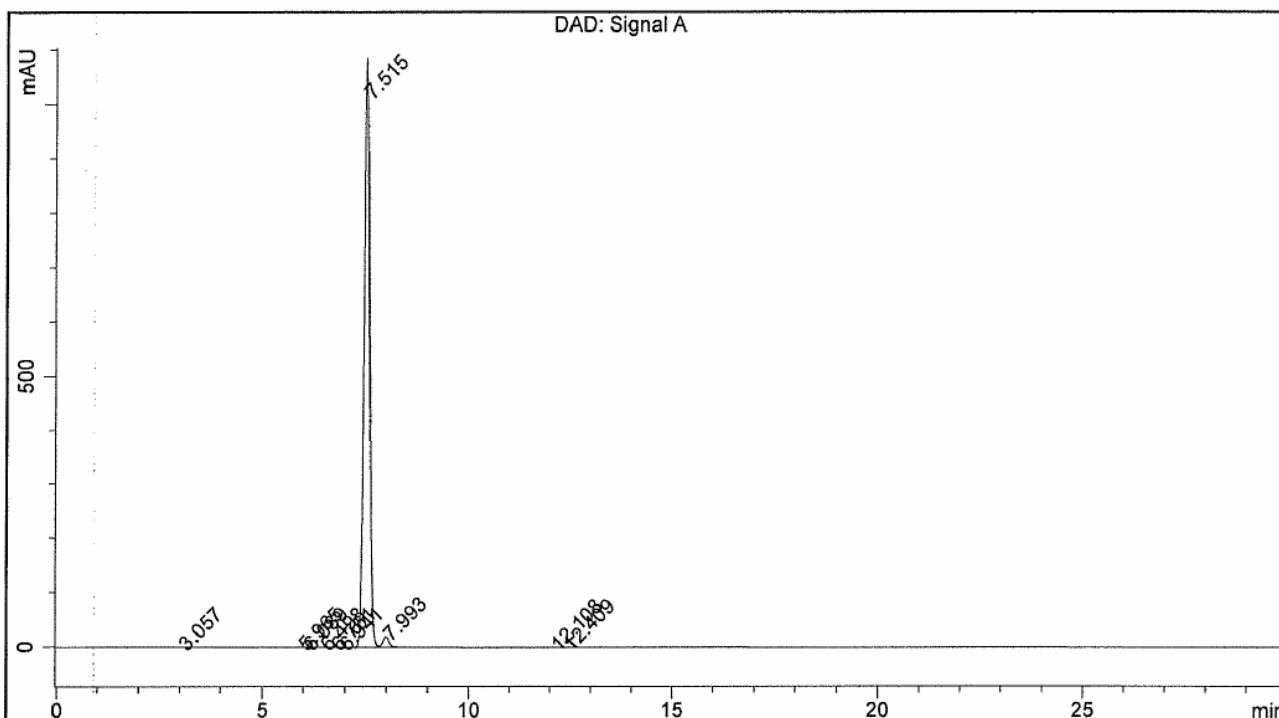
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BDG - Analysis of Glimepiride-d8

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 35:65 10 mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile
 Flow Rate : 1.0 mL/min
 Sample Solvent : Mobile Phase
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 230 nm

Sample Name	BDG 7655.1	Instrument	AnalyticalLC01
Acquisition	21/10/2008, 19:26:16	Method (rev.)	LC10296a (5)
Sequence	BDG_21Oct2008a - Reprocessed	Vial Position	42
Operator	solvation010\cerityadmin	Injection	2 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.06 min	0.2130	1.2184	0.0847 min	0.012 %
2	5.96 min	0.2246	1.4152	0.0895 min	0.014 %
3	6.09 min	0.3387	2.8239	0.1193 min	0.028 %
4	6.50 min	0.2512	1.9391	0.1181 min	0.019 %
5	6.76 min	0.3199	2.4927	0.1149 min	0.024 %
6	6.94 min	0.4998	4.3494	0.1335 min	0.043 %
7	7.51 min	1085.1338	9931.4410	0.1428 min	97.595 %
8	7.99 min	19.2242	219.3355	0.1711 min	2.155 %
9	12.11 min	0.4735	6.2470	0.1899 min	0.061 %
10	12.41 min	0.3763	4.9456	0.1873 min	0.049 %