BDG SYNTHESIS

Certificate of Analysis

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

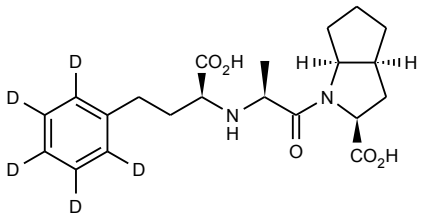
Barry Dent

Barry R. Dent, PhD, Director
6 February 2011

Name: **Ramiprilat-d_5**

CAS Number: 87269-97-4 (unlabelled)

Structure:



Molecular Weight: $C_{21}H_{23}D_5N_2O_5$ = 393.49

Lot Number: BDG 4422.4

Appearance: White powder

Corrected Purity: 96.5 % (HPLC) - 3.4 % (ethanol) - 7.8 % (water) = 85.3 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 6 February 2016

Storage and Handling:

Temperature:	ambient laboratory temperature; may be refrigerated.
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. Do not dry. Drying may remove water of crystallization and rehydration may be variable.

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Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. The complexity of the spectrum indicates two conformers of the product are present in solution.
Isotopic Labelling: signals at the sites of deuteration are greatly diminished, compared with what would be expected for unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of ethanol (3.4 % *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. The majority of the signals are duplicated indicating that two conformers of the product are present in solution.
Isotopic Labelling: signals at the sites of deuteration have collapsed to small multiplets compared with what would be expected for unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (FAB+)

Found *m/z* 394.2392. $C_{21}H_{24}D_5N_2O_5$ $[M+H]^+$ requires *m/z* 394.2390. The deviation of 0.5 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 broad, symmetrical peak is observed (96.5 %). 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 58.69, H 6.40, D 2.21, N 6.14 %
$C_{21}H_{23}D_5N_2O_5{\cdot}2.0H_2O$	Requires:	C 58.72, H 6.34, D 2.34, N 6.52 %
$C_{21}H_{23}D_5N_2O_5$	Requires:	C 64.10, H 5.89, D 2.56, N 7.12 %

The elemental analyses fall substantially 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.

Karl-Fischer Analysis

	Found:	H_2O 7.8 %
$C_{21}H_{23}D_5N_2O_5{\cdot}2.0H_2O$	Requires:	H_2O 8.4 %

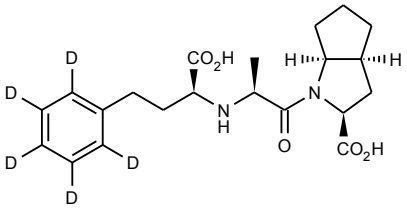
Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

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.

BDG SYNTHESIS

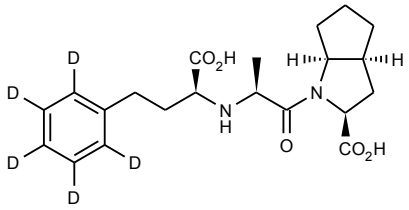
Proton NMR Spectrum of Ramiprilat-d_5 in Methanol-d_4



Lot Number: BDG 4422.4

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Ramiprilat-d_5 in Methanol-d_4



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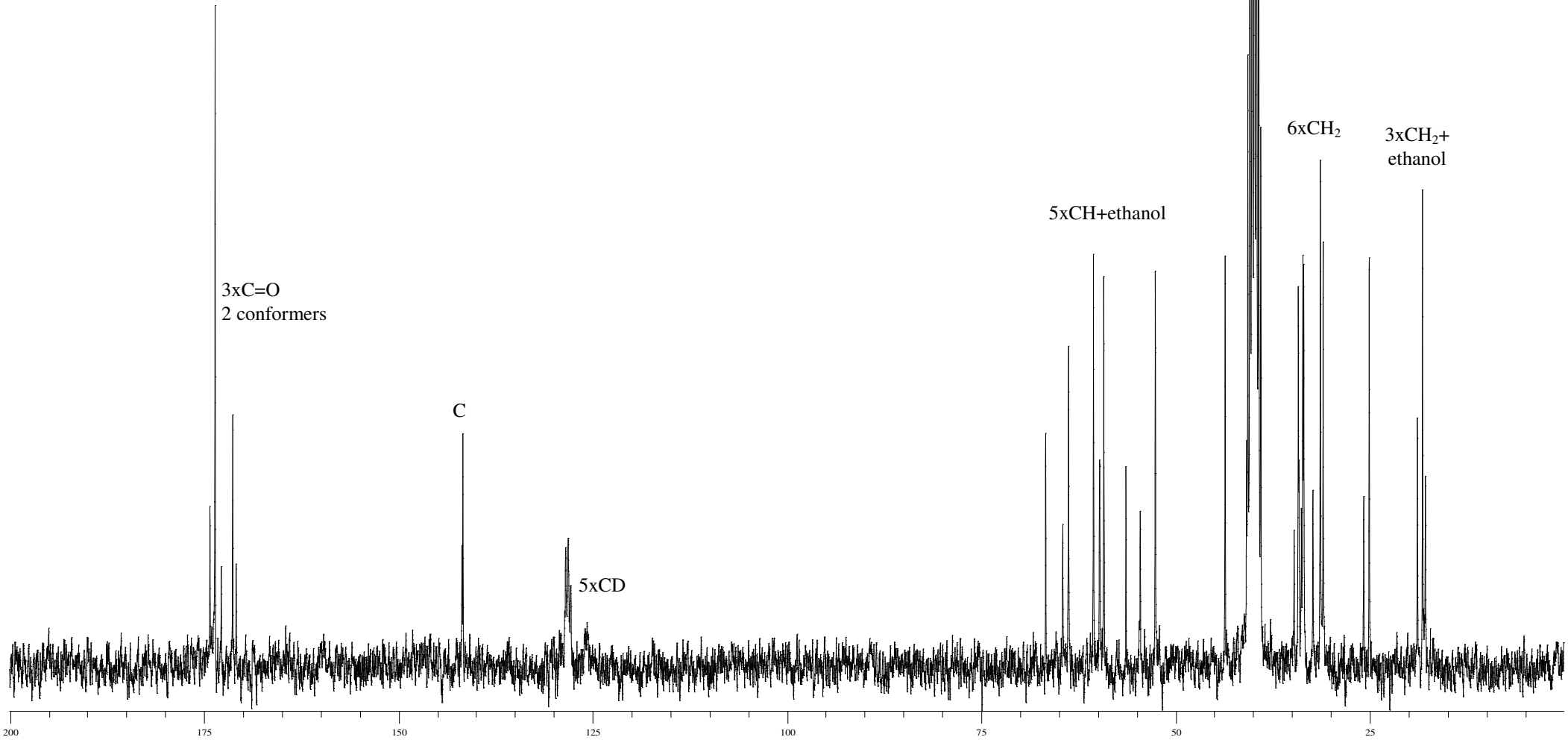
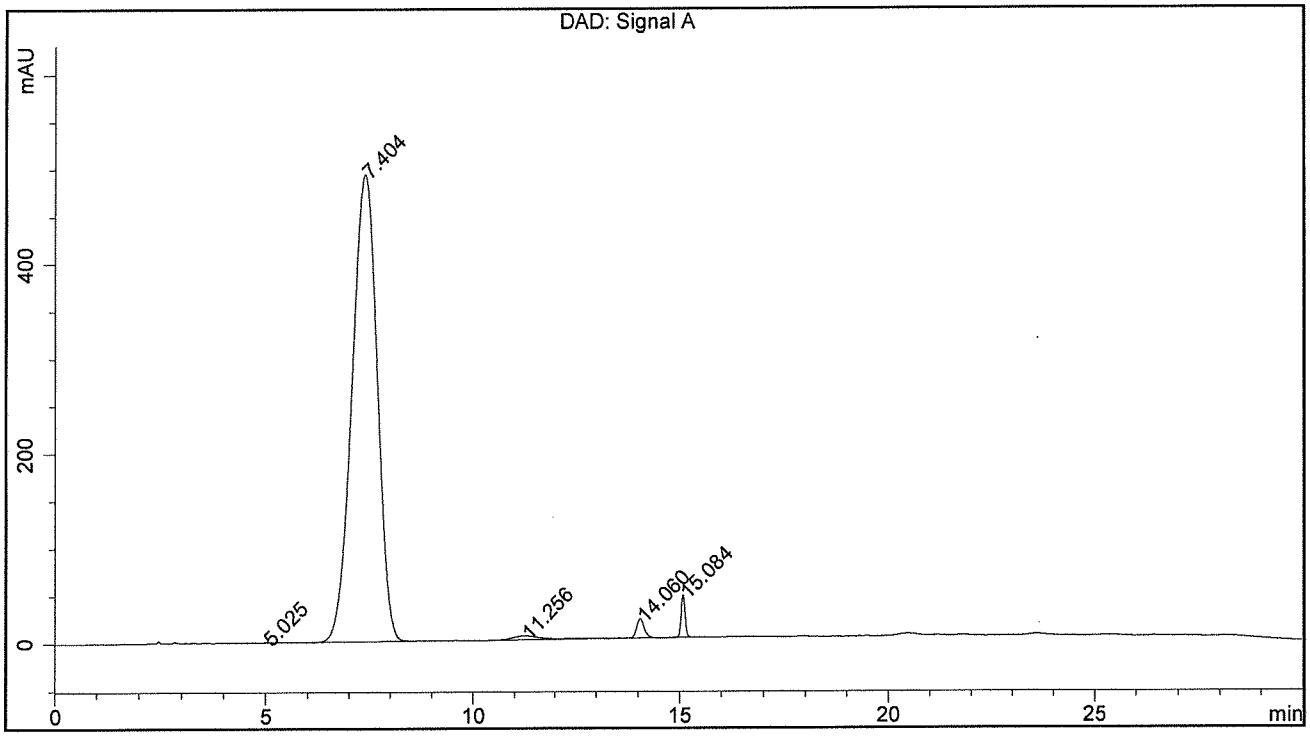


BDG - Analysis of Ramiprilat-d5

Column : Phenomenex Luna C18 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 4 x 3 mm
Mobile Phase : 90:10 0.2% Sodium Perchorate 0.05% Triethylamine pH=3.6 : Acetonitrile
Mobile Phase : 30:70 0.2% Sodium Perchorate 0.05% Triethylamine pH=2.6 : Acetonitrile
Gradient (A:B) : T0=90:10, T20=30:70, T25=30:70, T27=90:10, T30=90:10
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 60C
Injection Volume : 10 uL
Detection : UV at 210 nm

Sample Name	BDG 4422.4	**Instrument**	AnalyticalLC01
Acquisition	06/02/2011, 11:52:56	**Method (rev.)**	LC10241a (17)
Sequence	BDG_06Feb2011d - Reprocessed	**Vial Position**	1
Operator	solvation010\cerityadmin	**Injection**	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.03 min	0.6991	5.8251	0.1192 min	0.027 %
2	7.40 min	492.6251	20902.9410	0.6610 min	96.522 %
3	11.26 min	4.0811	200.9698	0.6265 min	0.928 %
4	14.06 min	20.2293	253.9639	0.1925 min	1.173 %
5	15.08 min	44.6489	292.5155	0.1024 min	1.351 %