BDG SYNTHESIS

Certificate of Analysis

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

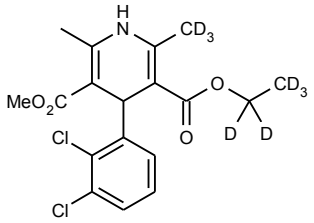
Barry Dent

Barry R. Dent, PhD, Director
1 July 2013

Name: **Felodipine-d_8**

CAS Number: 72509-76-3 (unlabelled)

Structure:



Molecular Weight: $C_{18}H_{11}D_8Cl_2NO_4$ = 392.30

Lot Number: BDG 5765

Appearance: Pale yellow, crystalline solid

Purity By HPLC: 98.6 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 1 July 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:	store in an amber vial and protect from bright light.
Caution:	only experienced laboratory personnel should handle the material. Do not expose to strong alkali.

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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.
Isotopic Labelling: signals at the sites of deuteration are absent for the ethyl ester group and diminished for the methyl group, compared with the spectrum of unlabelled material. This indicates clean deuteration for the ethyl group, whilst the signal for the labelled methyl group indicates that about half of the labels have been exchanged for protons.
Residual Solvents: no residual solvents 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 for the sites of deuteration are absent for the ethyl ester group, indicating clean deuteration. Some H/D exchange is evident in the signal for the labelled methyl group.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 390.1024. $C_{18}H_{10}D_8Cl_2NO_4$ $[M-H]^-$ requires *m/z* 390.1121. The deviation of 24.4 ppm is somewhat outside normally accepted limits for the establishment of identity by HRMS, and the mass spectral data should be considered in conjunction with other identity criteria. Significant M-1, M-2 and M-3 peaks are observed, but any M-8 peak is at approximately the background level of 0.5 %. We conclude that the compound comprises d_8 material, but with significant levels of d_5, d_6 and d_7 because of partial deuteration at the methyl group.

HPLC

A somewhat broadened, symmetrical peak is observed (98.6 %). 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 55.37, H 2.91, D 4.23, N 3.53 %
$C_{18}H_{11}D_8Cl_2NO_4$	Requires:	C 55.11, H 2.83, D 4.11, N 3.57 %

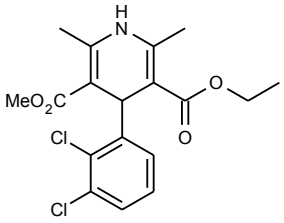
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

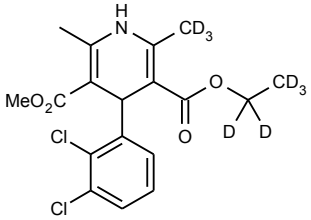
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

BDG SYNTHESIS

Proton NMR Spectrum of Felodipine (top) and Felodipine-d_8 (bottom) in $CDCl_3$

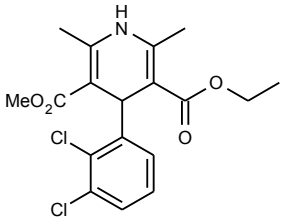


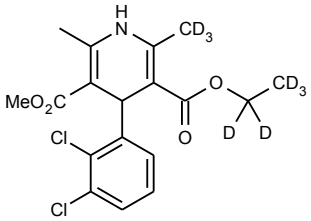


Lot Number: BDG 5765

BDG SYNTHESIS

Carbon-13 NMR Spectrum of Felodipine (top) and Felodipine-d_8 (bottom) in $CDCl_3$





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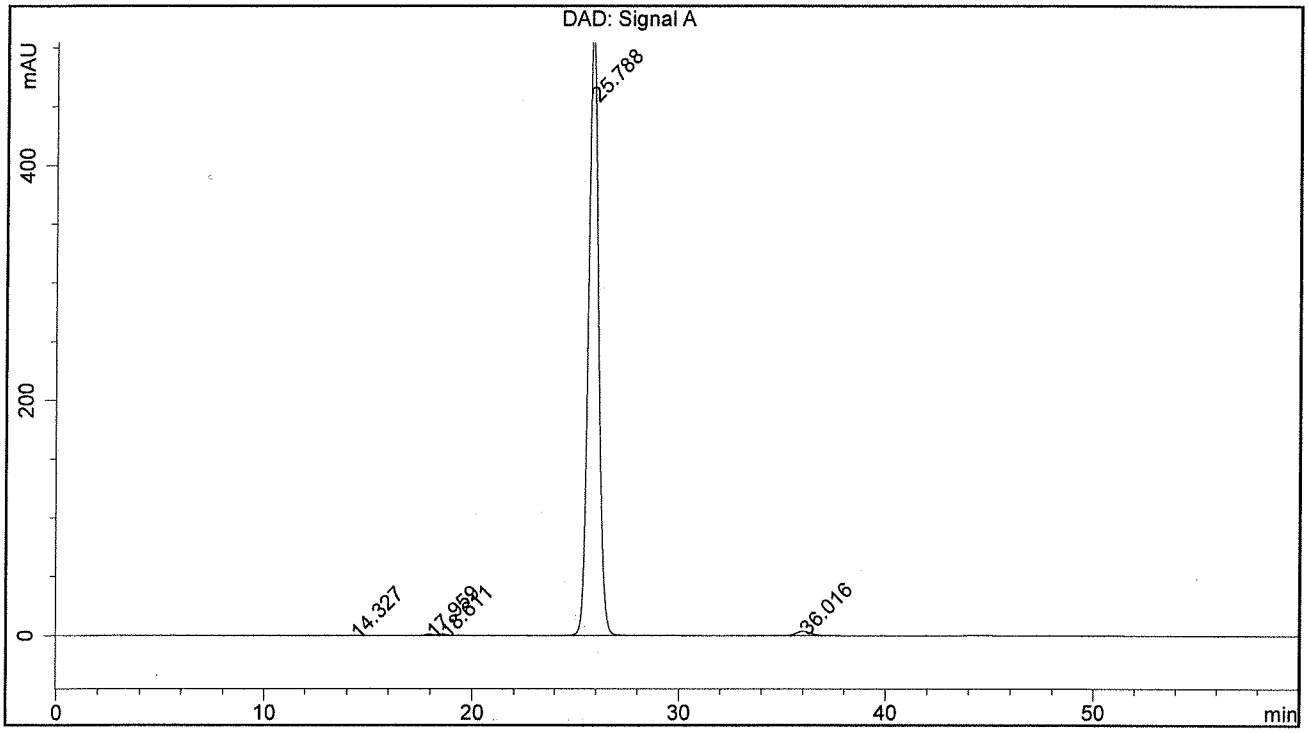
BDG - Analysis of Felodipine-d8

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase : 20:20:10 20mM Potassium diHydrogen Phosphate pH=3.0 : Acetonitrile : Methanol
Flow Rate : 1.0 mL/min
Sample Solvent : Mobile Phase
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 254 nm

Sample Name	BDG 5765	Instrument	AnalyticalLC01
Acquisition	01/07/2013, 16:30:26	Method (rev.)	LC10266a (11)
Sequence	BDG_01Jul2013a	Vial Position	1
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	14.33 min	0.1034	1.6174	0.2025 min	0.009 %
2	17.96 min	1.1126	26.8324	0.2994 min	0.150 %
3	18.61 min	1.1413	29.1108	0.3376 min	0.163 %
4	25.79 min	515.3461	17604.9120	0.5265 min	98.646 %
5	36.02 min	3.7232	184.1312	0.6250 min	1.032 %