



BDG SYNTHESIS

Certificate of Analysis

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

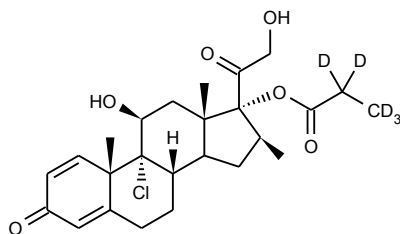
Neil Beare

Neil Beare, PhD, Director
12 September 2014

Name: Beclomethasone 17-Propionate-d₅

CAS Number: 5534-18-9 (unlabelled)

Structure:



Molecular Weight: C₂₅H₂₈D₅ClO₆ = 470.01

Lot Number: BDG 15087.2

Appearance: White, crystalline solid

Corrected Purity: 98.5 % (HPLC) - 0.5 % (ethyl acetate) = 98.0 %

Isotopic Purity: Under 0.5 % d₀

Re-test Date: 12 September 2019

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: the signal for the CD₃ group is absent compared with the spectrum of unlabelled material indicating high isotopic purity, but a significant signal is seen for the CD₂ group indicating some H/D exchange has occurred at this position.

Residual Solvents: a small amount of ethyl acetate (0.5 % 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.

Isotopic Labelling: the CD₃ signal has collapsed into a small multiplet compared with the spectrum of unlabelled material, indicating high isotopic purity, but the CD₂ signal contains a spike indicating some H/D exchange has occurred at this position.

High-resolution Mass Spectrum (ESI+)

Found m/z 470.2345. C₂₅H₂₉D₅ClO₆ [M+H]⁺ requires m/z 470.2334. The deviation of 2.8 ppm is within normally accepted limits for the establishment of identity by HRMS. Signals were observed for d₄ and d₃ material but no signal for d₀ material was seen (detection limit about 0.5 %).

HPLC

A sharp, symmetrical peak is observed (98.5 %). 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 63.89, H 5.88, D 2.10 %
C ₂₅ H ₂₈ D ₅ ClO ₆	Requires:	C 63.89, H 6.00, D 2.14 %

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).

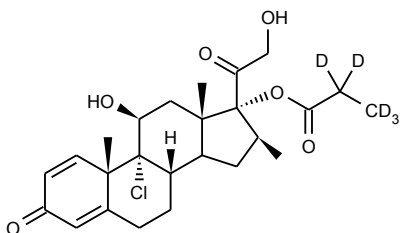
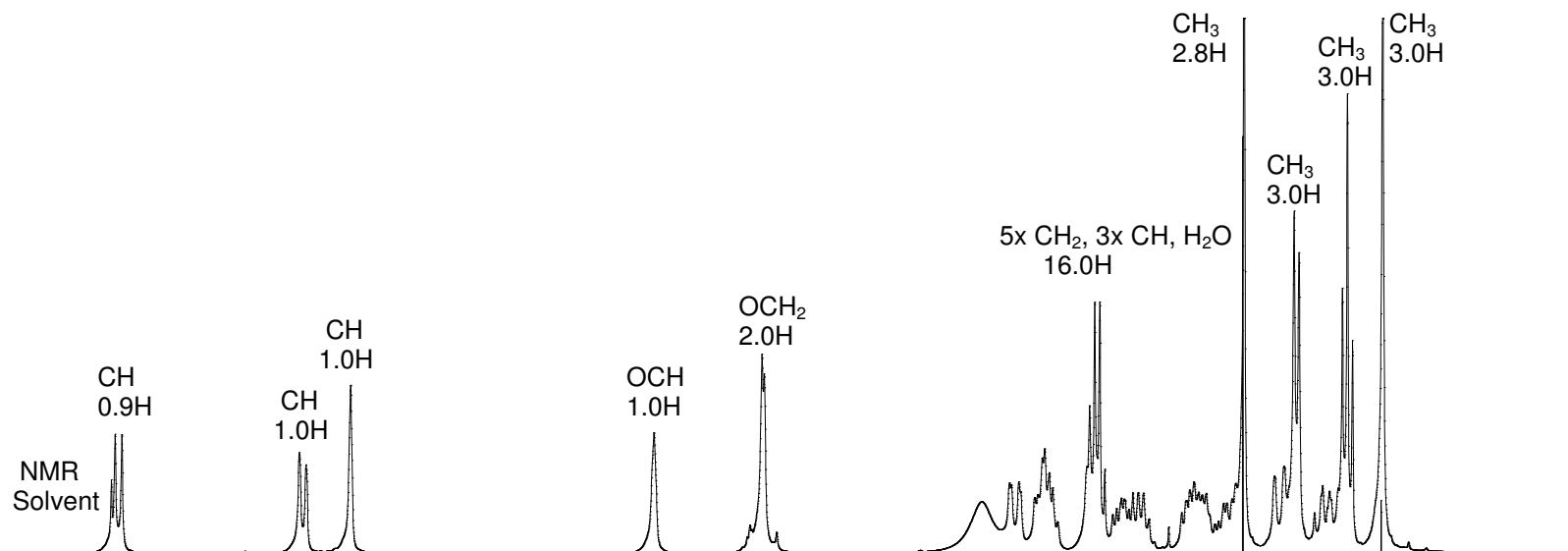
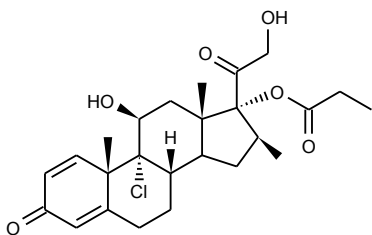
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

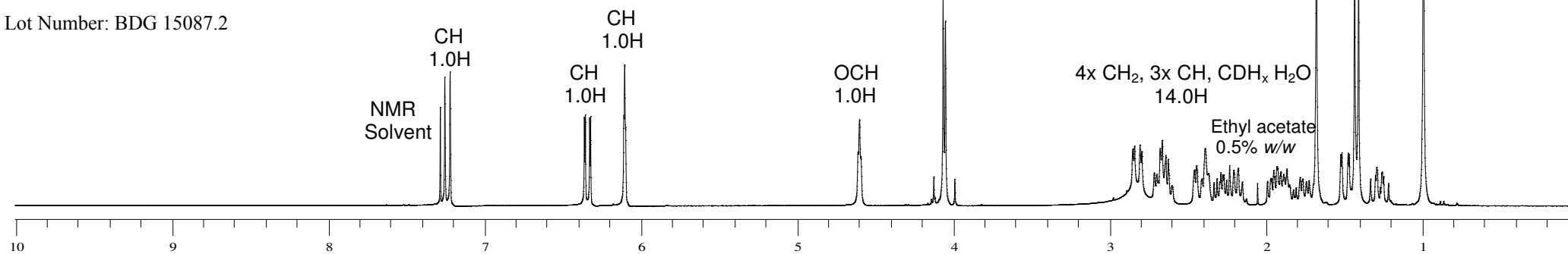


Proton NMR Spectrum of Beclomethasone 17-Propionate (top) and Beclomethasone 17-Propionate-d₅ (bottom) in CDCl₃

BDG SYNTHESIS



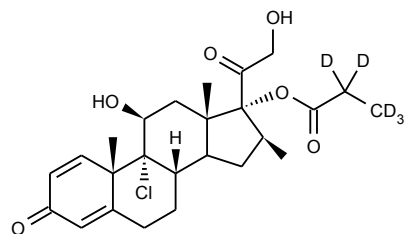
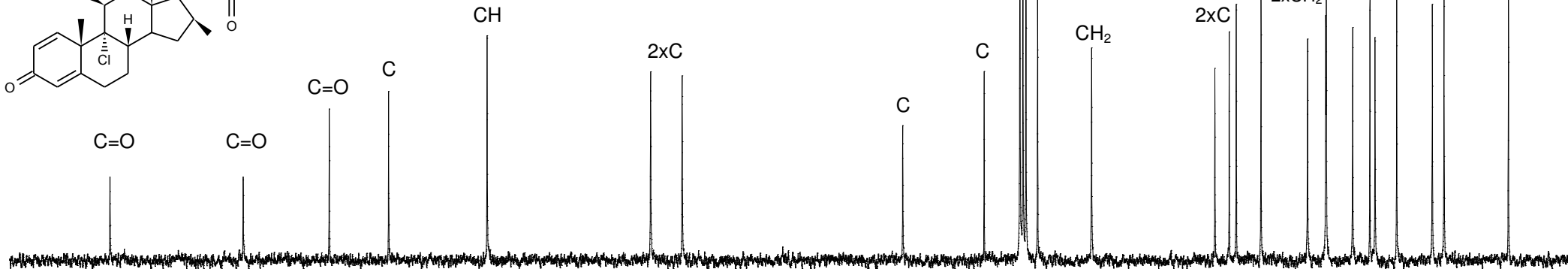
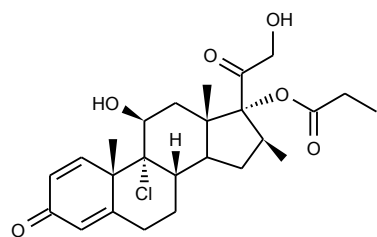
Lot Number: BDG 15087.2



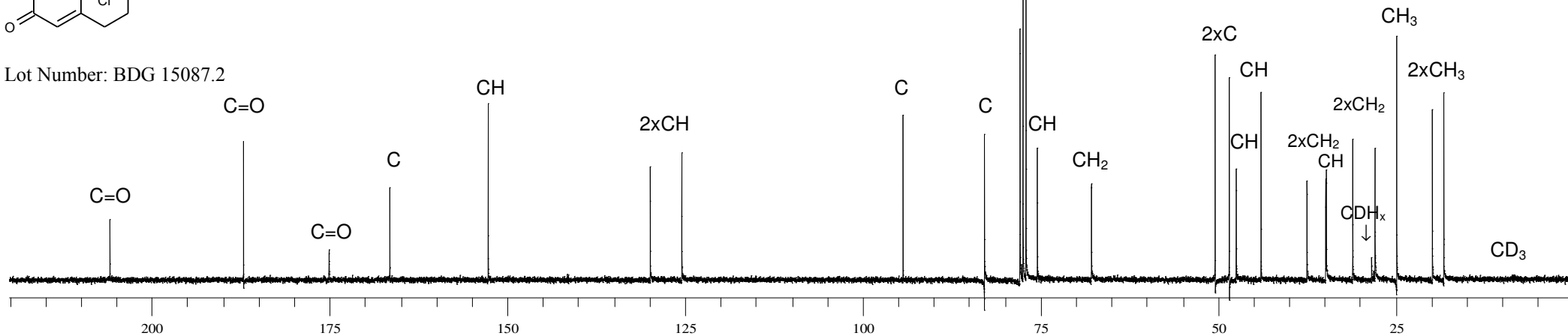


Carbon-13 NMR Spectrum of Beclomethasone 17-Propionate (top) and Beclomethasone 17-Propionate-d₅ (bottom) in CDCl₃

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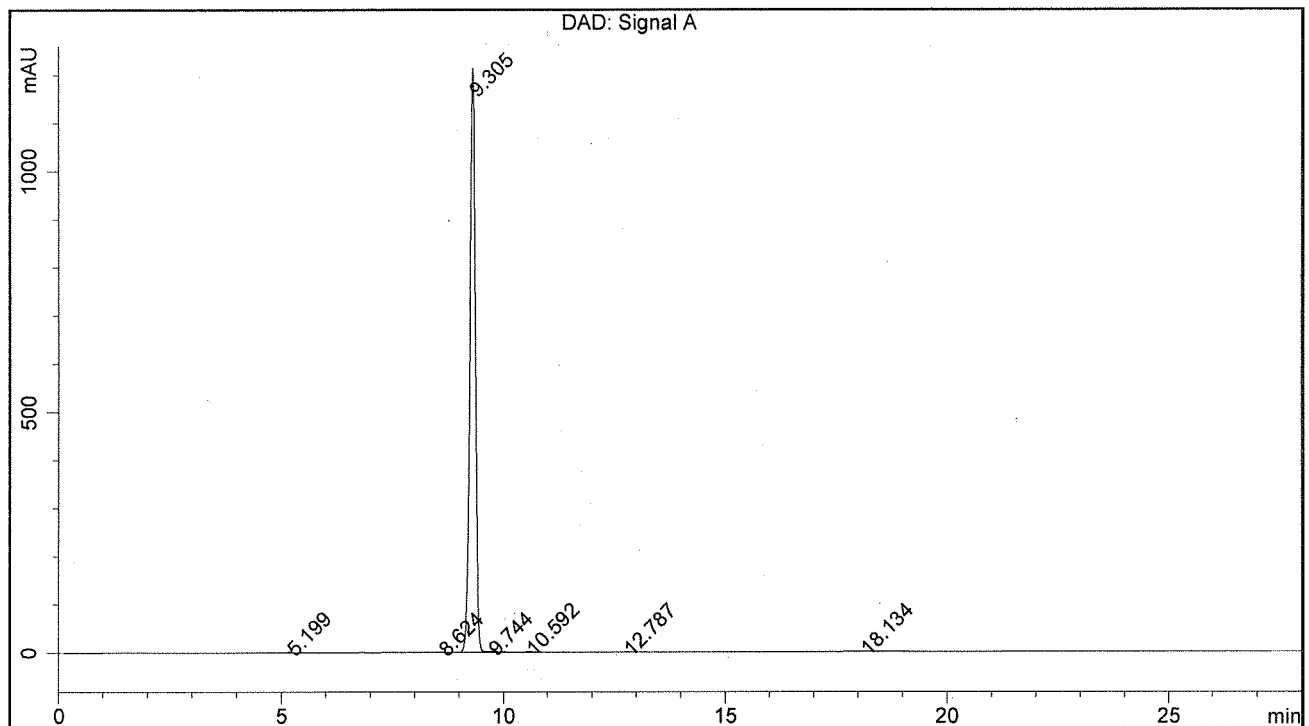
Lot Number: BDG 15087.2



BDG - Analysis of Beclomethasone 17-Propionate-d5

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase A: 50:50 Water : Acetonitrile
 Mobile Phase B: 20:80 Water :Acetonitrile
 Gradient (A:B) : T0=100:0, T20=0:100, T25=0:100, T28=100:0
 Flow Rate : 1.0 mL/min
 Sample Solvent : 1:1 Water : Acetonitrile
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 238 nm

Sample Name	BDG 15087.2	Instrument	AnalyticalLC01
Acquisition	12/09/2014, 12:20:36	Method (rev.)	LC10411a (8)
Sequence	BDG_12Sep2014a - Reprocessed	Vial Position	5
Operator	solvation010\cerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.20 min	2.1403	13.5024	0.0976 min	0.129 %
2	8.62 min	0.6495	5.5217	0.1312 min	0.053 %
3	9.30 min	1213.5598	10309.7575	0.1311 min	98.496 %
4	9.74 min	2.1542	62.1966	0.3809 min	0.594 %
5	10.59 min	1.8949	19.7779	0.1538 min	0.189 %
6	12.79 min	0.5942	6.4191	0.1580 min	0.061 %
7	18.13 min	0.7509	49.9855	0.7806 min	0.478 %