BDG SYNTHESIS

Certificate of Analysis

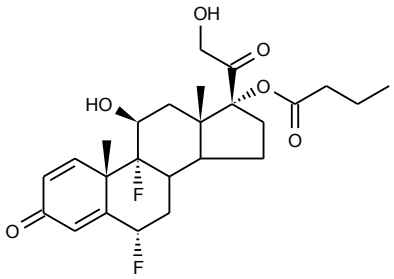
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
11 February 2016

Name: **6α,9α-Difluoroprednisolone-17-butyrate**

CAS Number: 23640-96-2

Structure:



Molecular Weight: $C_{25}H_{32}F_2O_6$ = 466.51

Lot Number: BDG 16355.1-01

Appearance: White, crystalline solid

Corrected Purity: 98.9 % (HPLC) - 0.3 % (acetone) - 3.6 % (water) = 95.0 %

Re-test Date: 11 February 2017

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.

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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.
Residual Solvents: a small amount of acetone (0.3 % *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.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 489.2066. $C_{25}H_{32}F_2NaO_6$ $[M+Na]^+$ requires *m/z* 489.2065. The deviation of 0.2 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A sharp, symmetrical peak is observed (98.9 %). 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 62.34, H 7.23 %
$C_{25}H_{32}F_2O_6{\cdot}0.9H_2O$	Requires:	C 62.20, H 7.06 %
$C_{25}H_{32}F_2O_6$	Requires:	C 64.36, H 6.91 %

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.

Karl-Fischer Analysis

	Found:	H_2O 3.6 %
$C_{25}H_{32}F_2O_6{\cdot}0.9H_2O$	Requires:	H_2O 3.4 %

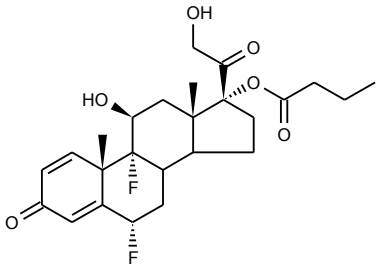
Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

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

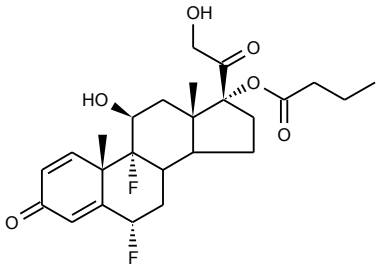
Proton NMR Spectrum of 6α,9α-Difluoroprednisolone-17-butyrate in DMSO-d_6



Lot Number: BDG 16355.1

BDG SYNTHESIS

Carbon-13 NMR Spectrum of 6α,9α-Difluoroprednisolone-17-butyrate in DMSO-d_6

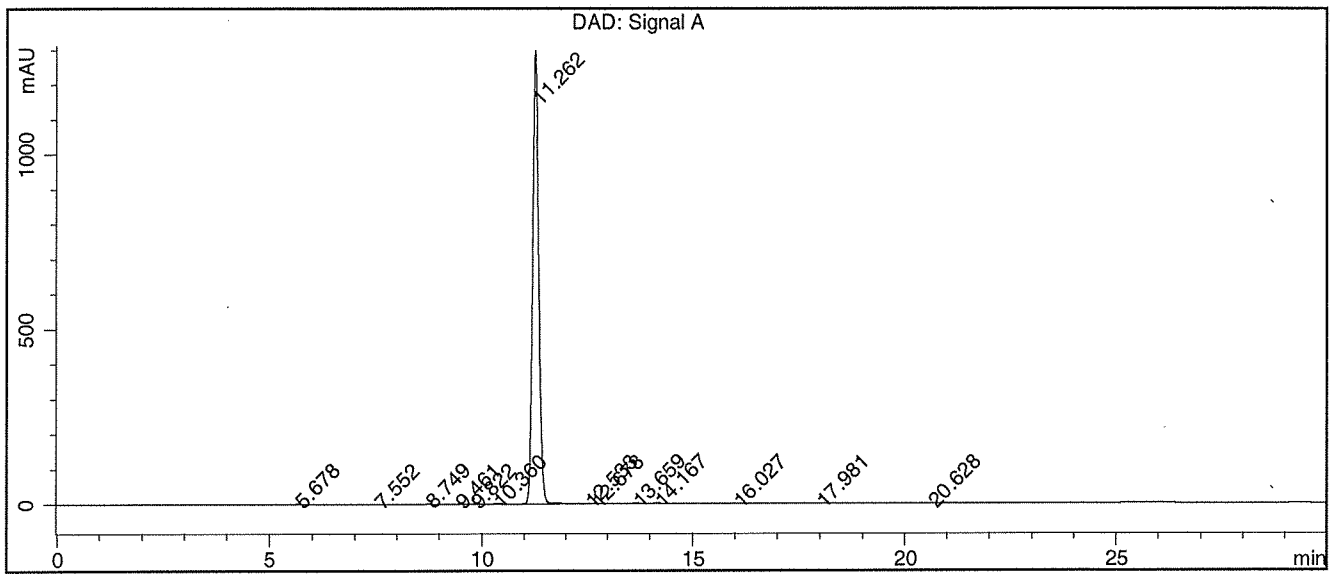


Lot Number: BDG 16355.1

BDG - Analysis of 6a,9a-Difluoroprednisolone-17-butyrate

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 60:40 10 mM diPotassium Hydrogen Phosphate pH=7.0 : Acetonitrile
Mobile Phase B : 25:75 10 mM diPotassium Hydrogen Phosphate pH=7.0 : Acetonitrile
Gradient (A:B) : T0=100:0, T20=0:100, T24=0:100, T27=100:0, T30=100:0
Flow Rate : 1.0 mL/min . . . . . Sample Solvent : 1:1 Water : Acetonitrile
Column Temperature : 20 C . . . . . Injection Volume : 10 uL . . . . . Detection : UV at 240 nm

Sample Name	BDG 16355.1	**Instrument**	AnalyticalLC01
Acquisition	11/02/2016, 13:14:06	**Method (rev.)**	LC10413a (11)
Sequence	BDG_11Feb2016a - Reprocessed	**Vial Position**	4
Operator	solvation010\cerityadmin	**Injection**	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	5.68 min	1.3364	11.0489	0.1265 min	0.083 %
2	7.55 min	0.3425	4.0104	0.1826 min	0.030 %
3	8.75 min	0.7206	8.1903	0.1666 min	0.062 %
4	9.46 min	0.3078	3.6505	0.1744 min	0.027 %
5	9.82 min	0.2697	3.1935	0.1621 min	0.024 %
6	10.36 min	0.9270	10.5261	0.1765 min	0.079 %
7	11.26 min	1298.0463	13137.9970	0.1561 min	98.903 %
8	12.53 min	1.2989	10.5692	0.1249 min	0.080 %
9	12.68 min	1.6360	18.0361	0.1626 min	0.136 %
10	13.66 min	2.6988	30.8176	0.1772 min	0.232 %
11	14.17 min	2.8363	30.2038	0.1642 min	0.227 %
12	16.03 min	0.4616	8.3701	0.2415 min	0.063 %
13	17.98 min	0.2869	3.5440	0.1841 min	0.027 %
14	20.63 min	0.2794	3.5970	0.1922 min	0.027 %