BDG SYNTHESIS

Certificate of Analysis

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

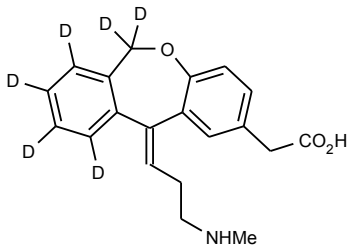
Barry Dent

Barry R. Dent, PhD, Director
29 April 2014

Name: ***N*-Desmethylolopatadine-d_6**

CAS Number: 113835-92-0 (unlabelled)

Structure:



Molecular Weight: $C_{20}H_{15}D_6NO_3$ = 329.42

Lot Number: BDG 9208

Appearance: White, crystalline solid

Corrected Purity: 98.9 % (HPLC) - 3.2 % (water) = 95.7 %

Isotopic Purity: Under 0.5 % d_0

Re-test Date: 29 April 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.

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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 greatly diminished, compared with the spectrum of unlabelled material, indicating clean deuteration.
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: signals at the sites of deuteration have collapsed to small multiplets compared with the spectrum of unlabelled material, indicating clean deuteration.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 330.1959. $C_{20}H_{16}D_6NO_3$ $[M+H]^+$ requires *m/z* 330.1971. The deviation of 3.6 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 (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 70.60, H 4.68, D 3.75, N 4.06 %
$C_{20}H_{15}D_6NO_3 \cdot 0.6H_2O$	Requires:	C 70.60, H 4.80, D 3.55, N 4.12 %, H_2O 3.18 %
$C_{20}H_{15}D_6NO_3$	Requires:	C 72.92, H 4.59, D 3.67, N 4.25 %

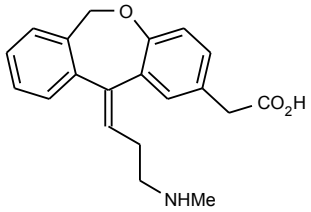
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

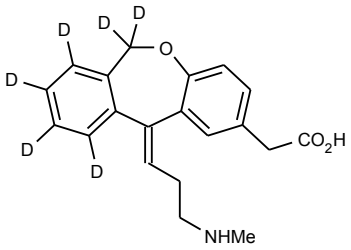
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials 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 *N*-Desmethylolopatadine (top) and *N*-Desmethylolopatadine-d_6 (bottom) in DMSO-d_6 + DCl

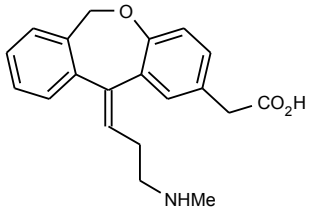


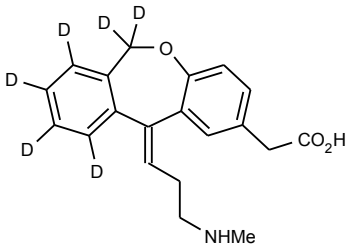


Lot Number: BDG 9208

BDG SYNTHESIS

Carbon-13 NMR Spectrum of *N*-Desmethylolopatadine (top) and *N*-Desmethylolopatadine-d_6 (bottom) in DMSO-d_6 + DCl





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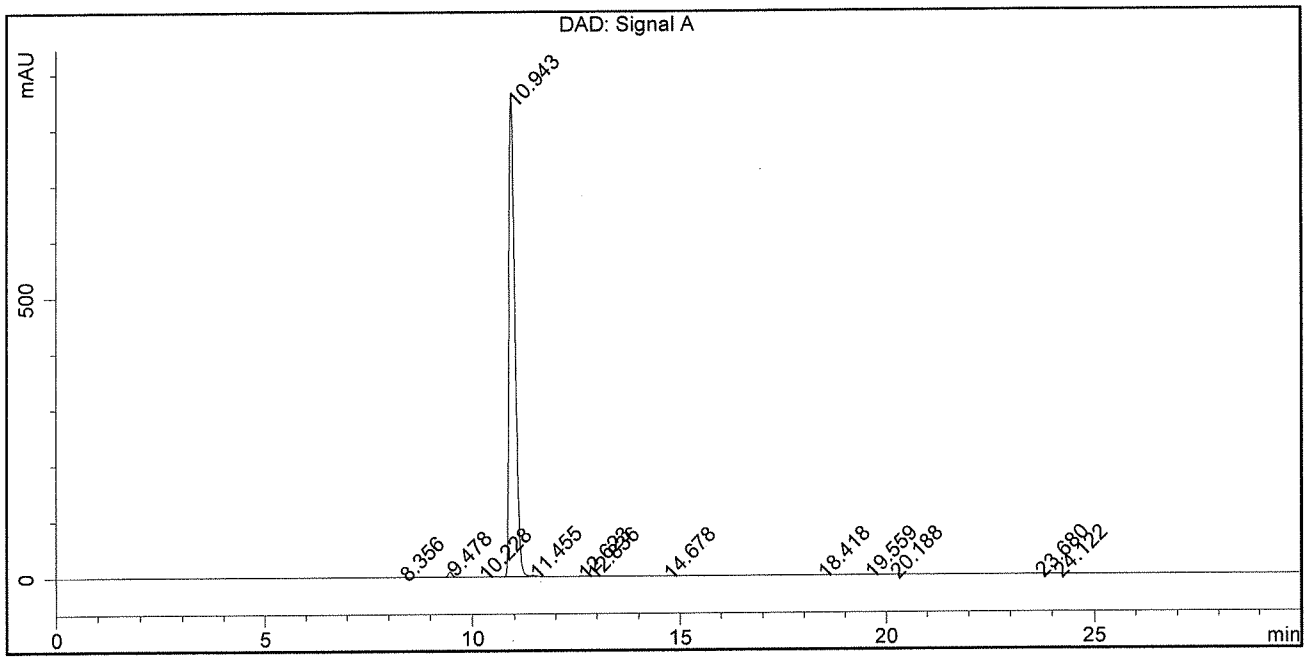
BDG - Analysis of Olopatadine derivatives

Column : Phenomenex Luna C18 (2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 80:20:0.01 Water : Acetonitrile :Trifluoroacetic Acid
Mobile Phase B : 50:50:0.01 Acetonitrile :Trifluoroacetic Acid
Gradient : T0=100:0, T25=0:100, T28=100:0, T30=100:0
Flow Rate : 1 mL/min
Sample Solvent : 1:1 Acetonitrile:Water
Column Temperature : 20C
Injection Volume : 10 uL
Detection : UV at 254 nm

Sample Name	BDG 9208	**Instrument**	AnalyticalLC01
Acquisition	29/04/2014, 16:07:58	**Method (rev.)**	LC10016c (12)
Sequence	BDG_29Apr2014a - Reprocessed	**Vial Position**	31
Operator	solvation010\cerityadmin	**Injection**	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	8.36 min	0.1691	1.9436	0.1501 min	0.022 %
2	9.48 min	9.0878	65.7439	0.1104 min	0.749 %
3	10.23 min	0.2288	1.7739	0.1145 min	0.020 %
4	10.94 min	864.7235	8679.2080	0.1571 min	98.868 %
5	11.46 min	1.0109	7.2151	0.1153 min	0.082 %
6	12.62 min	0.3472	2.2256	0.0988 min	0.025 %
7	12.84 min	0.4138	2.9095	0.1060 min	0.033 %
8	14.68 min	0.2931	3.2492	0.1573 min	0.037 %
9	18.42 min	0.1357	1.0959	0.1202 min	0.012 %
10	19.56 min	0.1719	2.8115	0.2148 min	0.032 %
11	20.19 min	0.1507	1.9361	0.1598 min	0.022 %
12	23.68 min	0.5334	6.5290	0.1868 min	0.074 %
13	24.12 min	0.1854	1.9385	0.1380 min	0.022 %