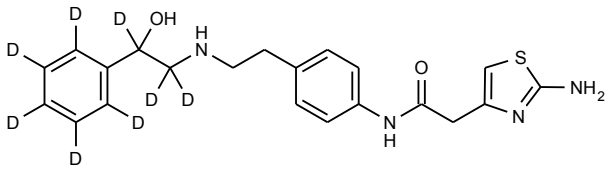
BDG SYNTHESIS

Certificate of Analysis

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

Barry Dent

Barry R. Dent, PhD, Director
9 July 2014

Name:	**Mirabegron-d_8**
CAS Number:	223673-61-8 (unlabelled)
Structure:	
Molecular Weight:	$C_{21}H_{16}D_8N_4O_2S$ = 404.56
Lot Number:	BDG 12920
Appearance:	Off-white, crystalline solid
Corrected Purity:	99.0 % (HPLC) - 0.1 % (ethanol) = 98.9 %
Isotopic Purity:	Under 0.5 % d_0
Re-test Date:	9 July 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 absent, compared with the spectrum of unlabelled material, indicating clean deuteration.
Residual Solvents: a small amount of ethanol (0.1 % *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: 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* 405.2200. $C_{21}H_{17}D_8N_4O_2S$ $[M+H]^+$ requires *m/z* 405.2200. The deviation of 0.0 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 (99.0 %). 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 62.30, H 3.95, D 3.95, N 13.90 %
$C_{21}H_{16}D_8N_4O_2S$	Requires:	C 62.35, H 3.99, D 3.98, N 13.85 %

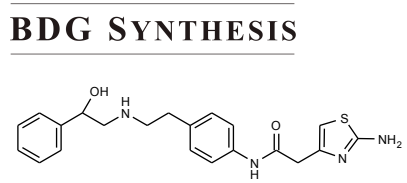
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

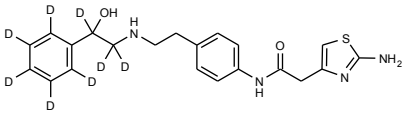
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

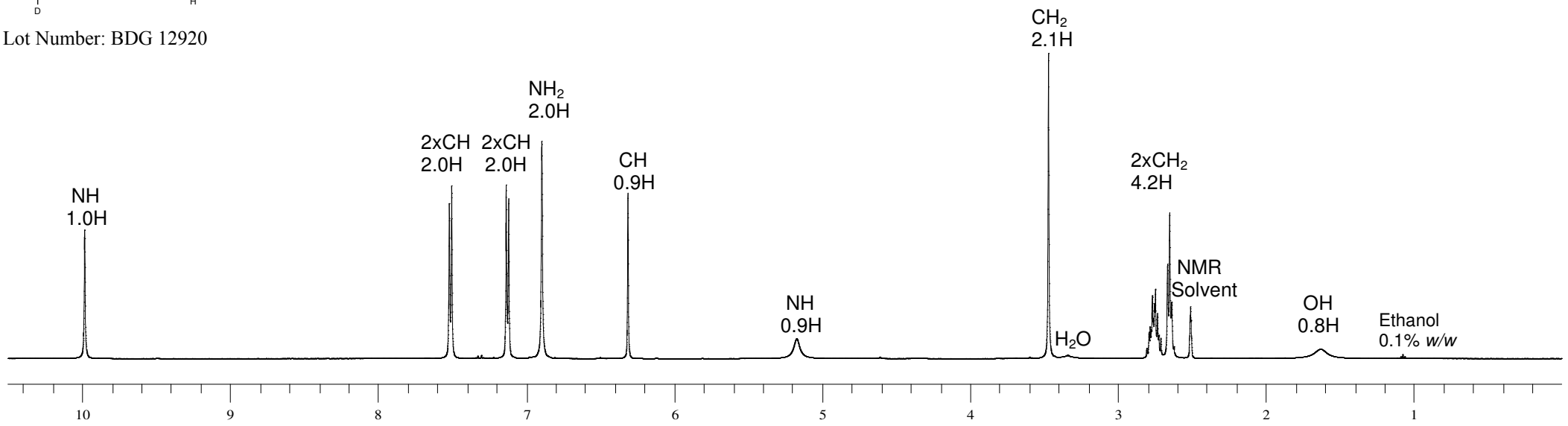
BDG SYNTHESIS

Proton NMR Spectrum of *rac*-Mirabegron (top) and Mirabegron-d_8 (bottom) in DMSO-d_6



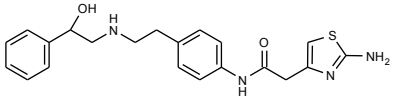


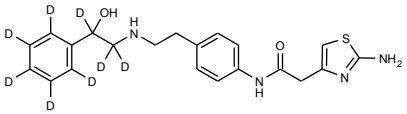
Lot Number: BDG 12920



BDG SYNTHESIS

Carbon-13 NMR Spectrum of *rac*-Mirabegron (top) and Mirabegron-d_8 (bottom) in DMSO-d_6





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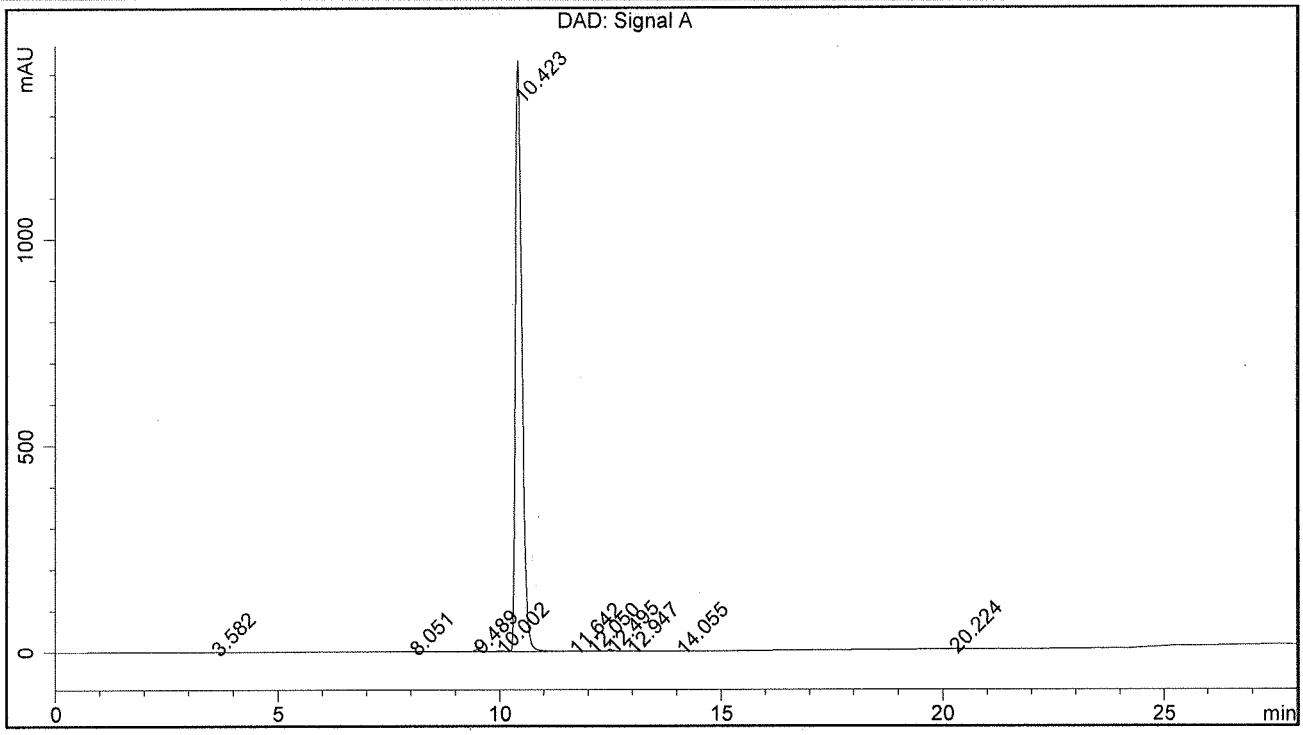
BDG - Analysis of Mirabegron-d8

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A: 85:15:0.05 Water : Acetonitrile : Trifluoroacetic Acid
Mobile Phase B: 100:0.05 Acetonitrile : Trifluoroacetic Acid
Gradient (A:B) : T0=100:0, T20=50:50, T24=0:100, T26=100:0, T30=100:0
Flow Rate : 1.0 mL/min . . . . . Sample Solvent : 80:20 Water : Acetonitrile
Column Temperature : 20 C . . . . . Injection Volume : 10 uL . . . . . Detection: UV 248 nm

Sample Name	BDG 12920	Instrument	AnalyticalLC01
Acquisition	09/07/2014, 16:29:26	Method (rev.)	LC10618a (17)
Sequence	BDG_09Jul2014h - Reprocessed	Vial Position	43
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	3.58 min	0.2283	4.6056	0.2513 min	0.031 %
2	8.05 min	0.3575	3.3405	0.1410 min	0.022 %
3	9.49 min	5.1729	54.5618	0.1591 min	0.362 %
4	10.00 min	2.0487	24.1817	0.1697 min	0.161 %
5	10.42 min	1428.1495	14908.7658	0.1658 min	99.032 %
6	11.64 min	0.5005	4.1145	0.1159 min	0.027 %
7	12.05 min	0.7435	5.0406	0.1031 min	0.033 %
8	12.49 min	4.6843	35.9128	0.1134 min	0.239 %
9	12.95 min	0.3881	2.3467	0.0945 min	0.016 %
10	14.05 min	0.3819	2.2179	0.0918 min	0.015 %
11	20.22 min	0.5181	9.4177	0.2681 min	0.063 %