



BDG SYNTHESIS

Certificate of Analysis

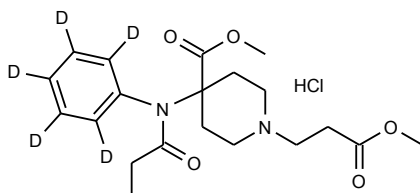
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Barry Dent

Barry R. Dent, PhD, Director
25 April 2010

Name: Remifentanil- d_5 HCl
CAS Number: 132539-07-2 (unlabelled)

Structure:



Molecular Weight: $C_{20}H_{23}D_5N_2O_5 \cdot HCl = 417.94$
Lot Number: BDG 10744.2
Appearance: White, crystalline solid
Corrected Purity: 97.6 % (HPLC) - 0.6 % (ethanol) - 1.3 % (acetone) = 95.7 %
Isotopic Purity: Under 0.5 % d_0
Re-test Date: 25 April 2015
Storage and Handling: Temperature: ambient laboratory temperature; may be refrigerated.
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. The complexity of the spectrum indicates two rotamers of the product are present in solution.

Isotopic Labelling: signals at the sites of deuteration are greatly diminished, compared with the spectrum of unlabelled material, indicating clean deuteration.

Residual Solvents: small amounts of ethanol (0.6 % w/w) and acetone (1.3 % w/w) 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. Most signals are duplicated indicating that two rotamers of the product are present in solution.

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 382.2391. $C_{20}H_{24}D_5N_2O_5$ $[M+H]^+$ requires m/z 382.2385. The deviation of 1.5 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 somewhat broadened, slightly tailing peak is observed (97.6 %). 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 57.40, H 5.87, D 2.44, N 6.50 %
$C_{20}H_{23}D_5N_2O_5 \cdot HCl$	Requires:	C 57.48, H 5.79, D 2.41, N 6.70 %

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).

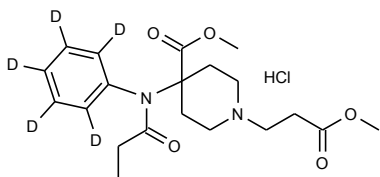
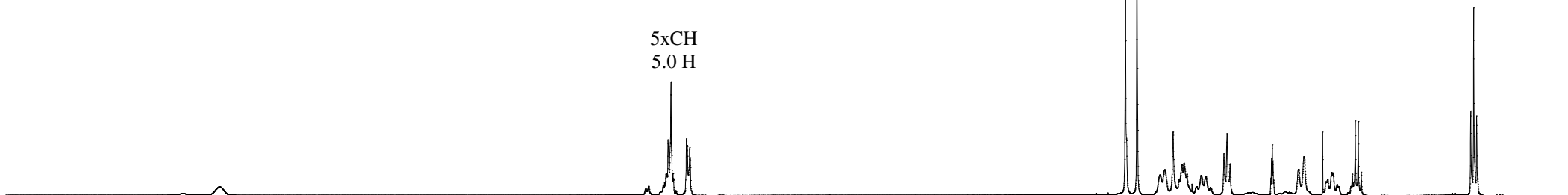
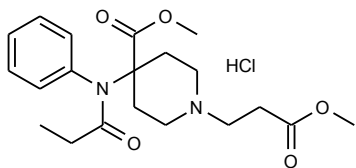
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

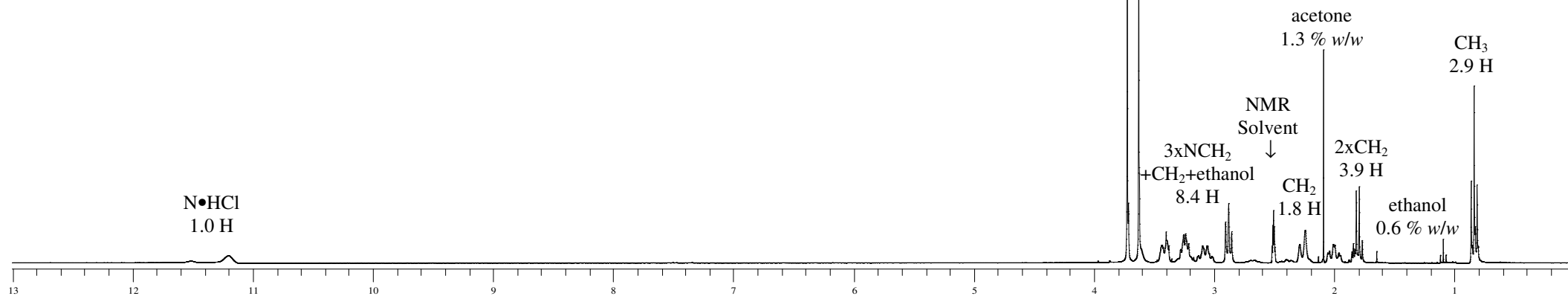


Proton NMR Spectrum of Remifentanil HCl (top) and Remifentanil-d₅ HCl (bottom) in DMSO-d₆

BDG SYNTHESIS



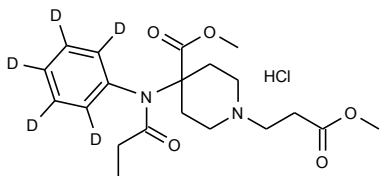
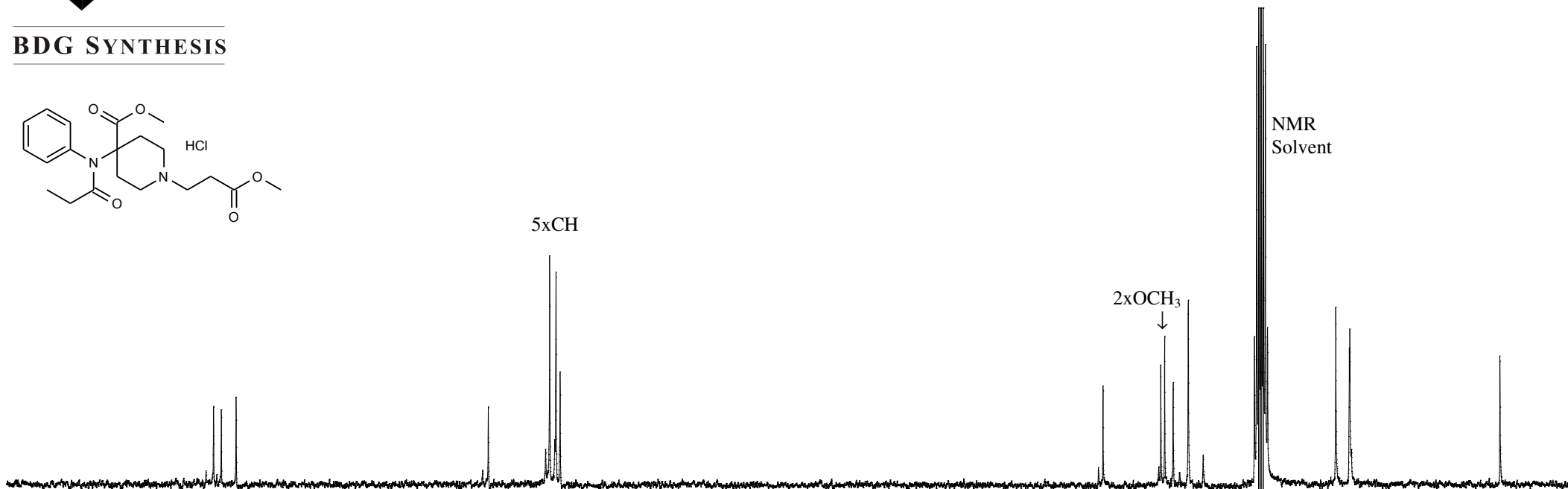
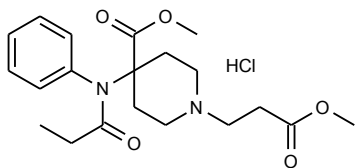
Lot Number: BDG 10744.2



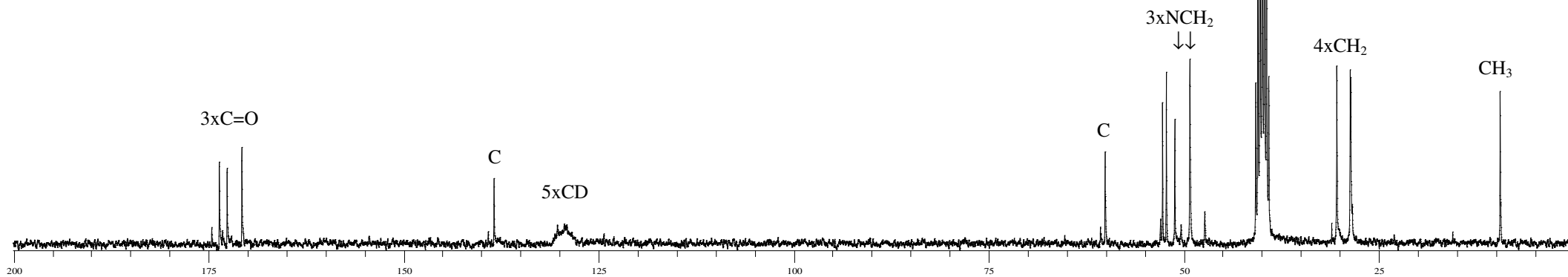


Carbon-13 NMR Spectrum of Remifentanil HCl (top) and Remifentanil-d₅ HCl (bottom) in DMSO-d₆

BDG SYNTHESIS



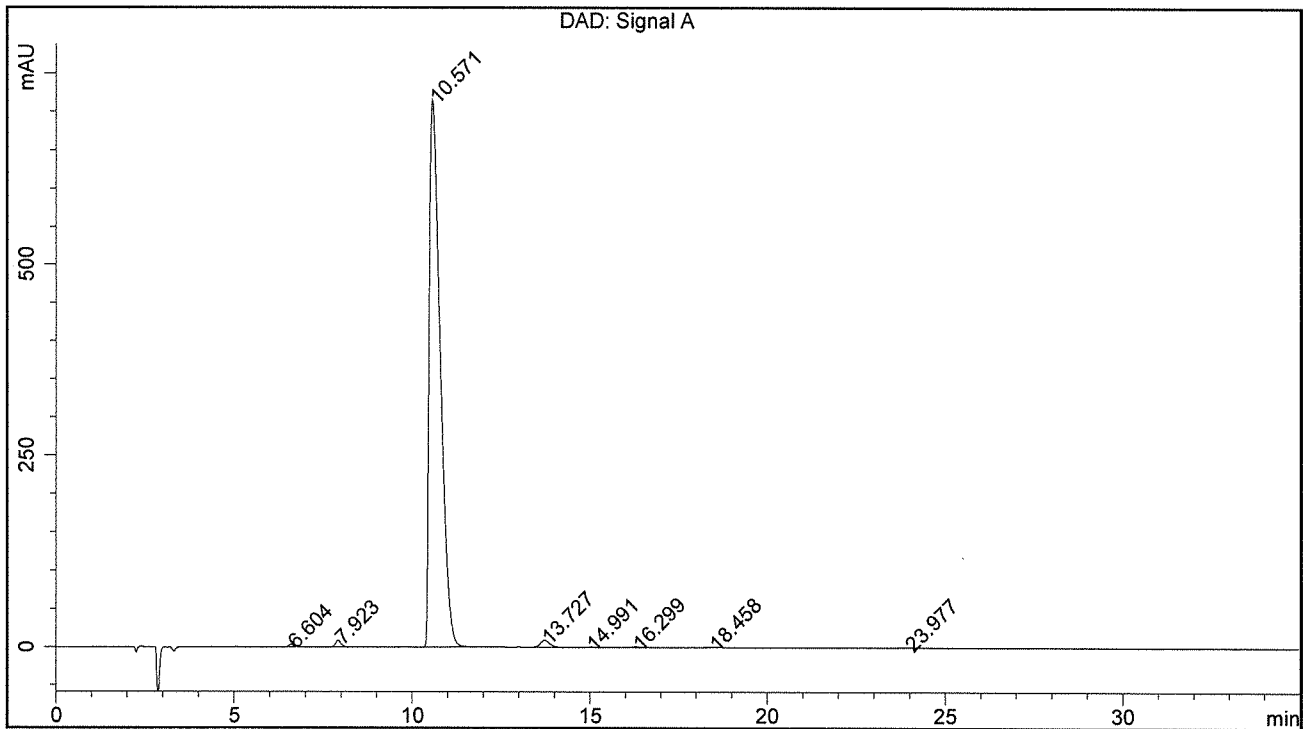
Lot Number: BDG 10744.2



BDG - Analysis of Remifentanil-d5 HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
 Mobile Phase : 75:25:0.1 Water : Acetonitrile : Trifluoroacetic Acid
 Flow Rate : 1.0 mL/min
 Sample Solvent : 7:3 Water : Acetonitrile
 Column Temperature : 20C
 Injection Volume : 10 uL
 Detection : UV at 210 nm

Sample Name	BDG 10744.2	Instrument	AnalyticalLC01
Acquisition	25/04/2010, 19:27:15	Method (rev.)	LC10373d (3)
Sequence	BDG_25Apr2010i	Vial Position	2
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	6.60 min	3.3517	34.0359	0.1545 min	0.217 %
2	7.92 min	8.6747	94.4115	0.1650 min	0.602 %
3	10.57 min	716.2644	15319.5517	0.3315 min	97.645 %
4	13.73 min	9.0522	165.7500	0.2856 min	1.056 %
5	14.99 min	0.5685	9.6536	0.2221 min	0.062 %
6	16.30 min	1.0935	22.7402	0.2746 min	0.145 %
7	18.46 min	0.9127	27.6486	0.3654 min	0.176 %
8	23.98 min	0.5097	15.1636	0.3591 min	0.097 %