



BDG SYNTHESIS

Certificate of Analysis

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

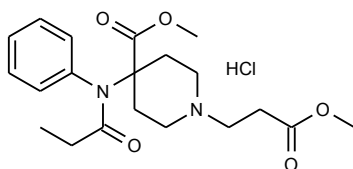
Barry Dent

Barry R. Dent, PhD, Director
26 April 2010

Name: Remifentanil HCl

CAS Number: 132539-07-2

Structure:



Molecular Weight: $C_{20}H_{28}N_2O_5 \cdot HCl = 412.91$

Lot Number: BDG 10740.4

Appearance: White, crystalline solid

Corrected Purity: 98.2 % (HPLC) - 0.5 % (acetone) = 97.7 %

Re-test Date: 26 April 2011

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.

Residual Solvents: a small amount of acetone (0.5 % w/w) and traces (under 0.1 % w/w) of methanol and 2-propanol 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.

High-resolution Mass Spectrum (ESI+)

Found m/z 377.2073. $C_{20}H_{29}N_2O_5$ $[M+H]^+$ requires m/z 377.2071. The deviation of 0.6 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A somewhat broadened, slightly tailing peak is observed (98.2 %). 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 58.25, H 7.17, N 6.78 % |
| $C_{20}H_{28}N_2O_5 \cdot HCl$ | Requires: | C 58.18, H 7.08, N 6.78 % |

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).

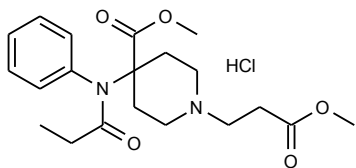
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

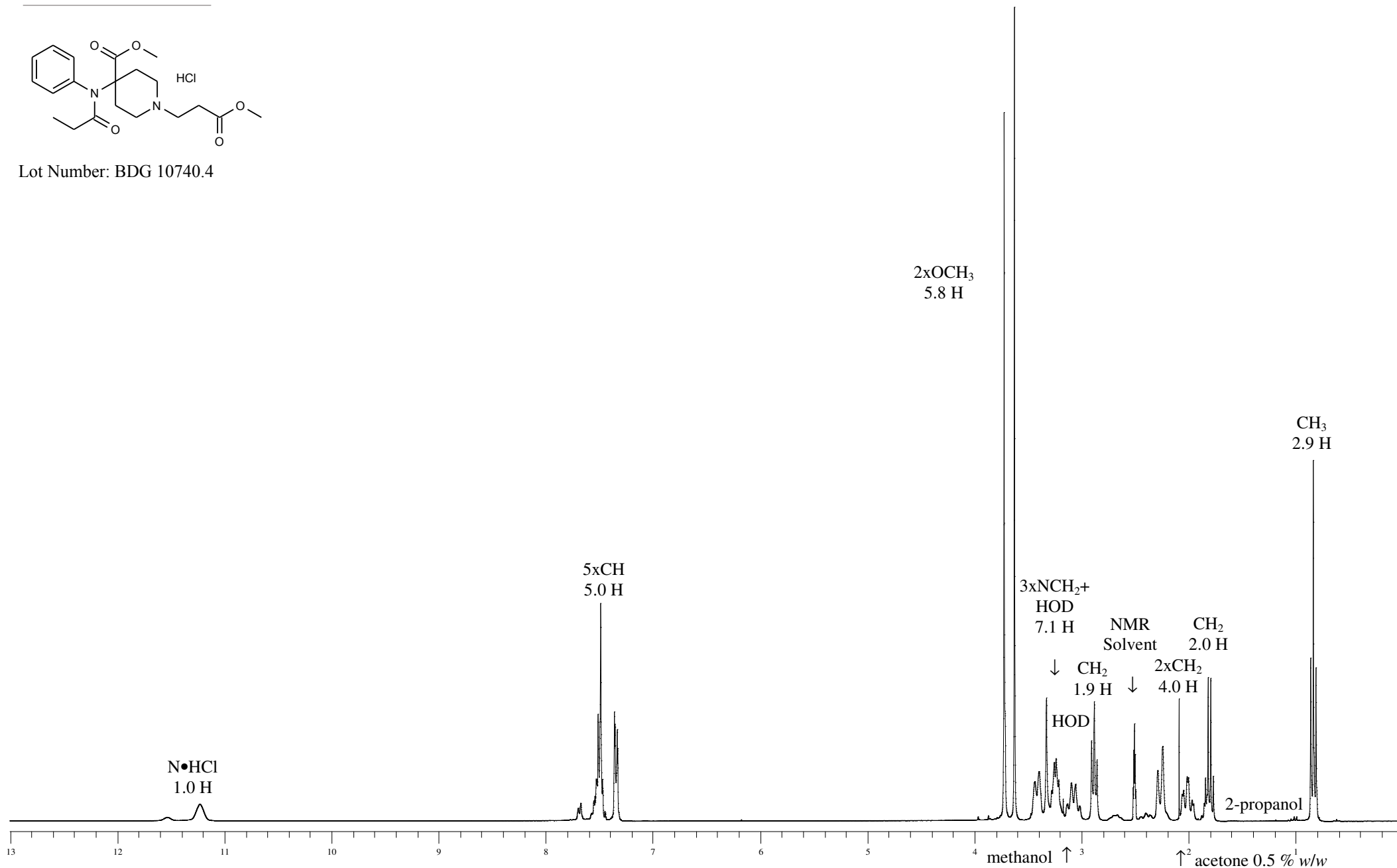


Proton NMR Spectrum of Remifentanil HCl in DMSO-d₆

BDG SYNTHESIS



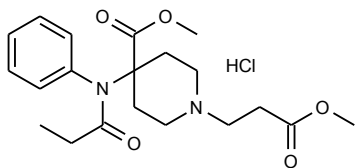
Lot Number: BDG 10740.4



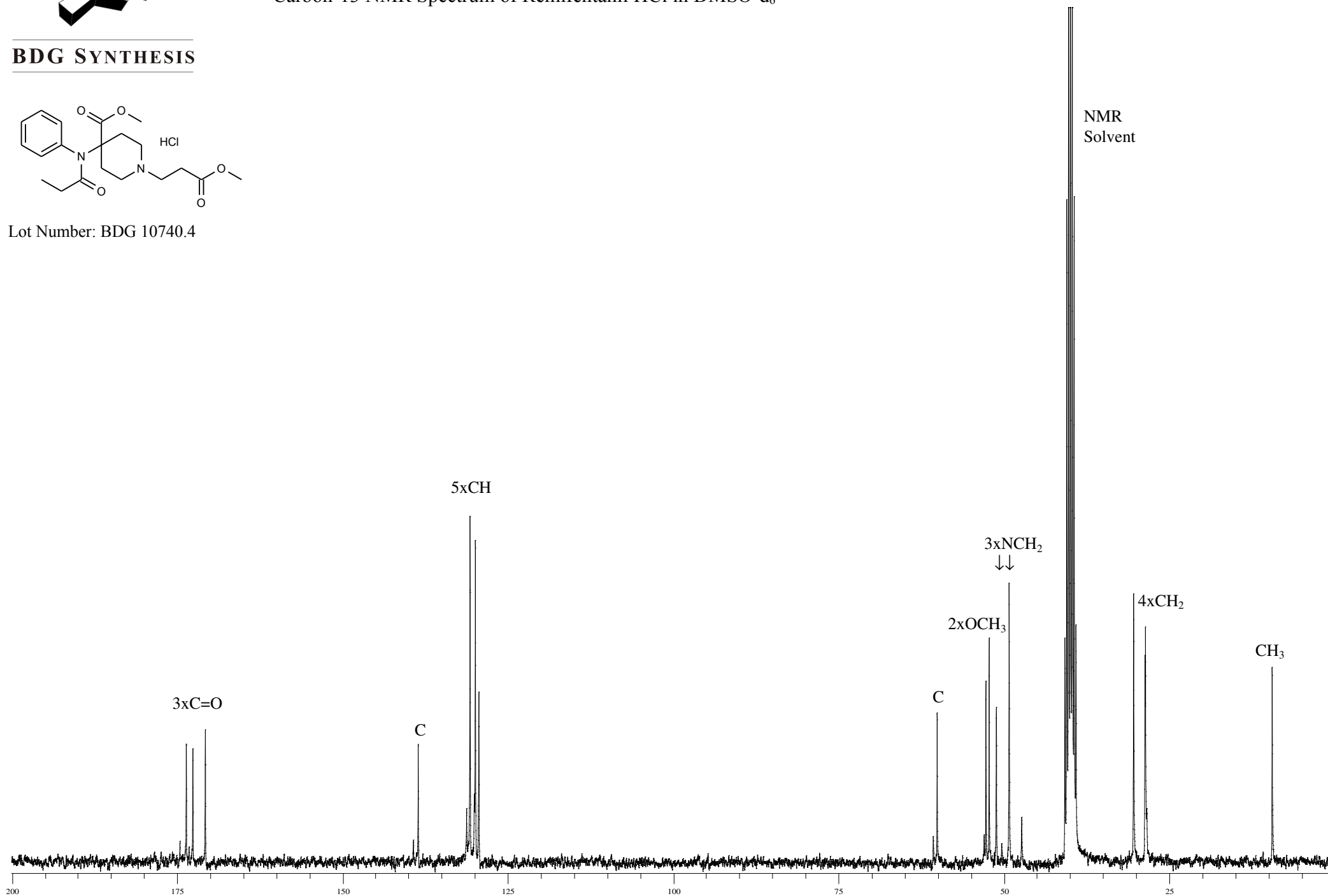


Carbon-13 NMR Spectrum of Remifentanyl HCl in DMSO-d₆

BDG SYNTHESIS



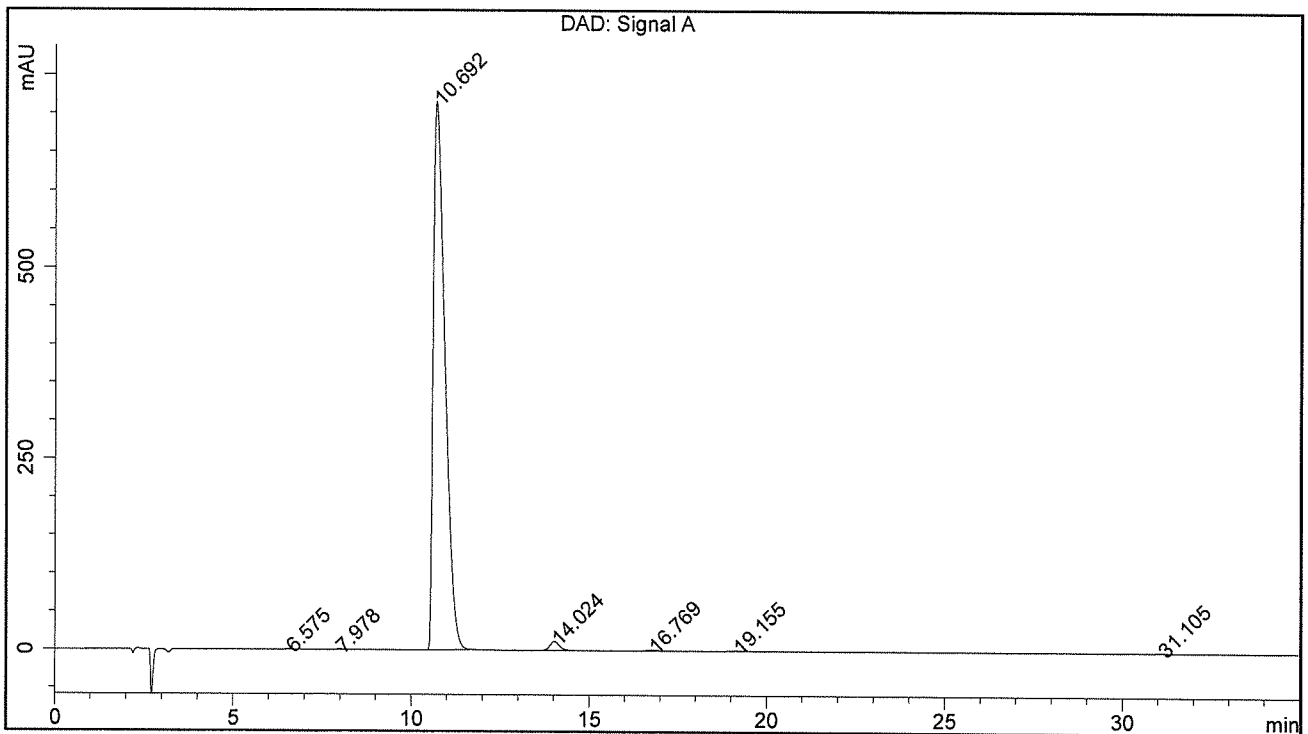
Lot Number: BDG 10740.4



BDG - Analysis of Remifentanil 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 10740.4 | Instrument | AnalyticalLC01 |
| Acquisition | 26/04/2010, 11:25:55 | Method (rev.) | LC10373b (15) |
| Sequence | BDG_26Apr2010a - Reprocessed | Vial Position | 21 |
| Operator | solvation010\cerityadmin | Injection | 1 of 1 |



Area Percent Report

| Peak# | RT | Peak Height | Peak Area | Width | Area % |
|-------|-----------|-------------|------------|------------|----------|
| 1 | 6.58 min | 0.9804 | 11.1120 | 0.1682 min | 0.067 % |
| 2 | 7.98 min | 0.8948 | 11.2713 | 0.1670 min | 0.068 % |
| 3 | 10.69 min | 715.9298 | 16301.2694 | 0.3476 min | 98.170 % |
| 4 | 14.02 min | 11.5564 | 218.9871 | 0.2911 min | 1.319 % |
| 5 | 16.77 min | 1.5435 | 33.8726 | 0.3100 min | 0.204 % |
| 6 | 19.16 min | 0.5383 | 13.5655 | 0.3240 min | 0.082 % |
| 7 | 31.10 min | 0.4087 | 15.1137 | 0.4414 min | 0.091 % |