



## BDG SYNTHESIS

### Certificate of Analysis

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

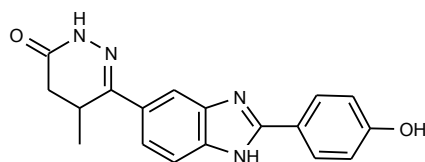
*Barry Dent*

Barry R. Dent, PhD, Director  
24 October 2009

**Name:** *O*-Desmethyimpibendan

**CAS Number:** 108381-22-2

**Structure:**



**Molecular Weight:**  $C_{18}H_{16}N_4O_2 = 320.35$

**Lot Number:** BDG 10621

**Appearance:** White, crystalline solid

**Corrected Purity:** 98.4 % (HPLC) - 0.2 % (methanol) - 5.1 % (water) = 93.1 %

**Re-test Date:** 24 October 2010

**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.

Residual Solvents: a small amount of methanol (0.2 % w/w) is 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. Several peaks associated with the benzimidazole moiety and evident in the spectra of impure material, have collapsed into the baseline.

### High-resolution Mass Spectrum (ESI+)

Found  $m/z$  321.1358.  $C_{18}H_{17}N_4O_2$   $[M+H]^+$  requires  $m/z$  321.1346. The deviation of 3.7 ppm is within normally accepted limits for the establishment of identity by HRMS.

### HPLC

A sharp, symmetrical peak is observed (98.4 %). 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 63.85, H 5.36, N 16.45 % |
| $C_{18}H_{16}N_4O_2 \cdot 1.0H_2O$ | Requires: | C 63.89, H 5.36, N 16.56 % |
| $C_{18}H_{16}N_4O_2$               | Requires: | C 67.49, H 5.03, N 17.49 % |

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 <sub>2</sub> O 5.1 % |
| $C_{18}H_{16}N_4O_2 \cdot 1.0H_2O$ | Requires: | H <sub>2</sub> O 5.3 % |

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.

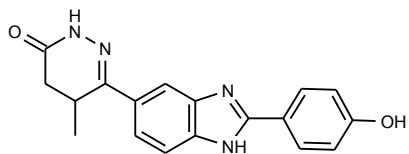
The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials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

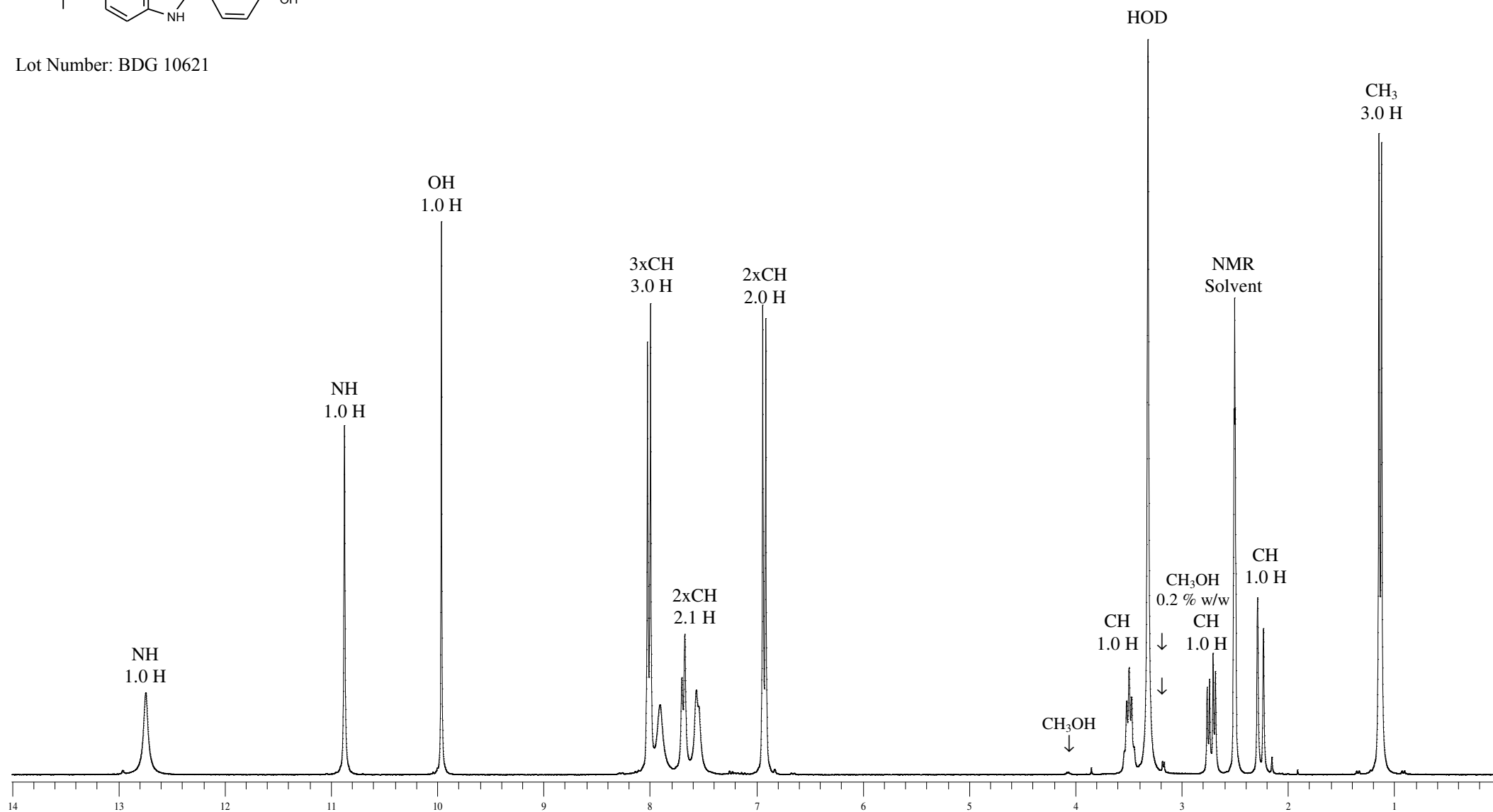


Proton NMR Spectrum of *O*-Desmethylpimobendan in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



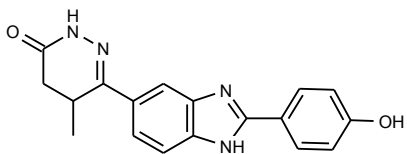
Lot Number: BDG 10621



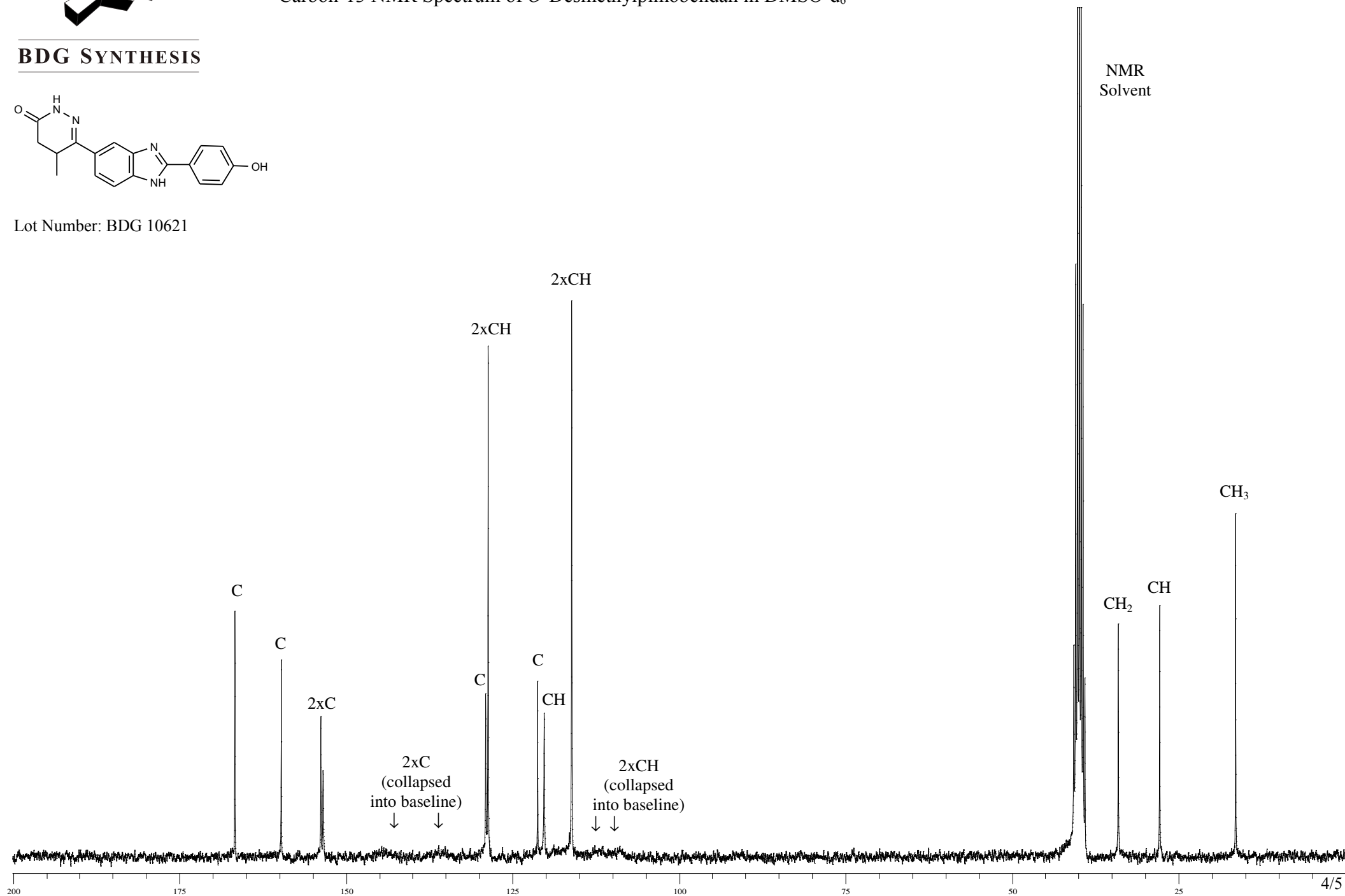


Carbon-13 NMR Spectrum of *O*-Desmethylpimobendan in DMSO-d<sub>6</sub>

**BDG SYNTHESIS**



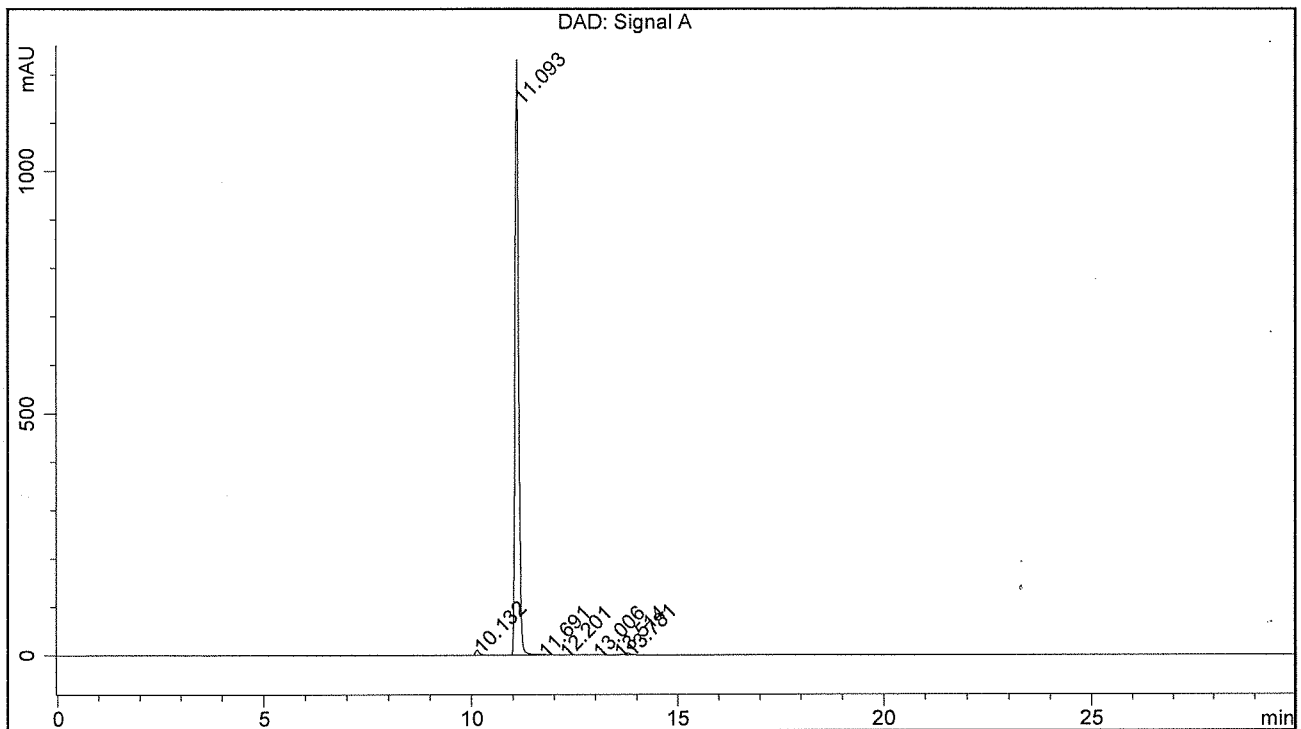
Lot Number: BDG 10621



BDG - Analysis of O-Desmethypimobendan

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm  
 Guard : Phenomenex Security Guard C18 RP 4 x 3 mm  
 Mobile Phase A : 70:30 Water : Acetonitrile  
 Mobile Phase B : 30:70 Water : Acetonitrile  
 Gradient (A:B) : T0=100:0, T24=0:100, T27=100:0, T30=100:0  
 Flow Rate : 1.0 mL/min . . . . . Sample Solvent : 1:1 Water : Acetonitrile  
 Column Temperature : 20C . . . . . Injection Volume : 10 uL . . . . . Detection : UV 328 nm

|                    |                              |                      |                |
|--------------------|------------------------------|----------------------|----------------|
| <b>Sample Name</b> | BDG 10621                    | <b>Instrument</b>    | AnalyticalLC01 |
| <b>Acquisition</b> | 24/10/2009, 14:23:26         | <b>Method (rev.)</b> | LC10347a ( 8)  |
| <b>Sequence</b>    | BDG_24Oct2009c - Reprocessed | <b>Vial Position</b> | 1              |
| <b>Operator</b>    | solvation010\cerityadmin     | <b>Injection</b>     | 1 of 1         |



Area Percent Report

| Peak# | RT        | Peak Height | Peak Area | Width      | Area %   |
|-------|-----------|-------------|-----------|------------|----------|
| 1     | 10.13 min | 10.7885     | 74.7105   | 0.1028 min | 0.986 %  |
| 2     | 11.09 min | 1231.3576   | 7454.0255 | 0.0926 min | 98.423 % |
| 3     | 11.69 min | 0.3619      | 3.8074    | 0.1468 min | 0.050 %  |
| 4     | 12.20 min | 0.3721      | 2.9417    | 0.1142 min | 0.039 %  |
| 5     | 13.01 min | 0.4506      | 3.2857    | 0.1131 min | 0.043 %  |
| 6     | 13.51 min | 0.6601      | 5.2884    | 0.1195 min | 0.070 %  |
| 7     | 13.78 min | 4.1015      | 29.3986   | 0.1076 min | 0.388 %  |