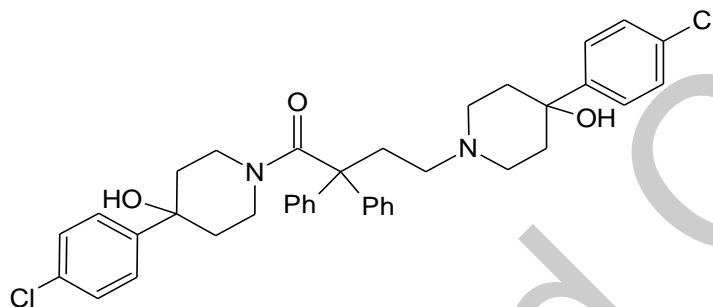


## Reference Material Product Information Sheet

Epichem's Quality System conforms to ISO9001:2015 as certified by ECAAS Pty Ltd - Certification number 616061.



<b>Name</b>	4-(4-chlorophenyl)-1-(4-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-2,2-diphenylbutanoyl)piperidin-4-ol
<b>BP Name</b>	Loperamide Impurity E
<b>Synonym(s)</b>	4-(4-chlorophenyl)-1-(4-(4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl)-2,2-diphenylbutanoyl)-4-hydroxypiperidine
<b>Epichem Item #</b>	EPL-AA159 Batch 1
<b>CAS #</b>	1426322-82-8
<b>Molecular Formula</b>	C <sub>38</sub> H <sub>40</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub>
<b>Molecular Weight</b>	643.66 g/mol
<b>Appearance</b>	White powder
<b>Melting Point</b>	142.5-209.7°C (decomposition)
<b>Combustion Analysis</b>	Required (%): C:70.9; H:6.3; N:4.4. Found (%): C:68.9; H:6.4; N:4.3.
<b>Purity</b>	97.2%
<b>Date of Manufacture</b>	15 December 2014
<b>Storage Requirements</b>	Protect from heat, light and moisture.
<b>Special Precautions</b>	<b>This compound is for laboratory use only. Its toxicological properties may not have been fully established. It should be handled only by suitably qualified personnel.</b>
<b>Date of Shipment</b>	TBA This certificate is valid for one year from the date of shipment provided the substance is unopened and stored under the recommended conditions.
<b>Retest Date</b>	TBA (Proper Storage and Handling Required)

EPL-AA159 Batch 1

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ABN 80 106 769 902

## I. Identity

The identity of this product was established using the following analyses:

### Ia. <sup>1</sup>HNMR Spectrum

Conditions: 400 MHz, DMSO-d<sub>6</sub>

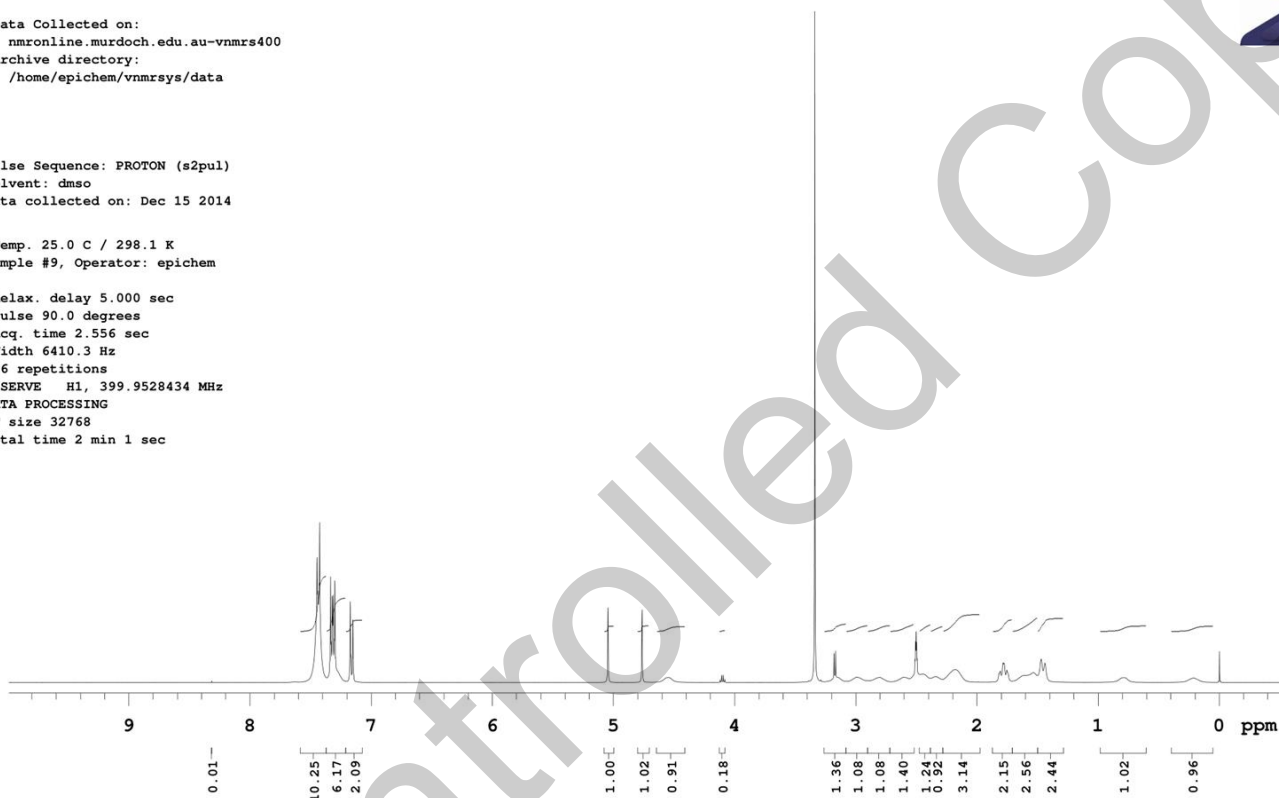
<sup>1</sup>HNMR spectrum consistent with chemical structure.

Data Collected on:  
nmronline.murdoch.edu.au-vnmrs400  
Archive directory:  
/home/epichem/vnmrsys/data

Pulse Sequence: PROTON (s2pul)  
Solvent: dmsc  
Data collected on: Dec 15 2014

Temp. 25.0 C / 298.1 K  
Sample #9, Operator: epichem

Relax. delay 5.000 sec  
Pulse 90.0 degrees  
Acq. time 2.556 sec  
Width 6410.3 Hz  
16 repetitions  
OBSERVE H1, 399.9528434 MHz  
DATA PROCESSING  
FT size 32768  
Total time 2 min 1 sec

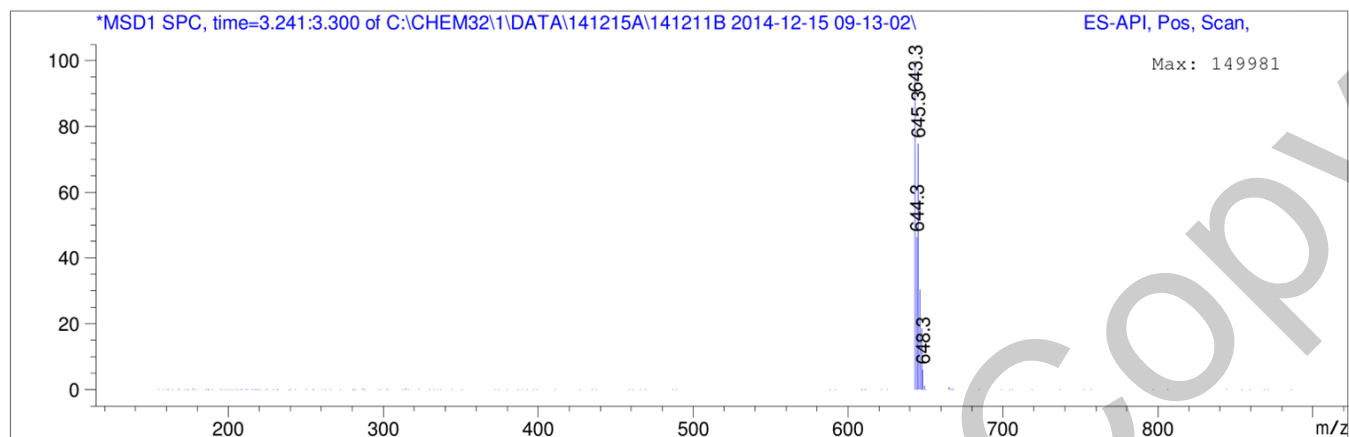


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## Ib. Mass Spectrum

Method: 5% to 100% ACN in water gradient (+0.1% formic acid)  
Poroshell 120 EC-C18, 4.6 x 50 mm, 2.7 micron



Theoretical value: 644.3 [M+H]<sup>+</sup>.

The signal of the Mass Spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.

EPL-AA159 Batch 1

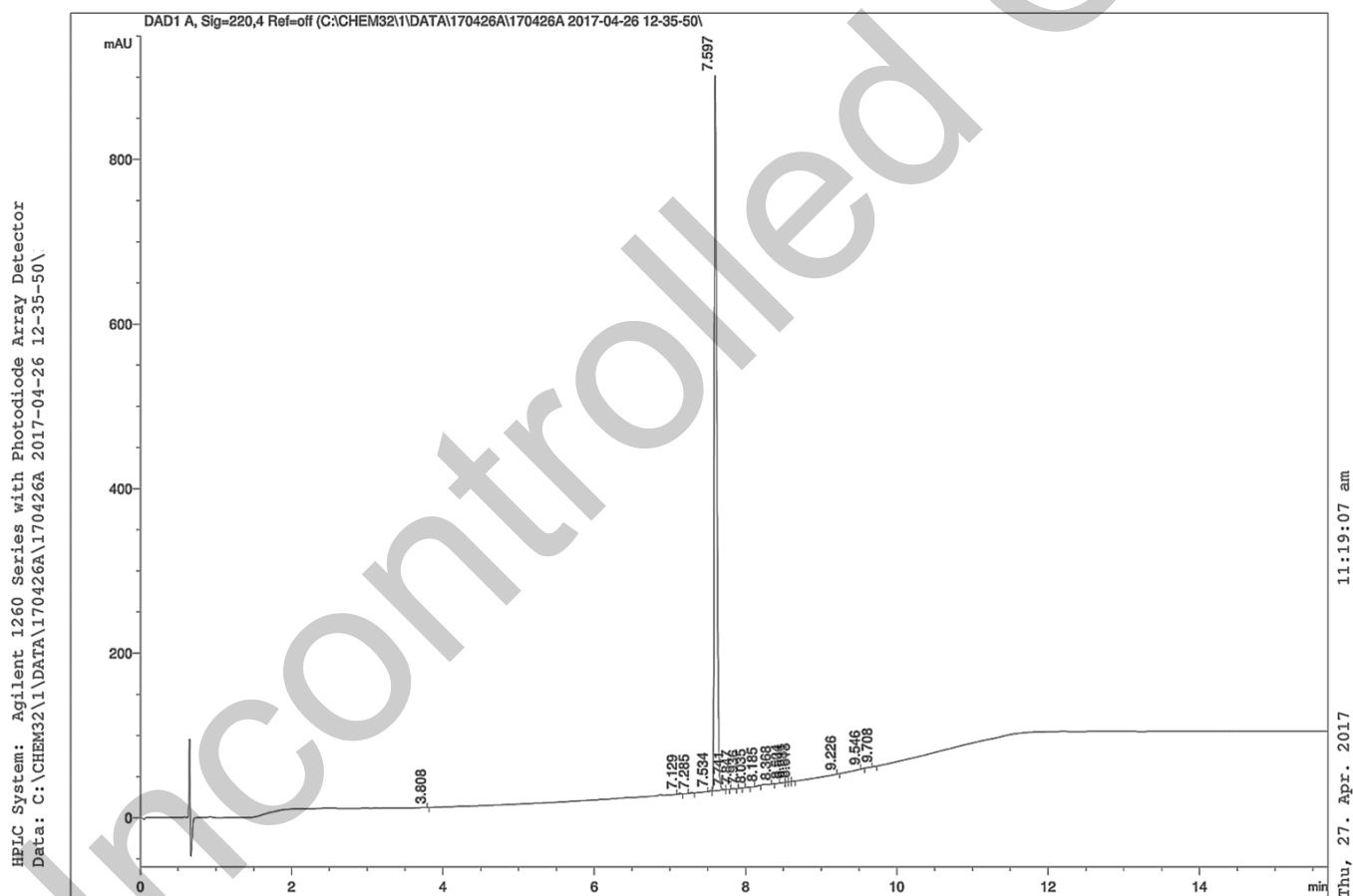
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## II. Purity

The purity of this material was analysed by high performance liquid chromatography (HPLC) using in-house EM005.WI07.

### HPLC Conditions:

Column	Conditions				Detector	Injector
Agilent Poroshell 120 EC-C18  4.6 x 50mm  2.7 micron	25°C				DAD 220nm	Auto 1.0 µL 0.63 mg/mL in 50% water / 50% acetonitrile (+0.1% TFA)  0.59 mg/mL in 50% water / 50% acetonitrile (+0.1% TFA) (duplicate)
	Time (min)	% Line A (Water + 0.1% (v/v) TFA)	% Line B (Acetonitrile + 0.1% (v/v) TFA)	Flow rate (mL/min)		
	0.00	95	5	1.0		
	10.00	5	95	1.0		
	14.50	5	95	1.0		
	15.50	95	5	1.0		
	18.50	95	5	1.0		



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### Area Percent Report – Sorted by Signal

Peak Number	Retention Time (rounded)	Area	Area % (rounded)
1	3.81	0.05	0.00
2	7.13	3.01	0.15
3	7.28	1.62	0.08
4	7.53	2.07	0.10
5	7.60	2018.81	99.36
6	7.74	0.37	0.02
7	7.85	1.26	0.06
8	7.94	0.24	0.01
9	8.04	0.64	0.03
10	8.18	0.59	0.03
11	8.37	0.12	0.01
12	8.50	0.28	0.01
13	8.54	0.67	0.03
14	8.58	0.47	0.02
15	8.62	0.23	0.01
16	9.23	0.16	0.01
17	9.55	0.39	0.02
18	9.71	0.76	0.04
Totals		2031.74	100.00

For the calculation the system peaks were ignored. The content of the analyte was determined as a ratio of the peak area of the analyte and the cumulative areas of the impurities, added up to 100%.

**Results:**

Average                    99.4% (average of duplicate analyses)

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### III. Water Content

Method: Karl-Fischer titration using in-house EM005.WI04.

#### Results:

Average 1.1%

### IV. Ash Content

Method: BP 2015 Appendix XII. Combustion adjuvant added.

#### Result:

Contains <0.1% ash.

### V. Residual Solvents

Method: <sup>1</sup>HNMR

#### Result:

<sup>1</sup>H NMR analysis showed chloroform (0.2% w/w) and methanol (0.9% w/w).

### VI. Final Result

Chromatographic purity (HPLC)	99.4%
Water content	1.1%
Ash content	<0.1%
Residual solvents	1.1%
Purity*	97.2%

This purity is assessed to be 97.2%.

Product Reviewed By:

Product Released By:

John Moursounidis, PhD  
Head Fine Chemicals and Technical Services

Boon Tan  
Quality Manager

Release Date: 29 November 2017

\*The calculation of the purity follows the formula:

$$\text{Purity(\%)} = \frac{((\text{Chromatographic purity [HPLC]}) \times (100 - (\text{water content} + \text{ash content} + \text{volatile contents})))}{100}$$

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