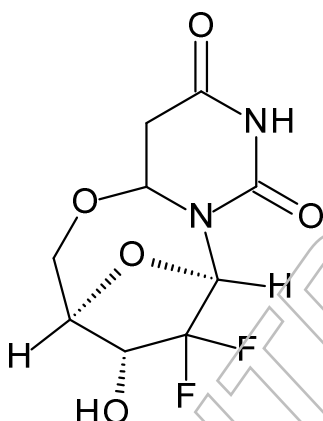




Certificate of Analysis

Reference Standard

(3R,4R,6R)-5,5-Difluorohexahydro-4-hydroxy-3,6-Epoxy-2H,8H-pyrimido-[6,1-b][1,3]oxazocine-8,10(9H)-dione



Molecular Formula: $C_9H_{10}F_2N_2O_5$
Molecular Weight: 264.18
CAS Number: 294177-31-4

Catalogue Number: MM1257.06
Lot Number: 132300
Long-term Storage: 2 to 8 °C, dark
Appearance: white solid
Melting Point: 131 °C
Assay 'as is': 95.1 %

Date of shipment: **2017-September-05**

This certificate is valid for one year from the date of shipment provided the substance is stored under the recommended conditions unopened in the original container.

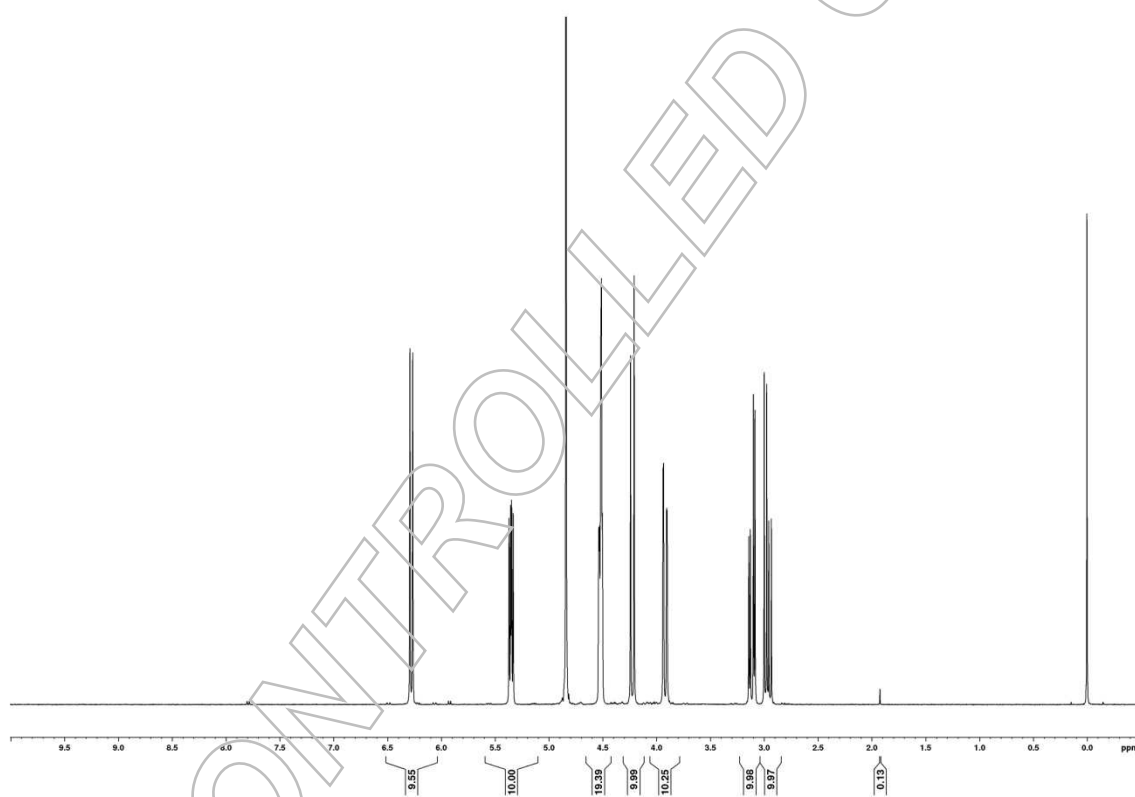


I. Identity

The identity of the reference substance was established by following analyses.

1a. ¹H-NMR Spectrum

Conditions: 400 MHz, D₂O

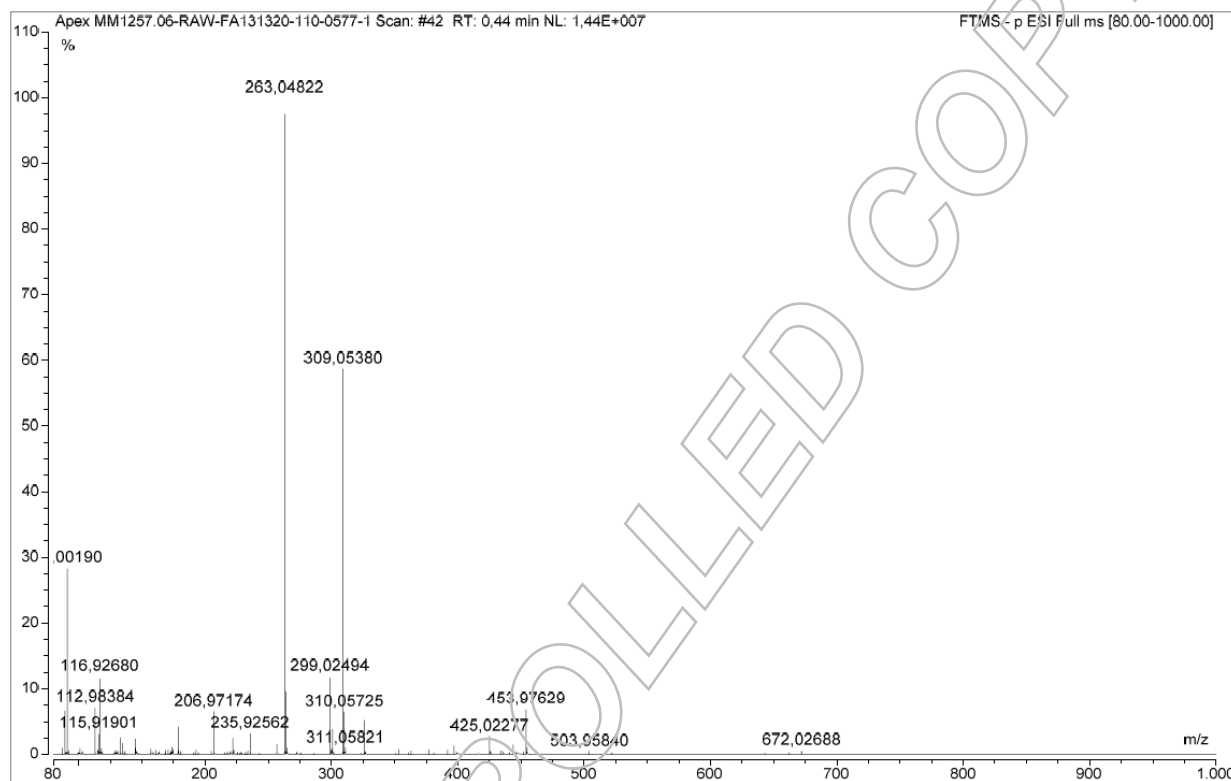


The structure is confirmed by the signals of the spectrum and their interpretation.



Ib. Mass Spectrum

Method: 3.2 kV ESI-; capillary temperature: 269 °C



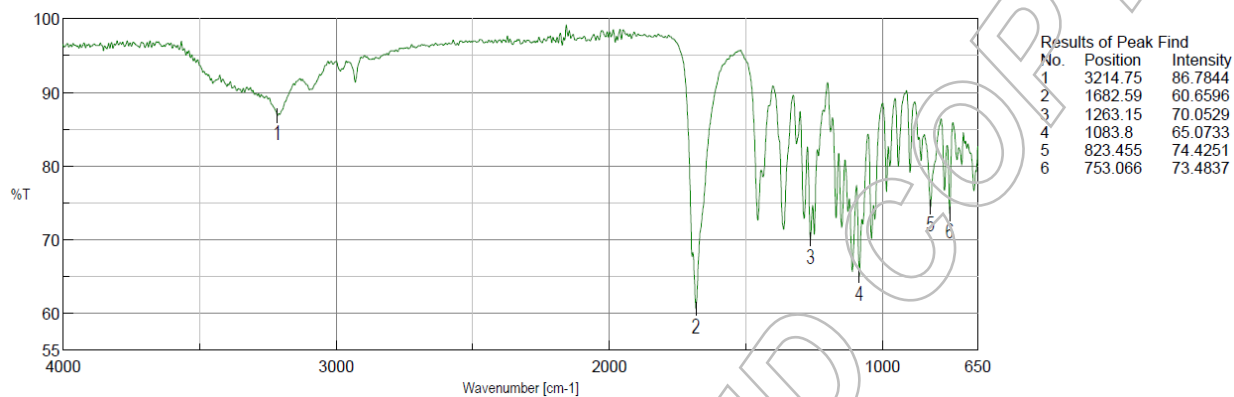
Theoretical value: 263.04850

The signal of the MS spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.



Ic. IR Spectrum

Method: Attenuated Total Reflection Fourier Transform Infrared (ATR-FTIR) Spectroscopy



The signals of the IR spectrum and their interpretation are consistent with the structural formula.

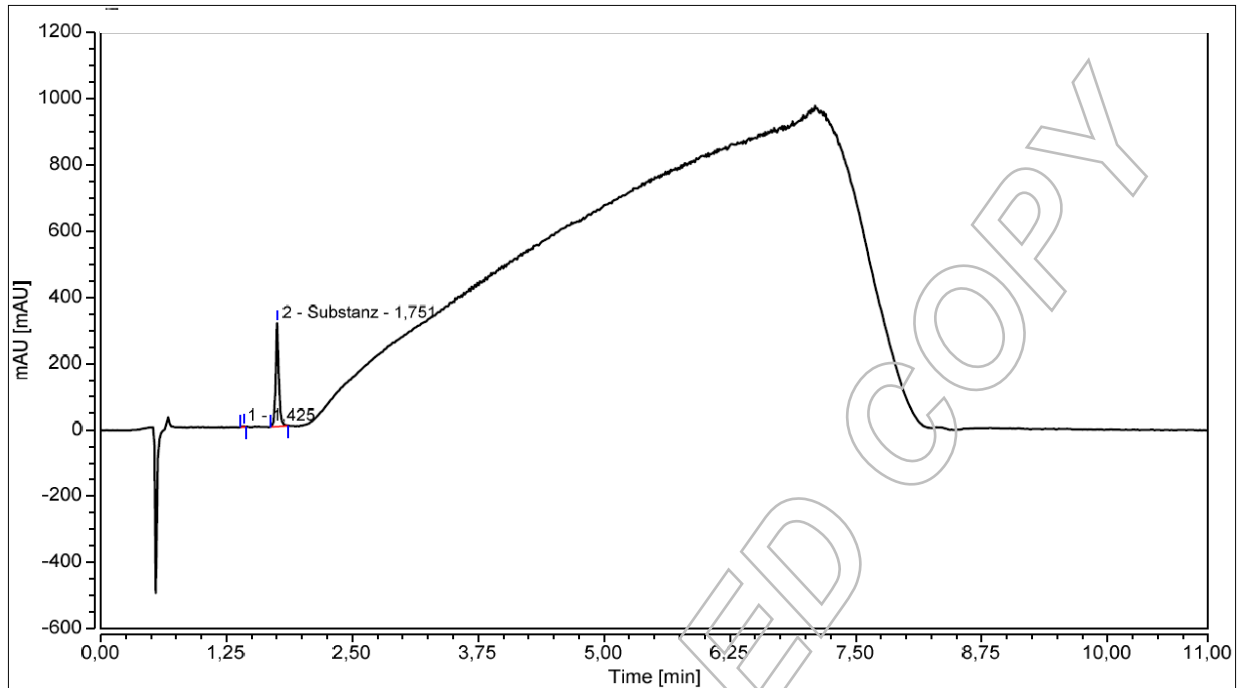
II. Purity

IIa. High Performance Liquid Chromatography (HPLC)

The purity of the reference substance was analysed by high performance liquid chromatography (HPLC).

HPLC Conditions:

Column:	Conditions:	Detector:	Injector:
Kinetex Phenyl-Hexyl 1.7 µm, 100 x 2.1 mm	0.5 ml/min, 40 °C 0-1 min Water/Acetonitrile 98/2 1-6 min Water/Acetonitrile to 1/99 6-7 min Water/Acetonitrile to 99/1 7-11 min Water/Acetonitrile 99/1 (v/v); 0.1 % HCOOH	DAD 210 nm	Auto 5 µl; 0.054 mg/ml in Water



Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	1.425	0.081	0.72
2	1.751	11.136	99.28
Totals		11.217	100.00

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

Results:

Average 99.27 %
Number of results n=3
Standard deviation 0.02 %



IIb. Water Content

Method: Karl Fischer titration

Results:

Average	4.06 %
Number of results	n=3
Standard deviation	0.05 %

IIc. Residual Solvents

Method: ¹H-NMR

Result: 0.10 % Acetic acid

III. Final Result

Chromatographic purity (HPLC)	99.27 %
Water content	4.06 %
Residual solvents	0.10 %
Assay (100 % method)¹	95.14 %

The assay is assessed to be 95.1 % 'as is'

The assay 'as is' is equivalent to the assay based on the not anhydrous and not dried substance respectively.

Release Date:

Luckenwalde, 2017-02-22

Dr. Sabine Schröder
Product Release

¹ The calculation of the 100 % method follows the formula:

$$\text{Assay (\%)} = (100 \% - \text{volatile contents}) * \frac{\text{Purity (\%)}}{100 \%}$$

Volatile contents are considered as absolute contributions, purity is considered as relative contribution.