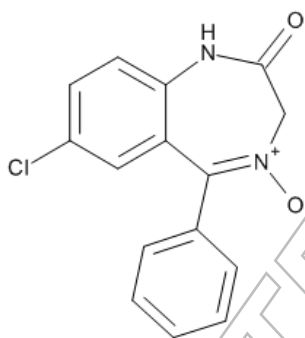




Certificate of Analysis

Reference Standard

7-Chloro-5-phenyl-1,3-dihydro-
2H-1,4-benzodiazepin-2-one
4-Oxide (Demoxepam)



Molecular Formula: $C_{15}H_{11}ClN_2O_2$
Molecular Weight: 286.71
CAS Number: 963-39-3

Catalogue Number: MM0028.02
Lot Number: 169611
Long-term Storage: 2 to 8 °C, dark
Appearance: white solid
Melting Point: 218 °C (dec.)
Assay 'as is': 99.5 %

Date of shipment: **2018-July-02**

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

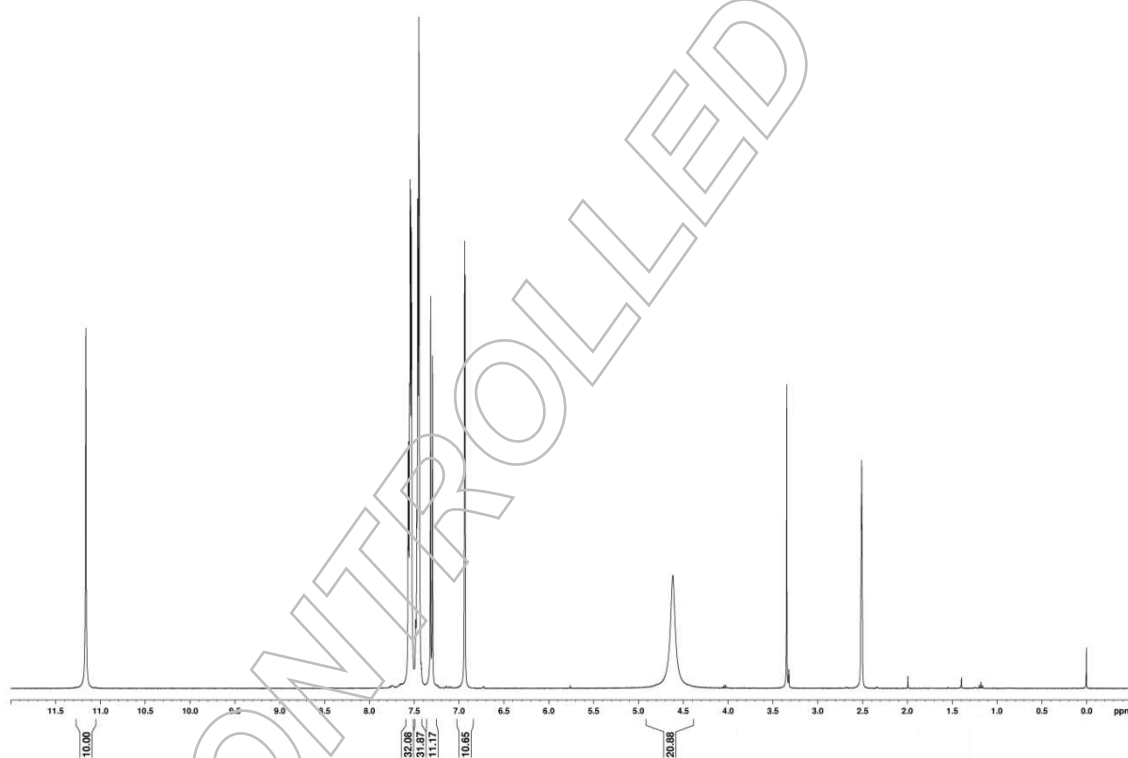


I. Identity

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

1a. ¹H-NMR Spectrum

Conditions: 400 MHz, DMSO-d₆

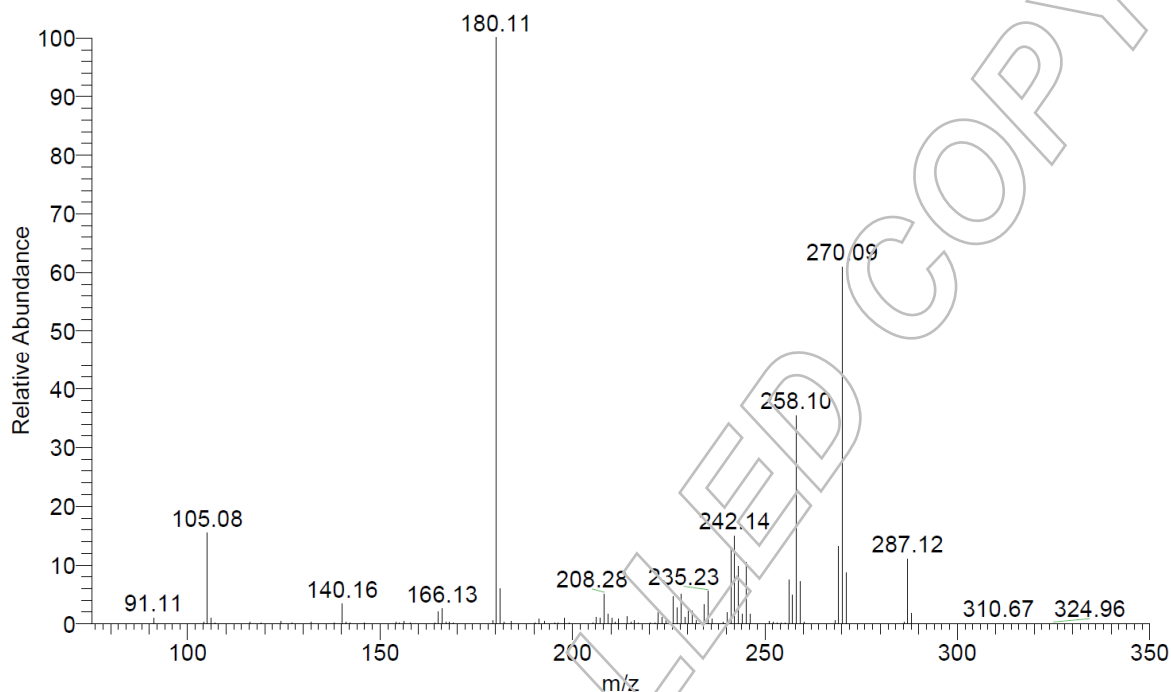


The structure is confirmed by the signals of the spectrum and their interpretation.



Ib. Mass Spectrum

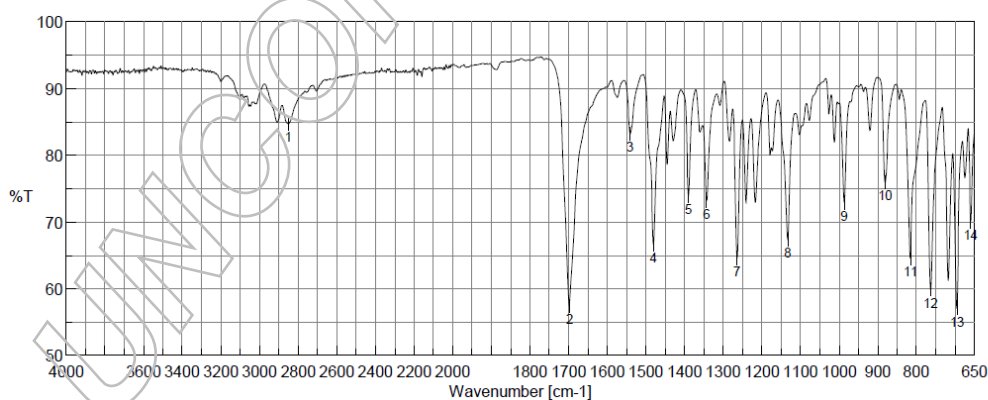
Method: 4.5 kV ESI+; vaporization temperature: 200 °C



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

Ic. IR Spectrum

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



No.	Position	Intensity
1	2850.27	84.6575
2	1698.02	57.3739
3	1540.85	83.1705
4	1480.1	66.6091
5	1389.46	73.9198
6	1343.18	73.1726
7	1264.11	64.6026
8	1132.97	67.2879
9	986.411	72.9069
10	881.309	75.8991
11	815.742	64.5651
12	763.673	59.8895
13	695.212	57.0119
14	659.536	70.0755

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:

LiChrospher
60 RP-select B
5 μm , 125 x 4 mm

Conditions:

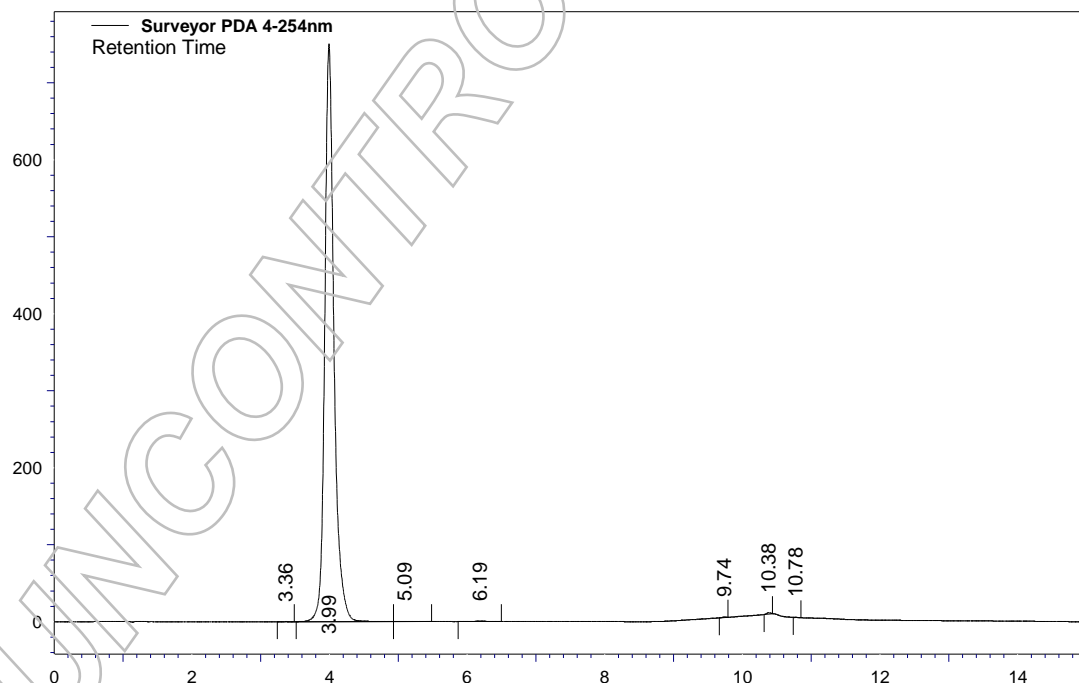
1.0 ml/min, 40 °C
0-6 min Water/Acetonitrile 70/30
6-9 min Water/Acetonitrile to 20/80
9-12 min Water/Acetonitrile to 70/30
12-15 min Water/Acetonitrile 70/30 (v/v);
0.1 % H_3PO_4

Detector:

DAD
254 nm

Injector:

Auto
4 μl ; 0.051 mg/ml in
Water/Acetonitrile 50/50 (v/v)





Area Percent Report - Sorted by Signal

Pk #	Retention Time	Area	Area %
1	3.36	375	0.01
2	3.99	6998049	99.66
3	5.09	5600	0.08
4	6.19	8764	0.12
5	9.74	2047	0.03
6	10.38	6732	0.10
7	10.78	617	0.01
Totals		7022184	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 99.66 %
Number of results n=3
Standard deviation 0.02 %

IIb. Water Content

Method: Karl Fischer titration

No significant amounts of water were detected (< 0.05 %).

IIc. Residual Solvents

Method: ¹H-NMR

Result: 0.12 % Ethyl acetate
0.04 % Cyclohexane
0.04 % Dichloromethane



III. Final Result

Chromatographic purity (HPLC)	99.66 %
Water content	No significant amounts of water were detected (< 0.05 %)
Residual solvents	0.20 %
Assay (100 % method)¹	99.46 %

The assay is assessed to be 99.5 % 'as is'

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

Release Date:

Luckenwalde, 2018-02-05

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.