Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

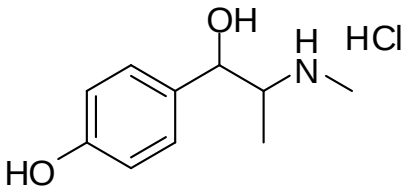
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D892: Oxilofrine hydrochloride

Report ID: D892.2017.02 (Bottled 180418)

Chemical Formula: $C_{10}H_{15}NO_2$.HCl

Molecular Weight: 217.7 g/mol (HCl), 181.2 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
05-D-09	942-51-8 (HCl) 365-26-4 (base)	100.0 ± 1.4%

The uncertainty has been calculated according to ISO Guide 35 and is stated at the 95% confidence limit (k = 2).

IUPAC name: 4-[1-Hydroxy-2-(methylamino)propyl]phenol hydrochloride

Expiration of certification: The property values are valid till 15 March 2022, i.e. five years from the date of re-certification provided the **unopened** material is handled and stored in accordance with the recommendations below. The material as issued in the unopened container and stored as recommended below should be suitable for use beyond this date, subject to confirmation of batch stability from the issuing body. The expiry date/shelf life does not apply to sample bottles that have been opened. In such cases it is recommended that the end-user conduct their own in-house stability trials.

Description: Off-white powder sourced from an external supplier, and certified for identity and purity by NMIA. Packaged in amber glass bottles with a septum and crimped aluminium cap or screw top cap.

Intended use: This certified reference material is suitable for use as a primary calibrator.

Instructions for use: Equilibrate the bottled material to room temperature before opening.

Recommended storage: When not in use this material should be stored at or below 25 ºC in a closed container in a dry, dark area.

Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. Quantitative NMR provides an independent direct measure of the mass fraction of the analyte of interest, calibrated with an internal standard certified for purity (mass fraction).

Stability: This material has demonstrated stability over a minimum period of three years. The measurement uncertainty at the 95% confidence interval includes a stability component which has been estimated from annual stability trials. The long-term stability of the compound in solution has not been examined.

Homogeneity assessment: The homogeneity of the material was assessed using purity assay by qNMR on five randomly selected 10 mg sub samples of the material. The material was judged to be sufficiently homogeneous at this level of sampling as the variation in analysis results between samples was not significantly different at a 95% confidence level from that observed on repeat analysis of the same sample.

Safety: Treat as a hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust. Refer to the provided safety data sheet.

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
8 April 2020

This report supersedes any issued prior to 8 April 2020

NATA logo notice: Accredited for compliance with ISO 17034. Accreditation No. 198 / Corporate Site No. 20844. The results of the tests, calibrations and/or measurements included in this document are traceable to Australian/national standards.

Legal notice: Terms and Conditions associated with the provision of this reference material can be found on the NMIA website.

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value was obtained by quantitative nuclear magnetic resonance (qNMR). The three-proton doublet at 1.05 ppm was measured against a certified internal standard of potassium hydrogen maleate or maleic acid.

Supporting evidence is provided by thermogravimetric analysis, Karl Fischer analysis and ^{1}H NMR spectroscopy, headspace GC-MS analysis of occluded solvents and elemental microanalysis.

Karl Fischer analysis:		Moisture content < 0.2 % mass fraction (April 2007, March 2012 & 2017)
Thermogravimetric analysis:		Initial volatile content < 0.1% and non-volatile residue < 0.2% mass fraction
QNMR:	Instrument:	Bruker DMX-500
	Field strength:	500 MHz
	Solvent:	D_2O (4.79 ppm)
	Internal standard:	Potassium hydrogen maleate (98.8% mass fraction)
	Initial analysis:	Mean (1.05 ppm) = 100.9%, s = 0.2% (4 sub samples, March 2007)
QNMR:	Instrument:	Bruker Avance-III-500 or 400
	Field strength:	500 or 400 MHz
	Solvent:	D_2O (4.79 ppm)
	Internal standard:	Maleic Acid (98.7% mass fraction)
	Initial analysis:	Mean (1.05 ppm) = 99.4%, s = 0.3% (5 sub samples, March 2012)
	Re-analysis:	Mean (1.05 ppm) = 99.5%, s = 0.1% (5 sub samples, March 2017)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	HP 6890/5973
	Column:	HP-Ultra 2, 17 m × 0.20 mm I.D. × 0.11 μm
	Program:	87 °C, 20 °C/min to 160 °C, 35 °C to 310 °C, (2 min)
	Injector:	250 °C
	Transfer line temp:	300 °C
	Carrier:	Helium, 1.2 mL/min
	Split ratio:	7.6/1
	The retention time of the free base is reported along with the major peaks in the mass spectrum. The latter are reported in as mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	Free base (5.9 min):	162 (5), 148 (3), 121 (9), 107 (4), 77 (9), 65 (4), 58 (100), 56 (23), 42 (5) *m/z*
	A peak observed at 5.0 min is attributed to the dehydration of oxilofrine upon injection at elevated temperature. Lowering the injection temperature decreases the size of this peak.	
ESI-MS:	Instrument	Micromass Quatro Micro
	Operation:	Positive ion mode, direct infusion at 5 μL/min
	Ionisation:	ESI spray voltage at 3.2 kV negative ion
	EM voltage:	600 V
	Cone voltage:	250 V
	The ions observed are reported in m/z and (in brackets) as a percentage relative to the base peak.	
	Peak:	204 ($M+Na^+$, 4), 182 ($M+H^+$, 67), 164 ($M+H^+-H_2O$, 100) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Conc. NH_3/Methanol (1.5/100) Single spot observed, R_f = 0.2. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400cm^{-1}, KBr powder
	Peaks:	3419, 2979, 2841, 2759, 2470, 1615, 1596, 1513, 1261, 1216, 989, 837, 810, 670, 532 cm^{-1}
^{1}H NMR:	Instrument:	DMX-500
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.07 (3H, d, *J* = 6.7 Hz), 2.74 (3H, s), 3.34 (1H, m), 5.09 (1H, d, *J* = 3.2 Hz), 6.80 (2H, d, *J* = 8.4 Hz), 7.22 (2H, d, *J* = 8.4 Hz) ppm
^{13}C NMR:	Instrument:	DMX-500
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 11.0, 32.5, 62.6, 72.7, 117.1, 129.1, 132.7, 159.2 ppm
Melting point:		207-209 °C
Microanalysis:	Found:	C = 55.5 %, H = 7.4 %; N = 6.5 % (December 2005)
	Calculated:	C = 55.2 %, H = 7.4 %; N = 6.4 % (Calculated for $C_{10}H_{15}NO_2$.HCl)