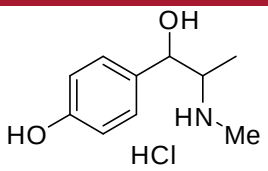
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA D892b: Oxilofrine hydrochloride



Report ID: D892b.2023.01 (Bottled 220301)

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

Molecular Weight: 217.7 g/mol (HCl), 181.3 g/mol (base)

Certified value

Batch No.	CAS No.	Purity (mass fraction)
21-D-10	**942-51-8 (HCl)** **365-26-4 (base)**	**98.7 ± 1.5%**

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 19 May 2026, three 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. The material will be re-tested on an annual basis to ensure that the property values are still valid. In the event a product fails the stability trial, notification will be sent to all impacted customers.

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.

Intended use: This reference material is recommended for qualitative analysis only and is not intended for use as a calibrator. The material does not have certified reference material status as metrological traceability of the stated purity value to the SI unit for mass (kg) has not been established.

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.

Stability: At the recommended storage conditions this material has demonstrated stability for a period of at least three years. The measurement uncertainty includes components for long term stability at the recommended storage conditions, and accelerated stability trials conducted at 40 ºC and 75% humidity for a 14 day period.

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 GC-FID on ten randomly selected 1-2 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.
23 May 2023

This report supersedes any issued prior to 23 May 2023

NATA Accreditation No. 198 / Corporate Site No. 14214.

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 indicative purity value was obtained by mass balance from a combination of traditional analytical techniques, including HPLC-UV, thermogravimetric analysis, Karl Fischer analysis, and ^{1}H NMR spectroscopy. The purity value is calculated as per Equation 1.

Purity = (100 % - I_{ORG}) x (100 % - I_{VOL} – I_{NVR}) Equation 1

I_{ORG} = Organic impurities of related structure, I_{VOL} = volatile impurities, I_{NVR} = non-volatile residue.

Supporting evidence is provided by GC-FID analysis and elemental microanalysis.

HPLC:	Instrument:	Thermo Scientific UltiMate 3000
	Column:	ACE Super C18 5 μm (4.6 mm x 250 mm)
	Column oven:	40 °C
	Mobile Phase:	Methanol/Ammonium acetate buffer 10mM (pH 9.6) in Milli Q water (15:85 v/v)
	Flow rate:	1.0 mL/min
	Detector:	RS PDA operating at 276 nm
	Relative peak area of the main component:	
	Initial analysis:	Mean = 99.7%, s = 0.02% (7 sub samples in duplicate, May 2023)
GC-FID:	Instrument:	Varian CP-3800
	Column:	DB-17, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	180 °C (10 min), 20 °C/min to 280 °C (10 min)
	Injector:	180 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative peak area of the main component as the free base:	
	Initial analysis:	Mean = 99.7%, s = 0.06% (10 sub samples in duplicate, January 2022)
Karl Fischer analysis:		Moisture content 0.5 % mass fraction (January 2022 and October 2022)
Thermogravimetric analysis:		Non-volatile residue 0.3% mass fraction (October 2021)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	DB-5MS, 30 m x 0.25 mm I.D. x 0.25 μm
	Program:	180 °C (10 min), 20 °C/min to 300 °C (5 min)
	Injector:	250 °C
	Split ratio:	20/1
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Scan range:	50-550 *m/z*
	The retention time of oxilofrine free base is reported with the major peaks in the mass spectra. The latter are reported as mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	Free base (5.0 min):	134 (11), 133 (9), 121 (12), 107 (6), 77 (9), 65 (7), 58 (100), 56 (18), 42 (17) *m/z*
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 mass/charge ratios 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}. Dichloromethane/Methanol (1:1). Single spot observed, R_f = 0.3. Visualisation with UV at 254 nm.
IR:	Instrument:	Bruker Alpha Platinum ATR
	Range:	4000-400 cm^{-1}, neat
	Peaks:	3410, 3094, 2971, 2841, 2758, 2469, 1615, 1596, 1511, 1462, 1442, 1213, 988, 851, 837, 670, 531 cm^{-1}.
^{1}H NMR:	Instrument:	Bruker Avance III-500
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.09 (3H, d, *J* = 6.5 Hz), 2.75 (3H, s), 3.35 (1H, dq, *J* = 3.3, 6.6 Hz), 5.01 (1H, d, *J* = 3.3 Hz), 6.81 (2H, m), 7.23 (2H, m) ppm
		Methanol was quantified at 0.2% mass fraction.
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	126 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 10.2, 31.6, 61.7, 71.8, 116.3, 128.3, 131.8, 158.4 ppm
Melting point:		207-209 °C
Microanalysis:	Found:	C = 55.2%; H = 7.5%; N = 6.4% (October 2021)
	Calculated:	C = 55.2%; H = 7.4%; N = 6.4% (Calculated for $C_{10}H_{15}NO_2$.HCl)