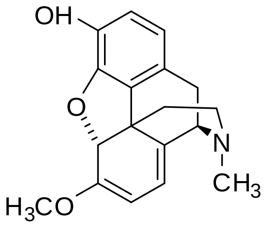
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

CERTIFIED REFERENCE MATERIAL
CERTIFICATE OF ANALYSIS

NMIA D734b: Oripavine



Report ID: D734b.2020.03

Chemical Formula: $C_{18}H_{19}NO_3$

Molecular Weight: 297.4 g/mol

Certified value

Batch No.	CAS No.	Purity (mass fraction)
08-D-07	**467-04-9**	**99.5 ± 0.4%**

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

IUPAC name: (5α)-6-Methoxy-17-methyl-6,7,8,14-tetradehydro-4,5-epoxymorphinan-3-ol

Expiration of certification: The property values are valid till 13 July 2030, i.e. ten 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: Light tan solid prepared by synthesis or sourced from an external supplier, 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.

Stability: In the absence of long term stability data the stability of this material has been judged from stability trials conducted on similar materials by NMI Australia over the last ten years. 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 HPLC with UV detection 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.

Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%. 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).

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
14 September 2022.

This report supersedes any issued prior to 14 September 2022.

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

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value was obtained from a combination of traditional analytical techniques and quantitative nuclear magnetic resonance (qNMR). The techniques used in the mass balance approach include HPLC with UV detection, thermogravimetric analysis, Karl Fischer analysis and ^{1}H NMR spectroscopy. The purity value is calculated as per Equation 1.

$$\text{Purity} = (100\ \% - I_{ORG}) \times (100\ \% - I_{VOL} - I_{NVR}) \qquad \text{Equation 1}$$

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

Supporting evidence is provided by elemental microanalysis.

QNMR:	Instrument:	Bruker DMX-400
	Field strength:	400 MHz
	Solvent:	d_6-DMSO
	Internal standard:	Triphenyl phosphine oxide (100% m/m)
	Initial analysis:	Mean = 98.5%, s = 1.0% (10 sub samples, June 2008)
	Re-analysis:	Mean = 99.2%, s = 0.4% (3 sub samples in duplicate, August 2011)
	Re-analysis:	Mean = 99.1%, s = 0.1% (5 sub samples in duplicate, July 2014)
	Re-analysis:	Mean = 99.1%, s = 0.1% (5 sub samples in duplicate, July 2020)
HPLC:	Instrument:	Shimadzu Binary pump LC-20AB, SIL-20 A HT autosampler or Waters alliance 2695
	Column:	X-Bridge C-18, 5 µm (4.6 mm x 150 mm)
	Column oven:	40 °C
	Mobile Phase:	Acetonitrile/MilliQ water (18:82)
		The aqueous phase was buffered at pH 10.9 using 20mM NH_4OAc and NH_4OH
	Flow rate:	1.0 mL/min
	Detector:	Shimadzu SPD-M20A or Waters 2998 PDA operating at 283 nm
	Relative mass fraction of the main component:	
	Initial analysis:	Mean = 99.7%, s = 0.05% (10 sub samples in duplicate, July 2014)
	Re-analysis:	Mean = 99.7%, s = 0.02% (5 sub samples in duplicate, June 2017)
	Re-analysis:	Mean = 99.9%, s = 0.003 (5 sub samples in duplicate, July 2020)
Karl Fischer analysis:		Moisture content < 0.2% mass fraction (April 2008 and May 2020) Moisture content 0.3% mass fraction (June 2014, May 2017)
Thermogravimetric analysis:		Initial volatile content < 0.1% and non-volatile residue < 0.2 % mass fraction (February 2008)

Spectroscopic and other characterisation data

ESI-MS:	Instrument:	Micromass Quatro Micro
	Operation:	Positive ion mode, direct infusion at 5 µL/min
	Ionisation:	ESI spray voltage at 3.2 kV positive ion
	EM voltage:	500 V
	Cone voltage:	20 V
	Peak:	298 (M^-H^+) *m/z.*
TLC:	Conditions:	Kieselgel 60F_{254}. $CHCl_3$/MeOH (10/1). Single spot observed, R_f = 0.23. Visualisation with UV at 254 nm.
IR:	Instrument:	Biorad FTS300MX FT-IR.
	Range:	4000-400cm^{-1}, KBr pellet.
	Peaks:	2929, 2840, 1669, 1605, 1501, 1462, 1231, 1140, 1020, 930, 822, 765, 689, 657, 515, 434 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX600
	Field strength:	600 MHz
	Solvent:	$CDCl_3$ (7.26ppm)
	Spectral data:	δ 1.72 (1H, dd, *J* = 2.3, 12.5 Hz), 2.23 (1H, dt, *J* = 5.0, 12.6 Hz), 2.47 (3H, s), 2.67-2.71 (2H, m), 2.89 (1H, dt, *J* = 3.5, 12.9 Hz), 3.30 (1H, d, *J* = 18.0 Hz), 3.61 (3H, s), 3.68 (1H, d, *J* = 7.0 Hz), 5.06 (1H, d, *J* = 6.5 Hz), 5.57 (1H, d, *J* = 6.4 Hz), 6.55 (1H, d, *J* = 8.1 Hz), 6.64 (1H, d, *J* = 8.1 Hz) ppm
^{13}C NMR:	Instrument:	Bruker DMX600
	Field strength:	151 MHz
	Solvent:	$CDCl_3$ (77.2ppm)
	Spectral data:	δ 30.6, 36.3, 41.8, 45.8, 46.4, 55.0, 60.7, 89.2, 96.4, 112.1, 116.8, 119.8, 126.4, 132.4, 132.9, 139.3, 143.3, 152.4 ppm
Melting point:		199-200 °C
Microanalysis:	Found:	C = 72.3 %, H = 6.5 %; N = 4.7% (February 2008)
	Calculated:	C = 72.7 %, H = 6.4 %; N = 4.7% (Calculated for $C_{18}H_{19}NO_3$)