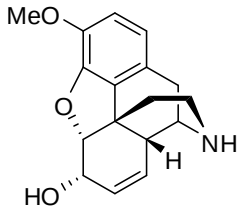
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D698: Norcodeine



Report ID: D698.2021.02

Chemical Formula: $C_{17}H_{19}NO_3$

Molecular Weight: 285.3 g/mol

Property value

Batch No.	CAS No.	Purity estimate
01-D-06	**467-15-2**	**94.2 ± 2.1%**

IUPAC name: (5α,6α)-3-Methoxy-7,8-didehydro-4,5-epoxymorphinan-6-ol

Expiration of certification: The property values are valid till 27 May 2026, 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: White micro-crystalline powder 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 4 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. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%.

Stability: This material has demonstrated stability over a minimum period of three years. The measurement uncertainty at the 95% coverage 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 GC-FID on eight randomly selected 1-2 mg 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 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.
14 September 2022

This report supersedes any issued prior to 14 September 2022.

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. Impurities of related structure were assessed by GC-FID. The purity value was obtained by mass balance from a combination of traditional analytical techniques, including GC-FID. 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 elemental microanalysis.

Note: **A major impurity, assigned as 7,8-dihydro-norcodeine, was quantified by ^{1}H NMR in $CDCl_3$. Under the GC conditions detailed in this report, this impurity could not be resolved from the norcodeine.**

GC-FID:	Instrument:	Agilent 6890N
	Column:	HP-1, 30 m × 0.32 mm I.D. × 0.25 μm [2001, 2008] or HP-5, 30 m × 0.32 mm I.D. × 0.25 μm [2016]
	Program:	180 °C (1 min), 10 °C/min to 250 °C, 20 °C/min to 300 °C (3 min) [2001, 2008] or 180 °C (1 min), 10 °C/min to 250 °C (5 min), 20 °C/min to 300 °C (3 min) [2016]
	Injector Temp:	250 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative peak area of the main component:	
	Initial analysis:	Mean = 96.8%, s = 0.06% (8 sub samples in duplicate, June 2001)
	Re-analysis:	Mean = 96.8%, s = 0.01% (5 sub samples in duplicate, September 2008)
	Re-analysis:	Mean = 96.6%, s = 0.03% (5 sub samples in duplicate, June 2016)
	Re-analysis:	Mean = 96.7%, s = 0.03% (5 sub samples in duplicate, May 2021)
HPLC:	Instrument:	Shimadzu or Waters HPLC
	Column:	X-Bridge C-18, 5 μm (4.6 mm x 150 mm)
	Mobile Phase:	A = 0.05% TFA in Milli-Q water, B = Methanol 0-2 min 10% B, 2-15 min 10% B to 20% B, 15-20min 20% B to 80% B (5 min), 25-26 min to 10% B (6 min)
	Flow rate:	1.0 mL/min, Gradient
	Detector:	Shimadzu or Waters Photodiode Array Detector operating at 210 nm
	Relative peak area of the main component:	
	Initial analysis:	Mean = 96.7%, s = 0.05% (5 sub samples in duplicate, August 2013)
Karl Fischer analysis:		Moisture content 2.4% mass fraction (September 2008) Moisture content 3.2% mass fraction (July 2013) Moisture content 3.1% mass fraction (June 2016) Moisture content 2.7% mass fraction (May 2021)
Thermogravimetric analysis:		Volatiles content 2.1% mass fraction. Non-volatile residue < 0.2% mass fraction (November 2005)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	HP6890/5973
	Column:	ZB-5, 30 m × 0.25 mm I.D. × 0.3 μm
	Program:	220 °C (1 min), 10 °C /min to 300 °C (3 min)
	Injector:	250 °C
	Transfer line temp:	300 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	20/1
	The retention time of the *bis*-TMS derivative is reported along with the major peaks in the mass spectrum. The latter are reported as mass/charge ratios (in brackets) as a percentage relative to the base peak.	
	8.5 min:	429 (M^+, 13), 357 (11), 164 (36), 73 (100) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol/acetone/30% aqueous NH_3 (50:40:10) Single spot observed, R_f = 0.5 (3 sub samples)
IR:	Instrument:	FT-IR, Biorad WIN FTS40
	Range:	4000-400 cm^{-1}, KBr pellet
	Peaks:	3311, 3031, 2930, 2838, 1633, 1602, 1508, 1451, 1285, 1200, 1167, 1134, 11617, 1061, 791 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX-500
	Field strength:	500 MHz
	Solvent:	$CDCl_3$ (7.26 ppm)
	Spectral data:	δ 2.44 (2H, br s), 2.93 (1H, ddd), 3.84 (3H, s), 4.85 (1H, dd), 5.24 (1H, m), 6.56 (1H, d), 6.66 (1H, d) ppm
^{13}C NMR:	Instrument:	Bruker DMX-500
	Field strength:	125 MHz
	Solvent:	$CDCl_3$ (77 ppm)
	Spectral data:	δ 31.3, 36.6, 38.5, 41.2, 43.8, 51.9, 56.3, 66.3, 92.0, 113.0, 119.4, 127.4, 128.1, 131.1, 133.6, 142.1, 146.4 ppm
Melting point:		181-184 °C
Microanalysis:	Found:	C = 70.3%; H = 6.9%; N = 4.9% (June 2001)
	Calculated:	C = 71.6%; H = 6.7%; N = 4.9% (Calculated for $C_{17}H_{19}NO_3$)