Australian Government
Department of Industry, Science and Resources

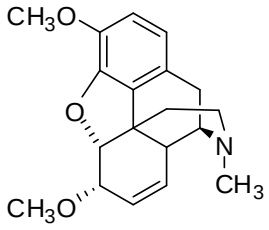
National Measurement Institute

CIPM MRA

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D924: Methyl codeine



Report ID: D924.2020.03

Chemical Formula: $C_{19}H_{23}NO_3$

Molecular Weight: 313.2 g/mol

Certified value

Batch No.	CAS No.	Purity (mass fraction)
08-D-02	**2859-16-7**	**98.8 ± 0.3%**

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

IUPAC name: (5α,6α)-3,6-Dimethoxy-17-methyl-7,8-didehydro-4,5-epoxymorphinan.

Expiration of certification: The property values are valid till 6 October 2025, 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: Pale tan solid 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 20 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 five 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 GC-FID on five 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.
19 September 2022

This report supersedes any issued prior to 19 September 2022.

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

CIPM MRA notice: This certificate is consistent with the capabilities that are included in Appendix C of the CIPM MRA drawn up by the CIPM. Under the CIPM MRA, all participating institutes recognize the validity of each other's calibration and measurement certificates for the quantities, ranges and measurement uncertainties specified in Appendix C. The "CIPM MRA Logo" and this statement attest only to the measurement(s) applied for determining the certified values on the certificate (for details see http://www.bipm.org).

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 mass balance from a combination of traditional analytical techniques, including GC-FID, 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 elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890N
	Column:	HP-1, 29.50 m × 0.32 mm I.D. × 0.25 μm
	Program:	150 °C (2 min), 50 °C/min to 200 °C, 4 °C/min to 230 °C, 30 °C/min to 300°C (3 min)
	Injector:	200 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative mass fraction of the main component:	
	Initial analysis:	Mean = 99.1%, s = 0.01 (10 sub samples in duplicate, January 2008)
	Re-analysis:	Mean = 99.2%, s = 0.02 (5 sub samples in duplicate, February 2009)
	Re-analysis	Mean = 99.2%. s = 0.01% (5 subsample in duplicate, February 2010)
GC-FID:	Instrument:	Varian CP3800
	Column	HP-5, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	160 °C (9 min), 30 °C/min to 220 °C (6.33 min), 30 °C/min to 300 °C (3 min)
	Injector:	250 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split Ratio:	20/1
	Relative mass fraction of the main component:	
	Re-analysis:	Mean = 99.3%, s = 0.03% (5 sub samples in duplicate, February 2011)
	Re-analysis	Mean = 99.2%. s = 0.03% (5 subsample in duplicate, January 2016)
	Re-analysis	Mean = 99.2%. s = 0.06% (5 subsample in duplicate, October 2020)
Thermogravimetric analysis:		Volatile content not determined and non volatile residue < 0.2 % mass fraction (February 2009).
Karl Fischer analysis:		Moisture content < 0.4% mass fraction (March 2008, February 2009, February 2010 & February 2011). Moisture content < 0.2% mass fraction (December 2015 and October 2020)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	ZB-5, 28 m × 0.25 mm I.D. × 0.25 μm
	Program:	200 °C (1 min), 4 °C/min to 260 °C, 20 °C/min to 300 °C, (3 min).
	Injector:	250°C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	20/1
	The retention time of the parent compound is reported along with the major peaks in the mass spectrum. The latter are reported as mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	Parent (8.6 min):	314 (M^++1, 21), 313 (M^+, 100), 282 (38), 229 (21), 176 (15), 138 (21) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. dichloromethane: methanol (95:5). Single spot observed, R_f = 0.24. Visualisation with UV at 254 nm.
IR:	Instrument:	Biorad FTS300MX FT-IR.
	Range:	4000-400cm^{-1}, KBr powder.
	Peaks:	3030, 2917, 2794, 1832, 1628, 1601, 1498, 1445, 1314, 1256, 1206, 1118, 1022, 929, 828, 789, 671 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX500
	Field strength:	500 MHz
	Solvent:	$CDCl_3$ (7.26 ppm)
	Spectral data:	δ 1.88 (1H, dd, *J* = 1.7, 12.6 Hz), 2.02 (1H, dt, *J* = 5.1, 12.5 Hz), 2.28 (1H, dd, *J* = 6.3, 18.6 Hz), 2.40 (1H, dt, *J* = 3.5, 12.2 Hz), 2.43 (3H, s), 2.56 (1H, dd, *J* = 4.2, 12.1 Hz), 2.64 (1H, t, *J* = 2.6 Hz), 3.02 (1H, d, *J* = 18.6 Hz), 3.34 (1H, dd, *J* = 1.6, 6.1 Hz), 3.52 (3H, s), 3.77 (1H, m), 3.81 (3H, s), 4.98 (1H, dd, *J* = 1.2, 5.9 Hz), 5.31 (1H, dt, *J* = 2.7, 9.8 Hz), 5.70-5.73 (1H, m), 6.49 (1H, d, *J* = 8.1 Hz), 6.61 (1H, d, *J* = 8.2 Hz) ppm. ^{1}H NMR shows the presence of dimethyl aniline in 0.23% mass fraction.
^{13}C NMR:	Instrument:	Bruker DMX500
	Field strength:	125 MHz
	Solvent:	$CDCl_3$ (77.16 ppm)
	Spectral data:	δ 20.3, 36.0, 41.2, 43.0, 43.4, 46.4, 56.3, 57.0, 58.8, 76.0, 89.3, 113.1, 118.6, 126.9, 128.7, 130.4, 130.7, 142.0, 147.4 ppm.
Melting point:		139-141 °C
Microanalysis:	Found:	C = 72.7%; H = 7.4%; N = 4.5% (February 2008)
	Calculated:	C = 72.8%; H = 7.4%; N = 4.5% (Calculated for $C_{19}H_{23}NO_3$)