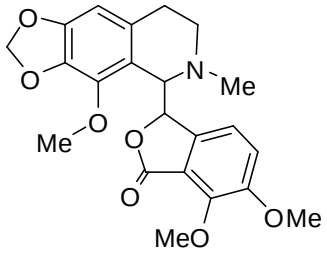
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D831b: Noscapine



Report ID: D831b.2019.03 (Bottled 140819)

Chemical Formula: $C_{22}H_{23}NO_7$

Molecular Weight: 413.42 g/mol

Certified value

Batch No.	CAS No.	Purity (mass fraction)
14-D-08	**128-62-1**	**99.3 ± 0.3%**

The uncertainty is stated at the 95% confidence limit.

IUPAC: (3S)-6,7-Dimethoxy-3-[(5R)-4-methoxy-6-methyl-5,6,7,8-tetrahydro[1,3]dioxolo[4,5-g]isoquinolin-5-yl]-2-benzofuran-1(3H)-one

Expiration of certification: The property values are valid till 1 March 2024, 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 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.

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).

Stability: This material has demonstrated stability over a minimum period of five 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.

Caution: 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.
15 September 2022

This report supersedes any issued prior to 15 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. The certified purity value was obtained by mass balance from a combination of traditional analytical techniques, including HPLC with UV detection, 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 qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

HPLC:	Instrument:	Shimadzu Binary pump LC-20AB, SIL-20 A HT autosampler
	Column:	XBridge C-18, 5 μm (4.6 mm x 150 mm)
	Column oven:	40 °C
	Mobile Phase:	Acetonitrile/MilliQ water 0-14 min 45%B, 14-15 min 45-80% B, 15-19 min 80% B, 19-20 min 80-45% B, 20-30 min 45% B 0.05% Diethylamine was present in both the organic and aqueous phases.
	Flow rate:	0.8 mL/min
	Detector:	Shimadzu SPD-M20A PDA operating at 310 nm
	Relative peak area of main component:	
	Initial analysis:	Mean = 99.5%, s = 0.02% (10 sub samples in duplicate, March 2014)
	Re-analysis:	Mean = 99.5%, s = 0.01% (5 sub samples in duplicate, March 2015)
	Re-analysis:	Mean = 99.5%, s = 0.02% (5 sub samples in duplicate, February 2016)
	Re-analysis:	Mean = 99.6%, s = 0.03% (5 sub samples in duplicate, March 2019)
Thermogravimetric analysis:		Volatile content < 0.1% and non volatile residue < 0.2% mass fraction (March 2014)
Karl Fischer analysis:		Moisture content 0.2% mass fraction (March 2014) Moisture content 0.1% mass fraction (March 2015) Moisture content 0.2% mass fraction (February 2016) Moisture content 0.1% mass fraction (March 2019)

Spectroscopic and other characterisation data

GC-MS:	Parent compound:	
	Instrument:	Agilent 6890/5973
	Column:	TG-1MS, 30 m x 0.25 mm I.D. x 0.25 µm
	Program:	220 °C (1 min), 10 °C/min to 300 °C (5 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 (10.7 min):	221 (14), 220 (100), 205 (13), 193 (6), 147 (8) *m/z*
LC/ESI -MS:	Instrument:	Micromass Quatro LC Micro
	Operation:	Positive ion mode, direct infusion at 10 µL/min
	Ionisation:	ESI spray voltage at 3.5 kV positive ion
	EM voltage:	650 V
	Cone voltage:	20 V
	Peak:	414.2 ($M+H^+$) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Hexane/ethyl acetate/diethyl amine (14/6/0.1) Single spot observed, R_f = 0.15. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3492, 2990, 2945, 2881, 2798, 1757, 1621, 1499, 1477, 1426, 1383, 1308, 1277, 1201, 1117, 1058, 1038, 1007, 934, 855, 845, 788 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance-400
	Field strength:	400 MHz
	Solvent:	$CDCl_3$ (7.26 ppm)
	Spectral data:	δ 1.89 (1H, m); 2.29-2.39 (2H, m), 2.53 (3H, s), 2.59 (1H, m), 3.85 (3H, s), 4.03 (3H, s), 4.08 (3H, s), 4.38 (1H, d, *J* = 4.1 Hz), 5.56 (1H, d, *J* = 3.9 Hz), 5.92 (1H, d, *J* = 1.4 Hz), , 5.93 (1H, d, *J* = 1.4 Hz), 6.05 (1H, d, *J* = 8.3 Hz), 6.30 (1H, s), 6.95 (1H, d, *J* = 8.3 Hz) ppm Isopropanol estimated at 0.03% mass fraction was observed in the ^{1}H NMR
^{13}C NMR:	Instrument:	Bruker Avance-400
	Field strength:	101 MHz
	Solvent:	$CDCl_3$ (77.2 ppm)
	Spectral data:	δ 28.2, 46.5, 50.2, 56.8, 59.5, 60.9, 62.4, 82.0, 100.9, 102.4, 117.2, 117.8, 118.1, 120.3, 132.3, 134.1, 140.5, 141.2, 147.7, 148.5, 152.3, 168.3 ppm
Melting point:		175-176 °C
Microanalysis:	Found:	C = 64.0%; H = 5.6%; N = 3.3% (March, 2014)
	Calc:	C = 63.9%; H = 5.6%; N = 3.4% (Calculated for $C_{22}H_{23}NO_7$)