Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

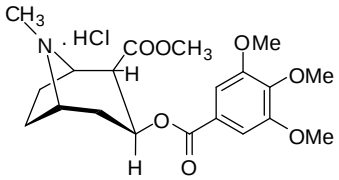
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D855b: 3,4,5-Trimethoxycocaine hydrochloride

Report ID: D855b.2024.01

Chemical Formula: $C_{20}H_{27}NO_7.HCl$

Molecular Weight: 429.9 g/mol (HCl), 393.4 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
22-D-02	**156301-59-6 (base)**	**95.2 ± 1.8%**

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

IUPAC name: Methyl (1R,2R,3S,5S)-8-methyl-3-[(3,4,5-trimethoxybenzoyl)oxy]-8-azabicyclo[3.2.1]octane-2-carboxylate hydrochloride

Expiration of certification: The property values are valid till 17 September 2029, 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. 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: White powder prepared by synthesis and certified for identity and purity by NMIA. Packaged in amber glass bottles with a septum and crimped aluminium 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.

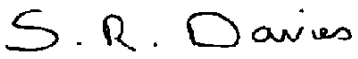
Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance all impurities are quantified as a mass fraction and subtracted from 100%.

Stability: At the recommended storage conditions this material has demonstrated stability for a period of up to ten 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.



Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
19 September 2024

This report supersedes any issued prior to 19 September 2024.

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 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 7890
	Column:	HP-1MS, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	150 °C (1 min), 10 °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 as the free base:	
	Initial analysis:	Mean = 99.3%, s = 0. 01% (10 sub samples in duplicate, February 2022)
	Re-analysis:	Mean = 99.2%, s = 0. 14% (5 sub samples in duplicate, November 2022)
	Re-analysis:	Mean = 99.3%, s = 0. 02% (5 sub samples in duplicate, September 2023)
	Re-analysis:	Mean = 99.5%, s = 0. 03% (5 sub samples in duplicate, September 2024)
Karl Fischer analysis:		Moisture content 4.2 % mass fraction (March 2022) Moisture content 4.1 % mass fraction (November 2022 and September 2023) Moisture content 4.2 % mass fraction (February 2024 and September 2024)
Thermogravimetric analysis:		Non-volatile residue < 0.2% mass fraction (February 2022). The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material and/or degradation at elevated temperatures.

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:	60 °C, (1 min), 10 °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 the 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 (25.0 min):	393 (M^+, 21), 362 (4), 212 (12), 195 (17), 182 (100), 94 (23), 82 (64) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol/conc. NH_3 (200:3) Single spot observed, R_f = 0.6, with UV light (254 nm)
IR:	Instrument:	BioRad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3561, 3418, 3376, 3056, 2955, 2837, 1747, 1724, 1590, 1504, 1461, 1417, 1334, 1223, 1125, 986, 763 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III-500
	Field strength:	500 MHz
	Solvent:	D_2O
	Spectral data:	δ 2.25 (2H, m), 2.40-2.60 (4H, m), 2.92 (3H, s), 3.63-3.65 (1H, m), 3.65 (3H, s), 3.84 (3H, s), 3.88 (6H, s), 4.13 (1H, m), 4.27 (1H, bd, *J* = 7.3 Hz), 5.54 (1H, m), 7.18 (2H, s) ppm Methanol and diethyl ether were quantified at 0.04% and 0.05% mass fraction respectively.
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	75.5 MHz
	Solvent:	D_2O
	Spectral data:	δ 22.5, 23.5, 32.4, 38.7, 45.9, 53.2, 56.1, 60.9, 63.0, 63.8, 64.6, 107.0, 124.1, 141.7, 152.4, 166.0, 173.1 ppm
Melting point:		179-182 °C
Microanalysis:	Found:	C = 53.6%; H = 7.0%; N = 3.1% (February 2022)
	Calculated:	C = 53.6%; H = 6.8%; N = 3.1% (Calculated for $C_{20}H_{27}NO_7.HCl.H_2O$)