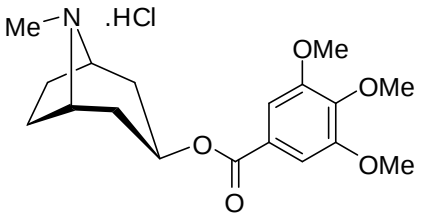
REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA D858b: 3,4,5-Trimethoxytropacocaine hydrochloride

Report ID: D858b.2014.04

Chemical Formula: $C_{18}H_{25}NO_5$.HCl

Molecular Weight: 371.9 g/mol (HCl salt), 335.4 g/mol (base)



Property value

Batch No.	CAS No.	Purity estimate
14-D-14	60820-69-1 (base)	95.5 ± 2.0%

IUPAC name: (3-exo)-8-Methyl-8-azabicyclo[3.2.1]oct-3-yl 3,4,5-trimethoxybenzoate hydrochloride

Expiration of certification: The property values are valid till 5 May 2017, i.e. three 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 or screw top cap.

Intended use: This reference material is recommended for qualitative analysis only.

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 GC-FID on nine 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.
13 October 2022

This report supersedes any issued prior to 19 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 estimate 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 Karl Fischer analysis, ^{1}H NMR spectroscopy qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID:	Instrument:	Varian CP-3800
	Column:	VF-1ms, 30 m × 0.32 mm I.D. × 0.25 µm
	Program:	120 °C (1 min), 15 °C/min to 250 °C (5 min), 30 °C/min to 300 °C (4 min)
	Injector:	250 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative peak area of the main component as the free base:	
	Initial analysis:	Mean = 99.8%, s = 0.05% (9 sub samples in duplicate, May 2014)
GC-FID:	Instrument:	Varian CP-3800
	Column:	HP-1, 30 m × 0.32 mm I.D. × 0.25 µm
	Program:	120 °C (1 min), 15 °C/min to 250 °C (5 min), 30 °C/min to 300 °C (4 min)
	Injector:	250 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative peak area of the main component as the free base:	
	Initial analysis:	Mean = 99.8%, s = 0.004% (9 sub samples in duplicate, May 2014)
Karl Fischer analysis:		Moisture content 3.8% mass fraction (May 2014)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	TG-1MS, 30 m × 0.25 mm I.D. × 0.25 □m
	Program:	60 °C (1 min), 10 °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 free base 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	
	22.6 min:	335 (M^+, 30), 212 (12), 195 (11), 124 (100), 94 (32), 82 (95), 67 (22) *m/z*
HS-GC-MS:	Instrument:	Agilent 6890/5973/G1888
	Column:	DB-624, 30 m x 0.25 mm I.D. x 1.4 µm
	Program:	50 °C (5 min), 7 °C/min to 120 °C, 15 °C/min to 220 °C (8.3 min)
	Injector:	150 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.2 mL/min
	Split ratio:	50/1
	Solvents detected:	Ethanol, diethyl ether
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol/conc NH_3 (200:3) Single spot observed, R_f = 0.26. Visualization with UV light (254 nm).
IR:	Instrument:	BioRad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3462, 3397, 2963, 2828, 2668, 2548, 1709, 1586, 1501, 1466, 1418, 1342, 1226, 1129, 1032, 999, 868, 766 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III -600
	Field strength:	600 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	δ 2.11-2.21 (4H, m), 2.27-2.43 (4H, m), 2.83 (2.7H, s), 3.09 (0.3H, s), 3.81 (3H, s), 3.86 (6H, s), 4.06 (2H, s), 5.35 (1H, septet, *J* = 6.1 Hz), 7.19 (2H, s) ppm Two conformational isomers are observed in the ^{1}H NMR spectrum Ethanol and diethyl ether estimated at 0.3 and 0.2% mass fraction respectively were observed in the ^{1}H NMR.
^{13}C NMR:	Instrument:	Bruker DMX-600
	Field strength:	151 MHz
	Solvent:	D_2O
	Spectral data:	δ 24.1, 35.2, 38.5, 56.4, 61.2, 63.7, 65.8, 107.4, 125.3, 141.7, 152.6, 167.1 ppm
Melting point:		206-208 °C
Microanalysis:	Found:	C = 56.2%; H = 6.9%; N = 3.7%; Cl = 9.1% (May 2014)
	Calculated:	C = 58.1%; H = 7.1%; N = 3.8%; Cl = 9.5% (for $C_{18}H_{25}NO_5$.HCl)
	Calculated:	C = 55.9%; H = 7.2%; N = 3.6%; Cl = 9.2% (for $C_{18}H_{25}NO_5$.HCl plus 3.8% H_2O)