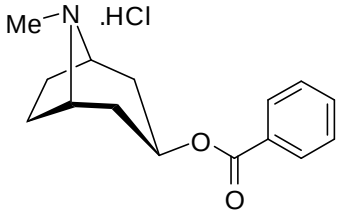
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D846b: Tropacocaine hydrochloride



Report ID: D846b.2020.03 (Bottled 170822)

Chemical Formula: $C_{15}H_{19}NO_2$.HCl

Molecular Weight: 281.8 g/mol (HCl salt); 245.3 g/mol (base)

Property value

Batch No.	CAS No.	Purity estimate
14-D-13	637-23-0 (HCl salt) 537-26-8 (base)	99.7%

IUPAC name: (3-exo)-8-Methyl-8-azabicyclo[3.2.1]oct-3-yl benzoate hydrochloride (1:1).

Expiration of certification: The property values are valid till 21 May 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: 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 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.

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.

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, 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.

GC-FID:	Instrument:	Varian CP-3800
	Column:	VF-1ms, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	100 °C (1 min), 10 °C/min to 200 °C (3 min), 30 °C/min to 300 °C (3 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 = 99.95%, s = 0.002% (10 sub samples in duplicate, May 2014)
	Re-analysis:	Mean = 99.9%, s = 0.02% (5 sub samples in duplicate, May 2017)
	Re-analysis:	Mean = 99.93%, s = 0.004% (5 sub samples in duplicate, May 2020)
GC-FID:	Instrument:	Varian CP-3800
	Column:	HP-5, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	100 °C (1 min), 10 °C/min to 200 °C (3 min), 30 °C/min to 300 °C (3 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 = 99.95%, s = 0.003% (10 sub samples in duplicate, May 2014)
Karl Fischer analysis:		Moisture content 0.2% mass fraction (May 2014) Moisture content < 0.1% mass fraction (June 2017) Moisture content < 0.1% mass fraction (May 2020)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	TG-1MS, 30 m × 0.25 mm I.D. × 0.25 μm
	Program:	60 °C (1 min), 10 °C/min to 300 °C (3 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 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	
	Free base (17.3 min):	245 (M^+, 20), 140 (6), 124 (100), 105 (17), 94 (34), 82 (77), 77 (22), 67 (17) *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
	Split ratio:	50/1
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.2 mL/min
	Solvents detected:	Ethanol, diethyl ether
TLC:	Conditions:	Kieselgel 60F_{254} Methanol/conc NH_3 (200:3) Single spot observed, R_f = 0.35. Visualisation with UV light (254 nm)
IR:	Instrument:	BioRad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	2959, 2683, 2492, 1711, 1450, 1289, 1118, 1031, 715 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III -600
	Field strength:	600 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	δ 2.12-2.22 (4H, m), 2.27-2.45 (4H, m), 2.82 (2.72H, s), 3.08 (0.3H, s), 4.04 (2H, t, *J* = 3 Hz), 5.4 (1H, septet, *J* = 6.2 Hz), 7.54 (2H, t, *J* = 7.7 Hz), 7.70 (1H, t, *J* = 7.4 Hz), 8.03 (2H, d, *J* = 7.3 Hz) ppm
		Two conformational isomers are observed in the ^{1}H NMR spectrum Ethanol and diethyl ether estimated at 0.04 and 0.01% mass fraction were observed in the ^{1}H NMR.
^{13}C NMR:	Instrument:	Bruker Avance III-600
	Field strength:	150 MHz
	Solvent:	D_2O
	Spectral data:	δ 23.7, 25.5, 28.1, 31.5, 34.8, 38.1, 60.2, 63.4, 65.1, 128.7, 129.1, 129.4, 134.0, 167.8 ppm
		Two conformational isomers are observed in the ^{13}C NMR spectrum.
Melting point:		280-282 °C
Microanalysis:	Found:	C = 63.8%; H = 7.2%; N = 5.0%; Cl = 12.7 % (May, 2014)
	Calculated:	C = 63.9%, H = 7.2%, N = 5.0%; Cl = 12.6 % (Calculated for $C_{15}H_{19}NO_2$.HCl)