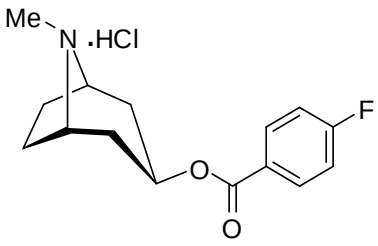
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA D949b: 4-Fluorotropacocaine hydrochloride



Report ID: D949b.2021.03

Chemical Formula: $C_{15}H_{18}FNO_2.HCl$

Molecular Weight: 299.8 g/mol (HCl), 263.3 g/mol (base)

Property value

Batch No.	CAS No.	Purity estimate
14-D-07	**172883-97-5 (base)**	**89.1% ± 1.5%**

IUPAC name: (3-exo)-8-Methyl-8-azabicyclo[3.2.1]oct-3-yl 4-fluorobenzoate (base).

Expiration of certification: The property values are valid till 13 May 2026, 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 seven 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.
20 September 2022

This report supersedes any issued prior to 20 September 2022.

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

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, 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:	VF-1MS, 30 m x 0.32 mm I.D. x 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 of main component as the free base:	
	Initial analysis:	Mean = 99.9%, s = 0.004% (7 sub samples in duplicate, February 2014)
	Re-analysis:	Mean = 99.9%, s = 0.002% (5 sub samples in duplicate, February 2015)
GC-FID:	Instrument:	Agilent 6890N or 7890A
	Column:	HP-5, 30 m x 0.32 mm I.D. x 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 main component as the free base:	
	Initial analysis:	Mean = 99.8%, s = 0.01% (7 sub samples in duplicate, February 2014)
	Re-analysis:	Mean = 99.8%, s = 0.008% (7 sub samples in duplicate, May 2021)
Karl Fischer analysis:		Moisture content 7.5% mass fraction (March 2014) Moisture content 10% mass fraction (February 2015) Moisture content 10.7% mass fraction (May 2021)
Thermogravimetric analysis:		Volatile content 7.5% and non-volatile residue < 0.2% mass fraction (February 2014)

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 (16.9 min):	263 (M^+, 20), 140 (8), 124 (100), 94 (35), 82 (65), 67 (16), 42 (15) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254} Methanol/$CHCl_3$ (20:80) Single spot observed, R_f = 0.30. Visualization with UV light (254 nm)
IR:	Instrument:	BioRad FTS3000MX FT-IR
	Range:	4000-500 cm^{-1}, KBr powder
	Peaks:	2962, 2824, 2678, 2490, 1718, 1603, 1508, 1292, 1116, 861, 770, 604 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III-300
	Field strength:	300 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 2.14-2.23 (4H, m), 2.39-2.44 (4H, m), 2.85 (3H, s), 4.04 (2H, m), 5.40 (1H, dddd, *J* = 6.3, 6.3, 11.0, 11.0 Hz), 7.22 (2H, m), 8.07 (2H, m)
	Isopropanol was observed in the ^{1}H NMR spectrum at 0.03 % mass fraction. Coupling between fluorine and hydrogen was observed.	
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	125 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 25.3, 36.2, 38.9, 64.6, 65.9, 116.7 (d, *J* = 22.5 Hz), 127.4 (d, *J* = 3.2 Hz), 133.4 (d, *J* = 9.5 Hz), 166.1, 167.4 (d, *J* = 253 Hz) ppm
	Coupling between fluorine and carbon was observed.	
Melting point:		283-285 °C
Microanalysis:	Found:	C = 55.3 %; H = 6.5 %; N = 4.1 %; Cl = 10.9%; F = 5.6% (March 2014)
	Calculated:	C = 55.4 %; H = 6.8 %; N = 4.3 %; Cl = 11.0%; F = 5.9% (Calc. for $C_{15}H_{18}FNO_2$.HCl containing 7.45% H_2O)
	Calculated:	C = 60.1 %; H = 6.4 %; N = 4.7 %; Cl = 11.8%; F = 6.8% (Calc. for $C_{15}H_{18}FNO_2$.HCl)