Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

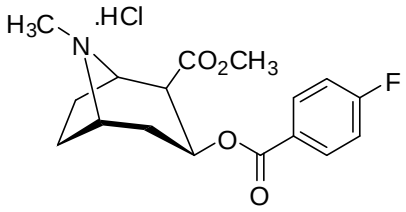
REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA D854b: 4-Fluorococaine hydrochloride

Report ID: D854b.2021.02

Chemical Formula: $C_{17}H_{20}FNO_4.HCl$

Molecular Weight: 357.8 g/mol (HCl), 321.3 g/mol (base)



Property value

Batch No.	CAS No.	Purity estimate
11-D-05	**134507-62-3 (base)**	**98.9 ± 0.9%**

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)-3-[(4-fluorobenzoyl)oxy]-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylate

Expiration of certification: The property values are valid till 22 November 2031, i.e. ten 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 and is not intended for use as a calibrator. The material does not have certified reference material status as metrological traceability of the stated purity value to the SI unit for mass (kg) has not been established.

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. 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 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.
13 October 2022

This report supersedes any issued prior to 19 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 qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID:	Instrument:	Varian CP-3800/Agilent 7890
	Column:	VF-1MS/HP-5, 30 m × 0.32 mm I.D. × 0.25 μm
	Program	120 °C (1 min), 15 °C/min to 220 °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 free base:	
	Initial analysis:	Mean = 99.2%, s = 0.01% (10 sub samples in duplicate, May 2011)
	Re-analysis:	Mean = 99.1%, s = 0.01% (5 sub samples in duplicate, March 2014)
	Re-analysis:	Mean = 99.2%, s = 0.01% (5 sub samples in duplicate, February 2017)
	Re-analysis:	Mean = 99.1%, s = 0.05% (5 sub samples in duplicate, November 2021)
GC-FID:	Instrument:	Varian CP-3800
	Column:	HP-5, 30.0 m × 0.32 mm I.D. × 0.25 μm
	Program	120 °C (1 min), 15 °C/min to 220 °C (5 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 free base:	
	Initial analysis:	Mean = 99.3%, s = 0.07% (10 sub samples in duplicate, May 2011)
Karl Fischer analysis:		Moisture content 0.2% mass fraction (May 2011, March 2014, February 2017) Moisture content 0.4% mass fraction (May 2013) Moisture content 0.1% mass fraction (November 2021)
Thermogravimetric analysis:		The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material

Spectroscopic and other characterisation data

GC-MS:	Instrument:	Agilent 6890/5973
	Column:	TG-1MS, 30 m x 0.25 mm I.D. x 0.25 µm
	Program:	100 °C (7 min), 20 °C/min to 300 °C (3 min)
	Injector:	250 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	30/1
	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 (15.1 min):	321 (M^+, 26), 290 (13), 198 (12), 182 (100), 123 (37), 94 (32), 82 (84) 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:	Diethyl ether
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol/conc. NH_3 (200:3) Single spot observed, R_f = 0.57 Visualization with UV light (254 nm)
IR:	Instrument:	BioRad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3041, 2971, 2774, 2551, 2362, 1731, 1713, 1602, 1265, 1234, 1151, 1113, 1092, 1026, 1012, 873, 774, 692, 774 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance DMX-600
	Field strength:	600 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	δ 2.25 (2H, m), 2.42-2.58 (4H, m), 2.92 (3H, s), 3.66 (3H, s), 3.68 (1H, dd, *J* = 2.5, 7.5 Hz), 4.13 (1H, m), 4.27 (1H, bd, *J* = 7.3 Hz), 5.6 (1H, q, *J* = 8.8), 7.27 (2H, m), 8.03 (2H, m) ppm. Diethyl ether (0.05%) and methanol (0.13%) mass fraction estimated by ^{1}H NMR spectrum in D_2O. Coupling between fluorine (^{19}F) and hydrogen (^{1}H) was observed.
^{13}C NMR:	Instrument:	Bruker GYRO-300
	Field strength:	75 MHz
	Solvent:	D_2O
	Spectral data:	δ 22.8, 23.9, 32.9, 39.1, 46.3, 53.6, 63.4, 64.1, 64.7, 116.2, 116.4, 125.08, 125.1, 132.6, 132.7, 165.7, 166.4, 167.4, 173.5 ppm. Coupling between fluorine (^{19}F) and carbon (^{13}C) was observed.
Melting point:		185-187 °C
Microanalysis:	Found:	C = 57.3%; H = 5.9%; N = 3.9%; Cl = 9.9%; F = 5.1% (May, 2011)
	Calculated:	C = 57.1%; H = 5.9%; N = 3.9%; Cl = 9.9%; F = 5.3% (Calculated for $C_{17}H_{20}FNO_4$.HCl)