



REFERENCE MATERIAL ANALYSIS REPORT

Report ID: D854b.2017.01

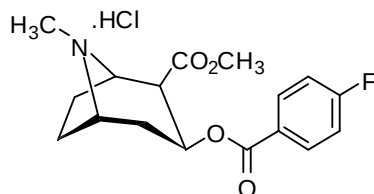
Compound Name: **4-Fluorococaine hydrochloride**

Collection number: D854b

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

CAS Registry Number: 134507-62-3 (base)

Structure:



Description: White powder

Batch number: 11-D-05

Molecular Weight: 357.8 (HCl), 321.3 (base)

Release Date: 14th June 2011

Synonyms: *p*-Fluorococaine hydrochloride
[1*R*-(exo,exo)]-3-[(4-Fluorobenzoyl)oxy]-8-methyl-8-azabicyclo[3.2.1]-octane-2-carboxylic acid methyl ester hydrochloride
(1*R*,2*R*,3*S*,5*S*)]-3-[(4-Fluorobenzoyl)oxy]-8-methyl-8-azabicyclo[3.2.1]-octane-2-carboxylic acid methyl ester hydrochloride
2 α -Carbomethoxy-3 α -(4-fluorophenyl)-tropane hydrochloride

Purity (mass fraction): $98.9 \pm 1.9\%$ (95% coverage interval)

This reference material is designed for use as an internal standard only. The stated purity value is indicative only as occluded diethyl ether and non-volatile residue (e.g. inorganic salts) content have not been quantified accurately. The elemental microanalysis suggests that both components are present in negligible quantities.

The indicative purity estimate by traditional analytical techniques was obtained by subtraction from 100% of total impurities by GC-FID, thermogravimetric analysis, Karl Fischer analysis and ^1H NMR analysis of the methanol content. Supporting evidence is provided by headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID: Instrument: Varian CP-3800
(Free base) Column: VF-1MS, 30 m $\times$ 0.32 mm I.D. $\times$ 0.25 μ m
Program 120 $^{\circ}C$ (1 min), 15 $^{\circ}C/min$ to 220 $^{\circ}C$ (3 min), 30 $^{\circ}C/min$ to 300 $^{\circ}C$ (3 min)
Injector: 250 $^{\circ}C$ Detector Temp: 320 $^{\circ}C$
Carrier: Helium Split ratio: 20/1
Relative peak area response of main component:
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)

GC-FID: Instrument: Varian CP-3800
(Free base) Column: HP-5, 30.0 m $\times$ 0.32 mm I.D. $\times$ 0.25 μ m
Program 120 $^{\circ}C$ (1 min), 15 $^{\circ}C/min$ to 220 $^{\circ}C$ (5 min), 30 $^{\circ}C/min$ to 300 $^{\circ}C$ (3 min)
Injector: 250 $^{\circ}C$ Detector Temp: 320 $^{\circ}C$
Carrier: Helium Split ratio: 20/1
Relative peak area response of main component:
Initial analysis: Mean = 99.3%, $s = 0.07\%$ (10 sub samples in duplicate, May 2011)

Thermogravimetric analysis: The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material

Karl Fischer analysis: Moisture content 0.2% mass fraction (May 2011)
Moisture content 0.4% mass fraction (May 2013)
Moisture content 0.2% mass fraction (March 2014)
Moisture content 0.2% mass fraction (February 2017)

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 μ m
	Program:	100 $^{\circ}$ C (7 min), 20 $^{\circ}$ C/min to 300 $^{\circ}$ C (3 min)
	Injector:	250 $^{\circ}$ C
	Carrier:	Helium, 1.0 mL/min
		Transfer line temp: 280 $^{\circ}$ C
		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 μ m
	Program:	50 $^{\circ}$ C (5 min), 7 $^{\circ}$ C/min to 120 $^{\circ}$ C, 15 $^{\circ}$ C/min to 220 $^{\circ}$ C (8.3 min)
	Injector:	150 $^{\circ}$ C
	Carrier:	Helium, 1.2 mL/min
		Transfer line temp: 280 $^{\circ}$ C
		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}
^1H NMR:	Instrument:	Bruker Avance DMX-600
	Field strength:	600 MHz
	Spectral data:	Solvent: D ₂ O (4.79 ppm) 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 ^1H NMR spectrum in D ₂ O. Coupling between fluorine (^{19}F) and hydrogen (^1H) was observed.
^{13}C NMR:	Instrument:	Bruker GYRO-300
	Field strength:	75 MHz
	Spectral data:	Solvent: D ₂ O 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 $^{\circ}$ C	
Microanalysis:	Found: C = 57.3%; H = 5.9%; N = 3.9%; Cl = 9.9%; F = 5.1% Calc: C = 57.1%; H = 5.9%; N = 3.9%; Cl = 9.9%; F = 5.3% (Calculated for C ₁₇ H ₂₀ FNO ₄ .HCl)	

Expiration of certification

The property values are valid till 16th February 2022, 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.

The long-term stability of the compound in solution has not been examined.

This material has been given a shelf life of three years from the date of re-certification. This material has demonstrated stability over a minimum period of five years. The measurement uncertainty at the 95% coverage interval includes a stability component which has been estimated from annual stability trials.

Homogeneity assessment

The homogeneity of the material was assessed using purity assay by GC-FID detection 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.

Recommended storage

When not in use this material should be stored at or below 25 °C in a closed container protected from ambient moisture and light.

Intended use

For *in vitro* laboratory analysis only.

Caution

Treat as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust.

Legal notice

Neither NMI nor any person acting on NMI's behalf assumes any liability with respect to the use of, or for damages resulting from the use of, this reference material or the information contained in this certificate.

Authorised by:

S. R. Davies

Dr Stephen R Davies
Team Leader,
Chemical Reference Materials, NMI
24 March 2017

Characterisation data and property values specified in this report supersede all reports issued prior to 24th March 2017.