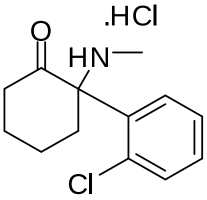
Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

NATA
ACCREDITED FOR TECHNICAL COMPETENCE

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D686c: Ketamine hydrochloride



Report ID: D686c.2021.02 (Bottled 210705)

Chemical Formula: $C_{13}H_{16}ClNO.HCl$

Molecular Weight: 274.2 g/mol (HCl), 237.7 g/mol (base)

Certified value

Batch No.	CAS No.	Purity (mass fraction)
13-D-10	**1867-66-9 (HCl)**	**99.5 ± 0.4%**

The uncertainty has been calculated according to ISO Guide 35 and is stated at the 95% confidence limit (k = 2).

IUPAC name: (±)-2-(2-Chlorophenyl)-2-(methylamino)-cyclohexanone hydrochloride (1:1).

Expiration of certification: The property values are valid till 26 June 2025, 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 crystalline solid sourced from an external supplier and certified for identity and purity by NMI Australia. Packaged in amber glass bottles with a septum and crimped aluminium cap or screw top cap.

Intended use: This certified reference material is suitable for use as a primary calibrator.

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.

Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%.Quantitative NMR provides an independent direct measure of the mass fraction of the analyte of interest, calibrated with an internal standard certified for purity (mass fraction)

Stability: This material has demonstrated stability over a minimum period of ten years. The measurement uncertainty at the 95% confidence interval includes a stability component which has been estimated from annual stability trials.

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.
4 July 2025

This report supersedes any issued prior to 04 July 2025.

NATA logo notice: Accredited for compliance with ISO 17034. Accreditation No. 198 / Corporate Site No. 14214. The results of the tests, calibrations and/or measurements included in this document are traceable to Australian/national standards.

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value 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 quantitative NMR (qNMR), qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis. The purity value obtained by qNMR was determined using combination of the four-proton multiplet at 7.6-7.9 ppm, and the one-proton multiplet at 3.35 ppm were measured against a certified internal standard of potassium hydrogen maleate.

GC-FID: Instrument: Varian CP-3800 or Agilent 8890
Column: VF-1MS or HP-1MS, 30 m x 0.32 mm I.D. x 0.25 µm
Program: 120 °C (1 min), 10 °C/min to 200 °C (2 min), 30 °C /min to 300 °C (3 min)
Injector: 200 °C Detector Temp: 320 °C
Carrier: Helium Split ratio: 20/1
Relative mass fraction of the main component as the free base:
Initial analysis: Mean = 99.9%, s = 0.02% (10 sub samples in duplicate, May 2013)
Re-analysis: Mean = 99.8%, s = 0.09% (5 sub samples in duplicate, March 2015)
Re-analysis: Mean = 99.9%, s = 0.01% (5 sub samples in duplicate, December 2017)
Re-analysis: Mean = 99.7%, s = 0.01% (5 sub samples in duplicate, July 2021)
Re-analysis: Mean = 99.6%, s = 0.03% (5 sub samples in duplicate, June 2025)

GC-FID: Instrument: Varian CP-3800
Column: HP-5, 30 m x 0.32 mm I.D. x 0.25 µm
Program: 120 °C (1 min), 10 °C /min to 200 °C (2 min), 30 °C /min to 300 °C (3 min)
Injector: 200 °C Detector Temp: 320 °C
Carrier: Helium Split ratio: 20/1
Relative mass fraction of the main component as the free base:
Initial analysis: Mean = 99.9%, s = 0.01% (10 sub samples in duplicate, May 2013)

Karl Fischer analysis: Moisture content 0.2% mass fraction (May 2013)
Moisture content 0.1% mass fraction (February 2015)
Moisture content < 0.1% mass fraction (January 2018)
Moisture content < 0.1% mass fraction (July 2021)

Thermogravimetric analysis: Non volatile residue < 0.2% mass fraction (June 2013). The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material and/or degradation at elevated temperatures.

QNMR: Instrument: Bruker Avance-III-500
Field strength: 500 MHz
Solvent: D_2O (4.79 ppm)
Internal standard: Potassium hydrogen maleate (99.7% mass fraction)

Initial analysis: Mean (3.35 ppm) = 100.1%, s = 0.1% (5 sub samples, September 2021)
Initial analysis: Mean (7.6-7.9 ppm) = 100.0%, s = 0.1% (5 sub samples, September 2021)

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:	120 °C (1 min), 10 °C /min to 200 °C (2 min), 30 °C /min to 300 °C (3 min)	
	Injector:	200 °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 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 (10.4 min):	237 (M+, 1), 210 (9), 208 (26), 182 (36), 180 (100), 154 (7), 152 (18), 138 (14), 115 (10), 102 (11) *m/z*	
ESI-MS	Instrument:	Waters Acquity UPLC/TQD	
	Operation:	Positive ion mode, direct infusion at 5 μL/min	
	Capillary voltage:	3.5 kV	
	Cone voltage:	30 V	
	Peak:	238.05 (M+H$^+$) *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:	Ethyl acetate	
TLC:	Conditions:	Kieselgel 60F254. NH3/methanol (3/200) Single spot observed, Rf = 0.7. Visualisation with UV at 254 nm	
IR:	Instrument:	Biorad FTS3000MX FT-IR	
	Range:	4000-400 cm^{-1}, KBr powder	
	Peaks:	2871, 2689, 2442, 1717, 1579, 1450, 1381, 1296,773, 718, 573 cm^{-1}	
^{1}H NMR:	Instrument:	Bruker Avance III-400	
	Field strength:	400 MHz	
	Solvent:	MeOH-d_4 (3.31 ppm)	
	Spectral data:	δ 1.67-1.85 (2H, m), 1.87-1.99 (2H, m), 2.13-2.18 (1H, m), 2.40 (3H, s), 2.51-2.62 (2H, m), 3.40 (1H, m), 7.59-7.67 (3H, m), 7.94 (1H, m) ppm Ethyl acetate estimated at 0.02% mass fraction was observed in the ^{1}H NMR	
^{13}C NMR:	Instrument:	Bruker Gyro-300	
	Field strength:	75 MHz	
	Solvent:	MeOH-d_4 (49.0 ppm)	
	Spectral data:	δ 22.8, 28.1, 31.0, 37.5, 40.8, 73.7, 129.2, 129.8, 133.3, 133.9, 135.8, 208.3 ppm	
Melting point:		256-259 °C	
Microanalysis:	Found:	C = 57.2%; H = 6.3%; N = 5.1%; Cl = 25.7% (May, 2013)	
	Calculated:	C = 57.0%; H = 6.3%; N = 5.1%; Cl = 25.9% (Calculated for $C_{13}H_{16}ClNO.HCl$)	