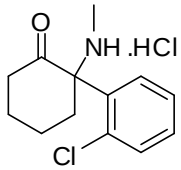
**Australian Government**

**National Measurement Institute**

## REFERENCE MATERIAL ANALYSIS REPORT

**Report ID: D686c.2013.01**

Compound Name: **Ketamine hydrochloride**
Collection Number: D686c
Chemical Formula: $C_{13}H_{16}ClNO.HCl$
CAS Number: 1867-66-9
Structure:




Description: White crystalline solid
Batch Number: 13-D-10
Molecular Weight: 274.2 (HCl), 237.7 (base)
Release date: 20th June 2013

Synonyms: (±)-2-(2-Chlorophenyl)-2-(methylamino)-cyclohexanone hydrochloride
(±)-2-(*o*-Chlorophenyl)-2-(methylamino)-cyclohexanone hydrochloride
Ketanarkonl
Ketavet

Purity (mass fraction): 99.7 ± 1.4% (95% coverage interval)

The purity value was obtained from a combination of traditional analytical. The purity estimate by traditional analytical techniques was obtained by subtraction from 100% of total impurities by GC-FID, thermogravimetric analysis, Karl Fischer analysis and $^1$H NMR. Supporting evidence is provided by headspace GC-MS analysis of occluded solvent and elemental microanalysis.

| | | | |
|---|---|---|---|
| GC-FID: | Instrument: | Varian CP-3800 | |
| | Column: | VF-1MS, 30 m × 0.32 mm I.D. × 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 peak area response of main component as the free base: | | |
| | Initial analysis: | Mean = 99.9%, s = 0.02% (10 sub samples in duplicate, May 2013) | |
| GC-FID: | Instrument: | Varian CP-3800 | |
| | Column: | HP-5, 30 m × 0.32 mm I.D. × 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 peak area response of main component as the free base: | | |
| | Initial analysis: | Mean = 99.9%, s = 0.01% (10 sub samples in duplicate, May 2013) | |

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.

Karl Fischer analysis: Moisture content 0.2% mass fraction (May 2013)

**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 60$F_{254}$. $NH_3$/methanol (3/200)<br>Single spot observed, $R_f$ = 0.67. 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: $CD_3OD$ (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: $d_4$-methanol (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)<br>Calc: C = 57.0%; H = 6.3%; N = 5.1%; Cl = 25.9% (Calculated for $C_{13}H_{16}ClNO.HCl$) |

**Expiration of certification**
The property values are valid till 21st May 2016, i.e. three years from the date of 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 certification. The material will be re-tested on an annual basis to ensure that the property values are still valid. In the event a product fails the stability trial, notification will be sent to all impacted customers.

In the absence of stability data the measurement uncertainty at the 95% coverage interval has been expanded to accommodate any potential change in the property value. The stability component has been estimated from stability trials conducted on similar materials by NMI Australia over the last 10 years.

**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 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 20 ºC in a closed container in a dry, dark area.

**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:

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Dr Stephen R. Davies,
Team Leader,
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Dated: 20 June, 2013.