



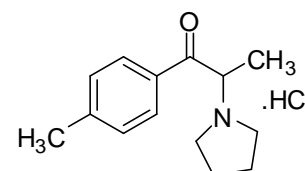
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D964: (\pm)-4'-Methyl-pyrrolidinopropiophenone hydrochloride

Report ID: D964.2023.01

Chemical Formula: C₁₄H₁₉NO.HCl

Molecular Weight: 253.8 g/mol (HCl), 217.3 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
11-D-02	1313393-58-6 (HCl) 28117-80-8 (base)	99.0 ± 1.3%

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

IUPAC name: 1-(4-Methylphenyl)-2-(1-pyrrolidinyl)-1-propanone hydrochloride.

Expiration of certification: The property values are valid till 29 March 2028, 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 solid prepared by synthesis, 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 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 °C 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 five 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 nine 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.
19 April 2023

This report supersedes any issued prior to 19 April 2023.

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

Legal notice: Terms and Conditions associated with the provision of this reference material can be found on the NMIA website.

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 ¹H NMR spectroscopy. The purity value is calculated as per Equation 1.

$$\text{Purity} = (100 \% - I_{\text{ORG}}) \times (100 \% - I_{\text{VOL}} - I_{\text{NVR}}) \quad \text{Equation 1}$$

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, HPLC-UV and elemental microanalysis.

GC-FID:	Instrument: Agilent 7890N Column: HP-1, 30 m × 0.32 mm I.D. × 0.25 μm Program: 165 °C (10 min), 30 °C/min to 300 °C (3 min) Injector: 250 °C Detector Temp: 320 °C Carrier: Helium Split ratio: 20/1 Relative mass fraction of the main component: Initial analysis: Mean = 99.2%, s = 0.07% (5 sub samples in duplicate, March 2012) Re-analysis: Mean = 99.0%, s = 0.08% (5 sub samples in duplicate, February 2013) Re-analysis: Mean = 99.4%, s = 0.01% (5 sub samples in duplicate, April 2015) Re-analysis: Mean = 99.5%, s = 0.02% (5 sub samples in duplicate, May 2018) Re-analysis: Mean = 99.4%, s = 0.03% (5 sub samples in duplicate, March 2023)
HPLC:	Instrument: Shimadzu Binary pump LC-20AB, SIL-20 A HT autosampler Column: X-Bridge C-18, 5 μm (4.6 mm x 150 mm) Column oven: 40°C Mobile Phase: Acetonitrile/MilliQ water (40:60) The aqueous phase was buffered at pH 10.8 using 20 mM NH ₄ OAc and NH ₄ OH Flow rate: 2.0 mL/min Detector: Shimadzu SPD-M20A operating at 225 nm Relative peak area response of main component: Initial analysis: Mean = 99.3%, s = 0.04% (10 sub samples in duplicate, March 2011)
Karl Fischer analysis:	Moisture content ≤ 0.3% mass fraction (April 2011, April 2012, February 2013, March 2015 and March 2023).
Thermogravimetric analysis:	Non volatile residue < 0.2 % mass fraction (April 2011). The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material.
QNMR:	Instrument: Bruker Avance DMX-600 Field strength: 600 MHz Solvent: D ₂ O (4.79 ppm) Internal standard: Maleic acid (98.7% mass fraction) Initial analysis: Mean (1.6 ppm) = 99.4%, s = 0.26% (5 sub samples, March 2011) Initial analysis: Mean (2.4 ppm) = 99.4%, s = 0.39% (5 sub samples, March 2011) Initial analysis: Mean (5.2 ppm) = 99.4%, s = 0.14% (5 sub samples, March 2011)

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:	60 °C (1 min), 10 °C/min to 100 °C, 15 °C/min to 250 °C (5 min), 30 °C/min to 300 °C (2 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 (12.7 min):	119 (9), 98 (100), 91 (8), 65 (4), 56 (8), 44 (8) <i>m/z</i>
ESI -MS:	Instrument:	Micromass Quatro LC Micro
	Operation:	Positive ion mode, direct infusion at 10 µL/min
	Ionisation:	ESI spray voltage at 3.5 kV positive ion
	EM voltage:	650 V
	Cone voltage:	3 V
	Peak:	218.2 (M+H ⁺) <i>m/z</i>
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, ethanol
TLC:	Conditions:	Kieselgel 60F254. Methanol/NH ₃ (100/1.5) Single spot observed, R _f = 0.7. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm ⁻¹ , KBr powder
	Peaks:	2955, 2640, 2579, 2447, 2361, 1686, 1606, 1457, 1388, 1339, 1295, 1244, 1135, 978, 830, 736, 586 cm ⁻¹
¹ H NMR:	Instrument:	Bruker Avance DMX-600
	Field strength:	600 MHz
	Solvent:	D ₂ O (4.79 ppm)
	Spectral data:	δ 7.91 (2H, d, <i>J</i> = 8.3 Hz), 7.44 (2H, d, <i>J</i> = 8.1 Hz), 5.23 (1H, q, <i>J</i> = 7.1 Hz), 2.80-4.10 (4H, m (br)), 2.44 (3H, s), 1.80-2.35 (4H, m (br)), 1.63 (3H, d, <i>J</i> = 7.1 Hz) ppm
	Ethanol and diethyl ether at 0.08% mass fraction were observed in the ¹ H NMR	
¹³ C NMR:	Instrument:	Bruker Avance DMX-600
	Field strength:	151 MHz
	Solvent:	D ₂ O
	Spectral data:	δ 16.1, 21.0, 22.9, 52.2, 54.4, 65.4, 129.1, 129.8, 130.0, 147.6, 197.2 ppm
Melting point:	222-223 °C	
Microanalysis:	Found:	C = 66.4%; H = 8.1%; N = 5.5%; Cl = 14.1% (April, 2011)
	Calculated:	C = 66.3%; H = 7.9%; N = 5.5%; Cl = 14.0% (Calculated for C ₁₄ H ₁₉ NO.HCl)