Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

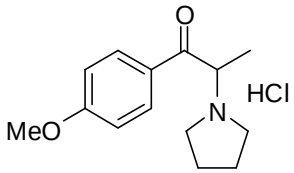
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D1024: (±)-1-(4-Methoxyphenyl)-2-(1-pyrrolidinyl)-1-propanone hydrochloride

Report ID: D1024.2023.01

Chemical Formula: $C_{14}H_{19}NO_2$.HCl

Molecular Weight: 269.8 g/mol (HCl), 233.3 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
14-D-23	478243-09-3 (free base)	96.8 ± 1.1%

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

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

Expiration of certification: The property values are valid till 21 September 2028, 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.

Description: Beige solid 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 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 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 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.
10 October 2023

This report supersedes any issued prior to 10 October 2023.

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value was obtained from a combination of traditional analytical techniques and quantitative nuclear magnetic resonance (qNMR). The techniques used in the mass balance approach include 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 elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890 or 7890
	Column:	HP-1, 30 m × 0.32 mm I.D. × 0.25 µm
	Program:	180 °C (10 min), 20 °C/min to 300 °C (4 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 = 98.2%, s= 0.08% (10 sub samples in duplicate, November 2014)
	Re-analysis:	Mean = 98.3%, s = 0.08% (5 sub samples in duplicate, October 2015)
	Re-analysis:	Mean = 98.2%, s = 0.02% (5 sub samples in duplicate, September 2016)
	Re-analysis:	Mean = 99.9%, s = 0.04% (5 sub samples in duplicate, September 2019)
	Re-analysis:	Mean = 99.9%, s = 0.01% (5 sub samples in duplicate, September 2023)
Thermogravimetric analysis:		Non volatile residue < 0.2% mass fraction (November 2014)
Karl Fischer analysis:		Moisture content 0.5% mass fraction (November 2014) Moisture content 0.5% mass fraction (October 2015) Moisture content 0.6% mass fraction (September 2016) Moisture content 0.5% mass fraction (September 2019) Moisture content 0.4% mass fraction (September 2023)
QNMR:	Instrument:	Bruker Avance-III
	Field strength:	500 MHz
	Solvent:	D_2O/DCl (4.79 ppm)
	Internal standard:	Maleic acid (98.7% mass fraction)
	Initial analysis:	Mean (7.98 ppm) = 96.9%, s = 0.1% (5 sub samples, August 2014)
	Initial analysis:	Mean (7.08 ppm) = 97.0%, s = 0.1% (5 sub samples, August 2014)
	Initial analysis:	Mean (1.59 ppm) = 96.6%, s = 0.1% (5 sub samples, August 2014)

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:	180 °C (10 min), 20 °C/min to 300 °C (4 min)
	Injector:	250 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	20/1
	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 (8.86 min): 135 (11), 98 (100), 56 (7) *m/z*	
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:	10 V
	Peak:	234.3 (M+H+) *m/z*
^{1}H NMR:	Instrument:	Bruker Avance-III
	Field strength:	500 MHz
	Solvent:	D2O/DCl (4.79 ppm)
	Spectral data:	δ 1.60 (3H, d, J = 7.0 Hz), 1.95-2.13 (3H, m), 2.18 (1H, m), 2.99 (1H, m), 3.27 (1H, m), 3.67 (1H, m), 3.74 (1H, m), 3.89 (3H, s), 5.16 (1H, q, J = 7.3 Hz), 7.08 (2H, d, J = 9.1 Hz), 7.98 (2H, d, J = 9.1 Hz) ppm
		Ethanol, diethyl ether, and the major brominated MOPPP hydrochloride were estimated at 0.2, 0.4 and 1.9% mass fraction respectively in the 1H NMR
^{13}C NMR:	Instrument:	Bruker Avance-III
	Field strength:	126 MHz
	Solvent:	D2O/DCl
	Spectral data:	δ 16.1, 22.8, 22.9, 51.9, 54.5, 55.7, 65.1, 114.6, 125.2, 131.6, 165.0, 195.8 ppm
Melting point:		193-199 °C
Microanalysis:	Found:	C = 62.2%; H = 7.5%; N = 5.2%; Cl = 13.1% (September, 2014)
	Calculated:	C = 62.3%; H = 7.5%; N = 5.2%; Cl = 13.1% (Calculated for $C_{14}H_{19}NO_2$.HCl)