Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

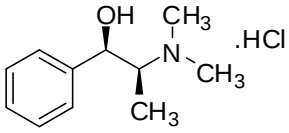
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA M243b: (-)-Methylephedrine hydrochloride

Report ID: M243b.2021.03 (Bottled 160810)

Chemical Formula: $C_{11}H_{17}NO.HCl$

Molecular Weight: 215.7 g/mol (HCl), 179.3 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
13-D-08	**38455-90-2 (HCl)** **552-79-4 (base)**	**99.6 ± 0.8%**

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

IUPAC name: (1R,2S)-2-(Dimethylamino)-1-phenyl-1-propanol hydrochloride.

Expiration of certification: The property values are valid till 07 May 2026, 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: White powder 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%.

Stability: This material has demonstrated stability over a minimum period of three 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.
1 August 2022

This report supersedes any issued prior to 01 August 2022.

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

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 qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890 or 7890
	Column:	HP-1, 30 m × 0.32 mm I.D. × 0.25 μm
	Program:	60 °C (1 min), 10 °C/min to 100 °C, 15 °C/min to 250 °C, 30 ºC/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 as the free base:	
	Initial analysis:	Mean = 99.8%, s = 0.03% (10 sub samples in duplicate, May 2013)
	Re-analysis:	Mean = 99.8%, s = 0.03% (5 sub samples in duplicate, August 2015)
	Re-analysis:	Mean = 99.8%, s = 0.02% (5 sub samples in duplicate, June 2018)
	Re-analysis:	Mean = 99.7%, s = 0.01% (5 sub samples in duplicate, May 2021)
Karl Fischer analysis:		Moisture content ≤ 0.2% mass fraction (May 2013, August 2015, June 2018 and May 2021)
Thermogravimetric analysis:		Non volatile residue < 0.2% mass fraction (May 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.

Spectroscopic and other characterisation data

GC-MS:	Parent compound:	
	Instrument:	HP6890/5973
	Column:	TG1-MS, 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, 30 ºC/min to 300 °C (3 min)
	Injector:	250 °C
	Split ratio:	20/1
	Transfer line temp:	280 °C
	Carrier:	Helium
	Scan range:	50-550 *m/z*
	Bis-TMS derivative:	
	Instrument:	HP 6890/5973
	Column:	TG1-MS, 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, 30 ºC/min to 300 °C (3 min)
	Injector:	250 °C
	Split ratio:	20/1
	Transfer line temp:	280 °C
	Carrier:	Helium
	Scan range:	50-550 *m/z*
	The retention times of the parent compound and MS derivative are 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 (10.0 min):	118 (5), 117 (8), 106 (13), 105 (14), 77 (17), 72 (100), 56 (10), 51 (6), 44 (11) *m/z*
	MS derivative (5.0 min):	236 (M^+-CH_3, 6), 163 (7), 117 (7), 102 (10), 91 (8), 72 (100) *m/z*
ESI-MS:	Instrument:	Micromass Quatro LC Micro
	Operation:	Positive ion mode, direct infusion at 5 μL/min
	Ionisation:	ESI spray voltage at 3.5 kV positive ion
	EM voltage:	650 V
	Cone voltage:	30 V
	Peak:	180.1 ($M+H^+$) *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:	Diethyl ether, isopropanol
TLC:	Conditions:	Kieselgel 60F_{254}. Methanol/ammonia (100/1.5) Single spot observed, R_f = 0.4
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3300, 3273, 2965, 2693, 2638, 1476, 1053, 1012, 746, 705 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DPX-300
	Field strength:	300 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.14 (3H, d, *J* = 6.8 Hz), 3.02 (6H, s), 3.52 (1H, dq, *J* = 2.6, 6.8 Hz), 5.36 (1H, d, *J* = 2.5 Hz), 7.28-7.47 (5H, m) ppm
^{13}C NMR:	Instrument:	Bruker DMX 600
	Field strength:	151 MHz
	Solvent:	MeOH-d_4 (49 ppm)
	Spectral data:	δ 7.9, 42.0, 68.09, 68.11, 71.2, 126.9, 128.9, 129.5, 142.2 ppm
Melting point:		200-202 °C
Microanalysis:	Found:	C = 61.3%; H = 8.1%; N = 6.5% (May, 2013)
	Calculated:	C = 61.3%; H = 6.4%; N = 6.5% (Calculated for $C_{11}H_{17}NO.HCl$)