Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

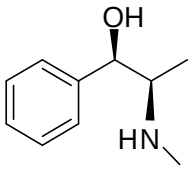
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D397: (-)-Pseudoephedrine

Report ID: D397.2022.01 (Bottled 190220)

Chemical Formula: $C_{10}H_{15}NO$

Molecular Weight: 165.2 g/mol



Certified value

Batch No.	CAS No.	Purity (mass fraction)
00-D-07	321-97-1	99.8 ± 0.3 %

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

Synonyms: Ψ- Ephedrine
α–[1-(Methylamino)ethyl]benzene-methanol
[1*R*, 2*R*]-(-)-2-Methylamino-1-phenylpropan-1-ol

Expiration of certification: The property values are valid till 22 August 2027, 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: Off-white powder prepared by synthesis or sourced from an external supplier, certified for identity and purity by NMIA. Packaged in amber glass bottles with a septum and crimped aluminium cap

Intended use: This certified reference material may be used for instrument calibration.

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 with flame ionisation detection on ten randomly selected 1-2 mg sub samples of the material. The material was judged to be sufficiently homogenous 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 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.
2 September 2022

This report supersedes any issued prior to 2 September 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 elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890N, 8890 or Varian 3800
	Column:	HP-1 or VF-1MS, 30 m x 0.32 mm I.D. x 0.25 µm
	Program:	100 °C (2 min), 10 °C/min to 220 °C, 20 °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 = 99.97%, s = 0.01% (10 sub samples in duplicate October 2000)
	Re-analysis:	Mean = 99.99%, s = 0.01% (5 sub sample in duplicate April 2007)
	Re-analysis:	Mean = 99.95%, s = 0.01% (5 sub samples in duplicate April 2010)
	Re-analysis:	Mean = 99.93%, s = 0.004% (5 sub samples in duplicate February 2013)
	Re-analysis:	Mean = 99.97%, s = 0.012% (5 sub samples in duplicate December 2017)
	Re-analysis:	Mean = 99.97%, s = 0.004% (6 sub samples in duplicate August 2022)
HPLC:	Column:	Waters X-Terra RP18, 5 µm (3.9 mm × 150 mm)
	Mobile Phase:	A = 5% Acetonitrile (ACN)/95% H_2O containing 2% by volume conc. NH_4OH, B = 100% ACN
	Gradient:	100% A hold 1 min, to 50% A over a 15 min, hold 10 min
	Flow Rate:	1.0 mL/min
	Detector:	PDA at 211 nm
	Relative mass fraction of the main component:	
	Initial analysis:	Mean = 99.75% s = 0.07% (3 sub samples in duplicate November 2000)
Karl Fischer titration:		Moisture content < 0.2% mass fraction (April 2007 and April 2010) Moisture content < 0.1% mass fraction (January 2013, December 2017 & June 2022)
Thermogravimetric analysis:		Non-volatile residue < 0.1% mass fraction

Spectroscopic and other characterisation data

GC-MS:

Parent compound:

Instrument:	HP6890/5973
Column:	HP Ultra 2, 17 m x 0.25 mm I.D. x 0.25 µm
Program:	180 °C (1 min), 15 °C/min to 300 °C (3 min)
Injector:	260 °C
Transfer line temp:	280 °C
Carrier:	Helium, 1.0 ml/min
Split ratio:	30/1

Pentafluorobenzyl derivative:

Instrument:	HP6890/5973
Column:	HP Ultra 2, 17 m x 0.20 mm ID x 0.11 µm
Program:	95 °C, 35 °C/min to 175 °C (6min), then 35 °C/min to 310 °C (3 min)
Injector:	260 °C
Transfer line temp:	300 °C
Carrier:	Helium
Split ratio:	15/1

The retention times of the parent material and PFB derivative are reported along with the major peaks in the mass spectrum. The latter are reported in mass / charge ratios and (in brackets) as a percentage relative to the base peak.

Parent (3.85 min): 146 (1), 117 (2), 105 (3), 79 (4), 77 (10), 58 (100), 56 (4) *m/z*

Spectrum obtained is consistent with published reference data.
PFB derivative (7.45 min): 253 (34), 252 (56), 234 (14), 218 (10), 195 (100), 167 (12) *m/z*

IR:

Instrument:	Perkin-Elmer FT-IR
Range:	4000-400 cm^{-1}, KBR disc
Peaks:	3321, 2977, 1479, 1438, 1155, 1064, 1024, 951, 763, 705 cm^{-1}

Spectrum obtained is consistent with published reference data

^{1}H NMR:

Instrument:	Bruker DMX-500
Field strength:	500 MHz
Solvent:	$CDCl_3$ (7.26 ppm)
Spectral data:	δ 0.86 (3H, d), 2.37 (3H, s), 2.59 (1H, m), 4.16 (1H, d), 7.27 (5H, m) ppm

^{13}C NMR:

Instrument:	Bruker DMX-500
Field strength:	125 MHz
Solvent:	$CDCl_3$ (77.16 ppm)
Spectral data:	δ 15.3, 33.3, 61.1, 77.4, 126.9, 127.5, 128.1, 142.4 ppm

Melting point: 119-120 °C by DSC

Microanalysis:

Found:	C = 72.8%; H = 9.0%; N= 8.5% (November 2000)
Calculated:	C = 72.7%; H = 9.2%; N= 8.5% (Calculated for $C_{10}H_{15}NO$)

Base titration: Acid base titration of pseudoephedrine; 99.43 % mass fraction, s = 0.17%