Australian Government
Department of Industry, Science and Resources

National Measurement Institute

CIPM MRA

NATA
WORLD RECOGNISED ACCREDITATION

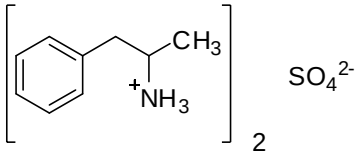
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D961: d-(+)-Amphetamine sulfate

Report ID: D961.2021.02 (Bottled 220630)

Chemical Formula: $(C_9H_{13}N)_2.H_2SO_4$

Molecular Weight: 368.5 g/mol (H_2SO_4), 135.2 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
10-D-18	51-63-8 (H_2SO_4) 300-62-9 (base)	99.8 ± 0.3%

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

IUPAC name: (2S)-1-Phenyl-2-propanamine sulfate (2:1)

Expiration of certification: The property values are valid till 15 April 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 sourced from an external supplier, and 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 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.
2 November 2022

This report supersedes any issued prior to 2 November 2022.

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

CIPM MRA notice: This certificate is consistent with the capabilities that are included in Appendix C of the MRA drawn up by the CIPM. Under the CIPM MRA, all participating institutes recognise the validity of each other's calibration and measurement certificates for the quantities, ranges and measurement uncertainties specified in the KCDB (for details see http://www.bipm.org/kcdb/). The "CIPM MRA Logo" and this statement attest only to the measurement(s) applied for determining the certified values on the certificate.

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 ^{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 quantitative nuclear magnetic resonance (qNMR) and qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

The purity value by qNMR was obtained using the three proton doublet at 1.31 ppm measured against a certified internal standard of potassium hydrogen maleate.

The enantiomeric purity of this material was estimated by capillary electrophoresis over dynamically coated capillaries using cyclodextrin as chiral additive in buffer. Supporting evidence was provided by relative peak area response of the Mosher's acid derivatised d and l enantiomer on GC-MSD.

Enantiomeric Purity: $d \approx 95.3\ \% = \frac{d}{(d+l)} \times 100 \quad [\text{ee} = 90.6\%\,(\text{d})]$

The main component of this material is d-(+)-amphetamine sulfate. The enantiomer l-(-)-amphetamine sulfate is also present. The stated chemical purity of the analyte represents the combined mass fractions of d and l enantiomer in the material.

GC-FID:	Instrument:	Varian CP-3800		
	Column:	VF-1ms, 30 m × 0.32 mm I.D. × 0.25 μm		
	Program:	60 °C (1 min), 10 °C/min to 100 °C, 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 as the free base:			
	Initial analysis:	Mean = 100%, s = 0.00% (10 sub samples in duplicate, October 2010)		
	Re-analysis:	Mean = 99.99%, s = 0.007% (5 sub samples in duplicate, April 2021)		
GC-FID:	Instrument:	Varian CP-3800		
	Column:	TG-17ms, 30 m × 0.32 mm I.D. × 0.25 μm		
	Program:	60 °C (1 min), 10 °C/min to 100 °C, 30 °C/min to 280 °C (10 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 = 100%, s = 0.00% (10 sub samples in duplicate, October 2010)		
	Re-analysis:	Mean = 100%, s = 0.002% (5 sub samples in duplicate, October 2013)		
Thermogravimetric analysis:		Volatile content < 0.1% and non-volatile residue < 0.2% mass fraction (October 2010)		
Karl Fischer analysis:		Moisture content 0.2% mass fraction (October 2010 and April 2021)		
QNMR:	Instrument:	Bruker Avance DMX-600		
	Field strength:	600 MHz		
	Solvent:	D_2O (4.79 ppm)		
	Internal standard:	Potassium hydrogen maleate (98.6% mass fraction)		
	Initial analysis:	Mean (1.31 ppm) = 100.6%, s = 0.4% (5 sub samples, October 2010)		

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 300 °C (3 min)
	Injector:	280 °C
	Split ratio:	20/1
	Transfer line temp:	300 °C
	Carrier:	Helium
	Scan range:	50-550 *m/z*
	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 (7.1 min):	134 (1), 120 (4), 91 (18), 65 (8), 44 (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:	15 V
	Peak:	369 ($2M.H_2SO_4+H^+$), 271 ($2M+H^+$), 136 ($M+H^+$) *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:	No solvents detected
TLC:	Conditions:	Kieselgel $60F_{254}$. Methanol/conc. ammonia (40/1.2) Single spot observed, R_f = 0.5
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3028, 2942, 2839, 2756, 2663, 2558, 2161, 1606, 1544, 1496, 1456, 1393, 1371, 1228, 1123, 1052, 740, 699, 619, 602, 461 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance III-400
	Field strength:	400 MHz
	Solvent:	D_2O (4.79 ppm)
	Spectral data:	δ 1.31 (3H, d, *J* = 6.6 Hz), 2.95 (2H, d, *J* = 7.2 Hz), 3.63 (1H, m), 7.31-7.45 (5H, m) ppm
^{13}C NMR:	Instrument:	Bruker Avance III-500
	Field strength:	126 MHz
	Solvent:	D_2O
	Spectral data:	δ 17.5, 40.1, 49.1, 127.4, 129.0, 129.4, 136.2 ppm
Melting point:		> 300 °C
Microanalysis:	Found:	C = 58.6%; H = 7.8%; N = 7.9%; S = 8.6% (October 2010)
	Calculated:	C = 58.7%; H = 7.7%; N = 7.6%; S = 8.7% (Calculated for $(C_9H_{13}N)_2.H_2SO_4$)