Australian Government
Department of Industry, Innovation and Science

National Measurement Institute

NATA
ACCREDITED FOR TECHNICAL COMPETENCE

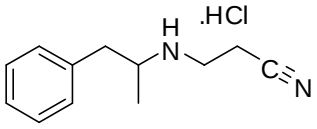
CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D500b: Fenproporex hydrochloride

Report ID: D500b.2019.01 (Bottled 160810)

Chemical Formula: $C_{12}H_{16}N_2.HCl$

Molecular Weight: 224.7 g/mol (HCl) 188.3 g/mol (base)



Certified value

Batch No.	CAS No.	Purity (mass fraction)
12-D-18	**18305-29-8**	**99.3 ± 1.2%**

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

IUPAC name: 3-[(1-Phenyl-2-propanyl)amino]propanenitrile hydrochloride (1:1)

Expiration of certification: The property values are valid till 20 June 2024, 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, 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% coverage 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 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.
28 June 2019

This report supersedes any issued prior to 28 June 2019

NATA logo notice: Accredited for compliance with ISO Guide 17034. Accreditation No. 198 / Corporate Site No. 20844. The results of the tests, calibrations and/or measurements included in this document are traceable to Australian/national standards.

Legal notice: Neither NMIA as a representative of the Commonwealth of Australia, nor any person acting on NMIA's behalf, assumes any liability with respect to the use of, or for damages resulting from the use of, this reference material or the information contained in this document.

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:	Varian CP-3800
	Column:	HP-5, 30 m × 0.32 mm I.D. × 0.25 µm
	Program:	100 °C (1 min), 10 °C/min to 220 °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:	
	Initial analysis:	Mean = 99.5%, s = 0.03% (10 sub samples in duplicate, November 2012)
	Re-analysis:	Mean = 99.6%, s = 0.02% (7 sub samples in duplicate, August 2016)
	Re-analysis:	Mean = 99.5%, s = 0.01% (5 sub samples in duplicate, June 2019)
GC-FID:	Instrument:	Varian CP-3800
	Column:	VF-1MS, 30 m × 0.32 mm I.D. × 0.25 µm
	Program:	100 °C (1 min), 10 °C/min to 220 °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:	
	Initial analysis:	Mean = 99.6%, s = 0.03% (10 sub samples in duplicate, November 2012)
	Re-analysis:	Mean = 99.5%, s = 0.01% (5 sub samples in duplicate, October 2013)
Thermogravimetric analysis:		Non-volatile residue < 0.2% mass fraction (October 2012). The volatile content (e.g. organic solvents and/or water) could not be determined because of the inherent volatility of the material.
Karl Fischer analysis:		Moisture content 0.2% mass fraction (October 2012, October 2013 and August 2016) Moisture content 0.3% mass fraction (June 2019)

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:	90 °C (1 min), 10 °C/min to 180 °C (7 min), 30 °C/min to 300 °C (3 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 (10.3 min):	97 (100), 91 (21), 56 (45), 44 (8) *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:	20 V
	Peak:	189.1 ($M+H^+$) *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:	*tert*-Butyl methyl ether
TLC:	Conditions:	Kieselgel 60F_{254}. Hexane/ethyl acetate/diethyl amine (10/10/1) Single spot observed, R_f = 0.47. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3004, 2765, 2634, 2453, 2260, 2060, 1582, 1483, 1453, 1281, 786 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Gyro-300
	Field strength:	400 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.25 (3H, d, *J* = 6.8 Hz), 2.75 (1H, dd, *J* = 10.1, 13.2 Hz), 3.01 (2H, dt, *J* = 1.2, 7.6 Hz), 3.27 (1H, dd, *J* = 4.4, 13.2 Hz), 3.40-3.51 (2H, m), 3.58 (1H, m), 7.27-7.38 (5H, m) ppm *tert*-Butyl methyl ether estimated at 0.1% mass fraction was observed in the ^{1}H NMR.
^{13}C NMR:	Instrument:	Bruker Bruker Gyro-300
	Field strength:	75 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 15.8, 15.9, 40.1, 41.9, 57.5, 117.5, 128.4, 130.0, 130.4, 137.1 ppm
Melting point:		140-144 °C
Microanalysis:	Found:	C = 64.2%; H = 7.7%; N = 12.6%; Cl = 15.9% (September, 2012)
	Calc:	C = 64.1%; H = 7.6%; N = 12.5%; Cl = 15.8% (Calculated for $C_{12}H_{16}N_2$. HCl)