Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

NATA
ACCREDITED FOR TECHNICAL COMPETENCE

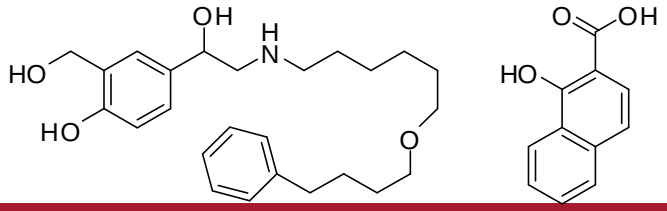
REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA M904: Salmeterol hydroxynaphthoate

Report ID: M904.2018.03

Chemical Formula: $C_{36}H_{45}NO_7$

Molecular Weight: 603.75 g/mol



Property value

Batch No.	CAS No.	Purity estimate
07-D-03	94749-08-3	97.6%

IUPAC name: 1-Hydroxy-2-naphthoic acid - 2-(hydroxymethyl)-4-(1-hydroxy-2-{[6-(4-phenylbutoxy)hexyl]amino}ethyl)phenol (1:1).

Expiration of certification: The property values are valid till 22 November 2023, 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 solid sourced from external supplier, 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 reference material is recommended for qualitative analysis only.

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 4 ºC in a closed container in a dry, dark area.

Stability: In the absence of long term stability data the stability of this material has been judged from stability trials conducted on similar materials by NMI Australia over the last ten years. This material has demonstrated stability over a minimum period of five years. 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 qNMR on five 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.
29 May 2020

This report supersedes any issued prior to 29 May 2020

NATA logo notice: Accredited for compliance with ISO 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: 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 purity value was obtained from quantitative nuclear magnetic resonance (qNMR). The purity estimate by qNMR was obtained using one proton doublet at 8.4 ppm against a certified internal standard of potassium hydrogen maleate. Supporting evidence is provided by Karl Fischer analysis, thermogravimetric analysis and elemental microanalysis.

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QNMR:	Instrument:	Bruker DMX-400
	Field strength:	400 MHz
	Solvent:	d_6-DMSO/D_2O
	Internal standard:	Potassium hydrogen maleate
	Initial analysis:	Mean (8.2 ppm) = 98.6%, s = 0.5% (5 sub samples, November 2008)
	Re-analysis:	Mean (8.2 ppm) = 97.6%, s = 0.5% (3 sub samples, December 2013)
QNMR:	Instrument:	Bruker Avance-500
	Field strength:	500 MHz
	Solvent:	d_4-acetic acid (2.05 ppm)
	Internal standard:	Potassium hydrogen maleate
	Re-analysis:	Mean (8.4 ppm) = 97.4%, s = 0.2% (3 sub samples, November 2018)
Karl Fischer analysis:		Moisture content < 0.7% mass fraction (June 2007) Moisture content < 0.2% mass fraction (December 2013)
Thermogravimetric analysis:		Volatile content < 0.1% and non-volatile residue < 0.2% mass fraction (June 2007)

Spectroscopic and other characterisation data

GC-MS:	*Tris*-TMS derivative	
	Instrument:	Agilent 5973MSD
	Column:	HP-1MS, 30 m × 0.2 mm I.D. × 0.2 μm
	Program:	150 °C (1 min), 20 °C/min to 300 °C, (10 min)
	Injector:	250 °C
	Split ratio:	20/1
	Transfer line temp:	320 °C
	Carrier:	Helium, 1.5 mL/min
	Scan range:	50-550 *m/z*
	The retention time of the *bis*-TMS derivative of hydroxynaphthoate (6.2 mins) and the *tris*-TMS derivative of salmeterol (15.8 mins) are reported along with the major peaks in the mass spectrum. The latter are reported as mass to charge ratios and (in brackets) as a percentage relative to the base peak.	
	Bis-TMS (6.2 min):	332 (M^+, 1), 319 (11), 318 (28) 317 (100), 243 (5), 185 (8) 147 (7), 141 (4), 73 (16) *m/z*
	Tris-TMS (15.8 min):	616 (1), 526 (2), 371 (8), 370 (18), 369 (53), 263 (19), 262 (100), 207 (3), 147 (4), 112 (6), 91 (12), 73 (19) 44 (4) *m/z*
ESI-MS:	Instrument:	Micromass Quatro Micro
	Operation:	Positive ion mode, direct infusion at 5 μL/min
	Ionisation:	ESI spray voltage at 3.0 kV positive ion
	EM voltage:	500 V
	Cone voltage:	20 V
	Peak:	416.1 ($M+H^+$) *m/z*
IR:	Instrument:	Biorad FTS300MX FT-IR
	Range:	4000-400cm^{-1}, KBr powder
	Peaks:	3309, 2940, 2859, 2361, 1579, 1557, 1466, 1409, 1302, 1275, 1096, 998, 884, 799, 775, 698 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX600
	Field strength:	600 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 1.32-1.40 (4H, m), 1.48-1.57 (4H, m), 1.60-1.65 (2H, m), 1.65-1.74 (2H, m), 2.59 (2H, t, *J* = 7.6 Hz), 2.99 (2H, m), 3.06-3.12 (2H, m), 3.35 (2H, t, *J* = 6.4 Hz), 3.37 (2H, t, *J* = 6.5 Hz), 4.66 (2H, s), 4.89 (1H, m), 6.78 (1H, d, *J* = 8.2 Hz), 7.11-7.25 (7H, m), 7.35 (1H, d, *J* = 2.2 Hz), 7.41 (1H, ddd, *J* =1.2, 6.8, 9.5 Hz), 7.48 (1H, ddd, *J* = 1.3, 6.9, 9.5 Hz), 7.72 (1H, bd, *J* = 8.2 Hz), 7.88 (1H, d, *J* = 8.6 Hz), 8.29 (1H, dt, *J* = 0.6, 8.3 Hz) ppm
^{13}C NMR:	Instrument:	Gyro 300
	Field strength:	150 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 26.8, 27.0, 27.4, 29.2, 30.3, 30.4, 36.6, 55.2, 60.8, 70.1, 71.6, 71.7, 112.9, 116.0, 117.7, 124.4, 125.6, 126.6, 126.7, 126.9, 127.0, 127.8, 128.3, 128.6, 128.9, 129.3, 129.4, 132.9, 137.9, 143.7, 156.3, 161.0, 176.9 ppm
Melting point:		138-140 °C
Microanalysis:	Found:	C = 72.1 %; H = 7.4 %; N = 2.3% (June 2007)
	Calculated:	C = 71.6 %; H = 7.5 %; N = 2.3% (Calculated for $C_{36}H_{45}NO_7$)