

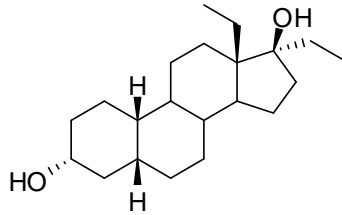


REFERENCE MATERIAL PRODUCT INFORMATION SHEET

Report ID: D818b.2018.01 (Ampouled 161208a)

This batch of ampoules was prepared from the bulk material on 8th December 2016.

Compound Name: (±)-18a-Homo-17α-ethyl-5β-estrane-3α, 17β-diol Description: White powder
Collection Number: D818b Batch Number: 16-S-08
Chemical Formula: C₂₁H₃₆O₂ Molecular Weight: 320.5
CAS Registry Number: 24366-75-4 Release date: 7th December 2016
Structure: Metabolite of norbolethone



Relative stereochemistry

Synonyms: (±)-18a-Homo-19-nor-17α-pregnane-3α, 17β-diol
(±)-13β, 17α-Diethyl-5β-gonane-3α, 17β-diol
(±)-(3α,5β,17α)-13-Ethyl-18,19-dinorpregnane-3,17-diol

The compound is supplied as a dried aliquot in a sealed ampoule and is intended for a single use to prepare a standard solution containing D818b. Open the ampoule and carefully rinse the interior at least three times with a suitable organic solvent (e.g. chloroform). This will transfer 982 ± 19 µg of anhydrous (±)-18a-homo-17α-ethyl-5β-estrane-3α, 17β-diol. The uncertainty is stated at the 95% coverage interval.

GC-FID: Instrument: Agilent 7890A
Column: HP-1MS, 30 m × 0.32 mm I.D. × 0.25 µm
Program: 180 °C (1 min), 15 °C/min to 250 °C (5 min), 30 °C/min to 300 °C (3 min)
Injector: 250 °C Detector Temp: 320 °C
Carrier: Helium Split ratio: 20/1
Relative peak area of main component :
Initial analysis: Mean = 98.4%, s = 0.01% (7 ampoules in duplicate, December 2016)
Re- analysis: Mean = 98.4%, s = 0.01% (5 ampoules in duplicate, November 2017)
Re- analysis: Mean = 98.5%, s = 0.00% (5 ampoules in duplicate, November 2018)

The following analytical data was obtained on the bulk material subsequently used in the preparation of the ampoules.

The purity value was obtained from a combination of traditional analytical techniques, by subtraction from 100% of total impurities by GC-FID, thermogravimetric analysis, Karl Fischer analysis and ¹H NMR spectroscopy. Supporting evidence is provided by headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID:	Instrument:	Agilent 7890A	
	Column:	HP-1MS, 30 m × 0.32 mm I.D. × 0.25 μm	
	Program:	180 °C (1 min), 15 °C/min to 250 °C (5 min), 30 °C/min to 300 °C (3 min)	
	Injector:	250 °C	Detector Temp: 320 °C
	Carrier:	Helium	Split ratio: 20/1
	Relative peak area of main component :		
	Initial analysis:	Mean = 98.4%, s = 0.02% (10 sub samples in duplicate, September 2016)	
Thermogravimetric analysis:	Volatile content < 0.1% and non volatile residue < 0.2% mass fraction (June 2016)		
Karl Fischer analysis:	Moisture content 0.3% mass fraction (September 2016)		

Spectroscopic and other characterisation data

GC-MS:	Parent compound:	
	Instrument:	Agilent 6890/5973
	Column:	HP-1MS, 30 m x 0.25 mm I.D. x 0.25 µm
	Program:	180 °C (1 min), 15 °C/min to 250 °C (5 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
	<i>Bis</i> -TMS derivative:	
	Instrument:	Agilent 6890/5973
	Column:	HP-1MS, 30 m x 0.25 mm I.D. x 0.25 µm
	Program:	180 °C (1 min), 15 °C/min to 250 °C (5 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 times of the parent compound and <i>bis</i> -TMS derivative are reported along 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.	
	Parent (11.3 min):	320 (M ⁺ , 2), 302 (17), 291 (21), 273 (82), 255 (100), 231 (35), 230 (35), 217 (29), 215 (29), 201 (30), 187 (14), 173 (13), 161 (20), 159 (21), 147 (29), 121 (40), 107 (34), 91 (43), 79 (37), 67 (34), 57 (34) <i>m/z</i>
	<i>Bis</i> -TMS (12.6 min):	435 (M ⁺ , 22), 345 (22), 255 (36), 157 (100), 144 (59), 75 (38), 73 (37) <i>m/z</i>
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:	Ethyl acetate, hexane
TLC:	Conditions:	Kieselgel 60F ₂₅₄ . Chloroform/ethyl acetate (4/1) Single spot observed, R _f = 0.38. Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS3000MX
	Range:	4000-400 cm ⁻¹ , KBr powder
	Peaks:	3370, 2929, 2871, 1454, 1374, 1150, 1031, 870 cm ⁻¹
¹ H NMR:	Instrument:	Bruker Avance III 500
	Field strength:	500 MHz Solvent: CDCl ₃ (7.26 ppm)
	Spectral data:	δ 0.85 (1H, m), 0.96 (3H, t, <i>J</i> = 7.3 Hz), 0.97 (3H, t, <i>J</i> = 7.3 Hz), 1.03 (1H, m), 1.10-1.30 (8H, m), 1.32-1.72 (15H, m), 1.74-1.84 (2H, m), 1.87-1.97 (2H, m), 3.63 (1H, m) ppm
	Ethyl acetate estimated at 0.6% mass fraction by ¹ H NMR	
¹³ C NMR:	Instrument:	Bruker Avance III 500
	Field strength:	126 MHz Solvent: CDCl ₃ (77.2 ppm)
	Spectral data:	δ 7.8, 10.1, 20.4, 23.2, 25.7, 26.2, 26.3, 28.0, 29.89, 29.92, 31.7, 34.5, 35.9, 36.6, 38.4, 40.0, 42.7, 48.1, 51.6, 71.9, 85.7 ppm
Melting point:	188 °C	
Microanalysis:	Found: C = 78.5%; H = 11.5% (September 2016) Calc: C = 78.7%; H = 11.3% (Calculated for C ₂₁ H ₃₆ O ₂)	

Expiration of certification

The property values are valid till 2nd November 2021, i.e. three 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 ampoules that have been opened. In such cases it is recommended that the end-user conduct their own in-house stability trials.

The long-term stability of the compound in solution has not been examined.

In the absence of stability data the measurement uncertainty at the 95% coverage interval has been expanded to accommodate any potential change in the property value. The stability component has been estimated from stability trials conducted on similar materials by NMI Australia over the last 10 years.

Homogeneity assessment

The homogeneity of the material was assessed using purity assay by GC-FID on seven randomly selected ampoules 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.

Recommended storage

When not in use, this material should be stored at or below 4 °C in a closed container in a dry, dark area.

Intended use

This reference material should be used for qualitative analysis only

Caution

Treat as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust.

Legal notice

Neither NMI nor any person acting on NMI'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 certificate.

Authorised by:

S. R. Davies

Dr Stephen R Davies
Team Leader,
Chemical Reference Materials, NMI
Dated: 14 December, 2018.

Characterisation data and property values specified in this report supersede those in all reports issued prior to 14th December 2018.