Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

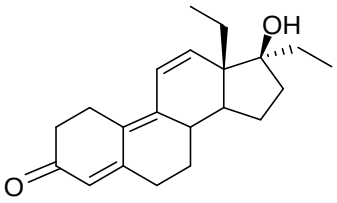
REFERENCE MATERIAL PRODUCT INFORMATION SHEET

NMIA D872e: Tetrahydrogestrinone

Report ID: D872e.2024.01

Chemical Formula: $C_{21}H_{28}O_2$

Molecular Weight: 312.5 g/mol



Property value

Batch No.	CAS No.	Purity by HPLC-UV (240 nm)
13-S-08	**618903-56-3**	**76.8 ± 1.3%**

The uncertainty is based on the standard deviation of five subsamples analysed in duplicate and is stated at the 95% confidence limit (k = 2).

IUPAC name: (8S,13S,14S,17S)-13,17-Diethyl-17-hydroxy-1,2,6,7,8,13,14,15,16,17-decahydro-3H-cyclopenta[a]phenanthren-3-one.

Expiration of certification: The property values are valid till 08 January 2029, 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: Yellow powder prepared by synthesis, 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 and is not intended for use as a calibrator. The material does not have certified reference material status as metrological traceability of the stated purity value to the SI unit for mass (kg) has not been established.

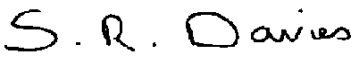
Instructions for use: Equilibrate the bottled material to room temperature before opening.

Recommended storage: When not in use this material should be stored at or below -18 ºC in a closed container in a dry, dark area.

Stability: This material has been shown to decompose over time (see ^{1}H quantitative NMR analysis summary). 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 HPLC with UV detection on seven 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.



Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
31 January 2024

This report supersedes any issued prior to 31 January 2024.

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 purity estimate was determined from quantitative NMR using dimethyl terephthalate as the internal standard.

Supporting evidence is provided by HPLC with UV detection, thermogravimetric analysis, Karl Fischer analysis and ^{1}H NMR spectroscopy, and elemental microanalysis.

QNMR:	Instrument:	Bruker Avance-500
	Field strength:	500 MHz
	Solvent:	$CDCl_3$ (7.26 ppm)
	Internal standard:	Dimethyl terephthalate (100% mass fraction)
	Initial analysis:	Mean (5.78 ppm) = 91.5%, s = 0.8% (5 sub samples, July 2013)
	Initial analysis:	Mean (6.58 ppm) = 91.5%, s = 0.9% (5 sub samples, July 2013)
	Re-analysis:	Mean (5.78 ppm) = 87.0%, s = 0.4% (3 sub samples, August 2013)
	Re-analysis:	Mean (5.78 ppm) = 80.2%, s = 0.9% (3 sub samples, January 2014)
	Re-analysis:	Mean (6.58 ppm) = 80.7%, s = 0.9% (3 sub samples, January 2014)
	Re-analysis:	Mean (5.79 ppm) = 80.7%, s = 0.3% (5 sub samples, June 2014)
	Re-analysis:	Mean (5.79 ppm) = 76.6%, s = 0.6% (3 sub samples, July 2015)
	Re-analysis:	Mean (5.79 ppm) = 79.3%, s = 0.5% (3 sub samples, June 2016)
	Re-analysis:	Mean (5.79 ppm) = 79.5%, s = 0.8% (5 sub samples, May 2017)
	Re-analysis:	Mean (5.79 ppm) = 78.3%, s = 0.7% (3 sub samples, May 2018)
HPLC:	Instrument:	Shimadzu Binary pump LC-20AB, SIL-20 A HT auto sampler
	Column:	Alltima C-18 (4.6 mm x 150 mm)
	Column oven:	40 °C
	Mobile Phase:	Acetonitrile/MilliQ water (50:50)
	Flow rate:	1 mL/min
	Detector:	Shimadzu SPD-M20A PDA detector operating at 240 nm
	Relative peak area response of main component:	
	Initial analysis:	Mean = 94.2%, s = 0.7% (7 sub samples in duplicate, August 2013)
	Re-analysis:	Mean = 76.8%, s = 0.2% (5 sub samples, July 2021)
	Re-analysis:	Mean = 76.6%, s = 0.1% (5 subsamples, January 2024)
Thermogravimetric analysis:		Volatile content 0.8% mass fraction Non volatile residue < 0.2% mass fraction (August 2013)
Karl Fischer analysis:		Moisture content 1.4% mass fraction (August 2013) Moisture content 1.7% mass fraction (December 2023)

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:	180 °C (1 min), 10 °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 parent compound is 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 (12.8 min):	312 (M^+, 47), 265 (55), 240 (45), 227 (100), 211 (29), 198 (15), 181 (13), 169 (15), 167 (14), 155 (14), 141 (21), 128 (16), 115 (14), 57 (17) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Chloroform/ethyl acetate (4/1) Single spot observed, R_f = 0.5 Visualisation with UV at 254 nm
IR:	Instrument:	Biorad FTS3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr powder
	Peaks:	3456, 2959, 2936, 2878, 1724, 1647, 1570, 1384, 1279, 1232, 1211, 1001, 857, 784 cm^{-1}
^{1}H NMR:	Instrument:	Bruker Avance-50
	Field strength:	500 MHz
	Solvent:	MeOH-d_4 (3.31 ppm)
	Spectral data:	δ 0.96 (3H, t, *J* = 7.4 Hz), 1.02 (3H, t, *J* = 7.4 Hz), 1.25 (1H, m), 1.40 (1H, m), 1.45-1.84 (7H, m), 1.92 (1H, m), 2.01 (1H, m) 2.44 (2H, t, *J* = 7.0 Hz), 2.53-2.65 (3H, m), 2.80 (1H, m), 2.91 (1H, m), 5.74 (1H, s), 6.46 (1H, d, *J* = 10.1 Hz), 6.65 (1H, d, *J* = 10.2 Hz) ppm
		Methanol estimated at 0.4% mass fraction was observed in the ^{1}H NMR
^{13}C NMR:	Instrument:	Bruker Avance III-400
	Field strength:	101 MHz
	Solvent:	MeOH-d_4 (49.0 ppm)
	Spectral data:	δ 7.9, 11.8, 23.4, 25.2, 25.4, 28.4, 31.2, 32.6, 33.8, 37.5, 39.1, 50.5, 52.5, 84.8, 123.5, 125.6, 127.8, 143.2, 144.8, 160.1, 202.0 ppm
Melting point:		76-78 °C
Microanalysis:	Found:	C = 78.0%; H = 8.8% (July, 2013)
	Calculated:	C = 80.7%; H = 9.0% (Calculated for $C_{21}H_{28}O_2$)