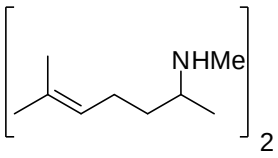
Australian Government
Department of Industry, Innovation and Science

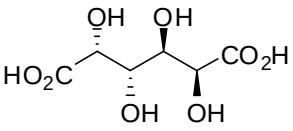
National Measurement Institute

NATA ACCREDITED FOR TECHNICAL COMPETENCE

# CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

## NMIA D940: Isometheptene mucate




Report ID: D940.2019.01

Chemical Formula: $C_{24}H_{48}N_2O_8$

Molecular Weight: 492.7 g/mol

## Certified value

| Batch No. | CAS No. | Purity (mass fraction) |
|---|---|---|
| 09-D-07 | 7492-31-1 | 99.5 ± 0.5% |

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

**IUPAC name:** N,6-Dimethyl-5-hepten-2-ammonium - D-galactarate

**Expiration of certification:** The property values are valid till 23 July 2029, i.e. ten 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 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 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:** 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 5 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 $^1$H NMR on five randomly selected 20 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.
7 August 2019

This report supersedes any issued prior to 7 August 2019

**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 certified purity value was obtained by quantitative nuclear magnetic resonance (qNMR). A combination of the three-proton doublet at 1.31 ppm, and the three-proton singlet at 2.68 ppm were measured against a certified internal standard of potassium hydrogen maleate or glycine.

Supporting evidence is provided by GC-FID, Karl-Fischer analysis, thermogravimetric analysis and elemental microanalysis.

| | | | | |
|---|---|---|---|---|
| GC-FID: | Instrument: | Agilent 6890 | | |
| | Column: | HP-1, 30 m × 0.32 mm I.D. × 0.25 μm | | |
| | Program: | 70 °C (15 min), 50 °C/min to 300 °C (5 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 = 99.9%, s = 0.1% (10 sub samples in duplicate, April 2009) | | |
| Karl Fischer analysis: | | Moisture content < 0.2% mass fraction (February 2009 and May 2019) | | |
| Thermogravimetric analysis: | | Volatiles content not determined due to the nature of the material. Non-volatile residue < 0.2% mass fraction (April 2009) | | |
| QNMR: | Instrument: | Bruker Avance-III-500 | | |
| | Field strength: | 500 MHz | Solvent: $D_2O$ | |
| | Internal standard: | Potassium hydrogen maleate | | |
| | Initial analysis: | Mean = 99.4%, s = 1.1% (3 sub samples, March 2009) | | |
| | Re-analysis: | Mean = 99.6%, s = 0.9% (5 sub samples, June 2010) | | |
| | Re-analysis: | Mean = 99.9%, s = 0.4% (5 sub samples, July 2013) | | |
| | Re-analysis: | Mean = 99.4%, s = 0.6% (5 sub samples, June 2016) | | |
| QNMR: | Instrument: | Bruker Avance-III-500 | | |
| | Field strength: | 500 MHz | Solvent: $D_2O$ | |
| | Internal standard: | Glycine (100.0% mass fraction) | | |
| | Initial analysis: | Mean (2.68 ppm) = 100.2%, s = 0.1% (4 sub samples, July 2019) | | |

## Spectroscopic and other characterisation data

| | | |
|---|---|---|
| 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: | 20 V |
| | Peak: | Isometheptene 142 ($M+H^+$) *m/z* |
| ESI-MS: | Instrument: | Micromass Quatro LC Micro |
| | Operation: | Negative ion mode, direct infusion at 5 μL/min |
| | Ionisation: | ESI spray voltage at 3.2 kV negative ion |
| | EM voltage: | 650 V |
| | Cone voltage: | 20 V |
| | Peak: | Mucate 209 ($M-H^+$) *m/z* |
| TLC: | Conditions: | Kieselgel 60F254. diethyl ether/tert-butyl methyl ether/diethylamine (45/45/10)<br>Single spot observed, $R_f$ = 0.5. Visualisation with vanillin |
| IR: | Instrument: | Bruker Alpha Platinum ATR |
| | Range: | 4000-400 $cm^{-1}$,neat |
| | Peaks: | 3287, 3163, 2960, 2740, 2441, 1590, 1424, 1367, 1107, 1050, 971, 767 $cm^{-1}$ |
| $^1$H NMR: | Instrument: | Bruker Avance III-500 |
| | Field strength: | 500 MHz |
| | Solvent: | $D_2O$ (4.79 ppm) |
| | Spectral data: | δ 1.31 (6H, d, *J* = 6.6 Hz), 1.54-1.65 (2H, m), 1.64 (6H, s), 1.71 (6H, d, *J* = 0.7 Hz), 1.73-1.82 (2H, m), 2.11 (4H, m), 2.68 (6H, s), 3.22 (2H, m), 3.95 (2H, s), 4.25 (2H, s), 5.19 (2H, m) ppm |
| $^{13}$C NMR: | Instrument: | Bruker Avance III-500 |
| | Field strength: | 126 MHz |
| | Solvent: | $D_2O$ |
| | Spectral data: | δ 14.9, 16.8, 23.1, 24.7, 29.6, 32.2, 55.0, 71.4, 71.7, 122.3, 134.7, 179.4 ppm |
| Melting point: | | 146-148 °C |
| Microanalysis: | Found: | C = 58.7%; H = 10.0%; N = 5.7% (February, 2009) |
| | Calculated: | C = 58.5%; H = 9.8%; N = 5.7% (Calculated for $C_{24}H_{48}N_2O_8$) |