

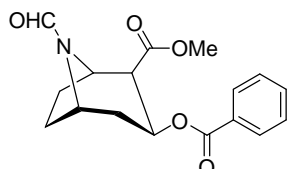


## REFERENCE MATERIAL ANALYSIS REPORT

Report ID: D857b.2017.01

Compound Name: *N*-Formylcocaine  
Collection Number: D857b  
Chemical Formula: C<sub>17</sub>H<sub>19</sub>NO<sub>5</sub>  
CAS Number: 137360-14-6  
Structure:

Description: Viscous oil  
Batch Number: 15-D-24  
Molecular Weight: 317.3  
Release date: 18<sup>th</sup> August 2016



Synonyms: [1*R*-(*exo*, *exo*)]-3-(Benzoyloxy)-8-formyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid methyl ester  
*N*-Formylcocaine

Purity (mass fraction): 91.5 ± 2.0% (95% coverage interval)

The purity value was obtained by quantitative nuclear magnetic resonance (qNMR). The one-proton multiplet at 5.5 ppm was measured against a certified internal standard of maleic acid. Supporting evidence is provided by HPLC with UV detection, thermogravimetric analysis, Karl Fischer analysis, <sup>1</sup>H NMR spectroscopy and elemental microanalysis.

HPLC: Instrument: Waters Model 1525 Binary pump, 717 plus  
Column: Alltima C-18, 5 μm (4.6 mm x 150 mm)  
Column oven: 25 °C  
Mobile Phase: Acetonitrile/MilliQ water (38:62), Isocratic  
Flow rate: 1.0 mL/min  
Detector: Waters 2998 PDA operating at 231.2 nm  
Relative peak area of main component:  
Initial analysis: Mean = 97.9%, s = 0.004% (7 sub samples in duplicate, May 2016)  
Re-analysis: Mean = 97.9%, s = 0.004% (5 sub samples in duplicate, May 2017)

Thermogravimetric analysis: Non-volatile residue < 0.2% mass fraction (January 2016). The volatile content (e.g. organic solvents and/or water) could not be determined by thermogravimetric analysis.

Karl Fischer analysis: Moisture content 1.5% mass fraction (January 2016)  
Moisture content 3.6% mass fraction (May 2017)

qNMR: Instrument: Bruker Avance-III-500  
Field strength: 500 MHz Solvent: DMSO-*d*<sub>6</sub> (2.50 ppm)  
Internal standard: Maleic acid (98.7% mass fraction)  
Initial analysis: Mean (5.5 ppm) = 93.6%, s = 0.1% (2 sub samples, July 2016)

### Spectroscopic and other characterisation data

GC-MS:	Instrument: Agilent 6890/5973 Column: HP-1MS, 30 m x 0.25 mm I.D. x 0.25 $\mu$ m Program: 60 $^{\circ}$ C (1 min), 10 $^{\circ}$ C/min to 300 $^{\circ}$ C (3 min) Injector: 250 $^{\circ}$ C Transfer line temp: 280 $^{\circ}$ 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 (21.9 min): 289 (47), 195 (46), 168 (100), 136 (42), 108 (56), 105 (92), 95 (26), 82 (16), 80 (23), 77 (57), 68 (48), 51 (12), 41 (11) m/z
ESI-MS:	Instrument: Micromass Quattro LC Micro Operation: Positive ion mode, direct infusion at 5 $\mu$ L/min Ionisation: ESI spray voltage at 3.5 kV positive ion EM voltage: 650 V Cone voltage: 20 V Peak: 340.1 (M+Na <sup>+</sup> ) m/z
TLC:	Conditions: Kieselgel 60F <sub>254</sub> . 100% Ethyl acetate. Single spot observed, R <sub>f</sub> = 0.23. Visualization with UV light (254 nm).
IR:	Instrument: BioRad FTS3000MX FT-IR Range: 4000-400 cm <sup>-1</sup> , Neat Peaks: 3464, 2954, 1739, 1718, 1669, 1436, 1389, 1276, 1113, 1035, 714 cm <sup>-1</sup>
<sup>1</sup> H NMR:	Instrument: Bruker Avance III-500 Field strength: 500 MHz Solvent: CDCl <sub>3</sub> (7.26 ppm) Spectral data: Major rotamer (53%) $\delta$ 1.86-1.97 (2H, m), 2.0-2.2 (3H, m), 2.37 (1H, ddd, <i>J</i> = 2.9, 12.1, 12.1 Hz), 3.26 (1H, dd, <i>J</i> = 2.1, 6.6 Hz), 3.65 (3H, s), 4.32 (1H, bd, <i>J</i> = 7.2 Hz), 4.81 (1H, m), 5.54 (1H, m), 7.43 (2H, m), 7.56 (1H, m), 7.95 (2H, m), 8.04 (1H, s) Minor rotamer (47%) $\delta$ 1.86-1.97 (2H, m), 2.0-2.2 (3H, m), 2.54 (1H, ddd, <i>J</i> = 3.1, 11.8, 11.8 Hz), 3.18 (1H, dd, <i>J</i> = 2.5, 6.2 Hz), 3.68 (3H, s), 4.28 (1H, m), 4.95 (1H, d, <i>J</i> = 5.4 Hz), 5.49 (1H, m), 7.43 (2H, m), 7.56 (1H, m), 7.97 (2H, m), 8.18 (1H, s) Ethyl acetate (1.0%) estimated mass fraction was observed in the <sup>1</sup> H NMR.
<sup>13</sup> C NMR:	Instrument: Bruker DMX-600 Field strength: 151 MHz Solvent: CDCl <sub>3</sub> Spectral data: $\delta$ 26.9, 27.4, 27.9, 28.4, 33.4, 35.4, 48.5, 48.7, 49.3, 51.1, 51.9, 52.0, 53.6, 55.5, 66.2, 66.3, 128.4, 128.4, 129.6, 129.7, 133.3, 133.3, 157.8, 158.0, 165.6, 165.7, 169.6, 170.0 ppm
Microanalysis:	Found: C = 62.7%; H = 6.3%; N = 4.3% (January 2016) Calc: C = 64.3%; H = 6.0%; N = 4.4% (Calculated for C <sub>17</sub> H <sub>19</sub> NO <sub>5</sub> )

### Expiration of certification

The property values are valid till 12<sup>th</sup> May 2020, 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 sample bottles 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.

This material has been given a shelf life of three years from the date of re-certification. The material will be re-tested on an annual basis to ensure that the property values are still valid. In the event a product fails the stability trial, notification will be sent to all impacted customers.

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 HPLC 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.

### 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

For *in vitro* laboratory 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: 1 June, 2017.

Characterisation data and property values specified in this report supersede those in all reports issued prior to 1<sup>st</sup> June 2017.