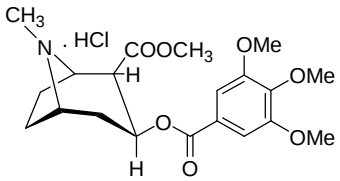
## REFERENCE MATERIAL ANALYSIS REPORT

**Report ID: D855.2017.01**

Compound Name: **3,4,5-Trimethoxycocaine hydrochloride**
Description: White powder
Collection Number: D855
Batch Number: 04-D-02
Chemical Formula: $C_{20}H_{27}NO_7.HCl$
Molecular Weight: 429.9 (HCl salt), 393.4 (base)
CAS Registry Number: 156301-59-6 (base)
Release Date: 22nd July 2004
Structure:




Synonyms: [1*R*-(*exo*,*exo*)-3-(3,4,5-Trimethoxybenzoyloxy)-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid methyl ester

Purity (mass fraction): 94.0 ± 1.2% (95% coverage interval)

Purity estimate obtained from a combination of traditional analytical techniques. The purity estimate by traditional analytical techniques was obtained by subtraction from 100% of total impurities by GC-FID, thermogravimetric analysis, Karl Fischer analysis and $^1$H NMR. Supporting evidence is provided by elemental microanalysis.

Identified impurities: Moisture (4.4% mass fraction)

GC-FID:
- Instrument: Agilent 6890N or 7890
- Column: HP-1, 30 m x 0.32 mm I.D. x 0.25 µm
  HP-1MS 30 m x 0.32 mm I.D. x 0.25 µm
- Program: 150 °C (1 min), 10 °C/min to 300 °C (3 min)
- Injector: 250 °C  Detector Temp: 320 °C
- Carrier: Helium  Split ratio: 20/1

Relative peak area response of main component:
- Initial analysis: Mean = 97.9%, s = 0.1% (10 sub samples in duplicate, January 2004)
- Re-analysis: Mean = 98.5%, s = 0.2% (5 sub samples in duplicate, February 2009)
- Re-analysis: Mean = 98.4%, s = 0.1% (5 sub samples in duplicate, February 2012)
- Re-analysis: Mean = 98.6%, s = 0.02% (5 sub samples in duplicate, February 2017)

Thermogravimetric analysis:
Volatiles content ca 3.6%,
Non-volatile residue < 0.2% mass fraction(January 2004)
Volatiles content ca 3.9% (April 2005)
Volatiles content ca 4.4% (January 2009)

Karl Fischer analysis:
Moisture content 4.3% mass fraction (January 2009)
Moisture content 4.4% mass fraction (February 2012 and March 2017)

**Spectroscopic and other characterisation data**

| | | | |
|---|---|---|---|
| GC-MS: | Instrument: | HP6890/5973 | |
| | Column: | ZB-5, 30 m x 0.25 mm I.D. x 0.30 μm | |
| | Program: | 150 °C, (1 min), 10 °C/min to 300 °C (2 min) | |
| | Injector: | 180 °C | Transfer line temp: 280 °C |
| | Carrier: | Helium, 1.0 mL/min | Split ratio: 20/1 |
| | The retention time is reported with the major peaks in the mass spectrum. The latter are reported as mass/charge ratio and (in brackets) as a percentage relative to the base peak. 16.3 min: 393 ($M^+$, 38), 362 (7), 212 (14), 195 (20), 182 (100), 94 (21), 82 (58) m/z | | |
| TLC: | Conditions: | Kieselgel 60$F_{254}$. Methanol/conc $NH_3$ (200:3). Single spot observed, $R_f$ = 0.59, with UV light (254 nm) | |
| IR: | Instrument: | BioRad FTS3000MX FT-IR | |
| | Range: | 4000-400 $cm^{-1}$, KBr powder | |
| | Peaks: | 3561, 3418, 3376, 3056, 2955, 2837, 1747, 1724, 1590, 1504, 1461, 1417, 1334, 1223, 1125, 986, 763 $cm^{-1}$ | |
| $^1$H NMR: | Instrument: | Bruker DMX-500 | |
| | Field strength: | 500 MHz | Solvent: $D_2O$ |
| | Key spectral data: | δ 2.90 (3H, s), 3.64 (3H, s), 3.81 (3H, s), 3.86 (6H, s), 4.26 (1H, bd), 5.50 (1H, m), 7.12 (2H, s) ppm | |
| $^{13}$C NMR: | Instrument: | Bruker Gyro-300 | |
| | Field strength: | 75.5 MHz | Solvent: $D_2O$ |
| | Spectral data: | δ 22.5, 23.5, 32.4, 38.7, 45.9, 53.2, 56.1, 60.9, 63.0, 63.8, 64.6, 107.0, 124.0, 141.8, 152.3, 165.9, 173.1 ppm | |
| Melting point: | | 173-176 °C | |
| Microanalysis: | | Found: C = 53.7%, H = 6.8%, N = 3.0% (February 2004)<br>Calc.: C = 53.6%, H = 6.8%, N = 3.1% (for $C_{20}H_{27}NO_7.HCl.H_2O$) | |

**Expiration of certification**
The property values are valid till 31st March 2022 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.

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

This material has demonstrated stability over a minimum period of three years. The measurement uncertainty at the 95% coverage interval includes a stability component which has been estimated from annual stability trials.

**Homogeneity assessment**
The homogeneity of the material was assessed using purity assay by GC-FID on ten 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 25 ºC 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: 12 April, 2017.

Characterisation data and property values specified in this report supersede those in all reports issued prior to 12th April 2017.