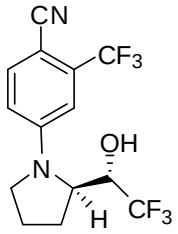
Australian Government
Department of Industry, Science, Energy and Resources

National Measurement Institute

NATA ACCREDITED FOR TECHNICAL COMPETENCE

# CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

## NMIA D1073: LGD-4033




Report ID: D1073.2021.01

Chemical Formula: $C_{14}H_{12}F_6N_2O$

Molecular Weight: 338.3 g/mol

## Certified value

| Batch No. | CAS No. | Purity (mass fraction) |
|---|---|---|
| **20-D-02** | **1165910-22-4** | **99.7 ± 1.3%** |

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

**IUPAC name:** 4-{(2R)-2-[(1R)-2,2,2-Trifluoro-1-hydroxyethyl]-1-pyrrolidinyl}-2-(trifluoromethyl)benzonitrile.

CAS registry number 1165910-22-4 represents the molecular structure as depicted above with the stereochemistry at C2 of the ethyl chain and C2 of the pyrrolidine ring assigned as the R configuration at both centres. The relative stereochemistry and enantiomeric purity for this material have not been confirmed.

**Expiration of certification:** The property values are valid till 4 June 2024, 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.

**Description:** Off-white powder 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.

**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:** The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%. 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:** In the absence of long term stability data the measurement uncertainty at the 95% coverage interval has been expanded to accommodate any potential change in the property value. In the absence of long term 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 short term accelerated stability trials and long term stability trials conducted on similar compounds. 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 GC-FID 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.

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
28 June 2021

This report supersedes any issued prior to 28 June 2021

**NATA logo notice**: Accredited for compliance with ISO 17034. Accreditation No. 198 / Corporate Site No. 14214. 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 mass balance from a combination of traditional analytical techniques, including GC-FID, thermogravimetric analysis, Karl Fischer analysis, and $^{1}$H NMR spectroscopy. The purity value is calculated as per Equation 1.

Purity = (100 % - $I_{ORG}$) x (100 % - $I_{VOL}$ – $I_{NVR}$) Equation 1

$I_{ORG}$ = Organic impurities of related structure, $I_{VOL}$ = volatile impurities, $I_{NVR}$ = non-volatile residue.

Supporting evidence is provided by quantitative NMR and elemental microanalysis.

The purity value obtained by quantitative nuclear magnetic resonance (qNMR). A combination of the one-proton doublet of doublets at 7.77 ppm, the two-proton multiplet at 4.23 ppm were measured against a certified internal standard of *bis*-(trimethylsilyl)benzene.

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

| | | |
|---|---|---|
| QNMR: | Instrument: | Bruker Avance-III-500 |
| | Field strength: | 500 MHz |
| | Solvent: | DMSO-$d_6$ (2.50 ppm) |
| | Internal standard: | *Bis*-(trimethylsilyl)benzene (100.0% mass fraction) |
| | Initial analysis: | Mean (4.23 ppm) = 99.8%, s = 0.4% (5 sub samples, August 2020) |
| | Initial analysis: | Mean (7.77 ppm) = 99.7%, s = 0.3% (5 sub samples, August 2020) |
| GC-FID: | Instrument: | Varian CP-3800 |
| | Column: | DB-17, 30 m × 0.32 mm I.D. × 0.25 μm |
| | Program: | 180 °C (1 min), 10 °C/min to 240 °C (10 min), 20 °C/min to 280 °C (10 min) |
| | Injector: | 250 °C |
| | Detector Temp: | 320 °C |
| | Carrier: | Helium |
| | Split ratio: | 20/1 |
| | Relative mass fraction of the main component: | |
| | Initial analysis: | Mean = 100.0%, s = 0.002% (7 sub samples in duplicate, July 2020) |
| | Re-analysis: | Mean = 100.0%, s = 0.002% (5 sub samples in duplicate, June 2021) |
| Karl Fischer analysis: | | Moisture content ≤ 0.1% mass fraction (August 2020 and May 2021) |
| Thermogravimetric analysis: | | Volatiles content < 0.1% and non-volatile residue < 0.2% mass fraction (September 2020) |

## Spectroscopic and other characterisation data

| | | |
|---|---|---|
| GC-MS: | Instrument: | Agilent 6890/5973 |
| | Column: | DB-5MS, 30 m x 0.25 mm I.D. x 0.25 μm |
| | Program: | 60 °C (1 min), 10 °C/min to 300 °C (5 min) |
| | Injector: | 250 °C |
| | Split ratio: | 20/1 |
| | Transfer line temp: | 280 °C |
| | Carrier: | Helium |
| | Scan range: | 50-550 *m/z* |
| | The retention time of the parent compound is reported 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 (18.9 min): | 338 ($M^+$, 7), 319 (2), 239 (100), 220 (2), 197 (18), 170 (19) *m/z* |
| IR: | Instrument: | Bruker Alpha Platinum ATR |
| | Range: | 4000-400 $cm^{-1}$, neat |
| | Peaks: | 3418, 2221, 1600, 1515, 1456, 1396, 1273, 1187, 1111, 1036, 990, 886, 818, 689, 593, 552, 475 $cm^{-1}$ |
| $^1$H NMR: | Instrument: | Bruker Avance III-500 |
| | Field strength: | 500 MHz |
| | Solvent: | $CDCl_3$ (7.26 ppm) |
| | Spectral data: | δ 2.02-2.22 (4H, m), 2.69 (1H, br s), 3.31 (1H, m), 3.63 (1H, t, *J* = 8.5 Hz), 3.91 (1H, quintet, *J* = 6.9 Hz), 4.24 (1H, t, *J* = 7.5 Hz), 6.91 (1H, dd, *J* = 2.5, 9.0 Hz), 7.07 (1H, d, *J* = 2.0 Hz), 7.56 (1H, d, *J* = 8.5 Hz) ppm |
| | | Dichloromethane estimated at 0.2% mass fraction was observed in the $^1$H NMR |
| $^{13}$C NMR: | Instrument: | Bruker Avance III-500 |
| | Field strength: | 126 MHz |
| | Solvent: | $CDCl_3$ (7.26 ppm) |
| | Spectral data: | δ 23.0, 29.3, 49.5, 58.6, 72.5 (q, $J_{C\text{-}F}$ = 28.9 Hz), 96.1, 111.1 (q, $J_{C\text{-}F}$ = 5.0 Hz), 115.4, 117.2, 122.7 (q, $J_{C\text{-}F}$ = 274 Hz), 124.7 (q, $J_{CF}$ = 282 Hz), 133.9 (q, $J_{C\text{-}F}$ = 31.4), 135.7, 151.3 ppm |
| Melting point: | | 108-109 °C |
| Microanalysis: | Found: | C = 49.6%; H = 3.5%; N = 8.3% (June, 2020) |
| | Calculated: | C = 49.7%; H = 3.6%; N = 8.3% (Calculated for $C_{14}H_{12}F_6N_2O$) |