National Institute of Advanced Industrial Science and Technology

National Metrology Institute of Japan

Reference Material Certificate

NMIJ CRM 4602-a
No. +++

1,4-Bis(trimethylsilyl)-2,3,5,6-tetrafluorobenzene for Quantitative NMR (\(^1H, ^19F\))

This certified reference material (CRM), 1,4-Bis(trimethylsilyl)-2,3,5,6-tetrafluorobenzene, was produced in accordance with the NMIJ’s management system and in compliance with ISO GUIDE 34:2009 and ISO/IEC 17025:2005. This CRM is intended for use in the calibration of \(^1H\) and \(^19F\) signal areas in nuclear magnetic resonance (NMR) spectroscopy. It is also intended for use in controlling the precision of analysis and confirming the validity of analytical methods.

Certified Value
The certified value of this CRM is the purity (mass fraction) given in the table below. The uncertainty of the certified value is the half-width of the expanded uncertainty interval calculated using a coverage factor \((k)\) of 2, which gives a level of confidence of approximately 95%.

<table>
<thead>
<tr>
<th>Substance</th>
<th>CAS No.</th>
<th>Certified value, Mass fraction (kg/kg)</th>
<th>Expanded uncertainty, Mass fraction (kg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,4-Bis(trimethylsilyl)-2,3,5,6-tetrafluorobenzene</td>
<td>16956-91-5</td>
<td>0.9998</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

Analysis
The certified value of this CRM is the weighted mean of purities determined by the mass balance approach and freezing point depression method. In the mass balance approach, impurities were analyzed using a high performance liquid chromatograph with an ultraviolet detector (HPLC-UV), a gas chromatograph with flame ionization detector (GC-FID) and a Karl-Fischer titrator (KF). In the freezing point depression method, an adiabatic calorimeter was used. The standard uncertainty was estimated by combining uncertainties from each analytical method, sample homogeneity, stability and difference between the methods.

Metrological Traceability
The certified value of this CRM was determined by the mass balance approach and the freezing point depression method which is the primary method. Organic impurities were determined by HPLC-UV and GC-FID using standard solutions prepared by the gravimetric method by NMIJ. Water content was determined by coulometric titrimetry which had been verified with a certified reference material (NMIJ CRM 4222-a: Water in mesitylene). An adiabatic calorimeter, in which the temperature, heating time, standard resistance, and voltage were calibrated, was used in the freezing point depression method. Therefore, the certified value is traceable to the International System of Units (SI).

Expiration of Certification
This certificate is valid for one year from the date of shipment, provided that the material remains unopened and is stored in accordance with the instructions given in this certificate.

Sample Form
This CRM is in the form of a white powder at room temperature. This CRM (100 mg) was bottled into a brown glass vial and stored in an aluminum-laminated bag.
Homogeneity
The homogeneity of this CRM was evaluated by analyzing 10 vials selected from 500 vials by a stratified random sampling method in order of subdivision. The total concentrations of impurities were measured by HPLC-UV and GC-FID. From the results, variation in purity (mass fraction) between and within vial was estimated by ANOVA. The water contents in the 10 vials selected above were measured by KF, and the result was lower than the limit of quantitation. It was estimated that the homogeneity of the water content fell below the limit of quantitation. This homogeneity is reflected in the uncertainty of the certified value.

Instructions for Storage
This CRM should be stored at a temperature between 2 °C and 10 °C and shielded from light in a clean area.

Instructions for Use
To ensure homogeneity, a minimum sample mass of 2 mg should be used. This CRM is for laboratory use only and not for in vivo use. This CRM should be allowed to warm to room temperature before opening, and used promptly owing to its slight volatility. 
A molar mass of (294.434 ± 0.007) g/mol (k=2) (IUPAC 2016) can be used for this CRM. As this CRM may become unstable in some solutions, it is recommended that the stability is checked before use by monitoring changes in the sample solution over time.

Precautions for Handling
Refer to the safety data sheet (SDS) on this CRM before use, and wear a protective mask and protective gloves when handling this CRM.

Preparation Method
The raw material of this CRM was synthesized by the Heteroatom Chemistry Team at the Interdisciplinary Research Center for Catalytic Chemistry in the National Institute of Advanced Industrial Science and Technology, and purified by recrystallization and sublimation. This CRM was then subdivided by Wako Pure Chemical Industries, Ltd. This CRM was bottled in a brown vial and sealed in an aluminum-laminated bag under dry argon atmosphere.

Information
The solubility and chemical shifts in the NMR spectra of this CRM in widely used solvents are shown below (next page). The following solubility and chemical shifts will be changed by temperature or coexisting solutes. Therefore, the overlap between signals originating from the calibrant (this CRM) and measurands must be checked. This CRM is insoluble in D2O (less than 0.5 mg/mL). The density of this CRM was 1.25 g/cm³ at 25 °C.
<table>
<thead>
<tr>
<th>Solvent</th>
<th>Solubility (mg/mL) (25 °C)</th>
<th>Chemical shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethylsulfoxide-d$_6$</td>
<td>5</td>
<td>$^1$H NMR (δ=0 ppm(TMS), 25 °C) 0.35</td>
</tr>
<tr>
<td>Methanol-d$_4$</td>
<td>≥ 20</td>
<td>0.38</td>
</tr>
<tr>
<td>Acetonitrile-d$_3$</td>
<td>≥ 20</td>
<td>0.40</td>
</tr>
<tr>
<td>Chloroform-d</td>
<td>≥ 20</td>
<td>0.38</td>
</tr>
<tr>
<td>Dicloromethane-d$_2$</td>
<td>≥ 20</td>
<td>0.39</td>
</tr>
<tr>
<td>Acetone-d$_6$</td>
<td>≥ 20</td>
<td>0.40</td>
</tr>
<tr>
<td>Toluene-d$_6$</td>
<td>≥ 20</td>
<td>0.30</td>
</tr>
<tr>
<td>Tetrahydrofuran-d$_8$</td>
<td>≥ 20</td>
<td>0.39</td>
</tr>
<tr>
<td>Benzene-d$_6$</td>
<td>≥ 20</td>
<td>0.24</td>
</tr>
</tbody>
</table>

TMS in the table shows the abbreviation for tetramethylsilane.

NMIJ Analysts
The technical manager for this CRM is M. Numata and the production manager is T. Yamazaki. The analysts are T. Yamazaki, Y. Shimizu, Y. Kitamaki, S. Nakamura and X. Bao.

Technical Information
Customer registration on the NMIJ Website (given below) will facilitate notification of any revision of the information given above. Technical reports regarding this CRM can be obtained from the contact details given below.

Reproduction of Certificate
In reproducing this certificate, it should be clearly indicated that the document is a copy.

March 14, 2018
Ryoji Chubachi
President
National Institute of Advanced Industrial Science and Technology

If you have any questions about this CRM, please contact:
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