

National Institute of Advanced Industrial Science and Technology

## National Metrology Institute of Japan



## Reference Material Certificate

NMIJ CRM 4601-a

No. +++

3,5-Bis(trifluoromethyl)benzoic Acid for Quantitative NMR ( $^1\text{H}$ ,  $^{19}\text{F}$ )

This certified reference material (CRM) is 3,5-Bis(trifluoromethyl)benzoic acid which 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  $^1\text{H}$  and  $^{19}\text{F}$  signal intensity by nuclear magnetic resonance (NMR) spectroscopy. It is also intended for controlling the precision of analysis and confirming the validity of the analytical methods.

**Certified Value**

The certified value of this CRM is the purity with the 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 %.

Substance	CAS No.	Certified value, Mass fraction (kg/kg)	Expanded uncertainty, Mass fraction (kg/kg)
3,5-Bis(trifluoromethyl)benzoic acid	725-89-3	0.9996	0.0006

**Analysis**

The certified value of this CRM is the weighted mean of purities determined by the mass balance approach, freezing point depression method and coulometric acidimetric titration method. In the mass balance approach, impurities were analyzed using a high performance liquid chromatograph with an ultraviolet detector (HPLC-UV), a gas chromatograph / flame ionization detector (GC-FID), a Karl-Fischer titrator (KF), and a thermogravimeter (TG). For the freezing point depression method in a continuous scan mode, a differential scanning calorimeter (DSC) was used. For the coulometric acidimetric titration, a coulometric titrator was used.

**Metrological Traceability**

The certified value of this CRM was determined by the mass balance approach, and by the freezing point depression method and coulometric acidimetric titration method which are primary methods. Organic impurities were determined with the HPLC-UV and GC-FID by using standard solutions prepared by gravimetric method by NMIJ. Water content was determined by coulometry with Karl-Fischer titrator which was validated. Ignition residue was determined with the TG calibrated with a JCSS-calibrated weight. The calibration of temperature and enthalpy of the DSC were performed with NIST SRM 2225 (mercury) and NIST SRM 2232 (indium). Purity by the coulometric acidimetric titration method was determined from the voltage, resistance and time (frequency) of the coulometric titrator calibrated by JCSS. 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 is stored in accordance with the instructions given in this certificate.

**Sample Form**

This CRM is in the form of a white powder. Two hundred milligrams of the material was bottled in a brown glass vial and kept

in an aluminum-laminated bag.

### Homogeneity

The homogeneity of the CRM was evaluated by analyzing ten vials selected from 200 vials by a stratified random sampling method in order of subdivision. The total concentrations of impurities were determined by HPLC-UV and GC-FID. From the results, the variation of purity (in mass fraction) between and within the vial(s) was estimated. The homogeneity is reflected in the uncertainty of the certified value.

### Instructions for Storage

This CRM should be stored at a temperature between 15 °C and 25 °C, and shielded from light in a clean desiccator.

### Instruction for Use

From the homogeneity, a minimum sample mass of 5 mg should be used. The CRM is for laboratory use only and not for in vivo use. The CRM should be used promptly once a vial is opened, and kept in a clean desiccator.

This reference value can be used for calibration of <sup>1</sup>H signal intensity in case of consideration for the amount of <sup>2</sup>H. As the molecular weight of this CRM, 3,5-Bis(trifluoromethyl)benzoic acid, 258.1165 ± 0.0031 (IUPAC 2011) should be used. The number after the ± means standard uncertainty.

### Precautions for Handling

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

### Preparation Method

This CRM was purified by recrystallization and subdivided by Wako Pure Chemical Industries, Ltd. This CRM was bottled into vials and sealed in an aluminum-laminated bag under dry air atmosphere.

### Information

The solubility and chemical shifts in the NMR spectra of this CRM in widely used solvents are shown below. The following solubility and chemical shifts will be changed by temperature or coexisting solutes. Therefore, the overlap between signals originated from the calibrant (this CRM) and measurands has to be checked.

Solvent	Solubility (mg/mL) (25 °C)	Chemical shift (ppm)	
		<sup>1</sup> H NMR (δ:0 ppm(TMS), 25 °C)	<sup>19</sup> F NMR (δ:-164 ppm(C <sub>6</sub> F <sub>6</sub> ),25 °C)
Dimethylsulfoxide- <i>d</i> <sub>6</sub>	over 20	8.42(1H), 8.44(2H)	-62.8
Methanol- <i>d</i> <sub>4</sub>	over 20	8.21(1H), 8.51(2H)	-66.0
Acetonitrile- <i>d</i> <sub>3</sub>	over 20	8.23(1H), 8.49(2H)	-64.0
Chloroform- <i>d</i>	0.5	8.12(1H), 8.54(2H)	-60.8
Dicloromethane- <i>d</i> <sub>2</sub>	1	8.15(1H), 8.55(2H)	-62.1
Acetone- <i>d</i> <sub>6</sub>	over 20	8.34(1H), 8.55(2H)	-64.2
0.1M NaOD/D <sub>2</sub> O	10	7.97(1H), 8.14(2H)	-62.9

This CRM is insoluble in D<sub>2</sub>O, benzen-*d*<sub>6</sub> or toluene-*d*<sub>8</sub> practically. 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, N. Hanari, T. Asakai, S. Taniguchi, R. Iwasawa and S. Nakamura.

### 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.

April 1, 2015

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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#### Revision history

April 1, 2015: "Metrology Management Center" was renamed to "Center for Quality Management of Metrology."

October 13, 2015: The description in "Expiration of Certification" was changed to "one year after the date of shipment."