National Institute of Advanced Industrial Science and Technology

National Metrology Institute of Japan

Reference Material

Certificate

NMIJ CRM 4601-b
No. +++

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

This certified reference material (CRM) is 3,5-Bis(trifluoromethyl)benzoic acid which is produced in accordance with the NMIJ's management system and is in compliance with ISO 17034 and ISO/IEC 17025. This CRM is intended for use in the calibration of ^{1}H and ^{19}F 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 the 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 %.

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	0.0003

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. The standard uncertainty was estimated by combining uncertainties due to each analytical method, sample homogeneity, stability and difference among the three methods.

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 mixing from 3,5-Bis(trifluoromethyl)benzoic acid (NMIJ CRM 4601-a). Water content was determined by coulometry with the Karl-Fischer titratior which was validated. Ignition residue was determined with the TG calibrated with a JCSS-calibrated weight. The calibration of temperature and enthalpy were performed with NMIJ CRM 5401-a (Cyclohexane) and NIST SRM 2232 (indium) for the freezing point depression method with the DSC. Purity by the coulometric acidimetric titration method was determined from the voltage, resistance and time (frequency) by using the coulometric titrator calibrated by Japan Calibration Service System (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. This CRM of ca. 200 mg in net volume is kept in a brown glass vial. The vial is sealed in an aluminum-laminated plastic bag.

Homogeneity

The homogeneity of the CRM was evaluated by analyzing ten vials selected from 202 vials by a stratified random sampling method in order of subdivision. The purity was determined as area percentage with the HPLC-UV and the GC-FID. From the results, the variation of purity (in mass fraction) between and within the vial(s) was estimated by ANOVA. The homogeneity is reflected in the uncertainty of the certified value, this CRM is homogeneous in the range of certified value.

Instructions for Storage

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

Instruction for Use

From the viewpoint of homogeneity, 5 mg or more of this CRM should be used for each analysis. 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.
As molar mass, (258.1165 ± 0.0062) g/mol (k=2) (IUPAC 2016) should be used for 3,5-Bis(trifluoromethyl)benzoic acid.

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

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.

Technical Information

The solubility and chemical shifts in the NMR spectra of this CRM in widely used deuterated solvents are shown below. The following solubility and chemical shifts will be changed by temperature or coexisting solutes. Therefore, possible overlap between signals originated from the calibrant (this CRM) and measurands has to be checked. This CRM is insoluble in D_2O, benzen-d_6 or toluene-d_8 practically (less than 0.5 mg/mL). The density of this CRM was 1.71 g/cm3 at 25 °C.

Solvent	Solubility (mg/mL) (25 °C)	Chemical shift (ppm)	
		^{1}H NMR (δ:0 ppm(TMS), 25 °C)	^{19}F NMR (δ:–164 ppm(C_6F_6),25 °C)
Dimethylsulfoxide-d_6	≥ 20	8.42(1H), 8.44(2H)	–62.8
Methanol-d_4	≥ 20	8.21(1H), 8.51(2H)	–66.0
Acetonitrile-d_3	≥ 20	8.23(1H), 8.49(2H)	–64.0
Chloroform-d	0.5	8.12(1H), 8.54(2H)	–60.8
Dicloromethane-d_2	1	8.15(1H), 8.55(2H)	–62.1
Acetone-d_6	≥ 20	8.34(1H), 8.55(2H)	–64.2
0.1M NaOD/D_2O	10	7.97(1H), 8.14(2H)	–62.9

TMS in the table shows the abbreviation for tetramethylsilane.

NMIJ Analysts

The technical manager for this CRM is NUMATA M. and the production manager is YAMAZAKI T., respectively. The analysts are YAMAZAKI T., SHIMIZU Y., KITAMAKI Y., ASAKAI T., NAKAMURA S., BAO X. and YAMANAKA N.

Information

If substantive technical changes occur that affect the certification before the expiration of this certificate, NMIJ will notify the registered customer. Customer registration on the NMIJ Website (given below) will facilitate notification. 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.

Note

Some parts of analytical methods were developed with support of a competitive grant (2013) by Chemicals Evaluation and Research Institute (CERI).

April 1, 2020

ISHIMURA Kazuhiko
President
National Institute of Advanced Industrial Science and Technology

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