

# Analysis of Tris(isopropylphenyl) Phosphate Using Agilent Triple Quadrupole 6475 LC/MS

## Author

Masahiko Takino

Agilent Technologies, Inc.

## Abstract

This application note describes a method for the analysis of tris(isopropylphenyl) phosphate using an Agilent 6475 triple quadrupole LC/MS.

Tris(isopropylphenyl) phosphate (TIPP) is a plasticizer and flame retardant additive used in polyvinyl chloride (PVC) and other synthetic resins. In January 2021, the U.S. Environmental Protection Agency (US EPA) announced restrictions on the manufacture and distribution of products and molded goods containing TIPP under the Toxic Substances Control Act (TSCA), causing a rise in the demand for its analysis. A method for the analysis of TIPP using GC/MS was reported in our previous research.<sup>1</sup> Additionally, LC/MS methods are promising alternatives to GC/MS due to their high sensitivity. This application note describes a TIPP analysis method using an Agilent 6475 triple quadrupole LC/MS. Our results showed that TIPP was analyzed with high sensitivity at a detection limit of 0.1 ng/mL or less, and with excellent linearity and reproducibility. Levels of TIPP in plastic products were also measured.

## Introduction

Tris(isopropylphenyl) phosphate (TIPP) (CAS No. 68937-41-7 or 26967-76-0) is a plasticizer and flame retardant additive used in polyvinyl chloride (PVC) and other synthetic resins. In January 2021, the U.S. Environmental Protection Agency (US EPA) announced restrictions on five persistent, bioaccumulative, and toxic (PBT) chemicals, including TIPP, under the Toxic Substances Control Act (TSCA) Section 6(h), regarding the manufacture and distribution of products and molded goods containing these chemicals. Therefore, an analytical method using triple quadrupole LC/MS was investigated. The plastic samples used were PVC components of toys and children's articles (Samples A and C) and PVC coating of cables (Samples B and D).

## Experimental

TIPP analytical standard was obtained from Santa Cruz Biotechnology. Calibration standard was prepared by dissolving neat standard in acetone to obtain 1 µg/mL solution, which was diluted with methanol as needed. Pretreatment of plastic materials was conducted according to the pretreatment method<sup>2</sup> proposed in previous research. Deactivated glass vials were used for sample vials.

### Instrumentation

#### System

1290 Infinity II Flexible Pump (G7104A)  
 1290 Infinity II Multisampler (G7167B)  
 1290 Infinity II Multicolumn Thermostat (G7116B)  
 6475 Triple Quadrupole LC/MS

Analysis of TIPP using the 6475 LC/TQ was performed by gradient analysis under the instrument conditions shown in Table 1, using the Agilent ZORBAX RRHD Eclipse Plus C18 column with a mobile phase of 2 mM ammonium acetate in ultrapure LC/MS water (mobile phase A) and acetonitrile (mobile phase B). Electrospray ionization (ESI) by Agilent Jet Stream (AJS) technology was used in multiple reaction monitoring (MRM) mode to take measurements as shown in Table 2.

**Table 1.** LC/MS instrument conditions for TIPP analysis.

| LC                 | Agilent 1290 Infinity II LC System  |
|--------------------|---|
| Column             | Agilent ZORBAX RRHD Eclipse Plus C18 column (2.1 mmx100 mm, 1.8 µm P/N: 959758-902) |
| Flow Rate          | 0.3 mL/min  |
| Mobile Phase       | A: 2 mM ammonium acetate in water B : Acetonitrile                                  |
| Gradient           | 30% B to 100% B in 15 min 100% B for 5 min  |
| Column Temperature | 40 °C   |
| Injection Volume   | 3 µL  |
| MS                 | Agilent 6475 Triple Quadrupole LC/MS  |
| Ion Source         | Agilent Jet Stream Technology ion source (AJS)                                      |
| Drying Gas         | 300 °C 10 L/min   |
| Sheath Gas         | 400 °C 12 L/min   |
| Nebulizer Pressure | 50 psi  |
| Capillary Voltage  | 4000 V  |
| Fragmentor Voltage | 100 V   |
| Nozzle Voltage     | 0 V   |

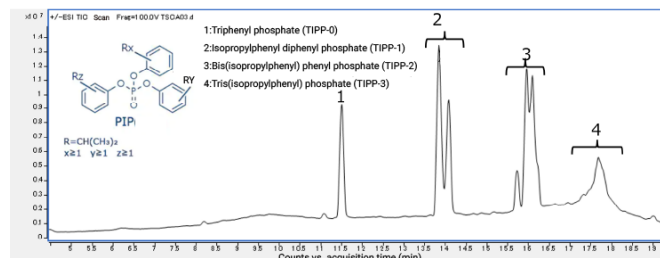
**Table 2.** MRM conditions for each TIPP.

| Compound                                       | Precursor Ion (m/z) | Product Ion (m/z) |                | Collision Energy (eV) |                |
|--|---------------------|-------------------|----------------|-----------------------|----------------|
|  |                     | Quant Ion         | Qualifier Ions | Quant Ion             | Qualifier Ions |
| (TIPP-0) Triphenyl phosphate                   | 327                 | 77                | 152            | 40                    | 40             |
| (TIPP-1) Isopropylphenyl diphenyl phosphate    | 369                 | 327               | 215            | 20                    | 35             |
| (TIPP-2) Bis(isopropylphenyl) phenyl phosphate | 411                 | 327               | 369            | 30                    | 20             |
| (TIPP-3) Tris(isopropylphenyl) phosphate       | 453                 | 369               | 327            | 25                    | 35             |

## Results

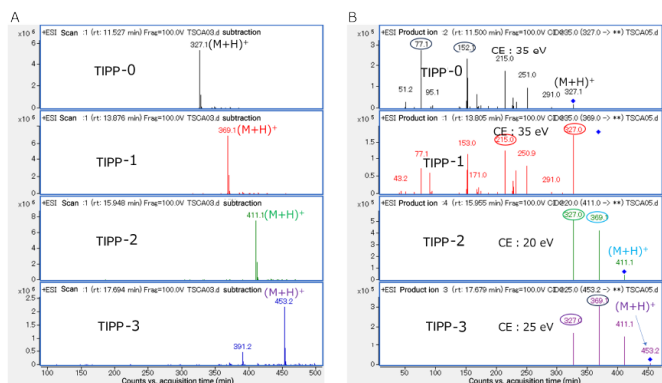
### Measurement of standard solution

Total ion chromatogram (TIC) of TIPP standard solution (10 µg/L) in scan mode is shown in Figure 1. As with the GC/MS results,<sup>1</sup> compounds with 0, 1, or 2 isopropyl groups were detected (peaks 1 to 3) in addition to TIPP (peak 4) which is regulated under TSCA. Isomers were detected at peaks 2 to 4. Isomers were treated as the same compound. Abundance ratio of the individual isomers are unknown, making isomer quantification difficult. Therefore, the concentration of each compound was set equal to that of TIPP standard solution.



**Figure 1.** TIC (Concentration: 10 µg/mL) of each TIPP compound.

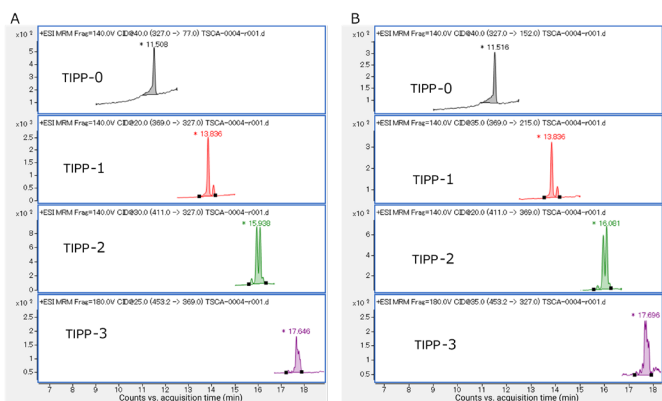
Mass spectra and product ion spectra of each TIPP compound are shown in Figure 2. In all compounds, protonated molecules (M+H)<sup>+</sup> were detected as base peaks in mass spectra obtained in scan mode. These ions were therefore treated as precursor ions in product ion scanning. Based on these results, the two strong ions observed were designated as product ions (Table 2).



**Figure 2.** Mass spectra of each TIPP compound (A) mass spectra and (B) product ion spectra (CE stands for collision energy).

### Sensitivity, linearity, and reproducibility

MRM chromatograms of TIPP standard solution (concentration: 0.1 ng/mL) are shown in Figure 3. Although the concentration of each TIPP compound is unknown, all compounds were measurable using the TIPP standard solution concentration of 0.1 ng/mL. S/N of TIPPs varied between 22 to 93 as shown in Table 3.



**Figure 3.** MRM chromatogram of each TIPP compound (TIPP standard solution concentration: 0.1 ng/mL). A: Quant ion B: Qualifier ions.

**Table 3.** S/N, linearity, and reproducibility of each TIPP compound.

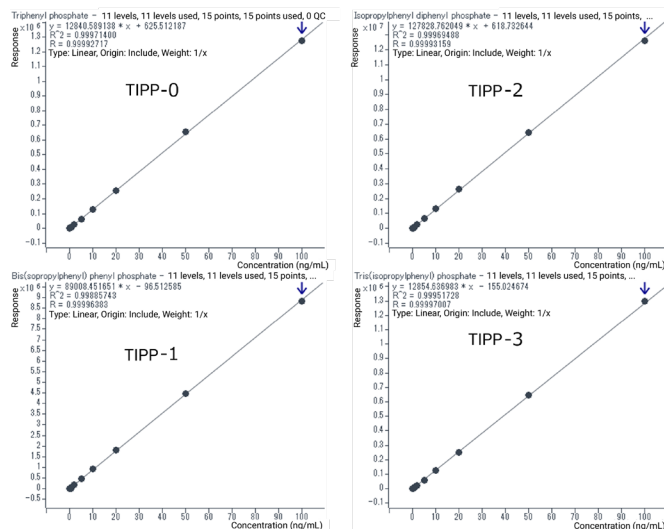
| Compound | S/N <sup>1</sup> | Linearity Correlation Coefficient <sup>2</sup> | Reproducibility Relative Standard Deviation (%) <sup>3</sup> |
|----------|------------------|--|--|
| TIPP-0   | 22               | 0.9999   | 1.38   |
| TIPP-1   | 37               | 0.9999   | 0.68   |
| TIPP-2   | 93               | 0.9999   | 0.46   |
| TIPP-3   | 38               | 0.9999   | 0.18   |

\*1: TIPP standard solution concentration 0.1 ng/mL

\*2: TIPP standard solution concentration 0.1 to 100 ng/mL

\*3: TIPP standard solution concentration 0.1 ng/mL n=5

Calibration curves of each TIPP compound are shown in Figure 4. Correlation coefficients were all 0.9999 or higher over the range of 0.1 to 100 ng/mL, indicating excellent performance.



**Figure 4.** Calibration curve of each TIPP compound (TIPP standard solution concentration range: 0.1 to 100 ng/mL).

The reproducibility for each TIPP compound when TIPP standard solution 0.1 ng/mL was measured five times is shown in Table 4. Relative standard deviation was 0.18 to 1.38%, indicating excellent performance.

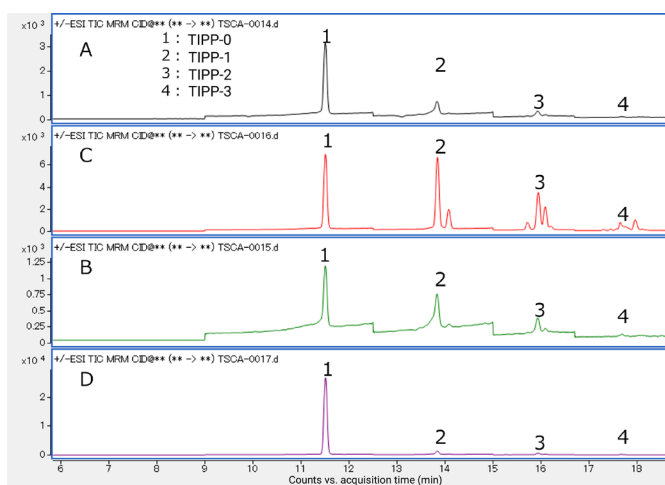
**Table 4.** Total intensity and relative intensity of each TIPP compound in plastic products.

| Compound                 | Relative Intensity Ratio (%) |       |                    |       |
|--------------------------|------------------------------|-------|--------------------|-------|
|                          | Children's Toys              |       | Cable Cord Coating |       |
|                          | A                            | C     | B                  | D     |
| TIPP-0                   | 67.2                         | 27.1  | 32.1               | 89.2  |
| TIPP-1                   | 24.4                         | 47.2  | 36.7               | 7.3   |
| TIPP-2                   | 7.7                          | 25.5  | 9.1                | 3.0   |
| TIPP-3                   | 0.7                          | 0.2   | 22.1               | 0.5   |
| Total TIPP <sup>*4</sup> | 14266                        | 78030 | 10624              | 93039 |

\*4: Sum of peak areas of each TIPP compound

Chromatograms of TIPP compounds in plastic products are shown in Figure 5. Intensity ratio of each TIPP compound differed markedly between products unlike the TIPP standards. Relative intensity and sum of area (plastic products only) of TIPP compounds in the TIPP standard solution and plastic products are shown in Table 4.

Relative intensity of TIPP-0 in TIPP standard solution was approximately 5%, but in plastic products it was markedly higher at 27.1 to 89.2%. Sensitivity of LC/MS may vary between different TIPP compounds. Therefore, it cannot be definitively concluded that the sum of the peak areas of each TIPP compound in plastic products is correlated to the total content of TIPP compounds. The cable cord coating D showed the highest value, approximately nine times higher than that of B.



**Figure 5.** Chromatograms of TIPP compounds in plastic products.

## Conclusion

A method for the measurement of TIPP was established and its sensitivity, linearity, and reproducibility were verified using standard solutions. In terms of sensitivity, S/N was higher than 20 for 0.1 ng/mL TIPP standard solution. The method showed excellent linearity with correlation coefficient higher than 0.9999 across the range of 0.1 to 100 ng/mL and excellent reproducibility with relative standard deviation of 0.18 to 1.38% for five measurements with 0.1 ng/mL. In addition, TIPP compounds were detected in plastic products that were analyzed as real-world samples, indicating that the Agilent 6475 triple quadrupole LC/MS is suitable for the analysis of TIPP.

## References

- 1) Analysis of Tris(isopropylphenyl) Phosphate in Polymer Materials Using Thermal Desorption–GC/MS. *Agilent Technologies application note*, 5994-4454JAJP, **2024**.
- 2) Analysis of Chlorinated Paraffins in Plastic Products and Waste Using the Agilent 6470 Triple Quadrupole LC/MS and InfinityLab Poroshell 120 EC-CN Column. *Agilent Technologies application note*, 5994-5521JAJP, **2022**.

Website

[www.agilent.com/chem/](http://www.agilent.com/chem/)

Contact Us

[www.agilent.com/en/contact-us/page](http://www.agilent.com/en/contact-us/page)

This information is subject to change without notice.

DE-014442

© Agilent Technologies, Inc. 2024  
Printed in the USA, May 15, 2024  
5994-7458EN