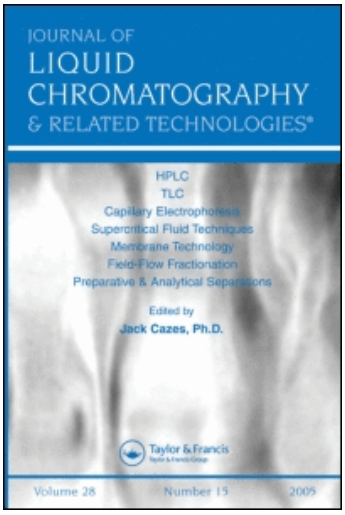

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

DETERMINATION OF o-TOLUIC ACID AND ITS MICRO AMOUNTS OF IMPURITIES IN INDUSTRIAL PRODUCTS BY HPLC

Hai-Jun Yang[a]; Ming-Yu Ding[a]
[a] Department of Chemistry, Tsinghua University, Beijing, P. R. China

Online publication date: 29 August 2002

To cite this Article Yang, Hai-Jun and Ding, Ming-Yu(2002) 'DETERMINATION OF o-TOLUIC ACID AND ITS MICRO AMOUNTS OF IMPURITIES IN INDUSTRIAL PRODUCTS BY HPLC', Journal of Liquid Chromatography & Related Technologies, 25: 17, 2709 — 2715
To link to this Article: DOI: 10.1081/JLC-120014387
URL: http://dx.doi.org/10.1081/JLC-120014387


MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

JOURNAL OF LIQUID CHROMATOGRAPHY & RELATED TECHNOLOGIES
Vol. 25, No. 17, pp. 2709–2715, 2002

DETERMINATION OF *o*-TOLUIC ACID AND ITS MICRO AMOUNTS OF IMPURITIES IN INDUSTRIAL PRODUCTS BY HPLC

Hai-Jun Yang and Ming-Yu Ding*

Department of Chemistry, Tsinghua University,
Beijing 100084, P. R. China

ABSTRACT

o-Toluic acid (OTA) is an important organic intermediate, and is broadly used in pesticides and medicines. Some micro amount of impurities, such as phthalic acid (PA), phathalide (PT), and benzoic acid (BA), can have a great effect on the following reactions. In order to control the quality of OTA products, it is important to establish an effective method to determinate OTA and its micro amount of impurities in the OTA industrial products. In this work, a high performance liquid chromatographic method is established for the simultaneous analysis of the OTA and its micro amount of impurities. The detection limits ($S/N = 3$) of OTA and its micro amount of impurities were $0.02 \sim 0.1$ mg/L at the detection wavelength 230 nm. The linear range of the peak area calibration curves for the analysts were over three orders of magnitude with a correlation coefficient of $0.996 \sim 0.999$. Using this method, many

*Corresponding author. E-mail: dingmy@chem.tsinghua.edu.cn

DOI: 10.1081/JLC-120014387
1082-6076 (Print); 1520-572X (Online)

industrial products are analyzed with good reproducibility and validity (RSD are below 5% and recoveries are between 96.5% and 103.2%).

INTRODUCTION

The application of organic intermediates becomes more and more important in pesticides, medicines, and other fields.[1] As a basic organic intermediate, *o*-toluic acid (OTA) plays a key role in industry.[2] Some impurities, such as phthalic acid (PA), phathalide (PT), and benzoic acid (BA) are produced with the OTA production process. Although, the amount of those impurities is very little, they can have a great effect on the following reactions. In order to control the quality of OTA products, it is important to establish an effective method to determine OTA and the impurities in the OTA industrial products.

Several analytical methods, such as capillary gel electrophoresis (CGE),[4] liquid chromatography/atmospheric pressure chemical ionization/mass spectrometry (LC/APCI/MS),[5] spectrophotometry,[6] high performance capillary zone electrophoresis (HPCZE),[7] and high performance liquid chromatography (HPLC),[8,9] have been used for the identification and quantification of OTA and the impurities, including the isomer of OTA, *m*-toluic acid (MTA), and *p*-toluic acid (PTA). High performance liquid chromatography is the most suitable method for OTA analysis. By the current HPLC methods, good results have been obtained for OTA analysis only. But, there are a few reports about simultaneous determination of OTA and its micro amount of impurities in our review.

In this work, a HPLC method was established for the simultaneous analysis of the OTA and the impurities MTA, PTA, PA, PT, and BA, in OTA industrial products.

EXPERIMENTAL

Reagents and Procedures

All reagents used in this study were of analytical purity. Methanol (HPLC grade) was from Tianjin Shield Co. (China), isopropyl alcohol from Beijing Yili Fine Chemical Plant (China). *o*-Toluic acid, MTA, PTA, BA, PA, and PT were purchased from Aldrich Chemical Company Inc. (USA) with purities greater than 98%. Water was deionized and doubly distilled. The mobile phase was filtered through a 0.45 μm membrane filter before use.

The stock solutions of OTA, MTA, PTA, BA, PA, and PT were prepared as methanol solutions at a concentration of 1 g/L for each compound.

Working standard mixtures were diluted from the stock solutions with methanol.

Instrumentation

A HP 1100 HPLC system (Hewlett-Packard, USA), which was equipped with a quaternary pump, a vacuum degasser, a column thermostat, a 20 μL manual injector, and a HP Chemstation for instrument control, data collection, and data handling was used to perform the analysis. Detection was carried out using a diode array detector (DAD).

A separation column (Zorbax SB-C_{18}, 250 mm × 4.6 mm I.D., 5 μm, Hewlett-Packard, USA) was used. Two types of mobile phase were used in this study. One was the aqueous solution containing 25% methanol, 25% isopropyl alcohol, and 10% phosphate buffer (7.1 g K_2HPO_4 + 6.9 g KH_2PO_4 + 14.5 mL H_3PO_4 in a liter of water), and the other containing 24% methanol, 24% isopropyl alcohol, 1% acetic acid, and 30% phosphate buffer (14.2 g K_2HPO_4 + 13.8 g KH_2PO_4 in a liter of water). The flow rate was 0.5 mL/min. The pH of both two mobile phases was about 5.3. The column temperature was room temperature. The detection wavelength was selected as 230 nm.

Sample Preparation

A 100 mg industrial OTA sample was weighed into a 100 mL volumetric flask (VF). The sample was dissolved in 50 mL methanol and diluted to the mark with doubly distilled water. A sample solution of 5 mL was added to a 50 mL of VF and diluted to the mark with the mobile phase. The concentration of the sample was 0.1 g/L. The sample solution was filtered through a 0.45 μm membrane filter and was injected into the HPLC using a 20 μL loop injector.

RESULTS AND DISCUSSION

Separation of OTA, MTA, PTA, BA, PA, and PT

Several methanol, aqueous-based mobile phases were studied, such as water–methanol in combination with isopropyl alcohol, acetic acid, and phosphate buffer. The gradient HPLC system was studied first. The base line drifted and a high noise level was observed when the gradient system was used. So, the isocratic system was selected in this work. It was shown, that the peak tailing would be improved when the concentration of isopropyl alcohol was

decreased in the mobile phase. When the concentration of methanol was increased in the mobile phase, the retention time and the resolution would be decreased. It was also proven, that the separation would become better and the retention time would be shorter when the concentration of phosphate buffer was increased. A very small amount of acetic acid in the mobile phase could have a great effect on the retention. It was found, that methanol–isopropyl alcohol–acetic acid–water–phosphate buffer eluent was the best for the separation of OTA, MTA/PTA, BA, PA, and PT. The mobile phase contained 24% methanol, 24% isopropyl alcohol, 30% phosphate buffer, and 0.22% acetic acid. The chromatogram of the standard mixture is shown in Fig. 1. It was very difficult to separate the isomers, MTA and PTA, but both MTA and PTA separated well from OTA. But, the mobile phase was complicated and the noise level was high.

Because MTA and PTA have not been detected in the OTA products, we can find a simpler mobile phase to separate OTA, BA, PA, and PT. Good separation of OTA, BA, PA, and PT was obtained when the mixture of water/methanol/isopropyl alcohol/phosphate buffer (40 : 25 : 25 : 10, v/v) was employed as a mobile phase. The chromatogram of a standard mixture and an OTA product is shown in Fig. 2.

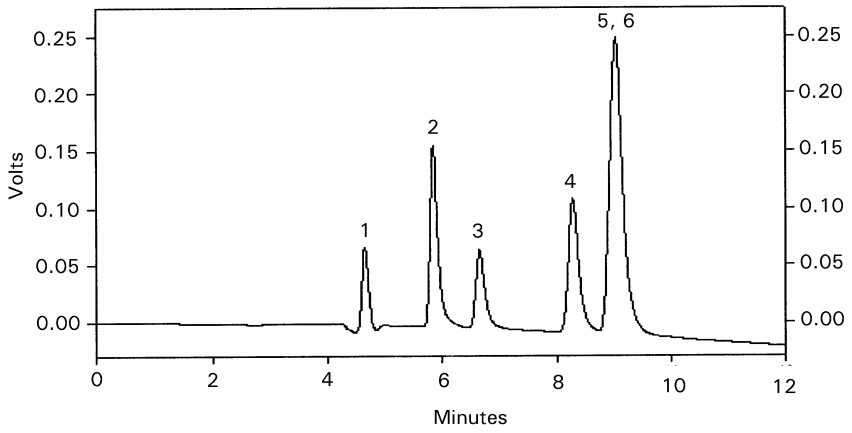

Figure 1. Separation of a standard mixture, mobile phase: 24% methanol and 24% isopropyl alcohol and 30% phosphate buffer in 1% acetic acid, flow rate: 0.5 mL/min. The detection wavelength was 230 nm. Peaks: 1. PT; 2. PA; 3. BA; 4. OTA; 5. MTA; 6. PTA. The standard mixture contained 20 mg/L of PT, PA, BA, OTA, MTA, and PTA.

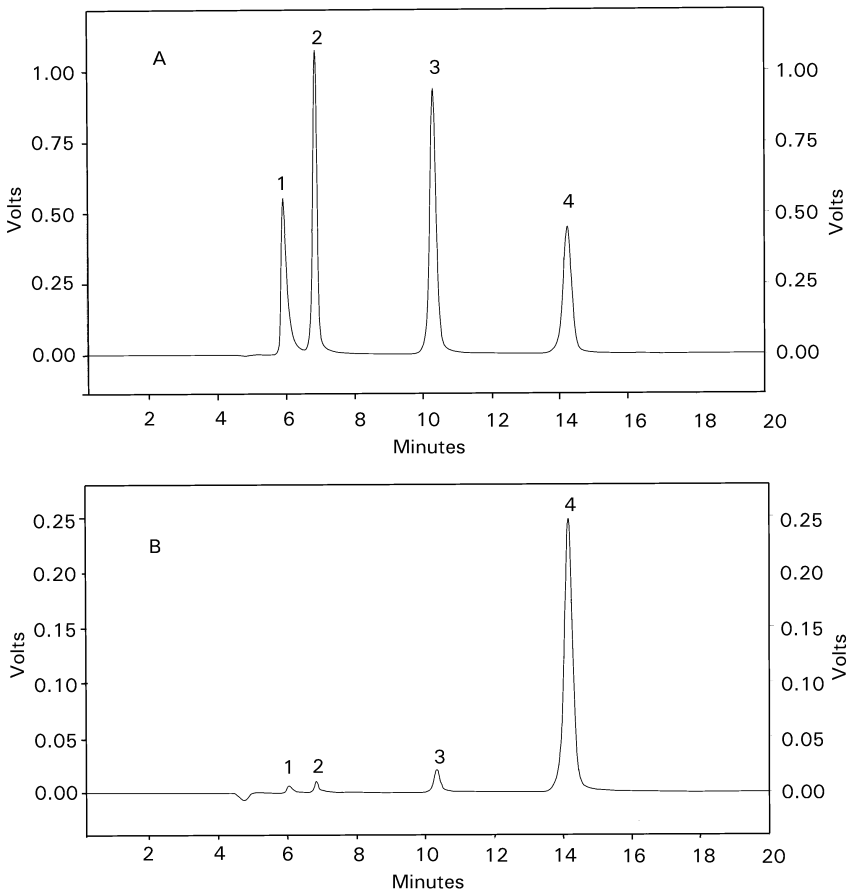

Figure 2. Separation of a standard mixture (A) and industrial OTA products (B) using mobile phase consisting of 25% methanol and 25% isopropyl alcohol containing 10% phosphate buffer, with flow rate of 0.5 mL/min. The detection wavelength was 230 nm. Peak identification: 1. PA; 2. PT; 3. BA; 4. OTA. The standard mixture contained 100 mg/L of PA, PT, BA, and OTA.

Parameters for Quantitative Analysis

The detection wavelength of 230 nm was selected in this study. At this wavelength, not only the highest detection sensitivity could be obtained for all analytes, but also the linearity of the calibration curves was the best, compared with that obtained at other wavelengths.

Table 1. Parameters of Quantitative Analysis for PA, PT, BA, OTA, PTA, and MTA

	Linear Range (mg/L)	Calibration Coefficient	Detection Limit (mg/L)	Recovery (%)
PT	0.08 ~ 40	0.996	0.04	96.5
PA	0.04 ~ 40	0.997	0.02	100.8
BA	0.08 ~ 40	0.997	0.04	100.2
OTA	0.20 ~ 400	0.999	0.10	102.1
PTA	0.20 ~ 400	0.999	0.10	102.8
MTA	0.20 ~ 400	0.999	0.10	103.2

The detection limits (S/N = 3) and linear range for OTA, MTA, PTA, BA, PA, and PT were investigated. The linear range of the calibration curves of peak areas for the all analytes, were over three orders of magnitude with a correlation coefficient of 0.996 ~ 0.999. The linear range of the peak height calibration curves was narrower than that of the peak areas. The detection limits of all analytes were 0.02 ~ 0.1 mg/L, which are suitable for the direct analysis of OTA, MTA, PTA, BA, PA, and PT in industrial products. The recoveries of standards are between 96.5% and 103.2%. Table 1 shows the above parameters.

Analysis of Industrial OTA Products

It is very important to control the quality of OTA products in industry. Some industrial products were analyzed for the contents of OTA, BA, PA, and PT. Because the linear range of the peak area calibration curves for all analytes were over three orders of magnitude, with a correlation coefficient of 0.996 ~ 0.999, good results were obtained for all analytes.

The determination results of several OTA products are shown in Table 2. Usually, the content of OTA must be above 97% in industry. We have found

Table 2. Determination Results of OTA and Its Micro Amount of Impurities ($n = 5$)

	1		2		3	
Sample	Mean/%	RSD (%)	Mean/%	RSD (%)	Mean/%	RSD (%)
PA	0.052	3.14	0.173	2.53	0.046	3.24
PT	0.152	3.22	0.148	3.59	0.134	4.13
BA	0.132	4.12	0.193	3.56	0.121	4.27
OTA	98.01	1.02	96.88	1.35	97.32	1.62

sample 2 is unqualified. At the same time, we found the contents of impurities of sample 2 greater than others. The reason is, that the impurities are the by-product in the production process. So, this result can guide the production process.

In conclusion, the HPLC method developed in this work, is practicable for the analysis of OTA and its micro amount of impurities in industrial products. The method is rapid and simple, with good reproducibility and validity (RSD are below 5% and recoveries are between 96% and 104%). This method has been applied in the determination of some industrial products with satisfactory results.

REFERENCES

1. Hildebran, K.C.; Cordray, T.L.; Chan, K.W.; Beam, C.F. Synth. Commun. **1994**, *24*, 779.
2. Besson, M.; Besson, P.; Neto, S.; Pinel, C. Tetrahedron: Asymmetry **2000**, *11*, 1809.
3. Bachiller-Baeza, B.; Rodriguez-Ramos, I.; Guerrero-Ruiz, A.; Besson, M.; Pinel, C. J. Molec. Catal. A: Chemical **2000**, *164*, 147.
4. Lin, J.M.; Nakagama, T.; Okazawa, H.; Wu, X.Z. Fresenius J. Anal. Chem. **1996**, *354*, 451.
5. Fang, J.S.; Barcelona, M.J. Anal. Let. **1999**, *32*, 1459.
6. Du, Y.X.; Chen, Y.Y.; Xia, X.Y. Chemical World (Chinese) **1994**, *8*, 428.
7. Wang, X.; Feng, Y.A. Chemical World (Chinese) **2001**, *6*, 296.
8. Park, J.S.; Park, K.M.; Kim, C.K. J. Liq. Chromatogr. & Relat. Technol. **2000**, *23*, 2513.
9. Abu-Qare, A.W.; Abou-Donia, M.B. J. Chromatogr. B **2000**, *749*, 171.

Received January 23, 2002
Accepted May 20, 2002
Manuscript 5730