Rapid Direct Analysis of *p*-Xylene Oxidation Products by Reversed-Phase High-Performance Liquid Chromatography

Antonello Viola and **Giacomo Cao***
Dipartimento di Ingegneria Chimica e Materiali, Università di Cagliari, Piazza D'Armi, 09123 Cagliari, Italy

Abstract

A reversed-phase high-performance liquid chromatographic (HPLC) method is developed for the determination of the products of liquid phase oxidation of *p*-xylene to terephthalic acid catalyzed by cobalt naphtenate with methyl benzoate as a solvent. Analyses are performed on a 250- × 4.6-mm octadecylsilica (ODS; C_{18}) bonded phase column with a 10- × 3-mm guard column in 22 min. A three-component mobile phase (methanol, acetonitrile, water) is used for gradient elution, and ultraviolet detection is selectively performed at 220 and 254 nm. The internal standard method (using cumene as the internal standard) is employed. The developed method avoids filtration, extraction, and derivatization pretreatment of the samples.

Introduction

Liquid-phase catalytic oxidation of *p*-xylene to terephthalic acid plays an important role in the petrochemical industry (1). This process has received a great amount of attention in the literature, with particular emphasis on the effects of the catalyst and promoter concentrations, the nature of the solvent, the reaction temperature, and other conditions on the oxidation rate (1,2 and references therein). Few studies have addressed the development of kinetic schemes of this process that are simple but yet provide a description of the product distribution sufficient to evaluate the performance of industrial processes (3–6). In these studies, the complex radical chain mechanism of this process has been typically lumped into appropriate kinetic schemes that account for the most important intermediates and final products, that is, *p*-tolualdehyde, 4-methylbenzyl alcohol, *p*-toluic acid, 4-hydroxymethylbenzoic acid, 4-carboxybenzaldehyde, terephthaldicarboxaldehyde, and terephthalic acid. As lumped kinetic schemes of this type can be proposed only on the basis of experimental evidence, a key point is represented in general by the analytical techniques employed. Cavalieri d'Oro and co-workers (3) analyzed reactants and intermediate products obtained from low-temperature oxidation of *p*-xylene in acetic acid by gas chromatography and high-performance liquid chromatography (HPLC), respectively. Solid products were analyzed after esterification by gas chromatography. Very few indications about the analytical conditions have been given; in addition, two different sets of equipment and a time-consuming pretreatment of the solid samples were employed. Jacobi and Baerns (4) analyzed the reaction products of *p*-xylene oxidation in the absence and presence of solvent (i.e., chlorobenzene and benzoic acid methylester) by HPLC. Depending upon the number of nuclei present in the products, different mixtures of eluent have been used by maintaining a constant mobile phase flow rate (i.e., 1 mL/min) at a temperature of 34°C. No information about the duration of the analysis has been reported. More recently, Cao and co-workers (5,6) investigated the liquid-phase catalytic oxidation of *p*-xylene to *p*-toluic acid and to terephthalic acid using methyl benzoate as a solvent by analyzing the reaction products with HPLC. For the analysis of oxidation products up to terephthalic acid formation, a relatively rapid and easy-to-use technique that represents the natural upgrade of the one developed for the detection of the products up to *p*-toluic acid formation (5) has been employed (6).

The aim of this work was to describe in detail the development and the performance of this technique that allows the rapid and simultaneous analysis of *p*-xylene, *p*-tolualdehyde, 4-methylbenzyl alcohol, *p*-toluic acid, 4-hydroxymethylbenzoic acid, 4-carboxybenzaldehyde, terephthaldicarboxaldehyde, terephthalic acid, methyl benzoate, and cumene. The method is free of filtration, extraction, and derivatization steps.

Experimental

Principle

For the determination of the oxidation products of *p*-xylene within a relatively wide range of concentrations, a reversed-phase HPLC method with ultraviolet detection was developed. It is based on the gradient elution technique in which a mobile phase consisting of methanol, acetonitrile, and water and an octadecylsilica (ODS; C_{18}) column were used.

* Author to whom correspondence should be addressed.

Selective detection of the various compounds at 220 and 254 nm was performed. Analyses were carried out by the combination of an isocratic period and a series of linear elution gradients of the mobile phase. The starting composition of the mobile phase resulted in a highly polar mixture that allowed effective interaction of 4-hydroxymethylbenzoic acid, terephthalic acid, terephthaldicarboxaldehyde, and 4-carboxybenzaldehyde with the stationary phase. In order to enhance the solvent strength of the mobile phase and reduce the analysis run time, the methanol and acetonitrile content were then progressively increased. Small quantities of phosphoric acid were added into the mobile phase to avoid asymmetrical effects and peaks tailing.

The internal standard method was adopted due to its capability of minimizing errors deriving from system and procedure variations (7–9). In addition, this method is particularly useful since it avoids frequent recalibrations because the response factors of all analytes remain practically constant for relatively long periods of time (10).

Table I. Maximum Absorption Wavelengths of all Analytes for HPLC Detection in the Range 195–320 nm

Analyte	Wavelength (nm)
p-Xylene	207, 263
p-Tolualdehyde	254
4-Hydroxymethylbenzoic acid	231
4-Carboxybenzaldehyde	249
Cumene	263
4-Methylbenzyl alcohol	215–225, 259
p-Toluic acid	246
Terephthaldicarboxaldehyde	257
Terephthalic acid	237
Methyl benzoate	225

Table II. Working Concentration Range of all Analytes

Analyte	Concentration (%)
p-Xylene	5–44
p-Tolualdehyde	1–3
4-Hydroxymethylbenzoic acid	0–1
4-Carboxybenzaldehyde	0–1
Cumene	13–16
4-Methylbenzyl alcohol	0–1.5
p-Toluic acid	0–7
Terephthaldicarboxaldehyde	0–1
Terephthalic acid	0–0.5
Methyl benzoate	45–58

Apparatus

The equipment used included a Hewlett-Packard 1050 liquid chromatograph equipped with a quaternary pump (Model 79852A, Hewlett-Packard; Palo Alto, CA), a helium degassing system for solvents, a multiple wavelength ultraviolet detector (Model 79854A) with an 8-µL volume and a 6-mm optical path internal flow cell, an autosampler (Model 79855A), and an integrator (Model 3396A) connected to an IBM PC-XT 8086 controlling a data acquisition system (Woodward McCoach, Inc.; West Chester, PA). A Chrompack Chromsep Spherisorb 5 ODS-2 column (250 × 4.6-mm; particle size, 5 µm; pore size, 8 nm; superficial area, 220 m^2/g; surface coverage, 2.2 $\mu mol/m^2$; carbon content, 10.5%) with a 10- × 3-mm guard column was used.

Reagents

HPLC-grade water (Art. n. 412142, Farmitalia Carlo Erba; Milano, Italy), HPLC-grade acetonitrile (Art. n. 412411, Farmitalia Carlo Erba), HPLC-grade methyl alcohol (Art. n. 412142, Farmitalia Carlo Erba), and 75% phosphoric acid (Art. n. 304051, Farmitalia Carlo Erba) were used as solvents for the mobile phase preparation. Standard solutions for calibration were prepared using the following: 4-hydroxymethylbenzoic acid (Art. n. H5892, Sigma; St. Louis, MO), terephthalic acid (Art. n. 18,536-1, Aldrich-Chemie; France), 4-carboxybenzaldehyde (Art. n. 12,491-5, Aldrich-Chemie), terephthaldicarboxaldehyde (Art. n. T 220-7, Aldrich-Chemie), 4-methylbenzyl alcohol (Art. n. 15.592.72, Janssen Chimica; Gardena, CA),

Table III. Routine Chromatographic Parameters of all Analytes for the Quality Test of the Analytical Method

Analyte	Retention time (min)	Resolution*	Capacity factor†	Asymmetry factor	No. theoretical plates
4-Hydroxymethylbenzoic acid	10.517		3.844	1.01	64,667
Terephthalic acid	11.615	12.76	4.35	1	128,839
4-Carboxybenzaldehyde	12.77	11.49	4.88	1	50,478
Terephthaldicarboxaldehyde	13.204	2.56	2.56 5.08	1	18,100
4-Methylbenzylalcohol	14.272	7.19	5.57	1	259,054
p-Toluic acid	15.229	15.2	6.04	1.15	280,132
p-Tolualdehyde	16.543	18.83	6.62	1.21	358,848
Methyl benzoate	17.049	7.84	6.85	1.3	393,140
p-Xylene	20.617	57.55	8.5	1.01	654,121
Cumene	21.346	12.25	8.83	1	725,168

* Corresponds to the analyte in the row and to the previous one.
† Calculated using the retention time of uracil (2.171).

p-toluic acid (Art. n. 13.906.35, Janssen Chimica), *p*-tolualdehyde (Art. 13.900.29, Janssen Chimica), *p*-xylene (Art. n. 492504, Farmitalia Carlo Erba), cumene (Art. n. 18.101.59, Janssen Chimica), and methyl benzoate (Art. m 12.634.24, Janssen Chimica). For sample dilution, HPLC-grade methyl alcohol (Art.n. 412533, Farmitalia Carlo Erba) was used. All the reagents were pure for analytical use.

Working conditions

The column was first conditioned for about 30 min with a mobile phase containing 95% water and 5% acetonitrile. The solvents of the mobile phase were degassed and maintained under a helium flux before and during the analyses (7). The volume of the samples injected by the autosampler was 20 µL, and the analyses were carried out with a flow rate of 1.5 mL/min by applying the following elution gradient program: isocratic conditions with 95% water and 5% acetonitrile for 5 min; gradient elution from 5 to 12 min until a mobile phase composition of 55% water, 35% acetonitrile, and 10% methanol was reached; a second linear gradient from 12 to 20 min, thus reaching the final composition of 15% water, 75% acetonitrile, and 10% methanol. To compensate for mobile phase compressibility, a value of 60E-6/bar and automatic stroke volume setting on the pump module were selected, thus obtaining an

Table IV. Relative Standard Deviations (%) of Peak Areas and Retention Times

	Analysis number							
Compound*	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**%RSD$_{Tr}$†**
p-Xylene								
Conc.	11	21.5	55	135	270	540	1085	0.018
%RSD	2.2	2.1	1.1	0.9	1	0.8	0.9	
4-Methylbenzyl alcohol								
Conc.	0.41	0.82	2	5.1	10.2	20.5	41	0.042
%RSD	7.6	3.1	2.6	1.2	2	0.7	0.6	
p-Tolualdehyde								
Conc.	0.78	1.6	3.9	9.7	19.5	39	77.9	0.037
%RSD	3.3	0.7	1.2	1.1	0.8	0.8	0.7	
p-Toluic acid								
Conc.	2	4	9.9	24.8	49.6	99.2	198	0.041
%RSD	8.3	1.4	1.1	1	1.9	0.9	1.8	
4-Hydroxymethylbenzoic acid								
Conc.	0.33	0.67	1.7	4.2	8.4	16.7	33.4	0.087
%RSD	7.8	3.8	3	3.3	3.1	3	1.9	
Terephthaldicarboxaldehyde								
Conc.	0.14	0.28	0.7	1.8	3.5	7.1	14.1	0.052
%RSD	5.5	3.8	2.6	0.7	1.6	0.9	1.9	
4-Carboxybenzaldehyde								
Conc.	0.33	0.67	1.7	4.2	8.4	16.9	33.7	0.052
%RSD	2.5	2.8	0.8	0.8	1.3	0.9	0.8	
Terephthalic acid								
Conc.	0.18	0.36	0.9	2.3	4.5	9.1	18.2	0.058
%RSD	9	3.1	1.3	0.9	1.7	1.1	1.1	
Cumene								
Conc.	2	4	28.5	70	140	285	565	0.019
%RSD	5.7	3.4	2.1	1.1	1	0.9	0.7	
Methyl benzoate								
Conc.	17.5	35.5	90	220	445	885	1770	0.03
%RSD	2.4	1	1.2	1	0.9	0.8	0.7	

* Concentrations are given in micrograms per milliliter of methanol. Percent relative standard deviations are for peak area counts.
† Percent relative standard deviation of retention times.

optimum pressure ripple within the whole analysis duration. After each run, the column was conditioned for 15 min at the starting mobile phase composition (95% water, 5% acetonitrile). The detection of various compounds was achieved by varying the wavelength as follows: 254 nm from 0 to 13.8 min; 220 nm from 13.8 to 15.9 min; 254 nm from 15.9 to 22 min. Note that the wavelength variation was selected in order to achieve a high degree of reproducibility and detection (good peak resolution and elution gradient characteristics). In fact, if a wavelength program in which the values of maximum absorption of all species (Table I) were used, quite low precision results due to signal drift and background noise would occur. In particular, detection was at 254 nm for 4-hydroxymethylbenzoic acid, terephthalic acid, terephthaldicarboxaldehyde, and 4-carboxybenzaldehyde. Detection occurred at 220 nm for 4-methylbenzyl alcohol and *p*-toluic acid. Finally, the second change of wavelength (i.e., 254 nm) allowed *p*-tolualdehyde, *p*-xylene, methyl benzoate, and cumene to be detected. On the detector module, the following bandwidths were used: 8 nm for the selected wavelengths; a reference wavelength of 400 nm with a bandwidth of 80 nm; and a multiplication factor of 0.5 for reducing the signal noise. A peak width with 0.1 s response time was selected for the signal to obtain a good detection of all peaks, which were narrow due to the high system efficiency. All analyses were carried out at room temperature.

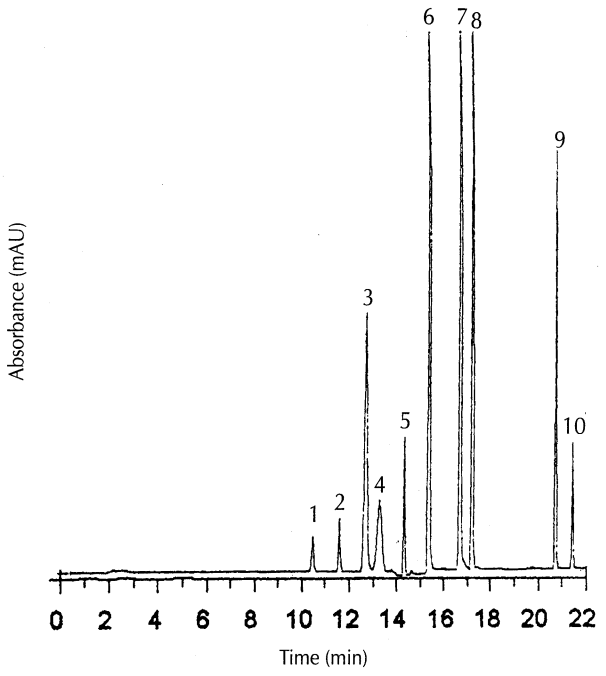

Figure 1. Chromatogram of a standard solution. Conditions: column, Chrompack Spherisorb 5 ODS-2 (250 x 4.6 mm); temperature, room; mobile phase, H_2O–CH_3CN–CH_3OH + 0.1% H_3PO_4; flow rate, 1.5 mL/min; injection, 20 µL; detection, ultraviolet at 254, 215, and 254 nm. The following gradient elution program was used: 0–5 min, 95% H_2O and 5% CH_3CN; 5–12 min, 55% H_2O, 35% CH_3CN, and 10% CH_3OH; 12–20 min, 15% H_2O, 75% CH_3CN, and 10% CH_3OH. Peaks: 1, 4-hydroxymethylbenzoic acid (10.52 min); 2, terephthalic acid (11.64 min); 3, 4-carboxybenzaldehyde (12.75 min); 4, terephthaldicarboxaldehyde (13.35 min); 5, 4-methylbenzyl alcohol (14.38 min); 6, *p*-toluic acid (15.4 min); 7, *p*-tolualdehyde (16.71 min); 8, methyl benzoate (17.24 min); 9, *p*-xylene (20.81 min); 10, cumene (21.55 min).

Standard preparation

Several standard solutions of the species involved during the oxidation of *p*-xylene to terephthalic acid were prepared to cover a wide calibration range of concentrations, as reported in Table II. In order to avoid solubility problems, solid species were weighted and then mixed with about 50 mL methanol in a 100-mL Pyrex Erlenmeyer flask. The solution was shaken and heated until the complete solubility of all components was achieved. It was then thoroughly transferred in a 100-mL volumetric flask where all liquid species (*p*-tolualdehyde, *p*-xylene, cumene, and methyl benzoate) had been previously weighted. The resulting solution was finally diluted up to 100 mL with methanol. For the analysis, 0.1 mL of each calibration standard was diluted to 5 mL with methanol.

Sample preparation

Determinations were performed on samples that were obtained directly from a batch oxidation laboratory reactor (5,6) where the oxidation of *p*-xylene to terephthalic acid (catalyzed by cobalt naphtenate with methyl benzoate as a solvent) was studied. About 0.5 mL of solution was taken from the reactor by means of a syringe or a pipette that was brought up to a temperature sufficiently high to prevent the precipitation of *p*-toluic acid and terephthalic acid. Each sample was accurately weighted and added with a precise quantity (15% of the sample weight) of cumene as an internal standard, and finally the mixture was diluted with 25 mL methanol. Only 0.1 mL of the sample obtained as described was diluted up to a volume of 1 mL with methanol in 1.5-mL vials that were finally used for analyses. Each sample was run in triplicate.

Results and Discussion

The system suitability was verified by checking all significant parameters for method validation, according to the guidelines and recommendations available in the literature (11–13). The resolution, R_S, of all components was calculated according to the following relationship (14):

$$R_s = \frac{t_{r2} - t_{r1}}{\frac{w_1 + w_2}{2}} \qquad \text{Eq 1}$$

where t_R is the retention time of each component as reported in Table III, and w is the mean peak width. All species displayed optimal resolution values (greater than or equal to 1.5), as indicated in Table III between each pair of components, corresponding to a complete baseline separation of all peaks.

The capacity factors for all compounds were estimated by injecting a Uracil standard solution (Chrompack, test mix 201) as the unretained component on the analytical stationary phase. The calculated values of the capacity factors were all acceptable (14) and are indicated in Table III. All peaks were found satisfactorily symmetrical with good asymmetry factors, which are also reported in Table III.

The system efficiency was evaluated in terms of number of theoretical plates of the column for each compound with which

satisfactory results could be obtained (Table III). Calculations were made according to the following relationship (14):

$$N = 5.545 \times \left(\frac{t_r}{w_h} \right)^2 \qquad \text{Eq 2}$$

where N represents the number of theoretical plates, t_R is the retention time, and w_h is the peak width at half height.

The precision of the developed analytical method was studied using several standard solutions in a wide range of concentrations. The results summarized in Table IV were achieved by running each standard six times, according to the literature guidelines (11,13); a typical chromatogram of a standard solution is also shown in Figure 1. Note from Table IV that the values of percent relative standard deviation are always less than 3.8%, except for the lowest level of concentration of each species where the maximum allowed limit of 15% indicated in the literature (15) is not exceeded. The values of the percent relative standard deviations of the retention time of each species are reported in Table IV. These results are extremely low, and in general, they come within 0.1%.

The accuracy of the method was tested by comparing the measured concentration values with the target concentrations. A series of standard solutions were prepared in a wide range of concentrations, and the highest values of the relative percent error are reported in Table V for each species. A value of 4% was never exceeded. Accuracy checks were performed by means of a multilevel calibration with linear fit on the Hewlett-Packard HP 3396A integrator. The level of accuracy of the method depends not only on good precision and resolution but also on system stability. The system stability, which should be guaranteed for at least 24 h (16), was checked up to 6 days by analyzing standard solution samples that were properly stored in a refrigerator during that time (Figures 2A–2C). The results show good stability for standard samples. The same conclusions are also valid for samples taken from the experimental oxidation reactor (5,6).

Detection and quantitation limits were evaluated with respect to signal-to-noise ratios of 2 and 10, respectively, through the following relationships (11,13):

$$DL = I \left(\frac{2}{S/N} \right) \qquad \text{Eq 3}$$

and

$$QL = I \left(\frac{10}{S/N} \right) \qquad \text{Eq 4}$$

where DL and QL represent the detection and the quantitation limits, respectively, I is the injected amount, and S/N is the signal-to-noise ratio, which can be calculated as follows (11):

$$S/N = \frac{h}{R_n} \qquad \text{Eq 5}$$

where h represents the signal height and $R_n = 6\Sigma$, where Σ is the standard deviation of the noise. The obtained values, which are reported in Table V, are satisfactory and refer to a standard solution containing very low quantities of those species, i.e.

Table V. Analytical Parameters for Method Validation

Compound	Accuracy (% relative error)	Detection limit ($S/N = 2$)	Quantitation limit ($S/N = 10$)	Selectivity (purity index)	Concentration in methenol (µg/mL)	Correlation coefficient (linearity)
4-Hydroxymethylbenzoic acid	0.9	4.2	20.8	1.06	0–17 0–10	0.997 0.9996
Terephthalic acid	1.9	1.2	6.3	1.06	0–10 0–5	0.998 0.9998
4-Carboxybenzaldehyde	3.9	0.5	2.8	1.2	0–17 0–10	0.997 0.9998
Terephthaldicarboxaldehyde	4	2.6	13.1	1.1	0–10 0–5	0.998 0.9999
4-Methylbenzyl alcohol	1.8	2.4	12.3	1.08	0–20 0–10	0.997 0.9998
p-Toluic acid	3.8	0.57	2.8	1.03	0–200	0.9994
p-Tolualdehyde	0.5			1.3	0–80 0–40	0.998 0.999
Methyl benzoate	2.4			1	0–1800 0–900	0.998 0.9997
p-Xylene	0.5			1.05	0–1100 0–300	0.997 0.999
Cumene				1.07	0–600	0.9991

4-hydroxymethylbenzoic acid (0.64 ng/µL), terephthalic acid (0.3 ng/µL), 4-methylbenzyl alcohol (0.69 ng/µL), and *p*-toluic acid (0.73 ng/µL), that can display low concentrations in the samples from the experimental oxidation reactor.

The specificity or selectivity of the method was checked by injecting, for each species, several samples with different concentrations and measuring the ratio of the peak areas at 220 and 254 nn. This ratio remained fairly constant and the values of the purity index reported in Table V were always less than the maximum limit of 1.5.

The linearity of the developed method was also verified. This was done by plotting the injected amount for each analyte as a function of the peak area counts. The corresponding regression lines were fitted through the least-squares method. As shown in Figure 3 for the case of terephthalic acid, the graph is linear over the concentration range presented in Table V. This result is also valid for the other analytes, as seen from the values of the regression coefficients listed in Table V, which were always greater than 0.997 over the concentration ranges presented in the same table. Note that the analytical method showed good precision, accuracy, and linearity over these ranges. However, as expected, better values were obtained by reducing the concentration range (Table V).

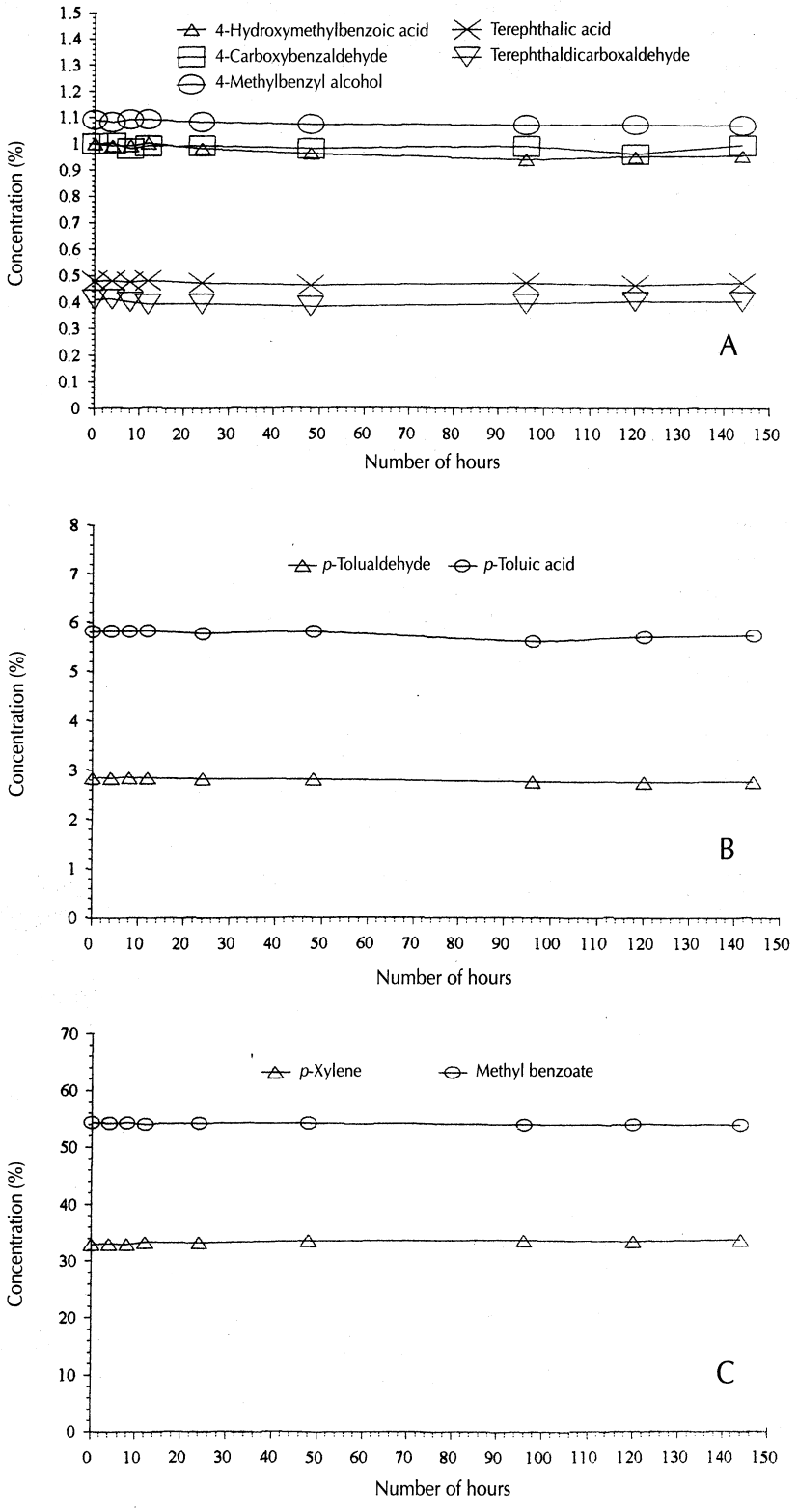

Figure 2. Representation of sample stability over 6 days.

As noted in the introduction, this analytical method has been used recently (5,6) to develop a lumped kinetic model for liquid-phase catalytic oxidation of *p*-xylene to terephthalic acid. A typical chromatogram of a sample from the oxidation reactor is shown in Figure 4. The analytical method allowed the determination of the products of *p*-xylene oxidation under a relatively wide range of operating conditions, i.e., seven temperature levels (80, 90, 100, 105, 110, 120, and 130°C), three different initial values of *p*-xylene (4, 6, and 9 mol/kg sol) and *p*-tolualdehyde concentrations (0.11, 0.17, and 0.22 mol/kgsol), and two partial pressure levels of oxygen (1 and 0.21 atm).

Conclusion

A reversed-phase HPLC method for the relatively quick determination of *p*-xylene and its catalytic liquid-phase oxidation products within a wide range of concentrations with limited sample manipulation was developed. The characteristics of the analytical method were described, and its reliability was successfully tested with respect to the recommended parameters available in the literature. The developed method has been used recently (5,6) to study the kinetics of *p*-xylene liquid-phase oxidation to terephthalic acid catalyzed by cobalt naphtenate using methyl benzoate as a solvent under a wide range of operating conditions.

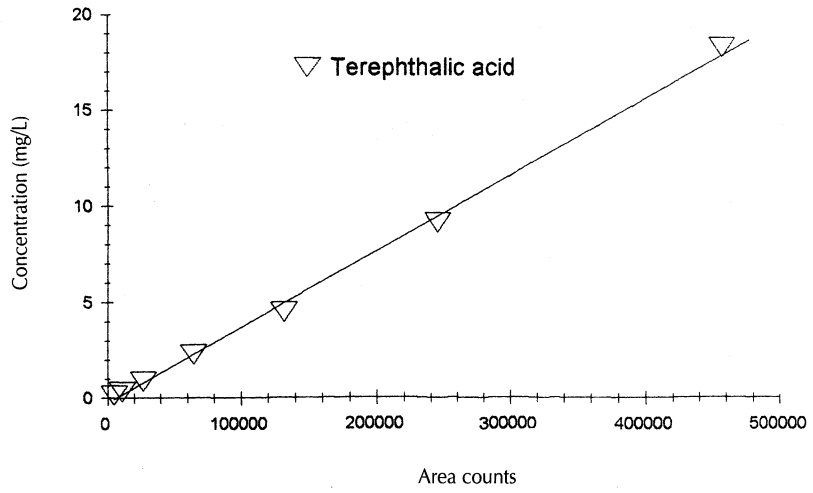

Figure 3. Linear regression curve of terephthalic acid.

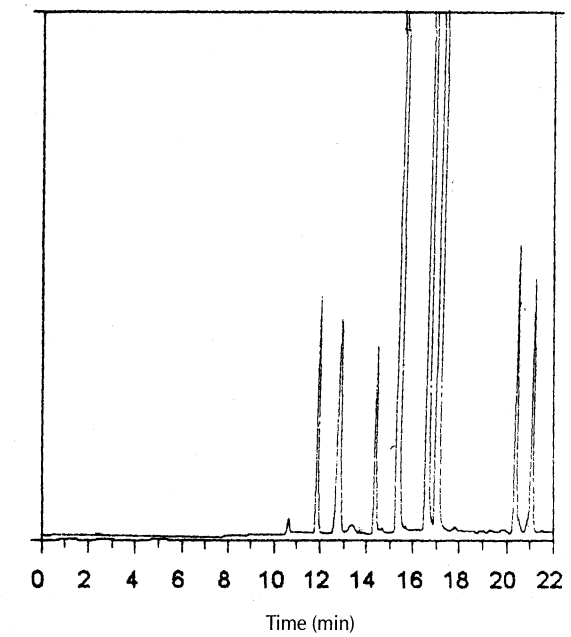

Figure 4. Chromatogram of an oxidation reaction sample. Conditions: column, Chrompack Spherisorb 5 ODS-2 (250 x 4.6 mm); temperature, room; mobile phase, H_2O–CH_3CN–CH_3OH + 0.1% H_3PO_4; flow rate, 1.5 mL/min; injection, 20 µL; detection, ultraviolet at 254, 215, and 254 nm. The following gradient elution program was used: 0–5 min, 95% H_2O, 5% CH_3CN; 5–12 min, 55% H_2O, 35% CH_3CN, 10% CH_3OH; 12–20 min, 15% H_2O, 75% CH_3CN, 10% CH_3OH.

Acknowledgments

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