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Short communication

Application of normal- and reversed-phase high-performance liquid chromatography for monitoring the progress of reactions of anthraquinone manufacturing processes☆

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Abstract

Two different methods for the separation and determination of the reactants, intermediates and products of anthraquinone manufacturing processes using normal- and reversed-phase high-performance liquid chromatography were developed. The separations were achieved on Spherisorb silica and reversed phase C_{18} columns using *n*-heptane–ethanol–chloroform–acetic acid (89:5:5:1, v/v) and acetonitrile–water (65:35, v/v) as the eluents, respectively. These methods were used not only for monitoring the reaction conditions but also the yields of anthraquinone.

1. Introduction

9,10-Anthraquinone is not only an important intermediate in the manufacture of various dyestuffs but is also used as a catalyst in the isomerization of vegetable oils [1]. It is produced in large amounts by the Friedel–Crafts reaction of phthalic anhydride and benzene in the presence of $AlCl_3$ catalyst [2]. Our laboratory has studied not only this process but also an alternative for the economic production of anthraquinone, involving the oxidation of toluene to benzoic acid followed by catalytic condensation [3]. The development of these two processes has required analytical methods for monitoring not only the reaction products but also the quality of anthraquinone.

Several gravimetric, titrimetric, polarographic and spectrophotometric techniques have been used for the evaluation of anthraquinone industrially [4,5], but they lack not only specificity but also accuracy owing to the influence of impurities present in anthraquinone. Anderson [6] and Mitra and Ghosh [7] determined anthraquinone in the vapour-phase oxidation products of toluene by gas–liquid chromatography. The separation was achieved on columns packed with 5% OV-101 on Chromosorb G using temperature programming. However, these methods were tedious and time consuming. Several high-performance liquid chromatographic (HPLC) methods for the determination of anthraquinone in environmental pollutants have been reported [8–10]. However, no suitable method for moni-

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toring the reaction conditions of anthraquinone processes is available.

In this paper, we describe two different methods for the separation, identification and determination of the reactants, intermediates, products and by-products of anthraquinone manufacturing processes by normal- and reversed-phase HPLC.

2. Experimental

2.1. Materials and reagents

All reagents were of analytical-reagent grade, unless stated otherwise. Glass-distilled water, acetonitrile, *n*-heptane, ethanol and chloroform (Spectrochem, Bombay, India) were used. Anthraquinone (BDH, Poole, UK) was used as a reference standard.

2.2. Apparatus

A Model ALC/GPC 244 high-performance liquid chromatograph (Waters, Milford, MA, USA) was used along with a U6K injector system and a Model 440 UV spectrophotometric detector. A Spherisorb silica column (250 mm × 4.6 mm I.D., particle size 5 μm) and a C_{18} column (250 mm × 4.6 mm I.D., particle size 5 μm) (Bischoff, Leonberg, Germany) were used for separation. The chromatograms and the integrated data were recorded with an Omniscribe D 5000 recorder and a Chromatopac E1A integrator, respectively.

2.3. Chromatographic conditions

Normal-phase HPLC

The mobile phase was *n*-heptane–ethanol–chloroform–acetic acid (89:5:5:1, v/v). Samples were dissolved in the mobile phase. The analysis was carried out under isocratic conditions at a flow-rate of 1 ml/min at room temperature (27°C). Chromatograms were recorded at 254 nm.

Reversed-phase HPLC

The mobile phase was acetonitrile–water (65:35, v/v). The flow-rate was 1 ml/min at room temperature (27°C). Chromatograms were recorded at 254 nm.

2.4. Analytical procedure

Samples of anthraquinone (10 mg) were dissolved in the mobile phase (50 ml) and 20 μl of each sample were injected and chromatographed. Synthetic and reaction mixtures were analysed under identical conditions. The amount of anthraquinone was calculated from the peak area.

3. Results and discussion

Fig. 1 shows the reaction pathways followed for the production of anthraquinone. The reaction mixtures and products of these processes were subjected to normal- and reversed-phase HPLC.

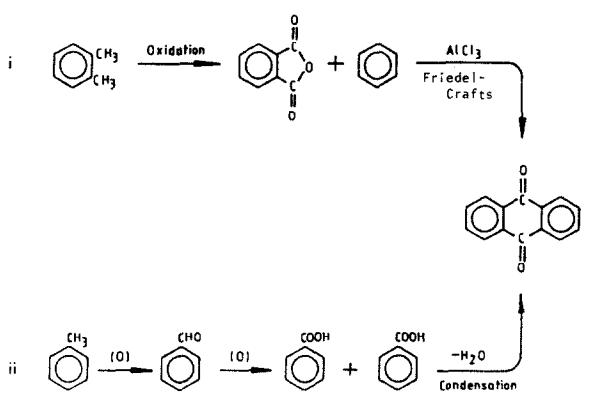

Fig. 1. Production of anthraquinone by (i) oxidation of *o*-xylene followed by Friedel–Crafts reaction of phthalic anhydride and benzene in the presence of $AlCl_3$ and (ii) oxidation of toluene to benzaldehyde to benzoic acid and its catalytical condensation.

3.1. Monitoring the reaction products of phthalic anhydride and benzene by normal-phase HPLC

The HPLC separation of anthraquinone and its impurities is shown in Fig. 2. The peaks were identified by injecting individual authentic compounds. It can be seen from Fig. 2 that anthraquinone is well separated from the process reactants, viz., *o*-xylene, benzene and phthalic anhydride. Maleic anhydride was used as an internal standard. It does not interfere in the determination and elutes at 6.83 min. The Spherisorb silica column was used with *n*-heptane–ethanol–chloroform–acetic acid (89:5:5:1, v/v) as mobile phase for separation. It may be noted that reversed-phase HPLC is not suitable for separation of the same reactants because phthalic anhydride is hydrolysed to phthalic acid in solvent systems containing water. The Spherisorb silica column provided the optimum resolution of peaks corresponding to the analytes under investigation. The retention data, response data and wavelengths of maximum absorption of all the compounds are given in Table 1. The linearity between the mass and integral responses of anthraquinone is good. When the UV detector is set at 0.005 AUFS the limit of detection for anthraquinone is $5.0 \cdot 10^{-9}$ g with a signal-to-noise ratio of 4.0.

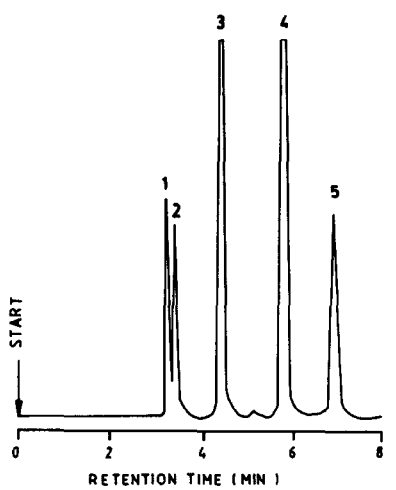

Fig. 2. Chromatogram of a mixture containing (2) benzene (1.8 μg), (1) *o*-xylene (1.6 μg), (4) phthalic anhydride (0.5 μg), (3) anthraquinone (0.1 μg) and (5) maleic anhydride (2.1 μg). Conditions: column, Spherisorb silica (250 mm × 4.6 mm I.D., particle size 10 μm); mobile phase, *n*-heptane–ethanol–chloroform–acetic acid (89:5:5:1, v/v); flow-rate, 1 ml/min; detection, UV at 254 nm.

Table 1
Retention data for reactants involved in the synthesis of anthraquinone by reaction (i)[a]

Compound	Retention time (min)	Response factor	λ_{max} (nm)
Benzene	3.35	1.00	255
o-Xylene	3.20	1.14	252
Phthalic anhydride	5.79	3.81	245
Anthraquinone	3.94	40.04	249
Maleic anhydride	6.83	1.28	225

[a] See Fig. 1.

Standard mixtures containing known amounts of the analytes were prepared and analysed by HPLC. The accuracy of the method was determined by the standard addition technique. Subsequent additions of small amounts of the analytes were accurately reflected in their peak heights. The measured amounts agreed well with the actual values (within 2.97%). The calibration graphs are shown in Fig. 3. The relative response factors were determined for all the compounds and used to determine the compositions of reaction mixtures obtained during the process development.

The method was applied not only to monitor the reaction conditions but also to determine the quality of anthraquinone periodically. Fig. 4 shows a typical chromatogram of a reaction mixture analysed during the course of reactions. The concentrations of various reactants were determined and the composition of reaction mixture was calculated. The levels of anthraquinone formed at different stages of the reaction are given in Table 2.

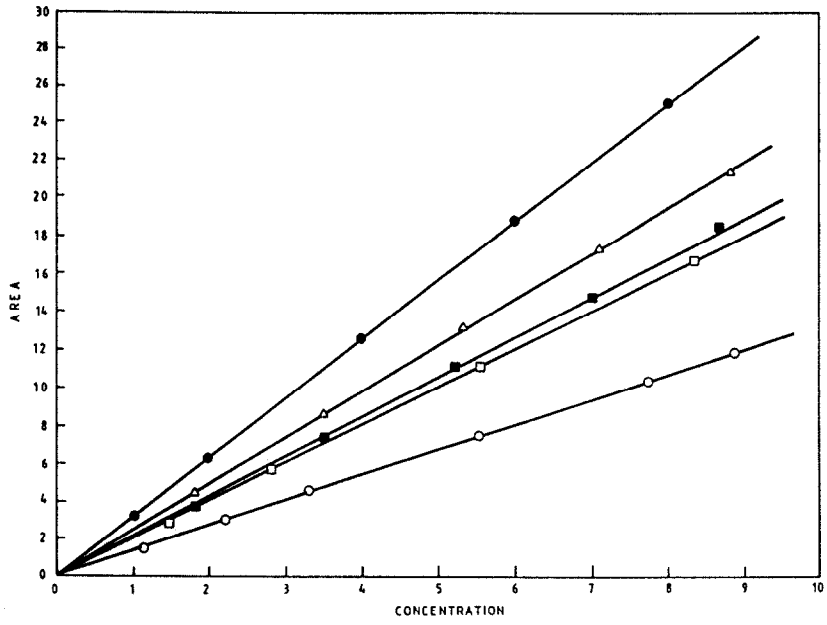

Fig. 3. Calibration graphs showing the linearity between concentration and integral response of (△) *o*-xylene, (■) benzene, (●) phthalic anhydride, (□) anthraquinone and (○) maleic anhydride. Concentration given in μg.

3.2. Monitoring the products of catalytic oxidation of toluene by reversed-phase HPLC

The reactants and products of this process were subjected to HPLC and their separation is shown in Fig. 5. It can be seen that anthraquinone is well separated from all the process impurities, viz., toluene, benzaldehyde and benzoic acid. The retention data are given in Table 3. The method was well standardized and used for process development. Fig. 6 shows a typical chromatogram of anthraquinone obtained by this process. The product yields were optimized by following the reaction conditions by HPLC. The results are given in Table 4. These results indi-

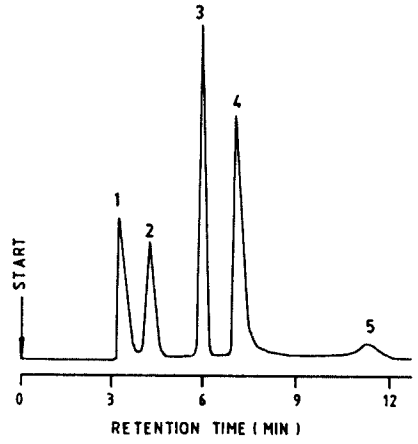

Fig. 4. Typical chromatogram of a reaction mixture collected during the course of reaction of phthalic anhydride with benzene in the presence of $AlCl_3$ as catalyst. Peaks: 1 = benzene; 2 = anthraquinone; 3 = phthalic anhydride; 4 = maleic anhydride; 5 = unknown. For conditions, see Fig. 2.

Table 2
Levels of anthraquinone formed at different stages of the reaction

Sample	Time (h)	Anthraquinone (%)[a]	S.D. (%)
React mixture 1	0.5	3.92	2.45
React mixture 2	1.0	9.75	1.98
React mixture 3	2.0	22.41	1.72
React mixture 4	4.0	49.38	1.64

[a] Average of three determinations.

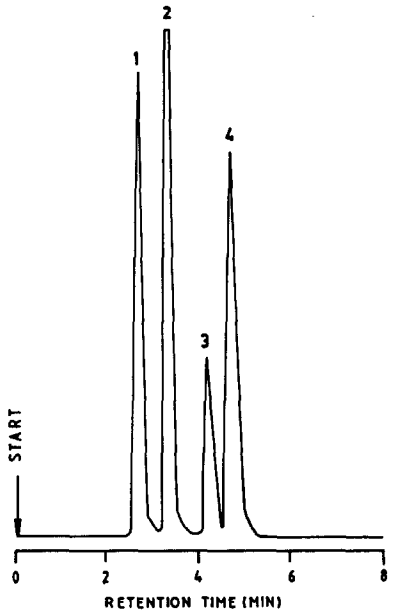

Fig. 5. Chromatogram of a typical mixture containing (1) benzoic acid (1.9 μg), (2) benzaldehyde (0.2 μg), (3) toluene (1.7 μg) and (4) anthraquinone (0.1 μg). Conditions: column, C_{18} (250 mm × 4.6 mm I.D., particle size 5 μm); mobile phase, acetonitrile–water (65:35, v/v); flow-rate, 1 ml/min; detection, UV at 254 nm.

cate that the method is suitable for monitoring the oxidation products of toluene.

4. Conclusions

The proposed HPLC methods are simple and rapid for monitoring the reaction products of anthraquinone manufacturing process. They are accurate and precise for the determination of process impurities and related products of industrial anthraquinone production.

Table 3
Retention data for reactants involved in the synthesis of anthraquinone by reaction (ii)[a]

Compound	Retention time (min)	Response factor	λ_{max} (nm)
Toluene	4.22	1.00	210
Benzaldehyde	3.32	45.19	243
Benzoic acid	2.60	3.39	226
Anthraquinone	4.72	87.51	252

[a] See Fig. 1.

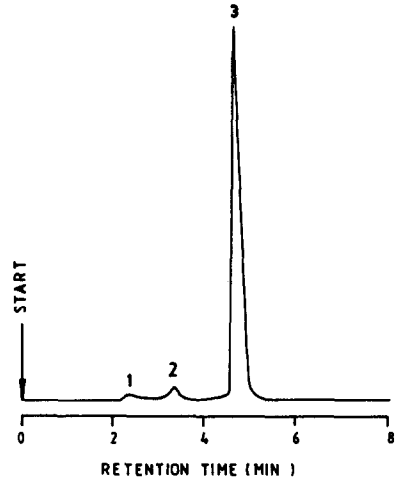

Fig. 6. Typical chromatogram of anthraquinone obtained during process development. Peaks: 1 = benzoic acid; 2 = benzaldehyde; 3 = anthraquinone. For conditions, see Fig. 5.

Table 4
Purity of anthraquinone

Sample	Purity by HPLC (%)[a]	S.D. (%)
Product 1	99.39	1.47
Product 2	98.74	1.82
Product 3	98.15	1.59

[a] Average of three determinations.

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