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Short Communication

High-performance liquid chromatography of isopropylphenols

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ABSTRACT

This paper presents a method for the direct determination of phenol, monoisopropylphenols (2-, 3- and 4-), diisopropylphenols (2,4-, 2,5-, 2,6- and 3,5-) and triisopropylphenols (2,4,5- and 2,4,6-) in technical alkylates. The possibility of controlling the alkylation reaction of phenol with propylene is shown. The 99% confidence limit is 10 ± 0.2%. The possibility of removing isopropylphenylethers from the alkylate and their determination are also discussed.

INTRODUCTION

The alkylphenols are important intermediates in the production of polymer additives with special applications. The most important of these compounds are the isopropylphenols. High-performance liquid chromatography (HPLC) has been used successfully in the separation of alkylphenols using both normal- [1–6] and reversed-phase [1–3,5,7,8] columns. The relationship between the molecular structure and retention of methylphenols has been studied [9]. Previously reported analytical procedures used UV and electrochemical detection [2,6,10] of alkylphenols.

This paper reports the direct determination of 4-isopropylphenol and other isomers as well as the products of side-reactions. The investigations were undertaken to develop an HPLC procedure capable of resolving and quantitating mixtures of isopropylphenols which would be applicable to the determination of industrially important isomers in technical mixtures [11].

EXPERIMENTAL

Chromatographic equipment

All separations were carried out using a Varian 2210 isocratic system, which includes a Model 2010 pump, a Model 2550 variable-wavelength UV detector, a Model 2081 column/valve mounting module and a Rheodyne injector. Retention data and the peak areas were measured and calculated by a Model SP 4200 computing integrator (Spectra-Physics).

Column

The column was a Separon SGX (Tessek, Czechoslovakia) consisting of 300 × 3.3 mm I.D. glass tubing packed with 5-μm silica.

Reagents

The chemicals were of analytical-reagent grade; *n*-hexane and dioxane were of spectroquality grade. Dioxane was dried and cleared of peroxidies by

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TABLE I
RELATIVE RETENTION TIMES OF ISOPROPYLPHENOLS

Compound	Relative retention time
2,4,6-Triisopropylphenol	0.228
2,6-Diisopropylphenol	0.243
2,4,5-Triisopropylphenol	0.380
2,5-Diisopropylphenol	0.416
2,4-Diisopropylphenol	0.492
2-Isopropylphenol	0.568
3,5-Diisopropylphenol	0.654
3-Isopropylphenol	0.791
4-Isopropylphenol	0.857
Phenol	1.000

passing through a 60 × 2 cm I.D. column filled with activated alumina.

The standards used (Table I) were prepared by the Division of Organic Chemistry in this Institute according to standard procedures; their purities and structures were established by elemental analysis, standard physicochemical techniques (Table II), ^{1}H NMR, ^{13}C NMR and gas chromatography–mass spectrometry.

Mobile phase

The mobile phase consisted of 2% (v/v) dioxane in *n*-hexane. The mobile phase for the separation of ethers was *n*-hexane.

Standard solutions

Standard solutions were prepared in the range 1–30 mg per 50 ml. Stock solutions of isopropylphenols were first prepared by dissolving 200 mg of the appropriate compound in 50 ml of mobile phase, then working standards were prepared by dilution of the stock solutions. The stock solutions were stable for up to 1 week when stored in the refrigerator.

TABLE II
BOILING AND FREEZING POINTS OF ISOPROPYLPHENOLS

Compound	Boiling point (°C)[a]	Freezing point (°C)
2,4,6-Triisopropylphenol	135	28
2,4,5-Triisopropylphenol	145	75
2,6-Diisopropylphenol	121	18
2,5-Diisopropylphenol	131	26
2,4-Diisopropylphenol	127	22
3,5-Diisopropylphenol	134	50
2-Isopropylphenol	94	15
4-Isopropylphenol	108	63

[a] 1.6 kPa.

Sample solution

For the analysis of technical mixtures of isopropylphenols 100–300 mg of sample were accurately weighed into a 50-ml calibrated flask, dissolved and diluted to volume with mobile phase.

Chromatographic procedure

The separations were performed in the isocratic mode at ambient temperature at a flow-rate of 1.0 ml/min (2 ml/min for the separation of ethers). Volumes of 10 μl of the solutions were introduced on to the column with a constant-volume loop injector. The detector was operated at 280 nm (0.32 a.u.f.s.).

Calculation

Calibration graphs were generated by plotting the peak area *versus* the concentration of standard substances in the concentration range 20–600 μg/ml. In all instances the calibration graphs were linear with a correlation coeficient of 0.999. Values of unknown sample concentrations were determined by comparison with the calibration graph.

Separation of ethers

Ethers were first isolated from the technical mixture with *n*-hexane on a 250 × 10 mm I.D. column packed with 100–160 μm Silasorb L (Lachema, Brno, Czechoslovakia). First three 100-ml fractions were concentrated to 10-ml volumes and reinjected onto an analytical column.

RESULTS AND DISCUSSION

To find the optimum chromatographic system the influence of the mobile phase on the retention time was studied. Combinations of methanol, acetonitrile and water were evaluated as mobile phases. Reversed-phase HPLC was found not to provide a satisfactory separation of closely related couples of the compounds 2-isopropylphenol, 3-isopropylphenol, 2,4-diisopropylphenol and 2,5-diisopropylphe-

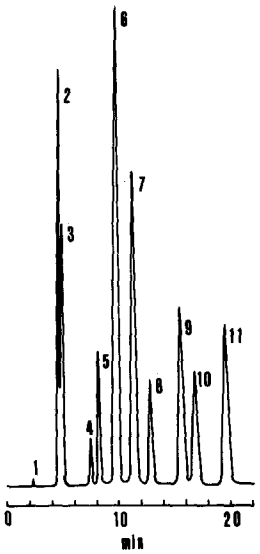

Fig. 1. High-performance liquid chromatogram of a mixture of isopropylphenols. Compact glass column, 300 × 3.3 mm I.D. Separon SGX, 5 μm; eluent, *n*-hexane–dioxane (98/2, v/v); flow-rate, 1 ml/min; UV detector, 280 nm. Peaks: 1 = phenyl isopropyl ether; 2 = 2,4,6-triisopropylphenol; 3 = 2,6-diisopropylphenol; 4 = 2,4,5-triisopropylphenol; 5 = 2,5-diisopropylphenol; 6 = 2,4-diisopropylphenol; 7 = 2-isopropylphenol; 8 = 3,5-diisopropylphenol; 9 = 3-isopropylphenol; 10 = 4-isopropylphenol; 11 = phenol.

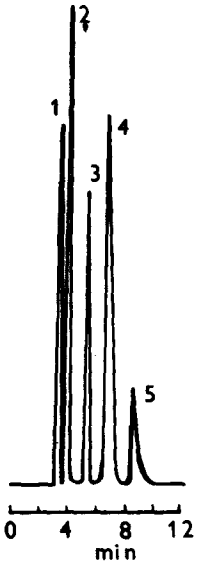

Fig. 2. High-performance liquid chromatogram of a mixture of isopropylphenylethers. Compact glass column, 300 × 3.3 mm I.D. Separon SGX, 5 μm; eluent, *n*-hexane; flow-rate, 2 ml/min; UV detector, 280 nm. Peaks: 1 = 2-isopropylphenyl isopropyl ether; 2 = 2,4-diisopropylphenyl isopropyl ether; 3 = phenyl isopropyl ether; 4 = 4-isopropylphenyl isopropyl ether and 2,6-diisopropylphenyl isopropyl ether; 5 = 2,4,6-triisopropylphenyl isopropyl ether.

nol [12]. Attempts to improve the peak shapes, retention time and resolution by altering the concentrations of the solvent were unsuccessful.

Good separation of isopropylphenols (Fig. 1) and isopropylphenylethers (Fig. 2) was achieved by normal-phase HPLC. As illustrated in Fig. 1, separation of mixtures of isopropylphenols can be obtained by the use of an isocratic solvent system *n*-hexane–dioxane (98:2, v/v). The use of dioxane as the modifier in the mobile phase for the separation of alkylphenols by normal-phase HPLC is in agreement with the principles of solvent selectivity (dioxane, tetrahydrofuran and propan-2-ol, respectively) discussed by Dzido and Soczewiński [13].

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