

High-performance liquid chromatographic determination of products of autoxidation of isopropylbenzene derivatives

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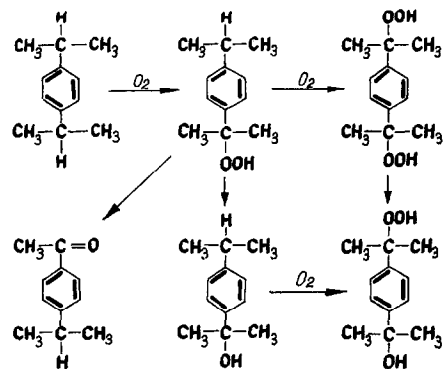
(First received August 7th, 1990; revised manuscript received July 15th, 1991)

ABSTRACT

The application of high-performance liquid chromatography to the qualitative and quantitative determination of the products of the autoxidation of cumene, *p*-cymene and 1,3- and 1,4-diisopropylbenzene is described.

INTRODUCTION

The autoxidation of isopropyl derivatives of benzene to hydroperoxides is the first reaction step in the process for the manufacture of phenols [1]. The autoxidation products are complicated mixtures containing unreacted hydrocarbons and compounds such as hydroperoxides, alcohols, ketones and many other oxygen derivatives. When two or more isopropyl groups are present on the benzene ring, the compositions of the mixtures are especially complicated. An example of such a process is the autoxidation of 1,4-diisopropylbenzene:



Such mixtures are not easily separated and analysed by conventional techniques. Gas chromatography (GC) [2–6] is not useful because some compounds are non-volatile and thermally unstable. Thin-layer chromatography (TLC) [7,8] and conventional column chromatography [9,10] offer insufficient separation efficiency and are slow. NMR techniques [10–12] offer unsatisfactory precision. IR [13–16], polarographic [17], density measurement [18] and iodimetric titration [19,20] methods enable only some of the components of the mixtures to be determined.

In contrast, high-performance liquid chromatography (HPLC [21–23]) is a versatile, efficient and relatively rapid separation method for non-volatile, thermally labile compounds and is ideal for the separation and study of the mixtures from autoxidation reactions.

In this paper the separation and determination of components of the autoxidation products of cumene, 1,3- and 1,4-diisopropylbenzene and *p*-cymene is reported. Isocratic elution was employed because of its simplicity and potential use in routine analysis.

EXPERIMENTAL

Materials and reagents

The solvents hexane, isopropanol and chloroform were of HPLC grade.

Standards

Cumyl hydroperoxide (technical product) was purified [24] and 1-methyl-1-phenylethanol [25], 1,3- and 1,4-diisopropylbenzene [26] and *p*-cymene derivatives [27,28] were prepared by published methods. Acetophenone was of analytical-reagent grade.

High-performance liquid chromatography

HPLC analyses were conducted utilizing an Philips LC XPD chromatograph, a Reodyne Model 7125 syringe-loading sample injector with a 20- μ l loop and 25 cm \times 4.6 mm I.D. stainless-steel column filled with LiChrosorb 60 (5 μ m) or Partisil 10 (10 μ m). The mobile phases were isopropanol-hexane mixtures at a flow-rate 1.0 cm³/min. Samples for injection (20 μ l) were solutions in the mobile phase. Compounds were detected at 257 nm with a LC XPD UV-VIS detector and integrated with a CDP4 integrator.

Quantitative procedures

Calibration was carried out according to one of two methods: external standardization using the external standard mode CDP4 integrator and internal standardization. In the external standardization mode, full 20- μ l loop repetitive injections of single-concentration standard solution were used for single-point calibration, based on principles where the test samples are "bracketed" by standards injected before and after test. An internal standard method was also used for comparison. The ratio of the peak area of the analysed compounds to that of the internal standard was used to construct a calibration graph. A number of possible internal standard were explored for quantification of each compound. The criteria applied in assessing a suitable candidate were the UV absorbance in the region of 257 nm, chemical similarity to analysed compounds, a capacity factor (k') close to each component and complete separation from other sample components.

For all mixtures examined 1-methyl-1-phenylethanol was chosen as the internal standard except for

the autoxidation products of cumene, where cumyl hydroperoxide was used.

RESULTS AND DISCUSSION

Selection of eluents

The conditions of analysis were investigated for the purpose of establishing routine analytical HPLC. It was important to know if there was any decomposition of hydroperoxides in the presence of LiChrosorb Si 60. The behaviour of cumyl hydroperoxide in the presence of LiChrosorb Si 60 (10 μ m) was examined. A 1-g amount of cumyl hydroperoxide was dissolved in 5 cm³ of *n*-hexane and stirred with 1-g of LiChrosorb Si 60 (10 μ m) for 8 h at room temperature. In the organic phase the hydroperoxide was determined by HPLC and iodimetric titration. HPLC did not provide evidence of hydroperoxide decomposition products. Iodimetric titration showed no change in hydroperoxide concentration.

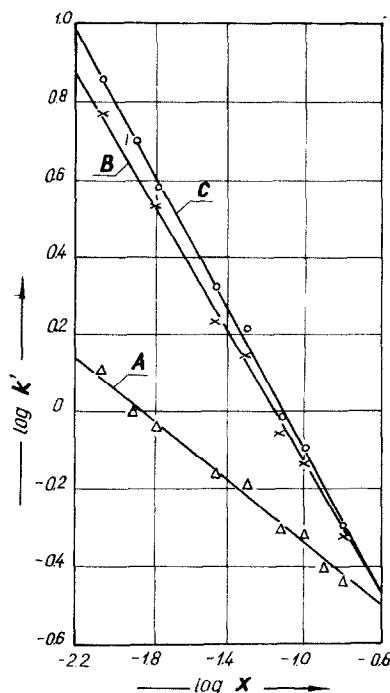


Fig. 1. Relationship between $\log k'$ of autoxidation products of cumene and $\log x$, where x = molar ratio of isopropanol to *n*-hexane. (A) Acetophenone; (B) cumene hydroperoxide; (C) 1-methyl-1-phenylethanol.

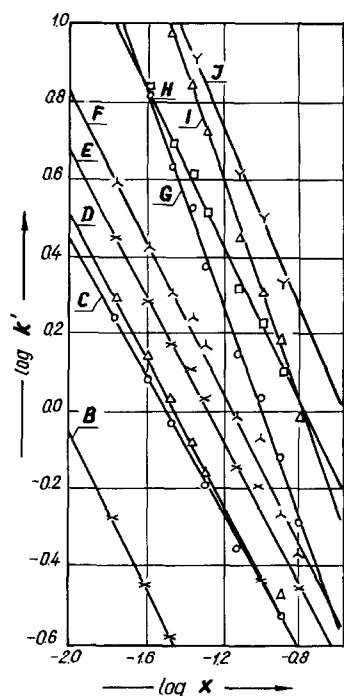


Fig. 2. Relationship between $\log k'$ of autoxidation products of 1,3-diisopropylbenzene and $\log x$, where x = molar ratio of isopropanol to *n*-hexane. (C) 1,3-Di(1-methylethyl)benzene monohydroperoxide; (E) 1-methyl-[3-(1-methylethyl)phenyl]-1-hydroxyethane; (F) 1-methyl-1-phenylethanol; (G) 1,3-di(1-methylethyl)benzene dihydroperoxide; (H) 1-[3-(1-hydroxymethylethyl)phenyl]-1-methylethane hydroperoxide. (A), (B), (D), (I) and (J) are unidentified compounds.

The performance of three solvent systems as eluents was examined: *n*-hexane-isopropanol, *n*-hexane-chloroform and chloroform-isopropanol. *n*-Hexane-isopropanol provided the best resolution. The dependence of $\log k'$ on \log (molar ratio

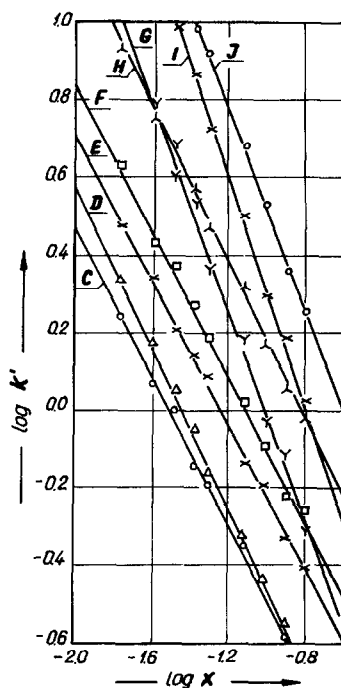


Fig. 3. Relationship between $\log k'$ of autoxidation products of 1,4-diisopropylbenzene and $\log x$, where x = molar ratio of isopropanol to *n*-hexane. (C) 1,4-Di(1-methylethyl)benzene monohydroperoxide; (E) 1-methyl-[4-(1-methylethyl)phenyl]-1-hydroxyethane; (F) 1-methyl-1-phenylethanol; (G) 1,4-di(1-methylethyl)benzene dihydroperoxide; (H) 1-[4-(1-hydroxymethylethyl)phenyl]-1-methylethane hydroperoxide. (A), (B), (D), (I) and (J) are unidentified compounds.

of components) is shown in Fig. 1-4.

For quantitative analyses, solvent compositions having $1 < k' < 10$ were chosen, because for $k' < 1$ poor resolution and a poorly defined baseline and for $k' > 10$ broad peaks were observed.

TABLE I

EXTERNAL STANDARD CALIBRATION: LINEAR REGRESSION BY LEAST-SQUARES METHOD FOR A PLOT OF PEAK AREA VERSUS MASS INJECTED FOR AUTOXIDATION PRODUCTS OF CUMENE

Number of calibration points for each compounds, $n=7$; number of replicates of each injection, $m=5$.

Compounds	Range (μg)	Slope, a	Intercept, b	Correlation coefficient, r
Acetophenone	0.1-1.0	$1.1201 \cdot 10^{10}$	14042	0.998
Cumene hydroperoxide	1.0-10.0	$1.2783 \cdot 10^9$	4152	0.999
1-Methyl-1-phenylethanol	1.0-5.0	$1.3795 \cdot 10^9$	1731	0.999

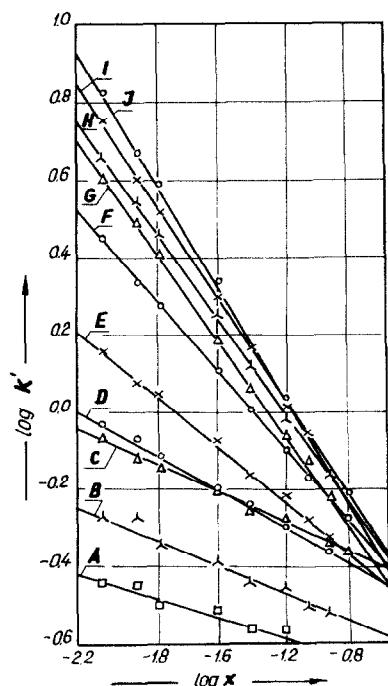


Fig. 4. Relationship between $\log k'$ of autoxidation products of *p*-cymene and $\log x$, where x = molar ratio of isopropanol to *n*-hexane. (B) [4-(1-Methylethyl)phenyl]methane hydroperoxide; (C) 4-methylacetophenone; (F) 1-methyl-1-(4-methylphenyl)ethane hydroperoxide; (G) 1-methyl-4-(hydroxy-1-methylethyl)benzene; (J) 1-methyl-1-phenylethanol. (A), (B), (E), (H) and (I) are unidentified compounds.

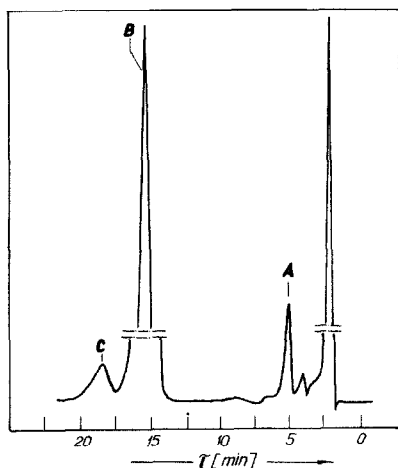


Fig. 5. Typical chromatogram of autoxidation products of cumene. Peaks: A = acetophenone; B = cumene hydroperoxide; C = 1-methyl-1-phenylethanol. Eluent, isopropanol-hexane (0.5:99.5); column Partisil 10 (10 μm) (25 cm); flow-rate, 1.0 ml/min.

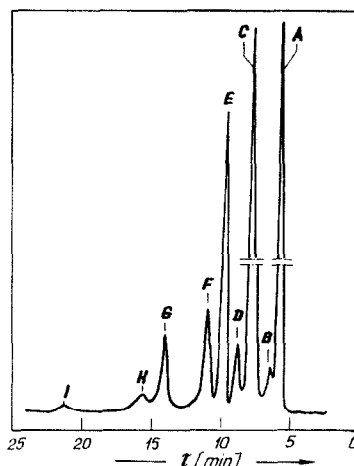


Fig. 6. Typical chromatogram of autoxidation products of 1,3-diisopropylbenzene. Peaks: A = 1,3-diisopropylbenzene; C = 1,3-di(1-methylethyl)benzene monohydroperoxide; D = 1,3-dihydroxybenzene; E = 1,3-di(1-methylethyl)benzene dihydroperoxide; F = 1-methyl-1-phenylethanol; G = 1-[3-(1-hydroxy-1-methyl)phenyl]-1-methylethane hydroperoxide; H = 1-methyl-[3-(1-methylethyl)phenyl]-1-hydroxyethane. B and I are unidentified compounds. Eluent, isopropanol-hexane (2.0:98.0); column, LiChrosorb Si 60 (5 μm) (25 cm); flow-rate, 1.0 ml/min.

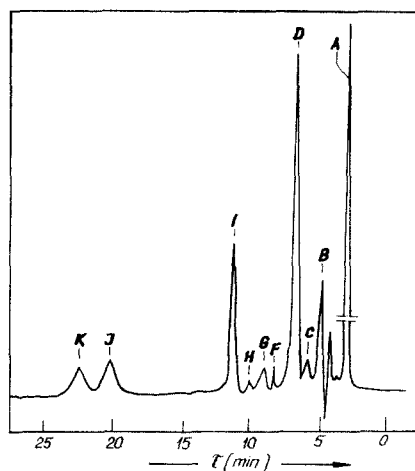


Fig. 7. Typical chromatogram of autoxidation products of 1,4-diisopropylbenzene. Peaks: A = 1,4-diisopropylbenzene; D = 1,4-di(1-methylethyl)benzene monohydroperoxide; F = 1,4-dihydroxybenzene; H = 1-methyl-1-phenylethanol; I = 1,4-di(1-methylethyl)benzene dihydroperoxide; J = 1-[4-(1-hydroxy-1-methylethyl)phenyl]-1-methylethane hydroperoxide; K = 1-methyl-[4-(1-methylethyl)phenyl]-1-hydroxyethane. B, C, E and G are unidentified compounds. Eluent, isopropanol-hexane (2.0:98.0); column, LiChrosorb Si 60 (5 μm) (25 cm); flow-rate, 1.0 ml/min.

TABLE II

EXTERNAL STANDARD CALIBRATION: LINEAR REGRESSION BY LEAST-SQUARES METHOD FOR A PLOT OF PEAK AREA *VERSUS* MASS INJECTED FOR AUTOXIDATION PRODUCTS OF 1,3-DIISOPROPYLBENZENENumber of calibration points for each compounds, $n = 7$; number of replicates of each injection, $m = 5$.

Compounds	Range (μg)	Slope, a	Intercept, b	Correlation coefficient, r
1,3-Di(1-methylethyl)benzene monohydroperoxide	1.0–10.0	$1.2193 \cdot 10^9$	2735	0.997
1-[3-(1-Hydroxy-1-methylethyl)phenyl]-1-methylethane hydroperoxide	1.0–5.0	$1.3145 \cdot 10^9$	3275	0.998
1-Methyl-[3-(1-methylethyl)phenyl]-1-hydroxyethane	1.0–5.0	$1.2831 \cdot 10^9$	4142	0.995
1,3-Di(1-methylethyl)benzene dihydroperoxide	1.0–10.0	$1.3543 \cdot 10^9$	5027	0.999
1,3-Dihydroxybenzene	0.5–1.0	$1.4579 \cdot 10^9$	10271	0.931

TABLE III

EXTERNAL STANDARD CALIBRATION: LINEAR REGRESSION BY LEAST-SQUARES METHOD FOR A PLOT OF PEAK AREA *VERSUS* MASS INJECTED FOR AUTOXIDATION PRODUCTS OF 1,4-DIISOPROPYLBENZENENumber of calibration points for each compounds, $n = 7$; number of replicates of each injection, $m = 5$.

Compounds	Range (μg)	Slope, a	Intercept, b	Correlation coefficient, r
1,4-Di(1-methylethyl)benzene monohydroperoxide	1.0–10.0	$1.3124 \cdot 10^9$	5431	0.998
1-[4-(1-Hydroxy-1-methylethyl)phenyl]-1-methylethane hydroperoxide	1.0–5.0	$1.3941 \cdot 10^9$	3725	0.989
1-Methyl-[4-(1-methylethyl)phenyl]-1-hydroxyethane	1.0–5.0	$1.2945 \cdot 10^9$	4211	0.995
1,4-Di(1-methylethyl)benzene dihydroperoxide	1.0–10.0	$1.4133 \cdot 10^9$	10182	0.985
1,4-Dihydroxybenzene	0.5–1.0	$1.5183 \cdot 10^9$	15041	0.981

TABLE IV

EXTERNAL STANDARD CALIBRATION: LINEAR REGRESSION BY LEAST-SQUARES METHOD FOR A PLOT OF PEAK AREA *VERSUS* MASS INJECTED FOR AUTOXIDATION PRODUCTS OF *p*-CYMENENumber of calibration points for each compounds, $n = 7$; number of replicates of each injection, $m = 5$.

Compounds	Range (μg)	Slope, a	Intercept, b	Correlation coefficient, r
1-Methyl-1-(4-methylphenyl)ethane hydroperoxide	1.0–5.0	$1.601 \cdot 10^9$	993	0.998
[4-(1-Methylethyl)phenyl]methane hydroperoxide	1.0–5.0	$1.336 \cdot 10^9$	735	0.995
4-Methylacetophenone	0.5–1.0	$2.736 \cdot 10^{10}$	7232	0.989
1-Methyl-4-(1-hydroxy-1-methylethyl)benzene	1.0–5.0	$1.405 \cdot 10^9$	7210	0.989
4-(1-Methylethyl)benzoic acid	0.5–2.0	$2.351 \cdot 10^9$	1351	0.897
4-Methylbenzoic acid	0.5–2.0	$2.532 \cdot 10^9$	10073	0.899
1-Hydroxy-4-methylbenzene	0.1–1.0	$2.103 \cdot 10^9$	12131	0.889

TABLE V

REPRODUCIBILITY OF EXTERNAL STANDARD METHOD FOR DETERMINATION OF AUTOXIDATION PRODUCTS OF CUMENE, 1,3-DIISOPROPYLBENZENE 1,4-DIISOPROPYLBENZENE AND *p*-CYMENENumber of injections for each determination, $m=8$.

Compounds	Amount added (μg)	Mean amount found (μg)	S.D. (μg)	R.S.D. (%)	Amount added (μg)	Mean amount found (μg)	S.D. (μg)	R.S.D. (%)
<i>Autoxidation products of cumene</i>								
Acetophenone	0.10	0.11	0.005	4.55	1.01	0.98	0.027	2.76
Cumene hydroperoxide	1.00	0.98	0.023	2.35	10.09	10.11	0.112	1.11
1-Methyl-1-phenylethanol	1.00	1.05	0.022	2.10	5.03	5.05	0.104	2.06
<i>Autoxidation products of 1,3-diisopropylbenzene</i>								
1,3-Di(1-methylethyl)benzene monohydroperoxide	1.02	1.03	0.022	2.14	10.01	10.51	0.198	1.88
1-[3-(1-Hydroxy-1-methylethyl)phenyl]-1-methylethane hydroperoxide	1.00	1.10	0.019	1.73	5.330	5.37	0.079	1.47
1-Methyl-[3-(1-methylethyl)phenyl]-1-hydroxyethane	1.02	0.95	0.028	2.95	4.99	5.42	0.069	1.27
1,3-Di(1-methylethyl)benzene dihydroperoxide	1.04	1.03	0.035	3.40	10.01	10.34	0.196	1.90
1,3-Dihydroxybenzene	0.51	1.07	0.027	2.52	1.35	1.29	0.032	2.48
<i>Autoxidation products of 1,4-diisopropylbenzene</i>								
1,4-Di(1-methylethyl)benzene monohydroperoxide	1.00	1.05	0.021	2.00	10.00	9.27	0.186	2.01
1-[4-(1-Hydroxy-1-methylethyl)phenyl]-1-methylethane hydroperoxide	1.01	1.02	0.019	1.86	5.02	5.15	0.141	2.74
1-Methyl-[4-(1-methylethyl)phenyl]-1-hydroxyethane	1.05	0.97	0.023	2.37	4.99	5.01	0.101	2.02
1,4-Di(methylethyl)benzene dihydroperoxide	1.00	0.98	0.020	2.04	10.04	10.08	0.197	1.95
1,4-Dihydroxybenzene	0.50	0.49	0.017	3.47	1.03	1.11	0.038	3.42
<i>Autoxidation products of p-cymene</i>								
1-Methyl-1-(4-methylphenyl)ethane hydroperoxide	1.02	1.03	0.023	2.33	5.01	5.21	0.139	2.67
[4-(1-Methylethyl)phenyl]methane hydroperoxide	1.01	1.05	0.021	2.00	5.05	5.03	0.095	1.89
4-methylacetophenone	0.49	0.97	0.039	4.02	0.98	0.99	0.025	2.52
1-Methyl-4-(1-hydroxy-1-methylethyl)-benzene	1.04	0.93	0.021	2.26	4.89	5.02	0.012	2.39
4-(1-Methylethyl)benzoic acid	0.51	0.49	0.019	3.73	2.00	1.98	0.024	1.21
4-Methylbenzoic acid	0.50	0.48	0.022	4.58	2.03	2.01	0.039	1.94
1-Hydroxy-4-methylbenzene	0.11	0.10	0.003	3.00	1.00	1.01	0.051	4.95

For the determination of the autoxidation products of cumene and *p*-cymene, the composition of the eluent was *n*-hexane-isopropanol (99.5:0.5, v/v) and for the autoxidation products of 1,3- and 1,4-diisopropylbenzenes the composition was 98.0:2.0 (v/v).

Figs. 5–8 are typical chromatograms of crude autoxidation products of cumene, 1,3- and 1,4-diisopropylbenzene and *p*-cymene.

Quantification

External and internal standard calibration gave a linear response for the peak-area ratio for standard concentrations over the range 1–10 $\mu\text{g}/\text{ml}$. The parameters derived from least-squares regression for the external standard method are given in Tables I–IV. The internal-standard method was also linear.

The relative standard deviations (R.S.D.) of replicate injections for the external standard method

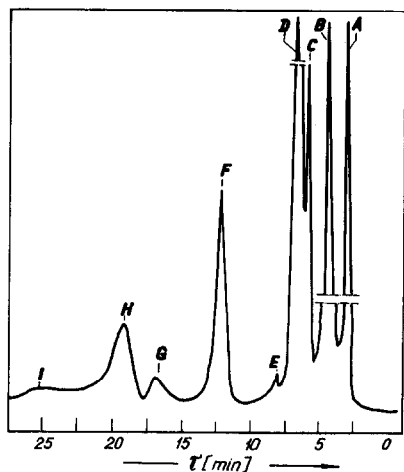


Fig. 8. Typical chromatogram of autoxidation products of *p*-cymene. Peaks: A = *p*-cymene; B = [4-(1-methylethyl)phenyl]methane hydroperoxide; C = 4-methylacetophenone; D = 1-methyl-1-(4-methylphenyl)ethane hydroperoxide; E = 1-methyl-4-(1-hydroxy-1-methyl)benzene; F = 1-methyl-1-phenylethanol; G = 4-(1-methylethyl)benzoic acid; H = 4-methylbenzoic acid; I = 1-hydroxy-4-methylbenzene. Eluent isopropanol-hexane (0.50:99.50); column, Partisil 10 (10 μ m) (25 cm); flow-rate, 1.0 ml/min.

are given in Table V. The method gave the possibility of determining the main products of the autoxidation of alkylaromatic compounds with good precision.

CONCLUSIONS

The possibility of the application of HPLC to the determination of the autoxidation products of some alkylaromatic compounds was studied. The method gave good results for the analysis of mixtures containing very unstable compounds such as hydroperoxides. The proposed procedure is rapid and simple.

ACKNOWLEDGEMENTS

We thank Dr. Ing. Aleksandra Burghardt, Institute of Organic Chemistry and Technology of Silesian Technical University, for samples of standards of *p*-cymene autoxidation products.

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