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CHROMATOGRAPHIC ANALYSIS OF A MIXTURE OF ISOMERIC METHYLCYCLOHEXANONES AND METHYLCYCLOHEXANOLS

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SUMMARY

A mixed stationary phase containing 2% of Reoplex 100 + 3% of Reoplex 400 on Chromaton N, AW-HMDS, has been investigated for the separation of a mixture of isomeric methylcyclohexanones and methylcyclohexanols. Measurements were made of the Kováts retention indices of all components in mixtures of these isomers at 76°. The polarity of the prepared mixed stationary phase was characterized by means of Rohrschneider constants.

INTRODUCTION

The chromatographic separation of mixtures of alicyclic ketones and alcohols has been investigated by only a few workers[1–5]. An integrated study with a theoretical interpretation of the chromatographic separation of alkylcyclohexanones and particularly of stereoisomeric alkylcyclohexanols was made by Komers and co-workers[2,3]. They verified that the separation of the mixtures examined can be effected only in strongly polar stationary phases, the molecules of most of which contain hydroxyl groups. The separation of the individual components of the mixture is made possible by the formation of hydrogen bonds between the hydroxyl groups of the stationary phase and the functional oxygen group of the substances being analyzed.

Various mixtures containing alicyclic ketones and alcohols have been separated using polar stationary phases that contain in their molecules different numbers of hydroxyl groups, such as alcoholic sugars[1–3,5], triethanolamine[5], pentaerythritol[3] and glycerol dicyanoethyl ether[4]. The separation of stereoisomeric alkylcyclohexanols, according to Komers and Kochloefl[3], is based on the formation of associates between the hydroxyl groups of the liquid phase and the separated alcohols, the stability of which is dependent on the steric accessibility of the hydroxyl groups of the individual conformers of the alkylcyclohexanols.

For the separation of mixtures of isomeric methylcyclohexanones and methylcyclohexanols, glycerol is most frequently recommended as the stationary phase, and diglycerol less often[3,6–8].

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A stationary phase containing 20% (w/w) of glycerol on Chromaton N, AW-HMDS, as carrier was therefore used for the quantitative analysis of the reaction mixture from the hydrogenation of cresylic acid. The separating capability of this stationary phase for the required analysis was high, the measured relative elution times being in good agreement with the results obtained by Komers and Kochloefl[3]. However, the stability of this phase was found to be unsatisfactory and its separating efficiency gradually decreased to a considerable extent. The changes in the separating properties of the glycerol phase are due to both its low thermal stability and particularly its modification as a result of the strong sorption of the cresols.

An improvement of the stability of stationary phases containing glycerol, with unchanged separating capabilities, was achieved by adding 1% (w/w) of sodium carbonate. We assume that the addition of such an alkaline substance resulted in the fixation of the acidic cresols in the initial zone of the chromatographic column.

Later, we found out that polyester stationary phases are more suitable for the separation of the reaction mixture from the hydrogenation of cresylic acid, and their application to the separation of this mixture is the subject of this paper.

EXPERIMENTAL

Materials

Two columns were prepared, one with 3% Reoplex 400 (Lachema, Brno, Czechoslovakia) on 0.16–0.20 mm Chromaton N, AW-HMDS (Lachema) and the other with 2% Reoplex 100 (Lachema) on the same support. The mixed polyester stationary phase was prepared by mixing the individual polyester phases.

The standards employed for peak identification in the chromatogram of the mixture of cycloaliphatic ketones and alcohols were prepared by high-pressure hydrogenation of phenol and cresols in the liquid phase with a palladium–charcoal catalyst[9]. The reaction mixtures obtained after hydrogenation of cresols, being catalyzed by a palladium catalyst, contained a major proportion of ketones and a small amount of the methylcyclohexanol stereoisomers, the proportions of which were not uniform. The differing contents of these isomers made possible their identification by separating them on a glycerol stationary phase on which the order of elution of all of the stereoisomers of methylcyclohexanols is known[3].

Procedure

In order to check the separating efficiency of the chromatographic phases, a synthetic mixture (A) was used (Table I). Its qualitative composition corresponded to the composition of the reaction product obtained by hydrogenation of cresylic acid, the various components, however, being present in comparable amounts.

Optimization of the conditions for the quantitative analysis was carried out using 3% Reoplex 400 on Chromaton N, AW-HMDS, as stationary phase. The resulting operating conditions are listed in Table II.

The separation of the cycloaliphatic components of the mixture being analyzed was carried out with isothermal operation of the chromatographic column under the conditions reported in Table II. After elution of the cycloaliphatic substances, the remaining (aromatic) components of the reaction mixture were likewise separated isothermally, but with an increase in the operating temperature to 150°. The aim of

TABLE I

COMPOSITION OF SYNTHETIC MIXTURE A

Component	*Amount (%, w/w)*
Cyclohexanone	6.7
2-Methylcyclohexanone	10.9
3-Methylcyclohexanone	8.1
4-Methylcyclohexanone	8.0
Cyclohexanol	14.1
2-*cis*-Methylcyclohexanol	1.4
2-*trans*-Methylcyclohexanol	0.6
3-*trans*-Methylcyclohexanol, 3-*cis*-Methylcyclohexanol, 4-*cis*-Methylcyclohexanol	6.7
4-*trans*-Methylcyclohexanol	8.2
Phenol	5.9
o-Cresol	13.5
m-Cresol, *p*-Cresol	16.0

this temperature increase between the separation of the cycloaliphatic and aromatic substances is to accelerate and increase the precision of the analysis of the aromatic components. The temperature is not increased above 150°, as at higher temperatures vaporization of the stationary phase (Reoplex 100) occurs.

For the determination of Kováts retention indices (I_t), synthetic mixture A was analyzed together with a mixture of C_{10}–C_{17} *n*-alkanes. These indices were calculated by the procedure reported by Kováts[10].

Rohrschneider constants were measured according to the original procedure[11] except for the amount of liquid phase used on the carrier.

RESULTS

The separation of the components of synthetic mixture A was studied on the column containing 3% Reoplex 400 on Chromaton N, AW-HMDS. At a higher

TABLE II

OPERATING CONDITIONS FOR THE CHROMATOGRAPHIC ANALYSIS OF THE MIXTURE OF CYCLOALIPHATIC KETONES AND ALCOHOLS

Condition	*Value*
Liquid phase	3% Reoplex 400 + 2% Reoplex 100
Carrier	Chromaton N, AW-HMDS, particle size 0.16–0.20 mm
Working temperature	76°
Column length	3.2 m
Column diameter	3 mm
Injector temperature	180–200°
Carrier gas	Nitrogen
Working pressure at the column inlet	0.56–0.6 kP/cm^2
Detector type	Flame ionization
Sample injected	0.2–0.5 μl

TABLE III

RELATIVE ELUTION TIMES OF SUBSTANCES SEPARATED AT 76° ON TWO TYPES OF POLYESTER STATIONARY PHASE

Eluted component	*Stationary phase on Chromaton N, AW-HMDS*	
	3% Reoplex 400	*2% Reoplex 100*
Cyclohexanone	1.0	1.0
2-Methylcyclohexanone	1.04	1.24
3-Methylcyclohexanone	1.24	1.42
4-Methylcyclohexanone	1.31	1.51
Cyclohexanol	—	1.76
2-*cis*-Methylcyclohexanol	1.67	2.0
2-*trans*-Methylcyclohexanol	—	—
3-*trans*-Methylcyclohexanol		
4-*cis*-Methylcyclohexanol	2.1	2.38
3-*cis*-Methylcyclohexanol	—	—
4-*trans*-Methylcyclohexanol	2.26	2.67

loading of the support (15%), the effectiveness of the separation was lower. The effect of the operating temperature on the effectiveness of the separation of methylcyclohexanones and methylcyclohexanols was studied at 60–90°.

The separation of the components of synthetic mixture A on the column containing 3% Reoplex 400 on Chromaton N, AW-HMDS was then investigated at 60–90°. The separation, especially of ketone isomers, proved to be more effective at lower temperatures, but the duration of the analysis was considerably prolonged owing to the higher solubility of the sample in the liquid phase. At temperatures above 80°, the separation of 3- and 4-methylcyclohexanones ceased altogether. Table III gives the relative elution times of the separated components of synthetic mixture A; the elution times were derived from the chromatogram of the analyzed mixture.

By comparing the relative elution times of methylcyclohexanone and methylcyclohexanol isomers with the results obtained by Komers and Kochloefl[3] using glycerol, it becomes obvious that the separating effectivenesses of the two stationary phases (glycerol and Reoplex 400) are similar. It was ascertained by Komers and Kochloefl[3] that the separation of isomeric mixtures of alicyclic ketones and alcohols is affected by the polarity of the stationary phase; the separating effectiveness in-

TABLE IV

ROHRSCHNEIDER CONSTANTS (*I*) FOR TWO TYPES OF POLYESTER PHASES

Column length (m)	*Liquid phase*	*I/100*				
		Benzene	*Ethanol*	*Methyl ethyl ketone*	*Nitromethane*	*Pyridine*
2	Reoplex 400	3.56	5.75	4.44	7.43	5.95
3.2	Reoplex 100 + Reoplex 400 (7:3)	2.19	4.16	2.98	5.17	4.24

creased on moving from non-polar (Apiezon L) to polar stationary phases (alcoholic sugars). With polar stationary phases containing hydroxyl groups, however, their effectiveness did not change monotonously with the increase in polarity, but an optimum occurred. Analogous behaviour was observed even with polyester stationary phases. The mutual separation capability of virtually all components of synthetic mixture A tended to be a better one (Table II), provided that a less polar polyester phase, Reoplex 100 (polypropylene sebacate), was used.

The differences in polarity of both of the polyester phases tested become evident by comparing the Rohrschneider constants for a column containing 20% Reoplex 400 on Kieselguhr[11] with those found here by using a column containing a mixture of 2% Reoplex 100 and 3% Reoplex 400 (7:3) on Chromaton N, AW-HMDS (Table IV).

It can be assumed that the differences in the polarities of the phases compared will actually be lower. The published values[11] for the liquid phase Reoplex 400 were measured for a loading of 20%, whereas we used a 3% loading; the polarity of such a column will most likely be affected to a considerable extent by the properties of the non-polar carrier.

The lower polarity of this stationary phase, in comparison with the Reoplex 400 (polyethylene adipate), had a favourable effect on the elution rate of the separated substances; the overall duration of the analysis of synthetic mixture A under comparable operating conditions was halved.

According to Komers and Kochloefl[3], the separation of stereoisomers of alkylcyclohexanols is made possible by the formation of hydrogen bonds (of different

TABLE V

$R_{t_{rel}}$ AND I_t VALUES OF SOME CYCLOALIPHATIC KETONES AND ALCOHOLS ON THE MIXED STATIONARY PHASE REOPLEX 100–REOPLEX 400 (7:3) AT 76°

No.	*Eluted component*	$R_{t_{rel}}$*	I_t
1	Cyclohexanone	1.0	1185
2	2-Methylcyclohexanone	1.16	1207
3	3-Methylcyclohexanone	1.38	1227
4	4-Methylcyclohexanone	1.47	1234
5	Cyclohexanol	1.74	1258
6	2-*cis*-Methylcyclohexanol	1.93	1275
7	2-*trans*-Methylcyclohexanol	2.09	1289
8	3-*trans*-Methylcyclohexanol	2.26	1302
9	4-*cis*-Methylcyclohexanol	2.30	1304
10	3-*cis*-Methylcyclohexanol	2.57	1315
11	4-*trans*-Methylcyclohexanol	2.58	1316
12	Phenol	(3.58)	—
13	2-Methylphenol	(3.76)	—
14	3-Methylphenol	(4.0)	—
15	4-Methylphenol	(4.0)	—
16	Cyclohexane	0.14	—
17	Benzene	0.20	—
18	Toluene	0.21	—

* The $R_{t_{rel}}$ values in parentheses are the relative elution times measured at operating conditions different to those for the other components. These operating conditions are listed on the time axis of the chromatogram in Fig. 1.

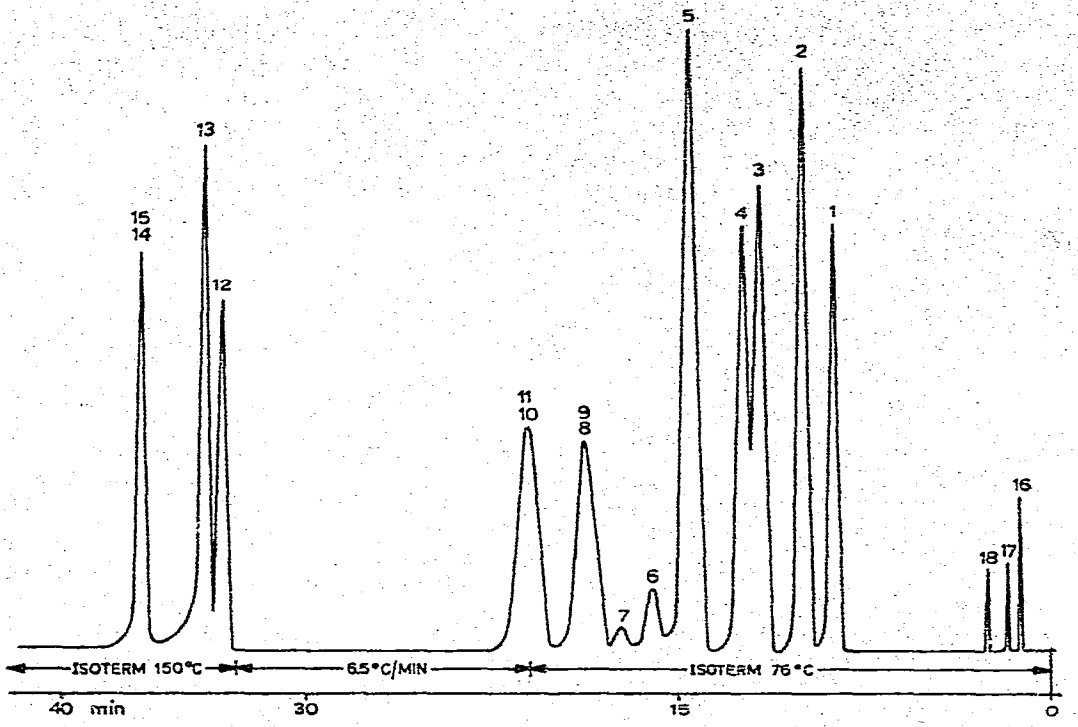

Fig. 1. Separation of isomeric methylcyclohexanones and methylcyclohexanols (analysis of synthetic mixture A). Column: 2% Reoplex 100 + 3% Reoplex 400 (7:3) on Chromaton N, AW-HMDS, 3.2 m × 3 mm glass, temperature 76°. Sample size, 0.20 μl. The numbers on the peaks correspond with the substances listed in Table V.

strengths) between the hydrogen atom of the hydroxyl group in the stationary phase and the free electron pair on the oxygen atom in the methylcyclohexanol molecule. The chromatographed substance was therefore the electron donor. In this work, the polyester stationary phase did not contain a hydroxyl group. Nevertheless, hydrogen bridges can be formed, but the electron donors are the free electron pairs on the oxygen atom of the carbonyl group.

In order to estimate the quality of the catalysts used for the hydrogenation of cresylic acid, it was necessary to determine the ratio of the overall contents of ketones and alcohols in the reaction mixture, the precision of the determination depending on the separation of 4-methylcyclohexanone and cyclohexanol. We therefore prepared a mixed stationary phase of Reoplex 100 plus Reoplex 400 (7:3). The separation properties of this mixed stationary phase confirmed that the properties of the component stationary phases are additive. Their separation effectiveness is characterized by the Kováts retention indices summarized in Table V. Fig. 1 shows an example of a chromatogram of synthetic mixture A.

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