

# High-temperature continuous counter-current gas–liquid chromatography

Katsunori Watabe

*Central Research Laboratory, Shimadzu Corporation, Kyoto (Japan)*

Hisashi Kanda

*Laboratory of Industrial Analytical Chemistry, Faculty of Technology, Tokyo Metropolitan University, Tokyo (Japan)*

Katsuya Sato

*Central Research Laboratory, Shimadzu Corporation, Kyoto (Japan)*

Toshiyuki Hobo\*

*Laboratory of Industrial Analytical Chemistry, Faculty of Technology, Tokyo Metropolitan University, 1-1 Minamiohsawa, Hachiohji-shi, Tokyo 192-03 (Japan)*

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## ABSTRACT

In continuous counter-current gas–liquid chromatography, which has a high resolving power and is suitable for the large-scale purification of organic solvents, it is very important that the samples that can be applied extend from easily separable to more difficult to separate, such as azeotropes, low-volatility compounds and stereoisomers. A system was designed and constructed for high-temperature operation up to 200°C, and was applied to the separation of dimethyl and diethyl phthalate, *trans*- and *cis*-decahydronaphthalene and *cis*-decahydronaphthalene and tetrahydronaphthalene. It was confirmed that over 99% of purity could be achieved for dimethyl and diethyl phthalate, *trans*-decahydronaphthalene, and tetrahydronaphthalene.

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## INTRODUCTION

Many attempts have been made to develop preparative-scale chromatography on account of its excellent separation capability. In conventional chromatography, however, samples cannot be introduced continuously, because it is a sequential method and the amount of sample applied each time is limited. Therefore, counter-current chromatography has been considered as an effective method for preparative separations. In counter-current chromatography, the difference in the partition coefficients of samples between two phases moving counter-

currently to each other is utilized for separation and purification.

Several methods have been proposed in order to realize the counter-current flow of two phases; (1) moving bed, to gravitate packing material coated with a liquid phase and to flow a carrier gas in the opposite direction of the flow of the packing material [1,2]; (2) rotation of a special type of column, to rotate doughnut-type tubing packed with absorbent [3,4]; and (3) circulation of liquid phase, to gravitate the stationary phase over the surface of the packing in the column against a gas stream [5–7]. Considering desirable attributes such as a simple scheme,

having little mechanical movement and direct control of liquid phase flow-rate, we chose the last method, and carried out studies on continuous counter-current gas-liquid chromatography (CCGLC). Despite its good resolving power, it has not become popular as a large-scale preparative separation method as it seems to have narrow range of application. The recent needs for the highly efficient separation and purification of large molecules with similar structures in the fields of fine chemistry and biochemistry encouraged us to develop further the capability of continuous counter-current chromatography.

However, the system reported previously [5-7] could be applied only up to 60°C and was used to separate volatile solvents with boiling points up to *ca.* 130°C. To extend the applicability of this method in practice, it is necessary that the system can be used above 150°C and be applicable to the separation of samples with the boiling points of more than 250°C.

In this work, we designed a high-temperature continuous CCGLC system, and applied it to the separation of high-boiling sample mixtures with close boiling points and to azeotropic systems.

## THEORETICAL

In previous papers we have discussed the separation conditions, the theoretical plate number and the

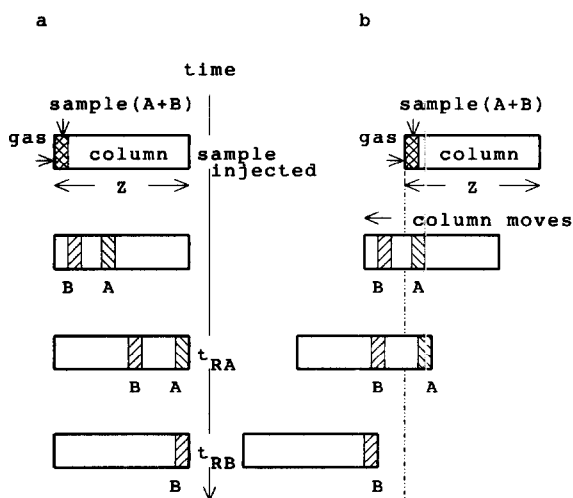


Fig. 1. Schematic comparison between (a) conventional gas chromatography and (b) continuous counter-current gas-liquid chromatography.

maximum sample feed rate [5-7]. The basic consideration required for the separating condition is as follows.

The separation of components depends on the difference in partition coefficients between two phases. In Fig. 1, schematic comparison between conventional gas chromatography (GC) and CCGLC is shown to clarify the difference between these two methods. In a column of length  $Z$  the retention times of component A and B are  $t_{RA}$  and  $t_{RB}$ , so that the velocities of the components in the column are  $Z/t_{RA}$  and  $Z/t_{RB}$ , respectively. When the column moves in the opposite direction to the gas flow and its velocity is between  $Z/t_{RA}$  and  $Z/t_{RB}$ , component A with a lower partition coefficient moves in the direction of the gas flow and component B with a higher partition coefficient moves in the direction of the column movement; components A and B move in different directions from the place of introduction. In order to determine the operational parameters, the principle of this method is expressed by using physico-chemical constants.

The partition coefficient  $K_{(n)}$  is defined as follows:

$$K_{(n)} = (\text{weight of component } n \text{ in unit volume of liquid phase}) / (\text{weight of component } n \text{ in unit of gas phase}) \quad (1)$$

This equation is also expressed as follows:

$$K_a = \frac{W_1}{W_g} = \frac{W_1}{W_g} \cdot \frac{G}{L} \quad (2)$$

where  $K_a$  = partition coefficient of component A,  $W_1$  = weight of component A contained in 1 ml of liquid phase (g),  $W_g$  = weight of component A contained in g ml of gas phase (g),  $L$  = flow-rate of liquid phase (ml/min) and  $G$  = flow-rate of gas phase (ml/min).

For component A, it is necessary that the amount of A in the gas phase is larger than that in the liquid phase in order to drive component A in the direction of the gas flow. That is,

$$\frac{W_1}{W_g} < 1 \quad (3)$$

Substituting eqn. 3 by eqn. 2,

$$\frac{G}{L} > K_a \quad (4)$$

Under the condition

$$\frac{G}{L} < K_b \quad (5)$$

component B moves in the direction of liquid flow in the same manner. From the eqns. 4 and 5, it is necessary that  $G/L$  is between  $K_a$  and  $K_b$  in order to separate components A and B:

$$K_a < \frac{G}{L} < K_b \quad (6)$$

The optimum separating conditions are defined by

$$(G/L)^{-1} = (1/K_a + 1/K_b)/2 \quad (7)$$

## EXPERIMENTAL

### Instrumentation

The basic scheme of the CCGLC system is shown in Fig. 2.

**Gas and liquid flows and sample introduction.** Liquid phase is fed from the tank  $R_L$  to the top of the column by a plunger-type constant-flow pump,  $P_1$ . The liquid phase as a thin film on the surface of packing materials gravitates in the column from the top to the bottom. The liquid phase is recycled through the tank  $R_L$ . A inert gas from a high-pressure cylinder, after removing trace amounts of oxygen by passing through a purifier C, is supplied to the system from the bottom of the column and moves towards the top of the column. In the middle of the column, the gas stream is separated into two streams. One leaves the column and vents through a cold trap and a flow meter. The other goes to the top of the column and out through a trap and a flow meter. Sample is injected continuously through the septum in the middle of the separating section into the column from tank  $R_S$  by pump  $P_2$ .

**Column.** A Pyrex glass tube (3 m  $\times$  17 mm I.D.) was used as a column. It consists of two sections, the separating section and the stripping section (both 1.5 m in length). The temperature of the separating section could be raised to 200°C and that of the stripping section to 260°C. Stainless-steel helical packing (NANIWAPAC No. 1, 0.9  $\times$  1.8  $\times$  1.8

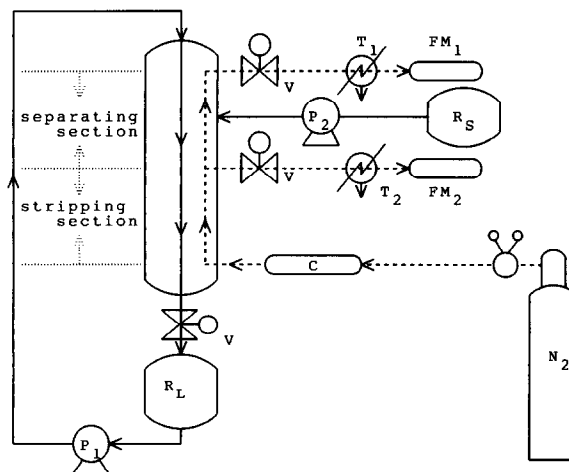


Fig. 2. Continuous counter-current gas-liquid chromatographic system,  $P_1$ ,  $P_2$  = Pumps;  $T_1$ ,  $T_2$  = traps; v = valve;  $FM_1$ ,  $FM_2$  = flow meters;  $R_L$  = liquid-phase tank;  $R_S$  = sample tank; C = purifier.

mm) was filled into the column. The surface area and density of the packing were 3.743 m<sup>2</sup>/m<sup>3</sup> and 1500 kg/m<sup>3</sup>, respectively.

In the stripping section, component B, which is moved from the separating section into the stripping section, is removed from the liquid phase at a higher temperature than that in the separating section, and is carried out from the middle of the column through a cold trap and a flow meter. To strip the component completely from the liquid phase in the stripping section, the following condition must be valid.

$$(G_s/L) > K_b^s \quad (8)$$

where  $G_s$  = flow-rate of the gas phase in the stripping section (ml/min),  $L$  = flow-rate of the liquid phase (ml/min) and  $K_b^s$  = partition coefficient of the component at the temperature of the stripping section.

**Trap.** A glass tube of (0.3 m  $\times$  17 mm I.D.) was used as a trap. The trap was set in a liquid nitrogen coolant vessel as shown in Fig. 3. The efficiency of the trap was about 80%, which was not sufficiently satisfactory, and further study of the trapping system is needed.

**Heating system.** The structure of the heating system is shown in Fig. 4. There were two layers of heater around the column and connecting tubings. As the first heating layer, glass tape was wrapped

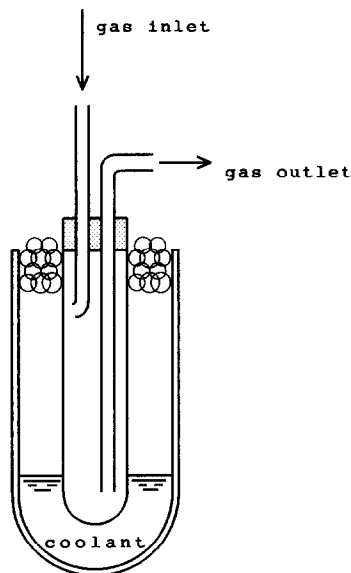


Fig. 3. Trap.

directly on the column and tubing and Nichrome wire and asbestos tape were wrapped over the glass tape. The second heating layer, overlapping the first, utilized the same structure as the first heating layer. The first layer was used for fine temperature control. Copper-constantan thermocouples were located at several positions, such as the separating section, stripping section and connectors, to measure the respective temperatures.

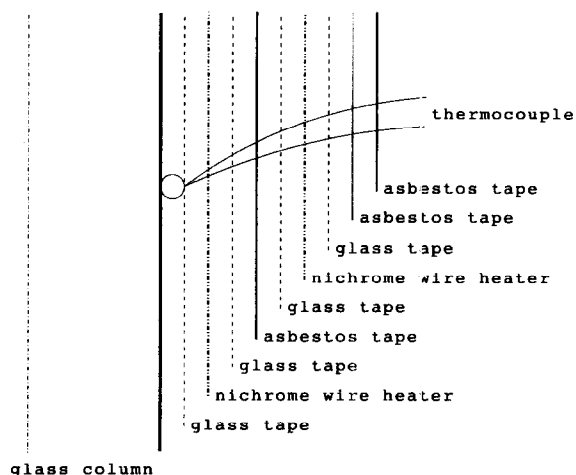


Fig. 4. Heating system.

**Mobile phases.** As thermally stable liquid mobile phases, silicone KF-54 (methylphenylsilicone; Shinetsu Kagaku) and poly(diethylene glycol succinate) were tested. For subsequent experiments KF-54 was selected for reasons given later.

**Carrier gas.** Nitrogen (B grade; Nippon Sanso) from a high-pressure cylinder was used after passing it through a purifier (0.3 m × 6 mm I.D. stainless-steel tube packed with reduced copper beads (1–2 mm diameter) in order to remove trace amounts of oxygen.

**Samples.** As test samples, three mixtures (50:50, w/w) of dimethyl phthalate (b.p. 283.7°C)–diethyl phthalate (b.p. 294.0°C), *trans*- (b.p. 187.2°C)–*cis*-decahydronaphthalene (b.p. 195.7°C) and *cis*-decahydronaphthalene–tetrahydronaphthalene (b.p. 207.2°C) were prepared by mixing the pure compounds purchased from Tokyo Kasei Kogyo (Tokyo, Japan). All sample systems are azeotropic and the components have close boiling points, and therefore they are very difficult to purify by distillation and other industrial methods.

#### Procedure

**Preparation of the system.** NANIWAPAC No. 1 helical wire packing was packed in the column by tapping the column gently. The column was washed with acetone and dried by passing nitrogen. The flow system, including tanks and traps, was connected with the column. The liquid phase was filled in the tank and allowed to circulate through the column to make a liquid film on the packing. To remove the highly volatile components present in the liquid phase, the whole system was heated gradually to 200°C with gas- and liquid-phase flows.

**Operating conditions.** Although the  $G/L$  values will be determined by eqn. 6, the maximum gas and liquid flow-rates are limited by the structure of the system. When silicone KF-54 was used as the liquid phase, the maximum liquid flow-rate with this system was found to be less than 1.7 ml/min to maintain a laminar flow as a thin film stream over the packing. At  $G/L$  values > 500, the gas flow became unstable and carried liquid phase out of the top of the column. Owing to the maximum  $G/L$  value, the range of the partition coefficients of the samples was limited. The operating temperature was determined from the partition coefficients and the vapour pressure of the samples. Considering the

amount of sample feed, the vapour pressure of the sample will be in the range 200–400 mmHg at the operating temperature. Partition coefficients were calculated from the gas chromatographic retention data by the equation

$$K = jF_c(t_R - t_0)/V_L \quad (9)$$

where

$$j = [3(P_i/P_o)^2 - 1]/[2(P_i/P_o)^3 - 1]$$

$P_i$  = inlet pressure of carrier gas ( $\text{kg}/\text{cm}^2$ ),  $P_o$  = outlet pressure of carrier gas ( $\text{kg}/\text{cm}^2$ ),  $F_c$  = flow-rate of carrier gas ( $\text{ml}/\text{min}$ ),  $t_R$  = retention time of component (min),  $t_0$  = retention time of air (min) and  $V_L$  = volume of liquid phase (ml).

A Shimadzu Model 3A gas chromatograph equipped with a thermal conductivity detector and with a stainless-steel column (3 m  $\times$  3 mm I.D.) of Chromosorb W AW (60–80 mesh) coated with 21.8% silicone KF-54 was used to measure partition coefficients.

Fig. 5 illustrates the plot of the logarithm of

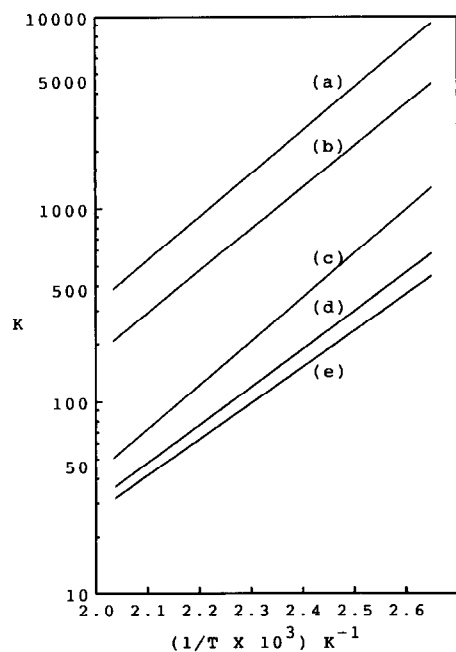


Fig. 5. Partition coefficients ( $K$ ) (measured on silicone KF-54) of (a) diethyl phthalate, (b) dimethyl phthalate, (c) tetrahydronaphthalene, (d) *cis*-decahydronaphthalene and (e) *trans*-decahydronaphthalene plotted against the reciprocal of the column temperature ( $1/T$ ).

partition coefficients *versus* the inverse of the column temperature.

*System setting and warm-up.* According to eqn. 6, the ratio of the flow-rates of the gas phase and liquid phase ( $G/L$ ) was set at a value between the partition coefficients of the two components. The total flow-rate of the gas phase was set at double that required for separation, *i.e.*, the flow-rate at the bottom of the column was double that at the top of the column. The temperature of the stripping section was 30–40°C higher than the temperature of the separating section, which was sufficient to satisfy eqn. (8).

The temperature of the system was kept at the set value by controlling the heater voltage with a variable transformer. The gas flow was controlled by a pressure regulator and liquid was circulated by a constant-flow pump. After about 2 h, the conditions became steady. Then, a sample mixture of two components was introduced continuously by a constant-flow pump.

*Retention time.* The retention time,  $t_{RA}$ , of component A, which is the travelling time of component A from the point of introduction to the top of the column, can be calculated with the equation [8]

$$t_{RA} = (K_A \cdot L_0/G \cdot 1/j)/[1 - (K_A \cdot L/G \cdot 1/j)] \quad (10)$$

and the retention time,  $t_{RB}$ , of component B, which is the travelling time of the component B from the point of introduction to the bottom of the separating section, can be calculated with the equation

$$t_{RB} = (K_B \cdot L_0/G \cdot 1/j)/[(K_B \cdot L/G \cdot 1/j) - 1] \quad (11)$$

where

$$j = [3(P_i/P_o)^2 - 1]/[2(P_i/P_o)^3 - 1]$$

$P_i$  = inlet pressure of carrier gas ( $\text{kg}/\text{cm}^2$ ),  $P_o$  = outlet pressure of carrier gas ( $\text{kg}/\text{cm}^2$ ) and  $L_0$  = volume of liquid phase in the upper half of the separating section of the column (ml).

It is important to calculate the retention time to establish whether the operating conditions are adequate. For example, the calculated retention times of dimethyl and diethyl phthalate were about 140 and 250 min, respectively, at 200°C with a  $G/L$  value of 430, a gas flow-rate of 250 ml/min and a volume of liquid phase of 34 ml.

*Sample feed rate.* If the feed rate of component A with a small partition coefficient is larger than the

maximum feed rate in an equilibrium state, an excess amount of component A flows down and leaves the bottom of the separating section with the other component. Therefore, the maximum sample feed rate is determined by the maximum feed rate of component A, which is equal to the eluting rate of the same component at the top of the column, without disturbing its partition equilibrium between the gas and liquid in the column. In this experiment, the sample feed rates were decided to be about half of the maximum sample feed rates calculated by the equation described in a previous paper [6], considering that the system was laboratory built.

*Analysis of eluates.* Eluates from the top and bottom of the column were collected by the traps. As the separation of the two components was the aim, GC was used to determine the ratios of the two components in the eluates. A Shimadzu Model 3A gas chromatograph equipped with a thermal conductivity detector was used with a stainless-steel column (3 m  $\times$  3 mm I.D.) packed with 21.8% silicone KF-54 on Chromosorb W AW (60–80 mesh).

## RESULTS AND DISCUSSION

### *Separation of dimethyl and diethyl phthalate*

The partition coefficients of dimethyl and diethyl phthalate with the KF54 column at 200°C were 300 and 560, respectively. As the difference between these two partition coefficients was large, their

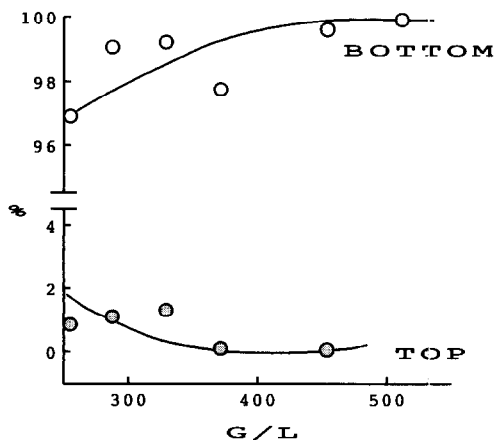


Fig. 6. Content of diethyl phthalate (%).

mixture was assumed to be a typical sample for CCGLC. A mixture of dimethyl and diethylphthalate (50:50, w/w) was introduced continuously into the column at 200°C.  $G/L$  values were adjusted in the range 256–512 by controlling the gas flow-rates. The highest purity of dimethyl phthalate obtained at the top of the column was 99.96% at  $G/L = 453$ . For diethyl phthalate, 99.69% purity was achieved at  $G/L = 329$ . In Fig. 6, the content of diethyl phthalate is plotted against  $G/L$ , and indicates that the best separation would be obtained at a  $G/L$  value of about 430.

### *Separation of trans- and cis-decahydronaphthalenes*

CCGLC is considered to be effective for the separation of these isomers. According to the partition coefficients (162 and 208) of the isomers on KF-54 at 140°C, the  $G/L$  values were adjusted in the range 173–212. A mixture of *trans*- and *cis*-decahydronaphthalene (50:50, w/w) was introduced at 140°C. The content of *cis*-decahydronaphthalene is plotted against  $G/L$  in Fig. 7. For small  $G/L$  values, the separation at the top of the column was better than that at the bottom, whereas for large  $G/L$  values this relationship was reversed.

### *Separation of cis-decahydronaphthalene and tetrahydronaphthalene*

*cis*-Decahydronaphthalene and tetrahydronaphthalene form an azeotropic mixture so that an effective separation cannot be achieved by conven-

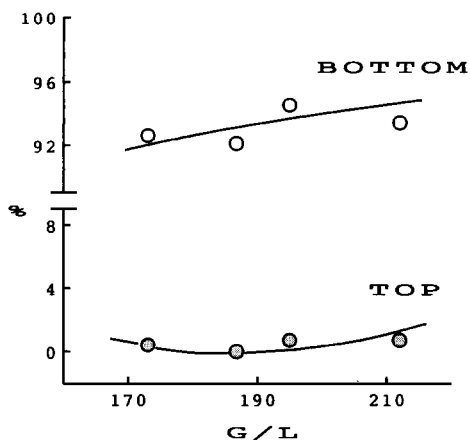


Fig. 7. Content of *cis*-decahydronaphthalene (%).

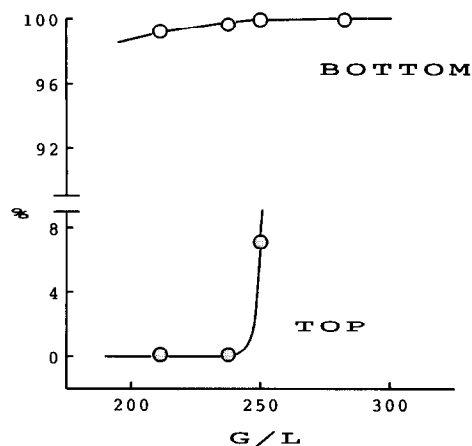


Fig. 8. Content of tetrahydronaphthalene (%).

tional distillation. They were separated by CCGLC at 140°C. The range of  $G/L$  values was set from 212 to 282. Over 99% purity of both components was obtained at  $G/L = 235$ . Fig. 8 shows the content of tetrahydronaphthalene vs.  $G/L$ . The relationship between  $G/L$  value and the purity of the eluate is similar to that for the separation of decahydronaphthalene stereoisomers.

#### *Optimum $G/L$ value for the separation of a two-component mixture*

Figs. 6 and 7 indicate that the best separation of the two-component mixture was obtained when the  $G/L$  values are set at the mid-point of the partition coefficients, *i.e.*, the optimum  $G/L$  value measured for the dimethyl–diethyl phthalate sample was 430, the partition coefficients of dimethyl and diethyl phthalate being 300 and 560, respectively, at 200°C. The optimum  $G/L$  value for the *trans*–*cis*-decahydronaphthalene sample at 140°C was about 185, the partition coefficients of these isomers being 162 and 208, respectively. This conclusion was also confirmed by the plot of the calculated theoretical plate numbers against  $G/L$  based on the equation in a previous paper [5]. For example, the maximum theoretical plate number for the dimethyl–diethyl phthalate separation was about 30 at  $G/L = 440$ , and that for the decahydronaphthalene stereoisomer separation was 62 at  $G/L = 185$ . For the *cis*-decahydronaphthalene–tetrahydronaphthalene sample, the optimum  $G/L$  value measured at 140°C was 235, which was about 45 lower than the calculated value. As

there was no observed change in the operating conditions except for prolonged use of the liquid phase, the partition coefficients of the components might be decreased owing to the partial deterioration of the liquid phase [9].

#### *Optimum $G/L$ value for purifying one particular component*

From Figs. 5–7, it is suggested that the larger the  $G/L$  value, the better is the resolution at the bottom of the column and the less is the separation at the top. Figs. 6 and 7 also indicate that with decreasing  $G/L$  value the resolution efficiency became higher at the top and lower at the bottom of the column. This means that if one particular component is required to be purified, the  $G/L$  value should be set close to the partition coefficient of the other component.

#### *Liquid phases*

The requirements for the liquid phase in CCGLC include not only high selectivity but also low viscosity. The liquid phase should flow by gravity as a thin film over the packing in the column. Durability and cost are also important factors. Poly(diethylene glycol succinate) and silicone KF-54 (methylphenyl-silicone) were studied with respect to these requirements. Poly(diethylene glycol succinate), a highly polar liquid phase for GC, was denatured quickly from a transparent brown liquid to a dark brown paste even during the warm-up period. Silicone KF-54, a slightly polar liquid phase, remained as a smooth liquid with long-term operation at 200°C. Using KF-54, over 99% purities of the samples of dimethyl–diethyl phthalate and *cis*-decahydronaphthalene–tetrahydronaphthalene were obtained. For the separation of decahydronaphthalene stereoisomers, about 94.5% purity of *cis*-decahydronaphthalene was obtained. It is necessary for more polar and stable liquid phases to be developed in order to extend the applicable range of this method. Precise temperature control system would also improve the separation, as the system used was made in the laboratory, and might have some temperature deviation.

#### CONCLUSION

The separation of test samples with high boiling points could have been achieved by using the

TABLE I  
COMPARISON OF THE SYSTEMS

Parameter	Previous system	Present system
Sample applicable	B.p. up to 130°C, <i>e.g.</i> , <i>n</i> -hexane, isooctane, benzene, toluene, ethanol	B.p. up to 300°C, <i>e.g.</i> , dimethyl phthalate, diethyl phthalate, decahydronaphthalene, tetrahydronaphthalene
Temperature of separating section	Up to 60°C	Up to 200°C
Temperature of stripping section	Up to 85°C	Up to 260°C
Liquid phase	PEG 400, squalane	Silicone KF-54

proposed system. The characteristics of the system are given in the Table I in comparison with the previous system.

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