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Katsuya Sato[a]; Osamu Motokawa[a]; Katsunori Watabe[a]; Toshihide Ihara[b]; Toshiyuki Hobo[b]
[a] CENTRAL RESEARCH LABORATORY SHIMADZU CORPORATION, KYOTO, JAPAN [b] LABORATORY OF INDUSTRIAL ANALYTICAL CHEMISTRY, FACULTY OF TECHNOLOGY, TOKYO METROPOLITAN UNIVERSITY, TOKYO, JAPAN

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Temperature Gradient Method for Continuous Countercurrent Gas–Liquid Chromatography

KATSUYA SATO, OSAMU MOTOKAWA, and KATSUNORI WATABE
CENTRAL RESEARCH LABORATORY
SHIMADZU CORPORATION
KYOTO, JAPAN

TOSHIHIDE IHARA and TOSHIYUKI HOBO
LABORATORY OF INDUSTRIAL ANALYTICAL CHEMISTRY
FACULTY OF TECHNOLOGY
TOKYO METROPOLITAN UNIVERSITY
TOKYO, JAPAN

ABSTRACT

Continuous countercurrent gas–liquid chromatography (CCGLC), where the gas and liquid phases move countercurrently and the sample can be introduced continuously, is a method suitable for separating binary sample systems. The flow ratio of the gas and liquid phases (G/L) in CCGLC should be between the partition coefficients of the two components to be separated. However, the larger the difference between the G/L and the partition coefficient of one component, the higher the separation efficiency of the other component. By shifting the partition coefficients from the point of introduction of the sample to the directions of the gas and liquid flows, we believed a more efficient separation of the components would be achieved. A separation tower with a temperature gradient was constructed to create an inclined arrangement of the partition coefficient. With this system, the separation of stereoisomers was investigated, and 99.9% purity of *trans*-decahydronaphthalene was achieved.

INTRODUCTION

In continuous countercurrent gas–liquid chromatography (CCGLC), the gas and liquid phases move countercurrently. The component having the larger moving velocity moves to the direction of the gas flow, and the component having the smaller moving velocity travels with the liquid phase, so that a two-component sample can be separated. Several methods have been proposed in order to realize countercurrent flow of two phases (1–5). For such advantages as a simple scheme, little mechanical movement, and direct control of the liquid-phase flow rate, we chose a liquid-phase circulation method and carried out studies on CCGLC (5–9). Essentially, separation depends on the difference between the partition coefficients of two components, so that precise separation of compounds in the fields of chemistry and biochemistry can be achieved by increasing the difference of partition coefficients. There are two ways to increase this difference: finding a new liquid phase and improving the methodology. We have reported on a study of the liquid phase (8, 9). In this paper we develop a temperature gradient method for CCGLC to improve the separation efficiency and we apply it to the separation of decahydronaphthalene stereoisomers.

THEORETICAL

The separation procedure of continuous countercurrent gas–liquid chromatography is shown in Fig. 1. In a column of length Z, the retention times of Components A and B are t_{RA} and t_{RB}, so that the moving velocities of the components in the column are Z/t_{RA} and Z/t_{RB}, respectively. When

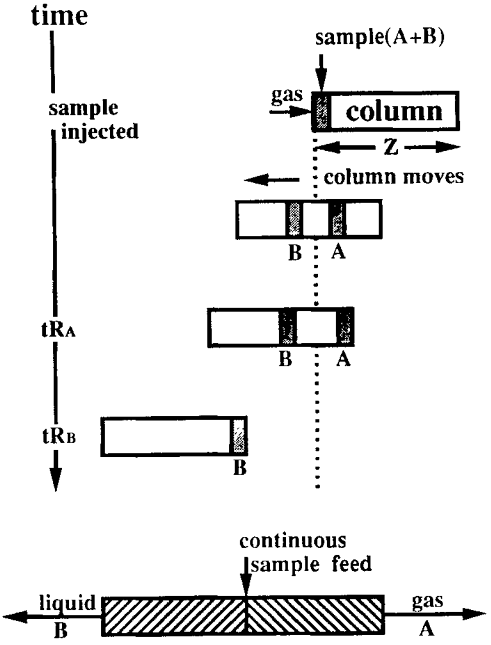

FIG. 1 Basic scheme of continuous countercurrent gas–liquid chromatography.

the column moves in the direction opposite of the gas flow and its velocity is between Z/t_{RA} and Z/t_{RB}, Component A, which has the smaller partition coefficient, moves in the direction of the gas flow, and Component B, which has the larger partition coefficient, moves in the direction in which the column is moving. Actually, the liquid-phase gravitation method is applied to the packing surface in a vertical separation tower instead of moving the column mechanically. Thus, Components A and B travel in different gas and liquid flow directions from the point of introduction; Component A with the gas phase to the top and Component B with the liquid phase to the bottom of the tower. This method enables continuous sample introduction. The separating condition is expressed by using the partition coefficient.

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

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

Equation (1) can also be expressed as

$$K_{\mathrm{A}} = \frac{\dfrac{W_l}{L}}{\dfrac{W_g}{G}} = \frac{W_l}{W_g}\frac{G}{L} \qquad (2)$$

where K_{A} = partition coefficient of Component A, W_l = weight (in grams) of Component A contained in 1 L of the liquid phase, W_g = weight (in grams) of Component A contained in 1 L of the gas phase, L = flow rate of the liquid phase (L/h), and G = flow rate of the gas phase (L/h).

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

$$W_l/W_g < 1 \qquad (3)$$

Substituting Eq. (3) into Eq. (2):

$$G/L > K_{\mathrm{A}} \qquad (4)$$

Under the condition in the following equation,

$$G/L < K_{\mathrm{B}} \qquad (5)$$

Component B moves in the direction of liquid flow in the same manner.

From Eqs. (4) and (5), it is necessary that G/L be between K_{A} and K_{B} in order to separate Components A and B, as shown in

$$K_{\mathrm{A}} < G/L < K_{\mathrm{B}} \qquad (6)$$

The optimum separating condition is defined by

$$(G/L)^{-1} = [(1/K_A) + (1/K_B)]/2 \tag{7}$$

From the point of view of the purification of one particular component, however, a larger difference between G/L and the partition coefficient of one component gives a higher separation efficiency for the other component. Figure 2 shows the content of impurities in the eluents from the top and bottom of the tower for decahydronaphthalene stereoisomer separation at 140°C. The partition coefficient of the *cis*-form, K_B, was 487 and the partition coefficient of the *trans*-form, K_A, was 382. When G/L was 447, near the midpoint of the two partition coefficients, the top eluent consisted of 97.5% *trans*- and 2.5% *cis*-form, and the bottom eluent consisted of 98.8% *cis*- and 1.2% *trans*-form. When G/L was 425, the top eluent consisted of 98.9% *trans*- and 1.1% *cis*-form, and the bottom eluent consisted of 96.6% *cis*- and 3.4% *trans*-form. When G/L was 459, the top eluent consisted of 97.1% *trans*- and 2.9% *cis*-form, and the bottom eluent consisted of 99.1% *cis*- and 0.9% *trans*-form. This means that by setting G/L far from K_A, a higher purity of the B component will be obtained, and vice versa. If differences between the partition coefficients and G/L could be increased by changing positions in the separation tower, more efficient separation of the components would be expected. A temperature gradient through the separation tower was adopted instead of varying the G/L from position to position because the partition coefficient depends on temperature and the tower is a closed system in which it is very hard to change G/L position by position. Figure 3 shows the scheme of the temperature gradient method, with the tower length (temperature gra-

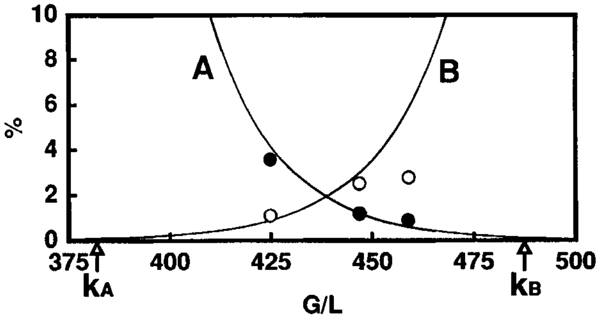

FIG. 2 Contents of impurities at the top and bottom eluent on separation of decahydronaphthalene stereoisomers at 140°C. Y axis: Isomer content. X axis: G/L. A: *trans*-form in the bottom product as an impurity. B: *cis*-form in the top product as an impurity. K_A: Partition coefficient of the *trans*-form. K_B: Partition coefficient of the *cis*-form.

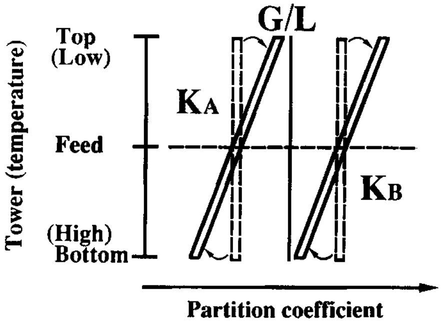

FIG. 3 Principle of the temperature gradient method. Y axis: Tower length, sample feed point taken as 0. X axis: Partition coefficient. The Y axis is also the mean temperature range from high to low (from bottom to top).

dient) as the ordinate and partition coefficient as the abscissa. At the middle of the tower, where the sample is introduced, G/L is about midpoint of two partition coefficients A and B. At the top of the tower, the partition coefficients increase by lowering the temperature; at the bottom of the tower, they decrease by raising the temperature, so that the difference between G/L and K_B increases toward the top of the tower and the difference between G/L and K_A increases toward the bottom of the tower. Thus, by the temperature gradient method, an inclined arrangement of the difference of the two factors is established throughout the tower.

EXPERIMENTAL

Tower

A diagram of the separation tower is shown in Fig. 4. Pyrex glass tubing (50 mm i.d. and 3 m in length) was used as the tower (9). The tower consisted of two sections, the separating section (1.5 m in length) and the stripping section (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 × 1.8 × 1.8 mm) was used to fill the tower. The surface area and the density of the packing was 3.743 m^2/m^3 and 1500 kg/m^3, respectively.

In the stripping section, a component, which is moved from the separating section into the stripping section, is removed from the liquid phase at a higher temperature than it had in the separating section, and it is carried out from the middle of the tower and goes through a cold trap and

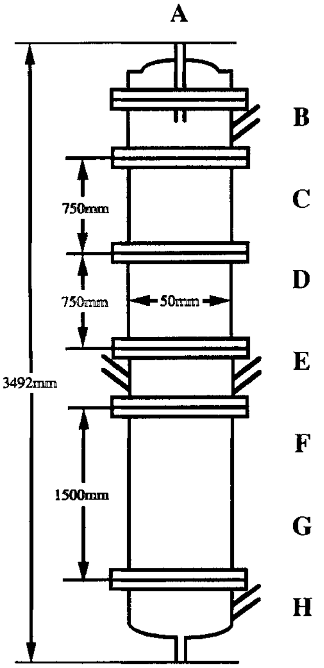

FIG. 4 Diagram of the tower. A: Liquid phase inlet. B: Outlet for Component A and gas phase. C: Upper separation section. D: Sample inlet. E: Lower separation section. F: Outlet for Component B and gas phase. G: Stripping section. H: Gas-phase inlet.

a flowmeter. To strip the component completely from the liquid phase in the stripping section, the following condition must be valid:

$$(G_s/L) > K_B^s \tag{8}$$

where G_s = flow rate of the gas phase in the stripping section (L/h), L = flow rate of the liquid phase (L/h), and K_B^s = partition coefficient of the component at the temperature of the stripping section.

Liquid and Gas Phases

Because of its high durability at high temperature, Apiezon C was used as the liquid phase. The liquid phase was fed to the top of the tower by a plunger-type constant-flow pump. As a thin film on the surface of the packing material, the liquid phase gravitated in the tower from the top to the bottom. The liquid phase was recycled through the stripping section.

Nitrogen (B grade, Nippon Sanso Co.) from a high-pressure cylinder was used as the gas phase after it was passed through a purifier (6 mm i.d. × 300 mm stainless steel tubing) packed with reduced copper beads 1–2 mm diameter) in order to remove any trace amount of oxygen gas. The nitrogen gas was supplied from the bottom of the tower and moved toward the top of the tower. At the middle of the tower, the gas stream is separated into two streams: One goes out of the tower by venting through a cold trap and a flowmeter, and the other goes to the top of the tower and exits through a trap and a flowmeter.

Samples

As a test sample, a mixture (50:50 wt%) of *trans-* (bp 187.2°C)/*cis*-decahydronaphthalene (bp 195.7°C) was prepared by mixing each component as a pure compound purchased from Tokyo Kasei Kogyo (Tokyo, Japan). The sample was fed by a plunger-type constant-flow pump continuously into the tower through the septum at the midpoint of the separating section.

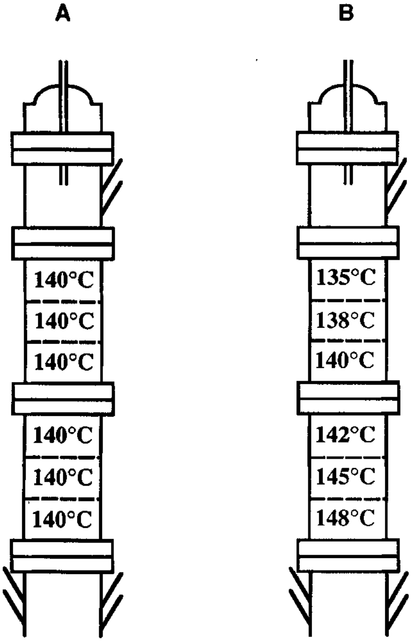

FIG. 5 Temperature settings of the tower. A: Isothermal operation. B: Temperature gradient operation.

Heating System

The tower was divided into 9 blocks: a liquid-phase inlet block, 3 blocks in the upper separation section, a sample inlet block, 3 blocks in the lower separation section, and a stripping block. A mantle heater was mounted in each section and independently controlled. For isothermal operation, the 6 heaters in the separating section were maintained at 140°C. For temperature gradient operation, they were controlled separately. An example of a temperature setting from 135 to 148°C is shown in Fig. 5. The temperatures of the liquid-phase inlet block, the sample inlet block, and the stripping block were kept at 140, 140, and 170°C, respectively.

RESULTS AND DISCUSSION

Isothermal Separation

A mixture of *trans*- and *cis*-decahydronaphthalene (50:50 wt%) was introduced continuously into the tower with the optimum operating condition as found after preliminary experiments (9). The separation temperature was 140°C, where the partition coefficients of *trans*- and *cis*-forms were 377 and 490, respectively. The gas flow rate was 87.1 L/h and the

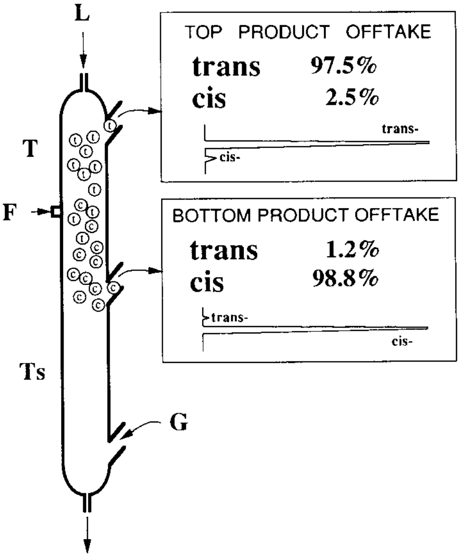

FIG. 6 Isothermal separation of decahydronaphthalene stereoisomer. T = temperature of the separation section, 140°C. T_S = temperature of the stripping section, 170°C. L = liquid-phase flow rate, 0.195 L/h. F = sample feed rate, 7.2 mL/h. G = gas-phase flow rate, 87.1 L/h.

liquid flow rate was 0.195 L/h, so that the G/L value was 447, near the theoretical value of 426. The rate of sample introduction was 7.2 mL/h. As shown in Fig. 6, the eluate from the top of the tower contained 97.5% *trans-* and 2.5% *cis*-forms. From the bottom of the tower, 1.2% *trans-* and 98.8% *cis*-forms were obtained. The theoretical number of plates calculated by the formula described elsewhere (5) was 17.

Temperature Gradient Separation

The gas flow rate was 82.6 L/h and the liquid flow rate was 0.195 L/h, so that the G/L value was 424. Under those conditions, several temperature gradient settings were studied, and the following condition was found to give the best result: increase the temperature 3°C for every 25 cm of length from 135 to 148°C. However, at 135°C, K_A was 434, which was larger than G/L (424), and at 148°C, K_B was 391, which was smaller than G/L. Accordingly, the relation of G/L and the partition coefficients did not satisfy Eq. (6) at both ends of the tower. The discrepancy between the theoretical and experimental optimum range could be explained by the difference between the measured temperature at the wall of the tower and the actual temperature at the center of the tower and also by considering that the

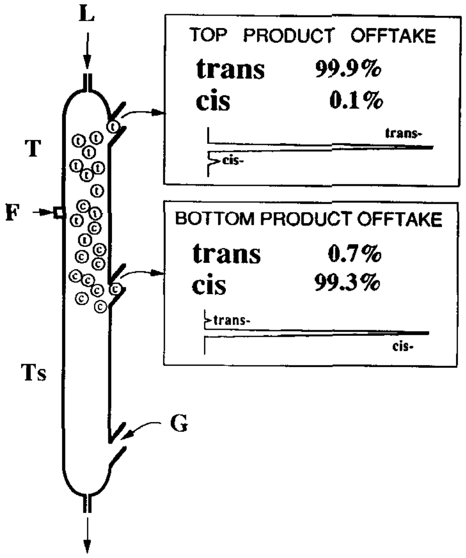

FIG. 7 Temperature gradient separation of decahydronaphthalene stereoisomer. T = temperature of the separation section, 135 to 148°C. T_S = temperature of the stripping section, 170°C. L = liquid-phase flow rate, 0.195 L/h. F = sample feed rate, 7.2 mL/h. G = gas-phase flow rate, 82.6 L/h.

temperature of the tower-top might be affected by the temperature of the lower part and that the bottom of the separation section might be cooled by the lower gas outlet block. In temperature gradient operation, the eluate from the top of the tower contained 99.9% *trans-* and 0.1% *cis*-forms, and from the bottom of the tower 0.7% *trans-* and 99.3% *cis*-forms were obtained. The theoretical number of plates calculated for isothermal operation at 140°C was 49. The result, shown as Fig. 7, indicates that the temperature gradient method greatly improved the separation efficiency of CCGLC.

Long-Term Operation

Because CCGLC is a method for preparative separation, stability in long-term operation is important. The stabilities of isothermal and temperature gradient CCGLC in long-term operation were compared. In Fig. 8, the *trans*-form contents in the eluents from the top and bottom of the separation section in isothermal separation are plotted as the ordinate with time as the abscissa. The temperature was 140°C with a gas flow rate of 8.7 L/h, a liquid flow rate of 0.195 L/h, and a sample feed rate of 7.2 mL/h. Over nearly 15 hours the *trans*-form content was more than 90% in the top product and less than 3% in the bottom product. In Fig. 9 the results

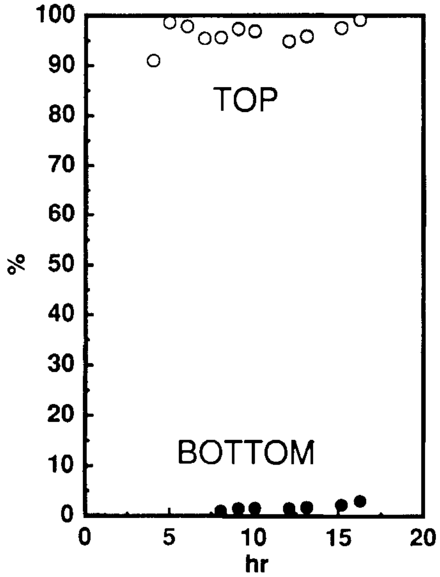

FIG. 8 Long-term operation of isothermal separation. Y axis: Content of *trans*-form. X axis: Time from the start of sample feeding (hours).

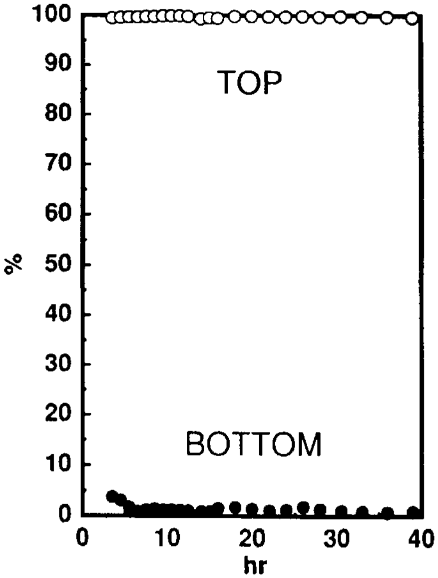

FIG. 9 Long-term operation of temperature gradient separation. Y axis: Content of *trans*-form. X axis: Time from the start of feeding (hours).

for temperature gradient separation in the same manner as for isothermal separation are plotted. The temperature range was 135 to 148°C, the gas flow rate was 82.6 to 91.8 L/h, the liquid flow rate was 0.195 L/h, and the sample flow rate was 7.2 mL/h. The figure indicates that over 30 hours the content of *trans*-form at the top of the tower was more than 99% and the content at the bottom, as impurity, was less than 1%. The data also indicate that the temperature gradient separation method was more stable than the isothermal operation method. The reason is that the temperature fluctuation was reduced through the effect of the temperature gradient while in isothermal separation the fluctuation directly influences the stability of the partition coefficient.

CONCLUSION

The temperature gradient method for continuous countercurrent gas–liquid chromatography has been investigated and confirmed as an effective method to separate a two-component sample system. It is applicable even in cases with a partition coefficient ratio as small as 1.3. Its stability in long-term operation has proved its capability for preparative-scale use.

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