Selective Transport of Saccharides through a Bulk Liquid Membrane Using Reversed Micelle Carriers

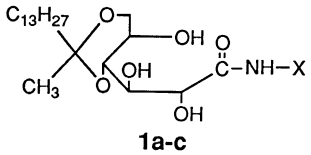
Toshiyuki Kida, Daisuke Furue, Araki Masuyama, Yohji Nakatsuji, and Isao Ikeda*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadaoka 2-1, Suita, Osaka 565

(Received May 7, 1996)

D-Ribose was selectively transported from a mixture of D-ribose, D-glucose, and D-fructose through a bulk liquid membrane including reversed micelles. Among amphiphiles examined in this study, a gluconamide-type amphiphile was found to form the best carrier from the point of both the selectivity and the velocity.

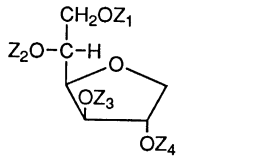
Recently, a system for selective saccharide transport through a liquid membrane including an artificial carrier has been developed and has attracted much attention, since such system is useful not only as a separation method for a particular saccharide but also as a model for clarifying the mechanism of action of saccharide transporter in a cell membrane. Until now, several researchers have reported the transport of monosaccharides or glycosides through an organic liquid membrane by use of phenylboronic acid or its analogues, which can covalently complex with saccharides to give cyclic boronate esters, as the carriers.[1] However, no other carrier for saccharide transport has been presented. We have a great interest in developing a new carrier for saccharide transport through a liquid membrane. In this communication, we report selective transport of saccharides using reversed micelle carriers. While the selective liquid-liquid extraction[2] and the transport[3] through a liquid membrane using reversed micelle systems have been described as good separation methods for proteins, there has been no report on transport of saccharides using the reversed micelle carrier to the best of our knowledge.

On the basis of the idea that the water pool formed in a reversed micelle may be an actual carrier for the transport of hydrophilic guest compounds across a liquid membrane, we designed amphiphiles **1a-c** bearing a highly lipophilic alkyl group and hydrophilic amide and polyhydroxyl groups that were supposed to be effective for forming a water pool, as reversed micelle-forming compounds. These compounds were prepared by acetalization of glucono-1,5-lactone with 2-pentadecanone, followed by amidation with the appropriate amines.[4] For the purpose of comparison, polyoxyethylene sorbitan trioleate (Tween 85), sorbitan stearate (Span 60), Aerosol-OT (AOT), dihexadecyldimethylammonium bromide (DHDMAB), and cetyltrimethylammonium bromide (CTAB) which are commercially available were selected as the typical reversed micelle-forming compounds.[5] Among them, AOT and CTAB were found to be inadequate for this transport because their good water solubilities caused them to leak from the organic liquid membrane into the aqueous phases during the transport.



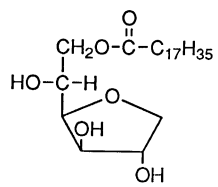
1a-c

1a : X = -$(CH_2)_2OH$
1b : X = -C_3H_7
1c : X = -$(CH_2)_2OCH_3$

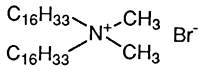


Z_1~ Z_4 =
$C_{17}H_{33}COO$-, $C_{17}H_{33}COO$-,
$C_{17}H_{33}COO$-, -$(C_2H_4O)_{20}H$

Tween 85



Span 60



DHDMAB

Transport experiments were carried out using a U tube apparatus (1.5 cm internal diameter, 14.6 cm high, 2 cm distance between two arms) equipped with a stirring rod and a magnetic stirrer (500 rpm) at 25 °C. An organic solution (15 mL) containing an amphiphilic compound was placed in the bottom of the tube, and two portions of aqueous solutions (both 3 mL) were carefully added on the tops of the organic solution. The details of transport conditions are summarized in the footnotes of Table 1. The concentration of saccharide in the receiving phase was determined by HPLC (Asahipack column, 4.6 mm internal diameter x 250 mm, acetonitrile/water = 75/25 as an eluent) using ethylene glycol as an internal standard. Water content in an organic liquid membrane after the transport experiment (1 day) was measured by Karl-Fischer titration method. Each experiment was repeated at least three times to ensure reproducibility (± 10%).

Table 1 shows the results of competitive transport toward D-ribose, D-glucose, and D-fructose using various reversed micelle carriers and water content in the organic liquid membrane after the transport experiments (1 day). These water content values were approximately equal to those obtained after the transport experiments over 4 days, indicating that the water content in the

Table 1. Competitive transport data[a]

Entry	Amphiphile	Transport Rate[b]			Water Content[c]
		Ri	Glu	Fru	
1	**1a**	6.3	1.1	1.3	1050
2	**1b**	2.7	1.0	1.2	880
3	**1c**	2.3	0.96	1.0	840
4	Tween 85	1.5	0.96	0.70	1050
5	Span 60	4.3	1.3	0.92	1040
6	DHDMAB	2.8	1.2	0.75	820

[a]Transport conditions: source phase (H_2O, 3 mL, [D-ribose] = [D-glucose] = [D-fructose] = 1.5 M); organic phase ($CHCl_3$, 15 mL, [amphiphile] = 1 x 10^{-2} M); receiving phase (H_2O, 3 mL), 25 °C, 500 rpm. [b]mM/day, Ri = D-Ribose, Glu = D-Glucose, Fru = D-Fructose. [c]ppm, after 1 day.

liquid membrane has come to equilibrium fully after 1 day. D-Ribose was transported faster than D-glucose and D-fructose, regardless of the type of carrier employed. The reversed micelle carrier formed by amphiphile **1a** bearing a terminal hydroxyl group in the hydrophilic moiety showed the highest D-ribose/D-glucose selectivity as well as the fastest transport rate for D-ribose among all types of carriers examined. On the other hand, when amphiphile **1b** (or **1c**), which has a CH_3 (or OCH_3) group in the terminal, was used as the reversed micelle-forming compound, both the transport rates for three types of saccharides and the D-ribose selectivity decreased. Concerning the carriers formed by the gluconamide-type amphiphiles **1a-c**, transport rates for these saccharides increased with an increase in water content in the liquid membrane. Since the water content relates to the amount of water pool formed in the reversed micelle, there should exist the close relationship between transport rates for saccharides and the amount of water pool in the liquid membrane. The D-ribose selectivity in the reversed micelle transport system may be explained by assuming that the more lipophilic the saccharide tends to transfer the faster from the source aqueous phase to the water pool (and from the water pool to the receiving aqueous phase) across a lipophilic region of the reversed micelle. The competitive transport toward methyl α-D-glucoside, D-xylose, and D-glucose using the carriers formed by compound **1a** resulted in clarifying the following order of increasing transport rate; methyl α-D-glucoside>D-xylose>D-glucose.[6] This order is in agreement with the increasing order of the lipophilicity of saccharide molecule, showing that the lipophilicity of saccharide molecule is an important factor among those affecting saccharide discrimination by the reversed micelle system.

Figure 1 shows the plots of saccharide concentration in the receiving phase after specific periods, for competitive transport toward D-ribose, D-glucose, and D-fructose using the reversed micelle carrier formed by amphiphile **1a**. The amounts of these saccharides transported into the receiving phase linearly increased with time.

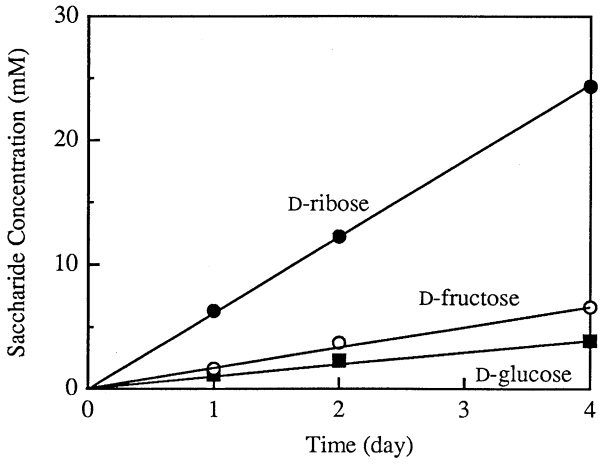


Figure 1. Plots of saccharide concentrations in the receiving phase *vs.* time. Transport conditions: the same as shown in Table 1.

In conclusion, the selective transport of D-ribose compared to D-glucose and D-fructose through a liquid membrane was achieved by using reversed micelles as the carrier. This is the first example for selective transport of monosaccharide through an organic liquid membrane using reversed micelle carriers. Optimization of transport conditions and elucidation of mechanism for the transport are now in progress.

References and Notes

1 T. Shinbo, K. Nishimura, T. Yamaguchi, and M. Sugiura, *J. Chem. Soc., Chem. Commun.*, **1986**, 349; B. F. Grotjohn and A. W. Czarnick, *Tetrahedron Lett.*, **30**, 2325(1989); L. K. Mohler and A. W. Czarnik, *J. Am. Chem. Soc.*, **115**, 2998(1993); M.-F. Paugam and B. D. Smith, *Tetrahedron Lett.*, **34**, 3723(1993); M.-F. Paugam, G.T. Morin, and B. D. Smith, *Tetrahedron Lett.*, **34**, 7841(1993); G. T. Morin, M.-F. Paugam, M. P. Hughes, and B. D. Smith, *J. Org. Chem.*, **59**, 2724(1994); G. T. Morin, M. P. Hughes, M.-F. Paugam, and B. D. Smith, *J. Am. Chem. Soc.*, **116**, 8895(1994); E. Lambert, E. C. Breinlinger, and V. M. Rotello, *J. Org. Chem.*, **60**, 2646(1995); J. A. Riggs, R. K. Litchfield, and B. D. Smith, *J. Org. Chem.*, **61**, 1148(1996).

2 R. S. Rahaman, J. Y. Chee, J. M. S. Cabral, and T. A. Hatton, *Biotechnol. Prog.*, **4**, 218(1989); J. M. Woll, T. A. Hatton, and M. L. Yarmush, *Biotechnol. Prog.*, **5**, 57(1989); M. R. Aires-Barros and J. M. S. Cabral, *Biotech. Bioeng.*, **38**, 1302(1991); V. M. Paradkar and J. S. Dordick, *Biotechnol. Prog.*, **9**, 199(1993).

3 P. L. Luisi, F. J. Bonner, A. Pellegrini, P. Wiget, and R. Wolf, *Helv. Chimica Acta*, **62**, 740(1979); P. L. Luisi, *Angew. Chem., Int. Ed. Eng.*, **24**, 439(1985); D. W. Armstrong and W. Li, *Anal. Chem.*, **60**, 86(1988); V. M. Paradkar and J. S. Dordick, *Biotechnol. Prog.*, **7**, 330(1991).

4 T. Kida, N. Morishima, A. Masuyama, and Y. Nakatsuji, *J. Am. Oil Chem. Soc.*, **71**, 705(1994).

5 M. Seno, K. Sawada, K. Araki, K. Iwamoto, and H. Kise, *J. Colloid Interface Sci.*, **78**, 57(1980); T. Sunamoto, T. Hamada, T. Seto, and S. Yamamoto, *Bull. Chem. Soc. Jpn.*, **53**, 583(1980); S. Goto, K. Nakata, T. Miyakawa, W. Zhang, and T. Uchida, *Yakugaku Zasshi*, **111**, 702(1991); N. Greenspoon and E. Wachtel, *J. Am. Chem. Soc.*, **113**, 7233(1991). C. F. Komives, D. E. Osborne, and A. J. Russell, *J. Phys. Chem.*, **98**, 369(1994); C. F. Komives, E. Lilley, and A. J. Russell, *Biotechnol. Bioeng.*, **43**, 946(1994).

6 This transport experiment was carried out under the same conditions as shown in the footnotes of Table 1 except that aqueous solution containing methyl α-D-glucoside (1.5 M), D-xylose (1.5 M), and D-glucose (1.5 M) was used as the source phase. The transport rates observed for methyl α-D-glucoside, D-xylose, and D-glucose were 11, 4.8, and 1.1 mM/day, respectively.