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# Creation of Novel Green Surfactants Containing Carbonate Linkages

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## 1. Introduction

### 1.1. What is green chemistry?

Chemistry has a key role to play in maintaining and improving our quality of life, such as in medicine, materials and electronics. However, it has also caused damage to human health and the natural environment. To make chemistry compatible with human health and the environment, Anastas and Warner have proposed 12 principles of green chemistry, which help to explain what it means in practice [1]. The principles cover a wide range of concepts, such as the molecular design and synthetic routes of product and the best means of waste disposal. In recent years, the establishment of a new field of green chemistry has been recognized as a necessary goal for sustainable development. The greening of chemistry will be realized by the discovery and development of new synthetic routes using renewable resources, reaction conditions and catalysts for improved selectivity and energy minimization, and the design of bio-/environmentally compatible chemicals. On the basis of these concepts, green polymer chemistry [2-4], synthetic organic chemistry using environmentally friendly processes [5,6] and technology for the production of bio-based product [7] have so far been developed and improved.

### 1.2. Requirements for green surfactants

Surfactants are widely used in large quantities in industrial fields including fibers, pharmaceutical agents and foods, and are also used as household detergents. Owing to the water-solubility of surfactants, they are generally difficult to recover or reuse; therefore, they are discharged as drainage into the environment if they are not biodegradable. On the other hand, surfactants should be chemically recycled, particularly after industrial use, in order to conserve

energy resources in addition to reducing their environmental impact. Therefore, the development of surfactants with improved biodegradability and chemical recyclability using renewable resources by an environmentally benign process is now needed with respect to the establishment of green chemistry. Also, increasing the performance of surfactants is one way to reduce their consumption. Figure 1 shows a simplified conceptual scheme of green surfactants.
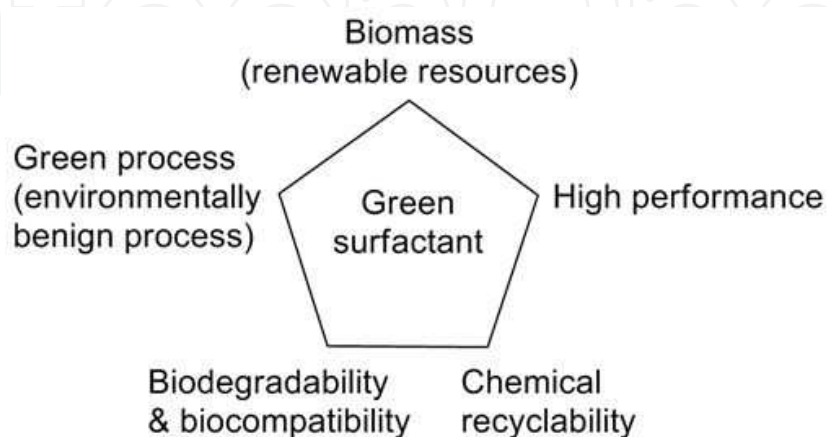


**Figure 1.** Simplified conceptual scheme of green surfactants.

Some green surfactants have been synthesized using renewable resources, such as amino acids, sugars and organic acids, and they have been used in human life because of their low toxicity and high biodegradability [8]. Surfactants containing the sugar moiety as a hydrophilic group have been synthesized by many researchers and used as detergents, emulsifiers and cosmetics [9]. The syntheses and properties of anionic, cationic and amphoteric surfactants containing amino acid moieties, such as arginine [10,11], tryptophan [12], lysine [13], cysteine [14], glutamate and aspartate [15] have also been reported. Microbially producible polycarboxylates may become versatile starting materials for the production of next-generation green surfactants. The polycarboxylates applicable to a biomass refinery system include fumaric acid, maleic acid, itaconic acid and aconitic acid [16]. The production of these polycarboxylates has been extensively studied with the aim of establishing a biomass refinery system as well as establishing green chemistry. Also, fatty acids and alcohols from plant oils occupy a concrete position as the hydrophobic group of a green surfactant. Furthermore, sugar-based biosurfactants produced by a variety of microorganisms exhibit unique properties, such as mild production conditions, multifunctionality and high environmental compatibility [17]. The numerous advantages of biosurfactants have led to their application not only in the food, cosmetic and pharmaceutical industries but also in environmental protection and energy-saving technology. These features of biosurfactants should broaden their range of applications in new advanced technologies.

It is known that ester- or amide-containing linear-type surfactants consisting of one hydrophobic group and one hydrophilic group are rapidly biodegraded by environmental microbes [18,19]. This is due to the high biodegradability of the degradation compounds produced by

the enzymatic hydrolysis of ester or amide linkage. However, ester-containing surfactants are generally labile to hydrolysis, particularly under alkaline conditions. Thus, more hydrolyti-cally stable and biodegradable surfactants are needed. Also, chemodegradable surfactants containing a labile linkage that is rapidly cleaved by a chemical stimulus have attracted considerable attention as biodegradable surfactants [20]. Acetal- or cyclic acetal-containing surfactants exhibit good surfactant properties and rapid hydrolyzability under acidic condi-tions [21,22]. On the other hand, the ester linkage of cationic surfactants is hydrolyzed to produce a fatty acid and a quaternary-ammonium alcohol at a high pH [23]. Furthermore, photolabile sulfonate-type anionic surfactants [24], ozone-cleavable anionic surfactants [25] and thermally cleavable anionic surfactants based on furan-maleimide Diels-Alder adducts [26] have been reported.

Recently, the syntheses and properties of gemini-type (dimeric) surfactants consisting of two hydrophobic alkyl chains, two hydrophilic groups and a linker in the same molecule have been extensively studied. The first report on dimeric cationics was published by Bunton *et al*. [27]. The term ''gemini-surfactants'' was coined for these dimeric surfactants by Menger *et al*. [28,29]. It was found that the surfactant properties of gemini-type surfactants, such as a low critical micelle concentration (cmc) and surface tension lowering, were superior to those of the corresponding linear-type (monomeric) surfactants [30-33]. These superior surfactant proper-ties are due to the stronger intra- and intermolecular hydrophobic interactions between the two hydrophobic alkyl chains of gemini-type surfactants. Therefore, gemini-type surfactants can be regarded as green surfactants because they exhibit higher functionalities that lead to a reduction in their consumption. Biodegradable sugar-derived gemini-type nonionic surfac-tants have already been reported by Wilk and co-workers [34,35]. Also, Ono *et al*. reported a tartrate-derived bis(sodium sulfate)-type chemocleavable gemini-type surfactant containing ester linkages that exhibited good biodegradability [36]. Moreover, oligomeric surfactants composed of three or four hydrophobic and hydrophilic groups have been synthesized and characterized [37-39]. Their surfactant properties are superior to those of gemini-type surfac-tants. However, there are few reports on oligomeric surfactants because their syntheses are complicated.

## 1.3. Role of carbonate linkage in surfactant molecule: their current use

The carbonate linkage is hydrolyzed in aqueous media by lipase to produce two hydroxyl groups and a carbon dioxide, and no acidic or alkaline species are produced. It will be advantageous for surfactants that the carbonate linkages are more stable than ester linkages in aqueous media [40]; because they are usually used in aqueous media. It has also been reported that carbonate-type nonionic surfactants are readily biodegraded by environmental microbes [40]. However, they are synthesized using an acid chloride. The synthesis of next-generation surfactants using halogen-free and environmentally benign processes is needed from the viewpoint of green chemistry.

Figure 2 shows a simplified conceptual scheme of the synthesis, chemical recycling and biodegradation of novel green surfactants containing carbonate linkages. The designed surfactants are hydrolyzed in the environment to produce a hydrophobic 1-alkanol and a

hydrophilic alcohol along with the evolution of carbon dioxide, which are further degraded by microbes as a part of their biodegradation or biorecycling process [40]. Also, the primary degradation products can be used for chemical recycling by lipase, which is an environmentally benign catalyst [41,42]. This sustainable chemical recycling may become an important issue for next-generation surfactants, particularly in industrial fields. A new strategy for molecular design involving ready chemical recyclability as well as biodegradability will be needed. Novel carbonate-type surfactants are produced by a two-step carbonate exchange reaction of 1-alkanol and a hydrophilic alcohol using diphenyl carbonate or dimethyl carbonate. Diphenyl carbonate is now industrially produced by the carbonate exchange reaction of dimethyl carbonate with phenol. Dimethyl carbonate can be produced from methanol and carbon dioxide by a green method [43-46].

In this paper, the design, synthesis and properties of novel cationic and nonionic surfactants containing carbonate linkages as biodegradable and chemically recyclable segments are described.

## 2. Synthesis and properties of novel green surfactants containing carbonate linkages

### 2.1. General methods

The equilibrium surface tensions of carbonate-type surfactants solutions were measured using an automatic digital Kyowa Precise Surface Tensiometer by the CBVP method (Kyowa Kagaku Co. Ltd., Tokyo, Japan). The measurement was carried out using the Wilhelmy vertical plate technique and a sandblasted glass plate. The test solutions were aged at 25 °C for at least 1 h before any measurements.

The antimicrobial activities of the surfactants were evaluated by the agar dilution method [47]. Gram-positive bacterial strains, *Staphylococcus aureus* KB210, *Bacillus subtilis* KB211 and *Micrococcus luteus* KB212, gram-negative bacterial strains, *Escherichia coli* KB213, *Salmonella typhimurium* KB20 and *Pseudomonas aeruginosa* KB115, six fungal strains, *Candida albicans* KF1, *Saccharomyces cerevisiae* KF25, *Trichophyton mentagrophytes* KF213, *Microsporium gypseum* KF64, *Penicillium chrysogenum* KF270 and *Aspergillus niger* KF103, were used. The bacteria and fungi were cultured by Nutrient agar and Sabouraud dextrose agar, respectively. The antimicrobial activity was expressed as the minimum inhibitory concentration (MIC). The MIC value shows the lowest concentration of a surfactant at which the tested microorganisms do not show visible growth.

The biodegradabilities of the carbonate-type surfactants were evaluated by the biochemical oxygen demand (BOD). The BOD was determined with a BOD Tester [VELP Scientifica s.r.l., Usmate (MI), Italy] using the oxygen consumption method according to the Modified MITI Test [48]. The BOD-biodegradation (BOD/ThOD) was calculated from the BOD values and the theoretical oxygen demand (ThOD).
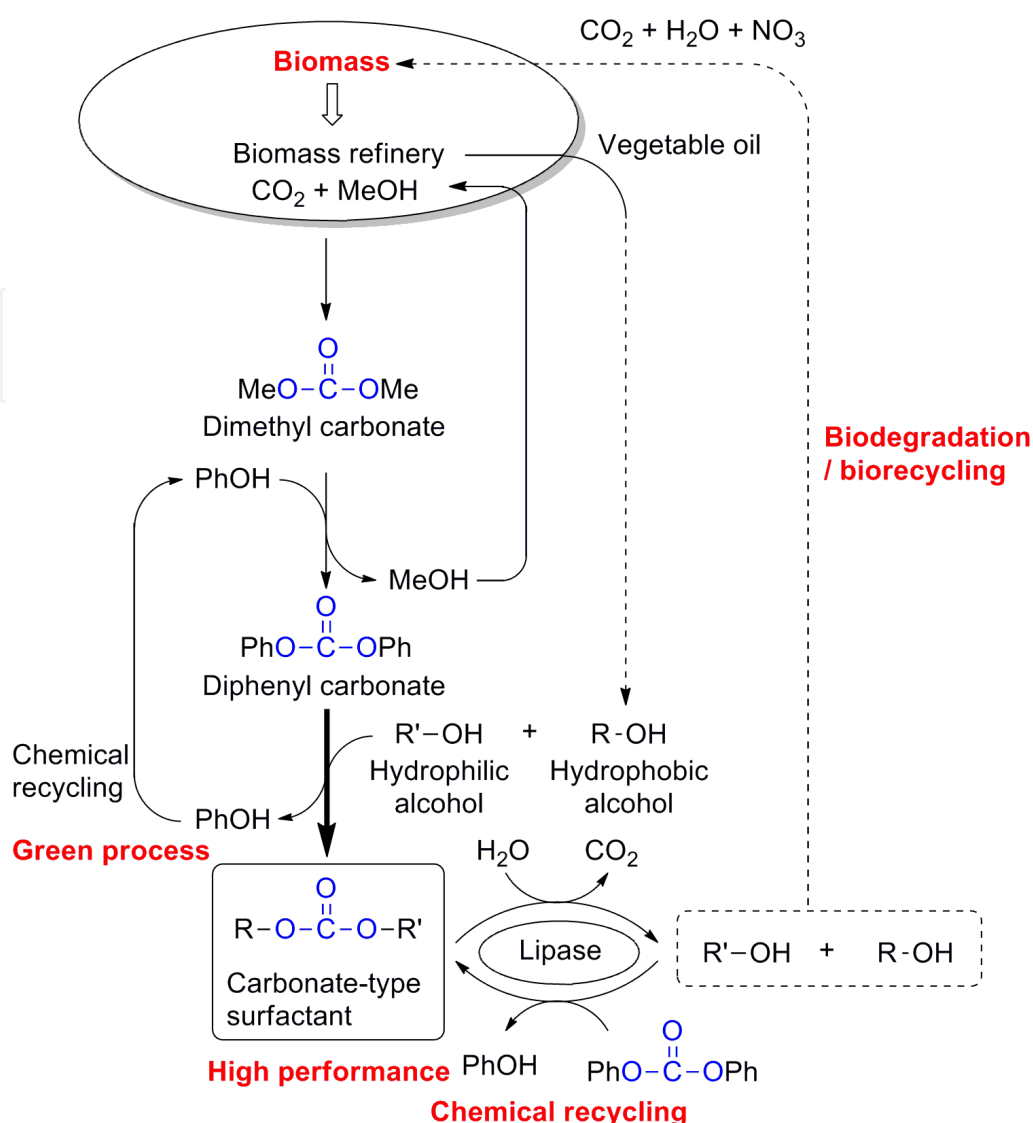
**Figure 2.** Simplified concepts of the synthesis, chemical recycling and biodegradation of novel green surfactants containing carbonate linkages.

## 2.2. Linear-type cationics containing carbonate linkage as green surfactants

In addition to good surfactant properties, it is known that cationic surfactants composed of quaternary-ammonium group and *n*-alkyl chain showed antimicrobial activities against a broad range of microorganisms such as gram-positive and gram-negative bacteria and fungi. However, they are generally highly resistant to biodegradation due to the lack of a primary degradation site in the molecule [49,50]. As a next-generation cationic surfactant, the biodegradabilities, chemical recyclabilities and higher functionalities that lead to a reduction in their consumption are needed as well as developing an environmentally benign synthetic route using renewable resources. Here, design and synthesis of linear-type cationics containing carbonate linkages (**SnX**) are described with respect to the effects of the introduction of carbonate linkages on biodegradation and chemical recycling (Figure 3) [51].
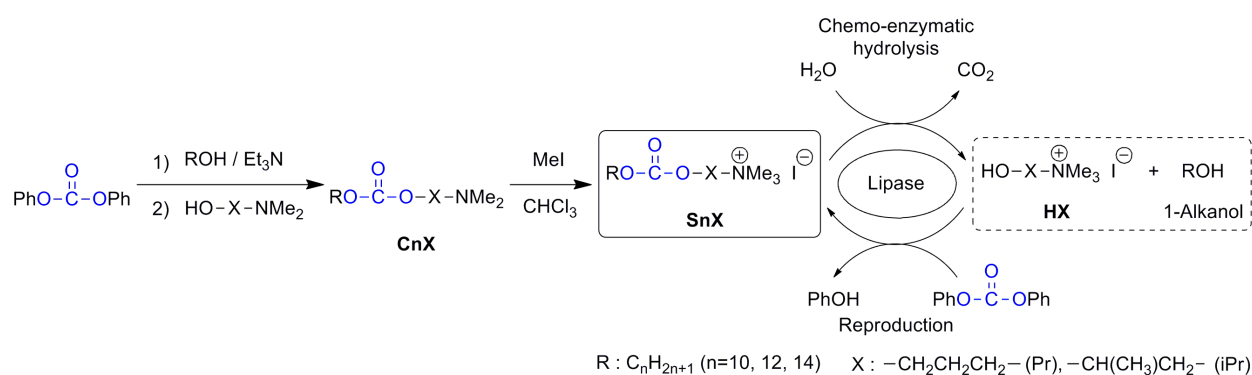
**Figure 3.** Synthesis and chemical recycling of novel linear-type cationics containing carbonate linkages (**SnX**) as biodegradable and chemically recyclable segments.

### 2.2.1. Synthesis of SnX

*n*-Alkyl-*N*,*N*-dimethylaminopropyl carbonate was first prepared by the reaction of diphenyl carbonate and 1-alkanol in the presence of Et$_3$N followed by the reaction of *N*,*N*-dimethylaminopropanol using one-pot, two-step reaction procedure. Then, the quaternarization of *N*,*N*-dimethylamino group of **CnX** readily occurred using CH$_3$I at room temperature (Figure 3). Purification was carried out by recrystallization from ethyl acetate to yield a series of quaternary-ammonium type cationics, **SnX**, in a total yield of 60-70%. The molecular structure was analyzed using $^1$H-NMR, $^{13}$C-NMR and elemental analysis.

### 2.2.2. Surfactant properties in aqueous solution

Carbonate-type cationics exhibited surfactant properties, such as surface tension lowering and micelle formation. From the surface tension *vs.* concentration plots for the cationic surfactants in distilled water, their cmc and the surface tension at the cmc ($\gamma_{cmc}$) are determined and listed in Table 1. The surfactant properties of a typical cationics, *N*-dodecyl-*N*,*N*,*N*-trimethylammonium iodide (**S12**), were also measured under the same conditions. The cmc of carbonate-type cationics was depended on the hydrocarbon chain length. The shorter hydrocarbon chain length tended to show a higher cmc value. The cmc value of carbonate-type cationics containing an *n*-dodecyl chain (**S12X**) showed a lower value compared to that of **S12**. This result indicates that the propylene or isopropylene group between the quaternary-ammonium group and carbonate linkage behave as a hydrophobic group and contribute the hydrophobic interaction between the surfactant molecules. It was also found the cmc value of **S12iPr** was higher than that of **S12Pr**. This is due to the steric hindrance between surfactant molecules caused by the branched group of **S12iPr** [52].

### 2.2.3. Antimicrobial activities

The MICs of cationic surfactants are summarized in Table 2. The carbonate linkage of cationic surfactants may be hydrolyzed by bacterial enzyme to produce the corresponding 1-alkanol and quaternary-ammonium alcohol as shown in Figure 3. The antimicrobial activities of **HPr**

| Cationics | cmc (mM) | $\gamma_{cmc}$ (mN/m) |
|---|---|---|
| S10Pr | 3.5 | 34 |
| S12Pr | 0.41 | 34 |
| S14Pr | 0.19 | 33 |
| S12iPr | 1.3 | 35 |
| S12 | 5.4 | 35 |

**Table 1.** Surfactant properties of cationics in aqueous solution at 25 °C.

were also evaluated under the same conditions. Althogh the antimicrobial activities of **HPr** were low, **SnPr** showed high activities against some strains. Therefore the carbonate linkage of **SnPr** was not hydrolyzed under the tested conditions. It was also found that cationic surfactants containing both the carbonate linkage and *n*-dodecyl group showed higher antimicrobial activities, especially toward *Staphylococcus aureus* and *Escherichia coli*, when compared to those of the conventional cationics, **S12**. The **S12Pr** showed similar activities towards **S12iPr**. That is, no significant differences in the antimicrobial activities were observed by the branched methyl group.

| Strain | MIC (μg/mL) | | | | | |
|---|---|---|---|---|---|---|
| | S10Pr | S12Pr | S14Pr | S12iPr | S12 | HPr |
| *S. aureus* | 25 | 2.5 | 2.5 | 2.5 | 10 | >400 |
| *B. subtilis* | 50 | 2.5 | 2.5 | 5 | 10 | >400 |
| *M. luteus* | 100 | 5 | 2.5 | 2.5 | 25 | >400 |
| *E. coli* | 20 | 10 | >400 | 10 | 25 | >400 |
| *S. typhimurium* | 200 | 200 | >400 | 200 | 100 | >400 |
| *P. aeruginosa* | 100 | 100 | 100 | 400 | 50 | >400 |
| *C. albicans* | >400 | >400 | >400 | 400 | 200 | >400 |
| *S. cerevisiae* | 400 | 400 | 400 | 400 | 100 | >400 |
| *T. mentagrophytes* | 200 | 50 | 100 | 400 | 50 | 100 |
| *M. gypseum* | 25 | 10 | 10 | 5 | 25 | 200 |
| *P. chrysogenum* | 400 | 200 | 400 | 100 | 100 | >400 |
| *A. niger* | >400 | >400 | >400 | >400 | 100 | >400 |

**Table 2.** Antimicrobial activities of cationics and **SnPr**-derived **HPr**.

### 2.2.4. Biodegradabilities

The quick and complete biodegradation after use is one of the significant factors for the next-generation surfactants, because water-soluble surfactants are generally difficult to recover or recycle. The biodegradation of the carbonate-type cationics may first occur by hydrolysis due to environmental microbial enzymes as shown in Figure 3. If the quaternarized degradation products (**HX**), show higher biodegradabilities, the parent surfactants would be regarded as biodegradable.

Figure 4 shows the BOD-biodegradation (BOD/ThOD) for 28 days of cationic surfactants and their degradation products. **S10Pr** was readily biodegraded and showed a 60% BOD-biode-gradability, which is the criterion for an acceptable biodegradation. The biodegradability of the carbonate-type cationics gradually decreased with the increasing hydrocarbon chain length. This is explained by the lower water solubility of cationics containing a longer hydrophobic alkyl chain. It was also found that **S12X**-derived 1-dodecanol (**DD**) was rapidly biodegraded by activated sludge. On the other hand, the biodegradability of **S12Pr**-derived **HPr** was better than that of **S12iPr**-derived **HiPr**: therefore, **S12Pr** showed a better biodegrad-ability than **S12iPr**.
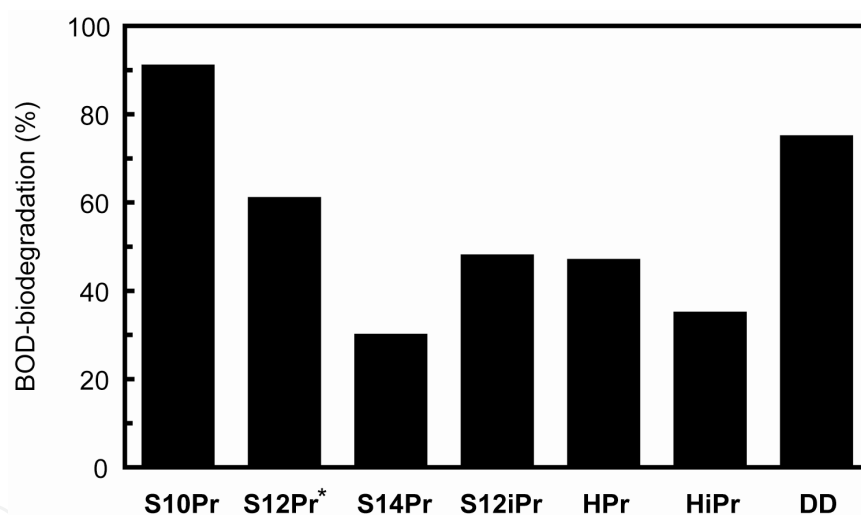


**Figure 4.** BOD-biodegradation of carbonate-type cationics and degradation intermediate (**HPr**, **HiPr** and **DD**) at 25 °C for 28 days (*45 days). Activated sludge: 30 ppm, carbonate-type cationics: ca. 40 ppm, **HPr** and **HiPr**: 57 ppm, **DD**: 38 ppm.

### 2.2.5. Enzymatic degradation and reproduction for chemical recycling

In the terms of green and sustainable chemistry, even water-soluble surfactants should be chemically recycled particularly in industrial fields. The **SnX** was hydrolyzed by lipase and accompanied by carbon dioxide evolution to produce the corresponding 1-alkanol and quaternary-ammonium alcohol, which could be converted into the initial cationics by the reaction with dialkyl carbonate. A lipase-catalyzed chemical recycling may become one of the green methods because lipase is a renewable catalyst with high catalytic activities [41,42].

The enzymatic degradation of **S12Pr** was carried out in toluene containing a small amount of water using immobilized lipase from *Candida antarctica* (CALB). The **S12Pr** was completely degraded at the carbonate linkage to produce **HPr** and **DD**. The **S12Pr** was regenerated in 69% yield by the lipase-catalyzed reaction of **HPr** and 1-dodecyl=phenyl=carbonate, which was prepared by the Et₃N-catalyzed reaction of **DD** and diphenyl carbonate (87% yield). The molecular structure of **S12Pr** was analyzed by ¹H- NMR. Based on these results, **S12Pr** showed a lipase-catalyzed chemical recyclability as shown in Figure 3.

## 2.3. Gemini-type cationics containing carbonate linkages as green surfactants

The syntheses and properties of gemini-type (dimeric) quaternary-ammonium cationics consisting of two hydrophobic alkyl chains and two quaternary-ammonium groups covalently attached through a linker moiety have been extensively studied by many researchers. Gemini-type cationics can be regarded as a next-generation green surfactant because they show higher functionalities that lead to a reduction in their consumption [32,33,53-55]. This saves carbon resources and production energies. However, there are few reports on the biodegradabilities of gemini-type cationics. It has been reported by Tehrani-Bagha *et al*. and Tatsumi *et al*. that gemini-type cationics containing ester linkages in the hydrophobic moiety were biodegraded by activated sludge [56-59]. However, ester linkages are generally labile to hydrolysis, particularly under alkaline conditions. More hydrolytically stable and biodegradable gemini-type cationics are, thus, needed. In this section, molecular design, synthesis and properties of gemini-type cationics containing carbonate linkages (**G12Pr** and **mG12Pr**) are described emphasizing the relations between carbonate linkage and biodegradation (Figure 5) [60,61].
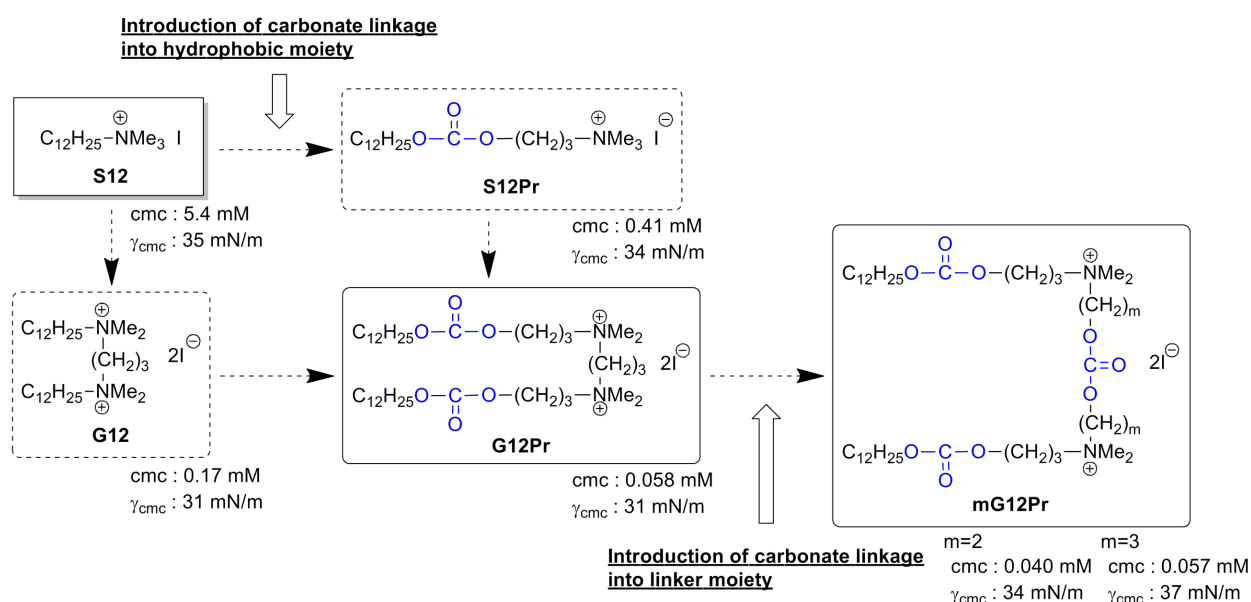


**Figure 5.** Design of biodegradable and chemically recyclable gemini-type cationics containing carbonate linkages.

## 2.3.1. Synthesis of gemini-type cationics containing carbonate linkages

Simultaneous gemini formation and quaternarization readily occurred at 80 ºC for 1 day by the reaction with **C12Pr** and 1,3-diiodopropane in dry acetonitrile to produce **G12Pr** containing carbonate linkages in the hydrophobic moiety in 86% yield as shown in Figure 6. The **mG12Pr** containing carbonate linkages both in hydrophobic and linker moieties was prepared at 80 ºC for 3 days by the reaction with **C12Pr** and α,ω-diiodide containing a carbonate linkage, which was prepared by the carbonate exchange reaction of diphenyl carbonate and iodoalkanol using K₂CO₃ (Figure 7). In a 1-day reaction, the yield of **2G12Pr** was only 20%. The maximum yield was 74% when the reaction time was 3 days. This could be due to the lower reactivity of the larger molecular size of di(iodoalkyl)carbonate.
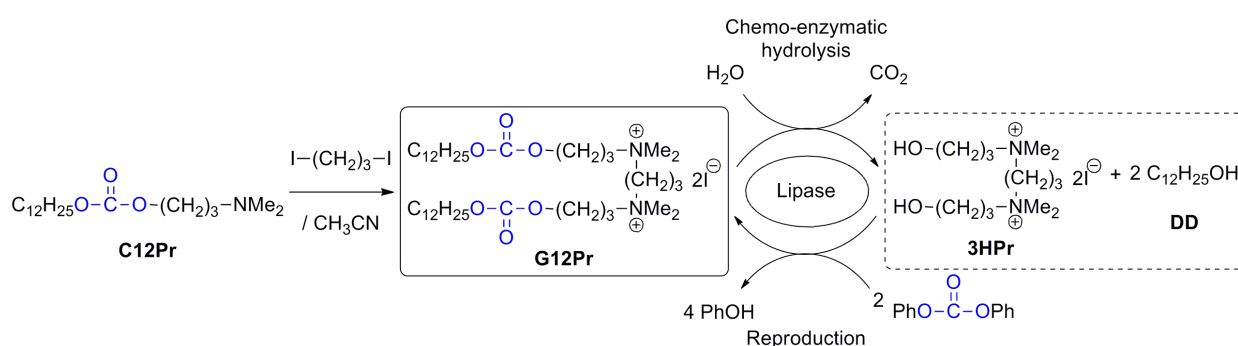


**Figure 6.** Synthesis and chemical recycling of **G12Pr** containing carbonate linkages in the hydrophobic moiety.
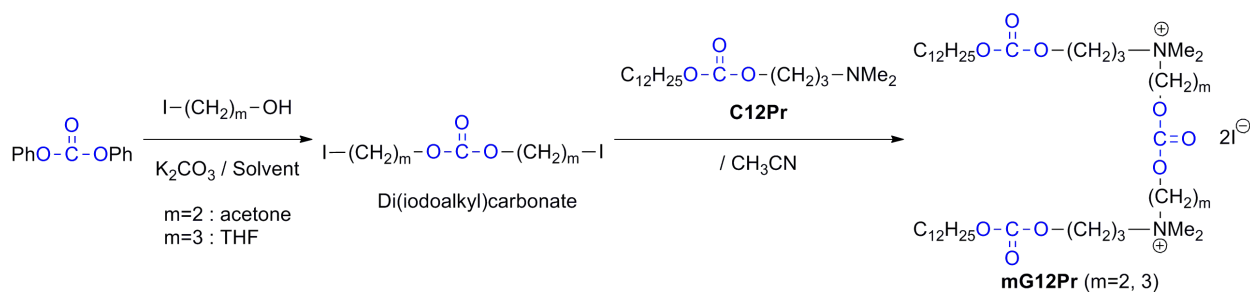


**Figure 7.** Synthesis of di(iodoalkyl)carbonate and **mG12Pr** containing carbonate linkages in both the linker and hydrophobic moieties.

## 2.3.2. Surfactant properties in aqueous solution

From the plots of surface tension *vs.* concentration of gemini-type cationics containing carbonate linkages in aqueous solution, the cmc and γ_cmc values are determined, and the results are shown in Figure 5. It was found that gemini-type cationics containing carbonate linkages showed lower cmc values compared to the corresponding linear-type cationics. These low cmc values of gemini-type surfactants were mainly caused by the simultaneous migration of the two alkyl chains, rather than one, from the aqueous phase to the micelle [32,33]. No significant

differences in the cmc values of the tested gemini-type cationics containing both the carbonate linkages and *n*-dodecyl groups were observed according to the linker structure. The $\gamma_{cmc}$ of **3G12Pr** was slightly higher than that of **2G12Pr**. This is due to the difference in the linker length between the quaternary-ammonium groups. That is, the **2G12Pr** having an ethoxycarbonyloxyethyl-type linker (m=2 in Figure 5) showed a lower $\gamma_{cmc}$ value when compared to the corresponding **3G12Pr** having a propoxycarbonyloxypropyl-type linker (m=3). The lower $\gamma_{cmc}$ of **2G12Pr** was due to the higher intra- and intermolecular hydrophobic interactions between the two hydrophobic alkyl chains of the gemini-type surfactant.

### 2.3.3. Enzymatic degradation and reproduction for chemical recycling

Gemini-type cationics containing carbonate linkages were hydrolyzed by lipase and accompanied by carbon dioxide evolution to produce the corresponding alcohol and quaternary-ammonium alkanol, which could be converted into the initial gemini-type cationics by the reaction with diphenyl carbonate. The enzymatic degradation of **G12Pr** was carried out in toluene containing a small amount of water using immobilized lipase CALB. The **G12Pr** was degraded at the carbonate linkage into the quaternary-ammonium alcohol (**3HPr**) and **DD** (92% yield). The **G12Pr** was regenerated by the reaction of **3HPr** and 1-dodecyl=phenyl=carbonate, which was prepared by the $Et_3N$-catalyzed reaction of **DD** and diphenyl carbonate (87% yield). That is, a mixture of **3HPr**, 1-dodecyl=phenyl=carbonate and immobilized lipase CALB was stirred in dry acetonitrile to obtain **G12Pr** in 30% yield (two-step). Based on these results, **G12Pr** showed chemical recyclability using lipase CALB (Figure 6).

### 2.3.4. Biodegradabilities

Figure 8 shows the BOD-biodegradation of gemini-type cationics and the **G12Pr**-derived degradation products, **3HPr** and **DD**. The conventional gemini-type cationics, **G12**, which had no hydrolytically cleavable moiety, showed no biodegradation by activated sludge. On the other hand, the **G12Pr** containing carbonate linkages showed higher biodegradability when compared to **G12**. It was found that the biodegradability was improved by the introduction of carbonate linkages into the hydrophobic moiety of the gemini-type cationics. However, the biodegradability of **G12Pr** was relatively low at around 25% after 28 days of incubation due to the relatively low biodegradability of **3HPr** as the primary biodegradation intermediate, i.e., 10% BOD-biodegradation after 28 days, as shown in Figure 8. On the other hand, **DD** as the degradation intermediate was readily biodegraded by activated sludge and its BOD-biodegradability exceeded 60% after 28 days. Based on these results, the low biodegradability of **G12Pr** was due to the low biodegradability of the degradation intermediate containing two quaternary-ammonium groups, **3HPr**.

The biodegradability of gemini-type cationics containing carbonate linkages was strongly affected by the linker structure. Though the **2G12Pr** was quickly biodegraded, the **3G12Pr** showed relatively low biodegradability (Figure 8). This is due to the difference in the primary degradation products. In order to compare the hydrolytic degradability of **2G12Pr** and **3G12Pr**, an accelerated hydrolytic degradation test was carried out by dissolving the gemini-type cationics in distilled water and stirring at a higher temperature of 60 ℃. The hydrolytic

degradation of **mG12Pr** was analyzed by comparing the $^1$H-NMR profiles of the reactants before and after the degradation, and the results are shown in Figure 9. Significant differences in the hydrolytic degradation were observed depending on whether the carbonate linkage was in the linker moiety or the hydrophobic moiety of the **2G12Pr** [Figure 9(a)]. Though the carbonate linkage in the linker moiety gradually hydrolyzed in water and only 18% remained after 9 h of reaction, 97% of the carbonate linkage in the hydrophobic moiety remained after 9 h of reaction. These results indicate that the carbonate linkage in the hydrophobic moiety was more stable against hydrolysis than the carbonate linkage in the linker moiety. Therefore, **2G12Pr** was readily hydrolyzed at the carbonate linkage in the linker moiety to produce the corresponding quaternary-ammonium alcohols having a similar molecular structure to the linear-type **S12Pr**, which exhibited a good biodegradability. On the other hand, both the carbonate linkages in the linker and hydrophobic moieties of **3G12Pr** were stable in water [Figure 9(b)]. It was found that the carbonate linkage in the linker moiety of **3G12Pr** was hydrolytically more stable than the carbonate linkage in the linker moiety of **2G12Pr**. Based on these results, **2G12Pr** was readily cleaved at the carbonate linkage in the linker moiety, indicating a higher degree of BOD-biodegradability than **3G12Pr**.
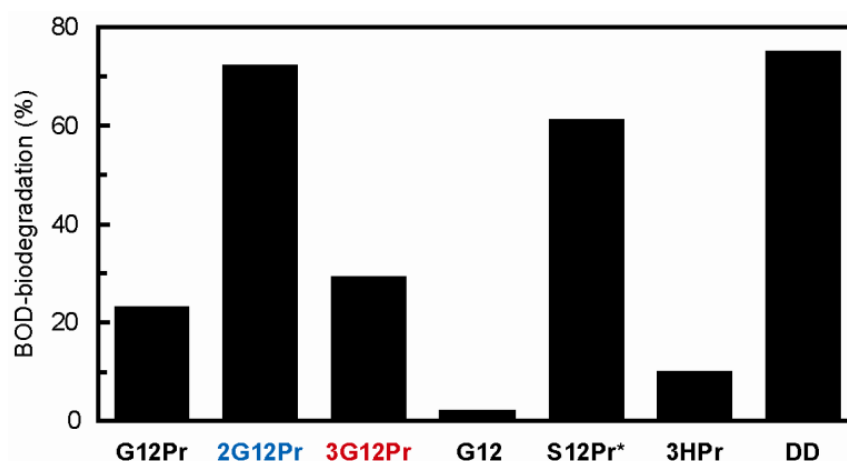


**Figure 8.** BOD-biodegradation of gemini-type cationics and **S12Pr** and **G12Pr**-derived degradation products, **3HPr** and **DD**, at 25 °C for 28 d (*45 d). Activated sludge: 30 ppm, cationics: ca. 40 ppm, **3HPr**: 52 ppm, **DD**: 38 ppm.

*2.3.5. Antimicrobial activities*

The gemini-type cationics were screened for their antimicrobial activities toward gram-positive and gram-negative bacterial strains and fungal strains based on the determination of their MICs. These results are shown in Table 3. It has been reported by some groups that cationic surfactants having multi-polar groups showed higher antimicrobial activities compared to the corresponding linear-type cationics because of the much higher charge density carried by multi-polar cationics [62,63]. However, **G12Pr** showed lower antimicrobial activities when compared to the corresponding linear-type **S12Pr**. The low antimicrobial activities of **G12Pr** could be due to the ready cleavability of the carbonate linkages of **G12Pr** by microbes forming surface-inactive molecules, **3HPr**, as shown in Figure 6. The **2G12Pr** containing
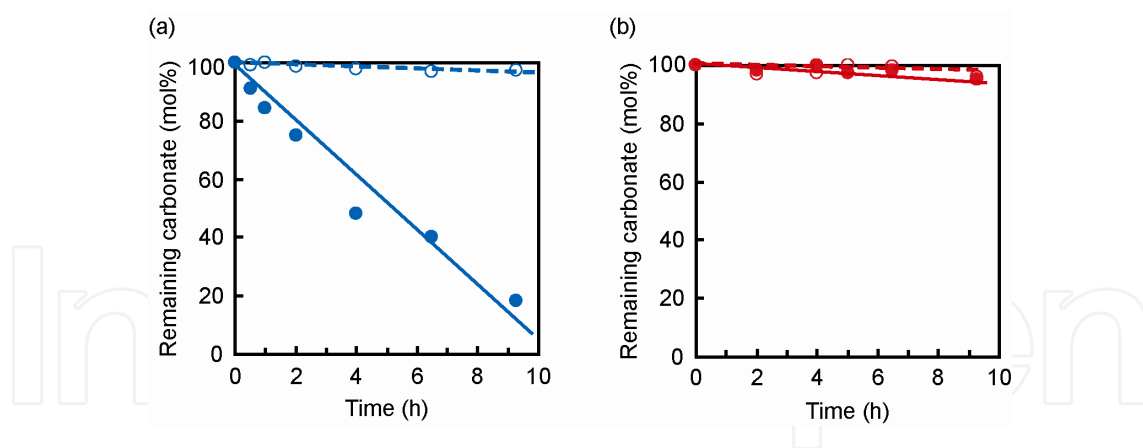
**Figure 9.** Time course of hydrolytic degradation of **mG12Pr** in distilled water at 60 °C. (a) Remaining carbonate in the hydrophobic moiety (○) and linker moiety (●) of **2G12Pr**. (b) Remaining carbonate in the hydrophobic moiety (○) and linker moiety (●) of **3G12Pr**. Concentration: 5 g/L.

carbonate linkages both in the hydrophobic and linker moieties showed higher antimicrobial activities than the **3G12Pr**. As discussed above, **2G12Pr** was readily hydrolyzed at the carbonate linkage in the linker moiety to produce the corresponding quaternary-ammonium alcohols having a similar molecular structure to the linear-type **S12Pr**, which exhibited strong antimicrobial activities. On the other hand, **3G12Pr** could be cleaved at the carbonate linkages in both the hydrophobic and linker moieties to produce the antimicrobially inactive alkyl chain-free fragments. Therefore the antimicrobial activities of **3G12Pr** were lower than those of **2G12Pr**.

| Strain | MIC (μg/mL) | | | | | |
|---|---|---|---|---|---|---|
| | G12Pr | 2G12Pr | 3G12Pr | G12 | S12Pr | 3HPr |
| *S. aureus* | 200 | 5 | 100 | 25 | 2.5 | >400 |
| *B. subtilis* | 200 | 10 | 50 | 10 | 2.5 | >400 |
| *M. luteus* | 400 | 25 | 100 | 25 | 5 | >400 |
| *E. coli* | 400 | 200 | 200 | 100 | 10 | >400 |
| *S. typhimurium* | >400 | 400 | >200 | 100 | 200 | >400 |
| *P. aeruginosa* | 400 | 200 | >200 | 100 | 100 | >400 |
| *C. albicans* | >400 | 400 | >200 | >400 | >400 | >400 |
| *S. cerevisiae* | >400 | 400 | >200 | >400 | 400 | >400 |
| *T. mentagrophytes* | >400 | 100 | >200 | 100 | 50 | 100 |
| *M. gypseum* | 400 | 25 | 100 | 50 | 10 | 200 |
| *P. chrysogenum* | >400 | 400 | >200 | 400 | 200 | >400 |
| *A. niger* | >400 | >400 | >200 | 400 | >400 | >400 |

**Table 3.** Antimicrobial activities of cationics and **G12Pr**-derived **3HPr**.

### 2.4. Chiral cationics containing carbonate linkages

The relationships between the physico-chemical properties and the stereochemistry of chiral surfactants derived from bio-based materials, such as sugars [64], amino acids [65,66], ascorbic acid [67] and succinic acid [68], have been studied by many researchers. Some of these showed better physico-chemical properties, such as surfactant properties and thermal properties, when compared to the corresponding stereochemically-mixed surfactants due to much stronger intermolecular interactions between the surfactant molecules. It is also known that the chirality of surfactants is a crucial issue in the interaction with a protein [69]. However, the syntheses of chiral surfactants are complicated, generating relatively low yields. Thus, a more facile synthetic route is required. Here, design, chemo-enzymatic synthesis, surface activities and biological properties of chiral cationics containing carbonate linkages [(R)-S12iPr and (S)-S12iPr] are described [70].

*2.4.1. Optical resolution of 1-(N,N-dimethylamino)-2-propanol using a lipase and synthesis of chiral cationics*

Optically active carbonate-type cationics were prepared using the (R)-alcohol or (S)-alcohol. The optical resolution of 1-(N,N-dimethylamino)-2-propanol using D-tartaric or L-tartaric acid has been reported by Chan *et al*. However, the yields of the optically active amino alcohols were relatively low at 7% [71]. Here, the optically active amino alcohol was prepared by the enantioselective transesterification of vinyl propionate and 1-(N,N-dimethylamino)-2-propanol using the lipase according to the method of Hull *et al*. as shown in Figure 10 [72].

First, the (R)-ester was prepared by the reaction of 1-(N,N-dimethylamino)-2-propanol (40 mmol) and vinyl propionate (20 mmol) using the lipase from *Burkholderia cepacia*, immobilized on diatomaceous (lipase PS-D). The (R)-ester was then hydrolyzed using sodium methoxide to obtain the (R)-alcohol. The two-step total yield of the (R)-alcohol was 43%. Next, the unreacted (S)-alcohol was collected by treatment with 1-(N,N-dimethylamino)-2-propanol (10 mmol) and vinyl propionate (10 mmol) in the presence of lipase PS-D. It is reported by Kazlauskas *et al*. that the (S)-secondary alcohol is the slower reacting enantiomer in lipase-catalyzed transesterifications [73]. The optical purity of the unreacted (S)-alcohol was 76% after 24 h of reaction. Thus, the recovered (S)-alcohol was further treated with vinyl propionate using lipase PS-D at room temperature for 24 h. Purification was carried out by silica gel column chromatography to obtain optically pure (S)-alcohol in 18% yield.

The intermediate was prepared by a two-step successive carbonate exchange reaction of diphenyl carbonate and 1-dodecanol in the presence of Et$_3$N followed by the reaction of the appropriate N,N-dimethylaminoalcohol as shown in Figure 3. The quaternarization of the N,N-dimethylamino group readily occurred by methyl iodide at room temperature. No significant differences in the yields of chiral intermediate and cationics were observed due to stereochemistry. However, the total yields were 28% for (R)-S12iPr and 10% for (S)-S12iPr, respectively.
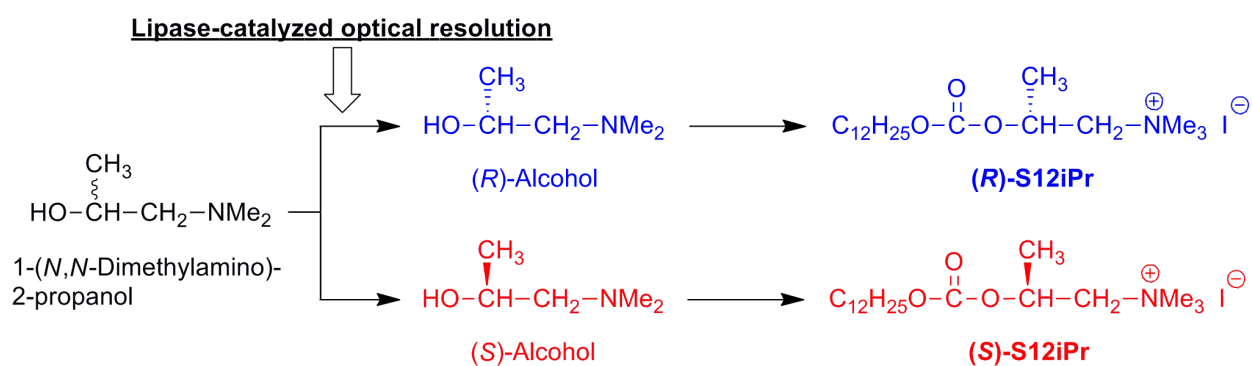
**Figure 10.** Preparation of chiral cationics by the lipase-catalyzed optical resolution of 1-(*N,N*-dimethylamino)-2-propanol.

### 2.4.2. Enantioselective hydrolysis of **S12iPr** using a lipase

To improve the yield of optically active cationics, the enantioselective hydrolysis of the **S12iPr** using lipase CALB was studied (Figure 11). Figure 12 shows the time course of the enzymatic hydrolysis of **(R)-S12iPr**, **(S)-S12iPr** and **S12iPr** in toluene containing a small amount of water. The enzymatic hydrolysis was strongly influenced by the stereochemistry of the cationics. Although the **(R)-S12iPr** was quickly hydrolyzed, the **(S)-S12iPr** was almost unchanged. The **S12iPr** was gradually hydrolyzed, and its hydrolysis rate exceeded 50% after 72 h. Therefore, it was hypothesized that the **(R)-S12iPr** would be preferentially hydrolyzed to produce the optically pure **(S)-S12iPr** as an unreacted material. Testing this hypothesis led to recovery the **(S)-S12iPr** in 27% yield (the theoretical yield was 50%) by the lipase-catalyzed hydrolysis of **S12iPr**.
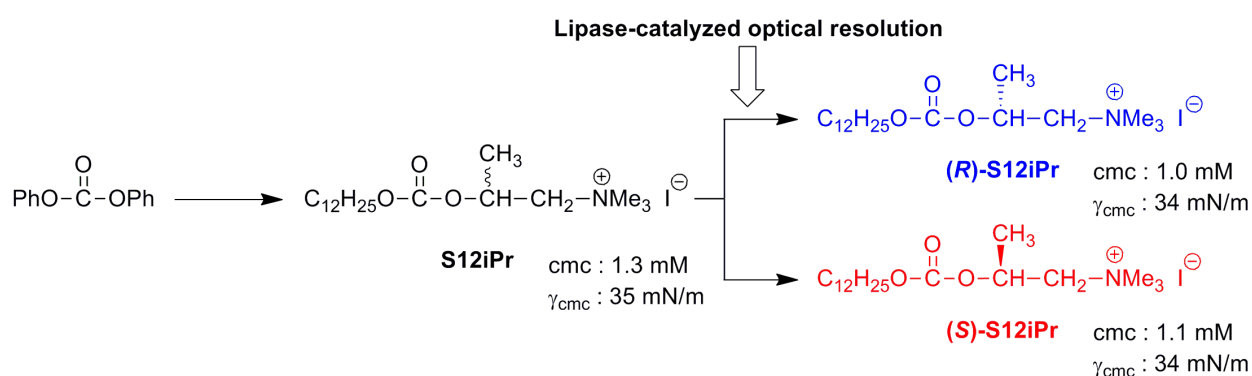
**Figure 11.** Preparation of chiral cationics by the lipase-catalyzed optical resolution of **S12iPr**.

### 2.4.3. Surfactant properties and antimicrobial activities

From the plots of surface tension *vs*. concentration curves of cationics in aqueous solution, the cmc and $\gamma_{cmc}$ values are determined and the results are shown in Figure 11. No significant differences in the surfactant properties were observed by the stereochemistry of the tested
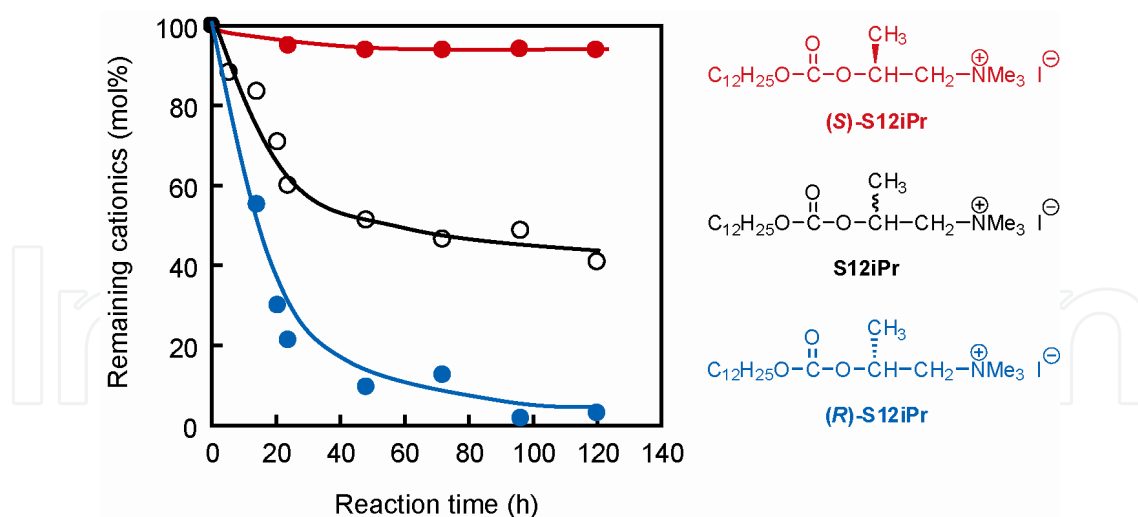
**Figure 12.** Time course of the enzymatic hydrolysis in toluene containing a small amount of water. Reaction conditions: cationics (10 mg) and 100 wt% immobilized lipase CALB (10 mg) were stirred in toluene (0.2 mL) and $H_2O$ (10 µL) at 65°C.

cationics. These results demonstrated that the optical activity in the hydrophobic moiety did not affect the surfactant properties. The surfactant properties of enantiomeric or diastereoisomeric surfactants show similar tendencies, i.e., those containing the chiral center in the hydrophobic moiety have been found to have similar properties to those of the corresponding stereochemically mixed surfactants [74,75].

Also, the cationics were screened for their antimicrobial activities toward gram-positive and gram-negative bacterial and fungal strains based on the determination of their MICs. No significant differences in the antimicrobial activities were observed due to the stereochemistry of the cationics.

### 2.4.4. Biodegradabilities

Figure 13 shows the BOD-biodegradability of the cationics and their degradation products [(**R**)-**HiPr**, (**S**)-**HiPr**, **HiPr** and **DD**]. The biodegradability was strongly affected by the stereochemistry of optically active cationics. Although the (**S**)-**S12iPr** was quickly biodegraded, (**R**)-**S12iPr** was biodegraded to a relatively lower extent at around 30%. This is due to both the hydrolyzability at the carbonate linkage and the biodegradability of the primary degradation products. To compare the non-enzymatic hydrolyzability of the chiral cationics, an accelerated hydrolytic degradation test was carried out by dissolving cationics in distilled water and keeping them at 60 °C for 48 h. It was found that both (**R**)-**S12iPr** and (**S**)-**S12iPr** were remained 95%. That is, no significant differences in the hydrolysis were observed due to the stereochemistry of the cationics. On the other hand, the biodegradability of the primary degradation product was affected by the stereochemistry. Though the (**S**)-**HiPr** derived from (**S**)-**S12iPr** was biodegraded by activated sludge, the (**R**)-**HiPr** derived from (**R**)-**S12iPr** was not biodegraded. This suggests that the better biodegradability of (**S**)-**S12iPr** was due to the higher biodegradability of (**S**)-**HiPr**. The **HiPr** was biodegraded, but at a lower rate than (**S**)-**HiPr**.

Therefore, the biodegradability of **S12iPr** was lower than **(S)-S12iPr**, but higher than **(R)-S12iPr**. As discussed above, the hydrolysis of **(R)-S12iPr** by lipase CALB was much higher than that of **(S)-S12iPr**. This implies that the microbial hydrolysis in the biodegradation of the cationics by the activated sludge exhibited (S)-specificity rather than (R)-specificity of lipase CALB.
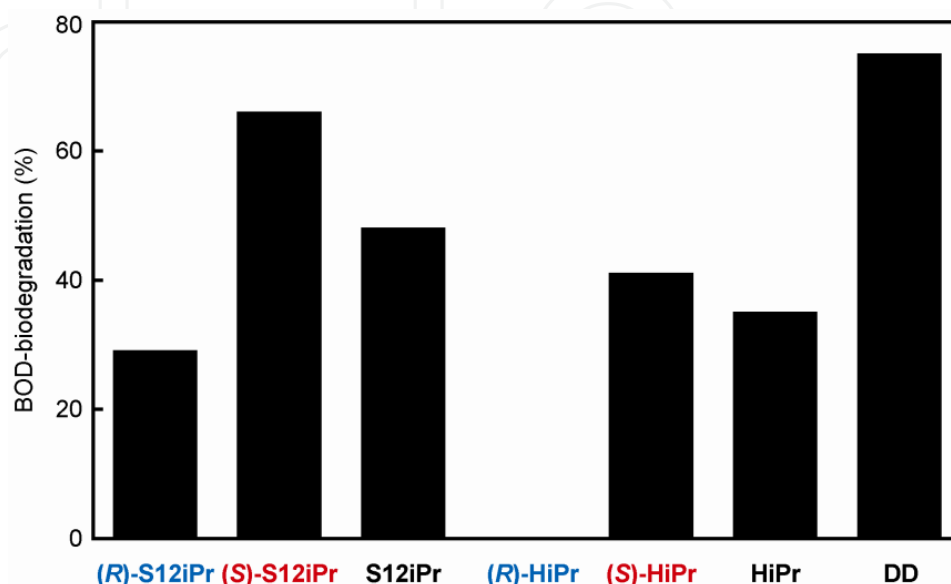


**Figure 13.** BOD-biodegradation of cationics and degradation intermediates at 25 °C for 28 d. Activated sludge: 30 ppm, cationics: ca. 40 ppm, **HiPr**: 57 ppm, **DD**: 38 ppm.

### 2.5. Green nonionics containing carbonate linkages

It has been reported that polyoxyethylene-type nonionic surfactant containing carbonate linkage was synthesized by the reaction of octanoyl chloroformate with tetra(ethylene glycol) [40]. More environmentally benign synthetic route without the use of halide is required in terms of green chemistry. Here, we describe synthesis of nonionics containing carbonate linkages (**mC-nEG**) using diphenyl carbonate as a green reagent in this section. We also report their properties and biodegradabilities [76].

#### 2.5.1. Synthesis of mC-nEG

A series of **mC-nEG** was prepared by the two-step carbonate exchange reaction of diphenyl carbonate and 1-alkanol followed by the reaction of poly(ethylene glycol) as shown in Figure 14. The **12C-Ph** was prepared by the carbonate exchange reaction of diphenyl carbonate and **DD** in the presence of Et$_3$N at 70°C for 15 h (87% yield). Then, **12C-4EG** was produced in 70% yield by the reaction of **12C-Ph** with tetra(ethylene glycol) in the presence of K$_2$CO$_3$ in acetone at room temperature for 24 h. In a similar procedure, a series of **mC-nEG** was prepared in 66-80% yield. On the other hand, the yield of **12C-4EG** was around 50% by the lipase-catalyzed synthesis of **12-Ph** and tetra(ethylene glycol). The slightly lower yield from the lipase-catalyzed

synthesis was due to the decarboxylation of the carbonate linkage of **12C-Ph** or **12C-4EG** during the reaction.
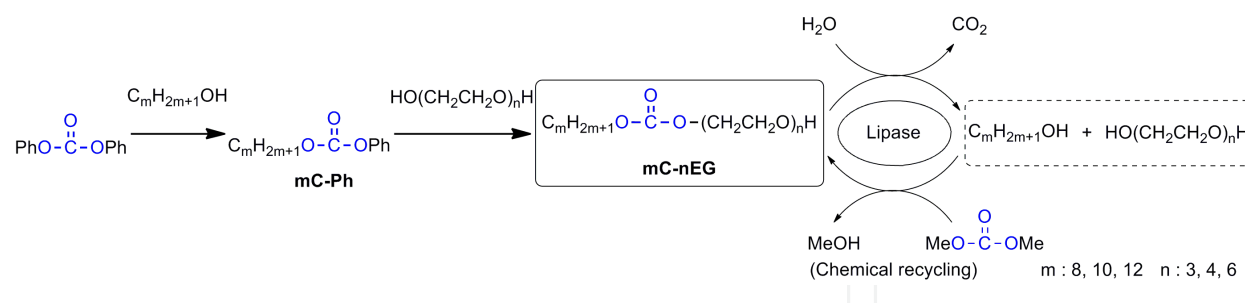


**Figure 14.** Synthesis and chemical recycling of **mC-nEG**.

### 2.5.2. Properties of *mC-nEG*

From the plots of surface tension *vs*. concentration curves of **mC-nEG**, their cmc and $\gamma_{cmc}$ values were determined and listed in Table 4. Table 4 also shows the surfactant properties of tetra(oxyethylene)dodecanoate (**12Es-4EG**) and dodecyl tetra(oxyethylene)ether (**12Et-4EG**) as a reference. It was found that the cmc values for the ester-type **12Es-4EG** and ether-type **12Et-4EG** were roughly the same. These results imply that the carbonyl and methylene groups provide similar contributions to the surfactant properties. Różycka-Roszak *et al.* and Menger *et al.* reported that the carbonyl groups of ester-type cationics can act as the hydrophobic moiety [77,78]. Also, the cmc of the carbonate-type **12C-4EG** was lower than the cmc of the ether-type **12Et-4EG**. These results indicate that the oxycarbonyl part of the carbonate linkage provides the same hydrophobic contribution as a methylene group. There existed a relationship between the alkyl chain length and the cmc, such that the addition of an extra methylene group decreased the cmc of the nonionics by a factor of three [40]. Carbonate-type nonionics having a tetra(oxyethylene) chain had similar $\gamma_{cmc}$ values. No significant differences in the $\gamma_{cmc}$ values were observed among the linkages between the hydrophobic and hydrophilic moieties (*cf.* **12C-4EG**, **12Es-4EG** and **12Et-4EG**). Among the tested carbonate-type nonionics containing an *n*-dodecyl group, the shorter oxyethylene chain tended to have a lower $\gamma_{cmc}$ value. The lowest $\gamma_{cmc}$ of **12C-3EG** is due to the highest intermolecular hydrophobic interactions between the surfactant molecules.

Next, we carried out a hydrolytic degradation test by dissolving **12C-4EG** and **12Es-4EG** in distilled water at 30°C. The hydrolytic degradation of the nonionics was measured by size exclusion chromatography. The carbonate linkage of **12C-4EG** was stable in water, and 99% of the surfactant remained after 21 d. On the other hand, the ester linkage of **12Es-4EG** gradually hydrolyzed in water, and only 35% remained after 21 d. Based on these results, it was confirmed that the carbonate-type **12C-4EG** was more stable in water than the ester-type **12Es-4EG**.

Also, the synthesized carbonate-type nonionics containing an *n*-dodecyl group were readily biodegraded by activated sludge. Their BOD-biodegradability exceeded 60% after a 28-d

| Surfactant | cmc (mM) | $\gamma_{cmc}$ (mN/m) |
|---|---|---|
| 8C-4EG | 1.6 | 30 |
| 10C-4EG | 0.17 | 30 |
| 12C-4EG | 0.019 | 30 |
| 12C-3EG | 0.015 | 29 |
| 12C-6EG | 0.029 | 32 |
| 12Es-4EG | 0.074 | 29 |
| 12Et-4EG | 0.055 | 29 |

**Table 4.** Surfactant properties of carbonate, ester and ether-type nonionics in aqueous solution at 25°C

incubation, which is a criterion for acceptable biodegradation. No significant differences in the biodegradabilities of carbonate-type surfactants were observed by the oxyethylene chain length.

Furthermore, the enzymatic degradation of **12C-4EG** was carried out in toluene containing a small amount of water using immobilized lipase CALB. The **12C-4EG** was completely degraded at the carbonate linkage to produce tetra(ethylene glycol) and **DD**. The **12C-4EG** was reproduced by the two-step lipase-catalyzed carbonate exchange reaction of dimethyl carbonate and **DD** followed by the reaction of tetra(ethylene glycol) in two-step total yield of 24%. Based on these results, **12C-4EG** showed a lipase-catalyzed chemical recyclability as shown in Figure 14.

# 3. Conclusion

The design, synthesis and properties of green surfactants containing carbonate linkages were summarized in this paper. It was clarified that the carbonate linkages in surfactant molecules are effective as biodegradable and chemically recyclable segments. In particular, it was found that the biodegradability and antimicrobial activity are improved by the introduction of a carbonate linkage into the linker moiety of gemini-type cationics. Therefore, we propose a novel biodegradable and chemically recyclable gemini-type cationics having both good surfactant properties and high antimicrobial activities. It was confirmed that the biodegradability was strongly affected by the stereochemistry of cationics. To the best of our knowledge, this is the first report on the relationship between the stereochemistry of surfactants and biodegradability. These carbonate-type surfactants may contribute to the sustainable development of society. It is also important that the emulsification processes using biodegradable green surfactants are clarified from the viewpoint of industrial fields, such as the washing, hygiene, medicine and food industries. For example, we have demonstrated that oil-in-water emulsion droplets exhibit autonomous locomotion in an aqueous solution containing an ester-type biodegradable surfactant [79]. Since the natural environment is an open system, the elucidation of emulsification processes in such a non-equilibrium state lies on the frontier of

surfactant research and development and is now needed for design the novel function of surfactants.

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