have been considered to be more polarizable than the corresponding normal amines having similar basicity, consequently they are expected to exhibit extra α-effect for the more polarizable thiol ester. Thus the result showing absence of polarizability effect on the α-effect in the present system is quite opposite to the generally known theory.

An explanation for the absent of polarizability effect on the α-effect is considered to be related with the rate determining step of the present reaction system. Since the formation of the tetrahedral intermediate is believed to be readily achieved for this mechanism[10], the nature of α-nucleophiles (*e.g.* low degree of solvation, ground-state destabilization, high polarizability) would not influence significantly the rate of intermediate formation. On the contrary, the presence of the nonbonding electrons adjacent to the reaction center for the α-effect amines is expected to stabilize the intermediate, while such a stabilization is absent for the normal amine system due to the absence of the nonbonding electrons. Since the stabilization of intermediate would also be considered to stabilize the transition-state for the α-amine system[11], the α-effect observed in the present reaction system is considered to originate from the stabilization of transition state. Thus the effect of polarizability is not considered to be important as the cause of the α-effect for the present system.

However more systematic studies would be required for a complete understanding of the present results. The kinetic study for IV and related esters are underway.

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Selective Transport of Amino Acids Derivatives through Calix[6]arene-Based Liquid Membrane

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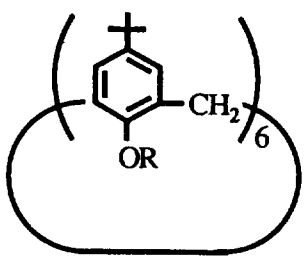
The understanding of selective recognition and transport of amino acids is one of the fundamental interests, in part from the point of view of mimicking the natural biological system.[1] Calixarene derivatives containing ester,[2] amide,[3] or ketone[4] groups have been reported to exhibit unique and selective ionophoric properties toward alkali and alkaline earth metal cations. In this study, the ionophoric property of calix[6]arene-based carrier was utilized for the separation of amino acids in carboxylate form, a common form of amino acids and proteins in physiological fluids.

Ethyl ester derivative of calix[6]arene was prepared by the reported procedure.[2] Transport experiment of N-benzoyl(Bz) derivative of amino acids was performed by using a U-tube (*i.d.* = 1.8 cm) through the chloroform liquid membrane containing a carrier, ethyl ester of calix[6]arene, at 25 °C. As summarized in Table 1, the liquid membrane containing the carrier exhibited the pronounced transport rate as well as selectivity toward amino acids, whereas no detectable amount of amino acid was transported without the carrier under the identical experimental conditions. It has been known that the transport efficiency strongly depends upon both the physicochemical nature of amino acids and the size of metal ions employed.[1] As can be seen from the Table 1, the transport rate for a given cation increased with increasing hydrophobicity of amino acids as follows; Bz-Gly<Bz-Ala<Bz-Val ≅ Bz-Trp<Bz-Phe. This trend is consistent with other results for the transport of amino acids and simple peptides.[5,6]



R = CH_2CO_2Et

Table 1. Transport of Amino Derivatives by Calix[6]arene Ester

Amino acid derivatives	Transport rate × 10^5 (mol/h/cm^2)				
	Li^+	Na^+	K^+	Cs^+	$(CH_3)_4N^+$
Bz-Gly	—	—	1.2	1.5	1.2
Bz-Ala	—	1.7	1.4	7.0	1.3
Bz-Val	—	1.1	4.1	10.9	1.7
Bz-Trp	1.0	1.0	4.2	9.9	2.4
Bz-Phe	1.9	5.4	23.0	38.6	9.0

Transport condition: Source phase; N-Bz amino acid (0.25 mmol), cation chloride (1.0 mmol) in 0.1 N LiOH (10 m*l*). Membrane; carrier (0.05 mmol) in $CHCl_3$ (15 m*l*). Receiving phase; deionized water (10 m*l*). The amount of transported amino acid was determined by UV spectrophotometry. (–): Not measurable.

For a given amino acid, the transport rate increases with increasing size of the metal cation employed ($Li^+ < Na^+ < K^+ < Cs^+$) besides tetramethylammonium (TMA) cation, which is known to act as a specific blocker for potassium channel in plasma membrane.[7] Although transport efficiency of amino acids with TMA cation is lower than those with K^+ and Cs^+, it is still significant. The preliminary extraction efficiency of N-Bz amino acids in dichloromethane containing the carrier, modelling partition of guests between the aqueous feed phase and the liquid membrane, demonstrated a similar trend with the transport rate obtained. Thus, the high transport efficiency for TMA cation is seemingly due to the specific interaction between TMA and the carrier.

The possible interaction between TMA and the carrier was confirmed by following observations. First, the CPK model demonstrates that TMA fits well to the pseudocavity of the carrier surrounded by oxygen atoms of phenyl ether and ester carbonyls. Secondly, in ^1H NMR titration of the picrate salt of TMA with the carrier in $CDCl_3$, methyl proton resonance of TMA was shifted upfield from 3.54 to 2.18 ppm with sharp break indicating 1:1 stoichiometry. Thirdly, in UV titration of TMA-picrate salt with carrier in THF, a large bathochromic shift from 368 to 382 nm was also observed. The λ_{max} of 368 nm of the uncomplexed picrate suggests the relative looseness of TMA-picrate ion pair in THF compared to those of the metal picrate salts (cf 357 nm for K^+ picrate[3] and 362 nm for Cs^+ picrate–)[8]. On the other hand, the λ_{max} of 382 nm denotes a typical solvent separated ion-pair state[8] of TMA-picrate salt, which manifests the complete encapsulation of TMA cation by carrier. All these observations cited above demonstrate the specific interaction between the carrier and TMA cation, which results in the significant transport behavior.

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Cyclization of β-Amino Acids to β-Lactams by Using Diethyl 2-(3-oxo-2,3,-dihydro-1,2-benzisosulfonazolyl)phosphonate

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A great deal of synthetic work has been already carried out in the formation of β-lactams from β-amino acids. One of the popular synthetic method for the β-lactam formation is based on the intramolecular cyclization of β-amino acids using coupling reagents.[1] Among various organophonsphorus coupling reagents currently available, triphenylphosphone-tetrahalomethane[2], triphenylphospline/2,2'-dipyridyl disulfide[3], bis[5'-nitro-2'-pyridyl]-2,2,2-trichloroethylphosphate[4], N,N'-bis[2-oxo-3-oxazolidinyl]phosphorodiamidic chloride[5], tris[2-oxo-3-oxazolinyl]phosphin oxide[6], and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate[7] are the most effective and reliable.

In connection with our on going research program directed toward the development of new synthetic methodoligies for the formation of β-lactam derivatives from β-amino acids, we have examined the β-lactam formation from β-amino acids using diethyl 2-(3-oxo-2,3-dihydro-1,2-benzisosulfonazolyl phosphonate (**DEBP** reagent, **3**). It has been reported that **DEBP** reagent in the effective coupling reagent for the synthesis of amides, esters, and thioesters.[8] On the other hand, there are no reports on the application DEBP reagent for β-lactam formation from β-amino acids. In this paper, we wish to report a new method for the preparation of β-lactam derivatives (**6**) from β-amino acids (**5**) by using **DEBP** reagent.

DEBP reagent was conveniently obtained by the reaction of diethyl chlorophosphate (**1**) with 3-oxo-2,3-dihydro-1,2-benzisosulfonazole (Saccharin, **2**), and triethylamine in dichloromethane at room temperature for 2 hr (eq. 1). Phsophorylation of **2** might be expected to give either the O- or N-phosphoryl product, because of its well-known tautomerism. The reaction of **1** with **2** in dichloromethane at 25 °C gave preferentially N-phosphoryl product **3**. The struc-