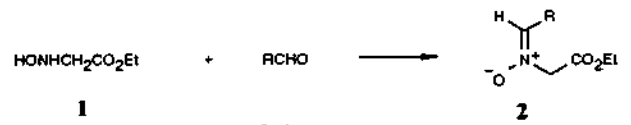
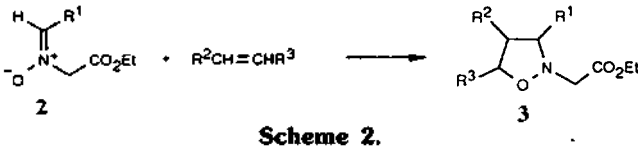


Scheme 1.

Table 1. Nitrones (2)[a] obtained from the condensation of *N*-hydroxyglycine ethyl ester with aldehydes

R	Temp. (℃)	Yield[b] (%)	R	Temp. (℃)	Yields[b] (%)
2a CH_3	20	89	**2g** *p*-HOC_6H_4	80	91
2b C_2H_5	20	90	**2h** *p*-$CH_3OC_6H_4$	80	91
2c C_3H_7	20	87	**2i** *p*-ClC_6H_4	80	95
2d $(CH_3)_2CH$	80	85	**2j** *p*-$NO_2C_6H_4$	80	100
2e $HOCH_2C(CH_3)_2$	80	90	**2k** *m*-$NO_2C_6H_4$	80	96
2f *o*-HOC_6H_4	80	99	**2l** *p*-$(CH_3)_2NC_6H_4$	80	85

[a]All the products gave satisfactory spectral and analytical data. [b]Isolated yields.



Scheme 2.

thylnitrones (**2**) could be synthesized easily by the condensation of *N*-hydroxyglycine ethyl ester (**1**) with aldehydes. Furthermore, the nitrones reacted with various alkenes very well to give 1,3-dipolar cycloadducts in good yields. In this communication we would like to report the results.

N-Hydroxyglycine ethyl ester (**1**) was synthesized following the method reported by the Herscheid[5]. Reduction of ethyl *N*-hydroxyiminoacetate was achieved with 5 eq. borane-pyridine complex in 54% yield. The condensation of *N*-hydroxyglycine ethyl ester with aldehydes at refluxing benzene gave the corresponding nitrones in good yields. Thus, refluxing of *N*-hydroxyglycine ethyl ester (**1**) (0.28 g, 2.35 mmol) with 2,2-dimethyl-3-hydroxypropanal (0.24 g, 2.35 mmol) in benzene (10 m*l*) for 3 hr under nitrogen gave the nitrone **2e** (0.43 g, yield 90%): ^{1}H-NMR ($CDCl_3$), δ, 1.22 (s, 1H), 1.28 (t, 3H), 3.57 (s, 2H), 4.23 (q, 2H), 4.50 (s, 2H), 4.85 (brs, 1H), 6.55 (s, 1H); IR (KBr), 3500, 1745, 1605, 1420, 1205 cm^{-1}; UV (95% EtOH), λ_{max} = 236 nm (ε = 36,000).

When acetaldehyde, propionaldehyde or butyraldehyde was stirred with *N*-hydroxyglycine ethyl ester in benzene in the presence of molecular seives 3 Å at room temperature, nitrones **2a**-**2c** were produced in good yields also. The nitrones obtained by these methods are summarized in Table 1.

Refluxing of the *N*-carbethoxymethylnitrones (**2**) with alkenes in benzene gave 1,3-cycloadducts (**3**) in good yields. Thus, refluxing of *N*-carbethoxymethly-C-ethylnitrone (**2b**) (0.159 g, 1.0 mmol) with diethyl fumarate (0.344 g, 2.00 mmol) in benzene (10 m*l*) for 8 hr under nitrogen gave a pale green liquid after removing solvent. It was purified by chromatography on silica gel using hexane-ethyl acetate (6 : 1) as an eluent to give 2-carbethoxymethyl-4,5-diethoxycarbonyl-3-ethylisoxazolidine (**3a**) (0.28 g, yield 84%): ^{1}H-NMR ($CDCl_3$), δ, 0.70-1.72 (m, 14H), 3.00-3.86 (m, 3H), 3.90-4.66 (m, 7H), 4.87 (d, J = 8.4 Hz, 1H); IR (neat), 2990, 1745, 1480, 1380, 1200, 1040 cm^{-1}. The isoxazolidine derivatives obtained by this method are summarized in Table 2.

Table 2. Isoxazolidine derivatives (3)[a] obtained from 1,3-dipolor cycloaddition of nitrones to alkenes

	R^1	R^2	R^3	Yield(%)[b]
3a	Et	CO_2Et	CO_2Et	84
3b	Pr	CO_2Et	CO_2Et	96
3c	Pr	H	CO_2Me	76
3d	Pr	CO_2Et	Me	82
3e	*p*-$NO_2C_6H_4$	H	CO_2Me	82
3f	*p*-$NO_2C_6H_4$	CO_2Me	H	10

[a]All the products gave satisfactory spectral and analytical data. [b]Isolated yields.

Currently, the transformation of the 1,3-dipolar cycloadducts to carbapenem skeletons is under investigation.

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Molecular Recognition of Butylamines by Calix [4]-crown Ethers

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Numerous attempts have been made to modify and endow unique binding characteristics to the crown ethers.[1] Of these,

Table 1. Extraction of Butylammonium Picrates[a]

Ligands	% Extraction of picrate				Selectivity, K_{ex}(*n*-Bu)/ K_{ex}(*tert*-Bu)
	n-Bu	*iso*-Bu	*sec*-Bu	*tert*-Bu	
1	2.0	2.2	1.4	1.0	2.66
2	20.3	13.8	9.3	3.1	9.70
DB18C6	23.8	18.5	18.5	17.8	1.56

[a]At 25℃, H_2O/CH_2Cl_2=5.0 mL/5.0 mL: [Ligand]=3.5×10^{-3} M, [$BuNH_3^+Pic^-$]=7.0×10^{-5} M.

Table 2. ^{1}H-NMR Induced Shifts (Δδ) of Calix-crown 2 upon Complexation with Butylammonium Guests[a]

Protons	Δδ(ppm)	
	n-Bu	*tert*-Bu
tert-Bu	−0.087	−0.024
tert-Bu	0.023	0.006
CH_2(eq)	0.084	0.015
H5	−0.140	−0.039
H4	−0.096	−0.034
H3	−0.054	−0.014
H2	−0.038	−0.020
H1	0.053	0.016
CH_2(ax)	−0.235	−0.057
ArH	−0.176	−0.032
OH	−0.329	−0.099
ArH	0.049	0.009

[a][2]=[$BuNH_3^+Pic^-$]=5.0×10^{-3} M in $CDCl_3$.

incorporation of subcyclic unit and intraannular functionality[2] to the crown ether backbone is one of the widely used approaches. Calixarenes attracted much interests as a versatile building block for the design of new biomimetic systems.[3] Recently, Ungaro and Reinhoudt have synthesized calix[4]-crown ethers and related derivatives which have calix[4] arene moiety as a subcyclic unit of crown ether, and characterized their ion-binding properties toward alkali and alkaline earth metal cations.[4,5] However, no studies have been performed for the binding properties of biologically important guests, such as biogenic amines.[6] Our interest in the structural characteristics of calix-crown led us to examine the possibility to achieve molecular recognition of butylamines[7] as a first step toward biologically important amine guests.

Calix[4]-crown ethers **1** and **2** were prepared by the reaction of *p-tert*-butylcalix[4]arene with appropriate oligoethylene glycol ditosylates according to the reported procedure of Ungaro *et al*[4]. The molecular recognition property of calix [4]-crowns toward varying structures of butylamines was investigated by the standard solvent extraction technique of alkylammonium picrates[8] into dichloromethane at 25℃ (Table 1). The stoichiometry of the host-guest complex was determined by the Job's method[9] and found to be 1 : 1 stoichiometric ratio by the UV and ^{1}H-NMR titration experiments. Calix [4]-crown-6 **2** exhibited pronounced discrimination behavior toward butylammonium picrates. The extraction efficiency decreases in the sequence *n*-Bu>*iso*-Bu>*sec*-Bu>*tert*-Bu, and

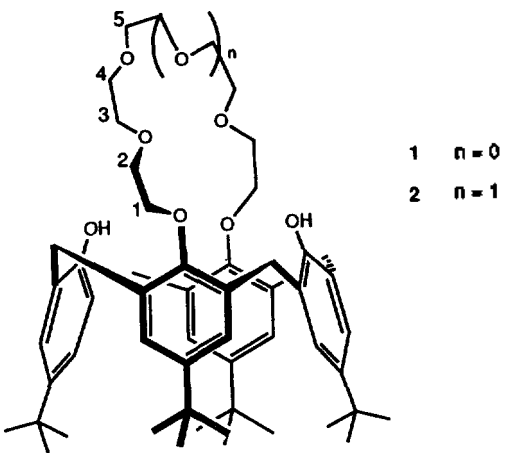

Figure 1. Structure and numbering scheme for calix[4]-crown ethers.

selectivity defined as the ratio of extraction constant K_{ex}[10], K_{ex}(*n*-Bu)/K_{ex}(*tert*-Bu), is as high as 9.70. This recognition behaviour might be originated from the lateral interaction between alkyl moiety of ammonium guests and the calix[4] arene backbone.

In contrast, calix[4]-crown-5 **1** has almost no selectivity and efficiency, which can be easily explained by the fact that the jaws of the crown ether ring is too small for the accommodation of the ammonium moiety of the guests.

The idea of utilizing the calixarene backbone as a recognition handle is well visualized by comparison with the result of dibenzo-18-crown-6(DB18C6). As can be seen from Table 1, DB18C6 exhibited somewhat higher efficiency but much inferior discrimination behavior (selectivity=1.56) than calix [4]-crown **2**, which might be due to the two dimensional nature of coronands.[11]

To elucidate the solution structure of the present host-guest complex, ^{1}H-NMR titration of **2** with *n*-butyl and *tert*-butylammonium picrate in $CDCl_3$ was performed[12] (Table 2). Upon interaction with one equivalent of *n*-butylammonium guest, the resonances of the host changed significantly. Particularly the resonances of the crown moiety moved to upfield (Δδ=−0.140 to 0.053), and the extent increased gradually from the methylene protons of phenolic ether to the central part of the crown moiety. However, the chemical shift of protons on phenolic ether carbon (C1) was relatively unchanged (Δδ=0.053), which might manifests that the guest interacts more strongly with the inner part ether oxygen atoms of crown ether. Another thing to be noted is the shift behavior of the bridging methylene protons. Higher field resonance (δ 3.281), which is ascribable to the equatorial protons,[13] shifted to downfield position (Δδ=0.084). And lower field one (δ 4.344), which is ascribable to the axial protons, moved to highfield position (Δδ=−0.235). The difference in chemical shift between axial and equatorial protons decreased from 1.063 ppm to 0.744 ppm, which suggests the adoption of more flattened cone conformation[14] upon complexation with *n*-butylammonium guest. The same phenomena were observed with the *tert*-butylammonium guest, although the changes in chemical shift are less pronounced, which can be easily explained by the lower binding strength of *tert*-Bu guest. All these observations strongly indicate that

Table 3. Competitive Transport of Butylammonium Perchlorates[a]

Carriers	Transport rates×10^5 mol/hr			
	n-Bu	*iso*-Bu	*sec*-Bu	*tert*-Bu
2	17.2	9.01	4.17	0.24
DB18C6	10.4	6.25	5.42	3.83

[a]Source Phase: Contains all four butylammonium perchlorates (each in 0.50 mmol/5.0 mL D_2O); membrane phase: carrier (0.05 mmol/15 mL $CDCl_3$); receiving phase: 5.0 mL D_2O. After 24 hrs of stirring the total transported guests were measured by Orion Ionalyzer 901 using a perchlorate ion-selective electrode and individual guests were determined by ^{1}H-NMR spectrometer (500 MHz), respectively.

the complexation occurs in the central part of crown periphery and significant conformational reorganization of the calixarene moiety was induced upon complexation with butylammonium guests.

To understand the molecular recognition properties of calix-crown ligands better, we performed competitive transport from the mixture containing all four butylammonium perchlorates through chloroform liquid membrane using U-tube at 25℃. After constant stirring of organic membrane layer for 24 hrs, the receiving phase was removed and the amount of transported butylammonium guests were determined by ^{1}H-NMR spectroscopy (Table 3). For the sake of detectability and convenience, deuterated solvents (D_2O and $CDCl_3$) were used for the constituents of liquid membrane. The transport efficiency of **2** for the varying structures of butylamine decreases in the order *n*-Bu>*iso*-Bu>*sec*-Bu≫*tert*-Bu. This order is in good agreement with the result of extraction experiments. Meanwhile the discrimination characteristics between *n*-Bu, *iso*-Bu and *sec*-Bu guests is moderate, the remarkably enhanced discrimination behavior between *n*-Bu and *tert*-Bu guests was observed. The selectivity in transport between *n*-butyl and *tert*-butylammonium salts is over 70-fold compared to the value of 2.70 for DB18C6.

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5-(π-*Endo*)-*exo* Vinyl Radical Cyclization Mediated by the Addition of Stannly Radicals to Triple Bonds

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Vinyl radical cyclization reactions can be subdivided into two classes; those in which the π-system of the vinyl radical is exocyclic to the ring formed and those in which it is endocyclic to the ring. These may be called as (*π-exo*) and (*π-endo*) type cyclizations.[1] Examples abound in each category when vinyl halides are used as substrates.[2,3] On the other hand, the usefulness of β-stannylvinyl radicals, formed by the addition of stannyl radicals to triple bonds, is manifested mainly by (*π-exo*) type cyclizations.[4] In each case, the reaction is initiated by the addition of a stannyl radical to the terminal carbon of the terminal triple bond. (*π-Endo*) type cyclizations of β-stannylvinyl radicals were used much less frequently,[4a] presumably due to the regioselectivity problem in reversible addition of stannyl radicals to internal triple bonds. We now wish to report here examples of (*π-endo*) cyclization of β-stannylvinyl radicals generated regioselectively from methoxycarbonyl-and trimethylsilyl-substituted alkynes.

The substrates **1a** and **1b** were converted into stannylcyclopentene derivatives **2a** and **2b** in reasonably good yields. The cyclization reactions are considered to proceed through the α-methoxycarbonyl-β-stannylvinyl radicals [A] in which the σ-vinyl radical (the semioccupied orbital is orthogonal