discontinued. After the reaction mixture had been purged with nitrogen, samples taken directly over the refluxing reaction mixture showed no detectable hydrocarbons in the reactor vessel. The gaseous hydrocarbon mixture was sampled and then analyzed by gas chromatography on Dowtherm (15%). The analytical method was found to be accurate upon preparing various mixtures of isobutane and *cis*-2-butene of known compositions in cyclohexane/ethyl Cellosolve/1-chlorobutane (1–5 M), separating the gaseous components by the method described above and gas chromatography.

The products from reactions of aryl halide pairs with alkali metals in **1** are benzene and toluene (nongaseous). The hydrocarbons were concentrated in the halide reaction mixture upon removing the ethyl Cellosolve by extraction with saturated sodium chloride solutions (3–5 extractions). The hydrocarbon ratios were determined by gas chromatography (20% SF-96 column) of the hydrocarbon/halide mixtures.

The nongaseous coupling products (Table I) were analyzed by a procedure identical with that used for benzene and toluene.

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Reactions of *N*-(Arylsulfonoxy)-*N*-benzylmethylamines with Sodium Methoxide in Methanol[1]

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Abstract: Reactions of *N*-(arylsulfonoxy)-*N*-benzylmethylamines (**1**) with MeONa in MeOH have been investigated. The eliminations are quantitative, producing only benzylidenemethylamines. The reactions are first order in substrate and first order in base, and an E2 mechanism is evident. Comparison of the rate data reveals that the arenesulfonates are better leaving groups than halogens in imine-forming eliminations. For eliminations from **1**, $\rho = 1.14$, $k_H/k_D = 3.6$, $\rho_{lg} = 1.30$, and $\beta_{lg} = -0.43$ have been calculated. Differences in the transition-state characters for imine-forming eliminations from $ArCH_2N(Cl)CH_3$ and **1** have been interpreted in terms of changes in the leaving-group propensities and base strength.

Extensive studies of olefin-forming β-elimination reactions have led to a qualitative understanding of the relationship between the structure of E2 transition state and changes in reactants and reaction conditions.[2,3a] Results from these studies indicate that the transition state shifts from central E2 to the E1cb borderline in the More O'Ferrall–Jencks reaction coordinate diagram as the β-phenyl substituent is made more electron withdrawing or the leaving group becomes poorer. In contrast, relatively little is known about factors that influence the shift of a central E2 transition state to the E1 borderline.

Earlier we reported that the reactions of *N*-chloro-*N*-benzylmethylamines with MeONa–MeOH proceeded via an E2-central transition state with appreciable C_β–H and N_α–Cl bond cleavage and significant double-bond character.[4-8] On the other hand, for reactions of *N*-(arylsulfonoxy)-*N*-benzylamines with benzylamine in MeOH, Hoffman and co-workers[9-12] found an E1-like transition state with extensive N_α–OSO_2Ar rupture, but limited C_β–H bond scission and carbon–nitrogen double-bond development. It appears that the transition-state differences for these two reactions may provide information regarding a shift in transition-state character from central E2 to the E1 borderline.

Table I. Rate Constants for Eliminations from $ArCH_2N(OSO_2Ar)CH_3$ Promoted by MeONa–MeOH[a]

entry	compd[b]	temp, °C	k_2,[c] $M^{-1}\,s^{-1}$
1	**1a**	25.0	1.98
2	**1a**	35.0	3.98
3	**1a**	45.0	7.68
4	**1b**	25.0	0.544
5	**1c**	25.0	1.49
6	**1d**	25.0	4.48
7	**1e**	25.0	5.44
8	**1f**	25.0	14.7
9	**1g**	25.0	0.439
10	**1h**	25.0	1.02
11	**1i**	25.0	3.64

[a] [MeONa] = 1.92×10^{-3} to 7.68×10^{-2} M. [b] [Substrate] = $(1.0\text{–}2.0) \times 10^{-4}$ M. [c] Estimated uncertainty, ±3%.

Hoffman suggested that the transition-state differences for these two reactions may be attributed to the large difference in the energies of N–Cl and N–OSO_2Ar bonds.[10] However, the validity of this interpretation is questionable because these two systems differ not only in the nature of the leaving group but also in the base strength and charge type. Recently, we reported that the

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[1] This research was supported by grants from the Korea Science and Engineering Foundation and the Korea Research Foundation.

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Table II. Leaving-Group Abilities of Cl, Br, and OSO_2Ar in Eliminations from $ArCH_2CH_2X$ and $ArCH_2N(X)CH_3$

	relative rate	
X	$ArCH_2CH_2X$[a]	$ArCH_2N(X)CH_3$[c]
Cl	1	1[d]
Br	60	16[d]
$OSO_2C_6H_4$-*p*-CH_3	6	24[e,f]
$OSO_2C_6H_4$-*m*-CF_3	26[b]	175[e]

[a] Reference 2b. Relative rate in reactions with EtONa in EtOH except as noted otherwise. [b] Estimated from ρ_{lg} for reactions with *t*-BuOK in *t*-BuOH. [c] Relative rate in reactions with MeONa in MeOH. [d] Reference 6. [e] This work. [f] Estimated from ρ_{lg}.

structure of imine-forming transition states changed only slightly with the variation of the leaving group from Cl to Br.[6,8] Assuming similar leaving-group propensities for bromide and arenesulfonate, the large differences in the transition-state structures between the MeONa-promoted eliminations from the *N*-bromoamines and the benzylamine-promoted eliminations from *N*-arenesulfonates were attributed to the change in base strength and charge type.[6] Here again the assumption remains to be verified.

In order to understand the transition-state differences for imine-forming eliminations wrought by changes in the leaving group and the base, it seems necessary to probe the influence of leaving-group variation from halogen to arenesulfonate as well as the change of the base from MeONa to $PhCH_2NH_2$. In this study we have investigated the reactions of *N*-(arylsulfonoxy)-*N*-benzylmethylamines (**1**) with MeONa–MeOH (eq 1). Thus,

$$\underset{\mathbf{1}}{XC_6H_4CL_2N(OSO_2C_6H_4Y)CH_3} + MeONa \xrightarrow{MeOH} \underset{\mathbf{2}}{XC_6H_4CL{=}NCH_3} \quad (1)$$

1a, X = H; Y = *m*-CF_3; L = H
b, X = H; Y = *m*-CF_3; L = D
c, X = *p*-CH_3; Y =*m*-CF_3; L = H
d, X = *p*-Cl; Y = *m*-CF_3; L = H
e, X = *m*-Br; Y = *m*-CF_3; L = H
f, X = *m*-NO_2; Y = *m*-CF_3; L = H
g, X = H; Y = H; L = H
h, X = H; Y = *p*-Cl; L = H
i, X = H; Y = *m*-NO_2; L = H

for the first time, the leaving-group abilities of Cl, Br, and arenesulfonates for imine-forming eliminations may be compared under the same conditions. The results of the kinetic studies depicted in eq 1 may now be compared with those for reactions of *N*-halo-*N*-benzylmethylamines with MeONa–MeOH and *N*-(arylsulfonoxy)-*N*-benzylamine with $PhCH_2NH_2$–MeOH to assess the factors that influence the change of the imine-forming transition state from E2-central to E1-like.

Results

N-(Arylsulfonoxy)-*N*-benzylmethylamines (**1**) were prepared in situ from the reactions of the corresponding benzylmethylamines with arylsulfonyl peroxides in EtOAc at −78 °C.[9] Reactions of **1** with MeONa–MeOH produced only benzylidenemethylamines (**2**). Eliminations were followed by monitoring the appearance of absorption at the λ_{max} for **2**. Excellent pseudo-first-order kinetic plots covering at least 2 half-lives were obtained. Plots of k_{obsd} vs [MeONa] gave straight lines passing through the origin. The slopes were the second-order rate constants. The k_2 values are summarized in Table I.

Relative rates of elimination from $ArCH_2N(X)CH_3$ compounds calculated from k_2 values determined in this study and those reported earlier are listed in Table II.

Rates of eliminations from **1a** promoted by MeONa–MeOH were measured at three temperatures spanning 30 °C. The Arrhenius plots were linear with excellent correlation. The calculated enthalpy of activation and entropy of activation are presented in Table III.

The influence of aryl substituents X and Y in **1** upon elimination rates correlated satisfactorily with the Hammett equation using σ values (Figure 1). A plot of log k_2 vs $pK_{lg}^{CH_3}$ values for the arenesulfonate leaving groups[12] was linear with excellent correlation. Hammett ρ, ρ_{lg}, and β_{lg} values are given in Table III.

Table III. Transition-State Parameters for Eliminations from $ArCH_2N(X)R$

	$ArCH_2N$-(Cl)CH_3[a]	$ArCH_2N$-(Br)CH_3[a]	$ArCH_2N$-(OSO_2Ar')CH_3[b]	$ArCH_2$-$NHOSO_2Ar'$[b,c]
base–solvent	MeONa–MeOH	MeONa–MeOH	MeONa–MeOH	$PhCH_2NH_2$–MeOH
ρ	1.73	1.60	1.14 ± 0.07	0.11
k_H/k_D	6.4	6.4	3.6	1.2
ρ_{lg}			1.30 ± 0.12	1.65[d]
β_{lg}			−0.43 ± 0.04	−0.55[e]
$\Delta H^{\ddagger}$, kcal/mol	14.2	14.4	12.2 ± 0.1	14.5
$\Delta S^{\ddagger}$, eu	−19.9	−13.7	−16.2 ± 0.1	−3.48

[a] Reference 6. [b] Ar′ = C_6H_4-*m*-CF_3. [c] Reference 10. [d] Ar = Ph. [e] Calculated from log k_2 and $pK_{lg}^{CH_3}$ values for arenesulfonate leaving groups.[12]

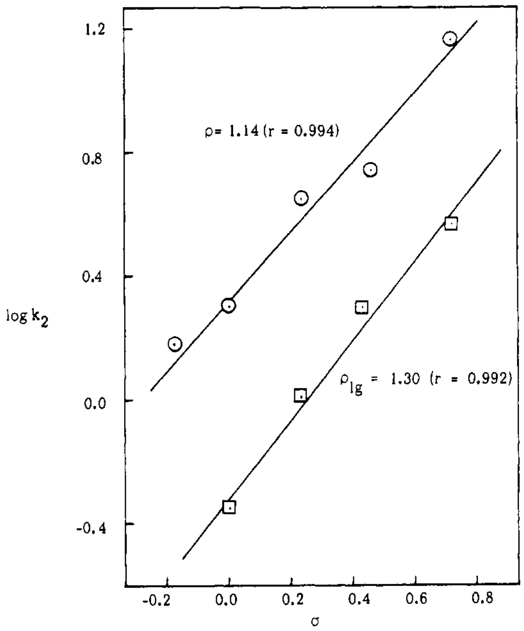

Figure 1. Hammett plots for eliminations from $XC_6H_5CH_2N(OSO_2C_6H_4$-*m*-$CF_3)CH_3$ (○) and $C_6H_5CH_2N(OSO_2C_6H_4Y)CH_3$ (□) promoted by MeONa in MeOH at 25.0 °C.

From the rate coefficients for eliminations from **1a** and its deuteriated analogue **1b**, the primary isotope effect value was calculated. The value is listed in Table III.

Discussion

Leaving-Group Abilities of Cl, Br, and OSO_2Ar in Imine-Forming Eliminations. The results of kinetic investigation and control experiments clearly establish that formation of **2** by MeONa-promoted elimination from **1** proceeds via an E2 mechanism. Since the plots of k_{obsd} vs [MeONa] were straight lines passing through the origin, solvolytic elimination is demonstrated to be unimportant. In addition, the observed second-order kinetics, first order in substrate and first order in base, rule out all but bimolecular reaction pathways. An E1cb mechanism is negated by the substantial values of k_H/k_D and β_{lg} (Table III).[2c]

Comparison of the leaving-group abilities of Cl, Br, and OSO_2Ar in elimination reactions (Table II) reveals that the arenesulfonates, which are poorer leaving groups than Br in alkene-forming eliminations, become better leaving groups in eliminations from $ArCH_2N(X)R$ compounds under comparable conditions. Thus the present result refutes our earlier assumption that Br and $OSO_2C_6H_4$-*m*-CF_3 might have similar leaving-group propensities in imine-forming eliminations.

Reversal in the order of leaving-group abilities of Br and OSO_2Ar in olefin- and imine-forming eliminations may in part be attributed to a bond strength effect. The C–OSO_2Ar bond is approximately 15 kcal/mol stronger than the C–Br bond,[10,13]

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whereas the N–OSO_2Ar bond is estimated to be much weaker than the N–Br bond.[14] Therefore, although the arenesulfonate is a poorer leaving group than Br in alkene-forming eliminations, it should become a better leaving group in elimination reactions that form carbon–nitrogen double bonds.

Effects of Leaving Group and Base Strength Variations upon the Imine-Forming Transition State. The transition-state parameters for MeONa-promoted eliminations from *N*-halo-*N*-benzylmethylamines and **1** (Table III) indicate that the structure of the transition state changes systematically when the leaving group is varied from Cl to Br to $OSO_2C_6H_4$-*m*-CF_3. As the leaving group is changed from Cl to better ones, the ρ value gradually decreases from 1.73 to 1.60 to 1.14. Thus, the carbanionic character at the β carbon is demonstrated to diminish in the transition state as the leaving group becomes better.

The primary deuterium isotope effect indicates the extent to which the benzylic proton is transferred to the base in the transition state. For eliminations from the *N*-halo-*N*-benzylmethylamines and **1**, the k_H/k_D value remains invariant and then decreases as the leaving group becomes better. Since the isotope effect has been demonstrated to increase to the maximum and then decrease as the degree of C_β–H bond rupture increases,[7,16] the present result may be interpreted as either a decrease or an increase in the extent of proton transfer in the transition state for a better leaving group. However, the former interpretation seems more compatible with the decreased ρ values.

The combined results reveal that the carbanionic character on the β carbon and the extent of proton transfer in the transition state decrease as the leaving group becomes better. The smaller change in transition-state structures produced by variation of the leaving group from Cl to Br correlates with the smaller difference in the leaving-group propensities between the halogens (Table II).

A similar change in the transition-state structure is also observed in eliminations from *N*-arenesulfonates with base strength variation.[17] Thus, the ρ and k_H/k_D values decrease and ρ_{lg} and $|\beta_{lg}|$ increase with the change of the base from MeONa to $PhCH_2NH_2$. Thus, the carbanionic character at the β carbon atom and the extent of C_β–H bond cleavage decrease, but the negative charge density on the leaving group and the degree of N_α–OSO_2Ar bond scission increase, in the transition state as the base becomes weaker.

The activation parameters for eliminations from *N*-halo-*N*-benzylmethylamines and **1** are included in Table III. The values of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ are similar for all of the systems, except for the large negative $\Delta S^\ddagger$ with the amine base. In no case is there a systematic change in $\Delta H^\ddagger$ values noted by Hoffman,[10] despite the large differences in leaving-group propensities and base strength. It seems extremely difficult to rationalize the transition-state differences only in terms of energies of the bonds involved in the reactions.

On the other hand, the present results can readily be interpreted by considering the relative effects of parallel and perpendicular motions in the reaction coordinate diagram.[19a,b] In previous work, it was established that the transition state for MeONa-promoted elimination from *N*-chloro-*N*-benzylmethylamine is unsymmetrical with approximately 40% proton transfer, a smaller extent of N_α–Cl bond cleavage, and limited carbanionic character[5-8] which would locate it somewhat toward the upper side from the center in the reaction coordinate diagram (Figure 2). A change to a better leaving group would decrease the energy of the lower edge of the diagram. This is expected to shift the transition state toward the reactant and the E1 intermediate. Assuming similar effects for parallel and perpendicular motion, the effect of change of the leaving group from Cl to Br to $OSO_2C_6H_4$-*m*-CF_3 would be to shift the transition state toward the right as indicated in the reaction coordinate diagram. This corresponds to less C_β–H bond cleavage and decreased carbanionic character in the transition state, as observed.

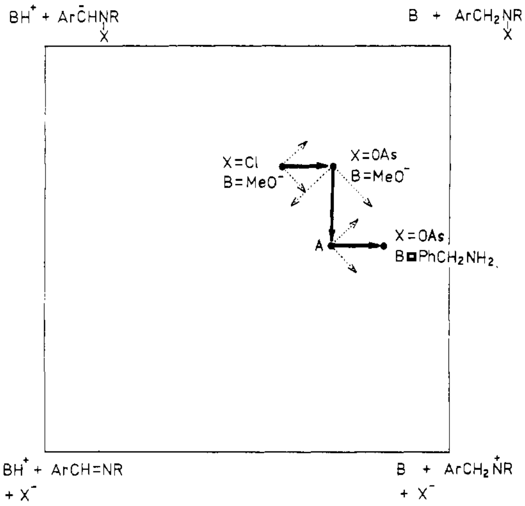

Figure 2. Reaction coordinate energy diagram for elimination reactions of $ArCH_2N(Cl)CH_3$ with MeONa–MeOH, $ArCH_2N(OAs)CH_3$ (OAs = $OSO_2C_6H_4$-*m*-CF_3) with MeONa–MeOH, and $ArCH_2NHOAs$ with $PhCH_2NH_2$–MeOH. The transition state for MeONa-promoted elimination from $ArCH_2N(Br)CH_3$, which should be located in between those for $ArCH_2N(Cl)CH_3$ and $ArCH_2N(OAs)CH_3$, is omitted. Effects of change in the leaving group and the base upon the position of the transition state are shown by solid lines.

Similarly, a change of the base from MeO^- to $PhCH_2NH_2$ would increase the energy of the left-hand edge of the reaction coordinate diagram. If one assumes that the leaving-group propensity of the arenesulfonate does not change with the base strength variation, this would shift the transition state directly downward to point A, increasing the extent of the cleavage of the bond to the leaving group (Figure 2). However, since the leaving ability of the $OSO_2C_6H_4$-*m*-CF_3 group would in fact increase as the degree of N_α–X bond ruputure increases due to its anion stabilizing ability,[20] the effect of the change of the base to a weaker one would be to further shift the transition state from A to the right (vide supra) as depicted in Figure 2. Thus the effect of the change in base from MeO^- to $PhCH_2NH_2$ would be to decrease the extent of C_β–H bond cleavage and carbanionic character at the β carbon, but to increase the N_α–OSO_2Ar bond scission and negative charge density on the leaving group. The prediction is borne out by the decrease in k_H/k_D and ρ values as well as the increase in ρ_{lg} and β_{lg} values.

Therefore it appears that the striking differences in the transition-state structures for MeONa-promoted elimination from $ArCH_3N(Cl)CH_3$ and $PhCH_2NH_2$-promoted elimination from $ArCH_2NHOSO_2Ar'$ result from changes in both the leaving-group propensity and the base strength. The present results clearly

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(14) Although the bond energy for H_2N–Br is not known, the bond energies for H_2N–OSO_2Ar, H_2N–Cl, and H_2N–I are estimated to be 32, 60, and 56 kcal/mol, respectively.[15,18] Therefore, the N–OSO_2Ar bond is expected to be much weaker than the N–Br bond.

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(17) A referee has pointed out that the compounds studied here are secondary amine derivatives while the work of Hoffman is for the primary amine system. There is indeed a possibility that compounds **1** might be more prone to undergo eliminations via an E2-central type of transition state due to the increased stability of the partial double bond character in the transition state by a Me substituent compared with the primary amine system. However, in view of the small differences in the transition-state structures noted in EtONa-promoted eliminations from $PhCH_2CH_2Br$ and $PhCH_2CH(Br)CH_3$,[2b,18] the influence of the change of the primary amine system to the secondary one upon the transition-state structure should be of minor importance.

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(19) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*; Harper and Row: New York, 1981: (a) pp 199–205, (b) pp 542–545, (c) pp 339–342.

(20) The k_{OTs}/k_{Br} ratios in nucleophilic substitution reactions increase with the increase in the extent of cleavage of the bond to the leaving group[19c,21] because the arenesulfonate ion can stablize a negative charge much more effectively than can bromide. Therefore, it seems reasonable to expect that the leaving-group ability of the arenesulfonate group should increase as the degree of N_α–X bond rupture increases in the imine-forming transition state.

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demonstrate that the E2-central transition state can be shifted toward the E1 borderline by utilizing a better leaving group and a weaker base.

Experimental Section

Reagents. Benzylidenemethylamines (**2**) and benzylmethylamines were available from previous work.[6-8] Arylsulfonyl peroxides were prepared by known methods.[22,23] *N*-(Arylsulfonoxy)-*N*-benzylmethylamines (**1**) were prepared from arylsulfonyl peroxides and benzylmethylamines in EtOAc according to the procedure of Hoffman.[9,10]

Kinetic Studies of Eliminations from 1. Base-promoted eliminations from **1** were followed by using a Cary 17D or Pye Unicam SP 500UV spectrophotometer with thermostated cuvette holders. Reactions were followed under pseudo-first-order conditions employing at least a tenfold excess of base. The solution of MeONa–MeOH (3.0 mL) was placed in a quartz cuvette and allowed to equilibrate in the cuvette compartment for 20 min. The cuvette was removed and 6 μL of the freshly prepared solution of **1** in EtOAc was injected with a microsyringe. The cuvette was quickly shaken and returned to the cuvette compartment. The increase of absorption at the λ_{max} for **2** with time was monitored. Plots of $-\ln [(A - A_t)/(A - A_0)]$ vs time were linear over at least 2 half-lives of the reaction. The slope was the pseudo-first-order rate constant, k_{obsd}. Values of k_{obsd} were determined at several base concentrations. Plots of k_{obsd} vs [MeONa] were straight lines passing through the origin. The second-order rate constants were obtained from the slope.

Product Studies of Eliminations from 1. For reactions of **1** with MeONa–MeOH, the yields of **2** determined by the absorbance of infinity samples from the kinetic reactions were 60–90% based upon the starting arylsulfonyl peroxide.

The product of reaction of **1g** with MeONa–MeOH was identified by using more concentrated solutions. *N*-(Phenylsulfonoxy)-*N*-benzylmethylamine (**1g**) was prepared by reaction of 0.37 mmol of phenylsulfonyl peroxide and 1.3 mmol of benzylmethylamine in 5 mL of EtOAc at −78 °C. The elimination reaction was conducted by adding 3.8 mL of 1.9 M MeONa–MeOH to the solution of **1g** and stirring for several hours at −78 °C. The solvent was removed in vacuo and the residue was extracted with diethyl ether. The diethyl ether extract was dried over $MgSO_4$, *m*-nitrotoluene (internal standard) was added, and the mixture was analyzed with a Hewlett-Packard Model HP 5890A gas chromatograph equipped with an HP 5970B mass-selective detector on a SE-54 cross-linked fused-silica capillary column (0.2 mm × 16 m) with temperature programming from 90–300 °C.[22] The products were benzaldehyde (9.4%), **2** (15.0%), benzylmethylamine (58.1%), and *N*-acetyl-*N*-benzylmethylamine (17.5%). Control experiments established that the benzaldehyde and *N*-acetyl-*N*-benzylmethylamine were the products from the hydrolysis of **2** and the reaction of benzylmethylamine with EtOAc, respectively, under the reaction conditions. Since an excess amount of benzylmethylamine was utilized in the preparation of **1**, the yield of elimination product (benzaldehyde + **2**) was calculated based on the starting peroxide. The yield was 85.6%.

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[24] We thank Dr. D. S. No at the Doping Control Center, Seoul, Korea, for performing the GC analysis.

Complexation of Neutral Molecules by Preorganized Macrocyclic Hosts[1]

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Contribution from the Laboratories of Organic Chemistry and Chemical Physics, University of Twente, 7500 AE Enschede, The Netherlands. *Received May 14, 1987*

Abstract: The complexation of functionalized hemispherands **1**–**4**, rigid ligands in which more than half of the binding sites are preorganized, with a neutral guest, viz. malononitrile, has been studied. The thermodynamic parameters of the complexation of these ligands with malononitrile were determined in $CDCl_3$ and C_6D_6. The binding free energies ($-\Delta G° = 1.2$–2.7 kcal/mol) were relatively favorable when compared with the stabilities of the corresponding complexes of flexible crown ethers. X-ray studies of the free (**2** and **4**) and complex (**1a**, **2**, and **4**) hemispherands revealed that both the methoxy oxygen atoms and the heteroatoms of the polyether chain are involved in the hydrogen bonding of the guest. The less organized ligand **1b** does not use the anisole binding sites of the terphenyl moiety according to X-ray studies. The ligands with the smallest conformational changes upon complexation generally form the strongest complexes. Molecular mechanics calculations of the free hosts confirm the different conformational flexibilities of the various macrocycles. Carbon-13 T_1 relaxation time studies of the free and complexed hemispherands clearly showed that the mobilities of the carbon-13 nuclei hardly decrease upon complexation, indicating that the host molecules are well preorganized.

In the past 2 decades many macrocyclic hosts capable of complexing cationic guests have been synthesized. Some guidelines can be derived by examining the thermodynamic parameters of the complex formation, and this has stimulated the rational design of host systems with defined properties. The so-called *principle of preorganization*, which states that "the smaller the changes in organization of host and guest, the stronger the binding", was first formulated by Cram.[2] The spherands,[3] a class of compounds with extremely selective and strong binding properties for Li^+ and Na^+ cations, are good examples of ligands based on this principle. However, the rather small cavities in these host molecules are not suited for the complexation of larger, polyfunctional guests. We are interested in the selective complexation of *neutral molecules*

[†] Laboratory of Organic Chemistry.

[‡] Laboratory of Chemical Physics.

[1] Part of this work appeared in preliminary form: van Eerden, J.; Grootenhuis, P. D. J.; Dijkstra, P. J.; van Staveren, C. J.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1986**, *51*, 3918–3920.

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