The failure to observe substantial amounts of deuterium in the five-membered ring of III would indicate that the *t*-BuOH involved in the nucleophilic addition to I must contain one of the original bridgehead protons. A substantial primary isotope effect in conjunction with a solvent cage during the protonation of I would account for preferential hydrogen incorporation into III. To date, we cannot completely factor the contribution due to solvent cage and isotope effects. However, the net result is that very little of the bulk deuterium of the solvent appears in III.

The fact that varying amounts of exchange of deuterium originally present at C_2 and C_3 of II occurred suggests that the eliminations are not concerted. Presumably, the intermediate cyclopentadienyl anion VII leading from VI to I can be reversably protonated on carbons other than the bridgehead, thus providing a mechanism for deuterium loss. Once again, a primary isotope effect would account for the failure to observe appreciable deuterium incorporation. Cram has commented on a similar experience in which deuterium was lost more easily to a protio solvent pool than a hydrogen to a deuterio one involving the base promoted isomerization of 1-protio- and 1-deuterio-1-methyl-3-*tert*-butylindenes.[16]

The conversion of II to III is summarized in Scheme I. Since labeling studies revealed loss of deuterium from C_2 and C_3, the anion VII must be reversably protonated at all ring positions. However, to maintain the stereochemical integrity discussed above, I once formed is converted to III in concerted reactions. If an anion of IV or V were formed, nonspecific protonation would obligate the C_2 deuterated triene to be converted to III which would contain deuterium at all four ring carbons. Moreover, the rearrangement of IV to V entails an unique instance of the σ asymmetry at C_6 distinguishing between two otherwise equivalent electrocyclic reactions.

Acknowledgment. We thank Research Corporation for financial support. We thank Dr. John McKelvey for assistance with the estimates of the acidity of I.

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Use of Circular Dichroism Measurements to Determine the Formation Constant of the Complex between an Optically Active Benzo-15-crown-5 and Sodium Ion

Sir:

Circular dichroism (CD) provides a powerful tool with which to study the conformation of molecules in solution.[1] An obviously essential condition is that the substrate under study be optically active. To facilitate interpretation of the CD data, the structure of the compound should be as simple as possible, and incorporate at least one chromophore which absorbs in an accessible region of the electronic spectrum, thereby exhibiting a measurable Cotton effect. Although conformational freedom makes unambiguous interpretation of CD data difficult in most cases, the number of possible conformers is conveniently restricted in the case of cyclic molecules. One subset of these, the cyclic polydentate molecules,[2] is especially interesting in that additional restrictions are imposed on the conformation of the molecule when it binds a cation. Blout[3] has recently reviewed much of the research on the cyclic peptide ionophores in this connection.

In our laboratory attention has been directed toward those macrocyclic polyethers termed "crowns" by their discoverer Pedersen.[4] They possess the advantage of a high degree of solvolytic stability due to the inertness of the ether bond, and can readily be designed with considerable symmetry, and to incorporate at least one aromatic ring. This in turn provides two useful absorption bands in the ultraviolet, each potentially leading to a Cotton effect in optically active derivatives. It is also helpful that the literature provides information about the preparation and characterization of a number of the parent (achiral) compounds.[5] In this communication we wish to report the synthesis of an optically active "15-crown-5", specifically (8*S*,12*S*)-8,12-dimethyl-5,6,8,9,11,12,14,15-octahydro[*b*]benzo-1,4,7,10,13-pentaoxacyclopentadecin (VII), and the use of circular dichroism measurements to calculate the equilibrium constant governing the formation of its complex with sodium ion (as the perchlorate) in spectrograde methanol at ambient temperature.

The polyether VII was synthesized as described in Scheme I; compound V is commercially available,[6] while the synthesis of I has been previously reported.[7] The elemental analysis of VII, its proton NMR, IR, and UV spectra were all consistent with the assigned structure. Its mass spectrum exhibited a strong parent ion peak at 296 mass units.

Figure 1 shows the CD spectra of a 1.51×10^{-4} M solution of VII in methanol, alone and in the presence of a 2000-fold molar (formal) excess of $NaClO_4$. (There were no significant differences between the latter curve, and those obtained with

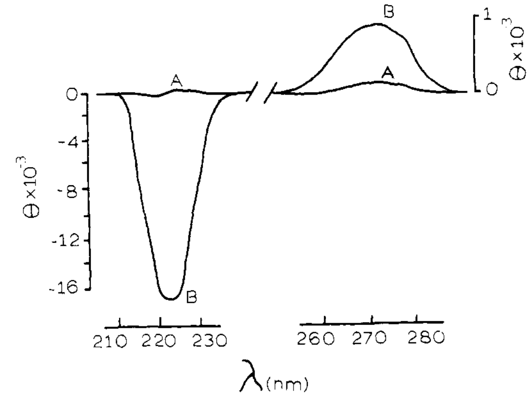


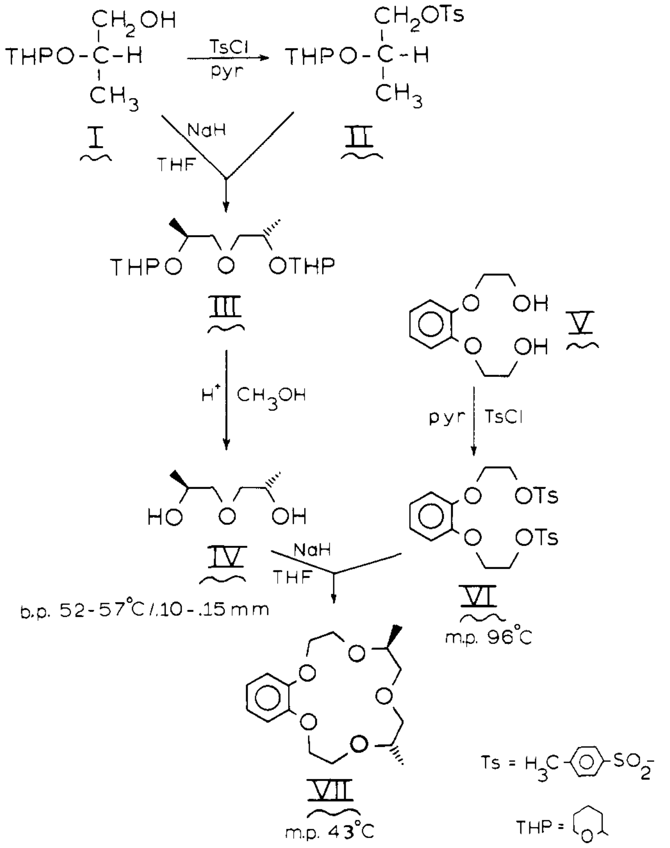
Figure 1. (A) CD spectrum of a 1.51×10^{-4} M solution of VII in anhydrous methanol, ambient temperature; JASCO ORD/CD/5, SS-20 modification. (B) Same as A except with addition of 250- to 2000-fold excess $NaClO_4$.

Table I

Cation/ crown ratio	222 nm		273 ± 1nm	
	θ = molar ellipticity	Log K	θ = molar ellipticity	Log K
200	-1.72×10^4		$+9.9 \times 10^2$	
1000	-1.72×10^4		$+9.3 \times 10^2$	
250	-1.72×10^4		$+9.9 \times 10^2$	
100	-1.58×10^4	2.88	$+9.3 \times 10^2$	2.93
54	-1.50×10^4	2.93	$+8.6 \times 10^2$	2.84
30	-1.26×10^4	2.79	$+7.9 \times 10^2$	2.88
20	-1.07×10^4	2.75	$+7.3 \times 10^2$	2.89
10	-8.1×10^3	2.79	$+5.2 \times 10^2$	2.75
7	-6.4×10^3	2.77	$+4.4 \times 10^2$	2.74
5	-5.0×10^3	2.76	$+3.8 \times 10^2$	2.77
4	-4.7×10^3	2.82	$+3.3 \times 10^2$	2.72
1	-1.7×10^3	2.91	$+3.0 \times 10^2$	3.31
0			$+1.3 \times 10^2$	
		2.82 ± 0.06		2.82 ± 0.07[a]

[a] Discounting value obtained for cation/crown = 1; see text.

Scheme I



a 250-fold excess of the same salt, or with correspondingly high concentrations of NaCl.) In Table I are given the molar ellipticities at the two spectral maxima for different ratios of sodium ion to macrocyclic ether, along with values for the formation constant K, calculated using the formula below which assumes a complex composed of one sodium ion and one ligand:

$$\frac{\theta_x - \theta_m}{(\theta_s - \theta_x)\left[C_s - C_m \dfrac{\theta_x - \theta_m}{\theta_s - \theta_m}\right]} = K$$

where θ = molar ellipticity, θ_x for sample, θ_m for macrocycle alone, θ_s for highest salt excess, C_m = *total* macrocycle concentration, and C_s = *total* cation concentration.

The existence in the crystalline state of 2:1 or "sandwich" complexes has been documented for the parent crown and potassium ion by Mallinson and Truter.[8] This type of behavior may account for the somewhat higher values of K obtained at the lower ratios of cation to macrocycle. (Naturally the CD signal to noise ratio is also lower where the bands are less intense.) The measured ellipticities at intermediate ratios were assumed to result from additive contributions of complex and free crown, values which can be found in the top and bottom lines of Table I. The ellipticity for the free macrocycle at 222 nm was taken as zero.

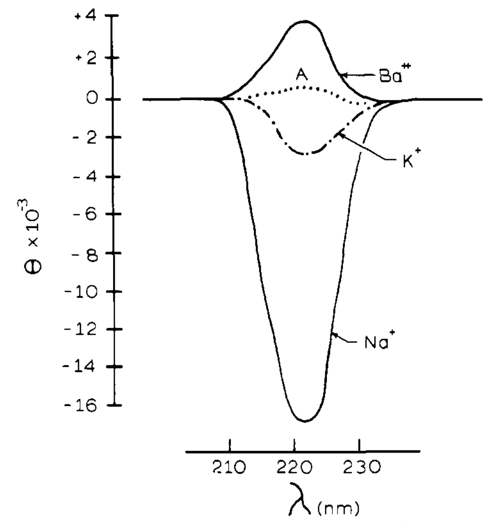


Figure 2. Low wavelength CD band of a 1.51×10^{-4} M solution of VII in anhydrous methanol, alone or in the presence of alkali and alkaline earth cations; (A) free crown or crown plus 100-fold excesses of $LiClO_4$, $RbClO_4$, $CsClO_4$, $Mg(ClO_4)_2$, or $Ca(ClO_4)_2{\cdot}6H_2O$. Other spectra in the presence of an excess of the cation indicated (as the perchlorate). The spectrum of the sodium ion complex is included for comparison.

A number of techniques have been utilized to determine the formation constants for crown ether complexes, including absorption spectroscopy, electrochemical procedures of various kinds, calorimetry, solvent-solvent distribution coefficients, and recently a competitive complexation technique based on ^{205}Tl NMR.[9] Many of these results have been tabulated and referenced in a review.[5b] Included among them is one report on the complex of benzo-15-crown-5 and sodium ion, based on calorimetric measurements in methanol-water mixtures. Extrapolation from these published figures to pure methanol leads to a value for K quite close to the average obtained for the dimethyl derivative in the present study.

Figure 2 illustrates the apparent limits of the response of the CD spectrum to large excesses of several cations, all as the perchlorates. Five of those employed can be seen to have had no measurable effect, in contrast to barium, potassium, and sodium; these in turn gave dramatically different results among themselves. Clearly, changes in cation size and charge profoundly influence the CD spectrum, probably by exerting different effects on the macrocycle's conformation, and thus on the relationship of chiral center (or region) to chromophore. We are continuing our studies in this area with considerable relish.

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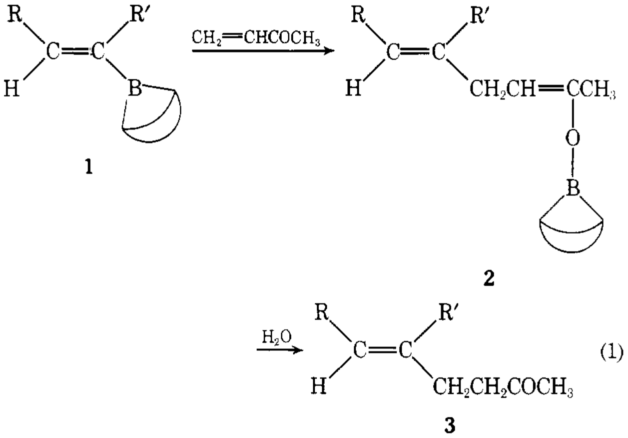
Conjugate Addition of *B*-Alkenyl-9-borabicyclo[3.3.1]nonanes to Methyl Vinyl Ketone. A Convenient Synthesis of γ,δ-Unsaturated Ketones

Sir:

B-Alkenyl-9-borabicyclo[3.3.1]nonanes (*B*-alkenyl-9-BBN) (**1**), readily prepared by the hydroboration of acetylenes with 9-BBN,[1] undergo a smooth 1,4-addition to methyl vinyl ketone (MVK) and related ketones in refluxing tetrahydrofuran. Hydrolysis of the initially formed enol borinate intermediate (**2**) provides the corresponding 4-alkenyl-2-butanones (**3**) (eq 1).



(1)

An important application for organocopper derivatives is their conjugate addition to α,β-enones.[2] Regretfully, easily polymerizable α,β-enones, such as methyl vinyl ketone, are not readily accommodated in this reaction.[3,4] However, the free radical addition of organoboranes to α,β-enones readily accommodates methyl vinyl ketone and related derivatives.[5]

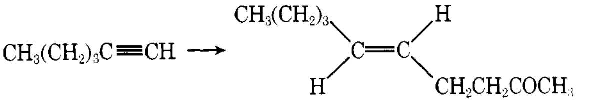
It would be highly desirable to extend such conjugate additions to the introduction of the vinyl group. Unfortunately, we have been unsuccessful in extending such conjugate additions to derivatives containing such groups. For example, our efforts to induce a free radical addition of *trans*-1-hexenyldiphenylborane to methyl vinyl ketone have failed.

Hooz and Layton were successful in achieving a conjugate addition with diisobutyl-*trans*-1-hexenylalane to α,β-enones.[4] However, even here they achieved their best yield, 67%, with stabilized substituted α,β-enones, such as benzalacetone. The optimum yield with methyl vinyl ketone was only 30%. They noted that the reaction proceeds satisfactorily only with cisoid enones (i.e., those ketones capable of adopting a cisoid conformation); transoid enones, such as 2-cyclohexenone, gave only complex mixtures not containing the desired product.

In the course of our efforts to achieve a free radical addition of vinylborane derivatives, we observed a new thermal reaction, one which led to the same product. It appears to be related to the reaction developed by Hooz and Layton in giving the same stereochemistry and in accommodating only cisoid enones. However, it gave greatly improved yields with methyl vinyl ketone. Since this particular derivative had proven to be a major stumbling block for previous workers, we decided to explore the range of applicability of various vinyl derivatives utilizing this labile reagent.

The conjugate addition reaction of alkenylboranes appears to be one of wide generality (Table I). A variety of structural modifications on the vinylic unit can be accommodated, including the presence of a heteroatom (eq 2-8).

We utilized *B*-1-hexenyl-9-BBN in a brief exploration of the applicability of this reaction to other α,β-enones (**11–14**). The cisoid ketones, **11** and **12**, reacted satisfactorily to give the



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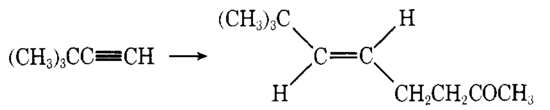

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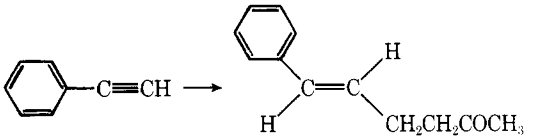

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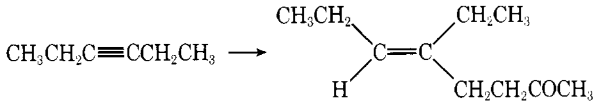

(5)

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Table I. Conversion of Alkynes into 4-Alkenyl-2-butanones by the Reaction of the Corresponding *B*-Alkenyl-9-BBN Derivatives with Methyl Vinyl Ketone

Alkyne	Product[a]	Yield,[b] %	n^{20}_{D}	Semicarbazone, mp (°C)
1-Hexyne[d]	*trans*-5-Decen-2-one (**4**)	87	1.4540	74.5–75.5
3,3-Dimethyl-1-butyne[e]	7,7-Dimethyl-*trans*-5-octen-2-one (**5**)	(85)[c]	1.4355	132.5–133.5
Phenylethyne[f]	*trans*-6-Phenyl-5-hexen-2-one (**6**)	93	1.5451	127–128
3-Hexyne[e]	5-Ethyl-*trans*-5-octen-2-one (**7**)	35	1.4460	129–130
1-Phenyl-1-propyne[f]	5-Methyl-*trans*-6-phenyl-5-hexen-2-one (**8**)	62	1.5400	144–145
5,5-Dimethyl-2-pentyne[e]	5,7,7-Trimethyl-*trans*-5-octen-2-one (**9**)	69	1.4456	133–134
5-Chloro-1-pentyne[g]	9-Chloro-*trans*-5-nonen-2-one (**10**)	66	1.4695	

[a] Satisfactory IR, ^{1}H NMR, and high resolution mass spectral data were obtained for all new compounds. [b] Yield by GLC analysis based on 9-BBN. [c] Isolated yield. [d] Distilled *B*-1-hexenyl-9-BBN was used. [e] A 10% excess of the alkyne was used. [f] A 50% excess of alkyne was used. [g] A 100% excess of alkyne was used. With straight-chain terminal alkynes, the excess is required to minimize double hydroboration.