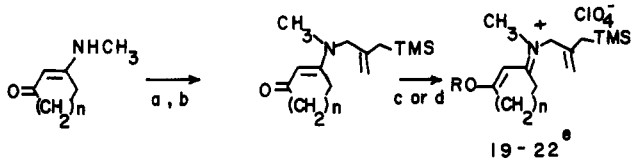
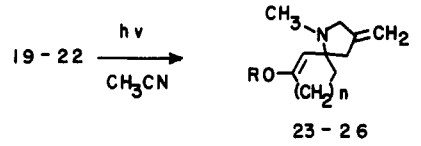
Scheme IV[a]



[a] (a) NaH, THF, (b) CH_2=C((CH_3)$_3$SiCH$_2$)CH_2OMs,[9] (c) CH_3I, $AgClO_4$, (d) $(CH_3)_3CCOCl$, $AgClO_4$, (e) yields for sequences are 89%, 85%, 90%, and 90%, respectively.

silylation of the intermediate diradical cation intermediates, and (3) provide by diradical cyclization pyrrolidine ring systems (17 and 18) with attractive exo- or endo-cyclic olefin functionality (Scheme III). The results from investigation of the *N*-[[(trimethylsilyl)methyl]allyl]iminium salts **19–22** illustrate the potential of strategies based on the sequence **15** → **17**. These salts are prepared in high yield by routes involving N-allylation followed by O-methylation or *tert*-butylacylation as shown in Scheme IV. Importantly, preparative irradiation of acetonitrile solutions of **19–22** with light $\lambda > 280$ nm provides, after basic workup and chromatography on Florisil or silica gel, excellent yields (84–95%)[10] of the spirocyclic amines **23–26** (Table I).



Several features of these *N*-[[(trimethylsilyl)methyl]-allyl]iminium salt photocyclization reactions require comment. The ease of formation and exceptionally high chemical efficiencies for reaction of these salts indicate that this methodology will be of general synthetic utility. The results also demonstrate the importance of the trialkylsilyl substituent in electron-transfer organic photochemical studies both as a mechanistic probe[2e] and as a group to control reaction efficiency and regiochemistry. Lastly, the photocyclization reactions described above, along with those related to **16** → **18**, which are under current investigation, appear to be applicable to our synthetic approaches to the harringtonine alkaloids.

Acknowledgment. These studies were supported by grants from the National Institutes of Health (GM-27251) and the National Science Foundation (CHE-09813).

Registry No. 3, 82444-46-0; **4**, 55998-74-8; **5**, 82444-48-2; **6**, 82444-50-6; **7**, 82444-52-8; **8**, 82444-54-0; **9** (n = 1; R = Me) isomer I, 82444-55-1; **9** (n = 1; R = Me) isomer II, 82444-56-2; **10** (n = 2; R = Me) isomer I, 82444-57-3; **10** (n = 2; R = Me) isomer II, 82444-58-4; **11** (n = 1; R = COBu-t) isomer I, 82444-73-3; **11** (n = 1; R = COBu-t) isomer II, 82456-18-6; **12** (n = 2; R = COBu-t) isomer I, 82444-74-4; **12** (n = 2; R = COBu-t) isomer II, 82444-75-5; **13**, 82456-19-7; **14**, 82444-60-8; **19**, 82444-62-0; **20**, 82444-64-2; **21**, 82444-66-4; **22**, 82444-68-6; **23**, 82444-69-7; **24**, 82444-70-0; **25**, 82444-71-1; **26**, 82444-72-2; $(CH_3)_2C$=$CHCH_2Br$, 870-63-3; CH_2=C($TMSCH_2$)-CH_2OMs, 74532-54-0; harringtonine, 26833-85-2.

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(10) The yields of these photocyclization reactions are near quantitative judged by ^{1}H NMR spectroscopic analysis of the crude photolysates. Thus, the less than quantitative isolated yields appear to be due to losses incurred during chromatographic purification of the photoproducts.

(11) The *N*-[[(trimethylsilyl)methyl]allyl]iminium perchlorates **19–23** resist fluoride ion induced ground-state cyclization to the corresponding spirocyclic amines. This is probably a result of the 5-endo-trig disfavored nature of the cyclization and the availability of intramolecular proton-transfer routes, which cause simple protodesilylation pathways to be preferred.

(12) A portion of these studies was conducted by TTH at The Department of Chemistry, Texas A&M University, College Station, TX, and in partial fulfillment of the requirement for the doctoral degree at that University.

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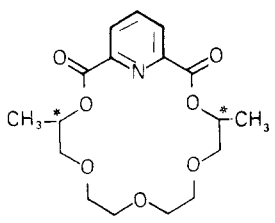
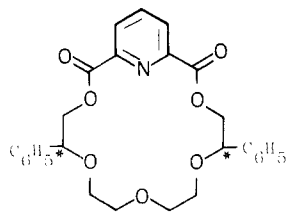
Chiral Recognition by the *S,S* and *R,R* Enantiomers of Dimethyldioxopyridino-18-crown-6 As Measured by Temperature-Dependent ^{1}H NMR Spectroscopy in CD_2Cl_2, Titration Calorimetry in CH_3OH at 25 °C, and Selective Crystallization[1a,b]

Summary: Enantiomeric recognition by the title compound for several chiral organic ammonium cations has been shown by independent experimental techniques. A similar chiral macrocycle, diphenyldioxopyridino-18-crown-6, does not show enantiomeric recognition for chiral organic ammonium cations when the same experimental methods are used.

Sir: The chiral macrocycles 1 and 2[2,3] have been syn-



1



2

thesized, and chiral recognition by the *S,S* enantiomer of 1 for several chiral alkylammonium cations has been shown by temperature-dependent ^{1}H NMR spectroscopy in CD_2Cl_2, titration calorimetry in CH_3OH, and selective crystallization. To the best of our knowledge, this is the first establishment of chiral recognition in a given system by more than one experimental method and the first report of log K, ΔH, and $T\Delta S$ values for a chiral-recognition reaction in a homogeneous solvent although Tundo and Fendler[4] have reported K values for similar reactions. Other workers[5-11] have also reported enantiomeric recog-

(1) (a) Presented in part at the National Meeting of the American Chemical Society, Las Vegas, NV, April 1982. (b) Contribution No. 275 from the Institute for Thermochemical Studies.

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(7) For example, see Sousa, L. R.; Sogah, D. Y. G.; Hoffman, D. H.; Cram, D. J. *J. Am. Chem. Soc.* **1978**, *100*, 4569–4576.

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Table I. Free Energies of Activation ($\Delta G_c^{\ddagger}$, kcal/mol) in CD_2Cl_2[a] for the Interaction of Chiral Macrocyclic Ligands with Chiral Alkylammonium Salts

ligand	value	(S)-NapEt[b]	(R)-NapEt[b]	(S)-PheOMe[b]	(R)-PheOMe[b]
(S,S)-1	T_c, °C	−19	12	−36	−25
	$\Delta G_c^{\ddagger}$	12.3	13.4	11.8	12.1
(R,R)-1	T_c, °C	13	−13	−25	−36
	$\Delta G_c^{\ddagger}$	13.4	12.5	12.1	11.8
(S,S)-2	T_c, °C			−28	−33
	$\Delta G_c^{\ddagger}$			11.6	11.5

[a] A Varian SC-300 spectrometer was used to record all ^1H NMR spectra. The CH_3 substituents on the macrocycle were used as the ^1H NMR probe. T_c = coalescence temperature. $\Delta G_c^{\ddagger}$ values are ±0.2. [b] NapEt = the hydrogen perchlorate salt of (R)- or (S)-α-(1-naphthyl)ethylamine; PheOMe = the hydrogen perchlorate salt of (R)- or (S)-methyl phenylalaninate.

Table II. Log K, ΔH (kcal/mol) and $T\Delta S$ (kcal/mol) Values[a] in CH_3OH at 25 °C for the Interaction of Chiral Macrocyclic Ligands with Chiral Alkylammonium Salts

ligand	value	(S)-NapEt[b]	(R)-NapEt[b]	(S)-AlaOMe[c]	(R)-AlaOMe[c]
(S,S)-1	ΔH	−6.32 ± 0.10	−6.59 ± 0.07	−3.48	−3.53 ± 0.05
	$T\Delta S$	−3.51	−3.22	−1.06	−0.78
	ΔG	−2.81	−3.37	−2.42	−2.75
	log K	2.06 ± 0.01	2.47 ± 0.01	1.78	2.02 ± 0.01
(S,S)-2	ΔH			−3.35 ± 0.15	−3.30 ± 0.09
	$T\Delta S$			−0.85	−0.79
	log K			1.84 ± 0.03	1.85 ± 0.03

[a] The average of three independent measurements.[14] Uncertainties are given as standard deviations. [b] See footnote b in Table I. [c] AlaOMe = the hydrogen chloride salt of (R)- or (S)-methyl alaninate.

nition that must reflect differences in the equilibrium constants for the reactions of the chiral ligand with the guest species. The relevant ^1H NMR and log K, ΔH, and $T\Delta S$ data are given in Tables I and II, respectively.

The formation of complexes by compounds **1** and **2** with alkylammonium salts is accompanied by significant chemical-shift changes in the ^1H NMR spectra as we reported also for the achiral pyridino ligands.[12] At low temperatures, the doublet attributed to the ring methyl substituents at δ 1.50 for the complex of (S,S)-**1** with (S)-methyl phenylalaninium perchlorate [(S)-PheOMe] separated into two sets of doublets. These peaks coalesced at −36 °C. The procedure of Sutherland[13] gives a free energy of activation ($\Delta G_c^{\ddagger}$) of 11.8 kcal/mol for the dissociation of the complex (Table I).

Variable-temperature ^1H NMR measurements demonstrated that (S,S)-**1** formed a kinetically more stable complex in CD_2Cl_2 with the perchlorate salt of (R)-α-(1-naphthyl)ethylamine[R-NapEt] than with the S form by 1.1 kcal/mol (Table I). This is one of the largest effects yet seen by the ^1H NMR method. That chiral recognition is involved in this result is confirmed by the fact that (R,R)-**1** formed a more stable complex with the salt of (S)-NapEt than with the salt of the R form, the difference in $\Delta G_c^{\ddagger}$ being 0.9 kcal/mol. The log K data[14] (Table II) show (S,S)-**1** to have a 2.5-fold preference in CH_3OH for the R form over the S form of NapEt, resulting in a $\Delta G°$ difference of 0.56 kcal/mol. Thus, this macrocycle exhibits chiral recognition through formation of both a thermodynamically and kinetically more stable (i.e., longer lived) complex with salts of (R)-NapEt than (S)-NapEt.

Similar results from the ^1H NMR experiments were found for the complex of **1** with the enantiomers of PheOMe although the effect is smaller. By analogy to the NapEt complexes with (S,S)-**1** and (R,R)-**1**, one would expect (R,R)-**1** to complex with (S)-PheOMe preferentially over (R)-PheOMe, and this does appear to be the case (Table I). The difference in $\Delta G_c^{\ddagger}$ found for the PheOMe isomers (0.3 kcal/mol) compared to that of the NapEt isomers (1.1 kcal/mol) may reflect greater steric effects in the larger NapEt species.

The log K data in Table II show that the (S,S)-**1** enantiomer has a nearly 2-fold preference for (R)-methyl alaninium chloride [(R)-AlaOMe] over (S)-AlaOMe, but (S,S)-**2** does not show chiral recognition for either enantiomer of AlaOMe. It was similarly found by the ^1H NMR procedure that (S,S)-**2** forms complexes of equal kinetic stability with (S)- or (R)-PheOMe. The absence of chiral recognition for alkylammonium salts by (S,S)-**2** is not unexpected even though the phenyl substituents in (S,S)-**2** are much larger than the methyl substituents of (S,S)-**1**. The phenyl substituents of **2** are further from the nitrogen binding site and are in the less rigid polyether portion of the macrocycle, while the methyl substituents of **1** are next to the rigid ester-pyridino groups. Comparison of log K values for complexation of the R and S forms of AlaOMe with (S,S)-**1** and (S,S)-**2** shows that steric effects due to the phenyl groups on (S,S)-**2** are comparable (log K values equal), but chiral recognition is absent. On the other hand, chiral recognition is evident in the (S,S)-**1** complexes (log K values differ by 0.24 log K unit). The correlation, if any, between steric factors and this difference in chiral recognition by (S,S)-**1** and (S,S)-**2** must await structure determinations on the complexes. Molecular models indicate that the smaller methyl groups may play a greater steric role than the phenyl groups.

Chiral recognition in the complexation of (S,S)-**1** with NapEt was also shown by a simple selective crystallization study. The chemical shift in the ^1H NMR spectrum for the complex of (S,S)-**1** with (R)-NapEt is slightly different than that for the complex with (S)-NapEt. The complex formed when 1 equiv of (S,S)-**1** was mixed with 2 equiv of racemic NapEt was found to contain 68% of the R and 32% of the S isomer of NapEt. A similar study was not completed for the complexes of (S,S)-**1** with AlaOMe and PheOMe since those complexes could not be crystallized.

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(14) For the details of this procedure, see Izatt, R. M.; Terry, R. E.; Nelson, D. P.; Chan, Y.; Eatough, D. J.; Bradshaw, J. S.; Hansen, L. D.; Christensen, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 7626–7630.

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Registry No. (*S,S*)-1, 82468-65-3; (*S,S*)-2, 80656-07-1; (*S*)-NapEt·$HClO_4$, 82431-48-9; (*R*)-NapEt·$HClO_4$, 82456-17-5; (*S*)-AlaOMe·HCl, 2491-20-5; (*R*)-AlaOMe·HCl, 14316-06-4.

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Preparation of Functionally Substituted Allenes from Methylacetylenes via Propargylic Lithium Alanate or Lithium Borate Intermediates

Summary: Propargylic lithium alanates or lithium borates react with allylic halides or with various carbonyl reagents in a highly regioselective manner to furnish 1,1-disubstituted allenes.

Sir: We herein report that addition of allylic halides or carbonyl reagents to readily accessible propargylic alanates or borates provides a convenient route to a variety of functionally substituted allenes. These are obtained in high yields and isomeric purities. Functionally substituted allenes are valuable synthetic intermediates and have been used as dienophiles in Diels–Alder reactions[1] and as substrates for 1,4-additions of organocuprates.[2]

Recently we have shown that propargylic boranes **1**, derived from lithium chloropropargylide and trialkylboranes, react with aldehydes to afford α-allenic alcohols (eq 1).[3] Unfortunately, attempts to develop this reaction

$$LiC{\equiv}CCH_2Cl \xrightarrow[-90 \rightarrow 25\ ^\circ C]{R_3B} RC{\equiv}CCH_2BR_2 \xrightarrow[2.\ [O]]{1.\ R'CHO} \underset{\mathbf{1}}{} \quad \begin{matrix} R \\ \diagdown \\ \quad C{=}C{=}CH_2 \\ \diagup \\ R'CHOH \end{matrix} \qquad (1)$$

into a general synthesis for functionally substituted allenes using carbon electrophiles other than aldehydes have not been successful. Thus, in a search for ways to circumvent the synthetic limitations attendant with the use of **1**, we have investigated the syntheses and reactions of the propargylic alanates **3** and borates **4**.

It has been well-established that conversion of triorganoalanes or triorganoboranes into the corresponding *ate* complexes results in an enhancement in their reactivity toward many electrophilic reagents.[4] In accord with this, we have now found that propargylic alanates and borates react readily with allylic halides[5] as well as with various carbonyl reagents. This provides the basis for an operationally simple procedure for preparing 1,1-disubstituted allenes bearing an α-functional group. Moreover, we have developed an efficient synthesis for the required organometallic *ate* complexes using the readily available 2-alkynes as precursors.

Metalation of 2-alkynes with *tert*-butyllithium in the presence of TMEDA (tetramethylethylenediamine) affords the corresponding lithium reagents **2** (eq 2).[6,7] Treatment

$$RC{\equiv}CCH_3 \xrightarrow[-78 \rightarrow 0\ ^\circ C]{t\text{-}C_4H_9Li,\ Et_2O\text{-}TMEDA} \underset{\mathbf{2}}{[RC{=}C{=}CH_2]^-Li^+} \xrightarrow{R_3'M} [RC{\equiv}CCH_2\bar{M}R'_3]Li^+ \qquad (2)$$

3, MR'_3 = $Al(i\text{-}C_4H_9)_3$
4, MR'_3 = $B\text{-}(sec\text{-}C_4H_9)_3$

of these with triisobutylalane or with tri-*sec*-butylborane furnishes the lithium alanates **3** or borates **4**, respectively.[8] The assignments of propargylic structures to **3** and **4** are based on IR and NMR data obtained from reaction mixtures containing these organometallic intermediates.

The propargylic moieties in **3** and **4** possess two potential nucleophilic sites. Attack of an electrophile "E" at the α carbon should afford a homopropargylic derivative, whereas attack at the γ carbon should produce, via bond transposition, an allenic compound (eq 3).[9]

$$[RC{\equiv}C{-}CH_2{-}MR'_3]Li^+ \xrightarrow[\gamma\ \text{attack}]{E} \begin{matrix} RC{\equiv}CCH_2E \\ \text{and} \\ \begin{matrix} R \\ \diagdown \\ \quad C{=}C{=}CH_2 \\ \diagup \\ E \end{matrix} \end{matrix} \qquad (3)$$

Treatment of the propargylic alanate **3** (R = n-C_4H_9) in ether at −78 °C with allyl bromide, prenyl bromide (1-bromo-3-methyl-2-butene), or (*Z*)-1-chloro-2-heptene followed by warming the reaction mixture to room temperature furnished, after hydrolytic workup, the corresponding allyl allenes **5** containing less than 4% of the α-coupling product **6** (eq 4).[10] Interestingly, substituting the n-butyl group on the γ carbon in **3** by the larger cyclohexyl group resulted in only a small increase in α prenylation (Table I). It is important to note that the structures of the allyl allenes derived from **3** and prenyl bromide or (*Z*)-1-chloro-2-heptene are consistent with a direct S_N2 attack on the electrophiles by the organometallic reagent.

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(5) The reactions of **3** and **4** with methyl iodide were too sluggish to be synthetically useful.
(6) (a) For alternative procedures for lithiation of methylacetylenes see: Klein, T. in "The Chemistry of Carbon–Carbon Triple Bonds"; Patai, L., Ed.; Wiley: New York, 1978; Vol. 1. (b) Despo, A. D.; Chin, S. K.; Flood, T.; Peterson, P. E. *J. Am. Chem. Soc.* **1980**, *102*, 5120.
(7) The organolithium reagents **2** exist as equilibrium mixtures of allenic and propargylic isomers.[6a]
(8) Reactions of the organolithium reagents **2** with diisobutylchloroalane or with dialkylchloroboranes provides an efficient synthesis for trigonal propargylic alanes and boranes, respectively. These, upon treatment with aldehydes, afford nearly exclusively the corresponding α-allenic alcohols. Zweifel, G.; Hahn, G.; Pearson, N. R., unpublished results.
(9) Although the following discussion focuses on the propargylic alanates and borates, it is conceivable that in certain cases the corresponding isomeric allenic organometallics may compete with **3** and **4** for the electrophile. The possibility that these species, in concentrations too low for spectroscopic detection, are in equilibrium with the thermodynamically favored propargylic organometallics **3** and **4** cannot be precluded.

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