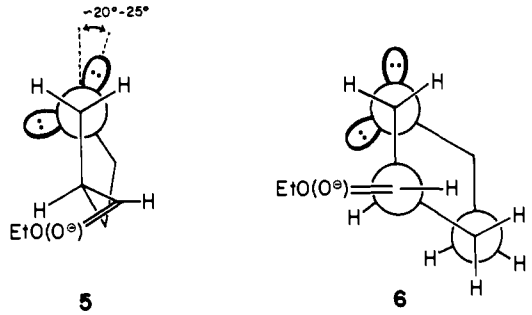
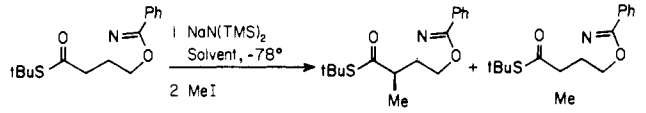


5 6

abilities of the Bu_3Sn group compared with the CH_2OR substituent.[11]

These results have obvious synthetic potential. For example, compound **7**, efficiently prepared from L-aspartic acid,[18] may be methylated through a chelated enolate (conformer B) in THF to favor isomer **8a**. Addition of HMPA, however, reverses the



Solvent	
THF (92% yield)	95:5
THF-HMPA (78% yield)	10:90

selectivity in favor of isomer **8b**, in agreement with a transition state modeled by conformer H.[19]

The results of this study supply experimental support for theoretical conclusions favoring the perpendicular transition states for electrophilic reactions of asymmetric π-systems.[1b-d,2b,c] These models also offer an explanation for the stereoselection observed in peracid epoxidations,[8,20] hydroborations,[1d,2c,8,21] halogenations,[22] oxymercurations,[23] osmylations,[2a,b,20a,24] and dipolar cycloadditions.[2b] Finally, by use of predictions from the transition-state model applied to our enolate alkylations, useful stereodirecting influences exerted by homoallylic substituents have been experimentally uncovered.[25] Recently, Houk and co-workers disclosed theoretical studies in agreement with this observation.[2c] Such predictions can be expected to lead to the rational design of new, highly selective transformations.

Acknowledgment is made to the National Institutes of Health for generous support of this work. We would also like to thank Professor Carl Trindle for helpful discussions during this study.

Registry No. (*E*)-EtOCOCH=CHCH$_3$, 623-70-1; (*E*)-EtOCOCH=CH(CH$_2$)$_2$OTBS, 94844-33-4; (*Z*)-EtOCOCH=CHCH$_3$, 6776-19-8; EtOCOCH$_2$CH(CH$_3$)CH$_2$OTBS, 94844-34-5; *t*-BuSCOCH$_2$CH(CH$_3$)CH$_2$OTBS, 94844-35-6; EtOCOCH$_2$CHCH$_2$OCH$_2$CH$_2$, 90113-46-5; EtOCOCH$_2$CHCH$_2$OCH$_2$CH$_2$CH$_2$, 94844-36-7; (*E*)-EtOCOCH=CHCH$_2$OTBS, 94844-37-8; EtOCOCH(CH$_3$)CH(CH$_3$)SnBu$_3$ (isomer 1), 94844-38-9; EtOCOCH(CH$_3$)CH(CH$_3$)SnBu$_3$ (isomer 2), 94844-39-0; EtOCOCH(CH$_3$)CH(SnBu$_3$)CH$_2$CH$_2$OTBS (isomer 1), 94844-41-4; EtOCOCH(CH$_3$)CH(SnBu$_3$)CH$_2$CH$_2$OTBS (isomer 2), 94844-40-3; EtOCOCH(CH$_3$)CH(CH$_3$)SiMe$_2$Ph (isomer 1), 89882-25-7; EtOCOCH(CH$_3$)CH(CH$_3$)SiMe$_2$Ph (isomer 2), 89882-22-4; EtOCOCH(CH$_3$)CH(CH$_3$)CH$_2$OTBS (isomer 1), 94844-42-5; EtOCOCH(CH$_3$)CH(CH$_3$)CH$_2$OTBS (isomer 2), 94844-43-6; *t*-BuSCOCH(CH$_3$)CH(CH$_3$)CH$_2$OTBS (isomer 1), 94844-44-7; *t*-BuSCOCH(CH$_3$)CH(CH$_3$)CH$_2$OTBS (isomer 2), 94844-45-8; EtOCOCH(CH$_3$)CHCH$_2$OCH$_2$CH$_2$ (isomer 1), 94844-46-9; EtOCOCH(CH$_3$)CHCH$_2$OCH$_2$CH$_2$ (isomer 2), 94844-47-0; EtOCOCH(CH$_3$)CHCH$_2$OCH$_2$CH$_2$CH$_2$ (isomer 1), 94844-48-1; EtOCOCH(CH$_3$)CHCH$_2$OCH$_2$CH$_2$CH$_2$ (isomer 2), 94844-49-2; EtOCOCH(CH$_3$)CH(SnBu$_3$)CH$_2$OTBS (isomer 1), 94844-50-5; EtOCOCH(CH$_3$)CH(SnBu$_3$)CH$_2$OTBS (isomer 2), 94844-51-6.

(18) This has been prepared by a route analogous to that previously reported: McGarvey, G. J.; Hiner, R. N.; Matsubara, Y.; Oh, T. *Tetrahedron Lett.* **1983**, 2733. Details will be disclosed at a later date.

(19) This result argues against a chelated enolate in the methylation described in entry 8 of Table I.

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(25) This effect may be an important contributor in other reactions.[2c,20,24]

Effect of Temperature on the Transport Capabilities of Some Common Ionophores

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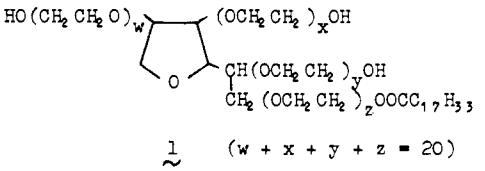
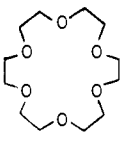
While studying the ionophoric properties of polysorbate 80 (Tween 80, **1**), work that will be published later, we determined the rate of transport of potassium ions at various temperatures through a model membrane (CH_2Cl_2) and were intrigued to find that it rose with a decrease in temperature.

In order to find whether such an inverse relationship between rate of transport and temperature was general, we repeated our experiments using the more common and extensively studied[2] ionophores 18-crown-6 (**2**) and polyethylene glycol-1000 (PEG-



1 (w + x + y + z ≈ 20)



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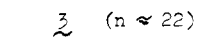

3 (n ≈ 22)

1000, **3**). The abilities of these carriers to transport potassium ions through CH_2Cl_2 also improved with decreasing temperature.

Our apparatus (Figure 1), consisting of a glass "cup" in a 600-mL beaker, was an adapted form of that used by Lamb et al.[3] The potassium ions were carried by the ionophore from the inner to the outer water layer; the thiocyanate counterions accompanying them reacted on arrival with the ferric ions in the outer layer to form the colored $Fe(SCN)^{2+}$ complex. Timely measurements of this visible complex's absorption at 480 nm led to the determination of the rate of transport. Our present ex-

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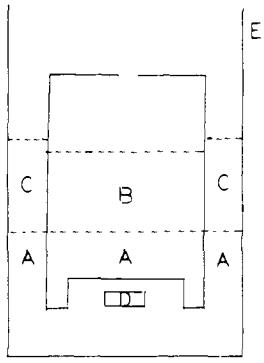

Figure 1. Apparatus used for transport studies. (A) Lower layer, 150 mL of 0.7 mM ionophore in CH_2Cl_2; (B) inner layer, 40 mL of 0.05 or 0.0125 M KSCN in deionized, distilled water; (C) outer layer, 50 mL of 0.02 M $Fe(NO_3)_3$ in 0.2 M aqueous HNO_3; (D) stirring bar; (E) 600-mL beaker.

Table I. Variation with Temperature of the Cation Flux[a] of KSCN through CH_2Cl_2 by Various Ionophores

	cation flux, J_m[a,b]		
T, °C	Tween 80, 0.05 M KSCN	18-crown-6, 0.0125 M KSCN	PEG-1000, 0.05 M KSCN
30	1.95 ± 0.14	6.54 ± 0.44	1.98 ± 0.19
23	2.60 ± 0.12	8.67 ± 0.47	3.10 ± 0.15
16	4.22 ± 0.23	12.54 ± 0.59	4.30 ± 0.28
2	7.03 ± 0.31	17.68 ± 1.17	6.67 ± 0.27
	Plot, J_m vs. T		
10^9 slope	-1.879	-4.076	-1.680
r	0.9921	0.9961	0.9999

[a] J_m = (mol 10^8)/(s m^2). [b] A minimum of three determinations were run at each temperature.

periments were conducted in a constant temperature bath at a stirring rate of 125 rpm.

Our results are summarized in Table I. Rates and fluxes at each temperature were determined from the slopes of lines (minimum $r = 0.9982$) resulting from the plotting of thiocyanate concentration in the outer layer vs. time. No transport was observed in the absence of ionophore. The lack of a reverse transport of ferric ions from the outer to the inner layer was shown by the total absence of the colored complex in the inner layer, even after several days. Thus, the thiocyanate transport accurately reflects the potassium ion transport. Note the large macrocyclic effect reflected by the 18-crown-6 rates compared to those of the two noncyclic ionophores.

A possible reason for this unusual temperature relationship may be found in the recent statement of Grandjean and Laszlo[4] that "many authors have shown that the rate determining step in ionic transport phenomena occurs at the water–membrane interface". Two interactions of the potassium ions at that interface can be cited: that with the solvent molecules in the water layer and that with the ionophore in the organic layer. Each of these attractions will increase at lower temperatures. If the strength of the potassium ion–ionophore interaction (within the ion pair KL^+ (org), SCN^- (org)) increases faster with a fall in temperature than the strength of the potassium ion–water molecule interaction, the partition coefficient would rise in favor of the ionophore complex and the rate of transport would also rise. This explanation is substantiated by the work of Ouchi et al.,[5] who found that the degree of extraction of potassium and sodium ions from water into CH_2Cl_2 with the help of crown ethers increased with decreasing temperature.

These variations merit further investigation, since ion transport figures so prominently in many important biochemical processes.

Registry No. 1, 9005-65-6; **2**, 17455-13-9; **3**, 25322-68-3; CH_2Cl_2, 75-09-2; K, 7440-09-7.

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A New Synthetic Strategy for the Penems. Total Synthesis of (5*R*,6*S*,8*R*)-6-(α-Hydroxyethyl)-2-(hydroxymethyl)penem-3-carboxylic Acid

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Woodward's original concepts regarding the penems[1] as well as their synthesis[2] stand as hallmarks of excellence in the area of β-lactam antibiotics.[3] Notable improvements have been recently reported with regard to the Wittig-type ring closure to 2-substituted thiazolines,[3] by resorting to reductive, thermal cyclizations of oxalimides, in the presence of trialkyl phosphites, or via anionic and other types of cyclizations.[4-8]

We wish to report on an operationally novel and practical process for the stereocontrolled assembly of an optically active penem nucleus, as exemplified in the total synthesis of the title compound, and its highly bioactive 2-*O*-carbamoyl derivative (FCE 22101).[9] The synthetic strategy is shown in the retrosynthetic analysis depicted in Scheme I. Two key features involve the exploitation of L-threonine as a versatile chiral template[10,11] for an optically active azetidinone precursor to the penem and the utilization of a unique ketene dithiol reagent[12] having ambident sites of reactivity, in a conceptually novel type of access to the thiazoline ring via in an intramolecular Michael addition.

The readily available L-threonine was converted into an epoxy acid $[\alpha]_D$ -9° (MeOH) via the corresponding α-bromide[10] in a modified, one-pot sequence and then to the epoxyamide **1**, mp 79–80 °C, $[\alpha]_D$ +176.4° (MeOH), in good overall yield. Treatment of **1** with potassium carbonate in DMF resulted in a remarkably facile ring closure to give the azetidinone **2**, mp 77–79 °C, $[\alpha]_D$ -68.2° (MeOH).[13,14] Protection of the hydroxyl group and removal of the *N*-(*p*-methoxyphenyl) group[15] led to **4**, mp 158–160 °C, $[\alpha]_D$ -28.2° ($CHCl_3$). Baeyer–Villiger oxidation

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