effects are 0.04 and 0.03 ppm, respectively. Thus, the magnitude of the isotope effect should be useful in spectral assignments.

An interesting phenomenon was observed with secondary ammonium ions of the type $A(NH_2^+)B$. The nitrogen atom in the monodeuterated species of such ions, $A(NHD^+)B$, is asymmetric. Therefore, if one of the substituents is isopropyl, e.g., $(CH_3)_2CHNH_2^+R$, the originally enantiotopic and isochronous isopropyl methyls become diastereotopic and anisochronous in the $(CH_3)_2CHNHD^+R$ species. This phenomenon is illustrated in Figure 2. For the partially deuterated diisopropylammonium ion both the CH and CH_3 resonances appear as triplets with large and small spacings, respectively (Figure 2A). However, for the ethylisopropylammonium ion the isopropyl methyls give rise to a clearly resolved quartet (Figure 2B). The spacing between the inner components of this quartet corresponds to the chemical shift difference (0.033 ppm) between the diastereotopic isopropyl methyls in the monodeuterated species. In the *N'*-isopropyl-2-methyl-1,2-propanediammonium ion this difference is approximately equal to the chemical shift (0.049 ppm) between the protio and deuterio forms, resulting in a doublet (Figure 2C). On the other hand, in the diisopropyl case the chemical shift between the diastereotopic methyls is smaller than the line-width (0.015 ppm), giving rise to a triplet (Figure 2A).

For amino acids and their derivatives, partial deuteration of the α ammonium group gives rise to isotopic multiplets in the carboxyl as well as in the backbone carbon resonances. Thus, isotopic multiplets should be useful in the assignment of such resonances and in the identification of terminal residues of peptides.

Acknowledgment. I thank David S. Rice for his excellent technical assistance.

Registry No. $H_3N(CH_2)_3NH_2(CH_2)_4NH_3^{3+}$, 74676-62-3; $[(CH_3)_2CH]_2NH_2^+$, 21445-72-7; $(CH_3)_2CHNH_2CH_2CH_3^+$, 94041-96-0; $(CH_3)_2CHNH_2CH_2C(CH_3)_2NH_3^{2+}$, 94859-78-6; L-$HOOCCH(NH_3)(CH_2)_4NH_3^{2+}$, 17829-44-6; D_2, 7782-39-0.

Stereoelectronic Controlling Features of Allylic Asymmetry. Application to Ester Enolate Alkylations

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Asymmetric transformations of unsaturated species have attracted considerable synthetic and theoretical interest.[1,2] An intriguing facet of the chemistry of **1** is the manner through which the asymmetric center renders the faces of the adjacent π-system chemically nonequivalent. Kinetic stereoselection in species **1** has been attributed to a number of conformational models that are conveniently classified as being eclipsed (A–D) or perpendicular (E–H, Figure 1).[1c,d] We present herein support for a transition-state model for electrophilic additions that is based upon conformer H, which finds considerable generality in predicting the stereochemical outcome of asymmetric reactions in this class.

Calculations modeling the transition states for the reaction of simple substrates with nucleophiles, electrophiles, radicals, and dipoles indicate a pronounced preference for perpendicular geometries in all cases.[1a,b] The approaching reagent is generally

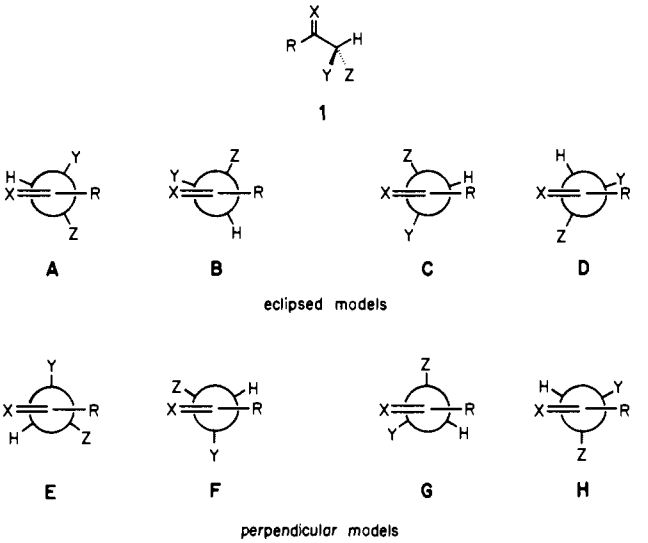

Figure 1.

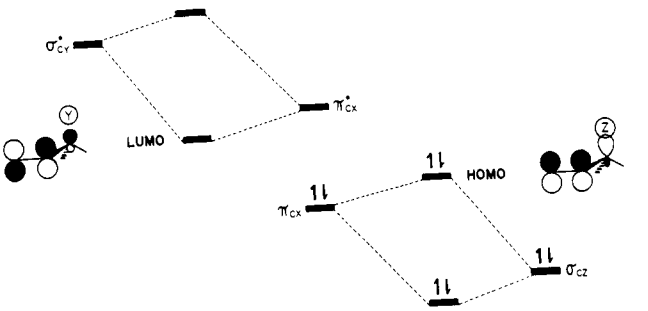

Figure 2.

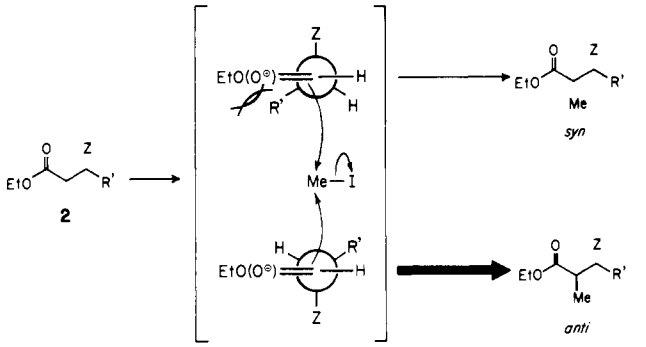

Figure 3.

directed antiperiplanar to the perpendicularly disposed substituent through secondary orbital interactions.[1-3] These theoretical conclusions find no contradictions in a rapidly growing body of experimental evidence. This being the case, the description of a given transition state requires the deployment of the appropriate substituent in the proper perpendicular position. In the MO formalism,[4] nucleophilic attack will seek the LUMO of the electrophile. This may be favorably affected through mixing of the π^* orbital with the lowest energy σ^* orbital, which is associated with the most electronegative substituent (e.g., Y; Figure 2).[5] In the event of electrophilic attack, however, the substrate's HOMO governs the course of the reaction. In this instance, the π orbital mixes with the highest energy σ orbital, belonging to the substituent that most efficiently participates in hyperconjugative

(1) For recent theoretical studies, see: (a) Ahn, N. T. *Top. Curr. Chem.* **1980**, *88*, 145. (b) Caramella, P.; Rondan, N. G.; Paddon-Row, N. M.; Houk, K. E. *J. Am. Chem. Soc.* **1981**, *103*, 2438. (c) Paddon-Row, M. N.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1982**, *104*, 7162. (d) Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277.

(2) For recent discussions on stereoselective electrophilic additions to olefins, see: (a) Schreiber, S. L.; Satake, K. *J. Am. Chem. Soc.* **1983**, *105*, 6723. (b) Houk, K. N.; Moses, S. R.; Wu, Y.-D.; Rondan, N. G.; Jäger, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. (c) Houk, K. N.; Rondan, N. G.; Wu, Y.-D.; Metz, J. J.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257.

(3) Franck, R. W.; John, T. V.; Olenjniczak, K. *J. Am. Chem. Soc.* **1982**, *104*, 1106.

(4) (a) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1977. (b) Epiotis, N. D.; Cherry, W. R.; Shaik, S.; Yates, R. L.; Bernardi, F. *Top. Curr. Chem.* **1977**, *70*, 1.

(5) Houk and co-workers have examined these orbitals with regard to the antiperiplanar effect.[1b]

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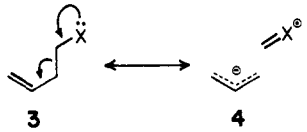
interactions (e.g., Z), to afford a more reactive MO.[5]

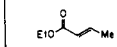
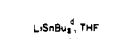
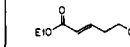
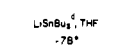
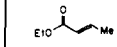
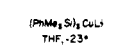
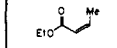
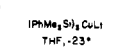
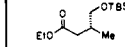
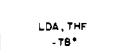
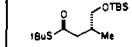
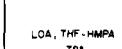
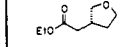
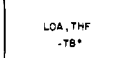
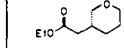
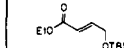
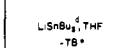
General agreement with this description is found for nucleophilic additions to carbon–carbon[6] and carbon–oxygen[7] π-systems in the absence of chelation effects. As recognized in the Felkin–Ahn model,[1a] the electronegative substituent (Y in **1**) occupies the perpendicular position in rotamer F. The case for electrophilic additions is less clear, however, with stereoselection often rationalized in terms of X-eclipsed conformer A,[8] reflecting the most stable geometry of the reactant π-system.[9] Recently, Houk and co-workers carried out theoretical studies on electrophilic additions to asymmetric olefins that indicated a marked preference for transition states arising from conformers G and H.[2b,c] Subtle effects associated with the structure of the olefinic substrate and the nature of the electrophilic reagent dictate which of these transition states is operative.

We chose to study the predictive value of the perpendicular models through a study of the methylation of enolates derived from β-substituted carbonyl compounds. As shown in Figure 3, analysis in terms of conformer H predicts the anti product *regardless* of enolate geometry. This model was favored over the alternative (conformer G) on the basis of destabilizing steric interactions (H $\leftrightarrow$ X in H vs. Y $\leftrightarrow$ X in G).[10] To ensure strong electron donation by the Z substituent in **2**, we examined trialkylstannyl-substituted enolates[11] formed in situ through conjugative addition of Bu_3SnLi[12] to α,β-unsaturated esters. Quenching these anions with MeI strongly favored the predicted anti stereoselection (entries 1 and 2, Table I). Analogous results were observed by Fleming and co-workers with silicon substitution on a range of substrates (e.g., entries 3 and 4).[13] These results are not consistent with a purely steric model based upon conformer A since the steric requirements of the asymmetric substituents apparently follow the order nBu$_3$Sn < Me < Me$_2$PhSi.[14] While a chelated intermediate is not rigorously excluded, the expected trans geometry of the generated enolate conflicts with this explanation.[15] In an effort to examine a less ambiguous example, we reasoned that a homoallylic heteroatom would enhance the donor ability of the substituted carbon via lone pair participation (**3** $\leftrightarrow$ **4**). With this in mind, the experiments in entries 5–10 were carried out.



3 **4**

Table I. Methylation of Ester Enolates

Entry	Starting Material[a]	Conditions of Enolate Generation	Major Product[b] major:minor[b]	Yield[c]
1		LiSnBu$_3$,[d] THF, -78°	 98:2	86%
2		LiSnBu$_3$,[d] THF, -78°	 93:7	78%
3[e]		(PhMe$_2$Si)$_2$CuLi, THF, -23°	 99:1	82%
4[e]		(PhMe$_2$Si)$_2$CuLi, THF, -23°	 98:2	75%
5		LDA, THF, -78°	 89:11	85%
6		LDA, THF-HMPA, -78°	90:10	96%
7		LDA, THF-HMPA, -78°	 91:9	98%
8		NaN(TMS)$_2$, THF-HMPA, -78°	90:10	90%
9		LDA, THF, -78°	 67:33	95%
10		LDA, THF, -78°	 87:13	94%
11		LiSnBu$_3$,[d] THF, -78°	 94:6	74%

[a] TBS = *t*-BuMe$_2$Si. [b] Isomer ratio determined by capillary GC analysis. [c] Isolated by column chromatography. [d] Prepared by the method of Still.[12] [e] This entry from the work of Fleming and co-workers.[13]

Noncyclic examples in entries 5–8 afforded uniformly high levels of anti stereoselection. The steric model (conformer A) again presents an inadequate explanation in view of the similar steric requirements of the Me and CH_2OR groups.[16] While it is highly improbable that stereoselection results from chelated enolates under the range of conditions employed, we examined the cyclic substrates in entries 9 and 10 because they offer stereochemical differentiation between methylation resulting from chelated and acyclic intermediates. In both cases the favored isomer is consistent with an unchelated enolate. The diminished stereoselection found that the five-membered ether (entry 9) is supportive of the proposed model (conformer H) since the oxygen lone pairs are prevented from achieving the optimal geometry for participation in the transition state (**5**). Higher levels of stereoselection are restored in the six-membered ether (entry 10) as an oxygen lone pair is permitted an ideal geometry (**6**).[17] The final example (entry 11) may be taken to reflect the relatively strong donor

(6) (a) Matsunga, H.; Sakamaki, T.; Nagaoka, H.; Yamada, Y. *Tetrahedron Lett.* **1983**, 3009. (b) Roush, W. R.; Lesur, B. M. *Tetrahedron Lett.* **1983**, 2231. (c) Fronza, G.; Fuganti, C.; Graselli, P.; Majori, L.; Pedrocchi-Fantoni, G.; Spreafico, F. *J. Org. Chem.* **1982**, *47*, 3289. (d) Isobe, M.; Kitamura, M.; Goto, T. *Tetrahedron Lett.* **1980**, 4727. (e) Dyong, I.; Bendlin, H. *Chem. Ber.* **1979**, *112*, 717.

(7) For representative examples, see: (a) Fuganti, C.; Grasselli, P.; Servi, S.; Spreafico, F.; Zirotti, C.; Casati, P. *J. Chem. Res.* **1984**, 112. (b) Mulzer, J.; Angermann, A. *Tetrahedron Lett.* **1983**, 2843. (c) Roush, W. R.; Harris, D. J.; Lesur, B. M. *Tetrahedron Lett.* **1983**, 2227. (d) Mukaiyama, T.; Yuki, Y.; Suzuki, K. *Chem. Lett.* **1982**, 1169. (e) Mukaiyama, T.; Suzuki, K.; Yamada, T. *Chem. Lett.* **1982**, 929. (f) Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pirrung, M. C.; White, C. T.; Van Derver, D. *J. Org. Chem.* **1980**, *45*, 3846.

(8) For examples of the utility of this empirical rationale, see: Kishi, Y. *Aldrichimica Acta* **1980**, *13*, 23.

(9) For a review on sp^2–sp^3 conformational isomerism, see: Karabatsos, G. J.; Fenolio, D. J. *Top. Stereochem.* **1969**, *5*, 167.

(10) An analogous transition state has been suggested to explain the stereoselection observed in a highly polarized cycloaddition: DeShong, P.; Leginus, J. M. *J. Am. Chem. Soc.* **1983**, *105*, 1686.

(11) For a measure of the donor abilities of trialkylstannyl groups, see: Traylor, T. G.; Berwin, H. J.; Jerkunica, J.; Hall, M. L. *Pure Appl. Chem.* **1972**, *30*, 599.

(12) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

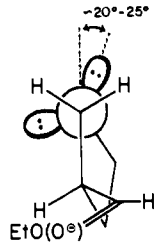
(13) Bernhard, W.; Fleming, I.; Waterson, D. *J. Chem. Soc., Chem Commun.* **1984**, 28.

(14) This order is based upon available *A* values. (a) *i*-Pr$_3$Sn = 1.10 kcal/mol: Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893. (b) Me = 1.70 kcal/mol: Hirsch, J. A. *Top. Stereochem.* **1967**, *1*, 199. (c) Me$_3$Si $\simeq$ 2.50 kcal/mol: Kitching, W.; Olszowy, H. A.; Drew, G. M.; Adcock, W. *J. Org. Chem.* **1982**, *47*, 5153.

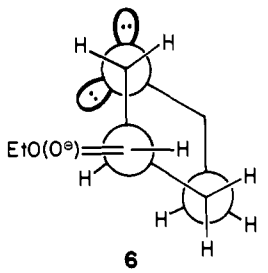
(15) Fleming and co-workers present several arguments against a chelated enolate, including the one suggested here.[13]

(16) These steric requirements are based upon A values:[14b] Me = 1.70 kcal/mol, TsOCH$_2$ = 1.7–1.8 kcal/mol.

(17) Possibly related stereoelectronic effects have been noted in a recent study of spiro-Claisen rearrangements: Fraser-Reid, B.; Tulshian, D. B.; Tsang, R.; Lowe, D.; Box, V. G. S. *Tetrahedron Lett.* **1984**, 4579.



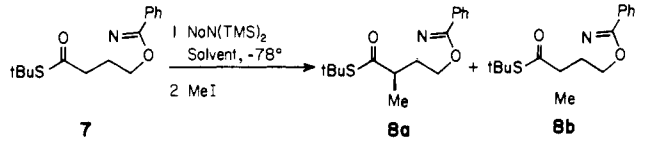
5



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



7 8a 8b

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.

(20) (a) Bognár, R.; Herczegh, P. *Carbohydr. Res.* **1976**, *52*, 11. (b) Johnson, M. R.; Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4343. (c) Johnson, M. R.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4347. (d) Hasan, I.; Kishi, Y. *Tetrahedron Lett.* **1980**, 4229. (e) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109.

(21) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487.

(22) (a) Midland, M. M.; Hatterman, R. L. *J. Org. Chem.* **1981**, *46*, 1227. (b) Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819.

(23) Paquet, F.; Sinaÿ, P. *Tetrahedron Lett.* **1984**, 3071.

(24) (a) Hauser, F. M.; Rhee, R. P. *J. Org. Chem.* **1981**, *46*, 227. (b) Katuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (c) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, 3943. (d) Christ, W. J.; Cha, J. K.; Kishi, Y. *Tetrahedron Lett.* **1983**, 3947. (e) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, 3951. (f) Larson, E. R.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 6715.

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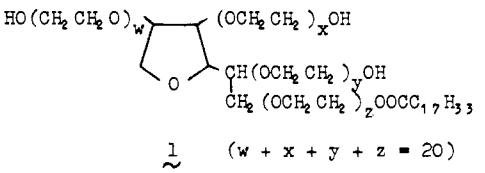
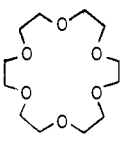
While studying the ionophoric properties of polysorbate 80 (Tween 80, **1**), work that will be published later, we determined the rate of transport of potassium ions at various temperatures through a model membrane (CH_2Cl_2) and were intrigued to find that it rose with a decrease in temperature.

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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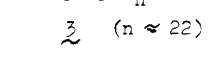

3 (n ≈ 22)

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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(2) (a) Lamb, J. D.; Christensen, J. J.; Oscarson, J. L.; Nielsen, B. L.; Asay, B. W.; Izatt, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 6820. (b) Yanagida, S.; Takahashi, K.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1386. (c) Balasubramanian, D.; Chandani, B. *J. Chem. Educ.* **1983**, *60*, 77.

(3) Lamb, J. D.; Christensen, J. J.; Izatt, S. R.; Bedke, K.; Astin, M. S.; Izatt, R. M. *J. Am. Chem. Soc.* **1980**, *102*, 3399.

0002-7863/85/1507-1437$01.50/0