Table II. Allylation of 6

entry	substrate	product[a]	yield, %	$[\alpha]_D$, deg (c, $CHCl_3$)
1	**6a**	**8a**	45	−39.4 (0.4)
2	**6b**	**8b**[4e]	71	−71.7 (0.8)
3	**6c**	**8c**[4e]	55	−74.2 (0.9)
4	**6f**	**8f**	72	−5.4 (0.6)
5	**6g**	**8g**[18]	76	+8.2 (1.1)
6	**6h**	**8h**	81	−31.2 (0.9)
7	**6i**	**8i**	60	−43.4 (0.6)
8	*cis*-**6i**	**8i**	20	
9	**6j**	**8j**	62	−3.7 (0.6)
10	**6k**	**8k**	81	−15.9 (0.7)
11	*cis*-**6k**	**8k**	30	
12	**6l**[b,c]	**8l**	57	−63.5 (1.0)

[a] All products were obtained as an oil except **8h**. **8h**: mp 80–81 °C. [b] 2.4:1 trans/cis mixture was used. [c] The reaction was continued for 40 h.

derived from **6a** and **6c**, respectively, by the procedure as outlined in Scheme II. *tert*-Butoxycarbonylation of **6a–c,e** (Boc_2O, Et_3N, 4-(dimethylamino)pyridine, THF) afforded **6f–i**, respectively, and acetylation of **6a,d** (Ac_2O, Et_3N, 4-(dimethylamino)pyridine, THF) gave **6j,k**, respectively.

Allylation of **6a–c,f–l** by modification of Keck's conditions[16] (0.5 M solution in toluene–CH_3CN (7:3), 4 equiv of allyltri-*n*-butylstannane, 1 equiv of $(Bu_3Sn)_2$, $h\nu$, 24 h, Pyrex filter, 300-W Hg lamp, 24 h) gave the corresponding 5-allyloxazolidin-2-ones **8a–l** as single diastereomers in the yields shown in Table II. The stereochemical assignment was clearly determined as 4*S*,5*S*-trans based on the ^1H NMR spectra.[3a,4e,5c] The optical purity of the allylation products was >99% ee by ^1H NMR (400 MHz) analysis of *N*-Boc Mosher esters[15] **7e,f** and MTPA imides **7g,h** prepared from **8h** and **8k**, respectively. Yields for 5-allylation products were increased by protection of nitrogen with Boc or acetyl groups (compare Table II, entry 1–3 with 4–6, 9). It is noteworthy that the reactivity of the 4,5-cis isomers toward generation of radical species is remarkably low compared with that of the trans isomers. This was clearly demonstrated by using **6i** and **6k**, which stereo isomers were available in a pure state (Table II, entry 8 and 11). These results indicate that the reaction is strongly affected by the stereochemistry and that the trans-oriented phenylthio group is more active than the cis-oriented one. The low reactivity of the cis isomers could be due to steric congestion, which restricts attack of the tri-*n*-butyltin radical on the sulfur atom.

These 5-allyloxazolidin-2-ones should be useful for the synthesis of β-oxygenated γ-amino acids. Oxidation of **8g** and **8h** ($RuCl_3$–$NaIO_4$, H_2O, CH_3CN, CCl_4)[17] under Sharpless conditions afforded the corresponding acids **9a**[18] (80%), $[\alpha]_D$ +23.3° (c 0.90, $CHCl_3$) (lit.[18] $[\alpha]_D$ +23.32° (c 0.92, $CHCl_3$)), and **9b** (45%), respectively. Compound **9a** was converted to (3*S*,4*S*)-statine (**1**) through hydrolysis[18] (80% yield) of **9a** and deprotection.[5a] Hydrolysis of **8k** (catalytic amount of Cs_2CO_3, MeOH, room temperature) gave **8d** (100%), which was converted to **10** ((1) $LiAlH_4$; (2) MeI/KH,[19] THF, 50% yield from **8d**), which should be a potentially useful intermediate for one isomer of **2**.

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(15) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(16) Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079.

(17) Carlsen, E.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.

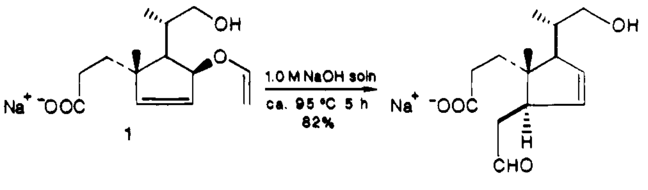
(18) Kano, S.; Yokomatsu, T.; Iwasawa, H.; Shibuya, S. *Tetrahedron Lett.* **1987**, *28*, 6331.

(19) Selective O-methylation of 2-amino alcohol system: Overman, L. E.; Kakimoto, M.; Okazaki, M. E.; Meier, G. P. *J. Am. Chem. Soc.* **1983**, *105*, 6622.

Effect of Polar Solvents on the Rates of Claisen Rearrangements: Assessment of Ionic Character

Summary: The first-order rate constants for Claisen rearrangement of carboxylate **3** and its methyl ester were determined in solvents ranging in polarity from cyclohexane to water.

Sir: The discovery by White[1] and the Cornell group[2] that polar solvents increase the rate of Claisen rearrangements has a profound consequence in synthetic methodology. While the vinyl ethers of cyclic allylic alcohols are most reluctant to undergo the 3,3-sigmatropic shift to the appropriate aldehyde in the gas phase or in hydrocarbon solvents, remarkably, compound **1** rearranges completely after only 5 h in boiling water.[3] From a mechanistic point of view, the nature of the transition state responding to the polar environment is of concern.



The Cornell group examined the rearrangement of allyl vinyl ethers in media as polar as 2:1 methanol–water.[2] However, the data could not be correlated with solvent E_t values. Further, more polar solvent systems could not be used because of solubility problems. The Cornell group interpreted the solvent response data in terms of an ionic-like transition state. In addition, Knowles has suggested that a dipolar or tight ion pair transition state is involved in the rearrangement of chorismate, **2**, and its diacid on the basis of faster rates in water relative to methanol solvent.[4] A dipolar transition state is also suggested by

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(1) White, W. N.; Wolfarth, E. F. *J. Org. Chem.* **1970**, *35*, 2196, 3585.

(2) Gajewski, J. J.; Jurayj, J.; Kimbrough, D. R.; Gande, M. E.; Ganem, B.; Carpenter, B. K. *J. Am. Chem. Soc.* **1987**, *109*, 1170.

(3) Unpublished observations, E. Brandes, Indiana University.

(4) Copley, S. D.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 5008.

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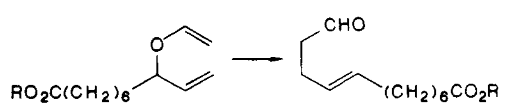
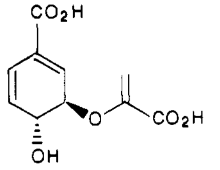
Table I. Rate Constants for the Claisen Rearrangement[a]



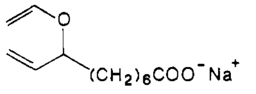
solvent	$k \times 10^{-5}$ s^{-1} R = Na	$k \times 10^{-5}$ s^{-1} R = Me
water	18	
75% H_2O–CF_3CH_2OH	6.9	
50% H_2O–$CF_3CH_2OH^b$	3.7	
25% H_2O–$CF_3CH_2OH^b$	2.8	
$CF_3CH_2OH^b$	2.6	4.7
75% H_2O–MeOH	11	
50% H_2O–MeOH	4.6	3.6
25% H_2O–MeOH	1.6	1.4
MeOH	0.79	0.72
75% H_2O–DMSO	3.0	
50% H_2O–DMSO	1.6	
25% H_2O–DMSO	0.93	0.82
10% H_2O–DMSO	0.27	0.50
EtOH		0.51
$(CH_3)_2CHOH$		0.42
CH_3CN		0.25
CH_3COCH_3		0.18
benzene		0.17
cyclohexane		0.084

[a] Reactions were carried out in sealed NMR tubes at 60 °C with ca. 0.01 M of **3** and 0.01 M of pyridine. Kinetic data was obtained by integration of 360-MHz ^1H NMR. [b] Containing ca. 0.1 M of pyridine.

Coates and Curran in the specific case of Claisen rearrangements of 6-alkoxyallyl enol ethers because of the large response to solvent polarity.[5]



2



3

We report here a solvent polarity study on the rate of the rearrangement of the allyl vinyl ether carboxylate salt, **3**, in solvent systems from pure methanol to water at 60 °C. The rate data correlates well with Y(Cl)[6] and Y(OTs)[7] with m values of 0.33 (r = 0.98) and 0.31 (r = 0.98), respectively. The corresponding methyl ester has also been examined in aqueous methanol mixtures allowing calculation of an m(OTs) value of 0.23 (r = 0.99).

Since previous workers postulate substantial polar character in the Claisen transition state, it is appropriate to examine the m values for model compounds using the solvent Y(OTs) values which might seem better for an oxygen leaving group than Y(Cl) values. Thus, m for isopropyl, cyclopentyl, and cyclohexyl tosylate solvolyses are 0.48, 0.55, and 0.69, respectively.[7] Further, conjugation increases the m value dramatically, judging by that for benzyl tosylate relative to ethyl tosylate (0.57 vs 0.14). For another point of calibration, the m(Cl) value for solvolysis of 3-chloro-1-butene is 0.79, which must indicate substantial ionic character at a secondary allylic site in a bona fide ionization process.[8] Finally, the internal return rates of *exo*-bicyclo[3.2.1]oct-3-enyl *p*-nitrobenzoate have been studied in 80% and 90% acetone–water mixtures with the relative rates being nearly identical with those of solvolysis; the ratio of the logarithm of the relative rates to the difference in Y(Cl) values (m(Cl)) is 0.95.[9]

The solvent–rate data provided by the Cornell group[3] yields an m(OTs) for allyl vinyl ether of 0.4 (only two data points are available), and for *trans,trans*-2,4-hexadienyl vinyl ether the m value is 0.29 (r = 0.98, three data points). These rearrangements do not appear to be much different than those of **3** and its ester studied here. It would appear that even in polar, hydroxylic solvents, the Claisen rearrangement has substantially less polar character than bona fide solvolyses.[10]

Finally, the origin of m value approaching 0.5 for the rearrangement of chorismate is of concern in light of the small values for the corresponding acid and 4-*O*-methyl chorismate (ca. 0.2). We would prefer to defer discussion of these observations until the much larger electrostatic interactions in the former case can be assessed and the not-necessarily linear perturbation of the energy surface by changes in solvent can be studied.

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(5) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.

(6) Grunwald, E.; Winstein, S. *J. Am. Chem. Soc.* **1948**, *70*, 846. See also: Smith, S. G.; Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1961**, *83*, 618 and references contained therein.

(7) Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667. Bentley, T. W.; Carter, G. E. *J. Org. Chem.* **1983**, *48*, 579.

(8) Vernon, C. A. *J. Chem. Soc.* **1954**, 423.

(9) Goering, H. L.; Anderson, R. P. *J. Am. Chem. Soc.* **1978**, *100*, 6469.

(10) The kinetic data from **3** correlates with Taft's solvatochromic equation[11] giving $\log k(\text{abs}) = [0.76\ (\pm 0.15)\pi^*] + [0.87\ (\pm 0.07)\alpha] - [0.41\ (\pm 0.12)\beta] - [6.13\ (\pm 0.01)]$. For comparison purposes, correlation of Y(OTs) values give $[8.8\ (\pm 0.3)\pi^*] + [3.9\ (\pm 0.2)\alpha] - [0.02\ (\pm 0.3)\beta] - 9.91$.

(11) Kamlet, M. J.; Abboud, J.-L. M.; Taft, R. W. *Prog. Phys. Org. Chem.* **1981**, *13*, 485. If the revised TFE parameters from Kamlet et al. (Kamlet, M. J.; Abboud, J.-L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877) are used, very different coefficients are obtained for Y(OTs) values, but the fit is a distinctly worse; if TFE is omitted, roughly the same coefficients cited above are obtained.