From eq 3, $[D^{\bullet+}]$ is obtained:

$$[D^{\bullet+}] = (k_p/k_{CH})[\mathbf{1}^{\bullet+}] \quad (4)$$

and substituting (4) into (2):

$$0 = k_i[\mathbf{1}][\mathbf{2}^{\bullet+}] - k_{-i}[\mathbf{1}^{\bullet+}][\mathbf{2}] - 2k_t[\mathbf{1}^{\bullet+}]^2 \quad (5)$$

The quadratic in $[\mathbf{1}^{\bullet+}]$ is easily solved, but the expression for $[\mathbf{1}^{\bullet+}]$ and thus the kinetic rate law has a simple form only if [2] is small:

$$[\mathbf{1}^{\bullet+}] = (8k_ik_t[\mathbf{1}][\mathbf{2}^{\bullet+}])^{1/2}/4k_t \quad (6)$$

Substituting (6) into (1):

$$\text{rate} = -d[\mathbf{1}]/dt = \sqrt{2}(k_pk_i^{1/2}k_t^{-1/2})[\mathbf{1}]^{3/2}[\mathbf{2}^{\bullet+}]^{1/2} \quad (7)$$

The analogous rate equation for the cyclodimerization of **3** is:

$$\text{rate} = -d[\mathbf{3}]/dt = (k_pk_ik'^{-1}_t)[\mathbf{3}]^2[\mathbf{2}^{\bullet+}]$$

The integrated rate equation corresponding to the rate law derived for the cyclodimerization of **1** and assuming $[Ar_3N^{\bullet+}]$ constant is

$$2([\mathbf{1}]_t^{-1/2} - [\mathbf{1}]_0^{-1/2})([\mathbf{2}^{\bullet+}])^{-1/2} = k_{app}t$$

Plots of:

$$2([\mathbf{1}]_t^{-1/2} - [\mathbf{1}]_0^{-1/2})([\mathbf{2}^{\bullet+}])^{-1/2}$$

vs. t yielded the rate constants, k_{app}, given in Table I. These plots maintained excellent linearity with varying [1], [2], and temperature. Plots which were first or second order with respect to [1] or those which were other than one-half order in $[\mathbf{2}^{\bullet+}]$ were found unsatisfactory.

The integrated rate equation which fit the data for the dimerization of **3** is:

$$([\mathbf{3}]_t^{-1} - [\mathbf{3}]_0^{-1})[\mathbf{2}^{\bullet+}]^{-1} = k_{app}t$$

Activation parameters were obtained in the usual way. The plots of ln k_{app} vs. T^{-1} had the following characteristics. For **1**, $r = -0.9952$, $y = 16.887$, $s = -4283.77$; for **3**, $r = -0.9965$, $y = 15.3887$, $s = -1358.37$. Arrhenius analysis gave for **1**, $E_a = 8.512$, $A = 2.16 \times 10^7$; for **3**, $E_a = 2.699$, $A = 4.822 \times 10^6$.

The separation of the $\Delta G^{\ddagger}_{app}$ into $\Delta G^{\ddagger}_p$ follows from the derivation below:

$$k_{app} = \sqrt{2}(k_pk_i^{1/2}k_t^{-1/2})$$

$$\Delta G^{\ddagger}_{app} = -RT \ln k_{app} =$$
$$-RT[\ln \sqrt{2} + \ln k_p + \tfrac{1}{2} \ln k_i - \tfrac{1}{2} \ln k_t]$$

$$\Delta G^{\ddagger}_{app} = \Delta G^{\ddagger}_p + \tfrac{1}{2}\Delta G^{\ddagger}_i - \tfrac{1}{2}\Delta G^{\ddagger}_t - RT \ln \sqrt{2}$$

$$\Delta G^{\ddagger}_p = \Delta G^{\ddagger}_{app} - \tfrac{1}{2}\Delta G^{\ddagger}_i + RT \ln \sqrt{2}$$

The preceding equation assumes the activation energy for termination (e.g., coupling) is negligible. The remainder of the separation into $\Delta H^{\ddagger}_p$ and $\Delta S^{\ddagger}_p$ is as follows:

$$\Delta H^{\ddagger}_p - T\Delta S^{\ddagger}_p =$$
$$\Delta H^{\ddagger}_{app} - T\Delta S^{\ddagger}_{app} - \tfrac{1}{2}(\Delta H^{\ddagger}_i - T\Delta S^{\ddagger}_i) + RT \ln \sqrt{2}$$

$$\Delta H^{\ddagger}_p = \Delta H^{\ddagger}_{app} - \tfrac{1}{2}\Delta H^{\ddagger}_i; \; -T\Delta S^{\ddagger}_p =$$
$$-T\Delta S^{\ddagger}_{app} + \tfrac{1}{2}T\Delta S^{\ddagger}_i + RT \ln \sqrt{2}$$

Finally, $\Delta H^{\ddagger}_i = \Delta G^{\ddagger}_i = \Delta E_p$ is assumed. That $\Delta S^{\ddagger}_i = 0$ is a reasonable approximation follows from the nature of the ionization equilibrium, which involves one cation radical and one neutral species on both reactant and products sides. The quantity ΔE_p is the difference in peak oxidation potentials of **1** and **2**, measured by cyclic voltammetry. Reversible potentials are not attainable, so that ΔE_p is not a true thermodynamic quantity. The potentials measured for **1** and **2**, respectively, are 1.60 and 1.05 V (ΔE_p = 0.55 eV = 12.68 kcal mol^{-1}).

Registry No. **1**, 592-57-4; $\mathbf{2}^{\bullet+}$, 24964-91-8; **3**, 4180-23-8; tris(4-bromophenyl)amine, 4316-58-9; acetonitrile, 75-05-8; diethyl ether, 60-29-7; octanol, 124-13-0; isopropyl alcohol, 67-63-0; triethyl amine, 121-44-8; 2,6-di-*tert*-butylpyridine, 585-48-8; 2,4-dimethyl-1,3-pentadiene, 1000-86-8.

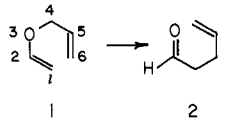
Synthesis and Claisen Rearrangement of Alkoxyallyl Enol Ethers. Evidence for a Dipolar Transition State

Robert M. Coates,*[†] Brian D. Rogers,[†1] Steven J. Hobbs,[†] David R. Peck,[‡] and Dennis P. Curran*[‡2]

Contribution from the Department of Chemistry, University of Illinois, Urbana, Illinois 61801, and Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260. *Received August 23, 1985. Revised Manuscript Received October 6, 1986*

Abstract: The synthesis and Claisen rearrangement of a series of 4-, 5-, and 6-alkoxyallyl vinyl ethers are reported. The 4- and 6-alkoxy derivatives (**4a-d**, **13**, and **15**) rearrange 9.5–159 times faster than the parent allyl vinyl ethers. In addition, a significant solvent effect is observed; the rates of rearrangement of the 4- and 6-alkoxy derivatives are increased 18–68-fold upon changing from benzene to methanol, ethanol, or 80% aqueous ethanol while the parent allyl vinyl ethers show a much smaller solvent effect. Further acceleration of the rearrangements from the combined influence of a 4-alkoxy group and a cyano or carbethoxy group at C-1 indicates a synergistic interaction of the donor and acceptor substituents. The substituent and solvent effects provide experimental evidence for a pronounced dipolar character of the transition state. 5-Methoxyallyl vinyl ether (**14**) rearranges 40 times slower than allyl vinyl ether itself. This contrasts with the results of a MNDO theoretical treatment by Dewar which predicted a 2-oxacyclohexane-1,4-diyl-like transition state and acceleration from the 5-methoxy substituent.

The Claisen rearrangement of allyl vinyl ethers (**1** → **2**)[3] and allyl aryl ethers is an important synthetic reaction for carbon–carbon bond formation[4] and a pericyclic transformation of considerable mechanistic interest.[5-8] Although the tolerance of the aliphatic Claisen rearrangement to various types of substituents has been amply demonstrated, the extent of quantitative infor-

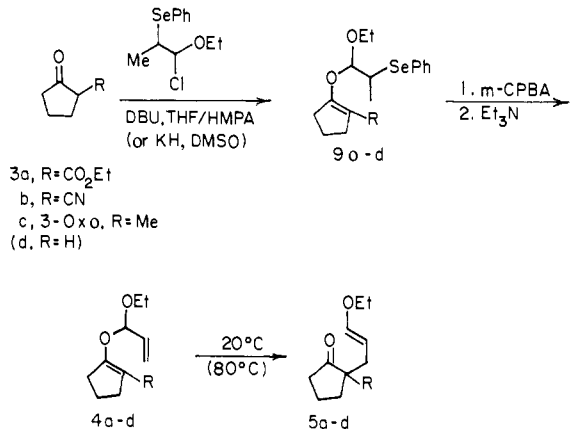


1 2

[†] University of Illinois.
[‡] University of Pittsburgh.

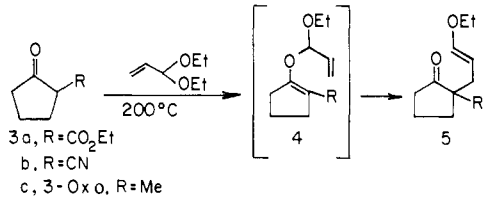
0002-7863/87/1509-1160$01.50/0

Scheme I

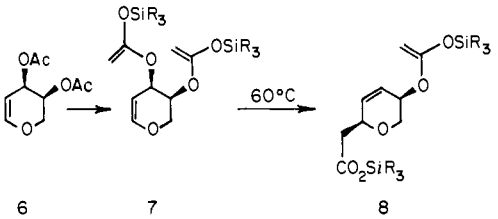


mation on substituent effects is quite limited. Carpenter and Burrows have reported a systematic evaluation of acceptor groups by kinetic measurements of cyano-substituted allyl vinyl ethers.[6b] The considerable rate-enhancing effect of donor substituents such as silyloxy,[9] amino,[10] and carbanion[11] at C-2 is now well-established, and recent evidence documents the accelerating influence of oxy anion,[12] amino,[13] and fluoro[14] substituents at C-1. Much less is known about the effect of donor substituents on the allyl group. We now report the results of our independent investigations on the effects of alkoxy donor substituents on the allyl group of allyl vinyl ethers.[15]

Previous publications from the Illinois laboratories[16] have proposed that the thermal condensation (100–200 °C) of acrolein diethyl acetal with β-dicarbonyl and related compounds (e.g., **3** → **5**) may take place via acetal exchange and Claisen rearrangement of the resulting α-alkoxyallyl vinyl ether **4**.[17] The putative α-alkoxyallyl vinyl ethers have now been generated under mild conditions by selenoxide elimination[18] and found to undergo Claisen rearrangement at remarkably low temperatures.



The Pittsburgh group has demonstrated the utility of the mono-Claisen rearrangement of polyacetylated glycal esters for the synthesis of C-glycosides (e.g., **6** → **7** → **8**) and has used this



approach in a total synthesis of (+)-pseudomonic acid C.[19] This selective rearrangement is made possible by an accelerating substituent effect of the endocyclic oxygen, and the acceleration has been rationalized as a consequence of a vinylogous kinetic anomeric effect.[8b] Implicit in this rationale was the dipolar nature of the transition state for the rearrangement.

The present studies afford a quantitative assessment of the rate-enhancing effects of the 4- and 6-alkoxy groups and the rate-retarding effect of the 5-alkoxy group. Kinetic measurements and solvent effects document a substantial polarizing effect of the 4- and 6-alkoxy groups on the transition state of the Claisen rearrangement.

Syntheses and Rearrangements

The α-ethoxy-β-phenylselenopropyl enol ethers required for the selenoxide elimination approach to the α-ethoxyallyl enol ethers were prepared by O-alkylation of the appropriate enolate anions with α-chloro-β-phenylselenopropyl ethyl ether (Scheme I). The latter unstable reagent was generated in pentane solution by reaction of benzeneselenenyl chloride and ethyl propenyl ether at room temperature.[18,20] Immediate reaction of the α-chloro ether with **3a–c** in tetrahydrofuran (THF)/hexamethylphosphoramide (HMPA) containing 1.5 equiv of diazabicyclo[5.4.0]undec-7-ene (DBU) afforded enol ethers **9a** (92%), **9b** (81%), and **9c** (58%), respectively, as ca 1:1 mixtures of the two diastereomers. The enol acetals were purified by chromatography on silica gel buffered with 1% triethylamine. The assignment of enol ether structures is based upon absorptions at 1640 cm^{-1} (C=C—OR) in their IR spectra and pairs of doublets at δ 5.0–5.6 (acetal protons) in their ^1H NMR spectra. The formation of O-alkylated products with the highly electrophilic α-chloro ether in the polar THF–HMPA medium was fully anticipated.[21]

Oxidation of the three seleno acetals (**9a,b,c**) and in situ elimination was carried out according to the procedure recommended by Reich and co-workers[22] for compounds sensitive to transient

(1) W. R. Grace Graduate Fellow, 1982–83. Chevron Graduate Fellow, 1983–84.

(2) Dreyfus Teacher-Scholar, 1986–91. Alfred P. Sloan Foundation Fellow, 1985–87. Lilly Grantee, 1985–87. Merck Young Faculty Development Awardee, 1986.

(3) The positional numbers of allyl vinyl ether are derived from those of 3-oxa-1,5-hexadiene.

(4) For recent reviews, see: (a) Bennett, G. G. *Synthesis* **1977**, 589. (b) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (c) Jefferson, A.; Scheinmann, F. *Quart. Rev. (London)* **1968**, *22*, 391.

(5) For reviews, see: (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim/Bergstr, 1970. (b) Hansen, H.-J.; Schmid, H. *Chimia* **1970**, *24*, 89. Hansen, H.-J.; Schmid, H. *Chem. Br.* **1969**, *5*, 107. (c) Shine, H. J. *Aromatic Rearrangements*; Elsevier: Amsterdam, 1967; p 89. (d) Rhoads, S. J. In *Molecular Rearrangements*; de Mayo, P. Ed.; Wiley-Interscience: New York, 1963; Vol. 1, pp 655–706.

(6) (a) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6984. (b) Burrows, C. J.; Carpenter, B. K. *Ibid.* **1981**, *103*, 6983. (c) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877.

(7) (a) Gajewski, J. J. *Acc. Chem. Res.* **1980**, *13*, 142. (b) Gajewski, J. J.; Gilbert, K. E. *J. Org. Chem.* **1984**, *49*, 11. (c) Gajewski, J. J.; Conrad, N. D. *J. Am. Chem. Soc.* **1979**, *101*, 2747.

(8) (a) Dewar, M. J. S.; Healy, E. F. *J. Am. Chem. Soc.* **1984**, *106*, 7127. (b) Curran, D. P.; Suh, Y.-G. *Ibid.* **1984**, *106*, 5002. (c) Addadi, L.; Jaffe, E. K.; Knowles, J. R. *Biochemistry* **1983**, *22*, 4494. (d) McMichael, K. D.; Korver, G. L. *J. Am. Chem. Soc.* **1979**, *101*, 2746.

(9) (a) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868. (b) Gajewski, J. J.; Emrani, J. *Ibid.* **1984**, *106*, 5733.

(10) (a) Wick, A. E.; Felix, D.; Steen, K.; Eschenmoser, A. *Helv. Chim. Acta* **1964**, *47*, 2425. (b) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Ibid.* **1969**, *52*, 1030. (c) Ficini, J.; Barbara, C. *Tetrahedron Lett.* **1966**, 6425. (d) Welch, J. T.; Eswarakrishnan, D. *J. Org. Chem.* **1985**, *50*, 5909.

(11) (a) Denmark, S. E.; Harmata, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 4972. (b) Denmark, S. E.; Harmata, M. A. *Tetrahedron Lett.* **1984**, *25*, 1543. (c) Ponaras, A. A. *J. Org. Chem.* **1983**, *48*, 3866.

(12) Koreeda, M.; Luengo, J. I. *J. Am. Chem. Soc.* **1985**, *107*, 5572.

(13) Barluenga, J.; Aznar, F.; Liz, R.; Bayod, M. *J. Chem. Soc., Chem. Commun.* **1984**, 1427.

(14) (a) Normant, J. F.; Reboul, O.; Sauvêtre, R.; Deshays, H.; Masure, D.; Villieras, J. *Bull. Soc. Chim. Fr.* **1974**, 2072. (b) Welch, J. T.; Samartino, J. S. *J. Org. Chem.* **1985**, *50*, 3663.

(15) Parallel investigations on the substituent contributions and mechanism of the Claisen rearrangement of chorismic acid to prephenic acid at Cornell University and Indiana University are described in the following paper.

(16) (a) Coates, R. M.; Hobbs, S. J. *J. Org. Chem.* **1984**, *49*, 140. (b) Coates, R. M.; Shah, S. K.; Mason, R. W. *J. Am. Chem. Soc.* **1982**, *104*, 2198.

(17) A similar addition–rearrangement mechanism was previously postulated by Dolby et al. to explain the *C*-alkylation of β-dicarbonyl compounds by 2-methoxy-1,3-butadiene: Dolby, L. J.; Elliger, C. A.; Esfandiara, S.; Marshall, K. S. *J. Org. Chem.* **1968**, *33*, 4508.

(18) (a) Pitteloud, R.; Petrzilka, M. *Helv. Chim. Acta* **1979**, *62*, 1319. (b) Petrzilka, M. *Ibid.* **1978**, *61*, 2286.

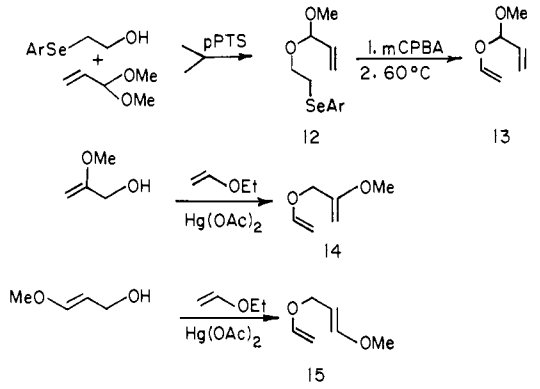
(19) (a) Curran, D. P.; Suh, Y.-G. *Carbohydr. Res.*, in press. (b) Curran, D. P.; Suh, Y.-G. *Tetrahedron Lett.* **1984**, *25*, 4179. (c) Curran, D. P. *Ibid.* **1982**, *23*, 4309.

(20) Nicolaou, K. C.; Magolda, R. L.; Sipio, W. J. *Synthesis* **1979**, 982.

(21) Coates, R. M.; Shaw, J. E. *J. Org. Chem.* **1970**, *35*, 2601.

(22) Reich, H. J.; Wollowitz, S.; Trend, J. E.; Chow, F.; Wendelborn, D. F. *J. Org. Chem.* **1978**, *43*, 1697.

Scheme II



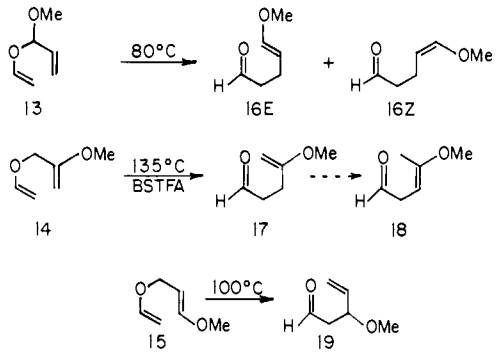
selenenyl electrophiles arising from benzeneselenenic acid generated in the elimination. This involves the following: (1) oxidation with 1 equiv of *m*-chloroperoxybenzoic acid (*m*-CPBA) in dichloromethane (−78 to 0 °C, 0.5–1.5 h); (2) addition of 2–4 equiv of triethylamine; and (3) dilution with pentane and warming to room temperature or reflux.[23] The products isolated from these reactions [**5a** (81%), **5b** (86%), **5c** (40%)] were identical with those previously formed by the thermal condensation of acrolein diethyl acetal with **3a–c**.[16a] The enol ether double bond was formed predominantly in the E configuration (93–98% E), in conformity with the usual stereoselectivity of the acrolein acetal condensations.[16] Evidently the intermediate α-ethoxyallyl enol ethers **4a–c** underwent rapid Claisen rearrangement at or below 20–35 °C!

The inability to detect the α-ethoxyallyl enol ethers **4a–c** during the preceding selenoxide eliminations raised the concern that the apparent Claisen rearrangements might have taken place via a dissociation–recombination mechanism. This possibility was readily discounted by a crossover experiment by using doubly labeled substrates. Oxidation of a 1:1 mixture of **9a-*d*$_5$** (acetal-OC_2D_5, 96% d_5) and **9b** (>99% d_0) provided **5a-*d*$_5$** (>90% d_5, <1% d_0) and **5b-*d*$_0$** (>99% d_0) after chromatographic separation. Clearly the migration of the ethoxyallyl group from oxygen to carbon is intramolecular.

The parent α-ethoxyallyl cyclopentenyl ether **4d** was more stable and proved amenable to isolation. Alkylation of the potassium enolate of cyclopentanone with the α-chloro ether in THF–dimethylsulfoxide (DMSO) at 25 °C gave seleno acetal **9d** in 18% yield after chromatographic purification. Oxidation of **9d** with mCPBA (CH_2Cl_2, $NaHCO_3/H_2O$, 25 °C),[25] followed by selenoxide elimination in pentane containing 4 equiv of dimethylamine,[22] afforded **4d** (44%) free of its ketonic isomer **5d**. When heated in benzene at reflux for 24 h, **4d** underwent smooth Claisen rearrangement to **5d** (97/3, E/Z) in 84% yield.

Allyl cyclopentenyl ether (**10**) and its 2-cyano derivative **11** were required as reference compounds for kinetic measurements. The former was prepared in 42% yield by acid-catalyzed elimination of allyl alcohol from cyclopentanone diallyl ketal at 110 °C.[26] The latter was prepared in 6% yield by the reaction of the potassium enolate of 2-cyanocyclopentanone with allyl bromide in DMSO.

Scheme III



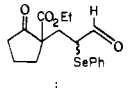
The syntheses of the simple methoxy-substituted allyl vinyl ethers **13–15** are outlined in Scheme II. The 4-methoxy derivative **13** was prepared by a two-step procedure.[27] Acetal exchange of excess acrolein dimethyl acetal with 2-(*o*-nitrophenylseleno)ethanol catalyzed by pyridinium *p*-toluenesulfonate provided mixed acetal **12** in 62% yield after flash chromatography. Oxidation of the selenide with mCPBA gave a stable selenoxide which was subjected to careful heating at 60 °C (1–2 mmHg) in a Kugelrohr apparatus. Enol acetal **13** distilled from the reaction in 48% yield. The use of the *o*-nitrophenylseleno derivative was crucial to the success of the elimination as the accelerating effect of the *o*-nitro group helps to offset the decelerating effect of the adjacent oxygen atom.[28] This method permitted isolation of **13** free of the rearrangement product **16**.

The 5- and 6-methoxyallyl vinyl ethers were each prepared by standard mercuric acetate-mediated exchange of the appropriate allylic alcohol with excess ethyl vinyl ether.[29] Enol ethers **14** and **15** were each isolated in about 30% yield by careful chromatography. The volatility of these compounds may have contributed to the modest yields. While compound **14** was quite stable, **13** and **15** were somewhat sensitive and decomposed upon prolonged storage at −20 °C. These new methoxy substituted allyl vinyl ethers all exhibit the expected simple ^{1}H NMR spectra (see Experimental Section).

Each allyl vinyl ether **13–15** underwent Claisen rearrangement in benzene to give the expected methoxy-substituted 4-pentenal **16**, **17**, and **19** (Scheme III). However, widely different temperatures were required to achieve reasonable reaction rates. Heating **13** in benzene at 80 °C (24 h, sealed tube) provided the known[30] aldehydes **16E** and **16Z** in 40% isolated yield. Again the E isomer predominated, but the ratio was somewhat lower than the above values (79/21). The allylically related isomer **15** rearranged to 3-methoxy-4-pentenal (**19**) at 100 °C. Aldehyde **19** was prone to elimination of methanol and was accordingly further characterized by sodium borohydride reduction to 3-methoxy-4-penten-1-ol (55% overall yield from **15**).

5-Methoxyallyl vinyl ether (**14**) was considerably less reactive, and heating at 135 °C for two days was required to complete the Claisen rearrangement. The rearrangement product **17** was invariably contaminated by substantial amounts of isomer **18** (stereochemistry not assigned). Control experiments demonstrated that **17** was converted to **18** under the reaction conditions. However, this annoying isomerization was completely suppressed by conducting the rearrangement in the presence of a small amount of *O,N*-bis(trimethylsilyl)trifluoromethylacetamide (BSTFA) as an acid/base scavenger. In this manner, **17** was isolated in 35% yield after flash chromatography.

(23) Oxidation of the seleno acetals with aqueous hydrogen peroxide[24] or sodium periodate[18] gave inferior yields of **5a–c** (31–48%). Seleno aldehyde **i** was isolated in 23% yield from the oxidation of **3a** with hydrogen peroxide. The presence of similar seleno aldehydes in the oxidations of **3b,c** was inferred from the ^{1}H NMR spectra of impure chromatography fractions. These byproducts presumably arise from the reaction of PhSeOH (or a related seleno electrophile) with the enol ether of the product. However, attempts to increase the yield of **4a**, by conducting the peroxide oxidation in the presence of 10 equiv of ethyl propenyl ether were unsuccessful, despite the formation of α-(phenylseleno)propionaldehyde in 52% yield.



i

(24) (a) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434. (b) Renga, J. M.; Reich, H. J. *Org. Synth.* **1979**, *59*, 58.
(25) Anderson, W. K.; Veysoglu, T. *J. Org. Chem.* **1973**, *38*, 2267.
(26) (a) Lorette, N. B.; Howard, W. L. *J. Org. Chem.* **1961**, *26*, 3112. (b) Lorette, N. B.; Howard, W. L. *Ibid.* **1960**, *25*, 521.
(27) For examples of this general approach, see: Rollin, P.; Bencomo, V. V.; Sinay, P. *Synthesis* **1984**, 134. Ho, T.-L.; Hall, T. W. *Synth Commun.* **1975**, *5*, 367.
(28) Sharpless, K. B.; Young, M. W. *J. Org. Chem.* **1975**, *40*, 947.
(29) (a) 2-Methoxyallyl alcohol was prepared by reduction of methyl 2-methoxyacrylate (Wermuth, C.-G.; Marx, H. *Bull. Soc. Chim. Fr.* **1964**, 732). (b) 3-Methoxyallyl alcohol: Vo Quang, Y.; Marias, D.; Vo Quang, L.; Legoffic, F. *Tetrahedron Lett.* **1983**, *24*, 5209.
(30) Arnould, J. C.; Pete, J. P. *Tetrahedron* **1975**, *31*, 815.

Table I. Rate Constants, Relative Rates, and Activation Parameters for Rearrangements of Allyl Vinyl Ethers in Various Solvents

enol ether	in benzene-d_6 at 80 °C				in other solvents at various temp		
	10^6k, s^{-1}	k_{rel}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	solvent	T, °C	k_{rel}
 1	0.649[a]	(1.0)[a]	25.4 ± 0.7[a]	−15.9 ± 1.5[a]	benzene-d_6	134	(1.0)
					acetonitrile-d_3	134	1.5
					methanol-d_4[b]	134	1.7
 13	62.1	96	22.4 ± 0.4	−14.7 ± 1.0	benzene-d_6	65	(1.0)
					acetonitrile-d_3	65	2.1
					methanol-d_4[b]	65	18
 14	0.0161	0.025	30.9 ± 0.9	−7.0 ± 2.0	benzene-d_6	139	(1.0)
					acetonitrile-d_3	139	1.5
					methanol-d_4	139	*c*
 15	6.12	9.5	24.7 ± 0.3	−12.8 ± 0.7	benzene-d_6	80	(1.0)
					acetone-d_6	80	1.5
					acetonitrile-d_3	80	3.2
					methanol-d_4[b]	80	68

[a] Kinetic data for allyl vinyl ether **1** taken from Carpenter and Burrows (ref 6b)—see ref 31. [b] The aldehyde product existed largely to exclusively in the hemiacetal form. [c] The Claisen rearrangement product was not detected in this solvent; however, the rate of disappearance of **14** was not consistent with a significant rate increase.

Table II. Rate Constants, Relative Rates, and Activation Parameters for Rearrangements of Allyl Cyclopentenyl Ethers in Various Solvents[a]

enol ether	solvent	T, °C	10^5k,[b] s^{-1}	k_{rel} 20.5 °C	k_{rel} 96.9 °C	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
 10	benzene-d_6	117.9	27.2				
		96.9	5.58		(1.0)	21.0 ± 1.0	−21.8 ± 3.0
		20.9	0.00025[c]	(1.0)			
	acetonitrile-d_3	96.9	10.5		1.9		
	ethanol-d_6[d]	96.9	15.0		2.7		
	80% aq ethanol-d_6[d]	96.9	21.9		3.9		
 11	benzene-d_6	117.9	17.6				
		96.9	3.66		0.66	20.8 ± 1.4	−23.1 ± 3.8
		20.5	0.00018[c]	0.70	1.6		
	acetonitrile-d_3	96.9	9.16		1.3		
	ethanol-d_6	96.9	7.23				
 4d	benzene-d_6	96.9	230[c]		41	17.2 ± 0.6	−24.4 ± 2.0
		63.2	19.4				
		44.8	4.56				
		20.5	0.405	159			
	acetonitrile-d_3	96.9	954[c]		170	18.2 ± 0.8	−18.9 ± 2.6
		44.8	14.3				
		20.5	1.21	456			
	ethanol-d_6[d]	96.9	1770[c]		320	14.4 ± 1.0	−28.0 ± 3.4
		44.8	61.9				
		20.5	8.63	3400			
	80% aq ethanol-d_6[d]	96.9	2810[c]		504	12.7 ± 0.4	−31.8 ± 1.5
		44.8	145				
		20.5	25.4	10000			

[a] In sealed NMR tubes under nitrogen at ca. 0.23 M. Kinetic data obtained by integration of 200-MHz ^{1}H NMR spectra. [b] Average of two, and in some cases three, runs. The deviation from the average was ±1–10%. [c] Extrapolated value. [d] Containing ca. 1 equiv of pyridine-d_5.

Kinetic Studies

The absolute first order rate constants for the Claisen rearrangement of 4-, 5-, and 6-methoxyallyl vinyl ether (**13**, **14**, and **15**) in benzene-d_6 at 80 °C are listed in Table I. For comparison, the rate of rearrangement of allyl vinyl ether itself is also included.[31] These rates were determined by conducting the rearrangements in benzene over a temperature range of about 40 °C, and the progress of the reactions was monitored by ^{1}H NMR. Each rearrangement followed first-order kinetics over several half-lives, and no products other than the rearranged aldehydes could be detected. The rates of rearrangement of the four substrates vary over a range of about 4000. 4-Methoxy derivative **13** rearranges quite rapidly at 80 °C ($t_{1/2}$ = 3.3 h), while its allylic isomer **15** is not quite as fast. On the other hand, allyl vinyl ether rearranges quite slowly at this temperature ($t_{1/2}$ = 13 days), and the 5-methoxy derivative **14** is virtually unreactive.

The results of a study of the solvent effects on the rate of rearrangement of the four substrates are also compiled in Table I. Because of the widely differing rates, the rearrangements were conducted at different temperatures and should not be quantitatively compared. However, the qualitative trends are quite evident. Both the 4- and 6-methoxyallyl vinyl ethers show a significant rate increase in methanol. On the other hand, allyl vinyl ether and the 5-methoxy derivative show at most a very small solvent effect.

The rates of Claisen rearrangement of the α-ethoxyallyl cyclopentenyl ether **4d** and reference compounds **10** and **11** are collected in Table II. These were determined at appropriate temperatures in the range of 20.5–117.9 °C by integration of the ^{1}H NMR spectra. About 1 equiv of pyridine-d_5 was added to the reactions conducted in ethanol-d_5 and aqueous ethanol-d_5. All reactions exhibited good first-order kinetics over 2 half-lives, and no products other than the γ-ethoxyallyl ketones could be detected in the NMR spectra. The deviation of the rate constants from the average of duplicate or triplicate runs was 1–6%. The rearrangement of **4d** is clearly accelerated by the presence of the 4-ethoxy group ($k_{rel}^{20.5°C}$ = 159 in benzene) and even occurs slowly

(31) These data are taken from Carpenter and Burrows (ref 6b). This study was performed in di-*n*-butyl ether, rather than benzene; however, a brief kinetic determination by the Pittsburgh group has indicated that the rates in the two solvents are very similar.

at room temperature ($t^{20.5°C}$ = 2 days). Again significantly larger rate increases are observed in ethanol and 80% aqueous ethanol compared to those of the reference compounds **10** and **11**.

Separate but identical oxidation–elimination operations were carried out on seleno acetals **9b** and **9d** in pentane containing triethylamine (25 °C) to obtain a lower limit for the rearrangement rate of the cyano-substituted α-ethoxyallyl vinyl ether **4b** relative to **4d**. The rate of rearrangement of **4b** is estimated to be at least 45 times that of **4d** in pentane at 25 °C based on approximate NMR detection limits for the presence of **4b** and **5d** in the products.

Discussion

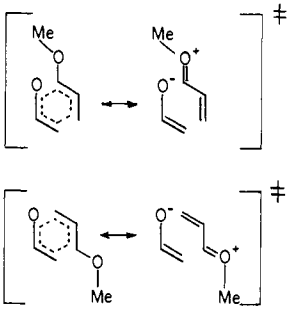
The accelerating influence of oxy substituents and other donor groups on the rates of the Cope,[32] Claisen,[8b,9-14] and various [1,3]sigmatropic rearrangements[33-36] has been amply demonstrated. Alkoxy and hydroxy in particular have been shown to lower the activation energies by 2.4–15.1 kcal/mol.[9,32a,33,34a,35a] The synthetic applications of sigmatropic rearrangements in general and the Claisen rearrangement in particular[9a,12,19,37] have been greatly enhanced by the use of such oxygenated substrates. An understanding of the origin of these substituent effects is clearly of both mechanistic and synthetic significance.

A number of recent theoretical treatments have attempted to predict and/or correlate the effect of alkoxy and other substituents on the rate of the aliphatic Claisen rearrangement. HMO calculations by Carpenter and Burrows[6] using phenyl anion as model for the cyclic transition state predict that a donor group at positions 1, 2, and 4 will lower the energy of the transition-state (TS) while a donor group at positions 5 and 6 should have the opposite effect. MNDO calculations by Dewar[8a] indicate a two-stage mechanism via an intermediate radicaloid that collapses to the product without activation energy. Methoxy groups at positions 2 and 5 are predicted to lower the activation energy. Finally, a thermochemically based empirical approach for estimating substituent effects on the Claisen and Cope rearrangements has been developed by Gajewski.[7] Stabilization of the products by resonance interactions (e.g., enol[38] or ester[9b]) is considered to be an important factor.

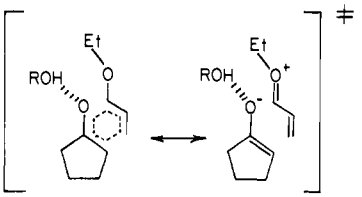
The kinetic data in Tables I and II document considerable rate enhancement from alkoxy substituents at positions 4 and 6. Thus, **4d** and **13** rearrange 159 and 96 times faster than the parent allyl vinyl ethers in benzene at 20.5 and 80 °C, respectively.[39] Allylically related isomer **15** rearranges 9.5 times faster than **1** in benzene at 80 °C. These rate enhancements occur despite appreciable thermodynamic stabilization of the reactants. Acetals **4d** and **13** must be stabilized by the anomeric effect[40] while **15** benefits from both enol ether resonance[41] and vinylogous anomeric effect stabilization.[8b,19a,43] In contrast, the 5-alkoxy substituent imparts a 40-fold rate retardation.

The rearrangement rates of the 4- and 6-alkoxyallyl enol ethers are quite sensitive to solvent polarity. While small but consistent increases are observed in acetonitrile (2.1–4.1-fold), the hydrogen bonding solvents—methanol, ethanol, and 80% aqueous ethanol—lead to marked rate enhancements ranging from 18- to 68-fold relative to the rates in benzene. In contrast, the two unsubstituted enol ethers **1** and **10** rearrange only slightly faster in the same hydrogen bonding solvents (**1**, $k_{MeOH}/k_{C_6H_6}$ = 1.7 at 134 °C; **10**, $k_{aq\ EtOH}/k_{C_6H_6}$ = 3.9 at 96.9 °C).

The accelerating influence of the 4- and 6-alkoxy groups and the pronounced solvent effects in hydrogen bonding media are attributed to an increased dipolar character of the TS for the Claisen rearrangement. That is, partial delocalization of a nonbonded electron pair from the donor substituent generates a significant degree of enolate–oxonium ion pair character that stabilizes the TS more than the ground state. The effects of substituents and solvents on the aromatic Claisen rearrangement[5d,43] have been similarly interpreted in terms of a weakly polarized TS.[5d] The small solvent effects on the rearrangements of the parent allyl vinyl ethers **1** and **10** probably reveal a nascent polarization which is magnified by the presence of the 4- and 6-alkoxy groups. On the other hand, the lack of a solvent effect on the rate of the [1,3] rearrangement of 7-alkoxynorbornadiene was taken as a sign of diradical character in the TS.[35a]



The exponential rate enhancements of aromatic Claisen rearrangements by protic and Lewis acid catalysts[44] no doubt arise from protonation or coordination at oxygen. Accordingly it seems reasonable to propose that hydrogen bonding specifically to the enol ether oxygen of 4- and 6-alkoxy substrates is responsible for a major part of the rate increases observed in alcohol solvents. The more negative entropies of activation for the rearrangement of **4d** in ethanol ($\Delta S^{\ddagger}$ = −28 eu) and 80% aqueous ethanol ($\Delta S^{\ddagger}$ = −31.8 eu) may reflect increased ordering of solvent molecules arising from stronger hydrogen bonding in the TS.



Previous studies by the Pittsburgh group with dihydropyrans such as **7** strongly suggested that a 6-alkoxy substituent accelerates the Claisen rearrangement.[8b,19] The present work confirms the generality of this phenomenon and supports the rationale of a "vinylogous kinetic anomeric effect".[8b] Similarly the influence of the 4-alkoxy substituents may be regarded as a kinetic anomeric

(32) (a) Berson, J. A.; Walsh, E. J., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4730. (b) Evans, D. A.; Golob, A. M. *Ibid.* **1975**, *97*, 4765. (c) Evans, D. A.; Nelson, J. V. *Ibid.* **1980**, *102*, 774.

(33) Vinylcyclopropane rearrangements: (a) Simpson, J. M.; Richey, H. G., Jr. *Tetrahedron Lett.* **1973**, 2545. (b) Trost, B. M.; Scudder, P. H. *J. Org. Chem.* **1981**, *46*, 506. (c) Paquette, L. A.; Wells, G. J.; Horn, K. A.; Yan, T.-H. *Tetrahedron* **1983**, *39*, 913.

(34) Vinylcyclobutane rearrangements: (a) Scheidt, F.; Kirmse, W. *J. Chem. Soc., Chem. Commun.* **1972**, 716. (b) Danheiser, R. L.; Martinez-Davila, C.; Sard, H. *Tetrahedron* **1981**, *37*, 3943.

(35) Norbornadiene to cycloheptatriene rearrangement: (a) Lustgarten, R. K.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1974**, *96*, 6393. (b) Franzus, B.; Scheinbaum, M. L.; Waters, D. L.; Bowlin, H. B. *Ibid.* **1976**, *98*, 1241.

(36) Dienyl alkoxides: (a) Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559. (b) Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050.

(37) (a) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48. (b) Whitesell, J. K.; Helbling, A. M. *Ibid.* **1980**, *45*, 4135. (c) Ager, D. J.; Cookson, R. C. *Tetrahedron Lett.* **1982**, *23*, 3419. (d) Sato, T.; Tajima, K.; Fujisawa, T. *Ibid.* **1983**, 729. (e) Kallmerten, J.; Gould, T. J. *Tetrahedron Lett.* **1983**, *24*, 5177. (f) Bartlett, P. A.; Tanzella, D. J.; Barstow, J. F. *J. Org. Chem.* **1982**, *47*, 3941. (g) Burke, S. D.; Fobare, W. F.; Pacofsky, G. J. *Ibid.* **1983**, *48*, 5221.

(38) Thies, R. W.; Wills, M. T.; Chin, A. W.; Schick, L. E.; Walton, E. S. *J. Am. Chem. Soc.* **1973**, *95*, 5281.

(39) It is interesting to note that the cyclopentenyl analogue **4d** rearranges 8 times faster than **13** at 70.5 °C in benzene. This effect may be attributed to the alkyl substituent at C-1 (see ref 9a).

(40) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: New York, 1983.

(41) Rhoads, S. J.; Waali, E. E. *J. Org. Chem.* **1970**, *35*, 3358.

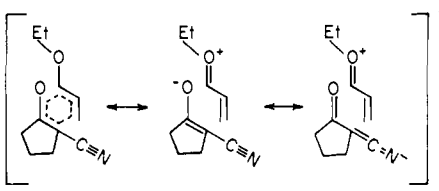
(42) (a) Denmark, S. E.; Dappen, M. S. *J. Org. Chem.* **1984**, *49*, 798. (b) Lessard, J.; Saunders, J. K.; Phan Viet, M. T. *Tetrahedron Lett.* **1982**, *23*, 2059.

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

(44) (a) Protic acid catalysis: Svanholm, U.; Parker, V. D. *J. Chem. Soc., Chem. Commun.* **1972**, 645. (b) Lewis acid catalysis: Borgulya, J.; Madeja, R.; Fahrni, P.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 14. (c) For a recent review, see: Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.

effect.[40] These expressions imply the existence of a stereoelectronic dependence of the rate acceleration upon the conformation of the 4- and 6-alkoxy groups. The larger rate enhancing effect of the 4-methoxy group (k_{rel} = 96 in benzene at 80 °C) compared to the 6-methoxy group (k_{rel} = 9.5 in benzene at 80 °C) is attributable to a partial gain of enol ether stabilization in the TS of the former and its partial loss in the latter.

The combination of a 6-ethoxy group with an electron-withdrawing group at C-1 as in **4a–c** results in even faster rates. Although the rapid rearrangement of these acetals under the conditions of selenoxide elimination precluded kinetic measurements, the rearrangement of **4b** (R = CN) is estimated to be at least 45 times faster than that of **4d** (R = H). In contrast, a cyano group alone (**11**) exerts a slight decelerating influence on the rate (k_{rel} = 0.66 in benzene at 96.9 °C).[6b] The synergistic effect of the cyano and ethoxy groups in **4b** can be rationalized by further delocalization of negative charge in the partially polarized TS.[45]



α-Ethoxyallyl enol ethers such as **4a–c** were postulated as intermediates in the O-alkylation–Claisen rearrangement mechanism for the thermal condensation of acrolein diethyl acetal with β-dicarbonyl compounds (**3** → **4** → **5**).[16,17] It is now apparent that acetal exchange rather than rearrangement must be the rate-determining step if this two-step mechanism is valid. The α-ethoxy allyl enol ethers rearrange spontaneously even at room temperature.

The 5-methoxy derivative **14** rearranges significantly slower than allyl vinyl ether itself, and no appreciable solvent effect could be detected in this case. This is one of the few substituents which retards the Claisen rearrangement, and the decelerating effect is the strongest to be quantified. This effect has recently been recognized by Parker and Farmar in the context of a series of intramolecular competition experiments.[46]

Carpenter's theoretical model[6b,c] for the TS correctly predicted the accelerating and decelerating effects of a donor group at the 4- and 5-positions on the allyl group. However, a decelerating effect was incorrectly predicted for a donor group at C-6. A MNDO treatment by Dewar[8a] indicated a bond-making TS that resembles 2-oxacyclohexane-1,4-diyl. However, the credibility of this model is diminished by its incorrect prediction of a rate acceleration from a 5-methoxy group. The relative magnitude of secondary deuterium and tritium isotope effects point to an early TS in which bond breaking is significantly more advanced than bond making.[7c,9b,8c]

It is appropriate to address the question whether the 4- and 6-alkoxy substituents might actually alter the mechanism of the Claisen rearrangement. The enhanced rates and solvent effects might be taken to indicate a two-step mechanism via a short-lived enolate–oxonium ion pair.[47] Although the distinction between concerted and two-step mechanisms may be subtle, in our opinion the likelihood of ion pair intermediates in the present cases is diminished by the following considerations. (1) The entropies of activation for the rearrangements of the unsubstituted, 4- and 6-alkoxy substrates are quite similar. This seems more consistent with a common mechanism and similar TSs. The possibility of a change from a cyclic conformation in the TS to an extended array seems unlikely for this reason. (2) The 19.2 kcal/mol rotational barrier for the 1-methoxyallyl carbonium ion (FSO_3H at −20 °C)[48] provides a reasonable estimate for the stabilization of an allyl carbonium ion by an alkoxy group. However, the ca. 10^3 rate increase resulting from the 4-ethoxy group (**4d**, $k_{rel} \leq$ 2600 in 80% aqueous ethanol at 20.5 °C) corresponds to only 4 kcal/mol stabilization of the TS. The 15 kcal/mol discrepancy seems too large to attribute to ion pair stabilization. (3) The solvent effects appear to be too small for a reaction producing ions. For example, the stepwise [2+2]cycloaddition of tetracyanoethylene to enol ethers via a zwitterionic intermediate proceeds ca. 10^3 times more rapidly in acetonitrile than in benzene.[49] This contrasts with the small rate increases (2–4-fold) for the rearrangements of **4d**, **13**, and **15** in the same solvents. The solvolysis rate of *tert*-butyl chloride is 100 times greater in 80% aqueous ethanol than in ethanol at 25 °C,[50] whereas the rearrangement rate of **4d** is increased only 3 times by the same solvent change at 20.5 °C. (4) One might expect to observe products arising from dissociation of the ion pairs and capture of the free ions in protic nucleophilic solvents.[51] However, the only products detected during the rearrangements of **4d**, **13**, and **15** were **5d**, **16**, and **18**, respectively.

While the preceding points argue strongly against the intermediacy of ion pairs having appreciable oxonium ion character, the possibility of a bidentate ion pair stabilized by simultaneous interactions at all four termini cannot be excluded. Such a species may not exhibit the characteristics normally associated with carbonium ions or ion pairs in solution. The existence of a bidentate allyl–carboxylate ion pair has been demonstrated.[52]

In conclusion, the accelerated rates and markedly enhanced solvent effects associated with the Claisen rearrangements of 4- and 6-alkoxyallyl enol ethers provide strong evidence for a pronounced dipolar character of the pericyclic TS. These findings should aid in the design of synthetically useful Claisen rearrangements which are accelerated by interactions with one or more substituents.

Experimental Section

General Aspects. Proton NMR spectra at 90, 200, 220, and 360 MHz were obtained with Varian EM-390, XL-200, and HR-220, and Nicolet NTC-360 spectrometers, respectively. ^{13}C NMR spectra were recorded at 15, 50, or 90 MHz through the use of JOEL FX-60, Varian XL-200, and Nicolet NTC-360 spectrometers, respectively. The ^{13}C NMR spectral data are reported in the following manner when isomers are assignable: chemical shifts (multiplicities, assignments, respective isomers). Infrared (IR) spectra were recorded on Perkin-Elmer 137 and 1320 and IBM IR/32 spectrometers. Mass spectra were obtained on Varian MAT CH-5 and 731 spectrometers by the Mass Spectrometry Center at the University of Illinois. Elemental analyses were provided by the Microanalytical Laboratory of the University of Illinois. Analytical gas chromatography (GC) was performed on a Varian Model 3700 gas chromatograph by using a 1.8-m × 6.4-mm column of 3% OV-17 on 100/120 mesh Chromosorb Q. Centrifugally enhanced preparative thin-layer chromatography was performed with a Harrison Research Model 7924T Chromatotron on either a 2- or 4-mm thickness of silica gel 60 PF_{254} "containing gypsum". The coated plates used were prepared in this laboratory and were suitable for use in the quantitative separation of 2 mg each of the 2,4-DNP derivatives of cyclopentanone and cyclohexanone with 1 mm or less of band wobble. Flash chromatography was performed according to the procedures of Still and coworkers[53] on Woelm 32-63 μ silica gel. Kugelrohr distillations were

(45) The possibility of a through-resonance interaction between donor and acceptor groups in a pseudo-para relationship on the pericyclic TS was brought to our attention in a letter from Dr. Barry Carpenter (July 12, 1983). We are grateful to Dr. Carpenter for helpful discussions and correspondence during the course of this research.

(46) Parker, K. A.; Farmer, J. G. *Tetrahedron Lett.* **1985**, *26*, 3655. Caution must be exercised in interpreting the results of such intramolecular competition experiments since each appendage must be regarded as a substituent in the rearrangement of its partner.

(47) The possibility of ion pair intermediates in the aromatic Claisen rearrangement has been given serious consideration. See: (a) Cram, D. J. In *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; J. Wiley: New York, 1956; Chapter 5, pp 295–303. (b) White, W. N.; Gwynn, D.; Schlitt, R.; Girardi, C.; Fife, W. *J. Am. Chem. Soc.* **1958**, *80*, 3271. (c) Goering, H. L.; Jacobson, R. R. *Ibid.* **1958**, *80*, 3277.

(48) (a) Childs, R. F.; Hagar, M. E. *Can. J. Chem.* **1980**, *58*, 1788. (b) Blackburn, C.; Childs, R. F.; Cremer, D.; Gauss, J. *J. Am. Chem. Soc.* **1985**, *107*, 2442.

(49) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117.

(50) (a) Fainberg, A. H.; Winstein, S. *J. Am. Chem. Soc.* **1956**, *78*, 2770. (b) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; J. Wiley: New York, 1963; pp 297–300.

(51) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 199.

(52) (a) Goering, H. L.; Doi, J. T.; McMichael, K. D. *J. Am. Chem. Soc.* **1964**, *86*, 1951. (b) Goering, H. L.; Pombo, M. M. *Ibid.* **1960**, *82*, 2515.

(53) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

performed with a Buchi GKR-50 apparatus. The temperatures associated with Kugelrohr distillations are oven temperatures. Boiling points are uncorrected.

Technical grade hexane and ethyl acetate used for chromatography were distilled prior to use. Quinoline, triethylamine, 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU), and dimethyl sulfoxide (Me_2SO) were purified by distillation from calcium hydride. Tetrahydrofuran (THF) and hexamethylphosphoramide (HMPA) were purified by distillation from sodium benzophenone ketyl and barium oxide, respectively. Pentane and dichloromethane were dried by storage over calcium sulfate and 4A molecular sieves, respectively. All other reagents and solvents were reagent grade or better and used without further purification.

Propionaldehyde diethyl acetal was prepared by the method of Adkins:[54] yield 29.90 g (74%); bp 122–125 °C (lit.[55] bp 123 °C).

Propionaldehyde Di(ethyl-d_5) Acetal: yield 3.81 g (70%); bp 122–123 °C; IR (neat) ν_{max} 2210, 2085 (C-D) cm^{-1}.

2-Oxocyclopentanecarbonitrile (2-cyanocyclopentanone) was prepared by the procedure of Thompson[56] and Thorpe.[57] The Thorpe–Ziegler condensation of adiponitrile with sodium *tert*-butoxide as base[56] afforded 2-aminocyclopent-1-enecarbonitrile in 60.78 g (56%) yield as tan crystals: mp 146.5–147.5 °C (lit.[56] mp 147–148 °C). The cyano enamine was hydrolyzed to the keto nitrile by the following modification of the procedure of Thorpe.[57]

To 400 mL of 1 N hydrochloric acid was added with stirring 60.8 g (0.562 mol) of 2-aminocyclopent-1-enecarbonitrile. After 3 h at room temperature, an additional 200-mL portion of 1 N hydrochloric acid was added. Stirring continued for 1 h, after which the solution was saturated with ammonium sulfate, and extracted with 3 portions of ether. The ethereal extracts were dried ($MgSO_4$) and evaporated. Distillation provided 54.9 g (89%) of 2-oxocyclopentanecarbonitrile: bp 93 °C (1.0 mmHg) [lit.[16a] bp 103–120 °C (2.8–4.8 mm)].

(*E*)- and (*Z*)-1-ethoxypropenes were prepared according to the procedure of Scheibler[58] with some modifications. A suspension of 4.23 g (29.8 mmol) of powdered phosphorus pentoxide in 3.22 g (24.9 mmol) of dry quinoline was stirred at 25 °C as a 3.29-g (24.9 mmol) portion of propionaldehyde diethyl acetal was added. The resulting suspension was distilled through a short-path apparatus into an ice bath cooled receiving flask. The oil bath temperature was increased so as to maintain a still-head temperature of 40–60 °C. The distillation was stopped when no more distillate was obtained at a bath temperature of 150 °C. The distillate was washed with several 5-mL portions of saturated aqueous sodium bicarbonate and once with water before drying (K_2CO_3). Filtration of the neat liquid gave 1.70 g (75%) of 1-ethoxypropene which was a 77:23 (Z:E) mixture of isomers as determined from the ^1H NMR spectrum. GC analysis showed that the product was contaminated with 6% by weight of ethanol and 11% by weight of starting acetal. This material was of sufficient purity for use in the next step. The ^1H NMR and IR spectral data for the product matched those of a commercial sample.

(*E*)- and (*Z*)-1-(ethoxy-d_5)propenes were prepared by the preceding procedure. The yield was 1.42 g (63%) as a colorless liquid which was a 75:25 (Z:E) mixture of isomers: MS (70 eV), *m/e* (rel abundance) 91 (33), 90 (1.5), 59 (55), 58 (base); deuterium distribution 96% d_5, 3.7% d_4, 0.1% d_3, 0.02% d_2, 0.02% d_1, 0.2% d_0.

Ethyl 2-[1-Ethoxy-2-(phenylseleno)propoxy]-1-cyclopentene-1-carboxylate (9a). A solution of α-chloro-β-(phenylseleno)propyl ethyl ether was prepared by adding a 5.4-mL (4.1 g, 49 mmol) portion of ethyl propenyl ether to a solution of 8.36 g (43.8 mmol) of benzeneselenyl chloride (Aldrich Chemical Co.) in 250 mL of pentane which was kept under nitrogen at 25–30 °C. The initial deep red color of the selenyl chloride solution immediately changed to a yellowish color, and this was judged to be the end of the reaction. The solution of crude α-chloro ether was used in the next step within 5 min of its preparation. The freshly prepared solution was stirred under nitrogen at room temperature as a solution of 5.47 g (35.0 mmol) of 2-carbethoxycyclopentanone, 7.97 g (52.4 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 6.2 mL (36 mmol) of hexamethylphosphoramide (HMPA) in 70 mL of THF was added over 45 min. The resulting suspension was stirred for an additional 30 min at room temperature, the suspended salts were filtered, and the resulting filtrate was evaporated. A solution of the residue in 200 mL of ether was washed 5 times with water and once with saturated sodium chloride, dried (K_2CO_3), and evaporated to afford 15.1 g of crude **9a**. Purification by flash chromatography (9% ethyl acetate, 1% triethylamine–hexane eluant) afforded 12.8 g (92%) of **9a** as a 60:40 mixture of diastereomers: IR (neat) ν_{max} 1710, 1690, (C=O), 1640 (C=C), 742, 692 (C_6H_5) cm^{-1}; ^1H NMR (360 MHz, C_6D_6), δ 0.99 (t, 1.5 H, *J* = 7.0 Hz, ether OCH_2CH_3), 1.05 (t, 1.5 H, *J* = 7.0 Hz, ether OCH_2CH_3), 1.07 (t, 3 H, *J* = 7.0 Hz, ester OCH_2CH_3), 1.39–1.57 (m, 2 H, ring CH_2), 1.62 (d, 1.5 H, *J* = 7.0 Hz, $SeCHCH_3$), 1.67 (d, 1.5 H, *J* = 7.1 Hz, $SeCHCH_3$), 2.08–2.19, 2.27–2.35, 2.58–2.69 (m, 4 H, ring CH_2), 3.23–3.67 (m, 3 H, SeCH and ether OCH_2), 4.05–4.18 (m, 2 H, ester OCH_2), 5.17 (d, 0.5 H, *J* = 5 Hz, acetal CH), 5.29 (d, 0.5 H, *J* = 4.1 Hz, acetal CH), 6.96–7.05 (m, 3 H, Ar H), 7.50–7.63 (m, 2 H, Ar H); ^{13}C NMR (15 MHz, C_6D_6) δ 14.7, 15.1, 15.7, 16.5, 19.7, 29.9, 32.4 (ring CH_2, ester and ether OCH_2CH_3, $SeCHCH_3$), 42.3, 43.0 ($SeCHCH_3$), 59.2, 62.5, 63.7 (ester and ether OCH_2), 104.7, 105.0, 107.3, 107.7 (acetal CH and C=COEt), 126.4, 127.8, 128.0, 129.3, 129.6, 134.9 (Ar C and C_6D_6), 164.4, 164.7, 165.4 (=COEt and ester C=O); MS (70 eV), *m/e* (rel abundance) 398 (M^+ for ^{80}Se, 0.6), 396 (M^+ for ^{78}Se, 0.4), 243 (19), 241 (11), 214 (15), 212 (8). An analytical sample was prepared in an earlier run by flash chromatography. Anal. Calcd for $C_{19}H_{26}O_4Se$: C, 57.43; H, 6.59; Se, 19.87. Found: C, 57.41; H, 6.78; Se, 19.81.

2-[1-Ethoxy-2-(phenylseleno)propoxy]-1-cyclopentene-1-carbonitrile (9b) was prepared according to the procedure used in the preparation of **9a**. Flash chromatography (19% ethyl acetate, 1% triethylamine–hexane eluant) provided 7.58 g (81%) of **9b** as a 50:50 mixture of diastereomers: IR (neat) ν_{max} 2200 (C≡N), 1640 (C=C), 742, 692 (C_6H_5) cm^{-1}; ^1H NMR (360 MHz, C_6D_6) δ 0.99 (t, 1.5 H, *J* = 7.0 Hz, OCH_2CH_3), 1.02 (t, 1.5 H, *J* = 7.1 Hz, OCH_2CH_3), 1.28 (m, 2 H, ring CH_2), 1.49 (d, 1.5 H, *J* = 6.7 Hz, $SeCHCH_3$), 1.50 (d, 1.5 H, *J* = 5.7 Hz, $SeCHCH_3$), 1.90–2.15 (m, 4 H, ring CH_2), 3.19–3.58 (m, 3 H, SeCH and OCH_2), 5.41 (d, 0.5 H, *J* = 4.7 Hz, acetal CH), 5.55 (d, 0.5 H, *J* = 4.4 Hz, acetal CH), 6.91–7.12 (m, 3 H, Ar H), 7.51–7.58, 7.62–7.72 (m, 2 H, Ar H); ^{13}C NMR (15 MHz, C_6D_6) δ 14.9, 15.7, 16.4 ($SeCHCH_3$ and OCH_2CH_3), 20.3, 30.3, 31.8 (ring CH_2), 41.8, 42.2 ($SeCHCH_3$), 63.5, 64.1 (OCH_2), 83.9 (N≡C*C*=C), 105.1, 105.3 (acetal CH), 116.3 (C≡N), 126.2, 127.8, 129.2, 129.5, 134.9, 135.3, 135.8 (Ar C and C_6D_6), 169.6, 170.2 (N≡CC=*C*); MS (70 eV), *m/e* (rel abundance) 351 (M^+ for ^{80}Se, 5), 349 (M^+ for ^{78}Se, 3), 243 (83), 241 (42), 214 (21), 212 (10); exact mass *m/e* calcd for $C_{17}H_{21}O_3{}^{80}Se$ 351.0737; found 351.0730.

3-[1-Ethoxy-2-(phenylseleno)propoxy]-2-methyl-2-cyclopentene-1-one (9c) was prepared by the procedure for the preparation of **9a**. Flash chromatography (49% ethyl acetate, 1% triethylamine–hexane eluant) gave 7.62 g (58%) of **9c** as a 60:40 mixture of diastereomers: IR (neat) ν_{max} 1690 (C=O), 1640 (C=C), 742, 694 (C_6H_5) cm^{-1}; ^1H NMR [360 MHz, C_6D_6, 60:40 (A:B) mixture of diastereomers] δ 0.94 (t, 1.8 H, *J* = 7.0 Hz, OCH_2CH_3, isomer A), 0.99 (t, 1.2 H, *J* = 7.0 Hz, OCH_2CH_3, isomer B), 1.39 (d, 1.8 H, *J* = 7.1 Hz, $SeCHCH_3$, isomer A), 1.46 (d, 1.2 H, *J* = 7.1 Hz, $SeCHCH_3$, isomer B), 1.69 (s, 1.2 H, ring CH_3, isomer B), 1.79 (s, 1.8 H, ring CH_3, isomer A), 1.88–2.14 (m, 4 H, ring CH_2), 2.99–3.45 (m, 3 H, OCH_2 and SeCH), 5.06 (d, 0.6 H, *J* = 4.9 Hz, acetal CH, isomer A), 5.15 (d, 0.4 H, *J* = 4.7 Hz, acetal CH, isomer B), 6.88–7.08 (m, 3 H, Ar H), 7.43–7.52 (m, 2 H, Ar H); ^{13}C NMR (15 MHz, C_6D_6) δ 6.3, 14.9, 15.8, 16.1 (ring CH_3, $SeCHCH_3$, and OCH_2CH_3), 25.4, 33.7 (ring CH_2), 41.9, 42.4 (SeCH), 63.3, 63.7 (OCH_2), 103.5, 103.9 (acetal CH), 117.0, 117.2 (*C*=COR), 126.2, 127.9, 129.2, 134.9 (Ar C and C_6H_6), 180.4, 180.9 (=COR), 203.0, 203.2 (ketone C=O); MS (10 eV), *m/e* (rel abundance) 354 (M+ for ^{80}Se, 2), 352 (M^+ for ^{78}Se, 1), 243 (13), 241 (6), 214 (48), 212 (27); exact mass *m/e* calcd for $C_{17}H_{22}O_3{}^{80}Se$ 354.0734, found 354.0720. Anal. Calcd for $C_{17}H_{22}O_3Se$: C, 57.79; H, 6.28; Se, 22.35. Found: C, 58.13; H, 6.38; Se, 22.37.

Ethyl 1-(3-Ethoxy-2-propenyl)-2-oxocyclopentanecarboxylate (5a). Method A. Oxidation with *m*-Chloroperoxybenzoic Acid (*m*-CPBA). A modification of the procedure of Reich and co-workers[22] was used. A solution of 1.82 g (4.57 mmol) of seleno acetal **9a** in 100 mL of dry dichloromethane was stirred and cooled at −78 °C as a solution of 0.986 g (4.57 mmol, 80–85%) of *m*-CPBA in 50 mL of dry dichloromethane was added slowly via cannula transfer. The added solution was precooled by allowing the drops to make first contact with the walls of the flask. Stirring was continued for an additional 20 min at −78 °C, after which the cooling bath was removed, and the reaction vessel was allowed to warm to 0 °C over 30 min. After 1 h, a 1.96-g (18.3 mmol, 2.7 mL) portion of triethylamine was added, and the solution immediately turned yellow. The reaction mixture was then rapidly added to a flask containing 200 mL of pentane at reflux. After 5 min at reflux temperature (31 °C), the reaction mixture was poured into a separatory funnel containing 150 mL of aqueous saturated sodium bicarbonate and 150 mL of ethyl ether. The ethereal layer was washed once with aqueous saturated sodium bicarbonate, twice with aqueous saturated copper(II) sulfate, and once with water. The organic layer was dried (K_2CO_3), the drying agent was filtered, and the solvent was evaporated under aspirator

(54) Adkins, H.; Nissen, B. H. *Organic Syntheses*; Wiley: New York, 1956, Collect. Vol. I., p 1.
(55) Kreevoy, M. M.; Taft, R. W., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 5590.
(56) Thompson, Q. E. *J. Am. Chem. Soc.* **1958**, *80*, 5483.
(57) Thorpe, J. F. *J. Chem. Soc.* **1909**, 1901.
(58) Scheibler, H.; Baganz, H. *Ann. Chem.* **1949**, *565*, 157.

vacuum. Purification of the residue by flash chromatography (20% ethyl acetate–hexane eluant) gave 896 mg (81%) of **5a**, as a 93:7 (E:Z) mixture of isomers as determined by the integrations of the doublets assigned to the α vinyl protons in the ^{1}H NMR spectrum. The chromatographic and ^{1}H NMR spectral properties correspond to those reported.[16a]

Method B. Oxidation with Hydrogen Peroxide.[24] A solution of 2.00 g (5.04 mmol) of **9a** and 0.800 g (10.1 mmol) of pyridine in 150 mL of dichloromethane at −1 °C (ice–salt bath) was rapidly stirred while a 1.4-mL portion of 30% hydrogen peroxide was added all at once, and the reaction mixture was allowed to warm to room temperature. After 1 h at room temperature, the mixture was poured into 150 mL of saturated sodium bicarbonate and 100 mL of dichloromethane. The dichloromethane phase was washed in succession with saturated sodium bicarbonate, 2 portions of saturated copper(II) sulfate, water, and saturated sodium chloride. The solution was dried (Na_2SO_4) and evaporated to afford 1.36 g of residue. Purification by flash chromatography (20% ethyl acetate–hexane eluant) provided the three following compounds: diphenyl diselenide, 0.122 g (8%); enol ether **5a**, 0.583 g (48%); ethyl 1-[2-formyl-2-(phenylseleno)ethyl]-2-oxocyclopentanecarboxylate (see structure i in ref 23), 0.425 g (23%). The selenoaldehyde appeared to be a mixture of two diastereomers (55:45 ratio) by the appearance of two spots on the TLC plates and the following resonances in its ^{1}H NMR spectrum (90 MHz, $CDCl_3$): δ 1.21 (t, 1.4 H, J = 7 Hz, minor isomer OCH_2CH_3), 1.23 (t, 1.6 H, J = 7 Hz, major isomer OCH_2CH_3). An analytically pure sample of the selenoaldehyde obtained from a different oxidation run as a single diastereomer (by TLC analysis) had the following analytical data: IR (neat) ν_{max} 1760, 1740 (C=O), 1590 (C=C), 748, 693 (C_6H_5) cm^{-1}; ^{1}H NMR (220 MHz, $CDCl_3$) δ 1.24 (t, 3 H, J = 7.1 Hz, OCH_2CH_3), 1.71–2.65 (m, 8 H, ring CH_2 and $CH_2CHSePh$), 3.89 (dt, 1 H, J = 3.6, 8.9 Hz, CH_2CHSePh), 4.15 (q, 2 H, J = 7.1 Hz, OCH_2CH_3), 7.09–7.73 (m, 5 H, Ar H), 9.33 (d, 1 H, J = 3.5 Hz, CHO); MS (70 eV), m/e (rel abundance) 368 (M^+ for ^{80}Se, 15), 366 (M^+ for ^{78}Se, 8). Anal. Calcd for $C_{17}H_{20}SeO_4$: C, 55.59; H, 5.49; Se, 21.50. Found: C, 55.87; H, 5.81; Se, 21.61.

Method C. Oxidation with Hydrogen Peroxide in the Presence of Ethyl Propenyl Ether. A 1.55-g (13.7 mmol) aliquot of 30% hydrogen peroxide was added all at once to a rapidly stirred solution of 2.00 g (5.05 mmol) of **9a**, 0.805 g (10.2 mmol) of pyridine, and 4.39 g (50.9 mmol) of ethyl propenyl ether at 5 °C (ice bath). The reaction mixture was warmed up to room temperature over 26 min and stirred for an additional 15 min at this temperature, after which the product was isolated as described above (method B). Purification of the residue (1.92 g) by flash chromatography (15% ethyl acetate–hexane), afforded three fractions, distillation of which in a Kugelrohr oven provided 0.574 g (53%) 2-(phenylseleno)propanol; 0.353 g (29%) of enol ether **5a**, and 0.162 g of a mixed fraction containing apparently 2-carbethoxycyclopentanone and enol ether **5a**. The ^{1}H NMR and IR spectra of 2-(phenylseleno)propanol compared closely to those of a sample prepared by hydrolysis of α-chloro-β-(phenylseleno)propyl ethyl ether.

1-(3-Ethoxy-2-propenyl)-2-oxocyclopentanecarbonitrile (5b). Method A. Oxidation with *m*-CPBA. The procedure used in the preparation of **5a** was followed, with the exception that 2 (instead of 4) equiv of triethylamine were used. The yield was 1.92 g of crude keto nitrile **5b**. Purification of the residue by flash chromatography (30% ethyl acetate–hexane eluant) gave 840 mg (86%) of **5b** as a 93:7 (E:Z) mixture of isomers as determined by its ^{1}H NMR spectrum. The chromatographic and ^{1}H NMR spectral properties of **5b** correspond to those reported in the literature.[16a]

Method B. Oxidation with Hydrogen Peroxide. The oxidation of 1.77 g (5.05 mmol) of **9b** was carried out as described above for **9a**. Purification of the product by flash chromatography (30% ethyl acetate–hexane) afforded 0.216 g (14%) of diphenyl diselenide, 0.382 g (39%) of ethoxyallyl cyano ketone **5b**, and 0.287 g of a mixed fraction containing both **5b** and an aldehyde byproduct. The aldehyde byproduct had the following resonances in its ^{1}H NMR spectrum: (90 MHz, $CDCl_3$) δ 3.81–4.08 (m, 1 H?, CHSe?), 7.11–7.64 (m, 5 H?, Ar H), 9.39, 9.46 (two, d, 1 H?, CHO).

(*E*)-2-(3-Ethoxy-2-propenyl)-2-methyl-1,3-cyclopentanedione (5c). Method A. Oxidation with *m*-CPBA. The procedure described above for the preparation of **5a** was followed. The solvent used for chromatography was 40% ethyl acetate–hexane. The yield was 400 mg (40%) of **5c** as a 98:2 (E:Z) mixture of isomers as determined by its ^{1}H NMR spectrum: ^{1}H NMR (200 MHz, C_6D_6) δ 0.94 (s, 3 H, CCH_3), 0.96 (t, 3 H, J = 7.0 Hz, OCH_2CH_3), 2.06 (s, 4 H, ring CH_2), 2.10 (dd, 2 H, J = 7.9, 1.1 Hz, allylic CH_2), 3.28 (q, 2 H, J = 7.0 Hz, OCH_2), 4.56 (dt, 1 H, J = 12.5, 7.9 Hz, CH=CHOEt), 6.17 (d, 1 H, J = 12.7 Hz, =CHOEt). The IR and ^{1}H NMR spectra match those reported previously.[16a]

Method B. Oxidation with Hydrogen Peroxide. Oxidation of 1.79 g (16.0 mmol) of **9c** was conducted by the procedure given for **9a** at room temperature for 47 min. Purification of the product by two successive flash chromatographies (60% ethyl acetate–hexane and 30% ethyl acetate–hexane) provided 0.268 g (15%) of diphenyl diselenide and 0.394 g (40%) of ethoxyallyl diketone **5c**. A mixed fraction (0.168 g) contained some enol ether **5c** and an aldehyde byproduct with the following ^{1}H NMR data: (90 MHz, $CDCl_3$) δ 7.13–7.63 (m, 5 H?, Ar H?), 8.34 (d, 1 H?, J = 2 Hz, CHO). The ^{1}H NMR and IR spectra of the diphenyl diselenide and enol ether **5c** matched those of authentic samples.

Ethyl 2-[1-(ethoxy-d_5)-2-(phenylseleno)propoxy]-1-cyclopentene-1-carboxylate (9a-d_5) was prepared according to the procedure for the preparation of **9a**. The yield was 3.46 g (61%) of **9a-d_5** as a 50:50 mixture of diastereomers, which contained 20% of what appeared to be an acetal impurity, as deduced from its ^{1}H NMR spectrum. This material was used in the cross-breeding experiment without further purification. Purification by chromatography on a chromatotron with 10% ethyl acetate, 1% triethylamine–hexane as the eluent, gave an analytical sample which consisted of a 60:40 mixture of diastereomers as determined from its ^{1}H NMR spectrum. The IR, ^{1}H NMR, and mass spectra are identical to those of **9a** with the following exceptions: IR (CCl_4) ν_{max} 2234, 2097 (C-D), cm^{-1}; ^{1}H NMR [200 MHz, C_6D_6] identical with that of **9a** except for the absence of the triplets at δ 0.99 and 1.05 and part of the multiplet at δ 3.23–3.67; MS (70 eV), m/e (rel abundance) 403 (M^+ for ^{80}Se, 2.8), 401 (M^+ for ^{78}Se, 1.5), 248 (base), 246 (69). Anal. Calcd for $C_{19}H_{21}O_4SeD_5$: C, 56.72; H, 6.51; Se, 19.63. Found: C, 56.96; H, 6.34; Se, 19.97.

Ethyl 1-[3-(Ethoxy-d_5)-2-propenyl]-2-oxocyclopentanecarboxylate (5a-d_5) and 1-(3-Ethoxy-2-propenyl)-2-oxocyclopentanecarbonitrile (5b-d_0). A solution of 1.02 g (2.53 mmol) of ester **9a-d_5** and 0.886 g (2.53 mmol) of nitrile **9b-d_0** in 20 mL of dichloromethane was stirred and cooled at −78 °C as a solution of 1.09 g (5.05 mmol, 80–85%) of *m*-CPBA in 20 mL of dichloromethane was added dropwise over 10 min, and the resulting mixture was allowed to warm to 0 °C over 15 min, and stirrred at 0 °C for 30 min. A 1.09-g (10.7 mmol) portion of triethylamine was added, and the resulting solution was then added in 1 portion to 100 mL of pentane at reflux. The resulting solution was held at reflux for an additional 5 min after which 150 mL of dichloromethane was added. The solution was washed twice with saturated aqueous sodium bicarbonate, twice with saturated aqueous copper(II) sulfate, and once with water. The organic layer was dried (Na_2SO_4) and evaporated. Elution of the crude reaction mixture from a 40 × 200 mm column of silica with 1.5 L of 10% ethyl acetate–hexane and then 1.5 L of 20% ethyl acetate–hexane provided 0.408 g (66%) of **5a-d_5** and 0.335 g (69%) of **5b-d_0** as colorless oils, both of which proved to be 93:7 (E:Z) mixtures of isomers as determined by their ^{1}H NMR spectra. The ^{1}H NMR spectrum of **5a-d_5** is identical with **5a** with the exception of the absence of the quartet at δ 3.69 and a decrease in intensity of the triplet at δ 1.27. The MS (10 eV), exhibited m/e (rel abundance) 245 (13), 240 (M^+, 0.2), 121 (33), 90 (base), 77 (47), 58 (64); deuterium distribution >90% d_5, 6 ± 3% d_4, <1% d_0. Anal. Calcd for $C_{13}H_{15}O_4D_5$: C, 63.66; H, 8.22. Found: C, 63.48; H, 8.09.

The chromatographic and ^{1}H NMR spectral properties for **5b-d_0** correspond to those reported in the literature:[16a] the MS (10 eV), exhibited m/e (rel abundance) 198 (0.05), 193 (M^+, 3.9), 85 (76), 57 (base); deuterium distribution <1% d_5, >99% d_0.

2-[1-Ethoxy-2-(phenylseleno)propoxy]cyclopentene (9d). A 10.24-g (89.4 mmol) portion of a 35% potassium hydride dispersion in mineral oil was washed 4 times with dry pentane, and the residual pentane was evaporated under a stream of dry nitrogen. To the resulting powder was added 200 mL of dry Me_2SO, and the effervescent mixture was stirred at room temperature. After hydrogen evolution ceased, a solution of 6.84 g (81.2 mmol) of cyclopentanone in 50 mL of Me_2SO was added dropwise over 1 h, and the resulting solution was stirred at room temperature for an additional 1 h. A freshly prepared solution of α-chloro-β-(phenylseleno)propyl ethyl ether in 180 mL of dry THF was added dropwise over 50 min. The solution of chloro ether in THF was prepared by adding 9.0 mL (7.0 g, 82 mmol) of ethyl propenyl ether to an ice-cold solution of 14.14 g (73.8 mmol) of benzeneselenyl chloride in 180 mL of THF and was used within 5 min of its preparation. After the addition of the chloro ether was complete, the resulting solution was immediately poured into a separatory funnel containing 1 L of ice-cold water and 400 mL of pentane. The mixture was shaken, and the layers were separated. The aqueous layers was extracted repeatedly with pentane, and the combined pentane layers were washed once with water, dried (Na_2SO_4), and filtered. Evaporation of the solvent under aspirator vacuum followed by filtration through a plug of silica gel using 2% ethyl acetate–1% triethylamine–hexane as the eluant gave 17.20 g of crude **9d**. Purification of the crude seleno acetal was accomplished by subjecting 200-mg portions of the crude product to chromatography on a chromatotron with a 4-mm plate using 2% ethyl acetate–1% triethylamine–hexane as the eluant. Kugelrohr distillation at 200 °C (0.3 mmHg) provided 4.39 g

(18%) of **9d** as a 60:40 mixture of diastereomers as determined from its ^{1}H NMR spectrum. The spectral properties of the product are as follows: IR (neat) ν_{max} 1642 (C=C), 742, 692 (C_6H_5) cm^{-1}; ^{1}H NMR [360 MHz, C_6D_6, 60:40 (A:B) mixture of diastereomers] δ 1.04 (t, 1.8 H, J = 7.1 Hz, OCH_2CH_3, isomer A), 1.08 (t, 1.2 H, J = 7.2 Hz, OCH_2CH_3, isomer B), 1.52 (d, 1.8 H, J = 7.1 Hz, $SeCHCH_3$, isomer A), 1.63 (d, 1.2 H, J = 7.1 Hz, $SeCHCH_3$, isomer B), 1.60–1.72 (16 line m, 2 H, ring $CH_2CH_2CH_2$), 2.17–2.29 (19 line m, 2 H, ring CH_2), 2.30–2.40 (20 line m, 2 H, ring CH_2), 3.30 (dq, 0.6 H, J = 9.2, 7.0 Hz, SeCH, isomer A), 3.36 (dq, 0.4 H, J = 9.2, 7.0 Hz, SeCH, isomer B), 3.64 (apparent dddq, 2 H, J = 24, 20, 9.4, 7.1 Hz, OCH_2), (28 line m, 2 H, OCH_2), 4.33 (t, 0.4 H, J = 1.9 Hz, ring CHCO, isomer B), 4.56 (t, 0.6 H, J = 2.0 Hz, ring CHCO, isomer A), 5.08 (d, 0.6 H, J = 4.8 Hz, acetal CH, isomer A), 5.28 (d, 0.4 H, J = 3.5 Hz, acetal CH, isomer B), 6.95–7.00 (8 line m, 3 H, Ar H), 7.65–7.62 (9 line m, 2 H, Ar H); ^{13}C NMR [90 MHz, C_6D_6, 55:45 (A:B) mixture of diastereomers] δ 15.1, 15.2 (q, ether OCH_2CH_3, BA), 15.6, 17.2 (q, $SeCHCH_3$, BA), 21.0, 21.1 (t, ring $CH_2CH_2CH_2$, BA), 29.5, 29.6, 32.4, 32.5 (t, ring CH_2CO and CH_2CH-CO, ABAB), 41.7, 42.1 (d, SeCH, BA), 63.4, 64.2 (t, ether OCH_2, AB), 95.9, 96.8 (d, ring CHCO, BA), 104.4, 104.7 (d, acetal CH, BA), 127.4 (d), 129.0 (d), 129.1 (s), 130.1 (s), 135.1 (d), 135.2 (d) (Ar C), 157.6, 158.2 (s, ring CHCO, BA); MS (70 eV), m/e (rel abundance) 326 (M^+ for ^{80}Se, 0.42), 324 (M^+ for ^{78}Se, 0.18), 243 (9.2), 241 (4.6), 214 (17), 212 (22); exact mass m/e calcd for $C_{16}H_{22}O_2Se$ 326.0785, found 326.0787. Anal. Calcd for $C_{16}H_{22}O_2Se$: C, 59.07; H, 6.82; Se, 24.27. Found: C, 58.85; H, 6.80; Se, 24.40.

1-(1-Ethoxy-2-propenoxy)cyclopentene (4d). A modification of the procedure of Anderson[25] was used. A solution of 2.26 g (10.5 mmol, 80–85%) of *m*-CPBA in 100 mL of dichloromethane was added dropwise over 2.5 h to a vigorously stirred ice-cold mixture of a solution of 3.40 g (10.5 mmol) of **9d** in 200 mL of dichloromethane and a 100-mL portion of 0.5 M aqueous sodium bicarbonate. The mixture was allowed to stir for an additional 15 min at 0 °C. The two phases were quickly separated, and the cold dichloromethane layer was added to a stirred solution of 3.07 g (42.0 mmol) of diethylamine in 400 mL of pentane at room temperature. The resulting solution was stirred without warming for 30 min, washed with saturated aqueous sodium bicarbonate, and dried (K_2CO_3). Evaporation of the solvent under reduced pressure and filtration through a plug of silica gel using 2% ethyl acetate–1% triethylamine–hexane as the eluant gave 2.16 g of crude **4d**. Purification by repeated chromatotron chromatography on a 4-mm plate using 2% ethyl acetate–1% triethylamine–hexane as the eluant provided 774 mg (44%) of **4d** as a colorless liquid. The product appeared as a mobile bluish band under UV irradiation which immediately precedes and overlaps with the yellowish band attributed to diphenyl diselenide. The spectral properties of the product are as follows: IR (CCl_4) ν_{max} 1642 (O-C=C), 1230 (C=C-O), 1175, 1125 (O-C-O), 978, 938 (C-C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 1.10 (t, 3 H, J = 7.1 Hz, OCH_2CH_3), 1.62–1.78 (5 line m, 2 H, $CH_2CH_2CH_2$), 2.24–2.46 (20 line m, 4 H, ring allylic CH_2), 3.39 (dq, 1 H, J = 9.2, 7.0 Hz, OCH_2), 3.64 (dq, 1 H, J = 9.2, 7.0 Hz, OCH_2), 4.69 (quintet, 1 H, J = 1.9 Hz, OC=CH), 5.09 (ddd, 1 H, J = 10.5, 1.6, 1.3 Hz, cis $=CH_2$), 5.32 (d, 1 H, J = 1.2 Hz, acetal CH), 5.38 (ddd, 1 H, J = 14.0, 1.6, 1.3 Hz, trans $=CH_2$), 5.86–6.03 (10 line m, 1 H, $CH=CH_2$); ^{13}C NMR (50 MHz, C_6D_6) δ 15.4 (q, OCH_2CH_3), 21.1 (t, $CH_2CH_2CH_2$), 29.7, 32.5 (t, ring allylic CH_2), 61.5 (t, OCH_2), 97.3, 101.2 (d, OC=CH and acetal CH), 118.0 (t, $=CH_2$), 135.3 (d, $CH=CH_2$), 157.0 (s, OC=CH); MS (70 eV), m/e (rel abundance) 168 (M^+, 4.5), 85 (82), 57 (base). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.50; H, 9.66.

(*E*)-2-(3-Ethoxy-2-propenyl)cyclopentanone (5d). A solution of 45.8 mg (0.272 mmol) of acetal **4d** in 15 mL of benzene was stirred and heated at reflux for 24 h. The benzene was removed by distillation through a short-path distillation head. Kugelrohr distillation of the residue at 130 °C (1.3 mm) gave 38.4 mg (84%) of **5d** as a 97:3 (E:Z) mixture of isomers as determined by the relative integrations for the pair of doublets assigned to the α-enol ether methine in its ^{1}H NMR spectrum. The spectral properties of the product are as follows: IR (neat) ν_{max} 1740 (C=O), 1655 (C=C), 1165 (C-O) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 1.02 (t, 3 H, J = 7.0 Hz, OCH_2CH_3), 1.10–1.36 (20 line m, 2 H, ring CH_2), 1.38–1.44 (13 line m, 1 H, ring CH_2), 1.58–1.80 (19 line m, 3 H, ring CH_2 and allylic CH_2), 1.84–2.04 (20 line m, 2 H, O=C-CH_2), 2.32 (dddd, 1 H, J = 14.3, 7.3, 4.2, 1.3 Hz, O=C-CH), 3.38 (q, 2 H, J = 7.0 Hz, OCH_2), 4.69 (dt, 1 H, J = 12.7, 7.6 Hz, CH=CHOEt), 6.21 (d, 1 H, J = 12.7 Hz, =CHOEt); ^{13}C NMR (50 MHz, C_6D_6) δ 14.8 (q, OCH_2CH_3), 20.7, 28.2, 28.6 (t, ring CH_2 and allylic CH_2), 38.1 (t, O=C-CH_2), 49.6 (d, O=C-CH), 64.4 (t, OCH_2), 100.7 (d, CH=CHOEt), 147.9 (d, =CHOEt), 217.9 (s, C=O); MS (70 eV), m/e (rel abundance) 168 (M^+, 8.8), 85 (48), 57 (base). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.31; H, 9.47.

Cyclopentanone diallyl ketal was prepared according to the procedure of Lorette and Howard.[26b] The yield was 88.00 g (45%) (lit.[11] 53%), bp 83–86 °C (10 mmHg) [lit.[26b] bp 98 °C (20 mmHg)]: IR (neat) ν_{max} 1647, 1424, 994, 918 (C=C), 1192, 1109, 1033 (O-C-O) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 1.51–1.61 (6 line m, 4 H, $O_2CCH_2CH_2$), 1.72–1.83 (10 line m, 4 H, O_2CCH_2), 3.94 (ddd, 4 H, J = 4.8, 1.8, 1.5 Hz, OCH_2), 5.04 (ddt, 2 H, J = 10.3, 2.1, 1.6 Hz, E $=CH_2$), 5.29 (ddt, 2 H, J = 17.4, 1.9, 1.9 Hz, Z $=CH_2$), 5.89 (centrosymmetric 10 line m, 2 H, CH=CH_2).

1-[2-Propenoxy]cyclopentene (10). The procedure reported by Lorette and Howard[26a] for the preparation of 1-(2-propenoxy)cyclohexene was used. The yield was 5.90 g (42%) of enol ether **10** as a colorless liquid, bp 58–60 °C (16 mmHg): IR (neat) ν_{max} 1642, 1242 (O-C=C), 993, 927 (C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 1.64–1.80 (19 line m, 2 H, $CH_2CH_2CH_2$), 2.23–2.44 (25 line m, 4 H, ring allylic CH_2), 4.08 (dt, 2 H, J = 5.1, 1.6 Hz, OCH_2), 4.36 (quintet, 1 H, J = 1.9 Hz, OC=CH), 5.01 (ddt, 1 H, J = 10.5, 1.6, 1.6 Hz, E $=CH_2$), 5.20 (ddt, 1 H, J = 17.1, 1.9, 1.6 Hz, Z $=CH_2$), 5.85 (centrosymmetric 10 line m, 1 H, $CH=CH_2$); ^{13}C NMR (50 MHz, C_6D_6) δ 21.6 (t, $CH_2CH_2CH_2$), 29.4, 32.3 (t, ring allylic CH_2), 70.1 (t, OCH_2), 93.9 (d, OC=CH), 116.4 (t, $=CH_2$), 134.1 (d, $C=CH_2$), 160.1 (s, OCCH); MS (70 eV), m/e (rel abundance) 124 (M^+, 16), 96 (24), 41 (base). Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.41; H, 9.51.

2-(2-Propenoxy)-1-cyclopentene-1-carbonitrile (11). A 1.92-g (16.8 mmol) portion of a 35% potassium hydride in mineral oil suspension was washed 4 times with dry pentane under nitrogen to remove the mineral oil, and the residual pentane was removed by a stream of dry nitrogen. A 100-mL portion of Me_2SO was added, and then 1.60 g (14.7 mmol) of 2-cyanocyclopentanone was added. A 2.85-g (23.6 mmol) portion of allyl bromide (distilled from P_2O_5) was added dropwise (CAUTION: EXOTHERMIC), and the resulting solution was stirred for 24 h at room temperature. The reaction mixture was diluted with 500 mL of ice-cold water, and the aqueous mixture was extracted repeatedly with pentane. The organic layers were combined, washed once with water, and dried (Na_2SO_4). Evaporation of the solvent gave 2.12 g of crude nitrile. Purification by flash chromatography (30% ethyl acetate–hexane eluant) provided two major components. The less polar fractions contained 142 mg (6%) of **11** as a yellowish liquid. The more polar fractions yielded 1.37 g (63%) of 1-(2-propenyl)-2-oxocyclopentanecarbonitrile. The ketone was identified by comparison of its IR and ^{1}H NMR spectra with those of a sample prepared by thermolysis of **11** (see below). The spectral properties of **11** are as follows: IR (neat) ν_{max} 2210 (C≡N), 1740, 1640 (O-C=C-C≡N), 936 (C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 1.13–1.30 (centrosymmetric 14 line m, 2 H, $CH_2CH_2CH_2$), 1.84 (ddd, 1 H, J = 8.3, 1.9, 1.6 Hz, OC=CCH_2), 1.88 (ddd, 1 H, J = 7.6, 1.9, 1.6 Hz, OC=CCH_2), 2.10 (ddd, 1 H, J = 7.6, 1.9, 1.6 Hz, $OCCH_2$), 2.15 (ddd, 1 H, J = 7.0, 1.9, 1.6 Hz, $OCCH_2$), 4.45 (dt, 2 H, J = 5.4, 1.6 Hz, OCH_2), 4.96 (ddt, 1 H, J = 10.5, 1.6, 1.3 Hz, E $=CH_2$), 5.10 (ddt, 1 H, J = 17.2, 1.6, 1.6 Hz, Z $=CH_2$), 5.52–5.72 (11 line m, 1 H, $CH=CH_2$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.3 ($CH_2CH_2CH_2$), 31.8, 33.2 (ring allylic CH_2), 71.6 (OCH_2), 79.8 (C-C≡N), 117.6 (C≡N), 118.5 ($=CH_2$), 132.0 ($CH=CH_2$), 171.6 (OC=C); MS (70 eV), m/e (rel abundance) 149 (M^+, 9.7), 41 (base). Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.69; H, 7.39; N, 9.50.

2-(2-Propenyl)cyclopentanone. A solution of 393 mg (3.16 mmol) of **10** in 15 mL of benzene was stirred and heated at reflux for 96 h. The benzene was removed by distillation through a short-path distillation head. Kugelrohr distillation of the residue at 90 °C (2.5 mm) gave 224 mg (57%) of E as a colorless liquid: IR (neat) ν_{max} 1738 (C=O), 1642, 997, 916 (C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 0.95–1.28 (27 line m, 2 H, ring CH_2), 1.34–1.48 (12 line m, 1 H, ring CH_2), 1.58–1.76 (14 line m, 3 H, ring CH_2 and allylic CH_2), 1.80–2.00 (15 line m, 2 H, $COCH_2$), 2.41–2.57 (centrosymmetric 21 line m, 1 H, COCH), 4.94 (ddt, 1 H, J = 11, 1.3, 1.0 Hz, E $=CH_2$), 4.95 (ddt, 1 H, J = 16, 1.9, 1.6 Hz, Z $=CH_2$), 5.55–5.75 (centrosymmetric 14 line m, 1 H, CH=CH_2). Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 76.98; H, 9.49.

1-(2-Propenyl)-2-oxocyclopentanecarbonitrile. A solution of 53.4 mg (0.358 mmol) of nitrile **11** in 15 mL of benzene was stirred and heated at reflux for 110 h. The benzene was removed by distillation through a short-path distillation head. Kugelrohr distillation at 120–130 °C (0.35 mmHg) provided 52.0 mg (97%) of the ketone as a colorless oil: IR (neat) ν_{max} 2220 (C≡N), 1745 (C=O), 1635 (C=C) cm^{-1}; ^{1}H NMR (200 MHz, C_6D_6) δ 0.94–1.10 (15 line m, 1 H, ring CH_2), 1.12–1.31 (21 line m, 2 H, ring CH_2), 1.34–1.78 (36 line m, 4 H, ring CH_2 and allylic CH_2), 2.27 (dddd, 1 H, J = 13.9, 6.7, 1.3, 1.3 Hz, allylic CH_2), 4.86 (ddt, 1 H, J = 17.2, 1.8, 1.6 Hz, Z $=CH_2$), 4.93 (ddt, 1 H, J = 10.0, 2.1, 1.0 Hz, E $=CH_2$), 5.45–5.67 (centrosymmetric 14 line m, 1 H, $CH=CH_2$). Anal. Calcd for $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.11; H, 7.54; N, 9.49.

2-(*o*-Nitrophenylseleno)ethanol.[27] (*o*-Nitrophenylseleno)cyanate (5.72 g, 25.2 mmol) was suspended in absolute ethanol (120 mL) at 0 °C, and sodium borohydride (1.20 g, 32 mmol) was added in small portions over 5 min.[28] After 90 min at 0 °C, the reaction was cooled to −20 °C, and liquid ethylene oxide (3.0 mL) was added. The mixture was warmed to room temperature, and after an additional 3 h the solvent was removed in vacuo. After addition of saturated NH_4Cl and extraction with ethyl acetate, the combined organic layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo. Flash chromatography of the residue (1:1 hexane/EtOAc) gave an orange-brown crystalline solid (4.14 g, 67%, R_f 0.38 in 1:2 hexanes/EtOAc): mp 97.5–98.0°; IR ($CHCl_3$) 3630, 3200–3450, 1585, 1562, 1505, 1325, 1298, 1100, 1050, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29 (1 H, dd, J = 1.2, 8.3 Hz), 7.61 (1 H, dd, J = 1.2, 8.0 Hz), 7.55 (1 H, dt, J = 1.3, 7.7 Hz), 7.34 (1 H, dt, J = 1.3, 7.7 Hz), 3.97 (1 H, t, J = 6.5 Hz), 3.17 (1 H, t, J = 6.5 Hz).

4-Methoxyallyl Vinyl Ether (13). 2-(*o*-Nitrophenylseleno)ethanol (130 mg, 0.52 mmol) was suspended in benzene (1 mL), and acrolein dimethyl acetal (0.50 mL, 4.2 mmol) and pyridinium *p*-toluenesulfonate (25 mg, 0.10 mmol) were added. The mixture was stirred at room temperature for 24 h. After filtration through Florisil (CH_2Cl_2) and concentration in vacuo, the residue was purified by flash chromatography (7:3 hexanes/EtOAc) to give **12** as a yellow oil (104 mg, 62% R_f 0.55 in 1:2 hexanes/EtOAc); IR ($CHCl_3$) 3070, 2990, 2880, 2830, 1590, 1568, 1510, 1335, 1300, 1100, 1060, 1035, 940, 905 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.29 (1 H, dd, J = 1.3, 8.2 Hz), 7.60 (1 H, dd, J = 1.2, 8.0 Hz), 7.53 (1 H, dt, J = 1.2, 7.7 Hz), 7.33 (1 H, dt, J = 1.3, 7.7 Hz), 5.81 (1 H, ddd, J = 4.7, 10.6, 17.5 Hz), 5.43 (1 H, br d, J = 17.5 Hz), 5.34 (1 H, br d, J = 10 Hz), 4.90 (1 H, br d, J = 10.6 Hz), 4.90 (1 H, br d, J = 4.7 Hz), 3.92 (1 H, dt, J = 10.4, 7.0 Hz), 3.82 (1 H, dt, J = 10.4, 7.0 Hz), 3.35 (3 H, s), 3.16 (2 H, t, J = 7.0 Hz); MS, (15 eV), m/e 317, 315, 230, 228, 203, 201, 186, 184, 71; exact mass m/e calcd for $C_{12}H_{15}NO_4{}^{78}Se$ 315.0173, found 315.0174.

Mixed acetal **12** (209 mg, 0.66 mmol) was dissolved in CH_2Cl_2 (1.2 mL) and cooled to −78 °C. *m*-Chloroperoxybenzoic acid (137 mg, 84%, 0.66 mmol) in CH_2Cl_2 (1 mL) was added dropwise, and the resulting mixture was warmed to −20 °C. After 40 min, the reaction was quenched with saturated aqueous $NaHCO_3$, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with 5% $Na_2S_2O_4$ and saturated $NaHCO_3$ and dried over Na_2CO_3/Na_2SO_4. Concentration in vacuo gave the crude selenoxide as a viscous yellowish oil (197 mg) which was directly heated in a Kugelrohr distillation apparatus for 45 min (60 °C, 1–2 mmHg). Compound **13** was collected (36 mg, 0.32 mmol, 48%) as a clear oil by cooling the receiving vessel to −78 °C; ^1H NMR (300 MHz, benzene-d_6) δ 6.40 (1 H, dd, J = 6.5, 14.0 Hz), 5.74 (1 H, ddd, J = 4.1, 10.7, 17.4 Hz), 5.34 (1 H, dt, J = 17.4, 1.4 Hz), 5.04 (1 H, dt, J = 10.7, 1.4 Hz), 4.90 (1 H, dt, J = 4.1, 1.4 Hz), 4.64 (1 H, dd, J = 1.1, 14.0 Hz), 4.09 (1 H, dd, J = 1.1, 6.5 Hz), 3.10 (s, 3 H); IR ($CHCl_3$) 3000, 2940, 2840, 1640, 1150, 1080, 1020, 985, 945 cm^{-1}.

2-Methoxyprop-2-en-1-ol (2-Methoxyallyl Alcohol). Methyl 2-methoxy acrylate[29a] (2.58 g, a 45 mol % mixture with the corresponding ketal, approximately 10 mmol) was added dropwise to a solution of $LiAlH_4$ (903 mg, 24 mmol) in ether at 0 °C over 10 min. The reaction was quenched carefully by dropwise addition of water (0.9 mL in 3 mL of THF), 15% NaOH (0.9 mL), and water (2.7 mL). The white precipitate was filtered and washed with CH_2Cl_2. The organic phase was dried (Na_2CO_3/Na_2SO_4), carefully concentrated in vacuo with a bath temperature of 0–5 °C, and purified by flash chromatography (silica, 1:1 pentanes/ether) followed by careful concentration to give a clear oil (47 mg, 53%, R_f 0.20 in 1:1 pentanes/ether): ^1H NMR (300 MHz, $CDCl_3$) δ 4.16 (1 H, d, J = 2.4 Hz), 4.06 (1 H, d, J = 6.2 Hz), 4.03 (1 H, d, J = 2.4 Hz), 3.60 (3 H, s); IR ($CHCl_3$) 3630, 3550–3200, 3015, 2960, 2948, 2920, 2875, 2850, 1670, 1630, 1455, 1300, 1262, 1200, 1095, 1080, 1035 cm^{-1}.

5-Methoxyallyl Vinyl Ether (14). 2-Methoxyallyl alcohol (431 mg, 4.89 mmol), mercuric acetate (160 mg, 0.50 mg), and ethyl vinyl ether (15 mL) were stirred at 25 °C for 36 h. Filtration through neutral alumina (washed with CH_2Cl_2), careful concentration in vacuo with a bath temperature of 0–5 °C, and flash chromatography (silica, 10:1 pentanes/ether) followed by careful concentration gave **14** as a sharp smelling clear oil (168 mg, 29%): ^1H NMR (300 MHz, benzene-d_6) δ 6.35 (1 H, dd, J = 6.8, 14.1 Hz), 4.22 (1 H, d, J = 2.0 *Hz*), 4.22 (1 H, dd, J = 2.0, 14.1 Hz), 4.02 (2 H, s), 3.93 (1 H, dd, J = 2.0, 6.8 Hz), 3.92 (1 H, d, 2.0 Hz), 3.12 (3 H, s); IR ($CHCl_3$) 3100, 3040, 2940, 2850, 1670, 1640, 1620, 1450, 1322, 1300, 1185, 1155, 1080 cm^{-1}; MS (15 eV), m/e 113, 86, 72, 71, 41; exact mass m/e (M − H) calcd for $C_6H_9O_2$ 113.0603, found 113.0605.

6-Methoxyallyl Vinyl Ether (15). 3-Methoxyallyl alcohol[29b] (205 mg, 2.32 mmol) and mercuric acetate (105 mg, 0.33 mmol) were dissolved in ethyl vinyl ether (15 mL) and stirred at 25 °C for 20 h. Filtration through neutral alumina, careful concentration in vacuo (bath temperature 0–5 °C), and flash chromatography (9:1 hexanes/ethyl acetate) gave **15** as a clear oil (85 mg, 32%, R_f 0.42 in 6:1 hexanes/EtOAc): ^1H NMR (300 MHz, benzene-d_6) δ 6.42 (1 H, dd, J = 6.9, 14.4 Hz), 6.32 (1 H, d, J = 12.7 Hz), 4.74 (1 H, dt, J = 12.7, 7.5 Hz), 4.23 (1 H, dd, 1.6, 4.4 Hz), 3.99 (1 H, dd, J = 1.6, 6.9 Hz), 3.89 (1 H, d, J = 7.5 Hz), 3.03 (3 H, s); IR ($CHCl_3$) 3120, 3000, 2960, 2945, 2880, 2840, 1660, 1638, 1620, 1465, 1320, 1175, 1040, 1000, 975, 950 cm^{-1}; MS (70 eV), m/e 114, 113, 85, 71, 58, 41; exact mass m/e (M − H) calcd for $C_6H_9O_2$ 113.0603, found 113.0602.

(*E*)- and (*Z*)-5-Methoxy-4-pentenal (16*E*, *Z*).[30] Freshly distilled enol ether **13** was dissolved in benzene-d_6 and heated in a sealed NMR tube for 24 h at 80 °C to give aldehydes **16Z** and **16Z** as the only detectable products: ^1H NMR (300 MHz, benzene-d_6) **16E** δ 9.3 (1 H, t, J = 1.5 Hz), 6.17 (1 H, br d, J = 12.6 Hz), 4.43 (1 H, dt, 12.7, 7.0 Hz), 3.05 (3 H, s); **16Z** 9.4 (1 H, t), 5.55 (1 H, dt, 6.1, 1.4 Hz), 4.20 (1 H, dt, 6.1, 7.2 Hz), 3.02 (3 H, s).

4-Methoxy-4-pentenal (17). Enol ether **14** was dissolved in benzene-d_6 containing BSTFA and heated at 135 °C for 2 days. Flash chromatography (silica, 6:1 pentanes/ether) gave aldehyde **17** as a clear oil (R_f 0.30 in 6:1 hexanes/EtOAc): ^1H NMR (300 MHz, benzene-d_6) δ 9.26 (1 H, t, J = 1.5 Hz), 3.77 (1 H, d, J = 2.0 Hz), 3.72 (1 H, d, J = 2.0 Hz), 3.09 (3 H, s), 2.20 (1 H, br t, J = 7.0 Hz), 2.07 (1 H, tt, J = 1.5, 7.0 Hz); IR ($CHCl_3$) 2960, 2910, 2840, 2735, 1716, 1380, 1170, 1090 cm^{-1}.

3-Methoxy-4-pentenal (19). Enol ether **15** was dissolved in benzene-d_6 and heated in a sealed NMR tube at 100 °C for 24 h to give aldehyde **19**: ^1H NMR (300 MHz, benzene-d_6) δ 9.40 (1 H, dd, J = 1.8, 2.5 Hz), 5.39 (1 H, ddd, J = 17.3, 10.1, 7.2 Hz), 4.97 (1 H, br d, J = 17.3 Hz), 4.90 (1 H, br d, J = 10.1 Hz), 3.68 (1 H, m), 2.98 (3 H, s), 2.27 (1 H, ddd, J = 16.3, 8.0, 2.5 Hz), 1.90 (1 H, ddd, J = 16.3, 4.7, 1.8 Hz).

3-Methoxy-4-penten-1-ol. Enol ether **15** (18 mg, 0.16 mmol) was dissolved in benzene-d_6, heated in a sealed NMR tube for 6 h at 100 °C, cooled, and poured into THF/MeOH (3:1) containing $NaBH_4$ (75 mg, 1.98 mmol) at 0 °C. After 90 min, water was added. After extraction with CH_2Cl_2, drying (Na_2SO_4), and concentration in vacuo, flash chromatography gave a clear oil (55 mg, 55%, R_f 0.28 in 1:1 hexanes/EtOAc): ^1H NMR (300 MHz, $CDCl_3$) δ 5.71 (1 H, ddd, J = 7.7, 9.9, 17.6 Hz), 5.24 (1 H, dd, J = 16.0, 0.8 Hz), 5.24 (1 H, dd, J = 11.0, 0.8 Hz), 3.73–3.84 (3 H, m), 3.30 (3 H, s), 1.73–1.85 (2 H, m); IR ($CHCl_3$) 3640, 3490 (br), 3080, 2990, 2940, 2830, 1420, 1260, 1100, 1070, 1020, 995, 930; MS (70 eV), m/e 115, 98, 97, 87, 84, 72, 71; exact mass m/e (M − 1) calcd for $C_6H_{11}O_2$ 115.0759, found 115.0761.

Kinetic Analyses (13, 14, and 15). For each kinetic run, five or six duplicate samples were prepared. The appropriate enol ether (3–4 mg) was dissolved in benzene-d_6 (500–600 μL) in an NMR tube, flushed with dry nitrogen, and flame sealed. In the case of 5-methoxyallyl vinyl ether, *O,N*-bis(trimethylsilyl)trifluoroacetamide (BSTFA) (3 μL) was also added. The NMR tubes had been base-washed with 10% (w/w) aqueous NaOH/KOH (1:1), thoroughly rinsed with distilled water, and oven-dried (135 °C) overnight. A constant temperature was maintained with a preequilibrated Neslabs EX-250-HT constant temperature bath (by using silicone oil for T > 80 °C, and water/ethylene glycol for T < 80 °C). The temperature of the bath was measured with certified NBS calibrated total immersion thermometer, with use of stem correction. The temperature was measured at several points during the reaction and did not vary from the average by more than 0.03 °C.

The duplicate samples were fully immersed in the bath, removed at appropriate intervals, and immediately frozen in a dry ice/acetone bath. The samples were stored at −20 °C until analysis by 300-MHz ^1H NMR. The yields of products were determined by integration of the ^1H NMR spectrum by using a relaxation delay sufficient to ensure uniform integration. Aside from starting material and expected aldehyde products, no other NMR peaks (<2–3%) were observed. Rate constants were determined by least-squares analysis by using a program kindly provided by Prof. J. Gajewski.[59] By using rate constants from five or six different temperatures, Eyring and Arrhenius parameters were also determined by least-squares analysis by using the same software.

Kinetic Measurements for Allyl Cyclopentenyl Ethers (4, 10, and 11). A solution of 0.21 mmol of the allyl vinyl ether and ca. 7 mg of tetramethylsilane in 0.847 mL of solvent (805 mg of C_6D_6, 705 mg of CD_3CN, 754 mg of C_2D_5OD + 17 mg of pyridine-d_5, 824 mg of 80% C_2D_5OD–20% D_2O + 17 mg of pyridine-d_5) was placed in an NMR tube and sealed under nitrogen with a ribbed pressure cap. The ^1H NMR spectrum was recorded at room temperature with a Varian XL-200, and the probe was then heated. A 5-min period was allowed for equilibration

(59) The software package is now available from Serena Software, 482 Serena Lane, Bloomington, IN 47401.

before data acquisition was begun (additional probe tuning was advisable after the probe had attained the desired temperature). Spectra were recorded after each estimated 3-5% of total conversion was achieved. Approximately 12 spectra were obtained for each kinetic plot within the first 2 half-lives. The rate constants were obtained by graphing $-\ln(X_{SM})$ vs. time, and the best line was estimated visually. The deviation of individual points along the ordinate was $<\pm 0.01$, and the average deviation of points was ± 0.0043. The rate constants listed in table II are averages of 2-3 kinetic runs. Three runs were generally used unless the rates obtained from the first two were within 5%. The data in Table II associated with the rearrangement rates of **11** in acetonitrile-d_3 and ethanol-d_6 were obtained from one kinetic run each. The integrals of the following absorptions were measured to determine the enol ether/ketone ratio: **10**, 4.08 (dt, CH_2O), 4.36 (quintet, OC=CH); 2-allylcyclopentanone, 4.94 (ddt, $=CH_2$), 4.95 (ddt, $=CH_2$), 5.55-5.76 (m, $=CH_2$); **11**, 4.45 (dt, CH_2O); **11** + 1-allyl-2-oxocyclopentanecarbonitrile, 4.8-5.1 ($=CH_2$); **4d**, 5.09 (ddd, $=CH_2$, 5.38 (ddd, $=CH_2$); **5d**, 6.21 (d, =CHOEt). The error in the integrals was less than 2%, and the reproducibility of the integrals was better than ±2%. No products other than the α-allylcyclopentanones were detected in any spectra. The probe temperatures were determined by application of the Van Geet equation[60] to the measured $\Delta\delta$ between the hydroxyl and methylene protons in ethylene glycol. The precision of the temperature measurements is ±1 °C and the reproducibility of the temperatures is ±0.3 °C. Extrapolations were performed through use of a least-squares program when more than two points were to be extrapolated from. The error limits cited for the activation parameters were calculated by propagating the maximum possible error through the calculations used for the parameters. The error in rate was assumed to be the average deviation from the mean, the error in temperature was assumed to be ±1 °C as given by Van Geet,[60] and the transmission coefficent in the Eyring equation was assumed to be unity.

Estimation of the Minimum Rate Ratio of 4b and 4d. Both **9b** and **9d** were oxidized separately and added to solutions of triethylamine in pentane at room temperature as described in the preparation of **4d**. Both reaction mixtures were stirrred, without externally warming the pentane solutions, for 30 min, and then a 50-mL aliquot was removed from both and cooled to -78 °C until their ^{1}H NMR spectra could be taken. The samples were later evaporated quickly and a 200-MHz ^{1}H NMR spectrum was obtained of both reaction mixture residues in benzene-d_6. In each case, the relative amounts of **4** and **5** were estimated by comparison of the integrals of the multiplets at δ 5.9 to the integrals of the doublets at δ 6.2, which are assigned to the allyl methine (**4b** and **4d**) and α-enol ether protons (**5b** and **5d**), respectively. The relative amounts of **4b** to **5b** was estimated to be less than 9:91, and the relative amounts of **4d** to **5d** was estimated to be greater than 95:5 after 50 and 45 min at room temperature, respectively. From these ratio estimates, the relative rate of rearrangement of **4b** and **4d** is estimated to be >45:1.

Acknowledgment. The research at the University of Illinois was supported in part by grants from the National Science Foundation (82-04485) and the National Institutes of Health (GM 13956). The Pittsburgh group thanks the National Institutes of Health (GM-34862) and the Petroleum Research Fund for support and is particularly grateful to Stuart Pharmaceuticals for an unrestricted gift.

Registry No. 1, 3917-15-5; **4d**, 106094-88-6; (*E*)-**5a**, 87698-30-4; (*Z*)-**5a**, 87698-31-5; (*E*)-**5a**-d_5, 106094-97-7; (*Z*)-**5a**-d_5, 106094-98-8; (*E*)-**5b**, 87711-07-7; (*Z*)-**5b**, 87698-14-4; (*E*)-**5c**, 87698-07-5; (*Z*)-**5c**, 87698-08-6; (*E*)-**5d**, 18802-25-0; (*Z*)-**5d**, 18802-26-1; **9a** (isomer 1), 106094-90-0; **9a** (isomer 2), 106094-91-1; **9a**-d_5 (isomer 1), 106094-96-6; **9a**-d_5 (isomer 2), 106095-06-1; **9b** (isomer 1), 106094-92-2; **9b** (isomer 2), 106094-93-3; **9c** (isomer 1), 106094-94-4; **9c** (isomer 2), 106094-95-5; **9d** (isomer 1), 106094-99-9; **9d** (isomer 2), 106095-00-5; **10**, 106094-86-4; **11**, 106094-87-5; **12**, 106095-01-6; **13**, 106094-84-2; **14**, 92127-02-1; **15**, 106094-85-3; (*E*)-**16**, 56175-41-8; (*Z*)-**16**, 56175-40-7; **17**, 106095-03-8; **19**, 106095-04-9; α-chloro-β-(phenylseleno)propyl ethyl ester, 106094-89-7; 2-cyanocyclopentanone, 2941-29-9; 2-methyl-1,3-cyclopentanedione, 765-69-5; cyclopentanone diallyl ketal, 62322-44-5; 2-(2-propenyl)cyclopentanone, 30079-93-7; 1-(2-propenyl)-2-cyclopentanecarbonitrile, 66984-19-8; 2-(*o*-nitrophenylseleno)ethanol, 94650-42-7; 2-methoxyallyl alcohol, 50717-56-1; 3-methoxyallyl alcohol, 106095-02-7; 3-methoxy-4-penten-1-ol, 106095-05-0; 2-carbethoxycyclopentanone, 611-10-9; cyclopentanone, 120-92-3.

(60) Van Geet, A. L. *Anal. Chem.* **1968**, *40*, 2227.

On the Mechanism of Rearrangement of Chorismic Acid and Related Compounds

Joseph J. Gajewski,*† Jurjus Jurayj,† Doris R. Kimbrough,‡ Matthew E. Gande,‡ Bruce Ganem,*‡ and Barry K. Carpenter*‡

Contribution from the Department of Chemistry, Indiana University, Bloomington, Indiana 47405, and the Department of Chemistry, Cornell University, Ithaca, New York 14853-1301. *Received September 23, 1985. Revised Manuscript Received October 18, 1986*

Abstract: The thermal reactions of the biochemically important molecule chorismic acid are studied in solution. It undergoes two competitive reactions, one is an unusually facile Claisen rearrangement, and the other an elimination to give *p*-hydroxybenzoic acid and pyruvic acid. Attempts are made to understand the factors responsible for the facility of the Claisen rearrangement by preparation of a variety of analogues of chorismate. Correlations of rate with structure as well as determinations of solvent and isotope effects are undertaken. The data from these experiments lead to the conclusion that chorismic acid and related molecules undergo the rearrangement and, where it occurs, the elimination, by reactions whose transition structures are dissociative in nature, i.e., there is substantial cleavage of the C-O bond linking the sidechain to the ring but little bond formation at the terminus of the sidechain. The roles of radical and zwitterionic structures are discussed, as are the implications of this work for the mechanism of enzyme catalysis of the chorismate to prephenate conversion.

Chorismic acid (**1**) is a key intermediate in the shikimate biosynthetic pathway which bacteria and lower plants use to convert glucose-6-phosphate into a wide variety of primary and secondary metabolites, including phenylalanine, tyrosine, tryptophan, the isoprenoid quinones, and the folate coenzymes.[1] The rearrangement of chorismic acid to prephenic acid (**2**), the first step in the conversion of chorismate to phenylalanine and tyrosine, is the focus of the present paper.

†Indiana University.
‡Cornell University.

(1) (a) Haslam, E. *The Shikimic Acid Pathway*; Halstead Press, Wiley: New York, 1974. (b) Ganem, B. *Tetrahedron* **1978**, *34*, 3353-3383. (c) Weiss, U.; Edwards, J. M. *The Biosynthesis of Aromatic Compounds*; Wiley: New York, 1980. (d) Dewick, P. M. *Nat. Prod. Rep.* **1984**, *1*, 451-469.

0002-7863/87/1509-1170$01.50/0