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Supplementary Material Available: Cartesian coordinates and Z-matrices are provided for 1, 2, and 3 (10 pages). Ordering information is given on any current masthead page.

Energetic and Rate Effects of the Trifluoromethyl Group at C-2 and C-4 on the Aliphatic Claisen Rearrangement

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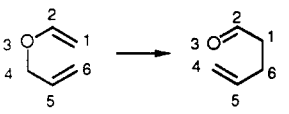
The rate of the Claisen rearrangement is accelerated by a factor of 73 over the parent system when a trifluoromethyl group is present at C-2 of allyl vinyl ether. Ground-state destabilization by the trifluoromethyl group may be responsible for this rate effect. There is little polar character in the transition state, and the transition-state structure has little carbonyl character and only moderate (ca. 1/3) bonding character between the two terminal carbons. The rate enhancement is not observed in the Cope rearrangement of the all-carbon analogue that has a trifluoromethyl group at C-2. At C-4, the trifluoromethyl group does not bring about a significant rate effect in the Claisen rearrangement relative to the parent system; this result is in contrast to an energetic benefit of 3.5 kcal/mol enjoyed by the system when a cyano group is at C-4, which suggests that radical-stabilizing ability and not electron-withdrawing ability is important in stabilizing the transition state.

Introduction

The synthetic usefulness of the Claisen rearrangement of aliphatic allyl vinyl ethers[1] to γ,δ-unsaturated carbonyl compounds has been well established.[2,3] That the Claisen rearrangement proceeds through a cyclic chair transition state[4] (when possible) as an intramolecular, concerted 3,3-sigmatropic rearrangement[5] has also been well established.[6] The high-energy species of the reaction is an aromatic[7] transition state that leads to the rearrangement product rather than an intermediate(s), although this picture is not without criticism.[8] The loss of entropy that would be expected for a cyclic transition state is confirmed by a −7.7 eu entropy of activation for allyl vinyl ether (AVE) in the gas phase at 180 °C.[9] The rearrangement is highly exothermic, downhill in enthalpy by 17 kcal as calculated by heats of formation of AVE and 5-hexenal.[10]



AVE (1)

Substituent effects on the rate of the Claisen rearrangment have been investigated, and various models have been proposed. One complication which should be addressed by a model is that 3,3-shift transition structures seem to respond to substituents as judged by secondary deuterium kinetic isotope effects.[11] A model suggested in our work is a nonlinear free-energy relationship to correlate the rates of a variety of substituted allyl vinyl ethers.[12] This model assumes that the transition-state structure takes on characteristics of reactant or product based on the exothermicity and takes on associative or dissociative character depending on how and where substituents can best stabilize such character.

Dewar[8a] has presented a model, based on MNDO calculations, that shows a biradical intermediate for the Claisen rearrangement (2-oxacyclohexane-1,4-diyl), which then decomposes to products without activation. This diyl is a highly polarizable specie, and the oxygen atom is said to favor a zwitterionic pathway. Most Claisen rearrangements do not respond dramatically to polar solvents (a rate factor of ca. 200 between benzene and aqueous environ-

(1) (a) Claisen, L. *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 3157. (b) Hurd, C. D.; Pollack, M. A. *J. Am. Chem. Soc.* **1938**, *60*, 1905.
(2) (a) Bennet, G. B. *Synthesis* **1977**, 589. (b) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423. (c) Rhoads, S. J.; Raulins, N. R. *Org. React.* **1975**, *22*, 1. (d) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205.
(3) (a) Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc.* **1957**, *79*, 2828. (b) Ireland, R. E.; Mueller, R. H. *J. Am. Chem. Soc.* **1972**, *94*, 5897. (c) Grubbs, R. H.; Brown-Wensley, K. A.; Buchwald, S. L.; Cannizzo, L.; Clawson, L.; Ho, S.; Meinhardt, D.; Stille, J. R.; Straus, D. *Pure Appl. Chem.* **1983**, *55*, 1733. (d) Stevenson, J. W. S.; Bryson, T. A. *Tetrahedron Lett.* **1982**, 3143. (e) Felix, D.; Gschwend-Steen, K.; Wick, A. E.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1030. (f) Johnson, W. S.; Werthemann, L.; Bartlett, W. R.; Brocksom, T. J.; Li, T.; Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741.
(4) Vittorelli, P.; Winkler, T.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1968**, *51*, 1457.
(5) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.
(6) (a) Hill, R. K.; Edwards, A. G. *Tetrahedron Lett.* **1964**, 3239. (b) Ralls, J. W.; Lundin, R. E.; Bailey, G. F. *J. Org. Chem.* **1963**, *28*, 3521.
(7) Evans, M. G. *Trans. Faraday Soc.* **1939**, *35*, 824.
(8) (a) Dewar, M. J. S.; Healy, E. F. *J. Am. Chem. Soc.* **1984**, *106*, 7127. (b) McIver, J. W., Jr. *Acc. Chem. Res.* **1974**, *7*, 72.
(9) Schuler, F. W.; Murphy, G. W. *J. Am. Chem. Soc.* **1950**, *72*, 3155.
(10) Benson, S. W.; O'Neal, H. E. *Kinetic Data on Gas Phase Unimolecular Reactions*; U.S. Department of Commerce: Washington, DC, 1970; NSRDS-NBS-21, p 363.
(11) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161.
(12) Gajewski, J. J.; Gilbert, K. E. *J. Org. Chem.* **1984**, *49*, 11.

0022-3263/90/1955-1813$02.50/0

ments) so the extent of polar character in the transition state is not high. Nonetheless it is argued by Dewar that both electron-withdrawing and electron-releasing groups at C-2 and C-5 should increase the rate of rearrangement, although an electron-withdrawing group at C-5 should facilitate the rearrangement to a greater extent than it should if it were at C-2. Burrows and Carpenter[13] supplied kinetic data for the rearrangement of various cyano-substituted allyl vinyl ethers. The compound with a cyano group at C-2 and also the one with a cyano group at C-5 indeed both rearrange faster than AVE itself. However, the C-5 cyano compound rearranges 8 times slower than the C-2 cyano compound, whereas Dewar's calculations predicted the C-5 cyano compound to rearrange 20 times faster than the C-2 cyano compound. Also, an alkoxy substituent at C-5 is predicted to rearrange 60 times more rapidly than unsubstituted AVE at 80 °C, while in actuality a methoxy group at C-5 causes a rate decrease by a factor of 40 relative to AVE.[14]

Carpenter[15] developed a theoretical model of the aliphatic Claisen transition state in which the conjugative electron-withdrawing and -donating abilities of substituents are assessed. In the model, Hückel molecular orbital (HMO) theory is used to evaluate the effect of a substituent on the transition state and reactant. The difference in HMO π-energy (ΔE_π) between the reactant and transition state is evaluated and compared with ΔE_π of the reaction of its unsubstituted analogue. The difference between ΔE_π of the reaction of interest and ΔE_π of its unsubstituted analogue, $\Delta\Delta E_\pi$, predicts the sign and magnitude of the substituent effect on the activation enthalpy of the reaction. In the model, electron-withdrawing and electron-donating substituents are represented by a carbocation and a carbanion, respectively, and the π-donor oxygen of AVE is replaced by a carbanion.

The model qualitatively predicts a rate enhancement for an electron-withdrawing substituent at C-2, C-4, and C-5 over AVE itself, while a rate retardation is expected for electron-withdrawing substituents at C-1 and C-6. Electron-releasing substituents should enhance the rate if at C-1, C-2, and C-4, while rate retardation is expected for such substitution at C-5 and C-6. The dramatic rate-accelerating effect of electron donors at C-2 can be rationalized by this effect. In an extensive investigation of the model, all possible monocyano-substituted allyl vinyl ethers were examined and found to fulfill the predictions of this HMO model. However, there should be concern that cyano is not only an electron-withdrawing group but a radical-stabilizing group of some merit, so that rate acceleration resulting from cyano substitution particularly at C-2 and C-4 may not be a result of the electron-withdrawing character of cyano.

There are other complications with the HMO model, namely that methoxy substitution at C-6 causes a rate enhancement,[16] although this may be a result of transition-state structure variation resulting from some cationic character at C-6 promoted by the good electron donor. Further, Jurayj found that methoxycarbonyl at C-2 causes a rate enhancement of 50 times at 80 °C,[17] and this appeared to be a result of increased stabilization of the 2-oxacyclohexan-1,4-diyl species as judged by secondary deuterium kinetic isotope effects in this system relative to those with the parent allyl vinyl ether. In order to differentiate between inductive and radical conjugative effects, the C-2 and C-4 trifluoromethyl allyl vinyl ethers have been prepared and studied, anticipating that CF_3 acts as an electron-withdrawing, π-acceptor substituent,[18] but not a radical-stabilizing substituent.[19]

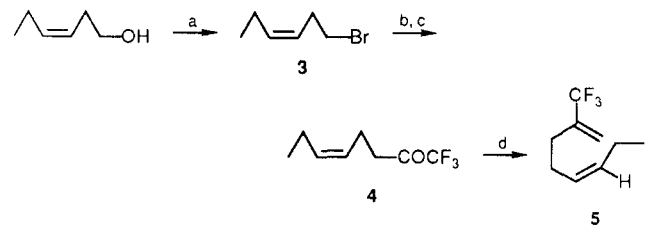
Table I. Kinetic Isotope Effects of C-2 Trifluoromethyl Allyl Vinyl Ether at 61 °C in Cyclohexane Solvent

BB:	run	k_{1a} ($\times 10^{-6}$, s^{-1})	k_{1b} ($\times 10^{-6}$, s^{-1})	k_{1a}/k_{1b}	EIE_{bb}
	1[a]	3.13 (0.11)	2.67 (0.07)	1.17 (0.030)	1.46
	2[a]	3.19 (0.05)	2.71 (0.03)	1.17 (0.017)	
	3	4.27 (0.02)	3.65 (0.03)	1.17 (0.014)	

BM:	run	k_{1a} ($\times 10^{-6}$, s^{-1})	k_{1c} ($\times 10^{-6}$ s^{-1})	k_{1a}/k_{1c}	EIE_{bm}
	1	3.89 (0.036)	4.29 (0.10)	0.906 (0.023)	0.781
	2	3.99 (0.071)	4.22 (0.085)	0.945 (0.025)	

[a] Compounds **1a** and **1b** prepared by alternate route by Jurayj[17] in BB runs 1 and 2.

Scheme I[a]



[a] (a) PBr_3, py; (b) Mg; (c) CF_3CO_2Et, Et_2O, −78 °C; (d) $Ph_3PCH_3{}^+I^-$, NaH, DMSO.

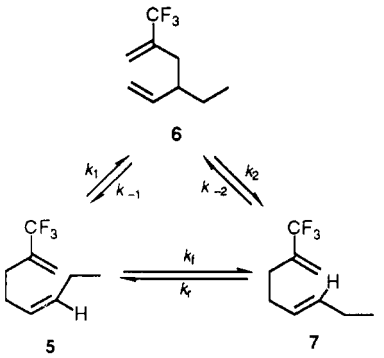
Results

Pyrolysis of C-2 Trifluoromethyl Allyl Vinyl Ethers: Activation Parameters and Secondary Deuterium Kinetic Isotope Effects. The rearrangement of C-2 trifluoromethyl allyl vinyl ether, **1a**, proceeded with a half-life of roughly 7.5 h in cyclohexane and roughly 2.4 h in DMSO at 80 °C.[17] This rate was about the same as that for the corresponding methoxycarbonyl derivative and was clearly acclerated relative to allyl vinyl ether itself. A study of the kinetics in cyclohexane over a 37.5 °C temperature range gave log k (/s) = 11.35 (0.13) − [25660 (280)]/2.303RT (E_a in kcal/mol). To examine the structure of the transition state in the rearrangement of **1a**, the secondary deuterium kinetic isotope effects at C-4 and C-6 were determined.

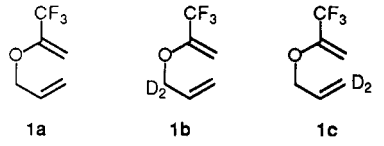
The C-2 trifluoromethyl allyl vinyl ethers **1a**, **1b**, and **1c** were prepared separately by a modification of the Takai method,[20] beginning with the appropriately deuterated allyl alcohols, taken up in cyclohexane and pyrolyzed simultaneously. Rearrangement to 1,1,1-trifluoro-5-hexen-

(13) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6983.
(14) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 1160.
(15) Burrows, C. J.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 6984.
(16) Curran, D. P.; Suh, Y. *J. Am. Chem. Soc.* **1984**, *106*, 5002.
(17) Jurayj, J. Ph.D. Thesis, Indiana University, 1986.
(18) Smart, B. E. In *Molecular Structure and Energetics*; Greenburg, A., Liebman, J. F., Eds.; Verlag Chemie: Deerfield Beach, FL, 1986; Vol. 3, Chapter 4.
(19) (a) See Gassman, P. G.; Harrington, C. K.; *J. Org. Chem.* **1984**, *49*, 2258 and references cited therein. (b) Creary, X.; Sky, A. F.; Mehrsheikh-Mohammadi, M. E. *Tetrahedron Lett.* **1988**, *29*, 6839 have shown that α-CF_3 is neither radical stabilizing or destabilizing based on its effect on biradical reactions. The very high C–H bond dissociation energy for 1,1,1-trifluoroethane reported by Wu, E.-C.; Rodgers, A. S. *J. Phys. Chem.* **1974**, *78*, 2315 probably has little to do with radical stabilization energies, rather the effect of CF_3 is to stabilize the ground state by hyperconjugative interactions. This is not an unknown effect; C–H bond energies are poor indicators of radical stabilization energies when the substituents are good π-acceptors such as cyano and carbonyl.
(20) Okazoe, T.; Takai, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1987**, *52*, 4410.

Scheme II



2-one (**2a**) proceeded cleanly with the results for the KIE experiments listed in Table I. The equilibrium isotope



effects are provided for comparison of the observed KIE's with the expected maximum KIE's for two deuteriums at this temperature.

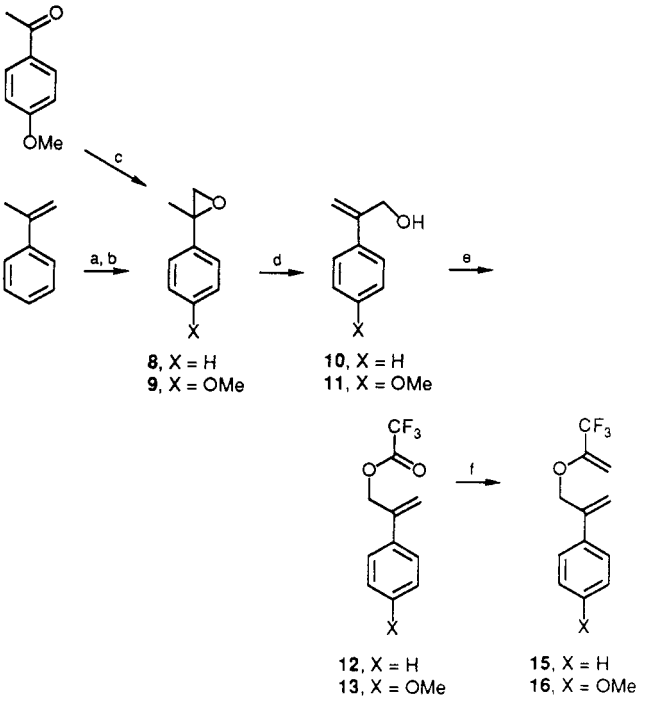
Synthesis and Pyrolysis of *cis*-2-(Trifluoromethyl)-1,5-octadiene (5). In order to test the effect of CF_3 at C-2 in [3,3] shifts in general, the all-carbon analogue **5** was prepared (Scheme I) from α-trifluoromethyl ketone **4**, which was prepared by the method of Creary.[21] Thus 1 equiv of *cis*-3-hexen-1-ylmagnesium bromide was reacted with 1.1 equiv of ethyl trifluoroacetate; Corey–Wittig methylenation[22] readily afforded the diene.

The *cis*-diene **5** was dissolved in benzene and sealed in capillary tubes. The tubes were immersed in a heat bath at 207 °C. Analysis by capillary gas chromatography (100-m supelcowax SPB-5 column in series with a 60-m supelcowax SP 2330 column) showed the starting material disappearing and a single product peak appearing; equilibrium of the two was reached after 7 days (K_{eq} = 3.46). The product peak was identified as *trans*-2-(trifluoromethyl)-1,5-octadiene (**7**) (Scheme II) by independent synthesis (following Scheme I, beginning with *trans*-3-hexen-1-ol) and co-injection with an equilibrium mixture. NMR analysis of the equilibrium mixture in hexachlorobutadiene at 300 MHz also showed the presence of only **5** and **7**; the diene **6** was never observed. Presumably the rate of Cope[23] rearrangement to either **5** or **7** from **6** is fast relative to the formation of **6** from **5** or **7**. Thus, the rearrangement can be analyzed as an equilibrium between **5** and **7**; application of a weighted least-squares program for reversible first-order kinetics reveals a forward rate constant, k_f, of 9.43 (0.15) × 10^{-6} s^{-1} and a reverse rate constant, k_r, of 2.72 (0.04) × 10^{-6} s^{-1}. These values correspond to an activation free energy, $\Delta G^{\ddagger}$ = 40.1 kcal/mol which is within 1 kcal/mol of that for the Cope rearrangement of unsubstituted 1,5-hexadiene.[24]

Synthesis and Pyrolysis of C-5 Phenyl-Substituted C-2 Trifluoromethyl Allyl Vinyl Ethers 15 and 16 and C-6 Phenyl C-2 Trifluoromethyl Allyl Vinyl Ether 17.

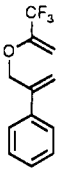
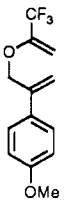
(21) Creary, X. *J. Org. Chem.* **1987**, *52*, 5026.
(22) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.
(23) Cope, A. C.; Hardy, E. M. *J. Am. Chem. Soc.* **1940**, *62*, 441.
(24) Doering, W. v. E.; Toscano, V. G.; Beasely, G. H. *Tetrahedron* **1971**, *27*, 5299.

Scheme III[a]



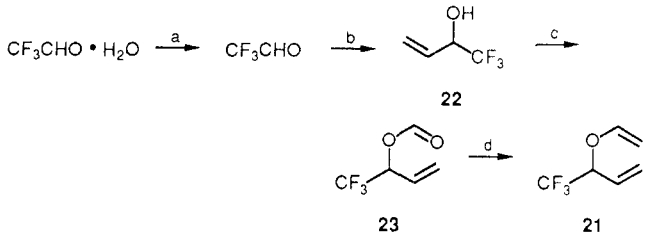
[a] (a) NBS, H_2O; (b) NaOH; (c) $(CH_3)_3SO^+$ I^-, NaH, DMSO; (d) LDA, Et_2O; (e) TFA; (f) $TiCl_4$, TMEDA, Zn, CH_2Br_2, THF.

Table II. Kinetic Data for the Claisen Rearrangement of 15 and 16

compd	T, °C	k (×10^{-5}, s^{-1})	solvent
	61.0	3.09 (0.11)	C_6D_{12}
	61.0	5.47 (0.42)	CD_3OD
15			
	61.0	3.33 (0.03)	C_6D_{12}
16			

The transition-state structure of the rearrangement of **1a** to **2a** was further probed by studying the rates of rearrangement of ethers **15**, **16**, and **17**. 2-Phenyl-2-propen-1-ol (**10**) was prepared by treatment of α-methylstyrene with wet *N*-bromosuccinimide followed by sodium hydroxide, and then cleavage of the epoxide **8** with LDA (Scheme III). 2-(4′-Methoxyphenyl)-2-propen-1-ol (**11**) was obtained from LDA cleavage of the epoxide **9**, which was prepared by methylenation of 4′-methoxyacetophenone with dimethyl sulfoxonium methylide. Allylic alcohol **10** was smoothly trifluoroacetylated with neat trifluoroacetic anhydride (TFA); however, trifluoroacetate **13** rapidly ionized under the acidic conditions generated by reaction of neat alcohol with TFA. Trifluoroacetylation of **11** was accomplished by using 1 equiv of a hindered base, 2,6-lutidine, in a solution of methylene chloride with an excess of TFA. Cinnamyl alcohol was reacted with TFA to give its trifluoroacetate (**14**); **12**, **13**, and **14** were all subject to me-

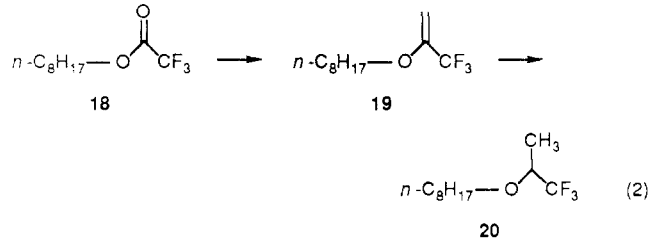
Scheme IV[a]



[a] (a) H_2SO_4, P_2O_5; (b) CH_2=CHMgBr, THF, (c) HCO_2H, $(CH_3CO)_2O$, DMAP, NEt_3, CH_2Cl_2; (d) $Cp_2Ti(Cl)(CH_2)AlMe_3$.

thylenation conditions described by Takai et al.[20] to yield ethers **15**, **16**, and **17** in moderate yield. The ethers were taken up in the indicated deuterated solvents and pyrolyzed (**17** did not rearrange after 2 weeks of 80 °C in $CDCl_3$); the results are listed in Table II. The lack of a polar transition state is indicated by the lack of a significant rate increase of **16** over **15** and of **15** in CD_3OD over **15** in C_6D_{12}.

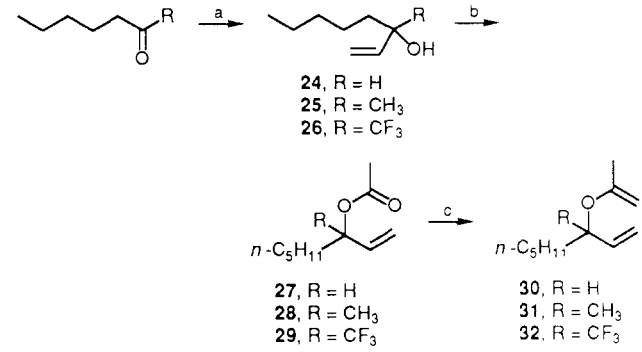
Heat of Hydrogenation of C-2 Trifluoromethyl Vinyl Octyl Ether (19). In order to gain further insight into ground-state destabilization afforded allyl vinyl ethers by a 2-CF_3 group, ether **19** was prepared by trifluoro-



acetaylation of 1-octanol to give trifluoroacetate **18** followed by titanium ylide methylenation. Ether **19** was hydrogenated to **20**, with the heat of hydrogenation (ΔH_{hyd}) determined by Prof. Donald Rogers of Long Island University to be −29.4 (0.53) kcal/mol.

Synthesis and Pyrolysis of C-4 Trifluoromethyl Allyl Vinyl Ether. In the study by Carpenter and Burrows[13] a cyano substituent at C-4 of allyl vinyl ether increased the rate of Claisen rearrangement by a factor of 270 over allyl vinyl ether itself at 100 °C in di-*n*-butyl ether. In order to further test the question of whether this was due to the electron-withdrawing capability of the cyano group or its radical stabilizing ability, C-4 trifluoromethyl allyl vinyl ether (**21**) was prepared in anticipation of comparing the rate of its Claisen rearrangement to that of allyl vinyl ether itself. The synthesis of **21** is outlined in Scheme IV. Trifluoroacetaldehyde was generated by dropwise addition of trifluoroacetaldehyde hydrate[25] into a hot mixture of concentrated sulfuric acid and phosphorous pentoxide and then trapped in a dry ice cooled flask. Admission of the gaseous aldehyde into a THF solution of vinylmagnesium bromide afforded the allylic alcohol **22**[26] as an azeotrope with THF. The formate **23** was prepared in moderate yield from DMAP-catalyzed reaction with formic acetic anhydride, prepared in situ.[27] Methylenation of **23** was accomplished by a slight modification of the method of Pine et al.[28] The Tebbe reagent[29]

Scheme V[a]



[a] (a) CH_2=CHMgBr; (b) "CH_3CO"; (c) $TiCl_4$, TMEDA, Zn, CH_2Br_2, THF.

was prepared and used without purification and was reacted with **23** in *m*-xylene; **23** was still in an inseparable mixture with THF. The volatile ether **21** was obtained in low yield and separated from its contaminants by preparative GC. Interestingly, a small amount of the acetate of **22**, formed during the formylation reaction and present with **23**, did not react with the Tebbe reagent in the time needed to consume all of **23**.

AVE and **21** were taken up in C_6D_6 and pyrolyzed; clean conversion to the respective aldehydes was observed, and the reaction was followed by capillary GC. At 118.6 °C, the ratio k_{32}/k_{AVE} = 1.30 (0.16) was observed. Activation parameters for both compounds were obtained and are listed in Table III.

Synthesis and Pyrolysis of C-4 Substituted Allyl Isopropenyl Ethers. To further examine the rate response of the Claisen rearrangement to a pure electron withdrawing group at C-4, C-4 trifluoromethyl C-4 *n*-pentyl allyl isopropenyl ether, **32**, was prepared, and its rearrangement rate was compared with model compounds **30**, **31**, and **33**. Ethers **30**, **31**, and **32** were prepared according to Scheme V. Reaction of vinylmagnesium bromide with hexanal, 2-heptanone, and 1,1,1-trifluoro-2-heptanone (prepared by the method of Dishart and Levine)[30] afforded allylic alcohols **24**, **25**, and **26**. Acetylation of alcohol **24** was normal; however, acetylation of tertiary alcohol **25** required 2 weeks at room temperature with acetic anhydride and dimethylaminopyride (DMAP). Acetylation of **26** was even more difficult, owing to the reduced nucleophilicity of the oxygen by the inductive withdrawing by CF_3. Reaction of acetyl chloride with the sodium salt of the conjugate base of **26** proceeded to give a poor, but sufficient, yield of acetate. Titanium ylide methylenation afforded ethers **30**, **31**, and **32**, which were dissolved in benzene and pyrolyzed. At 80 °C the C-4,C-4 dialkyl derivative, **31**, reacted roughly twice as fast as the C-4 trifluoromethyl, C-4 pentyl material, **32**, roughly 20 times faster than the C-4 pentyl derivative, **30**, and roughly 550 times faster than allyl isopropenyl ether (**33**) itself. The activation parameters were also determined and are listed in Table III.

Discussion

C-2 Trifluoromethyl Allyl Vinyl Ethers. The rate of the Claisen rearrangement of C-2 trifluoromethyl allyl

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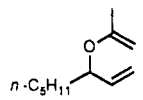
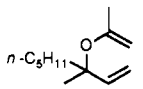
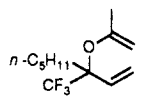
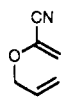
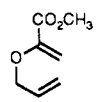
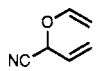
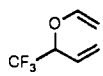
Table III. Activation Parameters for the Claisen Rearrangement of Some Allyl Vinyl Ethers

	temp range, °C	arrhenius parameters	enthalpy of activation, kcal/mol	entropy of activation, cal/mol K^{-1}
 **1a**	61.0–98.5 (C_6H_{12})	log k = 11.35 (0.13) – [25660 (280)]/2.3RT	24.95 (0.27)	–8.9 (0.59)
 **33**	80.0–125.2 (C_6H_6)	log k = 10.45 (0.14) – [25690 (270)]/2.3RT	24.94 (0.26)	–13.2 (0.64)
 **30**	40.0–79.0 (C_6D_6)	log k = 11.97 (0.02) – [25990 (483)]/2.3RT	25.32 (0.47)	–5.97 (0.09)
 **31**	39.9–76.4 (C_6D_6)	log k = 10.70 (0.01) – [21545 (603)]/2.3RT	20.89 (0.58)	–11.79 (0.04)
 **32**	40.0–79.0 (C_6D_6)	log k = 13.02 (0.34) – [26080 (561)]/2.3RT	25.42 (0.55)	–1.15 (1.5)
 AVE	118–153.1 (C_6D_6)	log k = 10.3 (0.14) – [26530 (260)]/2.3RT	25.72 (0.26)	–14.1 (0.64)
	66–115[a] (n-Bu_2O)	log k = 10.3 (0.38) – [23540 (196)]/2.3RT	22.84 (0.19)	–13.4 (0.5)
	40.5–80.0[b] (CCl_4)	log k = 11.44 (0.026) – [25754 (43)]/2.3RT	25.09 (0.05)	–8.3 (0.1)
	55–101[a] (n-Bu_2O)	log k = 10.4 (0.48) – [23000 (206)]/2.3RT	22.33 (0.20)	–13.0 (0.6)
 **21**	96.8–134.6 (C_6D_6)	log k = 10.1 (0.50) – [25980 (933)]/2.3RT	25.20 (0.93)	–14.8 (2.3)

vinyl ether in cyclohexane is accelerated by a factor of 73 over the parent compound at 100 °C in butyl ether. For comparison, C-2 cyano allyl vinyl ether (in butyl ether) is ca. 111 times faster,[13] and C-2 carbomethoxy allyl vinyl ether (in carbon tetrachloride)[31] is a factor of ca. 79 faster than allyl vinyl ether itself. Since solvent-rate effect studies show only small rate factors in the nonpolar regime, these 2-substituted materials have a free energy of activation which is 2–2.5 kcal/mol less than that for rearrangement of the parent ether.

The rate acceleration with the C-2 trifluoromethyl substituent does not appear to occur in the Cope rearrangement of a hydrocarbon derivative. The activation free energy at 20 °C for cis–trans equilibration of 2-(trifluoromethyl)-1,5-octadiene is similar to that for rearrangement of 1,5-hexadiene although exact comparisons are difficult. More directly, the forward rate constant for rearrangment of the *cis*-2-(trifluoromethyl)-1,5-heptadiene is only 3 times faster than the rate constant for the 3,3-shift of *cis*-1,5-heptadiene at 220 °C.[32]

In the case of the C-2 trifluoromethyl-substituted allyl vinyl ether, the product trifluoromethyl ketone would appear to be substantially destabilized relative to the case with hydrocarbon substituents. If this resulted in a less exothermic reaction, then the rate acceleration noted would be more remarkable. Ab initio calculations by D. A. Dixon and B. E. Smart[33] revealed that the energy difference between acetone and its enol is the same as that between trifluoroacetone and its enol. This suggests that the ground state of the C-2 trifluoromethyl allyl vinyl ether is itself destabilized to the same extent as the product. Since the usual destabilization of ketones by a flanking trifluoromethyl group is 10–20 kcal/mol, it was surprising that the heat of hydrogenation of *n*-octyl α-trifluoromethyl vinyl ether was found to be only 2.9 kcal/mol more exothermic than that of ethyl vinyl ether. Comparisons are

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difficult, however, since heats of hydrogenation require information about the effect of substitutents on the product. Nonetheless, there is some evidence for vinyl ether destabilization by α-trifluoromethyl, and it might be speculated that there is comparable destabilization of α-cyano- and α-carboalkoxy-substituted vinyl ethers as well; however, group additivity calculations indicate that the heats of hydrogenation of acrylonitrile and methyl acrylate are less exothermic than for ethylene, indicating some ground-state stabilization of these materials.

Because C-2 trifluoromethyl allyl vinyl ether and the product trifluoromethyl ketone are destabilized relative to allyl vinyl ether and its Claisen rearrangement product, the rate acceleration noted may result from less destabilization of the transition state. This would require that the transition state not have much carbonyl group character as is the case with the parent structure and the C-2 carbomethoxy derivative as judged by secondary deuterium kinetic isotope effects (DKIE). The DKIE at C-4 of the trifluoro derivative is 1.17 at 60 °C, but the maximum value expected at this temperature is 1.46 from equilibrium isotope effects (EIE). Using the Brønsted-like relationship KIE = EIE^i, i at the bond breaking site is 0.42 (0.04). From the inverse KIE at C-6, i at the bond making site is 0.31 (0.03). For comparison, the values with allyl vinyl ether[34] are i_{bb} 0.42 (0.02) and i_{bm} 0.17 (0.04), and those with the 2-carbomethoxy derivative[31] are i_{bb} = 0.30 and i_{bm} = 0.38. Thus the transition state in all these cases still has a substantial oxygen to C-4 bond, and there is partial bonding between the termini in the C-2 trifluoromethyl and the C-2 carbomethoxy derivatives. It appears to be the case that not much carbonyl group character is developing in the C-2 trifluoromethyl allyl vinyl ether Claisen transition state. In dramatic contrast, the i_{bb} value for the very fast rearrangement of allyl trimethylsilyl ketene acetal is 0.8, indicating that the donor group strongly stabilizes this transition state by stabilizing the carbonyl group and forcing the transition state to take on this character.[35]

To probe for radical or charged character at C-5 in the transition state for the Claisen rearrangement of C-2 trifluoromethyl allyl vinyl ether, the C-5 phenyl and C-5 *p*-anisyl derivatives were pryolyzed in cyclohexane solution at 61 °C. The rate constants for both are faster by a factor of 10 than that for the parent C-2 trifluoromethyl material, which argues that the aromatic group stabilizes the transition state approximately 1.5 kcal/mol more than it stabilizes the C-5,C-6 double bond. Furthermore, no strong polar character is evident since the rate for the C-5 phenyl derivative in methanol solvent is less than a factor of two faster than the rate in cyclohexane. It should be noted that in the Cope rearrangement of 2-(or 5-)phenyl-1,5-hexadienes, a rate factor of 70 is obtained relative to the parent compound at roughly 200 °C. Thus the Claisen rearrangement of C-2 trifluoromethyl allyl vinyl ether enjoys a little more than half of the energy benefit provided by a 5-phenyl group relative to the Cope rearrangement. This is a striking confirmation of the importance of bond making in the transition state for rearrangement of C-2 trifluoromethyl allyl vinyl ether, a reaction whose transition state is more reactant like than that for the Cope rearrangement.

To summarize, the introduction of a trifluoromethyl group at C-2 of allyl vinyl ether increases the rate of Claisen rearrangement by a factor of 73. The ground state is destabilized by the substituent, and this may be responsible for the acceleration. There is little polar character in the transition state, and the transition structure has little carbonyl group character and moderate (ca. 1/3) bonding character between the two terminal carbons.

C-4 Trifluoromethyl Allyl Vinyl Ethers. In contrast to the 3.5 kcal/mol lower E_a for Claisen rearrangement of C-4 cyano allyl vinyl ether relative to allyl vinyl ether itself,[13] the activation parameters for rearrangement of C-4 trifluoromethyl allyl vinyl ether are almost identical to those of the parent when both are done in benzene solvent. This suggests that it is not the electron withdrawing capability of the substituent to increase the reaction rate at C-4, but it is the ability to stabilize radical character at C-4 which is important in stabilizing the transition state.

Examination of more substituted materials revealed more complicated behavior. Here, a C-4 CF_3 group appeared to increase the rate to the same extent as a methyl group, namely by a factor of roughly 10, but the effect is almost entirely in the decreased entropy of activation. Unfortunately, a comparable C-4 cyano substituted material is not available for a rate comparison, but a much larger rate factor might be anticipated. Thus, in the two C-4 trifluoromethyl compounds examined, there appears to be a much smaller if not a nonexistent rate acceleration relative to the effect of a C-4 cyano group on the Claisen rearrangement.

Experimental Section

General. ^{1}H nuclear magnetic resonance spectra were obtained by using Varian EM-390, Varian XL300, Nicolet 360, and Bruker AM500 instruments with the indicated solvents. Chemical shifts are reported in δ units downfield from internal tetramethylsilane. NMR multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; *J*, coupling constant. Mass spectra were recorded on a Kratos GC/MS80 spectrometer. Capillary gas chromatography was performed using a Varian 3700 gas chromatograph equipped with a 60-m Supelcowax 10 (except where noted) column and a Hewlett-Packard 3390A integrator. Preparative vapor-phase chromatography (VPC) was performed on a Varian Aerograph Model 90-P instrument with the indicated columns. Infrared (IR) spectra were recorded on a Perkin-Elmer 298 instrument; peak frequencies are reported in wavemembers (cm^{-1}) with the polystyrene peak at 1601 cm^{-1} as the standard. Intensities are indicated using the following abbreviations: s, strong; m, medium; w, weak. Boiling and melting points are uncorrected. Reactions sensitive to air or moisture were carried out in glassware that had been oven-dried and cooled in a nitrogen atmosphere.

Tetrahydrofuran (THF) and ethyl ether were distilled from sodium benzophenone ketyl, methylene chloride was distilled from P_2O_5, and dimethyl sulfoxide and diisopropyl amine were distilled from calcium hydride. Pyridine, triethylamine, lutidine, and tetramethylethylenediamine (TMEDA) were distilled from KOH. Titanium(IV) chloride was purchased from Aldrich neat and as a 1.0 M solution in methylene chloride. Vinylmagnesium bromide (1.0 M in THF) and butyllithium in hexanes were also purchased from Aldrich. Allyl vinyl ether was prepared according to the method of Watanabe and Conlon[3a] and purified by VPC. Column chromatography was performed on Merck silica gel 60 (except where noted), and thin-layer chromatography was performed on Merck silica gel (0.25 mm) precoated glass sheets.

Kinetic Measurements. Absolute rate constants were measured by following the disappearance of reactant versus time using NMR and capillary GC integrations as quantitative measures of concentration. In a typical run to be monitored by NMR, a 25-μL sample of reactant was placed in an NMR tube with 500 μL of deacidified, deuterated solvent and 1 μL of deacidified internal standard, and the tube was tightly stoppered. The tube was heated at the indicated temperature, and the NMR spectrum was recorded periodically. Except for the case of **16** (which was followed by FT-NMR at 300 MHz), the spectra were obtained at 90 MHz. Random error was determined by averaging the differences between identical integrations throughout an experiment; the percent variability was applied to the equation[36]

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$$(\Delta k/k)^2 = (A_o/A_o - A)^2(\Delta A/A)^2 + (A/A_o - A)^2(\Delta A_o/A_o)^2 \quad (3)$$

where $(\Delta A/A)$ was in the range of 0.030.

In a typical run to be monitored by capillary GC, a 1-μL sample was dissolved in 200 μL of solvent, the solution was placed in capillary tubes in 15-μL portions, and the tubes were flame-sealed. A number of tubes were heated simultaneously and withdrawn one at a time for analysis. The injector port was held at 100 °C and the column at low temperature. Helium was the carrier gas. Random error was determined by averaging the differences between integrations of *cis*- and *trans*-decaline in a series of multiple injections of a solution of the two. The percent variability was applied to eq 3; $\Delta A/A = 0.003$ was determined.

The rate constants were determined by submitting the data to a weighted least-squares program. A statistical error was associated with this determination, and the error reported with each rate constant is the larger of the statistical error and the random error. All rearrangements proceeded cleanly to give the expected [3,3] shift products, which were characterized by NMR and IR analysis.

General Procedure for Enol Ether Formation via Titanium Ylide Chemistry. Compounds **15**, **16**, **17**, **19**, **31**, and **32** were prepared by methylenation of the appropriate acetates and trifluoroacetates according to the method of Takai et al.[20] In a typical reaction 40 mL of THF was cooled to 0 °C under nitrogen. Titanium(IV) chloride (16.0 mmol as a 1.0 M solution in methylene chloride) was added from a syringe, and the yellow solution was allowed to warm to room temperature. TMEDA (4.80 mL, 32.0 mmol) was added, and the yellow-brown solution was stirred for 10 min. Zinc dust (2.36 g, 36.0 mmol) was introduced, and the resulting suspension stirred for 30 min during which a mild exotherm was observed and the solution turned blue. A solution of acetate (4.0 mmol) and dibromomethane (1.53 g, 8.8 mmol) in 8 mL THF was added from a syringe, and stirring was continued for 3 h at room temperature, during which the color changed to dark brown. Saturated aqueous potassium carbonate (5.2 mL) was added to the reaction mixture at 0 °C, with stirring continued for 15 min at 0 °C. Ethyl ether (80 mL) was added, and the solution was passed rapidly through a short column of basic alumina (activity III) using 400 mL of ether/triethylamine (200:1) as eluant. Concentration by rotary evaporation and chromatography of the residue on basic alumina (activity III) using pentane as eluant afforded enol ethers.

***cis*-1,1,1-Trifluoro-5-octen-2-one (4).** The procedure of Creary was used. A Grignard reagent was formed from *cis*-1-bromo-3-hexane (**3**) (0.013 mol)[37] and magnesium turnings (0.013 mol) in 12 mL of anhydrous ether under nitrogen. Once the reagent was formed it was transferred via cannula to a dropping funnel and added dropwise to a solution of ethyl trifluoroacetate (1.85 g, 0.013 mol) in 12 mL of anhydrous ether held at −78 °C. When addition was complete the resulting suspension was allowed to warm to room temperature. Saturated aqueous ammonium chloride was added, followed by 5% HCl until the aqueous layer was neutralized. The layers were separated, and the organic layer was washed with brine and dried over magnesium sulfate. The ether was removed by distillation at atmospheric pressure through a 32-cm Vigreaux column. The residue was applied to a column of silica gel and eluted with pentane to afford 0.96 g of the ketone (41% yield): NMR (300 MHz, $CDCl_3$) 0.95 (t, J = 6.9 Hz, 3 H), 2.06 (m, 2 H), 2.41 (q, J = 6.9 Hz, 2 H), 2.77 (t, J = 6.3 Hz, 2 H), 5.28 (m, 1 H), 5.46 (dd, J = 16.8, 8.0 Hz, 1 H); IR (neat) 2960 (s), 2930 (s), 1765 (s), 1655 (w), 1150 (m) cm^{-1}.

***cis*-2-(Trifluoromethyl)-1,5-octadiene (5).** Sodium hydride (6.0 mmol as a 58 wt % dispersion) was washed twice with pentane under a nitrogen atmosphere. The system was alternately evacuated and flushed with nitrogen. Dimethyl sulfoxide (4 mL) was added via syringe; the solution was heated with stirring at 75 °C for 30 min followed by cooling to room temperature. Methyltriphenylphosphonium iodide (2.43 g, 6.0 mmol) was added as a solution in 6 mL of warm DMSO, and the resulting golden ylide solution was stirred for 10 min. **4** (0.74 g, 4.1 mmol) was added via syringe; the solution was immediately decolorized. It was stirred an additional 45 min at 50 °C. Water (15 mL) was added, and the solution was extracted with pentane (3 × 20 mL). The pentane extracts were combined and washed with brine (1 × 25 mL) and dried with magnesium sulfate. After concentration by distillation at atmospheric pressure, the yellow residue was applied to a column of neutral alumina (activity I) and eluted with 50 mL of pentane. Removal of the pentane by distillation afforded 0.55 g of the crude diene (75% yield). The crude product was purified by VPC on a 12 ft × $^1/_4$ in. OV-101 column (20% on 60/80 Chromosorb P), column temperature 95 °C, to yield the pure diene as a clear, colorless liquid: NMR (300 MHz, C_6D_6) 0.87 (t, J = 6.1 Hz, 3 H), 1.88 (m, 2 H), 2.01 (s, 2 H), 2.03 (s, 2 H), 4.81 (s, 1 H), 5.15 (m, 1 H), 5.36 (m, 1 H), 5.40 (s, 1 H); ^{19}F NMR (360 MHz, $CDCl_3$) s, −69.70 ppm, relative to external standard CF_3CO_2H at −78.9 ppm; NMR (300 MHz, C_4Cl_6) 0.89 (t, J = 7.2 Hz, 3 H), 1.81 (m, 2 H), 2.03 (br s, 4 H), 5.04 (br s, 3 H), 5.19 (m, 1 H), 5.53 (s, 1 H); IR (neat) 3100 (w), 2940 (s), 2865 (m), 1880 (m), 1655 (m), 1120 (m), 935 (m), 865 (m), 790 (w) cm^{-1}. $(M - CF_3)/e$ = 109.1017, calcd for C_8H_{13} 109.1018.

***trans*-1,1,1-Trifluoro-5-octen-2-one.** The procedure of Creary was again used. A Grignard reagent was formed from *trans*-1-bromo-3-hexene[38] (2.12 g, 13 mmol) and magnesium turnings (0.36 g, 15 mmol) in 15 mL of anhydrous ether. After transfer to a dropping funnel, it was added dropwise to a solution of ethyl trifluoroacetate (1.99 g, 14 mmol) in 15 mL of anhydrous ether held at −78 °C. After being allowed to warm to room temperature the reaction mixture was quenched with aqueous NH_4Cl, followed by the addition of 5% HCl. Removal of ether by fractional distillation followed by short path distillation at aspirator pressure afforded 1.07 g of the ketone, contaminated with ~0.30 g of 3,9-dodecadiene as a side product. Used without further purification (crude yield 46%): NMR (300 MHz, $CDCl_3$) 0.93 (t, J = 6.9 Hz, 3 H), 2.00 (m, 2 H), 2.35 (m, 2 H), 2.79 (t, J = 7.0 Hz, 2 H), 5.30–5.45 (m, 1 H), 5.46–5.61 (m, 1 H), 5.46–5.61 (m, 1 H).

***trans*-2-(Trifluoromethyl)-1,5-octadiene (7).** The same procedure used to prepare diene **5** afforded 0.89 g of **7** as a clear, colorless liquid (crude yield 85%). A portion of this crude was further purified by VPC using an OV-101 column (30 g, 20% on 60/80 Chromosorb P, 12 ft × $^1/_4$ in., 80 °C column temperature): NMR (300 MHz, $CDCl_3$) 0.91 (t, J = 7.5 Hz), 1.90 (t, J = 7.5 Hz, 2 H), 1.95–2.10 (m, 2 H), 4.82 (s, 1 H), 5.17–5.26 (m, 1 H), 5.31–5.40 (m, 1 H), 5.42 (s, 1 H). ^{19}F NMR (360 MHz, $CDCl_3$) −69.76 ppm, referenced from external standard CF_3CO_2H at −78.9 ppm; IR (neat) 3100 (w), 2960 (s), 2870 (m), 1880 (m), 1660 (m, sh), 1120 (m), 960 (m), 935 (m), 825 (m) cm^{-1}; low-res mass spec 178.

α-Methylstyrene Oxide (8).[39] α-Methylstyrene (29.55 g, 0.25 mol) was mixed with *N*-bromosuccinimide (44.5 g, 0.25 mol) in 100 mL of water and stirred vigorously at room temperature for 2 h. The bromohydrin was separated from the water layer, and the water layer was washed with ether (2 × 40 mL). The ether washes were combined with the bromohydrin, and the ether was removed by rotary evaporation. The crude bromohydrin was taken up in a 20% aqueous sodium hydroxide solution (75 mL) and stirred for 30 min at 60 °C. The oxide was separated from the aqueous layer, which was extracted with ether (2 × 40 mL). The combined organic portions were dried over sodium sulfate, and the ether was removed by distillation at atmospheric pressure. Short-path distillation of the residue at reduced pressure afforded 28.7 of the oxide as a clear, colorless liquid (86% yield): bp 77–78 °C (10 Torr); NMR (300 MHz, $CDCl_3$) 1.71 (s, 3 H), 2.79 (d, J = 5.5 Hz, 1 H), 2.96 (d, J = 5.5 Hz, 1 H), 6.40–6.20 (m, 5 H).

2-Phenyl-2-propen-1-ol (10).[40] *n*-Butyllithium as a 2.5 M solution in hexanes (68 mmol) was added to a stirred solution of dry diisopropylamine (6.71 g, 66 mmol) in 60 mL of anhydrous ether at room temperature in a nitrogen atmosphere. The solution was stirred for 45 min, and then 8 (6.00 g, 45 mmol) as a solution in 80 mL of anhydrous ether was added dropwise to the stirring LDA solution over a period of 1 h. The resulting deep red solution was refluxed for 4 h after stirring overnight at room temperature. The reaction was quenched with aqueous ammonium chloride,

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and the layers were separated. The aqueous layer was washed twice with ether; the combined organic portions were washed with 5% HCl until the aqueous layer remained acidic, and then with aqueous sodium carbonate and brine. Drying over sodium sulfate and rotary evaporation to remove ether afforded an oily yellow residue, which was applied to a column of 150 g of silica gel and eluted with 20% ether–hexane. The alcohol was obtained as a yellow liquid (1.55 g, 26% yield). It was purified further by vacuum distillation (bulb-to-bulb): bp 86–90 °C (2 Torr); R_f = 0.24 (20% ether/hexane); NMR (300 MHz, $CDCl_3$) 1.60 (s, 1 H), 4.56 (s, 2 H), 5.36 (s, 1 H), 5.48 (s, 1 H), 7.46–7.28 (m, 5 H); IR (neat) 3350 (s), 3080 (w), 3040 (w), 2920 (w), 1630 (w), 1600 (w), 1025 (w) cm^{-1}.

2-Phenyl-2-propen-1-yl Trifluoroacetate (12). Under anhydrous conditions freshly distilled **10** (0.72 g, 5.4 mmol) was added to stirring trifluoroacetic anhydride (7 mL) at room temperature. The resulting pale yellow solution was gently refluxed for 15 min. Trifluoroacetic anhydride and trifluoroacetic acid were removed by rotary evaporation, and the residue was distilled at reduced pressure (bulb-to-bulb) to yield the trifluoroacetate as a clear, colorless liquid, 1.14 g (92% yield): bp 67–70 °C (1.5 Torr); NMR (90 MHz, $CDCl_3$) 5.23 (s, 2 H), 5.42 (br s, 1 H), 5.63 (s, 1 H), 7.42 (br s, 5 H); IR (neat) 3060 (m), 3030 (m), 2960 (m), 1955 (w), 1785 (s), 1690 (w), 1630 (m), 1220 (m), 1150 (s) cm^{-1}.

5-Phenyl-2-(trifluoromethyl)-3-oxa-1,5-hexadiene (15). **15** was isolated in 30% yield from **12** via the titanium ylide method: R_f 0.51 (pentane); NMR (300 MHz, $CDCl_3$) 4.54 (m, 1 H), 4.72 (s, 2 H), 4.90 (d, J = 3.9 Hz, 1 H), 5.44 (s, 1 H), 5.62 (s, 1 H), 7.30–7.50 (m, 5 H); IR (neat) 3060 (m), 3030 (m), 2930 (m), 1950 (w), 1880 (w), 1810 (w), 1655 (m), 1150 (s) cm^{-1}; M/e = 228.0761, calcd for $C_{12}H_{11}OF_3$ 228.0762.

3-Phenyl-2-propen-1-yl Trifluoroacetate (14). Under nitrogen freshly distilled cinnamyl alcohol (2.50 g, 18.6 mmol) was added from a syringe to stirring trifluoroacetic anhydride (14 mL, 99 mmol) at room temperature. The solution turned red and was refluxed for 10 min. Trifluoroacetic anhydride and trifluoroacetic acid were removed by rotary evaporation, and the residue was purified by bulb-to-bulb distillation to afford the product as 1.08 g of a clear, colorless liquid (25% yield): bp 105–108 °C (4 Torr); NMR (90 MHz, $CDCl_3$) 4.99 (d, J = 5.0 Hz, 2 H), 6.29 (dt, J = 16.0, 6.0 Hz 1 H), 6.78 (d, J = 16.0 Hz, 1 H), 7.43 (m, 5 H).

6-Phenyl-3-oxa-2-(trifluoromethyl)-1,5-hexadiene (17). **17** was isolated in 53% yield from **14** via the titanium ylide method: NMR (300 MHz, $CDCl_3$) 4.52 (m, 3 H), 4.88 (d, J = 4.3 Hz, 1 H), 6.33 (dt, J = 16.0, 5.86 Hz, 1 H), 6.70 (d, J = 16.0 Hz, 1 H), 7.35 (m, 5 H).

1,2-Epoxy-2-(4′-methoxyphenyl)propane (9).[41] Under nitrogen, trimethyloxosulfonium iodide (11.0 g, 40 mmol) was introduced into a three-necked flask that contained sodium hydride (50 mmol, washed twice from the dispersion with pentane). DMSO (50 ml) was added slowly from a syringe; when addition was complete it was stirred another 20 min at room temperature. 4-Methoxyacetophenone (5.00 g, 33 mmol) was added from a syringe as a solution in 13 mL of DMSO, and the reaction mixture stirred at 50 °C for 15 h. Cold water (100 mL) was added, and the product mixture extracted with ether (3 × 50 mL). The combined ether extracts were washed with water (2 × 50 mL) and dried over sodium sulfate. Rotary evaporation afforded a clear brown oil that was purified by bulb-to-bulb distillation from potassium carbonate to yield 3.20 g of a clear colorless oil (59% yield). Note: This epoxide is extremely acid sensitive; any attempts at chromatography result in rearrangement to 2-(4′-methoxyphenyl)propionaldehyde: bp 109–112 °C (2.5 Torr); NMR (90 MHz, $CDCl_3$) 1.67 (s 3 H), 2.79 (d, J = 5.0 Hz, 1 H), 2.91 (d, J = 5.09 Hz, 1 H), 3.80 (s, 3 H) 6.87 (d, J = 9.0 Hz, 2 H), 7.30 (d, J = 9.0 Hz, 2 H); IR (neat) 2960 (s), 2910 (s), 2045 (m), 1890 (m), 1720 (m), 1675 (w), 1605 (m), 1245 (m), 1175 (m) cm^{-1}.

2-(4′-Methoxyphenyl)-2-propen-1-ol (11).[40] Lithium diisopropylamide was formed by adding n-butyllithium (47 mmol as a 2.5 M solution in hexane) to a solution of diisopropylamine (4.76 g, 47 mmol) in 40 mL ether and stirring for 30 min under nitrogen. 1,2-Epoxy-2-(4′-methoxyphenyl)propane (**9**) (5.10 g, 31 mmol) was added from a dropping funnel as a solution in 65 mL of ether over a period of 1 h. The dark red reaction mixture was stirred at room temperature for 20 h and then quenched with saturated NH_4Cl(aq). The layers were separated, and the aqueous layer was washed once with ether. The combined organic portions were washed successively with water, 5% HCl, and aqueous sodium carbonate, dried over sodium sulfate, and concentrated by rotary evaporation to afford a pale yellow solid. Chromatography on silica gel (100 g, 3:1 hexane/ether) afforded 1.37 g (27% yield) of the alcohol as fine white needles: R_f = 0.21 (15% ethyl acetate/hexane); mp 72–77 °C (lit.[19] mp 80–81 °C); NMR (300 MHz, $CDCl_3$) 1.55 (br s, 1 H), 3.81 (s, 3 H), 4.53 (br s, 2 H), 5.26 (br s, 1 H), 5.40 (s, 1 H) 6.89 (d, J = 7.2 Hz, 2 H), 7.40 (d, J = 7.2 Hz, 2 H).

2-(4′-Methoxyphenyl)-2-propen-1-yl Trifluoroacetate (13).[42] 2,6-Lutidine (0.29 g, 2.7 mmol) and **11** (0.44 g, 2.7 mmol) were stirred together in 10 mL of methylene chloride at 0 °C under nitrogen. Trifluoroacetic anhydride (0.79 mL, 4.8 mmol) was added dropwise from a syringe. The reaction mixture was stirred at 0 °C for 30 min, and then the ice bath was replaced with an oil bath and the reflux condenser with a distillation head. Methylene chloride and excess trifluoroacetic anhydride were removed by distillation at atmospheric pressure in a nitrogen atmosphere. Distillation of the residue at reduced pressure afforded 0.96 g of a clear, pale brown liquid that boiled at 112–117 °C/3 Torr and upon analysis proved to be a 71% mixture of product and lutidine. Used without further purification (crude yield 98%): R_f = 0.52 (5% ethyl acetate/hexane); bp 113–117 °C (2.0 Torr); NMR (300 MHz, $CDCl_3$) 3.83 (s, 3 H), 5.20 (s, 2 H), 5.37 (s, 1 H), 5.58 (s, 1 H), 6.91 (d, J = 7.2 Hz, 2 H), 7.36 (d, J = 7.2 Hz, 2 H); IR (neat) 3100 (m), 3040 (m), 2930 (s), 2840 (m, sh), 1785 (m), 1605 (s), 1250 (m), 1175 (w) cm^{-1}.

5-(4′-Methoxyphenyl)-2-(trifluoromethyl)-3-oxa-1,5-hexadiene (16). **16** was isolated in 8% yield from **13** via the titanium ylide method, contaminated with an equal amount of a side product, 4-bromo-2-(4′-methoxyphenyl)-1-butene. Product ether: R_f = 0.43 (5% ethyl acetate/hexane). Product ether: NMR (300 MHz, C_6D_{12}) 3.63 (s, 3 H), 4.33 (m, 1 H), 4.52 (br s, 2 H), 4.74 (d, J = 4.30 Hz, 1 H), 5.22 (br s, 1 H), 5.37 (br s, 1 H), 6.71 (d, J = 7.2 Hz, 2 H), 7.20 (d, J = 7.2 Hz, 2 H). Side product: R_f = 0.61 (5% ethyl acetate/hexane). Side product: NMR (300 MHz, C_6D_{12}) 7.18 (d, J = 7.2 Hz, 2 H), 6.70 (d, J = 7.2 Hz, 2 H), 5.18 (br s, 1 H), 4.95 (br s, 1 H), 3.63 (s, 3 H), 3.38 (t, J = 7.3 Hz, 2 H), 2.82 (t, J = 7.3 Hz, 2 H).

3-Oxa-2-(trifluoromethyl)-1-undecene (19). **19** was isolated in 28% yield from n-octyl trifluoroacetate (**18**) via the titanium ylide method: R_f = 0.90 (1% ether/pentane); NMR (500 MHz, $CDCl_3$) 0.89 (t, J = 6.9 Hz, 3 H), 1.30 (m, 10 H), 1.39 (m, 2 H), 1.74 (m, 2 H), 3.77 (t, J = 6.5 Hz, 2 H), 4.38 (dt, J = 3.6, 1.9 Hz), 4.76 (d, J = 3.6 Hz, 1 H); IR (neat) 2930 (s), 2860 (s), 1650 (s), 1190 (m), 1150 (s) cm^{-1}; $(M - CF_3)/e$ = 155.145, calcd for $C_{10}H_{19}O$ 155.144.

***n*-Octyl 1,1,1-Trifluoro-2-propyl Ether (20).** Atmospheric pressure hydrogenation of 3-oxa-2-(trifluoromethyl)-1-undecene (**19**) in methanol catalyzed by 5% palladium on charcoal afforded n-octyl 1,1,1-trifluoro-2-propyl ether as the only product: NMR (300 MHz, $CDCl_3$) 0.88 (t, J = 7.04 Hz, 3 H), 1.29 (m, 13 H), 1.58 (m, 2 H), 3.50–3.78 (m, 3 H); m/e = 226.1549, calcd for $C_{11}H_{21}OF_3$ 226.1545.

Allyl Trifluoroacetate. Allyl alcohol (5.00 g, 86.1 mmol) and 2,6-lutidine (10.18 g, 95.0 mmol) were stirred together under nitrogen and cooled to 0 °C. Trifluoroacetic anhydride (18.1 g, 86.1 mmol) was slowly added from a syringe. Distillation of the reaction mixture through a 20-cm Vigreaux column afforded 9.7 g of the acetate as a clear, colorless liquid (73% yield): bp 79–81.5 °C; NMR (90 MHz, $CDCl_3$) 4.84 (d, J = 7 Hz, 2 H), 5.30–5.52 (m, 2 H), 5.80–6.18 (m, 1 H).

3-Oxa-2-(trifluoromethyl)-1,5-hexadiene (1a). **1a** was prepared via the titanium ylide method from allyl trifluoroacetate with the following modifications. Titanium(IV) chloride was added neat, as were allyl trifluoroacetate and methylene bromide. The reaction was run in diglyme (anhydrous). After being stirred at room temperature for 4.5 h, the system was evacuated to 20 Torr with a vacuum-transfer tube leading to a liquid nitrogen

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cooled flask for 1 h. The distillate collected was predominantly diglyme, but the product ether **1a** was isolated pure in trace amounts by VPC purification using an OV-101 column (20% on Chromosorb P, 6 ft × $^1/_4$ in., injector port at 70 °C, column at 45 °C, and detector at ca. 100 °C). The compound had an identical retention time as that of an authentic sample by capillary GC analysis: NMR (300 MHz, authentic sample, $CDCl_3$) 4.36 (dt, J = 5.6, 1.7 Hz, 2 H), 4.43 (m, J = 2.0 Hz, 1 H), 4.83 (d, J = 3.9 Hz, 1 H), 5.27–5.42 (m, 2 H), 5.90–6.04 (m, 1 H); M/e = 152.0450, calcd for $C_6H_7OF_3$ 152.0449.

α,α-Dideuterioallyl Trifluoroacetate. The same method as described for allyl trifluoroacetate gave the deuterated trifluoroacetate from 1,1-dideuterioallyl alcohol[45] as 0.82 g of a clear, pale yellow liquid (54% yield); bp 76–78 °C; NMR (300 MHz, $CDCl_3$) 5.41 (ddd, J = 17.0, 10.5, 2.35 Hz, 2 H), 5.94 (dd, J = 17.0, 10.5 Hz, 1 H); m/e = 156.0344; calcd for $C_5H_3D_2O_2F_3$ 156.0367. NMR and mass spectral data indicated >96% deuteration.

4,4-Dideuterio-3-oxa-2-(trifluoromethyl)-1,5-hexadiene (1b). **1b** was prepared via the titanium ylide method used to prepare **1a**, using α,α-dideuterioallyl trifluoroacetate. It was obtained in a trace amount by VPC as for **1a**, having an identical retention time as that of an authentic sample by capillary GC analysis. The percent deuteration was taken to be the same as that for α,α-dideuterioallyl trifluoroacetate: NMR (360 MHz, authentic sample, $CDCl_3$) 4.43 (d, J = 5.6, 1.8 Hz, 1 H), 4.83 (d, J = 4.0 Hz, 1 H), 5.34 (ddd, J = 17.3, 10.4, 1.1 Hz, 2 H), 5.95 (dd, J = 17.3, 10.4 Hz, 1 H).

γ,γ-Dideuterioallyl Trifluoroacetate. 3,3-Dideuterioallyl alcohol was prepared according to the method of McMichael.[44] The same method as described for allyl trifluoroacetate gave 3.24 g of the acetate as a clear colorless liquid (57% yield): bp 72–75.5 °C; NMR (90 MHz, $CDCl_3$) 6.02 (m, 1 H), 4.85 (d, J = 7 Hz, 2 H); a small signal at 5.40 ppm was integrated to show at least 85% deuteration at the γ-position.

6,6-Dideuterio-3-oxa-2-(trifluoromethyl)-1,5-hexadiene (1c). **1c** was prepared via the titanium ylide method from γ,γ-dideuterioallyl trifluoroacetate, as described for **1a**, with the following modification. After the reaction mixture was stirred at room temperature for 5 h, gaseous nitrogen was rapidly bubbled through the stirring reaction mixture into a liquid nitrogen cooled flask for 3 h. The aspirated distillate was predominantly diglyme, and the product ether **1c** was obtained pure in a trace amount by VPC as described for **1a**. The percent deuteration, ≥85%, was taken to be the same as that observed for γ,γ-dideuterioallyl trifluoroacetate: NMR (360 MHz, authentic sample, $CDCl_3$) 4.36 (d, J = 5.4 Hz, 2 H), 4.43 (m, J = 1.8 Hz, 1 H), 4.83 (d, J = 3.9 Hz, 1 H), 5.95 (br s, 1 H).

1-Octen-3-yl Acetate (27). A 500-ml, three-necked round-bottom flask was charged with cyclohexane (150 ml), 1-octen-3-ol (2.95 g, 23.0 mmol), and pyridine (8.19 g, 0.103 mol) under a reflux condenser that was fitted with a drying tube containing calcium chloride. When the solution reached reflux, acetic anhydride (7.15 g, 0.070 mol) was added, and the solution was refluxed for 10 h. Cyclohexane was removed by rotary evaporation, and the residue was fractionally distilled to yield 2.66 g of the acetate as a clear, colorless liquid (68% yield): R_f = 0.82 ($CHCl_3$); bp 75–77 °C (11 Torr); NMR (300 MHz, $CDCl_3$) 0.89 (t, J = 6.3 Hz, 3 H), 1.29 (br s, 6 H), 1.60 (m, 2 H), 2.07 (s, 3 H), 5.25–5.14 (m, 3 H), 5.84–5.72 (m, 1 H); IR (neat) 3080 (m), 2930 (s), 2850 (m), 1735 (s), 1645 (m), 1235 (m) cm^{-1}.

2-Methyl-4-pentyl-3-oxa-1,5-hexadiene (30). **30** was isolated in 41% yield from **27** via the titanium ylide method: NMR (500 MHz, $CDCl_3$) 0.89 (t, 3 H), 1.45–1.22 (m, 6 H), 1.67–1.50 (m, 2 H), 1.81 (s, 3 H), 3.82 (d, J = 1.4 Hz, 1 H), 3.87 (s, 1 H), 4.32 (q, J = 6.4 Hz, 1 H), 5.15 (s, 1 H), 5.17 (d, J = 8.1 Hz, 1 H), 5.75 (m, 1 H); IR (neat) 3120 (w), 3080 (m), 2920 (s), 2850 (m), 1845 (m), 1655 (s), 1590 (m), 1270 (s), 985 (m), 920 (m), 790 (m) cm^{-1}; M/e = 168.1514, calcd for $C_{11}H_{20}O$ 168.1515.

3-Methyl-1-octen-3-yl Acetate (28).[27] 3-Methyl-1-octen-3-ol (**25**) (1.96 g, 13.8 mmol), triethylamine (2.77 mL, 20.8 mmol), acetic anhydride (2.12 g, 20.8 mmol), and (dimethylamino)pyridine (DMAP, 0.17 g) were stirred together at room temperature for 2 weeks. Ether (25 mL) was added, and the solution was washed with 5% HCl until the aqueous layer remained acidic. The organic layer was washed with saturated sodium carbonate solution (1 × 20 mL) and dried over magnesium sulfate. Concentration via rotary evaporation and bulb-to-bulb distillation afforded the acetate as 1.56 g of a clear, colorless liquid (61% yield): bp 75–78 °C (7 Torr); R_f 0.92 (15% ether/hexane); NMR (90 MHz, $CDCl_3$) 0.90 (t, 3 H), 1.30 (m, 6 H), 1.60 (s, 3 H), 1.81 (m, 2 H), 2.07 (s, 3 H), 5.19 (m, 2 H), 6.05 (m, 1 H).

2,4-Dimethyl-4-pentyl-3-oxa-1,5-hexadiene (31). **31** was isolated in 22% yield from **28** via the titanium ylide method, ca. 80% pure: NMR (500 MHz, C_6D_6) 0.90 (t, 3 H), 1.45–1.20 (m, 6 H), 1.42 (s, 3 H), 1.81 (s, 3 H), 2.28 (m, 2 H), 4.06 (s, 1 H), 4.19 (s, 1 H), 4.97 (m, 2 H), 6.04 (dd, J = 18.0, 10.8 Hz, 1 H); IR (neat) 3080 (w), 2920 (s), 2850 (s), 1660 (s), 1615 (m), 1370 (m), 1270 (m), 985 (w), 910 (w) cm^{-1}; M/e = 182.1667, calcd for $C_{12}H_{22}O$ 182.1672.

1,1,1-Trifluoro-2-heptanone. The method of Dishart and Levine[30] was employed. The Grignard reagent was formed from magnesium turnings (7.78 g, 0.32 mol) and dry pentyl bromide (37.2 mL, 0.30 mol) in 150 mL of anhydrous ether. After formation it was cooled in a dry ice–acetone bath, and trifluoroacetic acid (7.70 mL, 0.10 mol) was added dropwise as a solution in 10 mL of ether over a period of 45 min. After addition was complete the dry ice bath was removed, and the product mixture was allowed to stir at room temperature for 6 h. The gray solution was carefully poured through a water-cooled condenser into a flask containing concentrated HCl (50 mL) and 200 g of cracked ice. The resulting suspension was stirred until the residual magnesium was dissolved, and the layers were separated. The aqueous layer was washed with ether (2 × 100 mL), and the combined ethereal portions were washed with saturated sodium carbonate solution until the aqueous layer remained basic and once with brine (100 mL) and dried over magnesium sulphate. Removal of the solvent by rotary evaporation and reduced pressure short-path distillation afforded 9.72 g of a clear, colorless liquid (58% yield): bp 60–71 °C (87 Torr) (lit.[43] bp 112–113.5 °C (739 torr)); NMR (90 MHz, $CDCl_3$) 0.90 (t, J = 7 Hz, 3 H), 1.33 (m, 4 H), 1.68 (m, 2 H), 2.70 (t, J = 7 Hz, 2 H); IR (neat) 3500 (w), 2930 (s), 2860 (m), 1760 (s), 1205 (m), 1150 (m) cm^{-1}.

3-(Trifluoromethyl)-1-octen-3-ol (26). 1,1,1-Trifluoro-2-heptanone (4.00 g, 23.8 mmol) was added dropwise to vinylmagnesium bromide (26.0 mmol, 1.0 M in THF) as a solution in 25 mL of anhydrous ether. The vinyl Grignard solution was held at 0 °C under dry nitrogen. When addition was complete the reaction mixture was allowed to warm to room temperature. It was quenched with saturated ammonium chloride solution and filtered. The filtrate was washed with water (2 × 30 mL) and brine (1 × 30 mL), dried over sodium sulfate, and concentrated by rotary evaporation. Bulb-to-bulb distillation at reduced pressure of the residue afforded 3.36 g of the alcohol as a clear, colorless liquid (72% yield): bp 66–72 °C (15 Torr); NMR (300 MHz, $CDCl_3$) 0.88 (t, J = 6.9 Hz, 3 H), 1.40–1.20 (m, 8 H), 1.80–1.65 (m, 2 H), 2.14 (s, 1 H), 5.43 (d, J = 10.9 Hz, 1 H), 5.51 (d, J = 17.2 Hz, 1 H), 5.88 (dd, J = 17.2, 10.9 Hz, 1 H); IR (neat) 3450 (br s), 3090 (w), 2950 (s), 2870 (m), 1880 (m), 1640 (m), 1160 (m).

3-(Trifluoromethyl)-1-octen-3-yl Acetate (29). 3-(Trifluoromethyl)-1-octen-3-ol (**26**) (1.50 g, 7.6 mmol) was dissolved in 10 mL of THF at 0 °C under nitrogen. Sodium hydride (0.26 g, 10.7 mmol, washed from dispersion with two portions of dry pentane) was added portionwise, with each portion being added after the preceding evolution of hydrogen ceased. After all the sodium hydride had been added, acetyl chloride (0.600 g, 7.6 mmol freshly distilled from dimethylaniline) was added slowly from a syringe to the solution at 0 °C. An immediate reaction ensued, producing a reddish-brown precipitate. Once addition was complete the reaction mixture was allowed to warm to room temperature. It was poured into 20 mL of water, 20 mL of ether was added, and the layers were separated. The organic layer was washed with saturated sodium bicarbonate solution (1 × 10 mL) and brine (1 × 10 mL) and dried over sodium sulfate. Concentration by rotary evaporation and bulb-to-bulb distillation at reduced pressure, 67–72 °C, 7 Torr, afforded 1.36 g of a mixture of the acetate and starting alcohol. The mixture was applied to silica gel (100 g) and eluted with 10% ether/hexane to afford 0.42

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g of the acetate as a clear, colorless liquid (23% yield): R_f = 0.70 (10% ether/hexane); NMR (300 MHz, $CDCl_3$) 0.89 (t, J = 5.1 Hz, 3 H), 1.28 (m, 8 H), 2.12 (s, 3 H), 5.41 (d, J = 6 Hz, 1 H), 5.45 (s, 1 H), 5.90 (dd, J = 18.0, 11.6 Hz, 1 H); IR (neat) 3100 (w), 2960 (s), 2930 (s), 2870 (m), 1760 (s), 1645 (m, sh), 1185 (w), 1160 (w) cm^{-1}.

2-Methyl-4-pentyl-4-(trifluoromethyl)-3-oxa-1,5-hexadiene (32). 32 was isolated in 10% yield from **29** via the titanium ylide method: R_f = 0.80 (pentane); NMR (500 MHz, C_6D_6) 0.88 (t, J = 8.9 Hz, 3 H), 1.25–1.10 (m, 6 H), 1.72 (s, 3 H), 2.02 (m, 2 H), 4.04 (br s, 1 H), 4.11 (d, J = 1.8 Hz, 1 H), 5.16 (d, J = 11.2 Hz, 1 H), 5.29 (d, J = 17.7 Hz, 1 H), 5.89 (dd, J = 17.7, 11.2 Hz, 1 H); IR (neat) 3090 (w), 2960 (s), 2910 (s), 2860 (m), 1645 (s), 1165 (m), 1115 (m), 930 (w), 810 (m) cm^{-1}; low-resolution mass spec (relative intensity) 237 (10.4), 236 (1.2), 195 (53.8), 179 (18.6), 84 (100).

2-Methyl-3-oxa-1,5-hexadiene (33). 2-Methoxypropene (100 mL, freshly distilled from sodium), allyl alcohol (1.65 g, 28 mmol, freshly distilled), and crystalline mercuric acetate (1.0 g) were mixed together and brought to reflux while stirring under dry nitrogen. Each 2 h for 6 h an additional 0.5 g of mercuric acetate was added; the reaction mixture was then refluxed overnight. Saturated sodium bicarbonate solution (50 mL) was added, and the resultant two-phase solution was stirred vigorously for 30 min. The layers were separated, and the organic layer was washed with sodium bicarbonate solution (2 × 25 ml); the combined aqueous portions were extracted with ether (1 × 50 mL). The combined organic portions were dried over sodium sulfate, and the volatile components were removed by distillation at atmospheric pressure through a 32-cm Vigreaux column. The resulting pale yellow liquid was chromatographed (Florisil, 60–100 mesh, pentane as eluant) to afford 0.23 g of the product ether as a clear colorless liquid (8% yield). The ether was further purified by VPC (12 ft × $^1/_4$ in. column, 20% OV-101, 30 g on 60/80 Chromosorb P, column temperature 75 °C, injection port temperature 180 °C); however, in the process the ether rearranged 45% to 5-hexen-2-one: bp 89–90 °C (lit.[1b] bp 87.5–88 °C, 745 Torr); NMR (300 MHz, $CDCl_3$) 1.85 (s, 3 H), 3.86 (d, J = 10.9 Hz, 1 H), 4.22 (d, J = 6.3 Hz, 1 H), 5.28 (dd, J = 32.8, 13.7 Hz, 2 H), 5.98 (m, 1 H); IR (neat) 3070 (m), 2920 (s), 1655 (s), 1600 (m), 1280 (s), 990 (w), 920 (m), 850 (w), 790 (m) cm^{-1}; M/e = 98.0731, calcd for $C_6H_{10}O$ 98.0732.

1,1,1-Trifluoro-3-buten-2-ol (22). Trifluoroacetaldehyde hydrate (10.6 g, 0.090 mol) was added dropwise from a syringe into a mixture of 20 mL of sulfuric acid and 3 g of phosphorous pentoxide at 100 °C. The trifluoroacetaldehyde thus generated went through a cannula into a dry ice cooled flask. Exclusion of moisture is very important. Once all the gaseous aldehyde had been generated and trapped, it was slowly admitted via cannula into a THF solution of vinylmagnesium bromide (110 mL, 1.0 M, 0.110 mol) with stirring and cooling. The reaction mixture was stirred for 3 h after addition was complete. Following a quench with saturated ammonium chloride solution (20 mL) and filtration, the filtered solids were washed with ether and the combined ethereal portions fractionated through a 32-cm Vigreaux column. When the head temperature reached 80 °C, fractionation through a 20-cm column packed with glass helices up to a head temperature of 100 °C afforded 8.11 g of an alcohol–THF azeotrope, which was 67.8 wt % alcohol (49% yield): R_f = 0.71 (40% ether/hexane); NMR (300 MHz, $CDCl_3$) 3.08 (d, J = 6.25 Hz), 4.46 (m, 1 H), 5.47 (d, J = 10.6 Hz, 1 H), 5.59 (d, J = 17.2 Hz, 1 H), 5.92 (m, 1 H).

1,1,1-Trifluoro-3-buten-2-yl Formate (23). A solution of methylene chloride (300 mL), 1,1,1-trifluoro-3-buten-2-ol (5.43 g, 104 mmol), formic acid (4.79 g, 104 mmol), and triethylamine (21.96 g, 217 mmol) was cooled to −40 °C under nitrogen. Acetic anhydride (16.2 g, 159 mmol) was added, and the solution was stirred at −40 °C for 40 min, followed by gradual warming to room temperature over a period of 1.5 h. The resulting white suspension was washed with 5% HCl until the aqueous portion remained acidic, and then once with saturated sodium bicarbonate. After drying over sodium sulfate, concentration by distillation at atmospheric pressure followed by reduced pressure distillation through a 20-cm Vigreaux column afforded, at 46–48 °C/75 Torr, 0.99 g of a clear colorless distillate that was comprised of the desired formate (81%), the acetate of the starting alcohol (16%), and THF (3%). Distillation at lower temperature afforded the formate as well, being contaminated to a greater extent with THF. The total yield of formate was 3.08 g (46%), obtained as a mixture with an additional 4% acetate side product and 29% THF: R_f = 0.35 (2% ethyl acetate/hexane); NMR (300 MHz, $CDCl_3$) 5.59 (m, 2 H), 5.72–5.91 (m, 2 H), 8.14 (s, 1 H); IR (neat) 3100 (w), 1740 (s), 1180 (m), 1135 (s) cm^{-1}; mass spec 154; M − CHO/e 125.0225, calcd for $C_4H_4OF_3$ 125.0215.

3-Oxa-4-(trifluoromethyl)-1,5-hexadiene (21). 1,1,1-Trifluoro-3-buten-2-yl formate (**23**) (2.00 g, 13.0 mmol as a mixture with an additional 0.93 g of THF and 0.08 g of the acetate) was taken up in m-xylene (25 mL, distilled from sodium benzophenone ketyl) along with 200 μL of pyridine and cooled under nitrogen to −40 °C. The Tebbe reagent, (m-chloro)(μ-methylene)bis(cyclopentadienyl)titaniumdimethylaluminum (~4.3 g, ~15.0 mmol; prepared according to the method of Tebbe et al. and used crude; a purity of 75% was assumed), was added over a period of 15 min as a solution in 35 mL of m-xylene. The reaction mixture was stirred an additional 30 min at −40 °C and allowed to warm to room temperature over a period of 1.5 h. After the mixture was stirred overnight, workup and purification of an aliquot and GC analysis showed most of the formate to be consumed, with the acetate impurity still remaining. Additional stirring at room temperature brought about no further reaction, so the quench was effected at −5 °C with dropwise addition of 7 mL of 10% NaOH. Once gas evolution ceased, 30 mL of xylene was added, and the solution was dried over sodium sulfate. Filtration through Celite afforded a clear, dark orange filtrate; distillation through a short Vigreaux column up to a head temperature of 112 °C afforded 2.0 g of a distillate that was 10% the desired ether, the major impurities being THF and cyclopentadiene (10% crude yield). The product ether was isolated pure by preparative gas chromatography (12 ft × $^1/_4$ in. 20% OV-101 on chromosorb P 60/80, oven at 45 °C, injector port at 65 °C, and detector at 100 °C): R_f = 0.94 (2% ethyl acetate/hexane); NMR (500 MHz, C_6D_6) 3.92 (dd, J = 6.52, 2.25 Hz, 1 H), 3.95 (m, J = 6.39 Hz), 4.27 (dd, J = 14.0, 2.25 Hz, 1 H), 4.99 (d, J = 10.4 Hz, 1 H), 5.11 (d, J = 17.3 Hz, 1 H), 5.45 (m, 1 H), 5.90 (dd, J = 14.0, 6.52 Hz, 1 H); ^{13}C NMR (125 MHz, CD_3CN) 150.69, 129.03, 124.55 (q, J = 281 Hz), 123.92, 91.56, 77.97 (q, J = 31.4 Hz); FT-IR (C_6D_6) 1643 (m), 1624 (m), 1271 (m), 1184 (s), 1132 (m) cm^{-1}.

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Registry No. **1a**, 124581-20-0; **1b**, 124581-22-2; **1c**, 124602-49-9; **4**, 124581-23-3; **5**, 124581-24-4; **7**, 124581-25-5; **8**, 2085-88-3; **9**, 42432-42-8; **10**, 6006-81-1; **11**, 89619-03-4; **12**, 66966-42-5; **13**, 65374-30-3; **14**, 28664-25-7; **15**, 124581-26-6; **16**, 124581-27-7; **17**, 124581-28-8; **18**, 2561-21-9; **19**, 124581-29-9; **20**, 92244-84-3; **21**, 124581-32-4; **22**, 666-33-1; **23**, 124581-30-2; **25**, 24089-00-7; **26**, 124581-35-7; **27**, 2442-10-6; **28**, 66008-66-0; **29**, 124602-50-2; **30**, 124581-33-5; **31**, 124581-34-6; **32**, 124581-36-8; **33**, 7623-25-8; H_2C=$CHCH_2OH$, 107-18-6; $F_3CCOOCOCF_3$, 407-25-0; $F_3CCO_2CH_2CH$=CH_2, 383-67-5; CH_2Br_2, 74-95-3; H_2C=$CHCD_2OH$, 10475-51-1; $F_3CCO_2CD_2CH$=CH_2, 124581-21-1; D_2C=$CHCH_2OH$, 16315-95-0; $F_3CCO_2CH_2CH$=CD_2, 124602-48-8; D_2, 7782-39-0; (Z)-$BrCH_2CH_2CH$=$CHCH_2CH_3$, 5009-31-4; F_3CCO_2Et, 383-63-1; (E)-$HOCH_2CH_2CH$=$CHCH_2CH_3$, 928-97-2; PhCH=$CHCH_3$, 98-83-9; p-$MeOC_6H_4COCH_3$, 100-06-1; PhCH=$CHCH_2OH$, 104-54-1; $F_3CCOH{\cdot}H_2O$, 421-53-4; $F_3CCH(OAc)CH$=CH_2, 124581-31-3; CH_2=$CHOCH_2CH$=CH_2, 3917-15-5; $CH_3(Ch_2)_4CHO$, 66-25-1; H_2C=$CHCH(OH)(CH_2)_4CH_3$, 3391-86-4; $H_3CCO(CH_2)_4CH_3$, 110-43-0; $H_3C(CH_2)_4Br$, 110-53-2; F_3CCO_2H, 76-05-1; $F_3CCO(CH_2)_4CH_3$, 453-41-8; $H_3CC(OMe)$=CH_2, 116-11-0; (E)-$BrCH_2CH_2CH$=$CHCH_2CH_3$, 63281-96-9; (E)-$F_3CCOCH_2CH_2CH$=$CHCH_2CH_3$, 124581-37-9; CH_3CH_2CH=$CHCH_2CH_2OH$, 928-96-1.