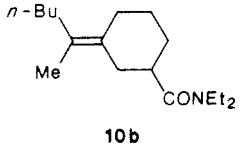
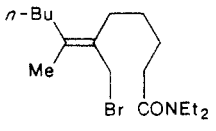
unequivocally establish the essential absence of the stereoisomeric impurities in each case.

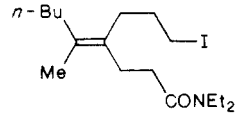
The potential versatility of the present strategy is indicated in Scheme I as well as in eq 3. ^{13}C NMR examination of three additional pairs of stereoisomeric exocyclic alkenes, i.e., **7d** and **7e**, **9a** and **9b**, and **10a** and **10b**, indicates that all of them are of >98% isomeric purity. The ^{13}C NMR spectra of all the other exocyclic alkene products also show only one set of signals, indicating that their isomeric purity is also >98%. It appears that so long as the reactions of allylic intermediates proceed without regio- or stereoisomerization the current strategy can readily provide exocyclic alkenes of essentially 100% isomeric purity. In addition to various forms of allylic rearrangement, however, certain types of reactions that can prevent the formation of exocyclic alkenes should be noted and avoided. For example, β elimination can be an undesirable side reaction especially in base-induced reactions for preparing six-membered rings. Thus, whereas treatment of **11** with LDA (−78 to 22 °C) gives **10b** in 98% yield, the corresponding reaction of **12** merely produces **13**.



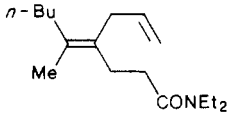
10b



11



12



13

All previously developed methodologies heavily depend on one to a few reactions in the crucial exocyclic alkene formation step with the possible exception of those involving alkenylmetal intermediates.[5] In contrast, a wide variety of reactions are available for the exocyclic alkene formation step, i.e., cyclization step, in the present strategy, as indicated and suggested by the results presented above. This and the ease with which essentially 100% regio- and stereoselectivity can be attained make this approach rather unique. Further exploration of its scope and its application to the synthesis of exocyclic alkenes of biological and medicinal interest, such as carbacyclin,[3b] are under active investigation.

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Supplementary Material Available: Physical data for **4**, **5a**, **5b**, **7a–e**, **8**, **9a**, **9b**, **10a**, and **10b** (4 pages). Ordering information is given on any current masthead page.

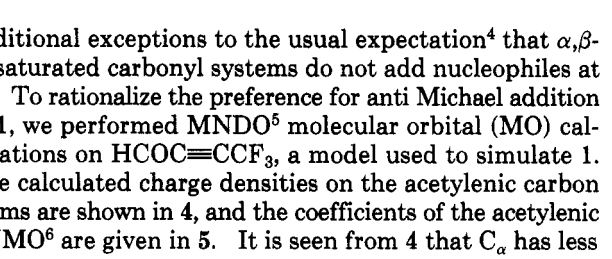
(16) In particular, the following pairs of signals for **5a** and **5b** respectively show chemical shift differences of >0.4 ppm: 18.03 and 18.67, 32.87 and 33.49, and 46.52 and 47.01.

Ei-ichi Negishi,* Yantao Zhang[2a]
Fredrik E. Cederbaum,[2b] Michael B. Webb
Department of Chemistry
Purdue University
West Lafayette, Indiana 47907
Received August 8, 1986

Michael and Anti-Michael Additions to Benzoyl(trifluoromethyl)acetylene

Summary: Kinetic and thermodynamic aspects of nucleophilic additions to benzoyl(trifluoromethyl)acetylene were examined.

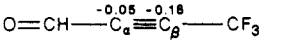
Sir: A recent report[1] on anti-Michael addition to ynamides prompts us to communicate our observations on the addition of PhS^- and PhO^- to benzoyl(trifluoromethyl)acetylene, $PhCOC{\equiv}CCF_3$ (**1**). As shown in eq 1, reaction of **1** with PhS^- and PhO^- leads cleanly to the anti-Michael adducts **2** and **3**, respectively.[2,3] These examples provide



(1)

2, >90% **3**, >90%

additional exceptions to the usual expectation[4] that α,β-unsaturated carbonyl systems do not add nucleophiles at C_α. To rationalize the preference for anti Michael addition to **1**, we performed MNDO[5] molecular orbital (MO) calculations on $HCOC{\equiv}CCF_3$, a model used to simulate **1**. The calculated charge densities on the acetylenic carbon atoms are shown in **4**, and the coefficients of the acetylenic LUMO[6] are given in **5**. It is seen from **4** that C_α has less



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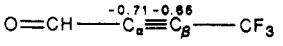

5

negative charge density than does C_β, so that a nucleophile will preferentially attack C_α, thereby leading to anti-Michael addition. The acetylenic LUMO shown in **5** has a larger coefficient at C_α than at C_β, which is also consistent with anti-Michael addition. These rationalizations are based on the properties of the substrate alone and thus imply that the preference for the above anti-Michael addition results from kinetic control.[11]

Consequently, we examined addition of PhS^- and PhO^- to **1** under a thermodynamically controlled condition, and these results are summarized in eq 2.[7] Heating the kinetic

(1) Klumpp, G. W.; Mierop, A. J. C.; Vrielink, J. J.; Brugman, A.; Schakel, M. *J. Am. Chem. Soc.* **1985**, *107*, 6740.

(2) A mixture containing $PhCOC{\equiv}CCF_3$[10] (5.00 mmol), PhSH (5.00 mmol), and 50 mg of *t*-BuOK in 15 mL of absolute ethanol was maintained under N_2 at 25 °C for 6 h. The mixture was then poured into water and extracted with ether. The ether solution was washed with dilute aqueous NaOH and water and dried over $MgSO_4$. Removal of drying agent and solvent left a residue which was chromatographed over silica gel. Compound **2** [mp 43 °C; ^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, Ar H), 6.0 (q, J = 9 Hz, vinyl H trans to PhS); ^{19}F NMR ($CFCl_3$) 58 ppm (d, J = 9 Hz, *gem* vinyl CF_3, H)] was isolated in 90% yield.[3] In similar fashion from $PhCOC{\equiv}CCF_3$ and PhOH, compound **3** [mp 92–93 °C; ^1H NMR ($CDCl_3$) δ 8.30–7.0 (m, Ar H), 5.8 (q, J = 9 Hz, vinyl H trans to PhO); ^{19}F NMR ($CFCl_3$) 57 ppm (d, J = 9 Hz, *gem* vinyl CF_3, H)] was isolated in 90% yield.[3]

(3) Satisfactory elemental analyses were obtained on all new compounds.

(4) March, J. *Advanced Organic Chemistry*, 2nd ed.; McGraw-Hill: New York, 1977; p 679.

(5) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899, 4907.

(6) The π^* orbital of a triple bond not in conjugation with the π framework of the substituent may be referred to as the acetylenic LUMO.

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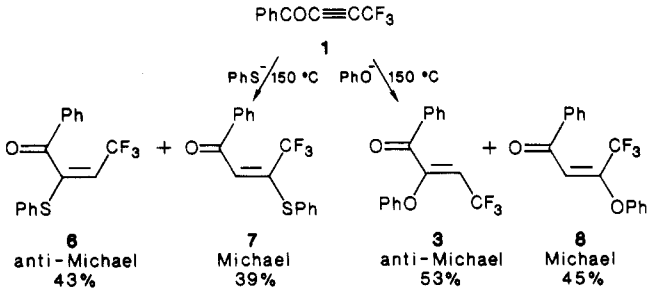
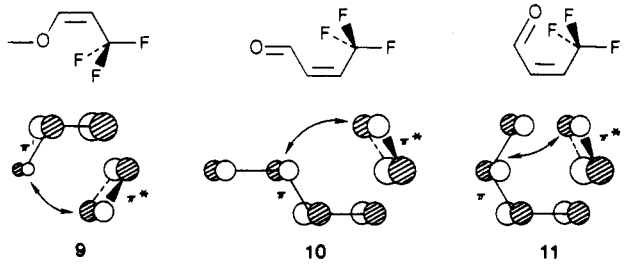


products **2** or **3** to 150 °C for 24 h with a catalytic amount of base produced essentially the same mixture as given in eq 2. Comparison of eq 1 and 2 reveals that although there is an overwhelming kinetic preference for anti-Michael addition, both the Michael and anti-Michael products are almost equally stable. The trans arrangement of CF_3 and carbonyl groups in the kinetic products **2** and **3** is a direct consequence of anti addition of nucleophile and H^+.[8] In the thermodynamic products of the reaction with PhS^-, both the Michael and anti-Michael products (**7** and **6**, respectively) have a cis arrangement of CF_3 and carbonyl groups. In the thermodynamic products of the reaction with PhO^-, however, the Michael and anti-Michael products (**8** and **3**, respectively) have cis and trans arrangements of CF_3 and carbonyl groups, respectively.

In the reactions of PhO^- and PhS^- with $PhC{\equiv}CCF_3$,[9] the thermodynamic product was found to have a cis arrangement of CF_3 and PhO groups for the PhO^- addition but a trans arrangement of CF_3 and PhS for the PhS^- addition. The preference for the cis arrangement of CF_3 and PhO is rationalized[9] in terms of secondary orbital interactions of $\pi^*_{CF_3}$ with the HOMO π' of the vinyl ether framework as shown in **9**. The secondary orbital interaction ($\pi' - \pi^*_{CF_3}$) is not significant for the case of PhS and CF_3.[9] Similarly, according to the interaction of $\pi^*_{CF_3}$ with the HOMO π of an enone framework shown in **10**, CF_3 and carbonyl groups are expected to prefer a cis arrangement as well. From eq 2 we see that indeed this preference is shown by the thermodynamic compounds **6–8**. The only exception, **3**, is accounted for if the ($\pi' - \pi^*_{CF_3}$) interaction is stronger than the ($\pi - \pi^*_{CF_3}$) interaction. Given the s-trans conformation of the enone framework, the trans



arrangement of CF_3 and carbonyl in **3** may be rationalized by simply invoking steric hindrance between the benzoyl benzene ring and the CF_3 group. This argument, however, would predict a trans arrangement of CF_3 and carbonyl for **6–8**, in disagreement with experiment. There is no need to invoke steric hindrance between the benzoyl group and the CF_3 groups, if the enone framework has a s-cis conformation. In such a case, the secondary orbital interaction of ($\pi - \pi^*_{CF_3}$) will increase the preference for a cis arrangement of carbonyl and CF_3 as depicted in **11**.

Registry No. **1**, 85694-32-2; **2**, 104322-88-5; **3**, 104322-89-6; **4**, 99048-75-6; **6**, 104322-90-9; (*E*)-**7**, 104322-91-0; (*Z*)-**7**, 104322-93-2; (*E*)-**8**, 104322-92-1; (*Z*)-**8**, 104322-94-3; PhO^-, 3229-70-7; PhS, 13133-62-5; PhSH, 108-98-5; PhOH, 108-95-2; PhCOCl, 98-88-4; $(CF_3C{\equiv}C)_2Zn$, 104322-95-4.

Carl L. Bumgardner,* John E. Bunch
Myung-Hwan Whangbo*
Department of Chemistry
North Carolina State University
Raleigh, North Carolina 27695-8204
Received May 27, 1986

Stereochemistry of the Asymmetric Oxidation of Ketone Enolates Using (Camphorylsulfonyl)oxaziridines

Summary: Asymmetric oxidation of the sodium enolates of ketones using chiral oxaziridines (+)-(2*R*,8a*S*)-**1** and (−)-(2*S*,8a*R*)-**2** affords α-hydroxy ketones **4** in high optical purity (69–95% ee). An open transition state, controlled by nonbonded steric interactions, is proposed as being responsible for the chiral recognition.

Sir: Chiral α-hydroxy carbonyl compounds are important reagents for the synthesis of complex optically active natural products and are useful stereodirecting groups.[1] Recently we reported a study of the asymmetric oxidation of ester and amide lithium enolates to α-hydroxy carbonyl compounds using (camphorylsulfonyl)oxaziridines (+)-(2*R*,8a*S*)-**1** and (−)-(2*S*,8a*R*)-**2** and oxaziridine (−)-(*S*,*S*)-**3**.[2] Both α-hydroxy carbonyl enantiomers, with enantioselectivities up to 85% ee, were accessible because the configuration of the oxaziridine three-membered ring determines the product stereochemistry.

In this paper we have extended these preliminary investigations to a detailed study of the asymmetric oxidation of ketone enolates (eq 1). From a consideration of the structure–stereoselectivity trends a transition-state hypothesis has been developed which also provides a useful probe into the solution chemistry of metal enolates.

(7) Heating the reaction mixtures described in ref 2 to 150 °C for 24 h gave, after workup and chromatography, the results shown in eq 2. Compound **6**: ^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, Ar H), 5.4 (q, J = 9 Hz, vinyl H cis to PhS); ^{19}F NMR ($CFCl_3$) 56 ppm (d, J = 9 Hz, *gem* CF_3, H).[3] Compound **7**: ^1H NMR ($CDCl_3$) δ 8.2–7.1 (m, Ar H), 6.4 (s, vinyl H trans to CF_3); ^{19}F NMR ($CFCl_3$) 69 ppm (s, CF_3 trans to vinyl H).[3] Compound **8**: ^1H NMR ($CDCl_3$) δ 8.3–7.0 (m, Ar H), 6.5 (s, vinyl H trans to CF_3); ^{19}F NMR ($CFCl_3$) 67 ppm (s, CF_3 trans to vinyl H).[3] In addition from $PhCOC{\equiv}CCF_3$ and PhS^- at 150 °C for 24 h a small amount (1%) of (*Z*)-PhCOCH=C(CF_3)SPh ([^1H NMR ($CDCl_3$) δ 8.2–7.0 (m, Ar H); ^{19}F NMR ($CFCl_3$) 64 ppm (d, J = 1–2 Hz, CF_3 cis to vinyl H)] was obtained.[3] Similarly from reaction of $PhCOC{\equiv}CCF_3$ and PhO^- at 150 °C for 4 h a trace of (*Z*)-PhCOCH=C(CF_3)OPh was isolated: ^1H NMR ($CDCl_3$) δ 7.2–6.8 (m, Ar H); ^{19}F NMR ($CFCl_3$) 64 ppm (d, J = 1–2 Hz, CF_3 cis to vinyl H).[3] In both of these cases the vinyl H signal was obscured by the aromatic resonance but the coupling clearly visible in the ^{19}F spectrum permitted assignments.

(8) Albright, T. A.; Burdett, J. K.; Whangbo, M.-H. *Orbital Interactions in Chemistry*; Wiley: New York, 1985; pp 175–178. Dickstein, J. I.; Miller, S. I. *The Chemistry of the Carbon–Carbon Triple Bond*; Patai, S., Ed.; Wiley: New York, 1978; Part 2, p 826.

(9) Bumgardner, C. L.; Bunch, J. E.; Whangbo, M.-H. *Tetrahedron Lett.* **1986**, *27*, 1883.

(10) $PhCOC{\equiv}CCF_3$ was prepared from PhCOCl and $Zn(C{\equiv}CCF_3)_2$. The physical properties of the ketone agreed with those reported by: Shen, Y.; Xin, Y.; Cen. W.; Huang, Y. *Synthesis*, **1984**, 35.

(11) The substrate properties are correlated with the observed regiochemistry when the transition state for addition is early and resembles the starting material. This would be the case if the rate-determining step is exothermic, a likely possibility given the protic medium where nucleophilic attack on the triple bond can be concerted with proton attachment.

(1) For leading references on chiral α-hydroxy carbonyl compounds, see: (a) Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, 3539. (b) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346. (c) Brown, H. C.; Pai, G. G.; Jadhav, P. K. *J. Am. Chem. Soc.* **1984**, *106*, 1531. (d) Gamboni, R.; Mohr, P.; Waespe-Sarcebvic, N.; Tamm, C. *Tetrahedron Lett.* **1985**, 203. (e) Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta* **1985**, *68*, 216.

(2) Davis, F. A.; Haque, M. S.; Ulatowski, T. G.; Towson, J. C. *J. Org. Chem.* **1986**, *51*, 2402.

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