A similar mechanism of hyperconjugation can also be suggested for the dimethylsulfilimines used in the present study. In the sulfonium ground state, hyperconjugation can occur by overlap between the methyl p orbitals and the low-lying d orbitals on the sulfur. The importance of this hyperconjugation is a simple measure of the energetic feasibility of this p–d overlap. Since it is very unlikely that the overlap intergrals for the tetrahedral sulfonium and bipyramidal sulfurane ground states would be identical, the observation of the small isotope effect for sulfurane formation strongly suggests that such hyperconjugative overlap is of little importance in sulfonium compounds.

Further support for this conclusion can be found in the very nature of the sulfilimine ground state, as measured by X-ray crystallography. For the cyclic sulfilimine, dehydromethionine,[15] the sulfilimine nitrogen is clearly tetrahedral in spite of the possibility of p–d overlap with the adjacent sulfonium center. Results from other sulfilimines are comparable.[1]

Another measure of the ability of sulfur d orbitals to overlap with adjacent π-systems is the magnitude of the "resonance contribution" to equilibrium ionization of thiophenols, relative to phenols. The resonance component of the Hammett ρ for the ionization equilibrium can be obtained from the dual parameter equation $\log (k/k_0) = [\sigma^n + (\rho^r/\rho)(\sigma^- - \sigma^n)]$ as described by Yukawa[16] and others.[17] Using this approach, the ratio ρ^r/ρ is 0.5 for thiophenols ($\rho = -1.87$; $\rho^r = -0.94$)[18] and 1.0 for phenols (by definition of the σ^- scale). This again indicates that overlap, even from a thiolate anion, with an adjacent carbon π-system is not energetically favorable.

If formal p–d overlap does not provide significant stabilization in these systems, the observed stabilization of carbanions adjacent to thioether or sulfonyl linkages most likely originates from d orbital polarization effects.[19,20]

Acknowledgment. This work was supported by a grant from the National Science Foundation, CHE 8511865.

Registry No. $(D_3C)_2S{=}NC_6H_5$, 104241-56-7; 3-$(D_3C)_2S{=}NC_6H_4Cl$, 104241-57-8; $(D_3C)_2S{=}NCOC_6H_5$, 104241-58-9; $(D_3C)_2S{=}NSO_2C_6H_5$, 104241-59-0; 4-$(D_3C)_2S{=}NC_6H_4Cl$, 104241-60-3; I_2^-, 12190-71-5; D_2, 7782-39-0.

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Communications

A Selective Method for the Synthesis of Stereodefined Exocyclic Alkenes via Allylmetalation of Propargyl Alcohols[1]

Summary: A potentially versatile and highly regio- and stereoselective method for preparing exocyclic alkenes involving the use of 2-allyl-substituted allylic alcohols 1 as key intermediates is described.

Sir: Despite advances over the past several years, highly selective synthesis of stereodefined exocyclic alkenes remains one of the underdeveloped areas in organic synthesis. In particular, procedures that are versatile and permit highly stereoselective (≥98%) synthesis of either *E* or *Z* isomers in high yields are scarce. Since a large number of natural and unnatural exocyclic alkenes of biological and medicinal importance, such as prostacyclin,[3a] carbacyclin,[3b] zoapatanol,[3c] pumiliotoxins,[3d] and fusidic acid,[3e] demand stereoselective methods for their satisfactory synthesis, development of such methods is highly desirable. In the past, exocyclic alkenes containing vinyl ethers and ω-alkylidene lactones have been prepared by cyclization via addition–elimination of stereodefined alkenes,[4a-c] stereoselective addition to alkynes,[4d-f] and epoxysilane opening–elimination.[4g] In cases where the exocyclic alkene moiety contains only H and C substituents, reactions of stereodefined alkenylsilanes[5a-e] and alkenylcoppers[5f] with carbon electrophiles have been successfully employed, although their applicability is still very limited. Also promising is partial hydrogenation of vinylcycloalkenes.[6] Controlling the stereochemistry of cyclic carbometalation has been generally difficult, although a few moderately successful examples[7] are known. Transition-

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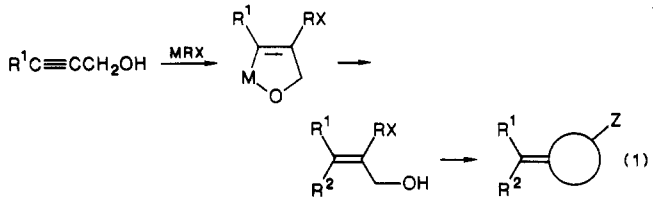
metal-promoted bicyclization reactions of enynes[8a] and diynes[8b] give stereoisomerically pure exocyclic alkenes. In general, synthesis of exocyclic alkenes via ring cleavage[9] can be highly stereoselective, but the current scope is very limited.

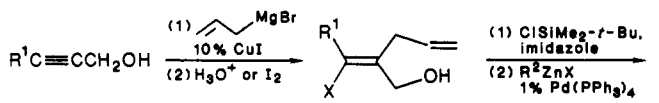
Herein described is a potentially versatile method permitting highly stereoselective (≥98%) synthesis of either *E* or *Z* isomers. The key strategy employed here is illustrated in eq 1. To our knowledge, this potentially versatile



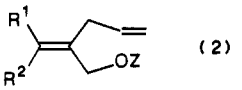
(1)

strategy has not been previously employed. Since addition of MRX to propargyl alcohols can be completely regio- and stereoselective, this methodology can provide exocyclic alkenes of essentially 100% isomeric purity. Another noteworthy feature is that both trisubstituted and tetrasubstituted exocyclic alkenes of either *E* or *Z* configuration can be readily synthesized.

Treatment of propargylic alcohols with allylmagnesium bromide in the presence of 10 mol % of CuI[10] followed by protonolysis or iodinolysis is known to produce **1** in a completely stereo- and regioselective manner. Quite unexpectedly, our attempts to convert **1b** and **1d** into **2** using either organocopper reagents[11] other than methylcopper reagents, e.g., $LiCu(n\text{-}Bu)_2$, or alkyllithiums,[12] e.g., *n*-BuLi, led only to very low yields of **2** heavily contaminated with byproducts. On the other hand, the reaction of **1b** and **1d** with organozinc halides[13] in the presence of 1 mol % of $Pd(PPh_3)_4$ can produce **2** in excellent yields, as indicated by the yield figures in parentheses.



1a: R^1 = Me, X = H
1b: R^1 = Me, X = I
1c: R^1 = *n*-Bu, X = H
1d: R^1 = *n*-Bu, X = I
1e: R^1 = *n*-Hex, X = I

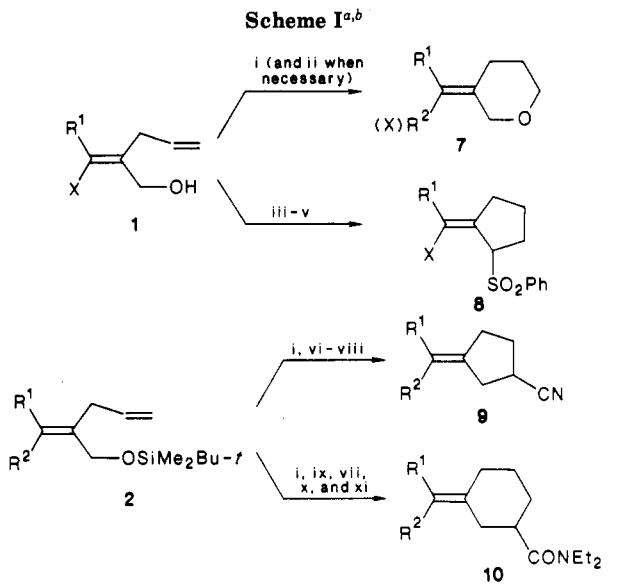


(2)

2a: R^1 = Me, R^2 = *n*-Bu, Z = $SiMe_2$-*t*-Bu (86%)
2b: R^1 = Bu, R^1 = Me, Z = $SiMe_2$-*t*-Bu (97%)

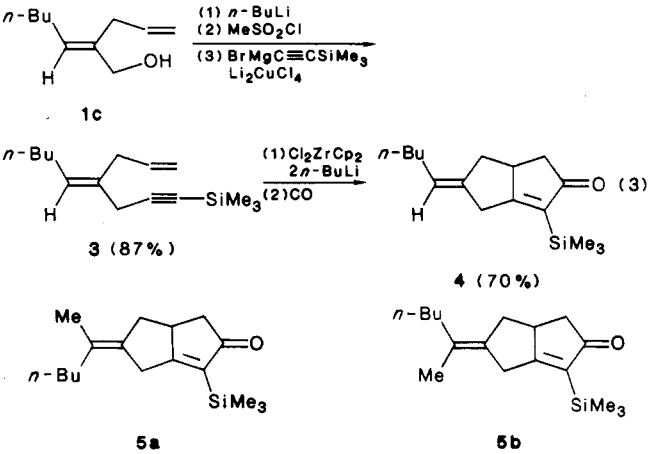
Sequential treatment of **1c** with *n*-BuLi (1.1 equiv, −78 °C, 30 min), $MeSO_2Cl$ (1.1 equiv, −78 °C, 1 h), $Me_3SiC{\equiv}CMgBr$ in THF (1.4 equiv) and Li_2CuCl_4[14] (0.05 equiv, 22 °C, 3 h) cleanly provided an 87% yield of **3** (>99% isomeric purity by ^{13}C NMR), which was identical with an authentic sample prepared via Zr-catalyzed allylalumination[15] of $HC{\equiv}CCH_2C{\equiv}CSiMe_3$ and subjected to the Zr-promoted bicyclization–carbonylation to give **4**.[8a] The present procedure for preparing **3** is not only more convenient but also more regioselective than previously reported.[8a]

Scheme I[a,b]



[a] (i) Sequential treatment with $(Me_2CHMeCH)_2BH$, I_2–NaOMe, and $NaOH$–H_2O_2; (ii) R^2ZnCl, $Pd(PPh_3)_4$ (1%); (iii) $(Me_2CHMeCH)_2BH$ then $NaOH$–H_2O_2; (iv) Br_2–PPh_3; (v) $NaSO_2Ph$, *n*-Bu_4NBr and then NaOH, HMPA; (vi) KCN, 18-crown-6 (5%); (vii) *n*-Bu_4NF; (viii) sequential treatment with LDA, $MeSO_2Cl$, and LDA; (ix) $LiCH_2CONEt_2$; (x) PBr_3; (xi) LDA. [b] **7a**: R^1 = *n*-Bu, X = H (91%). **7b**: R^1 = *n*-Bu, X = I (80%). **7c**: R^1 = Me, X = I (60%). **7d**: R^1 = *n*-Bu, R^2 = Me (74%). **7e**: R^1 = Me, R^2 = *n*-Bu (60%). **8**: R^1 = *n*-Hex, X = I (43%). **9a**: R^1 = Me, R^2 = *n*-Bu (43%). **9b**: R^1 = *n*-Bu, R^2 = Me (48%). **10a**: R^1 = Me, R^2 = *n*-Bu (38%). **10b**: R^1 = *n*-Bu, R^2 = Me (45%). The yields in parentheses are based on **1** or **2**.

The above stereochemical correlation and the known stereochemistry of allylmagnesiation of propargylic alcohols[10] support the stereochemical assignment shown in eq 3.



(3)

To unequivocally establish the essentially 100% stereoselectivity, **5a** (65% yield) and **5b** (73% yield) were similarly prepared from **2a** and **2b**, respectively, in yields indicated in parentheses. Although both IR and ^1H NMR spectra of **5a** and **5b** are indistinguishable, their ^{13}C NMR spectra show some readily noticeable differences[16] and

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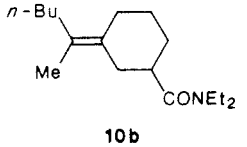
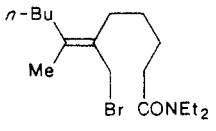
unequivocally establish the essential absence of the stereoisomeric impurities in each case.

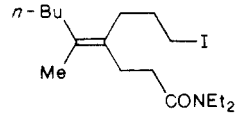
The potential versatility of the present strategy is indicated in Scheme I as well as in eq 3. ^{13}C NMR examination of three additional pairs of stereoisomeric exocyclic alkenes, i.e., **7d** and **7e**, **9a** and **9b**, and **10a** and **10b**, indicates that all of them are of >98% isomeric purity. 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**.



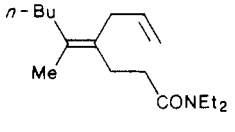
10b



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.

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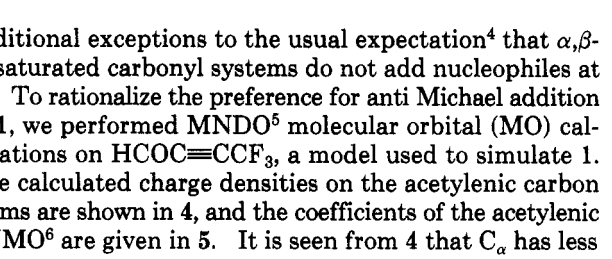
Michael and Anti-Michael Additions to Benzoyl(trifluoromethyl)acetylene

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

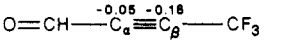
Sir: A recent report[1] on anti-Michael addition to ynamides prompts us to communicate our observations on the addition of PhS^- and PhO^- to benzoyl(trifluoromethyl)acetylene, $PhCOC{\equiv}CCF_3$ (**1**). As shown in eq 1, reaction of **1** with PhS^- and PhO^- leads cleanly to the anti-Michael adducts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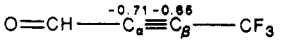

5

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.

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(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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