(Figure 2) which is ascribed to the attack of a second molecule of CD on the ester·CD complex:

$$\mathrm{S{\cdot}CD} + \mathrm{CD} \xrightarrow{k_{c2}} \tag{5}$$

In this case eq 2 must be expanded to eq 6 which fits our data for the C6, C7, and C8 esters (Figure 2) with the constants given in Table I (part b).

$$k^{\mathrm{obsd}} = \frac{(k_{\mathrm{u}}K_1 + k_{\mathrm{c}}[\mathrm{CD}] + k_{\mathrm{c2}}[\mathrm{CD}]^2)}{(K_1 + [\mathrm{CD}])} \tag{6}$$

For both α- and β-CD the variations of K_1 and k_c/k_u with chain length (Table I) are similar to those for other aryl esters.[4,5] Substrate binding becomes stronger whereas the "catalytic ratio" (k_c/k_u) and the "substrate specificity"[2a,d] ($k_2 = k_c/K_1$) decrease and then increase. Apparently, with a shorter, bound alkyl chain (C4 ester) the ester function sits too deeply in the CD cavity to be easily attacked by an ionized OH,[1,2] but with the longer esters it is held progressively higher and more accessible.

The unreactive 2:1 complexes of α-CD probably have the alkyl chain of 1 included in the first CD molecule (K_1) and the aryl group in the second (K_2) since the values of K_2 vary little with chain length. The additional catalysis seen with β-CD and the C6, C7, and C8 esters also involves two CD molecules, but, since the increases in k^{obsd} at high [CD] are linear (Figure 2), any 2:1 binding must be very weak. With increasing chain length the second-order process becomes more important (k_{c2} increases).

The different behaviors noted for the longer esters must relate to the cavity widths of α- and β-CD since their depths are the same.[1] Molecular (CPK) models suggest a fairly tight fit of alkyl chains in α-CD and a looser fit for β-CD. This seems to be the case with linear alcohols[3] and alkane sulfonate ions[8] (up to C8), but it is not clearly so with the present esters or with p-nitrophenyl alkanoates.[4] Nonetheless, the present results may mean that α-CD forms a 2:1 complex with the longer esters which is too tight to react whereas β-CD forms a weak, much looser 2:1 complex which can react.[9]

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(8) Satake, I.; Ikenoue, T.; Takshita, T.; Hayakawa, K.; Meda, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2747. Satake, I.; Yoshida, S.; Hayakawa, K.; Meda, T.; Kusumoto, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3991.

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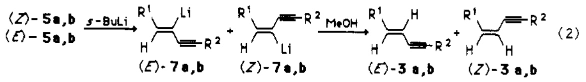
Configurational Instability of α-Alkenyl and α-Alkynyl Vinyllithiums. Syntheses of Stereodefined 2-Alkyl-1-en-3-ynes

Summary: Metal-halogen exchange of either (Z)-enynyl bromides or (Z)-dienyl bromides by *sec*-BuLi produces vinyllithiums that are configurationally stable only at temperatures below -120 °C and -78 °C, respectively. Allylation of (Z)-enynylalanates with allyl bromide or methylation of (Z)-enynyl bromides with CH_3MgI and $Fe(acac)_3$ catalyst furnishes the corresponding 2-alkyl-1-en-3-ynes.

Sir: The hydroalumination of conjugated diynes 1[2,3] with lithium trialkylaluminum hydrides is a highly stereo- and regioselective process, placing the aluminum at the internal position of the resultant double bond. With the silyl-substituted diynes **1b**,[3] the hydroalumination also occurs chemoselectively, with Al-H addition taking place exclusively at the non-silicon bearing triple bond. Protonolysis of the intermediate vinylalanates **2** cleanly affords the respective (*E*)-enynes **3**. In seeking to extend this methodology to carbon electrophiles to obtain stereodefined trisubstituted enynes, treatment of **2** with allyl bromide (2.0 equiv, 25 °C, 24 h) produced nearly quantitative yields of the isomerically pure (≥99%) allylated enynes (*E*)-**4a** (95%) and (*E*)-**4b** (94%) (eq 1). Unfortunately, however, the alkenylalanates **2** were unreactive toward other common alkylating agents, such as methyl iodide.[4]

In the course of our search for a general route for the alkylation of the vinylalanates **2**, we investigated their conversion into the more nucleophilic vinyllithiums. This was achieved by converting the vinylalanates **2** into the corresponding (*Z*)-enynyl bromides **5** and then via metal-halogen exchange to the vinyllithiums. Thus, treatment of **2** with 2 equiv of cyanogen bromide (-78 → 25 °C) furnished the enynyl bromides **5** (**a**, 91%; **b**, 92%) in high isomeric purity (≥98%). Lithiation of (*Z*)-**5a** by *sec*-BuLi (1.1 equiv, ether, -78 → 25 °C) occurred readily, yet produced the isomeric enynes (*E*)-**3a** (9%) and (*Z*)-**3a** (89%) upon protonolysis (eq 2). The formation of the *cis*-enyne **3a** from the (*Z*)-enynyl bromide **5a** points to an isomerization of the initially formed vinyllithium (*E*)-**7a** to the respective *Z* isomer **7a**. Similar results were obtained from the lithiation of the silylated (*Z*)-enynyl bromide **5b**. The enynyllithium isomerization is an extremely facile process, taking place readily at -78 °C but is nearly entirely suppressed at -120 °C.[5] The equilibrium ratio of (*E*)-**7a**:(*Z*)-**7a** at room temperature must be in the range of 10:90 to 5:95, since nearly the same distribution of enynes (*E*)-**3a** and (*Z*)-**3a**, respectively, was obtained from the lithiation/methanolysis of either pure (*Z*)-enynyl bromide **5a** or from the corresponding *E* isomer **5a**.[7] The configura-



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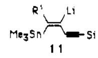
(1) Present address: Ethyl Corporation, Technical Center, P.O. Box 14799, Baton Rouge, LA 70898.

(2) Zweifel, G.; Lynd, R. A.; Murray, R. E. *Synthesis* **1977**, 52.

(3) Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc.* **1983**, *105*, 1383.

(4) Alkenylalanates derived from simple 1-alkynes are known to react readily with typical alkylating agents such as methyl iodide: Baba, S.; Van Horn, D. E.; Negishi, E. *Tetrahedron Lett.* **1976**, 1927. Eisch, J. J.; Damasevitz, J. E. *J. Org. Chem.* **1976**, *41*, 2214. Uchida, K.; Utimoto, K.; Nozaki, H. *J. Org. Chem.* **1976**, *41*, 2215.

(5) It is interesting to contrast the configurational instability of (*E*)-**7a** and (*E*)-**7b** with the observed stereochemical stability of **11**.[6] The geometrical rigidity of **11** probably results from the additional stability gained through maximum separation of the two olefinic metal atoms.



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(6) Miller, J. A. Doctoral Dissertation, University of California, Davis, 1982. Zweifel, G.; Leong, W. *J. Am. Chem. Soc.* **1987**, *109*, 6409.

(7) The *E* bromide **5a** was synthesized from (*Z*)-**5a** by sequential treatment with *sec*-BuLi (-78 °C, 0.5 h) and BrCN. The resulting mixture (85% *E*:15% *Z*) was purified by preparative GLC (Carbowax-20M) to furnish 97% isomerically pure (*E*)-**5a**.

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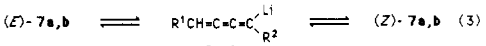
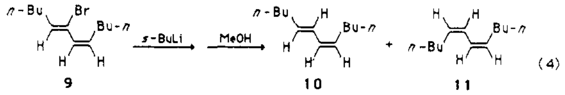
tional lability of vinyllithiums which possess α electron-withdrawing groups, such as aryl,[8,9b] cyano,[9] sulfoxy,[9a] carbomethoxy,[9b] and silyl,[10] has been previously reported. While the acetylenic moiety in **7a** and **7b** must also facilitate C=C isomerization through electron delocalization, it is worth noting that no cumulene products resulting from protonation or alkylation of **8a,b** have been detected (eq 3). Interestingly, vinyllithiums which bear α-alkenyl groups are also configurationally unstable. Thus, the stereochemically pure dienyl bromide **9** derived from hydroboration (disiamylborane)–protonolysis of **5a**,[11] on reaction with *sec*-BuLi (1.1 equiv, ether, −78 → 0 °C) furnished 50% yields each of the dienes **10** and **11** upon methanolysis. Carrying out the metal–halogen exchange of **9** at −78 °C, however, and adding methanol to the solution at that temperature, provided only the unrearranged diene **10** (eq 4). Hence, vinyllithiums which possess α-alkenyl groups appear to be less prone toward double-bond isomerization than are their α-alkynyl counterparts.

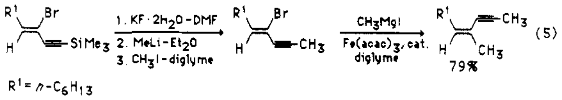


$$(E)\text{-}7a,b \rightleftharpoons \underset{8a,b}{R^1CH{=}C{=}C{=}C\begin{smallmatrix}Li\\R^2\end{smallmatrix}} \rightleftharpoons (Z)\text{-}7a,b \quad (3)$$



The nature of the α-substituent in the vinyl bromides **5a**, **5b**, and **9** has a marked effect not only on the ease of isomerization of the corresponding vinyllithiums but also on their rate of metal–halogen exchange. For example, addition of 1 equiv of *sec*-BuLi to an equimolar mixture of (*Z*)-**5a** and **9** at −78 °C followed by methanolysis furnished exclusively the enynes (*E*)-**3a** and (*Z*)-**3a** and none of the debrominated dienes **10** and **11**. Lithium–bromine exchange also occurred when the enynyl bromide (*Z*)-**5a** was treated at −78 °C with the dienyllithium derived from the reaction of **9** with *sec*-BuLi. Protonolysis of the reaction mixture afforded the enynes (*E*)-**3a** and (*Z*)-**3a** (91% combined yield) along with a quantitative recovery of the dienyl bromide **9**. The increased anion-stabilizing nature of the acetylenic moiety relative to the alkenyl group is readily evidenced from these experiments. Similarly, treatment of equal amounts of (*Z*)-**5a** and (*Z*)-**5b** with 1 equiv of *sec*-BuLi at −120 °C furnished, after protonolysis, the silyl-substituted enyne (*E*)-**3b** in 72% yield with only 10% of the competing enyne (*E*)-**3a** detected. Therefore, in terms of facilitation of vinyllithium formation as a consequence of anion-stabilizing ability, the trend for α-substituents seems to be $Me_3SiC{\equiv}C > RC{\equiv}C > RCH{=}CH$.

Although the vinyllithium route, as described above, did not provide a viable general method for stereoselective alkylations, methylation of the (*Z*)-enynyl bromide **5a** with either Me_2CuLi (1.2 equiv, −30 → 25 °C) or with a mixture of MeMgI (1.1 equiv) and $Fe(acac)_3$[12] (5 mol %) in diglyme (0 → 25 °C) furnished the (*Z*)-enyne-**6a** in 72% and 78% yields, respectively. Thus, net inversion of the double-bond geometry was observed in both methylation reactions.[13,14] It should be noted that the methylation reaction may also be applied to the preparation of unsymmetrically substituted enynes, as exemplified in eq 5. Thus, the stereodefined allylation (vide supra) and methylation reactions effectively extend the scope of existing methodologies[15] for the preparation of 2-alkyl-1-en-3-ynes.



Acknowledgment. This investigation was supported by the National Science Foundation under Grant No. CHE85-19555.

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[8] Nesmeyanov, A. N.; Borisov, A. E. *Tetrahedron* **1957**, *1*, 158. Curtin, D. Y.; Crump, J. W. *J. Am. Chem. Soc.* **1958**, *80*, 1922. Curtin, D. Y.; Koehl, W. J. *Ibid.* **1962**, *84*, 1967. Panek, E. J.; Neff, B. L.; Chu, H.; Panek, M. G. *Ibid.* **1975**, *97*, 3996. Knorr, R.; Lattke, E. *Tetrahedron Lett.* **1977**, 3969.

[9] (a) Schmidt, R. R.; Speer, H.; Schmidt, B. *Tetrahedron Lett.* **1979**, 4277. (b) Feit, B. A.; Haag, B.; Schmidt, R. R. *J. Org. Chem.* **1987**, *52*, 3825.

[10] Cunico, R. F. *J. Organomet. Chem.* **1973**, *60*, 219. Brook, A. G.; Duff, J. M.; Reynolds, W. F. *Ibid.* **1976**, *121*, 293. Zweifel, G.; Murray, R. E.; On, H. P. *J. Org. Chem.* **1981**, *46*, 1292. Negishi, E.; Takahashi, T. *J. Am. Chem. Soc.* **1986**, *108*, 3402.

[11] Zweifel, G.; Polston, N. L. *J. Am. Chem. Soc.* **1970**, *92*, 4068.

[12] Tamura, M.; Kochi, J. K. *J. Am. Chem. Soc.* **1971**, *93*, 1487. Tamura, M.; Kochi, J. K. *Synthesis* **1971**, 303. Molander, G. A.; Rahn, B. J.; Shubert, D. C.; Bonde, S. E. *Tetrahedron Lett.* **1983**, *24*, 5449.

[13] Attempted Cu- and Fe-based alkylations of (*Z*)-**5a** utilizing E groups other than Me have thus far yielded unsatisfactory results.

[14] It should be noted that treatment of the trimethylsilyl-substituted *Z* bromide **5b** with MeMgI and $Fe(acac)_3$ afforded mixtures of products.

[15] For example, see: Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259. Descoins, C.; Samain, D. *Tetrahedron Lett.* **1976**, 745. Brown, H. C.; Molander, G. A. *J. Org. Chem.* **1981**, *46*, 645. Arase, A.; Hoshi, M.; Masuda, Y. *Chem. Lett.* **1984**, 2093. Hoshi, M.; Masuda, Y.; Arase, A. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1683. Trost, B. M.; Chan, C.; Ruhter, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486.

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