REACTION OF DITHIO-SUBSTITUTED CINNAMYLLITHIUM WITH CARBONYL COMPOUNDS: A TEST OF THE HSAB PRINCIPLE

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Abstract-- By mediation of $BF_3.Et_20$, dithio-substituted cinnamyllithium 2 reacted predominantly at the *a*-site with carbonyl compounds. No selectivity was found when the reaction was performed in the absence of $BF_3.Et_20$.

We have recently observed the dichotomous regiochemistry of aldehyde and ketone in addition reactions with a lithium anion 1 generated from 2-propenyl-1,3-dithiane. While aldehydes reacted exclusively at the γ -site of 1, most ketones of modest size attacked the α -site of this unsymmetric allylic anion.¹ On the other hand, Murphy and Wattanasin have shown that percentage of alkylation at the α -site of the cinnamyl anion 2 increases as the hardness of electrophile RX (X = I, Br, Cl and OTs) increases.² We thus carried out the reaction of anion 2 with carbonyl compounds in order to see if the regioselectivity can be correlated with above mentioned results.

Cinnamyllithium 2 was generated from a THF solution of 2-styryl-1,3-dithiane with *n*-BuLi. On contrary to 1, anion 2 did not exhibit any regio- or stereoselectivity in reactions with various carbonyl compounds at -78 $^{\rm O}$ C, except for the reaction with benzophenone (Table). The discrepancy of selectivities of anions 1 and 2 can be attributed to difference of electronic properties of γ -substituents.³ On the other hand, treatment of the lithium anion 2 (in an ethereal solution) with one equivalent of boron trifluoride etherate prior to addition of carbonyl compounds afforded predominantly *a*-addition products, except for the reaction with isobutanal. The regioselectivity is consistent with the HSAB principle⁴ as well as in the trend of alkylations.² Accordingly, the hardness of carbonyl compound would significantly



increase when it coordinates with BF_3 ,⁵ and thus it preferred to attack the relatively hard *a*-site of 2. However, the possibility of anion 2 behaving as a cinnamylboron⁶ or as an "ate" complex⁷ was not excluded.

From the synthetic point of view, cinnamyl anion 2 serves as an equivalent of α,β -unsaturated acyl anion.⁸ Thus, α -addition products 4 were hydrolyzed with HgCl₂ to give

high yields of a' hydroxy enones 6, which are structural subunits of many natural products⁹ and the precursors of cyclopentenones (via Nazarov cyclization)¹⁰.

electrophile	in the absence of BF_3 $\alpha:\gamma$ (anti/syn) ^b total yield (%)		mediated by BF_3 $\alpha:\gamma$ (anti/syn) total yield (%)	
MeCH0 MeCH ₂ CH0 Me ₂ CHCH0 CH ₂ =CHCH0 CH ₂ =CHCH0 MeCH=CHCH0 PhCH0 cyclopentanone cyclohexanone 2-butanone 3-pentanone 2-heptanone 4-heptanone benzophenone CH ₂ =CHC0Me	53:47 (46/54) 56:44 (53/47) 38:62 (52/48) 49:51 (46/54) 46:54 (45/55) 48:52 (46/54) 51:49 (43/57) 64:36 77:23 53:47 (68/32) ~0:100	71 90 98 93 72 80 86 85 91 88	~100:0 66:34 (~100:0) ^c ~0:100 (~100:0) ^c 85:15 (~100:0) ^c 100:<1 ~100:0 98:2 100:<1 100:<1 100:<1 100:<1	92 91 88 90 92 95 93 95 86 83 78

Table. Reactions of Unsymmetric Allylic Anion 2 with Carbonyl Compounds.²

(a) Experimental procedure: To 2-styryl-1,3-dithiane (1 mmol) in ether (10 mL) was added dropwise n-BuLi (1.2 mmol, 1.6 M in hexane) at -40 °C. After stirring for 20 min, the solution was cooled to -78 °C, and 1 mmol of BF₃.Et₂0 (in 1 mL of ether) was added dropwise, followed by addition of 1.2 mmol of appropriate carbonyl compound. The addition reaction completed in 20 min as revealed by the TLC analysis. (b) All products had satisfactory elmental analyses and compatible spectra (IR, MS, ¹H and ¹³C NMR). The ratio of products was determined by the HPLC and ¹H NMR analyses and occasionally assisted with measurement of isolated weights of products. The structures of anti and syn isomers were rigorously determined by analyses of corresponding spiro dithianes (via acid-catalyzed cyclization)¹¹ and/or γ -lactones (via hydrolysis with HgCl₂).¹ (c) The anti products were obtained as their corresponding trans γ -lactones 5 (R group is bulkier than R' group).

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References:

1. (a) Fang, J. M.; Hong, B. C.; Liao, L. F. J. Org. Chem. 1987, 52, 855. (b) Fang, J. M.; Hong, B. C. *ibid.* 1987, 52, 3162.

2. Murphy, W. S.; Wattanasin, S. J. J. Chem. Soc., Perkin Trans 1 1980, 2678.

3. (a) Biellmann, J. F.; Ducep, J. B. Organic Reactions 1982, 27, 1. (b) Meyers, A. I.;

Strickland, R. C. J. Org. Chem. 1972, 37, 2579. (c) Koksal, Y.; Raddatz, P.; Winterfeldt, E. Liebigs Ann. Chem. 1984, 450.

4. Ho, T. L. Tetrahedron 1985, 41, 3.

5. Eis, M. J.; Wrobel, J. E.; Ganem, B. J. Am. Chem. Soc. 1984, 106, 3693.

6. (a) Yamamoto, Y.; Yatagai, K.; Maruyama, K. *Chemistry Lett.* 1979, 385. (b) Naruta, Y.; Ushida, S.; Maruyama, K. *ibid.* 1979, 919

7. Yamaguchi, M.; Hirao, I. Tetrahedron Lett. 1983, 24, 391.

8. (a) Seebach, D. Synthesis 1969, 17. (b) Seebach, D.; Maetzke, T.; Haynes, R. K.;

Paddon-Row, M. N.; Wong, S. S. Helv. Chim. Acta. 1988, 71, 299 and references cited therein.

9. Davis, F. A.; Vishwakarma, L. C.; Billmers, J. M.; Finn, J. J. Org. Chem. 1984, 49, 3241.

10. Santelli-Rouvier, C.; Santelli, M. Synthesis 1983, 429.

 Suzuki, K.; Tomooka, K.; Matsumoto, T.; Katayama, E.; Tsuchihashi, G. I. Tetrahedron Lett. 1985, 26, 3711.

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