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ON THE LITHIUM DIMETHYLCUPRATE INDUCED CONVERSION OF PROPARGYLIC ESTERS INTO ALLENES USING A STEROIDAL C/D FRAGMENT DERIVED FROM VITAMIN D_3 AS A STEREOCHEMICAL PROBE .

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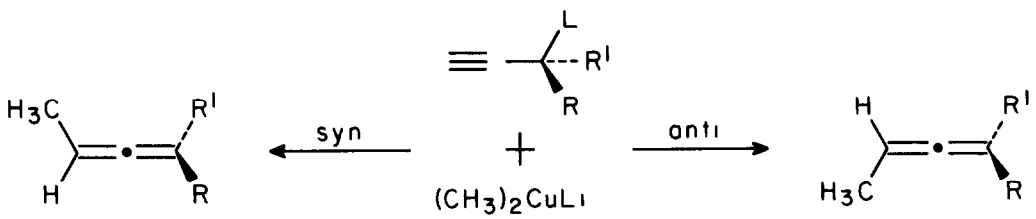
Summary: The reactions of $(CH_3)_2CuLi$ with various C-8 epimeric propargylic esters derived from Grundmann's ketone, a C/D steroid fragment originating from vitamin D_3, lead to the corresponding allenes, the stereochemistry of which indicate a preferred anti 1,3-substitution.

A very recent communication on the revision of literature data by Vermeer[1] prompts us to disclose our results in this field. There exists some confusion as to whether the organocopper promoted conversion of propargylic esters into the corresponding allenic compounds proceeds either by a syn or an anti attack of the copper reagent[2] (Scheme 1). Until recently, the

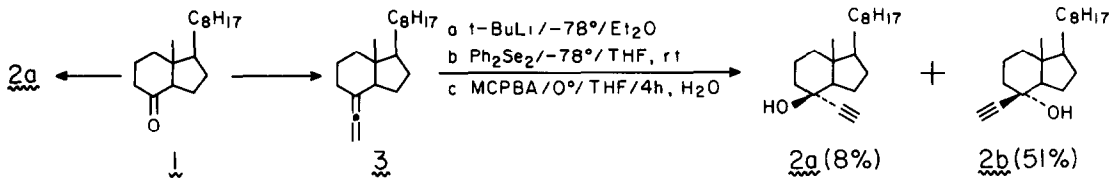
SCHEME I



notion evolved that an anti mode of substitution is favorable for acylic systems while in steroidal cyclic cases syn products were preferred. This has been revised on the basis of an X-ray analysis of the allene obtained from mestranol methane sulfinate and methylcopper, indicating that also in the steroidal cases the 1,3-substitution proceeds in an anti fashion. In our case we have used the C/D ring fragment (obtained from Grundmann's ketone 1[3,4]) as a convenient stereochemical probe for the conversion of propargylic esters into the allenes.

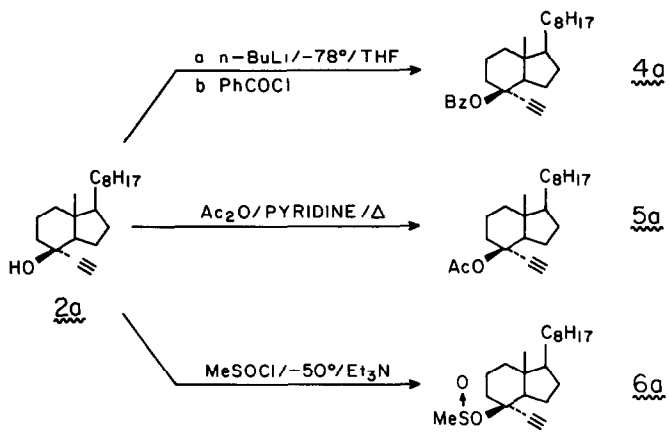
Scheme 2 summarizes the preparation of the two epimeric propargylic alcohols 2a and 2b starting from Grundmann's ketone 1.[3,4] Alcohol 2a has been previously reported,[4] while allene 3,[4] in a one-pot reaction, on treatment with tert-BuLi at -78 °C and then Ph_2Se_2 followed by MCPBA oxidation at 0 °C and hydrolysis, afforded a mixture of 2a and 2b,[5,6] which were separated by medium pressure LC (silica gel; 10% Et_2O in low-boiling petroleum ether). Propargylic alcohol 2a was converted into the corresponding benzoate 4a (88%),[4a] acetate 5a (88%)[4b] and

SCHEME 2



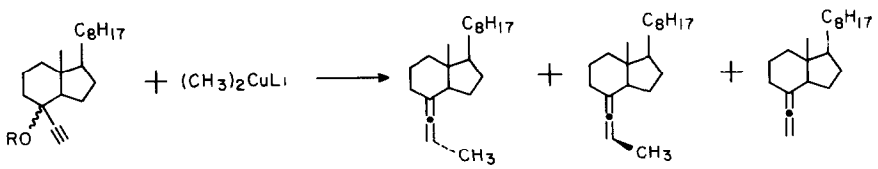
methane sulfinate 6a (74%) by standard procedures[9] as shown in Scheme 3. The epimeric alcohol 2b yielded, using analogous procedures, the corresponding esters 4b-6b in 65%, 70% and 90% yields, respectively.

SCHEME 3



Treatment of the propargylic esters 4a,b-6a,b with one equivalent of $(CH_3)_2CuLi$ in Et_2O for 4 hr at 0 °C and 1 hr at room temperature resulted in the formation of the C/D ring fragment allenes 7a, 7b and 3[10] as shown in the Table.[11]

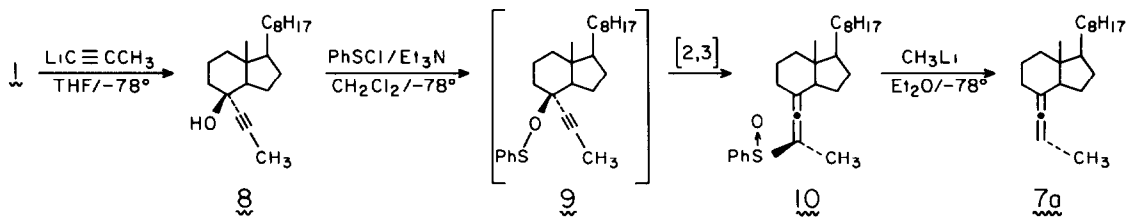
TABLE



	7a	7b	3
4a (R = Bz)	64%	5%	3%
5a (R = Ac)	67%	1%	6%
6a (R = MeSO)	64%	1%	4%
4b (R = Bz)	7%	85%	—
5b (R = Ac)	3%	83%	4%
6b (R = MeSO)	5%	61%	10%

The stereochemistry of the allenes 7a and 7b were assigned on the basis of a comparison of their ^{1}H-NMR spectral data with those of the product of the reaction sequence shown in Scheme 4. Grundmann's ketone 1 was converted into the propargylic alcohol 8 (88%),[4,12] which

SCHEME 4



was treated with one equivalent of PhSCl at -78 °C in the presence of excess base resulting in the formation of allene sulfoxide 10 (85%).[13] Allene 10 was desulfurized using Neef's procedure[13e,14] (treatment with 4 equivalents of CH_3Li at -78 °C) to give the allene 7a in 58% yield. Because both the [2,3]-sigmatropic rearrangement of the sulfinate ester 9 and the desulfurization proceed stereospecifically, the reaction shown in Scheme 4 gives rise to the formation of only the (6R)-allene 7a.

In conclusion, the present study shows that in all cases the predominant product in the organocopper promoted conversion of propargylic esters into allenes originates from an anti mode of displacement. This is in full agreement with Vermeer's recent revision[1] of his previously reported syn displacements.[2] It is of further interest to note that the nature of the leaving group does not affect the stereoselectivity significantly in the reaction of organocopper with the C/D ring propargylic esters (see Table).

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References and Notes

1. Elsevier, C. J., Meijer, J.; Westmijze, H., Vermeer, P., van Dijck, L. A. J. Chem. Soc., Chem. Commun. 1982, 84

2. (a) Rona, P ; Crabbé, P. J. Am. Chem. Soc. 1969, 91, 3289, (b) van Dijck, L. A., Lankwerden, B J., Vermeer, J G.C.M., Weber, A.J.M. Recl. Trav. Chim. Pays-Bas 1971, 90, 801, (c) Luche, J. L., Barreiro, E., Dollat, J M., Crabbé, P. Tetrahedron Lett. 1975, 4615, (d) Pirkle, W. M., Boeder, C. W. J. Org. Chem. 1978, 43, 1950; (e) Tadema, G.; Everhardus, R. M., Westmijze, H., Vermeer, P. Tetrahedron Lett. 1978, 3935, (f) Vermeer, P., Westmijze, H., Kleijn, H., van Dijck, L. A. Recl. Trav. Chim. Pays-Bas 1978, 97, 56; (g) Westmijze, H., Vermeer, P. Tetrahedron Lett. 1979, 4101, (h) Olsson, L-I., Claesson, A.

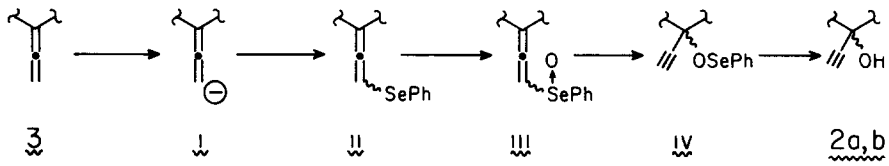
Acta Chem. Scand. B 1979, 33, 679; (i) Westmijze, H., Vermeer, P. Tetrahedron Lett. 1980, 1789; (j) chiral allenes are subject to racemization by organocuprates, Claesson, A., Olsson, L.-I. J. Chem. Soc. Chem. Commun. 1979, 524

3. Inhoffen, H. H., Quinkert, G.; Siegismund, S.; Kampe, D., Domagk, C F. Chem Ber. 1957, 90, 664.

4. (a) Condran, P., Jr., Hammond, M. L., Mouriño, A., Okamura, W. H. J. Am. Chem. Soc. 1980, 102, 6259; (b) Hammond, M. L., Mouriño, A., Okamura, W. H. J. Am. Chem. Soc. 1978, 100, 4907.

5. All new compounds gave satisfactory spectroscopic data.

6. The course of this reaction sequence is presumably as follows the allenic anion 1, obtained upon treatment of allene 3 with tert-BuLi, reacts stereoselectively[4a] with Ph_2Se_2



to afford primarily the (6R)-allene phenyl selenide II.[7] Oxidation of II results in the formation of the allene phenyl selenoxide III, which undergoes spontaneous [2,3]-sigmatropic rearrangement[8] to the selenate ester IV. The latter upon hydrolysis yields the alcohols 2a,b.

7. See, for a similar example, the reaction of an allenyllithium reagent with Ph_2S_2: Clinet, J.-C.; Linstrumelle, G. Synthesis 1981, 875.

8. Reich, H., Shah, S. K , Gold, P. M.; Olson, R. E. J. Am. Chem. Soc. 1981, 103, 3112.

9. Benzoate see Reference 4a and Kaiser, E. M.; Woodruff, R. A. J. Org. Chem. 1970, 35, 1198. Acetate. see Reference 4b. Methane sulfinate see Reference 2f.

10. Minor amounts of Grundmann's allene 3 are formed presumably due to quenching of the intermediate organocopper allenic species, in which no alkyl migration has occurred. See, for example, (a) Dollat, J-M.; Luche, J-L.; Crabbé, P. J. Chem. Soc. Chem. Commun. 1977, 761, (b) Crabbé, P.; Carpio, H J. Chem. Soc. Chem. Commun. 1972, 904.

11. The yields were calculated by ^{1}H-NMR by quantitatively adding vitamin D_3 to the product mixture and then integrating the peaks assigned to the allenic hydrogen and/or the C_{18} angular methyl group of each of the components. Pertinent chemical shifts include (6R)-allene 7a (allenic hydrogen at δ5.00, C_{18} methyl at δ0.62), (6S)-allene 7b (allenic hydrogen at δ5.00, C_{18} methyl at δ0.67), allene 3 (allenic hydrogens at δ4.66, C_{18} methyl at δ0.65), vitamin D_3 (C_{18} methyl at δ0.54). CuI was used for preparing the $(CH_3)_2CuLi$.

12. Midland, M. M. J. Org. Chem. 1975, 40, 2250.

13. (a) Braverman, S., Stabinsky, Y. Israel J. Chem. 1967, 5, 125, (b) Smith, G., Stirling, C.J.M. J. Chem. Soc. (C) 1971, 1530; (c) Horner, L.; Binder, V. Justus Liebigs Ann. Chem 1972, 757, 33, (d) VanRheenen, V , Paul Shephard, K. J. Org. Chem. 1979, 44, 1582, (e) Neef, G.; Eder, U., Seeger, A. Tetrahedron Lett. 1980, 903, (f) van Kruchten, E.M.G.A., Okamura, W. H. Tetrahedron Lett. 1982, 0000.

14. In our hands the use of diethyl ether instead of THF[13e] as solvent for the desulfurization reaction gave optimal results.

15. Dr. Menso P. Rappoldt of Duphar B.V. (Weesp, the Netherlands) provided generous samples of vitamin D_3 used in the preparation of 1.

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