Tetrahedron Letters No. 41, pp 3935 - 3936. 0040-4039/78/1008-3935$02.00/0

PREFERRED ANTI - 1,3- SUBSTITUTION BY ATTACK OF ORGANOCUPRATES ON THE METHANESULFINATE OF (R)-(−)-3-HYDROXY-3-PHENYLPROPYNE. AN ATTRACTIVE ROUTE TO CHIRAL ALLENES .

G.Tadema , R.H.Everhardus , H.Westmijze and P.Vermeer .

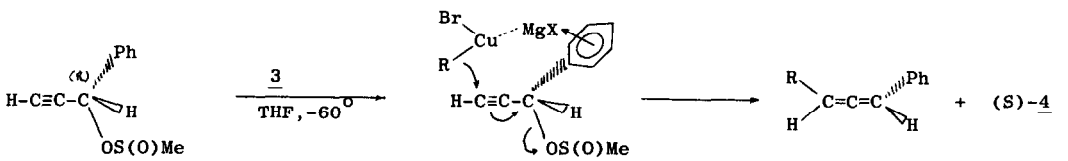
(Department for Organic Chemistry of the State University , Croesestraat 79 , Utrecht , The Netherlands)

The synthesis of optically pure chiral allenes has been the target of many studies [1].Several investigators have tried to achieve such a synthesis by reacting chiral propargylic substrates with organocuprates.Remarkably,the observed syn/anti - ratio of the organocuprate induced 1,3- substitutions appears at least to be dependent on the type of propargylic substrate which is used .

For instance , van Dijck et al. observed 80% syn - and 20% anti -1,3- substitution for the reaction of " Mestranol acetate " with lithium dimethylcuprate in diethyl ether [2].On the other hand , anti -1,3-substitution preferentially occurs if acetates or carbamates derived from chiral non-steroidal propargylic alcohols are reacted with lithium dialkylcuprates in diethyl ether [3,4]. Recently , we have shown that in " Mestranol methanesulfinate " the syn - route is exclusively followed if this sulfinic ester is treated with the heterocuprate [MeCuBr]MgCl.LiBr in tetrahydrofuran (THF) [5].

Hitherto , nothing was known about the stereochemical pattern of organocuprate induced 1,3-substitutions in non-steroidal propargylic sulfinates . We therefore extended our previous study to the reaction of the methanesulfinate 1 [6] - derived from (R)-(−)-3-hydroxy-3-phenylpropyne [7] - with some organoheterocuprates of the type [RCuBr]MgX.LiBr (3) in THF , and in this paper we wish to report our preliminary results.

Treatment of 1 (0.005 mol) with 3 (0.010 mol ; R = Me(X = Cl) or Ph(X = Br)) [5] in THF (30 ml) during 2 hours at -60° followed by protonolysis of the unreacted cuprate at -60° and usual work-up (cf [5]) , afforded the allenes (R,S)- 4 (R = Me or Ph) in a high yield (>90%) :



1 2 (R)-(−)-4

R = Me (X = Cl) or Ph (X = Br)

Both allenes showed negative optical rotations ($[\alpha]_D^{25}$ found for 4 with R = Ph : -868.8^o c = 0.47,$CHCl_3$) ; $[\alpha]_D^{25}$ found for 4 with R = Me : -197.7^o (c = 2.36 , acetone)) which is characteristic for an enantiomeric excess of (R)-(−)-4 and thus for the occurrence of more anti - than syn - 1,3 -substitution in both cases (see reference 1 and other references cited therein). The optical yield of the conversion of 1 into 4 seems to be very good if R = Ph. Based on the highest value of $[\alpha]_D^{25}$ reported for this compound , viz. -1137^o ($CHCl_3$)[1] , and on the assumption that our starting alcohol was optically pure (cf[7]) ,the enantiomeric purity of 4 (R = Ph) amounts 88% . In the literature no data are available concerning the specific rotation of optically pure (R)-(−)-4 with R = Me but the high value of $[\alpha]_D^{25}$ observed for our product is very promising (cf[4]).

Our observations are consistent with the results obtained by Crabbé[3] and Pirkle [4] for secondary substituted propargylic acetates and carbamates respectively.This could imply that the anti - 1,3-substitution route is the normal stereochemical pathway in esters derived from secondary propargylic alcohols while the syn - route is preferred if the esters are derived from tertiary propargylic alcohols [2,5] . Nevertheless , a study of sulfinic esters of type 1 bearing no aryl group on the chiral center is necessary to justify this assertion , as the formation of a cuprate- arene π - complex between 1 and 3 (intermediate 2 in the Scheme) could also be responsible for the preferred anti - 1,3 - substitution in 1 .

Currently, we are investigating the factors which determine the stereochemical course of organocuprate induced 1,3 - substitutions in propargylic compounds in more detail.

References and notes

1. For a review , see : R.Rossi, P.Diversi , Synthesis , 25 (1973).
2. L.A.van Dijck , B.J.Lankwerden , J.G.C.M. Vermeer , A.J.M.Weber , Recl.Trav.Chim.Pays-Bas , 90 , 801 (1971).
3. J.L.Luche, E.Barreiro,J.M.Dollat,P.Crabbé , Tetrahedron Lett. , 4615 (1975).
4. W.H.Pirkle , C.W.Boeder , J.Org.Chem. , 43 , 1950 (1978).
5. P.Vermeer,H.Westmijze,H.Kleijn,L.A.van Dijck,Recl.Trav.Chim.Pays-Bas, 97,56 (1978).
6. The sulfinate was prepared as described in reference 5.
7. (R)-(−)-3-hydroxy-3-phenylpropyne ($[\alpha]_D^{25}$: -20.8^o (c = 4.30, dioxan) ; Litt.value [8] :-17.68^o (c = 3.45 , dioxan)) was obtained by crystallization the ester of N-phtaloyl-(S)-phenylalanine and racemic 3-hydroxy-3-phenylpropyne from methanol to a constant specific rotation ($[\alpha]_D^{25}$: -146.3^o (c = 2.07 , acetone) ; m.p. 134.0 -135.5 ^{o}) followed by hydrolysis of the ester with sodium hydroxide.
8. R.Weidmann, A.Schoofs , A.Horeau , Bull.Soc.Chim.France , 1976 (3-4),645 .

(Received in UK 17 July 1978; accepted for publication 8 August 1978)