Tetrahedron Letters,Vol.28,No.21, pp 2363-2366,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

# ACETALS AS CHIRAL AUXILIARIES Part 4 (1)

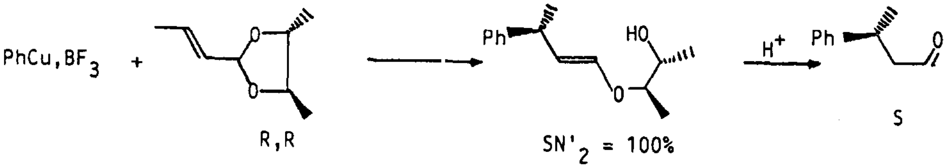
## Asymmetric synthesis of γ,δ-ethylenic aldehydes
## An approach to the California Red scale pheromone

P. Mangeney*, A. Alexakis, J.F. Normant

Laboratoire de Chimie des Organo-éléments, tour 44-45
Université P. et M. Curie, 4 place Jussieu F-75252 PARIS Cédex 05

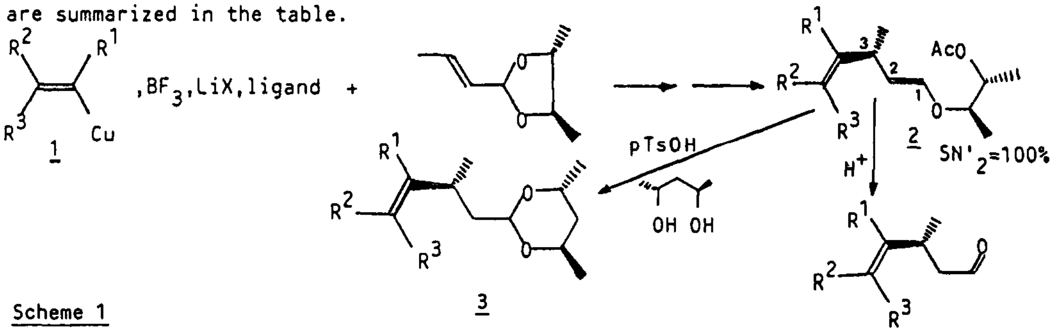
*Abstract - Alkenyl copper - $BF_3$ reagents, associated with tributylphosphine, react stereoselectively with chiral α, β-ethylenic acetals. A precursor of the California Red scale pheromone has been prepared.*

Chiral acetals with a twofold axis of symmetry have been extensively studied as "templates" these last few years (2) ; we have recently reported the regio and diastereoselective 1-4 addition of the $PhCu,BF_3$ reagent on such α, β ethylenic acetals, as a new way to β-phenylated aldehydes with fairly good ee (1a).



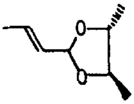
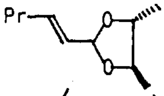
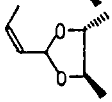
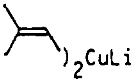
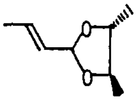
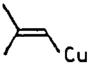
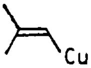
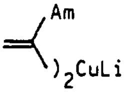
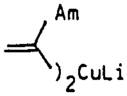
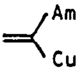
During this study we found that R,R-2,3-butanediol was among the most appropriate auxiliaries for best e.e's. In an effort to generalize the scope of this reaction we screened various $RCu,BF_3$ reagents and we observed that only alkenyl copper reagents <u>1</u> reacted regioselectively to give exclusively 1-4 adducts <u>2</u>.

Moreover we now wish to focus on the definite improvement brought in by addition of tributylphosphine in such reactions, leading to higher diastereomeric ratios. Our results are summarized in the table.

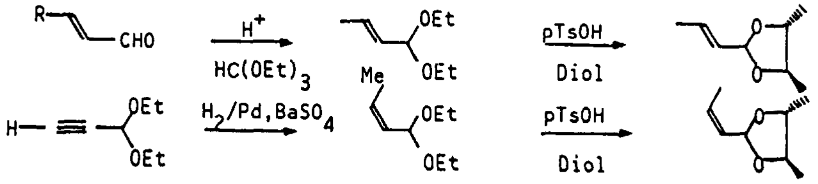


Scheme 1

Table (3)

| Entry | RCu | CuX-ligand | Acetal (a) | E/Z (b) | Yield (%) of 2 | d.e. (c) | $C_3$ conf. |
|---|---|---|---|---|---|---|---|
| 1 | PhCu | CuBr,$PBu_3$ |  | 100/0 | 75 | 95 | S |
| 2(4) | PhCu | CuBr,$PBu_3$ |  | 100/0 | 71 | 91 | S |
| 3(d) | PhCu | CuBr,- |  | 100/0 | 75 | 69 | R |
| 4 |  | CuI,- |  | 95/5 | 69 | 24 | S |
| 5 |  | CuBr,$Me_2S$ | " | 95/5 | 72 | 67 | S |
| 6 |  | CuBr,$PBu_3$ | " | 95/5 | 70 | 85 | S |
| 7 |  | CuI | " | 95/5 | 75 | 50 | S |
| 8 |  | CuBr,$Me_2S$ | " | 95/5 | 71 | 60 | S |
| 9 |  | CuBr,$PBu_3$ | " | 95/5 | 69 | 85 | S |
| 10 |  | CuBr,$Me_2S$ | " | 95/5 | 70 | 73 | S |
| 11 |  | CuBr,$PBu_3$ | " | 95/5 | 68 | 85 | S |

a/ The starting acetal was synthesized from the corresponding aldehyde except for entry 2



E/Z = 92/8

Z/E = 92/8

b/ Stereochemistry of $C_1$-$C_2$ double bond of 2

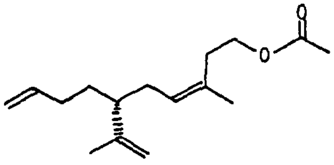
c/ The diastereoselectivity (d.e.) and the absolute configuration were assigned by $^{13}C$ NMR(5) and G.C. analysis on 3 (6). The d.e. was corrected taking into account the E/Z ratio of starting material.

d/ The reaction was complete after 1hr at -70°C.

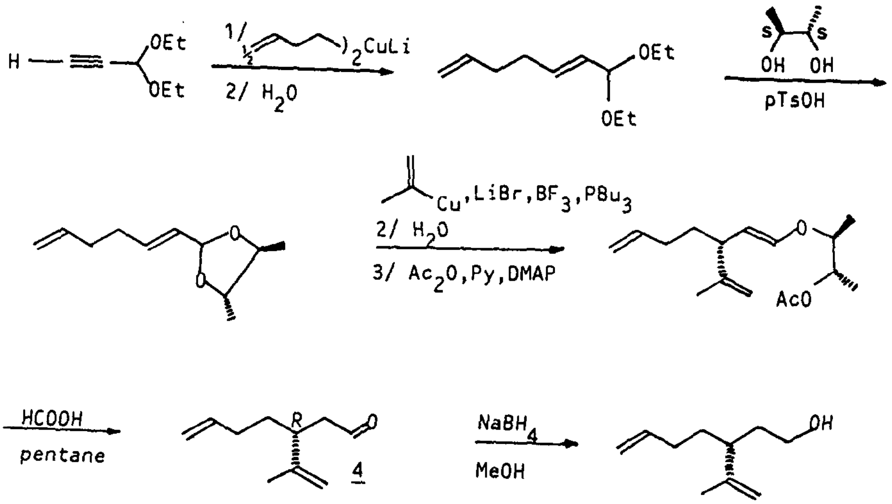
In all cases, the E enol ether 2 was purified by silica gel column chromatography and shown to be of $C_3$(S) configuration. Interestingly, the Z enol ether (5%) was of $C_3$(R) configuration with the same d.e.

We see that the use of more or less effective ligands ($Me_2S$ or $PBu_3$) has a large effect upon diastereoselectivity. Without any ligand (entries 3, 4, 7) the d.e. value is quite low. With $Me_2S$ (entries 5, 8, 10) an improvement is observed up to 75% and with $PBu_3$ (entries 1, 2, 6, 9, 11) the d.e. raises up to > 85% (95% for PhCu).

The good diastereoselectivity resulting from the presence of a phosphine ligand prompted us to explore the asymmetric synthesis (scheme 2) of the aldehyde 4, a precursor of the California red scale pheromone 5 (7).



5



overall yield 50%

$[\alpha]_D^{25} = +6,5(11,5)HCCl_3$

e.e. 85% from MTPA ester (8)

Scheme 2

*Acknowledgements* -

*We thank the C.N.R.S. for financial support (UA 473).*

**References and Notes -**

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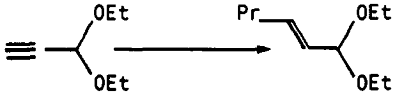
   g/ I.R. Silverman, C. Edington, J.D. Elliott, W.S. Johnson, J. Org. Chem., 52, 180 (1987)
3. The acetal was reacted with four equivalents of $RCu,LiX,BF_3$, ligand, in $Et_2O$ at -78°C. The mixture was allowed to warm up until all starting material was consumed. After usual work up, enol ether was purified by flash column chromatography and acetylated ($Ac_2O$, pyr., DMAP). The mixture of enol ether acetates 2 was purified by silica gel column chromatography. The pure E (or Z) enol ether 2 was then transacetalized with R,R-3,4 pentanediol.
4. $Pr_2CuLi$ +



100% E

according to

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(Received in France 20 March 1987)