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# REACTIONS OF 3-ALKYL- AND 3,3-DIALKYL-1-BROMOALLENES WITH ORGANOCUPRATES: EFFECTS OF THE NATURE OF THE CUPRATE REAGENT ON THE REGIO- AND STEREOSELECTIVITY

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**Summary:** Organocuprates induce 1,3- and direct substitution in 3-alkyl- and 3,3-dialkyl-1-bromo-1,2-dienes leading respectively to either terminal acetylenes or allenic hydrocarbons. The nature of the cuprate exerts a prominent role in determining both the regio- and the stereochemistry of these reactions.

Organocopper and cuprate reagents react with propargylic functional derivatives to afford allenes.[1] It has been well established[2] that this reaction proceeds with a prevalent 1,3-**ANTI** displacement independently of the nature of both the organocopper species and the propargylic precursor, as confirmed also by our recent data employing tertiary acyclic propargylic esters.[3]

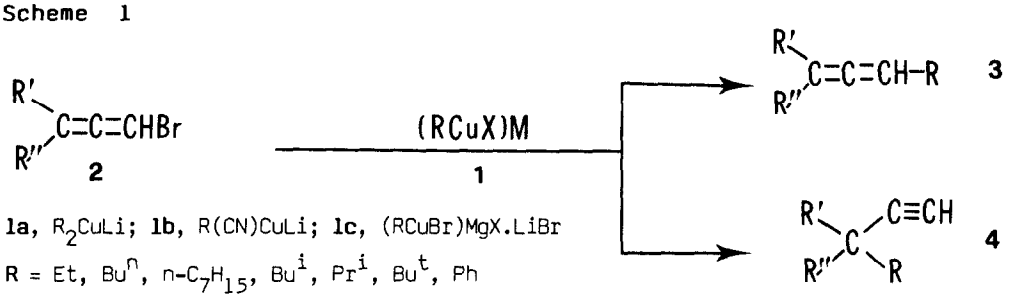
On the contrary, the regio- and the stereochemistry of the reactions of organocuprates with allenic substrates have been little studied. In fact, only few examples are reported concerning the reactivity of allenic bromides.[4,5] In particular, it has been observed that the reactions of 3-substituted- and 3,3-disubstituted-1-bromoallenes with lithium dialkylcuprates, $R_2CuLi$, give 1-alkylallenes <u>via</u> direct substitution,[4] while cyanocuprates, R(CN)CuLi, react with 1,3-disubstituted-1-bromoallenes to form mainly internal alkynes.[5]
In this connection, an high **ANTI** stereochemistry has been found for the conversion of bromoallenes into alkyl acetylenes,[6] but some confusion still exsists on the stereochemical course of the allenes formation.[2,4b,5]

We report here the evidence that both the nature and the structure of the organocopper reagent exert a prominent role in determining the regio- and the stereochemistry of the cuprate displacement reactions involving allenic bromides.

The reactions of 3-alkyl- and 3,3-dialkyl-1-bromo-1,2-dienes, **2**, with a number of cuprate

reagents **1a-1c** in diethyl ether or tetrahydrofuran at -70°C were examined (Scheme 1).[6]

**Scheme 1**




**1a**, $R_2CuLi$; **1b**, R(CN)CuLi; **1c**, (RCuBr)MgX.LiBr

R = Et, $Bu^n$, $n\text{-}C_7H_{15}$, $Bu^i$, $Pr^i$, $Bu^t$, Ph

**R'** = H, Me; **R"** = Me, Et, $Pr^n$, $Pr^i$, $Bu^t$

According to Landor,[4] compounds **2** react with the Gilman reagents **1a** to afford exclusively the allenic products **3**, regardless of the structure of the cuprate organic moiety (**R**= alkyl or phenyl).

On the other hand, the alkylcyanocuprates **1b** and the complex organocopper species **1c** lead to the acetylenic product **4** when **R** = n-alkyl (80-98% yield) and to the substituted allene **3** when **R** is a tertiary group (90-100% yield). The steric hindrance at the C-3 of the bromoallenic substrate becomes a dominant factor in products generation when we use secondary (**R**=$Pr^i$) or $\alpha$-branched primary copper reagents (**R**=$Bu^i$): 1-alkynes are in general obtained with mono-substituted substrates (**R'**=H; 80-96% yield) and allenes with the disubstituted ones (**R'**=Me; 70-100% yield).

Interestingly, in all the cases examined, the phenylcyanocuprate **Ph(CN)CuLi** selectively affords the phenylallenes **3** (70-80% yield) while with **(PhCuBr)MgBr.LiBr** the predominant products are the 3-phenyl-1-alkynes **4** (80-92% yield).[7]

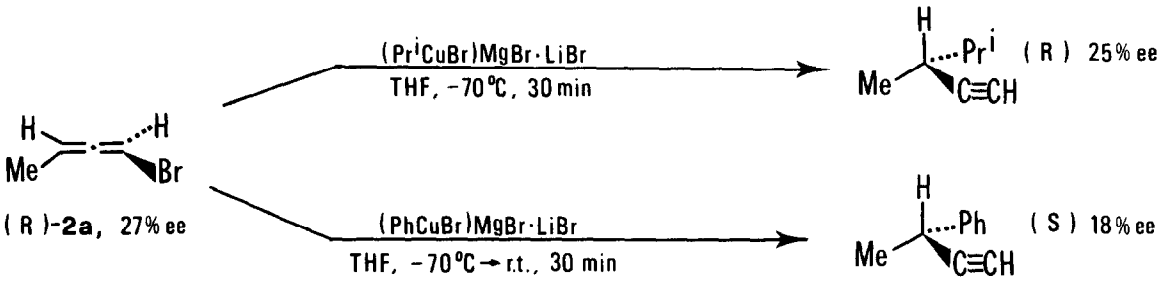
In order to elucidate the stereochemical behaviour of the above substitution reactions, we have employed as starting materials chiral bromoallenes **2**, prepared from the corresponding optically active propargylic alcohols by procedures described elsewere.[8,9]

Thus, the reaction of (R)-1-bromo-1,2-butadiene,[9] (R)(**2a**), with **($Pr^i$CuBr)MgBr.LiBr** and **(PhCuBr)MgBr.LiBr** gave, respectively, (R)-3,4-dimethyl-1-pentyne[10] and (S)-3-phenyl-1-butyne[7,11] of known ee. (Scheme 2).

These data are consistent with the results obtained by Corey[5] for internal acetylenes and imply that the formation of alkynes from allenic bromides and organocopper reagents should proceed in a highly **ANTI** stereochemical fashion.

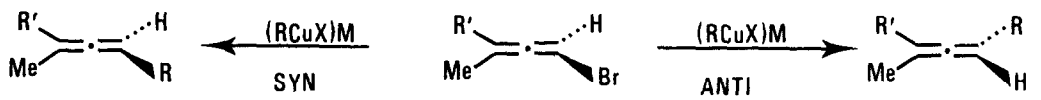
On the other hand, the results of the reactions carried out with various cuprates and (S)-1-bromo-3-methyl-1,2-pentadiene, (S)(**2b**),[8] and (S)-1-bromo-3,4,4-trimethyl-1,2-pentadiene,

**Scheme 2**




(S)(**2c**)[8] show that the direct substitution, which affords the allenic products **3**, proceeds with two opposite stereochemical pathways, depending on the nature and structure of the organocopper species (Table). In particular, the homocuprates **1a** and the **phenyl** reagents, irrespective to

**Table**




(S)-3 (S)-2 (R)-3

| Entry[a] | (S)-2,[b] | R' | Organocopper agent | 3 Absolute Configuration[c] | 3 $[\alpha]_D^{25}$[d] | 3 ee±5%[e] |
|---|---|---|---|---|---|---|
| 1 | (S)-**2b** | Et | $Bu^i_2CuLi$ | R | - 9.5(hexane) | 35 |
| 2 | (S)-**2b** | Et | $Bu^i(CN)CuLi$ | S | +17.8(hexane) | 66 |
| 3 | (S)-**2b** | Et | $(Bu^iCuBr)MgCl.LiBr$ | S | +24.3(hexane) | 90 |
| 4 | (S)-**2c** | $Bu^t$ | $(Bu^tCuBr)MgCl.LiBr$ | S | +37.8(pentane) | 64 |
| 5 | (S)-**2b** | Et | $Ph_2CuLi$ | R | -70.3(heptane) | 62 |
| 6 | (S)-**2b** | Et | Ph(CN)CuLi | R | -115 (heptane) | 100 |
| 7[f] | (S)-**2b** | Et | (PhCuBr)MgBr.LiBr | R | -72.3(heptane) | 63 |

[a]All reactions were carried out according to ref.6. [b]The ee values for (S)-**2b** and (S)-**2c** used in the experiments amounted to 51% and 38% respectively. [c]Deduced by the Runge "chirality functions approach"(see ref 12) and by preparing compounds **3** *via* 1,3-**ANTI** substitution reaction of the appropriate propargylic chiral substrate with cuprates **1a-c**(see ref 2,3). [d]The reported rotations refer to conversion of optically pure (S)-**2** and are extrapolated values. Allenes were purified by preparative GLC. [e]Determined by $^{195}$**Pt** NMR of the Pt-complexes obtained by reacting, in chloroform at r.t., the chiral allenic hydrocarbons with an excess of *trans*-dichloro|(S)-*α*-phenylethylamine||ethylene|Pt(II) (G.Uccello Barretta, et al., manuscript in preparation). [f]The reaction affords 3-methyl-3-phenyl-1-pentyne as main product (80%), the phenylallene **3** (20%) was recovered by preparative GLC.

their specific nature, lead to substituted allenes with prevalent inversion of configuration, viz. with **ANTI** stereoselectivity,[13] while **alkyl**heterocuprates **1b** and **1c** afford the allenic product with retention in the allenyl moiety (**SYN** substitution process). The nature and the structure of the organocopper species seem to affect also the degree of stereoselectivity, the best results being in general obtained with the cuprates **1b** and **1c**; the contact of the products with the cuprate excess during the reaction time could be responsible, however, for the high racemisation observed in some cases for the allenic derivatives.[14]

In conclusion, all these data suggest that different mechanisms must be operative for the reactions of bromoallenes with copper reagents, in relation to the different nature of the reagent itself.

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6. All experiments were run in a 10 mmol scale by reacting the allenic substrate **2** with 2 equiv. of organocuprates **1** at -70°C for 30 min (in diethyl ether with **1a** and **1b** and in THF with **1c**); when phenyl reagents were used, the reaction mixture was allowed to warm to room temperature. After hydrolysis with $NH_4Cl$ solution, the products were isolated by distillation or preparative GLC. All new compounds showed satisfactory analytical and spectral data.

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13. This result fights against the SYN stereoselectivity reported for the reaction of $Me_2CuLi$ with the allenic bromide derived from mestranol(see ref 4b).

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