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METAL CATALYSIS IN ORGANIC REACTIONS. 18.

STEREOCHEMISTRY OF THE TRANSITION-METAL CATALYZED CROSS-COUPLING OF (S)-1-BROMO-3-METHYL-1,2-PENTADIENE WITH ISOBUTYLMETAL COMPOUNDS.

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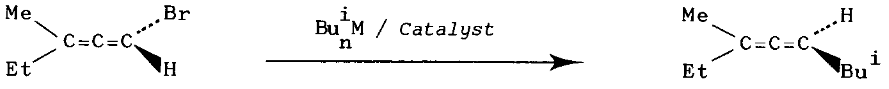
Summary : The stereochemical course of Ni- and Pd-catalyzed reactions of (+)(S)-1 with isobutylmetal reagents has been elucidated by preparing the allene (+)-2 via an *anti* stereoselective transformation of the propargylic acetate (+)(R)-4 with organocuprates.

In a recent paper[1] we reported an efficient synthesis of trisubstituted allenes by Ni-catalyzed reactions of 3,3-dialkyl-1-bromoallenes with typical organometallic reagents, R_nM, containing Mg, Zn, and Al. We proposed that the stereochemical course of such conversions proceed with prevalent inversion in the allenyl moiety.[1] The results obtained in the reactions between (+)(S)-1[2] and isobutylmetal compounds in the presence of bis(N-methylsalicylaldimine) nickel, Ni(mesal)$_2$, showed also that the degree of stereoselectivity depends upon the nature of the organometallic reagent employed (Scheme 1).[1] The *anti* stereochemistry of the process was based on the absolute R configuration assigned to dextrorotatory 3,7-dimethyl-3,4-octadiene, (+)-2, by relating this compound to (+)(S)-1 *via* the Pd(PPh$_3$)$_4$-catalyzed coupling with Bu^{i}ZnCl, according to the Vermeer procedure[3] (Scheme 1). In fact, this Pd-promoted reaction was reported to proceed in a highly stereoselective fashion, at least with phenylzinc reagents and 3-phenyl- or 3-alkyl-1-bromoallenes.[3] On the other hand, by reaction with MeZnCl and Pd(PPh$_3$)$_4$,[3] (+)(S)-1 (23% ee) was also converted into (-)-4-methyl-2,3-hexadiene, $[\alpha]_D^{20}$ -0.20, of known R configuration,[4] i.e. with inversion in the allenyl moiety.

SCHEME 1



(+)(S)-1

35% ee

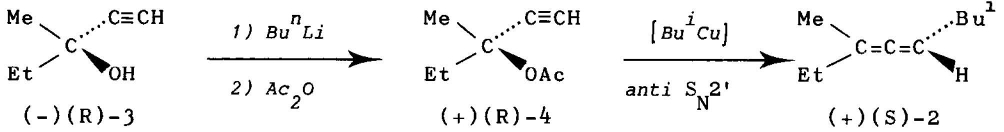
(+)(R)-2

Catalyst	M	$[\alpha]_D^{25}$
Ni(mesal)$_2$	Al	+ 10.0 (*hexane*)
"	MgCl	+ 4.1 "
"	ZnCl	+ 0.05 "
Pd(PPh$_3$)$_4$	ZnCl	+ 1.15 "

However, as the above catalytic reactions of (+)(S)-1 with Bu^{i}ZnCl and MeZnCl proceed with a very high degree of racemization (see Scheme 1 and ref 4), and the assignment of the R configuration to (+)-2 conflict with the Runge "chirality functions approach",[5] it seemed useful to confirm our previous stereochemical hypothesis[1] by preparing (+)-2 *via* an independent route of known stereochemistry.

Scheme 2 summarizes here the synthesis of (+)-2 from (R)-3-methyl-1-pentyn-3-ol,(-)(R)-3, through the reaction of the corresponding propargylic acetate, (+)(R)-4, with organocuprates.[6]

SCHEME 2



(-)(R)-3 (84% ee)[4] was converted into (+)(R)-4 $\{$72% yield, $[\alpha]_D^{20}$ +20.2 (heptane)$\}$ by reaction, at -70°C in THF, with one equivalent of Bu^nLi followed by addition of acetic anhydride.[7] Treatment of (+)(R)-4 (*28 mmol*) with $[Bu^iCuBr]MgCl\cdot LiBr$ (*56 mmol*) in THF during 12 h at -70°C afforded pure (+)-2 (70% yield) having $[\alpha]_D^{25}$ +19.6 (hexane).

Similarly, (+)-2 $\{$55% yield, $[\alpha]_D^{25}$ +9.9 (hexane)$\}$ was obtained from (+)(R)-4 by reaction with equimolar amounts of Bu^i_2CuLi in diethyl ether at -70°C.

Since it has been well established[8] that organocopper(I) reagents induce an *anti*-1,3-substitution reaction in esters of secondary and tertiary propargylic carbinols, dextrorotatory 2 must have the S absolute configuration, in contrast with our previous assignment.[1] Therefore, the Ni- and Pd-promoted reactions of (+)(S)-1 with isobutylmetal compounds (Scheme 1) proceed with prevalent retention in the allenyl moiety and not with inversion.[3]

The comparison of our results with those of Vermeer[3] shows that the stereochemistry and also the mechanism of the transition-metal-catalyzed allene synthesis from 1-halogenoallenes and organometallic reagents seems to depend drastically on the nature and structure of the organometallic compound employed as well as on the structure of the allenic substrate.

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