COPPER- AND NICKEL-CATALYSIS IN S_N2'- AND S_N2-REGIOSELECTIVE ALLYLATION OF ORGANOZINC REAGENTS

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Summary: Allylation of organozinc reagents in the presence of a copper catalyst takes place in a highly $S_N 2^i$ -selective manner, whereas that in the presence of a nickel catalyst occurs with excellent $S_N 2$ -selectivity.

Allylation of an organometallic reagent is an important carbon-carbon bond forming reaction, for which RLi and RMgX have generally been used as the source of the carbanionic moiety to be transferred to the allylating reagent.¹ The regiochemistry has been the primary problem, the reaction of an allylic halide (1) often giving a mixture of the S_N2' - (2) and the S_N2 -products (3).² We have found that readily available organozinc reagents undergo highly regio- and chemoselective allylation reaction under very mild conditions. Particularly notable among our present findings is that the mode of the regioselection can be completely changed from S_N2' to S_N2 simply by switching the catalyst from a copper-based to a nickel-base one (eq 1).



The examples of the allylation reactions are shown in Table 1. The reaction of MeZnCl, BuZnCl (from RLi and ZnCl₂ in THF), and Et₂Zn with cinnamyl chloride in the presence of CuBr·Me₂S³ (5 mol%) proceeded smoothly at 20 °C to afford S_N2'-allylation products (entries 1--3). The observed regioselectivity (92-98%) compares favorably with that of a more elaborate stoichiometric reagent, RCu-BF₃² (89-99.7% selective at -70 °C). The S_N2' selectivity was also found very high, even for the reaction in which a sterically congested quaternary center is created (entry 4).

The reaction also shows high chemoselectivity (entry 5). In contrast to the copper reagents based on RLi or RMgX,^{1,4} the organozinc/cat. copper reagent react neither with allylic acetate nor with alkyl halides. Eq 2 illustrates an even more striking example. Being quite non-nucleophilic and non-basic,⁵ this reagent shows strong preference to undergo an allylation reaction rather than reactions with ketones.

0.6 Et₂Zn + Ph c_1 + Ph c_1 + Ph room tempHMPA/1HF Ph room temp + Ph recovered (2)

A nickel-catalyzed reaction of MeZnCl with cinnamyl chloride took an entirely different course to give an S_N^2 substitution product⁶ with 92% regioselectivity (entry 6). More importantly, the organozinc/cat. nickel reagent has been found to offer a new solution to the problems of unsymmetrical allyl-allyl coupling, which has long been the subject of considerable interest, yet not been fully resolved.⁷ Thus, crotylzinc bromide (from <u>trans</u>-

crotvl bromide and zinc dust in THF),8 reacted with cinnamyl chloride (entry 7) and geranyl chloride (entry 8) through exclusive $S_N 2$ substitution with retention of the trans-crotyl molety (1 H NMR) in the S_F2 product.

Although it is too early to enumerate the advantages of the organozinc/cat. transition metal reagents⁹ over the conventional ones, it is already clear that such reagents are synthetically useful, particularly, for the control of regio- and chemoselectivity.¹⁰

Table	1.	S _N 2-'	and	S _N 2-Allylation	of	Organozinc	Reagentsa
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Entry	'RZn'	Cataly	vst Substrate	S _N 2' Product(s)	Product S _N 2'	ratio ^e : S _N 2	isolat yield	:ed (%)
1	MeZnCl	Cu ^b	Ph~~Cl	Ph	92	: 8	67	7
2	Et ₂ Zn	Cu ^b	Ph Cl	Ph	98	: 2	85	5
3	BuZnCl	Cu ^b	Ph CI	Ph	96	: 4	84	4
4	BuZnCl	Cu ^b	Landara I		91	: 9	62	2
5	BuZnCl	Cu ^b	Acondat	Acondada	100	: 0	65	5
6	MeZnCl	Ni ^c	Ph CI	`1:1 Ph∕∽∕	8	: 92	65	5
7	ZnBr	r Ni ^d	Ph~~CI	Ph~~~~ · Ph~~~~~	0 (76	:100 : 24)	95	5
8	ZnBr	. _{Ni} d	Landrei -	bulan · bulay	<pre> <3 (63</pre>	: 97 : 37)	69	9

^aAllylic chloride was allowed to react in THF with a zinc reagent (1-1.5 equiv) at 0-20 ^aAllylic chloride was allowed to react in THF with a zinc reagent (1-1.5 equiv) at 0-20 °C for 5-15 h. In entries 1, 2, and 4, HMPA (1 equiv) was used as an additive. The isomeric ratio was determined by capillary GLC analysis, and the regio- and stereochemical assignment was made by IR and 200 MHz ¹H NMR analysis. All products showed correct elemental analysis. ^bCuBr·Me₂S (5 mol%) was used as catalyst. ^cNiCl₂[1,2-bis(triphenylphosphino)ethane] (5 mol%). ^dNiCl₂(PPh₃)₂ (5 mol%). ^eS_E2/S_E2' ratio in parenthesis.

References

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