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A New Preparation of Diorganozincs from Olefins via a Nickel Catalyzed Hydrozincation.

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Summary: The reaction of olefins with diethylzinc in the presence of catalytic amounts of Ni(acac)₂ provides dialkylzincs (neat, 40-50 °C, 2-6 h). These zinc reagents can be trapped by various electrophiles or used for the catalytic asymmetric addition to aldehydes (> 85 % ee). Allylic and homoallylic alcohols are especially good substrates for the reaction.

Recently, we have reported that the treatment of functionalized alkyl iodides (or bromides) with diethylzinc in the presence of catalytic amounts of Ni(acac)₂ furnishes alkylzinc halides, which can be reacted further with a range of electrophiles. The presence of a double bond at an appropriate position in the alkyl halide allows the performance of efficient cyclization reactions.¹ In the course of this work, we have now found a new reaction, allowing the direct preparation of dialkylzincs from olefins and Et₂Zn (Eq. 1).

$$2 \operatorname{R} + \operatorname{Et_2Zn} \xrightarrow{\operatorname{neat}, 50 \ ^{\circ}C} \left(\operatorname{R} + 2 \operatorname{H_2C=CH_2} (1) \right)$$

Ni(acac)₂ (1-2 mol%)
COD (1-4 mol%)

The treatment of octene with Et₂Zn (0.5-0.6 equiv) in the presence of Ni(acac)₂ (1-2 mol %) and 1,5cyclooctadiene (COD; 1-4 mol %) at 50 °C for 3 h affords Oct₂Zn in 40-45 % yield. Lower conversions are obtained in the absence of COD. The use of NiCl₂(PPh₃)₂ as catalyst slows the reaction down and the addition of an excess of Et₂Zn did not improve the conversion. The dialkylzincs prepared under these conditions can be trapped by various electrophiles after transmetalation with CuCN·2 LiCl.² Moreover, the reaction of Oct₂Zn with benzaldehyde or cinnamaldehyde in the presence of a catalytic amount of (*IR*,*2R*)-1,2-bis(trifluormethanesulfonamido)cyclohexane³ 1 (8 mol %, toluene, Ti(Oi-Pr)₄ (1.25 - 2 equiv)) produces the expected alcohols **2a-b** in 62-76 % yield and 89-90 % *ee* (Scheme 1). This reaction can be extended to the preparation of chiral polyfunctional alcohols. The hydrozincation of the unsaturated ester 3 provides the corresponding zinc reagent in 40 % yield. Its reaction with the aldehyde **4** affords the chiral polyfunctional alcohol **2c** in 68 % yield and 95 % *ee* (Eq. 2).^{3e}





The presence of a charged heteroatom in the olefin at an allylic or homallylic position should considerably stabilize⁴ the zinc reagent obtained after hydrozincation,⁵ and should allow higher conversions.^{6,7} Thus, the treatment of allylic or homoallylic alcohols of type 5 with Et₂Zn (2.2 equiv) and COD (10 mol %) in the presence of Ni(acac)₂ (5 mol %) for 4-6 h at 40 °C affords the hydrozincated products 6 in \ge 85 % conversion. The addition of TMSCl (2.0 equiv) in THF converts the cyclic zinc reagent to an alkylzinc halide 7. This procedure protects the alcohol function in situ and affords an organozinc chloride which is readily transmetalated to the corresponding copper derivative by the addition of CuCN-2 LiCl (2.0 equiv).⁸



The addition of an electrophile such, as an allylic bromide, diethyl benzylidenemalonate, iodine, acid chloride or alkynyl bromide, leads to the expected products 8 in satisfactory yields (Eq. 3 and Table 1).



A tentative catalytic cycle for the reaction is proposed (Scheme 2). The reaction of Et₂Zn with Ni(acac)₂ should provide an ethylnickel(II) species of type 9 which leads, after β -hydride elimination, to the nickel hydride 10. The exchange of ethylene by an alkene will furnish the nickel-olefin complex 11 which affords, by a hydronickelation,⁹ a new alkylnickel(II) complex 12. Finally, the transmetalation of 12 with Et₂Zn gives

entry	alcohol 5	electrophile	product 8	yield ^a (%)
1	5a Me	I2		76
2	5a	Br—C≡C— Et	Me OH Me Me	68
3	5a	Ph CO ₂ Et	$Me \qquad Ph \qquad 8c$	65 ^b
4	5a	t-BuCOCl	Me OCOt-Bu	62
5	5b OH	PhCOCl	Me t-Bu 80 OCOPh n-Hex Ph	65
6	5 b	Br—C≡C—Ph	OH 8f	71
7	TIPSO OH 5c	CO ₂ Et	TIPSO OH CO ₂ Et	62
8	OPiv 5d	CO ₂ Et Br		67
9	5e OH	I ₂		70
10	5e	CO ₂ Et	Ph 8j CO ₂ Et	73

Table 1. Products **8a-j** obtained by the hydrozincation of the allylic and homallylic alcohols **5a-e** with Et_2Zn in the presence of catalytic amounts of Ni(acac)₂, and further reaction with an electrophile.¹⁰

^a All yields are isolated yields of analytically pure compounds. ^b The TMS-protecting group of 8c has been removed by treatment with Bu4NF in THF before aqueous workup.

the dialkylzinc 13 and regenerates the nickel(II) intermediate 9 making the whole process catalytic. Further extensions of this work are currently under investigation in our laboratories.

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- 10. Typical procedure: Ethyl 2-(4-hydroxy-7-pivaloxy)acrylate (8h). To a stirred suspension of 4-hydroxy-hex-5-enyl pivalate (5d) (0.50 g, 5.0 mmol), 1,5 cyclooctadiene (0.05 mL, 10 mol %) and Ni(acac)₂ (60 mg, 5 mol %, 0.25 mmol) was added at -78 °C neat Et₂Zn (1.1 mL, 11 mmol). The reaction mixture was slowly warmed to 40 °C leading to a black suspension. The reaction was completed by stirring at 40 °C for 4 hours. Excess Et₂Zn was pumped off at high vacuum (0.1 mm Hg / rt). The residual solid was dissolved in THF (5 mL) and treated with TMSCl (1.2 mL, 10 mmol) at -78 °C. The mixture was allowed to warm to rt overnight. Then a THF solution (10 mL) of CuCN (0.89 g, 10 mmol) and LiCl (0.84 g, 20 mmol) was added at -60 °C. After stirring at 0 °C for 30 min, the mixture was cooled again to -78 °C cand ethyl (2-bromomethyl)acrylate (1.3 g, 6.5 mmol) was added. The allylation reaction was complete after stirring at 0 °C for 30 min. The reaction mixture was then poured into ice-cooled saturated aqueous NH₄Cl (100 mL) and was extracted with ether (3x100 mL). The combined organic layers were washed with brine, dried over MgSO4 and concentrated. The crude product was purified by flash chromatography (hexanes/ether 9:1 to 4:1) affording the alcohol 8h (0.99 g, 3.35 mmol, 67 % yield).

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