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1,2-Addition of Alkyl- and Alkenylzirconocene Chlorides to Aldehydes Accelerated by Catalytic Amounts of $ZnBr_2$ as a Method of Synthesizing Secondary Alcohols, Secondary Allylic Alcohols, and *in-Situ* Oppenauer-Type Oxidation of the Alcohols to Ketones

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Organozirconocene chlorides do not readily react by 1,2-addition to carbonyls. Several protocols have recently been explored to try and rectify this problem. Suzuki has used various silver salts to accelerate the addition of alkyl- and alkenylzirconocene chlorides to aldehydes.[1] Wipf has added stoichiometric amounts of Me_2Zn to 1-alkenylzirconocene chlorides and shown that 1,2-addition occurs at 0 °C with various aldehydes, presumably by way of alkenylzinc species.[2] On the other hand, 1,2-alkylations of aldehydes with Cp_2ZrR_2 in the presence of 4−5 equiv of potassium *tert*-butoxide has been reported.[3] Only nonenolizable aldehydes may be used. An approach employing readily available reagents catalytically would greatly extend the chemistry of organozirconocenes in synthesis. In this communication we present our results and demonstrate the very general nature of the reaction of organozirconocene chlorides with aldehydes catalyzed by $ZnBr_2$ and the facile Oppenauer-type oxidation of the alcohols, if desired, to ketones.

When octylzirconocene chloride (**1**, R^1 = *n*-octyl) was treated with benzaldehyde (**2**, R^2 = phenyl) in the presence of 2.0 equiv of $ZnBr_2$ the initial yellow solution turned colorless (THF, 0.2 M, 6 h, 25 °C). After aqueous workup, GCMS, ^1H and ^{13}C NMR analysis indicated that 1-phenyl-1-nonanol had been obtained (**4**, R^1 = octyl, R^2 = phenyl; Scheme 1) in 82% yield. We quickly established that the addition could be made catalytic in $ZnBr_2$ and that the reaction time could be considerably reduced by running the reaction in more concentrated solution. The yield also went up. Additional transition metals were not required.[4] $ZnCl_2$ was ineffective in dilute solutions but could also catalyze the reaction, though less efficiently than $ZnBr_2$ in more concentrated solutions. Other zinc salts were not investigated.

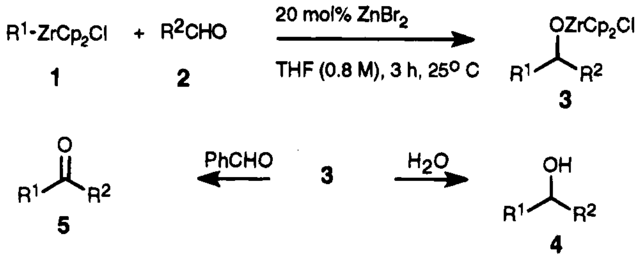
The reaction appears to be very general both for aliphatic and aromatic aldehydes. Coupled with the compatibility of organozirconium reagents with a variety of functional groups,[5] the present protocol represents a significant advance in the organometallic chemistry of zirconium. Results are summarized in Table 1.

Table 1. Preparation of Alcohols by 1,2-Addition of $RZrCp_2Cl$ to Aldehydes and Their in-Situ Conversion to Ketones, Catalyzed by $ZnBr_2$[a]

entry	R^1	aldehyde	% yield,[b] **4**	% yield,[b,f] **5**
1	*n*-octyl	benzaldehyde	88	83
2	5-chloropentyl	benzaldehyde	85	77
3	4-phenylbutyl	benzaldehyde	90	83
4	cyclohexyl	benzaldehyde	89	88
5	$Me_3Si(CH_2)_2CH_2$	benzaldehyde	91	87
6	$MeSi_3CH_2CH_2$	benzaldehyde	89	82
7	octyl	hydrocinnamaldehyde[c]	91	
8	$Me_3Si(CH_2)_2CH_2$	2-furaldehyde[d]	88	
9	$Me_3Si(CH_2)_2CH_2$	*p*-MeC_6H_4CHO	90	82
10	4-phenylbutyl	*n*-butanal	85	77
11	4-phenylbutyl	*p*-ClC_6H_4CHO	80	
12	1-hexenyl	benzaldehyde[e]	95	
13	2-cyclopentylvinyl	hydrocinnamaldehyde[e]	96	91
14	2-(trimethylsilyl)vinyl	*p*-MeC_6H_4CHO[e]	94	89
15	5-chloro-1-pentenyl	*n*-Butanal[e]	90	88
16	3-hexenyl	p-ClC_6H_4CHO[e]	87	

[a] Standard reaction conditions, unless indicated otherwise: THF, 0.8 M initial concentration of reactants, in a ratio of aldehyde:$RZrCp_2Cl$:$ZnBr_2$ = 1:1.1:0.2; 25 °C, 3 h. [b] Isolated by TLC. [c] Reaction worked up after 4 h. [d] Reaction worked up after 2.5 h. [e] Reaction run at 0 °C, 15 min. [f] One equivalent of benzaldehyde was added and the reaction stirred for 6 h at 25 °C for alkyl derivatives, and 3 h for alkenyl derivatives.

Scheme 1



When the reaction was carried out with a slight excess of aldehyde, a considerable amount of the corresponding ketone **5** (10−30%) was obtained! This seemed remarkable. A survey of the literature however revealed that Cp_2ZrH_2 has been used to oxidize alcohols to ketones at elevated temperatures and prolonged reaction times in the presence of suitable hydrogen acceptors.[6] Intrigued, we explored this aspect. When an additional 1 equiv of benzaldehyde was added to the reaction mixture (after analysis indicated that 1 equiv of aldehyde had been consumed, presumably forming $ROZrCp_2Cl$, **3**) the metalated secondary alcohol was converted to the corresponding ketone **5** (Scheme 1). The oxidation is thought to be of the Oppenauer-type.[7] Thus it is possible to obtain either the secondary alcohol **4** or the ketone **5** from the same reaction mixture by varying the ratio of reagents. While we have not optimized the conditions of oxidation, the yields of ketones with benzaldehyde as a hydrogen acceptor are satisfactory. Enolizable aldehydes, i.e., propanal, gave aldol side-products and should be avoided.

Regarding the mechanism of the addition reaction, a number of pathways are possible: (1) carbonyl activation by $ZnBr_2$ followed by 1,2-addition of the alkylzirconocene. (2) Transmetalation to form an organozinc halide. (3) Ionization of the zirconocene chloride. We do not favor the ionization mechanism since ionization of zirconocene chlorides under the present reaction conditions is unlikely.[8] While a facile transmetalation apparently occurs with alkenylzirconocene chlorides and Me_2Zn,[2,9] we have

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as yet no evidence of a similar mechanism with alkylzirconocene chlorides. On the other hand, complexation of aldehydes with zinc halides is well known.[10] Complexation can also explain the observed rate acceleration of the oxidation reaction. Alkoxyzirconocenes are known to undergo Oppenauer-type oxidation. Regarding the oxidation, Negishi has suggested a mechanism for this type of oxidation that postulates a hydride attack on the receptor carbonyl compound.[11] We independently prepared $ROZrCp_2Cl$[12] and reacted it with benzaldehyde. No appreciable rate increase was observed in the presence of $ZnBr_2$. Therefore carbonyl activation probably is not important here. The rate acceleration observed for the oxidation under our conditions as compared to the literature is probably due to the stoichiometric amount of $ROZrCp_2Cl$ used.

We next explored the addition of various *trans*-1-alkenylzirconocene chlorides to aldehydes in the catalytic presence of $ZnBr_2$. Not unexpectedly, their reaction with aldehydes was much faster (0 °C, 15 min). Again excellent yields of the secondary allylic alcohols were obtained (Table 1, entry 12–16). Addition of 1 equiv of benzaldehyde to **3** provided the α,β-unsaturated ketones in excellent yield, if desired. The addition reaction also works well with internal alkenylzirconocenes (Table 1, entry 16). The trans geometry of the double bond is retained in the secondary allylic alcohols and in the α,β-unsaturated ketones as determined by analysis of their ^1H NMR spectra.

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Supplementary Material Available: General experimental procedures for compounds in Table 1 (5 pages).

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