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A ZIRCONIUM-PROMOTED METHYLENATION OF ALDEHYDES, KETONES, AND ENONES

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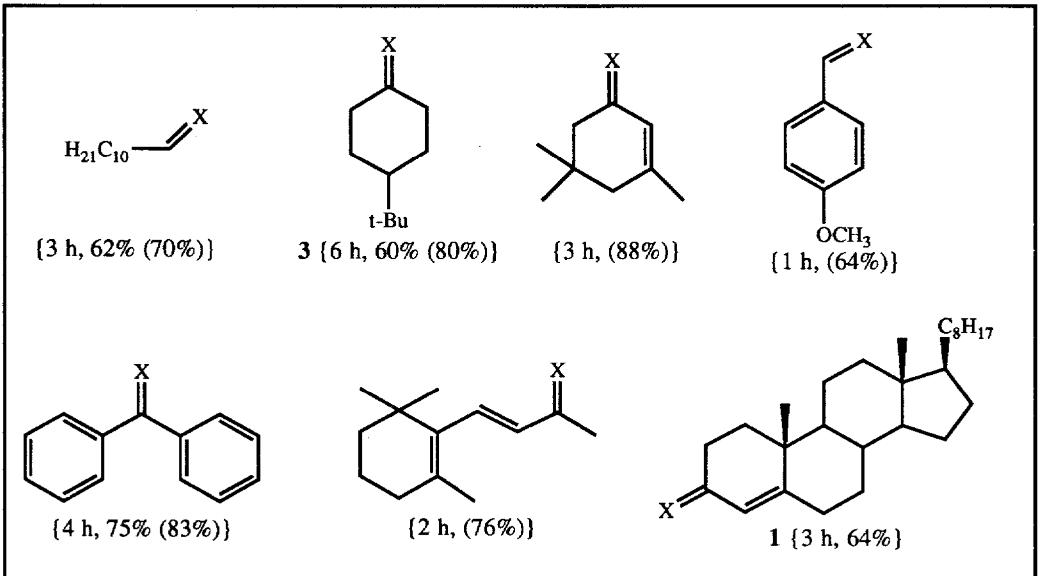
Abstract. Treatment of zirconocene dichloride with dibromomethane and zinc affords an organometallic intermediate which rapidly methylenates aldehydes, ketones, and enones at room temperature.

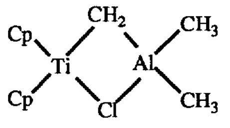
Although there have been several recent advances in the use of transition metal complexes for the alkenylation of carbonyl compounds, most of those methods require extended reaction times and/or extensive procedures to prepare the required organometallic complexes.[1-5] During the course of our investigations into the formation of transition metal carbenes, we found that the addition of dibromomethane to zinc metal and Cp_2ZrCl_2 afforded a reagent which rapidly and cleanly methylenated aldehydes and ketones. This Cp_2ZrCl_2-promoted methylenation procedure should prove to be especially useful for acid sensitive substrates when the more Lewis acidic titanium-based methodologies are unsuitable. All the reagents can be sequentially added at room temperature to form the active organometallic complex which then carries out the olefination to yield a single monomeric product. A representative procedure is as follows. A dry nitrogen flushed flask was sequentially charged with zinc metal[6] (0.52 g, 8.0 mmol), zirconocene dichloride (0.35 g, 1.2 mmol), (+)-4-cholesten-3-one (**1**, X=O) (0.385 g, 1.0 mmol), THF (2.5 mL), and dibromomethane (0.38 g, 154 µL, 2.2 mmol). The solution was stirred for 3 h at room temperature before being quenched with water (3 mL). The standard extractive work-up and flash chromatographic purification (silica gel, hexane) afforded 0.245 g (64%) of the pure diene **1** ($X=CH_2$).[7] Other results are summarized in Table 1.

Several aspects of the reaction are noteworthy. Firstly, there was no reaction of the carbonyl compounds with Zn and CH_2Br_2 in the absence of Cp_2ZrCl_2. Secondly, CH_2I_2 could be used in place of CH_2Br_2 while CH_2Cl_2 was unreactive under the standard conditions. Use of 1,1-dibromopentane as the dihalide did not form any olefinated material presumably due to ß-hydride elimination. The use of zinc-copper couple in place zinc metal depressed the yields of the methylenated products. Unlike Tebbe's reagent (**2**),[1] this zirconium procedure does not successfully methylenate esters and lactones. Though most transition-metal-promoted methylenation procedures utilize titanium-based organometallic complexes,[1] substitution of

Table 1. Conversion of carbonyls (X=O) to olefins (X=CH_2) using $Cp_2ZrCl_2/CH_2Br_2/Zn$.



All reactions were performed according to the standard conditions reported in the text. The yields in parentheses are VPC yields.



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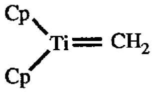
Cp_2ZrCl_2 in this reaction with Cp_2TiCl_2 lead to much lower yields of the olefinated product. For example, treatment of 4-*t*-butylcyclohexanone (**3**, X = O) with Cp_2TiCl_2, Zn, and CH_2Br_2 caused a rapid gas evolution from the reaction mixture and afforded only a 17% yield of the methylenated product **3** (X = CH_2) and 25% of the unreacted ketone remained. Treatment of Cp_2TiCl_2, and Zn with CH_2Br_2 in the absence of the ketone caused the same gas evolution. The gas was shown to be ethylene by passing it through a solution of bromine in chloroform and analyzing the 1,2-dibromoethane which was formed in 40% yield (relative to titanium) by capillary VPC analysis with *n*-nonane as an internal standard. The analogous experiment with Cp_2ZrCl_2, Zn, and CH_2Br_2 showed no formation of ethylene at room temperature and only a small amount of ethylene upon heating the reaction mixture. Similarly, the reaction of CH_2Br_2 and Zn in THF in the absence of titanium or zirconium did not form any ethylene even upon heating of the reaction mixture. It is unlikely that the Cp_2TiCl_2 yielded the titanocene methylidene complex **4** since it has been shown that the methylidene complex **4** would form predominantly ethane and the bridged dimer **5** in the absence of a supporting ligand such as trimethylphosphine. The bridged dimer **5** is stable at room temperature and would yield methane and only traces (<1%) of ethylene upon decomposition.[8]



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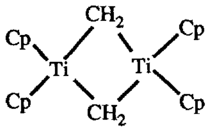

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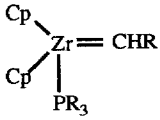
Presumably, under the reaction conditions, titanium(IV) is being reduced to lower valent titanium species which are causing the ethylene formation. Conversely, the reduction of zirconium(IV) to lower valent forms of zirconium is very unlikely under these reaction conditions.

*Zirconium carbene complexes (**6**) have been prepared by Schwartz,[2] in a three step* sequence. In the absence of a phosphine supporting ligand, complex **6** will dimerize to form complex **7**. Since the zirconium carbene complex **6**, once purified, can perform olefination reactions of ketones, esters and lactones while the zirconium species formed by the reaction conditions described herein do not olefinate esters and lactones nor do they dimerize to form unreactive bridged complexes **7**, the formation of a bimetallic zirconium species (**8**) is suggested under our conditions rather than the formation of a monometallic zirconium carbene such as **6**.



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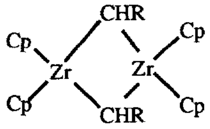

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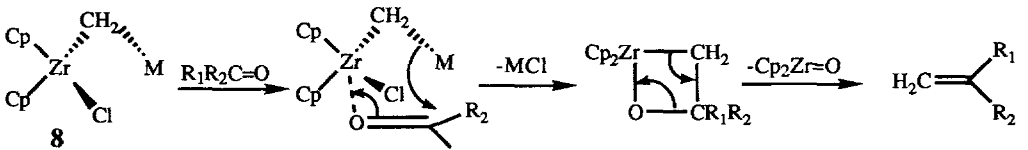
A possible mechanism for this zirconium-promoted methylenation is shown in eq 1. The bimetallic complex **8** which could be formed would have both a nucleophilic end and a Lewis acidic end. Attack on the carbonyl compound would afford the metallaoxacyclobutane which would rapidly yield zirconocene oxide and the methylenated product.



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(M= ZnCl or ZrCp$_2$Cl)

(1)

In summary, we have outlined a facile zirconium-promoted procedure for the rapid methylenation of aldehydes, ketones, and enones at room temperature. A bimetallic zirconium complex (**8**) is suggested as the active organometallic reagent.

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References and Notes

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5. For a W-based method, see: Aguero, A.; Kress, J.; Osborn, J. A. *J. Chem. Soc. Chem. Commun.* **1986**, 531.

6. Granular zinc metal (Aldrich, 30 mesh) was washed with 5% aqueous HCl, water, and ether. The activated metal was dried *in vacuo* and stored in a stoppered container.

7. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (br s, 1 H), 4.65 (br s, 1 H), 4.59 (br s, 1 H), 2.23 (m, 4 H), 2.06 (ddd, *J* = 14, 4, 2.5 Hz, 1 H), 1.98 (dt, *J* = 12.5, 5 Hz, 1 H), 1.8 (m, 2 H), 1.7 (m, 2 H), 1.6-1.0 (m with methyl s at δ 1.03, 22 H), 0.95-0.70 (m, 8 H), 0.66 (s, 3 H). ^{13}C NMR (20 MHz, $CDCl_3$) δ 149.16, 143.93, 122.59, 107.78, 56.25, 56.21, 54.22, 42.48, 39.97, 39.55, 37.46, 37.31, 36.20, 35.96, 35.81, 32.81, 32.49, 28.24, 28.02, 27.22, 24.29, 23.88, 22.83, 22.58, 21.49, 18.69, 18.44, 11.99. Calc'd for $C_{28}H_{46}$: 382.3599. Found: 382.3589.

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