Alkylation of Carbonyl Compounds with Dialkylzirconocene Complexes Promoted by Potassium *t*-Butoxide

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Abstract Potassium *t*-butoxide promotes alkylation of non-enolizable ketones and aldehydes by zirconocene dialkyls. The reaction proceeds with loss of cyclopentadienide ion from the metal center

Organozirconium complexes are finding increasing use in organic synthesis ¹ The majority of developments in this area involve bis(η^{5} -cyclopentadienyl)zirconium ("zirconocene") derivatives Whereas complexes of the type RZr(OR')₃ have long been known to react as nucleophiles toward carbonyl substrates,² zirconocene alkyls do not, transmetalation has been used previously to overcome this limitation ³ We report here that addition of 4-5 eq of KOt-Bu to a THF solution of Cp₂ZrR₂ (Cp = η^{5} -C₅H₅, R = CH₃, CH₂Ph) and

Entry	Substrate	R	Product(s) ^b	% Yıeld ^c
1	РһСНО	CH ₃	РһСН(СН3)ОН	78 (52) ^d
2	СНО	CH3	CH(CH ₃)OH	80 (40)
3	trans-PhCH=CHCHO	CH3	trans-PhCH=CH(CH3)OH	99 (46)
4	СНО	CH3	CH(CH ₃)OH	83 (69)
5	Ph ₂ C=O	CH ₃	Ph ₂ C(CH ₃)OH	100 (89)
6	PhCOCH ₃	CH ₃		0 ^e
7		CH ₃		0 ^e
8	РһСНО	CH ₂ Ph	PhCH(OH)CH ₂ Ph	31
			trans-PhCH=CHPh	50

Table 1 Alkylations with Cp2ZrR2/KOt-Bu/THF

a In a typical reaction appx 1 mmol Cp_2ZrR_2 is dissolved in 15 mL THF (distilled from sodium-benzophenone) in a Schlenk flask under nitrogen or argon atmosphere, then 2.2 mmol of the carbonyl compound (dried over 3A molecular sieves) is added and the solution is cooled to 0°C. With vigorous stirring, 4-5 mmol of a concentrated (appx 2M) solution of KOt-Bu/THF is added in one portion via syringe (yields are considerably lower if less KOt-Bu is used or if the reagent is added slowly). Alternatively, the base may be added before the substrate with comparable results. After stirring at 0°C for one hour the reaction is quenched with 5 mL of sat'd KF and worked up by standard techniques b. Products identified by GC and NMR comparison with authentic samples c. Yields by GC versus p-xylene or biphenyl internal standard, isolated yields in parentheses. Values based on transfer of both R groups from Zr. Solid products punfied by flash chromatography on silica gel and/or recrystallization liquid products were isolated by preparative GC d. A yield of 62% was obtained after 1 h at -50°C e. Starting material detected in nearly quantitative amount substrate leads to rapid transfer of both alkyl ligands to a variety of non-enolizable carbonyl compounds (eq 1 and Table 1) In the case of enolizable substrates (eg, entries 6 and 7, Table 1) rapid evolution of methane is

observed and the substrate is recovered after hydrolysis, suggesting metal enolate formation

$$R^{1} \xrightarrow{C} R^{2} \qquad \begin{array}{c} 1 \quad Cp_{2}ZrR^{3}_{2} \qquad OH \\ \hline 2 \quad 4-5 \text{ mol-equiv KOt-Bu/THF} \qquad R^{1} \xrightarrow{I} C-R^{2} \\ \hline 3 \quad aq \quad KF \end{array}$$
(1)

The requirement of a large amount of base in these reactions may be due to displacement of the cyclopentadienyl rings by t-butoxide We find that when $Cp_2Zr(CH_3)_2$ is treated with 3 mol-equiv KOt-Bu in THF solution for 12 h at room temperature and the mixture is cooled to -50°C, crystalline KCsH5 is isolated in 76% yield based on loss of both Cp rings from the metal This is one of relatively few examples of nucleophilic displacement of a coordinated Cp ligand as C₅H₅⁻⁴ The zirconium byproducts have not yet been identified Consistent with this observation, all of the reactions of aldehydes in Table 1 proceed with formation of deeply colored byproducts which have been identified as fulvenes for entries 1 and 2^{5} Apparently C₅H₅ competes with active Zr alkyl species for the carbonyl substrate The large amount of elimination product in entry 8 may result from direct elimination from an intermediate zirconium alkoxide 6

The alkylation reactions of eq 1 almost certainly involve alkyl transfer from a zirconium intermediate The selectivity for PhCHO versus Ph₂CO is 6 1 for Cp₂Zr(CH₃)₂ compared with 1 6 1 for CH₃Li⁷ Whether the active species are neutral alkoxyalkylzirconium complexes or zirconium "ate" complexes⁸ is presently being explored We are also attempting to find milder conditions with which to enhance the nucleophilicity of zirconocene alkyls without transmetallation and investigating these reactions with alkyl groups possessing β-hydrogens

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- 5 6-Phenylfulvene in entry 1 by GCMS and GC comparison with an authentic sample, 6-(2-furfuryl)fulvene in entry 2 by GCMS, both formed in appx 20% yield For a similar reaction involving a titanium alkoxide Reetz, M T, von Itzstein, M J Organomet Chem
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- In the competition experiments 2 mol-eq of each carbonyl compound were employed using the conditions of Table 1 The CH3Li competition was also run in THF at similar concentrations using 1 56 M CH3Li in 7 diethyl ether (Aldrich, 0 05 M halide) A Zr-free intermediate, such as CH₃K, would be expected to be
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