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A Convenient and Genuine Equivalent to $HZrCp_2Cl$ Generated in Situ from $ZrCp_2Cl_2$–DIBAL-H

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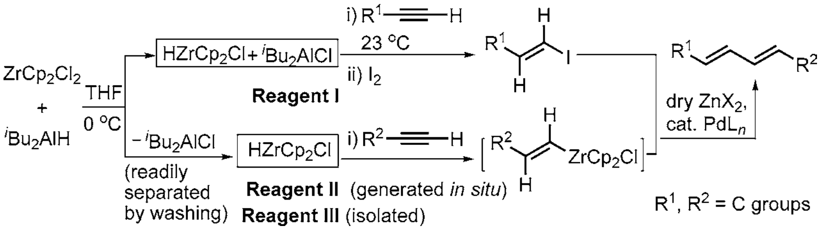
ABSTRACT



Slow addition of 1 equiv of $^iBu_2AlH$ to $ZrCp_2Cl_2$ in THF provides a convenient route to either $HZrCp_2Cl$-$^iBu_2AlCl$ (Reagent I) or $HZrCp_2Cl$ (Reagents II and III). The latter represents a highly convenient route to genuine $HZrCp_2Cl$, while Reagent I is useful for regio- and stereoselective conversion of 1- and 2-alkynes into (*E*)-1-iodo-1-alkenes and (*E*)-2-iodo-2-alkenes, respectively.

Despite the well-established significance of $HZrCp_2Cl$[1,2] in organic synthesis[3] including its hydrozirconation of alkenes[2a] and alkynes[1b,2b] as well as reduction of various other organic compounds,[3,4] its use has been plagued with difficulties in maintaining its purity over an extended period of time at the satisfactory level.[3d] This has made it desirable to develop procedures for its in situ generation and use. Thus, various methods have been devised, including treatment of considerably more stable and less expensive $ZrCp_2Cl_2$ with many different hydride sources, such as $LiAlH_4$,[5,6] $NaAlH_2(OCH_2CH_2OMe)_2$,[5] $LiBH(^sBu)_3$,[5,7] and ^tBuMgCl,[5,8] as well as modifications of some of these original procedures involving $LiAlH_4$[6] and ^tBuMgCl.[9] And yet, none of these in situ generation methods appears to be a true equivalent to isolated and pure $HZrCp_2Cl$. The use of basic metal hydrides, such as $LiAlH_4$ and $NaAlH_2(OCH_2CH_2OMe)_2$, is usually complicated by the production of undesirable byproducts that interfere with the desired reactions with $HZrCp_2Cl$ and/or cause technical difficulties, such as very sluggish and tedious filtration for their removal. The initially formed reagent generated by treating $ZrCp_2Cl_2$ with ^tBuMgCl is $^iBuZrCp_2Cl$, whose hydrogen-transfer hydrozirconation is much slower than that with $HZrCp_2Cl$.[5,8] Its acceleration through the use of various catalysts does speed up the desired hydrozirconation, but fails to match the results obtainable with pure $HZrCp_2Cl$.[9]

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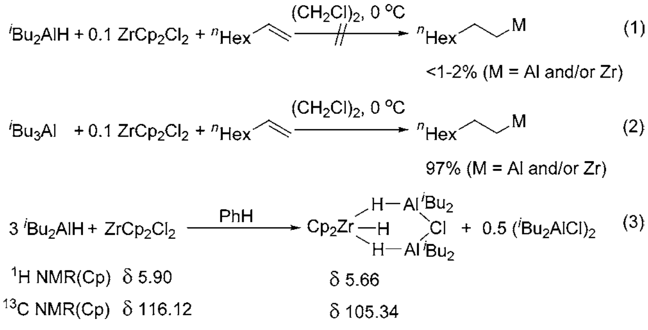
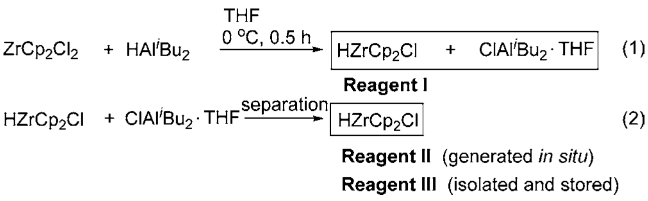
An obvious combination of $^{i}Bu_2AlH$ and $ZrCp_2Cl_2$ was briefly investigated by us in 1980 with the goal of catalyzing hydroalumination of alkenes with $ZrCp_2Cl_2$ (eq 1 in Scheme 1). This attempt failed, but the corresponding reaction of $^{i}Bu_3Al$ with alkenes in the presence of a catalytic amount of $ZrCp_2Cl_2$ led to a hydrogen-transfer hydroalumination of alkenes[10] (eq 2 in Scheme 1). A year earlier, Schwartz reported an intriguing but complex 1:3 reaction of $ZrCp_2Cl_2$ with $^{i}Bu_2AlH$ in benzene shown in eq 3 in Scheme 1.[11] We confirmed the reported results. Furthermore, we have found that the 1:3 stoichiometry is independent of the initial ratio of $ZrCp_2Cl_2$ and $^{i}Bu_2AlH$. Thus, the reaction fails to give $HZrCp_2Cl$.

Scheme 1



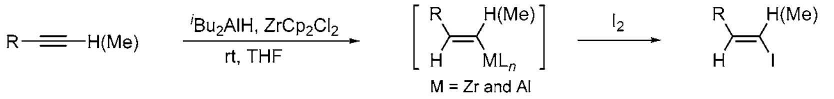
Despite the uninspiring results shown in Scheme 1, the reaction of $ZrCp_2Cl_2$ with $^{i}Bu_2AlH$ was reexamined in THF. Thus, $^{i}Bu_2AlH$ was slowly added to 1 molar equiv of $ZrCp_2Cl_2$ dissolved in THF at 0 °C, and the reaction was monitored by NMR spectroscopy. It induced precipitation of $HZrCp_2Cl$, which was accompanied by complete disappearance of the Cp signals for $ZrCp_2Cl_2$ [^{1}H NMR: δ 6.25 (s); ^{13}C NMR: δ 116.60 (s)]. These findings indicated clean formation of a 1:1 mixture of $HZrCp_2Cl$ and $^{i}Bu_2AlCl{\cdot}THF$ (Reagent I) according to eq 1 in Scheme 2. In marked contrast with other known procedures for the preparation of $HZrCp_2Cl$ by treating $ZrCp_2Cl_2$ with $LiAlH_4$, Red-Al, or other basic metal hydrides, the $^{i}Bu_2AlH{-}ZrCp_2Cl_2$ reaction was not seriously plagued with over-reduction of $ZrCp_2Cl_2$ to produce H_2ZrCp_2[12] or very sluggish and tedious filtration of the byproducts. The latter feature permits convenient and facile removal of $^{i}Bu_2AlCl{\cdot}THF$ by washing it through a sintered glass filter leading to in situ generation and direct use of $HZrCp_2Cl$ (Reagent II) without its transfer, reweighing, or, more dangerously, long-term storage. It goes without saying that this reaction also provides an unprecedentedly clean and convenient route to isolated and pure $HZrCp_2Cl$ (Reagent III) that can be stored and used (Scheme 2).

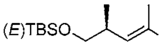
Scheme 2



As the results summarized in Table 1 indicate, Reagent I is a convenient reagent for hydrometalation of both terminal (entries 1−10) and internal (entries 11 and 12) alkynes as well as alkenes (entries 13 and 14). One unexpected but synthetically useful finding is that the hydrometalation−iodinolysis of 2-alkynes run at ≤25 °C (entries 11 and 12) is highly regioselective (≥98%) as long as 1.5 equiv of Reagent I is used.[13] This reagent is also convenient and satisfactory for a recently reported direct reduction of amides to aldehydes[4] at 23 °C (eq 3 in Scheme 3). Despite many favorable results shown in Table 1 and Scheme 3, Reagent I is clearly not a genuine equivalent to $HZrCp_2Cl$. In some cases, the presence of $^{i}Bu_2AlCl$ can be detrimental, as indicated by three mutually related cases of the hydrozirconation−Pd-catalyzed cross-coupling tandem reactions (eqs

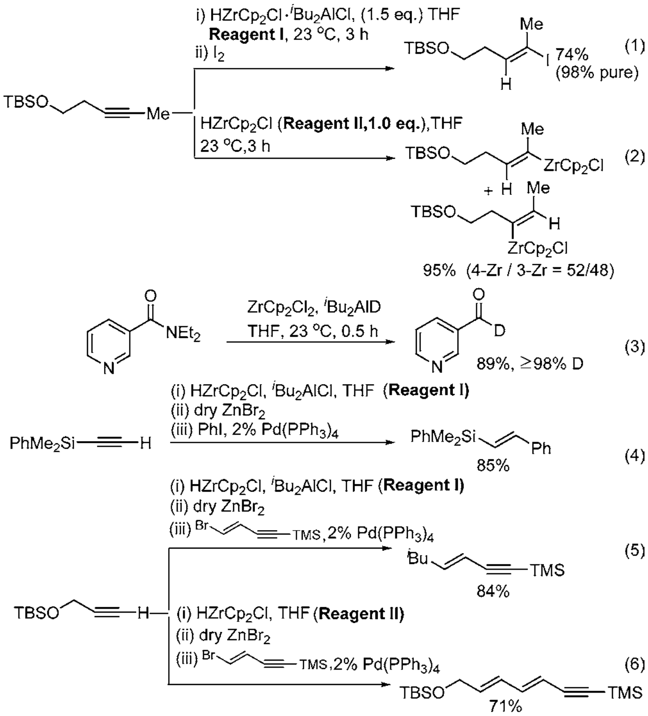
Table 1. Hydrometalation−Iodinolysis of Alkynes and Alkenes with $ZrCp_2Cl_2$−DIBAL-H in THF (Reagent I)



entry	R	H or Me	isolated yield of iodide[a] (%)	entry	R	H or Me	isolated yield of iodide[a] (%)
1	^{n}Hex	H	91[b]	8	(*E*)-$^{n}HexCH{=}CH$	H	95
2	$HOCH_2$	H	83	9	(*E*)-$TBSOCH_2CH{=}CH$	H	79
3	$HO(CH_2)_2$	H	85	10		H	87
4	$TBSOCH_2$	H	92	11	$TBSOCH_2$	Me	82
5	$TBSOCH(^{n}Pr)$	H	93	12	$TBSO(CH_2)_2$	Me	74
6	$TBSOCH_2CHMe$	H	90	13	$^{n}HexCH{=}CH_2$		87[c]
7	$PhMe_2Si$	H	81	14	$PhCH{=}CH_2$		89[c]

[a] All isolated products were isomerically ≥98% pure by ^{1}H and ^{13}C NMR spectroscopy. [b] The use of $^{i}Bu_2AlD$ gave the β-deuterio derivative in 90% yield with ≥98% D incorporation in the β position. [c] The alkene indicated was hydrometalated, and the corresponding iodoalkanes were the products obtained in the indicated yields.

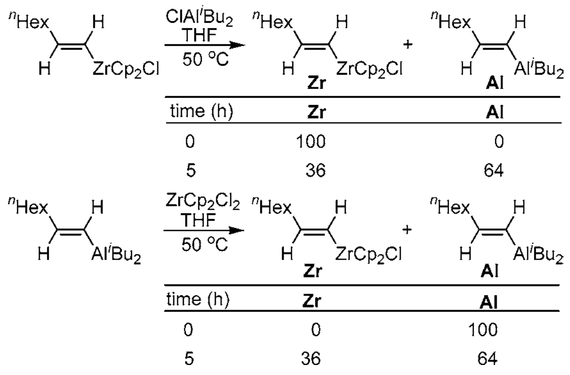
Scheme 3



4−6 in Scheme 3). In eq 4, Reagent I is highly satisfactory. In eq 5, however, an undesired participation by ^{i}Bu$_2$AlCl seriously diverts the course of the reaction. This side reaction is currently under investigation.

Another somewhat unexpected aspect of the hydrozirconation with Reagent I is that the desired hydrozirconation is accompanied by a slow reverse transmetalation in which the alkenyl group generated by hydrozirconation is transferred from Zr to Al to eventually give an equilibrium mixture. The reversible nature of the slow transmetalation can be readily observed, as exemplified in Scheme 4.

Scheme 4



time (h)	Zr	Al
0	100	0
5	36	64

time (h)	Zr	Al
0	0	100
5	36	64

As amply demonstrated in Scheme 5 summarizing the results of highly demanding cases of oligoenyne syntheses, Reagent II does appear to serve as a genuine and satisfactory equivalent to isolated and pure HZrCp$_2$Cl. Even so, fast addition or use of an excess ^{i}Bu$_2$AlH must be avoided so as not to generate H$_2$ZrCp$_2$.

The following experiments involving the use of Reagents I and II are representative.

(1*E*,3*S*)-4-(*tert*-Butyldimethylsiloxy)-1-iodo-3-methyl-1-butene (use of Reagent I): To ZrCp$_2$Cl$_2$ (321 mg, 1.1 mmol) in THF (2.5 mL) cooled to 0 °C was added slowly a solution of ^{i}Bu$_2$AlH (156 mg, 1.1 mmol) in THF (0.5 mL) under argon. The resultant suspension was stirred for 30 min at 0 °C, followed by addition of a solution of (3*S*)-4-(*tert*-butyldimethylsiloxy)-3-methyl-1-butyne (198 mg, 1.0 mmol) in THF (0.5 mL). The mixture was warmed to room temperature and stirred until a homogeneous solution resulted (ca. 1 h) and then cooled to −78 °C, followed by addition of I$_2$ (330 mg, 1.3 mmol) in THF (1.5 mL). After 30 min at −78 °C, GLC analysis indicated that the starting material had been completely consumed, and the desired product was formed in 94% yield by GLC. The reaction mixture was quenched with 1 N HCl, extracted with ether, washed successively with saturated Na$_2$S$_2$O$_3$, NaHCO$_3$, and brine, dried over MgSO$_4$, filtered, and concentrated. Flash chromatography (silica gel, hexanes) afforded 293 mg (90%) of the title compound.[14]

(3*E*,5*E*,7*E*)-1-(*tert*-Butyldimethylsilyl)-3,5,7-decatrien-1,9-diyne (5b) (use of Reagent II): To ZrCp$_2$Cl$_2$ (321 mg, 1.1 mmol) in THF (2.5 mL) in a two-necked flask was added dropwise a solution of ^{i}Bu$_2$AlH (156 mg, 1.1 mmol) in THF (0.5 mL) at 0 °C. The resultant suspension was stirred for 30 min at 0 °C. The supernatant liquid was filtered through a sintered glass filter attached to the flask under argon. The white solid (HZrCp$_2$Cl) remaining in the reactor was washed with THF (2.0 mL). To HZrCp$_2$Cl thus prepared was added a solution of **3b** (190 mg, 1.0 mmol) in THF (1.0 mL) at room temperature. After 1 h, a homogeneous solution thus obtained was cooled to 0 °C, and a solution of dry ZnBr$_2$ (261 mg, 1.0 mmol) in THF (1.0 mL) was added. After 30 min, (*E*)-BrCH═CHC≡CSiMe$_3$ (242 mg, 1.2 mmol) and Pd(PPh$_3$)$_4$ (23 mg, 0.02 mmol) in DMF (2.0 mL) were added, and the resultant mixture was stirred at room temperature and monitored by GLC analysis. The reaction was complete in 5 h, and the reaction mixture was quenched with aqueous NH$_4$Cl, extracted with ether, washed successively with saturated NaHCO$_3$ and brine, dried over MgSO$_4$, filtered, and concentrated to give the crude product as a viscous oil. To the crude product were added MeOH (4.0 mL) and K$_2$CO$_3$ (138 mg, 1.0 mmol). The resultant mixture was stirred at room temperature for 1 h, quenched with water, extracted with ether, dried over MgSO$_4$, filtered, and concentrated. Flash chromatography (silica gel,

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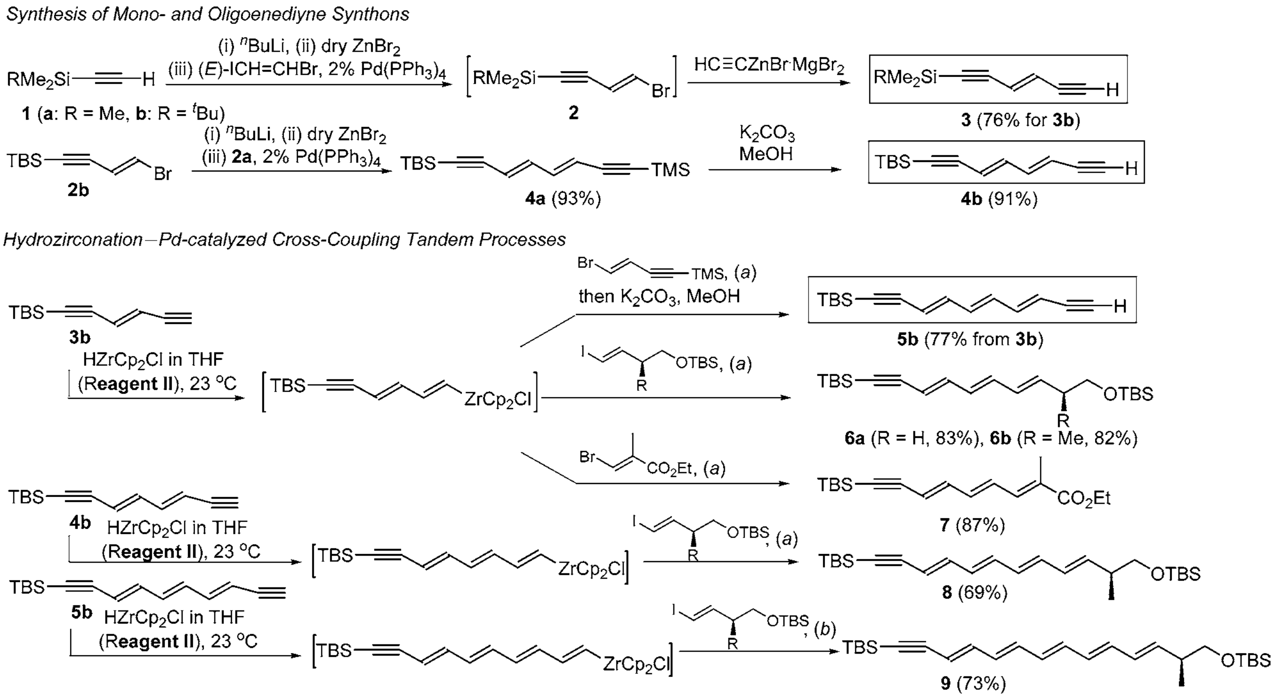
Scheme 5 [a]



[a] Reagents and conditions: (a) (i) dry $ZnBr_2$, (ii) 2% $Pd(PPh_3)_4$, THF–DMF. (b) Same as (a) except that 2 equiv each of **5b** and $HZrCp_2Cl$ were used and that the cross-coupling reaction was carried out at 50 °C.

hexanes) afforded the title compound (**5b**) (186 mg, 77% over 2 steps).

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Supporting Information Available: Experimental procedures and ^1H and ^{13}C NMR spectroscopic data for 9 terminally silylated oligoenynes including **4b**, **5b**, **8**, and **9**, iodoalkenes, and 3-pyridinecarboxaldehyde-α-d_1. This material is available free of charge via the Internet at http://pubs.acs.org.

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