ONE-POT CONVERSION OF ALKYNES AND ALKENES INTO ONE-CARBON HOMOLOGATED ALDEHYDES VIA HYDROZIRCONATION-ISOCYANIDE INSERTION-HYDROLYSIS¹

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SUMMARY: The reaction of monoorganozirconocene chlorides and diorganozirconocenes with relatively unhindered isocyanides, such as n-BuNC, followed by hydrolysis with 50% HOAc or dilute HCl can produce the corresponding aldehydes in good yields.

Conversion of alkenes into one-carbon homologated aldehydes via transition metalcatalyzed hydroformylation,² hydroboration-carbonylation,³ and hydrozirconationcarbonylation⁴ is a well established methodology. On the other hand, no well-developed method appears to exist for direct, one pot conversion of alkynes into the corresponding α , β -unsaturated aldehyde.⁵ Transition metal-catalyzed hydroformylation of alkynes mainly produces saturated aldehydes,² and hydroboration-carbonylation of alkynes has not been developed into a method for aldehyde synthesis.⁶ Although the reaction of alkenylzirconocene chlorides with CO has been reported,⁴ the synthesis of α , β -unsaturated aldehydes by this reaction does not appear to have been described. Finally, no reaction was observed between (E)-1-octenyldiisobutylalane and CO at 80°C and 1200 psi, as judged by ¹H NMR and GLC analysis after hydrolysis.

We now report that treatment of either monoorganozirconcene chlorides, obtained by hydrozirconation of alkynes or alkenes, or diorganozirconcenes, prepared by the reaction of Cl_2ZrCp_2 with organolithiums, with sterically unhindered isocyanides, such as <u>n</u>-BuNC, at room temperature followed by hydrolysis with 50% acetic acid or 3-6N HCl can produce the corresponding one-carbon homologated aldehydes in good yields (eqs 1 and 2). The experimental results are summarized in Table 1.

$$c_{P_2}Zr < \begin{pmatrix} R^1 \\ \chi \end{pmatrix} \xrightarrow{RNC} c_{P_2}Zr < \begin{pmatrix} R^1 \\ \chi \end{pmatrix} \xrightarrow{R^1} R^1CHO$$
 (1)



The reaction of organozirconocenes with isocyanides is known to give isocyanideinsertion products,⁷ and treatment of isocyanide-insertion products obtained from <u>t</u>-BuNC with iodine is known to provide one-carbon homologated cyanides.⁸ However, their successful conversion into aldehydes does not appear to have been reported.

The following observation are noteworthy. First, it is important to use sterically unhindered isocyanides, such as n-BuNC, for obtaining aldehydes in high yields. For example, the reaction of (E)-1-octenylzirconocene chloride with n-BuNC produced 1 in \geq 95% yield by ¹H NMR (Cp signal at 5.77 ppm) and its treatment with 50% HOAc provided (E)-2-nonenal in 93% yield by GLC. The corresponding reaction of t-BuNC also gave 2 in \geq 95% yield by ¹H NMR (Cp signal at 5.71 ppm). However, all attempts to hydrolyze 2 with HOAc, HCl, or CF₃COOH led to no reaction, with the chemical shift and integration of the Cp signal remaining essentially unchanged. Cyclohexyl and 2,6-xylyl isocyanides may be used in place of n-BuNC, but the product yields are lower.



Secondly, α , β -unsaturated aldehydes obtained by this method are >98% E. Thirdly, even in cases where diorganozirconocenes are used, clean and nearly quantitative single migratory insertion products can be obtained at room temperature. This appears to be in contrast with the corresponding carbonylation reaction, which has a tendency to produce competitively double migratory insertion products.⁹ The reaction of 3^{10} and with <u>n</u>-BuNC followed by treatment with iodine (1.2 equiv, 1 h, -78° C) and hydrolysis with 3N HCl provided 4^{11} in 60% yield (eq 3). These results indicate that, migratory insertion of <u>n</u>-BuNC involves, at least in this case, predominant participation of the alkyl-Zr bond and that iodinolysis of the isocyanide-insertion product occurs predominantly at the alkenyl-Zr bond. On the other hand, carbonylation of 3 at 1.1 atm and 25°C gives, after hydrolysis, 5^{12} in 68% yield, with no sign of the formation of a single migration product, e.g., **6**. Fourthly, our attempts to convert R₂ZrCp₂, where R was 1-octynyl, benzyl, or allyl, into the corresponding aldehyde did not lead to clean formation of the desired compound.



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The following procedure for converting 1-octyne into (<u>E</u>)-2-nonenal is representative. To a suspension of Cp₂Zr(H)Cl¹³ (1.52 g, 4.0 mmol) in 15 mL of THF was added 1-octene (0.44 g, 4.0 mmol) at 25°C. After stirring the mixture for 1 h, examination by ¹H NMR indicated the formation of (<u>E</u>)-1-octenylzirconocene chloride in >95% yield as judged by the integration of the Cp signal at 6.16 relative to benzene added as an internal standard. To this solution was added at 0°C <u>n</u>-BuNC (0.33 g, 4.0 mmol). The mixture was heated at 45°C for 3 h. Clean and essentially quantitative formation of **1** was indicated by analysis of the ¹H NMR Cp signal at 5.77. The mixture was cooled to -78°C, and 50% HOAc kept at -20°C was added. After warming to room temperature, the mixture was extracted with ether, washed (NaHCO₃ and brine), dried (MgSO₄), concentrated, and distilled to give 0.42 g (75%) of (<u>E</u>)-2-nonenal.¹⁴ IR (neat) 1660 (s), 1630 (m) cm⁻¹; ¹H NMR (CDCl₃, Me₄Si) & 0.88 (t, <u>J</u> = 6 Hz, 3 H), 1.1-1.7 (m, 8 H), 2.1-2.5 (m, 2 H), 6.11 (dd, <u>J</u> = 15 and 8 Hz, 1 H), 6.83 (dt, <u>J</u> = 15 and 7 Hz, 1 H), 9.48 (d, <u>J</u> = 8 Hz, 1 H); ¹³C NMR (CDCl₃, Me₄Si) & 13.92, 22.44, 27.74, 28.72, 31.46, 32.64, 132.90, 158.88, 193.99.

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Starting	Zirconium	Type of	R of	Hydrolysis	Yield ^a of
material	reagent	intermediate	RNC	reagent	R ¹ CHO (%)
<u>n</u> -C ₆ H ₁₃ C≡CH	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	n-Bu	50% НОАС	93 (75)
<u>п</u> -С ₆ Н ₁₃ С≡СН	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	2,6-Me ₂ C ₆ H ₄	50% HOAC	<5
n-C ₆ H ₁₃ C≡CH	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	2,6-Me ₂ C ₆ H ₄	6N HCl	69 (51)
<u>с</u> -С ₅ Н9С≡СН	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	n-Bu	50% HOAC	63 (54)
PhC≡CH	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	2,6-Me ₂ C ₆ H ₄	6N HC1	- (60)
t-BuC≡CH	Cp ₂ Zr(H)Cl	R ¹ ZrCp2C1	n-Bu	50% HOAC	76 (54)
n–BuC≡CBu–n_	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	n-Bu	50% HOAC	90 (72)
<u>п</u> -С ₆ Н ₁₃ СН=СН ₂	Cp ₂ Zr(H)Cl	R ¹ ZrCp ₂ C1	n–Bu	50% HOAC	88
n-OctLi	Cp ₂ ZrCl	R ¹ ₂ ZrCp ₂	n-Bu	50% HOAC	88 <mark>b</mark>
PhLi	Cp ₂ ZrCl ₂	$R_2^{\tilde{1}}ZrCp_2$	n-Bu	50% HOAC	77 <u>b</u>

Table 1. Synthesis of Aldehydes from monorganozirconocene Chlorides andDiorganozirconocenes via Isocyanide Insertion-Hydrolysis

 $\frac{a}{b}$ By GLC. The numbers in parentheses are isolated yields. $\frac{b}{b}$ Based on one of the two R¹ groups.

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- (11) 4: IR (neat) 1723 (s), 1610 (m), 1252 (s), 845 (s) cm⁻¹; ¹H NMR (CDCl₃, Me₄Si) &0.20s, 9 H), 2.58 (dd, <u>J</u> = 9 and 6 Hz, 1 H), 2.75 (d, <u>J</u> = 9 Hz, 1 H), 2.8–3.0 (m, 4 H), 3.2–3.3 (m, 1 H), 3.62 (s, 2 H), 72.–7.4 (m, 5 H), 9.75 (t, <u>J</u> = 2 Hz, 1 H); ¹³C NMR (CDCl₃) &0.49, 46.29, 48.14, 57.62, 59.58, 60.11, 101.92, 127.17, 128.34, 128.55, 138.04, 160.30, 200.71.
- (12) 5: IR (neat) 1697 (s, 1617 (s), 1248 (s), 840 (s) cm⁻¹; ¹H NMR (CDCl₃, CH₂Cl₂) δ 0.15 (s, 9 H), 1.9-2.2 (m, 2 H), 2.54 (dd, <u>J</u> = 6 and 18 Hz, 1 H), 2.85-3.2 (m, 3 H), 3.5-4.0 (m, 3 H), 7.0-7.3 (m, 5 H); ¹³C NMR (CDCl₃) δ -1.47, 41.21, 47.37, 54.67, 57.90, 60.07, 127.22, 128.43, 128.58, 135.31, 138.38, 193.55, 213.12.
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