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REACTION OF 3-ZIRCONA-1-CYCLOPENTENES AND ZIRCONACYCLOPENTANES
WITH ALDEHYDES. A SELECTIVE AND CONVENIENT SYNTHESIS OF
4-PENTEN-1-OLS, (Z)-5-IODO-4-PENTEN-1-OLS, AND RELATED ALKANOLS

Christophe Copéret and Ei-ichi Negishi*

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, U.S.A.

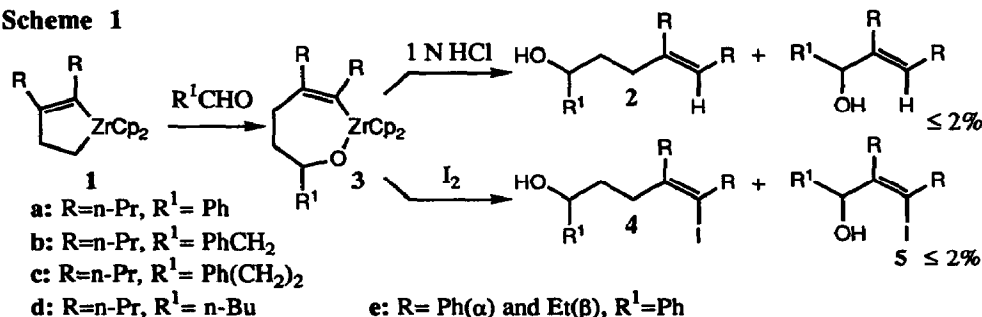
Zhenfeng Xi and Tamotsu Takahashi*

Coordination Chemistry Laboratories, Institute for Molecular Science, Myodaiji, Okazaki 444, Japan

SUMMARY: 3-Zircona-1-cyclopentenes and zirconacyclopentanes react with aldehydes at or below 25 °C to give the corresponding carbonyl addition products, i.e., 7-membered oxazirconacycles, which can be readily converted to the corresponding alcohols via protonolysis and 5-iodoalcohols via iodinolysis; the latter product can be further converted to 7-membered lactones via Pd-catalyzed carbonylation.

We recently reported that 3-zircona-1-cyclopentenes (**1**) react with alkynes, nitriles, and aldehydes to undergo coupling of these added reagents with the alkenylidene moiety of **1** with concomitant extrusion of ethylene.¹ In each of the reactions of aldehydes, however, a minor amount of another product was obtained at 50 °C. To our surprise, this became the major product, when the reaction was run at lower temperatures (≤ 25 °C). In the reaction of **1a** with PhCHO, the product obtained in 80% yield after protonolysis was identified as (*E*)-1-phenyl-4-(*n*-propyl)-4-octen-1-ol (**2a**),² and the spectral data for the Cp₂Zr-containing product were consistent with **3a**.³ Treatment of the reaction mixture containing **3a** with I₂ gave a 75% yield of **4a**, which was isomerically $\geq 98\%$ pure. The amount of **5a**, the major product at 50 °C, was $\leq 2\%$. The experimental results are summarized in Scheme 1 and Table I.

Scheme 1



The feasibility of converting bicyclic zirconacyclopentene derivatives into alkenols was also demonstrated by the reaction of **6**⁴ with benzaldehyde to give **7** in 80% NMR yield. Protonolysis of this reaction mixture containing **7** with 1 N HCl gave a 65% yield of **8** as an 85:15 mixture of the two possible epimers. Two minor byproducts, i.e., **9** and **10**, were also present to the extent of 3-5% each. Similarly, iodinolysis of **7** provided **11** in 65% yield as an 85:15 epimeric

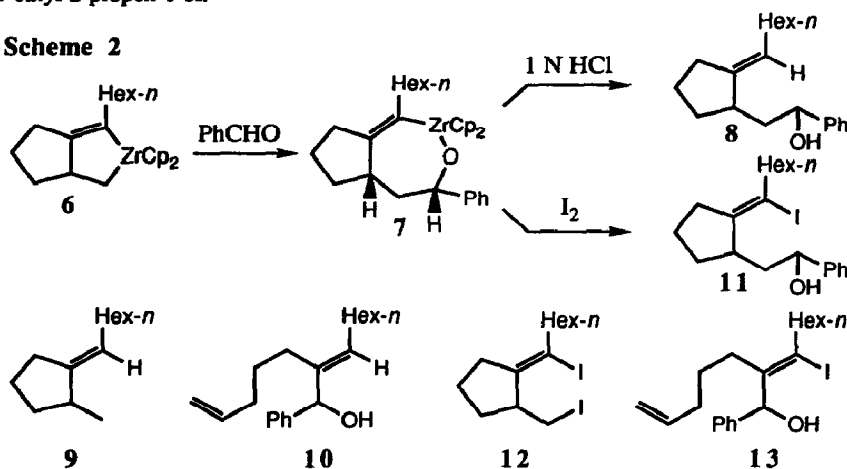
mixture along with a couple of unidentified minor byproducts, presumably 12 and 13.

Table I. Reaction of 3-Zircona-1-cyclopentenes with Aldehydes

Zirconacyclopentene(1)		R ¹ of	Electrophilic	Product	Yield ^{a,b} %	Byproduct (Yield, ^b %)
R(α)	R(β)	R ¹ CHO	reagent			
<i>n</i> -Pr	<i>n</i> -Pr	Ph	HCl	2a	69(80)	^c (≤ 2%)
<i>n</i> -Pr	<i>n</i> -Pr	Ph	DCl	^d	61(75)	^e (≤ 2%)
<i>n</i> -Pr	<i>n</i> -Pr	Ph	I ₂	4a	59(74)	5a(≤ 2%)
<i>n</i> -Pr	<i>n</i> -Pr	PhCH ₂	I ₂	4b	14(30)	5b(≤ 2%)
<i>n</i> -Pr	<i>n</i> -Pr	Ph(CH ₂) ₂	I ₂	4c	45(62)	5c(≤ 2%)
<i>n</i> -Pr	<i>n</i> -Pr	<i>n</i> -Bu	HCl	4d	42(51)	5d(≤ 2%)
Ph	Et	Ph	HCl	2e	42(61)	^f (≤ 2%)
Ph	Et	Ph	I ₂	4e	48(51)	5e(≤ 2%)

^a Isolated yield. ^b The number in parentheses is an NMR yield. ^c 1-Phenyl-2-(*n*-propyl)-2-hexen-1-ol. ^d 5-D derivative of 2a. ^e 1-Phenyl-2-(*n*-propyl)-3-deuterio-2-hexen-1-ol. ^f (*E*)-1,3-Diphenyl-1-ethyl-2-propen-1-ol.

Scheme 2



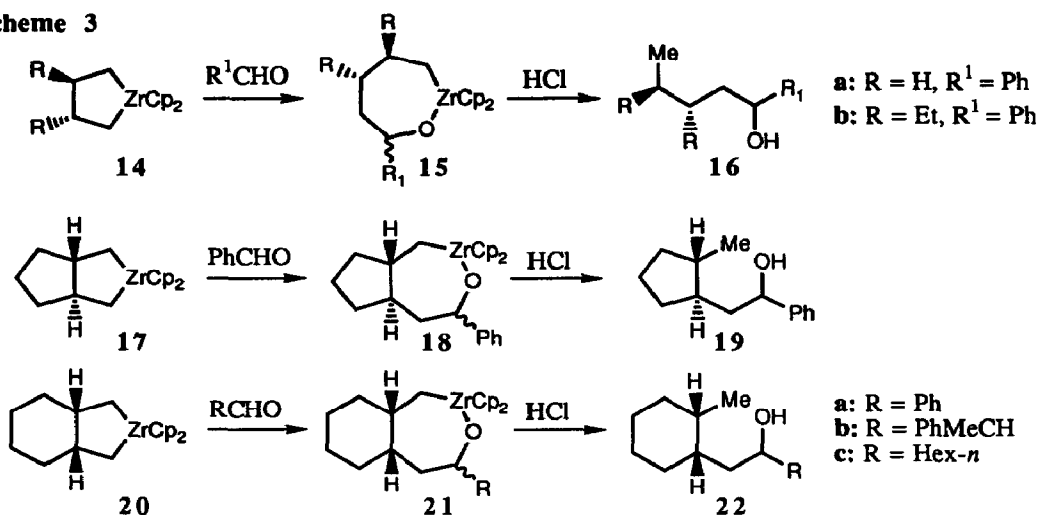
Interestingly, even monocyclic and bicyclic zirconacyclopentanes undergo the same addition reaction with aldehydes. These results are summarized in Table II and Scheme 3.

Table II. Reaction of Zirconacyclopentanes with Aldehydes Followed by Protonolysis

Zirconacyclopentane	R ¹ of R ¹ CHO	Product	Yield ^a %	Other notes
14a	Ph	16a	46	-
14b	Ph	16b	52	^b
17 ^c	Ph	19	37	^d
20 ^e	Ph	22a	69	^f
20	PhMeCH	22b	58	^g
20	<i>n</i> -Hex	22c	72	^h

^a Isolated yield. In cases when the product is a mixture of diastereomers, the combined yield is shown. ^b A 5:1 diastereomeric mixture. ^c ≥95% trans. ^d A 3:2 mixture of 2 diastereomers. ^e ≥95% cis. ^f A 1:1 diastereomeric mixture. ^g A 4:2:1:1 mixture of 4 diastereomers. ^h A 3:2 mixture of 2 diastereomers.

Scheme 3

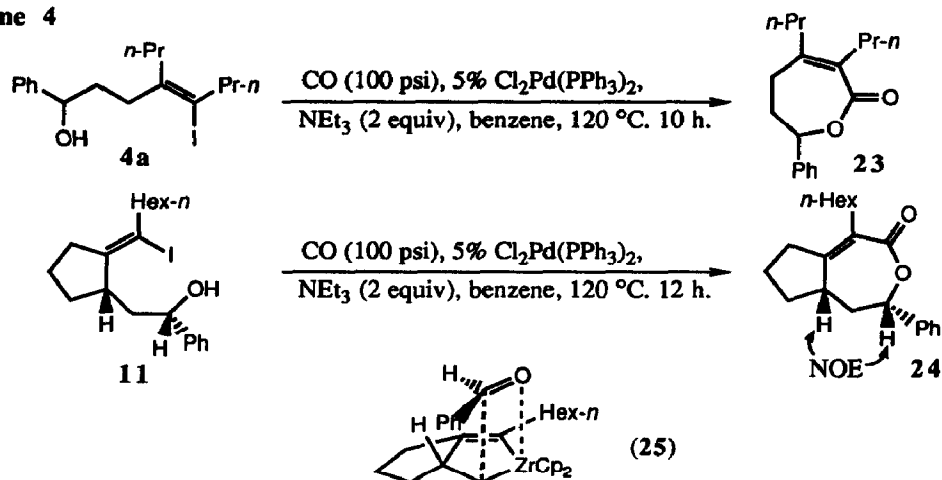


Although allylzirconocenes⁵ and related conjugated diene-zirconocenes⁶ are known to react readily not only with aldehydes but also with ketones, nitriles, alkenes, and alkynes, the corresponding reactions of alkyl- and alkenylzirconocene derivatives appear to be unprecedented.² Indeed, our repeated attempts to observe the reaction of Me₂ZrCp₂ with PhCHO or heptaldehyde have been uniformly unsuccessful. Thus, the reaction herein reported is totally unexpected, and it remains as an interesting puzzle. It is conceivable that interaction between a Zr empty orbital and the C_β-C_{β'} bond boosts the nucleophilicity of the Zr-C bonds of five-membered zirconacycles relative to Me₂ZrCp₂ and other diorganylzirconocenes that are without the benefit of such interactions. Irrespective of mechanistic details, however, the reaction promises to provide an efficient and convenient route to alkenols, some of which are not readily accessible via known methods.

The following additional features of the reaction are worth noting. First, attempts to observe related addition reactions of zirconacyclopentenes and zirconacyclopentanes with nitriles, alkenes, and alkynes have so far failed. Second, the reaction does not proceed beyond single addition to aldehydes even when an excess of an aldehyde is used. Third, treatment of (*Z*)-5-iodo-4-alken-1-ols with CO in the presence of a catalytic amount of a Pd-phosphine complex, e.g., Cl₂Pd(PPh₃)₂, gives the corresponding lactones⁷ (Scheme 4). Fourth, the lactonization, in turn, provides a convenient means of determining the 1,3-diastereochemistry of the aldehyde addition reaction. Specifically, 11 or its epimer was converted to 24 or its epimer, respectively, via carbonylation (Scheme 4). An NOE signal enhancement (8 ± 1%) observed between the bridgehead and benzylic protons of the major isomer indicates that these two protons are *cis* to each other. This stereochemical preference is consistent with attack by PhCHO on the *exo* side of 6 with the Ph group pointing outside the bicyclic framework, as shown in 25.

A typical procedure is as follows. A solution of Cp₂ZrCl₂ (0.88 g, 3.00 mmol) in THF (12 mL) was successively treated with EtMgBr (6.0 mL, 1 M, -78 °C, 1 h) in THF, 4-octyne (0.33 g, 0.44 mL, 3.00 mmol, -78 °C, 5 min and then 0 °C, 1 h), and benzaldehyde (0.35 g, 0.33 mL, 3.30 mmol, 0 °C, 3 h). Iodinolysis or hydrolysis of the reaction mixture followed by usual workup afforded 2a or 4a in 75 or 80% NMR yield, respectively.

Scheme 4



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- (2) During this study, we noted the reactions of 7,7-bis(cyclopentadienyl)-7-zirconabicyclo[4.3.0]non-1(6)-ene with isovaleraldehyde, acetone, and butyronitrile to give the corresponding 7-membered ring products presented as unpublished results (Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047). However, the zirconacyclopentene intermediate involved in the reported work behaves differently with nitriles, presumably due to the more difficult ethylene elimination, which would generate the more strained zirconocene-cyclohexyne complex.
- (3) ^1H NMR (C_6D_6 , Me_4Si) δ 0.99 (t, $J = 7$ Hz, 3 H), 1.02 (t, $J = 7$ Hz, 3 H), 1.2-2.4 (m, 12 H), 5.07 (t, $J = 5.5$ Hz, 1 H), 6.08 (s, 5 H), 6.14 (s, 5 H), 7.1-7.4 (m, 5 H). The following ^{13}C NMR signals were assignable to the compound: ^{13}C NMR (C_6D_6 , Me_4Si) δ 14.70, 15.47, 22.69, 24.81, 39.02, 39.65, 40.33, 81.95, 110.68, 111.33, 128.54, 128.69.
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