

Highly Chemoselective Reactions of Zirconacyclopentenes for Selective Functionalization

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Alcoholysis of zirconacyclopentenes proceeds at the alkyl carbon on Zr with high chemoselectivity in sharp contrast to monoiodination of zirconacyclopentenes with iodine; alcoholysis followed by iodination of zirconacyclopentenes produces stereodefined trisubstituted alkenyl iodides in high yields with high isomeric purities.

Cross coupling of alkynes with alkenes on zirconium complexes results in the formation of zirconacyclopentenes which contain two different zirconium–carbon bonds.¹ In order to transform the zirconacyclopentenes into useful organic compounds, for example, stereodefined trisubstituted alkenyl iodide, the chemoselective reactions of these two different zirconium–carbon bonds are important.

Herein we describe that alcoholysis of zirconacyclopentenes proceeded with high chemoselectivity at the alkyl carbon on zirconium which was in sharp contrast to the monoiodination of zirconacyclopentenes which was dependent on their substituents. We also demonstrate that alcoholysis of zirconacyclopentenes

followed by iodination gave stereodefined trisubstituted alkenyl iodides in high yields with high selectivities.

During our studies on the reactions of zirconacyclopentenes we found that monoiodination of zirconacyclopentene **1a** with iodine (method A) proceeded at the alkenyl carbon on Zr to afford stereodefined trisubstituted alkenyl iodide **2a** in 77% yield after hydrolysis. The regioisomer of monoiodination product **3a** was formed in 6% yield and the diiodination product **4a** in 4%. However, method A has a critical limitation

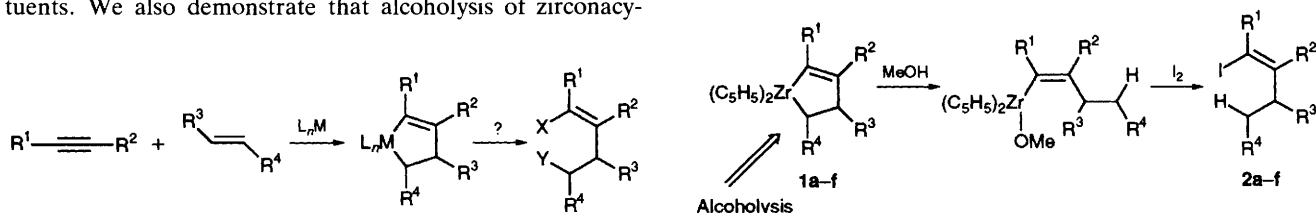


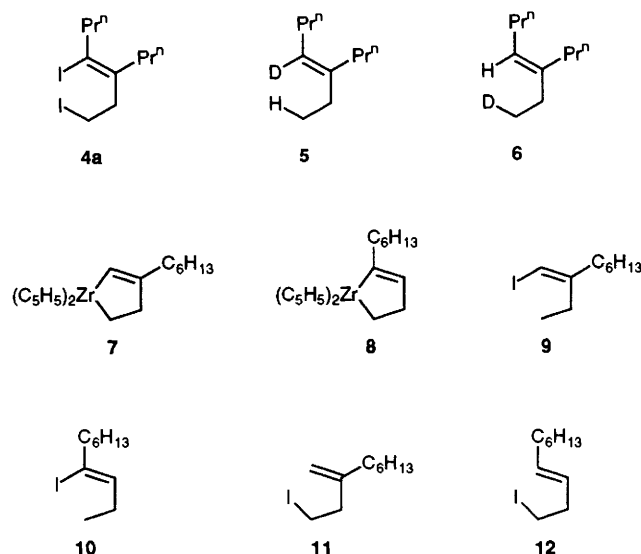
Table 1 Chemoselective reactions of zirconacyclopentenes

Zirconacyclopentenes	Reagents ^a	Product ^b	Yield (%) ^c
 1a	I ₂ /H ⁺ MeOH/I ₂	2a 3a	93 7 83 (83) >99 < 1 96 (85)
 1b	I ₂ /H ⁺ MeOH/I ₂	2b 3b	< 1 >99 80 (80) >99 < 1 97 (78)
 1c	I ₂ /H ⁺ MeOH/I ₂	2c 3c	>99 < 1 99 (78) >99 < 1 99 (81)
 1d	I ₂ /H ⁺ MeOH/I ₂	2d 3d	5 95 82 (82) >99 < 1 99 (80)
 1e	I ₂ /H ⁺ MeOH/I ₂	2e 3e	>99 < 1 93 (82) >99 < 1 95 (76)
 1f	I ₂ /H ⁺ MeOH/I ₂	2f 3f	>99 < 1 18 (14) >99 < 1 95 (75)

^a I₂/H⁺ (method A): Zirconacyclopentene was treated with 1.2 equiv. of I₂ at 0 °C for 1 h and then with dil. HCl (aq.). MeOH/I₂ (method B): Zirconacyclopentene was treated with 1.5 equiv. of MeOH at room temp. for 1 h and then with 1.2 equiv. of I₂. ^b NMR spectra and high resolution MS of the products were consistent with the formulae. ^c Combined yields of monoiodination products. Yields were determined by GC. Isolated yields are given in parentheses.

for its generality. For example, as shown in Table 1, some zirconacyclopentenes such as **1b** and **1d** reacted with iodine at the alkyl carbon on Zr to give homoallylic iodides, **3b** and **3d**, respectively. Furthermore, in the case of **1f**, monoiodination with iodine was not a clean reaction. Negishi *et al.*^{1d} and Mori *et al.*^{1f} reported that the alkyl carbon of the zirconacyclopentene moiety in a bi- or a tri-cyclic compound was attacked by the first reagent. However, selectivity of monoiodination of zirconacyclopentenes with iodine (method A) was strongly dependent on the substituents. This situation prompted us to develop chemoselective reactions of zirconacyclopentenes for selective functionalization. We found that alcoholysis followed by iodination (method B) led to chemoselective monoiodination of zirconacyclopentenes.

Alcoholysis of **1a** with methanol occurred chemoselectively only at the alkyl carbon on Zr and even in the presence of 2 equiv. of methanol only monoprotonation proceeded under



the conditions used. The following deuteration clearly revealed the selective alcoholysis with methanol. When **1a** was treated with an excess of methanol and then quenched with DCl, Z-4-deutero-5-ethyloct-4-ene **5** was obtained. However, treatment of **1a** with an excess of MeOD followed by quenching with HCl gave Z-4-(2-deuteroethyl)oct-4-ene **6**.

Subsequent iodination after alcoholysis of **1a** (method B) gave stereodefined trisubstituted alkenyl iodide **2a** in 96% yield with high isomeric purity (>99%). Formation of monoiodination isomer **3a** and diiodide **4a** was not detected. Stereoselectivities of the alkenyl moiety were also high due to >99% *syn* addition. The alcoholysis of zirconacyclopentenes was highly chemoselective and was not dependent on substituents. The chemoselectivity of alcoholysis is probably due to the stronger basicity of the alkyl carbon attached to Zr than alkenyl carbon. Alcoholysis of zirconacyclopentenes, **1b** and **1d**, similarly occurred only at the alkyl carbon and monoiodides **2b** and **2d** were obtained, respectively, after treatment with iodine (method B) in high yields with high selectivities. Regioselectivity for Ph and Me groups of **1d** was retained. In the case of zirconacyclopentenes **1e** and **1f** with a substituent such as trimethylsilyl at the alkyl carbon attached to zirconium, alcoholysis proceeded very selectively. For terminal alkynes such as oct-1-yne, it is known that zirconacyclopentene was formed as a mixture of two regioisomers **7** and **8**.^{1f} However, alcoholysis followed by iodination gave chemoselective products **9** and **10**, respectively, with high chemoselectivities; iodides **11** or **12** were not detected.

The high chemoselectivity of alcoholysis and also the high selective monoprotonation should be emphasized. Method B could avoid the formation of diiodide compounds, this selectivity was due to its selective monoprotonation. Monoprotonation products of **1** with methanol were inert toward an excess of methanol under conditions used here.^{2,3} This inertness allowed the treatment of zirconacyclopentenes with an excess of methanol to complete the monoprotonation. Therefore the formation of diiodide **4** was not detected using method B.

For preparing regio- and stereo-selective trisubstituted alkenyl iodide, carbometallations of alkynes using copper reagents or aluminium reagents/Zr catalyst have already been reported.^{4,5} However, internal alkynes are usually unreactive toward carbocupration,⁴ and the R groups of aluminium are very limited for selective carboalumination.⁵ Although selective preparative methods for various zirconacyclopentenes to provide a synthetically useful method have yet to be developed, the method shown here can provide some trisubstituted

alkenyl iodides, such as **2f**, in high stereoselectivity (>99% *syn* addition in all cases) which are not produced by the method already reported.^{3,4}

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