Chemoselective functionalization of zirconacyclopentenes

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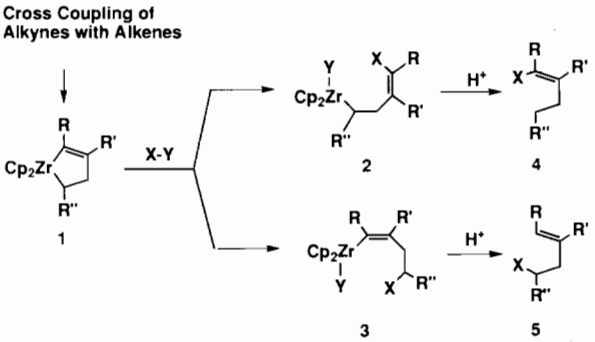
Abstract

Zirconacyclopentenes, which were readily prepared by the reaction of Cp_2ZrEt_2 with alkynes or by the reaction of vinylsilane with alkynes in the presence of Cp_2ZrBu_2 (Negishi reagent), reacted with iodine to give either stereodefined alkenyl iodides or homoallylic iodides selectively after hydrolysis. The chemoselectivity of this reaction was strongly dependent on the substituent R group of the C2 carbon attached to zirconium. When R was a phenyl group, homoallylic iodides were selectively formed. On the other hand, alkyl substituted zirconacyclopentenes reacted with iodine to afford alkenyl iodides selectively. A small amount of diiodides were produced as by-products. Reactions of zirconacyclopentenes with an excess of MeOH and iodine in this order gave only alkenyl iodides with excellent selectivities. The formation of diiodides was not detected. This monohalogenation procedure using an excess of $MeOH/I_2$ was not substituent dependent in the system used here. Treatment of alkylsubstituted zirconacyclopentenes with CBr_4 or CCl_3Br yielded only homoallylic bromides, after hydrolysis, with >99% chemoselectivity. It is in sharp contrast to the reaction with usual bromination reagents such as Br_2 and NBS which led to the selective formation of alkenyl bromides. A sequential treatment of zirconacyclopentenes with CBr_4 and I_2 in this order, afforded a mixed dihalogenation product selectively. Reaction with Me_3SnCl was not substituent dependent. The sp^3 carbon attached to Zr selectively reacted with Me_3SnCl to give homoallyltin compounds. Insertion reaction of isonitrile in the Zr–carbon bond of zirconacyclopentenes were chemoselective but neither substituent dependent nor reagent dependent in the system used here.

Key words: Chemoselective reaction; Substituent dependent; Substituent independent; Reagent dependent; Zirconium complexes; Zirconacyclopentene complexes

Introduction

Chemoselective functionalization of organometallic compounds is very attractive for organic synthesis. Zirconacyclopentene compounds have been readily prepared by intermolecular cross-coupling of alkynes with alkenes [1, 2] or intramolecular cyclization of enynes [3]. Zirconacyclopentene compounds have two different zirconium–carbon bonds. One is a zirconium–sp^3 carbon bond and the other is a zirconium–sp^2 carbon bond. These two zirconium–carbon bonds can be expected to have different reactivities (Scheme 1). Negishi *et al.* [4], Mori *et al.* [3g] and Buchwald and Nielsen [5] reported several reactions of zirconacyclopentenes in bicyclic or tricyclic systems with various reagents [3g]. The Zr–sp^3 carbon bond seemed to be more reactive than the Zr–sp^2 carbon bond towards those reagents. Interestingly, Negishi *et al.* reported that n-BuNC insertion occurred between Zr and the sp^3 carbon of a bicyclic zirconacyclopentene compound [4] while Buchwald and Nielsen showed that t-BuNC reacted at the Zr–sp^2 carbon of a bicyclo[3.1.0]zirconacyclopentene [5]. However, the factors of the opposite selectivities have not been elucidated yet.



Scheme 1.

Recently, we reported a convenient preparative method of zirconacyclopentenes using Cp_2ZrEt_2 [1a]

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and alkynes or a combination of Cp_2ZrBu_2 (Negishi reagent) [3b], an ethylene gas and alkynes [1b]. Surprisingly, we found that chemoselectivity of the iodination reaction of zirconacyclopentenes was dependent on their substituents, whereas the method using an excess of MeOH/I_2 gave only alkenyl iodides [6]. The use of an excess of MeOH was very important for achieving an excellent selectivity [7]. We also found that CBr_4 or $CClBr_3$ could be used as a bromination reagent for alkyl-substituted zirconacyclopentenes. This reagent afforded only homoallyl bromides, which is in sharp contrast to the usual bromination reagent such as Br_2 and NBS which gave alkenyl bromide selectively [8]. In this paper we describe in detail the chemoselective functionalization of zirconacyclopentenes.

Experimental

All reactions and manipulations were performed under an atmosphere of nitrogen using standard Schlenk techniques. THF was distilled from sodium/benzophenone. GC analyses were performed on a Shimadzu GC-14A equipped with a flame ionization detector using Shimadzu capillary column(CBP1-M25-025). The GC yields were determined using suitable hydrocarbon internal standards. NMR spectra were recorded on a Jeol EX-270 FT NMR spectrometer, GC-MS on a Shimadzu GCMS-QP1000EX and high resolution MS on a Shimadzu KRATOS CONCEPT IS.

Preparation of zirconacyclopentenes

Zirconacyclopentenes **1a–h** were prepared *in situ* in high yields as described previously [1] by the reaction of 1.2 mmol of Cp_2ZrEt_2 with 1.0 mmol of alkynes or by the reaction of 5.0 mmol of vinylsilane with 1.0 mmol of alkynes in the presence of 1.2 mmol of Cp_2ZrBu_2 (Negishi reagent). Yields obtained here were based on alkynes.

The alkynes, 1-(*p*-methoxyphenyl)-1-hexyne and 1-(*p*-chlorophenyl)-1-hexyne, were prepared according to the literature [9].

1-(p-Methoxyphenyl)-1-hexyne. Yield 78%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.94 (t, $J=7$ Hz, 3H), 1.40–1.63 (m, 4H), 2.38 (t, $J=7$ Hz, 2H), 3.76 (s, 3H), 6.79 (d, $J=9$ Hz, 2H), 7.32 (d, $J=9$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 13.68, 19.12, 22.07, 31.02, 55.20, 80.29, 88.73, 113.82, 116.33, 132.86, 159.01. High resolution mass spectroscopy (HRMS): calc. for $C_{13}H_{16}O$: 188.1201; found: 188.1203.

1-(p-Chlorophenyl)-1-hexyne. Yield 82%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.94 (t, $J=7$ Hz, 3H), 1.39–1.63 (m, 4H), 2.38 (t, $J=7$ Hz, 2H), 7.20–7.32 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 13.64, 19.12, 22.07, 30.78, 79.57, 91.50, 122.69, 128.48, 132.77, 133.40. HRMS: calc. for $C_{12}H_{13}Cl$: 192.0706; found: 192.0677.

Reaction of 1a with I_2

To a solution of **1a** was added 1.2 mmol (0.30 g) of I_2 at 0 °C and the mixture was stirred for 1 h at 0 °C. The reaction mixture was quenched with 3 N HCl. The aqueous layer was extracted with diethyl ether and the combined organic layers were washed with 25 wt./wt.% $Na_2S_2O_3$ and saturated NaCl, and dried over $MgSO_4$. After filtration and distillation, (*E*)-4-ethyl-5-iodo-4-octene (**4a**) was obtained in 83% yield.

(E)-4-Ethyl-5-iodo-4-octene (4a). ^{1}H NMR ($CDCl_3$, TMS): δ 0.90 (t, $J=7$ Hz, 3H), 0.91 (t, $J=7$ Hz, 3H), 0.97 (t, $J=7$ Hz, 3H), 1.41 (tq, $J=7$ Hz, 2H), 1.54 (tq, $J=7$ Hz, 2H), 2.13–2.25 (m, 4H), 2.47 (t, $J=7$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.15, 12.87, 14.09, 22.07, 23.04, 33.30, 35.76, 42.87, 104.35, 145.33. HRMS: calc. for $C_{10}H_{19}I$: 266.0532; found: 266.0531.

(Z)-1,2-Diphenyl-4-iodo-1-butene (5b). ^{1}H NMR ($CDCl_3$, TMS): δ 3.03–3.17 (m, 4H), 6.49 (s, 1H), 6.92–7.34 (m, 10H). ^{13}C NMR ($CDCl_3$, TMS): δ 4.73, 44.44, 126.63, 127.39, 127.89, 128.64, 128.75, 128.89, 129.00, 136.66, 139.32, 140.66. HRMS: calc. for $C_{16}H_{15}I$: 334.0219; found: 334.0218.

3-Ethyl-4-iodo-3-hexene (4c). ^{1}H NMR ($CDCl_3$, TMS): δ 0.97 (t, $J=7$ Hz, 3H), 0.99 (t, $J=7$ Hz, 3H), 1.05 (t, $J=7$ Hz, 3H), 2.15–2.27 (m, 4H), 2.53 (q, $J=7$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.04, 13.62, 14.75, 24.03, 34.88, 35.36, 105.46, 145.98. HRMS: calc. for $C_8H_{15}I$: 238.0219; found: 238.0213.

(E)-4-Iodo-2-methyl-1-phenyl-1-butene (5d). ^{1}H NMR ($CDCl_3$, TMS): δ 1.85 (d, $J=1$ Hz, 3H), 2.68–2.74 (m, 2H), 3.31 (t, $J=7$ Hz, 2H), 6.32 (s, 1H), 7.17–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS): δ 4.37, 17.06, 44.49, 126.27, 127.40, 128.05, 128.75, 136.86, 137.74. HRMS: calc. for $C_{11}H_{13}I$: 272.0062; found: 272.0064.

(E)-4-Iodo-2-butyl-(1-p-methoxyphenyl)-1-butene (5e). Yield 71%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.89 (t, $J=7$ Hz, 3H), 1.24–1.49 (m, 4H), 2.22–2.24 (m, 2H), 2.67–2.73 (m, 2H), 3.30 (t, $J=8$ Hz, 2H), 3.80 (s, 3H), 6.25 (s, 1H), 6.85 (d, $J=9$ Hz, 2H), 7.14 (d, $J=9$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 4.64, 13.91, 22.82, 29.90, 30.44, 41.62, 55.22, 113.58, 126.90, 129.68, 130.33, 140.52, 158.07. HRMS: calc. for $C_{15}H_{21}OI$: 344.0637; found: 344.0627.

(E)-4-Iodo-2-butyl-(1-p-chlorophenyl)-1-butene (5f). Yield 85%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.87 (t, $J=7$ Hz, 3H), 1.18–1.48 (m, 4H), 2.15–2.21 (m, 2H), 2.68–2.74 (m, 2H), 3.31 (t, $J=8$ Hz, 2H), 6.25 (s, 1H), 7.11–7.30 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 4.15, 13.87, 22.75, 29.83, 30.33, 41.24, 126.25, 128.30, 129.88, 132.06, 136.24, 142.55. HRMS: calc. for $C_{14}H_{18}ClI$: 348.0142; found: 348.0169.

(Z)-5-Iodo-4-[2-(trimethylsilyl)ethyl]-4-octene (4g). ^{1}H NMR ($CDCl_3$, TMS): δ 0.03 (s, 9H), 0.59–0.65 (m, 2H), 0.88–0.94 (m, 6H), 1.41 (tq, $J=7$ Hz, 2H), 1.54 (tq, $J=7$ Hz, 2H), 2.14–2.20 (m, 4H), 2.44 (t, $J=7$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ −1.78, 12.87, 14.11, 14.93, 22.10, 23.04, 33.24, 37.00, 42.89, 103.59, 146.29. HRMS: calc. for $C_{13}H_{27}ISi$: 338.0927; found: 338.0918.

(E)-1,2-Diphenyl-1-iodo-4-trimethylsilyl-1-butene (4h). ^{1}H NMR ($CDCl_3$, TMS): δ 0.03 (s, 9H), 0.65–0.72 (m, 2H), 2.74–2.81 (m, 2H), 6.23–7.08 (m, 10H). ^{13}C NMR ($CDCl_3$, TMS): δ −1.80, 14.43, 39.93, 98.15, 126.47, 126.79, 127.40, 127.69, 129.04, 129.86, 139.64, 144.45, 151.05. HRMS: calc. for $C_{19}H_{23}ISi$: 406.0614; found: 406.0630.

*Reaction of **1b** with an excess of MeOH and iodine*

Methanol (1.5 mmol) was added to a solution of **1b** (1 mmol) in THF (5 ml) at 0 °C. After stirring for 1 h, iodine (1.2 mmol, 0.30 g) was added to the reaction mixture and stirred for 3 h. The reaction mixture was quenched with 3 N HCl. The aqueous layer was extracted with diethyl ether and the combined organic layers were washed with 25 wt./wt.% $Na_2S_2O_3$ and saturated NaCl, and dried over $MgSO_4$. After filtration and distillation, (*E*)-1,2-diphenyl-1-iodo-1-butene **4b** was obtained in 78% yield.

(E)-1,2-Diphenyl-1-iodo-1-butene (4b). ^{1}H NMR ($CDCl_3$, TMS): δ 1.03 (t, $J=7$ Hz, 3H), 2.82 (q, $J=7$ Hz, 2H), 6.89–7.16 (m, 10H). ^{13}C NMR ($CDCl_3$, TMS): δ 11.77, 38.60, 98.90, 126.59, 126.93, 127.51, 127.78, 129.07, 129.90, 139.62, 144.53, 150.26. HRMS: calc. for $C_{16}H_{15}I$: 334.0219; found: 334.0231.

(Z)-1-Iodo-2-methyl-1-phenyl-1-butene (4d). ^{1}H NMR ($CDCl_3$, TMS): δ 1.10 (t, $J=7$ Hz, 3H), 1.72 (s, 3H), 2.43 (q, $J=7$ Hz, 2H), 7.17–7.33 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS): δ 11.72, 18.47, 37.43, 93.78, 127.28, 128.08, 128.89, 144.51, 144.85. HRMS: calc. for $C_{11}H_{13}I$: 272.0062; found: 272.0071.

(Z)-1-Iodo-2-ethyl-(1-p-methoxyphenyl)-1-hexene (4e). Yield 80%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.80 (t, $J=7$ Hz, 3H), 0.89–1.32 (m, 4H), 1.09 (t, $J=7$ Hz, 3H), 2.02–2.08 (m, 2H), 2.41 (q, $J=7$ Hz, 2H), 3.78 (s, 3H), 6.81 (d, $J=9$ Hz, 2H), 7.13 (d, $J=9$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.09, 13.80, 22.43, 30.84, 31.55, 34.34, 55.20, 95.65, 113.39, 129.85, 137.61, 148.80, 158.52. HRMS: calc. for $C_{15}H_{21}OI$: 344.0637; found: 344.0623.

(Z)-1-Iodo-2-ethyl-(1-p-chlorophenyl)-1-hexene (4f). Yield 82%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.76 (t, $J=7$ Hz, 3H), 1.09 (t, $J=7$ Hz, 3H), 1.14–1.39 (m, 4H), 2.00–2.05 (m, 2H), 2.41 (q, $J=7$ Hz, 2H), 7.06–7.30 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.01, 13.75, 22.37, 30.73, 31.59, 34.18, 93.39, 128.27, 129.97, 132.97, 143.34, 149.72. HRMS: calc. for $C_{14}H_{18}ClI$: 348.0142; found: 348.0116.

*Reaction of **1a** with Br_2*

This reaction was carried out in a similar way to the reaction described above using Br_2 (1.2 mmol, 0.062 ml) instead of I_2. (*E*)-4-Bromo-5-ethyl-4-octene was obtained in 79% yield. Isomerical purity was 94%.

(E)-4-Bromo-5-ethyl-4-octene (14a). ^{1}H NMR ($CDCl_3$, TMS): δ 0.90 (t, $J=7$ Hz, 3H), 0.91 (t, $J=7$ Hz, 3H), 1.00 (t, $J=7$ Hz, 3H), 1.42 (tq, $J=7$ Hz, 2H), 1.58 (tq, $J=7$ Hz, 2H), 2.06–2.12 (m, 4H), 2.22 (q, $J=7$ Hz, 2H), 2.44 (t, $J=7$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.06, 13.10, 14.11, 21.87, 21.96, 29.88, 34.18, 39.14, 123.16, 139.82. HRMS: calc. for $C_{10}H_{19}Br$: 218.0670; found: 218.0654.

(E)-3-Bromo-4-ethyl-3-hexene (14c). ^{1}H NMR ($CDCl_3$, TMS): δ 1.00 (t, $J=7$ Hz, 3H), 1.00 (t, $J=7$ Hz, 3H), 1.10 (t, $J=7$ Hz, 3H), 2.13 (q, $J=7$ Hz, 2H), 2.22 (q, $J=7$ Hz, 2H), 2.49 (q, $J=7$ Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS): δ 12.02, 13.46, 13.84, 25.12, 29.60, 30.94, 124.45, 140.39. HRMS: calc. for $C_8H_{15}Br$: 190.0357; found: 190.0374.

*Reaction of **1a** with NBS*

NBS (1.2 mmol, 0.21 g) was used as a bromination reagent instead of Br_2 in the above reaction. Bromination reaction of **1a** with NBS gave 98% of **14a** in 98% yield with 96% of isomerical purity.

*Reaction of **1a** with $CuBr_2$*

$CuBr_2$ (1.2 mmol, 0.29 g) was used as a bromination reagent. GC analysis of the reaction mixture showed that **14a** was formed in 30% yield.

*Reaction of **1a** with carbon tetrabromide*

To a solution of **1a** was added carbon tetrabromide (1.2 mmol, 0.40 g) at 0 °C and the mixture was stirred for 1 h at room temperature. After quenching with 3 N HCl, aqueous layers were extracted with diethyl ether. The combined organic layers were washed with saturated $NaHCO_3$, and dried over $MgSO_4$. The ether extract was evaporated. The product was purified by column chromatography. (*Z*)-3-Propyl-1-bromo-3-heptene was obtained in 94% yield with >99% isomerical purity.

1-Bromo-3-propyl-3-heptene (13a). ^{1}H NMR ($CDCl_3$, Me_4Si): δ 0.83 (t, $J=7.2$ Hz, 6H), 1.24–1.36 (m, 4H), 1.86–1.96 (m, 4H), 2.45 (t, $J=7.9$ Hz, 2H), 3.34 (t, $J=7.6$ Hz, 2H), 5.15 (t, $J=7.9$ Hz, 1H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.79, 14.02, 21.58, 22.97, 29.81, 31.83, 31.99, 40.40, 128.34, 136.26. HRMS: calc. for $C_{10}H_{19}Br$: 218.0670; found: 218.0651.

(Z)-3-Ethyl-1-bromo-3-hexene (13c). ^{1}H NMR ($CDCl_3$, TMS): δ 0.95 (t, $J=7$ Hz, 3H), 0.97 (t, $J=7$ Hz, 3H), 1.96–2.07 (m, 4H), 2.53 (t, $J=8$ Hz, 2H), 3.41 (t, $J=8$ Hz, 2H), 5.18 (t, $J=7$ Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS): δ 13.30, 14.48, 20.92, 22.82, 31.90, 40.13, 129.32,

137.39. HRMS: calc. for $C_8H_{15}Br$: 190.0357; found: 190.0335.

Dihalogenation of 1c with CCl_3Br and I_2

To a solution of **1c** (1 mmol) in THF (3.5 ml) was added CCl_3Br (0.22 g, 1.1 mmol) and the reaction mixture was stirred at room temperature for 3 h. Then iodine (0.51 g, 2 mmol) was added and after stirring at room temperature for 3 h the usual work-up gave **15** in 89% yield (>98% isomerically pure).

1-Bromo-3-ethyl-4-iodo-3-hexene (15). ^{1}H NMR ($CDCl_3$, Me_4Si): δ 0.9–1.2 (m, 6H), 2.23 (q, J=7.6 Hz, 2H), 2.57 (q, J=7.3 Hz, 2H), 2.7–2.9 (m, 2H), 3.3–3.5 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 13.48, 14.66, 25.03, 29.36, 35.11, 45.41, 106.43, 142.01. HRMS: calc. for $C_8H_{14}BrI$: 315.9324; found: 315.9344.

Dihalogenation of 1c with NBS and I_2

To a solution of **1c** (1 mmol) in THF (5 ml) was added NBS (196 mg, 1.1 mmol) and the reaction mixture was stirred at 0 °C for 1 h. Then iodine (0.51 g, 2 mmol) was added and after stirring at room temperature for 3 h the usual work-up gave 1-iodo-3-ethyl-4-bromo-3-hexene (**16**) in 74% yield along with 1-bromo-3-ethyl-4-iodo-3-hexene (**15**) (7%) and 1,4-diiodo-3-ethyl-3-hexene (**17**) (15%).

1-Iodo-3-ethyl-4-bromo-3-hexene (16). ^{1}H NMR ($CDCl_3$, Me_4Si): δ 1.01 (t, J=7.6 Hz, 3H), 1.11 (t, J=7.3 Hz, 3H), 2.16 (q, J=7.6 Hz, 2H), 2.48 (q, J=7.3 Hz, 2H), 2.7–2.9 (m, 2H), 3.1–3.3 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 1.29, 13.37, 13.64, 25.59, 31.00, 41.08, 127.74, 138.17. HRMS: calc. for $C_8H_{14}BrI$: 315.9324; found: 315.9330.

1,4-Diiodo-3-ethyl-3-hexene (17). ^{1}H NMR ($CDCl_3$, Me_4Si): δ 1.01 (t, J=7.6 Hz, 3H), 1.06 (t, J=7.3 Hz, 3H), 2.22 (q, J=7.6 Hz, 2H), 2.53 (q, J=7.3 Hz, 2H), 2.7–2.9 (m, 2H), 3.1–3.2 (m, 2H). ^{13}C NMR ($CDCl_3$, Me_4Si): δ 1.24, 13.53, 14.59, 24.73, 35.06, 46.52, 108.98, 143.90. HRMS: calc. for $C_8H_{14}I_2$: 363.9186; found: 363.9192.

Dihalogenation of 1c with I_2 and NBS

To a solution of **1c** (1 mmol) in THF (5 ml) was added iodine (0.28 g, 1.1 mmol) and the mixture was stirred at 0 °C for 1 h. Then NBS (0.27 g, 1.5 mmol) was added and after stirring at room temperature for 3 h the usual work-up gave **15** in 25% yield and **17** in 60% yield.

Reaction of dimethylzirconocene with CCl_3Br

To a freshly prepared solution of dimethylzirconocene in C_6D_6 (*c.* 0.7 M, 0.35 mmol), CCl_3Br (77 mg, 0.38 mmol) was added at room temperature and the mixture was monitored by NMR. Within 10 min dimethylzirconocene was completely consumed and $Cp_2Zr(CH_3)CCl_3$ was formed in 89% yield along with the formation of MeBr in 83% yield.

$Cp_2Zr(CH_3)CCl_3$. ^{1}H NMR (C_6D_6, Me_4Si): δ 0.24 (s, 3H), 5.93 (s, 10H). ^{13}C NMR (C_6D_6, Me_4Si): δ 35.09, 78.32, 112.73.

Reaction of 1a with Me_3SnCl

To a solution of **1a** (1 mmol) in THF (5 ml) was added 1.0 mmol of Me_3SnCl (0.20 g) at 0 °C and the mixture was stirred for 1 h. (*Z*)-3-Propyl-1-trimethylstannyl-3-heptene (**18a**) was formed in 91% yield. ^{1}H NMR ($CDCl_3$, TMS): δ 0.03 (s, 9H), 0.84–0.96 (m, 2H), 0.89 (t, J=7 Hz, 3H), 0.90 (t, J=7 Hz, 3H), 1.28–1.41 (m, 4H), 1.93–2.03 (m, 4H), 2.15–2.22 (m, 2H), 5.13 (t, J=7 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS): δ −10.10, 9.51, 14.02, 14.29, 21.65, 23.31, 29.92, 31.93, 33.37, 123.84, 141.90. HRMS: calc. for $C_{13}H_{28}Sn$: 304.1213; found: 304.1189.

(E)-1,2-Diphenyl-4-trimethylstannyl-1-butene. Yield 91%. ^{1}H NMR ($CDCl_3$, TMS): δ 0.03 (s, 9H), 0.92 (t, J=8 Hz, 2H), 2.62 (t, J=8 Hz, 2H), 6.38 (s, 1H), 6.68–7.48 (m, 10H). ^{13}C NMR ($CDCl_3$, TMS): δ −10.14, 9.18, 37.34, 125.01, 126.02, 126.81, 127.80, 128.44, 128.64, 128.96, 137.55, 141.40, 145.91. HRMS: calc. for $C_{19}H_{24}Sn$: 372.0900; found: 372.0874.

Reaction of 1b or 1c with isonitriles

To a THF solution of **1b** of **1c** prepared *in situ* using 1.2 mmol of Cp_2ZrEt_2 and 1.0 mmol of alkynes was added t-BuNC (1 mmol, 0.083 g) or n-BuNC (1 mmol, 0.083 g) at 0 °C. The mixture was stirred for 2 h at 0 °C. The reaction mixture was evaporated and dissolved in C_6D_6. The solution was monitored by NMR spectroscopy.

20b. Yield 96% based on diphenylacetylene. ^{1}H NMR (C_6D_6, TMS): δ 1.06 (s, 9H), 2.55–2.77 (m, 4H), 5.45 (s, 10H), 6.91–7.21 (m, 10H). ^{13}C NMR (C_6D_6, TMS): δ 28.84, 29.22, 37.68, 58.92, 106.54, 121.13, 124.13, 127.22, 127.47, 128.62, 143.00, 151.28, 158.88, 177.36, 231.23.

20c. Yield 95% based on 3-hexyne. ^{1}H NMR (C_6D_6, TMS): δ 1.01 (s, 9H), 1.27 (t, J=7.4 Hz, 3H), 1.33 (t, J=7.4 Hz, 3H), 2.24–2.27 (m, 2H), 2.40–2.53 (m, 6H), 5.53 (s, 10H). ^{13}C NMR (C_6D_6, TMS): δ 14.41, 16.46, 29.47, 30.33, 30.40, 33.10, 35.44, 58.33, 105.44, 142.50, 170.89, 232.49.

21b. Yield 94% based on diphenylacetylene. ^{1}H NMR (C_6D_6, TMS): δ 0.87 (t, J=7.1 Hz, 3H), 1.10–1.22 (m, 2H), 1.33–1.41 (m, 2H), 2.32–2.36 (m, 2H), 2.72–2.76 (m, 2H), 3.08 (t, J=7.3 Hz, 2H), 5.46 (s, 10H), 6.91–7.24 (m, 10H). ^{13}C NMR (C_6D_6, TMS): δ 13.93, 20.84, 26.99, 31.39, 37.63, 51.55, 106.70, 121.29, 124.27, 127.35, 127.53, 129.90, 143.12, 151.21, 158.58, 177.91, 232.02.

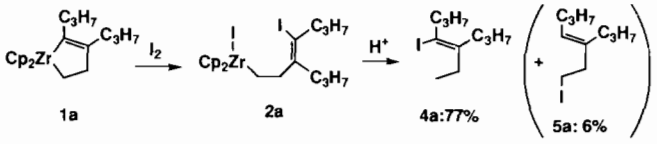
21c. Yield 88% based on 3-hexyne. ^{1}H NMR (C_6D_6, TMS): δ 0.85 (t, J=7.3 Hz, 3H), 1.08–1.19 (m, 2H), 1.23–1.34 (m, 6H), 1.36–1.42 (m, 2H), 2.18–2.23 (m,

2H), 2.29–2.32 (m, 2H), 2.36–2.48 (m, 2H), 3.07 (t, $J=7.3$ Hz, 2H), 5.54 (s, 10H). ^{13}C NMR (C_6D_6, TMS): δ 13.93, 14.41, 16.37, 20.81, 28.12, 30.26, 31.55, 32.78, 35.40, 50.53, 105.53, 142.30, 171.30, 232.99.

Results and discussion

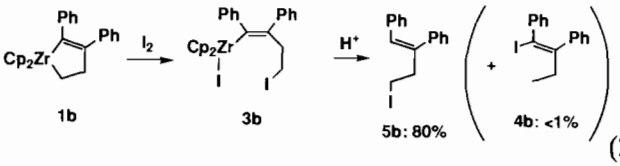
Substituent-dependent chemoselective monohalogenation reaction of zirconacyclopentenes

Treatment of 1,1-bis(η^5-cyclopentadienyl)-2,3-dipropyl-2-zirconacyclopentene (**1a**) prepared *in situ* with iodine gave, after hydrolysis, (*E*)-4-ethyl-5-iodo-4-octene (**4a**) in 77% yield along with the formation of **5a** (6%) (eqn. (1)). Diiodination product was obtained in 4% yield. The Zr–sp^2 carbon bond reacted selectively with iodine. This chemoselectivity of iodination was observed for **1c** or **1g** which have an alkyl substituent on the C2 carbon.



(1)

However, reaction of **1b**, which has a phenyl substituent on the C2 carbon, afforded **5b** in 97% yield (isolated yield 78%) with a high selectivity after hydrolysis (eqn. (2)). The Zr–sp^3 carbon bond reacted chemoselectively with iodine. Other aryl substituted zirconacyclopentenes such as **1d–f** except **1h** showed a similar chemoselectivity. The reaction of **1h** with iodine was not clean. *Para*-substituted phenyl groups such as *p*-$MeOC_6H_4$- and *p*-ClC_6H_4- were used in **1e** and **1f**, respectively, no significant change in chemoselectivities was observed.



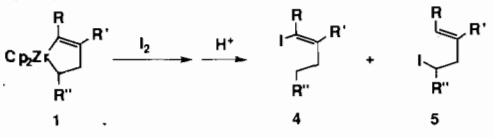
(2)

The result obtained here (see Table 1) revealed that the chemoselectivity of iodination of **1** was highly dependent on the substituents and, interestingly, the iodination was selective.

Substituent-independent chemoselective monohalogenation of zirconacyclopentenes

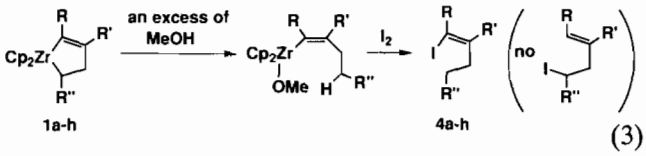
In order to develop a useful and a general procedure for organic synthesis, substituent-independent chemoselective reaction is much more attractive. Recently we reported that the treatment of diorganozirconocene such as zirconacyclopentene with an excess of methanol led to a selective monoprotonation reaction [7]. The zirconium containing reaction product with methanol, organozirconocene alkoxide, was relatively inert toward methanol. This inertness allowed the complete monoprotonation of diorganozirconocene compounds. Therefore highly selective monohalogenation products could be obtained after halogenation with I_2, NBS or Br_2.

TABLE 1. Substituent-dependent monoiodination of zirconacyclopentenes with iodine[a]



Zirconacyclopentene				Product		Yield[b] (%)
R	R'	R''		4	5	
n-Pr	n-Pr	H	(**1a**)	93	7	83
Ph	Ph	H	(**1b**)	<1	>99	80
Et	Et	H	(**1c**)	>99	<1	>99
Ph	Me	H	(**1d**)	5	95	82
p-MeO-C_6H_4	n-Bu	H	(**1e**)	10	90	83
p-Cl-C_6H_4	n-Bu	H	(**1f**)	10	90	>99
n-Pr	n-Pr	Me_3Si	(**1g**)	>99	<1	93
Ph	Ph	Me_3Si	(**1h**)	>99	<1	18

[a]Zirconacyclopentenes were prepared *in situ*. The reaction was carried out at 0 °C using 1.2 equiv. of I_2. Reaction time: 1 h. Solvent: THF. [b]Combined GC yields of **4** and **5** based on alkynes.



(3)

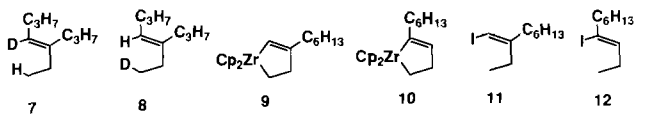
We employed the method of an excess of MeOH/I_2 for monoiodination of **1a–h** (eqn. (3)). Results are shown in Table 2. Surprisingly, this method was substituent independent and in all cases only stereodefined alkenyl iodides **4a–h** were obtained in high yields with an excellent chemoselectivity. Formation of diiodides was not detected. Stereochemistry of carbon–carbon double bonds was retained (>99% *syn*) during monoiodination. Monoprotonation proceeded at the sp^3 carbon on Zr chemoselectively. Treatment of **1a** with an excess of MeOH/DCl and an excess of MeOD/HCl gave (*Z*)-4-deutero-5-ethyloct-4-ene (**7**) and (*Z*)-4-(2-deuteroethyl)-oct-4-ene (**8**). The highly chemoselective protonation is probably due to the stronger basicity of the sp^3 carbon attached to Zr rather than the sp^2 carbon. Monoiodination of **1h** with iodine gave, after hydrolysis, a low yield of **4h** (18%), whereas this method afforded **4h** in 95% yield. In the case of **9** and **10** which are prepared as a mixture of isomers from 1-

TABLE 2. Substituent-independent iodination of **1** with an excess of MeOH/I_2[a]

Zirconacyclopentene	Product		Yield[b] (%)
	4	**5**	
1a	>99	<1	96
1b	>99	<1	99
1c	>99	<1	97
1d	>99	<1	99
1e	>99	<1	80
1f	>99	<1	82
1g	>99	<1	95
1h	>99	<1	95

[a]Zirconacyclopentenes were prepared *in situ*. Solvent: THF. Temperature: 0 °C. Time: 3 h. The reaction was carried out using 1.5 equiv. of MeOH and then 1.2 equiv. of I_2. [b]Combined yields of **4** and **5** based on alkynes.

octyne, similarly, monoiodination products **11** and **12** were obtained, respectively.

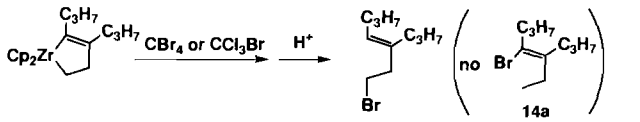


7 8 9 10 11 12

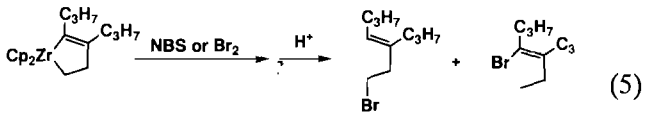
Reagent-dependent chemoselective monobromination of zirconacyclopentenes

Chemoselective monohalogenation reaction of **1** described above could provide alkenyl halides in all cases and homoallylic halides for aryl-substituted zirconacyclopentenes. However, there was no procedure to produce homoallylic halides from alkyl-substituted zirconacyclopentenes such as **1a** and **1c**. During the course of our study to develop a new reagent for halogenation of **1**, we found a new reagent CBr_4 or CCl_3Br which afforded homoallylic halides.

Reaction of **1a** with CBr_4 gave, after hydrolysis, 3-propyl-3-heptenyl-1-bromide (**13a**) in 94% yield (eqn. (4)). Formation of alkenyl bromide was not detected. This is in sharp contrast to the bromination of **1a** with the usual bromination reagents such as NBS and Br_2 which afforded **14a** selectively (eqn. (5)). It is noteworthy that monobromination of **1a** of **1c** with CCl_3Br or CBr_4 had an opposite chemoselectivity to the usual bromination reagents. In addition, treatment of **1a** and **1c** with NBS or Br_2 usually produced 4–10% of isomers **13a** and **13c**, respectively. However, bromination with CBr_4 or CCl_3Br showed an excellent chemoselectivity. Results are given in Table 3.



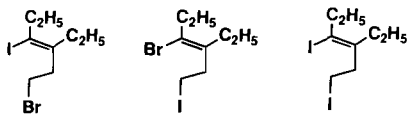
13a: 94% (4)



13a: 4-10% 14a: 80-90% (5)

When Cp_2ZrMe_2 was treated with 1.1 equiv. of CCl_3Br, MeBr was obtained in 83% yield in benzene at 10 °C. NMR spectra of zirconium species were consistent with $Cp_2Zr(Me)(CCl_3)$ (89%). In its ^1H NMR spectrum there were two singlets at 5.93 and 0.24 ppm which were assignable to Cp protons and a methyl group, respectively. ^{13}C NMR spectrum showed three carbons at 112.73, 78.32 and 35.09 ppm assignable to Cp–Zr, Cl_3C–Zr and Me–Zr, respectively.

Mixed dihalogenation of zirconacyclopentenes has been practically difficult, since selectivity of halogenation was not high. However, chemoselectivity of bromination with CBr_4 or CCl_3Br was satisfactory for mixed dihalogenation of **1**. Conventional bromination–iodination of **1c** with NBS (1.1 equiv.) and I_2 (2 equiv.) gave the desired product 1-iodo-3-ethyl-4-bromo-3-hexene (**16**) in 74% yield along with the formation of by-products **15** and **17** in 7% and 15% yields, respectively. The opposite treatment sequence of I_2 and NBS in this order for **1c** predominantly led to diiodide **17** in 60% yield. The desired compound **15** was obtained only in 25% yield. This is probably because of a halide exchange reaction of the zirconium-containing intermediate **2c** with NBS. Reaction of the Zr–I moiety with NBS might produce an iodination reagent such as NIS in the reaction mixture.



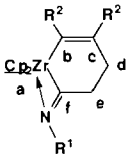
15 16 17

TABLE 3. Reagent-dependent chemoselective bromination of zirconacyclopentenes with various reagents[a]

Zirconacyclopentene	Reagent[b]	Temp. (°C)	Time (h)	Products		Yield[c] (%)
				13	**14**	
1a	Br_2	0	1	94	6	79
	NBS	0	1	96	4	98
	$CuBr_2$	35	1	90	10	30
	CCl_3Br	r.t.	1	<1	>99	76
	CBr_4	r.t.	1	<1	>99	94
1c	NBS	0	3	90	10	87
	CBr_4	r.t.	3	<1	>99	90

[a]Zirconacyclopentenes were prepared *in situ*. Solvent: THF. [b]1.2 equiv. [c]Combined yields of **13** and **14** based on alkynes.

TABLE 4. ^{13}C NMR spectra data of **20a,c** and **21a,c** produced by the reaction of zirconacyclopentenes with t-BuNC or n-BuNC[a]



20: R^1 = t-Bu
21: R^1 = n-Bu

Product	R^1	R^2	Ca	Cb	Cc	Cd	Ce	Cf	Yield[b] (%)
20b	t-Bu	Ph	106.54	177.36	143.00	28.84	37.68	231.23	96
20c	t-Bu	C_2H_5	105.44	170.89	142.50	30.33	35.44	232.49	95
21b	n-Bu	Ph	106.70	177.91	143.12	26.99	37.63	232.02	94
21c	n-Bu	C_2H_5	105.53	171.30	142.30	28.12	35.40	232.99	88

[a]Zirconacyclopentenes were prepared *in situ* using 1.2 mmol of Cp_2ZrEt_2 and 1.0 mmol of alkynes. The reaction was carried out in THF at 0 °C using 1 mmol of t-BuNC or n-BuNC. Reaction time: 2 h. [b]NMR yield based on alkynes.

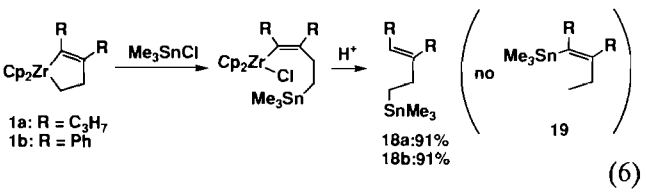
On the other hand treatment of **1c** with CCl_3Br and I_2 in this order gave **15** in 89% yield with >98% of isomerical purity. Formation of isomer **16** or diiodide **17** was not detected.

The monohalogenation procedures of **1** are summarized in Scheme 2. Both stereodefined alkenyl halides and homoallylic halides could be selectively obtained from **1**.

Chemoselective reaction of zirconacyclopentenes with trimethyltin chloride

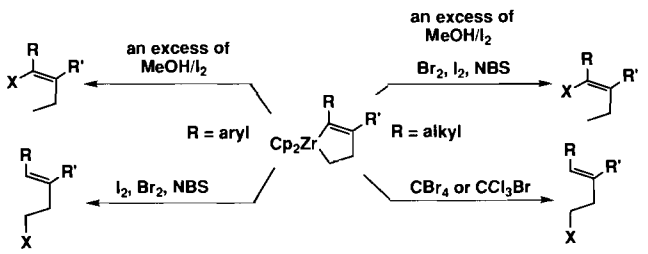
A Zr–sp^3 carbon bond of zirconacyclopentane is known to react with Sn–X of Ph_2SnCl_2 [10]. On the other hand, one Zr–sp^2 carbon bond also reacted with the Sn–X bond of Me_2SnBr_2 [11]. It is interesting to compare the reactivities of Zr–sp^3 and Zr–sp^2 carbon bonds in zirconacyclopentenes towards the Sn–X moiety.

Reaction of **1a** with 1 equiv. of Me_3SnCl at room temperature in THF gave the homoallyltin compound (**18a**) in 91% yield selectively, after hydrolysis (eqn. (6)). The alkenyltin compound (**19**) was not formed. Phenyl substituted zirconacyclopentene **1b** also reacted with 1 equiv. of Me_3SnCl to afford only **18b**. These results indicated that the reaction of **1** with Me_3SnCl was not substituent dependent like the reaction with iodine but highly chemoselective. Other metal halides such as Ph_3GeCl, Me_3GeCl, Me_3SiCl and Me_3SiI did not give positive results.



1a: R = C_3H_7
1b: R = Ph
18a:91%
18b:91%

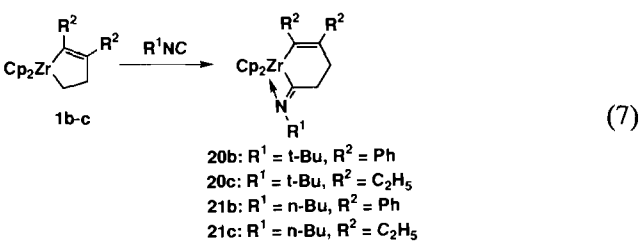
(6)



Scheme 2.

Reaction of zirconacyclopentenes with isonitriles

We investigated the reaction of t-BuNC and n-BuNC with **1b** and **1c**, (eqn. (7)), since two different chemoselectivities have been reported for the reaction of isonitriles with different types of zirconacyclopentenes [4, 5]. The reaction was carried out at 0 °C and completed within 2 h. ^1H and ^{13}C NMR spectra of those products showed a clean formation of isonitrile insertion products **20** or **21**. Their ^{13}C NMR data are summarized in Table 4. A resonance at 231–232 ppm was characteristic for the η^2-iminoacyl group [12, 13]. The result obtained here indicated the insertion reaction of isonitrile was highly chemoselective but neither substituent dependent nor reagent dependent in our system.



1b-c

20b: R^1 = t-Bu, R^2 = Ph
20c: R^1 = t-Bu, R^2 = C_2H_5
21b: R^1 = n-Bu, R^2 = Ph
21c: R^1 = n-Bu, R^2 = C_2H_5

(7)

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