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γ-Trimethylsilyl-substituted allylzirconcenes in organic synthesis. Stereoselective synthesis of terminal 1,3-butadienes and functionalized vinylsilanes

Jin-Hong Pi and Xian Huang*

Department of Chemistry, Zhejiang University, Xi-xi Campus, Hangzhou 310028, PR China
State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, PR China

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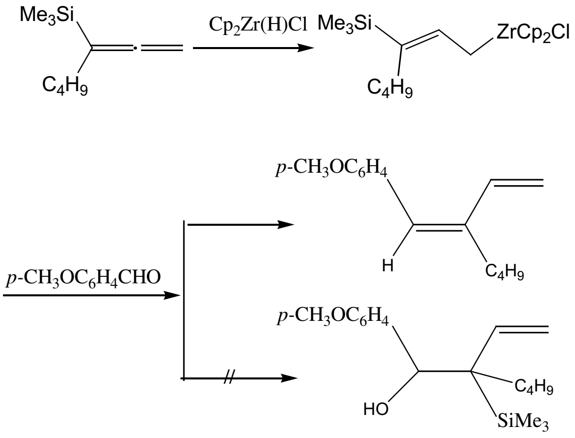
Abstract—γ-Trimethylsilyl-substituted allylzirconcenes, prepared by hydrozirconation of trimethylsilyl-substituted terminal allenes, react with aldehydes at the γ-position to give 1,3-butadienes in one step with good stereoselectivity and undergo conjugate addition to α,β-unsaturated aromatic ketones at the α-position to selectively afford functionalized vinylsilanes in the presence of catalytic $CuBr\cdot SMe_2$.

Heteroatom-stabilized allyl organometallics, which can be used as homoenolate anion synthons and reversed polarity synthetic equivalents, are of great importance in organic synthesis and a great deal of effort has been exerted to control the regioselectivity and stereoselectivity in their reactions with electrophiles.[1] Silicon-substituted allylic anions, which can react with a variety of aldehydes and ketones, are often used to prepare lactols,[2] diols,[3] vinylsilanes,[4] and terminal 1,3-dienes.[5] Organozirconocenes have emerged as one of the most useful classes of transition metal derivatives for use in organic synthesis owing to the widely used zirconocene-mediated tansformations and the relative ease of their preparation.[6] In this paper, we wish to report the condensation reactions of γ-trimethylsilyl-substituted allylzirconcenes with aldehydes to give terminal 1,3-butadienes in one step and their conjugate additions to α,β-unsaturated aromatic ketones to afford functionalized vinylsilanes in the presence of catalytic $CuBr\cdot SMe_2$.

γ-Trimethylsilyl-substituted allylzirconcenes are easily prepared by hydrozirconation of trimethylsilyl-substituted terminal allenes.[7] Initially we investigated the reaction of γ-trimethylsilyl-γ-butyl-allylzirconcene with *p*-anisaldehyde. We found the reaction proceeded smoothly at −78 °C. To our surprise, the obtained product was not the expected β-hydroxysilane, as was the case for various other allylzirconiums,[8] Instead the 1,3–terminal butadiene with *E* configuration was isolated as the major product (Scheme 1).

Obviously, γ-trimethylsilyl-substituted allylzirconcene **1** reacted with the aldehydes at the γ-position, probably via the chair-like transition state **2**, to give **3**, this was



Scheme 1.

Keywords: Allylzirconcene; Peterson olefination reaction; Conjugation addition; 1,3-Butadiene; Vinylsilane.

* Corresponding author. Fax: +86-571-8807077; e-mail: huangx@mail.hz.zj.cn

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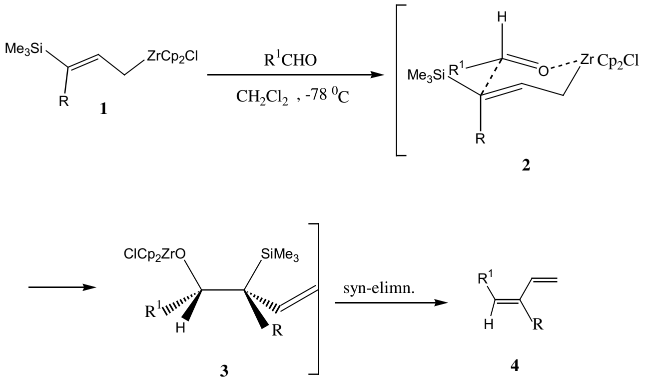
followed immediately by the Peterson olefination reaction in a syn manner, which led to the formation of 1,3–terminal butadiene **4** in one step (Scheme 2).

With this result in mind, we further investigated the reactions of different γ-trimethylsilyl-substituted allylzirconcenes with different carbonyl compounds and the results are summarized in Table 1. It shows that in most cases 1,3-terminal butadiene **4** could be obtained with good stereoselectivity. However, unsatisfactory results were obtained when ketones were used and when R was a more sterically bulky phenyl group, even aldehyde was used (entry 9). This unusual reactivity in comparison with the other γ-monosubstituted-allylzironiums reported[8] maybe is ascribed to the additional substituted group on the γ-position. Obviously, increasing steric hindrance could suppress reaction mentioned above.

Recognizing the fact that increasing steric hindrance can prevent **1** from reacting with the electrophile at the γ-position, we explored its copper-catalyzed addition to α,β-unsaturated ketones at the α-position (Scheme 3).

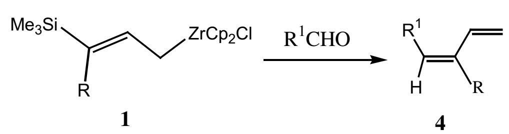
Transmetalation of organic ligands from zirconium to copper had been intensely researched due to the wide application of organocopper reagents in synthetic chemistry. Wipf and Smitrovich reported the first example of addition of alkyl zirconocenes with catalytic $CuBr{\cdot}SMe_2$ to enones.[6] We found in the presence of a $CuBr{\cdot}SMe_2$, allylzirconocene **1** underwent clean conjugate addition to α,β-unsaturated ketones when R^2 is a phenyl group at the α-position. The results are summarized in Table 2. The reactions proceeded smoothly with high stereo and regioselectivity, and the major products were (*E*)-vinylsilanes. However, no reaction result was observed when R^2 was an aliphatic group (entry 9 and 10). Nevertheless, this is, to our knowledge, the first example of the copper-catalyzed addition of allylzirconocene to α,β-unsaturated ketones.[11]

The stereochemistry of the resulting compounds was established on the basis of ^1H NMR as well as from NOESY experiments. In the case of **5c**, a major triplet at δ 6.12 is attributed to the vinylic hydrogen of the *E*-isomer, whereas a minor triplet at δ 5.95 was attributed to the vinylic hydrogen of the *Z*-isomer. The assignment of the major signal at δ 5.75 to *E*-isomer is based on earlier reports that vinylic hydrogens *cis*-to the trimethylsilyl group consistently exhibited ca. 0.3 ppm upfield shift with respect to the corresponding vinylic hydrogen *trans*-to the trimethylsilyl group.[12] Additionally, there was a strong cross peak between the hydrogen



Scheme 2.

Table 1. Stereoselective synthesis of terminal 1,3-butadienes[9]

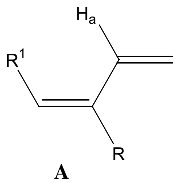


Entry	R	R^1	Product	Yield (%)[a]	*E*:*Z* ratio[b,c]
1	Me	p-BrC_6H_4	**4a**	64	89:11
2	Me	p-$CH_3OC_6H_4$	**4b**	62	88:12
3	Et	p-BrC_6H_4	**4c**	63	90:10
4	Et	p-$CH_3OC_6H_4$	**4d**	65	88:12
5	*n*-Bu	C_6H_5	**4e**	71	90:10
6	*n*-Bu	p-$CH_3OC_6H_4$	**4f**	73	91:9
7	$C_6H_5CH_2$	C_6H_5	**4g**	84	88:12
8	$C_6H_5CH_2$	p-$CH_3OC_6H_4$	**4h**	86	89:11
9	C_6H_5	p-$CH_3OC_6H_4$	—	—	—

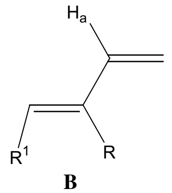
[a] Isolated yield.

[b] The isomer ratio was determined by the integration of the 400 MHz ^1H NMR spectrum.

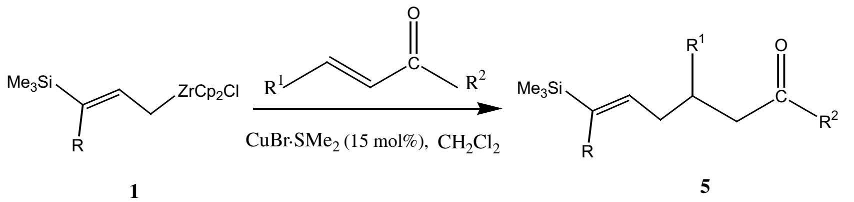
[c] The double-bond geometry of the dienes in Table 1 was determined by comparing the ^1H and ^{13}C NMR spectra of our compounds to data reported for known compounds and in combination with the fact that the chemical shift of H_a in isomer **A** is generally ca. 0.4 ppm downfield from that of isomer **B**.[10]



A



B



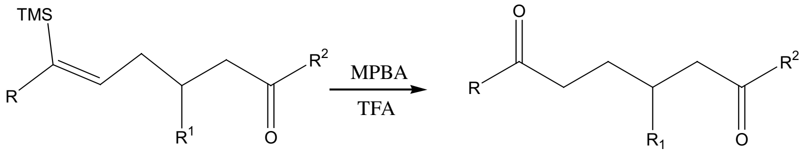
Scheme 3.

Table 2. $CuBr{\cdot}SMe_2$ catalyzed conjugate addition of **1** to α,β-unsaturated ketones[13]

Entry	R	R^1	R^2	Product	Yield (%)[a]	*E*:*Z* ratio[b]
1	Et	C_6H_5	C_6H_5	**5a**	63	95:5
2	Et	*p*-$CH_3OC_6H_4$	C_6H_5	**5b**	62	97:3
3	*n*-Bu	*p*-$CH_3C_6H_4$	C_6H_5	**5c**	68	98:2
4	*n*-Bu	*p*-$CH_3OC_6H_4$	C_6H_5	**5d**	73	97:3
5	$C_6H_5CH_2$	*p*-BrC_6H_4	C_6H_5	**5e**	66	92:8
6	$C_6H_5CH_2$	*p*-$CH_3OC_6H_4$	C_6H_5	**5f**	65	93:7
7	C_6H_5	*p*-$CH_3C_6H_4$	C_6H_5	**5g**	63	88:12
8	C_6H_5	C_6H_5	C_6H_5	**6h**	69	87:13
9	C_6H_5	*p*-$CH_3OC_6H_4$	CH_3	—	—	—
10	C_6H_5	*p*-$CH_3OC_6H_4$	CH_3CH_2	—	—	—

[a] Isolated yield.

[b] The isomer ratio was determined by the integration of the 400 MHz ^1H NMR spectrum.



5 **6**

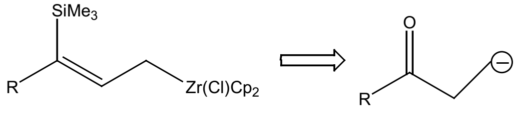
6a: R = C_6H_5, R^1= *p*-$CH_3C_6H_4$, R^2 = C_6H_5 (64%)
6b: R = C_2H_5, R^1= *p*-$CH_3OC_6H_4$, R^2 = C_6H_5 (66%)

Scheme 4.

at δ 0.08 ppm in the trimethylsilyl group and the hydrogen at δ 5.75 ppm in the NOESY spectrum, which further supports that the major isomer is the *E*-isomer.

Vinylsilanes serve as important synthetic intermediates, and have been converted to other useful compounds in organic synthesis.[14] In order to test the synthetic utility of the functionalized vinylsilanes **5**, we studied their epoxidation. Epoxidation of **5** with *m*-chloroperbenzoic acid, followed by hydrolysis with trifluoroacetic acid in refluxing methanol afforded 1,6-ketones **6** (Scheme 4).[15] In this process, the polarity of the vinylic carbon atom adjacent to silyl group was reversed, and therefore the γ-trimethylsilyl-substituted allylzirconcene served as polarity umploung synthetic equivalent **7** (Scheme 5).

In conclusion, we found that γ-trimethylsilyl-substituted allylzirconcenes, prepared by hydrozirconation of trimethylsilyl-substituted terminal allenes, react with aldehydes at the γ-position to give 1,3-butadienes in one step with good stereoselectity. They also undergo conjugate addition to α,β-unsaturated aromatic ketones at the α-position to stereoselectively afford functionalized vinylsilanes in the presence of catalytic $CuBr{\cdot}SMe_2$.



2 **7**

Scheme 5.

Acknowledgements

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9. General procedure for preparation of **4**. Under a nitrogen atmosphere at −78 °C, to a stirred suspension of $Cp_2Zr(H)Cl$ (2 mmol) in CH_2Cl_2 (5 mL) was added allene1 (3 mmol) in CH_2Cl_2 (3 mL). The reaction was gradually warmed up to room temperature, where a red solution resulted. The reaction was rechilled to −78 °C, and a solution of aldehyde (1 mmol) in CH_2Cl_2 (5 mL) was then added. After 30 min, the reaction was stopped by adding

sat. aq. $NaHCO_3$. Extractive workup was followed by purification (SiO_2 preparative TLC, hexane) giving **4**. (b) Selected data for **4f**: IR (neat): 1930, 1875, 1600, 1490, 1450, 1410, 1375, 1325, 1175, 1060, 853 cm^{-1}. ^1H NMR (400 MHz. $CDCl_3$): $\delta = 7.18$ (d, $J = 8.0$ Hz, 2H), 6.86 (d, $J = 8.0$ Hz, 2H), 6.79 (dd, $J = 17.8$, 10.8 1H), 6.41 (s, 1H), 5.36 (dd, $J = 17.8$, 0.8 Hz 1H), 5.15 (dd, $J = 10.8$, 1 Hz, 1H), 3.80 (s, 3H), 2.35 (t, $J = 7.2$ Hz, 2H), 1.51–1.59 (m, 2H), 1.37–1.44 (m, 2H), 0.95 (t, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz. $CDCl_3$): $\delta = 168.3$, 138.1, 134.4, 130.6, 130.2 130.1 128.7 127.8, 114.4, 113.5, 55.2, 33.6, 31.2, 22.8, 14.0. Anal. calcd for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.30; H, 9.37.

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13. General procedure for preparation of **5**: Under a nitrogen atmosphere at −78 °C, to a stirred suspension of $Cp_2Zr(H)Cl$ (2 mmol) in CH_2Cl_2 (5 mL) was added allene **1** (3 mmol) in CH_2Cl_2 (3 mL). The reaction was gradually warmed up to room temperature, where a red solution resulted. To the resultant mixture was added $CuBr{\cdot}SMe_2$ (0.025 mmol) and α,β-unsaturated ketone (1 mmol), and stirred at rt. This was monitored by TLC, and quenched with wet Et_2O. Extractive workup was followed by purification (SiO_2 preparative TLC, hexane–EtOAc 10:1) giving **5**. (b) Selected data for **5c**: IR (neat): 1690, 1665, 1611, 1590, 1565, 1485, 860, 750, 695 cm^{-1}. ^1H NMR (400 MHz. $CDCl_3$): $\delta = 7.15$–7.99 (m, 9H), 5.75 (t, $J = 6.8$ Hz, 1H), 3.47–3.54 (m, 1H), 3.32–3.39 (m, 2H), 2.50–2.67 (m, 1H), 2.44–2.51 (m, 1H), 2.39 (s, 3H), 2.10–2.17 (m, 2H), 1.23–1.40 (m, 4H), 0.97 (t, $J = 6.8$ Hz, 3H), 0.08 (s, 9H). ^{13}C NMR (100 MHz. $CDCl_3$): $\delta = 199.4$, 143.5, 142.1, 137.8, 137.7, 136.1, 133.3, 129.5, 128.9, 128.5, 127.8, 45.0, 41.4, 35.9, 32.8, 30.0, 23.6, 21.4, 14.5, 0.9. MS (EI): m/z (%) = 392 (3.5). Anal. calcd for $C_{26}H_{36}OSi$: C, 79.53; H, 9.24. Found: C, 79.54; H, 9.19.
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15. General procedure for preparation of **6**. To the solution of MCPBA (0.33 mmol) in CH_2Cl_2 (10 mL) was added **5** (0.3 mmol). The mixture was stirred at rt until the vinylsiane disappeared as determined by TLC. The mixture was washed in turn with sat. aq. $NaHCO_3$, sat. brine, and water. The solvent solution of TFA (0.33 mmol) in MeOH (10 mL) was added. After refluxing for 2 h, the reaction was worked up and a pure product was obtained by column chromatography (silca gel; ligHt petroleum–EtOAc, 15:1). (b) Selected data for **6a**. IR (neat): 1679, 1596, 1579, 823, 746, 689 cm^{-1}. ^1H NMR (400 MHz. $CDCl_3$): $\delta = 7.09$–7.94 (m, 14H), 3.40–3.47 (m, 1H), 3.33–3.35 (m, 2H), 2.90–2.99 (m, 1H), 2.75–2.83 (m, 1H), 2.30 (s, 3H), 2.20–2.28 (m, 1H), 2.03–2.13 (m, 1H). ^{13}C NMR (100 MHz. $CDCl_3$): $\delta = 200.0$, 198.8, 140.8, 137.1, 136.9, 136.1, 132.9, 132.8, 129.3, 128.5, 128.0, 127.9, 127.5, 46.2, 40.3, 36.8, 30.6, 210. MS (EI): m/z (%) = 357 (76.5), 105 (100). Anal. calcd for $C_{25}H_{24}O_2$: C, 84.24; H, 6.79. Found: C, 84.27; H, 6.84.