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Selective Protonation/Iodination of Unsymmetrical Zirconacyclopentadienes

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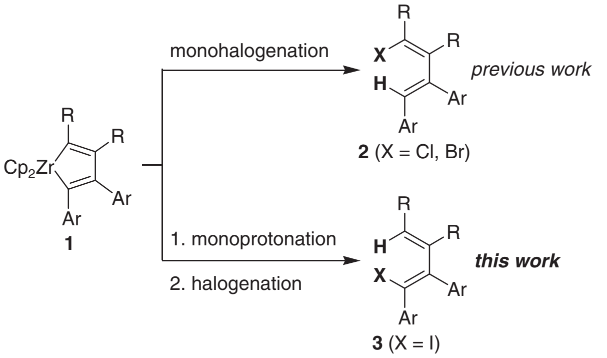
Selective monohalogenation reaction of unsymmetrical zirconacyclopentadienes was developed by selective protonation and iodination reactions. Among the examined acids, acetic acid and acetylacetone showed the best yield and selectivity to afford the corresponding monoiododienes. For the zirconacyclopentadiene prepared from 3-hexyne and diphenylacetylene, the Et-bearing carbon–zirconium bond was selectively protonated with more than 90% selectivity.

Development of selective reaction of unsymmetrical metallacycles which have two different metal–carbon bonds is attractive and important.[1] In particular, selective cleavage of one of the two metal–carbon bonds is very attractive for organic synthesis. Previously we have developed selective monohalogenation reaction by NCS or NBS of unsymmetrical zirconacyclopentadienes[2] which were conveniently prepared from two different alkynes; one is alkyl-substituted alkyne and the other is aryl-substituted alkyne as shown in eq 1.[3] This selective reaction could be applied for linear triene or tetraene formation from three or four different alkynes.[4] However, by this method opposite monohalogenation product **3** could not be prepared. In this paper we would like to report a novel procedure to provide the opposite monohalogenation product **3** from the unsymmetrical zirconacyclopentadienes.

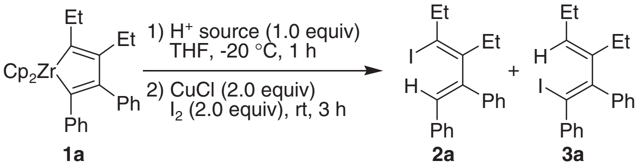


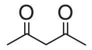
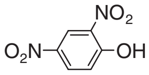
(1)

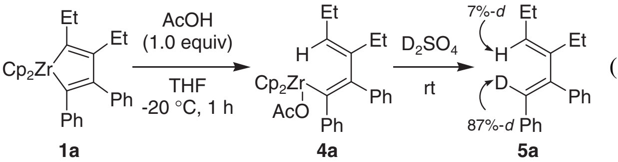
We found that when zirconacyclopentadiene **1a** was treated with 1 equiv of CH_3CO_2H, selective cleavage proceeded to give **4a** as shown in eq 2. Its ^1H NMR spectrum clearly showed a triplet signal at 5.5 ppm assignable to the diene proton and a singlet at 6.1 ppm assigned to Cp protons. Deuterolysis of **4a** with D_2SO_4 afforded monodeuterated product **5a** in 77% NMR yield, predominantly. Deuterium incorporations were 87% for the phenyl-bearing carbon, and 7% for the ethyl-substituted one.

This selective protonation can be rationalized by the different basicity of the two carbons attached to zirconium atom, one with an alkyl group and the other with an aryl group. The carbon attached to the alkyl group is more basic and protonation occurs at the more basic carbon predominantly.

Table 1. Formation of monoiododienes **2a** and **3a** by selective protonation/iodination of zirconacyclopentadiene **1a**



Entry	Proton source	Yield of **2a** + **3a**/%	Ratio of **2a**:**3a**
1	*t*-BuOH	17	35:65
2	H_2O	37	16:84
3	MeOH	53	19:81
4	PhOH	57	11:89
5		74	8:92
6	PPTS	55	10:90
7	AcOH	80	9:91
8	$PhCO_2H$	52	12:88
9		34	13:87
10	CSA	0	–



77%

(2)

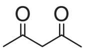
In order to make this selective protonation useful, we converted **4** into monoiodinated diene derivatives **3**.[5,6] Our previous selective chlorination and bromination with NCS or NBS of **1** afforded monohalogenation product **2** after hydrolysis.[3] Therefore, this selective protonation/halogenation provides **3** as products which are the isomers of **2**.

Monoiodination was carried out by the selective protonation with various proton sources followed by iodination with CuCl giving **2a** and **3a**. The results are shown in Table 1.

Reactions with 1 equiv of alcohols or water afforded the products in relatively low yields. This is due to weak acidity of alcohols. High yields and high selectivity were achieved by using acetic acid and acetylacetone. The yield of **2a** was 74% when **1a** was treated with acetylacetone followed by iodination in the presence of CuCl. High selectivity (8:92) was achieved in this case. The reaction of **1a** with acetic acid gave **3a** in 80% combined yield with the selectivity of **2a**:**3a** = 9:91.

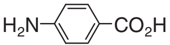
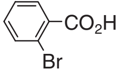
Table 2 summarized the results of the protonation/iodination sequence with acetylacetone or acetic acid at various

Table 2. Temperature effects on the selective protonation/iodination of zirconacyclopentadiene **1a**

Entry	H^+ source	Temp/°C	Time/h	Yield of $\mathbf{2a} + \mathbf{3a}$/%^{a}	Ratio of **2a**:**3a**
1		0	12	65	8:92
2		50	12	96	5:95
3	AcOH	0	12	71	7:93
4	AcOH	−20	1	96	7:93
5	AcOH	−40	3	68	13:87
6	AcOH	−78	3	33	9:91

^{a}NMR yield.

Table 3. Reactions with various carboxylic acids

Entry	H^+ source	Yield of $\mathbf{2a} + \mathbf{3a}$/%^{a}	Ratio of **2a**:**3a**
1	HCO_2H	93	9:91
2	$CH_3CH_2CO_2H$	92	11:89
3	$PhCOCH_2CH_2CO_2H$	94	9:91
4		93	11:89
5		92	4:96
6	$C_6F_5CO_2H$	70	6:94
7	CF_3CO_2H	78	13:87
8	CCl_3CO_2H	74	11:89
9	$HO_2CCO_2H^b$	70	7:93
10	$HO_2C{-}C{\equiv}C{-}CO_2H^b$	84	8:92

^{a}NMR yield. ^{b}0.5 equiv.

Table 4. Formation of monoiododienes with various substituents

Entry	R	Ar	Yield of $\mathbf{2} + \mathbf{3}$/%^{a}	Ratio of **2**:**3**
1	Bu	Ph	74	9:91
2	Bn	Ph	81	8:92
3	Et	*p*-Tol	87	6:94
4	Et	*p*-$MeOC_6H_4$	78	9:91
5	Et	*p*-FC_6H_4	76	4:96
6	Et	3-thienyl	75	31:69

^{a}NMR yield.

temperatures. Among them, the reaction with acetylacetone at 50 °C provided the highest yield and selectivity. The yield was 96% and the ratio of **2a** and **3a** was 5:95. In contrast, protonation with acetic acid at −20 °C for 1 h gave the best result.

Table 3 shows the results of the protonation/iodination of **1a** with various carboxylic acids. The ratio of **2a** and **3a** was around 10:90. When relatively stronger acids such as C_6F_5COOH, CF_3COOH, CCl_3COOH, and HOOCCOOH (Entries 6–9) were used, the yields were not high.

Zirconacyclopentadienes with other substituents were also examined for the monoiodination.[7] The results are shown in Table 4. A series of monoiododienes having Bu and Bn groups for alkyl groups (Entries 1 and 2), electron-donating or -withdrawing aryl groups (Entries 3–5) and heterocycle (Entry 6) were obtained in high yields with high selectivity.

When the monoiododiene **3** formed, the stereochemistry of the C=C bonds was kept. However, column separation with silica gel led to isomerization of stereochemistry of **3**. Even though the crude NMR spectra showed one set of peaks for **3**, after purification another set of peaks was also observed. Previously we met the similar C=C isomerization of arylated iodobutadienes.[8] In that case, the isomerization occurred during the iodination reaction of a Zr–C bond. In the present case, however, it occurred during silica gel column purification. Actually, stirring of monoiododiene **3** with silica gel in hexane under nitrogen did not afford the isomerized product, while 10% of isomerization was observed under air after 1 d. After several trials, we found that the use of an eluent containing triethylamine was effective for avoiding the isomerization during the column separation.

In summary, we realized another selective synthesis of monoiodobutadienes in contrast to our previous report.[3] The key step was establishment of highly selective monoprotonation of unsymmetrical zirconacyclopentadienes. Further functionalization and conversion of thus obtained iododienes are now in progress.

References and Notes

1 For unsymmetrical metallacyclopentadienes, see: a) J. R. Strickler, P. A. Wexler, D. E. Wigley, *Organometallics* **1988**, *7*, 2067. b) J. R. Strickler, P. A. Wexler, D. E. Wigley, *Organometallics* **1991**, *10*, 118. c) B. C. V. Wagenen, T. Livinghouse, *Tetrahedron Lett.* **1989**, *30*, 3495. d) S. L. Buchwald, B. T. Watson, J. C. Huffman, *J. Am. Chem. Soc.* **1986**, *108*, 7411. e) S. L. Buchwald, R. B. Nielsen, *J. Am. Chem. Soc.* **1989**, *111*, 2870. f) R. Hara, Z. Xi, M. Kotora, C. Xi, T. Takahashi, *Chem. Lett.* **1996**, 1003. g) T. Takahashi, D. R. Swanson, E. Negishi, *Chem. Lett.* **1987**, 623. h) J. E. Hill, G. Balaich, P. E. Fanwich, I. P. Rothwell, *Organometallics* **1993**, *12*, 2911.

2 Unsymmetrical zirconacyclopentadienes were prepared according to the literature. a) T. Takahashi, F.-Y. Tsai, Y. Li, K. Nakajima, M. Kotora, *J. Am. Chem. Soc.* **1999**, *121*, 11093. b) T. Takahashi, Z. Xi, A. Yamazaki, Y. Liu, K. Nakajima, M. Kotora, *J. Am. Chem. Soc.* **1998**, *120*, 1672. c) T. Takahashi, M. Kotora, Z. Xi, *J. Chem. Soc., Chem. Commun.* **1995**, 361. d) Z. Xi, R. Hara, T. Takahashi, *J. Org. Chem.* **1995**, *60*, 4444. e) T. Takahashi, M. Kageyama, V. Denisov, R. Hara, E. Negishi, *Tetrahedron Lett.* **1993**, *34*, 687.

3 H. Ubayama, Z. Xi, T. Takahashi, *Chem. Lett.* **1998**, 517.

4 K. Kanno, E. Igarashi, L. Zhou, K. Nakajima, T. Takahashi, *J. Am. Chem. Soc.* **2008**, *130*, 5624.

5 For the iodination of zirconacyclopentadienes, see: a) C. Xi, S. Huo, T. H. Afifi, R. Hara, T. Takahashi, *Tetrahedron Lett.* **1997**, *38*, 4099. b) E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson, T. Takahashi, *J. Am. Chem. Soc.* **1989**, *111*, 3336. c) H.-J. Zhang, Z. Song, C. Wang, C. Bruneau, Z. Xi, *Tetrahedron Lett.* **2008**, *49*, 624. d) ref. 1e.

6 For the preparation of halo-dienes, see: a) E. Negishi, F. E. Cederbaum, T. Takahashi, *Tetrahedron Lett.* **1986**, *27*, 2829. b) S. Yamaguchi, R. Jin, K. Tamao, F. Sato, *J. Org. Chem.* **1998**, *63*, 10060. c) Z. Xi, X. Liu, J. Lu, F. Bao, H. Fan, Z. Li, T. Takahashi, *J. Org. Chem.* **2004**, *69*, 8547. d) Z. Xi, Z. Song, G. Liu, X. Liu, T. Takahashi, *J. Org. Chem.* **2006**, *71*, 3154. e) ref. 1e, 1h, and 5b.

7 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

8 T. Takahashi, D. Y. Kondakov, Z. Xi, N. Suzuki, *J. Am. Chem. Soc.* **1995**, *117*, 5871.