Highly regio- and diastereo-selective carbon–carbon bond formation reaction of unsymmetrical zirconacyclopentanes using copper salt

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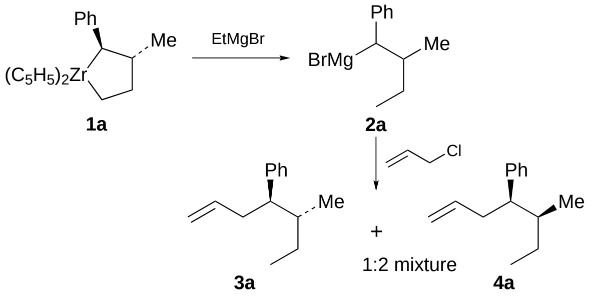
Reaction of unsymmetrical zirconacyclopentanes with allyl chloride or benzoyl chloride in the presence of copper chloride gave allylated or benzoylated products with high regio- and diastereo-selectivities.

Regio- and stereo-selective reactions are attractive and useful for organic synthesis. Recently we reported the unprecedented highly regioselective transmetalation of zirconacyclopentanes such as **1a** with EtMgBr to afford Grignard compound **2a**.[1] It is known that zirconacyclopentane **1a** is prepared by the reaction of $(C_5H_5)_2Zr(CH_2{=}CH_2)$,[2] which is generated from $(C_5H_5)_2ZrCl_2$, 2 equiv. of EtMgBr and β-methylstyrene with high stereo- and regio-selectivity.[3] However, further reaction of **1a**, for example with allyl chloride by transmetalation from zirconium to magnesium, gave a mixture of two diastereomers **3a** and **4a** in a ratio of almost 1 : 2 (Scheme 1). Here we report the regio- and diastereo-selective C–C bond formation reactions of unsymmetrical zirconacyclopentanes.

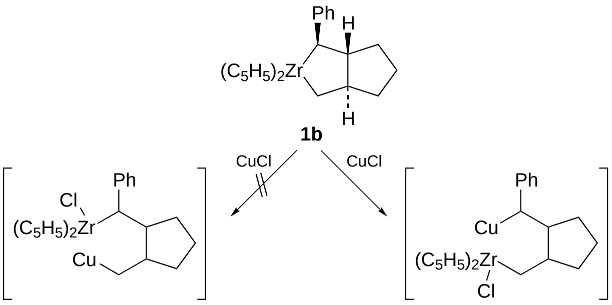


Scheme 1

Unsymmetrical zirconacyclopentanes **1a**–**d** were prepared by the reaction of β-methylstyrene with $(C_5H_5)_2ZrEt_2$[1,3] or by the reaction of dienes[3] or trienes[4] with $(C_5H_5)_2ZrBu_2$ (the Negishi reagent).[5] The unsymmetrical zirconacyclopentanes have two different Zr–C bonds. One of the most attractive aspects of these species is the regioselective C–C bond formation reactions of these two different Zr–C bonds. Reaction of zirconacyclopentane **1a** with allyl chloride in the presence of a stoichiometric amount of copper(I) chloride gave product **3a** in 64% yield as the sole product. The C–C bond formation reaction selectively proceeded at the carbon which had a phenyl substituent. The formation of the regioisomer was not observed (regioselectivity > 98%). More interestingly, the ^{13}C NMR spectrum of **3a** showed that the only one diastereoisomer was formed. This is in sharp contrast to the case with EtMgBr.

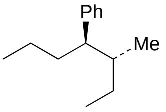
The stereochemistry of the product **3a** was determined by comparison of the ^{13}C NMR spectrum of its hydrogenation product with those of the two diastereomers **5** and **6** which were prepared as authentic samples. The ^{13}C NMR spectrum of the hydrogenation product of **3a** was identical to that of **5**. This result clearly indicated that this type of copper mediated C–C bond formation reaction of **1a** with allyl chloride gave diastereomerically pure product **3a** and no formation of its stereoisomer **4a** was observed. The stereochemistry between the Ph and Me substituents was maintained during this allylation reaction of **1a**.

Unsymmetrical bicyclic zirconacyclopentane **1b** also showed the same selectivity for the copper catalysed allylation reaction as shown in Table 1. Allylation product **3b** was obtained in 94% yield after hydrolysis. Iodinolysis instead of hydrolysis afforded **7b** in 90% yield. The allylation selectively occurred at the carbon which had a phenyl substituent. In the reaction of **1b** with BzCl the regioselectivity was very high (> 98%). The first step of this reaction is a transmetalation reaction from zirconium to copper as reported.[6–10] This suggests that this step is highly regioselective. The more sterically hindered carbon attached to zirconium is transferred to copper (Scheme 2) due to the repulsion between cyclopentadienyl ligands and the substituent. Even a methyl group at the β-position has a remarkable effect on the regioselectivity, as shown in the case of **1c** and **1d**. Allylation product **3c** and benzoylation product **8d** were obtained with > 98% regioselectivity.



Scheme 2

When **1b** reacted with allyl chloride or benzoyl chloride (Scheme 3), only one diastereomer was obtained as observed in the case of **1a**. The stereochemistry of the product **8b** was determined by X-ray analysis as shown in Fig. 1. It clearly showed that the stereochemistry of **1b** was also maintained during the reactions. There are two possible paths to explain this stereochemistry (Scheme 4). One is a retention-retention path for the transmetalation step and the C–C bond formation step. The other is an inversion-inversion path. The former path is more likely, although the mechanism is not clear yet.



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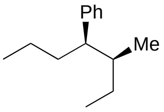

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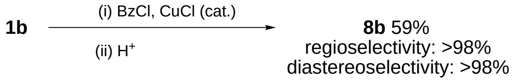
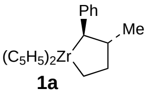
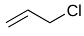
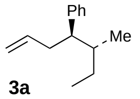
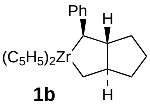
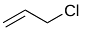
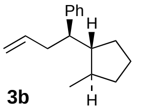
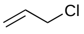
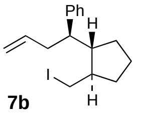
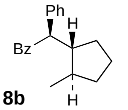
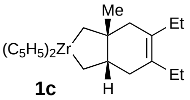
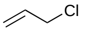
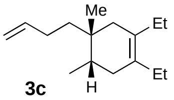
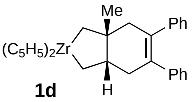
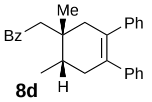


Scheme 3

Table 1 Regio- and diastereo-selective carbon–carbon bond formation reactions of unsymmetrical zirconacyclopentanes[a]

Zircona-cyclopentane	Chloride	*t*/h	*T*/°C	Product	Yield (%)[b]	Regio-selectivity	Diastereo-selectivity
 **1a**		1	0	 **3a**	64[c] (48)	>98	>98
 **1b**		6	0	 **3b**	94 (83)	>98	>98
		6	0	 **7b**	90 (78)	>98	>98
	BzCl	1	0	 **8b**	59 (49)	>98	>98
 **1c**		1	0	 **3c**	74 (58)	>98	*d*
 **1d**	BzCl	1	0	 **8d**	70 (59)	>98	*d*

[a] Catalytic amount (0.1 equiv.) of CuCl was used. [b] Yields were determined by GC. Isolated yields are shown in parentheses. [c] One equivalent of CuCl was used. [d] Product was diasteromerically pure.

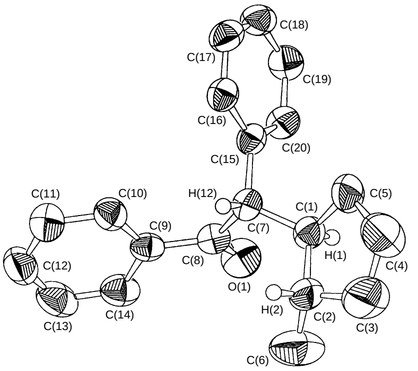
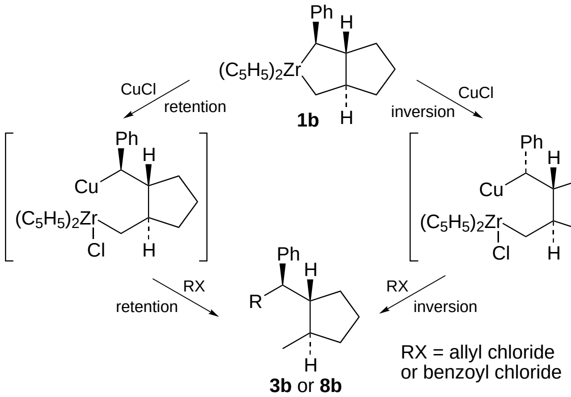


Fig. 1 ORTEP Drawing of **8b**



Scheme 4

Further investigations on the selective C–C bond formation characteristics of zirconacycles are in progress.

Footnotes and References

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† *Selected crystallographic data* for **8b**: CCDC 182/511.

1 T. Takahashi, T. Seki, M. Saburi and E. Negishi, XIVth International Conference on Organometallic Chemistry, Detroit, MI, 1990, B17; T. Takahashi, T. Seki, Y. Nitto, M. Saburi, C. J. Rousset and E. Negishi, *J. Am. Chem. Soc.*, 1991, **113**, 6266. For related catalytic reactions involving the transmetalation step of zirconacyclopentanes with RMgX, see also U. M. Dzhemilev, O. S. Vostrikova and G. A. Tolstikov, *J. Organomet. Chem.*, 1985, **285**, 43; A. H. Hoveyda and Z. Xu, *J. Am. Chem. Soc.*, 1991, **113**, 5079; K. S. Knight and R. H. Waymouth, *J. Am. Chem. Soc.*, 1991, **113**, 6268; D. P. Lewis, P. M. Muller and R. J. Whitby, *Tetrahedron Lett.*, 1991, **32**, 6297.

2 T. Takahashi, N. Suzuki, M. Kageyama, Y. Nitto, M. Saburi and E. Negishi, *Chem. Lett.*, 1991, 1579.

3 E. Negishi, D. Choueiry, T. B. Nguyen, D. R. Swanson, N. Suzuki and T. Takahashi, *J. Am. Chem. Soc.*, 1994, **116**, 9751.

4 T. Takahashi, M. Kotora, K. Kasai and N. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1994, 2693.

5 E. Negishi, F. E. Cederbaum and T. Takahashi, *Tetrahedron Lett.*, 1986, **27**, 2829.

6 T. Takahashi, M. Kotora and Z. Xi, *J. Chem. Soc., Chem. Commun.*, 1995, 1503.

7 K. Kasai, M. Kotora, N. Suzuki and T. Takahashi, *J. Chem. Soc., Chem. Commun.*, 1995, 109; B. H. Lipshutz and M. Segi, *Tetrahedron*, 1995, **51**, 4407.

8 L. M. Venanzi, R. Lehman, R. Keil and B. H. Lipshutz, *Tetrahedron Lett.*, 1992, **33**, 5857; T. Takahashi, M. Kotora, K. Kasai and N. Suzuki, *Tetrahedron Lett.*, 1994, **35**, 5685.

9 T. Takahashi, M. Kotora, K. Kasai and N. Suzuki, *Organometallics*, 1994, **13**, 4183.

10 T. Takahashi, R. Hara, Y. Nishihara and M. Kotora, *J. Am. Chem. Soc.*, 1996, **118**, 5154.

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