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## Zirconocyclisation : Access to New Racemic (di) Phosphines<sup>1</sup>

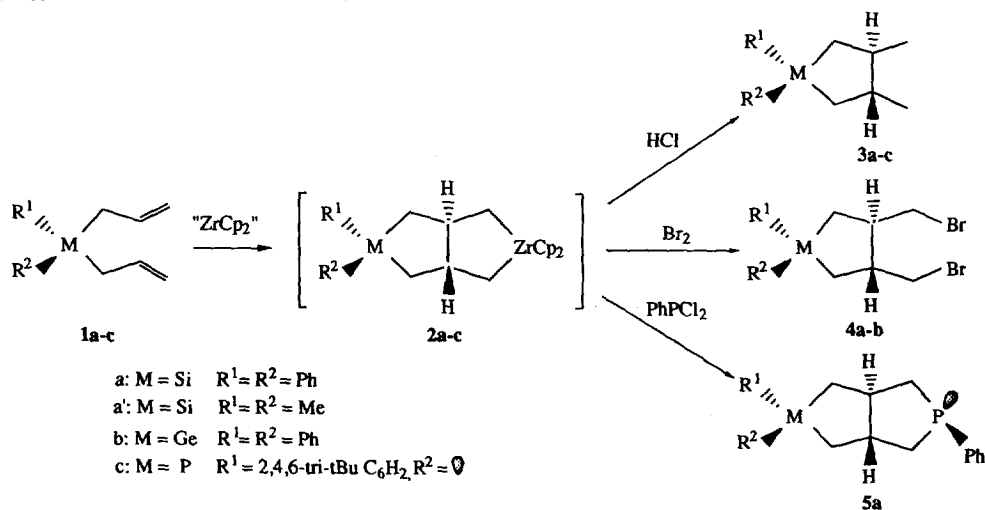
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**Abstract** - The bis-allylic **1** and the bis-propargylic **6** derivatives react with the zirconocene "ZrCp<sub>2</sub>" and lead, after electrophilic addition, to the corresponding chiral *trans* heterocyclopentanes (M=Si,Ge,P) **3-5** and bis-methylenecyclopentanes **8**. New chiral diphosphine **9** is obtained starting from the intermediate complex **2** or the functionalized heterocyclopentane **4**.  
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We have reported the stabilization of heteroallylic compounds by transition metal complexes (Mo, Co, W) leading to  $\sigma$  or  $\pi$  allylic complexes,<sup>2</sup> whereas an important part of the work of some of us was focused on the synthesis of various functionalized sila- and germacyclopentanes.<sup>3</sup> At the same time and independently, Nugent<sup>4</sup> and Negishi<sup>5</sup> developed a convenient method for generating metallocenes and their use in cyclisation of alkenes, alkynes, dienes, enynes and diynes. This metal-promoted cyclisation allowed various heterocyclisations.<sup>6-9</sup> Recent advances in the chemistry of zirconocene and related compounds show the interdisciplinary character of this research area and its usefulness as a versatile tool in synthetic chemistry.<sup>10</sup>

In view to prepare new chiral phosphine or diphosphine ligands for asymmetric catalysis,<sup>11-13</sup> we present the extension of the synthesis of various functionalized main group heterocyclopentanes **3**, **4**, **5** and **8** (Si, Ge, P) by the reaction of zirconocene "ZrCp<sub>2</sub>" with the corresponding bis-allylic **1a-c** (scheme 1) and bis-propargylic **6a-c** derivatives (scheme 2).



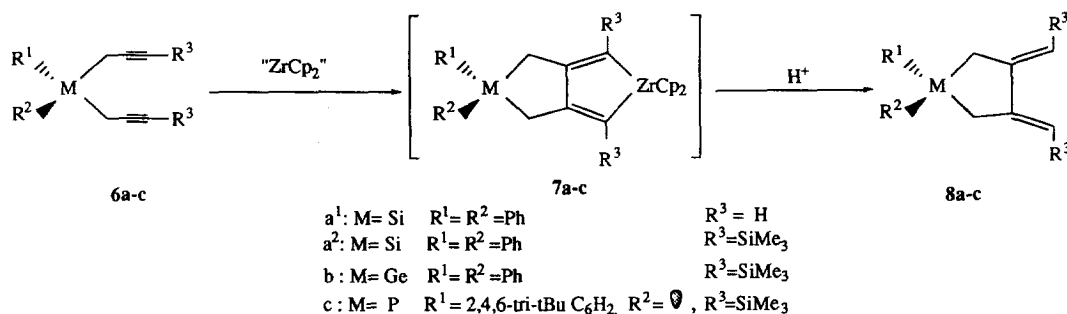
Scheme 1

The zirconocene "ZrCp<sub>2</sub>" was preliminary prepared following the well described methods<sup>5b</sup> by reaction of 2 molar equivalents of nBuLi with the dichlorozirconocene in THF solution at -78 °C. The unsaturated diallylic derivatives **1a-c** were added to this yellow solution maintained at low temperature. The mixture was then allowed to warm to room temperature and stirring was continued for 2 h until the red characteristic coloration of the **2a-c** complexes was obtained.

The protonolysis of the mixture with 10 % HCl afforded the corresponding heterocyclopentanes **3a-c** which were purified by silica column chromatography. **3a** was obtained as a white solid in 83% yield (eluent : hexane; m.p. 29°C), **3a'** as a colorless oil (eluent : pentane/ether 98/2) in 61 % isolated yield, **3b** as a colorless oil (eluent : hexane) in 45 % isolated yield, and the phospholane **3c** ( $\delta^{31}\text{P} = + 7.6$ ) as a yellow solid (eluent: CH<sub>2</sub>Cl<sub>2</sub>/ether 10/90) in 33 % yield.

The bromination of the zirconacyclopentadiene intermediates **2a-b** with an excess of Br<sub>2</sub> in CCl<sub>4</sub> at temperatures ranging from -78 to 20 °C afforded, after addition of 10 % H<sub>2</sub>SO<sub>4</sub> and workup followed by a purification on silica column, the corresponding functionalized heterocyclopentanes as white crystals : **4a** (eluent : hexane/ether 99/1; m.p. 73 - 75 °C) in 45% yield and **4b** (eluent : hexane/ether 90/10; m.p. 87 - 89 °C) in 45% yield.

The addition of the dichlorophenylphosphine as electrophile to the zirconabicyclopentane intermediate **2a** at room temperature led to the bicyclic compound **5a** which after purification on silica column (eluent : hexane/ether 97/3) is obtained as a white powder ( $\delta^{31}\text{P} = - 1.6$ ; m.p. 108 - 111 °C) in 46 % isolated yield.

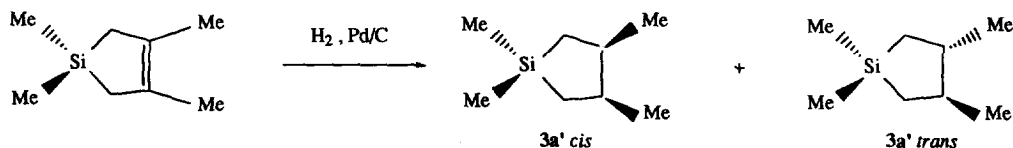


**Scheme 2**

Using the same protonolysis method than above, the zirconocyclisation was then extended to the diynes **6a-c** (Scheme 2). Thus, the bis-propargylsilane **6a**<sup>1</sup> led to the bis-methylene-1,1'-diphenyl-1-silacyclopentane **8a**<sup>1</sup> via the zirconabicyclopentadiene **7a**<sup>1</sup> but its low yield (10%) induced us to substitute the propargylic hydrogen by the SiMe<sub>3</sub> group. So, **8a**<sup>2</sup> was obtained after purification on silica column (eluent : hexane/ether 98/2) as a colorless oil in 60 % yield, **8b** (eluent : hexane/ether 99/1) as a pale yellow oil in 40 % yield, and **8c** (eluent : hexane/ether 95/5) as a yellow oil ( $\delta^{31}\text{P} = - 11.1$ ) in 50 % isolated yield. The structures of all these compounds were determined by their spectroscopic and analytical data.

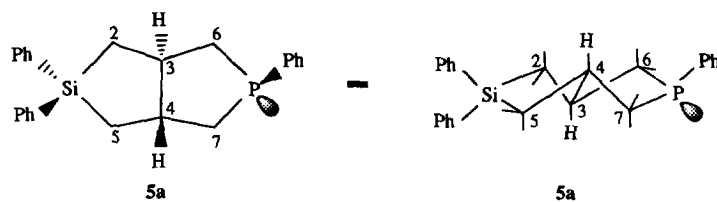
In the literature, the zirconium-mediated ring construction allows the selective cyclisation for dienes to either *cis*- or *trans*-1,2-disubstituted cyclopentanes.<sup>4e,5d,14</sup> In our approach, the reaction leading to the formation of heterocyclopentanes is regio and stereoselective. In any case, the zirconocyclisation gave stereoselectively *trans*-3,4-dialkyl-heterocyclopentanes **3-5**. In the particular case of sila- and germa-cyclopentanes **3-4(a-b)**, the *trans* configuration makes the R<sup>1</sup> and R<sup>2</sup> substituents magnetically equivalent, *i.e.*, for **3a'**, the methyl

substituents linked to silicon atom appear as a singlet ( $\delta^1\text{H} = 0.07$  and  $\delta^{13}\text{C} = -1.07$ ) and all the *ipso* carbon atoms of the phenyl substituents are equivalent for **3** and **4** [ $\delta^{13}\text{C}$  : 137.2 (**3a**); 139.0 (**3b**); 153.9 (**3c**); 135.4 (**4a**) and 137.3 (**4b**)]. In order to compare the NMR parameters of the *cis* and *trans* isomers, we have synthesized the silacyclopentane **3a'** in the two configurations. Starting from the corresponding silacyclopentene, the catalytic hydrogenation upon 10 % palladium on charcoal in hexane under 100 bar hydrogen pressure at 100 °C for 1 h leads to **3a'** as a 76/24 mixture of *cis* / *trans* isomers.

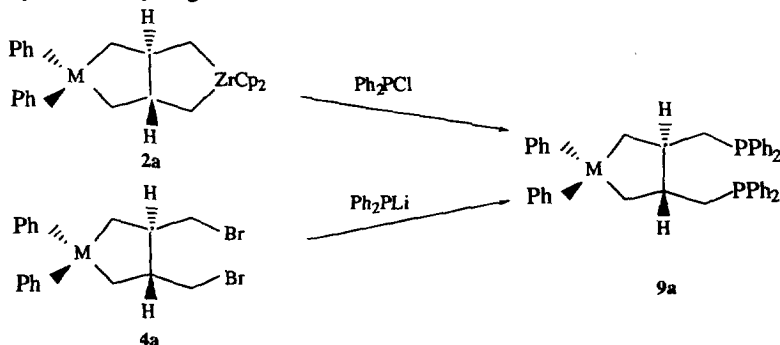


The two isomers are separated by GPC [DI 200, 10 % SE30, temperature gradient : 10 °C / mn, retention time for **3a'***cis* 243 s and for **3a'***trans* 210 s]. The methyl groups linked to silicon atom are diastereotopic for the *cis* isomer and exhibit two resonances ( $\delta^1\text{H} = 0.06$  and 0.15 ;  $\delta^{13}\text{C} = -0.87$  and 0.19).

In the case of the heterobicyclic compound **5a**, the *trans* configuration induces the non-equivalence of all the intra- and extracyclic carbons and we observe the  $^2\text{J}_{\text{CP}}$  and  $^3\text{J}_{\text{CP}}$  coupling constants only for C<sub>3</sub> ( $^2\text{J}_{\text{CP}} = 4.3$  Hz) and C<sub>5</sub> ( $^3\text{J}_{\text{CP}} = 4.4$  Hz) intracyclic carbon and not for C<sub>4</sub> and C<sub>2</sub>. Furthermore, the proton linked to the C<sub>3</sub> carbon is coupled with the phosphorus atom ( $^3\text{J}_{\text{HP}} = 30$  Hz) whereas any coupling is detected for the proton linked to the C<sub>4</sub> carbon. The notable effects observed for  $^3\text{J}_{\text{HP}}$  values are a consequence of the relative positions of the phosphorus lone pair and the ring atoms : their respective *syn* position involves a more important interaction with enhancement of the corresponding coupling constants.<sup>15</sup> Consequently, the *trans* configuration induces an intrinsic chirality to the phosphine **5**.



An evident application of this heterocyclisation is the easy access to new chiral diphosphines similar to the DIOP models synthesized by Kagan and co-workers.<sup>11</sup>



A direct synthesis of diphosphines **9** is carried out by addition of two equivalent of chlorodiphenyl phosphine to the corresponding intermediates **2** or by addition of  $\text{Ph}_2\text{PLi}$  to the functionalized cyclopentanes **4**. For example, the diphosphine **9a** was obtained after purification on silica column (eluent : hexane/ether 98/2) as a white powder ( $\delta^{31\text{P}} = -19$ ) in 40% yield. The resolution of the racemic phosphines **5** and diphosphines **9** will be performed using the procedure developed by Otsuku and co-workers *via* diastereoisomeric transition metal complexes.<sup>13</sup>

## References

1. Communication to *Société Française de Chimie* "5<sup>ème</sup> Journée Grand Sud-Ouest", Montpellier, Nov. 1995.
2. (a) Etemad-Moghadam, G.; El-Ouatib, R.; Ballivet-Tkatchenko, D. and Koenig, M. *Phosphorus, Sulfur and Silicon* **1993**, *76*, 41-44. (b) El-Ouatib, R.; Ballivet-Tkatchenko, D.; Etemad-Moghadam, G. and Koenig, M. *J. Organomet. Chem.* **1993**, *453*, 77-84.
3. (a) Manuel, G. and Boukherroub, R. *J. Organomet. Chem.* **1993**, *447*, 165-175. (b) Boukherroub, R.; Manuel, G.; Mignani, S.; Damour, D. *ibid* **1994**, *487*, 119-127. (c) Manuel, G.; Weber, W. P. and Boukherroub, R. *Main Group Met. Chem.* **1996**, *3* (in press)
4. (a) Nugent, W. A. and Calabrese, J.C. *J. Am. Chem. Soc.* **1984**, *106*, 6422-6424. (b) Nugent, W. A.; Thorn, D. L. and Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788-2796. (c) Fagan, P. J. and Nugent, W. A. *ibid.* **1988**, *110*, 2310-2312. (d) Rajanbabu, T. V.; Nugent, W. A.; Taber, D. F. and Fagan, P. J. *ibid.* **1988**, *110*, 7128-7135. (e) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 6435-6437.
5. (a) Negishi, E.; Holmes S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.*, **1985**, *107*, 2568-2569. (b) Negishi, E.; Cederbaum, F. E.; and Takahashi, T. *Tetrahedron Letters*, **1986**, *27*, 2829-2832. (c) Negishi, E.; Swanson, D. R.; Cederbaum, F. E. and Takahashi, T. *ibid* **1987**, *28*, 917-920. (d) Rousset, C. J.; Swanson, D. R.; Lamaty, F. and Negishi, E. *ibid* **1989**, *30*, 5105-5108.
6. Tour, J. T.; Wu, R. and Schumm, J. S., *J. Am. Chem. Soc.* **1990**, *112*, 5662-5663.
7. Horn, T.; Baumgarten, M.; Gerghel, L.; Enkelmann, V. and Müllen, K. *Tetrahedron Letters* **1993**, *34*, 5889-5892.
8. Dzhemilev, U. M., *Tetrahedron* **1995**, *51*, 4333-4346.
9. Barluenga, J.; Sanz, R. and Fananas, F. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1009-1010.
10. Negishi, E. I. Ed. *Tetrahedron Symposia -in -Print n°57*, *Tetrahedron* **1995**, *51*, 4255-4570.
11. Kagan, H.B. and Dang, T.P., *Chem. Comm.*, **1971**, 481.
12. Caplar, V., Comisso, G. and Sunjic, S. *Synthesis*, **1981**, 85-115.
13. (a) Knowles, W.S. *Acc. Chem. Res.*, **1983**, 106-112. (b) Pietrusiewicz, K.M. and Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375-1411.
14. (a) Knight, K. S.; Wang, D.; Waymouth, R. M. and Ziller, J.J. *J. Am. Chem. Soc.* **1994**, *116*, 1845-1854. (b) Wischmeyer, U.; Knight, K. S. and Waymouth, R. M. *Tetrahedron Letters* **1992**, *33*, 7735-7738.
15. Phosphorus-31 NMR Spectroscopy in Stereochemical Analysis., Ed. Verkade, J. G. and Quin, L. D. *VCH Publishers, Inc.* **1987**.

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