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Zirconocyclisation : Access to New Racemic (di) Phosphines¹

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Abstract - The bis-allylic 1 and the bis-propargylic 6 derivatives react with the zirconocene "ZrCp₂" 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. Copyright © 1996 Elsevier Science Ltd

We have reported the stabilization of heteroallylic compounds by transition metal complexes (Mo, Co, W) leading to σ or π allylic complexes,² whereas an important part of the work of some of us was focused on the synthesis of various functionalized sila- and germacyclopentanes.³ At the same time and independently, Nugent⁴ and Negishi⁵ 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.⁶⁻⁹ 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.¹⁰

In view to prepare new chiral phosphine or diphosphine ligands for asymmetric catalysis,¹¹⁻¹³ 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 "ZrCp₂" with the corresponding bis-allylic **1a-c** (scheme 1) and bis-propargylic **6a-c** derivatives (scheme 2).



Scheme 1

The zirconocene "ZrCp₂" was preliminary prepared following the well described methods^{5b} 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** (δ ³¹P = + 7.6) as a yellow solid (eluent: CH₂Cl₂/ether 10/90) in 33 % yield.

The bromination of the zirconacyclopentadiene intermediates **2a-b** with an excess of Br₂ in CCl₄ at temperatures ranging from -78 to 20 °C afforded, after addition of 10 % H₂SO₄ 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 ($\delta^{31}P = -1.6$; m.p. 108 - 111 °C) in 46 % isolated yield.



Using the same protonolysis method than above, the zirconocyclisation was then extended to the diynes **6a-c** (Scheme 2). Thus, the bis-propargylsilane **6a¹** led to the bis-methylene-1,1'-diphenyl-1-silacyclopentane **8a¹** via the zirconabicyclopentadiene **7a¹** but its low yield (10%) induced us to substitute the propargylic hydrogen by the SiMe₃ group. So, **8a²** 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 ($\delta^{31}P = -11.1$) 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.^{4e,5d,14} 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^1 and R^2 substituents magnetically equivalent, *i.e.*, for 3a', the methyl

substituents linked to silicon atom appear as a singlet ($\delta^{1}H = 0.07$ and $\delta^{13}C = -1.07$) and all the *ipso* carbon atoms of the phenyl substituents are equivalent for 3 and 4 [$\delta^{13}C$: 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 (δ ¹H = 0.06 and 0.15; δ ¹³C = -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 ${}^{2}J_{CP}$ and ${}^{3}J_{CP}$ coupling constants only for C₃ (${}^{2}J_{CP} = 4.3 \text{ Hz}$) and C₅ (${}^{3}J_{CP} = 4.4 \text{ Hz}$) intracyclic carbon and not for C₄ and C₂. Furthermore, the proton linked to the C₃ carbon is coupled with the phosphorus atom (${}^{3}J_{HP} = 30 \text{ Hz}$) whereas any coupling is detected for the proton linked to the C₄ carbon. The notable effects observed for ${}^{3}J_{HP}$ 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.¹⁵ 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.¹¹



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 Ph₂PLi to the funtionalized cyclopentanes 4. For example, the diphosphine 9a was obtained after purification on silica column (eluent : hexane/ether 98/2) as a white powder ($\delta^{31}P = -19$) 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.¹³

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