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Zirconium-mediated conversion of homoallylic ethers into cyclopropane derivatives

Vincent Gandon, Christophe Laroche and Jan Szymoniak*

Réactions Sélectives et Applications (UMR 6519), CNRS and Université de Reims, 51687 Reims Cedex 2, France

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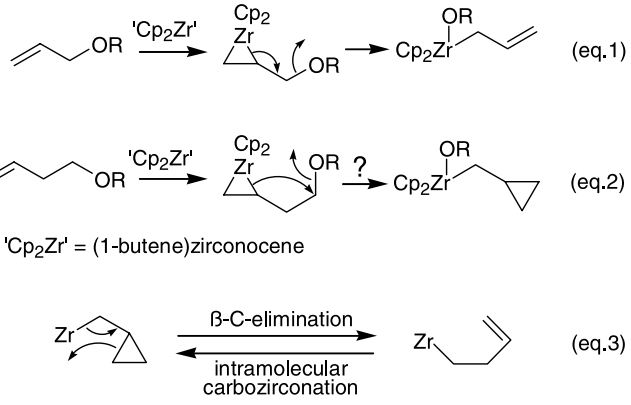
Abstract—Homoallylic ethers react with Cp_2ZrCl_2/2 *n*-BuLi reagent to afford cyclopropane derivatives. Cyclopropylcarbinyl–homoallyl rearrangements involving zirconium species are observed depending on the substrate structure. © 2003 Elsevier Science Ltd. All rights reserved.

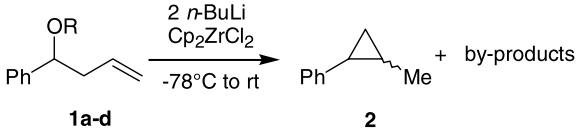
Allylic ethers react with (1-butene)zirconocene to afford allylzirconium derivatives.[1] This reaction proceeds through ligand exchange, formation of a zirconacyclopropane and the following β-elimination of the alkoxy group (Scheme 1, Eq. (1)). We speculated that, analogously, homoallylic ethers might be converted into cyclopropylcarbinylzirconium complexes through the γ-elimination of the alkoxy-group (Eq. (2)).[2] The corresponding cyclopropanes could then be generated from these species under protonolysis conditions.[3] Here we report on the feasibility of performing such transformations.

Various cyclopropylcarbinyl- or (cyclopropylmethyl)metal complexes have been described, based on transition metals such as Fe, Co, Pd, Ni, Rh, Mn, Pt and Ti.[4] Some of them were demonstrated to equilibrate through the cyclopropylcarbinyl–homoallyl rearrangement (Scheme 1, Eq. (3)) and to react with ring opening, thus operating as homoallyl equivalents. Furthermore, the hypothetical cyclopropylcarbinyl–homoallyl rearrangement involving zirconium was estimated to be slightly exothermic ($\Delta H \sim -6$ kcal/mol).[5] We began our study bearing these features in mind.

In the first experiments, unsaturated ethers **1a–d** (Scheme 2) were used in ligand exchange with (1-butene)$ZrCp_2$, preformed in situ from Cp_2ZrCl_2 and *n*-BuLi.[6] Typically, Cp_2ZrCl_2 (1 mmol) and compound **1** (1 mmol) were dissolved in THF (5 mmol), *n*-BuLi (2 mmol) was added at −78°C, and the mixture was allowed to warm to 20°C. The reactions were monitored by ^1H NMR and ended after a 3–5 h period with a hydrolytic work-up. Starting from **1c** (R = MOM) and **1d** (R = $SiMe_3$) complex mixture of products were observed. In contrast, significant amounts of the cyclo-



Scheme 1.



a: R=Me; b: R=Bn; c: R=MOM; d: R=$SiMe_3$
1a gives **2** (*trans*:*cis* = 2.7) , 65% NMR yield.

Scheme 2.

Keywords: cyclopropanes; homoallylic ethers; rearrangement; zirconium.

* Corresponding author. Fax: +33-326-913-166; e-mail: jan.szymoniak@univ-reims.fr

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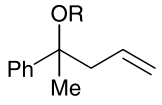
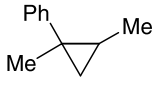
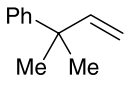
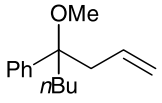
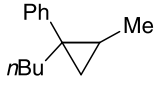
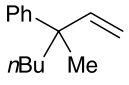
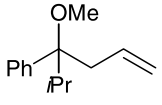
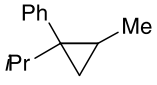
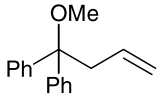
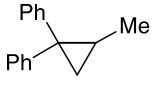
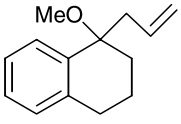
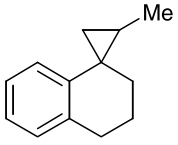
propane **2** were formed from **1a** (R = Me) and **1b** (R = Bn). In the first case (**1a**), the cyclopropane **2** was even the major product (65% NMR yield). It was accompanied by smaller quantities of 1-phenyl-1-butene and 1-phenyl-2-octene. In the second case (**1b**), a mixture of **2** and the same as well as two other deoxygenation and coupling products were formed. Similar results were obtained when using benzene as solvent in place of THF.

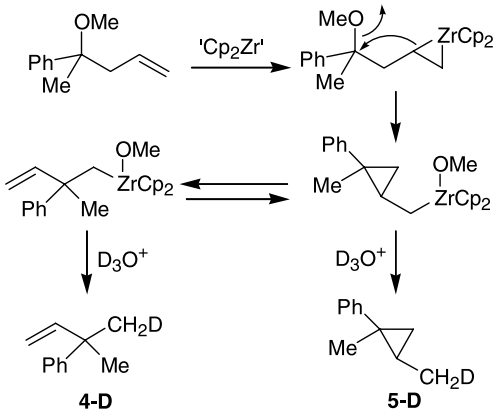
To further investigate the cyclopropanation reaction we next used homoallylic ethers with a tertiary α-C atom as substrate. These reactions, performed as previously, led to trisubstituted cyclopropanes which proved to be major or even unique products as shown in Table 1. Starting from ethers **3** and **6** with Ph and respectively Me or *n*-Bu groups on α-C atom, mixtures of cyclopropanes (major) and alkenes were formed (entries 1 and 2). In contrast, cyclopropanes were solely obtained from ethers **9** or **11** with Ph and *i*-Pr or Ph groups (entries 3 and 4). Furthermore, spirocyclopropane **14** was formed in good yield starting from **13** (entry 5). The *trans* configuration was assigned to the major diastereomers of compounds **4**, **7** and **10** based on their ^{1}H NMR spectra and in accordance with the literature data.[7,8] The degree of diastereoselectivity does not depend significantly neither on the solvent used (THF, Et_2O, PhH) nor on the nature of the -OR group (R = Me, Bn, MOM) (entry 1).

The ratios of cyclopropanes versus the open chain-products in entries 1 and 2 (respectively **4**:**5** and **7**:**8**) are not sharply influenced by the solvent nor the OR group. We have noticed, however, that these ratios were markedly increased in favour of the cyclopropane by deacreasing of the temperature for hydrolysis. For example, when starting from **3a** and hydrolysing the reaction mixture at 50, 20, −10 and −40°C, the ratios of **4**:**5** were 6.8, 7.8, 10.4 and 14.0, respectively (GC monitoring). The **4**:**5** ratio seems almost constant during the

Table 1. Reaction of homoallylic ethers with 2 *n*-BuLi/Cp_2ZrCl_2[a]

Entry	Ether	Products	Yield (%) *(trans:cis)*
1		 	
	3a-c	**4** **5**	
	3a (R = Me)	7.8 : 1	85[b] (2.8:1)
	3b (R = Bn)	6.3 : 1	50[b] (3.2:1)
	3c (R = MOM)	7.4 : 1	60[b] (3.0:1)
2		 	79[c] (1.1:1)
	6	**7** **8**	
		14.5 : 1	
3			80 (1.4:1)
	9	**10**	
4			80
	11	**12**	
5			76 (1:1)
	13	**14**	

[a] Reaction performed in THF and hydrolysed at 20°C.
[b] Overall yield of two products.
[c] Isolated yield of cyclopropane.



Scheme 3.

reaction, which was demonstrated to come to completion within 3 h. Finally, deuterolysis of the reaction mixture with D_2O/D_2SO_4 (1 M) afforded the deuterated compounds **4-D** and **5-D** (Scheme 3).

The concomitant formation of cyclopropanes and alkenes in entries 1 and 2 is consistent with a cyclopropylcarbinyl–homoallyl rearrangement as shown in Scheme 3. Particularly, the deuteration experiments and the temperature effect further support an equilibrium between the cyclopropyl- and homoallyl zirconium species. In this context, the lack of rearrangement for the homoallylic ethers **9**, **11** and **13** is noteworthy. It might be attributed to the Thorpe–Ingold effect, i.e. angle compression at the substituted carbon.[9] Thus, the equilibrium totally in favour to the cyclopropyl zirconium species with **9**, **11** and **13**, would be attributed to a steric repulsion of the attached groups stronger than with **3** and **6**.

In summary, we have shown that cyclopropanes can be obtained from homoallylic ethers via zirconium-mediated γ-elimination reaction. In several cases, cyclopropylcarbinyl–homoallyl rearrangement has been noticed to occur. We are currently exploring these new transformations and particularly focus on their synthetic potential.

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7. Selected data for 1,2-dimethyl-1-phenylcyclopropane (**4**). Major isomer (*trans*): ^{1}H NMR ($CDCl_3$, 250 MHz) δ: 0.21–0.30 (m, 1 H), 0.93–1.06 (m, 2 H), 1.13 (d, $J=5.8$, 3 H), 1.30 (s, 3 H), 7.15–7.30 (m, 5 H); ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ: 14.1, 19.8, 20.5, 22.1, 23.4, 125.2, 126.6, 128.1, 148.9; MS (EI) m/z (%) 146 (22, $M^{+\bullet}$), 131 (100), 91 (42), 77 (24). Minor isomer (*cis*): ^{1}H NMR ($CDCl_3$, 250 MHz) δ: 0.51–0.59 (m, 1 H), 0.66 (d, $J=$ 5.8, 3 H), 0.71–0.90 (m, 2 H), 1.26 (s, 3 H), 7.15–7.30 (m, 5 H); NOE +5%: irrad. Me-1, obs. H-2; ^{13}C NMR ($CDCl_3$, 62.5 MHz) δ: 16.0, 19.2, 19.6, 26.1, 28.6, 128.0, 128.1, 129.5; MS (EI) m/z (%): 146 (24, $M^{+\bullet}$), 131 (100).
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9. (a) Sammes, P. G.; Weller, D. J. *Synthesis* **1995**, 1205; (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc*. **1991**, *113*, 224.