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Reaction of (cycloalkenyl)alkylzirconium compounds with alkynes: novel procedure for the formation of bicyclic compounds

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Abstract

Reaction of (cycloalkenyl)alkyl zirconium compounds with alkynes in the presence of MAO afforded bicyclic tetrahydroindene derivatives with a methyl group at the ring junction. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: zirconium; alkyne; MAO; cyclization.

The reactions of zirconium cationic species with unsaturated bonds have received considerable attention in recent years, and both alkyl- and alkenylzirconium cationic species were shown to react with alkenes and alkynes as well as with a carbonyl group under different conditions.[1] For example, cationic alkylzirconium compounds are very efficient catalysts for alkene polymerization,[1] cationic zirconium complexes generated by the reaction of alkyl- or alkenylchlorozirconocenes with $AgClO_4$ or similar salts reacted with aldehydes to give saturated secondary and secondary allylic alcohols,[2] cationic zirconium complexes formed by the reaction of Cp_2ZrCl_2 and MAO[3] or $Cp^*{}_2ZrMe_2$ and $B(C_6F_5)_3$ with excess of Me_3Al[4] cyclize 1,5-, 1,6-, 1,7-dienes to the corresponding five-, six, and seven-membered ring compounds. Recently, it has also been shown that alkyl- and allylchlorozirconium complexes reacted in the presence of a catalytic amount of $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ or MAO with carbon–carbon triple bonds to give functionalized alkenes.[5]

During our research of cyclization reactions by means of zirconocene derivatives we realized that it would be of interest to develop a reaction sequence capable of constructing a bicyclic framework in one step from easily accessible starting material. While studying cyclization reactions of 2-chloro-1,ω-dienes, prepared by double allylation of alkynes,[6] with the Negishi

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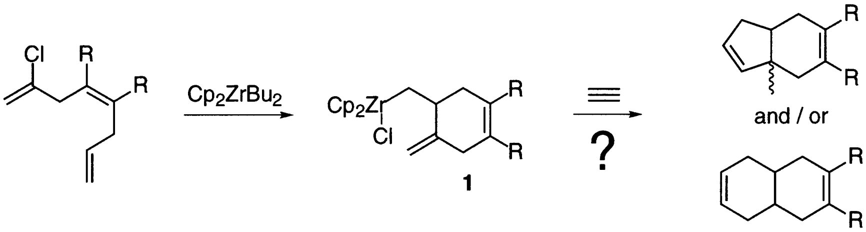
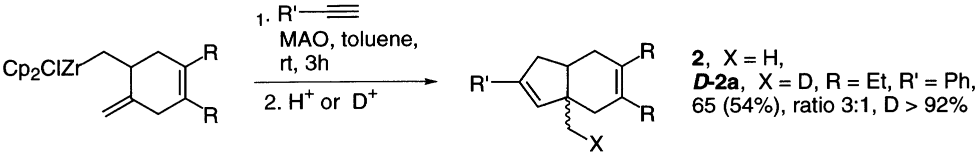
reagent to give 1-methylene-2-methylcycloalkanes, as it was initially reported by us[7] and later by others,[8] we came to the conclusion that the intermediate organozirconium compound **1** could be utilized in subsequent C–C bond formation reactions with alkenes and alkynes followed by intramolecular cyclization with the participation of the *exo* double bond to give 5–6 or 6–6 fused bicyclic compounds (Eq. 1).



(1)

Herein, we would like to present a novel method for the formation of bicyclic compounds based on the reaction of (cycloalkenyl)alkylzirconium compounds **1** with terminal alkynes. Typically, organozirconium compound **1**, prepared by the reaction of the Negishi reagent with 2-chloro-1,4,7-trienes,[7] reacted with alkynes in the presence of MAO at room temperature, followed by hydrolysis to afford 5–6-fused bicyclic compounds **2** (Eq. 2).[9] It is noteworthy that the reaction gave only *exo*-trig cyclization products. Moreover, this cyclization renders it possible to construct a quaternary carbon at the ring junction, where construction is generally considered to be a difficult task. Some representative examples of the bicycle formation are given in Table 1.



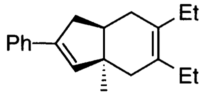
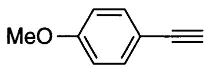
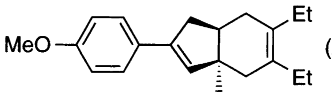
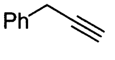
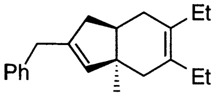
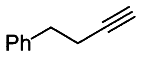
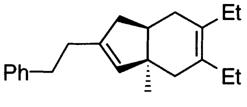
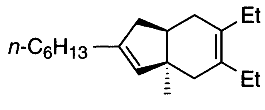
(2)

Generally, in all instances the addition proceeded at the substituted carbon of the triple bond, followed by *exo-trig* cyclization. Initially, the cyclization of chlorodiene was carried out in THF, which was then removed under reduced pressure and substituted for 1,2-dichloroethane prior to the addition of MAO and phenyl acetylene. In this case, the bicycle **2a** was obtained as a 3:1 mixture of isomers in reasonable yield (61%). However, the change of the solvent during the course of the reaction was not considered practical and we found that the overall reaction sequence can be conveniently carried out in toluene. Thus, the reaction of **1** with phenylacetylene (entry 1) in toluene afforded **2a** in higher yield (71%) in comparison with the previous case, also as a 3:1 mixture of isomers. The stereochemistry of the isomers **2a** was determined by comparison with the authentic sample of the *cis* isomer of **2a** which was prepared using a known procedure.[10] The methyl groups at the bridge-head of the *cis* isomers showed characteristic chemicals shifts 28.6–29.0 ppm in their ^{13}C NMR spectra. The methyl signals of the *trans* isomers appeared at 26.7–26.9 ppm in their ^{13}C NMR spectra.

The use of 4-methoxyphenylacetylene (entry 2) furnished the bicycle **2b** in reasonable yield (65%) as a 1.6:1 mixture of isomers. The reaction with 3-phenylpropyne (entry 3) gave the bicycle **2c** in good yield (72%) as a 1:1 mixture of isomers.

Alkyl substituted acetylenes such as 4-phenylbutyne (entry 4) and 1-octyne (entry 5) reacted as well and afforded the bicycles **2d** and **2e** in moderate yields of 56% (3:1 ratio of isomers) and

Table 1
Reaction of **1a** with alkynes to give bicycles **2** in the presence of MAO

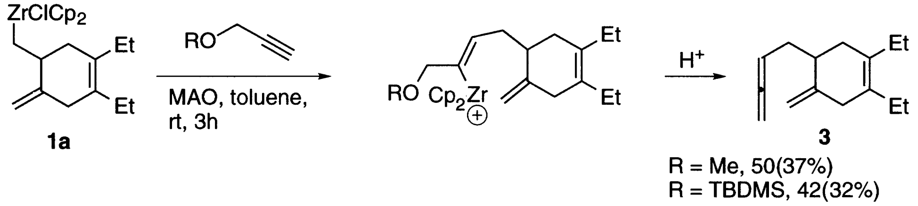
Run	Alkyne	Major products	Isomer ratio	Yield (%)[a]
1	Ph—≡	 **(2a)**	3:1	71 (56)
2		 **(2b)**	1.6:1	65 (49)
3		 **(2c)**	1:1	72 (52)
4		 **(2d)**	3:1	56 (40)
5	*n*-C_6H_{13}—≡	 **(2e)**	1:1	57 (41)

[a] GC yields. Isolated yields are in parentheses. Mixture of cis and trans isomers.

57% (1:1 ratio of isomers), respectively. Quenching of the reaction mixture with DCl afforded *D*-2a in 65% (54%) yield (a 3:1 mixture of diastereoisomers) with deuterium incorporation in >92% (Eq. 2). Internal alkynes such as 4-octyne did not give the desired product.

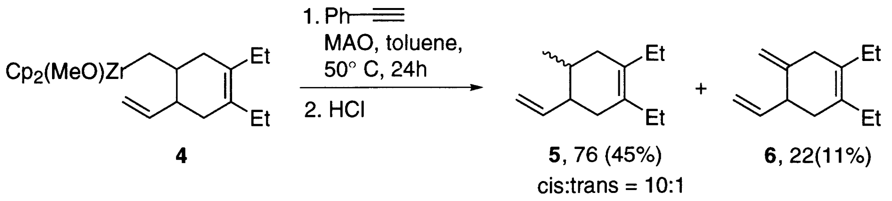
The reaction of **1a** with phenylacetylene was used to check other methods for the generation of a cationic species as well. The obtained results can be summarized as follows: (i) the change of MAO to Me_3Al did not result in any reaction, (ii) a combination of Me_3Al with a catalytic amount of $B(C_6F_5)_3$ (5%) furnished **2a** albeit in a low yield of 10%, (iii) the use of $AgOSO_2CF_3$ to generate the cationic species did not result in the formation of any observable products, and (iv) in the presence of a catalytic amount of $Ph_3CB(C_6F_5)_4$ (5 mol%) the reaction proceeded smoothly to give **2a** in good yield (64%).

Surprisingly, the reaction of **1** with methyl- or dimethyl(*t*-butyl)silylpropargyl ethers afforded the allene derivative **3** instead of the expected bicyclic compound in 50 and 42% yields, respectively. The insertion obviously proceeded at the unsubstituted carbon of the triple bond, giving rise to the α-organozirconium-β-alkoxy compound which underwent dealkoxymetalation to afford the allene **3** after hydrolysis (Eq. 3). Although the cause of the change in the regioselectivity of the insertion is not clear, coordination or interaction of the oxygen atom of the propargyl ethers to the zirconium atom during the course of the reaction is reasonably presumed. A similar phenomenon has been observed in the reactions of propargylic ether with organocopper compounds.[11]



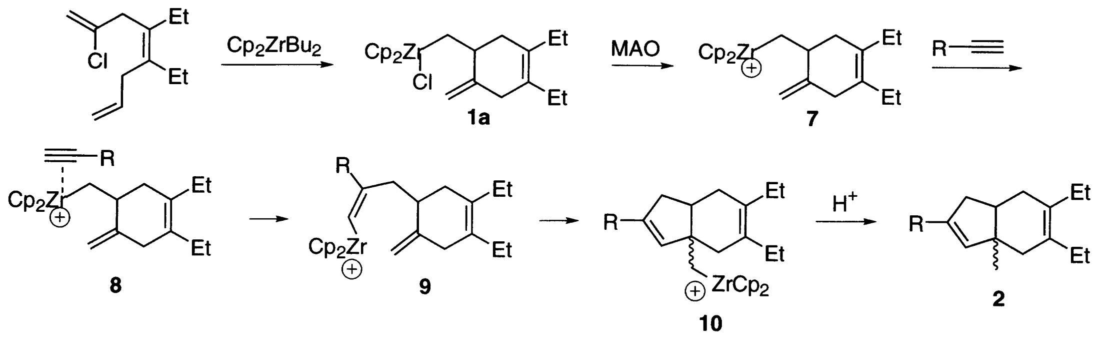
(3)

Interestingly, when compound **4**, prepared by the reaction of the Negishi reagent with 9-methoxy-4,5-diethylnona-1,4(*Z*),7(*E*)-triene,[10] was treated with MAO and phenylacetylene under the identical conditions, no insertion reaction was observed (Eq. 4). Even after heating the reaction mixture at 50°C for 24 h, insertion of the triple bond into the Zr–C bond did not take place. After hydrolysis, a mixture of **5** and **6** was formed in 76% (*cis*:*trans* = 10:1) and 22% yields, respectively. Inhibition of the insertion of an alkyne may be explained by coordination of the vinyl group, which blocks the vacant site of the Zr atom of the cationic species. This would effectively prevent an alkyne from approaching the metal–carbon bond.



(4)

It is reasonable to assume that the mechanism of the reaction of **1a** with an alkyne proceeds as follows: (i) formation of **1a** by the reaction of Negishi's reagent with 2-chloro-4,5-diethyl-1,4,7-triene, (ii) reaction of **1a** with MAO to produce the cationic species **7**, (iii) coordination of an alkyne to the Zr atom giving **8**, (iv) insertion of an alkyne into the Zr–sp^3C bond of **8** to give **9**, (v) intramolecular insertion of the *exo*-methylene moiety into the Zr–sp^2C bond to afford **10**, and finally hydrolysis furnishes **2** (Scheme 1).



Scheme 1.

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9. Typical experimental procedure: To a solution of **1a** (1 mmol) in toluene, prepared 'in situ' from 1 equiv. of Negishi reagent and 2-chloro-4,5-diethyl-1,4,7-triene (199 mg, 1 mmol), was added 1 mL of toluene solution of MAO (9 wt%) and phenylacetylene (102 mg, 1 mmol) at −78°C followed by warming to ambient temperature. After stirring for 3 h, the reaction mixture was quenched with 3N HCl to furnish the corresponding bicyclic compounds **2**. (**3a***R**,**7a***R**)-**3a**,**4**,**7**,**7a**-Tetrahydro-2-phenyl-3a-methyl-5,6-diethylindene (**2a**). Isolated yield 56%. A 3:1 mixture of isomers. *Cis* isomer: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, $J = 7.5$ Hz, 6H), 1.12 (s, 3H), 1.19–1.27 (m 10H), 2.92–2.99 (m, 1H), 5.87 (s, 1H), 7.17–7.44 (m, 5H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.42, 13.47, 25.89, 25.98, 28.61, 34.12, 40.42, 40.44, 43.76, 49.73, 125.48, 126.73, 127.49, 127.92, 128.17, 131.98, 132.96, 135.76, 136.78, 139.17. *Trans* isomer: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 0.90 (t, $J = 7.5$ Hz, 6H), 1.12 (s, 3H), 5.73 (s, 1H), other peaks are covered by the major isomer; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.27, 16.16, 25.76, 26.17, 26.75, 32.65, 37.38, 39.27, 46.34, 49.05, 125.34, 126.51, 126.82, 127.03, 128.25, 130.92, 131.94, 136.50, 138.20, 141.45. HRMS cacld for $C_{20}H_{26}$: 266.2034, found: 266.2034.
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