C–H Insertion

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Intramolecular Concerted Insertion of Vinyl Cations into C–H Bonds: Hydroalkylating Cyclization of Alkynes with Alkyl Chloroformates To Give Cyclopentanes**

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Recently we reported on the hydroalkylation of alkenes with alkyl chloroformates induced by ethylaluminum sesquichloride (Et3Al2Cl3).[7] The reaction of the Lewis acid, for example, with isopropyl chloroformate (1a) gives the isopropyl cation, which adds across the alkene. Transfer of a hydride ion from an ethylaluminum sesquichloride species to the adduct carbenium ion takes place by formation of the hydroalkylation product (Scheme 1).

Scheme 1. Mechanism of the hydroalkylation of alkenes with isopropyl chloroformate (1a) induced by ethylaluminum sesquichloride. R = alkyl.

The application of this reaction to alkynes was expected to give analogously alkylated alkenes. The reaction of 4-octyne (2a) and 1a under similar reaction conditions in the presence of Et3Al2Cl3 and with Et3SiH as an additional hydride donor[8] was expected to proceed via vinyl cation 3a to give 4-isopropyl-4-octene (4a) (Scheme 2). To our surprise this product was formed only as a side product (<5%). We isolated 1-isopropyl-2-propylcyclopentane (5a) in 79% yield as a mixture of two diastereomers in a ratio of 4.6:1. The analogous reaction of 5-decyne (2b) afforded the 1,2,3-trialkyl-substituted cyclopentane 5b in 74% yield as a mixture of four diastereomers in a ratio of 11:6:1:1. In this case, too, the hydroalkylation product 4b was obtained in about 12% yield. Reaction of 1-octyne (2d) with 1a in the presence of Et3Al2Cl3/Et3SiH proceeding via vinyl cations 3a–d. Products 5a,b and 6c,d as well as the side products 4a–d were obtained as mixtures of diastereomers. Products derived from the exocyclic cyclopentyl cation 8 were not observed.

Scheme 2. Reactions of alkynes 2a–d with 1a in the presence of Et3Al2Cl3/Et3SiH proceeding via vinyl cations 3a–d. Products 5a,b and 6c,d as well as the side products 4a–d were obtained as mixtures of diastereomers. Products derived from the exocyclic cyclopentyl cation 8 were not observed.

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The formation of products 4–6 can be explained as follows: The initially formed 2-propyl cation adds across the C=C triple bond to give vinyl cations 3. If a C–H bond is available in position 5 of 3 an intramolecular 1,5-hydride shift takes place to give cyclopentyl cations 7a and 7b, respectively, with formation of a new C–C bond. Finally, intermolecular hydride transfer leads to the products 5a and 5b, respectively. The intramolecular 1,5-hydride shift is definitely faster than the intermolecular hydride transfer from Et₃Al₂Cl₃ or Et₃SiH yielding hydroalkylation products 4. In the case of alkyne 2c a 1,5-hydride shift is not possible. Therefore vinyl cation 3c is mainly trapped by transfer of a chloride ion from chloroformate 1a or an EtAlCl₃⁻ species to give chloroalkanes 6c. Apparently the transfer of a chloride ion to the vinyl cation intermediate is faster than the transfer of a hydride ion. Marcuzzi and Melloni reported on the chloroalkylation of alkynes using chloroalkanes in the presence of Lewis acids. In analogy, the cyclization of vinyl cation 3d should be possible by formation of the exocyclic carbenium ion 8. However, products derived from 8 were not observed, giving evidence that a fast 1,5-hydride shift takes place only if an endocyclic carbenium ion such as 7a,b is formed. Thus, alkynes 2e and 2f were treated with 2-buty1 chloroformate (1b) in the presence of Et₃Al₂Cl₃ and Et₃SiH. As expected, we observed the formation of the cyclopentane derivatives 10c and 10d via vinyl cations 9c and 9d, respectively (Scheme 3). The diastereomeric mixtures of compounds 10c and 10d were obtained in yields of 26% (GC) and 13% (GC), respectively. Interestingly, the reaction of alkyne 2a with alkyl chloroformate 1b via vinyl cation 9a gave cyclopentane 10a as well as 11 (total yield: 52%) in a ratio of 1:3.

There are some questions concerning the mechanism of the formation of the cyclopentanes. Schegolev et al. reported on the formation of cyclopentane derivatives by additions of acyl cations to alkynes. They discussed a 1,5-hydride shift of the initially formed acyl vinyl cation followed by an addition–elimination reaction AₓE or alternatively an intramolecular electrophilic substitution SₓE. In our case both mechanistic alternatives can be excluded with certainty. Cyclopentane derivatives formed as products of a SₓE reaction were not observed even in trace amounts. The alternative 1,5-hydride transfer followed by an addition reaction to give a cyclopentyl cation, which under our reaction conditions could be trapped by a hydride donor, can be excluded, too, because in this case the vinyl cation intermediates 3a and 3b should give initially a primary and secondary alkyl carbenium ion, respectively. Our investigations of hydroalkylations of alkynes have shown that 1,2-H shifts of the alkyl carbenium ion intermediates are always faster than all kinds of possible inter- and intramolecular trapping reactions. However, products of these rearranged carbenium ions, such as cyclobutanes, were not observed. Thus, the 1,5-H shift and the cyclization must proceed in a concerted reaction (Scheme 4).

Our quantum-mechanical calculations (MP2/6-311 + G(d,p)//MP2/6-31G(d) + ZPVE) predict that this concerted insertion of vinyl cation 3a into a C–H bond is a possible pathway. After the exothermic formation of 3a (−197 kJ mol⁻¹), the reaction proceeds via the transition state of the concerted process (Figure 1), leading directly to the cyclopentane 7a. While the latter is stabilized by about 130 kJ mol⁻¹ relative to 3a, the activation energy for the cyclization and simultaneous hydrogen transfer is only 8 kJ mol⁻¹. The formation of a primary alkyl carbenium ion by 1,5-hydride shift followed by C–C bond formation can be ruled out because the carbenium ion is not a minimum on the potential energy surface but rearranges by a 1,2-hydrogen shift to give a secondary alkyl carbenium ion, which cannot form cyclopentanes. Analysis of the transition state’s single imaginary frequency reveals a motion of the bond-forming carbon atoms towards each other, while the hydrogen atom is moving above the ring system. The relevant distances are in accordance with those of an insertion of the ethenyl cation into the C–H bond of ethane and those of comparable C–H insertion reactions of carbenes.

Surprisingly, vinyl cation 3d does not form an exocyclic secondary cyclopentyl cation 8. The reason could be that the generation of a secondary cation is energetically less favorable than formation of a tertiary endocyclic carbenium ion. Our calculations with the model vinyl cation 3e (R¹ = Pr, R² = Bu) demonstrate that the formation of the exocyclic carbenium ion 12 is in particular kinetically disfavored (Scheme 5).
While the cyclopentyl cation $7e$ as the *endo* product is as stable as the corresponding *exo* product $12$, there is a significant difference in the transition states. The formation of the exocyclic carbenium ion $12$ is no longer a concerted process, but its transition state corresponds more to a hydride transfer transition state.[16] Its barrier is calculated to be about 20 kJ mol$^{-1}$ higher in energy than that for the formation of the observed endocyclic cation $7e$.

Our experimental results and the quantum mechanical calculations clearly indicate that 1,5-H shift and cyclization of vinyl cations $3a, b$ as well as $9a, c, d$ should be concerted processes, allowing the preparatively useful intramolecular insertion of a vinyl cation into C–H bonds$^{[4-6]}$ in solution, in analogy to the insertion of singlet carbenes$^{[3, 17]}$.

Keywords: alklylation · alkynes · C–H insertion · cyclopentanes · vinyl cations

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