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Intermolecular versus intramolecular Pauson-Khand reaction in gas phase: Limitation and feasibility

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ABSTRACT

The intermolecular Pauson-Khand reaction has been reproduced in the gas phase by using electrospray ionization coupled to modified tandem mass spectrometry. It has been found, as in solution, that the use of a strained alkene is preferred because of its relatively high reactivity. To observe the final cyclopentenone product, the cobaltacycle produced after a first ion-molecule reaction must necessarily collide with CO. Furthermore, when competition between an inter versus an intra-molecular reaction is possible, the intermolecular reaction is favored.

1. Introduction

The Pauson-Khand reaction (PKR), a cobalt-mediated joining of an alkyne, an alkene, and carbon-monoxide, is a highly useful method for the synthesis of cyclopentenone derivatives (Chart 1) [1].

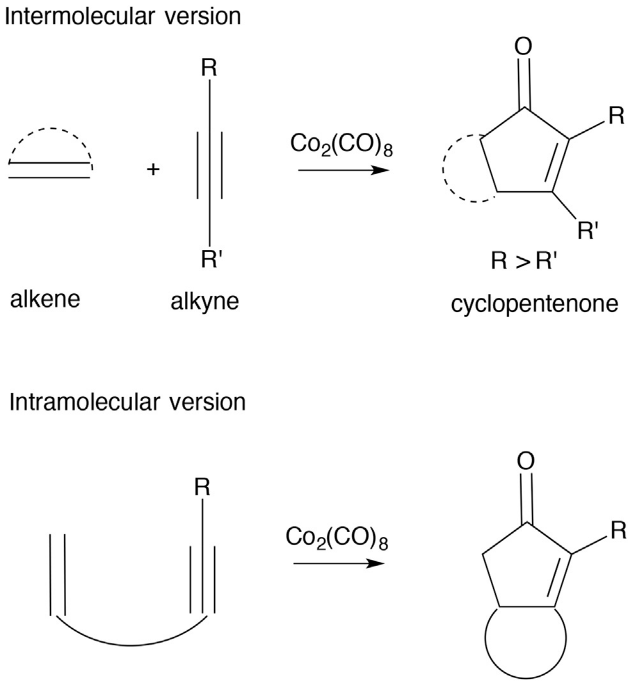

Chart 1. The Pauson-Khand reaction.

The intramolecular version of this reaction has been abundantly exemplified, but the intermolecular variant appears to be more limited in scope. There are several reasons for this: Firstly, the intermolecular PKR can yield a mixture of regioisomers, which is not the case for the intramolecular PKR. Secondly, compared with the intramolecular process, which is energetically reasonable, the intermolecular transformation is limited to a few highly reactive strained alkenes, such as norbonene (NBN) and norbornadiene (NBD). Less reactive alkenes require higher temperatures and/or prolonged reaction times, which leads to a degradation of the cobalt complex and thus a reduced yield. The relatively high reactivity of norbornene can be appreciated by comparison of the yield produced with phenylethyne in THF at 65 °C (80%, 4 h) with those obtained with another cyclic alkene (cyclopentene, 47%, 12 h) and a linear alkene (decene, 25%, 24 h), or also dihydrofuran (37%, 36 h at 70 °C) [2,3]. In 2004, we proposed [4] an explanation for the

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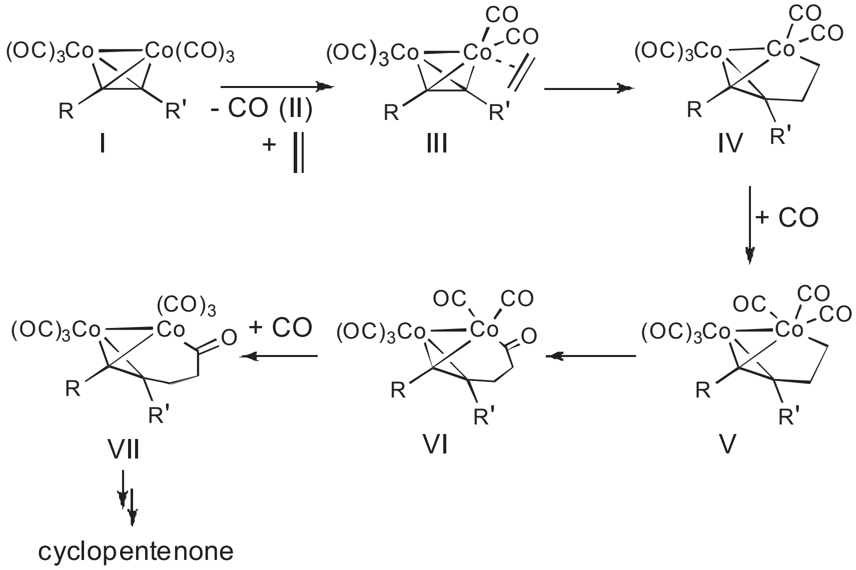


Scheme 1. Commonly accepted Magnus mechanism.

reactivity differences observed with strained and unstrained alkenes, based on consideration of the LUMO of the coordinated olefin and the HOMO of the $Co_2(CO)_5$-alkyne complex: the greater the back-donation, the higher the alkene coordination capability and thus reactivity.

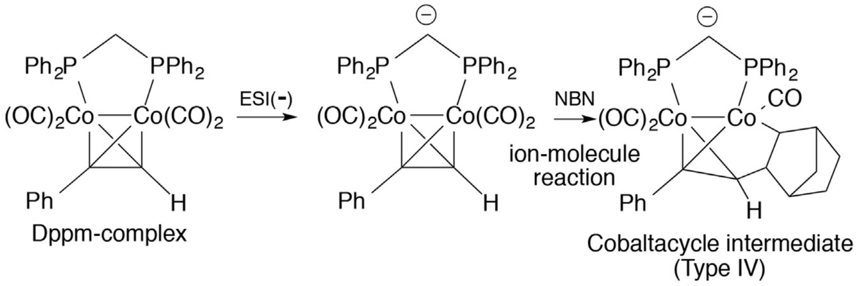
Several DFT studies [5] have been performed that have led to a better evaluation, and some modification [6], of the mechanism originally proposed by Magnus et al. (Scheme 1) [7]. Experimental confirmation of proposed intermediates, however, has been a challenge [8], *e.g.*, that of the cobaltacycle IV, which results from the formation of the first C—C bond after the coordination of the alkene to a Co atom [9].

Tandem mass spectrometry coupled with electrospray ionization (ESI) has proven to be a valuable tool for elucidating various organometallic structures and for studying their reactivity in the gas phase [10], and thus seemed to offer a possible means to investigate this type of intermediate. In 2003, we reported [11] the first gas phase ion-molecule reaction, studied with a modified triple quadrupole mass spectrometer, involving Pauson-Khand reaction precursors phenylethyne-dicobaltetracarbonyl-Dppm complex and norbornene (Scheme 2). Since the available time for an ion-molecule reaction is quite short (a few milliseconds), this highly reactive alkene was used to increase the possibility of forming an adduct. Because of an absence of CO in the space where the collision between the alkene and the Co complex occurs, it was hoped that the reaction could be stopped at the cobaltaclycle stage and thus allow the observation of a type IV intermediate.

At the time, we were not able to perform a collision ion-molecule reaction, followed by a collision induced dissociation (two collision cells are required), to permit the acquisition of supplementary details on the structure of the adduct. DFT calculations were realized, however, to clarify the nature of the adduct obtained in this approach: an association complex (Scheme 1, type III) and/or a cobaltacycle complex (Scheme 1, type IV). In the light of the computational model, we proposed the formation of a cobaltacycle.

In 2009, we modified once again the mass spectrometer to allow the transfer hexapole H0 to be used as a second collision cell (Scheme 3) [12]. With this change now not only a succession — reactive collision, then dissociative collision-can be performed, but also a reactive collision, followed by a second reactive collision. In 2011, an article of McIndoe et al. [13] guided us toward the choice of a cobalt complex derived from a cationic alkyne precursor, which allowed the observation of the final reaction product, a result that was not possible with our initial choice in 2003 (because the charge was carried by the dicobalt species and not the organic partner in the final reaction mixture). The results obtained with this new approach led to a new study of an aspect of the PKR mechanism [6].

Interestingly, McIndoe et al. reported in the same paper that in gas phase cycloadducts were not produced with alkenes such as cyclopentene, dihydrofuran, and hexene. It therefore seemed of interest to study with our modified instrument the reaction of norborne, an exceptionally reactive alkene (see above), compared with those of alkenes less reactive such as cyclopentene and hexene as previously mentioned at the beginning of the manuscript. In this



Scheme 2. Observation in gas phase of a cobaltacycle intermediate in PKR.