

THE 1,4- AND 1,6-ADDITION OF VINYLOGOUS DONOR SYSTEMS IN ON-WATER AND ORGANOCATALYZED REACTIONS*

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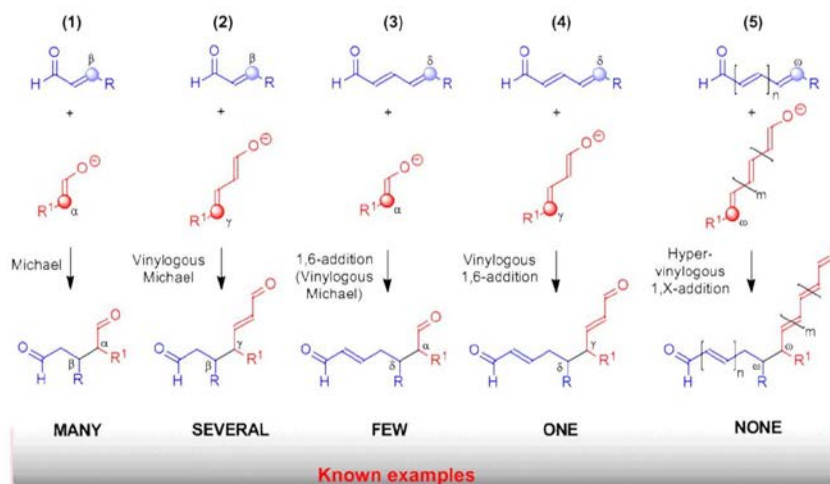
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The vinylogy principle, which explains the transmission of the electronic effects through a conjugated system, has increasingly attracted the curiosity of organic chemists while challenging their abilities. The design of new synthetic methodologies based on the application of this principle experienced an exponential growth in the past few years, especially when this topic was connected to other emerging fields such as eco-friendly synthetic methods or enantioselective catalysis. In this brief contribution we will present how the vinylogy principle was applied to on-water vinylogous Michael additions of pyrrole-based dienolates to diazadiene acceptors and to organocatalyzed 1,6-addition of vinylogous lactones to 2,4-dienals.

Le addizioni 1,4- e 1,6- di sistemi donatori viniloghi in reazioni in acqua e organo-catalizzate

Il principio di vinilogia, il quale descrive la trasmissione degli effetti elettronici attraverso sistemi coniugati, è stato efficacemente applicato a donatori di natura pirrolica e lattonica in reazioni di addizione viniloga. La presenza di molecole di acqua o di organocatalizzatori a base amminica, ha permesso lo sviluppo di due nuove metodologie sintetiche, le quali portano alla formazione di complessi scaffolds eterociclici.

The Michael addition reaction emerged in the past century as one of the pillars for the construction of carbon-carbon bonds. Considering its vinylogous extension - employing vinylogous donor systems - several applications were reported (Scheme 1, eq. 2), while a still limited number of works were published on the use of vinylogous acceptors (1,6-, 1,8-, etc. additions, eq. 3)¹, testifying the inherent difficulties in the propagation of the electrophilic characteristics through a long series of conjugated double bonds to the remote position. Thus, vinylogous and hyper-vinylogous 1,6-additions still remain almost unexplored domains, worth to be pursued. In the following sections the results recently obtained for on-water vinylogous 1,4-additions and organocatalyzed vinylogous 1,6-addition will be briefly presented.

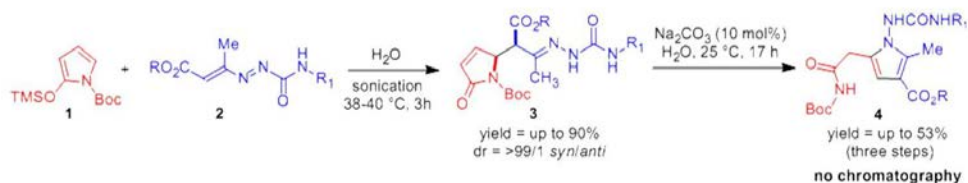


Scheme 1 - The evolution of the Michael chemistry. Increasing vinylogation means increasing molecular diversity

*Relazione presentata lo scorso 18 dicembre in occasione della XIII Giornata della Chimica dell'Emilia Romagna.

Results and discussion

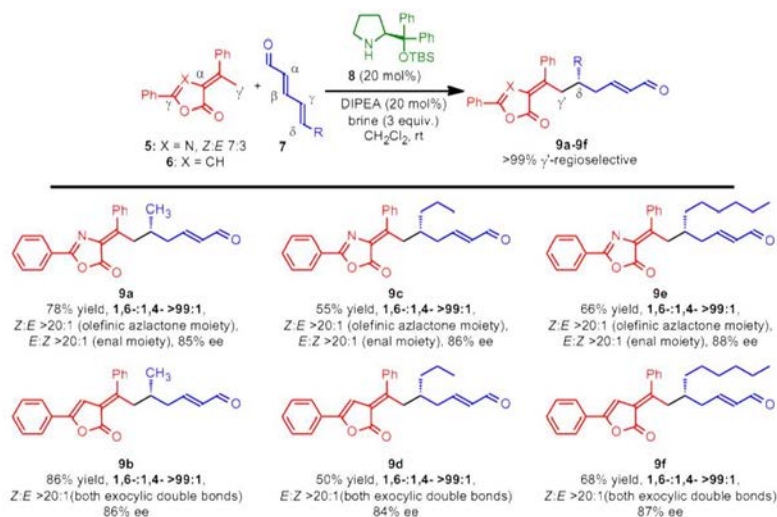
A novel eco-friendly vinylogous Mukaiyama-Michael addition reaction was reported, where heterocyclic 2-silyloxydienes of type **1** and 1,2-diaza-1,3-dienes **2** were coupled on-water in open-air vessels under ultrasound irradiation at 38-40 °C (Scheme 2)².



Scheme 2 - Developed vinylogous 1,4-addition and related manipulation products

The butenolide-type Michael products **3** were easily isolated, without need of flash chromatography. The superior role of water allowed for the efficient synthesis of the desired vinylogous 1,4-adduct in excellent yield and *syn*-diastereoselectivity. On the other hand, lactams **3** could be involved in base-triggered, *all-on-water* reaction cascades, ultimately resulting in production of highly functionalized pyrrole-carboxylates **4**. The generality of the reaction was proven for differently substituted diazadiene **2**, leading to the formation of variously adorned pyrrole-carboxylates **4**².

Methyl-substituted olefinic azalactones **5** and butyrolactones **6** were found to be useful substrates for the first examples of organocatalyzed intermolecular vinylogous 1,6-addition to 2,4-dienals (Tab. 1)³. Several commercially available δ -substituted dienals were evaluated to demonstrate the generality of the reaction. Methyl, propyl, and hexyl groups were found to be suitable remote substituents and high level of enantio- and regiocontrol were obtained. The geometry of both exocyclic double bonds in the products was fully controlled in all of the cases. Interestingly, no substituents on the 2,4-dienals were needed to guide the regioselectivity of the process, and full γ' , δ -regiocontrol was obtained in the transformations.



Tab. 1 - Scope of the doubly vinylogous Michael addition of olefinic lactones to 2,4-dienals

Conclusions

It was demonstrated that vinylogous Michael reactions could be efficiently carried out using different vinylogous donor systems, exploiting either eco-friendly on-water conditions or secondary amine organocatalysts. The synthetic potential of the presented methods was highlighted by the construction of complex heterocyclic structures.

References

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