A MECHANISTIC PROPOSAL FOR THE FORMATION OF UNEXPECTED PYRROLES IN REACTIONS OF CARBOETHOXYCARBENE WITH ENAMINONES

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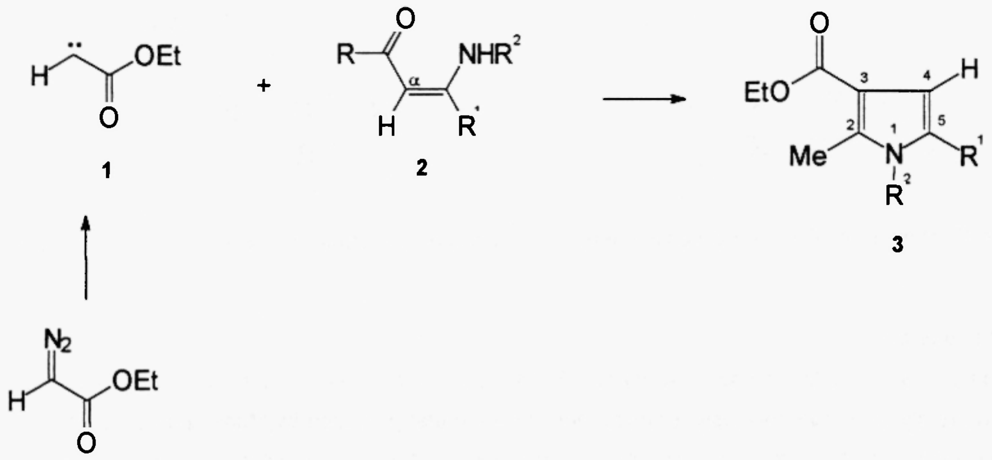
Abstract

A reaction mechanism is proposed for the unexpected formation of 3-carboethoxy-2-methyl pyrroles in reactions of acyclic enaminones with carbethoxycarbene, formed *in situ* from cupric acetilacetonate catalyzed decomposition of ethyl diazoacetate.

Introduction

Carbenes, very useful and highly reactive intermediates in organic synthesis (1, 2), are generated when diazo compounds decompose in the presence of copper and rhodium salts (3). Enaminones (4, 5, 6) are also easily accessible, multifunctional, and versatile reagents in organic synthesis as they contain several centers subject to either nucleophilic or electrophilic attack. We have studied the structure (7) and reactivity (8) of enaminones, and the synthetic utility of their reactions with α-ketocarbenes, generated *in situ* from cupric acetylacetonate catalyzed decomposition of α-diazoketones (9), and developed new methods for the synthesis of pyrroles (9) and triazoles (10, 11).

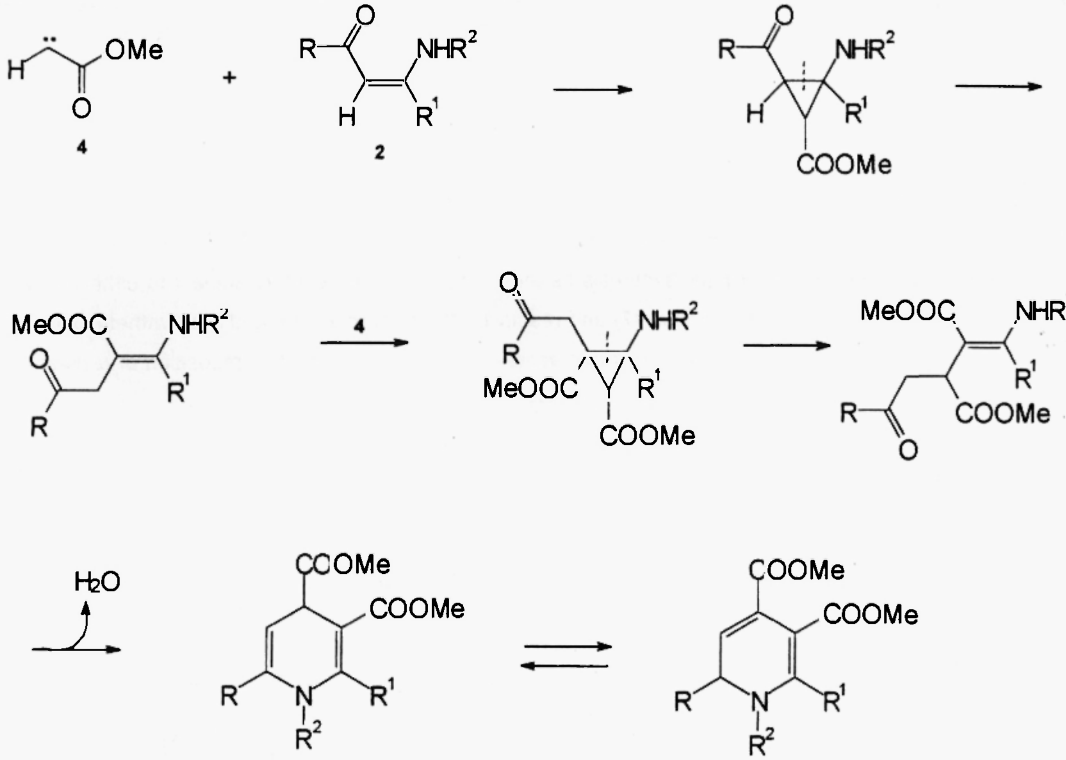
When reacting the carboethoxycarbene 1 (generated *in situ* from the cupric acetilacetonate catalyzed decomposition of ethyl diazoacetate) with acyclic enaminones 2, we observed the unexpected formation of pyrroles 3 (12) (Scheme 1).



Scheme 1- Unexpected formation of pyrroles 3 in the reaction of carbene 1 with acyclic enaminones 2

By varying the substituents in specific positions of the enaminones backbone, we verified that the fragment C4(H)-C5(R^1)NR^2 of the pyrrole structure is provided by 2 whereas, surprisingly, we found that the fragments C2(Me)C3CO$_2$Et is provided by two carbenes 1 in an overall 1:2 molar ratio reaction. We conclude therefore that the initial reaction step occurs through insertion of 1 into the Cα-H bond of 2 (12). In spite of having most likely elucidated the origin of the whole pyrrole backbone and having determined the initial reactional step, we were unable by that time to postulate a plausible, complete mechanism for this puzzling reaction.

Recently, Maas and co-workers (13, 14) reacted cyclic and acyclic enaminones 2 with carbomethoxycarbene 4 (the methyl analog of 1) generated *in situ* by copper triflate catalyzed decomposition of methyl diazoacetate. They reported that dihydropyridines were formed also via a 1:2 molar ratio reaction. Maas and co-workers then proposed a reaction mechanism initiated by insertion of 4 into the double bond of 2 and the subsequent rupture of the so formed cyclopropane ring. A second insertion of 4 into a double carbon bond of the reaction intermediate followed by cyclopropane ring-opening and water loss form the final products (Scheme 2).

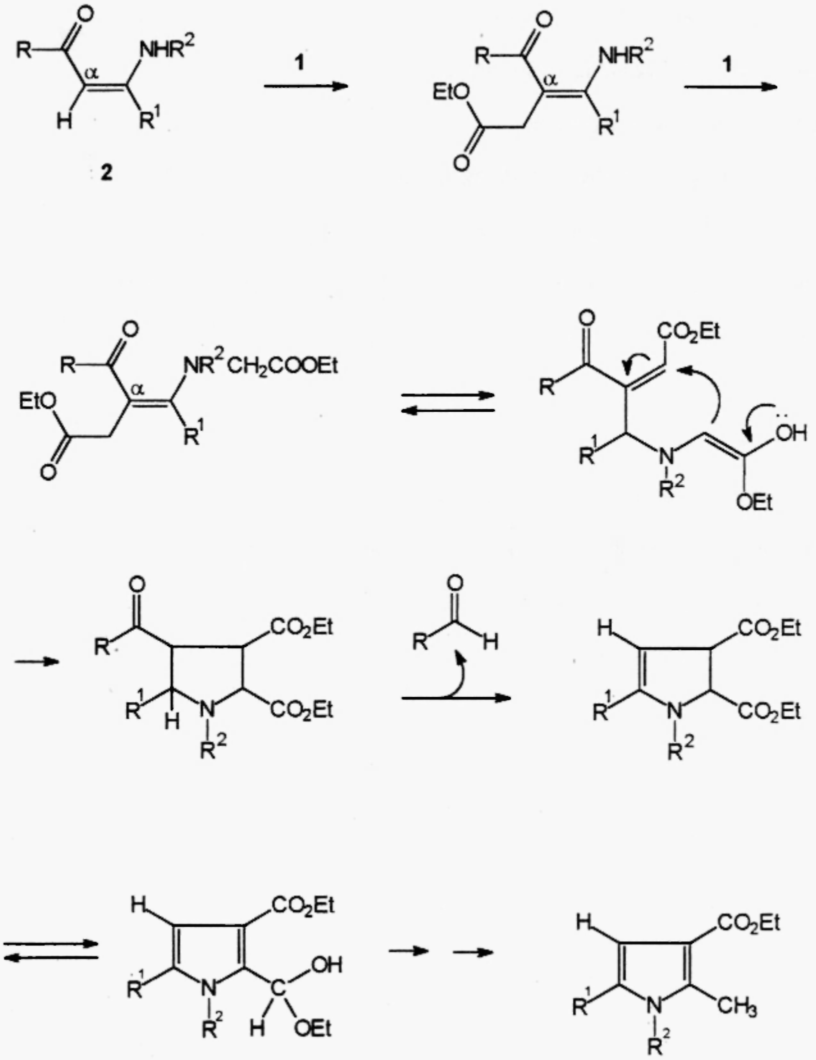


Scheme 2- Formation of dihydropyridines in the reaction of carbomethoxycarbene 4 with acyclic enaminones 2

Results and Discussion

Although we (6d) and Maas and co-workers (13, 14) have used similar reaction conditions and reactants, the products formed greatly differ and obviously a similar mechanism to that proposed by Maas and co-workers (7) (Scheme 2) cannot be postulated for the formation of pyrroles 3 in reactions of 1 with 2 (Scheme 1). Therefore, and owing to the continuous and growing interest in the synthetic applications of carbenes and enaminones (3), we have directed our efforts so as to propose a plausible mechanism for the intriguing formation of pyrroles 3.

Scheme 3 summarizes our present proposal. The reaction is initiated by insertion of 1 into both the Cα-H and N-H bonds of the enaminone 2 (12). The subsequent steps involve a keto-enolic equilibrium, intramolecular cyclization, and subsequent or simultaneous decarbonylation to form a dihydro dicarboethoxy pyrrole intermediate. The most puzzling process then began as aromatization must occur with reduction of the C2-COOEt group to a methyl group (3, Scheme 1). A keto-enolic equilibrium may be invoked followed by aromatization, hydrolysis of the acetal and formation of a C2-COH aldehyde group. Reduction of CO to CH_2 should then occur if pyrrole 3 is to be formed. The pathway by which this reduction occurs is however still obscure and it is the subject of our present investigation.



Scheme 3- Mechanism for pyrrole 3 formation in the reaction of carboethoxycarbene 1 with acyclic enaminones 2

Conclusion

In conclusion, we hope that this work contributes to the elucidation of an intriguing mechanism that involves an increasingly and interesting area: the enaminones and ketocarbenes reactivities.

Acknowledgments

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