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Nucleophilic Addition Reaction of Unsaturated Methyl Lactones with Pyridine Aldehydes

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Received: 11 July 1997 / Uploaded: 13 August 1997

Abstract: New interpretation of the mechanism of CH-acid condensation with aldehydes using quantum chemical method is reported in this work.

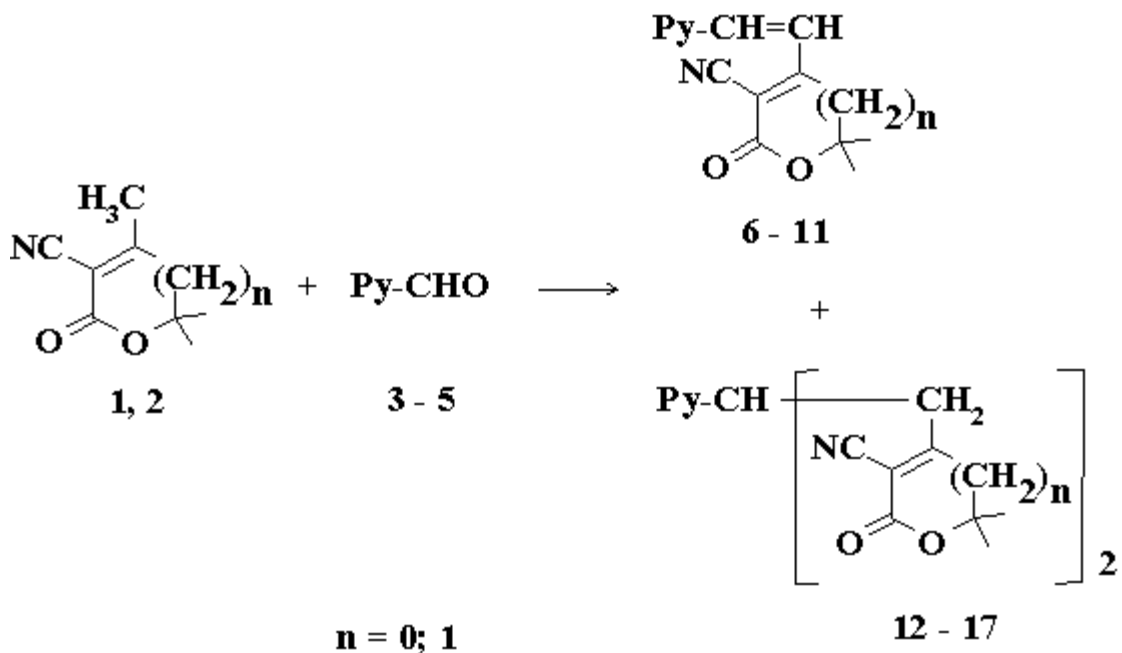
Keywords: Methyl lactone, pyridine aldehyde, nucleophilic addition reaction, Michael-type reaction, quantum chemical calculation.

Introduction

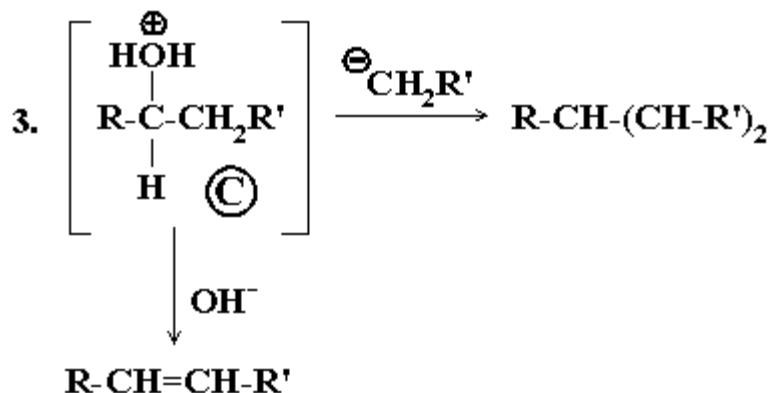
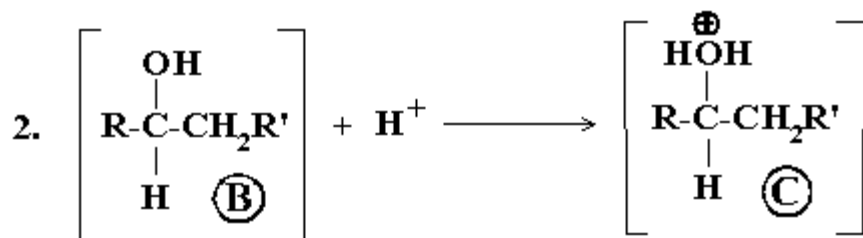
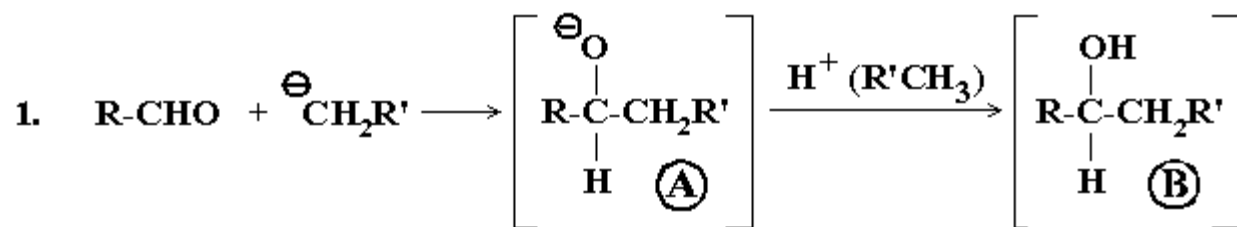
Base catalyzed condensation of pyridine aldehydes with CH-acids (acetophenone, methyl pyridine and etc.) generally afforded the vinyl- and/or hydroxyethyl derivatives of pyridine [1]. In the case of acetophenone the formation of the Michael-type addition products in 5-6% yield was also observed. According to the traditional point of view the Michael-type addition products are formed in this case step-wise *via* aldol condensation of aldehyde with CH-acid followed by addition to double bond of second molecule of methyl derivative [2]. During the reaction of pyridine aldehydes with gamma- and delta-lactones we observed the formation of aldol condensation products and Michael-type addition products in 2-80% yield. The quantum chemical method was used in present work to receive the information on the reaction mechanism.

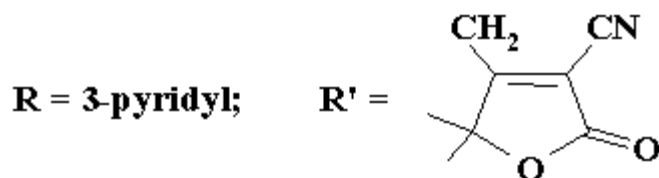
Results and Discussion

We have found that the reaction of 3-cyano-4,5,5-trimethyl-2-(5H)-furanone (**1**) and 3-cyano-4,6,6-trimethyl-2-(5,6-dihydro)-pyrone (**2**) with 2-, 3- and 4-pyridinealdehydes (**3** - **5**) in the presence of NaOH resulted in the unsaturated condensation products (**6** - **11**) and Michael-type addition products (**12** - **17**):



According to the TLC data compounds **6 - 11** and **12 - 17** under the reaction condition studied (NaOH, methanol, 20°C) are formed simultaneously. Application of quantum chemical calculation method allowed to propose a possibility of their formation *via* the following steps and intermediates, as it is shown for pyridine aldehyde **4** and lactone **1**:





The ion-adduct **A** is characterized by C--C bond order 0.7. This bond is considerably strengthened after addition of H⁺. Bond C-C order of intermediate **B** is 1.5. The calculations showed that the participation of furanone molecules R¹CH₃ in OH group formation is possible but energetic less favourably (stabilization energy of intermediate **B** in this case is 1.24 eV) in comparison with H⁺ (proton affinity 12.8 eV). According to the above scheme both compounds - unsaturated condensation products and Michael adducts are formed *via* one and the same intermediate **C**. As noted above according to literature data such bis-pyrone derivatives as **12** - **17** would be resulted by Michael-type addition reaction, i.e. by joining second anion ⁻CH₂R¹ to nucleophilic olefin **6** - **11**. The negative charges on both olefinic C atoms (according to our calculations) also confirm high possibility of the scheme proposed. It has been also shown that a negative charge on C atom of anion ⁻CH₂R¹ formed from methyl pyrone is larger than that of anion formed from methyl furanone. Probably, it defines a higher efficiency of methyl pyrone as a nucleophilic reagent than that of methyl furanone in Michael reaction.

Conclusion

The employment of quantum chemical method gave the possibility to suggest the new mechanism of condensation reaction of active methyl group with aldehydes.

Experimental Part

The synthesis of compounds **6** -**17** and their physicochemical characteristics presented in [3]. The quantum chemical calculations were carried out by means of semiempirical method AM1 using Program MOPAC 5.0. Geometric parameters of all the structures considered were exposed to full optimization (algorithm of Broyden-Fletcher-Goldfarb-Shanno). The computerized design of the starting molecules was performed using the LabVision Software package [4].

References

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4. LabVision (Version 1, 1992), TRIPOS associates Inc., 1699 S.Hanley Rd., St. Louis, MO, 63144, USA.

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