Synthesis of Ureidomethylene Compounds: a short review

Shrishnu Kumar Kundu

Acharya Prafulla Chandra Roy Government College, Himachal Bihar, Matigara,

Siliguri-734 010, West Bengal, India.

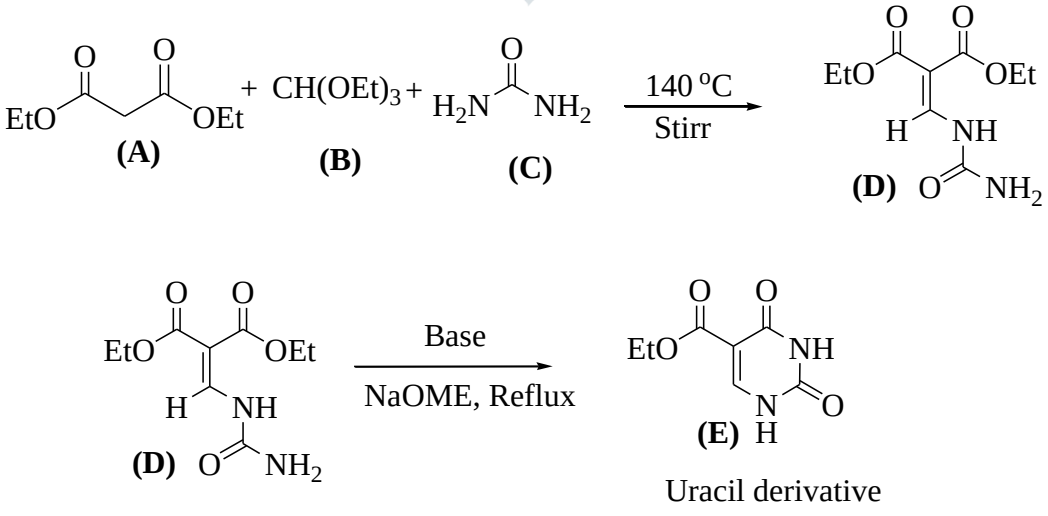
Abstract: Hetero-atom in organic molecules was always important, especially Nitrogen. Nitrogenous organic compounds were found in many natural products, drugs, dyes etc. Ureidomethylene Compounds were one of the important nitrogenous organic molecules. It is basically a derivative of urea. It was used as intermediate for synthesis of many heterocyclic and nitrogenous organic molecules.

Creating of new Carbon-Nitrogen bond is always very important and effective in organic synthesis. It is found in a tremendous variety of organic compounds such as amines, amides, anilides, nitriles, synthetic intermediates, organic solvents, dyes, drugs, amino acids, DNA and RNA bases, pesticides, agrochemicals, organocatalysts[1] etc.

Ureidomethylene Compounds is an important class of compounds in organic synthesis. It is actually vinylogous derivatives of urea. Urea derivatives are important class of organic nitrogenous compounds. They exhibits a variety of biological activities such as antifungal and larvicidal activity[2], Antimicrobial and Antioxidant activity[3], anti-inflammatory agents[4], Antiinfectives[5] as anticancer agents[6] etc.

Miyasheta *and his co-worker* [7] synthesised of uracil derivative **E**. Firstly they condensed diethyl malonate (**A**), triethyl orthoformate (**B**) and urea (**C**) to form Ureidomethylene derivatives (**D**) which on treatment with base gives the desired product, uracil derivatives (**E**) (Scheme 1).

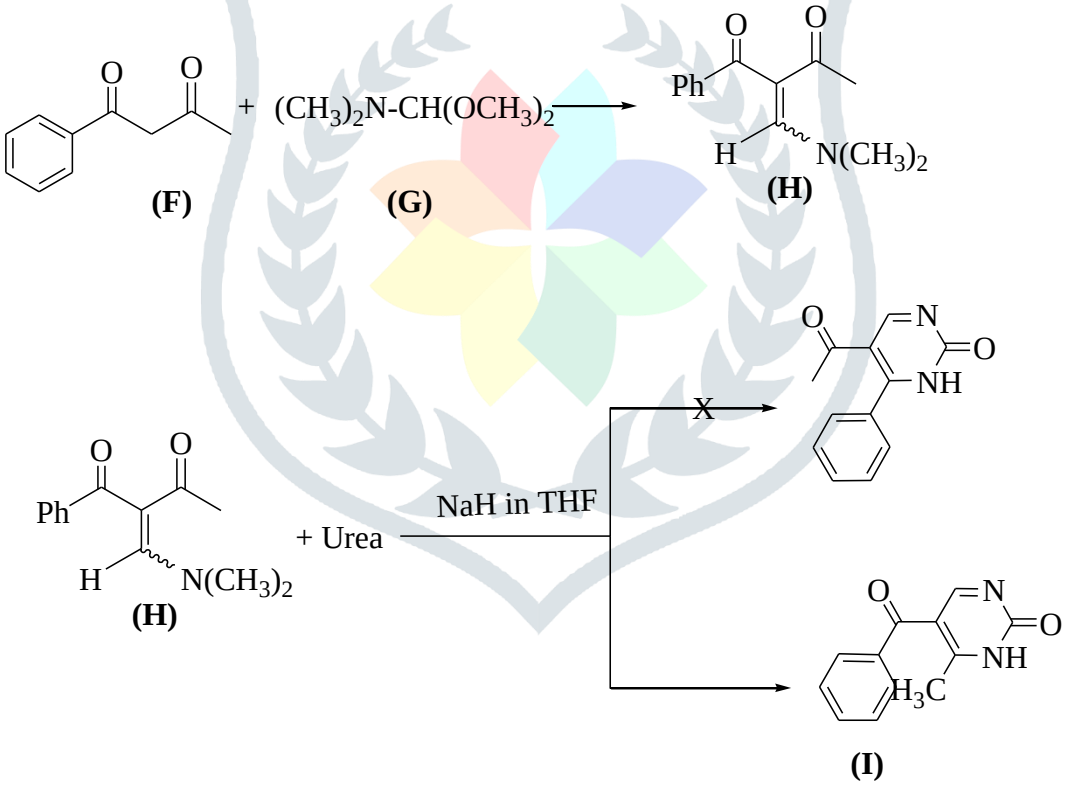
Scheme - 1



In the reaction procedure they have used a mixture of urea **7** (1.5 mol), diethyl malonate **5** (1 mol) and triethylorthoformate **6** (1.1 mol) and heated at 140 ^{o}C for 4 hours with continue stirring. They distilled off the by-product, ethanol, liberated during the course of the reaction. Then water and methanol was added to the reaction mixture was chilled in ice bath and dried over P_2O_5 in vacuo which gives ethyl 2-ureidomethylene-malonicacid diethyl ester **8**. The yield of the reaction was 66%. Then the Intermediate, ethyl 2-ureidomethylene-malonicacid diethyl ester **8,** was allowed to react with sodium methoxide and was refluxed for 10 minutes, cooled the reaction mixture with ice-water and acidify with conc. HCl to get the final product **9** as colorless needle.

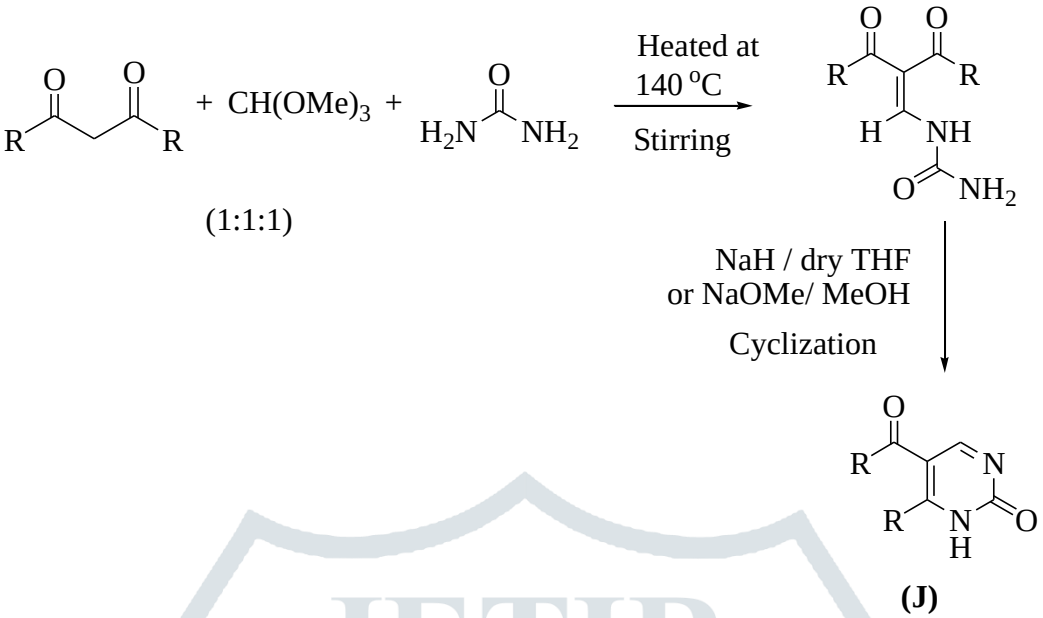
In 1987 Winton D. Jones, Jr and his co-worker[8] synthesized 5 and 6-acyl-2 (1H)-pyrimidones by by cyclization with vinylogous amide and urea using NaH in dry THF (Scheme 1) They synthesized 5 and 6-acyl-2 (1H)-pyrimidones **(I).** For this firstly they condensed benzylacetone **(F)** and dimethyl formamide.dimethyl acetal **(G)** to form vinylogous amide **(H)** after this cyclization of vinylogous amide with urea using NaH in dry THF (Scheme 2). The overall yield of this reaction is 30 %.

Scheme - 2



W. D. Jones, Jr.[8] and his co-worker also modified their procedure (scheme 1) for synthesis of 5 and 6-acyl-2 (1H)-pyrimidones **1** in an alternative route. In the reaction procedure they have used 1, 3-dicarbonyl compound (1 mol), urea (1 mol) and trimethyl orthoformate (1mol) heated at 140^{0}C with continue stirring until the mixture solidified. The solidified froduct was then allowed to react with sodium hydride or sodium methoxide to get the cyclic product **(J)** (Scheme 3). The overall yield of the reaction was only 45- 66 %.

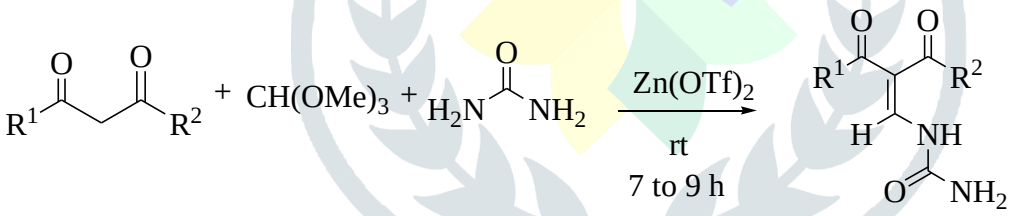
Scheme - 3



(J)

In both of the two case the yield of the Ureidomethylene Compounds was very poor.

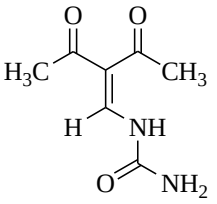
Later on in 2014 Majee *et al.*[9] concentrated of increasing the yield of Ureidomethylene derivatives. In this the reaction procedure they have used 1,3-dicarbonyl compounds (1 mmol), urea (1.5 mmol) and trimethylorthoformate (1 mmol) in presence of $Zn(OTf)_2$ (5 mol%) under solvent-free conditions (Scheme 4) to yield the Ureidomethylene derivatives(**K**).



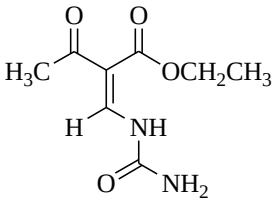
(K)

It was a solvent free one pot three component condensation reaction. They have shown that Zinc Triflate was an efficient catalyst for this conversation, the reaction proceeds in room temperature with good yield. They increased the yield of Ureidomethylene Compounds upto 85% (Table 1).

Table - 1



85%



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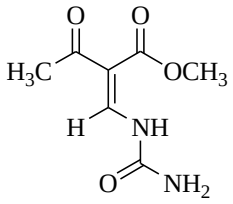

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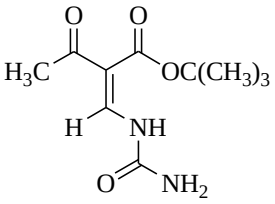
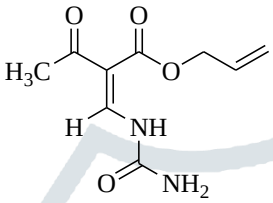


78%



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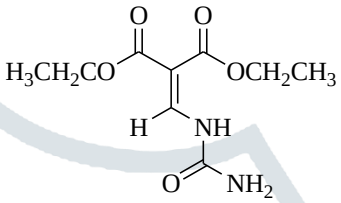
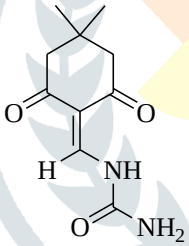


80%

They also extend the reaction for cyclic diketone and N-substituted urea. They observed that in both the case desired product were formed with moderate to good yield (Table 2).

Table - 2



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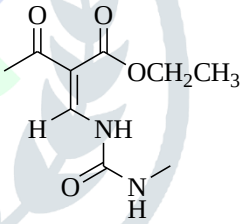

56%

Thus they developed a very good methodology for the synthesis of Ureidomethylene Compounds with high yield. As it was a solvent free reaction, it was eco-friendly procedure also.

In conclusion I have tried to highlight the synthesis of Ureidomethylene derivatives through this review. Although, this review is very short but still it will be very important for academic as well as industrial purpose.

Reference:

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