

# Recent Developments in Intramolecular Stetter Reaction

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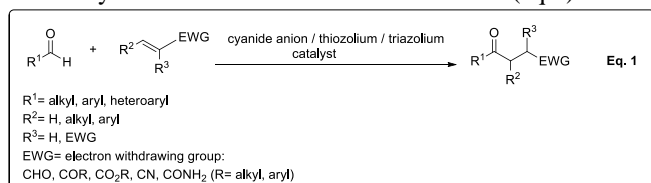
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**Abstract-** The Stetter reaction is an important carbon-carbon bond forming reaction between an electrophile and a Michael acceptor in the presences of NHC catalysts. Intramolecular Stetter reaction is possible if both the nucleophile and Michael acceptor in the same molecule. This article highlights recent developments of the intramolecular version of the Stetter reaction.

**Keywords-** Carbon-carbon bond forming reaction, electrophile, Michael acceptor, NHC catalysts.

## INTRODUCTION

In the synthetic organic chemistry quite a few Carbon-Carbon bond forming reactions have been well established in the literature. New approaches for development of carbon-carbon bonds have been constant attractive challenge to synthetic organic chemists. The Stetter reaction<sup>1</sup> is one among important carbon-carbon bond forming reaction which is developing fast in recent years. For the first time in 1973 Hermann Stetter reported the conjugate addition of aldehydes to  $\alpha, \beta$ -unsaturated compounds which yield 1,4-dicarbonyl compounds. 1,4-Addition of aldehydes to Michael acceptors in the presence of cyanide anion or thiazolium or triazolium salt catalyst has been known as Stetter reaction (eq 1).

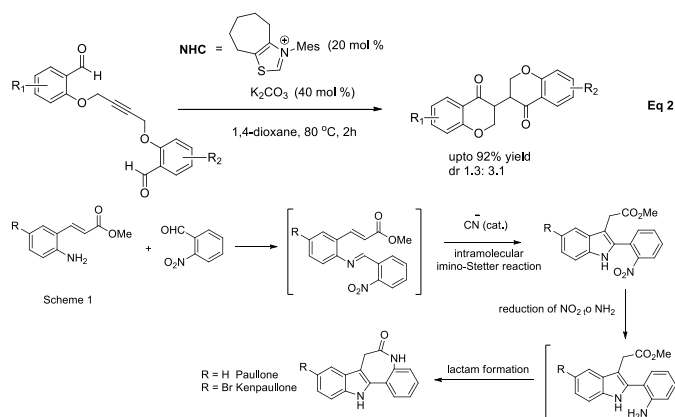


## INTRAMOLECULAR STETTER REACTION

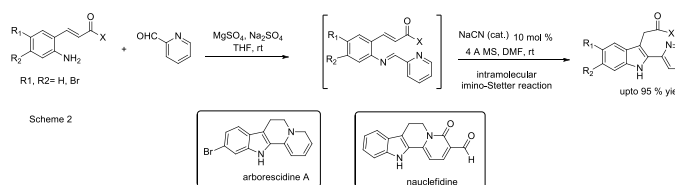
Stetter reaction growing in the three essential components *i.e.* electrophiles, Michael acceptors and catalysts. A verity of electrophiles, Michael acceptors and catalysts has been employed successfully. The intramolecular Stetter reaction is possible if both the nucleophile and Michael acceptor in the same molecule. This article highlights recent developments of the intramolecular version of the Stetter reaction.

Zhou and co-workers<sup>2</sup> reported an efficient synthesis of symmetrical and unsymmetrical bisbenzopyrones via intramolecular hydroacylation-Stetter reaction cascade in the presence of NHC (20 mol %) and K<sub>2</sub>CO<sub>3</sub> (40 mol %) in 1,4-dioxane at 80 °C (Eq 2).

Cheon and co-workers<sup>3</sup> described the total synthesis of Paullone and Kenpaullone *via* intramolecular imino-Stetter reaction. The methyl 2-aminocinnamate derivatives and 2-nitrobenzaldehyde offer 2-(2'-aminophenyl)indole-3-acetic acid derivatives followed by reduction of nitro to amino with Zink will form spontaneous lactam (Scheme 1).

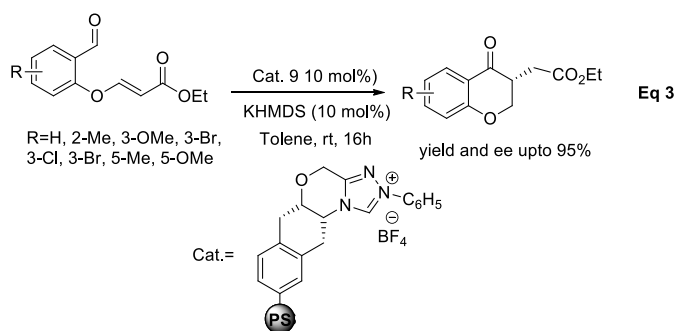


Subsequently Cheon and co-workers<sup>4</sup> reported an exciting intramolecular Stetter reaction of aldimines obtained from 2-aminocinnamic acid derivatives and 2-pyridinecarboxaldehydes. They further prolonged these derivatives for the synthesis of indoloquinolizines and the total synthesis of arborescidine A and nauclefidine (Scheme 2).

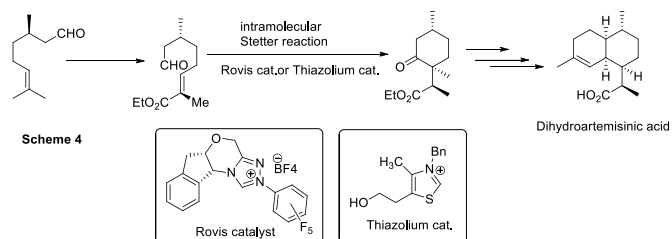


Cheon and co-workers<sup>5</sup> reported another fascinating intramolecular Stetter reaction of aldimines obtained from 2-aminocinnamic acid derivatives and 2-aromatic aldehydes

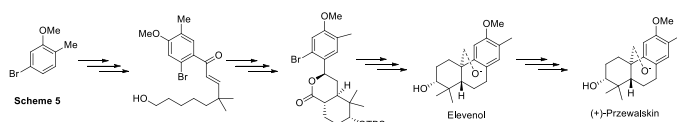
affording 2-aryl-substituted indole-3-acetic acid derivatives. They extended these methodology for the synthesis of biologically important FPTase inhibitor (Scheme 3). Massi and co-workers<sup>6</sup> reported an interesting intramolecular Stetter reaction in the presence of polystyrene-supported Rovis triazolium carbene catalyst. They were observed a good recyclability of the catalyst in batch experiments in the excellent yields and ee (Eq 3).



Nanda and co-workers<sup>7</sup> reported the synthesis of enantiopure dihydroartemisinic acid. In this strategy intramolecular Stetter reaction using Ravis or Thiazolium catalyst explored for the synthesis of functionalized enantiopure cyclohexanone from acyclic precursor (Scheme 4).

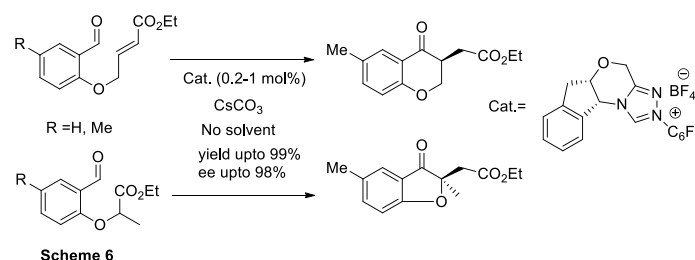
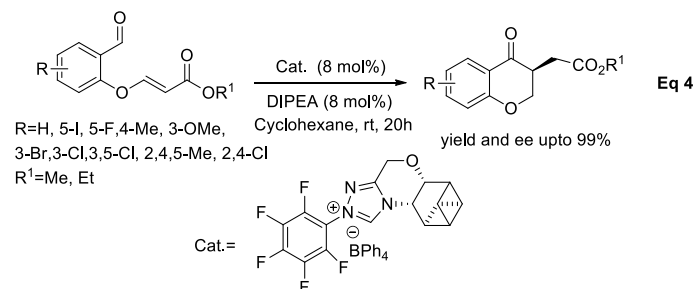


Koert and co-workers<sup>8</sup> reported an efficient synthesis of 7,20-oxo-bridged abietane type natural products. In this approach the significant steps are asymmetric Mukaiyama aldol, intramolecular Stetter type Michael addition and Tishchenko reaction. This approach was applied for the first time to the total synthesis of (+) Elevenol and (+)-Przewalskin (Scheme 5).



Rafinski<sup>9</sup> reported the synthesis of a series of chiral triazolium salts and further applied these chiral triazolium salts for intramolecular Stetter reaction (Eq. 4)

Ema and co-workers<sup>10</sup> reported an interesting intramolecular asymmetric Stetter reaction under solvent free condition (Scheme 6).



## CONCLUSIONS AND FUTURE OF THE REACTION

This article demonstrates the recent advances of intramolecular Stetter reaction. The details in this article clearly specify that Stetter reaction has developed one of the most useful carbon-carbon bond forming reaction. Further this article will open an opportunity to organic chemists to discover novel methodologies to synthesize important biological molecules by using the inspiring Stetter reaction.

## ACKNOWLEDGEMENTS

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