

## Synthesis of Flavone Skeleton by Different Methods

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### ABSTRACT

Flavones (flavus = yellow), are a class of flavonoids based on the backbone of 2-phenylchromen-4-one. Flavones are mainly found in cereals and herbs. Flavones are biologically active compounds. Therefore number of synthetic methods were developed. In this mini review we have tried to cover various synthetic strategies for the synthesis of flavones. Some of the well known methods used for synthesis of flavones are Baker & Venkatraman synthesis and Claisen-Schmidt condensation.

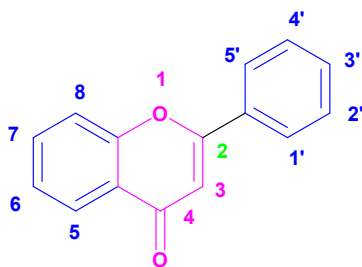
**Key words:** Flavones, Biologically Active Compounds, Synthetic Methods

### INTRODUCTION

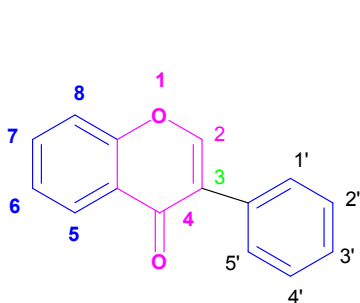
Flavones (flavus = yellow), are a class of flavonoids based on the backbone of 2-phenylchromen-4-one. Apart from flavones other flavonoids are isoflavonoids, derived from 3-phenylchromen-4-one structure neoflavonoids,

derived from 4-phenylcoumarine structure. The three flavonoid classes are all ketone-containing compounds, and as such, are anthoxanthins (flavones and flavonols)

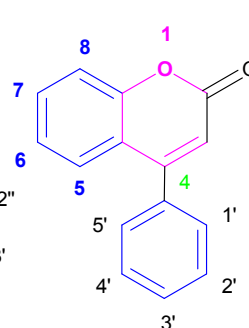
Flavones are well known for their various biological activities such as anticancer<sup>1</sup> Anti



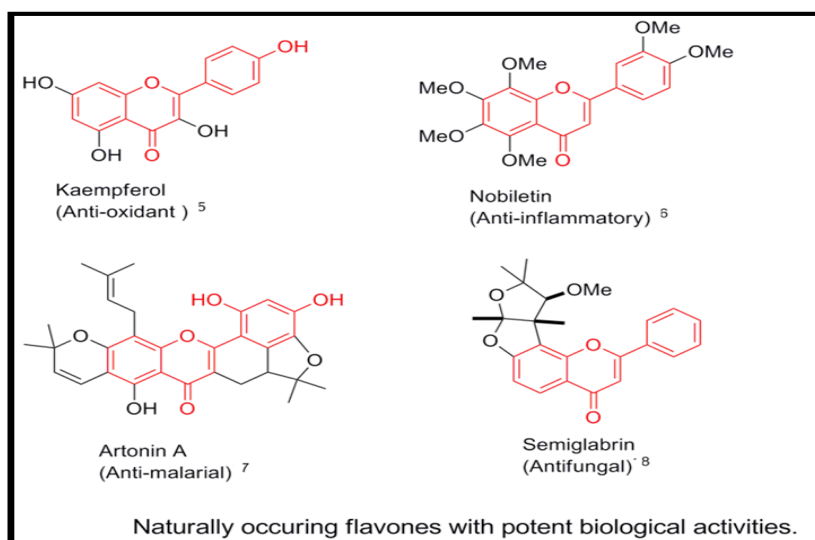
**Flavone**



**Isoflavone**



**Neoflavone**

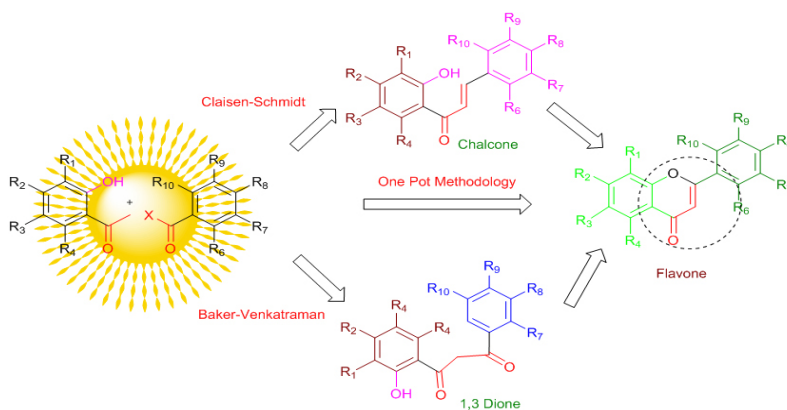


inflammatory<sup>2</sup>, anti-osteoporotic<sup>3</sup>, anti-diabetic<sup>4</sup>, etc. some of the examples as shown as under.

### Synthetic strategies of flavones

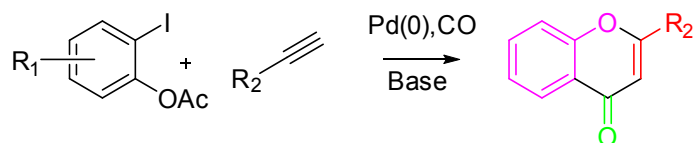
Traditionally, flavones have been prepared by Baker-Venkatraman rearrangement and Claisen-Schmidt condensation, which involves the conversion of 2-hydroxyacetophenones into

benzoyl esters, followed by rearrangement in base to 1,3-diphenylpropane-1,3-diones which upon cyclization under acidic conditions furnishes flavones. On the other hand hydroxychalcone synthesized from 2-hydroxyacetophenone and benzaldehyde under Claisen-Schmidt conditions can undergo oxidative cyclization to furnish flavones ring.

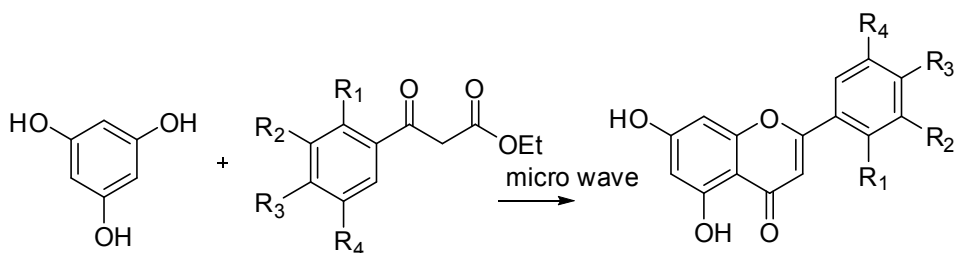


**Fig. 1: Basic reactions for the synthesis of flavones**

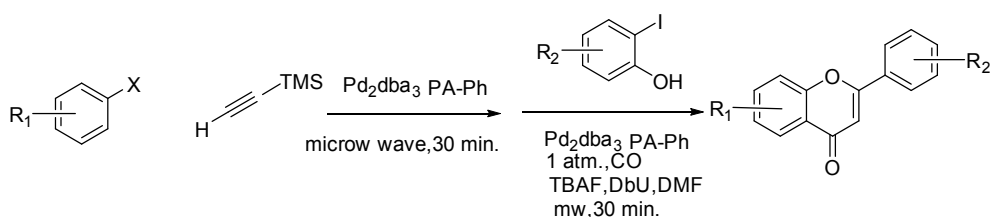
Basic schemes related to synthesis of flavones is mentioned below (Scheme 1-43),



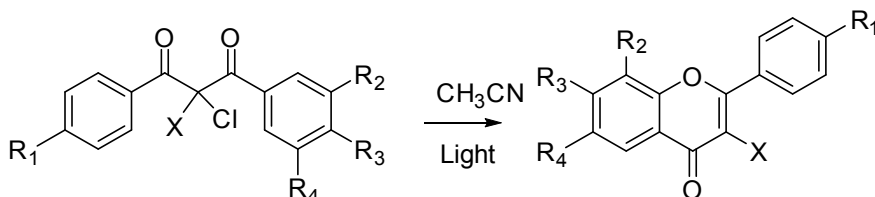
**Scheme 1: Palladium catalysed synthesis is carried out in presence of basic environment by Hua & Yang<sup>9</sup>**



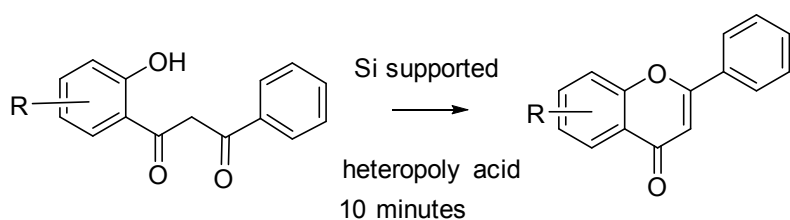
**Scheme 2: Solvent free synthesis of flavone is carried out by Julia & co-workers<sup>10</sup>**



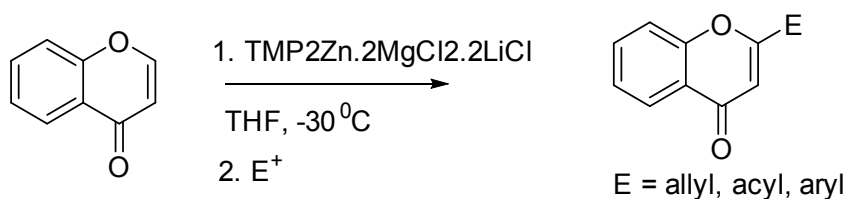
**Scheme 3: Flavones via a Micro-Assisted, One-Pot Sonogashira-Carbonylation Annulation Reaction is used by E. Awuah & A. Capretta<sup>11</sup>**



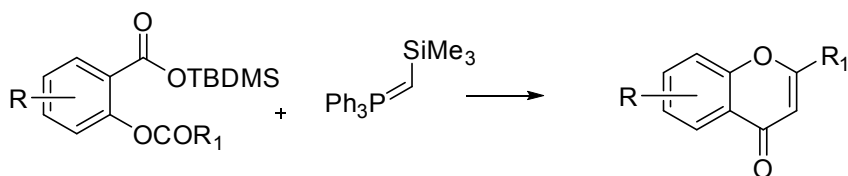
**Scheme 4: Photo cyclization of 2-chloro-substituted 1,3-diarylpropan-1,3-diones to flavones is invented by B. Kosmrrji & co-workers<sup>12</sup>**



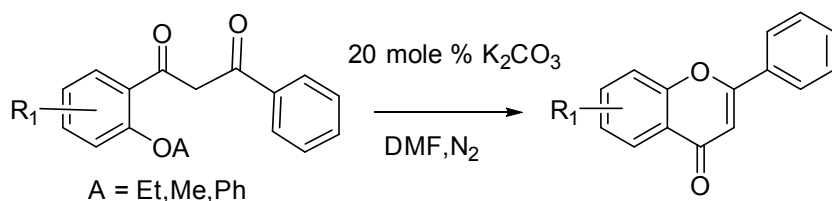
**Scheme 5: Conversion of intermediate 1,3-dione is carried by G. Romanelli & co-workers<sup>13</sup>**



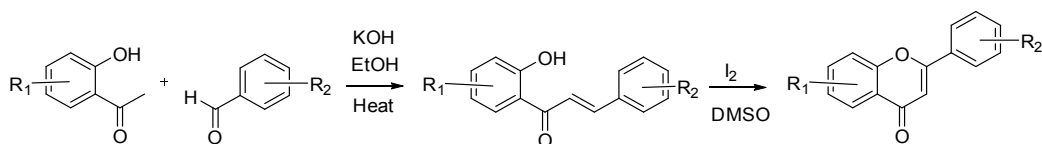
**Scheme 6: Alkene hydrogen is replaced by L. Klier & T. Bresser<sup>14</sup>**



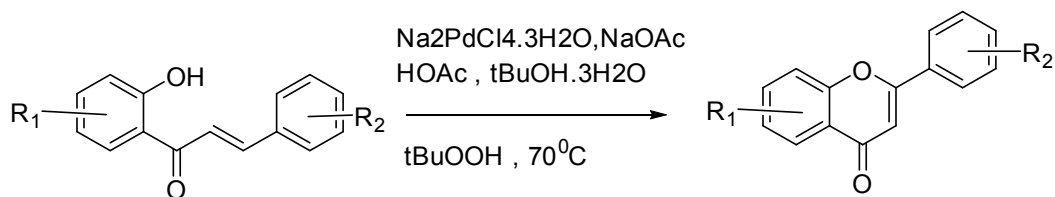
**Scheme 7: A Novel Synthesis of 4H-Chromen-4-ones via Intramolecular Wittig Reaction is used for the synthesis of flavones<sup>15</sup>**



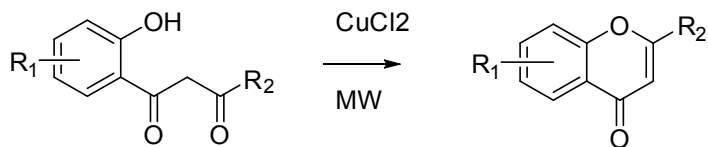
**Scheme 8: This invention converts 1,3 dione into flavones. Only base is used for this purpose<sup>16</sup>**



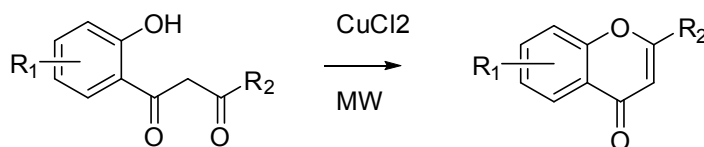
**Scheme 9: Koneni & his group first time invented flavones in which oxygen of flavone come from water molecule<sup>17</sup>**



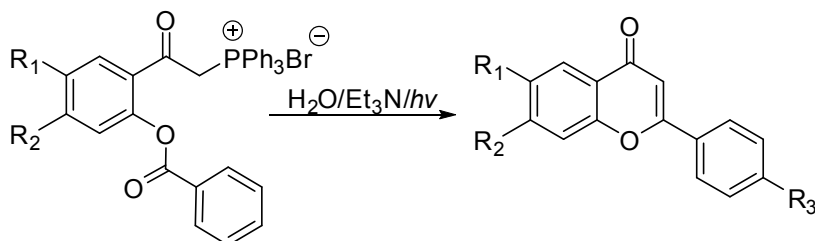
**Scheme 10: A two step synthesis of flavones via Wacker oxidation is carried out in this process<sup>18</sup>**



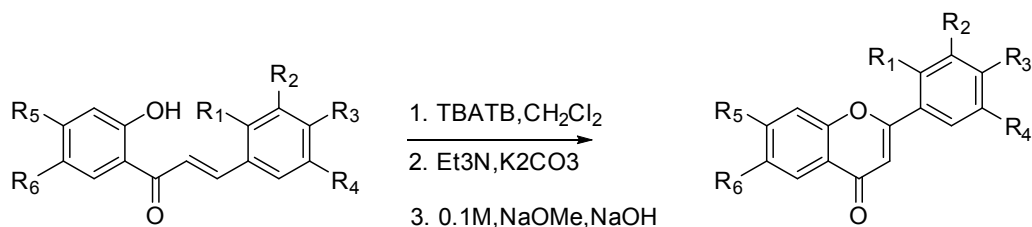
**Scheme 11: G.Kabalka & A.Meredy carried microwave assisted synthesis of flavones. Copper chloride is used as a catalyst for this process<sup>19</sup>**



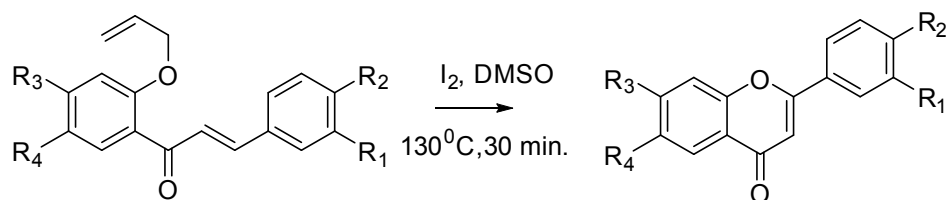
**Scheme 12:** Photo-Wittig reaction is applied for the synthesis of flavones<sup>20</sup>



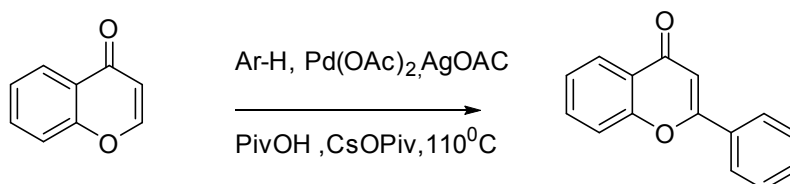
**Scheme 13:** Oxidative cyclisation of chalcone to flavone is carried out for the synthesis of flavones. Here n-tetrabutylammonium tribromide is used as a catalyst<sup>21</sup>



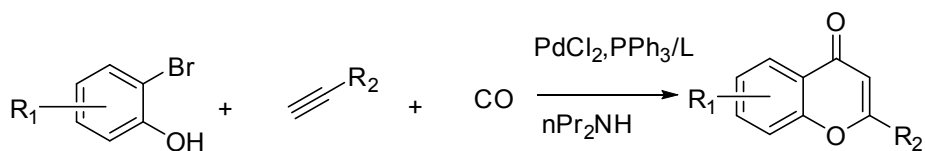
**Scheme 14:** 2'-allyloxy chalcone undergoes oxidative coupling when treated with iodine & DMSO<sup>22</sup>



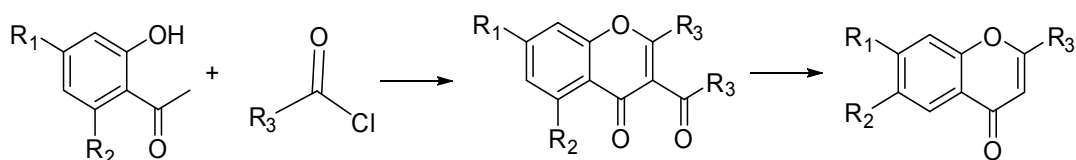
**Scheme 15:** Palladium acetate is used catalyst for the synthesis of flavones<sup>23</sup>



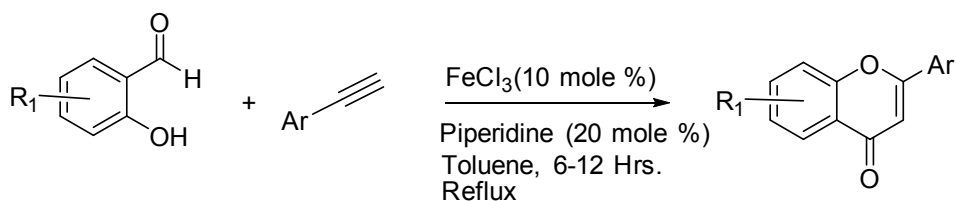
**Scheme 16:** Construction of flavones through regioselective carbonylative annulation of 2 bromo phenols & terminal alkynes is carried out<sup>24</sup>



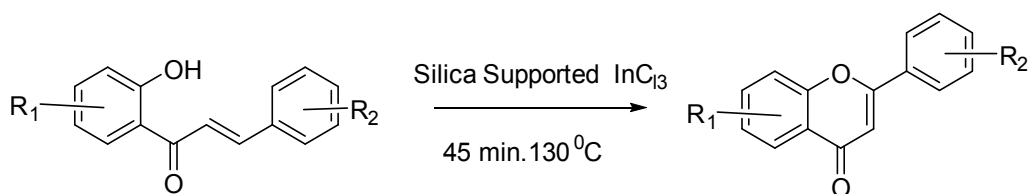
**Scheme 17:** Ganguly's synthesis includes synthesis of flavones using O-hydroxy acetophenone & acetyl chloride as a precursor<sup>25</sup>



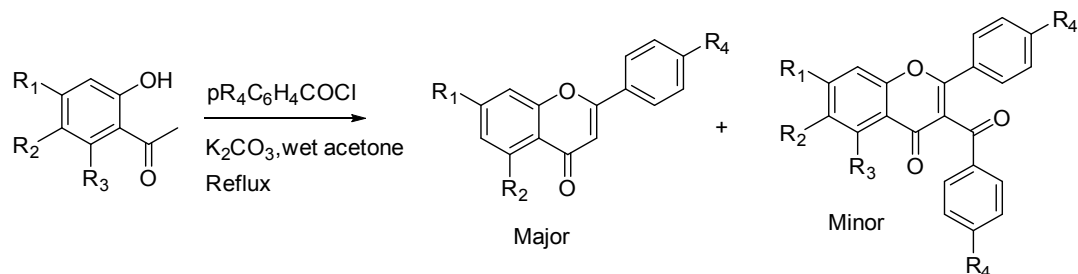
**Scheme 18:** One pot synthesis of flavones using ferric chloride is efficient method carried out by Rajiv Karmarkar & co-worker<sup>26</sup>



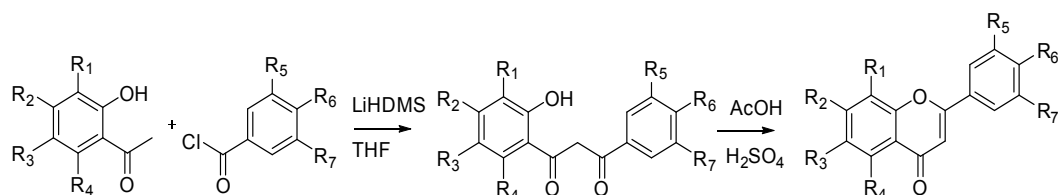
**Scheme 19:** Silica supported Lewis acids indium chloride & indium bromide undergoes oxidative coupling to give flavones<sup>27</sup>



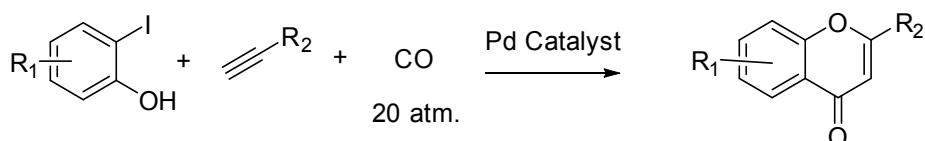
**Scheme 20:** Wet acetone is efficient catalyst for the one pot synthesis of flavones from 2-hydroxy acetophenone & acetyl chloride<sup>28</sup>



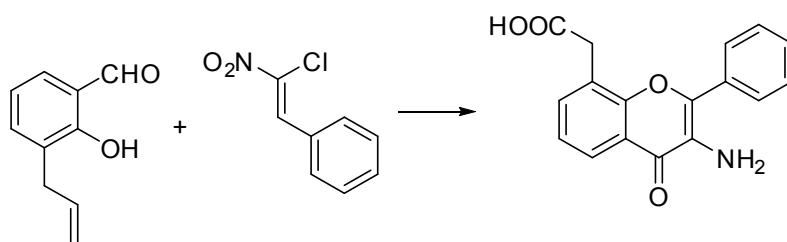
**Scheme 21:** Formation of 1,3 dione using LiHDMs followed by cyclisation using acid catalyst is achieved<sup>29</sup>



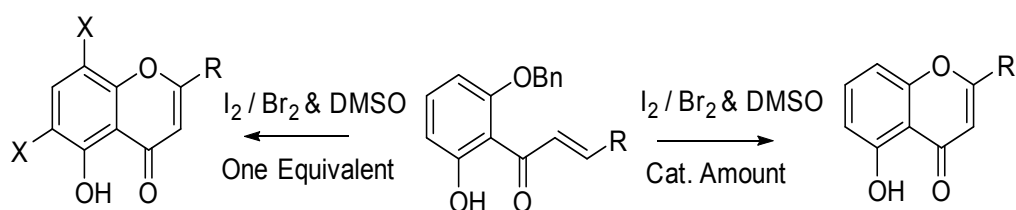
**Scheme 22: Carbonylative coupling using Pd catalyst is invention of this method<sup>30</sup>**



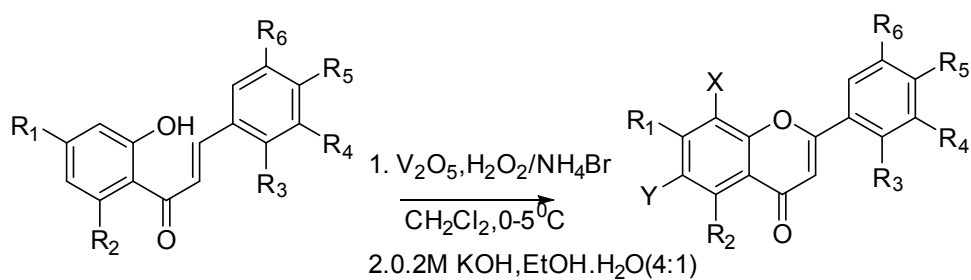
**Scheme 23: Daniel et al<sup>31</sup> suggested the following methodology consisting of five steps**



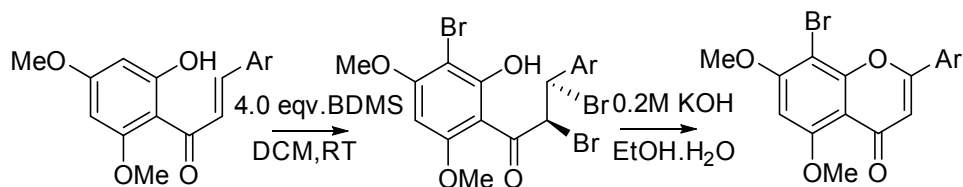
**Scheme 24: Iodo & bromo derivatives of flavones were synthesized by this method<sup>32</sup>**



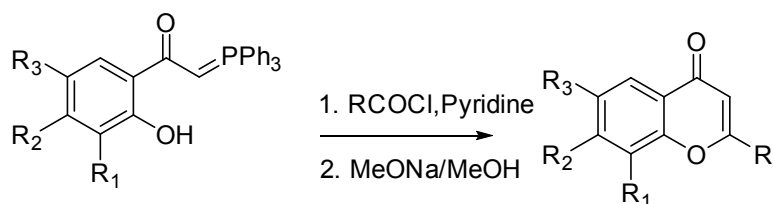
**Scheme 25: Oxidative cyclisation followed by bromination is carried out by this process<sup>33</sup>**



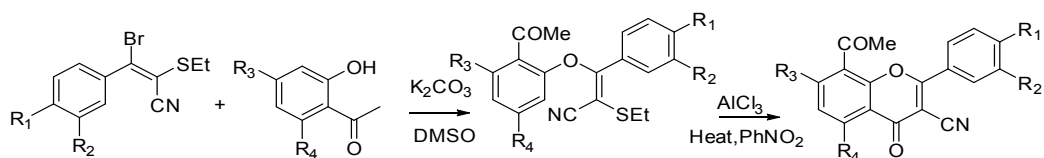
**Scheme 26: Base is used for cyclisation of intermediate to flavone<sup>34</sup>**



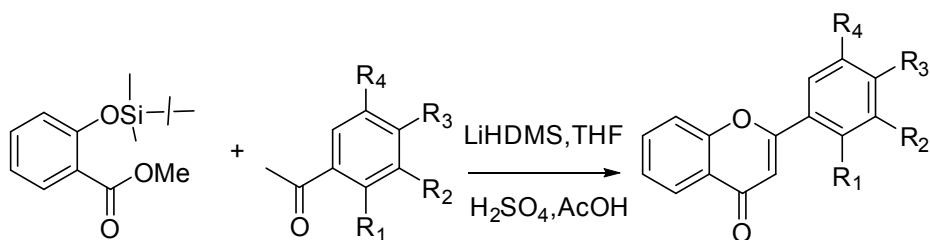
**Scheme 27: Wittig reaction is applied for the synthesis of flavones<sup>35</sup>**



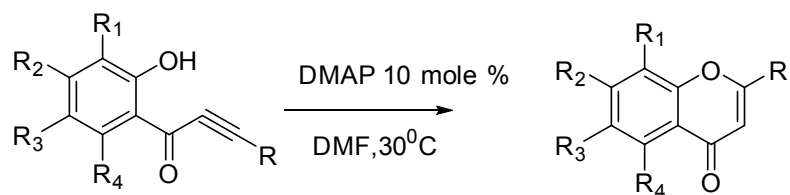
**Scheme 28: Frédéric et al<sup>36</sup> suggested**



**Scheme 29: Dhanapalan N<sup>37</sup> et al and Scheme<sup>30</sup>. Yoshida et al<sup>38</sup> suggested the following methodologies respectively**

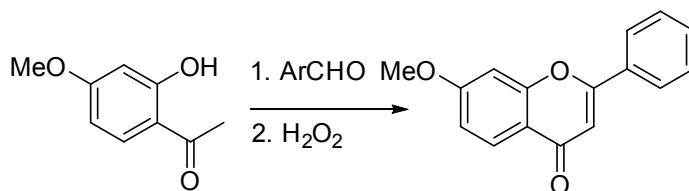


**Scheme 30:**



**Scheme 31: Hydrogen peroxide is used as catalyst for this one pot method<sup>39</sup>**

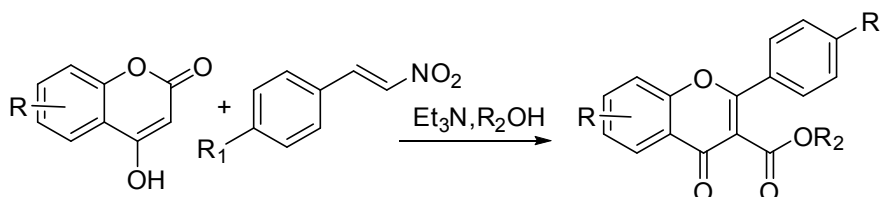




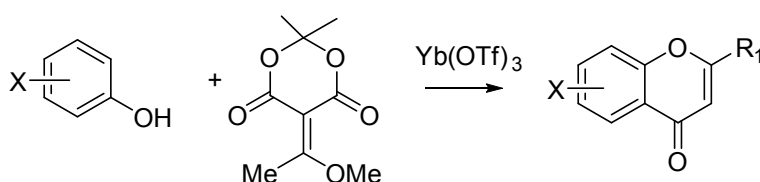
**Scheme 32:** Lewis acid ferric chloride is applied for the synthesis of flavones via oxidative coupling by Kumar & Perumal<sup>40</sup>



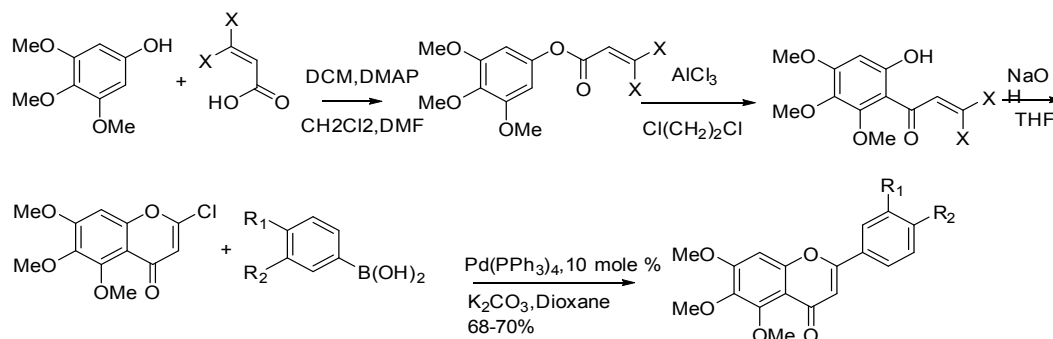
**Scheme 33:** Zanwar, M. R41 suggested the following methodology



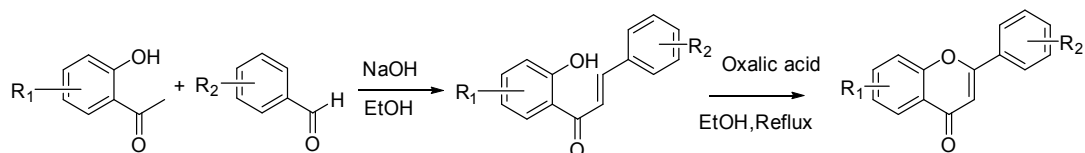
**Scheme 34:** Ytterbium triflate is used for the one pot synthesis of flavones in this paper<sup>42</sup>



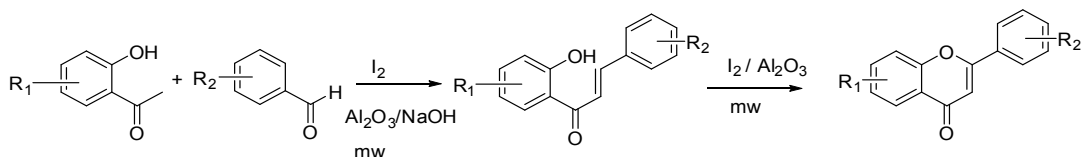
**Scheme 35:** Suzuki-Miyaura coupling used for the synthesis of flavone by Kraus & Gupta<sup>43</sup>



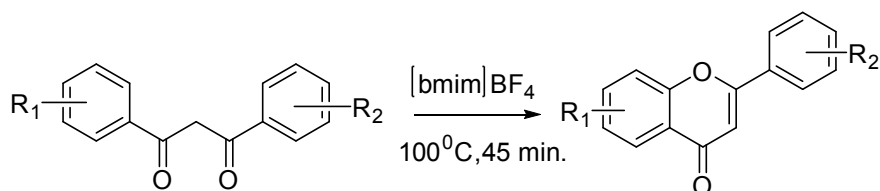
**Scheme 36:** Zambre & Sangshetti used oxalic acid for oxidative coupling method<sup>44</sup>



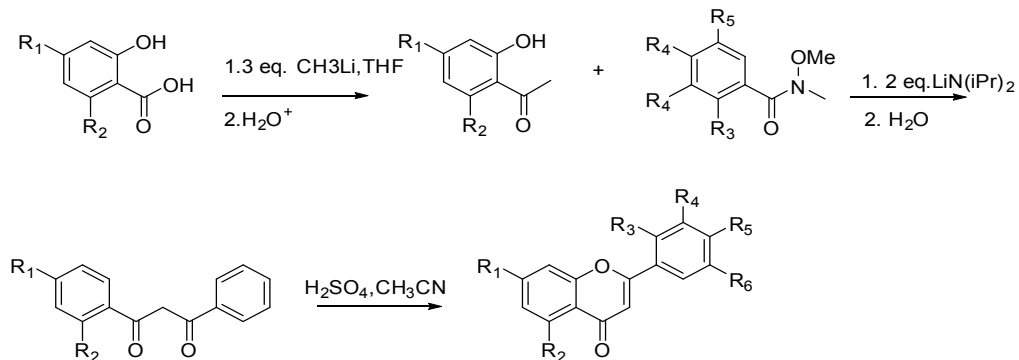
**Scheme 37: Iodine is used as catalyst for both Claisen-Schmidt condensation and oxidative coupling<sup>45</sup>**



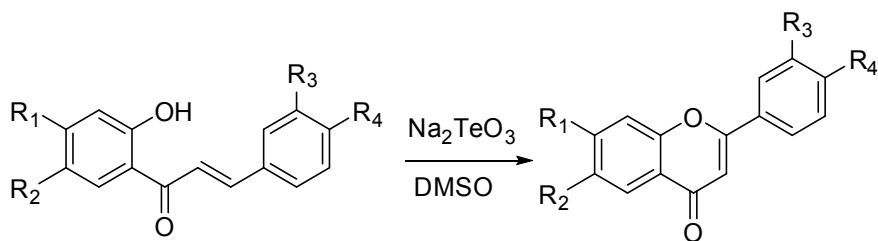
**Scheme 38: Bosale & Sarda used ionic liquid for the synthesis of flavones from dione intermediate<sup>46</sup>**



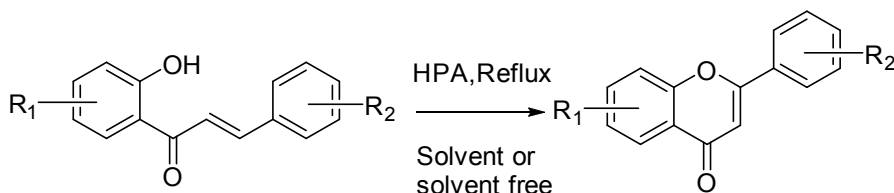
**Scheme 39: Jae In Lee *et al.*<sup>47</sup> suggested the following methodology**



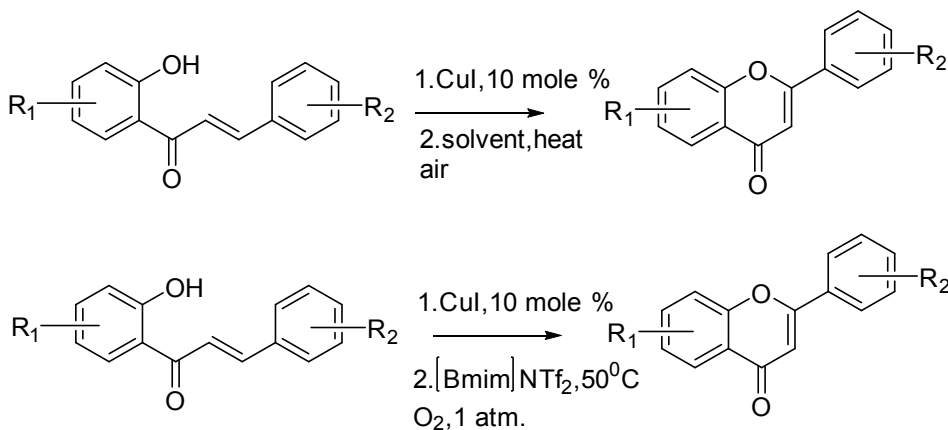
**Scheme 40: Sodium tellurite is used for the oxidative coupling method by the author KumarS & Sharma D<sup>48</sup>**



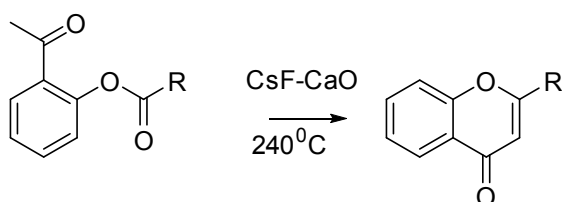
**Scheme 41: New catalyst at present is use of heteropolyacid is used for the synthesis of flavones. This solvent free synthesis avoids excess loss of solvents<sup>49</sup>**



**Scheme 42:** CuI is another important catalyst invented by Zhiyun, Du & Huifen N.. This method gives new catalyst for oxidative coupling of flavones<sup>50</sup>



**Scheme 43:** Ortho acetyl acetophenone get converted to flavone directly without conversion to 1,3 dione intermediate<sup>51</sup>



## CONCLUSION

In conclusion I try to give most of the schemes related to flavones. This review provides ready data for the people working in this field.

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