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Various Synthetic Pathways of Flavanones Focused on their Biological Activity: A Review

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ABSTRACT

Flavanones are a diverse group of phytonutrients found in most plants. They act as pigments, producing many colours like yellow, red and orange found in plant-based diets. Flavanones have become an essential component in a wide range of nutraceutical, pharmacological, therapeutic, and cosmetic applications. This is due to their ability to control critical cellular enzyme activity as well as their anti-inflammatory, Flavanones were discovered in 1938 by a Hungarian scientist named Dr. Albert Szent-Gyorgyi, who identified them as vitamin P. The challenge is that the chemistry of Flavanones is difficult because there are over 6,000 distinct compounds that belong to the flavonoid family. These challenges could be overcome by optimization techniques, novel technology, fermentation and metabolic engineering. The functional recommendations that could be added here are population heterogeneity, high study cost and time. Many different chemical families of compounds such as Flavonols, dihydroflavonols, flavones, isoflavones, flavanones, anthocyanins, and anthocyanidins are among these groups. Hundreds, if not thousands, of distinct Flavanones can be found in each of these families. Examples of some well-known flavonols include quercetin, rutin, and hesperidin while well-known apigenin and luteolin.

Keywords: Flavanones, Antimicrobial activity, Anticancer activity, Bio Flavanones, Antibacterial characteristics.

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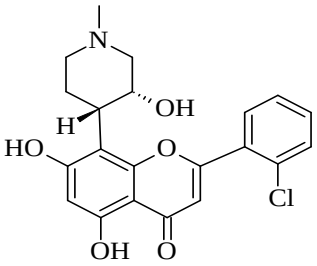
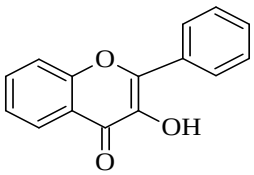
INTRODUCTION

The study of seaweeds as sources of bioactive chemicals has gotten a lot more popular in the last ten years[1]

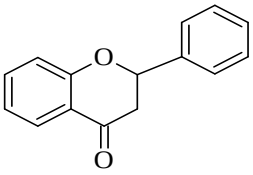
Flavopiridol are a type of polyphenolic substance that can be found in abundance in nature and are frequently used in food and medicine. They've been proven to have anti-cancer, anti-inflammatory, anti-microbial, and anti-viral qualities, among other things[2] Flavanones are distinguished by the presence of one or more hydroxylated benzene rings[3] Suzuki coupling or Ullmann coupling can be used to make them from halogen-substituted Flavanones[4] Flavanones can operate directly against infectious microorganisms, in combination with other antibiotics (synergistic interaction), or against bacterial virulence characteristics such as cell-binding capacity or pathogen-released toxins in theory[5]



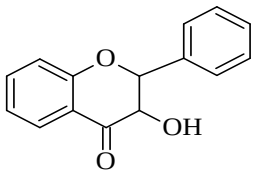
2-(2-chlorophenyl)-5,7-dihydroxy-8-(3-hydroxy-1-methylpiperidin-4-yl)-4*H*-1-benzopyran-4-one



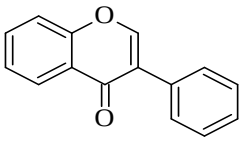
3-hydroxy-2-phenyl-4*H*-1-benzopyran-4-one



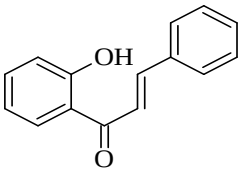
2-phenyl-2,3-dihydro-4*H*-1-benzopyran-4-one



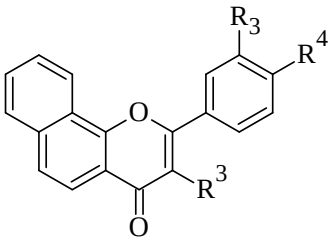
3-hydroxy-2-phenyl-2,3-dihydro-4*H*-1-benzopyran-4-one



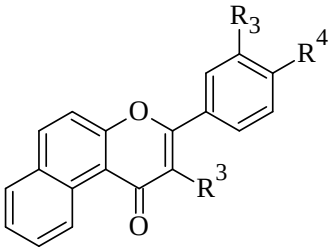
3-phenyl-4*H*-1-benzo pyran-4-one



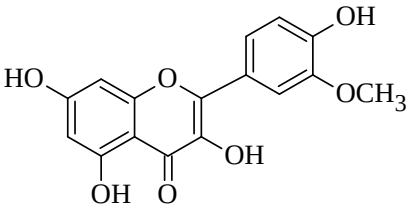
(2*E*)-1-(2-hydroxyphenyl)-3-phenylprop-2-en-1-one



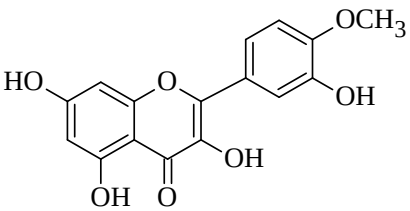
2-phenyl-4*H*-naphtho [1,2-*b*]pyran-4-one



3-phenyl-1*H*-naphtho [2,1-*b*]pyran-1-one



3,5,7-trihydroxy-2-(4-hydroxy-3-methoxy phenyl)-4*H*-1-benzopyran-4-one



3,5,7-trihydroxy-2-(3-hydroxy-4-methoxy phenyl)-4*H*-1-benzopyran-4-one

Figure 1: Various structure of flavanone

THERAPEUTICAL APPLICATIONS

Drug-resistant bacteria are a major source of worry in today's society, so finding new antibiotics that can combat these infections is critical. Some Flavanones have antibacterial characteristics, which might be beneficial.to be used for this purpose Flavanones have the potential to function in a variety of ways[6] They can be employed directly against infectious bacteria. When used in conjunction with other antibiotics (synergistic relationship), may act against bacterial virulence factors such as cell-binding ability or pathogen-produced toxins [7] These chemicals of antibacterial properties have been studied. Gram-positive bacteria, Gram-negative bacteria, and human pathogenic fungus have antimicrobial action[8]

Anti-cancer:

Cancer, also known as malignant neoplasm, is a condition in which a group of cells divides uncontrolled beyond the normal limit, then invades nearby or distant organs (metastasis), eventually resulting in cell death[9]

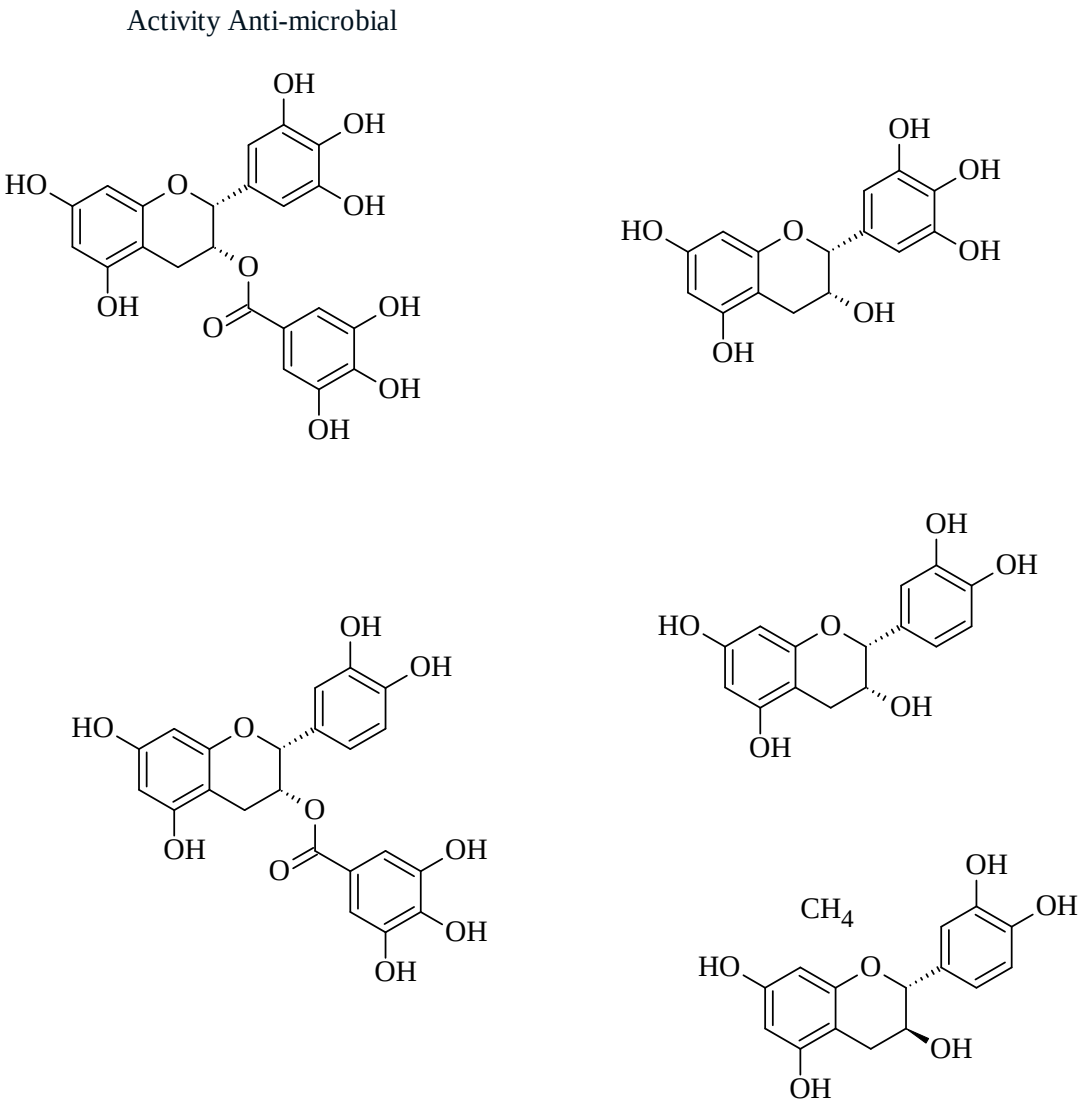
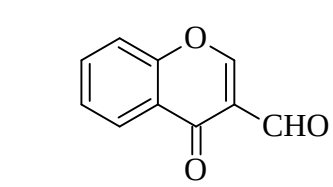
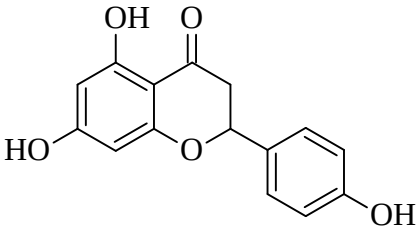


Figure 2: Few promising compounds with flavanones ring system

Flavones (also known as 2-aryl-4H-1-benzopyran-4-ones) are naturally occurring flavonoid chemicals. Bicyclic heterocycles containing oxygen have a wide range of biological actions, including anticancer, antioxidant, anti-inflammatory, antiviral, anti-mutagenic, anti-HIV, antibacterial, DNA cleavage, and so on[10]



4-oxo-4*H*-1-benzopyran
-3-carbaldehyde



5,7-dihydroxy-2-(4-hydroxyphenyl)-2,
3-dihydro-4*H*-1-benzopyran-4-one

Figure 3: Some important flavanones derivatives

Natural chemicals found in plants are gaining popularity as potential chemo preventive or chemotherapeutic treatments for different malignancies Phytochemicals have been a significant component of anticancer medicines in recent years. In fact, between 1981 and 2007, nearly 75% of nonbiological anticancer medicines authorized were either natural compounds or based on them[11]

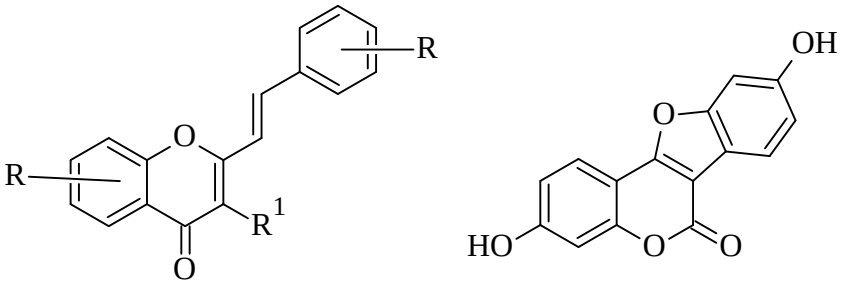


Figure 4: Some anticancer medicines of flavanones derivatives

CONVENTIONAL METHODS OF SYNTHESIS

Gammill and his coworkers described first the addition reaction of amines to 3-bromochromone in 1983[12.]

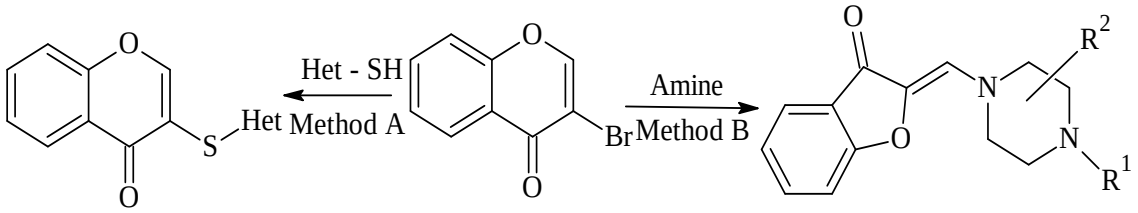


Figure 5: Various conventional routs for the synthesis of flavanones derivatives

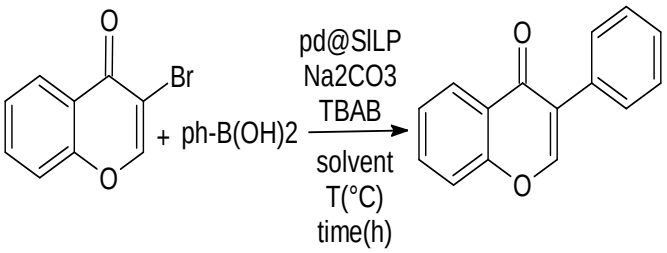
The structural core of flavanones has been generally synthesized by various conventional named reactions such as Gammill, Claisen-Schmidt condensation[13].

Though many of these methods are very effective, they often involve the use of various acids or reagents that are environmentally compatible, produce a large amount of waste and require longer reaction times[14].

Our recent success in application of microwave irradiation prompted us to carry out microwave-assisted synthesis of the target compounds. By optimizing the temperature, reaction time, solvent, base, and molar ratios of base, the optimized conditions were obtained[15].

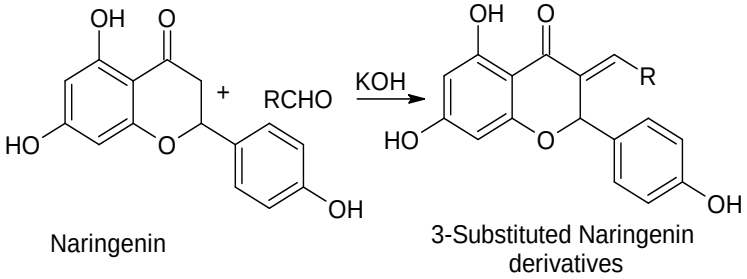
SYNTHETIC PATHWAYS

Silva *et al*



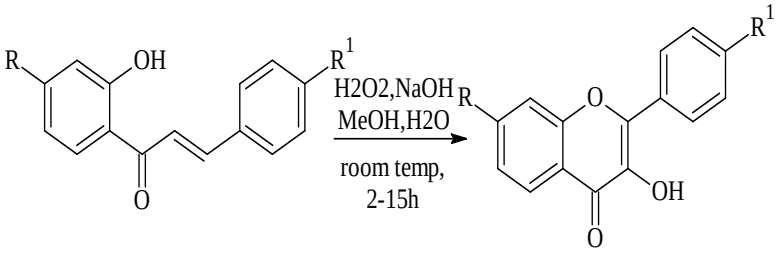
Silva *et al* were reported Ionic Liquids and Ohmic Heating in Combination for Pd-Catalyzed Cross-Coupling Reactions: Sustainable Synthesis of Flavanones his methodology was applied to the synthesis of a series of flavonoid derivatives[16].

Yogesh Murti *et al*



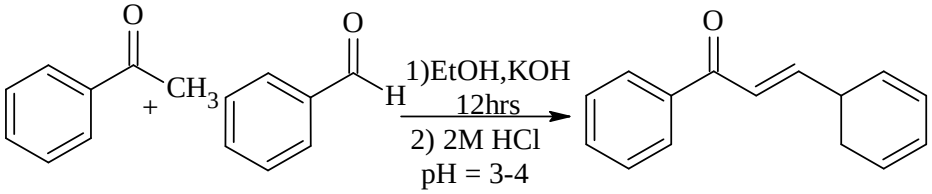
Yogesh Murti *et al* were reported Synthesis, Characterization, and Biological Evaluation of Novel Naringenin Derivatives as Anticancer Agents In the present study, a series of substituted naringenin derivatives was synthesized by Claisen–Schmidt reaction using grinding technique[17].

Błażejowski *et al*



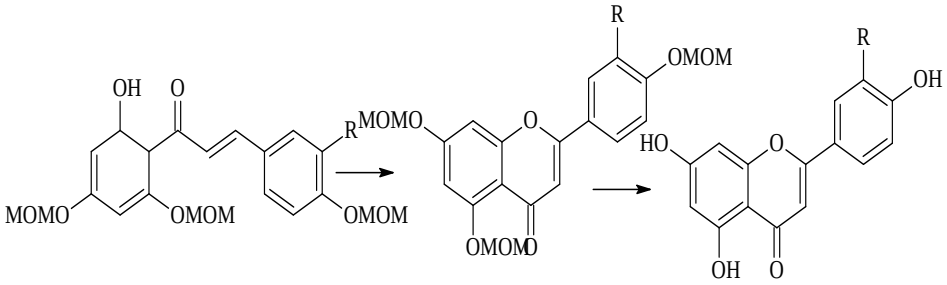
Błażejowski *et al* were reported quantum-chemical analysis of the Algar–Flynn–Oyamada reaction mechanism This work better to understanding the Algar-Flynn-Oyamada reaction mechanism and to investigate the elements that impact flavanones production[18].

Julio Alarc *et al*



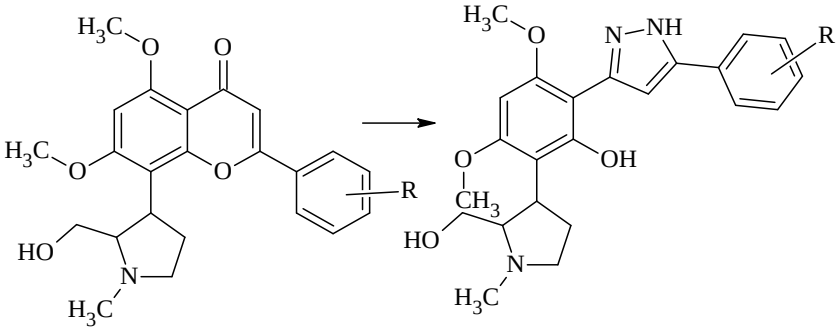
Julio Alarc et *al* were reported Aspergillus Niger catalyses the synthesis of Flavanones from chalcones Aspergillus Niger is capable of cyclizing chalcones to flavanones, affording a mimic of plant biosynthetic processes[19].

Hong-Quan Duan *et al*



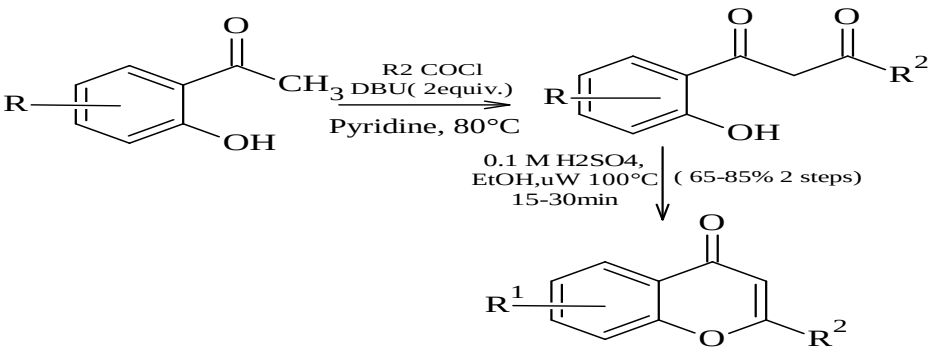
Hong-Quan Duan *et al* were reported Synthesis and Antidiabetic Activity of 5,7-DihydroxyFlavanones and Analogs in the Synthesis of structural elements are essential for antidiabetic activity, we prepared two series of flavonoid as follows the above the synthesis[20].

B. P. Bandgar *et al.*



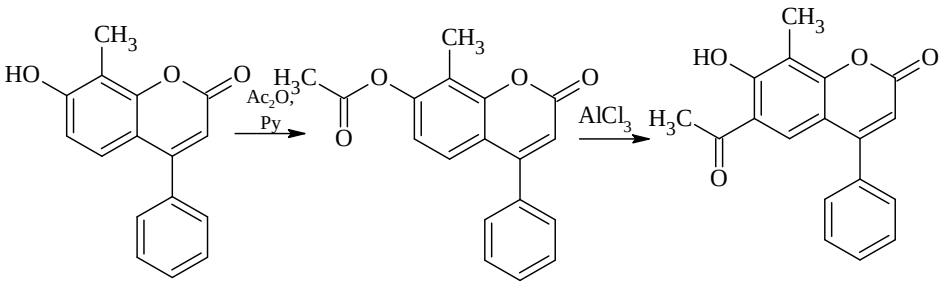
B. P. Bandgar *et al.* were reported Synthesis of novel 3,5-diaryl pyrazole derivatives using combinatorial chemistry as inhibitors of tyrosinase as well as potent anticancer, anti-inflammatory agents. In pyrazole derivatives, we have synthesized total 15 compounds with significant anticancer, anti-inflammatory and Tyrosinase inhibitory activity. Compounds we identified as the potent anti-cancer and inflammatory agent against all selected cell lines respectively[21].

S. B. Abdel Ghani *et al.*



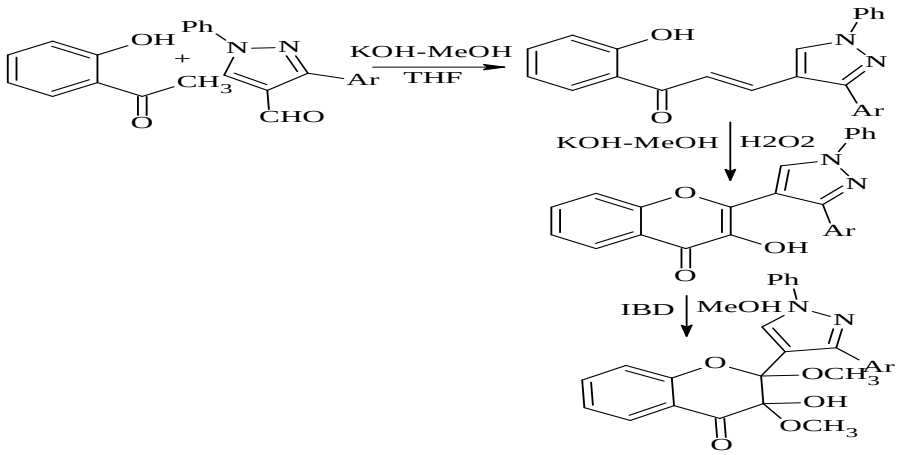
S. B. Abdel Ghani *et al.* were reported Microwave-assisted synthesis and antimicrobial activities of flavonoid derivatives. The modified Baker – Venkataraman rearrangement and consequent microwave assisted closure of the heterocyclic ring have been used to make flavanones derivatives. Antifungal activity was found in synthesised substances[22]

V. S. Moskvina *et al*



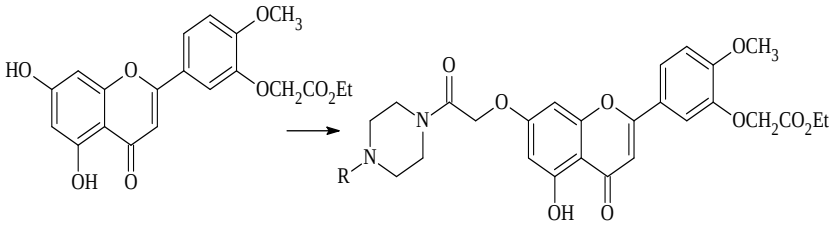
V. S. Moskvina *et al* . were reported Synthesis of Pyrano[2,3-F]Chromen-2,8-diones and Pyrano[3,2-G]Chromen-2,8-diones based on O-Hydroxy formyl(Acyl)Neo Flavanones . The flavanones from the 4-phenylcoumarin group are widely used as antioxidants, insecticides and bactericides because they have insecticidal and antibacterial properties. They are also ant atherosclerotic, anticonvulsive, antituberculosis and antimalarial properties[23]

Om Prakash *et al*



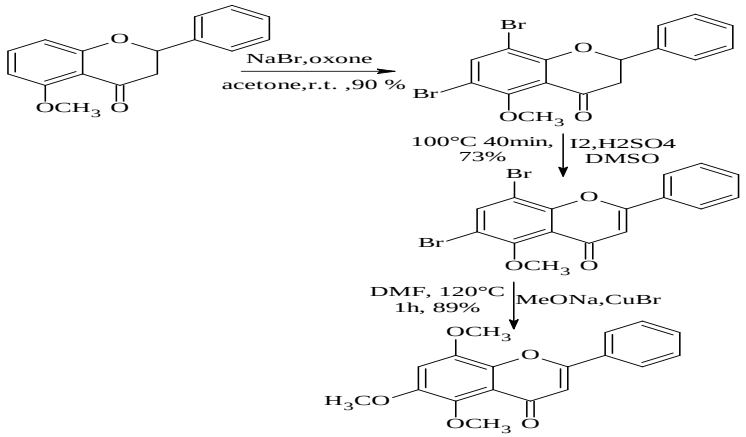
Om Prakash *et al* . were reported synthesis and antibacterial activity of some new 2,3-dimethoxy-3- hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl)chromanones. The Compounds were tested *in vitro* for antibacterial activity against three Gram-positive bacteria and both Gram-positive and Gram-negative bacteria showed good antibacterial activity[24]

G. Auffret *et al*



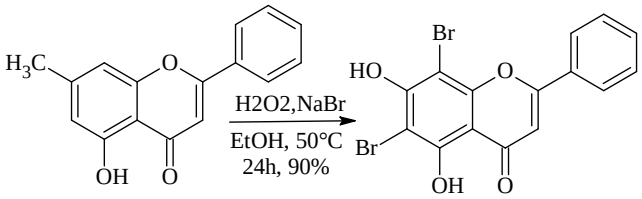
G. Auffret *et al* . were reported Synthesis and antimalarial evaluation of a series of piperazinyl flavones. Piperazinyl-chained flavanone derivatives have been synthesised and tested for ant plasmodial action. Different substitution patterns on piperazinyl and flavone moieties were tested and found to have different effects on activity[25]

Paolo Bovicelli *et al*



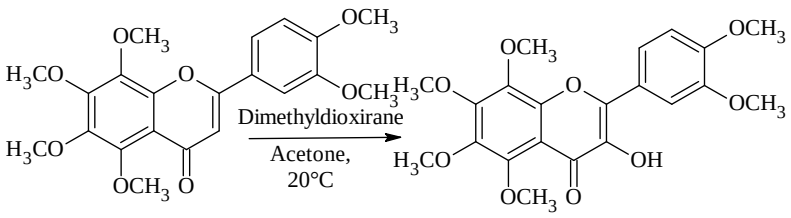
Paolo Bovicelli *et al* . were reported Efficient synthesis of polyoxygenated flavones from naturally occurring flavanones. Flavanones are components of human diet foods and beverages, and they provide a variety of biological functions in organisms, including antioxidant activity[26]

Paolo Bovicelli *et al*



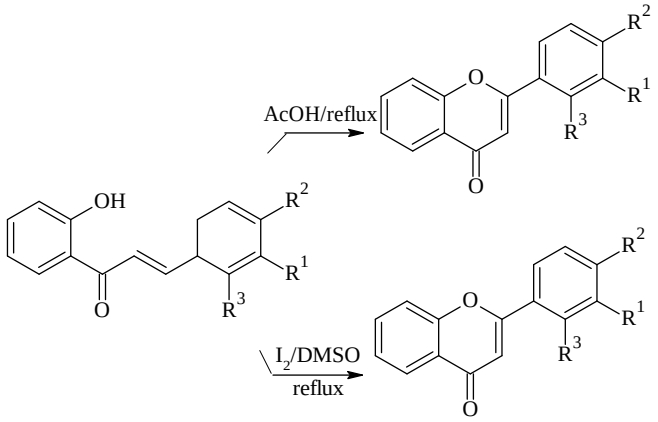
Paolo Bovicelli *et al* . were reported Radical-scavenging polyphenols: new strategies for their synthesis. The development of new methodologies for the production of polyphenols, antioxidant chemicals found in all types of plants was discussed[27]

Shiming Li *et al*



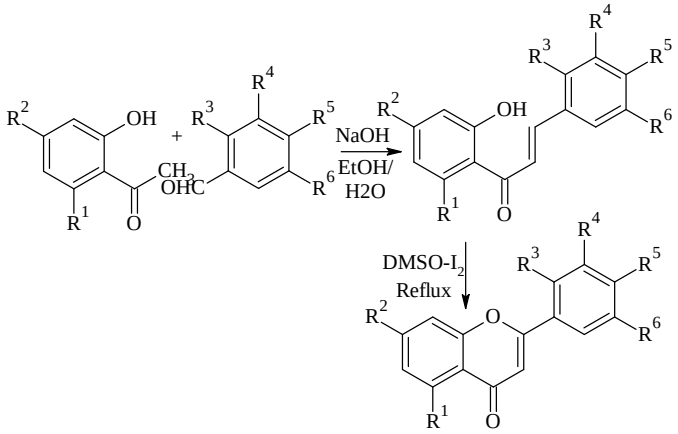
Shiming Li *et al* were reported Isolation and syntheses of polymethoxyflavones and hydroxylated polymethoxyflavones as inhibitors of HL-60 cell lines. To study their biological activity, polymethoxyflavones (PMFs) and hydroxylated PMFs were extracted and synthesised from sweet orange (Citrus sinensis) peel extract. In HL-60 cancer cell proliferation and apoptosis induction experiments, all substances were investigated[28]

M. Cabrera *et al*



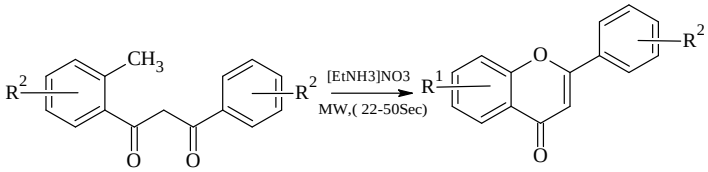
M. Cabrera *et al* were reported Synthetic chalcones, flavanones, and flavones as antitumoral agents: Biological evaluation and structure–activity relationships. The Synthetic flavanones were synthesised and tested for anticancer efficacy against human kidney carcinoma cells TK-10, human mammary adenocarcinoma cells MCF-7, and human colon adenocarcinoma cells HT-29[29]

Mostahar *et al*



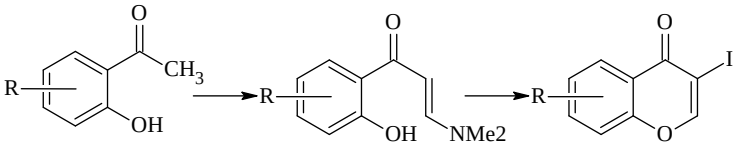
Mostahar *et al* were reported Cytotoxic and antimicrobial activities of some synthetic flavones. Several flavanones have been synthesised and their biological activity against several bacterial and fungal strains, as well as brine shrimp nauplii, has been examined[30]

Rajendra P. Pawar *et al*



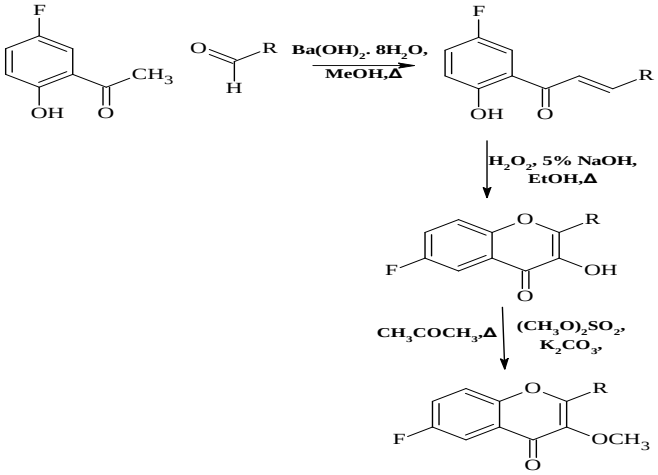
Rajendra P. Pawar *et al* were reported A facile synthesis of flavones using recyclable ionic liquid under microwave irradiation. This microwave irradiation method is more useful due to its shorter reaction time, simple reaction conditions, and higher yield. The method is simple and easy, and it can be used in instead of current methods[31]

Vasselin *et al*



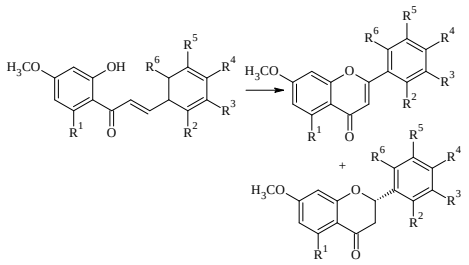
Vasselin *et al* were reported Structural Studies on Bioactive Compounds. 40.1 Synthesis and Biological Properties of Fluoro-, Methoxyl-, and Amino-Substituted 3-Phenyl-4H-1-benzopyran-4-ones and a Comparison of Their Antitumor Activities with the Activities of Related 2-Phenylbenzothiazoles. Due to its structural similarities to known flavanones, a new series of fluoro-, Methoxyl-, and amino-substituted isoflavones have been synthesised as potential anticancer drugs[32]

Conti et al.



Conti *et al.* were reported Synthesis and anti-rhinovirus properties of fluoro-substituted Flavanones Fluoro-substituted flavones and 2-styrylchromones were synthesised, identified, and tested for anti-rhinovirus action[33]

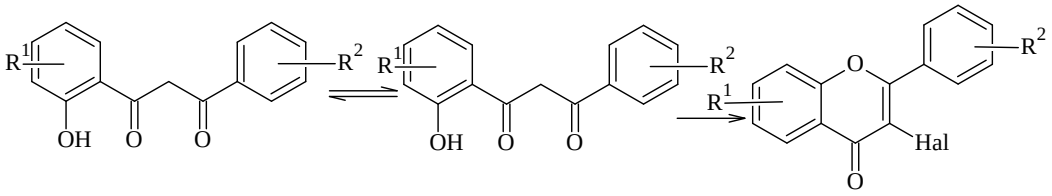
Y. K. Rao *et al*



Y. K. Rao *et al* were reported Synthesis, growth inhibition, and cell cycle evaluations of novel flavonoid derivatives. A variety of flavonoid derivatives were produced by cyclization

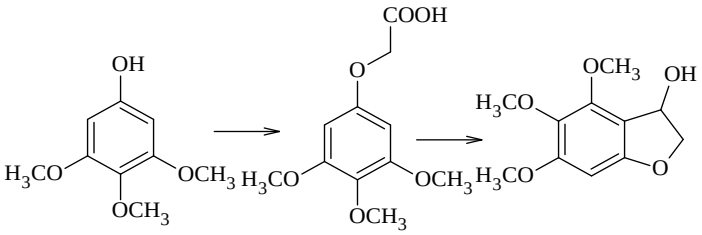
of substituted coumarins as part of our ongoing investigation for potential novel anticancer drugs[34]

Silva *et al*



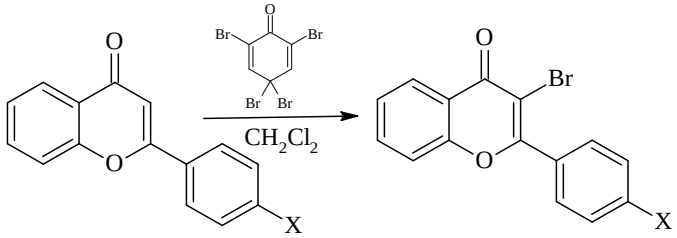
Silva *et al* were reported Synthesis and Transformation of Halochromones. the most significant developments in the synthesis and reactivity of halogen-containing chromones, especially simple flavanones[35]

N. J. Lawrence *et al*



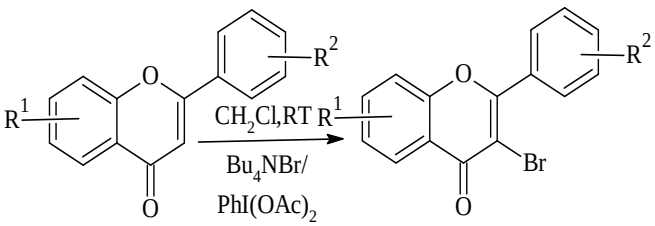
N. J. Lawrence *et al* were reported The Total Synthesis of an Aurone Isolated from Uvaria hamiltonii: Aurones and Flavones as Anticancer Agents. The anticancer activity of naturally occurring flavanones extracted from Uvaria hamiltonii, as well as a variety of flavanone derivatives based structurally on recognised tubulin binding agents, was investigated[36]

Yung Hyup Joo *et al*



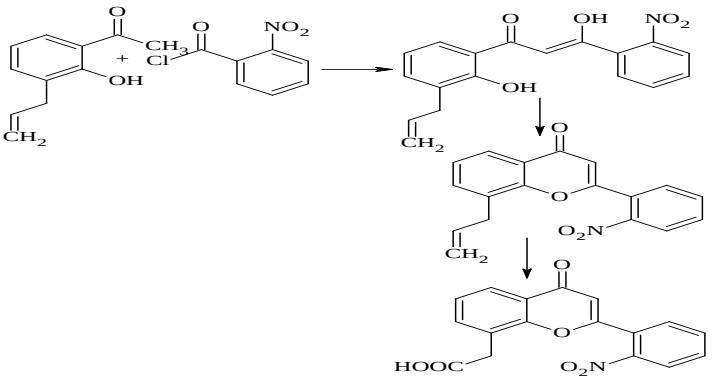
Yung Hyup Joo *et al* were reported a convenient synthesis of 3-bromoflavones. Flavanones with easily degradable functional groups were also brominated without producing harmful oxidation products[37]

Ho Sik Rho *et al*



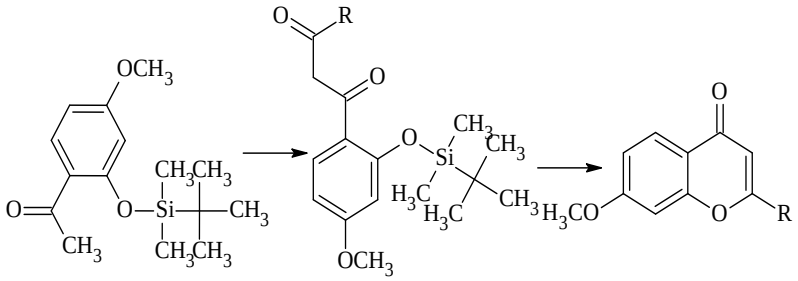
Ho Sik Rho *et al* were reported synthesis of 3-bromo derivatives of flavones The reaction of the relevant flavanone derivatives provided a variety of 3-halo flavanones[38]

Daniel Dauzonne *et al*



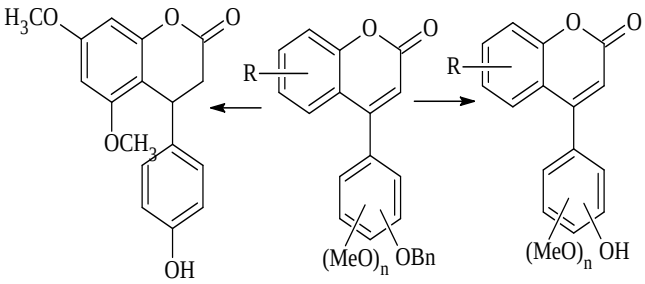
Daniel Dauzonne *et al* were reported Synthesis and Biological Evaluation of Novel Flavone-8-acetic Acid Derivatives as Reversible Inhibitors of Aminopeptidase N/CD13. The cell surface aminopeptidase N (APN/CD13), which is overexpressed in tumour cells, is essential for angiogenesis. However, effective, selective, and particularly noncytotoxic inhibitors of this protein are limited, and the present work was done with the aim of generating a new category of noncytotoxic APN/CD13 inhibitors[39]

Khadiga Ahmed Ismail *et al*



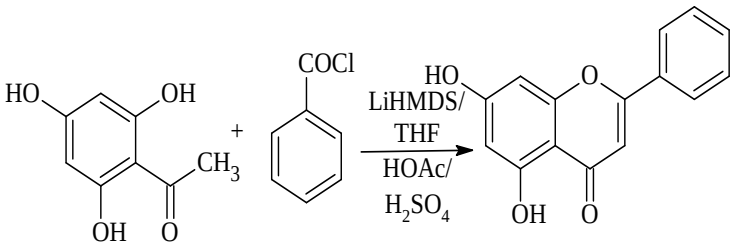
Khadiga Ahmed Ismail *et al* were reported Synthesis and biological evaluation of some novel 4H-benzopyran-4-one derivatives as nonsteroidal antioestrogens. The preparation and characterisation outline the synthesis of two series of flavones substituted at the 2- or 3-position in order to investigate the influence of structural modulation around the flavone nucleus on estrogenic and antifertility actions[40]

Jean-Pierre Finet *et al*



Jean-Pierre Finet *et al* were reported Synthesis of c-ring hydroxylated neo-Flavanones by ligand coupling reactions. When palladium-catalyzed hydrogenolysis was done in the presence of acetic acid, selective debenzylation occurred in high yields[41]

Geahle *et al*



Geahle *et al* were reported synthesis and evaluation of hydroxylated flavones and related compounds as potential inhibitors of the protein-tyrosine kinas a variety of hydroxylated flavones and related compounds were synthesised and tested for their ability to inhibit the in vitro protein-tyrosine activity of an enzyme known to be important in mediating signal transduction from the CD4 receptor during lymphocyte activation[42]

CONCLUSION

Flavanones are a class of chemicals having a wide range of biological functions that are useful in a variety of industries, including food, medicines, and cosmetics. As a result of today's customer demands for products that significantly improve their quality of life. For its wide variety of applications. this review will be extremely beneficial to researchers in this field. It would also assist them in developing a new environmentally friendly, efficient, and cost-effective technique. This is vital today because we require an ecologically friendly approach for the large-scale manufacture of such an important biological component, which may then be employed in a variety of processes to produce a future effective pharmacophore.

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CONFLICT OF INTEREST

All the authors have no conflicts of interests.

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