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SYNTHESIS OF COUMARIN AND THEIR DERIVATIVES WITH THEIR APPLICATINS BY DIFFERENT METHODS

Shilpa V. Narale*

Assistant Professor, Department of Chemistry, Dr. D. Y. Patil Arts, Commerce and Science College, Pimpri, Pune – 411018. Maharashtra, India.

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***Corresponding Author**
Shilpa V. Narale
Assistant Professor,
Department of Chemistry,
Dr. D. Y. Patil Arts,
Commerce & Science
College, Pimpri, Pune –
411018. Maharashtra, India.

ABSTRACT

Coumarin is a natural product obtained from mullein (Verbascum spp.), sweet grass (Hierochloe odorata), cassia cinnamon (Cinnamomum cassia) tonka bean (*Dipteryx odorata*), vanilla grass (*Anthoxanthum odoratum*) and sweet wood ruff (*Galium odoratum*). Coumarins are classified as a member of the benzopyrone family all of which consist of benzene ring joined to pyrone ring. The benzopyrones can be classified into the benzo alpha-pyrones to which the coumarins belong and the benzo gamma-pyrones of which the flavonoids are principal members. Umbliferone, esculetin and scopoletin are the most widespread coumarins in nature. During the synthesis of these compounds ortho-hydroxylation should respectively takes place on p-coumaric, caffeic and ferulic acid. The coumarins are of great interest due to their pharmalogical properties. In particular their physiological, bacteriostatic and anti tumor activity make these compounds attractive backbone derivatisation and screening as novel therapeutic agents. It also shows anti-HIV, anti-fungal, and anti-cancer activity. Coumarins are nowadays an important group of organic compounds that are used as additives to food and cosmetics, optical brightening agents, and dispersed fluorescent and laser dyes. The derivatives of coumarin usually occur as secondary metabolites present in seeds, root, and leaves of many plant species.

KEYWORDS: Coumarin is a natural leaves of many plant species.

INTRODUCTION

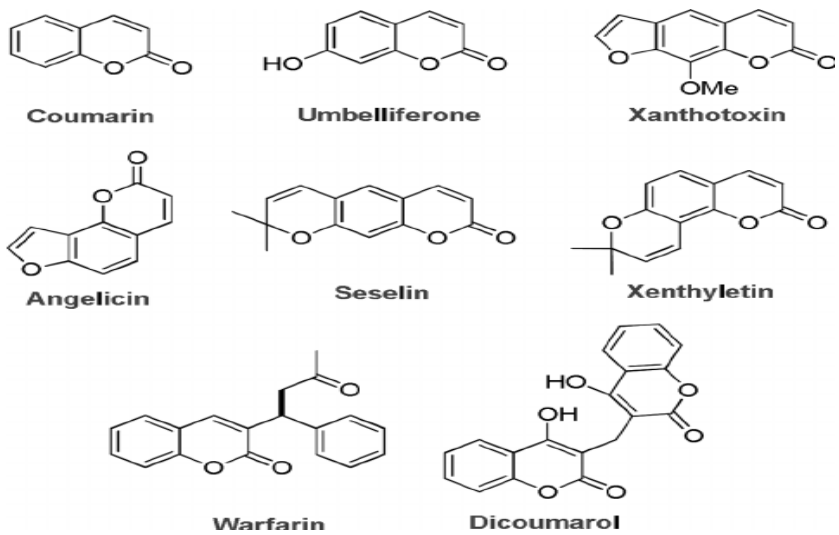
Coumarin is an organic compound that has two six-membered rings fused together, with one of the rings being a benzene ring and the other containing alkenes functionality and an ester

functional group. Coumarins play an important role in both natural systems like plants and also in medicinal applications as drug molecules. The primary topics in our lesson will be the general structure of coumarin, how it's made synthetically, and some important derivatives of coumarin in terms of application.

Coumarin is a fragrant organic compound that is of importance in perfumery, medicines, and dyes. Coumarins can be synthesised by one of such methods as the Kostanecki Acylation, Wittig reaction, Claisen rearrangement, Knoevenagel condensation, Pechmann reaction as well as Perkin reaction. Some of the industrially important coumarins are the 4-methylsubstituted group (e.g., 7-hydroxy-4-methylcoumarin and 7-diethylamino-4-methylcoumarin. The reactions are monitored by UV, IR, and NMR. Melting points are in good agreement with literature data.

Experimental

Structure of Coumarin: Actually, Coumarin belongs to a broader class of compounds called the benzopyrones. It is simple to identify, it's just two six-membered rings fused together in which one of the rings being a benzene ring, and the other ring containing an alkenes and functional group inside the ring is ester.

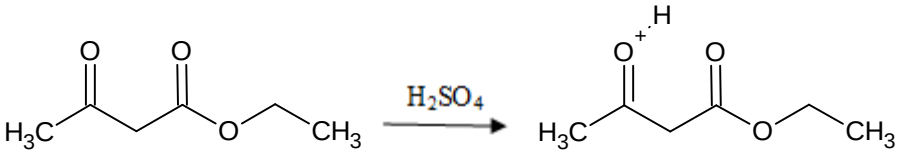


General structure of coumarin

Synthesis of Coumarin: Now that we know how to identify a coumarin based on its structure, let's talk about how it's made synthetically. (Note: coumarin and derivatives of coumarin can be isolated from plant sources in nature but here we are going to focus on man-made methods of its preparation).

1) Knoevenagel condensation: It is reaction in which there is a nucleophilic addition of an active hydrogen compound to a compound containing carbonyl group product formed followed by a dehydration in which a molecule of water is eliminated hence condensation. The product is αβ-unsaturated ketone (a conjugatedenone).

1.



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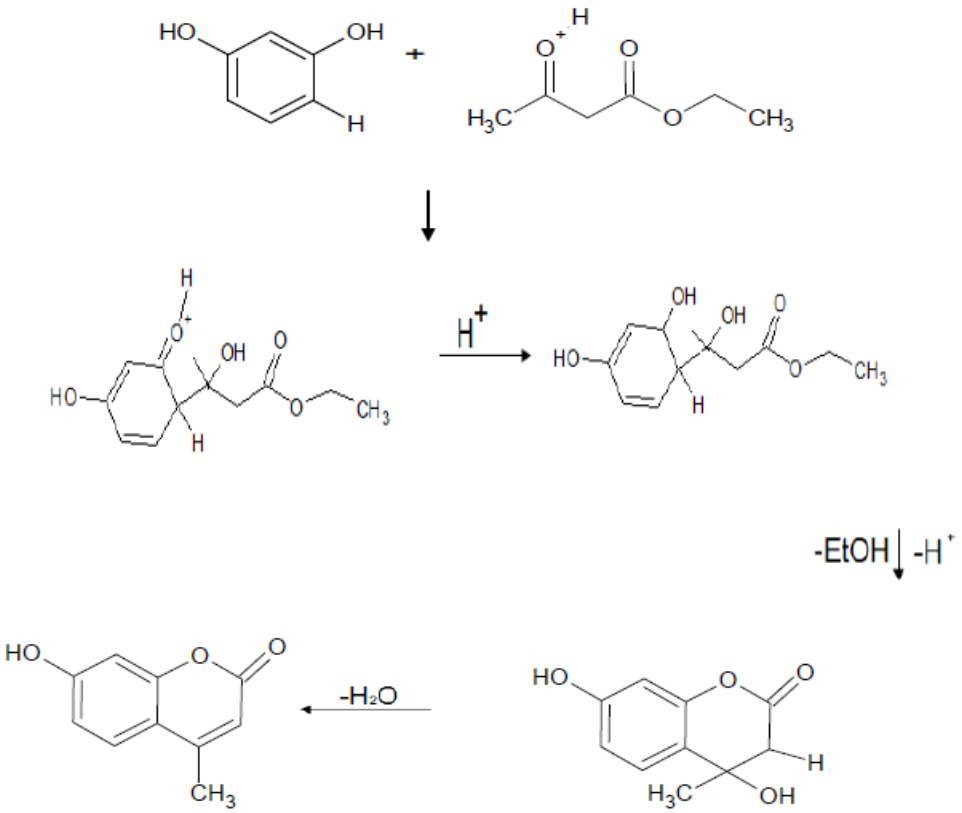
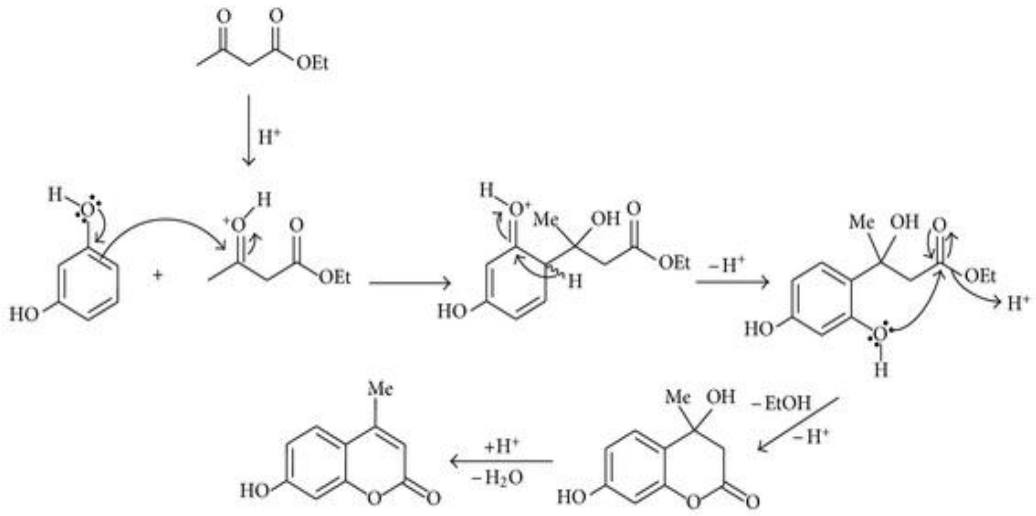


2) Pechmann Condensation

This involves phenol and carboxylic acid or ester containing β-carbonylgroup undergocondensation to give coumarin. The mechanism involves an estertification/transesterification followed by attack of the activated carbonyl ortho to the oxygen to generate the new ring.

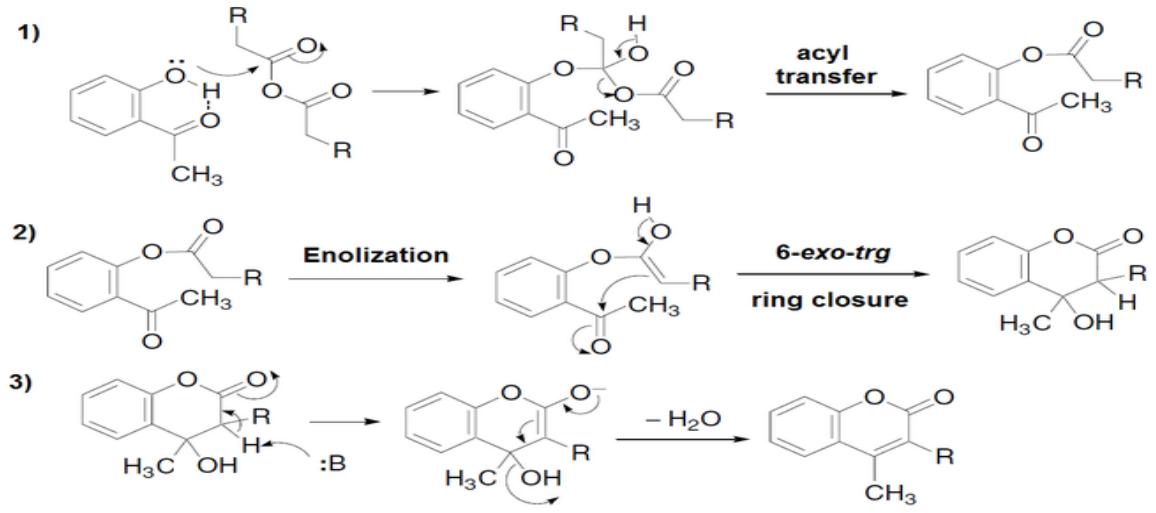


Pechmann condensation of phenol and ethyl acetoacetate to make 4-methylcoumarin

3) Kostanecki Acylation

Another popular method of making coumarins is by a reaction called the Kostanecki acylation, which involves the use of an Ortho-hydroxyaryl ketone (an aromatic ketone with an -OH group adjacent to it) with an anhydride of some sort. Much like the Pechmann condensation, this transformation is a great way to make coumarins because it has pretty mild reaction conditions and uses cheap and abundant starting materials.

Note: in this reaction any anhydride can be used, which is why we use the 'R' group designation for the anhydride reactant.



Kostanecki acylation of an ortho-hydroxyaryl ketone with an anhydride to make a 4-methylcoumarin product.

Application

In this work, coumarin was synthesized by Perkin reaction using salicylaldehyde, acetic acid and sodium acetate. Due to the misuse of acetic anhydride in narcotics synthesis, acetic acid was substituted for acetic anhydride in Perkin reaction. On the basis of this substitution a hypothesis was proposed that "acetic acid could be substituted as an acetylating agent in place of acetic anhydride in coumarin synthesis via Perkin reaction". In the present research project, salicylaldehyde was prepared from phenol, sodium hydroxide and chloroform for further procedure. Then four different coumarin samples were synthesized by changing the parameter of reactants proportions. From this parameter, we designed a trend of high product yield. Yields of Coumarin samples will lead towards either acceptance or rejection of the above proposed hypothesis. In the next step, these Coumarin samples were characterized by age yield (%), solubility and melting points. At last Antibacterial activities of all the four coumarin samples were evaluated against two bacterial strains; E.coli and S.aureus. As a consequence of all above, it was inferred that the yields of all coumarin samples obtained were low as compared to the yield obtained by the use of acetic anhydride in previous reports. This led to the rejection of proposed hypothesis. Among four Coumarin samples, sample-4 obtained by taking equal amounts of all the reactants had shown maximum yield, best characterization and excellent antibacterial activity. In spite of low yields obtained, the remarkable antibacterial activities of Coumarin samples have enabled us to suggest coumarin as a strong antibacterial agent and it must be employed for further applications. Coumarin is a **flavouring substance** which is contained in relatively high concentrations in **cinnamon** varieties collectively known as "**Cassia cinnamon**". In especially **sensitive** persons, even comparatively small quantities of coumarin can cause **liver** damage, although the effect is usually reversible.

These oral **anticoagulants** are derived from **coumarin**, which is found in many plants. A prominent member of this class is warfarin (Coumadin). It takes at least 48 to 72 hours for the anticoagulant effect to develop.

When highly diluted, the scent is reminiscent of freshly-mown hay. In **cosmetics** and personal care products, **Coumarin** is used in the formulation of aftershave lotions, bath products, bubble baths, cleansing products, moisturizers, skin care products and suntan products. **Coumarin** functions as a fragrance ingredient.

Anticoagulants and antiplatelet drugs eliminate or reduce the risk of blood clots. They're often called blood thinners, but these medications don't really thin your blood. Instead, they help prevent or break up dangerous blood clots that form in your blood vessels or heart Their function is far from clear, though suggestions include waste products, plant growth regulators, fungistats and bacteriostats. It is therefore of utmost importance that the synthesis of coumarin and its derivatives should be achieved by a simple and effective method.

Antifungal activities of the synthesized coumarins and angelicin derivatives were reported against Candida albicans, Cryptococcus neoformans, Saccharomyces cerevisiae and Aspergillusniger. Human cell line cytotoxicity of several coumarins was evaluated against KB cells. Angelicin and several potent antifungals showed to be non-toxic in this assay.

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