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Research Article

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DESIGN AND SYNTHESIS OF SOME NEW AND NOVEL ANALOGUES OF CURCUMIN OF POTENTIAL ANTICANCER ACTIVITY

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Abstract

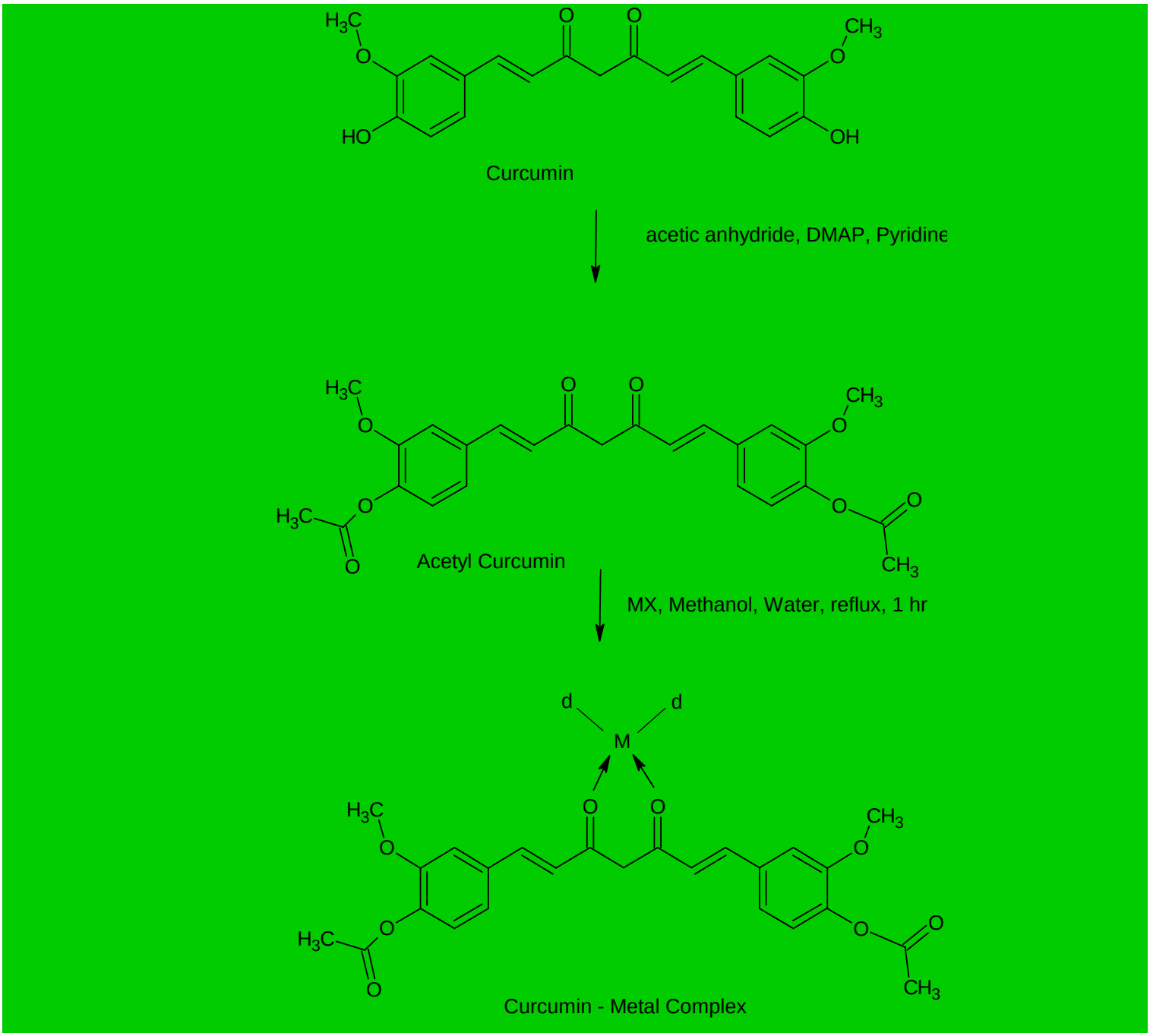
Curcumin,1,7-bis(4-Hydroxy-3-Methoxy Phenyl)-1,6-heptane-dione-3,5-dione,or Diferuloyl methane(CR) is a yellow pigment obtainale from the rhizomes of the plant Curcuma longa, which is one of the major species used in the Indian Culinary practices.It is considered to be a safe Phytochemical without having any toxic , genotoxic and teratogenic properties even at high doses.There is compelling evidience that curcumin has cancer chemopreventive properties in a range of animal models of chemical carcinogenesis .A few natural products such as curcuminoids have both phenolic and B-diketone groups in the same molecule and thus become potential Antioxidants .Curcuminoids were reprted to possess antioxidant,anti-inflammatory,anticancer and antiviral properties.The compound has antioxidative and Antiinflamatory properties, and several mechanisms have been proposed by which it might block initiation and progression of cancer.Loo and Co-workers have proposed that H2O2 is the indirect DNA damaging agent in curcumin treated Jurkat T-Lymphocites .The remarkable antioxidant properties of curcumin are thought to arise from the Hydroxyl groups in the aromatic side chains or from the CH2 group of the B-diketone moiety.It has also been indicated that the Hydrogen abstraction from the methylene CH2 group is responsible for the remarkable antioxidant activity of curcumin. Recently Priyadarshani etal have confirmed that phenolic OH is mainly responsible for the activity of curcumin .Attempts have been made wherein the phenolic OH is blocked on both the rings keeping the B-diketone moity intact.However modifications in the B-diketone are less explored except where

this moity ids modified with Hydrazide and Cyclohexanone groups.Lack of systematic study of Antioxidant activity of phenolic curcumin analogues and their extreme potential to be the ideal Anticancer drugs , prompted us to synthesize and evaluate the Antioxidant activity and Anticancer activity.

Results and Discussion

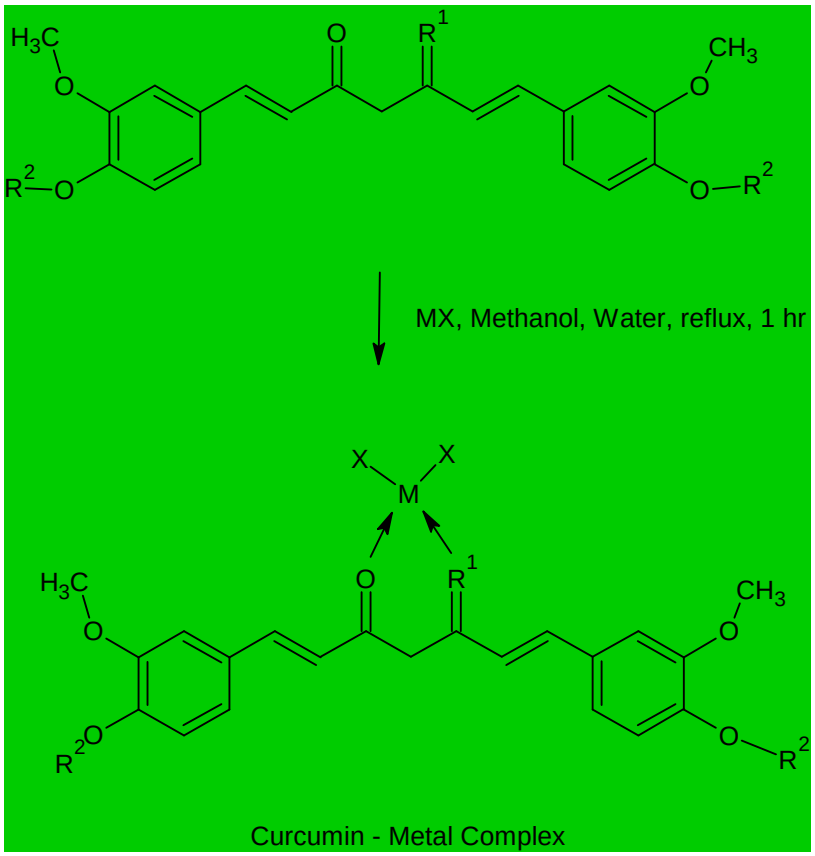
As Curcumin is found to be one of the most important starting point for making new anti-cancer compounds, and several research groups around the world are actively working on Curcumin because of the promising results observed by Curcumin and its analogs, We became interested and envisaged several novel analgues and derivatives. The approach to our design involve several steps. Firstly synthesize appropriate starting materials, followed by the synthesis of the corresponding Schiff bases, with several amines, phenyl hydrazine, semicarbazones, thiocarbazones etc. The compounds thus prepared are complexed with transition metals like Copper, Nickel, Cobalt, Zinc, Chromium, Gold, Platinum, Palladium, and Ruthenium.

Initially we have designed several derivatives like Acetyl, benzoyl, methyl curcumins as the starting points. These derivatives are prepared according to the standard literature methods. The acetyl curcumin was obtained in excellet yield from the acetylation of Curcumin with excess of acetic anhydride, using N,N-dimethyl amino pyridine as catalyst, and Pyridine as solvent. The reaction proceeded smoothly resulting in the formation of a single product according to the precoated silicagel TLC. The product obtained after usual workup procedure has shown a single spot on TLC, and taken as such for the next reaction i.e. complexation with the metal using Copper (II) Sulfate. The reaction of metal complexation was carriedout in a mixture of methanol and water at refluxing temperature for one hour. The change in the color of the reaction mixture indicated that the complexation has taken place which is usually the case in case of metal complexation reactions. The metal complex of acetylcurcumin obtained as the crude product is isolated and further characterization is in progress. Similar reactions are carriedout on other derivatives of curcumin as well and show promising results. Further results will be published in due course.



Scheme 1

M = Cu, Ni



R1 = O, R2 = Acetyl, Bezoyl, Methyl

R1 = NOH, R2 = Acetyl, Bezoyl, Methyl

R1 = NNHCONH2, R2 = Acetyl, Bezoyl, Methyl

R1 = NNHCSNH2, R2 = Acetyl, Bezoyl, Methyl

Scheme 2

Typical Experimental Procedure

1. Acetyl Curcumin

Curcumin (1 g, moles) was dissolved in pyridine (5 ml), followed by the addition of DMAP (10 mg) as catalyst. The resulting reaction mixture was cooled to 0 deg C, followed by the addition of excess acetic anhydride (5 ml). The reaction mixture was stirred for 1 hour initially at 0 deg C followed by stirring at room temperature. The reaction mixture was poured in water acidified with dilute hydrochloric acid. The resulting reaction mixture was extracted

with dichloromethane (3 times), followed by drying over anhydrous sodium sulfate and concentration of solvent provided acetyl curcumin in almost quantitative yield. TLC was checked on precoated silicagel TLC plates which showed a single spot. The product obtained after workup was taken as such to the next step of metal complexation. Similarly benzoyl curcumin and methyl curcumin are prepared.

Preparation of Curcuminoid ligands:

The above mentioned Curcuminoid ligands are prepared according to the standard literature procedures.

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