

Antioxidant Activities of Imino Chromene Derivatives with Even Alkyl tail: Synthesis and Characterisation

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Abstract: The reaction between substituted 4-hydroxybenzaldehyde, active methylene compounds iminochromene derivatives. Structures of the were established upon the basis of IR, ¹HNMR, ¹³CNMR, and MASS data. *In vitro*, antioxidant activities of these compounds against superoxide anion radical, nitric oxide radical, DPPH radical and hydrogen peroxide were evaluated and compared with standard natural antioxidants ascorbic acid.

Keywords: chromenes, imines, amines, antioxidants

I. INTRODUCTION

Multicomponent reactions (MCRS) are reactions where numerous reactants involved in single synthetic operation and give new compounds.¹ This type of reactions avoids purification process and often wide variety of complex molecule in a single step, in turn it is very useful for saving solvent and reagents. Among many heterocyclic compounds, chromenes are very important due to its biological activity such as antioxidants,² anticancer, anti-microbial, ³ anti-inflammatory,⁴ anti-HIV,⁵ and anti-tumor,^{6,7} Alzheimer disease, ^{8,9} antihypertensive¹⁰ and antileishmanial.⁹ There are many reports shown that synthesis of different chromene derivatives and its applications (Figure 1).^{11, 12, 13} A Knoevenagel condensation is the reaction between salicylaldehyde with active methylene compounds followed by intramolecular cyclisation to give imino derivatives. ¹⁴ As per reports, different products are obtained by control of a solvent,¹⁵ ratio of reagents and temperature¹⁶ etc.,. Due to importance of these chromene derivatives, numerous green approaches¹⁷ have been developed under distinct conditions like thermal heating,¹⁸ microwave, ultrasonic, electrochemical, infrared, and solvent free conditions. We could not find many reports on variation of an alkyl side chain to see the effect on antioxidant properties of chromene derivatives. So we are motivated to synthesis imino and amino

chromenes by taking alkylated aldehyde and malonitrile. Currently, many investigations are going on effect of free radicals in biological systems such as lipids, DNA and protein, also create many diseases like atherosclerosis, neurodegenerative disease, rheumatoid arthritis, age related disease, cancer initiation and tumor.^{19, 20, 21} It is necessary to keep a proper level of natural antioxidant such as vitamin E, C and glutathione in a biological system in order to avoid serious health problems.^{22, 23, 24} All these health problems are caused by action of free radical oxygen (ROS) and reactive nitrogen (RNS) species, commonly known as (RSs).^{25, 26.}[1]-[7]

II. EXPERIMENTAL METHOD AND TECHNIQUES

Experimental

All NMR spectra were recorded using Bruker (300MHz) spectrometer. JASCO-FTIR spectrometer (4000-400cm⁻¹) used for recording Infrared spectra. Electro spray ionization mass spectrometry (ESI-MS) analysis was performed in the negative ion mode on a liquid chromatography-ion trap mass spectrometer (LCQ Fleet, Thermo Fisher Instruments Limited, US). The DPPH radical scavenging action of the compounds was dignified rendering to the method of Blies.²⁰ The assay of nitric oxide (NO[•]), H₂O₂, (O₂^{•-}) scavenging activity was determined using the method available in literature.

III. RESULTS AND DISCUSSION

A. Antioxidant activities

In the present study, antioxidant potential of synthesized 3-cyano-2-imino-2H-chromen-7-yl 4-(alkyloxy)benzoate (6a-h) were studied using DPPH, NO[•], O₂^{•-}, H₂O₂ radical scavenging [8]-15]

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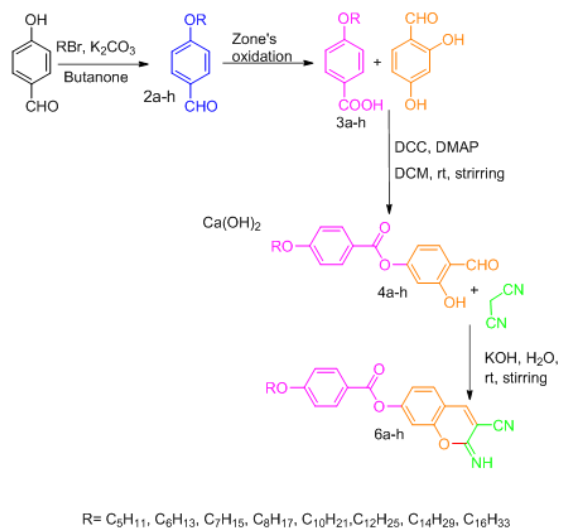
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Table II. Antioxidant activity of chromene derivatives (6a-h)

S.No	Entry	IC ₅₀ (μM)				
		DPPH	NO*	O ₂ ⁻	H ₂ O ₂	
1	Vitamin C	32.52±0.11	55.00±0.12	52.00±0.56	43.00±0.65	
2	6a	27.16±0.41	22.48±0.41	35.04±0.49	42.48±0.82	
3	6b	27.95±0.32	24.62±0.03	31.96±0.38	35.67±0.15	
4	6c	27.93±0.36	27.72±0.36	31.08±0.40	34.88±0.38	
5	6d	28.75±0.18	27.37±0.92	28.90±0.11	33.17±0.54	
6	6e	28.11±0.22	27.23±0.23	30.83±0.92	33.15±0.45	
7	6f	30.65±0.38	27.28±0.53	29.76±0.36	29.76±0.43	
8	6g	31.04±0.58	29.13±0.35	28.48±0.53	30.60±0.82	
9	6h	31.04±0.45	33.72±0.18	27.96±0.13	26.89±0.22	

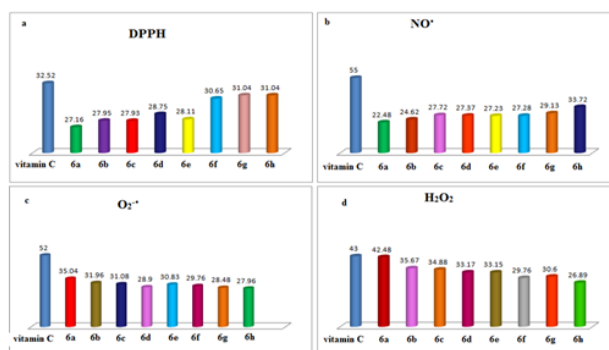
technique by spectrophotometrically. Radical scavenging activities of all derivatives were determined from the interacting ability of derivatives with DPPH, NO*, O₂⁻, H₂O₂ radicals. The antioxidant activities were expressed as 50% inhibitory concentration values in Table 2,

Figure 2, and compared with that of standard ascorbic acid. The hydrogen donating ability of amines and imine groups present as part of all synthesized derivatives in the series 5a-h and 6a-h might be responsible for their antioxidant properties. Lower IC₅₀ value gives better radical-scavenging activity. From the table, it was clear that almost all the compounds were shown radical scavenging activities in DPPH assay. It was important to note that **6a, 6b and 6c** [16]-[22]

**FIG 1 1. Synthetic procedures for series 5 and 6**

Shown better DPPH scavenging activity than vitamin with IC₅₀ values 27.16, 27.95 and 27.93 μM respectively. The DPPH activities of tested were found to be in the decreasing order of **6a, 6c, 6b, 6e, 6d, 6f, 6g** and **6h**. We can find in case of NO* radical scavenging activities, compound 6a and 6b have very low IC₅₀ values are 22.48 and 24.52 μM respectively. The decreasing orders of antioxidant activity of these compounds were 6a, 6b, 6e, 6d, 6c, 6f, 6g and 6h. The results of the NO* assay were expressed as IC₅₀ values in Table 2 revealed that **6h, 6g** showed better super oxide radical scavenging activity than natural antioxidant vitamin with IC₅₀ of 27.96, and 28.48 μM respectively. Surprisingly, IC₅₀ values of all synthesized derivatives were lower than IC₅₀ Vitamin C. The superoxide anion radical scavenging

activities of tested was found to be in the decreasing order of **6h, 6g, 6d, 6f, 6e, 6c, 6b, 6a** and **Vitamin C**. The hydrogen peroxide radical scavenging activities of tested was found to be in the decreasing order of **6h, 6f, 6g, 6e, 6d, 6c, 6b, 6a** and **Vitamin C**.

**Fig.2. Antioxidant activity of 6a-h in IC₅₀ values**

IV. CONCLUSION

A series of 3-cyano-2-imino-2H-chromen-7-yl 4-(alkyloxy) benzoate have been synthesized. The structures were confirmed by ¹H-NMR, ¹³C-NMR, FT-IR and mass spectroscopic techniques. The compounds exhibited excellent radical scavenging activities against super oxide anion radical, nitric oxide radical, DPPH radical and hydrogen peroxide. Among all the derivatives 6a, 6c (DPPH), 6a, 6b (NO*), 6g, 6h (O₂⁻), 6h, 6f (H₂O₂) having better free radical scavenging ability. Based on the result, it is clear that these can be used as good antioxidant in the field of medicinal and food industry.

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