

Abstract

This thesis comprises four chapters:

1- An introduction which consists of a brief survey of different methods to synthesize coumarin containing compounds and their anticancer activity, in addition to their antioxidant activity.

2- The second chapter deals with the aim of the work and Schemes that have been carried out to obtain the new required coumarin derivatives.

3-The third chapter clarifies the theoretical discussion of the experimental work. 3-Acetyl-chromen-2-one derivatives **IIIa-i** were prepared by Knoevenagel condensation followed by intra-molecular transesterification process of salicylaldehyde derivatives **Ia-f** and **IIa-c**.

Pechmann condensation of resorcinol **IV** with ethyl acetoacetate gave 7-hydroxy-4-methyl-2*H*-chromen-2-one derivative **V**. Alkylation of 7-hydroxy coumarin derivatives **V** and **VIII** with ethyl chloroacetate gave **VI** and **IX** followed by hydrazinolysis to afford the acid hydrazide **VII** and **X** that were reacted with the corresponding acetyl derivative **IIIa-i** to yield bicoumarinyl hydrazone derivatives **XIa-i**, and **XIIa-d**, respectively.

Reaction of **IIIa-f** in the presence of ammonium acetate afforded bicoumarin derivatives containing fused pyridocoumarin derivatives **XIIIa-f**.

Condensation of **IIIc-f** with dimethylformamide dimethylacetal resulted in enaminone derivatives **XIVa-d** which upon reaction with hydroxylamine hydrochloride yielded isoxazole derivatives **XVa-d**. On

the other hand, reaction of **XIVa-d** with phenyl hydrazine hydrochloride gave the pyrazole derivatives **XVIa-d**.

Fusion of **IIIa**, **IIIc** or **IIId** with thiourea in the presence of iodine yielded the respective 2-aminothiazole derivatives **XVIIa-c**, which upon acetylation with chloroacetyl chloride gave 2-chloroacetamide derivatives **XVIIIa-c**. Compounds **XVIIIa-c** were used for alkylation of primary aromatic amines yielding **XIXa-e** derivatives.

Also, theoretical discussion of biological anticancer and antioxidant activity screening were given.

4- The fourth chapter consists of the experimental part of this work which contains the detailed procedures used for the synthesis of the starting compounds **IIIa-i**, **VII** and **X**, the intermediates **IIa-c**, **V**, **VI**, **IX**, **XIVa-d**, **XVIIa-c** and **XVIIIa-c**, in addition to the target new coumarin derivatives **XIa-i**, **XIIa-d**, **XIIIa-f**, **XVa-d**, **XVIa-d** and **XIXa-e**. The structure elucidation of the new compounds was supported by element analysis, IR, ¹H NMR, ¹³C NMR in addition to mass spectral data. It also, sheds the light on the anticancer and antioxidant activities of the newly synthesized derivatives compared with doxorubicin and cisplatin as standard anticancer agents and silymarin as a standard antioxidant agent.

5- The fifth chapter includes 158 references from 1935 to 2015.