بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

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بالرسالة صفحات لم ترد بالاصل

SYNTHESIS AND EVALUATION OF NITROGEN HETEROCYCLIC COMPOUNDS OF ANTITUMOR EFFECTS

A THESIS
Submitted In Partial Fulfillment Of The Requirements Of M.Sc. Degree In Organic Chemistry

Presented by
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TO
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Title of (M.Sc.) Thesis : "Synthesis and evaluation of nitrogen hetero-cyclic compounds of antitumor effects".

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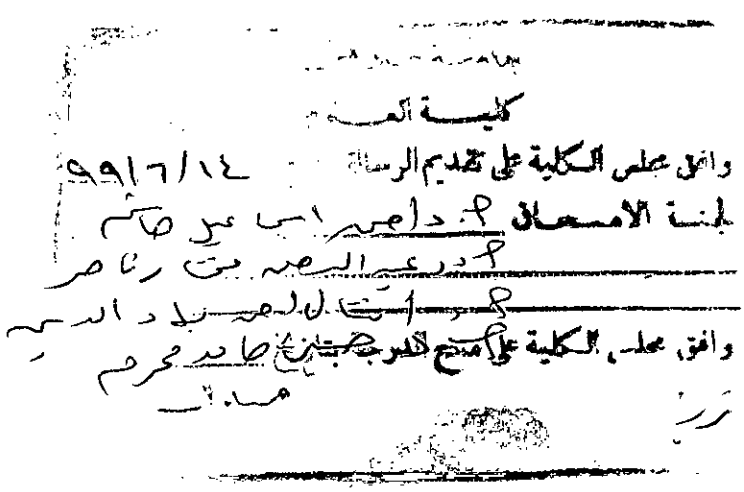
LIST OF CONTENTS



To MY FAMILY

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AIM OF THE WORK

Our research work at the National Organization for Drug Control and Research is usually oriented to the chemistry of biologically active compounds. The reported pharmacological activities of thiohydantoin derivatives as antitumor and antiviral agents promoted my interest to synthesize and study the reactions of some new thiohydantoin derivatives. Evaluation of the antitumor and antiviral activities of the compounds obtained is also carried out.

SUMMARY

SUMMARY

The biological activity of many drugs containing the thiohydantoin moiety led many investigators to synthesize several new compouunds containing this moeity and evaluate their pharmacological activites as antitumor and antiviral agents. Our research work at the National Organization for Drug Control and Research is usually oriented to the chemistry of biologically active compounds.

In this investigation, the following two topics are studied :

a) Synthesis and reactions of some thiohydantoin derivatives.
b) Evaluation of the antitumor and antiviral activities of the compounds obtained.

a) Synthesis and reactions of some thiohydantoin derivatives :

2-Thiohydantoin condenses with salicylaldehyde, furfural, and N,N-dimethyl-p-aminobenzaldehyde to give the corresponding arylidene derivatives (CLXIIa-c). Alkylation of these arylidene derivatives with alkyl iodides in alkaline medium leads to S-alkylation with the formation of the corresponding 2-S-alkyl derivatives (CLXIIIa-g). When the latter derivatives are allowed to react with hydrazine hydrate or phenylhydrazine in boiling ethanol, the corresponding 2-hydrazino derivatives (CLXIVa-c) and 2-phenyl hydrazino derivatives (CLXIVd-f) are formed with the removal of the S-alkyl group.

Condensation of the hydrazino derivatives (CLXIVa-c) with benzaldehyde, salicylaldehyde, furfural and N,N-dimethyl-p-aminobenzaldehyde gives the corresponding Schiff's bases (CLXVa-l).

Phosphorus oxychloride reacts with the 2-alkylmercapto-5-arylidene derivatives (CLXIIIa-g) to give the corresponding 4-chloroimidazoles (CLXVIa-g).

It was interesting to test the reactivity of chlorine atom in the latter compounds (CLXVIa-g) towards some nitrogen nucleophiles. Thus, the 4-choroimidazoles (CLXVIa-g) react with p-toluidine, and hydrazine to give the 4-(p-tolylamino) (CLXVIIa-g) and 4-hydrazino derivatives (CLXVIIIa-g) respectively.

The latter hydrazino derivatives (CLXVIIIc-g) are converted into the corresponding tetrazoloimidazoles (CLXIXa-e) by the action of nitrous / acetic acid mixture. On the other hand, treating these hydrazino derivatives with formic acid leads to the formation of the triazoloimidazoles (CLXXa-e).

The structures of all the products synthesized were established from their analytical data, chemical behaviour and spectroscopic properties.

The reactions carried out in this investigation are illustrated by the following scheme.