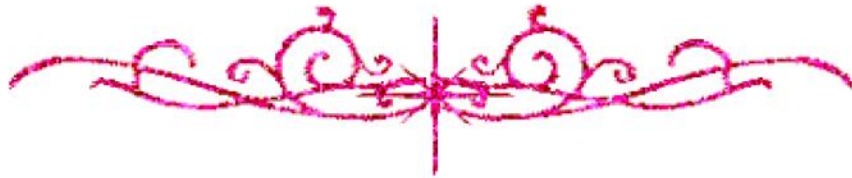


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شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



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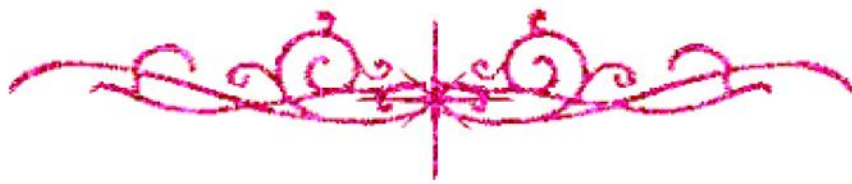


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**SYNTHESIS OF SOME
TETRAHYDROACRIDINE DERIVATIVES OF
POSSIBLE PHARMACOLOGICAL ACTIVITY**

THESIS

Presented By

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M. PHARM. SCI. (1990)

SUBMITTED FOR DEGREE OF DOCTOR OF PHILOSOPHY

IN

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- Date 17/6/1998

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ABSTRACT

ABSTRACT

Synthesis of Some Tetrahydroacridine Derivatives of Possible Pharmacological activity

In the present work, certain 9-substituted anilino (or phenoxy)-1,2,3,4-tetrahydroacridine derivatives were synthesized, hoping that the resultant compounds may exhibit favorable antimicrobial, antifungal, anticholinesterase (cholinesterase inhibitor) and/or anticancer activities.

The thesis consists of the following parts :

I. Introduction :

This part includes a review on the various methods of synthesis and biological activities of 1,2,3,4-tetrahydroacridine and its derivatives.

II. Aim of the Present Investigation :

In this part the pharmacological basis (on which the synthesized compounds were chosen) is discussed.

III. Theoretical Discussion of the Experimental Part:

This part deals with explanation of the reactions involved in the synthesis of both the key intermediates and the new final compounds as well as the elucidation of their structures spectroscopically. Schemes for the synthesis of the suggested compounds were given.

9-[p-(4-Methyl-3-cyano-2-iminopyran-6-yl)anilino]-1,2,3,4-tetrahydroacridine (20)

9-[p-[(2-cyclohexylimino-4-oxo-thiazolidin-3-yl)carboxamido]anilino]-1,2,3,4-tetrahydroacridine (21a)

9-[p-(2-phenylimino-4-oxo-oxazolidin-3-yl)carboxamido]anilino]-1,2,3,4-tetrahydroacridine (21b)

9-[p-(5-Methyl-1,3-dihydro-3-oxo-pyrazol-2-yl)carbonyl]anilino]-1,2,3,4-tetrahydroacridine (22)

9-[p-(3,5-Methyl-1,3-dihydro-pyrazole-2-yl)carbonyl]anilino]-1,2,3,4-tetrahydroacridine (23)

9-[p-(4-methoxybenzylidenehydrazide)anilino]-1,2,3,4-tetrahydroacridine (24)

V. Biological Part :

In this part, a number of the newly prepared 9-substituted 1,2,3,4-tetrahydroacridines were biologically tested as follow :

a) Compounds 1, 2, 6a, 6c, 6e, 7, 8, 13, 16a, 16c, 16d, 17b, 17e, 18a, and 18e were tested as antimicrobial agents against G+Ve, G-Ve, bacteria, yeast and fungi.

b) Compounds 1, 2, 3, 9, 10b, 15a, 19, 23 and 24 were tested as antitumor agents in mice.

Tables and discussion of the results were given.

c) LD₅₀ of some compounds were achieved.

d) compounds 1, 2, 3, 9, 10b, 11e and 23 were tested as choline esterase inhibitors on isolated frog rectus abdominus.

IV. Experimental :

This part includes the synthesis of two known intermediates, two new starting compounds, thirteen new intermediates, as well as thirty nine new end products.

Known intermediates :

1,2,3,4-tetrahydroacridone (IX)

9-Chloro-1,2,3,4-tetrahydroacridine (XXXIV)

New Starting Compounds

Scheme I

9-(p-Acetylanilino)-1,2,3,4-tetrahydroacridine (1)

Ethyl-p-[1,2,3,4-tetrahydroacridin-9-yl]-aminobenzoate (2)

New Intermediates :

Scheme II

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-phenylpropen-1-one (6a)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(p-anisyl)propen-1-one (6b)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(p-tolyl)propen-1-one (6c)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(nitrophenyl)propen-1-one (6d)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(p-chlorophenyl)propen-1-one (6e)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(p-dimethylaminophenyl)-propen-1-one (6f)

1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(3,4,5-trimethoxyphenyl)-propen-1-one (6g)

(1-[p-[9-(1,2,3,4-Tetrahydroacridinyl)amino]-phenyl]-3-(2-thienyl)propen-1-one (6h)

9-[p-Bromoacetylanilino]-1,2,3,4-tetrahydroacridine (7)

Schemes III and IV :

1-[4-(1,2,3,4-Tetrahydroacridin-9-yl)-amino]phenyl]butane-1,3-dione (8)

p-(1,2,3,4-Tetrahydroacridin-9-yl)-aminobenzoic acid hydrazide (9)

1-[4-(1,2,3,4-Tetrahydroacridin-9-yl)-aminobenzoyl]-4-cyclohexylthiosemicarbazide (10a)

1-[4-(1,2,3,4-Tetrahydroacridin-9-yl)-aminobenzoyl]-4-phenylsemicarbazide (10b)

The New End Products

Scheme I

9-(4-Aminophenoxy)-1,2,3,4-tetrahydroacridine (3)

9-(3,4-dimethylphenoxy)-1,2,3,4-tetrahydroacridine (4)

9-(2,4,6-trinitrophenoxy)-1,2,3,4-tetrahydroacridine (5)

Scheme II :

9-[p-[1-Acetyl-5-phenyl- Δ^2 -pyrazolin-3-yl]anilino]-1,2,3,4-tetrahydroacridine (11a)

9-[p-[1-Acetyl-5-(p-chlorophenyl)- Δ^2 -pyrazolin-3-yl]anilino]-1,2,3,4-tetrahydroacridine (11b)

9-[p-[1-Acetyl-5-(p-anisyl)- Δ^2 -pyrazolin-3-yl]anilino]-1,2,3,4-tetrahydroacridine (11c)