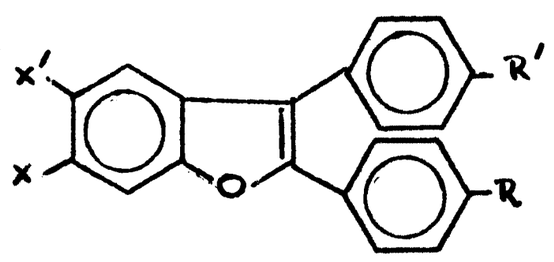
SUMMARY

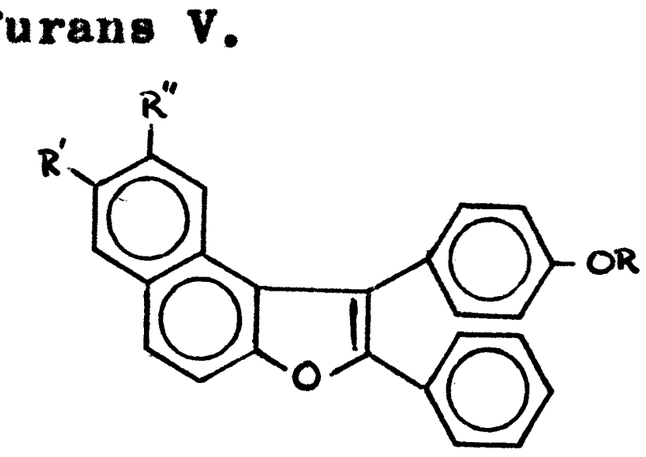
In a search of new antifertility agents which, unlike the presently used steroidal anti-ovulatory agents, would not alter the hormonal balance of the body and may be taken as and when needed post-coitally, diphenyl-benzofurans of the type I, which incorporate in their



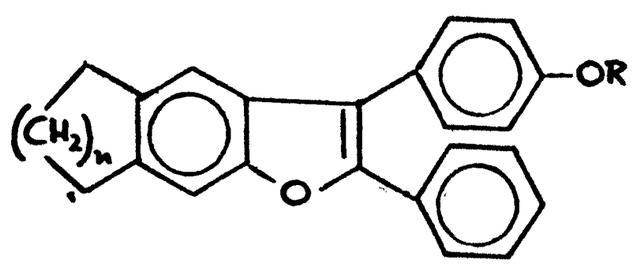
I

structure the triphenylethylene pattern in a rigid form, seemed a worthwhile group for exploration. A number of 5,6-substituted 2-phenyl-3-[p-(β-tertiary aminoethoxy) phenyl]benzofurans were therefore prepared. Some of them, and particularly 2-phenyl-3-[p-(β-pyrolidinoethoxy)phenyl]-6-methoxybenzofuran, showed good anti-implantation activity.

This work was next extended to the synthesis of the corresponding naphthofurans II, 5,6-polymethylene-benzofurans III (n=1 to 3), benzodifurans IV and naphtho-difurans V.



II



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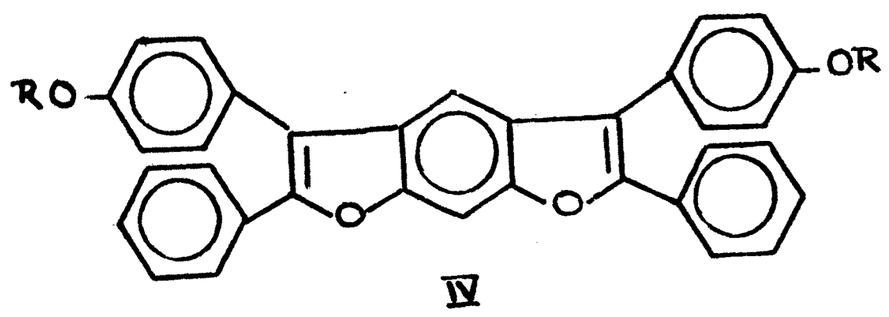

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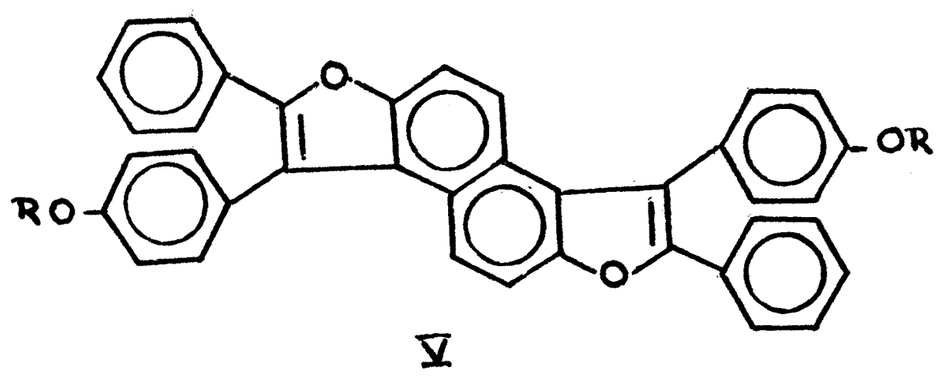
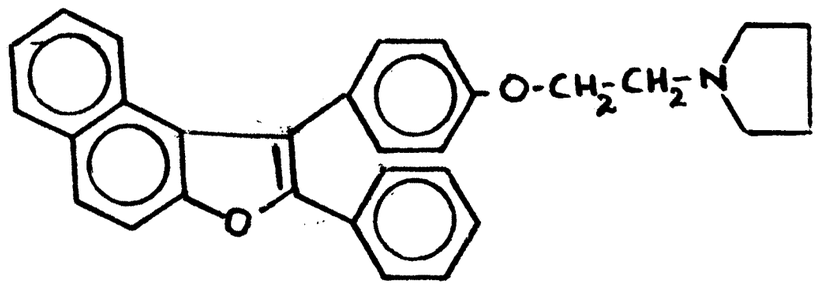
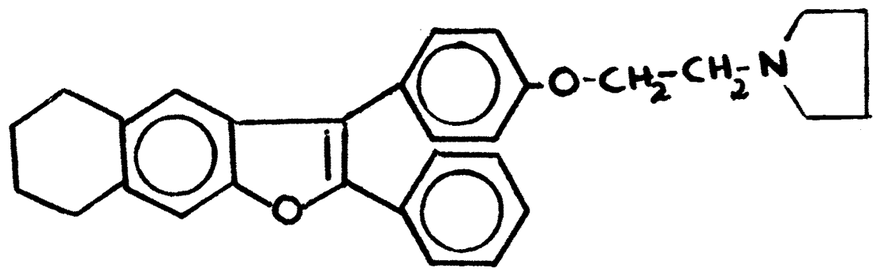


V

The benzodifurans and naphthodifurans did not possess any anti-implantation activity, while a number of naphthofurans and polymethylenebenzofurans proved to be active anti-fertility agents. Of these, VI and VII, were particularly active, causing complete inhibition of implantation at 2 mg/kg, and without having any effect on the endocrine spectrum. These are now undergoing chronic toxicity studies.

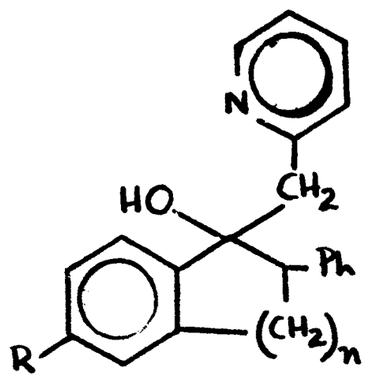


VI

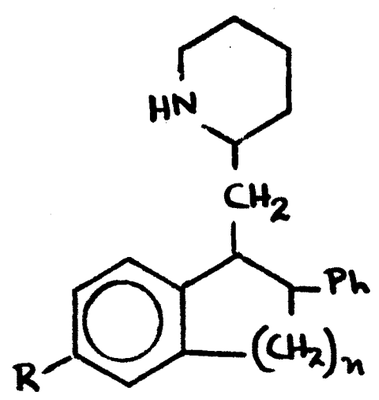


VII

This work was further extended to the synthesis of 2-phenyl-3-(2-pyridylmethyl)indanes and 1-(2-pyridyl-methyl)-2-phenyltetrahydronaphthalenes (VIII) and the corresponding piperidyl analogs IX. These compounds bear resemblance to indenes and tetrahydronaphthalenes, reported by Bencze et al. to cause marked enzyme inhibition of certain stages of steroidogenesis.



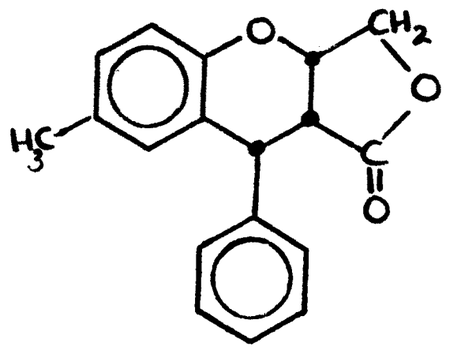
VIII



IX

A number of 2,3-bis(p-methoxyphenyl)benzofurans were submitted for anti-inflammatory testing. Of these, 2,3-bis(p-methoxyphenyl)-5,6-dimethylbenzofuran proved to be a potent anti-inflammatory agent.

Chapter III of the thesis describes a convenient synthesis of 7-methyl-9-phenyl-1-oxo-tetrahydrofurano (3,4-b) (1)benzofuran (X), an isostere of podophyllum lignans, which have come to occupy a prominent place in clinical medicine as anti-cancer agents. The acid hydrazide of podophyllotoxin has also been reported to

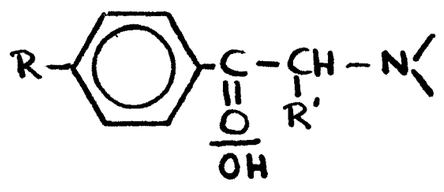


X

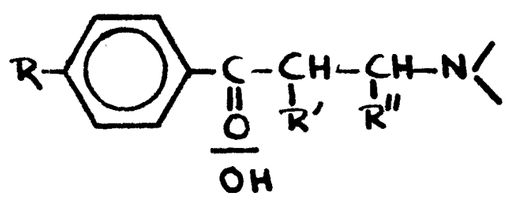
possess antispermatogenic activity. A very suitable intermediate for the synthesis of X, 2-carboxy-3-ethoxy-carbonyl-4-phenyl-6-methylchromene was obtained in one step by the condensation of sodium salt of 2-hydroxy-4-methylbenzophenone and diethyl maleate. This on reduction, followed by cyclisation and hydrogenation, gave the required benzopyran X. The NMR spectra of these compounds possess interesting features and are discussed in detail.

A method has been standardised for the preparation of 2-hydroxy-4,5,3',4',5'-pentamethoxybenzophenone needed as an intermediate for the synthesis of 6,7-dimethoxy-9-(3,4,5-trimethoxyphenyl)-1-oxo-tetrahydrofurano(3,4-b)(1)benzopyran.

In a search of new central muscle relaxants, the synthesis of certain 1-arylalkanones and alkanols of the type XI and XII have been carried out and forms Part II



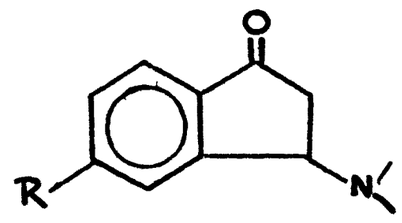
XI



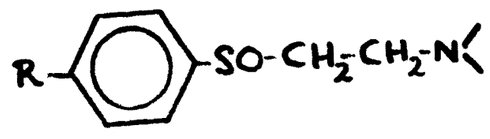
XII

of the thesis. These compounds were synthesised because of their close structural resemblance with sympathomimetic amines and known psychotropic agents, and incorporate in their structure features likely to favour access to the CNS and interaction with bio-receptors present therein.

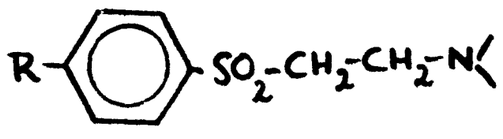
Whereas β-tertiary aminopropiophenones possessed CNS depressant activity, the corresponding alkanols and α-tertiary aminopropiophenones showed markedly reduced activity; some of them, instead, showed stimulant action. This difference in activity may be related to the ability of the former to undergo a retro-Michael reaction, thus generating an aryl vinyl ketone, which being a reactive species, could alkylate a nucleophillic centre in the biophase. Therefore, in a SAR study, apart from introducing substituents of different stereo-electronic character, it seemed of interest to change the electronegativity of position 1 of β-tertiary aminopropiophenones. Compounds of the type XIII to XVI were thus synthesised. During the course of this work new



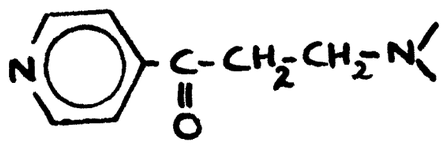
XIII



XIV



XV



XVI

activities were discovered for some of these compounds which include antifungal, antiviral, and diuretic activities. SAR of these compounds is discussed.