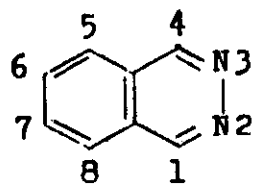
INTRODUCTION

PHTHALAZINE AND ITS DERIVATIVES

Phthalazine is benzo[d]pyridazine. The fundamental ring systems involved in this thesis are named, numbered and oriented as shown in formula I.



(I)

The chemistry of the phthalazines has been reviewed by Vaughan[1].

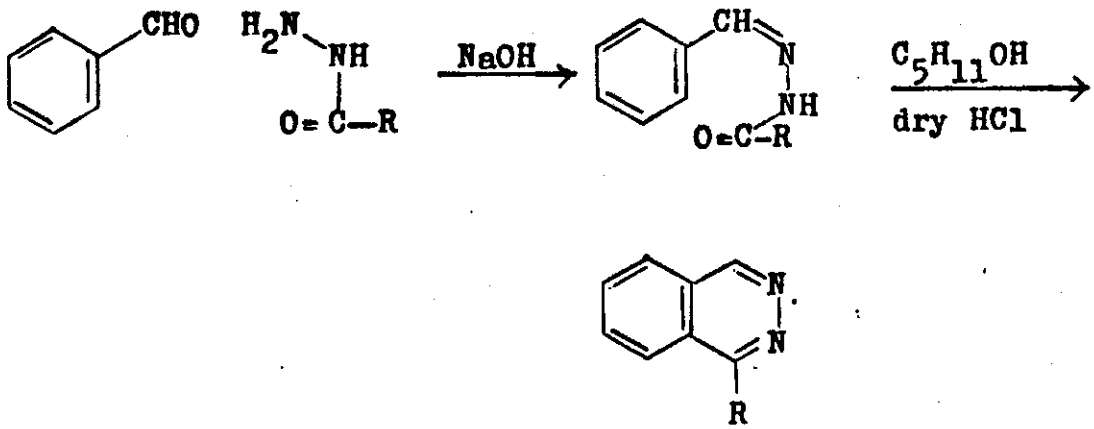
SYNTHESIS OF PHTHALAZINES

All known synthesis of phthalazines proceed through closure of the pyridazine ring either between the 1 position and the benzene ring (Type I) or between the 1 and 2 (or 3 and 4) positions (Type II).

Type I ring closures :

When an aromatic aldehyde is condensed with a hydrazide of an acid, an acyl hydrazone of the aldehyde is formed. On cyclodehydration of this hydrazone a

1-substituted phthalazine results (II)[2,3].



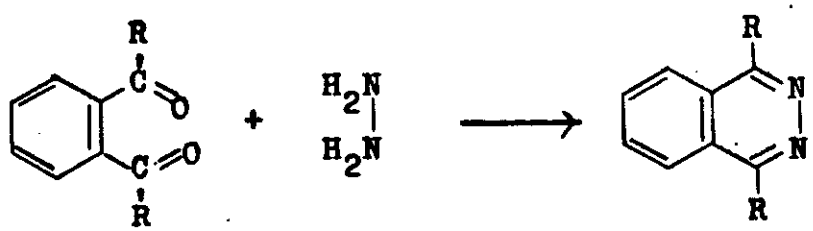
(II)

The yields of phthalazines in general do not exceed 50 %. The reaction has been successful with veratric and p-anisic aldehydes, piperonal, benzaldehyde, and o-methoxy-benzaldehyde. Some doubt exists as to whether meta-substituted benzaldehydes (CH_3O or NO_2) yield phthalazines[2]. Hydrazides of benzoic; phenylacetic, piperonylic, and veratric acids have been used.

Type II Ring Closures:

When an o-diaroylbenzene is condensed with hydrazine, a 1,4-diarylphthalazine (IV) results directly[4-10]. The reaction also proceeds with phthalaldehyde[11], and there seems to be no reason other than the inaccessability of the requisite o-diacyl benzenes to suppose that it will

not proceed when R = alkyl in formula III.

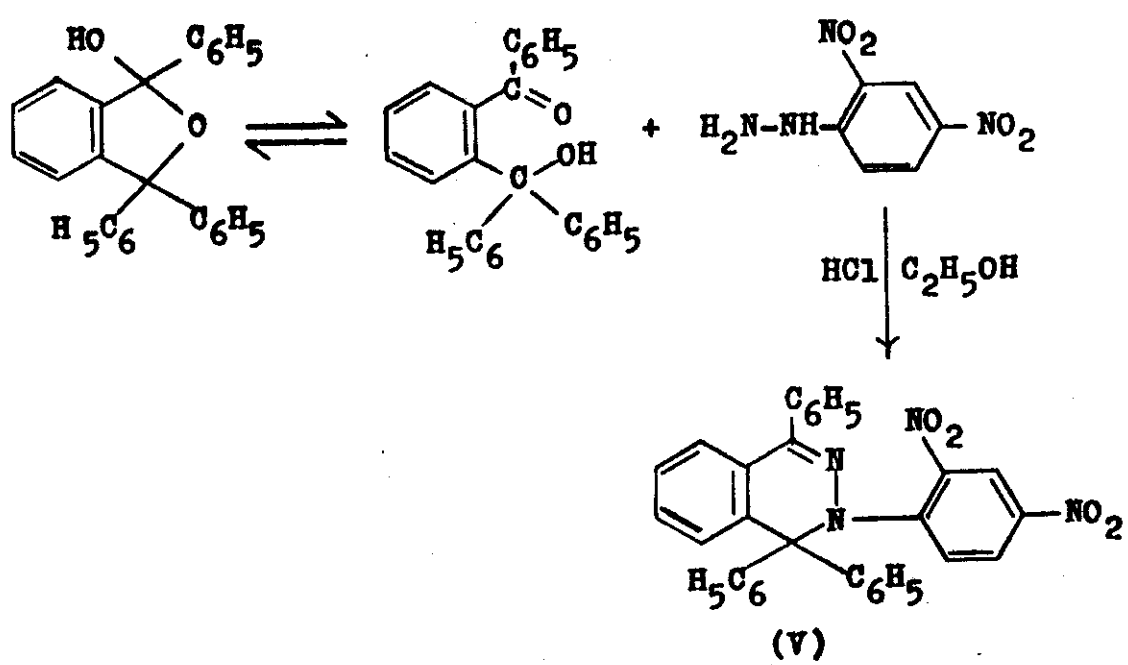


(III) (IV)

R = aryl

Closely related to the above reaction is the condensation of α , α , α`, α`-tetrahalo-o-xylene derivatives with hydrazine which gives phthalazines[11,12].

A 1,2-dihydrophthalazine derivative has been prepared by the following reaction[13].



(V)

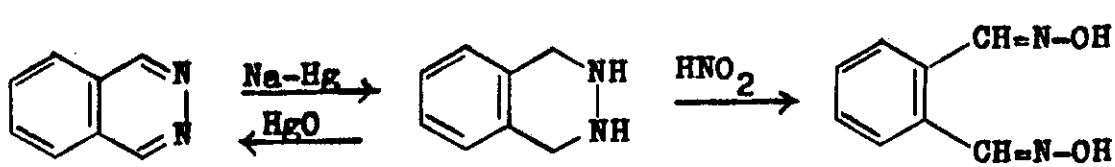
V is remarkable for the tenacity with which it retains solvent of crystallization. It crystallizes with benzene, water, or alcohol of crystallization.

Phthalazines are also prepared by reduction of the readily available 1-chlorophthalazines.

Properties of phthalazines:

Phthalazine itself is a white crystalline substance, m.p. 90°. It forms monoacidic salts[12,14,15], as does tetrahydrophthalazine (VI)[14,15].

On reduction with sodium amalgam, phthalazine yields tetrahydrophthalazine[14,15]. Tetrahydrophthalazine with nitrous acid gives the dioxime of o-phthalaldehyde[11], or under the influence of mercuric oxide, it is oxidized to phthalazine[11]. Although tetrahydrophthalazine forms only monoacidic salts, it yields a dibenzoyl derivative.



(I) (VI)

More vigorous reduction of phthalazine (I) with zinc and hydrochloric acid results in ring cleavage and