

CARBON-CARBON ALKYLATION OF ENAMINES WITH MANNICH BASES II.<sup>1</sup>  
A NEW SYNTHESIS OF PYRAN CONTAINING FUSED RING SYSTEMS.

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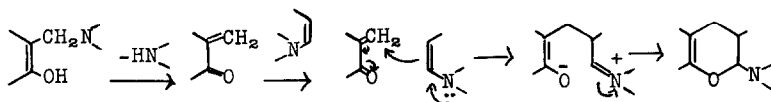
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In a previous communication<sup>1</sup> we have reported on the alkylation of enamines with Mannich bases. One of the reactions described was a spontaneous intramolecular hemiketalization of the primary product of the alkylation of cyclohexanone pyrrolidine enamine with 1-dimethylaminomethyl-2-naphthol. The resulting compound was shown to be 7a,8,9,10,11a,12-hexahydro-9H-benzo[a]xanthin-7a-ol (**1**, Table I). Further exploration of this cyclization has shown that the formation of **1** is representative of a general synthesis suitable for the preparation of a wide variety of pyran containing fused ring systems. In a recent communication<sup>2</sup> Paquette disclosed a related reaction of phenolic aldehydes with enamines which gave derivatives of pyran-4-ol. The similarity of the mechanism of both reactions prompts us to publish a preliminary account of our results in this field.

We have found that refluxing a phenolic Mannich base with an equivalent quantity of a suitable enamine in dioxane, until evolution of basic fumes has ceased, results in the

formation of cyclic O,N-acetals having the pyran nucleus. The likely mechanism for this reaction is the elimination of the dialkylamine followed by a Michael-type addition of the unsaturated species to the enamine. The resulting charged intermediate cyclizes readily to an  $\alpha$ -aminopyran derivative as shown in the following scheme:



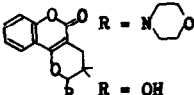
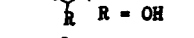
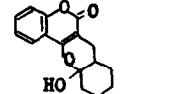
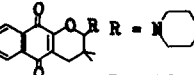

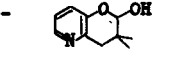
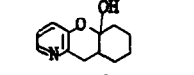
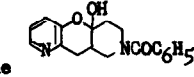
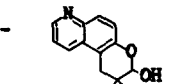
If water is added to the reaction mixture, hydrolysis ensues and  $\alpha$ -hydroxypyranones are obtained as the final products.

Reactions illustrative of the versatility of this synthesis are summarized in Table I.

TABLE I

## Reaction of Phenolic Mannich Bases with Enamines

	Mannich Base	Enamine	Product	M.p., °C
1.	1-Dimethylaminomethyl-2-naphthol	Cyclohexanone pyrrolidine enamine		143.5-145
2.	"	N-isobutenyl-morpholine		154-156
3.	"	N-benzoyl-4-piperidone pyrrolidine enamine		192-194

4.	3-Dimethylaminomethyl-4-hydroxycoumarin	N-isobutenyl-morpholine		R = N(CH <sub>2</sub> ) <sub>2</sub> O	142-144
5.	"	"		R = OH	135-139
6.	"	Cyclohexanone pyrrolidine enamine			190-194
7.	2-Dimethylaminomethyl-3-hydroxynaphthoquinone	N-isobutenyl-morpholine		R = N(CH <sub>2</sub> ) <sub>2</sub> O	153-154.5
8.	"	"		R = OH	191-193
9.	2-Dimethylaminomethyl-3-hydroxypyridine	N,N-dimethylisobutenylamine			114-117
10.	"	Cyclohexanone pyrrolidine enamine			153-157.5
11.	"	N-benzoyl-4-piperidone pyrrolidine enamine			176-178
12.	5-Dimethylaminomethyl-6-hydroxyquinoline	N,N-dimethylisobutenylamine			201.5-203.5

Some of the products contain new ring systems (Table I - 3,9,10,11). The two hitherto undescribed starting materials, N-benzoyl-4-piperidone pyrrolidine enamine (not characterized) and 5-dimethylaminomethyl-6-hydroxyisoquinoline (m.p., 106-107.5°), were prepared by standard procedures<sup>3,4</sup>. Correct analyses were obtained for all compounds described. The infrared and p.m.r. spectra are consistent with the assigned structures.

## REFERENCES

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