

Reaction of Phenolic Mannich Bases with Imines and Oximes.
Synthesis of Fused Ring Systems Containing 1,3-Oxazines.

M. von Strandtmann, M. P. Cohen and J. Shavel, Jr.

Department of Organic Chemistry, Warner-Lambert Research Institute

In preceding communications we have described some reactions of Mannich bases with enamines (1,2) and with phosphoranes (3). Presently, our exploration of newer Mannich base reactions has been extended into the fields of imines and oximes.

When phenolic Mannich bases are allowed to react with imines, 1,3-oxazines are formed according to scheme 1.

SCHEME 1

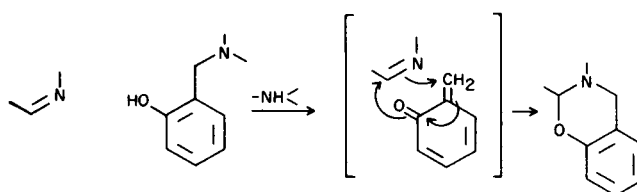


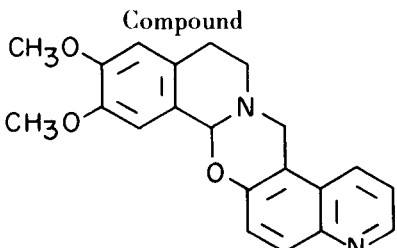
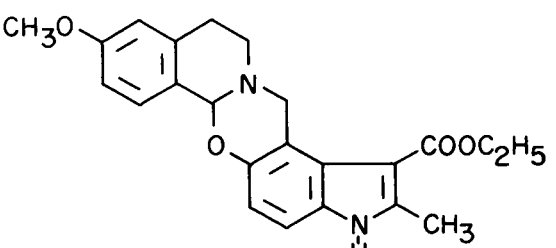
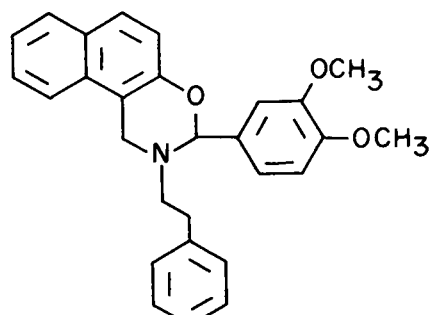
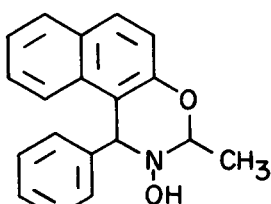
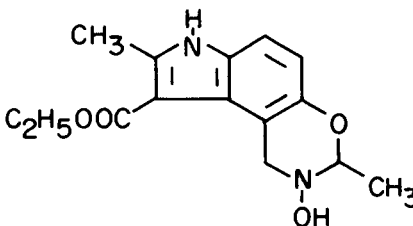
TABLE I

1,3-Oxazines Prepared from Phenolic Mannich Bases and Imines or Oximes

Compound	M.P. °C (a)	Calcd. %			Found %			Yield % (b)
		C	H	N	C	H	N	
<p>1</p>	185-187	76.06	6.09	4.03	76.13	6.02	4.15	36
<p>2</p>	200-202	80.95	5.56	8.58	80.83	5.55	8.48	26
<p>3</p>	183-185	75.48	4.67	9.27	75.34	4.64	9.49	50

TABLE I (continued)

1,3-Oxazines Prepared from Phenolic Mannich Bases and Imines or Oximes

Compound	M.P. °C (a)	Calcd. %		Found %		Yield % (b)		
	175-177	72.39	5.79	8.04	72.62	5.74	8.32	15
	191-192	70.39	6.16	7.14	70.28	6.28	7.05	54
	128-131	79.03	6.40	3.29	78.86	6.54	3.36	19
	193-199	78.33	5.88	4.81	78.51	6.13	4.83	62
	161-165	62.05	6.25	9.65	62.14	6.44	9.42	15

(a) Melting points were determined with the Thomas Hoover capillary melting point apparatus which was calibrated against known standards. (b) The yields stated in the table represent materials of analytical purity. They reflect losses incurred by recrystallization to constant melting point.

The reaction is particularly facile when the azomethine function is part of a partially hydrogenated heteroaromatic ring system; however, some linear Schiff bases and oximes were found to react similarly. Table 1 summarizes the compounds prepared by this method. (Table 1).

The structures assigned are based on elemental analyses, absence of the imine and hydroxyl absorption bands in the infrared spectra, and absence of the phenolic proton signal in the nmr spectrum.

EXPERIMENTAL

General Procedure.

A solution of 0.02 mole of a phenolic Mannich base and 0.02 mole of imine or oxime in 20 ml. of dioxane was allowed to

reflux for 3 hours under nitrogen. The solution was cooled and the precipitate was collected by filtration, washed with cold dioxane and recrystallized from acetonitrile (compounds **1** and **6**), ethanol (**3**, **4** and **7**), ethyl acetate (**5** and **8**), or ethanol-tetrahydrofuran (**2**).

Melting points and analytical data are listed in Table I.

REFERENCES

- (1) M. von Strandtmann, M. P. Cohen and J. Shavel, Jr., *Tetrahedron Letters*, 3103 (1965).
- (2) M. von Strandtmann, M. P. Cohen and J. Shavel, Jr., *J. Org. Chem.*, **30**, 3240 (1965).
- (3) M. von Strandtmann, M. P. Cohen, C. Puchalski and J. Shavel, Jr., *J. Org. Chem.*, **33**, 4306 (1968).

Received March 18, 1969

Morris Plains, New Jersey 07950