

STUDIES ON 1,3-BENZOXAZINES V.<sup>1</sup> REACTION OF IMIDOYL CHLORIDES  
OF 1,3-BENZOXAZINES WITH 2-AMINOPHENOLS, o-PHENYLENEDIAMINES  
AND 2-AMINOTHIOPHENOL

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Abstract --- A general synthetic method for benzoxazoles, benzimidazoles and benzthiazole is described. Treatment of the imidoyl chloride of 1,3-benzoxazine with 2-aminophenols gave the corresponding 2-hydroxyphenylbenzoxazoles in good yields. Similarly, 2-hydroxyphenylbenzimidazoles and 2-hydroxyphenylbenzthiazole were obtained using o-phenylenediamines and 2-aminothiophenol, respectively.

In earlier studies on 1,3-benzoxazines, we reported the reactions of imidoyl chlorides of 1,3-benzoxazines with pyridine N-oxides<sup>2a</sup> and sulfoxide derivatives.<sup>1</sup> In this communication, we wish to report a simple preparation of 2-phenylbenzoxazoles, 2-phenylbenzimidazoles and 2-phenylbenzthiazole under mild reaction conditions.

Treatment of 4-chloro-2,2-dimethyl-2H-1,3-benzoxazine (1) with two molar equivalents of 2-aminophenol (2a) in acetonitrile under reflux for 1h afforded 2-(2-hydroxyphenyl)benzoxazole (3a) in 89 % yield. The structure of 3a was determined on the basis of the following results, and unambiguously confirmed by comparison with an authentic sample prepared from phenyl salicylate and 2a according to the method of the literature.<sup>3a</sup>

On the other hand, when this reaction was carried out in methylene chloride instead of acetonitrile under reflux for 6h, 2,2-dimethyl-4-(2-hydroxyphenyl)amino-2H-1,3-benzoxazine (4a) was obtained in 89 % yield, mp 184-186°C, Anal. Calcd. for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>2</sub>: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.39; H, 5.84; N, 10.53, nmr (CDCl<sub>3</sub>) δ (ppm) 1.57 (6H, s, <math>\begin{matrix} \text{CH}\_3 \\ | \\ \text{C} \\ | \\ \text{CH}\_3 \end{matrix}</math>), 6.70-8.30 (8H, m, aromatic H), mass (M<sup>+</sup>: m/e 268). Compound 4a was readily converted into 3a by refluxing

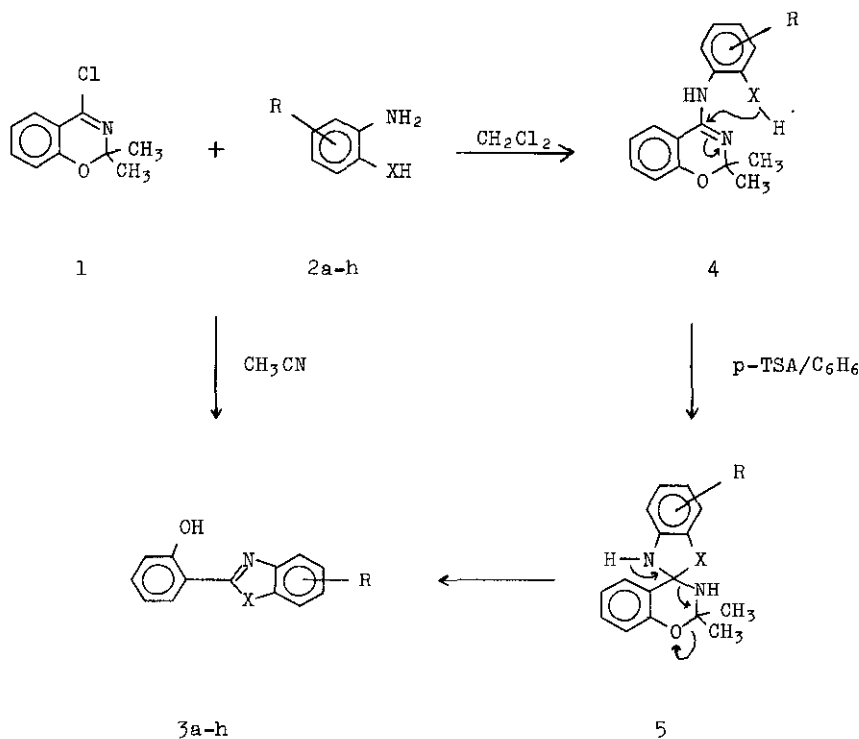


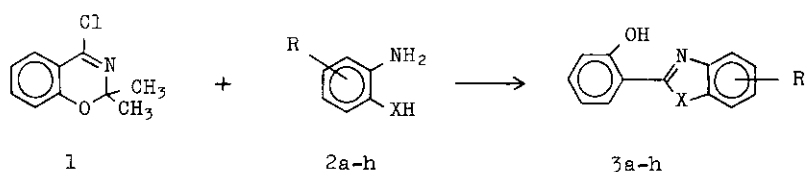
Chart 1

in benzene in the presence of p-toluenesulfonic acid (p-TSA) in 96 % yield. Similar reactions were undertaken with several aminophenol derivatives,<sup>3a</sup> and the results are summarized in Table I. However, 2-amino-5-nitrophenol (2d) gave no benzoxazole derivative even in refluxing in acetonitrile for a long period of time, but afforded only substituted compound (4d), mp 180-182°C (decomp.), Anal. Calcd. for C<sub>16</sub>H<sub>15</sub>N<sub>3</sub>O<sub>4</sub>: C, 61.33; H, 4.83; N, 13.41. Found: C, 61.23; H, 4.75; N, 13.30, nmr (DMSO-d<sub>6</sub>) δ (ppm) 1.57 (6H, s, <math>\langle \frac{\text{CH}\_3}{\text{CH}\_3}</math>), 6.90-8.70 (7H, m, aromatic H), 9.35 (2H, br s, -OH, -NH), mass (M<sup>+</sup>: m/e 313). Compound 4d, however, was also converted into 3d on heating in xylene in the presence of p-TSA in 92 % yield. Likewise, benzimidazoles (3e-g)<sup>4a,b,c</sup> and benzthiazole (3h)<sup>5</sup> were obtained by the reactions of 1 with o-phenylenediamines and 2-aminothiophenol,

respectively. The results are summarized in Table I.

A possible mechanism for the formation of  $\underline{3}$  is shown in Chart 1. The initially formed substituted compound ( $\underline{4}$ ) undergoes an intramolecular cyclization, followed by the elimination of isopropylideneimine to give  $\underline{3}$ .

Table I. Benzoxazole, Benzimidazole and Benzthiazole Derivatives ( $\underline{3}$ )



Compd. No.	R	X	mp ( $^{\circ}$ C)	Yield (%)
$\underline{3a}$	H	O	123-125	89
$\underline{3b}$	5-Cl	O	140-142	92
$\underline{3c}$	5-CH <sub>3</sub>	O	133-135	90
$\underline{3d}$	5-NO <sub>2</sub>	O	212-214	92 <sup>a)</sup>
$\underline{3e}$	H	NH	241-242	91
$\underline{3f}$	5-Cl	NH	279-281	93
$\underline{3g}$	5-NO <sub>2</sub>	NH	297-299	94 <sup>b)</sup>
$\underline{3h}$	H	S	130-132	89

a) from  $\underline{4d}$ . b) from  $\underline{4g}$ .<sup>6</sup>

#### References and Notes

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- 3) a) K.V. Auwers and O. Jordan, *Chem. Ber.*, **58**, 26 (1925); b) K. Brewster, R.A. Chittenden, J.M. Harrison and T.D. Inch, *J. Chem. Soc.*, 1976, 1291.
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- 5) R. Gompper and R.R. Schmidt, *Chem. Ber.*, **98**, 1385 (1965).
- 6) In the reaction of  $\underline{1}$  with 4-nitro-o-phenylenediamine ( $\underline{2g}$ ), the product,  $\underline{4g}$ ,

