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STUDIES ON 1,3-BENZOXAZINES V.[1] 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[2a] and sulfoxide derivatives.[1] 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.[3a]

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 $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.39; H, 5.84; N, 10.53, nmr ($CDCl_3$) δ (ppm) 1.57 (6H, s, $<^{CH_3}_{CH_3}$), 6.70-8.30 (8H, m, aromatic H), mass (M^+: m/e 268). Compound **4a** was readily converted into **3a** by refluxing

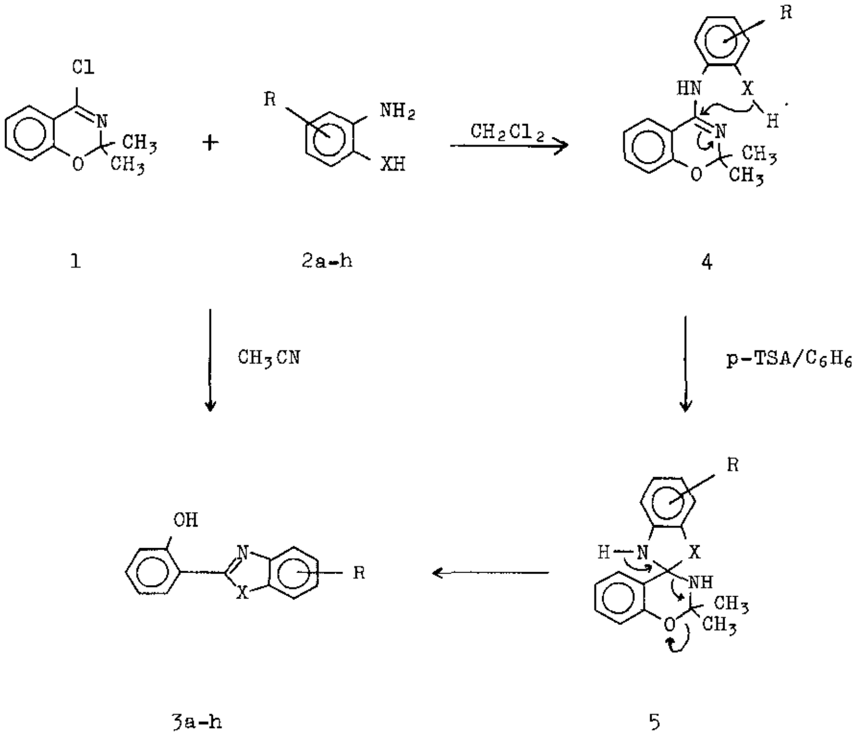
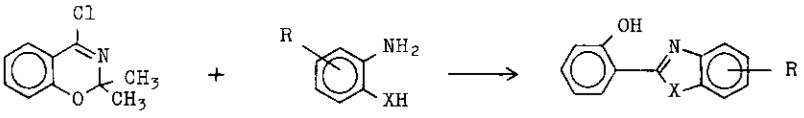


Chart 1

in benzene in the presence of p-toluenesulfonic acid (p-TSA) in 96 % yield. Similar reactions were undertaken with several aminophenol derivatives,[3a] 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 (decompd.), Anal. Calcd. for $C_{16}H_{15}N_3O_4$: C, 61.33; H, 4.83; N, 13.41. Found: C, 61.23; H, 4.75; N, 13.30, nmr (DMSO-d_6) δ (ppm) 1.57 (6H, s, $<{}^{CH_3}_{CH_3}$), 6.90-8.70 (7H, m, aromatic H), 9.35 (2H, br s, -OH, -NH), mass (M^+: m/e 313). Compound 4d, however, was also converted into 3d on heating in xylene in the presence of p-TSA in 92 % yield. Likeweise, benzimidazoles (3e-g)[4a,b,c] and benzthiazole (3h)[5] 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 **3** is shown in Chart 1. The initially formed substituted compound (**4**) undergoes an intramolecular cyclization, followed by the elimination of isopropylideneimine to give **3**.

Table I. Benzoxazole, Benzimidazole and Benzthiazole Derivatives (**3**)



1 2a-h 3a-h

Compd. No.	R	X	mp (°C)	Yield (%)
3a	H	O	123-125	89
b	5-Cl	O	140-142	92
c	5-CH_3	O	133-135	90
d	5-NO_2	O	212-214	92[a)]
e	H	NH	241-242	91
f	5-Cl	NH	279-281	93
g	5-NO_2	NH	297-299	94[b)]
h	H	S	130-132	89

a) from **4d**. b) from **4g**.[6]

References and Notes

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2) a) K. Wachi and A. Terada, Chem. Pharm. Bull., **28**, 465 (1980); b) idem, ibid., **28**, 3020 (1980).

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.

4) a) D.W. Hein, R.J. Alheim and J.J. Leavitt, J. Am. Chem. Soc., **79**, 427 (1957); b) N.V.S. Rao and C.V. Ratnam, Proc. Indian Acad. Sci., **49**A, 139 (1959); c) L.L. Zaika and M.M. Joullie, J. Heterocycl. Chem., **3**, 444 (1966).

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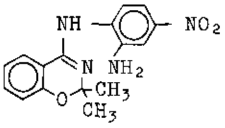
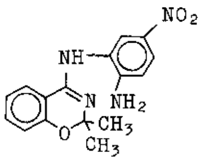
6) In the reaction of **1** with 4-nitro-o-phenylenediamine (**2g**), the product, **4g**,

might be A or B. The structure of the product was not clear which is correct from the following results. mp 171-172°C, Anal. Calcd. for $C_{16}H_{16}N_4O_3$: C, 61.53; H, 5.16; N, 17.94. Found: C, 61.53; H, 5.16; N, 17.98; nmr ($CDCl_3$) δ (ppm) 1.60


A

;


B

(6H, s, $<^{CH_3}_{CH_3}$), 4.56 (2H, br s, $-NH_2$), 5.43 (1H, br s, $>NH$), 6.60-8.30 (7H, m, aromatic H), ir (Nujol) 3500, 3400, 3330, 1505 and 1340 cm^{-1}, mass (M^+: m/e 312).

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