effect of the fluorine atom the electron density at oxygen will increase during the course of the reaction. The different reactivities of the *p*-halogenophenols now become understandable if the site of attack is oxygen and not the ortho-carbon atom. The rate constants for *p*-chloro-, *p*-bromo- and *p*-iodophenols are either equal to or lower than phenol since the *d*-orbital resonance reduces the electron density at oxygen. The singular behaviour of *p*-fluorophenol, that is its higher rate constant, results due to the + M effect of fluorine. If the above explanation is correct one should expect all the *m*-halogenophenols to behave in a similar manner since contributions from structure A is not possible. In fact the experimental results indicate that all the four *m*-halogenophenols have lower rate constants than phenol (*see* Table I).

If the attack is at oxygen one should expect that when an electron-releasing group is present in a para-substituted phenol then it will have a higher rate constant than phenol and the rate constant will be lower if the substituent is electron-withdrawing. The results in Table I substantiate this prediction. *p*-Methoxyphenol is oxidised about 20 times faster than phenol and *p*-cyanophenol about 10 times lower than phenol. It appears, therefore, that in the absence of steric effects the electrophilic attack is at oxygen.

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School of Chemistry, Madurai University, Madurai 625 021,
July 11, 1977.

C. SRINIVASAN.
S. RAJAGOPAL.

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1, 3-ADDITION REACTIONS OF BENZONITRILE OXIDES TO BENZIMIDAZOLES : SYNTHESIS OF 1-[(HYDROXYIMINO)ARYLMETHYL]-1*H*-BENZIMIDAZOLES AND THEIR 2-METHYL ANALOGS

PRIMARY and secondary amines undergo 1, 3-addition reactions with benzonitrile oxides to give the corresponding benzamide oximes[1,2]. Such reactions have not been investigated so far using heterocyclic bases containing N–H function. The 1, 3-addition of benzonitrile oxides with benzimidazoles have now been carried out to know the course of the reaction and the nature of the products formed.

When benzhydroximic acid chloride[3] (0·01 mole) was allowed to react with benzimidazole (0·02 mole) in methanol at room temperature, a colourless crystalline compound, m.p. 181° C (M+237) separated out from the reaction mixture. Its i.r. spectrum (KBr) showed an intense, broad absorption at 3100–2500 cm^{-1} (oxime O–H) and another absorption of medium intensity at 1600 cm^{-1} (C=N). On the basis of this evidence and analytical data, the compound has been assigned the 1-[(hydroxyimino) phenyl methyl]-1H-benzimidazole (*I*, R = H, Ar = Ph) structure. Similarly, 2-methyl-benzimidazole also reacted with benzhydroximic acid chloride to give I (R = CH_3, Ar = Ph). This reaction has been extended to differently substituted benzhydroximic acid chlorides and the products obtained have been characterised as I (Table I) by analogy. That the reaction is proceeding through the intermediacy of benzonitrile oxide is confirmed by reacting the latter, freshly generated from benzhydroximic acid chloride and triethylamine, with benzimidazole (R = H), when I (R = H, Ar = Ph) is obtained in almost quantitative yield.

TABLE I

1-[*Hydroxyimino*) *arylmethyl*]-1H-*benzimidazoles*, I[1]

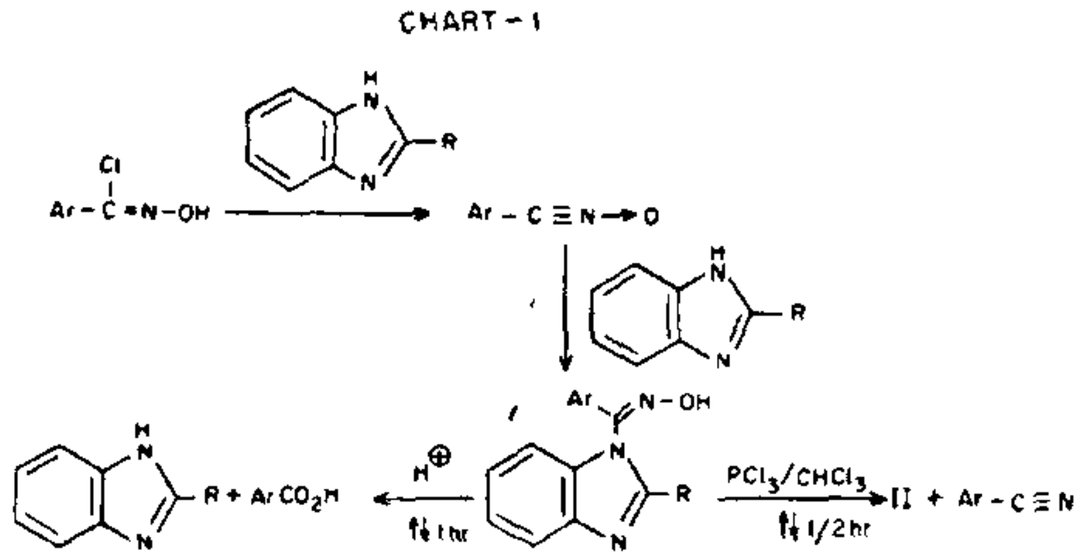
Sl. No.	Ar	R=H		R=CH_3	
		Yield (%)	M.P.[2] (°C)	yield (%)	M.P.[2] (°C)
1.	Phenyl	75	181	73	218
2.	4′-methylphenyl	87	201	80	210
3.	2′-chlorophenyl	70	196	88	221
4.	4′-chlorophenyl	72	199	72	233
5.	3′-nitrophenyl	96	221	70	231
6.	4′-nitrophenyl	75	227	72	247
7.	4′-methoxyphenyl	78	210	..	..
8.	3′, 5′-dichloro-4′-methoxyphenyl	75	221	..	..

1. All the compounds are recrystallised from methanol and gave satisfactory analytical values for carbon, hydrogen and nitrogen.
2. Melting points are uncorrected.

I (Ar = Ph, R = H) on acid hydrolysis under refluxing conditions resulted in the formation of benzimidazole (II, R = H) and the acid (III, Ar = Ph). Beckmann rearrangement of I using reagents like thionyl chloride, phosphorus pentoxide and polyphosphoric acid did not result in the formation of either of the two possible anilides.

Attempted dehydrogenative cyclisation reactions of I (Ar = Ph, R = H) to 3-phenyl-(1, 2, 4)-oxadiazolo-(4, 5-*a*)-benzimidazole using reagents like alkaline potassium ferricyanide, ferric chloride were also unsuccessful. However reaction of I (Ar = 3, 3'-dichloro-4'-methoxyphenyl, R = H) with phosphorus trichloride in chloroform gave II (R = H) and the nitrile IV (Ar = 3, 3'-dichloro-4-methoxyphenyl). The results are summarised in Chart I.

CHART - I



II III IV

Full details of the dehydrogenative cyclisation and pyrolysis results of I will be published elsewhere.

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Department of Chemistry, Osmania University, Hyderabad 7.
B. Ramamohan Rao.
Khalil Ahmed.

August 3, 1977.

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AMMONIUM SULPHATE AS A THYROID INHIBITOR IN THE FRESHWATER TELEOST *CLARIAS BATRACHUS* (L.)

Presence of pesticide residues has been reported in the fishes by several investigators[3,9]. But very little is known about the effect of commonly used fertilizers on the endocrine physiology of the fishes. As the thyroid gland of the teleosts is in the form of scattered follicles in the pharyngeal region, surgical thyroidectomy is not possible. Hence, thyroidectomy is accomplished with the aid of radioiodine[5,6]. Thyroid inhibitors like propylthiouracil and thiourea[2,4,10] are used to inhibit the secretion of thyroxine. It is known that when thyroxine level in the blood is reduced by the use of inhibitors or through radiothyroidectomy the thyrotrophs of the pituitary are stimulated to produce more of thyroid stimulating hormone (TSH). This feedback phenomenon is utilized to identify the thyrotrophs in the fishes[1,5–8,10].

60 *C. batrachus* used in this study were divided into three groups of twenty each, and, ten fish in each group were kept as controls. Group 1 was administered intraperitoneally 1·0 mCi of radioiodine (I-131) in four equal instalments of 250 μCi at three monthly intervals. Group 2 was kept in 0·01% ammonium sulphate for a year. Group 3 was maintained in 0·03% thiourea as used by several earlier investigators[2,7,10] for three months. The aquarium water containing these salts was replaced three times a week for groups 2 and 3. All of them were sacrificed by decapitation and their pharyngeal region with the thyroid and pituitary were fixed in Boun's fluid and Bouyin's sublimate respectively. The thyroid was stained in periodic acid Schiff (PAS) and haematoxylin. The pituitary was stained in PAS and lead haematoxylin, Herlant's tetrachrome and Alcian blue-PAS-Orange-G.

In *C. batrachus* the thyrotrophs are situated in the ventral aspect of the proximal pars distalis and in the adjacent neurohypophysial branches of the pars intermedia, comparable to that of *Heteropenustes fossilis*[1]. In the ammonium sulphate treated fishes, the thyroid follicles exhibited hypertrophy and hyperplasia and reduction in their colloid content (Fig. 5) in comparison to the controls (Fig. 1). This compares well with those treated with thiourea (Fig. 3). The thyrotrophs of all the fishes treated with thiourea (Fig. 4), radioiodine (Fig. 6) and ammonium sulphate (Fig. 7) exhibited marked hypertrophy and degranulation. Their large rounded nuclei have prominent nucleoli. In the control fishes the thyrotrophs are small and the nuclei have clumps of chromatin material and lack prominent nucleoli (Fig. 2).

Thus, the histological picture of the thyroid and thyrotrophs of the fishes treated with known thyroid inhibitors are comparable with those exposed to ammonium sulphate. The thyroid inhibiting property of this commonly used fertilizer is apparently reported for the first time. Further studies on the radioactive iodine uptake and protein bound iodine (PBI) are in progress.