SEARCH FOR PHYSIOLOGICALLY ACTIVE COMPOUNDS

Part IX. Synthesis of Naphthoxazoles from Amino-naphthols and Aromatic Aldehydes

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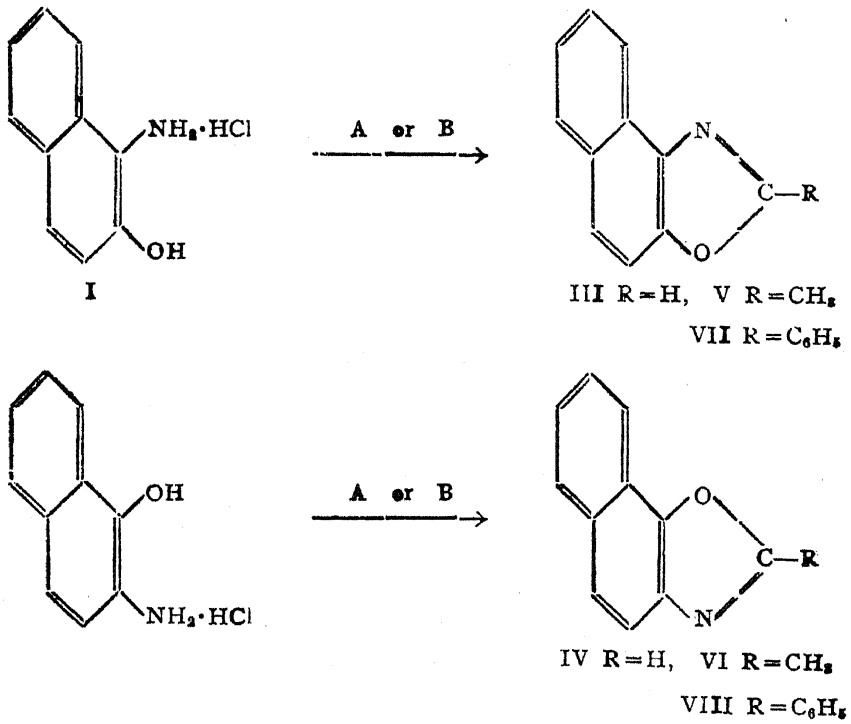
THE two isomeric parent naphthoxazoles III and IV were first prepared by Fischer[1] by heating amino-naphthol hydrochlorides (I and II) with sodium formate and formic acid. Fischer and Hamer[2] obtained 2-methyl napth-(1, 2) oxazole (V) and 2-methyl napth-(2, 1) oxazole (VI) by condensing the corresponding amino-naphthol hydrochlorides with sodium acetate and acetic anhydride.



I

III R=H, V R=CH_3

VII R=C_6H_5

IV R=H, VI R=CH_3

VIII R=C_6H_5

A=$(RCO)_2O$ + RCOONa, B=R·CHO+ $C_6H_5NO_2$

Fries, Walter and Shiling[3] carried out pyrolysis with the mono, di- and triacetyl derivatives of 1-amino 2-naphthol and obtained in all cases 2-methyl

naphth-(1, 2) oxazole (V). 2-Amino naphth-(1, 2) and (2, 1) oxazoles were prepared by Desai and co-workers[4] by treating hydroxynaphthyl thiourea with mercuric oxide and alcohol. Worms[5] claimed that benzoates of 1-nitrosc 2-naphthol and 2-nitroso 1-naphthol on reduction gave the corresponding 2-phenyl naphthoxazoles VII and VIII. However, Botcher[6] reported that he was unable to repeat this work.

With a view to studying the physiological activity associated with the oxazole ring when fused to other ring systems such as naphthalene, a convenient method of preparation of naphthoxazoles has now been worked out. As nitrobenzene was found to be a successful dehydrogenating and condensing agent in the preparation of benzoxazoles,[7, 8] isomeric (1, 2) and (2, 1) amino naphthol hydrochlorides have been condensed with nine aromatic aldehydes in nitrobenzene medium. The products in these condensations are crystalline solids with sharp melting points. The similarity of the method of preparation to that of benzoxazoles indicates that the products might be naphthoxazoles, and this is confirmed by the analysis of these compounds. The product obtained by condensing 1-amino 2-naphthol hydrochloride with benzaldehyde in nitrobenzene medium has been found to be identical with 2-phenyl naphth-(1, 2) oxazole (VII) prepared by the procedure of Fischer and Hamer.[2] The properties and analytical data of the naphthoxazoles obtained are given in Tables I and II. After the work had been completed,[9] the preparation of a few 2-aryl naphth-(1, 2) and (2, 1) oxazoles by condensing the corresponding amino-naphthols with aromatic aldehydes has been reported by others.[10, 11]

Spectra of Naphthoxazoles

The ultra-violet absorption spectra of 2-phenyl and 2-(*p*-chlorophenyl) naphth-(1, 2) oxazoles and 2-phenyl, 2-(*o*-chlorophenyl) napth (2, 1) oxazoles have been recorded in Fig. 1. The following absorption maxima are common between the (1, 2) and (2, 1) naphthoxazoles: 220–222 mμ, 290–300 mμ, 300–312 mμ, 331–332 mμ, and 345–347 mμ. In the case of napth-(2, 1) oxazoles, however, two additional absorption maxima at 266 mμ and 276 mμ have been observed. This appears to be a distinctive difference between the two isomeric naphthoxazoles. The infra-red absorption spectra of 2-phenyl naphth-(1, 2) oxazole and 2-phenyl naphth-(2, 1) oxazole have been recorded in Fig. 2. As in the case of benzoxazoles absorption bands at 6·45 μ, 6·94 μ, 8·0–8·1 μ and 9·4–9·5 μ have been observed in both the types of naphthoxazoles. Intensity variations are however noticeable between the two. While naphth-(1, 2) oxazoles have more intense absorption at 6·9 μ, naphth-(2, 1) oxazoles have intense absorption at 9·5 μ.

TABLE I

Products of condensation with 1-amino-2-naphthol hydrochloride

Sl. No.	Name of the aldehyde	Name of the Naphth (1,2) oxazole	Yield %	Colour	m.p. °C.	Formula	Found			Required		
							C	H	N	C	H	N
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
1	Benzaldehyde ..	2 Phenyl naphth (1, 2) S oxazole	79·0	Colourless needles	134	$C_{17}H_{11}NO$	83·0	4·8	5·6	83·3	4·5	5·7
2	Salicylaldehyde ..	2-(*o*-Hydroxyphenyl) S	69·1	do.	142	$C_{17}H_{11}NO_2$	78·2	4·6	5·1	78·2	4·2	5·4
3	*m*-Hydroxy benzaldehyde ..	2-(*m*-Hydroxyphenyl) Z	91·0	Colourless rectangular plates	205	$C_{17}H_{11}NO_2$	77·8	4·3	5·1	78·2	4·2	5·4
4	*o*-Chlorobenzaldehyde ..	2-(*o*-Chlorophenyl) S	65·0	Colourless	110	$C_{17}H_{10}NOCl$	72·6	3·8	5·3	72·9	3·6	5·0
5	*p*-Chlorobenzaldehyde ..	2-(*p*-Chlorophenyl) S	62·2	Colourless needles	183	$C_{17}H_{10}NOCl$	72·8	4·0	5·3	72·9	3·6	5·0
6	2: 4-Dichlorobenzaldehyde	2-(2: 4-Dichlorophenyl) S	72·2	do.	135	$C_{17}H_9NOCl_2$	65·1	3·1	4·6	64·9	2·9	4·4
7	*o*-Nitrobenzaldehyde ..	2-(*o*-Nitrophenyl) Z	86·0	Pale yellow plates	137	$C_{17}H_{10}N_2O_3$	70·1	3·9	9·6	70·3	3·5	9·7
8	*m*-Nitrobenzaldehyde ..	2-(*m*-Nitrophenyl) Z	86·0	Rectangular needles	225	$C_{17}H_{10}N_2O_3$	70·3	3·4	9·8	70·3	3·5	9·7
9	*p*-Nitrobenzaldehyde ..	2-(*p*-Nitrophenyl) Z	81·2	Micro crystalline	227	$C_{17}H_{10}N_2O_3$	70·3	3·8	9·3	70·3	3·5	9·7

TABLE II

Products of condensation with 2-amino-1-naphthol hydrochloride

Sl. No.	Name of the aldehyde	Name of the Naphth (2,1) oxazole	Yield %	Colour	m.p. °C.	Formula	Found			Required		
							C	H	N	C	H	N
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
1	Benzaldehyde ..	2-Phenyl naphth (2, 1) oxazole P	57·0	Colourless needles	89	$C_{17}H_{11}NO$	83·1	4·6	5·4	83·3	4·5	5·7
2	*m*-Hydroxy benzaldehyde ..	2-(*m*-Hydroxyphenyl) Z	94·0	do.	255	$C_{17}H_{11}NO_2$	77·9	4·0	5·2	78·2	4·2	5·4
3	*p*-Hydroxy benzaldehyde ..	2-(*p*-Hydroxyphenyl) Z	87·0	do.	253	$C_{17}H_{11}NO_2$	78·0	4·3	5·2	78·2	4·2	5·4
4	*p*-Methoxy benzaldehyde ..	2-(*p*-Methoxyphenyl P	83·0	Colourless plates	125	$C_{18}H_{13}NO_2$	78·4	4·8	5·3	78·6	4·7	5·1
5	*p*-Chlorobenzaldehyde ..	2-(*p*-Chlorophenyl) B	74·0	Colourless needles	105	$C_{17}H_{10}NOCl$	72·7	3·3	5·2	72·9	3·6	5·0
6	2 : 4-Dichloro benzaldehyde	2-(2: 4-Dichlorophenyl N	86·0	Yellow tiny rods	248	$C_{17}H_9NOCl_2$	65·2	3·0	4·5	64·9	2·9	4·4
7	3 : 4-Dichlorobenzaldehyde	2-(3′4′-Dichlorophenyl) A.P.	80·0	Yellow prismatic rods	196	$C_{17}H_9NOCl_2$	65·3	3·2	4·7	64·9	2·9	4·4
8	*m*-Nitrobenzaldehyde ..	2-(*m*-Nitrophenyl) Z	88·0	Light yellow rectangular rods	220	$C_{17}H_{10}N_2O_3$	70·0	3·6	9·8	70·3	3·5	9·7
9	*p*-Nitrobenzaldehyde ..	2-(*p*-Nitrophenyl) Z	82·0	Yellow needles	225	$C_{17}H_{10}N_2O_3$	69·9	3·5	9·5	70·3	3·5	9·7

Crystallised from: Z, Xylene; P, Petroleum ether; B, Benzene; N, Nitrobenzene; A.P., Mixture of acetone and petroleum ether. S., Steam distillate.

EXPERIMENTAL

1-Amino 2-naphthol hydrochloride and 2-amino 1-naphthol hydrochloride were prepared by standard methods.[12, 2]

General Method

The above amino naphthol hydrochlorides and aromatic aldehydes (in 1 : 1 molar proportion) were refluxed in nitrobenzene for one hour and a half. The products were steam-distilled to eliminate nitrobenzene and the unreacted aldehyde. Some of the naphth-(1, 2) oxazoles could be isolated

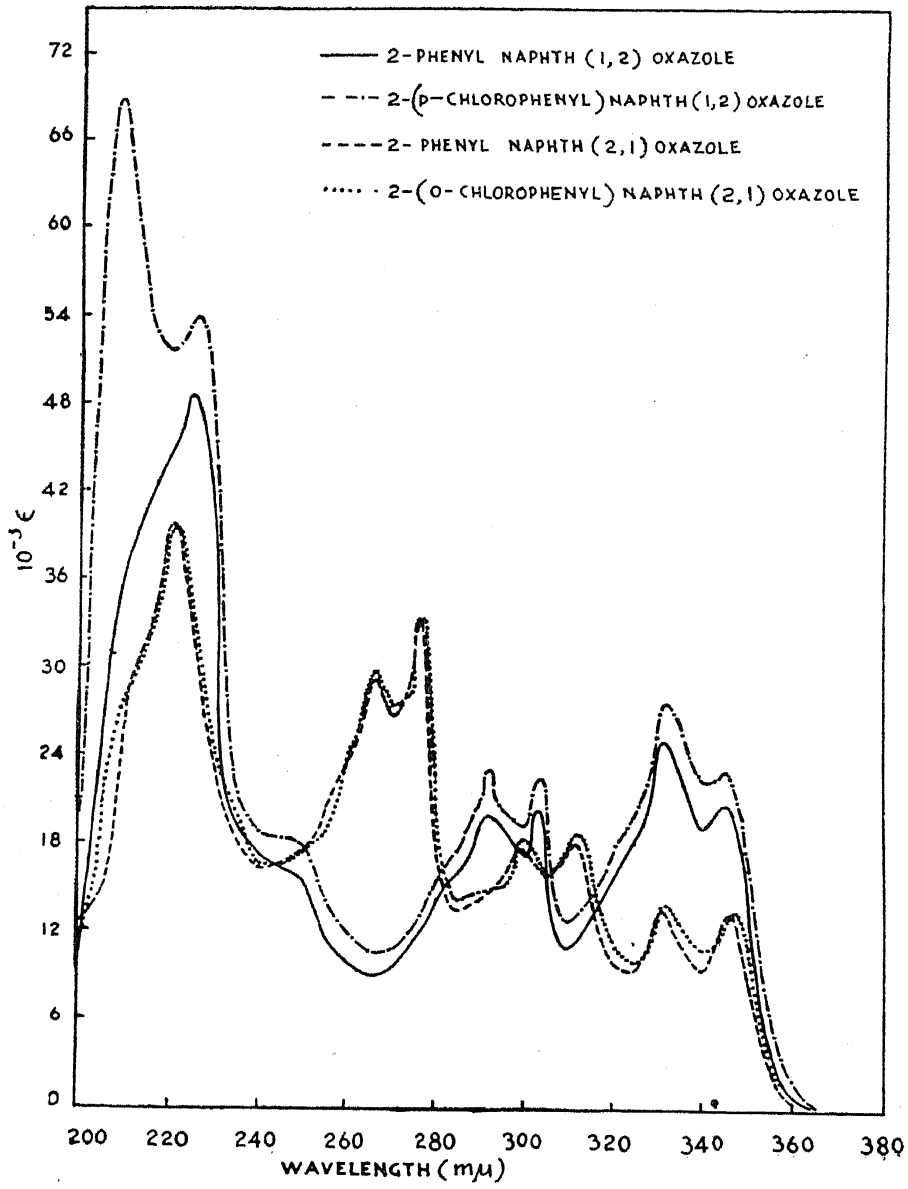


FIG. 1

in the steam distillate, whereas in other cases, the residue after steam distillation was worked up with suitable solvents to isolate the naphthoxazoles.

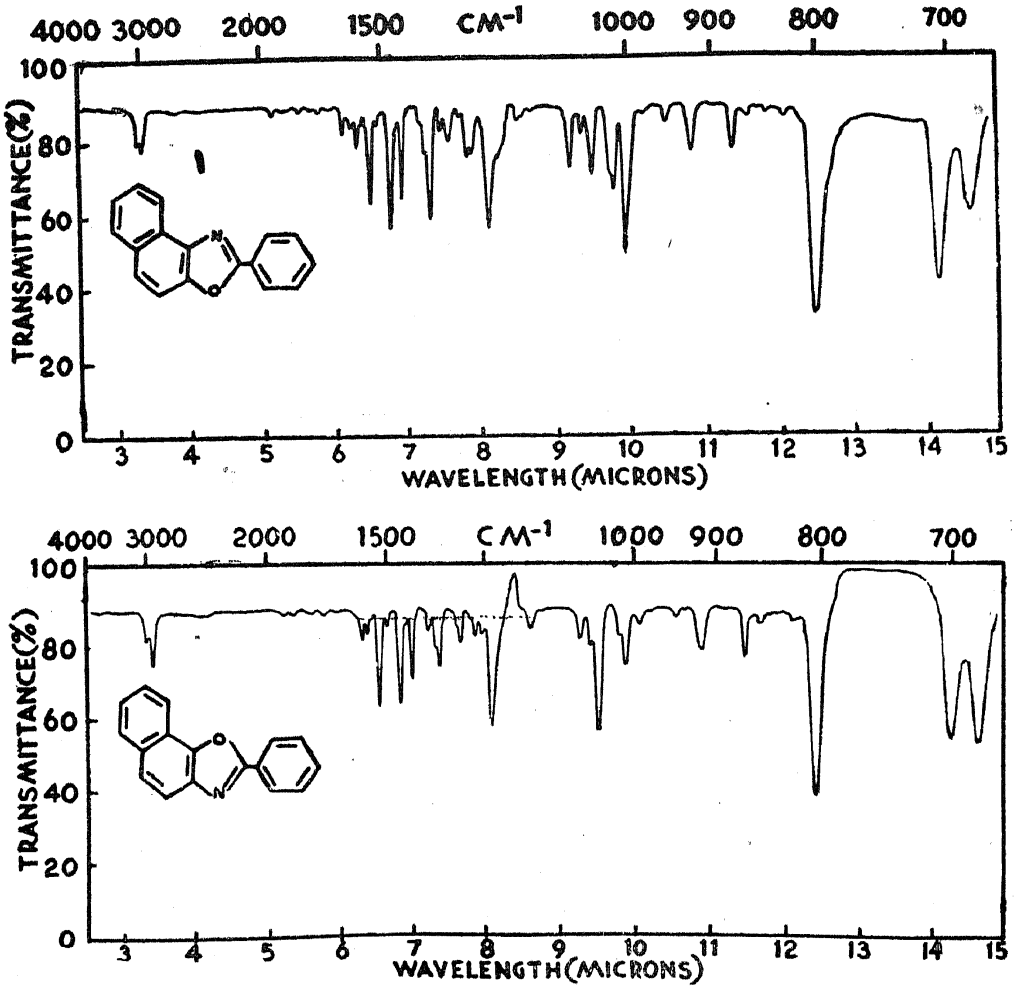


FIG. 2

Adopting the above procedure, benzaldehyde, *o*-hydroxy, *m*-hydroxy, *p*-chloro, 2:4-dichloro-, *m*-nitro and *p*-nitro benzaldehydes have been condensed with both the amino-naphthol hydrochlorides. In addition, *o*-chloro and *o*-nitro benzaldehydes have been condensed with 1-amino 2-naphthol hydrochloride and *p*-hydroxy and 3:4-dichlorobenzaldehydes with 2-amino 1-naphthol hydrochloride.

2-Phenyl naphth-(1, 2) *oxazole.*—This compound was prepared following the method of Fischer and Hamer.[2]

1-Amino 2-naphthol hydrochloride (1 g.), benzoic anhydride (1·2 g.) and sodium benzoate (0·75 g.) were heated in an oil-bath at 150–160° for eight hours. The product was treated with excess of sodium bicarbonate

solution and the residue steam-distilled when 2-phenyl naphth-(1, 2) oxazole was obtained in the steam distillate, m.p. 134° C. The mixed melting point with the compound obtained from benzaldehyde condensation was not depressed.

SUMMARY

2-Aryl naphth-(1, 2) and naphth-(2, 1) oxazoles have been prepared by condensing 2-amino 1-naphthol and 1-amino 2-naphthol hydrochlorides respectively with nine aldehydes. The isomeric naphthoxazoles can be distinguished by the IR and UV absorption spectra.

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