

STUDIES IN THE FORMATION OF HETEROCYCLIC RINGS CONTAINING NITROGEN

Part VII. Condensation of 4-Nitro-*o*-Phenylenediamine with Aromatic Aldehydes

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PINNOW AND WISKOTT¹ reported the formation of mono and disubstituted benziminazoles in the condensation of 4-nitro-*o*-phenylenediamine hydrochloride with two moles of benzaldehyde and *m*-nitro benzaldehyde. However, they could not succeed in their attempts to fix the position of nitro group (5 or 6) in the disubstituted benziminazoles; this has been recently established by the present authors² to be 6 adopting definite synthetic methods. Feitelson and collaborators³ carried out the condensation of the diamine with one mole of *p*-nitrobenzaldehyde by refluxing in acetic acid for 5 hours, and obtained the corresponding mono and disubstituted benziminazoles, the former being formed in minute amounts. They did neither mention about the isomerism nor made any attempts to determine the position of nitro group in the disubstituted benziminazole, but named it as 1-(*p*-nitrobenzyl)-2-(*p*-nitrophenyl)-5-nitrobenziminazole. Perhaps, these workers did not pay attention to this problem.

Condensation of 4-nitro-*o*-phenylenediamine with seventeen aromatic aldehydes (other than benzaldehyde²) has now been investigated with a view to studying the influence of substituents in the aldehydes as well as of the nitro group of the diamine on the nature and relative yields of the reaction products. The condensations have been carried out following the modified Hinsberg's procedure,⁴ except that hot acetic acid has been used on account of the low solubility of the diamine in the cold acid. It has been found that the mono and disubstituted benziminazoles formed in the condensations with aldehydes other than hydroxy aldehydes could be conveniently separated making use of 5% potassium hydroxide solution in which the monosubstituted benziminazoles are preferentially soluble.

In the case of a few aldehydes, dianils (II) or monoanils (I) have been isolated along with the corresponding benziminazoles. 5-Nitrosalicylaldehyde gave the dianil only. The anils isolated have been identified by cyclising them to the corresponding benziminazoles and comparing with those obtained

TABLE II
Properties and analytical data of the new compounds

No.	Name of the Compound	Colour and crystalline shape	m.p. (°C.)	Formula	% of N	
					Found	Required
1	1-(<i>p</i> -methylbenzyl)-2-(<i>p</i> -methylphenyl)-6-nitro benzimidazole ^a	light yellow prismatic rods	160	C ₂₂ H ₁₉ N ₃ O ₂	11.7	11.8
2	2-(<i>p</i> -methylphenyl)-5 (or 6)-nitro benzimidazole ^a	colourless plates	215	C ₁₄ H ₁₁ N ₃ O ₂	16.2	16.6
3	1-(<i>o</i> -hydroxybenzyl)-2-(<i>o</i> -hydroxyphenyl)-6-nitro benzimidazole ^b	pale yellow rectangular rods	211	C ₂₀ H ₁₅ N ₃ O ₄	11.0	11.6
4	2-(<i>o</i> -hydroxyphenyl)-5 (or 6)-nitro benzimidazole ^b	pale yellow needles	297	C ₁₃ H ₉ N ₃ O ₂	16.6	16.5
5	1-(<i>m</i> -hydroxybenzyl)-2-(<i>m</i> -hydroxyphenyl)-6-nitro benzimidazole ^c	pale yellow plates	276	C ₂₀ H ₁₅ N ₃ O ₄	11.7	11.6
6	1-(<i>p</i> -hydroxybenzyl)-2-(<i>p</i> -hydroxyphenyl)-6-nitro benzimidazole ^c	pale yellow rectangular rods	245	C ₂₀ H ₁₅ N ₃ O ₄	11.0	11.6
7	2-(<i>p</i> -hydroxyphenyl)-5 (or 6)-nitro benzimidazole ^c	yellow microcrystalline	328*	C ₁₃ H ₉ N ₃ O ₃	15.9	16.5
8	1-(<i>m</i> -methoxy- <i>p</i> -hydroxybenzyl)-2-(<i>m</i> -methoxy- <i>p</i> -hydroxyphenyl)-6-nitro benzimidazole ^a	orange rectangular plates	216	C ₂₂ H ₁₉ N ₃ O ₆	10.1	10.0
9	2-(<i>m</i> -methoxy- <i>p</i> -hydroxyphenyl)-5 (or 6)-nitro benzimidazole ^a	yellow plates	283*	C ₁₄ H ₁₁ N ₃ O ₄	14.5	14.7
10	1-(3:4-methylenedioxybenzyl)-2-(3:4-methylenedioxyphenyl)-6-nitro benzimidazole ^a	tiny yellow rods	224	C ₂₂ H ₁₅ N ₃ O ₆	9.8	10.1
11	2-(3:4-methylenedioxyphenyl)-5 (or 6)-nitro benzimidazole ^a	yellow rectangular rods	248	C ₁₄ H ₉ N ₃ O ₄	14.3	14.8
12	1-(<i>p</i> -methoxybenzyl)-2-(<i>p</i> -methoxyphenyl)-6-nitro benzimidazole ^a	light yellow prismatic rods	132	C ₂₂ H ₁₉ N ₃ O ₄	10.3	10.8
13	2-(<i>p</i> -methoxyphenyl)-5 (or 6)-nitro benzimidazole ^a	yellow needles	234	C ₁₄ H ₁₁ N ₃ O ₄	15.6	15.6

14	N: N'- <i>di</i> -(<i>o</i> -chlorobenzylidene)-4-nitro- <i>o</i> -phenylenediamine ^a	175	C ₂₀ H ₁₃ N ₃ O ₂ Cl ₂	11.0	10.6
15	1-(<i>p</i> -chlorobenzyl)-2-(<i>p</i> -chlorophenyl)-6-nitro benzimidazole ^a	208	C ₂₀ H ₁₃ N ₃ O ₂ Cl ₂	10.8	10.6
16	2-(2:4-dichlorophenyl)-5 (or 6)-nitro benzimidazole ^a	242	C ₁₃ H ₇ N ₃ O ₂ Cl ₂	13.8	13.6
17	N: N'- <i>di</i> -(3:4-dichlorobenzylidene)-4-nitro- <i>o</i> -phenylenediamine ^a	166	C ₂₀ H ₁₁ N ₃ O ₂ Cl ₄	9.3	9.0
18	1-(3:4-dichlorobenzyl)-2-(3:4-dichlorophenyl)-6-nitrobenzimidazole ^a	223	C ₂₀ H ₁₁ N ₃ O ₂ Cl ₄	9.5	9.0
19	2-(3:4-dichlorophenyl)-5 (or 6)-nitro benzimidazole ^a	295	C ₁₃ H ₇ N ₃ O ₂ Cl ₂	13.2	13.6
20	N-(<i>o</i> -nitrobenzylidene)-4-nitro- <i>o</i> -phenylenediamine ^a	218	C ₁₃ H ₁₀ N ₄ O ₄	19.0	19.6
21	1-(<i>o</i> -nitrobenzyl)-2-(<i>o</i> -nitrophenyl)-6-nitro benzimidazole ^a	270	C ₂₀ H ₁₃ N ₅ O ₆	17.2	16.7
22	2-(<i>o</i> -nitrophenyl)-5 (or 6)-nitro benzimidazole ^a	222	C ₁₃ H ₈ N ₄ O ₄	19.5	19.7
23	N: N'- <i>di</i> -(<i>m</i> -nitrobenzylidene)-4-nitro- <i>o</i> -phenylenediamine ^a	188†	C ₂₀ H ₁₃ N ₅ O ₆	16.5	16.7
24	N: N'- <i>di</i> -(2-hydroxy-5-nitro benzylidene)-4-nitro- <i>o</i> -phenylenediamine ^a	238	C ₂₀ H ₁₃ N ₅ O ₈	16.0	15.5
25	1-(2-hydroxy-5-nitrobenzyl)-2-(2-hydroxy-5-nitrophenyl)-6-nitro benzimidazole ^a	315*	C ₂₀ H ₁₃ N ₅ O ₈	16.1	15.5
26	2-(<i>p</i> -dimethylaminophenyl)-5 (or 6)-nitro benzimidazole ^a	220	C ₁₆ H ₁₄ N ₄ O ₂	19.5	19.9
27	1-(1-naphthyl methyl)-2-(1-naphthyl)-6-nitro benzimidazole ^a	218	C ₂₈ H ₁₉ N ₃ O ₂	9.5	9.8
28	2-(1-naphthyl)-5 (or 6)-nitro benzimidazole ^a	226	C ₁₇ H ₁₁ N ₃ O ₂	14.0	14.5

Solvents of recrystallisation: ^a alcohol; ^b benzene-alcohol; ^c benzene; ^d ethyl acetate; ^e alcohol-acetone; ^f nitrobenzene; ^g benzene-acetone.

* Decomposition;

† Melting at 188°, resolidifying to an yellow mass by 210°, which melts at 230°.

of refluxing for cyclisation, while attempts to cyclise the anil from *o*-chloro-benzaldehyde were unsuccessful.

Products of condensation.—In the condensation of the diamine with *p*-tolualdehyde, piperonal, and anisaldehyde, no solids separated from the glacial acetic acid solution. The products obtained from the dilute acid solution, on fractionation with alkali, yielded alkali insoluble compounds characterised as disubstituted benziminazoles, and alkali soluble substances identified as monosubstituted benziminazoles.

The products that separated by cooling the acetic acid solution in the *p*-chlorobenzaldehyde and 1-naphthaldehyde reactions were completely soluble in alkali and could be characterised as monosubstituted benziminazoles, while the products obtained from the dilute acid solution were found to be mostly the alkali insoluble disubstituted derivatives.

In the condensation with *o*- and *p*-hydroxybenzaldehydes, the substances that separated by cooling the acetic acid solution were found to be monosubstituted benziminazoles, while the compounds from dilute acid solution were the disubstituted derivatives. No substance was isolated from the acetic acid solution in the case of *m*-hydroxybenzaldehyde, and the compound that separated from the dilute acid solution was found to be disubstituted benziminazole.

No solid separated from the acetic acid solution in the condensation with vanillin, and the product isolated from the dilute acid solution yielded two compounds on fractionation with alcohol. The alcohol insoluble compound was identified as the monosubstituted benziminazole and the alcohol soluble compound as the disubstituted derivative.

The products that separated from the acetic acid solution in 2:4-dichloro and *p*-dimethylamino benzaldehyde reactions were found to be the alkali soluble monosubstituted benziminazoles.

In the condensation with 3:4-dichloro and *m*-nitro benzaldehydes, the products that separated from the acetic acid solution were found to be mixtures of dianils and monosubstituted benziminazoles which could be separated on the basis of the solubility of the latter in alkali; the compounds obtained by diluting the acid filtrates were identified as the disubstituted benziminazoles.

The substances obtained from the acetic acid solution in the *o*- and *p*-nitrobenzaldehyde reactions, on fractionation with alkali, gave alkali soluble monosubstituted benziminazoles, and alkali insoluble products, which on fractional crystallisation from alcohol gave alcohol insoluble monoanils

and alcohol soluble disubstituted benziminazoles. The products that separated by diluting the acid filtrates, in both the cases, were found to be mostly the disubstituted benziminazoles.

In the condensation with *o*-chlorobenzaldehyde, the solid that separated from acetic acid solution on cooling as well as that obtained from dilute acid solution were found to be mixtures of dianil and monosubstituted benziminazole. The compound that separated from acetic acid solution in 5-nitrosalicylaldehyde reaction was found to be the dianil.

The properties and analytical data of the new compounds isolated during this investigation are given in Table II.

SUMMARY

On condensation with aromatic aldehydes 4-nitro-*o*-phenylenediamine has been found to yield mono and disubstituted benziminazoles, as well as mono or dianils in a few cases. The formation of monosubstituted benziminazoles or monoanils in greater proportion in these condensations than in those with methyl and chloro diamines may be attributed to the predominating influence of the nitro group of the diamine. The results provide strong support to the step-wise mechanism for the formation of benziminazoles through the intermediate anils.

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