

Tris(benzimidazo)-1,3,5-triazine from the Thermolysis of 2-Aryloxybenzimidazoles

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2-Aryloxybenzimidazoles gave tris(benzimidazo)-[1,2-*a*: 1',2'-*c*: 1'',2''-*e*]-1,3,5-triazine and phenol in almost quantitative yields upon heating at 230—250 °C, while in the reaction in cumene small amounts of 2-aryloxy-1,2'-dibenzimidazole and dicumyl were obtained along with the major products. On the other hand, 2-phenylthiobenzimidazole gave diphenyl disulfide and 1,2'-dibenzimidazole, together with tris(benzimidazo)-1,3,5-triazine. The thermolysis is assumed to proceed by step-by-step radical processes involving the formation of such intermediates as 2-aryloxy-1,2'-dibenzimidazole and 2-aryloxy-1,2'-1'',2''-trisbenzimidazole.

In a previous paper,¹⁾ we reported that 2-aryloxybenzazoles rearrange photochemically to give 2-(2-and/or 4-hydroxyphenyl)benzazoles upon irradiation with a low-pressure mercury lamp, and that 2-(2-amino-phenoxy)benzazoles undergo a photo-Smiles rearrangement. During the course of our studies of the reactions of 2-substituted benzazoles, it was found that 2-aryloxybenzimidazoles undergo an interesting thermal reaction. This paper will report on the thermal decomposition of 2-aryloxybenzimidazoles.

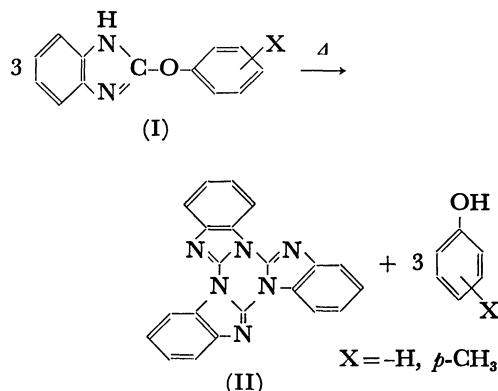
Results and Discussion

Thermal Decomposition of 2-Aryloxybenzimidazoles.

Ordinary 2-aryloxybenzazoles are thermally stable; in the cases of 2-aryloxy derivatives of benzoxazole and benzothiazole, no decomposition took place upon heating at 200 °C for 5 hr. However, not only 2-aryloxy derivatives of benzoxazole and benzothiazole, but also 2-aryloxybenzimidazoles gradually decomposed above 200 °C, and the TG curves showed a weight loss. Although the weight losses of the derivatives of benzoxazole and benzothiazole during heating were not simple, the TG curves of 2-aryloxybenzimidazoles (I) showed a weight loss, just corresponding to a fission of the phenol moiety; in fact, by heating 2-aryloxybenzimidazoles at 230—250 °C for 5 hr, the corresponding phenol and a product of a high melting point (above 360 °C) were obtained in almost quantitative yields.

The same product with a high melting point was obtained even when benzimidazole derivatives of different aryloxy components (phenol and *p*-cresol were used as the phenol components) were decomposed; it was found to be a cyclic trimer of the benzimidazolyl residue (tris(benzimidazo)-[1,2-*a*: 1',2'-*c*: 1'',2''-*e*]-1,3,5-triazine) (II) (hereafter we will call the compound

merely a trimer), as is shown below:



Recently, similar thermal trimerizations have been observed with 2-chlorobenzimidazole and related derivatives,²⁾ although the yields of the trimers were quite low. The mechanisms of these reactions, however, have not been investigated.

The thermal trimerization of 2-aryloxybenzimidazoles took place also in various organic solvents, such as cumene, toluene, *o*-dichlorobenzene, and ethanol, as is shown in Table 1; when 2-phenoxybenzimidazole was heated in cumene at 250 °C under pressure, a small amount of dicumyl was obtained along with the trimer and phenol, suggesting that the reaction took place *via* a radical process. However, at present the details of the solvent effect are not clear.

Effect of Substituent on the Thermal Trimerization of 2-Substituted Benzimidazoles. When the substituent of benzimidazole at the 2-position is -OH, -SH, -NH₂, or -NHC₆H₅, the compounds are thermally very stable; even after heating at 250 °C for a long period, no decomposition to give the trimer was observed. On the other hand, 2-chloro, 2-phenylthio, and 2-phenoxy derivatives gave the trimer under similar reaction conditions, as is shown in Table 2. The derivatives of benzimidazole substituted at the 1-position, such as 1-methyl-2-chlorobenzimidazole, did not yield the trimer upon heating, as might have been anticipated.

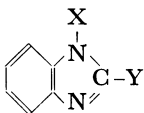
From these results, it is obvious that the thermal trimerization of 2-substituted benzimidazoles depends remarkably upon the substituent at the 2-position; when the hetero atom of the 2-substituent possesses an active hydrogen atom, the trimerization became difficult. This is considered to be due to an increase in the bond strength between the ring carbon and hetero

TABLE 1. YIELDS OF TRIMER IN THE THERMOLYSIS OF 2-PHENOXYBENZIMIDAZOLE IN ORGANIC SOLVENTS

Solvent	Yield of trimer (%) ^{a)}
Cumene	81.8
Toluene	38.0
<i>o</i> -Dichlorobenzene	34.4
Ethanol	21.7

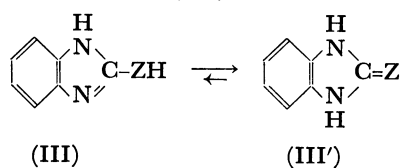
a) Yield of trimer when heated at 250 °C for 5 hr.

TABLE 2. THERMOLYSES OF 2-SUBSTITUTED BENZIMIDAZOLES

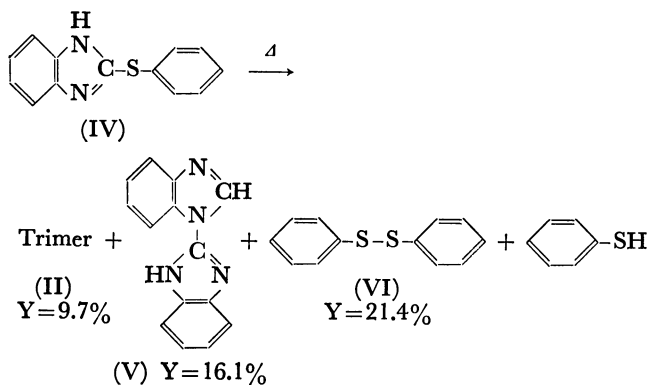
		Reaction temp. (°C)	Yield of trimer (%) ^{a)}
X	Y		
-H	-OC ₆ H ₅	220—230	90<
-H	-OC ₆ H ₄ -CH ₃ (<i>p</i>)	220—230	90<
-H	-SC ₆ H ₅	220—230	9.7
-H	-Cl	200—210	14.0

a) Yield of trimer after heating for 2.5 hr.

atoms, because these compounds (III) are known to exist as their tautomers (III)', as is shown below:

Z = -S-, -NH-, -O-, -NC₆H₅, etc.

Although 2-Cl, -OAr, and 2-SAr benzimidazoles all underwent the thermal trimerization, the reactivity to give the trimer differed significantly from one to the other; among them, -OAr was the best and -SAr was the worst substituent for the reaction, as can be seen in Table 2. When the 2-phenylthio derivative (IV) was heated at 230 °C for 2.5 hr, the trimer (II) was obtained in a low yield, along with 1,2'-dibenzimidazole (V), diphenyl disulfide (VI), and the undecomposed starting material.



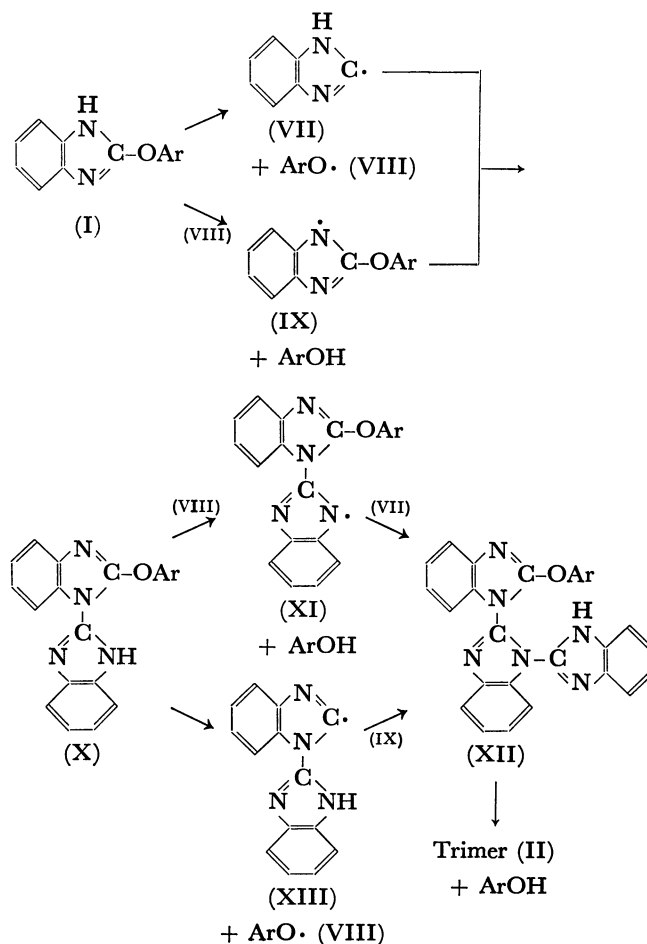
1,2'-Dibenzimidazole (V) should be formed by a combination between 2- and 1-benzimidazolyl radicals; the former may be produced by a homolytic fission of the C-S bond of the starting material, while the latter may be formed by an intramolecular N→C migration of the hydrogen atom in the former. However, it is unlikely that Compound (V) is a necessary intermediate for the trimerization, and dibenzimidazole of the 1,1'- or 2,2'-type and benzimidazole were not obtained.

On the other hand, in the case of 2-phenoxybenzimidazole, the thermal trimerization took place almost quantitatively, without any appreciable side reaction, and in the reactions in organic solvents, only a small amount of a dimer of the benzimidazolyl residue

possessing one phenoxy group (2-phenoxy-1,2'-dibenzimidazole) (X) was obtained, along with the major products (II), as can also be seen in the reaction in cumene; benzimidazole and dibenzimidazole containing no phenoxy group of 1,1'-, 2,2'-, or 1,2'-type were not obtained in this case. 2-Phenoxy-1,2'-dibenzimidazole is considered to be not a mere by-product, but an intermediate for the trimerization, as will be discussed later; the difference in thermal reactivity between phenoxy and phenylthio derivatives is considered to depend mainly upon the difference in readiness for dimerization between the phenoxy and phenylthiyl radicals; the phenylthiyl radical produced by the homolytic fission of the C-S bond would dimerize readily to give diphenyl disulfide. Consequently, in the case of phenylthio derivative, the abstraction of the NH hydrogen would be incomplete in the production of the trimer (II) in a good yield.

On the other hand, in the case of the phenoxy derivative, the phenoxy radical (VIII) once produced by a homolytic cleavage of the C-O bond would rapidly abstract the NH hydrogen atom from the starting material to give phenol and the 1-(2-phenoxy)benzimidazolyl radical (IX), which may then react with the 2-benzimidazolyl radical (VII) to give 2-phenoxy-1,2'-dibenzimidazole (X).

However, 2-alkoxy- and 2-alkylthiobenzimidazoles behave in different manners upon heating. For example, 2-ethoxybenzimidazole is known to decompose thermally to give 1-ethyl-2-ethoxybenzimidazole and



2-(3*H*)-benzimidazolinone upon heating at 200–230 °C,³⁾ indicating that the bond fission took place at O–C₂H₅. In the case of the aryloxy derivative, the bond fission may occur more readily at C–OAr than at O–Ar, because the O–Ar bond should be stronger than the C–OAr bond as a result of the overlap of the lone pair of electrons on the oxygen with the aromatic π electrons; in addition, the stabilization of the resultant radical by the aryl group may favor the fission at C–OAr. When 2-methylthiobenzimidazole was heated at 230 °C, a decomposition took place to give various decomposition products, although in this case the (II) trimer was not detected in the reaction mixture, showing that substituents at the 2-position consisting of a hetero atom and an alkyl group are not suitable for the thermal trimerization. It can be said that the aryloxy group is the best substituent for the thermal trimerization of 2-substituted benzimidazoles.

Reaction Sequences of the Thermal Trimerization of 2-Aryloxybenzimidazoles. From the results described above, it seems reasonable to assume that the thermal trimerization of 2-substituted benzimidazoles proceeds homolytically by step-by-step processes such as are shown in the case of 2-aryloxybenzimidazoles.

1. The homolytic fission of the C–O bond of 2-aryloxybenzimidazole (I) to give aryloxy (VIII) and 2-benzimidazolyl radicals (VII).

2. The abstraction of the NH hydrogen of I by VIII to give the 1-(2-aryloxy)benzimidazolyl radical (IX) and phenol.

3. The combination of IX and VII to give 2-aryloxy-1,2'-dibenzimidazole (X).

4. From the dimer (X), several possible routes can be considered. A trimer possessing one aryloxy group (2-aryloxy-1,2'-1'-2''-trisbenzimidazole) (XII) is the most probable intermediate, even though it has not been isolated. For the formation of XII, two routes are possible; one is a combination of XIII, produced by a homolytic fission of the C–O bond of X, with IX, while the other is a reaction of XI, formed by an abstraction of the NH hydrogen of X by VIII, with VII. The actual reaction would proceed *via* both of the two routes.

5. The formation of the final product from XII by a fission of the C–O bond and an abstraction of the NH hydrogen by the resulting phenoxy radical therefrom, followed by an intramolecular combination of the resultant biradical.

Experimental

All the melting points are uncorrected. The NMR spectra were taken on a Varian A-60D spectrometer, using tetramethylsilane as the internal standard. The IR spectra were measured in potassium bromide discs on a Jasco D-301 spectrometer. The UV spectra were recorded on a Hitachi-124 UV-VIS spectrometer. The Mass spectra were recorded on a JEOL-JMS-07 mass spectrometer. The elemental analyses were performed in the Micro-analytical Center of Gunma University. The structural assignments of the reaction products were done by means of their NMR, IR, UV, and MS spectra and by elemental analyses.

Materials. Preparation of 2-Substituted Benzazoles; 2-

Aryloxybenzazoles were prepared by the condensation of 2-chlorobenzazoles with the equimolar corresponding phenolates.¹⁾ A typical procedure will be described in the case of 2-phenoxybenzimidazole.

After 10.0 g (0.066 mol) of 2-chlorobenzimidazole and 10.0 g (0.086 mol) of sodium phenoxide in 150 g of phenol had been heated at 150 °C for 7 hr, the reaction mixture was steam distilled and the residue was filtered and washed with a 1% aqueous NaOH solution and water. The precipitate was then recrystallized from ethanol to give an analytical sample of 2-phenoxybenzimidazole.

Other 2-substituted benzimidazoles were prepared by the methods described in the literature: 2-OH, mp 312–313 °C (ethanol) (lit,⁴⁾ 307–308 °C); 2-SH, mp 302–303 °C (ethanol) (lit,⁵⁾ 303–304 °C); 2-NH₂, mp 223–224 °C (ethanol) (lit,⁶⁾ 222 °C); 2-NHC₆H₅, mp 190–191 °C (benzene) (lit,⁷⁾ 190 °C); 2-OC₆H₅, mp 229–230 °C (ethanol) (lit,¹⁾ 228–229 °C); 2-OC₆H₄-CH₃(p), mp 257–258 °C (dioxane) (lit,¹⁾ 259–260 °C); 2-SC₆H₅, mp 202–203 °C (benzene) (lit,⁸⁾ 201–202 °C); 2-Cl, mp 191–193 °C (ethanol–water) (lit,⁹⁾ 180 °C, lit,¹⁰⁾ 210–212 °C; Found: C, 55.35; H, 3.33%. Calcd for C₇H₅ClN₂: C, 55.11; H, 3.31%; 2-Cl, 1-CH₃, mp 113–115 °C (petroleum ether) (lit,⁹⁾ 114–116 °C). 2-Methylthiobenzimidazole was prepared by the condensation of 2-mercaptobenzimidazole with methyl iodide in the presence of potassium hydroxide in a mixture of ethanol and water, as in the case of the 2-nonylthio derivative.¹¹⁾ Mp 203–204 °C (benzene). Yield, 25%. Found: C, 58.56; H, 4.93%. Calcd for C₈H₈N₂S: C, 58.51; H, 4.92%.

Thermolyses of 2-Substituted Benzimidazoles; The thermolyses were carried out both without and with a solvent, as follows.

a) Thermolysis of 2-substituted benzimidazoles without a solvent; A 0.5 g portion of 2-substituted benzimidazole was heated in a small test tube under an atmosphere of nitrogen. The decomposed mixture was then treated with dioxane to give the trimer as a sparingly soluble product. Recrystallization from a large amount of dioxane gave an analytical sample. Mp > 360 °C. IR (KBr disc) cm⁻¹, 1624 (–C=N); 1600, 1578, 1480 (phenyl). NMR (in trifluoroacetic acid) δ 7.85 (m, 6H), 8.10 (m, 3H), 8.64 (m, 3H). *M/e* 348.1138 (Calcd for C₂₁H₁₂N₆ = 348.1124). UV $\lambda_{\text{max}}^{\text{dioxane}}$ (nm) ($\epsilon \times 10^4$) 282 (7.8), 260 (9.8). Found: C, 72.61; H, 3.64; N, 24.06%. Calcd for C₂₁H₁₂N₆: C, 72.40; H, 3.47; N, 24.12%. The compound is identical with that obtained in the thermolysis of 2-chlorobenzimidazole.^{2a)}

Decomposed products soluble in dioxane were purified by thin-layer chromatography on silica gel, using benzene as the developing solvent. Thus, in the case of the 2-phenylthio derivative, diphenyl disulfide (yield, 21.4%; mp 60–61 °C) and 1,2'-dibenzimidazole (yield, 16.1%) were obtained from the filtrate. The latter was recrystallized from benzene. Mp 212–213 °C. *m/e* 234 (Calcd for C₁₄H₁₀N₄ = 234). NMR (DMSO-*d*₆) δ 8.91 (s, 1H), 8.50 (broad, 1H), 7.60 (m, 8H). Found: C, 71.69; H, 4.33; N, 23.98%. Calcd for C₁₄H₁₀N₄: C, 71.79; H, 4.30; N, 23.91%.

b) Thermolysis of 2-aryloxybenzimidazoles in organic solvents. A typical run is shown below in the decomposition of 2-phenoxybenzimidazole in cumene. A mixture of 1.0 g of 2-phenoxybenzimidazole and 50 ml of cumene was heated in an autoclave at 250 °C for 5 hr. After the mixture had stood at room temperature for 1 night, the crystals which had separated out were filtered and washed with ether to give the crude trimer (II) in an 81.8% yield. The filtrate was extracted with a 10% aqueous sodium hydroxide solution, and the aqueous layer was acidified with hydrochloric acid to give 2-phenoxy-1,2'-dibenzimidazole (V) in a yield of 13%. Recrystallization from ethanol gave an analytical sample of

(V). Mp 228—230 °C. m/e 326 (Calcd for $C_{20}H_{14}N_4O=$ 326). NMR (DMSO- d_6) δ 8.20 (broad, 1H), 7.55 (m, 13H). Found: C, 73.36; H, 4.48; N, 17.11%. Calcd for $C_{20}H_{14}N_4O$: C, 73.60; H, 4.32; N, 17.17%.

The cumene layer was evaporated *in vacuo*, and the residue was purified by vacuum sublimation to give 3.0 mg of dicumyl (mp 118—119 °C),¹² which was identified by a mixed-melting-point test with an authentic sample.

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