# Synthesis of Benzimidazoles from Anils of *o*-Azidoaniline

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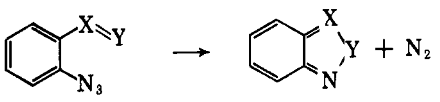
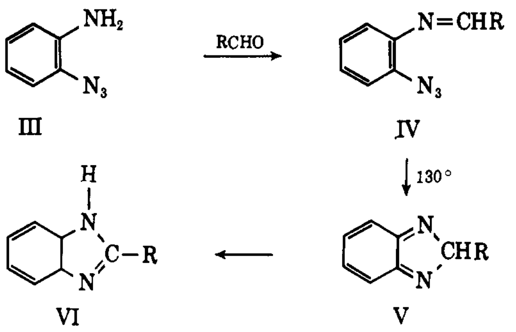
When aryl azides which have substituents *ortho* to the azido group are thermally decomposed, cyclization frequently occurs. This is particularly true when the *ortho* substituent has formal $\alpha,\beta$-unsaturation as represented in structure I. Cyclization has been reported



I II

to be the major product when X=Y is N=O as in the nitro group, N=N in aromatic azo compounds, C=O in aldehydes and ketones, and C=C as part of an aromatic ring.[2] This list has recently been extended to the case where X=Y is C=N in Schiff bases, hydrazones, and azines.[3a] The present paper is concerned with extension of this type of cyclization reaction to the system where X=Y is N=C in anils of *o*-azidoaniline. While this paper was in preparation, Krbechek and Takimoto reported a similar study.[3b]

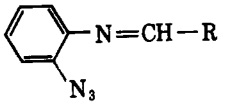


III IV V VI

A series of anils have been prepared by direct condensation of *o*-azidoaniline[4] with selected aldehydes. The condensation of aldehydes with *o*-azidoaniline is limited by two factors. First, the *o*-azidoaniline undergoes thermal decomposition at *ca.* 65°, which limits the temperature at which the condensation can be carried out. Second, the presence of the *o*-azido group decreases the basicity of the aniline ($K_b$ = $2.30 \times 10^{-11}$ compared with $25.7 \times 10^{-11}$ for aniline in 45% methanol[4]), which makes the condensation difficult. Both benzaldehyde and *p*-chlorobenzaldehyde failed to react with *o*-azidoaniline when the reaction was carried out in benzene at 35°. Krbechek and Takimoto, however, succeeded in condensing these aldehydes with *o*-azidoaniline by carrying the reaction out in ethanol with a trace of acetic acid catalyst.[3b] When a strong electron-withdrawing group such as a nitro group, cyano group, or heterocyclic nitrogen was placed *ortho* or *para* to the formyl group of the aldehyde, the condensation with *o*-azidoaniline occurred readily without a catalyst. Furfural failed to react. Simple aliphatic aldehydes did not condense with *o*-azidoaniline to give products that could be purified. However, a moderate yield of the anil was obtained when diphenylacetaldehyde was used. With chloral, the primary reaction was apparently alkylation. The only product that could be isolated and purified was *o*-azidoaniline hydrochloride.

TABLE I

ANILS DERIVED FROM *o*-AZIDOANILINE



| R | Yield, % | M.p., °C. | Asym. $N_3$ stretch, cm.$^{-1}$ [a] | Formula | Calcd., % C | Calcd., % H | Calcd., % N | Found, %[b] C | Found, %[b] H | Found, %[b] N |
|---|---|---|---|---|---|---|---|---|---|---|
| *p*-Nitrophenyl | 51 | 132[c,d] | 2090, 2120 | $C_{13}H_9N_5O_2$ | 58.5 | 3.40 | 26.2 | 58.7 | 3.26 | 26.1 |
| *o*-Nitrophenyl | 63 | 80–81[e] | 2080, 2110 | $C_{13}H_9N_5O_2$ | 58.5 | 3.40 | 26.2 | 58.7 | 3.25 | 26.1 |
| *p*-Cyanophenyl | 60 | 99.5–100.5[c] | | $C_{14}H_9N_5$ | 68.1 | 3.67 | 28.4 | *f* | 3.66 | 28.3 |
| *o*-Pyridyl | 67 | 54–55[g] | 2090, 2125 | $C_{12}H_9N_5$ | 64.6 | 4.06 | 31.4 | 64.2 | 4.09 | 31.4 |
| *p*-Pyridyl | 61 | 81–82[g] | 2080, 2120 | $C_{12}H_9N_5$ | 64.6 | 4.06 | 31.4 | 64.4 | 4.33 | 31.4 |
| *o*-Nitrostyryl | 78 | 87[e] | 2090, 2130 | $C_{15}H_{11}N_5O_2$ | 61.5 | 3.78 | 23.9 | 61.6 | 3.77 | 23.9 |
| 2-Quinoxalinyl | 84 | 144[c] | 2100, 2150 | $C_{15}H_{10}N_6$ | 65.7 | 3.67 | 30.6 | 66.1 | 3.37 | 30.6 |
| Diphenylmethyl | 43 | 138[c] | 2090, 2120 | $C_{20}H_{16}N_4$ | 77.0 | 5.17 | 17.9 | 77.2 | 5.02 | 18.1 |

[a] Nujol mulls. [b] Analyses by G. Weiler and F. B. Strauss Microanalytical Laboratories, Oxford, England. [c] Recrystallized from ethanol. [d] Lit.[3b] m.p. 132°. [e] Recrystallized from methanol. [f] Three different samples gave values of 66.93, 63.55, and 66.83. Also a sample of *p*-cyanobenzaldehyde gave a low carbon analysis. [g] The crude product was dissolved in petroleum ether, the insoluble impurities were filtered off, and the filtrate was evaporated to give the pure solid.

It was interesting to note that the asymmetrical stretching frequency (Table I) of the azido group in these anils appeared in their infrared spectrum as a doublet rather than the usual singlet.[5] This splitting has been observed before in other types of azides,[6] but apparently not with aromatic azides.

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[1] The research described in this paper was abstracted from the thesis presented by D. R. Kamm in partial fulfillment for the M.A. degree, Aug. 1964.

[2] (a) J. H. Boyer and F. C. Canter, *Chem. Rev.*, **54**, 1 (1954); (b) L. Horner and A. Christmann, *Angew. Chem., Intern. Ed. Engl.*, **2**, 599 (1963); (c) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).

[3] (a) L. Krbechek and H. Takimoto, *J. Org. Chem.*, **29**, 1150 (1964); (b) *ibid.*, 3630 (1964).

[4] P. A. S. Smith, J. H. Hall, and R. O. Kan, *J. Am. Chem. Soc.*, **84**, 485 (1962).

[5] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 273.

[6] E. Lieber, C. N. R. Rao, A. E. Thomas, E. Oftedahl, R. Minnis, and C. V. N. Nambury, *Spectrochim. Acta*, **19**, 1135 (1963).

The anils of *o*-azidoaniline, that are listed in Table I, were decomposed by heating in dimethylformamide. In each case, the azide was found to decompose at about 130°. With one exception, cyclization occurred to give the anticipated 2-substituted benzimidazole (VI). The yields obtained are listed in Table II.

Table II

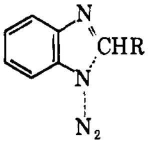
2-Substituted Benzimidazoles

| Benzimidazole | Yield, % | M.p., °C. |
|---|---|---|
| 2-(*p*-Nitrophenyl)- | 48[a] | 318[b] |
| 2-(*o*-Nitrophenyl)- | 56[c] | 208[d] |
| 2-(*p*-Cyanophenyl)- | 53[e] | 262.5[f] |
| 2-(*o*-Pyridyl)- | 52[g] | 215.5[h] |
| 2-(*p*-Pyridyl)- | 48[i] | 216[j] |
| 2-(*o*-Nitrostyryl)- | 62[a] | 216[k] |
| 2-(2-Quinoxalinyl)- | 71[a] | 255[l] |
| 2-Diphenylmethyl- | 0 | m |

[a] Recrystallized from ethanol. [b] Lit.[7] m.p. 322°. No mixture melting point depression with authentic sample. [c] Recrystallized from methanol. [d] R. Walther and T. Pulawski [*J. prakt. Chem.*, **59**, 261 (1899)] report m.p. 208°. [e] Recrystallized from chloroform. [f] Lit.[8] m.p. 260°. Infrared spectrum was identical with that of an authentic sample. [g] Recrystallized from aqueous methanol. [h] B. L. Bastic [*Bull. soc. chim. Belgrade*, **16**, 141 (1951)] reports m.p. 217°. [i] Recrystallized from water. [j] R. Meyer and J. Maier [*Ann.*, **327**, 50 (1903)] report m.p. 214°. [k] H. Rupe and A. Porai-Koschitz [*Chem. Zentr.*, **751**, 102 (1904)] report m.p. 215°. [l] *Anal.* Calcd. for $C_{15}H_{10}N_4$: C, 73.2; H, 4.06; N, 22.7. Found: C, 72.8; H, 4.27; N, 22.7. [m] No crystalline compound could be isolated.

The structures of two of the benzimidazoles were verified by independent synthesis. The procedure of Hinsberg and Funk[7] was used to prepare a sample of 2-(*p*-nitrophenyl)benzimidazole and the procedure of Stephen and Bower[8] was used to prepare a sample of 2-(*p*-cyanophenyl)benzimidazole. These compounds were found to be identical with the products produced by decomposing *p*-nitrobenzal *o*-azidoaniline and *p*-cyanobenzal *o*-azidoaniline, respectively.

The decomposition temperature (130°) of the anils of *o*-azidoaniline is 20–30° below that of phenyl azide. The lower decomposition temperature suggests that the reaction is concerted, involving considerable participation by carbon in the transition state (VII).



VII

Krbechek and Takimoto[3b] reported that the anils of *o*-azidoaniline, which they prepared, decompose at *ca.* 140°. Their compounds included benzal and *p*-methylbenzal *o*-azidoanilines. The results of their work and the work reported here suggest that the decomposition temperature is not very dependent on the nature of substituents and hence that the transition state is not particularly polar.

### Experimental[9]

**Preparation of Anils from *o*-Azidoaniline.**—The anils were prepared by condensing *o*-azidoaniline[4] with an equimolar quantity of the corresponding aldehyde in benzene solution. The water formed was azeotroped out of the reaction by distilling the benzene. This was done under vacuum at temperatures below 35° to prevent decomposition of *o*-azidoaniline (decomposition temperature *ca.* 65°). The following procedure is typical.

*o*-Azidoaniline (1.0 g., 0.0074 mole) and *p*-nitrobenzaldehyde (1.1 g., 0.0074 mole) were dissolved in 100 ml. of anhydrous benzene. The reaction mixture was warmed to 35°, and the benzene was slowly distilled under vacuum. The crude residue was recrystallized from ethanol to give 1.01 g. (51%) of yellow *p*-nitrobenzal *o*-azidoaniline, m.p. 132°.

**Preparation of 2-Substituted Benzimidazoles.**—The anils of *o*-azidoaniline were all decomposed by heating them in dimethylformamide. The following procedure is representative. In 25 ml. of dimethylformamide was dissolved 1.0 g. of *o*-nitrocinnamal *o*-azidoaniline. The solution was refluxed for 2 hr. After cooling, the solution was poured into water to precipitate the crude product. The solid was filtered off and recrystallized from ethanol. The yield of 2-(*o*-nitrostyryl)benzimidazole was 0.45 g. (62%), m.p. 216°.

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[7] O. Hinsberg and F. Funk, *Ber.*, [3] **27**, 2191 (1894).

[8] F. F. Stephens and J. D. Bower, *J. Chem. Soc.*, 2971 (1949).

[9] Melting points are corrected. They were obtained using a Thomas-Hoover capillary melting point apparatus.

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## Bromine Addition to N-(Diarylphosphinyl)iminophosphoranes

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Diarylphosphinic azides have been found to react with a variety of tertiary phosphorus compounds to yield N-(diarylphosphinyl)iminophosphoranes.[1] As a result of continuing studies in this area, we now wish to report on the novel addition of bromine to the N-(diarylphosphinyl)iminophosphoranes.

During the attempted nuclear bromination of N-(diphenylphosphinyl)-P,P,P-triphenyliminophosphorane (I) in carbon tetrachloride by means of bromine and iron powder, it was observed that there was not any evolution of hydrogen bromide with the concurrent precipitation of a yellow-orange crystalline material. These results then suggested that the bromine was reacting additively to yield a phosphorane dibromide II rather than substituting the aromatic groups of I. This novel bromination was, however, complicated somewhat by the inclusion of chlorine in the yellow-orange crystalline product when the addition was carried out in carbon tetrachloride and by apparently low bromine contents of the products from reactions in benzene or chloroform. The low bromine content was reflected in the high (~106%) yields of the phosphorane I recovered from the hydrolysis studies.

$$\underset{\text{I}}{(C_6H_5)_2P(O)N{=}P(C_6H_5)_3} + Br_2 \underset{\text{acetone—water}}{\rightleftarrows} \underset{\text{II}}{(C_6H_5)_2P(O)N{=}P(C_6H_5)_3Br_2}$$

Hydrolysis of the yellow-orange solids with dilute sodium hydroxide or simply with acetone and water resulted in the nearly quantitative recovery of the parent phosphorane I. In contrast, under the same mild conditions, nuclear halogen is not removed from the phenyl groups of the haloarylphosphorane III.

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[1] R. A. Baldwin and R. M. Washburn, *J. Am. Chem. Soc.*, **83**, 4466 (1961).