Manganese Dioxide Oxidation of Aryl 1,2-Diaminoimidazoles

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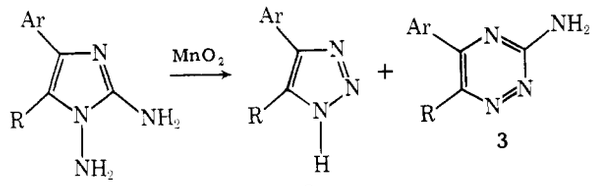
The oxidation of aryl 1,2-diaminoimidazoles (1) with manganese dioxide to 1,2,3-triazoles (2) and/or 3-amino-1,2,4-triazoles (3) is described. Aroyldiazomethanes (4), benzonitriles (5), and acetophenones (6) were minor products of this oxidation. The formation of 2 and 3 from the monoaryl imidazoles (1a–c) is viewed as proceeding via the formation of the *C*-nitrenes (or nitrenoids) which open to the α-hydrazono-*N*-cyanoimines (8), followed by cyclization to either 2 or 3. The α-hydrazono-*N*-cyanoimines (8) can also account for the formation of 4 and 5, while fragmentation of the *N*-nitrenes would explain the presence of the acetophenones (6). The mechanism of the oxidation of 4,5-diphenyl-1,2-diaminoimidazole (1d) and 1,2-diaminobenzimidazole (1e) is also discussed.

The manganese dioxide oxidation of 4-phenyl-1,2-diaminoimidazole (**1a**) to 4(5)-phenyl-1,2,3-triazole (**2a**) and 3-amino-5-phenyl-1,2,4-triazine (**3a**) has been recently described in a communication.[2a] The formation of **2a** and **3a** was

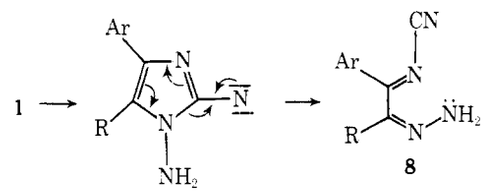


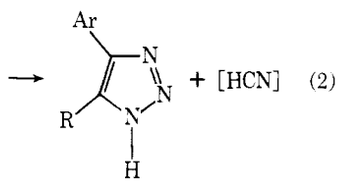
+ ArCOCHN⁻–N⁺ + ArC≡N + ArCOCH₃ (1)

4 5 6

a, R = H; Ar = Ph
b, R = H; Ar = *p*-BrC$_6$H$_4$
c, R = H; Ar = *p*-CH$_3$OC$_6$H$_4$
d, R = Ar = Ph
e, R, Ar =

rationalized via formation of the *C*-nitrene (or nitrenoid) **7a** which could then undergo ring opening to the α-hydrazono-*N*-cyanoimine (8) thence to the observed products **2a** and **3a.**



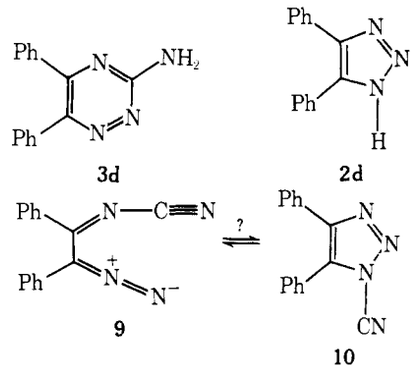


+ [HCN] (2)

The possible alternate reaction paths of the postulated intermediates, coupled with the need to determine the scope and mechanism of this oxidation, made a more detailed investigation desirable. This paper reports the oxidation of 4-aryl- (**1a–c**), 4,5-diphenyl-1,2-diaminoimidazoles (**1d**), and 1,2-diaminobenzimidazole (**1e**).

Results

The oxidation of 4-aryl-1,2-diaminoimidazoles (**1**)[2b] with manganese dioxide in benzene at reflux gave 4-aryl-1,2,3-triazoles (**2**) and 3-amino-5-aryl-1,2,4-triazines (**3**) as the major products (Table I). However, careful workup of the reaction mixtures permitted the isolation of minor products **4, 5,** and **6.** Oxidation of 4,5-diphenyl-1,2-diaminoimidazole (**1d**) gave the corresponding 3-amino-5,6-diphenyl-1,2,4-triazine (**3d**) as the major product (62%) while only 10% of 4,5-diphenyl-1,2,3-triazole (**2d**) was isolated; in addition, benzonitrile (**5a**), benzil, and a compound which appears to be compound **9** (or in equilibrium with the isomeric 4,5-diphenyl-1-cyanotriazole **10**) were isolated. No benzotriazole could be detected from the oxidation of 1,2-diaminobenzimidazole (**1e**); the major



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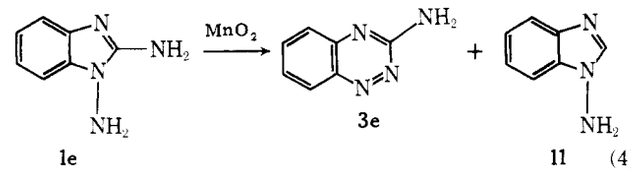
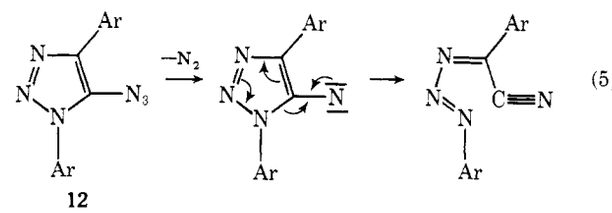


(4)

product (33%) was 3-aminobenzotriazine (**3e**) along with trace amounts of 1-aminobenzimidazole (**11**).

Discussion

The formation of the triazoles **2** can be best rationalized in terms of *C*-nitrene (or nitrenoid) intermediates (**7**) which then undergo fragmentation to α-hydrazono-*N*-cyanoimines (**8**). Cyclization of **8** by displacement of cyanide by the NH_2 group would then yield the 1,2,3-triazoles with elimination of hy-



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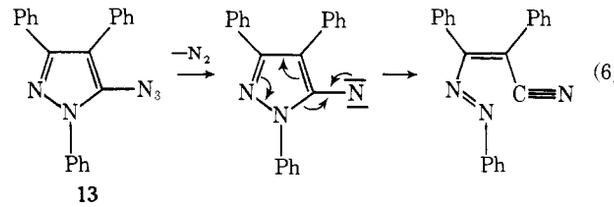

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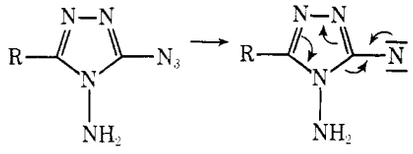
Table I. Oxidation of 4-Aryl-1,2-diaminoimidazoles

Ar	Registry no.	R	Triazole (2), %	Registry no.	Triazine (3), %	Registry no.
p-BrC_6H_4	15970-41-9	H	55	5301-98-4	6	65943-30-8
C_6H_5	15970-40-8	H	46	1680-44-0	11	942-60-9
p-$CH_3OC_6H_4$	15965-79-4	H	35	5301-97-3	25	65943-31-9



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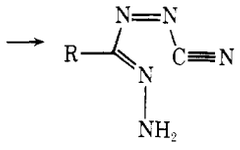

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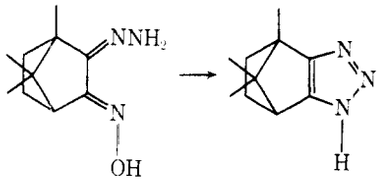

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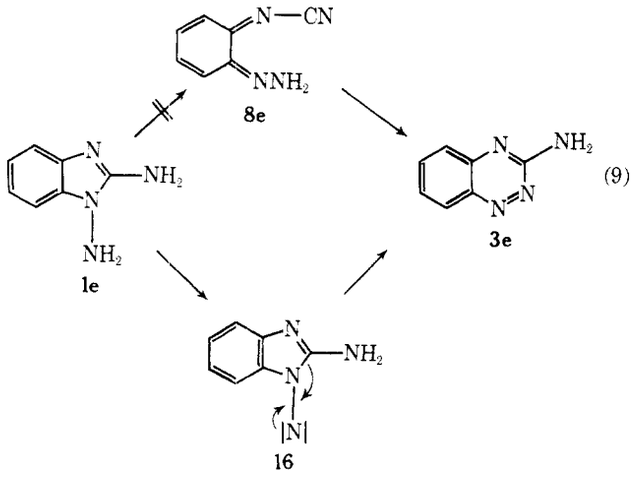
(8)

drogen cyanide. There exists ample precedent in the literature for both of these reactions. Smith and his group[4] had reported the fragmentation of 1,4-diaryl-5-azidotriazoles (**12**) and of 5-azidopyrazoles (**13**). Takimoto and Denault described the formation of 3-amino-*s*-tetrazines from the thermal decomposition of 1-amino-3-azido-*s*-triazoles (**14**).[5] The cyclization of α-hydrazono oximes (**15**) to 1,2,3-triazoles (eq 8)[6] provides an analogy for the cyclization of **8** to **2**.

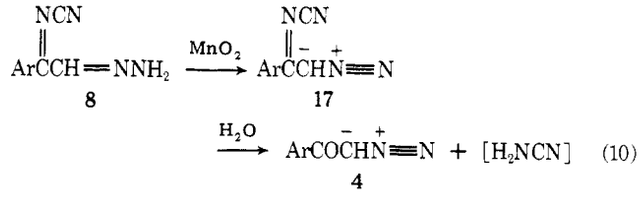
The absence of benzotriazole from the oxidation of **1e** is consistent with the formation of the α-hydrazono-*N*-cyanoimine intermediate (**8**) in the case of the other imidazoles **1**. Indeed the participation of an intermediate of type **8** (**8e**)



(9)

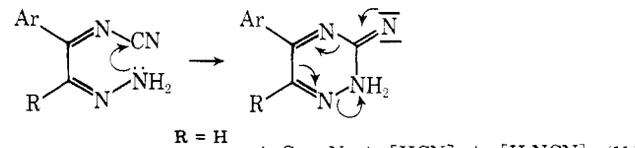
in this case would result in disruption of the aromatic ring.[7] The formation of **3e** must then be understood via oxidation to the *N*-nitrene (**16**) followed by a diazene–hydrazone rearrangement.[8]

Although the diazene–hydrazone rearrangement could account economically for the formation of the 3-amino-5-aryl-1,2,4-triazines (**3**) from the *N*-nitrenes which might be derived from **1**, the presence of aroyldiazomethanes (**4**) and benzonitriles (**5**) strongly favors the α-hydrazono-*N*-cyanoimines **8** as intermediates which explain not only the formation of **3**[2a] but also that of the nitriles and of the diazo ketones. Further oxidation of the hydrazone **8** would lead to the α-diazocyanoimines **17** which could then be hydrolyzed to **4** (eq 10). The possible formation of related compound **9** was



(10)

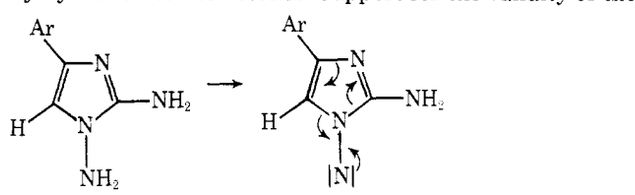
mentioned earlier. The generation of the benzonitriles may also be understood in terms of yet another novel path of **8** as shown below. It is interesting to note that **2d** (R = Ph) gave a sufficient amount of benzonitrile (in this case a second



(11)

molecule of benzonitrile would be generated instead of hydrogen cyanide) to be characterized in subsequent chromatography of the reaction mixture.

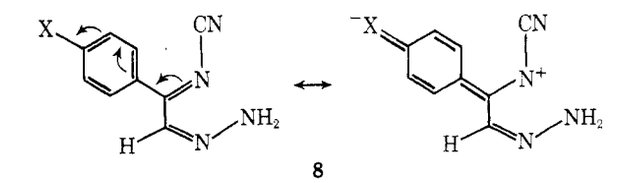
On the other hand, the presence of the acetophenone **6** (and of benzil in the case of **2d**) must be ascribed to the anticipated *N*-nitrene (**18**) fragmentation path[9] to the acetylenes followed by hydration to the ketones. Support for the validity of the



(12)

hydration step came from control experiments (see Experimental Section); desoxybenzoin is known to be oxidized to benzil under these conditions.[10]

The variation in the yields of triazoles **2** and triazines **3** further militates against the diazene–hydrazone rearrangement as a rationalization for the formation of the 1,2,4-triazines in the case of **1a–c**, as both the generation and rearrangement of the *N*-nitrene would not be expected to be substantially affected by the para substituent of the 4-aryl group. On the other hand if α-hydrazono-*N*-cyanoimines (**8**)



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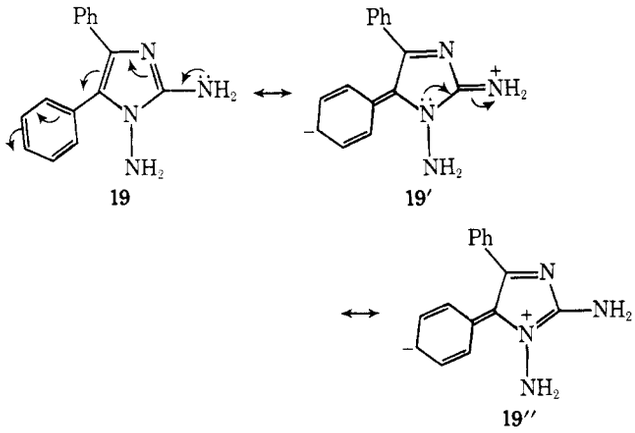
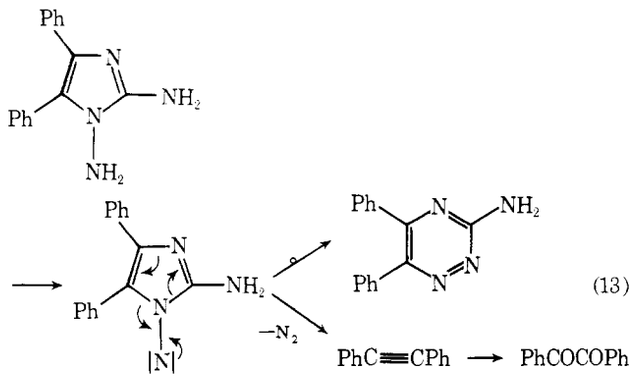
are intermediates, an electron-withdrawing substituent in the para position would favor formation of the triazole while an electron-donating substituent would not, as was observed (Table I).

The unexpectedly high yield of **3d** (and the correspondingly low yield of triazole **2d**) in the oxidation of **1d** would suggest that the triazines **3d** arose via the diazene–hydrazone rear-



19 19′ 19″

rangement of the *N*-nitrene since the susceptibility of the 2-amino group to oxidation would be reduced by the 5-phenyl substituent (structure **19′**) while the *N*-amino group should remain unaffected (the contribution of structure **19″** should be negligibly small). This view would be further supported by the measurable amount (8%) of benzil isolated in this reaction.



(13)

Experimental Section

All melting points were taken on a Thomas-Hoover capillary apparatus (below 250 °C) or on a Mel-Temp apparatus (above 250 °C) and are uncorrected. Infrared spectra were determined neat or as KBr pellets using a Perkin-Elmer 137. ^{1}H NMR spectra were obtained on a Hitachi Perkin-Elmer R24. Elemental analyses were performed by the Microanalysis Laboratory, University of Massachusetts at Amherst. The notation for solvents used in chromatography, e.g., 9:1–6:4 v/v, means that this particular combination of solvents was used in the range 9:1 to 6:4. Precoated TLC plates (silica gel 60 F-254 supported on a glass plate) were used and the eluent was chloroform–ethanol (1:1 v/v).

4-Aryl- and **4,5-diphenyl-1,2-diaminoimidazoles** were prepared by the procedure of Beyer et al.[2b] **1,2-Diaminobenzimidazole**[11] was obtained from 2-(*o*-aminophenyl)-1-acetylhydrazine[12] and cyanogen bromide.

Oxidation of 1,2-Diaminoimidazoles with Manganese Dioxide. General Procedure. A suspension of the 1,2-diaminoimidazole (10 mmol) and activated manganese dioxide (7.0 g)[10] in benzene (40 mL) was heated to reflux for 17 h. The inorganic material was removed by filtration and washed with hot ethanol (20 mL × 3). The combined filtrates were evaporated to near dryness. The residual material was deposited on a preparative chromatographic column (silica gel, mesh 60–200, 35–40 g). Elution was performed with hexane–benzene, benzene, benzene–chloroform, chloroform, chloroform–ethanol, and finally ethanol.

4-Phenyl-1,2-diaminoimidazole. The reaction mixture (from 10 mmol of the imidazole) was worked up as described in the general procedure. Elution with benzene gave acetophenone (17 mg, 1.4%) and benzoyldiazomethane (16 mg, 1.1%). The identity of these compounds was determined by comparison of their IR spectra with those of authentic samples. Elution with chloroform–benzene (1:7 v/v) gave an unknown compound (13 mg) whose IR spectrum indicated the presence of an NH group. Elution with chloroform gave 4(5)-phenyl-1,2,3-triazole (672 mg, 46%), mp 147–147.5 °C (lit.[13] mp 147–148 °C). Its IR spectrum was superimposable upon that of an authentic sample. Elution with chloroform–ethanol (9:1 v/v) gave 3-amino-5-phenyl-1,2,4-triazine (187 mg, 11%), mp 233–234 °C (lit.[14] mp 233–235 °C). Its IR spectrum was superimposable upon that of an authentic sample.

4-(*p*-Bromophenyl)-1,2-diaminoimidazole. The reaction mixture (from 10 mmol of the imidazole) was worked up as described in the general procedure. Elution with benzene gave a mixture (25 mg) of *p*-bromobenzonitrile and *p*-bromoacetophenone whose IR spectrum showed a characteristic nitrile band (2220 cm^{-1}). The presence of *p*-bromoacetophenone was confirmed by derivatization as its 2,4-dinitrophenylhydrazone whose IR spectrum was superimposable upon that of an authentic sample. Further elution with benzene gave a colored compound (10 mg), whose IR spectrum showed a typical diazo band (2110 cm^{-1}) and a carbonyl band (1600 cm^{-}). Continued elution with benzene gave an unknown compound (72 mg), mp 174–180 °C dec, whose IR spectrum indicated the presence of an NH group. Elution with benzene ethanol (95:5 v/v) gave 4(5)-(*p*-bromophenyl)-1,2,3-triazole (1.24 g, 55%), mp 184–185 °C (lit.[15] mp 185–187 °C). Its IR spectrum showed a characteristic NH absorption (3150 cm^{-1}). Elution with benzene–ethanol (6:4 v/v) gave 5-(*p*-bromophenyl)-3-amino-1,2,4-triazine (0.15 g, 5.8%), mp 249–253 °C dec, whose IR spectrum showed typical NH_2 absorption (3270 and 3100 cm^{-1}). Anal. Calcd for $C_9H_7BrN_4$: C, 43.05; H, 2.81; N, 22.31. Found: C, 43.05; H, 2.87; N, 22.20.

4-(*p*-Methoxyphenyl)-1,2-diaminoimidazole. The reaction mixture (from 10 mmol of the imidazole) was worked up as described in the general procedure. Elution with benzene–hexane (1:1 v/v) gave *p*-anisonitrile (3 mg, 0.2%) whose identity was confirmed by its IR spectrum and its NMR spectrum. Elution with benzene gave a mixture (9 mg), consisting mainly of *p*-methoxyacetophenone. Its IR spectrum was superimposable upon that of *p*-methoxyacetophenone, but additional absorptions at 2220 (w) and 2170 cm^{-1} (w) suggested the presence of the *N*-cyanotriazole. Elution with benzene–chloroform (6:1 v/v) gave *p*-methoxyacetophenone (6 mg, 0.4%) whose IR spectrum was superimposable upon that of an authentic sample. Elution with benzene–chloroform (1:1–1:3 v/v) gave a colored compound (4 mg). Its IR spectrum showed a typical diazo ketone, 2120 and 1620 cm^{-1}. Elution with chloroform gave an unknown compound (8 mg). Its IR spectrum indicated the presence of an NH group. Further elution with chloroform gave 4(5)-(*p*-methoxyphenyl)-1,2,3-triazole (610 mg, 34.7%), mp 167–168 °C (lit.[13] mp 171–171.5 °C). Its IR spectrum showed a characteristic triazole type NH absorption (3130 cm^{-1}): ^{1}H NMR (Me_2SO-d_6, Me_4Si as standard) δ 3.82 (s, 3 H), 6.80–7.20 (d, 2 H, J_{ab} = 8.7 Hz), 7.60–8.00 (d, 2 H, J_{ab} = 8.7 Hz), 8.21 (s, 1 H). Elution with chloroform–ethanol (8.2 v/v) gave 3-amino-5-(*p*-methoxyphenyl)-1,2,4-triazine (514 mg, 25.5%), mp 214–216 °C. Its IR spectrum showed NH_2 absorptions (3300 and 3150 cm^{-1}) and was similar to that of 3-amino-5-phenyl-1,2.4-triazine: ^{1}H NMR (Me_2SO, Me_4Si as standard) δ 4.08 (s, 3 H), 6.70–7.30 (d, 2 H, J_{ab} = 9.1 Hz), 7.85–8.35 (d, 2 H, J_{ab} = 9.1 Hz), 9.05 (s, 1 H).

4,5-Diphenyl-1,2-diaminoimidazole. The reaction mixture (from 10 mmol of the imidazole) was worked up as described in the general procedure. Elution with benzene gave a mixture (174 mg) of benzil and benzonitrile whose identities were determined by comparison of their IR spectra with those of authentic samples. Benzil was also identified as its 2,4-dinitrophenylhydrazone whose IR spectrum was superimposable upon that of an authentic sample. Elution with benzene gave an unknown oily product (135 mg) and a compound (284 mg) which seems to be *N*-cyanoimino-1,2-diphenyldiazoethane. The IR spectrum of the latter compound showed a strong absorption at 2180 cm^{-1}, a value which had been reported for *N*-cyanoiminodiazoalkane.[3] Elution with benzene–chloroform (9:1–6:4 v/v) gave 4,5-diphenyl-1,2,3-triazole (148 mg, 9.6%), mp 138–139 °C (lit.[13] mp 140 °C). Its IR spectrum was superimposable upon that of an authentic sample. Elution with chloroform and with chloroform–ethanol (4:1 v/v) gave 3-amino-5,6-diphenyl-1,2,4-triazine (1.53 g, 62%), mp 163–169 °C (lit.[16] mp 175 °C). Its IR spectrum showed characteristic NH_2 absorptions (3420, 3250 cm^{-1}).

Oxidation of 1,2-Diaminobenzimidazole with Manganese Dioxide. A mixture of 1,2-diaminobenzimidazole (1.247 g, 8.4 mmol) and activated manganese dioxide (6.0 g) in benzene (50 mL) was heated to reflux for 17 h. The inorganic material was removed by filtration and washed with benzene (20 mL × 3). Evaporation of benzene gave 3-amino-1,2,4-benzotriazine (333 mg, 27.1%), which was purified by sublimation (120–130 °C (0.5 mmHg)) to yield a yellow solid, mp 205–206 °C (lit.[17] mp 207 °C). The inorganic material was then washed with hot ethanol (30 mL × 3). Evaporation of the ethanol gave a residue (0.526 g) which was deposited on a preparative column chromatography (silica gel mesh 60–200, 40 g). Elution with ethyl acetate (250 mL) gave yellow colored material (0.2374 g) which was

purified further by sublimation (120–130 °C (10.5 mmHg)) to afford a yellow solid (0.2337 g). Recrystallization of the yellow solid from benzene gave yellow crystals, mp 133–135 °C. Further sublimation of these yellow crystals at 70–85 °C (0.5 mmHg) gave 71 mg of 3-amino-1,2,4-benzotriazine, mp 160–180 °C. The residue from this sublimation was white solid, mp 146–147 °C. TLC showed this compound to consist mainly of 1-aminobenzimidazole, mp 150–152 °C.[18] Elution with ethyl acetate–ethanol and ethanol gave a brown colored material (0.1646 g), which was ecrystallized from benzene–chloroform to give an unknown solid, mp 128–132 °C dec.

Preparation of 1-Cyano-4- and 5-phenyltriazoles. Oil-free sodium hydride was prepared from a 50% oil dispersion of sodium hydride (0.69 g) by washing with petroleum ether (30–60 °C). The petroleum ether was decanted and the residue was evacuated under reduced pressure (0.5 mmHg). Dry THF (25 mL) was added to the sodium hydride and the mixture was stirred for 1 h. A solution of 4(5)-phenyltriazole (1.40 g, 10 mmol) in dry THF (20 mL) was added dropwise to the mixture. The resulting thick emulsion was stirred for 1 h. To this mixture was added a solution of cyanogen bromide (1.38 g, 13 mmol) in dry THF (15 mL) at such a rate that the temperature remained below 25 °C. The mixture was stirred for an additional 1.5 h. Sodium bromide was filtered and evaporation of THF gave a yellow solid (1.78 g, ~100%). The IR spectrum of this yellow solid showed a strong nitrile band (2250 cm^{-1}) and a weak diazo band (2180 cm^{-1}), mp 38–39 °C.

Reaction of *N*-Cyanotriazoles with Manganese Dioxide in Benzene. The mixture of triazoles (0.742 g) prepared above and activated manganese dioxide (0.388 g) in benzene (20 mL) was heated to reflux for 17 h. The inorganic material was filtered and the filtrate was evaporated to give a residue (0.759 g) whose IR spectrum showed the isolated products to be the starting *N*-cyanotriazoles.

Oxidation of 4-Phenyl-1,2-diaminoimidazole with Manganese Dioxide in the Presence of Phenylacetylene. A mixture of the imidazole (1.537 g, 8.8 mmol), phenylacetylene (500 mg), and activated manganese dioxide (7.0 g) in benzene (40 mL) was heated to reflux for 17 h. The workup was as described in the general procedure. Elution with benzene–hexane (1:1–9:1 v/v) gave acetophenone (39 mg) whose identity was confirmed by its IR and its NMR spectra. Elution with benzene–hexane (9:1 v/v) and with benzene gave benzoyldiazomethane (12 mg, 0.9%). Elution with benzene–chloroform (1:1 v/v) gave an unknown compound (55 mg). Elution with benzene–chloroform (1:9 v/v) gave 4(5)-phenyl-1,2,3-triazole (240 mg, 19%). Its IR spectrum was superimposable upon that of an authentic sample. Elution with chloroform and chloroform–methanol (9:1 v/v) gave a mixture (398 mg) of the triazole and 3-amino-5-phenyl-1,2,4-triazine. The yields of the triazole and the triazine were estimated to be 20 and 9.6% respectively by integration of the NMR spectrum (the peaks at δ 8.52 and 8.95 were used with CH_3COOH as solvent).

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Registry No.—**1d,** 19933-51-8; **1e,** 29540-87-2; **2d,** 5533-73-3; **3d,** 4511-99-3; **3e,** 20028-80-2; **11,** 6299-92-9; 2-(*o*-aminophenyl)-1-acetylhydrazine, 6299-91-8; cyanogen bromide, 506-68-3; 1-cyano-4-phenyl-1,2,3-triazole, 65969-54-2; 1-cyano-5-phenyl-1,2,3-triazole, 65943-32-0; manganese dioxide, 131-13-9.

References and Notes

(1) (a) Taken from the Master of Science Thesis of Masayuki Nakajima, University of Massachusetts at Boston, June 1977. (b) Faculty of Education, Shizuoka University, Shizuoka, Japan.
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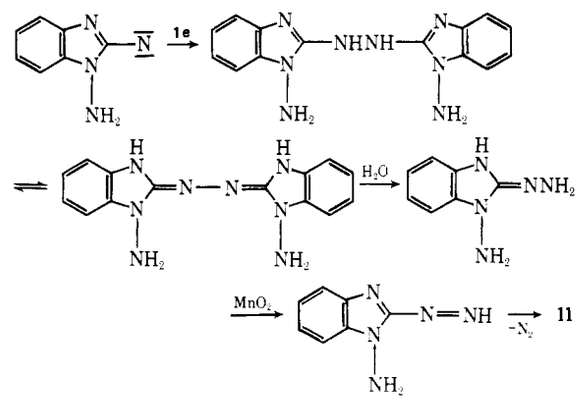
(7) Further support for this view comes from the isolation of 1-aminobenzimidazole (**11**) in trace amounts. Although the path by which **11** is formed is not obvious, one may speculate that it arose from the *C*-nitrene as shown below.



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