The Reaction of *para*-Substituted β-Aminocinnamonitriles with Benzonitrile Oxides

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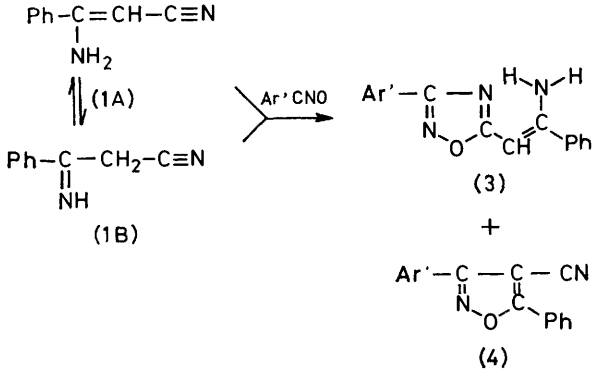
β-Aminocinnamonitrile *para*-substituted by electron-withdrawing groups (5a,b) with benzonitrile oxides (2) give the expected cycloadducts (6) to the C–N triple bond. The *p*-methyl derivative (5c) behaves similarly, but the yields are smaller. Reactions of (2) with derivatives *para*-substituted by electron-donating groups (5d,e) give two bis-adducts, the structures of which have been elucidated.

RECENTLY we reported that β-aminocinnamonitrile (1) reacts with benzonitrile oxides (2) to give chiefly the oxadiazoles (3) together with lesser amounts of the expected isoxazoles (4).[1]



Some evidence suggested to us that structure (1B) rather than (1A) is responsible for the unexpected reactivity of the terminal C≡N group [2] and that the more the Ar–C(=NH)– system is electron-withdrawing, the more it must activate the C≡N triple bond. On the other hand an electron-releasing residue could affect the dipolarophilic activities of the different sites of the molecule, the terminal C≡N triple bond becoming less reactive in comparison with the C=C or C=N double bonds. Furthermore in the second case, taking into account the greater availability of the nitrogen lone pair, an exclusive nucleophilic attack of compounds (5) on the 1,3-dipole could be rationalized.

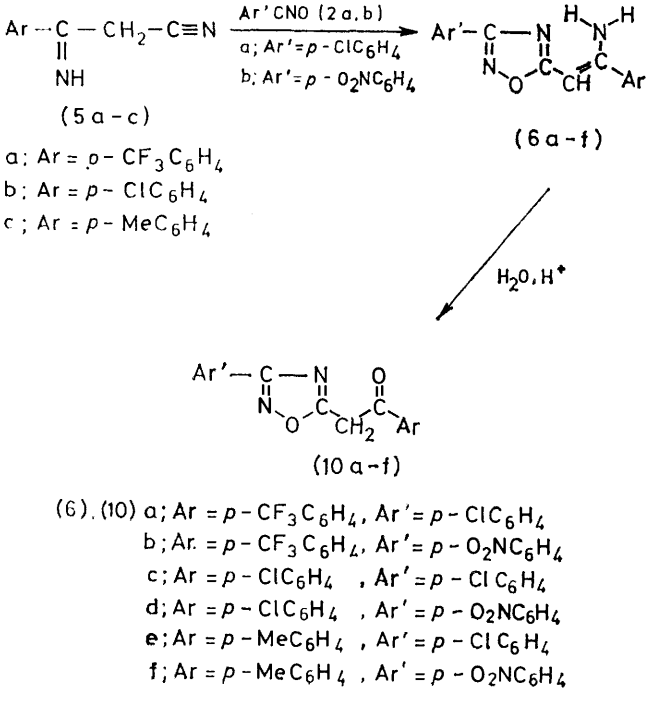
In order to verify these possibilities, compounds (5a—e) were allowed to react with benzonitrile oxides (2a,b) under the same conditions used previously.[1]

RESULTS AND DISCUSSION

Data obtained (Table 1) indicate that *para*-substituents in the phenyl ring of (5) and (2) can notably affect the reaction course qualitatively and/or quantitatively. In particular, according to expectation, *p*-trifluoromethyl (5a) and *p*-chloro (5b) derivatives react with (2a,b) to yield only the corresponding monoadducts (6a—d). β-Amino-*p*-methylcinnamonitrile (5c) behaves similarly, but the yields are smaller.

The reactions of compounds (5d,e) with 1,3-dipoles (2a,b) allow us to verify the surprising influence of electron-releasing *para*-substituents. Reaction of (5d) with (2a) (2 equiv.) leads to the oxadiazole (6 g) as the predominant product together with small amounts of 3-(*p*-chlorophenyl)-5-(*p*-methoxyphenyl)-1,2,4-oxadiazole (7 g).† On the other hand, (5d) reacts in the same ratio with (2b) to give *N*-{2-[3-(*p*-nitrophenyl)-1,2,4-oxadiazol-5-yl]-1-(*p*-methoxyphenyl)vinyl}-*p*-nitrobenzamide oxime (8h) as the major component of the reaction mixture. In this case the monoadduct (6h) and the bis-adduct 3-(*p*-nitrophenyl)-5-[3-(*p*-nitrophenyl)-5-(*p*-methoxyphenyl)-1,2-oxazol-4-yl]-1,2,4-oxadiazole (9h) are also isolated together with trace amounts of the isoxazole (4h).

The fact that oxadiazole (6h) is the only product



(6), (10) a; Ar = *p*-$CF_3C_6H_4$, Ar' = *p*-ClC_6H_4
b; Ar = *p*-$CF_3C_6H_4$, Ar' = *p*-$O_2NC_6H_4$
c; Ar = *p*-ClC_6H_4, Ar' = *p*-ClC_6H_4
d; Ar = *p*-ClC_6H_4, Ar' = *p*-$O_2NC_6H_4$
e; Ar = *p*-MeC_6H_4, Ar' = *p*-ClC_6H_4
f; Ar = *p*-MeC_6H_4, Ar' = *p*-$O_2NC_6H_4$

obtained in the reaction of (5d) with an equimolar amount of (2b), and that (8h) can also be produced starting from (6h), indicates a possible two-step pathway for the formation of (8h) (see Experimental section).

In this case the presence of the nitro-group in the

† As reported in the case of the reaction between (1) and (2b),[1] the production of (7g) can be attributed to the interaction of (2a) with the >C=NH group of (5d) and to the subsequent elimination of acetonitrile.

benzonitrile oxide enhances the electrophilic character of the carbon of the CNO system, making the latter capable of undergoing nucleophilic attack by the amino-group of (6h), activated by the conjugation with the methoxy-group. It is worthy of note that in no other case are compounds (8) obtained from the monoadducts (6).

TABLE 1

Yields[a] (%) of adducts (6), (8), and (9)

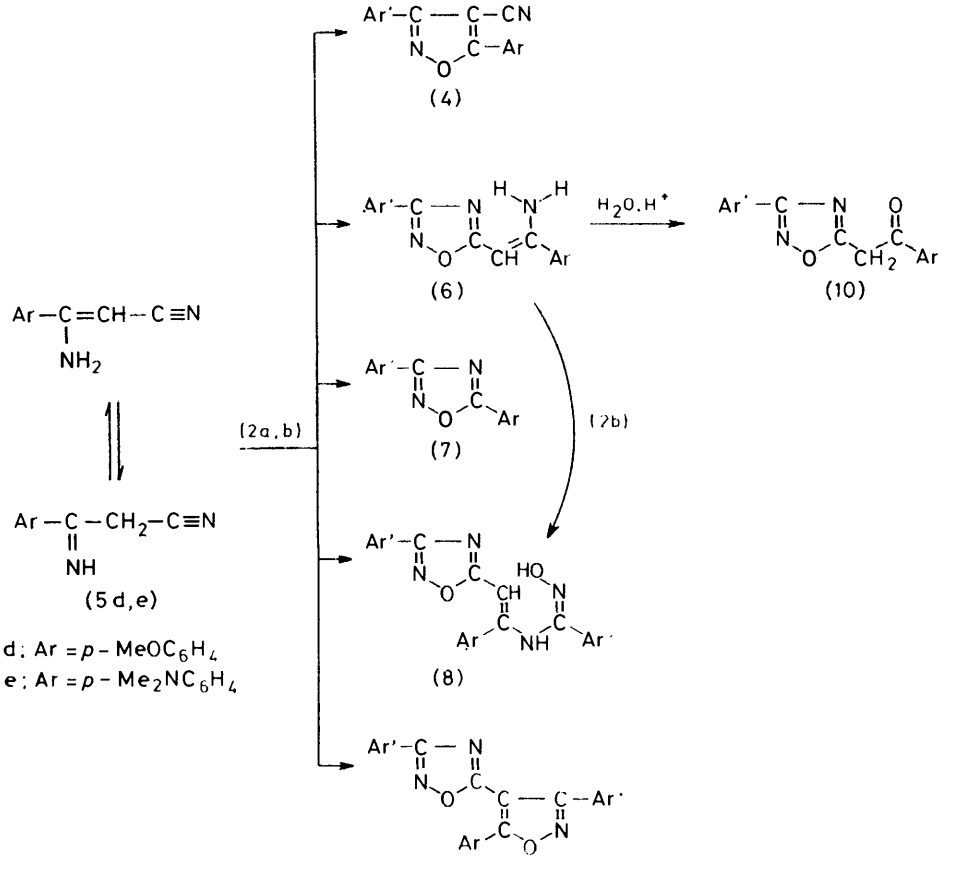
Starting material	With (2a)			With (2b)		
	(6)	(8)	(9)	(6)	(8)	(9)
(5a)	**41**			**57**		
(5b)	**34**			**42**		
(5c)	**26** [b]			**34**		
(5d)	**15** [b]			9	51	5
(5e)	6		50		1	58

[a] Yields are calculated considering the recovered amounts of the starting enamines. [b] Yields of hydrolysis products, obtained during column chromatography, are also included.

amounts of the mono-adduct (6i), while there is no evidence of the production of (8i). In contrast the corresponding (8l), with (9l) as the major product, is isolated from the reaction mixture obtained from (5e) and (2b), but formation of compounds (4l) and (6l) does not occur. This suggests to us that compound (6l), as it is formed, reacts with a second equivalent of (2b) to give (8l), since it is more nucleophilic than (6h) because of conjugation with the dimethylamino-group.

With reference to the production of compounds (9), we conclude that they derive from two synchronous cycloaddition processes, since (9h) is never isolated among the reaction products of (6h) with (2b), but (8h) is.

The structure of compounds (4) and (6) was substantiated on the basis of their chemical and/or spectral data, which are in agreement with those shown by

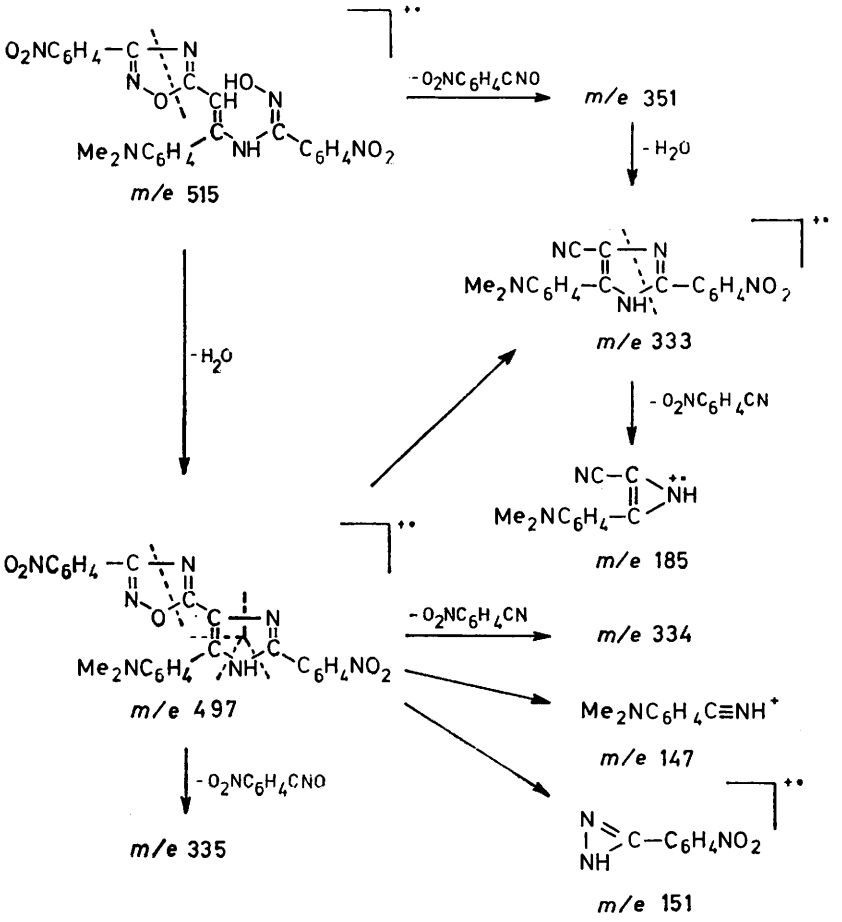


(4), (6), (7), (8), (9), (10) g; Ar = p-MeOC$_6$H$_4$, Ar' = p-ClC$_6$H$_4$
h; Ar = p-MeOC$_6$H$_4$, Ar' = p-O$_2$NC$_6$H$_4$
i; Ar = p-Me$_2$NC$_6$H$_4$, Ar' = p-ClC$_6$H$_4$
l; Ar = p-Me$_2$NC$_6$H$_4$, Ar' = p-O$_2$NC$_6$H$_4$

Reactions of (5e) with *p*-chlorobenzonitrile oxide (2a) carried out in the ratios (1 : 2) and (1 : 1) give the bis-adduct (9i) as the prominent product, besides very small similar compounds reported previously [1] (see Experimental section).

The structure of compounds (8) was elucidated by means of spectral evidence. I.r. spectra show a broad band at 3 450 cm^{-1} for the associated OH and bands at

1 600, 1 578, and 1 556 cm^{-1} for both the disubstituted phenyl systems and five-membered hetero-aromatic rings. The mass spectra show the molecular ions at *m/e* 502 and 515, respectively, for (8h) and (8l), and the base peaks correspond to the loss of water. Further prominent fragment-ions correspond to the subsequent cleavage of the two heteroaromatic rings. The scheme indicates the fragmentation pattern of the most significant fragment-ions derived from the fission of (8l). Attempts to record n.m.r. spectra failed because of the insolubility of the compounds in common deuteriated solvents. However, the spectra of solutions in deuteriated trifluoroacetic acid indicate the presence of exchangeable protons. Also, attempts to effect the Beckmann rearrangement to the two *para*-substituted benzonitrile ions, in accordance with the fission of similar compounds.[3] Other intense peaks derive from the formation of the ions $[Ar'CNO]^+$, $[Ar'CN_2]^+$, and $[ArCO]^+$.



EXPERIMENTAL

M.p.s were determined on an electrothermal apparatus and are uncorrected. I.r. spectra (KBr discs, unless otherwise stated) were recorded with a Perkin-Elmer 137 spectrophotometer, u.v. spectra (solutions in 95% ethanol) with a Beckmann DB-GT spectrophotometer and ^1H n.m.r. spectra (60 MHz) with a Varian A-60 spectrometer (solvent, unless otherwise stated, $CDCl_3$; $SiMe_4$ as internal standard). Mass spectra were obtained with an LKB 9000 S mass-spectrometer. T.l.c. was carried out with silica gel F 254 plates [developing solvents light petroleum–benzene (20:80), benzene, and benzene–ethyl acetate (90:10)]. Chromatography was performed with Merk silica gel (0.05—0.2 mm).

Materials.—Solvents were purified and dried according to the literature methods. The benzonitrile oxides (2a,b) were not isolated, but prepared directly in solution ($CHCl_3$) from equivalent amounts of purified triethylamine (TEA) and the corresponding benzohydroxamoyl chlorides.[4,5] Enamines (5b—e) were prepared by reported procedures.[6-10] The enamine (5a) was prepared by following the literature procedure starting from *p*-trifluoromethylbenzonitrile (17 g) and acetonitrile (5 g) with sodium (2.5 g) in refluxing

reaction failed. Elemental analyses agree with the assigned structures.

Compounds (9) were identified on the basis of their spectroscopic data. The i.r. spectra exhibit only the bands of the heteroaromatic systems and the bands of disubstituted phenyl rings. N.m.r. spectra, besides the proton signals of the different phenyl substituent groups, show only the signals of aromatic protons. In each case the mass spectrum shows the molecular ion in high abundance; the base peaks occur at *m/e* 148 for both (9h) and (9l), and at *m/e* 137 for (9i). They correspond

benzene. The crude material on crystallization from light petroleum–benzene gave β-*amino*-p-*trifluoromethylcinnamonitrile* (5a) (13 g, 40%), m.p. 133—134 °C (Found: C, 56.3; H, 3.4; N, 13.1. $C_{10}H_7F_3N_2$ requires C, 56.1; H, 3.3; N, 13.2%); $\lambda_{max.}$ (EtOH) 303 nm (ε 1.1 × 10^4); $\nu_{max.}$ (KBr) 3 333 and 3 230 (NH_2), 2 176 (C≡N), 1 638 (enamine C=C), and 1 600 and 1 566 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$) 4.32 (1 H, s, CH), 5.05 (2 H, br, NH_2), and 7.3—8.05 (4 H, m, aromatic); *m/e* 212.

All compounds were purified until they were observed as single spots on t.l.c. (Kieselgel PF 254).

General Procedure for the Reaction of Compounds (2a,b) *with Enamines* (5a—e).—A solution of TEA (6 mmol) in chloroform (10 ml) was added dropwise to a mixture of the appropriate benzohydroxamoyl chloride (6 mmol) with enamine (3 mmol) in chloroform (30 ml) with stirring. The mixture was then kept at room temperature for 48 h. Triethylammonium hydrochloride was filtered off and the filtrate was distilled under reduced pressure. The reaction products were separated by column chromatography. In every case the benzonitrile oxide dimers and small amounts of the starting enamine were recovered. Where necessary further purification of products was achieved by crystallization from ethanol or by washing with hot benzene, in which impurities were soluble.

Reactions of p-*Chlorobenzonitrile Oxide* (2a).—(i) *With* β-*amino*-p-*trifluoromethylcinnamonitrile* (5a). Elution with light petroleum–benzene (20 : 80) gave only 3-(p-*chlorophenyl*)-5-(β-*amino*-p-*trifluoromethylstyryl*)-1,2,4-*oxadiazole* (6a) (0.448 g, 41%), m.p. 129—130 °C (from EtOH) (Found: C, 55.6; H, 3.1; N, 11.3. $C_{17}H_{11}ClF_3N_3O$ requires C, 55.8; H, 3.0; N, 11.5%); $\lambda_{max.}$ (EtOH) 332 (ε 1.6 × 10^4) and 246 nm (ε 2.8 × 10^4); $\nu_{max.}$ (KBr) 3 448 and 3 229 (NH_2), 1 640 (enamine C=C), and 1 587 and 1 550 cm^{-1} (aromatic C=C and C=N); δ($CDCl_3$) 5.68 (1 H, s, CH), 6.80 (2 H, br, NH_2), and 7.50—8.30 (8 H, m, aromatic); *m/e* 365.

(ii) *With* β-*amino*-p-*chlorocinnamonitrile* (5b). Chromatography with light petroleum–benzene (20 : 80) as eluant gave 3-(*p-chlorophenyl*)-5-(β-*amino*-p-*chlorostyryl*)-1,2,4-*oxadiazole* (6c) (0.331 g, 34%), m.p. 164—165 °C (from EtOH) (Found: C, 54.3; H, 3.1; N, 14.8. $C_{16}H_{11}Cl_2N_3O$ requires C, 54.2; H, 2.9; N, 14.9%); $\lambda_{max.}$ (EtOH) 335 (ε 1.5 × 10^4) and 250 nm (ε 2.0 × 10^4); $\nu_{max.}$ (KBr) 3 412 and 3 229 (NH_2), 1 639 (enamine C=C), and 1 587 and 1 562 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$) 5.63 (1 H, s, CH), 6.72 (2 H, br, NH_2), and 7.40—8.30 (8 H, m, aromatic); *m/e* 331.

(iii) *With* β-*amino*-p-*methylcinnamonitrile* (5c). Elution with light petroleum–benzene (20 : 80) gave as the major product 3-(p-*chlorophenyl*)-5-(β-*amino*-p-*styryl*)-1,2,4-*oxadiazole* (6e) (0.149 g, 16%), m.p. 170 °C (from EtOH) (Found: C, 57.7; H, 3.4; N, 21.1. $C_{17}H_{14}ClN_3O$ requires C, 57.8; H, 3.3; N, 12.7%); $\lambda_{max.}$ (EtOH) 325 (ε 2.2 × 10^4) and 245 nm (ε 2.4 × 10^4); $\nu_{max.}$ (KBr) 3 410 and 3 312 (NH_2), 1 610 (enamine C=C), and 1 590 and 1 570 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$) 2.4 (3 H, s, Me), 5.6 (1 H, s, CH), 6.4 (2 H, br, NH_2), and 7.1—8.2 (8 H, m, aromatic); *m/e* 311.

Elution with benzene gave 3-(p-*chlorophenyl*)-5-(p-*methylphenacyl*)-1,2,4-*oxadiazole* (10e) (0.095 g, 10%), m.p. 128—129 °C (from EtOH) (Found: C, 57.3; H, 3.2; N, 8.4. $C_{17}H_{13}ClN_2O_2$ requires C, 57.7; H, 3.0; N, 8.4%); $\lambda_{max.}$ (EtOH) 315 (ε 0.6 × 10^4) and 255 nm (ε 2.9 × 10^4); $\nu_{max.}$ (KBr) 3 446 cm^{-1} (associated OH); $\nu_{max.}$ ($CHCl_3$) 1 695 cm^{-1} (C=O); δ ($CDCl_3$) 2.41 (3 H, s, Me), 4.62 (2 H, s, CH_2 of keto-form), 6.21 (1 H, s, CH of enol form), and 7.12—8.10 (8 H, m, aromatic); *m/e* 312. The structure (10e) was confirmed by comparison with an authentic sample obtained from hydrolysis of (6e). Clearly it is produced during the column chromatography.

(iv) *With* β-*amino*-p-*methoxycinnamonitrile* (5d). The first compound eluted with light petroleum was 3-(*p*-chlorophenyl)-5-(*p*-methoxyphenyl)-1,2,4-oxadiazole (7) (0.068 g, 8%), m.p. 158—160 °C (from EtOH) (lit.,[11] m.p. 155—157 °C). Elution with light petroleum–benzene (20 : 80) gave, after dimers, 3-(p-*chlorophenyl*)-5-(β-*amino*-p-*methoxystyryl*)-1,2,4-*oxadiazole* (6g) (0.102 g, 11%), m.p. 162—163 °C (from EtOH) (Found: C, 55.8; H, 3.0; N, 16.2. $C_{17}H_{14}ClN_3O_2$ requires C, 56.0; H, 3.2; N, 16.3%); $\lambda_{max.}$ (EtOH) 340 (ε 2.1 × 10^4) and 250 nm (ε 1.6 × 10^4); $\nu_{max.}$ (KBr) 3 436 and 3 280 (NH_2), 1 624 (enamine C=C), and 1 600 and 1 564 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$) 3.80 (3 H, s, OMe), 5.60 (1 H, s, CH), 6.7 (2 H, br, NH_2), and 6.9—8.2 (8 H, m, aromatic); *m/e* 327. The last compound eluted (with benzene) was 3-(p-*chlorophenyl*)-5-(p-*methoxyphenacyl*)-1,2,4-*oxadiazole* (10g) (0.045 g, 4%), m.p. 120—121 °C (from EtOH) (Found: C, 55.6; H, 3.2; N, 12.3. $C_{17}H_{13}ClN_2O_3$ requires C, 55.9; H, 2.9; N, 12.2%); $\lambda_{max.}$ (EtOH) 325 (ε 0.4 × 10^4) and 245 nm (ε 2.9 × 10^4); $\nu_{max.}$ (KBr) 3 400 cm^{-1} (associated OH); $\nu_{max.}$ ($CHCl_3$) 1 690 cm^{-1} (C=O); *m/e* 328. In this case the structure (10g) was confirmed by comparison with an authentic sample obtained from hydrolysis of (6g), and it was produced during the column chromatography.

(v) *With* β-*amino*-p-*dimethylaminocinnamonitrile* (5e). Elution with light petroleum–benzene (20 : 80) gave 3-(p-*chlorophenyl*)-5-[3-(p-*chlorophenyl*)-5-(p-*dimethylaminophenyl*)*isoxazol*-4-*yl*]-1,2,4-*oxadiazole* (9i) (0.715 g, 50%), m.p. 138 °C (from EtOH) (Found: C, 62.7; H, 3.7; N, 14.7. $C_{25}H_{18}Cl_2N_4O_2$ requires C, 62.9; H, 3.8; N, 14.9%); $\lambda_{max.}$ (EtOH) 277 nm (ε 2.5 × 10^4); $\nu_{max.}$ (KBr) 1 616 and 1 592 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$) 3.2 (6 H, s, NMe_2), and 6.8—8.3 (12 H, m, aromatic); *m/e* 476. Further elution gave 3-(p-*chlorophenyl*)-5-(β-*amino*-p-*dimethylaminostyryl*)-1,2,4-*oxadiazole* (6i) (0.061 g, 6%), m.p. 196—197 °C (from EtOH) (Found: C, 65.8; H, 4.7; N, 13.3. $C_{18}H_{17}ClN_4O$ requires C, 65.5; H, 4.5; N, 13.5%); $\lambda_{max.}$ (EtOH) 315 (ε 1.6 × 10^4) and 235 nm (ε 2.3 × 10^4); $\nu_{max.}$ (KBr) 3 472 and 3 289 (NH_2), 1 639 (enamine C=C), and 1 615 and 1 540 cm^{-1} (aromatic C=C and C=N); δ ($CDCl_3$–DMSO) 3.2 (6 H, s, NMe_2), 5.7 (1 H, s, CH), and 6.8—8.3 (10 H, NH_2 and aromatic); *m/e* 340.

Reactions of p-*Nitrobenzonitrile Oxide* (2b).—(i) *With* β-*amino*-p-*trifluoromethylcinnamonitrile* (5a). Elution with light petroleum–benzene (20 : 80) gave only the mono-adduct 3-(p-*nitrophenyl*)-5-(β-*amino*-p-*trifluoromethylstyryl*)-1,2,4-*oxadiazole* (6b) (0.642 g, 57%), m.p. 172—173 °C (from EtOH) (Found: C, 63.2; H, 4.4; N, 17.2. $C_{17}H_{11}F_3N_4O_3$ requires C, 63.3; H, 4.4; N, 17.4%); $\lambda_{max.}$ (EtOH) 330 (ε 1.0 × 10^4) and 268 nm (ε 3.0 × 10^4); $\nu_{max.}$ (KBr) 3 508 and 3 333 (NH_2), 1 639 (enamine C=C), 1 587 and 1 562 (aromatic C=C and C=N), 1 515 (asym. NO_2), and 1 324 (sym. NO_2); δ ($CDCl_3$) 5.76 (1 H, s, CH), 6.84 (2 H, br, NH_2), and 7.7—8.7 (8 H, m, aromatic); *m/e* 376.

(ii) *With* β-*amino*-p-*chlorocinnamonitrile* (5b). As above the only product isolated was 3-(p-*nitrophenyl*)-5-(β-*amino*-p-*chlorostyryl*)-1,2,4-*oxadiazole* (6d) (0.423 g, 42%), m.p. 175—176 °C (from EtOH) (Found: C, 62.4; H, 4.1; N, 12.8. $C_{16}H_{11}ClN_4O_3$ requires C, 62.3; H, 4.3; N, 12.8%); $\lambda_{max.}$ (EtOH) 338 (ε 1.7 × 10^4) and 258 nm (ε 2.4 × 10^4); $\nu_{max.}$ (KBr) 3 442 and 3 230 (NH_2), 1 625 (enamine C=C), 1 574 and 1 550 (aromatic C=C and C=N), 1 532 (asym NO_2),

and 1 340 cm^{-1} (sym. NO_2); δ ($CDCl_3$) 5.7 (1 H, s, CH), 6.8 (2 H, br, NH_2), and 7.4—8.5 (8 H, m, aromatic); *m/e* 342.

(iii) *With* β-*amino*-p-*methylcinnamonitrile* (5c). In this case also the only product separated was the mono-adduct 3-(p-*nitrophenyl*)-5-(β-*amino*-p-*methylstyryl*)-1,2,4-*oxadiazole* (6f) (0.33 g, 34%), m.p. 181—182 °C (from EtOH) (Found: C, 60.3; H, 4.4; N, 16.3. $C_{17}H_{14}N_4O_3$ requires C, 60.3; H, 4.2; N, 16.5%); $\lambda_{max.}$ (EtOH) 325 (ε 2.1 × 10^4) and 270 nm (ε 2.2 × 10^4); $\nu_{max.}$ (KBr) 3 490 and 3 307 (NH_2), 1 621 (enamine C=C), 1 610 and 1 570 (aromatic C=C and C=N), 1 510 (asym. NO_2), and 1 350 cm^{-1} (sym. NO_2); δ ($CDCl_3$) 2.4 (2 H, s, Me), 5.6 (1 H, s, CH), 6.4 (2 H, br, NH_2), 7.2—8.5 (8 H, m, aromatic); *m/e* 322.

(iv) *With* β-*amino*-p-*methoxycinnamonitrile* (5d). By treatment of the reaction-mixture residue with hot benzene, the *bis-adduct* (8h) (0.768 g, 51%) was separated as a red powder, m.p. 322—324 °C (from DMF) (Found: C, 57.1; H, 3.7; N, 16.7. $C_{24}H_{18}N_6O_7$ requires C, 57.4; H, 3.6; N, 16.8%); $\lambda_{max.}$ (EtOH) 360 (ε 3.7 × 10^4) and 285 nm (ε 3.2 × 10^4); $\nu_{max.}$ (KBr) 3 420 br (associated OH), 1 612 and 1 578 (aromatic C=C and C=N), 1 532 (asym. NO_2), and 1 342 cm^{-1} (sym. NO_2); δ (CF_3CO_2D) 3.8 (3 H, s, OMe), and 8.05—8.64 (12 H, m, aromatic); *m/e* 502. The benzene solution was distilled off and the residue was chromatographed. In the first eluate [light petroleum–benzene (80 : 20)] trace amounts of 3-(*p*-nitrophenyl)-4-cyano-5-(*p*-methoxyphenyl)isoxazole (4h) were identified on the basis of i.r. and n.m.r. spectra. The second eluate [light petroleum–benzene (20 : 80)] gave the mono-adduct 3-(p-*nitrophenyl*)-5-(β-*amino*-p-*methoxystyryl*)-1,2,4-*oxadiazole* (6h) (0.091 g, 9%), m.p. 183—184 °C (from EtOH) (Found: C, 63.2; H, 5.2; N, 16.5. $C_{17}H_{14}N_4O_4$ requires C, 63.4; H, 5.0; N, 16.4%); $\lambda_{max.}$ (EtOH) 333 (ε 1.9 × 10^4) and 270 nm (ε 2.9 × 10^4); $\nu_{max.}$ (KBr) 3 440 and 3 228 (NH_2), 1 633 (enamine C=C), 1 612 and 1 567 (aromatic C=C and C=N), 1 515 (asym. NO_2), and 1 351 cm^{-1} (sym. NO_2); δ ($CDCl_3$) 3.8 (3 H, s, OMe), 5.7 (1 H, s, CH), 6.8 (2 H, br, NH_2), and 7.0—8.5 (8 H, m, aromatic); *m/e* 338. The evaporation of the third eluate [benzene–ethyl acetate (90 : 10)] left a residue which was separated into two components by treatment with pyridine. The pyridine-insoluble compound was the bis-adduct (8h), while the pyridine-soluble one was identified as 3-(p-*nitrophenyl*)-5-[3-(p-*nitrophenyl*)-5-(p-*methoxyphenyl*)*isoxazol*-4-*yl*]-1,2,4-*oxadiazole* (9h) (0.0 718 g, 5%), m.p. 284 °C (from EtOH) (Found: C, 60.2; H, 3.4; N, 17.0. $C_{24}H_{15}N_5O_7$ requires C, 60.2; H, 3.6; N, 16.9%); $\lambda_{max.}$ (EtOH) 278 nm (ε 2.5 × 10^4); $\nu_{max.}$ (KBr) 1 604, 1 576, and 1 554 (aromatic C=C and C=N), 1 524 (asym. NO_2), and 1 348 cm^{-1} (sym. NO_2); *m/e* 485. The n.m.r. spectrum could not be recorded because of its insolubility.

(v) *With* β-*amino*-p-*dimethylaminocinnamonitrile* (5e). The treatment of the reaction mixture residue with cold ethanol gave a mixture of dimers and an orange compound, which by further washing with hot ethanol was separated and identified as 3-(p-*nitrophenyl*)-5-[3-(p-*nitrophenyl*)-5-(p-*dimethylaminophenyl*)*isoxazol*-4-*yl*]-1,2,4-*oxadiazole* (9l) (0.866 g, 58%), m.p. 265—266 °C (from THF) (Found: C, 62.6; H, 4.0; N, 11.4. $C_{25}H_{18}N_6O_6$ requires C, 62.9; H, 3.8; N, 11.7%); $\lambda_{max.}$ (EtOH) 277 nm (ε 2.2 × 10^4); $\nu_{max.}$ (KBr) 1 620, 1 577, and 1 558 (aromatic C=C and C=N), 1 530 (asym. NO_2), and 1 344 cm^{-1} (sym. NO_2); δ ($CDCl_3$) 3.2 (6 H, s, NMe_2), and 7.2—8.5 (12 H, m, aromatic); *m/e* 498. Column chromatography of the ethanolic solution residue, besides further amounts of (9l), gave the bis-adduct N-{2-[3-(p-*nitrophenyl*)-1,2,4-*oxadiazol*-5-*yl*]-1-(p-*dimethylaminophenyl*)*vinyl*}-p-*nitrobenzamide oxime* (8l) (0.015 g, 1%), m.p. 299—301 °C (from DMF) (Found: C, 58.4; H, 4.1; N, 18.9. $C_{25}H_{18}N_6O_6$ requires C, 58.2; H, 4.1; N, 19.0%); $\lambda_{max.}$ (EtOH) 340 (ε 3.7 × 10^4) and 274 nm (ε 4.2 × 10^4); $\nu_{max.}$ (KBr) 3 390 br (associated OH), 1 615 and 1 564 (C=C and C=N), 1 528 (asym. NO_2), and 1 340 cm^{-1} (sym. NO_2); δ (CF_3CO_2D) 3.2 (6 H, s, NMe_2) and 8.12—8.72 (12, m, aromatic); *m/e* 515.

(vi) *With* β-*amino*-p-*methoxycinnamonitrile* (5d) (*ratio* 1 : 1). Following the general procedure reported above, from the reaction mixture only the mono-adduct (6h) was separated. It was identified by t.l.c., m.p., and mixed m.p. with an authentic sample.

(vii) *With* β-*amino*-p-*dimethylaminocinnamonitrile* (5e) (*ratio* 1 : 1). The reaction mixture residue gave the same products obtained in the case where the ratio of 2 : 1 was used. Compounds (8l) and (9l) were isolated and identified by t.l.c., m.p., and mixed m.p. with an authentic sample.

(viii) *With mono-adduct* (6h). A solution of TEA (1 mmol) in chloroform (2 ml) was added to a mixture of *p*-nitrobenzohydroxamoyl chloride (1 mmol) with (6h) (1 mmol) in chloroform (5 ml) with stirring. The mixture was kept at room temperature for 48 h and then treated according to the same procedure followed for the reaction of enamine (5d) with (2b). Besides dimers and the starting mono-adduct (6h), only the bis-adduct (8h) was isolated, and identified by t.l.c., m.p., and mixed m.p. with an authentic sample.

Hydrolysis of Compound (6).—A solution of compounds (6) (0.5 mmol) in ethanol (20 ml) containing 15% hydrochloric acid (3 ml) was refluxed for 4 h [hydrolysis of *para*-nitro-derivatives required 36% HCl and 12 h]. On dilution with water, compounds (10) were precipitated. They were filtered off and washed repeatedly with water. Crystallization from ethanol gave nearly quantitative yields. M.p.s and elemental analyses are given in Table 2. Compounds (10) showed $\lambda_{max.}$ (EtOH) in the ranges 320—345 and 248—276 nm; $\nu_{max.}$ (KBr) in the range 3 300—3 350 cm^{-1} (associated OH); $\nu_{max.}$ ($CHCl_3$) in the range 1 680—1 695 cm^{-1} (C=O); δ ($CDCl_3$), besides the signals of aromatic protons and those of the substituent groups, 4.7 (2 H, s, CH_2 of keto-form) and 6.3 (1 H, s, CH of enol form). The OH signals were broad and were not observed.

TABLE 2

M.p.s and elemental analyses of compounds (10)

Compound	M.p. (°C)	Analysis: Found C	Found H	Found N	Required C	Required H	Required N
(10a)	115—116	55.6	3.0	7.7	55.7	2.8	7.6
(10b)	138—140	54.0	2.8	11.0	54.1	2.7	11.1
(10c)	141—142	57.4	3.0	8.5	57.7	3.0	8.4
(10d)	139	55.6	2.8	12.0	55.9	2.9	12.2
(10e)	128—129	65.4	4.4	8.9	65.3	4.2	8.9
(10f)	151—152	63.1	4.1	13.1	63.1	4.0	13.0
(10g)	119—121	62.0	3.9	8.5	62.1	4.0	8.5
(10h)	165	60.0	3.9	12.3	60.2	3.8	12.4
(10i)	146—148	63.3	4.5	12.2	63.2	4.7	12.3

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