The Chemistry of Cyanoacetylenes. Part II.[1] Cyanoenamines, their Preparation and Reactions

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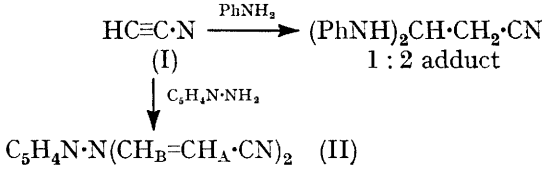
Cyanoenamines were prepared by addition of cyclic secondary amines to cyanoacetylene. Acidic hydrolysis of 3-morpholinoacrylonitrile afforded formylacetic acid. Treatment of the same cyanoenamine with acyl chlorides gave, unexpectedly, 4-morpholinobutadiene-1,3-dicarbonitrile. Reactions of 3-aziridin-1-ylacrylonitrile with *p*-nitrobenzoic acid, sodium iodide in acetone, and sodium iodide in carbon disulphide afforded 2-(2-cyanovinylamino)ethyl *p*-nitrobenzoate, 3-(2,2-dimethyl-1,3-oxazolidin-1-yl)acrylonitrile, and 3-(2-thioxo-1,3-thiazolidin-1-yl)acrylonitrile, respectively.

CYANOENAMINES were prepared by addition of cyclic secondary amines (morpholine, pyrrolidine, piperidine, aziridine, and imidazole) to an ethereal solution of cyanoacetylene (I); the results are summarized in the Table. The products have the *trans*-configuration, as expected [2,3] (see Table for spectroscopic evidence of structure).

With primary amines such as aniline, cyanoacetylene is reported to give a mixture of 1 : 1 and 1 : 2 adducts.[4] Our repetition of the same experiment, however, gave exclusively a 1 : 2 adduct (65%). Treatment of cyanoacetylene with 2-aminopyridine under similar conditions (in ether at room temperature) gave 1-pyridyliminobisacrylonitrile, a 2 : 1 adduct (II); the structure was confirmed by the n.m.r. spectrum.

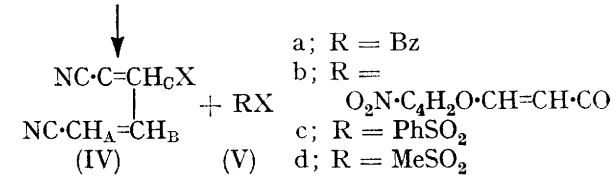


Alt and Speziale [5] have reported that a keto-enamine can be benzoylated with benzoyl chloride (2 equiv.); in this case, the benzoyl chloride attacks the enamine carbon, not the ketone oxygen. Expecting to obtain a similar compound (IV'), we treated 3-morpholinoacrylonitrile (III) with acyl chlorides (benzoyl chloride, 5-nitro-2-furylacryloyl chloride,[6] and benzenesulphonyl and methanesulphonyl chloride) under the conditions specified by Campbell and Jung.[7] All the reactions gave the same product (IV), together with the *N*-acylmorphiline (Va—d). The product (IV) was identified as 4-morpholinobutadiene-1,3-dicarbonitrile (H_A and H_B *trans*) by analysis and n.m.r. data. Since in these reactions morpholine elimination seems to be favoured in acidic media,[8] (III) was treated with acyl chloride (1 equiv.) in the presence of triethylamine. However, the products were mostly intractable tars, together with a small amount of (IV).

Cyanoenamines (*trans*-NC·CH$_A$=CH$_B$X)

X	M.p.	Yield (%)	Found (%) C	H	N		Required (%) C	H	N	$\nu_{max.}$ (CN) (cm.$^{-1}$)	τ(CDCl$_3$) H_A	H_B	J_{AB} (c./sec.)
Morpholine	56—57°	85	60·5	7·6	20·4	$C_7H_{10}N_2O$	60·85	7·3	20·3	2219	6·07	3·13	14·0
Pyrrolidin-1-yl...	46—47 ·	75	68·4	8·4	22·6	$C_7H_{10}N_2$	68·8	8·25	22·3	2220	6·36	2·86	13·5
Piperidino	56 [a]	85								2220	6·10	3·15	14·0
Aziridin-1-yl ...	(B.p. 32°/0·3 mm.) [b]	60	63·9	6·3	29·8	$C_5H_6N_2$	63·8	6·4	29·8	2220 [c]			
Imidazol-1-yl ...	75	80	60·2	3·9	35·45	$C_6H_5N_3$	60·5	4·2	35·3	2220	4·91	2·71	10·5

[a] Lit. (ref. 4) 55·5—56°. [b] An unstable liquid which decomposes gradually to black tars at room temperature on exposure to air. [c] Liquid film; all others as KBr epllets.



We suggest that the reactions take place by initial electrophilic attack of acyl cation on the enamine nitrogen; this *N*-acylation converts the enamine system into an electrophilic olefin, since the nitrogen lone pair is no longer available for enamine activation. Further reaction is possible as shown (Scheme).

Treatment of (III) with strong organic acids (trichloro- and monochloro-acetic acid) also afforded (IV), together with the corresponding morpholine salts.

Treatment of the cyanoenamine (VI), which contains a reactive aziridine ring,[9] with *p*-nitrobenzoic acid

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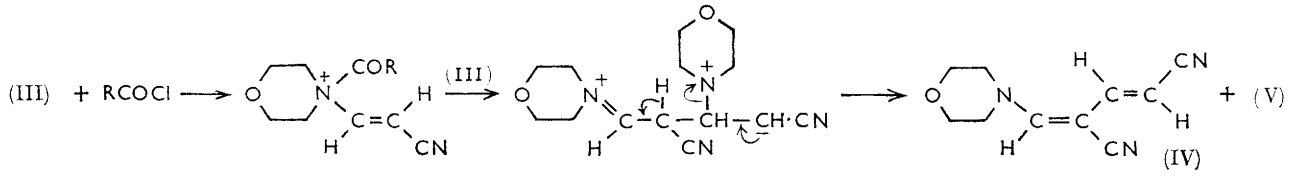
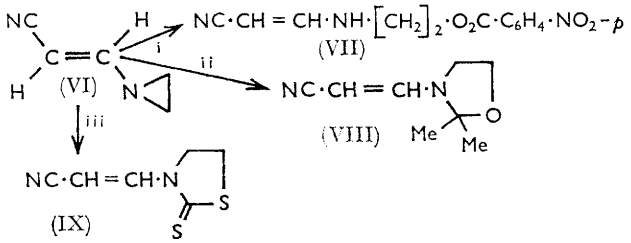


SCHEME

afforded a ring-opened compound (VII). When a solution of (VI) in acetone was heated under reflux with sodium iodide, a new type of recyclization product (VIII) was obtained, identified (analysis and n.m.r. spectrum) as 3-(2,2-dimethyl-1,3-oxazolidin-1-yl)acrylonitrile. Similar treatment with sodium iodide in carbon disulphide afforded 3-(2-thioxo-1,3-thiazolidin-1-yl)acrylonitrile (IX).



Reagents: i, *p*-$O_2N{\cdot}C_6H_4{\cdot}CO_2H$; ii, Me_2CO–NaI; iii, CS_2–NaI.

EXPERIMENTAL

M.p.s were determined with a Yanagimoto apparatus. Microanalyses were carried out with a Yanagimoto MT-1 C.H.N. Corder. I.r. spectra were recorded for potassium chloride pellets with a JASCO IR-S spectrophotometer. N.m.r. spectra were obtained with a Varian A-60 spectrometer, with tetramethylsilane as internal standard. Mass spectra were determined with a Hitachi RMU-7HR high-resolution spectrometer, operating at 70 ev. Chromatography was carried out with a column of silica gel (Mallinckrodt 100 mesh), eluted with chloroform.

3-Morpholinoacrylonitrile (III).—To a stirred solution of cyanoacetylene (2·2 g., 0·04 mole) in absolute ether (30 ml.) cooled in ice was added dropwise a solution of morpholine (4 g., 0·04 mole) in absolute ether (10 ml.). Stirring was continued at room temperature overnight; removal of the solvent then left the product (III) (5·0 g., 85%), which was recrystallized from ethanol. The results of similar reactions with several cyclic secondary amines are summarized in the Table.

Cyanoacetylene and Aniline.—To a stirred solution of aniline (1 g., 0·01 mole) in ether (10 ml.) cooled in ice was added a solution of cyanoacetylene (0·5 g., 0·01 mole) in ether (10 ml.). The mixture was kept at room temperature overnight. The product was a 1 : 2 adduct (0·8 g., 65%), m.p. 133° (lit.,[4] 133·5—134·5°).

Cyanoacetylene and 2-Aminopyridine.—To a stirred solution of 2-aminopyridine (1 g., 0·01 mole) in ether (20 ml.) was added a solution of cyanoacetylene (0·5 g., 0·01 mole) in ether (10 ml.) under similar conditions. The crude product gave the adduct (II) (0·6 g., 65%), m.p. 220—221° (from benzene) (Found: C, 67·5; H, 4·3; N, 28·35%. $C_{11}H_8N_2$ requires C, 67·3; H, 4·1; N, 28·5%), $\nu_{max.}$ 2200 (CN) and 1650 (C=C) cm.$^{-1}$ (no NH), τ ($CDCl_3$) 5·34 (d, *J* 13·0 c./sec., H_A) and 2·95 (d, *J* 13·0 c./sec., H_B).

Acidic Hydrolysis of (III).—A solution of the nitrile (III) (0·5 g.) in N-hydrochloric acid (30 ml.) was heated at 80° for 0·5 hr. Water was removed under reduced pressure and the residue was dissolved in ethanol (20 ml.). To this solution was added an ethanolic solution of dinitrophenylhydrazine. The resulting precipitate gave *formylacetic acid 2,4-dinitrophenylhydrazone* (0·15 g., 15%), m.p. 160° (decomp.) (from ethanol) (Found: C, 40·5; N, 2·9; N, 21·1%. $C_9H_8N_4O_6$ requires C, 40·3; H, 3·0; N, 20·9%), no CN peak in i.r. spectrum.

Reactions of (III) *with Acyl Chlorides.*—(a) *Benzoyl chloride.* To a stirred solution of benzoyl chloride (0·35 g., 0·0025 mole) in dry benzene (20 ml.) cooled in ice was added a solution of the nitrile (III) (0·7 g., 0·005 mole) in dry benzene (20 ml.). Stirring was continued at room temperature overnight. The precipitate was washed with hot benzene and then with water to give the *dinitrile* (IV) (0·21 g.), m.p. 180° (from ethanol). The residue after removal of benzene from the filtrate was dissolved in chloroform and chromatographed. A colourless oil (0·3 g.) obtained from the first fraction solidified when cooled (m.p. 74°) and was identified as *N*-benzoylmorpholine [10] by comparison of the i.r. spectrum with that of an authentic specimen. From the later fractions, more (IV) (0·13 g.) was obtained (total yield 71%) [Found: C, 63·6; H, 5·8; N, 21·8%; M^+ 189 (30%). $C_{10}H_{11}N_3O$ requires C, 63·5; H, 5·9; N, 22·2%; *M* 189], $\lambda_{max.}$ (EtOH) 318 mμ (ε 32,800), $\nu_{max.}$ 2260 (CN) and 970 (*trans*-C=C) cm.$^{-1}$, τ ($CDCl_3$) 6·28 (s, morpholine ring), 4·83 (d, *J* 16 c./sec., H_A), 3·16 (d, *J* 16 c./sec., H_B), and 3·18 (s, H_C; see ref. 11).

(b) *5-Nitro-2-furylacryloyl chloride.* Similar treatment of (III) with 5-nitro-2-furylacryloyl chloride [6] afforded the dinitrile (IV) (68%) and *N*-(*5-nitro-2-furylacryloyl*)*morpholine* (Vb) (65%), m.p. 180° (from ethanol) (Found: C, 52·6; H, 4·7; N, 11·2%. $C_{11}H_{12}N_2O_5$ requires C, 52·4; H, 4·8; N, 11·1%), $\nu_{max.}$ 1650 (CO) cm.$^{-1}$.

(c) *Benzenesulphonyl chloride.* Similar treatment of (III) with benzenesulphonyl chloride afforded the dinitrile (IV) (70%) and *N*-phenylsulphonylmorpholine (Vc) (60%), m.p. 118—119° (lit.,[12] 118°).

Reaction of (III) *with Methanesulphonyl Chloride in the Presence of Triethylamine.*—Equivalent amounts of the three components were treated under the conditions given by Stork and Borowitz.[13] When methanesulphonyl chloride was added to a mixture of (III) and triethylamine at 0°, the yield of (IV) was as high as 70%; however when (III) was added to a solution of methanesulphonyl chloride and triethylamine in dioxan at 0°, it was lowered to 45% and some unchanged (III) was recovered.

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Reaction of (III) *with Trichloroacetic Acid.*—To a stirred solution of (III) (0·8 g.) in chloroform (10 ml.) was added a solution of trichloroacetic acid (0·85 g.) in chloroform (10 ml.) at room temperature. The mixture was stirred at room temperature for 1 day. The precipitate gave *morpholine trichloroacetate* (0·9 g., 65%), m.p. 125—127° (decomp.) (from benzene) (Found: C, 29·05; H, 4·0; N, 5·55%. $C_5H_{10}Cl_3NO_3$ requires C, 28·8; H, 4·0; N, 5·6%). This was readily converted into its hydrochloride by treatment with hydrochloric acid. From the benzene filtrate the dinitrile (IV) (0·45 g., 75%) was obtained. Similar treatment of (III) with monochloroacetic acid afforded (IV) (33%).

Reactions of the Dinitrile (IV).—All attempts at acidic or alkaline hydrolysis, the Ritter reaction with t-butyl alcohol, photoreaction with acetophenone, and the Diels–Alder reaction with maleic anhydride were unsuccessful; unchanged (IV) was always recovered.

Reactions of 3-*Aziridin*-1-*ylacrylonitrile*.—(a) *With* p-*nitrobenzoic acid.* A solution of the nitrile (VI) (0·8 g., 8·5 mmoles) and *p*-nitrobenzoic acid (1·12 g., 6·6 mmoles) in a mixture of benzene (10 ml.) and ethanol (10 ml.) was heated under reflux for 21 hr. The solvents were removed under reduced pressure, and the residue was treated with water–ethanol (5 : 1). The precipitate gave 2-(2-*cyanovinylamino*)*ethyl* p-*nitrobenzoate* (VII) (1·9 g., 90%), m.p. 125—127° (from ethanol) (Found: C, 54·9; H, 4·3; N, 15·8%. $C_{12}H_{11}N_3O_4$ requires C, 55·1; H, 4·2; N, 16·1%), $\nu_{max.}$ 3300 (NH), 2300 (CN), 1710 (CO), and 1620 (C=C) cm.$^{-1}$.

(b) *With acetone in the presence of sodium iodide.* A mixture of (VI) (0·85 g., 0·01 mole) and sodium iodide (0·18 g., 0·001 mole) in acetone (15 ml.) was heated under reflux for 26 hr. Acetone was removed, water (15 ml.) was added to the residue, and the mixture was extracted with ether (2 × 15 ml.). The extracts were washed with water (30 ml.), dried (Na_2SO_4), and evaporated to yield 3-(2,2-*dimethyl*-1,3-*oxazolidin*-1-*yl*)*acrylonitrile* (VIII) (1·2 g., 87%), m.p. 60—62° [from light petroleum–ethanol (1 : 1)] (Found: C, 43·3; H, 2·7; N, 15·9%. $C_8H_{12}N_2O$ requires C, 43·1; H, 2·6; N, 16·0%), $\nu_{max.}$ 2300 (CN) and 1616 (C=C) cm.$^{-1}$, τ ($CDCl_3$) 2·97 (d, *J* 13 c./sec., =CH–N), 6·21 (d, *J* 13 c./sec., NC–CH=), and 8·60 (s, CMe_2).

(c) *With carbon disulphide in the presence of sodium iodide.* A mixture of (VI) (1 g.) and sodium iodide (0·2 g.) in carbon disulphide (10 ml.) was gently heated under reflux on a water-bath for 8 hr. The residual oil obtained after removal of the solvent under reduced pressure was extracted with ethanol (10 ml.). The undissolved yellow crystals were recrystallized three times from ethanol to give 3-(2-*thioxo*-1,3-*thiazolidin*-1-*yl*)*acrylonitrile* (IX) (0·4 g., 30%), m.p. 128—130° (Found: C, 42·2; H, 3·5; N, 16·4%. $C_6H_6N_2S_2$ requires C, 42·4; H, 3·6; N, 16·5%), $\nu_{max.}$ 2300 (CN), 1615 (C=C), and 1205 (C=S) cm.$^{-1}$, τ ($CDCl_3$) 1·87 (d, *J* 15 c./sec., =CH–N), 4·50 (d, *J* 15 c./sec., NC–CH=), 5·70 (t, *J* 8 and 9 c./sec., CH_2–S), and 6·46 (t, *J* 8 and 9 c./sec., =N–CH_2).

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