Allenes. Part 40.[1] 2:1 Bis-adducts from Allenic Nitriles and Phenylpropynenitriles with Difunctional Nucleophiles and their Conversion into Heterocycles

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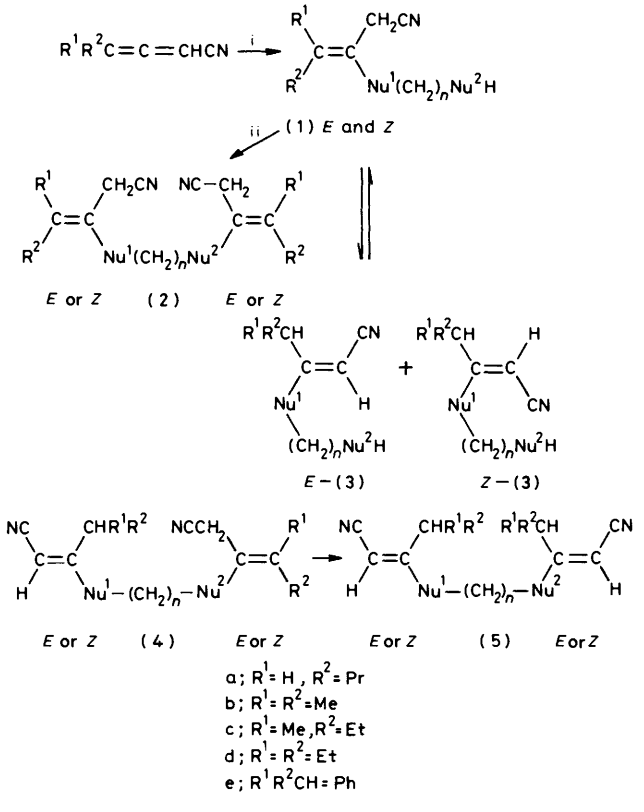
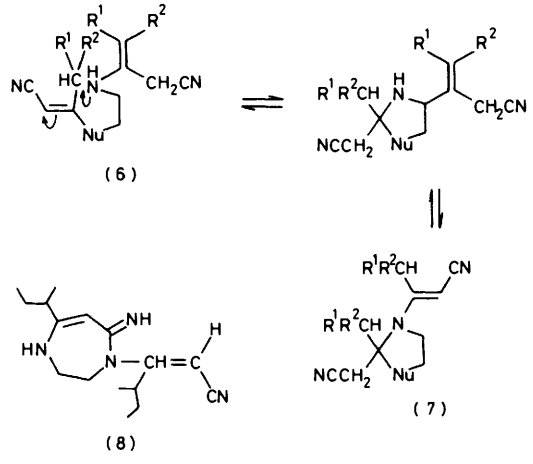
Two equivalents of allenic nitrile or phenylpropynenitrile add to 1,2- and 1,3-diamines, 2-aminoethanethiol, ethanedithiol, and 4-aminopyridine to give 2:1 adducts of structures (2), (4), and (5). Ring closure and elimination of one equivalent each of allenic nitrile (or phenylpropynenitrile) and acetonitrile gave the imidazolines (29), the thiazolines (30), and the tetrahydropyrimidines (31). Mass spectral fission patterns are discussed.

Careful addition of allenic nitriles to difunctional nucleophiles has been shown to yield monoadducts, the enaminic nitriles (1), in near quantitative yields.[2] However, small quantities of a solid were sometimes precipitated from the reaction mixture which analysed as the 2:1 bis-adduct. We now report that the sparingly soluble, high melting 2:1 bis-adducts are always formed from two equivalents of allenic nitriles of alkynenitriles and dinucleophiles under mild conditions. Alternatively, the bis-adducts may be formed quantitatively from the monoadducts by reaction with one equivalent of nitrile. Furthermore, certain monoadducts disproportionate on heating, or even when kept for prolonged periods at room temperature, to give 2:1 bis-adducts, one equivalent of the original dinucleophile being liberated in the process. A number of structures, (2), (4), and (5), can be envisaged for the bis-adducts as shown in Scheme 1.



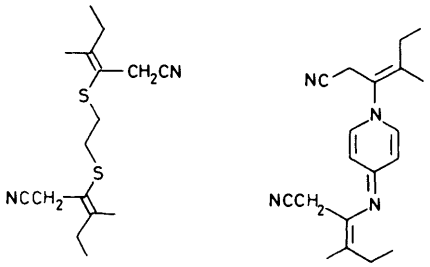
Scheme 1. *Reagents:* i, $HNu^1(CH_2)_nNu^2H$; ii, $R^1R^2C{=}C{=}CHCN$

Cyclised products such as the imidazolidines (7) and 1,4-diazepines (8) could also be formed when at least one of the nucleophiles is an amino group. We have evidence that imidazolidines are formed at elevated temperatures, but there is no indication that 1,4-diazepines are amongst the products of any of the reactions. In view of the low nucleophilicity of the nitrogen of the conjugated enamine nitrile, cyclisation is seen as proceeding *via* the unconjugated enamine nitrile group, as in structure (6), which may then revert to the conjugated enamine nitrile group as in structure (7). Formation of the diazepine (8) is probably not favoured owing to considerable constraints to coplanarity of the enamine and amidine moiety, both in the transition state and product, as shown by Dreiding models.

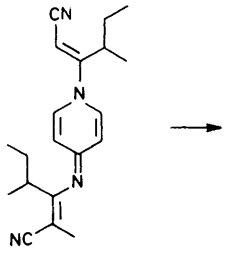


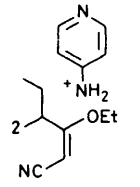
Nucleophiles add to allenic nitriles to give first the unconjugated adducts (1) which are stable under the reaction conditions if the nucleophile is a sulphide anion, but which usually rearrange fast to the conjugated adducts (3) if the nucleophile is a primary amino group.[2] Thus, ethanedithiol gives the bis-adduct (9) with two equivalents of allenic nitrile. More surprising is the isolation of only one bis-adduct (10) from 4-aminopyridine in which both enaminic nitrile groups are unconjugated. Apparently, as soon as any conjugated adduct (11) is formed during the reaction it undergoes fast ethanolysis in the presence of an excess of base to give two equivalents of 3-ethoxy-4-methylhex-2-enenitrile (12) and one of 4-aminopyridine.

The ^1H n.m.r. spectrum of (10) indicates that approximately equal amounts of *E* and *Z* isomers are formed in the


(9)

(10)


(11)

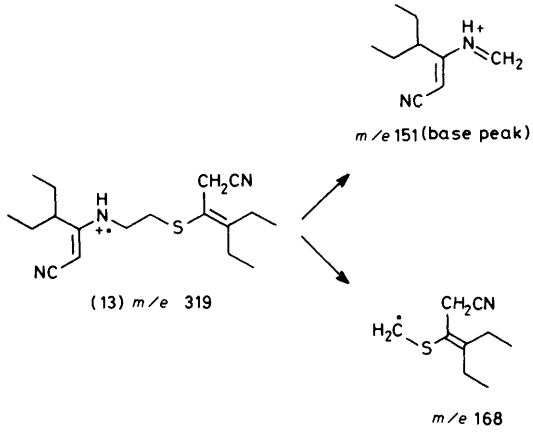

(12)

enamine group attached to the ring nitrogen, and possibly the same ratio for the enamine attached to the exocyclic nitrogen, although the alkyl substituents on the latter have similar chemical shifts and cannot be distinguished in this way.

The bis-adduct from 2-aminoethanethiol and 4-ethylhexa-2,3-dienenitrile predictably has one conjugated and one unconjugated enamine nitrile group and probably has structure (13). The u.v. maxima at $\lambda_{max.}$ 260 (ε 17 600) and 206 nm (ε 10 800) represent the enamine and enesulphide chromophores with the enamine shifted from the usual $\lambda_{max.}$ 262 nm by the superimposed low intensity enesulphide at $\lambda_{max.}$ *ca.* 255 nm. α-Cleavage in the mass spectrum gives the base peak at *m/e* 151.

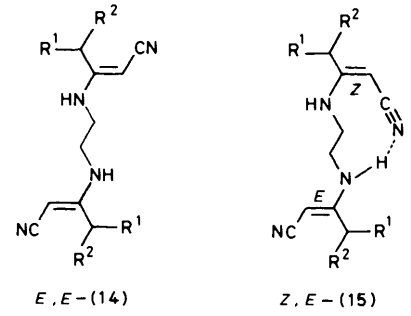
Bis-adducts were formed readily from diaminoethane and two equivalents of the allenic nitriles $R^1R^2C{=}C{=}CHCN$ (where R^1 = Pr, R^2 = H; $R^1 = R^2$ = Me; R^1 = Me, R^2 = Et; and $R^1 = R^2$ = Et). Reaction with any one allenic nitrile under varying conditions (temperature, time, and solvent variation) gave bis-adducts with identical melting points, mass spectra and i.r. spectra, but slight variations in n.m.r. signals and wide variations in the intensities of the absorption at $\lambda_{max.}$ 260—265 nm in the u.v. from ε 30 000 to 40 000. The most plausible explanation is that initial formation of the unconjugated enamine nitrile bis-adducts (2) and (4) gives liquids (these are formed at low temperature in dichloromethane) which rapidly rearrange to the crystalline conjugated adducts at room temperature to give the (*E,E*)-bis-adducts (14). If the bis-adducts are formed at elevated temperature, or if the low-temperature product is subjected to heat, the product shows a progressive reduction of the NH signal near τ 3.5—4 from 2 H to 1 H and a progressive decrease in the extinction coefficient from 40 000 to 30 000 with a slight hypsochromic shift in the wavelength. This could be explained by a $E \rightleftharpoons Z$ equilibrium of one of the enamines with crystallization of a stable hydrogen-bonded *Z,E*-isomer (15).

The *Z,E*-isomer is more soluble in most solvents (CH_2Cl_2, MeOH, EtOH, Me_2SO) than the *E,E*-isomer (14), but the melting points, which are all above 200 °C, are not affected by isomeric content. Equilibration, as the sample is being heated above 200 °C, apparently gives the *Z,E*-form and the recorded melting points are probably all for *Z,E*-isomers;

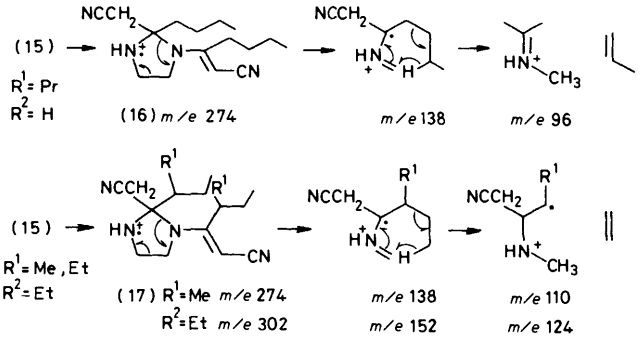


however, the possibility of imidazolidine (7; Nu = NH) formation cannot be ruled out. Mass spectral evidence suggests imidazolidines as intermediates at elevated temperature.

Particularly revealing are the mass spectra for the isomeric butyl (R^1 = Pr, R^2 = H) and 1-methylpropyl (R^1 = Me, R^2 = Et) substituted bis-adducts. Both show molecular ions at *m/e* 274 and intense peaks at *m/e* 150, 151, 138, 137, with the butyl substituted compound base peak at 96 and metastable ion at *m/e* 66.8, and the 1-methylpropyl substituted bis-adduct base peak at 110 and metastable ion at 87.7. Most of the fission pattern may be rationalised by postulating cyclisation of the two isomeric bis-adducts (15) to the imidazolidines (16) and (17) (Scheme 2) at injection temperature (this is known to occur during the pyrolytic conversion of bis-adducts into imidazolines) followed by fission to *m/e* 138 in each case. The butyl isomer immediately loses propene to give the base peak *m/e* 96 with the metastable ion at 66.8, whereas the 1-methylpropyl isomer (17) loses ethene to give the base peak at *m/e* 110 with the metastable ion at 87.7.

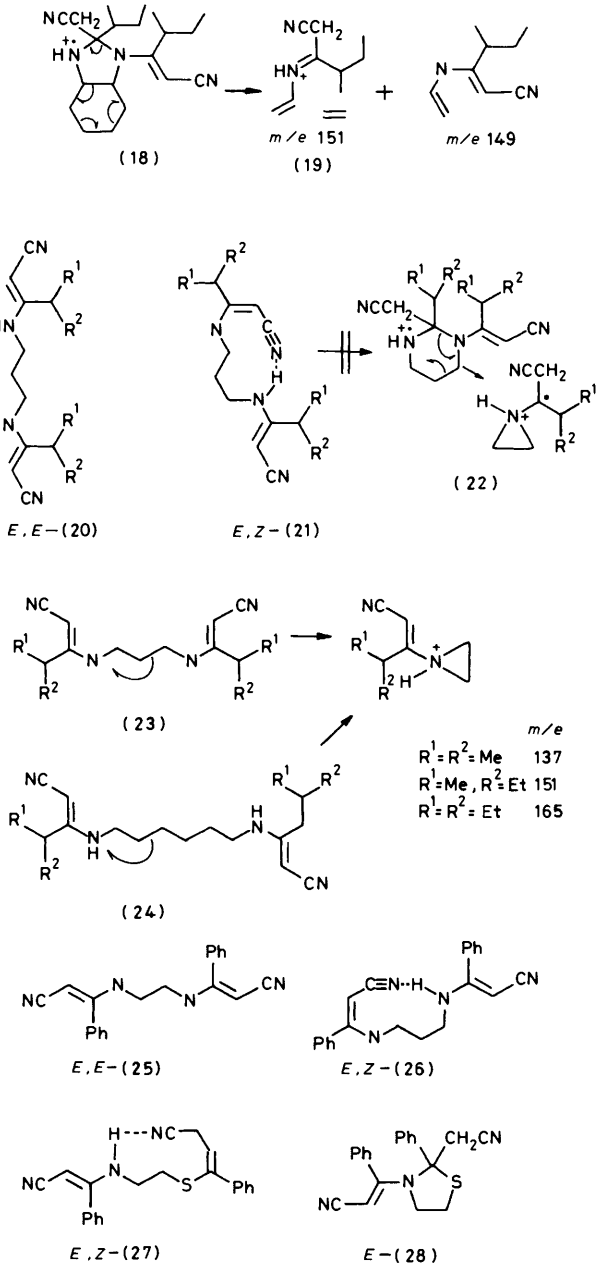

E,E-(14)

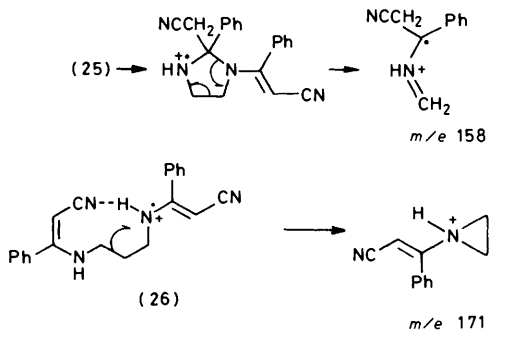
Z,E-(15)



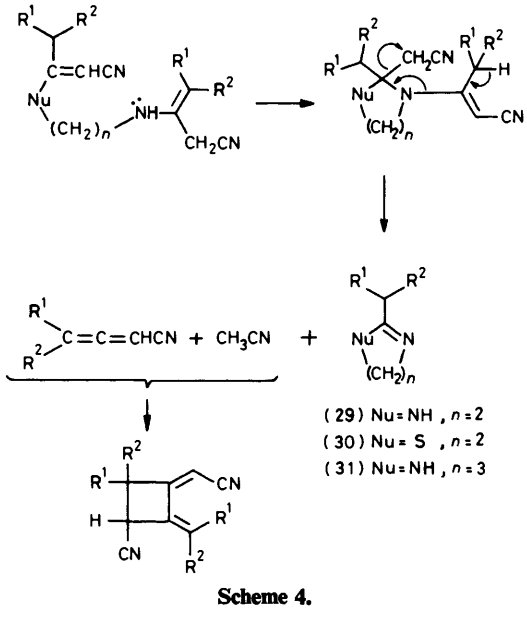
Scheme 2.

Similarly for the diethyl analogue (15; $R^1 = R^2$ = Et), the molecular ion *m/e* 302 breaks down *via* the imidazolidine to





Scheme 3.



Scheme 4.

fragment *m/e* 152 which eliminates ethene to give the base peak *m/e* 124 with metastable ion at *m/e* 101.2. The dimethyl compound (15; $R^1 = R^2 = Me$), with molecular ion at *m/e* 246, gives the base peak at *m/e* 124 directly from the imidazolidine which cannot eliminate an alkene by the route shown above and so loses a methyl radical to give *m/e* 109 (66% of base peak) with a small metastable ion at *m/e* 95.8. However the bis-adduct from diaminocyclohexane (18) shows no obvious metastable ion, the base peak at *m/e* 151 probably arising from a retro-[2π + 2π + 2π]-cycloaddition with imidazolidine ring-opening to give the stable ion (19). The alternative retro-[2π + 2π + 2π]-cycloaddition gives *m/e* 138 (83% of base peak).

Bis-adducts from 1,3-diaminopropane have considerably lower melting points (127—179 °C) than those derived from diaminoethane (m.p.s 209—242 °C) but similar absorption in the u.v. at $\lambda_{max.}$ 263 (ε 27 000—31 000). Low extinction coefficients indicate a stable *E,Z*-configuration with hydrogen bonding as in (21). The *E,Z*-compounds are formed even at low temperatures, which favour *E,E*-isomer formation with 1,2-diaminoethane. Mass spectra show little evidence of hexahydropyrimidine intermediates (22) and base peaks are derived from simple β-cleavage of the aminopropane chain of the molecular ions (23). Confirmation comes from the fission of the bis-adducts from 1,6-diaminohexane and 4-methylhexenenitrile (24; $R^1 = Me$, $R^2 = Et$) which gives the same base peak of *m/e* 151 as the identically substituted (23).

3-Phenylpropynenitrile gave bis-adducts with diaminoethane, diaminopropane, and 2-aminoethanethiol which are tentatively assigned structures (25), (26), and (27) respectively. The mass spectrum of (25) shows a molecular ion *m/e* 314 with base peak at *m/e* 158 by α-cleavage, whereas the usual β-cleavage of the 1,3-diaminopropane chain of the molecular ion of (26) gave the stable aziridinium ion as the base peak at *m/e* 171 (Scheme 3). I.r. and n.m.r. spectra of the thiaza compound (27) suggest that it contains *ca.* 50% of the thiazolidine (28) which, however, did not separate on t.l.c.

When the bis-adducts are heated to 300 °C or above they cyclise to 5- or 6-membered rings and then eliminate one equivalent each of allenic or acetylenic nitrile and acetonitrile. At that temperature the allenic nitriles dimerise to cyclobutane derivatives and acetylenic nitriles polymerise. Imidazolines (29), thiazolines (30), and tetrahydropyrimidines (31) were formed as shown in Scheme 4.

Unsaturated diamines have been reported to be inhibitors of blood platelet inhibition [3] and bis-quaternary ammonium salts have been described as anthelmintics. Some of the compounds reported here are being tested as anti-tumour agents.

Experimental

4,7-Diaza-3,8-dibutyldeca-2,8-diene-1,10-dinitrile (5a; $Nu^1 = Nu^2 = NH$, $n = 2$).—(*a*) Freshly redistilled hepta-2,3-dienenitrile (10.7 g, 0.1 mol), dissolved in ether (150 ml), was added dropwise with stirring over a period of 2 h to a solution of 1,2-diaminoethane (6.0 g, 0.1 mol) in ether (150 ml). The mixture was stirred for a further 2 h then kept overnight at room temperature. A solid separated out and was recrystallised from dimethyl sulphoxide–water to give *4,7-diaza-3,8-dibutyldeca-2,8-diene-1,10-dinitrile* (5a; $Nu^1 = Nu^2 = NH$, $n = 2$) (3.1 g, 12%), m.p. 222—223 °C (Found: C, 69.9; H, 9.2; N, 20.6. $C_{16}H_{26}N_4$ requires C, 70.1; H, 9.4; N, 20.5%); $\lambda_{max.}$ 3 250 (NH), 2 180 (C≡N), 1 560 (C=C), and 1 500 cm^{-1} (NH def.); $\lambda_{max.}$ 263 nm (ε 32 300); τ($CDCl_3$–Me_2SO) 9.00 (6 H, t, CH_3CH_2), 8.90—8.00 [8 H, m, (CH_3-$CH_2CH_2CH_2$)$_2$], 7.72—7.40 [4 H, td, (CH_2CH_2C=)$_2$] 7.05 (4 H, s, NCH_2CH_2N), 6.10 [2 H, s, (=CHCN)$_2$], and 4.00 [2 H, s, $(NH)_2$, disappears on deuteriation]; *m/e* 274, 150, 151, 138, 137, and 96 (100%), metastable ion 66.8.

The ethereal solution was dried ($MgSO_4$) and solvent removed, and the residue was then chromatographed (alumina, activity 3, elution with ether) to give 3-(2-aminoethylamino)hept-2-enenitrile (9.0 g, 52%).[2]

(*b*) Hepta-2,3-dienenitrile (2.14 g, 0.02 mol), dissolved in dichloromethane (50 ml), was added to a solution of 1,2-diaminoethane (0.6 g, 0.1 mol) in dichloromethane (50 ml) and the mixture refluxed with stirring overnight. Removal of solvent followed by recrystallisation from ethanol gave 4,7-diaza-3,8-dibutyldeca-2,8-diene-1,10-dinitrile (2.52 g, 93%), m.p. 222—223 °C, $\lambda_{max.}$ 263 nm (ε 34 000).

4,7-Diaza-3,8-di(1-methylpropyl)deca-2,8-diene-1,10-dinitrile (5c; $Nu^1 = Nu^2 = NH$, $n = 2$).—(*a*) 4-Methylhexa-2,3-dienenitrile (2.14 g, 0.02 mol) was added rapidly to 1,2-diaminoethane (0.6 g, 0.01 mol) with shaking. An exothermic reaction took place, the temperature rising to 170 °C. The solid which separated on cooling was recrystallised from ethanol to give *4,7-diaza-3,8-di(1-methylpropyl)deca-2,8-diene-1,10-dinitrile* (5c; $Nu^1 = Nu^2 = NH$, $n = 2$) (2.6 g, 95%), m.p. 223 °C (Found: C, 70.2; H, 9.3; N, 20.3. $C_{16}H_{26}N_4$ requires C, 70.1; H, 9.4; N, 20.5%); $\lambda_{max.}$ 3 250 (NH), 2 180 (C≡N), 1 580 (C=C), and 1 500 (NH def.); $\lambda_{max.}$ 263 nm (ε 34 500); δ($CDCl_3$–Me_2SO) 9.20 [6 H, t, ($CH_3CH_2CHCH_3$)$_2$], 8.86 [6 H, d, ($CH_3CH_2CHCH_3$)$_2$], 8.80—8.30 [4 H, m, ($CH_3CH_2CHCH_3$)$_2$], 7.70—7.15 [2 H, m, ($CH_3CH_2CHCH_3$)$_2$], 6.90 (4 H, s, NCH_2CH_2N), 6.86—7.3 (0.3 H br, N · · · NC), 6.28 [2 H, s, (=CHCN)$_2$], and 3.80 [1.7 H, s, $(NH)_2$, disappears on deuteriation]; *m/e* 274 ($C_{16}H_{26}N_4$ requires 274), 151, 150, 138, 137, and 110 (base peak); metastable ion at 97.7.

(*b*) 4-Methylhexa-2,3-dienenitrile (2.14 g, 0.02 mol) in dichloromethane (100 ml) was added dropwise with stirring to 1,2-diaminoethane (0.6 g, 0.01 mol) in dichloromethane (100 ml). After being stirred for 24 h, evaporation gave a thick oil which crystallised on refrigeration overnight. Suspension in cold ethanol, filtration and drying gave the product (2.5 g, 90%), $\lambda_{max.}$ 263 nm (ε 38 100); τ 3.80 (2 H, br s, NH disappears on deuteriation).

(*c*) 3-(2-Aminoethylamino)-4-methylhex-2-enenitrile [2] (3.34 g, 0.02 mol) was refluxed in absolute ethanol (100 ml) for 12 h. The solution was cooled to 0 °C. A solid separated out and was recrystallised from ethanol to give the product (2.5 g, 91%), m.p. 223 °C; $\lambda_{max.}$ 263 nm (ε 33 300).

(*d*) 3-(2-Aminoethylamino)-4-methylhex-2-enenitrile (1.67 g, 0.01 mol) in dichloromethane (50 ml) was added to 4-methylhexa-2,3-dienenitrile (1.07 g, 0.01 mol) in dichloromethane (50 ml). The mixture was refluxed for 24 h to give 4,7-diaza-3,8-di(1-methylpropyl)deca-2,8-diene-1,10-dinitrile (2.6 g, 94%), m.p. 223 °C.

4,7-Diaza-3,8-di(1-ethylpropyl)deca-2,8-diene-1,10-dinitrile (5d; $Nu^1 = Nu^2 = NH$, $n = 2$).—(*a*) 4-Ethylhexa-2,3-dienenitrile (2.42 g, 0.02 mol), dissolved in dichloromethane (50 ml), was added to a solution of 1,2-diaminoethane (0.6 g, 0.01 mol) in dichloromethane (50 ml) and the mixture stirred overnight to give a crude product which was recrystallised from ethanol to give *4,7-diaza-3,8-di(1-ethylpropyl)deca-2,8-diene-1,10-dinitrile* (5d; $Nu^1 = Nu^2 = NH$, $n = 2$) (2.8 g, 95%), m.p. 241—242 °C (Found: C, 71.4; H, 10.0; N, 18.5. $C_{18}H_{30}N_4$ requires C, 71.5; H, 9.9; N, 18.5%); $\nu_{max.}$ 3 250 (NH), 2 170 (C=N), 1 570 (C=C), 1 500 cm^{-1} (NH def.); $\lambda_{max.}$ 263 nm (ε 38 600); τ(Me_2SO–$CDCl_3$) 9.18 {12 H, t, [(CH_3CH_2)$_2$CH]$_2$}, 8.85—8.25 {8 H, m [(CH_3CH_2)$_2$CH]$_2$}, 7.75—7.35 {2 H, m, [(CH_3CH_2)$_2$CH]$_2$}, 6.90 (4 H, s, NCH_2-CH_2N), 6.18 [2 H, s, (=CHCN)$_2$)], and 3.90 [2 H, s, $(NH)_2$, disappears on deuteriation]; *m/e* 302 ($C_{18}H_{30}N_4$ requires 302), 152, 124 (100%), and 109; metastable ion 101.2.

(*b*) 3-(2-Aminoethylamino)-4-ethylhex-2-enenitrile [2] (1.81 g, 0.01 mol) was allowed to stand at room temperature for 7 days to give 4,7-diaza-3,8-di(1-ethylpropyl)deca-2,8-diene-1,10-dinitrile (1.4 g, 93%); $\lambda_{max.}$ 263 nm (ε 39 000).

4,7-Diaza-3,8-di(1-methylethyl)deca-2,8-diene-1,10-dinitrile (5b; $Nu^1 = Nu^2 = NH$, $n = 2$).—(*a*) 4-Methylpenta-2,3-dienenitrile (1.86 g, 0.02 mol) was added to 1,2-diaminoethane (0.6 g, 0.01 mol) to give *4,7-diaza-3,8-di(1-methylethyl)deca-2,8-diene-1,10-dinitrile* (2.2 g, 90%), m.p. 209 °C (Found: C, 68.4; H, 9.1; N, 22.7. $C_{14}H_{22}N_4$ requires C, 68.3; H, 8.9; N, 22.8%); $\nu_{max.}$ 3 250 (NH), 2 180 (C≡N), 1 580 (C=C), and 1 500 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 262 nm (ε 30 100); τ(Me_2SO–$CDCl_3$) 8.85 {12 H, d, [(CH_3)$_2$CH]$_2$}, 7.30—6.90 {3 H, m, [(CH_3)$_2$CH_2] and (NH · · · NC)}, 7.00 (4 H, s, NCH_2CH_2N), 6.32 [2 H, s, (=CHCN)$_2$], 3.80 (1 H, s, NH, disappears on deuteriation); *m/e* 246 ($C_{14}H_{22}N_4$ requires 246), 137, 136, 124 (100%) 123, and 109; metastable ion 95.8.

(*b*) Similarly the reagents, as in (*a*), were heated under reflux in ethanol for 24 h to give the product (2.1 g, 89%), m.p. 209 °C; $\lambda_{max.}$ (EtOH) 262 nm (ε 25 600); τ 3.7 (1 H, s, NH), 6.6—7.1 [3 H, m, (CH_3)$_2$C*H* and NH · · · NC].

Bis-adduct from 1,2-Diaminocyclohexane and 4-Methylhexa-2,3-dienenitrile.—4-Methylhexa-2,3-dienenitrile (2.14 g, 0.02 mol) in dichloromethane (30 ml) was added to 1,2-diaminocyclohexane (1.15 g) in dichloromethane (20 ml) and the solution heated under reflux for 12 h. On cooling, the bis-adduct separated and was filtered (3.0 g, 91%), m.p. 256 °C, $\nu_{max.}$ 3 250, 2 185 (CN), 1 590 and 1 530 cm^{-1}; τ 9.10 (6 H, t, CH_3CH_2), 8.80 (6 H, d, CH_3CH), 8.65—8.10 (12 H, m), 6.2 (2 H, s, C=CHCN), 4.1 [2 H, br s, $(NH)_2$]; *m/e* 328, 204, 151 (100%), and 138.

4,7-Dithio-3,8-di(1-methylethylidene)decane-1,10-dinitrile (2b; $Nu^1 = Nu^2 = S$, $n = 2$).—4-Methylpenta-2,3-dienenitrile (1.86 g, 0.02 mol), ethane-1,2-dithiol (0.94 g, 0.01 mol), and sodium carbonate (1.0 g) in ethanol (90%, 100 ml) for 26 h gave the title *compound* (2.38 g, 86%), m.p. 48—49 °C; $\nu_{max.}$ 2 250, 2 215 (CH_2CN), 1 660, and 1 620 cm^{-1} (C=C); $\lambda_{max.}$ 207 (ε 20 700) and 254 (ε 8 400); τ($CDCl_3$) 8.08 (6 H, s, CH_3 *cis* to S), 7.90 (6 H, s, CH_3 *trans* to S), 7.15 (4 H, s, SCH_2CH_2S), 6.57 (2 H, s, CH_2CN), and 6.55 (2 H, s, CH_2-CN) (Found: C, 59.9; H, 7.1; N, 9.95. $C_{14}H_{20}N_2S_2$ requires C, 60.00; H, 7.14; N, 10.00%).

3-(1-*Ethylpropylidene*)-8-(1-*ethylpropyl*)-4,7-*thiazadec*-8-*ene*-1,10-*dinitrile* (4d; Nu^1 = NH, Nu^2 = S, n = 2).—4-Ethylhexa-2,3-dienenitrile (2.42 g, 0.02 mol), 2-aminoethanethiol hydrochloride (1.14 g, 0.01 mol), and sodium carbonate (0.53 g, 0.005 mol) were refluxed in ethanol (100 ml) with stirring for 6 h. Removal of solvent gave a semi-solid which was purified by chromatography (alumina, activity V, eluting with hexane–ethyl acetate) to give the title *compound* (2.1 g, 70%), m.p. 58 °C (Found: C, 67.6; H, 9.0; N, 13.3. $C_{18}H_{29}N_3S$ requires C, 67.7; H, 9.1; N, 13.2%); $\nu_{max.}$ 3 300 (NH), 2 225 ($CH_2C{\equiv}N$), 2 180 (=CHCN), 1 600 (C=C), 1 580 (C=C), and 1 525 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 206 (ε 10 800) and 260 nm (ε 17 600); τ($CDCl_3$) 9.10 [6 H, t, (CH_3CH_2)$_2$CH], 9.00 [6 H, t, (CH_3CH_2)$_2$C=], 8.75—8.20 [4 H, m, (CH_3CH_2)$_2$CH], 8.00—7.45 [4 H, q, (CH_3CH_2)$_2$C=], 8.75 [1 H, m, (CH_3CH_2)$_2$CH], 7.12—6.65 (4 H, m, NCH_2CH_2N), 6.62 (2 H, s, CH_2CN), 6.20 (1 H, s, =CHCN), and 5.45 (1 H, s, NH, disappears on deuteriation); *m/e* 319 ($C_{18}H_{29}N_3S$ requires 319), 181 (71%), 151 (100), and 138 (63).

4,8-*Diaza*-3,9-*di*(1-*methylpropyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (5c; Nu^1 = Nu^2 = NH, n = 3).—(*a*) 4-Methylhexa-2,3-dienenitrile (1.07 g, 0.01 mol) was added to a solution of 1,3-diaminopropane (0.37 g, 0.005 mol) in dichloromethane (50 ml) and the mixture refluxed for 3 h. Removal of the solvent gave a thick oil which on chromatography (alumina, activity 4, eluting with dichloromethane–hexane) gave a solid fraction. Recrystallisation (hexane–dichloromethane) gave 4,8-*diaza*-3,9-*di*(1-*methylpropyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (1.31 g, 91%), m.p. 158 °C (Found: C, 70.8; H, 9.8; N, 19.5. $C_{17}H_{28}N_4$ requires C, 70.8; H, 8.7; N, 19.4%); $\nu_{max.}$ 3 300 (NH), 2 170 (C≡N), 1 580 (C=C), and 1 530 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 263 nm (ε 30 200); τ($CDCl_3$) 9.10 [6 H, t, ($CH_3CH_2CHCH_3$)$_2$], 8.85 [6 H, d, ($CH_3CH_2CHCH_3$)$_2$], 8.74—7.90 [6 H, m, ($CH_3CH_2CHCH_3$)$_2$, $NCH_2CH_2CN_2$N], 7.55—6.85 [6 H, m, ($CH_3CH_2CHCH_3$)$_2$, $NCH_2CH_2CH_2$], 6.32 [2 H, s, (=CHCN)$_2$], and 5.15 (2 H, t, $NHCH_2CH_2CH_2$-NH, disappears on deuteriation). This signal shifted to δ 3.85 when the spectrum was determined in CCl_4–$(CD_3)_2SO$; *m/e* 288 ($C_{17}H_{28}N_4$ requires 288), 151 (100%), and 110 (10.2).

(*b*) 3-(3-Aminopropylamino)-4-methylhex-2-enenitrile [2] (1.81 g, 0.01 mol) was allowed to stand at room temperature for 6 weeks. An amorphous mass formed which was purified by column chromatography, followed by recrystallisation (hexane–dichloromethane) to give 4,8-diaza-3,9-di(1-methylpropyl)undeca-2,9-diene-1,11-dinitrile (1.29 g, 90%), m.p. 158 °C. Spectroscopic data as in (*a*).

(*c*) 4-Methylhexa-2,3-dienenitrile (1.07 g, 0.01 mol) in chloroform (50 ml) was added to 3-(3-aminopropylamino)-4-methylhex-2-enenitrile [2] (1.81 g, 0.01 mol) in chloroform (50 ml). The mixture was stirred under reflux for 24 h and then worked up as in (*b*) to give 4,8-diaza-3,9-di(1-methylpropyl)undeca-2,9-diene-1,11-dinitrile (1.17 g, 88%), m.p. 158 °C. Spectroscopic data as in (*a*).

4,8-*Diaza*-3,9-*di*(1-*ethylpropyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (5d; Nu^1 = Nu^2 = NH, n = 3).—4-Ethylhexa-2,3-dienenitrile (2.42 g, 0.02 mol) and 1,3-diaminopropane (0.74 g, 0.01 mol) in dichloromethane gave after chromatography and recrystallisation (hexane–chloroform) 4,8-*diaza*-3,9-*di*(1-*ethylpropyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (5d; Nu^1 = Nu^2 = NH, n = 3) (3.0 g, 94%), m.p. 179 °C (Found: C, 72.2; H, 10.1; N, 17.6. $C_{19}H_{32}N_4$ requires C, 72.2; H, 10.1; N, 17.7%); $\nu_{max.}$ 3 280 (NH), 2 160 (C≡N), 1 580 (C=C), and 1 520 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 263 nm (ε 27 500); τ($CDCl_3$) 9.18 [12 H, t, (CH_3CH_2)$_2$CH)$_2$], 8.85—8.10 {10 H, m, [(CH_3CH_2)$_2$CH]$_2$, $NCH_2CH_2CH_2N$}, 7.85—7.30 {2 H, m, [(CH_3CH_2)$_2$CH]$_2$}, 7.30—6.30 (4 H, m, $NCH_2CH_2CH_2N$), 6.37 [2 H, s, (=CHCN)$_2$], and 5.1 [2 H, t, $(NH)_2$ disappears on deuteriation]; *m/e* 316 ($C_{19}H_{32}N_4$ requires 316), 165 (100%).

4,8-*Diaza*-3,9-*di*(1-*methylethyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (5b; Nu^1 = Nu^2 = NH, n = 3).—4-Methylpenta-2,3-dienenitrile (1.86 g, 0.02 mol) in chloroform (100 ml) was treated with 1,3-diaminopropane (0.74 g, 0.01 mol) and then stirred at room temperature for 48 h to give an oil which was chromatographed and then recrystallised from acetone–hexane–ether to give 4,8-*diaza*-2,8-*di*(1-*methylethyl*)*undeca*-2,9-*diene*-1,11-*dinitrile* (5b; Nu^1 = Nu^2 = NH, n = 3) (2.2 g, 85%), m.p. 127—128 °C (Found: C, 69.2; H, 9.4; N, 21.6. $C_{15}H_{24}N_4$ requires C, 69.2; H, 9.2; N, 21.5%); $\nu_{max.}$ 3 300 (NH), 2 160 (C≡N), 1 570 (C=C), and 1 520 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 262 nm (ε 30 300); τ($CDCl_3$) 8.80 {12 H, d, [(CH_3)$_2$CH]$_2$}, 8.40—7.95 (2 H, m, $NCH_2CH_2CH_2N$), 7.65—7.25 {6 H, m, [(CH_3)$_2$CH]$_2$, $NCH_2CH_2CH_2N$}, 6.60 (2 H, s, =CHCN$_2$), and 4.90 [2 H, t, $(NH)_2$, disappears on deuteriation]; *m/e* 260 ($C_{15}H_{24}N_4$ requires 260), 137 (100%).

4,8-*Diaza*-3,9-*dibutylundeca*-2,9-*diene*-1,11-*dinitrile* (5a; Nu^1 = Nu^2 = NH, n = 3).—Hepta-2,3-dienenitrile (2.14 g, 0.02 mol) and 1,3-diaminopropane (0.74 g, 0.01 mol) in chloroform (100 ml) gave 4,8-*diaza*-2,8-*dibutylundeca*-2,9-*diene*-1,11-*dinitrile* (5a; Nu^1 = Nu^2 = NH, n = 3) (2.6 g, 90%), m.p. 142 °C (Found: C, 70.7; H, 9.9; N, 19.4. $C_{17}H_{28}N_4$ requires C, 70.8; H, 9.7; N, 19.4%); $\nu_{max.}$ 3 300 (NH), 2 165 (C≡N), 1 590 (C=C), and 1 530 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 263 nm (ε 30 700); τ($CDCl_3$) 9.10 {6 H, t, [$CH_3(CH_2)_3$]$_2$}, 8.83—7.90 [10 H, m, ($CH_3CH_2CH_2CH_2$)$_2$, $NCH_2CH_2CH_2$N], 7.67 [4 H, t, ($CH_2CH_2C=$)$_2$], 7.25—6.86 (4 H, m, NCH_2CH_2-CH_2N), 6.33 [2 H, s, (CHCN)$_2$], and 5.00 [2 H, t, $(NH)_2$, disappears on deuteriation].

4,7-*Diaza*-3,8-*diphenyldeca*-2,8-*diene*-1,10-*dinitrile* (5e; Nu^1 = Nu^2 = NH, n = 2).—3-Phenylpropynenitrile (1.6 g, 0.0126 mol) and 1,2-diaminoethane (0.375 g, 0.006 25 mol) were refluxed in dichloromethane (20 ml) for 2 h to give, after recrystallization (ethanol), 4,7-*diaza*-3,8-*diphenyldeca*-2,8-*diene*-1,10-*dinitrile* (1.88 g, 95%), m.p. 222 °C (Found: C, 76.3; H, 5.7; N, 17.9. $C_{20}H_{18}N_4$ requires C, 76.4; H, 5.7; N, 17.8%); $\nu_{max.}$ 3 320 (NH), 2 180 (C≡N), 1 580 (C=C), and 1 520 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 205 (ε 31 400), 226 (ε 25 300), and 282 nm (ε 17 100); τ($CDCl_3$–Me_2SO) 6.70 (4 H, s, NCH_2CH_2), 5.90 (2 H, s, (=CHCN)$_2$], 3.13 [2 H, s, $(NH)_2$, disappears on deuteriation], and 2.52 (10 H, s, CH aromatic); *m/e* 314 ($C_{20}H_{18}N_4$ requires 314).

4,8-*Diaza*-3,9-*diphenylundeca*-2,9-*diene*-1,11-*dinitrile* (5e; Nu^1 = Nu^2 = NH, n = 3).—3-Phenylpropynenitrile (2.54 g, 0.02 mol) and 1,3-diaminopropane (0.74 g, 0.01 mol) were refluxed in dichloromethane for 2 h and then recrystallized (ethanol) to give 4,8-*diaza*-3,9-*diphenylundeca*-2,9-*diene*-1,11-*dinitrile* (5e; Nu^1 = Nu^2 = NH, n = 3) (3.15 g, 96%), m.p. 182 °C (Found: C, 76.6; H, 6.0; N, 17.1. $C_{21}H_{20}N_4$ requires C, 76.8; H, 6.1; N, 17.1%); $\nu_{max.}$ 3 300 (NH), 2 170 (C≡N), 1 580 (C≡C), and 1 520 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 207 (ε 27 400), 227 (ε 25 800), and 283 nm (ε 16 000); τ($CDCl_3$–Me_2SO), 8.35—7.85 (2 H, quin., $NCH_2CH_2CH_2N$), 6.90 (4 H, t, $NCH_2CH_2CH_2N$), 5.95 [2 H, s, (=CHCN)$_2$)], 3.05 [2 H, t, $(NH)_2$, disappears on deuteriation], and 2.55 (10 H, s, CH aromatic); *m/e* 328 ($C_{21}H_{20}N_4$ requires 328), 171 (100%), and 157.

3,8-*Diphenyl*-4,7-*thiazadeca*-2,8-*diene*-1,10-*dinitrile* (5e; Nu^1 = NH, Nu^2 = S, n = 2).—3-Phenylpropynenitrile (1.27 g, 0.01 mol), 2-aminoethanethiol hydrochloride (0.565 g,

0.005 mol), and sodium carbonate (0.2 g, 0.0025 mol) were dissolved in ethanol and the mixture refluxed with stirring for 72 h. The solvent was distilled off, the residue dissolved in dichloromethane (100 ml) and washed with water (3 × 50 ml), and dried ($MgSO_4$). Removal of the solvent gave the crude product which solidified on standing at room temperature. Recrystallization from ethanol gave 3,8-*diphenyl*-4,7-*thiazadeca*-2,8-*diene*-1,10-*dinitrile* (5e; Nu^1 = NH, Nu^2 = S, n = 2) (1.25 g, 76%), m.p. 118 °C (Found: C, 72.6; H, 5.3; N, 12.8. $C_{20}H_{17}N_3S$ requires C, 72.5; H, 5.1; N, 12.7%). T.l.c. (Si gel, C_6H_6–EtOAc, 3 : 2) gave one spot, R_F 0.57, $\nu_{max.}$ 3 320 (NH), 2 210 (SC=CCN), 2 180 (NC=CCN), 1 580 (C=C), and 1 510 cm^{-1} (NH def.); $\lambda_{max.}$ (EtOH) 205 (ε 33 500), 225 (ε 23 400) and 280 nm (ε 16 200); τ($CDCl_3$) 7.40—6.80 (4 H, m, SCH_2CH_2N), 6.58 (1 H, s, NHC=C*H*CN), 5.25 (1 H, br s, NH, disappears on deuteriation), 4.53 (1 H, s, SC=CHCN), 2.70 (5 H, aromatic), and 2.65 (5 H, aromatic); *m/e* 331 ($C_{20}H_{17}N_3S$ requires 331).

4,11-*Diaza*-3,12-*di*(1-*methylpropyl*)*tetradeca*-2,12-*diene*-1,14-*dinitrile* (5c; Nu^1 = Nu^2 = NH, n = 6).—4-Methylhexa-2,3-dienenitrile (2.14, 0.02 mol) was added to 1,6-diaminohexane (1.18 g, 0.01 mol) in ethanol (95%, 50 ml) and heated under reflux for 24 h. Removal of the solvent followed by chromatography gave the *bis-adduct* (5c; Nu^1 = Nu^2 = NH, n = 6) (3.0 g, 90%), m.p. 125 °C (Found: C, 72.57; H, 10.12; N, 17.11. $C_{20}H_{34}N_4$ requires C, 72.72; H, 10.30; N, 16.97%; *M* 330); *m/e* 330, 151 (100%); $\nu_{max.}$ 3 250 (NH) and 2 200 (CN); $\lambda_{max.}$ (EtOH) 262 nm (ε 32 300); τ($CDCl_3$–Me_2SO) 9.10 (6 H, t, CH_3), 8.86 (6 H, d, $CHCH_3$), 8.70—8.10 (12 H, m, CH_2), 7.50—6.90 (6 H, m, CH and CH_2N), 6.35 (2 H, s, =CHCN), and 4.37 (2 H, br t, NH exchanges D_2O).

Bis-adduct (10) *from* 4-*Aminopyridine and* 4-*Methylhexa*-2,3-*dienenitrile*.—4-Methylhexa-2,3-dienenitrile (1.0, 0.09 mol) and 4-aminopyridine (0.88 g, 0.09 mol) were dissolved in ethanol (150 ml) and refluxed for 72 h. Evaporation of solvent followed by chromatography (neutral alumina; activity 4) and elution with hexane gave 3-ethoxy-4-methylhex-2-enenitrile (0.9 g, 63%). $\nu_{max.}$ 2 220 (CN) and 1 580 cm^{-1} (C=C). Elution with dichloromethane–hexane (3 : 17) gave the 3-[1-(1-*cyano*-3-*methylpent*-2-*en*-2-*yl*)-1,4-*dihydro*-4-*pyridylideneamino*]-4-*methylhex*-3-*enenitrile* (10) (0.44 g, 30%), m.p. 142 °C; $\nu_{max.}$ 2 240 (CN), 1 595 (C=C) and 1 500 cm^{-1} (C=C); $\lambda_{max.}$ (EtOH) 207 (ε 18 200) and 265 nm (ε 14 500); τ($CDCl_3$) 9.15—8.69 (6 H, two overlapping triplets CH_3-CH_2C=), 8.38 (4.2 H, s, CH_3C=, *trans* to pyridyl, 8.06 (1.8 H, s, CH_3C=, *cis* to pyridyl), 6.82 [4 H, s, $(CH_2CN)_2$] 3.42 (2 H, d, 3,5-ring H), and 1.70 (2 H, d, 2,6-ring H) (Found: C, 73.9; H, 7.7; N, 18.2. $C_{19}H_{24}N_4$ requires C, 74.03; H, 7.79; N, 18.18%; *M* 308); *m/e* 308, 160, and 94 (100%). Elution with dichloromethane–hexane (7 : 3) gave 4-aminopyridine (0.52 g), m.p. 157 °C.

Formation of Imidazolines and Thiazolines from Bis-adducts.—(*a*) 2-(1-*Methylpropyl*)-2-*imidazoline*. 4,7-Diaza-3,8-di(1-methylpropyl)deca-2,8-diene-1,10-dinitrile (2.74 g, 0.01 mol) was distilled (bath temperature 300 °C). Acetonitrile (0.3 g, 73%), b.p. 80—85 °C, was collected, followed by crude product which was redistilled to give 2-(1-methylpropyl)-2-imidazoline [4] (1.1 g, 87%), b.p. 218—219 °C. It solidified in the receiver (m.p. 38 °C) and crude 3-cyanomethylene-2-ethyl-2-methyl-4-(1-methylpropylidene)cyclobutanecarbonitrile [5] (0.45 g) was left in the residue. Spectroscopic data as previously described.

(*b*) 2-(1-*Ethylpropyl*)-2-*imidazoline*. 4,7-Diaza-3,8-di(1-ethylpropyl)deca-2,8-diene-1,10-dinitrile (6.0 g, 0.02 mol) was distilled at atmospheric pressure (bath temperature 300 °C) to give acetonitrile and 2-(1-ethylpropyl)-2-imidazoline (2.3 g, 82%), m.p. 86 °C (lit.,[4] m.p. 87 °C). The residue in the flask was 3-cyanomethylene-2,2-diethyl-4-(1-ethylpropylidene)cyclobutanecarbonitrile.[5]

(*c*) 2-*Phenyl*-2-*imidazoline*. 4,7-Diaza-3,8-diphenyldeca-2,8-diene-1,10-dinitrile (5 g, 0.016 mol) was heated at 300—350 °C to give 2-phenyl-2-imidazoline (1.7 g, 73%), m.p. 100 °C (lit.,[4] m.p. 100—101 °C) and a polymeric residue.

(*d*) 2-(1-*Ethylpropyl*)-2-*thiazoline*. 3-(1-Ethylpropylidene)-8-(1-ethylpropyl)-4,7-thiazadec-8-ene-1,10-dinitrile (4.8 g) was distilled at 300 °C at atmospheric pressure. After a forerun of acetonitrile, 2-(1-ethylpropyl)-2-thiazoline, b.p. 220—222 °C at 750 mmHg was collected as an oil (1.7 g, 70%). Spectroscopic data were identical with those obtained previously.[6]

Formation of Tetrahydropyrimidines.—(*a*) 2-(1-*Ethylpropyl*)-1,4,5,6-*tetrahydropyrimidine*. (i) 4,8-Diaza-3,9-di(1-ethylpropyl)undeca-2,9-diene-1,11-dinitrile (1.58 g, 0.005 mol) was heated under reflux in ethanol (50 ml) for 72 h. Removal of solvent gave the starting material. (ii) Repeating (i) in refluxing dimethyl sulphoxide (50 ml) for 72 h gave the starting material. (iii) 4,8-Diaza-3,9-di(1-ethylpropyl)undeca-2,9-diene-1,11-dinitrile (3.16 g, 0.01 mol) was heated in a distillation set at 320—350 °C. Acetonitrile (0.28 g, 68%) distilled off, followed by crude product which solidified in the condenser. Recrystallization from hexane gave 2-(1-ethylpropyl)-1,4,5,6-tetrahydropyrimidine (1.25 g, 81%), m.p. 105 °C (lit.,[7] m.p. 122 °C. Repeating the literature preparation gave m.p. and mixed m.p. 105—106 °C).

(*b*) 2-(1-*Methylpropyl*)-1,4,5,6-*tetrahydropyrimidine*. 4,8-Diaza-3,9-di(1-methylpropyl)undeca-2,9-diene-1,11-dinitrile (5.76 g, 0.02 mol) was distilled (bath temperature 320—350 °C) to give acetonitrile followed by 2-(1-methylpropyl)-1,4,5,6-tetrahydropyrimidine (2.1 g, 75%), m.p. 48 °C (lit.,[7] 48 °C).

(*c*) 2-*Phenyl*-1,4,5,6-*tetrahydropyrimidine*. 4,8-Diaza-3,9-diphenylundeca-2,9-diene-1,11-dinitrile (5 g, 0.01 mol) was heated at 300—350 °C. Acetonitrile distilled off followed by 2-phenyl-1,4,5,6-tetrahydropyrimidine which solidified in the receiver. Recrystallization from hexane–chloroform gave the *product* (1.82 g, 76%), m.p. 73 °C (Found: C, 74.9; H, 7.6; N, 17.5. $C_{10}H_{12}N_2$ requires C, 75.0; H, 7.5; N, 17.5%); $\nu_{max.}$ 3 180 (NH), 1 620 (C=C), 1 560 (C=N), and 1 520 cm^{-1} (NH def.); $\lambda_{max.}$ 203 (ε 23 800), 230 (14 300), and 275 nm (1 800); τ($CDCl_3$) 8.28 (2 H, quin, $NCH_2CH_2CH_2N$), 6.58 (4 H, t, $NCH_2CH_2CH_2N$), 5.12 (1 H, s, NH exchanges on deuteriation), 2.80—2.60 (3 H, m, 3-, 4-, 5-H on Ph), and 2.50—2.30 (2 H, m, 2, 6-H on Ph).

References

1. Allenes. Part 39, Z. T. Fomum, S. R. Landor, P. D. Landor, and G. W. P. Mpango, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2997.
2. Z. T. Fomum, P. M. Greaves, P. D. Landor, and S. R. Landor, *J. Chem. Soc., Perkin Trans. 1*, 1973, 1108.
3. R. D. Mackenzie, T. R. Blohm, and J. M. Grisar, *J. Med. Chem.*, 1973, **16**, 688.
4. S. R. Landor, P. D. Landor, Z. T. Fomum, and G. W. P. Mpango, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2289.
5. C. W. N. Cumper, Z. T. Fomum, P. M. Greaves, and S. R. Landor, *J. Chem. Soc., Perkin Trans. 2*, 1973, 885.
6. Z. T. Fomum, J. T. Mbafor, S. R. Landor, P. D. Landor, and G. W. P. Mpango, *Tetrahedron*, in the press.
7. S. R. Landor, P. D. Landor, Z. T. Fomum, and J. T. Mbafor, *Heterocycles*, 1981, **16**, 1889.

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