

## Allenes. Part XXVI.<sup>1</sup> The Synthesis of Enaminic Nitriles by the Nucleophilic Addition of Amines to Allenic Nitriles

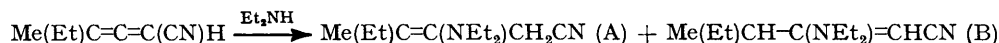
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Unconjugated or conjugated enaminic nitriles may be obtained quantitatively by Michael addition of amines to 1-cyanoallenes, according to the reaction conditions. Both series of enamines are hydrolysed to  $\beta$ -keto-nitriles. I.r., u.v., and n.m.r. spectra are discussed.

PREVIOUSLY<sup>2</sup> we outlined the formation of both unconjugated (II) and conjugated enaminic nitriles (III) by a Michael addition of a primary or secondary amine to a series of monoalkyl and dialkyl substituted cyanoallenes (I). At the time we postulated separate and distinct

conjugated enamines, exceptionally intense stretching bands in the i.r. for CN at 2190 and for C=C at 1590  $\text{cm}^{-1}$ , and absorption maxima in the u.v. near 262 for enamines derived from primary amines and 273–282 nm for those prepared from secondary amines (both  $\epsilon$  ca. 20,000);

TABLE 1



A (%)	B (%)	Condition of experiment	Extinction coefficient of product mixture		
			$\lambda_{\text{max.}}$ 204 nm	$\lambda_{\text{max.}}$ 247 nm	$\lambda_{\text{max.}}$ 277 nm
100	0	Reaction at $-10^\circ$	5700	1500	
98	2	Reaction at room temp. for 15 min *	5600	1450	900
94	6	Reflux in $\text{CHCl}_3$ for 15 min	5400	1300	1900
81	19	Reflux in superdry ethanol for 15 min	4600	1000	3100
75	25	Heated at $96^\circ$ for 1 h	4200	900	4200
26	74	Heated in <i>NN</i> -dimethylformamide for 25 min at $150^\circ$	1500	300	14200
0	100	Heated at $150^\circ$ for 45 min			19400

\* Temperature of initial reaction reached  $85^\circ$ .

mechanisms for the formation of the enamines (II) and (III). However more detailed work has since shown that unconjugated enamines are frequently converted into conjugated enaminic nitriles during distillation and that unconjugated enaminic nitriles (II) are always formed first and then rearrange to conjugated enaminic nitriles either spontaneously or when heated at higher temperatures (Table 1).

The unconjugated enaminic nitriles (II) (Table 2) are best prepared by treating the cyanoallenes with a primary or secondary amine in equimolar proportion at temperatures between  $-33$  and  $0^\circ$ . The crude products, which are formed quantitatively, are completely converted into conjugated enamines (III) of  $>99\%$  purity on g.l.c. at  $200^\circ$  thus showing that no other products [besides (II) and (III)] are formed.

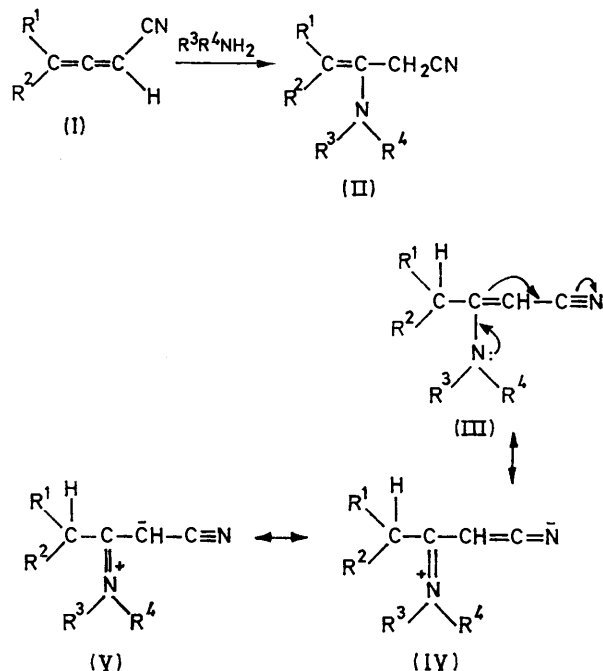
Even at lower temperatures some interconversion takes place and g.l.c. cannot be used readily for the estimation of the proportion of unconjugated enamine present. This is best achieved by the application of u.v. spectra. Enamines (II) show low intensity stretching bands in the i.r. for CN at ca. 2250 and for C=C at ca. 1660  $\text{cm}^{-1}$  together with a maximum in the u.v. in the 204–207 region ( $\epsilon$  5000) with weaker secondary absorption in the 230–250 nm region in some cases.

Conjugated enaminic nitriles (III) (Table 3) are best prepared by heating the reaction mixture, after the initial exothermic reaction has subsided, at  $150$ – $200^\circ$  for up to 2 h and are usually isolated in ca. 90% yield. They have substantially higher b.p.s than the un-

<sup>1</sup> Part XXV, C. W. N. Cumper, Z. T. Fomum, P. M. Greaves, and S. R. Landor, *J.C.S. Perkin II*, 1973, 885.

<sup>2</sup> P. M. Greaves and S. R. Landor, *Chem. Comm.*, 1966, 322.

these data are consistent with a substantial contribution from a highly polarised structure such as (IV). The n.m.r. spectra showed a strongly shielded olefinic



proton near  $\tau$  6.2 (Table 4) (the normal signal for  $=\text{CHCN}$  is near  $\tau$  5.0<sup>1,3</sup>) suggesting a partial negative charge on C-2 as in (V). Both *cis*- and *trans*-compounds

<sup>3</sup> P. M. Greaves, S. R. Landor, and D. R. J. Laws, *J. Chem. Soc. (C)*, 1968, 291.

TABLE 2  
Preparation of unconjugated enaminic nitriles (II)

Nitrile		Amine		Condition of experiment	B.p./°C (mmHg)	Yield (%)	$\lambda_{\max.}/\text{nm}$		Found (%)			Requires (%)				
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>				$\epsilon$	$\epsilon$	C	H	N	C	H	N		
Me	Me	Bu <sup>a</sup>	H	Reaction at -33° for 35 min		92 <sup>a</sup>	222	6700								
Me	Me	Et	Et	Room temp. for 15 min, distilled	46 (0.25)	94	204	4800	230	2200	72.2	10.7	17.0	72.2	10.7	16.9
Me	Me	[CH <sub>2</sub> ] <sub>5</sub>		Reaction at -10° for 30 min		90 <sup>b</sup>	204	4200	236	3100	74.1	10.1	15.8	74.2	10.1	15.7
Me	Me	[CH <sub>2</sub> ] <sub>4</sub>		Reaction at -33° for 30 min		94 <sup>c</sup>	204	4400	245	5300						
Me	Et	Bu	H	Reaction at -33° for 25 min		90 <sup>d</sup>	218	5100	230	4700						
Me	Et	Et	Et	Reaction at 0° for 15 min, distilled *	54 (0.4)	92	206	7200	247	1900	73.2	11.1	15.6	73.3	11.1	15.6
Me	Et	[CH <sub>2</sub> ] <sub>4</sub>		Reaction at -33° for 1 h		89 <sup>e</sup>	204	4800	244	5700						
Me	Et	[CH <sub>2</sub> ] <sub>5</sub>		Reaction at -10° for 30 min		86 <sup>f</sup>	205	4000	232	2300	74.2	10.2	14.0	75.0	10.5	14.6
Et	Et	Bu <sup>a</sup>	H	Reaction at 0° for 1 h		92 <sup>g</sup>	215	4200	228	5300						
Et	Et	Et	Et	Reaction at 0° for 25 min, distilled *	72 (0.6)	92	204	7600	250	1100	73.2	11.3	15.4	73.3	11.3	15.4
Et	Et	[CH <sub>2</sub> ] <sub>4</sub>		Reaction at -33° for 1 h		90 <sup>h</sup>	206	6900	245	3500						
Et	Et	[CH <sub>2</sub> ] <sub>5</sub>		Reaction at -10° for 30 min		87 <sup>i</sup>	206	5000	236	3100						

\* Some rearrangement during distillation.

Contains <sup>a</sup> 4%. <sup>b</sup> 15%. <sup>c</sup> 12%. <sup>d</sup> 5%. <sup>e</sup> 10%. <sup>f</sup> 13%. <sup>g</sup> 10%. <sup>h</sup> 8%. <sup>i</sup> 12% rearrangement product.

TABLE 3  
Preparation of conjugated enaminic nitriles (III)

Nitrile		Amine		Condition of experiment	B.p./°C (mmHg)	Yield (%)	$\lambda_{\max.}/\text{nm}$		Found (%)			Required (%)		
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>				$\epsilon$	$\epsilon$	C	H	N	C	H	N
H	Pr	Et	Et	Reflux for 12 min, distilled	106 (0.4)	91	273	24,000	73.3	11.3	15.4	73.3	11.2	15.7
D	Pr	Et	Et	Room temp. for 5 min, distilled	118 (1.0)	88	274	21,600	73.9	10.7	15.4	73.8	10.6	15.6
Me	Me	Bu <sup>a</sup>	H	Room temp. for 2 h, distilled <sup>a</sup>	118 (0.5)	94	263	19,900	71.6	10.7	16.9	72.2	10.7	17.0
Me	Me	Et	Et	Heated at 180° for 1 h, distilled	90 (0.6)	90	277	18,700	72.2	10.8	16.8	72.3	10.7	17.0
Me	Me	[CH <sub>2</sub> ] <sub>5</sub>		Heated at 180° for 1 h, distilled	121 (0.9)	92	277	22,400	74.0	10.1	15.8	74.2	10.1	15.7
Me	Me	[CH <sub>2</sub> ] <sub>4</sub>		Heated at 180° for 1.5 h, distilled	130 (1)	89	277	22,600	72.9	10.1	16.8	73.2	9.8	17.1
Me	Et	Bu <sup>a</sup>	H	Room temp. for 4 h, distilled <sup>b</sup>	110 (0.2)	88	262	20,500	73.6	11.4	15.4	73.3	11.2	15.6
Me	Et	Et	Et	Heated at 180° for 2 h, distilled	112 (0.8)	93	277	20,100	73.2	11.1	15.6	73.3	11.2	15.6
Me	Et	[CH <sub>2</sub> ] <sub>4</sub>		Heated at 180° for 2 h, distilled	110 (0.2)	91	274	23,000	74.2	9.9	15.7	74.1	10.2	15.7
Me	Et	[CH <sub>2</sub> ] <sub>5</sub>		Heated at 180° for 2 h, distilled	110 (0.3)	92	277	18,700	74.9	10.5	14.6	75.0	10.5	14.6
Et	Et	Bu <sup>a</sup>	H	Room temp. for 12 h, distilled <sup>c</sup>	140 (0.5)	88	264	20,600	74.0	11.2	14.5	74.2	11.3	14.4
Et	Et	Et	Et	Heated at 200° for 50 min, distilled	112 (0.8)	93	277	20,900	74.1	11.3	14.5	74.2	11.3	14.4
Et	Et	H	H	Heated at 60—70° for 4 h, distilled	90 (0.2)	60	261	18,300	69.5	10.4	20.1	69.5	10.2	20.3
Et	Et	[CH <sub>2</sub> ] <sub>5</sub>		Heated at 200° for 2 h, distilled	125 (0.1)	91	277	23,700	74.8	10.7	14.4	75.7	10.8	13.6
Et	Et	[CH <sub>2</sub> ] <sub>4</sub>		Heated at 200° for 2 h, distilled	130 (0.2)	92	274	23,500	75.1	10.4	14.5	75.0	10.4	14.8
Et	Et	C <sub>9</sub> H <sub>10</sub> *		Room temp. for 30 min		60	274	16,000						
Et	Et	C <sub>9</sub> H <sub>10</sub> †		Room temp. for 6 h <sup>d</sup>		0								
Me	Bu <sup>t</sup>	Et	Et	Heated at 96° for 2.5 h, distilled	110 (0.5)	46	282	18,300	74.9	11.5	13.6	74.9	11.6	13.5
Me	Bu <sup>t</sup>	[CH <sub>2</sub> ] <sub>4</sub>		Heated at 96° for 1 h, distilled	120 (2 × 10 <sup>-2</sup> )	83	279	21,000	75.9	10.9	13.4	75.7	10.8	13.6
Me	Bu <sup>t</sup>	[CH <sub>2</sub> ] <sub>5</sub>		Heated at 120° for 1 h		80	284	16,000	76.4	10.8	12.5	76.3	11.0	12.7
Pr <sup>i</sup>	Pr <sup>i</sup>	Et	Et	Heated at 150° for 2 h	115 (0.15)	82	277	22,500	75.1	11.8	13.3	75.6	11.8	12.6

<sup>a</sup> M.p. 46—47°. <sup>b</sup> M.p. 53—54°. <sup>c</sup> M.p. 67°. <sup>d</sup> Not tried at higher temperature.

\* 1,2,3,4-tetrahydroisoquinoline.

† 1,2,3,4-tetrahydroquinoline.

appear to be formed since the *NN*-diethylamino-adducts show a quartet centred on  $\tau$  6.75 which is attributed to the methylene hydrogens of the *N*-ethyl group *trans* to the  $C\equiv N$  groups and an overlapping quartet centred at  $\tau$  6.51 which is probably due to the presence of the methylene hydrogens of the *N*-ethyl groups *cis* to the  $C\equiv N$  group.

of the tautomeric imino-nitrile. Corresponding imino-nitriles could not, however, be detected in the product from *n*-butylamine and allenic nitriles.

Acid-catalysed hydrolysis of the corresponding unconjugated and conjugated enaminc nitriles (II) and (III) gave the  $\beta$ -keto-nitrile (VI) as the only isolated product<sup>4</sup> (Table 5).

TABLE 4  
N.m.r. data of enaminc nitriles

Nitrile		Amine		Unconjugated enaminc nitriles *	Conjugated enaminc nitriles
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>		
Me	Me	Bu <sup>a</sup>	H		9.1(6H,m); 8.85(3H,d); 8.3—8.75(4H,m); 6.9—7.4(5H,m); 6.26(1H,s); 5.2—5.6br(1H,s)
Me	Me	Et	Et	9.05(6H,t); 8.20(6H,s); 7.59—6.58(4H, overlapping q); 7.03(2H,s)	8.83(6H,dt); 8.47(6H,d); 7.50(1H,m); 7.14—6.47(4H, overlapping q); 6.25(1H,d)
Me	Et	Et	Et	8.8—9.2(9H,tt); 8.2(3H,s); 7.75(2H,q); 7.37(4H,qd); 7.04(2H,s)	8.9(3H,t); 8.86(3H,t); 8.64(3H,d); 8.2(2H,dq); 7.3(1H,m); 6.75(4H,q); 6.23(1H,d)
Me	Et	[CH <sub>2</sub> ] <sub>5</sub>			9.05(3H,t); 8.7(3H,d); 8.5(2H,q); 7.1(6H,m); 6.7—6.95(4H,m); 6.03(1H,d)
Et	Et	H	H		9.1(6H,m); 8.5(4H,m); 6.2(1H,t); 5.83(1H,d); 5—5.8(3H,m)
Et	Et	Et	Et	9.16—8.85(12H, overlapping 5); 7.94—7.28(8H, overlapping q); 7.05(2H,s)	9.08(6H,t); 8.87(6H,t); 8.50—8.03(4H,m); 7.50(1H,m); 6.91—6.50(4H, overlapping q); 6.22(1H,d)
Me	Bu <sup>t</sup>	Et	Et		9.03(9H,s); 8.85(3H,m); 8.5(3H,d); 7.55(1H,q); 6.6(2H,m); 6.3(1H,s)

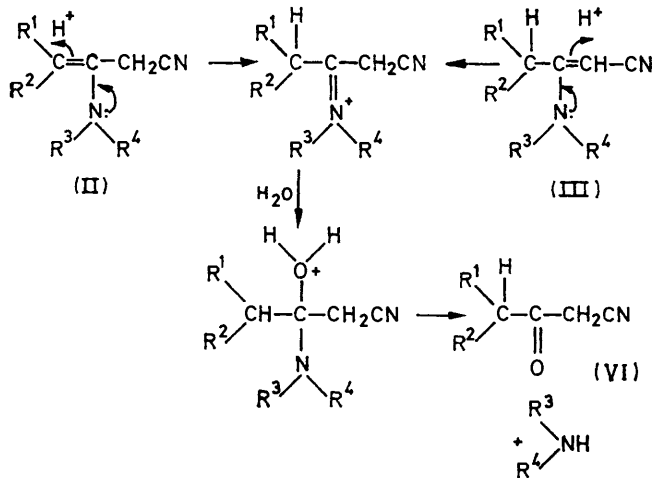
\* The n.m.r. spectra of pure unconjugated enaminc nitriles only are given here. The rest are obtained *ca.* 90% pure, the contaminant being the conjugated enaminc nitrile.

TABLE 5  
Data for  $\beta$ -keto-nitriles (R<sup>1</sup>R<sup>2</sup>CHCOCH<sub>2</sub>CN)

R <sup>1</sup>	R <sup>2</sup>	Yield (%)	B.p./°C (mmHg)	$\nu_{\max}$ /cm <sup>-1</sup>	$\lambda_{\max}$ /nm	$\epsilon$	Found (%)				Requires (%)			
							C	H	O	N	C	H	O	N
Et	Me	81 <sup>a</sup>	70 (0.5)	2260, 1730, 780	232	4100	67.1	8.7	13.0	11.2	67.2	8.9	12.8	11.2
Et	Et	78 <sup>b</sup>	65 (0.4)	2280, 1730, 785	232	4400	69.0	9.4	11.6	10.6	69.0	9.4	11.5	10.1
Me	Bu <sup>t</sup>	52 <sup>c</sup>	80 (0.15)	2280, 1730, 710	234	3200	70.6	9.7	10.4	9.3	70.6	9.8	10.6	9.2

<sup>a</sup> From 3-diethylamino-4-methylhex-3-enitrile, 3-diethylamino-4-methylhex-2-enitrile, 4-methyl-3-piperidinopent-2-enitrile, and 4-methyl-3-piperidinopent-3-enitrile. <sup>b</sup> From 3-diethylamino-4-ethylhex-3-enitrile, 3-amino-4-ethylhex-2-enitrile, 4-ethyl-3-(1,2,3,4-tetrahydroisoquinolin-2-yl)pent-2-enitrile, and 4-ethyl-3-(1,2,3,4-tetrahydroisoquinolin-2-yl)pent-3-enitrile. <sup>c</sup> From 3-diethylamino-3,4,4-trimethylpent-2-enitrile, 3-piperidino-3,4,4-trimethylpent-2-enitrile, 3-piperidino-3,4,4-trimethylpent-3-enitrile, and 3-pyrrolidin-1-yl-3,4,4-trimethylpent-2-enitrile.

It is interesting to note that ammonia reacts very slowly and then only on heating the reactants to 60—70°,



showing that it is a much weaker nucleophile than either primary or secondary amines. The n.m.r. of the resulting enaminc nitrile showed the presence of *ca.* 12%

## EXPERIMENTAL

I.r. spectra were determined for liquid films with Perkin-Elmer Infracord and 257 spectrophotometers. U.v. spectra were obtained for ethanolic solutions with Bausch and Lomb Spectronic 505 and Pye-Unicam 1800 spectrometers. N.m.r. spectra were determined with Perkin-Elmer R 10 and Varian T 60 spectrometers for solutions in deuteriochloroform with tetramethylsilane as internal standard. G.l.c. was carried out with a Pye 104 instrument on glass columns (5 ft) using nitrogen as a carrier gas at a flow rate of 2.5 l h<sup>-1</sup>.

*Preparation of Unconjugated Enaminc Nitriles (II).*—A typical example is given below; variations in conditions for individual enamines, analyses, and physical data are given in Table 2.

*3-Diethylamino-4-methylhex-3-enitrile.* Redistilled diethylamine (0.37 g, 0.005 mol) was cooled to 0° and added to 4-methylhexa-2,3-dienitrile (0.52 g, 0.005 mol) also cooled to 0°. The mixture was kept at 0° for 15 min and then allowed to warm to room temperature. The crude product gave  $\nu_{\max}$  2242 (C≡N) and 1660 cm<sup>-1</sup> (C=C), and complete absence of  $\nu_{\max}$  1950 cm<sup>-1</sup> (C=C=C),  $\lambda_{\max}$  206 nm ( $\epsilon$  7200),  $\tau$  7.04 [2H, s, =C(NEt<sub>2</sub>)CH<sub>2</sub>CN] and complete absence of a signal centred on  $\tau$  4.9 (C=C=CHCN).

<sup>4</sup> M. E. Kuehne, *J. Amer. Chem. Soc.*, 1959, **81**, 5400.

Distillation of the product from an experiment on a 0.05 mol scale gave pure enamine, b.p. 54° at 0.4 mmHg, together with higher boiling fractions of a mixture of partially rearranged conjugated and unconjugated enamines.

*Preparation of Conjugated Enaminic Nitriles (III).*—A typical example is given below; variations in conditions for individual enamines, analyses, and physical data are given in Table 3.

*3-Diethylamino-4-methylhex-2-enenitrile.* Redistilled diethylamine (1.5 g, 0.02 mol) was added slowly to 4-methylhexa-2,3-dienenitrile (1.6 g, 0.015 mol) cooled in ice and the mixture was then heated under reflux for 15 min. Excess of diethylamine was removed under reduced pressure and the product distilled yielding 3-diethylamino-4-methylhex-2-enenitrile (2.45 g, 91%), b.p. 143° at 4.9 mmHg,  $\nu_{\max}$  2195 ( $=C-CN$ ) and 1575 ( $C=C-CN$ )  $cm^{-1}$ ,  $\lambda_{\max}$  277 nm ( $\epsilon$  19,400),  $\tau$  6.23 (1H, d,  $C=CHCN$ ).

*Thermal Rearrangement of 3-Diethylamino-4-methylhex-3-enenitrile to 3-Diethylamino-4-methylhex-2-enenitrile.*—3-Diethylamino-4-methylhex-3-enenitrile (1.8 g, 0.01 mol) was heated under nitrogen at 150°. The reaction was monitored by i.r. absorption and was complete after 40 min,  $\nu_{\max}$  2195 ( $=C-CN$ ) and 1575  $cm^{-1}$  ( $C=C-CN$ ) and complete absence of  $\nu_{\max}$  2240 ( $CH_2CN$ ) and 1660  $cm^{-1}$  ( $C=C-CH_2$ ),  $\lambda_{\max}$  277 nm ( $\epsilon$  19,400).

*3-Amino-4-ethylhex-2-enenitrile.*—Anhydrous ammonia

gas was passed through 4-ethylhexa-2,3-dienenitrile (6 g, 0.05 mol) at room temperature for 10 h when i.r. showed little reaction had taken place. After heating at 60–70° with passage of ammonia for a further 4 h the absence of the 1950  $cm^{-1}$  band in the i.r. showed the reaction had gone to completion. Distillation gave 3-amino-4-ethylhex-2-enenitrile (4.1 g, 60%), b.p. 90° at 0.2 mmHg,  $\nu_{\max}$  3430, 3350, 3220 (NH and  $=NH$  stretch), 2200 ( $=C-C\equiv N$ ), 1645 (NH deformation), and 1585 ( $C=C-CN$ )  $cm^{-1}$ ;  $\lambda_{\max}$  261 nm ( $\epsilon$  18,300),  $\tau$  6.2 (0.88H, t,  $=CHCN$ ), 5.83 (0.24H, d,  $CH_2CN$ ), and 5–5.5br (1.88H,  $NH_2$  and  $=NH$ ).

*Hydrolysis of Enamines to  $\beta$ -Keto-nitriles.*—Variations in conditions for individual enamines, analyses, and physical data are given in Table 5.

*4-Methyl-3-oxohexanenitrile.* (a) 3-Diethylamino-4-methylhex-3-enenitrile (9.0 g, 0.05 mol) was stirred with 5% hydrochloric acid (50 ml) at 100° for 2.5 h. The mixture was cooled, extracted with ether (3  $\times$  100 ml), and dried ( $MgSO_4$ ). Distillation gave 4-methyl-3-oxohexanenitrile (5.1 g, 81%), b.p. 70° at 0.5 mmHg,  $\nu_{\max}$  2280 (CN) and 1730 ( $C=O$ )  $cm^{-1}$ ,  $\lambda_{\max}$  232 nm ( $\epsilon$  4100), g.l.c. gave one peak,  $t_R$  5 min (silicone oil; SE 30; 150°).

(b) 3-Diethylamino-4-methylhex-3-enenitrile (9.0 g, 0.05 mol) by the same procedure gave the same product (3.8 g, 60%) with identical spectra and g.l.c. behaviour.

[2/2648 Received, 22nd November, 1972]