

*A Novel Method of Cyanoethylation. Part III.\* The Mechanism of the Reaction.*

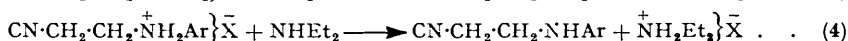
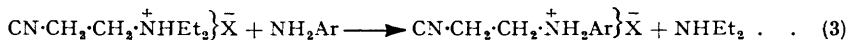
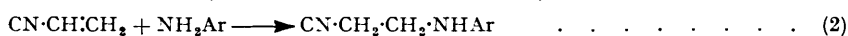
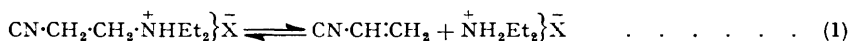
By J. CYMERMAN-CRAIG, M. MOYLE, A. J. C. NICHOLSON, and R. L. WERNER.

[Reprint Order No. 6478.]

Reaction of 2-diethylaminoethyl cyanide with arylamine salts to give *N*-2-cyanoethylarylamines is shown to proceed by a substitution mechanism, rather than by elimination followed by addition. The use of *N*-deuterio-diethylamine confirms this conclusion.

IN Part I (*J.*, 1951, 3311) the reaction of 2-diethylaminoethyl cyanide with arylamine salts at 180° was shown to lead to *N*-2-cyanoethylarylamines. This amine-exchange cyanoethylation may proceed either by elimination (reaction 1) followed by Michael addition (reaction 2), or alternatively by a substitution mechanism (reaction 3) followed by proton transfer to the more strongly basic dialkylamine (reaction 4).

After Part I had been submitted, a paper by Bekhli came to hand [*J. Gen. Chem. (U.S.S.R.)*, 1951, 21, 86] in which he prepared *N*-2-cyanoethylarylamines from 2-cyanoethyldiethylammonium chloride and arylamines at 140—160° (2 hr.). He states that the reaction proceeds by cleavage followed by addition, *i.e.*, reactions 1 and 2, and cites as evidence his finding that, whereas 2-diethylaminoethyl cyanide remained substantially unchanged at 193° for 3 hr., its hydrochloride when heated alone to 160—190° gave 77% of vinyl cyanide. The dissociation of Mannich bases, on distillation, into



the amine and an ethylene is well known, and it is expected that salt formation will enhance the rate of such elimination, which presumably proceeds by the “*E1cB*” mechanism (Ingold, “Structure and Mechanism in Organic Chemistry,” Bell, London, 1953, p. 695) or, in a medium of low dielectric constant, by an equivalent synchronous step avoiding the separation of free ions.

However, reference to Bekhli’s paper showed that under his conditions (continuous removal of vinyl cyanide from a distilling flask) the elimination reaction would be expected

\* Part II, *J.*, 1954, 1153.

to go towards completion, and that his findings are therefore inadmissible as proof of the "cleavage and addition" mechanism. Indeed, our own results contradict Bekhli's conclusions in this respect: we find that 2-cyanoethyldiethylammonium chloride was recovered substantially (73%) unchanged after being refluxed at 180° for 1.5 hr., thus affording evidence of the stability of this compound in the conditions used for cyanoethylation.

Further, Bekhli (*loc. cit.*) showed that no product was obtained from anilinium chloride and 2-cyanoethyldiethylammonium chloride and ascribes the formation of *N*-2-cyanoethylarylamines to reaction 2. We find, however, that no reaction occurs between vinyl cyanide and aniline, or between this cyanide and *p*-anisidinium chloride, at 180° during 1.5 hr., whereas in the same conditions 2-diethylaminoethyl cyanide and *p*-anisidinium chloride gave 78% of *N*-2-cyanoethyl-*p*-anisidine. Moreover, a mixture, in the same proportions, of vinyl cyanide, diethylamine, and *p*-anisidinium chloride afforded the same product in 67% (1.5 hr.) and 76% (2.5 hr.) yield, and reaction of vinyl cyanide, diethylammonium chloride, and *p*-anisidine gave 79% of the same substance, accompanied by some of the *NN*-di-(2-cyanoethyl) compound.

Although vinyl cyanide failed to react with either aniline or *p*-anisidinium chloride, addition of 0.1 mol. of diethylammonium benzenesulphonate to a mixture of vinyl cyanide and *p*-anisidine (1 mol. of each) led to *N*-2-cyanoethyl-*p*-anisidine in 59% yield. These results (see Table) support the hypothesis that the reaction proceeds by a substitution mechanism (reaction 3).

Reactants	Temp. (time, hr.)	Product	Yield (%)
Vinyl cyanide, diethylamine	Reflux (0.5)	2-Diethylaminoethyl cyanide	93 <sup>4</sup>
2-Cyanoethyldiethylammonium chloride	180° (1.5)	2-Cyanoethyldiethylammonium chloride	73
Vinyl cyanide, aniline	180 (1.5)	Unchanged	—
Vinyl cyanide, <i>p</i> -anisidinium chloride	180 (1.5)	"	—
2-Diethylaminoethyl cyanide, aniline	180 (1)	"	— <sup>1</sup>
2-Cyanoethyldiethylammonium chloride, anilinium chloride	140—150 (2)	None obtained	— <sup>2</sup>
2-Diethylaminoethyl cyanide, <i>p</i> -anisidinium chloride	180 (1.5)	<i>N</i> -2-Cyanoethyl- <i>p</i> -anisidine	78
Vinyl cyanide, diethylamine, <i>p</i> -anisidinium chloride	180 (1.5)	"	68
	180 (2.5)	"	76
Vinyl cyanide, diethylammonium chloride, <i>p</i> -anisidine	180 (1.5)	"	79 <sup>3</sup>
Vinyl cyanide, <i>p</i> -anisidine, 0.1 mol. of diethylammonium benzenesulphonate	180 (1.5)	"	59

<sup>1</sup> *J.*, 1951, 3311. <sup>2</sup> Bekhli, *loc. cit.* <sup>3</sup> Also isolated: *NN*-di-(2-cyanoethyl)-*p*-anisidine (7%).

<sup>4</sup> Whitmore, Mosher, Adams, Taylor, Chapin, Weisel, and Yanko, *J. Amer. Chem. Soc.*, 1944, **66**, 725.

Further evidence has been obtained by the use of *N*-deuterodiethylamine, prepared from diethylaminomagnesium bromide and deuterium oxide and shown by mass-spectrometric analysis to contain at least 80% of *NDEt*<sub>2</sub>; its infrared spectrum showed absorption at 2434 cm.<sup>-1</sup> attributable to the stretching vibration of the N-D bond (cf. deuterohydrazoic acid, 2457 cm.<sup>-1</sup>; Randall, Fowler, Fuson, and Dangel, "Infrared Determination of Organic Structures," Van Nostrand, New York, 1949). This band was absent from the spectrum of diethylamine, which showed only the band at 3284 cm.<sup>-1</sup> due to N-H.

*N*-Deuterodiethylamine was condensed with vinyl cyanide, the resulting 1-deutero-2-diethylaminoethyl cyanide containing, by mass-spectrometric analysis, about 80% of the deutero-compound whose infrared spectrum showed a strong band at 2244 cm.<sup>-1</sup> (C≡N; cf. 2252 cm.<sup>-1</sup> in 2-hydroxyethyl cyanide; Randall *et al.*, *op. cit.*) and a band at 2192 cm.<sup>-1</sup> attributable to the C-D stretching vibration (cf. 2151 cm.<sup>-1</sup> in 2-deuteropropane; Condon, McMurry, and Thornton, *J. Chem. Phys.*, 1951, **19**, 1010). The former, but not the latter, band was present in 2-diethylaminoethyl cyanide.

Reaction of 1-deutero-2-diethylaminoethyl cyanide and *p*-anisidinium benzenesulphonate gave diethylammonium benzenesulphonate which, on treatment with saturated

sodium hydroxide solution, evolved diethylamine containing no  $\text{NDEt}_2$ : the mass-spectrometer would have detected 2% of this substance.

The absence of deuterium in the diethylammonium benzenesulphonate shows that the  $\text{CH}_2\cdot\text{CHD}\cdot\text{CN}$  group remained intact during the reaction and hence provides further evidence for a nucleophilic substitution mechanism. The *N*-2-cyanoethyl-*p*-anisidine was not volatile enough to give a reading in the ion chamber of the mass-spectrometer, but its infrared spectrum showed both a strong band at  $2243\text{ cm}^{-1}$  ( $\text{C}\equiv\text{N}$ ) and a very weak peak at  $2192\text{ cm}^{-1}$  (C-D) corresponding exactly in wavelength with that found in 1-deutero-2-diethylaminoethyl cyanide.

#### EXPERIMENTAL

*Stability of 2-Cyanoethyldiethylammonium Chloride.*—2-Cyanoethyldiethylammonium chloride [32.5 g., 0.2 mole; Terent'ev and Kost, *J. Gen. Chem. (U.S.S.R.)*, 1946, 16, 859] was heated under reflux for 1.5 hr. at  $180^\circ$ . The cooled material was thoroughly washed (dry  $\text{C}_6\text{H}_6$ ), and the residue basified with sodium hydroxide solution (pH >12) and extracted with ether. Removal of solvent from the dried ( $\text{Na}_2\text{SO}_4$ ) extracts on the steam-bath gave 2-diethylaminoethyl cyanide (18.4 g., 73%),  $n_D^{25}$  1.4342 (Whitmore, Mosher, Adams, Taylor, Chapin, Weisel, and Yanko, *J. Amer. Chem. Soc.*, 1944, 66, 725, give  $n_D^{25}$  1.4356).

*Attempted Reaction of Vinyl Cyanide with Arylamines.*—(i) An equimolecular mixture of vinyl cyanide and aniline was refluxed at  $180^\circ$  for 1.5 hr. Distillation afforded only the starting materials (90% recovery); no residue remained. (ii) Vinyl cyanide (5.3 g., 1.5 mols.) and *p*-anisidinium chloride (10.65 g., 1 mol.) were heated under reflux at  $180^\circ$  for 1.5 hr. The cold mixture was washed with acetone (10 c.c.) and ether (40 c.c.), leaving unchanged *p*-anisidinium chloride (10.4 g.), m. p. and mixed m. p. undepressed. The filtrates left no residue of b. p.  $>100^\circ$ .

*N-2-Cyanoethyl-*p*-anisidine.*—(i) A mixture of 2-diethylaminoethyl cyanide (12.6 g., 1.5 mols.) and *p*-anisidinium chloride (10.65 g., 1 mol.) was heated under reflux at  $180^\circ$  for 1.5 hr. On cooling, addition of acetone (10 c.c.) gave diethylammonium chloride (5.2 g., 95%), which when washed with acetone and ether had m. p. and mixed m. p.  $218\text{--}220^\circ$ . Distillation of the filtrate gave two fractions: (1) b. p.  $84\text{--}106^\circ/3\text{ mm.}$  (3.1 g.), containing 2-diethylaminoethyl cyanide (2.25 g.) and *p*-anisidine (0.85 g., 10%, estimated as the acetyl derivative); (2) b. p.  $136\text{--}150^\circ/0.001\text{ mm.}$  (9.45 g., 78%), needles, m. p. and mixed m. p.  $62\text{--}64^\circ$ , of *N*-2-cyanoethyl-*p*-anisidine.

(ii) A mixture of diethylamine (7.3 g., 1.5 mols.), vinyl cyanide (5.3 g., 1.5 mols.), and *p*-anisidinium chloride (10.65 g., 1 mol.) was heated under reflux at  $180^\circ$  for 1.5 hr. Working up as in (i) gave diethylammonium chloride (6.3 g., 86%), m. p. and mixed m. p.  $218\text{--}220^\circ$ , and distillation gave two fractions: (1) b. p.  $65\text{--}120^\circ/2\text{ mm.}$  (5.8 g.), containing 2-diethylaminoethyl cyanide (3.95 g.) and *p*-anisidine (1.8 g., 22%); (2) b. p.  $136\text{--}150^\circ/0.001\text{ mm.}$  (7.9 g., 68%), m. p. and mixed m. p.  $62\text{--}64^\circ$ , of *N*-2-cyanoethyl-*p*-anisidine.

(iii) An experiment identical with (ii) but extending over 2.5 hr. gave 15% of recovered *p*-anisidine and 76% of *N*-2-cyanoethyl-*p*-anisidine.

(iv) A mixture of vinyl cyanide (8 g., 1.5 mols.), diethylammonium chloride (10.95 g., 1 mol.), and *p*-anisidine (12.3 g., 1 mol.) was refluxed at  $180^\circ$  for 1.5 hr. The cooled mixture was treated with sodium hydroxide solution and extracted with chloroform. Distillation of the dried extracts gave three fractions: (1) unchanged 2-diethylaminoethyl cyanide and *p*-anisidine; (2) b. p.  $140\text{--}150^\circ/0.001\text{ mm.}$  (14 g., 79%), m. p. and mixed m. p.  $62\text{--}64^\circ$ , of *N*-2-cyanoethyl-*p*-anisidine; (3) b. p.  $180^\circ/0.001\text{ mm.}$  (1.6 g., 7%), of *NN*-di-(2-cyanoethyl)-*p*-anisidine, m. p.  $103\text{--}104^\circ$ , as needles from alcohol (Braunholtz and Mann, *J.*, 1953, 1817, give m. p.  $103^\circ$ ).

(v) A mixture of vinyl cyanide (5.3 g., 1.5 mols.), *p*-anisidine (8.2 g., 1 mol.), and diethylammonium benzenesulphonate (1.54 g., 0.1 mol.) was heated under reflux at  $180^\circ$  for 1.5 hr. The cooled melt, treated as in (i), gave diethylammonium benzenesulphonate (0.35 g., 22%), m. p. and mixed m. p.  $137\text{--}139^\circ$ . Distillation gave two fractions: (1) b. p.  $94\text{--}110^\circ/2\text{ mm.}$  (2.6 g., 32%), of *p*-anisidine, m. p. and mixed m. p.  $55\text{--}57^\circ$ ; (2) b. p.  $135\text{--}145^\circ/0.001\text{ mm.}$  (6.85 g., 59%), of *N*-2-cyanoethyl-*p*-anisidine (mixed m. p.).

*N-Deuterodiethylamine.*—Diethylamine (4.2 c.c., 1 mol.) was added to a stirred solution of ethylmagnesium bromide (from 9.6 g. of magnesium) in ether (135 c.c.), and the mixture refluxed for 0.5 hr. The ether was distilled off, and diisooamyl ether (100 c.c.) added simultaneously. The cooled (ice) reaction mixture was decomposed by addition of deuterium oxide (12 g., 1.5 mol., 99.7%  $\text{D}_2\text{O}$ ). Distillation through a column ( $6'' \times \frac{3}{8}''$ ) filled with single-turn glass helices gave *N*-deuterodiethylamine, b. p.  $52\text{--}56^\circ/760\text{ mm.}$ , in 50% yield.

*1-Deutero-2-diethylaminoethyl Cyanide.*—Prepared by reaction of equimolar quantities of *N*-deuterodiethylamine and vinyl cyanide, this had b. p. 100—101°/30 mm.,  $n_D^{17}$  1.4350.

*Reaction with p-anisidinium benzenesulphonate.* The above cyanide (2.7 g., 1.5 mols.) and *p*-anisidinium benzenesulphonate (4 g., 1 mol.) were heated under reflux for 1.5 hr. at 180°. Cooling and addition of dry acetone (2 c.c.) gave diethylammonium benzenesulphonate which was filtered off and washed with dry acetone (2 c.c.) and dry ether (5 × 5 c.c.) Distillation of the filtrate gave (after a first fraction containing recovered cyanide and *p*-anisidine) *N*-2-cyanoethyl-*p*-anisidine, b. p. 135—140°/0.001 mm., solidifying to white needles.

*Spectroscopic Technique.*—The spectra were obtained with a double-beam infrared spectrometer based on the "optical null" principle, constructed by one of us (R. L. W.), and with sodium chloride optics. Calibration was effected in the usual manner by means of Oetjen, Kao, and Randall's data (*Rev. Sci. Instr.*, 1942, **13**, 515). Solids were examined as mulls in hexachlorobutadiene, and liquids as capillaries or in a 0.050-cm. cell.

*Mass-spectrometric Technique.*—Mass-spectra were measured with a Consolidated 21-103 mass-spectrometer. No spectra were available to check the purity of the diethylamine and *N*-deuterodiethylamine. Both samples contained a small quantity of an unidentified impurity with a peak at mass 86, but it was assumed that this impurity did not interfere with the peaks at masses 72, 73, and 74 used in the analytical calculations. The further assumption was made that the sensitivity (mass-spectrometer deflection per unit of pressure) was the same for the parent peak (73) of  $\text{NHEt}_2$  as for that (74) of  $\text{NDEt}_2$ . The *N*-deuterodiethylamine sample was then found to contain at least 80% of  $\text{NDEt}_2$  and a comparison of the ratio of the 72 and the 73 peak in the  $\text{NHEt}_2$  sample with the 73/74 ratio in the  $\text{NDEt}_2$  sample showed that the impurity in the latter was not  $\text{NHEt}_2$ . Similarly, the  $\text{NEt}_2 \cdot \text{CH}_2 \cdot \text{CHD} \cdot \text{CN}$  was at least 80% pure, although, in this case, the impurity could have been  $\text{NEt}_2 \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CN}$ .

The presumed diethylammonium benzenesulphonate, when treated with sodium hydroxide solution, gave  $\text{NHEt}_2$  with a mass-spectrum almost identical with that of the original sample of diethylamine. The sensitivity of the mass-spectrometer was such that 2% of  $\text{NDEt}_2$  would have been detected if present in this sample. As a further check, the water formed in the reaction of the benzenesulphonate with alkali was examined for deuterium content but none was found. This shows that deuterium could not have been lost from the amine salt by exchange with the water present.

The authors are grateful to Professor C. K. Ingold, F.R.S., for helpful discussion.

(J. C.-C. and M. M.) ORGANIC CHEMISTRY DEPARTMENT, UNIVERSITY OF SYDNEY.

(A. J. C. N.) CHEMICAL PHYSICS SECTION, DIVISION OF INDUSTRIAL CHEMISTRY,  
C.S.I.R.O., MELBOURNE.

(R. L. W.) DEPARTMENT OF PHYSICAL CHEMISTRY,  
N.S.W. UNIVERSITY OF TECHNOLOGY.

[Received, June 3rd, 1955.]