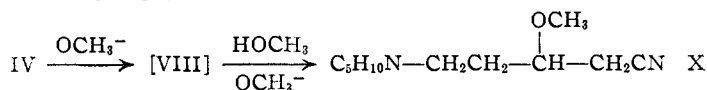


TABLE I

Compound, 1-cyano-2-butenes	Yield, %	B. p., °C.	Mm.	Refract. index, n_D^{20}	Picrate m. p., °C.	Neut. equiv.		Formula	Analyses, %			
						Calcd.	Found		Carbon		Hydrogen	
									Calcd.	Found	Calcd.	Found
4-Piperidino-	82.7	106-109	5	1.4865	130-131	164	164.0	C ₁₀ H ₁₆ N ₂	73.12	72.89	9.82	9.65
4-Morpholino-	89.5	114-119	3	1.4872	174-175	166	165.7	C ₉ H ₁₄ ON ₂	65.03	65.34	8.49	8.32
4-Diethylamino-	80.0	83-95	3	1.4591	90-92	152	154.8	C ₉ H ₁₆ N ₂	71.00	71.14	10.60	10.26
1-Cyanobutanes												
4-Piperidino-	86.2 ^d	106-109	3	1.4659	123-123.5							
4-Morpholino-	80.6 ^d	110-115	3	1.4650	121-121.5							
4-Diethylamino-	46.1 ^d	67-70	8	1.4444								
1-Aminopentanes												
5-Piperidino- ^b	75.5	72-83	3	1.4750	139-140	85	85.0	C ₁₀ H ₂₂ N ₂	70.52	70.99	13.02	12.64
5-Morpholino-	63.0	111-126	5	1.475	144-145	86	86.2	C ₂₁ H ₂₆ N ₂ O ₁₁ ^e	40.00	40.30	4.16	4.27
5-Diethylamino ^c	76.6	106-115	32	1.4485		79	80.8					

^a Hydrochloride derivative m. p. 150-151°. *Anal.* Calcd. for C₁₀H₁₈N₂·HCl: Cl, 17.5. Found: 17.3. ^b Chloroplatinate, m. p. found 221-224° dec. Manasse, *Ber.*, **35** 1370 (1902), reports a m. p. of 228° dec. for this derivative. ^c Magidson and Gregorowsky, *ibid.*, **69B**, 396 (1936). ^d These are the yields obtained by the reaction of 1-cyano-4-chlorobutane with the secondary amine. The yields obtained by the catalytic reduction of the corresponding butenes were 80-90%. ^e This analysis is on the dipicrate derivative.

Methanol added to 1-cyano-4-piperidino-2-butene (IV) in the presence of sodium methylate to give an 80% yield of purified 1-cyano-2-methoxy-4-piperidinobutane (X).



The 1-cyano-1,3-butadiene was prepared both by the pyrolysis of the benzoate of crotonaldehyde cyanohydrin^{9,10} and by the dehydration of butadiene cyanohydrin.¹¹

It was realized during this investigation that the 1-cyano-1,3-butadiene being used must be a mixture of both *cis* and *trans* forms.⁹ However, careful fractionation always resulted in the preferential polymerization of the high refractive index form, leaving as much as 50% of the charge as a non-volatile residue. The material used in the earlier experiments was carefully fractionated and therefore corresponded closely in properties to the substance reported by Snyder, *et al.*,⁹ as the *cis* isomer. In the later experiments a mixture of isomers boiling between fifty and sixty degrees at thirty-five millimeters pressure was used. No apparent difference was noted in the reactions of these two materials with the secondary amines.

Acknowledgment.—We wish to thank Parke, Davis and Company, whose support made this work possible, and the Columbia Chemicals Division of Pittsburgh Plate Glass Company, and in particular Dr. William E. Bissinger, for a generous supply of butadiene cyanohydrin.

Experimental

Reaction of Secondary Amines with 1-Cyano-1,3-butadiene.—In a 500-ml. three-necked flask equipped with mechanical stirrer, thermometer and dropping funnel was placed 67.4 g. (0.85 mole) of 1-cyano-1,3-butadiene (b. p. 50-60° (35 mm.), n_D^{20} 1.4912). While the tem-

perature was maintained at 5-10°, 76.5 g. (0.9 mole) of redistilled piperidine was added. The addition, which was accompanied by an exothermic reaction, required one hour. After remaining for thirty-six hours at 10° the mixture was distilled giving 115.3 g. of product, 82.7% yield. Morpholine and diethylamine underwent reaction in a similar manner. Properties and yields are given in Table I. The reaction was probably complete in two to three hours in the cold but the reaction mixtures were always

stored for a time as indicated above, since this procedure was found to result in better yields in the analogous addition of secondary amines to acrylonitrile.

If an excess of piperidine was employed, the reaction was complicated as indicated in the following experiment. When 0.79 mole of 1-cyano-1,3-butadiene and 3 moles of piperidine were allowed to react essentially as described above, there was obtained 78.2 g. (62.5%) crude yield of 1-cyano-4-piperidino-2-butene as well as 22 g. (12% yield) of crude 1-cyano-2,4-dipiperidinobutane, b. p. 175° (3 mm.), n_D^{20} 1.497, neutral equivalent found (on titration to methyl orange end-point in 50% ethanol) 126.3, calculated 124.5. The picrate derivative, m. p. 151.5-162° was analyzed.

Anal. Calcd. for C₁₆H₂₇N₃: C, 45.83; H, 4.70. Found: C, 45.77; H, 4.64.

Even when an excess of morpholine or diethylamine was employed no diaddition product was isolated.

The Reaction of Secondary Amines with the 1-Cyano-4-substituted-amino-2-butenes.—1-Cyano-4-piperidino-2-butene (IV), 5 g. (0.03 mole), was stirred with piperidine, (0.09 mole), while the solution was refluxed for ten hours. Distillation of the reaction mixture from a Claisen flask gave approximately 3 g. of recovered IV, b. p. 83-94° (2 mm.), n_D^{20} 1.4880-1.4901, and 3.2 g. of 1-cyano-2,4-dipiperidinobutane (VIII), b. p. 174-176° (2 mm.), n_D^{20} 1.4953. Based on IV taken the yield is about 43%; considering recovered IV the yield is quantitative. Similar experiments with morpholine and diethylamine failed to give any addition of the second molecule of the amine. A reaction conducted with morpholine and III in a sealed tube at 120° for eleven hours gave no addition product and 75% of III was recovered.

Several attempts were made to increase the yield by addition of a more strongly basic catalyst. Piperidine, 17 g. (0.20 mole), was mixed with IV, 16.5 g. (0.10 mole), and one drop of Triton B (40% solution of trimethylbenzyl ammonium hydroxide). After the mixture had remained at 10° for five days and at room temperature for one day, it was distilled, giving 11.8 g. (72%) of recovered IV and 2.4 g. (10%) of VIII. The yield, considering recovered starting material, was 33%. The use of either a higher

(10) Gudgeon, Canadian Patent 389,840, Aug. 26 (1941).

(11) Bissinger, *et al.*, THIS JOURNAL, **69**, 2958 (1947).

temperature or more catalyst resulted in lower yields and greatly increased amounts of non-distillable residues.

Although the yields were poor, the use of Triton B as a catalyst made possible the addition of a second molecule of diethylamine or morpholine to II and III, respectively. Thus 15.2 g. of II, 14.6 g. of diethylamine and one drop of Triton B gave 11.6 g. of recovered II, 1.5 g. of the addition product, presumably 1-cyano-2,4-di-(diethylamino)-butane, b. p. 155–160° (0.1 mm.), n_D^{20} 1.4808, and 1.8 g. of residue. Similarly 16.6 g. of III, 17.4 g. of morpholine and one drop of Triton B gave 3.3 g. of the addition product (presumably 1-cyano-2,4-dimorpholinobutane), b. p. 195–200° (0.6 mm.), n_D^{20} 1.5124 as a viscous yellow oil and the remainder was a non-distillable polymer. Crystalline picrates could not be prepared of either of these two addition compounds and they undoubtedly were impure.

1-Cyano-2-methoxy-4-piperidinobutane.—Into a mixture of 14.2 g. (0.44 mole) of absolute methanol and 0.8 g. (0.015 mole) of sodium methylate in a 100-ml. flask was dropped 16.4 g. (0.10 mole) of 1-cyano-4-piperidino-2-butene over a thirty-minute period; there was no appreciable evolution of heat. The reaction mixture was stirred for two hours, allowed to remain at room temperature for ten hours and worked up by neutralization of the base with 0.4 ml. (0.0075 mole) of concentrated sulfuric acid, filtration and distillation. After the alcohol was removed, only one material distilled, b. p. 152–153° (3 mm.), n_D^{20} 1.4683, 15.7 g. (80%). The picrate, m. p. 143.0–143.5°, was analyzed.

Anal. Calcd. for $C_{17}H_{22}N_2O_3$: C, 48.00; H, 5.45. Found: C, 48.30; H, 5.49.

Preparation of the 1-Cyano-4-substituted-aminobutanes.—The products from the addition of piperidine, morpholine and diethylamine to 1-cyano-1,3-butadiene were each reduced catalytically in ethanol solvent under three atmospheres pressure of hydrogen in the presence of Adams catalyst. At room temperature absorption of hydrogen proceeded only until one mole was absorbed. The boiling points and refractive indices of these products agreed very closely to the corresponding properties of the same products made from 1-chloro-4-cyanobutane and the respective secondary amine as indicated below. The picrates of the products made by these two different methods melted at the same temperatures (see Table I) and these melting points were undepressed by mixing. A mixture melting point of the picrate of 1-cyano-4-morpholinobutane (m. p. 120.5–121.5°) and picric acid (m. p. 122°) was greatly depressed, as was also the melting point of a mixture of 1-cyano-4-piperidinobutane (m. p. 122.5–123.5°) and picric acid.

1-Cyano-4-substituted-aminobutanes from 1-Cyano-4-chlorobutane.—Piperidine, morpholine and diethylamine were refluxed with δ -chlorovaleronitrile¹² in dry benzene as already described for the next lower homolog.¹³ The yields and properties are given in Table I.

Reduction of 1-Cyano-4-substituted-aminobutanes to the Corresponding 5-Substituted Amino-1-aminopentanes.

(12) Starr and Hixon, *THIS JOURNAL*, **56**, 1595 (1934).

(13) Whitmore, Mosher, *et al.*, *ibid.*, **66**, 725 (1944).

—The products resulting from the addition of the secondary amines to 1-cyano-1,3-butadiene were catalytically reduced in absolute alcohol solvent which was saturated with ammonia. The reductions were conducted with initial hydrogen pressures of 2000 p. s. i., temperatures of 90–100°, and in the presence of Raney nickel catalyst. The properties of the resulting 5-amino-1-aminopentanes are given in Table I.

2-Methoxy-6-chloro-9-(ϵ -piperidinoamyl)-aminoacridine.—The 5-piperidino-1-aminopentane, 8.5 g. (0.05 mole), from the above reduction was added to a mixture of 6,9-dichloro-2-methoxyacridine, 13.9 g. (0.05 mole), in 60 g. of phenol. After three hours of heating on the steam-bath, the mixture was poured into 500 ml. of 2 *N* sodium hydroxide, and extracted with 500 ml. of chloroform in three portions. The chloroform extracts were shaken with 10% acetic acid and the acetic acid extracts treated with ammonium hydroxide. A yellow oil separated which was converted to the hydrochloride by dissolving in absolute ethanol and bubbling in dry hydrogen chloride gas. The product was twice crystallized from ethanol; 11 g., m. p. 237–238°.

Anal. Calcd. for $C_{24}H_{33}ON_2Cl_2$: N, 8.06. Found: N, 7.98.

A mixture melting point with this material and the product made in the same manner, from 5-piperidino-1-aminopentane prepared by another method,¹⁴ was undepressed.

Summary

1. Three secondary amines, piperidine, morpholine and diethylamine, have been shown to react with 1-cyano-1,3-butadiene to give 1-cyano-4-amino-2-butenes in good yields.

2. A second molecule of the secondary amine will react in the presence of an added basic catalyst to give 1-cyano-2,4-diaminobutenes but with more difficulty.

3. The 1-cyano-4-amino-2-butenes may be reduced catalytically either to 1-cyano-4-aminobutanes or to ϵ -aminoamylamines.

4. In the presence of sodium methylate, methyl alcohol will add to 1-cyano-4-piperidino-2-butene to give 1-cyano-2-methoxy-4-piperidinobutane. These reactions offer possibilities of synthesizing various di-functional derivatives of valeronitrile and amylamine which are otherwise very difficultly accessible.

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(14) E. C. Chapin, Ph.D. Thesis, The Pennsylvania State College, Oct. 1944, p. 98. The melting point reported here was 140° but this particular sample was found to melt at 237–238° when the melting point was redetermined at a later date.