from ethanol or benzene gave a product that softened at 133° and melted at 142–144°. When the melt was allowed to solidify, the new m.p. was 146–147°. These interconversions were reproducible.

Anal. Calcd. for $C_{14}H_8N_4O_2$: C, 63.63; H, 3.05. Found: C, 63.59; H, 3.26.

N-(*p*-Azidophenyl)-phthalimide.—Owing to the insolubility of the salts of N-(*p*-aminophenyl)-phthalimide with common acids, resort was made to isethionic acid (2-hydroxyethanesulfonic acid) in the diazotization procedure. A solution of this acid was prepared from 51 g. of commercial sodium isethionate, which was first freed from sulfate by filtering its hot solution in 400 ml. of 95% ethanol and 50 ml. of water through a layer of Celite. The addition of 700 ml. of absolute ethanol to the ice-cooled filtrate precipitated 44 g. of product which did not give a precipitate with barium chloride. A water solution of the sulfate-free salt was then passed through a column containing 150 g. of 20–30 mesh Dowex ion-exchange resin in the acid form. The effluent solution, approximately 0.29 *N*, was used directly in the diazotization.

To a slurry prepared from 16.9 g. (0.0712 mole) of finely powdered N-(*p*-aminophenyl)-phthalimide and 500 ml. of water was added 365 ml. of 0.29 *N* isethionic acid; much of the salt formed precipitated. After 15 minutes of stirring, the mixture was cooled to 0–5° and diazotized by the addition of 5.4 g. of sodium nitrite in water. After 5 hours of stirring at 0–5° the salt had dissolved, leaving only a small amount of a finely divided solid. The filtered solution was treated with a solution of 5.1 g. of sodium azide, in the presence of a little ether to reduce foaming. When gas evolution ceased, the ether was evaporated in an air stream, and after a further 20 minutes the precipitated azide was collected and washed with water; wt. 17.0 g. (90%), m.p. 187° dec. An analytical sample recrystallized from benzene had m.p. 190° dec.

Anal. Calcd. for $C_{14}H_8N_4O_2$: C, 63.63; H, 3.05. Found: C, 63.61; H, 3.11.

***o*-Azidoaniline.**—A slurry of 19.6 g. (0.0742 mole) of powdered N-(*o*-azidophenyl)-phthalimide in 200 ml. of 95% ethanol was stirred with 3.72 g. (0.0742 mole) of hydrazine hydrate for 90 minutes, whereupon 100 ml. of water followed by 30 ml. of 20% sodium hydroxide solution was added. Most of the solid dissolved in a few minutes; filtration gave 0.35 g. of unreacted starting material. Dilution of the filtrate with 2 l. of water and chilling in ice precipitated 4.4 g. of *o*-azidoaniline, m.p. 61–63°. The mother liquors yielded a further 1.3 g., m.p. 56–69°, by extraction with ether; total yield 57%. Several recrystallizations from aqueous methanol gave an analytical sample, m.p. 63–63.5°. *o*-Azidoaniline decomposes to an intensely red substance at about 65°; consequently, all operations in its preparation and purification must be carried our at mild temperatures.

Anal. Calcd. for $C_6H_6N_4$: C, 53.72; H, 4.51. Found: C, 53.79; H, 4.58.

***m*- and *p*-azidoanilines** were prepared from the corresponding azidophenylphthalimides by procedures essentially similar to that described for the *o*-isomer. *p*-Azidoaniline was obtained in 46% yield and had m.p. 65–66° (reported[24] m.p. 65°); it turns dark red at its melting point. *m*-Azidoaniline was obtained as an oil from its ether solution in 47% yield, b.p. 76° (0.6 mm.), 70° (0.4 mm.), $n^{21}\text{D}$ 1.6251. Its preparation has been reported,[25] but neither properties nor analysis were given.

Anal. Calcd. for $C_6H_6N_4$: C, 53.72; H, 4.51. Found: C, 53.79; H, 4.56.

Azidobenzoic Acids.—*o*-, *m*- and *p*-azidobenzoic acid were prepared from the corresponding aminobenzoic acids by diazotization and coupling to sodium azide[26]; the samples used were purified by repeated recrystallization from aqueous ethanol.

Ionization Constants of Azidoanilines and Azidobenzoic Acids.—Samples of approximately 0.0015 mole of the benzoic acids were accurately weighed, dissolved in a mixture of 100 ml. of methanol and 100 ml. of water, and titrated with 0.03721 *N* aqueous sodium hydroxide, using a Beckman model G *p*H meter. The apparent ionization constants were determined from the *p*H at the half-neutralization points, at which the solvent composition was 45.4 ±0.2% methanol by volume, taking $pK_w = 14.00$. Three determinations were made for each acid, and the average for each is reported in Table I; the average deviations of pK_a were 0.03 or less. The neutralization equivalents were from 163.3 to 164.3 (calcd. 164.1).

Samples of approximately 0.0017 mole of the anilines were treated similarly, using 0.04429 *N* hydrochloric acid for titration. The solvent composition at the half neutralization point was 45.4 ± 0.4%, and the average deviation of pK_b among determinations was 0.02 or less. The average value for each compound is given in Table II.

---

[24] P. Griess, *Ber.*, **21**, 1559 (1888).

[25] P. Griess, *ibid.*, **18**, 963 (1885).

[26] K. A. N. Rao and P. R. Venkataraman, *J. Indian Chem. Soc.*, **15**, 201 (1938).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA 4, PENNA.]

A Crystalline Hexamer from Acrylonitrile

BY NAOMITSU TAKASHINA[1] AND CHARLES C. PRICE

RECEIVED AUGUST 21, 1961

In the presence of several alcohols, triphenylphosphine has been found to catalyze the conversion of acrylonitrile to a crystalline hexamer, m.p. 240°, which has been shown to be identical with the cyanoethylation product of 1,4-dicyano-*trans*-2-butene and is assigned the structure of 1,1,4,4-tetra-(2-cyanoethyl)-1,4-dicyano-*trans*-2-butene (I). The corresponding acid and methyl and ethyl esters have been prepared and characterized.

In view of the stereoregular polymerization of vinylic compounds containing electron-donating groups by a wide variety of Lewis acids, the corresponding possibility of stereoregular coördination polymerization of vinylic compounds containing electron-withdrawing groups by hindered Lewis bases seemed worthy of investigation. While this objective has not been achieved in experiments described herein, we have obtained a new crystalline hexamer of acrylonitrile.

Experimental[2]

1,1,4,4-Tetracyanoethyl-1,4-dicyano-*trans*-2-butene (I). A. From Acrylonitrile Polymerization.—A mixture of 16 g. of acrylonitrile, 0.4 g. of triphenylphosphine and 5 ml. of ethanol was sealed under nitrogen and heated in the dark at 80° for 2-4 weeks. The resulting mixture of crystals and viscous brown oil was extracted with acetone. The insoluble crystals were recrystallized from dimethylformamide (DMF)-ethanol (or acetonitrile); 4.5 g. (28%), m.p. 240°.

Anal. Calcd. for C_3H_3N: C, 67.90; H, 5.69; N, 26.40. Found: C, 68.04; H, 6.17; N, 26.36.

---

[1] Supported in part by a grant from the General Tire and Rubber Co.

[2] Analyses by Midwest Microlab, Inc., Indianapolis, Ind., and Galbraith Laboratories, Knoxville, Tenn. All m.p.'s are uncorrected.

From the acetone by distillation, 6 g. (71% based on ethanol) of **β-ethoxypropionitrile** was isolated, b.p. 77–77.5° (25 mm.), $n^{24.5}_D$ 1.4070 (lit.[3] b.p. 77–78° (25 mm.), n^{20}_D 1.4068).

Recrystallization of the distillation residue produced a small amount of **triphenylphosphine oxide**, m.p. 154–155°.

The yields of hexamer obtained in a number of other experiments are summarized in Tables I and II.

TABLE I

FORMATION OF $(C_3H_3N)_6$ IN THE PRESENCE OF ETHANOL AT 80° FOR 18 DAYS

Acrylonitrile, ml.[a]	Ethanol, ml.	$(C_6H_5)_3$, g.	Yield of $(C_3H_3N)_6$, g.
20	5	0.4	3.0, 3.5[b]
15	10	.4	1.5
10	15	.4	Trace
20	5	.8	4.0
10	15	.8	3.0
20	1	.4	3.5, 3.7[c]

[a] d^{20} = 0.81. [b] After 25 days. [c] After 22 days.

TABLE II

FORMATION OF $(C_3H_3N)_6$ IN THE PRESENCE OF ALCOHOLS OTHER THAN ETHANOL

Temp., °C.	Time, days	Acrylonitrile,[a] ml.	Alcohol, ml.	Yield of $(C_3H_3N)_6$, g.
80	5	20	5 (methyl)	None
80	18	20	5 (methyl)	Trace
80	30	20	5 (isopr.)	5.0
80	22	20	5 (*n*-hexyl)	4.3
25	30	10	10 (*t*-butyl)	None
80	30	20	5 (*t*-butyl)	3.85

[a] Each reaction contained 0.4 g. of triphenylphosphine.

B. Cyanoethylation of 1,4-Dicyano-*trans*-2-butene.—The reaction of 1,4-dibromo-*trans*-2-butene (m.p. 54°[4]) with cuprous cyanide in acetonitrile produced the corresponding dinitrile in 48% yield, m.p. 75.5–76°,[5] a considerable improvement over the yield using sodium cyanide in ethanol.[6]

When 200 mg. of 40% Triton B solution in 10 ml. of *t*-butyl alcohol was added to 1 g. of the dinitrile, 10 ml. of acrylonitrile and 10 ml. of *t*-butyl alcohol, crystals formed immediately. Recrystallization from DMF–ethanol yielded 2.2 g. (73%) of hexamer, m.p. 240°. A similar experiment using 0.5 ml. of 20% potassium hydroxide as base gave 2.3 g. and the results of a number of cyanoethylations using triphenylphosphine as base are summarized in Table III.

TABLE III

FORMATION OF $(C_3H_3N)_6$ FROM 1,4-DICYANO-*trans*-2-BUTENE AT ROOM TEMPERATURE

$(C_6H_5)_3P$, g.	1,4-Dicyano-*trans*-2-butene, g.	Acrylonitrile,[a] ml.	Time, days	Yield of $(C_3H_3N)_6$, g.
0.10	1.00	10	1	0.54
.10	1.00	10	2	1.40
.10	1.00	10	5	1.58
.10	1.00	10	10	1.64
.10	2.00	10	10	2.44
.20	1.00	10	10	1.70
.20	2.00	10	10	2.76
.10	None	10	10	None (clear)[b]
.20	1.00	25	10	2.10
.20	1.00	25	15	2.13
.20	None	25	15	None (clear)[b]

[a] All reaction mixtures also contained 10 ml. of *t*-butyl alcohol. [b] On standing for longer than 15 days in diffuse daylight, these control samples began to precipitate fluffy, amorphous polyacrylonitrile.

Hexacrylic Acid (II).—Refluxing I with concentrated hydrochloric acid or 10% alkali overnight gave the corresponding acid in 98 and 68% yields, respectively. The acid could be recrystallized from dioxane–benzene or small volumes of water; m.p. 236–237°.

Anal. Calcd. for $(C_3H_4O_2)_6$: C, 50.02; H, 5.53; neut. equiv., 72. Found: C, 50.21; H, 5.91; neut. equiv., 74.

Methyl hexacrylate (III) was prepared by conventional esterification in 67% yield. It crystallized from ether–petroleum ether as needles, m.p. 66°. The molecular weight was measured cryoscopically in camphor (506, 475) and exaltone (533, 521) and ebullioscopically in benzene (536) and carbon tetrachloride (503). These values all are in satisfactory agreement with that expected for a hexamer of methyl acrylate (516).

Anal. Calcd. for $(C_4H_6O_2)_6$: C, 55.83; H, 6.97. Found: C, 55.76; H, 7.09.

Ethyl hexacrylate was an oil, b.p. 269–270° (1.4 mm.), n^{25}_D 1.4682.

Anal. Calcd. for $(C_5H_8O_2)_6$: C, 59.98; H, 8.00. Found: C, 60.19; H, 8.12.

1,2-Dicyanocyclobutane, b.p. 95–97° (1 mm.), n^{25}_D 1.4628, was prepared in 2% yield by the procedure of Coyner and Hillman.[6] Attempted cyanoethylation under the same conditions used successfully on the isomeric unsaturated dinitrile (see Table III) gave no crystalline hexamer, even after 7 days.

Polyacrylonitrile.—Addition of 0.4 ml. of **triethylphosphine**,[7] b.p. 127–128°, in 10 ml. of petroleum ether to a solution of 20 ml. of acrylonitrile in 50 ml. of benzene, cooled in a Dry Ice–acetone-bath,[8] gave a quantitative yield of amorphous white polymer. In contrast to ordinary polyacrylonitrile, this polymer turned yellow immediately in air and gradually darkened further to reddish-brown.

Triethylarsine[9] failed to catalyze the polymerization of acrylonitrile even at 75°.

A solution of 0.4 g. of **triphenylphosphine** in 20 ml. of acrylonitrile was sealed and heated at 70°. In a few days, an oil separated at the bottom. After 2 weeks the contents had solidified in upper opaque and lower transparent resins. On dissolution in DMF and reprecipitation from methanol, the upper part gave 8.5 g., the lower 3–4 g. of amorphous polyacrylonitrile.

Experiments on polymerization with the arsenic, antimony and bismuth analogs are summarized in Table IV.

TABLE IV

POLYMERIZATION OF ACRYLONITRILE (20 ML. AND 5 ML. OF ETHANOL) AT 25° WITH VARIOUS CATALYSTS

Catalyst, g.	Time, days	Yield, g.	$[\eta]$[a]
$(C_6H_5)_3As$[b]			
0.468	18[c]	Trace	...
0.450		3.0	0.326
$(C_6H_5)_3Sb$[b]			
0.54	18[c]	0.630	0.294
0.54		4.1	...
$(C_6H_5)_3Bi$[b]			
0.622	3	0.632	...
0.768	3	0.757	0.262
1.129	3	1.116	...
0.622	3	Trace[d]	...
0.673	60	None[e]	...

[a] Intrinsic viscosity in dl./g. in dimethylformamide at 25°. [b] From Distillation Products, Inc., Rochester, N. Y. [c] These two samples did not polymerize for 45 days at 80° in darkness. When they were taken out to diffused light, they started polymerizing soon and were left for an additional 30 days. [d] Kept in total darkness. [e] Contained 0.1 g. of hydroquinone and kept in total darkness.

---

[3] W. P. Utermohlen, *J. Am. Chem. Soc.*, **67**, 1505 (1945).

[4] L. N. Owen, *J. Chem. Soc.*, 243 (1949).

[5] W. Reppe, *et al.*, *Ann.*, **596**, 133 (1956).

[6] E. C. Coyner and W. S. Hillman, *J. Am. Chem. Soc.*, **71**, 324 (1949).

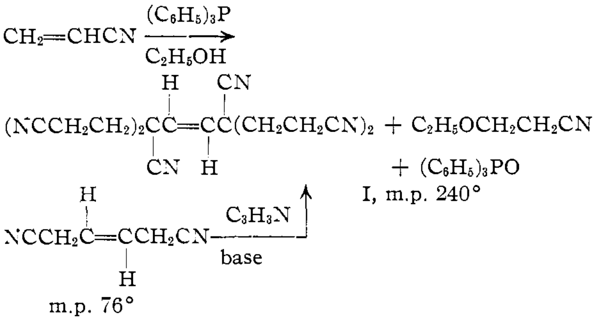
[7] H. Hibbert, *Ber.*, **39**, 161 (1906).

[8] The reaction was violent at room temperature.

[9] W. Steinkopf and J. Mueller, *Ber.*, **54B**, 844 (1921).

Discussion

While the polymerization of acrylonitrile in the presence of triphenylphosphine produces amorphous high polymer, in the presence of ethanol (and other alcohols), the principal products of the reaction are a high-melting, insoluble hexamer, the addition product of alcohol to acrylonitrile and a small amount of triphenylphosphine oxide.



$$CH_2{=}CHCN \xrightarrow[C_2H_5OH]{(C_6H_5)_3P} (NCCH_2CH_2)_2C\underset{CN}{\overset{H}{C}}{=}\underset{H}{\overset{CN}{C}}C(CH_2CH_2CN)_2 + C_2H_5OCH_2CH_2CN + (C_6H_5)_3PO$$

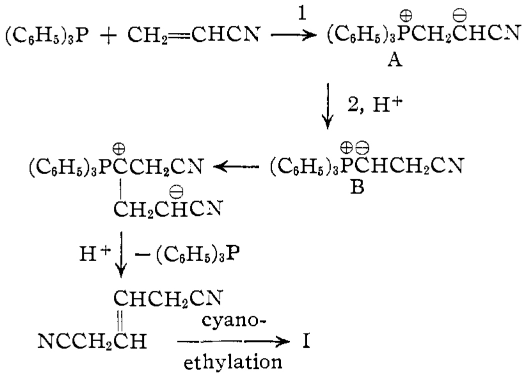
$$NCCH_2\overset{H}{C}{=}\underset{H}{C}CH_2CN \xrightarrow[\text{base}]{C_3H_3N} \text{I, m.p. } 240°$$

m.p. 76°

This new hexanitrile, for which we suggest the trivial name of hexacrylonitrile, readily was converted to the corresponding hexacrylic acid II, m.p. 237°, and esters.

The structure we propose is based on (a) the synthesis of the compound in good yield from cyanoethylation of 1,4-dicyano-*trans*-2-butene, (b) molecular weight measurements on the methyl hexacrylate, (c) the infrared spectra which showed no functional group other than the nitrile band at 4.44μ, and (d) a preliminary analysis of the X-ray pattern, which indicated that the molecule must have a center of symmetry.[10]

The mechanism of the formation of I presents an interesting problem since one pair of acrylonitrile units must unite in a head-to-head manner. Normally, this would appear to be unlikely in a conventional base-catalyzed polymerization. However, for triphenylphosphine, by invoking a phosphorus ylid intermediate, we can propose a sequence of reactions.



$$(C_6H_5)_3P + CH_2{=}CHCN \xrightarrow{1} (C_6H_5)_3\overset{\oplus}{P}CH_2\overset{\ominus}{C}HCN \ \text{(A)}$$

$$\text{A} \xrightarrow{2,\ H^+} (C_6H_5)_3\overset{\oplus}{P}\overset{\ominus}{C}HCH_2CN \ \text{(B)}$$

$$\text{B} \longrightarrow (C_6H_5)_3\overset{\oplus}{P}\underset{CH_2\overset{\ominus}{C}HCN}{C}CH_2CN \xrightarrow{H^+,\ -(C_6H_5)_3P} NCCH_2CH{=}CHCH_2CN \xrightarrow[\text{ethylation}]{\text{cyano-}} \text{I}$$

Addition of acrylonitrile to A would produce normal high polymer, as was observed in the absence of ethanol. The proton migration (step 2) would be promoted by a protolytic solvent like ethanol. The stability of a carbanion in an ylid such as B is enhanced not only by the adjacent positive charge but by the possibility of accommodation of the electron by bonding overlap with unfilled 3d-orbitals on the phosphorus.

Since Coyner and Hillman[6] have reported a cyclic dimer of acrylonitrile, 1,2-dicyanocyclobutane, we have prepared a sample and attempted to convert it to I, but without success.

---

(10) X-Ray diffraction analysis was carried out independently by Dr. R. E. Hughes (University of Pennsylvania) and Dr. R. R. Pfeiffer (Eli Lilly and Co.). They found the space symmetry to be $P2_1/a$, the dimension of the unit cell to be a_0 = 15.53 Å., b_0 = 6.46 Å., c_0 = 9.12 Å. and β = 107.5°, and the density 1.20. This requires that there be twelve acrylonitrile units (or two hexamer molecules) per unit cell. Details of this work will be published elsewhere by Dr. R. E. Hughes.

COMMUNICATIONS TO THE EDITOR

CONFORMATIONAL CHANGES ACCOMPANYING AN ENZYME CATALYZED REACTION[1]

Sir:

We wish to report that the catalytic reaction of α-chymotrypsin with diisopropylphosphorofluoridate or *p*-nitrophenyl acetate is accompanied by conformational changes of the enzyme. These conformational changes may have a pronounced effect on the activation of the substrate and therefore make a major contribution to the velocities observed in the enzymatic reactions.[2] Since the hydrolysis of specific substrates for α-chymotrypsin most probably involves the same mechanism as the hydrolysis of *p*-nitrophenyl acetate,[3] this report is of interest for an understanding of α-chymotrypsin catalysis. To our knowledge, conformational changes which accompany a reaction catalyzed by an enzyme consisting of amino acids only, have not been reported previously.

Earlier studies[4-8] demonstrated that the catalytic reaction of α-chymotrypsin with either diisopropylphosphorofluoridate or *p*-nitrophenyl acetate is accompanied by spectral changes of the enzyme. These spectral changes are intimately related to the formation of diisopropylphosphoryl-α-chymo-

---

(1) This research was supported by grants from the National Institutes of Health and the National Science Foundation.

(2) R. Lumry and H. Eyring, *J. Phys. Chem.*, **58**, 110 (1954); H. Eyring, R. Lumry, and J. D. Spikes in "The Mechanism of Enzyme Action," W. D. McElroy and B. Glass, Eds., The Johns Hopkins Press, Baltimore, Md., 1954, p. 123.

(3) T. Spencer and J. M. Sturtevant, *J. Am. Chem. Soc.*, **81**, 1874 (1959); H. Gutfreund and B. R. Hammond, *Biochem. J.*, **73**, 526 (1959); M. L. Bender and B. Zerner, *J. Am. Chem. Soc.*, **83**, 2391 (1961).

(4) G. P. Hess and J. F. Wootton, *Fed. Proc.*, **19**, 340 (1960).

(5) J. F. Wootton and G. P. Hess, *Nature*, **188**, 4752 (1960).

(6) J. F. Wootton and G. P. Hess, *J. Am. Chem. Soc.*, **83**, 4234 (1961).

(7) J. F. Wootton and G. P. Hess, *ibid.*, **84**, 440 (1962).

(8) B. H. Havsteen and G. P. Hess, *ibid.*, **84**, 448 (1962).