Electrolytic Reductive Coupling. VIII.[1] Utilization and a New Preparation of α-Methyleneglutaronitrile

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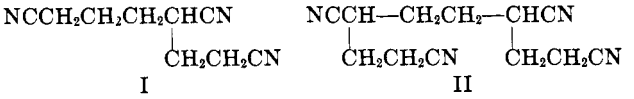
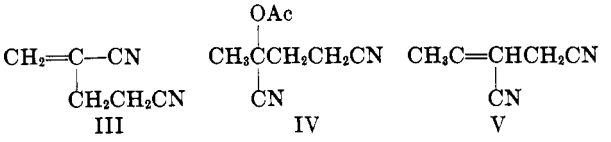
α-Methyleneglutaronitrile (III) has been electrolytically hydrodimerized to yield 1,3,6,8-tetracyanooctane (II). Electrolysis of a mixture of III and acrylonitrile yielded II and adiponitrile—the two hydro dimers—and 1,3,6-tricyanohexane, the product of mixed coupling. III and higher oligomers of acrylonitrile have been prepared by the reaction of acrylonitrile with catalytic quantities of tertiary phosphines in the presence of proton donors.

The formation of the new nitriles, 1,3,6-tricyanohexane (I) and 1,3,6,8-tetracyanooctane (II), during the



electrolysis of acrylonitrile in the presence of a limited amount of proton donor has been described. These nitriles are also formed in very small yield in the electrolytic adiponitrile (ADN) process. In order to provide for the potentially useful intermediates I and II a route that would be independent of ADN production we undertook electrolytic reductive coupling experiments with α-methyleneglutaronitrile [III, α-(2-cyanoethyl)-acrylonitrile].

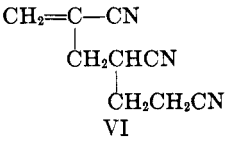


Electrolyses with α-Methyleneglutaronitrile (III).—III was found to undergo reduction on a mercury cathode at about the same cathode voltage (−1.8 to −1.9 v. *vs.* s.c.e.) as is needed for acrylonitrile reduction (*ca.* −1.9 v.). Hydrodimerization of III gave a 93% current yield of II, mainly as one diastereoisomer, m.p. 119°. The tetraethyl ester prepared from II was identical with a sample previously prepared by an independent synthesis.[1]

Mixed reductive coupling of III with an equimolar quantity of acrylonitrile (AN) yielded the expected three products: ADN, I, and II.

Synthesis of α-Methyleneglutaronitrile (III) from Acrylonitrile.—The search for a convenient synthesis of III led to the discovery of a new procedure for oligomerizing AN.[2] It has been claimed[3] that III and V are formed upon pyrolysis of the acetate of levulinonitrile cyanohydrin (IV), although Kurtz, *et al.*,[4] report that under apparently identical conditions this reaction leads to only V.[5] The need for repeated fractionation[3] of the mixture of isomers in order to obtain pure III was not attractive. Rauhut and Currier[6] disclose that treatment of ethyl acrylate with a catalytic quantity of tributylphosphine in acetonitrile yields the dimer diethyl α-methyleneglutarate. An attempt to apply this procedure to AN led to vigorous polymerization at the distillation stage. Since we had found previously[1] that it requires more proton donor to arrest acrylonitrile electrolytic coupling at the hydro trimer and hydro tetramer stage than to arrest multiple ethyl acrylate reductive couplings, we modified, for acrylonitrile oligomerization, Rauhut and Currier's acrylate ester procedure by incorporating more acidic proton donors in the reaction mixture.

Addition of stabilized acrylonitrile to a solution of tributylphosphine[7] in acetonitrile containing water or *t*-butyl alcohol followed by separation of the phosphorus compounds before isolation of the products yielded the dimer III, the trimer VI, and a benzene-insoluble



tar from which higher oligomers[8] could undoubtedly be isolated after the development of suitable isolation procedures. The variation in yield of III with change of catalyst and proton donor concentration is shown in Table I.

III was hydrolyzed to the known α-methyleneglutaric acid and catalytically reduced to α-methylglutaronitrile.[9] The latter was purer than a reference prepared according to Zahn and Schäfer's three-step synthesis from ethyl α-cyanopropionate.[11] Catalytic reduction of VI yielded a saturated trinitrile for which boiling point, refractive index, and elemental analysis indicated agreement with 1,3,5-tricyanohexane prepared by the above workers in a six-step synthesis from malonic ester.[12]

(1) Paper VII: M. M. Baizer and J. D. Anderson, *J. Org. Chem.*, **30**, 1351 (1965).

(2) After this work was completed P. Charardes, C. Grard, P. Lafont, and M. Thiers [French Patent 1,366,081 (June 1, 1964)] described a procedure for preparing α-methyleneglutaronitrile from AN and tertiary phosphines.

(3) M. Tanaka, *et al.*, *Kogyo Kagaku Zasshi*, **62**, 1786 (1959); *Chem. Abstr.*, **57**, 13972*i* (1962).

(4) P. Kurtz, H. Schwarz, and H. Disselnkotter, *Ann.*, **631**, 21 (1960).

(5) Kurtz's reduction of his product to α-methylglutaronitrile does not, of course, distinguish between structures III and V.

(6) M. Rauhut and H. Currier (to American Cyanamid), U. S. Patent 3,074,999 (Jan. 22, 1963).

(7) L. Horner, W. Jurgeleit, and K. Klupfel [*Ann.*, **591**, 108 (1955)] obtained relatively high molecular weight polymers on treatment of acrylonitrile with triethylphosphine in anhydrous media and tars in the presence of water.

(8) From several of the experiments yellow solids were isolated which after recrystallization from dimethylformamide–ethanol decomposed at *ca.* 185–200°, 220–230°. The structure of these oligomers has not been determined.

(9) This provides a formal route from acrylonitrile to nicotinic acid *via* reductive deamination and ring closure of α-methylglutaronitrile to 3-methylpiperidine,[4] dehydrogenation to 3-picoline,[10] etc.

(10) H. Adkins and L. G. Lunsted, *J. Am. Chem. Soc.*, **71**, 2964 (1949).

(11) H. Zahn and P. Schäfer, *Chem. Ber.*, **92**, 736 (1959).

(12) An alternate synthesis yielding a product of b.p. 195–196° (2.5 mm.), $n^{25}D$ 1.4609, is reported by T. Takata, *et al.* [*Chem. High Polymers* (Tokyo), 693 (1959)].

TABLE I

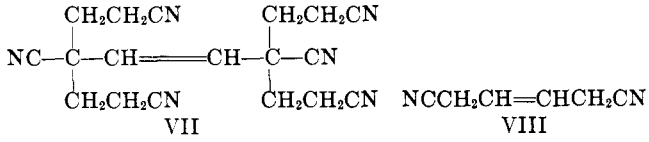
PREPARATION OF α-(2-CYANOETHYL)ACRYLONITRILE FROM ACRYLONITRILE

Expt. no.	AN, moles	Phosphine (moles)	Acetonitrile, ml.	Other proton source (moles)	Reactn. temp., °C.	Reactn. time, hr.	CEAN,[a] g.	Remarks
1	0.94	Bu_3P (0.005)	30	...	45–50	1	4.0	
2	0.94	Bu_3P (0.005)	35	H_2O (0.056)	45–50	1	~4.0	
3	0.94	Bu_3P (0.005)	70	H_2O (0.28)	45–50	1	4.3	
4	0.94	Bu_3P (0.005)	35	*t*-BuOH (0.28)	45–50	1	5.1	
5	0.94	Bu_3P (0.005)	110	H_2O (0.56)	45–50	1	4.8	
6	0.94	Bu_3P (0.005)	35	*t*-BuOH (0.56)	45–50	1	5.3	
7	0.94	Bu_3P (0.015)	35	*t*-BuOH (0.56)	45–50	1	7.0	
8	9.4	Bu_3P (0.15)	350	*t*-BuOH (5.6)	45–50	2	54.3	
9	0.94	Ph_3P (0.005)	60	...	78	19	...	
10	0.94	Ph_3P (0.019)	0.4	...	78	19	...	Polymer obtained
11	0.94	Ph_3P (0.019)	3	...	78	19	...	Polymer obtained
12	0.94	Ph_3P (0.019)	10	...	78	5	0.3	No polymer

[a] α-(2-Cyanoethyl)acrylonitrile.

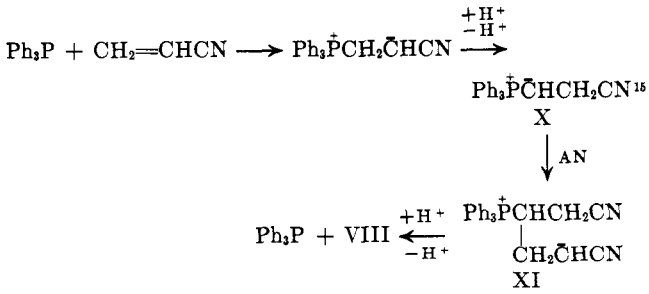
Oligomerization of AN with triphenylphosphine was more sluggish than with tributylphosphine. An experiment whose conditions were intermediate in severity between those which yielded no products at all and those which yielded solid polymers afforded a small yield of III (expt. 12, Table I).

The above dimerizations of AN to α-methyleneglutaronitrile like Rauhut and Currier's formation of diethyl α-methyleneglutarate from ethyl acrylate yield products which are the result of α to β coupling of monomers. In the former case *our* findings are in apparent contradiction to the report[13] that under specified conditions triphenylphosphine (with ethanol) converts AN to a hexamer VII presumably *via* the intermediate 1,4-dicyano-2-butene (VIII), a product of β to β coupling.



VII VIII

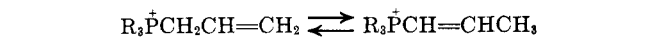
To rationalize the postulated intermediacy of VIII,[14] Takashina and Price[13] proposed essentially the following transformations.



(13) N. Takashina and C. C. Price, *J. Am. Chem. Soc.*, **84**, 489 (1962).

(14) Takashina and Price[13] did obtain VII by cyanoethylation of VIII.

(15) While P. T. Keough and M. Grayson [*J. Org. Chem.*, **29**, 631 (1964)] have recently reported the base-catalyzed rearrangement of allyltriphenylphosphonium salts to propenyltriphenylphosphonium salts, indicating that



phosphonium has an "acidifying effect" upon adjacent methylene, no data are available on the relative "acidifying effect" of triphenylphosphonium *vs.* -CN. An attempt to determine these relative effects by electrolytic reductive coupling of $R_3\dot{P}CH{=}CHCN$ with a suitable acceptor is planned.

These questions then presented themselves: (a) are *both* IX and X formed? (b) are IX and X in equilibrium? (c) can X, a "homo-ylid", be intercepted by reaction with *p*-nitrobenzaldehyde?[16] (d) can X undergo a Michael reaction with suitable acceptors?[17] (e) does XI, if formed, indeed collapse to VIII? (f) can another rational pathway be formulated leading from IX to both III and VII *via* a common intermediate? Experimental answers were found to some of these questions by studying the relatively slow reaction of triphenylphosphine[18] with acrylonitrile and with ethyl acrylate in more detail.

Aliquots of a stock solution containing AN, *t*-butyl alcohol, and triphenylphosphine were kept at 45° under nitrogen and analyzed over various intervals during a reaction time of 198 hr. There were identified: (a) α-methyleneglutaronitrile (III); (b) *cis*- and *trans*-1,4-dicyano-1-butene (XII); and (c) VII, the AN hexamer. III and XII were formed at about the same rate initially[19]; the concentration of the latter species fell off as the formation of hexamer (VII) increased (see Figure 1). No 1,4-dicyano-2-butene (VIII) was found.[20] It would then appear that XI, if formed, collapses to XII rather than to VIII and that the hexamer is formed by cyanoethylation of XII.[21,22] No product of a Wittig reaction was isolated from a mixture of triphenylphosphine, AN, *p*-nitrobenzaldehyde, and *t*-butyl alcohol kept under conditions suitable for yielding AN dimers in the absence of the aldehyde.[16]

(16) A. J. Speziale and D. Bissing, *J. Am. Chem. Soc.*, **85**, 3878 (1963). Since our work was completed R. Oda, T. Kawabata, and S. Tanimoto [*Tetrahedron Letters*, 1653 (1964)] have reported moderate yields of Wittig products from X and benzaldehyde.

(17) J. P. Freeman [*Chem. Ind.* (London) 1254 (1959)] reports addition of triphenylphosphinemethylene to α,β-unsaturated ketones.

(18) Tributylphosphine reacted rapidly and gave exclusively the products of α to β coupling. The profound influence of the substituents attached to phosphorus upon the allylphosphonium–propenylphosphonium equilibrium has been noted.[15]

(19) Mixtures of triphenylphosphine with III and with XII were allowed to stand separately for several days at 45–50°. No isomerization of the nitriles occurred.

(20) If the collapse of the intermediate XI is visualized as proceeding *via* addition of HX (*e.g.*, HOR) followed by Hofmann degradation of the resulting phosphonium salt, the loss of the proton β to Ph_3P and α to CN (leading to XII) is *a priori* more reasonable than the loss of the proton β to Ph_3P and β to CN.

(21) The cyanoethylation of XII to VII is reported by J. Lichtenberger and A. Lantz [*Bull. soc. chim. France*, 27 (1963)].

(22) Crotononitrile and allyl cyanide yield the same cyanoethylation products: H. A. Bruson, *Org. Reactions*, **5**, 106 (1949).

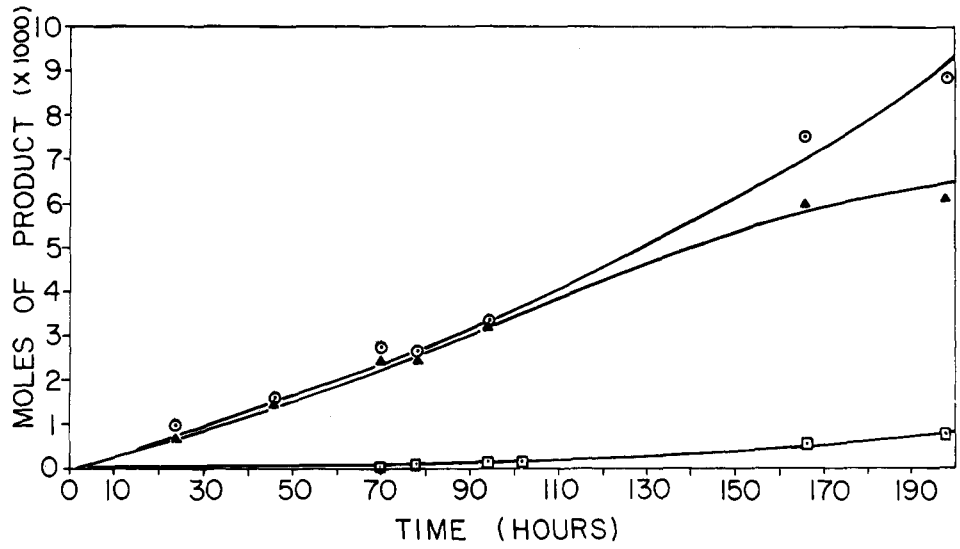
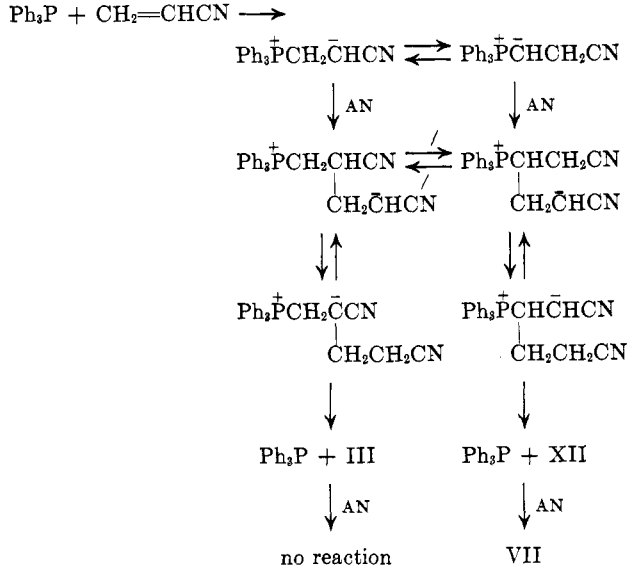


Figure 1.—Quantities of products obtained from the reaction of 0.9 g. of triphenylphosphine with 10 ml. of acrylonitrile in the presence of 0.9 ml. of *t*-butyl alcohol at 45°: ⊙, α-methyleneglutaronitrile; △, 1,4-dicyano-1-butene; □, acrylonitrile hexamer.

Our results may be accommodated by the proposal[23] shown in Scheme I.

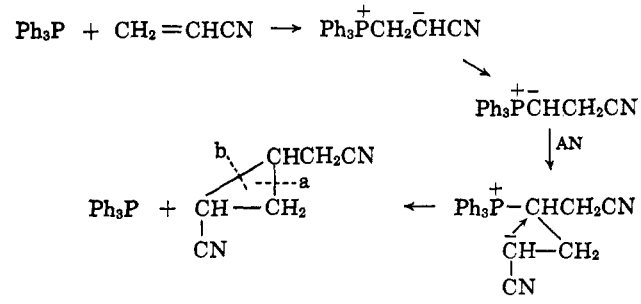
SCHEME I



A solution of triphenylphosphine, ethyl acrylate, and *t*-butyl alcohol kept at 40° was monitored analytically over a 2-week period as in the above AN experiment. There were found (a) a preponderant amount of diethyl α-methyleneglutarate, (b) a very small quantity of *trans*-1,4-dicarbethoxy-1-butene, and (c) too little *cis*-1,4-dicarbethoxy-1-butene (if any were formed) to detect by vapor phase chromatography.

These results, when considered in conjunction with those reported above for acrylonitrile, suggest that in the equilibrium $Ph_3\overset{+}{P}CH_2\overset{-}{C}HR \rightleftarrows Ph_3\overset{+}{P}\overset{-}{C}HCH_2R$ carbethoxy (R = $COOC_2H_5$) in competition with triphenylphosphonium is much more able to stabilize an α-carbanion than is cyano (R = CN) in competition with triphenylphosphonium.[15]

(23) This is a slight modification of a suggestion made by a referee. We had originally made an alternate proposal involving cyclopropane intermediates which could be formed by analogy with Freeman's results.[17] Cleavage of XIII at a would lead to α-methyleneglutaronitrile; cleavage at b would lead to dicyanobutenes.



Experimental[24]

Electrolytic Hydrodimerization of α-Methyleneglutaronitrile.—The apparatus and general procedure for carrying out this type of reaction has been described previously.[25] The catholyte contained 50.0 g. of methyltriethylammonium (*o*-, *p*-) toluenesulfonate, 53.0 g. (0.50 mole) of III, 40 g. of DMF, 10 g. of water, and a trace of *p*-nitrosodimethylaniline. The anolyte was a concentrated aqueous solution of the above salt. The cathode was 110 ml. of mercury. The electrolysis was conducted at 23–28° at 2.0 amp. for a total of 4.4 amp.-hr. The cathode voltage was −1.80 to −1.89 v. (s.c.e.). Acetic acid was added dropwise to the catholyte to prevent it from becoming excessively alkaline. The catholyte was then diluted with water and extracted with four 75-ml. portions of methylene chloride. The extracts were washed and dried. Volatile products were removed on the water bath at *ca.* 20 mm. The residual liquid (57.3 g.) was vacuum distilled through a 2-ft. jacketed Vigreux column. There was recovered 33.2 g. of distillate containing 95% III and 2% α-methylglutaronitrile (v.p.c. analysis). The undistilled portion (15.7 g., 93.5% yield based on current input) crystallized. Recrystallization from DMF–ethanol yielded white crystals of 1,3,6,8-tetracyanooctane (II) softening at 115–117°, m.p. 119°.

Anal. Calcd. for $C_{12}H_{14}N_4$: C, 67.26; H, 6.59; N, 26.15; mol. wt., 214. Found: C, 67.54; H, 6.94; N, 25.59; mol. wt., 215 (osmometrically in dioxane, extrapolated to infinite dilution).

A sample of II was hydrolyzed by refluxing hydrochloric acid. The crude acid was esterified with ethanol–sulfuric acid. The tetraethyl ester obtained had satisfactory elemental analyses; its infrared spectrum and v.p.c. retention time were identical with those of a sample previously prepared by an independent synthesis.[2]

(24) Boiling points are not corrected.

(25) Paper I: M. M. Baizer, *J. Electrochem. Soc.*, **111**, 215 (1964).

Mixed Electrolytic Coupling of III and AN.—The catholyte contained 26.5 g. (0.50 mole) of AN, 53.0 g. (0.50 mole) of III, 50.0 g. of the quaternary salt, 10 g. of water, 25 ml. of DMF, and a trace of stabilizer. Electrolysis was conducted at 25° and 3.0 amp. for a total of 13.4 amp.-hr. Work-up as above and fractionation yielded the products listed in Table II.

TABLE II

Fraction	B.p., °C. (mm.)	Wt., g.	Products,[a] g. A[b]	B[c]	C[d]
1	87–103 (0.1)	30.1	4.5	...	...
2	103–175 (0.1)	2.1	1.8	0.1	...
3	175–182 (0.1)	14.2	...	14.2	...
4	203–210 (0.2)	0.5	...	...	...
5	Residue	20.1	...	...	...
Total			6.3	14.3	20.1 crude

[a] Analyses by v.p.c. [b] Adiponitrile. [c] Compound I (1,3,6-tricyanohexane). [d] Compound II (1,3,6,8-tetracyanooctane).

Fraction 5 was distilled at 264–198° (0.1–0.25 mm.); $n^{25}D$ 1.4820. The distillate crystallized and was recrystallized from DMF–ethanol; m.p. 116–118°.

The distribution of products that would have been expected from equal electron uptake by III and AN and statistical coupling of the intermediates is 6.6 g. of adiponitrile, 20 g. of I, and 13.4 g. of II.

Preparation of III from Acrylonitrile.—In a typical experiment there was added under nitrogen with stirring 50.0 g. of stabilized AN dissolved in 20.7 g. of *t*-butyl alcohol to a solution of 1.0 g. of tributylphosphine in 35 ml. of acetonitrile. The mixture was cooled intermittently to keep the temperature below 45°. After stirring 3 hr. at room temperature, the mixture was acidified with hydrochloric acid and extracted with benzene. The extracts were washed with water and dried with Drierite. Some polymeric material separated from the benzene. From the filtered solution volatile material was removed on the water bath (house vacuum); the residue (11.1 g.) was fractionated. The cut having b.p. 65° (0.1 mm.), $n^{25}D$ 1.4550, was III (5.3 g.).

A 2.0-g. sample of product was heated under reflux with 8 ml. of 20% sulfuric acid for 4 days. The contents of the flask were then concentrated to *ca.* 8 ml. At room temperature the crystals were removed by filtration, washed with ice–water and benzene, and recrystallized from water; m.p. 134–135°. A sample of α-methyleneglutaric acid prepared by hydrolysis of diethyl α-methyleneglutarate[6] likewise melted at 134–135°; lit.[26] m.p. 131–132°.

A 10.6-g. sample of III (from several preparations) was dissolved in 100 ml. of ethanol containing 0.2 g. of 5% palladium on charcoal. Hydrogenation of the Parr shaker at an initial pressure of 38.75 p.s.i. was complete in 12 min. The product, α-methylglutaronitrile, had b.p. 116–118° (4.7–5.0 mm.), $n^{25}D$ 1.4320. V.p.c. analysis showed identity with the major component of the preparation according to Zahn.[11] Infrared analysis was consistent with the structure.

Isolation and Examination of VI.—From an oligomerization on 12 times the scale of the above there was obtained from the benzene-soluble fraction 67.6 g. of III; 2.5 g. of an intermediate fraction, b.p. 96–150° (0.15 mm.); 9.2 g. of crude VI, b.p. 152–164° (0.15–0.2 mm.), $n^{25}D$ 1.4762; and 12.7 g. of higher boiling residue.

Anal. Calcd. for $C_9H_9N_3$ (VI): C, 67.90; H, 5.70; N, 26.40; mol. wt., 159. Found: C, 67.12; H, 6.48; N, 24.62; mol. wt., 165.

A 7.8-g. sample of VI was hydrogenated in the Parr shaker as above. The product, 1,3,5-tricyanohexane, b.p. 158–166° (0.20–0.15 mm.), $n^{25}D$ 1.4620, was about 92–94% pure by v.p.c. analysis.

Anal. Calcd. for $C_9H_{11}N_3$: C, 67.05; H, 6.87; N, 26.07. Found: C, 66.76; H, 7.16; N, 25.63.

Reaction of Triphenylphosphine with Acrylonitrile.—A stock solution was prepared by stirring under nitrogen until homogeneous at 0° a mixture of 120 ml. of AN, 10 ml. of *t*-butyl alcohol, and 10 g. of triphenylphosphine. Ten-milliliter aliquots were charged to vials under nitrogen and placed in a constant-temperature water bath at 45°. The contents of the several vials were analyzed at various times during a 198-hr. period (Figure 1) as follows. The vial content was shaken vigorously with 1 ml. of 6 *N* HCl and the AN hexamer, practically quantitatively precipitated, was removed by filtration. The organic layer of the filtrate was separated, dried, weighed, and analyzed by vapor phase chromatography using a 12-ft. column of 2% RJ 100 on Teflon. The individual fractions were identified by (a) comparison of the retention time with that of an authentic sample of the given component, (b) enrichment of the sample with an authentic sample of the given component and observation of the enhancement of the concentration of the chromatographic fraction, and (c) collection of individual v.p.c. fractions and comparison of the infrared spectra with those of authentic samples. There were found α-methyleneglutaronitrile[27] and *cis*- and *trans*-1,4-dicyano-1-butenes.[28] The AN hexamer obtained was identical in properties with the product described in the literature[13]; the melting point of a mixture with an authentic sample was undepressed.

Reaction of Triphenylphosphine with Ethyl Acrylate.—The stock solution was prepared at room temperature under nitrogen from 100 ml. of ethyl acrylate, 5 ml. of *t*-butyl alcohol, and 10 g. of triphenylphosphine. The 10-ml. aliquots in vials were stored at 40° and analyzed in the course of 2 weeks as follows. The vial content was shaken with 2 ml. of 6 *N* HCl. The water-insoluble organic material was extracted with methylene chloride. The extracts were dried and concentrated to *ca.* 1 ml. before v.p.c. analysis on a 3-m. column of 12% silicone grease on 35–48-mesh Chromasorb W at 150°. There were found diethyl α-methyleneglutarate[29] and *trans*-1,4-dicarbethoxy-1-butene.[30] The identity of a given v.p.c. fraction with a given authentic sample was established by the procedures described in the experiment immediately above. The rate of conversion was very low; after 2 weeks only a few milligrams of products was obtained.

(26) E. R. Buchman, A. O. Reims, and M. J. Schlatter, *J. Am. Chem. Soc.*, **64**, 2705 (1942).

(27) Authentic sample prepared from tributylphosphine and AN as above.

(28) An authentic sample was prepared by isomerization of 1,4-dicyano-2-butene according to the method of C. M. Langkammerer [U. S. Patent 2,478,285 (Aug. 9, 1949)]. The 1,4-dicyano-2-butene was prepared according to Takashina and Price.[13]

(29) Authentic sample prepared according to ref. 6.

(30) Prepared by the triethylenediamine-catalyzed isomerization of diethyl Δ^2-dihydromuconate. The structure was confirmed by infrared spectrum, elemental analysis, and polarography.