

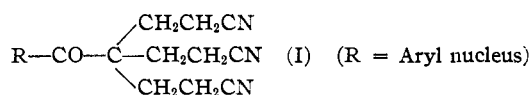
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The Chemistry of Acrylonitrile. II. Reactions with Ketones

BY HERMAN ALEXANDER BRUSON AND THOMAS W. RIENER

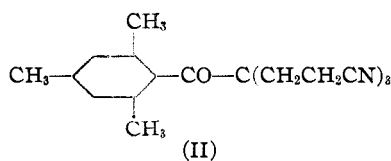
The powerful cyanoethylating action of acrylonitrile in the presence of strong bases upon organic compounds possessing labile hydrogen atoms¹ is strikingly evident with various types of ketones.

Aromatic methyl ketones of the type R—CO—CH₃ as exemplified by acetophenone, *p*-methylacetophenone, *p*-methoxyacetophenone, *p*-chloroacetophenone, *p*-bromoacetophenone, *p*-acetyldiphenyl, and 2-acetylnaphthalene readily took up three molecular equivalents of acrylonitrile in the presence of strong alkali catalysts such as trimethylbenzylammonium hydroxide or potassium hydroxide to form crystalline *tri*-cyanoethylation products (I).

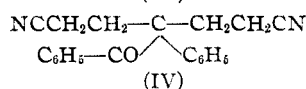
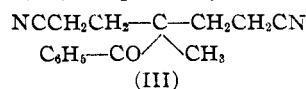


These are listed in Table I together with their physical and analytical data. Upon hydrolysis with aqueous sodium hydroxide or potassium hydroxide these *tri*-(cyanoethyl)-methyl aryl ketones yielded the corresponding aryl keto tricarboxylic acids R—CO—C(CH₂CH₂COOH)₃. These are listed in Table II.

Even acetomesitylene which because of steric hindrance reacts sluggishly, gave a small yield (30%) of the *tri*-cyanoethylation product (II).



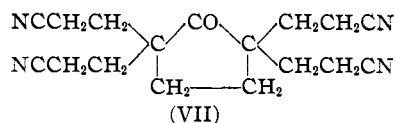
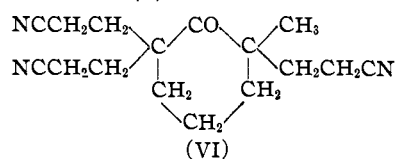
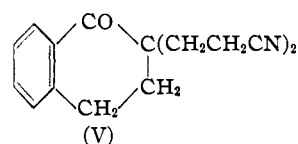
Propiophenone and desoxybenzoin which possess only two active hydrogen atoms contiguous to the carbonyl group, each took up two molecular equivalents of acrylonitrile to form γ -benzoyl- γ -methylpimelonitrile (III) and γ -benzoyl- γ -phenylpimelonitrile (IV), respectively.



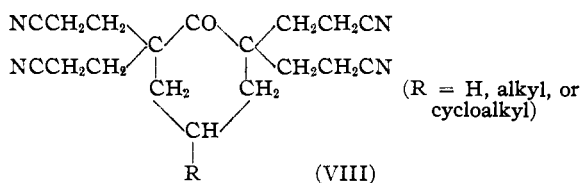
Upon hydrolysis with aqueous sodium hydrox-

ide, compounds III and IV yielded γ -benzoyl- γ -methylpimelic acid and γ -benzoyl- γ -phenylpimelic acid, respectively.

In a similar manner acrylonitrile reacted with α -tetralone, *o*-methylcyclohexanone and cyclopentanone to form compounds V, VI and VII, respectively.



Cyclohexanone itself as well as *p*-methylcyclohexanone, *p*-*t*-amyl cyclohexanone, *p*-($\alpha,\alpha,\gamma,\gamma$ -tetramethylbutyl)-cyclohexanone and *p*-cyclohexylcyclohexanone each took up four moles of acrylonitrile to yield crystalline 2,2,6,6-tetracyanoethylation products of the general type (VIII) in 80–95% yields (Table III).



Upon alkaline hydrolysis compounds VI, VII, and VIII were converted into the corresponding ketonic polycarboxylic acids. The tetra-carboxylic acids derived from (VIII) are listed in Table IV.

When cyclohexanone reacted with only one or two molecular equivalents of acrylonitrile, it was possible to isolate a mono-cyanoethylation product, 2-(β -cyanoethyl)-cyclohexanone, and a dicyanoethylation product, very probably 2,2-di-(β -cyanoethyl)-cyclohexanone, from the reaction mixture in addition to considerable tetra-cyanoethylation product.

(1) Bruson, THIS JOURNAL, 64, 2457 (1942); U. S. Patent 2,287,510.

TABLE I
TRICYANOETHYLATION PRODUCTS R—CO—C(CH₂CH₂CN)₃, R = Aryl

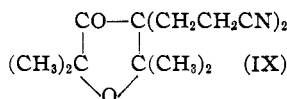
Value of R	M. p., °C.	Formula	Analyses, %					
			Calcd.			Found		
			C	H	N	C	H	N
Phenyl	128–129 ^a	C ₁₇ H ₁₇ N ₃ O	73.08	6.14	15.04	73.10	6.29	15.13
2-Naphthyl	122 ^b	C ₂₁ H ₁₉ N ₃ O	76.59	5.82	12.76	77.03	5.58	12.71
<i>p</i> -Phenylphenyl	178 ^d	C ₂₃ H ₂₁ N ₃ O	77.70	5.96	11.83	77.80	6.23	11.86
<i>p</i> -Methoxyphenyl	133 ^c	C ₁₈ H ₁₉ N ₃ O ₂	69.87	6.19	13.59	69.40	6.04	13.72
<i>p</i> -Methylphenyl	161–162 ^b	C ₁₈ H ₁₉ N ₃ O	73.68	6.53	14.33	73.12	6.42	14.63
2,4,6-Trimethylphenyl	126 ^b	C ₂₀ H ₂₃ N ₃ O	74.72	7.22	13.08	75.20	7.10	13.49
<i>p</i> -Chlorophenyl	141–142 ^c	C ₁₇ H ₁₆ N ₃ OCl	Cl, 11.30		13.39	Cl, 10.87		13.12
<i>p</i> -Bromophenyl	151–152 ^b	C ₁₇ H ₁₆ N ₃ OBr	Br, 22.32		11.73	Br, 21.98		11.67

^a Recrystallized from "Cellosolve." ^b From ethanol. ^c From methanol. ^d From dioxane.

TABLE II
R—CO—C(CH₂CH₂COOH)₃, R = Aryl

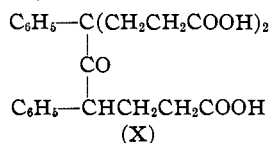
Value of R	M. p., °C.	Formula	Analyses, %					
			Calcd.			Found		
			C	H		C	H	
Phenyl	143–145	C ₁₇ H ₂₀ O ₇	60.69	6.00		60.50		6.39
2-Naphthyl	173–174	C ₂₁ H ₂₂ O ₇	65.25	5.74		65.21		5.81
<i>p</i> -Phenylphenyl	236–238	C ₂₃ H ₂₄ O ₇	66.95	5.87		67.01		5.77
<i>p</i> -Methoxyphenyl	219	C ₁₈ H ₂₂ O ₈	58.99	6.06		58.70		5.94
<i>p</i> -Methylphenyl	226	C ₁₈ H ₂₂ O ₇	61.68	6.33		61.80		6.25
<i>p</i> -Chlorophenyl	225–227	C ₁₇ H ₁₉ O ₇ Cl	55.04	5.17		55.20		5.00
<i>p</i> -Bromophenyl	241–243	C ₁₇ H ₁₉ O ₇ Br	49.15	4.61		49.19		4.63

In an analogous manner, the heterocyclic ketone 2,2,5,5-tetramethyltetrahydrofuranone-3 reacted with acrylonitrile to yield the crystalline dicyanoethylation product (IX).



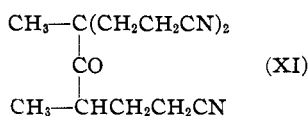
Upon alkaline hydrolysis it formed the corresponding 4,4-di-(β -carboxy-ethyl)-2,2,5,5-tetramethyltetrahydrofuranone-3.

An attempt was made to *tetra*-cyanoethylate dibenzyl ketone but the only product that could be isolated after saponification, from the resinous mixture obtained, was a crystalline tricarboxylic acid (X).



instead of the expected *tetra*-carboxylic acid.

In a similar manner, an attempt to *tetra*-cyanoethylate diethyl ketone gave a resinous product from which a crystalline *tri*-cyanoethylation product (XI) could be isolated by vacuum distillation.

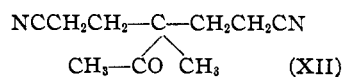


Upon alkaline saponification (XI) yielded the corresponding 2,4,4-tri-(β -carboxyethyl)-pentanone-3.

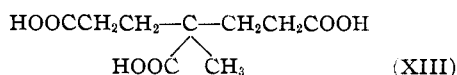
In all of the above examples, the positions occupied by the entering cyanoethyl groups can hardly be other than those indicated since these are established by the only available active hydrogen atoms in the ketones employed.

However, in the case of the saturated aliphatic methyl ketones of the type CH₃—CO—CH₂—alkyl, such as methyl ethyl ketone, methyl propyl ketone, methyl iso-butyl ketone, methyl *n*-amyl ketone, and methyl *n*-hexyl ketone, which could presumably react on either the —CH₂— group, or the CH₃—group, or both, it was of interest to determine the exact location of the entering cyanoethyl groups and also the maximum number that could be introduced.

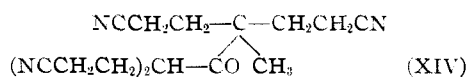
Methyl ethyl ketone reacted with acrylonitrile to first take up two cyanoethyl radicals on the methylene group and give 4-acetyl-4-methylpimelonitrile (XII) in yields up to 90%.



The structure of this compound was established by saponifying it to the corresponding γ -acetyl- γ -methylpimelic acid, and subjecting the latter in alkaline hypochlorite solution to the haloform reaction, whereby chloroform was evolved and the new tricarboxylic acid XIII isolated.

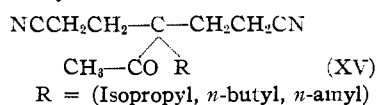


Upon treating 4-acetyl-4-methylpimelonitrile with one molecular equivalent of acrylonitrile in an attempt to cyanoethylate one of the hydrogen atoms of the remaining active methyl group, a resin was obtained from which a crystalline tetra-cyanoethylation product (XIV) could be distilled under high vacuum.

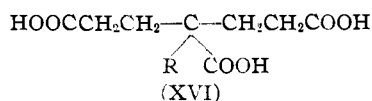


Acrylonitrile also combined with methyl propyl ketone to give a crystalline di-cyanoethylation product, which by conversion to the corresponding dicarboxylic acid and subjection of the latter to the haloform reaction, was shown to have both cyanoethyl groups on the methylene group. It was also possible to isolate a crystalline *tri*-cyanoethylation product, namely, 1,3,3-*tri*-(β -cyanoethyl)-pentanone-2 from the original di-cyanoethylation reaction mixture.

In the same manner methyl isobutyl ketone, methyl *n*-amyl ketone and methyl *n*-hexyl ketone gave crystalline γ -acetyl- γ -alkyl pimelonitriles (XV) upon treatment in alkaline solution with two moles of acrylonitrile.



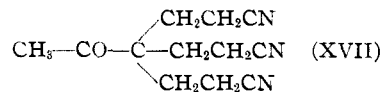
The above γ -acetyl- γ -alkyl pimelonitriles were saponified to the corresponding γ -acetyl- γ -alkyl-pimelic acids, which were isolated in the pure form. The latter in turn were each oxidized by means of alkaline hypochlorite solution to chloroform and the γ -alkyl- γ -carboxypimelic acids (XVI).



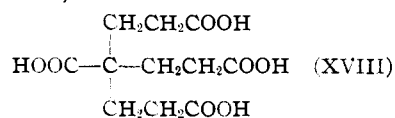
The positions taken by the two entering cyanoethyl radicals in the homologs of methyl ethyl ketone having thus been established as being on the $-\text{CH}_2-$ group, it was of interest to study the cyanoethylation of acetone itself since this possesses two active methyl groups of equal value and might perhaps distribute the cyanoethyl radicals between both of them.

Upon treating acetone with three moles of acrylonitrile in the presence of potassium hydroxide as the catalyst, a crystalline *tri*-cyanoethyla-

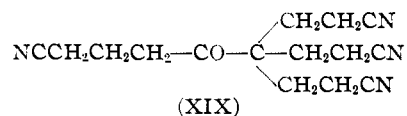
tion product was obtained in 75-80% yield. This compound is 1,1,1-*tri*-(β -cyanoethyl)-acetone (XVII).



Upon alkaline hydrolysis it yielded the corresponding 1,1,1-*tri*-(β -carboxyethyl)-acetone which, upon oxidation with alkaline hypochlorite solution, gave chloroform and the tetra-carboxylic acid (XVIII).

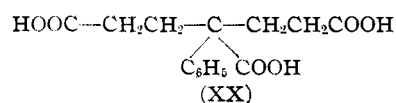


The *tri*-cyanoethylation of acetone therefore takes place first on one methyl group. Upon further cyanoethylation of the 1,1,1-*tri*-(β -cyanoethyl)-acetone, a crystalline *tetra*-cyanoethyl acetone could be isolated from the resinous residue, and consequently must possess formula (XIX).

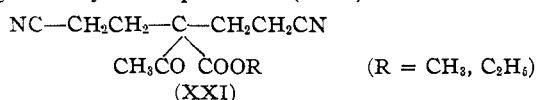


It is highly probable that the resinous residue contains a *penta*- or a *hexa*-cyanoethylation product, but the purification offers considerable difficulty.

In the case of phenylacetone, which also possesses two possible points of reaction, di-cyanoethylation took place on the methylene group to give the crystalline γ -acetyl- γ -phenylpimelonitrile in 86% yield. Upon saponification it yielded γ -acetyl- γ -phenylpimelic acid which upon oxidation with alkaline hypochlorite solution cleaved to give chloroform and γ -carboxy- γ -phenylpimelic acid (XX).



Finally, acrylonitrile was condensed with acetoacetic esters. Both methyl acetoacetate and ethyl acetoacetate gave good yields of crystalline di-cyanoethylation products (XXI).



From the foregoing it appears therefore that with aliphatic or arylaliphatic ketones possessing the reactive grouping $-\text{CH}_2-\text{CO}-\text{CH}_3$ cyano-

ethylation first occurs on the $-\text{CH}_2-$ group and after this has been satisfied further cyanoethylation can occur on the remaining methyl radical.

In conclusion it may be said that certain methylene ketones were incapable of being cyanoethylated by the method here described, namely, camphor, iso-phorone, and di-isobutyl ketone. Furthermore, attempts to utilize α -methyl acrylonitrile or crotonitrile in place of acrylonitrile were unsuccessful.

Experimental

$\text{R}-\text{CO}-\text{C}(\text{CH}_2\text{CH}_2\text{CN})_3$ (R = Aryl).—The general method of condensing aryl alkyl ketones with acrylonitrile consisted in dissolving the ketone $\text{R}-\text{CO}-\text{CH}_3$ (R = aryl) in dioxane or in tertiary butyl alcohol so as to form a 25–50% solution, adding a small quantity of aqueous 40% trimethylbenzylammonium hydroxide² corresponding to about 5–10% on the weight of the ketone, and then adding dropwise three molecular equivalents of acrylonitrile to the stirred reaction mixture while maintaining the temperature of the mixture between 25 and 40° by means of external water cooling and by regulating the rate of addition of the acrylonitrile. The mixture was then usually stirred for two to four hours longer at room temperature, and the tricyanoethylation product separated either by filtration or by neutralizing the alkali with dilute hydrochloric acid, evaporating off the solvent under reduced pressure on a steam-bath, and crystallizing the residue from a suitable solvent.

A typical procedure using acetophenone, for example, is as follows:

To a solution of 60 g. of acetophenone (0.50 mole) in 60 g. of dioxane and containing 5 g. of "Triton B," was added 79.5 g. of acrylonitrile (1.5 mole) dropwise during a period of two hours while the mixture was stirred and maintained between 30 and 40° by external water cooling. During the addition crystals separated. After all the acrylonitrile had been added, the mixture was stirred for one hour and then filtered by suction. The pinkish crystalline product weighed 79 g., corresponding to a 57% yield of 1,1,1-tri-(β -cyanoethyl)-acetophenone. After recrystallization from glycol monoethyl ether ("Cellosolve") it formed colorless crystals melting at 128–129°.

In Table I are given the physical and analytical data of the various homologs of acetophenone prepared in the above manner. All of the melting points given in this paper are uncorrected for stem exposure.

$\text{R}-\text{CO}-\text{C}(\text{CH}_2\text{CH}_2\text{COOH})_3$, R = Aryl.—The general method of hydrolyzing the cyanoethylated ketones consisted in boiling the tricyanoethylation products given in Table I with an excess of sodium hydroxide or potassium hydroxide in aqueous solution for a period of from four to twelve hours until all the product had dissolved and evolution of ammonia had ceased. The solution was then clarified with charcoal, filtered, and the filtrate acidified with concentrated hydrochloric acid. The tricarboxylic acids usually precipitated first as viscous oils or dough-like masses which gradually solidified to a crystalline product.

(2) Available commercially as "Triton B."

After recrystallization from hot water, or from a mixture of water-dioxane (4:1), they were obtained in pure form as colorless crystals.

A typical procedure using 1,1,1-tri-(β -cyanoethyl)-acetophenone is as follows:

A mixture consisting of 400 g. of water, 39 g. of potassium hydroxide and 55.8 g. of 1,1,1-tri-(β -cyanoethyl)-acetophenone was stirred rapidly and boiled under reflux for six hours. The solution was clarified with charcoal, filtered, and the filtrate acidified with concentrated hydrochloric acid. The 1,1,1-tri-(β -carboxyethyl)-acetophenone separated as a white, resinous mass which soon became crystalline. It was purified by recrystallization from hot water, yield 58 g. or 80%.

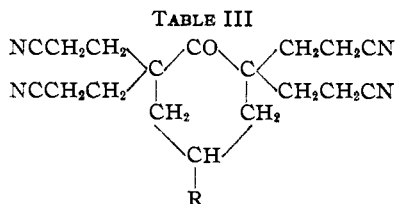
In Table II are given the physical and analytical data of the various 1,1,1-tri-(β -carboxyethyl)-methyl aryl ketones prepared in the above manner. The yields of pure product were between 80 and 85%.

III. γ -Benzoyl- γ -methylpimelonitrile.—To a solution of 26.9 g. of propiophenone (0.2 mole), 50 g. of dioxane and 2 g. of "Triton B" there was added dropwise 21.2 g. of acrylonitrile (0.4 mole) during the course of twenty minutes while the reaction mixture was stirred and maintained between 25 and 30° by external water cooling. The mixture was stirred for five hours longer, then neutralized with dilute hydrochloric acid and poured into 300 cc. of water. The oil layer was separated, taken up in ethylene dichloride, washed thoroughly with water, and the ethylene dichloride layer evaporated under reduced pressure on a steam-bath. The residual oil (48 g.) was mixed with an equal weight of ethanol and chilled whereupon the product crystallized. After recrystallization from ethanol the γ -benzoyl- γ -methylpimelonitrile formed colorless crystals m. p. 66°. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}$: C, 74.96; H, 6.72; N, 11.66. Found: C, 75.10; H, 6.65; N, 11.71.

γ -Benzoyl- γ -methylpimelic Acid.—A mixture of 150 g. of water, 10 g. of sodium hydroxide, and 16.5 g. of III was boiled under reflux for six and one-half hours, treated with charcoal and the clear filtrate acidified with concentrated hydrochloric acid. The precipitated product was crystallized from hot water; m. p. 166–167°. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_5$: C, 64.73; H, 6.52. Found: C, 64.50; H, 6.29.

IV. γ -Benzoyl- γ -phenylpimelonitrile.—Acrylonitrile (13.5 g.) was added dropwise to a stirred solution of 50 g. of dioxane, 25 g. of desoxybenzoin and 2 g. of "Triton B" while the reaction temperature was maintained at 30–35° by external cooling. After all the acrylonitrile had been added, the mixture was stirred for three hours at 45° to complete the reaction. It was then cooled, acidified with dilute hydrochloric acid, taken up in ethylene dichloride and washed with water. The ethylene dichloride layer was evaporated to dryness under reduced pressure on a steam-bath and the residual crystalline product (38 g.) washed with a little alcohol and purified by recrystallization from ethanol. The yield of pure product melting at 149–150°, was 31 g. *Anal.* Calcd. for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{O}$: N, 9.27. Found: N, 9.06.

γ -Benzoyl- γ -phenylpimelic Acid.—A mixture of 12 g. of IV, 150 g. of water and 6 g. of sodium hydroxide was boiled under reflux for twenty-one hours. The solution was treated with charcoal, filtered and the filtrate acidified with



Value of R	M. p., °C.	Formula	Analyses, %					
			C	Calcd. H	N	C	Found H	N
H	165	C ₁₅ H ₂₂ N ₄ O	69.64	7.15	18.05	69.80	7.08	18.20
Methyl	138	C ₁₉ H ₂₄ N ₄ O	17.27	17.26
<i>t</i> -Amyl	145	C ₂₃ H ₃₂ N ₄ O	14.72	14.54
<i>t</i> -Octyl	155-156	C ₂₆ H ₃₈ N ₄ O	73.88	9.07	13.26	74.10	9.04	13.15
Cyclohexyl	223-224	C ₂₄ H ₃₂ N ₄ O	14.27	14.28

hydrochloric acid. The product precipitated as a white solid. Upon repeated recrystallization from water and drying in an oven at 70° for twenty-four hours the analytical sample melted at 172-173°. *Anal.* Calcd. for C₂₀H₂₆O₅: C, 70.55; H, 5.93. Found: C, 70.21; H, 5.85.

V. 2-Di-(β -cyanoethyl)-tetralone-1.—Acrylonitrile (21.2 g.) was added at room temperature to a mixture of 29.2 g. of α -tetralone, 50 g. of dioxane, and 4 g. of "Triton B." The mixture was stirred for twenty-four hours, then neutralized with dilute hydrochloric acid, washed well with water and distilled under reduced pressure at 1 mm. The fraction boiling at 250-260° (1 mm.) formed a pale yellow oil which gradually solidified to a waxy, crystalline mass. After recrystallization from ethanol, the product formed colorless crystals melting at 80°. *Anal.* Calcd. for C₁₈H₁₈N₂O: C, 76.15; H, 6.39; N, 11.10. Found: C, 76.59; H, 6.05; N, 11.09.

VI. 2,2,6-Tri-(β -cyanoethyl)-6-methyl-cyclohexanone.—Acrylonitrile (63.5 g.) was added dropwise to a stirred solution of 44.8 g. of *o*-methylcyclohexanone, 200 g. of benzene, and 5 g. of "Triton B" while maintaining the reaction temperature at 30-40°. The mixture was then stirred at room temperature for eighteen hours and, after neutralization with hydrochloric acid and thorough washing with water, was filtered to remove some polyacrylonitrile which was present. The filtrate was evaporated to dryness under reduced pressure on a steam-bath and the residual oil (103 g.) distilled under high vacuum. The product (41 g.) came over at 270-285° (1-2 mm.) as a viscous, amber-colored sirup which gradually crystallized on long standing. Upon recrystallization from ice-cold methanol it was obtained in the form of colorless crystals melting at 69-70°. *Anal.* Calcd. for C₁₈H₂₁N₃O: C, 70.82; H, 7.79; N, 15.49. Found: C, 71.00; H, 7.49; N, 15.86.

VII. 2,2,5,5-Tetra-(β -cyanoethyl)-cyclopentanone.—To a solution of 42 g. of cyclopentanone (0.5 mole) in 200 g. of benzene, there was added 5 g. of "Triton B." The mixture was stirred rapidly and cooled to 35-45° while 106 g. of acrylonitrile (2 moles) was added dropwise during two hours. Crystals began to separate within a few minutes after the addition was begun. As the reaction proceeded it was necessary to add 200 cc. of benzene to prevent clogging the stirrer by the crystalline mass. The mixture was allowed to stand for eighteen hours before the crystals were filtered by suction. The yield was 144 g. or 97%. The product can be recrystallized from hot methyl ethyl ketone or glycol monoethyl ether, from which it separates in

colorless crystals, m. p. 175°. *Anal.* Calcd. for C₁₇H₂₀N₄O: N, 18.90. Found: N, 18.93.

VIII. 2,2,6,6-Tetra-(β -cyanoethyl)-cyclohexanone.—To 935 g. of tertiary butyl alcohol there was added 15 g. of aqueous 40% potassium hydroxide solution and 294 g. of cyclohexanone (3 moles). The solution was stirred rapidly in a three-neck flask surrounded by running tap water, and 636 g. of acrylonitrile (12 moles) added dropwise thereto during one and one-half hours, while the temperature of the reaction mixture was maintained between 35 and 45°. During the addition crystals separated. The mixture was stirred for an additional fifteen hours at room temperature and the crystalline product filtered off by suction, washed with water, and dried; yield 820 g. of faintly yellow crystals, or 88%. Upon recrystallization from acetone it formed colorless fine needles, melting at 165°.

In Table III are given the physical and analytical data of the various 2,2,6,6-tetra-(β -cyanoethyl)-cyclohexanones of type VIII prepared in the above manner. The *p*-*t*-octylcyclohexanone used was obtained from *p*-($\alpha,\alpha,\gamma,\gamma$ -tetramethylbutyl)-phenol by catalytic hydrogenation with Raney nickel to *p*-($\alpha,\alpha,\gamma,\gamma$ -tetramethylbutyl)-cyclohexanol and oxidation of the latter with potassium dichromate-sulfuric acid mixture.³

Tetra-(β -carboxyethyl)-cycloalkanones.—The general method of hydrolysis used consisted in boiling the tetra-cyanoethylated cycloalkanones given in Table III with an excess of potassium hydroxide or sodium hydroxide in aqueous solution for a period of from four to eight hours until ammonia ceased to be evolved, then treating the hot solution with Norite decolorizing charcoal, filtering, and acidifying the filtrate with concentrated hydrochloric acid. The crude tetra-carboxylic acids precipitated in crystalline form and were then recrystallized from appropriate solvents.

The following procedures were typical:

2,2,5,5-Tetra-(β -carboxyethyl)-cyclopentanone.—A mixture of 600 g. of water, 80 g. of sodium hydroxide and 95 g. of 2,2,5,5-tetra-(β -cyanoethyl)-cyclopentanone (VII) was stirred and boiled under reflux for twenty-three hours. The clear, amber-colored solution was treated with charcoal, filtered and acidified with concentrated hydrochloric acid. The clear solution obtained was cooled in an ice-bath to 10-15° whereupon it set to a white crystalline magma, which after filtration and drying at room temperature weighed 108 g.

(3) Nieder, *Ind. Eng. Chem.*, 30, 1270 (1938).

Upon recrystallization from water the product formed colorless crystals melting at 173°, containing one mole of water of crystallization. *Anal.* Calcd. for $C_{17}H_{24}O_7 \cdot H_2O$: C, 52.28; H, 6.72. Found: C, 52.20; H, 6.78.

2,2,6,6-Tetra-(β -carboxyethyl)-cyclohexanone.—A mixture consisting of 1900 g. of water, 196 g. of potassium hydroxide and 217 g. of 2,2,6,6-tetra-(β -cyanoethyl)-cyclohexanone was stirred and boiled under reflux for five hours. The clear solution was acidified with 350 g. of concentrated hydrochloric acid, and cooled to 15–20° whereupon the product crystallized. It was filtered off and washed with a little ice water; yield 199 g. of air-dried, white crystals. Upon recrystallization from water the compound formed colorless needles melting at 179–180°.

In Table IV are given the physical and analytical data of various tetra-(β -carboxy-ethyl)-cyclohexanones prepared in the above manner from the tetra-cyanoethylation products of cyclohexanone, *p*-methylcyclohexanone, *p*-*t*-amylcyclohexanone, *p*-($\alpha,\alpha,\gamma,\gamma$ -tetramethylbutyl)-cyclohexanone, and *p*-cyclohexylcyclohexanone, respectively.

TABLE IV

Value of R	M. p., °C.	Formula	Analyses, %			
			Calcd.		Found	
			C	H	C	H
H	179–180	$C_{18}H_{24}O_7$	55.93	6.79	56.30	6.59
Methyl	205–206	$C_{19}H_{26}O_7$	56.96	7.05	57.01	7.10
<i>t</i> -amyl	205	$C_{23}H_{30}O_7$	60.49	7.95	60.89	7.94
<i>t</i> -Octyl	185–186	$C_{26}H_{34}O_7$	62.60	8.49	61.90	8.49
Cyclohexyl	205–206	$C_{24}H_{30}O_7$	61.50	7.74	61.61	7.40

2-(β -Cyanoethyl)-cyclohexanone.—To a stirred mixture of 98 g. of cyclohexanone (1 mole) and 5 g. of "Triton B," was added dropwise 53 g. of acrylonitrile (1 mole) at 30–35° during the course of eighty minutes. The mixture was stirred at 35–40° for one hour thereafter and finally for eighteen hours at room temperature. The partially crystalline mixture was acidified with dilute hydrochloric acid and the crystalline tetracyanoethylation product (30 g.) was filtered off by suction. The filtrate was washed with water and distilled in vacuum. About 31 g. of unchanged cyclohexanone was recovered.

The 2-(β -cyanoethyl)-cyclohexanone distilled over at 138–142° (10 mm.) as a colorless oil; yield 16.5 g. *Anal.* Calcd. for $C_9H_{14}NO$: N, 9.27. Found: N, 9.03.

The fraction boiling at 195–198° (1 mm.) was a viscous yellow oil; yield 12.5 g. On standing it gradually crystallized. After recrystallization from benzene it formed colorless crystals melting at 69°, the analysis of which corresponds to a di-cyanoethylation product of cyclohexanone. *Anal.* Calcd. for $C_{12}H_{16}N_2O$: C, 70.54; H, 7.90; N, 13.71. Found: C, 70.90; H, 7.85; N, 13.78.

IX. 4,4-Di-(β -cyanoethyl)-2,2,5,5-tetramethyltetrahydrofuranone-3.—Acrylonitrile (24.4 g.) was added dropwise to a stirred solution consisting of 50 g. of dioxane, 3 g. of aqueous 40% Triton B, and 33 g. of 2,2,5,5-tetramethyltetrahydrofuranone-3 while the reaction temperature was maintained at 35–40° by external cooling. The

mixture was then stirred three hours longer at 25°. During the addition crystals separated. The mixture was neutralized with dilute hydrochloric acid, the white crystalline product filtered off, and washed with a little ethanol; yield 41 g. After recrystallization from ethanol, the product formed colorless needles melting at 153°. *Anal.* Calcd. for $C_{14}H_{20}N_2O_2$: N, 11.28. Found: N, 11.16.

4,4-Di-(β -carboxy-ethyl)-2,2,5,5-tetramethyltetrahydrofuranone-3.—A mixture of 120 g. of water, 12 g. of sodium hydroxide and 27 g. of compound IX was boiled under reflux for eight hours. The solution was treated with charcoal, filtered and the filtrate acidified with concentrated hydrochloric acid. The product crystallized on cooling; yield 18 g. Upon recrystallization from water it formed colorless crystals, m. p. 170–171°. *Anal.* Calcd. for $C_{14}H_{22}O_6$: C, 58.70; H, 7.75. Found: C, 58.61; H, 7.57.

X. 1,3-Diphenyl-1,1,3-tri-(β -carboxyethyl)-propanone-2.—Acrylonitrile (21.2 g.) was added dropwise during forty minutes to a stirred mixture of 21 g. of dibenzyl ketone, 50 g. of dioxane and 2 g. of "Triton B" at 30–35°. The mixture was allowed to stand eighteen hours at room temperature. It was then acidified with dilute hydrochloric acid and taken up in ethylene dichloride. The solution was washed thoroughly with water and evaporated to dryness *in vacuo* at 30 mm. on a steam-bath. The residue was a viscous, sticky sirup weighing 42 g. which could not be made to crystallize. It was therefore saponified directly by boiling 36 g. of it with a solution of 200 g. of water and 18 g. of sodium hydroxide for eight and one-half hours under reflux. The product was treated with charcoal and filtered. Upon acidifying the clear filtrate with hydrochloric acid, the product separated as a dough-like material which solidified to a hard mass. Upon recrystallization from a mixture of dioxane–water (30:70), with Norite to remove the color, the product was obtained in colorless crystals, m. p. 205° after drying at 60° for twenty-four hours. *Anal.* Calcd. for $C_{24}H_{28}O_7$: C, 67.57; H, 6.15. Found: C, 68.18; H, 6.15.

XI. 2,4,4-Tri-(β -cyanoethyl)-pentanone-3.—To a stirred solution of 34.4 g. diethyl ketone (0.4 mole), 35 g. of tertiary butyl alcohol, and 4 g. of "Triton B," there was added dropwise 84.8 g. of acrylonitrile (1.6 mole) at 30–40° during the course of two hours. The reaction mixture was allowed to stand for twenty-four hours at room temperature. It was then acidified with dilute hydrochloric acid, taken up in ethylene dichloride, and washed thoroughly with water. The solvent was removed *in vacuo* on a steam-bath and the residual oil weighing 123 g. was distilled in high vacuum. The fraction boiling at 280–300° (2 mm.) was a viscous sirup (45 g.) which crystallized from methanol in colorless crystals melting at 90–91°; yield 30 g. pure product. *Anal.* Calcd. for $C_{14}H_{18}N_3O$: C, 68.55; H, 7.79; N, 17.14. Found: C, 68.80; H, 7.60; N, 17.38.

2,4,4-Tri-(β -carboxyethyl)-pentanone-3.—A mixture of 21 g. of compound XI, 150 g. of water and 32 g. of sodium hydroxide was boiled under reflux for fourteen and one-half hours, then treated with carbon black and filtered. Upon acidifying the clear filtrate with concentrated hydrochloric acid an oil separated on cooling. The water layer was poured off and the oil layer was dissolved in 60 cc. of warm water and allowed to crystallize in a refrigerator for

about a week. The air-dried crystalline product weighed 21 g. Upon recrystallization from nitromethane it formed colorless crystals melting at 116°. *Anal.* Calcd. for $C_{14}H_{22}O_7$: C, 55.59; H, 7.34. Found: C, 55.55; H, 7.35.

XII. 4-Acetyl-4-methylpimelonitrile.—A solution consisting of 160 g. of acrylonitrile and 100 g. of tertiary butyl alcohol was added dropwise during the course of three hours, to a rapidly stirred, ice-cold solution of 144 g. of methyl ethyl ketone, 200 g. of tertiary butyl alcohol, and 10 g. of methanolic potassium hydroxide (30% solution) care being taken that the reaction temperature did not exceed 5°. During the addition a crystalline solid separated. After all the acrylonitrile had been added, the mixture was stirred for two hours longer at 5–10°, then filtered by suction while still cold. After air-drying for twenty-four hours the product was obtained as an almost white crystalline material; yield 239 g. or 89%. Upon recrystallization from benzene it forms colorless crystals, m. p. 67°. *Anal.* Calcd. for $C_{10}H_{14}N_2O$: C, 67.37; H, 7.92; N, 15.72. Found: C, 67.80; H, 7.82; N, 15.90.

γ -Acetyl- γ -methylpimelic Acid.—A mixture of 50 g. of compound XII, 400 g. of water, and 39.2 g. of potassium hydroxide was gradually heated to boiling under reflux (exothermal reaction). Boiling was continued for three hours. The product was then evaporated to expel the ammonia and acidified with hydrochloric acid. The mixture was evaporated to dryness on a steam-bath and the powdered residue extracted with boiling ethylene dichloride. Upon chilling the extract, 38 g. of colorless crystals was obtained. After recrystallization from ethylene dichloride the product melted at 125°. *Anal.* Calcd. for $C_{10}H_{16}O_6$: C, 55.52; H, 7.46. Found: C, 55.70; H, 7.46.

XIII. γ -Carboxy- γ -methylpimelic Acid.—A solution of alkaline potassium hypochlorite was prepared by stirring at 50° a solution of 660 g. of water and 165 g. of calcium hypochlorite ("HTH" containing 70% available Cl) with a solution of 115 g. of anhydrous potassium carbonate, 33 g. of potassium hydroxide and 330 g. of water for about ten minutes and filtering off the precipitate of calcium carbonate. The clear filtrate was stirred and to it was added dropwise a solution of 71 g. of γ -acetyl- γ -methylpimelic acid in 200 g. of 20% sodium hydroxide solution, while maintaining the reaction mixture between 60 and 70° by external cooling. Chloroform was evolved. After all had been added, the mixture was stirred for one hour longer at 60–70° and any excess hypochlorite destroyed by adding a solution of sodium bisulfite. The product was then acidified with hydrochloric acid and the clear solution evaporated to dryness on a steam-bath, under reduced pressure. The solid residue was extracted with hot acetone. Upon evaporation of the acetone from the extract, 64 g. of a viscous sirup was obtained which gradually set to a solid mass. Upon recrystallization from nitromethane it separated in colorless crystals. The analytical sample was dried in a vacuum desiccator over phosphorus pentoxide for several days. It melted at 111°. *Anal.* Calcd. for $C_9H_{14}O_6$: C, 49.51; H, 6.47. Found: C, 49.21; H, 6.33.

XIV. 1,1,3,3-Tetra-(β -cyanoethyl)-butanone-2.—To a solution of 100 g. of dioxane, 53.4 g. of compound XII (0.3 mole) and 3 g. of "Triton B," there was added 15.9 g. (0.3 mole) of acrylonitrile while stirring at 25–40°. The reaction mixture was then allowed to stand for forty-eight hours

at room temperature. The product was acidified with dilute hydrochloric acid, taken up in ethylene dichloride, washed thoroughly and dried *in vacuo* at 90°. The residual oil weighing 62 g. was then distilled under high vacuum. About 40 g. of unchanged XII boiling at 180–200° (2 mm.) was recovered. The fraction boiling at 345–355° (2 mm.) distilled as a thick oil (11 g.) which crystallized when stirred with ethanol. After several recrystallizations from ethanol it was obtained as colorless crystals, m. p. 84–85°; yield 4 g. *Anal.* Calcd. for $C_{16}H_{20}N_4O$: C, 67.57; H, 7.09; N, 19.70. Found: C, 67.40; H, 6.97; N, 19.79.

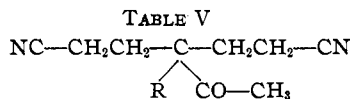
4-Acetyl-4-ethylpimelonitrile.—To a stirred solution of 60 g. of methyl *n*-propyl ketone, 10 g. of tertiary butyl alcohol and 1 g. of "Triton B," there was added dropwise 74 g. of acrylonitrile during the course of one and one-half hours while maintaining the reaction temperature at 10–15° by means of an ice-bath. The mixture was stirred for one hour longer at 15° after all the acrylonitrile had been added. It was then made slightly acid with dilute hydrochloric acid, and the crystalline precipitate filtered off and washed with a little ethanol; yield 57 g. Upon recrystallization from ethanol the compound formed colorless crystals, m. p. 109°. *Anal.* Calcd. for $C_{11}H_{16}N_2O$: C, 68.70; H, 8.39; N, 14.57. Found: C, 68.50; H, 8.15; N, 14.49.

1,3,3-Tri-(β -cyanoethyl)-pentanone-2.—The filtrate from the above preparation was mixed with ethylene dichloride and washed thoroughly with water. The ethylene dichloride was evaporated off under reduced pressure on a steam-bath and the residual oil (67 g.) distilled in high vacuum. The fraction boiling at 200–270° (1 mm.) amounting to 10 g. was crystalline and consisted almost entirely of 4-acetyl-4-ethylpimelonitrile. The fraction boiling at 270–285° (1 mm.) amounted to 26 g. and consisted almost entirely of 1,3,3-tri-(β -cyanoethyl)-pentanone-2. Upon recrystallization from ethanol it melted at 90–91°. *Anal.* Calcd. for $C_{14}H_{18}N_3O$: C, 68.53; H, 7.81; N, 17.13. Found: C, 68.51; H, 7.61; N, 17.27.

γ -Acetyl- γ -ethylpimelic Acid.—A mixture of 400 g. of water, 88 g. of sodium hydroxide, and 192 g. of 4-acetyl-4-ethylpimelonitrile was boiled under reflux for five hours. The clear solution was treated with "Norite," filtered, and acidified with 210 g. of concentrated hydrochloric acid while it was cooled and stirred. The product separated as a white crystalline mass (yield 170 g.) which, upon recrystallization from hot water, melted at 112–113°. *Anal.* Calcd. for $C_{11}H_{18}O_6$: C, 57.36; H, 7.88. Found: C, 57.70; H, 7.83.

γ -Carboxy- γ -ethylpimelic Acid.—To a stirred filtered solution of potassium hypochlorite made from 250 g. of calcium hypochlorite, 1500 g. of water, 175 g. of potassium carbonate and 50 g. of potassium hydroxide, there was added gradually at 60–70°, 115 g. of γ -acetyl- γ -ethylpimelic acid in 300 g. of 20% sodium hydroxide solution. Chloroform was evolved. The product was worked up as described for compound XIII. Upon evaporation of the acetone, 105 g. of crystalline product was obtained. Upon recrystallization from water or nitromethane it melted at 172°. *Anal.* Calcd. for $C_{10}H_{16}O_6$: C, 51.69; H, 6.95. Found: C, 51.30; H, 6.51.

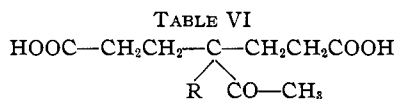
γ -Acetyl- γ -alkylpimelonitriles (Alkyl = Isopropyl, *n*-butyl, *n*-amyl).—In Table V are given the physical and



Value of R	°C.	B. p., Mm.	M. p., °C.	Formula	Analyses, %					
					C	Calcd. H	N	C	Found H	N
Iso-propyl	200-205	2	101	C ₁₂ H ₁₈ N ₂ O	13.58	13.50
<i>n</i> -Butyl	205-210	2	63	C ₁₃ H ₂₀ N ₂ O	70.86	9.16	12.71	71.09	9.09	12.71
<i>n</i> -Amyl	195-200	1	47	C ₁₄ H ₂₂ N ₂ O	71.74	9.47	11.96	71.60	9.81	12.06

analytical data of various dicyanoethylated homologs of methyl propyl ketone, prepared, respectively, from methyl isobutyl ketone, methyl *n*-amyl ketone, and methyl *n*-hexyl ketone. These dinitriles were prepared in the same manner as compound XII, but since they did not separate as solids from the reaction mixture, they were isolated by vacuum distillation after neutralizing the alkaline catalyst with dilute hydrochloric acid. The distilled products were then crystallized from ethanol to constant melting point. The yields of dicyanoethylation product were 50 to 60% in the case of methyl *n*-amyl ketone and methyl *n*-hexyl ketone, but only about 20% in the case of methyl isobutyl ketone, which reacted very sluggishly.

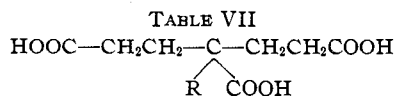
γ -Acetyl- γ -alkylpimelic Acids (Alkyl = Isopropyl, *n*-butyl, *n*-amyl).—These were obtained by saponification of the dinitriles of Table V, by boiling with an excess of aqueous sodium hydroxide solution, bleaching the resulting solution with charcoal, filtering, and acidifying the filtrate with concentrated hydrochloric acid, by the method described in the preparation of γ -acetyl- γ -ethylpimelic acid. They are listed in Table VI.



Value of R	M. p., °C.	Formula	Calcd., %		Found, %	
			C	H	C	H
Isopropyl ^a	148	C ₁₂ H ₂₀ O ₆	58.98	8.26	59.10	8.15
<i>n</i> -Butyl ^b	60-61	C ₁₃ H ₂₂ O ₆	60.42	8.59	60.70	8.39
<i>n</i> -Amyl ^b	73-74	C ₁₄ H ₂₄ O ₆	61.72	8.88	61.50	8.95

^{a,b} Recrystallized from *a* water; *b* benzene.

γ -Alkyl- γ -carboxypimelic Acids (Alkyl = Isopropyl, *n*-butyl, *n*-amyl).—These were prepared by treating the above γ -acetyl- γ -alkylpimelic acids dissolved in aqueous sodium hydroxide solution with an excess of potassium hypochlorite solution containing free potassium hydroxide at 60-70°, destroying the excess hypochlorite after eight hours of reaction, by means of sodium bisulfite, acidifying the solution with hydrochloric acid and evaporating the mixture to dryness, by exactly the same procedure as described above in the preparation of γ -carboxy- γ -ethylpimelic acid. The dried residue was extracted with acetone, and the acetone extract evaporated to dryness in



Value of R	M. p., °C.	Formula	Calcd., %		Found, %	
			C	H	C	H
Isopropyl ^a	160-161	C ₁₁ H ₁₈ O ₆	53.63	7.37	53.50	7.23
<i>n</i> -Butyl ^b	125	C ₁₂ H ₂₀ O ₆	55.35	7.75	55.01	7.65
<i>n</i> -Amyl ^b	114-115	C ₁₃ H ₂₂ O ₆	56.90	8.09	56.70	7.90

^{a,b} Recrystallized from *a* nitromethane; *b* water.

vacuum on a steam-bath. The resulting crude tri-carboxylic acids were each recrystallized from water or nitromethane and dried over phosphorus pentoxide for analysis. These are listed in Table VII.

XVII. 1,1,1-Tri-(β -cyanoethyl)-acetone.—To a solution of 29 g. of acetone, 30 g. of tertiary butyl alcohol and 2.5 g. of ethanolic 30% potassium hydroxide solution, cooled to 0° there was added dropwise, with rapid mechanical stirring, a solution consisting of 80 g. of acrylonitrile and 37 g. of tertiary butyl alcohol during a period of one and one-half hours while the reaction mixture was maintained between 0 and 5° by an ice-salt cooling bath. The mixture was stirred thereafter for two hours at 5° and the crystalline product filtered off by suction; yield 84 g. After recrystallization from hot water or from glycol monomethyl ether it formed colorless crystals; m. p. 154°. *Anal.* Calcd. for C₁₂H₁₈N₃O: C, 66.32; H, 6.96; N, 19.34. Found: C, 66.80; H, 6.91; N, 19.40.

1,1,1-Tri-(β -carboxyethyl)-acetone.—A mixture consisting of 140 g. of potassium hydroxide, 800 cc. of water, and 120 g. of XVII was boiled under reflux for four hours. The solution was treated with "Norite," cooled to 50° and filtered. The filtrate was acidified to congo red indicator with concentrated hydrochloric acid, and then evaporated to dryness under reduced pressure on a steam-bath. The residue was extracted with hot acetone. Upon cooling the hot filtered acetone extract, tri-(carboxyethyl)-acetone separated in colorless crystals; yield 80 g. More can be obtained from the mother liquor. The compound forms colorless needles from acetone melting at 149-150°. It is readily soluble in water or in ethanol. *Anal.* Calcd. for C₁₂H₁₈O₇: C, 52.53; H, 6.62. Found: C, 52.30; H, 6.68.

XVIII. Tri-(β -carboxyethyl)-acetic Acid.—To a stirred filtered solution of potassium hypochlorite prepared from 85 g. of calcium hypochlorite ("HTH" containing 70% available chlorine), 59.5 g. of anhydrous potassium carbonate, 17 g. of potassium hydroxide and 510 g. of water, there was added dropwise at 60-70° a solution of 136 g. of 20% sodium hydroxide solution and 46.5 g. of 1,1,1-tri-(β -carboxyethyl)-acetone. Chloroform was evolved. The mixture was stirred for two hours after reaction had apparently ceased. The product was worked up as described for compound XIII. The acetone extract upon evaporation yielded a white powdery residue which after several recrystallizations from water melted at 192° after softening at 182°. *Anal.* Calcd. for C₁₁H₁₆O₈: C, 47.80; H, 5.84. Found: C, 47.70; H, 5.67.

XIX. 1,3,3,3-Tetra-(β -cyanoethyl)-acetone.—A solution of 43.4 g. of 1,1,1-tri-(β -cyanoethyl)-acetone in 150 g. of acetonitrile was prepared by warming at 50°. To this stirred solution, 5 g. of "Triton B" was added. Acrylonitrile (31.6 g.) was then added dropwise during twenty

minutes, while stirring and maintaining the temperature at 40–42°. The mixture was stirred for two hours longer, then cooled, acidified with dilute hydrochloric acid, poured into water, and the oil taken up in ethylene dichloride. The ethylene dichloride solution was washed with water and dried in vacuum on a steam-bath. The residual oil weighed 53 g. Upon distillation in high vacuum, 27 g. of material distilled over up to 320° (1–3 mm.) This was mostly tri-(cyanoethyl)-acetone. The fraction which came over at 320–340° (1–3 mm.) weighed 7 g. Upon recrystallization from methanol it formed colorless needles, m. p. 121–122°. *Anal.* Calcd. for $C_{15}H_{12}N_4O$: C, 66.63; H, 6.71; N, 20.73. Found: C, 66.04; H, 6.63; N, 20.39.

γ -Acetyl- γ -phenylpimelonitrile.—Acrylonitrile (53 g.) was added dropwise to a stirred solution of 100 g. of tertiary butyl alcohol, 67 g. of phenylacetone, and 5 g. of "Triton B" while the reaction mixture was stirred and maintained at 20–25° by cooling. After one hour of additional stirring the almost solid mixture of crystalline product was filtered off and washed with about 50 cc. of methanol; yield 104 g. of colorless crystals. Upon recrystallization from ethanol it melted at 109–110°. *Anal.* Calcd. for $C_{15}H_{12}N_2O$: C, 74.95; H, 6.71; N, 11.66. Found: C, 74.70; H, 6.67; N, 11.63.

γ -Acetyl- γ -phenylpimelic acid.—A mixture of 40 g. of sodium hydroxide, 400 g. of water, and 87 g. of γ -acetyl- γ -phenylpimelonitrile was boiled under reflux for nine hours, treated with "Norite," filtered, and acidified with concentrated hydrochloric acid. The product separated as a thick oil which rapidly solidified. After recrystallization from water, the analytical sample melted at 171–172°. *Anal.* Calcd. for $C_{15}H_{12}O_3$: C, 64.72; H, 6.52. Found: C, 64.85; H, 6.64.

XX. γ -Carboxy- γ -phenylpimelic Acid.—To a stirred filtered potassium hypochlorite solution made from 50 g. of calcium hypochlorite ("HTH" containing 70% available Cl), 35 g. of anhydrous potassium carbonate, 10 g. of potassium hydroxide and 300 g. of water, there was added dropwise at 60–70° a solution of 27.8 g. of γ -acetyl- γ -phenylpimelic acid in 60 g. of aqueous 20% sodium hydroxide, while stirring. Chloroform was evolved. The mixture was stirred for one hour after reaction had ceased, and worked up as described for compound XIII. Upon evaporation of the acetone, 19 g. of resin-like material was obtained. Upon crystallization of the resin from nitromethane the product separated in the form of colorless crystals melting at 154°. *Anal.* Calcd. for $C_{14}H_{10}O_6$: C, 59.97; H, 5.76. Found: C, 59.67; H, 5.85.

XXI. α,α -Di-(2-cyanoethyl)-acetoacetic Methyl Ester.—(a) To a solution of 58 g. of methyl acetoacetate, 100 g. of dioxane and 7 g. of "Triton B," there was added 53 g. of acrylonitrile while the solution was stirred and cooled to

30–40°. After stirring for one hour the crystalline product was filtered off; yield 55 g. After recrystallization from acetone it formed colorless crystals melting at 154°. A further quantity can be obtained from the original filtrate on addition of water. *Anal.* Calcd. for $C_{11}H_{14}N_2O_3$: C, 59.43; H, 6.35; N, 12.60. Found: C, 59.80; H, 6.29; N, 12.59.

(b) The ethyl ester can be obtained in the same manner by using 65 g. of ethyl acetoacetate in the above procedure. The crude reaction product was poured into one liter of ice water whereupon the compound separated in crystalline form. After recrystallization from ethanol it melts at 82°. *Anal.* Calcd. for $C_{12}H_{16}N_2O_3$: C, 60.98; H, 6.83; N, 11.85. Found: C, 61.60; H, 6.88; N, 11.84.

Acknowledgment.—The analyses of the above products were performed by the semi-micro method by Mr. C. W. Nash of these laboratories.

Summary

1. Acrylonitrile condenses in the presence of aqueous trimethylbenzylammonium hydroxide or other strong alkali as a catalyst, with reactive ketones having a $-\text{CH}-$, $-\text{CH}_2-$, or CH_3- group adjacent to the carbonyl, so as to replace one or more of the reactive hydrogen atoms thereof by β -cyanoethyl radicals. The reaction furnishes a simple method for preparing a wide variety of ketonic polynitriles and polycarboxylic acids.

2. Acetophenone and its aryl substituted derivatives gave tri-cyanoethylation products $\text{R}-\text{CO}-\text{C}(\text{CH}_2\text{CH}_2\text{CN})_3$; cyclopentanone, cyclohexanone and para-substituted cyclohexanones gave tetra-cyanoethylation products; *o*-methylcyclohexanone gave a tri-cyanoethylation product, and α -tetralone gave a dicyanoethylation product.

3. Acetone gave a crystalline tri-cyanoethylation product, $\text{CH}_3\text{CO}-\text{C}(\text{CH}_2\text{CH}_2\text{CN})_3$. Substituted acetones of the type $\text{R}-\text{CH}_2-\text{CO}-\text{CH}_3$ (R is alkyl or aryl) reacted first on the $-\text{CH}_2-$ group to give dicyanoethylation products. These products are cyanoethylated further on the residual CH_3 group.

4. Acetoacetic esters similarly gave crystalline dicyanoethylation products.

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