High Pressure–High Temperature Reactions. II. The Reactions of Aliphatic Nitriles and Amides[1]

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Under the extreme conditions of high pressure (35,000–50,000 atm.) and temperatures ranging from ambient to 475°, certain aliphatic nitriles are not trimerized to *sym*-triazines as previously observed for aromatic nitriles. Instead, phenylacetonitrile, ethyl cyanoacetate, and adiponitrile undergo polymerizations which probably involve the addition of α-methylene groups to the triply bonded nitrile function (Thorpe reaction). Acrylonitrile is converted to a carbonaceous residue by the mere application of high pressure alone. Amides, due to resonance stabilization, are relatively unreactive under these conditions; acrylamide, like the nitrile, is also degraded to a carbonaceous product, but the simultaneous application of pressure and heat is required.

Discussion

Nitriles.—Pure aromatic nitriles have been observed to trimerize readily, in the course of a few minutes, to the corresponding 2,4,6-tris(aryl)-1,3,5-triazines under the extreme conditions of high pressure (35,000–50,000 atm.) and high temperature (350–500°).[3]
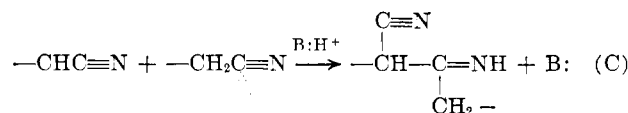

$$3ArC{\equiv}N \longrightarrow \qquad\qquad (A)$$
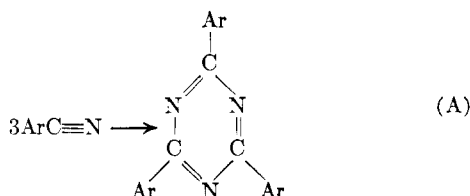
The reaction involves a decrease in multiple bond character (C=N of the product as compared to C≡N of the reagent); such aggregation reactions are facilitated by the application of pressure since the reaction's transition state is of smaller volume than that of the uncombined reagents.[4]

In their pioneering work on the subjection of solutions of nitriles to pressures of 7000–8500 atm., Cairns, Larchar, and McKusick[5] observed that aliphatic nitriles as well as aromatic nitriles, are trimerized to the corresponding triazines; the trimerization, however, did not occur either in the absence of a solvent (especially methanol), or at pressures below 1000 atm. It was of interest, therefore, in the present survey of the behavior of organic compounds under the simultaneous application of high pressures and high temperatures (HPHT) to determine whether aliphatic nitriles, without solvents, would trimerize under the extreme reaction conditions.

It has been observed that although the products from the HPHT treatment of an organic reagent differ in *degree* of reaction, they are usually of the same *kind* as those obtained by the acid- or base-catalyzed treatment of that reagent at atmospheric pressure. Thus, the condensation of cyclohexanone to dodecahydrotriphenylene is an example of acid-catalysis mimetic HPHT behavior, while the base-catalysis mimetic character has been observed in the polymeric condensation reaction of acetone.[6]

Because of this acid- or base-catalysis behavior, the HPHT reactions of aliphatic nitriles are more complex

than the simple trimerizations observed for their aromatic analogues. The complicating factor is due to the reactivity of the α-methylene group of the nitrile which can add *inter*- or *intra*-molecularly to the triplybonded —C≡N group to give rise to cyanoketimines; the latter, which still contain both α-methylene and nitrile groups, are then capable of further similar reaction to yield polymeric materials. The behavior of aliphatic nitriles under HPHT conditions, therefore, represents an extension of their behavior upon treatment with base (Thorpe reaction),[7] along with their trimerization reaction.

$$-CH_2C{\equiv}N + B{:} \longrightarrow B{:}H^+ + -\bar{C}HC{\equiv}N \qquad (B)$$

$$-CHC{\equiv}N + -CH_2C{\equiv}N \xrightarrow{B:H^+} -CH-C{=}NH + B{:} \qquad (C)$$

Thus, adiponitrile, an unactivated aliphatic dinitrile, gives HPHT products which are clear, brown, infusible, insoluble, amberlike resins. The elementary analyses and infrared spectral data suggest that the HPHT product is derived from a series of Thorpe-like addition reactions and trimerizations. The HPHT experiments with adiponitrile are particularly satisfying for they provide a clear-cut example of the primary and dominating effects of temperature and time at a given pressure. Thus, at 40 kbars (1 bar = 0.98692 atm.) and 155° for 30 min., the dinitrile is recovered unchanged. For a similar pressure and reaction time but an increased temperature (255°), however, the reaction product is the amber-like resin. If the pressure is still maintained at 40 kbars and the temperature is further increased to 370–400°, one can now decrease the reaction time in half (15 min.) and still obtain the same polymeric resinous product. A further increase of reaction temperature to 475° and the pressure to 50 kbars results in the production of a similar polymeric material after only six minutes' reaction time. Even at these high temperatures, the polymerization of the dinitrile proceeded with a minimum of decomposition; no odor of ammonia was present.

The HPHT situation with acetonitrile, a simple unactivated mononitrile, however, is different. Most of this liquid reagent at 50 kbars and 300–325° for 6–8

(1) Presented at the 134th National Meeting of the American Chemical Society, Chicago, Ill., September, 1958.

(2) U. S. Borax Research Corporation, Anaheim, Calif.

(3) I. S. Bengelsdorf, *J. Am. Chem. Soc.*, **80**, 1442 (1958).

(4) M. G. Evans and M. Polanyi, *Trans. Faraday Soc.*, **31**, 875 (1935).

(5) T. L. Cairns, A. W. Larchar, and B. C. McKusick, *J. Am. Chem. Soc.*, **74**, 5633 (1952).

(6) I. S. Bengelsdorf, 130th National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1956, Abstracts, p. 74-O; *cf.* S. D. Hamann, "Physico-Chemical Effects of Pressure," Butterworths Scientific Publications, London, 1957, p. 187.

(7) The first paper in a series of works on this reaction is by H. Baron, F. G. P. Remfry, and J. F. Thorpe, *J. Chem. Soc.*, **85**, 1726 (1904).
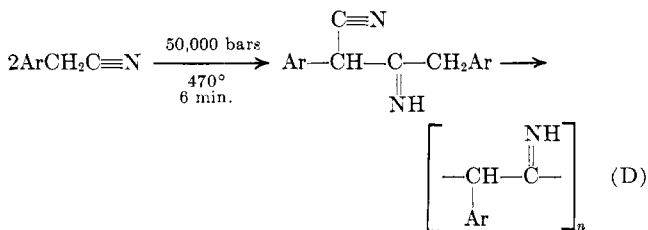
min. is decomposed to a dark, sooty solid; the odor of ammonia is evident. Sublimation of the product at reduced pressure gives a small yield of the unsymmetrical trimer, 4-amino-2,4-dimethylpyrimidine (I). This

$$
\begin{array}{c}
N \\
CH_3-C \quad\quad C-CH_3 \\
| \quad\quad\quad | \\
CH \quad\quad N \\
\quad C \\
\quad | \\
\quad NH_2 \\
I
\end{array}
$$
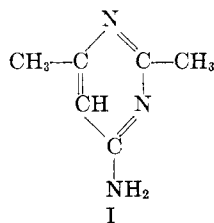
observation corroborates the previous report by Cairns, Larcher, and McCusick.[5] They found that the trimerization of acetonitrile, at pressures in the 7.5 kbar region, gives predominantly I as the reaction temperature increased. This is particularly true in the presence of a base, such as, ammonia. The pyrimidine I is also the chief product of the treatment of acetonitrile with base at atmospheric pressure.[8] All of these studies indicate that the presence of ammonia in the decomposition reaction of acetonitrile under HPHT conditions would tend, therefore, to produce some pyrimidine (I); this is observed.

If the methylene group of a mononitrile substrate, however, is more activated than is the case for acetonitrile, then the more intimate molecular environment of the severe HPHT conditions causes the nitrile to react far beyond the relatively simple reaction sequence described (B and C). Thus, instead of a decomposition and trimerization reaction as observed for the non-activated acetonitrile, the HPHT reactions of phenylacetonitrile and ethyl cyanoacetate lead to extensive polymerization and decomposition, respectively.

The complete absence of the —C≡N group vibration in the infrared spectrum of the polymers, and the appearance of C=N and NH bands not originally present, strongly suggest the following *inter*molecular addition polymerization sequence for phenylacetonitrile.

$$
2ArCH_2C\equiv N \xrightarrow[\substack{470° \\ 6\ min.}]{50,000\ bars}
\begin{array}{c}
C\equiv N \\
| \\
Ar-CH-C-CH_2Ar \\
\| \\
NH
\end{array}
\longrightarrow
\left[\begin{array}{c}
NH \\
\| \\
-CH-C- \\
| \\
Ar
\end{array}\right]_n \quad (D)
$$

The HPHT polymerization of ethyl cyanoacetate, an even more reactive nitrile, shows marked temperature dependence. Thus, at 40 kbars, up to 170° and 30-min. reaction time, the ester is recovered unchanged. At 200° and 15 min., however, the ester is converted to dark-colored, insoluble, infusible solids. If the reaction temperature is raised to 275–340°, and the time is decreased to 12 min., one observes the production of even darker (black) solids with similar physical properties as above; the odor of liberated ammonia, a reduced molecule, is indicative of the occurrence of deep-seated decomposition reactions.

An attempt to treat acrylonitrile at 40,000 bars and 300° for 14 min., through the simultaneous trimerization of the cyano group and the polymerization of the

vinyl group led to a carbonaceous residue and ammonia. Since other unsaturated substrates, e.g., isoprene, have been observed to carbonize by the application of pressure alone,[9] acrylonitrile was again subjected to 40,000 bars but with no thermal input. Again, the nitrile was decomposed to a carbonaceous solid and ammonia. This observation may be explained by the fact that the application of pressure alone must result in a rapid polymerization of the monomer. The subsequent rapid rise in temperature from the heat of polymerization cannot be dissipated from the thermally insulated reaction vessel and this internally generated energy results in the degradation of the reagent. Similar explosive polymerizations due to temperature increases under pressure have been observed and described previously.[10] A recent observation states that polyacrylonitrile reacts with bases to form polycyclic imidines[11]; that the dark color of the HPHT product may be due to such extensive polymeric cyclization reactions, of the initially produced polyacrylonitrile, in the presence of the liberated ammonia, could not be substantiated since the infrared spectrum of the HPHT product exhibited no absorption bands whatsoever.

The HPHT data concerning the experiments with furmaronitrile, β,β'-thio-dipropionitrile, and terephthalonitrile are presented in the table.

Amides.—Whereas nitriles are readily trimerized or polymerized under HPHT conditions, amides are extremely resistant towards change under similar extreme experimental conditions. This is undoubtedly due to the stabilization of amides by resonance; if any HPHT reaction occurs at all it is one of decomposition or carbonization.

One exception to the above observations is that of benzamide, an aromatic amide. It is partially dehydrated to benzonitrile *in situ;* the latter is then readily trimerized to 2,4,6-triphenyl-1,3,5-triazine (*cf.* equation A).[3]

In contrast, the HPHT treatment of *sym*-diphenylurea, a carbamide, at 50,000 bars and 360° partially converts it to a carbonaceous residue. Colorless starting urea, however, is recovered as a sublimate from the dark HPHT product. This indicates that those molecules of diphenylurea which survived the decomposition carbonization reaction are completely unaffected, *i.e.*, the HPHT reaction is one of degradation or no reaction at all.

The rather indiscriminate nature of the HPHT conditions as concluded from the above amide reactions and the ethyl cyanoacetate reactions, is pointedly illustrated by the behavior of acrylamide. The experimental data show that between 200° and 250° at 40,000 bars this monomer undergoes a violent decomposition reaction leading to carbonization and ammonia formation. Obviously, the heat of reaction added to the thermal input energy provides a thermal shock within the insulated reaction vessel which is too great to be dissipated and a violent decomposition ensues. Thus, both pressure and heat lead to the same degradative type of reaction in acrylamide as is observed for acrylonitrile by the application of pressure alone.
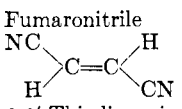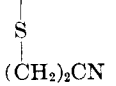
(8) A. R. Ronzio and W. B. Cook, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N.Y., 1951, p. 71.

(9) I. S. Bengelsdorf, unpublished work.
(10) K. H. Klaasens and J. H. Gisolf, *J. Polymer Sci.*, **10**, 149 (1953).
(11) E. M. LaCombe, *ibid.*, **24**, 152 (1957).

TABLE I. THE HIGH PRESSURE–HIGH TEMPERATURE REACTIONS OF ALIPHATIC NITRILES AND AMIDES[a]

Reagent	Pressure[b] bar × 10³	Temp., °C.	Time, min.	Results and products
Adiponitrile $NC(CH_2)_4CN$	40	155	30	Nitrile recovered unchanged
	40	255	14	Partial polymerization
	40	255	30	Complete polymerization to clear yellow-brown resin which looked like amber. Began to darken, but did not melt at 360°. *Anal.* Calcd. for $C_6H_8N_2$: C, 66.6; H, 7.4. Found: C, 65.7; H, 7.1.[c] Strong CN band at 2240 is missing, while bands at 3300, 3130, 1634, 1582, 1515 suggest NH, C=N, NH_2 functional groups are present in the product[d]
	40	370	15	Same as above. The absence of NH_3 indicated a minimum of degradative reactions[3]
	40	400	15	Same product and infrared spectrum as above
	50	475	6	Same product and infrared spectrum as above
Acetonitrile CH_3CN	50	325	6	Decomposition to a dark, sooty solid. Vacuum sublimation isolated a small yield of colorless, grainy crystals of 4-amino-2,6-dimethyl pyrimidine, m.p. 183°; lit.[e] m.p. 182–183°
	50	300	8	Same as above
Phenylacetonitrile $C_6H_5CH_2CN$	50[f]	410	7	Nitrile recovered unchanged
	50	470	6	Yellow polymeric solid. Strong CN stretching band at 2240 is missing, while bands at 3500, 3410, 3310, 1568, 1555 suggest NH, C=N, NH_2 functional groups are present in the product. *Anal.* Calcd. for C_8H_7N: C, 82.0; H, 6.0. Found: C, 78.4; H, 5.9[e]
Ethyl cyanoacetate $C_2H_5OOCCH_2CN$	40	55	30	Ester recovered unchanged
	40	170	15	Same as above
	35	200	15	Dark orange-colored infusible solid. Sharp 2270-CN band is missing. Extreme broadness of bands in the 1300–1800 and 3000 region is indicative of mixtures of functional groups
	40	200	15	Dark red-purple solid insoluble in alcohol, benzene, acetone, methanol, or ether. Begins to darken at 240°, but is not molten at 320°. *Anal.* Calcd. for $C_5H_7O_2N$: C, 53.1; H, 6.2. Found: C, 51.0; H, 4.5[e]
	35	275	12	Decomposition to ammonia and a black solid which neither sublimed or melted in a free flame
	35	340	12	Same as above
Acrylonitrile $CH_2=CHCN$	40	300	14	Carbonized solid product and ammonia
	40	. . .	30	Same as above
	40	. . .	15	Same as above. Infrared spectrum of product revealed absence of absorption bands
Fumaronitrile $NC \diagdown C=C \diagup H$ $H \diagup \diagdown CN$	40	340	15	The major part of the starting dinitrile was recovered
	40	335	15	Same as above. No dimerization or polymerization was observed
β,β'-Thiodipropionitrile $(CH_2)_2CN$ $|$ S $|$ $(CH_2)_2CN$	40	305	10	Extensive degradation to a carbonized solid and hydrogen sulfide
Terephthalonitrile[g] $p\text{-}NC\text{—}C_6H_4\text{—}CN$	39	400	11	Carbonized solid product (not molten at 330°); partial recovery of starting material
s-Diphenylurea $C_6H_5NHCONHC_6H_5$[g]	50[h]	360	6	Partial carbonization. Infrared spectrum of colorless solid recovered by sublimation is identical with that of starting material
Acrylamide $CH_2=CHCONH_2$	40	150	25	The amide melted in the capsule, but was recovered unchanged
	40	195	15	Same as above
	40	260	15	Extensive decomposition to carbonaceous residue and ammonia
	40	300	15	Same as above
Oxamide $H_2NCO\text{—}CONH_2$	40	260	18	Amide recovered unchanged
	40	330	18	Partial degradation to dark residue and ammonia
	40	345	16	Same as above
Urea–pyromellitic anhydride	40	355	17	Partial degradation to ammonia and recovery of unchanged urea

[a] All HPHT reactions were conducted in lead reaction vessels unless otherwise indicated. [b] 1 atm. = 1.0133 bar or 1 bar = 0.98692 atm. [c] The analytical value for carbon in the noncarbonized polymeric products is somewhat lower, in all cases, than that for the starting nitrile; this may be due to partial loss of HCN. [d] Infrared absorption bands are reported in wave numbers (cm.⁻¹). [e] *Cf.* ref. 5. [f] This reaction was conducted in a nickel capsule. [g] An aromatic compound included in this study. [h] This reaction was conducted in a stainless steel capsule.

The case of oxamide is further illustrative of the resistance of amides to HPHT change. Paracyanogen, a carbon–nitrogen polymer, has been reported to have been prepared in 30–40 % yield by heating oxamide at 270° for one week.[12] Attempts to accelerate this dehydration of oxamide, by HPHT conditions, failed. At 40 kbars and 260° for 18 min. oxamide is recovered unchanged. Elevation of the temperature to 333°, under identical pressure–time conditions, leads to extensive decomposition to a carbonaceous materials and ammonia.

A single experiment involving the HPHT reaction of urea with pyromellitic anhydride to produce a polymeric phthalocyanine also failed; ammonia was liberated as evidence of a deep-seated decomposition reaction.

(12) L. L. Bircumshaw, F. M. Taylor, and D. H. Whiffen, J. Chem. Soc., 931 (1954).

Experimental

Apparatus.—The experimental apparatus used in this investigation is the "belt" high pressure–high temperature apparatus developed in this laboratory[13]; suitable modifications were made to facilitate the study of liquid and solid organic substrates. Thus, the reaction vessels are small metallic cylinders fabricated so that they are closed at one end, and capable at the other. Their dimensions (0.200-in. diameter and 0.450 in. long) permitted a sample capacity of ca. 0.2 ml. of liquid and 0.13 g. of solid. Cylinders fabricated of nickel, stainless steel, and lead were used; the latter soft metal is preferred for the reaction capsule since it can be opened easily with a razor blade after the reaction is completed. Liquid products and reagents were manipulated by suitable glass capillary milligram techniques.

Reactions.—The details of the HPHT reactions are summarized in Table I.

(13) H. T. Hall, Rev. Sci. Instr., 31, 125 (1960); H. T. Hall, J. Phys. Chem., 59, 1144 (1955).

The Reaction of Diketene with Glycine

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Department of Biochemistry, Columbia University, College of Physicians and Surgeons, New York 32, N. Y.

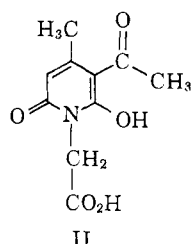The reaction between diketene and glycine in basic solution yields 3-acetyl-1-carboxymethylene-4-hydroxy-6-methyl-2-pyridone (I).
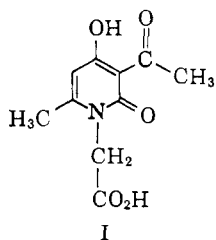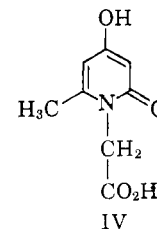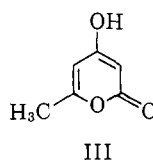
In the course of a biosynthetic investigation, the preparation of acetoacetylglycine by the reaction of glycine with diketene was attempted. Instead, a crystalline compound was obtained in about a 15% yield which was not the desired material. We have recently re-investigated the reaction and have shown the compound to be 3-acetyl-1-carboxymethylene-4-hydroxy-6-methyl-2-pyridone (I).

Elemental analysis gave the empirical formula $C_{10}H_{11}NO_5$ which is satisfied by the condensation of two molecules of diketene with one molecule of glycine and the elimination of one molecule of water. The compound is acidic (neutralization equivalent 112, pK_{a_1}, 3.25, pK_{a_2} 8.0) and the infrared spectrum showed three carbonyl peaks which were assigned as follows: 5.78 μ, $-CH_2CO_2H$; 6.00 μ, $>NCO-$, and 6.18 μ, α,β-unsaturated-β-hydroxy ketone.[1] There was no hydroxyl absorption. The carbonyl of the acetyl function formed a 2,4-dinitrophenylhydrazone and also gave a positive iodoform test. Kuhn Roth oxidation gave two C-methyl groups. The ultraviolet spectrum implied a pyridone rather than a pyrrolidone structure and therefore I and II were considered most probable.

The acid could be esterified easily to give the ethyl or methyl ester and the increased solubility of these compounds in deuterated chloroform enabled their n.m.r. spectra to be studied.[2] The methyl ester showed 6 singlets at τ values, -5.3 (1H); 4.2 (1H); 5.35 (2H, $-CH_2CO_2CH_3$); 6.3 (3H, $-CO_2CH_3$); 7.4 (3H, $-COCH_3$); 7.75 (3H, $C-CH_3$). The singlet at -5.3 τ was attributed to the hydroxyl hydrogen in the α,β-unsaturated-β-hydroxy ketone function.[3]

On heating with concentrated sulfuric acid, the compound was deacetylated,[4] and the acetic acid which distilled was characterized as the S-benzylthiouronium salt. The infrared spectrum of the deacetylated product lacked the band at 6.18 μ and the ultraviolet spectrum was identical with that of 1,6 dimethyl-4-hydroxy-2-pyridone and unlike that of 2,6 dihydroxypyridine. Thus structure I was assigned to the original compound and this was verified by a partial synthesis.

III   IV

By analogy with the well known reaction of triacetic acid lactone (III) to give 1,4 dihydroxypyridines with ammonia and amines,[5] glycine reacted with triacetic acid lactone in sodium hydroxide solution and the prod-

(2) N.m.r. spectra were taken on a Varian A60 instrument at 60 Mc. using deuterated chloroform solutions and tetramethylsilane as internal reference.

(3) L. M. Jackman, "Applications of Nuclear Magnetic Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p. 71.

(4) O. Mumm and G. Hingst, Ber., 56, 2301 (1923).

(5) N. Collie and W. W. Myers, J. Chem. Soc., 722 (1892); H. M. Woodburn and M. Hellmann, Rec. trav. chim., 70, 813 (1951).

I   II

(1) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 124.