(B) **Dibromo Derivative of II.**—A solution of 4.5 g. of II, 6.0 g. of N-bromosuccinimide and 60 cc. of carbon tetrachloride was placed in a desiccator containing sodium hydroxide pellets, and the desiccator was partially evacuated. After five days at room temperature the mixture was filtered, and the filtrate was concentrated *in vacuo*. The resulting solid was crystallized from a mixture of ethanol and benzene and 4 g. of solid, m.p. 164–165°, was obtained.

Anal. Calcd. for $C_{16}H_{10}Br_2S_2$: C, 45.09; H, 2.36. Found: C, 45.17; H, 2.38.

The identical material was obtained in 63% yield by the treatment of the above mentioned monobromo compound with an excess of N-bromosuccinimide in the presence of catalytic amounts of benzoyl peroxide using carbon tetrachloride as the solvent and room temperature conditions.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF BROOKLYN COLLEGE]

The Pyrolysis of Amides

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In its early stages the thermal conversion of an amide to the corresponding nitrile is characterized by the evolution of ammonia, the appearance of the secondary amide (imide) and the accumulation of the corresponding carboxylic acid. These facts may be accounted for by assuming that the primary step in the pyrolysis is the bimolecular deammonation of the amide to the isoimide, RC(=NH)OCOR. In part, the isoimide may then decompose to nitrile and carboxylic acid and, in part, rearrange reversibly to the imide. The carboxylic acid, in turn, may react with the ammonia being formed to regenerate one molecule of amide and yield water. It is only under conditions favorable for this last reaction that the thermal conversion of amides to nitriles becomes a dehydration reaction. The exchange reaction, $CH_3CONH_2 + PhCOOH \rightarrow CH_3COOH + PhCONH_2$, appears to involve a partial decomposition of the acetamide according to the scheme given above; *i.e.*, $2CH_3CONH_2 \rightarrow CH_3CN + CH_3COOH + NH_3$, coupled with the reaction of benzoic acid with the ammonia formed to yield benzamide and water. Once water is formed the reaction may take the course, $CH_3CONH_2 + H_2O \rightarrow CH_3COOH + NH_3$ and $PhCOOH + NH_3 \rightarrow PhCONH_2 + H_2O$, the water thus serving a catalytic function in the exchange. It is also possible that the amide and acid react to form the isoimide and water; after rearrangement to the imide, the product would be capable of hydrolyzing to regenerate the original amide and acid or the exchanged pair. The previously observed reactivity of partially pyrolyzed amides toward aniline is probably due to catalysis by the carboxylic acids present.

Amides have been found to pyrolyze in two ways: (a) to nitrile and water[1,2]; (b) to nitrile, carboxylic acid and ammonia.[3] The second of these has been said to result from the direct dehydration of one molecule of amide followed by the hydrolysis of a second molecule. A third mode of pyrolysis has been hypothesized,[4] *i.e.*, scission to ketene and ammonia. While partially pyrolyzed amides were found to be much more reactive toward aniline than the original amides, this behavior was not restricted to amides in which the formation of ketenes was structurally possible but was also shown by benzamide. Suffice it to say that the evolution of ammonia has been generally recognized to accompany the pyrolysis of amides.

The observation[5] that monocarboxylic acids yield anhydrides when heated above 250° suggested that the evolution of ammonia from amides might be due to the analogous deammonation to imides. Isoimides are possible intermediates in this reaction. N-Substituted isoimides rearrange readily to N-substituted imides.[6,7]

The formation of cyclic imides by heating certain diamides such as phthalamide is well known[8] and the formation of acyclic imides from monoamides has been shown to occur in the presence of hydrogen chloride.[9] Furthermore, acyclic imides undergo facile pyrolysis to nitriles and acids,[10] presumably reverting to isoimides in the process.[11] In sum, the reactions involving the formation and pyrolysis of the imide equal the result given above as mode (b) for the pyrolysis of amides. Since carboxylic acids react with ammonia to form amides and water,[12] it follows that the thermal dehydration

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[1] R. S. Boehner and C. E. Andrews, THIS JOURNAL, **38**, 2503 (1916), refluxed amides with massive amounts of contact agents such as alumina, pumice, glass, sand and graphite.

[2] R. S. Boehner and A. L. Ward, *ibid.*, **38**, 2505 (1916), passed the vapors of amides over the same contact agents at 425°.

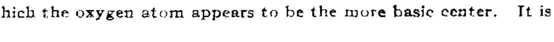
[3] A. W. Ralston, H. J. Harwood and W. O. Pool, *ibid.*, **59**, 986 (1937), distilled stearamide at atmospheric pressure.

[4] C. D. Hurd, M. F. Dull and K. E. Martin, *ibid.*, **54**, 1974 (1932).

[5] D. Davidson and P. Newman, *ibid.*, **74**, 1515 (1952).

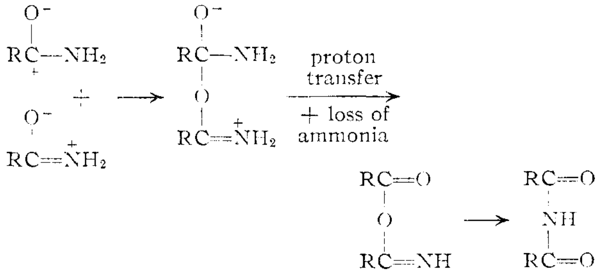
[6] M. L. Sherrill, F. L. Schaeffer and E. P. Shoyer, *ibid.*, **50**, 474 (1928).

[7] Amides are resonance hybrids,



$$R\overset{O}{\overset{\|}{C}}-NH_2 \longleftrightarrow R\overset{O^-}{\overset{|}{C}}=\overset{+}{N}H_2 \longleftrightarrow R\underset{+}{\overset{O^-}{\overset{|}{C}}}-NH_2,$$

in which the oxygen atom appears to be the more basic center. It is, therefore, possible that the addition of one molecule of amide to the carbonyl carbon atom of another will take place as



$$R\underset{+}{\overset{O^-}{\overset{|}{C}}}-NH_2 + R\overset{O^-}{\overset{|}{C}}=\overset{+}{N}H_2 \longrightarrow R\overset{O^-}{\overset{|}{C}}(-NH_2)-O-RC=\overset{+}{N}H_2 \xrightarrow[\text{+ loss of ammonia}]{\text{proton transfer}} RC(=O)-O-RC=NH \longrightarrow RC(=O)-NH-RC=O$$

The process may also be looked upon as the addition of one molecule of amide in the enol form to a second in either enol or keto form. The finding of Q. E. Thompson, THIS JOURNAL, **73**, 5841 (1951), that tribenzamide is formed more rapidly from benzamide than from dibenzamide is readily explained by the assumption that the isoimide is the primary product in the benzoylation of benzamide.

[8] F. W. Stacey, J. G. Lindsay and A. N. Bourns, *Can. J. Chem.*, **30**, 135 (1952).

[9] J. B. Polya and T. M. Spotswood, *Rec. trav. chim.*, **67**, 927 (1948).

[10] C. D. Hurd and M. F. Dull, THIS JOURNAL, **54**, 2432 (1932).

[11] H. Meyer and A. Hofmann, *Monatsh.*, **38**, 343 (1917).

[12] J. A. Mitchell and E. E. Reid, THIS JOURNAL, **53**, 321, 187 (1931).

of amides to nitriles (mode a of pyrolysis) may actually consist of three steps: (1) deammonation to imide; (2) pyrolysis of the imide and (3) ammonolysis of the resulting carboxylic acid. If the isoimide is an intermediate, it is likely that much of it decomposes as it is formed from the amide and before it rearranges to the imide.

It has now been found that deammonation of amides takes place even more readily than the dehydration of monocarboxylic acids,[5] marked reaction occurring in the vicinity of 220°. Sufficient imide survives to permit detection by means of hydroxylamine.[13] In cases such as propionamide and isobutyramide, where the solubility relationships are favorable, the imides are readily isolated in low yields by merely adding water to the pyrolyzed amides.

When simply refluxed at their boiling points, the lower aliphatic amides and benzamide follow mainly the nitrile–acid type of pyrolysis. Of the amides examined in the present study only phenylacetamide exhibited marked dehydration, the molar ratio of nitrile to acid here alone being much greater than unity. Apparently, the rate of ammonolysis of the acid gradually approaches the rate of formation of ammonia since in an extended experiment with acetamide, ammonia no longer escaped from the refluxing amide after five hours although the pyrolysis was far from complete and nitrile continued to be formed. The formation of water from amides, previously observed at higher temperatures[2,4] or in the presence of finely divided solids,[1,2] is probably due not to direct dehydration but to a differential increase in the rate of ammonolysis of the acid over the rate of deammonation of the amide under these conditions.

That ammonolysis of acids may be occurring in the pyrolysis of amides is shown by adding an equivalent of an unrelated acid to the amide being pyrolyzed. Refluxing an equimolecular mixture of acetamide and benzoic acid while removing volatile products gives a fair yield of benzamide.[14] No ammonia is evolved and acetonitrile and water appear in the distillate, which is mainly acetic acid. The reaction thus seems to involve a partial pyrolysis of the acetamide to nitrile and acid coupled with the ammonolysis of the benzoic acid. The water thus formed may set off another mode of exchange, *i.e.*, the hydrolysis of the acetamide followed by the ammonolysis of the benzoic acid. In this process the water is regenerated. Another possibility for the exchange, which is not excluded, is the interaction of acetamide with benzoic acid to form N-acetylbenzamide and water; these two may revert to acetic acid and benzamide.

The reactivity toward aniline of partially pyrolyzed amides[4] requires explanation. It has been shown that benzoic acid catalyzes the exchange reaction between acetanilide and *p*-anisidine.[15] Since it is probable that acids were present in the partially pyrolyzed amides previously studied, it seems likely that their enhanced reactivity toward aniline was due to acid catalysis. In the present work equivalent amounts of acetamide and *p*-toluidine (*p*-toluidine was employed rather than aniline because of the lower solubility of its acetyl derivative) gave no aceto-*p*-toluide after 15 minutes of refluxing, whereas the addition of 0.1 of an equivalent of acetic acid to the reaction mixture resulted in a 67% yield of aceto-*p*-toluide.

The conversion of aliphatic diamides to cyanoacids[16] represents a variation of the nitrile–acid type of pyrolysis. Thus, $NH_2CO(CH_2)_nCONH_2$ may yield a polyimide, $NH_2[CO(CH_2)_nCONH]_mH$, which contains the structural element, –CONH-CO–, flanked by hydrocarbon residues. Since the imide grouping undergoes scission to –CN and –COOH, it may be anticipated that 50% of the polyimide units will emerge as cyanoacid, 25% as dicarboxylic acid and 25% as dinitrile. The dinitrile, being the most volatile species, may be removed by distillation. Since nitriles and acids combine to form imides,[17,18] the cyanoacid may reform the polyimide and the yield of dinitrile thus be enhanced.

Imides react with methanolic hydroxylamine in the presence of potassium hydroxide to yield hydroxamic acids.[13,19] The reaction occurs quite readily even in the cold, which is not the case with amides. Amides, on the other hand, react readily with methanolic hydroxylamine hydrochloride to form hydroxamic acids, while imides do not. Acyclic imides are distinguished from acyclic anhydrides (which also yield hydroxamic acids) by the fact that they fail to dehydrate α-(*p*-nitrobenzoyl)-aminotoluic acid in pyridine.[20] Most characteristic of acyclic imides is their behavior toward 0.05 *M* potassium hydroxide in 1:1 pyridine–methanol solution containing the indicators Alizarin Yellow R and brom thymol blue (the A–I indicator reagent).[21] At first, an immediate color change from purple to green occurs. This signifies that acyclic imides are weak acids (their pK_a's probably lie somewhere between 7 and 12). In about one minute the purple color is restored indicating that the imide has disappeared. Within 24 hours a second and permanent change to green occurs. These color changes reflect the following events.

$$(RCO)_2NH + CH_3O^- \text{ (strong base)} \rightleftarrows CH_3OH + (RCO)_2N^- \text{ (interm. base)}$$

$$(RCO)_2N^- \text{ (interm. base)} + CH_3OH \longrightarrow RCOOCH_3 + RCONH^- \text{ (strong base)}$$

$$RCOOCH_3 + RCONH^- \text{ (strong base)} + H_2O \longrightarrow RCONH_2 + CH_3OH + RCOO^- \text{ (weak base)}$$

Experimental[22]

The Pyrolysis of Amides at their Boiling Points.—One-third mole of an amide was placed in a 125-ml. Claisen flask which had been modified by replacing the side-tube by an 8-in. Vigreux column. A receiver consisting of an 8 × 1" side-arm test-tube was attached to the side-arm of the Claisen flask and connected through a Y-tube to a safety bottle charged with mineral oil and to a delivery tube dipping into a 100-ml. cylinder containing 20 ml. of saturated boric acid

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[13] J. B. Polya and P. L. Tardew, *Anal. Chem.*, **23**, 1036 (1951).

[14] J. F. Norris and A. J. Klemka, THIS JOURNAL, **62**, 1432 (1940).

[15] R. Jauvin, M. B. Piccoli and J. Charlambous, *Helv. Chim. Acta*, **37**, 216 (1954).

[16] B. S. Biggs and W. L. Bishop, *Org. Syntheses*, **25**, 95 (1945).

[17] C. E. Colby and F. D. Dodge, *Am. Chem. J.*, **13**, 1 (1891).

[18] W. König, *J. prakt. Chem.*, [2] **69**, 1 (1904).

[19] D. Davidson, *J. Chem. Educ.*, **17**, 81 (1940).

[20] D. Davidson, *Anal. Chem.*, **26**, 576 (1954).

[21] D. Davidson, *J. Chem. Educ.*, **19**, 221 (1942).

[22] All temperatures given are corrected.

solution to which a few drops of methyl red–methylene blue indicator had been added. One thermometer extended into the bulb of the flask and another was in the usual position in the side-tube. The receiver was cooled in a beaker of ice-water. Heating by flame was so regulated that the amide refluxed in the lower part of the side-tube but nitrile or water or both could distil. As ammonia was evolved and the indicator in the boric acid solution turned, 2 *M* hydrochloric acid was added from a buret to restore the acidity of the solution. The temperature of the boiling amide gradually declined while the temperature at the top of the side-tube rose. At the end of the heating period (3–5 hr.) the residue was cooled somewhat, rinsed out of the flask with water, cooled to room temperature and titrated with 2 *M* sodium hydroxide to the phenolphthalein end-point. If the nitrile had not distilled out during the heating it was then steam distilled, the distillate being salted out with sodium chloride. In favorable cases (benzamide, phenylacetamide) unchanged amide could be recovered by chilling the residue and filtering; solid acids agreeing closely in amount with that determined by the alkali titration could be obtained by acidifying the filtrate with concd. hydrochloric acid. Table I gives the results with a number of amides.

In an extended experiment with acetamide it was found that the evolution of ammonia ceased after five hours although the distillation of acetonitrile continued. If, beyond this point, the flame was raised, a two-phase distillate containing acetonitrile, water, acetic acid and ammonium acetate passed over and the evolution of ammonia began again.

TABLE I

THE NITRILE–ACID RATIO IN THE PYROLYSIS OF AMIDES AT THEIR BOILING POINTS

Amide	Time, hr.	Temp. range, °C.	Mole of products (per mole of amide) NH_3	Nitrile	Acid	Nitrile–acid ratio
Acet-	3.5	220–217	0.096	0.058[b]	0.048	1.2
Propion-	3.5	226–217	.12	.15	.11	1.3
Isobutyr-	3	220–213	.11	.13	.13	1.0
Butyr-	3.5	227–217	.18	.19	.17	1.1
Capro-	5	252–207	.25	.37	.31	1.2
Capro-[a]	2.5	252–216	.17	.18	.18	1.0
Benz-[a,c]	3.5	284–228	.26	.33	.32	1.0
Phenylacet-[a,d]	4.5	279–244	.19	.50	.19	2.6

[a] In these cases the nitrile was not distilled out of the refluxing amide but was subsequently recovered from the residue by steam distillation. [b] Water was separated from the distillate by treating with solid potassium carbonate. [c] 31% of the amide was recovered unchanged on chilling the residue after removal of the nitrile; acidification of the filtrate gave 90% of the benzoic acid indicated by titration. [d] 11% of unchanged amide was recovered as in (*c*) followed by recrystallization from water which removed 2.3 g. of resin; acidification of the original filtrate yielded 106% of the acid indicated by titration.

The Isolation of Imides from the Pyrolysis of Amides. A. Dipropionamide from Propionamide.—One-gram samples of propionamide were refluxed for varying lengths of time in 8 × 1″ test-tubes loosely closed by means of glass stoppers. The residues were then cooled and stirred with 3 ml. of water. The insoluble material was filtered and air-dried. The periods of heating in hours and the yields of dipropionamide in mg., respectively, were: 0, 0; 0.5, 22; 1, 47; 1.5, 43; 2, 49. These precipitates melted at 154° and gave the tests for imides described below.

B. Diisobutyramide from Butyramide.—In like manner, 1-g. samples of isobutyramide after pyrolysis and treatment with 5 ml. of water yielded: 0, 0; 1, 11; 2, 12. The products melted at 174° and responded to the tests for imides mentioned below.

The Qualitative Analytical Behavior of Acyclic Imides.—The acyclic imides encountered in this work gave the following tests. When 30 mg. of the imide was dissolved in 1 ml. of the A–I indicator reagent,[21] the purple color of the reagent turned to green at once, but within a minute the green color changed back to purple. On standing, a second and permanent change from purple to green occurred.

The acyclic imides responded *in the cold* to the hydroxamic acid test[19] when the hydroxylamine hydrochloride and potassium hydroxide were mixed before treating the imide. Under these conditions amides gave negative results. On the other hand, if the potassium hydroxide was omitted and the test conducted in the hot, amides responded but the acyclic imides did not.

The diacetamide used in the preceding experiment was prepared by a modification of an existing method.[18] A mixture of 76 ml. of acetic annydride, 34.5 g. of acetamide and 3 g. of ammonium chloride was refluxed for 30 min. in an all-glass apparatus and then fractionated in vacuum at 9 mm. in the Claisen flask described above. The fraction boiling at 110–120° (mainly at 114°) weighed 21.5 g., had a m.p. of 81° and gave the tests for acyclic imides described above but not the test for acetamide with hydroxylamine hydrochloride.

A Qualitative Pyrolytic Test for Amides.—One-tenth of a gram of an amide in a small (4 × 1/2″) test-tube was refluxed while moist, red litmus paper was inserted into the gas space of the tube. The presence of ammonia was indicated almost at once and after one minute the cooled residue gave a marginal hydroxamic acid test (see above). Refluxing for three min. was sufficient to give a marked test. The azlactone test for acyclic anhydrides[20] was negative. Positive tests were given by the amides listed in Table I. At a controlled bath temperature of 220° all of these amides yielded positive hydroxamic acid tests after 15 min. heating.

Catalysis of the Reaction between Acetamide and *p*-Toluidine by Acetic Acid.—A mixture of 1.1 g. (0.01 mole) of *p*-toluidine and 0.6 g. (0.01 mole) of acetamide was refluxed for 15 min. in a loosely stoppered, 8 × 1″ test-tube, cooled and treated with 5 ml. of water. This precipitated an oil which dissolved on the further addition of 5 ml. of 2 *M* hydrochloric acid. In a similar run in which 0.06 ml. (0.001 mole) of glacial acetic acid was included, the addition of water caused the precipitation of a solid which did not dissolve on the further addition of 5 ml. of 2 *M* hydrochloric acid. Filtration, washing and air-drying yielded 1.0 g. (67% of the theoretical amount) of aceto-*p*-toluide, m.p. 146°.

The Exchange between Acetamide and Benzoic Acid.—A mixture of 29.5 g. (0.50 mole) of acetamide and 61 g. (0.50 mole) of benzoic acid was heated in the apparatus described above under the pyrolysis of amides. The heating was regulated so that acetic acid and lower-boiling products distilled. No ammonia was evolved and 27.2 g. (30 g. was the theoretical amount of acetic acid) was obtained in 3.5 hrs. During the first 20 min., the temperature of the boiling reaction mixture fell from 224 to 220° after which it rose gradually to 232°. Titration of a sample of the distillate with standard sodium hydroxide showed it to contain 71% of acetic acid. Karl Fischer titration gave a water content of 13%. The nitrile content (by difference) was 16%. This last was confirmed by treating 1 ml. of the distillate with 1 ml. of water and saturating with potassium carbonate which gave 0.2 ml. of an upper, oily layer. Redistillation of 18.8 g. of the acid distillate gave 3.0 g. of a first fraction, b. 81–94° (d^{20}_4 0.843) and 4.3 g. of a third fraction, b. 112–119° (d^{20}_4 1.047). On a molecular basis the figures given above become: acetic acid recovered, 64% of the theoretical amount; water, 39%; acetonitrile, 22%. Thus 86% of the amide taken was accounted for as acid and nitrile, of which quantity about half reacted according to the nitrile–acid pyrolysis scheme. No benzonitrile was apparent in the distillate which gave a clear solution on dilution with water.

The original residue gave a positive hydroxamic acid test but negative azlactone test. It was removed from the flask while molten, allowed to solidify in a beaker, transferred to a mortar, ground with 25 ml. of water and titrated with 2 *M* sodium hydroxide to the phenolphthalein end-point. This required 84 ml. of solution. Steam distillation of the precipitate and of the mother liquor followed by salting out of the distillate gave 2.0 g. (4% of the theoretical amount) of benzonitrile. Cooling the residue from the steam distillation of the precipitate gave 28.1 g. (46% of the theoretical amount) of benzamide. Acidification of the residue from the original filtrate gave 19.7 g. of benzoic acid (32% of the acid taken). Thus, 82% of the benzoic acid taken was accounted for.

Similar experiments with 0.33-mole quantities of benzoic acid and 0.33 mole each of propionamide, butyramide and isobutyramide gave very similar results.

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