THE CHEMISTRY OF THE ALKALI AMIDES

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I. INTRODUCTION

The history of science is filled with numerous examples of laboratory or museum curiosities which became after a time common laboratory reagents or commercially useful substances. Such in a general way has been the case with the alkali amides, compounds known for well over a hundred years, but which, with the exception of occasional isolated and sporadic researches, remained without systematic investigation for perhaps ninety years following their discovery. Then arose a period of active and far-reaching research which continues unabated today. Sodium amide has become a much used reagent in synthetic organic chemistry because of its ability to promote condensation reactions, to introduce amino groups into a molecule, and to remove the elements of water or of a hydrohalide acid. Moreover, the use of the alkali amides for the commercial production of indigo, cyanides, and azides has resulted in a rapid growth of the literature dealing with the alkali amides. So much work has now been done in this field that anyone desirous of acquainting himself with the chemistry of the alkali amides is faced with a tremendous task. It is the purpose of this article to give a review of the chemistry of the alkali amides in as brief a manner as is consistent with thoroughness and accuracy.

II. HISTORICAL

The discovery of sodium and potassium amides[1] belongs rightly to that golden age of chemical development, the early part of the nineteenth century. At that time chemistry was in a state of flux. The elementary nature of chlorine had as yet not been established and many substances now known to be compounds were regarded as elementary in nature. In 1807 Davy (22) electrolyzed the supposed elements, soda and potash, and obtained sodium and potassium. This discovery immediately caused considerable discussion and speculation and likewise precipitated a good deal of experimentation. Gay-Lussac and Thénard (55, 56) held that the new substances were compounds of hydrogen with soda and potash and showed that these metals could be prepared in quantity much more easily by the reaction of iron with the hydroxides. During the course of their examination of the properties of these newly found alkali metals, Gay-Lussac and Thénard (57, 58) examined their reaction with ammonia and first prepared sodium and potassium amides. They found in these substances a proof for their views concerning the nature of sodium and potassium, because in their experiments on the preparation of the amides and subsequent hydrolysis they obtained a volume of hydrogen greater than that of the ammonia with which they began; this experimental error may very likely have arisen from the incomplete conversion of the

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[1] The names "sodamide" and "potassamide" are not used here because it is felt that the general usage of such contractions would be confusing.

metal to the amide. Davy (23) worked with these compounds at the same time as Gay-Lussac and Thénard and saw in his work the confirmation of his view that the volatile alkali, ammonia, like the solid alkalis contained oxygen. It is interesting that the first two investigations upon the alkali amides led their pursuers to erroneous conclusions which had soon to be abandoned.

Gay-Lussac and Thénard (58) later arrived at the formulas $NaNH_2$ and KNH_2 for sodium and potassium amides by indirect analysis, while Beilstein and Geuther (2) made the first direct analyses of sodium amide. Titherley (96) made a thorough study of the composition of these substances by synthetical methods. Gay-Lussac and Thénard (58) called the substances which they obtained "ammoniures," while Davy seems to attach no name to the amides in his papers. Beilstein and Geuther speak of sodium amide but they do not claim the nomenclature as their own; they speak, instead, of some earlier work of Wöhler and Kolb on sodium amide, but give no reference. The amides of lithium (79, 96), rubidium (98), and cesium (83) have also been prepared. One group of investigators, including Titherley, Dennis and Browne, and others, have studied the preparation of the alkali amides from the molten metals and gaseous ammonia, while another group, including in part Joannis, Ruff, Franklin, and Kraus, have investigated the action of liquid ammonia upon the alkali metals.

The chemistry of the alkali amides has been the subject of a large number of investigations. Davy (24) studied in a superficial manner the reaction of potassium amide with tellurium and arsenic. Gay-Lussac and Thénard (58) found that several metals were attacked by potassium amide. The next workers in this field were Beilstein and Geuther (2), who investigated the action of sodium amide on carbon monoxide, carbon dioxide, and carbon disulfide; Baumert and Landolt (1), who studied the reactions of sodium amide with some simple organic substances; and Drechsel (27), who reinvestigated the reaction of carbon dioxide with sodium amide and established the steps.

In the last decade of the nineteenth century there were several investigations upon the alkali amides, which are recorded in the publications of Joannis (64), Wislicenus (103) (use in preparing sodium azide), Titherley (96 to 98), and Moissan (79), as well as patent literature bearing upon the use of amides as intermediate products in the manufacture of cyanides (115). The first decade of the twentieth century saw the beginning of the use of sodium amide in organic syntheses as recorded in the papers of Haller and Bauer (61), Claisen (20), Lebeau (73), Meunier and Desparmet (77), and Sachs (88), as well as important contributions to the inorganic chemistry of the amides through the work of Franklin (36 to 41), Kraus (67), Winter (102), Dennis and Browne (26), and Ephraim (29).

In 1918 Wöhler and Stang-Lund (104) published an important paper bearing upon the ionization and electrolysis of the fused alkali amides. Other papers of the decade were those of Stollé (93), Chablay (17), Chichibabin (18), and Miles (78).

In 1923 the senior author (3 to 12) began a series of researches upon the reactions of the elements with the alkali amides in liquid ammonia solution. Contemporaneous papers were those of McGee (76), Wibaut (101), Picon (82), Bourguel (15), Seide (92), Verley (99, 100), and Guntz and Benoit (60). The most recent work on the reactions of the fused amides is that of Fernelius and Bergstrom (31) and of Fulton and Bergstrom (54), who employed a number of refinements and special precautions in their studies.

III. THE ALKALI AMIDES AS THE CAUSTIC ALKALIS OF THE AMMONIA SYSTEM

That theory which best serves to explain and classify the reactions of the alkali amides is the conception of an ammonia system of compounds. Franklin's ideas in this connection are sufficiently well-known so that it is necessary here only to recall a few of the major points of Franklin's thesis: first, that water and ammonia are abnormal in their properties when compared to the hydrides of the other elements in groups six and five, respectively, of the periodic table, and that both water and ammonia are good solvents of a polar character; second, that, whereas the familiar salts, acids, and bases are compounds of oxygen which may be regarded either as substituted water molecules or dehydration products of substituted water molecules, there are numerous nitrogen compounds which may in a similar manner be regarded as derivatives of ammonia, and these substances constitute the salts, acids, and bases of the ammonia system of compounds (38, 118 to 122). Franklin distinguishes between the representatives of these two systems of compounds by calling the first *aquo* salts, etc., and the latter *ammono.* Furthermore, it is to be understood that the best solvent for the study of the representatives of the ammonia system is anhydrous liquid ammonia.

Whenever an alkali metal reacts with water a strong base and hydrogen result through a vigorous reaction:

$$2Na + 2H_2O \longrightarrow 2NaOH + H_2$$

It is customary to say that the alkali metal has displaced one of the hydrogen atoms of water. Similarly, the alkali metals displace hydrogen from ammonia to produce an alkali amide:

$$2K + 2NH_3 \xrightarrow{\text{catalyst}} 2KNH_2 + H_2$$

This similarity in the formation of an amide and an hydroxide suggests that the alkali amides are the strong bases of the ammonia system. All that is known about the basic amides is consistent with this view.

Action on indicators; neutralization reactions

In liquid ammonia solution, the alkali amides effect the same color changes in indicators as do the alkali hydroxides in aqueous solution. Thus the addition of a very small amount of a liquid ammonia solution of potassium amide to a neutral colorless solution of phenolphthalein in the same solvent immediately turns the solution a deep red (36, 38). A colorless solution of triphenylmethane similarly develops a deep red color, owing to the formation of a colored salt (71). Liquid ammonia solutions of safranine are red (53) in color but become blue in the presence of potassium amide. Carmine and alizarin also exhibit color changes in solutions of these ammono bases (36). A yellow solution of an aromatic hydrazo compound in liquid ammonia is colored dark brown by the addition of a drop of potassium amide solution (91).

Closely associated with the ability of the alkali amides to affect the colors in indicators is the production of salts by the neutralization of acids by these ammono bases. This property was first investigated by Franklin and Stafford (37), who prepared the potassium and dipotassium sulfamides, $O_2S(NH_2)NHK$ and $O_2S(NHK)_2$. A large number of salts of organic ammono and mixed aquo-ammono acids have been made by the use of the alkali amides. These will be discussed in Part II of this paper.

Precipitation of insoluble bases

Just as potassium hydroxide acts on metallic salts in solution in water to form insoluble metallic hydroxides or oxides, as the case may be, so potassium amide added to liquid ammonia solutions of the salts of heavy metals gives, in certain instances, precipitates of the amides, in others of the imides, and in still others of the nitrides. The following equations representing the formation of barium amide, lead imide, and mercuric nitride illustrate this behavior of the alkali amides:

$$\begin{aligned}
Ca(NO_3)_2 + 2KOH &\longrightarrow \underline{Ca(OH)_2} + 2KNO_3 \\
Ba(SCN)_2 + 2KNH_2 &\longrightarrow \underline{Ba(NH_2)_2} + 2KSCN \text{ (49)} \\
PbI_2 + 2KNH_2 &\longrightarrow \underline{Pb{=}NH} + NH_3 + 2KI \text{ (38)} \\
Hg(NO_3)_2 + 2KOH &\longrightarrow \underline{HgO} + H_2O + 2KNO_3 \\
3HgI_2 + 6KNH_2 &\longrightarrow \underline{Hg_3N_2} + 4NH_3 + 6KI \text{ (38)}
\end{aligned}$$

Other amides, etc., prepared by similar reactions are the following: Cu_2NH and Cu_3N (34, 45); silver amide, $AgNH_2$ (38); impure cadmium amide, $Cd(NH_2)_2$ (14); thallous nitride, Tl_3N (44); bismuth nitride, BiN (38); manganous amide, $Mn(NH_2)_2$ (4); impure ferrous nitride, Fe_3N_2; ammonous cobaltous nitride, $Co_3N_2 \cdot xNH_3$ (5); and nickelous amide, $Ni(NH_2)_2$ (14). Attempts to prepare the amides of beryllium (10), aluminum (12, 38, 47), and chromium (14) by this method have been unsuccessful.

Amphoteric amides

Just as certain metallic hydroxides such as those of zinc, lead, and aluminum dissolve in aqueous solutions of potassium hydroxide to form potassium zincate, plumbite, and aluminate, respectively, so zinc amide (34), lead imide (38, 42), and ammonous aluminum nitride (12) are acted upon by potassium amide in liquid ammonia solution to form the analogous ammono salts, potassium ammonozincate, ammonoplumbite, and ammonoaluminate:

$$2H_2O + Zn(OH)_2 + 2NaOH \rightarrow Zn(ONa)_2\cdot 4H_2O$$

$$Zn(NH_2)_2 + 2KNH_2 \rightarrow Zn(NHK)_2\cdot 2NH_3$$

It will be recalled that because of the hydrolyzing action of water on salts of weak acids, the preparation of alkali metal aluminates, zincates, and plumbites is attended with serious manipulative difficulties.

In sharp contrast to the behavior of water solutions of the aquo salts it has been found that from liquid ammonia solutions the analogous ammono salts may be easily obtained, for the most part beautifully crystallized and of definite composition. It is a matter of much interest furthermore to observe that whereas, on the one hand, a very limited number of metallic hydroxides react after the manner of aluminum hydroxide with potassium hydroxide in aqueous solution, on the other hand, the number of metallic amides which react with potassium amide in liquid ammonia is very large. Not only have an ammonoaluminate, $Al(NH_2)_2NHK\cdot 2NH_3$, an ammonozincate, and an ammonoplumbite, $PbNK\cdot 2.5NH_3$, of potassium been prepared, but the list of such compounds has been extended to include the following: a cadmiate, $Cd(NHK)_2\cdot 2NH_3$ (14); a cuprite, $CuNK_2\cdot 3NH_3$ (34, 45); an argentate, $AgNHK\cdot NH_3$ (48); a hypomanganite, $Mn(NHK)_2\cdot 2NH_3$ (4); a thallite, $TlNK_2\cdot 4NH_3$ (44); a nickelite, $KN(NiNK_2)_2\cdot 6NH_3$ (14); a berylliate, $Be(NH_2)NHK\cdot NH_3$ (10); a cerite, $Ce(NHK)_3\cdot 3NH_3$; a lanthanite, $La(NHK)_3\cdot 3NH_3$ (6); a titanate, $NTiNHK$ (43); a molybdite, $Mo(NK)_2NH_2$; a tungstite, $W(NK)_2NH_2$ (7); a magnesiate, $Mg(NHK)_2\cdot 2NH_3$ (46); a bariate, $BaNK\cdot 2NH_3$; a strontiate, $SrNK\cdot 2NH_3$; a calciate,

$CaNK \cdot 2NH_3$ (49); and even a sodiate, $NaNK_2 \cdot 2NH_3$, and a lithiate, $LiNK_2 \cdot 2NH_3$ (50). Sodium ammonoberylliate, $Be(NH_2)NHNa \cdot NH_3$ (10), sodium ammonomagnesiate, $Mg(NHNa)_2 \cdot 2NH_3$ (8), sodium ammonoaluminate, $Al(NH_2)_2NHNa \cdot NH_3$ (3, 4), and sodium ammonostannite, $SnNNa \cdot 2NH_3$ (9), are also known, as well as two rubidium ammonosodiates, $NaNHRb \cdot NH_3$ and $NaNRb_2 \cdot 2NH_3$, and a rubidium ammonolithiate, $LiNHRb \cdot NH_3$ (50).

Ammonobasic salts

Occasionally the addition of a base to an aqueous solution of a salt results in the precipitation not of an hydroxide or an oxide but of a basic salt. Nitrogen compounds analogous to basic salts, which may for convenience be called ammonobasic salts, are sometimes formed upon the addition of a soluble ammono base, such as potassium amide, to an ammonia solution of a salt. Ammonobasic salts so prepared are the following: NH_2HgCl; Hg_2NCl; Hg_2NBr; Hg_2NI; $Pb_2NI \cdot NH_3$ (38, 39); $Al(NH_2)_3 \cdot AlI_3 \cdot 6NH_3$ and $Al(NH_2)_3 \cdot Al(NH_2)_2I \cdot NH_3$ (47); as well as certain ammonobasic salts of beryllium (10, 11), such as $3Be(NH_2)_2 \cdot BeBr_2 \cdot 4NH_3$ and $5Be(NH_2)_2 \cdot BeI_2 \cdot 4NH_3$, which are best made by the action of an ammonium salt on an excess of metallic beryllium in liquid ammonia.

The above discussion should serve to show that the alkali amides may be regarded as the caustic bases of the ammonia system of compounds. Before proceeding with a detailed account of the reactions of the elements with the alkali amides and of the reactions of the latter substances in the fused state, it seems advisable to treat such subjects as the preparation, preservation, and physical properties of the amides.

IV. PREPARATION OF THE ALKALI AMIDES

When the alkali amides are desired in any but the smallest amounts, they are best made by the reaction of gaseous ammonia upon the molten metal. Great care must be taken when using this method of preparation both to use pure materials and to exclude all air and moisture during the interaction of metal and ammonia and during the storage of the amide. Convenient arrangements of apparatus for carrying out this synthesis are described in the papers of Dennis and Browne (26), Kraus and Cuy (70), Fernelius and Bergstrom (31), and Fulton and Bergstrom (54). The metal, sodium or potassium, contained in a nickel crucible, first melts to a silvery liquid with a high surface tension that does not wet the sides of the container. As the reaction begins small green-blue drops form on the surface of the metal and dart about for a time before sinking to the bottom of the vessel. These drops are thought to be a solution of metal in the amide.[2] As the reaction continues, the metal floats about on the denser amide, oftentimes, as the drops of metal become small, moving about rather rapidly. All the while the amide remains green-blue in color, more particularly in the region immediately in contact with the metal. Finally, all of the metal disappears and shortly afterward the liquid becomes clear light yellow in color. The melt now consists of pure amide and will set, on cooling, to a white, crystalline solid.

Mention was made above of the care necessary in obtaining pure materials from which to generate the amides. Investigators until very recent years have taken elaborate precautions to obtain pure ammonia. With the present wide-spread use of liquid ammonia and the ease of obtaining this substance in steel tanks no such precautions are necessary. Ammonia distilled from a tank in which a few grams of sodium has been dissolved as a drying agent gives a very pure amide (36, 65). The sodium or other metal that is used to generate the amide must be relatively free from oxide, hydroxide, moisture, etc. Dennis and Browne (26) advise cutting the sodium from the center of large sticks so that the metal will be free from the hydrocarbon in which it has been preserved, and to warm all apparatus with which the sodium is to be brought in contact in order to drive off the film of moisture that is present at ordinary temperatures. Where small amounts of very pure amide are desired, they are

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[2] The alkali and alkaline earth metals as well as magnesium dissolve in liquid ammonia to give blue solutions. Likewise solutions of lithium in methyl- and ethyl-amines, of potassium in ethylenediamine, and of cesium in methyl- and ethyl-amines are all blue in color (67,123,124). Finally sodium dissolves in fused sodium hydroxide to give a blue solution (31).

best prepared by melting the metal in an ammonia atmosphere and filtering from the oxide crust, etc., through a fine capillary (30, 31, 54). Several different reaction vessels have been used for the conversion of the alkali metal to amide, but those constructed of nickel appear to be the most generally useful. Vessels of glass, porcelain, etc., although used in several cases (29, 76, 103) are out of the question because they are attacked by the melt and hence give a contaminated product. The reports on the action of the fused amides on various metallic vessels are somewhat conflicting. Titherley (96) found that platinum was only slowly corroded by sodium amide, but after a week's use the metal becomes friable and much corroded. Dennis and Browne (26) report that the action is very marked, and McGee (76) states that platinum dissolves with evolution of ammonia. Titherley (96; cf. 29) used silver boats for his studies of lithium, sodium, potassium, and rubidium amides and reported that the fused amides have no appreciable action on the silver. Dennis and Browne (26), however, found that sodium amide attacks a silver crucible to such an extent that the melt adheres firmly to the sides of the crucible on cooling. Winter (102) reports that a silver-plated crucible is rapidly attacked by sodium amide. Miles (78) used a silver boat in his experiments with sodium amide but he did not work above 300°C. Ruff and Goerges (86) also used silver dishes for heating lithium amide and lithium imide between 360°C. and 450°C. Wöhler and Stang-Lund (104) used a silver-nickel element for temperature measurements in fused sodium and potassium amides and found that it was not acted upon chemically. They state that only iron and nickel are sufficiently resistant at 220°C. for a study of the anode gases when electrolyzing the above amides. Titherley (96) suggested the use of a polished iron retort for preparing the amides in large quantity and De Forcrand (25) made sodium amide in iron dishes. The use of iron vessels is open to some objection, however, because the carbon in this metal introduces cyanides into the amide (26, 95), and because all iron vessels become rusty in time. On the other hand, Winter (102) seems to have had good success using a pure wrought iron crucible for preparing sodium amide.

Following the recommendations of Dennis and Browne, nickel vessels have been used in the laboratories of Stanford University for several years with entire success (19, 62, 66, 81; cf. 31, 60). Although the pure sodium and potassium amides of themselves do not attack nickel, there are formed frequently, by the reaction of substances introduced into the melt, mixtures which do etch and discolor the nickel boats, sometimes badly (31). Franklin (51) has on occasion used a gold crucible with satisfactory results. The authors from their own experience would place monel metal second only to nickel as an amide fusion vessel, leaving gold out of consideration because of its cost. Although copper is not attacked by sodium amide, its use as a containing vessel seems never to have been investigated. In any event, air and moisture would have to be carefully excluded both during conversion of the metal and storage of the amide, because a mixture of moist air and ammonia attacks copper.

Temperature is a very important factor in the conversion of alkali metals to the amides. In the case of sodium amide, this factor has been rather carefully studied.

> "The rapidity of action of the ammonia upon the molten sodium was found to increase with the temperature, as was to be expected. But at temperatures much above 350° (which was the temperature found on the whole to give the best practical results) there seems to be some loss of the product by sublimation. This was noted also by Titherley, who worked chiefly between temperatures of 300° and 400°. At temperatures below 250°, on the other hand, rather curious results were obtained in our work. Although in every case the reaction seemed to have been completed, analysis invariably showed too low a percentage of nitrogen, and too high a percentage of sodium. Moreover, the deficit of nitrogen and excess of sodium showed a tendency to increase as the temperature became lower. At first this was attributed to the possible presence of uncombined sodium dissolved in the amide; but when pieces of the product were thrown upon water beneath an inverted glass tube filled with water, no hydrogen was liberated." (26)

Certainly these authors are slightly in error in their last statement. Winter (102) examined numerous specimens of sodium amide and found that all of them gave hydrogen and some nitrogen upon reaction with water. This behavior had previously been noted by Davy (23) in the case of potassium amide. The ratio between hydrogen and nitrogen depends not only on the way in which the sodium amide is prepared, but also on the length of time and manner in which it is kept previous to analysis. Furthermore, Winter found that "the relative proportion of nitrogen to hydrogen is low in sodamide that has been insufficiently heated, but high in sodamide properly prepared."

The keynote to an explanation of these anomalous results was sounded in a recent paper by Guntz and Benoit (60). Following an accident caused by sodium amide in their laboratory, they examined specimens of commercial sodium amide and found them to contain from 1.85 to 11.75 per cent of sodium hydride. They found, also, that in making sodium amide if the melt be cooled before all of the sodium has disappeared, it contains as much as 3 to 6 per cent of sodium hydride. Miles (78) had previously shown the reaction,

$$NaNH_2 + H_2 = NaH + NH_3$$

to take place in a stream of hydrogen between 200°C. and 300°C. Guntz and Benoit showed that this reaction is reversible in a stream of ammonia. Going back to Dennis and Browne's results, let us make the assumption that the presence of sodium hydride is responsible for the high percentage of sodium and low percentage of nitrogen. Table 1 shows how well this assumption checks with the actual analyses of Dennis and Browne (26). They state in their paper: "In Table I are given the results of three experiments conducted at different temperatures in the neighborhood of the temperature limit below which apparently a good product cannot be obtained. In the second and third of these experiments, about 100 grams of sodium were employed in each case, while in the first a somewhat smaller amount was used. The method of bubbling (through the molten metal) was used in each case, and the reaction was allowed to proceed to completion."

The first two columns show the results of the analyses of Dennis and Browne. From the percentage of nitrogen we can calculate the percentage of sodium amide in each sample (column 3) and by difference the percentage of sodium hydride (column 4). From these values it is possible to calculate further the percentage of sodium as amide (column 5) and as hydride (column 6). The sum of these two partial percentages (last column) should agree with the actual percentage of sodium determined by analysis. The agreement is very close and we may conclude that the formation of sodium hydride is responsible for the impure amide obtained below 250°C.

Winter (102) claimed that the nitrogen which he always obtained upon the hydrolysis of sodium amide arose through the oxidation of sodium amide. Probably the nitrogen is generated by the following reaction,

TABLE 1

	1 Na	2 N	3 $NaNH_2$	4 NaH	5 Na as $NaNH_2$	6 Na as NaH	7 Total Na
					per cent	*per cent*	
Theory for $NaNH_2$	58.9	35.9	100.0		58.9	0.0	58.9
Theory for NaH	95.8					95.8	95.8
No. 1, 250°C	59.4	35.3	98.3	1.7	57.9	1.6	59.5
No. 2, 240°C	61.4	33.6	93.6	6.4	55.1	6.1	61.2
No. 3, 200°C	71.2	23.4	65.2	34.8	38.4	33.3	71.7

$$NaNO_2 + NaNH_2 = 2NaOH + N_2$$

since sodium nitrite is known to be the principal oxidation product of sodium amide (see below). However, the decomposition of sodium amide by water takes place with extreme violence and a sudden local rise in temperature which may be sufficiently high to promote the direct decomposition of some of the amide or of the ammonia liberated in the reaction. When pure sodium amide is slowly hydrolyzed with water vapor no insoluble gases are formed (13, 52). The nitrous oxide observed by Winter (102) to be formed during the acid hydrolysis of sodium amide undoubtedly had its origin in the traces of sodium hyponitrite which this investigator found to be present in specimens of the amide which had been exposed to the air for some time.

For preparing the alkali amides, Kraus and Cuy (70) used gaseous ammonia at a pressure of approximately ten atmospheres in a steel tube. They state that the higher pressure serves to accelerate the reaction between the metal and the ammonia vapor. Dennis and Browne (26) stress the importance of having the largest possible surface of contact between the metal and gaseous ammonia. Bubbling the ammonia through the molten sodium, rather than merely conducting the gas over the surface of the metal, greatly accelerates their interaction. During the formation of the amides, the tendency of these substances to sublime and creep over the sides of the containing vessel is frequently troublesome.

The alkali metals dissolve in liquid ammonia without any chemical action,[3] and such solutions are perfectly stable at low temperatures or over short periods of time. The reaction of the metal with ammonia to form the amide, however, becomes noticeable on long standing or at more elevated temperatures.[4] Joannis (64) observed no appreciable formation of amide with sodium and potassium solutions at $-78°C$. Ruff and Geisel (85) claim that at room temperature half-saturated solutions require the lapse of the following times before they are completely decomposed: Cs, 1 to 2 hrs.; Rb, 6 to 10 hrs.; K, 2 to 3 days; Na and Li, 2 to 3 weeks. Leighton, Bergstrom, and Ogg (74) have, however, prepared in quartz very dilute transparent solutions of cesium in ammonia that could be kept for several days at room temperature without decolorization. The contention of Joannis

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[3] There is considerable confusion in chemical literature on this particular point. The erroneous interpretation of vapor pressure data for solutions of the alkali metals in liquid ammonia led Joannis to the conclusion that there existed in such solutions compounds of the type $Na \cdot NH_3$ or $NaNH_3 \cdot NaNH_3$, which he called "metal-ammoniums." Later work has clearly demonstrated that solutions of the alkali metals in liquid ammonia contain no such combinations but are simply solutions of metals. Despite the fact that the death knell of the "metal-ammonium" theory was sounded over twenty years ago, the influence of Joannis and his followers has been so wide-spread that even today one finds references to the "metal-ammoniums" (67,123,124).

[4] The difference in the rate of reaction of the alkali metals with water and with ammonia may be explained as being due to two factors: (1) the greater affinity of the metals for oxygen than for nitrogen, and (2) the much greater concentration of hydrogen-ion in water.

that, in a closed system, the pressure of hydrogen resulting from the conversion of sodium to sodium amide has an inhibiting effect upon the rate of the reaction has been shown by Kraus to be untenable (67). The reactions of the alkali metals with liquid ammonia are greatly influenced by catalysts. Whereas a solution of potassium in ammonia may be preserved for a couple of weeks even at room temperature, in the presence of iron oxide or finely divided platinum the potassium is completely converted to potassium amide within an hour—oftentimes in a very few minutes (38, 85). This catalyzing effect is less with lithium and sodium. Many metals, and metallic oxides and hydroxides serve to catalyze these reactions. The catalytic effect of solid sodium amide makes the conversion of sodium an autocatalytic reaction (67). Short ultra-violet light also catalyzes the reaction of the alkali metals with liquid ammoia (74; cf. 64).

There are numerous patents covering the manufacture of the alkali amides (106 to 113).

V. PROPERTIES OF THE ALKALI AMIDES

The alkali amides are white or translucent, crystalline solids which melt to clear liquids frequently tinged slightly yellow or green. The green and black tints noticed by some of the earlier investigators were due to impurities (boron from glass (?), etc.). All the amides are hydrolyzed vigorously by water according to the following equation,

$$MNH_2 + H_2O = NH_3 + MOH$$

where M is any alkali metal. In accordance with this reaction, Stollé (93) has used sodium amide to obtain anhydrous hydrazine from hydrazine hydrate.

Our knowledge of the physical constants of the amides is very incomplete (table 2), the melting points being about the only constants known with any certainty for all the amides. Probably much of the material given below under the individual substances is in error.

Lithium amide

Lithium amide is a white substance, markedly crystalline, which melts to a clear liquid with a greenish tinge at 380–400°C. It volatilizes somewhat around 400°C. and may be sublimed under pressure in an ammonia atmosphere (96). On heating, lithium amide is decomposed into the imide and ammonia

$$2LiNH_2 \rightarrow Li_2NH + NH_3$$

The reaction begins at 240°C. and is rapid at 450°C. (86). The imide forms a white, partly sintered mass which does not melt at 600°C. but assumes a yellow color. At higher temperatures, it decomposes into lithium nitride (m.p. 849°C.). It is very interesting to note that lithium amide is the only alkali amide which is converted into the imide and nitride on heating.

TABLE 2

Physical constants of the alkali amides

AMIDE	MELTING POINT	DENSITY	HEAT OF FORMATION	SOLUBILITY IN LIQUID AMMONIA
	degrees C.		*calories*	
$LiNH_2$....	380–400 (96)*	1.178 (17.5°C.) (86)	86.7 (59)	Insoluble (50)
$NaNH_2$...	210 (76, 104)		33.04 (25)	1 gram per liter (52)
KNH_2....	338 (104)			Very soluble (36)
$RbNH_2$...	285–287 (98)			Very soluble (50)
$CsNH_2$....	260 (83)			Very soluble (83)
Li_2NH....		1.303 (19°C.) (86)	52.6 (59)	

* The figures in parentheses refer to the bibliography.

Sodium amide

Sodium amide has been studied to a much greater extent than any other of the amides. Gaseous ammonia reacts very readily with molten sodium at a temperature of 300°C., as described above. The molten amide is clear, usually with a slight yellow tinge. The waxy appearing solid has a conchoidal fracture and a marked crystalline structure. In liquid ammonia, beautiful dodecahedra of sodium amide are easily obtained. Titherley

(96) studied the thermal decomposition of this compound. A little above the melting point the liquid becomes pale green. Between 300°C. and 400°C. the liquid darkens but remains apparently unchanged; at 400°C. the substance begins to volatilize; between 500°C. and 600°C., gas is evolved rapidly, owing to the decomposition of the amide. The gas proved to be hydrogen and nitrogen in the approximate ratio 2:1, with a slight but consistent deficiency of hydrogen from this ratio. Titherley attributed this behavior to the reducing action of hydrogen gas upon glass and to its absorption by sodium. Metallic sodium remains behind after the decomposition or distills off. In a current of ammonia, the sodium formed by the decomposition of the amide reacts with the ammonia so that there is virtually a decomposition of ammonia. There is no tendency to form an imide or nitride either by heating sodium amide alone or with sodium metal. The evolution of ammonia which McGee (76) attributed to a decomposition of sodium amide into imide or nitride undoubtedly had its origin in the reaction of the amide with the glass container and, possibly, also in the reaction with the platinum present.

Sodium amide reacts violently with water. When thrown upon water, a piece of the amide darts about on the surface with a hissing noise much as a piece of sodium. Frequently the amide bursts into flame and after a time often explodes. Sodium amide heated in contact with air catches fire. This substance may be safely hydrolyzed in quantity by first allowing it to react with alcohol and then adding water or by first covering the solid with benzene and then slowly adding water (54).

As the strong bases of the ammonia system, it would seem that sodium and potassium amides dissolved in liquid ammonia should be good conductors of the electric current. The facts are however, that sodium amide is a poor conductor. The reason for this discrepancy is not known (36, 41, 69).

The specific conductivity of molten sodium amide, measured with nickel electrodes at 210°C., is 0.593 mho, and the decomposition voltage is 0.71 volt with the temperature coefficient 1.52 $\times 10^{-3}$ (104). The above value of Wöhler and Stang-Lund's for the specific conductivity is probably more accurate than that found by McGee (76) (1.665 ± 0.005 mho at 210°C.), who used platinum electrodes which were attacked by the melt. Indeed, these platinum electrodes were dissolved by the amide to such an extent that McGee could not determine accurately the temperature coefficient but could only note qualitatively that it was positive.

Potassium amide

Potassium amide, like its sodium analogue, has formed the subject of numerous researches. Potassium behaves much like sodium toward gaseous ammonia but the reaction is more rapid. On heating, colorless molten potassium amide acquires a faint greenish tinge which increases with the temperature. There is no decomposition of this amide at 350°C. At 400°C., it commences to volatilize. At 500°C., the distillation increases and the amide darkens. At a full red heat it distills rapidly but decomposes only slowly into its elements. In fact, potassium amide is so stable that, at a full red heat, it may be distilled in a current of hydrogen (hydride formed ?). It condenses as a bluish-green liquid or a fine white sublimate. Crystalline potassium amide has the same waxy appearance as sodium amide, but it is softer and less brittle (96).

The specific conductivity of potassium amide at 340°C. (nickel electrodes) is 0.389 mho and the decomposition voltage is 0.870 volt (104).

Rubidium amide

Investigations on rubidium amide have not been numerous (50, 84, 98). Metallic rubidium is more reactive toward gaseous ammonia at all temperatures than is either sodium or potassium. The molten amide solidifies to a white, crystalline, glistening mass of small plates similar to potassium amide. Rubidium amide has a tendency to creep when fused and distills unchanged above 400°C.

Cesium amide

Cesium amide has been prepared by Rengade (83). When made in liquid ammonia, the amide may be made to crystallize from this solvent in small prisms or plates. Rengade found the reaction between ammonia and cesium to be very rapid at a temperature slightly above the melting point of the amide (260°C.).

Mixtures of the alkali amides

Kraus and Cuy (70) have studied the system, potassium amide–sodium amide. The melting point diagram shows the existence of a compound $NaNH_2 \cdot 2KNH_2$ (transition point 120°C.), which is largely dissociated in the melt, and a eutectic mixture, containing 33 mole per cent of potassium amide and melting between 92 and 97°C. Such a mixture of these amides should prove very useful for low temperature fusions which are particularly desirable in some organic work.

Franklin (50) found that rubidium and potassium amides form isomorphous mixtures when crystallized from ammonia solution. "It is interesting to note that the crystals are obtained relatively richer in rubidium than the solution from which they are deposited. In one experiment recrystallization repeated three times gave a preparation which was nearly pure rubidium amide from a solution containing relatively a large quantity of potassium amide."

VI. DETERIORATION OF THE AMIDES DURING STORAGE

When using the alkali amides it is imperative that they be freshly prepared and preserved out of contact with the air. These substances are not only intensely hygroscopic but they are also very susceptible to oxidation. Numerous investigators have commented on the above properties of the amides. The observations of these men will be considered in the order of publication of their results. Drechsel (28) first showed that sodium nitrite is present in sodium amide which has been in contact with the air. DeForcrand (25) states that on exposure to air sodium amide absorbs water, oxygen, and carbon dioxide and is converted into a mixture of sodium hydroxide, sodium nitrite, and sodium carbonate (cf. 62a; Part II, ref. 64, and ref. 171, p. 384). Winter (102) found sodium nitrite and traces of sodium hyponitrite in sodium amide that had become yellow through exposure to air. Cesium amide is likewise readily oxidized with formation of cesium nitrite, cesium hydroxide, and ammonia according to Rengade (83; cf. 84). Muthmann (80) noted that sodium amide is gradually oxidized by the oxygen of the air, forming explosive mixtures which detonate apparently without external cause. He even measured the reaction velocity between oxygen and amide at different temperatures. Schrader (89) obtained a yellowish-red oxidation product on the exposure of finely divided sodium amide to air in the presence of a little moisture. He thought that this substance was a peroxide, probably of the formula, $NaNH_2 \cdot O_2$. He states that in dry air autoxidation does not take place at the ordinary temperature, but at 100°C. to 110°C. the peroxide is slowly formed. The most accurate work on the oxidation of the amides is that of Kraus and Whyte (72), who found that potassium amide in liquid ammonia solution is completely oxidized to potassium nitrite and potassium hydroxide by gaseous oxygen.

$$4KNH_2 + 3O_2 = 2KOH + 2KNO_2 + 2NH_3$$

Browne and Wilcoxon (16) in another connection observed that the addition of sodium nitrite to fused sodium amide resulted in immediate evolution of gas followed by a violent detonation. Even heating solid potassium amide and solid potassium nitrite *in vacuo* results in a vigorous explosion which shatters the containing vessel (32; cf. 62a).

This mass of observations shows that the alkali amides are rapidly acted upon by oxygen, carbon dioxide, and moisture of the air to give mixtures which are not only dangerously explosive but also contain a sufficient number of impurities to render them useless for many purposes. When a slight amount of contamination is not harmful, the amides may be preserved in bottles fitted with well greased glass stoppers. Even here, however, the amide deteriorates in time, losing much of its activity and becoming dangerous in that it may explode on heating. The best practice and the only one possible when a pure amide is desired is either to generate the amide in the vessel in which the desired fusion is to take place, or to keep the amide always in an atmosphere of ammonia or of an inert gas. Following the latter practice it is advisable to seal in each container, i.e., glass tube or bottle, a sufficient quantity of the amide for one experiment or, at least, to use all of the amide shortly after opening the container. There is no observation on record which would indicate that the pure amides are in any way explosive or even unstable compounds. They become dangerous only when mixed with their oxidation products. An examination of the literature shows that in many, if not in most, cases of laboratory accident an impure amide was used for investigation. Such a procedure not only influences the yield of product but conceivably may even change the entire course of a reaction.

VII. ANALYSIS OF THE AMIDES AND OF THEIR REACTION PRODUCTS

Different methods of analysis have been used to demonstrate the composition of the amides. Gay-Lussac and Thénard (58) arrived at the formulas of potassium and sodium amides by measuring the amount of ammonia absorbed and the amount of hydrogen evolved in their formation. These investigators stressed the fact that the amount of hydrogen evolved on treating potassium with ammonia is the same as that which is evolved in the reaction of the same amount of potassium with water. Davy (23) determined the gain in weight of potassium on being converted to the amide. Beilstein and Geuther (2) determined the ratio of nitrogen to sodium by dissolving sodium amide in hydrochloric acid solution, determining the total solids formed, and then noting the loss of weight on ignition of the solid chlorides. Baumert and Landolt (1) analyzed potassium amide by observing both the gain in weight of potassium when ammonia is passed over it and the ratio of potassium chloride to ammonium chloride on dissolving the amide in hydrochloric acid solution. Titherley (96) made a thorough study of the composition of sodium amide by synthetic means. He determined first the weight of sodium amide formed from a given weight of sodium (repeated later by Miles (78)) and, second, the ratio between this increase in weight and the weight of hydrogen evolved. He further determined the gain in weight when potassium, lithium, and rubidium (98) are converted into the amides. In the case of lithium amide, Titherley added a known weight of this substance to water, distilled off the ammonia into standard acid, titrated the lithium hydroxide remaining behind, and, finally, determined the lithium as sulfate. This last scheme of analysis is the one used and recommended by Dennis and Browne (26) for sodium amide and used since by Wöhler and Stang-Lund (104) and McGee (76). In the case of cesium amide, Rengade (83) noted only the amount of hydrogen evolved from a given weight of cesium. All the evidence available is consistent with the formula, MNH_2, for the alkali amides.

Winter (102), when working with sodium amide, was interested solely in the gases evolved on hydrolysis and determined them simply by placing the amide under water and collecting the gases by displacement of water in an inverted calibrated tube. In Miles' studies (78) concerning the action of hydrogen on sodium amide, he found a good agreement between the hydrogen evolved when the melt is treated with water and that calculated from the loss in weight of the amide during its reaction with hydrogen.

When studying the action of the fused amides upon various substances, the almost invariable practice has been to hydrolyze the melt and then examine the products of hydrolysis. Such a technique is open to serious objections because many of the amide fusion products are entirely destroyed or greatly altered by water. By carrying on fusions in such a way that the cold melt could be extracted with liquid ammonia, Fernelius and Bergstrom (31) were able to isolate in a pure state many of the products of amide fusions and to subject these products to direct analysis. The apparatus of these investigators also permitted them to observe visually the course of the reactions.

VIII. THE NATURE OF THE FUSED AMIDES

In view of suggestions in the literature that, in the reactions of sodium amide, the group NaNH— acts as a unit (97) and that potassium amide undergoes an acidic dissociation,

$$KNH_2 \rightleftharpoons KNH^- + H^+ \quad (94)$$

it is advisable to point out what is known concerning the ionic species present in the fused amides. Wöhler and Stang-Lund (104) proved the existence of amide ion, NH_2^-, and of sodium or potassium ion in the respective fused amides and found no evidence for the presence of any other ion. In this respect the alkali amides resemble the alkali hydroxides. By measuring the amount of electricity passed through the melt and by analyzing the anode gases, these investigators showed the validity of the equation,

$$6NH_2^- + 6 \oplus = 4NH_3 + N_2$$

for the decomposition of the anion. At 210°C. with a low current density no trace of gas was generated at the cathode, although at a higher temperature and with greater current densities, the diffusion of the alkali metal (liberated at the cathode) into the anode region was sufficient to necessitate a correction for the ammonia used up and the hydrogen liberated by the reaction.

$$2Na + 2NH_3 = 2NaNH_2 + H_2$$

Electrolysis and migration experiments on solutions of the alkali amides in liquid ammonia indicate the presence of metal cations and amide anions (68).

IX. REACTIONS OF THE ELEMENTS WITH THE ALKALI AMIDES

The reactions of the alkali amides on the elements given below are grouped according to the Mendeléeff classification. These reactions are carried out in three ways: (1) in liquid ammonia solution; (2) in an inert solvent such as xylene, in which the amides are insoluble; and (3) in the fused amide. In general the three methods yield the same results, except that with the fused amides complications frequently arise, owing to the instability of the reaction products at the temperature of the melt. Unless otherwise noted, the reactions of the fused amides are those of Fernelius and Bergstrom (31).

Group I, Subgroup A

Hydrogen. Miles (78) found that sodium amide was partially converted into sodium hydride in a stream of hydrogen between 200°C. and 300°C.

$$NaNH_2 + H_2 = NaH + NH_3$$

Titherley (96) did not find this reaction to take place when sodium amide is heated with hydrogen in an enclosed space up to 300°C. Guntz and Benoit (60) have shown the above reaction to be reversible in a stream of ammonia. They state that pure sodium hydride cannot be prepared by the action of hydrogen on sodium amide because with more than 33 per cent hydride, the melt becomes pasty and creeps along the walls of the vessel. Ruff and Geisel (85) several years before showed that the alkali hydrides react with liquid ammonia, yielding hydrogen and metal amides.

Dafert and Miklauz (21) reported a compound, trilithium ammonium, Li_3NH_4, which they obtained by heating (at 220–250°C.) lithium nitride in a current of hydrogen. In repeating this work Ruff and Goerges (86) showed this substance to be a mixture, or possibly a solid solution, of lithium amide (1 mole) and lithium hydride (2 moles).

$$Li_3N + 2H_2 = LiNH_2 + 2LiH$$

On heating this mixture at 340–480°C., the amide is converted into imide and ammonia, and the latter immediately combines with the hydride, forming lithium imide and hydrogen. Hence the total reaction is given by the equation.

$$2LiNH_2 + 4LiH = 2Li_2NH + 2LiH + 2H_2$$

These investigators support their contention by the known decomposition of lithium amide into lithium imide at 240–450°C. and by the fact that at a slightly higher temperature lithium hydride reacts with ammonia with the formation of lithium amide.

Alkali metals. The alkali metals are, so far as has been observed, without action upon their amides. A small amount of the metal seems to dissolve in the fused amide, forming a true solution (see above).

Group I, Subgroup B

Copper. Fused sodium amide does not act upon copper (29), while heated lithium nitride rapidly attacks this metal (21).

Silver. The resistance of silver to the fused amides has already been discussed. It seems justifiable to conclude that silver is relatively unattacked by these substances.

Gold. Fused sodium amide is without action on a gold crucible (51).

Group II, Subgroup B

Beryllium. Beryllium is dissolved slowly by fused sodium amide, with the production of sodium ammonoberylliate. Bergstrom (10) has prepared both sodium and potassium ammonoberylliates by the action of the respective amides on metallic beryllium in liquid ammonia.

$$Be + KNH_2 + 2NH_3 = Be(NH_2)NHK \cdot NH_3 + H_2$$

The mechanism of this reaction will be discussed in connection with a related reaction of magnesium.

Magnesium. Ephraim (29) examined the reaction between magnesium and sodium amide. He found that ammonia, hydrogen, and nitrogen are evolved, and that the reaction product, when an excess of magnesium was used, gives off ammonia in contact with water, which led him to assume that magnesium nitride, Mg_3N_2, was formed. He also says that his results point to the formation of free sodium because of the production of hydrogen, but he does not say that he showed the presence of this metal in the melt.

The senior author (3, 4, 6, 8, 9, 10) in a series of investigations has examined the reactions of sodium and potassium amides with numerous elements in liquid ammonia. Sodium amide and magnesium in this solvent react to give sodium ammonomagnesiate, in the following stepwise manner.

Magnesium first dissolves to a slight extent in ammonia to give magnesium ions, Mg^{++}, and solvated electrons, e^-,

$$Mg \rightleftarrows Mg^{++} + 2e^-$$

and sodium amide dissolves to give sodium and amide ions.

$$NaNH_2 \rightleftarrows Na^+ + NH_2^-$$

Since magnesium amide, $Mg(NH_2)_2$, is the least soluble of the various substances capable of formation from the four available ions, the following equilibrium lies far to the right.

$$Mg + 2NaNH_2 \rightleftarrows Mg(NH_2)_2 + 2Na$$

That metallic sodium is liberated is evidenced by the fact that (1) the solution becomes opaque blue in color, and (2) the sodium may be extracted from the solution by means of mercury. Liquid ammonia solutions of sodium are not particularly stable, however, especially in the presence of a metal which acts as a catalyst for the conversion of sodium into amide.

$$2Na + 2NH_3 = 2NaNH_2 + H_2$$

Furthermore, magnesium amide is an amphoteric substance which reacts with sodium amide to form the salt, sodium ammonomagnesiate.

$$Mg(NH_2)_2 + 2NaNH_2 = Mg(NHNa)_2 \cdot 2NH_3$$

In this manner the equilibrium between sodium amide and magnesium is continually shifted to the right-hand side until one of these substances has reacted completely.

The course of the reaction between fused sodium amide and magnesium is essentially the same as that in ammonia solution. Immediately upon adding magnesium to the amide, globules of sodium form and float about on the surface of the melt. A white precipitate, visible through the clear melt and repeatedly observed, indicates the presence of magnesium amide. On continuing the fusion in an atmosphere of ammonia, the sodium is converted into amide and the melt becomes clear. The sodium ammonomagnesiate which is undoubtedly present cannot be isolated because of the very low solubility of both the magnesiate and sodium amide in ammonia.

The course of the reaction between magnesium and potassium amide both in liquid ammonia (3) and in the fused state is identical with that for sodium amide described above. In the present instance, however, the soluble potassium amide can be extracted and the insoluble potassium ammonomagnesiate isolated in the pure state.

Zinc. Potassium ammonozincate, $Zn(NHK)_2 \cdot 2NH_3$, is formed by the action of the fused amide or its liquid ammonia solution (34) upon metallic zinc. The reaction is slow, however, and no blue color due to free potassium has been observed. Potassium amide in liquid ammonia solution readily attacks zinc amalgam (6), forming a mixture of zinc amide and potassium ammonozincate.

Cadmium. Fused potassium amide has little, if any, solvent action on cadmium. Likewise a liquid ammonia solution of potassium amide has no detectable action upon a cadmium rod over a period of months, although the same solution readily reacts with a liquid cadmium amalgam (6), forming a mixture of cadmium amide and potassium ammonocadmiate.

Mercury. Wöhler and Stang-Lund (104) report that mercury alone has no action upon molten sodium amide. When mercury is heated in contact with potassium amide for some time a dilute potassium amalgam results from the very slow decomposition of the amide into its elements.

Group II, Subgroup A

Calcium. Metallic calcium reacts with fused potassium amide to give potassium ammonocalciate, $CaNK \cdot 2NH_3$ and hydrogen.

Group III, Subgroup B

Boron. Boron appears to be slightly atacked by potassium amide although the reaction product has not been established.

Aluminum. Sodium and potassium amides in liquid ammonia react with aluminum (3, 4) after the fashion mentioned above for magnesium, to produce the very soluble aluminates. Aluminum is readily attacked by sodium and potassium amides in the fused condition. In the latter case an impure aluminum nitride was obtained by extracting the melt with liquid ammonia.

Thallium. Metallic thallium is unattacked by fused potassium amide over a space of four and one-half hours. A moderately strong solution of potassium amide in liquid ammonia has but very slight action on lump thallium over a period of eight months (6).

Rare earths

Cerium. It seems not unlikely that a potassium ammonocerite or an impure cerous nitride is formed by the reaction of fused potassium amide on metallic cerium. A solution of potassium amide in liquid ammonia attacks cerium with the formation of potassium ammonocerite, $Ce(NHK)_3 \cdot 3NH_3$ (6).

Group IV, Subgroup A

Titanium and *zirconium* are attacked only very slightly, if at all, by fused potassium amide.

Thorium is but slightly attacked by fused potassium amide over a period of a few hours. The reaction product has not been obtained in sufficient amount for identification.

Group IV, Subgroup B

Carbon. One of the first references to the action of alkali amides upon carbon is that of Titherley (96), who says, "It is interesting to note that when complex organic matter is charred by the amides, sodium or potassium cyanide is found amongst the products of the decomposition." At about this same time patents for the production of cyanides by the interaction of carbon and the alkali amides were issued (115, 116). Szarvasy (95) and Dennis and Browne (26) have both mentioned that an iron retort introduces cyanides into sodium amide because of the carbon contained in the iron. At about 500–600°C., carbon in the form of charcoal or coal reacts with sodium amide to form disodium cyanamide and hydrogen.

$$2NaNH_2 + C = Na_2NCN + 2H_2$$

Near 800°C., the cyanamide reacts with the excess of carbon to form cyanide.

$$Na_2NCN + C = 2NaCN$$

These reactions seem to depend upon temperature, because hydrogen and cyanamide are formed when sodium cyanide is dissolved in fused sodium amide at 400°C.

$$NaCN + NaNH_2 = Na_2NCN + H_2 \text{ (116)}$$

Silicon. Silicon is slightly attacked by fused potassium amide, probably with the formation of a potassium ammonosilicate.

Germanium. Finely divided metallic germanium reacts readily with fused potassium amide to liberate hydrogen and form a mixture of potassium ammonogermanate, $KHNGeN$, and potassium ammonogermanite, $KNGe \cdot NH_3$.

$$Ge + KNH_2 + NH_3 = KHNGeN + 2H_2$$
$$Ge + KNH_2 + NH_3 = KNGe \cdot NH_3 + H_2$$

Germanium, in the form of either powder or lumps, is not appreciably attacked by a 0.6 *N* solution of potassium amide in two months (9).

Tin. Bergstrom has established the following equation as representing the reaction of dilute solutions of sodium and potassium amides upon tin in liquid ammonia.

$$10Sn + 6KNH_2 = \underset{\substack{\text{Potassium} \\ \text{ammonostannite}}}{2SnNK \cdot 2NH_3} + \underset{\substack{\text{Potassium} \\ \text{polystannide}}}{K_4Sn_8}$$

Although both the ammonostannites and the polystannides so formed are soluble in ammonia, the polystannides can be removed from solution by metallic mercury (9). This is an example of a very general type of reaction in which an element, electronegative or at least not strongly electropositive (amphoteric), reacts with a strong base to produce one compound, stannite, in which the element functions in an electropositive capacity, and another compound, polystannide, in which the element functions in an electronegative capacity. The reaction is to be compared to the reaction of chlorine, or better, of sulfur, with potassium hydroxide.

$$Cl_2 + 2KOH \rightarrow KOCl + KCl + H_2O$$

$$3S + 6KOH \rightarrow K_2SO_3 + 2K_2S + 3H_2O$$

The reaction of sulfur is complicated somewhat by subsequent reactions of the products of the first reaction with more sulfur.

$$2(x + 1)S + 2K_2S \rightarrow 2K_2Sx$$

$$S + K_2SO_3 \rightarrow K_2S_2O_3 \text{ (cf. 117)}$$

Lead. Although sodium amide in liquid ammonia fails to react with lead, potassium amide reacts at times to give a green solution containing potassium polyplumbide, K_4Pb_9, and, presumably, potassium ammonoplumbite. Lead amalgam is not appreciably attacked by a solution of potassium amide (9).

Group V, Subgroup A

Tantalum is unattacked by fused potassium amide over a period of several hours.

Group V, Subgroup B

Nitrogen. Nitrogen is without action upon the fused amides (96).

Phosphorus. Winter (102) reports that, on warming, an energetic reaction occurs between sodium amide and yellow phosphorus with the production of sodium phosphide and other substances, including probably an amide of phosphorus. The water decomposition of his reaction product yielded hydrogen, phosphine, and ammonia. Winter was troubled because of the lack of a method for examining the substances obtained.

Both red and yellow phosphorus react readily with a liquid ammonia solution of potassium amide at room temperature to form a solution containing a polyphosphide of potassium and a light yellow precipitate, perhaps a potassium ammonophosphite. Sodium amide reacts in a similar manner with red phosphorus (9).

Arsenic. Arsenic reacts slowly with a solution of potassium amide at room temperature with the production of red solutions indicative of the presence of complex anions containing arsenic. Sodium amide reacts slowly with arsenic in liquid ammonia (9).

Antimony. Antimony reacts with a liquid ammonia solution of potassium amide in the same manner that arsenic does. The reaction with sodium amide under similar conditions is very slow (9).

Bismuth. Potassium amide, and more particularly sodium amide, react with extreme slowness with bismuth in liquid ammonia (9).

Group VI, Subgroup A

Chromium gives no evidence of any reaction with a 0.5 *N* solution of potassium amide in liquid ammonia in four months (6) nor with molten potassium amide over a period of several hours.

Molybdenum. A moderately strong ammonia solution of potassium amide has only an extremely slight action upon lump molybdenum over a period of a year (6).

Tungsten. Lumps of tungsten are very slightly attacked by a moderately strong solution of potassium amide over a period of action of one year (6).

Uranium appears to be slightly attacked by fused potassium amide over a period of about three hours, but the product of the reaction has not been identified.

Group VI, Subgroup B

Oxygen. The reaction of oxygen and the alkali amides has already been discussed; an alkali hydroxide and nitrite are obtained. The further reaction of the nitrite and excess amide to give nitrogen and hydroxide (see below),

$$KNO_2 + KNH_2 = 2KOH + N_2$$

places the reaction of oxygen in a line with the reactions of the halogens and sulfur which also liberate nitrogen.

Sulfur. Ephraim (29) found that finely divided sodium amide suspended in xylene reacts with an excess of sulfur on heating to give nitrogen, ammonia, sodium polysulfide, and apparently, in addition, a substance rich in nitrogen. The reactions of sodium amide with molten sulfur Ephraim found to be explosively violent. In liquid ammonia sulfur readily reacts with the alkali and alkaline earth amides to form polysulfides and soluble salts of unidentified ammono sulfur acids (9).

Selenium and *tellurium* react with liquid ammonia solutions of the alkali amides in essentially the same manner as sulfur. The products of the reactions are dependent upon the concentration of the reactants. The analysis of some of the ammono salts of selenium and tellurium is difficult because of their explosive character.

Group VII, Subgroup A

Manganese is only slightly attacked by fused sodium and potassium amides over a period of hours. The resulting compound is probably the hypomanganite which has been prepared by the slow reaction of potassium amide dissolved in liquid ammonia on lump manganese (4).

Group VII, Subgroup B

The halogens. Chlorine, bromine, and iodine all react vigorously with sodium amide to give sodium and ammonium halides and nitrogen (29). By modifying the conditions so that the reaction is not violent, it is possible to obtain nitrogenous halogen compounds such as chloramine or nitrogen chloride (104). The following equation represents the reaction of iodine with potassium amide in liquid ammonia at −33°C.

$$3I_2 + 6KNH_2 = 6KI + 4NH_3 + N_2 \quad (9)$$

Group VIII

Transition elements. The resistance of this group of elements to the fused amides has been discussed. None of them so far investigated is attacked to any great extent. The conversion of iron into ferric nitride, FeN, by means of heated barium nitride, Ba_3N_2, at once recalls to mind the related action of the metallic amides on the more electropositive elements (105).

Platinum appears to be slowly attacked by the molten amides (76). Iridium is unattacked by molten potassium amide over a period of fusion of four hours.

X. REACTIONS OF THE ALKALI AMIDES WITH COMPOUNDS

The reactions of salts with liquid ammonia solutions of the alkali amides have already been discussed. The reactions of compounds with the fused alkali amides follow in the main two courses: (1) the compound is reduced by the amide, or (2) the compound is ammonolyzed by the amide to form the corresponding compound of the ammonia system. The nature of the reducing action of the alkali amides has not been investigated. The most comprehensive investigation on this subject is that of Ephraim (29), and references unless otherwise noted are to his paper. It is to be borne in mind continually that the course of the reaction is judged by the products of hydrolysis of the fusion and not by the fusion products themselves.

Sulfur dioxide on warming with sodium amide reacts violently to give ammonia, hydrogen sulfide (ammonium sulfides?), and polysulfides (104); with potassium amide, sulfur dioxide reacts similarly giving amidosulfonic acids, ammonia, and other products (90).

Nitrous oxide bubbled into molten sodium amide gives sodium azide, ammonia, and sodium hydroxide (26, 63, 103, 104).

$$N_2O + 2NaNH_2 = NaN_3 + NH_3 + NaOH$$

This reaction serves as a starting point for the preparation of the azides.

Phosphorus pentoxide heated with sodium amide yields phosphine among other products (104). Carbon monoxide gives sodium cyanide when passed over heated sodium amide (2). Carbon dioxide, gives sodium cyanamide with some sodium carbonate and sodium cyanate (2, 27, 51, 66, 102). The factors which determine the relative amounts of these substances have not as yet been completely determined. Silica and boric oxide are supposed to react with sodium amide to give sodium silicate and sodium borate, respectively, together with the nitrides of silicon and boron (96). More likely mixed aquoammono-silicates and -borates are formed (81). Aluminum, calcium, magnesium, and stannic oxides are not acted upon by sodium amide. Cupric oxide, cadmium oxide, chromic anhydride, CrO_3, chromium trioxide, Cr_2O_3, ferric oxide, manganic oxide, and zinc oxide are all reduced, most of them to the metal. Lead oxide on heating with sodium amide gives metal globules and a green black powder [polyplumbide (?)]. Mercuric oxide furnishes a sodium amalgam. Antimony and arsenic trioxides, Sb_2O_3 and As_2O_3, react to give sodium antimonite and sodium arsenite, respectively, together with some metal. Likewise, tungsten trioxide, WO_3, and vanadium pentoxide, V_2O_5, react energetically to produce sodium tungstate and sodium vanadate, respectively.

Nitrosyl chloride reacts in the following manner when passed over warm potassium amide (96).

$$NOCl + 2KNH_2 = KCl + KOH + N_2 + NH_3$$

The reaction of carbon disulfide with sodium amide resembles that of carbon dioxide (2, 27), in that a mixed thioammonocarbonate, NaSCN, is formed. Lead and copper sulfides and lead, sodium, and copper sulfates are all reduced by sodium amide. Bismuth sulfide gives a sodium–bismuth alloy on heating with sodium amide, while antimony sulfide gives sodium sulfantimonite, and arsenic sulfide gives arsine, arsenic, and sodium sulfarsenite.

The chlorides of lead, mercury, zinc, and barium are similarly reduced, while calcium and potassium chlorides are not acted upon by heated sodium amide. The acid chlorides react very vigorously with sodium amide (96, 102).

Similarly phosphates, nitrates, and other oxygen salts of the heavy metals are reduced. The hydroxides of these metals are dehydrated to the corresponding oxides.

Sodium nitrate and molten sodium amide give sodium azide (16),

$$NaNO_3 + 3NaNH_2 = NaN_3 + 3NaOH + NH_3$$

a simple ammonolysis, while sodium nitrite and sodium amide (also potassium nitrite and potassium amide; cf. 32) explode on heating. It seems likely from the analogous reaction of nitrosyl chloride above and from the reactions of certain organic derivatives of nitrous acid (33) that the reaction proceeds as follows:

$$KNO_2 + KNH_2 = 2KOH + N_2$$

This reaction can be interpreted likewise as a simple, though violent, ammonolysis—potassium aquonitrite is ammonolyzed by an ammono base to an aquo base and nitrous anammonide.

Glass. Titherley (96, 98) reports that the amides of lithium, sodium, potassium and rubidium all attack glass with the evolution of ammonia, but that the action of rubidium amide is not as marked as that of either sodium or potassium amide. Dennis and Browne (26) found that glass was clouded when heated in contact with fused sodium amide, but that it was not eaten away appreciably. McGee (76) used flint glass as a containing vessel for molten sodium amide and found that the cell became slightly etched after exposure to the fused amide for two or three days. Jena glass is likewise attacked to a slight extent by both sodium and potassium amides (104). It has been the experience of the authors that soda glass is attacked to a greater extent than the literature would lead one to believe, while Pyrex glass is fairly resistant but becomes etched within a few hours.

Porcelain. Titherley (96) reports that sodium amide does not attack porcelain very rapidly up to 300°C., but that the action increases considerably as the temperature is raised. Other investigators found that porcelain lost its glaze and assumed a dark brown color in contact with molten sodium amide (26). Fused lithium nitride (850°C.) rapidly attacks porcelain and other silicates. At 870°C. this nitride will eat through any containing vessel. It penetrates through vessels of magnesia as through a filter (21).

Silicates. Peterson (81) has been able to decompose finely ground silicate minerals sufficiently for a complete analysis by fusing them with sodium amide.

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Part II. Organic Reactions

I. INTRODUCTION

In the first part of this article, a review was made of the preparation and properties of the alkali metal amides and of their applications in the domain of inorganic chemistry. In the second part, the rather more extended field of the use of the metallic amides in organic chemistry will be taken up, with the hope that all types of reaction in which these amides play a part will be mentioned. Because of the limitations of space, it is inadvisable to include a discussion of all of the compounds that have been made with the use of these highly reactive ammono bases.

In reading the present article, it should be borne in mind that many of the older investigators worked with sodium amide of unknown or rather doubtful purity, Titherley (327), for example, using material having a melting point 55°C. low, indicating the presence of significant quantities of sodium hydroxide or sodium oxide. Guntz and Benoit (159) have recently shown that commercial sodium amide—besides containing sodium hydroxide and small quantities of iron—may be contaminated with as much as 11.75 per cent of sodium hydride, which could readily have been eliminated by prolonged treatment with gaseous ammonia at 250–350°C. Air oxidation of potassium and sodium amide produces nitrites (311, 240, 270, 64), which may be converted by heat into explosive nitrogen compounds—possibly mixed aquo-ammononitrites. Sodium amide is often made commercially (116, 151a) by passing ammonia through heated molten sodium to which there has been added a catalyst, such as sodium hydroxide or an oxide of one of the less electropositive metals. The influence of these impurities upon the course of the reactions in which sodium amide is used is naturally a matter of conjecture. Nevertheless, it is probable that most of the reactions described in the following pages are due primarily to sodium amide itself.

II. THE OXIDES OF CARBON AND CARBON DISULFIDE

According to Beilstein and Geuther (28) carbon monoxide attacks warm sodium amide vigorously, the amide melting and finally becoming solid again when the reaction is complete. Sodium cyanide is formed, together with water, the latter of course reacting with unused sodium amide to form sodium hydroxide and ammonia. The reaction may be interpreted as the ammonolysis of a derivative of divalent carbon, carbon monoxide, to a salt of an ammonocarbonous acid, potassium cyanide (132).

These authors have likewise found that carbon dioxide reacts vigorously with warm sodium amide to form disodium cyanamide, sodium hydroxide, and ammonia. A repetition of this work under more carefully controlled conditions has shown that sodium cyanate may be formed in this reaction as well as disodium cyanamide and sodium aquocarbonate (109a, 230). The first named salt appears to result from the action of carbon dioxide upon disodium cyanamide (230). Carbon dioxide is therefore ammonolyzed by sodium amide and converted to a sodium ammonocarbonate, disodium cyanamide, and then by the further action of carbon dioxide, to the sodium salt of a mixed aquo-ammonocarbonic acid, sodium cyanate (40). It should be noted that if sodium cyanate is the primary product of the above reaction between carbon dioxide and fused sodium amide in excess, it would soon be converted to cyanamide (127a, 109a) and therefore could not be detected.

Beilstein and Geuther (28) and Drechsel (109b) report that sodium thiocyanate, a mixed thioammonocarbonate, is found among the products of the action of carbon disulfide on sodium amide.

III. AMMONOCARBONIC ACIDS (CYANAMIDE, GUANIDINE, ETC.)

Franklin (127) has shown that the progressive deammonation of the hypothetical ammonoorthocarbonic acid, $C(NH_2)_4$, leads to a series of ammonocarbonic acids, which include the known substances guanidine, biguanide, cyanamide, dicyanodiamide, melamine, and the less well-known melam, melem, and hydromelonic acid.

$$\begin{tikzcd}
C(NH_2)_4 \arrow[r] & NH{=}C(NH_2)_2 \arrow[r] & N{\equiv}C{-}NH_2 \\
& \text{Guanidine} & \text{Cyanamide} \arrow[d] \\
& H_6C_3N_6 & H_4C_2N_4 \arrow[l] \\
& \text{Melamine} & \text{Dicyanodiamide}
\end{tikzcd} \tag{1}$$

While a detailed review of this interesting class of substances is outside the scope of the present article, it may be pointed out that Franklin was able to prepare salts of all of the definitely known ammonocarbonic acids by treating them in liquid ammonia solution with the ammono base, potassium amide. Thus, dipotassium guanidine is formed as a precipitate when guanidine nitrate is added to an excess of a solution of potassium, the reaction proceeding in accordance with the equation

$$H_5CN_3{\cdot}HNO_3 + 3KNH_2 = K_2H_3CN_3 + KNO_3 + 3NH_3 \tag{2}$$

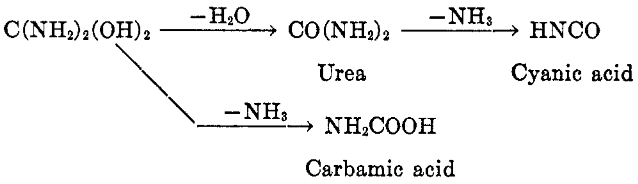
Guanidine nitrate, rather than guanidine itself, is used in this reaction because the latter substance is very hygroscopic. Disodium triphenylguanidine is formed as a readily soluble salt by the action of the sparingly soluble sodium amide upon a liquid ammonia solution of triphenylguanidine, a triphenyl acid ester of an ammonocarbonic acid.

$$(C_6H_5)_3CN_3H_2 + 2NaNH_2 = (C_6H_5)_3CN_3Na_2 + 2NH_3 \tag{3}$$

Franklin furthermore makes the interesting observation that disodium cyanamide is the only ammonocarbonic acid formed when any of the other ammonocarbonic acids, or for that matter any of the aquocarbonates, carbon dioxide or the mixed aquoammonocarbonic acids of the type of urea are fused with an excess of sodium amide or potassium amide.

IV. MIXED AQUOAMMONOCARBONIC ACIDS

Blair (40, 41) has pointed out the existence of a class of substances which may be regarded as carbonic acids related to the water and ammonia systems at the same time, and which may therefore logically be termed mixed aquoammonocarbonic acids. Thus, the hypothetical mixed aquoammonoorthocarbonic acid, $C(NH_2)_2(OH)_2$, may lose water or ammonia, in the manner of the scheme below, to give the mixed type acids, urea, carbamic acid, and cyanic acid.



$$\begin{tikzcd}
C(NH_2)_2(OH)_2 \arrow[r, "-H_2O"] \arrow[ddr, "-NH_3"'] & CO(NH_2)_2 \arrow[r, "-NH_3"] & HNCO \\
 & \text{Urea} & \text{Cyanic acid} \\
 & NH_2COOH & \\
 & \text{Carbamic acid} &
\end{tikzcd} \qquad (4)$$

Blair has verified the earlier work of Franklin and Stafford (136) and has prepared the mono- and di-potassium salts of urea by the action of potassium amide upon a liquid ammonia solution of urea, in accordance with the equation

$$CO(NH_2)_2 + KNH_2 = CO(NH_2)(NHK) + NH_3 \qquad (5)$$
$$CO(NH_2)NHK + KNH_2 = CO(NHK)_2 + NH_3$$

The symmetrical structure of the dipotassium salt has not been proven. Blair has similarly prepared the potassium salts of carbamic acid, biuret, and allophanic acid. It is perhaps needless to mention that many of these salts are incapable of existence in water solution.

V. HYDROCARBONS

A. Saturated and unsaturated (ethylenic) hydrocarbons

In accordance with our expectations, the saturated paraffin hydrocarbons exhibit no acid properties whatsoever in liquid ammonia towards the bases, sodium amide and potassium amide. At more elevated temperatures, in the neighborhood of the melting points of the amides, the paraffin hydrocarbons containing several atoms of carbon are cracked to lower hydrocarbons and hydrogen, with the simultaneous formation of some dipotassium cyanamide (146).

The effect of sodium amide upon ethylenic hydrocarbons does not appear to have been investigated. The senior author has made the observation (34) that dipentene, a mixture of trimethylethylene and *sym*-methylethylethylene, pentene-2, cyclohexene, stilbene, and styrene react with potassium amide in liquid ammonia at room temperatures to form red or reddish-brown solutions. The reactions, which are far from complete with all of the above named compounds except stilbene and styrene, may indicate salt formation in which a hydrogen atom of the hydrocarbon is replaced by potassium, or they may indicate that potassium amide has added to the ethylenic double bond. Muskat (269) has found that potassium amide, dissolved in liquid ammonia, adds to one of the double bonds of 1-phenylbutadiene, forming an addition compound which is converted to an unsaturated amine by hydrolysis.

B. Acetylenic and aromatic hydrocarbons

Acetylene itself, and all true acetylenic hydrocarbons that contain a free methine group, $\equiv CH$, react with sodium amide in liquid ammonia to form salts of the composition, $R \cdot C \equiv C \cdot Na$, in theoretical yield (281; cf. 251). The sodium derivatives of some of the higher true acetylenes may conveniently be made in boiling benzene, as Picon has found, but it is stated that the lower homologues fail to react with sodium amide under these conditions. A few years later, Bourguel (71b, 56a) came to the conclusion that Picon's failure to prepare the sodium derivatives of acetylenic hydrocarbons in cold ether or benzene was due to the alteration of the surface of the amide by the action of moist air. Sodium amide, ground to a fine powder under vaseline oil or other suitable inert liquid, and suspended in ether, reacts readily with all true acetylenes (that is, with hydrocarbons containing a free methine group) at room temperatures with only a slight evolution of heat (56a, 58). Both Picon and Bourguel recommend the use of sodium amide for the preparation of the sodium salts of the true acetylenes, since the reaction is more rapid and complete than when metallic sodium is used for the purpose, and the possibility of the formation of reduction products is eliminated (cf. 245). Meunier and Desparmet (261) have prepared the sodium salts of a number of acetylenic hydrocarbons without the use of a solvent.

Disubstituted acetylenes of the type, $R \cdot C \equiv C \cdot CH_3$, $R \cdot C \equiv C \cdot C_2H_5$, etc., are transformed by sodium amide into a true acetylene, in accordance with the equations

$$R \cdot C \equiv C \cdot CH_3 + NaNH_2 = R \cdot CH_2C \equiv C \cdot Na + NH_3 \quad (6a)$$

$$R \cdot C \equiv C \cdot C_2H_5 + NaNH_2 = R \cdot CH_2CH_2C \equiv C \cdot Na + NH_3 \quad (6b)$$

$$R' \cdot C \equiv C \cdot Na + (\text{ice})\ H_2O = R'C \equiv CH + NaOH \quad (6c)$$

These transpositions best take place when one mole of the disubstituted acetylene is heated to 150–160°C. with 1.2 equivalents of sodium amide under vaseline or paraffin oil. The isomerization is not always complete. In order to isolate the reaction product, the vaseline oil, together with any unchanged disubstituted acetylene, is distilled from the solid, which consists of the sodium salt of the desired hydrocarbon. The hydrocarbon itself is obtained by hydrolysis of its salt (see equation 6c) (59). The rearrangement expressed in equations 6a and 6b was first observed by Favorsky (117), who heated a disubstituted acetylene with metallic sodium in a sealed tube.

A few years later, Bourguel (72) reinvestigated this reaction in an attempt to elucidate its mechanism. He found that sodium amide, even at 60–70°C., slowly isomerizes methylphenylacetylene, $C_6H_5C \equiv CCH_3$, to phenylpropine, $C_6H_5CH_2C \equiv CH$, and a new hydrocarbon, believed to be $C_6H_5CH=C=CH_2$. This latter, on further treatment with sodium amide, is changed to phenylpropine.

Lebeau and Picon (244; cf. 251) prepared a few monoalkylated acetylenes in satisfactory yield by the action of the lower alkyl iodides on monosodium acetylene in liquid ammonia at temperatures ranging from −50°C. to −30°C., depending upon the nature of R in the equation

$$CH{\equiv}C \cdot Na + RI = NaI + CH{\equiv}C \cdot R \tag{7}$$

$$R = CH_3,\ n\text{-}C_4H_9,\ \text{etc.}$$

In continuation of this work, Picon (278a, 280) carried out the reaction of equation 7 in an autoclave at room temperatures, likewise using liquid ammonia as the solvent. Homologous acetylenes were in this manner prepared from monosodium acetylene and the primary alkyl iodides, *n*-heptine and *n*-decine thus being obtained in yields of 40 and 65 per cent of the theoretical, respectively. A little platinum black often acts favorably as a catalyst.

Alkyl iodides with a branched chain either on the carbon carrying the halogen, or on the adjacent carbon, are converted by monosodium acetylene in ammonia to the corresponding ethylenic hydrocarbon, with elimination of hydrogen iodide.

$$CH{\equiv}C \cdot Na + R \cdot CHR' \cdot CH_2I = CH{\equiv}CH + RR'C{=}CH_2 + NaI \tag{8}$$

As illustrations of this reaction, isopropyl and *sec*-hexyl iodides, submitted to the process of equation 8, were converted to propylene and hexylene in yields of 83 and 79 per cent, respectively.

A possible, although untested, explanation of the formation of ethylenic hydrocarbons in this reaction may be advanced by assuming that monosodium acetylene is slightly ammonolyzed in liquid ammonia to acetylene and sodium amide. (Acetylene is slightly soluble in ammonia.) The latter base is known from the work of Chablay (79) to react with primary alkyl halides in liquid ammonia to form unsaturated hydrocarbons. Presumably, secondary halides of the type of isopropyl iodide would be changed to olefin even by the very low concentration of sodium amide in equilibrium with a solution of monosodium acetylene.

Bourguel (61), at a later date, found that dimethyl sulfate reacts rapidly with monosodium acetylene under ether at ordinary temperatures in accordance with the equation

$$R \cdot C{\equiv}C \cdot Na + (CH_3)_2SO_4 = R \cdot C{\equiv}C \cdot CH_3 + Na(CH_3)SO_4 \tag{9}$$

Monosodium acetylene readily absorbs carbon dioxide, either in the presence or absence of a solvent, such as benzene, to form the salt of an acetylenic acid (56b, 261, 60).

$$R{\cdot}C{\equiv}C{\cdot}Na + CO_2 = R{\cdot}C{\equiv}C{\cdot}COONa \tag{10}$$

Bourguel (60) has described an interesting method for increasing the length of the carbon chain of an acetylenic hydrocarbon. A monosubstituted acetylene, $R{\cdot}C{\equiv}CH$, is converted to its sodium salt and then methylated, in accordance with equation 9. The resulting disubstituted acetylene, $R{\cdot}C{\equiv}C{\cdot}CH_3$, is isomerized by sodium amide to $R{\cdot}CH_2C{\equiv}C{\cdot}Na$ (equation 6a), this is again methylated, and the process repeated until the desired product is synthesized. The yield in each step is about 80 per cent of the theory. Thus from 500 grams of cyclohexylpropine, $C_6H_{11}CH_2C{\equiv}CH$, there was obtained 200 grams of cyclohexylhexine, $C_6H_{11}(CH_2)_4C{\equiv}CH$, by the method just described.

The foregoing section has dealt with the direct replacement of the hydrogen atom of a methine group by sodium. The observation has been made by Grignard and Lapyre (157) that a methylene group, activated by the influence of a triple and a double bond (and presumably also by the influence of two triple bonds), reacts with sodium amide with the evolution of ammonia, indicating the formation of a sodium salt. Thus, ammonia in slight excess of one mole is given off when 1-phenylpentene-4-ine-1, $C_6H_5C{\equiv}C{-}CH_2{-}CH{=}CH_2$, is heated with sodium amide in boiling toluene, suggesting the partial rearrangement of the hydrocarbon to a true acetylene (cf. equations 6a and 6b).

The activation of a methane hydrogen atom by phenyl groups attached to the same carbon atom has been known for a number of years. Kraus and Rosen (239) were the first to observe that potassium amide, in liquid ammonia solution, reacts with triphenylmethane to form a potassium salt of the composition, $(C_6H_5)_3C{\cdot}K$. As this salt dissolves readily in ammonia with an intense red color which may be discharged by acids (such as ammonium salts, etc.), it may be used as an indicator.

Wooster and Mitchell (351) and later Wooster and Ryan (352) in extending the observations of Kraus and Rosen, have shown that hydrocarbons containing a benzohydryl group, $(C_6H_5)_2CH$—, react with potassium amide (or with metallic sodium) to form red colored salts of the type of potassium triphenylmethyl. Thus, diphenylmethane, triphenylmethane, diphenylbenzylmethane, and *sym*-tetraphenylethane so react, but toluene, ethylbenzene, tetraphenylmethane, etc., fail to react because they do not contain the benzohydryl group.

Hexaphenylethane is reported by Wooster and Mitchell (351) to add potassium amide in liquid ammonia solution. No experiments are described. Supposedly, this addition is similar to the reaction between sodium amide and hexamethylstannoethane in liquid ammonia (238), which is known to follow the scheme

$$\begin{array}{llll} [(CH_3)_3Sn]_2 + NaNH_2 = (CH_3)_3Sn \cdot Na + & (CH_3)_3Sn \cdot NH_2 & & (11) \\ \text{or } 2(CH_3)_3Sn & \text{(as Na salt?)} & & \end{array}$$

Aside from the fact that chlorine is not measurably dissociated under ordinary conditions into atoms, this reaction is analogous to the conversion of chlorine into sodium chloride and hypochlorite by cold aqueous sodium hydroxide, in accordance with the equation

$$Cl_2 + 2NaOH = NaCl + ClONa + H_2O \qquad (12)$$

Naphthalene is stated by Germuth (152) to be attacked by fused sodium amide at 215–220°C. with the formation of pure α-naphthylamine. No experiments are described. Sachs (300a) in an attempt to prepare aminophenols by fusing sodium amide with phenol in the presence of naphthalene, was surprised to obtain, instead of the expected products, α-naphthylamine and 1,5-naphthylenediamine. Hydrogen was evolved when the melt was hydrolyzed with water, possibly because of the presence of sodium hydride. This may have been formed, however, by the action of hydrogen upon the sodium amide (268a). Here, as in Germuth's experiments, an amino group is introduced into the aromatic nucleus, just as is a hydroxyl group in the well-known reaction between fused sodium hydroxide and phenol or resorcinol to form phloroglucinol (13). It will be noted that 1,5-naphthylenediamine is formed in the reaction of Sachs, in accordance with the theory that the amino group will activate the ring of which it is a member for reactions with negative center-seeking reagents, such as nitric acid (the NO_2^+ of which is active in nitrations), but will deactivate it for reactions with positive center-seeking reagents, such as sodium amide or sodium hydroxide (the OH^- or NH_2^- in this case being active in substitution) (226).

Kraus and Neal (238) have observed that trimethylstannane, $(CH_3)_3SnH$, is converted to a sodium salt, $(CH_3)_3Sn \cdot Na$, by sodium amide in liquid ammonia. At the same time, hydrogen and trimethylstannylamine are formed in the peculiar reaction

$$2(CH_3)_3SnH + NaNH_2 = (CH_3)_3\,Sn \cdot Na + (CH_3)_3SnNH_2 + H_2 \qquad (13)$$

VI. HALOGEN COMPOUNDS

A. Paraffin monohalides

Shortly after the middle of the last century, Baumert and Landolt (25) examined the reaction between potassium amide and the ethyl halides, but without definite results. At a later date Titherley (328, 329) reported that sodium amide either does not react with ethyl iodide and ethylene dibromide in the absence of solvent, or, when change does occur at higher temperature, complete decomposition and charring takes place. Alexieff (5) reports that sodium amide reacts with amyl iodide in a sealed tube at 152°C. to form a mixture of the three amylamines, the tertiary predominating. Chablay (79), working under more regulated conditions, added alkyl halides gradually to suspensions of sodium amide in liquid ammonia at its normal boiling point. With methyl iodide, the reaction is very vigorous and is said to lead to the formation of methylamine, although it is known that some tetramethylammonium iodide is formed by the action of methyl iodide on liquid ammonia alone (345). The higher alkyl halides react with sodium amide to produce unsaturated hydrocarbons in amounts increasing with the molecular weight of the halide. Thus, ethylene is obtained in 5.4 per cent yield from ethyl iodide, propylene in 37 and 69.6 per cent yields from *n*-propyl iodide and *n*-propyl chloride, respectively, and isobutylene in 62.4 per cent yield from isobutyl iodide or in 83.6 per cent yield from isobutyl chloride.

Picon (279), finding that mixtures of primary, secondary, and tertiary ethylamines were formed by the action of liquid ammonia on the ethyl halides, attempted to prepare pure ethylamine by the action of sodium amide on ethyl chloride at 0°C. (autoclave). The low yield of ethylamine, 30 per cent of the theory, is due to the formation of considerable quantities of ethylene, partly, perhaps, because the heat liberated in the reaction warmed the contents of the autoclave to 50°C. Less satisfactory results were obtained with ethyl iodide or bromide, owing to the production of secondary and tertiary amines.

The reactions that have just been discussed consist (1) in the ammonolysis of ethyl chloride by a base of the ammonia system, sodium amide, to sodium chloride and an ammono alcohol, ethylamine, and (2) in the abstraction of hydrogen halide from the alkyl halide to form an unsaturated hydrocarbon, a reaction in which alcoholic potash is usually used in place of sodium amide.

Mlle. Amagat (6) has found that unsaturated hydrocarbons are formed when phenylalkylethyl bromides are heated with sodium amide in boiling xylene for five to six hours, in accordance with the general equation

$$\begin{gathered} C_6H_5\cdot CHR\cdot CH_2Br + NaNH_2 = \\ C_6H_5\cdot CH{=}CHR\ (+\text{ some } C_6H_5CR{=}CH_2) + NaBr + NH_3 \qquad (14) \\ R = CH_3,\ C_2H_5,\ (CH_3)_2CH \end{gathered}$$

It will be noted that one of the groups has migrated during the reaction. The expected hydrocarbon, $C_6H_5CR{=}CH_2$, is obtained in very small amount. 1-Bromo-3-phenylpropane, $C_6H_5CH_2CH_2CH_2Br$, is not attacked by sodium amide under the conditions of the previous experiments, but in boiling diphenylmethane it is converted to a mixture of the corresponding secondary and tertiary amines.

B. *Unsaturated monohalides*

Bourguel and Lespieau (58, 67, 248), following earlier work of Meunier and Desparmet (260, 259), have obtained acetylenic hydrocarbons by treating halogen derivatives of ethylenic hydrocarbons with sodium amide in an inert liquid (toluene, xylene, but generally vaseline or paraffin oil boiling at or above 160°C.

(56c)) whose boiling point is governed by the difficulty with which the reaction occurs. The two equations below express in the main the course of the reactions.

$$R{\cdot}CH{=}CHX + 2NaNH_2 = NaX + 2NH_3 + R{\cdot}C{\equiv}C{\cdot}Na \qquad (15)$$

$$R{\cdot}C{\equiv}C{\cdot}Na + H_2O \text{ (ice)} = NaOH + R{\cdot}C{\equiv}CH \qquad (16)$$

(X = a halogen, generally Cl or Br; R = an alkyl or hydroaromatic radical.)

Bourguel (68, 69), as the result of a series of investigations, has come to the conclusion that sodium amide is superior to sodium or potassium hydroxide for the preparation of acetylenic hydrocarbons by the abstraction of halogen acids from a paraffin dihalide, or from an ethylenic monohalide, in that polymerization and reduction are minimized, yields are increased, and the products are purer.

Since it is the purpose of this review to include, in an article of not too great a length, a discussion of all of the known types of reaction in which sodium amide plays a part, it has been found necessary to abbreviate some topics, such as the present one dealing with the synthesis of acetylenic hydrocarbons. Mention therefore can be made of only a few specific preparations.

(1) Lespieau and Bourguel (250) made cyclohexylpropine, $C_6H_{11}CH_2C{\equiv}CH$, in 66 per cent yield by heating cyclohexylbromopropene, $C_6H_{11}CH_2CBr{=}CH_2$, with 3 mole proportions of sodium amide in mineral oil at a temperature of 160–165°C. The reaction followed the type equation (15), and required three to four hours for completion. The authors emphasize the necessity for using a finely pulverized sodium amide, as free as possible from sodium hydroxide.

(2) By treatment with phosphorus pentachloride, diethyl ketone, $(C_2H_5)_2C{=}O$, was converted to a mixture of the chlorides, $C_2H_5CCl{=}CHCH_3$ and $(C_2H_5)_2CCl_2$, which were heated for five hours with sodium amide in boiling xylene (57a). The reaction was considered complete when the evolution of ammonia, formed in accordance with equations 17 to 19 below, had practically ceased.

$$C_2H_5CCl{=}CHCH_3 + NaNH_2 = C_2H_5C{\equiv}CCH_3 + NaCl + NH_3 \qquad (17)$$

$$C_2H_5CCl_2C_2H_5 + 2NaNH_2 = 2NaCl + C_2H_5C{\equiv}CCH_3 + 2NH_3 \qquad (18)$$

$$C_2H_5C{\equiv}CCH_3 + NaNH_2 = C_2H_5CH_2C{\equiv}CNa + NH_3 \qquad (19)$$

The contents of the reaction flask were distilled directly, to remove the paraffin oil and a small amount of pentine-2 (see equation 17) that escaped the rearrangement of equation 19. The main reaction product, pentine-1, $CH_3CH_2CH_2C\equiv CH$, was obtained in 30 per cent yield by hydrolyzing the solid remaining in the flask with ice and water (cf. equation 6c). It is thus seen that under the proper conditions, a true acetylenic hydrocarbon, $R\cdot C\equiv CH$, is generally the principal product of the abstraction of hydrogen halide from a paraffin dihalide, $RCCl_2R'$ or from an unsaturated monohalide, $RCCl{=}CH_2R'$ (R' equals an aliphatic radical), irrespective of the position of the halogen atoms in the molecule.

(3) In a similar fashion, 4-chloroheptene-3, $C_3H_7\cdot CCl{=}CH\cdot C_2H_5$, is converted by sodium amide in pseudocumene, at 140°C., into heptine-3, $C_3H_7C\equiv CC_2H_5$ and heptine-1, $CH_3(CH_2)_4C\equiv CH$, in yields of 40 and 15 per cent, respectively. The former compound may be converted into the latter, in the manner of equation 6b, by the long continued action of sodium amide at 170°C. It is especially to be noted that heptine-3 undergoes this transposition more slowly than do the acetylenic hydrocarbons with the triple bond in the 2-position (octine-2, nonine-2) (62). Better yields of the true acetylenic hydrocarbons, $R\cdot C\equiv CH$, have been obtained by Bourguel in other reactions of the type just discussed (66).

In accordance with equation 15, one might logically expect that the abstraction of hydrogen halide from a halogenated hydrocarbon $R{-}CX{=}CH_2$, followed by a subsequent reaction of the acetylenic hydrocarbon so formed with another molecule of sodium amide, would give a sodium salt of the composition, $R\cdot C\equiv C\cdot Na$. Peculiarly enough, Bourguel (63) found that the solid product of these reactions did not behave as a homogeneous substance, for it contained in addition to the salt, $R\cdot C\equiv C\cdot Na$, a substance whose properties are in agreement with one of the formulas,

$$R\cdot C\equiv CH\cdot NaNH_2 \quad \text{or} \quad R\cdot C\equiv CNH_3Na \qquad (20)$$

The second alternative structure is improbable, since the so-called "sodammonium," $NaNH_3$, to which it is related, does not exist

(235, 237, 287). Furthermore, a reasonable electronic structure cannot be assigned to it.

Leaving constitutional questions out of consideration for the present, it has been found that a portion of the solid resulting from the action of sodium amide on an unsaturated monohalide reacts with carbon dioxide and dimethyl sulfate to regenerate the parent acetylene, $R \cdot C \equiv CH$, while another part of the solid, consisting of the sodium salt, $R \cdot C \equiv C \cdot Na$, is converted to the expected products, $R \cdot C \equiv C \cdot COONa$ and $R \cdot C \equiv C \cdot CH_3$, in accordance with equations 9 and 10.

C. Paraffin polyhalides

Meunier and Desparmet (260; cf. 28) report that sodium amide reacts with chloroform and bromoform, in the absence of a solvent, to form sodium halide and sodium cyanide. The reaction, although slow to start, may become violent.

$$4NaNH_2 + CHCl_3 = NaCN + 3NaCl + 3NH_3 \qquad (21)$$

Since hydrocyanic acid may be regarded as a derivative of formic acid (cf. 132), the above reaction is related to the synthesis of orthoformic esters by the action of alkali alcoholates on chloroform.

A benzene solution of equimolecular amounts of chloroform and aniline, heated with three equivalents of sodium amide, gives phenyl isocyanide, in accordance with the equation

$$CHCl_3 + 3NaNH_2 + C_6H_5NH_2 = C_6H_5NC + 3NaCl + 3NH_3 \qquad (22)$$

The yields are not given. Muthmann (270) subsequently reports a qualitative verification of this reaction.

Meunier and Desparmet (259, 260) found that sodium amide reacts with ethylene dibromide at 100°C., in the absence of solvent, to form acetylene, sodium bromide, and ammonia. Titherley (328) previously examined this reaction without satisfactory results.

Bourguel (69) as well as Meunier and Desparmet (261) and Lespieau (247) prepared acetylenic hydrocarbons by treating 1,1- or 1,2-paraffin dihalides with sodium amide under an inert hydrocarbon of high boiling point (toluene, xylene, paraffin oil, etc.). The equations which represent these reactions are generalized below.

$$R\cdot CHX\cdot CH_2X + 3NaNH_2 = R\cdot C\equiv C\cdot Na + 2NaBr + 3NH_3 \qquad (23)$$

$$R\cdot CX_2\cdot CH_3 + 3NaNH_2 = R\cdot C\equiv C\cdot Na + 2NaBr + 3NH_3 \qquad (24)$$

$$R\cdot CH_2CHX_2 + 3NaNH_2 = R\cdot C\equiv C\cdot Na + 2NaBr + 3NH_3 \qquad (25)$$

The sodium salts of the acetylenic hydrocarbons may be converted by hydrolysis into the acetylenes themselves (equation 6c).

It will be remembered from the preceding section (B) that unsaturated monohalides of the type, $R\cdot CX{=}CHCH_3$, react with sodium amide at elevated temperatures to form the sodium salt of a true acetylene, $R\cdot CH_2C\equiv C\cdot Na$ (cf. equations 6a, 6b, 19). Similarly, true acetylenes, $R\cdot C\equiv CH$, are generally the chief products of the action of sodium amide under these conditions on any of the dihalides whose formulas are given in equations 23 to 25.

The reactions just discussed will be made more understandable by the consideration of a few concrete examples. Ethylbenzene, $C_6H_5C_2H_5$, is brominated to styrene dibromide, $C_6H_5\cdot CHBr\cdot CH_2Br$, and this is slowly introduced into a mixture of sodium amide with a high-boiling petroleum fraction heated to about 160°C. The reaction is rapid, and is practically complete half an hour after the addition of the last of the dibromide. Distillation of the petroleum fraction from the solid residue yields a small quantity of styrene, $C_6H_5CH{=}CH_2$, which has been formed by the removal of two atoms of bromine from the styrene dibromide. Although metallic sodium would have caused this side reaction, it was not present in the sodium amide which Bourguel used in these experiments. The water-ice hydrolysis of the solid residue left after the distillation yields phenylacetylene in about 40 per cent of the theory (58a).

Because of the formation of ethylenic hydrocarbons in the reactions of equations 23 and 24, it is often profitable first to convert a ketone dihalide, $R\cdot CX_2\cdot CH_2\cdot R'$, to an unsaturated monohalide, $RCX{=}CHR'$ by the action of alcoholic potash, and then by the action of sodium amide to an acetylenic hydrocarbon (equations 15, 17, 19).

Secondary octyl alcohol, $C_6H_{13}\cdot CHOH\cdot CH_3$, is dehydrated by zinc chloride to a mixture of octenes, in which the compound $C_5H_{11}\cdot CH{=}CH\cdot CH_3$ predominates. Bromine changes this to a dibromide, $C_5H_{11}\cdot CHBr\cdot CHBr\cdot CH_3$, from which there may be obtained octylene (40 per cent), octine-1, $C_6H_{13}C{\equiv}CH$ (25 per cent), and a mixture of octines-2 and -3 (8 per cent) (compare equations 17, 19). It is evident that the chief reaction product is an ethylenic hydrocarbon, formed by a parasitic reaction. To avoid this, it is best to start with a monobromoöctylene, of the composition, $C_5H_{11}CBr{=}CHCH_3$. The yield of octine-1 may thereby be increased (57).

Titherley (329) states that "carbon hexachloride" (hexachloroethane?) is decomposed by sodium amide to form a mixture of products which include sodium cyanide, chloride, and cyanamide. The reaction has not been carried out under regulated conditions.

D. Aromatic halides

Titherley (329) may be credited with the first qualitative observation to the effect that sodium amide slowly attacks chlorobenzene, ammonia and phenyl isocyanide being isolated from the rather complex reaction mixture. The latter compound may owe its origin to the presence of cyanide in the sodium amide used. Sachs (298), by "melting" chloro- or bromo-benzene with sodium amide, obtained aniline in poor yield. Gilkey (153), working in the laboratories of Stanford University, has shown that chloro- and bromo-benzene react vigorously with a liquid ammonia solution of potassium amide at −33°C., a somewhat unexpected fact when one remembers the inertness of the halogeno benzenes toward cold aqueous alkali. By adding chlorobenzene to three equivalents of potassium amide in ammonia, Gilkey obtained 50 per cent of the theoretical amount of aniline expected from equation 26,

$$C_6H_5Cl + KNH_2 = C_6H_5NH_2 + KCl \qquad (26)$$

$$C_6H_5NH_2 + KNH_2 = C_6H_5NHK + NH_3 \qquad (27)$$

$$C_6H_5NHK + C_6H_5Cl = (C_6H_5)_2NH + KCl \qquad (28)$$

together with smaller quantities of diphenylamine, which one might expect to result from reactions 27 and 28. Preliminary experiments have indicated that very little if any of the diphenylamine is formed in this way. This is in agreement with the work of Eatough (114) and White, Morrison, and Anderson (345). α-Bromonaphthalene, *o*- and *p*-chlorodiphenyl, *o*-chloroaniline, and *o*-dichlorobenzene likewise react readily with a liquid ammonia solution of potassium amide, but the reactions often appear complex. α-Fluoronaphthalene is more slowly converted by an excess of potassium amide in liquid ammonia at room temperatures to α-naphthylamine in fairly good yield. Fluorobenzene appears more inert and is not completely decomposed by potassium amide in the same time (34).

E. Triphenylgermanyl bromide, phenyl mercuric iodide, and tetraalkylammonium halides

Triphenylgermanium bromide, $(C_6H_5)_3GeBr$, is converted by potassium amide in liquid ammonia to triphenylgermanylamine, $(C_6H_5)_3GeNH_2$ (241). Under similar conditions, Chambers and Scherer (80) found that phenyl mercuric iodide, C_6H_5HgI, is converted to phenyl mercuric amine, $C_6H_5HgNH_2$.

Attempts of Franklin (123) to prepare tetramethylammonium amide, $(CH_3)_4N \cdot NH_2$, trimethylsulfonium amide, $(CH_3)_3S \cdot NH_2$, and diphenyliodonium amide, $(C_6H_5)_2I \cdot NH_2$, by the action of potassium amide on tetramethylammonium chloride, trimethylsulfonium iodide, and diphenyliodonium iodide, respectively, were unsuccessful. Kraus and his students are reëxamining the first of these reactions (236) and conclude that the tetraalkylammonium amides are unstable in ammonia.

VII. ALCOHOLS AND PHENOLS

In view of the fact that a substance as weakly acidic as triphenylmethane reacts with sodium amide and potassium amide in liquid ammonia (239), it may confidently be predicted that aliphatic alcohols and phenols will similarly be converted to alkali metal salts. Baumert and Landolt (25) and White, Morrison, and Anderson (345) report this to be the case in liquid ammonia or benzene solution, although very few individual alcohols and phenols were examined. Sachs (300a), and White, Morrison, and Anderson (345), have observed that α- and β-naphthol react with sodium amide or potassium amide to form alkali metal salts. Sachs furthermore has examined the action of sodium amide upon β-naphthol at 200–220°C. in the presence of naphthalene, finding the chief product of the reaction to be 1-amino-6-naphthol. Hydrogen is evolved in approximately the amount corresponding to the equation

$$C_{10}H_7OH + 2NaNH_2 = C_{10}H_6(ONa)(NHNa) + H_2 + NH_3 \qquad (29)$$

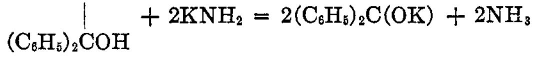
In two experiments, the total yield of mixed aminonaphthols was 35 and 56 per cent. Sachs also reports that α-naphthol, fused with sodium amide and naphthalene at 190°C., is converted in 20 per cent yield to 1-amino-5-naphthol. At higher temperatures, the formation of 1,5-naphthylenediamine predominates. Fused sodium amide converts phenol to benzene, but if this reaction is carried out in the presence of naphthalene, α-naphthylamine and 1,5-naphthylenediamine are formed, as has previously been reported.

Wooster (350) has found that potassium amide reacts with a liquid ammonia solution of benzohydrol, in the sense of equation 30, to form ammonia and dipotassium benzophenone.

$$(C_6H_5)_2CHOH + 2KNH_2 = 2NH_3 + (C_6H_5)_2C(K)(OK) \qquad (30)$$

The latter substance may also be formed by the action of benzophenone upon an excess of a liquid ammonia solution of potassium (350).

Under similar conditions, benzopinacol is converted by potassium amide to ammonia and potassium benzophenone, a metal ketyl (349). The reaction follows the equation



$$\begin{array}{l}(C_6H_5)_2COH\\ \quad\ \ |\\ (C_6H_5)_2COH\end{array} + 2KNH_2 = 2(C_6H_5)_2C(OK) + 2NH_3 \qquad (31)$$

Benzopinacol Potassium benzophenone

VIII. AMINES

A. Aliphatic amines

Titherley (330) states that sodium amide does not react with the aliphatic amines. The experimental conditions are not described. According to the experience of Wood and the senior author (38), the lower aliphatic amines do not react with potassium or sodium amide in liquid ammonia solution at ordinary temperatures.

Fernelius (119) has found that fused sodium amide reacts with the primary aliphatic amines with the formation of cyanamide (sodium ammonocarbonate) and a mixture of hydrogen and hydrocarbons. Fry (142, 144), Otto, Schulze, and Weitkamp have similarly found that alcohols may be changed to alkali carbonates, hydrocarbons, and hydrogen by fused bases of the water system.

B. Aromatic amines

Aromatic amines, on the other hand, are the ammonia analogues of the phenols of the water system. Consequently, they should be more prone to form alkali metal salts, and this in fact proved to be the case. It has long been known that aniline reacts with potassium and sodium amides, both in the presence and absence of liquid ammonia, to form a monosodium or monopotassium salt, in accordance with the following equation (344, 330, 259, 260).

$$C_6H_5NH_2 + NaNH_2 = NH_3 + C_6H_5NHNa \tag{32}$$

White, Morrison, and Anderson (344) are of the opinion that dipotassium anilide, $C_6H_5NK_2$, is not formed, except in small amounts, when aniline is treated with an excess of potassium amide in liquid ammonia at −33°C., although White and Knight (343) state that disodium anilide, $C_6H_5NNa_2$, is stable in ammonia solution, if it is formed by reduction of azo- or nitro-benzene with sodium. Monosodium anilide can be alkylated in liquid ammonia by treatment with alkyl halides.

According to Meunier and Desparmet, Titherley, and White, Morrison, and Anderson (259, 344, 331, 119), diphenylamine reacts with sodium or potassium amide in benzene or in ammonia to form a salt and this in turn is converted to *N*-ethyldiphenylamine by ethyl bromide (344), in the sense of the equation

$$(C_6H_5)_2NK + C_2H_5Br = KBr + (C_6H_5)_2NC_2H_5 \qquad (33)$$

Titherley (330) prepared the monosodium derivatives of aniline, *p*-toluidine, β-naphthylamine, and diphenylamine by the action of sodium amide upon a benzene solution of the amine. Meunier and Desparmet (259, 260) similarly prepared sodium anilide and sodium diphenylamide.

Sachs (300a) found that α-naphthylamine, fused with a mixture of sodium amide and naphthalene at 230°C., was converted in 47 per cent yield to a fairly pure 1,5-naphthylenediamine with evolution of hydrogen. β-Naphthylamine, under similar conditions, was converted to 2,5-naphthylenediamine in about 45 per cent yield, together with a small amount of an *ortho* diamine, probably 2,3-naphthylenediamine. Hydrogen was evolved, but not in quite the expected quantity, pointing to the possible formation of hydronaphthalenes. The main reaction follows the equation

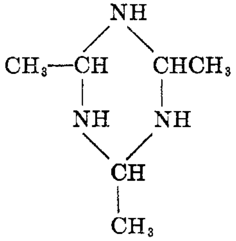
$$C_{10}H_7NH_2 + NaNH_2 = H_2 + C_{10}H_6(NH_2)_2 \text{ (as a sodium salt)} \qquad (34)$$

Kraus and Wooster (241), report that triphenylgermanylamine, $(C_6H_5)_3GeNH_2$, reacts with potassium amide in liquid ammonia to form a salt of the composition, $(C_6H_5)_3GeNHK$.

IX. ALDEHYDES AND ALDEHYDE AMMONIAS

A. Aliphatic aldehydes, trimeric ethylidenimine

Aside from an earlier observation of Meunier and Desparmet (259, 260) to the effect that sodium amide reacts with acetaldehyde, possibly to form $CH_3CH{=}NNa$, the literature fails to record that anyone has directly treated aldehydes with metallic amides. Strain (325) has obtained trimolecular ethylidenimine, a close although not exact ammonia analogue of paraldehyde, by treating a liquid ammonia solution of aldehyde ammonia with the almost insoluble calcium amide. It may be recalled in this connection that Delépine (109) regards aldehyde ammonia as having the formula, $(CH_3CH{=}NH)_3 \cdot 3H_2O$, which represents a trihydrate of a trimolecular ethylidenimine. Removal of water from this compound in a vacuum desiccator gives the anhydrous trimer, of the probable constitution,



This is the compound that Strain has prepared in liquid ammonia. Potassium amide, presumably because of its high solubility in this solvent, converts acetaldehyde ammonia into dark colored condensation products, in much the fashion that potassium hydroxide causes the formation of colored aldehyde resins from acetaldehyde.

B. Aromatic aldehydes

Haller and Bauer (170a) treated benzaldehyde with sodium amide in benzene or toluene and obtained benzamide (undoubtedly as the sodium salt) and benzyl alcohol, in accordance with the equation

$$2C_6H_5CHO + NaNH_2 = C_6H_5CH_2OH + C_6H_5CONHNa \qquad (35)$$

It is probable that the benzyl alcohol is converted by an excess of sodium amide to sodium benzylate. Both benzyl alcohol and benzamide are obtained when this mixture is hydrolyzed. Since benzamide is a mixed aquoammonobenzoic acid (128), this is clearly an example of the Cannizzaro reaction. Anisic aldehyde is similarly converted to anisamide and anisyl alcohol. Kasiwagi (229) has verified the work of Haller and Bauer on the reaction between benzaldehyde and sodium amide, and has in addition found that furfuraldehyde is converted to furyl alcohol and pyromucic acid (or its amide?) by sodium amide in boiling toluene.

X. ALDIMINES, HYDRAMIDES, AND SCHIFF BASES

A. Benzylideneimine and hydrobenzamide

It has long been known that benzaldehyde reacts with aqueous ammonia to form hydrobenzamide, possibly in the manner of the following scheme.

$$\underset{\text{Benzaldehyde}}{3C_6H_5CHO} \xrightarrow{+3NH_3} \underset{\text{Benzylideneimine}}{(3C_6H_5CH{=}NH)} \xrightarrow{-NH_3} \underset{\text{Hydrobenzamide}}{(C_6H_5CH{=}N)_2{=}CHC_6H_5} \qquad (36)$$

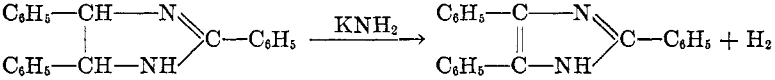
The first reaction, in which benzaldehyde is converted to the assumed intermediate, benzylideneimine, may be regarded as an ammonolysis of an aquo aldehyde to an aldehyde-alcohol of the ammonia system (321). The unfamiliar complexity of a substance that is simultaneously an alcohol and an aldehyde because of a single grouping within the molecule, is to be attributed to the trivalence of nitrogen as compared with the divalence of oxygen.

When three molecules of benzylideneimine lose ammonia to form hydrobenzamide, a compound is produced in which no hydrogen atoms are attached to nitrogen, yet this substance is not a strict ammonia analogue of benzaldehyde, because of the fact that the $C_6H_5CH{=}$ group on the right side of the formula is attached by single bonds to each of two nitrogens. Therefore, hydrobenzamide is not only an aldehyde, but also an acetal of the ammonia system.

With these brief definitions of ammono aldehyde-alcohols and ammono aldehyde-acetals in mind, it is possible to understand the often apparently complex effects of potassium amide upon substances of this class.

Strain (321) found that benzylideneimine could be prepared by the long continued action of liquid ammonia at room temperatures upon hydrobenzamide, a direct reversal of the second step of equation 36. With potassium and sodium amides in liquid ammonia, benzylidineimine forms very soluble, deep red colored salts of the typical composition, $C_6H_5CH{=}N \cdot K$. When heated with an excess of a liquid ammonia solution of potassium amide for one day at 210°C., the potassium salt is converted to potassium benzamidine, $C_6H_5 \cdot C(NH)NHK$ (a potassium ammonobenzoate), benzylamine, $C_6H_5CH_2NH_2$ (an ammonobenzyl alcohol), and lophine, a product of the action of potassium amide upon amarine. Amarine is known to be formed by the slow decomposition of benzylideneimine in liquid ammonia (323).

Amarine, which is formed from hydrobenzamide by a process akin to a benzoin condensation (320), is converted by potassium amide in liquid ammonia to lophine and hydrogen, in accordance with the equation

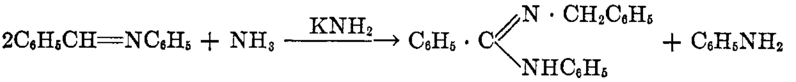


$$\begin{matrix} C_6H_5-CH-N \\ | \\ C_6H_5-CH-NH \end{matrix} \!\!>\! C-C_6H_5 \xrightarrow{KNH_2} \begin{matrix} C_6H_5-C-N \\ \| \\ C_6H_5-C-NH \end{matrix} \!\!>\! C-C_6H_5 + H_2 \qquad (37)$$

A reaction of this type is especially noteworthy because it takes place in liquid ammonia at room temperatures. Potassium hydroxide attacks many organic compounds with the evolution of hydrogen, but these reactions as a rule occur only at elevated temperatures (142, 143, 144).

B. Schiff bases

Schiff bases, $R \cdot CH{=}N \cdot R'$, are ammono aldehyde-acetals. In conformity with this view, Strain (323a) found that benzylideneaniline, $C_6H_5CH{=}NC_6H_5$, is converted into benzylphenylbenzamidine by the action of a solution of two or more equivalents of potassium amide in liquid ammonia at room temperatures, in accordance with the equation



$$2C_6H_5CH{=}NC_6H_5 + NH_3 \xrightarrow{KNH_2} C_6H_5 \cdot C\begin{matrix} \nearrow N \cdot CH_2C_6H_5 \\ \searrow NHC_6H_5 \end{matrix} + C_6H_5NH_2 \qquad (38)$$

Benzylphenylbenzamidine

Benzylphenylbenzamidine is at the same time a benzyl and a phenyl ester of ammonobenzoic acid (benzamidine, $C_6H_5 \cdot C({=}NH)NH_2$). The overall reaction is therefore analogous to the formation of benzyl benzoate from potassium hydroxide and benzaldehyde. The phenyl group attached to the third valence of the nitrogen of benzylideneaniline naturally complicates matters somewhat, in that the reaction product still contains one phenyl group, while another one has been eliminated as aniline. It should be noted that Lachmann (242) has obtained evidence for the intermediate formation of benzyl benzoate in the Cannizzaro reaction between sodium hydroxide and benzaldehyde (cf. 143).

Pyridine, quinoline, isoquinoline, and their derivatives, which may be regarded as cyclic Schiff bases (76, 35), will be discussed further on in this article.

XI. KETONES

A. Aliphatic ketones

Titherley (334) treated a solution of dry acetone in benzene with sodium amide and found that a gelatinous precipitate was formed, with the simultaneous evolution of ammonia. The precipitate, consisting of the sodium salts of the enolic forms of the various condensation products, was hydrolyzed and the benzene layer fractionated to give mesityl oxide, phorone, and isophorone. Freund and Speyer (138) repeated the work of Titherley without using benzene as a medium, and report isophorone to be the chief product.

Strain (324) prepared the sodium salt of the enol form of acetone by treating acetone with sodium amide in liquid ammonia. (For the preparation of this salt in ether, etc., see reference 27a.)

$$(CH_3)_2CO + NaNH_2 = CH_3C({=}CH_2)ONa + NH_3 \tag{39}$$

Pinacolone, $(CH_3)_3C{\cdot}CO{\cdot}CH_3$, refluxed for one to three hours with sodium amide under ether, is converted to the sodium salt of the enolic modification, and this readily reacts with the lower saturated and unsaturated aliphatic halides to form monoalkyl pinacolones. Di- and tri-alkyl derivatives of the general formulas, $(CH_3)_3C{\cdot}CO{\cdot}CHRR'$ and $(CH_3)_3C{\cdot}CO{\cdot}CRR'R''$ are successively obtained by repetitions of the alkylation process. The formation of a monoalkyl pinacolone may be represented as follows (200, 177a).

$$(CH_3)_3C{\cdot}CO{\cdot}CH_3 + NaNH_2 = (CH_3)_3C{\cdot}C({=}CH_2)ONa + NH_3 \tag{40}$$

$$(CH_3)_3C{\cdot}C({=}CH_2)ONa + C_2H_5Br = (CH_3)_3C{\cdot}CO{\cdot}CH_2{\cdot}C_2H_5 + NaBr$$

According to Haller (193, 194, 178, 177a), aliphatic and mixed aliphatic-aromatic ketones containing the residues $CH_2=$ and $CHR=$ attached to a carbonyl group are capable of reaction with sodium amide, the resulting salts reacting with the lower alkyl halides to form homologous ketones. Acetone is an exception, in that phorone and other condensation products are formed, and it may be inferred that some of the other less complex aliphatic ketones will behave in the same manner. Pentanone-3, methyl isohexyl ketone and others of similar complexity have been successfully alkylated (353).

B. Mixed aliphatic-aromatic ketones

1. The alkylation of mixed ketones of the type of acetophenone and acetonaphthone. Claisen and Feyerabend (96), following the earlier work of Haller (166) on the alkylation of menthone with the use of sodium amide and an alkyl halide, found that acetophenone, dissolved in benzene, readily reacts with sodium amide to form a soluble sodium salt, together with ammonia. Haller and Bauer (172b) later demonstrated that the reaction follows the equation

$$C_6H_5 \cdot CO \cdot CH_3 + NaNH_2 = NH_3 + C_6H_5C(ONa){=}CH_2 \text{ (or, } C_6H_5 \cdot CO \cdot CH_2Na) \quad (41)$$

The first formula, representing the product as a derivative of the enol form of acetophenone, is undoubtedly to be preferred. Hydrolysis of this salt by water alone results in the almost quantitative regeneration of the acetophenone. This is not the case if the sodium salt is heated for some time in xylene, since a small quantity of dypnone, $C_6H_5(CH_3)C{=}CH \cdot CO \cdot C_6H_5$, is formed, together with a larger amount of a resinous condensation product from which no definite compounds can be isolated. The presence of sodium hydroxide in the sodium amide increases the relative amount of dypnone in the above reaction (177).

Strain (324) has obtained sodium acetophenone in definite crystalline form by carrying out the reaction of equation 41 in liquid ammonia. The senior author has prepared potassium acetophenone by the action of acetophenone on potassium quinaldine in liquid ammonia (30).

Claisen and Feyerabend (96) slowly added sodium amide to equivalent proportions of a solution of acetophenone and ethyl iodide in anhydrous ether, obtaining a reaction mixture which yielded ethyl acetophenone (i.e., *n*-butyrophenone) on hydrolysis, together with smaller amounts of diethylacetophenone and unchanged acetophenone. The two reactions may be expressed by the following equations.

$$C_6H_5 \cdot C(ONa){=}CH_2 + C_2H_5I = C_6H_5 \cdot CO \cdot CH_2CH_2CH_3 + NaI \quad (42)$$

The butyrophenone is converted either by the sodium amide or by the sodium acetophenone to a sodium salt, and this may be ethylated in accordance with the equation

$$C_6H_5 \cdot C(ONa){=}CHCH_2CH_3 + C_2H_5I = C_6H_5 \cdot CO \cdot CH(C_2H_5)_2 + NaI \quad (43)$$

The reaction between ethylacetophenone and sodium acetophenone to give acetophenone and sodium ethylacetophenone is undoubtedly reversible.

Claisen and Feyerabend in a similar manner have obtained benzylacetophenone from sodium amide, acetophenone, and benzyl chloride. In a repetition of this reaction, Haller and Bauer (175) have isolated in addition a small quantity of dibenzylacetophenone.

A number of years later, Haller and Bauer (190, 200, 198a, 172) began a rather extended series of investigations on the alkylation of acetophenone and its derivatives, with the result that they were able to prepare a large number of ketones of the general formulas, $C_6H_5 \cdot CO \cdot CH_2R$, $C_6H_5 \cdot CO \cdot CHRR'$, and $C_6H_5 \cdot CO \cdot CRR'R''$, where R, R′ and R″ are usually methyl, ethyl, propyl, allyl, or benzyl. The aromatic groups, such as phenyl, as well as the higher aliphatic groups, can not be introduced into acetophenone by this method.

The manner in which a mixed aliphatic-aromatic ketone is alkylated will be made clear by the description of a typical experiment. Sodium amide, ground to a powder under ether or some other inert liquid, is introduced into a balloon flask provided with a dropping funnel and a reflux condenser terminated by a mercury bubbler. A suitable amount of ether or benzene is then added, and the ketone which is to be alkylated is introduced gradually through the dropping funnel. The reaction, whose velocity depends upon the nature of the ketone, is complete when the evolution of ammonia (equation 41) has ceased, this generally occurring in from thirty minutes to three hours. The sodium derivative of the ketone is often soluble in the ether or benzene used as a reaction medium. Maintaining the solvent at the boiling temperature, an alkyl halide is slowly introduced through the dropping funnel. The reaction is often vigorous, and with methyl and ethyl iodides is terminated in a short while. With less reactive halides, prolonged heating of the reaction mixture is often necessary. The substitution having taken place, water is cautiously added to dissolve the sodium halide, the ether or benzene layer is washed several times with water and finally distilled. The residue remaining after the evaporation of the solvent is fractionated in a vacuum to give the desired alkylated ketones.

Haller and Bauer, Dumesnil, Albesco, Blondeau, Ramart-Lucas (190, 192, 200, 198a, 283, 172, 110, 3, 43, 204) and others who have used this method for the alkylation of the mixed alkyl aryl ketones have concerned themselves principally with the preparation of the di- and tri-substituted acetophenones of the general formulas, $C_6H_5 \cdot CO \cdot CHRR'$ and $C_6H_5 \cdot CO \cdot CRR'R''$. It will be impossible to give more than a very few specific examples.

(1) Trimethylacetophenone, $(CH_3)_3C \cdot CO \cdot C_6H_5$, or pivalophenone, was prepared by Nef (273) in poor yield by heating a mixture of acetophenone, methyl iodide, and aqueous sodium hydroxide in a sealed tube. It was very difficult to effect a satisfactory separation of this compound from the mono- and dimethylacetophenones which were formed at the same time. Haller and Bauer (172a) discarded the synthesis of trimethylacetophenone by the successive methylation of acetophenone with sodium amide and methyl iodide in favor of the simpler preparation from phenyl isopropyl ketone, in accordance with the equation

$$(CH_3)_2CHCOC_6H_5 \xrightarrow{NaNH_2} (CH_3)_2CNa \cdot CO \cdot C_6H_5$$

$$\xrightarrow{CH_3I} (CH_3)_3C \cdot CO \cdot C_6H_5 \qquad (44)$$

The yields generally ranged between 88 and 93 per cent of the theoretical, indicating conclusively the marked superiority of sodium amide over sodium hydroxide in this synthesis.

(2) Ethyl phenyl ketone, $C_2H_5 \cdot CO \cdot C_6H_5$, is converted by sodium amide in benzene to a sodium salt, $CH_3CH{=}C(ONa) \cdot C_6H_5$, which reacts readily with ethyl iodide to form methylethylacetophenone, $(CH_3)(C_2H_5)CH \cdot CO \cdot C_6H_5$, together with smaller quantities of methyldiethylacetophenone, $(CH_3)(C_2H_5)_2 \cdot CO \cdot C_6H_5$. The two were separated by fractional distillation in a vacuum. The former, by the successive action of sodium amide and *n*-propyl iodide, was changed to methylethyl-*n*-propylacetophenone, $(CH_3)(C_2H_5)(n\text{-}C_3H_7)COC_6H_5$ (173). Here, as elsewhere, alkylation has occurred exclusively on the α-carbon atom.

(3) Phenylethylpropiophenone, $(C_6H_5)(C_2H_5)CHCH_2 \cdot CO \cdot C_6H_5$, reacts with sodium amide in benzene to form a sodium salt, $(C_6H_5)(C_2H_5)CHCHNa \cdot COC_6H_5$, and this in turn reacts with methyl iodide to give phenylmethylethylpropiophenone, $(C_6H_5)(C_2H_5)CH \cdot CH(CH_3) \cdot CO \cdot C_6H_5$ (4).

Previously, a reference has been made to the impossibility of introducing the higher alkyl groups into acetophenone and related ketones by an extension of the methods which have just been described. This statement is amply supported by the work of Haller and his associates. *n*-Propylacetophenone (*n*-valerophenone) is obtained in poor yield, unaccompanied by higher alkylated ketones (176), by treating acetophenone with sodium amide and then with *n*-propyl iodide. At the same time, a small quantity of dypnone, $C_6H_5C(CH_3){=}CH \cdot CO \cdot C_6H_5$, is formed by the condensation of two molecules of acetophenone with the elimination of a molecule of water. (Compare the formation of mesityl oxide from acetone.) Isobutyl iodide and sodium amide convert acetophenone into dypnone and other condensation products, without the formation of appreciable quantities of alkylated ketones (177).

The higher branched chain homologues of acetophenone must therefore be prepared by starting with ketones of the general formula, $C_6H_5 \cdot CO \cdot CH_2C_nH_{2n+1}$ or $C_6H_5 \cdot CO \cdot CHRR'$, which may be converted to sodium salts by the action of sodium amide and then to the desired alkylated acetophenones by means of the lower alkyl halides. In this manner, α-methyl and α, α-dimethyllaurophenone may be prepared in fair yield from laurophenone (174).

$$C_6H_5 \cdot CO \cdot CH_2 \cdot C_{10}H_{21}(n) \xrightarrow[CH_3I]{NaNH_2} C_6H_5 \cdot CO \cdot CH(CH_3)C_{10}H_{21}(n) \quad (45)$$

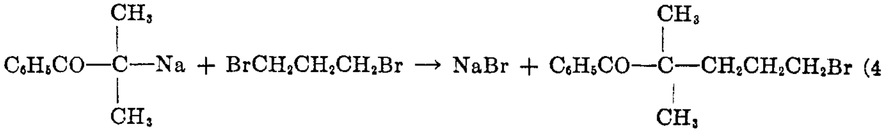
$$\xrightarrow[CH_3I]{NaNH_2} C_6H_5 \cdot CO \cdot C(CH_3)_2C_{10}H_{21}(n)$$

α- and β-Acetonaphthones may be alkylated in the same manner as acetophenone, again with the limitation that only the lower alkyl groups may be introduced (340).

The allyl group, for some unknown reason, cannot be directly introduced into acetophenone or into the acetonaphthones, as can the methyl or ethyl groups (173, 190, 200, 204). The allyl alkyl and allyl dialkyl ketones can be prepared only by the alkylation of previously formed ω-monoallylacetophenones or acetonaphthones. It is interesting to note that monoallylacetophenone, reacting successively with sodium amide and allyl iodide, is converted into di- and tri-allylacetophenone.

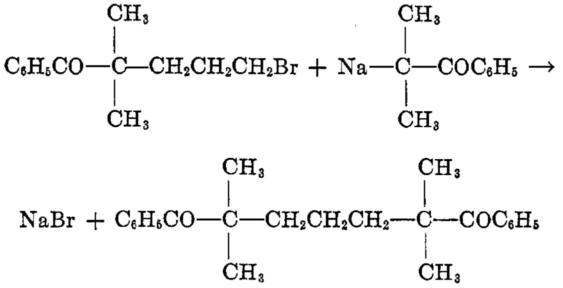
A tabulation of the numerous compounds prepared by Haller and members of the contemporary French school appears inadvisable in this article, not only because of the limitations of space, but particularly because of the existence of an excellent review of this field by Haller himself (161). Therefore, the abbreviation of this work, and the simultaneous inclusion in other parts of this article of numerous reactions of less interest to the synthetic organic chemist is for the sole purpose of describing the effect of the alkali amides on a maximum number of compound types.

2. The action of ethylene and trimethylene dihalides on the sodium salts of mixed aliphatic-aromatic ketones. Ethylene dibromide and ethylene chlorobromide are indifferent toward the sodium salt of isopropyl phenyl ketone, whatever the solvent. Trimethylene dibromide and chlorobromide, on the other hand, react with sodium isopropyl phenyl ketone, first to form a monobrominated ketone (196, 218),



$$C_6H_5CO-\underset{CH_3}{\overset{CH_3}{C}}-Na + BrCH_2CH_2CH_2Br \rightarrow NaBr + C_6H_5CO-\underset{CH_3}{\overset{CH_3}{C}}-CH_2CH_2CH_2Br \quad (46)$$

which is difficult to isolate in a pure state, and then, with a second molecule of the sodium salt, a diketone.



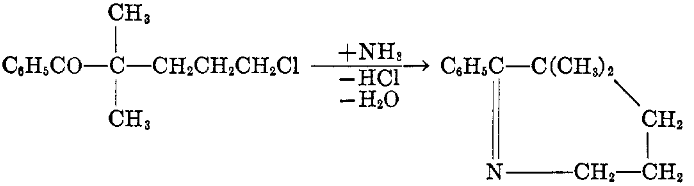
$$C_6H_5CO-\underset{CH_3}{\overset{CH_3}{C}}-CH_2CH_2CH_2Br + Na-\underset{CH_3}{\overset{CH_3}{C}}-COC_6H_5 \rightarrow$$

$$NaBr + C_6H_5CO-\underset{CH_3}{\overset{CH_3}{C}}-CH_2CH_2CH_2-\underset{CH_3}{\overset{CH_3}{C}}-COC_6H_5 \qquad (47)$$

The representation of the sodium salt above as a derivative of the keto form is only for purposes of convenience.

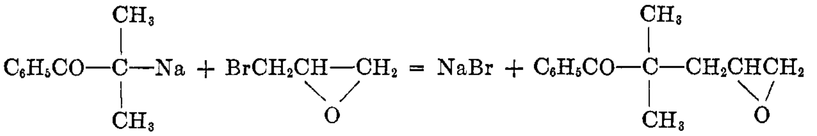
This synthesis has been extended by Haller and Ramart (218), Dumesnil (113), and Billon (39) the last named author having succeeded in preparing in a pure state chlorinated ketones of the type, $(CH_3)_2CH \cdot CO \cdot C(CH_3)_2CH_2CH_2CH_2Cl$, which are aliphatic analogues of the ketones of equation 46.

The intermediate halogenated ketone of equation 46 may be converted to a tetrahydropyridine derivative by heating with alcoholic ammonia in a sealed tube (217). In this way, 2-phenyl-3,3-dimethyltetrahydropyridine may be made from 2-methyl-2-benzoyl-5-chloropentane.



(48)

3. The action of epihalohydrins on the sodium salts of dialkyl acetophenones. Sodium acetophenone reacts with the epihalohydrins to give viscous products of an indefinite nature (219). On the other hand, the sodium derivative of the more complex phenyl isopropyl ketone reacts with epichlorohydrin and epibromohydrin to give the oxide of propylenedimethylacetophenone, in accordance with the equation



$$C_6H_5CO{-}C(CH_3)_2{-}Na + BrCH_2CH{-}CH_2(O) = NaBr + C_6H_5CO{-}C(CH_3)_2{-}CH_2CHCH_2(O) \quad (49)$$

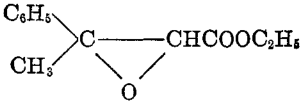
4. The action of monochloroacetic esters on ketones in the presence of sodium amide. Claisen and Feyerabend (97) slowly added sodium amide to a solution of equimolecular amounts of acetophenone and ethyl monochloroacetate in ether, anticipating thereby the preparation of a 1,4-diketone. Unexpectedly, a good yield of β-phenylmethylglycidic ester was obtained, in a manner which may be represented as follows: (1) Addition of sodium amide to the carbonyl group of the ketone,

$$C_6H_5{\cdot}CO{\cdot}CH_3 + NaNH_2 = C_6H_5C(ONa)(NH_2)CH_3 \qquad (50)$$

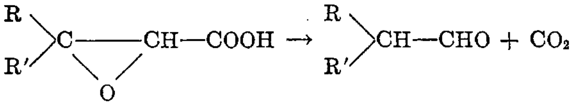
(2) Condensation of this addition product with chloroacetic ester, with elimination of ammonia, to form

$$C_6H_5(CH_3)C(ONa){\cdot}CHCl{\cdot}COOC_2H_5$$

(3) Elimination of sodium chloride with the formation of the glycidic ester.



The free glycidic acid, which results when the ester is saponified, readily passes into an aldehyde by loss of carbon dioxide, in the sense of the equation

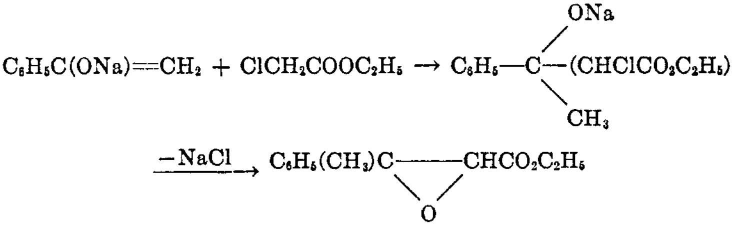


$$RR'C{-}CH{-}COOH\,(O) \rightarrow RR'CH{-}CHO + CO_2 \qquad (51)$$

Accordingly, this affords a method for the preparation from a ketone of an aldehyde containing one more carbon atom.

Quite recently, Rutovskii and Daev (292) have reinvestigated this reaction and favor a mechanism involving the sodium salt of the enol form of acetophenone.

$$C_6H_5COCH_3 + NaNH_2 \rightarrow C_6H_5C(ONa){=}CH_2 + NH_3 \qquad (52)$$

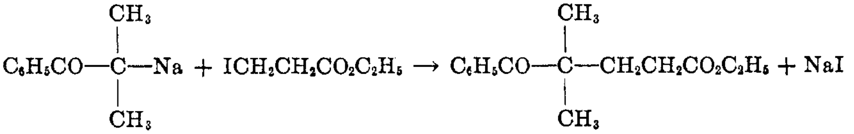


$$C_6H_5C(ONa){=}CH_2 + ClCH_2COOC_2H_5 \rightarrow C_6H_5-\overset{ONa}{\underset{CH_3}{C}}-(CHClCO_2C_2H_5)$$

$$\xrightarrow{-NaCl} C_6H_5(CH_3)\underset{O}{\underbrace{C{-\!\!-\!\!-}CH}}CO_2C_2H_5$$

Strangely enough, the elimination of chlorine does not occur in either of the above mechanisms until the last step of the reaction.

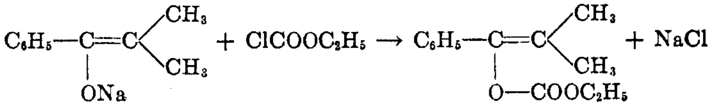
5. The action of α-iodoacetic and β-iodopropionic esters on the sodium salts of ketones. These reactions proceed in the expected manner, that is, in accord with the type equation



$$C_6H_5CO-\overset{CH_3}{\underset{CH_3}{C}}-Na + ICH_2CH_2CO_2C_2H_5 \rightarrow C_6H_5CO-\overset{CH_3}{\underset{CH_3}{C}}-CH_2CH_2CO_2C_2H_5 + NaI \qquad (53)$$

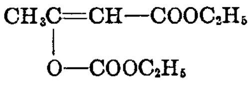
to form γ- or δ-ketonic esters (219a).

6. The action of chlorocarbonic esters on the sodium salts of ketones. Haller and Bauer found (195) that sodium isopropyl phenyl ketone reacts with ethyl chlorocarbonate in benzene to give a derivative of the enol form of the ketone,



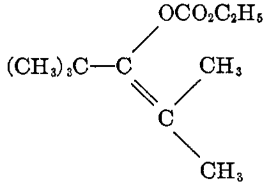
$$C_6H_5-\underset{ONa}{C}{=}C\begin{matrix}CH_3\\CH_3\end{matrix} + ClCOOC_2H_5 \rightarrow C_6H_5-\underset{O-COOC_2H_5}{C}{=}C\begin{matrix}CH_3\\CH_3\end{matrix} + NaCl \qquad (54)$$

It will be recalled that chlorocarbonic ester similarly reacts with sodium acetoacetic ester to give a substitution product of the enol, of the constitution (264, 94)

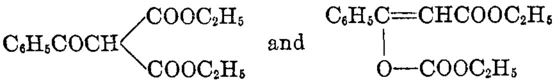


$$CH_3\underset{O-COOC_2H_5}{C}{=}CH-COOC_2H_5$$

Sodium pentamethylacetone, $(CH_3)_3CC(ONa){=}C(CH_3)_2$, is similarly converted by ethyl chlorocarbonate to the enolic ester (186a),



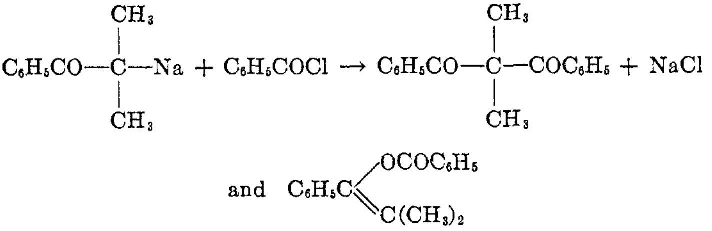
while sodium acetophenone gives a mixture of products of the formulas,



$C_6H_5COCH(COOC_2H_5)_2$ and $C_6H_5C(O{-}COOC_2H_5){=}CHCOOC_2H_5$

The first is obtained by the di-*C* alkylation of acetophenone, the second probably by successive *C* and *O* alkylations (195, 186).

7. *The action of acid chlorides on the sodium salts of ketones.* As an illustration, benzoyl chloride reacts with the sodium salts of a number of ketones to give a β-diketone, together with the corresponding enolic isomer (197, 21).

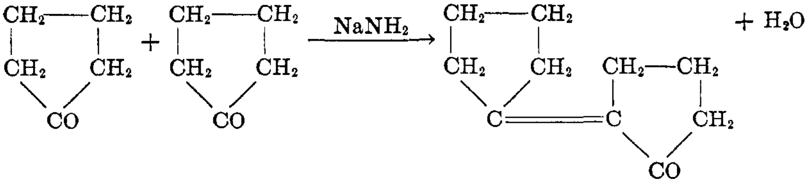


$$C_6H_5CO{-}C(CH_3)_2{-}Na + C_6H_5COCl \rightarrow C_6H_5CO{-}C(CH_3)_2{-}COC_6H_5 + NaCl \quad (55)$$

$$\text{and}\ C_6H_5C(OCOC_6H_5){=}C(CH_3)_2$$

C. Cyclic ketones

1. *The alkylation of substituted cyclopentanones, thujone, isothujone, and indanone.* Cyclopentanone undergoes a crotonaldehyde type condensation in the presence of sodium amide to form cyclopentylidenecyclopentanone, in accordance with the equation

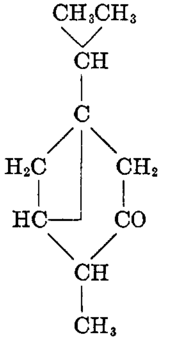


(56)

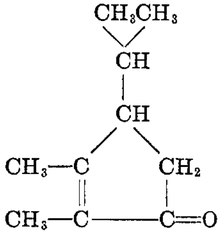
If suitable precautions are observed, one may prepare α-methylcyclopentanone in poor yield by the successive action of sodium amide and methyl iodide on the unsubstituted ketone (211; cf. 27a).

β-Methylcyclopentanone, like cyclopentanone itself, undergoes the crotonaldehyde type condensation of equation 56, and it is not possible to prepare alkylation products in satisfactory yield (211). α-Methyl- and α,β′-dimethyl-cyclopentanone, may, on the other hand, be alkylated in the usual manner. As an end-product of a series of successive alkylations, an α,α,α′,α′-tetrasubstituted or an α,α,α′,α′,β′-pentasubstituted cyclopentanone is obtained. (See also reference 358.)

It was found difficult even to introduce the *n*-propyl group into cyclopentanone or its derivatives, while the introduction of the higher alkyl groups was in general impossible. It will be recalled that similar difficulties were encountered in the alkylation of acetophenone.



Thujone

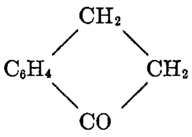


Isothujone

Both thujone and isothujone contain cyclopentanone rings and are capable of alkylation in the same manner as the simple derivatives of cyclopentanone. Three alkyl groups may be introduced in place of the three available α and α′ hydrogen atoms of thujone, while isothujone can be alkylated only two times (168, 169a).

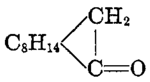
Monomethyl-, ethyl-, propyl- and allyl-thujones were prepared in this manner, and from the first and last named, dimethyl-, diallyl-, and triallyl-thujones were obtained by further alkylation. The inability to synthesize a trimethylthujone is of interest.

Indanone,

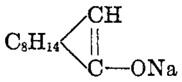


has two hydrogen atoms in the α position with respect to carbonyl, and these may be replaced successively by methyl groups in the usual manner (185).

2. The alkylation of camphor. Camphor,

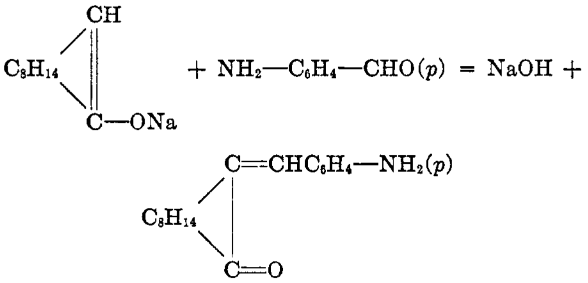


is readily converted by sodium amide in ether or benzene to a sodium salt,



which reacts with the lower aliphatic halides to form monoalkyl camphors. A second alkyl group may be introduced by a repetition of this process (164, 181, 213, 214).

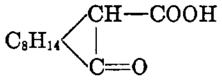
p-Aminobenzylidenecamphor and other compounds of a like nature may readily be formed by the action of *p*-aminobenzaldehyde or a homologue upon the sodium salt of camphor in an inert liquid (191, 208, 164).



(57)

Substituted benzylidene camphors do not appear to have been made by the action of aromatic aldehydes upon free camphor. It will be recalled that benzaldehyde condenses with many ketones containing an active methylene group, although often rather slowly and in the presence of zinc chloride or a similar dehydrating agent.

Camphorcarboxylic acid,



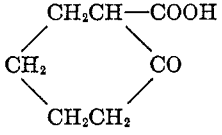
(as sodium salt)

is obtained by passing dry carbon dioxide through sodium camphor under benzene (75).

Bromocamphor reacts slowly and incompletely with sodium amide in boiling benzene. Aminocamphor is formed only in traces, while the chief isolable product appears to be sodium camphor, which was identified by conversion to camphorcarboxylic acid. The yield of the latter, calculated on the basis of the bromocamphor, is 30 per cent (75).

3. The alkylation of cyclohexanone, menthone, and their derivatives. According to Haller (169), sodium amide converts cyclohexanone in a large measure to cyclohexylidenecyclohexanone by a crotonaldehyde type condensation similar to that of equation 56 (cf. reference 27a). It is therefore not possible to alkylate cyclohexanone itself with altogether satisfactory results, although Haller has reported the preparation of a number of alkylated derivatives. Cornubert (104, 105) in a subsequent investigation finds that the extent to which this condensation takes place is a maximum at about room temperatures, but is a minimum in the more dilute ethereal solutions. Bearing this in mind, he succeeded in synthesizing a series of allyl- and methylallyl-cyclohexanones. All four hydrogen atoms in the α and α' positions with respect to carbonyl may be replaced by allyl groups.

Gardner, Perkin, and Watson (148a) and Luff and Perkin (148a) prepared cyclohexanone-2-carboxylic acid,



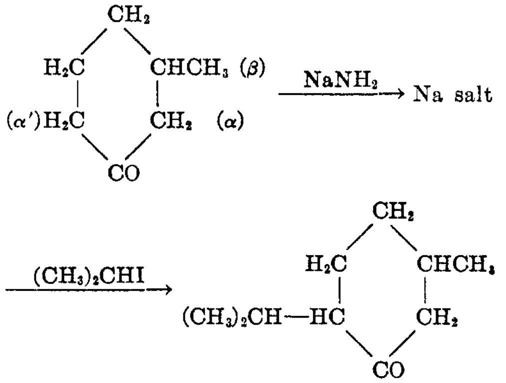
(as sodium salt)

by treating cyclohexanone successively with sodium amide and carbon dioxide in ether. α-, β-, and γ-Methylcyclohexanones may be converted to carboxylic acids in a similar manner.

The condensation of equation 56 is evident to some extent even with α-, β-, and γ-methylcyclohexanones. Nevertheless, it is possible to alkylate all three of these compounds in a satisfactory manner (170, 166, 167, 216, 209, 212, 359).

When α-methylcyclohexanone is monoalkylated and γ-methylcyclohexanone is dialkylated, both alkyl groups are found to be attached to the same carbon atom, as may be shown by the fact that the products contain a —CH_2CO— group which condenses with benzaldehyde (170, 9, 212a, 360). Subsequent investigations revealed the fact that there are formed smaller quantities of the isomeric products in which the two entering alkyl groups are attached to different (α and α′) carbon atoms (360). All available α and α′ hydrogen atoms of these two substances may be replaced by allyl groups.

β-Methylcyclohexanone, on the other hand, is first alkylated in the α′ position, isopropyl iodide thus reacting with the sodium derivative of the ketone to form isopropylmethylcyclohexanone, or menthone (216).



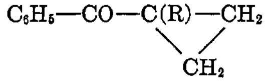
(58)

The second entering alkyl group goes to the α′ position if the group already in this position (CH_3, etc.) is small. A large group, such as isopropyl (which is present in menthone), causes a second radical to enter into the α position, possibly because of steric influences (166, 167).

All of the three available α and α' hydrogens of menthone may be replaced by allyl but not by methyl groups (166). The final product of the methylation of β-methylcyclohexanone is α, α, α', α', β-pentamethylcyclohexanone (170). Owing to an unfortunate oversight, a number of important investigations of Cornubert, Haller and their associates, dealing with problems relating to the alkylation of substituted cyclopentanones and cyclohexanones, were not reviewed for this article. The references have been added to the proof (358, 359, 360, 361).

4. The alkylation of other ketones. Because of the limitations of space, it will not be possible to mention more than a few of the many other ketones that have been alkylated with the use of sodium amide.

Haller and Benoist (205) have prepared the methyl, benzyl, and allyl derivatives of benzoyltrimethylene, of the typical constitution,



$$\begin{array}{l} C_6H_5—CO—C(R)—CH_2 \\ \qquad\qquad\qquad\quad \diagdown \ \diagup \\ \qquad\qquad\qquad\quad\ CH_2 \end{array}$$

by treating benzoyltrimethylene with pure sodium amide in dry benzene, and then with the appropriate alkyl halide. Moist sodium amide or moist benzene favors the scission of the ketone into benzamide and a substituted trimethylene.

Godchot and Cauquil (154) have methylated cycloöctanone with sodium amide and methyl iodide, while Ruzicka, Stoll, and Schinz (295) have methylated cyclopentadecanone in a similar fashion.

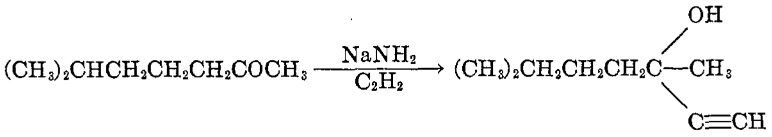
Maxim (257) has extended the method of Haller to the synthesis of furanic ketones of the types,

$$C_4H_3O \cdot CHRCHR' \cdot COC_6H_5 \text{ and } C_4H_3O \cdot CHRCR'R'' \cdot COC_6H_5$$

where the radicals R′ and R″ are aliphatic and R is either aliphatic or aromatic.

C′. The preparation of acetylenic carbinols

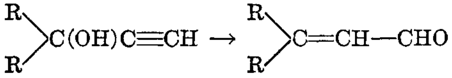
Ruzicka, Rupe, and their coworkers (293, 294, 288, 289, 290) have found that acetylenic carbinols are easily formed by treating ketones with acetylene in the presence of sodium or sodium amide, the reaction following the type equation



$$(CH_3)_2CHCH_2CH_2CH_2COCH_3 \xrightarrow[C_2H_2]{NaNH_2} (CH_3)_2CH_2CH_2CH_2C(OH)(CH_3)C{\equiv}CH \quad (59)$$

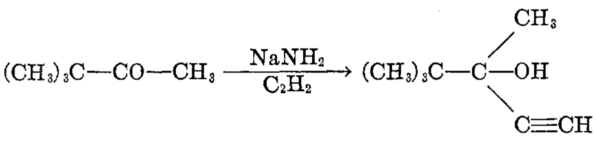
This synthesis was discovered by Nef (272), and later extended by many workers, whose investigations are reviewed in an article by Hess and Munderloh (220). It is of course possible first to form the sodium salt of acetylene by the action of sodium or sodium amide on acetylene, and then allow this to react with a ketone.

Heated with an excess of strong formic acid, the acetylenic carbinols are isomerized to unsaturated aldehydes in the manner of the equation



$$R_2C(OH)C{\equiv}CH \rightarrow R_2C{=}CH{-}CHO \quad (60)$$

Ruzicka and Fornasir (293) have converted methylheptenone into linalool, while Wouseng (352a) has prepared methyl-*tertiary*-butylethinylcarbinol and a number of related substances in very good yield.



$$(CH_3)_3C{-}CO{-}CH_3 \xrightarrow[C_2H_2]{NaNH_2} (CH_3)_3C{-}C(CH_3)(OH){-}C{\equiv}CH \quad (61)$$

Pinacolone Methyl-*tert.*-butylethinylcarbinol

Fischer and Löwenberg (121) have made use of these reactions in their synthesis of phytol.

According to German patents issued to Baeyer and Co. (27) sodium amide reacts with acetone in ether at low temperatures to form the sodium salt of the enol, apparently without any of the condensations which accompany the reaction at higher temperatures. Acetylene readily unites with this sodium salt in the following manner:

$$CH_3C(ONa){=}CH_2 + C_2H_2 = (CH_3)_2C(OH)C{\equiv}CH \text{ (as the sodium salt)} \qquad (62)$$

Reduction of this acetylenic carbinol gives 3-methylbutene-1-ol-3, $(CH_3)_2CH(OH)CH{=}CH_2$, which passes into isoprene, $CH_2{=}C(CH_3)CH{=}CH_2$, by the loss of a molecule of water. Several modifications of this synthesis are described in the patents referred to.

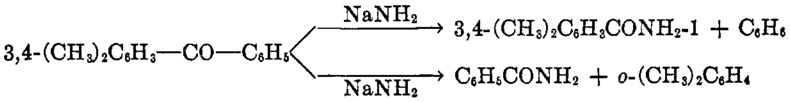
D. *The scission of ketones by means of sodium amide*

1. *Decomposition of diaryl ketones.* In the course of investigations concerning the condensation of benzene solutions of certain diaryl ketones with sodium camphor, Haller and Bauer (170a) observed that the water used for the hydrolysis of the reaction mixture contained aromatic acids and their amides, while the expected condensation products remained dissolved in the hydrocarbon layer. Subsequently, it was shown that the acids and acid amides were formed by the action of sodium amide upon the diaryl ketone, benzophenone thus decomposing into benzamide and benzene, in accordance with the equations

$$(C_6H_5)_2CO + NaNH_2 = (C_6H_5)_2C(NH_2)(ONa) \qquad (63)$$

$$(C_6H_5)_2C(NH_2)(ONa) + H_2O = C_6H_5CONH_2 + C_6H_6 + NaOH \qquad (64)$$

The first product of the action of sodium amide on benzophenone is assumed to be the addition compound on the right side of equation 63 (however, see reference 312). This is converted by hydrolysis into benzamide and benzene (equation 64). The alkaline wash waters from the precipitate of benzamide always contain a little sodium benzoate, resulting from the hydrolysis of the benzamide. 3,4-Xylyl phenyl ketone similarly is converted to approximately equal amounts of xylenic amide and benzamide, the scission therefore taking place in both of the possible ways, as shown by the following equations (252).



$$3,4\text{-}(CH_3)_2C_6H_3{-}CO{-}C_6H_5 \begin{cases} \xrightarrow{NaNH_2} 3,4\text{-}(CH_3)_2C_6H_3CONH_2\text{-}1 + C_6H_6 \\ \xrightarrow[NaNH_2]{} C_6H_5CONH_2 + o\text{-}(CH_3)_2C_6H_4 \end{cases} \qquad (65)$$

p-Tolyl phenyl ketone is split by sodium amide under the same conditions into benzamide and *p*-toluamide, while anisyl phenyl ketone yields benzamide and anisamide (170a).

The reaction expressed by equations 63, 64, and 65 appears to be general for all aromatic ketones, as well as for many of the mixed aliphatic-aromatic ketones, as will be seen later. The decomposition of benzophenone by fused potassium hydroxide follows a similar course, yielding benzene and potassium benzoate (80a, 108a).

Schönberg (312) extended these observations of Haller and determined a series representing the relative affinities of organic radicals for the carbonyl group of a ketone. In the reaction,

$$\mathrm{R{-}CO{-}R' + NaNH_2 = RCONHNa + R'H} \qquad (66)$$

the radical R′, eliminated as hydrocarbon, has a smaller relative affinity for the carbonyl group than R. The following order has been established. *p*-Anisyl > β-naphthyl > *p*-diphenylyl > phenyl > *p*-chlorophenyl > *p*-bromophenyl > *m*-chlorophenyl > *m*-bromophenyl. The dimethyl-*p*-aminophenyl radical has a greater, and the thienyl and triphenylmethyl radicals lower "affinities" than phenyl. In carrying out these reactions, the ketones, dissolved in benzene or toluene, were heated for several hours with sodium amide, the mixture cooled and hydrolyzed, the acid amide alone generally being the only reaction product determined. Since a mixture of amides is often obtained, the one found in least amount contains the radical of least "affinity" (i.e., more of the hydrecarbon containing this radical has been produced). It is interesting to note that in these experiments sodium amide has very little effect on the nuclear halogen.

Recently, de Cuester (78) has questioned the validity of Schönberg's method for determining relative affinities, or bond strengths, in that the course of these elimination reactions was found to depend upon the reagent used. Of fifty-seven ketone scissions described in the literature, fourteen are in agreement with Schönberg's theory, thirty-four in disagreement, and nine inconclusive. de Cuester himself has split twelve asymmetric diaryl ketones by at least two different methods, finding that four conformed with the theory, five were in disagreement, and three were inconclusive. It is concluded that this reaction does not afford a sure method of measuring affinities.

2. The scission of trialkylacetophenones and trialkylacetonaphthones. Haller, Bauer, Ramart, Dumesnil and others (178, 3, 283, 112, 179) have decomposed trialkylacetophenones by means of sodium amide, in accordance with the general equation

$$C_6H_5—CO—CRR'R'' + NaNH_2 = C_6H_6 + RR'R''CONHNa \quad (67)$$

the reactions taking place in boiling benzene, toluene, or xylene, depending upon the resistance of the ketone. Occasionally, as when the benzyl, *p*-methylbenzyl, benzohydryl, or ethylphenylcarbinyl [$(C_2H_5)(C_6H_5)CH—$] radicals are among those that have been introduced into the methyl group of acetophenone, the scission partially takes place in the reverse sense, with the formation of a branched chain hydrocarbon and benzamide.

$$C_6H_5—CO—CRR'R'' + NaNH_2 = C_6H_5CONHNa + RR'R''CH \quad (68)$$

Thus, benzyldialkylacetophenones give benzene and benzyldialkylacetamides, as well as a branched chain hydrocarbon containing a benzyl group, according to both of the possible modes of decomposition represented by equations 67 and 68. It may be remarked that the reaction proceeds the more in accordance with equation 68 the heavier the radicals R and R′. Under favorable conditions, some branched chain hydrocarbons, as well as the more complex acid amides may best be synthesized in this manner.

As an illustration of this type of reaction, a solution of methylethylbenzylacetophenone, $(CH_3)(C_2H_5)(C_6H_5CH_2)C \cdot COC_6H_5$, was heated with four equivalents of sodium amide in xylene to about 140°C., where a vigorous reaction occurred, making necessary the cooling of the containing vessel. After the first reaction was over, the contents of the flask were refluxed for six hours, then cooled and hydrolyzed with water. Methylethylbenzylacetamide was obtained in 30 per cent yield, together with a smaller quantity of 2-benzylbutane (112a).

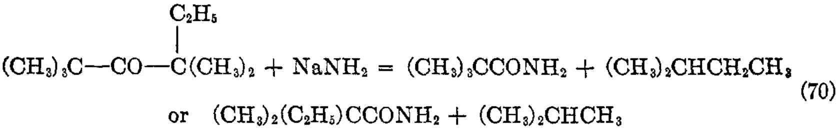
α,α-Dimethyl-β,β-diphenylpropiophenone is scarcely attacked by an excess of sodium amide in benzene or toluene, although reaction does take place in boiling xylene. α,α-Diphenyl-β-methylpropane and β,β-diphenyl-α,α-dimethylpropionamide are formed approximately to the same extent, in accordance with the equations

$$(C_6H_5)_2CHC(CH_3)_2COC_6H_5 \begin{cases} \xrightarrow{NaNH_2} C_6H_5CONHNa + (C_6H_5)_2CHCH(CH_3)_2 \\ \xrightarrow[NaNH_2]{} C_6H_6 + (C_6H_5)_2CHC(CH_3)_2CONH_2 \end{cases} \quad (69)$$

At the same time a fair quantity of *sym*-tetraphenylethane, $(C_6H_5)_2CHCH(C_6H_5)_2$, is obtained as a by-product. The manner in which it is formed is not clearly understood (3a).

The α-trialkylacetonaphthones normally decompose into trisubstituted acetamides ($RR'R''CCONH_2$) and naphthalene, while the β-isomers usually undergo the other method of scission with the production of trialkylmethanes and β-naphthoamide (254, 340).

3. The scission of hexaalkylacetones. Pentamethylethylacetone is decomposed by sodium amide in both possible ways to give pivalic acid amide, 2-methylbutane, the amide of dimethylethylacetic acid, and isobutane (178).



$$(CH_3)_3C{-}CO{-}\overset{\displaystyle C_2H_5 \atop |}{C}(CH_3)_2 + NaNH_2 = (CH_3)_3CCONH_2 + (CH_3)_2CHCH_2CH_3 \quad \text{or} \quad (CH_3)_2(C_2H_5)CCONH_2 + (CH_3)_2CHCH_3 \qquad (70)$$

With ketones of the structure $R''R'RC{-}CO{-}CRR'R''$ and $R''R'RC{-}CO{-}CR_3$ the reaction with sodium amide is far from being as general as it is with the trialkylacetophenones (178, 194). The scission proceeds with unsymmetrically substituted ketones in both of the possible directions (cf. equation 70), but certain symmetrical ketones do not react at all with sodium amide. In the latter case, where decomposition does take place, only two products can be formed instead of four. Hexaethylacetone and $\alpha,\alpha,\alpha',\alpha'$-tetramethylisovalerone thus will not react with sodium amide; pentamethylethylacetone decomposes in the manner described above (equation 70); α,α',-dibenzyl-$\alpha,\alpha,\alpha',\alpha'$-tetramethylacetone decomposes only into the amide of benzyldimethylacetic acid and dimethylbenzylmethane.

4. The scission and decomposition of diketones. Diketones similar to 2,6-dibenzoyl-2,6-dimethylheptane are decomposed by sodium amide (196) in accordance with the type equation

$$C_6H_5COC(CH_3)_2{-}CH_2CH_2CH_2{-}C(CH_3)_2COC_6H_5 \xrightarrow{NaNH_2} \qquad (70)$$

$$NH_2COC(CH_3)_2{-}CH_2CH_2CH_2{-}C(CH_3)_2CONH_2 + 2C_6H_6$$

α, α, α′, α′-Tetramethylpimelamide

to give amides of dibasic acids, as would be predicted from the known method of scission of the trialkylacetophenones.

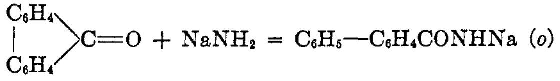
The complex diketones of Dumesnil (111) are ruptured according to the equation

$$C_6H_4[CH_2C(CH_3)_2COC_6H_5]_2\ (o,\ m,\ \text{or}\ p) \xrightarrow[\text{boiling xylene}]{NaNH_2}$$

$$C_6H_4[CH_2C(CH_3)_2CONH_2]_2 + 2C_6H_6 \qquad (72)$$

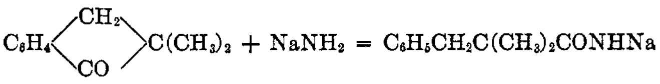
Kasiwagi (229) heated a toluene solution of benzil with sodium amide and obtained a good yield of benzilic acid from the products of hydrolysis of the reaction mixture. Unfortunately, the sodium hydroxide formed in the hydrolysis may have aided the rearrangement of benzil to benzilic acid, although it is certain that sodium amide alone would have sufficed. Haller (162) had previously published a brief note concerning the formation of benzilic acid from sodium amide and benzil.

5. The scission of cyclic ketones. Ketones in which the carbon of the carbonyl group is part of a ring system are split by sodium amide in the expected manner, with the formation of but a single product. Fluorenone is thus converted in almost quantitative yield to diphenyl-*o*-carboxylic acid amide (170a), as expressed by the equation



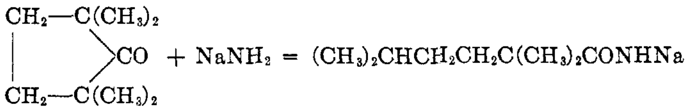
$$\begin{matrix} C_6H_4 \\ | \\ C_6H_4 \end{matrix}\!\!>\!C{=}O + NaNH_2 = C_6H_5{-}C_6H_4CONHNa\ (o) \qquad (71)$$

2,2-Dimethylindanone, under approximately the same conditions, is changed to α,α-dimethylhydrocinnamamide (184).



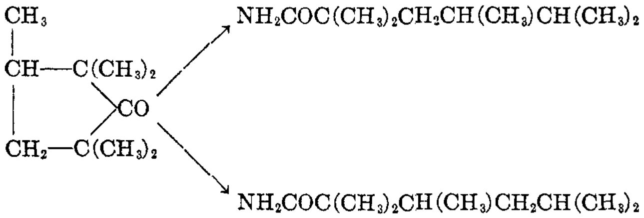
$$C_6H_4\!<\!\begin{matrix} CH_2 \\ CO \end{matrix}\!>\!C(CH_3)_2 + NaNH_2 = C_6H_5CH_2C(CH_3)_2CONHNa \qquad (72)$$

Tetraalkylcyclopentanones are decomposed by sodium amide with the opening of the ring. Thus, $\alpha,\alpha,\alpha',\alpha'$-tetramethylcyclopentanone is broken down into 2,2,5-trimethylcaproamide (210; cf. 17)



(73)

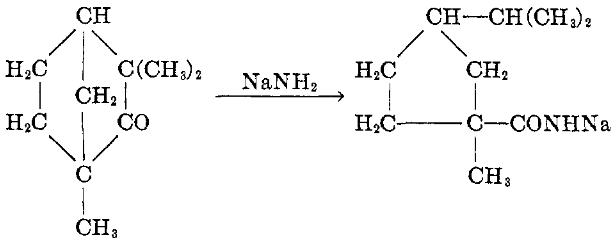
while $\alpha,\alpha,\alpha',\alpha',\beta$-pentamethylcyclopentanone is cleaved in both of the theoretically possible ways.



(74)

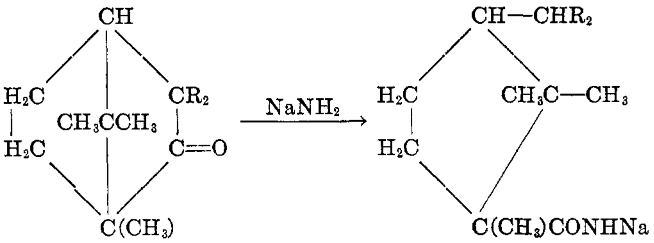
Other unsymmetrically substituted cyclopentanones are ruptured in the manner of equation 74.

Fenchone and camphor each contain two cyclopentane rings, in one of which there is a carbonyl group. Sodium amide should therefore split these ketones in accordance with one of the equations (71 to 74) above. Semmler (317) has indeed shown that fenchone is changed into fencholamide in the sense of the equation



(75)

Haller and Bauer (182) and Haller and Louvrier (213a) have shown that the dialkylcamphors, prepared by the alkylation of camphor with sodium amide and alkyl iodides, further react with an excess of the former reagent under a heated hydrocarbon oil to form dialkylcampholamides. The reaction is expressed by the following equation

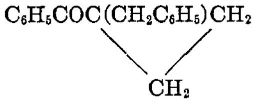


(76)

Nametkin (271) has similarly decomposed β-methylcamphenilone into β-methylcamphenylic acid amide.

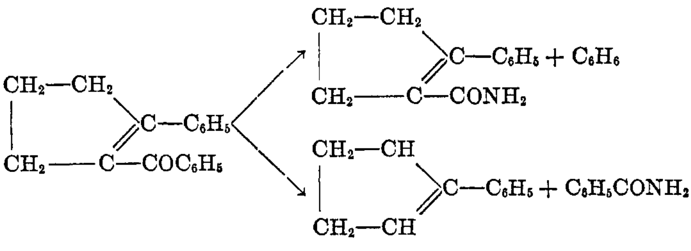
Tetrasubstituted cyclohexanones fail to react appreciably with sodium amide, even after long heating in boiling xylene (163).

Benzoyltrimethylene is cleaved by moist sodium amide under benzene to benzamide and trimethylene (206), while benzoylbenzyltrimethylene



is split into benzene and the amide of benzyltrimethylenecarboxylic acid (207).

Benzoyl-1-phenyl-2- Δ_1-cyclopentene and related compounds break up in both of the possible ways (17).

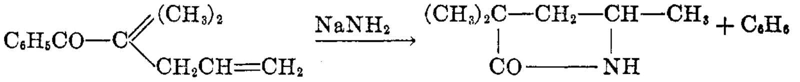


(77)

Sachs (299) obtained diphenyl by heating phenanthrenequinone with fused sodium amide.

E. Condensation reactions of the allylalkylacetophenones and acetonaphthones

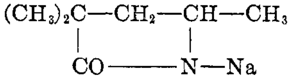
The unsaturated ketones named in the heading are condensed to substituted pyrrolidones, in accordance with the type equation below.



$$C_6H_5CO-C\begin{cases}(CH_3)_2\\ CH_2CH=CH_2\end{cases} \xrightarrow{NaNH_2} \begin{array}{l}(CH_3)_2C-CH_2-CH-CH_3\\ \qquad|\qquad\qquad\quad|\\ \qquad CO\text{————}NH\end{array} + C_6H_6 \qquad (78)$$

3,3,5-Trimethylpyrrolidone

This apparently complex reaction was explained by Haller, who assumed that sodium amide first cleaves the ketone to benzene and the sodium salt of an acid amide of the composition, $NaNHCOC(CH_3)_2CH_2CH=CH_2$. The —NH— portion of the molecule adds to the double bond of the allyl group to form



$$\begin{array}{l}(CH_3)_2C-CH_2-CH-CH_3\\ \qquad|\qquad\qquad\quad|\\ \qquad CO\text{————}N-Na\end{array}$$

and this passes by hydrolysis into the substituted pyrrolidone on the right side of equation 78 (201, 203, 213b).

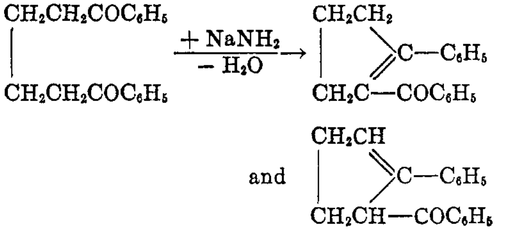
Dimethylallylacetonaphthone (α) either yields allyldimethylacetamide and naphthalene, decomposing therefore in the manner of a trialkylacetophenone, or else it yields naphthalene and trimethylpyrrolidone, as in the reaction of equation 78.

F. Cyclization of ketones by sodium amide

Sodium amide will cause many ketones, acids, and acid amides to lose water intramolecularly with the formation of cyclic compounds. The synthesis of indoxyl from phenylglycine and of substituted indoles from acyl derivatives of *o*-toluidine are illustrations of this type of reaction, but a further discussion will be reserved for a later section of this review.

The conversion of a ketone to a cyclic compound by means of sodium amide is usually the result of a crotonaldehyde type reaction involving the loss of water between the oxygen of carbonyl and two hydrogens of a methyl or methylene group favorably situated spatially elsewhere within the molecule.

Bauer (14) has thus found that 1,6- and 1,7-diketones are converted to acyl derivatives of cyclopentene and cyclohexene, respectively, in the manner of the type equation



(77a)

The second compound is formed from the first by a prototropic (i.e., a tautomeric) change (223).

XII. ACIDS AND THEIR DERIVATIVES, EXCLUSIVE OF ESTERS

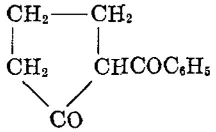
A. Acids

It has been the general experience of a number of investigators that sodium or potassium amide react with substances that are recognized as acids of the water system to form alkali metal salts. Literature references to such evident facts are not necessary. R. A. Fulton (145; cf. 319), working in the laboratories of Stanford University, has observed the formation of methane when sodium acetate is fused with sodium amide, the reaction resembling the well-known method for the preparation of this gas from sodium acetate and soda lime.

Staudinger and Meyer (319) state that potassium diphenylacetate is converted by heated potassium amide to the dipotassium salt of diphenylmethylenecarbonic acid, in accordance with the equation

$$(C_6H_5)_2CHCOOK + KNH_2 = (C_6H_5)_2CH(OK)_2NH_2 = (C_6H_5)_2C{=}C(OK)_2 + NH_3 \tag{79}$$

Bauer (22, 18a) treated δ-benzoylvaleric acid, $C_6H_5COCH_2CH_2CH_2CH_2COOH$, with sodium amide and obtained the cyclic compound, α-benzoylcyclopentanone.



B. *Acid amides and proteins*

Franklin and his coworkers (126, 136, 128, 129) have shown that the acid amides, $RCONH_2$, are mixed acids of the water and ammonia systems, and as such should show the properties of acids, at least in liquid ammonia solution. While it is true that only a few acid amides show well defined acidic properties in water (cf. 256), it is equally true that every acid amide examined by Franklin and his students forms salts in liquid ammonia with bases of the type of sodium or potassium amide. Furthermore, these salts may generally be obtained in definite crystalline form, and therefore in an analytically pure state. In most cases they are hydrolyzed by water to a base of the water system and an acid amide, a reminder of the fact that the ionic product of water ($H^+ \times OH^-$) is much greater than that of ammonia, ($H^+ \times NH_2^-$) (140, 134, 125 footnote).

As an illustration, Franklin and Stafford (136), and Miss R. V. Fulton (148) prepared monopotassium acetamide by bringing together liquid ammonia solutions of potassium amide and acetamide, the reaction proceeding rapidly in accordance with the equation

$$KNH_2 + CH_3CONH_2 = CH_3CONHK + NH_3 \qquad (80)$$

The salt is very soluble in liquid ammonia at room temperature, but can be crystallized at $-40°C.$ from a solution of proper concentration. It is perhaps needless to say that, as far as the evidence goes, potassium acetamide may as well be represented by the formula, $CH_3C(OK){=}NH$. Since the salt is ionic in nature, it may be meaningless to attempt to distinguish between the two structures. Potassium acetamide is decomposed by hydrolysis into acetamide and potassium hydroxide.

$$CH_3CONHK + H_2O = CH_3CONH_2 + KOH \qquad (81)$$

The acetamide, under favorable conditions, may of course be further hydrolyzed to acetic acid.

Franklin, Franklin and Stafford (122, 102, 136, 40), and Miss Fulton (148) prepared the sodium and potassium salts of a number of acid amides by the general reaction illustrated in equation 80. Among these were the monopotassium salts of phenylacetamide, benzamide, urea, benzenesulfonamide, *m*-methoxybenzenesulfonamide, saccharin, propionamide, butyramide, valeramide, capramide, palmitamide, and the dipotassium salts of benzamide, benzenesulfonamide, *m*-methoxybenzenesulfonamide, and urea.

The pioneer work of Franklin and Stafford was not the first recorded preparation of metallic salts of the acid amides. Titherley (331) treated formamide, acetamide, propionamide, and benzamide with sodium amide under boiling benzene, and isolated the monosodium salts of each of these in a fairly pure condition. Similar salts had been made before the date of publication of Titherley's article, but without the use of metallic amides.

Since the paper of Franklin and Stafford, a number of articles have been written upon the subject of the acid amides and their salts, but it would unduly lengthen this review to include more than the references (122, 102, 40, 148, 136). In reading some of the older articles, it should be borne in mind that the acid amides are mixed aquoammonocarboxylic acids (carboxyazylic acids) and not ammono acids, as has often been incorrectly stated.

Miss R. V. Fulton (148) prepared monopotassium formamide, HCONHK, by the action of a liquid ammonia solution of potassium amide on an excess of formamide. If, conversely, more than one molecular proportion of potassium amide is used in this preparation, at room temperatures, hydrogen is evolved in close agreement with the equation

$$\mathrm{HCONHK} = \mathrm{H_2} + \mathrm{KNCO} \tag{82}$$

Potassium cyanate, a salt of a mixed aquoammonocarbonic acid, may readily be isolated from the reaction mixture.

A related, although not strictly comparable, reaction of the water system is the conversion of sodium formate into hydrogen and sodium oxalate, by the action of an excess of heated sodium hydroxide (155, 115, 233). If a mixed aquoammonooxalate is formed in Miss Fulton's reaction, it is converted under the influence of the excess of potassium amide, to potassium cyanate and hydrogen.

The potassium salts of the higher fatty acid amides (acetamide to *n*-caproamide) when heated by themselves, and therefore in the absence of excess potassium amide, decompose in two different ways: (1) to give a hydrocarbon and a cyanate,

$$\mathrm{RCONHK} = \mathrm{KNCO} + \mathrm{RH} \tag{83}$$

a reaction closely akin to the preparation of methane by heating sodium acetate with soda lime, and (2) to give a nitrile and potassium hydroxide.

$$\mathrm{RCONHK} = \mathrm{KOH} + \mathrm{RCN} \tag{84}$$

In the latter decomposition, the acid amide has merely been dehydrated to an acid anammonide, or nitrile. Specifically, potassium *n*-caproamide heated to 220°C., decomposes in accordance with equations 83 and 84 to the extent of about 28 per cent and 72 per cent, respectively. The purity of the pentane formed in reaction 83 was not determined.

R. A. Fulton (145) treated a series of the lower aliphatic acid amides with an excess of fused potassium amide, obtaining hydrocarbons and dipotassium cyanamide, a salt of an ammonocarbonic acid.

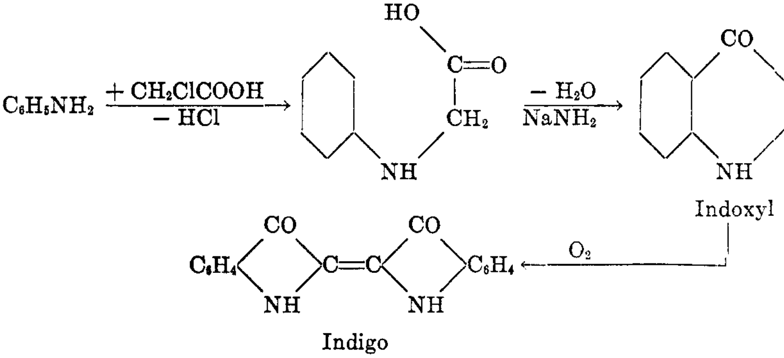
$$\mathrm{RCONH_2} + 3\mathrm{KNH_2} = \mathrm{RH} + \mathrm{K_2CN_2} + \mathrm{KOH} + 2\mathrm{NH_3} \tag{85}$$

The higher hydrocarbons (i.e., above ethane) that would be anticipated in the reaction of equation 85 are cracked to hydrocarbons of lower carbon content and hydrogen by the fused amide.

McChesney and Miller (255) have observed that proteins are partially ammonolyzed by solutions of sodium and potassium amide in liquid ammonia, the latter ammono base being the more effective. As a rule, it is advisable to heat the protein with the alkali metal amide and ammonia to about 110–120°C. for two or three days, but even then the ammonolysis is incomplete. The extent of the decomposition is found by determining the ratio of amide nitrogen to total nitrogen in the reaction product. Under the most favorable conditions, in an experiment when silk was heated with sodium amide and ammonia at 120°C. for four days, this ratio was only 0.306.

C. The indigo synthesis

Sodium amide has long been used in the conversion of phenylglycine to indoxyl, an intermediate in the commercial synthesis of indigo. The complete equations for the preparation of this important dyestuff from aniline are the following:

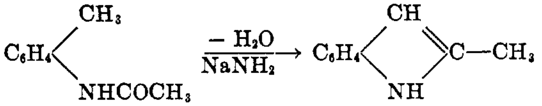


(86)

Rather unsatisfactory yields of indoxyl were obtained in the second stage of the reaction when fused alkali hydroxides were used to bring about the ring closure (2, 141), but sodium amide (151b), either alone or mixed with sodium hydroxide, has been of great advantage in making this process a commercial success. Many other intermediates of the type of phenylglycine have been converted to bicyclic ring systems by the use of sodium amide (222).

D. The preparation of substituted indoles

With the synthesis of indoxyl as a prototype, Verley (338) and Verley and Berdurvé (339) heated the acetyl derivative of *o*-toluidine with 2.5 parts of sodium amide at 250°C. and obtained α-methylindole in good yield, the reaction proceeding in accordance with the equation



(87)

2-Ethyl-, 2-*n*-propyl-, and 2-isobutyl-indoles were synthesized in a like manner. Indole itself was prepared by heating form-*o*-toluide with sodium amide and kieselguhr in the presence of an inert liquid.

E. Acid chlorides

Baumert and Landolt (25) state that dibenzamide as well as benzamide is formed by the action of sodium or potassium amide on benzoyl chloride, in the sense of the following equation, in which the formation of dibenzamide is illustrated.

$$2C_6H_5COCl + 3NaNH_2 = (C_6H_5CO)_2N \cdot Na + 2NaCl + 2NH_3 \qquad (88)$$

$$(C_6H_5CO)_2\,N \cdot Na + H_2O = NaOH + (C_6H_5CO)_2NH$$

While sodium hydroxide and benzoyl chloride react to form sodium benzoate, sodium amide reacts to form also the sodium salt of a mixed aquoammono*di*benzoic acid, a strict analogue of which in the water system alone is impossible. Undoubtedly the products obtained in the reaction of equation 88 will depend to a large extent upon experimental conditions.

Alexieff (5) prepared acetamide, isovaleramide, benzamide, and benzenesulfonamide by adding sodium amide to a solution of the corresponding acid chloride in benzene or xylene. Succinic and phthalic anhydrides are attacked much more slowly by sodium amide with the formation chiefly of salts of acids which contain one COOH and one $CONH_2$ group.

F. Nitriles and related compounds

1. The formation of amidines, of salts, and of cyanphenins and cyanalkines from nitriles. Cornell (103, 130), working under Dr. E. C. Franklin, advanced the hypothesis that the acid nitriles are anammonides of "carbazylic" acids of the ammonia system, since they are related to a class of ammono acids, the acid amidines, in much the same manner that the familiar acid anhydrides of the water system are related to their parent acids.

$$\begin{array}{ll} 2CH_3COOH - H_2O = (CH_3CO)_2O & \\ CH_3C({=}NH)NH_2 - NH_3 = CH_3CN & (89) \\ \text{Acetamidine} \qquad\qquad \text{Acetonitrile} & \end{array}$$

The fact that nitrogen is trivalent while oxygen is divalent makes it possible to prepare an acid anammonide by loss of ammonia from a single molecule of ammonoacetic acid.

With the relationship of the nitriles to the acids of the ammonia system in mind, Franklin and Cornell reasoned that it should be possible to prepare salts of the amidines by treating liquid ammonia solutions of the nitriles with potassium or sodium amide. These reactions were indeed found to proceed very rapidly in liquid ammonia at room temperatures, in accordance with the equation

$$\mathrm{RCN + KNH_2 = RC({=}NH)NHK} \qquad (90)$$

Cornell thus prepared alkali metal salts of acetamidine, propionamidine, isocaproamidine, palmitamidine, benzamidine, butyramidine, valeramidine, succinamidine, and *p*-toluamidine. In some cases, the free amidine was isolated from the products of the water hydrolysis of its salt.

Previous to the publication of Cornell's article, Mlle. Ramart (282) refluxed solutions of *n*-valeronitrile, caprylonitrile, and diethylacetonitrile with sodium amide in ether, forming sodium salts that were not isolated. Addition of benzyl chloride to the reaction mixtures, with a subsequent working up of the products, gave α-benzyl derivatives of the nitriles. One may assume for the time that the reaction follows the course,

$$\mathrm{RCH_2CN + NaNH_2 = RCHNaCN + NH_3} \qquad (91)$$
$$\mathrm{RCHNaCN + C_6H_5CH_2Cl = RCH(CH_2C_6H_5)CN + NaCl}$$

Quite recently, Ziegler and Ohlinger (354) have greatly extended the earlier work of Ramart, and have succeeded in developing a general method for the alkylation of aliphatic nitriles. In the course of their investigations, it was found that the higher nitriles react with a suspension of sodium amide in benzene at 60–70°C. to give the sodium salts of the acid amidines (compare equation 90), which were not isolated as such but were hydrolyzed to form the free amidines in good yield. In this fashion, Ziegler and Ohlinger prepared diethylacetamidine, diethylallylacetamidine, and triethylacetamidine.

Lithium salts of the aliphatic nitriles, presumably of the constitution, $R_2C(Li)CN$ or $R_2C{=}C{=}N{-}Li$, were readily prepared by the action of lithium diethylamide, $(C_2H_5)_2NLi$, upon the nitrile, diethylamine of course being the other reaction product. The lithium diethylamide was most readily made by adding diethylamine to an ethereal solution of lithium phenyl. Therefore, a small amount of a suitable secondary amine, in the presence of lithium phenyl, will serve as a catalyst for converting a large amount of a nitrile to its lithium salt. Addition of an alkyl halide to the solution of the lithium salt of the nitrile gave an α-alkyl derivative of the nitrile, in accordance with the equation

$$(C_2H_5)_2CLiCN + CH_2{=}CHCH_2Cl = LiCl + (C_2H_5)_2C(CH_2CH{=}CH_2)CN \quad (92)$$

A further improvement in this method consisted in the use of a very fine suspension of sodium amide in benzene, prepared by grinding these two substances together for several days in a ball mill. To lessen the formation of amidine, in accordance with equation 90, this suspension of sodium amide in benzene was refluxed for some time with a mixture of the alkyl halide and nitrile and then carefully hydrolyzed with water. Alkylated nitriles were isolated in good yield.

Among the nitriles that Ziegler and Ohlinger prepared are the following: diethylacetonitrile, diallylethylacetonitrile, dibenzylpropionitrile, diisopropylacetonitrile, diethylacetonitrile, and *n*-capronitrile, the latter being made by refluxing a mixture of acetonitrile, *n*-butyl bromide, and sodium amide in absolute ether. It is of interest that diethylacetonitrile was prepared by two methods: first, by heating a mixture of ethyl bromide, ether, and *n*-butyronitrile with sodium amide; and, second, in the same manner, except that the butyronitrile was replaced by half an equivalent of acetonitrile, which therefore was alkylated twice in the alpha position. Ziegler (357), who has recently patented this process, states that several of the nitriles can be hydrolyzed to acid amides which may prove of value as hypnotics.

Under altered conditions, sodium amide is reported to cause the trimerization of nitriles to cyanalkines or cyanphenins. E. von Meyer (262) has obtained these substances in good yield by heating sodium amide with methyl, ethyl, benzyl, and phenyl cyanides. Unfortunately the original article is not available and it is not possible to state the conditions under which the reactions were carried out.

2. The action of highly heated or fused amides on the nitriles. Cornell (103) heated the potassium salts of a number of amidines with potassium amide and obtained hydrocarbons in accordance with the equation

$$RC(=NH)NHK + KNH_2 = RH + K_2NCN + NH_3 \qquad (93)$$

Previously, Miss R. V. Fulton (148) had carried out similar experiments. The reactions are analogous to the decomposition of sodium acetate by heated soda lime into methane and sodium carbonate, since dipotassium cyanamide is a potassium carbonate of the ammonia system (127).

Knowing that the higher hydrocarbons cannot be prepared in a pure state by the action of heated alkalis on the salts of the aquo fatty acids, R. A. Fulton and Bergstrom (146) passed a number of aliphatic nitriles through molten potassium amide. The potassium salt of the amidine, first formed (see equation 90), is at once decomposed into a mixture of hydrocarbon gases, in which the lower hydrocarbons predominate. Hydrogen is always present in the gaseous reaction products from the decomposition of the nitriles containing three or more carbon atoms.

Kirkish (231, 232) has found that phenyl, benzyl, *p*-tolyl, and α-naphthyl cyanides are decomposed by fused sodium amide into benzene, toluene and naphthalene, respectively, and disodium cyanamide. The yield of hydrocarbon is 30 to 60 per cent of the theoretical.

3. Phenylacetonitrile. Phenylacetonitrile, $C_6H_5CH_2CN$, presents a case of especial interest, since it does not form an amidine when treated with the alkali metal amides, because of the great reactivity of the hydrogen atoms of the methylene group. Instead, the reaction follows the course of the equation,

$$NaNH_2 + C_6H_5CH_2CN \underset{\text{in ether or benzene}}{=} NH_3 + C_6H_5CHNaCN \text{ (or } C_6H_5 \cdot CH{=}C{=}NNa) \qquad (94)$$

There is some question as to the structure of the sodium salt so formed, although most investigators seem to prefer the latter, or "nitride," formula (cf. also 286, 336).

Sodium phenylacetonitrile is converted by alkyl halides in ether solution into α-alkylated phenylacetonitriles, according to the equation,

$$C_6H_5CHNaCN + RX = C_6H_5CHRCN + NaX \qquad (95)$$

$$X = \text{halogen}$$

The α-alkylacetonitriles obtained in this reaction may again be alkylated, by a repetition of the processes represented by equations 94 and 95, to give $C_6H_5CRR'CN$ (51, 53, 54, 55, 199, 221, 282a, 283a, 285, 286, 337).

The sodium salt of phenylacetonitrile condenses very readily with suitable esters, aromatic acid halides, and ketones, in the manner of the following equations.

$$2C_6H_5CHNaCN + CH_2(COOC_2H_5)_2 = CH_2[COCH(C_6H_5)CN]_2 + 2C_2H_5ONa \text{ (45, 49)} \qquad (96)$$

$$C_6H_5CHNaCN + C_6H_5CHO = C_6H_5CH{=}C(C_6H_5)CN + NaOH \text{ (52, 50)} \qquad (97)$$

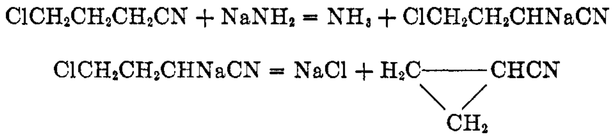
A little benzoic acid is formed at the same time.

$$C_6H_5COC_6H_5 + C_6H_5CHNaCN = (C_6H_5)_2C{=}C(C_6H_5)CN + NaOH \text{ (46, 47, 48)} \qquad (98)$$

$$C_6H_5COCl + C_6H_5CHNaCN = C_6H_5COCH(C_6H_5)CN + NaCl \text{ (45, 46)} \qquad (99)$$

The illustrations that have been given are taken from the articles of Bodroux, who used sodium amide in preparing sodium phenylacetonitrile. This salt can also be made by the action of sodium on phenylacetonitrile and condensations of the latter can be effected without the previous preparation of its sodium derivative, provided the nitrile, the substance with which it is to condense, and an alcoholic solution of sodium ethylate are refluxed together. References to reactions in which sodium amide has not been used are omitted.

Cloke, Anderson, Lachmann, and Smith (101) successfully prepared cyclopropyl cyanide by adding a suspension of sodium amide in toluene to a solution of γ-chlorobutyronitrile in liquid ammonia. The reaction follows the equations

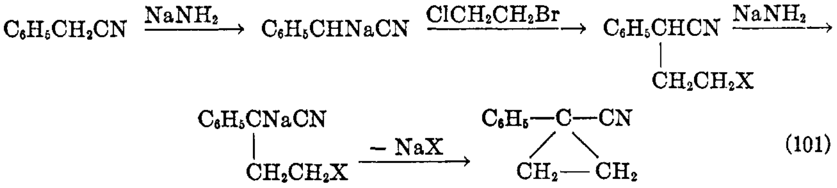


(100)

and consistently gives yields varying between 75 and 90 per cent of the theoretical. Omission of the liquid ammonia very definitely decreases the yield, while even less satisfactory results are obtained by using potassium hydroxide in place of sodium amide (206, 275, 100).

Using the same method, Knowles and Cloke (234) prepared 1-phenyl-1-cyanocyclopropane by treating a liquid ammonia solution of α-phenyl-γ-chlorobutyronitrile with sodium amide.

More simply, phenylacetonitrile was treated with 2 mole proportions of sodium amide in ether, the resulting sodium salt then reacting with ethylene chlorobromide, in the presence of the excess of sodium amide, to give 1-phenyl-1-cyanocyclopropane.



(101)

X = Cl or Br

The first step in the reaction is an extension of the earlier work of Bodroux and Taboury (51, 55).

4. Hydrocyanic acid, the cyanides, isocyanides, and cyanogen. Hydrocyanic acid may be considered either as a nitrile of formic acid, H—CN (therefore a formic acid anammonide) or an ammonocarbonous acid, HN=C (132). The reaction of this substance with potassium amide in liquid ammonia results in the formation of potassium cyanide to the exclusion of a salt of formamidine, HC(=NH)NHK (a potassium ammonoformate) (103a).

Perret and Krawczynski (277) very recently have found that hydrocyanic acid gas reacts with sodium amide at temperatures between 150°C. and 250°C. to form a mixture of sodium cyanamide and sodium cyanide, the former arising from the reaction

$$NaNH_2 + HCN = H_2 + NCNHNa \qquad (102)$$

$$NCNHNa + \text{excess } NaNH_2 = NCNNa_2 + NH_3$$

It will be recalled that sodium cyanide has previously been reported to react with sodium amide to form disodium cyanamide (see Part I, reference 116).

Cornell (103a) has found that cyanogen reacts with a liquid ammonia solution of potassium amide to form potassium cyanide and cyanamide, in qualitative agreement with the equation

$$C_2N_2 + 3KNH_2 = K_2CN_2 + CNK + 2NH_3 \qquad (103)$$

Perret and Krawczynski (277) have made an extended investigation of the action of cyanogen gas on sodium amide in the absence of a solvent, and have observed that between 90°C. and 120°C. there is no reaction other than a polymerization of the cyanogen to paracyanogen. With an increase in the temperature (which may reach 350°C.) sodium cyanamide is formed, apparently as the primary product of the reaction, while variable quantities of cyanide are obtained at the same time.

$$NaNH_2 + (CN)_2 \text{ (or } (CN)_x) = NaNHCN + HCN \qquad (104)$$

In the presence of an excess of sodium amide, it is probable that the monosodium cyanamide is converted to disodium cyanamide. Hydrocyanic acid is not liberated in the free state, since it reacts with an excess of heated sodium amide to form both sodium cyanide and sodium cyanamide (equation 102). The relative extent to which these reactions occur depends upon the experimental conditions. The reaction of Castner (Part I, reference 116)

$$NaNH_2 + NaCN = Na_2CN_2 + H_2 \qquad (105)$$

does not appear to be of importance in the present work, since it was found not to take place at temperatures up to 250°C., although hydrocyanic acid itself is stated to react with sodium amide in the manner of equation 102.

Franklin (132a) has shown that ethyl isocyanide reacts with potassium or sodium amide in liquid ammonia (at 80°C.) to form ethylamine (an ammono alcohol) and potassium or sodium cyanide.

$$C_2H_5NC + KNH_2 = C_2H_5NH_2 + KCN \qquad (106)$$

Therefore, ethyl isocyanide behaves as an ester of an ammonocarbonous acid, HN=C, undergoing saponification in the anticipated manner. It is clear from the preceding paragraphs that the normal alkyl cyanides, or nitriles, cannot be considered as esters of hydrocyanic acid.

XIII. ESTERS

A. Esters not undergoing the Claisen condensation (exclusive of alkyl halides, etc.)

Sodium amide, a base of the ammonia system, should saponify an ester in one of the following ways:

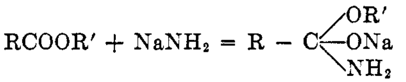
$$\mathrm{RCOOR'} + \mathrm{NaNH_2} = \mathrm{RCONHNa} + \mathrm{R'OH} \qquad (107)$$

yielding the sodium salt of an acid amide (mixed aquoammono acid) and an aquo alcohol, or

$$\mathrm{RCOOR'} + \mathrm{NaNH_2} = \mathrm{RCOONa} + \mathrm{R'NH_2} \qquad (108)$$

giving the sodium salt of an aquo acid and an amine (ammono alcohol). Experiment has shown that the first mode of decomposition generally predominates, if the sodium amide does not cause the ester to undergo condensation.

Titherley (333) examined the action of sodium amide on benzene solutions of a number of typical esters, and found that the reaction in the cold apparently first leads to the formation of an unstable addition compound,



$$\mathrm{RCOOR'} + \mathrm{NaNH_2} = \mathrm{R} - \mathrm{C}\left\langle\begin{matrix}\mathrm{OR'}\\ \mathrm{ONa}\\ \mathrm{NH_2}\end{matrix}\right. \qquad (109)$$

It will be recalled that the carbonyl group of an ester in many cases adds potassium or sodium hydroxide or the alkali metal alcoholates. Intermediate products of the type represented in equation 109 were observed in the reactions between sodium amide and esters of acetic, oxalic, and benzoic acids. The mode in which this addition compound decomposes depends upon the ester, as well as upon experimental conditions.

Ethyl, butyl, and amyl formates react with sodium amide in benzene to give ammonia and sodium formate (333). The experiments are not described in detail sufficient to decide between the two alternatives: first, that the sodium formate is produced in accordance with equation 108, in which case an amine should likewise be formed; and, second, that the sodium formate is a secondary product resulting from the subsequent hydrolysis of formamide in alkaline solution (cf. equation 107).

Ethyl benzoate reacts slowly with sodium amide in warm benzene to form sodium benzamide, sodium benzoate, and sodium ethylate, the relative proportions of which vary with the proportions of ester and amide entering the reaction (333).

Scheibler (301) in his controversial preparation of carbon monoxide diethyl acetal, $C(OC_2H_5)_2$, states that sodium amide reacts with ethyl formate in ethereal solution to give ammonia and sodium oxy-ethoxymethylene, $C(OC_2H_5)(ONa)$, in accordance with the equation

$$HCOOC_2H_5 + NaNH_2 = NH_3 + C(OC_2H_5)(ONa) \qquad (110)$$

Nitrogen-containing by-products are formed at the same time. Titherley (333) previously reported his inability to obtain a sodium salt of ethyl formate, while Wood and the senior author (38) did not succeed in preparing it in liquid ammonia.

Phenyl benzoate is saponified in the approximate manner of equation 107 to phenol and the sodium salt of dibenzamide, $(C_6H_5CO)_2NNa$. The latter may be formed by the action of the expected product, sodium benzamide, $C_6H_5CONHNa$, upon a molecule of the unchanged ester (333).

$$C_6H_5CONHNa + C_6H_5COOC_6H_5 = (C_6H_5CO)_2NNa + \underset{(\text{or } C_6H_5ONa)}{C_6H_5OH} \qquad (111)$$

Diethyl oxalate reacts very vigorously with sodium amide in the absence of a diluent (335). The reaction is more regular in the presence of an excess of benzene, but in spite of this the sodium salts of oxamic acid and of oxamide are formed only in poor yield.

Benzimino ethyl ether, $C_6H_5C(=NH)OC_2H_5$, an *O*-ester of a mixed aquoammonobenzoic acid, benzamide, reacts with sodium amide in benzene to form sodium ethylate, benzonitrile, and ammonia (335).

$$C_6H_5C(=NH)OC_2H_5 + NaNH_2 = C_6H_5CN + C_2H_5ONa + NH_3 \quad (112)$$

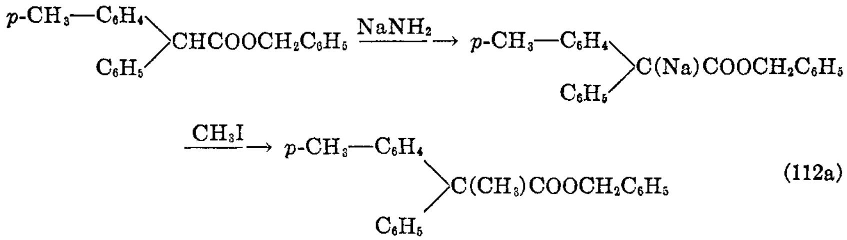
A molecule of ethyl alcohol is removed, converting the ester to benzonitrile, an anammonide of ammonobenzoic acid, $C_6H_5C(=NH)NH_2$. As we have seen, benzonitrile may itself react with sodium amide (cf. equation 90).

Ramart and Haller (284), in extending the earlier work of Titherley, have likewise come to the conclusion that the action of sodium amide on esters varies with the nature of the ester and with the experimental conditions. Phenyl formate is decomposed by sodium amide into sodium phenolate, carbon monoxide, and ammonia, a more deep-seated decomposition than Titherley observed with the alkyl esters of formic acid. Phenyl acetate is converted to sodium phenolate and acetamide, in the manner to be expected from equation 107. Benzyl isobutyrate and sodium amide react, in the absence of solvent, with the evolution of ammonia, but the unchanged ester alone is recovered after hydrolysis of the reaction mixture. This would indicate the formation of a salt. If the reaction is carried out at higher temperatures, under xylene, the ester is to some extent saponified.

The benzyl ester of phenylacetic acid reacts with sodium amide suspended in warm ether or benzene with the slow evolution of ammonia. The addition of benzyl chloride, after completion of the reaction, gives sodium chloride, phenylacetamide and its *N*-benzyl derivative (cf. equation 107), the latter obviously formed by the action of benzyl chloride on sodium phenylacetamide.

If benzyl phenylacetate and sodium amide react at 0°C. in the absence of solvent, a sodium salt of the ester is formed, $C_6H_5CHNaCOOCH_2C_6H_5$. The sodium salt may well have the enolic structure, $C_6H_5CH=C(ONa)OCH_2C_6H_5$.

Ramart (282a) and Ramart and Amagat (283b) have alkylated esters of diphenyl- and phenyl-*p*-tolylacetic acids in accordance with the illustrative equation



$$\begin{matrix}p\text{-}CH_3\text{—}C_6H_4\\C_6H_5\end{matrix}\!\!>CHCOOCH_2C_6H_5 \xrightarrow{NaNH_2} \begin{matrix}p\text{-}CH_3\text{—}C_6H_4\\C_6H_5\end{matrix}\!\!>C(Na)COOCH_2C_6H_5$$

$$\xrightarrow{CH_3I} \begin{matrix}p\text{-}CH_3\text{—}C_6H_4\\C_6H_5\end{matrix}\!\!>C(CH_3)COOCH_2C_6H_5 \qquad (112a)$$

The sodium salt pictured above is undoubtedly derived—at least in large measure—from the enol form of the ester.

Staudinger and Meyer (319a) state that methyl diphenylacetate reacts with potassium amide in liquid ammonia to form an addition compound, from which ammonia can be removed by heating in a vacuum at 100–110°C., presumably leaving the salt of the enol, $(C_6H_5)_2C{=}C(ONa)OCH_3$. This is converted to the methyl ester of methyldiphenylacetic acid by the action of methyl iodide.

Titherley (332) reports that potassium ethyl sulfate reacts with sodium amide at 180°C. in "petrol" to form ammonia, ethylene, and ethylamine, the latter in about 10 per cent of the theoretical yield. Picon (279) has obtained similar results.

Chichibabin and Rjasanjew (85a) treated 2-aminopyridine with sodium amide and the resulting sodium salt with isoamyl nitrite, obtaining a comparatively stable isodiazotate of 2-aminopyridine, $C_5H_4N \cdot N{=}NONa$. It is known that aniline is converted by a solution of sodium ethylate and isoamyl nitrite into the sodium salt of isodiazobenzene, $C_6H_5\text{—}N{=}N\text{—}ONa$ (11, 92).

Blair (42) finds that ethyl allophanate, $NH_2CONHCOOC_2H_5$, reacts with a solution of potassium amide in liquid ammonia to form a monopotassium salt, as would be predicted from the fact that we are dealing with an acid ester of a mixed aquoammonocarbonic acid. Potassium replaces one of the three hydrogens attached to nitrogen. Heated in the absence of liquid ammonia to 215°C., this salt is split into urethan and potassium cyanate, an ethyl ester and a potassium salt of two different mixed aquoammonocarbonic acids. Using potassium amide in excess of three equivalents, Blair was able to saponify ethyl allophanate in liquid ammonia at ordinary temperatures. The reaction appears to be complex.

Ethylcarbamate, or urethan, $NH_2COOC_2H_5$, is readily saponified by potassium amide in liquid ammonia at room temperatures (42), in accordance with the equation

$$NH_2COOC_2H_5 + KNH_2 = KNCO + C_2H_5OH \text{ (or } C_2H_5OK) + NH_3 \qquad (113)$$

Since cyanamide, NH_2CN, is an ammonocarbonic acid (127), it follows that the dialkylcyanamides, R_2NCN, are esters. In conformity with this view, Griswold (158) reports that a dialkyl amine (an ammono alcohol) and dipotassium cyanamide result from the action of a liquid ammonia solution of two or more equivalents of potassium amide on these esters at temperatures above 35°C. Diethylcyanamide is thus decomposed in the manner of the equation

$$(C_2H_5)_2NCN + 2KNH_2 = (C_2H_5)_2NH + K_2NCN + NH_3 \qquad (114)$$

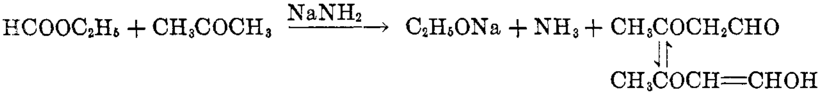
At the temperature of an ice-salt freezing mixture (−6°C. or below) equimolecular proportions of potassium amide and a dialkylcyanamide unite to form crystalline addition compounds which appear to be derivatives of guanidine.

$$(C_2H_5)_2NCN + KNH_2 = (C_2H_5)_2NC({=}NH)NHK \qquad (115)$$

B. Esters undergoing the Claisen condensation

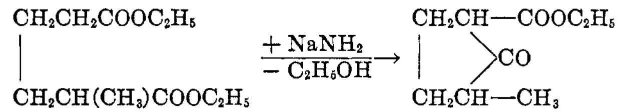
Titherley (333) was the first to observe that sodium amide reacts with ethyl acetate dissolved in benzene to form the sodium salt of ethyl acetoacetate and ammonia. The yield of product is not as good as in the reaction between ethyl acetate and metallic sodium. Freund and Speyer (138) almost simultaneously condensed ethyl acetate with sodium amide in the absence of an inert liquid and obtained sodium acetoacetic ester, likewise in poor yield. A few years later, Claisen and Feyerabend (98) extended the earlier work of Titherley and of Freund and Speyer, and discovered that sodium amide can be used to advantage in the condensation of ketones with esters to form 1,3-diketones, in that the reactions often run more smoothly and rapidly and give better yields of product. As an illustration, sodium amide was slowly introduced into a mixture of ethyl acetate and acetone, cooled in a freezing mixture. After a few hours standing at 0°C. and about twelve hours standing at room temperatures, ice water was slowly added to hydrolyze the reaction products, and the acetylacetone contained in the aqueous layer was isolated as the copper salt, after previously acidifying the solution with acetic acid. From 34 grams of sodium amide, 120 cc. of ethyl acetate, and 32 cc. of acetone, there was obtained 20 grams of acetylacetone, while only 16 to 17 grams could be prepared by the older method in which sodium was used. It is of significance that these directions have been transferred to Gattermann-Wieland, *Die Praxis des organischen Chemikers* (149).

Benzoylacetone was obtained in 77 per cent of the theoretical yield by condensing ethyl acetate and acetophenone with sodium amide in ether (98). Acetophenone, ethyl benzoate, and sodium amide in ether gave dibenzoylmethane in good yield. Oxymethylene ketones of the type, $CH_3COCH{=}CHOH$, may be prepared by the condensation of formic acid esters with ketones in the presence of sodium amide.



$$HCOOC_2H_5 + CH_3COCH_3 \xrightarrow{NaNH_2} C_2H_5ONa + NH_3 + \begin{array}{c} CH_3COCH_2CHO \\ \downarrow\uparrow \\ CH_3COCH{=}CHOH \end{array} \quad (116)$$

An internal Claisen condensation, or Dieckmann reaction, may be occasioned by sodium amide in long chain esters of suitable constitution. Bouveault and Locquin (74) have carried out a number of syntheses of this type, of which the following is an example.



(116a)

Diethyl α-methyladipate

Ethyl α-methylcyclopentanone-α′-carboxylate

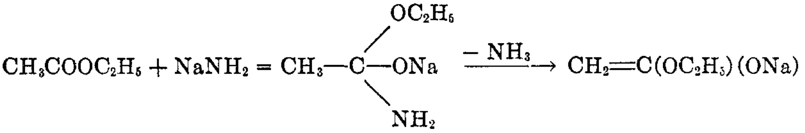
Bauer (18a) in a like manner prepared α-benzoylcyclopentanone and α-benzoylcyclohexanone by the action of sodium amide on esters of δ-benzoylvaleric and ε-benzoylcaproic acids, respectively. The latter may also be made by condensing ethyl benzoate with cyclohexanone in the presence of sodium amide (20). (See also reference 361.)

Claisen and Schulze (95) obtained 32 per cent of the calculated amount of isonitrosoacetophenone by the action of sodium amide on a mixture of amyl nitrite and acetophenone, while the same substance was prepared in 50 per cent yield by using sodium ethylate in place of the sodium amide. There is accordingly no advantage in the use of the latter in this synthesis.

A number of years later, Scheibler and his coworkers, in a series of investigations of the action of finely divided alkali metals on the esters of the lower fatty acids, came to the conclusion that the first product of the action of potassium upon ethyl acetate in absolute ether has the structure, $CH_2{=}C(OC_2H_5)(OK)$, this representing the sodium salt of the enolic form of the ester (306, 307, 303).

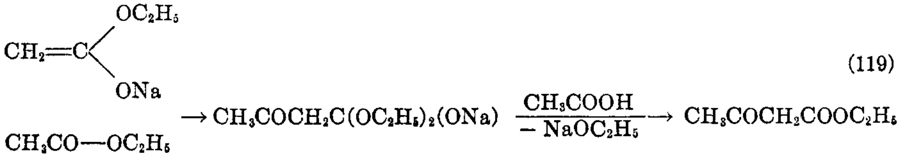
$$CH_3COOC_2H_5 + K \rightarrow CH_2{=}C(OC_2H_5)(OK) + \tfrac{1}{2}H_2 \qquad (117)$$

Since sodium amide may replace metallic sodium in the acetoacetic ester condensation, it naturally became of interest to examine further the reaction between this ammono base and ethyl acetate. This was done by Scheibler and Ziegner (307) who conclude that the reaction follows the course,



$$CH_3COOC_2H_5 + NaNH_2 = CH_3{-}\overset{OC_2H_5}{\underset{NH_2}{C}}{-}ONa \xrightarrow{-\,NH_3} CH_2{=}C(OC_2H_5)(ONa) \qquad (118)$$

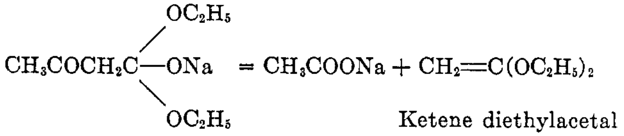
The conversion of the sodium enolate of ethyl acetate into ethyl acetoacetate may be expressed by the equation



$$\begin{matrix} CH_2{=}C\begin{smallmatrix}OC_2H_5\\ ONa\end{smallmatrix} \\ CH_3CO{-}OC_2H_5 \end{matrix} \rightarrow CH_3COCH_2C(OC_2H_5)_2(ONa) \xrightarrow[-\,NaOC_2H_5]{CH_3COOH} CH_3COCH_2COOC_2H_5 \qquad (119)$$

K. Meyer holds a similar view concerning the mechanism of this condensation (263) and speculations concerning the possible existence of the enolic salt of equation 117 are found in Gattermann-Wieland, *Die Praxis des organischen Chemikers* (149a).

When the product of the action of sodium amide upon an excess of ethyl acetate (to which ether was later added) is freed by vacuum distillation from the excess of ester and ether, there is left a colorless solid consisting of the addition product, $CH_3COCH_2C(OC_2H_5)_2(ONa)$. If this is added very slowly to ice water, some sodium acetate and ketene diethylacetal are formed in the sense of the equation (309),



$$CH_3COCH_2C(OC_2H_5)_2ONa = CH_3COONa + \underset{\text{Ketene diethylacetal}}{CH_2{=}C(OC_2H_5)_2} \qquad (119a)$$

The yield is not over 16 per cent of the theoretical amount calculated on the basis of the sodium amide.

According to Scheibler, Marhenkel, and Nikolić (305), ketene diethylacetal is decomposed by eight hours refluxing with sodium amide under diethyl ether into ethinyl ethyl ether, according to the scheme

$$CH_2{=}C(OC_2H_5)_2 \xrightarrow[-\,C_2H_5ONa]{+\,NaNH_2} CH_2{=}C(OC_2H_5)NH_2 \xrightarrow{-\,NH_3} \begin{array}{c} CH{\equiv}COC_2H_5 \\ +\,NaNH_2 \downarrow \\ NaC{\equiv}COC_2H_5 \end{array} \qquad (120)$$

Phenylketene diethylacetal, $C_6H_5CH{=}C(OC_2H_5)_2$, was submitted to a similar series of operations to give phenylethinyl ethyl ether, $C_6H_5C{\equiv}COC_2H_5$. It should be mentioned that both of these acetylenic ethers were qualitatively recognized by their reactions but were not isolated.

Scheibler and Ziegner (308) have briefly investigated the action of sodium amide upon a mixture of ethyl acetate and ethyl benzoate.

Finally, it is only fair to say that the views of Scheibler and his coworkers concerning the mechanism of the acetoacetic ester synthesis have been attacked by Adickes (1) and by M. C. Franklin and Short (137). The latter authors have not been able to duplicate in all particulars the work of Scheibler and his coworkers on the sodium amide–ethyl acetate reaction. They have observed the formation of sodium acetate and sodium acetamide, in qualitative agreement with the earlier work of Titherley (333).

XIV. ORGANIC DERIVATIVES OF HYDROXYLAMINE, HYDRAZINE, DIIMIDE, AND TRIAZENE

Oximes, such as acetone oxime, are readily converted by sodium amide in warm benzene to salts of the type, $(CH_3)_2C{=}NONa$ (329). Phenylhydrazine reacts with sodium amide in benzene at 40°C. to form a pale yellow monosodium salt, in which the alkali metal is supposed to be attached to the nitrogen nearest the phenyl group (329).

Titherley (330) makes the unsupported statement that sodium hydrazobenzene has been prepared in a manner similar to sodium phenylhydrazine. Schurman and Fernelius (314) state that hydrazobenzene reacts with potassium amide in liquid ammonia to form a very soluble strongly colored reddish-brown salt. As the color is discharged by ammonium salts, which act as acids in liquid ammonia (125, 133, 135, 33), hydrazobenzene is suitable for use as an indicator of the Ostwald type.

White and Knight (343) observed that potassium amide reacts with phenylhydroxylamine in liquid ammonia at −33°C. to form a sparingly soluble, red precipitate, which they consider to be identical with the red dipotassium phenylhydroxylamine formed by the action of potassium metal on nitrobenzene in liquid ammonia.

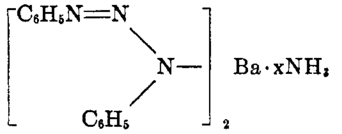
$$C_6H_5NO_2 + 4K + NH_3 = KOH + KNH_2 + C_6H_5N(K)OK \qquad (121)$$

Sachs (299) claims to have obtained hydrazobenzene as one of the products of the reaction between fused sodium amide and azobenzene.

Meunier and Desparmet (260) state that diazoaminobenzene reacts with sodium amide in ether to form a sodium salt, in the manner of the equation

$$C_6H_5NHN{=}NC_6H_5 + NaNH_2 = C_6H_5NNaN{=}NC_6H_5 + NH_3 \qquad (122)$$

Fernelius (118) has found that diazoaminobenzene reacts with the amides of calcium and barium in liquid ammonia to form salts of the general formula,



in agreement with Franklin's theory (124) that the parent compound is a diphenyl ester of an ammononitrous acid, $HN{=}N{-}NH_2$. (The central nitrogen is the nitrous acid nitrogen.) Potassium and sodium amide in liquid ammonia convert diazoaminobenzene to extremely soluble salts that can not be isolated in crystalline form.

XV. NITRO COMPOUNDS

In an attempt to reverse the ordinary method of formation of diazonium salts, in which a salt of aniline is treated with sodium nitrite and an acid, Bamberger and Wetter (12; cf. Sachs reference 298, and Titherley, reference 328) treated nitrobenzene with sodium amide suspended in cold petroleum ether, to which β-naphthol had been added. From the products of the hydrolysis of the reaction mixture, there was isolated a small quantity of phenylazo-β-naphthol, a compound that is likewise formed by the coupling of potassium benzene normal diazotate with an alkaline solution of β-naphthol in water,

$$C_6H_5{-}N{=}N{-}OK + C_{10}H_7OH = \underset{\text{Phenylazo-}\beta\text{-naphthol}}{C_6H_5{-}N{=}\overset{1}{N}{-}\overset{2}{C_{10}}H_6OH} + KOH \qquad (123)$$

Williams (347), working in the laboratories of Stanford University, undertook the examination of this reaction in liquid ammonia at −33°C., and found that nitrobenzene, added slowly to a solution of an excess of potassium amide and β-naphthol gives a fair yield of phenylazo-β-naphthol (see equation 123).

The senior author (34) found that nitrobenzene reacts vigorously with a liquid ammonia solution of potassium amide at −33°C. or at room temperature, with the evolution of nitrogen. The product of the reaction must therefore be rather unstable in ammonia, a not unexpected fact since benzenediazonium nitrate reacts with this solvent to give an indefinite mixture of a somewhat similar nature. *p*-Nitroaniline, *o*-nitroaniline and 1-nitronaphthalene also react with a liquid ammonia solution of potassium amide at room temperatures to give mixtures from which no definite compounds have been isolated. *p*-Nitrotoluene, reacting with β-naphthol and an excess of potassium amide in ammonia at room temperatures, is converted in good yield to a red colored dye.

Angeli (8a) has mentioned this reaction of Bamberger and Wetter's as an indication of the correctness of his proposed structure for normal potassium benzene diazotate, $C_6H_5\text{—N(=NK)O}$ (8, 8a).

Fernelius and Watt (120) report that diphenylnitrosoamine, a diphenyl ester of a mixed aquoammononitrous acid, reacts with potassium amide to give diphenylamine, nitrogen, and potassium hydroxide

$$(C_6H_5)_2N\text{—}NO + 2KNH_2 = NH_3 + (C_6H_5)_2NK + (O\text{=}N\text{—}NHK) \quad (124)$$
$$(O\text{=}N\text{—}NHK) = KOH + N_2$$

the two latter substances possibly resulting from the decomposition of a primarily formed potassium salt of a mixed aquoammononitrous acid, O=N—NHK. Similar reactions were observed with the amides of lithium, sodium, and calcium.

XVI. FIVE-MEMBERED HETEROCYCLIC NITROGEN RING SYSTEMS

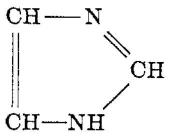
The *N*-hydrogen atoms of pyrrole, indole, and carbazole, as is well known, are slightly acidic in character, since they may be replaced by metals. The reason why these substances do not show the basic properties usually associated with trivalent nitrogen is probably due to the inclusion of the unshared electron pair of the nitrogen atom in a group of six electrons inside of the heterocyclic ring (10, 224, 156). Nitrogen thus has no unshared electron pairs external to the nucleus and this will hinder its coördination with the hydrogen-ion. It is thought that the aromatic properties of benzene are due to this same stable grouping of six electrons within the molecule.

Although not the first to prepare alkali salts of pyrrole, indole, and carbazole, Franklin (131) was the first to observe that these heterocyclic nitrogen compounds react with the metallic amides in liquid ammonia. Sodium and silver amides convert pyrrole, indole, and carbazole to their sodium and silver salts, which may readily be obtained in crystalline form by cooling their liquid ammonia solutions. The formation of sodium pyrrole may serve as an illustration.

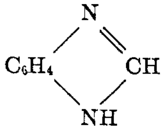
$$C_4H_4NH + NaNH_2 + (x - 1)NH_3 = C_4H_4NNa \cdot xNH_3 \qquad (125)$$

Calcium carbazole is readily prepared by treating carbazole with calcium amide in liquid ammonia. Potassium amide reacts with pyrrole, indole, and carbazole, but with the exception of potassium carbazole, none of the salts were isolated and analyzed.

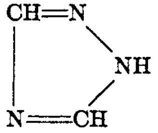
Strain (322) refers to the work of Wenzel (342), who prepared the potassium, sodium, calcium, and silver salts of imidazole



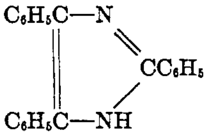
by the action on this substance of the appropriate metallic amide in liquid ammonia. Bergstrom and Wood (38) made the monosodium and monopotassium salts of benzimidazole,



and Strain obtained the monosodium, silver, and cuprous salts of 1,2,4-triazole



and the monopotassium, sodium, cuprous, silver, and lithium salts of triphenylglyoxaline (lophine),



by the general methods outlined above (322).

As may be seen from the formulas above, these substances may be regarded as acid esters of ammonoformic acid, $H—C(=NH)-NH_2$. Tetrazole is also an ester of a hydrazide of formic acid.

XVII. SIX-MEMBERED HETEROCYCLIC NITROGEN RING SYSTEMS

A. Pyridine and its derivatives

Chichibabin and his coworkers (310, 81, 87, 150) prepared 2- or α-aminopyridine, $C_5H_4N—NH_2$, in yields that are reported as high as 70 per cent, by the action of sodium amide upon pyridine in boiling xylene, toluene, or benzene, the reaction following the equation

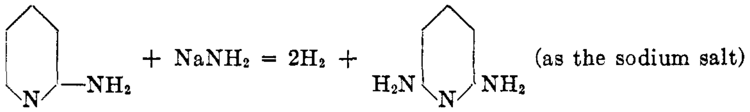
$$C_5H_5N + NaNH_2 = H_2 + C_5H_4N—NHNa \tag{126}$$

Water converts the sodium salt above into 2-aminopyridine, which may be extracted from the aqueous solution with benzene. The preparation of 2-aminopyridine has been the subject of a number of patents (81, 310).

Several years later, Wibaut and Dingemanse (346) again investigated the action of sodium amide on pyridine in toluene, and obtained results differing in a few details from those of Chichibabin. Distillation in a vacuum of the ether extract of the hydrolysate of the sodium amide–pyridine reaction mixture gave 2-aminopyridine in 46 to 55 per cent yield, along with higher boiling fractions which contained smaller amounts of 4,4′-dipyridyl, 2,2′-dipyridylamine and unidentified products. Chichibabin likewise obtained higher boiling fractions, but he was unable to identify any constituent with certainty.

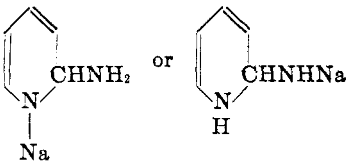
Wibaut and Dingemanse (346) made the interesting observation that the yield of 2-aminopyridine depends to a large extent upon the condition of the sodium amide used in the synthesis. Strangely enough, it was found that the purest sodium amide, prepared in accordance with the method of Titherley (327), failed to react appreciably with pyridine during eight hours heating at 120–125°C. in toluene, while good yields of 2-aminopyridine were obtained when sodium amide of less purity was used (i.e., material of commercial origin or material that had been standing in laboratory bottles for some time). It would appear that impurities in the sodium amide have catalytically influenced the course of the reaction.

If the relative proportion of sodium amide is increased above that used in the preparation of 2-aminopyridine, it is possible under suitable conditions to introduce another amino group into the pyridine nucleus and obtain 2,6-diaminopyridine in yields of about 50 per cent (87).



(127)

The mechanism of these syntheses has been discussed by Ziegler and Zeiser (356), who suggest that the sodium amide first adds to the —CH═N— bond of pyridine to give



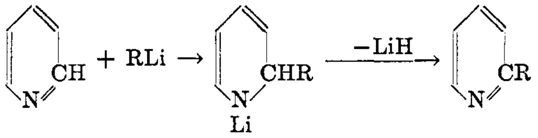
(127a)

this passing by loss of sodium hydride into 2-aminopyridine. The sodium hydride cannot be isolated as such, since it converts 2-aminopyridine into a sodium salt and hydrogen.

$$C_5H_4N—NH_2 + NaH = (C_5H_4N—NH)Na + H_2 \qquad (128)$$

One could equally well assume that the direct loss of a molecule of hydrogen from 127a gives sodium 2-aminopyridine.

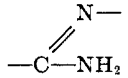
Although this mechanism received no direct experimental support, it appeared reasonable because the addition products formed between pyridine and the lithium alkyls or aryls lose lithium hydride on heating and pass into 2-alkyl- or 2-arylpyridines.



(129)

In a series of unpublished investigations, one of us (34) has shown that pyridine reacts slowly with a liquid ammonia solution of a large excess of potassium amide at room temperatures to yield 2-aminopyridine in amounts not greater than 30 per cent of the theoretical. A large excess of pyridine, on the other hand, results in the formation, in poor yield, of a soluble blue colored monopotassium salt of a partly reduced 4,4′-dipyridyl. (Compare the blue color produced when 4,4′-dipyridyl is treated with zinc dust and acetic acid, as in the qualitative test for this substance (cf. reference 115a). Very little or no 2-aminopyridine is formed. The other product of the reactions is an amorphous, apparently polymerized substance that chars without melting.

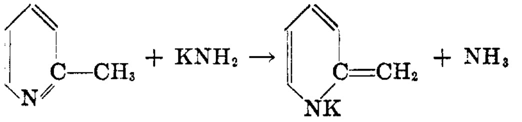
Heated to 100–130°C. with an excess of a liquid ammonia solution of potassium amide, pyridine is partly converted to the potassium salts of 2-aminopyridine and 2,6-diaminopyridine, with the evolution of some hydrogen. The potassium salt of 2-aminopyridine is readily soluble in liquid ammonia, while the dipotassium salt of diaminopyridine is practically insoluble. Bergstrom and McAllister (35) have pointed out the formal structural relationship of the —CH═N— group of pyridine to the —CH═O group of the aquo aldehydes. The formation of 2-aminopyridine is therefore the nitridation of an aldehyde of the ammonia system to the corresponding carbazylic acid, which contains the group



$$-\mathrm{C}(=\mathrm{N}-)-\mathrm{NH_2}$$

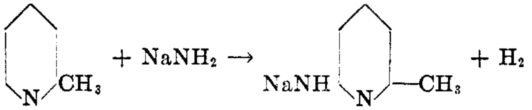
It is well known from the work of Chichibabin (86) that 2-aminopyridine is readily converted to a sodium salt by reaction with sodium amide under benzene. This salt, when heated with alkyl halides or with dimethyl sulfate, is changed to 2-*N*-alkylated aminopyridines.

2-Methylpyridine (α-picoline) reacts with sodium and potassium amide in liquid ammonia to form salts of an enamic, or ammono enolic, modification (31), in the manner of the equation



(130)

Working with sodium amide in a boiling hydrocarbon solvent, Seide (315b) and Chichibabin (86, 81, 310) have found that 2-methylpyridine is converted in fair yield to 2-methyl-6-aminopyridine.



(131)

3-Methylpyridine (316), 4-methylpyridine (315a), 2-methyl-5-ethylpyridine (aldehyde collidine) (90), and nicotine (83, 84), when treated with sodium amide under similar conditions, are converted respectively to 2-amino-3-methylpyridine, 2-amino-4-methylpyridine, 2-methyl-5-ethyl-6-aminopyridine and to a mixture of α- and α′-aminonicotines.

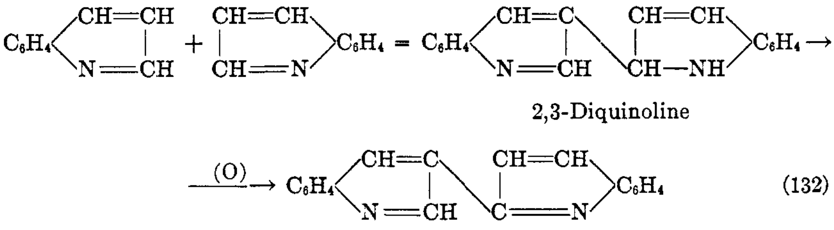
Symmetrical collidine (2,4,6-trimethylpyridine) is changed by an excess of potassium amide in liquid ammonia solution at room temperature to the potassium salt of an ammono enol (enam), but barium and sodium amide, having a low solubility in ammonia, do not react to completion (32).

From the above reactions it would appear that the nitrogen atom has in some way activated the hydrogen atoms in the α and α′ positions alone, so that one or both may be replaced by amino groups. Whether this activation can be attributed other than in a purely formal manner to the inclusion of the ammono aldehyde group, —CH=N—, in the pyridine ring, is a matter that must await further investigation.

Chichibabin believed that he found a little 4-aminopyridine among the products of the action of sodium amide on pyridine, but this was not confirmed by Wibaut and Dingemanse. Nevertheless, Chichibabin (82) reports that sodium amide and 2,6-dimethylpyridine slowly react to form a small amount of the 4-amino derivative.

B. Quinoline, isoquinoline, and their derivatives

Chichibabin and Zatzepina (91) prepared 2-aminoquinoline in rather poor yield (25 per cent) by heating quinoline and sodium amide in the presence of a boiling hydrocarbon. 2,3-Diquinoline is formed at the same time, and this readily loses two atoms of hydrogen by oxidation and passes into 2,3-diquinolyl. The formation of 2,3-diquinoline from quinoline may be regarded as an example of the aldol condensation, if one accepts the thesis that quinoline has some of the properties of an aldehyde of the ammonia system (35). The condensation may be represented by the equation



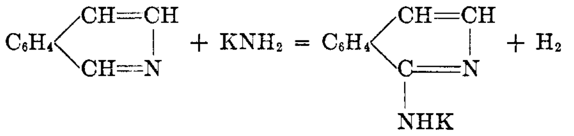
2,3-Diquinoline

2,3-Diquinolyl

(132)

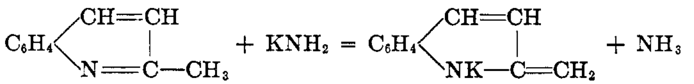
In liquid ammonia solution at room temperatures, both sodium and potassium amide convert quinoline into low-melting resinous compounds of an indefinite nature (34). 2-Aminoquinoline is, however, formed in good yield, together with the calculated amount of hydrogen, by the action of barium amide upon quinoline in liquid ammonia, possibly because the reaction is slower as a result of the low solubility of the barium amide (34). One may recall in this connection that strong aqueous or alcoholic potassium hydroxide converts acetaldehyde into indefinite "aldehyde resins," while weaker alkalis, such as potassium carbonate, favor the formation of a definite compound, which in this case is an aldol (265, 274).

1-Aminoisoquinoline may be prepared in 38 per cent yield by the action of sodium amide upon isoquinoline in the presence of hot indifferent solvents (85). A solution of potassium amide in liquid ammonia at room temperatures reacts with isoquinoline to give 1-aminoisoquinoline in 75 per cent yield (34), together with approximately the amount of hydrogen that corresponds to the equation



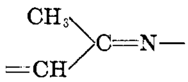
(133)

Quinaldine, 2-methylquinoline, reacts readily with potassium or sodium amide in liquid ammonia, either at −33°C. or at room temperatures, to form soluble red colored salts of an ammono enolic, or enamic, modification (29), in the manner represented by the equation

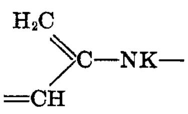


(134)

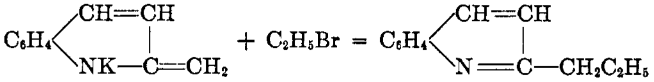
Regarding quinaldine as a cyclic ammono ketone (acetal) because of the



group, it is perfectly logical to assign to the reaction product of equation 134 the structure of an ammono enol, which contains the group,



These salts may readily be alkylated in liquid ammonia or in absolute ether to form homologues of quinaldine, in accordance with the type equation

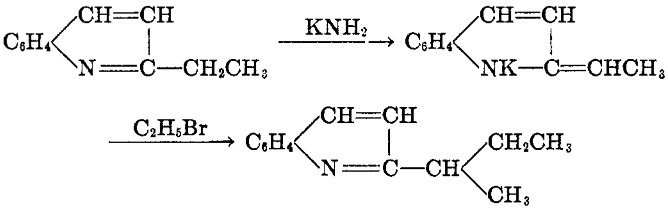


$$C_6H_4\left\langle\begin{array}{l}CH{=}CH\\ \quad\;\;|\\ NK{-}C{=}CH_2\end{array}\right. + C_2H_5Br = C_6H_4\left\langle\begin{array}{l}CH{=}CH\\ \quad\;\;|\\ N{=}C{-}CH_2C_2H_5\end{array}\right. + KBr \quad (135)$$

(75 per cent yield)

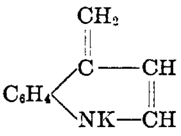
The reaction proceeds less satisfactorily with *n*-butyl and *n*-amyl bromide, the yield of *n*-amylquinoline with the former amounting to about 25 per cent. 2-Ethyl- and 2-*n*-butyl quinolines have been prepared in fair yields by this method.

All quinoline derivatives with a —CH_2— group in the 2-position (as, for example, 2-ethyl- and 2-ω-phenylethylquinoline) react with potassium amide to form homologues of potassium quinaldine, in the manner of equation 134. These salts may be alkylated by treatment with alkyl halides in the *absence* of liquid ammonia, as in the typical preparation of 2-*sec*-butylquinoline from 2-ethylquinoline (32a).



$$C_6H_4\left\langle\begin{array}{l}CH{=}CH\\ \quad\;\;|\\ N{=}C{-}CH_2CH_3\end{array}\right. \xrightarrow{KNH_2} C_6H_4\left\langle\begin{array}{l}CH{=}CH\\ \quad\;\;|\\ NK{-}C{=}CHCH_3\end{array}\right. \xrightarrow{C_2H_5Br} C_6H_4\left\langle\begin{array}{l}CH{=}CH\\ \quad\;\;|\\ N{=}C{-}CH\left\langle\begin{array}{l}CH_2CH_3\\ CH_3\end{array}\right.\end{array}\right. \quad (136)$$

4-Methylquinoline (lepidine) reacts with potassium, sodium, and barium amides in liquid ammonia to form salts of the probable type constitution,



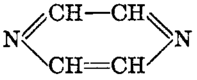
$$C_6H_4\left\langle\begin{array}{l}\overset{\displaystyle CH_2}{\overset{\|}{C}}{-}CH\\ \qquad\;\;\|\\ NK{-}CH\end{array}\right.$$

These salts can be alkylated by treatment with the lower alkyl halides in ethereal solution. 4-Ethyl- and 4-*n*-propyl-quinolines were thus prepared (32a).

Ziegler and Zeiser have alkylated quinoline through the lithium salt of the enamic modification, prepared by the action of lithium alkyls or aryls on quinaldine in ether (356).

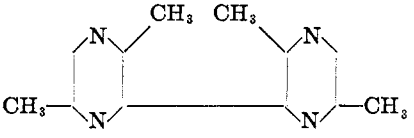
C. Pyrazine and 2,5-dimethylpyrazine

Bergstrom and Ogg (37) found that pyrazine

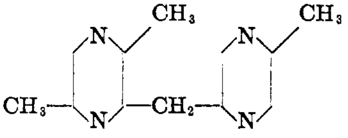


is attacked by a liquid ammonia solution of potassium amide to form an opaque dirty green solution from which no definite products were isolated.

According to Chichibabin and Shchukina (89), 2,5-dimethylpyrazine slowly reacts with sodium amide in xylene to give 2,5-dimethyl-3-aminopyrazine in poor yield. In the absence of solvent, some dimethylpiperazine is formed by reduction of the dimethylpyrazine and there is also obtained a tetramethyldipyrazyl and a trimethyldipyrazylmethane, of the formulas.



Tetramethyldipyrazyl

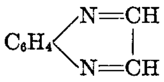


Trimethyldipyrazylmethane

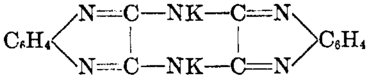
(137)

D. Quinoxaline and its derivatives

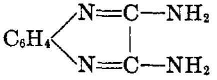
Quinoxaline



is readily formed by the action of glyoxal, CHO-CHO, on *o*-phenylenediamine, a reaction which may be interpreted as the ammonolysis of an aquo dialdehyde by a substituted ammonia to give the *o*-phenylene diacetal of a glyoxal of the ammonia system. The resemblance of quinoxaline to glyoxal is often rather striking. Confining ourselves only to reactions in which the alkali amides have a part, we find that potassium amide, in ammonia solution, converts quinoxaline into a mixture which appears to contain the dipotassium salt of fluorubin (36).



Dipotassiumfluorubin



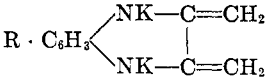
2,3-Diaminoquinoxaline

(138)

Fluorubin is a product of the nitridation of quinoxaline, since it may be regarded as derived from two molecules of 2,3-diaminoquinoxaline by the loss of two molecules of ammonia. Diaminoquinoxaline is the ammono diacid ester corresponding to the ammono dialdehyde-diacetal quinoxaline.

Peterson (278) reports a similar reaction between potassium amide and toluquinoxaline in liquid ammonia.

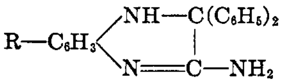
2,3-Dimethylquinoxaline and 2,3-dimethyltoluquinoxaline are reported by Ogg and Bergstrom (276) and by Peterson (278) to react readily with potassium amide to form the dipotassium salt of an ammono dienol (dienam) of the probable formula,



R = H or CH_3 in position 6

Ethyl bromide converts these salts to di-*n*-propyl-quinoxaline or -toluquinoxaline in a manner similar to that of equation 135. Di-*n*-propyltoluquinoxaline reacts with sodium amide to form a sodium salt (278).

2,3-Diphenylquinoxaline and 2,3-diphenyltoluquinoxaline, while sparingly soluble in liquid ammonia at room temperatures, dissolve easily in potassium amide, presumably to form an addition compound, in which one or both of the —CH=N— groups has been converted to —CH(NH—)(NHK). Further action of potassium amide in ammonia at 130–140°C. produces compounds which may have the structure of the product of a benzilic acid rearrangement of the diphenylquinoxalines.

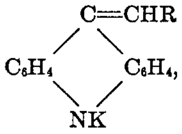


(139)

R, in position 6, is H or CH_3

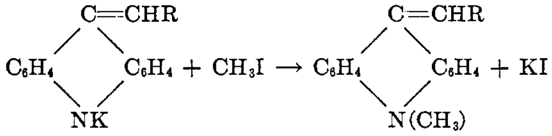
E. Acridine and tetrazine

Mesomethyl- and mesobenzyl-acridine react with potassium and sodium amides to form salts of the typical composition,



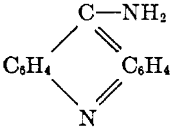
where R is H or C_6H_5

These salts appear to be converted in poor yield by the lower alkyl halides chiefly to *N*-alkyl-mesomethylenedihydroacridines, in accordance with the equation

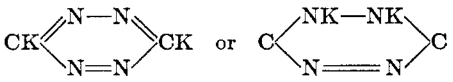


(140)

Acridine itself reacts with potassium or barium amides in liquid ammonia to yield a mixture of products which contains *ms*-aminoacridine (7).



Tetrazine, a crimson colored and somewhat unstable compound, reacts with a liquid ammonia solution of potassium amide at −33°C. to form an insoluble, explosive dipotassium salt, to which either of the following structures may be assigned.



(141)

When freshly made, it may be converted by a liquid ammonia solution of ammonium bromide to potassium bromide and tetrazine, but the latter cannot be isolated from specimens of the salt which have stood for a long time at −33°C. or which have been prepared at room temperatures.

The evidence so far obtained does not enable one to distinguish between the two structures of 141, the second of which contains divalent carbon, and is therefore a derivative of ammonocarbonous acid. Perhaps, if the compound is ionic, the two forms of the ion will be in resonance with each other, and it will be meaningless to speak of the structure of the salt (348).

XVIII. ORGANIC COMPOUNDS OF SULFUR

A. Tetraalkylthiodiamines and tetraalkyldithiodiamines

C. K. Clark (99) and G. W. Smith (318) found that the tetraalkyl-thiodiamines and -dithiodiamines of Lengfeld and Stieglitz (246) and of Michaelis (267, 268) are saponified by a liquid ammonia solution of potassium amide, as one might expect in view of the fact that they are the tetraalkyl esters of the ammono acids, $S({=}NH)_2$ and $S_2(N{=}H)_2$ (sulfazylic and thiosulfazylic acids). The decomposition of tetraethylthiodiamine may be represented by the equation

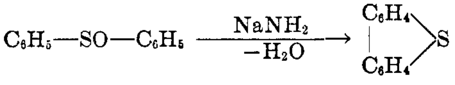
$$S(NEt_2)_2 + 2KNH_2 = S(NHK)_2 + 2Et_2NH \qquad (142)$$

$$Et = C_2H_5$$

The potassium salt of sulfazylic acid, represented on the right hand side of equation 142, decomposes to some extent into nitrogen and potassium sulfide, so it can not be isolated in a pure state. Potassium thiosulfazylate, $S_2(NHK)_2$, is supposedly formed by the saponification of $S_2(NEt_2)_2$ in accordance with type equation 142, but it can not be isolated because of a further reaction with potassium amide, in which nitrogen and potassium monosulfide are formed. Presumably, potassium sulfazylate, $S(NHK)_2$, is an intermediate in this reaction.

B. Sulfoxides

Schönberg (313) refluxed a solution of diphenyl sulfoxide in toluene with sodium amide for six hours. The only product isolated from the resulting reaction mixture was diphenylene sulfide, in a 25 per cent yield. Insofar as the formation of this compound is concerned, the sodium amide has acted only as a dehydrating agent, in the sense of the equation



$$C_6H_5\text{—}SO\text{—}C_6H_5 \xrightarrow[-H_2O]{NaNH_2} \left.\begin{matrix}C_6H_4\\ |\\ C_6H_4\end{matrix}\right\rangle S \qquad (143)$$

Recently, Courtot, Chaix, and Nicolas (107) have reëxamined this reaction and have improved the yield of diphenylene sulfide to 32 per cent. Smaller quantities of diphenyl sulfide, diphenyl disulfide, and the sodium salt of benzenesulfinic acid were also obtained, together with a very small amount of aniline. Courtot, Chaix, and Kelner (106), in discussing the mechanism of this reaction, conclude that the following equation represents the formation of some of the by-products mentioned above.

$$C_6H_5SOC_6H_5 + NaNH_2 = C_6H_5SONa + C_6H_5NH_2 \qquad (143a)$$

The sodium salt of benzenesulfenic acid, C_6H_5SOH, is unstable, and is either oxidized at the expense of the diphenyl sulfoxide to benzenesulfinic acid, or else undergoes disproportionation to the latter and sodium thiophenate, C_6H_5SNa, which in turn may be converted to diphenyl disulfide by the action of atmospheric oxygen. Diphenyl sulfide apparently results from the removal of an atom of oxygen from diphenyl sulfoxide.

Di-*p*-bromophenylsulfoxide and di-*p*-tolylsulfoxide are not dehydrated by sodium amide in the manner of equation 143.

C. Sulfonic acids

Jackson and Wing (228) heated sodium benzenesulfonate with sodium amide in a test tube and obtained about 10 per cent of the amount of aniline theoretically expected from the reaction,

$$C_6H_5SO_2ONa + NaNH_2 = C_6H_5NH_2 \text{ (probably as sodium salt)} + Na_2SO_3 \qquad (144)$$

together with a smaller quantity of diphenylamine. As is well known, phenol is formed when sodium benzenesulfonate is fused with sodium hydroxide.

Sachs, in repeating the work of Jackson and Wing, was able to obtain 30 per cent of the theoretical amount of aniline (300).

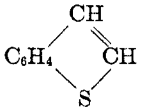
β-Naphthylamine was obtained in 32 per cent yield by heating sodium naphthalene-β-sulfonate with sodium amide and naphthalene at 200°C. Phenol-*p*-sulfonic acid is reported to yield none of the expected *p*-aminophenol under similar conditions (300).

A careful investigation of the action of fused sodium amide on the sodium salt of Schaeffer's Beta Acid (2-naphthol-6-sulfonic acid) in the presence of naphthalene enabled Sachs to obtain as high as 51 per cent of the theoretical amount of 1-amino-6-naphthol. No comment was made concerning the apparent absence of 2-amino-6-naphthol (300). Sodium 2-naphthol-7-sulfonate, fused with naphthalene and sodium amide, is converted to a mixture of aminonaphthols, among which 2-amino-7-naphthol and 1-amino-6-naphthol were identified. The two compounds together were formed in 57 per cent yield (300). Sodium 2-naphthol-8-sulfonate is changed under similar conditions to a mixture of aminonaphthols, the chief constituent of which is 1-amino-6-naphthol (300). Disodium 2-naphthol-1-sulfonate apparently yields only a single product, which was however not identified with any of the known aminonaphthols (300). Sodium 1-naphthol-5- and -8-sulfonates are converted to the expected aminonaphthols (300). Naphtholdisulfonic acids R (2,3,6) and G (2,6,8) gave products of an indefinite nature. Anthraquinone-β-sulfonic acid gave a small yield of anthraquinone, together with an unidentified substance that appeared to be an aminoanthraquinone (300).

The investigations of Sachs indicate that molecular rearrangements may occur in the fusion of the naphtholsulfonic acids with sodium amide. This is not surprising in view of the experiments of Meharg and Allen (258) and of Button (77), who have observed molecular rearrangements in the hydrolysis of the chlorotoluenes with aqueous alkali at high temperatures.

D. *Thionaphthene*

Weissgerber and Kruber (341) have utilized sodium amide in the separation of thionaphthene,



from crude naphthalene, or from the enriched concentrates containing a larger proportion of the sulfur compound. Thionaphthene itself reacts with sodium amide under xylene at temperatures from about 60°C. to 120°C. to form a yellow brown sodium salt, which is decomposed by water with regeneration of the thionaphthene. In order to find out which hydrogen atoms were replaced by sodium in the formation of this salt, an experiment was performed in which 400 grams of thionaphthene was heated at 100–145°C. with 3.75 equivalents of sodium amide under xylene, dry carbon dioxide then being passed through the mixture for some time at 100–110°C. After methylation of the reaction product, approximately equal quantities of the methyl esters of thionaphthene-2-carboxylic acid and thionaphthene-2,3-dicarboxylic acid were obtained, indicating that some disodium thionaphthene was formed under these conditions.

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