Table II

Effect of Added Cyclohexanone

Aliquot	Time, hr.	% I	% II[a]	% V[b]	% IV[c]
1	. . .	3.0	97.0	. . .	. .
2	0.0[d]	7.0	93.0	*ca.* 100	Trace
3	2.8	49.4	50.6	62.3	37.7
4	16.8	84.5	15.5[e]	26.7	73.3
5	24.9	79.9	20.1	15.7	84.3
6	48.0	68.9	31.1	17.1	82.9
7	165.0	40.7	59.3	11.3	88.7

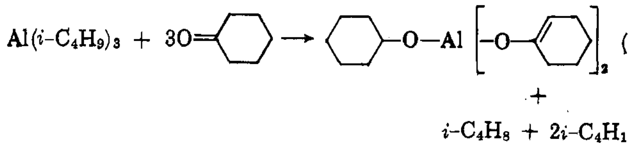
[a] *cis*- + *trans*-II. I and II are normalized to 100%. [b] V = cyclohexanone. [c] IV = cyclohexanol. V + IV are normalized to 100%. [d] Zero time taken as end of cyclohexanone addition. [e] The fourth and subsequent aliquots showed no detectable amount of *trans*-II.

Table III

Variation of C_9/C_6 Ratio

Aliquot	2	3	4	5	6	7
C_9/C_6 ratio[a]	1.3	1.5	1.5	1.9	2.0	3.9

[a] C_9 = I + II; C_6 = cyclohexanone + cyclohexanol. C_9/C_6 was determined by ratio of peak areas.


(4)

reduction of I under similar conditions, nor was any condensation (aldol) product isolated.

Ziegler, *et al.*,[1c] has reported that cyclohexanone forms an enolate with triisobutylaluminum after the initial reduction step, according to equation 4.

During analyses of the compositions of various reduction products, controls and synthetic mixtures were used to test the reliability of the analytical method. The data obtained on analysis of a five-component synthetic mixture are given in Table IV. All analyses were done by gas chromatography using a Carbowax 20M column. Measurement of peak areas was done by the peak-height half-width method.

Table IV

Analysis of a Synthetic Mixture

	% *cis*-II	% *trans*-II[a]	% I	% II[b]	% V[c]	% IV[d]
Theory	63.8	36.2	61.1	38.9	33.2	66.8
Found	64.7	35.3	62.0	38.0	33.0	67.0

[a] *cis*- and *trans*-II are normalized to 100%. [b] *cis*- + *trans*-II. I and II are normalized to 100%. [c] V = cyclohexanone. [d] IV = cyclohexanol. IV + V are normalized to 100%.

Acknowledgment.—The authors would like to express their appreciation to Dr. Ernest L. Eliel for providing samples of *cis*- and *trans*-II and for helpful advice. Also the authors would like to thank the Chemicals Research Division of the Esso Research and Engineering Company for providing the facilities necessary to carry out this work.

The Preparation of Lithium Acetylide·Ethylenediamine

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A procedure has been developed for the preparation and isolation of N-lithioethylenediamine. A thermally stable form of monolithium acetylide has been produced by allowing N-lithioethylenediamine to react with acetylene in a variety of organic solvents. Some physical properties of the resulting lithium acetylide·ethylenediamine complex are given.

In 1898 Moissan[1] prepared monolithium acetylide by adding acetylene to a solution of lithium in liquid ammonia. Although this process has undergone some refinements during the intervening years,[2] it is still the only method used today for preparing monolithium acetylide. A British patent[3] was granted on the preparation of monolithium acetylide by allowing acetylene to react with lithium dispersion in tetrahydrofuran. We were unable to duplicate this work. Attempts to isolate the monolithium acetylide from liquid ammonia have failed because the monolithium acetylide disproportionated to dilithium acetylide and acetylene.[4] The presence of ammonia probably imparted some stability through complex formation. Detection of such a complex has been reported.[4] Removal of this complexing agent led to decomposition.

$$2LiC{\equiv}CH \longrightarrow LiC{\equiv}CLi + HC{\equiv}CH$$

The object of this work was to find a complexing agent which would impart sufficient stability to permit isolation and eliminate the need for liquid ammonia. Ethylenediamine was found to give such a complex. This complex, monolithium acetylide·ethylenediamine can be prepared by the reaction of lithium metal dispersion with ethylenediamine to form N-lithioethylenediamine, followed by the reaction of the N-lithioethylenediamine with acetylene.

$$Li + H_2NCH_2CH_2NH_2 \longrightarrow LiHNCH_2CH_2NH_2 + 0.5H_2$$

$$LiHNCH_2CH_2NH_2 + HC{\equiv}CH \longrightarrow LiC{\equiv}CH{\cdot}H_2NCH_2CH_2NH_2$$

Several references are available in the literature for the preparation of N-lithioethylenediamine by adding lithium metal to refluxing ethylenediamine.[5] No reference is made to its isolation. Isolation is complicated by the high solubility of the lithium salt in ethylenediamine.

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[1] H. Moissan, *Compt. rend.*, **127**, 911 (1898).

[2] K. N. Campbell and B. K. Campbell, *Proc. Indiana Acad. Sci.*, **50**, 123 (1940).

[3] Badische Anilin- and Soda-Fabrik Akt.-Ges., British Patent 771,708 (April 3, 1957).

[4] M. Corbellini and L. Turner, *Chim. Ind.* (Milan), **42**, 251 (1950); *Chem. Abstr.*, **54**, 19250 (1960).

[5] (a) L. Reggel, R. A. Friedel, and I. Wender, *J. Org. Chem.*, **22**, 891 (1957); (b) L. Reggel, S. Friedman, and I. Wender, *ibid.*, **23**, 1136 (1958); (c) L. Reggel, J. P. Henry, and I. Wender, *ibid.*, **26**, 1837 (1961); B. S. Tyagi, B. B. Ghatge, and S. C. Bhattacharyya, *ibid.*, **27**, 1430 (1962).

Aliphatic hydrocarbons can be used as solvents for the preparation of N-lithioethylenediamine since they are completely inert to the system and since the product is insoluble. However, since the solubility of ethylenediamine in aliphatic hydrocarbons is very low near room temperature, and since lithium metal floats and ethylenediamine sinks, vigorous stirring is required to maintain contact between the two. The reaction proceeds slowly below 70–80° and becomes very fast above 85°. Yields in excess of 90% are obtained in five hours.

In aromatic hydrocarbons, ethylenediamine is completely miscible and reaction proceeds readily even at room temperature. In benzene at reflux, reaction is very rapid and nearly quantitative yields of very pure material are obtained in about an hour. However, the rate of hydrogen evolution is drastically reduced. Vapor phase chromatography and infrared spectra showed that cyclohexene was formed in yields as high as 95% based on the lithium metal when benzene was the solvent. This intermediate reduction of the benzene facilitates the formation of N-lithioethylenediamine.[6]

Although the reaction of lithium metal dispersion with ethylenediamine proved to be the method of choice for preparing N-lithioethylenediamine, it is possible to use other lithiating agents to obtain the same product. Others tested include lithium nitride, lithium hydride, lithium amide, and *n*-butyllithium.

The reaction between N-lithioethylenediamine and acetylene was studied in detail. A sample of N-lithioethylenediamine was suspended in dioxane, and acetylene was bubbled through the slurry. Acetylene was absorbed and heat was evolved. When one-half mole of acetylene was absorbed, the reaction stopped. Analysis of the product showed it to be dilithium acetylide. When the addition of acetylene was continued beyond this point for an extended period of time, heat was evolved and another one-half mole of acetylene was absorbed with renewed vigor. The product in this case consisted of colorless crystals whose analysis indicated the structure $LiC{\equiv}CH \cdot H_2NCH_2CH_2NH_2$. The initiation of this further reaction can be very difficult without the presence of seed crystals. In subsequent runs, the crystalline material could always be obtained by seeding the reaction at the half-way point.

In order to determine the reaction path, a seeded run was interrupted several times during the course of a reaction and an aliquot removed and analyzed. The results are tabulated in Table I.

TABLE I

PRODUCTS OF THE REACTION BETWEEN N-LITHIOETHYLENEDIAMINE AND ACETYLENE IN 1,4-DIOXANE AT 25°

% C_2H_2 absorbed	% $LiHNCH_2$-CH_2NH_2	% Li_2C_2	% $LiC_2H \cdot$-$H_2NCH_2CH_2NH_2$
0	100	0	0
27	58	42	0
53	0	100	0
62	0	63	37
83	0	20	80
100	0	0	96

The data in Table I indicate the reaction sequence shown.

$$2LiHNCH_2CH_2NH_2 + HC{\equiv}CH \longrightarrow LiC{\equiv}CLi + 2H_2NCH_2CH_2NH_2 \quad (1)$$

$$LiC{\equiv}CLi + HC{\equiv}CH + 2H_2NCH_2CH_2NH_2 \longrightarrow 2LiC{\equiv}CH \cdot H_2NCH_2CH_2NH_2 \quad (2)$$

This is consistent with the results obtained. Reaction 1, of course, represents several reactions. It is not certain at this time just what they are, but the reactions indicated by the following two equations are likely.

$$LiHNCH_2CH_2NH_2 + HC{\equiv}CH \longrightarrow LiC{\equiv}CH \cdot H_2NCH_2CH_2NH_2 \quad (3)$$

$$LiC{\equiv}CH \cdot H_2NCH_2CH_2NH_2 + LiHNCH_2CH_2NH_2 \longrightarrow LiC{\equiv}CLi + 2H_2NCH_2CH_2NH_2 \quad (4)$$

In order to check equation 4, equivalent amounts of monolithium acetylide·ethylenediamine and N-lithioethylenediamine were placed together in benzene at room temperature. The reaction was followed analytically and was found to be proceeding slowly as written.

Interestingly, by forming the ethylenediamine complex of monolithium acetylide it has not only been possible to prevent the disproportionation of monolithium acetylide to dilithium acetylide at room temperature, but this disproportionation reaction can actually be reversed. When dilithium acetylide (obtained by the reaction between *n*-butyllithium and acetylene) was placed in dioxane with two moles of ethylenediamine and acetylene was passed into the seeded slurry, lithium acetylide·ethylenediamine was isolated.

The effect of reaction temperature on the product of reaction of N-lithioethylenediamine and acetylene was studied. Results are shown in Fig. 1.

The reaction between N-lithioethylenediamine and acetylene was carried out in a variety of solvents (1,4-dioxane, tetrahydrofuran, diethyl ether, diethylcarbitol, 1,2-dimethoxyethane, *n*-butylamine, di-*n*-butylamine, tri-*n*-butylamine, pyridine, ethylenediamine, benzene, xylene, heptane, and hexane). The reaction also was run neat. Good yields were obtained in every case.

Lithium acetylide·ethylenediamine is a white-to-light tan crystalline solid. The crystals are octahedral and, although they are normally less than one

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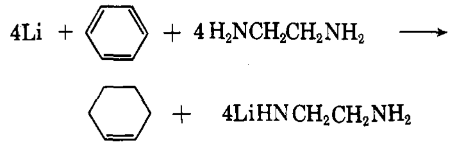
[6] In a paper concerning reductions with lithium in ethylenediamine, Reggel, *et al.* (ref. 5a), point out that benzene can be reduced to cyclohexene and cyclohexane in a solution of lithium in ethylenediamine. It also is pointed out that there is a competition between direct amide formation and the reduction reaction. Above 85° a vigorous reaction takes place with the evolution of a considerable amount of hydrogen.

In studying the formation of N-lithioethylenediamine, we confirmed these results. The competing reactions appear to be the following.

$$Li + H_2NCH_2CH_2NH_2 \longrightarrow LiHNCH_2CH_2NH_2 + 0.5H_2 \quad (A)$$



(B)

Above 85° reaction A becomes very fast and considerable direct amide formation takes place. Our system refluxes at about 80° and gives nearly quantitative reduction (reaction B). Direct amide formation also is minimized by the fact that free ethylenediamine is kept to a minimum. In contrast to the work cited where ethylenediamine is the solvent and, therefore, is present in large excess, the ethylenediamine was added as it reacted while the hydrocarbon was in excess. The net result of the two factors favoring reduction over direct amide formation is a yield of 85–95% based on lithium metal in contrast to a yield of 51% cyclohexene and 1.4% cyclohexane based on benzene using a fourfold excess of lithium over benzene. No cyclohexane was detected in our work.

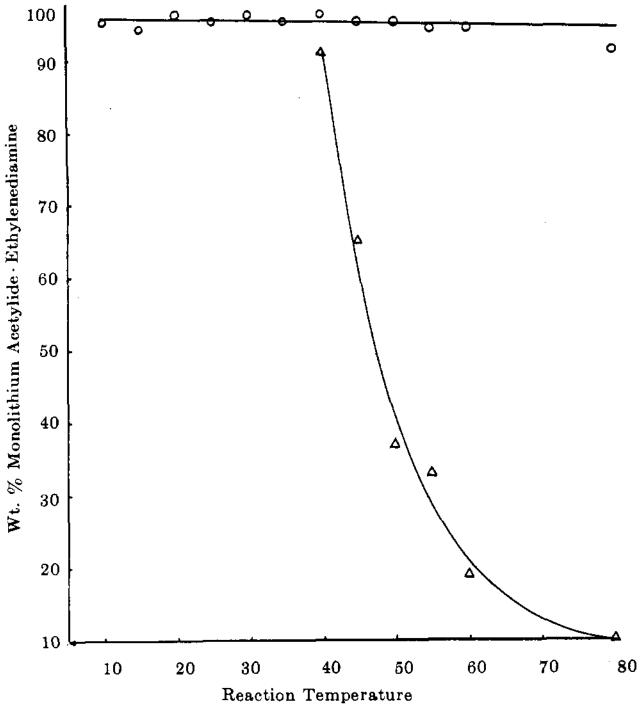


Fig. 1.—Effect of reaction temperature on formation of monolithium acetylide·ethylenediamine in dioxane: ○ —, brought to 25° under acetylene after reaction was complete at given temperature; Δ —, brought to 25° under argon after the reaction was complete at given temperature.

millimeter across as they are formed in the foregoing reaction, crystals up to two centimeters have been grown. On standing in the light they slowly darken in color. This discoloration is accelerated by the presence of free ethylenediamine. Samples have been stored at room temperature for six months, with negligible decomposition.

Contact with water causes vigorous evolution of acetylene. However, addition of the complex to water or the addition of water to it has never resulted in a fire. On exposure to the atmosphere, a slow reaction occurs with moisture, oxygen, and carbon dioxide. Although there is no hazard, exposure results in a loss of activity.

Repeated blows with a hammer could not induce detonation. Even when ignited with a match the complex burned with a low red flame.

In a closed system it is thermally stable up to about 45°. Above 45° it decomposes slowly to dilithium acetylide, acetylene, and ethylenediamine. It also decomposed under vacuum giving the same products. In twenty-four hours at one-millimeter pressure, a sample was decomposed 42% at 25° and 56% at 40°.

Solubility was checked in a number of organic solvents. Table II gives the results of these tests. Interestingly, there is some solubility in all but the aliphatic hydrocarbons. Even N,N-dimethylformamide and N,N-dimethylacetamide are suitable solvents as reaction media if reaction is carried out below room temperature and contact time is held to a minimum.

This new, stable form of lithium acetylide should be a welcome addition to anyone interested in ethynylation reactions. It can easily be obtained solvent-free and is storage stable. A wide variety of solvents is available as a reaction medium, and preliminary application studies show that it is possible to obtain high yields from both coupling reactions with alkyl chlorides and bromides, and carbonyl reactions with ketones. Some reactions utilizing this new ethynylating agent will be described in subsequent publications.

Table II

Solubility of Monolithium Acetylide·Ethylenediamine in Various Solvents

	25°, g./100 g. of solvent	40°, g./100 g. of solvent
Hexane	0.00	0.00
Heptane	0.00	0.00
Benzene	0.08	0.20
Toluene	0.02	0.06
Xylene	0.04	0.04
Diethyl ether	0.05	...
Tetrahydrofuran	0.4	0.4
1,4-Dioxane	0.6	1.6
n-Propylamine	17.0	19.5
n-Butylamine	12.1	14.3
Di-*n*-butylamine	0.03	0.03
Tri-*n*-butylamine	0.6	0.4
Pyridine	5.4	9.2
Ethylenediamine	130.0	32.0
Dimethyl sulfoxide	50.0	49.0
N,N-Dimethylformamide	Reacts slowly	
N,N-Dimethylacetamide	Reacts slowly	

Experimental

General.—The lithium metal powder was obtained by filtering a lithium dispersion (75 μ) in mineral oil, washing with hexane, and drying under argon.

Ethylenediamine (98%) was used as obtained. Acetylene (welding grade) was purified by passage through columns containing activated alumina. All solvents were dried over sodium wire unless otherwise stated. All reactions were carried out under argon atmospheres.

Preparation and Isolation of N-Lithioethylenediamine.—A 1-l., three-necked flask, equipped with a dropping funnel, oil-cooled condenser, crescent-blade stirrer, electric stirring motor, and thermometer, served as the reactor. A glass "T" above the condenser served as a means for argon cover and as an exit for escaping gases.

Lithium metal powder (2.0 moles) was placed in the reactor and was followed by benzene (400 ml.). After stirring had been initiated, ethylenediamine (2.0 moles) was added dropwise over a period of 1 hr. The temperature rose quickly to reflux during the addition and was maintained at reflux by gentle heating for 2 hr. after the addition was complete.

After cooling to room temperature, the resultant white slurry was transferred under an argon atmosphere to a large double-cone filter which had been thoroughly flushed with argon. Filtration was facilitated by a small argon pressure. The product was washed several times with hexane and dried by argon passage.

The resultant white, free-flowing crystalline solid was recovered in 97% yield; assay, 99% $LiNHCH_2CH_2NH_2$, 0.2% free lithium metal.

Detection of Cyclohexene.—The filtrate from the previous preparation was saved. A few milliliters of water were added to decompose dissolved N-lithioethylenediamine. After filtration and separation of the water layer, the benzene layer was dried over calcium chloride, weight 240 g.

The liquid was chromatographed through a Fisher-Gulf partitioner (Model #11-130) containing tri-*m*-cresyl phosphate packing (85°; 0.005-ml. sample; 30 ml. He/min., carrier gas; peaks, 18, 28 min.; calibrated against cyclohexene, 18 min., and benzene, 28 min.). A peak at 18 min. represented 15.3% of the total weight. The yield of cyclohexene is 90% based on lithium.

Conversion of N-Lithioethylenediamine to Lithium Acetylide·Ethylenediamine in Various Solvents.—The apparatus was the same as that used in the N-lithioethylenediamine preparation, except that the dropping funnel was replaced by an acetylene inlet tube and rotameter.

N-Lithioethylenediamine (2.8 moles) was placed in the reactor followed by 1,4-dioxane (700 ml.). Vigorous stirring was initiated, and acetylene (3.0 moles) was introduced over a period of 1 hr. The temperature was maintained at 25° by external cooling. The reaction was seeded at 50% acetylene absorption.

The resultant slurry was poured into a 2-l. resin-type filtering funnel containing 1 l. of hexane, to precipitate the product. Filtration was facilitated by a small argon pressure. The product was washed with pentane and dried by argon passage. The resultant off-white, free-flowing, crystalline solid was recovered in 95% yield; assay, 95% $LiC_2H \cdot NH_2CH_2CH_2NH_2$.

The general procedure as described, using 1,4-dioxane, was carried out using a wide variety of ether, amine, and hydrocarbon solvents. In cases of high solubility it was necessary to use a larger proportion of hexane. Some product was still lost with some amine type solvents.

Conversion of N-Lithioethylenediamine to Lithium Acetylide·Ethylenediamine without Solvent.—A 500-ml., two-necked stainless steel flask equipped with a gas inlet attachment and thermometer served as the reactor. A pressure-relief regulator was attached to the gas inlet attachment (set at 0.5 p.s.i.g.). The reactor was thoroughly flushed with argon.

N-Lithioethylenediamine (0.4 mole) and seeds were placed in the reactor. Acetylene was introduced into the system, and the flask was shaken by hand to supply agitation. The temperature increased rapidly, but there was negligible pressure within the reactor for several minutes. When the pressure built up to 0.5 p.s.i.g., it was maintained for 10 min., and then the thermometer was loosened to vent any hydrogen produced by free lithium metal and ethylenediamine. This procedure was continued two more times, and then the reactor was subjected to a 0.5-p.s.i.g. acetylene pressure for 3 days; yield, 94% $LiC_2H \cdot NH_2CH_2CH_2NH_2$.

Reaction between N-Lithioethylenediamine and Monolithium Acetylide·Ethylenediamine.—Monolithium acetylide·ethylenediamine (0.54 mole) was placed in a reactor followed by benzene (200 ml.). Vigorous stirring was initiated and N-lithioethylenediamine (0.54 mole) was added. There was no exothermic effect. The slurry was stirred at room temperature for 5 hr., filtered, washed with ether, and dried under argon.

A purple solid was obtained (30 g.). It was found to contain only dilithium acetylide and ethylenediamine.

Conversion of Dilithium Acetylide to Monolithium Acetylide·Ethylenediamine.—Dilithium acetylide (0.6 mole) was placed in a reactor followed by 1,4-dioxane (300 ml.). Ethylenediamine (1.2 moles) was added dropwise with stirring. Acetylene (0.9 mole) was introduced over a period of 1 hr., the temperature being maintained at 25° by external cooling.

At completion, an equal volume of hexane was added. The resultant white slurry was filtered and dried; yield, 95%; assay, 96% $LiC_2H \cdot NH_2CH_2CH_2NH_2$.

Conversion of N-Lithioethylenediamine to Lithium Acetylide·Ethylenediamine at Various Temperatures.—N-Lithioethylenediamine (2.8 moles) was placed in the reactor followed by 1,4-dioxane (700 ml.). Vigorous stirring was initiated and acetylene was introduced. The temperature was maintained at the desired temperature by external cooling. When the heat effect was complete, the desired temperature was maintained for an additional 30 min. to ensure complete reaction.

A small sample was removed under an argon atmosphere, filtered, washed with diethyl ether to remove occluded ethylenediamine, and dried under a slight argon pressure. The per cents of dilithium acetylide and monolithium acetylide·ethylenediamine were then determined.

The reaction temperature was brought to 25° under acetylene and maintained at this temperature by external cooling until the final reaction was complete. A small sample was removed and treated as previously described.

Solubility.—Solubility tests were carried out in 40-ml. glass test tubes containing Viton A stoppers. Excess monolithium acetylide·ethylenediamine was placed in each tube along with the desired solvent in an argon atmosphere. Each sample was thoroughly shaken and allowed to remain at the given temperature for 24 hr. Clear samples were removed by means of a hypodermic syringe, weighed, hydrolyzed, and the lithium determined by spectrophotometry. In the few cases where clear samples could not be obtained directly, it was necessary to centrifuge and replace them in the desired bath for several additional hours. The weight of monolithium acetylide·ethylenediamine was calculated from the lithium present.

All amine solvents with the exception of ethylenediamine were dried over potassium hydroxide. Ethylenediamine, dimethyl sulfoxide, N,N-dimethylformamide, and N,N-dimethylacetamide were used as obtained. Tetrahydrofuran was distilled from lithium aluminum hydride.

Analytical Procedure for N-Lithioethylenediamine. A. Introduction.—The quantity of unchanged free lithium metal was determined by measurement of the hydrogen evolved upon hydrolysis of a weighed sample. Ethylenediamine and lithium were determined by acid–base titration. The total basicity was first determined by titration with standard hydrochloric acid to pH 3.90. Upon addition of cupric ions the ethylenediamine formed a complex and in so doing released two moles of hydrochloric acid per mole of ethylenediamine. Titration with standard sodium hydroxide to pH 5.25 determined the ethylenediamine. Lithium was determined by the difference between the total base titration and the ethylenediamine titration. It was necessary to run blanks on each titration.

Any lithium hydroxide which may have been present was determined independently by a modified Karl Fischer titration in anhydrous methanol, glacial acetic acid being added to react with the ethylenediamine.[7]

B. Procedure.—A 250-ml., three-necked flask equipped with a magnetic stirrer, thermometer, single bubble trap, and glass stopper served as a controlled-hydrolysis reactor. A 100-ml. pressure equalizing gas buret was attached to the reactor above the single bubble trap by means of a three-way stopcock, the third arm of which permitted a means of venting the system. The apparatus was flushed with argon. Water (15 ml.), which had previously been saturated with hydrogen, was placed in the reactor and allowed to equilibrate by stirring with the stopcock in the venting position.

A sample (0.2–0.3 g.) in a gelatin capsule was placed in the reactor and the stopcock set in the gas buret position. When hydrolysis was complete, time was allowed for the solution to return to room temperature (t). The increase in volume (v) was directly proportional to the free lithium content.

$$\%\text{ free Li} = \frac{v}{22{,}400} \cdot \frac{(p - p')}{760} \cdot \frac{273}{273 + t} \cdot \frac{1388}{W}$$

where p = atmospheric pressure, mm.
p' = vapor pressure of water at given temperature t, mm.
W = sample weight in grams

The reactor was removed and its contents washed into a 400-ml. beaker with about 50 ml. of distilled water. The solution was titrated with standard 0.1 N hydrochloric acid to pH 3.90 with the aid of a pH meter. Copper nitrate solution (15 ml., 1.5 g. $Cu(NO_3)_2 \cdot 3H_2O$) was added. The freed hydrochloric acid was titrated with standard 0.1 N sodium hydroxide to pH 5.25.

The hydroxide blank, B_h, was determined by placing 50 ml. of distilled water and 50.00 ml. of standard sodium hydroxide in a clean 400-ml. beaker and titrating with standard hydrochloric acid to pH 3.90. Copper nitrate solution (10 ml.) was added and the resulting solution titrated to pH 5.25 to obtain the ethylenediamine blank, B_E.

$$B_h = \text{ml. HCl} - 50.00\,\frac{(\text{normality NaOH})}{(\text{normality HCl})}$$

$$B_E = \text{ml. NaOH}$$

$$\%\text{ N-Lithioethylenediamine} = [(\text{ml. HCl} - B_h)\,(\text{normality HCl}) - \frac{(\text{ml. NaOH} - B_E)}{2}\,\frac{(\text{normality NaOH})}{(\text{normality HCl})} - L_h]\,\frac{6604}{W}$$

where L_h = moles lithium as lithium hydroxide

Analytical Procedure for Monolithium Acetylide·Ethylenediamine. A. Introduction.—An analytical procedure was developed for the determination of monolithium acetylide·ethylenediamine, dilithium acetylide, N-lithioethylenediamine, lithium hydroxide, and free ethylenediamine in the presence of each other.

When monolithium acetylide·ethylenediamine was heated at 125° for 24 hr. under a reduced pressure of 1 mm., it quantitatively decomposed to dilithium acetylide, acetylene, and ethyl-

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(7) J. Mitchell, Jr., and D. M. Smith, "Aquametry," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 127, 249.

enediamine. Therefore, the variation of acetylene obtained upon hydrolysis of a given material with respect to lithium before and after this decomposition treatment is a direct measure of the monolithium acetylide·ethylenediamine content. Definitions follow.

A = moles acetylene initially per mole of lithium
A_f = moles acetylene present after decomposition per mole of lithium
L = moles lithium present in initial sample
L_f = moles lithium present in decomposed sample
a = moles dilithium acetylide per mole of lithium
b = moles monolithium acetylide·ethylenediamine per mole of lithium

$$A/L = a + b \qquad b = 2(A/L - A_f/L_f)$$

$$A_f/L_f = a + \frac{b}{2} \qquad a = (A/L - b)$$

B. Procedure.—The apparatus employed was the same as that used in the N-lithioethylenediamine determination. After thoroughly flushing the apparatus with argon, water (15 ml.), which had been previously saturated with acetylene, was placed in the reactor and allowed to equilibrate. A sample (about 0.35 g. in a gelatin capsule) was hydrolyzed and the volume increase (v), room temperature (t), and atmospheric pressure (p) were noted.

$$\text{moles acetylene} = \frac{v}{22{,}030} \cdot \frac{(p - p')}{760} \cdot \frac{273}{263 + t}$$

Ethylenediamine and total lithium were determined on the aforementioned solution as described under procedure for N-lithioethylenediamine.

$$\text{moles ethylenediamine} = E = \frac{(\text{ml. NaOH} - B_E)}{2000} \times \frac{(\text{normality NaOH})}{(\text{normality HCl})}$$

$$\text{total moles lithium} = L = \frac{(\text{ml. HCl} - B_h)}{1000} (\text{normality HCl}) - E$$

A sample was decomposed in a vacuum desiccator at 125° for 24 hr. at 1 mm. Samples (0.14 g.) of the resulting material were taken and analyzed as before for moles acetylene, A_f, and moles lithium, L_f.

$$\%\ \text{monolithium acetylide}\cdot\text{ethylenediamine} = \frac{9207\,bL}{W}$$

$$\%\ \text{dilithium acetylide} = \frac{3800\,aL}{W}$$

$$\%\ \text{N-lithioethylenediamine} = \frac{6604\,(L - 2aL - bL - L_h)}{\text{W}}$$

$$\%\ \text{ethylenediamine} = \frac{6010\,[E - (L - 2aL - L_h)]}{W}$$

where L_h = moles lithium hydroxide
E = moles ethylenediamine

Lithium hydroxide was determined independently by the same method used for its determination in N-lithioethylenediamine.

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Amine Exchange Reactions. Mannich Bases from Primary Aliphatic Amines and from Amino Acids[1]

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The exchange reaction between tertiary Mannich bases (I) and primary alkylamines has been shown to give the monosubstituted secondary Mannich bases (II), and the nonavailability of the latter by the normal Mannich reaction is accounted for by their instability to base, including the basic group in the same molecule. The exchange reaction has been further extended by the use of amino acids as the primary alkylamines and makes readily available the amino acid Mannich bases of type V, of possible application for N-terminal labeling of peptides.

The Mannich condensation between ketones, formaldehyde, and secondary alkylamines affords tertiary Mannich bases of type I.[3]

The reaction using primary alkylamines is more complicated since the first-formed product (II) can react further with the ketone and formaldehyde to give a bis-Mannich base (III). Considerable disagreement exists in the literature with regard to the actual products obtained in the reaction between ketones, formaldehyde, and primary alkylamines. Mannich and Heilner[4] report the preparation of bis(β-benzoylethyl)methylamine (IIIa) ,as well as β-methylaminopropiophenone (IIa) from the condensation between acetophenone, formaldehyde, and methylamine hydrochloride in the molar ratio 2:2:1. Blicke and Burckhalter[5] obtained the same products (IIIa and IIa) using equivalent amounts of the three reagents. Mannich and Heilner[4] found that steam distillation converted IIIa to IIa, while treatment of IIa with alkali[5] led to IIIa, also formed by reaction of phenyl vinyl ketone with methylamine. Warnat[6] reported yet a third product, N-methyl-3-benzoyl-4-hydroxy-4-phenylpiperidine (IVa); this work was confirmed by Mannich and Hieronimus.[7] Plati and Wenner[8] have shown that the product isolated and assumed by Blicke and Burckhalter[5] to be the bis-Mannich base (IIIa) was in fact the substituted piperidine (IVa) obtained by Warnat. Plati and Wenner[8] suggest that this piperidine derivative is not a primary product of the Mannich reaction, but is formed from the bis-Mannich base (IIIa) *via* an internal Claisen reaction brought about by the action of alkali used in the isolation procedure by the previous

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