refluxing ethanol) and 3 ml of methyl isocyanate (3.1 g, 0.054 mole). The bottle was sealed, heated for 0.5 hr on a steam bath, cooled for 1 hr, and then opened. The solution had turned a deep red, and a gas evolved. Water was added slowly, causing a further evolution of gas and the precipitation of a yellow solid. The solid was filtered and recrystallized from 50% ethanol to give yellow needles, mp 160° dec.

Anal. Calcd for $C_{12}H_{10}N_2O_3$: C, 62.60; H, 4.33; N, 12.17. Found: C, 62.87; H, 5.03; N, 13.08; also C, 63.36; H, 4.60; N, 9.38.

The infrared spectrum showed the following bands, which received the indicated assignments: 2.98 (ms) and 3.03 (sh), NH stretching; 3.43 (w) and 3.51 (sh), CH_3 stretching in NCH_3; 5.83 (s), C=O in carbamate; 6.04 (s), C=O in conjugation; 6.70 (s), C=C; 8.17 (s), C—O—C in carbamate; 10.46 (vs) μ, N—O stretching band in the oxime. The nmr spectrum (DMSO-d_6 solution) showed a doublet at 169.5 (J = 4.5 Hz) due to CH_3NH, an AB pattern (J = 10.6 Hz; ω_A = 404.5 Hz, ω_B = 480.0 Hz) due to protons on the quinone ring, and a complex absorption from 450 to 515 Hz due to the aromatic protons on the other ring.

Methylation of 2-Formylcyclohexanone.—About 63 ml of a solution of CH_2N_2 in ethyl ether (20 mg/ml) was added to 3.0 g (neat) of 2-formylcyclohexanone at 0°. The solution was allowed to warm gradually to 15°. Most of the ether was flash evaporated.

The nmr spectrum showed a 1:2:1 triplet at 423 Hz with a line separation of 2.2 Hz due to —(CH_2—)C=C(O—)H; it also showed two peaks for aldehydic protons (608 and 520 Hz), the cyclohexane proton peaks, and normal peaks for residual ethyl ether and OCH_3.

Attempted Carbamylation of Acetylacetone.—In a 125-ml conical flask were mixed 2.5 g (0.025 mole) of acetylacetone, 0.5 ml of pyridine, and 7.8 ml (0.027 mole) of 20% methyl isocyanate in ether. The mixture was shaken and allowed to stand at room temperature. After 6 days the nmr spectra of the solution indicated that only a trace of product, if any, was formed.

Registry No.—**2**, 13866-74-5; **4**, 13970-40-6; **6**, 13866-63-2; **7**, 13866-64-3; **8**, 5819-21-6; **9**, 10369-95-6; **10**, 13866-67-6; methyl isocyanate, 624-83-9.

Acknowledgments.—The authors wish to thank Joseph N. Damico for obtaining the mass spectral data, Nicholas Duy for obtaining the nmr data, and George Yip for preparing the CH_2N_2 solution.

Conversions of Certain Amides into Nitriles by Means of *n*-Butyllithium[1]

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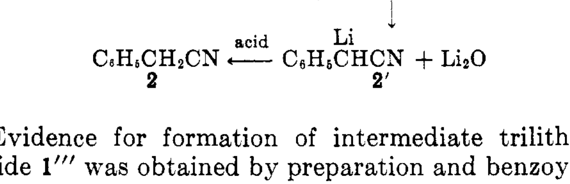
Phenyl- and diphenylacetamides were converted readily into the corresponding nitriles in good yields by means of three mole equivalents of *n*-butyllithium in inert solvents. The mechanism presumably involves β elimination of lithium oxide from an intermediate trilithioamide. However, *n*-heptamide afforded nitrile in ony a fair yield and benzamide in only trace amounts. Phenylacetamide was converted into nitrile in fair yield by lithium aluminum hydride, but potassium amide and lithium amide failed to effect the reaction.

It is well-known that amides can be dehydrated readily to form nitriles by means of acidic reagents[2] or by a combination of an acidic reagent and an amine such as tosyl chloride and pyridine.[3]

Although certain amides have been converted to nitriles with basic reagents, special procedures and/or relatively drastic conditions appear to have been employed. Some examples have involved benzamide with lithium aluminum hydride,[4,5] heptamide and benzamide with sodium hydroxide or potassium hydroxide (pyrolysis of sodio or potassio salt),[6] 2-methoxy-3-naphthamide with methylmagnesium iodide,[7] trimethylacetamide with *t*-butylmagnesium chloride in refluxing ether (16 hr),[8] and some hindered amides such as mesitamide with sodium hydroxide in refluxing ethylene glycol.[9]

It has now been found that phenyl- and diphenylacetamides can be converted readily to the corresponding nitriles by means of *n*-butyllithium which functions as a very strong base. Thus, phenylacetamide (**1**) reacted with 3 mol equiv of this reagent in tetrahydrofuran (THF)–hexane or ether–hexane to give phenylacetonitrile in good yield (45–77%). Presumably, **1** was trilithiated to form trilithioamide **1‴**, which decomposed to produce lithiophenylacetonitrile (**2′**) and lithium oxide (Scheme I).[10]

SCHEME I



$$C_6H_5CH_2CONH_2 \ (\mathbf{1}) \xrightarrow[\text{THF–hexane or ether–hexane}]{3LiC_4H_9} C_6H_5\overset{Li}{C}H—\overset{OLi}{C}=N—Li \ (\mathbf{1'''}) \longrightarrow C_6H_5\overset{Li}{C}HCN \ (\mathbf{2'}) + Li_2O \xrightarrow{\text{acid}} C_6H_5CH_2CN \ (\mathbf{2})$$

Evidence for formation of intermediate trilithioamide **1‴** was obtained by preparation and benzoylation of trilithioamide **1‴** at −80° to form the N-benzoyl derivative **3** and the dibenzoyl derivative **4** in yields of 30 and 14%, respectively (Scheme II).[10]

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[1] Supported by the Army Research Office (Durham) and by the National Science Foundation. A preliminary communication has appeared: E. M. Kaiser, R. L. Vaulx and C. R. Hauser, *Tetrahedron Letters*, **40**, 4833 (1966).

[2] D. T. Mowry, *Chem. Rev.*, **42**, 257 (1948).

[3] C. R. Stevens, E. J. Bianco, and F. J. Pilgrim, *J. Am. Chem. Soc.*, **77**, 1701 (1955).

[4] M. S. Newman and T. Fukunaga, *ibid.* **82**, 693 (1960).

[5] (a) W. G. Brown, *Org. Reactions*, **6**, 484 (1955). The special conditions required for this reaction, which were not reported in detail in the original paper,[4] involved addition of 19 mmoles of a standardized 0.26 *M* solution of lithium aluminum hydride in THF to a solution of 5.0 mmoles of benzamide in THF at 30-35° during 90 min, gradual heating to reflux during 30 min, and final refluxing for 4 hr. (b) However, only spectroscopic amounts of the nitrile were obtained when the lithium aluminum hydride solution was added at 0-5°, and the reaction mixture was stirred at this temperature for several hours and then refluxed for 4 hr (Private communication from Dr. T. Fukunaga).

[6] See F. W. Bergestrom and W. C. Fernelius, *Chem. Rev.*, **12**, 133 (1933).

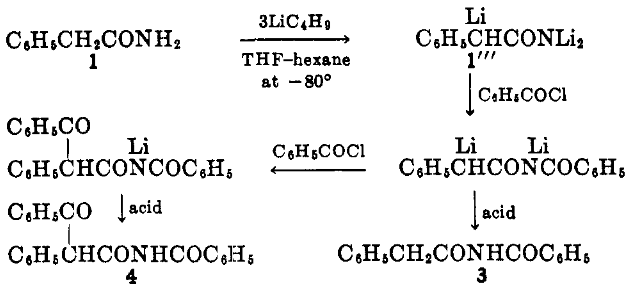
[7] K. Fries and K. Schimmelschmidt, *Ber.*, **B58**, 2835 (1925).

[8] F C. Whitmore, C. I. Noll, and V. C. Meunier, *J. Am. Chem. Soc.*, **61**, 683 (1939).

[9] L. Tsai, T. Miwa and M. S. Newman, *ibid.*, **79**, 2530 (1957).

[10] For convenience, mono- di-, and trilithio salts are designated by prime, double prime, and triple prime, respectively.

SCHEME II



Although the combined yield of the two products **3** and **4** was only 44%, this result is considered satisfactory as 43% of the starting phenylacetamide was recovered giving a material balance of 87%. Since none of the α-benzoyl derivative of phenylacetamide was found, the N,α-dibenzoyl derivative **4** probably arose through further benzoylation of the dilithio salt of the N-benzoyl derivative as indicated in Scheme II. The observed preferential N-benzoylation of trilithioamide **1‴** was anticipated as the doubly charged nitrogen of **1‴** was expected to be more nucleophilic than the singly charged α carbon.

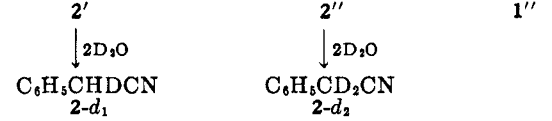
Further evidence for intermediate trilithioamide **1‴** in the conversion of phenylacetamide to lithiophenylacetonitrile (see Scheme I) was obtained from deuteration at −80° to form trideuterioamide **1-d_3** (eq 1).[11]

$$\underset{\mathbf{1}}{C_6H_5CH_2CONH_2} \xrightarrow[2.\ D_2O]{1.\ 3LiC_4H_9(-80°)} \underset{\mathbf{1\text{-}d_3}}{C_6H_5CHDCOND_2} \qquad (1)$$

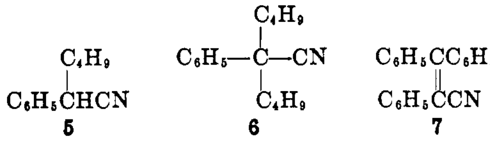
Structure **1-d_3** was supported by the absorption spectra. Its nmr spectrum exhibited chemical shifts due to aromatic and benzyl protons in the ratio 5.0:1.078 indicating the presence of 0.922 benzyl deuterium atoms per molecule. Its mass spectrum contained fragments ascribed to the molecular ion of **1-d_3** and to the N,N-dideuterocarboxamido ion (see Experimental Section).

As indicated in Scheme I, the decomposition of trilithioamide **1‴** is considered to form the lithionitrile **2′**, from which the free nitrile **2** is liberated on acidification. That **2′** was present in the reaction mixture was shown by deuteration to afford monodeuteronitrile **2-d_1** and dideuteronitrile **2-d_2**; the latter presumably arose through equilibration of **2′** with trilithioamide **1‴** to form dilithionitrile **2″**[12] and dilithioamide **1″** (Scheme III).[10,13]

SCHEME III

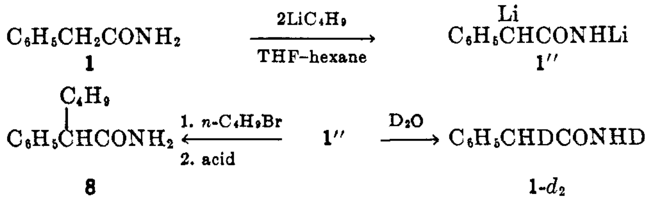


Further support for mono- and dilithionitriles **2′** and **2″** (see Scheme III) was obtained by alkylation with n-butyl bromide to give mono- and dibutyl derivatives **5** and **6**, respectively; also, condensation with benzophenone afforded unsaturated adduct **7**.



The triionization of phenylacetamide to form trilithioamide **1‴** (see Scheme I) evidently involved primary ionization of an amido hydrogen, secondary ionization of an α hydrogen, and tertiary ionization of the second amido hydrogen. The instability of the trilithio salt **1‴** is to be contrasted with the relative stabilities of the di- and monolithiophenylacetamides. Thus, whereas **1‴** decomposed to the lithionitrile **2′** even at 0°, the dilithioamide **1″** was n-butylated even at 25-30° to afford the α derivative **8** in 87% yield; also, **1″** was deuterated at 0° to give the dideuterioamide **1-d_2** (Scheme IV).

SCHEME IV

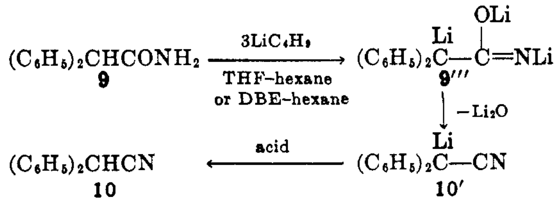


Structure **1-d_2** was supported by absorption spectra. Its nmr spectrum showed chemical shifts due to aromatic and benzylic protons in the ratio of 5.0:1.1 indicating the presence of 0.9 benzyl deuterium atoms per molecule. Its mass spectrum contained a fragment ascribed to the molecular ion of **1-d_2**, but none that was attributable to **1-d_3** or to the N,N-dideuteriocarboxamido ion (see Scheme IV).

It should be mentioned that the monolithioamide, presumably $C_6H_5CH_2CONHLi$, failed to undergo α deuteration, α n-butylation, or α or N benzoylation; most of the phenylacetamide was usually recovered.

Similarly, diphenylacetamide (**9**) underwent dehydration with 3 mol equiv of n-butyllithium in THF-hexane or di-n-butyl ether (DBE)-hexane to form diphenylacetonitrile (**10**); presumably, trilithioamide **9‴** was an intermediate (Scheme V).[10]

SCHEME V



Evidently, the intermediate trilithioamide **9‴** decomposed less readily than trilithioamide **1‴**. Thus, the yield of nitrile was only 26% (compared to the

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[11] An attempt to effect tetraionization of the second α hydrogen under similar conditions was unsuccessful; thus, treatment of phenylacetamide with 4 mol equiv of the reagent followed by 4 mol equiv of deuterium oxide introduced only about as much deuterium as 3 equiv.

[12] See E. M. Kaiser and C. R. Hauser, *J. Am. Chem. Soc.*, **88**, 2348 (1966).

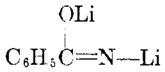
[13] Higher yields of nitrile were obtained when slightly more than 3 mol equiv of n-butyllithium were used; conversion of monolithionitrile **2′** to dilithionitrile **2″** may have been effected also by the excess reagent.

77% yield of nitrile 2) when the reaction mixture in THF–hexane was refluxed for 20 min. However, the yield of **10** was 62% when the reaction was effected in DBE–hexane.

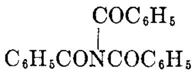
That the trilithioamide **9‴** was formed with 3 equiv of the reagent (see Scheme V) was supported by deuteration to give **9**-d_3; also, the dilithio salt, prepared by means of 2 equiv of the reagent, was deuterated to produce **9**-d_2 (see Experimental Section).

$(C_6H_5)_2CDCOND_2$ **9**-d_3 $(C_6H_5)_2CDCONHD$ **9**-d_2

Although phenyl- and diphenylacetamides were converted by *n*-butyllithium to nitriles in good yields, *n*-heptamide afforded nitrile in only 21% yield, and benzamide no appreciable nitrile, under similar conditions (see Experimental Sections); yet benzamide was readily converted by this reagent to dilithio salt **11″**, as evidenced by dibenzoylation with benzoyl chloride to form triamide **12**.


$C_6H_5\overset{OLi}{\overset{|}{C}}=N-Li$

11′


$C_6H_5CO\overset{COC_6H_5}{\overset{|}{N}}COC_6H_5$

12

Obviously, dilithioamide **11″** of benzamide is much more stable than trilithioamides **1‴** and **9‴** of phenyl- and diphenylacetamides, respectively. Also, the dilithioamide **11″**, which arose from mono- and diionizations of amido hydrogens, is to be distinguished from the dilithioamides of phenyl- and diphenylacetamides, for example, **1″**, which was formed through primary ionization of an amido hydrogen and secondary ionization of an α hydrogen.

Like *n*-butyllithium, lithium aluminum hydride was observed to convert phenylacetamide to phenylacetonitrile; however, the yield was only 31% which is less than half that (72–77%) obtained with *n*-butyllithium under similar conditions. Moreover, lithium aluminum hydride was unsatisfactory with benzamide under the usual conditions (see Experimental Section).

Finally, in contrast to *n*-butyllithium (or lithium aluminum hydride), alkali amides were found incapable of converting phenylacetamide to phenylacetonitrile. Thus, none of the nitrile was obtained with 3 mol equiv of lithium amide or potassium amide in liquid ammonia or refluxing THF (3 hr), and most of the phenylacetamide was recovered. Alkali amides, however, can convert phenylacetamide to its dialkali salt, as evidenced by alkylation at the α carbon.[14]

Discussion

The trilithiation of phenyl- and diphenylacetamides appear to be the first examples of such a triionization of an amide, which evidently requires a stronger base than an alkali amide. The success of this novel triionization by *n*-butyllithium, and also that of the diionization, seems to be dependent on an initial deactivation of the carbonyl group through primary ionization of an amido hydrogen, since a free carbonyl group usually undergoes an addition reaction with the organolithium reagent. For example, N,N-dimethylbenzamide, which has no amido hydrogen, reacts with *n*-butyllithium to afford valerophenone.[15]

The mechanism of the decomposition of the trilithioamides, for example, that of **1‴** to form the lithionitrile **2′**, presumably involves β elimination of lithium oxide as indicated in Scheme I. The similar β elimination of lithium oxide from intermediate **11″** was suggested by Newman and Fukunago[4] to account for their observed conversion of benzamide to benzonitrile by lithium aluminum hydride under special conditions.

Since trilithioamides **1‴** and **9‴** (of phenyl- and diphenylacetamides, respectively) decomposed much more readily than dilithioamide **11″** of benzamide, the presence of the negative charge on the α carbon apparently facilitates β elimination of the lithium oxide. The greater ease of decomposition of trilithioamide **1‴** than trilithioamide **9‴** seems attributable to less delocalization of the negative charge, which may be distributed in one phenyl group in **1‴** but in two phenyl groups in **9‴**. On this basis, the trilithio salt of a purely aliphatic amide, such as that of *n*-heptamide, should be expected to decompose even more readily than that (**1‴**) of phenylacetamide. Since *n*-heptamide was converted less readily to nitrile, its α hydrogen was either not ionized or was ionized very slowly.

The present basic method of dehydration of amides should be preferable in certain cases to the more common acidic methods, especially when the amide contains a group susceptible to attack by an acid. Recently, the *n*-butyllithium method was found useful in connection with the preparation of some pure α-alkylphenylacetonitriles which were obtained through decomposition of intermediate trilithio-α-alkylphenylacetamides.[16]

Experimental Section[17]

Trilithiation of Phenylacetamide (1) with *n*-Butyllithium to Form Trilithioamide 1‴. Decomposition to Form Phenylacetonitrile. A. In THF–Hexane.—To a stirred suspension of 6.75 g (0.05 mole) of phenylacetamide in 101.4 ml of anhydrous THF, under nitrogen at room temperature (25–30°), was added during 7–8 min, 101.4 ml (0.1625 mole)[18] of a solution of 1.6 *M* *n*-butyllithium in hexane.[19] The first equivalent of the reagent produced a voluminous white precipitate, which dissolved on adding the second equivalent to afford a yellow solution; addition of the third equivalent caused the color to become yellow-orange. Sufficient heat was evolved spontaneously during addition of the reagent to cause the medium to reflux (64°), but the temperature decreased to 25–30° within 30 min. After standing at this temperature for 30 min longer, the reaction mixture was cooled in an ice bath, and acidified with 100 ml of 3 *N* hydrochloric acid (dropwise addition with stirring). The two layers were separated and the aqueous layer was extracted with three 50-ml portions of ether. The combined extracts were dried (calcium sulfate) and concentrated. Distillation *in vacuo* afforded 4.2 g (72%) of phenylacetonitrile, bp 102–104° (11.5 mm), lit.[20] bp 234° (760 mm). The infrared spectrum of

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[14] See, for example, R. B. Meyer and C. R. Hauser, *J. Org. Chem.*, **26**, 3696 (1961).

[15] See W. H. Puterbaugh and C. R. Hauser, *ibid.*, **29**, 853 (1964).

[16] E. M. Kaiser and C. R. Hauser, *ibid.*, **31**, 3873 (1966).

[17] Melting points were taken on a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were determined with Perkin-Elmer Infracords, Models 137 and 237, with potassium bromide disks or nujol mulls. Nmr spectra were obtained with a Varian Associates A-60 spectrometer using trifluoroacetic acid as the solvent and tetramethylsilane as the internal standard. Mass spectra were determined on a Bendix time-of-flight Model 14 spectrometer.

[18] This is a 10% excess over the 3 equiv required for trilithiation. The use of just 3 equiv gave a slightly lower yield.

[19] Supplied by the Foote Mineral Co., Exton, Pa.

[20] "Tables for Identification of Organic Compounds," The Chemical Rubber Co., Cleveland, Ohio, 1964, p 266.

this product as well as the vpc retention time (10-ft silicone gum rubber column at 200°) was identical with that of an authentic sample.

When the reaction mixture was refluxed for 20 min (after the 7–8 min addition of the reagent), the yield of nitrile was 77%.

When the suspension of phenylacetamide in THF–hexane was cooled in an ice bath and the cooled reagent added during the 7–8 min, the temperature rose to 44°; the reaction mixture was neutralized immediately to give the nitrile in 55% yield. The yield was 33% when the starting temperature was about $-5°$ and the reagent added so slowly (58 min) that the temperature did not rise.

B. In Diethyl Ether–Hexane.—*n*-Butyllithium (101.4 ml, 0.1625 mole) in hexane[19] was added to a suspension of 6.75 g (0.05 mole) of phenylacetamide in 101.4 ml of anhydrous ethyl ether essentially as described above using THF as cosolvent. The solvent refluxed spontaneously. After 1 hr, the reaction mixture was worked up to afford 2.65 g (45%) of phenylacetonitrile. A similar reaction in which the mixture was refluxed for 3 hr produced this nitrile in 53% yield.

Benzoylation of Trilithioamide 1''' to Form 4.—Phenylacetamide (6.75 g, 0.05 mole), suspended in 101.4 ml of anhydrous THF at $-80°$ under nitrogen, was treated with 101.4 ml (0.1625 mole) of 1.6 *M* *n*-butyllithium in hexane[19] added during 30 min. After 1 hr, the clear yellow solution was treated with a solution of 22.8 g (0.1625 mole) of benzoyl chloride in 50 ml of THF added during 40 min. The resulting clear orange solution was stirred for 2 hr at $-80°$ and the cold bath was then removed. After 3 hr, the resulting yellow suspension was treated with 100 ml of water. The layers were separated and the aqueous layer was extracted with three 50-ml portions of ethyl ether. The combined extracts were dried (calcium sulfate) and the solvent was then removed to afford an oil. Crystals soon formed which were separated from the oil and recrystallized from absolute ethanol to afford 2.25 g (14%) of α,N-dibenzoylphenylacetamide (**4**), mp 210–211°. The infrared spectrum contained bands due to N–H at 3310 cm^{-1} and to carbonyl moieties at 1710 and 1670 cm^{-1}. In addition, this spectrum contained a band at 1250 cm^{-1} presumably due to carbonyl absorption from a ketone. The compound exhibited chemical shifts in the nmr at δ 6.93 (complex multiplet, aromatic) and at 6.03 (singlet, aliphatic hydrogen adjacent to two carbonyl moieties and phenyl) in the calculated ratio of 15:1.

Anal. Calcd for $C_{22}H_{17}NO_3$: C, 76.96; H, 4.95; N, 4.08. Found: C, 76.79; H, 5.00; N, 4.08.

In addition, the above recrystallization afforded 3.55 g (30%) of a second product, N-benzoylphenylacetamide (**3**), mp 133.5–135°, lit.[21] mp 129–130°. The infrared spectrum of this compound contained bands due to N–H at 3100, and to carbonyl at 1725 cm^{-1}. The compound exhibited chemical shifts in the nmr at δ 7.52 (singlet, aromatic) and at 4.13 (singlet, benzylic) in the calculated ratio of 5:1.

Finally, the initial oil above was dissolved in benzene and chromatographed on Merck Reagent alumina to afford 2.9 g (43%) of recovered phenylacetamide, mp, mmp 158–159°.

Deuteration of Trilithioamide 1'''.—Phenylacetamide (6.75 g, 0.05 mole) suspended in 101.4 ml of anhydrous THF was treated at $-80°$ (Dry Ice–acetone bath) under nitrogen, with 101.4 ml (0.1625 mole) of 1.6 *M* *n*-butyllithium in hexane[19] at a rate (33 min) sufficient to maintain the reaction mixture at this temperature. After 5 min more, the reaction mixture was treated during 4 min with a solution of 3.1 ml (0.17 mole) of deuterium oxide[22] in 22 ml of THF; the temperature rose to $-65°$. The resulting white suspension was stirred for 5 min, allowed to warm to room temperature, and the solid was collected under suction. Extraction of this solid with ethyl ether in a Soxhlet extractor afforded 6.17 g of deuterated phenylacetamide, mp 159–160°. This compound exhibited chemical shifts in the nmr at δ 7.37 (singlet, aromatic) and 3.82 (singlet, benzylic) in the ratio of 5.0:1.078 indicating the presence of 0.922 benzyl deuterium atoms per molecule. Its mass spectrum contained fragments due to *m/e* 138 $[(C_6H_5CHDCOND_2)^+]$ (14% of the base peak), *m/e* 46 $[^+O{\equiv}C{-}ND_2]$ (57.3%), *m/e* 137 $[(C_6H_5CHDCONHD)^+]$ (20.8%), *m/e* 45 $[^+O{\equiv}C{-}NHD]$ (62.9%), and *m/e* 92 $[(C_6H_5CHD)^+]$ (97%).

In a blank experiment, a suspension of 6.75 g (0.05 mole) of phenylacetamide in 101.4 ml each of anhydrous THF and hexane, at $-80°$ under nitrogen, was treated with 3.75 g (0.15 mole) of lithium deuteroxide and 3.1 ml (0.17 mole) of deuterium oxide[22] in 25 ml of THF (added all at once). After 5 min, the reaction mixture was worked up as above to afford 5.88 g of deuterated amide, mp 158–160°. The nmr of this product showed singlets at δ 7.37 and 3.82 in the ratio of 5:2; thus the benzyl protiums did *not* exchange under these conditions. The infrared spectrum, however, showed bands due to N–H at 3300 (broad) and 3225 cm^{-1} (broad), and bands due to N–D at 2510 (shoulder), 2455 (shoulder), 2415 (shoulder), and 2350 cm^{-1} (broad). Thus, some of the amido protium exchanged with deuterium under these conditions.

Decomposition of Trilithioamide 1''' to Form Lithiophenylacetonitrile (2'). A. Deuteration.—To a suspension of 6.75 g (0.05 mole) of phenylacetamide in 93.7 ml of anhydrous THF, under nitrogen at room temperature, was added during 5 min, 93.7 ml (0.15 mole) of 1.6 *M* *n*-butyllithium[19] in hexane. After 1 hr, the reaction mixture was treated with a solution of 2.71 ml (0.15 mole) of deuterium oxide[22] in 21 ml of anhydrous THF (added all at once). The resulting white suspension was filtered under suction. After washing thoroughly with ethyl ether, the solid was discarded. The filtrate and washings were dried (calcium sulfate), concentrated, and distilled to give 3.44 g (60%) of phenylacetonitrile, bp 88–89° (6 mm).[20] The nmr showed a singlet at δ 7.18 (aromatic) and a multiplet at δ 3.42 (benzylic) in the ratio of 5.0:0.477; thus, the product consisted of approximately 50% each of phenylacetonitrile-α-d_1 and phenylacetonitrile-α,α-d_2.

B. *n*-Butylation.—This reaction was effected essentially as described above under A, except that at the end of 1 hr, a solution of 7.19 g (0.0525 mole) of *n*-butyl bromide in 50 ml of THF was added during 5 min. After 3 hr, the reaction mixture was treated with 100 ml of water. The organic layer was dried (calcium sulfate) and the solvent was stripped. Distillation at 70–125° (3 mm) afforded 1.28 g (15%) of 2-phenylhexanenitrile (**5**) and 5.5 g (48%) of 5-cyano-5-phenylnonane (**6**) (by vpc).[23]

C. Condensation with Benzophenone.—Lithiophenylacetonitrile, formed *in situ* as described under A, was treated at room temperature during 12 min with a solution of 14.6 (0.08 mole) of benzophenone in 80 ml of anhydrous ethyl ether. After refluxing for 24 hr, the reaction mixture was worked up as previously described[24] to afford 6.55 g (47%) of α,β-diphenylcinnamonitrile (**7**), mp, mmp 165–166°.

Dilithiation of Phenylacetamide (1) with *n*-Butyllithium. A. *n*-Butylation to Form 8.—A suspension of 6.75 g (0.05 mole) of phenylacetamide in 62.5 ml of anhydrous THF under nitrogen at 0° was treated during 3 min, with 62.5 ml (0.1 mole) of 1.6 *M* *n*-butyllithium in hexane,[19] followed after 5 min by a solution of 6.85 g (0.05 mole) of *n*-butyl bromide in 50 ml of THF added during 5 min. After removing the ice bath, the solution was stirred for 1 hr, then hydrolyzed by the addition of 100 ml of 3 *N* hydrochloric acid. The layers were separated and the aqueous layer was extracted with three 50-ml portions of ether. The combined extracts were dried over magnesium sulfate and the solvent was removed on the rotary evaporator. The resulting crude solid was recrystallized from aqueous ethanol, then from aqueous methanol to afford 8.15 g (86%) of 2-phenylhexanamide (**8**), mp, mmp 97–98° (lit.[14] mp 97.5–98.5°).

Deuteration to Form 1-d_2.—A suspension of 6.75 g (0.05 mole) of phenylacetamide in 62.5 ml of anhydrous THF under nitrogen at 0° was treated, during 2.3 min, with 62.5 ml (0.1 mole) of 1.6 *M* *n*-butyllithium in hexane[19] followed after 5 min by a solution of 2.17 ml (0.12 mole) of deuterium oxide[22] in 23 ml of THF (added all at once). The resulting white precipitate was worked up as above in the deuteration of trilithioamide **1'''** to afford 5.02 g of phenylacetamide, mp 159–160°; more (0.33 g) of this product was obtained by concentration of the combined original filtrate and subsequent washings and extractions. The nmr of this compound showed a singlet at δ 7.37

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[21] H. L. Wheeler, T. B. Johnson, and D. F. McFarland, *J. Am. Chem. Soc.*, **25**, 795 (1903).

[22] Supplied by the Columbia Chemical Co., Columbia, S. C.; minimum isotopic purity, 99.8%.

[23] W. G. Kenyon, E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, **30**, 4135 (1965).

[24] See S. Wawzonek and E M. Smolin, "Organic Syntheses," Coll. Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1963, p 387.

(aromatic) and a singlet at 3.82 (benzylic) in the ratio of 5.0:1.1; thus, the compound contained 0.9 benzyl deuterium atoms per molecule. The mass spectra contained fragments due to *m/e* 137 $[(C_6H_5CHDCONHD)^+]$ (8% of the base peak), *m/e* 45 $[^+O{\equiv}C{-}NHD]$ (5%), *m/e* 136 $[(C_6H_5CHDCONH_2)^+]$ (20%), *m/e* 44 $[^+O{\equiv}C{-}NH_2]$ (13%), and *m/e* 92 $[(C_6H_5CHD)^+]$ (100%).

Preparation and Attempted Reactions of Monolithiophenylacetamide (1′).—N-Lithiophenylacetamide (**1′**) was prepared at an appropriate temperature by adding 34 ml (0.0525 mole) of 1.6 *M* *n*-butyllithium in hexane[19] to a suspension of 6.75 g (0.05 mole) of phenylacetamide in an appropriate amount of THF. The details are given below.

A. Benzoylation.—A suspension of the anion in 101.4 ml of THF at −30° was treated with a solution of 7.025 g (0.05 mole) of benzoyl chloride in 50 ml of THF added during 40 min. After stirring the mixture for 2 hr at −80°, the cold bath was removed and the reaction was then stirred for an additional 3 hr. Subsequent hydrolysis and work-up as above afforded 5.2 g (77%) of phenylacetamide, mp and mmp 158–159°.

B. Butylation.—A suspension of the anion in 62.5 ml of THF at 0° was treated with a solution of 6.85 g (0.05 mole) of *n*-butyl bromide in 50 ml of THF added during 5 min. After removing the cold bath, the reaction was stirred for 1 hr. Subsequent hydrolysis and work-up as above gave none of 2-phenylhexanamide (**8**); there was recovered 5.10 g (76%) of phenylacetamide, mp 158–160°.

C. Deuteration.—A suspension of the anion in 62.5 ml of THF at 0° was treated with a solution of 2.17 ml (0.12 mole) of D_2O[22] in 23 ml of THF (added all at once). The resulting white suspension was worked up as above to afford 4.8 g of phenylacetamide, mp 159–160°. The nmr of this product showed a singlet at δ 7.37 (aromatic) and a singlet at 3.82 (benzylic) in the ratio 5.0:2.0; thus, this compound contained no benzyl deuterium.

Trilithiation of Diphenylacetamide (9) with *n*-Butyllithium to Form Trilithioamide 9‴. Decomposition to Form Diphenylacetonitrile. A. In THF–Hexane.—To a suspension of 10.55 g (0.05 mole) of diphenylacetamide in 101.4 ml of anhydrous THF, was added, during 6 min under nitrogen, 101.4 ml (0.1625) mole of 1.6 *M* *n*-butyllithium in hexane.[19] Addition of the first equivalent of the reagent dissolved the solid to afford an orange solution which quickly turned red, then red-orange. The latter color persisted while the solution was refluxed (65°) for 20 min. After cooling to 0°, the solution was treated with 100 ml of 3 *N* hydrochloric acid; the resulting solid was collected under suction to afford 1.57 g (30%) of recovered amide, mp, mmp 168–169°. The layers of filtrate were separated. The aqueous layer was extracted with three 50-ml portions of ethyl ether, and the combined extracts were dried, then concentrated to give 2.47 g (26%) of diphenylacetonitrile (**10**), mp, mmp 72–73°. The yield was not improved by refluxing for 1 hr before work-up.

B. In DBE–Hexane.—A suspension of 10.55 g (0.05 mole) of diphenylacetamide in 108 ml of anhydrous dibutyl ether upon treatment, under nitrogen at room temperature, with 108 ml (0.1625 mole) of 1.5 *M* *n*-butyllithium in hexane[19] (8 min) generated much heat and produced a dark brown mixture. After 1 hr, the reaction mixture was worked up as above to afford 6.0 g (62%) of diphenylacetonitrile, mp, mmp 72–73.5°.

Deuteration of Trilithioamide 9‴.—Diphenylacetamide (5.28 g, 0.025 mole) was suspended in 54 ml of anhydrous THF under nitrogen at 0° and 54 ml (0.081 mole) of 1.6 *M* *n*-butyllithium in hexane[19] was added during 3 min. After 5 min, the solution was treated with 2.0 ml (0.111 mole) of deuterium oxide[22] in 25 ml of THF (added all at once) to afford a white precipitate. The solid was collected and worked up as described above for the deuteration of phenylacetamide to afford 2.97 g of deuterated diphenylacetamide, mp 167–169°. Its nmr showed singlets at δ 7.35 (aromatic) and 5.19 (benzhydrylic) in the ratio 10:0.097; thus, the compound possessed 0.903 benzhydrylic deuterium atoms per molecule. Its mass spectrum contained fragments due to *m/e* 214 $[(C_6H_5)_2CDCOND_2)^+]$ (3% of the base peak), *m/e* 46 $[^+O{\equiv}C{-}ND_2]$ (18%), *m/e* 213 $[(C_6H_5)_2CDCONHD)^+]$ (9%), *m/e* 45 $[^+O{\equiv}C{-}NHD]$ (64%), and *m/e* 168 $[(C_6H_5)_2C^+D]$ (100%).

Deuteration of Dilithioamide 9″.—This reaction was effected essentially as described above for the deuteration of trilithiophenylacetamide **1‴** using 10.55 g (0.05 mole) of diphenylacetamide, 62.5 ml (0.1 mole) of 1.6 *M* *n*-butyllithium in hexane[19] and 62.5 ml of THF. Deuteration was effected with 2.17 ml (0.12 mole) of deuterium oxide[22] in 23 ml of THF. Upon work-up, 5.36 g of deuterated diphenylacetamide was obtained, mp 167–168°. The nmr showed singlets at δ 7.35 (aromatic) and 5.29 (benzhydrylic) in the ratio 10:0.3; thus, the compound contained 0.7 benzhydrylic deuterium atoms per molecule. The mass spectrum of the product contained fragments due to *m/e* 213 $[(C_6H_5)_2CDCONHD)^+]$ (8% of the base peak), *m/e* 45 $[^+O{\equiv}C{-}NHD]$ (3%), *m/e* 212 $[(C_6H_5)_2CDCONH_2)^+]$ (9%), *m/e* 44 $[^+O{\equiv}C{-}NH_2]$ (3%), and *m/e* 168 $[(C_6H_5)_2{}^+CD]$ (100%).

Conversion of Heptamide to Heptanenitrile.—To a solution of 6.45 g (0.05 mole) of heptamide in 108 ml of anhydrous THF was added 108 ml (0.1625 mole) of 1.5 *M* *n*-butyllithium in hexane[19] as described above. After 1 hr, the mixture was cooled to 0° and hydrolyzed by 100 ml of 3 *N* hydrochloric acid. After the usual work-up, the crude product was vacuum distilled to afford 1.2 g (21%) of heptanenitrile, bp 56–58° (8 mm). The vpc of this material showed one product whose infrared spectrum contained only bands due to aliphatic C—H and to the nitrile moiety. Crystals which formed in the pot were collected and dried to afford 2.0 g (31%) of recovered heptamide, mp, mmp 93–95°.

Dilithiation of Benzamide with *n*-Butyllithium.—To a solution of 6.05 g (0.05 mole) of benzamide dissolved in 70.3 ml of anhydrous THF under nitrogen at room temperature, was added during 6 min, 70.3 ml (0.1125 mole) of 1.6 *M* *n*-butyllithium in hexane[19] to form presumably dilithiobenzamide (**11″**). Addition of the first equivalent of the reagent produced a white precipitate, which turned yellow as the second equivalent was added. After refluxing for 20 min, the reaction mixture was worked up as above to afford only recovered benzamide, mp, mmp 128–129°.

When the reaction was repeated with a 24-hr reflux period before work-up, 0.08 g (2%) of benzonitrile was obtained, bp 68–70° (15 mm), lit.[20] bp 190° (760 mm). The infrared spectrum and vpc retention times agreed with those of an authentic sample.

In another experiment, the THF–hexane was replaced with 2,2′-dimethoxydiethyl ether (diglyme) after 20 min and the resulting mixture was refluxed for 5 hr to give 0.69 g (14%) of benzonitrile, bp 68–70° (15 mm). The remainder of the product consisted of tarry material.

Dilithiobenzamide (**11″**), prepared in THF–hexane as described above and refluxed for 20 min, was benzoylated with 16.1 g (0.1125 mole) of benzoyl chloride dissolved in 50 ml of anhydrous THF (added during 50 min). After refluxing for 5 hr longer, the mixture was cooled to room temperature and treated with 100 ml of water. The layers were separated. The organic layer (with which was combined three etheral extracts of the aqueous layer) was dried and concentrated. The resulting precipitate was recrystallized from absolute ethanol to give 5.91 g (35%) of tribenzamide (**12**), mp 211–212°, lit.[25] mp 207–208°. The infrared spectrum of this product was consistent with the structure assigned.

Similarly, monolithiobenzamide, prepared from 6.05 g (0.05 mole) of benzamide in 31.3 ml of anhydrous THF and 31.3 ml (0.05 mole) of 1.6 *M* *n*-butyllithium in hexane,[19] was treated with 7.025 g (0.05 mole) of benzoyl chloride. The reaction mixture was worked up to give 5.53 g (50%) of dibenzamide, mp, mmp 147–148°; none of the tribenzamide **12** was isolated.

Results with Lithium Aluminum Hydride. A. With Phenylacetamide.—To a suspension of 3.38 g (0.025 mole) of phenylacetamide in 50 ml of anhydrous THF was added during 15 min, a suspension of 0.542 g (0.0143 mole) of lithium aluminum hydride in 100 ml of anhydrous THF. Although much foaming occurred and the color changed to bright yellow, the reaction was not exothermic. The reaction mixture was refluxed for 4 hr during which time it turned light brown. After cooling to 0°, the suspension was treated with 50 ml of water, 100 ml of 15% sodium hydroxide solution, and finally with 100 ml of water. The layers were separated and the aqueous layer was extracted with three 50-ml portions of ethyl ether. The combined extracts were dried (calcium sulfate) and the solvent was removed to afford a liquid. Distillation afforded 0.9 g (31%) of phenylacetonitrile, bp 77–78° (4 mm).[20] The remainder of the product consisted of tarry material.

In another experiment, the suspension of phenylacetamide

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[25] C. Blacher, *Ber.*, **28**, 435 (1895).

and lithium aluminum hydride in THF was refluxed for 20 min before work-up to afford 0.83 g (28%) of phenylacetonitrile and 0.83 g (25%) of recovered phenylacetamide. As before, the remainder of the product consisted of tarry materials.

B. **With Benzamide.**—To a solution of 3.025 g (0.025 mole) of benzamide in 50 ml of anhydrous THF was added, during 8 min, a suspension of 0.361 g (0.0095 mole) of lithium aluminum hydride in 100 ml of THF. Although much foaming occurred, the reaction was only slightly exothermic. The gray suspension was refluxed for 4 hr during which time it lightened in color. Upon cooling to 0°, the reaction mixture was worked up as described in method A. Although the odor of benzonitrile could be detected, the amounts present were insufficient for isolation. Instead, 2.2 g (73%) of benzamide was recovered, mp, mmp 127–129°. A similar result was obtained in another experiment on four times the scale.

Registry No.—**1**, 103-81-1; **$1'$**, 14072-58-3; **$1'''$**, 14072-59-4; **1**-d_2, 14072-60-7; **$2'$**, 6393-50-6; **3**, 14072-62-9; **4**, 14072-63-0; **5**, 3508-98-3; **6**, 3508-99-4; **7**, 6304-33-2; **8**, 14072-67-4; **9**, 4695-13-0; **$9''$**, 14072-69-6; **$9'''$**, 14072-70-9; **10**, 86-29-3; **$11''$**, 14072-71-0; **12**, 602-88-0; *n*-butyllithium, 109-72-8; heptamide, 628-62-6; phenylacetonitrile, 140-29-4; phenylacetonitrile-α-d_1, 14072-73-2; heptanenitrile, 1885-40-1; dibenzamide, 614-28-8; phenylacetonitrile-α,α-d_2, 935-66-0.

The Reaction of Methanesulfinyl Chloride with Water[1a]

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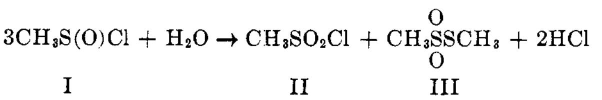
Methanesulfinyl chloride (I) reacts with a limited amount of water (mole ratio 3:1) or deuterium oxide yielding methanesulfonyl chloride (II) and methyl methanethiolsulfonate (III) as the only sulfur-containing products, according to the stoichiometry $3CH_3S(O)Cl + H_2O \rightarrow CH_3SO_2Cl + CH_3SO_2SCH_3 + 2HCl$. Evidence is presented that the reaction may occur by formation of methylsulfinyl methyl sulfone, $CH_3S(O)SO_2CH_3$, which subsequently reacts with unhydrolyzed I. With greater quantites of water (up to I:H_2O = 0.33), although initially large amounts of methanesulfinic acid (IV) are formed, the final products are again II and III with lesser amounts of methanesulfonic acid (V). Although there is a rapid initial hydrolysis of I to form IV, as long as the mole ratio of water to sulfinyl chloride does not exceed 4:1, nmr spectroscopy reveals the presence of sulfinyl chloride in the reaction mixture. Its persistence is apparently due to reaction between hydrogen chloride and the sulfinic acid.

The ease with which methanesulfinyl chloride, $CH_3S(O)Cl$(I), can be prepared by the controlled solvolysis of methylsulfur trichloride[2] or the chlorination of a mixture of methyl disulfide and acetic acid[3] has made this compound readily available.

We have always assumed that I reacts quantitatively with water to form methanesulfinic acid. Titration of its aqueous solutions with sodium hydroxide consumes 2 moles of base/mole of I. Our inability to obtain a satisfactory pmr spectrum of methanesulfinic acid from an equimolar mixture of the sulfinyl chloride and water, however, led to a systematic study of the reaction between I and different stoichiometric quantities of water.

In one case water and methanesulfinyl chloride were mixed in a molar ratio of 1:2.2. On distilling the reaction products, 12% of the initial sulfur was recovered as methanesulfonyl chloride (II), and 70% as methyl methanethiolsulfonate (III). These results suggested that the reaction shown in eq 1 might be taking place.



$$\underset{\text{I}}{3CH_3S(O)Cl} + H_2O \rightarrow \underset{\text{II}}{CH_3SO_2Cl} + \underset{\text{III}}{CH_3\overset{O}{\underset{O}{S}}SCH_3} + 2HCl \qquad (1)$$

The stoichiometry was later confirmed by adding I to water and determining the proton magnetic resonance (pmr) spectrum of the reaction mixture in carbon tetrachloride (CCl_4). Reverse addition of the reactants or the use of D_2O instead of H_2O had no effect upon the relative proportions of II and III.

Further experiments were carried out by mixing larger quantities of D_2O with I and periodically determining the pmr spectra of both the neat solutions and their carbon tetrachloride extracts. Results are given in Table I which contains data obtained by integrating spectra of neat solutions. Since the pmr spectra of the CCl_4 extracts could be run at spectrum amplitudes up to 40 times greater than those of the neat solutions, these were used to detect the presence of methanesulfinyl chloride traces. In all experiments a vigorous exothermic reaction was observed on mixing the reactants. With mixtures of up to 3 moles of D_2O to 1 mole of I, however, even though large quantities of methanesulfinic acid (IV) were initially formed, I was not completely destroyed. The final reaction products were principally II and III with smaller quantities of methanesulfonic acid (V).

With 4 moles of D_2O/mole of I only a faint trace of I could be detected in the reaction mixture. The methanesulfinic acid formed under these conditions remained virtually unchanged after 120 hr.

The unexpected persistence of I in the presence of excess water is believed to be due to an equilibrium reaction (eq 2). The reverse reaction was demonstrated by passing gaseous hydrogen chloride into a solution of IV obtained by saponification of its methyl ester. Extraction of the resulting solution with carbon tetrachloride and pmr analysis clearly demonstrated the presence of I.

$$\underset{\text{I}}{CH_3S(O)Cl} + H_2O \rightleftharpoons \underset{\text{IV}}{CH_3SO_2H} + HCl \qquad (2)$$

The formation of II and III may be explained in two ways, both involving an initial rapid attainment of the equilibrium shown in eq 2. In the first, one may pos-

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[1] (a) Taken in part from a thesis presented by R. V. Norton in partial fulfillment of the requirements of the Ph.D. degree, June 1967. (b) To whom inquiries should be directed.

[2] I. B. Douglass and D. R. Poole, *J. Org. Chem.*, **22**, 536 (1957).

[3] I. B. Douglass, B. S. Farah, and E. G. Thomas, *ibid.*, **26**, 1996 (1961); *Org. Syn.*, **40**, 62 (1960).