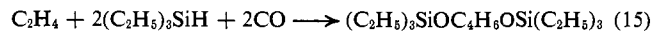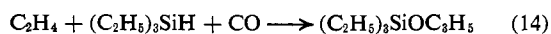very complex, but it was established that, among the reactions occurring between ethylene, triethylsilane, and carbon monoxide, eq 14 and 15 took place. The products of both reactions are unsaturated alkoxysilanes, a number of isomers being possible.

$$C_2H_4 + (C_2H_5)_3SiH + CO \longrightarrow (C_2H_5)_3SiOC_3H_5 \quad (14)$$

$$C_2H_4 + 2(C_2H_5)_3SiH + 2CO \longrightarrow (C_2H_5)_3SiOC_4H_6OSi(C_2H_5)_3 \quad (15)$$

A discussion of all the possible reaction paths would be largely speculative so that only two points will be made. (i) Since no reaction occurred in the absence of olefin, no facile carbon monoxide insertion occurs for silylcobalt carbonyls, unlike the corresponding

alkylcobalt carbonyls. (ii) In view of the above, it seems most probable that the reaction in the presence of olefins occurs by carbon monoxide insertion in an alkylcobalt carbonyl as in the hydroformylation reaction. Reactions 14 and 15 would then be analogous to the hydrosilation reaction but with an additional carbonyl insertion step. The resulting products would then rearrange from α-silyl ketones to unsaturated alkoxysilanes, e.g.

$$(C_2H_5)_3SiCOC_2H_5 \quad \longrightarrow \quad (C_2H_5)SiOC_3H_5$$
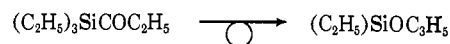
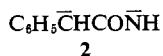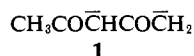The product of reaction 15 could then be formed from further reaction of this olefin.

Formation of 1,3-Dianions of Acetanilide and Related Amides by Means of n-Butyllithium. Condensations with Electrophilic Compounds[1]

Robert L. Gay and Charles R. Hauser

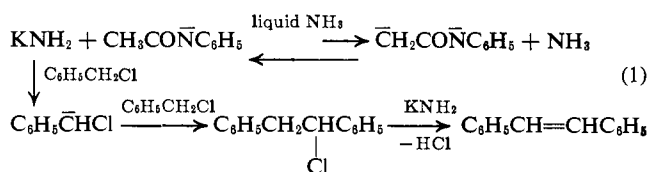Contribution from the Department of Chemistry, Duke University, Durham, North Carolina. Received October 28, 1966

Abstract: The 1,3-dianion of acetanilide, which could not be prepared satisfactorily with potassium amide in liquid ammonia, was made by means of n-butyllithium in an inert solvent and condensed at its α-carbon with various electrophilic compounds. Similarly, several other secondary amides were converted to their 1,3-dianions, which were condensed at their α-carbon with benzophenone. The method appears to be quite general and useful for the synthesis of a number of α-substituted secondary amides.

Many unsymmetrical 1,3-dianions have previously been prepared from appropriate active hydrogen compounds by means of 2 molar equiv of an alkali amide in liquid ammonia and alkylated to form derivatives that are isomeric with the alkyl derivatives of the intermediate monoanions. For example, 1,3-dianions 1 and 2 have been made by this method from acetylacetone[2] and phenylacetamide[3] and benzylated at the terminal position[2b] and at the α-carbon,[3] respectively. Also, other types of condensations at these positions have been realized.[2a,4,5]

$$\text{CH}_3\text{CO}\bar{\text{C}}\text{H}\text{CO}\bar{\text{C}}\text{H}_2 \qquad \text{C}_6\text{H}_5\bar{\text{C}}\text{H}\text{CO}\bar{\text{N}}\text{H}$$
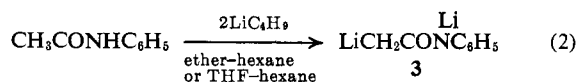$$\mathbf{1} \qquad\qquad\qquad \mathbf{2}$$

The 1,3-dianion of acetanilide, however, could not be formed satisfactorily by this method even though this amide is isomeric with phenylacetamide which is readily converted to dianion 2. Thus, treatment of acetanilide with 2 molar equiv of potassium amide in liquid ammonia followed by 1 molar equiv of benzyl chloride

has afforded stilbene instead of α-benzylacetanilide.[6] This result may be rationalized by eq 1, since benzyl chloride is known to be converted by this reagent to stilbene.[7]

$$\text{KNH}_2 + \text{CH}_3\text{CO}\bar{\text{N}}\text{C}_6\text{H}_5 \xrightarrow{\text{liquid NH}_3} \bar{\text{C}}\text{H}_2\text{CO}\bar{\text{N}}\text{C}_6\text{H}_5 + \text{NH}_3$$

$$\Big\downarrow \text{C}_6\text{H}_5\text{CH}_2\text{Cl} \qquad\qquad\qquad\qquad (1)$$

$$\text{C}_6\text{H}_5\bar{\text{C}}\text{HCl} \xrightarrow{\text{C}_6\text{H}_5\text{CH}_2\text{Cl}} \text{C}_6\text{H}_5\text{CH}_2\text{CH}\text{C}_6\text{H}_5 \xrightarrow[-\text{HCl}]{\text{KNH}_2} \text{C}_6\text{H}_5\text{CH}=\text{CHC}_6\text{H}_5$$
$$\qquad\qquad\qquad\qquad \underset{\text{Cl}}{\big|}$$

We have now found that the 1,3-dianion of acetanilide (3) can be prepared satisfactorily by means of 2 molar equiv of n-butyllithium in ether–hexane or tetrahydrofuran (THF)–hexane (eq 2), as evidenced by condensations at the α-carbon of 3 with various electrophilic compounds (Table I).

$$\text{CH}_3\text{CONHC}_6\text{H}_5 \xrightarrow[\substack{\text{ether–hexane} \\ \text{or THF–hexane}}]{2\text{LiC}_4\text{H}_9} \overset{\text{Li}}{\text{LiCH}_2\text{CO}\bar{\text{N}}\text{C}_6\text{H}_5} \quad (2)$$
$$\mathbf{3}$$

Dilithioamide 3 was alkylated with benzyl chloride to form 4, which was independently synthesized from hydrocinnamoyl chloride and aniline (eq 3).

(1) (a) Supported by the Petroleum Research Fund administered by the American Chemical Society and by the Public Health Service, Research Grant No. CA-04455 from the National Cancer Institute. (b) For a preliminary communication on part of this work, see R. L. Gay, S. Boatman, and C. R. Hauser, Chem. Ind. (London), 1789 (1965).

(2) (a) C. R. Hauser and T. M. Harris, J. Am. Chem. Soc., 80, 6360 (1958); (b) K. G. Hampton, T. M. Harris and C. R. Hauser, J. Org. Chem., 30, 61 (1965).

(3) R. B. Meyer and C. R. Hauser, ibid., 26, 3696 (1961).

(4) R. J. Light and C. R. Hauser, ibid., 25, 538 (1960); R. J. Light and C. R. Hauser, ibid., 26, 1716 (1961).

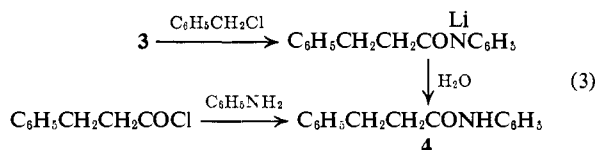(5) E. M. Kaiser and C. R. Hauser, ibid., 31, 3317 (1966).

(6) D. R. Bryant, Ph.D. Thesis, Duke University, 1962; stilbene and its dimer were obtained in yields of 54 and 22%, respectively, and 68% of the starting acetanilide was recovered.

(7) See C. R. Hauser, W. R. Brasen, P. S. Skell, S. W. Kantor, and A. E. Brodhag, J. Am. Chem. Soc., 78, 1653 (1956); D. R. Bryant, S. D. Work, and C. R. Hauser, J. Org. Chem., 29, 236 (1964).

Table I. Yields of Products from Dilithioacetanilide (3) and Electrophilic Compounds in Ether–Hexane and THF–Hexane

| Electrophilic compound | Product | Yield, % | |
		Ether–hexane[a]	THF–hexane[b]
Benzyl chloride	4	69	. .[c]
1,2-Dibromoethane	5a	21	59
1,4-Dibromobutane	5b	22	86
Cyclohexene oxide	6	41	. . .[c]
Carbon dioxide	7	58	37
Benzaldehyde	8	80	86
Benzophenone	10	84	91
Cyclohexanone	13	92	81
Cyclopentanone	14	84	94
Benzonitrile	15	63	74

[a] Effected at 25–35°. [b] Effected at 0–5°. [c] Unsatisfactory result.

$$3 \xrightarrow{C_6H_5CH_2Cl} C_6H_5CH_2CH_2\overset{Li}{CONC_6H_5}$$

$$\downarrow H_2O \quad (3)$$

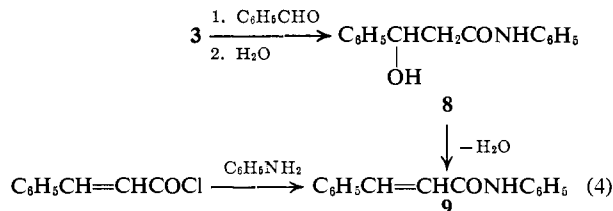$$C_6H_5CH_2CH_2COCl \xrightarrow{C_6H_5NH_2} \underset{4}{C_6H_5CH_2CH_2CONHC_6H_5}$$

Similarly, dilithioamide 3 underwent twofold alkylations with ethylene bromide and 1,4-dibromobutane to give the bis products 5a and 5b, respectively.

$$\underset{\substack{5a, n = 2 \\ b, n = 4}}{C_6H_5NHCOCH_2(CH_2)_nCH_2CONHC_6H_5}$$
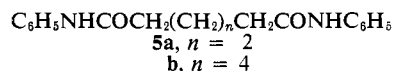
Dilithioamide 3 was condensed with cyclohexene oxide to form hydroxyamide 6 which, presumably, has *trans* orientation with respect to the cyclohexane rings.[8] Dilithioamide 3 was carbonated to afford acid amide 7, which was subsequently decarboxylated to regenerate acetanilide.
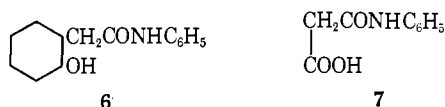

Dilithioamide 3 underwent an addition reaction with benzaldehyde to form β-hydroxyamide 8, which was dehydrated to give cinnamanilide (9), which was independently synthesized from cinnamoyl chloride and aniline (eq 4).
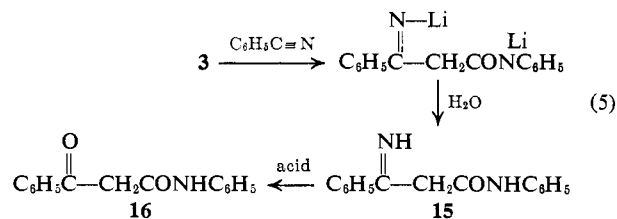
$$3 \xrightarrow[\text{2. H}_2O]{\text{1. C}_6\text{H}_5\text{CHO}} \underset{OH}{C_6H_5CHCH_2CONHC_6H_5}$$

$$8$$

$$\downarrow -H_2O$$

$$C_6H_5CH=CHCOCl \xrightarrow{C_6H_5NH_2} \underset{9}{C_6H_5CH=CHCONHC_6H_5} \quad (4)$$

Similarly, dilithioamide 3 was condensed with benzophenone to form β-hydroxyamide 10, which was dehydrated with hot 20% sulfuric acid to give 11 and cyclized with cold, concentrated sulfuric acid to afford 12. Likewise, 3 was condensed with cyclohexanone and cyclopentanone to produce 13 and 14, respectively.

(8) See (a) J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry," W. A. Benjamin, Inc., New York, N. Y., 1964, p 414; (b) C. C. Price and J. V. Karabinos, *J. Am. Chem. Soc.*, 62, 1159 (1940).
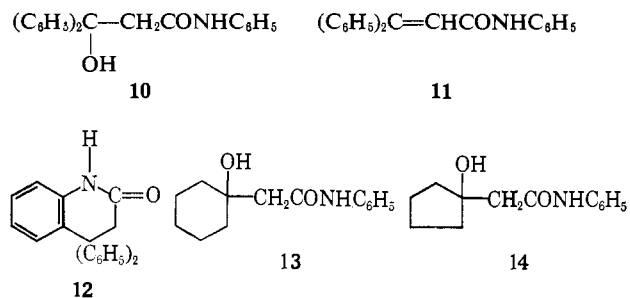
Dilithioamide 3 reacted with benzonitrile to form β-imine amide 15, which was hydrolyzed with dilute hydrochloric acid to give β-keto amide 16 (eq 5). Also

$$3 \xrightarrow{C_6H_5C\equiv N} C_6H_5\overset{N-Li}{\underset{}{C}}-CH_2CON\overset{Li}{C_6H_5}$$

$$\downarrow H_2O \quad (5)$$

$$\underset{16}{C_6H_5\overset{O}{\overset{\|}{C}}-CH_2CONHC_6H_5} \xleftarrow{acid} \underset{15}{C_6H_5\overset{NH}{\overset{\|}{C}}-CH_2CONHC_6H_5}$$
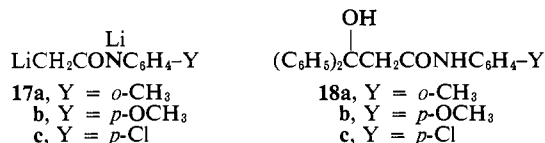
the method was successful with five other secondary amides, which were condensed with benzophenone (Table II). Thus, o-methyl-, p-methoxy-, and p-chloro-

Table II. Yields of Products from Other Secondary Amides and Benzophenone

| Secondary amide | Product | Yield, % | |
		Ether–hexane	THF–hexane
o-Methylacetanilide	17a	94	23
p-Methoxyacetanilide	17b	66	76
p-Chloroacetanilide	17c	48	74
Propionanilide	22	47	71
N-n-Butylacetamide	24	89	. . .[a]

[a] Not attempted.

acetanilides were converted by n-butyllithium to dilithioamides 17a–c, which were condensed with this ketone to form hydroxyamides 18a–c, respectively.

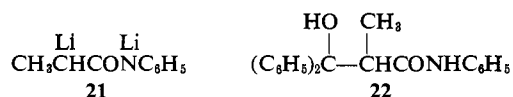$$\underset{\substack{\textbf{17a, Y} = o\text{-CH}_3 \\ \textbf{b, Y} = p\text{-OCH}_3 \\ \textbf{c, Y} = p\text{-Cl}}}{\overset{Li}{LiCH_2CONC_6H_4-Y}} \qquad \underset{\substack{\textbf{18a, Y} = o\text{-CH}_3 \\ \textbf{b, Y} = p\text{-OCH}_3 \\ \textbf{c, Y} = p\text{-Cl}}}{\overset{OH}{(C_6H_5)_2CCH_2CONHC_6H_4-Y}}$$

That o-methylacetanilide was lithiated at an α-hydrogen to form 17a, not an o-methyl hydrogen to lead to hydroxyamide 19, was supported by cyclization of the product with sulfuric acid to afford cyclic amide 20, the infrared spectrum of which was very similar to that of cyclic amide 12.
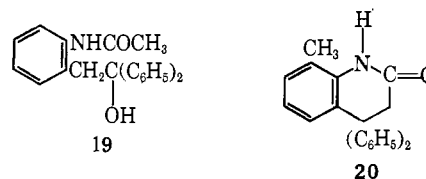

As an example of an anilide of an acid higher than acetic, propionanilide was converted to dilithioamide

21, which was condensed with benzophenone to form hydroxyamide 22.

$$\underset{21}{\underset{\text{Li} \quad \text{Li}}{CH_3CHCONC_6H_5}} \qquad \underset{22}{\underset{\text{HO} \quad CH_3}{(C_6H_5)_2C-CHCONHC_6H_5}}$$

As an example of a purely aliphatic secondary amide, N-n-butylacetamide was converted to dilithioamide 23, which was condensed with benzophenone to afford hydroxyamide 24.

$$\underset{23}{\underset{\text{Li}}{LiCH_2CONC_4H_9\text{-}n}} \qquad \underset{24}{\underset{\text{OH}}{(C_6H_5)_2CCH_2CONHC_4H_9\text{-}n}}$$
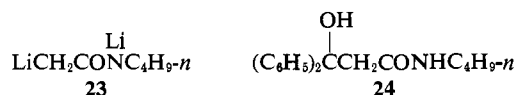
It should be mentioned that N-benzylacetamide has recently been condensed with benzaldehyde by means of n-butyllithium and the resulting hydroxyamide dehydrated, but no yields were reported.[9] However, p-hydroxy- and p-nitroacetanilides and crotonanilide, which is a vinylog of acetanilide, failed to afford satisfactory results on treatment with the reagent followed by benzophenone in THF–hexane under the usual conditions. Possibly the last reaction involved addition of the n-butyllithium to the carbon–carbon double bond, a type of reaction observed with crotonic acid and Ivanov reagents.[10]

Tables I and II show that most of the condensation products were obtained in good to excellent yields (58–94%) by at least one of the two procedures. The yield was better for certain products in ether–hexane, but for certain others in THF–hexane; some of the low yields could probably be improved by further study. The two procedures were equally convenient.

The condensation products from benzaldehyde and benzophenone were obtained apparently in two crystalline modifications, each of which melted rather sharply. A single recrystallization converted the lower melting form to the higher melting one; only the latter, however, was fully characterized (see Experimental Section).

The infrared spectra for the condensation products and their derivatives are summarized in Table III. Because of the dominance of the amido group peaks, the spectra of many of the products resembled those of the starting amides. Although the peaks for the hydroxyl group in the hydroxyamides were difficult to distinguish from those of the amido hydrogen, characteristic peaks for some of the other functional groups were readily detected. Thus, the spectra of 5b, 6, 13, and 14 exhibited peaks near 2926 and 2853 cm^{-1}, presumably arising from enhanced -CH$_2$- absorption;[11] compounds 5b, 6, and 13 showed a peak near 720 cm^{-1} for an aliphatic chain,[12] -(CH$_2$)$_n$- ($n \geq 4$); compound 7 showed a strong peak at 1736 cm^{-1} for a carboxylic acid carbonyl group;[13] compound 16 exhibited a peak at 1689 cm^{-1} for an aryl ketone carbonyl group;[14] and compounds 18a–b and 24 showed peaks for five adjacent free aromatic hydrogens.[15]

Discussion

These preparations of the 1,3-dianions of acetanilide and other secondary amides by means of n-butyllithium represent a significant advance in this field, since these resonance dianions cannot be made with alkali amides which have generally been employed for this purpose. Success in such dianion formation with n-butyllithium appears to be dependent on initial nullification of the carbonyl addition tendency of this reagent through formation of a monolithioamide, for example, 25, which then undergoes secondary ionization of an α-hydrogen with a second molecule of the reagent. Although the detailed mechanism of this secondary ionization has not been established, it may involve coordination of the lithium of the reagent with the nitrogen in the monolithioamide, thereby bringing the potential butyl carbanion in close proximity to the α-hydrogen, as in 26.

$$\underset{25}{\underset{CH_3C-NC_6H_5}{\overset{O|Li}{|}}} \qquad \underset{26}{}$$
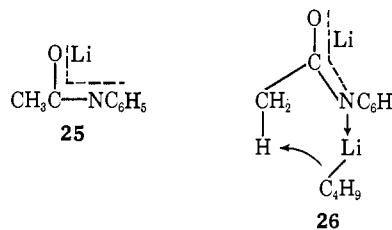
The observed preferential condensation of the electrophilic compound at the α-carbon of dilithioamide 3, rather than at the amido nitrogen, is not surprising since the anion formed by the secondary ionization might be expected to be more nucleophilic. Although further condensation of the electrophilic compound at the amide nitrogen of the resulting monolithio salt was possible, none was observed under the conditions employed.

This method is useful for the synthesis of not only the new products 5b, 6, 13–15, 18c, 22, and 24 but also of certain of the known compounds. Thus, the method is more convenient and produces better yields than earlier methods for β-hydroxyamides 8, 10, 18a, and 18b; 8 was prepared from acetylenic compound 27 and aniline,[16] and 10, 18a, and 18b were made from β-hydroxy ester 28 and the appropriate anilinomagnesium

$$\underset{27}{\underset{OH}{\overset{|}{C_6H_5CHC\equiv COC_2H_5}}} \qquad \underset{28}{\underset{OH}{\overset{|}{(C_6H_5)_2CCH_2COOC_2H_5}}}$$
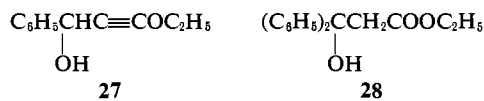
bromides.[17]

The present method could probably be extended not only to other electrophilic compounds but also to other secondary amides and even to certain other types of active hydrogen compounds. It appears to be quite general with amides of type 29 and it may be general with amides of type 30, where R and R' are alkyl or aryl. Since the method is satisfactory with propionanilide (30, R = phenyl, R' = methyl), it would presumably be suitable also with secondary amides of higher aliphatic acids. In contrast, the alkali amide method would probably not be satisfactory for such

$$\underset{29}{CH_3CONHR} \qquad \underset{30}{R'CH_2CONHR}$$

(9) N. S. Narasimhan and H. C. Ranade, Tetrahedron Letters, 46, 4145 (1965); this article appeared after our communication on the present work.[1b]

(10) F. F. Blicke and H. Zinnes, J. Am. Chem. Soc., 77, 4849 (1955).

(11) See L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 15.

(12) See ref 11, p 27.

(13) See ref 11, p 167.

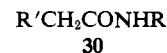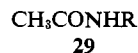(14) See ref 11, p 137.

(15) See ref 11, p 76.

(16) J. C. W. Postma and J. F. Arens, Rec. Trav. Chim., 75, 1377 (1956).

(17) P. A. Petyunin and A. S. Pesis, J. Gen. Chem. USSR, 23, 1033 (1952).

compounds, though it is successful with compounds of type **30** where R' is phenyl.[18]

Experimental Section

Melting points, taken on a Thomas-Hoover capillary melting point apparatus, are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord using samples prepared as potassium bromide pellets; peak positions were corrected relative to a polystyrene film standard. Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer using deuteriochloroform solutions containing tetramethylsilane as an internal standard; spectra were integrated three times, and the average value was used to calculate the relative number of hydrogens associated with each peak. Elemental analyses were performed by Paul Demoen, Janssen, Pharmaceutical Research Laboratories, Beerse, Belgium.

I. Lithiation of Acetanilide and Condensation with Electrophilic Compounds in Ether–Hexane. To a solution of 6.75 g (0.05 mole) of acetanilide in 600 ml of anhydrous ether, stirred under nitrogen at room temperature,[19] was added 69 ml (0.105 mole) of 1.55 M n-butyllithium in hexane[20] during 15 min. The addition of the first equivalent of this reagent caused slight refluxing of the solvent and formation of a white precipitate, which usually redissolved as the second equivalent was added. After stirring for 30 min, the resulting solution was assumed to contain 0.05 mole of dilithioamide **3**. To this stirred solution was added a solution of 0.06 mole of the electrophilic compound (0.025 mole of the methylene halides) in anhydrous ether (50 ml), and the stirring was continued for 30–60 min. The reaction mixture was hydrolyzed with 100 ml of water (stirred 30 min) to give a two-phase solution or suspension, the work-up of which is described below for each electrophilic compound.

A. With Benzyl Chloride. The two layers of the hydrolyzed reaction solution were separated. The organic layer, which was combined with two ethereal extracts of the aqueous layer, was dried over anhydrous magnesium sulfate and concentrated on a rotary evaporator. After cooling in an ice bath, filtration afforded 7.80 g (69%) of hydrocinnamanilide (**4**), mp 91.5–95°, and 97–98.5° after two recrystallizations from ligroin (bp 60–90°) containing a few drops of ethanol; lit.[21] mp 97–98°.

An independent synthesis of **4** was achieved by refluxing 7.5 g (0.05 mole) of hydrocinnamic acid with 7 ml of thionyl chloride in 25 ml of dry benzene for 1 hr. After removing the excess thionyl chloride and benzene, the residue was shaken with 10 ml of aniline and 100 ml of 3 M sodium hydroxide to give, after recrystallization from ligroin–ethanol, 6.72 g (60%) of **4**, mp 96–98°, undepressed on admixture with a sample of **4** obtained as described above. Infrared spectra of the two samples were identical.

B. With 1,2-Dibromoethane. The suspension resulting from the hydrolysis of the reaction mixture was filtered, and the solid was recrystallized from 95% ethanol to afford 1.56 g (21%) of adipanilide (**5a**), mp 229–232°; lit.[22] mp 234–236°.

C. With 1,4-Dibromobutane. The hydrolyzed reaction suspension (obtained after a 135-min condensation period) was filtered. The solid was recrystallized from acetonitrile to afford 1.80 g (22%) of suberanilide (**5b**); mp 186–187.5°.

Anal. Calcd for $C_{20}H_{24}N_2O_4$: C, 74.03; H, 7.46; N, 8.64. Found: C, 74.09; H, 7.43; N, 8.85.

D. With Cyclohexene Oxide. The hydrolyzed reaction suspension was filtered and the solid was recrystallized from acetonitrile to give 4.82 g (41%) of γ-hydroxycyclohexaneacetanilide (**6**), mp 175–177°.

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.03; H, 8.20; N, 6.03. Found: C, 71.93; H, 8.14; N, 6.19.

E. With Carbon Dioxide. This reaction was effected by dropping the solution of dilithioamide **3** from an inverse addition flask into a slurry of powdered Dry Ice (large excess) and anhydrous ether. After the Dry Ice had evaporated, the reaction mixture was shaken with 100 ml of water and acidified with 25 ml of concentrated hydrochloric acid. The two layers were separated and proc-

essed as described above for benzyl chloride to afford 5.16 g (58%) of malonanilic acid (**7**), mp 132.5–134.5°; lit.[23] mp 131–132°.

Decarboxylation of 7 (1.59 g, 0.009 mole) was effected by heating at 140° under nitrogen until gas ceased to be evolved (about 30 min). After cooling, the resulting solid was recrystallized from boiling water to give 0.72 g (60%) of acetanilide, mp 112–114.5°; lit.[24] mp 113–114°.

F. With Benzaldehyde. The hydrolyzed reaction suspension was filtered to afford 7.94 g (65.7%) of crystals, mp 140–143°, which was apparently a lower melting crystalline modification of hydrocinnamanilide (**8**), since one recrystallization from acetonitrile afforded **8**, mp 158–160°. The layers of the filtrate were separated and processed as described above for benzyl chloride to give 1.68 g (13.9%) of **8**, mp 156–158.5°; the total yield of **8** was 80%. Several recrystallizations from acetonitrile raised the melting point to 160–161.5°; lit.[16] mp 162–162.5°.

Dehydration of 8 (2.0 g, 0.0083 mole) was accomplished by dissolving it in 40 ml of cold, concentrated sulfuric acid at 0°. After 30 min, the solution was poured with stirring into 150 ml of ice and water. The insoluble solid was filtered and recrystallized from ethanol–water to give 1.40 g (75%) of cinnamanilide (**9**), mp 146–149°, and at 151–152° after several recrystallizations from acetonitrile; lit.[25] mp 152–154°.

G. With Benzophenone. This reaction was run on a 0.037 M scale. The hydrolyzed reaction suspension was worked up as described above for benzaldehyde to afford 6.01 g (51.2%) of crystals, mp 128.5–130.5°, and 3.80 g (32.4%) of crystals, mp 162–165°, of β-phenylhydracinnamanilide (**10**); the total yield was 84%. A single recrystallization of the lower melting material from acetonitrile produced the higher melting material. After two further recrystallizations from acetonitrile, the product melted at 168–170°; lit.[17] mp 166.5°.

Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.48; H, 6.03; N, 4.41. Found: C, 79.28; H, 5.94; N, 4.64.

Dehydration of 10 (3.0 g, 0.0095 mole) was carried out by refluxing it in 50 ml of 20% sulfuric acid for 24 hr. Cooling and filtration afforded 2.55 g (90%) of β-phenylcinnamanilide (**11**), mp 128–132°, and 132–133.5° after several recrystallizations from anhydrous ether; lit.[26] mp 133.5–134°.

Dehydration and cyclization of 10 (1.96 g, 0.0062 mole) was effected by dissolving it in 25 ml of cold, concentrated sulfuric acid at 0°. After 20 min, the solution was poured into ice and water, and the resulting solid was recrystallized from absolute ethanol to give 1.20 g (65%) of 4,4-diphenyl-3,4-dihydrocarbostyril (**12**), mp 247–248°; lit.[27] mp 242.2–243.5°.

Anal. Calcd for $C_{21}H_{17}NO$: C, 84.28; H, 5.73; N, 4.67. Found: C, 84.13; H, 5.78; N, 4.60.

H. With Cyclohexanone. The hydrolyzed reaction solution was worked up as described above for benzyl chloride (see section I-A) to afford 10.73 g (92%) of β-hydroxycyclohexaneacetanilide (**13**), mp 125–128°, and 128.5–130.5° after several recrystallizations from acetonitrile.

Anal. Calcd for $C_{14}H_{19}NO_2$: 72.04; H, 8.21; N, 6.02. Found: C, 71.81; H, 8.21; N, 6.02.

I. With Cyclopentanone. The hydrolyzed reaction solution was worked up as described above (see I-A) to afford 9.20 g (84%) of β-hydroxycyclopentaneacetanilide (**14**), mp 131–135°, and 136.5–137.5° after several recrystallizations from absolute ethanol.

Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.38. Found: C, 70.90; H, 7.77; N, 6.56.

J. With Benzonitrile. The hydrolyzed reaction solution was worked up as described above (see I-A) to afford 7.45 g (63%) of α-benzimidoylacetanilide (**15**), mp 125–127.5°, and 126.8–128.2° after several recrystallizations from cyclohexane–ethanol.

Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.58; H, 5.92; N, 11.97. Found: C, 75.20; H, 5.91; N, 11.58.

Hydrolysis of 15 was effected by warming a 2-g (0.0084 mole) sample of it with 60 ml of 1 M hydrochloric acid on the steam bath for 10 min. After cooling, the mixture was filtered to afford 2.10 g (100%) of α-benzoylacetanilide (**16**), mp 104–106°; lit.[28] mp 106–106.5°.

(18) S. D. Work, D. R. Bryant, and C. R. Hauser, *J. Org. Chem.*, **29**, 722 (1964).

(19) Because of the limited solubility of acetanilide in ether, lithiation at lower temperatures in this solvent did not seem feasible.

(20) This reagent was used as obtained from Foote Mineral Co., New Johnsonville, Tenn.

(21) G. Natta, P. Pino, and R. Erocoli, *J. Am. Chem. Soc.*, **74**, 4496 (1952).

(22) A. V. Kirsanov and N. L. Egorova, *Zh. Obshch. Khim.*, **23**, 1920 (1953); *Chem. Abstr.*, **49**, 899i (1955).

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(26) J. H. Boyer and M. Sanders, *ibid.*, **26**, 1644 (1961).

(27) P. A. Petyunin and A. S. Pesis, *J. Gen. Chem. USSR*, **22**, 1235 (1952).

(28) C. F. H. Allen and W. J. Humphlett, *Org. Syn.*, **37**, 3 (1957).

II. **Lithiation of Acetanilide and Condensation with Electrophilic Compounds in Tetrahydrofuran (THF)–Hexane.** To a solution of 6.75 g (0.05 mole) of acetanilide in 125 ml of dry THF (freshly distilled from lithium aluminum hydride), stirred under nitrogen at 0–5°, was added 69 ml (0.105 mole) of 1.55 M n-butyllithium in hexane during 15 min. After stirring for 15 min, the clear solution was assumed to contain 0.05 mole of dilithioamide **3**. To this solution was added 0.06 mole of the electrophilic compound (0.025 mole of the methylene halides) in 25 ml of dry THF, and the stirring was continued for 15 min. Water (100 ml) was added to give a two-phase solution or suspension, which was worked up as described below for each electrophilic compound.

A. **With Benzyl Chloride.** The hydrolyzed reaction solution was distilled until most of the THF and hexane had been removed, as evidenced by the temperature of the distillate vapor reaching about 90°. After cooling, the aqueous mixture in the flask was stirred with 200 ml of ether for 1 hr. The two layers were separated and processed essentially as described above under I-A for the corresponding reaction with benzyl chloride. The result was much less satisfactory than that obtained under I-A.

B. **With 1,2-Dibromomethane.** The hydrolyzed reaction suspension was filtered to afford 4.06 g of adipanilide (**5a**), mp 227–229°. The filtrate was distilled until the temperature of the vapors reached about 90°. After cooling, the aqueous mixture in the flask was stirred with 200 ml of ether for 1 hr. The resulting suspension was filtered to give 0.94 g more of **5a**, mp 227–229°. The combined solid was recrystallized from 95% ethanol to give 4.35 g (59%) of **5a**, mp 231–233°.

C. **With 1,4-Dibromobutane.** The hydrolyzed reaction suspension was worked up as described above under II-B to afford 6.94 g (86%) of suberanilide (**5b**), mp 181–185°, and 186.5–187.5° after recrystallization from acetonitrile.

D. **With Cyclohexene Oxide.** The hydrolyzed reaction suspension was worked up as described above under II-B, but none of the desired product was isolated.

E. **With Carbon Dioxide.** This reaction was effected as described under I-E, employing THF instead of ether. After the Dry Ice had evaporated and the water had been added, most of the THF was removed by heating (temperature of the distillate vapors, 80°). The residual liquid was then worked up to give 3.28 g (37%) of maloanilic acid (**7**), mp 131–133°, and a small amount of an unidentified higher melting material.

F. **With Benzaldehyde.** The hydrolyzed reaction solution was heated to remove the THF (temperature of the distillate vapors, 95°). After cooling, the residual liquid was stirred with 200 ml of ether for 30 min and filtered. The solid consisted of 9.73 g (80.7%) of crystals, mp 136.5–138°, which was converted by a single recrystallization from acetonitrile to crystals of **8**, mp 158–160°. More of the latter (total yield, 86%) was isolated from the ethereal layer of the filtrate.

G. **With Benzophenone.** The hydrolyzed reaction solution was worked up as described above under II-F to afford 10.96 g (69.0%) of crystals, mp 128–130°, and 3.43 g (21.5%) of crystals, mp 168–169°, of β-phenylhydracinnamanilide (**10**); the total yield was 91%. One recrystallization of the lower melting material from acetonitrile produced the higher melting material. A mixture of the higher and lower melting crystalline modifications obtained from this reaction melted at 138–143°.

H. **With Cyclohexanone.** The hydrolyzed reaction solution was worked up as described above in II-A to afford 9.41 g (81%) of β-hydroxycyclohexaneacetanilide (**13**), mp 128–132°.

I. **With Cyclopentanone.** The hydrolyzed reaction solution was worked up as described in II-A to give 10.31 g (94%) of β-hydroxycyclopentaneacetanilide (**14**), mp 130–134°.

J. **With Benzonitrile.** The hydrolyzed reaction solution was worked up as described in II-A to give 8.40 g (71%) of α-benzimidoylacetanilide (**15**), mp 125.5–128°.

III. **Lithiation of Other Secondary Amides and Condensation with Benzophenone.** These reactions were effected in ether–hexane and/or in THF–hexane essentially as described in sections I and II,

respectively. The results with the different secondary amides are given below.

A. **With o-Methylacetanilide.** This amide (7.46 g, 0.05 mole) was lithiated in ether–hexane, and the resulting dilithioamide **17a** was treated with 10.95 g (0.06 mole) of benzophenone in 100 ml of dry ether to afford, on hydrolysis and processing (see I-F), 11.90 g (71.8%) of crystals, mp 128–129°, and 3.63 g (21.9%) of crystals, mp 175–177°, of 2′-methyl-β-phenylhydracinnamanilide (**18a**); total yield, 94%. The former modification was converted to the latter (mp 175–177°) by one recrystallization from acetonitrile; lit.[17] mp 167°.

Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.74; H, 6.38; N, 4.23. Found: C, 79.43; H, 6.38; N, 4.37.

When the lithiation and condensation were effected in THF–hexane and the hydrolyzed reaction solution processed as described in II-G, 3.87 g (23%) of **18a**, mp 175–177°, was obtained.

Dehydration and cyclization of 18a (2.0 g, 0.006 mole) was carried out essentially as described above under I-G for **12**. Recrystallization of the resulting solid from ethanol afforded 1.60 g (85%) of 8-methyl-4,4-diphenyl-3,4-dihydrocarbostyril (**20**), mp 197–199°; lit.[27] mp 198.5°.

B. **With p-Methoxyacetanilide.** This amide (8.25 g, 0.05 mole) was lithiated in THF–hexane, and the resulting dilithioamide **17b** was treated with 0.06 mole of benzophenone in 25 ml of dry THF to give, on hydrolysis and processing (see II-F), two crops of solid product. These were combined and recrystallized from acetonitrile to afford 13.21 g (76%) of 4′-methoxy-β-phenylhydracinnamanilide (**18b**), mp 155–158°, and 158–160° after several more recrystallizations; lit.[17] mp 160°.

When this reaction was carried out in ether–hexane (see I-F), 11.51 g (66%) of a lower melting modification of **18b**, mp 126–129°, was obtained; this product was converted to the higher melting form, mp 157–159°, by one recrystallization from acetonitrile.

C. **With p-Chloroacetanilide.** This amide (8.47 g, 0.05 mole) was similarly lithiated in THF–hexane and the resulting dilithioamide **17c** was condensed with 0.06 mole of benzophenone to give on hydrolysis and processing (see II-F) 3.47 g (20%) of crystals, mp 130–132°, and 9.59 g (54%) of crystals, mp 172.5–174°, of 4′-chloro-β-phenylhydracinnamanilide (**18c**); total yield, 74%. The lower melting material was converted to the higher melting material by a single recrystallization from acetonitrile.

Anal. Calcd for $C_{21}H_{18}ClNO_2$: C, 71.71; H, 5.16; N, 3.98. Found: C, 71.46; H, 5.18; N, 4.24.

When the lithiation and condensation were effected in ether–hexane and the hydrolyzed reaction solution was processed as described under I-A, 8.4 g (48%) of crystals, mp 127–134°, was obtained; one recrystallization from acetonitrile converted this product to crystals of **18c**, mp 170–173°.

D. **With Propionanilide.** This amide (7.46 g, 0.05 mole) was lithiated in THF–hexane and the resulting dilithioamide **21** was condensed with 0.06 mole of benzophenone to afford 11.75 g (71%) of α-methyl-β-phenylhydracinnamanilide (**22**), mp 167–172°, and 173–174° after several recrystallizations from 95% ethanol or acetonitrile.

Anal. Calcd for $C_{22}H_{21}NO_2$: C, 79.75; H, 6.38; N, 4.22. Found: C, 79.80; H, 6.37; N, 4.24.

The nmr spectrum of **22** exhibited the following chemical shifts and relative numbers of hydrogens: a doublet ($J = 7$ cps) centered at 1.28 ppm, 2.9 H; a quartet ($J = 7$ cps) centered at 3.52 ppm, 1.1 H; a singlet at 5.28 ppm, 0.9 H; and a multiplet at 6.87–8.00 ppm, 14.9 H. This agrees with the theoretical ratio of 3:1:1:15 for the methyl:methyne:hydroxyl or amido:aromatic (included in which is ether the hydroxyl or amido hydrogen) hydrogens of structure **22**.

E. **With N-n-Butylacetamide.** This amide (5.75 g, 0.05 mole) was lithiated in ether–hexane and condensed with 0.06 mole of benzophenone to give, after hydrolysis and processing (see I-F), 13.24 g (89%) of N-n-butyl-β-phenylhydracinnamanilide (**24**), mp 85–86° (recrystallized from cyclohexane).

Anal. Calcd for $C_{19}H_{23}NO_2$: 76.74; H, 7.79; N, 4.71. Found: C, 76.94; H, 7.85; N, 4.99.