J. Org. Chem. 1983, 48, 4349–4357

Reactions of Primary Amines with Organolithium Compounds[1]

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Received August 16, 1982

Primary amines react under mild conditions with an excess of an organolithium compound to form imines and α-substituted primary amines. Frequently, *N*-alkylimines that result from the condensation of these products are also isolated. For example, reactions of $PhCH_2NH_2$ with RLi (R = *n*-Bu) in refluxing hexane furnish (after hydrolysis) $PhCHRNH_2$, PhRC=O, PhRC=NCHRPh, and $R_2C{=}O$. The organic group of the primary amine can be a primary, secondary, or tertiary alkyl group. A reaction scheme is proposed that has three types of steps: (1) Mono- and dilithiation of the primary amine by an organolithium compound (both lithiations generally at nitrogen). (2) Elimination from the mono- or dilithiated amine of lithium hydride or (when the alkyl group is tertiary) of the elements of an organolithium compound to produce an *N*-lithioimine. (3) Addition of an organolithium compound to the lithioimine to produce a new dilithiated amine. The scheme rationalizes both the structures of the products and the effects of reaction conditions on product composition. Reaction of benzonitrile with an excess of *n*-butyllithium furnishes (after hydrolysis) di-*n*-butyl ketone as the major product. Since this reaction must also proceed through an *N*-lithioimine, formation of this product provides additional evidence for the proposed addition and elimination steps.

In extending a study of reactions of Grignard reagents and unsaturated amines,[3] we have discovered some new reaction chemistry. Reactions of organolithium compounds with some tertiary amines furnished products of addition to the alkene functions,[4] just as had the reactions with Grignard reagents. However, reactions with unsaturated primary amines gave unexpected products. For example, a reaction (eq 1) in which allylamine (1) and

$$\underset{\textbf{1}}{CH_2{=}CHCH_2NH_2} \xrightarrow[2.\ H_2O]{1.\ RLi} \underset{\textbf{2},\ R\ =\ n\text{-Bu}}{RCH_2CH_2(R)C{=}O} \quad (1)$$

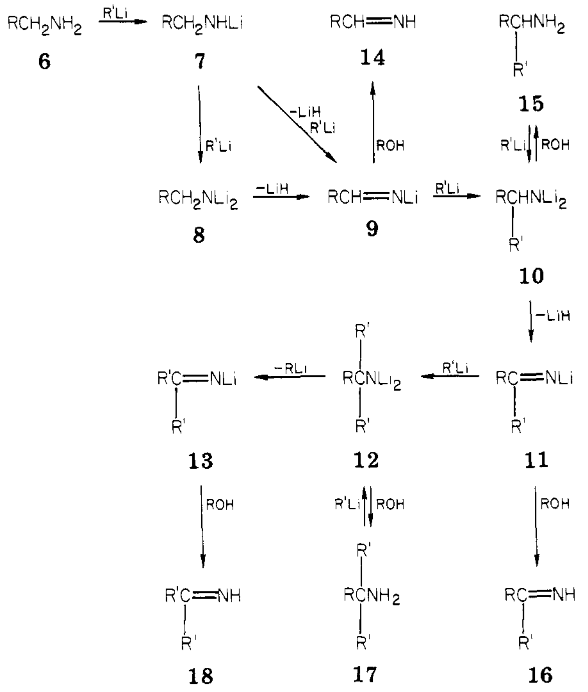
n-butyllithium (1:6 molar ratio) were heated at reflux in hexane followed by hydrolysis gave a complex mixture in which **2** was the largest component (35% yield). A reaction (eq 2) of **3** with *n*-butyllithium followed by hydrolysis

$$\underset{\textbf{3}}{PhC{\equiv}CCH_2NH_2} \xrightarrow[2.\ H_2O]{1.\ RLi} \underset{\textbf{4}}{PhC{\equiv}CH} + \underset{\textbf{5}}{R_2C{=}O} \quad (2)$$

furnished **4** and **5** (R = *n*-Bu). Investigations with saturated primary amines soon showed that multiple bonds are not essential for unexpected products to form.

It may be helpful to first present Scheme I that successfully rationalizes both the formation of the products and the effects of reaction conditions on the product compositions. The reactants in the scheme are primary amines having primary (**6**), secondary (**15**), or tertiary (**17**) alkyl groups. The products are compounds **14**–**18**. The lithiated compounds (**7**–**13**) constitute a hypothetical sequence of intermediates whose formation and transformation involve three types of reaction steps: (1) mono- and dilithiation of a primary amine by an organolithium compound; (2) elimination from a dilithiated (or monolithiated) amine of lithium hydride or (if the alkyl group is tertiary) of the elements of an organolithium compound to produce an *N*-lithioamine; (3) addition of an organolithium compound to the *N*-lithioimine to produce a new dilithiated amine.

Scheme I



The composition of the product mixtures isolated after protonolysis can be complicated by secondary reactions. For example, hydrolysis of lithiated imines (e.g., **11**, **13**) should initially furnish imines (**16**, **18**). If not sterically hindered, however, these imines are hydrolyzed rapidly to the corresponding ketones.[5] Even if a proton source other than water (e.g., an alcohol) is used, the imine products are susceptible to hydrolysis by adventitious moisture, making it difficult to isolate and characterize them without some contamination by the corresponding ketones. Furthermore, imines can react (eq 3) with any primary amines

$$R_2C{=}NH + R'NH_2 \rightarrow R_2C{=}NR' + NH_3 \quad (3)$$

that are present in the reaction mixtures to furnish *N*-alkylimines.[6] Results already in the literature indicate

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[1] Most of this work is taken from ref 2a, which contains some additional experiments and experimental details. Some of this work was presented in preliminary communications.[2b,c]

[2] (a) Erickson, W. F. Ph.D. Dissertation, The Pennsylvania State University, University Park, PA, 1972. (b) Richey, H. G., Jr.; Erickson, W. F.; Heyn, A. S. *Tetrahedron Lett.* **1971**, 2187. (c) Erickson, W. F.; Richey, H. G., Jr. *Ibid.* **1972**, 2811.

[3] Richey, H. G., Jr.; Moses, L. M.; Domalski, M. S.; Erickson, W. F.; Heyn, A. S. *J. Org. Chem.* **1981**, *46*, 3773.

[4] Richey, H. G., Jr.; Heyn, A. S.; Erickson, W. F. *J. Org. Chem.* **1983**, *48*, 3821.

[5] For a review of imine chemistry see: Layer, R. W. *Chem. Rev.* **1963**, *63*, 489.

0022-3263/83/1948-4349$01.50/0

that reactions of amines with imines can be considerably faster than with the corresponding ketones.[7] In qualitative experiments, we found that the amine–imine reaction can be rapid on the time scale of ordinary workup procedures. In summary, the products often contain amines, imines, *N*-alkylimines, and ketones. The amount of an imine and of products that can result from its reactions are very susceptible to workup conditions.

Results

In the most common reaction procedure, the amine was added to a cooled solution of organolithium compound (1:3 molar ratio), and the resulting reaction mixture was heated at reflux for 4 h. The solvent was hexane for reactions with *n*-butyllithium, pentane for *tert*-butyllithium, diethyl ether for methyllithium, and benzene–diethyl ether (70:30) for phenyllithium. Any significant deviations from this standard procedure (described more fully in the Experimental Section) are indicated. Where not specifically noted in the Experimental Section, identification of a product was by comparison with an authentic sample.

The various procedures (A–D) used to determine yields are described in the Experimental Section; the procedure used for each experiment is indicated specifically in this section. Solvent was removed at reduced pressure from crude products; the residues were frequently subjected to simple distillation followed by GC analysis of the distillates. These procedures decrease the relative amounts of any very high- or low-boiling components (particularly of components present in small amounts). The assumptions used in GC analyses (see Experimental Section) also led to low values for some products. Yields of many products probably could be increased by working on a larger scale (2 g of amine was typically used) and optimizing reaction and workup procedures more than we did in this exploratory study.

Reactions of Primary Amines Having Primary Saturated Alkyl Groups. A representative of each general structure shown in eq 4 was isolated from at least one reaction of an amine of this type. As shown by the data in Table I, the composition of the product mixtures obtained from reactions of 1-hexanamine (**19a**) and *n*-butyllithium was very dependent on the amine:RLi ratio. Additional experiments (1:3 ratio of reactants) which used "inverse addition" (organolithium compound added to the cold solution of amine before the reflux period) or addition of the amine to an already refluxing (instead of a cold) solution of *n*-butyllithium did not give significantly different results. The crude product from a reaction (1:3) worked up with methanol (no water) was distilled to give a 32% yield (A) of imine **23a** contaminated only slightly with the corresponding ketone (**22a**).

$$\underset{\textbf{19}}{\mathrm{RCH_2NH_2}} \xrightarrow[\text{2. H}_2\text{O}]{\text{1. R}'\text{Li}} \underset{\textbf{20}}{\mathrm{RCH{=}NCH_2R}} + \underset{\textbf{21}}{\mathrm{R'RCHNH_2}} +$$

$$\underset{\textbf{22}}{\mathrm{R'RC{=}O}} + \underset{\textbf{23}}{\mathrm{R'RC{=}NH}} + \underset{\textbf{24}}{\mathrm{R'RC{=}NCH_2R}} +$$

$$\underset{\textbf{25}}{\mathrm{R'RC{=}NCHRR'}} + \underset{\textbf{5}}{\mathrm{R'_2C{=}O}} + \underset{\textbf{26}}{\mathrm{R'_2C{=}NCH_2R}} \qquad (4)$$

19, a, R = $CH_3(CH_2)_4$; b, R = Et; c, R = $PhCH_2$; d, R = *t*-Bu; e, R = H_2NCH_2; f, R = Ph
20, R = Ph
21, a, R = Ph, R′ = *n*-Bu; b, R = R′ = Ph
22, a, R = $CH_3(CH_2)_4$, R′ = *n*-Bu; b, R = Et, R′ = *n*-Bu; c, R = $PhCH_2$, R′ = *n*-Bu; d, R = Ph, R′ = *n*-Bu; e, R = Ph, R′ = Me; f, R = Ph, R′ = *t*-Bu
23, a, R = $CH_3(CH_2)_4$, R′ = *n*-Bu; b, R = R′ = *t*-Bu; c, R = Ph, R′ = *n*-Bu; d, R = Ph, R′ = *t*-Bu; e, R = R′ = Ph
24, a, R = $CH_3(CH_2)_4$, R′ = *n*-Bu; b, R = $PhCH_2$, R′ = *n*-Bu; c, R = Ph, R′ = *t*-Bu; d, R = Ph, R′ = Me
25, a, R = $CH_3(CH_2)_4$, R′ = *n*-Bu; b, R = Ph, R′ = *n*-Bu; c, R = R′ = Ph
5, R′ = *n*-Bu
26, R = $PhCH_2$, R′ = *n*-Bu

A reaction of 1-propanamine (**19b**) and *n*-butyllithium furnished (A) 18% of **22b** as well as a larger amount of unidentified higher boiling material.

The composition of the product mixture obtained from 2-phenylethanamine (**19c**) and *n*-butyllithium also depended strongly on the reactant ratio. A 1:1.5 ratio (amine:RLi) gave (C) 2% of **24b**, 6% of **26**, 20% of recovered **19c**, and traces of two other components. A 1:3 ratio gave (C) 6% of **22c** and 30% of **5**, however, and a 1:6 ratio gave 20% and 41% of the same compounds.

The crude product from a reaction (24 h) of neopentylamine (**19d**) and *tert*-butyllithium was distilled to give imine **23b** in 20% yield (A).[8] A reaction of ethylenediamine (**19e**) and *n*-butyllithium (1:3 molar ratio, or 1:1.5 per amino group) gave **5** in 23% yield (C) as the only volatile product.

The product mixtures obtained from benzylamine (**19f**) and *n*-butyllithium also exemplified the importance of reaction conditions. A 1:1 ratio (ambient temperature) led to recovered **19f** and a trace of **21a** as the only volatile products. A similar reaction[9] (reflux temperature) led to 89% recovery of benzylamine. A 1:2 ratio (amine:RLi) gave (D) 1% of **19f**, 6% of **21a**, 3% of **22d**, and large amounts of three unidentified materials having much longer retention times. These were not separated satisfactorily by GC in amounts sufficient for spectral analysis, but one was probably **25b**. In parallel experiments, the product compositions were similar for reactions run at ambient temperature or for reactions with inverse addition (organolithium compound added to the cold solution of amine before the reflux period). A 1:3 ratio gave (D) 13% of **22d**, 7% of **23c**, 12% of **25b**, and 7% of **5**. The crude product from a similar reaction was distilled to give 20% (A) of **22d**. A reaction with a 1:6 ratio gave (C) 1% of **22d** and 84% of **5**.

Distillation of the crude product from a reaction (3 h) of benzylamine and *tert*-butyllithium (1:3) gave (A) 56% of **23d** and 16% of **24c**. By contrast, a 1:6 ratio gave imine **23d** as the only volatile product, isolated in 63% yield by distillation.

Distillation of the crude product from a reaction of benzylamine and phenyllithium furnished a 33% yield of imine **23e** that appeared to be contaminated with a trace of **21b**. After the distillate had stood at room temperature for several months, a small amount of **25c** precipitated from it.

Reactions of benzylamine and methyllithium did not progress as far along Scheme I as did the reactions using other organolithium compounds. A standard reaction in which diethyl ether was used as the solvent gave (C) mostly starting amine (45%) along with a small amount of **20** (7%). A reaction in which most of the ether was replaced by hexane, to give a higher reflux temperature (57 °C), furnished a similar product mixture: 3% of **20**, a trace of

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(6) *N*-Alkylimines also can form by condensation of ketones and amines, but this condensation is much slower.

(7) For example, see: Elvidge, J. A.; Linstead, R. P. *J. Chem. Soc.* **1952**, 5000.

(8) A higher yield reported for **23b** in ref 2c is incorrect.

(9) This was performed by R. C. McLane.

Table I. Composition of Product Mixtures Obtained from Reactions of 1-Hexanamine and *n*-Butyllithium

ratio amine:RLi	analytical procedure	yield, % 19a	22a	23a	24a	25a	5
1:1	B	53	0	0	0	0	0
1:2	C[a]	0	5	1	40	5	0
1:3[b]	D	0	41	8	20	11	0
1:3[c]	A	0	32	6	0	0	5
1:6	C	0	54	50	0	0	5

[a] Contains ca. 2% of an unidentified component. [b] Ambient temperature for 24 h. [c] Heated at reflux for 5 h.

Table II. Composition of Product Mixtures Obtained from Reactions of 1-Phenylethanamine (27) and *n*-Butyllithium

ratio amine:RLi	temperature	time, h	analytical procedure	yield,[a] % 22e	28	22d	5	29
1:3	ambient	5	A	4	41	0	0	0
1:3	ambient	20	C	3	50	2	2	0
1:3	reflux	4	A	6	25	6	30	0
1:3	reflux	0.5	C	5	27	6	15	0
1:3	reflux	4	C	3	25	2	15	14
1:3	reflux	20	C	5	21	2	28	3
1:6	reflux	20	C	6	3	0	20	52

[a] Three unidentified components (see Experimental Section for details) were observed in some of the GC analyses.

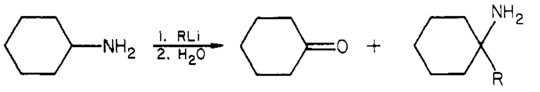
24d, and 46% of recovered benzylamine. However, a reaction in diethyl ether in which the solvent was accidentally boiled away, presumably leading to an even higher reaction temperature, gave a product mixture in which **24d** was the major volatile component. At least five minor components, one of which was **22e**, also were present.

Reactions of Primary Amines Having Secondary, Saturated Alkyl Groups. The data in Table II show that the composition of product mixtures obtained from reactions (eq 5; R = *n*-Bu) of 1-phenylethanamine (**27**) and

$$\underset{\mathbf{27}}{PhCH(CH_3)NH_2} \xrightarrow[2.\ H_2O]{1.\ RLi} \underset{\mathbf{22e}}{Ph(CH_3)C{=}O} + \underset{\mathbf{28}}{PhRC(CH_3)NH_2} + \underset{\mathbf{22d}}{PhRC{=}O} + \underset{\mathbf{5}}{R_2C{=}O} + \underset{\mathbf{29}}{R_2C{=}NH} \qquad (5)$$

n-butyllithium depended greatly on amine:RLi ratio, reaction time, and temperature. The material isolated after 0.5 h at ambient temperature (1:3 ratio of amine to RLi) consisted mainly of the reactant (**27**); this compound, however, was not detected in any of the reactions included in Table II. Ketone **5** was sometimes accompanied by the corresponding imine (**29**); the variation in relative amounts of **5** and **29** presumably is due to the ease of hydrolysis of the imine.

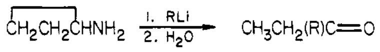
A standard reaction of cyclohexylamine and *n*-butyllithium (eq 6) gave (C) 30% of cyclohexanone and 20%



(6)

30 **31** **32**, R = *n*-Bu

of **32**. Distillation of the product from a similar reaction of cyclopropylamine (eq 7) gave (A) a 14% yield of **22b**.



(7)

33 **22b**, R = *n*-Bu

Reaction of a Primary Amine Having a Tertiary, Saturated Group. The only volatile materials from a reaction of a small sample of **28** and *n*-butyllithium using standard conditions were (C) 18% of **5** and 28% of recovered **28**.

Reactions of Unsaturated Primary Amines. GC analysis of the crude products obtained from reactions (eq 1) of allylamine and *n*-butyllithium (1:3) for 5 or 22 h showed at least eight volatile components. Reaction of a 1:5 ratio of the reactants for 4 h, however, gave a simpler product mixture containing (C) 35% of **2** plus several minor unidentified components.

A reaction (eq 8) of **34** and *n*-butyllithium (3.5 h) gave (A) 9% of **35**, 2% of **36**, 7% of **37**, 3% of **38**, and a large

$$\underset{\mathbf{34}}{PhCH{=}CHCH_2NH_2} \xrightarrow[2.\ H_2O]{1.\ RLi} \underset{\mathbf{35}}{PhCH_2CH_2(R)C{=}O} + \underset{\mathbf{36}}{PhCH_2CH_2(R)C{=}NH} + \underset{\mathbf{37}}{PhCHRCH_2(R)C{=}O} + \underset{\mathbf{38}}{PhCHRCH_2(R)C{=}NH} \qquad (8)$$

$$R = n\text{-Bu}$$

pot residue. Structure **39**, differing only in the position

$$\underset{\mathbf{39}}{PhCH_2CHR(R)C{=}O}$$

of one butyl group, might be possible for the compound assigned structure **37**. However, the position of the NMR absorption (τ 6.96) assigned to the methine hydrogen is more in accord with **37** than with **39**.[10] Also more consistent with **37** is the observation that upon addition of increments of the shift reagent europium tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate) [Eu(fod)$_3$], the multiplet at τ 6.96 moved downfield less than did a doublet at τ 7.44, assigned to $CH_2C{=}O$, although the ratio (0.93:1.00) was small. Amine **34** was recovered in 84% yield (B) from a reaction with methyllithium.

A reaction of **3** and *n*-butyllithium (eq 2) gave (C) 53% of **4** and 40% of **5**. A reaction at ambient temperature (21 h) led to the same products in yields (A) of 63% and 38%.

Reactions of Secondary Amines. The ^1H NMR spectrum of the undistilled product obtained from a reaction of *N*-methylbenzylamine under standard conditions showed it to be essentially pure reactant (75% recovery). No more than a few percent of any other components could have been present. Similarly, the ^1H NMR spectrum of material obtained from a reaction of dibenzylamine was 90% reactant (83% recovery), and GC analysis showed no

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[10] Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: Oxford, 1969; Chapter 3-2.

significant new peaks. The IR and NMR spectra of the dibenzylamine recovered when a reaction was hydrolyzed with D_2O indicated that no more than 0.1 D could have been incorporated into the methylene positions. Although the ^1H NMR spectrum of material isolated from a reaction of dibenzylamine for 24 hr (instead of the standard 4 h) showed significant new absorptions, more than 50% of the material was still dibenzylamine.[9]

Gases and Solids Produced by Reactions of Amines and Organolithium Compounds. Addition of excess *n*-butyllithium to benzylamine at ambient temperature instantaneously produced approximately 1 mol of gas (presumably butane).

In one instance, the solid observed during the reactions of **27** and *n*-butyllithium was isolated and washed repeatedly with hexane. Addition of methanol to the solid immediately generated a large volume of gas, shown by GC and mass spectral analysis to contain H_2 and some CH_4; workup of the remaining material showed the presence of **22e**, **28**, and at least one unidentified component.

Reactions of Benzonitrile. A reaction (eq 9) of benzonitrile and *n*-butyllithium (1:1) furnished (C) 21% of **22d**

$$\underset{\mathbf{40}}{\mathrm{PhC{\equiv}N}} \xrightarrow[2.\ \mathrm{H_2O}]{1.\ \mathrm{RLi}} \underset{\mathbf{22d}}{\mathrm{PhRC{=}O}} + \underset{\mathbf{5}}{\mathrm{R_2C{=}O}} \qquad (9)$$

$$R = n\text{-Bu}$$

and 6% of **5**, as well as significant amounts of two unidentified components. With increasing amounts of *n*-butyllithium, the yield of **22d** decreased and that of **5** increased. For example, a 1:3 ratio (nitrile:RLi) furnished 4% of **22d** and 49% of **5**, as well as three unidentified components.

Reactions of Benzyl Alcohol. Benzyl alcohol was recovered almost completely from reactions with *n*-butyllithium for 4 or 28 h, although a few percent of benzaldehyde and of an unidentified, less volatile compound were detected.

Reactions of Imines with Amines To Produce *N*-Alkylimines. The reaction (in diethyl ether) of imine **23a** with 1-hexanamine to produce **24a** was at least 500 times faster than the same reaction of the corresponding ketone (**22a**). Similarly, the reaction of imine **23d** with benzylamine to produce **24c** was at least 100 times faster than the reaction of the corresponding ketone (**22f**).

Discussion

Scheme I, proposed for the reactions of primary amines and organolithium compounds, has three types of reaction steps. We will consider each step individually and then discuss matters related to the overall reaction sequence.

Lithiation and Dilithiation of Primary Amines. Reactions of amines (e.g., **19a** and **19f**) with organolithium compounds in 1:1 ratio gave large amounts of recovered starting materials and only traces of products.[11] Because more than 1 equiv of organolithium compound is needed for significant reaction to occur and also because secondary amines do not as readily give comparable reactions, we think it likely that eliminations are mainly from dilithiated rather than from monolithiated, primary amines. For example, **9** probably arises predominantly by elimination of lithium hydride from **8** rather than from **7** (followed by metalation).

We originally reported[2b] that the secondary amine *N*-methylbenzylamine did not react when heated at reflux with *n*-butyllithium in hexane and subsequently observed[2a] that dibenzylamine also did not react significantly. These control experiments used the standard reaction time of 4 h. It has more recently been reported[12] that some secondary amines when treated with *n*-butyllithium for 24 h at 24 °C give, besides recovered amine, mixtures of imines and α-alkylamines that must form by elimination of lithium hydride, followed sometimes by addition of the organolithium compound. Moreover, aldimines (RCH=NR), when treated with *n*-butyllithium in refluxing hexane for 24 h, react partially to form products that must result from addition of butyllithium, followed sometimes by elimination of lithium hydride and a second addition of butyllithium. Therefore, we reinvestigated[9] the control reactions and found that after 4 h at reflux temperature, formation of any products could not have exceeded 5% from *N*-methylbenzylamine and 10% from dibenzylamine. After 24 h, however, nearly 50% of the dibenzylamine had reacted in some manner.[13] Therefore, some reaction of secondary amines does occur. However, in our experiments, such reactions are slow by comparison to those of the primary amines; for example, note the virtually complete disappearance of **19f** and **27** in reactions for 4 h at ambient temperature.

The necessity for a primary amino group is readily explained if both metalation steps occur at the amino function.[14,15] While the second metalation conceivably could occur at an α-carbon, then secondary amines should similarly be metalated. However, dibenzylamine disappeared more slowly than primary amines. This was not because an α-metalated species formed but was stable, since dibenzylamine recovered after D_2O quenching had no significant amount of C–D in its methylene groups.[16] Since α-metalation of dibenzylamine is not significant, it is unlikely that metalations of the less acidic C–H linkages of alkylamines that lack an electron-withdrawing group such as phenyl play an important role in the reactions discussed here.

The second metalation step must be much slower than the first. Only 1 mol of gas (butane) formed rapidly when benzylamine was treated with an excess of *n*-butyllithium at ambient temperature. Furthermore, alterations in product composition were not large when (a) inverse addition (organolithium compound added to the amine) preceded the reflux period, (b) the amine was added to the organolithium compound at low (rather than ambient temperature) before the reflux period, or (c) the amine was added to an already refluxing (rather than to a cooled) solution of organolithium compound. If the second metalation occurred rapidly then these alterations in conditions should alter product composition, since in some in-

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(11) Under more vigorous conditions, RNHLi (and RNHNa) undergo a reaction that produces secondary amines (R_2NH): Richey, H. G., Jr.; Erickson, W. F. *Tetrahedron Lett.* **1972**, 2807.

(12) Hu, L.; Mauzé, B.; Miginiac, L. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1977**, *284*, 195.

(13) Although not investigated in detail, the reaction mixture did not seem to include large amounts of $PhCH{=}NCH_2Ph$ or $PhCHRNHCH_2Ph$ (R = *n*-Bu), products that would correspond to those noted[12] from reactions of some other secondary amines and from some imines.

(14) Dilithiation at carbon is well established. For a review see: West, R. *Adv. Chem. Ser.* **1974**, *No. 130*, 211.

(15) Primary amines are known to react slowly with a second mole of a Grignard reagent: Kharasch, M. S.; Reinmuth, O. "Grignard Reactions of Nonmetallic Substances"; Prentice-Hall; New York, 1954; Chapter 18. The formation of stable *N,N*-dilithioamines has been claimed; for a collection of references see: Pozharskii, A. F.; Zvezdina, E. A. *Russ. Chem. Rev. (Engl. Transl.)* **1973**, *42*, 37; *Usp. Khim.* **1973**, *42*, 65.

(16) Significant N,α-dilithiation of dibenzylamine by *n*-butyllithium has been observed in diethyl ether, a solvent more favorable for metalation: Gilman, H.; Woods, L. A. *J. Am. Chem. Soc.* **1943**, *65*, 33. A small amount of N,α-dilithiation and a large amount of N,*o*-dilithiation of *N*-methylbenzylamine by *n*-butyllithium have been observed in the presence of tetramethylethylenediamine, a reagent that greatly facilitates metalation: Ludt, R. E.; Hauser, C. R. *J. Org. Chem.* **1971**, *36*, 1607.

stances all of the organolithium compound could be consumed before the last portion of the amine was added.

Eliminations from Lithiated Amines. The isolation of imines and products resulting from their hydrolysis (ketones) or reaction with primary amines (*N*-alkylimines) suggests that elimination of lithium hydride from the lithiated amines is occurring. Precipitates were often observed in the reaction vessels during the reflux period, and the solid isolated from a reaction of **27** and *n*-butyllithium was found to contain lithium hydride. Other instances of loss of lithium hydride from organolithium compounds are known, but not ones that generally occur with such facility.[17] For example, eliminations of lithium hydride from the monolithiated amines that result from 1,2-additions of organolithium compounds to pyridines ordinarily require higher temperatures, *even though aromatic systems are generated*.[18] Elimination of organic groups from lithium alkoxides has been observed, but generally is also associated with much higher temperatures[19] or with substituents[20] that might afford considerable stabilization to transition states for cleavage of radicals or carbanions. We assume that dilithiation contributes to the relative rapidity of the eliminations observed in our reactions.

Formation of di-*n*-butyl ketone (**5**) from reactions of *n*-butyllithium with many amines that contain no *n*-butyl groups is most readily explained by postulating the elimination at some stage of an organolithium compound to form a carbon–nitrogen double bond (e.g., **12** → **13**). The organic groups that were eliminated generally were small, and the hydrocarbons formed by their protonation would not have been detected by the usual workup procedures. However, phenylacetylene was sufficiently nonvolatile to be isolated from the reaction of **3**. Moreover, some methane, presumably formed from methyllithium, was noted along with the hydrogen obtained from hydrolysis of the solid present after a reaction of **27**. Elimination of an organic group obviously occurred in the reaction of **28**, an amine that has a tertiary alkyl group.[22]

We assume that the eliminations generally produce *N*-lithioimines, the most reasonable source of the imine, ketone, and *N*-alkylimine products. In those instances in which the amine has a primary alkyl group, it is conceivable that elimination could lead to a nitrile (RCH_2NLi_2 or $RCHLiNHLi \rightarrow RC{\equiv}N$). Organolithium compounds add to nitriles (eq 10) to form *N*-lithioimines (**11**),[23] a step

$$RC{\equiv}N \xrightarrow{R'Li} \underset{\mathbf{11}}{R'RC{=}NLi} \xrightarrow{R'Li} \underset{\mathbf{12}}{R_2'RCNLi_2} \qquad (10)$$

that would produce the products observed in this work. However, nitriles are susceptible to α-metalation by organolithium compounds.[23] Since α-metalated nitriles probably would not react further, some of the nitrile should be obtained upon hydrolysis. However, a nitrile never was noted in any product mixture.

Additions of Organolithium Compounds to *N*-Lithioimines. Although additions of organolithium compounds to *N*-alkylimines ($R_2C{=}NR$) have been noted,[23] we have found no prior reports of direct additions to simple imines, $R_2C{=}NH$ (of course, lithiated to $R_2C{=}NLi$ by the organolithium compound). The observation that the major product obtained from the reaction of benzonitrile and an excess of *n*-butyllithium (eq 9) was not *n*-butyl phenyl ketone but di-*n*-butyl ketone (**5**) suggests that organolithium compounds can add to *N*-lithioimines. In fact, products that result from two additions (to produce **12**, eq 10) have recently been observed in reactions of *n*-butyllithium with some α-oxygenated nitriles.[24,25] Moreover, some of these products were accompanied by small amounts of di-*n*-butyl ketone (**5**).[24]

In Scheme I, the reactions of amines having primary alkyl groups (**6**) proceed through *N*-lithioaldimines ($RCH{=}NLi$, **9**). No aldimines ($RCH{=}NH$) were observed. From reactions of benzylamine with methyllithium, however, small amounts were obtained of a product (**20**) that presumably arose from a reaction of aldimine $PhCH{=}NH$ with unreacted benzylamine. The rapidity of addition of organolithium compounds to **9** probably is the major cause of the failure to obtain products derived more directly from **9**. However, methyllithium is an organolithium compound of particularly low reactivity, so its addition to **9** may be unusually slow. It is possible that small amounts of aldimines were among the products formed upon quenching some other reactions but were lost due to the ready polymerization processes to which these compounds are susceptible.[5] The reactions in which **20** was isolated were carried out only to low conversion, so upon quenching, considerable benzylamine was present to rapidly trap the aldimine.

The product compositions indicate that additions to *N*-lithioketimines ($R_2C{=}NLi$) are considerably slower than to *N*-lithioaldimines ($RCH{=}NLi$). It is not surprising that the lower reactivity of ketones than of aldehydes toward nucleophilic reagents is paralleled by the reactivities of the corresponding *N*-lithioimines. The results also suggest that addition becomes slower with increasing bulk of the organic groups of the *N*-lithioketimine and of the organolithium compound. For example, compare the reactions of benzylamine (**19f**) and *tert*-butyllithium, which gave no products that result from further reaction of **11** in Scheme I, with the reactions of benzylamine (**19f**) and *n*-butyllithium.

The Overall Reaction Sequence and Product Composition. Scheme I accounts satisfactorily for the formation of the various products. Even more important, this scheme is qualitatively consistent with the variations in product composition when reaction conditions are altered. Increasing severity of conditions (more time, higher temperature, or greater RLi:amine ratio) always favors products further along the scheme. For example, note in the reaction of **27** and *n*-butyllithium (eq 5 and Table II) the appearance first of **22e** and **28**, those products whose formation requires the fewest steps, then of **22d**, and finally of **5** and **29**. Note in the reaction of **19f** and *tert*-butyllithium that *N*-alkylimine **24c**, presumably a product of reaction during workup of imine **23d** with recovered **19f**, was observed when a 1:3 but not when a 1:6 ratio (amine:RLi) was used.

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(17) Besides the observations in ref 12, the most closely related observation that we have found is a report of formation of the corresponding imine upon treating 9-aminofluorene with potassium amide in ammonia: Hauser, C. R.; Brasen, W. R.; Skell, P. S.; Kantor, S. W.; Brodhag, A. E. *J. Am. Chem. Soc.* **1956**, *78*, 1653.

(18) For a summary see: Yale, H. L. *Chem. Heterocycl. Comp.* **1961**, *14, Part 2*, 421; **1974**, *14 Suppl., Part 2*, 489.

(19) Zook, H. D.; March, J.; Smith, D. F. *J. Am. Chem. Soc.* **1959**, *81*, 1617.

(20) Extensive studies of such systems by Cram and his co-workers are summarized in ref 21.

(21) Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965; Chapter 4.

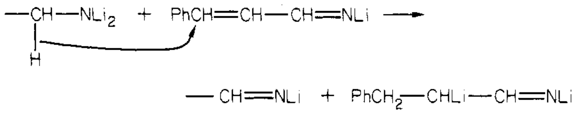
(22) Additional examples of cleavage of such amines are presented in another publication: Richey, H. G., Jr.; Cabré, S. *J. Org. Chem.* **1983**, *48*, 3822.

(23) Wakefield, B. J. "The Chemistry of Organolithium Compounds"; Pergamon Press: Oxford, 1974; Chapter 8.

(24) Gauthier, R.; Axiotis, G. P.; Chastrette, M. *J. Organomet. Chem.* **1977**, *140*, 245.

(25) Chastrette, M.; Axiotis, G. P. *Synthesis* **1980**, 889. Amouroux, R.; Axiotis, G. P. *Ibid.* **1981**, 270.

The reactions of cyclopropylamine and of the unsaturated primary amines present additional features. At some stage, the reaction of cyclopropylamine probably involves the well-known ring opening of anions having α-cyclopropyl substituents.[26] The reactions with allylic amines give products whose formation must involve addition of the organolithium compound to the alkene functions. In the formation of **2** from **1**, addition could be directly to the alkene function of lithiated **1**, in analogy to ready additions of organolithium compounds to alkene functions of some alkenols.[27] Alternatively, addition might occur at some later stage to a carbon–carbon double bond activated by conjugation with a carbon–nitrogen double bond ($CH_2{=}CHCH{=}NLi$). Products **37** and **38** (eq 8) must have a similar origin. One possibility for the reduction of the double bond in the formation of **35** and **36** is hydride transfer from a lithiated amine to a carbon–carbon double bond conjugated with a carbon–nitrogen double bond (eq 11).[28]



(11)

Unraveling the stoichiometries of the reactions and understanding the compositions of the product mixtures that ultimately result from certain ratios of reactants are interrelated and complicated problems. Scheme I predicts minimal ratios of organolithium reagents to amine that are necessary for particular conversions. For example, conversions of **6** to **16** and of **15** to **18** formally require 3 mol of organolithium compound per mol of amine, 2 acting as a metalating agent and 1 as a nucleophile. However, the product mixtures indicate that the reality is more complex. At least four types of complications will affect product composition.

(1) Some reaction steps (e.g., **7** → **8**) may be slow compared to subsequent steps (e.g., **8** → **9** → **10**). Therefore, molecules that have passed the rate determining step may proceed rapidly through several subsequent steps. Such behavior probably is largely responsible for conversion of *part* of a reactant to products whose formation theoretically requires a larger ratio of organolithium compound to amine than is used.

(2) The elimination reactions generate species that could reduce the requirement for the organolithium compound. For example, the conversion of **6** to **16** considered above produces 2 mol of lithium hydride, and the conversion of **15** to **18** produces 1 mol of lithium hydride and 1 mol of the elements of an organolithium compound (it has not been demonstrated that the eliminated groups actually are present in significant amounts in the form of organolithium compounds). To the extent that these species metalate the amines (and that potential sites for metalation remain), the requirement for the initial organolithium compound is reduced. Lithium hydride is not very soluble in the reaction solutions, and perhaps for that reason plays little role in the reactions. In fact, the effects on product composition of increasing amounts of organolithium compound suggest that more (not less) organolithium compound than predicted by Scheme I is often consumed.

(3) Reactions not shown in Scheme I undoubtedly contribute to destruction of the organolithium compound. Abstraction of protons by organolithium compounds (and perhaps also by other strong bases such as $RNLi_2$) from various species in solution probably is occurring. Such metalation of the alkanes used as solvents in most of this work should not occur significantly. However, metalation of imine intermediates having α-hydrogens is a likely possibility.[29] Metalation of the aryl hydrogens of systems having phenyl rings is another possibility.[30] Some thermal decomposition of organolithium compounds may also be occurring.[31]

(4) Reactions not shown in Scheme I and insolubility may prevent further reaction of some components. For example, α-metalation of an *N*-lithioimine would not only destroy an organolithium compound but also convert the imine to a form that probably would not undergo further reaction. The elimination reactions are potentially reversible. It is conceivable that insolubility of lithium hydride (or of other components) is important in favoring formation of significant amounts of *N*-lithioimines.

Conclusion

This exploratory study shows that primary amines and organolithium compounds react under surprisingly mild conditions to produce new primary amines, in which a group from the organolithium compound is incorporated into the α-position, and imines or products that result from their hydrolysis or condensation with amines. Some of these reactions might be useful preparatively. Several essentially pure imines (e.g., **23a**, **23b**, **23d**, **23e**), for example, were isolated in preparatively useful amounts simply by distillation. The reactions probably proceed mainly by the sequence of steps shown in Scheme I. The conclusion that dimetalation at nitrogen facilitates ready eliminations suggests that polymetalation at the same or at adjoining atoms of other systems may also lead to new reaction chemistry.

Experimental Section

^1H NMR spectra were taken at 60 MHz with Me_4Si as an internal standard. Absorptions are reported with the following notations (b is added when the multiplicity is poorly defined or has additional fine splitting): s, singlet; d, doublet; t, triplet; q, quartet; m, a more complex multiplet or overlapping multiplets. IR spectra were taken in 0.5-mm cells and calibrated against a polystyrene film. Mass spectra were obtained with an AEI MS 902 spectrometer at an ionization potential of 70 eV. For low-resolution mass spectra, m/z values (and relative intensities) are given for the molecular ion (M^+) and base ion. Melting points were taken in capillary tubes and are uncorrected. Presentation of high-resolution mass spectral data or an elemental analysis implies that the compound has not previously been reported.

Analytical and preparative GC separations were performed by using a thermal conductivity instrument with helium as the carrier gas and the following columns constructed out of aluminum tubing: A, XE-60 (15%) on Gas Chrom Q (80–100 mesh), 0.25 × 6 ft; B, Versamid 900 (20%) on Gas Chrom P (60–80 mesh), 0.25 in. × 10 ft; C, XE-60 (20%) on Gas Chrom P (60–80 mesh), 0.25 in. × 10 ft; D, SF-96 (10%) on Chromosorb W (45–60 mesh), 0.25 in. × 6 ft. Peak areas were ordinarily measured by using a planimeter. Samples were collected for spectral analysis by using glass U-shaped tubes inserted into the exit port of the gas

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[26] Reference 21, Chapter 6.

[27] Crandall, J. K.; Clark, A. C. *Tetrahedron Lett.* **1969**, 325. Felkin, H.; Swierczewski, G.; Tambuté, A. *Ibid.* **1969**, 707. Crandall, J. K.; Clark, A. C. *J. Org. Chem.* **1972**, *37*, 4236. Dimmel, D. R.; Huang, S. *Ibid.* **1973**, *38*, 2756. Dimmel, D. R.; O'Malley, J. P. *Ibid.* **1975**, *40*, 132. Olsson, L.-I.; Claesson, A. *Acta Chem. Scand., Ser. B* **1976**, *30*, 521. Richey, H. G., Jr.; Wilkins, C. W., Jr.; Bension, R. M. *J. Org. Chem.* **1980**, *45*, 5042.

[28] Compare with the hydride transfer proposed in ref 11.

[29] Metalation of *N*-alkylimines is well-known.[23] For an example of metalation of an *N*-lithioimine, although in a solvent mixture more favorable for metalation than are alkanes, see: Cuvigny, T.; Normant, H. *C. R. Hebd. Seances Acad. Sci., Ser. C.* **1967**, *265*, 245.

[30] Evidence for some metalation of phenyl rings under comparable reaction conditions has been noted in other work: McLane, R. C. Ph.D. Dissertation, The Pennsylvania State University, University Park, PA, 1975.

[31] Reference 23, Chapter 15.

chromatograph and cooled in liquid nitrogen.

Materials. All amines used as substrates were commercial samples. The solutions of organolithium compounds were obtained from Alfa Inorganics, Inc. (typical concentrations are shown in parentheses): *n*-butyllithium in hexane (2.3 M), *tert*-butyllithium in pentane (2.1 M), methyllithium in diethyl ether (1.9 M), phenyllithium in (70:30) benzene–diethyl ether (1.9 M). Diethyl ether and benzene were dried over sodium. Hexane and pentane were dried over molecular sieves (4 Å).

Procedure for Reactions with Organolithium Compounds. Except where otherwise noted, the following procedure was used. Reactions were carried out in a standard-taper, three-necked flask containing a magnetic stirring bar and fitted with a condenser having a gas inlet tube at the top, a pressure-equalizing addition funnel, and a rubber septum. After assembly, the apparatus was heated gently with a Bunsen burner while nitrogen was flowing rapidly through it. During a reaction, a positive pressure of nitrogen was maintained in the closed reaction system.

The solution of organolithium compound was introduced into the flask with a syringe. A solution of the amine (typically 2.0 g) dissolved in the same solvent as the organolithium compound (typically 25 mL) was added over 15 min to the ice-cooled, stirred solution of organolithium compound. The resulting reaction mixture was heated at reflux for 4 h before cooling again. Methanol (5 mL) and then water (5 mL) were added carefully and the resulting mixture was taken into water and either benzene or diethyl ether. The layers were separated, the aqueous layer was washed with two additional portions of hexane or diethyl ether, and the combined organic layers were dried (MgSO$_4$). The solvent was removed at reduced pressure to give the crude product.

The crude product was sometimes subjected to GC analysis. In other cases, it was distilled, followed often by GC analysis. Small samples of each significant component noted in GC analyses were ordinarily collected for spectral analysis. Spectra are reported here for all compounds for which authentic samples are not readily available.

Calculation of Yields. One of the following procedures was used. (A) The yield of a compound was determined from the weight of a distillate that spectral and GC analytical data showed to be essentially pure, or alternatively from some combination of spectral and GC analysis of a distillate, assuming that the observed peaks included all of the injected material (a reasonable assumption since materials having little volatility had been removed). (B) A yield of a compound was determined from the weight of a crude (undistilled) product that spectral (and sometimes also GC analytical) data showed to be essentially completely that compound. (C) A known weight of a linear alkane (whose GC peak did not overlap with those of the components of the reaction mixture) was added as a standard to the undistilled product; yields were determined from the ratios of the GC peaks due to each product relative to the area of the peak due to the standard. (D) Yields were determined from GC analysis of a crude product, assuming that the observed peaks included all of the injected material. High column temperatures and flow rates were always used initially to ensure that components of little volatility would be noted. In all GC analyses, it was assumed that the detector responded equally to equal weights of different compounds.

Reactions of 1-Hexanamine (19a) and *n*-Butyllithium. Typical GC conditions (column B, 155 °C) gave the following relative retention times: **5** (0.6), **22a** (1.0), **23a** (1.5), **24a** (4.3), **25a** (7.4). An unidentified component (3.1) having 3% of the combined areas of the other peaks was present in the 1:2 reaction (entry 2 in Table I). Dodecane was used as the internal standard for calculating yields.

22a: ^{1}H NMR (CCl$_4$) τ 7.70 (t, J = 6 Hz, 4, CH$_2$CO), 8.67 (m, 10, all other CH$_2$'s), 9.04 (m, 6, CH$_3$); IR (CCl$_4$) 1720 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 156 (M$^+$, 14), 58 (100).

23a: ^{1}H NMR (CCl$_4$) τ 1.66 (very broad, 1, NH), 7.78 (m, 4, CH$_2$CN), 8.68 (m, 10, all other CH$_2$'s), 9.06 (m, 6, CH$_3$); IR (CCl$_4$) 1645 cm^{-1} (C=N).[32]

24a: ^{1}H NMR (CCl$_4$) τ 6.82 (m, 2, CH$_2$N), 7.77 (m, 4, CH$_2$CN), 8.65 (m, 18, all other CH$_2$'s), 9.10 (m, 9, CH$_3$); IR (CCl$_4$) 1655 cm^{-1} (C=N); low-resolution mass spectrum, m/z (relative intensity) 239 (M$^+$, 8), 43 (100); high-resolution mass spectrum, m/z 239.2646 (M$^+$ calcd for $C_{16}H_{33}N$: 239.2612).

25a: ^{1}H NMR (CCl$_4$) τ 6.70 (m, 1, CHN), 7.80 (m, 4, CH$_2$CN), 8.64 (m, 24, all others CH$_2$'s), 9.06 (m, 12, CH$_3$); IR (CCl$_4$) 1655 cm^{-1} (C=N); low-resolution mass spectrum, m/z (relative intensity) 295 (M$^+$, 3), 43 (100); high-resolution mass spectrum, m/z 295.3249 (M$^+$ calcd for $C_{20}H_{41}N$: 295.3238).

An IR spectrum of the crude product from the 1:1 reaction (entry 1 in Table I) was identical with that of **19a** and GC analysis (column A, 140 °C) gave only one peak. The analysis of the 1:3 reaction (entry 4 in Table I) was of a distillate, bp 40–80 °C (0.12 torr). Distillation of a similar reaction (4 h) worked up only by the addition of methanol gave a fraction, bp 160–214 °C, shown by ^{1}H NMR and IR spectra to be **23a** (32% yield), slightly contaminated with **22a**.

Reaction of 1-Propanamine (19b) and *n*-Butyllithium. Distillation of the crude product gave a liquid with ^{1}H NMR, IR, and mass spectra identical with those of **22b**: bp 90–103 °C [lit.[33] bp 147–148 °C]. The IR spectrum (CCl$_4$) of the large pot residue had strong absorptions at 1720 and 1660 cm^{-1}.

Reactions of 2-Phenylethanamine (19c) and *n*-Butyllithium. GC analysis (column C, 185 °C initially, raised at a rate of 7 °C/min to 215 °C after the second component (**26**) had eluted) of the 1:1.5 reaction had the following relative retention times: **19b** (1.0), minor unidentified component (2.0, probably **22c**), **26** (2.7), minor unidentified component (6.3), **24b** (10.4). Heptadecane was used as the internal standard for calculating yields in this reaction. GC analysis (column C, 170 °C) of the products from the other reactions had the following relative retention times: **5** (1.0), **22c** (5.6). Octadecane was used as the internal standard for calculating yields in these reactions.

22c: ^{1}H NMR (CCl$_4$) τ 2.78 (m, 5, Ph), 6.43 (s, 2, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 7.66 (bt, J = 7 Hz, 2, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CO}$), 8.64 (m, 4, $\mathrm{CH_3(C}\mathit{H}_2)_2$), 9.13 (m, 3, CH$_3$); IR (CCl$_4$) 1720 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 176 (M$^+$, 10), 57 (100).

24b:[34] ^{1}H NMR (CCl$_4$) τ 2.85 (m, 10, Ph), 5.66–6.83 (m, 2, CH$_2$N), 6.47 (s, 2, $\mathrm{PhC}\mathit{H}_2\mathrm{CN}$), 7.18 (m, 2, $\mathrm{CH_2C}\mathit{H}_2\mathrm{Ph}$), 7.68 (bt, J = 6 Hz, 2, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CN}$), 8.63 (m, 4, $\mathrm{CH_3(C}\mathit{H}_2)_2$), 9.10 (m, 3, CH$_3$); IR (CCl$_4$) 1660 cm^{-1} (C=N).

26: ^{1}H NMR (CCl$_4$) τ 2.84 (m, 5, Ph), 6.53 (t, J = 6 Hz, 2, CH$_2$N), 7.15 (bt, J = 6 Hz, 2, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 7.91 (m, 4, CH$_2$CN), 8.70 (m, 8, $\mathrm{CH_3(C}\mathit{H}_2)_2$), 9.08 (m, 6, CH$_3$); IR (CCl$_4$) 1660 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 245 (M$^+$, 1), 57 (100).

Reaction of Neopentylamine (19d) and *tert*-Butyllithium. GC analysis (column C, 150 °C) of the crude product gave only one peak, and distillation gave a liquid that was essentially pure **23b**: bp 64–109 °C [lit.[35] bp 166 °C]: ^{1}H NMR (CCl$_4$) τ 0.36 (very broad, 1, NH), 8.74 (s, 18, CH$_3$); IR (CCl$_4$) 1601 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 141 (M$^+$, 2), 57 (100). This compound has a very strong musty odor.

Reaction of Ethylenediamine (19e) and *n*-Butyllithium. The IR spectrum of the crude product was essentially identical to that of **5**, and GC analysis (column C, 170 °C) gave only one peak, a retention time identical with that of **5**. Octadecane was used as the internal standard for determining yields.

Reactions of Benzylamine (19f) and *n*-Butyllithium. GC analysis conditions (column C, 155 °C) used for the 1:2 reactions gave the following relative retention times: **19f** (1.0), **21a** (1.8), **22d** (3.0), and three unidentified components (20, 24, and 34). The last three peaks comprised 12%, 15%, and 25% of the total area of the GC peaks for the 1:2 reaction reported under Results. These three peaks were not sufficiently resolved on this or some other columns to permit collection of samples large enough for spectral analysis. An IR spectrum (CCl$_4$) of the material representing all three peaks, however, had a strong absorption at 1640 cm^{-1}. A similar GC analysis of the 1:1 reaction that had been run at ambient temperature showed the presence only of **19f** and a trace of **21a**. The ^{1}H NMR spectrum of the crude product from the 1:1 reaction at reflux temperature also showed it to be essentially only **19f**. GC analysis conditions (column C, 145 °C

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[32] This imine is a new compound, but no analysis was obtained because it was always contaminated with the corresponding ketone.

[33] Pickard, R. H.; Kenyon, J. *J. Chem. Soc.* **1913**, *103*, 1923.

[34] This is a new compound, but was inadvertently not analyzed.

[35] Hansley, V. L. U.S. Patent 2742503, 1956; *Chem. Abstr.* **1956**, *50*, 16830.

initially, but raised at the rate of 10 °C/min to 195 °C after the third component (**23c**) had eluted) used for the 1:3 reaction gave the following relative retention times: **5** (1.0), **22d** (6.4), **23c** (7.2), **25b** (16). Distillation of a crude product from a 1:3 reaction gave a liquid shown by its ^{1}H NMR and IR spectra to be essentially pure **22d**: bp 74–83 °C (0.5 torr) [lit.[36] bp 135–140 °C (25 torr)]. A 2,4-dinitrophenylhydrazone derivative, recrystallized from dichloromethane–methanol, had mp 170–171 °C [lit.[37] mp 167–168 °C]. The ^{1}H NMR and IR spectra of the pot residue showed it to be mainly **25b**. Similar GC conditions and a tridecane internal standard were used for analysis of the 1:6 reaction.

21a: ^{1}H NMR (CCl_4) τ 2.75 (m, 5, Ph), 6.15 (t, J = 7 Hz, 1, CH), 7.54 (bs, disappears on shaking sample with D_2O, 2, NH_2), 8.40 (m, 2, CH_2CH), 8.73 (m, 4, $(CH_2)_2CH_3$), 9.08 (t, J = 6 Hz, 3, CH_3); IR (CCl_4) 3310 and 3390 cm^{-1} (very weak, NH stretch), 1600 cm^{-1} (NH bend).

22d: ^{1}H NMR (CCl_4) τ 2.07 (m, 2, *o*-H's), 2.53 (m, 3, *m*- and *p*-H's), 7.12 (t, J = 6 Hz, 2, CH_2CO), 8.39 (m, 4, $(CH_2)_2CH_3$), 9.03 (m, 3, CH_3); IR (CCl_4) 1685 cm^{-1} (C=O).

23c: IR (CCl_4) 1635 cm^{-1} (C=N). Formed **22d** on exposure to water.

25b: ^{1}H NMR (CCl_4) τ 2.23 (m, 2, *o*-H's of PhCN), 2.78 (m, 8, other Ph H's), 5.43 (t, J = 6 Hz, 1, CH), 7.42 (m, 2, CH_2CN), 8.70 (m, 10, all other CH_2's), 9.11 (m, 6, CH_3); IR (CCl_4) 1635 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 307 (M^+, 5), 91 (100).

Reactions of Benzylamine (19f) and *tert*-Butyllithium. Distillation of the crude product from the 1:3 reaction gave two fractions. The first was **23d** (56%): bp 46–47 °C (0.35 torr);[38] ^{1}H NMR (CCl_4) τ 1.70 (very broad, 1, NH), 2.85 (m, 5, Ph), 8.80 (s, 9, CH_3); IR (CCl_4) 1620 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 161 (M^+, 21), 105 (100). When an ether solution of this compound was stirred with aqueous hydrochloric acid, it was converted to **22f**: ^{1}H NMR (CCl_4) τ 2.42 (m, 2, *o*-H's), 2.67 (m, 3, *m*- and *p*-H's), 8.69 (s, 9, CH_3); IR (CCl_4) 1680 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 162 (M^+, 3), 105 (100). The second fraction was **24c** (16%): bp 139–140 °C (0.8 torr) [lit.[39] bp 114 °C (0.2 torr)]; solidified after standing for several months, mp 62–63 °C; ^{1}H NMR (CCl_4) τ 2.87 (m, 10, Ph), 5.90 (s, 2, CH_2Ph), 8.85 (s, 9, CH_3); IR (CCl_4) 1640 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 251 (M^+, 2), 91 (100). The IR and NMR spectra of the liquid and solid were identical.

GC analysis (column C, 150 °C) of such reaction mixtures had the following relative retention times: **23d** (1.0), **24c** (7.4). GC analysis of the crude product from the 1:6 reaction showed the presence only of **23d**. Distillation gave only **23d** (63%): bp 36–37 °C (0.18 torr).

Reaction of Benzylamine (19f) and Phenyllithium. GC analysis (column C) showed only two significant components. The first as biphenyl, presumably an impurity in the phenyllithium solution. The second component was **23e**: ^{1}H NMR (CCl_4) τ 0.29 (bs, 1, NH), 2.65 (m, 10, Ph); IR (CCl_4) 1605 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 181 (M^+, 58), 180 (100). Distillation gave a liquid that was mainly **23e** (33%): bp 123–139 °C (0.9 torr) [lit.[40] bp 127 °C (3.5 torr)]. However, weak alkyl C–H absorptions at 3000–2900 cm^{-1} in the IR spectrum and a weak absorption at τ 4.94 in the ^{1}H NMR spectrum suggested the presence of a small amount of **21b**. After the distillate had stood for several months, a small amount of a solid precipitated from it and was identified as **25c**: mp 155–157 °C (lit.[41] mp 153 °C); ^{1}H NMR (CCl_4) τ 2.27 (m, 2, Ph), 2.72 (m, 18, Ph), 4.43 (s, 1, CH); IR (CH_2Cl_2) 1622 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 347 (M^+, 29), 167 (100).

Reactions of Benzylamine (19f) and Methyllithium. GC analysis (column A, 205 °C) of the crude products from the normal reactions gave the following relative retention times: **19f** (1.0), **20** (9.0), **24d** (13). Heptadecane was used as the internal standard for calculating yields.

20: ^{1}H NMR (CCl_4) τ 1.68 (bs, 1, CH), 2.27 (m, 2, *o*-H's of PhCN), 2.73 (m, 8, other Ph H's), 5.23 (s, 2, CH_2); IR (CCl_4) 1645 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 195 (M^+, 52), 91 (100). The compound was identical with an authentic sample prepared from benzaldehyde and benzylamine.[42]

24d: ^{1}H NMR (CCl_4) τ 2.20 (m, 2, *o*-H's of PhCN), 2.72 (m, 8, other Ph H's), 5.34 (s, 2, CH_2Ph), 7.75 (s, 3, CH_3); IR (CCl_4) 1640 cm^{-1} (C=N); mass spectrum, m/z (relative intensity) 209 (M^+, 25), 91 (100).

Reactions of 1-Phenylethanamine (27) and *n*-Butyllithium. Typical GC conditions (column B, 200 °C) gave the following relative retention times: **5** (1.0), **29** (1.3), **22e** (2.0), **28** (3.7), **22d** (4.6). Three unidentified components (2.6, 5.6, 7.3) totaled about 10–20% of the total GC peak area in the analyses of the reactions that are entries 2 and 4–7 in Table II. Heptadecane was used as the internal standard for calculating yields in the 1:6 reaction, and tetradecane or octadecane in the others. Analysis of the 1:3 reaction for 5 h at ambient temperature (entry 1 in Table II) was of a distillate, bp 76–115 °C (0.3 torr), and of the 1:3 reaction for 5 h at reflux temperature (entry 3 in Table II) of a distillate, bp 40–80 °C (0.15 torr).

28: ^{1}H NMR (CCl_4) τ 2.75 (m, 5, Ph), 8.40 (m, 2, CH_2CN), 8.60 (s, 3, CH_3CN), 8.74 (m, 6, decreased by about 2 when the sample was shaken with D_2O, $(CH_2)_2CH_3$ and NH_2), 9.15 (m, 3, CH_3CH_2); IR (CCl_4) 3370 and 3300 (weak, NH stretch), 1600 (NH bend) cm^{-1}; mass spectrum, m/z (relative intensity) 176 (M^+, 1), 120 (100). The effects of adding europium tris(2,2,6,6-tetramethylheptane-3,5-dionate) upon the positions of ^{1}H NMR absorptions were consistent with this structure. When this reagent was added, the shifts of absorptions due to the *o*-H's, CH_3CN, and CH_2CN were similar, that due to the other CH_2's was about a third as great, and those for the *m*- and *p*-H's and CH_3CH_2 were very much smaller.

29: This compound was identified by having a retention time similar to that of the corresponding ketone, as did other imines on this GC column, and in forming that ketone upon hydrolysis.

Reaction of Cyclohexylamine (30) and *n*-Butyllithium. GC analysis (column A, 140 °C) gave two peaks shown to be due to **31** and **32** (relative retention times 1.0 and 1.6). Pentadecane as used as the internal standard for calculating yields.

32: ^{1}H NMR (CCl_4) τ 8.67 (m, 16, all CH_2's), 9.07 (m, 3, CH_3), 9.30 (bs, 2, disappears on shaking with D_2O, NH_2); IR (CCl_4) 1608 cm^{-1} (NH); mass spectrum, m/z (relative intensity) 155 (M^+, 7), 98 (100).

Reaction of Cyclopropylamine (33) and *n*-Butyllithium. GC analysis (column D, 100 °C) indicated the presence of one major and at least seven minor components. Distillation yielded a liquid that was virtually pure **22b**: bp 84–102 °C. A large amount of pot residue remained.

Reactions of Allylamine (1) and *n*-Butyllithium. GC analysis (column A, 205 °C) of the crude product showed one large and several small peaks. The large peak was due to **2**: ^{1}H NMR (CCl_4) τ 7.92 (bt, J = 7 Hz, 4, CH_2CO), 8.68 (m, 12, all other CH_2's), 9.07 (m, 6, CH_3); IR (CCl_4) 1713 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 170 (M^+, 8), 58 (100). Octadecane was used as the internal standard for determining the yield.

Reactions of Cinnamylamine (34) and *n*-Butyllithium. Distillation of the crude product gave a liquid, bp 106–168 °C (0.5 torr), and left a large pot residue. GC analysis (column B, 205 °C) of the distillate gave the following relative retention times: **35** (1.0), **36** (1.2), **37** (2.0), **38** (2.4).

35: ^{1}H NMR (CCl_4) τ 2.86 (m, 5, Ph), 7.27 (m, 4, $(CH_2)_2Ph$), 7.73 (bt, J = 7 Hz, 2, $CH_2(CH_2)_2CH_3$), 8.62 (m, 4, $(CH_2)_2CH_3$), 9.08 (m, 3, CH_3); IR (CCl_4) 1708 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 190 (M^+, 33), 91 (100). a 2,4-dinitrophenylhydrazone derivative, recrystallized from dichloromethane–methanol, had mp 132–132.5 °C (lit.[43] 133–134.5 °C).

36: ^{1}H NMR (CCl_4) τ 2.82 (m, 5, Ph), 7.23 (m, 4, $(CH_2)_2Ph$), 7.67 (m, 2, $CH_2(CH_2)_2CH_3$), 8.60 (m, 4, $(CH_2)_2CH_3$), 9.04 (m, 3,

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CH_3); IR (CCl_4) 1650 cm^{-1} (C=N). Samples of this compound were somewhat contaminated with **35**.[32] When a portion of the crude product was stirred with aqueous hydrochloric acid (5%) prior to GC analysis, **36** was not observed.

37: ^{1}H NMR (CCl_4) τ 2.87 (m, 5, Ph), 6.96 (m, 1, CH), 7.44 (bd, J = 6 Hz, 2, $\mathrm{CHC}H_2\mathrm{CO}$), 7.87 (bt, J = 6 Hz, 2, $\mathrm{CH_2C}H_2\mathrm{CO}$), 8.78 (m, 10, all other CH_2's), 9.15 (m, 6, CH_3); IR (CCl_4) 1704 cm^{-1} (C=O); mass spectrum, m/z (relative intensity) 246 (M^+, 4), 91 (100).

38: ^{1}H NMR (CCl_4) τ 2.82 (m, 5, Ph), 6.92 (m, 1, CH), 7.42 (bd, J = 7 Hz, 2, $\mathrm{CHC}H_2\mathrm{CN}$), 7.92 (m, 2, $\mathrm{CH_2C}H_2\mathrm{CN}$), 8.68 (m, 10, all other CH_2's), 9.08 (m, 6, CH_3); IR (CCl_4) 1640 cm^{-1} (C=N). Samples of this compound were somewhat contaminated with **37**.[32]

Reactions of 3-Phenyl-2-propyn-1-amine (3) and *n*-Butyllithium. GC analysis (column A, 150 °C) of the crude products gave the following relative retention times: **4** (1.0), **5** (2.0). Hexadecane was used as the internal standard for determining yields.

Reactions of Benzonitrile (40) with *n*-Butyllithium. GC analyses (column C, 150 °C) of the crude products had the following relative retention times: **5** (1.0), **22d** (6.0), and three unidentified components (2.0, 6.9, and 8.0). Tetradecane was used as the internal standard for determining yields. The peaks due to the unidentified components constituted 0%, 17%, and 50% of the total GC peak area of a 1:1 reaction and 4%, 18%, and 8% of a 1:3 reaction.

Reactions of 22a and 23a with 19a. GC analysis (column A, 120 °C initially, but raised at a rate of 10 °C/min to 185 °C after **23a** had eluted) gave the following retention times: **19a** (1.0), **22a** (5.0), **23a** (6.0), **24a** (13). GC analysis of a solution of a mixture of **22a** and **23a** (18 mg) in diethyl ether (0.5 mL) gave a peak area ratio **23a**:(**22a** + **23a**) of 0.31. This solution was mixed rapidly with a solution of **19a** (17 mg) in diethyl ether (0.5 mL). GC analysis of a sample injected after only 1 min showed the absence of **23a** and a substantial peak for **24a**; the peak area ratio **24a**:(**22a** + **24a**) was 0.53. In another reaction, a solution of **22a** (20 mg) in diethyl ether (0.5 mL) was mixed rapidly with a solution of **19a** (18 mg) in diethyl ether (0.5 mL). The peak area ratio **24a**:(**22a** + **24a**) was 0 after 1 min, 0.05 after 30 min, and 0.30 after 522 min.

Reactions of 22f and 23d with 19f. GC analysis (column A, 145 °C initially, but raised at a rate of 8 °C/min to 204 °C after **22f** had eluted) gave the following relative retention times: **19f** (1.0), **23d** (1.9), **22f** (2.3), **24c** (6.4). GC analysis of a solution of a mixture of **22f** and **23d** (41 mg) in diethyl ether (0.5 mL) gave a peak area ratio **23d**:(**22f** + **23d**) of 0.33. This solution was mixed rapidly with a solution of **19f** (29 mg) in diethyl ether (0.5 mL). GC analysis of a sample injected after only 1 min gave a peak area ratio **23d**:(**22f** + **23d**) of 0.22 and a peak area ratio **24c**:(**22f** + **23d** + **24c**) of 0.14. After 45 min, the same ratios were 0.16 and 0.25, respectively. A solution of **22f** (24 mg) in diethyl ether (0.5 mL) was mixed rapidly with a solution of **19f** (17 mg) in diethyl ether (0.5 mL). GC analysis showed no **24c**, even after 180 min.

Acknowledgment. We are grateful to the National Science Foundation for support of this research and for aiding in the purchase of the NMR spectrometers and the mass spectrometer. We thank Dr. Raymond C. McLane for performing some control experiments.

Registry No. **1**, 107-11-9; **2**, 33083-83-9; **3**, 78168-74-8; **4**, 536-74-3; **5**, 502-56-7; **19a**, 111-26-2; **19b**, 107-10-8; **19c**, 64-04-0; **19d**, 5813-64-9; **19e**, 107-15-3; **19f**, 100-46-9; **20**, 780-25-6; **21a**, 61501-03-9; **21b**, 91-00-9; **22a**, 820-29-1; **22b**, 106-35-4; **22c**, 25870-62-6; **22d**, 1009-14-9; **22d** 2,4-dinitrophenylhydrazone, 2121-88-2; **22e**, 98-86-2; **22f**, 938-16-9; **23a**, 37027-36-4; **23b**, 29097-52-7; **23c**, 16659-09-9; **23d**, 33611-54-0; **23e**, 1013-88-3; **24a**, 37027-39-7; **24b**, 86885-94-1; **24c**, 86885-95-2; **24d**, 14428-98-9; **25a**, 37027-40-0; **25b**, 86885-96-3; **25c**, 5350-59-4; **26**, 86885-97-4; **27**, 98-84-0; **28**, 33083-81-7; **29**, 36653-37-9; **30**, 108-91-8; **31**, 108-94-1; **32**, 2626-61-1; **33**, 765-30-0; **34**, 4360-51-4; **35**, 19969-04-1; **35** 2,4-dinitrophenylhydrazone, 19969-05-2; **36**, 86885-98-5; **37**, 30242-38-7; **38**, 86885-99-6; **40**, 100-47-0; *n*-BuLi, 109-72-8; phenyllithium, 591-51-5; methyllithium, 917-54-4.

Synthesis of Heptiptycenes with Face-to-Face Arene Rings via a 2,3:6,7-Anthradiyne Equivalent

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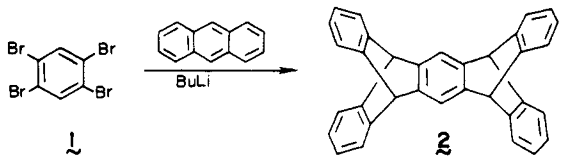
Received April 20, 1983

1,2,4,5-Tetrabromobenzene reacts with 2 equiv of butyllithium and furan to give 1,4:5,8-diepoxy-1,4,5,8-tetrahydroanthracene (**3**). Both double bonds in **3** are effective dienophiles. Thus **3** gives a bis(adduct) with anthracene which on dehydration gives the pentiptycene **6**. That is, **3** is a 2,3:6,7-anthradiyne equivalent. The central anthracene moiety in **6** adds benzyne to give the novel heptiptycene **12** with face-to-face arene rings. Analogous experiments with a dimethoxy analogue are also described. The crystal structure of *anti*-diepoxide **3** was determined.

Diaryne equivalents[1] have considerable potential for the rapid assembly of multiring systems. For example, the pentiptycene **2** was prepared in one step from anthracene and the diaryne equivalent 1,2,4,5-tetrabromobenzene (**1**).[2]



In this paper we use a different type of diaryne equivalent to synthesize analogues of **2** in which the "central" ring is an anthracene moiety. These analogues react with benzyne to give iptycenes with face-to-face arene rings.

Results and Discussion

Treatment of **1** with *n*-butyllithium and excess furan gave the bis(adduct) **3**.[3] Both isomers (syn and anti) are

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[†] To whom inquiries regarding the X-ray structure of **3** should be directed.

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(3) This adduct was first prepared by Dr. Yoshikazu Takehira, whom we thank.