Preparation of a Series of Highly Hindered Secondary Amines, Including Bis(triethylcarbinyl)amine

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A series of highly branched secondary amines was prepared by coupling propargylamines with propargyl chlorides. Hydrogenation of the resultant dipropargylamines was accomplished with Raney nickel in the presence of potassium hydroxide. The resultant amines, including bis(triethylcarbinyl)amine, are among the most hindered secondary amines reported to date. The pK_a values of the conjugate acids of the series of secondary amines exhibit a regular decrease with increasing size of the amine. The bulkier members of the series are inert to methyl iodide. Bis(triethylcarbinyl)amine reacts with boron trifluoride etherate to give a primary amine adduct and 3-ethyl-2-pentene.

Secondary amines with highly branched alkyl groups are valuable synthetic reagents. Major applications depend on the increased substrate selectivity resulting from steric factors. For example, 2,2,6,6-tetramethylpiperidine is probably the most hindered commercially available secondary amine. The lithium base (LiTMP) of this amine[2] is largely proton selective and nonnucleophilic. A variety of applications based on this useful property have been reported by Olofson.[3] Similarly, the *N*-chloro derivative of *tert*-butylneopentylamine[4] was shown by Deno[5] to produce a radical cation which exhibits increased selectivity for secondary hydrogen over tertiary hydrogen abstraction. Clearly, it would be useful to know if secondary amines with more hindered alkyl groups would show even greater substrate selectivity.

A report by Brown[6] on the base strength of potassium alkoxides as a function of alkyl group size suggested a second reason for preparing such amines. Potassium tricyclohexylmethoxide is an appreciably stronger base than potassium *tert*-butoxide (by about 1.2 pK_a units). This effect is attributed to decreased solvation or ion-pair stabilization of the more hindered base. It would be useful to know if such an effect also applies to the amide bases derived from hindered secondary amines.

Accordingly, we have prepared a series of highly hindered secondary amines. We report here the details of the syntheses of these amines and some observations on their chemistry.

Results and Discussion

Coupling Reaction. The sequence used to prepare the series of secondary amines is summarized in eq 1–5. The propargyl alcohols of eq 1 and propargyl chlorides of eq 2 can be obtained in nearly quantitative yields or are commercially available in many cases. The key steps in the synthesis, eq 3 and 4, are based on the observations of Hennion[7,8] that tertiary propargyl chlorides react with nucleophiles (HNu in eq 6) in the presence of strong base

$$R_2CO + NaC{\equiv}CH \rightarrow HC{\equiv}CCR_2OH \quad (1)$$

$$HC{\equiv}CCR_2OH + HCl \rightarrow HC{\equiv}CCR_2Cl \quad (2)$$

$$HC{\equiv}CCR_2Cl + NH_3 \xrightarrow{NaNH_2} HC{\equiv}CCR_2NH_2 \quad (3)$$

$$HC{\equiv}CCR_2NH_2 + HC{\equiv}CCR_2Cl \rightarrow (HC{\equiv}CCR_2)_2NH \quad (4)$$

$$(HC{\equiv}CCR_2)_2NH + H_2 \xrightarrow{Ni} (CH_3CH_2CR_2)_2NH \quad (5)$$

Table I. Coupling of Propargylamines with Propargyl Chlorides

$$HC{\equiv}CCR_1R_2NH_2 + HC{\equiv}CCR_3R_4Cl \rightarrow HC{\equiv}CCR_1R_2NHR_3R_4CC{\equiv}CH$$

R_1	R_2	R_3	R_4	% yield[a]
CH_3	CH_3	CH_3	CH_3	70
CH_3	CH_3CH_2	CH_3	CH_3	62
CH_3	CH_3CH_2	CH_3	CH_3CH_2	55
CH_3CH_2	CH_3CH_2	CH_3	CH_3CH_2	55
CH_3CH_2	CH_3CH_2	CH_3CH_2	CH_3CH_2	48
$-CH_2(CH_2)_3CH_2-$		$-CH_2(CH_2)_3CH_2-$		66

[a] Isolated yield.

$$HC{\equiv}CCR_2Cl \xrightarrow{base} {}^-C{\equiv}CCR_2Cl \rightarrow {}^-C{\equiv}CCR_2^+ \xrightarrow{HNu} HC{\equiv}CCR_2Nu \quad (6)$$

(usually KOH or $NaNH_2$) to give clean substitution at the tertiary carbon, presumably by a zwitterionic (carbene) mechanism. By this means, Hennion[9] synthesized compound 1 in a yield of 47% (eq 7).

$$HC{\equiv}CC(CH_3)_2Cl + HC{\equiv}CC(CH_3)_2NH_2 \xrightarrow[Cu^0,\ Cu_2Cl_2,\ 8\ days,\ 30\ °C]{40\%\ KOH} [HC{\equiv}CC(CH_3)_2]_2NH \quad (7)$$

We find that the coupling procedure exemplified by eq 7 does not give significant yields when applied to more hindered reactants. The coupling of 3-amino-3-ethyl-1-pentyne (**2**) with the corresponding chloride was attempted with a variety of bases (eq 8). No detectable amount of the coupled product, **3**, was obtained with 40% KOH in

$$\underset{\mathbf{2}}{HC{\equiv}CC(CH_3CH_2)_2NH_2} + HC{\equiv}CC(CH_3CH_2)Cl \xrightarrow[base]{Cu^0,\ Cu_2Cl_2} \underset{\mathbf{3}}{[HC{\equiv}CC(CH_3CH_2)_2]_2NH} \quad (8)$$

(1) Dow summer fellow, 1980.
(2) Rathke, M. W.; Kow, R. *J. Am. Chem. Soc.* **1972**, *94*, 6854.
(3) (a) Olofson, R. A.; Dougherty, C. M. *J. Am. Chem. Soc.* **1973**, *95*, 582. (b) *Ibid.* **1973**, *95*, 581.
(4) Hennion, G. F.; Hanzel, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 4908.
(5) Deno, N. C.; Fishbein, R.; Wyckoff, J. C. *J. Am. Chem. Soc.* **1971**, *93*, 2065.
(6) Brown, C. A. *J. Chem. Soc., Chem. Commun.* **1974**, 680.
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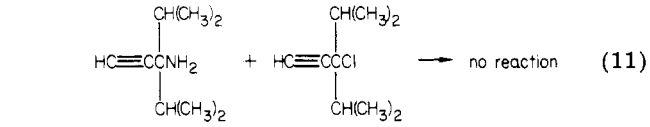
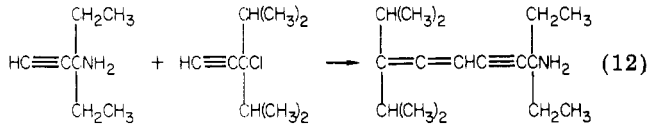
H_2O or with NaH, KH, or $KOC(CH_3)_3$ in tetrahydrofuran[10] (THF). However, use of an extra equivalent of **2** as base gave, after 3 days of reaction at 4 °C in DMF, a 60% GLC yield of **3**. Triethylamine or diisopropylamine in place of excess **2** gave only low yields (<7%) of **3**. The coupling reaction fails when the Cu^0–Cu_2Cl_2 catalyst is omitted or with the saturated amine **4**, derived from **2** (eq 9), and it

$$(CH_3CH_2)_3CNH_2 + HC{\equiv}CC(CH_3CH_2)_2Cl \rightarrow \underset{\mathbf{4}}{} \text{no coupled product} \quad (9)$$

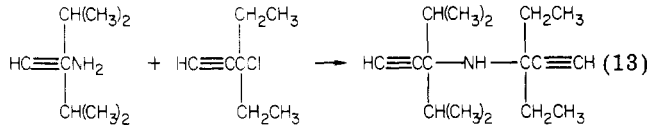
$$CH_2{=}CHC(CH_3CH_2)_2NH_2 + HC{\equiv}CC(CH_3CH_2)_2Cl \rightarrow \underset{\mathbf{5}}{} CH_2{=}CHC(CH_3CH_2)_2NH(CH_2CH_3)_2CC{\equiv}CH \quad (10)$$
17% yield

is less effective with the olefinic amine **5** (eq 10). Results obtained for the coupling reaction (eq 4) for a series of propargyl chlorides with propargyl amines are given in Table I. As expected, the lowest yields were obtained with the more highly substituted members of the series. Results obtained with even more hindered reagents (eq 11–13) help to define the ultimate steric limitations of the reaction.





6, 10% yield

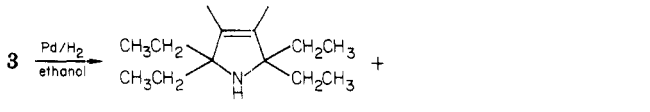


7, 5% yield

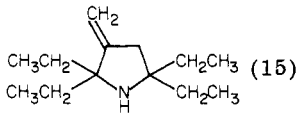
Hydrogenation of Propargyl Amines. Hydrogenation (eq 5) of the series of propargyl amines of Table I was by no means as straightforward as anticipated. Hydrogenation of **3** or its hydrochloride with platinum catalysts in a variety of solvents gave almost exclusively the corresponding primary amine (eq 14). Palladium catalysts gave

$$3 \xrightarrow[H_2,\ 3\ atm]{PtO_2} \underset{90\text{–}100\%}{(CH_3CH_2)_3CNH_2} \quad (14)$$

similar results in aprotic solvents. Surprisingly, in absolute ethanol the major products were the heterocycles **8** and **9** (eq 15).[11] A successful preparation of the desired bis-



8, 48% yield



9, 15% yield

(10) Easton, N. R.; Dillard, R. D.; Doran, W. J.; Livezey, M.; Morrison, D. E. *J. Org. Chem.* **1961**, *26*, 3772.

(11) Similar reactions have been observed for sodium/NH_3 reduction of related propargylamines: Hennion, G. F.; Ode, R. H. *J. Org. Chem.* **1966**, *31*, 1975.

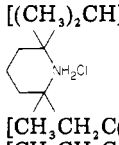
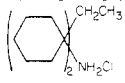
Table II. Hydrogenation of Dipropargylamines

$$HC{\equiv}CCR_1R_2NHR_3R_4CC{\equiv}CH \xrightarrow[KOH,\ Ni]{H_2} CH_3CH_2CR_1R_2NHR_3R_4CCH_2CH_3$$

R_1	R_2	R_3	R_4	% yield[a]
CH_3	CH_3	CH_3	CH_3	80
CH_3	CH_3CH_2	CH_3	CH_3	78
CH_3	CH_3CH_2	CH_3	CH_3CH_2	75
CH_3CH_2	CH_3CH_2	CH_3	CH_3CH_2	75
CH_3CH_2	CH_3CH_2	CH_3CH_2	CH_3CH_2	72
$-CH_2(CH_2)_3CH_2-$		$-CH_2(CH_2)_3CH_2-$		80

[a] Isolated yield.

Table III. Acidity Constants of R_2NH_2Cl in 90% Ethanol

R_2NH_2Cl	pK_a
$[(CH_3)_2CH]_2NH_2Cl$	9.8[a]
	10.1[b]
$[CH_3CH_2C(CH_3)_2]_2NH_2Cl$	9.9
$[CH_3CH_2C(CH_3)_2NH_2C(CH_3)(CH_2CH_3)_2]Cl$	9.4
$[(CH_3CH_2)_2C(CH_3)]_2NH_2Cl$	8.7
$[(CH_3CH_2)_3CNH_2C(CH_3)(CH_2CH_3)_2]Cl$	8.0
$[(CH_3CH_2)_3C]_2NH_2Cl$	7.1
	9.0

[a] Lit.[23a] pK_a = 11.07 (water solvent). [b] Lit.[23b] pK_a = 11.24 (water solvent).

(triethylcarbinyl)amine (**10**) was achieved in 20% yield by low-pressure hydrogenation over W_2 grade Raney Nickel (eq 16). The major side reaction was again hydrogenolysis

$$3 \xrightarrow[H_2,\ ethanol]{Ni} \underset{\mathbf{10}}{[(CH_3CH_2)_3C]_2NH} \quad (16)$$

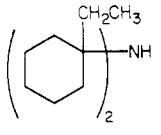
to the primary amine. More reactive grades of Raney nickel (W_4 and W_6) gave more hydrogenolysis. Presumably hydrogenolysis occurs at the diallylamine stage since it was possible to isolate the diallylamine corresponding to **3** in 80% yield by interrupting the hydrogenation. Finally, a 72% yield of **10** was obtained by adding an excess of potassium hydroxide to the W_2 catalyst to suppress hydrogenolysis. Results obtained with a series of propargylamines with this last procedure are given in Table II.

Acidity Constants of Amine Hydrochlorides. The acidity constants of the amine hydrochlorides obtained from the secondary amines of Table II were determined by potentiometric titration with standard ethanolic potassium hydroxide. Ethanol (90%) was chosen as the solvent since both amine and amine hydrochloride are completely soluble in this solvent at the concentrations employed (0.01 M).[12] Results are given in Table III. For reference, values obtained with the hydrochlorides of diisopropylamine and 2,2,6,6-tetramethylpiperidine are also given. A regular increase in acidity (decrease in pK_a) is observed with increasing size of the alkyl groups. The most highly substituted amine (**10**) in the series appears to be the weakest base (pK_a of conjugate acid = 7.1) of any saturated aliphatic amine yet reported. Presumably, de-

(12) The effect of increasing ethanol concentration on apparent pK_a values of typical aliphatic amines is to lower the observed pK_a by approximately 1–2 units (relative to water) and to compress the range of pK_a values for a given series of amines.[23] Thus, the differences in pK_a values shown in Table III are expected to be even greater in water solution.

creased solvation of the highly hindered ammonium salt accounts for this effect.[13,14] Similar observations, of smaller magnitude, were reported by Brown for highly branched pyridine bases.[13] Interestingly, Brown also reports that 2,6-di-*tert*-butylpyridine does not form a simple hydrochloride; only a dihydrochloride is formed. He attributes this effect to the inability of chloride ion to form a hydrogen bond to the nitrogen-bound hydrogen. A second molecule of hydrogen chloride is then required to form a hydrogen bond with the chloride ion. We observed that treatment of amine **10** with an excess of either hydrochloric acid or hydrogen chloride in ether gives a dihydrochloride. The second molecule of hydrogen chloride was not removed even after prolonged heating under vacuum. However, the monohydrochloride of **10** was readily obtained by treating the amine with slightly less than 1 equiv of hydrochloric acid.

Reaction of Amines with Methyl Iodide. The rate of reaction of a number of secondary amines with methyl iodide was briefly studied. When 2,2,6,6-tetramethylpiperidine was mixed with an equivalent amount of methyl iodide in chloroform solution, a white precipitate of the corresponding *N*-methyl ammonium iodide was formed within a few minutes. Under similar conditions no precipitate was formed with amines **10** or **11** and, after several



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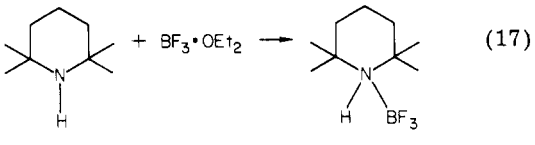
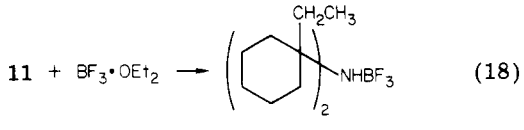
weeks, NMR analysis of the reaction mixtures showed only unreacted methyl iodide and secondary amine. Addition of excess methyl iodide to **10** or **11** in refluxing ethanol again gave only recovered starting amine.

Reaction of Amines with Boron Trifluoride. Addition of boron trifluoride etherate to either 2,2,6,6-tetramethylpiperidine or amine **11** in hexane solution gave, within a few minutes, a white precipitate of the corresponding adducts (eq 17 and 18). Under the same con-



(17)



(18)

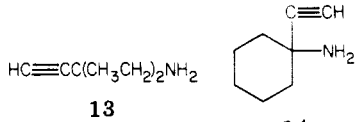
ditions, amine **10** formed only the adduct of a secondary amine (**12**) and the olefin, 3-ethyl-2-pentene. It seems likely that the boron trifluoride adduct of this hindered amine is formed but rapidly eliminates even at room temperature as shown in eq 19.

$$BF_3{\cdot}OEt_2 \rightarrow [(CH_3CH_2)_3C]_2NHBF_3 \rightarrow CH_3CH{=}C(CH_2CH_3)_2 + (CH_3CH_2)_3CNH_2BF_3 \quad (19)$$

12

Conclusions

The synthesis of a series of highly hindered secondary amines has been achieved. Studies on synthetic applications, particularly of the corresponding lithium amides, are in progress. While the syntheses of the amines are straightforward and readily adaptable to a large scale, the number of steps involved may be a handicap to their practical application. In this regard we note that both propargylamines **13** and **14** are commercially available and the preparation of the corresponding secondary amines (**10** and **11**) is greatly simplified.



13 **14**

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Elemental analyses were performed by Spang Microanalytical Labs, Inc. IR spectra were obtained as neat films on NaCl plates with a Perkin-Elmer 237-B spectrophotometer, and ^1H NMR spectra were taken on a Varian T-60 spectrometer with Me_4Si internal standard. ^{13}C NMR spectra were taken with a Varian CFT-20 spectrometer and are calibrated in parts per million downfield from Me_4Si; the J values are given in hertz. Mass spectra were taken with a Hitachi RMU-6 mass spectrometer. Gas–liquid chromatography (GLC) was performed with a Varian 920 gas chromatograph. All reagents and solvents were dried and purified before use. Absolute ethanol (Gold Shield) was used for all hydrogenations. Dimethylformamide (DMF) was dried over calcium hydride and distilled under vacuum. Anhydrous ammonia (Matheson) was used without further drying. Anhydrous cuprous chloride (Cu_2Cl_2), used for converting the propargyl alcohols to the propargyl chlorides, was obtained as a 95% pure brown powder from Ventron. Cuprous chloride was prepared immediately before use in the amine coupling reaction by a published procedure.[15] Copper bronze powder was obtained from the Illinois Bronze Powder Co. Raney nickel alloy was obtained from Ventron, Inc.

Propargyl Alcohols. 3-Methyl-1-butyn-3-ol, 3-methyl-1-pentyn-3-ol, and 1-ethynyl-1-cyclohexanol were commercially available (Aldrich). All other propargyl alcohols were synthesized from the corresponding ketones by previously reported methods.[16,17]

Propargyl Chlorides. All propargyl chlorides were prepared[19] from the corresponding propargyl alcohols and used without further purification. All were dried and stored over anhydrous potassium carbonate. The purity of the propargyl chlorides was determined by GLC (10% Carbowax 20M on Chromasorb W, AW-DMCS).

Propargylamines. 1-Ethynylcyclohexylamine and 3-amino-3-ethyl-1-pentyne were obtained commercially (Aldrich). All other propargylamines were made by a previously reported method.[18]

Preparation of 3-Ethyl-1-pentyn-3-ol. This compound was prepared according to the procedure of Vaughn and co-workers,[16] and its preparation is representative for the preparation of tertiary propargyl alcohols. A 5-L, three-necked, round-bottomed flask was fitted with an efficient mechanical stirrer mounted through a glass bushing along with two gas inlet tubes for acetylene and ammonia, both of which were immersed in liquid ammonia. The third neck of the flask was fitted with a dry ice condenser which was connected to a KOH drying tower by rubber tubing. The flask was flame-dried, purged with NH_3 gas, and insulated with a 5-L heating mantle. The flask was charged with 3500 mL of liquid ammonia, the stirrer was started and a rapid stream of acetylene was passed into the solution for about 30 min to saturate the solution. Additional ammonia gas was condensed in from time to time to keep the solution volume at about 4 L. Sodium (115

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(17) Midland, M. M. *J. Org. Chem.* **1975**, *40*, 2250.
(18) Hennion, G. F.; Teach, E. G. *J. Am. Chem. Soc.* **1953**, *75*, 1653.
(19) Hennion, G. F., Boisselle, A. P. *J. Org. Chem.* **1961**, *26*, 725.

g, 5 mol) was cut into strips and added at such a rate that the entire solution did not turn blue. The addition required about 1.5 h, depending on the rate of passage of acetylene. Stirring and addition of acetylene was continued for 1 h.

3-Pentanone (430.6 g, 4.95 mol, 98%) was added dropwise over 1 h to the ammonia solution. The solution was stirred overnight. Then the heating mantle was removed, and the reaction mixture was allowed to stand until all the ammonia had evaporated. The solid residue was decomposed by adding abut 1500 mL of ice and water. The mixture was carefully acidified with 50% H_2SO_4 (300–350 mL). The organic layer was dissolved in 400 mL of ether and washed with 200 mL of brine. The original aqueous phase and the brine wash were then extracted with two 200-mL portions of ether. The combined ethereal solutions were dried over anhydrous $MgSO_4$ and filtered, and the ether was removed under reduced pressure. The product was distilled under reduced pressure through a 15-cm Vigreux column. The yield of 3-ethyl-1-pentyn-3-ol was 520 g (93% yield): bp 135–136 °C; ν_{max} 3413, 3300, 2970, 1470, 1375, 910 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (6 H, t, J = 7), 1.65 (4 H, q, J = 7), 2.3 (1 H, s), 2.38 (1 H, s); n^{25}_D 1.4207.

Preparation of 4-Methyl-3-isopropyl-1-pentyn-3-ol. Application of the above procedure to 2,4-dimethyl-3-pentanone gave 133 g of 4-methyl-3-isopropyl-1-pentyn-3-ol: 89% yield; bp 69 °C (16 mm); ν_{max} 3490, 3315, 2970, 1475, 985 cm^{-1}; NMR ($CDCl_3$) δ 0.98 (12 H, d, J = 7), 1.92 (3 H, m, J = 7), 2.35 (1 H, s); n^{25}_D 1.4435.

Preparation of 3-Chloro-3-ethyl-1-pentyne. The following procedure for the conversion of 3-ethyl-1-pentyn-3-ol to 3-chloro-3-ethyl-1-pentyne is representative for preparing the chlorides.[19] A 1-L, three-necked flask provided with a magnetic stirrer, thermometer, and dropping funnel was charged with 56 g (0.5 mol) of calcium chloride, 40 g (0.4 mol) of Cu_2Cl_2 (95% brown powder), 400 mg of copper bronze powder, and 430 mL (5 mol) of cold concentrated hydrochloric acid. The mixture was flushed with argon and cooled (ice bath) with stirring. One mole of 3-ethyl-1-pentyn-3-ol (112.2 g) was added dropwise over 30 min. Stirring was continued for 1 h (0–5 °C). The upper organic layer was separated and washed immediately with three 100-mL portions of cold concentrated hydrochloric acid, with two 100-mL portions of water, and once with 100-mL portion of saturated aqueous sodium carbonate. The colorless product was dried superficially with anhydrous K_2CO_3 and then thoroughly with fresh K_2CO_3. Analysis of the sample by GLC (10% Carbowax 20M on Chromasorb W) showed the sample to be 96% pure. The chloride was used without further purification. The total isolated yield of the chloride was 73%: ν_{max} 3290, 2970, 1950, 1460, 1380, 1315, 835 cm^{-1}; NMR ($CDCl_3$) δ 1.47 (6 H, t, J = 7), 1.92 (4 H, q, J = 7), 2.58 (1 H, s); n^{25}_D 1.4387.

Preparation of 3-Chloro-3-methyl-1-pentyne. Application of the above procedure to 3-methyl-1-pentyn-3-ol (196 g, 2 mol) gave 176 g of 94% pure product (76% yield). This solution was used without further purification: ν_{max} 3290, 2975, 1950, 1460, 1380, 1210, 815, 750 cm^{-1}; NMR ($CDCl_3$) δ 1.05 (3 H, t, J = 7), 1.73 (3 H, s), 1.93 (2 H, q, J = 7), 2.53 (1 H, s); n^{25}_D 1.3749.

Preparation of 3-Chloro-3-methyl-1-butyne. Application of the above procedure to 2-methyl-3-butyn-2-ol (168 g, 2 mol) followed by distillation at atmospheric pressure through a 20-cm Vigreux column gave 62 g of 97% pure product: 30% yield; bp 74–76 °C; ν_{max} 3290, 2110 cm^{-1}; NMR ($CDCl_3$) δ 1.82 (6 H, s), 2.57 (1 H, s); n^{25}_D 1.4156.

Preparation of 3-Chloro-4-methyl-3-isopropyl-1-pentyne. Application of the above procedure to 4-methyl-3-isopropyl-1-pentyn-3-ol (137 g) gave 115 g of the corresponding propargyl chloride (70%), 94% pure by GLC. The chloride was used without further purification: bp 57–60 °C (15 mm); ν_{max} 3290, 2960, 1475, 1390, 810 cm^{-1}; NMR ($CDCl_3$) δ 1.10 (12 H, d, J = 6), 2.13 (2 H, m, J = 6), 2.55 (1 H, s); n^{25}_D 1.4559.

Preparation of 3-Amino-3-ethyl-1-pentyne. The following procedure for converting 3-chloro-3-ethyl-1-pentyne into 3-amino-3-ethyl-1-pentyne is adapted from a published procedure[18] and is representative for preparing all other primary propargylamines from the corresponding propargyl chlorides. Sodium (24 g, 1.04 mol) was converted to the amide (catalyzed by 0.3 g of $FeCl_3$) in 1 L of liquid ammonia (anhydrous) in a 3-L, three-necked, round-bottomed flask provided with a mechanical stirrer, dry ice condenser, and a long stem gas inlet tube for introducing ammonia. Then 130.6 g of 96% pure 3-chloro-3-ethyl-1-pentyne (0.96 mol) diluted with 4 volumes of anhydrous ether was added dropwise over a 1.5-h period with continuous stirring. The flask was insulated with a 3-L heating mantle and allowed to stir overnight. The ammonia was allowed to evaporate, and chopped ice (500 g) and ether (150 mL) were then added. The ether layer was separated and the aqueous layer extracted once with 100 mL of ether. The combined ethereal extract was washed with cold water and filtered. The extract was acidified with concentrated HCl (60 mL). The ether layer was discarded and the solution was extracted once with 50 mL of ether. The aqueous solution was then treated with 29 g of NaOH in 30 mL of water to release the amine, which was recovered by extraction with ether. Distillation gave 81.2 g (73% yield) of pure 3-amino-3-ethyl-1-pentyne: bp 36–38 °C (2 mm); ν_{max} 3360, 3290, 3280, 2080 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (6 H, t, J = 7), 1.53 (6 H, m), 2.27 (1 H, s); n^{25}_D 1.4392.

Preparation of 3-Amino-3-methyl-1-butyne. About 105 g of 97% pure 3-chloro-3-methyl-1-butyne (1.0 mol) was added to sodamide (1.1 mol) in liquid amonia. After workup, 35 g (42% yield) of 3-amino-3-methyl-1-butyne was obtained: bp 79–80 °C (760 mm); ν_{max} 3370, 3290, 3210, 1620 cm^{-1}; NMR ($CDCl_3$) δ 1.4 (6 H, s), 1.67 (2 H, br s), 2.25 (1 H, s); n^{25}_D 1.4180.

Preparation of 3-Amino-3-methyl-1-pentyne. 3-Chloro-3-methyl-1-pentyne (120 g, 97%, 1.0 mol) was added to sodamide (1.1 mol) in liquid ammonia. After workup and distillation, 59 g (61% yield) of 3-amino-3-methyl-1-pentyne was obtained: bp 53–54 °C (100 mm); ν_{max} 3360, 3300, 3290, 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (3 H, t, J = 7), 1.53 (4 H, m), 2.25 (1 H, s); n^{25}_D 1.4302.

Preparation of 3-Amino-4-methyl-3-isopropyl-1-pentyne. 3-Chloro-4-methyl-3-isopropyl-1-pentyne (51 g, 0.32 mol) was added to sodamine (0.35 mol) in liquid ammonia. After workup and distillation, 14.5 g (41% yield) of 3-amino-4-methyl-3-isopropyl-1-pentyne was obtained: bp 56–67 °C (3 mm); ν_{max} 3370, 3290, 3250 cm^{-1}; NMR ($CDCl_3$) δ 0.98 (12 H, d, J = 6), 1.27 (2 H, br s), 1.85 (2 H, m, J = 6), 2.2 (1 H, s); n^{25}_D 1.4501.

Preparation of 3-Amino-3-ethyl-1-pentene from 3-Amino-3-ethyl-1-pentyne. This experiment was adapted from a previously published procedure.[20] Sodium metal (2.3 g, 0.1 mol) was added in small pieces with stirring to a solution of 22.2 g (0.2 mol) of 3-amino-3-ethyl-1-pentyne in a 500-mL, three-necked, round-bottomed flask containing 200 mL of anhydrous liquid ammonia. Ammonium chloride (0.1 mol, 5.4 g) was then added slowly. Alternate additions of sodium and ammonium chloride were repeated until a total of 11.3 g (0.47 mol) of sodium and 27 g (0.5 mol) of ammonium chloride had been added. A constant total volume was maintained by periodic addition of ammonia. Ether (50 mL) was added, and the liquid ammonia was allowed to evaporate overnight. The mixture was filtered, and the solid was washed with two 50-mL portions of ether. The combined ether solutions were dried over anhydrous K_2CO_3. Distillation gave 9.44 g (42% yield) of 3-amino-3-ethyl-1-pentene: bp 128–129 °C (760 mm); ν_{max} 3350, 3290, 3075, 1685 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (8 H, q, J = 7), 1.42 (4 H, q, J = 7), 4.8–5.9 (3 H, m).

Attempted Coupling of 3-Amino-3-ethyl-1-pentyne with 3-Chloro-3-ethyl-1-pentyne in Aqueous KOH Solution. This experiment was adapted from a previously published procedure.[20] 3-Amino-3-ethyl-1-pentyne (4.5 g, 40 mmol), 2 mL of 40% KOH solution, 10 mg of copper bronze powder, and 8.6 g of 3-chloro-3-ethyl-1-pentyne were mixed together and maintained at 25–30 °C. After 24 h, an additional 30-mL portion of KOH solution and 10 mg of copper bronze were added. Five additional 30-mL portions of KOH were added, one after each 24-h period. After the eighth day, an aliquot of the sample's organic top layer was analyzed by GLC (10% Carbowax 20M Chromasorb W, AW-DMCS treated, 6-ft column). Analysis of the separated components indicated that the propargyl chloride had hydrolyzed to the propargyl alcohol, and the primary amine was recovered quantitatively. No high-boiling coupled products were seen.

Attempted Coupling of 3-Amino-3-ethyl-1-pentyne with 3-Chloro-3-ethyl-1-pentyne with Equimolar Quantities of either KH or $KOC(CH_3)_3$. Potassium hydride suspension (2

(20) Hennion, G. F.; DiGiovanna, C. V. *J. Org. Chem.* **1965**, *30*, 2645.

mmol, 0.4 mL of 5.4 M KH) was injected into a flame-dried, 10-mL, round-bottomed flask fitted with septum inlet, a flow control valve, and a Teflon-coated stirring bar. The flask was flushed with argon. The mineral oil was removed via syringe by washing with three 2-mL aliquots of dry pentane. Copper bronze (15 mg) was suspended in 2 mL of dry THF and injected into the flask. Then 1 mmol of 3-amino-3-ethyl-1-pentyne was injected. The flask was thermostated at 22 °C, and a gas manometer was attached. Then 0.16 g (1 mmol) of 3-chloro-3-ethyl-1-pentyne was injected dropwise. About 0.8 mmol of H_2 was evolved over a 5-h period. After the reaction was quenched with H_2O (0.5 mL), no coupled secondary amine was detected by GLC. Identical results were obtained with NaH and $KOC(CH_3)_3$. In each case, there was partial H_2 evolution, but no coupled amine was formed.

Preparation of Bis(1,1-diethyl-2-propynyl)amine (7). The following procedure for the coupling of 3-amino-3-ethyl-1-pentyne with 3-chloro-3-ethyl-1-pentyne is representative for the formation of dipropargylamines. A 500-mL, round-bottomed flask equipped with a magnetic stirring bar, septum inlet, and gas inlet valve was flame-dried under argon. Copper bronze powder (220 mg) and freshly prepared Cu_2Cl_2 (220 mg) were added followed by 109 mL of DMF (dried over CaH_2 and distilled) and 3-amino-3-ethyl-1-pentyne (29.8 g, 260 mmol). The flask was flushed with argon for 10 min and cooled to 4 °C in a cold room. Then 18.3 g (133 mmol) of 95% 3-chloro-3-ethyl-1-pentyne was injected. After 72 h, the solution was quenched with 30 mL of 20% aqueous NaOH (150 mmol). Water (100 mL) was added and the solution was steam distilled. The organic layer was separated from the distillate, and the aqueous layer was extracted with three 50-mL aliquots of ether. The combined ether extracts were dried over $MgSO_4$. The ether was removed under vacuum and the residue distilled through a short Vigreux column. The primary propargylamine was recovered (12.7 g, 110 mmol, 86% of extra equivalent), and the coupled amine was distilled under vacuum; bp 61–64 °C (0.5 mm). There was obtained 12.9 g (48% yield) of bis(1,1-diethyl-2-propynyl)amine: ν_{max} 3290, 2965, 2925, 2870, 1460, 1375, 1170 cm^{-1}; NMR ($CDCl_3$) δ 0.93 (13 H, t, J = 7), 1.73 (8 H, q, J = 7), 2.25 (2 H, s); mass spectrum, m/e (relative intensity) 206 (M^+ + 1), 176 (17), 82 (100), 67 (16), 55 (15), 41 (15).

Preparation of Bis(1,1-dimethyl-2-propynyl)amine. 3-Chloro-3-methyl-1-butyne (0.5 mol, 51 g) was reacted with 3-amino-3-methyl-1-butyne (1.1 mol, 92.5 g) for 24 h and was worked up as previously described. After distillation, 52.5 g (70% yield) of bis(1,1-dimethyl-2-propynyl)amine was isolated: bp 60–65 °C (20 mm); ν_{max} 3290, 2300, 1465, 1375, 1360, 1210, 1065 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (1 H, s), 1.48 (12 H, s), 2.23 (2 H, s); mass spectrum, m/e (relative intensity) 149 (M^+), 134 (46), 118 (3), 91 (3), 68 (100), 67 (16), 41 (30).

Preparation of (1′-Ethyl-1′-methyl-2-propynyl)(1,1-dimethyl-2-propynyl)amine. 3-Chloro-3-methyl-1-pentyne (0.78 mol, 113 g) was reacted with 3-amino-3-methyl-1-butyne (2 mol, 168 g) for 72 h, and the mixture was worked up as previously described. After distillation, 79 g (62% yield) of the product was obtained: bp 60–62 °C (5 mm); ν_{max} 3290, 2290, 1380, 1065 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (3 H, t, J = 7), 1.35 (1 H, s), 1.55 (9 H, s), 1.58 (2 H, m), 2.3 (2 H, s); mass spectrum, m/e (relative intensity) 163 (M^+), 68 (100).

Preparation of Bis(1-ethyl-1-methyl-2-propynyl)amine. 3-Chloro-3-methyl-1-pentyne (0.91 mol, 123 g) was reacted with 3-amino-3-methyl-1-pentyne (1.95 mol, 187 g) for 72 h and was worked up as previously described. After distillation, 89 g (55% yield) of product was isolated: bp 50–52 °C (5 mm); ν_{max} 3290, 2960, 2920, 2860, 1510, 1375, 1180 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (7 H, m), 1.41 (6 H, s), 1.60 (4 H, m) 2.25 (2 H, s); mass spectrum, m/e (relative intensity) 178 (M^+ + 1), 148 (42), 82 (48), 68 (100), 53 (39), 41 (35).

Preparation of (1-Ethyl-1-methyl-2-propynyl)(1′,1′-diethyl-2-propynyl)amine. 3-Chloro-3-ethyl-1-pentyne (0.75 mol, 98 g) was reacted with 3-amino-3-methyl-1-pentyne (1.5 mol, 149 g) for 72 h and was worked up as previously described. After distillation, 79 g (55% yield) of product was isolated: bp 67–68 °C (5 mm); ν_{max} 3310, 2970, 2940, 2880, 1470, 1380, 1170 cm^{-1}; NMR ($CDCl_3$) δ 0.95 (10 H, t, J = 6), 1.5 (3 H, s), 1.65 (6 H, q, J = 6), 2.2 (2 H, s); mass spectrum, m/e (relative intensity) 192 (M^+ + 1), 162 (36), 82 (100), 68 (67), 53 (25), 41 (29).

Preparation of Bis(cyclohexylethynyl)amine. 1-Chloro-1-ethynylcyclohexane (1.08 mol, 154 g) was reacted with (1-ethynylcyclohexyl)amine (2.16 mol, 265 g) for 48 h, and the mixture was worked up as previously described. After distillation, 155 g (65% yield) of product was obtained: bp 105–106 °C (2 mm); ν_{max} 3290, 2300, 1070 cm^{-1}; mp 71–72 °C; NMR ($CDCl_3$) δ 1.55 (13 H, m), 2.0 (8 H, m), 2.35 (2 H, s); mass spectrum, m/e (realtive intensity) 230 (M^+ + 1), 229 (M^+), 229 (17), 200 (21), 186 (52), 172 (73), 118 (50), 80 (100), 67 (49), 41 (58).

Preparation of Bis(1,1-diethylallyl)(1,1-diethyl-2-propynyl)amine. The procedure for preparing this compound was identical with the procedure for preparing the other secondary dipropargylic amines, except that a 2:1 molar ratio of 3-amino-3-ethyl-1-pentene to 3-chloro-3-ethyl-1-pentyne was used. Characterization and yield determination was accomplished by GLC purification: ν_{max} 3280, 3045 cm^{-1}; mass spectrum, m/e (relative intensity) 208 (M^+ + 1), 188 (5), 178 (50), 84 (100), 82 (85), 67 (13), 55 (44); NMR ($CDCl_3$) δ 0.88 (13 H, q, J = 7), 1.4 (8 H, q, J = 7), 2.18 (1 H, s), 4.73–6.18 (3 H, m); yield (GLC) 17%.

Preparation of (1,1-Diisopropyl-2-propynyl)(1,1-diethyl-2-propynyl)amine. 3-Chloro-3-ethyl-1-pentyne (0.12 mol, 14.6 g) was added to 80 mL of DMF containing 0.16 g of Cu_2Cl_2, 0.16 g of copper bronze, and 3-amino-4-methyl-3-isopropyl-1-pentyne (0.24 mol, 30.2 g) at 4 °C. The reaction mixture was allowed to react for 1 week at 4 °C and then warmed to 23 °C for 24 h. After workup, the mixture was distilled under vacuum to collect the high-boiling organic components. GLC analysis (10% Carbowax 20M) and collection of the highest boiling peak showed it to be the title compound: ν_{max} 3290, 2950, 2920, 2860, 1455, 1375, 1150, 1060 cm^{-1}; NMR δ 1.0 (19 H, m), 1.8 (6 H, br m), 2.05 (1 H, s), 2.15 (1 H, s); mass spectrum, m/e (relative intensity) 223 (M^+), 190 (60), 96 (100); yield (GLC) 5%.

Preparation of 6. 3-Chloro-4-methyl-3-isopropyl-1-pentyne (0.14 mol, 22.6 g) was added to 56 mL of DMF containing 0.11 g of Cu_2Cl_2, 0.11 g of copper bronze and 3-amino-3-ethyl-1-pentyne (0.26 mol, 28.9 g) at 0 °C. The reaction mixture was allowed to react for 4 days at 0 °C. After workup, the mixture was distilled under high vacuum and the distillate analyzed by GLC (10% Carbowax 20M). The largest GLC peak was collected and characterized as the coupled primary allylamine **6**: ν_{max} 3360, 3280, 2960, 2925, 2870, 1940, 1460, 1380, 1370 cm^{-1}; NMR ($CDCl_3$) δ 1.05 (18 H, d over q), 1.4–2.4 (8 H, m), 5.35 (1 H, s); mass spectrum, m/e (relative intensity) 233 (M^+), 204 (100), 146 (30).

Hydrogenation of Bis(1,1-diethyl-2-propynyl)amine in Absolute Ethanol with 10% Palladium on Charcoal. A 50-mL, round-bottomed flask equipped with a magnetic stirring bar, septum inlet, and gas inlet valve was attached with rubber tubing to a mineral oil gas buret. A 10-mg sample of 10% palladium on charcoal (Engelhard Industries, Inc.) and 5 mL of absolute ethanol (Gold Shield U.S.P.) were added. Hydrogen gas (Matheson 99.9%) was flushed through the system, and the buret was charged with the same. The solution was cooled to 0 °C with an ice bath. Then 1 mmol (0.23 mL) of **3** was added to the rapidly stirred solution. Hydrogen uptake was monitored with a gas buret and product formation via GLC (10% Carbowax 20M on Chromasorb W) at 160 °C. Hydrogen uptake (74 mL, 2.9 mmol) ceased within 1 h. The GLC trace showed two distinct high-boiling products and a low-boiling product eluting with the solvent. Preparative GLC and subsequent spectroscopic analysis identified the high-boiling components as 3,4-dimethyl-2,2,5,5-tetraethyl-3-pyrroline (**8**) and 3-methylene-4-methyl-2,2,5,5-tetraethyl-3-pyrrolidine (**9**). Repeating the experiment with tridecane as an internal standard established the yields of **8** and **9** as 48% and 15%, respectively. Spectral data for **8**: ν_{max} 2970, 2925, 2875, 2350, 1465, 1420, 1385, 990 cm^{-1}; ^{13}C NMR ($CDCl_3$, Me_4Si) δ 134.2, 70.69, 29.79, 8.69, 7.15; ^1H NMR ($CDCl_3$) δ 0.80 (t, 13 H, J = 6), 1.43 (14 H, s superimposed on m); mass spectrum, m/e (relative intensity) 209 (M^+), 180 (100), 152 (22), 136 (27). Spectral data for **9**: ν_{max} 3055, 2960, 2925, 2860, 1650, 1460, 885 cm^{-1}; NMR ($CDCl_3$) δ 0.83 (13 H, t, J = 6), 1.2 (8 H, m), 2.4 (1 H, m), 4.63 (2 H, t, J = 3); mass spectrum, m/e (relative intensity) 209 (M^+), 180 (100).

Hydrogenation of Bis(1,1-diethyl-2-propynyl)amine in Absolute Ethanol with Platinum Oxide. The same experimental conditions were used as in the palladium-catalyzed procedure, except that 5 mg of PtO_2 was substituted for 5 mg of 10%

palladium on charcoal. A total of 93 mL (3.8 mmol) of hydrogen was taken up. By GLC, only trace amounts of products (<2%) having the same retention times as **8** and **9** were seen; the rest of the starting material was hydrogenated to 1,1-diethyl-1-aminopropane.

Hydrogenation of Bis(1,1-diethyl-2-propynyl)amine (1) to Bis(1,1-diethylallyl)amine in Ligroin. A 10-mmol sample of **3** (2.05 g) was dissolved in 30 mL of ligroin in a 250-mL centrifuge bottle. Then 20 mg of 10% palladium on charcoal was added. The bottle was placed in a Parr hydrogenation apparatus and hydrogenated for 10 h; the initial H_2 pressure was 50 psi and the pressure dropped 37 psi. The GLC analysis revealed three peaks, one of which was the bis(1,1-diethylallyl)amine. Its spectral properties were identical with the semihydrogenation product of **3** obtained by using W2 Raney nickel in ethanol. Addition of 10 mL of absolute ethanol to the ligroin solution and continuation of the hydrogenation completely hydrogenolyzed the bis(1,1-diethylallyl)amine. Spectral data for the diallyl amine are as follows: ν_{max} 3380, 3045, 1630 cm^{-1}; NMR ($CDCl_3$) δ 0.75 (13 H, t, J = 7), 1.43 (8 H, q, J = 7), 4.67–6.0 (6 H, m); mass spectrum, m/e (relative intensity) 209 (M^+), 180 (100).

Hydrogenation of Bis(1,1-diethyl-2-propynyl)amine in Absolute Ethanol with W2 Raney Nickel Catalyst. Raney nickel alloy was activated by a literature procedure.[21] W2 Raney nickel (2 g) was added to a solution of 50 mL of absolute ethanol and 10 mmol (2.05 g) of **3** in a 500-mL centrifuge bottle. The bottle was placed in a Parr hydrogenation apparatus and purged with hydrogen five or six times. The bottle was pressurized to 60 psi and the shaker turned on. The pressure dropped 5 psi in 18 h. The solution was filtered to remove the catalyst and the ethanol evaporated under reduced pressure. Bulb to bulb distillation [62–64 °C (0.2 mm)] gave 0.43 g (20%) of the saturated amine **10**. GLC analysis (5% OV-101 Chromasorb W, acid washed, DMSC treated) showed it to be 95% pure; the remaining 5% was Bis(1,1-diethylallyl)(1,1,1-triethylcarbinyl)amine.

The same experiment was performed with W4 and W6 Raney nickel under identical conditions. Tridecane was added as an internal standard in each case. Analysis of the products of each experiment by GLC showed that as the reactivity of the catalyst increased, the degree of hydrogenation of the dipropargyl secondary amine decreased. Thus W2 Raney nickel was the most satisfactory catalyst for the hydrogenation of **3** to the saturated secondary amine. The same experiment was performed under identical conditions, except that 20 mmol (1.12 g) of potassium hydroxide was dissolved in the ethanolic solution of **3** before the W2 Raney nickel catalyst was added. The catalyst was filtered, and ethanol was removed under reduced pressure. Water (20 mL) was added to the viscous residue. The solution was transferred to a separatory funnel and the aqueous layer extracted with two 20-mL portions of ether. The ether layer was pooled, dried over anhydrous potassium carbonate, and then evaporated under reduced pressure. The amine was distilled bulb to bulb under reduced pressure. About 1.52 g (71% yield) of the saturated amine **10** was obtained (91% pure). The remaining unsaturated secondary amine was separated by spinning-band distillation. All subsequent hydrogenations with the remaining dipropargylamines were carried out under identical conditions with the same proportions of amine, solvent, catalyst, and base and were scaled up to a 50-mmol scale. In the case of bis(cyclohexylethynyl)amine, hydrogenation without KOH gave a higher yield and increased purity of the saturated amine than when KOH was present. The amount of semihydrogenated amine decreased from a maximum of 9% for the most hindered amine to less than 3% for the least hindered amine.

Product Analysis of Bis(1,1-diethyl-2-propyl)amine: NMR ($CDCl_3$) δ 0.78 (19 H, t, J = 6), 1.4 (12 H, q, J = 6); mass spectrum, m/e (relative intensity) 214 (M^+ + 1), 184 (8), 86 (100), 57 (32), 56 (10), 43 (14), 41 (23); yield 7.6 g (71%). Anal. Calcd for $C_{14}H_{31}N$: C, 78.79; H, 14.64; N, 6.56. Found: C, 78.68; H, 14.57; N, 6.60.

Product Analysis of Bis(1,1-dimethyl-2-propyl)amine: NMR ($CDCl_3$) δ 0.83 (7 H, t, J = 6), 1.07 (12 H, s), 1.3 (4 H, q, J = 6); mass spectrum, m/e (relative intensity) 156 (M^+ – 1), 142 (7), 128 (7), 72 (88), 58 (100), 43 (30); yield 6.3 g (80%). Anal. Calcd for $C_{10}H_{23}N$: C, 76.35; H, 14.74; N, 8.90. Found: C, 76.16; H, 14.57; N, 8.83.

Product Analysis of (1′-Ethyl-1′-methyl-2-propynyl)(1,1-dimethyl-2-propynyl)amine: NMR ($CDCl_3$) δ 0.80 (10 H, t, J = 6), 1.1 (6 H, s), 1.4 (6 H, q, J = 6); mass spectrum, m/e (relative intensity) 172 (M^+ + 1), 142 (17), 86 (11), 72 (100), 58 (64), 43 (33); yield 6.7 g (78%). Anal. Calcd for $C_{11}H_{25}N$: C, 77.12; H, 14.71; N, 18.18. Found: C, 76.85; H, 14.57; N, 8.09.

Product Analysis of Bis(1-ethyl-1-methyl-2-propyl)amine: NMR ($CDCl_3$) δ 0.52 (1 H), 0.8 (12 H, t, J = 6), 1.05 (6 H, s), 1.3 (8 H, q, J = 6); mass spectrum, m/e (relative intensity) 186 (M^+ + 1), 156 (15), 86 (16), 72 (100), 55 (17), 43 (46); yield 7.0 g (75%). Anal. Calcd for $C_{12}H_{25}N$: C, 77.76; H, 14.68; N, 7.56. Found: C, 77.61; H, 14.58; N, 7.46.

Product Analysis of (1-Ethyl-1-methyl-2-propynyl)-(1′,1′-diethyl-2-propynyl)amine: NMR ($CDCl_3$) δ 0.49 (1 H, s), 0.78 (15 H, t, J = 6), 1.05 (3 H, s), 1.35 (10 H, q, J = 6); mass spectrum, m/e (relative intensity) 200 (M^+ + 1), 170 (14), 112 (2), 86 (100), 72 (95), 57 (26), 43 (39); yield 7.5 g (75%). Anal. Calcd for $C_{13}H_{29}N$: C, 78.31; H, 14.66; N, 7.03. Found: C, 78.43; H, 14.54; N, 7.08.

Product Analysis of Bis(1-ethylcyclohexyl)amine: NMR ($CDCl_3$) δ 0.80 (7 H, t, J = 6), 1.40 (24 H, M); mass spectrum m/e (relative intensity) 237 (M^+), 184 (4), 128 (5), 98 (11), 86 (100), 72 (15), 57 (20); yield 9.5 g (80%). Anal. Calcd for $C_{16}H_{31}N$: C, 81.01; H, 13.08; N, 5.91. Found; C, 81.11; H, 12.94; N, 5.79.

Reaction of Bis(1,1-diethyl-2-propyl)amine with Methyl Iodide. Methyl iodide (0.75 mL, 10 mmol) was added to a 50-mL, round-bottomed flask containing a stir bar, side arm septum, gas inlet valve, and 25 mL of THF. Then 10 mmol (2.52 mL) of **10** was injected. The flask was sealed, and the solution was stirred for 2 weeks. The solvent was evaporated under vacuum and the product analyzed by GLC and NMR spectroscopy. Analysis showed that no ammonium salt was formed; amine **3** was recovered quantitatively.

Reaction of BF_3·OEt_2 with Bis(1-ethylcyclohexyl)amine. BF_3·OEt_2 (1 mmol; distilled and stored under argon, 0.125 mL) was added to hexane (1 mL) under argon in a round-bottomed flask equipped with a gas inlet valve, septum side arm, and stir bar. A white, air-stable solid was quickly formed. Drying under vacuum overnight gave a white crystalline powder free of ether (by NMR): NMR ($CDCl_3$) δ 1.05 (6 H, t, J = 7), 1.6 (20 H, br m), 1.95 (4 H, br q, J = 7), 5.6 (1 H, br s); mass spectrum, m/e 237 (M^+), remainder identical with spectrum of free amine. Anal. Calcd for $C_{16}H_{31}NBF_3$: C, 62.96; H, 10.23; N, 4.59; B, 3.54; F, 18.67. Found: C, 61.11; H, 10.43; N, 4.39; B, 4.83; F, 19.22.

Reaction of BF_3·OEt_2 and BF_3 Gas with Bis(1,1-diethyl-2-propyl)amine. BF_3·OEt_2 (1 mmol, 0.125 mL) and **10** (1 mmol, 0.25 mL) were injected into a pyrolysis tube, and the glass tube was flame sealed. The neat solution reacted for 1 h at 25 °C. The tube was opened and the liquid removed. The remaining air-stable solid was analyzed by NMR and mass spectroscopy. It was identified as the aminolysis product $(CH_3CH_2)_3CNH_2BF_3$ (**12**): NMR ($CDCl_3$) δ 0.93 (9 H, t, J = 6), 1.65 (6 H, q, J = 6), 5.76 (2 H, s, D_2O exchangeable); mass spectrum, m/e 184 (M^+). Repetition of the same reaction but with BF_3 gas (24 mL) gave a liquid fraction as well as the BF_3 amine complex. The liquid was identified by NMR and mass spectrometry as 3-ethyl-2-pentene.

Titration of Amine Hydrochlorides in 90% Ethanol with 0.1075 N KOH under Argon. The procedure for the titration reactions was taken from a previously reported procedure.[22] Potassium hydroxide was prepared by dissolving potassium metal in absolute ethanol under argon and diluting with degassed H_2O to the required concentration. All solutions were stored in polypropylene containers under argon. All transferring of solutions was done via cannula, and the titrations were done under argon. The amines were converted to the hydrochlorides by stoichiometric titration with standardized aqueous HCl (0.0954 N). Water was removed from the amine hydrochlorides by drying for 1 week under high vacuum in a desiccator over phosphorus pentoxide. The titration was followed by using an Orion 1601-A Digital Ionalizer with a Markson combination pH reference electrode at

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20 °C. All of the titrations were carried out so that the solution was 0.01 N at the equivalence point. The pK_a was calculated as the pH of the solution at half the equivalence point volume. All titrations were carried out three times, and the theoretical equivalence point was within 0.25% of the experimental value. In each case, only a single inflection point was observed. For a discussion on the effect of ethanol on the apparent strength of organic amine bases and for a method for the extrapolation of the pK_a from solutions which are progressively less alcoholic, see the paper of Hall et al.[23]

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Registry No. 1, 2809-93-0; 2, 3234-64-8; 3, 74986-44-0; 4, 1571-51-3; 5, 3234-65-9; 6, 74986-45-1; 7, 74986-46-2; 8, 74986-47-3; 9, 74986-48-4; 10, 74986-49-5; 11, 74986-50-8; 12, 74986-51-9; 14, 30389-18-5; acetylene, 74-86-2; 3-pentanone, 96-22-0; 3-ethyl-1-pentyn-3-ol, 6285-06-9; 2,4-dimethyl-3-pentanone, 565-80-0; 4-methyl-3-isopropyl-1-pentyn-3-ol, 5333-87-9; 3-chloro-3-ethyl-1-pentyne, 6080-79-1; 3-chloro-3-methyl-1-pentyne, 14179-94-3; 3-methyl-1-pentyn-3-ol, 77-75-8; 3-chloro-3-methyl-1-butyne, 1111-97-3; 2-methyl-3-butyn-2-ol, 115-19-5; 3-chloro-4-methyl-3-isopropyl-1-pentyne, 74986-52-0; 3-amino-3-methyl-1-butyne, 2978-58-7; 3-amino-3-methyl-1-pentyne, 18369-96-5; 3-amino-4-methyl-3-isopropyl-1-pentyne, 74986-53-1; (1'-ethyl-1'-methyl-2-propynyl)(1,1-dimethyl-2-propynyl)amine, 74986-54-2; bis(1-ethyl-1-methyl-2-propynyl)amine, 74986-55-3; (1-ethyl-1-methyl-2-propynyl)(1,1'-diethyl-2-propynyl)-amine, 74986-56-4; bis(cyclohexylethynyl)amine, 74986-57-5; 1-chloro-1-ethynylcyclohexane, 6209-75-2; bis(1,1-diethylallyl)(1,1-diethyl-2-propynyl)amine, 74986-58-6; bis(1,1-diethylallyl)amine, 74986-59-7; bis(1,1-diethylallyl)(1,1,1-triethylcarbinyl)amine, 74998-56-4; bis(1,1-dimethylpropyl)amine, 2978-47-4; (1'-ethyl-1'-methylpropyl)(1,1-dimethylpropyl)amine, 74986-60-0; bis(1-ethyl-1-methylpropyl)amine, 74986-61-1; (1-ethyl-1-methylpropyl)(1',1'-diethylpropyl)amine, 74986-62-2; bis(1-ethylcyclohexyl)amine trifluoroboron salt, 74986-63-3; 3-ethyl-2-pentene, 816-79-5; 1-ethynyl-1-cyclohexanol, 78-27-3; diisopropylamine HCl, 819-79-4; 2,2,6,6-tetramethylpiperidine HCl, 935-22-8; bis(1,1-dimethylpropyl)amine HCl, 3374-96-7; (1'-ethyl-1'-methylpropyl)(1,1-dimethylpropyl)amine HCl, 74986-64-4; bis(1-ethyl-1-methylpropyl)-amine HCl, 74986-65-5; (1-ethyl-1-methylpropyl)(1',1'-diethylpropyl)amine HCl, 74986-66-6; bis(1,1-diethylpropyl)amine HCl, 74986-67-7; bis(1-ethylcyclohexyl)amine HCl, 74986-68-8.

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Preparation and Stereochemistry of Some Substituted 4-Selenanones and 4-Selenanols

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The preparation of a number of substituted 4-selenanones and four epimeric pairs of 4-selenanols has been described. The configuration and conformation of the 4-selenanones and 4-selenanols were assigned on the basis of IR, ^1H NMR, and ^{13}C NMR spectral data, and the selenane ring was shown to be predominantly in the chair form. The dissociation constants of cyanohydrins from six substituted 4-selenanones were measured in 80% dioxane at 25 °C, and the results were analyzed in terms of steric parameters in the flattened ring systems.

Simple six-membered heterocyclic ketones and the corresponding alcohols containing sulfur,[2-4] oxygen,[2,5,6] nitrogen,[6,7] and phosphorus[8-10] are known to exist mostly in the chair conformation. However, there has been little work on functionalized selenium heterocycles.[6] We report herein general methods of preparation of these systems with spectral and chemical evidence regarding the configuration and conformation for the saturated, six-membered selenium heterocyclics.

Results and Discussion

Lalezari[11a] and co-workers reported the formation of some 2,6-diaryl-4-selenanones during the reaction of symmetrical distyryl ketones with hydrogen selenide in the presence of sodium acetate. In the present investigation, several substituted 4-selenanones were prepared by the condensation of unsymmetrical distyryl ketones with hydrogen selenide. The procedure used for the synthesis of selenanones **2a–d** was similar to that published[11a] but with

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