Synthesis of 2,3-Disubstituted Pyrroles from 3,*N*-Dilithio-*N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine

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Received March 20, 2001

N-(Trialkylsilyl)allylamines can be deprotonated at the *cis*-vinylic position to yield 3,*N*-dilithio-*N*-(trialkylsilyl)allylamines under mild conditions. *N*-(Trialkylsilyl)allylamines with terminal alkyl substituents were reported not to form dianions under the same conditions. During our investigations we found that *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine (**1**) is deprotonated under the reaction conditions reported in the literature, but the resulting dianion is quenched by ethereal solvents. Consequently, new reaction conditions were developed that allow the generation of stable dianions from allylamines with terminal alkyl substituents. Thus, 2,3-disubstituted pyrroles hitherto unattainable via this methodology were formed from 3,*N*-dilithio-*N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine (**2**) and various carbonyl electrophiles in good yields.

Introduction

Pyrroles represent an important class of heterocyclic compounds.[1,2] They are abundant in nature[3] and are of great interest as subunits for natural products.[4] In addition, substituted pyrroles often display biological activity.[1a,5] Pyrroles are also building blocks for porphyrins,[2a,6] and polymers of pyrroles have found use as conducting and nonlinear optics materials.[7] Because of their utility and interest there are numerous synthetic pathways by which pyrroles can be synthesized.[8] The classical methods include the Hanzsch method using chloroacetone and 3-amino ethyl crotonate,[9] the Knorr[10] and Paal−Knorr[11] syntheses, as well as various 1,3-dipolar cycloaddition reactions, such as the reaction of nitrile ylides with alkynes,[12] and reactions involving substrates such as oxazolones, azalactones, and alkynes.[13] More recently some new methods have come to light, such as the rhodium-catalyzed reaction of α-diazo ketoacyl amides,[14] the reaction of chromium carbene complexes with 1-azadienes,[15] the reaction of dichloroazodienes with electron-rich olefins,[16] and McMurry's intramolecular type II alkylidenation of acylamidocarbonyls.[17] In addition, several reviews have recently been published on the synthesis of pyrroles.[18]

2,3-Disubstituted pyrroles can be prepared by the Trofimov reaction between appropriately substituted oximes and ethyne,[19] chloroethene,[20] or 1,2-dichloroeth-

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(1) For biologically important pyrroles, see: (a) Lainton, J. A. H.; Huffman, J. W.; Martin, B. R.; Compton, D. R. *Tetrahedron Lett.* **1995**, *36*, 1401. (b) de Leon, C. Y.; Ganem, B. *Tetrahedron* **1997**, *53*, 7731. (c) Gupton, J. T.; Krumpe, K. E.; Burnham, B. S.; Dwornik, K. A.; Petrich, S. A.; Du, K. X.; Bruce, M. A.; Vu, P.; Vargas, M.; Keertikar, K. M.; Hosein, K. N.; Jones, C. R.; Sikorski, J. A. *Tetrahedron* **1998**, *54*, 5075. (d) Jacobi, P. A.; Coutts, L. D.; Guo, J.; Hauck, S. I.; Leung, S. H. *J. Org. Chem.* **2000**, *65*, 205.

(2) For the chemistry of macrocycles containing pyrrole units; see: (a) Sessler, J. L.; Weghorn, S. J. *Expanded, Contracted & Isomeric Porphyrins*; Pergamon Press: Oxford, 1997. (b) Thoresen, L. H.; Kim, H.; Welch, M. B.; Burghart, A.; Burgess, K. *Synlett* **1998**, *11*, 1276.

(3) Pinder, A. R. In *The Alkaloids*; Grundon, M. F., Ed., The Royal Chemical Society: London, 1982; Vol. 12, Chapter 2, p 35.

(4) See (a) Herbert, R. B. In *The Alkaloids*; Grundon, M. F., Ed.; The Royal Chemical Society: London, 1982; Vol. 12, Chapter 1, p 1. (b) Falk, H. *The Chemistry of Linear Oligopyrroles and Bile Pigments*; Springer-Verlag: Wienna, 1989. (c) *Biosynthesis of Tetrapyrroles*; Jordan, P. M., Ed.; Elsevier: Amsterdam, 1991.

(5) (a) Korostova, S. E.; Sobenina, L. N.; Nersterenko, R. N.; Aliev, I. A.; Mikhaleva, A. I. *Zh. Org. Khim.* **1984**, 1960; *Chem. Abstr.* **1985**, *102*, 131860. (b) Itoh, S.; Fukui, Y.; Haranou, S.; Ogino, M.; Komatsu, M.; Ohshiro, Y. *J. Org. Chem.* **1992**, *57*, 4452. (c) Woo, J.; Sigurdsson, S. T.; Hopkins, P. B. *J. Am. Chem. Soc.* **1993**, *115*, 3407.

(6) (a) *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975. (b) Franck, B.; Nonn, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1795.

(7) (a) Niziurski-Mann, R. E.; Cava, M. P. *Heterocycles* **1992**, *34*, 2003. (b) Naarmann, H.; Theophilou, N. In *Electroresponsive Molecular and Polymeric Systems*; Skotheim, T. A., Ed.; Marcel Dekker Inc.: New York, 1988; Vol. 1. (c) Bauerle, P. *Adv. Mater.* **1993**, *5*, 879.

(8) (a) Patterson, J. M. *Synthesis* **1976**, *5*, 281. (b) Jones, R. A.; Bean, G. P. *The Chemistry of Pyrroles*; Academic Press, Inc.: London, 1977. (c) Bean, G. P. In *The Chemistry of Heterocyclic Compounds*; Jones, A. R., Ed.; John Wiley & Sons: New York, 1990; Vol. 48, Part 1, Chapter 2, p 105. (d) Trofimov, B. A.; Mikhaleva, A. I. *Heterocycles* **1994**, *37*, 1193. (e) Enders, D.; Maassen, R.; Han, S.-H. *Liebigs Ann* **1996**, *10*, 1565. (f) Jones, G. B.; Chapman, B. J. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, p 1. (g) Black, D. St. C. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, p 39. (h) Sundberg, R. J. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, p 119. (i) Gribble, G. W. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, p 207. (j) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 615.

(9) (a) Hantzsch, A. *Chem. Ber.* **1890**, *23*, 1474. (b) Beelen van, D. C.; Wolters, J.; Gen van der, A. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 437.

(10) (a) Knorr, L. *Ber.* **1884**, *17*, 1635. (b) Knorr, L. *Annalen* **1886**, *236*, 290. (c) Kleinspehn, G. G. *J. Am. Chem. Soc.* **1955**, *77*, 1546.

(11) (a) Paal, C. *Ber.* **1885**, *18*, 367. (b) Knorr, L. *Ber.* **1885**, *18*, 1568. (c) See ref 8b, Chapter 3.

(12) (a) Huisgen, R.; Stangl, H.; Sturm, H. J.; Wagenhofer, H. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 50. (b) Berrée, F.; Marchand, E.; Morel, G. *Tetrahedron Lett.* **1992**, *33*, 6155.

(13) (a) Bayer, H. O.; Gotthardt, H.; Huisgen, R. *Chem. Ber.* **1970**, *103*, 2356. (b) Huisgen, R.; Gotthardt, H.; Bayer, H. O.; Schaefer, F. C. *Chem. Ber.* **1970**, *103*, 2611.

(14) Padwa, A.; Deen, D. C.; Hertzog, D. C.; Nadler, W. R.; Zhi, L. *Tetrahedron* **1992**, *48*, 7565.

(15) Danks, T. N.; Velo-Rego, D. *Tetrahedron Lett.* **1994**, *35*, 9443.

(16) South, M. S.; Jakuboski, T. L.; Westmeyer, M. D.; Dukesherer, D. R. *Tetrahedron Lett.* **1996**, *37*, 1351.

(17) Furstner, A.; Bogdanovic, B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2442.

(18) (a) Sundberg, R. J. *Prog. Heterocycl. Chem.* **1992**, *4*, 81. (b) Gilchrist, T. L. *Contemp. Org. Synth.* **1994**, *1*, 205. (c) Sundberg, R. J.; Nguyen, P. V. *Prog. Heterocycl. Chem.* **1994**, *6*, 110. (d) Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 615.

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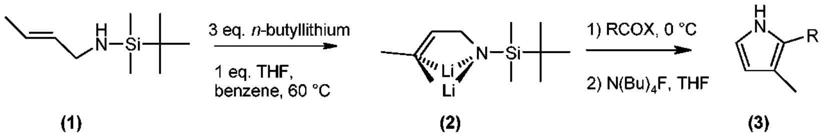
Scheme 1



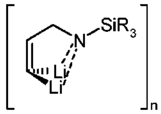
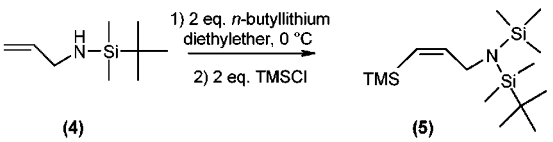


Figure 1. Central unit of 3,*N*-dilithio-*N*-(trialkylsilyl)allylamines as observed by X-ray crystallography.

Scheme 2



ane,[21] in the presence of KOH or NaOH and elevated temperatures, in yields around 40−50%. While 1,4-conjugate addition reactions followed by cyclization normally lead to pyrroles containing electron-withdrawing groups at the 3-position, the addition of enamines to chloroacrylonitrile yields 2,3-disubstituted pyrroles.[8c]

In this paper we wish to present a synthesis of 2,3-disubstituted pyrroles from a simple butenylamine precursor. Deprotonation of silyl-protected 2-*E*-buten-1-amine with 3 equiv of *n*-butyllithium in benzene in the presence of 1 equiv of THF at 60 °C to form the 3,*N*-dilithio species, followed by the addition of various carbonyl compounds at 0 °C, gives 2,3-disubstituted pyrroles in good yields (Scheme 1).

Results and Discussion

N-(Trialkylsilyl)allylamines can be deprotonated at the *cis*-vinylic position to yield 3,*N*-dilithio-*N*-(trialkylsilyl)allylamines under surprisingly mild conditions (Scheme 2).[22] We have characterized a series of such dianions by X-ray crystallography[23] (Figure 1), and the synthesis of 2-substituted pyrroles from the addition of dianions to carbonyl electrophiles was reported in the literature.[22]

However, *N*-(trialkylsilyl)allylamines with terminal alkyl substituents were reported not to form dianions under the same conditions (i.e., 2 equiv of *n*-butyllithium, in diethyl ether at 0 °C).[22] During our investigations we found that, contrary to previous reports, **1** is deprotonated under these reaction conditions, but the resulting dianion is quenched by ethereal solvents (Scheme 3). This increased basicity of the substituted vinyllithium species is not surprising as the basicity of organolithiums is known to increase with increasing substitution.[24]

The method of the previous investigators involved the generation of dianion over a 48 h period, followed by quenching with chlorotrimethylsilane. Over such a long period of time the dianion would likely have been reprotonated by the solvent to regenerate the lithium amide of the starting amine. Consequently, the only observed product was bis-*N*,*N*-disilylated crotylamine,[22] misleadingly indicating lack of dianion formation. Our experience suggested that dianion formation may be complete as soon as 0.5 h after the addition of base. Indeed, our NMR investigation into the reaction progress of the vinylic deprotonation of **1** in THF-d_8 indicated that dianion was completely formed after 90 min. This dianionic species then went on to deprotonate solvent (THF-d_8) overnight to generate *E*-3-Deutero-*N*-lithio-*N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine **(6)**. (Figures 2 and 3)

Attempts to generate useful amounts of the dianion in nondeuterated THF or diethyl ether by varying the reaction conditions failed, most likely because quenching competes more effectively with dianion formation in nondeuterated solvents. When the reaction was followed by ^{1}H NMR using benzene-d_6 or toluene-d_8 as the solvent, none or only very small amounts of dianion were generated, even at elevated temperatures (+60 °C and +90 °C, respectively) and over extended periods of time. This observation is in agreement with our previous experience that the generation of dianions from *N*-(trialkylsilyl)allylamines in hydrocarbon solvents, such as pentane or hexane, is sluggish at best and most often unsuccessful. Upon addition of 1 equiv of THF, however, the reaction proceeds smoothly, and the dianionic species is fully generated at room temperature in less than 2 h (Scheme 4). This amount of THF appears to only catalyze the formation of the vinylic anion and does not appear to quench the formed dianion to any appreciable extent. The reaction also proceeds to completion in the presence of 0.1 equiv of THF, but the rate of dianion formation is reduced considerably. The mode of catalysis is currently under investigation, as are attempts to crystallize the dianionic species. It is interesting to note that the equivalent ^{1}H NMR experiment with 1 equiv of TMEDA, instead of 1 equiv of THF, did not generate any discernible amount of dianion.

Synthetically useful dianions of **1** can be generated with 3 equiv of *n*-butyllithium and 1 equiv of THF in benzene. The presence of dianion **2** can be confirmed by GC/MS, after quenching a small aliquot of the reaction mixture with D$_2$O. The dianions react with carbonyl electrophiles to yield 2,3-disubstituted pyrroles **3** (Scheme 1).

The products are obtained as mixtures of the silylated and desilylated 2,3-disubstituted pyrroles as detected by

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(19) For some examples, see: (a) Trofimov, B. A.; Korostova, S. E.; Balabanova, L. N.; Mikhaleva, A. I. *J. Org. Chem. USSR* **1978**, *14*, 2018. (b) Korostova, S. E.; Mikhaleva, A. I.; Sobenina, L. N.; Shevchenko, S. G.; Shcherbakov, V. V. *Khim. Geterotsikl. Soedin.* **1985**, *11*, 1501.

(20) For some examples, see (a) Aliev, I. A.; Zeinalova, S. N.; Gasanov, B. R.; Mikhaleva, A. I.; Korostova, S. E. *J. Org. Chem. USSR* **1988**, *24*, 2198. (b) Aliev, I. A.; Mikhaleva, A. I.; Gasanov, B. R.; Golovanova, N. I. *Khim. Geterotsikl. Soedin.* **1990**, *10*, 1337.

(21) For some examples, see: (a) Trofimov, B. A.; Mikhaleva, A. I.; Vasil'ev, A. N.; Korostova, S. E.; Schevchenko, S. G. *Khim. Geterotsikl. Soedin.* **1985**, *1*, 59. (b) Korostova, S. E.; Nesterenko, R. N.; Mikhaleva, A. I.; Polovnikova, R. I.; Golovanova, N. I. *Khim. Geterotsikl. Soedin.* **1989**, *7*, 901.

(22) Burns, S. A.; Corriu, R. J. P.; Huynh, V.; Moreau, J. J. E. *J. Organomet. Chem.* **1987**, *333*, 281.

(23) Williard, P. G.; Jacobson, M. A. *Org. Lett.* **2000**, *2*, 2753.

(24) Sapse, A.-M.; Schleyer, P. von R. *Lithium Chemistry: A Theoretical and Experimental Overview*; John Wiley & Sons: New York, 1995.

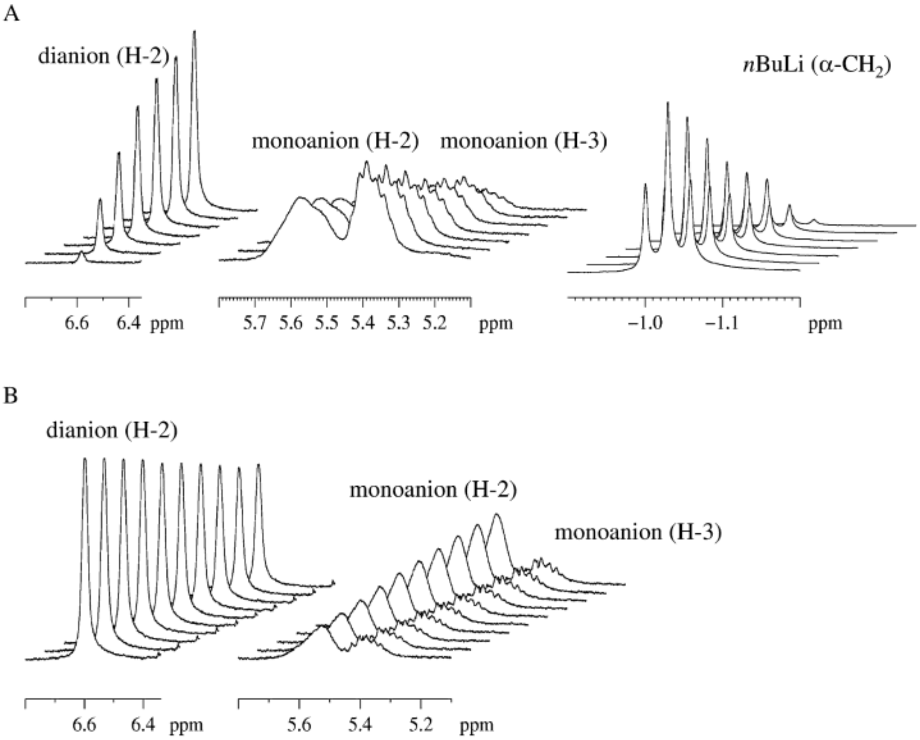
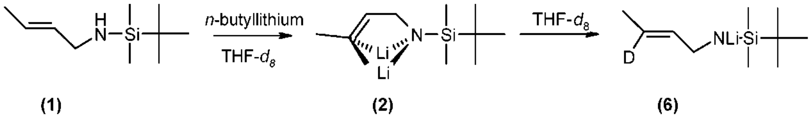


Figure 2. Generation and quenching of dianion **2**. Reaction progress followed by ^{1}H NMR in THF-d_8 at 25 °C. Stacked NMR spectra. A: Appearance of dianion and disappearance of monoanion as *n*-butyllithium is consumed. B: Deuteration of the dianion to regenerate monoanionic lithium amide.

Scheme 3



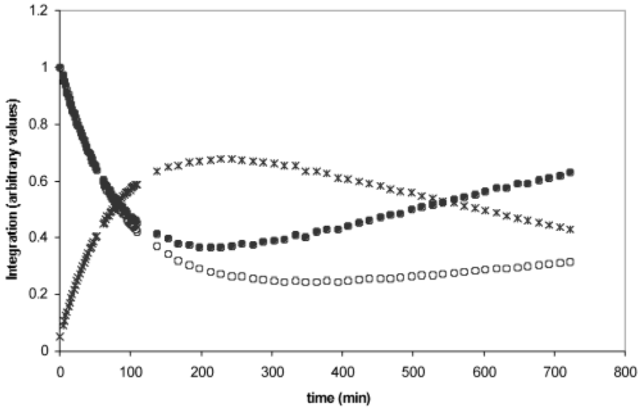
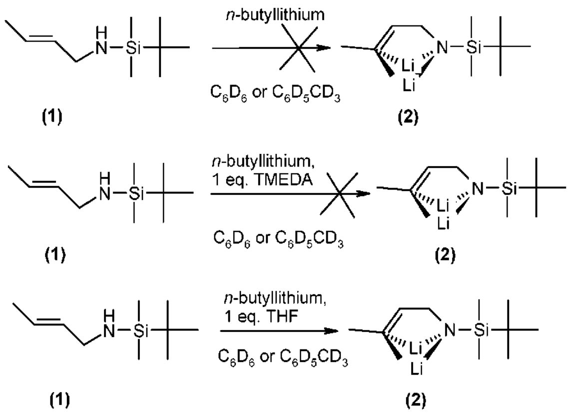


Figure 3. Generation and quenching of dianion **2**. Reaction progress followed by ^{1}H NMR in THF-d_8 at 25 °C. Plot of peak areas as a function of time. ∗ dianion (H-2), ● monoanion (H-2), ○ monoanion (H-3).

GC/MS, and confirmed by ^{1}H NMR.[25] Table 1 illustrates some typical reactions and conversions. Acid chlorides (entries 1 and 2), anhydrides (entries 3−5), and esters (entries 6−8) all react readily, except for entry 6, ethyl acetate. This entry's lower yield is most likely due to a competing reaction, namely enolization of the electrophile by the dianionic species. This competing reaction is also

Scheme 4



seen in reactions with amides. The reaction with *N*,*N*-dimethylformamide (entry 9) proceeds readily and in high yields, while the reaction with *N*,*N*-dimethylacetamide (entry 10), *N*,*N*-diethylpropionamide (entry 11), and 1-methyl-2-pyrrolidinone (entry 12) give no pyrrole product with recovery of starting amine. *N*,*N*,2-Trimethylpropionamide (entry 13) and *N*,*N*-dimethylbenzamide (entry 14), on the other hand, give 87% and 89% of the 2,3-disubstituted pyrrole, respectively.

For entries 10−12, the R group is enolizable, while for entries 9, 13, and 14 the R group is less so, or not at all. If the electrophile is reactive enough, as in the case of acid chlorides and anhydrides, addition of the dianion to

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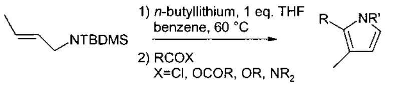
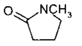
[25] Desilylation is presumed to occur by lithium siloxide elimination from a cyclized intermediate as described in ref 22 and references therein.

Table 1. Pyrrole Formation from 2 and Various Carbonyl Electrophiles in Benzene at 0 °C



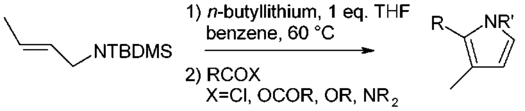
Entry	Electrophile		Pyrrole, % conversion[a]		
	R	X	R'=TBDMS	R'=H	Total
1	CH_3	Cl	54	ND[b]	54[c]
2	Ph	Cl	46	54	100
3	CH_3	$OCOCH_3$	54	ND[b]	54[c]
4	CF_3	$OCOCF_3$	16	0	16[d]
5	Ph	OCOPh	65	28	93
6	CH_3	OCH_2CH_3	27	ND[b]	27[c]
7	Furan	OCH_2CH_3	48	35	83
8	Ph	OCH_2CH_3	71	29	100
9	H	$N(CH_3)_2$	87	ND[b]	87[c]
10	CH_3	$N(CH_3)_2$	0	0	0[e]
11	CH_3CH_2	$N(CH_2CH_3)_2$	0	0	0[e]
12			0	0	0[e]
13	$(CH_3)_2CH$	$N(CH_3)_2$	30	57	87
14	Ph	$N(CH_3)_2$	46	43	89
15	$CH_2{=}CH$	$N(CH_3)_2$	0	0	0[e]

[a] The % conversion was calculated based on unreacted *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine as determined by GC/MS. The presence of pyrrole product was confirmed by ^1H NMR after workup. [b] Not detected. The presence of unprotected pyrrole product would not be detected by GC/MS; see footnote c. [c] The limit of detection for the GC/MS was molecular weights of 100. Any formation of pyrroles (unprotected) with a molecular weight less than this could therefore not be detected. In these cases the total % conversion should be considered a lower limit for possible yield of pyrrole product. [d] The balance of amine was converted to mono-trifluoroacetylated (26%) and di-trifluoroacetylated (48%) *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine. [e] **1** recovered.

the carbonyl group, followed by cyclization to yield the 2,3-disubstituted pyrrole product dominates. If the electrophile is less reactive—as in the case of esters (entry 6) and amides with enolizable protons (entries 10−12)—enolization of the electrophile is the preferred reaction pathway, and the reaction gives none or very little 2,3-disubstituted pyrrole product. The amides (entries 10−13)[26] illustrate that the bulkier the R group is to enolize, the more pyrrole product will be seen and vice versa. However, experiments using trimethylacetyl chloride and trimethylacetic anhydride indicate that if the R group is too bulky, much lower yields and complex reaction mixtures are observed. Consequently, sterically hindered carbonyls are expected to give lower yields, regardless of their activity.

For an enolizable electrophile (as R = CH_3) the nature of the leaving group X greatly effects the yield (Table 2). More reactive carbonyl compounds, such as acid chlorides and anhydrides, give little or no amount of enolized electrophile and consequently high yields of 2,3-disubstituted pyrrole. Less reactive carbonyls, such as esters and amides, give more of the enolized electrophile and lower yields of the 2,3-disubstituted pyrrole. For a nonenolizable electrophile, such as R = Ph, the nature of the leaving group has little or no effect on the yield of pyrrole product (Table 2).

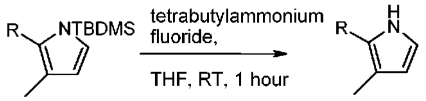
Table 2. Pyrrole Formation from 2 and Various Carbonyl Electrophiles in Benzene at 0 °C, Arranged by R. Effect of the Leaving Group



electrophile		pyrrole, % conversion[a]		
R	X	R' = TBDMS	R' = H	total
CH_3	Cl	54	ND[b]	54[c]
CH_3	$OCOCH_3$	54	ND[b]	54[c]
CH_3	OCH_2CH_3	27	ND[b]	27[c]
CH_3	$N(CH_3)_2$	0	0	0[d]
Ph	Cl	46	54	100
Ph	OCOPh	65	28	93
Ph	OCH_2CH_3	71	29	100
Ph	$N(CH_3)_2$	46	43	89

[a] The % conversion was calculated based on unreacted *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine as determined by GC/MS. The presence of pyrrole product was confirmed by ^1H NMR after workup. [b] Not detected. In this case the presence of unprotected pyrrole product would not be detected by GC/MS; see footnote c. [c] The limit of detection for the GC/MS was molecular weights of 100. Any formation of pyrroles (unprotected) with a molecular weight less than this could therefore not be detected. In these cases the total % conversion should be considered a lower limit for possible yield of pyrrole product. [d] **1** recovered.

Table 3. Some Representative Examples of Isolation of Pyrrole Product



(3)

R	electrophile	% yield[a]
furan (**3a**)	ethyl 2-furoate	71
Ph (**3b**)	PhCOCl	43[b]
Ph (**3c**)	$(PhCO)_2O$	41
Ph (**3d**)	$PhCON(CH_3)_2$	46

[a] After purification by column chromatography, as described in the Experimental Section. Yield based on *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine. [b] After purification by preparative thin-layer chromatography, as described in the Experimental Section. Yield based on *N*-(*tert*-butyldimethylsilyl)-2-buten-1-amine.

In the final step, the mixtures of silylated and desilylated pyrrole product were treated with tetrabutylammonium fluoride, and the resulting desilylated product was purified by chromatography. Table 3 shows some representative examples of isolation of 2,3-disubstituted pyrroles, with yields varying from 41−71%.

We have here demonstrated the hitherto unknown reactivity of *N*-(trialkylsilyl)allylamines with terminal alkyl substituents to form dianionic species when exposed to *n*-butyllithium in the presence of 1 equiv of THF in benzene. These dilithiated species react with various carbonyl electrophiles to form 2,3-disubstituted pyrroles in good yields. We anticipate that highly substituted pyrroles could be prepared from appropriately substituted butenylamines. The mode of catalysis, which requires

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(26) When acrylamide (entry 15) was mixed with the dianion **2**, a white solid preciptated. GC/MS and ^1H NMR indicated that most of the dianion **2** remained in solution. The solid is likely polyacrylamide, as the poylmerization of acrylamide in the presence of electrons is a known phenomenon. Reaction of dianion **2** with acryloyl chloride yielded a jellylike material and otherwise similar results. Most likely a polymer was formed in this case as well.

THF to be present for the dianionic species to form, is currently under investigation. We expect that THF-induced changes in aggregation play an important role in facilitating these reactions.[27] In light of the inability of TMEDA to catalyze this reaction, the possibility of a unique aggregate with ethereal solvation is especially intriguing. We are currently attempting to characterize these interesting aggregates by X-ray crystallography and NMR.

Experimental Section

General. Diethyl ether and THF were distilled from sodium/benzophenone under a nitrogen atmosphere. *n*-Buthyllithium was obtained from Aldrich Chemical Co. (2.5 M in hexanes), and the exact concentration of the solution was determined by direct titration with 2,5-dimethoxybenzyl alcohol in THF. All chemicals were purchased from Aldrich Chemical Co. and distilled prior to use when appropriate. Benzene and toluene were dried over CaH_2 and distilled before use. Deuterated NMR solvents were dried over 3 Å Linde sieves prior to use. All reactions and NMR studies were carried out under argon atmosphere, using flame-dried glassware. Aldrich silica gel (70−230 mesh, 60 Å) and Analtech silica gel thin layer plates (20 × 20 cm, 1000 μm) were used for chromatography. GC analyses were performed on a Hewlett-Packard 5890 series II gas chromatograph equipped with a Hewlett-Packard 5972 mass selective detector. IR spectra were recorded on a Perkin-Elmer 1600 FTIR. NMR spectra were collected on Bruker DRX400 or DPX300 spectrometers operating at 400 and 300 MHz for ^{1}H and 100 and 75 MHz for ^{13}C observation. The chemical shifts were referenced to $CDCl_3$ (^{1}H 7.27 ppm and ^{13}C 77.23 ppm) as an internal standard. HRMS were performed on a Kratos MS80RFA instrument.

The synthesis of 2-*E*-buten-1-amine from 3-buten-2-ol was adapted from literature procedures:[28]

2,2,2-Trichloroacetimidic Acid 1-Methylallyl Ester (7). NaH (1.4 g, 0.059 mol) was weighed into a flask, and 14 mL of dry THF was added. This slurry was placed in an icebath (at about 5 °C), and a solution of 3-buten-2-ol (18.6 g, 0.258 mol) in 25 mL of dry THF was added dropwise, with a syringe pump. The temperature of the bath was maintained. After stirring for 1 h, the solution was added to trichloroacetonitrile (37.3 g, 0.258 mol) in 240 mL of dry THF at 0 °C, over the course of 30 min. Stirring for 2 h, followed by evaporation of the solvent, yielded a brown oil. This crude product was used for the next step without further purification. ^{1}H NMR ($CDCl_3$): δ 8.35 (br, 1H), 5.96 (ddd, 1H, $J = 17.3$ Hz, 10.6 Hz, 5.6 Hz), 5.55 (m, 1H), 5.35 (dt, 1H, $J = 17.3$ Hz, 1.3 Hz), 5.20 (dt, 1H, $J = 10.6$ Hz, 1.3 Hz), 1.43 (d, 3H, $J = 6.55$ Hz).

***N*-But-2-enyl-2,2,2-trichloroacetamide (8).** Crude **7** was refluxed in 340 mL of toluene for 2 h, and the solvent was evaporated. The crude product was purified by fractional distillation (106 °C/0.25 mmHg) to yield 29.4 g (53%) as a white solid, mp 28−29 °C. ^{1}H NMR ($CDCl_3$): δ 6.71 (br, 1H), 5.76 (dqt, 1H, $J = 15.3$ Hz, 6.5 Hz, 1.3 Hz), 5.52 (dtq, 1H, $J = 15.2$ Hz, 6.3 Hz, 1.6 Hz), 3.93 (m, 2H), 1.74 (ddt, 3H, $J = 6.5$ Hz, 1.6 Hz, 1.3 Hz). ^{13}C NMR ($CDCl_3$): δ 18.1, 43.7, 93.0, 125.3, 130.8, 162.0. EIMS *m/z* 182 (16), 180 (25), 55 (100). HRMS calculated for $C_6H_8NOCl_3Na$: 237.9569. Found: 237.9567.

2-*E*-Buten-1-amine (9). A mixture of molten **8** (29.4 g, 0.136 mol) in 9 mL of DMF was added to 345 mL of 3 M KOH in several portions over the course of 30 min, resulting in a slightly exothermic reaction. After stirring at room temperature for 2 h, the reaction mixture was extracted with diethyl ether (4 × 60 mL). The combined ethereal layer was washed with brine (4 × 30 mL), dried over KOH pellets, and filtered. The solvent was not evaporated, but the presence of amine was confirmed by ^{1}H NMR. The ether layer was used, as was, in the next step.

***N*-(*tert*-Butyldimethylsilyl)-2-buten-1-amine (1).** Triethylamine (11.0 g, 0.109 mol) was added to the ether layer containing **9**. *tert*-Butyldimethylsilyl chloride (16.3 g, 0.109 mol) dissolved in 40 mL of distilled diethyl ether was added to the amine/triethylamine mixture. Within a few minutes, a white solid precipitated. The reaction mixture was stirred at room temperature for 12 h, and the presence of **1** was confirmed by GC/MS. The reaction mixture was filtered through florisil, and the filtrate was stirred with CaH_2 for 4 h. Filtration, followed by fractional distillation (52 °C, 0.25 mmHg), resulted in 6.4 g (26% yield) of **1**. FTIR (neat): ν (cm^{-1}) 3410, 2926, 2854, 1670. ^{1}H NMR ($CDCl_3$): δ 5.52 (m, 2H). 3.30 (m, 2H), 1.68 (m, 3H), 0.89 (s, 9H), 0.02 (s, 6H). ^{13}C NMR ($CDCl_3$): δ −4.6, 18.0, 18.8, 26.1, 44.9, 124.4, 134.1. EIMS *m/z* 185 (6, M$^+$), 170 (4), 128 (100), 99 (35). 73 (23), 59 (23). HRMS calculated for $C_{10}H_{23}NSi$: 185.1599. Found: 185.1593.

General Procedure for the Preparation of Dianion 2 To Follow the Reaction by NMR. *n*-Butyllithium (0.13 mmol) in hexanes was placed in a flame-dried NMR tube under argon atmosphere. The hexanes were removed in vacuo, and 0.6 mL of THF-d_8 was added. To this clear and colorless solution (12 mg, 6.6×10^{-5} mol) was added **1**.

General Procedure for the Generation of Dianion 2 from 1. 1 (167 mg, 0.9 mmol) was weighed into a flask, and 3.4 mL of benzene was added. *n*-Butyllithium (1.8 mmol) was added at 0 °C, followed by the addition of 1 equiv of dry THF. The temperature was raised to +60 °C, and another 0.9 mmol of *n*-butyllithium was added. The mixture was stirred at this temperature for another 1 h. The presence of dianion was confirmed by injecting a small aliquot of the reaction mixture into D_2O, extracting with hexanes, and detecting the M + 2 ion by GC/MS.

General Procedure for the Preparation of 2,3-Disubstituted Pyrroles from 2. The electrophile (1.8 mmol) was added dropwise to the dianion mixture at 0 °C. Solid electrophiles were dissolved in 1 mL of benzene prior to addition. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The reaction mixture was poured into water, and the aqueous layer was extracted with benzene (3 × 5 mL). The combined organic layer was dried over Na_2SO_4 and the solvent evaporated to yield the crude 2,3-disubstituted pyrroles.

General Procedure for Desilylating *N*-(*tert*-Butyldimethylsilyl)pyrroles. The crude mixture of silyl-protected and non-silyl-protected pyrroles was dissolved in 3 mL of dry THF. To this solution was added tetrabutylammonium fluoride (1.4 mmol, 365 mg) dissolved in 3 mL of dry THF, and the resulting slightly red liquid was stirred for 1 h at room temperature. The reaction mixture was poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with dichloromethane (3 × 5 mL). The combined organic layer was dried over Na_2SO_4, and the solvents were evaporated to yield the 2,3-disubstituted pyrroles as oils.

Some Representative Examples of Purification of 2,3-Disubstituted Pyrroles. 2-(2-Furyl)-3-methylpyrrole (3a).[29] Crude **3a** was purified by flash column chromatography using 1:9 dichloromethane:pentane, with 0.5% triethylamine, as the eluent. **3a** was subsequently isolated as a clear, colorless oil in 71% yield. ^{1}H NMR ($CDCl_3$): δ 7.40 (dd, 1H, $J = 1.8$ Hz, 0.8 Hz), 6.76 (m, 1H), 6.51 (dd, 1H, $J = 3.3$ Hz, 1.8 Hz), 6.34 (dd, 1H, $J = 3.3$ Hz, 0.8 Hz), 6.15 (m, 1H), 2.31 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 12.8, 103.1, 112.0, 112.1, 116.6, 117.7, 121.1, 140.2, 148.8. EIMS *m/z* 147 (100, M$^+$), 118 (81), 104 (18), 91 (21). HRMS calculated for C_9H_9N: 147.0684. Found: 147.0683.

3-Methyl-2-phenylpyrrole (3b−d).[30] Prepared from benzoyl chloride. The crude pyrrole was purified by preparative thin-layer chromatography, using 1:2.3 acetone:hexanes as the eluent. **3b** was isolated as a colorless oil in 43% yield.

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[27] For reviews on R_2NLi structures, see: (a) Gregory, K.; Schleyer, P. v. R.; Snaith, R. *Adv. Inorg. Chem.* **1991**, *37*, 47. (b) Mulvey, R. E. *Chem. Soc. Rev.* **1991**, *20*, 167. (c) Collum, D. B. *Acc. Chem. Res.* **1993**, *26*, 227. (d) Mulvey, R. E. *Chem. Soc. Rev.* **1998**, *27*, 339.

[28] (a) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901. (b) Jordis, U.; Grohmann, F.; Kuenburg, B. *Org. Prepr. Proc., Int.* **1997**, *5*, 549.

[29] Trofimov, B. A. *Bull. Acad. Sci. USSR Div. Chem. Sci.* **1979**, *28*, 2195.

[30] Thompson, T. W *Chem. Commun.* **1968**, 532.

Prepared from benzoic anhydride. Flash column chromatography, using 1:4 dichloromethane:pentane, with 0.5% triethylamine as the eluent gave **3c** as a colorless oil in 41% yield.

Prepared from *N*,*N*-dimethylbenzamide. Preparative thin-layer chromatography, using 1:3.5 ethyl acetate:hexanes as the eluent, followed by further purification by flash column chromatography with 1:4 ethyl acetate:hexanes as the eluent, gave **3d** as a colorless oil in 46% yield.

^{1}H NMR (CDCl$_3$): δ 8.15 (br, 1H), 7.45 (m, 4H), 7.25 (m, 1H), 6.8 (t, 1H), 6.2 (t, 1H), 2.3 (s, 3H). ^{13}C NMR (CDCl3): δ 12.8, 112.1, 116.2, 117.7, 126.0, 126.8, 128.5, 128.9, 133.8. EIMS *m*/*z* 157 (75, M$^+$), 156 (100), 128 (14), 77 (10), 51 (8). HRMS calculated for C$_{11}$H$_{11}$N: 157.0891. Found **3b**: 157.0894, **3c**: 157.0888, **3d**: 157.0894.

Acknowledgment. This work was supported by PHS grant GM35980. HRMS were performed by Dr. Tun-Li Shen, Brown University.

Supporting Information Available: ^{1}H and ^{13}C NMR of compounds **1**, **3a**, **3b**, and **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO015638N