[1-(Phenylthio)-2-carbamoylallyl]lithium Reagents. Electrophilic Substitution and Formal Anionic 3 + 2 Cyclization–Elimination

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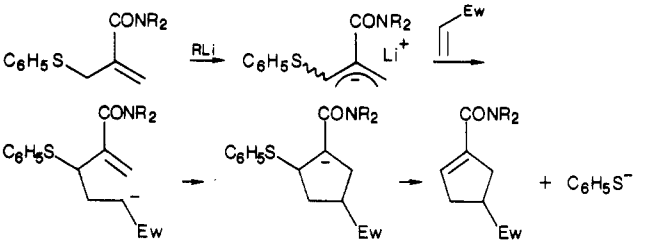
The formation and reaction of a number of [1-(phenylthio)-2-carbamoylallyl]lithium reagents is reported. Lithiation of the β′- and β-(phenylthio)-α,β-unsaturated carbamates provides **8**, **13**, and **35** from tertiary amides and **26**, **32**, and **45** from secondary amides. These reagents are geometrically stable and react regioselectively with a variety of electrophiles. The reaction of **8** with *N*-methyl-*N*-phenylacrylamide gives the cyclopentenes **42** and **43** while reactions of **13** and **45** with azobenzene gives the dihydropyrazoles **44** and **46**, respectively. These sequences involve β′-directed lithiations, stepwise anionic 3 + 2 cyclizations, and thermodynamically driven eliminations. The formation of the quinoline **47** from **12**, an adduct of **8** and azobenzene, is reported.

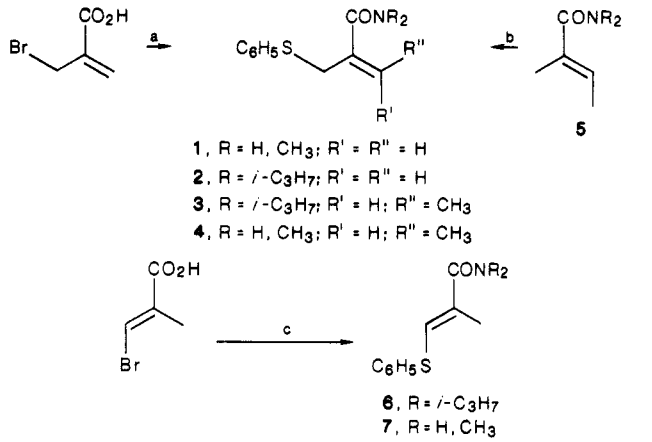
Efficient syntheses of cyclopentane rings have been the focus of a large number of methodological studies.[1] One of the most attractive approaches, the anionic 3 + 2 cyclization route, first studied extensively by Kauffmann, appears not to have been fully developed because of the limited availability of allyl carbanions that bear a strongly electron withdrawing group at the 2-position.[2] We have reported that β′-lithiation of α-methyl-β-alkyl-α,β-unsaturated tertiary amides gives (1-alkyl-2-carbamoylallyl)-lithium reagents which undergo stepwise 3 + 2 cyclizations with acrylamides to provide 1,4-dicarboxamido-2-alkylcyclopentanes.[3] While those results demonstrated the cyclization to be possible, the limitations of that specific system led us to investigate other tertiary amide derivatives. In this report we discuss the formation and reaction of [1-(phenylthio)-2-carbamoylallyl]lithium reagents.

The postulated advantage of such a species for cyclopentene synthesis is illustrated in Scheme I. The β′-phenylthio group should increase the reactivity of the reactant and the stability of the product in the metalation step, give regiocontrol of electrophilic addition in the second step, and provide a thermodynamically driven reaction, by acting as a leaving group, in the final step of the proposed 3 + 2 cyclization sequence.[4,5]

Scheme I



Scheme II[a]



[a] (a) C_6H_5SH, K^+-O-*t*-Bu; H_3O^+; $SOCl_2$; R_2NH; (b) *sec*-BuLi–TMEDA; $(C_6H_5S)_2$; H_2O; (c) C_6H_5SCu; H_3O^+; $SOCl_2$; R_2NH.

Uda and co-workers have reported the dilithiation and electrophilic substitution of the secondary amides 2-[(phenylthio)methyl]-*N*-*tert*-butylpropenamide and (*E*)-2-methyl-3-(phenylthio)-*N*-*tert*-butylpropenamide to give [1-(phenylthio)-2-carbamoylallyl]lithium reagents.[6] They

(1) For recent examples, see: Demuth, M., Schaffner, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *20*, 820. Bal, S. A.; Marfat A.; Helquist, P. *J. Org. Chem.* **1947**, *47*, 5047. Piers, E.; Karunaratine, V. *Ibid.* **1983**, *49*, 1774. Leone-Bay, A.; Paquette, L. *Ibid.* **1982**, *47*, 4173. Trost, B. M.; Chan, B. M. J. *J. Am. Chem. Soc.* **1983**, *102*, 2315. Calligaris, M.; Cartusan, G.; Nardin, G.; Sirivanti A.; Wojciki, A. *Organometallics* **1983**, *2*, 865. Santelli-Rouvier C.; Santelli, M. *Synthesis* **1983**, *429*. Denmark, S.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642. Magnus, P.; Quagliato, D.; Huffman, J. C. *Organometallics* **1982**, *1*, 1240. Danheiser, R. L.; Carini, D. J.; Basar, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. Little, R. D.; Muller, G. W.; Vengas, M. G.; Carroll, G. C.; Kukhari, A.; Patton, L.; Stone, J. *Tetrahedron Lett.* **1981**, *22*, 4371. Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1984**, *106*, 805. For a recent summary, see: Trost, B. M. *Chem. Soc. Rev.* **1982**, *11*, 141.

(2) The anionic 3 + 2 cyclization reaction was first recognized as a general process for cyclopentane synthesis by Kauffmann: Kauffmann, T. H. *Top. Curr. Chem.* **1980**, *92*, 109 and references cited therein.

(3) Beak, P.; Wilson, K. D. *J. Org. Chem.* **1986**, *51*, 4627.

(4) For examples of the Michael addition–elimination sequence, see Nelson, R. P.; Lawton, R. G. *J. Am. Chem. Soc.* **1966**, *88*, 3884. Mitra, S.; Lawton, R. G. *Ibid.* **1979**, *101*, 3067. Saddler, J. C.; Donaldson, R. E.; Fuchs, P. L. *Ibid.* **1981**, *103*, 2110. Anzeveno, P. B.; Matthews, D. P.; Barney, C. L.; Barbuch, R. J. *J. Org. Chem.* **1984**, *49*, 3134. Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, *26*, 425. For cases of intermolecular conjugate addition–elimination reactions of organocuprates with β-(alkylthio)-α,β-unsaturated carbonyl compounds see Dieter, R. K.; Fishpaugh, J. R.; Silks, L. A. *Tetrahedron Lett.* **1982**, *23*, 3751. Coates, R. M.; Sanderfur, L. O. *J. Org. Chem.* **1974**, *39*, 275. For an addition–elimination of a β-bromo ketone by a copper sulfide, see: Piers, E.; Cheng, K. F.; Nagakura, I. *Can. J. Chem.* **1982**, *60*, 1256.

(5) (a) The phenylthio group has been shown to decrease the pK_a of a carbon–hydrogen bond by about 10 pK_a units in dimethyl sulfoxide. Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1983**, *48*, 2216. For recent cases involving phenylthio activation, see: Katritzky, A. R.; Saczewski, F.; Marson, C. M. *J. Org. Chem.* **1985**, *50*, 1351. Takano, K.; Yasuda, A.; Urabe, H.; Kuwajima, I. *Tetrahedron Lett.* **1985**, *26*, 6228. (b) For recent cases of sulfone activation in systems similar to the present cases, see: Tanaka, K.; Yoda, H.; Kaji, A. *Tetrahedron Lett.* **1985**, *26*, 4747. Beak, P.; Burg, D. A. *Tetrahedron Lett.*, in press.

(6) (a) Kitaoka, M.; Takahashi, Y.; Kosugi, H.; Uda, H. *Chem. Lett.* **1983**, 1065. Uda and co-workers reported that (*Z*)-2-methyl-3-(phenylthio)-1-butylpropenamide gives vinyl lithiation. The difference between these *Z* and *E* isomers is consistent with the importance of complexation between the amide function and the organolithium base in directing the metalation.[7] Uda et al. also report dilithiations of the corresponding acids to give the β′-lithiated species. (b) Miyata, O.; Schmidt, R. R. *Tetrahedron Lett.* **1982**, *23*, 1793 and references cited therein.

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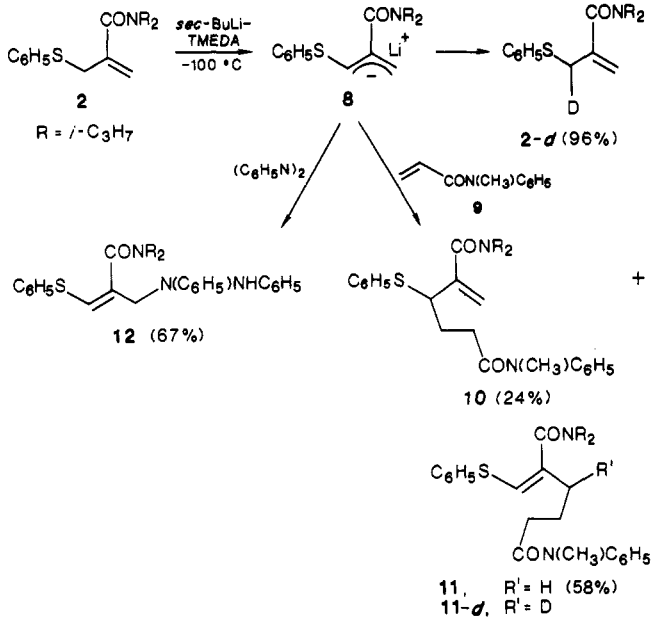
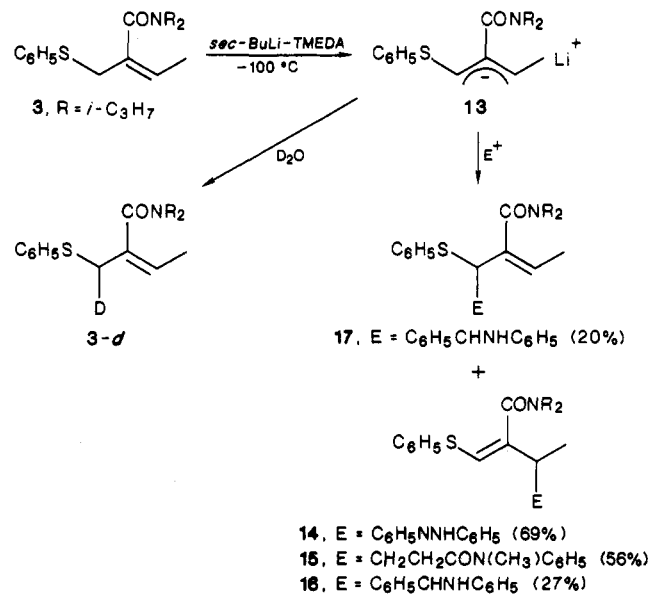
Scheme III



Scheme IV



found that these derivatives react with a number of electrophiles to give *E*-substituted products. Uda also reported that 2-[(phenylthio)methyl]-*N*,*N*-diisopropylpropenamide undergoes β' lithiation to give a species which is unstable above −50 °C and reacts with acetone to give β and β' adducts. We chose derivatives of tertiary amides to test Scheme I because of the presumed ability of the carbonyl group of a tertiary amide to promote the cyclization step more effectively than a lithiated secondary amide.

We have found that β' lithiations of β'- and β-(phenylthio)-substituted tertiary methacryl amides give stable [1-(phenylthio)-2-carbamoylallyl]lithium reagents **8**, **13**, and **35** and these react regioselectively with a variety of electrophiles. Addition of **8** to *N*-methyl-*N*-phenylacrylamide or of **13** to azobenzene give five-membered ring products via stepwise processes albeit as a mixture of olefine isomers, in the former case. We have also found that **45**, a β'-lithiated secondary amide, adds to azobenzene to give an adduct which can be cyclized. In addition we report a novel cyclization of **12**, an adduct of **8** with azobenzene to the quinoline **47**.

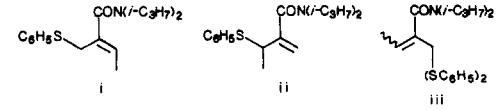
Results and Discussion

Preparation, Structure, and Electrophilic Substitution of [1-(Phenylthio)-2-carbamoylallyl]lithium Reagents. The (phenylthio)-substituted α,β-unsaturated carboxamides required for preparation of the [1-(phenylthio)-2-carboxamoylallyl]lithium reagents were prepared by standard methods as shown in Scheme II. The amides **1** and **2** are derived from 2-bromoacrylic acid. The butenamides **3** and **4** were prepared by lithiation of the corresponding tiglamide **5** followed by reaction with diphenyl disulfide.[8,9] The (*E*)-3-(phenylthio)propenamides **6** and **7** were prepared from 2-methyl-3-bromopropenoic acid. The geometry about the double bond is assigned to **3** on the basis of the method of Uda in which 0.3 to 0.5 ppm downfield shift is observed in the ^{1}H NMR spectra for the signal of the vinyl or methyl protons cis to the sulfur when the thioether is converted to the sulfoxide.[3,8,10,11] The *E* geometry about the double bond of **7** was established by conversion of the acid chloride used to make the amide to the ethyl ester of known configuration.[8,9]

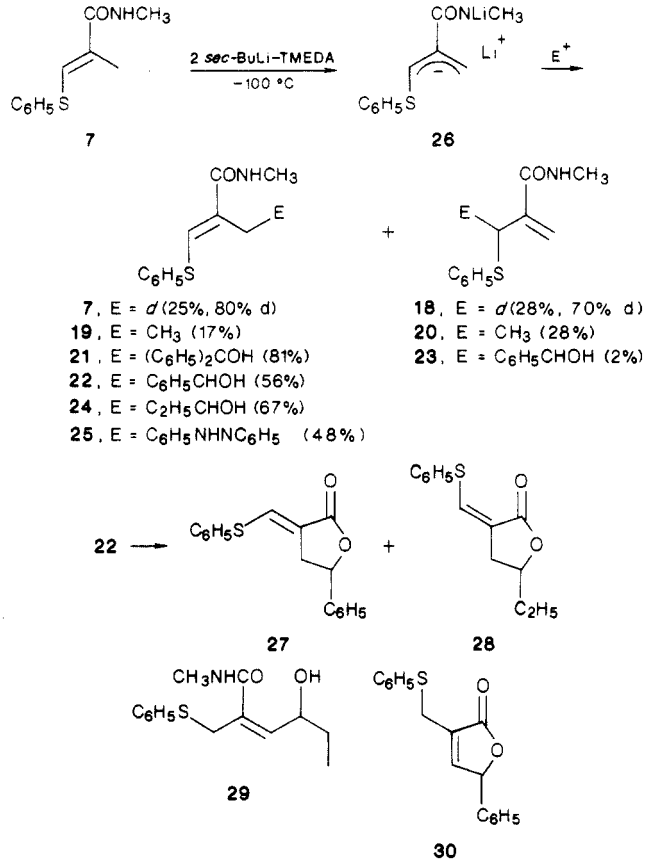
The β' lithiations of the α,β-unsaturated carboxamides **1**–**4** and **6**–**7** to give [1-(phenylthio)-2-carbamoylallyl]lithium reagents and electrophilic reactions of these reagents are straightforward. Metalation of the tertiary amide **2** with *sec*-butyllithium–tetramethylethylenediamine (*sec*-BuLi–TMEDA) at −100 °C provides **8** which reacts with deuterium oxide to give **2**-*d* in 96% yield (Scheme III). The use of lithium tetramethylpiperdide as the base provides **2**-*d* in 69% yield. Addition of **8** to *N*-methyl-*N*-phenylacrylamide (**9**) followed by hydrolysis at −60 °C gives the diamides **10** and **11**. The sulfoxide from **11** shows the diastereotopic allyl protons to have a chemical shift within δ 0.08 of the corresponding protons in **11**. Accordingly the sulfoxide and alkyl group are assigned a trans disposition about the double bond and this geometry is assigned to **8** as well. Addition of **8** to azobenzene provides **12** in which the assignment of double-bond geometry is based on analogy to **11** and preparation of a nonidentical *E* isomer (vide infra).

Scheme IV illustrates the lithiation and electrophilic substitution of **3**. Since the sequence using deuterium oxide provides **3**-*d* which has retained double-bond geometry, the intermediate (2-carbamoylallyl)lithium is considered to be **13**, also with retained geometry. Addition of **13** to azobenzene and aqueous workup at −60 °C gives **14**. Addition of **13** to **9** gives **15** in 56% yield, while addition to *N*-phenylbenzylidenimine provides the amines **16** and **17**. Retention of the double-bond geometry is

(7) This may be described as a complex-induced proximity effect. Beak P.; Meyers, A. I. *Acc. of Chem. Res.*, in press.
(8) Wilson, K. D. Ph.D. Thesis, University of Illinois, 1984, available form University Microfilms, Ann Arbor, MI.
(9) Takahashi, Y.; Kosugi, H.; Uda, H. *Tetrahedron Lett.* **1982**, *23*, 815.
(10) Yamagiwa, S.; Hoshi, N.; Sato, H.; Kosugi, H.; Uda, H. *J. Chem. Soc., Perkin Trans. 1* **1978**, 214.
(11) The formation of **3** is accompanied by its geometrical isomer (*E*)-2-(phenylthio)-*N*,*N*-diisopropyl-2-butenamide (i). The formation of the two geometrical isomers **3** and i from the geometrically defined tiglamide **5** is the only case of isomerization we have encountered and is attributed to equilibration by protonation–deprotonation under the reaction conditions. The formation of **3** and its geometrical isomer is accompanied by 4% of ii and 18% of iii. The latter product indicates the possibility of a second deprotonation after substitution.



Scheme V

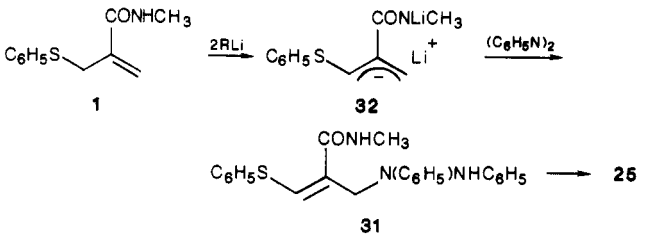


presumed for **14**, **15**, and **16**.

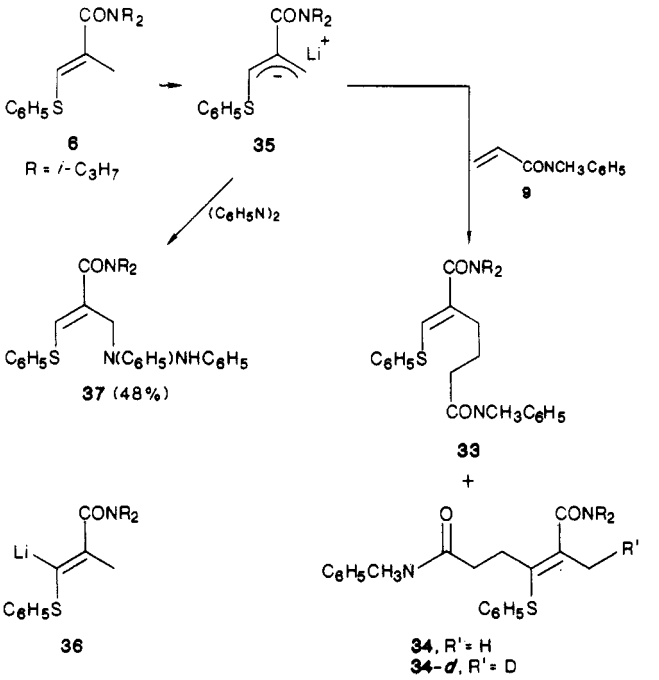
The lithiations of **2** and **3** contrast with the earlier findings that acrylamide systems, which lack the phenylthio group or have a syn β-methyl, undergo self-condensation or γ-lithiation respectively.[3,12] The β'-phenylthio group clearly provides additional activation for β' lithiation and stabilization of the intermediate (2-carboxamoylallyl)lithium reagent. Thus the phenylthio group meets the requirement of the first steps of Scheme I.

The geometry of the intermediate [1-(phenylthio)-2-carbamoylallyl]lithium reagents and the regiochemistry of their reactions with electrophiles was investigated for additional systems. The secondary amide **7** was found to be a suitable precursor for a [*N*-lithio-1-(phenylthio)-2-carbamoylallyl]lithium reagent consistent with Uda's recent work.[6] Lithiation of **7** with 2 equiv of *sec*-BuLi–TMEDA at −100 °C followed by reaction with deuterium oxide, methyl iodide, benzophenone, benzaldehyde, propional, and azobenzene gives the products **7**-*d* and **18**–**25** as shown in Scheme V. The low isolated yields of deuterated products were due to mechanical problems in their separation as the mixture is obtained in 94% yield. Retention of the double-bond geometry, consistent with the intermediacy of **26**, is assigned by oxidation and ^{1}H NMR analysis of unpurified sulfoxides which have appropriate chemical shifts.[8,13] The regioisomers **19** and **20** from the reaction of **26** with methyl iodide are obtained in comparable and modest yields but additions to benzophenone

Scheme VI



Scheme VII



and benzaldehyde proceed regioselectively in good yields to provide **21** and **22**. The isomeric lactones **27** and **28**, characterized only by their spectral properties, are obtained in 45% and 15% yields, respectively, when **22** is heated for 20 min at 200 °C, geometrical isomerization of the double bond must occur under the cyclization conditions. The major product of the reaction of **26** with propional is **24** but it is accompanied by 8% of an isomer, **29**, and 1% of a lactone, **30**. Apparently **30** results from cyclization of **29** which, in turn, is the result of isomerization of **24**.

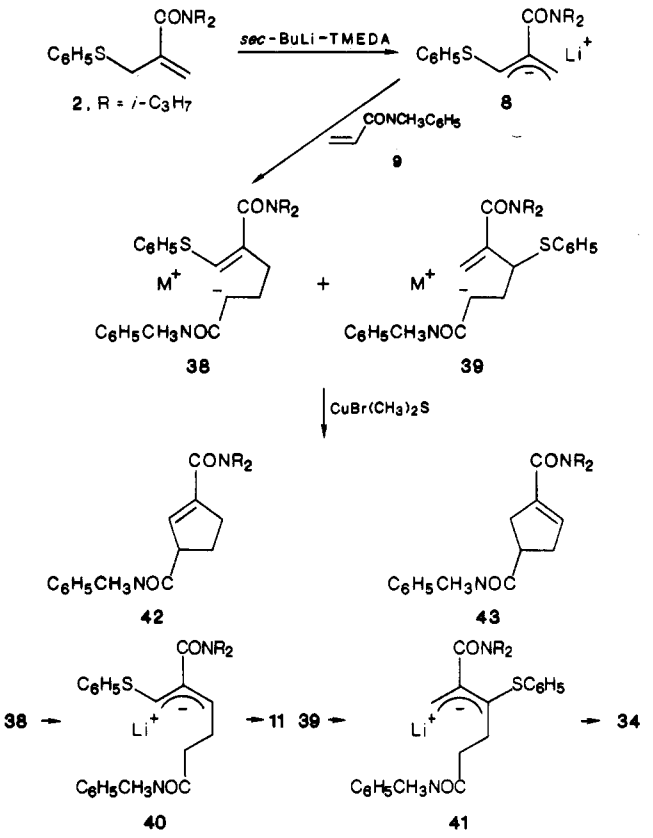
Reaction of **26** with azobenzene gives **25**, a geometrical isomer of **31** which is produced from lithiation of **1** and reaction with azobenzene as shown in Scheme VI. The hydrazine **31** was characterized by ^{1}H NMR and undergoes isomerization to **25** on standing. The formation of different isomers from **1** and **7** is consistent with the intermediacy of two geometrically isomeric allyllithium species **26** and **32**.

Additional support for the geometric stability of [1-(phenylthio)-2-carbamoylallyl]lithium reagents is provided by the lithiation of the β-(phenylthio)-α,β-unsaturated tertiary amide **6** to give, after addition to the acrylamide **9**, the products **33** and **34** as shown in Scheme VII. The diamide **33** is the geometric isomer of **11** produced from **8**. These results show that **35** formed from **6** and **8** formed from **2** are geometrically isomers and add to **9** with retention of geometry. The formation of **34** could involve the vinyllithium **36** as an intermediate, consistent with the work of Uda and Schmidt, and of the importance of proximity in amide-directed lithiations.[6,7] Another possible route to **34** involves proton transfer in the initial adduct

(12) Beak, P.; Kempf, D. J.; Wilson, K. D. *J. Am. Chem. Soc.* **1985**, *107*, 4745.

(13) For other cases of geometrically stable sulfide-substituted allyl anions, see: Ruel, O.; Ekogha, B. B.; Julia, S. A. *Tetrahedron Lett.* **1983**, *24*, 4829. Biellmann, J. F.; Ducep, J. B. *Tetrahedron* **1971**, *27*, 5861. Hartmann, J.; Muthukrishnan, R.; Schlosser, M. *Helv. Chim. Acta* **1974**, *57*, 2261.

Scheme VIII



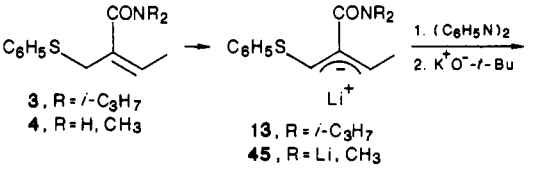
(Scheme VIII). If azobenzene is used as the electrophile for **35**, **37** is obtained in 48% yield. The hydrazine **37** is isomeric with **12**. The apparent preference for electrophilic substitution in the position γ to the sulfide is different from the usual preference of 1-sulfur-substituted allyllithium reagents for a substitution.[14] These results also show the reactions of the geometrically stable [1-(phenylthio)-2-carbamoylallyl]lithium reagents with electrophiles to be regioselective.

Cyclizations to Five-Membered Rings. The formations of the [1-(phenylthio)-2-carbamoylallyl]lithium reagents **8**, **13**, and **35** and their regioselective additions to azobenzene and to *N*-methyl-*N*-phenylacrylamide (**9**) show that the first two steps of Scheme I can be achieved. Cyclization of the adducts is required to illustrate the feasibility of the overall sequence.

If the solution produced from addition of **8** to **9** is allowed to warm to room temperature before hydrolysis, the acyclic amides **11** and **34** are obtained in 21% and 9% yields, respectively. If the hydrolysis is carried out with deuterium oxide, **11**-*d* and **34**-*d* with deuterium in the allylic positions are found in 13% and 6% yields, respectively. The formation of these products is postulated to involve proton transfer of the initially formed adducts **38** and **39** (bottom of Scheme VIII) to give **40** and **41**, respectively, prior to quenching. Apparently the inhibition of a 5-endo-trig cyclization is sufficient to prevent ring closure under these conditions.[13,15]

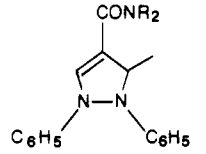
Cyclopentenes can be obtained from these reactants, however, if lithiation and addition is followed by warming to ambient temperature for 48 h in the presence of cuprous bromide–dimethyl sulfide as shown in Scheme VIII. In this case, an unseparated 1:3 mixture of **42** and **43** is obtained in 39% yield. The ratio of the isomers was established by capillary GLPC and the structural assignments are based on the MS, IR, and ^{1}H and ^{13}C NMR spectral properties as well as elemental analysis of the mixture. In the major isomer, **43**, the vinyl hydrogen appears at δ 5.56 as a triplet with J = 1.5 Hz. A single hydrogen at δ 3.12 is assigned to the position α to the anilide carbonyl group because it is coupled to two sets of methylene groups. In the minor isomer the vinyl hydrogen at δ 5.50 is a quartet with a coupling of 0.6 Hz due to adjacent and long range coupling and the single hydrogen at δ 3.58 adjacent to the anilide group is coupled only to a single adjacent methylene group. The formation of these cyclopentenes show that the postulate of Scheme I, the coupling of an anionic 3 + 2 cyclization with an elimination step, is feasible.[2,4,15-17] The isolation of **11** and **34** in the absence of cuprous bromide confirms the stepwise nature of the reaction.[2,3]

The cyclization–elimination sequence may also be demonstrated for the formation of a heterocyclic ring. If the lithiation of **3** to give **13** followed by the addition of azobenzene is subsequently allowed to warm to room temperature in the presence of potassium *tert*-butoxide the dihydropyrazole **44** is obtained in 72% yield. Since quenching of the reaction of **13** with azobenzene at −60 °C gives **14**, this reaction also proceeds in a stepwise mechanism.



3, R = *i*-C$_3$H$_7$
4, R = H, CH$_3$

13, R = *i*-C$_3$H$_7$
45, R = Li, CH$_3$



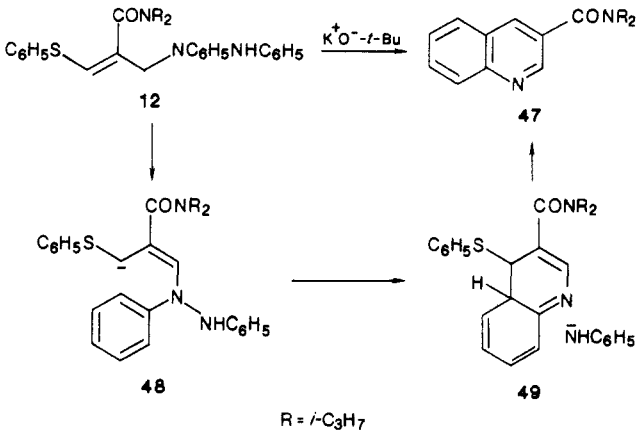
44, R = *i*-C$_3$H$_7$
46, R = H, CH$_3$

We also tested a secondary amide in this sequence. Thus lithiation of **4** to give **45** when followed by addition of azobenzene and reaction with potassium *tert*-butoxide provides the dihydropyrazole **46** in 60% yield. While the cyclization in this case appears to be slower than for the sequence from **3**, it appears that derivatives of secondary amides can be used in this sequence.

Cyclization to a Quinoline. In the course of investigating the cyclizations, the hydrazine derivative **12** was treated with potassium *tert*-butoxide. The product from reaction is identified as *N*,*N*-diisopropyl-3-quinolinecarboxamide (**47**) in 91% yield. The structural assignment rests on analytical and spectral properties as well as independent synthesis from the corresponding acid. We postulate that the reaction proceeds by formation of the allyl anion **48** followed by cyclization–elimination to give the dihydroisoquinoline derivative **49** which can undergo loss of thiophenol to provide **47**.

Conclusion. The present work demonstrates that [1-(phenylthio)-2-carbamoylallyl]lithium reagents can be readily formed, retain their geometry, and can add to an α,β-unsaturated amide and to azobenzene to give intermediates which can further react in a cyclization–elimination sequence to provide five-membered ring products.

(14) Biellmann, J. F.; Ducep, J. B. *Org. React.* (*N.Y.*) **1982**, *27*, 1.
(15) Baldwin, J. E.; Husch, M. J. *Tetrahedron* **1982**, *38*, 2939 and references cited therein.
(16) Klupp, G. W.; Schmatz, R. C. *Tetrahedron Lett.* **1974**, 2911.
(17) Allylic substitution of a sulfide is known: Smith, A. B. III; Wexler, B. A.; Slade, J. S. *Tetrahedron Lett.* **1980**, *21*, 3237.



The proposal in Scheme I is thus demonstrated. However regiospecificity and use of a wider range of electrophiles is desirable for the second step of the sequence. Extension of the approach to related systems will be explored.[5b]

Experimental Section

General. Proton chemical shifts are reported in δ (ppm) downfield from an internal tetramethylsilane standard for solutions in $CDCl_3$, unless otherwise noted. All decoupling, two-dimensional, and NOE experiments were performed on a Nicolet NT-360 spectrometer. Mass spectra were recorded by Mr. Carter Cook and associates on Varian MAT CH-5 or 731 mass spectrometers. Elemental analyses were performed by Mr. J. Nemeth and associates.

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The temperatures for bulb-to-bulb distillations in a Kugelrohr apparatus represent the temperature of the air bath used and may not be an accurate measure of the boiling point. High pressure liquid chromatographic (HPLC) separations were performed on a Waters M6000 HPLC on a 50 cm × 1 cm column containing irregular 10 ± 4 μm silica gel. Medium pressure liquid chromatographic (MPLC) separations were performed on a 36 in. × 1 in. column packed with Ventron 43–64-mesh silica gel.

Materials. All compounds obtained from commercial sources were used without further purification unless otherwise noted. Tetrahydrofuran (THF), diethyl ether (Et_2O), and dimethoxyethane (DME) were freshly distilled from sodium/benzophenone under an atmosphere of dry nitrogen. Pentane was dried and stored over calcium hydride under an atmosphere of dry N_2. Tetramethylethylenediamine (TMEDA) was distilled from CaH_2 under N_2. Diisopropylamine (DA) and 2,2,6,6-tetramethylpiperidine (TMP) were azeotropically dried then distilled under N_2. Thionyl chloride was distilled before use. Commercial solutions of *n*-butyllithium (*n*-BuLi) in hexanes and *sec*-butyllithium (*sec*-BuLi) in cyclohexane were titrated by using a modification of Tischler and Tischler's procedure.[18] The preparations of **1**, **2**, **3**, **4**, **6**, **7**, **27**, and **28** are described in the supplementary material.

Lithiations of Amides. The typical procedures for the lithiation of 1–2 mmol of amide are shown below. The amount of reagent used, purification method, spectroscopic and analytical data, and any variations in these procedures are included with specific cases.

Procedure A. A dry three-necked, round-bottomed flask is equipped with an overhead stirring apparatus, alcohol thermometer, and pressure equalizing dropping funnel and is flushed with N_2. The TMEDA, 1–2 mg of *N*-benzylbenzamide indicator, and 30–60 mL of THF are added to the flask and the solution is cooled with stirring in an ice/acetone bath. To this solution is added *sec*-BuLi dropwise until a pale blue solution just forms and persists (usually 1–5 drops). This ensures that the solvent and apparatus are completely anhydrous. The solution is cooled to −70 °C, the required amount of *sec*-BuLi is added, and the mixture is stirred for 15 min and then cooled to −100 to −105 °C by using a bath prepared by adding liquid N_2 to 2:1 mixture of pentane and methanol. The amide in 5–10 mL of THF is added dropwise over 5 min to the vigorously stirred solution maintaining the temperature at −95 to −105 °C. After 5 additional min either 1 mL of D_2O, or MeOD, in 5 mL of THF is added. Alternatively the solution is warmed to −70 °C and the electrophile is added as a solution in 5 mL of THF. The mixture is allowed to stir for ca. 15 min and then hydrolyzed by pouring into ca. 20 mL of 5% HCl, or if the product is an amine into H_2O. The resulting solution is concentrated in vacuo, the organics are extracted with 50–100 mL of Et_2O, and the extract is dried over either $CaSO_4$ or $MgSO_4$ and concentrated in vacuo to give the crude product.

Procedure B. A dry solution of TMEDA, 1–2 mg of *N*-benzylbenzamide in 30–60 mL of THF in a one-necked flask equipped with a magnetic stirrer and pressure equalizing dropping funnel, is prepared as described above. The required amount of *sec*-BuLi is added at −78 °C and stirred for 15 min. The amide and then electrophile are introduced and the mixture is worked up as described above.

(*Z*)-6-(Phenylthio)-5-(*N*,*N*-diisopropylcarbamoyl)-*N*-methyl-*N*-phenyl-5-hexenamide (11) and 4-(Phenylthio)-5-(*N*,*N*-diisopropylcarbamoyl)-*N*-methyl-*N*-phenyl-5-hexenamide (10). According to procedure A: 2.68 mmol of *sec*-BuLi and 405 μL (2.68 mmol) of TMEDA in 100 mL of THF, 677 mg (2.44 mmol) of **2** in 10 mL of THF, 393 mg (2.68 mmol) of **9** in 10 mL of THF; reaction conditions: −100 °C, 5 min, **9** is added at −70 °C, stirred for 1 h, and then poured into 5% HCl. Workup as usual and chromatographic separation by MPLC using 30% EtOAc/hexanes and then 70% EtOAc/hexanes on a 40 × 0.5 in. (10 ± 4 μm) silica gel column gives 258 mg (24%) of **10**: $bp^{0.15}$ 120–130 °C; ^1H NMR δ 1.103 (unresolved m, 6 H), 1.234 (unresolved m, 6 H), 2.071 (m, 1 H), 2.221 (m, 2 H), 2.348 (m, 1 H), 3.229 (s, 3 H), 3.4 (br m, 1 H), 4.020 (t, J = 6 Hz, 1 H), 4.19 (m, 1 H), 5.043 (s, 1 H), 5.182 (s, 1 H), 7.10–7.39 (m, 10 H); ^{13}C NMR δ 20.6 (q), 29.9 (t), 31.9 (t), 37.3 (q), 45.6 (br d), 50.6 (br d), 50.7 (d), 112.9 (t), 126.5 (d), 127.3 (d), 127.6 (d), 128.8 (d), 129.7 (d), 130.6 (d), 135.7 (s), 144.2 (s), 145.3 (s), 170.2 (s), 172.3 (s); MS, *m*/*e* (relative intensity) 438 (17), 338 (14), 329 (52), 290 (12), 230 (36), 134 (30), 120 (37), 119 (31), 111 (19), 105 (42), 100 (22), 97 (26), 85 (58), 83 (92), 71 (56), 57 (100); IR (thin film) 2960, 1660, 1645, 1625, 1600, 1500, 1450, 1390, 1350, 1210, 1170, 1130, 1050, 925, 780, 745, 702 cm^{-1}.

Anal. Calcd for $C_{28}H_{34}N_2O_2S$: C, 71.19; H, 7.81; N, 6.39. Found: C, 71.15; H, 7.65; N, 6.16.

Also obtained is 614 mg (58%) of **11** (three crops): mp 101–103 °C, mmp 101–103 °C; ^1H NMR δ 1.188 (unresolved m, 6 H), 1.467 (unresolved m, 6 H), 1.834 (tt, J = 7 Hz, 2 H), 2.160 (t, J = 7 Hz, 2 H), 2.260 (t, J = 7 Hz, 2 H), 3.249 (s, 3 H), 3.390 (m, 1 H), 3.99 (m, 1 H), 6.015 (s, 1 H), 7.15–7.42 (m, 10 H); ^{13}C NMR δ 21.0 (br q), 23.3 (t), 33.2 (t), 34.4 (t), 37.3 (q), 45.9 (br d), 50.4 (br d), 119.2 (d), 126.4 (d), 127.5 (d), 127.7 (d), 128.9 (d), 129.0 (d), 129.8 (d), 136.2 (s), 141.3 (s), 144.1 (s), 168.7 (s), 172.4 (s); MS, *m*/*e* (relative intensity) 438 (35), 338 (5), 329 (73), 289 (72), 231 (34), 230 (33), 222 (28), 204 (27), 200 (26), 189 (49), 134 (43), 107 (49), 106 (51), 100 (13), 92 (32), 86 (38), 77 (38), 43 (100), 28 (95); IR (Nujol) 2920, 1660, 1620, 1600, 1490, 1450, 1365, 1335, 1275, 1210, 1140, 1040, 1020, 1010, 920, 880, 865, 840, 776, 750, 700 cm^{-1}.

Anal. Calcd for $C_{28}H_{34}N_2O_2S$: C, 71.19; H, 7.81; N, 6.39; S, 7.31. Found: C, 70.82; H, 7.83; N, 6.12; S, 7.27.

(*Z*)-1-(Phenylthio)-*N*,*N*-diisopropyl-4,5-diphenyl-4,5-diaza-1-pentene-2-carboxamide (12). According to procedure A: 4.52 mmol of *sec*-BuLi and 684 μL (4.52 mmol) of TMEDA in 150 mL of THF, 1.144 g (4.12 mmol) of **2** in 10 mL of THF, 826 mg (4.52 mmol) of azobenzene in 10 mL of THF; reaction conditions −70 °C, 5 min, azobenzene is added and after 15 min the solution is poured into brine. Workup as usual and chromatographic separation by MPLC using 5% EtOAC/hexanes gives 1.274 g (67%) of **12**: mp 109–110 °C (from pentane); ^1H NMR δ 1.27 (br d, 12 H), 3.47 (br m, 2 H), 4.42 (s, 2 H), 6.27 (s, 1 H), 6.7–7.3 (m, 15 H); ^{13}C NMR (nitromethane-d_3) δ 20.7 (q), 21.6 (q), 46.8 (d), 52.1 (d), 55.8 (t), 113.8 (d), 114.5 (d), 119.9 (d), 120.5 (d), 124.5 (d), 128.0 (d), 129.9 (d), 130.3 (d), 130.5 (d), 130.6 (d), 136.4 (s), 137.7 (s), 148.7 (s), 150.9 (s), 169.2 (s); MS, *m*/*e* (relative intensity) 459 (2), 331 (3), 277 (30), 183 (13), 177 (39), 168 (100), 105 (11), 77 (70), 43 (41); IR (film with CCl_4) 3270, 3050, 2970, 1615, 1600, 1490, 1440, 1365, 1270, 1210, 1155, 1085, 1035, 1020, 985, 880, 790, 760, 690 cm^{-1}.

(18) Tischler, A. N.; Tischler, M. H. *Aldrichimica Acta* **1978**, *11*, 20.

Anal. Calcd for $C_{28}H_{33}N_3OS$: C, 73.11; H, 7.24; N, 9.14; S, 6.98. Found: C, 72.78; H, 7.34; N, 9.18; S, 6.85.

(*Z*)-1-(Phenylthio)-*N*,*N*-diisopropyl-4,5-diphenyl-3-methyl-4,5-diaza-1-pentene-2-carboxamide (14). According to procedure A: 1.13 mmol of *sec*-BuLi and 171 μL (1.13 mmol) of TMEDA in 23 mL of THF, 300 mg (1.03 mmol) of **3** in 10 mL of THF; reaction conditions: −90 °C, 5 min; azobenzene is added and stirred for 1 h at −50 °C and then poured into brine, extractive workup and purification by preparative TLC with 15% EtOAc/hexanes and then recrystallization from hexane/CH_2Cl_2 gives 338 mg (69%) of **14**: mp 128–135 °C; ^{1}H NMR δ 1.20 (br d, 6 H), 1.45 (br d, 6 H), 1.52 (d, *J* = 6 Hz, 3 H), 3.25 (m, 1 H), 4.05 (m, 1 H), 4.81 (q, *J* = 6 Hz, 1 H), 6.23 (s, 1 H), 6.7–7.3 (m, 11 H); ^{13}C NMR δ 17.3, 19.5, 20.0, 21.0, 21.5, 46.1, 50.8, 60.2, 111.8, 115.0, 118.2, 119.4, 123.9, 126.8, 129.1, 129.3, 135.5, 139.1, 149.0, 149.6, 168.6; MS, *m*/*e* (relative intensity) 473 (10), 370 (13), 364 (7), 342 (6), 290 (48), 191 (100), 182 (41), 161 (10), 147 (17), 128 (38), 109 (14), 100 (35), 86 (82), 81 (73), 77 (40), 55 (27), 43 (92), 41 (29); IR (KBr) 3440, 2970, 1616, 1600, 1495, 1445, 1370, 1350, 1310, 1250, 1210, 1160, 1035, 830, 750, 694 cm^{-1}.

Anal. Calcd for $C_{39}H_{35}N_3OS$: C, 73.53; H, 7.45; N, 8.87; S, 6.77. Found: C, 73.66; H, 7.63; N, 8.87; S, 6.91.

(*Z*)-6-(Phenylthio)-5-(*N*,*N*-diisopropylcarbamoyl)-*N*,4-dimethyl-*N*-phenyl-5-hexenamide (15). According to procedure A: 3.24 mmol of *sec*-BuLi and 488 μL (3.24 mmol) of TMEDA in 150 mL of THF, 786 mg (2.70 mmol) of **3** in 10 mL of THF; 457 mg (3.24 mmol) of **9** in 10 mL of THF; reaction conditions: −100 °C, 5 min, **9** is added at −60 °C and then stirred for 4 h at −60 °C. Workup as usual and chromatographic separation by MPLC using 20% EtOAc/hexanes gives 688 mg (56%) of **15**: mp 101–103 °C (from EtOAc/pentane); ^{1}H NMR δ 1.08 (d, *J* = 6 Hz, 3 H), 1.21 (br d, 6 H), 1.50 (br d, 6 H), 1.73 (m, 1 H), 1.96 (m, 1 H), 2.21 (m, 2 H), 2.41 (m, 1 H), 3.25 (s, 3 H), 3.4 (br m, 1 H), 3.98 (m, 1 H), 6.02 (s, 1 H), 7.20–7.45 (m, 10 H), decoupling [irradiation at δ 1.08 simplifies 2.41 to dd, 2.41 simplifies 1.08 to s, 1.73 and 1.96]; ^{13}C NMR δ 19.3 (q), 21.0 (br q), 31.3 (t), 31.7 (t), 37.3 (q), 38.3 (d), 45.7 (br d), 50.2 (br d), 118.9 (d), 126.4 (d), 127.2 (d), 127.6 (d), 128.8 (d), 129.0 (d), 129.7 (d), 136.3 (s), 144.2 (s), 145.4 (s), 168.4 (s), 172.7 (s); MS, *m*/*e* (relative intensity) 452 (94), 352 (7), 343 (100), 304 (94), 242 (12), 236 (19), 203 (18), 149 (17), 110 (30), 107 (18), 100 (7); IR (Nujol) 3020, 2920, 1655, 1610, 1490, 1450, 1370, 1350, 1210, 1110, 1040, 1020, 845, 820, 775, 740, 700 cm^{-1}.

Anal. Calcd for $C_{27}H_{35}N_2O_2S$: C, 71.64; H, 8.02; N, 6.19; S, 7.08. Found: C, 71.54; H, 7.74; N, 6.28; S, 7.10.

(*Z*)-1-(Phenylthio)-*N*,*N*-diisopropyl-4,5-diphenyl-3-methyl-5-aza-1-pentene-2-carboxamide (16) and (*Z*)-3-(Phenylthio)-*N*,*N*-diisopropyl-1,2-diphenyl-1-aza-4-hexene-4-carboxamide (17). According to procedure A: 1.40 mmol of *sec*-BuLi and 424 μL (2.80 mmol) of TMEDA in 28 mL of THF, 372 mg (1.28 mmol) of **3** in 10 mL of THF, 254 mg (1.40 mmol) of *N*-phenylbenzaldehydimine in 10 mL of THF; reaction conditions: −105 °C, 5 min; the imine is added at −60 °C and after 30 min brine is added. Workup as usual and chromatographic separation by MPLC using 5% EtOAc/hexanes and a 40 × 0.5 in. (10 ± 4 μm) silica gel column gives 78 mg (21%) of a 1:1 mixture of **3** and i identified by ^{1}H NMR and 164 mg (27%) of **16**: mp 163–164 °C (from CH_2Cl/hexanes); ^{1}H NMR (Me_2SO-d_6) δ 0.98 (d, *J* = 7 Hz, 3 H), 1.19 (unresolved m, 6 H), 1.42 (unresolved m, 6 H), 2.69 (m, 1 H), 3.48 (m, 1 H), 4.03 (m, 1 H), 4.53 (dq, *J* = 7 Hz, 1 H), 6.06 (s, 1 H), 6.46 (t, *J* = 7 Hz, 3 H), 6.9–7.6 (m, 13 H); ^{13}C NMR δ 18.0, 20.5 (br), 46.1 (br), 50.1 (br), 64.5, 133.1, 116.3, 126.5, 127.0, 127.8, 128.3, 129.9, 135.5, 143.0, 148.4, 169.1; FDMS, *m*/*e* 472; EIMS, *m*/*e* (relative intensity) 472 (2), 290 (20), 191 (11), 182 (100), 104 (20), 77 (28), 43 (19); IR (Nujol) 3280, 2920, 1590, 1530, 1440, 1360, 1320, 1265, 1200, 1140, 1030, 830, 750, 740, 695 cm^{-1}.

Anal. Calcd for $C_{30}H_{36}N_2OS$: C, 76.14; H, 7.67; N, 5.92; S, 6.77. Found: C, 75.88; H, 7.68; N, 5.85; S, 6.84.

Also obtained is 120 mg (20%) of **17**: mp 143–145 °C (from hexanes/CH_2Cl); ^{1}H NMR δ 0.56–0.94 (m, 6 H), 1.18 (d, *J* = 7 Hz, 3 H), 1.40–1.74 (m, 6 H), 3.03 (m, 1 H), 4.07 (m, 1 H), 4.39 (d, *J* = 5.9 Hz, 1 H), 5.20 (t, *J* = 5.9 Hz, 1 H), 5.32 (q, *J* = 7.0 Hz, 1 H), 6.83 (t, *J* = 7.4 Hz, 1 H), 6.89–7.18 (m, 12 H), 7.76 (d, *J* = 7.4 Hz, 2 H), decoupling [irradiation at δ 4.39 simplifies 5.20 to d, 5.32 simplifies to s]; FDMS, *m*/*e* 472.363; EIMS, *m*/*e* (relative intensity) 472 (2), 363 (2), 291 (26), 191 (9), 182 (100), 128 (6), 104 (13), 84 (72), 77 (16), 43 (35): IR (Nujol) 3220, 2920, 1580, 1530, 1440, 1370, 1340, 1310, 1200, 1150, 1020, 980, 920, 755, 735, 695, 690 cm^{-1}.

Anal. Calcd for $C_{30}H_{36}N_2OS$: C, 76.14; H, 7.67; N, 5.92; S, 6.77. Found: C, 76.22; H, 7.59; N, 5.69; S, 6.85.

3-(Phenylthio)-*N*-methyl-1-butene-2-carboxamide (20) and (*E*)-1-(Phenylthio)-*N*-methyl-1-butene-2-carboxamide (19). According to procedure B: 6.33 mmol of *sec*-BuLi and 955 μL (6.33 mmol) of TMEDA in 50 mL of THF, 665 mg (3.01 mmol) of **7** in 10 mL of THF, 206 μL (3.31 mmol) of methyl iodide in 10 mL of THF; reaction conditions: −70 °C, 5 min then 0 °C for 10 min, the solution is recooled to −70 °C and CH_3I is added, and after 5 min poured into water. Workup as usual followed by chromatographic separation by MPLC using a gradient from 20% to 40% EtOAc/hexanes gives 185 mg (28%) of **20**: bp$^{0.4}$ 165–170 °C; ^{1}H NMR δ 1.40 (d, *J* = 7 Hz, 3 H), 2.81 (d, *J* = 5 Hz, 3 H), 4.27 (q, *J* = 7 Hz, 1 H), 5.23 (s, 1 H), 5.59 (s, 1 H), 6.78 (m, 1 H), 7.11–7.48 (m, 5 H); MS, *m*/*e* (relative intensity) 221 (3), 220 (10), 189 (9), 168 (100), 137 (15), 113 (16), 109 (19), 101 (13), 84 (13), 69 (34), 58 (54), 55 (31), 43 (19), 41 (27), 28 (26); IR (thin film) 3550, 3010, 2920, 1630, 1570, 1530, 1470, 1440, 1420, 1310, 1160, 1090, 1030, 1000, 860, 815, 740, 705, 690 cm^{-1}.

Anal. Calcd for $C_{12}H_{15}NOS$: C, 65.13; H, 6.83; N, 6.33; S, 14.49. Found: C, 65.12; H, 6.59; N, 6.30; S, 14.47.

Also obtained is 115 mg (17%) of **19**: bp$^{0.4}$ 170–180 °C; ^{1}H NMR δ 1.05 (t, *J* = 7 Hz, 3 H), 2.43 (q, *J* = 7 Hz, 2 H), 2.79 (d, *J* = 5 Hz, 3 H), 6.24 (m, 1 H), 7.12 (s, 1 H), 7.15–7.45 (m, 5 H); ^{13}C NMR (1:1 $CDCl_3$/Me_2SO-d_6) δ 12.5 (q), 22.3 (t), 26.3 (q), 127.2 (d), 129.1 (d), 129.1 (d), 129.7 (d), 131.3 (s), 134.5 (s), 166.9 (s); MS, *m*/*e* (relative intensity) 221 (100), 191 (62), 162 (33), 147 (36), 144 (25), 135 (20), 130 (23), 129 (22), 121 (15), 112 (60), 109 (33), 91 (33), 85 (13), 77 (23), 65 (27), 58 (69), 53 (20), 52 (25), 45 (21); IR (thin film) 3550, 3020, 2930, 1630, 1580, 1530, 1475, 1455, 1405, 1305, 1260, 1155, 1090, 1075, 1055, 1025, 955, 945, 870, 795, 740, 705, 690 cm^{-1}; high resolution MS, calcd for $C_{12}H_{15}NOS$ 221.0874, found 221.0872.

Anal. Calcd for $C_{12}H_{15}NOS$: C, 65.12; H, 6.83; N, 6.33; S, 14.49. Found: C, 64.57; H, 6.68; N, 6.02; S, 14.35.

(*E*)-1-(Phenylthio)-4,4-diphenyl-4-hydroxy-*N*-methyl-1-butene-2-carboxamide (21). According to procedure B: 7.7 mmol of *sec*-BuLi and 1.16 mL (7.7 mmol) of TMEDA in 50 mL of THF, 762 mg (3.68 mmol) of **7** in 10 mL of THF, 737 mg (4.04 mmol) of benzophenone in 10 mL of THF; reaction conditions: −78 °C, 5 min; then −10 °C, 15 min, the solution is recooled to −70 °C, the benzophenone is added, stirred for 5 min, and poured into 5% HCl. Workup as usual and recrystallization of the resulting solid from EtOAc/pentane gives 1.158 g (81%) of **21**: mp 164–166 °C; ^{1}H NMR δ 2.61 (d, *J* = 5 Hz, 3 H), 3.47 (s, 2 H), 4.85 (s, 1 H, exchanges in D_2O), 5.78 (br q, 1 H), 6.87 (s, 1 H), 7.09–7.58 (m, 15 H); MS, *m*/*e* (relative intensity) 371 (2) $M^+ - H_2O$, 358 (34), 207 (59), 183 (11), 176 (100), 148 (73), 105 (17), 30 (11); IR (Nujol) 3650, 2920, 1645, 1510, 1450, 1160, 1050, 980, 915, 850, 750, 745, 700, 695 cm^{-1}.

Anal. Calcd for $C_{24}H_{23}NO_2S$: C, 74.00; H, 5.95; N, 3.40; S, 8.23. Found: C, 73.66; H, 5.84; N, 3.48; S, 8.28.

(*E*)-1-(Phenylthio)-*N*-methyl-4-hydroxy-4-phenyl-1-butene-2-carboxamide (22) and 3-(Phenylthio)-4-hydroxy-*N*-methyl-4-hydroxy-4-phenyl-1-butene-2-carboxamide (23). According to procedure B: 3.92 mmol of *sec*-BuLi and 536 μL (3.92 mmol) of TMEDA in 50 mL of THF, 368 mg (1.78 mmol) of **7** in 10 mL of THF, 420 μL (4.0 mmol) of benzaldehyde in 10 mL of THF; reaction conditions: −70 °C, 5 min, then −15 °C, 10 min, the solution is recooled to −70 °C, benzaldehyde is added and after 20 min pour into 5% HCl. Workup as usual and chromatographic separation by MPLC using 20% EtOAc/hexanes and a 40 × 0.5 in. (10 ± 4 μm) silica gel column gives 296 mg (56%) of **22**: mp 114–116 °C (triturated with pentane/EtOAc); ^{1}H NMR δ 2.73 (m, 2 H), 2.80 (d, *J* = 5 Hz, 3 H), 4.40 (d, *J* = 3 Hz, 1 H, exchanges in D_2O), 4.96 (ddd, *J* = 3 Hz, 5 Hz, 8 Hz, 1 H); ^{13}C NMR δ 26.7 (q), 40.2 (t), 73.0 (d), 125.5 (d), 127.3 (d), 127.8 (d), 128.3 (d), 129.3 (d), 130.6 (d), 130.8 (s), 133.8 (s), 136.6 (d), 144.5 (s), 169.4 (s); IR (powder) 3400, 3250, 2890, 1620, 1560, 1470, 1440, 1320, 1090, 1055, 1025, 865, 810, 747, 700, 685 cm^{-1}.

Anal. Calcd for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; N, 4.47; S, 10.23. Found: C, 68.59; H, 6.42; N, 4.43; S, 10.43.

Also obtained is 12 mg (2%) of **23**: ^{1}H NMR δ 2.834 (s, 2 H), 2.847 (s, 1 H), 4.167 (d, J = 4 Hz, 0.7 H, exchanges in D_2O), 4.205 (d, J = 4 Hz, 0.3 H), 5.257 (s, 0.7 H), 5.437 (s, 0.3 H), 5.90 (br q, 0.7 H), 5.95 (br q, 0.3 H), 7.1–7.5 (m, 10 H); ratio, 7:3.

(*E*)-1-(Phenylthio)-*N*-methyl-6-hydroxy-1-hexene-2-carboxamide (24), 1-(Phenylthio)-*N*-methyl-4-hydroxy-2-hexene-2-carboxamide (29), and 2-[(Phenylthio)methyl]-4-ethyl-2-butyrolactone (30). According to procedure B: 8.9 mmol of *sec*-BuLi and 1.34 mL (8.93 mmol) of TMEDA in 30 mL of THF, 880 mg (4.25 mmol) of **7** in 10 mL of THF, 338 μL (4.68 mmol) of propanal in 10 mL of THF; reaction conditions: −70 °C, 5 min, then −10 °C for 10 min, the solution is recooled to −70 °C and propanal is added, stirred for 15 min, and then poured into 5% HCl. Workup as usual and chromatographic separation by MPLC using 20% EtOAc/hexanes gives 760 mg (67%) of **24**: mp 82–84 °C (from Et_2O/pentane); ^{1}H NMR δ 1.02 (t, J = 6 Hz, 3 H), 1.57 (dq, J = 6 Hz, 2 H), 2.52 (m, 2 H), 2.78 (d, J = 5 Hz, 3 H), 3.64 (br s, 1 H), 3.76 (m, 1 H), 6.8 (br q, 1 H), 7.2–7.5 (m, 6 H); ^{13}C NMR δ 10.0 (q), 26.6 (q), 30.7 (t), 36.800 (t), 72.8 (d), 127.6 (d), 128.9 (d), 129.2 (d), 130.2 (s), 134.1 (s), 135.8 (d), 169.4 (s); MS, m/e (relative intensity) 265 (1), 236 (4), 234 (4), 207 (100), 176 (33), 148 (39), 130 (13), 116 (15), 98 (20), 58 (14), 32 (16).

Anal. Calcd for $C_{14}H_{19}NOS$: C, 63.36; H, 7.22; N, 5.28; S, 12.08. Found: C, 63.67; H, 7.38; N, 5.22; S, 12.04.

Also obtained is 96 mg (8%) of **29**: mp 83–86 °C (from $CHCl_3$/pentane); ^{1}H NMR (1:1 $CDCl_3$/Me_2SO-d_6) δ 0.86 (t, J = 7 Hz, 3 H), 1.37 (dq, J = 7 Hz, 2 H), 2.76 (d, J = 5 Hz, 3 H), 3.89 (s, 2 H), 4.12 (m, J = 9 Hz, 7 Hz, 5 Hz, 1 H), 4.54 (d, J = 5 Hz, 1 H), 6.19 (d, J = 9 Hz, 1 H), 7.15–7.50 (m, 5 H), 7.81 (br q, 1 H).

Anal. Calcd for $C_{14}H_{19}NOS$: C, 63.36; H, 7.22; N, 5.28; S, 12.08. Found: C, 63.31; H, 7.05; N, 5.47; S, 12.13.

Also obtained is 12 mg (1%) of **30**: mp 112–113.5 °C (from pentane/EtOAc); ^{1}H NMR δ 0.86 (t, J = 6 Hz, 3 H), 1.61 (dq, J = 6 Hz, 2 H), 3.68 (s, 2 H), 4.77 (dt, J = 1.2 Hz, 6 Hz, 1 H), 6.96 (d, J = 1.2 Hz, 1 H), 7.2–7.4 (m, 5 H); MS, m/e (relative intensity) 234 (48), 173 (11), 147 (28), 125 (85), 110 (58), 109 (72), 97 (40), 81 (59), 79 (65), 77 (28), 69 (20), 65 (57), 57 (100), 51 (32), 45 (27), 43 (21), 41 (59), 39 (80), 29 (87), 27 (39); IR (melt) 3030, 2850, 1650, 1580, 1480, 1455, 1340, 1280, 1200, 1155, 1075, 1050, 1030, 1000, 965, 909, 860, 795, 745, 690 cm^{-1}.

(*E*)-1-(Phenylthio)-4,5-diphenyl-*N*-methyl-4,5-diaza-1-pentene-2-carboxamide (25). According to procedure B: 7.93 mmol of *sec*-BuLi and 1.20 mL (7.93 mmol) of TMEDA in 50 mL of THF, 782 mg (3.77 mmol) of **7** in 10 mL of THF, 756 mg (7.92 mmol) of azobenzene in 10 mL of THF; reaction conditions: −78 °C, 5 min, then −10 °C, 15 min, the solution is recooled to −78 °C and azobenzene is added. Workup as usual and chromatographic separation by MPLC on a 12 × 0.5 in. silica gel column using a gradient from 5% to 50% EtOAc/hexane gives 700 mg (48%) of **25**: mp 102–104 °C (from hexanes), mmp 101–104 °C; ^{1}H NMR δ 2.64 (d, J = 5 Hz, 3 H), 4.34 (s, 2 H), 6.01 (s, 1 H), 6.25 (br q, 1 H), 6.57–7.38 (m, 16 H); ^{13}C NMR (nitromethane-d_3) δ 26.9 (q), 51.8 (t), 113.7 (d), 114.8 (d), 120.4 (d), 129.0 (d), 130.3 (d), 130.6 (d), 131.4 (d), 131.8 (s), 135.3 (s), 137.4 (d), 149.3 (s), 151.1 (s), 168.6 (s).

(*Z*)-1-(Phenylthio)-4,5-diphenyl-*N*-methyl-4,5-diaza-1-pentene-2-carboxamide (31). According to procedure A: 5.38 mmol of *sec*-BuLi and 811 μL (5.38 mmol) of TMEDA in 50 mL of THF, 530 mg (2.57 mmol) of **1** in 10 mL of THF, 513 mg (2.82 mmol) of azobenzene in 10 mL of THF; reaction conditions: −78 °C, 5 min, the azobenzene is added stirred for 15 min at −60 °C and then 1 mL of D_2O is added. Workup as usual and chromatographic separation by MPLC using 40% EtOAc/hexanes gives 542 mg (54%) of **31** as an oil: ^{1}H NMR δ 2.50 (d, J = 5 Hz, 3 H), 4.33 (s, 2 H), 6.22 (s, 1 H), 6.37 (q, J = 5 Hz, 1 H), 6.55–7.35 (m, 15 H). This amine slowly crystallizes over ca. 2 weeks at room temperature: ^{1}H NMR (after 2 weeks) δ 2.68 (d, J = 5 Hz, 3 H), 4.49 (s, 2 H), 5.5 (br q, 1 H), 6.03 (s, 1 H), 6.65–7.40 (m, 15 H). ^{13}C NMR (nitromethane-d_3) δ 27.2, 52.2, 114.1, 115.4, 120.8, 129.4, 130.6, 131.0, 131.8, 132.1, 135.6, 137.9, 149.7, 151.5, 169.0.

(*E*)-6-(Phenylthio)-5-(*N*,*N*-diisopropylcarbamoyl)-*N*-methyl-*N*-phenyl-5-hexenamide (33) and (*E*)-4-(Phenylthio)-5-(*N*,*N*-diisopropylcarbamoyl)-*N*-methyl-*N*-phenyl-4-hexenamide (34). According to procedure A: 3.87 mmol of *sec*-BuLi and 585 μL (3.87 mmol) of TMEDA in 60 mL of THF, 977 mg (3.52 mmol) of **6** in 10 mL of THF, 625 mg (3.87 mmol) of **9** in 10 mL of THF; reaction conditions: −105 °C, 5 min; **9** is added at −70 °C and after 15 min the solution is poured into 5% HCl. Workup as usual and chromatographic separation by MPLC using 20% EtOAc/hexanes gives 62 mg (4%) of **34**: mp 119–121 °C; mmp 116–121 °C: ^{1}H NMR (Me_2SO-d_6) δ 1.154 (d, J = 7 Hz, 3 H), 1.16 (d, J = 7 Hz, 3 H), 1.42 (d, J = 6.8 Hz, 3 H), 1.50 (d, J = 6.8 Hz, 3 H), 1.97 (s, 3 H), 2.29 (m, 2 H), 2.44 (t, J = 7 Hz, 1 H), 2.62 (t, J = 7 Hz, 1 H), 3.18 (s, 3 H), 3.40 (qq, J = 6.8 Hz, 1 H), 3.91 (qq, J = 7 Hz, 1 H), 7.07–7.39 (m, 10 H); ^{13}C NMR (1:1 $CDCl_3$/Me_2SO-d_6) δ 18.3 (q), 20.2 (q), 20.3 (q), 20.6 (q), 21.0 (q), 30.1 (t), 32.8 (t), 36.9 (q), 45.2 (d), 50.2 (d), 126.1 (d), 127.0 (d), 127.5 (d), 128.8 (d), 128.8 (d), 129.2 (s), 129.6 (d), 134.6 (s), 140.9 (s), 143.6 (s), 169.5 (s), 171.2 (s); MS, m/e (relative intensity) 438 (3), 338 (5), 329 (100), 228 (48), 202 (30), 200 (13), 134 (34), 128 (16), 106 (27), 86 (40), 77 (15), 43 (58); IR (Nujol) 3920, 1650, 1620, 1590, 1490, 1430, 1370, 1330, 1280, 1120, 1025, 830, 780, 740, 730, 700 cm^{-1}.

Also obtained is 291 mg (19%) of **33**: mp 117–118 °C; ^{1}H NMR δ 1.28 (unresolved m, 12 H), 1.77 (tt, J = 7.6 Hz, 2 H), 2.17 (t, J = 7.6 Hz, 2 H), 2.39 (t, J = 7.6 Hz, 2 H), 3.26 (s, 3 H), 3.7 (br m, 2 H), 6.18 (s, 1 H), 7.13–7.41 (m, 10 H); ^{13}C NMR δ 20.7 (q), 23.2 (t), 20.5 (t), 33.8 (t), 37.3 (q), 47.8 (br d), 123.3 (d), 126.8 (d), 127.3 (d), 127.7 (d), 129.1 (d), 129.5 (d), 129.7 (d), 135.3 (s), 138.9 (s), 144.0 (s), 169.9 (s), 172.4 (s); MS, m/e (relative intensity) 438 (33), 329 (100), 290 (60), 231 (35), 230 (36), 228 (15), 222 (33), 203 (26), 200 (26), 191 (28), 189 (53), 180 (16), 149 (17), 134 (44), 128 (11), 109 (17), 107 (35), 106 (40), 100 (15), 95 (11), 92 (25), 86 (35), 77 (25), 66 (16), 65 (15), 43 (88), 41 (43); high resolution MS, calcd for $C_{26}H_{34}O_2N_2S$ 438.2347, found 438.2339; IR (melt) 2940, 1655, 1625, 1590, 1490, 1435, 1385, 1335, 1210, 1155, 1120, 1040, 1030, 925, 830, 780, 740, 700 cm^{-1}.

(*E*)-1-(Phenylthio)-*N*,*N*-diisopropyl-4,5-diphenyl-4,5-diaza-1-pentene-2-carboxamide (37). According to procedure A: 3.6 mmol of *sec*-BuLi and 454 μL (3.90 mmol) of TMEDA in 60 mL of THF, 901 mg (3.25 mmol) of **6** in 10 mL of THF, 711 mg (3.90 mmol) of azobenzene in 10 mL of THF; reaction conditions: −105 °C, 5 min; azobenzene is added at −70 °C, stirred for 10 min, and then poured into brine. Workup as usual and chromatographic separation by MPLC using a gradient of 10% to 50% EtOAc/hexanes gives 728 mg (48%) of **37** as a glass: ^{1}H NMR (nitromethane-d_3) δ 1.09 (br d, 12 H), 3.61 (m, 2 H), 4.54 (s, 2 H), 6.43 (s, 1 H), 6.7–7.2 (m, 15 H); ^{13}C NMR (nitromethane-d_3) δ 20.08, 47.16 (br), 51.45, 113.96, 119.70, 120.77, 127.75, 128.79, 130.52, 130.64, 130.78, 131.05, 136.18, 136.98, 149.01, 150.85, 170.26; ^{13}C NMR (1:1 $CDCl_3$/Me_2SO-d_6) δ 20.2 (q), 45.7 (br d), 50.2 (t), 50.4 (br d), 112.2 (d), 112.7 (d), 118.3 (d), 119.4 (d), 127.1 (d), 127.5 (d), 129.0 (d), 129.3 (d), 129.8 (d), 134.4 (s), 134.7 (s), 147.3 (s), 149.0 (s), 168.8 (s); MS, m/e (relative intensity) 459 (8), 350 (1), 277 (26), 183 (16), 177 (38), 168 (100), 129 (9), 105 (11), 77 (66), 43 (31); IR (film from CCl_4) 3280, 2920, 1620, 1600, 1520, 1490, 1430, 1365, 1330, 1255, 1240, 1160, 1090, 1035, 995, 965, 925, 885, 837, 785, 760, 748, 695 cm^{-1}.

Anal. Calcd for $C_{28}H_{33}N_3OS$: C, 73.16; H, 7.24; N, 9.14; S, 6.98. Found: C, 73.23; H, 7.10; N, 9.02; S, 6.78.

***N*,*N*-Diisopropyl-*N*'-methyl-*N*'-phenyl-1-cyclopentene-1,4-dicarboxamide (43) and *N*,*N*-Diisopropyl-*N*'-methyl-*N*'-phenyl-1-cyclopentene-1,3-dicarboxamide (42).** According to procedure A: 2.91 mmol of *sec*-BuLi and 440 μL (2.91 mmol) of TMEDA in 150 mL of THF, 770 mg (2.78 mmol) of **2** in 10 mL of THF, 470 mg (2.91 mmol) of **9** in 10 mL of THF; reaction conditions: −100 °C, 5 min, **9** is added at −78 °C followed after 5 min by 471 mg (2.78 mmol) of CuBr–Me_2S in 20 mL of THF. The slurry is stirred for 94 h at room temperature, poured into saturated NH_4Cl, and worked up as usual. Separation by MPLC using 50% EtOAc/hexanes gives 179 mg (7%) of **11**: mp 100–103 °C, mmp 100–103 °C.

Also obtained is 354 mg (39%) of ca. a 3:1 mixture of **43** and **42**: mp 71–76 °C (from pentane/Et_2O); ^{1}H NMR (for **43**) δ (br m, 12 H), 2.41 (dd, $J_{H5H5'}$ = 12 Hz, J_{H5H4} = 7 Hz, 1 H), 2.60 (dd, slightly broadened, $J_{H3H3'}$ = 13 Hz, J_{H3H4} = 8 Hz, 1 H), 2.78 (dd, $J_{H3'H3}$ = 13 Hz, $J_{H3'H4}$ = 7 Hz, 1 H), 2.84 (dd, $J_{H5'H5}$ = 12 Hz, $J_{H5'H4}$ = 7 Hz, 1 H), 3.12 (dddd, J's = 7 Hz, 1 H, H-4), 3.28 (s, 3 H), 3.4 (br m, 1 H), 4.2 (br m, 1 H), 5.56 (t, J = 1.2 Hz, 1 H, H-2), 7.18 (d, J = 7.4 Hz, 2 H), 7.35 (t, J = 7.4 Hz, 1 H), 5.56 (t, J = 1.2 Hz, 1 H, H-2), 7.18 (d, J = 7.4 Hz, 2 H), 7.35 (t, J = 7.4 Hz, 1

H), 7.42 (t, J = 7.4 Hz, 2 H), decoupling [irradiation at δ 3.12 simplifies 2.41 to d, 2.60 to d, 2.78 to d, 2.84 to d, 2.41 simplifies 3.12 to q, 2.84 to d, 2.60 simplifies 2.78 to d, 3.12 to q]. Resonances attributed to **42**: δ 1.90 (m, 1 H, H-4), 1.91 (dd, J = 13 Hz, 7 Hz, 1 H, H-5), 2.11 (dd, J = 13 Hz, 8 Hz, 1 H, H-5′), 2.15 (m, 1 H, H-4′), 3.29 (s, 3 H), 3.58 (dd, broadened slightly, J = 7 Hz, 1 H, H-3), 5.50 (q, J = 0.6 Hz, 1 H, H-2), 7.20 (d, 2 H); other resonances are obscured by **43**, decoupling [irradiation at δ 3.58 simplifies 1.90, 2.15, 2.1 (H-4′, H-5′) simplifies 3.58 to d, 1.90 to d, 2.11 to d]. ^{13}C NMR (nitromethane-d_3) for **43**: δ 20.1 (q), 37.8 (q), 38.8 (t), 39.9 (t), 40.6 (d), 48.3 (br), 127.2 (d), 128.0 (d), 128.7 (d), 130.7 (d), 140.2 (s), 145.5 (s), 169.2 (d), 176.1 (s); for **42**: δ 28.9 (t), 35.1 (t), 50.4 (d), 130.3 (d), 144.0 (s), 169.4 (s), 174.8 (s); other resonances obscured by **43**; MS, m/e (relative intensity) 328 (10), 285 (3), 228 (24), 194 (100), 134 (97), 128 (13), 107 (35), 106 (37), 100 (36), 93 (24), 86 (46), 77 (27), 67 (40), 65 (29), 43 (59), 41 (23); IR (melt) 3020, 2920, 1660, 1620, 1600, 1495, 1440, 1375, 1345, 1260, 1220, 1160, 1125, 1040, 980, 925, 835, 780, 702 cm^{-1}.

The mixture of **43** and **42** was analyzed by GLPC using a SE 52/54 FSOT capillary column with programmed heating from 120 °C to 220 °C at 10°/min. Retention time and peak areas are given. **43**: t_R 22.04 min (74%). t_R **42**: 21.32 min (26%).

Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 73.13; H, 8.59; N, 8.53. Found: C, 73.19; H, 8.69; N, 8.53.

***N,N*-Diisopropyl-2,3-dihydro-1,2-diphenyl-3-methyl-4-1*H*-pyrazolecarboxamide (44).** According to procedure A: 1.47 mmol of *sec*-BuLi and 443 μL (2.94 mmol) of TMEDA in 29 mL of THF, 389 mg (1.33 mmol) of **3** in 10 mL of THF, 268 mg (1.47 mmol) of azobenzene in 20 mL of THF; reaction conditions: −105 °C, 5 min, azobenzene is added at −65 °C followed by 330 mg (2.94 mmol) of KO-*t*-Bu and the mixture is stirred at 0 °C for 10 min and then poured into brine. Workup as usual and recrystallization from hexanes (3×) gives 350 mg (72%) of **44**: mp 140.5–141.0 °C; ^1H NMR δ 1.295 (d, J = 6 Hz, 6 H), 1.312 (d, J = 6 Hz, 6 H), 1.487 (d, J = 6.4 Hz, 3 H), 3.9 (br m, 2 H), 4.740 (q, J = 6.4 Hz, 1 H), 6.9–7.05 (m, 6 H), 7.205 (s, 1 H), 7.244 (t, J = 7.2 Hz, 4 H); ^{13}C NMR δ 20.8 (q), 21.3 (q), 23.9 (q), 48.1 (d), 70.4 (d), 114.5 (d), 115.7 (d), 116.4 (s), 128.9 (d), 130.0 (d), 129.3 (d), 145.4 (s), 151.8 (s), 164.7 (s); MS, m/e (relative intensity) 363 (22), 348 (100), 271 (27), 249 (44), 144 (59), 118 (34), 104 (43), 100 (23), 86 (20), 84 (13), 81 (21), 77 (69), 57 (54), 56 (57), 43 (97), 41 (72); IR (KBr) 2970, 1620, 1596, 1490, 1450, 1370, 1315, 1210, 1160, 1032, 759, 695 cm^{-1}.

Anal. Calcd for $C_{23}H_{29}N_3$: C, 75.99; H, 8.04; N, 11.56. Found: C, 76.09; H, 8.31; N, 11.57.

1,2-Diphenyl-2,3-dihydro-*N*,3-dimethyl-4-1*H*-pyrazolecarboxamide (46). According to procedure B: 800 mg (3.62 mmol) of **4** in 10 mL of THF, 7.95 mmol of *sec*-BuLi and 1.20 mL (7.95 mmol) of TMEDA in 100 mL of THF, 790 mg (4.34 mmol) of azobenzene in 20 mL of THF; reaction conditions: −60 °C, 5 min; then 0 °C, 10 min; the solution is recooled to −70 °C, azobenzene is added, followed by 1.30 g (11.6 mmol) of KO-*t*-Bu, and the mixture is stirred for 40 h at room temperature and then poured into brine. Extractive workup with Et_2O and recrystallization from EtOAc/hexanes gives 634 mg (60%) of **46**: mp 168–169.5 °C; ^1H NMR (Me_2SO-d_6) δ 1.350 (d, J = 5.2 Hz, 3 H), 2.630 (d, J = 4 Hz, 3 H), 4.560 (q, J = 5.2 Hz, 1 H), 6.892 (t, J = 7.2 Hz, 1 H), 6.967 (d, J = 7.2 Hz, 2 H), 6.989 (d, J = 7.2 Hz, 2 H), 6.999 (t, J = 7.2 Hz, 1 H), 7.247 (t, J = 7.2 Hz, 2 H), 7.291 (t, J = 7.2 Hz, 2 H), 7.652 (br q, 1 H, exchanges in D_2O/H_3PO_4), 8.121 (s, 1 H); MS, m/e (relative intensity) 293 (11), 278 (100), 247 (10), 235 (3), 221 (9), 185 (11), 146 (16), 144 (35), 118 (18), 104 (43), 82 (21), 77 (100), 58 (18), 51 (27); IR (KBr) 1627, 1594, 1496, 939, 759, 695 cm^{-1}.

Anal. Calcd for $C_{18}H_{19}N_3O$: C, 73.69; H, 6.53; N, 14.33. Found: C, 73.40; H, 6.28; N, 14.17.

***N,N*-Diisopropyl-3-quinolinecarboxamide (47).** To 204 mg (0.44 mmol) of **12** in 15 mL of THF at −78 °C is added 100 mg (0.89 mmol) of KO-*t*-Bu in 5 mL of THF, and the slurry is warmed quickly and stirred at room temperature for 15 min. The resulting solution is poured into water, the organics are extracted with Et_2O, dried ($CaSO_4$), and concentrated, and the product is purified by HPLC using 7.5% EtOAc/hexanes to give 103 mg (91%) of **47**: mp 86–89 °C (from pentane/Et_2O); ^1H NMR (acetone-d_6) δ 1.4 (unresolved m, 12 H), 3.8 (br m, 2 H), 7.619 (t, J = 8.3 Hz, 1 H), 7.777 (t, J = 8.2 Hz, 1 H), 7.985 (d, J = 8.1 Hz, 1 H), 8.083 (d, J = 8.4 Hz, 1 H), 8.258 (d, J = 1.8 Hz, 1 H), 8.875 (d, J = 1.8 Hz, 1 H), decoupling [irradiation at δ 7.62 simplifies 7.78 to d, 7.99 to s, 7.99 simplifies 7.62 to d, 8.08 simplifies 7.78 to d, 8.26 simplifies 8.88 to s]; MS, m/e (relative intensity) 256 (14), 241 (4), 213 (21), 156 (100), 128 (41), 101 (16), 75 (6); IR (melt) 2920, 1625, 1595, 1485, 1460, 1420, 1370, 1340, 1310, 1210, 1160, 1135, 1040, 980, 925, 910, 810, 790, 760 cm^{-1}.

Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.75; H, 7.63; N, 10.82.

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Supplementary Material Available: Experimental details of **1**, **2**, **6**, **3**, **i**, **4**, **7**, **27**, **28**, and **47** (7 pages). Ordering information is given on any current masthead page.