Formation, Electrophilic Substitution, and Formal 3 + 2 Cyclization of (2-Carbamoylallyl)lithium Reagents

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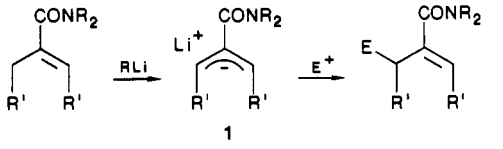
Directed β′-lithiations of α,β-unsaturated amides and reactions of the resulting (2-carbamoylallyl)lithium reagents with electrophiles are reported. Treatment of (*E*)-*N*,*N*-diisopropyl-2-methyl-2-butenamide (**5**) provides [(*E*)-2-(*N*,*N*-diisopropylcarbamoyl)-3-methylallyl]lithium (**6**), which has retained the double bond geometry of **5** and undergoes reaction with a variety of electrophiles to provide the β- and β′-substituted products **7–20**. High regioselectivity can be achieved in some cases. The (2-carbamoylallyl)lithium reagents **21**, **22**, and **23** are also available by directed β′-lithiations. The reaction of **6** with a number of α,β-unsaturated amides in a 3 + 2 cyclization gives cyclopentanes **28**, **29**, **30**, **32**, **33**, **35**, **36**, **38**, **39**, **42**, **45**, and **46** in acceptable yields, accompanied by lower yields of acyclic products. Electrophilic trapping of the cyclopentane enolates is illustrated by formation of **50–53**. Addition of **6** to azobenzene is shown to give the pyrazole **48** in low yield. The formation of the cyclic products is considered to occur in a stepwise fashion because quenching the reactions of **6** with **25** or **26** at −60 °C provides acyclic products which are derived from the logical precursors to the observed cyclopentanes. Analogous reactions of **54** and **27** give **55** and **56**. These results establish that β′-lithiation of β-alkyl-α,β-unsaturated tertiary amides can provide in high yields (2-carbamoylallyl)lithium reagents which retain double-bond geometry and react regioselectively with a variety of electrophiles. The (2-carbamoylallyl)lithium reagents can participate in stepwise 3 + 2 cyclizations with acrylamides to give substituted cyclopentanes with high regioselectivity and stereoselectivity.

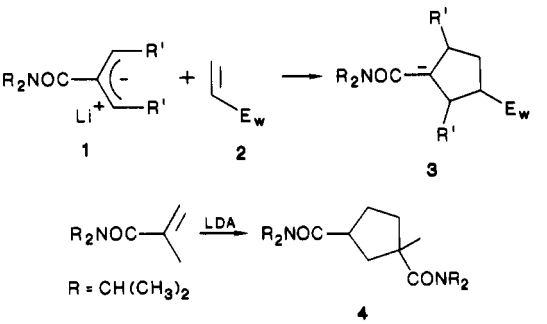
Organolithium reagents that can be formed by a kinetically controlled directed metalation of a weakly acidic hydrogen in the presence of thermodynamically more acidic hydrogens or other potentially reactive groups can be of special synthetic value. Of recent interest are the (2-carbamoylallyl)lithium reagents **1** which can be formed by the β′-metalation of secondary and tertiary α,β-unsaturated amides as outlined in Scheme I. These reagents have been used in the syntheses of a variety of β′-substituted-α,β-unsaturated amides and of methylene lactones.[1-4]

A prospective use for tertiary amide derivatives of **1** is as a π^4 component in a formal 3 + 2 cyclization with a π^2 partner. The reaction of **1** with **2** could provide cyclopentane enolate **3** by pathways investigated by Kauffmann and outlined in Scheme II.[3,4] In fact, Kauffmann and co-workers have reported that treatment of *N*,*N*-diisopropylmethacrylamide with lithium diisopropylamide (LDA) provides the cyclopentane **4** in situ. They suggested that **1** (R = $CH(CH_3)_2$, R′ = H) is formed as a transient intermediate and adds to starting methacrylamide to afford the substituted cyclopentane after hydrolysis.[4b] Similar anionic 3 + 2 cyclizations have also been reported for cases in which the allylic and olefinic components have aryl or heteroatom substitution.[5,6] However, this strategy

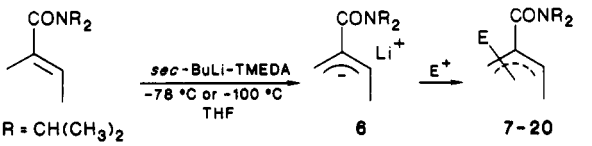
Scheme I



Scheme II



Scheme III



appears not to have been investigated for the general synthesis of cyclopentanes. This may be due, in part, to the lack of convenient procedures for preparation of the

(1) For recent communications on this type of lithiation of α,β-unsaturated amides, see: (1) Beak, P.; Kempf, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 4550. (b) Fitt, J. J.; Gschwend, H. W. *J. Org. Chem.* **1980**, *45*, 4257. (c) Tanaka, K.; Nozaki, Y.; Tamura, N.; Tanikaga, R.; Kaji, A. *Chem. Lett.* **1980**, 1576. (d) Tamura, Y.; Kagotani, N.; Yoshida, Z. *Tetrahedron Lett.* **1981**, *22*, 3409. (e) Tamura, Y.; Kagotani, M.; Furukawa, Y.; Amino, Y.; Yoshida, Z. *Ibid.* **1981**, *22*, 3413.

(2) For reports, see: (a) Kitaoka, N.; Takahashi, Y.; Kosugi, H.; Uda, H. *Chem. Lett.* **1983**, 1065. (b) Beak, P.; Kempf, D. J.; Wilson, K. D. *J. Am. Chem. Soc.* **1985**, *107*, 4745.

(3) For a preliminary report, see: Kempf, D. J.; Wilson, K. D.; Beak, P. *J. Org. Chem.* **1982**, *47*, 1610.

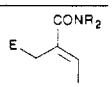
(4) (a) Kauffmann, T.; Berg, H.; Koppelmann, E. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 380. (b) Bannworth, W.; Eidenschink, R.; Kauffmann, T. *Ibid.* **1974**, *13*, 468. (c) Kauffmann, T. *Ibid.* **1974**, *13*, 427.

(5) Böche, G.; Martens, D. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 724. (b) Kolobielski, M.; Pines, H. *J. Am. Chem. Soc.* **1957**, *79*, 5820. (c) Eidenschink, R.; Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 292. (d) Klumpp, G. W.; Schmitz, R. F. *Tetrahedron Lett.* **1974**, 2911. (e) Luteri, G. F.; Ford, W. F. *J. Organomet. Chem.* **1976**, *105*, 139. (f) Luteri, G. F.; Ford, W. F. *J. Org. Chem.* **1977**, *42*, 820. For a summary, see: Kauffmann, T. *Top. Curr. Chem.* **1980**, *92*, 109. For a discussion of this cyclization in the gas phase, see: Kleingeld, J. C.; Nibbering, M. *Red. Trav. Chim. Pays-Bas* **1984**, *103*, 87.

(6) Many ingenious cyclopentane syntheses involving the combination of three- and two-carbon fragments have been devised in recent years. For summaries and applications, see: (a) Demuth, M.; Schaffner, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *20*, 820. (b) Bal, S. A.; Marfat, A.; Helquist, P. *J. Org. Chem.* **1981**, *47*, 5047. (c) Piers, E.; Karunaratine, V. *Ibid.* **1983**, *49*, 1774. (d) Leono-Bay, A.; Paquette, L. *Ibid.* **1982**, *47*, 4173. (e) Trost, B. M.; Chan, B. M. J. *J. Am. Chem. Soc.* **1983**, *102*, 2315. (f) Calligaris, M.; Cartusan, G.; Nardin, G.; Sirivanti, G.; Wojciki, A. *Organometallics* **1983**, *2*, 865. (g) Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, 429. (h) Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642. (i) Magnus, P.; Quagliato, D.; Huffman, J. C. *Organometallics* **1982**, *1*, 1240; (j) Danheiser, R. L.; Carinid, D. J.; Basar, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604. (k) Little, R. D.; Muller, G. W.; Vengas, M. G.; Carroll, G. C.; Kikhari, A.; Patton, L.; Stone, J. *Tetrahedron Lett.* **1981**, *22*, 4371. (l) Boger, D. L.; Brotherton, C. E. *J. Am. Chem. Soc.* **1984**, *106*, 805.

0022-3263/86/1951-4627$01.50/0

Table I. Lithiation and Electrophile Substitution of (*E*)-*N*,*N*-Diisopropyl-2-methylbutenamide (5)

electrophile	products (yield, %) 	
D_2O	7 (12)	8 (81)
$(CH_3)_2C{=}CHCCl$	9[a] (24)	10[a] (42)
$(CH_3)_2CO$	11 (32)	12 (49)
$(CH_3)_2CO$, $MgBr_2$	11 (57)	
$(C_6H_5)_2CO$	13 (44)	14 (37)
$(C_6H_5)_2CO$, $MgBr_2$	13 (79)	
$C_6H_5NNC_6H_5$	15 (46)	16 (29)
$CH_3(CH_2)_3I$		17 (63)
$(CH_3)_3SiCl$		18 (58)
$C_6H_5CHNC_6H_5$	19 (26)	20 (21)

[a] Isolated as a mixture and not separated.

appropriately 2-substituted allyl anion reagents of the type represented by **1**.

In this report we describe the β′-lithiations of β-alkyl-α,β-unsaturated tertiary amides to form (2-carbamoylallyl)lithium reagents **1**, the reaction of **1** with electrophiles to give β-substituted-α,β-unsaturated amides, and the anionic 3 + 2 cyclization reactions of **1** with acrylamides to afford cyclopentanes.[4,7-10]

Results and Discussion

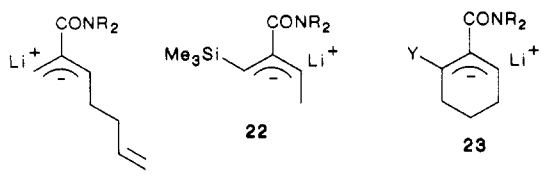
Unless otherwise noted the β′-lithiations were accomplished at −78 °C or −100 °C with 1 equiv of *sec*-butyllithium/*N*,*N*,*N*′,*N*′-tetramethylethylenediamine (*sec*-BuLi/TMEDA) in dry tetrahydrofuran for 5 to 10 min.[11,12] Excess organolithium reagent is not necessary and may be detrimental. The electrophiles were added at −50 °C to −70 °C and the reactions completed as described in the text. All isomeric products were separated, each was characterized spectrally, and yields are reported for analytically pure compounds unless otherwise noted.

β′-Lithiation and Electrophilic Substitution of α,β-Unsaturated Tertiary Amides. (*E*)-*N*,*N*-Diisopropyl-2-methyl-2-butenamide (**5**) was used as a prototype to study the directed metalation, electrophilic substitution, and 3 + 2 cyclization of α,β-unsaturated tertiary amides. Treatment of **5** with *sec*-BuLi/TMEDA for 5 min at −78 °C or −100 °C in tetrahydrofuran affords the (2-carbamoylallyl)lithium reagent **6** which is converted to the β′-substituted products **7**–**20** upon reaction with electrophiles as shown in Scheme III and summarized in Table I.[12] Two regioisomers are obtained upon reaction of **6** with deuterium oxide, 1-chloro-3-methyl-2-butene, acetone, benzophenone, azobenzene, or 1,2-diphenylimine, whereas reaction with 1-iodobutane or chlorotrimethylsilane affords only single products **17** and **18**, respectively, having a trisubstituted double bond. If magnesium bromide is added to **6** prior to the addition of acetone or benzophenone, only a single product, **11** and **13**, respectively, having a disubstituted double bond is obtained. The regiochemical preference observed in the electrophilic substitution of **6** is similar to that of other formal allylic carbanions in which alkylation occurs preferentially at the primary site, while addition to ketones, in the presence of magnesium bromide, occurs predominately at the more substituted site.[13,14] The regioselective preference observed with these tertiary amides is opposite of that seen with corresponding secondary amides, suggesting that regiocontrol might be achieved by proper choice of amide precursor.[2]

In all of the cases examined only a single geometric double-bond isomer is obtained. Retention of geometry was established for **8** by comparison with **5**. The geometries of the α,β-disubstituted double bonds of **14** and **16** were established by NOE experiments. For example, irradiation of the β-methylene signal of **14** at 3.26 ppm causes a 4.5% enhancement in the intensity of the methyl resonance at 1.29 ppm and no change in the signal for the β-vinyl hydrogen at 5.53 ppm. Similarly irradiation of the vinyl hydrogen has no effect on the β-methylene resonance, indicating that **14** has retained the geometry of **5**. Similar results indicate that **16** also has the same double-bond geometry as **5**. Since only one geometric isomer of **10**, **12**, **17**, **18**, and **20** is observed, these are also considered to have retained double-bond geometry and we suggest that this geometry is also retained in the intermediate allyllithium reagent **6**.

Each pure isomer was treated with lithium hydride in tetrahydrofuran, in order to determine whether the isomer ratios of **13**:**14** and **15**:**16** obtained from the reactions of benzophenone and azobenzene with **6** result from equilibration. Gas evolution was observed, indicating generation of the intermediate lithium salts, and no interconversion between **13** and **14** or between **15** and **16** is observed, indicating that their formation is kinetically controlled.

We have generated **21**, **22**, and **23** as representative examples of (2-carbamoylallyl)lithium reagents. Treatment



22 **23**

21

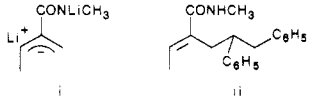
R = $CH(CH_3)_2$; Y = H, $(CH_3)_3Si$, C_6H_5S

(7) For a case in which BuLi complexation to an amide provides a driving force for kinetic lithiation that overcomes the more well-known resonance and inductive effects, see: Beak, P.; Hunter, J. E.; Jun, Y. M. *J. Am. Chem. Soc.* **1983**, *105*, 6350.

(8) This cyclization is considered to be a geometrically disfavored reaction: (a) Baldwin, J. E.; Husch, M. J. *Tetrahedron* **1982**, *38*, 2939. (b) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. However, examples of anionic 5-endo-trio ring closures are known: (c) Grigg, R.; Gunaratne, N. Q. H. *J. Chem. Soc., Chem. Commun.* **1982**, 384. (d) Grigg, R.; Kemp, J.; Malone, J.; Tangthongkum, A. *Ibid.* **1980**, 648. (e) Griff, R.; Kemp, J. *Tetrahedron Lett.* **1980**, *21*, 2461. (f) Falling, S. F.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 1260. (g) Scherrer, V.; Jackson-Mully, M.; Findely, J.; Schmid, H. *Helv. Chim. Acta* **1978**, *61*, 716. (h) Grigg, R.; Kemp, J.; Sheldrick, G.; Trotter, J. *J. Chem. Soc. D* **1978**, 109. (i) Anselme, J. P. *Tetrahedron Lett.* **1977**, 3615. (j) Kijkink, J.; Jonjee, J. N.; deJong, B. S.; Speckamp, W. N. *Heterocycles* **1983**, *20*, 1255. (k) Veenstra, S. J.; Speckamp, W. N. *J. Chem. Soc., Chem. Commun.* **1982**, 369.

(9) For examples of β additions to α,β-unsaturated amides, see: (a) Mpango, G. P.; Mahalgnasis, K. K.; Mahdaui-Danghari, Z.; Snieckus, V. *Tetrahedron Lett.* **1980**, *21*, 4823, 4827. (b) Baldwin, J.; Dupont, W. A. *Ibid.* **1980**, *21*, 1881.

(10) In fact, reaction of the secondary amide i, prepared by lithiation of *N*-methyl-2-butenamide, with *trans*-stilbene provides the acyclic product ii in low yield.[11]



i ii

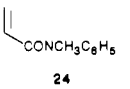
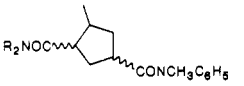
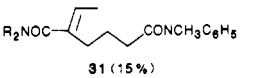
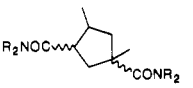
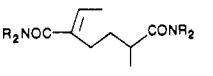
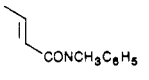
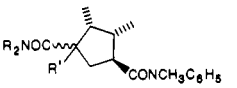
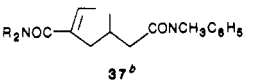
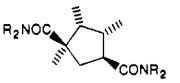
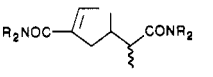
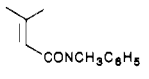
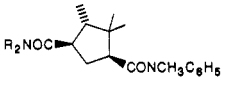
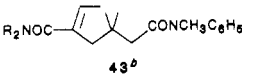
(11) For details including optimization of metalation conditions, characterizations of other products, and spectroscopic experiments and discussion, see: Kempf, D. J. Ph.D. Thesis, 1982; Wilson, K. D. Ph.D. Thesis, 1984, University of Illinois Urbana–Champaign, available from University Microfilm, Ann Arbor, MI.

(12) Lower reaction temperatures gave slightly high yields of **7** and **8** and fewer side products such as **40**, **41**.[11]

(13) α-Hetero-substituted allyl organometallics are of considerable synthetic value. Biellmann, J. F.; Ducep, J. B. *Org. React. (N.Y.)* **1982**, *27*, 1. Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1980**, *102*, 5004. Ahlbrecht, H. *Chimia* **1977**, *31*, 391 and references cited therein.

(14) Benkeser, R. A. *Synthesis* **1971**, 347. Courtois, G.; Miginiac, L. *J. Organomet. Chem.* **1974**, *69*, 1.

Table II. Lithiation and Reaction of 5 with Acrylamides 5, 24, 25, 26, and 27[a]

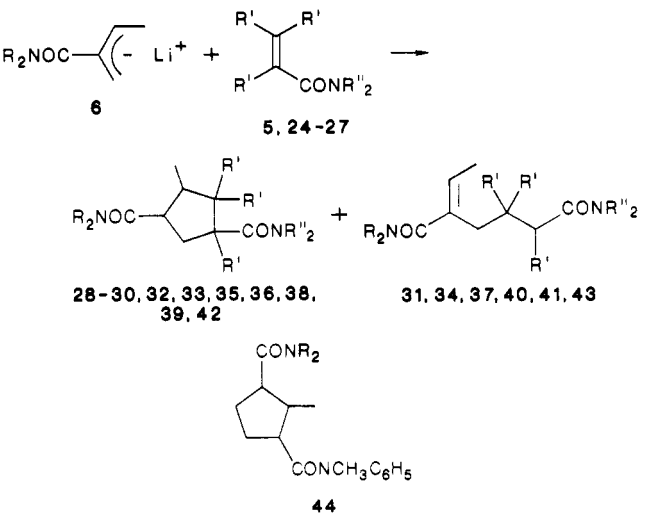
acrylamide electrophile	products (yield, %)
 24	 28 (17%) 29 (12%) 30 (26%)  31 (15%)
 25	 32 (17%) 33 (42%)  34 (21%)
 26	 35 (34%) R' = H 36 (17%) R' = H  37[b]
 5	 38 (64%) 39 (8%)[c]  40 (12%) 41 (9%)
 27	 42 (81%)  43[b]

[a] R = $CH(CH_3)_2$. [b] Trace products identified by NMR only. [c] 39 was identified as a component in impure 38 by VPC analysis and spectral properties.

of the appropriate α,β-unsaturated amide with *sec*-BuLi/TMEDA followed by deuterium oxide affords β'-deuterio-α,β-unsaturated amides.[11] Attempts to prepare and trap the unsubstituted allyllithium reagent from **25** resulted in the formation of complex mixtures of β'-substituted amides, self-condensation products, and products from 1,4-addition of *sec*-BuLi to **25**, in agreement with Kauffmann's earlier reports.[4b,11,15] The facile formation of stable solutions of **6**, **21**, **22**, and **23** under conditions which fail to produce the corresponding species from **25** suggests that the presence of a substituent on the prospective allyllithium reagent is needed to minimize undesired reactions during metalation.

Anionic 3 + 2 Cyclizations of Tertiary (2-Carbamoylallyl)lithium Reagents with Substituted Acrylamides. In a test of the formal 3 + 2 cyclization of Scheme II, we have found that the lithiation of **5** to form **6**, followed by addition of acrylamides **5** or **24–27** and warming to ambient temperature, affords the 2-methylcyclopentane-1,4-dicarboxamides **28**, **29**, **30**, **32**, **33**, **35**, **36**, **38**, **39**, and **42**. The results are shown in Scheme IV and Table II. Each of these cyclopentanes results from bonding between the more substituted β-carbon of **5** and the β-carbon of the acrylamide and bonding between the β'-carbon of **5** and the α-carbon of the acrylamide. The acyclic products **31**, **34**, **37**, **40**, **41**, and **43** result from addition of the less-substituted β'-carbon of **6** to the β-carbon of the acrylamide.[16]

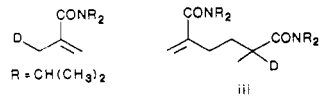
Scheme IV[a]



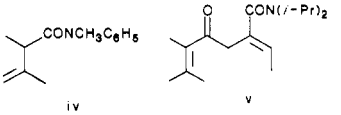
[a] R = $CH(CH_3)_2$, R' = H, alkyl; R'' = $CH(CH_3)_2$, $CH_3C_6H_5$.

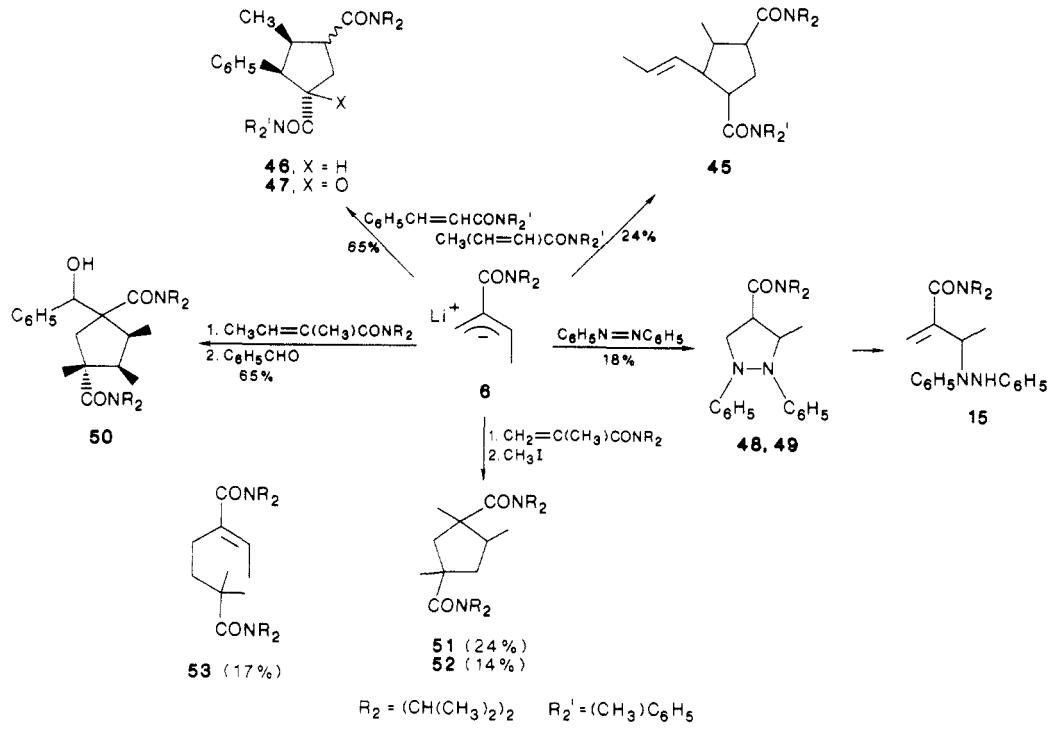
The structural assignments for **28–36**, **38**, and **40–42** were based on infrared, ^1H, ^{13}C NMR, and mass spectral data and NMR decoupling and NOE experiments. For example, homonuclear decoupling experiments establish that **28** has a proton adjacent to a methyl group and to three other ring hydrogens, thus ruling out structure **44**. The

(15) Addition of *sec*-butyllithium to **3** is normally observed; however, metalation of **3** by lithium 2,2,6,6-tetramethylpiperidide at −120 °C in THF/pentane with exposure to methanol-*O*-*d* gave *N*,*N*-diisopropylmethacrylamide-*3'*-*d* and the diamide iii.[2b]



(16) Attempted addition of **6** to *N*-methyl-*N*-phenyl-2,3-dimethyl-2-butenamide, a trisubstituted acrylamide, resulted in the formation of iv and v.[11]



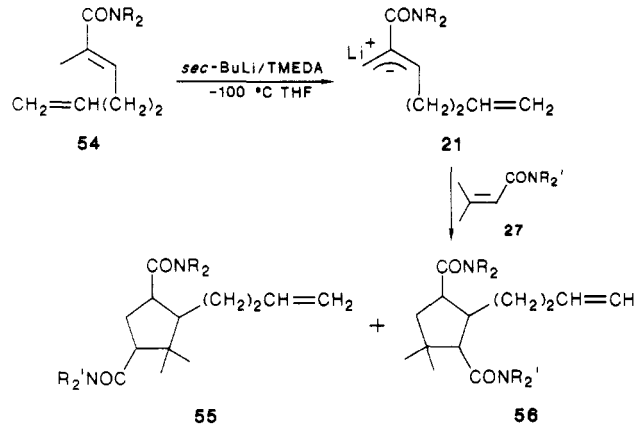


structures of the other compounds in Table I were similarly assigned and details are available.[11] In the case of **36** the spectral-based assignment was independently confirmed by single-crystal X-ray analysis.[17]

The lithiation of **5** followed by the reaction of **6** with the *N*-methylanilides of sorbic and cinnamic acids provides the cyclopentanes **45** and **46**, respectively, in 24% and 65% yields, respectively. The structures of **45** and **46** were established spectrally, although in the case of **46** it was necessary to determine which hydrogen was α to the anilide group. To do this **46** was treated with potassium hydride in dimethyl-d_6 sulfoxide and the ^{1}H NMR spectrum obtained. In addition to the disappearance of a resonance due to an α proton, the benzylic resonance and the geminal resonances are simplified to a doublet and to two doublet of doublets, respectively, in accordance with structure **47**. Decoupling experiments with **47** established that H-2 and the benzylic hydrogen are coupled and hence that the C-2 methyl and phenyl groups are at adjacent positions as depicted in **46** and **47**. Only partial stereochemical assignment for **46** and **47** are made due to the overlap of the signals in the NOE spectra.

The diastereomeric pyrazoles **48** and **49** are obtained in low yield following treatment of **6** with azobenzene and warming to ambient temperature. These pyrazoles are also obtained in 41% and 19% yields, respectively, when **15** is treated with *n*-BuLi then potassium *tert*-butoxide and warmed to ambient temperature in tetrahydrofuran. The isomeric amine **16**, obtained from **6** and azobenzene, did not cyclize under these conditions.

Electrophilic substitution of the cyclopentane enolates formed in this sequence can be accomplished in situ. When a solution of **6** is treated with **5**, warmed, and then treated with benzaldehyde, **50** is obtained in 65% yield simply by precipitating the product from the concentrated reaction mixture. Upon heating above 200 °C, **50** loses benzaldehyde to give **38**. This simple one-pot preparation of **50**, in which three new carbon–carbon bonds and formal asymmetric centers are selectively generated, illustrates the synthetic potential for cyclopentane formation via sequential 3 + 2 cyclization and electrophilic substitution of (2-carbamoylallyl)lithium reagents. The in situ alkylation of cyclopentyl enolates is also possible as illustrated by the reaction of **6** with **25** followed by treatment with methyl iodide to give **51** and **52**, along with **53**, in 24%, 14% and 17% yields, respectively.[18]



The presence of a substituent on the β-carbon of the α,β-unsaturated tertiary amide precursor appears to be necessary for formation of the (2-carbamoylallyl)lithium reagent in high yield (vide supra).[4b,11,15] An example of an extension of the reaction of **5** is the lithiation of **54** to form **21**. Reaction of **21** with **27** affords isomers **55** and **56** in 28% and 12% yields, respectively.[19]

Mechanism of the 3 + 2 Cyclization of (2-Carbamoylallyl)lithium Reagents with Acrylamides. Although a concerted cycloaddition is an allowed process for the anionic 3 + 2 cycloaddition, the evidence for related cases favors a stepwise mechanism.[4,5] Low-temperature

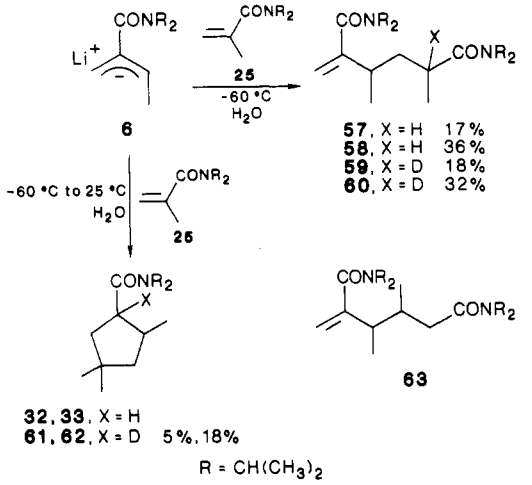
(17) Data for this assignment is provided in the supplementary material. See paragraph at end of paper for ordering information.

(18) In addition, 3% of 1,3-dimethyl-*N*,*N*,*N*',*N*'-tetraisopropyl-1,3-dicarbamylcyclopentane was obtained.[4b,11]

(19) The product from 1,2-addition to **27** was also obtained in 13% yield.

trapping experiments provide evidence supporting a stepwise mechanism for the formation of the cyclopentane rings in the present cases also.

Lithiation of **5** to give **6** followed by addition of **25** at −60 °C, hydrolysis with water prior to warming, and chromatography provides the diastereomers **57** and **58** in 17% and 36% yields, respectively, along with **34** in 5% yield. Similar hydrolysis of the reaction mixture with



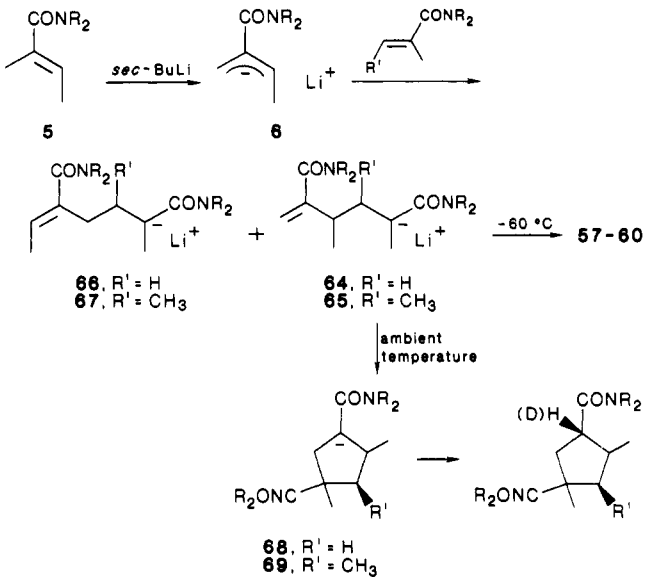
deuterium oxide affords **59** and **60** in 18% and 32% yields. ^1H and ^{13}C NMR experiments established that deuterium is incorporated only at the carbon α to the carbamoyl group. The cyclopentanes **32** and **33**, which are obtained in 17% and 42% yields when the reaction mixture is allowed to warm to ambient temperature prior to quenching, are not detected among the reaction products under these conditions. However, if the reaction mixture is allowed to warm prior to hydrolysis with deuterium oxide, the α-deuteriocyclopentanes **61** and **62** are obtained in 5% and 18% yields.[20] In another case, when the reaction of **6** with **26** was quenched after 1 h, rather than after the usual 10 h at ambient temperature, the acyclic diamide **63** was obtained in 10% yield.

The formation of **57–60** is considered to result from amide-directed metalation of **5** to form **6**, followed by addition of the more substituted allylic position of **6** to **25** or **26** to form enolates **64** or **65**, respectively, as shown in Scheme V. The formation of **64** at low temperature is evident from the fact that deuterium is incorporated specifically at the position α to the carbamoyl groups in **59** and **60**. The 5-endo-trig cyclization of the enolates **64** and **65**, to form cyclopentane enolates **68** and **69** as shown in Scheme V, occurs only after warming as evidenced by the absence of cyclopentanes in the reaction mixtures that have been quenched at low temperatures.[8] Specific deuterium incorporation α to the diisopropylcarbamoyl group in **61** and **62** after hydrolysis with deuterium oxide demonstrates the intermediacy of the cyclopentane enolates **68** and **69**.

Alternative reaction of **6** at the less-substituted allylic position gives enolates **66** and **67**. Cyclization of **66** and **67** to form cyclopentanes apparently does not proceed at ambient temperature. The cyclization appears to be sensitive to methyl substitution at the β-carbon of the double bond. A similar pattern of reactivity, in which ring closure occurs only for enolates having unsubstituted β-vinyl positions, is observed for other cyclizations of **6** with α,β-unsaturated amides and for the cyclization of **15** but not

(20) The α-deuterio derivative of **34** (**34-d**) was also obtained in 9% yield.

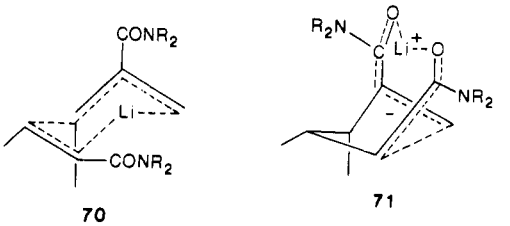
Scheme V[a]



[a] R = $CH(CH_3)_2$.

of **16**. The regioselective formation 2-methyl-1,4-cyclopentanedicarboxamides from **6** in these studies and the absence of 2-methyl-1,3-cyclopentanedicarboxamides is rationalized by this cyclization preference. However, the formation of **56** from **54** does demonstrate that the less-favorable ring closure can occur at ambient temperature.

The cyclizations illustrated in Scheme IV for the conversion of **6** to cyclopentanes are regioselective and stereoselective. The predominant isomers have a C-2 methyl group that is cis to the C-3 substituent and trans to the C-4 carbamoyl group. In general the two major cyclopentane stereoisomers obtained are epimeric at C-1. The formation of the predominant isomers can be rationalized by an extension of the Heathcock–Zimmerman model for addition reactions to carbonyl groups, a model that takes into account the possibility of chelation of the two reactants by lithium and is shown as **70**.[21] In this pseudo-chair transition state, the groups on the acceptor acrylamide begin to occupy pseudo-equitorial positions while the lithium interacts with the faces of the π systems. If the lithium ion bears two solvent molecules, the unsubstituted end of the allyllithium component could be the more sterically congested in **70** and the new carbon–carbon bond



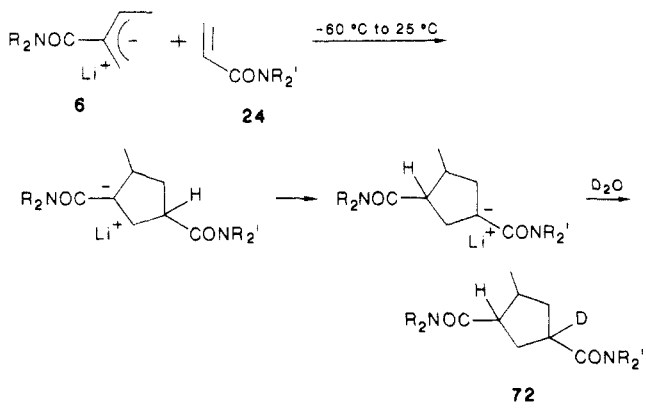
thus formed at the site remote from that hinderance. A cyclic chelated-transition-state model is also useful for rationalizing the stereochemistry of the ring-closure reaction.[22] Thus, the transition state represented by **71** would allow the lithium to coordinate to both amides, albeit on the faces of the π systems.[23] It must be noted

(21) (a) Heathcock, C.; Lampe, J. *J. Org. Chem.* **1983**, *48*, 4330 and references cited therein. (b) Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

(22) For an eight-membered complex in a lithium-directed enolization, see: Majewski, M.; Green, J. R.; Snieckus, V. *Tetrahedron Lett.* **1986**, *27*, 531.

these are speculative rationales; while they serve to rationalize the stereochemistry of the products indicated, they do not offer a compelling explanation for the high yield of **42**, a result which could be taken to suggest a one-electron process.

The relative stereochemistry at C-1 is established by protonation of the cyclopentyl enolate and generally occurs on hydrolysis as evidenced by the formation of **61** and **62**. In one instance this protonation occurred after equilibration, prior to hydrolysis, as evidenced by the isolation of **72** following reaction of **6** with **24** and then with deuterium oxide. However, this was the only case in which enolate equilibration was observed and it may account for the low stereoselectivity observed in the formation of **28–30**.



$R_2 = (CH(CH_3)_2)_2$, $R_2' = (CH_3)C_6H_6$

In summary, these results establish the viability of the cyclization proposed in Scheme II. However, the need to use tertiary carbamoyl groups to drive the cyclization steps of the reaction limits the synthetic potential of this approach. A solution to this difficulty is presented in a subsequent report.[24]

Experimental Section[25]

All reactions involving organolithiums were performed in oven-dried glassware under a nitrogen atmosphere. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone ketyl before use. *n*-Butyllithium and *sec*-butyllithium were titrated prior to use according to the procedure of either Watson and Eastham, Shapiro et al., or Tischler and Tischler.[26] *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) and diisopropylamine were distilled from calcium hydride. All other solvents and reagents were of reagent grade or higher. Unless otherwise noted, ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ or CCl_4 with tetramethylsilane as an internal standard.

Determination of Nuclear Overhauser Enhancements (NOEs). A sample of 10 mg of material was dissolved with 1.5 mL of $CDCl_3$ in a NMR tube equipped with a ground-glass fitting. The charged apparatus was connected to a vacuum line, the solution was cooled in liquid N_2, and the system was evacuated. After 4 freeze–thaw cycles, the tube was sealed under vacuum and the ^1H NMR and ^1H NOE spectra were recorded by using the PRESAT experiment described by Hall and Sanders.[27]

Procedure A. Metalation of Amides and Reactions with Electrophiles. To a stirred solution of TMEDA in 30–60 mL of tetrahydrofuran under a N_2 atmosphere at −100 °C were added *sec*-butyllithium followed after 5 min by a solution of the amide in 10–20 mL of tetrahydrofuran. After being allowed to stir for 5–10 min, the solution was warmed to between −60 °C and −70 °C, treated with a solution of the electrophile in 10 mL of tetrahydrofuran, stirred for 10–120 min, and then poured into 50 mL of saturated NH_4Cl. Following extraction with diethyl ether, the organic portion was washed with 2% HCl and then brine, dried over either $CaSO_4$ or $MgSO_4$, and concentrated in vacuo to give the crude product. Deuterium oxide, when used, was added as a solution of 1–2 mL in 10 mL of tetrahydrofuran just prior to aqueous workup. Variations of this procedure, the amounts of reagents used, and the purification methods used are given with the spectroscopic and analytical data of the individual products.

Procedure B. To a stirred solution of TMEDA in 30–60 mL of tetrahydrofuran under a N_2 atmosphere at −78 °C were added *sec*-butyllithium followed after 5–10 min by a solution of the electrophile in 10 mL of tetrahydrofuran. After stirring for 10–120 min at between −60 °C and −70 °C, the products were separated as described in procedure A.

Procedure C. Preparation of Cyclopentanedicarboxamides. To a stirred solution of TMEDA in tetrahydrofuran under a N_2 atmosphere at −100 °C were added *sec*-butyllithium followed by a solution of the amide in 10–20 mL of tetrahydrofuran. After being stirred for 5 min, the solution was warmed to −78 °C and treated with the acrylamide as a solution in 10–20 mL of tetrahydrofuran. After stirring for 15 min, the cooling bath was removed and the solution allowed to warm and stir at ambient temperature for 1–12 h and then poured into 50 mL of saturated NH_4Cl. Following extraction into diethyl ether, the organic portion was washed with 2% HCl and then brine, dried over either $CaSO_4$ or $MgSO_4$, and concentrated in vacuo to give the crude product. Alternatively the reaction mixture was treated with deuterium oxide, benzophenone, or methyl iodide and stirred for 10–15 min at ambient temperature just prior to the aqueous workup.

***(E)*-*N,N*-Diisopropyl-1,1-diphenyl-1-hydroxy-3-pentene-3-carboxamide (14) and *N,N*-Diisopropyl-1,1-diphenyl-1-hydroxy-2-methyl-3-butene-3-carboxamide (13). Procedure B**: 534 mg (2.92 mmol) of **5** in 10 mL of THF, 3.21 mmol of *sec*-BuLi and 484 μL (3.21 mmol) of TMEDA in 80 mL of THF, 1.063 g (5.84 mmol) of benzophenone in 10 mL of THF. After treatment with benzophenone the solution was stirred for 5 min. Chromatographic separation of the crude semisolid by MPLC with 10% EtOAc/hexanes and recrystallization of the products from EtOAc/pentane gave 468 mg (44%) of **13** and 395 mg (37%) of **14**.

13: mp 165–167 °C; ^1H NMR δ 1.09 (d, J = 7 Hz, 3 H), 1.1–1.6 (unresolved m, 12 H), 3.41 (m, 1 H), 3.64 (q, J = 7 Hz, 1 H), 4.31 (m, 1 H), 5.63 (s, 1 H), 5.74 (s, 1 H), 7.0–7.7 (m, 11 H); MS, m/e (relative intensity) 228 (2), 183 (67), 168 (100), 140 (25), 105 (33), 83 (37), 77 (20), 55 (16), 43 (13); FD MS, m/e, 365; IR (KBr) 3430, 3200, 2980, 1625, 1594, 1450, 1370, 1350, 1240, 1205, 1180, 1160, 1135, 1055, 1040, 919, 830, 750, 709 cm^{-1}.

Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.49; H, 8.65; N, 3.88.

14: mp 128–131 °C; ^1H NMR δ 1.20 (d, J = 7 Hz, 15 H), 3.25 (s, 2 H), 3.71 (br m, 2 H), 5.53 (q, J = 7 Hz, 1 H), 6.12 (s, 1 H, exchanges with D_2O), 7.0–7.6 (m, 10 H); MS, m/e (relative intensity) 288 (1), 265 (1), 247 (4), 183 (100), 168 (88), 140 (26), 83 (11); FAB MS, m/e, 365; IR (KBr) 3295, 2960, 1650, 1597, 1490, 1445, 1370, 1355, 1340, 1205, 1160, 1060, 1050, 1025, 950, 875, 771, 760, 702 cm^{-1}.

Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 78.67; H, 8.58; N, 4.19.

After treatment with benzophenone the solution was warmed to ambient temperature and stirred for 1 h prior to workup and

(23) For some other cases where "metal chelate" transition-state models have been proposed, see: (a) Tamaru, Y.; Amino, Y.; Furukawa, Y.; Kagotani, M.; Yoshida, Z. *J. Am. Chem. Soc.* **1982**, *104*, 4018. (b) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 2. (c) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203.

(24) For an approach which leads to an unsubstituted cyclopentyl derivative, see: Beak, P.; Wilson, K. D. *J. Org. Chem.*, in press.

(25) Mass spectra were recorded by Carter Cook and associates on Varian MAT CH-5 and 731 mass spectrometers. Elemental analyses were performed by J. Nemeth and associates. Melting points are uncorrected. The temperatures reported for bulb-to-bulb distillations in a Kugelrohr apparatus represent the temperature of the hot air bath and are not necessarily an accurate measure of the boiling points. Vapor pressure chromatography (VPC) was performed on a 1.25-m Hewlett-Packard SE 52/54 cross-linked dimethyl silicone capillary column (0.2 mm in diameter).

(26) (a) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165. (b) Lipton, M. F.; Sorensen, C. M.; Sadler, A. C.; Shapiro, R. H. *Ibid.* **1980**, *186*, 155. (c) Tischler, A. N.; Tischler, M. H. *Aldrichimica Acta* **1978**, *11*, 20.

(27) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703.

isolation to give 490 mg (44%) of **13** and 426 mg (38%) of **14**.

13: mmp 165–167 °C.

14: mmp 128–131 °C.

Determination of NOE for **14**. PRESAT parameters: P2 = 6 μs, D3 = 15 sc, D4 = 100 μs, D5 = 200 μs. Irradiation at δ 1.29 enhanced 3.26 by 20% and 5.53 by 22%; δ 3.26 enhanced 1.29 by 4.5%; 5.53 enhanced 3.26 by 0%.

Attempted Isomerization of 14 to 13. To a slurry of 125 mg (15.6 mmol) of lithium hydride in 20 mL of THF was added a solution of 250 mg (0.68 mmol) of **14** in 5 mL of THF. Immediate gas evolution was observed. The slurry was stirred for 80 min and then carefully poured into 30 mL of saturated NH_4Cl. Workup as usual gave 294 mg (93%) of **14**: mp 126–130 °C, mmp 126–130 °C.

Attempted Isomerization of 13 to 14. As described in the preceding experiment: 94 mg (0.26 mmol) of **13** in 5 mL of THF was added to 21 mg (30 mmol) of lithium hydride in 20 mL of THF. TLC analysis shows no spots with R_f the same as **14**. The crude solid was recrystallized from EtOAc/hexanes and gave 76 mg (81%) of **13**: mp 163–165 °C, mmp 164–166 °C.

Preparation of 13 Using $MgBr_2$–Et_2O. Procedure A: 8.30 mmol of *sec*-BuLi and 1.25 mL (8.30 mmol) of $MgBr_2$–Et_2O in 25 mL of THF, 1.51 g (8.30 mmol) of benzophenone in 5 mL of THF. Following addition of the *sec*-BuLi the solution was warmed to −70 °C and then treated with $MgBr_2$–Et_2O, stirred 15 min, and treated with benzophenone. The crude semisolid was recrystallized from EtOAc/hexanes to give (two crops of crystals) 1.989 g (71%) of **13**: mp 166–167.5 °C, mmp 166–167 °C.

Anal. Calcd for $C_{24}H_{31}NO_2$: C, 78.86; H, 8.55; N, 3.83. Found: C, 79.15; H, 8.62; N, 3.95.

(*E*)-*N*,*N*-Diisopropyl-5,6-diphenyl-5,6-diazahex-2-ene-3-carboxamide (16) and *N*,*N*-Diisopropyl-4,5-diphenyl-3-methyl-4,5-diazapent-1-ene-2-carboxamide (15). Procedure B:[28] 1.275 g (6.96 mmol) of **5** in 15 mL of THF, 7.65 mmol of *sec*-BuLi and 1.16 mL (7.65 mmol) of TMEDA in 190 mL of THF, 2.53 g (13.9 mmol) of azobenzene in 15 mL of THF. After treatment with azobenzene at −60 °C, the solution was stirred for 15 min. The crude oil was separated by MPLC with 5% EtOAc/hexanes and the two products were recrystallized from CH_2Cl_2/petroleum ether (30–60 °C) to give 1.179 g (46%) of **15** and 745 mg (29%) of **16**. **16**: mp 99–100 °C; ^1H NMR δ 0.8–1.5 (br peak, 12 H), 1.48 (s, 1 H, exchanges in D_2O), 1.67 (d, J = 7 Hz, 3 H), 2.9–4.6 (two broad overlapping m, 2 H), 4.39 (s, 2 H), 5.63 (q, J = 7 Hz, 1 H), 6.6–7.4 (m, 10 H); MS, *m*/*e* (relative intensity) 365 (22), 273 (7), 264 (7), 183 (65), 172 (26), 168 (100), 140 (31), 100 (17), 83 (32), 77 (65), 55 (18), 43 (25); IR (KBr) 3440, 1597, 1495, 1445, 1370, 1345, 750, 694 cm^{-1}.

Anal. Calcd for $C_{23}H_{32}N_3O$: C, 75.72; H, 8.50; N, 11.48. Found: C, 75.77; H, 8.48; N, 11.34.

15: mp 110.5–112 °C; ^1H NMR δ 1.03 (d, J = 7 Hz, 12 H), 1.50 (d, J = 7 Hz, 3 H), 3.26 (qq, J = 7 Hz, 1 H), 4.06 (qq, J = 7 Hz, 1 H), 4.92 (q, J = 7 Hz, 1 H), 5.10 (s, 1 H), 5.20 (s, 1 H), 5.26 (s, 1 H), 6.5–7.3 (m, 10 H); MS, *m*/*e* (relative intensity) 365 (18), 183 (85), 168 (100), 140 (27), 83 (9), 77 (7); IR (KBr) 3440, 3295, 1600, 1495, 1445, 1370, 1200, 1040, 919, 750, 694 cm^{-1}.

Anal. Calcd for $C_{23}H_{32}N_3O$: C, 75.71; H, 8.50; N, 11.48. Found: C, 75.92; H, 8.60; N, 11.48.

Determination of NOE for 16. PRESAT parameters: P2 = 6 μs, D3 = 15 s, D4 = 100 μs, D5 = 200 μs. Irradiation at δ 1.67 enhanced 4.39 by 4.5% and 5.63 by 17%; 5.63 enhanced 4.39 by 0%.

(*E*)-*N*,*N*-Diisopropyl-2-octene-3-carboxamide (17). According to procedure B: 444 mg (2.42 mmol) of **5** in 5 mL of THF, 2.67 mmol) of *sec*-BuLi and 414 μL (2.75 mmol) of TMEDA in 60 mL of THF, 304 μL (2.67 mmol) of 1-iodobutane in 5 mL of THF; reaction conditions: −78 °C, 5 min. The iodobutane solution is added, stirred 15 min, and poured into saturated NH_4Cl. Workup as usual gives 763 mg of crude oil, of which 581 mg is chromatographically separated by MPLC using 30% EtOAc/hexanes, and bulb-to-bulb distilled to give 280 mg (63%) of **17**: $bp^{3.0}$ 95–100 °C; ^1H NMR δ 0.88 (t, J = 6 Hz, 3 H), 1.31 (d, J = 7 Hz, 12 H), 0.95–1.50 (unresolved m, 6 H), 1.65 (d, J = 7 Hz, 3 H), 2.23 (m, 2 H), 3.73 (m, 2 H), 5.40 (q, J = 7 Hz, 1 H); MS, *m*/*e* (relative intensity) 239 (11), 224 (15), 196 (16), 182 (60), 168 (11), 139 (100), 86 (26), 69 (88), 55 (1), 43 (52), 41 (50); IR (thin film) 2900, 1624, 1435, 1315, 1330, 1210, 1160, 1130, 1045, 828, 758 cm^{-1}.

(*E*)-*N*,*N*-Diisopropyl-1-(trimethylsilyl)-2-butene-2-carboxamide (18). According to procedure B: 926 mg (5.06 mmol) of **5** in 10 mL of THF, 5.57 mmol of *sec*-BuLi and 839 μL (5.57 mmol) of TMEDA in 140 mL of THF, 1.28 mL (10.1 mmol) of chlorotrimethylsilane in 20 mL of THF; reaction conditions: −78 °C, 5 min, chlorotrimethylsilane is added and stirred for 20 min. Workup as usual and bulb-to-bulb distillation gives 743 mg (58%) of **18**: $bp^{0.9}$ 95–105 °C; ^1H NMR (δ vs. $CHCl_3$ (7.28 ppm)) 0.12 (s, 9 H), 1.31 (d, J = 7 Hz, 12 H), 1.62 (d, J = 7 Hz, 3 H), 1.67 (s, 2 H), 3.74 (m, 2 H), 5.36 (q, J = 7 Hz, 1 H); ^{13}C NMR δ −0.9 (q), 13.2 (q), 19.5 (t), 20.7 (q), 47.6 (d), 119.2 (d), 137.1 (s), 173.0 (s); MS, *m*/*e* (relative intensity) 255 (5), 240 (100), 212 (37), 198 (19), 156 (13), 83 (42), 73 (30), 55 (8); isotope ratio, *m*/*e* (relative intensity) 259 (1.4), 257 (9.8), 256 (13.3), 255 (51.4), 254 (24.1); IR (thin film) 2960, 1629, 1536, 1368, 1336, 1245, 1210, 1159, 1130, 104, 1028, 980, 910, 850, 819 cm^{-1}.

Anal. Calcd for $C_{14}H_{29}NOSi$: C, 65.82; H, 11.44; N, 5.48.

(*E*)-*N*,*N*-Diisopropyl-2-methyl-2,6-heptadienamide (54). A mixture of 3.10 g (22.1 mmol) of (*E*)-2-methyl-2,6-heptadienoic acid and 10 mL of thionyl chloride was stirred for 3 h at room temperature; then the excess thionyl chloride was distilled in vacuo leaving the crude acid chloride: IR (thin film) 1740, 1640, 1000, 920, 860 cm^{-1}. The crude acid chloride in 10 mL of THF was added dropwise over 15 min to a stirred 0 °C solution of 3.5 mL (25 mmol) of diisopropylamine and 3.5 mL (26 mmol) of Et_3N in 50 mL of THF and then warmed and stirred at room temperature for 10 h. The resulting slurry was filtered and the solid washed with sequentially 50 mL of THF and 200 mL of Et_2O. The combined solutions were washed successively with 5% HCl, 5% NaOH, and brine, dried (Na_2SO_4), and concentrated, and the crude oil was bulb-to-bulb distilled to give 3.42 g (70%) of **54**: $bp^{0.30}$ 85–95 °C; ^1H NMR δ 1.24 (d, J = 6 Hz, 12 H), 1.78 (s, 3 H), 2.12 (m, 4 H), 3.63 (m, 2 H), 4.88 (d, J = 10 Hz, 1 H), 4.92 (d, J = 17 Hz, 1 H), 5.31 (t, J = 5 Hz, 1 H), 5.69 (m, 1 H); ^{13}C NMR δ 14.33 (q), 20.68 (q), 26.79 (t), 33.24 (t), 46.3 (br d), 49.3 (br d), 115.02 (t), 126.88 (d), 133.97 (s), 137.91 (d), 173.16 (s); MS, *m*/*e* (relative intensity) 223 (11), 208 (47), 181 (25), 168 (25), 166 (23), 153 (83), 139 (27), 134 (27), 126 (62), 123 (91), 95 (95), 83 (100), 67 (93), 55 (69), 43 (67), 41 (97); IR (thin film) 3020, 2910, 1625, 1430, 1360, 1330, 1210, 1160, 1130, 1040, 995, 915, 885, 775 cm^{-1}.

Anal. Calcd for $C_{14}H_{25}NO$: C, 75.28; H, 11.28; N, 6.27. Found: C, 75.16; H, 11.40; N, 5.97.

VPC analysis using a SE52/54 FSOT capillary column with programmed heating from 120 °C (3 min) to 220 °C at 15°/min showed one peak with a retention time (t_R) of 8.46 min.

Generation of 21 from (*E*)-*N*,*N*-Diisopropyl-2-methyl-2,6-heptadienamide (54). Procedure A: 375 mg (1.68 mmol) of **54** in 10 mL of THF, 1.85 mmol of *sec*-BuLi and 279 μL (1.85 mmol) of TMEDA in 50 mL of THF. The crude oil was bulb-to-bulb distilled to afford 325 mg (86%) of a 79:21 mixture of **(*E*)-*N*,*N*-diisopropyl-2-methyl-2,6-heptadienamide-*3′-d* (ix) and *N*,*N*-diisopropyl-1,6-heptadiene-2-carboxamide-*3-d* (x)**, $bp^{0.30}$ 85–95 °C; analysis using a SE 52/54 FSOT capillary column with programmed heating from 120 °C (3 min) to 220 °C at 15°/min showed two peaks having an area ratio of 79:21 (ix:x) and retention times (t_R) of 8.40 and 7.68 min, respectively. ^1H NMR δ 1.24 (d, J = 6 Hz, 12 H), 1.52 (m, 0.4 H), 1.78 (s, 1.6 H), 2.12 (m, 4 H), 3.3 (br m, 0.2 H), 3.68 (m, 1.6 H), 4.2 (br m, 0.2 H), 4.87 (s, 0.2 H), 4.88 (d, J = 10 Hz, 1 H), 4.92 (d, J = 17 Hz, 1 H), 5.01 (s, 0.2 H), 5.31 (t, 0.8 H), 5.69 (m, 1 H); MS, *m*/*e* (relative intensity) 224 (2), 209 (40), 181 (31), 169 (27), 124 (97), 100 (13), 96 (100), 86 (25), 84 (20), 83 (12), 70 (16), 68 (32), 67 (31), 58 (23), 56 (32), 55 (28), 43 (51), 41 (57). For ix: ^{13}C NMR δ 14.13 (trio), 20.68, 26.79, 33.24, 46.3 (br), 49.3 (br), 115.02, 126.88, 133.97, 137.91, 173.16. For x: ^{13}C NMR δ 20.68, 26.53, 29.95 (trio), 33.31, 45.9 (br), 50.2 (br), 111.53, 114.88, 133.96, 138.27, 146.87, 171.73.

***N*,*N*-Diisopropyl-*N′*,2-dimethyl-*N′*-phenyl-1,4-cyclopentanedicarboxamide (28–30) and 5-(Diisopropylcarbamoyl)-*N*-methyl-*N*-phenyl-5-heptenamide (31).** Procedure C: 6.28 mmol of *sec*-BuLi and 948 μL (6.28 mmol) of TMEDA in 180 mL of THF, 1.097 g (5.98 mmol) of **5** in 10 mL

(28) During workup, washing of the organic phase with 2% HCl was not carried out.

of THF, 965 mg (5.98 mmol) of **24** in 5 mL of THF. After warming, the solution was stirred for 12 h. The crude oil was bulb-to-bulb distilled, the second fraction ($bp^{0.4}$ 140–210 °C) was separated by MPLC with a solvent gradient of 30% to 100% EtOAc/hexanes. The products were each bulb-to-bulb distilled to give 353 mg (17%) of **28**, 239 mg (12%) of **29**, 543 mg (26%) of **30**, and 312 mg (15%) of **31**. The isomeric purity of each product was determined by VPC using a SE 52/54 FSOT capillary column with temperature program from 220 °C (4 min) to 250 °C at 20°/min. *Retention time (t_R) and % relative area of the peak are reported.* **30**: $bp^{0.3}$ 180–195 °C; ^1H NMR δ 0.850 (d, J = 6.4 Hz, 3 H, Me-2), 1.107 (d, J = 6 Hz, 6 H), 1.237 (d, J = 6 Hz, 6 H), 1.404 (ddd, $J_{H3H3'}$ = 12 Hz, J_{H3H4} = 10 Hz, J_{H3H2} = 12 Hz, 11 H), 1.554 (ddd, $J_{H5H5'}$ = 12 Hz, J_{H5H1} = 10 Hz, J_{H5H4} = 10 Hz, 1 H), 1.750 (ddd, $J_{H3'H3}$ = 12 Hz, $J_{H3'H4}$ = 7 Hz, $J_{H3'H2}$ = 6 Hz, 1 H), 2.099 (ddd, $J_{H5'H5}$ = 12 Hz, $J_{H5'H1}$ = 9 Hz, $J_{H5'H4}$ = 10 Hz, 1 H), 2.110 (m, 1 H, H-2), 2.501 (ddd, J_{H1H2} = 10 Hz, J_{H1H5} = 10 Hz, $J_{H1H5'}$ = 9 Hz, 1 H), 2.724 (dddd, J_{H4H3} = 10 Hz, $J_{H4H3'}$ = 7 Hz, J_{H4H5} = 10 Hz, $J_{H4H5'}$ = 10 Hz, 1 H), 3.165 (s, 3 H), 3.39 (m, 1 H), 3.20 (m, 1 H), 7.052 (d, J = 8.2 Hz, 2 H), 7.248 (t, J = 8.2 Hz, 1 H), 7.319 (t, J = 8.2 Hz, 2 H); decoupling, irradiation at δ 0.850 simplifies 2.110; 2.724 simplifies 1.404 to dd, 1.554 to dd, 1.750 to dd, and 2.099 to dd; at 2.501 simplifies 2.110, 2.099 to dd, and 1.554 to dd; 1.554 simplifies 2.099 to dd, 2.501 to dd, 2.724 to m; 1.750 simplifies 1.404 to dd, 2.110, 2.724 to m; ^{13}C NMR δ 17.92 (q), 20.67 (q), 20.80 (q), 21.32 (q), 21.42 (q), 35.01 (t), 137.58 (q), 39.22 (d), 39.73 (t), 40.29 (d), 45.60 (d), 47.88 (d), 50.50 (d), 127.28 (d), 127.60 (d), 129.78 (d), 143.91 (s), 173.49 (s), 176.59 (s); IR (Nujol) 2960, 1620, 1590, 1440, 1370, 1310, 1270, 1210, 1120, 1035, 1780, 700 cm^{-1}; VPC (t_r) 12.51 min (94%).

Anal. Calcd for $C_{21}H_{32}N_2O_2$: C, 73.21; H, 9.36; N, 8.13. Found: C, 73.50; H, 9.40; N, 7.90.

29: $bp^{0.3}$ 180–200 °C; mp 71–75 °C (from EtOAc/hexanes), mp 92–93 °C (from melt); ^1H NMR δ 0.688 (d, J = 7.0 Hz, 3 H, C-2Me), 1.170 (d, J = 6.2 Hz, 3 H), 1.183 (d, J = 6.2 Hz, 3 H), 1.336 (d, J = 6.7 Hz, 3 H), 1.354 (d, J = 6.5 Hz, 3 H), 1.474 (ddd, J_{H3H2} = 2.4 Hz, $J_{H3H3'}$ = 12 Hz, J_{H3H4} = 10 Hz, 1 H), 1.868 (ddd, J_{H5H1} = 7 Hz, J_{H5H4} = 8.5 Hz, $J_{H5H5'}$ = 12 Hz, 1 H), 2.163 (ddd, $J_{H3'H2}$ = 7.5 Hz, $J_{H3'H3}$ = 12 Hz, $J_{H3'H4}$ = 7 Hz, 1 H), 2.284 (ddd, $J_{H5'H1}$ = 10 Hz, $J_{H5'H4}$ = 10 Hz, $J_{H5'H5}$ = 12 Hz, 1 H), 2.421 (dddq, J_{H2H1} = 7.5 Hz, J_{H2H3} = 2.4 Hz, $J_{H2H3'}$ = 7.5 Hz, J_{H2Me-2} = 7.0 Hz, 1 H) 2.894 (dddd, J_{H4H3} = 10 Hz, $J_{H4H3'}$ = 7.0 Hz, J_{H4H5} = 8.5 Hz, $J_{H4H5'}$ = 10 Hz, 1 H), 3.200 (ddd, J_{H1H2} = 7.5 Hz, J_{H1H5} = 7 Hz, $J_{H1H5'}$ = 10 Hz, 1 H), 3.255 (s, 3 H), 3.39 (br m, 1 H), 4.159 (m, 1 H), 7.170 (d, J = 7.3 Hz, 2 H), 7.323 (t, J = 7.3 Hz, 1 H), 7.404 (t, J = 7.3 Hz, 2 H); decoupling, irradiation at δ 0.688 simplifies 2.421; 2.421 decouples 1.474 to dd, 0.688 to s, 2.163 to dd, and 3.200 to dd; 3.200 decouples 1.868 to dd, 2.284 to dd, and simplifies 2.421; 1.868 decouples 2.284 to dd, 3.200 to dd, and dimplifies 2.894; 2.284 decouples 1.868 to dd, and simplifies 2.894 and 3.200; 2.894 decouples 1.868 to dd, 2.284 to dd, 2.163 to dd, and simplifies 1.474; 1.474 decouples 2.163 to dd, and simplifies 2.421 and 2.894; 2.163 decouples 1.474 to dd, and simplifies 2.421 and 2.894; ^{13}C NMR δ 16.07 (q), 20.59 (q), 21.01 (q), 21.08 (q), 21.32 (q), 32.13 (t), 36.71 (t), 37.64 (q), 38.36 (d), 38.92 (d), 45.71 (d), 46.92 (d), 48.06 (d), 127.45 (d), 127.67 (d), 129.74 (d), 144.19 (s), 171.76 (s), 177.35 (s); IR (melt) 2940, 1650, 1640, 1600, 1495, 1440, 1380, 1270, 1220, 1130, 1045, 779, 702 cm^{-1}; MS, m/e (relative intensity) 344 (14), 343 (15), 287 (3), 244 (48), 216 (37), 210 (25), 170 (16), 134 (22), 107 (100), 100 (26), 86 (54), 80 (27), 77 (15), 58 (28), 5 (12), 43 (73), 41 (22); VPC, t_R 13.91 min (98%).

Anal. Calcd for $C_{21}H_{32}N_2O_2$: C, 73.21; H, 9.36; N, 8.13. Found: C, 73.49; H, 9.54; N, 7.81.

28: $bp^{0.3}$ 180–200 °C; ^1H NMR δ 0.853 (d, J = 6.5 Hz, 3 H, M3-2), 1.120 (d, J = 7 Hz, 3 H), 1.140 (d, J = 7 Hz, 3 H), 1.352 (d, J = 6.5 Hz, 6 H), 1.759 (ddd, $J_{H5H5'}$ = 12 Hz, J_{H5H1} = 7 Hz, J_{H5H4} = 7 Hz, 1 H), 2.049 (ddd, $J_{H5'H5}$ = 12 Hz, $J_{H5'H1}$ = 11 Hz, $J_{H5'H4}$ = 11 Hz), 2.15 (m, 3 H, H3, H3', and H1), 2.594 (m, J_{H2Me-2} = 6.5 Hz, J_{H2H1} = 9 Hz, J_{H2H3} = 9 Hz, $J_{H2H3'}$ = 8 Hz, 1 H), 2.768 (m, 1 H), 3.249 (s, 3 H), 3.37 (br m, 1 H), 3.918 (qq, J = 7 Hz, 1 H), 7.190 (d, J = 7.4 Hz, 2 H), 7.356 (t, J = 7.4 Hz, 1 H), 7.435 (5, J = 7.4 Hz, 2 H); Decoupling, irradiation at δ 0.853 simplifies 2.594 to q; 2.594 simplifies 2.15 to m; 2.768 simplifies 1.759 to d, 2.049 to d, 2.15 to m; 1.759 simplifies 2.049 to dd, 2.15 to m, 2.768 to ddd; ^1H NMR (benzene-d_6) δ 0.664 (d, J = 6.8 Hz, 3 H), 0.690 (d, J = 6.8 Hz, 3 H), 0.791 (d, J = 6.8 Hz, 3 H, Me-2), 1.009 (ddd, $J_{H3H3'}$ = 12 Hz, J_{H3H2} = 10 Hz, J_{H3H4} = 8 Hz, 1 H), 1.384 (d, J = 6.6 Hz, 6 H), 1.615 (ddd, $J_{H5H5'}$ = 10 Hz, J_{H5H4} = 9 Hz, 1 H), 1.840 (ddd, J_{H1H5} = 10 Hz, $J_{H1H5'}$ = 10 Hz, J_{H1H2} = 9 Hz, 1 H), 2.319 (ddd, $J_{H3'H3}$ = 12 Hz, $J_{H3'H2}$ = 8 Hz, $J_{H3'H4}$ = 5 Hz, 1 H), 2.419 (ddd, $J_{H5'H5}$ = 12 Hz, $J_{5'H4}$ = 10 Hz, $J_{5'H1}$ = 10 Hz, 1 H), 2.705 (dddd, J_{H4H3} = 8 Hz, $J_{H4H3'}$ = 5 Hz, J_{H4H5} = 9 Hz, $J_{H4H5'}$ = 10 Hz, 1 H), 3.029 (s, 3 H), 3.17 (br m, 1 H), 3.434 (qq, J = 6.8 Hz, 1 H), 6.680 (d, J = 6.8 Hz, 2 H), 6.848 (t, J = 7 Hz, 1 H), 6.912 (t, J = 7.0 Hz, 2 H); decoupling, irradiation at δ −0.791 simplifies 2.956 to ddd; 2.956 simplifies 0.791 to s, 1.009 to dd, 1.840 to dd, and 2.319 to dd; 1.840 simplifies 1.615 to dd, 2.419 to dd, and simplifies 2.956; 1.615 simplifies 1.840 to dd, 2.419 to dd, 2.705 to ddd; 2.419 simplifies 1.615 to dd, 1.840 to dd, and 2.705 to ddd; 1.009 simplifies 2.319 to dd, 2.705 to ddd, and 2.956 to m; 2.705 simplifies 1.009 to dd, 1.615 to dd, 2.319 to dd, and 2.419 to dd; ^{13}C NMR δ 19.14 (q), 20.85 (q), 21.37 (q), 35.94 (t), 37.63 (d), 37.70 (q), 37.83 (t), 40.61 (d), 45.76 (d), 47.69 (d), 51.50 (d), 127.67 (d), 127.90 (d), 129.62 (d), 144.51 (s), 172.50 (s), 175.33 (s); IR (thin film) 3060, 2940, 1655, 1600, 1495, 1440, 1380, 1310, 1260, 1215, 1125, 1045, 780, 705 cm^{-1}; VPC, t_R 14.91 (96%).

Anal. Calcd for $C_{21}H_{32}N_2O_2$: C, 73.21; H, 9.36; N, 8.13. Found: C, 72.97; H, 9.56; N, 7.95.

31: $bp^{0.3}$ 170–195 °C; ^1H NMR δ 1.12 (unresolved m, 12 H), 1.618 (d, J = 6.8 Hz, 3 H), 1.629 (tt, J's = 7 Hz, 1 H), 2.083 (t, J = 7 Hz, 1 H), 2.166 (t, J = 7 Hz, 2 H), 3.228 (s, 3, H), 3.3 (br m, 1 H), 4.08 (br m, 1 H), 5.391 (q, J = 6.8 Hz, 1 H), 7.139 (d, J = 7.3 Hz, 2 H), 7.200 (t, J = 7.3 Hz, 1 H), 7.381 (t, J = 7.3 Hz, 2 H); ^{13}C NMR δ 12.87 (q), 20.73 (q), 23.74 (t), 28.00 (t), 33.86 (t), 37.26 (q), 47.7 (br d), 122.41 (d), 127.28 (d), 127.62 (d), 129.71 (d), 138.63 (s), 144.25 (s), 172.46 (s), 174.98 (s); MS, m/e (relative intensity) 344 (40), 244 (50), 238 (45), 222 (10), 216 (36), 196 (100), 182 (49), 168 (24), 154 (9), 136 (16), 134 (54), 111 (16), 107 (57), 106 (45), 100 (32), 92 (12), 86 (16), 81 (28), 77 (30), 67 (17), 58 (15), 55 (21), 43 (55), 41 (39); IR (thin film) 2940, 1655, 1620, 1600, 1500, 1435, 1380, 1330, 1218, 1160, 1120, 1040, 776, 702 cm^{-1}; VPC, t_R 13.43 min (94%).

Anal. Calcd for $C_{21}H_{32}N_2O_2$: C, 73.21; H, 9.36; N, 8.13. Found: C, 73.40; H, 9.70; N, 8.02.

2,4-Dimethyl-*N*,*N*,*N'*,*N'*-tetraisopropyl-1,4-cyclopentanedicarboxamide (32, 33) and *N*,*N*-Diisopropyl-5-(diisopropylcarbamoyl)-2-methyl-5-heptenamide (34). Procedure C: 4.23 mmol of *sec*-BuLi and 638 μL (4.23 mmol) in 150 mL of THF, 705 mg (3.85 mmol) of **5** in 10 mL of THF, 716 mg (4.23 mmol) of **25** in 10 mL of THF. After warming, the solution was stirred for 5 h. The crude oil was bulb-to-bulb distilled, and the higher boiling fraction (bp 140–220 °C) was separated by MPLC with a solvent gradient of 10–30% EtOAc/hexanes to give 225 mg (17%) of **32** and 228 mg (21%) of **34** after bulb-to-bulb distillation and 570 mg (42%) of **33** after recrystallization.

33: mp 109–111 °C (from EtOAc/pentane); ^1H NMR δ 0.921 (d, J = 7 Hz, 3 H, Me-2), 1.142 (d, J = 6.7 Hz, 3 H), 1.182 (d, J = 0.67 Hz, 3 H), 1.187 (d, J = 6.7 Hz, 3 H), 1.200 (d, J = 6.8 Hz, 3 H), 1.279 (dd, J_{H3H2} = 7 Hz, $J_{H3H3'}$ = 13 Hz, 1 H), 1.377 (d, J = 7 Hz, 6 H), 1.390 (s, 3 H, Me-4), 1.398 (d, J = 7 Hz, 6 H), 2.088 (dd, $J_{H5H5'}$ = 13 Hz, J_{H5H1} = 11 Hz, 1 H), 2.310 (m, J_{H2Me-2} = 7 Hz, J_{H2H1} = 8 Hz, J_{H2H3} = 7 Hz, $J_{H2H3'}$ = 7 Hz, 1 H), 2.345 (dd, $J_{H5'H5}$ = 13 Hz, $J_{H5'H1}$ = 7 Hz, 1 H), 2.574 (dd, $J_{H3'H3}$ = 13 Hz, $J_{H3'H2}$ = 7 Hz, 1 H), 2.926 (ddd, J_{H1H2} = 8 Hz, J_{H1H5} = 11 Hz, $J_{H1H5'}$ = 7 Hz, 1 H), 3.283 (qq, J = 6.8 Hz, 1 H), 3.43 (br m, 1 H), 4.01 (m, 1 H), 4.218 (qq, J = 6.7 Hz, 1 H); decoupling, irradiation at δ 0.921 simplifies 2.310 to ddd; 1.279 simplifies 2.574 to d, 2.310 to m; 2.574 simplifies 2.310 to m, 1.279 to d; 2.926 simplifies 2.088 to d, 2.310 to m, 2.345 to d; at 2.088 simplifies 2.345 to d, 2.926 to dd; ^{13}C NMR δ 17.1 (q), 20.5 (q), 20.9 (q), 21.3 (q), 25.6 (q), 34.8 (d), 40.7 (t), 45.5 (d), 46.2 (d), 47.4 (t), 47.6 (br d), 48.2 (d), 49.1 (s), 172.3 (s), 175.4 (s); MS, m/e (relative intensity) 352 (s), 309 (3), 252 (18), 224 (100), 128 (9), 100 (25), 95 (24), 86 (35), 43 (54); isotope ratio 351 (3.0), 352 (160), 353 (42), 354 (5.7); IR (Nujol) 2920, 1620, 1440, 1360, 1300, 1210, 1120, 1030 cm^{-1}.

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.65; H, 11.20; N, 7.99.

32: $bp^{0.1}$ 120–145 °C; ^1H NMR δ 0.917 (d, J = 6.4 Hz, 3 H, Me-2), 1.140 (dd, J_{H3H2} = 8 Hz, $J_{H3H3'}$ = 13 Hz, 1 H), 1.188 (d, J = 6.8 Hz, 6 H), 1.210 (d, J = 6.8 Hz, 3 H), 1.220 (d, J = 6.8 Hz, 3 H), 1.313 (s, 3 H, Me-4), 1.35–1.42 (overlapping d's, 12 H), 1.765 (dd, J_{H5H1} = 8 Hz, $J_{H5H5'}$ = 12 Hz, 1 H), 2.335 (dd, $J_{H5'H5}$ = 12

Ha, $J_{H5'H1}$ = 10 Hz, 1 H), 2.416 (ddd, J_{H1H2} = 8 Hz, J_{H1H5} = 8 Hz, $J_{H1H5'}$ = 10 Hz, 1 H), 2.514 (m, J_{H2Me-2} = 6.4 Hz, J_{H2H1} = 8 Hz, J_{H2H3} = 8 Hz, $J_{H2H3'}$ = 10 Hz, 1 H), 2.587 (dd, $J_{H3'H2}$ = 10 Hz, $J_{H3'H3}$ = 13 Hz, 1 H), 3.273 (qq, J = 6.7 Hz, 1 H), 3.53 (br m, 1 H), 4.033 (m, 2 H); decoupling, irradiation at δ 0.971 simplifies 2.514 to ddd; 1.140 simplifies 2.587 to d, 2.514 to m; 1.765 simplifies 2.355 to d, 2.416 to dd; ^{13}C NMR δ 19.84 (q), 20.61 (q), 20.81 (q), 21.51 (q), 28.12 (q), 37.61 (d), 44.05 (t), 45.40 (d), 46.31 (d), 47.65 (s), 47.95 (t), 49.28 (d), 172.41 (s), 176.01 (s); MS, *m/e* (relative intensity) 352 (2), 309 (2), 252 (81), 224 (51), 210 (15), 182 (12), 128 (15), 100 (88), 95 (36), 81 (15), 57 (26), 55 (29), 43 (100); IR (thin film) 2960, 1630, 1440, 1380, 1320, 1210, 1140, 1040 cm^{-1}.

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.76; H, 11.25; N, 7.87.

34: bp$^{0.2}$ 130–140 °C; ^{1}H NMR δ 1.091 (d, J = 6.8 Hz, 3 H), 1.193 (d, J = 6.4 Hz, 3 H), 1.209 (d, J = 6.4 Hz, 3 H), 1.3 (unresolved m, 12 H), 1.385 (d, J = 6.1 Hz, 6 H), 1.46 (m, 1 H), 1.666 (d, J = 6.8 Hz, 3 H), 1.802 (m, 1 H), 2.229 (m, 2 H), 2.705 (m, 1 H), 3.45 (br m, 2 H), 4.07 (m, 2 H), 5.458 (q, J = 6.8 Hz, 1 H); ^{13}C NMR δ 12.94 (q), 18.02 (q), 20.69 (q), 20.84 (q), 21.23 (q), 26.26 (t), 32.43 (t), 36.60 (d), 45.70 (d), 45.8 (br d), 48.0 (br d), 50.1 (br d), 122.41 (d), 138.62 (s), 172.73 (s), 175.09 (s); IR (thin film) 2960, 1716, 1624, 1440, 1370, 1330, 1210, 1140, 1040, 723 cm^{-1}; MS, *m/e* (relative intensity) 352 (12), 252 (45), 224 (20), 196 (100), 183 (33), 182 (32), 170 (29), 168 (31), 157 (31), 150 (12), 140 (15), 138 (17), 114 (80), 100 (89), 95 (17), 86 (43), 58 (24), 55 (32), 43 (86), 41 (25).

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.31; H, 11.17; N, 8.02.

***N,N*-Diisopropyl-*N'*-phenyl-*N'*,2,3-trimethyl-1,4-cyclopentanedicarboxamide (35, 36) and *N,N*-Diisopropyl-5-(diisopropylcarbamoyl)-3-methyl-5-heptenamide (37).** According to procedure A: 8.10 mmol of *sec*-BuLi and 1.22 mL (8.10 mmol) of TMEDA in 180 mL of THF, 1.414 g (7.72 mmol) of **5** in 10 mL of THF, 1.372 g (8.10 mmol) of **26** in 10 mL of THF. After warming, the solution was stirred for 10 h. The crude oil was bulb-to-bulb distilled, the second fraction (bp$^{0.4}$ 140–240 °C) was separated by MPLC with a solvent gradient of 7.5–40% EtOAc/hexanes, and the products were distilled to give 934 mg (34%) of **35**, 471 mg (17%) of **36**, and 124 mg (5%) of impure **37**. The isomeric purity of each product was determined by VPC using a SE 52/54 capillary column with temperature programming from 120 °C (3 min) to 250 °C at 10°/min. Retention times (t_R) and % relative peak areas are given. **35**: ^{1}H NMR δ 0.764 (d, J = 7 Hz, 3 H, Me-2), 0.784 (d, J = 7 Hz, 3 H, Me-3), 1.170 (d, J = 6.8 Hz, 3 H), 1.186 (d, J = 6.8 Hz, 3 H), 1.310 (d, J = 6.6 Hz, 3 H), 1.388 (d, J = 6.6 Hz, 3 H), 1.592 (ddd, J_{H5H1} = 10.2 Hz, J_{H5H4} = 6.2 Hz, $J_{H5H5'}$ = 12.8 Hz, 1 H), 1.771 (ddq, J_{H2H1} = 6.3 Hz, J_{H2H3} = 6.3 Hz, J_{H2Me-2} = 7.0 Hz, 1 H), 2.289 (ddq, J_{H3H2} = 6.3 Hz, J_{H3H4} = 9.7 Hz, J_{H3Me-3} = 7.2 Hz, 1 H), 2.552 (ddd, J_{H4H3} = 9.7 Hz, J_{H4H5} = 6.2 Hz, $J_{H4H5'}$ = 10.3 Hz, 1 H), 2.643 (ddd, $J_{H5'H1}$ = 7.9 Hz, $J_{H5'H4}$ = 10.3 Hz, $J_{H5'H5}$ = 12.8 Hz, 1 H), 3.019 (ddd, J_{H1H2} = 6.3 Hz, J_{H1H5} = 10.2 Hz, $J_{H1H5'}$ = 7.9 Hz, 1 H), 3.260 (s, 3 H), 3.45 (br m, 1 H), 4.06 (m, 1 H), 7.156 (d, J = 7.3 Hz, 2 H), 7.333 (t, J = 7.3 Hz, 1 H), 7.404 (t, J = 7.3 Hz, 2 H); decoupling, irradiation at δ 1.771 decouples 0.764 to s, simplifies 2.289 and 3.019; 2.289 decouples 0.874 to s, simplifies 1.771 and 2.552; 3.019 simplifies 1.771, 1.592, and 2.643; 1.592 simplifies 2.552, 2.643 and 3.019; 2.552 simplifies 1.592, 2.289, and 2.643; ^{13}C NMR δ 10.49 (q), 14.15 (q), 20.39 (1), 20.49 (q), 20.98 (q), 30.96 (t), 37.48 (q), 40.11 (d), 127.59 (d), 129 (45), 143.39 (s), 172.84 (s), 173.89 (s); MS, *m/e* (relative intensity) 358 (9), 357 (11), 258 (27), 230 (16), 224 (25), 170 (20), 134 (24), 128 (8), 107 (100), 94 (15), 86 (36), 77 (10), 59 (15), 43 (49); IR (thin film) 2940, 1650, 1600, 1595, 1440, 1380, 1330, 1260, 1110, 1050, 970, 930, 777, 732, 703 cm^{-1}; VPC, t_R 23.54 min (97%).

Anal. Calcd for $C_{22}H_{34}N_2O_2$: C, 73.70; H, 9.56; N, 7.82. Found: C, 73.74; H, 9.29; N, 7.66.

36: mp 78–81 °C (from benzane/Et$_2$O); ^{1}H NMR (3:1 $CDCl_3$/benzene-d_6) δ 0.698 (d, J = 6.8 Hz, 6 H, Me-2 and Me-3), 1.020 (d, J = 6.7 Hz, 3 H), 1.050 (d, J = 6.8 Hz, 3 H), 1.346 (br d, 6 H), 1.758 (ddd, J_{H5H1} = 8 Hz, J_{H5H4} = 8 Hz, $J_{H5H5'}$ = 13 Hz, 1 H), 2.026 (ddd, $J_{H5'H1}$ = 10 Hz, $J_{H5'H4}$ = 10 Hz, $J_{H5'H5}$ = 13 Hz, 1 H), 2.305 (ddd, J_{H1H2} = 7 Hz, J_{H1H5} = 8 Hz, $J_{H1H5'}$ = 10 Hz, 1 H), 2.380 (ddd, J_{H4H3} = 7 Hz, J_{H4H5} = 8 Hz, $J_{H4H5'}$ = 10 Hz, 1 H), 2.519 (ddq, J_{H3H2} = 7 Hz, J_{H3H4} = 7 Hz, J_{H3Me-3} = 7 Hz, 1 H), 2.549 (ddq, J_{H2H1} = 7 Hz, J_{H2H3} = 7 Hz, J_{H2Me-2} = 7 Hz, 1 H), 3.208 (s, 3 H), 3.327 (m, 1 H), 3.804 (m, 1 H), 7.070 (d, J = 7.2 Hz, 2 H), 7.232 (t, J = 7.2 Hz, 1 H), 7.3 (t, 2 H); decoupling, irradiation at δ 0.698 decouples 2.519 to t, and 2.549 to t; 1.758 simplifies 2.026, 2.305, and 2.380; 2.026 simplifies 1.758, 2.305, and 2.380; 2.305 simplifies 1.758, 2.305 and 2.380; 2.305 simplifies 1.758, 2.026, and 2.549; 2.380 simplifies 1.758, 2.026 and 2.519; ^{13}C NMR (acetone-d_6) δ 14.80 (q), 15.34 (q), 21.01 (q), 21.31 (q), 21.41 (q), 35.09 (t), 37.60 (q), 40.81 (d), 41.65 (d), 45.95 (d), 48.41 (d), 48.71 (d), 49.23 (d), 128.28 (d), 128.72 (d), 130.43 (d), 145.45 (s), 173.48 (s), 175.09 (s); MS, *m/e* (relative intensity) 358 (3), 343 (1), 258 (24), 252 (100), 230 (12), 224 (5), 210 (6), 150 (20), 149 (18), 134 (23), 122 (7), 107 (13), 106 (13), 100 (8), 97 (11), 95 (20), 86 (21), 77 (12), 69 (12), 55 (18), 43 (59), 41 (21); IR (Nujol) 2920, 1650, 1620, 1590, 1490, 1460, 1370, 1310, 1270, 1200, 1120, 1040, 775, 700 cm^{-1}; VPC, t_R 22.87 min (99%).

Anal. Calcd for $C_{22}H_{34}N_2O_2$: C, 73.70; H, 9.56; N, 7.82. Found: C, 73.76; H, 9.56; N, 7.89.

37: (ca. 85% pure): bp$^{0.5}$ 170–220 °C; ^{1}H NMR δ 0.71 (d, 3 H), 1.1–1.4 (m, 12 H), 1.61 (d, 3 H), 1.9–2.6 (m, 5 H), 3.28 (s, 3 H), 3.41 (m, 1 H), 3.95 (m, 1 H), 5.51 (q, 1 H), 7.0–7.5 (m, 5 H).

Determination of NOEs for 35 and 36. Solvents: $CDCl_3$ was used for **35** and a 3:1 mixture of $CDCl_3$ and benzene-d_6 was used for **36**. PRESAT parameters: P2 = 6 μs, D3 = 15 s, D4 = 100 μs, D5 = 200 μs. **36**: irradiation at δ 0.698 (Me-2, Me-3) enhances 2.305 (H-1) 17%, 2.519 (H-3) 18%, 2.549 (H-2) 18%, and 2.380 (H-4) 17%; 2.380 (H-4) enhances 1.758 (H-5) 2%, and 0.698 (Me-2, Me-3) 3%; 1.758 (H-5) enhances 2.026 (H-5') 9%, 2.305 (H-1) 9%, and 2.380 (H-4) 13%; 2.026 (H-5') enhances 1.758 (H-5) 2%, 2.519 (H-3) 2%, 2.549 (H-2) 4%.

35: irradiation at δ 3.019 (H-1) enhances 1.771 (H-2) 8%, and 1.592 (H-5) 7%; 1.771 (H-2) enhances 3.019 (H-1) 21%, and 2.289 (H-3) 6%; 0.81 (Me-2, Me-3) enhances 1.771 (H-2) 9%, 2.289 (H-3) 22%, 2.643 (H-5') 14%, and 2.552 (H-4) 14%; 2.289 (H-3) enhances 3.019 (H-1) 16%, and 1.592 (H-5) 2%.

***N,N,N',N'*-Tetraisopropyl-2,3,4-trimethyl-1,4-cyclopentanedicarboxamide (38, 39) and *N,N*-Diisopropyl-5-(diisopropylcarbamoyl)-2,3-dimethyl-5-heptenamide (40, 41).** Procedure C: 538 mmol of *sec*-BuLi and 810 μL (5.38 μL) of TMEDA in 100 ml of THF, 1.794 g (9.79 mmol) of **5** in 10 mL of THF. After warming the solution, the solution was stirred for 3 h. The crude oil was distilled, and the higher boiling fraction was separated by MPLC with 25% EtOAc/hexanes and redistilled to give 1.292 g (72%) of **38** and **39** as a 9:1 mixture, 258 mg (12%) of **40** and 216 mg (9%) of **41**. Further separation of the mixture of **38** and **39** in 15% EtOAc/hexanes and distillation gave 1.115 g (64%) of **38**. **38**: bp$^{0.3}$ 130–145 °C; ^{1}H NMR δ 0.842 (d, J = 7 Hz, 3 H, Me-2), 1.012 (d, J = 7 Hz, 3 H, Me-3), 1.19 (overlapping d's, 12 H), 1.138 (s, 3 H, Me-4), 1.40 (overlapping d's, 12 H), 2.173 (dd, $J_{H5H5'}$ = 13 Hz, J_{H5H1} = 8 Hz, 1 H), 2.238 (ddq, J_{H2H1} = 9 Hz, J_{H2H3} = 8 Hz, J_{H2Me-2} = 7 Hz, 1 H), 2.416 (dd, $J_{H5'H5}$ = 13 Hz, $J_{H5'H1}$ = 10 Hz, 1 H), 2.784 (dq, J_{H3H2} = 8 Hz, J_{H3Me-3} = 7 Hz, 1 H), 3.058 (ddd, J_{H1H2} = 9 Hz, J_{H1H5} = 8 Hz, $J_{H1H5'}$ = 10 Hz, 1 H), 3.295 (qq, J = 6.8 Hz, 1 H), 3.42 (m, 1 H), 4.139 (qq, J = 6.8 Hz, 1 H), 4.211 (qq, J = 6.8 Hz, 1 H); decoupling, irradiation at δ 0.842 decouples 2.238 to dd; 1.012 decouples 2.784 to d; 2.238 decouples 2.784 to q, 0.842 to s, and 3.058 to dd; 2.784 decouples 1.012 to s; and simplifies 2.238; 2.173 decouples 2.146 to d, and 3.058 to dd; 2.416 decouples 2.173 to d, and 3.058 to dd; ^{13}C NMR δ 11.29 (q), 11.90 (q), 20.34 (q), 20.53 (q), 20.67 (q), 20.68 (q), 20.94 (q), 21.01 (q), 21.16 (q), 21.46 (q), 22.99 (q), 39.62 (t), 39.95 (d), 44.32 (d), 45.68 (d), 45.86 (d), 46.34 (d), 47.91 (d), 48.34 (d), 50.02 (s), 171.83 (s), 176.78 (s); MS, *m/e* (relative intensity) 366 (2), 266 (7), 238 (27), 128 (7), 109 (7), 100 (10), 97 (11), 86 (20), 71 (36), 69 (25), 57 (76), 55 (39), 43 (100), 41 (50); IR (thin film) 2960, 1630, 1440, 1370, 1315, 1160, 1030 cm^{-1}.

Anal. Calcd for $C_{22}H_{42}N_2O_2$: C, 72.08; H, 11.65; N, 7.64. Found: C, 72.43; H, 11.83; N, 7.60.

For **39** in the mixture of **38** and **39**: ^{13}C NMR δ 11.02 (q), 15.33 (q), 21.86 (q), 39.68 (d), 41.76 (t), 42.79 (d), 45.96 (d), 47.22 (d), 48.11 (d), 48.48 (s), 171.67 (s), 175 (s).

Anal. Calcd for $C_{22}H_{42}N_2O_2$: C, 72.08; H, 11.65; N, 7.64. Found: C, 72.34; H, 11.67; N, 7.50.

40: mp 96–97 °C (from EtOAc/hexanes); ^{1}H NMR δ 0.910 (d, J = 6.7 Hz, 3 H), 1.041 (d, J = 6.8 Hz, 3 H), 1.198 (d, J = 6.7 Hz, 12 H), 1.371 (d, J = 6.4 Hz, 12 H), 1.702 (d, J = 6.9 Hz, 3 H), 1.925

(m, 1 H), 2.101 (dd, J = 9.8 Hz, 12 Hz, 1 H), 2.287 (dd, J = 9.8 Hz, 3 Hz, 1 H), 2.605 (ddq, J = 6.8 Hz, 1 H), 3.45 (br m, 2 H), 4.10 (br m, 2 H), 5.580 (q, J = 6.9 Hz, 1 H); ^{13}C NMR δ 13.26 (q), 13.67 (q), 15.63 (q), 20.63 (q), 20.74 (q), 20.79 (q), 20.89 (q), 21.38 (q), 34.14 (t), 35.16 (d), 41.71 (d), 45.65 (d), 47.93 (br d), 124.51 (d), 138.11 (s), 172.73 (s), 175.01 (s); MS, m/e (relative intensity) 366 (24), 238 (14), 210 (100), 196 (9), 184 (70), 168 (25), 144 (38), 100 (64), 86 (29); IR (KBr) 2960, 1660, 1630, 1615, 1440, 1365, 1335, 1210, 1135, 1110, 1040, 850, 765, 745 cm^{-1}.

Anal. Calcd for $C_{22}H_{42}N_2O_2$: C, 72.08; H, 11.65; N, 7.64. Found: C, 72.45; H, 11.72; N, 7.63.

41: mp 110.5–112 °C (from EtOAc/hexanes); ^{1}H NMR δ 0.914 (d, J = 6.6 Hz, 3 H), 1.114 (d, J = 6.7 Hz, 3 H), 1.201 (d, J = 6.5 Hz, 6 H), 1.270 (d, J = 6.5 Hz, 6 H), 1.370 (d, J = 6.2 Hz, 12 H), 1.685 (d, J = 6.8 Hz, 3 H), 1.899 (m, 1 H), 2.054 (dd, J = 12 Hz, 10.2 Hz, 1 H), 2.459 (dd, J = 4.2 Hz, 10.6 Hz, 1 H), 2.550 (m, 1 H), 3.43 (br m, 2 H), 4.052 (m, J = 6.5 Hz, 2 H), 5.561 (q, J = 6.7 Hz, 1 H), MS, m/e (relative intensity) 366 (7), 323 (1), 266 (6), 238 (8), 210 (100), 194 (9), 184 (26), 168 (10), 157 (12), 114 (27), 100 (14), 86 (9); IR (KBr) 2960, 1660, 1630, 1615, 1440, 1370, 1335, 1320, 1210, 1160, 1130, 1040, 1030, 825, 765, 755 cm^{-1}.

Anal. Calcd for $C_{22}H_{42}N_2O_2$: C, 72.08; H, 11.55; N, 7.64. Found: C, 72.10; H, 11.60; N, 7.60.

Determination of NOEs for 38. PRESAT parameters: P2 = 6 μs, D3 = 15 s, D4 = 100 μs, D5 = 200 μs. Irradiation at δ 3.058 (H-1) enhanced 2.238 (H-2) 4%; 2.784 (H-3) enhanced 2.238 (H-2) 14%, 1.012 (Me-3) 1%; 1.138 (Me-4) enhanced 2.173 (H-5) 10%; 0.842 (Me-2) enhanced 2.238 (H-2) 22%, 1.138 (Me-4) 2%.

***N*,*N*-Diisopropyl-*N*′,2-dimethyl-*N*′,3-diphenyl-1,4-cyclopentanedicarboxamide (46).** Procedure C: 6.55 mmol of *sec*-BuLi and 988 μL (6.55 mmol) of TMEDA in 150 mL of THF, 2.000 g (5.46 mmol) of **5** in 10 mL of THF, 1.553 g (6.55 mmol) of (*E*)-*N*-methyl-3,*N*-diphenylpropenamide in 10 mL of THF. After warming, the solution was stirred for 10 h. The crude oil was separated by MPLC with 15% EtOAc/hexanes to give 1.456 g (65%) of **46**: bp$^{0.2}$ 270–290 °C; ^{1}H NMR (1:1 $CDCl_3$/benzene-d_6) δ 0.464 (d, J = 6.2 Hz, 3 H, Me-2), 0.984 (d, J = 6.4 Hz, 3 H), 1.076 (d, J = 6.7 Hz, 3 H), 1.277 (d, J = 6.6 Hz, 3 H), 1.332 (d, J = 6.3 Hz, 3 H), 1.976 (ddd, J_{H5H1} = 8.0 Hz, J_{H5H4} = 10.5 Hz, $J_{H5H5'}$ = 12.8 Hz, 1 H), 2.606 (dd, J_{H3H2} = 7 Hz, J_{H3H4} = 7 Hz, 1 H), 2.675 (ddq, J_{H2H1} = 6 Hz, J_{H2H3} = 7 Hz, J_{H2Me} = 6.2 Hz, 1 H), 2.778 (ddd, J_{H1H2} = 6 Hz, J_{H1H5} = 8.0 Hz, $J_{H1H5'}$ = 10.5 Hz, 1 H), 2.857 (s, 3 H), 3.177 (ddd, $J_{H5'H1}$ = 10.5 Hz, $J_{H5'H4}$ = 8.5 Hz, $J_{H5'H5}$ = 12.8 Hz, 1 H), 3.36 (br m, 1 H), 3.591 (ddd, J_{H4H3} = 7 Hz, J_{H4H5} = 10.5 Hz, $J_{H4H5'}$ = 8.5 Hz, 1 H), 4.00 (br m, 1 H), 6.821 (d, J = 7.2 Hz, 2 H), 7.069 (d, J = 7.4 Hz, 2 H), 7.14–7.29 (m, 6 H); decoupling, irradiation at δ 0.464 simplifies 2.675 to dd; 2.675 simplifies 0.464 to s, 2.606 to d, and 2.778 to dd; 2.606 simplifies 2.675 and 3.591 to dd's; 3.591 simplifies 1.976 to dd, 2.778 to dd, and 3.591 to dd; 1.976 simplifies 2.778 to dd, 3.177 to dd, and 3.591 to dd; ^{13}C NMR δ 15.26 (q), 20.62 (q), 20.71 (q), 21.35 (q), 21.46 (q), 32.43 (t), 37.75 (q), 43.33 (d), 45.62 (d), 47.09 (d), 47.11 (br d), 47.80 (br d), 53.04 (d), 126.33 (d), 127.55 (d), 127.69 (d), 129.39 (d), 129.47 (d), 129.57 (d), 139.40 (s), 143.55 (s), 172.12 (s), 173.82 (s); IR (thin film) 2940, 1640 (vs), 1590, 1490, 1440, 1370, 1325, 1260, 1215, 1135, 1110, 1050, 810, 776, 701 cm^{-1}; MS, m/e (relative intensity) 420 (30), 320 (17), 292 (14), 286 (100), 265 (10), 170 (20), 157 (17), 134 (30), 128 (27), 107 (98), 100 (12), 91 (15), 86 (64), 77 (12), 58 (13), 43 (83); isotope ratio, m/e (relative intensity) 419 (24.3), 420 (55.5), 421 (17.1), 422 (2.7).

Anal. Calcd for $C_{27}H_{36}N_2O_2$: C, 77.10; H, 8.63; N, 6.66. Found: C, 77.18; H, 8.69; N, 6.83.

Determination of NOEs for 46. Solvent: 1:1 $CDCl_3$/benzene-d_6. PRESAT parameters: P2 = 6 μs, D3 = 15 s, D4 = 100 μs, D5 = 200 μs. Irradiation at δ 0.464 enhanced 2.675 (H-2) 17%, 7.069 (ortho) 1%; 3.591 (H-4) enhanced 1.976 (H-5) 4%, 7.069 (ortho) 2%; 1.976 (H-5) enhanced 3.591 (H-4) 7%, 3.177 (H-5′) 14%; 3.177 (H-5′) enhanced 1.976 (H-5) 14%.

***N*,*N*-Diisopropyl-*N*′,2-dimethyl-*N*′,3-diphenyl-1,4-cyclopentanedicarboxamide-*4*-*d* (47).** A solution of 293 mg (0.697 mmol) of **46** and 300 mL (35% slurry in mineral oil) of KH in 3 mL of Me_2SO-d_6 was stirred at 20 °C for 18 h and then carefully hydrolyzed with 3 mL of D_2O in 10 mL of THF under N_2. Workup according to procedure C and separation by MPLC with 20% EtOAc/hexanes gave 273 mg (91%) of **47**: bp$^{0.2}$ 270–290 °C; ^{1}H NMR (1:1 $CDCl_3$/benzene-d_6) was identical with **46** except δ 1.976 (dd, J_{H5H1} = 7.8 Hz, $J_{H5H5'}$ = 13 Hz, 1 H), 2.606 (d, J_{H3H2} = 6.9 Hz, 1 H), 3.177 (dd, $J_{H5'H1}$ = 10.9 Hz, $J_{H5'H5}$ = 13 Hz, 1 H), 3.591 (no signal); ^{13}C NMR (nitromethane-d_3) δ 15.73, 21.13, 21.16, 21.67, 33.42, 28.01, 44.44, 46.57, 48.14 (trio), 48.34, 49.11, 54.57, 127.49, 128.79, 129.01, 130.76, 131.33, 141.08, 145.36, 172.91, 174.91; IR (film with $CDCl_3$) 2940, 1640, 1590, 1490, 1440, 1370, 1325, 1260, 1215, 1110, 1050, 810, 776, 700 cm^{-1}; MS, m/e (relative intensity) 421 (53), 321 (32), 293 (14), 287 (97), 266 (20), 239 (13), 171 (19), 158 (25), 134 (55), 128 (42), 108 (98), 100 (18), 91 (20), 86 (99), 84 (35), 77 (19), 69 (13), 58 (24), 43 (100); isotope ratio, m/e (relative intensity) 419 (0.9), 420 (21.22), 421 (54.9), 422 (19.1), 423 (3.6): 91% *d*.

***N*,*N*-Diisopropyl-1,2-diphenyl-3-methyl-2,3,4,5-tetrahydropyrazole-4-carboxamide (48 and 49).** To 556 mg (1.52 mmol) of **15** in 25 mL of THF at −78 °C was added 1.67 mmol of *n*-BuLi followed by 341 mg (3.04 mmol) of KO-*t*-Bu. The mixture was warmed, stirred at 20 °C for 16 h, then poured into saturated NH_4Cl, and extracted with diethyl ether. The organic layer was dried over $CaSO_4$, concentrated, and separated by MPLC with a solvent gradient of 2–5% EtOAc/hexanes to give 99 mg (18%) **49**, 226 mg (41%) of **48**, and 203 mg (37%) of a 2:1 mixture of **48** and **49**.

49: mp 153–155 °C (from hexanes); ^{1}H NMR δ 1.073 (d, J = 6.8 Hz, 3 H, Me-3), 1.137 (d, J = 6.7 Hz, 3 H), 1.240 (d, J = 6.6 Hz, 3 H), 1.380 (d, J = 6.8 Hz, 3 H), 1.417 (d, J = 6.8 Hz, 3 H), 3.395 (m, 1 H), 3.477 (ddd, J_{H4H3} = 6.4 Hz, J_{H4H5} = 9 Hz, $J_{H4H5'}$ = 10 Hz, 1 H), 3.873 (dd, J_{H5H4} = 9 Hz, $J_{H5H5'}$ = 11 Hz, 1 H), 3.993 (m, 1 H), 4.164 (dq, J_{H3H4} = 6.4 Hz, J_{H3Me-3} = 6.8 Hz, 1 H), 4.225 (dd, $J_{H5'H5}$ = 11 Hz, $J_{H5'H4}$ = 10 Hz, 1 H), 6.768 (t, J = 7.2 Hz, 1 H), 6.848 (d, J = 7.4 Hz, 2 H), 6.942 (t, J = 7.2 Hz, 1 H), 7.031 (d, J = 7.4 Hz, 2 H), 7.187 (t, J = 7.3 Hz, 2 H), 7.263 (t, J = 7.3 Hz, 2 H); decoupling, irradiation at δ 4.164 simplifies 1.073 to s, 3.477 to dd; 3.477 simplifies 4.164 to q, 3.873 to d and 4.225 to d; ^{13}C NMR δ 15.6 (q), 20.17 (q), 20.77 (q), 20.98 (q), 21.28 (q), 46.17 (d), 47.06 (d), 48.41 (d), 50.65 (t), 61.79 (d), 112.66 (d), 115.58 (d), 118.36 (d), 121.19 (d), 129.01 (d), 129.09 (d), 151.25 (s), 153.45 (s), 167.05 (s); MS, m/e (relative intensity) 365 (55), 237 (39), 221 (9), 195 (16), 160 (20), 154 (21), 147 (61), 120 (50), 119 (58), 105 (24), 100 (65), 86 (50), 77 (67), 71 (27), 57 (98), 43 (100); IR (Nujol) 2910, 1650, 1601, 1500, 1490, 1450, 1380, 1330, 1300, 1290, 1150, 1100, 1040, 998, 873, 800, 767, 751, 695 cm^{-1}.

Anal. Calcd for $C_{23}H_{31}N_3O$: C, 75.57; H, 8.55; N, 11.50. Found: C, 75.70; H, 8.43; N, 11.74.

48: mp 120–122 °C (from hexanes); ^{1}H NMR δ 1.198 (d, J = 7.5 Hz, 3 H), 1.218 (d, J = 7.2 Hz, 3 H), 1.249 (d, J = 6.8 Hz, 3 H), 1.323 (d, J = 6.7 Hz, 3 H), 1.463 (d, J = 6.4 Hz, 3 H, Me-3), 3.145 (ddd, J_{H4H3} = 6.8 Hz, J_{H4H5} = 9.5 Hz, $J_{H4H5'}$ = 6.5 Hz, 1 H), 3.490 (m, 1 H), 3.593 (dd, J_{H5H4} = 9.5 Hz, $J_{H5H5'}$ = 11 Hz, 1 H), 3.893 (dd, $J_{H5'H5}$ = 11 Hz, $J_{H5'H4}$ = 6.5 Hz, 1 H), 3.977 (m, 1 H), 4.391 (dq, J_{H3Me-3} = 6.4 Hz, J_{H3H4} = 6.8 Hz, 1 H), 6.819 (t, J = 7.3 Hz, 1 H), 6.892 (t, J = 7.3 Hz, 1 H), 6.933 (d, J = 7.4 Hz, 2 H), 7.054 (d, J = 7.4 Hz, 2 H), 7.203 (t, J = 7.4 Hz, 2 H), 7.256 (t, J = 7.4 Hz, 2 H); decoupling, irradiation at δ 4.391 simplifies 1.463 to s, 3.145 to dd; 3.145 simplifies 3.593 to d, 3.893 to d, and 4.391 to q; ^{13}C NMR δ 20.34 (q), 20.63 (q), 21.31 (q), 21.54 (q), 21.59 (q), 46.12 (d), 48.12 (d), 52.84 (d), 54.48 (t), 63.44 (d), 113.56 (d), 114.44 (d), 119.43 (d), 120.105 (d), 128.79 (d), 129.01 (d), 150.59 (s), 151.738 (s), 168.54 (s); MS, m/e (relative intensity) 365 (80), 237 (100), 195 (8), 172 (14), 160 (50), 154 (13), 146 (29), 144 (31), 133 (24), 120 (20), 119 (25), 118 (29), 104 (18), 100 (85), 86 (29), 77 (54), 43 (45).

Anal. Calcd for $C_{23}H_{32}N_3O$: C, 75.57; H, 8.55; N, 11.50. Found: C, 75.25; H, 8.85; N, 11.56.

2:1 mixture of 48 and 49. Anal. Calcd for $C_{23}H_{31}N_3O$: C, 75.57; H, 8.55; N, 11.50. Found: C, 75.25: H, 8.85; N, 11.56.

***N*,*N*-Diisopropyl-1,2-diphenyl-3-methyl-2,3,4,5-tetrahydropyrazole-4-carboxamide (48).** Procedure C:[28] 10.3 mmol of *sec*-BuLi and 1.55 mL (10.3 mmol) of TMEDA in 190 mL of THF, 1.712 g (9.36 mmol) of **5** in 10 mL of THF, 2.55 g (14.0 mmol) of azobenzene in 25 mL of THF. After warming, the solution was stirred for 2 h. The crude product was separated by MPLC with 2% EtOAc/hexanes to afford 2.843 g (83%) of a mixture of **48**, **49** and **16**. Further separation by MPLC with 1% EtOAc/hexanes and then recrystallization 3 times from EtOAc/pentane gave 524 mg (22%) of **48**: mp 119–122 °C, mmp 119–122 °C.

Anal. Calcd for $C_{22}H_{31}N_3O$: C, 75.57; H, 8.55; N, 11.50. Found: C, 75.87; H, 8.78; N, 11.38.

1-(α-Hydroxybenzyl)-*N*,*N*,*N*′,*N*′-tetraisopropyl-2,3,4-trimethyl-1,4-cyclopentanedicarboxamide (50). Procedure C: 2.73 mmol of *sec*-BuLi and 411 μL (2.73 mmol) of TMEDA in 150 mL of THF, 1.00 g (5.46 mmol) of **5** in 10 mL of THF, 277 μL (2.73 mmol) of benzaldehyde. After being warmed and stirred for 5 h, benzaldehyde was added. Ethyl acetate was used in place of diethyl ether to extract the organics and the precipitate that formed upon concentration of the organic layer was triturated with cold diethyl ether to afford 821 mg (65%) of **50**: mp 234–235 °C dec; ^{1}H NMR δ 0.348 (d, J = 6.4 Hz, 3 H), 0.922 (d, J = 7.3 Hz, 3 H, Me-3), 0.989 (d, J = 6.5 Hz, 3 H), 1.040 (d, J = 7 Hz, 3 H, Me-2), 1.239 (br d, 6 H), 1.294 (s, 3 H, Me-4), 1.352 (d, J = 6.5 Hz, 3 H), 1.438 (d, J = 6.5 Hz, 3 H), 1.456 (d, J = 6.5 Hz, 3 H), 1.558 (d, J = 6.5 Hz, 3 H), 2.021 (d, $J_{H5H5'}$ = 13 Hz, 1 H), 2.595 (d, $J_{H5'H5}$ = 13 Hz, 1 H), 3.010 (dq, J_{H3Me-3} = 7.3 Hz, J_{H3H2} = 6.2 Hz, 1 H), 3.159 (m, J = 6.5 Hz, 2 H), 3.285 (dq, J_{H2Me-2} = 7 Hz, J_{H2H3} = 6.2 Hz, 1 H), 3.399 (m, 1 H), 4.124 (m, 1 H), 4.567 (d, J = 9.1 Hz, 1 H, benzyl), 5.691 (d, J = 9.1 Hz, 1 H, exchanges in D_2O), 7.210 (t, J = 7.2 Hz, 1 H), 7.269 (t, J = 7.2 Hz, 2 H), 7.328 (d, J = 7.2 Hz, 2 H); decoupling, irradiation at δ 0.922 simplifies 3.010 to d; 1.040 simplifies 3.285 to d; 3.010 simplifies 0.922 to s, 3.285 to q; 2.595 decouples 2.021 to s; 4.567 decouples 5.691 to s; ^{13}C NMR δ 12.05 (q), 12.17 (q), 19.43 (q), 19.68 (q), 20.32 (q), 20.57 (q), 20.71 (q), 20.81 (q), 21.05 (q), 21.85 (q), 24.72 (q), 37.30 (d), 42.05 (t), 46.26 (d), 46.72 (d), 47.67 (d), 48.15 (d), 48.63 (d), 49.95 (s), 63.77 (s), 75.01 (d), 127.50 (d), 127.84 (d), 128.29 (d), 142.51 (s), 175.50 (s), 176.31 (s); IR (Nujol) 3360, 2930, 1594, 1460, 1370, 1320, 1295, 1135, 1055, 1030, 757, 701 cm^{-1}.

Anal. Calcd for $C_{29}H_{48}N_2O_3$: C, 73.68; H, 10.24; N, 5.93. Found: C, 73.77; H, 10.45; N, 5.97.

A sample of 20 mg of **50** was heated at 250 °C as a melt for 5 min, and a gas, which smelled like benzaldehyde, was evolved. The remaining oil was cooled and dissolved in $CDCl_3$ and the ^{1}H NMR and ^{13}C NMR spectra were recorded. For **38** in the oil: ^{13}C NMR δ 11.2, 11.9, 20.3, 20.8, 21.0, 21.2, 21.5, 23.1, 39.3, 39.9, 44.1, 45.4, 46.0, 47.8, 48.1, 50.0, 171.8, 177.1.

For benzaldehyde: ^{13}C NMR δ 129.0, 129.8, 134.1, 136.9, 192.6. VPC comparison of the oil with **38** using a SE 52/54 FSOT capillary column with temperature programming from 60 °C (2.5 min) to 250 °C at 10°/min showed that the high boiling component in the oil had a retention time (t_R 12.95 min) identical with authentic **38**.

2-(3′-Butenyl)-*N*,*N*-diisopropyl-*N*′-phenyl-*N*′,3,3-trimethyl-1,4-cyclopentanedicarboxamide (55), 2-(3′-Butenyl)-*N*,*N*-diisopropyl-*N*′-phenyl-*N*′,4,4-trimethyl-1,3-cyclopentanedicarboxamide (56), and *N*,*N*-Diisopropyl-10-methyl-8-oxoundeca-1,5,9-triene-6-carboxamide (viii). Procedure C: 7.08 mmol of *sec*-BuLi and 1.07 mL (7.08 mmol) of TMEDA in 150 mL of THF, 1.507 g (6.75 mmol) of **54** in 15 mL of THF, 1.34 g (7.08 mmol) of **27** in 15 mL of THF. After being warmed, the solution was stirred for 12 h. Separation of the crude oil by MPLC with 15% EtOAc/hexanes gave 271 mg (18%) of **54**, 269 mg (13%) of viii, 321 mg (12%) of **56**, and 768 mg (28%) of **55**.

56: bp$^{0.2}$ 180–210 °C; ^{1}H NMR δ 0.725 (s, 3 H, Me-4), 1.073 (s, 3 H, Me-4), 1.138 (d, J = 6.9 Hz, 3 H), 1.157 (d, J = 7.0 Hz, 3 H), 1.346 (br d, 6 H), 1.248 (m, 1 H, H-1′), 1.466 (m, $J_{H1'H1'}$ = 12 Hz, J's = 6 Hz, 1 H), 1.552 (dd, J_{H5H5} = 12 Hz, J_{H5H1} = 9.2 Hz, 1 H), 1.579 (dd, J_{H5H5} = 12 Hz, J_{H5H1} = 10.6 Hz, 1 H), 1.937 (m, 1 H, H-2′), 2.011 (m, 1 H, H-2′), 2.321 (d, J_{H3H2} = 1-.4 Hz, 1 H), 2.400 (ddd, J_{H1H5} = 9.2 Hz, J_{H1H5} = 10.6 Hz, J_{H1H2} = 9 Hz, 1 H), 3.231 (m, J_{H2H1} = 9 Hz, J_{H2H3} = 10.4 Hz, $J_{H2H1'}$ = 6 Hz, $J_{H2H1'}$ = 6 Hz, 1 H), 3.291 (s, 3 H), 3.451 (m, 1 H), 3.903 (m, 1 H), 4.921 (d, J = 10.2 Hz, 1 H), 3.291 (s, 3 H), 3.451 (m, 1 H), 5.820 (ddt, J = 17 Hz, 10.2 Hz, 6.5 Hz, 1 H), 7.152 (d, J = 7.2 Hz, 2 H), 7.330 (t, J = 7.2 Hz, 1 H), 7.419 (t, J = 7.2 Hz, 2 H); decoupling, irradiation at δ 5.820 simplifies 4.962 to s, 4.921 to s, 2.011 and 1.937; 1.937 simplifies 5.820 to ddd, 1.456, 1.248, and 2.011; 2.011 simplifies 5.820 to dd, 1.466, 1.248, and 1.937; 1.248 and 1.466 simplifies 3.231 to ddd, 1.937 and 2.011; at 3.231 simplifies 1.466, 1.248, 2.321 to s, and 2.400 to dd; 2.400 simplifies 3.231, 1.552 to d, and 1.579 to d; ^{13}C NMR δ 20.95 (q), 21.24 (q), 21.54 (q), 26.58 (q), 30.68 (q), 33.27 (t), 35.22 (t), 38.09 (q), 42.63 (s), 46.44 (d), 47.61 (d), 48.03 (t), 48.98 (d), 57.71 (d), 114.55 (t), 128.70 (d), 129.58 (d), 130.68 (d), 140.51 (d), 145.89 (s), 174.28 (s), 174.65 (s); MS, m/e (relative intensity) 412 (1), 371 (5), 312 (17), 306 (100), 134 (25), 107 (16), 106 (14), 95 (10), 86 (31), 77 (11), 69 (12), 55 (16), 43 (69), 41 (21); IR (thin film) 3020, 2940, 1645, 1500, 1445, 1375, 1330, 1270, 1220, 1115, 1050, 1000, 912, 773, 700 cm^{-1}.

Anal. Calcd for $C_{26}H_{40}N_2O_2$: C, 75.68; H, 9.77; N, 6.79. Found: C, 75.38; H, 9.96; N, 6.46.

55: bp[1.8] 220–240 °C; ^{1}H NMR (3:2 $CDCl_3$/benzene-d_6) δ 0.520 (s, 3 H, Me-3), 0.971 (d, J = 6.7 Hz, 3 H), 1.020 (d, J = 6.7 Hz, 3 H), 1.065 (m, 2 H, H-1′), 1.124 (s, 3 H, Me-3), 1.35 (unresolved m, 6 H), 1.794 (ddd, J_{H5H1} = 8 Hz, J_{H5H4} = 8 Hz, J_{H5H5} = 12 Hz, 1 H), 1.964 (m, 1 H, H2′), 2.064 (m, 1 H, H2′), 2.267 (ddd, J_{H5H5} = 12 Hz, J_{H5H1} = 10 Hz, J_{H5H4} = 8 Hz), 2.374 (ddd, J_{H1H2} = 10 Hz, J_{H1H5} = 8 Hz, J_{H1H5} = 10 Hz, 1 H), 2.511 (ddd, J_{H2H1} = 10 Hz, $J_{H2H1'}$ = 9 Hz, $J_{H2H1'}$ = 5 Hz, 1 H), 2.642 (dd, J_{H4H5} = 8 Hz, J_{H4H5} = 8 Hz, 1 H), 3.170 (s, 3 H), 3.24 (br m, 1 H), 3.828 (m, J = 6.7 Hz, 1 H), 4.883 (d, J = 10.2 Hz, 1 H), 4.947 (d, J = 17.1 Hz, 1 H), 5.774 (ddt, J = 10.2 Hz, 17.1 Hz, 6.6 Hz, 1 H), 6.969 (d, J = 7.4 Hz, 2 H), 7.118 (t, J = 7.4 Hz, 1 H), 7.204 (t, J = 7.4 Hz, 2 H); decoupling, irradiation at δ 5.774 simplifies 4.947 to s, 4.883 to s, 2.064 and 1.964; 2.064 or 1.964 simplifies 1.065, and 5.774 to ddd; 2.511 simplifies 1.065, and 2.374 to dd; 2.374 simplifies 2.511 to dd, 2.267 to dd, and 1.794 to dd; 2.642 simplifies 2.267 to dd, and 1.794 to dd; 1.794 simplifies 2.642 to d, 2.374 to dd, 2.267 to dd; ^{13}C NMR (nitromethane-d_3) δ 20.89 (q), 21.69 (q), 21.79 (q), 21.85 (q), 25.60 (q), 25.78 (q), 30.30 (t), 33.76 (t), 34.44 (t), 37.81 (d), 45.23 (s), 46.49 (d), 48.42 (d), 48.87 (br d), 51.88 (d), 52.29 (d), 114.38 (t), 128.57 (d), 129.01 (d), 130.76 (d), 140.92 (d), 146.15 (s), 174.75 (s), 175.68 (s); MS, m/e (relative intensity) 412 (3), 371 (7), 312 (26), 306 (100), 134 (41), 109 (11), 107 (29), 106 (25), 95 (20), 93 (12), 86 (28), 81 (12), 77 (18), 67 (13), 55 (20), 43 (99), 41 (29): IR (thin film) 3060, 2930, 1645, 1590, 1490, 1440, 1390, 1320, 1260, 1215, 1120, 1045, 1000, 913, 778, 703 cm^{-1}.

Anal. Calcd for $C_{26}H_{40}N_2O_2$: C, 75.68; H, 9.77; N, 6.79. Found: C, 75.41; H, 9.51; N, 6.82.

viii: bp$^{0.3}$ 140–160 °C; ^{1}H NMR δ 1.28 (br, 12 H), 1.878 (s, 3 H), 2.120 (s, 3 H), 2.173 (m, 4 H), 3.471 (s, 2 H), 3.5 (br m, 2 H), 4.982 (d, J = 11 Hz, 1 H), 5.028 (d, J = 17.4 Hz, 1 H), 5.593 (t, J = 6.6 Hz, 1 H), 5.794 (ddt, J = 11 Hz, 17 Hz, 6.6 Hz, 1 H), 6.133 (s, 1 H); ^{13}C NMR (nitromethane-d_3) δ 20.68 (q), 27.27 (t), 27.65 (q), 33.08 (t), 44.31 (t), 47.8 (br d), 115.26 (t), 123.56 (d), 130.65 (d), 131.91 (s), 137.71 (d), 155.67 (s), 172.14 (s), 197.19 (s); MS, m/e (relative intensity) 305 (8), 272 (6), 250 (4), 220 (31), 208 (27), 205 (29), 182 (17), 180 (27), 168 (19), 100 (12), 83 (100), 58 (12); IR (thin film) 3060, 2940, 1695, 1630, 1440, 1370, 1340, 1215, 1160, 1140, 1120, 1050, 1000, 920, 980, 775 cm^{-1}.

3,5-Dimethyl-2-methylene-*N*,*N*,*N*′,*N*′-tetraisopropylhexanediamide (57, 58) and *N*,*N*-Diisopropyl-5-(diisopropylcarbamoyl)-2-methyl-5-heptenamide (34). Procedure A: 8.02 mmol of *sec*-BuLi and 1.21 mL (8.02 mmol) of TMEDA in 160 mL of THF, 1.337 g (7.29 mmol) of **5** in 20 mL of THF; 1.358 g (8.01 mmol) of **25** in 20 mL of THF. After addition of **25**, the solution was stirred for 1 h. The crude oil was distilled, and the higher boiling fraction was separated by MPLC with 5% EtOAc/hexanes to give 437 mg (17%) of **57**, 926 mg (36%) of **58**, and 377 mg of **34**.

57: bp$^{0.3}$ 130–145 °C; ^{1}H NMR δ 1.053 (d, J = 7 Hz, 3 H), 1.072 (d, J = 7 Hz, 3 H), 1.14 (unresolved m, 6 H), 1.169 (d, J = 6.8 Hz, 3 H), 1.187 (d, J = 6.8 Hz, 3 H), 1.394 (d, J = 6.3 Hz, 6 H), 1.44 (unresolved m, 6 H), 1.586 (ddd, J = 4 Hz, 8 Hz, 13 Hz, 1 H), 1.806 (ddd, J = 7 Hz, 12 Hz, 13 Hz, 1 H), 2.517 (ddq, J = 8 Hz, 7 Hz, 7 Hz, 1 H), 2.834 (ddq, J = 4 Hz, 12 Hz, 7 Hz, 1 H), 3.3 (br m, 1 H), 3.39 (m, 1 H), 4.12 (m, 1 H), 4.22 (m, 1 H), 4.894 (s, 1 H), 4.944 (s, 1 H); ^{13}C NMR δ 18.63 (q), 19.40 (1), 20.61 (q), 20.73 (q), 20.98 (q), 21.27 (q), 34.835 (d), 37.53 (d), 39.36 (t), 45.44 (d), 45.80 (d), 47.88 (d), 50.14 (d), 110.93 (t), 150.66 (s), 171.00 (s), 175.26 (s); MS, m/e (relative intensity) 352 (11), 309 (2), 252 (39), 224 (5), 196 (25), 183 (64), 170 (47), 168 (42), 157 (15), 140 (9), 128 (15), 114 (28), 100 (100), 86 (17), 83 (11); IR (thin film) 2930, 1635, 1630, 1435, 1370, 1330, 1260, 1215, 1155, 1135, 1045, 910 cm^{-1}.

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.43; H, 11.59; N, 7.61.

58: mp 59–60 °C (from hexanes); ^{1}H NMR δ 1.083 (d, J = 6.6 Hz, 3 H), 1.087 (d, J = 6.7 Hz, 3 H), 1.16 (unresolved m, 6 H), 1.188 (d, J = 6 Hz, 6 H), 1.378 (d, J = 6 Hz, 6 H), 1.44 (unresolved

m, 7 H), 2.004 (ddd, J = 13 Hz, 7 Hz, 7 Hz, 1 H), 2.452 (ddq, J = 7 Hz, 7 Hz, 6.6 Hz, 1 H), 2.821 (ddq, J's = 7 Hz, 1 H), 3.40 (m, 2 H), 4.18 (m, 2 H), 4.972 (s, 1 H), 5.015 (s, 1 H); decoupling, irradiation at δ 2.821 decouples 1.087 to s, 2.004 to dd; 2.455 decouples 1.083 to s, 2.004 to dd; ^{13}C NMR δ 18.2 (q), 19.8 (q), 20.7 (q), 21.2 (q), 34.1 (d), 35.5 (d), 39.6 (t), 45.4 (br d), 45.6 (d), 47.9 (d), 50.2 (br d), 110.4 (t), 151.6 (s), 171.5 (s), 175.4 (s); MS, m/e (relative intensity) 352 (8), 309 (2), 252 (39), 224 (6), 196 (21), 183 (47), 170 (47), 168 (38), 157 (13), 150 (7), 140 (8), 128 (19), 114 (33), 100 (100), 86 (32), 43 (8); IR (KBr) 2960, 1635, 1625, 1440, 1370, 1340, 1210, 1140, 1040, 909 cm^{-1}.

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.48; H, 11.42; N, 7.70.

34: bp$^{0.1}$ 110–135 °C; ^{1}H NMR (benzene-d_6) δ 0.824 (d, J = 6.7 Hz, 3 H), 0.886 (d, J = 6.6 Hz, 3 H), 1.005 (d, J = 6.8 Hz, 3 H), 1.2 (unresolved m, 12 H), 1.462 (d, J = 7 Hz, 3 H), 1.483 (d, J = 7 Hz, 3 H), 1.589 (d, J = 6.8 Hz, 3 H), 1.702 (m, 1 H), 2.120 (ddd, J = 13 Hz, 7 Hz, 7 Hz, 1 H), 2.383 (t, J = 7 Hz, 2 H), 2.557 (ddq, J = 6.8 Hz, 7 Hz, 7 Hz, 1 H), 3.12 (m, 1 H), 3.5 (br m, 2 H), 3.755 (m, 1 H), 5.415 (q, J = 6.8 Hz, 1 H).

Anal. Calcd for $C_{21}H_{40}N_2O_2$: C, 71.54; H, 11.44; N, 7.95. Found: C, 71.38; H, 11.69; N, 8.04.

3,5-Dimethyl-2-methylene-*N*,*N*,*N*′,*N*′-tetraisopropylhexanediamide-*5*-*d* (59, 60) and *N*,*N*-Diisopropyl-5-(diisopropylcarbamoyl)-2-methyl-5-heptenamide-*2*-*d* (34-*d*). Procedure A: 6.00 mmol of *sec*-BuLi and 906 μL (6.00 mmol) of TMEDA in 120 mL of THF, 1.00 g (5.46 mmol) of **5** in 10 mL of THF, 923 mg (6.00 mmol) of **25** in 10 mL of THF. After addition of **25**, the solution was stirred for 1 h and then treated with the deuterium oxide solution. Isolation according to the procedure for **57** and **58** gave 355 mg (18%) of **59**, 618 mg (32%) of **60**, and 172 mg (9%) of **34**-*d*.

59: bp$^{0.5}$ 150–165 °C; ^{1}H NMR δ 1.053 (d, J = 6.8 Hz, 3 H), 1.064 (s, 3 H), 1.136 (br m, 6 H), 1.169 (d, J = 6.8 Hz, 3 H), 1.188 (d, J = 7 Hz, 3 H), 1.392 (br d, 6 H), 1.44 (br m, 6 H), 1.582 (dd, J = 13 Hz, 8.6 Hz, 1 H), 1.807 (dd, J = 13 Hz, 6.3 Hz, 1 H), 2.514 (ddq, J = 8.6 Hz, 6.8 Hz, 6.3 Hz, 1 H), 3.39 (br m, 2 H), 4.105 (m, 1 H), 4.218 (m, 1 H), 4.890 (s, 1 H), 4.942 (s, 1 H); decoupling, irradiation at δ 1.053 decouples 2.514; 2.514 decouples 1.053, 1.582, and 1.807; ^{13}C NMR δ 18.5 (q), 19.4 (q), 20.6 (q), 20.7 (q), 21.0 (q), 21.3 (q), 34.5 (trio), 37.6 (d), 39.8 (t), 45.4 (br d), 45.6 (d), 47.8 (d), 50.2 (br d), 111.0 (t), 150.5 (s), 171.0 (s), 175.3 (s); MS (EI, 10 eV), m/e (relative intensity) 353 (9.28), 153 (36.85), 196 (25.69), 183 (51.11), 171 (38.59), 168 (23.11), 158 (15.73), 128 (12.95), 115 (32.67), 100 (100), 86 (31.53), 43 (11.76); IR (thin film) 2930, 1635, 1630, 1435, 1370, 1330, 1215, 1155, 1135, 1045, 910 cm^{-1}.

60: bp$^{0.5}$ 150–155 °C; mp 58.5–60.0 °C, mmp with **58**, 58–60 °C; ^{1}H NMR δ 1.083 (d, J = 6.6 Hz, 3 H), 1.087 (s, 3 H), 1.16 (unresolved m, 6 H), 1.189 (d, J = 6 Hz, 6 H), 1.378 (d, J = 6 Hz, 6 H), 1.44 (br, 7 H), 2.004 (dd, J = 7.2 Hz, 13.6 Hz, 1 H), 2.455 (ddq, J = 7.2 Hz, 7 Hz, 6.6 Hz, 1 H), 3.40 (br m, 2 H), 4.2 (br m, 2 H), 4.972 (s, 1 H), 5.015 (s, 1 H); decoupling, irradiation at δ 1.083 decouples 2.455; 2.455 decouples 2.004 and 1.083: ^{13}C NMR δ 18.1 (q), 19.7 (q), 20.7 (q), 20.8 (q), 21.2 (q), 21.3 (q), 33.7 (trio), 35.5 (d), 39.6 (t), 45.4 (br d), 45.6 (d), 47.9 (d), 50.2 (br d), 110.4 (t), 151.6 (s), 171.5 (s), 175.4 (s); MS, m/e (relative intensity) 353 (8.73), 253 (38.08), 196 (19.18), 183 (37.61), 171 (28.18), 168 (19.38), 151 (11.54), 128 (14.66), 115 (28.83), 100 (100), 96 (12.47), 86 (47.34), 58 (14.51), 55 (14.93), 43 (86.49); IR (melt) 2920, 1630, 1625, 1440, 1370, 1330, 1220, 1155, 1135, 1045, 975, 910 cm^{-1}.

34-*d*: bp$^{0.5}$ 150–160 °C; ^{1}H NMR δ 1.077 (s, 3 H), 1.15–1.40 (unresolved m, 12 H), 1.196 (d, J = 7 Hz, 3 H), 1.212 (d, J = 7 Hz, 3 H), 1.380 (d, J = 7 Hz, 6 H), 1.454 (m, 1 H), 1.662 (d, J = 6.9 Hz, 3 H), 1.781 (m, 1 H), 2.228 (m, 2 H), 3.45 (br m, 2 H), 4.08 (m, 2 H), 5.446 (q, J = 6.9 Hz, 1 H); ^{13}C NMR δ 12.94 (q), 18.02 (q), 20.70 (q), 20.84 (q), 21.23 (q), 21.32 (q), 26.26 (t), 32.43 (t), 36.49 (trio), 45.70 (d), 48.01 (br d), 122.41 (d), 138.62 (s), 172.73 (s), 175.09 (s); IR (thin film) 2960, 1716, 1624, 1440, 1370, 1330, 1210, 1140, 1040 cm^{-1}.

2,4-Dimethyl-*N*,*N*,*N*′,*N*′-tetraisopropyl-1,4-cyclopentanedicarboxamide-*1*-*d* (61, 62). Procedure C: 12.1 mmol of *sec*-BuLi and 1.83 mL (12.1 mmol) of TMEDA in 400 mL of THF, 1.84 g (10.1 mmol) of **5** in 25 mL of THF, 1.70 g (12.01 mmol) of **25** in 25 mL of THF. After being warmed and stirred for 3 h, the deuterium oxide solution was added. The crude oil was purified as described for **32**–**34** to give 1.28 g (18%) of **62**, 350 mg (5%) of **61**, and 278 mg (4%) of **34**-*d*.

62: mp 108–110 °C (from EtOAc/hexanes), mmp with **33**, 108–111 °C; ^{1}H NMR δ 0.932 (d, J = 7 Hz, 3 H, Me-2), 1.142 (d, J = 6.7 Hz, 3 H), 1.182 (d, J = 6.7 Hz, 3 H), 1.186 (d, J = 6.7 Hz, 3 H), 1.200 (d, J = 6.8 Hz, 3 H), 1.279 (dd, J = 7 Hz, 13 Hz, 1 H, H-3), 1.377 (d, J = 7 Hz, 6 H), 1.390 (s, 3 H), 1.398 (d, J = 7 Hz, 6 H), 2.088 (d, J = 13 Hz, 1 H, H-5), 2.310 (ddq, J = 7 Hz, 7 Hz, 7 Hz, 1 H, H-2), 2.345 (d, J = 13 Hz, 1 H, H-5′), 2.574 (dd, J = 13 Hz, 7 Hz, 1 H, H-3′), 3.282 (qq, J = 6.8 Hz, 1 H), 3.43 (br m, 1 H), 4.01 (m, 1 H), 4.218 (qq, J = 6.7 Hz, 1 H); ^{13}C NMR δ 16.91 (q), 20.37 (q), 20.72 (q), 21.16 (q), 25.40 (q), 34.67 (d), 40.66 (t), 45.04 (trio), 45.33 (d), 46.06 (d), 47.21 (t), 47.54 (br d), 48.03 (d), 48.98 (s), 172.12 (s), 175.15 (s); MS, m/e (relative intensity) 353 (5), 310 (3), 253 (10), 225 (10), 128 (7), 100 (5), 96 (19), 86 (28), 43 (43); isotope ratio 352 (7.5), 353 (169), 354 (45), 355 (6.1), 97% d.

61: bp$^{0.2}$ 120–170 °C; ^{1}H NMR δ 0.971 (d, J = 6.4 Hz, 3 H, Me-2), 1.140 (dd, J = 8 Hz, 13 Hz, 1 H, H-3), 1.188 (d, J = 6.8 Hz, 6 H), 1.210 (d, J = 6.8 Hz, 3 H), 1.220 (d, J = 6.8 Hz, 3 H), 1.313 (s, 3 H), 1.35–1.42 (overlapping d's, 12 H), 1.765 (d, J = 12 Hz, 1 H, H-5), 2.355 (d, J = 12 Hz, 1 H, H-5′), 2.514 (m, J = 6.4 Hz, 8 Hz, 10 Hz, 1 H, H-1), 2.587 (dd, J = 10 Hz, 13 Hz, 1 H, H-3′), 3.273 (qq, J = 6.7 Hz, 1 H), 3.53 (br m, 1 H), 4.033 (m, 2 H); MS, m/e (relative intensity) 353 (4), 310 (2), 253 (74), 225 (63), 183 (13), 169 (7), 128 (17), 123 (10), 100 (100), 96 (35), 86 (59), 43 (80); isotope ratio 352 (9.8), 353 (160), 354 (54), 355 (9.2), 97% d.

34-*d*: bp$^{0.2}$ 130–180 °C; ^{1}H NMR δ 1.077 (s, 3 H), 1.196 (d, J = 6.4 Hz, 3 H), 1.217 (d, J = 6.4 Hz, 3 H), 1.3 (unresolved m, 12 H), 1.380 (d, J = 6.6 Hz, 6 H), 1.454 (m, 1 H), 1.663 (J = 6.8 Hz, 3 H), 1.788 (m, 1 H), 2.228 (br t, J = 7 Hz, 2 H), 3.45 (br m, 2 H), 4.065 (qq, J = 6.8 Hz, 1 H), 4.1 (br m, 1 H), 5.446 (q, J = 6.8 Hz, 1 H).

35, **33**, **61**, and **62** were analyzed by VPC using coinjection techniques and a SE 52/54 FSOT capillary column with programmed heating from 60 °C (2.5 min) to 250 °C at 10°/min. **33** and **62** had an identical retention time of 12.23 min and **32** and **61** had an identical retention time of 12.41 min.

5-(Diisopropylcarbamoyl)-*N*-phenyl-*N*,3,4-trimethyl-5-hexenamide (63). Procedure C: 7.2 mmol of *sec*-BuLi and 1.189 mL (7.88 mmol) of TMEDA in 160 mL of THF, 1.204 g (6.59 mmol) of **5** in 10 mL of THF, 1.38 g (7.88 mmol) of **26** in 10 mL of THF. After warming, the solution was stirred for 1 h. The crude oil was separated as described for **35** and **36** to give 680 mg (29%) of **35**, 228 mg (10%) of **63**, and 137 mg (6%) of **36**.

63: bp$^{0.5}$ 190–205 °C; ^{1}H NMR δ 0.80 (d, J = 6 Hz, 3 H), 0.91 (d, J = 6 Hz, 3 H), 1.21 (br d, 12 H), 1.65–1.45 (m, 4 H), 3.23 (s, 3 H), 3.8 (br m, 2 H), 4.89 (s, 1 H), 4.94 (s, 1 H), 7.05–7.5 (m, 5 H); ^{13}C NMR δ 14.94 (q), 18.36 (q), 20.71 (q), 33.20 (d), 37.00 (t), 37.40 (q), 41.96 (d), 45.59 (br d), 49.78 (br d), 11.85 (t), 127.49 (d), 127.59 (d), 129.68 (d), 144.29 (s), 149.70 (s), 171.74 (s), 172.64 (s); MS, m/e (relative intensity) 358 (10), 258 (30), 252 (100), 231 (15), 210 (35), 183 (20), 182 (35), 176 (16), 168 (35), 151 (18), 140 (12), 134 (39), 128 (14), 123 (27), 107 (77), 100 (69), 95 (17), 86 (60), 77 (28), 69 (21), 55 (31), 43 (85); IR (thin film) 2920, 1650, 1620, 1600, 1490, 1435, 1365, 1330, 1215, 1150, 1110, 1075, 1040, 912, 848, 778, 701 cm^{-1}.

Anal. Calcd for $C_{22}H_{34}N_2O_2$: C, 73.70; H, 9.56; N, 7.83. Found: C, 73.50; H, 9.47; N, 7.42.

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Registry No. **5**, 80997-47-3; **7**, 80997-49-5; **8**, 96759-51-2; **9**, 104642-91-3; **10**, 104642-92-4; **11**, 81011-47-4; **12**, 96759-54-5; **13**, 80997-53-1; **14**, 96759-55-6; **15**, 80997-51-9; **16**, 104642-93-5; **17**, 96759-52-3; **18**, 96759-53-4; **19**, 104642-94-6; **20**, 104642-95-7; **24**, 6273-94-5; **25**, 51745-62-1; **26**, 104642-97-9; **27**, 20886-47-9; **28**, 104642-98-0; **31**, 104642-99-1; **32**, 80997-70-2; **34**, 104643-00-7; **34-d**, 104643-27-8; **35**, 104643-01-8; **36**, 104713-93-1; **37**, 104643-02-9; **38**, 104713-94-2; **40** (isomer 1), 104643-03-0; **40** (isomer 2), 104643-04-1; **42**, 104643-05-2; **43**, 104643-06-3; **45**, 104643-07-4; **46**, 104643-08-5; **47**, 104643-09-6; **48** (isomer 1), 104643-10-9; **48** (isomer 2), 104643-11-0; **50**, 104643-12-1; **51**, 104643-13-2; **53**, 104643-14-3; **54**, 104643-15-4; **55**, 104643-16-5; **56**, 104663-58-3; **57** (isomer 1), 104643-17-6; **57** (isomer 2), 104643-18-7; **59** (isomer

1), 104643-19-8; **59** (isomer 2), 104643-20-1; **61**, 104643-21-2; **63**, 104643-22-3; **72**, 104643-29-0; vii, 104643-28-9; viii, 104643-26-7; ix, 104642-96-8; **x**, 104643-25-6; PhCHNPh, 538-51-2; deuterium oxide, 7789-20-0; 1-chloro-3-methyl-2-butene, 503-60-6; acetone, 67-64-1; benzophenone, 119-61-9; azobenzene, 103-33-3; 1-iodobutane, 542-69-8; chlorotrimethylsilane, 75-77-4; (*E*)-2-methyl-2,6-heptadienoic acid, 104643-23-4; (*E*)-2-methyl-2,6-heptadienoyl chloride, 104643-24-5; (*E*)-*N*-methyl-3,*N*-diphenylpropenamide, 33603-46-2; benzaldehyde, 100-52-7; aniline, 62-53-3; (*E,E*)-*N*-methyl-*N*-phenyl-2,4-hexadienamide, 61859-43-6; ethyl sorbate, 2396-84-1; sorbic acid, 110-44-1; sorbic acid chloride, 2614-88-2; *N*-methylaniline, 100-61-8; 3,3-dimethylacryloyl chloride, 3350-78-5; acryloyl chloride, 814-68-6; cinnamoyl chloride, 102-92-1; crotonyl chloride, 10487-71-5.

Supplementary Material Available: Experimental details for remaining compounds in this study (13 pages). Ordering information is given on any current masthead page.

Indolizines. 2. Preparation of 1- and 3-Indolizinols and Their Esters

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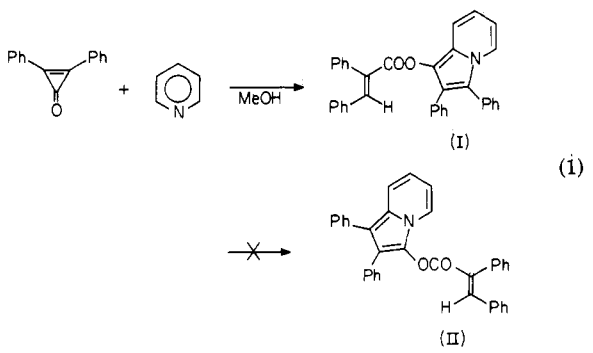
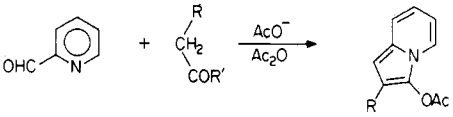
2,3-Diarylcyclopropenones react smoothly with pyridine and substituted pyridines in a variety of solvents to produce 1- and/or 3-indolizinols. The regioisomeric indolizines were characterized by X-ray crystallography of their acetate derivatives. The synthesis and spectroscopic properties of a number of indolizinols and their ester derivatives are described.

The preparation of 1-[(*cis*-2,3-diphenylacryl)oxy]-2,3-diphenylindolizine (I) from pyridine and 2,3-diphenylcyclopropenone (eq 1) was first reported by Breslow et al.[1]

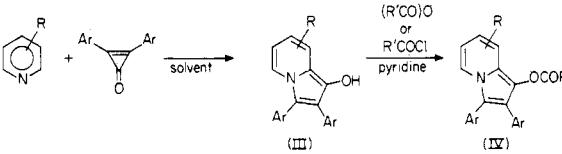


and elaborated on by Lown and Matsumoto.[2] The latter authors assigned the 3-oxy structure II, but we have now established the correct regiochemistry as I by X-ray crystallography[3] and have expanded the reaction to encompass a variety of substituted pyridines and cyclopropenones for the preparation of both 1- and 3-indolizinols. In the extensive indolizine literature, the few reported indolizinols are characterized as unstable intermediates that can be isolated only as esters or salts. Basic hydrolysis of ester I, for instance, furnished *cis*-diphenylacrylic acid but apparently destroyed the unstable indolizinol fragment.[1] In a series of papers, Pohjala[4-6] described the formation (via a Perkin reaction, eq 2) and reactions of some 3-(acyloxy)indolizines but not the isolation or characterization of any of the free indolizinols.



We report here facile, high-yield syntheses of a variety of 2,3-diaryl-1-hydroxyindolizines (III) and their esters (IV), a novel method of preparation of 1,2-diaryl-3-hydroxyindolizines V and their esters VI, and a comparison of NMR chemical shifts and coupling constants.

We have found that pyridines substituted with electron-withdrawing substituents react smoothly with a variety of diarylcyclopropenones to form the corresponding 1-indolizinols III in good yield (eq 3). With the 4-substituted pyridines, near-quantitative yields of the corresponding 7-substituted 1-indolizinols III were formed. The 3-substituted pyridines furnished good yields of ~50–50 mixtures of 6- and 8-substituted indolizinols III, which could be separated by crystallization and/or column chromatography. 2-Substituted pyridines were unreactive, even with prolonged heating. Although all indolizinols substituted with electron-withdrawing groups were reasonably stable in air, they slowly oxidized, forming radical species [as evidenced by a strong ESR signal (g = 2.003 65 ± 0.000 07, ΔH = 5.6 ± 0.2 G) from an aerated solution of 7-cyano-2,3-diphenyl-1-indolizinol (**32**, free base)].[7] Ad-



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