Applications of the β-Azidonation Reaction to Organic Synthesis. α,β-Enones, Conjugate Addition, and γ-Lactam Annulation

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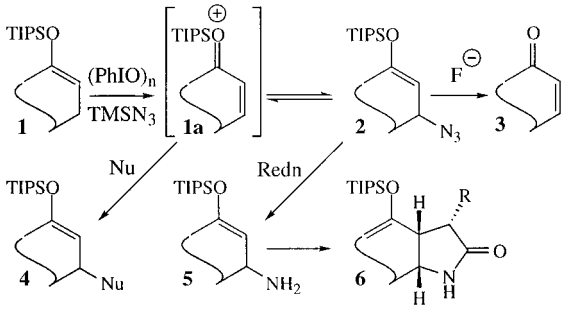
Abstract: The β-azido functionalization reaction provides a mechanistically different enone synthesis that involves treatment of **2** with fluoride anion to effect desilylation and concomitant β-elimination to give **3**. Table 1 lists a number of examples of the direct conversion of a TIPS enol ether into the corresponding α,β-enone via a β-azido TIPS enol ether. The β-azido group can be ionized with Me_3Al or Me_2AlCl and the intermediate enonium ion trapped by a variety of nucleophiles such as an allylstannane, electron-rich aromatics, TMS enol ethers, Et_2AlCN, Me_2AlCCR, Me_4AlLi, and vinylaluminum reagents to give the products listed in Table 2. The diastereoselectivity of the reaction of a 4-substituted enonium ion with indole shows an unusual increase of selectivity with increasing temperature. Reduction of the azide **2** provides access to β-amino TIPS enol ethers **5**, which, for example, can be converted into a cinnamide derivative and cyclized via a putative "ene" process into a γ-lactam.

Introduction

We recently reported the full details of the conversion of triisopropylsilyl (TIPS) enol ethers **1** into β-azido TIPS enol ethers **2** using the reagent combination of (PhIO)n/$TMSN_3$, Scheme 1.[1] The reaction appears to proceed via the enonium ion **1a**, which is trapped by azide ion to give **2**. Attempts to trap **1a** in situ, intermolecularly with nucleophiles other than azide were unsuccessful, and only **2** was formed. The adducts **2** can, in principle, be used as synthetic intermediates for a number of processes, and here we describe the conversion of **2** into α,β-unsaturated ketones **3**,[2] β-substituted TIPS enol ethers **4**,[3] and γ-lactams **6**[4] via β-amino TIPS enol ethers **5**.[5]

Scheme 1



α,β-Unsaturated Enones. The main methods for the synthesis of α,β-unsaturated ketones[6] from saturated ketones are (a) halogenation, followed by dehydro-halogenation,[7] (b) utilizing sulfur[8] or selenium[9] derivatives, (c) DDQ,[10] and (d) palladium(II) complexes.[11,12]

The β-azido functionalization methodology provides a mechanistically different enone synthesis that involves treatment of **2** with fluoride anion to effect desilylation and concomitant β-elimination to give **3**, Scheme 1. The intermediate β-azido TIPS enol ether **2** need not be isolated but can be directly converted by treatment with *n*-Bu_4NF (TBAF) into the α,β-unsaturated ketone **3**. The examples listed in Table 1 give yields for the two steps and refer to chromatographically purified material. The reaction is completely regiospecific (entries 4/5 and 6/7), and for entry 6 where there is the possibility of regioisomeric azides we found that **18** and **18a** were formed (ca. 6:1). A particularly interesting example is shown in entry 9. The β-azidonation reaction reintroduces the azide functionality which undergoes fluoride induced elimination to give the ketone−enone **24** (see also Table 2, entry 5). No existing methodology allows these manipulations without protection of the saturated carbonyl group. The overall conversion of a TIPS

(1) Magnus, P.; Lacour, J.; Evans, P. A.; Roe, M. B.; Hulme, C. *J. Am. Chem. Soc.* **1996**, *118*, 3406.
(2) Magnus, P.; Evans, P. A.; Lacour, J. *Tetrahedron Lett.* **1992**, *33*, 2933.
(3) Magnus, P.; Lacour, P. *J. Am. Chem. Soc.* **1992**, *114*, 3993.
(4) Magnus, P.; Rigollier, P.; Lacour, J.; Tobler, H. *J. Am. Chem. Soc.* **1993**, *115*, 12629.
(5) The synthesis (+)-pancratistatin using a β-aminoTIPS enol ether. Magnus, P.; Sebhat, I. K. *J. Am. Chem. Soc.* **1998**, *120*, 5341.
(6) For a review, see: Buckle, D. R.; Pinto, I. L. In Oxidation Adjacent to C=X Bonds by Dehydrogenation. *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 7.
(7) Slotter, P. L.; Hill, K. A. *J. Org. Chem.* **1973**, *38*, 2576. Ladjama, D.; Riehl, J.-J. *Synthesis* **1979**, 504. Jung, F.; Ladjama, D.; Riehl, J.-J. *Synthesis* **1979**, 507. Blanco, L.; Amice, P.; Conia, J.-M. *Synthesis* **1976**, 194. Ravid, U.; Ikan, R. *Synth. Commun.* **1975**, *5*, 137.
(8) Trost, B. M.; Saltzman, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.
(9) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434. Barton, D. H. R.; Motherwell, W. B.; Wozniak, J.; Zard, S. Z. *J. Chem. Soc., Perkin Trans. I* **1985**, 1865. Clive, D. L. J. *Tetrahedron* **1978,** *34*, 1049.
(10) Ryu, I.; Murai, S.; Hatayama, Y.; Sonoda, N. *Tetrahedron Lett.* **1978**, 3455. Fleming, I.; Paterson, I. *Synthesis* **1979**, 736.
(11) Kane, V. V. *Synth. Commun.* **1976**, *6*, 237. Ringold, H. J.; Turner, A. B. *Chem. Ind. (London)* **1962**, 211. Ito, Y.; Hirao, T.; Saegusa, T. *J. Org. Chem.* **1978**, *43*, 1011. Tsuji, J.; Minami, I. *Acc. Chem. Res.* **1987**, *20*, 140. Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1983**, *24*, 5635. Tsuji, J.; Minami, I.; Shimizu, I. Kataoka, H. *Chem. Lett.* **1984**, 1133. Shimizu, I.; Tsuji, J. *J. Am. Chem. Soc.* **1982**, *104*, 5844.
(12) For an example of a large scale Tsuji reaction see: Magnus, P.; Miknis, G. F.; Press: N. J.; Grandjean, D.; Taylor, G. M.; Harling, J. *J. Am. Chem. Soc.* **1997**, *119*, 6739.

10.1021/ja9829564 CCC: $15.00
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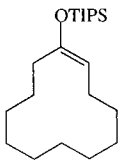
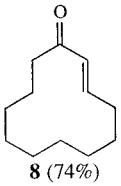
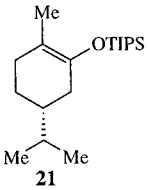
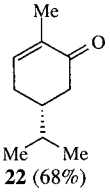
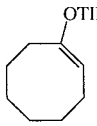
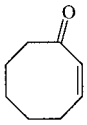
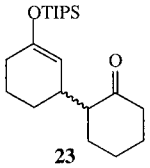
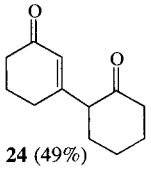
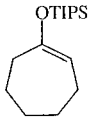
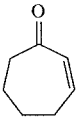
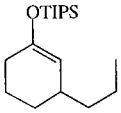
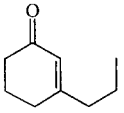
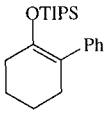
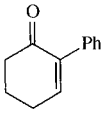
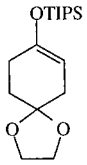
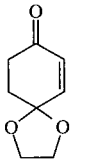
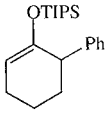
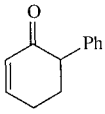
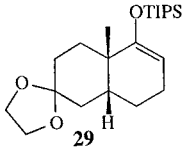
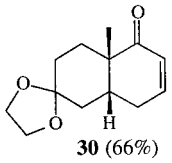
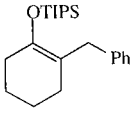
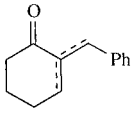
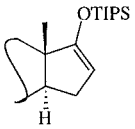
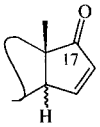
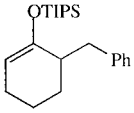
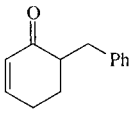
Table 1.

Entry	Substrate	Enone (%)	Entry	Substrate	Enone (%)
1[13]	 **7**	 **8** (74%)	**8**	 **21**	 **22** (68%)
2[14]	 **9**	 **10** (62%)	**9**	 **23**	 **24** (49%)
3	 **11**	 **12** (64%)	**10**	 **25**	 **26** (55%)
4[15]	 **13**	 **14** (60%)	**11**[16]	 **27**	 **28** (68%)
5[17]	 **15**	 **16** (68%)	**12**[18]	 **29**	 **30** (66%)
6[19]	 **17**	 **18/18a** (78%) 6:1 endo:exo	**13**[20]	 **31**	 **32** (75%)
7	 **19**	 **20** (73%)			

enol ether to an enone takes place very rapidly, and under mild reaction conditions. For example (entry 1), $TMSN_3$ was added to a mixture of **7** and PhIO in dichloromethane at 5 °C; after 5 min the solution was warmed to 25 °C and cooled to −5 °C, and TBAF/THF was added. The mixture was warmed to 25 °C and worked-up to give the enone **8** (74%). The conversion of **29** into **30** (entry 12) is noteworthy since conventional phenylselenation of the saturated ketone followed by oxidation and elimination gave **30** in an overall yield of 32%.[18] The example entry 13 (ring D of O-methyl estrone-17-TIPS enol ether) was complicated by the fact that β,γ-isomerization leads to a mixture of *cis*- and *trans*-ring D isomers.

In all cases it is important to use the TIPS enol ether derivative in this chemistry since less sterically encumbered silyl

(13) Leonard, N. J.; Owens, F. H. *J. Am. Chem. Soc.* **1958**, *80*, 6039. Wasserman, H. H.; Gosselink, F.; Keith, D. D.; Nadelson, J.; Sykes, R. J. *Tetrahedron* **1976**, *32*, 1863.

(14) Cope, A. C.; Kinter, M. R.; Keler, R. T. *J. Am. Chem. Soc.* **1954**, *76*, 2757. See also ref 9.

(15) Elad, D.; Ginsburg, D. *J. Chem. Soc.* **1953**, 2664. Bachmann, W. E.; Wick, L. B. *J. Am. Chem. Soc.* **1950**, *72*, 3388.

(16) Hung, S.-C.; Liao, C.-C. *J. Chin. Chem. Soc. (Taipei)* **1994**, *41 (2)*, 191.

(17) Wildman, W. C.; Wildman, R. B. *J. Org. Chem.* **1952**, *17*, 581. Marino, J. P.; Jaen, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165.

(18) Magnus, P.; Leapheart, T.; Walker, C. *J. Chem. Soc., Chem. Commun.* **1985**, 1185. Unpublished results, Leapheart, T., Ph. D thesis, Indiana University, Bloomington, 1983. Hayakawa, K.; Ohsuki, S.; Kanematsu, K. *Tetrahedron Lett.* **1986**, *27*, 4205. Yeo, S.-K.; Hatae, N.; Seki, M.; Kanematsu, K. *Tetrahedron* **1995**, *51*, 3499.

Table 2.

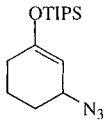
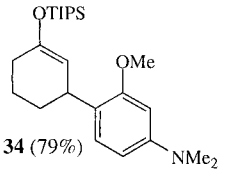
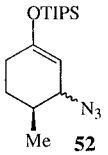
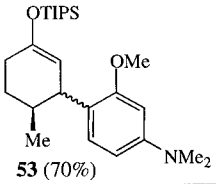
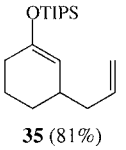
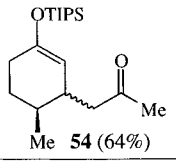
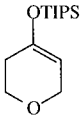
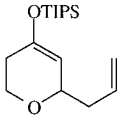
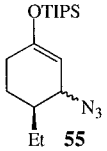
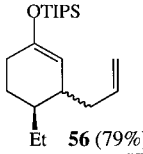
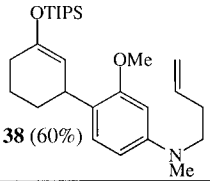
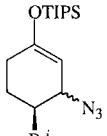
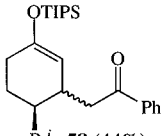
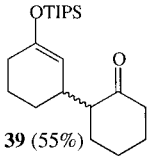
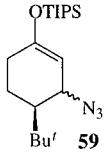
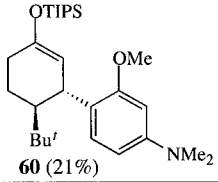
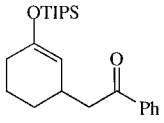
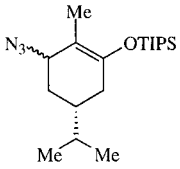
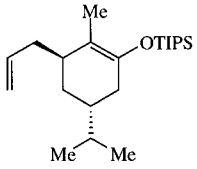
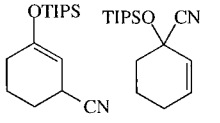
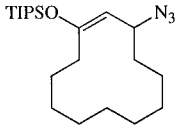
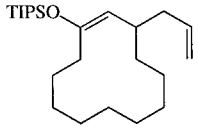
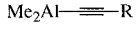
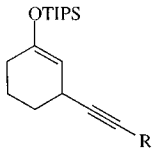
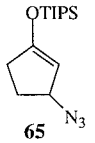
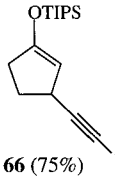
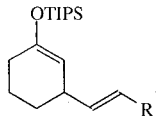
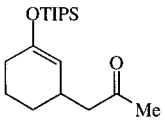
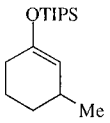
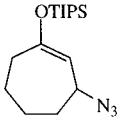
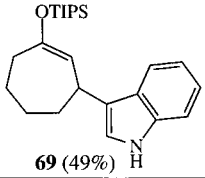
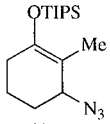
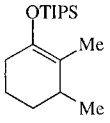
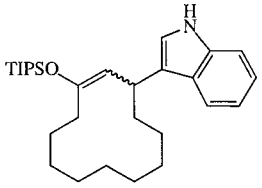
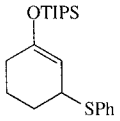
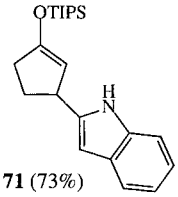
Entry	Substrate	Enone (%)	Entry	Substrate	Enone (%)
1	 **33**	 **34** (79%)	13	 **52**	 **53** (70%)
2	**33**	 **35** (81%)	14	**52**	 **54** (64%)
3	 **36**	 **37** (62%)	15	 **55**	 **56** (79%)
4	**34**	 **38** (60%)	16	 **57**	 **58** (44%)
5	**33**	 **39** (55%)	17	 **59**	 **60** (21%)
6	**33**	 **40** (68%)	18	 **61**	 **62** (56%)
7	**33**	 **41** (60%) **42** (23%)	19	 **63**	 **64** (59%)
8	**33** 	 **43** (R = Ph) (98%) **44** (R = TMS) (70%) **45** (R = *n*-Bu) (84%)	20	 **65**	 **66** (75%)

Table 2. (Continued)

Entry	Substrate	Enone (%)	Entry	Substrate	Enone (%)
9	**33**	 **46** (R = Ph) (46%) **47** (R = *n*-Bu) (45%)	**21**	**65**	 **67** (44%)
10	**33**	 **48** (44%)	**22**	 **68**	 **69** (49%)
11	 **49**	 **50** (45%)	**23**	**63**	 **70** (81%)
12	**33**	 **51** (97%)	**24**	**65**	 **71** (73%)

enol ethers (TMS and TBDMS) are desilylated in the β-azidonation step to give the unfunctionalized saturated ketone as the major product.

Conjugate Additions

The conjugate addition of a stabilized carbanion to an α,β-unsaturated ketone was first reported by Michael,[21] and now forms one of the most widely used reactions for the formation of carbon−carbon bonds.[22−25]

We expected that the β-azido TIPS enol ether **2** would require a Lewis acid to ionize it to the enonium ion **1a**, which in the presence of a nucleophile would be converted into **4**, Scheme 1. It should be noted that conjugate addition of Me_2CuLi to cyclohexenone followed by attempted trapping of the resulting enolate with either TIPSCl or TIPSOTf gave no more than 5% of the product **48** (Table 2, entry 10). Consequently, the products in Table 2 are not accessible via conventional conjugate addition/trapping methodology.

The β-azido TIPS enol ethers did not react with Grignard reagents, with or without copper(I) catalysis, cuprates, or organozirconium derivatives. Several reactions were performed with a range of Lewis acids, and eventually the following features emerged. The Lewis basic solvents such as tetrahydrofuran or ether completely inhibited the reaction. Hexane and dichloromethane were the two solvents most commonly used. Most reactions proceeded at 25 °C as well as at low temperatures. However, in some cases the yields were improved by an increase in temperature. Two equivalents of Me_2AlCl were shown to be necessary to obtain the best yields. Generally, at least 2 equiv of the nucleophile are also utilized during these reactions. Lewis acid assisted conjugate addition was carried out by two different experimental procedures: (1) The nucleophile was mixed with the β-azido silyl enol ether in the reaction mixture. Then, the Lewis acid was added at the required temperature. This procedure is designated *direct addition*. (2) The Lewis acid was premixed with the nucleophile, and then, the β-azido silyl enol ether was added in solution at the required temperature. This procedure is designated *reverse addition*.

Treatment of a mixture of **33** and 3-*N*,*N*-dimethylaminoanisole in hexane with Me_2AlCl (2 equiv) for 10 min at 25 °C gave **34** (79%). Employing $NaBPh_4/CH_2Cl_2$ at reflux as the Lewis acid gave **34** (46%). Sakurai[26] and Mobilio[27] have reported syntheses of ketones substituted at the β-position by an allyl group utilizing $(Et_2Al)_2SO_4$ and titanium tetrachloride as Lewis acids. Treatment of **33** with allyltri-*n*-butylstannane

(19) Auwers, K von.; Treppmann, W. *Chem. Ber*. **1915**, *48*, 1207. Evans, P. A.; Longmire, J. M.; Modi, D. P. *Tetrahedron Lett*. **1995**, *36*, 3985. Vorläender, D.; Kunze, K. *Chem. Ber*. **1926**, *59*, 2078. House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem*. **1971**, *36*, 2361.

(20) Cantrall, E. W.; Littell, R.; Bernstein, S. *J. Org. Chem*. **1964**, *29*, 64. Johnson, W. S.; Johns, W. F. *J. Am. Chem. Soc*. **1957**, *79*, 2005.

(21) Michael, A. *J. Prakt. Chem*. **1887**, *35*, 349. Michael, A. *Am. Chem. J*. **1887**, *9*, 115. Michael, A. *J. Prakt. Chem*. **1894**, *49*, 20.

(22) Kharash, M. S.; Tawney, P. O. *J. Am. Chem. Soc*. **1941**, *63*, 2308.

(23) House, H. O.; Respess, W. L.; Whitesides, G. M. *J. Org. Chem*. **1966**, *31*, 3128.

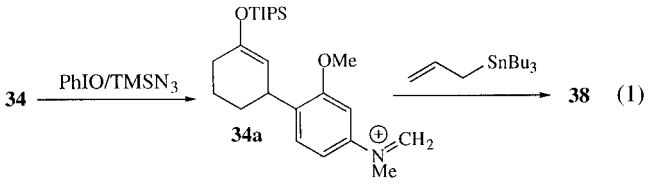
(24) Gilman, H.; Kirby, R. *J. Am. Chem. Soc*. **1941**, *63*, 2046.

(25) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc*. **1977**, *99*, 8068. Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc*. **1978**, *100*, 3240.

(26) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc*. **1977**, *99*, 1673. Hosomi, A.; Iguchi, H.; Endo, M.; Sakurai, H. *Chem. Lett*. **1979**, 977.

(27) Mobilio, D.; De Lange, B. *Tetrahedron Lett*. **1987**, *28*, 1483.

(2 equiv) and Me_2AlCl (2 equiv) in hexane at −70 °C produces the TIPS enol ether **35** (81%). A one-pot procedure (β-azidonation plus conjugate addition) was carried out with **36** to give **37** (62%). Application of the same procedure as above to **34** resulted in the unexpected formation of the *N*-butenyl derivative **38** (60%) (entry 4). The probable mechanism of its formation is outlined in eq 1. Dehydrogenation of **34** with PhIO/



(1)

$TMSN_3$ produces the iminium ion intermediate **34a**, which undergoes addition of the allylstannane to give **38**. The selectivity toward the *tert*-amine functionality versus the TIPS enol ether is in agreement with our studies on the oxidation of amines and amides using the $PhIO/TMSN_3$ reagent combination.[28]

Conjugate addition of a silyl enol ether to an α,β-unsaturated ketone, catalyzed by titanium tetrachloride, is a key reaction in synthetic organic chemistry (Mukaiyama−Michael reaction).[29] Other variations such as CsF,[30] montmorillonite clay,[31] $BF_3 \cdot Et_2O$[32] also form 1,5-diketones. Conjugate addition catalyzed by trityl perchlorate produces δ-keto silyl enol ethers.[33] The addition of silyl enol ethers to 4-*tert*-butyldimethylsilyl(oxy)-1-benzopyrylium salts is closely related.[34]

Treatment of **33** with 2 equiv of cyclohexanone TMS enol ether and Me_2AlCl at −70 °C, in hexane, gave the carbonyl derivative **39** (55%) as a (3:1) mixture of diastereoisomers (entry 5). In an analogous manner, the reaction of **33** and 1-trimethylsilyl(oxy)styrene forms the silyl enol ether **40** (68%).

Nagata reported the conjugate hydrocyanation of α,β-unsaturated ketones using Et_2AlCN.[35] β-Cyano silyl enol ethers are obtained when α,β-unsaturated ketones are treated with trimethylsilyl cyanide and Me_2AlCl.[36] Treatment of **33** with Et_2AlCN in dichloromethane at reflux gave the conjugate addition product **41** and the 1,2-adduct **42**. If the reaction between **33** and Et_2AlCN is performed in tetrahydrofuran at reflux, only **41** (60%) was obtained. This result further adds support to the credibility of the intermediate α,β-unsaturated oxonium ion **1a**, Scheme 1.

Earlier attempts of conjugate addition reactions between a terminal acetylene and a conjugated enone were unsuccessful.[37] Among several methods now available,[38] nickel-catalyzed conjugate addition of organoaluminum acetylides to α,β-enones seems to be the most effective and reliable.[39] In 1990, Kim reported a trialkylsilyl trifluoromethanesulfonate-promoted addition of alkynylzinc compounds to α,β-enones to afford γ,δ-acetylenic silyl enol ethers.[40] The terminal alkynes (entry 8) were first converted into their lithium salts and then treated with Me_2AlCl and **33** to give the γ,δ-acetylenic TIPS enol ethers **43** (98%), **44** (70%), and **45** (84%), respectively.

Hydroalumination[41] and hydrozirconation[42] of terminal acetylenes is a useful reaction for several reasons: the mild reaction conditions, short reaction times, commercial availability of the reagents, and excellent regio- and stereochemical control of the reagent addition. Unfortunately, the lack of reactivity of the alkenylzirconium derivatives in C−C bond formation have limited their use. Transmetalation chemistry to give a more reactive organometallic species was developed to broaden their reactivity.[43−45] Zirconocene complexes have also been used catalytically to control the monocarboalumination and hydroalumination of alkynes.[46] These new organometallic species have been used in conjugate addition reactions to α,β-enones.[47] A solution of phenylacetylene and diisobutylaluminum hydride was heated at 50 °C for 2 h, and cooled to −70 °C, and **33** was added to give the *trans*-γ,δ-alkenic **46** (46%) and γ,δ-acetylenic **43** (10%). Phenylacetylene and hexyne-1, respectively, were treated with bis-(η^5-cyclopentadienyl) chlorohydridozirconium and then with Me_2AlCl. The vinylaluminum derivatives formed in this manner react with **33** to give, respectively, **46** (46%) and **47** (45%).

We decided to study the reaction of a β-azido silyl enol ether with Me_3Al and the derived "ate" complex Me_4AlLi. Treatment of **33** with Me_4AlLi complex gave **48** (44%, 25% recovered **33**). Exposure of **49** to Me_3Al in toluene for 10 min at 25 °C gave **50** (45%). Using a preformed solution of Me_4AlLi also converted **49** into **50** (45%).

Attempts to trap **1a** with various oxygen- and nitrogen-nucleophiles were unsuccessful. Sulfur reagents are known to be softer nucleophiles and to perform well in conjugate additions.[48] Treatment of **33** with thiophenol in the presence of Me_3Al gave the β-mercapto-silyl enol ether **51** (97%). When this reaction was performed using direct addition conditions, traces of 3-methyl-silyl enol ether **48** were also isolated.

Stereochemical Outcome of the Conjugate Addition. The diastereoselectivity of dialkylcuprate conjugate addition to

(28) Magnus, P.; Lacour, J.; Weber, W. *J. Am. Chem. Soc*. **1993**, *115*, 9347. Magnus, P.; Hulme, C.; Weber, W. *J. Am. Chem. Soc*. **1994**, *116*, 4501. Magnus, P.; Lacour, J.; Weber, W. *Synthesis* **1998**, 547.

(29) Narasaka, K.; Soai, K.; Mukaiyama, T. *Chem. Lett.* **1974**, 1223. Narasaka, K.; Soai, K.; Aikawa, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 779. Saigo, K.; Osaki, M.; Mukaiyama, T. *Chem. Lett.* **1976**, 163. Heathcock, C. H.; Norman, M. H.; Uehling, D. E. *J. Am. Chem. Soc.* **1985**, *107*, 2797. Heathcock, C. H.; Uehling, D. E. *J. Org. Chem.* **1986**, *51*, 279.

(30) Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *J. Organomet. Chem. Commun.* **1980**, *184*, 157. Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *J. Chem. Soc., Chem. Commun.* **1981**, 122. Boyer, J.; Corriu, R. J. P.; Perz, R.; Reye, C. *Tetrahedron* **1983**, *39*, 117.

(31) Kawai, M.; Onaka, M.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 1203.

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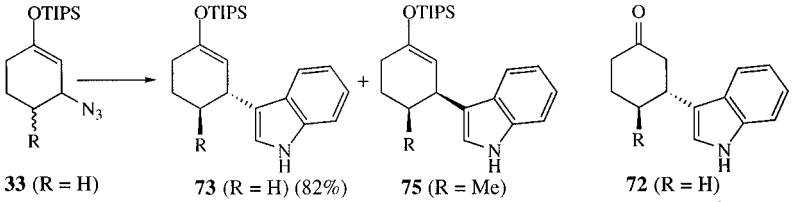
Scheme 2



33 (R = H)
52 (R = Me)
55 (R = Et)
57 (R = Pr^i)
59 (R = Bu^t)

73 (R = H) (82%)
74 (R = Me)
76 (R = Et)
78 (R = Pr^i)
80 (R = Bu^t) (63%)

75 (R = Me)
77 (R = Et)
79 (R = Pr^i)
81 (R = Bu^t) (not detected)

72 (R = H)
82 (R = Pr^i)

Table 3. Reverse Addition with Indole and **52**

reaction temperature	ratios β-indolo SEE *trans* **74**/*cis* **75**	yields (%)
−70 °C	none	no reaction
0 °C	4.5:1	71
+50 °C	4.5:1	75

Table 4. Direct Addition with Indole and **52**

reaction temperature	ratios β-indolo SEE *trans* **74**/*cis* **75**	yields (%)
−70 °C	2.3:1	68
−40 °C	3.0:1	36
0 °C	4.0:1	70
+25 °C	5.0:1	63
+50 °C	10.0:1	54

cyclohexenones has been studied with substituents at the 4-[49] and the 5-positions.[50] Conjugate addition of an organocuprate or Grignard reagent, with copper(I) catalysis, leads to the predominant formation of the *trans*-cyclohexanone products. In general the larger the nucleophile and the larger the group at the 4-position are, the greater the diastereoisomeric excess.

4-Me Series. Treatment of **52** and 3-*N*,*N*-dimethylaminoanisole with Me_2AlCl gave **53** (70%, 3:1, trans-/cis-, entry 13). Similarly, **52** and 2-trimethylsilyl(oxy)-prop-1-ene gave **54** (64%, 4.8:1, trans-/cis-, entry 14). An interesting and unusual temperature effect was observed in the case of the aromatic nucleophile. The diastereoselectivity of the reaction increases with the reaction temperature! This effect was more thoroughly studied using indole as the nucleophile. Treatment of **52** with indole and Me_3Al leads to the formation of *trans*-**74** and *cis*-**75** β-indolo silyl enol ethers (SEE) (4:1 at 0 °C), Scheme 2. The two different procedures (reverse or direct) were examined. With the reverse addition procedure, no or little temperature effect was detected (Table 3), whereas in the case of the direct addition procedure, a strong temperature effect was observed (Table 4).

4-Et Series. The direct addition procedure at 0 °C and at +50 °C was used with **55** and allyl tri-*n*-butyltin using Me_2AlCl to give **56** (79%, 1.7:1, trans-/cis- at 0 °C; 83%, 2.6:1, trans-/cis- at 50 °C). The *trans*-/*cis*- ratio was determined by ^1H NMR and was confirmed by treatment of **56** with tetra-*n*-butylammonium fluoride, and the crude reaction mixture was analyzed by gas chromatography, (1.7:1) at 0 °C and (2.6:1) at 50 °C. By using indole as the nucleophile and utilizing the reverse addition procedure, slightly better ratios in favor of the *trans*-isomer **76**:**77** (~5:1) were obtained, compared to the 4-Me series. The reverse addition procedure at +50 °C was also performed. This time a slight temperature effect was observed (Table 5). The best ratio was, as expected, obtained using the direct addition procedure at higher temperature.

Table 5.

procedure	reaction temperature	ratios β-indolo SEE *trans* **76**/*cis* **77**	yields (%)
reverse	0 °C	4.8:1	83
reverse	+50 °C	5.3:1	72
direct	+55 °C	8.5:1	51

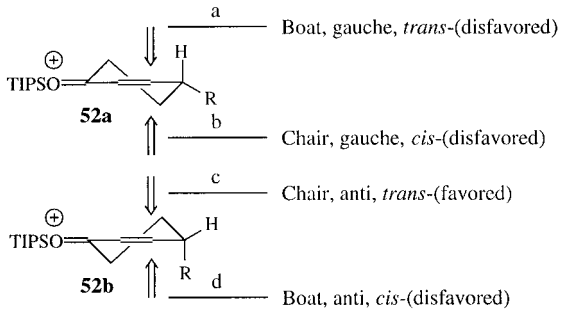
Table 6.

procedure	reaction temperature	ratios β-indolo SEE *trans* **78**/*cis* **79**	yields (%)
reverse	0 °C	12:1	72
direct	−70 °C	5:1	53

Table 7.

substituent at the 4 position	procedure	reaction temperature	ratios β-indolo SEE *trans*/*cis*
Me	reverse	0 °C	4.5:1
Et	reverse	0 °C	4.8:1
Pr^i	reverse	0 °C	12:1
Bu^t	reverse	0 °C	>20:1

Scheme 3



4-Pr^i Series. The direct addition procedure at 0 °C was used with **57**, 1-trimethylsilyl(oxy)styrene, and Me_2AlCl to give **58** (44%, 12:1, trans-/cis-, entry *16*). With indole as the nucleophile, a much better ratio in favor of the *trans*-isomer (**78**:**79**, 12:1) was obtained using the reverse procedure at 0 °C. The direct addition procedure at −70 °C was performed to confirm the temperature trend. As expected, a lower ratio (5:1) of diastereoisomers was observed, (Table 6).

4-Bu^t Series. Compound **59** was prepared in situ and used immediately without purification. Treatment of **59** with indole, following the reverse addition procedure, leads to the formation of only one β-indolo silyl enol ether **80** (63%), the *cis*-diastereomer **81** was not detected (^1H NMR). Similarly, **59** and 3-*N*,*N*-dimethylaminoanisole on treatment with Me_2AlCl gave **60** (21%, entry *17*), and two regioisomeric dienes (55%) formed by elimination of the azide from **59** followed by proton loss.

(49) Rivière, H.; Tostain, J. *Bull. Soc. Chim. Fr.* **1969**, 568. Hoye, T. R.; Magee, A. S.; Rosen, R. E. *J. Org. Chem.* **1984**, *49*, 3224.
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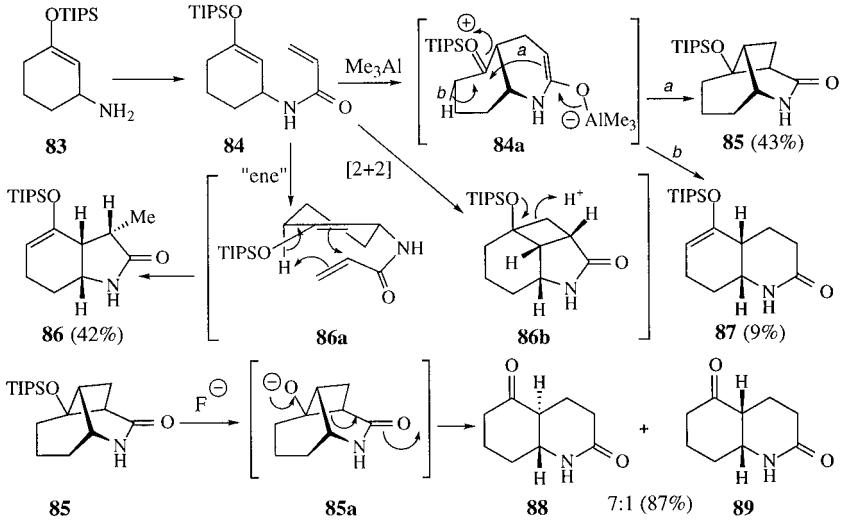
Scheme 4



Using the same temperature (0 °C) and the reverse addition procedure, we have shown that the diastereoisomeric excess increases with the size of the substituent at the C4-position (Table 7).

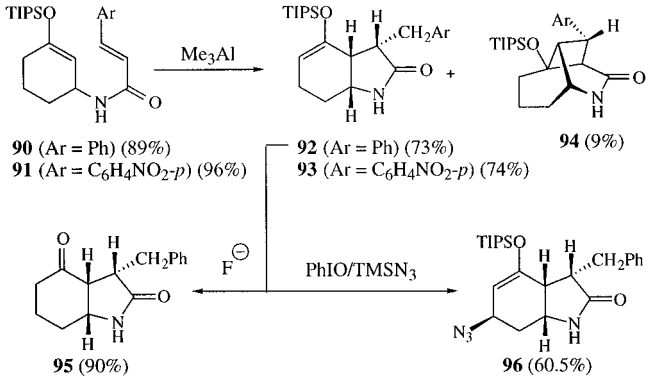
The two lower energy conformations of the intermediate enonium ion derived from **52**, **55**, **57**, and **59** are **52a** (*R* equatorial) and **52b** (*R* axial), the former being more stable than the latter, Scheme 3. Each of the two conformations (**52a** and **52b**) of the enonium ion has two possible modes of nucleophilic addition to it, which lead to four transition states and two products. The pathways leading to a boat transition state or having a gauche 1,2-interaction with the substituent at C4-position are disfavored. This leads to the conclusion that the less stable enonium ion conformer **52b** (chair/substituent axial), which is more reactive than the more stable conformer **52a**, forms the major observed *trans*-products.

The reaction profile is best described as following the Curtin−Hammett principle. The ratio of the products is not determined by the conformer population ratio but by the relative energy of the two transition states.[51]

***γ*-Lactam Annulation.** Reactions that retain the nitrogen functionality would be particularly interesting since *β*-amino silyl enol ethers are an unknown functional group array.[4] The *β*-azido functionalization reaction allows ready access to *β*-amino TIPS enol ethers by reduction of the azido group in **33** with lithium aluminum hydride to give **83**, Scheme 4. The compound **83** is relatively stable and can be stored as its hydrochloride salt without noticeable decomposition to cyclohexenone.

It was decided to examine the intramolecular conjugate addition reaction depicted in Scheme 4. The cyclization of the acrylamide **84** to give the octahydroquinoline **87** is a favored process (6-*endo*-trig),[52,53] but would require the higher energy *cis*-amide conformer in order to arrive at **6**.[54] The amine **3** was readily converted into the α,*β*-unsaturated amide derivative **84** by treatment with acryloyl chloride/Et_3N/THF at −78 °C.

Scheme 5



Initial attempts to induce intramolecular 1,4-addition of **84** with Lewis acids such as $TiCl_4$, trimethylsilyltriflate, Me_2AlCl or $BF_3{\cdot}OEt_2$, all failed. The only product isolated, apart from the starting material, was 3-(propenoylamino)-cyclohexanone. However, desilylation of **84** was avoided by the use of Me_3Al. Treatment of **84** with 1.3 equiv of Me_3Al (2.0 *M* solution in toluene) in 1,2-dichloroethane for 42 h produced the compound **87** (9%) as a minor component. To our surprise the major product has the structure **85** (43%, structure by X-ray crystallography).

Treatment of **85** with tetra-*n*-butylammonium fluoride (1.2 equiv) in THF at 0 °C (5 min) caused cyclobutane opening to the known hydroquinoline-2,5-diones **88** and **89** (87%).[55] The *trans*-fused product most probably resulted from epimerization of the *cis*-fused compound under the reaction conditions.

The formation of the tricyclic amide **85** might involve the intermediate **84a** which can either react by pathway *a* leading to **85** or undergo proton loss (pathway *b*) resulting in the minor product **87**.

In an effort to improve the yield of **87**, a series of experiments were run at different temperatures. It was found that treatment of **84** with 2.5 equiv of Me_3Al in anhydrous 1,2-dichlorobenzene at 180 °C gave the lactam **87** in 10% yield. The major product of the above reaction was shown to have structure **86** (42%, structure by X-ray crystallography). These two products were obtained in similar yields under the following conditions. Me_3-

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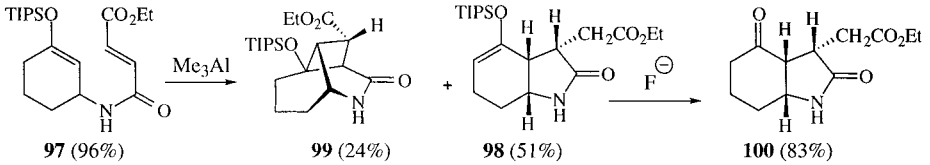
(53) The closest analogy to the reaction depicted in Scheme 4 (**84** → **87**) is the intramolecular Michael addition of a cyclic *β*-ketoester to a conjugated ketone. Berthiaume, G.; Lavallée, J.-F.; Deslongchamps, P. *Tetrahedron Lett.* **1986**, *27*, 5451.

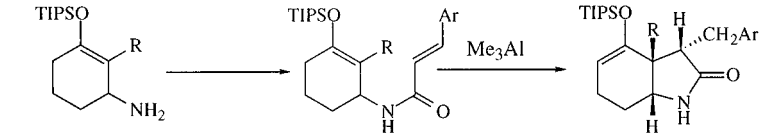
(54) LaPlanche, L. A.; Rogers, M. T. *J. Am. Chem. Soc.* **1964**, *86*, 337.

(55) Momose, T.; Miyata, T.; Imanishi, T. *Heterocycles* **1978**, *9*, 17. Momose, T.; Uchida, S.; Miyata, T.; Ohshima, K.; Chiamchittrong, K.; Imanishi, T. *Heterocycles* **1979**, *12*, 393. Witiak, D.; Patch, R. J.; Enna, S. J.; Fung, Y. K. *J. Med. Chem.* **1986**, *29*, 2.

Scheme 6



Scheme 7



Al (1.2 equiv), 1,2-dichloroethane, 150 °C, 22 h, **87** (12%) and **86** (42%) or Me_3Al (1.2 equiv), benzene, 150 °C, 22 h, **87** (7%) and **86** (45%). No reaction occurred if **84** was heated to 180 °C without Me_3Al. In all of the above experiments appreciable amounts of material less polar than **84** was observed. One of these nonpolar products was **48**, presumably resulting from ionization of **84** to give **1a** and conjugate addition of a methyl group from Me_3Al. Other reagents [such as CsF (1.0 equiv), CH_3CN, reflux, 30 min; Ag_2CO_3 (1.0 equiv) benzene, reflux, 23 h; MAD (2.0 equiv), toluene, RT to reflux, 23 h; $Pd(OAc)_2$ (0.2 equiv), benzoquinone (1.0 equiv), acetonitrile, 25 to 50 °C, 16 h] did not produce any of the products **85**, **86**, or **87**.

We originally postulated[4] that **86** arose from a [2 + 2] pathway **86b**, but attempts to incorporate deuterium at the benzylic position in the conversion of **91** into **93** (workup with DCl) were unsuccessful, Scheme 5. Therefore it appears that the more plausible "ene" process **86a** is responsible for the formation of **86**.

Treatment of **90** with 2.5 equiv of Me_3Al at 80 °C for 22 h gave only one cyclization product **92** in 44% yield. Optimal yields were obtained by using a small excess of Me_3Al (1.1 equiv) in *o*-dichlorobenzene at reflux for 20 h to give **92** (73%), Scheme 5. Similar results were observed for the cyclization of the more activated compound **91**. Optimal reaction conditions were obtained when **91** was treated with Me_3Al (1.1 equiv) at 120 °C for 22 h to give **93** (74%). At lower temperatures (83 °C, dichloroethane reflux), the γ-lactam **93** (46%) was formed along with the cyclobutane adduct **94** (9%).

Irradiation of **91** gave an equilibrium mixture of *E*-**91**/*Z*-**91** (1.6:1) with no indication of any [2+2] cyclization. Treatment of *Z*-**91** with $Me_3Al/Cl(CH_2)_2Cl$ at reflux gave **93** as the major product along with small amounts of *E*-**91**. Careful monitoring of the reaction demonstrated that *Z*-**91** is first converted into *E*-**91**, which is then transformed into **93** and **94**.

Treatment of **92** with TBAF resulted into desilylation to the product **95** in 90% yield. When **92** was exposed to the β-azidonation reaction conditions ($PhIO/TMSN_3$), a single epimer **96** was produced very cleanly as shown by the ^1H NMR of the crude reaction mixture.

Treatment of the *E*-isomer **97** with Me_3Al (2.0 equiv) in toluene heated at reflux gave a mixture of **98** (51%) and **99** (24%), Scheme 6. To confirm the structure, **98** was treated with TBAF/THF to give **100** (83%).

It was of interest to see if the "ene" reaction would tolerate the presence of an angular substituent. Reduction of the corresponding azides[1] gave **101** and **102**. The derived cinnamide **103** on treatment with Me_3Al/PhMe reflux gave the γ-lactam **105** (46%). Similarly, the 2-phenyl derivative **104** was heated in xylene at reflux with Me_3Al (1.1 equiv) to give **106** in a modest 24% yield. Given the rather sterically crowded nature of the *cis*-hexahydroindolones **105** and **106**, it is quite surprising that they are formed at all and that elimination of the cinnamide appendage was not completely dominant (Scheme 7).

Summary

The β-azido TIPS enol ether functionality appears to quite flexible in its applications to organic synthesis. Depending on the specific reaction conditions, they may be converted into α,β-enones, β-substituted TIPS enol ethers, and γ-lactams. These transformations are further illustrations of the increasing value of the enhanced stability of TIPS enol ethers.[56]

Experimental Section[57]

General Procedure for the Synthesis of α,β-Unsaturated Ketones. (*E*)-Cyclododec-2-en-1-one (8). Trimethylsilyl azide (500 μL, 3.77 mmol, 2.4 equiv) was added to a suspension of **7** (530 mg, 1.57 mmol, 1 equiv) and iodosobenzene (416 mg, 1.89 mmol, 1.2 equiv) in CH_2Cl_2 (10 mL) at 5 °C. After 5 min the mixture (now a clear solution) was warmed to 25 °C (N_2 evolution), after 10 min the solution was cooled to −5 °C, and tetra-*n*-butylammonium fluoride (4.0 mL, 1.0 M in THF, 4.0 mmol, 4.0 equiv) were added. The mixture was warmed to 25 °C, saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) was added, and the phases were separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (2 × 15 mL) and brine (15 mL). The aqueous phase was extracted with Et_2O (2 × 10 mL), and the combined extracts dried ($MgSO_4$), filtered, and evaporated in vacuo. The residue was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (17:3) to give **8** (209 mg, 74%) as a colorless oil: IR

(56) Rücher, C. *Chem. Rev.* **1995**, *95*, 1009.

(57) Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium/benzophenone under nitrogen prior to use. *N*,*N*-Dimethylformamide (DMF), hexane, and benzene were distilled from calcium hydride. Methanol (MeOH) was distilled from magnesium methoxide and stored over 3 Å molecular sieves under argon. Triethylamine was distilled from calcium hydride and stored under argon. All reactions involving organometallic reagents or other moisture-sensitive reactants were executed under an atmosphere of dry nitrogen or argon using oven-dried and/or flame-dried glassware. ^1H NMR spectra were recorded at 300 MHz as solutions in deuteriochloroform ($CDCl_3$), unless otherwise indicated. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.24 ppm) as internal standard. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. Coupling constants are given in hertz (Hz). ^{13}C NMR spectra were recorded at 75 MHz as solutions in $CDCl_3$ unless otherwise indicated. Chemical shifts are reported in parts per million (ppm, δ) downfield from TMS and are referenced to the center line of $CDCl_3$ (77.0 ppm) as internal standard; or indicate even or odd numbers of hydrogens carried by the carbon. IR spectra were recorded either neat on sodium chloride plates or as solutions in the solvent as indicated.

(film) 2931, 2860, 1690 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 6.71−6.61 (1H, m), 6.18 (1H, d, J = 15.8 Hz), 2.37 (2H, t, J = 6.6 Hz), 2.17−2.10 (2H, m), 1.60 (2H, quint, J = 6.6 Hz), 1.52−1.44 (2H, m), 1.31−1.10 (10H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 203.2, 146.6, 131.1, 39.9, 32.5, 26.5, 25.2, 25.1, 25.1, 24.7, 24.5, 23.8. HRMS (M^+) calcd for $C_{12}H_{20}O$ 180.151, found 180.152.

3-(2-Methoxy-4-*N*,*N*-dimethylaminophenyl)-1-triisopropylsilyl-(oxy)-cyclohexan-1-ene (34). Direct Addition Procedure. Me_2AlCl (1.0 mL, 1.0 M in hexane, 1.0 mmol, 2 equiv) was added to a solution of **33** (148 mg, 0.50 mmol, 1.0 equiv) and 3-*N*,*N*-dimethylaminoanisole (302 mg, 2.0 mmol, 4 equiv) in hexane (4 mL) at 25 °C. After 10 min saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added, the mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL), and the aqueous phases were extracted with Et_2O (2 × 15 mL). The combined extracts were dried (Na_2SO_4) and evaporated in vacuo. The residue was placed under high vacuum (2 mmHg) at 115 °C for 1 h. The product was purified by flash chromatography over Florisil eluting with CH_2Cl_2 to give **34** (159 mg, 79%) as a colorless oil: IR (film) 2943, 2865, 1665 cm^{-1}. ^1H NMR (300 MHz, C_6D_6) δ 7.38 (1H, d, J = 8.4 Hz), 6.38 (1H, dd, J = 8.4, 2.4 Hz), 6.20 (1H, d, J = 2.4 Hz), 5.12 (1H, d, J = 3.4 Hz), 4.30−4.20 (1H, m), 3.46 (3H, s), 2.59 (6H, s), 2.25−2.03 (3H, m), 1.77−1.57 (3H, m), 1.25−1.05 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 158.0, 152.0, 150.9, 129.4, 124.0, 107.5, 105.5, 96.8, 54.8, 40.7, 33.5, 31.0, 30.4, 21.7, 18.4, 13.1. HRMS (M^+) calcd for $C_{24}H_{41}NO_2Si$ 403.291, found 403.291.

$NaBPh_4$ Mediated Reaction. A suspension of $NaBPh_4$ (111 mg, 0.32 mmol, 2 equiv), **33** (48 mg, 0.16 mmol, 1.0 equiv), and 3-*N*,*N*-dimethylaminoanisole (98 mg, 0.64 mmol, 4.0 equiv) in CH_2Cl_2 (4 mL) was heated at reflux. After 15 min the solution was cooled to 25 °C, filtered through Celite, and washed with CH_2Cl_2. The solvent was evaporated in vacuo and the residue purified by Kugelrohr distillation at 100 °C for 1 h under high vacuum and then by flash chromatography over silica gel eluting with CH_2Cl_2 to give **34** (30 mg, 46%).

3-(2-Propenyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (35). Direct Addition Procedure. Me_2AlCl (2.0 mL, 1.0 M in hexane, 2.0 mmol, 2 equiv) was added to a solution of **33** (295 mg, 1.0 mmol, 1.0 equiv) and allyl tri-*n*-butylstannane (620 μL, 2.0 mmol, 2 equiv) in hexane (5 mL) at −70 °C. After 30 min the mixture was warmed to 25 °C. Saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added, the mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL). The aqueous phases were extracted with CH_2Cl_2 (2 × 15 mL), and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes to give **35** (220 mg, 81%) as a colorless oil: IR (film) 2946, 1662, 1640 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 5.77−5.63 (1H, m), 4.94 (1H, d, J = 4.8 Hz), 4.85 (1H, s), 4.75 (1H, s, br), 2.16−2.10 (1H, m), 2.03−1.90 (4H, m), 1.74−1.42 (4H, m), 1.22−0.95 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 151.4, 137.6, 115.9, 107.7, 41.9, 35.0, 30.3, 29.1, 22.1, 18.3, 13.1. HRMS (MH^+) calcd for $C_{18}H_{34}OSi$ 294.238, found 294.237.

2-(2-Propenyl)-4-triisopropylsilyl(oxy)-pyran-3-ene (37). Trimethylsilyl azide (500 μL, 2.4 mmol, 2.4 equiv) was added to a suspension of **36** (408 mg, 1.57 mmol) and iodosobenzene (416 mg, 1.886 mmol, 1.2 equiv) in CH_2Cl_2 (10 mL) at −15 °C. After 10 min the mixture was warmed to 25 °C, and then cooled to −70 °C. Allyl tri-*n*-butylstannane (775 μL, 2.50 mmol, 1.6 equiv) and Me_2AlCl (2.5 mL, 1.0 M in hexane, 2.5 mmol, 1.6 equiv) were added successively. After 30 min the mixture was warmed to 25 °C, and saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added. The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 15 mL), and the combined extracts were dried (Na_2SO_4) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes to separate the tin derivatives, followed by hexanes/EtOAc (17:3) to give **37** (290 mg, 62%) as a colorless oil: IR (film) 2945, 1670, 1642 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 5.87−5.73 (1H, m), 5.09−5.02 (2H, m), 4.77 (1H, s), 4.18−4.10 (1H, m), 4.00 (1H, ddd, J = 11.0, 6.0, 2.05 Hz), 3.62 (1H, td, J = 11.0, 3.8 Hz), 2.41−2.14 (3H, m), 1.94−1.87 (1H, m), 1.20−1.00 (21H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 149.1, 134.7, 116.9, 105.0, 73.3, 63.9, 40.8, 30.3, 17.9, 12.5. HRMS (MH^+) calcd for $C_{17}H_{33}O_2Si$ 297.225, found 297.225.

3-(2-Oxo-cyclohexyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (39). A solution of Me_2AlCl (1.0 mL, 1.0 M in hexane, 1.0 mmol, 2 equiv) was added to a solution of **33** (148 mg, 0.50 mmol, 1.0 equiv) and 1-trimethylsilyl(oxy)cyclohexene (240 mg, 1.4 mmol, 2.8 equiv) in hexane (5 mL) at −70 °C. After 2 h the mixture was warmed to 25 °C, and saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added. The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL). The aqueous phase was extracted with Et_2O (15 mL), and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (9:1) to give **39** (97 mg, 55%) as a colorless oil. The product was a (3:1) mixture of diastereoisomers: IR (film) 2939, 1712, 1665 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ (major isomer) 4.82−4.79 (1H, m), 2.88−2.75 (1H, m), 2.48−2.20 (3H, m), 2.10−1.50 (11H, m), 1.20−1.00 (21H, m). δ (minor isomer) 4.75−4.72 (1H, m), 2.78−2.68 (1H, m), 2.48−1.00 (35H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ (major isomer) 213.1, 151.6, 104.9, 55.5, 42.0, 32.8, 29.8, 29.6, 28.0, 26.8, 24.3, 21.6, 17.9, 12.6. HRMS (M^+) calcd for $C_{21}H_{38}O_2Si$ 350.264, found 350.263.

3-Cyano-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (41). A solution of Et_2AlCN (500 μL, 1.0 M in toluene, 0.50 mmol, 2 equiv) was added to a solution of **33** (74 mg, 0.250 mmol, 1.0 equiv) in THF (4 mL). The mixture was heated at reflux for 60 h and cooled to 25 °C. Saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added, and the mixture was filtered through Celite, and the phases were separated. The extracts were washed with brine (2 × 10 mL), dried ($MgSO_4$), and evaporated in vacuo. ^1H NMR analysis of the crude mixture reveals only the 1,4-addition adduct **41**, which was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (4:1) to give **41** (42 mg, 60%) as a colorless oil: IR (film) 2945, 2237, 1661 cm^{-1}. ^1H NMR (300 MHz, C_6D_6) δ 4.67 (1H, d, J = 4.1 Hz), 2.64−2.59 (1H, m), 1.78−1.70 (2H, m), 1.51−1.31 (2H, m), 1.25−1.00 (23H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 154.8, 121.5, 98.5, 29.4, 26.4, 26.3, 20.6, 18.1, 12.8. HRMS (M^+) calcd for $C_{16}H_{29}NOSi$ 279.202, found 279.202.

1-Cyano-1-triisopropylsilyl(oxy)-cyclohexan-2-ene (42). A solution of Et_2AlCN (680 μL, 1.0 M in toluene, 0.68 mmol, 2 equiv) was added to a solution of **33** (100 mg, 0.34 mmol, 1.0 equiv) in CH_2Cl_2 (5 mL) at 25 °C. The mixture was heated at reflux for 2 h, cooled to 25 °C, and quenched with saturated aqueous $NaHCO_3$ (10 mL) and Et_2O (50 mL). The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with an aqueous brine (2 × 10 mL), dried ($MgSO_4$), and evaporated in vacuo. ^1H NMR analysis of the crude mixture shows a (2:1) mixture of **41** and **42**. The 1,2-adduct was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (17:3) to give **42** (22 mg, 23%) as a colorless oil: IR (film) 2946, 2229, 1653 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 5.92 (1H, dt, J = 9.9, 3.6 Hz), 5.73 (1H, d, J = 9.9 Hz), 2.17−2.09 (1H, m), 2.04−1.97 (2H, m), 1.90 (1H, ddd, J = 12.8, 9.4, 3.4 Hz), 1.80−1.78 (2H, m), 1.20−0.95 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 132.1, 128.2, 122.1, 67.0, 37.7, 24.3, 18.6, 18.3, 13.2.

3-(2-Phenyl-ethynyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (43). A solution of *n*-BuLi (420 μL, 2.4 M in hexane, 1.0 mmol, 2 equiv) followed by Me_2AlCl (1.0 mL, 1.0 M in hexane, 1.0 mmol, 2 equiv) was added to phenylacetylene (102 mg, 1.0 mmol, 2.0 equiv) in hexane (5 mL). After 5 min a solution of **33** (148 mg, 0.50 mmol, 1.0 equiv) in hexane (3 mL) was added to the mixture. After 1.5 h saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added. the mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL), and the aqueous phases were combined and extracted with Et_2O (2 × 15 mL). The extracts were dried (Na_2SO_4), and evaporated in vacuo. The product was purified by flash chromatography over Florisil eluting with hexanes/EtOAc (19:1) to give **43** (174 mg, 98%) as a colorless oil: IR (film) 3056, 2945, 2139, 1661 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.31−7.27 (2H, m), 7.20−7.16 (3H, m), 4.89 (1H, d, J = 3.9 Hz), 3.29−3.25 (1H, m), 2.04−1.99 (2H, m), 1.88−1.73 (2H, m), 1.68−1.54 (2H, m), 1.17−

0.90 (21H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 151.8, 131.5, 128.1, 127.4, 124.1, 104.4, 93.4, 80.1, 29.6, 29.1, 27.4, 21.0, 18.0, 12.6. HRMS (MH^+) calcd for $C_{23}H_{35}OSi$ 355.246, found 355.247.

3-((*E*)-2-Phenyl-ethenyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (46). Hydroalumination Procedure. A solution of phenylacetylene (110 μL, 1.0 mmol, 2.0 equiv) and DIBAL-H (0.67 mL, 1.5 M in hexane, 1.00 mmol, 2.0 equiv) in hexane (4 mL) was heated at 50 °C for 2 h. The mixture was cooled to −70 °C, and a solution of **33** (148 mg, 0.50 mmol, 1.0 equiv) in hexane (2 mL) was added. After 40 min saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added. The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL). The combined aqueous phases were extracted with CH_2Cl_2 (2 × 15 mL). The extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash chromatography over Florisil eluting with hexanes to give **46** (83 mg, 46%) as a colorless oil: IR (film) 3025, 2942, 1661, 1646 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 7.30−7.00 (5H, m), 6.45 (1H, d, J = 15.8 Hz), 6.17 (1H, dd, J = 15.8, 7.25 Hz), 5.01 (1H, d, J = 3.2 Hz), 3.00−2.96 (1H, m), 2.09−2.03 (2H, m), 1.69−1.61 (2H, m), 1.52−1.41 (1H, m), 1.37−1.19 (1H, m), 1.13−1.01 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 152.2, 138.3, 135.4, 129.6, 128.8, 127.2, 126.5, 105.9, 38.6, 30.3, 29.5, 21.2, 18.3, 13.1. HRMS (M^+) calcd for $C_{23}H_{36}OSi$ 356.254, found 356.253.

3-((*E*)-1-Hexenyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (47). Cp_2ZrHCl (172 mg, 0.66 mmol, 2.0 equiv) was added to a solution of hex-1-yne (75 μL, 0.66 mmol, 2.0 equiv) in CH_2Cl_2 (4 mL) at 25 °C. After 45 min, Me_2AlCl (666 μL, 1.0 M in hexane, 0.66 mmol, 2 equiv) was added to the yellow solution, which immediately became orange. After 5 min a solution of **33** (98 mg, 0.33 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL) was added. After 1.5 h, saturated aqueous $NaHCO_3$ (20 mL) and Et_2O (40 mL) were added, the mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (2 × 10 mL). The combined aqueous phases were extracted with Et_2O (2 × 15 mL), and the extracts were dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash chromatography over Florisil eluting with hexanes to give **47** (51 mg, 45%) as a colorless oil: IR (film) 2929, 2867, 1661 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 5.50−5.46 (2H, m), 5.02−4.98 (1H, m), 2.92−2.82 (1H, m), 2.07−1.97 (4H, m), 1.69−1.62 (2H, m), 1.53−1.42 (1H, m), 1.37−1.20 (5H, m), 1.16−1.10 (21H, m), 0.86 (3H, t, J = 7.0 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 151.5, 135.5, 129.6, 106.9, 38.4, 32.6, 32.2, 30.3, 29.9, 22.5, 21.4, 18.3, 14.2, 13.1. HRMS (M^+) calcd for $C_{21}H_{40}OSi$ 336.285, found 336.284.

3-Methyl-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (48). Me_3Al (1.0 mL, 2.0 M in toluene, 2.00 mmol, 2 equiv) was added to a solution of MeLi (833 μL, 1.2 M in Et_2O, 1.00 mmol, 2.0 equiv) in hexane (6 mL) at 0 °C, and after 5 min a solution of **33** (295 mg, 1.00 mmol, 1.0 equiv) in hexane (1 mL) was added to the mixture. After 1 h saturated aqueous $NaHCO_3$ (10 mL) was added, the mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (15 mL). The aqueous phases were combined and extracted with Et_2O (15 mL), and the extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes to give **48** (58.6 mg, 44%) as a colorless oil. ^{1}H NMR analysis of the crude mixture shows that 25% of the starting β-azido silyl enol ether was present in the crude reaction mixture: IR (film) 2945, 2867, 1667 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.76−4.72 (1H, m), 2.25−2.18 (1H, m), 2.04−1.98 (2H, m), 1.79−1.40 (4H, m), 1.20−1.05 (2H, m), 0.92 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 151.0, 109.9, 31.5, 30.2, 29.9, 22.8, 22.2, 18.3, 13.1. HRMS (MH^+) calcd for $C_{16}H_{33}OSi$ 269.230, found 269.231.

2,3-Dimethyl-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (50). Me_3Al (1.0 mL, 2.0 M in toluene, 1.00 mmol, 2 equiv) was added to a solution of **49** (295 mg, 1.00 mmol, 1.0 equiv) in hexane (5 mL) at 25 °C. After 10 min, Et_2O (1 mL) and saturated aqueous $NaHCO_3$ (1 mL) were added. The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with brine (5 mL), and the aqueous phases were combined and extracted with Et_2O (10 mL). The extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes to give **50** (63 mg, 45%) as a colorless oil: IR (film) 2943, 2867, 1678 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 2.10−2.02 (3H, m), 1.74 (3H, s), 1.68−1.57 (2H, m), 1.55−1.43 (1H, m), 1.25−1.05 (22H, m), 0.98 (3H, d, J = 6.9 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 144.0, 115.0, 34.2, 31.6, 31.1, 20.9, 20.1, 18.4, 14.8, 13.6. HRMS (MH^+) calcd for $C_{17}H_{35}OSi$ 283.246, found 283.245.

3-(Thiophenyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (51). Me_3Al (2.0 mL, 2.0 M in toluene, 4.0 mmol, 2 equiv) was added to a solution of thiophenol (410 μL, 4.0 mmol, 2.0 equiv) in hexane (10 mL) at 0 °C. After 5 min a solution of **33** (591 mg, 2.0 mmol, 1.0 equiv) in hexane (3 mL) was added at 0 °C. After 30 min Et_2O (20 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added. The mixture was filtered through Celite, and the organic phase was washed with saturated aqueous $NaHCO_3$ (2 × 20 mL) and brine (10 mL). The aqueous phase was extracted with Et_2O (15 mL), and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by Kugelrohr distillation at 80 °C under high vacuum for 2 h to give **51** (703 mg, 97%) as a colorless oil: IR (film) 3059, 2866, 1657 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 7.35 (1H, d, J = 7.85 Hz), 7.05−6.94 (3H, m), 5.17−5.13 (1H, m), 3.94−3.90 (1H, m), 2.05−1.95 (3H, m), 1.72−1.38 (3H, m), 1.17−1.00 (21H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 154.3, 136.4, 131.3, 128.7, 126.4, 103.7, 44.9, 29.8, 28.1, 19.2, 18.0, 12.5. HRMS (M^+) calcd for $C_{21}H_{34}OSSi$ 362.210, found 362.210.

***cis*- and *trans*-4-Methyl-3-(2-oxo-propyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (54).** Me_2AlCl (2.0 mL, 1.0 M in hexane, 2.00 mmol, 2 equiv) was added to a solution of **52** (155 mg, 1.00 mmol, 1.0 equiv) and 2-trimethylsilyl(oxy)-prop-1-ene (195 mg, 1.50 mmol, 3.0 equiv) in hexane (6 mL) at 0 °C. After 25 min at 0 °C, Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added, the mixture was filtered through Celite, and the organic phase was washed with brine (15 mL). The aqueous phases were extracted with Et_2O (15 mL), and the combined extracts were dried ($MgSO_4$), and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (10:1) to give **54** (104 mg, 64%) as a colorless oil. ^{1}H NMR analysis showed the product to be a mixture of diastereoisomers (4.8:1) in favor of the *trans*-isomer: IR (film) 2944, 1721, 1667 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ (major isomer) 4.90−4.86 (1H, m), 2.42−2.35 (1H, m), 2.20 (1H, dd, J = 16.2, 4.85 Hz), 2.05−1.98 (3H, m), 1.96 (1H, dd, J = 16.2, 8.8 Hz), 1.69 (3H, s), 1.52−1.47 (1H, m), 1.32−0.95 (23H, m), 0.83 (1H, d, J = 6.5 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ (major isomer) 206.1, 151.1, 106.2, 49.5, 37.6, 33.0, 30.0, 29.6, 28.8, 19.4, 18.3, 13.0. HRMS (MH^+) calcd for $C_{19}H_{37}O_2Si$ 325.256, found 325.256.

***trans*- and *cis*-4-Isopropyl-3-(2-oxo-2-phenyl-ethyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (58).** Prepared in an analogous manner to **40** from **57** (169 mg, 0.50 mmol, 1.0 equiv), 1-trimethylsilyl(oxy)-styrene (234 mg, 1.00 mmol, 2.0 equiv) and Me_2AlCl (2.0 mL, 1.0 M in hexane, 2.00 mmol, 2 equiv). The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (19:1) to give **58** (91 mg, 44%) as a colorless oil. ^{1}H NMR analysis shows the product to be a mixture of diastereoisomers (12:1) in favor of the *trans*-isomer: IR (film) 3060, 1690, 1667 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ (major isomer) 7.90−7.85 (2H, m), 7.15−7.03 (3H, m), 5.02 (1H, d, J = 3.6 Hz), 3.07−3.02 (1H, m), 2.86 (1H, dd, J = 16.0, 5.3 Hz), 2.70 (1H, dd, J = 16.0, 8.4 Hz), 2.15−1.98 (2H, m), 1.75−1.20 (3H, m), 1.20−1.04 (22H, m), 0.96 (3H, d, J = 6.8 Hz), 0.78 (3H, d, J = 6.8 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ (major isomer) 200.4, 151.2, 137.6, 132.8, 128.5, 128.0, 106.4, 44.8, 44.0, 33.6, 28.3, 27.3, 21.8, 21.2, 18.2, 17.9, 12.5. HRMS (M^+) calcd for $C_{26}H_{42}O_2Si$ 414.295, found 414.295.

***trans*-5-Isopropyl-3-(2-propenyl)-2-methyl-1-triisopropylsilyl-(oxy)-cyclohexan-1-ene (62).** Prepared in an analogous manner to **35** using the direct addition procedure with **61** (88 mg, 0.250 mmol, 1.0 equiv), allyl tri-*n*-butylstannane (166 mg, 0.50 mmol, 2.0 equiv), and Me_2AlCl (500 μL, 1.0 M in hexane, 2.0 equiv). The product was purified by flash chromatography over silica gel eluting with hexanes to give **62** (49.5 mg, 56%). ^{1}H NMR analysis shows the product to be a single diastereoisomer: $[\alpha]^{25}_D = +34°$ (c = 0.94, CH_2Cl_2). IR (film) 2945, 1682, 1640 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82−5.68 (1H, m), 4.98 (1H, d, J = 3.7 Hz), 4.95 (1H, s), 2.35−2.25 (1H, m), 2.05−1.98 (2H, m), 1.93−1.82 (2H, m), 1.70−1.30 (4H, m), 1.64 (3H,

s), 1.15−1.05 (21H, m), 0.85 (6H, d, $J = 6.5$ Hz). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 144.2, 138.5, 115.5, 113.6, 39.2, 37.4, 36.1, 34.6, 32.3, 28.9, 19.9, 19.8, 18.1, 15.1, 13.2. HRMS (MH^+) calcd for $C_{22}H_{43}OSi$ 351.308, found 351.308.

(*E*)-3-(2-Propenyl)-1-triisopropylsilyl(oxy)-cyclododecan-1-ene (64). Prepared in an analogous manner to **35** using the direct addition procedure with **63** (190 mg, 0.50 mmol, 1.0 equiv), allyl tri-*n*-butylstannane (331 mg, 1.0 mmol, 2.0 equiv), and Me_2AlCl (1.0 mL, 1.0 M in hexane, 1.0 mmol, 2.0 equiv). The product was isolated by flash chromatography over silica gel eluting with hexanes to give **64** (112 mg, 59%) as a colorless oil. ^{1}H NMR analysis of the crude mixture shows only one isomer. The major isomer was assigned as the *E*-stereoisomer (^{13}C, δ major isomer 42.1 and δ minor isomer 44.0): IR (film) 2931, 1660, 1644 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83−5.69 (1H, m), 5.00−4.91 (2H, m), 4.23 (1H, d, $J = 10.3$ Hz), 2.48−2.37 (1H, m), 2.37−2.25 (1H, m), 2.12−2.03 (1H, m), 1.97−1.92 (1H, m), 1.90−1.72 (2H, m), 1.55−1.22 (13H, m), 1.20−1.02 (21H, m), 0.89 (2H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 151.9, 137.8, 115.7, 111.4, 42.1, 35.6, 34.9, 28.3, 25.2, 25.1, 24.9, 24.7, 23.8, 23.4, 22.6, 18.5, 18.4, 13.2. HRMS (MH^+) calcd for $C_{24}H_{47}OSi$ 379.340, found 379.341.

3-(2-Phenyl-ethynyl)-1-triisopropylsilyl(oxy)-cyclopentan-1-ene (66). Prepared in an analogous manner to **43** with β-azido silyl enol ether **65** (141 mg, 0.50 mmol, 1.0 equiv), phenylacetylene (102 mg, 1.0 mmol, 2.0 equiv), *n*-BuLi (400 μL, 1.00 mmol, 2.5 M in hexane), and Me_2AlCl (1.0 mL, 1.0 M in hexane, 1.0 mmol, 2.0 equiv). The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (97:3) to give **66** (127 mg, 75%) as colorless oil: IR (film) 3081, 2945, 2139, 1644 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 7.23−7.16 (2H, m), 6.76−6.70 (3H, m), 4.53 (1H, m), 3.41−3.36 (1H, m), 2.18−1.71 (4H, m), 0.95−0.85 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 157.0, 131.9, 128.5, 127.4, 124.9, 103.6, 94.1, 81.2, 33.6, 33.3, 30.2, 18.1, 12.8. HRMS (M^+) calcd for $C_{22}H_{32}OSi$ 340.222, found 340.222.

3-(2-Oxo-propyl)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (67). $LiBPh_4$ tris(1,2-dimethoxyethane) (298 mg, 0.500 mmol, 1 equiv) was added to a solution of **33** (148 mg, 0.500 mmol, 1.0 equiv) and 2-trimethylsilyl(oxy)-prop-1-ene (195 mg, 1.50 mmol, 3.0 equiv) in CH_2Cl_2 (2 mL) at 25 °C. After 48 h, Et_2O (20 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added, and the phases were separated. The organic phase was washed with brine (2 × 10 mL), and the aqueous phases were extracted with Et_2O (15 mL) and EtOAc (15 mL). The combined extracts were dried (Na_2SO_4) and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (9:1) to give **67** (69 mg, 44%) as a colorless oil: IR (film) 2943, 1716, 1668 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6) δ 4.79−4.75 (1H, m), 2.65−2.57 (1H, m), 1.93−1.85 (2H, m), 1.89 (2H, d, $J = 7.1$ Hz), 1.55 (3H, s), 1.53−1.23 (4H, m), 1.10−0.90 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 205.8, 151.7, 107.3, 50.2, 30.8, 30.2, 29.9, 29.0, 21.6, 18.3, 13.0. HRMS (M^+) calcd for $C_{18}H_{35}O_2Si$ 311.241, found 311.240.

3-Indolo-1-triisopropylsilyl(oxy)-cycloheptan-1-ene (69). Prepared in an analogous manner to **74**/**75** using the reverse addition procedure with β-azido silyl enol ether **68** (155 mg, 0.50 mmol, 1.0 equiv), indole (117 mg, 1.0 mmol, 2.0 equiv), and Me_3Al (500 μL, 2.0 M in toluene, 1.0 mmol, 2.0 equiv). The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (17:3) to give **69** (95 mg, 49%): mp 93−94 °C (Et_2O). IR (film) 3469, 2925, 1653 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (1H, s, br), 7.62 (1H, d, $J = 7.8$ Hz), 7.30 (1H, d, $J = 9.0$ Hz), 7.22−7.06 (2H, m), 6.94 (1H, d, $J = 2.0$ Hz), 5.19 (1H, d, $J = 4.6$ Hz), 3.79−3.75 (1H, m), 2.54 (1H, dd, $J = 15.6$, 9.2 Hz), 2.31 (1H, dd, $J = 15.6$, 7.1 Hz), 2.04−1.61 (6H, m), 1.10−1.00 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 155.6, 137.2, 127.0, 122.7, 122.1, 120.2, 120.0, 112.5, 111.5, 35.8, 35.3, 34.9, 30.1, 25.7, 18.3, 13.0. HRMS (M^+) calcd for $C_{24}H_{37}NOSi$ 383.264, found 383.265.

(2*E*)- and (2*Z*)-3-Indolo-1-triisopropylsilyl(oxy)-cyclododecan-1-ene (70). Prepared in an analogous manner to **74**/**75** using the reverse addition procedure with **63** (190 mg, 0.50 mmol, 1.0 equiv), indole (117 mg, 1.0 mmol, 2.0 equiv), and Me_3Al (500 μL, 2.0 M in toluene, 1.0 mmol, 2.0 equiv). ^{1}H NMR analysis of the crude mixture shows a (5:1) mixture of stereoisomers in favor of the *E*-isomer. The stereochemistry was assigned using ^{13}C NMR [for the allylic carbon, δ (major isomer) 35.5 and δ (minor isomer) 38.0]. The isomers were not separable by chromatography but were isolated together by flash chromatography over silica gel eluting with hexanes/EtOAc (4:1) to give **70** (184 mg, 81%) as a colorless oil: IR (film) 3470, 3043, 1655 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ (major isomer) 7.75 (1H, s, br), 7.62 (1H, d, $J = 7.9$ Hz), 7.23 (1H, d, $J = 7.9$ Hz), 7.16−7.04 (2H, m), 6.84 (1H, d, $J = 2.2$ Hz), 4.72 (1H, d, $J = 10.5$ Hz), 3.84−3.76 (1H, m), 2.76−2.67 (1H, m), 2.00−1.20 (17H, m), 1.20−1.00 (21H, m); δ (minor isomer) there were two distinguishable signals at 4.81 (1H, d, $J = 10$ Hz), 4.10−4.00 (1H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ (major isomer) 151.3, 137.0, 127.5, 122.1, 121.6, 120.1, 119.8, 119.2, 111.7, 111.4, 35.5, 32.8, 28.4, 25.4, 25.0, 24.8 (2), 24.1, 23.4, 22.7, 18.4, 13.2. HRMS (M^+) calcd for $C_{29}H_{47}NOSi$ 453.343, found 453.342.

3-(3-Indolo)-1-triisopropylsilyl(oxy)-cyclopentan-1-ene (71). Prepared in an analogous manner to **74**/**75** using the reverse addition procedure with β-azido silyl enol ether **65** (141 mg, 0.50 mmol, 1.0 equiv), indole (117 mg, 1.0 mmol, 2.0 equiv), and Me_3Al (500 μL, 2.0 M in toluene, 1.0 mmol, 2.0 equiv). The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (17:3) to give **71** (129.6 mg, 73%) as a colorless oil: IR (film) 3416, 1651 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (1H, s, br), 7.65 (1H, d, $J = 7.8$ Hz), 7.28 (1H, d, $J = 7.9$ Hz), 7.19−7.05 (2H, m), 6.88 (1H, d, $J = 2.1$ Hz), 4.85 (1H, d, $J = 1.6$ Hz), 4.15−4.10 (1H, m), 2.47−2.36 (3H, m), 1.96−1.85 (1H, m), 1.15−1.00 (21H, m). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 155.9, 136.7, 126.7, 122.2, 121.8, 120.1, 119.4, 118.9, 111.1, 105.8, 38.6, 33.6, 30.6, 17.4, 12.5. HRMS (M^+) calcd for $C_{22}H_{33}NOSi$ 355.233, found 355.232.

3-(3-Indole)-1-triisopropylsilyl(oxy)-cyclohexan-1-one (72). Copper trifluoromethane sulfonate (II) (122 mg, 0.34 mmol, 1.0 equiv) was added to a solution of **33** (100 mg, 0.34 mmol, 1.0 equiv) and indole (54 mg, 0.47 mmol, 1.4 equiv) in CH_2Cl_2 (4 mL) at 25 °C. After 20 min CH_2Cl_2 (5 mL), a saturated aqueous solution of NH_4Cl and NH_4OH (1:1) (10 mL), and water (5 mL) were added. The phases was separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 10 mL). The organic phases were combined, washed with brine, and dried ($MgSO_4$). After filtration, the solvent was evaporated in vacuo, and the residue was purified by flash chromatography over silica gel eluting with CH_2Cl_2 to give **72** (38 mg, 52%): mp 105−106 °C (CH_2Cl_2). IR (CH_2Cl_2) 3468, 1708 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (1H, s, br), 7.55 (1H, d, $J = 7.8$ Hz), 7.28 (1H, d, $J = 8.0$ Hz), 7.17−7.02 (2H, m), 6.89 (1H, d, $J = 2.2$ Hz), 3.42−3.22 (1H, m), 2.76−2.69 (1H, m), 2.55 (1H, ddd, $J = 14.0$, 10.6, 0.7 Hz), 2.43−2.27 (2H, m), 2.21−2.14 (1H, m), 2.03−1.71 (3H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 209.6, 136.9, 126.7, 122.2, 120.6, 119.6, 119.5, 119.4, 111.5, 47.9, 41.5, 35.8, 31.7, 24.6. HRMS (M^+) calcd for $C_{14}H_{15}NO$ 213.115, found 213.115.

3-(3-Indole)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (73). Direct Addition Procedure. Me_3Al (250 μL, 2.0 M in toluene, 0.50 mmol, 2 equiv) was added to a solution of **33** (74 mg, 0.250 mmol, 1.0 equiv) and indole (58.6 mg, 0.50 mmol, 2 equiv) in CH_2Cl_2 (4 mL) at −65 °C. After 20 min a solution of saturated aqueous $NaHCO_3$ (10 mL) and water (10 mL) were added. The mixture was filtered through a Celite pad, and the aqueous phase was extracted with CH_2Cl_2 (4 × 10 mL). The combined extracts were washed with a brine, dried ($MgSO_4$), and evaporated in vacuo. The residue was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (4:1) to give **73** (71 mg, 82%) as a colorless oil: IR (film) 3419, 1662 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (1H, br), 7.63 (1H, d, $J = 7.8$ Hz), 7.33 (1H, d, $J = 8.0$ Hz), 7.17 (1H, td, $J = 7.6$, 0.85 Hz), 7.09 (1H, td, $J = 7.6$, 0.85 Hz), 6.93 (1H, d, $J = 2.1$ Hz), 5.06 (1H, d, $J = 3.45$ Hz), 3.83−3.79 (1H, m), 2.15−2.00 (2H, m), 1.99−1.93 (1H, m), 1.78−1.63 (4H, m), 1.25−1.00 (21H, m). ^{13}C NMR (75 MHz, APT, C_6D_6) δ 151.7, 137.4, 127.5, 122.4, 121.7, 121.5, 119.6, 119.3, 111.4, 107.1, 32.5, 30.5, 30.4, 21.4, 18.3, 13.1. HRMS (M^+) calcd for $C_{23}H_{35}NOSi$ 369.249, found 369.248.

***trans*- and *cis*-4-Methyl-3-(3-indolo)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (74 and 75). Direct Addition Procedure.** Me_3Al (500 μL, 2.0 M in toluene, 1.0 mmol) was added to a solution of **52** (155

mg, 0.500 mmol, 1.0 equiv) and indole (117 mg, 1.00 mmol, 2 equiv) in hexane (5 mL) at 0 °C. After 15 min Et_2O (10 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added. The mixture was filtered through Celite, and the phases were separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (15 mL) and brine (15 mL). The aqueous phase was extracted with Et_2O (15 mL) and EtOAc (15 mL), and the combined extracts were dried ($MgSO_4$) and evaporated in vacuo. The product was purified by flash chromatography over Florisil eluting with hexanes to give (**74** and **75**) (134 mg, 70%) as a colorless oil. ^{1}H NMR analysis shows the product to be a 4:1 mixture of diastereoisomers in favor of the *trans*-isomer **74**. At −70 °C, a *trans* and *cis* mixture (**74**:**75**, 2.3:1) was observed (130 mg, 68%). At −35 °C, from **52** (77 mg, 0.25 mmol), a *trans* and *cis* mixture (**74**:**75**, 3:1) was observed (34.7 mg, 36%). At 25 °C, from **52** (77 mg, 0.25 mmol), a *trans* and *cis* mixture (**74**:**75**, 5:1) was observed (60.7 mg, 63%). At 50 °C, a *trans* and *cis* mixture (**74**:**75**, 10:1) was observed (103 mg, 54%).

Reverse addItion Procedure. Me_3Al (0.5 mL, 2.0 M in toluene, 1.0 mmol, 2 equiv) was added to a solution of indole (117 mg, 1.0 mmol, 2.0 equiv) in hexane (5 mL) at 0 °C. After 5 min a solution of **33** (148 mg, 0.50 mmol, 1.0 equiv) in hexane (3 mL) was added. After 20 min Et_2O (20 mL) and saturated aqueous $NaHCO_3$ (10 mL) were added. Workup as above gave (**74** and **75**) (137 mg, 71%) as a colorless oil. ^{1}H NMR analysis showed the product to be a mixture of diastereoisomers (4.5:1) in favor of the *trans*-isomer. At 50 °C, a *trans* and *cis* mixture (**74**:**75**, 4.5:1) was observed (130 mg, 75%). At −70 °C, no formation of products was observed: IR (film) 3418, 1668 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ (major isomer) **74** 7.84 (1H, br), 7.63 (1H, d, J = 7.8 Hz), 7.30 (1H, d, J = 8.0 Hz), 7.19−7.04 (3H, m), 6.93 (1H, d, J = 2.2 Hz), 4.95−4.91 (1H, m), 3.34−3.30 (1H, m), 2.33−2.04 (2H, m), 1.88−1.77 (2H, m), 1.65−1.44 (1H, m), 1.20−1.05 (21H, m), 0.93 (3H, d, J = 6.5 Hz); δ (minor isomer) **75** 7.90 (1H, br), 7.63−7.04 (3H, m), 6.88 (1H, d, J = 2.2 Hz), 5.03 (1H, d, J = 4.4 Hz), 3.89−3.87 (1H, m), 2.33−1.4 (5H, m), 1.20−1.05 (21H, m), 0.66 (3H, d, J = 7.0 Hz). ^{13}C NMR (75 MHz, APT, C_6D_6) δ (major isomer) **74** 150.8, 137.1, 127.4, 122.0, 121.7, 121.0, 120.2, 119.2, 111.4, 107.5, 40.8, 35.2, 30.7, 29.8, 20.2, 18.4, 13.0; δ (minor isomer) **75** 150.9, 136.7, 128.6, 123.4, 121.9, 119.9, 119.4, 118.2, 111.3, 107.3, 36.4, 32.9, 29.6, 27.5, 20.2, 18.4, 13.1. HRMS (M^+) calcd for $C_{24}H_{37}NOSi$ 383.264, found 383.264.

***trans*-4-Isopropyl-3-indolo-1-cyclohexan-1-one (82).** Tetra-*n*-butylammonium fluoride (650 μL, 1.0 M in THF, 650 μmol) was added to a solution of **78** and **79** (130 mg, 0.32 mmol) in THF (3 mL). The mixture was stirred for 30 min, Et_2O (10 mL) and water (10 mL) were added, and the phases were separated. The organic layer was washed with water and brine. The aqueous layers were combined and extracted with Et_2O (10 mL). The combined extracts were dried (Na_2SO_4), and evaporated in vacuo. The product was purified by flash chromatography over silica gel eluting with hexanes/EtOAc (7:3) to give **82** (62 mg, 75%) as a colorless oil: IR (film) 3414, 1699 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (1H, s, br), 7.66 (1H, d, J = 7.9 Hz), 7.35 (1H, d, J = 7.9 Hz), 7.22−7.08 (2H, m), 6.96 (1H, d, J = 2.25 Hz), 3.28 (1H, dt, J = 4.7, 10.6 Hz), 2.83 (1H, dd, J = 11.2, 14.2 Hz), 2.63 (1H, ddd, J = 1.5, 4.7, 14.2 Hz), 2.54−2.46 (2H, m), 2.18−2.00 (2H, m), 1.86−1.72 (1H, m), 1.66−1.52 (1H, m), 0.93 (3H, d, 6.9 Hz), 0.75 (3H, d, J = 6.9 Hz). ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 212.1, 137.8, 126.0, 121.9, 121.5, 119.2, 119.1, 118.3, 11.4, 48.3, 46.1, 40.9, 39.5, 27.2, 24.5, 21.7, 16.1. HRMS (M^+) calcd for $C_{17}H_{21}NO$ 255.162, found 255.162.

3-Amino-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (83). To a mixture of 1-triisopropylsilyl(oxy)cyclohexene (15.26 g, 60.0 mmol) and iodosylbenzene (15.84 g, 72.0 mmol) in CH_2Cl_2 (600 mL) at −20 °C (internal temperature) under argon was added trimethylsilyl azide (19.1 mL, 144.0 mmol) over a 15 min period. The cold bath was removed after 15 min, and the mixture was allowed to warm to 25 °C. The solution was concentrated in vacuo to a yellow paste. The paste was dissolved in Et_2O (100 mL) and added slowly to a suspension of $LiAlH_4$ (2.28 g, 60.0 mmol) in Et_2O (200 mL) at 0 °C. After the reaction was complete (30 min), the solution was quenched at 0 °C by sequential addition of water (2.3 mL), 15% aqueous NaOH solution (2.3 mL), and water (7.0 mL). After stirring for 1 h the white precipitate was filtered, and the filtrate was dried (Na_2SO_4) and concentrated in vacuo. The residue was chromatographed over silica gel eluting with EtOAc/MeOH/NH_4OH (16:4:1), and the product fractions were combined and concentrated in vacuo. The residue was taken up in CH_2Cl_2 (300 mL), washed with a 3 N aqueous NaOH solution (2 × 40 mL), and dried (Na_2SO_4). Concentration in vacuo afforded **83** (11.69 g, 73%) as an oil: IR (neat) 3352, 1662 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 4.84, (1 H, d, J = 4.3 Hz), 3.37 (1H, m), 1.97 (2H, m), 1.73 (2H, m), 1.54 (1H, m), 1.26 (2H, s), 0.95−1.30 (22H, m). ^{13}C NMR ($CDCl_3$) δ 152.3, 109.3, 47.0, 33.4, 29.8, 19.8, 17.9, 12.6. MS-CI *m/e* 270 (M + 1), 253 (100). Used directly in the next stage.

3-(Propenoylamino)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (84). A solution of **83** (1.347 g, 5.00 mmol) and Et_3N (1.050 mL, 7.50 mmol) in THF (30 mL) was treated at −78 °C with acryloyl chloride (0.490 mL, 6.00 mmol). After 10 min the mixture was warmed to 25 °C and partitioned between Et_2O (30 mL) and 50% saturated aqueous $NaHCO_3$ (30 mL). The aqueous phase was extracted with Et_2O (2 × 15 mL). The organic phases were combined, washed with water (25 mL), dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography over silica gel eluting with EtOAc to give **84** (1.444 g, 89%) as an oil which crystallized upon standing: mp 66−67 °C. IR (neat) 3274, 1653, 1623 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 6.19, (1H, dd, J = 16.9, 1.6 Hz), 6.03 (1H, dd, J = 17.0, 10.1 Hz), 5.77 (1H, d, J = 7.9 Hz), 5.54 (1H, dd, J = 10.1, 1.6 Hz), 4.78 (1H, d, J = 4.2 Hz), 4.58 (1H, m), 2.00 (2H, m), 1.4−1.8 (4H, m), 0.8−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 164.4, 154.9, 131.1, 125.9, 103.9, 44.7, 29.7, 28.8, 19.4, 17.8, 12.5. HRMS (CI) calcd for $C_{18}H_{34}NSiO_2$ 324.236, found 324.236.

***cis*-Octahydro-5-triisopropylsilyl(oxy)-quinoline-2-one (87), 5-Aza-10-triisopropylsilyl(oxy)-tricyclo[4.4.0.0^{3,10}]-4-decanone (85) and (88/89). Cyclization of 84 at 80 °C.** To a solution of **84** (0.162 g, 0.50 mmol) in dry 1,2-dichloroethane (5 mL) was added Me_3Al (0.33 mL, 0.65 mmol, 2.0 *M* solution in toluene) at 0 °C. The mixture was heated at reflux under argon for 42 h, cooled to 0 °C, dissolved in CH_2Cl_2 (30 mL), washed with saturated aqueous $NaHCO_3$ (35 mL), and dried (Na_2SO_4). Concentration in vacuo followed by flash chromatography afforded **87** (0.015 g, 9%): mp 118−119 °C. IR (neat) 3209, 1668, 1658 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 5.70 (1H, s), 4.83 (1H, t, J = 3.6 Hz), 3.68 (1H, m), 2.45 (1H, m), 2.30 (2H, m), 1.9−2.1 (4H, m), 1.5−1.7 (6H, m), 0.9−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 172.5, 149,1, 102.2, 51.7, 37.0, 29.5, 27.7, 22.2, 20.5, 18.1, 16.7. HRMS (MH^+) calcd for $C_{18}H_{34}NSiO_2$ 324.2359, found 324.2349. **85** (0.070 g, 43%): mp 166−167 °C. IR ($CHCl_3$) 3680, 2946, 1669 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 7.29 (1H, s), 3.38 (1H, s), 2.97 (1H, t, J = 5.8 Hz), 2.68 (1H, dt, J = 8.3, 5.4 Hz), 1.98 (1H, q, J = 5.3 Hz), 1.88 (1H, m), 1.2−1.5 (5H, m), 0.8−1.1 (21H, m). ^{13}C NMR (C_6D_6) δ 178.5, 78.6, 54.5, 49.7, 44.8, 33.1, 29.0, 28.4, 18.6, 17.8, 13.6. HRMS (MH^+) calcd for $C_{18}H_{34}NSiO_2$ 324.2359, found 324.2363. A solution of **85** (6 mg, 0.019 mmol) in THF (2 mL) was treated with TBAF (0.020 mL, 1.05 equiv 1, M in THF) at −78 °C for 5 min. The mixture was concentrated in vacuo, and the residue was dissolved in dichloromethane (10 mL), washed with saturated aqueous $NaHCO_3$ (2 × 3 mL), and dried (Na_2SO_4). Evaporation of the extract in vacuo gave **88**/**89** (3.5 mg, 97%, 7:1 ratio).[55]

Cyclization of 84 at 180 °C. A solution of **84** (0.050 g, 0.15 mmol) in dry 1,2-dichlorobenzene (5 mL) was treated at 0 °C with Me_3Al (0.190, 0.38 mmol, of 2.0 *M* solution in toluene). The solution was heated to reflux under argon. Upon reaction completion (30 min) the solution was quenched at 0 °C with saturated aqueous $NaHCO_3$ (1 mL). The organic phase was dried ($MgSO_4$) and evaporated in vacuo. The residue was purified by flash chromatography over silica gel eluting with EtOAc to give **87** (0.005 g, 10%) and **86** (0.021 g, 42%): mp 110−111 °C. IR (neat) 3237, 1699, 1665 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 6.13 (1H, s), 4.99 (1H, t, J = 3.8 Hz), 3.72 (1H, m), 3.03 (1H, t, J = 8.6 Hz), 2.59 (1H, dt, J = 9.4, 7.7 Hz), 1.9−2.2 (2H, m), 1.80 (1H, m), 1.45 (1H, m), 1.25 (3H, d, J = 7.7 Hz), 0.9−1.2 (21H, m). ^{13}C

(58) **Important Cautionary Information:** Reactions involving $TMSN_3$ are capable of being violently explosive. It is important to make certain that the evolution of dinitrogen is *complete* before work-up. The reactions must *not* be allowed to run dry and should be conducted behind a *safety shield*.

NMR ($CDCl_3$) δ 180.6, 148.7, 104.1, 53.0, 41.9, 38.7, 29.4, 20.8, 18.0, 14.2, 12.6. HRMS (CI) calcd for $C_{18}H_{34}NSiO_2$ 324.236, found 324.235.

3-((*E*)-3-Phenylpropenoylamino)-1-triisopropylsilyl(oxy)-cyclohexan-1-ene (90). A solution of **83** (1.88 g, 7.00 mmol) and Et_3N (1.50 mL, 10.50 mmol) in THF (40 mL) was treated at −78 °C with cinnamoyl chloride (1.290 g, 7.70 mmol) in THF (4 mL). After completion of the reaction (5 min), the cold bath was removed and the solution partitioned between Et_2O (30 mL) and saturated aqueous $NaHCO_3$ (30 mL). The aqueous phase was extracted with Et_2O (2 × 15 mL). The extracts were combined, washed with water (2 × 10 mL), and dried ($MgSO_4$). Concentration in vacuo afforded an oil which crystallized from *n*-pentane to give **90** (2.480 g, 89%) as a white powder: mp 152−153 °C. IR (neat) 3267, 1654 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.59 (1H, d, J = 15.6 Hz), 7.47 (2H, m), 7.33 (3H, m), 6.34 (1H, d, J = 15.6 Hz), 5.57 (1H, d, J = 8.1 Hz), 4.86 (1H, d, J = 4.3 Hz), 4.70 (1H, m), 2.07 (2H, t, J = 5.5 Hz), 1.5−1.9 (4H, m), 0.9−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 164.8, 155.2, 140.8, 134.9, 129.5, 128.7, 127.7, 121.1, 104.0, 45.0, 29.8, 29.0, 19.5, 17.9, 12.6. HRMS (CI) calcd for $C_{24}H_{37}NSiO_2$ 399.259, found 399.260.

3-[(*E*)-3-(4-Nitrophenyl)-propenoylamino]-1-triisopropylsilyl-(oxy)-cyclohexan-1-ene (91). A solution of 4-nitrocinnamoyl chloride (1.164 g, 5.50 mmol) in THF (10 mL) was added to **83** (1.348 g, 5.00 mmol) and Et_3N (1.050 mL, 7.50 mmol) in THF (25 mL) at −78 °C. After the reaction was complete, the cold bath was removed, and the solution was partitioned between CH_2Cl_2 (80 mL) and saturated aqueous $NaHCO_3$ (40 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic phase was washed with brine (40 mL), and water (20 mL) and dried ($MgSO_4$). Concentration in vacuo gave **91** (2.124 g, 96%): mp 62 °C. IR (neat) 3261, 2943, 1657 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.19 (2H, d, J = 8.7 Hz), 7.63 (1H, d, J = 15.9 Hz), 7.61 (2H, d, J = 8.2 Hz), 6.47 (1H, d, J = 15.6 Hz), 5.69 (1H, d, J = 8.0 Hz), 4.85 (1H, d, J = 4.1 Hz), 4.69 (1H, m), 2.07 (1H, t, J = 5.5 Hz), 1.5−1.9 (4H, m), 0.9−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 163.7, 155.4, 148.0, 141.2, 138.0, 128.2, 125.3, 124.0, 103.6, 45.3, 29.7, 28.9, 19.4, 17.9, 12.5. HRMS (MH^+) calcd for $C_{24}H_{37}N_2SiO_4$ 445.252, found 445.252.

3-Benzyl-4-triisopropylsilyl(oxy)-1,3,3a,6,7,7a-hexahydro-2H-indol-2-one (92). A solution of **90** (0.40 g, 1.0 mmol) in dry 1,2-dichlorobenzene (40 mL) was treated at 0 °C with Me_3Al (0.550 mL, 1.10 mmol, 2.0 *M* solution in toluene). The ice bath was removed and the solution warmed to 25 °C and then heated to reflux under argon. After 20 h the mixture was cooled to 0 °C and quenched with saturated aqueous $NaHCO_3$ (1 mL) and concentrated under high vacuum at 50 °C. The residue was dissolved in CH_2Cl_2 (100 mL), washed with saturated aqueous $NaHCO_3$ (2 × 15 mL) and water (10 mL), and dried (Na_2SO_4). Flash chromatography over silica gel eluting with EtOAc gave **92** (0.292 g, 73%): mp 156 °C. IR (neat) 3223, 1698, 1664 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.82 (1H, s), 7.55 (2H, d, J = 7.3 Hz), 7.0−7.2 (3H, m), 4.92 (1H, dd, J = 4.5, 2.9 Hz), 3.27 (1H, dd, J = 14.2, 3.6 Hz), 3.12 (1H, m), 3.00 (1H, dd, J = 14.2, 8.5 Hz), 2.86 (1H, td, J = 8.8, 3.7 Hz), 2.76 (1H, t, J = 8.3 Hz), 1.7−1.9 (1H, m), 1.6−1.7 (1H, m), 1.3−1.5 (1H, m), 0.9−1.2 (22H, m). ^{13}C NMR ($CDCl_3$) δ 170.8, 148.2, 140.6, 129.2, 128.0, 125.9, 105.2, 52.7, 44.9, 42.7, 35.5, 29.2, 21.2, 18.1, 12.6. HRMS (MH^+) calcd for $C_{24}H_{38}NSiO_2$ 400.267, found 400.268.

3-(4-Nitrobenzyl)-4-triisopropylsilyl(oxy)-1,3,3a,6,7,7a-hexahydro-2H-indol-2-one (93) and 8-(4-Nitrophenyl)-5-aza-10-triisopropylsilyl(oxy)-tricyclo[4.4.0.0^{3,10}]-decan-4-one (94). A solution of **91** (0.444 g, 1.00 mmol) in toluene (45 mL) was treated at 0 °C with Me_3Al (0.550 mL, 1.10 mmol, 2.0 *M* solution in toluene). The solution was heated to reflux under argon. After 22 h the mixture was cooled to 0 °C and quenched with water (0.5 mL), partitioned between Et_2O (200 mL) and saturated aqueous Rochelle's salt solution (100 mL). The organic phase was washed with a 50% saturated aqueous $NaHCO_3$ (50 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography over silica gel eluting with EtOAc gave **93** (0.326 g, 74%): mp 146−148 °C. IR ($CHCl_3$) 3430, 1694, 1665 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.09 (2H, d, J = 8.6 Hz), 7.41 (2H, d, J = 8.6 Hz), 6.47 (1H, s), 5.10 (1H, t, J = 3.7 Hz), 3.71 (1H, m), 3.23 (1H, dd, J = 13.4, 3.0 Hz), 3.16 (1H, t, J = 8.0 Hz), 2.82 (1H, m), 2.80 (1H, qd, J = 13.4, 3.6 Hz), 1.95−2.20 (2H, m), 1.80−1.95 (1H, m), 0.60−1.40 (22H, m). ^{13}C NMR ($CDCl_3$) δ 178.3, 148.7, 147.9, 146.4, 129.9, 123.4, 105.7, 52.8, 44.6, 42.5, 35.4, 29.3, 21.1, 18.0, 12.5. HRMS (MH^+) calcd for $C_{24}H_{37}N_2SiO_4$ 445.252, found 445.251. **94** (40 mg, 9%). IR ($CHCl_3$) 3421, 3023, 2946, 2867, 1692 cm^{-1}. ^1H NMR ($CDCl_3$) δ 8.12 (2H, d, J = 8.6 Hz), 7.36 (2H, d, J = 8.6 Hz) 5.52 (1H, b), 4.21−4.17 (1H, m), 3.85 (1H, d, J = 7.2 Hz), 3.42−3.36 (1H, m), 2.85−2.78 (1H, m), 2.0−1.0 (6H, m), 0.95−0.80 (21H, m). ^{13}C NMR ($CDCl_3$) δ 178.9, 146.5, 145.7, 129.4, 122.9, 77.1, 52.6, 51.8, 41.6, 40.0, 36.3, 28.4, 18.0, 16.7, 13.1. HRMS (MH^+) calcd for $C_{24}H_{37}N_2SiO_4$ 445.252, found 445.251.

1,3,3a,6,7,7a-hexahydro-3-benzyl-2H-indol-2,4-dione (95). To a solution of **92** (50 mg, 0.125 mmol) in THF (5 mL) at −78 °C was added *n*-Bu_4NF (0.13 μL, 1.0 M in Et_2O). The solution was warmed to 25 °C and after 20 min the solution was evaporated in vacuo and the residue purified by chromatography over silica gel eluting with EtOAc to give **95** (27 mg, 90%): mp 119−121 °C (Et_2O). IR (neat) 3251, 1695 cm^{-1}. ^1H NMR ($CDCl_3$) δ 7.99 (1H, s), 7.29 (2H, d, J = 7.2 Hz), 7.15 (2H, m), 7.07 (1H, d, J = 7.3 Hz), 3.73 (1H, dd, J = 14.0, 9.8 Hz), 3.43 (1H, dd, J = 14.0, 5.1 Hz), 3.20 (1H, dt, J = 5.1, 4.2 Hz), 2.48 (1H, m), 2.15 (1H, t, J = 6.6 Hz), 1.88 (1H, dt, J = 13.8, 4.6 Hz), 1.4−1.7 (2H, m), 1.2−1.4 (1H, m), 1.0−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 210.3, 178.3, 139.8, 129.1, 128.3, 126.2, 55.0, 49.7, 47.8, 41.3, 32.0, 27.9, 20.2. HRMS (MH^+) calcd for $C_{15}H_{18}NO_2$ 244.134, found 244.135.

6-Azido-1,3,3a,6,7,7a-hexahydro-3-benzyl-4-triisopropylsilyl(oxy)-2H-indol-2-one (96). Iodosobenzene (660 mg, 3 mmol, 3.0 equiv) was added to a solution of **92** (400 mg, 1 mmol) in CH_2Cl_2 (20 mL) at −20 °C, and trimethylsilylazide 95% (728 mg, 0.84 mL, 6 mmol, 6 equiv) was added via syringe. The cooling bath was removed and the reaction temperature allowed to warm to 25 °C. After 1 h the clear yellow solution was concentrated under reduced pressure (first at the rotaevaporator, then in a Kugelrohr at high vacuum at 70 °C) to give an oily residue (663 mg). Chromatography over Florisil eluting with EtOAc/hexanes (1:2) followed by pentane washing of the resulting solid gave **96** (266.5 mg, 60.5%): mp 147−148 °C (MeCN). IR ($CHCl_3$) 2094, 1692, 1649 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) 7.28−7.16 (5H, m), 5.74 (1H, br), 5.26 (1H, d, J = 5.9 Hz), 4.16 (1H, m), 3.97 (1H, m), 3.29 (1H, t, J = 8.8 Hz), 3.14 (1H, d,d, J = 3.5, 13.6 Hz), 2.87 (1H, dt, J = 3.6, 9.3 Hz), 2.74 (1H, dd, J = 13.6, 9.2 Hz), 1.96 (1H, d, J = 13.5 Hz), 1.4−1.0 (22H, m). ^{13}C NMR ($CDCl_3$) 178.2, 154.1, 139.5, 129.4, 128.2, 126.4, 102.5, 55.7, 48.8, 44.3, 42.5, 35.1, 34.8, 18.1, 18.0, 12.5. HRMS (MH^+) calcd for $C_{24}H_{37}N_4O_2Si$ 441.269, found 441.268.

(*E*)-3-(Carboethoxy)-propenoylamino-1-triisopropylsilyl(oxy)-cyclohexan-1-ene 97. A solution of fumaric acid monoethyl ester (0.303 g, 2.10 mmol) and *N*-methylmorpholine (0.250 mL, 2.28 mmol) in THF (50 mL) was treated with isobutylchloroformate (0.275 mL, 2.10 mmol) at 0 °C. After 15 min at 0 °C, **83** (0.472 g, 1.75 mmol) in THF (10 mL) was added. The ice bath was removed after 15 min, and the mixture was dissolved in Et_2O (60 mL), washed with saturated aqueous $NaHCO_3$ (2 × 15 mL), and dried (Na_2SO_4). Chromatography over silica gel eluting with EtOAc gave **97** (0.666 g, 96%) as a white powder: mp 99−100 °C. IR (neat) 1726, 1661, 1634 cm^{-1}. ^1H NMR ($CDCl_3$) δ 6.97 (1H, d, J = 15.4 Hz), 6.75 (1H, d, J = 15.4 Hz), 6.45 (1H, d, J = 8.2 Hz), 4.77 (1H, d, J = 4.1 Hz), 4.60 (1H, m), 4.15 (2H, q, J = 7.1 Hz), 2.00 (2H, t, J = 6.3 Hz), 1.4−1.8 (4H, m), 1.23 (3H, t, J = 7.1 Hz), 0.8−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 165.8, 162.5, 155.1, 137.1, 129.7, 103.3, 61.0, 45.1, 29.7, 28.7, 19.3, 17.8, 14.0, 12.4. HRMS (CI) calcd for $C_{21}H_{37}NSiO_4$ 395.249, found 395.249.

3-Carboethoxymethyl-4-triisopropylsilyl(oxy)-1,3,3a,6,7,7a-hexahydro-2H-indol-2-one (98) and 8-Carboethoxy-5-aza-10-triisopropylsilyl(oxy)-tricyclo[4.4.0.0^{3,10}]-decan-4-one (99). A solution of **97** (0.079 g, 0.20 mmol) in 1,2-dichloroethane (8 mL) was treated with Me_3Al (0.200 mL, 0.40 mmol, 2.0 *M* solution in toluene) at 0 °C. The solution was heated to reflux under argon until completion of the reaction (3 h). The mixture was cooled to 0 °C and quenched with water (0.5 mL). The crude mixture was dissolved in CH_2Cl_2 (20 mL), washed with saturated aqueous $NaHCO_3$ (2 × 5 mL), and dried (Na_2SO_4). After concentration in vacuo the residue was purified by flash chromatography over silica gel eluting with EtOAc to give **98** (0.040 g, 51%) and **99** (0.019 g, 24%). For **98**: mp 100−102 °C. IR (neat) 1734, 1700, 1684, 1668, 1653 cm^{-1}. ^1H NMR ($CDCl_3$) δ 6.19 (1H, s), 5.00 (1H, t, J = 4.4 Hz), 4.0−4.2 (2H, m), 3.92 (1H, dt, J = 6.0, 5.1 Hz), 3.21 (1H, dt,

J = 9.0, 6.9 Hz), 3.09 (1H, t, J = 7.9 Hz), 2.75 (1H, dd, J = 17.1, 7.1 Hz), 2.64 (1H, dd, J = 17.1, 6.6 Hz), 2.10 (1H, m), 1.90 (1H, m), 1.60 (2H, m), 1.22 (3H, t, J = 7.1 Hz), 0.8−1.2 (21H, m). ^{13}C NMR ($CDCl_3$) δ 178.2, 172, 5, 148.4, 105.4, 60.4, 52.4, 41.6, 41.1, 32.8, 27.3, 19.4, 18.0, 14.1, 12.6. HRMS (MH^+) calcd for $C_{21}H_{38}NSiO_4$ 396.257, found 396.258. For **99**: mp 120 °C. IR (neat) 3216, 2942, 2867, 1739, 1699 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 6.20 (1H, s), 4.19 (1H, m), 4.08 (1H, m), 3.99 (1H, m), 3.51 (1H, dd, J = 9.0, 6.6 Hz), 3.30 (1H, d, J = 6.7 Hz), 2.73 (1H, t, J = 9.4 Hz), 2.00 (1H, d, J = 12.9 Hz), 1.6−1.8 (3H, m), 1.4−1.5 (2H, m), 1.21 (3H, t, J = 7.1 Hz), 1.00 (21H, s). ^{13}C NMR ($CDCl_3$) δ 178.5, 169.0, 76.4, 60.7, 51.9, 51.5, 42.0, 36.4, 35.8, 28.6, 18.2, 16.4, 14.1, 13.1. HRMS (MH^+) calcd for $C_{21}H_{38}NSiO_4$ 396.257, found 396.256.

3-Carboethoxymethyl-1,3,3a,6,7,7a-hexahydro-2H-indol-2,4-dione (100). A solution of **98** (0.040 g, 0.101 mmol) in THF (4 mL) at 0 °C was treated with *n*-Bu_4NF (0.111 mL, 0.111 mmol, 1.0 *M* solution in THF). After the reaction was complete (5 min), the solution was concentrated in vacuo and applied to a short column of silica gel eluting with EtOAc to give **100** (0.020 g, 83%) as an oil: IR (neat) 3261, 2939, 1699 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 6.00 (1H, s), 4.19 (1H, m), 4.10 (2H, q, J = 7.1 Hz), 3.16 (1H, t, J = 7.6 Hz), 3.04 (1H, m), 2.93 (2H, d, J = 6.4 Hz), 2.40 (1H, m), 2.30 (1H, m), 1.7−2.1 (4H, m), 1.23 (3H, t, J = 7.1 Hz). ^{13}C NMR ($CDCl_3$) δ 209.9, 177.4, 172.7, 60.6, 53.5, 48.6, 41.8, 40.8, 31.0, 27.5, 18.4, 14.16. HRMS (MH^+) calcd for $C_{12}H_{18}NO_4$ 240.124, found 240.124.

3-((*E*)-4-Nitrocinnamoylamino)-2-methyl-1-triisopropylsilyl(oxy)-cyclohex-1-ene (103). To a solution of **101** (1.8 g) in THF (50 mL) and Et_3N (2.75 mL, ca. 3 equiv) was treated with (*E*)-4-nitrocinnamoyl chloride (1.2 g) at −70 °C. After 20 min the cooling bath was removed and the slurry diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and evaporated in vacuo. The residue was purified by chromatography over silica gel eluting with EtOAc/hexanes (1:4) to give **103** (336 mg) of pure product as a viscous oil along with 468 mg of a slightly impure fraction: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (2H, d, J = 9 Hz), 7.7 (1H, d, J = 13 Hz), 7.65 (2H, d, J = 9 Hz), 6.5 (1H, d, J = 13 Hz), 5.65 (1H, d, J = 10 Hz), 4.55 (1H, br), 2.25−2.0 (2H, m), 1.9−1.4 (4H, m), 1.65 (3H, s), 1.3−0.9 (21H). Used directly in the next step.

3a-Methyl-3-(4-nitrobenzyl)-4-triisopropylsilyl(oxy)-1,3,3a,6,7,7a-hexahydro-2H-indol-2-one (105). All glassware was treated with hexamethyldisilazane for 24 h and oven dried prior to use. A solution of **103** (266 mg, 0.58 mmol) in toluene (10 mL) was treated with Me_3-Al (0.34 mL, 2M in toluene, 1.2 equiv) at 25 °C and heated at reflux for 41 h. The solution was cooled to 25 °C and water (1 mL) added. The mixture was extracted with EtOAc (2 × 10 mL), washed twice with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$), and concentrated in vacuo. The crude oil (228 mg) was purified by chromatography over silica gel eluting with Et_2O/pentane (4:1) to give **105** (122 mg, 46%): mp 134−136 °C (pentane). IR ($CHCl_3$) 3430, 1696 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (2H, d, J = 8.6 Hz), 7.42 (2H, d, J = 8.6 Hz), 6.02 (1H, s), 5.00 (1H, t, J = 4.2 Hz), 3.38 (1H, dd, J = 3.9, 10.2 Hz), 3.30 (1H, dd, J = 2.8 Hz, 14.2 Hz), 2.85 (1H, dd, J = 11.4, 14 Hz), 2.40 (1H, dd, J = 3.0, 11.3 Hz), 2.2−1.95 (2H, m), 1.65−1.45 (1H, m), 1.43 (3H, s), 1.37−0.9 (21H, m). ^{13}C NMR ($CDCl_3$) δ 177.7, 151.2, 148.8, 146.3, 129.8, 123.4, 103.1, 60.4, 52.9, 46.3, 35.9, 28.5, 26.7, 20.6, 18.3, 12.8. HRMS (MH^+) calcd for $C_{25}H_{39}N_2O_4Si$ 459.268, found 459.266.

3-((*E*)-4-Nitrocinnamoylamino)-2-phenyl-1-triisopropylsilyl(oxy)-cyclohex-1-ene (104). 4-Nitrocinnamoyl chloride (1.7 g, 8 mmol) was added to a solution of **102** [2.79 g, crude, assay approximately 50−60%, Et_3N (2.45 g, 3.4 mL, 24 mmol)] in THF (100 mL) at −60 °C. After 5 min the temperature was allowed to rise to 25 °C and after 10 h diluted with EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (10 mL) followed by brine (10 mL), dried ($MgSO_4$), and concentrated to give **104** (4.2 g of crude material). Purification by chromatography over silica gel eluting with hexanes/EtOAc (5:1 to 4:1) gave **104** (1.217 g): mp 160−162 °C (Et_2O). Further purification of the mixed fractions including mother liquors yielded another crop of **104** (495 mg, mp 157 °C). Overall yield of **104** based on the azide is 32.9%: IR ($CHCl_3$) 3434, 1662, 1625 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.18 (2H, d, J = 8.7 Hz), 7.55 (2H, d J = 8.7 Hz), 7.50 (1H, d, J = 15.5 Hz), 7.35 (2H, d, J = 7.3 Hz), 7.26 (2H, t, J = 7.5 Hz), 7.14 (1H, t, J = 7.3 Hz), 6.30 (1H, d, J = 15.5 Hz), 5.60 (1H, d, J = 7.5 Hz), 5.11−5.09 (1H, m), 2.4−2.2 (2H, m), 2.1−2.0 (1H, m), 1.95−1.7 (3H, m), 1.0−0.8 (21H, m). ^{13}C NMR (75 MHz, C_6D_6) δ 163.6, 150.7, 148.0, 141.1, 138.4, 137.9, 129.6, 126.7, 125.4, 123.7, 116.5, 48.6, 31.5, 28.8, 19.2, 18.0, 13.5. HRMS (MH^+) calcd for $C_{30}H_{41}N_2O_4Si$ 521.284, found 521.283.

3-(4-Nitrobenzyl)-3a-phenyl-4-triisopropylsilyl(oxy)-1,3,3a,6,7,7a-hexahydro-2H-indol-2-one (106). A solution of the amide **104** (521 mg. 1 mmol) in *p*-xylene (10 mL) was treated with Me_3Al (0.55 mL, 2 M in toluene, 1.1 equiv) at 25 °C. and then heated to reflux for 24 h. The mixture was cooled to 25 °C and EtOAc (10 mL) added. The mixture was washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried ($MgSO_4$), treated with activated charcoal, and concentrated to give **106** (508 mg of crude). Purification by chromatography over silica gel eluting with Et_2O/hexanes (4:1) gave the starting material (58 mg, 11%), and **106** (113 mg, 24.4%): mp 203−204 °C (Et_2O). IR ($CHCl_3$) 3431, 1700 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 (2H, d, J = 8.6 Hz), 7.51 (2H, d, J = 8.6 Hz), 7.43 (2H, d, J = 7.4 Hz), 7.33 (2H, t, J = 7.4 Hz), 7.26 (1H, d, J = 7,4 Hz), 5.71 (1H, br), 5.28 (1H, t, J = 4.2 Hz), 3.66 (1H, dd, J = 3.8 Hz, J = 8.6 Hz), 3.40 (2H, d, J = 11.6 Hz), 3.07 (1H, dd, J = 11.7, 14.4 Hz), 2.4−2.2 (2H, m), 2.1−1.9 (1H, m), 1.9−1.7 (1H, m), 1.2−0.8 (21H, m). ^{13}C NMR (75 MHz, $CDCl_3$) 177.0, 150.2, 148.8, 146.5, 143.7, 130.0, 128.5, 127.1, 126.8, 123.6, 105.2, 62.0, 55.2, 49.1, 35.3, 26.8, 20.5, 18.3, 18.0, 12.7. HRMS (MH^+) calcd for $C_{30}H_{41}N_2O_4Si$ 521.284, found 521.284.

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Supporting Information Available: Complete experimental details and spectral information for compounds **10**, **12**, **14**, **16**, **18**, **18a**, **20**, **22**, **24**, **26**, **28**, **30**, **32**, **38**, **40**, **44**, **45**, **46**, **53**, **56**, **60**, **73**, **76**, **77**, **78**, **79**, **101**, **102**, and X-ray crystallographic data for **85** and **86** is available (22 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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