Hypervalent Iodine Chemistry: New Oxidation Reactions Using the Iodosylbenzene−Trimethylsilyl Azide Reagent Combination. Direct α- and β-Azido Functionalization of Triisopropylsilyl Enol Ethers

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Abstract: Treatment of triisopropylsilyl (TIPS) enol ethers with PhIO/$TMSN_3$/at −18 to −15 °C rapidly (5 min) gave β-azido TIPS enol ethers in high yields, with only traces of the α-azido adduct. The reaction is very sensitive to temperature changes, with the α-pathway being favored at −78 °C and the β-pathway at −15 to −20 °C. Addition of catalytic amounts of the stable radical TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl) significantly reduced the β-azidonation and increased the α-azidonation reaction. A mechanistic hypothesis is presented that offers a clear distinction between the α- and β-functionalization pathways. The key difference between the two reactions is that the α-pathway is an azide radical addition process and the β-pathway involves ionic dehydrogenation. Efforts to extend the unusual β-functionalization reaction to other trimethylsilyl derivatives (TMSX) were unsuccessful. The reagent combination PhIO/$TMSN_3$ is the only system we have found that results in clean, high-yield β-functionalization. Attempts to substitute iodine with S, Se, P, As, or Te did not result in an active oxidant, although in the case of diphenyltelluroxide we were able to isolate the stable crystalline adduct bis[azidodiphenyltellurium(IV)] oxide.

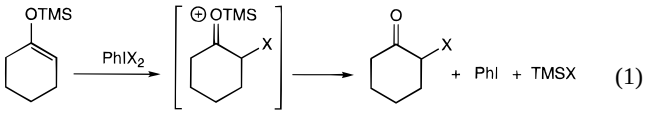
Introduction

The last decade has witnessed a substantial renaissance in hypervalent iodine chemistry, and a number of useful new reactions have been discovered.[1] Most of these transformations involve oxidation of an organic substrate with concomitant reduction of I^{III} to the more stable monovalent oxidation state.[2] Much of the organic chemistry of iodosylarenes ($ArI^{III}O$) is similar to that of lead tetraacetate and derives its driving force from the less stable hypervalent oxidation states compared to the lower I^{I} and Pb^{II} oxidation levels. This should be contrasted with sulfur and selenium chemistry, where the hypervalent oxidation states are relatively stable.

Part of the recent attraction of iodosylarene chemistry is that the reduction product iodoarene is usually inert to the reaction conditions, easy to remove from the other reaction product(s), and relatively innocuous. This should be compared with the notorious toxicity of lead, tellurium, and selenium compounds. The recent excellent review articles by Moriarty, Vaid, Koser and Stang and an outstanding book by Varvoglis provide an up-to-date critical picture of the past, present, and potential future of hypervalent organoiodine chemistry.[3]

We were particularly attracted to reactions that produce electrophilic aminating reagents, since our studies on the synthesis of calicheamicin γ_1 have involved in part the introduction of nitrogen functionality adjacent to a carbonyl group.[4] Trimethylsilyl azide ($TMSN_3$) has been used in combination with $Pb(OAc)_4$ and reacts with carbon−carbon double bonds to give α-azido ketones.[5] Ehrenfreund and Zbiral have treated alkenes with $PhI(OAc)_2$/$TMSN_3$ and isolated either α-azido ketones or cyano acid derivatives where the double bond had been cleaved, depending on the substitution of the alkene. Moriarty and Khosrowshahi have treated alkenes with a combination of iodosylbenzene/acetic acid/sodium azide and isolated vicinal bis-azido derivatives.[6] It appears that this reaction and the equivalent $PhI(OAc)_2$/$TMSN_3$ reagent combination involve the production of azido radicals. In the last few years azido radicals have been implicated in a number of reactions.[7]

Introduction of a substituent α to a carbonyl group utilizing hypervalent iodine chemistry is known and has been well studied. For example, treatment of trimethylsilyl (TMS) enol ethers or β-diketones with hypervalent iodine compounds ($PhIX_2$) generates ketones substituted at the α-position by the ligand X that was bound to iodine, eq 1.[8]



(1)

Because of the diversity of ligands that can be bound to iodine(III), this chemistry allows the synthesis of a large number of α-substituted derivatives such acetate, tosylate, chloride,

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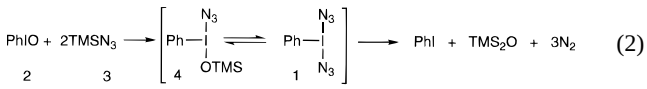
bromide, and azide (for β-dicarbonyl compounds).[9] Since our objective was the introduction of a nitrogen functional group, the use of (diazidoiodo)benzene $PhI(N_3)_2$ (**1**) was considered for the introduction of nitrogen functionality as an azido group. Compound **1** is made *in situ* from a combination of $(PhIO)_n$ (**2**) and $TMSN_3$ (**3**). It was assumed that the derivatives formed from the combination of **2** and **3** are **1** and **4**, eq 2.[10]



2 3 4 1 (2)

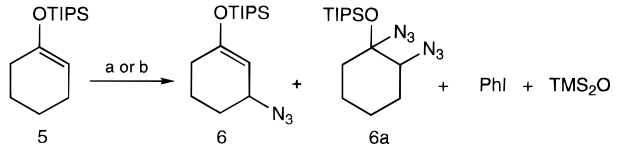
(PhIO is a polymeric solid, but for convenience it is written as a monomer)

Zefirov, Zhdankin, and Stang have reported a general method for the synthesis of hypervalent iodine compounds $PhIX_2$, also based on the reaction of **2** with trimethylsilyl reagents TMSX.[11] The thermodynamically favored formation of two silicon−oxygen bonds (TMS_2O) shifts the equilibrium of this reaction toward $PhIX_2$. The reaction between **2** and **3** takes place between −78 and −50 °C to form a pale yellow solution (in CH_2Cl_2). If the solution is warmed to −30 °C, the reaction products (or product) decompose(s) and dinitrogen is evolved. Presumably the dinitrogen arises from the dimerization of azido radicals ($N_3^\bullet$) to give N_6 (?) and fragmentation to $3N_2$. The adduct **1** has never been characterized, but by analogy with the recent X-ray structure obtained for the *o*-$(CF_3)_2COC_6H_4IN_3$ adduct, it appears most likely that **1** can be represented by the formula $PhI(N_3)_2$.[12]

Results

Our recent interest in the amination of triisopropylsilyl (TIPS) enol ethers prompted an investigation of the reagent combination PhIO/$TMSN_3$, eq 2.[13,14] We were intrigued at the prospect of generating **1**/**4** (eq 2) in the presence of a TIPS enol ether to see if an electrophilic form of azide can be trapped in the "normal" (α) fashion to give **6a**.[15] When a suspension of PhIO in dichloromethane at −45 °C was treated with $TMSN_3$, the solution became canary yellow and homogeneous. At this temperature the evolution of dinitrogen is very slow. Warming the solution to −20 °C causes rapid dinitrogen evolution and the formation of iodobenzene and hexamethyldisiloxane. If the above reaction is carried out in the presence of **5** (at −45 °C), we observed the rapid formation of two compounds, **6** and **6a**. While the α-azidonation product **6a** was the expected product of trapping an electrophilic azide radical ($N_3^\bullet$), the β-azido adduct **6** was completely unexpected, Scheme 1. The regiochemistry of **6** was first determined by ^{1}H NMR spectroscopy. Selective irradiation of the hydrogen α to the azide decouples the vinylic proton from a doublet to a singlet, consistent with a β-azido derivative **6** (see Scheme 2 for conclusive proof by X-ray of a derivative).

Scheme 1[a]



[a] Reagents and conditions: (a) PhIO (1.2 equiv)/$TMSN_3$ (2.4 equiv)/CH_2Cl_2; (b) PhIO (1.5 equiv)/$TMSN_3$ (3.0 equiv)/CH_2Cl_2/TEMPO (10 mol %).

The unprecedented nature of the β-azide product **6** initiated a survey of reaction conditions to improve the ratio of **6** to **6a**. Initially, we found that conducting the reaction at −45 °C in the presence of 2,6-di-*tert*-butyl-4-methyl pyridine caused the β-adduct **6** to become the major product (ca. 4:1). This was found to be inconvenient because of the difficult separation of the product from the pyridine base. However, it was found that the product ratio was extremely sensitive to the reaction temperature. For example, adding $TMSN_3$ to a suspension of PhIO and the TIPS enol ether **5** at −18 to −15 °C rapidly (5 min) gave the β-azido enol ether **6** (>95%, crude), with only traces of the α-adduct **6a**.

Table 1 shows that at −78 °C α-azidonation is the favored pathway, and increasing temperature causes the β-pathway to become dominant. At 0 °C the decomposition of the reagent to give PhI + N_2 + TMS_2O is very rapid, and only β-azidonation was observed. It was found that the stable radical TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxyl) can be used to modify the outcome of this reaction. Catalytic quantities of TEMPO (10 mol %) significantly reduced the β-azidonation and increased the α-azidonation reaction.[16] Consequently, the ratio of **6** to **6a** can be controlled by a combination of temperature and the addition of TEMPO, whereby **6** or **6a** almost becomes the predominant product. It should be noted that, if TMS or *tert*-butyldimethylsilyl (TBS) enol ethers are used as substrates for the β-azidonation reaction, they are rapidly desilylated (presumably by azide anion) to give the starting ketone. The small amounts of β-azido TMS and TBS enol ethers that are formed are extremely labile and decompose to the corresponding enone through β-elimination of the azide group.

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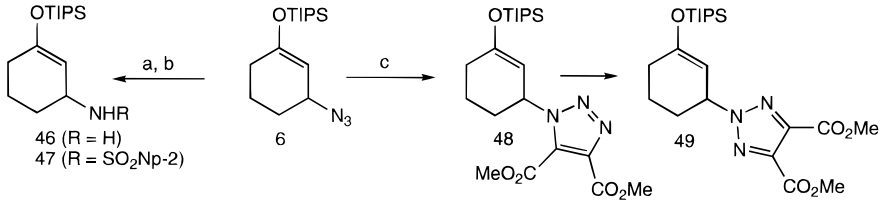
Scheme 2[a]



[a] Reagents and conditions: (a) $LiAlH_4/Et_2O$ (85%); (b) 2-$NpSO_2Cl$ (85%); (c) dimethyl acetylenedicarboxylate.

Table 1. Temperature Variation of the Azidonations Shown in Scheme 1

	6:6a	
temp °C	without TEMPO	with TEMPO (10 mol %)
−78	1:9	
−60	1:3	
−45	1:1	1:>10
−20	20:1	1:4
0	>99:1	1:1.5

Table 2 lists a number of TIPS enol ethers that have been converted into their respective β-azido adducts. In all cases the reaction is complete within a few minutes at −15 °C and the β-azido products are formed in very high yield. The only other products are iodobenzene and hexamethyldisiloxane, which are removed under vacuum. While the regiochemistry is excellent, the stereoselectivity is modest. Presumably, this is due to the low steric requirements of the N_3 group.

The β-azidonation reaction of substrates **9**, **11**, **13**, **15**, **17**, **24**, **26**, and **28** leads to the formation of epimeric mixtures. An axial configuration for the azide is assigned to the major isomer of **29** (6:1). Low diastereoselectivities were observed for the 4-substituted TIPS enol ether series **11**, **13**, **15**, and **17**, Table 3. For these derivatives, the diastereomeric excess changes from 13% to 47% with the increasing size of the substituent at the C4-position. The ^{1}H NMR spectroscopic data are consistent within the series; the major diastereomer always has chemical shifts for the vinylic and allylic protons at higher field than the minor one. The major diastereomers of these reactions are the *trans*-β-azido TIPS enol ethers.

β-Azidonation of a TIPS enol ether already substituted at the β-position is also possible, **42**. The product **43** is sensitive to chromatography and readily decomposes to a triene. The β-azidonation reaction of a mixture (*Z*:*E*, 3.7:1) of TIPS enol ethers **40** forms two β-azido TIPS enol ethers **41** in favor of the *E* isomer (*Z*:*E*, 1:4). It is interesting to note that the same composition of products is obtained from the β-azidonation of pure *E*-**40**. This result indicates that isomers *E*-**40** and *Z*-**40** form the same enonium ion intermediate (cf. **6b**), which results in **41** (see Scheme 7 concerning mechanistic hypothesis).

A variety of reducing agents were tried in order convert **6** into the amine **46**. It was found that $LiAlH_4$ in ether gave **46** (85%). Conversion of amine **46** into the 2-naphthalenesulfonamide derivative **47** provided crystals suitable for X-ray analysis and thus confirmed the assigned structure.

While attempting to form a crystalline derivative of the β-azido group, we treated **6** with dimethyl acetylenedicarboxylate heated at reflux in dichloromethane for 17 h. Two β-triazole TIPS enol ethers **48** and **49** were formed in a 1:1.4 ratio. The first compound **48** corresponds to the expected triazole, and **49** to its symmetric triazole isomer (readily distinguished by ^{1}H and ^{13}C NMR). These compounds were separated, and solutions of **48** and **49** were heated at reflux in dichloromethane. **48** transforms itself into **49**. The latter remains unchanged under these reaction conditions. Analogous shifts of substituents on a triazole, from the 1- to the 2-position, have been reported. The migrating entities were a trimethylsilyl group and α-aminoalkyl derivatives.[17]

The most likely explanation for the above equilibration is that the initial 1,3-dipolar adduct **48** ionizes to give the enonium ion **6b** and the triazole anion **48b**, which recombine at the central nitrogen atom, resulting in **49**, Scheme 3. A [1,5]-sigmatropic shift mechanism is of course another reasonable possibility. While we have no experimental evidence to distinguish between these two plausible options, the ionization pathway to an enonium ion intermediate **6b** did suggest that β-azido TIPS enol ethers themselves may be capable of dissociation to an ion pair. A simple way in which to test this notion was to treat a diastereomeric mixture of β-azido TIPS enol ethers with a Lewis acid (non-nucleophilic counterion) and see if the ratio of *cis* and *trans* diastereomers changes, Scheme 4.

We decided to use two Lewis acids based on the tetraphenylboron counterion; lithium tetraphenylboron tris(dimethoxyethane) and sodium tetraphenylboron. The 4-methyl-β-azido TIPS silyl enol ether **12** was chosen as the substrate for these experiments. The ratios of *cis*- and *trans*-**12** were determined by ^{1}H NMR spectroscopy. The sodium salt was less reactive than the lithium salt: heating at reflux and 1 equiv of $Na^+BPh_4^-$ were needed to ensure some epimerization, while for the lithium compound only 20 mol % was necessary at 25 °C, Tables 4 and 5, respectively.

Equilibration favors the 3,4-diequatorial *trans* isomer *versus* the *cis* isomer. Prolonged reaction times with the Lewis acids or an increase in temperature leads to decomposition of the β-azido silyl enol ethers into mixtures of dienes.

Effect of TEMPO

We have explored the effect of certain additives on the reagent combination $PhIO/TMSN_3$. The stable radical TEMPO can be used to modify the outcome of this reaction. Catalytic quantities of TEMPO significantly reduced the β-azidonation and increased the α-azidonation reaction, Scheme 1, Table 1.

The use of TEMPO and choice of temperature allow the 1,2-bis-azide **6a** to be obtained predominantly, and in good yield. Table 6 lists the results for the conversion of a number of substituted cyclic TIPS enol ethers to their 1,2-bis-azido derivatives.

The yields varied from 91% for the unsubstituted compound **6a** to 41% for the product **56**. The reaction is stereoselective, and in three cases, **6a**, **50**, and **52**, none of the minor diastereomer could be detected (^{1}H NMR). The relative stereochemistry of the 1,2-bis-azides **6a**, **50**, and **52** is assigned as *trans*-diaxial on the basis of the CH−N_3 coupling. In the case of **58**, the *trans*-diaxial relationship of the 1,2-bis-azide was determined by X-ray crystallography. Figure 1 show an ORTEP representation of **58** which clearly indicates the 1,2-diaxial conformation of the *trans*-bis-azide array. In a blank

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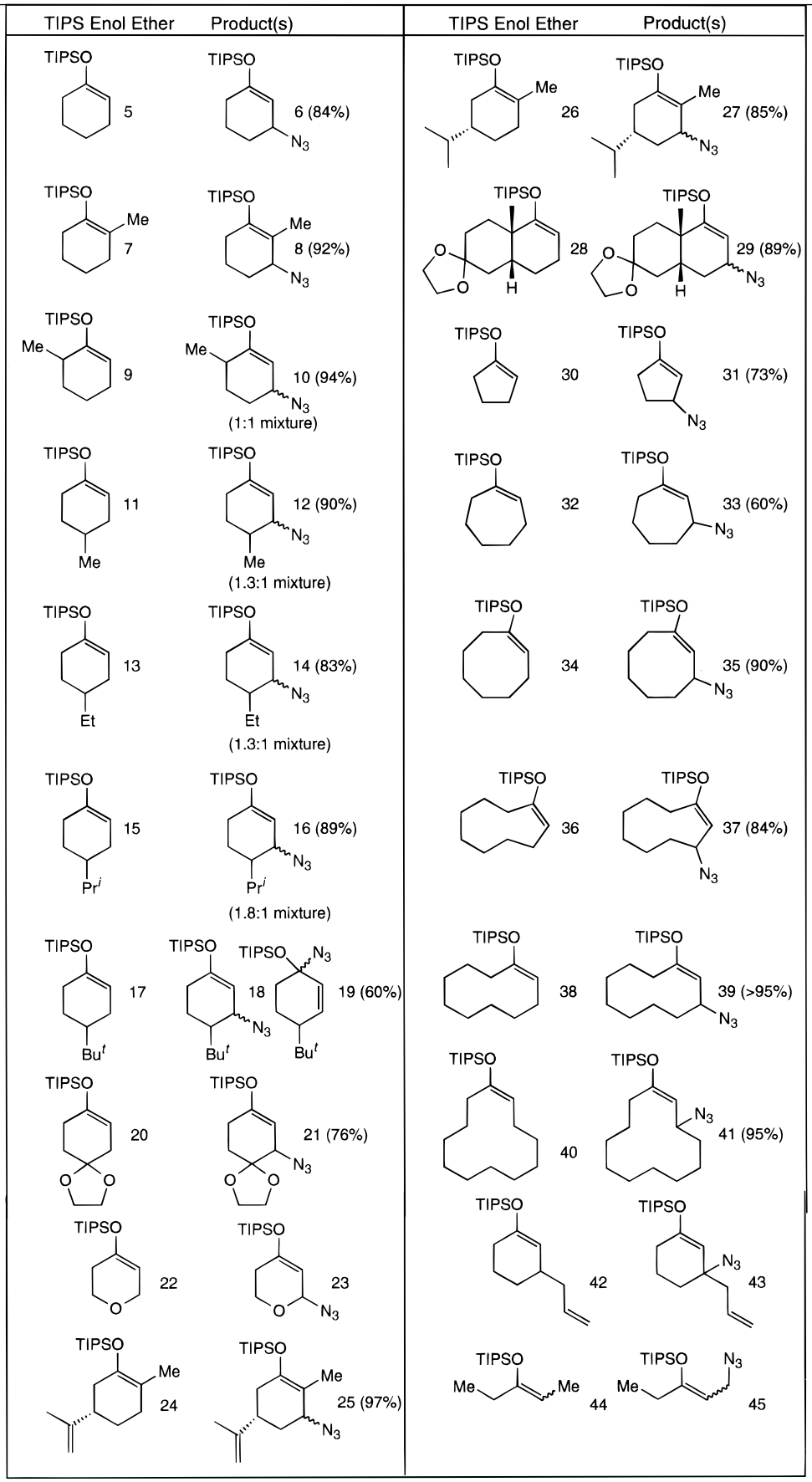
Table 2



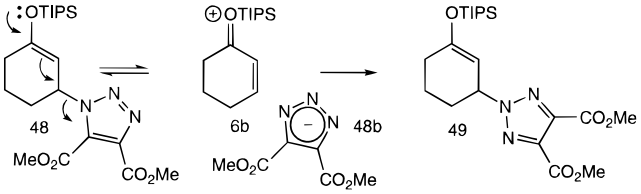
reaction a TIPS enol ether was treated with $TMSN_3$ and a stoichiometric amount of TEMPO in the absence of iodosylbenzene. No reaction occurred.

In the above reactions (Table 6) the TEMPO additive was consumed, and for the substrate **5** we could isolate the adduct **59** (5%). Also, conducting the reaction in the presence of 2,6-

Table 3

enol ether	ratio	de (%)	^{1}H NMR shift (ppm) major isomer	^{1}H NMR shift (ppm) minor isomer
11	1.3:1	13	δH vinylic = 4.87 δH α-N_3 = 3.52	δH vinylic = 5.03 δH α-N_3 = 3.83
13	1.3:	13	δH vinylic = 4.88 δH α-N_3 = 3.63	δH vinylic = 5.05 δH α-N_3 = 3.93
15	1.8:1	29	δH vinylic = 4.86 δH α-N_3 = 3.77	δH vinylic = 5.03 δH α-N_3 = 4.00
17	2.8:1	47	δH vinylic = 4.83 δH α-N_3 = 3.72	δH vinylic = 5.01 δH α-N_3 = 3.98

Scheme 3



Scheme 4

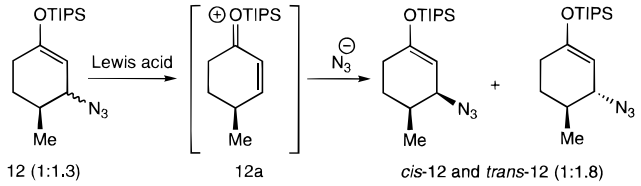


Table 4. Reaction of **12** with Lithium Tetraphenylboron Tris(dimethoxyethane)[a]

equiv of $LiBPh_4(C_4H_{10}O_2)_3$	reaction time	*cis*:*trans* **12**
0.2	0	1:1.3
0.2	4 min	1:1.4
0.2	11 min	1:1.5
0.2	26 min	1:1.75
0.2	57 min	1:1.8
0.2	15 h	(1:1.7) + 33% dec[b]
1.0	30 min	1:2.3 + dec

[a] Solvent: $CDCl_3$. [b] Decomposition.

Table 5. Reaction of **12** with Sodium Tetraphenylboron[a]

solvent	reaction time (h)	temp °C	*cis*:*trans* **12**
$CDCl_3$	1.5	25	1:1.3 (no change)
$CDCl_3$	1	reflux	1:2
$CDCl_3$	15	reflux	1:2 + dec[b]
$(CD_3)_2CO$	2	25	1:1.3 (no change)

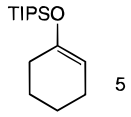
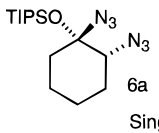
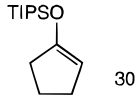
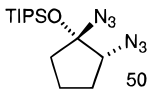
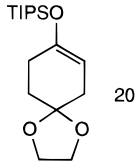
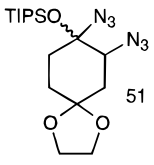
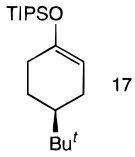
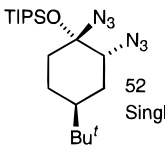
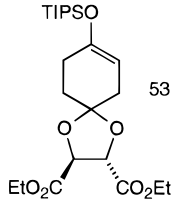
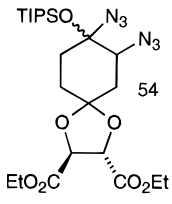
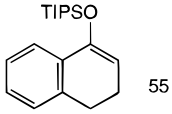
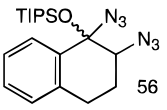
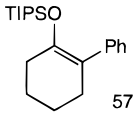
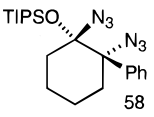
[a] Equivalents of $NaBPh_4$: 1.0. [b] Decomposition.

di-*tert*-butyl-4-methylphenol (10%, no TEMPO) caused formation of **6**/**6a** (1:1 at −45 °C) and the adduct **60** (6%). The formation of **59** strongly implicates the radical intermediate **5a**, whereas **60** could arise from **5a** or the onium ion **5b**, Scheme 5.

The generation of azide radicals from similar reagent systems such as $PhI(OAc)_2$ and NaN_3 is well precedented.[18] Evidence for a radical addition process is shown in Scheme 6. Treatment of **62** with the PhIO/$TMSN_3$/TEMPO reagent system gave the ring-opened product **63** (90%). Presumably, the azido radical adds to **62** to give **62a**, which undergoes ring cleavage to the tertiary radical **62b**. The substrate **61** gave a complex mixture

(18) Radical cations have been proposed as intermediates in the reactions of $PhI(OCOCF_3)_2$/$TMSN_3$ with electron-rich phenolic ethers resulting in electrophilic substitution. Kita, Y.; Tohma, H.; Hatanaka, K.; Takada, T.; Fujita, S.; Mitoh, S.; Sakurai, H.; Oka, S. *J. Am. Chem. Soc.* **1994**, *116*, 3684. See ref 7.

Table 6. Reactions of TIPS Enol Ethers with PhIO/$TMSN_3$/10 mol % TEMPO[a]

TIPS Enol Ether	1,2-*bis*-azido product(s)	Yield[b]
 5	 6a	91%[d] Single diastereoisomer
 30	 50	60% Single diastereoisomer
 20	 51	82%(3:1)[c]
 17	 52	71% Single diastereoisomer
 53	 54	67%(4:2:1)[c]
 55	 56	41%(4:1)[c]
 57	 58	59%(5:1)[c, e]

[a] PhIO (1.5 equiv)/$TMSN_3$ (3.0 equiv)/TEMPO (0.1 equiv)/CH_2Cl_2, −45 °C, 16 h. [b] Isolated yield of diastereomeric mixture after chromatography. [c] Diastereomeric ratio determined by ^{1}H NMR. [d] Reaction carried out in toluene. [e] Structure confirmed by X-ray crystallography.

of products from which we could isolate the adduct **65** (7%). Again, this can be rationalized by formation of a primary radical **61b** (from **61a**), combination with TEMPO to give **64**, and β-azidonation (TEMPO has been consumed) to give **65**.

Azide radical trapping occurs when cyclohexene is treated with the PhIO/$TMSN_3$/TEMPO reagent system to yield **66** (5%) and the known bis-azide **67** (80%), Scheme 6. For comparison, this reaction was carried out in the absence of TEMPO; the yield of **67** dropped to 49% (lit.[19] 40%), and the diastereomeric ratio changed to ∼1:1.

Mechanistic Hypothesis

Scheme 7 represents a mechanistic proposal that offers a clear distinction between the α- and β-functionalization pathways. The key difference between the two reactions is that the

(19) Moriarty, R. M.; Khosrowshahi, J. S. *Tetrahedron Lett.* **1986**, *27*, 2809.

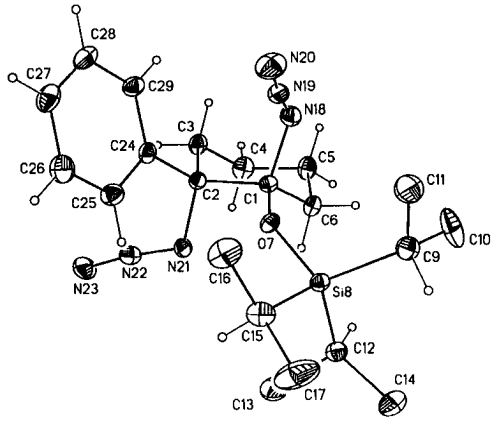


Figure 1. ORTEP representation of **58** showing the 1,2-diaxial azido groups.

α-pathway is an azide radical addition process, and the *β*-pathway involves ionic dehydrogenation.

Iodosylbenzene (**2**) and $TMSN_3$ (**3**) can interact to form the oxonium ion **3a**, which is in equilibrium with the tricoordinate adduct **4**. The oxonium/iodonium ion **3a** should be capable of hydride (H^-) abstraction from **5** to form the enonium ion **6b** [removal of H(*β*)] and initially **3b**. Reductive elimination of **3b** results in the production of iodobenzene and trimethylsilanol, which leads to hexamethyldisiloxane and water. It is also possible that **4a** can abstract a hydride anion. The alternative H(α) hydride abstraction would lead to the oxyallyl cation **6c**, which is a much higher energy intermediate than **6b** since it does not allow oxonium ion stabilization of the cationic charge. The enonium ion **6b** adds azide anion (1,4) to give the observed product **6**. The alternative 1,2-addition is possible, and in the case of **17** (Table 2) we have observed this regiochemistry. It is also known that allylic azides can undergo [3,3]-sigmatropic rearrangements. Consequently, it is quite possible that the kinetic product is the 1,2-adduct, which rapidly rearranges to the thermodynamic 1,4-adduct.[20]

At lower temperatures (−45 °C, see Table 1) the dissociation of **4** into **3a** is slow, and **4** can form **1**, which leads to azide radicals *via* **1a**. Eventually, azide radicals can combine to give the putative N_6 species and decompose to dinitrogen. Clearly, the latter pathway is unproductive since it removes azide radicals and azide anions from the reaction required to give either **6** or **6a**. Overall, it appears that the low-temperature pathway favors homolytic dissociation (radicals), and as the temperature is increased, the higher energy heterolytic (ionic) dissociation pathway becomes the favored mode of decomposition of the putative hypervalent iodine intermediates **1** and **4**.

The addition of TEMPO markedly suppresses the *β*-pathway in favor of the α-pathway (Table 1). It is reasonable to speculate that TEMPO intercepts **1** or **4** or both (shown for **4**) by radical addition to give **4b**. Homolytic dissociation of **4b** leads to **4c** and $N_3^{\bullet}$ radicals. These reactions should be reversible. The adduct **4c** can also dissociate and regenerate TEMPO and **4d**. Combination of **4d** with $N_3^{\bullet}$ completes the cycle by reforming **4**. Once the reaction is complete (TEMPO and the TIPS enol ether consumed), the intermediate(s) **1/4** will decompose to iodobenzene, dinitrogen, hexamethyldisiloxane, and water.

We considered that the putative enonium ion **6b** should be capable of being trapped in an intramolecular fashion, thus providing evidence for the intermediacy of this species. While at first sight this seems to be a simple experimental proposition, it must be remembered that azide anion is an extremely good nucleophile and it may be difficult to construct a substrate that can compete effectively (intramolecularly) with the intermolecular azide anion trapping. To this end we treated the lithium carboxylate **68** under the usual *β*-azidonation reaction conditions (although at 0 °C) and obtained **69** and **70** (Scheme 8); see Table 7 for relative ratios. The lactone **70** is only a minor product under the usual *β*-azidonation reaction conditions, but if the reaction is carried out under high-dilution conditions to suppress intermolecular processes, the amount of lactone **70** increases. Indeed, at 0.005 M the lactone **70** is the major product. It should be noted that amide or ester analogs of **68** did not form any lactone and only the analogous *β*-azido TIPS enol ether was observed.

Overall, these experiments provide strong circumstantial evidence for the intermediacy of an enonium ion species formulated as **68a**.

Why Azide?

We were interested to know whether or not the unusual *β*-functionalization reaction could be extended to other trimethylsilyl derivatives (TMSX) and the ratio of α-addition *versus β*-oxidative functionalization. Scheme 9 summarizes the overall results we have observed for a number of TMSX systems, X = Cl, Br, I, CN, SPh, NCO.[21]

Trimethylsilyl chloride (1.2 equiv) and PhIO (1.2 equiv) in CH_2Cl_2 generated iodosylbenzene dichloride ($PhICl_2$). Addition of **5** to this solution at −78 °C, followed by warming to 25 °C, gave **71**/**72** (X = Cl) (59%, 1:1), traces of the dichloride **73** (X = Cl), and cyclohexenone **74**. Similarly, trimethylsilyl bromide (1.2 equiv) and PhIO (1.2 equiv) in CH_2Cl_2 generated iodosylbenzene dibromide ($PhIBr_2$), which on treatment with **5** gave a mixture of **71** and **72** (X = Br) (1:1). Carrying out the same reaction in the presence of 2,6-di-*tert*-butyl-4-methyl pyridine gave **71** and **72** (X = Br) (1:9). Attempted extension of these reactions to more complicated substrates gave inseparable mixtures of halogenated products along with small amounts of α,*β*-unsaturated ketones.[22]

Treatment of PhIO with TMSCN generated the adduct $PhI(CN)_2$,[23] which did not react with **5** even at 40 °C. Addition of TMSOTf (0.1 equiv) at −78 °C and warming to 25 °C (16 h) gave the α-cyano TIPS enol ether **71** (X = CN) (72%). Treatment of trimethylsilyl phenyl sulfide with PhIO at 0 °C gave diphenyl disulfide and iodobenzene. Likewise, treatment of trimethylsilyl iodide with PhIO at 0 °C gave iodine and iodobenzene. Trimethylsilyl isocyanate did not give any discernible reaction.

It is clear from the above experiments that the *β*-azidonation reaction is unique in leading almost exclusively to oxidative *β*-substitution. The iodosylbenzene/TMSCN, -TMSCl, and -TMSBr combinations behave more normally and give predominantly α-electrophilic substitution. The small amounts of α,*β*-unsaturated ketones that we observe in these reactions most probably arise from the competitive *β*-pathway (Scheme 7), since it would be difficult to imagine that the α-cyano/α-chloro

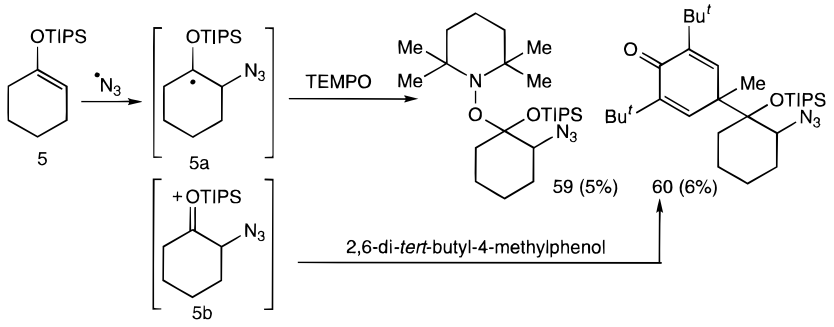
(20) Gagneux, A.; Winstein, S.; Young, W. G. *J. Am. Chem. Soc.* **1960**, *82*, 5956. VanderWerf, C. A.; Heasley, V. L. *J. Org. Chem.* **1966**, *31*, 3534.

(21) Gusarsky, E.; Treinin, A. *J. Phys. Chem.* **1965**, *69*, 3176. The reducing power of the halide and pseudo halide ions increases in the following order F^-, NCO^-, Cl^-, N_3^-, Br^-, SCN^-, I^-.

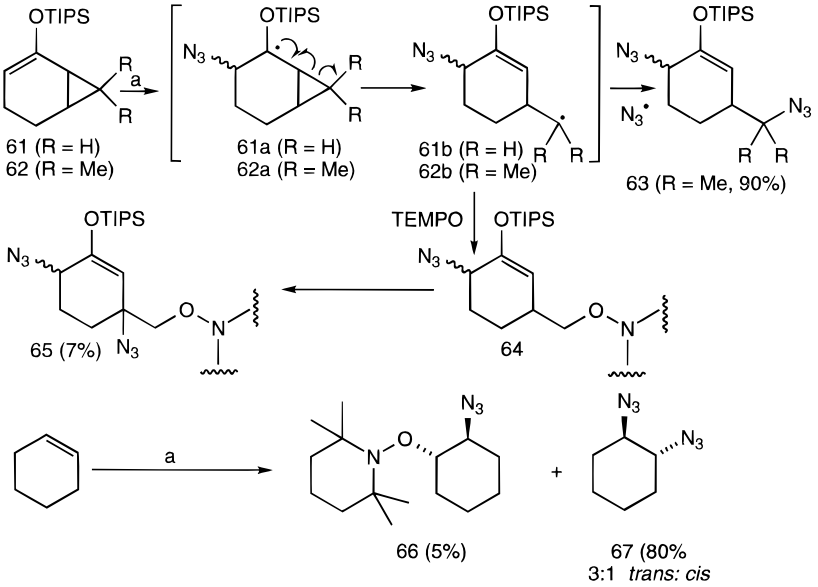
(22) Koser's reagent oxidizes halide anions to halogens. Bovonsombat, P.; Djuardi, E.; Mc Nelis, E. *Tetrahedron Lett.* **1994**, *35*, 2841 and references therein.

(23) Zhdankin, V. V.; Tykwinski, R.; Williamson, B. L.; Stang, P. J. *Tetrahedron Lett.* **1991**, *32*, 733. Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Mismash, B.; Woodward, J. K.; Simonsen, A. J. *Tetrahedron Lett.* **1995**, *36*, 7975.

Scheme 5

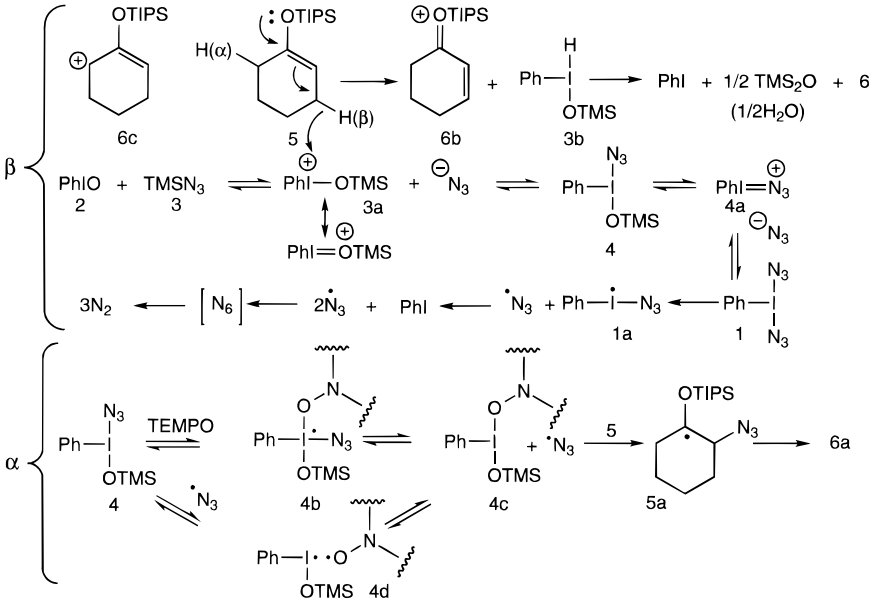


Scheme 6[a]



[a] (a) PhIO (1.5 equiv)/$TMSN_3$ (3.0 equiv)/TEMPO (0.1 equiv)/CH_2Cl_2 −45 °C, 16 h.

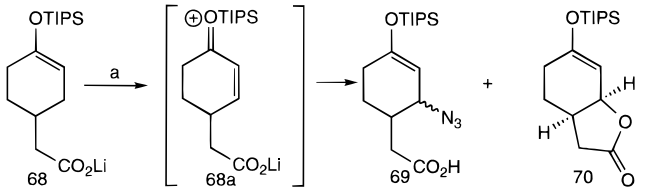
Scheme 7



derivatives would eliminate to the enones under such mild reaction conditions. In summary, the reagent combination PhIO/$TMSN_3$ is the only system we have found that results in clean, high-yield β-functionalization.

Why is this? A plausible explanation is that if the X component of TMSX is readily oxidized by PhIO, it will rapidly form X_2 + PhI ($PhIX_2$), and the intermediate iodosonium ion **3a**, Scheme 7, will have to compete with X_2 for the TIPS enol ether. Azide anion is oxidized by PhIO to $(N_3)_2$, and hence to $3N_2$, but of course this is benign and merely reduces the effective oxidant. Consequently, for the case where X = N_3 the TIPS enol ether is not removed by reaction(s) with X_2, and β-oxidative functionalization can occur without substantial competitive interference from the transformations shown in Scheme 9.

Scheme 8[a]

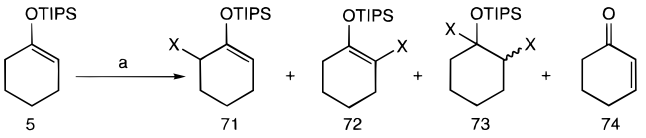


[a] (a) $(PhIO)_n$ (1.2 equiv), $TMSN_3$ (1.2 equiv)/CH_2Cl_2.

Table 7

[M]	temp (°C)	**69**:**70**
0.1	0	3:1
0.1	−40	95:5
0.1	25	1:1
0.02	25	1:3
0.005	25	>1:95

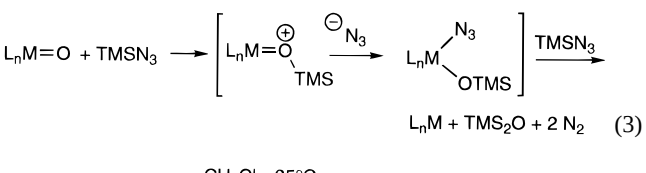
Scheme 9[a]

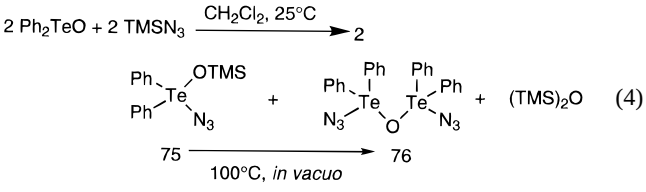


[a] (a) $(PhIO)_n$ (1.2 equiv), TMSX (1.2 equiv)/CH_2Cl_2.

Replacement of PhIO with Ph_nMO

Equation 2 can be written in a more generalized form as shown in eq 3. M may be a suitable replacement for iodine. It was found that Ph_2SeO, Ph_3AsO, and Ph_3PO were cleanly reduced to Ph_2Se, Ph_3As, and Ph_3P (and TMS_2O and N_2), respectively, when treated with $TMSN_3$ at −20 °C. When the reaction was conducted in the presence of the TIPS enol ether **5**, no azidonation occurred. Selenium, arsenic, and phosphorus have stable hypervalent oxidation states compared to lower ones, which may explain why no oxidation products are observed. However, the elements in the fifth row of the periodic table have less stable hypervalent oxidation states and are correspondingly more reactive.[24] With this in mind it was decided to examine diphenyltelluroxide. Diphenyltelluroxide was treated with $TMSN_3/CH_2Cl_2$ at room temperature, eq 4.

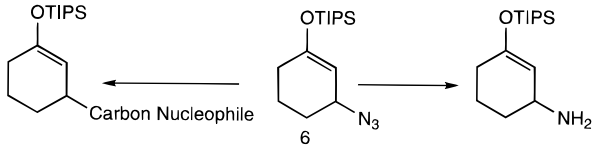




Nitrogen gas was not evolved. After 3 h, evaporation of solvent yielded a mixture of two products, **75** and **76**. The mixture was heated without solvent under high vacuum to 100 °C for 2 h to drive conversion of **75** to **76** to completion. Crystallization from dichloromethane and diethyl ether afforded pure bis-[azidodiphenyltellurium(IV)] oxide, **76** (92% yield), as white needles. Heating **76** to 200 °C (mp 174−176 °C, without decomposition,) caused decomposition and gas evolution (presumably N_2).[25]

(24) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 4th ed.; Wiley: New York, 1980.

Scheme 10



Conclusions

The β-azidonation reaction appears to be quite specific for the hypervalent tricoordinate iodine reagents ($PhIO_2$ is inert), although there exists the possibility that other elements (yet to be examined) may undergo this type of chemistry. The delicately balanced temperature dependence between α- and β-azidonation points to a change in mechanism which can be rationalized by radical and ionic pathways, respectively. While the products from these reactions might appear to be somewhat esoteric, the β-azido TIPS enol ethers have proven to be versatile synthetic intermediates and provide access to new TIPS enol ether derivatives, Scheme 10.[26] The reagent combination PhIO/$TMSN_3$ also readily oxidizes amines and amides to the corresponding α-azido derivative.[27]

The ability to fine-tune the reactivity of aryl hypervalent iodine reagents by substitution in the aryl component provides an added degree of flexibility and possible selectivity that can be readily explored.[3]

Experimental Section

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.

Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a General Electric QE-300 (300 MHz) spectrometer 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 on a General Electric QE-300 (75 MHz) instrument 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; e and o indicate even and odd numbers of hydrogens, respectively, carried by the carbon. IR spectra were recorded either neat on sodium chloride plates or as solutions in solvent as indicated using a Perkin-Elmer 1600 FT-IR spectrometer and are reported in wavenumbers (cm^{-1}). Low-resolution chemical ionization (CI) mass spectra were obtained on a TSQ 70 instrument,

(25) Magnus, P.; Roe, M. B.; Lynch, V.; Hulme, C. *J. Chem. Soc. Chem. Commun.* **1995**, 1609.

(26) See ref 13. Magnus, P.; Evans, P. A.; Lacour, J. *Tetrahedron Lett.* **1992**, *33*, 2933. Magnus, P.; Rigollier, P.; Lacour, J.; Tobler, H. *J. Am. Chem. Soc.* **1993**, *115*, 12629. Magnus, P.; Roe, M. B. *Tetrahedron Lett.*, in press. Magnus, P.; Lacour, J.; Evans, P. A. *Janssen Chim. Acta* **1993**, *11* (1), 3.

(27) Magnus, P.; Lacour, J.; Weber, W. *J. Am. Chem. Soc.* **1993**, *115*, 9347. Magnus, P.; Hulme, C. *Tetrahedron Lett.* **1994**, *35*, 8097. Magnus, P.; Hulme, C.; Weber, W. *J. Am. Chem. Soc.* **1994**, *116*, 4501.

and the exact mass determinations were obtained on a VG analytical ZAB2-E instrument.

Routine monitoring of reactions was performed using Merck Alufolien Kieselgel 60 F_{254} silica gel, aluminum-backed TLC plates. Flash chromatography was performed using silica gel Merck Kieselgel 60H F_{254} and Florisil 100−200 mesh with the solvent indicated.

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 workup. The reactions must *not* be allowed to run dry and should be conducted behind a *safety shield*. We have carried out some β-azidonation reactions on scales up to 40 g (**20** into **21**) without problems.

3-Azido-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (6). General Procedure for the Synthesis of β-Azido TIPS Enol Ethers. At −15 °C, in an oven-dried, three-necked, round-bottomed 250 mL flask, equipped with a thermometer, a magnetic stirring bar and an argon inlet, trimethylsilyl azide (3.19 mL, 24 mmol, 2.4 equiv) was added to a suspension of **5** (2.55 g, 10 mmol, 1 equiv) and iodosylbenzene (2.64 g, 12 mmol, 1.2 equiv) in dichloromethane (100 mL). After 1 min, gas evolution (dinitrogen) was usually observed. Ten minutes later, the reaction mixture, which had become a clear solution, was warmed to 25 °C (N_2 evolution complete). The solvent was removed under reduced pressure. ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **6**. The product was purified by flash chromatography (very short column of silica gel, 20 g, eluent 9:1 hexanes/ethyl acetate) and then placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **6** as a yellow oil (2.47 g, 84%): IR (film) 2946, 2867, 2093, 1656, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.96 (1H, d, J = 4.3 Hz), 4.04−3.98 (1H, m), 2.12−2.05 (2H, m), 1.87−1.62 (4H, m), 1.25−1.0 (21H, m); ^{13}C NMR (75 MHz, $CDCl_3$, APT) δ 156.7 (e), 100.8 (o), 57.0 (o), 29.7 (e), 28.6 (e), 19.1 (e), 17.9 (o), 12.5 (o); CIMS (MH^+) *m/e* 296 (22), base 253 (100), 295 (2), 294 (3), 268 (2); HRMS (MH^+) *m/e* calcd for $C_{15}H_{30}N_3OSi$ 296.216, found 296.215.

1,2-Diazido-1-[(triisopropylsilyl)oxy]cyclohexane (6a). General Procedure for the Synthesis of 1,2-Diazido Compounds (without TEMPO). At −45 °C, trimethylsilyl azide (250 μL, 1.89 mmol, 2.4 equiv) was added to a suspension of **5** (200 mg, 0.79 mmol, 1 equiv) and iodosylbenzene (208 mg, 0.94 mmol, 1.2 equiv) in dichloromethane (15 mL). The mixture was stirred for 3 h. The reaction mixture, which had become a clear solution, was warmed to 25 °C, and the solvent was removed under reduced pressure. The crude product was analyzed by ^{1}H NMR spectroscopy to determine the (1:1) ratio between β-azido silyl enol ether **6** and 1,2-diazido compound **6a**. The product was purified by flash chromatography over silica gel (120 g, eluent 19:3 hexanes/ethyl acetate) to give **6a** as a yellow oil (127 mg, 48%). See below for characterization.

3-Azido-2-methyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (8) was synthesized analogously to **6** from **7** (392 mg, 1.46 mmol), trimethylsilyl azide (500 μL, 3.78 mmol, 2.6 equiv) and iodosylbenzene (416 mg, 1.89 mmol, 1.2 equiv); ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **8**. The product was purified by flash chromatography over silica gel (very short column of silica gel, 15 g, eluent 9:1 hexanes/ethyl acetate) and then placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **8** as an oil (417 mg, 92%): IR (film) 2944, 2867, 2095, 1673, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (1H, br), 2.18−2.10 (2H, m), 1.75 (3H, s), 1.87−1.66 (4H, m), 1.20−1.05 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 149.4 (e), 108.9 (e), 62.7 (o), 30.1 (e), 29.1 (e), 19.2 (e), 17.9 (o), 14.5 (o), 13.2 (o); CIMS (MH^+) *m/e* 310 (5), base 267 (100), 309 (3), 268 (96), 266 (12); HRMS (M^+) *m/e* calcd for $C_{16}H_{31}N_3OSi$ 309.224, found 309.223.

***cis*- and *trans*-3-azido-6-methyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (10)** was synthesized analogously to **6** from **9** (422 mg, 1.57 mmol, 1 equiv), trimethylsilyl azide (500 μL, 3.78 mmol, 2.4 equiv), and iodosylbenzene (416 mg, 1.89 mmol, 1.2 equiv). ^{1}H NMR spectroscopic analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and epimers **10** (1:1). The epimers were not separable by chromatography but were isolated together by flash chromatography (column of silica gel, 150 g, eluent 9:1 hexane/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **10** as an oil (457 mg, 94%): IR (film) 2945, 2868, 2092, 1656, 1648 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2 epimers 4.85−4.75 (2H, m), 3.97−3.91 (2H, m), 2.27−2.17 (2H, m), 1.97−1.40 (8H, m), 1.25−1.00 (48H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 2 epimers 160.56 (e), 160.1 (e), 99.4 (o), 98.7 (o), 57.7 (o), 57.4 (o), 34.0 (o), 33.6 (o), 27.7 (e), 27.5 (e), 27.2 (e), 26.0 (e), 18.4 (o), 18.0 (3, i), 12.7 (o), 12.2 (o); CIMS (MH^+) *m/e* 310 (9), base 267 (100), 309 (2), 282 (10), 269 (28), 268 (49), 223 (3); HRMS (M^+) *m/e* calcd for $C_{17}H_{34}N_3OSi$ 309.224, found 309.221.

***cis*- and *trans*-3-azido-4-methyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (12)** was synthesized analogously to **6** from **11** (842 mg, 3.14 mmol, 1.0 equiv), an excess of trimethylsilyl azide (1.0 mL, 7.54 mmol, 2.8 equiv), and iodosylbenzene (828 mg, 3.77 mmol, 1.2 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and epimers **12** (1.3:1). The epimers were not separable by chromatography but were isolated together by flash chromatography (very short column of silica gel, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **12** as an oil (878 mg, 90%): IR (film) 2945, 2867, 2095, 1654, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major epimer 4.89−4.85 (1H, m), 3.55−3.50 (1H, m), 2.25−1.40 (5H, m), 1.30−0.95 (24H, m); irradiation at 4.87 ppm decouples the signal at 3.52 ppm to a doublet (J = 6.9 Hz); δ minor epimer 5.03 (1H, d, J = 4.6 Hz), 3.83 (1H, t, J = 4.6 Hz), 2.25−1.40 (5H, m), 1.30−0.95 (24H, m); irradiation at 5.03 ppm decouples the signal at 3.83 ppm to a doublet (J = 3.6 Hz); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ both isomers 157.2 (e), 155.7 (e), 100.8 (o), 100.3 (o), 64.3 (o), 61.4 (o), 33.7 (o), 33.4 (o), 30.1 (e), 28.5 (e), 27.8 (e), 25.9 (e), 18.1 (o), 17.9 (2, i), 17.7 (o), 12.5 (2, i); CIMS (MH^+) *m/e* 310 (15), base 267 (100), 309 (7), 308 (24), 282 (3), 269 (14), 268 (45), 266 (26); HRMS (MH^+) *m/e* calcd for $C_{16}H_{32}N_3OSi$ 310.232, found 310.232.

***cis*- and *trans*-3-azido-4-ethyl-1-[(triisopropylsilyl)oxy]-cyclohex-1-ene (14)** was synthesized analogously to **6** from **13** (1.4 g, 5.0 mmol, 1.0 equiv), trimethylsilyl azide (1.73 mL, 13 mmol, 2.6 equiv), and iodosylbenzene (1.43 g, 6.5 mmol, 1.3 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and epimers **14** (1.3:1). The epimers were not separable by chromatography but were isolated together by flash chromatography (short column of Florisil, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **14** as an oil (1.35 g, 83%): IR (film) 2943, 2866, 2095, 1657 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major isomer 4.90−4.86 (1H, m), 3.65−3.60 (1H, m), 2.2−1.4 (7H, m), 1.25−1.06 (21H, m), 0.96−0.90 (3H, m), δ minor isomer 5.05 (1H, d, J = 5.7 Hz), 3.95−3.90 (1H, m), 2.20−1.40 (7H, m), 1.25−1.06 (21H, m), 0.96−0.90 (3H, m); ^{13}C NMR (75 MHz, APT, C_6D_6) δ major isomer 157.8 (e), 156.2 (e), 100.8 (o), 100.3 (o), 62.6 (o), 59.2 (o), 40.6 (o), 40.3 (o), 30.7 (e), 28.5 (e), 25.3 (e), 24.7 (e), 24.4 (e), 24.2 (e), 18.2 (o, 2), 12.9 (o, 2), 11.7 (o), 11.5 (o); CIMS (MH^+) *m/e* 324 (5), base 281 (100), others 322 (6), 309 (2), 296 (2), 282 (22); HRMS (MH^+) *m/e* calcd for $C_{17}H_{34}N_3OSi$ 324.246, found 324.246.

***cis*- and *trans*-3-azido-4-isopropyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (16)** was synthesized analogously to **6** from **15** (1.19 g, 4.0 mmol, 1.0 equiv), trimethylsilyl azide (1.38 mL, 10.4 mmol, 2.6 equiv), and iodosylbenzene (1.14 g, 5.2 mmol, 1.3 equiv). ^{1}H NMR analysis of the crude reaction showed only a mixture of TMS_2O, iodobenzene, and epimers (1.8:1). The epimers were not separable by chromatography, but were isolated together by flash chromatography (short column of Florisil, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 1 h under high vacuum (0.6 mmHg) at 90 °C to give **16** as an oil (1.208 g, 89%): IR (film) 2945, 2867, 2093, 1660 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major isomer 4.88−4.84 (1H, m), 3.79−3.74 (1H, m), 2.2−0.80 (33H, m), δ minor isomer 5.03 (1H, d, J = 6.1 Hz), 4.02−3.98 (1H, m), 2.20−0.80 (33H, m); ^{13}C NMR (75 MHz, APT, C_6D_6) δ major isomer 156.3 (e), 101.4 (o), 60.5 (o), 44.8 (o), 29.3 (e), 27.3 (o), 21.2 (e), 21.1 (o), 18.4 (o), 18.2 (o), 12.9 (o), δ minor isomer 157.9 (e), 100.1 (o), 58.3 (o), 46.0 (o), 31.0 (e), 29.1 (o), 22.1 (e), 21.0 (o), 20.8 (o), 18.2 (o), 12.9 (o); CIMS (MH^+) *m/e* 338 (5), base 295 (100), others 337 (3), 336 (9), 308 (3), 297 (7), 296 (5), 294 (19); HRMS (MH^+) *m/e* calcd for $C_{18}H_{36}N_3OSi$ 338.263, found 338.262.

***cis*- and *trans*-3-azido-4-*tert*-butyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (18) and *cis*- and *trans*-1-azido-4-*tert*-butyl-1-[(triisopro-**

pylsilyl)oxy]cyclohex-2-ene (19) was synthesized analogously to **6** from **17** (155 mg, 0.50 mmol, 1.0 equiv), trimethylsilyl azide (212 μL, 1.60 mmol, 3.2 equiv), and iodosylbenzene (176 mg, 0.80 mmol, 1.6 equiv). ^{1}H NMR analysis of the crude reaction mixture showed a mixture of TMS_2O, iodobenzene, and epimers **18** (2.8:1, ~33%) and products of 1,2-addition **19** (~66%). Iodobenzene and TMS_2O were removed by Kugelrohr distillation for 12 h under high vacuum (0.6 mmHg) at 25 °C to give an oil containing **18** and **19** (170 mg, 97%): IR (film) 2946, 2868, 2101, 1661, 1651 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ **19** 5.90−5.68 (2H, m), 2.20−0.80 (34H, m), δ **18**, major β-azido silyl enol ether 4.85−4.80 (1H, m), 3.75−3.70 (1H, m), 2.20−0.80 (34H, m), δ **18**, minor β-azido silyl enol ether 5.01 (1H, d, J = 5.9 Hz), 4.00−3.96 (1H, m), 2.20−0.80 (34H, m); CIMS (MH^+) *m/e* 352 (25), base 309 (100), others 350 (25), 324 (4), 322 (7), 310 (39), 308 (33); HRMS (MH^+) *m/e* calcd for $C_{19}H_{38}N_3OSi$ 352.278, found 352.274.

3-Azido-4,4-(ethylenedioxy)-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (21) was synthesized analogously to **6** from **20** (368 mg, 1.18 mmol), an excess of trimethylsilyl azide (500 μL, 3.77 mmol, 3.2 equiv), and iodosylbenzene (416 mg, 1.87 mmol, 1.6 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **21**. The product was purified by flash chromatography (very short column of silica gel, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **21** as an oil (315 mg, 76%): IR (film) 2946, 2867, 2097, 1661 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.80 (1H, d, J = 4.1 Hz), 4.08−3.92 (4H, m), 3.77 (1H, d, J = 3 Hz), 2.31−2.25 (2H, m), 1.95−1.89 (1H, m), 1.78−1.68 (1H, m), 1.25−1.00 (21H, m); irradiation of signal at 2.26 ppm decouples the signals at δ 3.77 (1H, d, J = 4.0 Hz), 1.90 (1H, d, J = 13.7 Hz), 1.70 (1H, d, J = 13.7 Hz); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 155.7 (e), 108.1 (e), 99.6 (o), 65.3 (e), 65.2 (e), 61.5 (o), 29.0 (e), 28.5 (e), 17.8 (o), 12.4 (o); CIMS (MH^+) *m/e* 354 (10), base 311 (100), 353 (8), 326 (6), 325 (6), 312 (22), 311 (100), 310 (11), 253 (16), 252 (18), 126 (11), 114 (11); HRMS (MH^+) *m/e* calcd for $C_{17}H_{32}N_3O_3Si$ 354.221, found 354.220.

2-Azido-4-[(triisopropylsilyl)oxy]pyran-3-ene (23) was synthesized analogously to **6** from **22** (408 mg, 1.57 mmol). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **23**. The product could not be purified by flash chromatography due to its instability over silica gel. The iodobenzene and TMS_2O were removed under high vacuum for 12 h: IR (film) 2944, 2867, 2138, 2101, 1667 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 5.26 (1H, dd, J = 1.5, 3.0 Hz), 4.68 (1H, dd, 3.0, 2.0 Hz), 3.75 (1H, dt, J = 11.2, 3.7 Hz), 3.51 (1H, ddd, J = 11.2, 6.0, 2.0 Hz), 2.17−2.05 (1H, m), 1.68−1.55 (1H, ddd, J = 17.0, 3.7, 1.5 Hz), 1.15−0.95 (21H, m); ^{13}C NMR (75 MHz, APT, C_6D_6) δ 153.9 (e), 100.8 (o), 86.9 (o), 59.9 (e), 29.9 (e), 18.0 (o), 12.8 (o); CIMS (MH^+) *m/e* 298 (40), base 175 (100), 297 (15), 270 (11), 256 (14), 255 (61); HRMS (MH^+) *m/e* calcd for $C_{14}H_{28}N_3O_2Si$ 298.195, found 298.194.

***cis*- and *trans*-3-azido-(5*S*)-5-isopropenyl-2-methyl-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (25)** was synthesized analogously to **6** from **24** (255 mg, 0.83 mmol). The trimethylsilyl azide was added at 0 °C. ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of iodobenzene and epimers (1.6:1) **25**. The epimers were not separable by chromatography but were isolated together by flash chromatography (very short column of Florisil, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **25** as an oil (280 mg, 97%): IR (film) 2945, 2868, 2098, 1674, 1645 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) two epimers δ 4.77−4.66 (6H, m), 3.64−3.57 (1H, m), 3.57−3.49 (1H, m), 2.54−2.48 (2H, m), 2.21−0.84 (62H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) two epimers δ 149.1 (e), 147.7 (e), 147.6 (e), 147.3 (e), 110.2 (e), 109.8 (e), 109.6 (e), 108.2 (e), 63.3 (o), 63.0 (o), 40.0 (o), 37.2 (o), 35.7 (e), 35.5 (e), 34.0 (e), 33.8 (e), 20.8 (o), 20.6 (o), 18.0 (2, i), 14.8 (o), 14.3 (o), 13.2 (o), 13.1 (o); MS (FAB) (MH^+) *m/e* 350 (4), base 307 (100), 349 (6), 348 (6), 322 (6); HRMS (MH^+) *m/e* calcd for $C_{19}H_{36}N_3OSi$ 350.263, found 350.262.

***cis*- and *trans*-3-azido-5-isopropyl-2-methyl-1-[(triisopropylsilyl)-oxy]cyclohex-1-ene (27)** was synthesized analogously to **6** from **26** (600 mg, 1.932 mmol, 1.0 equiv), trimethylsilyl azide (670 μL, 5.02 mmol, 2.6 equiv), and iodosylbenzene (553 mg, 2.51 mmol, 1.3 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and epimers (1.6:1) **27**. The epimers were not separable by chromatography but were isolated together by flash chromatography (short column of Florisil, 15 g, eluents 9:1 hexanes/ethyl acetate) and placed for 1 h under high vacuum (0.6 mmHg) at 85 °C to give **27** as an oil (579 mg, 85%): IR (film) 2946, 2868, 2096, 1678 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major isomer 3.60−3.58 (1H, m), 2.20−1.25 (9, m), 1.25−1.00 (21H, m), 0.80−0.70 (6H, m), δ minor isomer 3.56−3.48 (1H, m), 2.20−1.25 (9, m), 1.25−1.00 (21H, m), 0.80−0.70 (6H, m); ^{13}C NMR (75 MHz, APT, C_6D_6) δ major isomer 149.6 (e), 108.6 (e), 63.3 (o), 36.9 (e), 34.6 (o), 33.0 (o), 32.2 (e), 20.0 (o), 19.6 (o), 18.3 (o), 15.1 (o), 13.6 (o); CIMS (MH^+) *m/e* 352 (6), base 309 (100), others 310 (22), 308 (14), 265 (5); HRMS (M^+) *m/e* calcd for $C_{19}H_{37}N_3OSi$ 351.271, found 351.269.

***cis*-3α/*β*-Azido-6-(ethylenedioxy)-1-[(triisopropylsilyl)oxy]-8a-methylbicyclo[4.4.0]dec-1-ene (29)** was synthesized analogously to **6** from **28** (598 mg, 1.57 mmol), trimethylsilyl azide (500 μL, 3.78 mmol, 2.4 equiv), and iodosylbenzene (416 mg, 1.89 mmol, 1.2 equiv). The ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and epimers (6:1) **29**. The epimers were not separable by chromatography but were isolated together by flash chromatography (very short column of silica gel, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **29** as an oil **29** (589 mg, 89%): IR (film) 2946, 2139, 2091, 1645, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major epimer 4.67 (1H, d, J = 3.86 Hz), 3.95−3.80 (5H, m), 2.13−1.98 (1H, m), 1.98−1.82 (2H, m), 1.82−1.35 (6H, m), 1.20 (3H, s), 1.28−1.00 (21H, m); irradiation of the signal at 4.67 ppm decouples the signal at 3.95 ppm to (t, J = 6.5 Hz); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ major epimer 160.3 (e), 108.9 (o), 97.5 (e), 64.2 (e), 64.1 (e), 57.0 (o), 38.5 (e), 38.3 (o), 36.1 (e), 31.5 (e), 31.2 (e), 30.8 (e), 26.0 (o), 18.1 (o), 12.8 (o); CIMS (MH^+) *m/e* 422 (11), base 379 (100), 420 (16), 394 (2), 380 (21), 365 (3), 326 (3); HRMS (MH^+) *m/e* calcd for $C_{22}H_{40}N_3O_3Si$ 422.284, found 422.283.

3-Azido-1-[(triisopropylsilyl)oxy]cyclopent-1-ene (31) was synthesized analogously to **6** from **30** (378 mg, 1.57 mmol), trimethylsilyl azide (500 μL, 3.78 mmol, 2.4 equiv), and iodosylbenzene (416 mg, 1.89 mmol, 1.2 equiv). ^{1}H NMR analysis of the crude reaction showed only a mixture of TMS_2O, iodobenzene, and **31**. The product was purified by flash chromatography (very short column of silica gel, 15 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **31** as an oil (324 mg, 73%): IR (film) 2946, 2868, 2091, 1637, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78−4.74 (1H, m), 4.34−4.32 (1H, m), 2.58−2.49 (1H, m), 2.33−2.19 (2H, m), 1.95−1.84 (1H, m), 1.15−1.00 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 161.5 (e), 100.3 (o), 66.0 (o), 32.5 (e), 28.6 (e), 17.8 (o), 12.4 (o); CIMS (MH^+) *m/e* 282 (30), base 239 (100), 281 (11), 280 (38), 254 (14, (MH^+) − 28), 240 (53), 238 (32); HRMS (MH^+) *m/e* calcd for $C_{14}H_{28}N_3OSi$ 282.198, found 282.199.

3-Azido-1-[(triisopropylsilyl)oxy]cyclohept-1-ene (33) was synthesized analogously to **6** from **32** (1.0 g, 3.73 mmol, 1.0 equiv), trimethylsilyl azide (1.83 mL, 13.73 mmol, 3.6 equiv), and iodosylbenzene (1.51 g, 6.87 mmol, 1.8 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **33**. The product was purified by flash chromatography (short column of Florisil, 15 g, 9:1 eluents hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 85 °C to give **33** as an oil (0.68 g, 60%): IR (film) 2944, 2867, 2098, 1661, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.93 (1H, d, J = 5.5 Hz), 4.08−4.02 (1H, m), 2.34−2.23 (2H, m), 1.96−1.73 (4H, m), 1.70−1.63 (4H, m), 0.25−1.00 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 159.3 (e), 105.6 (o), 59.2 (o), 35.1 (e), 32.7 (e), 25.8 (e), 24.7 (e), 18.0 (o), 12.5 (o); CIMS (MH^+) *m/e* 310 (9), base 267 (100), others 282 (8), 281 (9), 280 (13); HRMS (MH^+) *m/e* calcd for $C_{16}H_{32}N_3OSi$ 310.231, found 310.231.

3-Azido-1-[(triisopropylsilyl)oxy]cyclooct-1-ene (35) was synthesized analogously to **6** from **34** (0.295 g, 1.04 mmol, 1.0 equiv), trimethylsilyl azide (0.62 mL, 4.18 mmol, 4.0 equiv), and iodosylbenzene (0.45 g, 2.09 mmol, 2.0 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **35**. The product was purified by flash chromatography (short column of Florisil, 15 g, eluents 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 85 °C to give **35** as an oil (0.303 g, 90%): IR (film) 2944, 2869, 2102, 1658, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (1H, t, J = 8.4 Hz), 4.60 (1H, d, J = 8.2 Hz),

4.64 (1H, m), 4.15 (1H, m), 2.4−0.8 (29H, m); CIMS (MH^+) *m/e* 324 (8), 296 (10), base 281 (100), others 280 (44), 267 (8), 252 (29); HRMS (MH^+) *m/e* calcd for $C_{17}H_{34}N_3OSi$ 324.247, found 324.248.

3-Azido-1-[(triisopropylsilyl)oxy]cyclonon-1-ene (37) was synthesized analogously to **6** from **36** (0.312 g, 1.05 mmol, 1.0 equiv), trimethylsilyl azide (0.47 mL, 3.15 mmol, 3.0 equiv), and iodosylbenzene (0.35 g, 1.57 mmol, 1.5 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **37**. The product was purified by flash chromatography (short column of Florisil, 15 g, eluents 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 85 °C to give **37** as an oil (0.299 g, 84%): IR (film) 2946, 2869, 2097, 1658, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.58 (1H, d, J = 9.4 Hz), 4.28 (1H, m), 2.31 (1H, m), 2.20−1.00 (32H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 155.7 (e), 104.6 (o), 60.8 (o), 34.5 (e), 32.6 (e), 27.0 (e), 25.5 (e), 24.6 (e), 23.9 (e), 17.9 (o), 12.5 (o); CIMS (MH^+) *m/e* 338 (8), 297 (14), 296 (26), base 295 (100); HRMS (MH^+) *m/e* calcd for $C_{18}H_{36}N_3OSi$ 338.263, found 338.262.

3-Azido-1-[(triisopropylsilyl)oxy]cyclodec-1-ene (39) was synthesized analogously to **6** from **38** (0.295 g, 0.95 mmol, 1.0 equiv), trimethylsilyl azide (0.74 mL, 5.58 mmol, 5.5 equiv), and iodosylbenzene (0.55 g, 2.5 mmol, 2.5 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **39**. The product was purified by flash chromatography (short column of Florisil, 15 g, eluents 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 85 °C to give **39** as an oil (0.332 g, 99%): IR (film) 2948, 2868, 2096, 1652, 1466 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (1H, d, J = 10.7 Hz), 4.44 (1H, dt, J = 4.8, 10.8 Hz), 2.56 (1H, dt, J = 4.5, 13.5 Hz), 2.25−1.00 (34H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 155.1 (e), 105.1 (o), 61.1 (o), 35.1 (e), 28.9 (e), 27.2 (e), 24.8 (e), 23.6 (e), 20.8 (e), 20.1 (e), 17.9 (o), 12.6 (o); CIMS (MH^+) *m/e* 352 (1), 310 (22), base 209 (100); HRMS (MH^+) *m/e* calcd for $C_{19}H_{38}N_3OSi$ 352.278, found 352.284.

3-Azido-1-[(triisopropylsilyl)oxy]cyclododec-1-ene (41) was synthesized analogously to **6** from a (3.7:1) mixture of isomers (*E:Z*) **40** (532 mg, 1.57 mmol), trimethylsilyl azide (500 μL, 3.78 mmol, 2.4 equiv), and iodosylbenzene (416 mg, 1.89 mmol, 1.2 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene ,and isomers (4:1, *E*/*Z*) **41**. The isomers were not separable by chromatography but were isolated together by flash chromatography (very short column of silica gel, 20 g, eluents 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C to give **41** as an oil (553 mg, 95%). Use of a pure sample of (*E*)-**40** (180 mg, 0.53 mmol), trimethylsilyl azide (85 μL, 1.28 mmol, 2.4 equiv), and iodosylbenzene (70 mg, 0.64 mmol, 1.2 equiv) gives exactly the same composition (4:1, *E*/*Z*) of products **41**: IR (film) 2940, 2865, 2091, 1646, 1463 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ major isomer (*E*) 4.57 (1H, d, J = 10.4 Hz), 4.23 (1H, td, J = 6.8, 10.4 Hz), 2.52−2.43 (1H, m), 1.95 (1H, td, J = 13.9, 5.1 Hz), 1.81−1.70 (1H, m), 1.60−1.05 (36H, m), δ minor isomer (*Z*) 4.45 (1H, d, J = 9.7 Hz), 4.34−4.22 (1H, m), 2.52−2.43 (1H, m), 2.60−1.05 (39H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ major isomer (*E*) δ 156.8 (e), 105.3 (o), 58.9 (o), 33.8 (e), 28.4 (e), 25.0 (e), 24.3 (2, e), 23.4 (e), 22.5 (e), 22.4 (e), 22.1 (e), 18.0 (o), 12.7 (o); CIMS (MH^+) *m/e* 380 (9), base 337 (100), 387 (11), 352 (3), 339 (18), 309 (1), 308 (5); HRMS (MH^+) *m/e* calcd for $C_{21}H_{42}N_3OSi$ 380.310, found 380.310.

3-Azido-3-(2-propenyl)-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (43) was synthesized analogously to **6** from **42** (126 mg, 0.43 mmol), trimethylsilyl azide (140 μL, 1.03 mmol, 2.4 equiv), and iodosylbenzene (114 mg, 0.52 mmol, 1.2 equiv). ^{1}H NMR analysis of the crude reaction mixture showed only a mixture of TMS_2O, iodobenzene, and **43**. The product could not be purified by flash chromatography over Florisil or silica gel without decomposition. Iodobenzene and TMS_2O were removed after 12 h under high vacuum (0.6 mmHg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90−5.75 (1H, m), 5.18−5.08 (2H, m), 4.90 (1H, s), 2.38−2.20 (2H, m), 2.15−2.05 (2H, m), 1.90−1.40 (4H, m), 1.15−0.98 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 156.7 (e), 133.1 (o), 118.5 (e), 103.6 (o), 64.9 (e), 46.3 (e), 33.9 (e), 29.7 (e), 19.1 (e), 17.9 (o), 12.5 (o); HRMS (MH^+) *m/e* calcd for $C_{18}H_{34}N_3OSi$ 336.239, found 336.240.

(*Z*)-1-Azido-3-[(triisopropylsilyl)oxy]pent-2-ene (45) was synthesized analogously to **6** from **44** (305 mg, 1.26 mmol), trimethylsilyl azide (500 μL, 3.77 mmol, 3.0 equiv), and iodosylbenzene (416 mg, 1.89 mmol, 1.5 equiv). ^{1}H NMR analysis of the crude reaction mixture showed a mixture of TMS_2O, iodobenzene, and **45** *Z* (42%), *E* (30%), and 1,2-diazido compounds (28%). The two β-azido silyl enol ethers were not separable by chromatography but were isolated together by flash chromatography (very short column of silica gel, 50 g, eluent 9:1 hexanes/ethyl acetate) and placed for 2 h under high vacuum (0.6 mmHg) at 80 °C: IR (film) 2945, 2869, 2105, 1660, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (1H, t, J = 7.4 Hz), 3.83 (2H, d, J = 7.4 Hz), 2.15 (2H, q, J = 7.5 Hz), 1.15−0.95 (24H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 158.6 (e), 97.8 (o), 46.1 (e), 29.1 (e), 18.0 (o), 13.3 (o), 11.6 (o); CIMS (MH^+) *m/e* 284, base 284 (100), 256 (14), 243 (21), 242 (84), 241 (65); HRMS (MH^+) *m/e* calcd for $C_{14}H_{30}N_3OSi$ 284.216, found 284.216. **(*E*)-1-Azido-3-[(triisopropylsilyl)oxy]pent-2-ene (45)** isolated along with the *Z* isomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (1H, t, J = 8.2 Hz), 3.71 (2H, d, J = 8.2 Hz), 2.15 (2H, q, J = 7.5 Hz), 1.15−0.95 (24H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 160.8 (e), 97.0 (o), 48.5 (e), 24.8 (e), 18.0 (o), 12.6 (o), 12.3 (o).

3-Amino-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (46). Lithium aluminum hydride (380 mg, 10 mmol, 1.8 equiv) was added, at 0 °C, to a solution of **6** (1.63 g, 5.50 mmol, 1.0 equiv) in ether (30 mL). Hydrogen evolution was observed during the addition. The mixture was stirred for 2 h at 25 °C. The reaction was cautiously quenched with an aqueous solution of ammonium chloride (5 × 2 mL) and filtered through a Celite pad which was washed with ether. The phases were separated, and the aqueous phase was extracted with ether (6 × 20 mL). The organic phases were combined and dried (Na_2SO_4), and after filtration, the solvent was removed under reduced pressure to give **46** as a colorless oil (1.26 g, 85%). No further purification was necessary: IR (film) 3347, 2949, 2892, 2865, 1665, 1661, 1580, 1463 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6) δ 4.90 (1H, d, J = 3.35 Hz), 3.42−3.38 (1H, m), 2.05−1.90 (5H, m), 1.85−1.65 (2H, m), 1.60−1.50 (1H, m), 1.20−0.95 (21H, m); ^{13}C NMR (75 MHz, C_6D_6, APT) δ 152.8 (e), 108.5 (o), 47.2 (o), 33.2 (e), 30.1 (e), 20.0 (e), 18.2 (o), 13.0 (o); CIMS (MH^+) *m/e* 270 (18), base 189 (100), 268 (14), 253 (73), 217 (20), 190 (13), 189 (100), 188 (11); HRMS (M^+) *m/e* calcd for $C_{15}H_{31}NOSi$ 269.217, found 269.216.

3-[(2-Naphthalenylsulfonyl)amino-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (47). At 0 °C, in an oven-dried 50 mL flask, triethylamine (560 μL, 4.0 mmol, 2.0 equiv) and 2-naphthalenesulfonyl chloride (907 mg, 4.0 mmol, 2.0 equiv) were added to a solution of **46** (539 mg, 2.0 mmol, 1 equiv) in dichloromethane (10 mL). The mixture was stirred under argon at 25 °C for 12 h and quenched with a saturated solution of ammonium chloride. The phases were separated. The organic phase was washed with an aqueous solution of sodium chloride (20 mL). The aqueous phase was extracted several times with dichloromethane. The organic phases were combined and dried over magnesium sulfate. After filtration, the solvent was removed under reduced pressure. The product was purified by flash chromatography over silica gel (eluent 85:15 hexanes/ethyl acetate) to give **47** as a colorless solid (780 mg, 85%). The product was recrystallized from hexane at 4 °C. The solvent was removed at 4 °C with a Pasteur pipet to avoid redissolution: mp 71−73 °C (hexane); IR (film) 3272, 3058, 2943, 2892, 2866, 1661, 1464 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (1H, s), 7.95−7.80 (4H, m), 7.65−7.50 (2H, m), 4.98 (1H, d, J = 8.8 Hz), 4.30 (1H, d, J = 4.0 Hz), 4.05−3.95 (1H, br), 1.98−1.92 (2H, m), 1.70−1.55 (2H, m), 1.55−1.45 (2H, m), 1.05−0.85 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 155.1 (e), 138.3 (e), 134.6 (e), 132.1 (e), 129.3 (o), 129.1 (o), 128.5 (o), 127.9 (o), 127.8 (o), 127.4 (o), 122.2 (o), 103.1 (o), 49.7 (o), 30.0 (e), 29.2 (e), 19.1 (e), 17.6 (o), 12.3 (o); CIMS (MH^+) *m/e* 461 (7), base 253 (100), 350 (5), 349 (16), 332 (11), 331 (37), 305 (11), 271 (20), 262 (21), 261 (29), 255 (8), 254 (15), 253 (100), 227 (25); HRMS (M^+) *m/e* calcd for $C_{25}H_{38}NO_3SiS$ 460.234, found 460.232.

3-(4,5-Dicarbomethoxy-1,2,3-triazolyl)-1-[(triisopropylsilyl)oxy]cyclohex-1-ene (48). A solution of dimethyl acetylenedicarboxylate (200 μL, 1.65 mmol, 2.0 equiv) and **6** (243 mg, 0.822 mmol, 1.0 equiv) in dichloromethane (4 mL) was heated at reflux for 17 h. The solution was cooled to 25 °C, and the solvent was removed under reduced pressure. ^{1}H NMR spectroscopic analysis showed the product to be a (1.4:1) mixture of isomers. The less polar product **49** (major isomer after the reaction) (R_f 0.36, eluent 3:1 hexanes/ethyl acetate) appears only after 5 h at reflux while the more polar **48** (minor product) (R_f

0.24, eluent 75:25 hexanes/ethyl acetate) appears from the start. Purification by flash chromatography over silica gel (eluent 4:1 hexanes/ethyl acetate) gave **48** as a colorless oil (97.6 mg, 27%): IR (film) 2949, 2867, 1732, 1667, 1545, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (1H, m), 4.91 (1H, d, $J = 3.8$ Hz), 3.93 (3H, s), 3.90 (3H, s), 2.25−1.98 (4H, m), 1.96−1.80 (1H, m), 1.78−1.62 (1H, m), 1.20−0.95 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 160.6 (e), 159.9 (e), 157.4 (e), 138.7 (e), 130.8 (e), 100.4 (o), 58.3 (o), 53.5 (o), 52.4 (o), 29.6 (e), 29.4 (e), 18.2 (e), 17.8 (o), 12.4 (o); CIMS (MH^+) *m/e* 438 (13), base 253 (100), others 437 (4), 409 (1), 394 (7), 342 (42), 316 (5), 298 (2); HRMS (M^+) *m/e* calcd for $C_{21}H_{35}N_3O_5Si$ 437.235, found 437.235.

The adduct **49** is the major compound of a (1.4:1) mixture of isomers. This less polar compound **49** was purified by flash chromatography over silica gel (eluent 3:1 hexanes/ethyl acetate) to give a colorless oil **49** (161.2 mg, 45%): IR (film) 2948, 2867, 1732, 1667, 1515, 1470 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.35−5.22 (1H, m), 4.96 (1H, d, $J = 3.8$ Hz), 3.90 (6H, s), 2.22−1.98 (4H, m), 1.95−1.85 (1H, m), 1.72−1.62 (1H, m), 1.20−0.95 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 160.5 (e), 158.8 (e), 139.2 (e), 100.6 (o), 63.1 (o), 52.6 (o), 29.4 (e), 28.6 (e), 19.1 (e), 17.8 (o), 12.5 (o); CIMS (MH^+) *m/e* 438 (23), base 253 (100), others 437 (14), 436 (18), 394 (23), 370 (12), 343 (20), 342 (90), 298 (10), 254 (54); HRMS (M^+) *m/e* calcd for $C_{21}H_{35}N_3O_5Si$ 437.235, found 437.234.

Isomerization of 48 to 49. A solution of **48** (2 mg, 4.6 μmol) in dichloromethane (2 mL) was heated at reflux for 15 h. The solution was cooled to 25 °C, and the solvent was removed under reduced pressure. ^1H NMR spectroscopic analysis showed a mixture (1:1.5) of **48** and **49**. If a solution of **48** (50 mg, 169 μmol) in dichloromethane (4 mL) was heated at reflux for 72 h, only **49** was observed at the end of the reaction. When **49** was placed under the same conditions, no isomerization was observed. If a sample of **48** was placed for a month at −18 °C, isomerization to **49** was observed (**48**:**49**, 1.7:1).

***trans*-1,2-diazido-1-[(triisopropylsilyl)oxy]cyclohexane (6a). General Procedure for the Synthesis of α-Bis-Azido TIPS Adducts.** Iodosylbenzene (165 mg, 0.75 mmol) and TEMPO (8 mg, 0.05 mmol) were added to a solution of the silyl enol ether **5** (127 mg, 0.50 mmol) in dry toluene (6 mL) under argon. The resulting suspension was cooled to −45 °C. Trimethylsilyl azide (0.20 mL, 173 mg, 3.0 mmol) was added dropwise. The mixture turned orange after approximately 10 min. The reaction was judged to be complete when the mixture had become a clear solution (16 h on this scale, longer times on larger scales). The mixture was allowed to warm slowly to 25 °C and evaporated *in vacuo*. Flash column chromatography (SiO_2, 1% ethyl acetate, 99% hexanes) afforded the bis azide **6a** as clear, colorless oil (154 mg, 91%): purification by flash chromatography on silica gel (eluent hexanes); IR (film) 2946, 2894, 2868, 2110, 1464, 1387, 1368, 1348, 1253 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.50 (1H, t, $J = 5.1$ Hz), 1.92 (1H, ddd, $J = 3.6$, 8.8, 12.7 Hz), 1.85−1.75 (2H, m), 1.72−1.30 (5H, m), 1.25−1.05 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 92.2, 65.5, 34.9, 28.1, 22.1, 20.9, 18.0, 13.2; CIMS (MH^+) *m/e* parent 339; HRMS (M^+) *m/e* calcd for $C_{15}H_{30}OSiN_6$ 338.225, found 338.226.

***trans*-1,2-Diazido-1-[(triisopropylsilyl)oxy]cyclopentane (50):** purification by flash chromatography on silica gel (eluent hexanes); IR (film) 2947, 2869, 2104, 1464, 1337, 1252, 1152 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (1H, dd, $J = 3.7$, 6.2 Hz), 2.12−1.52 (6H, m), 1.34−0.82 (21H, m); CIMS (MH^+) *m/e* parent 325; HRMS (MH^+) *m/e* calcd for $C_{14}H_{29}OSiN_6$ 325.217, found 325.217.

***cis*- and *trans*-1,2-diazido-4,4-(ethylenedioxy)-1-[(triisopropylsilyl)oxy]cyclohexane (51):** purification by flash chromatography on silica gel (eluent 95:5 hexanes/EtOAc); IR (film) 2946, 2868, 2102, 1463, 1367, 1257, 1116, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), 3:1 ratio of diastereomers, δ 4.14−3.82 (4H, m), 3.76 (minor isomer only, 1H, dd, $J = 11.0$ Hz, 5.0 Hz), 3.58 (major isomer only, 1H, dd, $J = 10.7$, 4.8 Hz), 2.16−1.76 (5H, m), 1.76−1.62 (1H, m), 1.38−0.74 (21H, m); CIMS (MH^+) *m/e* parent 397; HRMS ($M^+ - 1$) *m/e* calcd for $C_{17}H_{31}O_3SiN_6$ 395.223, found 395.223.

***trans*-1,2-Diazido-4-*tert*-butyl-1-[(triisopropylsilyl)oxy]cyclohexane (52):** purification by flash chromatography on silica gel (eluent hexanes); IR (film) 2949, 2869, 2106, 1466, 1367, 1237, 1127 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.74 (1H, d, $J = 1.8$ Hz), 1.86−1.74 (3H, m), 1.66−1.46 (3H, m), 1.24 (1H, tt, $J = 11.0$Hz, 3.0 Hz), 1.20−0.96 (21H, m), 0.82 (9H, s); CIMS (MH^+) *m/e* parent 395; HRMS (M^+) *m/e* calcd for $C_{19}H_{38}OSiN_6$ 394.288, found 394.289.

***cis*- and *trans*-1,2-diazido-4,4-[1,2-(dicarbethoxy)ethylenedioxy]-1-[(triisopropylsilyl)oxy]cyclohexane (54):** purification by flash chromatography on silica gel (eluent 90:10 hexanes/EtOAc); IR (film) 2946, 2868, 2109, 1759, 1465, 1369, 1243, 1126, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), 4:2:1 ratio of diastereomers, δ 4.92−4.74 (2H, m), 4.38−4.14 (4H, m), 3.88−3.60 (1H, m), 2.28−1.72 (6H, m), 1.40−1.24 (6H, m), 1.24−0.76 (21H, m); CIMS (MH^+) *m/e* parent 541; HRMS (MH^+) *m/e* calcd for $C_{23}H_{41}O_7SiN_6$ 541.281, found 541.280.

***cis*- and *trans*-1,2-diazido-1-[(triisopropylsilyl)oxy]1,2,3,4-tetrahydronaphthalene (56):** purification by flash chromatography on silica gel (eluent hexane); IR (film) 2946, 2868, 2101, 1464, 1253, 1157 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), 4:1 ratio of diastereomers, major isomer shown, δ 7.82−7.62 (1H, m), 7.38−7.22 (2H, m), 7.20−7.04 (1H, m), 3.80 (1H, dd, $J = 3.5$, 6.7 Hz), 3.03 (1H, dt, $J = 17.7$, 7.7 Hz), 2.86 (1H, dt, $J = 17.7$, 6.2 Hz), 2.44−2.16 (2H, m), 1.36−0.80 (21H, m); CIMS (MH^+) *m/e* parent 387; HRMS ($M^+ - 1$) *m/e* calcd for $C_{19}H_{29}OSiN_6$ 385.219, found 385.217.

***cis*- *and trans*-1,2-diazido-1-[(triisopropylsilyl)oxy]2-phenylcyclohexane (58):** purification by flash chromatography on silica gel (eluent hexanes); mp 86−87 °C (from CH_3NO_2); IR (film) 2945, 2867, 2099, 1464, 1254, 1164, 1102 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$), 5:1 ratio of diastereomers, major isomer shown, δ 2.64 (1H, ddd, $J = 14.1$, 11.0, 5.9 Hz), 2.11 (1H, td, $J = 13.0$, 4.0 Hz), 2.01 (1H, dq, $J = 14.1$, 2.1 Hz), 1.87 (1H,dt, $J = 13.0$, 3.0 Hz), 1.82−1.44 (4H, m), 1.36−0.72 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 137.7, 129.1, 128.3, 128.0, 92.6, 73.6, 35.8, 31.2, 22.8, 20.7, 18.3, 18.1, 13.7; CIMS (MH^+) *m/e* parent 415; HRMS (MH^+) *m/e* calcd for $C_{21}H_{35}OSiN_6$ 415.264, found 415.263.

Adduct 59: purification by flash chromatography on silica gel (eluent 98:2 hexanes/EtOAc); IR (film) 2943, 2867, 2100, 1464, 1361, 1257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.00−3.80 (1H, m), 2.20−0.80 (47H, m); CIMS (MH^+) *m/e* parent 453 (MH^+); HRMS calcd for $C_{24}H_{48}O_2SiN_4$ M^+ 452.355, found *m/e* 452.354.

Adduct 60: purification by flash chromatography on silica gel (eluent 75:25 hexanes/EtOAc); IR (film) 2947, 2867, 2099, 1667, 1646, 1463, 1364, 1259 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.64 (1H, d, $J = 3.0$ Hz), 6.54 (1H, d, $J = 3.0$ Hz), 3.68 (1H, dd, $J = 3.0$, 10.0 Hz), 1.95−1.40 (8H, m), 1.30 (3H, s), 1.21 (9H, s), 1.20 (9H, s), 1.10−0.80 (21H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 186.1, 147.1, 146.9, 142.2, 142.0, 104.8, 62.4, 34.7, 34.4, 29.3, 28.4, 24.9, 22.6, 22.5, 18.4, 18.1, 16.4, 13.2; HRMS (M^+) *m/e* calcd for $C_{30}H_{53}O_2SiN_3$ 515.391, found 515.390.

Adduct 63: purification by flash chromatography on silica gel (eluent 99:1 hexanes/EtOAc); IR (film) 2946, 2868, 2100, 1652, 1484, 1371, 1256 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.18−4.95 (1H, m), 3.96−3.80 (1H, m), 2.36−1.40 (5H, m), 1.40−0.80 (27H, m); CIMS (MH^+) *m/e* parent 379; HRMS ($M^+ - 1$) *m/e* calcd for $C_{18}H_{33}OSiN_6$ 377.248, found 377.247.

Adduct 65: purification by flash chromatography on silica gel (eluent 99:1 hexanes/EtOAc); IR (film) 2945, 2869, 2101, 1651, 1464, 1362, 1257 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.31 (1H, s), 3.88 (1H, dd, $J = 1.9$, 4.2 Hz), 3.78 and 3.71 (each 1H, ABq, $J = 8.8$ Hz), 2.16−1.96 (1H, m), 1.84−1.72 (1H, m), 1.70−1.40 (8H, m), 1.38−0.80 (33H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 153.5, 103.1, 83.0, 63.6, 60.2, 59.3, 39.7, 33.1, 32.8, 26.4, 25.3, 20.1, 20.0, 17.9, 16.9, 12.5; CIMS (MH^+) *m/e* parent 506; HRMS (MH^+) *m/e* calcd for $C_{25}H_{48}O_2SiN_7$ 506.364, found 506.363.

Adduct 66: purification by flash chromatography on silica gel (eluent 90:10 hexanes/EtOAc); IR (film) 2935, 2868, 2097, 1451, 1360, 1260, 1133 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.69 (1H, td, $J = 10.0$, 3.8Hz), 3.30 (1H, td, $J = 10.0$, 4.6Hz), 2.40−2.26 (1H, m), 2.00−1.86 (1H, m), 1.80−0.82 (24H, m); ^{13}C NMR (75 MHz, APT, $CDCl_3$) δ 83.8, 65.0, 60.7, 58.9, 40.5, 40.3, 34.6, 34.3, 31.0, 30.7, 24.2, 23.7, 20.5, 17.3; CIMS (MH^+) *m/e* parent 281; HRMS (M^+) *m/e* calcd for $C_{15}H_{28}ON_4$ 280.226, found 280.226.

Adduct 67: purification by flash chromatography on silica gel (eluent 98:2 hexanes/EtOAc). Data compares well to literature values.[28] IR

(28) Emmer, G.; Zbiral, E. *Liebigs Ann. Chem.* **1979**, 796. Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1976**, *59*, 2100.

(film): 2939, 2861, 2096, 1260 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): 3:1 mixture of diastereomers, δ 3.62 (minor isomer only, 2H, d, J = 10Hz) (*cis* isomer), 3.28−3.08 (major isomer only, 2H, m) (*trans* isomer), 2.18−2.00 (8H, m).

Lactone 70. Treatment of **68** (72 mg, 0.23 mmol) with trimethylsilyl azide (36 μL, 0.27 mmol, 1.3 equiv) and iodosylbenzene (60 mg, 0.27 mmol, 1.3 equiv) in dichloromethane (48 mL) under the usual conditions except that the solution is 0.0047 M with respect to **68** gave **70** (12 mg, 17%) after purification: IR (film) 1775 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.03 (1H, d, J = 3.5 Hz), 4.95 (1H, t, J = 3.5, 5.5 Hz), 2.74 (1H, dd, J = 14, 7 Hz), 2.48 (1H, m), 2.30 (1H, dd, J = 14, 2 Hz), 2.15 (2H, m), 1.75 (1H, m), 1.60 (1H, m), 1.1 (21H, bs); ^{13}C NMR (75 MHz, $CDCl_3$, APT) δ 176.7, 158.2, 99.6, 78.7, 35.7, 33.2, 28.2, 24.4, 18.1, 18.0, 12.0; HRMS (MH^+) *m/e* calcd for $C_{17}H_{30}O_3Si$ 311.204, found 311.204.

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Supporting Information Available: Full details of the X-ray structure determination of **47** and **58** and tables of fractional coordinates, isotropic thermal parameters, anisotropic thermal parameters, bond lengths, and bond angles (32 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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