N,N-Dimethyldimesitylacetamide (10). To a stirred solution of dimesitylketene (610 mg, 2.2 mmol) in THF (10 mL) at 0 °C was added a solution of 26% Me_2NH in water (w/w) (6.5 mL, approximately 36 mmol). After stirring overnight at room temperature, the THF was evaporated. The solution was extracted with ether (3 × 30 mL) and separated, and the organic phase was dried ($MgSO_4$) and evaporated, giving an orange oil (0.59 g). The ^1H NMR ($CDCl_3$) indicated the presence of 10 along with several other compounds. Chromatography on a Si-60 column with 1:1 (v/v) petroleum ether (40-60 °C)/ether eluent gave a light orange solid (325 mg, 46%). Further chromatography of 175 mg of this solid yielded a light orange solid (141 mg). Recrystallization (ether-petroleum ether) gave N,N-dimethyldimesitylacetamide (10), mp 144.5 °C: UV λ_{max} (hexane) 233 nm sh (ϵ) (14 500), 250 (260), 268 (480); IR ν_{max} (Nujol) 1620-1640 (s) cm^{-1}. The ^1H NMR, TLC, and IR are identical with those of 10 obtained above in HMPA.

Anal. Found: C, 81.42; H, 9.01; N, 4.34. Calcd for $C_{22}H_{29}NO$: C, 81.69; H, 9.04; N, 4.33.

X-ray Crystal Structure Analysis. Data were measured on a Philips PW1100 four-circle computer-controlled diffractometer. The method is identical with that described previously,[29] except that the unit cell dimensions were obtained by a least squares fit of 24 centered reflections in the range of 21° < θ < 28°. Intensity data were collected by the ω-2θ technique to a maximum of 2θ of 110°. The scan width $\Delta\omega$ for each reflection was 0.80 ± 0.15 tan θ with a scan speed of 8.24°/min. All non-hydrogen atoms were found by using the results of the SHELX5-86 direct method analysis.[30]

Crystallographic data for 6: $C_{24}H_{35}N_2O_2P$, M 414.5, space group $P_{ca}2_1$; a = 20.520 (4) Å, b = 10.064 (2) Å, c = 11.426 (4) Å; V = 2359.6 (7) Å^3; Z = 4; ρ_{calcd} = 1.17 g cm^{-3}; μ(Cu K$_\alpha$) = 11.02 cm^{-1}; no. of unique reflections 1547, reflections with $I > 2\sigma_I$ = 1475; R = 0.058; R_w = 0.093; $w^{-1} = \sigma_F^2 + 0.00045F^2$.

14: $C_{21}H_{29}N_2O_2P$, M = 456.5, monoclinic, space group $P2_{1/n}$; a = 13.278 (7) Å, b = 15.630 (8) Å, c = 10.049 (5) Å; β = 91.56 (2)°; Z = 4; R = 0.067, R_w = 0.059. For 2520 reflections [$F_o > 1.5\sigma(F_o)$; $w = 1.530[\sigma^2(F) + 0.0002F^2]$].

Acknowledgment. We are indebted to Dr. S. Cohen and to Prof. M. Kaftory for the X-ray diffraction analysis. This work was supported by the United States-Israel Binational Science Foundation (BSF), to whom we are indebted.

Supplementary Material Available: Tables of X-ray data of 6 and 14 (12 pages). Ordering information is given on any current masthead page.

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A New Route to 3,5-Disubstituted Isoxazolidines via the Iodocyclization of Homoallylic Hydroxylamines

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N,N-Dialkyl-*O*-trialkylsilyl homoallylic hydroxylamines reacted with iodine, *N*-iodosuccinimide, or iodine chloride to give 3,5-disubstituted isoxazolidines in good yield. The relative configuration that was generated at C3 and C5 was controlled by the nature of the nitrogen substituent of the parent hydroxylamine: the presence of a primary alkyl group favored the formation of a *cis*-isoxazolidine, whereas the presence of a *tert*-butyl group favored the formation of a *trans*-isoxazolidine. The effects that the *N*- and *O*-substituents and the nature of the iodinating agent exerted on the stereoselectivity of the cyclization were examined. The synthesis of enantiomerically pure isoxazolidines from hydroxylamines carrying a chiral *N*-mannofuranosyl group is described.

Introduction

Isoxazolidines[1] are important intermediates in the synthesis of such naturally occurring substances as Biotin,[2] amino glycosides,[3] alkaloids,[4] and the antibiotics Thienamycin[5] and Negamycin.[6] The usefulness of isoxazolidines arises from the transformations possible for these versatile compounds. For example, they can be readily converted to 1,3-amino alcohols. The most general route to isoxazolidines involves the 1,3-dipolar cycloaddition of nitrones to alkenes. This reaction was first described by Lebel,[7] was later studied by Huisgen,[8] and has been extensively

Scheme I

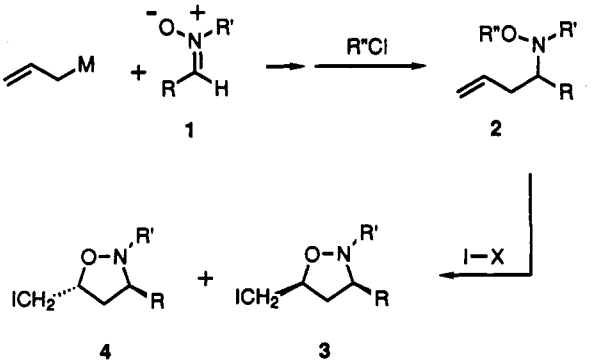

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Table I. Iodocyclization of *N,N*-Dialkyl-*O*-(trialkylsilyl)hydroxylamines 2

entry	2	R	R′	R″	reaction time (h)	iodinating agent	product yield 3 + 4[a] (%)	product ratio 3:4[b]
1	2a	Ph	Me	Me_3Si	25	I_2	29 (20)[c]	7.0 (5.4)[c]
2	2a	Ph	Me	Me_3Si	24	NIS	80	6.0
3	2a	Ph	Me	Me_3Si	1	ICl	62	1.65
4	2a′	Ph	Me	*t*-$BuMe_2Si$	24	I_2[c,d]	7	30.0
5	2a′	Ph	Me	*t*-$BuMe_2Si$	21	NIS[d]	66	24.7
6	2a′	Ph	Me	*t*-$BuMe_2Si$	7	ICl	57	3.3
7	2b	Ph	$PhCH_2$	Me_3Si	4	NIS	72	9.0
8	2b	Ph	$PhCH_2$	Me_3Si	4	ICl	66	1.4
9	2c	Ph	*t*-Bu	Me_3Si	20	NIS	43	0.21
10	2d	*n*-C_5H_{11}	Me	Me_3Si	12	NIS	74	4.7
11	2e	Me_2CH	$PhCH_2$	Me_3Si	12	NIS	61	35.0
12	2e	Me_2CH	$PhCH_2$	Me_3Si	1.5	ICl	66	3.5

[a] Unless otherwise stated, the reactions were performed in CH_2Cl_2. Yields are of the pure isolated compounds. [b] Determined by GLC. [c] Reaction performed in THF. [d] Reaction performed at 20 °C.

applied in both its inter- and intramolecular versions by several groups.[9]

We devised an alternative route to isoxazolidines, starting from nitrones (Scheme I). This route involved the nucleophilic addition of an allylic organometallic compound to an aldonitrone[10] to give a homoallylic hydroxylamine. The hydroxylamine, after *O*-trialkylsilylations, was cyclized to an isoxazolidine by treatment with an iodinating agent.

Formally, the reactions described here construct the same C3–C4 and C5–O bonds that are formed by the 1,3-dipolar cycloaddition. The advantage of this new two-step procedure is that the regiochemistry of the ring-forming step can be controlled. Moreover, the relative configuration that is generated at C3 and C5 can also be controlled by proper choice of the N-substituent R′, the trialkylsilyl group, and the iodinating agent.

Results and Discussion

N,N-Dialkyl homoallylic hydroxylamines were prepared in 60–90% yield (the yield depended on the nature of R and R′ groups) by the reaction of allyl organometallic compounds with nitrones. Two different reactions gave similar results. In the first, a 2 M THF solution of allylmagnesium chloride was introduced at 0 °C to a THF solution of the nitrone. The corresponding hydroxylamine was formed in good yield. In the second reaction, a THF solution of allyl bromide and nitrone was introduced into a stirred suspension of zinc–graphite[11] in THF. The allylzinc bromide that was formed in situ added to the nitrone to produce the corresponding hydroxylamine in a yield comparable to that obtained from the reaction of the Grignard reagent. The *N,N*-dialkylhydroxylamines so formed could be purified by silica gel column chromatography. However they were unstable toward oxidizing agents[12] like halogens and molecular oxygen, which convert them to nitroxide radicals.[13] *O*-Trialkylsilylation stabilized the hydroxylamines. The *O*-trialkylsilyl derivatives 2 could be stored for several weeks without appreciable decomposition. The *O*-(trialkylsilyl)hydroxylamines **2a–e** were iodocyclized[14] by treatment with I_2 in CH_2Cl_2 or THF, *N*-iodosuccinimide (NIS) in $CHCl_3$, or ICl in CH_2Cl_2, at 0 or 20 °C. Under these conditions, cyclization proceeded in a strictly Markovnikov fashion to yield products of 5-*exo-trig* heterocyclization.

In all of the iodocyclizations listed in Table I, with the exception of entry 9, the major product was the *cis*-isoxazolidine **3**. Each of the cis isomers **3a–e** always displayed a higher R_f than the corresponding trans isomer **4a–e**. Thus, each cis/trans pair could be separated by flash chromatography. The relative configurations of C3 and C5 of **3** and **4** were established by analysis of the ^1H NMR spectra of the compounds. As was previously reported,[8,15] the multiplets due to the protons at C4 (H4 protons) of the *cis*-isoxazolidines **3** were broad, well-resolved, and well-separated ($\Delta\delta$ ranged from 0.93 ppm in the case of **3d** to 0.66 ppm in the case of **3e**), whereas in the spectra of the trans isomers, the signals due to the C4 protons were collapsed into an incompletely resolved multiplet. The results of nuclear Overhauser effect (NOE)[16] experiments performed with **3b** and **3e** confirmed the stereochemical assignments and proved that the downfield multiplet was due to the C4 proton that was cis to both H3 and H5 in compounds **3**.

The striking effect that the nature of the iodinating agent had on the rate of the reaction and on the stereochemical outcome was immediately apparent in the case of *O*-(trialkylsilyl)hydroxylamine **2a** (entries 1,3). GLC analysis of the mixture of products formed from the reaction of **2a** and I_2 (entry 1) revealed, after 1 h at 0 °C: **2a** (60%), **3a** (35%), **4a** (5%). Analyses after 3, 9, and 25 h at 0 °C showed no appreciable change in product composition. These results suggested that the thermodynamic equilibrium depicted in Scheme II had already been attained. This belief was reinforced by the observation that the reaction of pure **3a** with in situ generated iodotrimethylsilane[17] in CH_2Cl_2 afforded a mixture of **2a**, **3a**, and

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Scheme II

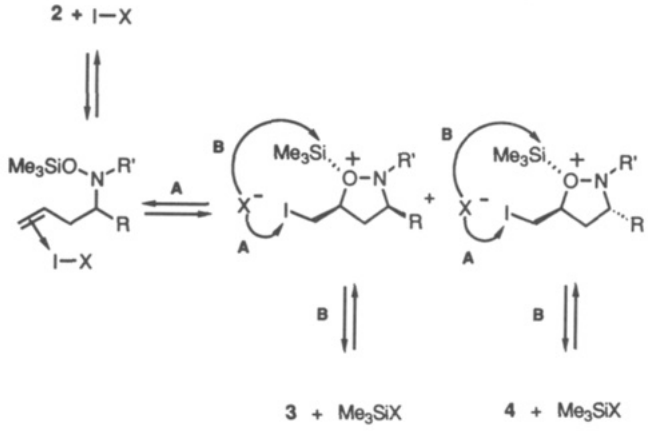
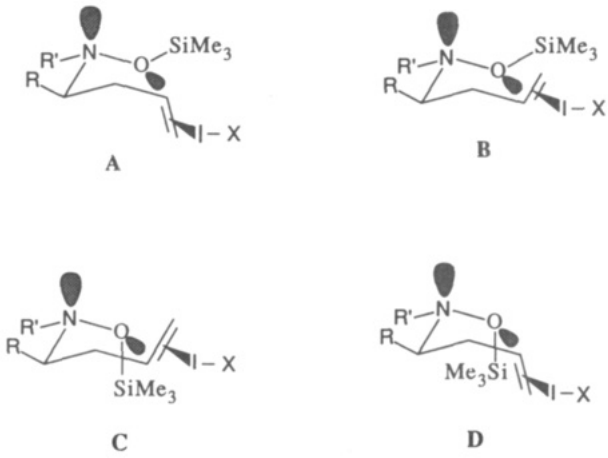


Chart I



4a, the composition of which was similar to that obtained from the I_2-induced cyclization of **2a**.

The nature of the halide ions, X^-, played an important role in the process depicted in Scheme II. When the iodinating agent was I_2, I^- (a typical "soft" base) showed a remarkable preference for attacking the iodomethyl group of the intermediate oxonium ion (path A) rather than the *O*-trialkylsilyl group (path B). Thus, the cyclization step was reversible. Moreover, the iodotrimethylsilane that could be formed in path B is a powerful silylating agent and may react to regenerate the intermediate oxonium ion from isoxazolidines **3** and **4**. Completely different results were observed when ICl was used (entry 3). After 1 h at 0 °C, GLC analysis of the reaction mixture showed the complete disappearance of **2a**. The major product was again *cis*-**3a**. However, the selectivity of the reaction, expressed as the ratio **3**:**4**, fell to 1.65. In this case, Cl^- (a "hard" base) exhibited a sharp preference for attacking the *O*-trialkylsilyl group (path B). This behavior was consistent with the great difference between the strengths of the I–Cl (214 kJ mol^{-1}) and Si–Cl (~410 kJ mol^{-1}) bonds. The poor selectivity displayed reflected the impossibility of exercising thermodynamic control over the formation of the oxonium ion. That the desilylation step was irreversible was confirmed by treating pure **3a** with chlorotrimethylsilane in CH_2Cl_2. After 2 days, no trace of either **2a** or **4a** was detected in the reaction mixture.

The reaction of **2a** with NIS, (which was used in a 10-fold lower concentration than I_2 or ICl for solubility reasons) represented an intermediate case (entry 2). GLC analysis of the reaction mixture showed a 70% conversion to products after 1 h, 80% after 2 h, 90% after 5 h, 95% after 10 h, and 100% after 24 h. The ratio **3**:**4** remained stable at 5.9 over that time interval. The selectivity that was attained in this last case (which approached the optimum value that was obtained in the I_2-induced cyclization), and the possibility that the reaction could be driven to completion, made NIS the electrophilic reagent of choice for the cyclization. The same trend of selectivity was observed in the NIS- and ICl-induced cyclizations of **2a'** (entries 5, 6), **2b** (entries 7, 8), and **2e** (entries 11, 12).

The bulkiness of the *O*-trialkylsilyl group also played an important role in the selectivity of the cyclization. In the reaction of the *t*-$BuMe_2Si$ hydroxylamine **2a'** with I_2, the rate of conversion was exceedingly low. This was in agreement with the greater steric hindrance to attack on silicon by I^- that would be presented by the bulky *t*-$BuMe_2Si$ group (entry 4). When either NIS or ICl were used (entries 5 and 6), the rate of conversion increased at the expense of selectivity, as has already been discussed. In all cases, the replacement of a Me_3Si group by a *t*-$BuMe_2Si$ group gave rise to increased selectivity (compare entries 1 and 4, 2 and 5, 3 and 6).

As to the effect of the nitrogen substituent R', it was observed that, whereas the presence of a primary alkyl group (methyl or benzyl) favored the formation of a *cis*-isoxazolidine, the presence of a tertiary alkyl group (entry 9) favored the formation of the trans product **4**.

Finally, a 7-fold increase in selectivity was observed when the substituent R was changed from a primary alkyl group to a secondary alkyl (entries 10, 11).

A mechanism that attempts to account for the factors that determine the diastereofacial selectivity of the process is proposed. The mechanism features the transition state structures A–D[18] (Chart I).

In the structures A–D, R and R' are trans to each other in order to minimize nonbonded interactions. A lone pair of electrons of the oxygen atom is directed toward one diastereotopic π-face of the carbon–carbon double bond. For steric reasons, the conformer A, which leads to the *trans*-isoxazolidine **4**, is the most thermodynamically favored. Conformer B suffers from a destabilizing interaction between the Me_3Si group and the carbon–carbon double bond. However, as has been seen, the formation of **4** is favored only when R' = *tert*-butyl. Thus the preferential formation of *cis*-isoxazolidines **3** when R' = primary alkyl must be the result of electronic effects that play an important role in determining the preferred orientations of the substituents. When R' is not sterically demanding, a stabilizing anomeric effect that can be attributed to an interaction between the nitrogen n-orbital and the Si–O σ^* bond can be present.[19] This would explain why the Me_3Si group adopts a pseudoaxial orientation that ensures that an antiperiplanar relationship exists between the nitrogen lone pair and the O–$SiMe_3$ bond (structure C and D). However, in conformer D, a significant destabilizing nonbonded interaction occurs between the Me_3Si group and the carbon–carbon double bond. Hence, *cis*-isoxazolidines **3** are expected to be formed preferentially, via C.

Finally, the method described here has been applied to the synthesis of optically active isoxazolidines from the *N*-(α-D-mannofuranosyl)nitrone **5**.[20] The reaction of **5**

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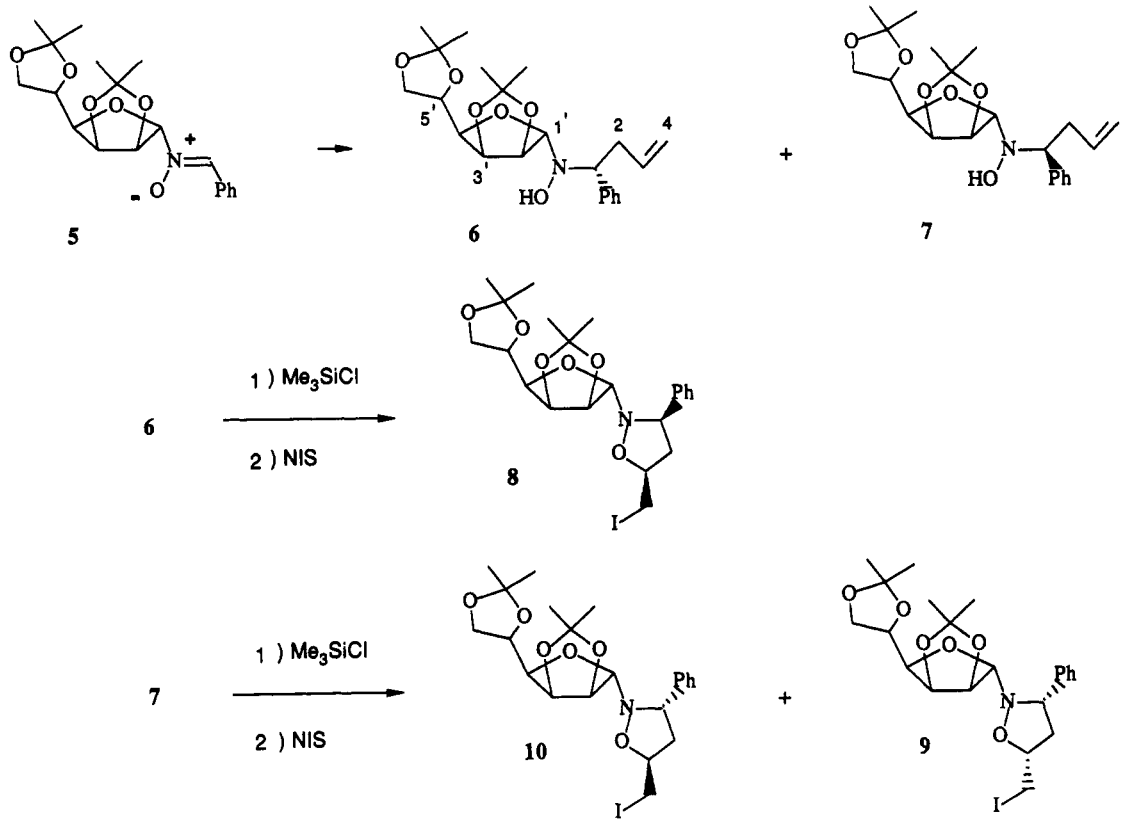
Scheme III



with allylmagnesium chloride afforded the diastereomeric hydroxylamines (1*R*)-**6**[21] and (1*S*)-**7** in 24 and 36% yield, respectively. Similar results were obtained from the reaction of allylzinc bromide formed in situ. Products **6** and **7** were obtained in 20 and 35% yield, respectively.[22] However, when **6** and **7** were silylated and cyclized (NIS, $CHCl_3$), somewhat surprising results were obtained (Scheme III).

O-Trimethylsilylated **6** gave the (3*R*,5*S*)-*cis*-isoxazolidine **8** in 66% yield (the cis stereochemistry was confirmed by the results of a NOE experiment) and no more than a trace of the trans isomer. However, *O*-trimethylsilylated **7** gave the diastereomeric (3*S*,5*R*)-*cis*- and (3*S*,5*S*)-*trans*-isoxazolidines **9** and **10** in 18 and 53% yield, respectively. It is not clear why *O*-trimethylsilylated **6** gave a cis product and *O*-trimethylsilylated **7** gave predominantly a trans product. Obviously, when the *N*-alkyl substituent of the hydroxylamine is α-D-mannofuranosyl or another chiral group, the mere bulkiness of the substituent is not the only factor that determines whether a *cis*- or *trans*-isoxazolidine is formed predominantly. In such cases, the stereogenic center at C-1 of the hydroxylamine and the other stereocenters in the *N*-alkyl substituent can act in concert or counteract each other in influencing the approach of the nucleophilic oxygen atom to one or the other diastereotopic face of the carbon–carbon double bond.

Conclusions

The racemic hydroxylamines obtained by allylation of aldonitrones are useful substrates for iodocyclizations. Iodocyclization, a traditional means of functionalizing a carbon–carbon double bond with generation of new stereocenters, yielded mixtures of cis and trans 3,5-disubstituted isoxazolidines. The cis/trans ratio could be controlled by a proper choice of the *N*- and *O*-substituents in **2** and the iodinating agent. Finally, the asymmetric synthesis of isoxazolidines is possible by the use of suitable chiral groups as *N*-substituents.

Experimental Section

General Procedures. ^1H NMR and ^{13}C NMR spectra of $CDCl_3$ solutions were recorded at 300 and 75 MHz, respectively. Chemical shifts are reported in ppm relative to internal standard Me_4Si (δ). High- and low-resolution mass spectra (MS) were recorded at 70 eV. Gas chromatographic–mass spectrometric analyses (GCMS) were performed with a HP-1 cross-linked methyl silicone glass capillary column (0.33-μm film thickness) connected to a quadrupole mass detector. The column temperature was programmed from 50 to 250 °C at 10 °C/min and was then held at 250 °C for 10 min. The helium carrier gas flow rate was 1 mL/min. Retention times (t_R) are reported in minutes. Analytical thin-layer chromatography (TLC) was performed with Kieselgel 60 F_{254} plates. Kieselgel 60 (230–400 mesh) was used for flash chromatography. Melting points (mp) are uncorrected. The silylated hydroxylamines **2**, **6**, and **7** were purified by chromatography and were sufficiently pure (>95% by ^1H NMR analysis) to be used directly in the subsequent cyclization reactions. The isoxazolidines **3**, **4**, and **8–10** gave acceptable elemental analyses (C and H ±0.3%). Reactions were performed in oven-dried glassware under an atmosphere of dry argon. All solvents were purified before use. *N*-Iodosuccinimide,[23] nitrones **1a–c**,[24] **1d–e**,[25]

(21) The *R* configuration was assigned to **8** after the physical properties of (*S*)-1-phenylbutanamine were compared to those of the product that was obtained by exposing **8** to, successively, acid (to remove the glycosyl group) and H_2 in the presence of $Pd(OH)_2/C$. See: Yamamoto, Y.; Shimoda, H.; Oda, J.; Inouie, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3247–3249.

(22) The slight preference displayed by allylmagnesium chloride and allylzinc bromide for attacking the π *si* face of the nitrone is in agreement with the mechanism proposed by Vasella for the addition of phosphorus nucleophiles to **5**. See: (a) Bernet, B.; Krawczyk, E.; Vasella, A. *Helv. Chim. Acta* **1985**, *68*, 2299. (b) Huber, R.; Vasella, A. *Tetrahedron* **1990**, *46*, 33–58.

(23) Djerassi, C.; Lenk, C. T. *J. Am. Chem. Soc.* **1953**, *75*, 3493–3495.

and 7[20] were prepared by literature procedures.

N-[(Trimethylsilyl)oxy]-N-methyl-α-2-propenylbenzenemethanamine (2a). To a stirred solution of nitrone **1a** (1.3 g, 10 mmol) at 0 °C was added drop-by-drop a THF solution of allylmagnesium chloride (Aldrich, 5 mL of 2 N solution, 10 mmol). The mixture was stirred at 0 °C for 1 h. The reaction was quenched with water (2 mL), and the mixture was filtered. The filtrate was concentrated, and the residue of crude *N*-hydroxy-*N*-methyl-α-2-propenylbenzenemethanamine (1.67 g, 94%) was used without further purification: mp 94–95 °C; ^{1}H NMR δ 7.28 (m, 5 H, ArH), 5.55 (m, 1 H, H_2C=C*H*), 4.90 (m, 2 H, H_2C=CH), 3.55 (m, 1 H, H1), 2.95 (m, 1 H, =CHCH_2) 2.55 (m, 1 H, =CHCH_2), 2.50 (s, 3 H, CH_3); ^{13}C NMR δ 139.7, 135.3, 128.9, 128.5, 127.8, 117.0, 74.1, 45.9, 37.8; IR 3200, 3070, 3000, 2920, 2850, 1635, 1595, 1490, 1450, 1375, 1345, 1330, 1180, 1100, 920, 840, 750, 700 cm^{-1}; GCMS *m/z* (relative intensity) 137 (9), 136 (M^+ – C_3H_5, 100), 131 (M^+ – CH_3NOH, 11%), 129 (8), 120 (34), 119 (9), 118 (20), 116 (10), 104 (9), 91 (41), 77 (16), 42 (25).

Compound **2a** was also prepared by the alternative procedure. To a suspension of zinc–graphite[11] (15 mmol) in THF (20 mL) were added, in turn, allyl bromide (0.50 mL, 6 mmol) and nitrone **1a** (0.68 g, 5 mmol) at room temperature. The mixture was stirred for 45 min, and then the reaction was quenched with water (2 mL) and was filtered. Solvent was evaporated from the filtrate. The crude hydroxylamine (0.72 g, 82%) was trimethylsilylated without further purification. To a solution of the hydroxylamine (1.8 g, 10 mmol) in DMF (5 mL), Et_3N (1.4 mL, 12.5 mmol), and Me_3SiCl (1.25 mL, 12.5 mmol) were added at 0 °C. The resulting suspension was stirred at room temperature for 9 h then was filtered through Celite. The solid collected by filtration was washed with cyclohexane. The combined organic phases were concentrated in vacuo. The product **2a** (2.37 g, 92%) was purified by flash chromatography (cyclohexane/Et_2O (9:1)): ^{1}H NMR δ 7.23 (m, 5 H, ArH), 5.45 (m, 1 H, H_2C=C*H*), 4.85 (m, 2 H, CH_2=CH), 3.50 (m, 1 H, H1), 2.85 (m, 1 H, =CHCH_2), 2.35 (m + s, 4 H, CH_3 + =CHCH_2), 0.20 (s, 9 H, CH_3); ^{13}C NMR δ 135.8, 129.1, 128.9, 128.3, 127.6, 116.6, 75.6, 46.4, 38.9, 0.45; MS *m/z* (relative intensity): 243 (M^+ – 15, 2%), 208 (M^+ – 41, 100), 131 (8), 130 (12), 118 (15), 104 (4), 91 (18), 89 (10), 75 (9), 73 (23), 59 (7), 42 (8).

N-[(*tert*-Butyldimethylsilyl)oxy]-N-methyl-α-2-propenylbenzenemethanamine (2a'). Et_3N (0.56 mL, 5 mmol) and *t*-BuMe_2SiCl (0.76 g, 5 mmol) were added to a solution of *N*-hydroxy-*N*-methyl-α-2-propenylbenzenemethanamine (0.70 g, 5 mmol) in DMF (2 mL) at room temperature. The resulting suspension was stirred at room temperature for 9 h. The mixture was filtered through Celite. The filtrate was concentrated, and the residue of crude **2a'** (1.13 g, 78%) was purified by flash chromatography with a short silica gel column (cyclohexane/Et_2O (95:5)): ^{1}H NMR δ 7.25 (s, 5 H, ArH), 5.50 (m, 1 H, H_2C=C*H*), 4.85 (m, m, 2 H, H_2C=CH), 3.52 (m, 1 H, H1), 2.72 (m, 1 H, =CHCH_2), 2.31 (s + m, 4 H, CH_3 + =CHCH_2), 0.85 (s, 9 H), 0.1 (s, 3 H), 0.05 (s, 3 H); GCMS *m/z* (relative intensity) 250 (M^+ – C_3H_5, 100), 234 (M^+ – 57,19), 130 (39), 120 (58), 91 (25), 75 (86).

N-[(Trimethylsilyl)oxy]-N-(phenylmethyl)-α-2-propenylbenzenemethanamine (2b). Allylation of nitrone **1b** with allylmagnesium chloride afforded the corresponding crude hydroxylamine (68%): ^{1}H NMR δ 7.35 (s, 5 H, ArH), 7.25 (s, 5 H, ArH), 5.55 (m, 1 H, CH_2=C*H*), 4.95 (m, 2 H, CH_2=CH), 3.75 (m, 4 H, H1 + CH_2Ph + OH), 2.80 (m, 1 H, =CHCH_2), 2.60 (m, 1 H, =CHCH_2); IR (neat) 3450, 3010, 2910, 2850, 1640, 1600, 1490, 1450, 1375, 920, 840, 820, 760, 735, 700 cm^{-1}; GCMS *m/z* (relative intensity) 177 (M^+ – Ph, 62), 136 (42), 131 (100), 129 (22), 118 (29), 105 (21), 91 (56), 77 (43), 43 (31), 42 (43). Silylation of the hydroxylamine with Me_3SiCl in Et_3N/DMF gave **2b** in 88% yield after purification by flash chromatography on a short column of silica gel (hexane/Et_2O (9:1)): ^{1}H NMR δ 7.30 (m, 5 H, ArH), 7.25 (s, 5 H, ArH), 5.55 (m, 1 H, CH_2=C*H*), 4.90 (m, 2 H, CH_2=CH), 3.9 (m, 1 H, CH_2Ph), 3.75 (dd, *J* = 5.0, 9.9 Hz, 1 H, H1), 3.48 (m, 1 H, CH_2Ph), 2.89 (m, 1 H, =CHCH_2), 2.55 (m, 1 H, =CHCH_2), 0.05 (s, 9 H); ^{13}C NMR δ 138.2, 136.1, 130.1, 129.8, 128.2, 127.6, 127.3, 116.5, 72.1, 60.9, 37.4, 0.4; GCMS *m/z* (relative intensity) 284 (M^+ – C_3H_6, 31), 131 (7), 92 (7), 91 (100), 75 (7).

N-[(Trimethylsilyl)oxy]-N-(1,1-dimethylethyl)-α-2-propenylbenzenemethanamine (2c). Allylation of nitrone **1c** with allylmagnesium chloride afforded the corresponding hydroxylamine, which was purified (48%) by column chromatography (cyclohexane/Et_2O (9:1)): ^{1}H NMR δ 7.42 (m, 2 H, ArH), 7.27 (m, 3 H, ArH), 5.71 (m, 1 H, CH_2=C*H*), 4.95 (m, 2 H, CH_2=CH), 4.31 (s, 1 H, OH), 4.01 (t, *J* = 7.4 Hz, 1 H, H1), 2.82 (m, 1 H, =CHCH_2), 2.62 (m, 1 H, =CHCH_2), 0.97 (s, 9 H, CH_3); ^{13}C NMR δ 142.3, 136.6, 128.6, 127.5, 126.4, 115.0, 64.0, 58.8, 39.0, 25.9. Silylation of the hydroxylamine in the manner described previously and flash chromatography of the product (cyclohexane/Et_2O (95:5)) on a short silica gel column gave **2c** (68%): ^{1}H NMR δ 7.42 (m, 2 H, ArH), 7.27 (m, 3 H, ArH), 5.69 (m, 1 H, CH_2=C*H*), 4.97 (m, 2 H, CH_2=CH), 4.00 (m, 1 H, H1), 2.79 (m, 1 H, =CHCH_2), 2.55 (m, 1 H, =CHCH_2), 1.01 (s, 9 H, CH_3), 0.1 (m, 9 H, CH_3); GCMS *m/z* (relative intensity): 276 (M^+ – CH_3, 3), 250 (39), 194 (100), 178 (32), 131 (92), 104 (55), 91 (68), 75 (89), 57 (98).

N-[(Trimethylsilyl)oxy]-N-methyl-1-nonen-4-amine (2d). Allylation of nitrone **1d** with allylmagnesium chloride in the manner described previously afforded the crude hydroxylamine (74%): ^{1}H NMR δ 5.85 (m, 1 H, H2), 5.08 (m, 2 H, H1), 2.65 (m + s, 4 H, H4 + CH_3), 2.46 (m, 1 H, H3), 2.23 (m, 1 H, H3), 1.65–1.25 (m, 8 H, H5–H8), 0.9 (t, *J* = 7.0 Hz, 3 H, H9); ^{13}C NMR δ 137.0 116.6, 67.8, 43.9, 34.3, 32.3, 29.8, 26.2, 22.7, 14.1. After silylation and flash chromatography (cyclohexane/Et_2O (95:5)), **2d** was obtained in 90% yield: ^{1}H NMR δ 5.78 (m, 1 H, H2), 4.95 (m, 2 H, H1), 2.65 (m, 1 H, H4), 2.38 (s, 3 H, CH_3), 2.2–1.8 (m, 2 H, H3), 1.45–1.15 (m, 8 H, H5–H8), 0.85 (t, *J* = 7.1 Hz, 3 H, H9), 0.05 (s, 9 H, CH_3); ^{13}C NMR δ 137.4, 115.8, 67.4, 31.9, 26.7, 26.2, 22.4, 13.8, –0.7; GCMS *m/z* (relative intensity) 228 (M^+ – CH_3, 8), 202 (100), 172 (6), 73 (20).

N-[(Trimethylsilyl)oxy]-N-(phenylmethyl)-2-methyl-5-hexen-3-amine (2e). Allylation of nitrone **1e** with allymagnesium chloride afforded the crude hydroxylamine (65%): ^{1}H NMR δ 7.37 (m, 5 H, ArH), 5.95 (m, 1 H, H5), 5.04 (m, 2 H, H6), 4.75 (s, 1 H, OH), 3.95 (d, *J* = 13.1 Hz, 1 H, CH_2Ph), 3.81 (d, *J* = 13.1 Hz, 1 H, CH_2Ph), 2.52 (m, 2 H, H3 + H4), 2.32 (m, 1 H, H4), 2.00 (m, 1 H, H2), 1.00 (d, *J* = 8 Hz, 3 H, H1), 0.98 (d, *J* = 8 Hz, 3 H, CH_3); ^{13}C NMR δ 139.1, 138.8, 129.4, 128.4, 127.2, 115.4, 70.9, 60.9, 30.7, 29.7, 20.2, 19.4. Silylation and flash chromatography on a short silica gel column (cyclohexane/Et_2O (95:5)) gave pure **2e** (89%): ^{1}H NMR δ 7.25 (m, 5 H, ArH), 6.91 (m, 1 H, H5), 4.96 (m, 2 H, H6), 3.73 (m, 2 H, CH_2Ph), 2.58 (m, 2 H, H3 + H4), 2.18 (m, 1 H, H4), 1.89 (m, 1 H, H2), 1.01 (d, *J* = 7.0 Hz, 3 H, H1), 0.92 (d, *J* = 7.0 Hz, 3 H, CH_3), –0.18 (s, 9 H, CH_3); ^{13}C NMR δ 139.3, 139.0, 128.5, 128.1, 127.2, 115.0, 71.9, 59.5, 30.7, 29.8, 21.4, 20.1, 0.5.

General Procedure for the I_2-Induced Cyclization of O-(Trimethylsilyl)hydroxylamines 2a–e. The reaction of **2a** with I_2 (Table I, entry 1) was typical. The reaction was performed under dry Ar in a vessel protected against light. I_2 (2.28 g, 9 mmol) was added to a solution of **2a** (1.55 g, 6 mmol) in CH_2Cl_2 (9 mL) at 0 °C. The reaction was quenched after 25 h at 0 °C with saturated aqueous $Na_2S_2O_3$ (3 mL). After the mixture was diluted with Et_2O (10 mL), the two liquid layers were separated. The aqueous phase was extracted with Et_2O (3 × 5 mL). The combined organic phases were dried (Na_2SO_4), and the solvent was evaporated in vacuo. The crude cyclic products **3a** and **4a** were separated by flash chromatography on silica gel (cyclohexane/Et_2O (8:2)).

General Procedure for the NIS-Induced Cyclization of O-(Trimethylsilyl)hydroxylamines 2a–e. A solution of **2a** (1.55 g, 6 mmol) in $CHCl_3$ (2 mL) was added to a 0.1 M solution of NIS (75 mL) in $CHCl_3$ at 0 °C (Table I, entry 2). Stirring was continued at 0 °C for 24 h. Quenching and workup were performed as in the previously described procedure.

General Procedure for the ICl-Induced Cyclization of O-(Trimethylsilyl)hydroxylamines 2a–e. A solution of **2a** (1.55 g, 6 mmol) in CH_2Cl_2 (1.5 mL) was added to a 1 M solution of ICl (7.5 mL) in CH_2Cl_2 at 0 °C over 3 min (Table I, entry 3). The reaction was quenched after 1 h. The apparatus used and the workup were the same as those of the I_2-induced reaction.

***cis*-2-Methyl-3-phenyl-5-(iodomethyl)isoxazolidine (3a):** IR (neat) 3060, 3020, 2960, 2870, 2850, 2770, 1600, 1490, 1450,

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1430, 1350, 1165, 1110, 1070, 1025, 1000, 990, 920, 900, 820, 750, 695 cm^{-1}; ^{1}H NMR δ 7.35 (s, 5 H, ArH), 4.36 (dddd, J = 5.75, 5.90, 8.34, 8.50 Hz, 1 H, H5), 3.58 (dd, J = 7.65, 9.76 Hz, 1 H, H3), 3.49 (dd, J = 5.75, 9.45 Hz, 1 H, CH_2I), 3.29 (dd, J = 8.50, 9.45 Hz, 1 H, CH_2I), 2.91 (ddd, J = 8.34, 7.65, 12.80 Hz, 1 H, H4), 2.56 (s, 3 H, NCH_3), 2.14 (ddd, J = 5.90, 9.76, 12.80 Hz, 1 H, H4); ^{13}C NMR δ 139.5, 129.5, 128.7, 128.3, 77.4 (C5), 74.8 (C3), 46.9 (C4), 43.8 (NCH_3), 10.6 (CH_2I); GCMS (t_R 16.2) m/z (relative intensity) 303 (M^+, 71), 257 (7), 226 (8), 176 (31), 134 (30), 131 (100), 91 (56), 77 (22), 51 (11), 42 (17).

***trans*-2-Methyl-3-phenyl-5-(iodomethyl)isoxazolidine (4a)**: IR (neat) 3060, 3030, 2920, 2850, 2770, 1600, 1490, 1450, 1430, 1355, 1335, 1210, 1170, 1110, 1030, 1005, 980, 915, 865, 845, 750, 695 cm^{-1}; ^{1}H NMR δ 7.35 (m, 5 H, ArH), 4.28 (br m, 1 H, H5), 3.62 (m, 1 H, H3), 3.35 (dd, J = 4.72, 10.2 Hz, 1 H, CH_2I), 3.28 (dd, J = 6.48, 10.2 Hz, 1 H, CH_2I), 2.60 (s, 3 H, NCH_3), 2.37–2.55 (m, 2 H, H4); ^{13}C NMR δ 139.2, 129.2, 128.5, 128.2, 76.3 (C5), 73.1 (C3), 45.8 (C4), 43.6 (NCH_3), 8.3 (CH_2I); GCMS (t_R 16.5) m/z (relative intensity) 303 (M^+, 97), 257 (8), 226 (9), 176 (29), 134 (27), 131 (100), 91 (42), 77 (13), 42 (11).

***cis*-2-(Phenylmethyl)-3-phenyl-5-(iodomethyl)isoxazolidine (3b)**: mp 102 °C; IR (KBr) 2920, 2850, 1450, 1370, 1160, 1140, 1000, 980, 925, 755, 735, 700 cm^{-1}; ^{1}H NMR δ 7.2 (m, 10 H, ArH), 4.27 (dddd, J = 5.4, 5.6, 7.6, 9.4 Hz, 1 H, H5), 3.85 (d, J = 14.6 Hz, 1 H, CH_2Ph), 3.73 (dd, J = 7.6, 9.1 Hz, 1 H, H3), 3.62 (d, J = 14.6 Hz, CH_2Ph), 3.33 (dd, J = 7.6, 9.4 Hz, 1 H, CH_2I), 3.18 (t, J = 9.4 Hz, 1 H, CH_2I), 2.81 (dt, J = 7.6, 12.7 Hz, 1 H, H4), 2.05 (ddd, J = 5.6, 9.1, 12.7 Hz, 1 H, H4); ^{13}C NMR δ 139.1, 137.8, 128.9, 128.6, 128.3, 128.0, 127.7, 127.2, 76.8 (C5), 71.2 (C3), 59.4 (CH_2Ph), 45.6 (C4), 9.9 (CH_2I); GCMS (t_R 21.9) m/z (relative intensity) 379 (M^+, 10), 252 (4), 132 (6), 131 (86), 104 (7), 92 (7), 91 (100), 65 (12), 51 (5), 41 (2).

***trans*-2-(Phenylmethyl)-3-phenyl-5-(iodomethyl)isoxazolidine (4b)**: mp 86 °C; IR (KBr) 2920, 2850, 1490, 1480, 1450, 1370, 1175, 1070, 1040, 1005, 975, 845, 755, 705 cm^{-1}; ^{1}H NMR δ 7.3 (m, 10 H, ArH), 4.21 (m, 1 H, H5), 3.91 (d, J = 14.3 Hz, 1 H, CH_2Ph), 3.84 (t, J = 8.4 Hz, 1 H, H3), 3.72 (d, J = 14.3 Hz, 1 H, CH_2Ph), 3.27 (dd, J = 3.9, 10.1 Hz, 1 H, CH_2I), 3.17 (dd, J = 7.3, 10.1 Hz, 1 H, CH_2I), 2.45 (m, 2 H, H4); ^{13}C NMR δ 139.2, 137.6, 129.1, 128.9, 128.3, 128.1, 128.0, 127.4, 76.0 (C5), 69.7 (C3), 60.1 (CH_2Ph), 44.9 (C4), 8.6 (CH_2I); GCMS (t_R 22.1) m/z (relative intensity) 379 (M^+, 13), 252 (4), 131 (87), 104 (7), 92 (7), 91 (100), 65 (12), 51 (5), 41 (2).

***cis*-(1,1-Dimethylethyl)-3-phenyl-5-(iodomethyl)isoxazolidine (3c)**: IR (neat) 2910, 2850, 1455, 1375, 1355, 1220, 1160, 1000, 930, 880, 760, 700 cm^{-1}; ^{1}H NMR δ 7.40 (m, 2 H, ArH), 7.32 (m, 3 H, ArH), 4.27 (br m, 2 H, H5 + H3), 3.31 (dd, J = 5.8, 9.6 Hz, 1 H, CH_2I), 3.11 (dd, J = 7.9, 9.6 Hz, 1 H, CH_2I), 2.83 (ddd, J = 5.9, 7.4, 12.5 Hz, 1 H, H4), 2.05 (ddd, J = 8.4, 8.5, 12.5 Hz, 1 H, H4), 1.62 (m, 9 H, CH_3); ^{13}C NMR δ 143.6, 128.8, 128.6, 127.1, 77.9 (C5), 64.0 (C3), 59.7 (C), 48.7 (C4), 26.7 (CH_3), 7.0 (CH_2I); GCMS (t_R 17.2) m/z (relative intensity): 345 (M^+, 29), 330 (58), 289 (100), 257 (15), 162 (53), 131 (38), 91 (30), 57 (41).

***trans*-(1,1-Dimethylethyl)-3-phenyl-5-(iodomethyl)isoxazolidine (4c)**: IR (neat) 2910, 2850, 1455, 1375, 1360, 1220, 1160, 1010, 930, 880, 760, 700 cm^{-1}; ^{1}H NMR δ 7.45 (m, 2 H, ArH), 7.28 (m, 3 H, ArH), 4.22 (dd, J = 6.4, 8.5 Hz, 1 H, H3), 4.14 (ddd, J = 4.6, 6.9, 11.5 Hz, 1 H, H5), 3.31 (dd, J = 4.6, 10.0 Hz, 1 H, CH_2I), 3.27 (dd, J = 6.9, 10.0 Hz, 1 H, CH_2I), 2.36 (m, 2 H, H4), 1.04 (s, 9 H, CH_3); ^{13}C NMR δ 144.3, 128.6, 127.3, 127.2, 74.6 (C5), 62.5 (C3), 58.8 (C), 47.2 (C4), 26.0 (CH_3), 6.8 (CH_2I); GCMS (t_R 17.3) m/z (relative intensity) 345 (M^+, 13), 330 (21), 289 (76), 257 (12), 162 (100), 131 (63), 121 (66), 91 (47), 77 (26), 57 (60).

***cis*-2-Methyl-3-pentyl-5-(iodomethyl)isoxazolidine (3d)**: IR (neat) 2960, 2955, 2855, 1460, 1370, 1160, 725 cm^{-1}; ^{1}H NMR δ 4.32 (m, 1 H, H5), 3.35 (dd, J = 5.5, 9.4 Hz, 1 H, CH_2I), 3.14 (dd, J = 8.6, 9.4 Hz, 1 H, CH_2I), 2.50–2.72 (br m, 2 H, H3 + H4), 2.67 (s, 3 H, NCH_3), 1.72 (ddd, J = 2.0, 6.0, 8.4 Hz, 1 H, H4), 1.31 (m, 8 H), 0.91 (t, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR δ 76.1 (C5), 69.5 (C3), 43.9 (NCH_3), 42.7 (C4), 32.6, 31.8, 26.2, 22.3, 13.7 (CH_3), 9.4 (CH_2I); GCMS (t_R 14.4) m/z (relative intensity) 297 (M^+, 15), 226 (100), 99 (24), 73 (18), 42 (20).

***trans*-2-Methyl-3-pentyl-5-(iodomethyl)isoxazolidine (4d)**: IR (neat) 2960, 2955, 2850, 1460, 1370, 1165, 720 cm^{-1}; ^{1}H NMR δ 4.09 (m, 1 H, H5), 3.28 (dd, J = 4.5, 10.0 Hz, 1 H, CH_2I), 3.16 (dd, J = 7.3, 10.0 Hz, 1 H, CH_2I), 2.70 (s, 3 H, NCH_3), 2.57 (m, 1 H, H3), 2.13 (m, 2 H, H4), 1.27 (m, 8 H), 0.86 (t, J = 7.3 Hz, 3 H, CH_3); ^{13}C NMR δ 75.9 (C5), 68.4 (C3), 43.3 (NCH_3), 41.7 (C4), 31.8, 30.0, 26.2, 22.3, 13.7 (CH_3), 8.3 (CH_2I); GCMS (t_R 14.5) m/z (relative intensity) 297 (M^+, 15), 226 (100), 99 (20), 73 (22), 42 (20).

***cis*-2-(Phenylmethyl)-3-(α-methylethyl)-5-(iodomethyl)isoxazolidine (3e)**: IR (neat) 3065, 3030, 2960, 2930, 2870, 1590, 1475, 1455, 760, 695 cm^{-1}; ^{1}H NMR δ 7.32 (m, 5 H, ArH), 4.41 (m, 1 H, H5), 3.97 (d, J = 13.7 Hz, 1 H, CH_2Ph), 3.92 (d, J = 13.7 Hz, 1 H, CH_2Ph), 3.32 (dd, J = 5.1, 9.5 Hz, 1 H, CH_2I), 3.18 (dd, J = 8.4, 9.5 Hz, 1 H, CH_2I), 2.82 (quartet, J = 14.0 Hz, 1 H, H3), 2.56 (ddd, J = 7.6, 12.6, 14.0 Hz, 1 H, H4), 1.90 (ddd, J = 7.1, 12.6, 14.0 Hz, 1 H, H4), 1.78 (sextet, J = 6.7 Hz, 1 H CH(CH_3)$_2$), 0.95 (d, J = 6.7 Hz, 3 H, CH_3), 0.92 (d, J = 6.7 Hz, 3 H, CH_3); ^{13}C NMR (C_6D_6) δ 138.5, 129.1, 128.0, 127.3, 76.2 (C5), 71.5 (C3), 61.0 (NCH_2Ph), 37.0 (C4), 30.1 (CH), 20.0 (CH_3), 17.0 (CH_3), 7.93 (CH_2I); GCMS (t_R 18.6) m/z (relative intensity) 345 (M^+, 4), 303 (6), 302 (54), 92 (7), 91 (100), 65 (7), 55 (5), 43 (4).

***trans*-2-(Phenylmethyl)-3-(α-methylethyl)-5-(iodomethyl)isoxazolidine (4e)**: IR (neat) 3065, 3030, 2960, 2930, 2870, 1590, 1470, 1455, 765, 700 cm^{-1}; ^{1}H NMR δ 7.20 (m, 5 H, ArH), 4.06 (m, 1 H, H5), 3.91 (d, J = 13.7 Hz, 1 H, CH_2Ph), 3.85 (d, J = 13.7 Hz, 1 H, CH_2Ph), 3.25 (dd, J = 4.1, 9.7 Hz, 1 H, CH_2I), 3.10 (dd, J = 8.4, 9.7 Hz, 1 H, CH_2I), 2.78 (m, 1 H, H3), 2.26 (ddd, J = 5.0, 7.6, 12.7 Hz, 1 H, H4), 1.98 (ddd, J = 6.4, 7.8, 12.7 Hz, 1 H, H4), 1.69 (m, 1 H, CH(CH_3)$_2$), 0.89 (d, J = 3.3 Hz, 3 H, CH_3), 0.85 (d, J = 3.3 Hz, 3 H, CH_3); ^{13}C NMR δ 138.7, 129.2, 128.3, 127.2, 76.5 (C5), 70.6 (C3), 61.8 (NCH_2Ph), 36.2 (C4), 29.1 (CH), 19.9 (CH_3), 16.6 (CH_3), 8.5 (CH_2I); GCMS (t_R 18.9) m/z (relative intensity) 345 (M^+, 3), 303 (6), 302 (55), 92 (7), 91 (100), 65 (7), 55 (5), 43 (5).

(1*R*)-*N*-Hydroxy-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-D-mannofuranosyl)-α-2-propenylbenzenemethanamine (6): [α]^{22}D +20.2° (*c* 2.0, $CHCl_3$); ^{1}H NMR δ 7.35 (m, 5 H, ArH), 5.51 (m, 1 H, H3), 4.75–5.26 (m, 4 H), 4.58 (s, 1 H), 4.32 (m, 2 H), 4.09 (m, 3 H), 2.69 (m, 1 H, H2), 2.56 (m, 1 H, H3), 1.52 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3); ^{13}C NMR δ 141.0, 134.5 (C3), 128.6, 128.4, 127.5, 117.3 (C4), 112.3 (C), 109.2 (C), 96.4 (C1′), 84.5 (CH), 84.4 (CH), 81.0 (CH), 73.8 (CH), 67.4 (C6′), 66.8 (C1), 37.4 (C2), 26.7 (CH_3), 25.8 (CH_3), 25.1 (CH_3), 24.1 (CH_3).

(1*R*)-*N*-[(Trimethylsilyl)oxy]-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-D-mannofuranosyl)-α-2-propenylbenzenemethanamine: ^{1}H NMR δ 7.35 (m, 5 H, ArH), 5.54 (m, 1 H, H3), 4.95 (m, 2 H, H4), 4.78 (m, 3 H,), 4.43 (dd, J = 4.1, 7.0 Hz, 1 H), 4.31 (dt, J = 5.5, 7.6 Hz, 1 H), 4.10 (m, 3 H), 2.98 (m, 1 H, H2), 2.70 (m, 1 H, H2), 1.5 (s, 3 H, CH_3), 1.43 (s, 6 H, 2CH_3), 1.39 (s, 3 H, CH_3), 0.08 (s, 9 H, 3CH_3).

(1*S*)-*N*-Hydroxy-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-D-mannofuranosyl)-α-2-propenylbenzenemethanamine (7): ^{1}H NMR δ 7.28 (m, 5 H, ArH), 5.60 (m, 1 H, H3), 4.90 (m, 4 H), 4.74 (d, J = 3.2 Hz, 1 H), 4.42 (s, 1 H), 4.33 (m, 2 H), 4.13 (m, 3 H), 2.82 (m, 1 H, H2), 2.56 (m, 1 H, H2), 1.50 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3); ^{13}C NMR δ 139.9, 136.2 (C3), 129.9, 129.5, 128.7, 117.8 (C4), 113.1 (C), 110.1 (C), 97.2 (C1′), 85.6 (CH), 85.0 (CH), 81.7 (CH), 74.7 (CH), 67.7 (C6′), 67.3 (C1), 39.1 (C2), 27.6 (CH_3), 26.5 (CH_3), 26.1 (CH_3), 24.8 (CH_3); MS m/z (relative intensity) 405 (1, M^+), 390 (10, $M^+ - 15$), 364 (35, $M^+ - 41$), 348 (14), 306 (27), 185 (36), 149 (100), 131 (50), 101 (15), 91 (19), 59 (54).

(1*R*)-*N*-[(Trimethylsilyl)oxy]-*N*-(2′,3′:5′,6′-*O*-diisopropylidene-α-D-mannofuranosyl)-α-2-propenylbenzenemethanamine: [α]^{22}D +31.0° (*c* 2.0, $CHCl_3$); ^{1}H NMR δ 7.3 (m, 5 H, ArH), 5.43 (m, 1 H, H3), 4.9 (m, 2 H, H4), 4.78 (m, 2 H), 4.43 (s, 1 H), 4.34 (m, 1 H), 4.26 (m, 1 H), 4.07 (m, 2 H), 2.82 (m, 1 H, H2), 2.41 (m, 1 H, H2), 1.48 (s, 3 H, CH_3), 1.40 (s, 6 H, 2CH_3), 1.31 (s, 3 H, CH_3), 0.27 (s, 9 H, 3CH_3); ^{13}C NMR δ 139.8, 135.4 (C3), 129.3, 128.4, 127.6, 117.0 (C4), 112.0 (C), 109.1 (C), 96.9 (C1′), 84.5 (CH), 84.0 (CH), 80.8 (CH), 73.9 (CH), 67.6 (C6′), 66.8 (C1), 38.1 (C2), 26.7 (CH_3), 25.6 (CH_3), 25.2 (CH_3), 24.1 (CH_3), 0.7 (CH_3).

(3*R*,5*S*)-*N*-(2′,3′:5′,6′-*O*-Diisopropylidene-α-D-mannofuranosyl)-3-phenyl-5-(iodomethyl)isoxazolidine (8): [α]$^{22}_D$ −40° (*c* 1.0, $CHCl_3$); mp 134 °C; ^{1}H NMR δ 7.32 (m, 5 H, ArH), 5.01 (d, J = 6.0 Hz, 1 H, H2′), 4.80 (dd, J = 3.6, 6.0 Hz, 1 H, H3′), 4.58 (s, 1 H, H1′), 4.45 (pseudo dq, J = 5.5, 7.5 Hz, 1 H, H5), 4.22 (dd, J = 7.5, 8.6 Hz, 1 H, H3), 4.18 (ddd, J = 8.5, 6.4, 4.9 Hz, 1

H, H5'), 3.76 (dd, J = 6.4, 8.6 Hz, 1 H, H6'), 3.66 (dd, J = 3.6, 8.5 Hz, 1 H, H4'), 3.39 (dd, J = 5.5, 9.8 Hz, 1 H, CH_2I), 3.21 (dd, J = 7.7, 9.8 Hz, 1 H, CH_2I), 2.98 (dd, J = 8.6, 4.9 Hz, 1 H, H6'), 2.93 (m, 1 H, H4), 2.17 (ddd, J = 7.3, 8.6, 12.7 Hz, 1 H, H4), 1.42 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3), 1.27 (s, 6 H, $2CH_3$); ^{13}C NMR δ 140.5, 128.8, 127.7, 127.0, 112.5 (C), 109.2 (C), 99.8 (C1'), 83.8 (CH), 82.4 (CH), 80.2 (CH), 77.8 (CH), 72.6 (CH), 68.6 (C3), 66.5 (C6'), 46.1 (C4), 26.5 (CH_3), 25.8 (CH_3), 25.1 (CH_3), 24.4 (CH_3), 6.53 (CH_2I); MS m/z (relative intensity) 531 (72, M^+), 430 (18), 318 (32), 185 (50), 141 (34), 129 (62), 104 (38), 101 (75), 91 (45), 85 (46), 69 (31), 59 (44), 43 (100).

(3*S*,5*R*)-*N*-(2',3':5',6'-*O*-Diisopropylidene-α-D-mannofuranosyl)-3-phenyl-5-(iodomethyl)isoxazolidine (9): $[\alpha]^{22}_D$ +115.8° (*c* 1.0, $CHCl_3$); ^1H NMR δ 7.35 (m, 5 H, ArH), 5.04 (dd, J = 0.5, 6.6 Hz, 1 H, H2'), 4.92 (dd, J = 4.0 Hz, 6.6 Hz, 1 H, H3'), 4.55 (d, J = 0.5 Hz, 1 H, H1'), 4.43 (dd, J = 7.2, 9.9 Hz, 1 H), 4.35 (m, 3 H,), 4.15 (m, 2 H,), 3.45 (dd, J = 6.7, 9.8 Hz, 1 H, CH_2I), 3.29 (dd, J = 6.9, 9.8 Hz, 1 H, CH_2I), 2.68 (dt, J = 7.0, 12.5 Hz, 1 H, H4), 2.10 (ddd, J = 6.6, 10.0, 12.5 Hz, 1 H, H4), 1.53 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3); ^{13}C NMR δ 137.8, 128.9, 128.3, 128.0, 112.5 (C), 109.2 (C), 94.4 (C1'), 85.0 (CH), 84.8 (CH), 80.5 (CH), 77.1 (CH), 73.9 (CH), 66.7 (C6'), 63.9 (C3), 45.2 (C4), 26.7 (CH_3), 25.7 (CH_3), 25.1 (CH_3), 24.0 (CH_3), 8.4 (CH_2I); high-resolution mass spectrum for $C_{22}H_{30}NO_6I$ calcd 531.11179, found 531.11093; MS m/z (relative intensity) 531 (61, M^+), 516 (26), 430 (51), 318 (52), 257 (30), 185 (87), 130 (47), 129 (65), 101 (70), 91 (29), 85 (48), 59 (43), 43 (100).

(3*S*,5*S*)-*N*-(2',3':5',6'-*O*-Diisopropylidene-α-D-mannofuranosyl)-3-phenyl-5-(iodomethyl)isoxazolidine (10): $[\alpha]^{22}_D$ +85.6° (*c* 1.0, $CHCl_3$); ^1H NMR δ 7.32 (m, 5 H, ArH), 5.30 (s, 1 H, H1'), 5.01 (d, J = 6.0 Hz, 1 H, H2'), 4.90 (dd, J = 4.1, 6.0 Hz, 1 H, H3'), 4.51 (dd, J = 4.1, 7.9 Hz, 1 H), 4.48 (s, 1 H), 4.39 (t, J = 5.5 Hz, 1 H), 4.32 (m, 1 H), 4.16 (m, 3 H), 3.35 (dd, J = 5.5, 10.6 Hz, 1 H, CH_2I), 3.29 (dd, J = 4.8, 10.6 Hz, 1 H, CH_2I), 2.40 (m, 2 H, H4), 1.52 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3); ^{13}C NMR δ 137.8, 128.9, 128.3, 127.0, 112.4 (C), 109.3 (C), 93.5 (C1'), 85.1 (CH), 84.8 (CH), 80.5 (CH), 75.6 (CH), 73.8 (CH), 67.0 (CH_2), 62.5 (C3), 44.3 (C4), 26.7 (CH_3), 25.7 (CH_3), 25.3 (CH_3), 24.0 (CH_3), 7.9 (CH_2I); MS m/z (relative intensity) 531 (74, M^+), 516 (26), 430 (38), 318 (47), 257 (21), 185 (56), 129 (41), 101 (50), 91 (26), 85 (38), 59 (32), 43 (100); high-resolution mass spectrum for $C_{22}H_{30}NO_6I$ calcd 531.11179, found 531.11146.

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(Nitroaryl)sulfinyl-Substituted Allenes. Novel and Convenient Propargyl Alcohol Synthons in 4 + 2 Cycloaddition Chemistry

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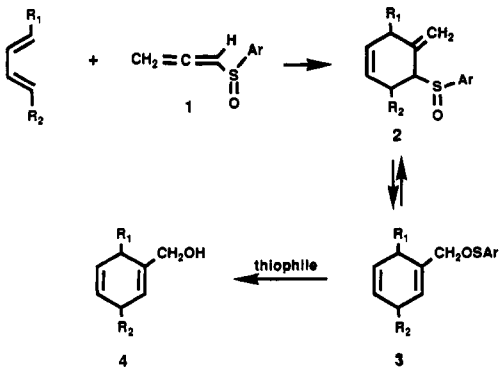
(Nitroaryl)sulfinyl-substituted allenes are conveniently prepared by treating propargyl alcohol or methyl 3-hydroxy-2-butynoate with a (nitroaryl)sulfenyl chloride and triethylamine. These activated allenes undergo 4 + 2 cycloaddition across the C_1C_2 π-bond. The initially formed allylic sulfoxide readily undergoes a 2,3-sigmatropic rearrangement to produce a stable sulfenate ester that is easily cleaved with thiophilic reagents. The dienophilic reactivity of the (nitroaryl)sulfinyl-substituted allene is much greater than the corresponding propargyl alcohol, and the cycloaddition also proceeds with high regioselectivity. The Diels-Alder reaction of [(2-nitrophenyl)sulfinyl]propadiene with Danishefsky's diene affords meta-substituted benzyl alcohols in high yield. Reaction of the more highly activated methyl 2-[(2-nitrophenyl)sulfinyl]-2,3-butadienoate with Danishefsky's diene followed by treatment of the resulting sulfenate ester with triethyl phosphite produces substituted phthalides in excellent yield. The (2,4-dinitrophenyl)sulfinyl-substituted allene was found to react smoothly with a variety of nitrones to give sulfenate esters of isoxazolidines. These allenyl sulfoxides correspond to formal equivalents of propargyl alcohol, which itself is too unreactive to undergo Diels-Alder chemistry or 1,3-dipolar cycloaddition with nitrones or nitrile oxides.

4 + 2 cycloadditions represent one of the most efficient methods for generating complex ring systems.[1-5] Two useful examples of this class are the Diels-Alder and 1,3-dipolar cycloaddition reactions. A limitation of these reactions is the poor reactivity of unactivated acetylenes with most 1,3-dienes and 1,3-dipoles, preventing the introduction of another degree of unsaturation into the newly formed ring.[6,7] To circumvent the forcing and often deleterious thermal conditions required for 4 + 2 cycloadditions involving such alkynes, several imaginative alternatives employing alkyne equivalents have been developed.[8] Among these, nitro olefins[9,10] vinyl sulfoxide,[11]

Scheme I



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