Synthesis and Iodocyclization of Homoallylic Hydroxylamines

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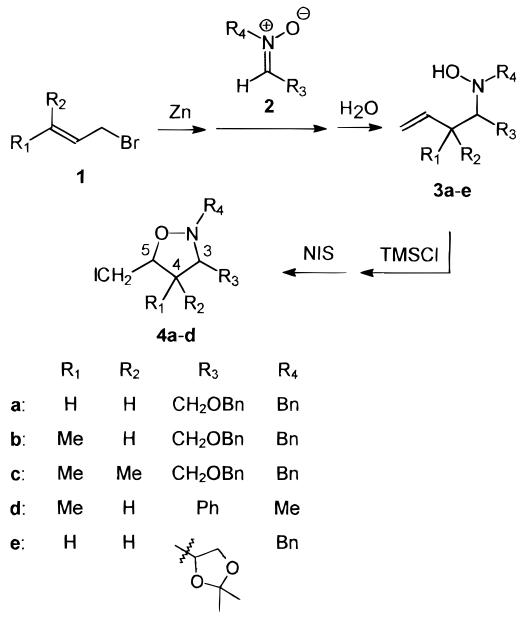
The allylation of nitrogen derivatives of carbonyl compounds such as imines and oximes,[1] etc., has received special attention due to the synthetic versatility of the final homoallylic amines and their applications as chiral modifiers or auxiliaries in asymmetric synthesis.

We recently reported the simple allylation of prochiral and chiral nitrones with allylmagnesium chloride; the resulting homoallylic *N*-hydroxylamines were exploited in iodocyclization reactions to give 5-(iodomethyl)isoxazolidines.[2]

We now wish to report that allylic zinc bromides generated *in situ* from allylic bromides **1** and zinc powder in THF regioselectively add to model aldonitrones **2** in very good yields. The simple diastereoselectivity of reactions involving crotylzinc bromide and the facial selectivity displayed by allylzinc bromide toward the *N*-benzylnitrone of glyceraldehyde were examined. Finally, homoallylic hydroxylamines **3** were *O*-silylated and subjected to iodocyclization to **4** in order (i) to get information about the *syn*/*anti* stereorelationship in hydroxylamines **3** and (ii) to observe stereodirecting effects of methyl substituents on the isoxazolidine-forming reaction (Scheme 1). In a first set of experiments (Table 1), we examined the allylation, crotylation, and prenylation of *O*-benzyl glycolaldehyde *N*-benzylnitrone. Reaction rates were found to be dependent on the degree of substitution on the allylic moiety, as expected on steric grounds (Table 1, entries 1, 2, and 6), the prenyl complex being the least reactive. The crotyl complex displayed an *anti* diastereoselectivity. Interesting observations were made when the reaction was carried out in the presence of Et_2AlCl (DEAC). Independent of the order of addition, reaction rates tremendously increased, the addition step could be carried out at much lower temperature, and a reversed *syn* selectivity was displayed (Table 1, entries 4 and 5). We also tested the crotylation of benzaldehyde *N*-methylnitrone, and again, we observed the inversion of simple diastereopreference with and without DEAC. The results are reported in Table 2. The *syn* selectivity displayed by DEAC could be accounted for by the adoption of an acyclic anti-periplanar transition state (TS); this TS geometry explains the stereoconvergent *syn* selectivity in the addition of crotylstannanes to aldehydes in the presence of Lewis acids, independent of the crotyl double bond configuration.[3] In the absence of DEAC, synclinal TS's, leading to the *anti* product, could be stabilized by attractive interactions between nitrone oxygen and zinc atom.[3b]

The last set of experiments was performed on (*R*)-glyceraldehyde acetonide *N*-benzylnitrone (Table 3). Using allylzinc bromide, we observed a slightly higher diastereofacial *anti* selectivity with respect to the previously reported allylmagnesium chloride[2b] (Table 3, entries 1 and 2). Again, an inversion of diastereopreference was

Scheme 1



	R_1	R_2	R_3	R_4
a:	H	H	CH_2OBn	Bn
b:	Me	H	CH_2OBn	Bn
c:	Me	Me	CH_2OBn	Bn
d:	Me	H	Ph	Me
e:	H	H		Bn

Table 1. Reaction of *O*-Benzyl Glycolaldehyde *N*-Benzylnitrone with Allylic Zinc Complexes

entry	**1** (method)[a]	*T* (°C)	*t* (h)	product[b]t(%)	*syn*/*anti*[c]
1	allyl (A)	25	0.5	**3a** (94)	
2	crotyl (A)	25	3.5	**3b** (95)	1/4
3	crotyl (A)	−40	4	**3b** (23)	1/5
4	crotyl (B)	−40	1.5	**3b** (91)	4/1
5	crotyl (C)	−40	1.5	**3b** (89)	4/1
6	prenyl (A)	25	24	**3c** (59)	
7	prenyl (B)	−40	1	**3c** (38)	
8	prenyl (B)	20	1	**3c** (80)	

[a] Method A involves the addition of the allylic zinc complex to nitrone at the reported temperature. Method B involves the addition of the allylic zinc complex to a preequilibrated mixture of nitrone and DEAC. Method C involves the addition of nitrone at −40 °C to a preequilibrated mixture of crotylzinc bromide and DEAC. [b] Isolated yield. [c] Determined by integral ratios in the ^1H NMR of crude reaction mixture.

Table 2. Reaction of Benzaldehyde *N*-Methylnitrone with Crotylzinc Bromide

entry	method[a]	*T* (°C)	*t* (h)	**3d**[b] (%)	*syn*/*anti*[c]
1	A	25	24	80	3/7
2	A	−40	24	traces	not det
3	B	−40	1	38	9/1

[a−c] See corresponding footnotes in Table 1.

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(1) Owing to the huge number of references on this topic, we only refer to the most recent papers and to references therein: (a) Itsuno, S.; Watanabe, K.; Ito, K.; El-Shehawy, A. A.; Sarhan, A. A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 109. (b) Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6641. (c) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 8489. (d) Alvaro, G.; Savoia, D. *Tetrahedron: Asymmetry* **1996**, *7*, 2083. (e) Alvaro, G.; Boga, C.; Savoia, D.; Umani-Ronchi, A. *J. Chem. Soc. Perkin Trans. 1* **1996**, 875. (f) Hanessian, S.; Yang, R.-Y. *Tetrahedron Lett.* **1996**, *37*, 5273. (g) Wang, D.-K.; Dai, L.-X.; Hou, X.-L.; Zhang, Y. *Tetrahedron Lett.* **1996**, *37*, 4187. (h) Wang, J.; Zhang, Y.; Bao, W. *Synth. Commun.* **1996**, *26*, 2473. (i) Yanagisawa, A.; Ogasawara, K.; Yasue, K.; Yamamoto, H. *J. Chem. Soc., Chem. Commun.* **1996**, 367.

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Table 3. Reaction of (*R*)-Glyceraldehyde Acetonide *N*-Benzylnitrone with Allylzinc Bromide

entry	method[a]	*T* (°C)	*t* (h)	**3e**[b] (%)	*syn*/*anti*[c]
1[a]	[d]	−30	2	90	44/56
2	A	0	1	92	25/75
3	B	0	0.5	88	58/42
4	B	−40	0.5	80	65/35

[a−c] See corresponding notes to Table 1. [d] Reaction carried out with allylmagnesium chloride, taken from ref 2b.

Table 4. Iodocyclization Reaction of *O*-Silylated Hydroxylamines 3 Promoted by NIS

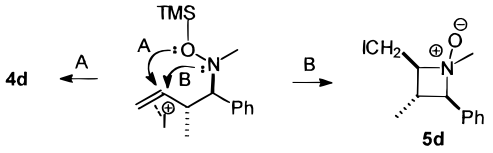
entry	substrate	*t* (h)	products[a] (%)
1	**3a**	2	3,5-*cis*-**4a** (41) + 3,5-*trans*-**4a** (50)
2	*syn*-**3b**[b]	3	**4b** (traces)
3	*anti*-**3b**[c]	3	3,4-*trans*-4,5-*trans*-**4b** (56) + 3,4-*trans*-4,5-*cis*-**4b** (19)
4	**3c**	4	3,5-*trans*-**4c** (41)[d]
5	*syn*-**3d**[e]	3	3,4-*cis*-4,5-*trans*-**4d** (55)
6	*anti*-**3d**[f]	3	3,4-*trans*-4,5-*trans*-**4d** (58)

[a] Isolated yields. [b] Reaction carried out on an 80% enriched mixture of the reported isomer. [c] Reaction carried out on an 80% enriched mixture of the reported isomer. [d] No trace of 3,5-cis isomer was observed and isolated. [e] Reaction carried out on a 90% enriched mixture of the reported isomer. [f] Reaction carried out on a 70% enriched mixture of the reported isomer.

recorded in the presence of DEAC, even though the absolute level of stereoselectivity was not impressive. An analogous reversal of facial stereoselection had previously been reported by Dondoni in the addition of nucleophiles such as 2-lithiothiazole,[4] 2-lithiofuran,[5] and simple Grignard reagents[6] to chiral nitrones in the presence of DEAC.

A classical solution to the assignment of the relative stereochemistry of contiguous centers requires their incorporation on the ring system of a 5- or 6-membered cyclic derivative. The iodocylization reaction of products **3** to isoxazolidines **4** not only allowed us to establish the *syn*/*anti* stereorelationships of **3b** and **3d** by inspecting coupling constants and NOE effects[7] on H-3 and H-4 of **4** but also gave interesting information about the effect of methyl groups on the ring closure process. The reactions were promoted by *N*-iodosuccinimide (NIS) in chloroform at 0 °C. The results are summarized in Table 4. Hydroxylamine **3a** afforded the expected mixture of 3,5-*cis* and 3,5-*trans* products on the basis of previous results on related hydroxylamines (Table 4, entry 1).[2a] Interestingly, the presence of two methyl groups on **3c** completely inhibited the formation of the 3,5-*cis* product (Table 4, entry 4). As far as homoallylic hydroxylamines **3b** and **3d** are concerned, the methyl group confers a marked preference for the formation of the 4,5-*trans* isoxazolidines, which are the sole products in entries 5 and 6 (Table 4) and the major one in entry 3 (Table 4). In general, products possessing the 3,4-*cis*-4,5-*cis* stereochemistry were never detected; in particular, hydroxylamine *syn*-**3b** underwent only oxidative decomposition into a plethora of unidentified products upon standing with NIS.[8] On the other hand, *N*-methylhydroxylamine *syn*-**3d** proved to be less sensitive to oxidative

Scheme 2



decomposition than *N*-benzylhydroxylamine *syn*-**3b** and was stereoselectively converted into 3,4-*cis*-4,5-*trans*-isoxazolidine **4d**. Noteworthy is that entry 6 represents the only iodocyclization experiment so far reported by us in which a product coming from a 4-*exo*-*trig* ring closure (Scheme 2, path B) has been observed. In fact, we isolated, besides isoxazolidine 3,4-*trans*-4,5-*trans*-**4d** coming from the normal 5-*exo*-*trig* mode (path A), azetidine *N*-oxide **5d** in 17% yield.

In conclusion, regiocontrolled allylation of nitrones combined with the iodocyclization reaction of the resulting homoallylic hydroxylamines could offer an interesting route to highly functionalized carbon frameworks. The attainment of the best stereocontrol in this process is the goal of our present studies.

Experimental Section

General Methods. All reactions were carried out in oven-dried glassware under an atmosphere of dry argon. All reagents were commercially available and were used without further purification, unless otherwise stated. ^{1}H and ^{13}C NMR were recorded at 300 and 75 MHz, respectively, using tetramethylsilane as an internal standard. Melting points are uncorrected.

Glycolaldehyde *N*-Benzylnitrone. 2-(Benzyloxy)ethanal (1.0 g, 6.7 mmol) and *N*-benzylhydroxylamine, freshly freed from the hydrochloride (1.07 g, 6.7 mmol), were allowed to react in CH_2Cl_2 (5 mL) at 20 °C overnight. After solvent evaporation and recrystallization (cyclohexane:ether), the pure nitrone (1.71 g, 97%) was obtained as a white solid: mp 95−96 °C; ^{1}H NMR ($CDCl_3$) δ 4.48 (d, J = 4.1 Hz, 2H), 4.54 (s, 2H), 4.87 (s, 2H), 6.79 (t, J = 4.1 Hz, 1H), 7.32−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 66.1, 69.0, 73.8, 127.9, 128.0, 128.5, 129.0, 129.2, 129.6, 132.0, 137.1, 137.4. Anal. Calcd for $C_{16}H_{15}NO_2$: C, 75.26; H, 6.72; N, 5.49. Found: C, 75.31; H, 6.58; N, 5.33.

Preparation of Allylic Zinc Bromide Solutions. To a suspension of activated zinc powder[9] (1.1 g, 16.8 mmol) in anhydrous THF (5 mL) was added a solution of allyl bromide (0.36 mL, 4.2 mmol) in THF (2 mL) at 0 °C. The heterogeneous mixture was allowed to reach rt and stirred for 2 h. After filtration through a glass frit under argon, the resulting solution of organozinc complex was titrated[10] and directly used for the addition reaction. For the preparation of crotyl- and prenylzinc bromide solutions, the corresponding allylic bromide was stirred with zinc at 0 °C for 3 h, so avoiding a Wurtz-type side reaction.

***N*-Hydroxy-*N*-benzyl-1-(benzyloxy)-4-penten-2-amine (3a). Method A (Table 1, Entry 1).** A solution of allylzinc bromide (5 mL, 0.6 M, 3 mmol) was added to glycolaldehyde *N*-benzylnitrone (383 mg, 1.5 mmol) dissolved in THF (2 mL), and the solution was stirred at rt for 30 min. The reaction mixture was quenched with aqueous $NaHCO_3$, filtered (Celite), and extracted

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(7) The following ranges of NOE values were observed: *cis* H-3/H-4 and *cis* H-4/H-5 5−8%; *trans* H-3/H-4 and *trans* H-4/H-5 <2%; *cis* H-4/CH_2I and *cis* H-4/CH_2OBn 3−5%.

(8) In three different experiments we got untractable reaction mixtures; after thiosulfate quenching, we identified a significant amount of benzaldehyde. We believe that oxidation might convert the starting *N*-benzyl group into a *C*-phenyl nitrone, which undergoes hydrolysis to benzaldehyde on aqueous workup.

(9) A number of methods for the activation of zinc or for the *in situ* preparation of active forms of zinc are available; see, for example (a) Rieke, R. D.; Hanson, M. V. *Tetrahedron* **1997**, *53*, 1925. (b) Erdik, E. *Tetrahedron* **1987**, *43*, 2203. For our purposes, activation was simply carried out by heating zinc powder (Janssen) at about 300 °C with a heat gun for 5 min under argon.

(10) An aliquot of allylic zinc bromide solution was quenched with 1 N HCl, and zinc was titrated by EDTA.

with ether (3 × 5 mL). The combined organic layers were dried (Na_2SO_4) and concentrated at reduced pressure. Hydroxylamine **3a** was obtained as a yellow oil (420 mg, 94%) after purification using flash chromatography (cyclohexane:ethyl acetate 95/5). **3a**: ^{1}H NMR ($CDCl_3$) δ 2.36 (dt, J = 7.6/14.3 Hz, 1H), 2.52 (dt, J = 6.0/14.3 Hz, 1H), 3.07 (ddt, J = 4.2/6.0/7.6 Hz, 1H), 3.63 (dd, J = 4.2/10.1 Hz, 1H), 3.78 (dd, J = 6.0/10.1 Hz, 1H), 3.97 (s, 2H), 4.54 (s, 2H), 5.03−5.12 (m, 2H), 5.19 (br s, 1H), 5.86 (ddt, J = 6.0/7.6/13.8 Hz, 1H), 7.28−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 32.8, 60.7, 64.9, 69.4, 73.2, 116.5, 127.1, 127.6, 128.2, 128.4, 129.2, 136.0, 138.2, 138.4. Anal. Calcd for $C_{19}H_{23}NO_2$: C, 76.72; H, 7.80; N, 4.71. Found: C, 76.92; H, 7.75; N, 4.83.

Method B (Table 1, Entry 4). Nitrone (383 mg, 1.5 mmol) and DEAC (∼1.8 M in hexane, 0.82 mL) in THF (2 mL) were equilibrated at −40 °C for 20 min. At the same temperature, a solution of crotylzinc bromide (6 mL, 0.5 M, 3 mmol) was added, and the reaction mixture was stirred for 1.5 h.

Method C (Table 1, Entry 5). A solution of crotylzinc bromide (5 mL, 0.16 M, 0.8 mmol) was treated with DEAC (0.21 mL, 0.8 mmol) at −40 °C for 30 min. Solid nitrone (100 mg, 0.39 mmol) was added at −40 °C, and stirring was continued for 1.5 h.

***N*-Hydroxy-*N*-benzyl-1-(benzyloxy)-3-methyl-4-penten-2-amine (3b).** The product was obtained as a solid mixture of the two *syn*/*anti* isomers having the same R_f on silica gel. The following spectroscopic data were drawn from the enriched mixtures obtained in entries 3 and 4 of Table 1. *syn*-**3b**: ^{1}H NMR ($CDCl_3$) δ 1.17 (d, J = 6.8 Hz, 3H), 2.54−2.67 (m, 1H), 2.82 (ddd, J = 3.0/5.8/8.7 Hz, 1H), 3.75 (dd, J = 3.0/10.2 Hz, 1H), 3.87 (dd, J = 5.8/10.2 Hz, 1H), 3.92 (d, J = 13.7 Hz, 1H), 4.16 (d, J = 13.7 Hz, 1H), 4.53 (s, 2H), 4.99 (ddd, J = 0.7/1.9/10.2, 1H), 5.05 (ddd, J = 1.0/1.9/17.2, 1H), 5.32 (br s, 1H), 5.79 (ddd, J = 8.3/10.2/17.2 Hz, 1H), 7.20−7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 18.1, 38.8, 61.3, 68.9, 73.4, 80.9, 114.5, 127.1, 127.7, 128.3, 128.4, 128.7, 130.3, 135.7, 139.1, 141.8. *anti*-**3b**: ^{1}H NMR ($CDCl_3$) δ 1.08 (d, J = 6.8 Hz, 3H), 2.52−2.67 (m, 1H), 2.89 (ddd, J = 3.2/5.7/7.4 Hz, 1H), 3.73 (dd, J = 3.2/10.2 Hz, 1H), 3.78 (dd, J = 5.7/10.2 Hz, 1H), 3.88 (d, J = 13.9 Hz, 1H), 4.15 (d, J = 13.9 Hz, 1H), 4.56 (s, 2H), 5.00−5.07 (m, 2H), 5.39 (br s, 1H), 5.97 (ddd, J = 7.7/10.3/17.1 Hz, 1H), 7.21−7.38 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 17.4, 38.4, 60.6, 67.1, 69.6, 73.2, 113.3, 127.0, 127.6, 128.1, 128.2, 128.4, 129.4, 138.3, 138.9, 142.8. Anal. (of a purified mixture of *syn*-**3b**/*anti*-**3b** in a 4:1 ratio) Calcd for $C_{20}H_{25}NO_2$: C, 77.12; H, 8.10; N, 4.50. Found: C, 77.36; H, 8.04; N, 4.21.

***N*-Hydroxy-*N*-benzyl-1-(benzyloxy)-3,3-dimethyl-4-penten-2-amine (3c):** Oil; ^{1}H NMR ($CDCl_3$) δ 1.10 (s, 3H), 1.14 (s, 3H), 2.83 (dd, J = 3.5/6.9 Hz, 1H), 3.69 (dd, J = 3.5/10.3 Hz, 1H), 3.95 (d, J = 13.7 Hz, 1H), 4.15 (dd, J = 6.9/10.3 Hz, 1H), 4.24 (d, J = 13.7 Hz, 1H), 4.51 (br s, 1H), 4.54 (d, J = 11.8 Hz, 1H), 4.60 (d, J = 11.8 Hz, 1H), 4.96 (dd, J = 1.4/10.7 Hz, 1H), 4.99 (dd, J = 1.4/17.5 Hz, 1H), 5.98 (dd, J = 10.7/17.5 Hz, 1H), 7.25−7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 24.4, 26.1, 40.7, 64.0, 66.6, 72.8, 73.2, 111.1, 126.9, 127.5, 127.6, 128.2, 128.4, 129.1, 138.4, 139.2, 146.8. Anal. Calcd for $C_{21}H_{27}NO_2$: C, 77.49; H, 8.37; N, 4.31. Found: C, 77.71; H, 8.56; N, 4.62.

***N*-Methyl-α-(1-methyl)-2-propenylbenzenemethanamine (3d).** The product was obtained as a mixture of the two *syn*/*anti* isomers having the same R_f on silica gel. The following spectroscopic data were drawn from the enriched mixtures obtained in entries 1 and 3 of Table 2. *syn*-**3d**: ^{1}H NMR ($CDCl_3$) δ 0.95 (d, J = 6.9 Hz, 3H), 2.53 (s, 3H), 3.00−3.08 (m, 1H), 3.41 (d, J = 2.2 Hz, 1H), 4.95−5.00 (m, 2H), 5.75−5.87 (m, 1H), 7.26−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.6, 39.2, 46.3, 78.8, 114.6, 127.4, 127.8, 128.5, 129.6, 137.5, 140.4. *anti*-**3d**: ^{1}H NMR ($CDCl_3$) δ 0.85 (d, J = 6.8 Hz, 3H), 2.44 (s, 3H), 2.90−2.99 (m, 1H), 3.38 (s, 1H), 4.73 (br s, 1H), 5.05 (ddd, J = 0.6/1.9/10.2 Hz, 1H), 5.13 (ddd, J = 0.9/1.9/17.1, 1H), 5.87 (ddd, J = 8.6/10.2/17.1, 1H), 7.25−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 16.9, 40.7, 45.4, 77.9, 113.5, 127.4, 127.8, 128.4, 128.7, 137.0, 143.2. Anal. (of a purified mixture of *syn*-**3d**/*anti*-**3d** in a 7:3 ratio) Calcd for $C_{12}H_{17}NO$: C, 75.34; H, 8.96; N, 7.33. Found: C, 75.38; H, 8.84; N, 7.52.

2-Benzyl-3-[(benzyloxy)methyl]-5-(iodomethyl)isoxazolidine (4a). General Procedure for the Iodocyclization Reaction. Imidazole (190 mg, 2.8 mmol) and TMSCl (0.36 mL, 2.8 mmol) were added to a solution of **3a** (420 mg, 1.4 mmol) in dry CH_2Cl_2 (5 mL), and the reaction mixture was stirred at rt overnight. Hexane (2 mL) was added, and the solution was filtered (Celite) and evaporated under reduced pressure to afford silylated hydroxylamine (442 mg, 86%) as a dense oil.[11] The product was dissolved in $CHCl_3$ (5 mL), the solution was cooled at 0 °C, and NIS (540 mg, 2.4 mmol) was added. After being stirred in the dark for 2 h at 0 °C, the reaction was quenched with aqueous $Na_2S_2O_3$, and the aqueous layer was extracted with $CHCl_3$ (3 × 5 mL). *cis*-**4a** (208 mg, 41%) and *trans*-**4a** (254 mg, 50%) were separated using flash chromatography eluting with cyclohexane/ethyl acetate 95:5. 3,5-*cis*-**4a**: oil; ^{1}H NMR ($CDCl_3$) δ 1.92 (dt, J = 6.2/12.7 Hz, 1H), 2.66 (dt, J = 7.9/12.7 Hz, 1H), 3.13 (dd, J = 8.4/9.6 Hz, 1H), 3.29 (dd, J = 5.0/9.6 Hz, 1H), 3.29−3.38 (m, 1H), 3.49 (dd, J = 5.8/9.6 Hz, 1H), 3.57 (dd, J = 6.9/9.6 Hz, 1H), 3.99 (d, J = 13.8 Hz, 1H), 4.12 (d, J = 13.8 Hz, 1H), 4.39 (m, 1H), 4.49 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 7.22−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 8.1, 38.3, 61.5, 65.0, 71.8, 73.3, 76.6, 127.2, 127.7, 128.2, 128.4, 128.8, 136.2, 139.8. Anal. Calcd for $C_{19}H_{22}NO_2I$: C, 53.89; H, 5.24; N, 3.31. Found: C, 53.96; H, 4.98; N, 3.28. 3,5-*trans*-**4a**: oil; ^{1}H NMR ($CDCl_3$) δ 2.18 (dt, J = 7.8/12.7 Hz, 1H), 2.30 (dt, J = 7.3/12.7 Hz, 1H), 3.15 (dd, J = 8.0/9.9 Hz, 1H), 3.30 (dd, J = 4.7/9.9 Hz, 1H), 3.27−3.34 (m, 1H), 3.53 (d, J = 5.5 Hz, 2H), 4.01 (d, J = 13.7 Hz, 1H), 4.12 (br dq, J = 4.7/7.7 Hz, 1H), 4.24 (d, J = 13.7 Hz, 1H), 4.52 (s, 2H), 7.26−7.41 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 8.3, 38.6, 62.7, 64.4, 71.3, 73.4, 76.6, 127.2, 127.6, 127.7, 128.2, 128.4, 129.1, 135.5, 137.9. Anal. Calcd for $C_{19}H_{22}NO_2I$: C, 53.89; H, 5.24; N, 3.31. Found: C, 53.72; H, 5.12; N, 3.47.

2-Benzyl-3-[(benzyloxy)methyl]-5-(iodomethyl)-4-methylisoxazolidine (4b). 3,4-*trans*-4,5-*trans*-**4b**: oil; ^{1}H NMR ($CDCl_3$) δ 1.24 (d, J = 6.8 Hz, 3H), 2.09−2.26 (m, 1H), 2.85 (dt, J = 5.6/11.7 Hz, 1H), 3.28 (d, J = 6.4 Hz, 2H), 3.59 (d, J = 5.6 Hz, 2H), 3.82 (q, J = 6.4 Hz, 1H), 3.94 (d, J = 14.0 Hz, 1H), 4.31 (d, J = 14.0 Hz, 1H), 4.53 (s, 2H), 7.22−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 8.0, 18.2, 47.2, 61.7, 71.1, 73.2, 73.3, 82.6, 127.0, 127.5, 127.6, 128.1, 128.4, 128.7, 137.8, 137.9. Anal. Calcd for $C_{20}H_{24}NO_2I$: C, 54.91; H, 5.53; N, 3.20. Found: C, 54.65; H, 5.61; N, 3.37. 3,4-*trans*-4,5-*cis*-**4b**: oil; ^{1}H NMR ($CDCl_3$) δ 1.09 (d, J = 7.1 Hz, 3H), 2.40−2.51 (m, 1H), 2.79−2.85 (m, 1H), 3.07 (dd, J = 7.8/10.0 Hz, 1H), 3.18 (dd, J = 6.2/10.0 Hz, 1H), 3.52−3.57 (m, 2H), 3.98 (d, J = 14.0 Hz, 1H), 4.24−4.34 (m, 1H), 4.26 (d, J = 14.0 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 7.27−7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 1.3, 13.5, 42.3, 62.9, 71.6, 72.6, 73.4, 79.2, 127.2, 127.6, 127.7, 128.2, 128.4, 129.3, 137.4, 137.9. Anal. Calcd for $C_{20}H_{24}NO_2I$: C, 54.91; H, 5.53; N, 3.20. Found: C, 55.12; H, 5.58; N, 3.14.

2-Benzyl-3-[(benzyloxy)methyl]-5-(iodomethyl)-4,4-dimethylisoxazolidine (4c). 3,5-*trans*-**4c**: oil; ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 6H), 3.06 (d, J = 6.6 Hz, 1H), 3.34 (dd, J = 6.6/11.2 Hz, 1H), 3.65 (d, J = 15.3 Hz, 1H), 3.75 (d, J = 11.2 Hz, 1H), 3.88 (dd, J = 4.4/11.0 Hz, 1H), 4.13 (t, J = 11.0 Hz, 1H), 4.22 (dd, J = 4.4/11.0 Hz, 1H), 4.26 (d, J = 15.3 Hz, 1H), 4.46 (d, J = 11.8 Hz, 1H), 4.51 (d, J = 11.8 Hz, 1H), 7.21−7.38 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 27.7, 37.5, 45.8, 59.3, 69.5, 72.6, 72.9, 73.8, 126.6, 127.6, 127.8, 127.9, 128.1, 128.5, 137.5, 139.2. Anal. Calcd for $C_{21}H_{26}NO_2I$: C, 55.86; H, 5.81; N, 3.10. Found: C, 55.73; H, 5.92; N, 3.14.

5-(Iodomethyl)-2,4-dimethyl-3-phenylisoxazolidine (4d). 3,4-*cis*-4,5-*trans*-**4d**: oil; ^{1}H NMR ($CDCl_3$) δ 0.76 (d, J = 7.3 Hz, 3H), 2.53 (ddq, J = 5.7/7.3/8.3 Hz, 1H), 2.68 (s, 3H), 3.33 (dd, J = 5.7/10.4 Hz, 1H), 3.38 (dd, J = 5.7/10.4 Hz, 1H), 3.72 (q, J = 5.7 Hz, 1H), 3.77 (d, J = 8.3 Hz, 1H), 7.20−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 7.2, 15.8, 44.0, 48.1, 76.2, 83.7, 127.5, 128.2, 128.3, 136.8. Anal. Calcd for $C_{12}H_{16}NOI$: C, 45.42; H, 5.09; N, 4.42. Found: C, 45.38; H, 5.24; N, 4.46. 3,4-*trans*-4,5-*trans*-**4d**: oil; ^{1}H NMR ($CDCl_3$) δ 1.18 (d, J = 6.8 Hz, 3H), 2.38 (ddq, J = 5.7/6.8/9.3 Hz, 1H), 2.55 (s, 3H), 3.10 (d, J = 9.3 Hz, 1H), 3.41 (dd, J = 7.7/9.7 Hz, 1H), 3.48 (dd, J = 5.7/9.7 Hz, 1H), 3.96 (dt, J = 5.7/7.7 Hz, 1H), 7.28−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 9.3, 16.9, 43.3, 54.1, 82.4, 83.1, 127.8, 128.1, 128.7, 137.5. Anal.

(11) All the *O*-silylated hydroxylamines, contrary to starting hydroxylamines, are easily analyzed by GC−MS and show the characteristic fragment due to the loss of the allylic moiety from the molecular ion.

Calcd for $C_{12}H_{16}NOI$: C, 45.42; H, 5.09; N, 4.42. Found: C, 45.48; H, 5.02; N, 4.51.

2-(Iodomethyl)-1,3-dimethyl-4-phenylazetidine 1-Oxide (5d). Oil; ^{1}H NMR ($CDCl_3$) δ 1.22 (d, J = 6.8 Hz, 3H), 2.31 (ddq, J = 5.8/6.8/8.8 Hz, 1H), 2.70 (q, J = 5.8 Hz, 1H), 2.91 (s, 3H), 3.31 (dd, J = 5.8/10.4 Hz, 1H), 3.37 (dd, J = 5.8/10.4 Hz, 1H), 4.81 (d, J = 8.8 Hz, 1H), 7.30−7.42 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 8.0, 16.4, 46.2, 54.3, 76.4, 106.8, 127.2, 128.7, 129.0, 135.4. Anal. Calcd for $C_{12}H_{16}NOI$: C, 45.42; H, 5.09; N, 4.42. Found: C, 45.36; H, 5.17; N, 4.48.

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