135 (base peak), 92, 77; CH_3O ^1H NMR (100 MHz) δ 3.45 (s), 3.74 (s); ^{13}C NMR δ 68.8 (C-4), 60.3, 55.5, 53.8. Anal. Calcd for $C_{32}H_{28}O_4S$: C, 75.57; H, 5.55: S, 6.30. Found: C, 75.29, H, 5.54; S, 6.13.

Single-Crystal X-ray Analysis of 5, 6, and 8.[17] Compound **5** crystallized in the monoclinic space group *Cc* with a = 8.461 (1), b = 23.159 (2), and c = 14.862 (2) Å, and β = 89.08 (1)°. All unique diffraction maxima with $2\theta \leq 144°$ were collected by using a computer-controlled four-circle diffractometer and graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.5478 Å) with variable speed, 1° ω-scans. Of the 1967 reflections surveyed in this fashion, 1835 (93%) were judged observed. The structure was solved routinely and refined by block-diagonal least-squares refinements to a conventional crystallographic residual of 0.0545 for the observed reflections. Additional crystallographic data are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

Compound **6** crystallized in the orthothrombic space group $P2_1nb$ with a = 9.199 (2), b = 11.251 (3), and c = 28.593 (8) Å. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer with graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 2139 reflections collected in this manner, 2006 (94%) were judged observed and used in subsequent refinements. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.0795 for the observed reflections. Additional crystallographic data are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

(17) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF written by P. T. Beurskens et al., University of Nijmegen, Netherlands, 1981; BLS78A, an anisotropic block-diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu, Cornell University, 1978.

In the case of **8**, preliminary X-ray photographs displayed only Friedel's law symmetry and belonged to the triclinic crystal class. Lattice constants were obtained from a least-squares fitting of 15 moderate angle 2θ values and were α 9.9507 (20), b = 12.8833 (29), and c = 11.8464 (27) Å, α = 117.97 (2)°, β = 99.398 (17)°, δ = 83.331 (17)°. A rough density measurement indicated that two molecules of composition $C_{32}H_{28}O_4S$ were in the unit cell. The space group was assumed to be $P\bar{1}$, and this assumption was verified by successful refinement. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer with graphite-monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 3554 reflections measured in this fashion, 3212 (90%) were judged observed ($|F_o| \geq 3\sigma(F_o)$) after correction for Lorentz, background, and polarization effects. A phasing model was found easily by using a multisolution sign determining approach. All of the non-hydrogen atoms were clearly visible on the resulting E-synthesis. Block-diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a conventional crystallographic residual of 0.0595 for the observed reflections. Additional crystallographic parameters are available and are described in the paragraph entitled Supplementary Material Available at the end of this paper.

Acknowledgment. We thank Dr. Philip Borer and Mr. Gene Bailey of the NIH Resource for Multi-Nuclei NMR and Data Processng, Department of Chemistry, Syracuse University, for the 500-MHz ^1H NMR spectra. We thank Mr. Bruce Prosser of Bristol-Myers Company and Mr. Timothy Ullman of Corporate Research and Development Center, General Electric Company, for elemental and HRMS analyses. We also thank Dr. Ronald Eby and Dr. Francis Webster, who provided us with the NMR simulator program. The Cornell authors thank NSF INT14133 for financial support.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, bond distances, and bond angles for compounds **5**, **6**, and **8**, the direct-bond ^1H–^{13}C 2D heteronuclear-correlated spectra for compounds **5**, **9**, and **12**, 2D ^1H–^1H NMR (COSY) spectra for compounds **5** and **9**, and three-dimensional plots illustrating the relation of δ^{H-3} and δ^{H-4} to vicinal and geminal thiolane substitution (29 pages). Ordering information is given on any current masthead page.

Factors Affecting the Regioselection of the Allylic Imidates Iodocyclization

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The regiochemistry of the iodocyclization reaction of allylic imidates leading to 4,5-dihydro-1,3-oxazoles or to 4,5-dihydro-1,3-oxazines strongly depends on the configuration of the double bond: (*E*)-allylic imidates afford preferentially 4,5-dihydro-1,3-oxazines through a 6-endo closure, whereas (*Z*)-allylic imidates afford preferentially 4,5-dihydro-1,3-oxazoles through a 5-exo closure. Furthermore a study on the effect of an oxygen atom vicinal to the double bond is reported.

Cyclic intermediates have been widely utilized in the total synthesis of complex molecules.[1] The use of cyclic systems in asymmetric induction relies on the propensity of a cyclic transition state to assume a configuration compatible with the smallest interaction among the substituents.[2]

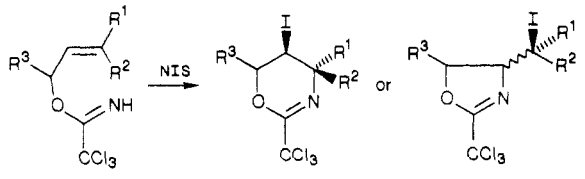
In this field we have developed methods for functionalization of double bonds of allylic and homoallylic alcohols and amine derivatives, through iodonium-initiated cycli-

(1) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3.

(2) (a) Bartlett, P. A.; Jernstedt, K. K. *J. Am. Chem. Soc.* **1977**, *99*, 4829. (b) Bartlett, P. A.; Meadows, J. D.; Brown, E. G.; Morimoto, A.; Jernstedt, K. K. *J. Org. Chem.* **1982**, *47*, 4013. (c) Pauls, H. W.; Fraser-Reid, B. J. *J. Am. Chem. Soc.* **1980**, *102*, 3956. (d) Chamberlin, A. R.; Dezube, M.; Dussault, P. *Tetrahedron Lett.* **1981**, *22*, 4611.

0022-3263/86/1951-4905$01.50/0

Table I. Product Distribution of the Iodocyclization of Allylic Imidates as a Function of Electronic Factors and *E* Geometry of the Double Bond



1 2 3

entry		yield of 2,[a] %	yield of 3,[a] %
a	R^1 = H; R^2 = C_6H_5; R^3 = H	80	
b	R^1 = H; R^2 = (*E*)-CH=CHCH$_3$; R^3 = H	90	
c	R^1 = H; R^2 = (*E*)-CH=CH$C_{13}H_{27}$; R^3 = H	95	
d	R^1 = $C_{15}H_{31}$; R^2 = H; R^3 = H		90
e	R^1 = H; R^2 = CH_3; R^3 = CH_3	85	

[a] Isolated yield of chromatographed product.

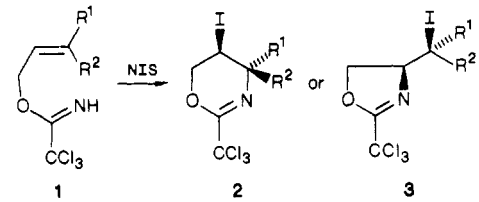
zation. Thus, starting from readily accessible acyclic adducts, we have synthesized heterocyclic intermediates whose hydrolysis leads to diols, amino diols, or triols.[3] Although both 5-exo and 6-endo closures can be obtained in cyclization of allylic imidates,[4] we have noticed that the regiochemical outcome of the ring closure is influenced by the incipient carbonium ion stabilization and strongly depends on the *E* or *Z* double bond configuration.[5] In particular we have observed that (*E*)-allylic imidates give 4,5-dihydro-1,3-oxazines through a 6-endo closure, whereas (*Z*)-allylic imidates give 4,5-dihydro-1,3-oxazoles through a 5-exo closure.[6] This observation prompted us to further investigate the regioselection of this reaction. Moreover a further study on the role of an oxygen atom vicinal to the double bond in controlling the regiochemistry of the ring closure of the reaction is reported.

Results and Discussion

Cyclization of (*E*)-cinnamyl imidate **1a** (Table I) with *N*-iodosuccinimide in chloroform gives exclusively the 4,5-dihydro-1,3-oxazine **2a** as confirmed by the C=N IR absorption at ν 1670 cm^{-1}, which is the characteristic feature for the six-membered ring of 2-(trichloromethyl)-4,5-dihydro-1,3-oxazines.[3c,7] This result is clearly due to the *E* configuration of the double bond and to the presence of the phenyl group stabilizing an incipient carbonium ion.

A series of substrates, where the regioselection is controlled both by electronic factors and by the *E* configuration of the double bond is reported in Table I.

Table II. Product Distribution of the Iodocyclization of Allylic Imidates as a Function of Olefin Geometry



1 2 3

entry		yield of 2,[a] %	yield of 3,[a] %
f	R^1 = C_2H_5; R^2 = H	90	
g	R^1 = H; R^2 = C_2H_5		88
h	R^1 = C_3H_7; R^2 = H	87	
i	R^1 = $C_{15}H_{31}$; R^2 = H	90	
j	R^1 = H; R^2 = $C_{15}H_{31}$		90
k	R^1 = H; R^2 = C_6H_5		92[b]

[a] Isolated yield of chromatographed product. [b] A mixture 47:53 of oxazolines with unassigned stereochemistry has been obtained.

For imidates **1b** and **1c**, the 6-endo closure can be expected on the basis of the above reported results. In fact the cyclization of 2(*E*),4(*E*)-hexadien-1-yl imidate **1b** in $CHCl_3$ with *N*-iodosuccinimide at room temperature affords in 90% yield the corresponding 4,5-dihydro-1,3-oxazine **2b** (IR 1670 cm^{-1}). Concerning the stereochemistry of this reaction, the trans relationship between 4-H and 5-H is predictable on the basis of mechanistic considerations; in addition in the proton magnetic resonance spectrum of **2b**, the vicinal coupling constant ($J_{4H,5H}$ = 7 Hz) shows these hydrogens to be trans axially oriented.[8]

The cyclization of the imidate **1c**, a useful intermediate in the synthesis of sphingosine,[9] gives **2c** as a single diastereoisomer with H-4 and H-5 in trans configuration, as confirmed by the ^{1}H NMR and ^{13}C NMR spectra.

On the other hand the cyclization of 1-octadecen-3-yl imidate **1d** proceeds with a total regioselection as already reported,[5] leading to a 4,5-dihydro-1,3-oxazole ring (IR absorption at 1650–1660 cm^{-1} is typical of the C=N bond in this class of compounds).[3c,7] The driving force, in this case, is the formation of the more stable carbonium ion. This behavior is in agreement with the cyclization of secondary 1-alkenyl lactones,[1d] urethanes,[10] imidates,[3c] amides,[3d,11] and carbonates,[2b,3b] which afford five-membered heterocyclic rings exclusively. Concerning the stereochemistry of the ring formation, it is observed that a diastereomeric trans/cis mixture with high trans stereoselection is generally obtained.

The cyclization of imidate **1e** is again controlled by electronic factors: the tertiary cation forces the closure in a 6-endo mode, and the 4,5-dihydro-1,3-oxazine **2e** is exclusively obtained in 85% yield, showing that electronic factors in this case outweigh steric hindrance (see further discussion).

A deeper insight on the factors affecting the regioselection of the iodocyclization of allylic imidates can be attained studying the cyclization of **1f–h** (Table II).

In fact, after treatment of 2(*E*)-penten-1-yl imidate **1f** with *N*-iodosuccinimide in $CHCl_3$, a single *trans*-4,5-di-

(3) (a) Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *J. Chem. Soc., Chem. Commun.* **1981**, 466. (b) Bongini, A.; Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *J. Org. Chem.* **1982**, *47*, 4626. (c) Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *J. Chem. Soc., Chem. Commun.* **1982**, 1308. (d) Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *Ibid.* 1982, 1309.

(4) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(5) (a) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1339. (b) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Ibid.* **1986**, 1345.

(6) These results are in agreement with the data reported by Parker and O'Fee (Parker, K. A.; O'Fee, R. *J. Am. Chem. Soc.* **1983**, *105*, 654): the cyclization of (*E*)-*p*-nitrocinnamyl urethane gives exclusively the corresponding oxazolidone, while the (*Z*)-*p*-nitrocinnamyl urethane gives the corresponding oxazolidinone and oxazolidone in a 5:1 ratio. An analogous regioselection has been recently reported by Freeman and Robarge (Freeman, F.; Robarge, K. D. *Tetrahedron Lett.* **1985**, *26*, 1943) in the cyclization of (*Z*)- and (*E*)-D-ribohept-2-enoates, leading to ribofuranose and ribopyranose derivatives, respectively.

(7) Foglia, T. A.; Gregory, L. M.; Maerker, G. *J. Org. Chem.* **1970**, *35*, 3779.

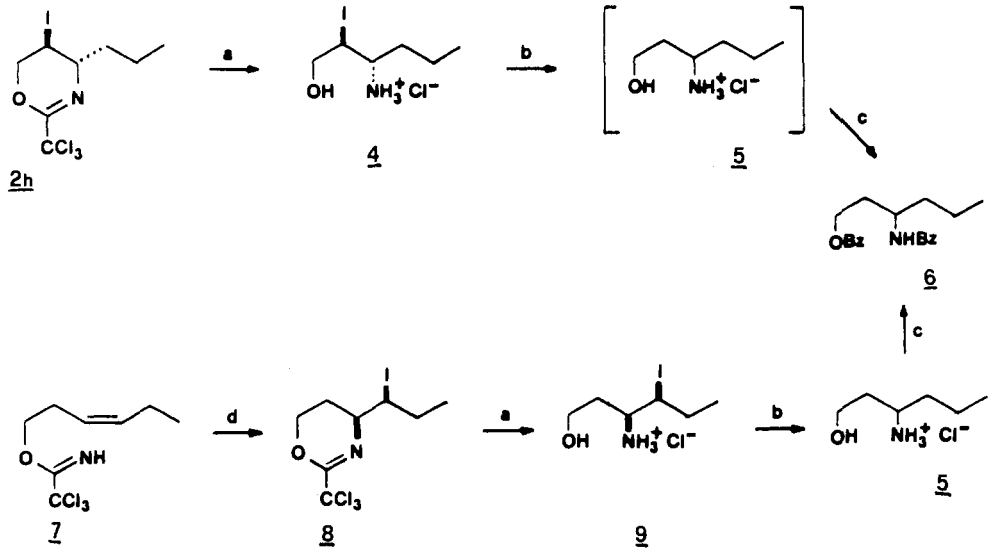
(8) Foglia, T. A.; Swern, D. *J. Org. Chem.* **1969**, *34*, 1680.

(9) Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Tetrahedron* **1986**, *42*, 917.

(10) (a) Hirama, M.; Iwashita, M.; Yamazaki, Y.; Ito, S. *Tetrahedron Lett.* **1984**, *25*, 4963. (b) Kobayashi, S.; Toshiyuki, I.; Ohno, M. *Ibid.* **1984**, *25*, 5079.

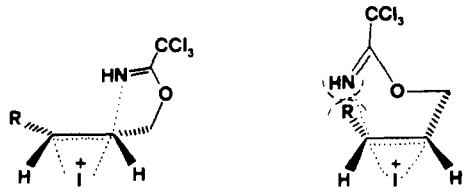
(11) (a) Cardillo, G.; Orena, M.; Sandri, S. *J. Chem. Soc., Chem. Commun.* **1983**, 1489. (b) Tamaru, Y.; Mizutani, M.; Furukawa, Y.; Kawamura, S.; Yoshida, Z.; Yanagi, K.; Minobe, M. *J. Am. Chem. Soc.* **1984**, *106*, 1079.

Scheme I[a]



[a] (a) 2 N HCl; (b) Bu_3SnH/ABIN; (c) BzCl/pyridine; (d) NIS/$CHCl_3$.

Scheme II

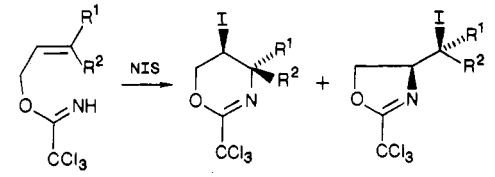


hydro-1,3-oxazine **2f** in 80% yield is obtained, while the 2*Z* isomer **1g** affords exclusively in 88% yield the 4,5-dihydro-1,3-oxazole **3g**, whose configuration is assigned on the basis of mechanistic considerations. In addition the cyclization of 2(*E*)-hexen-1-yl imidate **1h** gives in 87% yield the 4,5-dihydro-1,3-oxazine **2h**. To confirm the oxazine structure, **2h** has been hydrolyzed under acidic conditions to the corresponding salt **4**; the iodine is removed with tri-*n*-butyltin hydride and the resulting product is directly treated with benzoyl chloride and pyridine in CH_2Cl_2 to afford the compound **6** which shows IR, ^1H NMR, and ^{13}C NMR spectra identical with those of an authentic sample obtained from the iodocyclization of 3(*Z*)-hexen-1-yl imidate **7** and successive deiodination (Bu_3SnH/ABIN)[12] (Scheme I).

The entries **1i** and **1j**, providing the 4,5-dihydro-1,3-oxazine **2i** and the 4,5-dihydro-1,3-oxazole **3j**, respectively, support this trend.[5] It is therefore apparent that the reaction of these imidates strongly depends on the *E* or *Z* double bond configuration. The preferential formation of a five-membered ring, starting from a (*Z*)-allylic imidate, could be in fact attributed to the steric hindrance in the transition state for cyclization of the (*Z*)-allylic imidate.

To rationalize the observed regioselection, we have analyzed the positions of the atoms in the two possible cyclic transition states, by inspection of molecular models,[13] and we have found that for allylic imidates, the 6-endo closure is favored with respect to the 5-exo one, since a nearer approach to C-3 and a more collinear line of attack on iodine axis can occur.[14] In contrast, the imino group of a *Z* substrate has to move to about 1.4 Å to C-4 to perform an attack on C-3 and this distance is far inferior than the Van der Waals interaction, so that the imino group is forced to attack C-2, leading to a 5-exo closure (Scheme II).

Table III. Product Distribution of the Iodocyclization of Allylic Imidates as a Function of the Oxygen Effect



1 2 3

entry		yield of **2**,[a] %	yield of **3**,[a] %
l	$R^1 = H$; $R^2 = CH_2OCH_3$		87
m	$R^1 = H$; $R^2 = CH_2OTHP$		81
n	$R^1 = H$; $R^2 = CH_2OCH_2C_6H_5$		98
o	$R^1 = CH_2OCH_3$; $R^2 = H$	30	61
p	$R^1 = CH_2OTHP$; $R^2 = H$	38	55
q	$R^1 = CH_2OCH_2C_6H_5$	18	75

[a] Isolated yield of chromatographed product.

To test the role of a bulky substituent (i.e., phenyl group) on the regiochemistry of cyclization of a *Z* olefin with respect to a stabilized carbonium ion, we have cyclized the (*Z*)-cinnamyl imidate **1k**, where an incipient benzylic carbonium ion can arise during the cyclization. A mixture of 4,5-dihydro-1,3-oxazoles **2k** (IR 1650 and 1660 cm^{-1}) with unassigned configuration has been obtained, in 47:53 ratio, as determined by ^1H and ^{13}C NMR spectra of the reaction mixture.[15]

In a further study on the regioselection of the iodocyclization of allylic imidates we have examined the role of an oxygen atom vicinal to the double bond. Thus, 5-exo closure is exclusively observed for imidates **1l–n**[16] (Table III). These compounds, besides a *Z* double bond, show a protected hydroxyl group that favors the attack to the carbon atom C-2, because of the inductive and steric effects of the alkoxy group.[17a,b,c]

(12) Corey, E. J.; Suggs, J. W. *J. Org. Chem.* **1975**, *40*, 2555.
(13) We have identified the geometry of the transition state by the help of an easy program whose input data were the interatomic distances and the plane angle of the iodonium intermediate. The calculations were performed by varying the dihedral angles.
(14) Stork, G.; Cohen, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 5270.
(15) This result could probably be ascribed to the epimerization of the C–I bond, due to the presence of the α-phenyl group.
(16) Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Chem. Soc., Perkin Trans. 1* **1985**, 935.

On the contrary, a mixture of six- and five-membered rings **2o** and **3o** (33:66 ratio) has been obtained from **1o**, confirming the propensity of *E* double bond to promote a 6-endo closure, in opposition to the oxygen effect, which favors a 5-exo closure. To confirm this result, we have cyclized the imidates **1p** and **1q**: the former has given **2p** and **3p** in 40:60 ratio, while the latter has given **2q** and **3q** in 20:80 ratio. This result can be explained through the effect of the oxygen atom on the iodonium ion, which directs the attack of the nucleophile on the halonium ion away from the oxygen atom.

Conclusions

The regioselection of the iodocyclization of allylic imidates is controlled by electronic effects and by the double bond configuration. A *Z* substitution pattern, owing to a steric effect, favors a 5-exo closure, while an *E* substitution pattern favors a 6-endo closure. On the other hand, when an oxygen atom is introduced β to the *E* double bond, the steric effect leading to a 6-endo closure is balanced by the oxygen effect, and a predominant 5-exo closure is observed. Moreover, when an oxygen atom is introduced β to a *Z* double bond, the steric and oxygen effects act jointly, and a 5-exo closure is exclusively observed.

Experimental Section

General Methods. Tetrahydrofuran (THF) was distilled from $LiAlH_4$ or sodium benzophenone immediately prior to use. All reactions involving organometallic reagents were carried out under an argon atmosphere. Melting points (Pyrex capillary) were determined on a Buchi 510 hot-stage apparatus and are uncorrected. IR spectra were obtained with a Perkin-Elmer Model 682 spectrophotometer either on films or, for solids, on Nujol mulls. ^1H NMR spectra were recorded on a Varian EM-390 (90 MHz) spectrometer with tetramethylsilane as internal reference. ^{13}C NMR spectra (20 MHz) were recorded with a Varian FT 80-A spectrometer. All chemical shifts were measured relative to tetramethylsilane ($\delta_C = 0$). Analytical GLC was carried out on a Carlo Erba capillary gas chromatograph (Fractovap 4160) equipped with a SE-52 flexible glass capillary column (25 m × 0.3 mm i.d.; carrier gas, He; p_{He} 0.6 kg cm^{-2}). Chromatograms, peak areas, and retention times were obtained by using a Perkin-Elmer Sigma 10 data processor. TLC and column chromatography were carried out on Kieselgel GF_{254} (Merck). Solvent ratios are in volume before mixing. Solutions were dried over anhydrous magnesium sulfate.

General Procedure for Preparation of 1-(1-Imino-2,2,2-trichloroethoxy)alk-2-enes 1a–q. A solution of allylic alcohol (20 mmol) in dry THF (30 mL) under argon was added to a stirred suspension of NaH (50% in mineral oil; 100 mg, 2 mmol; previously washed with dry pentane) in dry THF (20 mL) at 0 °C. After 1 h the resulting mixture was added dropwise to a solution of trichloroacetonitrile (22 mmol) in dry THF (30 mL) with stirring at 0 °C. After 1.5 h at room temperature the volatiles were evaporated under reduced pressure, and pentane (20 mL) containing methanol (2 mL) was added to the residue: successive filtration through Celite pad, removal of the solvent and silica gel chromatography (95:5 cyclohexane/ethyl acetate) gave **1a–q** in good yield as colorless oils.

1-(1-Imino-2,2,2-trichloroethoxy)-3-phenyl-2(*E*)-propene (1a): 90%; IR 3340, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.00 (d, 2 H, J = 6 Hz), 6.40 (dt, 1 H, J = 6 Hz, J = 15 Hz), 7.40 (m, 5 H), 8.40 (br s, 1 H, NH). Anal. Calcd for $C_{11}H_{10}NOCl_3$: C, 47.43; H, 3.62; N, 5.03. Found: C, 47.5; H, 3.6; N, 5.0.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*E*),4(*E*)-hexadiene (1b): 85%; IR 3350, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.85 (d, 3 H, J = 6 Hz), 4.90 (d, 2 H, J = 5 Hz), 5.35–6.35 (m, 4 H), 8.45 (br s, 1 H, NH). Anal. Calcd for $C_8H_{10}NOCl_3$: C, 39.62; H, 4.16; N, 5.78. Found C, 39.5; H, 4.2; N, 5.8.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*E*),4(*E*)-octadecadiene (1c): see ref 9.

3-(1-Imino-2,2,2-trichloroethoxy)-1-octadecene (1d): see ref 5.

1-(1-Imino-2,2,2-trichloroethoxy)-3-methyl-3-butene (1e): 66%; IR 3340, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.70 (s, 3 H), 2.80 (s, 3 H), 4.80 (d, 2 H, J = 6 Hz), 5.55 (t, 1 H, J = 6 Hz), 8.25 (br s, 1 H, NH). Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.4; H, 4.4; N, 6.1.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*E*)-pentene (1f): 89%; IR 3340, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (t, 3 H, J = 6 Hz), 2.05 (q, 2 H, J = 6 Hz), 4.7 (d, 2 H, J = 6 Hz), 5.8 (m, 2 H), 8.25 (br s, 1 H, NH). Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.4; H, 4.4; N, 6.1.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*Z*)-pentene (1g): 78%; IR 3345, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (t, 3 H, J = 6 Hz), 2.1 (q, 2 H, J = 6 Hz), 4.85 (d, 2 H, J = 6 Hz), 5.7 (m, 2 H), 8.3 (br s, 1 H, NH). Anal. Calcd for $C_7H_{10}NOCl_3$: C, 36.47; H, 4.37; N, 6.08. Found: C, 36.5; H, 4.4; N, 6.0.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*E*)-hexene (1h): 88%; IR 3340, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H), 1.30–1.60 (m, 2 H), 1.90–2.30 (m, 2 H), 4.75 (d, 2 H, J = 7 Hz), 5.60–6.05 (m, 2 H), 8.35 (br s, 1 H, NH). Anal. Calcd for $C_8H_{12}NOCl_3$: C, 39.29; H, 4.95; N, 5.73. Found: C, 39.3; H, 4.9; N, 5.7.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*E*)-octadecene (1i): see ref 5.

1-(1-Imino-2,2,2-trichloroethoxy)-2(*Z*)-octadecene (1j): see ref 5.

1-(1-Imino-2,2,2-trichloroethoxy)-3-phenyl-2(*Z*)-propene (1k): 90%; IR 3340, 1665 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.05 (d, 2 H, J = 6 Hz), 5.95 (dt, 1 H, J = 6 Hz, J = 11 Hz), 6.75 (d, 1 H, J = 11 Hz), 7.3 (br s, 5 H), 8.3 (br s, 1 H, NH). Anal. Calcd for $C_{11}H_{10}NOCl_3$: C, 47.43; H, 3.62; N, 5.03. Found: C, 47.4; H, 3.6; N, 5.0.

1-(1-Imino-2,2,2-trichloroethoxy)-4-methoxy-2(*Z*)-butene (1l): 85%; IR 3340, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 4.1 (d, 2 H, J = 4 Hz), 4.9 (d, 2 H, J = 4 Hz), 5.85 (t, 2 H, J = 4 Hz), 8.35 (br s, 1 H, NH). Anal. Calcd for $C_7H_{10}NO_2Cl_3$: C, 34.11; H, 4.09; N, 5.68. Found: C, 34.1; H, 4.1; N, 5.7.

1-(1-Imino-2,2,2-trichloroethoxy)-4-(tetrahydropyranyloxy)-2(*Z*)-butene (1m): 80%; IR 3340, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (m, 6 H), 3.80 (m, 2 H), 4.50 (m, 3 H), 4.80 (m, 2 H), 5.80 (m, 2 H), 8.30 (br s, 1 H, NH). Anal. Calcd for $C_{11}H_{16}NO_3Cl_3$: C, 41.73; H, 5.09; N, 4.42. Found: C, 41.7; H, 5.1; N, 4.4.

1-(1-Imino-2,2,2-trichloroethoxy)-4-(benzyloxy)-2(*Z*)-butene (1n): see ref 16.

1-(1-Imino-2,2,2-trichloroethoxy)-4-methoxy-2(*E*)-butene (1o): 83%; IR 3345, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.35 (s, 3 H), 3.95 (m, 2 H), 4.85 (m, 2 H), 5.90 (m, 2 H), 8.35 (br s, 1 H, NH). Anal. Calcd for $C_7H_{10}NO_2Cl_3$: C, 34.11; H, 4.09; N, 5.68. Found: C, 34.0; H, 4.1; N, 5.7.

1-(1-Imino-2,2,2-trichloroethoxy)-4-(tetrahydropyranyloxy)-2(*E*)-butene (1p): 82%; IR 3340, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (m, 6 H), 3.80 (m, 2 H), 4.50 (m, 3 H), 4.80 (m, 2 H), 5.80 (m, 2 H), 8.30 (br s, 1 H, NH). Anal. Calcd for $C_{11}H_{16}NO_3Cl_3$: C, 41.73; H, 5.09; N, 4.42. Found: C, 41.8; H, 5.0; N, 4.4.

1-(1-Imino-2,2,2-trichloroethoxy)-4-(benzyloxy)-2(*E*)-butene (1q): 80%; IR 3330, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.15 (m, 2 H), 4.50 (s, 2 H), 4.85 (m, 2 H), 5.90 (m, 2 H), 7.30 (m, 5 H), 8.30 (br s, 1 H, NH). Anal. Calcd for $C_{13}H_{14}NO_2Cl_3$: C, 48.40; H, 4.37; N, 4.34. Found: C, 48.3; H, 4.4; N, 4.4.

General Procedure for the Iodocyclization of 1a–q. To a solution of **1a–q** (15 mmol) in $CHCl_3$ (150 mL) was added *N*-iodosuccinimide (3.6 g, 16 mmol), and the mixture was stirred for 12 h. Then a 10% $Na_2S_2O_3$ aqueous solution was added, the organic phase was separated, and the volatiles were removed in vacuo. After chromatography on silica gel (9:1 cyclohexane/ether) the oxazine and/or the oxazoline were recovered in good yield

(17) (a) Sato, A.; Ogiso, A.; Nogushi, H.; Mitsui, S.; Kaneto, I.; Shimada, Y. *Chem. Pharm. Bull.* **1980**, *28*, 1509. (b) Snider, B. B.; Johnson, M. I. *Tetrahedron Lett.* **1985**, *26*, 5497. (c) The same results have been obtained for the imidates employed in the synthesis of sugars ristosamine and daunosamine (Bongini, A.; Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *Tetrahedron* **1983**, *39*, 3801. Pauls, H. W.; Fraser-Reid, B. J. *Org. Chem.* **1983**, *48*, 1392. Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Org. Chem.* **1984**, *49*, 3951. Pauls, H. W.; Fraser-Reid, B. J. *J. Chem. Soc., Chem. Commun.* **1983**, 1031).

as colorless oils or low-melting solids.

***trans*-5-Iodo-4-phenyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2a)**: 80%; IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.07 (m, 1 H, CHI), 4.30 (m, 2 H, CH_2O), 4.90 (d, 1 H, CHN, J = 6 Hz), 7.25 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 128.1, 127.3, 70.5, 64.4, 22.1. Anal. Calcd for $C_{11}H_9NOCl_3I$: C, 24.86; H, 1.71; N, 2.64. Found: C, 24.8; H, 1.7; N, 2.6.

***trans*-5-Iodo-4-prop-1(*E*)-enyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2b)**: 90%; IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.75 (d, 3 H, J = 6 Hz), 4.05 (dt, 1 H, CHI, J = 7 Hz, J = 5 Hz), 4.30–4.80 (m, 3 H, CHN, CH_2O), 5.30–6.20 (m, 2 H); ^{13}C NMR (acetone-d_6) δ 135.4, 128.7, 71.1, 62.5, 27.3, 23.1. Anal. Calcd for $C_8H_9NOCl_3I$: C, 19.40; H, 1.83; N, 2.83. Found: C, 19.4; N, 1.9; H, 2.8.

***trans*-5-Iodo-4-pentadec-1(*E*)-enyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2c)**: see ref 9.

***cis*- and *trans*-4-(iodomethyl)-5-pentadecyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3d)**: see ref 5.

5-Iodo-4,4-dimethyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2e): 85%; IR 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 6 H), 4.30 (m, 1 H, CHI), 4.57 (m, 2 H, CH_2O); ^{13}C NMR ($CDCl_3$) δ 69.7, 54.3, 29.9, 29.2, 27.5. Anal. Calcd for $C_7H_9NOCl_3I$: C, 17.40; H, 1.88; N, 2.90. Found: C, 17.4; H, 1.8; N, 2.8.

***trans*-5-Iodo-4-ethyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2f)**: 90%; IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.0 (t, 3 H, J = 6 Hz), 1.6 (m, 1 H), 2.0 (m, 1 H), 3.72 (dt, 1 H, CHN, J = 3 Hz, J = 9 Hz), 4.1 (m, 1 H, CHI), 4.35 and 4.6 (*AB*X, 2 H, CH_2O, $J_{(AB)}$ = 12 Hz); ^{13}C NMR (DCl_3) δ 71.5, 61.9, 27.2, 20.6, 9.1. Anal. Calcd. for $C_7H_9NOCl_3I$: C, 17.40; H, 1.88; N, 2.90. Found: C, 17.4; H, 1.9; N, 2.9.

***threo*-4-(1-Iodopropyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3g)**: 88%; IR 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.1 (t, 3 H, J = 7 Hz), 1.8 (m, 2 H), 4.0–4.8 (complex pattern, 4 H); ^{13}C NMR ($CDCl_3$) δ 75.4, 71.8, 41.2, 28.1, 14.7. Anal. Calcd for $C_7H_9NOCl_3I$: C, 17.40; H, 1.88; N, 2.90. Found: C, 17.4; H, 1.8; N, 2.9.

***trans*-5-Iodo-4-propyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2h)**: 87%; IR 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (t, 3 H), 1.20–1.50 (m, 4 H), 3.50–5.00 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 71.2, 60.5, 36.2, 21.3, 17.9, 13.7. Anal. Calcd for $C_8H_{11}NOCl_3I$: C, 19.32; H, 2.23; N, 2.82. Found: C, 19.4; H, 2.2; N, 2.8.

***trans*-5-Iodo-4-pentadecyl-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2i)**: see ref 5.

***threo*-4-(1-Iodohexadecyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3j)**: see ref 5.

***threo*- and *erythro*-4-(α-iodobenzyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3k)**: 92%; IR 1660, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ [major isomer] 4.3–4.8 (complex pattern, 3 H), 5.45 (m, 1 H), 7.2–7.7 (complex pattern, 5 H), [minor isomer] 4.3–4.8 (complex pattern, 3 H), 5.15 (m, 1 H), 7.2–7.7 (complex pattern, 5 H); ^{13}C NMR δ [major isomer] 129.1, 128.7, 128.2, 76.6, 72.8, 37.0, [minor isomer] 128.8, 128.7, 128.2, 74.9, 72.5, 34.5.

***threo*-4-(2-Methoxy-1-iodoethyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3l)**: 87%; IR 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.4 (s, 3 H), 3.85 (dd, 2 H, J = 2 Hz, J = 7 Hz), 4.2–4.8 (complex pattern, 4 H); ^{13}C NMR ($CDCl_3$) δ 76.0, 74.8, 67.4, 58.8, 35.0. Anal. Calcd for $C_7H_9NO_2Cl_3I$: C, 16.84; H, 1.82; N, 2.81. Found: C, 16.8; H, 1.8; N, 2.9.

***threo*-4-[2-(Tetrahydropyranyloxy)-1-iodoethyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3m)**: 81%; IR 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70 (m, 6 H), 3.40–4.20 (m, 3 H), 4.70 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 99.6, 98.3, 77.2, 70.2, 69.9, 68.8, 68.2, 62.7, 62.4, 36.5, 36.3, 30.1, 26.8, 25.3, 19.3, 19.2. Anal. Calcd for $C_{11}H_{15}NO_3Cl_3I$: C, 23.20; H, 2.66; N, 2.46. Found: C, 23.3; H, 2.7; N, 2.4.

***threo*-4-[2-(Benzyloxy)-1-iodoethyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3n)**: see ref 16.

***trans*-5-Iodo-4-(methoxymethyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2o)**: 30%; IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (s, 3 H), 3.70 (m, 2 H, CH_2OMe), 3.90 (m, 1 H, CHN), 4.43 (m, 1 H, CHI), 4.60 (m, 2 H, CH_2O); ^{13}C NMR ($CDCl_3$) δ 72.7, 71.1, 61.3, 59.6, 16.3. Anal. Calcd for $C_7H_9NO_2Cl_3I$: C, 16.84; H, 1.82; N, 2.81. Found: C, 16.9; H, 1.8; N, 2.9.

***erythro*-4-(2-Methoxy-1-iodoethyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3o)**: 61%; IR 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.40 (s, 3 H), 3.75 (*AB*X, 2 H, CH_2OBn), 4.35–4.75 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 75.9, 74.8, 68.3, 58.8, 35.6. Anal. Calcd for $C_7H_9NO_2Cl_3I$: C, 16.84; H, 1.82; N, 2.81. Found: C, 16.8; H, 1.8; N, 2.8.

***trans*-5-Iodo-4-[(tetrahydropyranyloxy)methyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2p)**: 38%; IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (m, 6 H), 3.40–4.20 (m, 5 H), 4.20–4.80 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 99.6, 97.6, 71.5, 71.4, 67.7, 66.6, 62.3, 61.8, 61.4, 61.0, 30.3, 26.9, 25.4, 19.6, 19.4, 18.5, 16.7. Anal. Calcd for $C_{11}H_{15}NO_3Cl_3I$: C, 23.20; H, 2.66; N, 2.46. Found: C, 23.1; H, 2.6; N, 2.4.

***erythro*-4-[2-(Tetrahydropyranyloxy)-1-iodoethyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3p)**: 55%; IR 1658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65 (m, 6 H), 3.40–4.10 (m, 4 H), 4.40–4.80 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 99.3, 98.3, 76.2, 70.6, 69.7, 68.9, 68.5, 62.4, 62.3, 36.4, 36.1, 30.3, 26.9, 25.3, 19.3, 19.2. Anal. Calcd for $C_{11}H_{15}NO_3Cl_3I$: C, 23.20; H, 2.66; N, 2.46. Found: C, 23.2; H, 2.7; N, 2.4.

***trans*-5-Iodo-4-[(benzyloxy)methyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (2q)**: 18%; IR 1678 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.47 (m, 1 H, CHN), 3.87 (m, 2 H, CH_2OBn), 4.15–4.85 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 128.2, 127.5, 127.4, 73.3, 71.2, 70.1, 61.5, 16.5. Anal. Calcd for $C_{13}H_{13}NO_2Cl_3I$: C, 27.14; H, 2.28; N, 2.43. Found: C, 27.1; H, 2.3; N, 2.4.

***erythro*-4-[2-(Benzyloxy)-1-iodoethyl]-2-(trichloromethyl)-4,5-dihydro-1,3-oxazole (3q)**: 75%; IR 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.30–4.10 (*AB*X, 2 H, CH_2OBn), 4.40–4.80 (m, 6 H), 7.30 (br s, 5 H); ^{13}C NMR ($CDCl_3$) δ 128.5, 128.4, 127.7, 76.0, 73.1, 72.5, 68.6, 35.6. Anal. Calcd for $C_{13}H_{13}NO_2Cl_3I$: C, 27.14; H, 2.28; N, 2.43. Found: C, 27.2; H, 2.3; N, 2.5.

***erythro*-2-Iodo-3-aminohexan-1-ol Hydrochloride (4).** A solution of 4,5-dihydro-1,3-oxazine **2h** (5.0 g, 10 mmol) in methanol (40 mL) containing 2 N HCl (4 mL) was stirred for 12 h at room temperature. After removal of the solvent, the residue was taken up in dry ether, to give after filtration the hydrochloride **4** (3.7 g; 91% yield) as a low-melting solid: IR (Nujol 3380 cm^{-1}; ^1H NMR (CD_3OD) δ 0.90 (t, 3 H), 1.20–1.60 (m, 4 H), 3.20–3.40 (m, 2 H), 3.80–4.00 (m, 2 H), 4.20 (br s, 4 H, OH, NH_3^+).

3-Benzamido-1-(benzoyloxy)hexane (6). To a solution of hydrochloride **4** (3.25 g; 8 mmol) and azobisisobutyronitrile (1.32 g; 8 mmol) in benzene (25 mL) and methanol (5 mL) was added dropwise tri-*n*-butyltin hydride (4.6 g; 16 mmol), and the mixture was refluxed for 5 h. The solvents were removed under vacuum, and the residue was chromatographed on silica gel column (ethyl acetate) and directly benzoylated with benzoyl chloride (2 mL) and pyridine (2 mL) in CH_2Cl_2 (20 mL) to give 1.9 g (73% yield) of **6** as a white solid: mp 85–88 °C; IR (Nujol) 3300, 1690, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3 H, J = 6 Hz), 1.50 (m, 4 H), 2.00 (q, 2 H, J = 6 Hz), 4.40 (t, 2 H, CH_2O, J = 6 Hz), 4.35 (m, 1 H, CHN), 7.00 (d, 1 H, NH, J = 9 Hz), 7.30–8.20 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 132.9, 131.3, 129.5, 128.4, 127.0, 68.1, 62.3, 47.3, 37.2, 33.9, 25.1, 13.9. Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found: C, 73.9; H, 7.1; N, 4.2.

1-(1-Imino-2,2,2-trichloroethoxy)-3(*Z*)-hexene (7). A solution of 3(*Z*)-hexen-1-ol (1.5 g; 15 mmol) in dry THF (20 mL) under argon was added to a stirred suspension of NaH (50% in mineral oil; 75 mg; 1.5 mmol; previously washed with dry pentane) in dry THF (20 mL) at 0 °C. After 1 h the resulting mixture was added dropwise to a solution of trichloroacetonitrile (16 mmol) in dry THF (30 mL) with stirring at 0 °C. After 1.5 h at room temperature the volatiles were evaporated under reduced pressure, and pentane (20 mL) containing methanol (2 mL) was added to the residue: successive silica gel chromatography (98:2 cyclohexane/ethyl acetate) gave **7** in 85% yield (3.1 g): IR (neat) 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (t, 3 H), 1.40 (m, 4 H), 4.80 (m, 2 H), 5.60 (m, 2 H), 8.20 (br s, 1 H, NH). Anal. Calcd for $C_8H_{12}NOCl_3$: C, 39.29; H, 4.95; N, 5.73. Found: C, 39.2; H, 4.9; N, 5.7.

***threo*-4-(1-Iodopropyl)-2-(trichloromethyl)-4,5-dihydro-1,3-oxazine (8).** To a solution of **7** (2.4 g, 10 mmol) in $CHCl_3$ (150 mL) at room temperature was added NIS (2.5 g; 11 mmol) under stirring. After 10 h, a 10% $Na_2S_2O_3$ aqueous solution was added, the organic phase was separated, and the volatiles were removed in vacuo. After chromatography on silica gel (cyclohexane) the oxazine **8** was recovered (4.5 g; 90% yield) as a colorless oil: IR 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10 (t, 3 H, J = 7 Hz), 1.50–2.40 (m, 4 H), 3.50 (m, 1 H), 4.00–4.80 (m, 3 H).

Anal. Calcd for $C_8H_{11}NOCl_3I$: C, 19.32; H, 2.23; N, 2.82. Found: C, 19.3; H, 2.2; N, 2.9.

***threo*-3-Amino-4-iodohexan-1-ol Hydrochloride (9).** A solution of oxazine **8** (4.0 g; 8 mmol) in methanol (35 mL) containing 2 N HCl (3 mL) was stirred for 11 h at room temperature. After removal of the solvent, the residue was taken up in dry ether, to give after filtration the hydrochloride **9** (2.8 g; 87% yield) as a low-melting solid: IR (Nujol) 3260 cm^{-1}; ^1H NMR (CD_3OD) δ 1.00 (t, 3 H), 1.30-1.80 (m, 4 H), 3.50 (m, 1 H), 3.80 (t, 2 H), 4.90 (br s, 4 H, OH, NH_3^+).

3-Benzamido-1-(benzyloxy)hexane (6). To a solution of hydrochloride **9** (2.0 g; 5 mmol) and azobisisobutyronitrile (0.8 g; 5 mmol) in benzene (15 mL) and methanol (3 mL) was added dropwise tri-*n*-butyltin hydride (2.9 g; 10 mmol), and the mixture was refluxed for 5 h. The solvents were removed under vacuum, and the residue was chromatographed on silica gel column (ethyl acetate) and directly benzoylated with benzoyl chloride (1.5 mL) and pyridine (1.5 mL) in CH_2Cl_2 (15 mL) to give **6** in 70% yield (1.1 g).

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Registry No. **1a**, 59874-81-6; **1b**, 104808-41-5; **1c**, 104808-42-6; **1d**, 104808-43-7; **1e**, 104808-44-8; **1f**, 104808-45-9; **1g**, 104808-46-0; **1h**, 51479-70-0; **1i**, 104808-47-1; **1j**, 104808-48-2; **1k**, 59874-82-7; **1l**, 104808-49-3; **1m**, 104808-50-6; **1n**, 97186-53-3; **1o**, 104808-51-7; **1p**, 104808-52-8; **1q**, 104808-53-9; **2a**, 104808-54-0; **2b**, 104808-55-1; **2c**, 104808-77-7; **2e**, 104808-58-4; **2f**, 104808-59-5; **2h**, 104808-61-9; **2i**, 104808-62-0; **2o**, 104808-67-5; **2p**, 104808-69-7; **2q**, 104808-70-0; *cis*-**3d**, 104808-56-2; *trans*-**3d**, 104808-57-3; **3g**, 104808-60-8; **3j**, 104808-63-1; **3k** (isomer 1), 104808-64-2; **3k** (isomer 2), 104808-78-8; **3l**, 104808-65-3; **3m**, 104808-66-4; **3n**, 104834-04-0; **3o**, 104808-68-6; **3p**, 104872-73-3; **3q**, 104808-71-1; **4**, 104808-72-2; **5**, 104808-73-3; **6**, 104808-74-4; **7**, 104808-75-5; **8**, 84820-38-2; **9**, 104808-76-6; (*E*)-$HOCH_2CH{=}CHPh$, 4407-36-7; (*E*,*E*)-$HOCH_2CH{=}CHCH{=}CHCH_3$, 17102-64-6; $HOCH_2CH{=}C(CH_3)_2$, 556-82-1; (*E*)-$HOCH_2CH{=}CHCH_2CH_3$, 1576-96-1; (*Z*)-$HOCH_2CH{=}CHCH_2CH_3$, 1576-95-0; (*E*)-$HOCH_2CH{=}CH(CH_2)_2CH_3$, 928-95-0; (*Z*)-$HOCH_2CH{=}CHCH_2OCH_3$, 30339-05-0; (*Z*)-$HOCH_2CH{=}CHCH_2OTHP$, 57323-06-5; (*E*)-$HOCH_2CH{=}CHCH_2OCH_3$, 22427-04-9; (*E*)-$HOCH_2CH{=}CHCH_2OTHP$, 77741-47-0; (*E*)-$HOCH_2CH{=}CHCH_2OCH_2Ph$, 69152-88-1; 3-(*Z*)-hexen-1-ol, 928-96-1; trichloroacetonitrile, 545-06-2.

Polymer-Supported Cryptands. Problems Arising in the Synthesis of Highly Loaded Polymers

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The attachment of a hydroxymethyl[2.2.2]cryptand to lightly loaded chloromethylpolystyrene (≤1 mequiv of Cl/g) cross-linked with divinylbenzene leads to polymer-supported cryptands that are highly efficient catalysts in anion-promoted reactions carried out under phase-transfer conditions. However, the condensation with polystyrenes having a higher content of chloromethyl groups occurs in low yields, apparently affording immobilized cryptands with very low catalytic activity. This behavior results from extensive structural modifications of the bicyclic ligand, most likely promoted by neighboring chloromethyl groups.

In addition to the well-known quaternary onium salts, lipophilic macrocyclic and macrobicyclic polyethers have been largely used as anion activators under phase-transfer conditions.[1] Their immobilization in insoluble polymer supports allows a very easy recovery and recycling of the catalyst.[2] This is especially important in the case of the expensive cryptands, which show very high catalytic efficiency and chemical stability for almost any kind of reaction carried out under aqueous organic two-phase conditions.[1b]

Factors affecting catalytic activity of polymer-supported quaternary onium salts[3] and crown ethers[4] have been thoroughly investigated and the extension of this study to polymeric cryptands appears important. In this context one of the main factors is the percent of ring substitution (prs). In this line it was necessary to synthesize a homogeneous series of immobilized cryptands in a wide range of loading. Cryptands with a low prs had been previously prepared by us;[5] however, unlike the quaternary salts and crown ethers, the synthesis of highly loaded catalysts by the attachment of a functionalized cryptand to chloromethylated polystyrenes turned out to be impossible. Many unexpected difficulties were met with, and they will be described in the present paper.

Results and Discussion

The polymeric catalysts here examined have structures **1** and **2**.

Hydroxymethyl[2.2.2]cryptand **13** was condensed with commercial chloromethylated polystyrenes **3a-d**, 1% cross-linked with divinylbenzene, with 0.67, 1.04, 2.63, and 5.0 mequiv of Cl/g, respectively, to afford catalysts **1a-d**. Reactions were carried out in the presence of *t*-BuOK in boiling tetrahydrofuran (THF). Catalysts **1a** and **1b** were obtained in 39% and 53% yields (2.8 and 6.0 prs), respectively, but in the case of **1c** and **1d**, the yields of binding were much lower (8% and 9%, 2.6 and 5.9 prs, respectively).

Catalysts **1a** and **1b** were highly efficient, as was proved in nucleophilic aliphatic substitutions (Tables II and III, see also below), and the catalytic activities of **1c,d**, however, were very low (Table II). Binding yields, starting from **3c,d**, could be improved (up to 29%, catalysts **1e-g**) by

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