under argon, for 4 h. The mixture was cooled, concentrated in vacuo, and passed through a small column of basic alumina. The compound was eluted with ethyl acetate and then recrystallized from ethyl acetate–petroleum ether to give 209 mg (63%) of pure **38** as a light yellow crystal: mp 182–183 °C; ^{1}H NMR δ 2.52 (3 H, CH_3CO, s), 6.22 (1 H, H_8, m), 6.47 (1 H, H_9, dd), 7.06 (1 H, H_7, d), 7.28–8.42 (18 H, m) ($J_{7,8}$ = 7.6) Hz, $J_{8,9}$ = 3.5 Hz, $J_{8,10}$ = 1.5 Hz, $J_{9,10}$ = 10 Hz); high-resolution mass spectrum mass obsd 552.1443, calcd 552.1572.

3-Hydroxy-*trans*-7,8-dihydroxy-7,8-dihydrobenzo[*a*]pyrene (40). Triester **38** (83 mg, 0.15 mmol) was dissolved in deaerated THF (2 mL) and MeOH (2 mL), and 30 mg of powdered NaOH was added. The mixture was stirred at room temperature, under Ar, for 1 h. The reaction mixture was then adjusted to pH 6–7 with dilute HCl and extracted with ethyl acetate (50 mL). The ethyl acetate solution was washed with water (1 × 15 mL), dried (Na_2SO_4), and concentrated under reduced pressure to yield a yellowish brown solid. The solid was triturated with 25% ethyl acetate–hexane and filtered to give 40.7 mg (90%) of pure triol **40**: mp 360 °C dec; ^{1}H NMR (270 MHz, DMSO-d_6 + CD_3OD) δ 4.42 (1 H, H_8, d), 4.88 (1 H, H_7, d), 6.16 (1 H, H_9, dd), 7.44 (1 H, H_{10}, dd), 7.54 (1 H, H_2, d), 7.98–8.28 (5 H, m), 8.29 (1 H H_6, s) ($J_{1,2}$ = 8.2 Hz, $J_{7,8}$ = 10.6 Hz, $J_{8,9}$ = $J_{8,10}$ = 1.0 Hz, $J_{9,10}$ = 10.2 Hz); high-resolution mass spectrum mass obsd 302.0956, calcd 302.0944; UV (1% THF–EtOH) λ_{max} (ϵ) 389.7 (22 500), 370.6 (22 300), 350 (sh, 12 900), 298.9 (13 200), 286.2 (14 200); the fluorescence spectrum (0.25% THF–EtOH, excitation at 391 or 260 nm) exhibited an emission, with a maximum at 429 nm.

Supplementary Material Available: Synthetic methods and spectral data (^{1}H NMR, MS, and/or UV) for **8**, **10**, **18**, **21**, **25** (method B), **26** (method A), **37**, **39**, and **41** and ^{1}H NMR data for **11**, **12**, **13**, **20**, and **23** (6 pages). Ordering information is given on any current masthead page.

Conversion of Unsaturated Alcohols into Functionalized Tetrahydrofurans and Tetrahydropyrans via Nitrile Oxide Dipolar Cycloadditions[1]

Alfred Hassner* and K. S. K. Murthy

Department of Chemistry, Bar-Ilan University, Ramat-Gan 52100, Israel

Albert Padwa,* Ugo Chiacchio,[2] Dennis C. Dean, and Allen M. Schoffstall

Department of Chemistry, Emory University, Atlanta, Georgia 30322

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The intramolecular nitrile oxide cycloaddition (INOC) of a series of unsaturated oximino ethers has been investigated. The synthesis of the olefinic nitrile oxides involves treating an unsaturated alcohol with a α-bromoalkanal *O*-(trimethylsilyl)oxime in the presence of fluoride ion followed by subsequent sodium hypochlorite oxidation. The nitrile oxides were not isolated but spontaneously underwent intramolecular cycloaddition to give fused five- and six-membered ring ethers. The preferred stereoisomer in the formation of the five-membered ring ethers is trans, whereas in the six-membered ring ethers the cis isomer predominates. MM2 calculations help rationalize the observed stereoselectivity. The ratio of diastereomeric products from the INOC reaction appears to correlate with product stabilities. Simple heating of some of the oximino ethers led to intramolecular cycloaddition. The ring closure apparently proceeds subsequent to a tautomeric equilibration of the oxime with a transient nitrone which is trapped by the neighboring π-bond.

In recent years intramolecular nitrile oxide–olefin cycloadditions (INOC) have been of considerable synthetic and mechanistic interest, especially since the resulting isoxazoline ring can serve as a precursor to hydroxy ketones or to other functional groups.[3-9] Substituted and functionalized tetrahydrofurans and pyrans are of interest as analogues of carbohydrates.[10,11] This is particularly true if these compounds can be prepared in a stereoselective manner. On the basis of previous work by us and others on intramolecular dipolar cycloadditions,[12-22] we envisioned

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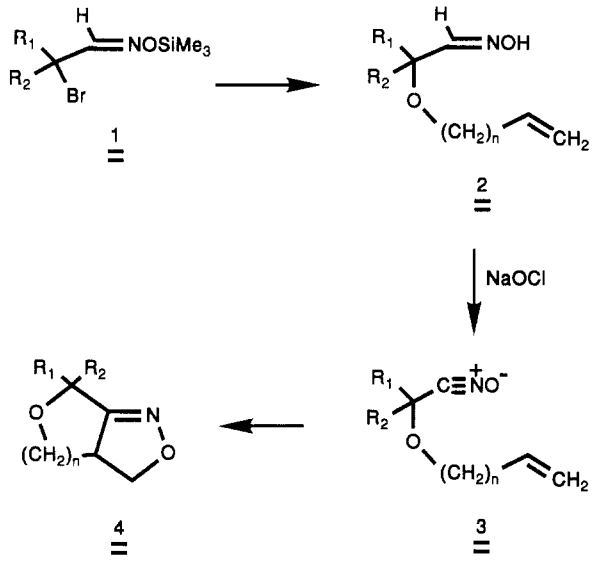
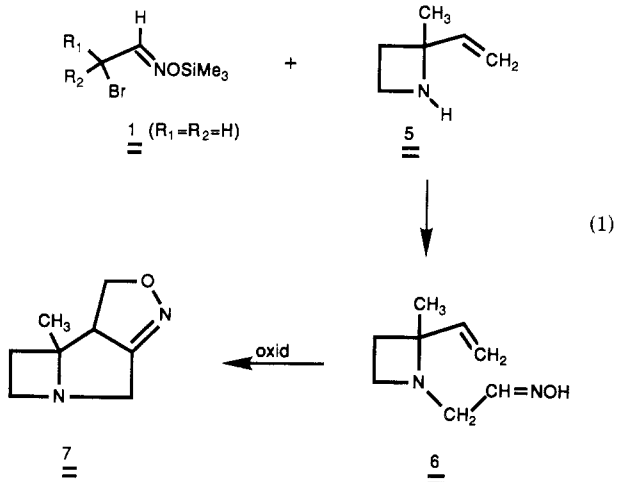
a general approach to such systems via a ring closure of unsaturated ethers of type **3**. Such unsaturated nitrile



oxides might be accessible from unsaturated alcohols and α-brominated aldoximes. Unfortunately, the latter, unlike α-bromo ketoximes, are difficult to prepare and unstable. Recently, we have shown that protection of aldoximes as the silyl ether permits their facile α bromination by means of *N*-bromosuccinimide.[12,14] The resulting oxime derivatives **1** can be isolated and used in reaction with nucleophiles such as vinyl azetidines.[14] The aminated intermediates served as building blocks for unsaturated nitrile oxides, which undergo spontaneous intramolecular dipolar cycloaddition, in some cases with high stereoselectivity (see eq 1). We now report the application of this approach to

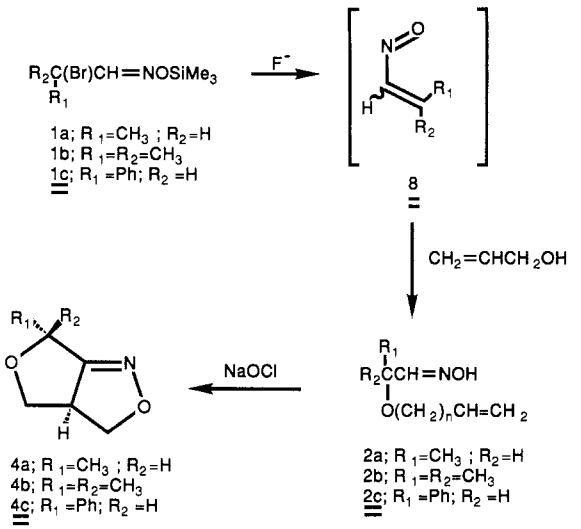


(1)

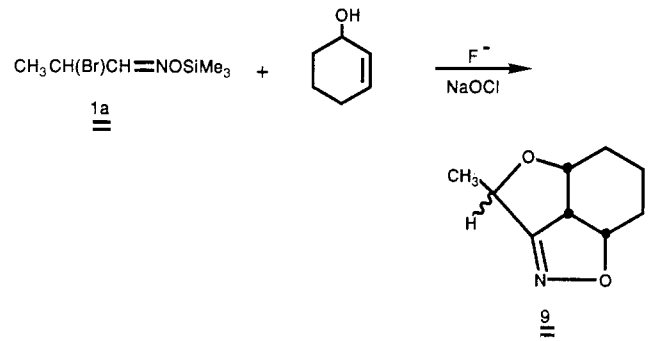
the conversion of unsaturated alcohols into functionalized five- and six-membered ring ethers, via intramolecular dipolar cycloaddition.[23]

Results and Discussion

When α-bromopropanal *O*-(trimethylsilyl)oxime (**1a**) was treated with allyl alcohol in the presence of fluoride ion, α-(allyloxy)propanal oxime (**2a**) was produced. Most likely this reaction involves a nitrosoalkene intermediate (i.e., **8**) since an analogous process is known to occur upon



treatment of α-halo oximes with base.[24] Nitrosoalkenes so generated undergo rapid addition of a variety of nucleophiles resulting in an overall nucleophilic functionalization α to the oxime center.[25-28] In our case the resulting unsaturated ether **2** possesses an aldoxime functionality which should be readily convertible to a nitrile oxide. Indeed, further treatment of the unsaturated aldoxime **2a** with NaOCl at room temperature led in 71% yield to **4a**, a cyclic ether fused to an isoxazoline and the result of spontaneous cyclization of an olefinic nitrile oxide (i.e., **3a**). Using the same procedure and starting with aldoxime derivatives **1b** and **1c**, we were able to prepare in good yield substituted tetrahydrofurans **4b,c** from allyl alcohol. The tricyclic ether **9** was obtained in a similar manner by



NaOCl oxidation of the unsaturated oxime, formed on treatment of α-bromo aldoxime **1a** with cyclohexen-3-ol. An examination of the behavior of *O*-silylated bromo oxime **1a** in the presence of fluoride ion revealed the transient appearance of a green color, indicative of the presence of an α,β-unsaturated nitroso compound, **8**. This pathway emphasizes the special feature of synthon **1**, inasmuch as it permits the use of a neutral nucleophile such as an alcohol, under mild conditions (room temperature), in the trapping of the vinyl nitroso intermediate **8**.

The stereochemical course of these intramolecular ring closures is a point of interest in stereoselective syntheses. We found that formation of the phenyl-substituted tetrahydrofuran **4c** proceeded with exclusive formation of the

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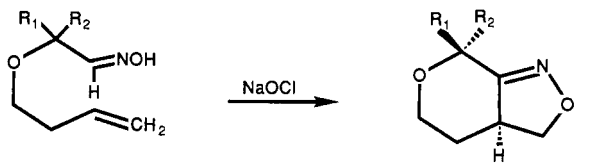
trans isomer (see Experimental Section), while the methyl analogue **4a** was formed in a 2.4:1 ratio of trans:cis isomers. Ring closure to the tricyclic system **9** proceeded with stereospecific introduction of three stereocenters (as in the synthesis of the carbon analogue ptilocaulin);[22] the fourth center was introduced as a 1:1 mixture of diastereomers.

To show that these oxazolines can be useful for formation of functionalized tetrahydrofuran derivatives, we examined the Raney Ni opening of the isoxazoline ring in **4b** and **4c**.[29] This led to keto alcohols **10b** and **10c** in 65% and 80% yield, respectively.

4b; R_1=R_2=CH_3
4c; R_1=Ph; R_2=H

10b; R_1=R_2=CH_3
10c; R_1=Ph; R_2=H

We next tested the possibility of forming stereoselectively a six-membered cyclic ether from the intramolecular cycloaddition reaction. For this purpose, 1-buten-4-ol was reacted with aldoxime derivative **1c** in the presence of tetrabutylammonium fluoride to produce in 56% yield **11c**, a homologue of **2c**. Reaction of **11c** with NaOCl led to **12c**

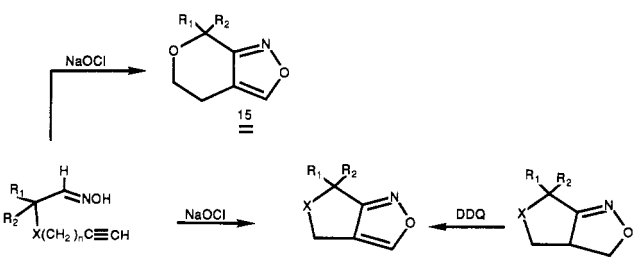


11a; R_1=CH_3; R_2=H
11b; R_1=R_2=CH_3
11c; R_1=Ph; R_2=H

12a; R_1=CH_3; R_2=H
12b; R_1=R_2=CH_3
12c; R_1=Ph; R_2=H

as a 6:1 mixture of stereoisomers. The major isomer in this case proved to be the cis isomer as indicated by NOE experiments (e.g. strong enhancement of the axial C-7 proton (adjacent to phenyl group) upon irradiation of the ring junction axial proton (at C-3a)). This is the opposite stereochemical result from that observed in the tetrahydrofuran case, where the major isomer was trans. MM2 calculations (vide infra) supports the stereochemical assignment and indicates the predictive value of such molecular mechanics calculations. In an analogous manner, fused tetrahydropyran **12a** was prepared in 78% (one isomer) from **11a**, and **12b** was formed from **11b** in 45% yield.

The use of propargyl alcohol in the reaction of **1b** and **1c** led, via the acetylenic oximes **13a** and **13c**, respectively, to the fused tetrahydrofurano[3,4-*c*]isoxazoles **14a** and **14c**.



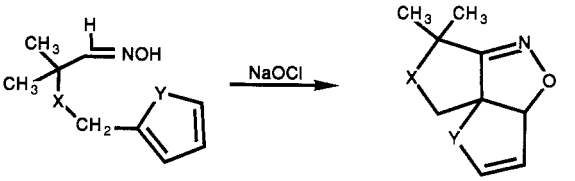
13a; R_1=R_2=CH_3; X=O; n=1
13b; R_1=R_2=CH_3; X=O; n=2
13c; R_1=Ph; R_2=H; X=O; n=1
13d; R_1=R_2=CH_3; X=S; n=1

14a; R_1=R_2=CH_3; X=O
14b; R_1=R_2=CH_3; X=S
14c; R_1=Ph; R_2=H; X=O

4b; R_1=R_2=CH_3; X=O

Isoxazoline **4b** was converted to isoxazole **14a** by DDQ oxidation. Furthermore, the same method can be employed, albeit in lower yield, for the synthesis of the fused tetrahydrothiophen **14b**, starting with propargyl thiol which reacted with **1b** followed by the sodium hypochlorite induced cycloaddition of **13d**. The six-membered ring tetrahydropyranoisoxazole **15** was prepared in 95% yield by NaOCl-induced ring closure of the homopropargyl ether **13b**, which resulted from reaction of 1-butyn-4-ol with oxime **1b**.

We also succeeded in extending the reaction of the α-bromo oxime **1b** with unsaturated alcohols to the heterocyclic system furfuryl alcohol and 2-thiophenemethanol. The furanyl and thiophenyl oximes **16a–c** were treated



16a; X=Y=O
16b; X=O; Y=S
16c; X=S; Y=O

17a; X=Y=O
17b; X=O; Y=S
17c; X=S; Y=O

with sodium hypochlorite, and the resulting heterocyclic nitrile oxides were found to undergo spontaneous intramolecular dipolar cycloaddition to produce the unusual tricyclic isoxazolines **17a–c** in high yield. In these systems, the heterocyclic ring acts as the dipolarophile with one of the double bonds adding to the nitrile oxide.[30] In all cases NMR and high-resolution mass spectra were consistent with the proposed structures (see Experimental Section).

To assess the geometrical requirements of an sp^2 (C=O) instead of an sp^3 center, we decided to compare nitrile oxide–olefin cycloaddition of ethers to tetrahydrofurans (i.e., **3** → **4**) with that of esters to furanones. The required oximes **18** of the unsaturated glyoxalic esters were prepared as shown in Scheme I. Sodium hypochlorite treatment of all three oximes (**18a–c**) led primarily to furoxans **19** (nitrile oxide dimers). In the phenyl-substituted case **18a**, ring closure to oxazoline **20** occurred in 24% yield. That the lack of intramolecular cycloaddition to form the oxazoline was not due to absence of nitrile oxide formation was established by trapping the 1,3-dipole with styrene to give oxazolines **21a–c**. Previous work by Garanti and Zecchi on cycloaddition of glyoxalic ester derivatives of type **18** also showed reluctance toward ring closure.[31] These results indicate that introduction of a carbonyl group in **18** has an unfavorable effect on the ring closure to the five-membered ring product during nitrile oxide–olefin cycloaddition.

Furthermore, we found that simple heating of the unsaturated oxime **2c** in benzene led to cycloaddition product **22a**. Grigg and co-workers have reported that aldoximes and ketoximes can react with olefins that serve as good Michael acceptors to produce isoxazolidines bearing a N-substituent. It is believed that first the oxime is transformed into a nitrone by reaction with 1 equiv of the electron-deficient olefin, and the nitrone then cycloadds to a second molecule of the acceptor olefin.[32]

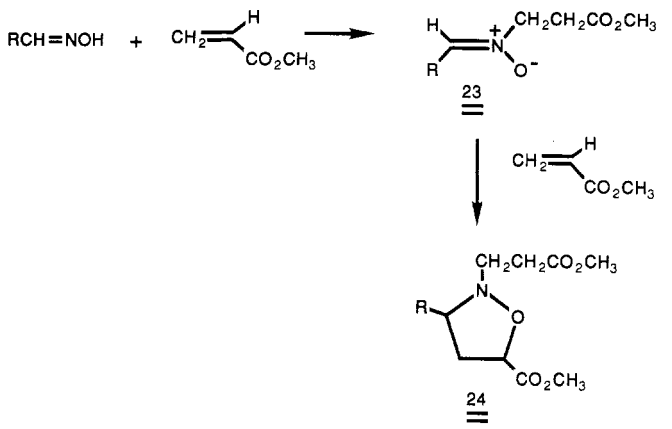
In the case of **2c**, the cycloaddition takes place simply on heating alone. This ring closure apparently proceeds

(29) Curran, D. P. *Advances in Cycloaddition*; Curran, D. P., Ed.; JAI Press: Greenwich, CT, 1988; Vol. 1.

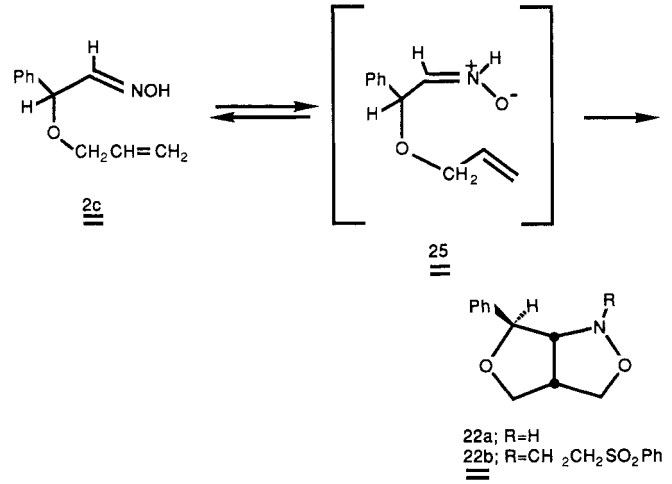
(30) For other examples of dipoles adding across a π-bond of a furan see: Heinze, I.; Eberbach, W. *Tetrahedron Lett.* **1988**, 2051.

(31) Garanti, L.; Zecchi, Z. *J. Heterocycl. Chem.* **1980**, *17*, 609.

(32) Grigg, R.; Jordan, M.; Tangthongkum, A.; Einstein, F. W. B.; Jones, T. *J. Chem. Soc., Perkin Trans. 1* **1984**, 47. For a related example see: Padwa, A.; Norman, B. H. *Tetrahedron Lett.* **1988**, 2417.



subsequent to a tautomeric equilibration of the oxime with nitrone **25**, which is trapped intramolecularly by the double



bond in a [3+2] cycloaddition.[33] Though 2-oximes of 1,2,3-tricarbonyl systems have been shown to undergo an unassisted proton transfer from O to N to generate a 1,3-dipole as a reactive intermediate,[34] attempts to extend this cycloaddition process to a simple aldehyde or keto oxime were generally unsuccessful.[35] Perhaps the facility of cycloaddition with **2c** is related to the availability of the heteroatom in the side chain which promotes the tautomerization process.[33]

Heating of α-(allyloxy)phenylacetaldoxime (**2c**) in toluene in the presence of phenyl vinyl sulfone as a Michael acceptor gave **22a** in 15% yield, together with 34% of its *N*-2-(phenylsulfonyl)ethyl derivative **22b**. The formation of **22b** may involve conjugate addition of **22a** onto phenyl vinyl sulfone or, alternatively, a mechanism similar to that described by Grigg with methyl acrylate and various oximes.[32] Tetrahydroisoxazole **22a** corresponds to a single stereochemical isomer. Hence, these ring closures are of potential interest in the stereospecific formation of cyclic ethers bearing 1,3-amino alcohol functions.

Molecular Mechanics Calculations

One important feature of the above cyclization process in which two rings are formed is one of stereoselectivity,

Table I. Molecular Mechanics Calculations of the INOC Reaction of Unsaturated Oximino Ethers

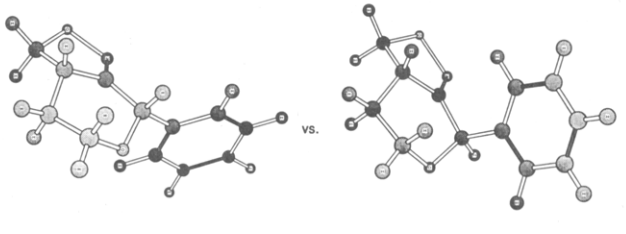
INOC reaction	cycloadduct cis	cycloadduct trans	ΔE,[a] kcal	cis/trans ratio
2a → **4a**	28.44	28.06	0.38	1:2.4
2c → **4c**	38.50	37.54	0.96	<1:100
11a → **12a**	18.53	20.08	1.55	>100:1
11c → **12c**	29.07	29.41	0.34	6:1
2c → **22a**	30.79	28.58	2.21	<1:100
CH_2=$CHCH_2OCH_2C$≡N^+O^-			GS[b] = −15.23 kcal	
	TS[c] = +18.98 kcal		(E_{TS} − E_{GS}) = 34.19 kcal	
CH_2=$CHCH_2OCOC$≡N^+O^-			GS = −35.68 kcal	
	TS = +13.76		(E_{TS} − E_{GS}) = 49.44 kcal	

[a] MM2 calculations were performed on a Vax 11/785 using Model 2.93. [b] Ground state using the Gajewski–Gilbert MMX program. [c] Transition-state energies were calculated by using the MMX program. The program is parameterized for transition-state carbon (C$,C#,C*) as well as transition-state oxygen. Transition-state bond orders of 0.3 were used.

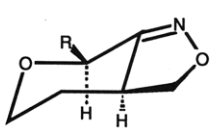
and it is useful to be able to predict the preferred stereochemistry of the products. In recent years, molecular mechanics has developed into an important technique for the calculation of molecular properties.[36] We have used the Still–Steliou model 2.93 program to model energy differences in the diastereomeric transition states for the INOC reaction. The stability of the diastereomeric cycloadducts can be determined by calculation of their steric energies, the direct sum of the force-field increments. These steric energies represent the thermally averaged energies relative to the same molecule but with all bond lengths, bond angles, and torsional angles set to their strainless values and the atoms having van der Waals and electrostatic interactions corresponding to infinite separation.[37] We assume that the relative energy differences of the two lowest energy conformations of the diastereomeric cycloadducts will parallel the energy differences in the transition state. These calculations help rationalize the exclusive formation of cycloadduct **4c** and account for a mixture of isomers with the methyl system (i.e., **4a**). The calculations reveal a 0.96 kcal difference between the two diastereomeric transition states for the phenyl case but only a 0.38 kcal difference for the methyl system (see Table I). In both cases the lower energy isomer corresponds to the trans isomer. This is a subtle effect that is not immediately obvious on inspection of molecular models but for which MM2 calculations serve well to predict stereochemistry in such intramolecular dipolar cycloadditions.[38]

That the preferred stereoisomer in the formation of the five-membered-ring ethers (i.e., **4**) in trans whereas in the six-membered-ring ethers (i.e., **12**) the cis isomer predominates coincides with the more stable isomer in each set, as revealed by MM2 calculations (see Table I) and thus can be explained on conformational grounds. In the six-membered-ring ether the cis configuration **26** with both R and CH_2 equatorial is expected to be more stable, while in the five-membered-ring ether the trans configuration,

(33) For another example of this type of [3+2] cycloaddition see: Norman, M. H.; Heathcock, C. H. *J. Org. Chem.* **1987**, *52*, 226. Hassner, A.; Maurya, R.; Mesko, E. *Tetrahedron Lett.* **1988**, *29*, 5313.
(34) Grigg, R.; Thianpantangul, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 653.
(35) Grigg, R. *Chem. Soc. Rev.* **1987**, *16*, 89.
(36) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. Burket, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, D.C., 1982.
(37) Kao, J.; Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 975.
(38) For some MM2 calculations on bimolecular nitrile oxide cycloadditions, see: Houk, K. N.; Moses, S. R.; Wu, Y. D.; Rondan, N. G.; Jager, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. Houk, K. N.; Duh, H. Y.; Wu, Y. D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754.



12c-cis isomer (Et=29.07 kcal) 12c-trans isomer (Et=29.41 kcal)



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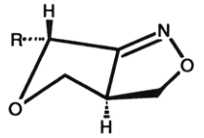


27

as indicated by conformer **27**, may be preferred. The MM2 calculations of the energy relationships between the cis and trans isomers of **22a** are also in good agreement with the isolation of a single product from the thermolysis of nitrone **2c**. The calculations show that the trans isomer is 2.21 kcal more stable than the cis isomer.

We have also probed the stereochemical effects operative during the INOC reaction of the glyoxalic ester system using MM2 calculations. Here we are dealing with an sp^2 hybridized carbonyl carbon instead of an sp^3 center at the position α to the nitrile oxide center. Widening of the bond angle will certainly lengthen the distance between the interacting dipole and π-bond and would be expected to diminish the rate of cycloaddition relative to the furan system. Although it is not realistic to directly compare ground- or transition-state energies for the two cycloadducts, it is admissible to compare activation energies ($E_{TS} - E_{GS}$) for the ring closure. We find that these differences (see Table I) are consistent with the experimental results. Thus, the glyoxalic esters are predicted to undergo the INOC reaction with greater difficulty than the corresponding ethers.

In conclusion, the work reported herein establishes the utility of the INOC reaction for the construction of fused heteroisoxazolines. MM2 calculations help rationalize the observed stereoselectivity. Extensions of the scope and synthetic potential of these cyclizations are being further investigated.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting-point apparatus and are uncorrected. Infrared spectra were run on a Perkin Elmer Model 283 infrared spectrometer. Spectral data were obtained on compounds that were judged to be >95% pure by ^{13}C and/or ^1H NMR analysis. Proton NMR spectra were obtained on a GE 300, Varian EM-390, or Nicolet NMC-360 MHz spectrometer. ^{13}C NMR spectra were recorded on a Bruker 300 or an IBM NB 200 SY FT spectrometer. Microanalyses were performed at Atlantic Microlabs, Atlanta, GA. Mass spectra were determined with a VG MM-7070S mass spectrometer at an ionizing voltage of 70 eV.

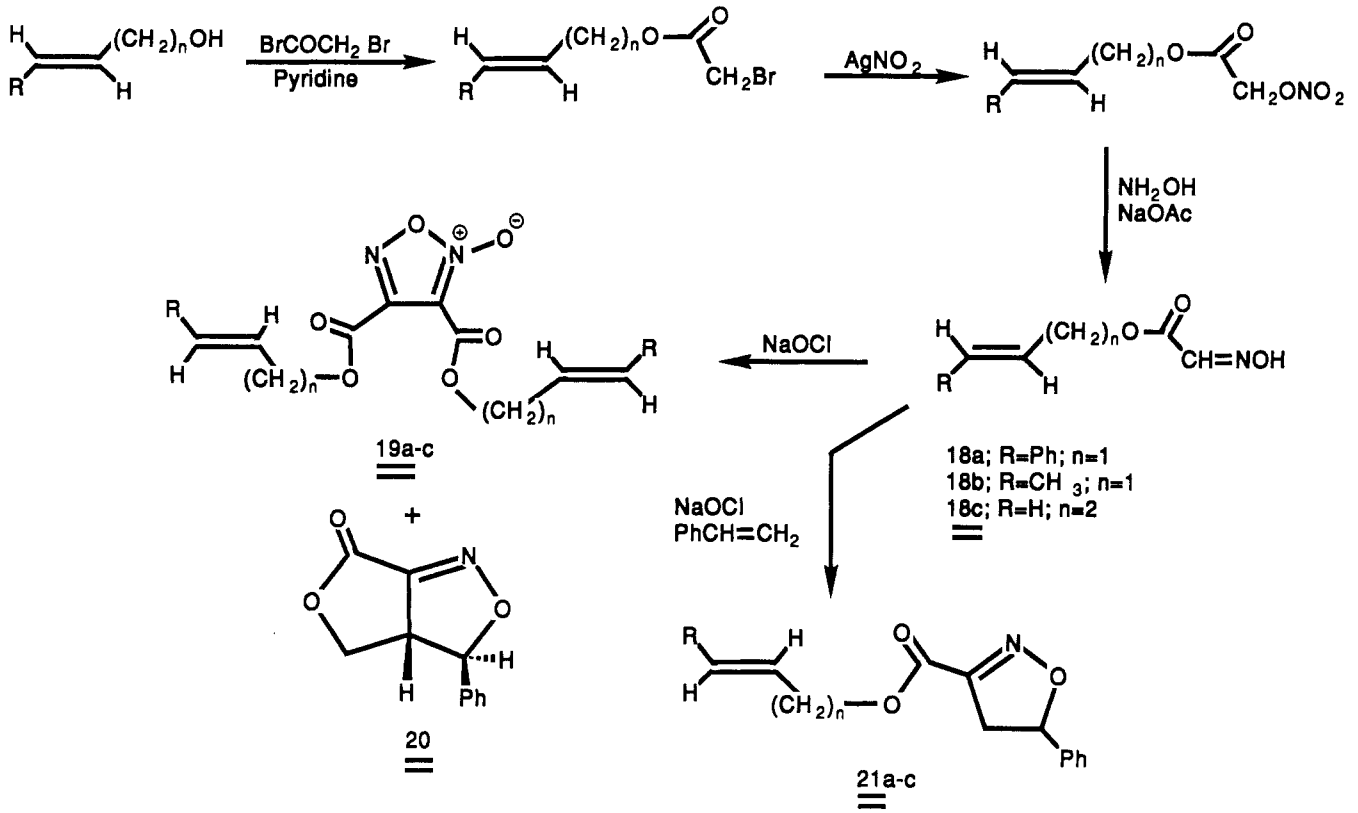
Reaction of 2-Bromopropanal *O*-(Trimethylsilyl)oxime (1a) with Allyl Alcohol Followed by Hypochlorite Oxidation. To a stirred solution containing 0.87 g of propanal oxime and 1.01 g of triethylamine in 30 mL of dry carbon tetrachloride at 0–5 °C was added dropwise 1.08 g of trimethylsilyl chloride in 5 mL of carbon tetrachloride. The mixture was slowly brought to room temperature and was stirred under argon for 2 h. The mixture was filtered, and the solid triethylamine hydrochloride that formed was washed with 20 mL of carbon tetrachloride. To the combined filtrate were added 1.78 g of *N*-bromosuccinimide and 120 mg of benzoyl peroxide. The stirred suspension was heated at reflux for 3.5 h (or irradiated for 2 h) under argon. The solution was filtered, and the filtrate was washed with a 10% aqueous sodium thiosulfate solution and water and then dried over sodium sulfate. Removal of the solvent under reduced pressure gave 2.25 g (95%) of 2-bromopropanal *O*-(trimethylsilyl)oxime (**1a**) as a colorless oil, bp 50–52 °C (7 mmHg). This material is stable in the refrigerator as an oil or as a carbon tetrachloride solution for at least 1 week but partially polymerizes upon distillation.

To a stirred solution containing 67 mg of the above α-bromosilyl oxime and 174 mg of allyl alcohol in 2 mL of tetrahydrofuran at 25 °C was added 0.3 mL of a 1.0 M tetrabutylammonium fluoride solution. The solution was stirred at 25 °C for 30 min. After removal of the solvent under reduced pressure, the mixture was taken up in 30 mL of methylene chloride and was extracted with water. The organic layer was washed with brine and dried over sodium sulfate, and the solvent was removed under reduced pressure to give α-(allyloxy)propanal oxime (**2a**) as a light yellow oil: ^1H NMR δ 1.32 (d, 3 H, J = 8.0 Hz), 3.85–3.94 (m, 1 H), 3.95–4.13 (m, 2 H), 5.13–5.31 (m, 2 H), 5.8–5.95 (m, 1 H), 7.29 (d, 1 H, J = 8.0 Hz), and 8.70 (br s, 1 H). This material was taken up in 20 mL of methylene chloride, and to this solution was added 0.6 mL of a 9% sodium hypochlorite solution at 6 °C. The temperature was allowed to warm to 25 °C, and the mixture was stirred vigorously for 1.5 h at room temperature. The organic layer was separated, and the aqueous layer was extracted with methylene chloride. The combined organic layer was washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure to leave behind a light yellow oil. This material was subjected to silica flash chromatography to give cycloadduct **4a** as a 2.4:1 mixture of isomers (27 mg, 71% yield): IR (neat) 2980, 2940, 2870, 1090, 1065, 1050, 1015, 970, 835, and 815 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ doublets at 1.43 and 1.46 (d, J = 6.5 Hz, 3 H), 3.59–3.74 (m, 1 H), 3.92–4.05 (m, 1 H), 4.15–4.31 (m, 2 H), and 4.5–4.72 (m, 2 H); ^{13}C NMR δ 16.1, 17.6, 18.5, 19.5, 29.2, 29.6, 29.8, and 31.8; MS, m/e 127 (M^+), 113, 111, 97, 88, 86, 84, 68, and 67; HRMS calcd for $C_6H_9NO_2$ 127.0633, found 127.0633.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with Allyl Alcohol Followed by Hypochlorite Oxidation. To a stirred solution containing 8.7 g of 2-methylpropanal oxime and 10.1 g of triethylamine in 250 mL of dry carbon tetrachloride at 0–5 °C was added 10.8 g of trimethylsilyl chloride in 30 mL of carbon tetrachloride. The mixture was slowly brought to room temperature and was then heated at reflux for 6 h. The mixture was filtered, and the solid triethylamine hydrochloride that formed was washed with carbon tetrachloride. The combined filtrates were distilled to give 13.7 g (87%) of 2-methylpropanal *O*-(trimethylsilyl)oxime: ^1H NMR ($CDCl_3$, 80 MHz) δ 0.16 (s, 9 H), 1.10 (d, 6 H, J = 7.0 Hz), 2.51 (oct, 1 H, J = 7.0 Hz), and 7.42 (d, 1 H, J = 7.0 Hz). To a stirred carbon tetrachloride solution containing 1.59 g of the above oxime was added 1.78 g of *N*-bromosuccinimide. The solution was irradiated for 2 h under a nitrogen atmosphere and was then filtered, washed with a 10% aqueous sodium thiosulfate solution followed by water, and then dried over sodium sulfate. Removal of the solvent under reduced pressure gave 1.54 g (65%) of 2-bromo-2-methylpropanal *O*-(trimethylsilyl)oxime (**1b**) as a colorless oil, bp 52 °C (0.5 mmHg); ^1H NMR ($CDCl_3$, 80 MHz) δ 0.20 (s, 9 H), 1.90 (s, 6 H) and 7.71 (s, 1 H).

To a stirred solution containing 710 mg of bromosilyl oxime **1b** and 1.74 g of allyl alcohol in 10 mL of tetrahydrofuran at 25 °C was added 3 mL of a 1.0 M tetrabutylammonium fluoride solution. The solution was stirred at 25 °C for 40 min, and then the solvent was removed under reduced pressure. The mixture was taken up in 30 mL of methylene chloride and was extracted with water. The organic layer was washed with brine and dried over sodium sulfate, and the solvent was removed under reduced pressure to leave behind 107 mg (25%) of α-(allyloxy)-2-methylpropanal oxime (**2b**) as a light yellow oil after silica gel chromatography (cyclohexane–ethyl acetate (9:1)): IR (neat) 3360, 2980, 2930, 2860, 1650, 1430, 1380, 1150, 1060, 1000, 950, 930, and 810 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.38 (s, 6 H), 3.87 (t, 1 H, J = 1.8 Hz), 3.95 (t, 1 H, J = 1.8 Hz), 5.02–5.40 (m, 2 H), 5.7–6.16 (m, 1 H), 7.41 (s, 1 H), and 8.45 (br s, 1 H).

Scheme I



A 500-mg sample of the above oil was taken up in 20 mL of methylene chloride. To this solution was added 10 mL of a 4.9% sodium hypochlorite solution at 0 °C, and the temperature was allowed to warm to 25 °C. The mixture was stirred vigorously for 1.5 h at room temperature, and the organic layer was extracted with methylene chloride. The combined organic extracts were washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure to leave behind a light yellow oil. This material was chromatographed on a silica gel plate using 5% ethyl acetate–cyclohexane mixture as the eluent. The first fraction contained 450 mg (95%) of cycloadduct **4b**: IR (neat) 2980, 2940, 2880, 1660, 1470, 1390, 1370, 1270, 1150, 1020, 900, and 840 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.47 (s, 3 H), 1.51 (s, 3 H), 3.7–4.6 (m, 5 H); HRMS calcd for $C_7H_{12}NO_2$ 142.0857, found 142.0867.

A 50-mg sample of the above material was dissolved in 20 mL of a 5:1 methanol–water mixture and was hydrogenated at atmospheric pressure at 25 °C for 4 h using 6 mg of W-2 Raney nickel as the catalyst. The mixture was filtered through Celite and concentrated under reduced pressure. The crude residue was chromatographed on a silica gel column using a 25% ethyl acetate–hexane mixture as the eluent. The major fraction isolated contained 65% of tetrahydrofuran-3-one **10b**: IR (neat) 3400, 2985, 2960, 2870, 1750, 1580, 1470, 1385, 1370, 1150, 1020, and 960 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.51 (s, 6 H), 2.72 (br s, 1 H), 3.65–4.45 (m, 5 H); MS, *m/e* 145 (MH^+).

Sodium Hypochlorite Oxidation of α-(Allyloxy)phenylacetaldoxime (2c). To a dry 500-mL round-bottom flask were added 2.7 g of phenylacetaldoxime, 2.02 g of triethylamine, and 200 mL of carbon tetrachloride. A sample containing 2.17 g of trimethylsilyl chloride was added dropwise over a 10–15-min period. A white precipitate soon appeared, and stirring was continued for an additional 12 h. The solution was concentrated under reduced pressure to give the silylated oxime, which was used in the next step without further purification; ^1H NMR (CCl_4, 90 MHz) δ 0.10 (s, 9 H), 3.50 (d, 2 H), 6.75 (t, 1 H), and 7.10 (m, 5 H). To a carbon tetrachloride solution of the above-silylated oxime were added 3.56 g of *N*-bromosuccinimide and 0.1 g of benzoyl peroxide. The flask was fitted with a septum and magnetic stirrer, and the mixture was photolyzed for 3 h by using a 450-W Hanovia lamp. The solution was filtered, and the filter cake was washed with 25 mL of carbon tetrachloride. The resulting solution contained 5.43 g of 2-bromophenylacetaldehyde *O*-(trimethylsilyl)oxime (**1c**) which could be stored in the cold for up to a week; IR (neat) 1715, 1500, 1455, 1250, 955, 845, 750, and 695 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.20 (s, 9 H), 5.70 (d, 1 H, J = 8.0 Hz), 7.4 (m, 5 H), and 7.9 (d, 1 H, J = 8.0 Hz).

A carbon tetrachloride solution containing the above bromo oxime was concentrated under reduced pressure, and the resulting oil was taken up in 50 mL of tetrahydrofuran. This solution was added to a solution containing 11.6 g of allyl alcohol and 20 mL of a 1.0 M tetrabutylammonium fluoride solution in 50 mL of tetrahydrofuran over a period of 1 h at 25 °C. After stirring for an additional hour, the solution was concentrated under reduced pressure, and the residue was taken up in 100 mL of ether. The organic layer was washed with a 20% brine solution, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give 2.5 g (65%) of α-(allyloxy)phenylacetaldoxime (**2c**) as a yellow oil: IR (neat) 3300, 1705, 1600, 1490, 1450, 1065, 935, 765, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 4.05 (d, 1 H, J = 5.0 Hz), 5.03 (d, 1 H, J = 7.0 Hz), 5.30 (m, 1 H), 5.80 (m, 1 H), 7.40 (m, 6 H), and 8.90 (br s, 1 H); MS, *m/e* 174, 134, 105, 91, 77, and 63; HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0938.

A 0.38-g sample of α-(allyloxy)phenylacetaldoxime (**2c**) was dissolved in 30 mL of methylene chloride. To this solution was added 9.3 mL of a 5.2% sodium hypochlorite solution at 0–5 °C over a period of 15 min. The mixture was slowly allowed to warm to 25 °C with vigorous stirring. The aqueous layer was extracted with 15 mL of methylene chloride, and the organic layer was dried over magnesium sulfate, filtered, and concentrated to give 330 mg (88%) of a light yellow oil. Silica gel chromatography of this material using a 20% ethyl acetate–hexane mixture as the eluent afforded 6-phenyl-2,3,4,5-tetrahydrofuranyl[3,4-*c*]-4,5-dihydroisoxazole (**4c**) as a pale yellow oil: IR (neat) 1710, 1605, 1500, 1450, 1020, 740, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.81 (t, 1 H, J = 8.4 Hz), 4.06 (dd, 1 H, J = 12.2 and 8.4 Hz), 4.23 (m, 1 H), 4.42 (t, 1 H, J = 8.4 Hz), 4.58 (t, 1 H, J = 8.4 Hz), 5.61 (s, 1 H), and 7.39 (m, 5 H). External irradiation of the triplet at δ 4.58 collapsed the doublet of doublets at δ 4.06 to a doublet and collapsed the multiplet at δ 4.23 to a doublet of doublet of doublets. External irradiation of the triplet at δ 4.42 collapsed the triplet at δ 3.81 to a doublet and collapsed the multiplet at δ 4.23 to a doublet of doublet of doublets; ^{13}C NMR ($CDCl_3$, 20 MHz) δ 54.4,

69.9, 72.9, 73.6, 125.6, 128.4, 128.6, 137.3, and 170.2; MS, *m/e* 175, 159, 131, 119, 105, 77, and 69 (base); HRMS calcd for $C_{11}H_{11}NO_2$ 189.0790, found 189.0789.

The relative trans stereochemistry of cycloadduct **4c** was assigned on the basis of NOE difference studies. Irradiation of the C-6 proton at δ 5.61 led to a moderate enhancement of the C-4 α-proton signal at δ 3.81 with no enhancement of the C-3a multiplet. Irradiation of the C-3a multiplet at δ 4.23 resulted in a strong enhancement of the C-3 β-proton signal at 4.58, a somewhat weaker enhancement of the C-4 β-proton at δ 4.06, and no enhancement of the C-6 proton signal. Molecular models show this information to be most consistent with a trans relationship between the C-6 and the C-3a protons.

Raney Nickel Reduction of 6-Phenyl-2,3,4,5-tetrahydrofuro[3,4-*c*]-4,4-dihydroisoxazole (4c). To a solution containing 80 mg of dihydroisoxazole **4c** in 10 mL of methanol/water (5:1) were added 53 mg of boric acid and approximately 15 mg of W-2 Raney nickel (base free). The mixture was shaken with hydrogen at 15 psi for 4 h by using a Parr apparatus. The catlayst was filtered, and the filtrate was concentrated under reduced pressure. The residue was taken up in 25 mL of methylene chloride and 25 mL of water. The aqueous layer was washed with an additional 25 mL of methylene chloride. The organic layer was dried over magnesium sulfate, and the solution was concentrated to give 65 mg (80%) of 2-phenyl-4-(hydroxymethyl)-2,3,4,5-tetrahydrofuran-3-one (**10c**) as a yellow oil. Silica gel chromatography of this material using a 10% ethyl acetate–hexane mixture afforded a pure sample of **10c** as a pale yellow oil: IR (neat) 3470, 2890, 1750, 1500, 1455, 1275, 1085, 965, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.84 (m, 1 H), 3.87 (dd, 1 H, J = 11.2 and 5.0 Hz), 3.98 (dd, 1 H, J = 11.2 and 5.0 Hz), 4.15 (t, 1 H, J = 9.6 Hz), 4.64 (t, 1 H, J = 9.1 Hz), 4.72 (s, 1 H); MS, *m/e* 192 (M^+), 164, 124, 122, 107, and 105 (base); HRMS calcd for $C_{11}H_{12}O_3$ 192.0786, found 192.0795.

Reaction of Cyclohexenol with 2-Bromopropanal *O*-(Trimethylsilyl)oxime (1a) Followed by Hypochlorite Oxidation. Following a similar procedure as was used with the other oximino ethers, cycloadduct **9** was formed in 67% yield as a 1:1 mixture of diastereomers: ^1H NMR ($CDCl_3$, 80 MHz) δ 1.42 (d, 1.5 H, J = 7.0 Hz), 1.52 (d, 1.5 H, J = 7.0 Hz), 1.15–2.0 (m, 6 H), 4.11–4.21 (m, 1 H), 4.3–4.43 (m, 1 H), 4.57 (dq, 0.5 H, J = 7.0 and 1.0 Hz), 4.71 (dq, 0.5 H, J = 7.0 and 2.0 Hz) and 4.87 (m, 1 H); MS, *m/e* 167 (M^+), 152, 126, 110, 96, and 68; ^{13}C NMR δ 16.1, 17.6, 18.5, 19.5, 29.2, 29.6, 29.8, 31.8, 53.8, 54.6, 66.6, 67.3, 71.2, 73.2, 80.2, 80.5, 168.2, and 170.9.

Reaction of 1-Buten-4-ol with 2-Bromopropanal *O*-(Trimethylsilyl)oxime (1a) Followed by Hypochlorite Oxidation. Following a similar procedure as outlined above, cycloadduct **12a** was prepared in 78% yield as a colorless oil: IR (neat) 3000, 2860, 1110, 1085, 1060, 940, 860, and 825 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.52 (d, 3 H, J = 6.5 Hz), 1.77 (dddd, 1 H, J = 17.0, 13.0, 12.0, and 5.0 Hz), 2.15 (ddt, 1 H, J = 13.0, 6.5, and 2.0 Hz), 3.39 (ddddd, 1 H, J = 17.0, 12.0, 10.3, 6.5, and 1.0 Hz), 3.57 (dt, 1 H, J = 12.0 and 2.0 Hz), 3.78 (dd, 1 H, J = 12.0 and 8.0 Hz), 4.06 (ddd, 1 H, J = 12.0, 5.0, and 2.0 Hz), 4.20 (dq, 1 H, J = 6.5 and 1.0 Hz), and 4.62 (dd, 1 H, J = 10.3 and 8.0 Hz); ^{13}C NMR δ 16.9, 32.8, 46.2, 65.9, 70.8, 73.7, and 158.6; MS, *m/e* 141 (M^+), 126, 111, 97, 91, 83, 81, and 68; HRMS calcd for $C_7H_{11}NO_2$ 141.0791, found 141.0789.

Reaction of 1-Buten-4-ol with 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) Followed by Hypochlorite Oxidation. Following a similar procedure as outlined above, the oxybutenyl-substituted oxime **11b** was prepared in 35% yield: IR (neat) 3330, 3080, 2970, 2940, 2880, 1650, 1380, 1365, 1260, 1240, 1160, 1070, 1020, 950, 920, and 800 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.35 (s, 6 H), 2.32 (q, 2 H, J = 6.9 Hz), 3.38 (t, 2 H, J = 6.9 Hz), 4.9–5.2 (m, 2 H), 5.5–6.1 (m, 1 H), 7.37 (s, 1 H), and 8.25 (br s, 1 H). This material was converted into cycloadduct **12b** in the normal manner in 45% yield: IR (neat) 2975, 2940, 2880, 1550, 1386, 1370, 1270, 1160, 1070, 1020, 950, 860, and 810 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.43 (s, 3 H), 1.55 (s, 3 H), 1.77 (m, 1 H), 2.09 (ddt, 1 H, J = 12.0, 6.0, and 2.0 Hz), 3.49 (tdd, 1 H, J = 11.0, 10.1, and 6.0 Hz), 3.72–3.81 (m, 3 H), and 4.62 (dd, 1 H, J = 10.1 and 7.9 Hz). External irradiation of the signal at δ 4.62 narrowed the mutliplet at 3.72 and collapsed the signal at 3.49 to a td (J = 11.0 and 6.0 Hz). External irradiation of the multiplet at δ 3.8 collapsed the signal at 2.09 to a dd (J = 12 and 11 Hz) and collapsed the multiplet at 1.77 to a dd (J = 12 and 11 Hz); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ 22.7, 26.4, 33.1, 43.9, 59.8, 72.5, 73.8, and 161.4; MS, *m/e* 156 (MH^+); HRMS calcd for $C_8H_{14}NO_2$ 156.1024, found 156.1038.

Sodium Hypochlorite Oxidation of α-(3-Butenyloxy)phenylacetaldoxime (11c). To a solution containing 4.57 mL of a 1.0 M tetrabutylammonium fluoride solution and 3.57 g of 1-buten-4-ol in 20 mL of tetrahydrofuran at 25 °C was added a solution containing 1.5 g of α-bromophenylacetaldehyde *O*-(*tert*-butyldimethylsilyl)oxime in 5 mL of tetrahydrofuran over a period of 2 h. The solution was concentrated under reduced pressure, and the residue was taken up in ether and washed with water. The ether layer was dried over sodium sulfate, and the solvent was removed to give 520 mg (56%) of α-(3-butenyloxy)phenylacetaldoxime (**11c**) as a yellow oil, which was used in the next step without further purification; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.38 (m, 2 H), 3.55 (m, 2 H), 4.95 (d, 1 H, J = 7.2 Hz), 5.08 (d, 1 H, J = 10.8 Hz), 5.18 (d, 1 H, J = 15 Hz), 5.8 (m, 1 H), 7.35 (m, 5 H), and 7.52 (d, 1 H, J = 7.2 Hz).

To a solution containing 0.48 g of α-(3-butenyloxy)phenylacetaldoxime (**11c**) in 35 mL of dichloromethane at 0–5 °C was added 9.3 mL of a 5.2% sodium hypochlorite solution dropwise over a period of 15 min. The mixture was allowed to reach room temperature with vigorous stirring. After stirring for an additional 2 h, the two layers were separated, and the aqueous phase was extracted with dichloromethane. The combined dichloromethane extracts were washed with water and dried over sodium sulfate. The solvent was removed under reduced pressure to leave behind a yellow oil, which was purified via silica gel flash chromatography using an ether–ethyl acetate mixture as the eluent to give 0.185 g (40%) of *cis*-[3aα,7α]-7-phenyl-4,5-dihydroisoxazolo[3,4-*c*]-2,3,5,6-tetrahydropyran (**12c**) as a pale yellow solid, mp 77–79 °C; IR ($CHCl_3$) 2980, 2875, 1510, 1460, 1345, and 1110 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (m, 1 H), 2.23 (m, 1 H), 3.52 (m, 1 H), 3.75 (m, 1 H), 3.87 (dd, 1 H, J = 9.9 and 8.05 Hz), 4.25 (m, 1 H), 4.67 (dd, 1 H, J = 9.9 and 8.1 Hz), 5.17 (s, 1 H) and 7.40 (m, 5 H); HRMS calcd for $C_{12}H_{13}NO_2$ 203.0946, found 203.0941. The minor *trans*-[3aα,7β] diastereomer was obtained in 7% yield as a pale yellow solid, mp 71–72 °C; IR ($CHCl_3$) 2980, 2890, 1718, 1510, 1460, 1350, and 1080 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.88 (m, 1 H), 2.09 (m, 1 H), 3.38 (m, 1 H), 3.62 (dt, 1 H, J = 12 and 1.9 Hz), 3.85 (m, 2 H), 4.65 (dd, 1 H, J = 10 and 8 Hz) and 7.40 (m, 5 H); HRMS calcd for $C_{12}H_{13}NO_2$ 203.0946, found 203.0934.

This cis stereochemistry of the major cycloadduct **12c** was assigned on the basis of NOE difference studies. Irradiation of the C-7 proton at δ 5.17 produced a strong positive enhancement of the C-5 β-proton at δ 3.75 and a definite, but weaker, effect on the C-3a proton at δ 3.52. Upon irradiation of the C-3a multiplet at δ 3.52, a strong NOE was observed for the C7 proton at δ 5.17 and also at δ 4.67 (corresponding to the C-3 β-proton, respectively). In addition, a somewhat weaker enhancement of the C-4 β-proton at δ 2.23 was produced. Inspection of molecular models clearly shows that only a cis relationship between the C-7 and C-3a protons can accommodate this data.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with Propargyl Alcohol Followed by Hypochlorite Oxidation. To a stirred solution containing 710 mg of α-bromosilyl oxime **1b** and 1.77 g of propargyl alcohol in 10 mL of dry tetrahydrofuran at 25 °C was added 3 mL of a 1.0 M solution of tetrabutylammonium fluoride. The solution was stirred at 25 °C for 40 min. After removal of the solvent under reduced pressure, the mixture was taken up in 30 mL of methylene chloride and extracted with water. The organic layer was washed with brine and dried over sodium sulfate, and the solvent was removed to give 100 mg (26%) of 2-methyl-2-(propargyloxy)propanal oxime (**13a**) after silica gel chromatography (cyclohexane–ethyl acetate (9:1)); ^1H NMR ($CDCl_3$, 80 MHz) δ 1.39 (s, 6 H), 2.43 (t, 1 H, J = 2.8 Hz), 4.07 (d, 2 H, J = 2.8 Hz), 7.42 (s, 1 H), and 8.31 (br s, OH); IR (neat) 3420, 3290, 2995, 2990, 2110, 1630, 1370, 1260, 1160, 1060, and 630 cm^{-1}.

To a stirred solution containing 50 mg of oxime **13a** in 20 mL of methylene chloride was added 1 mL of a 4.9% sodium hypochlorite solution at 0 °C. The temperature was allowed to warm to 25 °C, and the mixture was stirred vigorously for 1.5 h. The

organic layer was separated, and the aqueous layer was washed with ether. The combined ether layer was washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure to leave behind a light yellow oil. This material was chromatographed on a silica gel plate using a 7% ethyl acetate–cyclohexane mixture as the eluent. The first fraction contained 47 mg of cycloadduct **14a** (95% yield): IR (neat) 2980, 2940, 2800, 1640, 1460, 1380, 1370, 1150, 1070, 1000, 960, and 820 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.59 (s, 6 H), 4.83 (d, 2 H, J = 1.5 Hz), and 7.95 (t, 1 H, J = 1.5 Hz); MS, m/e 140 (MH^+); HRMS calcd for $C_7H_{10}NO_2$ 140.0712, found 140.0709.

A mixture containing 75 mg of cycloadduct **4b** and 200 mg of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in 5 mL of benzene was heated with stirring at 80 °C for 18 h. The mixture was filtered, and the residue was subjected to silica gel chromatography using a 10% ethyl acetate–hexane mixture as the eluent to give 48 mg (61%) of cycloadduct **14a** that was identical in every detail with the material obtained from the hypochlorite oxidation of **13a**.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with 1-Butyn-4-ol Followed by Hypochlorite Oxidation. Following a procedure similar to that outlined above, the butynyloxy-substituted oxime **13b** was prepared in 28% yield: IR (neat) 3300, 2990, 2940, 2880, 2110, 1385, 1370, 1160, 1080, and 950 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.36 (s, 6 H), 1.97 (t, 1 H, J = 2.6 Hz), 2.41 (dt, 2 H, J = 7.0 and 2.6 Hz), 3.48 (t, 2 H, J = 7.0 Hz), 7.41 (s, 1 H), and 8.30 (br s, 1 H). This material was converted into cycloadduct **15** in the normal manner in 95% yield: IR (neat) 2990, 2930, 2860, 1620, 1460, 1360, 1270, 1150, 1100, 1080, and 830 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.61 (s, 6 H), 2.67 (dt, 2 H, J = 7.0 and 1.3 Hz), 3.87 (t, 2 H, J = 7.0 Hz), and 8.2 (t, 1 H, J = 1.3 Hz); MS, m/e 154 (MH^+); HRMS calcd for $C_8H_{12}NO_2$ 154.0868, found 154.0855.

Sodium Hypochlorite Oxidation of α-(Propargyloxy)-phenylacetaldoxime (13c). To a solution containing 10 mL of tetrabutylammonium fluoride and 5.60 g of propargyl alcohol in 40 mL of tetrahydrofuran was added a solution containing 2.86 g of α-bromophenylacetaldde *O*-(trimethylsilyl)oxime (**1c**) in 40 mL of tetrahydrofuran over a period of 90 min. Stirring was continued for 1 h, the solution was concentrated under reduced pressure, and the residual oil was taken up in 75 mL of ether. The ether layer was washed with brine, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give 1.0 g of α-(propargyloxy)phenylacetaldoxime (**13c**) as a yellow oil (53%): IR (neat) 3290, 1710, 1495, 1450, 1070, 910, 735, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.47 (m, 1 H), 4.25 (d, 2 H, J = 9.0 Hz), 5.27 (d, 1 H, J = 18.0 Hz), and 7.45 (m, 6 H); MS, m/e 187 (M^+), 172, 145, 133, 115, and 105 (base); HRMS calcd for $C_{11}H_{11}NO_2$ 189.0790, found 189.0785.

Oxime **13c** (0.28 g) was converted with sodium hypochlorite in the usual manner to 6-phenyl-2,3,4,5-tetrahydrofuranyl[3,4-*c*]isoxazole (**14c**) as a clear oil (0.175 g, 75%): IR (neat) 2890, 1720, 1665, 1635, 1600, 1070, 1015, 760, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.95 (d, 1 H, J = 12.0 Hz), 5.02 (d, 1 H, J = 12.0 Hz), 6.13 (s, 1 H), 7.38 (m, 5 H), and 8.03 (s, 1 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 63.9, 76.3, 122.8, 126.2, 128.4, 128.6, 137.8, 148.1, and 172.3; MS, m/e 187 (M^+), 130, 116, and 105 (base); HRMS calcd for $C_{11}H_9NO_2$ 187.0633, found 187.0630.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with Propargyl Mercaptan Followed by Hypochlorite Oxidation. To a stirred solution containing 711 mg of α-bromosilyl oxime **1b** and 1.88 g of propargyl mercaptan in 10 mL of dry tetrahydrofuran at 25 °C was added 0.3 mL of a 1.0 M solution of tetrabutylammonium fluoride. The solution was stirred at 25 °C for 30 min. After removal of the solvent under reduced pressure, the mixture was taken up in 30 mL of methylene chloride and was extracted with water. The organic layer was washed with brine and dried over sodium sulfate. The solvent was removed under reduced pressure to give oxime **13d**: ^1H NMR ($CDCl_3$, 80 MHz) δ 1.45 (s, 6 H), 2.42 (t, 1 H, J = 2.6 Hz), 3.67 (d, 2 H, J = 2.6 Hz), 7.40 (s, 1 H), and 8.27 (br s, 1 H). This material was taken up in 20 mL of methylene chloride. To this stirred solution was added 0.6 mL of a 4.9% sodium hypochlorite solution at 0 °C. The temperature was allowed to reach 25 °C, and the mixture was stirred vigorously for 1.5 h. The organic layer was separated and the aqueous layer was extracted with methylene chloride. The combined organic layer was washed with water and dried over sodium sulfate, and the solvent was removed under reduced pressure to leave behind a light yellow oil. This material was chromatographed on a silica gel column to give 50 mg of cycloadduct **14b**: IR (neat) 2990, 2950, 2880, 1600, 1380, 1370, 1320, 1040, 1000, 910, 850, and 810 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.78 (s, 6 H), 3.86 (d, 2 H, J = 1.3 Hz), and 7.96 (t, 1 H, J = 1.3 Hz); MS, m/e 156 (MH^+); HRMS calcd for $C_7H_{10}NOS$ 156.0483, found 156.0463.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with 2-Furfuryl Alcohol Followed by Hypochlorite Oxidation. Following a procedure similar to that outlined above, the 2-furfuryl-substituted oxime **16a** was prepared in 25% yield: IR (neat) 3360, 2960, 2940, 2880, 1510, 1470, 1380, 1160, 1050, 950, 930, 810, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.41 (s, 6 H), 4.37 (s, 2 H), 6.21–6.36 (m, 2 H), 7.3–7.45 (m, 2 H), and 8.32 (br s, 1 H). This material was converted into cycloadduct **17a** in the normal fashion in 95% yield: mp 93–94 °C; IR (KBr) 2980, 2935, 2870, 1460, 1160, 1050, 1000, and 910 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 1.54 (s, 3 H), 1.57 (s, 3 H), 3.93 (d, 1 H, J = 10.3 Hz), 4.24 (d, 1 H, J = 10.3 Hz), 5.41 (dd, 1 H, J = 2.9 and 2.6 Hz), 5.70 (d, 1 H, J = 2.9 Hz), and 6.71 (d, 1 H, J = 2.6 Hz); MS, m/e 182 (MH^+); HRMS calcd for $C_9H_{12}NO_3$ 182.0817, found 182.0796.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with Thiophene-2-methanol Followed by Hypochlorite Oxidation. Following a procedure similar to that outlined above, the 2-thiophenemethyl-substituted oxime **16b** was obtained in 25% yield: IR (neat) 3380, 3100, 2980, 2940, 2880, 1580, 1470, 1380, 1370, 1260, 1160, 940, and 800 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.43 (s, 6 H), 4.59 (s, 2 H), 6.92–7.02 (m, 2 H), 7.21–7.45 (m, 2 H), and 8.31 (br s, 1 H). This material was converted into cycloadduct **17b** in the normal manner in 90% yield: IR (neat) 3080, 2990, 2930, 2860, 1580, 1460, 1390, 1370, 1170, 1010, 980, 850, 830, 730, and 690 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.54 (s, 6 H), 4.12 (d, 1 H, J = 9.5 Hz), 4.32 (d, 1 H, J = 9.5 Hz), 5.75–5.88 (m, 2 H), 6.64–6.73 (m, 1 H); MS, m/e 198 (MH^+); HRMS calcd for $C_9H_{12}NO_2S$ 198.0588, found 198.0567.

Reaction of 2-Bromo-2-methylpropanal *O*-(Trimethylsilyl)oxime (1b) with Furanyl-2-methanethiol Followed by Hypochlorite Oxidation. Following a procedure similar to that outlined above, the 2-thiomethyl-substituted oxime **16c** was prepared in 25% yield: IR (neat) 3320, 3120, 2970, 2950, 2870, 1600, 1500, 1390, 1370, 1250, 1150, 1130, 1070, 1010, 940, 810, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.46 (s, 6 H), 3.69 (s, 2 H), 6.14–6.32 (m, 2 H), 6.81 (br s, 1 H) and 7.29–7.43 (m, 2 H). This material was converted into cycloadduct **17c** in the normal manner in 35% yield: IR (neat) 3070, 2980, 2940, 1600, 1390, 1370, 1320, 1150, 1040, 920, 810, and 740 cm^{-1}; ^1H NMR ($CDCl_3$, 80 MHz) δ 1.53 (s, 6 H), 2.88 (d, 1 H, J = 14.0 Hz), 3.12 (d, 1 H, J = 14.0 Hz), 5.43 (dd, 1 H, J = 2.9 and 2.5 Hz), 5.78 (d, 1 H, J = 2.9 Hz) and 6.52 (d, 1 H, J = 2.5 Hz); MS, m/e 198 (MH^+); HRMS calcd for $C_9H_{12}NO_2S$ 198.0588, found 198.0570.

Preparation and Sodium Hypochlorite Oxidation of (*E*)-3-Phenyl-2-propenyl Glyoxylate Oxime (18a). Following a procedure similar to that used for 3-butenyl glyoxylate (vide infra), (*E*)-3-phenyl-2-propenyl (nitrooxy)acetate was converted to (*E*)-3-phenyl-2-propenyl glyoxylate oxime (**18a**) in 86% yield as a light tan solid, mp 44–45 °C; IR (neat) 3360, 1730, 1460, 1315, 1265, and 1205 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 4.90 (d, 2 H, 7.0 Hz), 6.25 (m, 1 H), 6.72 (d, 1 H, J = 15.0 Hz), 7.30 (m, 5 H), 7.73 (s, 1 H), and 10.0 (br s, 1 H). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.82. Found: C, 64.10, H, 5.39; N, 6.75.

To a solution containing 0.25 g of (*E*)-3-phenyl-2-propenyl glyoxylate oxime (**18a**) in 10 mL of dichloromethane at 0 °C was added 6 mL of a 5.25% sodium hypochlorite solution with vigorous stirring over a 45-min period. The mixture was stirred vigorously at 0 °C for an additional hour. The layers were separated, and the aqueous phase was extracted with 20 mL of dichloromethane. The combined organic extracts were washed with 20 mL of water and dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography, eluting with a 25% ethyl acetate–hexane mixture to give 74 mg (30%) of the furoxan dimer **19a** as a white solid, mp 71–72 °C; IR ($CHCl_3$) 1770, 1640, 1475, 1355, 1250, and 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.97 (d, 2 H, J = 6.3 Hz), 5.07 (d, 2 H, J = 6.3 Hz), 6.30 (m, 2 H), 6.65 (d, 1 H, J = 6.3 Hz), 6.73

(d, 1 H, J = 6.3 Hz), and 7.37 (m, 10 H). The minor product contained 0.057 g (24%) of [3α,3aα]-3-phenylfuro[3,4-c]isoxazoline **20** as a light yellow solid: mp 116–117 °C; IR ($CHCl_3$) 1780, 1635, 1300, and 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.28–4.45 (m, 2 H), 4.75 (td, 1 H, J = 12.2 and 8.2 Hz), 5.75 (d, 1 H, J = 12.2 Hz), and 7.4 (s, 5 H); HRMS calcd for $C_{11}H_9NO_3$ 203.0582, found 203.0579.

To a solution containing 1.25 mmol of glyoxylate oxime **18a** and 1.9 mmol of styrene in 8 mL of dichloromethane at 0 °C was added 6 mL of a 5.25% sodium hypochlorite solution dropwise over a period of 45 min with vigorous stirring. The mixture was stirred vigorously for an additional 1 h at 0 °C. The layers were separated, and the aqueous phase was extracted with 20 mL of dichloromethane. The combined organic extracts were washed with 15 mL of water and dried over sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography using an ethyl acetate–hexane mixture as the eluent to give (*E*)-3-phenyl-2-propenyl 5-phenylisoxazoline-3-carboxylate (**21a**) as a colorless oil (51% yield): IR (neat) 3030, 2990, 1735, 1590, 1510, 1270, 1130, and 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.24 (dd, 1 H, J = 17.8 and 8.9 Hz), 3.75 (dd, 1 H, J = 17.8 and 11.6 Hz), 4.97 (d, 2 H, J = 6.6 Hz), 5.78 (dd, 1 H, J = 11.6 and 8.9 Hz), 6.38 (m, 1 H), 6.75 (d, 1 H, J = 15.9 Hz), and 7.40 (m, 10 H); HRMS calcd for $C_{19}H_{17}NO_3$ 307.1208, found 307.1208.

Preparation and Sodium Hypochlorite Oxidation of (*E*)-2-Butenyl Glyoxylate Oxime (18b). Following a procedure similar to that used with 3-butenyl glyoxylate oxime (vide infra), (*E*)-2-butenyl (nitrooxy)acetate was converted to (*E*)-2-butenyl glyoxylate oxime (**18b**) in 91% yield as a colorless oil: IR (neat) 3350, 3080, 2970, 1730, 1630, 1450, 1320, 1270, and 1210 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.75 (d, 3 H, J = 6.5 Hz), 4.65 (d, 2 H, J = 6.5 Hz), 5.60 (m, 1 H), 5.85 (m, 1 H), 7.58 (s, 1 H), and 10.50 (br s, 1 H).

To a solution containing 0.5 g of (*E*)-2-butenyl glyoxylate oxime (**18b**) in 20 mL of dichloromethane at 0 °C was added 16 mL of a 5.25% sodium hypochlorite solution with vigorous stirring over a 45-min period. The mixture was stirred vigorously at 0 °C for an additional hour. The layers were separated, and the aqueous phase was extracted with 20 mL of dichloromethane. The combined organic phases were washed with 20 mL of water and dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography eluting with a 20% ethyl acetate–hexane mixture to give 340 mg (60%) of the furoxan dimer **19b** as a colorless oil: IR (neat) 2980, 1760, 1635, 1460, 1390, 1340, and 1295 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.79 (m, 6 H), 4.77 (d, 2 H, J = 6.5 Hz), 4.83 (d, 2 H, J = 6.5 Hz), 5.62 (m, 2 H), and 5.90 (m, 2 H).

The nitrile oxide was trapped with styrene to give (*E*)-2-butenyl 5-phenylisoxazoline-3-carboxylate (**21b**) as a clear oil (50% yield): IR (neat) 2960, 1730, 1595, 1460, 1255, 1125, and 930 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.75 (d, 3 H, J = 6.5 Hz), 3.20 (dd, 1 H, J = 17.7 and 8.8 Hz), 3.62 (dd, 1 H, J = 17.7 and 11.6 Hz), 4.72 (d, 2 H, J = 6.5 Hz), 5.65 (m, 1 H), 5.90 (m, 1 H), and 7.33 (m, 5 H); HRMS calcd for $C_{14}H_{15}NO_3$ 245.1052, found 245.1050.

Preparation and Sodium Hypochlorite Oxidation of 3-Butenyl Glyoxylate Oxime (18c). A solution containing 10 g of 3-buten-1-ol and 21 mL of pyridine in 150 mL of dichloromethane was cooled to 0 °C. A solution containing 36.47 g of bromoacetyl bromide in 100 mL of dichloromethane was added dropwise with stirring over a period of 15 min.[39] The mixture was stirred for 30 min, poured into 30 mL of ice water, and extracted with 150 mL of dichloromethane. The combined organic extracts were washed with 200 mL of a 5% hydrochloric acid solution and 200 mL of water and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the residual oil was distilled to give 21.6 g (81%) of 3-butenyl bromoacetate: bp 55 °C (0.1 mmHg); IR (neat) 2980, 1740, 1430, 1290, 1170, and 1118 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 2.40 (q, 2 H, J = 7.0 Hz), 3.85 (s, 2 H), 4.29 (t, 2 H, J = 7.0 Hz), 5.15 (m, 2 H), and 5.80 (m, 2 H).

A solution containing 20 g of the above bromo ester and 35.2 g of silver nitrite in 180 mL of anhydrous acetonitrile was stirred at 25 °C in the dark for 24 h. The solvent was removed under reduced pressure, and the residue was taken up in 150 mL of ether and filtered. The filtrate was washed with 300 mL of ether, and the combined organic extracts were washed with water and dried over magnesium sulfate. Removal of the solvent under reduced pressure gave 11 g (61%) of 3-butenyl (nitrooxy)acetate as a colorless oil: IR (neat) 2980, 1765, 1750, 1665, 1645, 1420, 1400, 1375, 1230, 1065, and 1000 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 2.40 (q, 2 H, J = 7.0 Hz), 4.30 (t, 2 H, 7 Hz), 4.82 (s, 2 H), 5.15 (m, 2 H), and 5.70 (m, 1 H).[40]

To a solution containing 5 g of the above nitrate ester and 3 g of hydroxylamine hydrochloride in 53 mL of dimethyl sulfoxide was added 7 g of anhydrous sodium acetate. The mixture was stirred at 25 °C for 30 min, poured into 150 mL of ice–brine, and extracted with ether. The combined ether extracts were washed with water and dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by silica gel flash chromatography eluting with a 1:1 hexane–ethyl acetate mixture to give 3.5 g (85%) of 3-butenyl glyoxylate oxime (**18c**) as a light blue oil: IR (neat) 3350, 2980, 1730, 1630, 1610, 1450, and 1315 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 2.45 (q, 2 H, J = 6.5 Hz), 4.40 (t, 2 H, J = 6.5 Hz), 5.15 (m, 2 H), 5.78 (m, 1 H), 7.55 (s, 1 H), and 9.50 (br s, 1 H).

To a solution containing 0.5 g of the above compound in 20 mL of dichloromethane at 0 °C was added 16 mL of a 5.25% sodium hypochlorite solution with vigorous stirring over a 45-min period. The mixture was stirred vigorously for an additional hour. The layers were separated, and the aqueous phase was extracted with 20 mL of dichloromethane. The combined organic phases were washed with 20 mL of water and dried over magnesium sulfate, and the solvent was removed under reduced pressure. The residue was purified by silica gel chromatography, giving the furoxan dimer **19c** in 57% yield as a light yellow oil: IR (neat) 2995, 1755, 1630, 1470, 1355, 1250, 1200, and 1075 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.50 (m, 4 H), 4.45 (m, 4 H), 5.20 (m, 4 H), and 5.82 (m, 2 H). The nitrile oxide was trapped by using styrene to give 3-butenyl 5-phenylisoxazoline-3-carboxylate (**21c**) as a clear oil (60% yield): IR (neat) 2990, 1730, 1600, 1370, 1350, 1260, 1135, and 1030 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.45 (q, 2 H, J = 6.8 Hz), 3.15 (dd, 1 H, J = 17.8 and 8.9 Hz), 3.60 (dd, 1 H, J = 17.8 and 11.6 Hz), 4.30 (t, 2 H, J = 6.8 Hz), 5.18 (m, 2 H), 5.75 (m, 1 H), and 7.32 (m, 5 H); HRMS calcd for $C_{14}H_{15}NO_3$ 245.1052, found 245.1050.

Thermal Cycloaddition of α-(Allyloxy)phenylacetaldoxime (2c). A solution containing 2.5 g of α-(allyloxyphenyl)acetaldoxime (**2c**) in 20 mL of acetonitrile was heated at 80 °C in the presence of silica gel for 24 h. Chromatography of the crude residue on silica gel using a 50% ethyl acetate–hexane mixture as the eluent afforded 620 mg (25%) of 6-phenyltetrahydrofuro[3,4-c]isoxazolidine (**22a**) as a yellow oil: IR (neat) 2880, 1495, 1450, 1145, 1045, 755, and 700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.32 (m, 1 H), 3.57 (m, 2 H), 3.98 (m, 2 H), 4.42 (t, 1 H, J = 8.5 Hz), 4.52 (d, 1 H, 6.2 Hz), 5.26 (br s, 1 H), and 7.32 (m, 5 H); external irrdiation of the signal at δ 4.42 collapsed the doublet at δ 4.52 to a singlet and narrowed the multiplet at δ 3.32; ^{13}C NMR ($CDCl_3$, 20 MHz) δ 49.7, 72.9, 74.1, 75.9, 85.2, 125.7, 127.6, 128.3, and 140.3; MS, m/e 191, 161, 132, and 107 (base); HRMS calcd for $C_{11}H_{13}NO_2$ 191.0946, found 191.0944.

Reaction of α-(Allyloxy)phenylacetaldoxime (2c) with Phenyl Vinyl Sulfone. A mixture containing 130 mg of α-(allyloxy)phenylacetaldoxime (**2c**) and 115 mg of phenyl vinyl sulfone in 30 mL of toluene was heated at reflux for 16 h. The solution was concentrated under reduced pressure, and the residue was purified by using preparative silica gel chromatography. Elution using a 35% ethyl acetate–hexane mixture gave 35 mg (30%) of recovered phenyl vinyl sulfone and 20 mg (15%) of 6-phenyltetrahydrofuro[3,4-c]isoxazolidine (**22a**). Elution with 50% ethyl acetate–hexane afforded 84 mg (34%) of *N*-[(2-phenylsulfonyl)ethyl]-6-phenyltetrahydrofuro[3,4-c]isoxazolidine (**22b**) as a pale yellow oil: IR (neat) 3070, 1490, 1350, 1190, 1140, 960, 780, and 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.95 (m, 1 H), 3.15 (m, 1 H), 3.35 (t, 1 H, J = 7.8 Hz), 3.43 (t, 2 H, J = 7.5 Hz), 3.53 (dd, 1 H, J = 8.6 and 6.1 Hz), 3.65 (m, 2 H), 3.93 (dd, 1 H, J = 9.0 and 6.7 Hz), 4.34 (t, 1 H, J = 8.5 Hz), 4.49 (d, 1 H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 48.7, 49.1, 54.4, 69.4, 73.3, 80.1, 84.5, 125.6, 127.8, 128.0, 128.6, 129.5, 133.7, 139.4,

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and 140.1; MS, m/e 359 (M^+), 161, 132, 105, and 77 (base); HRMS calcd for $C_{19}H_{21}NO_4S$ 359.1191, found 359.1203.

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Supplementary Material Available: NMR spectra for HRMS compounds (37 pages). Ordering information is given on any current masthead page.

Rearrangement and Cleavage of the Grignard Reagent from 5-(Chloromethyl)norbornene[1]

E. Alexander Hill,* King Hsieh, Kevin Condroski, Heidi Sonnentag, Donald Skalitzky, and Donald Gagas

Department of Chemistry, University of Wisconsin—Milwaukee, Milwaukee, Wisconsin 53201

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The Grignard reagents **1**-Mg and **2**-Mg from *endo*- and *exo*-5-(chloromethyl)norbornene rearrange with ring cleavage on heating to yield an allylcyclopentenyl organomagnesium compound (**3**-Mg). This, in turn, undergoes competitively a variety of reactions, including an alternative cyclization to a bicyclo[3.3.0]octene organomagnesium (**4**-Mg) and *formal* loss of hydrogen or propene to produce allylcyclopentadienyl- (**5**-Mg) and cyclopentadienylmagnesium compounds. Endo and exo isomers **1**-Mg and **2**-Mg rearrange at comparable rates and are partially interconverted, probably via their cleavage and recyclization. Mechanistic possibilities are discussed.

Several years ago, Freeman and co-workers[3] published a study of the reactions of *endo*- and *exo*-5-(chloromethyl)norbornene with sodium. The monomeric hydrocarbon products isolated were explained by a series of ring-cleavage and cyclization rearrangements of organosodium intermediates and their subsequent protonation.

We were interested in seeing how the organomagnesium compounds might compare with their sodium analogues in these rearrangements. Several questions, raised by features of the earlier work, were of particular relevance in this respect. First, cleavage of the five-membered ring in cyclopentylmethyl organometallic compounds is thermodynamically unfavorable,[4] and norbornylmethyl chlorides fail to cleave under similar conditions.[3] Is the double bond's effect sufficient to allow the ring cleavage of the *organomagnesium* compound to occur? The conversion of *exo*- to *endo*-5-(chloromethyl)norbornene was observed under the reaction conditions, presumably via reversal of the cleavage reaction. Would the Grignard reagents undergo the same exo-endo isomerization? Finally, the subsequent cyclization of the initial ring-opened organometallic product is of interest, since it occurs opposite to the customary orientation in organometallic cylization rearrangements.[2,4,5] Is the observed behavior unique to the highly ionic character of the organosodium derivative, or does it result from structural features independent of the metal, such as ring strain or allylic structure?

We report in this paper that norbornenylmethyl Grignard reagents do undergo analogous rearrangements when heated and that an additional reaction path, which does not appear to occur for the sodium derivatives, is important for the organomagnesium.

Results

Grignard reagents were prepared in tetrahydrofuran (THF) from a mixture of endo and exo isomers containing about 87% of *endo*-5-(chloromethyl)norbornene (**1**-Cl) and from a pure sample of the exo isomer **2**-Cl and heated to temperatures of 80–120 °C in sealed tubes. The progress of the reaction was followed by observation of the ^{13}C NMR spectrum of the Grignard solutions, and samples were also hydrolyzed after partial reaction to allow isolation and characterization of the hydrocarbon products. Less extensive studies were done in ethyl ether solution. Scheme I summarizes the observed transformations, and Table I lists ^{13}C NMR data for the Grignard reagents and related structures.

The ^{13}C NMR spectra of Grignard solutions before heating indicated nearly quantitative formation of the unrearranged organomagnesium compounds. After heating for several hours at 115 °C, both norbornenylmethyl Grignard reagent isomers had partially rearranged with ring cleavage to the allylcyclopentenyl organomagnesium compound **3**-Mg. This should exist as a mixture of rapidly equilibrating allylic isomers. Averaged ^{13}C NMR signals were readily recognized for all carbons except for the two that are rapidly interconverted between allylic and olefinic environments by the exchange. This signal may have been obscured by solvent or may have been broadened by the exchange to the point where it could not be detected. No significant change in the spectrum was observed over the temperature range 12–80 °C, except for a sharpening of several of the Grignard reagent resonances at higher temperature. Hydrolysis produced a nearly equal mixture of 3- and 4-allylcyclopentenes **3a**-H and **3b**-H, in addition to

(1) A summary of some of this material in preliminary form has been included in reviews[2] and in the M.S. thesis of K.H., University of Wisconsin—Milwaukee, 1968.

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