H), 4.00 (septet, J = 8 Hz, 1 H), and 6.60 (s, 2 H).

6-Acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one (2), mp 87.5–89 °C (lit.[12] mp 84 °C), was prepared in 51% yield by reaction of 2,4,6-trimethylphenol with lead tetraacetate in chloroform, according to the procedure employed for the preparation of 6-acetoxy-2,6-dimethylcyclohexa-2,4-dien-1-one.[13]

Reaction of 6-Acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one with Isopropylmagnesium Bromide. The general procedure was as follows.

Into each of six 50-mL three-necked flasks equipped with glass-coated magnetic stirring bars, reflux condensers leading to mercury traps, and nitrogen inlet tubes were pipetted aliquots of freshly prepared and standardized solutions of isopropylmagnesium bromide. These solutions were diluted with anhydrous ether to give a range of concentrations varying from ca. 0.08 to 1.8 M. To each solution was added a sample of the quinol acetate dissolved in 1 mL of anhydrous ether. The samples of quinol acetate did not exceed 0.11 times the number of moles of Grignard reagent employed. The reaction mixtures were stirred overnight at room temperature and were then quenched with either saturated ammonium chloride solution or 0.1 M hydrochloric acid solution. Each mixture was extracted 4 times with 10 mL of methylene chloride, washed with 10 mL of water, and dried over magnesium sulfate. The solvent was evaporated, the residual oil was weighed, and a known weight of hexamethylbenzene was added to act as an internal GLPC standard. GLPC analysis at 150 °C showed the presence of three major components with retention times of 1.0, 3.2, and 7.6 min. Comparison of the areas of these peaks (corrected for thermal conductivity differences, as determined from isolated samples) with that of hexamethylbenzene showed that these peaks comprised ca. 99 mol % of the product. Very minor peaks with retention times of 4–5 min were also observed.

The three components were isolated by preparative GLPC on column B. The components with retention times 1.0 and 3.2 min were identified as isopropyl 2,4,6-trimethylphenyl ether and 2,4,6-trimethylphenol, respectively by comparison with authentic samples. The component with a retention time of 7.6 min was identified as 3-isopropyl-2,4,6-trimethylphenol. Its NMR spectrum showed peaks at δ 1.30 (d, J = 8 Hz, 6 H), 2.11 (s, 3 H), 2.25 (s, 6 H), 3.39 (m, J = 8 Hz, 1 H), 4.59 (br s, 1 H), 6.71 (br s, 1 H). Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.41; H, 11.40.

Reactions of **2** with solutions containing various percentages of dioxane or THF were carried out as described above, except that measured volumes of the other solvents were added to the ethereal Grignard solutions before reaction with **2**. Reactions of **2** with diisopropylmagnesium were carried out in the same manner as reactions with isopropylmagnesium bromide.

Reactions of **2** with isopropylmagnesium chloride were carried out as described for reaction with isopropylmagnesium bromide. A sample of products with retention times on column A of ca. 4–5 min was isolated by preparative GLPC on column B. Its IR spectrum showed strong absorptions at 1710 and 1680 cm^{-1}. It had a very complex NMR spectrum.

Reactions of **2** with isopropyllithium in pentane were carried out and analyzed in a manner similar to that described for reaction with isopropylmagnesium bromide.

Reaction of 2 with Isopropylmagnesium Bromide Formed from Grignard Grade Magnesium. The reaction was carried out as described above by employing magnesium turnings ("for Grignard Reactions") obtained from the Fisher Scientific Co. The reaction was worked up and analyzed as usual. In addition to peaks for **3**, **4**, and **5**, a peak with a retention time of 4.9 min was observed. This component was isolated by preparative GLPC as a pale yellow oil and identified as **2,6-dimethyl-4-isobutylphenol.** Its NMR spectrum showed peaks at δ 0.87 (d, J = 7.8 Hz, 6 H), 2.18 (m, 9 H), 4.47 (br s, 1 H), and 6.85 (s, 2 H). Addition of $Eu(fod)_3$ (4.85×10^2 mmol to 1.58×10^1 mmol of the phenol) converted the multiplet at δ 2.18 into peaks at δ 2.96 (s, 6 H), 2.50 (d, J = 7.8 Hz, 2 H), and 2.3 (m, 1 H). Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 81.04; H, 10.41.

Reaction of 2 with Diethylmagnesium. Reactions of **2** with diethylmagnesium were carried out in a manner similar to that described for reaction with isopropylmagnesium bromide. GLPC analysis (column A, 140 °C) of the reaction products after workup showed components with retention times of 1.1, 3.1, 4.1–5.2 (at least three overlapping peaks) and 6.8 min. The peaks with retention times of 1.1, 3.1, and 6.8 min were isolated by preparative GLPC and identified as ethyl 2,4,6-trimethylphenyl ether, mesitol, and 3-ethyl-2,4,6-trimethylphenol by comparison of their spectra with those of authentic samples.[1a] The products with retention times of 4.1–5.2 min could not be separated but were isolated as a mixture. Its IR spectrum showed strong peaks at 1667 and 1650 cm^{-1}. Its UV spectrum (in methanol) had a λ_{max} of 330 μm.

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Registry No. **2**, 4906-82-5; **3**, 13605-05-5; **4**, 527-60-6; **5**, 54337-56-3; **6**, 91083-11-3; **8**, 61248-71-3; $(Et)_2Mg$, 557-18-6; $(i\text{-}Pr)_2Mg$, 3536-97-8; *i*-PrMgCl, 1068-55-9; *i*-PrLi, 1888-75-1; *i*-PrMgBr, 920-39-8; ethyl 2,4,6-trimethylphenyl ether, 61248-63-3; isoproyl 2,4,6-trimethylphenyl ether, 13605-05-5; 2,6-dimethyl-4-isobutylphenol, 35993-75-0.

(12) Wessely, F.; Sinwel, F. *Monatsh. Chem.* **1950**, *81*, 1055.
(13) Budzikiewicz, H.; Schmidt, G.; Stockhammer, P.; Wessely, F. *Monatsh. Chem.* **1959**, *90*, 609.

Generation and [3 + 2] Cycloaddition Reactions of Oxazoline *N*-Oxides

Stephen P. Ashburn and Robert M. Coates*

Department of Chemistry, University of Illinois, Urbana, Illinois 61801

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2,4,4-Trimethyloxazoline *N*-oxide (**6a**) and 2-ethyl-4,4-dimethyloxazoline *N*-oxide (**6b**) have been prepared by condensation of 2-(hydroxyamino)-2-methyl-1-propanol hydrochloride (**7**) with triethyl orthoacetate and orthopropionate. [3 + 2] Cycloaddition reactions of nitrones **6a** and **6b** and the related 2,5,5-trimethylpyrroline *N*-oxide (**12**) with phenyl isocyanate, dimethyl acetylenedicarboxylate, methyl phenylpropiolate, phenylpropiolonitrile, methyl acrylate, and acrylonitrile were carried out. Competition experiments demonstrated that **6a** is at least 6800 times more reactive than **12** towards phenyl isocyanate. The oxazoline *N*-oxide (**6a**) proved to be 160 times more reactive than the pyrroline *N*-oxide in similar competitive cycloadditions with dimethyl acetylenedicarboxylate. Reaction of **6a** with acrylonitrile afforded 3-substituted cycloadducts as major products (3:1 ratio of regioisomers) in contrast to **12** which gave only a 2-substituted cycloadduct under kinetically controlled conditions at room temperature.

Nitrones[1] readily undergo 1,3-dipolar cycloaddition reactions with multiply bonded dipolarophiles to yield synthetically useful heterocyclic derivatives.[2] For example, the inter- and intramolecular reactions of nitrone functions

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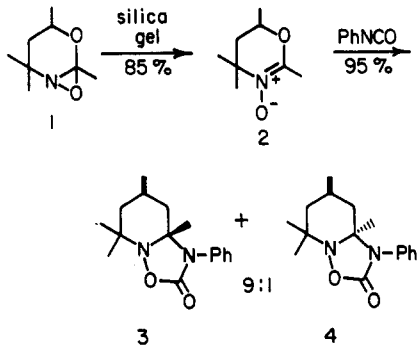
with alkenes lead stereoselectively to isoxazolidines,[3] which can be reduced to β-amino alcohols.[4] This approach has been employed to advantage in total syntheses of members of several alkaloid classes.[5]

Recently a new class of cyclic nitrones has been reported,[6] bearing an oxygen atom α to the carbon of the nitrone (e.g., **2** and **6a**). We have devised a new route to these oxazoline *N*-oxides **6a,b** and have studied their 1,3-dipolar cycloaddition reactions in order to determine the effect of the oxygen substituent upon the reactivity of the nitrone function.[7]

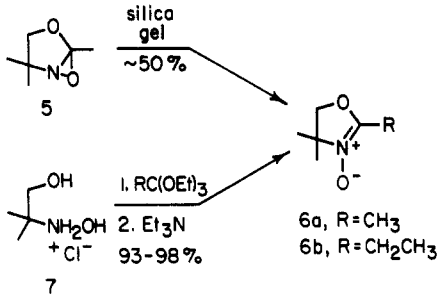
Results and Discussion

Isomerization of oxaziridine **1** on silica gel according to the procedure of Keana and Lee[6] yielded nitrone **2** as a flaky, crystalline powder in 85% yield. This material

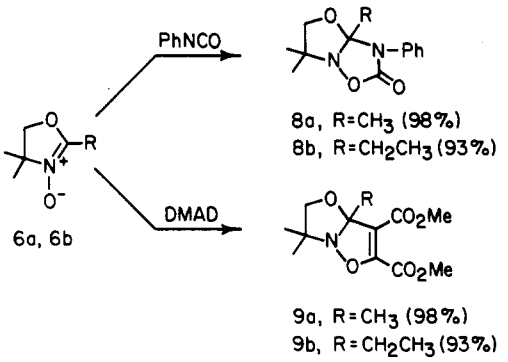


liquified within a few min of exposure to air, and could not be kept in a powder form for more than 12 h under vacuum or under an argon atmosphere. Nitrone **2** reacted exothermically with phenyl isocyanate in chloroform solution to give a 9:1 mixture of adducts **3** and **4**. The structural assignments are based on the assumption that cycloaddition of phenyl isocyanate occurs preferentially on the less sterically hindered face of the nitrone.

Oxazoline *N*-oxide **6a** was selected as a suitable substrate for further studies of α-alkoxy nitrone cycloaddition reactions. Isomerization of oxaziridine **5** on silica gel[6] led



to nitrone **6a** as a crude oil of ~50% purity. However, a new method was devised which led cleanly and efficiently to the desired nitrone. Hydroxylamino alcohol **7**[8,9] was prepared by zinc reduction of the nitro compound by the method of Janzen and Zawaski[8] and isolated as the hydrochloride salt in 93% yield. Condensation[10] of **7** with triethyl orthoacetate in dichloromethane (25 °C, 1 h) followed by neutralization of the nitrone hydrochloride salt with triethylamine yielded solutions of nitrone **6a** almost quantitatively as shown by subsequent cycloaddition reactions. Solutions of nitrone **6b** were generated in the same



manner from triethyl orthopropionate in high yield. Since attempts to isolate **6a** by precipitation of the triethylamine hydrochloride and concentration led to the formation of impurities,[11] the oxazoline *N*-oxide was generated in solution and immediately allowed to react with dipolarophile. Thus, addition of phenyl isocyanate to a solution of **6a** gave adduct **8a** as colorless prisms in 98% yield (based on hydroxylamine salt **7**). In a similar fashion, treatment of nitrone **6a** with dimethyl acetylenedicarboxylate (DMAD) afforded adduct **9a** (98%) as an oil. The high yields of these exothermic cycloaddition reactions demonstrate that nitrone **6a** is formed nearly quantitatively from hydroxylamine salt **7**. When the two reactions were carried out by means of isomerization of oxaziridine **5**, the yields of **8a** and **9a** were 45% and 56% (based on oxaziridine **5**), respectively. Solutions of nitrone **6b** also reacted exothermically with phenyl isocyanate and dimethyl acetylenedicarboxylate to yield cycloadducts **8b** (93%) and **9b** (93%), respectively.

Oxazoline *N*-oxides **6a,b** and the analogous 2,5,5-trimethylpyrroline *N*-oxide **12**[12] were allowed to react with unsymmetrical dipolarophiles to determine the regioselectivity of the cycloaddition reactions. Interaction of **6a** with methyl phenylpropiolate gave a single regioisomer (**10a**) as colorless prisms. The structural assignment is based on the low C=O stretching frequency at 1705 Cm^{-1}, which is consistent with the vinylogous carbonate structure **10a**.

Nitrones **6b** and **12** reacted analogously, yielding cycloadducts **10b** and **13**, with $\delta_{max}^{C=O}$ at 1710 and 1690 cm^{-1}, respectively. Oxazoline *N*-oxides **6a,b** and pyrroline *N*-oxide **12** also underwent regiospecific cycloaddition with phenylpropiolonitrile to give **11a,b** and **14**, the structures of which are based on analogy with the preceding cases. These assignments are consistent with the recent report that 5,5-dimethyloxazoline *N*-oxide adds regiospecifically

(1) For reviews of the chemistry of nitrones, see: (a) Hamer, J.; Macaluso, A. *Chem. Rev.* **1964**, *64*, 473–495. (b) Delpierre, G. R.; Lamchen, M. *Q. Rev., Chem. Soc.* **1965**, *19*, 329–348.

(2) (a) Black, D. St. C.; Crozier, R. F.; Davis, V. C. *Synthesis* **1975**, *7*, 205–221. (b) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123–136. (c) Huisgen, R. *Ibid.* **1963**, *2*, 565–598. (d) Oppolzer, W. *Ibid.* **1977**, *16*, 10–23. (e) Freeman, J. P. *Chem. Rev.* **1983**, *83*, 241–261.

(3) LeBel, N. A.; Hwang, D. *Org. Synth.* (*N.Y.*) **1978**, *58*, 106–112.

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(5) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396–403.

(6) Lee, T. D.; Keana, J. F. W. *J. Org. Chem.* **1976**, *41*, 3237–3241.

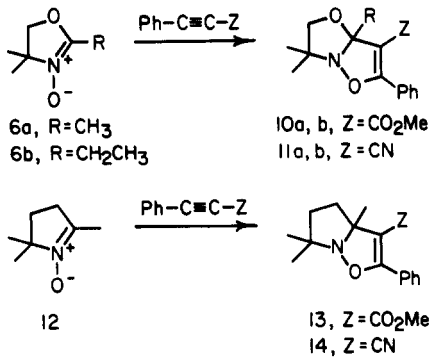
(7) The cyclic dimer of 4,4-dimethyloxazoline *N*-oxide has recently been reported by Hendrickson and Pearson. Cycloaddition reactions of the monomeric nitrone generated in situ with maleic anhydride and methyl propiolate were also described. Hendrickson, J. B.; Pearson, D. A. *Tetrahedron Lett.* **1983**, *24*, 4657–4660.

(8) Janzen, E. G.; Zawalski, R. C. *J. Org. Chem.* **1978**, *43*, 1900–1903.

(9) Kliegel, W.; Becker, H. *Chem. Ber.* **1977**, *110*, 2067–2089.

(10) Exner, O. *Collect. Czech. Chem. Comm.* **1951**, *16*, 258–267.

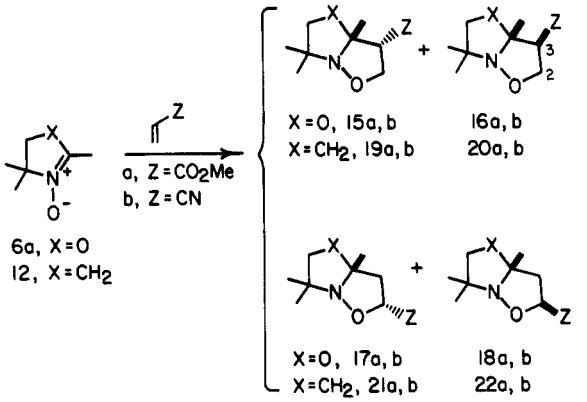
(11) Evaporation of solvent, addition of ether, filtration of the precipitated triethylamine hydrochloride, and concentration afforded impure **6a** as a viscous oil. NMR spectra in deuterium oxide, methanol-d_4, and chloroform-*d*, showed impurity peaks in the region δ 1–1.4. The purity of the nitrone was estimated to be about 50%. Since the NMR spectrum in deuterium oxide showed no time dependence, the nitrone is evidently stable to hydrolysis.



to methyl propiolate to yield the 3-substituted adduct.[7]

A series of complex mixtures resulted from reactions of **6a** and **12** with methyl acrylate and acrylonitrile. The mixtures of diastereometric adducts were partially separated by flash chromatography and the individual fractions were analyzed by proton NMR spectroscopy at 360 MHz.

Regioisomers are easily identified by the number of C-2 protons in the δ 4.0–5.0 range and by the number of C-3 protons in the δ 2.0–3.5 range. Unfortunately the NMR spectral data do not allow a definitive assignment of the exo/endo stereochemistry at C-2 and C-3. Nitrone **6a**



showed little regioselectivity with methyl acrylate but gave mainly 3-substituted adducts with acrylonitrile (see Table I). Nitrone **12** afforded mainly 2-substituted adducts with methyl acrylate and a single 2-substituted cycloadduct (**21b** or **22b**) with acrylonitrile at 25 °C. At elevated temperature (reflux, ca. 77 °C), however, reaction of **12** with acrylonitrile gave mainly the 3-substituted adduct (**19b** or **20b**) along with some of the same isomer obtained at 25 °C.

When solutions of purified cycloadducts **19b** or **20b**, and **21b**, or **22b** in acrylonitrile were heated at reflux (ca. 77 °C) for 35 h, the same 5:1 mixture of the two isomers (**19b** or **20b**:**21b** or **22b**) was formed in both cases. This demonstrates that the cycloaddition is reversible at the elevated temperature and that the 3-substituted isomer (**19b** or **20b**) is more stable. The thermal reversibility of cycloaddition reactions with pyrroline *N*-oxides has been noted in the literature[5,12] and Lamchen has reported that 5,5-dimethylpyrroline *N*-oxide and ethyl acrylate similarly afford the 2-substituted adduct at 25 °C and the 3-substituted isomer at 100 °C.

The reactions of nitrones **6a** and **12** with methyl acrylate and of **6a** with acrylonitrile each produced mixtures of four diastereomers. Although stereochemical assignments for three pairs of 2-substituted diastereomers (**17a** or **18a**, **17b** or **18b**, **21a** or **22a**) are not given owing to the similarity of their NMR spectra, the exo/endo orientation of the Z

(12) Delpierre, G. R.; Lamchen, M. *J. Chem. Soc.* **1963**, 4693–4701.

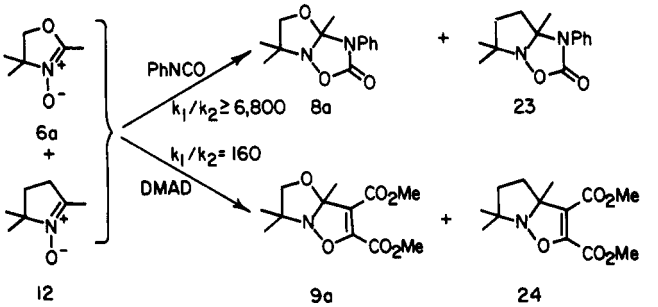
Table I. Regioselectivity of [3 + 2] Cycloaddition Reactions of 2,4,4-Trimethyloxazoline (6a) and 2,5,5-Trimethylpyrroline *N*-Oxides (12) with Methyl Acrylate and Acrylonitrile

nitrone	dipolarophile	temp, °C		regioisomer ratio	yield, %
6a	methyl acrylate	25	(**15a** + **16a**): (**17a** + **18a**)[a]	53:47	84
12	methyl acrylate	80[b]	(**19a** + **20a**): (**21a** + **22a**)[c]	37:63	72
6a	acrylonitrile	25	(**15b** + **16b**): (**17b** + **18b**)[d]	75:25	81
12	acrylonitrile	25	**21b** or **22b**	0:100	49
12	acrylonitrile	77[e]	(**19b** or **20b**): (**21b** or **22b**)	69:31	40

[a] The endo/exo isomer ratios for **15a**/**16a** and **17a**/**18a** (or **18a**/**17a**) were 38:15 and 12:35, respectively. [b] Refluxing methyl acrylate. [c] The endo/exo isomer ratios for **19a**/**20a** and **21a**/**22a** (or **22a**/**21a**) were 15:22 and 33:30, respectively. [d] The endo/exo isomer ratios for **15b**/**16b** and **17b**/**18b** (or **18b**/**17b**) were 56:19 and 7:18, respectively. [e] Refluxing acrylonitrile.

group of 3-substituted diastereomers is tentatively assigned by the relative chemical shifts of the methyl group at C-4. A β-carbomethoxy group (Z = CO_2Me) at C-3 is assumed to have a shielding effect, for conformational reasons, on the C-4 methyl, and a β-cyano group (Z = CN) at C-3 is assumed to have a deshielding effect on the methyl group at C-4.

A competitive cycloaddition reaction between nitrones **6a** and **12** and phenyl isocyanate was carried out. The



ratio of products was measured by NMR, and the rate ratio k_1/k_2 was calculated by the method of Ingold and Shaw[13] to be greater than 6800. Peaks from adduct **23** were not visible in the NMR spectrum, and a lower limit to the rate ratio was calculated from the noise level of the NMR spectrum. When dimethyl acetylenedicarboxylate (DMAD) was used in the competition experiment, both adducts were clearly visible in the NMR spectrum and the rate ratio was calculated to be approximately 160.

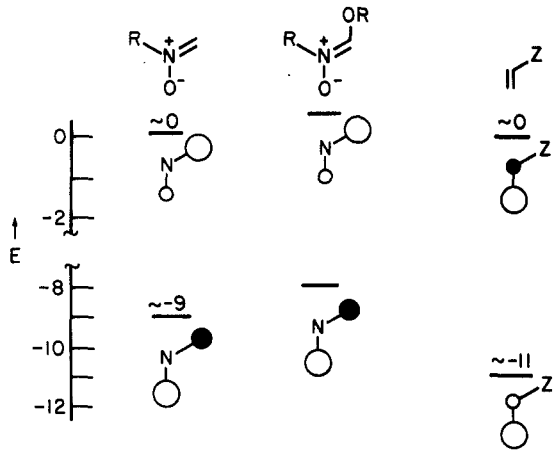
The enhanced reactivity of **6a** can be rationalized in terms of frontier molecular orbital theory.[14] The substitution of oxygen α to the nitrone releases electrons into the π-system, thereby raising the HOMO and LUMO of **6a**.[15] This has the effect of lowering the HOMO–LUMO gap between **6a** and the dipolarophiles and increases the interaction energy between them in the transition state for cycloaddition.

The regioselectivity of nitrone cycloadditions may also be considered in terms of frontier orbital theory.[14] For the

(13) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2918–2926.

(14) (a) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361–369. (b) Houk, K. N.; Sims, J.; Duke, R. E.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7287–7301. (c) Houk, K. N.; Sims, J.; Watts, C. R.; Luskus, L. J. *Ibid.* **1973**, *95*, 7301–7315.

(15) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976; p 128.



reaction of an *N*-alkyl, methylene nitrone with an electron deficient alkene, the dipole HOMO/dipolarophile LUMO interaction is larger. Since the coefficients on carbon and oxygen of the dipole HOMO are nearly the same, the orientation of the reaction is determined by the dipole LUMO/dipolarophile HOMO interaction which favors the transition state leading to the 2-substituted isomer (e.g., **21**). On the other hand, substitution of an oxygen atom α to the carbon of the nitrone should enhance the HOMO coefficient on *N*-oxide oxygen.[15] Thus, the dipole HOMO/dipolarophile LUMO interaction should also influence the regioselectively of the reaction to favor the 3-substituted product (e.g., **15**). Although this effect is apparently slight in the reaction of **6a** with methyl acrylate, it is more pronounced in the reaction with acrylonitrile, which affords the 3-substituted cycloadduct as the major product. The pyrroline *N*-oxide (**12**) yields mainly the 2-substituted cycloadduct, with acrylonitrile, as predicted by the theory.

Experimental Section

Melting points were determined on a Thomas-Hoover melting point apparatus or a Reichert micro-hot stage melting point apparatus and are uncorrected. IR spectra were determined on a Perkin-Elmer Model 137 spectrophotometer. ^{1}H NMR spectra were obtained on a Varian EM-390 (90 MHz) or a Nicolet NT-360 (360 MHz) spectrometer. The frequency was 360 MHz unless specified otherwise. Mass spectra were obtained on a Varian CH-5 mass spectrometer. Microanalyses were performed by J. Nemeth and his associates in the University of Illinois Microanalytical Laboratory.

All reagents and solvents were reagent grade and were used without further purification unless otherwise specified. Technical grade hexane and ethyl acetate used for flash chromatography[16] were distilled prior to use. Woelm 32–63 μm silica gel was used for isomerizing the oxaziridines and was dried in vacuum (<0.005 mm) before use.

Silica gel chromatographic purifications were performed by flash chromatography[16] with Woelm 32–63 μm silica packed in glass columns. The weight of the silica was approximately 100 times the weight of the material. Thin-layer chromatography was used to determine the appropriate solvent system for elution, which was 10–50% ethyl acetate in hexane. The fraction size was 30 mL in most cases, and all fractions are stated in order of elution. All flash chromatographic purifications were carried out in this manner.

5,6-Dihydro-2,4,4,6-tetramethyl-1,3-oxazine 2,3-oxide (1) was prepared according to a modification of the procedure of Keana.[6] A solution of 9.77 g (0.62 mol) of 5,6-dihydro-2,4,4,6-tetramethyl-1,3-oxazine[17] in 200 mL of ether was cooled to −23 °C and a solution of 13.43 g of 80–90% *m*-chloroperoxybenzoic acid (0.62 mol based on 80% purity) in 50 mL of ether was added dropwise over 25 min. The solution was allowed to warm to −10 °C, washed with three 50-mL portions of a 10% aqueous sodium carbonate solution, and dried over potassium carbonate. Evaporation of solvent and distillation of the residual oil gave 8.33 g (85% based on dihydrooxazine) of a deep blue oil, bp 25 °C (2 mm), which was judged to be 94% pure by NMR. The NMR spectral data agree with those reported by Keana.[6] The product exhibited the following NMR spectral properties: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.23 (d, 3 H, J = 6 Hz, CH_3 at C-6), 1.27 (s, 6 H, *gem*-dimethyl), 1.63 (s, 3 H, CH_3 at C-2), 4.00 (m, 1 H, 1 H at C-6).

5,6-Dihydro-2,4,4,6-tetramethyl-1,3-oxazine *N*-oxide (2) was prepared according to a modification of the procedure of Keana.[6] A solution of 0.64 g of crude oxaziridine **1** (3.5 mmol based on 85% purity) in 5 mL of dry chloroform was placed on top of a dry silica gel column under argon equipped with flash chromatography apparatus, and an additional 5 mL of chloroform was used to rinse the residual solution on to the column. The adsorbed solution was allowed to stand for 1 h, and the column was then eluted with 100 mL of a 2:1 mixture of chloroform and methanol and 100 mL of methanol under 3 psi head pressure of argon. The fast-moving blue band (nitroso compound) was discarded and all subsequent eluate was collected. (Attempts to increase the scale above 1 g led to decomposition and low yields, evidently owing to the exothermicity of the reaction.) Evaporation of solvent gave a partially crystalline solid which was washed three times with hexane to yield 0.46 g (85% based on oxaziridine) of flaky white crystals, mp 82–83 °C. These crystals quickly deliquesced upon exposure to air and could not be stored under vacuum or under argon. The combusion analyses of the product were always low on carbon, even though the sample was rigorously protected from atmospheric moisture. The NMR spectral data agree with those reported by Keana. The product exhibited the following spectral properties: IR ($CHCl_3$) ν_{max} 2890, 1620, 1125 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.37 (d, 3 H, J = 6 Hz, CH_3 at C-6), 1.52 and 1.55 (2 s, 6 H, *gem*-dimethyl), 1.95 (d, 1 H, J = 6 Hz, CH_2 at C-5), 2.03 (s, 1 H, 2 H at C-5), 2.26 (s, 3 H, CH_3 at C-2), 4.1–4.5 (m, 1 H, 1 H at C-6). Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 59.58; H, 9.48; N, 8.75.

Adducts of Nitrone 2 and Phenyl Isocyanate (3–4). A solution of 0.70 g (4.5 mmol, 70%) of nitrone **2**, 0.55 mL (5.1 mmol) of phenyl isocyanate and 5 mL of chloroform was heated at 45 °C for 3 h. Evaporation of the solvent yielded 1.17 g of a solid which was a 9:1 mixture of adducts **3**:**4**. Crystallization from hexane gave 0.27 g of adduct **3** as colorless prisms (anal.), mp 102–103 °C: IR ($CHCl_3$) ν_{max} 1750, 1390, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) adduct **3** δ 1.35 (d, 3 H, J = 6 Hz, $CHCH_3$), 1.39 and 1.41 (2 s, 6 H, *gem*-dimethyl), 1.62 (s, 3 H, CH_3 at C-4), 2.05 (dd, 2 H, J = 7, 14 Hz, 2 H at C-7), 4.10–4.20 (m, 1 H, $CHCH_3$), 7.20–7.50 (m, 5 H, C_6H_5); adduct **4** δ 1.27 (d, 3 H, J = 6 Hz, $CHCH_3$), 1.45 and 1.46 (2 s, 6 H, *gem*-dimethyl), 1.49 (s, 3 H, CH_3 at C-4). Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 65.20; H, 7.30; N, 10.14. Found: C, 65.40; H, 7.30; N, 9.87.

2,4,4-Trimethyloxazoline 2,3-oxide (5) was prepared according to a modification of the procedure of Keana and Lee.[6] A solution of 5.00 g (0.44 mol) of 4,5-dihydro-2,4,4-trimethyloxazoline[18] in 80 mL of ether was cooled to −10 °C and a solution of 9.54 g of 80–85% *m*-chloroperoxybenzoic acid (0.44 mol based on 80% purity) in 80 mL of ether was added dropwise over 1 h. The solution was allowed to stand at 2 °C for 48 h, then it was washed with three 50-mL portions of a 10% aqueous sodium carbonate solution, and the organic layer was dried over potassium carbonate. Evaporation of the solvent and distillation of the residual oil gave 4.63 g (81% based on oxazoline) of blue oil, bp 25 °C (2 mm), which was judged to be 92% pure by NMR. The product exibited the following spectral properties: IR (film) ν_{max} 1410, 1270, 1040 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.14 and 1.36 (2 s, 6 H, *gem*-dimethyl), 1.79 (s, 3 H, CH_3 at C-2), 3.37 and 3.50 (2 d, 2 H, J = 8 Hz, CH_2O).

2,4,4-Trimethyloxazoline *N*-oxide (6a) was prepared according to the procedure described above for oxazine *N*-oxide **2** from 0.78 g of crude oxaziridine **5** (5.2 mmol based on 86% purity).

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Evaporation of solvent gave 0.92 g (>100%) of a crude oil, the purity of which was judged to be about 50% based on the integrated ratio of peaks in the 1 to 2 ppm region of the ^{1}H NMR spectrum. Preparation of nitrone **6a** by ortho ester condensation followed by isolation[11] gave a similar purity of nitrone. The ^{1}H NMR spectral properties of nitrone **6a** are as follows: (D_2O) δ 1.43 (s, 6 H, *gem*-dimethyl), 2.16 (s, 3 H, CH_3), 4.49 (s, 2 H, CH_2O); (MeOH-d_4) δ 1.45 (s, 6 H), 2.18 (s, 3 H), 4.49 (s, 2 H); ($CDCl_3$) δ 1.51 (s, 6 H), 2.20 (s, 3 H), 4.30 (s, 2 H). Impurity peaks appeared as a series of lines from δ 1.00–1.40 in all spectra.

2-(Hydroxyamino)-2-methyl-1-propanol hydrochloride (7) was prepared according to the following procedure.[8,9] A solution of 16.25 g (0.30 mol) of ammonium chloride in 200 mL of water was added to a solution of 29.75 g (0.25 mol) of 2-methyl-2-nitro-1-propanol (Commercial Solvents, Inc.) in 600 mL of absolute ethanol. The combined solution was stirred and cooled in an ice bath while 65 g (1 mol) of zinc dust was added in small portions over 15 min. The addition rate was adjusted so as to maintain the temperature at or below 10 °C. The mixture was stirred at 25 °C for 4 h and filtered. The precipitate was washed with 350 mL of hot 95% ethanol and 350 mL of hot chloroform. The filtrate was evaporated and the resulting clear oil was dried (K_2CO_3) and dissolved in chloroform. The chloroform solution was saturated with hydrogen chloride gas. The resulting precipitate was filtered, washed with chloroform and ether, and dried in vacuum, yielding 28.93 g (93% based on 2-methyl-2-nitro-1-propanol) of white crystals, mp 99–100 °C: IR (nujol) ν_{max} 3150, 1050 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.32 (s, 6 H, *gem*-dimethyl), 3.57 (s, 2 H, CH_2O), 4.80 (s, 4 H, OH and NH_2OH). Anal. Calcd for $C_4H_{12}NO_2Cl$: C, 33.93; H, 8.54; N, 9.89; Cl, 25.04. Found: C, 33.90; H, 8.67; N, 9.51; Cl, 25.36.

3,3a,5,6-Tetrahydro-3a,6,6-trimethyl-3-phenyl-2*H*-oxazolo[3,2-*b*]-1,2,4-oxadiazol-2-one (8a). Representative Procedure for the in Situ Generation of 2-Ethyl- and 2,4,4-Trimethyloxazoline *N*-Oxides. A suspension of 0.25 g (1.8 mmol) of hydroxylamine hydrochloride **7** in a solution of 0.35 g (2.2 mmol) of triethyl orthoacetate (or 0.39 g (2.2 mmol) of triethyl orthopropionate for nitrone **6b**) in 2 mL of dichloromethane was stirred at 25 °C for 1 h. Aliquots of 0.25 mL (1.8 mmol) of triethylamine and 0.24 mL (2.2 mmol) of phenyl isocyanate were added in succession and the solution was stirred at 25 °C for 5 h. Purification by flash chromatography and crystallization from hexane gave 0.43 g (98% based on hydroxylamine hydrochloride **7**) of colorless prisms, mp 65–66 °C: IR ($CHCl_3$) ν_{max} 1750, 1600, 1490, 1385, 1030 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 and 1.43 (2 s, 6 H, *gem*-dimethyl), 1.68 (s, 3 H, CH_3 at C-3a), 3.81 and 3.88 (2 d, 2 H, J = 9 Hz, CH_2O), 7.20–7.60 (m, 5 H, C_6H_5); (benzene-d_6) δ 0.89 and 1.03 (2 s, 6 H, *gem*-dimethyl), 1.40 (s, 3 H, CH_3 at C-4), 3.16 and 3.22 (2 d, 2 H, J = 9 Hz, CH_2O), 6.92–7.54 (m, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{16}N_2O_3$: C, 62.89; H, 6.50; N, 11.28. Found: C, 62.64; H, 6.25; N, 11.56.

3a-Ethyl-3,3a,5,6-tetrahydro-6,6-dimethyl-3-phenyl-2*H*-oxazolo[3,2-*b*]-1,2,4-oxadiazol-2-one (8b). A solution of nitrone **6b** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride **7**), an aliquot of 0.21 mL (1.9 mmol) of phenyl isocyanate, and 1 mL of dichloromethane was stirred at 25 °C for 3 h. Purification by flash chromatography and crystallization from hexane yielded 0.43 g (93% based on hydroxylamine hydrochloride **7**) of colorless prisms, mp 97–98 °C: IR ($CHCl_3$) ν_{max} 1750, 1600, 1490, 1390 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.32 and 1.42 (2 s, 6 H, *gem*-dimethyl), 1.75 and 2.09 (2 dq, 2 H, J = 7, 15 Hz, CH_2CH_3), 3.81 and 3.87 (2 d, 2 H, J = 9 Hz, CH_2O), 7.26–7.55 (m, 5 H, C_6H_5). Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.68. Found: C, 64.00; H, 6.73; N, 10.55.

Dimethyl 3a,6-Dihydro-3a,6,6-trimethyl-5*H*-oxazolo[3,2-*b*]isoxazole-2,3-dicarboxylate (9a). A solution of nitrone **6a** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride **7**), 0.27 mL (2.2 mmol) of dimethyl acetylenedicarboxylate, and 2 mL of dichloromethane was stirred at 25 °C for 2 h. Purification by flash chromatography yielded 0.47 g (98% based on hydroxylamine salt) of a clear oil: IR (film) ν_{max} 1750, 1720, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30 and 1.35 (2 s, 6 H, *gem*-dimethyl), 1.89 (s, 3 H, CH_3 at C-3a), 3.33 and 3.78 (2 d, 2 H, J = 9 Hz, CH_2O), 3.77 and 3.91 (2 s, 6 H, OCH_3). Anal. Calcd for $C_{12}H_{17}NO_6$: C, 53.13; H, 6.32; N, 5.16. Found: C, 52.74; H, 6.23; N, 5.28.

Dimethyl 3a-Ethyl-3a,6-dihydro-6,6-dimethyl-5*H*-oxazolo[3,2-*b*]isoxazole-2,3-dicarboxylate (9b). A solution of nitrone **6b** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride **7**), 0.27 mL (2.2 mmol) of dimethyl acetylenedicarboxylate, and 2 mL of dichloromethane was stirred at 25 °C for 3 h. Purification by flash chromatography gave 0.47 g (93% based on hydroxylamine salt) of a clear oil: IR (film) ν_{max} 1750, 1720, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.27 and 1.35 (2 s, 6 H, *gem*-dimethyl), 1.77 and 2.53 (2 dq, 2 H, J = 7, 14 Hz, CH_2CH_3), 3.34 and 3.76 (2 d, 2 H, J = 9 Hz, CH_2O), 3.77 and 3.91 (2 s, 6 H, OCH_3). Anal. Calcd for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71; N, 4.91. Found: C, 54.74; H, 6.56; N, 4.96.

Methyl Phenylpropiolate. A solution of 3 g (71.4 mmol) of diazomethane in 250 mL of ether was added to a solution of 10.43 g (71.4 mmol) of phenylpropiolic acid (mp 136–137 °C) in 50 mL of ether. The solution was immediately washed with 10% aqueous sodium carbonate solution, dried (Na_2SO_4), and evaporated. Distillation of the remaining liquid at 74–76 °C (0.1 mm) (lit.[19] 120–121 °C (16 mm)) gave 8.04 g (70% based on phenylpropiolic acid) of a clear oil: IR (film) ν_{max} 2215, 1710, 1280 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.84 (s, 3 H, CO_2CH_3), 7.2–7.6 (m, 5 H, C_6H_5).

Phenylpropiolonitrile. A solution of 5.00 g (49.0 mmol) of phenylacetylene (Aldrich Chemical Company) in 100 mL of ether was stirred at 0 °C as a 31.6-mL (49.0 mmol) aliquot of 1.55 M *tert*-butyllithium in *n*-pentane (Alfa Products) was added dropwise by syringe. Cyanogen chloride gas (Matheson Gas Products) was bubbled through the resulting mixture at 0 °C until the mixture became saturated. The solvent was evaporated, the resulting brown solid was suspended in water, and the product was extracted with ether. The ethereal solution was washed with 5% aqueous hydrogen chloride, 10% aqueous sodium carbonate, and saturated aqueous sodium chloride and dried (Na_2SO_4). Evaporation of the solvent and distillation of the residue at 35 °C (0.1 mm) afforded 2.77 g (44% based on phenylacetylene) of a crystalline solid, mp 38 °C (lit.[20] 39 °C): IR (film) ν_{max} 2260, 1440, 755, 685 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.10–7.70 (m, 5 H, C_6H_5). Anal. Calcd for C_9H_5N: C, 85.02; H, 3.96; N, 11.02. Found: C, 84.81; H, 3.91; N, 11.09.

2,4,4-Trimethylpyrroline *N*-oxide (12) was prepared from 34 g (0.21 mol) of 5-methyl-5-nitro-2-hexanone[21] according to the procedure of Delpierre and Lamchen.[12] The yield of colorless oil, bp 84–86 °C (2 mm) was 26 g (0.20 mol, 95%; IR (film) ν_{max} 2870, 1590, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 6 H, *gem*-dimethyl), 2.03 (s, 3 H, CH_3), 2.00 and 2.58 (2 t, 4 H, J = 7 Hz, CH_2CH_2); ^{13}C NMR ($CDCl_3$) δ 13.04 (q, 1 C, J = 129 Hz, CH_3), 25.43 (q, 2 C, J = 128 Hz, *gem*-dimethyl), 29.05 (t, 1 C, J = 134 Hz, CH_2), 32.21 (t, 1 C, J = 133 Hz, CH_2), 73.05 (s, 1 C, C-5), 140.79 (s, 1 C, C-2).

Methyl 3a,6-Dihydro-3a,6,6-trimethyl-2-phenyl-5*H*-oxazolo[3,2-*b*]isoxazole-3-carboxylate (10a). A solution of nitrone **6a** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride **7**), 0.28 g (1.8 mmol) of methyl phenylpropiolate, and 2 mL of dichloromethane was stirred at 35 °C for 24 h and filtered through basic aluminum oxide. Crystallization of the remaining oil (0.45 g) from hexane afforded 0.38 g (74% based on hydroxylamine hydrochloride) of colorless prisms, mp 62–63 °C: IR ($CHCl_3$) ν_{max} 1705, 1630, 1130, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 and 1.38 (2 s, 6 H, *gem*-dimethyl), 1.96 (s, 3 H, CH_3 at C-3a), 3.38 and 3.80 (2 d, 2 H, J = 9 Hz, CH_2O), 3.71 (s, 3 H, CO_2CH_3), 7.4–7.7 (m, 5 H, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.51 (q, 1 C, J = 129 Hz, CH_3 at C-3a), 25.82 (q, 1 C, J = 125 Hz, CH_3 at C-6), 26.71 (q, 1 C, J = 129 Hz, CH_3 at C-6), 51.08 (q, 1 C, J = 147 Hz, OCH_3), 68.58 (s, 1 C, C-6), 72.54 (t, 1 C, J = 147 Hz, CH_2), 102.22 and 108.67 (2 s, 2 C, C-3 and C-4), 127.27 (s, 1 C, C_6H_5), 127.86 and 129.12 (2 d, 4 C, *o*- and *m*-C_6H_5), 130.89 (d, 1 C, *p*-C_6H_5), 163.92 and 165.10 (2 s, 2 C, C-2 and C=O). Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.19; H, 6.54; N, 4.57.

Methyl 3a-Ethyl-3a,6-dihydro-6,6-dimethyl-2-phenyl-5*H*-oxazolo[3,2-*b*]isoxazole-3-carboxylate (10b). A solution of nitrone **6b** (prepared from 0.25 g (1.8 mmol) of hydroxylamine

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hydrochloride 7), 0.31 g (1.9 mmol) of methyl phenylpropiolate, and 1 mL of dichloromethane was stirred at 25 °C for 48 h. Purification by flash chromatography afforded 0.39 g (73% based on hydroxylamine hydrochloride) of an oil: IR (film) ν_{max} 1710, 1640, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.33 and 1.38 (2 s, 6 H, *gem*-dimethyl), 1.81 and 2.64 (2 dq, 2 H, J = 7, 14 Hz, CH_2CH_3), 3.38 and 3.78 (2 d, 2 H, J = 9 Hz, CH_2O), 3.70 (s, 3 H, OCH_3), 7.26–7.67 (m, 5 H, C_6H_5). Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.25; H, 6.72; N, 4.51.

3a,6-Dihydro-3a,6,6-trimethyl-2-phenyl-5*H*-oxazolo[3,2-*b*]isoxazole-3-carbonitrile (11a). A solution of nitrone **6a** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride 7), 0.28 g (2.2 mmol) of phenylpropiolonitrile, and 2 mL of dichloromethane was stirred at 45 °C for 24 h. Purification by flash chromatography yielded 0.43 g (95% based on hydroxylamine hydrochloride 7) of an oil: IR (film) ν_{max} 2200, 1640, 1345, 1175, 1035 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 and 1.42 (2 s, 6 H, *gem*-dimethyl), 1.90 (s, 3 H, CH_3 at C-3a), 3.34 and 3.80 (2 d, 2 H, J = 9 Hz, CH_2O), 7.40–7.95 (m, 5 H, C_6H_5). Anal. Calcd for $C_{15}H_{16}N_2O_2$: C, 70.29; H, 6.29; N, 10.92. Found: C, 70.29; H, 6.31; N, 10.59.

3a-Ethyl-3a,6-dihydro-6,6-dimethyl-2-phenyl-5*H*-oxazolo-[3,2-*b*]isoxazole-3-carbonitrile (11b). A solution of nitrone **6b** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride 7), 0.25 g (1.9 mmol) of phenylpropiolonitrile, and 1 mL of dichloromethane was stirred at 25 °C for 48 h. Purification by flash chromatography gave 0.43 g (90% based on hydroxylamine hydrochloride 7) of an oil: IR (film) ν_{max} 2100, 1630, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.09 (t, 3 H, J = 7 Hz, CH_2CH_3), 1.31 and 1.42 (2 s, 6 H, *gem*-dimethyl), 1.91 and 2.31 (2 dq, 2 H, J = 7, 14 Hz, CH_2CH_3), 3.35 and 3.79 (2 d, 2 H, J = 9 Hz, CH_2O), 7.26–7.93 (m, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.99; H, 6.58; N, 10.51.

Methyl 3a,4,5,6-Tetrahydro-3a,6,6-trimethyl-2-phenylpyrrolo[1,2-*b*]isoxazole-3-carboxylate (13). A solution of 0.50 g (3.9 mmol) of nitrone **12**, 0.16 g (1.0 mmol) of methyl phenylpropiolate, and 2 mL of benzene was heated at reflux for 32 h. Purification by flash chromatography yielded 0.27 g (94% based on methyl phenylpropiolate) of an oil: IR (film) ν_{max} 1690, 1640, 1095 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 6 H, *gem*-dimethyl), 1.62 (s, 3 H, CH_3 at C-3a), 1.74 (t, 2 H, J = 7 Hz, CH_2CH_2), 1.98 and 2.42 (2 dt, 2 H, J = 7, 13 Hz, CH_2CH_2), 3.64 (s, 3 H, CO_2CH_3), 7.4–7.7 (m, 5 H, C_6H_5). Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 71.07; H, 7.13; N, 4.90.

3a,4,5,6-Tetrahydro-3a,6,6-trimethyl-2-phenylpyrrolo[1,2-*b*]isoxazole-3-carbonitrile (14). A solution of 0.20 g (1.6 mmol) of nitrone **12**, 0.25 g (2.0 mmol) of phenylpropiolonitrile, and 2 mL of benzene was heated at reflux for 40 h. Purification by flash chromatography gave 0.38 g (95% based on nitrone **12**) of an oil: IR (film) ν_{max} 2190, 1640, 775, 690, cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 and 1.32 (2 s, 6 H, *gem*-dimethyl), 1.63 (s, 3 H, CH_3 at C-3a), 1.70–2.35 (m, 4 H, CH_2CH_2), 7.30–8.00 (m, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{18}N_2O$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.91; H, 7.03; N, 11.34.

Isomers of Methyl 3,3a,5,6-Tetrahydro-3a,6,6-trimethyl-2*H*-oxazolo[3,2-*b*]isoxazole-2- and -3-carboxylate (15a–18a). A solution of nitrone **6a** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride 7) in 7 mL (77.7 mmol) of methyl acrylate was stirred at 25 °C for 16 h. Purification by flash chromatography yielded two fractions: 50 mg (13% based on hydroxylamine hydrochloride 7) of adduct **16a** as an oil and 271 mg (71% based on hydroxylamine hydrochloride) of an oil which was a 45:14:41 mixture of adducts **15a**:(**17a** or **18a**):(**18a** or **17a**) by NMR analysis. Adduct **16a** exhibited the following spectral properties: IR (film) ν_{max} 1735, 1205, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 and 1.31 (2 s, 6 H, *gem*-dimethyl), 1.52 (s, 3 H, CH_3 at C-3a), 3.29 (dd, 1 H, J = 7, 10 Hz, 1 H at C-3), 3.65 and 3.71 (2 d, 2 H, J = 8 Hz, CH_2O), 3.77 (s, 3 H, CO_2CH_3), 3.96 (t, 1 H, J = 10 Hz, 1 H at C-2), 4.10 (dd, 1 H, J = 7, 10 Hz, 1 H at C-2). Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.89; H, 7.84; N, 6.37.

The mixture of **15a**, **17a**, and **18a** exhibited the following spectral properties: IR (film) ν_{max} 1735, 1210, 1050 cm^{-1}; ^{1}H NMR ($CDCl_3$) adduct **15a** δ 1.25 and 1.32 (2 s, 6 H, *gem*-dimethyl), 1.78 (s, 3 H, CH_3 at C-3a), 3.43 (t, 1 H, J = 8 Hz, 1 H at C-3), 3.57 and 3.59 (2 d, 2 H, J = 3 Hz, CH_2O), 3.99 and 4.14 (2 t, 2 H, J = 8 Hz, 2 H at C-2); adduct **17a** or **18a** δ 1.42 (s, 3 H, CH_3 at C-6), 1.61 (s, 3 H, CH_3 at C-3a), 2.54–2.64 (m, 2 H, 2 H at C-3), 4.43 (dd, 1 H, J = 7, 8 Hz, 1 H at C-2); adduct **18a** or **17a** δ 1.25 and 1.35 (2 s, 6 H, *gem*-dimethyl), 1.62 (s, 3 H, CH_3 at C-3a), 2.67 (d, 2 H, J = 7 Hz, 2 H at C-3), 4.56 (t, 1 H, J = 7 Hz, 1 H at C-2). Anal. Calcd for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51. Found: C, 55.79; H, 7.98; N, 6.64.

Isomers of 3,3a,5,6-Tetrahydro-3a,6,6-trimethyl-2*H*-oxazolo[3,2-*b*]isoxazole-2- and -3-carbonitrile (15b–18b). A solution of nitrone **6a** (prepared from 0.25 g (1.8 mmol) of hydroxylamine hydrochloride 7) and 5 mL (76.0 mmol) of acrylonitrile was stirred at 25 °C for 24 h. Purification by flash chromatography yielded 0.26 g (81% based on hydroxylamine hydrochloride) of an oil which was a 56:19:7:18 mixture of adducts **15b**:**16b**:(**17b** or **18b**):(**18b** or **17b**) by NMR analysis. A 70-mg portion of this oil was rechromatographed yielding 3 fractions: 25 mg of a 1:1 mixture of adducts **16b**:(**18b** or **17b**), 10 mg of a 2:1 mixture of adducts **15b**:(**17b** or **18b**), and 35 mg of adduct **15b** as oils. Adduct **15b** exhibited the following spectral properties: IR (film) ν_{max} 2230, 1380, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 and 1.34 (2 s, 6 H, *gem*-dimethyl), 1.70 (s, 3 H, CH_3 at C-3a), 3.44 (t, 1 H, J = 6 Hz, 1 H at C-3), 3.78 and 3.84 (2 d, 2 H, J = 8 Hz, CH_2O), 4.02 and 4.08 (2 dd, J = 8, 9 Hz, 2 H at C-2). Anal. Calcd for $C_{10}H_{17}N_2O_4$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.25; H, 7.69; N, 15.09.

The mixture of adducts **15b**, **16b**, **17b**, and **18b** exhibited the following spectral properties: IR (film) ν_{max} 2230, 2180, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) adduct **16b** δ 1.25 and 1.32 (2 s, 6 H, *gem*-dimethyl), 1.77 (s, 3 H, CH_3 at C-3a), 3.35 (dd, 1 H, J = 7, 9 Hz, 1 H at C-3), 3.56 and 3.61 (AB q, 2 H, J = 8 Hz, CH_2O), 3.82 (t, 1 H, J = 9 Hz, 1 H at C-2), 4.23 (dd, 1 H, J = 7, 9 Hz, 1 H at C-2); adduct **17b** or **18b** δ 1.30 and 1.38 (2 s, 6 H, *gem*-dimethyl), 1.63 (s, 3 H, CH_3 at C-3a), 2.76 (d, 2 H, J = 6 Hz, 2 H at C-3), 3.84 and 3.91 (2 d, 2 H, J = 8 Hz, CH_2O), 4.67 (t, 1 H, J = 6 Hz, 1 H at C-2); adduct **18b** or **17b** δ 1.26 and 1.32 (2 s, 6 H, *gem*-dimethyl), 1.73 (s, 3 H, CH_3 at C-3a), 2.63 (dd, 1 H, J = 3, 13 Hz, 1 H at C-3), 2.70 (dd, 1 H, J = 7, 13 Hz, 1 H at C-3), 3.69 and 3.73 (2 d, 2 H, J = 8 Hz, CH_2O), 4.85 (dd, 1 H, J = 3, 7 Hz, 1 H at C-2). Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.60; H, 7.61; N, 15.00.

Isomers of Methyl Hexahydro-3a,6,6-trimethylpyrrolo-[1,2-*b*]isoxazole-2- and -3-carboxylate (19a–22a). A solution of 200 mg of nitrone **12** in 20 mL of methyl acrylate was heated at reflux (ca. 80 °C) for 84 h. Purification by flash chromatography yielded three fractions as oils: 49 mg (15% based on nitrone) of adduct **20a** (contaminated with about 2% of adduct **21a** or **22a**), 119 mg (35% of a 24:4:64:8 mixture of adducts **19a**:**20a**:(**21a** or **22a**):(**22a** or **21a**), and 74 mg (22%) of a 6:12:82 mixture of adducts **19a**:(**21a** or **22a**):(**22a** or **21a**) by NMR analysis. Adduct **20a** exhibited the following spectral properties: IR (film) ν_{max} 1735, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.13 and 1.26 (2 s, 6 H, *gem*-dimethyl), 1.27 (s, 3 H, CH_3 at C-3a), 1.65–2.20 (m, 4 H, CH_2CH_2), 3.01 (dd, 1 H, J = 7, 11 Hz, 1 H at C-3), 3.73 (s, 3 H, CO_2CH_3), 4.02 (t, 1 H, J = 11 Hz, 1 H at C-2), 4.10 (t, 1 H, J = 7 Hz, 1 H at C-2); exact mass calcd for $C_{11}H_{19}NO_3$ m/e 213.13649, found m/e 213.13632.

The mixture of adducts **19a**, **20a**, **21a**, and **22a** exhibited the following spectral properties: IR (film) ν_{max} 1755, 1735, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) adduct **19a** δ 1.19 and 1.27 (2 s, 6 H, *gem*-dimethyl), 1.56 (s, 3 H, CH_3 at C-3a), 1.60–1.95 (m, 4 H, CH_2CH_2), 3.24 (dd, 1 H, J = 8, 9 Hz, 1 H at C-3), 3.74 (s, 3 H, CO_2CH_3), 4.01 (t, 1 H, J = 8 Hz, 1 H at C-2), 4.05 (t, 1 H, J = 9 Hz, 1 H at C-2); adduct **21a** or **22a** δ 1.16 and 1.25 (2 s, 6 H, *gem*-dimethyl), 1.38 (s, 3 H, CH_3 at C-3a), 1.60–1.95 (m, 4 H, CH_2CH_2), 2.40 (dd, 1 H, J = 8, 13 Hz, 1 H at C-3), 2.46 (dd, 1 H, J = 6, 13 Hz, 1 H at C-3), 3.76 (s, 3 H, CO_2Me), 4.60 (dd, 1 H, J = 6, 8 Hz, 1 H at C-2). Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57. Found: C, 62.08; H, 9.02; N, 6.50.

The mixture of adducts **19a**, **21a**, and **22a** exhibited the following spectral properties: IR (film) ν_{max} 1755, 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) adduct **22a** or **21a** δ 1.12 and 1.34 (2 s, 6 H, *gem*-dimethyl), 1.40 (s, 3 H, CH_3 at C-3a), 1.60–2.10 (m, 2 H, CH_2CH_2), 2.16 (t, 1 H, J = 11 Hz, 1 H at C-3), 2.35 (dd, 1 H, J = 6, 11 Hz, 1 H at C-3), 3.75 (s, 3 H, CO_2CH_3), 4.45 (dd, 1 H, J = 6, 11 Hz, 1 H at C-2). Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H, 8.98; N, 6.57.

Found: C, 61.68; H, 8.97; N, 6.32.

Isomers of Hexahydro-3a,6,6-trimethylpyrrolo[1,2-*b*]-isoxazole-2- and -3-carbonitrile (19b–22b). A solution of 200 mg of nitrone **12** in 10 mL of acrylonitrile was stirred at 25 °C for 54 h. Purification by flash chromatography yielded 139 mg (49% based on nitrone **12**) of adduct **21b** or **22b** as an oil. When a solution of 200 mg of nitrone **12** in 20 mL of acrylonitrile was heated at reflux for 96 h, purification by flash chromatography yielded two fractions: 35 mg (12%) of adduct **21b** or **22b** and 80 mg (28%) of adduct **19b** or **20b** as oils. A solution of 7 mg of adduct **21b** or **22b** in 5 mL of acrylonitrile was heated at reflux for 40 h. Evaporation of the solvent and filtration through silica gel gave 6 mg of a 5:1 mixture of adducts (**19b** or **20b**):(**21b** or **22b**) from the integrated ratios of the C-2 and C-3 absorbtions in the NMR spectrum. The ratios of the peak heights of the visible methyl groups was also 5:1. A solution of 44 mg of adduct **19b** or **20b** in 5 mL of acrylonitrile was heated at reflux for 35 h. Evaporation of the solvent and filtration through silica gel gave 33 mg of 5:1 mixture of nitrones (**19b** or **20b**):(**21b** or **22b**). Adduct **21b** or **22b** exhibited the following spectral properties: IR (film) ν_{max} 2910, 1145, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 and 1.27 (2 s, 6 H, *gem*-dimethyl), 1.56 (s, 3 H, CH_3 at C-3a), 1.60–1.85 (m, 4 H, CH_2CH_2), 2.39 (dd, 1 H, J = 8, 13 Hz, 1 H at C-3), 2.50 (dd, 1 H, J = 2, 13 Hz, 1 H at C-3), 4.80 (dd, 1 H, J = 2, 8 Hz, 1 H at C-2); exact mass calcd for $C_{10}H_{16}N_2O$ m/e 180.12627, found m/e 180.12655. Anal. Calcd for $C_{10}H_{16}N_2O$: C, 66.64; H, 8.95; N, 15.54. Found: C, 66.82; H, 8.88; N, 15.34.

Adduct **19b** or **20b** exhibited the following spectral properties: IR (film) ν_{max} 2230, 1460, 1150, 1070, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 and 1.28 (2 s, 6 H, *gem*-dimethyl), 1.56 (s, 3 H, CH_3 at C-3a), 1.65–2.05 (m, 4 H, CH_2CH_2), 3.03 (dd, 1 H, J = 7, 10 Hz, 1 H at C-3), 3.83 (dd, 1 H, J = 9, 10 Hz, 1 H at C-2), 4.23 (dd, 1 H, J = 7, 9 Hz, 1 H at C-2). Anal. Calcd for $C_{10}H_{16}N_2O$: C, 66.64; H, 8.95; N, 15.54. Found: C, 66.72; H, 8.95; N, 15.41.

Competitive Cycloaddition Reaction between Nitrones 6a and 12 for Dimethyl Acetylenedicarboxylate. A solution of nitrone **6a** (prepared from 0.25 g (1.77 mmol) of hydroxylamine hydrochloride **7**) and 2.95 g (23.23 mmol) of nitrone **12** in 20 mL of dichloromethane was prepared and was stirred rapidly at 0 °C. An aliquot of 0.17 mL (1.38 mmol) of dimethyl acetylenedicarboxylate was added dropwise over 1 min. The solution was stirred for 2.5 h at 25 °C. Evaporation of the solvent and purification of the residue by flash chromatography yielded 0.34 g (90% based on dimethyl acetylenedicarboxylate) of an oil. The ratio of cycloadducts **9a**:**24** was established by the average value of the ratio of peak heights of each methyl group in adduct **9a** compared to the corresponding methyl group in adduct **24** in the proton NMR spectrum at 360 MHz, and was calculated to be 87:13 (±2). The rate ratio was calculated from Ingold's equation[13] to be 154 (±39):1. A second experiment, carried out in the same manner, yielded a rate ratio of 163 (±17):1 for an average rate ratio of approximately 160:1.

Competitive Cycloaddition Reaction between Nitrones 6a and 12 for Phenyl Isocyanate. A solution of nitrone **6a** (prepared from 0.05 g (0.35 mmol) of hydroxylamine hydrochloride **7**), 4.76 g (37.48 mmol) of nitrone **12**, and 20 mL of dichloromethane was prepared and an aliquot of 0.025 mL (0.23 mmol) of phenyl isocyanate was added dropwise over 30 s. The solution was stirred for 3 h at 25 °C. Evaporation of solvent and chromatography of the residue yielded 0.06 g (>100% based on phenyl isocyanate) of a solid which was pure oxazoline adduct **8a** by NMR analysis and which showed no trace of pyrroline adduct **23**. A maximum amount of adduct **23** was calculated to be 2.4% from the relative heights of a peak in the noise region of the NMR spectrum in benzene-d_6 at δ 1.11 and the C-6 methyl group of adduct **8a** at δ 1.03. A lower limit to the rate ratio was calculated from Ingold's equation[13] to be 6800:1. A second experiment, carried out with a 16:1 ratio of nitrones **12**:**6a**, yielded a product which also showed no trace of adduct **23**. A maximum amount of adduct **23** was calculated to be 2.4% in the same manner as above for a lower limit to the rate ratio of 1300:1.

Hexahydro-3a,6,6-trimethyl-3-phenylpyrrolo[1,2-*b*]-1,2,4-oxadiazol-2(3*H*)-one (23). A solution of 0.28 g (2.2 mmol) of nitrone **12**, 0.24 mL (2.2 mmol) of phenyl isocyanate, and 1 mL of chloroform was heated at 40 °C for 3 h. Evaporation of the solvent and crystallization of the residue from hexane afforded 0.41 g (76%) of colorless tetragonal prisms mp 81–82 °C: IR ($CHCl_3$) ν_{max} 1750, 1601, 1500, 1360 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 6 H, *gem*-dimethyl), 1.65 (s, 3 H, CH_3 at C-3a), 1.70–2.40 (m, 4 H, CH_2CH_2), 7.20–7.60 (m, 5 H, C_6H_5); ^1H NMR (benzene-d_6) δ 1.04 and 1.11 (2 s, 6 H, *gem*-dimethyl), 1.25 (s, 3 H, CH_3 at C-4), 1.15–1.30 (m, 3 H, CH_2CH_2), 1.75–1.90 (m, 1 H, CH_2CH_2), 6.90–7.35 (m, 5 H, C_6H_5). Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.40; H, 7.41; N, 11.39.

Dimethyl 3a,4,5,6-Tetrahydro-3a,6,6-trimethylpyrrolo-[1,2-*b*]isoxazole-2,3-dicarboxylate (24).[22] A solution of 0.25 g (2.0 mmol) of nitrone **12** and 0.27 mL (2.2 mmol) of dimethyl acetylenedicarboxylate in 1 mL of dichloromethane was stirred at 25 °C for 1 h. The solvent was evaporated and excess dimethyl acetylenedicarboxylate was removed under reduced pressure, leaving 0.51 g (96% based on nitrone **12**) of a clear oil: IR (film) ν_{max} 1750, 1710, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.23 and 1.26 (2 s, 6 H, *gem*-dimethyl), 1.57 (s, 3 H, CH_3 at C-3a), 1.72 (t, 2 H, J = 7 Hz, CH_2CH_2), 1.92 and 2.35 (2 dt, 2 H, J = 7, 13 Hz, CH_2CH_2), 3.73 and 3.89 (2 s, 6 H, OCH_3). Anal. Calcd for $C_{13}H_{19}NO_5$: C, 57.98; H, 7.11; N, 5.20. Found: C, 58.32; H, 7.34; N, 5.17.

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Registry No. **1**, 59813-18-2; **2**, 59813-19-3; **3**, 90900-21-3; **4**, 90900-22-4; **5**, 62539-46-2; **6a**, 90900-23-5; **6b**, 90900-24-6; **7**, 63829-84-5; **8a**, 90900-25-7; **8b**, 90900-26-8; **9a**, 90900-27-9; **9b**, 90900-28-0; **10a**, 90900-29-1; **10b**, 90900-30-4; **11a**, 90900-31-5; **11b**, 90900-32-6; **12**, 4567-18-4; **13**, 90900-33-7; **14**, 90900-34-8; **15a**, 90900-35-9; **15b**, 90900-36-0; **16a**, 90900-37-1; **16b**, 90900-38-2; **17a**, 90900-39-3; **17b**, 90900-40-6; **18a**, 90900-41-7; **18b**, 90900-42-8; **19a**, 90900-43-9; **19b**, 90900-44-0; **20a**, 90900-45-1; **20b**, 90900-46-2; **21a**, 90900-47-3; **21b**, 90900-48-4; **22a**, 90900-49-5; **22b**, 90990-38-8; **23**, 90900-50-8; **24**, 7713-51-1; 5,6-dihydro-2,4,4,6-tetramethyl-1,3-oxazine, 26939-18-4; 4,5-dihydro-2,4,4-trimethyloxazole, 1772-43-6; 2-methyl-2-nitro-1-propanol, 76-39-1; methyl phenylpropiolate, 4891-38-7; triethyl orthoacetate, 78-39-7; triethyl orthopropionate, 115-80-0; phenyl isocyanate, 103-71-9; dimethyl acetylenedicarboxylate, 762-42-5; phenylpropiolonitrile, 935-02-4.

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