cell, a = 3.8421 ± 0.001 Å, b = 15.542 ± 0.003 Å, c = 9.662 ± 0.002 Å, β = 95.32 ± 0.01°, calculated density for $C_5H_6N_2O_2$, M, 126.1, is 1.46 g cm^{-3}. The intensities of 871 reflections were measured on a four-angle diffractometer using monochromatic copper radiation. The structure was solved by direct methods (SHELXTL) and refined by the least-squares method to R = 0.047. See supplementary material for ORTEP drawing of the molecule (Figure 1), atomic coordinates, bond distances, and angles (Tables I–V).

4-Chloro-5-methoxypyrimidine (10). Compound **8** (120 mg, 0.95 mmol) was treated with phosphorus oxychloride according to the method of Chesterfield, McOmie, and Tute,[13] giving 100 mg (73%) of a crystalline solid (mp 60–61 °C). The crude solid was sublimed [80 °C (10 mm)], affording **10** as fine white needles: mp 60–62 °C (lit.[13] mp 63–64 °C); IR ($CHCl_3$) 3000, 1562, 1547, 1461, 1449, 1430, 1400 cm^{-1}; UV (ethanol) λ_{max} (log ϵ) 275 (3.69), 221 nm (3.81); mass spectrum, m/e (%) 144–146 (80), 109 (100); NMR ($CDCl_3$) δ 8.62 (H-2, s, 1 H), 8.33 (H-6, s, 1 H), 4.03 (CH_3, s, 3 H).

Anal. Calcd for $C_5H_5N_2ClO$: C, 41.54; H, 3.49; N, 19.38. Found: C, 41.74; H, 3.49; N, 19.25.

4(3*H*)-Pyrimidinone (12). Pyrimidine (**11**) (8.0 g, 0.1 mol) was treated according to the procedure described for the preparation of **3**. Continuous extraction of the aqueous phase (24 h) with chloroform afforded after drying and filtration of the organic phase 470 mg (4.7%) of **12** as a white powder. Repetition of this experiment using acetone as the solvent gave 900 mg (9.3%) of **12**. Crystallization from ethanol yielded fine needles, mp 163–164 °C (lit.[15] mp 163–164 °C). This material was identical in all respects with an authentic sample prepared from 2-thiouracil by using the method of Brown:[17] IR ($CHCl_3$) 1704, 1675 cm^{-1}; UV (ethanol) λ_{max} (log ϵ) 221 (3.91), 268 mn (3.56); mass spectrum, m/e (%) 96 (100), 68 (40); NMR (Me_2SO-d_6) δ 8.19 (H-2, s, 1 H), 7.91 (H-6, d, 1 H, $J_{5,6}$ = 6.7 Hz), 6.33 (H-5, dd, 1 H, $J_{2,5}$ = 0.6 Hz, $J_{5,6}$ = 6.7 Hz).

(17) Brown, D. J. *J. Chem. Soc. Ind.* **1950**, *69*, 356.

Treatment of 2 with Peracetic Acid–Sulfuric Acid. To a solution of **2** (300 mg, 1.7 mmol) in 15 mL of water at 25 °C was added a mixture of 0.74 mL (3.4 mmol) of 35% peracetic acid and 0.09 mL (1.7 mmol) of 18 M sulfuric acid. This mixture was stirred at ambient temperature for 1.5 h and treated as described in the preparation of **8** and **9**. TLC on the isolated product (205 mg, 68% recovery) showed only **2** and no trace of compound **3**.

Treatment of 7 with Peracetic Acid–Sulfuric Acid. A solution of **7** (315 mg, 2.5 mmol) in 10 mL of water, 1.0 mL (6.0 mmol) of 40% peracetic acid, and 0.14 mL (2.5 mmol) of 18 M sulfuric acid was allowed to stir at ambient temperature for 4 days. The solution was treated as described in the preparation of **8** and **9**, affording a white solid (180 mg, 90% recovery), which by TLC showed only **7** and no trace of **8** or **9**.

Treatment of 8 with Peracetic Acid–Sulfuric Acid. A solution of **8** (70 mg, 0.55 mmol), 1.0 mL of D_2O, 0.03 mL (0.55 mmol) of sulfuric acid, and 0.22 mL (1.32 mmol) of 40% peracetic acid was placed in an NMR tube at 25 °C. The original spectrum of **8** (see experimental above) remained unchanged after 24 h. Another NMR sample of **8** prepared as described above showed no change after standing for 5 h at 48 °C.

Acknowledgment. I am indebted to Dr. Noel Jones and John Swartzendruber of Eli Lilly and Co. for determining the X-ray crystal structure of compound **9** and to Dr. R. D. G. Cooper for an authentic sample of this substance. I thank Dr. D. W. Balogh for reading the manuscript and Professor E. C. Taylor for many stimulating conversations.

Registry No. **1**, 4595-59-9; **2**, 36529-69-8; **3**, 19808-30-1; **3**·$^1/_2H_2SO_4$, 97234-97-4; **6**, 31458-33-0; **7**, 36529-70-1; **8**, 695-87-4; **9**, 17325-26-7; **10**, 695-85-2; **11**, 289-95-2; **12**, 4562-27-0.

Supplementary Material Available: Tables of atomic coordinates, bond lengths, and bond angles and structure for **9** (6 pages). Ordering information is given on any current masthead page.

Preparation of Oxazoline *N*-Oxides and Imidate *N*-Oxides by Amide Acetal Condensation and Their [3 + 2] Cycloaddition Reactions

Stephen P. Ashburn and Robert M. Coates*

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

Received January 21, 1985

2,4,4-Trimethyloxazoline *N*-oxide (**3a**), 4,4-dimethyl-2-phenyloxazoline *N*-oxide (**3b**), and ethyl *N*-methylbenzimidate *N*-oxide (**4**) have been prepared by condensation of 2-(hydroxyamino)-2-methyl-1-propanol hydrochloride (**1**) with acetamide or benzamide acetals (**2a** or **2b**). ^{13}C NMR and UV spectral data are reported for **3a,b**, as well as the related pyrroline *N*-oxides (**5a,b**) and oxazolines (**6a,b**). [3 + 2] Cycloaddition reactions of **3a**, **3b**, **4**, and **5b** with phenyl isocyanate, dimethyl acetylenedicarboxylate, and methyl phenylpropiolate were carried out. Similar reactions of **3b** with the acetylenic dipolarophiles in the presence of dimethylamine hydrochloride afforded isoxazoles **11a,b**. A mechanism involving protonation of a zwitterionic intermediate, electrocyclic ring closure, and fragmentative elimination of isobutylene oxide is proposed to explain the formation of the isoxazoles. Rate constants for the cycloaddition reactions of nitrones **3b** and **5b** with phenyl isocyanate and dimethyl acetylenedicarboxylate were determined by NMR. These data indicate that the nitrone **3b** is approximately 76 000 times more reactive than **5b** toward phenyl isocyanate and 70 times more reactive than **5b** toward dimethyl acetylenedicarboxylate.

Oxazoline *N*-oxides **3** are endocyclic nitrones at the carboxylic oxidation state. These heterocyclic compounds have been generated in solution by rearrangement of oxaziridines,[1] by thermal dissociation of a dimer,[1b] and by cyclocondensation of hydroxylamino alcohol **1** with ortho esters.[2] The ready availability and high reactivity of amide acetals[3] suggested that these activated carboxyl derivatives might also be suitable substrates for preparation of oxa-

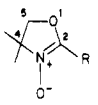
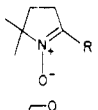
(1) (a) Lee, T. D.; Keana, J. F. W. *J. Org. Chem.* **1976**, *41*, 3237–3241. (b) Hendrickson, J. B.; Pearson, D. A. *Tetrahedron Lett.* **1983**, *24*, 4657–4660.

(2) Ashburn, S. P.; Coates, R. M. *J. Org. Chem.* **1984**, *49*, 3127–3133.

(3) (a) Feugeas, C.; Olschwang, D. *Bull. Soc. Chim. Fr.* **1968**, 4985–4990. (b) Feugeas, C.; Olschwang, D.; Chatzopoulos, M. *C. R. Acad. Seances, Ser. C.* **1967**, *265*, 113–116. (c) Salomon, R. G.; Raychaudhuri, S. R. *J. Org. Chem.* **1984**, *49*, 3659–3660. (d) Meerwein, H.; Florian, W.; Schon, N.; Stopp, G. *Justus Liebigs Ann. Chem.* **1961**, *641*, 1–39. (e) DeWolfe, R. H. "Carboxylic Ortho Acid Derivatives"; Academic Press: New York, 1970; pp 420–506.

0022-3263/85/1950-3076$01.50/0

Table I. UV and ^{13}C NMR Spectral Parameters for Oxazoline *N*-Oxides, Pyrroline *N*-Oxides, and Oxazolines

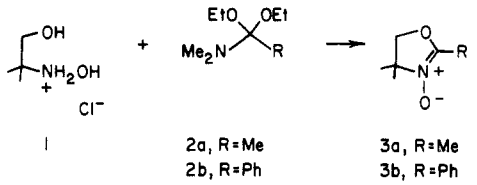
compd[a]	no.	λ_{max},[b] nm	ϵ_{max}	^{13}C chemical shifts and multiplicities[c] C-1	C-2	C-4	C-5
	**3a**, R = Me				151.91 (s)	67.31 (s)	78.40 (t)
	3b, R = Ph	231	12380		145.84 (s)	69.63 (s)	76.84 (t)
		308	9770				
	**5a**, R = Me	230	9950	32.21 (t)[d]	140.79 (s)	73.05 (s)	29.05 (t)[d]
	5b, R = Ph	224	8580	31.85 (t)[e]	137.32 (s)	75.59 (s)	26.73 (t)[e]
		292	15790				
	**6a**, R = Me				162.81 (s)	67.04 (s)	79.14 (t)
	6b, R = Ph	236	10460		162.19 (s)	67.48 (s)	79.13 (t)

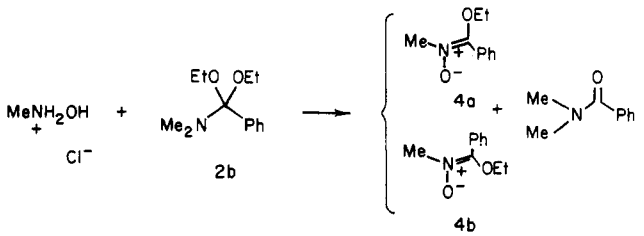
[a] The ring atoms are numbered according to the rules for dihydrooxazoles (oxazolines). [b] Solvent: 95% ethanol. [c] Chemical shifts are in parts per million in deuteriochloroform with reference to internal Me_4Si. Multiplicities are given in parenthesis: s = singlet, t = triplet. [d] Assignments may be interchanged. [e] Assignments may be interchanged.

zoline *N*-oxides by cyclocondensation. We wish to report the use of the amide acetal condensation to prepare a stable, isolable 2-phenyloxazoline *N*-oxide and the first imidate *N*-oxides. The [3 + 2] cycloaddition reactions of these novel nitrones with various dipolarophiles have been carried out to evaluate further the effect of the α-oxy substituent.

Results and Discussion

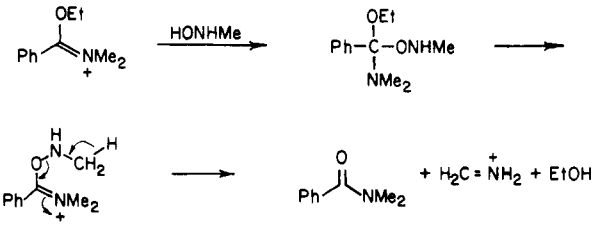
Condensation of hydroxylamino alcohol **1**[2] as its hydrochloride salt with *N*,*N*-dimethylacetamide diethyl acetal (**2a**)[3a] in dichloromethane at 25 °C for 1 h gave rise



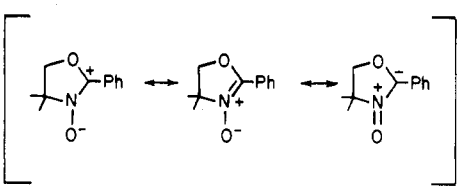


to solutions of 2,4,4-trimethyloxazoline *N*-oxide (**3a**). Since earlier attempts to isolate **3a** led to formation of impurities,[2] the presence of the oxazoline *N*-oxide was demonstrated by trapping the nitrone as a cycloadduct (**7a**) in 82% yield upon addition of phenyl isocyanate. Similar condensation of benzamide acetal **2b**[3a] with **1** afforded a 2:1 mixture of 4,4-dimethyl-2-phenyloxazoline *N*-oxide (**3b**) and *N*,*N*-dimethylbenzamide that could be separated by distillation. The crystalline phenyl-substituted oxazoline *N*-oxide, mp 93–94 °C, proved to be nonhygroscopic and stable indefinitely at ambient temperature in the open atmosphere, in contrast to the corresponding 2-methyl analogue (**3a**) and other nitrones. Like its alkyl counterpart, **3b** appeared to be stable in water, judging from the appearance of its ^1H NMR spectrum in deuterium oxide.

Condensation of benzamide acetal **2b** with 0.9 equiv of *N*-methylhydroxylamine hydrochloride produced a mixture of the *E* and *Z* imidate *N*-oxides **4a** and **4b** (14%) and *N*,*N*-dimethylbenzamide (51%). Although the *E* and *Z* isomers could be separated by flash chromatography on silica gel with methanol as eluant, the purified fractions reverted quickly to the original 5:2 mixture of isomers upon evaporation. The *E* and *Z* stereochemistry of **4a** and **4b** is tentatively assigned on the basis of the ^1H NMR chemical shifts for the *N*-methyl groups (δ 3.83 and 3.51, respectively).[4] The imidate *N*-oxides **4a** and **4b** may be regarded as nitrones of esters and are, to our knowledge, the first acyclic compounds of this type to be reported. Since the yield of **4a** and **4b** was not increased when the condensation was conducted with 1.5 equiv of amide acetal, the formation of *N*,*N*-dimethylbenzamide is evidently not caused by adventitious moisture. A plausible mechanism to rationalize the competing formation of *N*,*N*-dimethylbenzamide involves initial O-alkylation of the hydroxylamine followed by fragmentation of the N–O bond in the amino–oxy iminium ion.



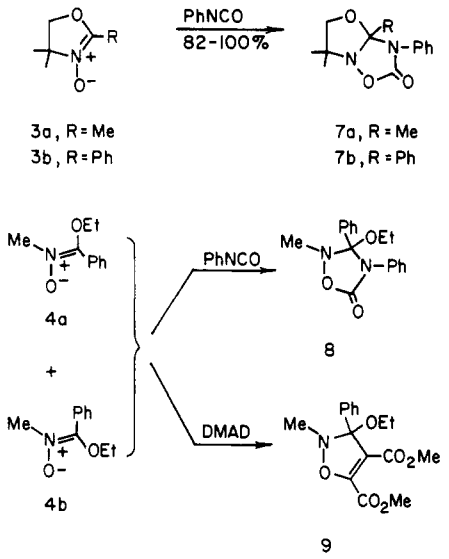
UV and ^{13}C NMR spectral data for oxazoline *N*-oxides **3a** and **3b**, as well as related pyrroline *N*-oxides (**5a** and **5b**) and oxazolines (**6a** and **6b**), are presented in Table I. The 16-nm shift of the λ_{max} of phenyloxazoline *N*-oxide **3b** compared to pyrroline analogue **5b** evidently indicates that the oxy substituent of the former lowers the HOMO–LUMO gap somewhat. The relatively high field position of the imidate carbon (δ_C 151.91 and 145.84) in the ^{13}C NMR spectra of the oxazoline *N*-oxides compared to that of the oxazolines **6a** and **6b** (δ_C 162.81 and 162.19) is interesting. It seems reasonable to attribute this upfield shift to electron donation by the *N*-oxide onto the imidate carbon via the nitrosonium resonance form. The imine



carbon of (*Z*)-*N*-methylbenzaldimine *N*-oxide (δ_C 135.0)[5a] is similarly found upfield from that of *N*-methyl benz-

(4) The resonance for the *N*-methyl groups of (*E*)- and (*Z*)-methyl *N*-methylbenzenecarboximidothioate *N*-oxide ($PhC(SCH_3)=N(O)CH_3$) appear at δ 4.08 and 3.51. The stereochemistry of the *Z* isomer was established by an X-ray crystallographic analysis. Unpublished results in this laboratory by S. Firsan.

(5) (a) Albright, T. A.; Freeman, W. J. *Org. Magn. Reson.* **1977**, *9*, 75–79. (b) Olah, G. A.; Donovan, D. J. *J. Org. Chem.* **1978**, *43*, 860–865.

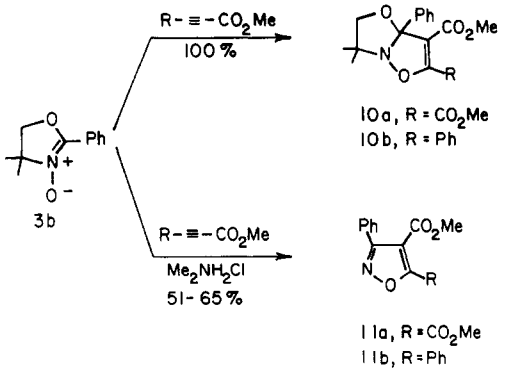


aldehyde imine (δ_C 162.2).[5b] A steric interaction between the phenyl and *N*-oxide groups may also contribute to these upfield shifts.

Phenyloxazoline *N*-oxide **3b** and the mixture of imidate *N*-oxides underwent smooth [3 + 2] dipolar cycloaddition reactions with phenyl isocyanate, dimethyl acetylenedicarboxylate (DMAD), and methyl phenylpropiolate. The 5:2 ratio of **4a** and **4b** remained unchanged after cycloadditions with less than 1 equiv of phenyl isocyanate according to NMR analysis of the product mixtures. Thus, either the *E* and *Z* isomers react at about the same rate or they undergo equilibration during or subsequent to the reaction.

The 360-MHz ^{1}H NMR spectrum of **8** exhibits signals for two *N*-methyl groups and two ethoxy groups in a 20:1 ratio. A similar doubling of peaks, but in a 1:1 ratio, is observed in the NMR spectrum of **9**. This is attributed to the presence of cis and trans isomers with respect to the *N*-methyl and ethoxy groups, which undergo interconversion by pyramidal inversion at nitrogen slowly on the NMR time scale. Slow inversion at nitrogen in various isoxazolidines has been reported in the literature.[6,7]

Cycloaddition of the two acetylenic dipolarophiles with **3b** afforded the expected bicyclic adducts **10a** and **10b** in quantitative yield. Structure **10b** is assigned to the



Scheme I

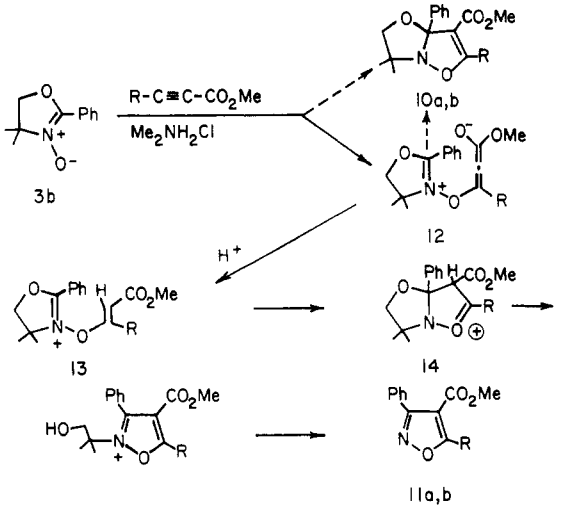


Table II. Rate Constants for the [3 + 2] Cycloaddition Reactions of Nitrones 3b and 5b with Phenyl Isocyanate and Dimethyl Acetylenedicarboxylate (DMAD) in Deuteriochloroform

nitrone	dipolarophile	adduct	k,[a,b] L mol^{-1} s^{-1}	k_{rel}
3b	phenyl isocyanate	**7b**	7.0 ± 0.4	~76 000
5b	phenyl isocyanate	**15**	9.22 (±0.05) × 10^{-5}	1
3b	DMAD	**10a**	1.12 (± 0.03) × 10^{-2}	~120
5b	DMAD	**16**	1.62 (±0.09) × 10^{-4}	21.8

[a] Average of three independent kinetic runs. [b] Rates with **3b**: concentration, 0.0015 M; temperature, 17 °C. Rates with **5b**: concentration, 0.8 M; temperature, 19 °C.

product from phenylpropiolate on the basis of a carbonyl peak at 1700 cm^{-1} in its IR spectrum[8] (vinylogous carbonate) and literature precedent.[2,9] However, when the same reactions were carried out with solutions of **3b** generated by amide acetal condensation, isoxazoles **11a** (65%) and **11b** (51%) were obtained instead of the expected cycloadducts.

The formation of isoxazoles **11a** and **11b** is attributed to the presence of dimethylamine hydrochloride in the dichloromethane solutions of **3b** resulting from amide acetal condensation. Reaction of purified oxazoline *N*-oxide **3b** with DMAD in the presence of 1 equiv of dimethylamine hydrochloride in dichloromethane afforded a 93:7 mixture of isoxazole **11a** and cycloadduct **10a**. Although a similar reaction of DMAD with **3b** and 1 equiv of triethylamine hydrochloride gave only the normal cycloadduct, this result is attributed to the insolubility of the tertiary amine salt in the reaction medium. Adducts **10a** and **10b** were shown to be stable to the reaction conditions (2 M Me_2NH_2Cl, EtOH, CH_2Cl_2 at 25 °C) and could be distilled in a Kugelrohr apparatus at 200 °C with complete recovery. Since (*N*,*N*-dimethylamino)maleate is known to be formed from conjugate addition of the amine to DMAD,[10] the possibility that this enamine is an intermediate in isoxazole formation was considered. However, no reaction occurred between independently prepared (*N*,*N*-dimethylamino)maleate[10c] and oxazoline *N*-oxide **3b** (CH_2Cl_2, 25 °C).

(6) (a) Raban, M.; Kost, D. *Tetrahedron* **1984**, *40*, 3345–3381. (b) Riddell, F. G. *J. Chem. Soc., Chem. Commun.* **1968**, 1403. (c) Muller, K.; Eschenmoser, A. *Helv. Chim. Acta* **1969**, *52*, 1823–1830. (d) Griffith, D. L.; Olson, B. L. *J. Chem. Soc., Chem. Commun.* **1968**, 1682–1683. (e) Raban, M.; Jones, F. B.; Carlson, E. H.; Banucci, E.; LeBel, N. A. *J. Org. Chem.* **1970**, *35*, 1496–1499.

(7) A referee has suggested that the complex NMR spectra of **8** and **9** might also be attributed to an equilibrium with the isoxazolium ethoxide ion pair. We consider this explanation less likely since the compounds were stable to chromatography on silica gel. Further more such an equilibrium would presumably be very rapid, leading to a time-averaged, but simple NMR spectrum.

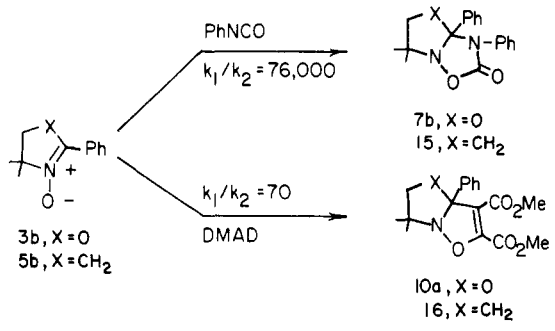
(8) Nakanishi, K.; Solomon, P. H. "Infrared Absorbtion Spectroscopy"; Holden-Day: San Francisco, 1977; p 40.

(9) (a) Houk, K. N.; Sims, J. *J. Am. Chem. Soc.* **1973**, *95*, 5798–5800. (b) Freeman, J. P. *Chem. Rev.* **1983**, *83*, 241–261.

(10) (a) Reich, H. J.; Renga, J. M.; Trend, J. E. *Tetrahedron Lett.* **1976**, 2217–2220. (b) Huisgen, R.; Giese, B.; Huber, H. *Ibid.* **1967**, 1883–1888. (c) Huisgen, R.; Herbig, K.; Siegel, A.; Huber, H. *Chem. Ber.* **1966**, *99*, 2526–2545.

A plausible mechanism for the formation of the isoxazoles is outlined in Scheme I. Protonation of zwitterionic adduct **12** would give rise to vinyloxy imminium ion **13**. Electrocyclic ring closure of the latter to amino oxonium ion **14** followed by opening of the oxazoline ring and elimination of isobutylene oxide leads to the observed isoxazoles **11a** and **11b**. The electrocyclic transformation represented by the **13** → **14** conversion is analogous to the disrotatory ring closure of *N*-vinyl azomethine imines[11] and is similar to the photochemical cyclizations of aryl vinyl ethers and amines.[12] It is not clear whether zwitterionic adduct **12** is also on the pathway to cycloadducts **10a** and **10b**. The small solvent effects associated with dipolar cycloadditions are generally considered to be inconsistent with a two-step mechanism involving a free zwitterionic intermediate solution.[13] However, if the mechanism in Scheme I is correct, it appears that nitrone **3b** and electron-deficient acetylenes readily form zwitterionic adducts (**12**) in dichloromethane. Thus, the cycloadditions of **3b** with the acetylenic dipolarophiles are probably stepwise, and this may well be the case for other nitrone 1,3-dipolar additions.[14]

Rate constants for the [3 + 2] cycloaddition reactions of oxazoline *N*-oxide **3b** and pyrroline *N*-oxide **5b** with phenyl isocyanate and dimethyl acetylenedicarboxylate were determined by NMR and are listed in Table II. The



relative rates given for the oxazoline *N*-oxides are approximate since the molar concentrations and temperatures used for **3b** and **5b** were somewhat different (0.0015 M and 17 °C vs. 0.8 M and 19 °C). Nevertheless, the data indicate that the oxazoline *N*-oxide is approximately 76 000 times more reactive toward phenyl isocyanate than the pyrroline *N*-oxide and about 70 times more reactive toward dimethyl acetylenedicarboxylate than the pyrroline *N*-oxide. The rate ratios are consistent with those calculated from independently conducted competitive experiments between nitrones **3b** and **5b** for phenyl isocyanate ($k_1/k_2 \geq 4200$) and DMAD ($k_1/k_2 = 80$) and with those previously reported[2] from competitive cycloadditions between nitrones **3a** and **5a** for the same dipolarophiles ($k_1/k_2 \geq 6800$ and $k_1/k_2 = 160$, respectively). The enhanced reactivity of oxazoline *N*-oxides has been rationalized[2] in terms of frontier molecular orbital theory.[15]

Experimental Section

Melting points were determined on a Reichert micro-hot-state melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. UV spectra were obtained on a Perkin-Elmer Lambda 3 UV–vis spectrophotometer. NMR spectra were determined on a Nicolet NT-360 spectrometer. The frequency for proton was 360 MHz and for carbon was 90 MHz. 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 were distilled prior to 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.

1,1-Diethoxy-*N*,*N*-dimethylethanamine (2a) was prepared from 8.71 g (100 mmol) of *N*,*N*-dimethylacetamide (Aldrich Chemical Co.) according to the procedures of Feugeas and Olschwang.[3a] The yield of colorless oil, bp 43–44 °C (10 mm) [lit.[3a] bp 32 °C (8 mm)], was 4.84 g (30 mmol, 30%): IR (film) ν_{max} 2900, 1170, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (t, 6 H, J = 7 Hz, CH_2CH_3), 1.22 (s, 3 H, CH_3), 2.28 (s, 6 H, CH_3), 3.47 and 3.53 (2 dq, 4 H, J = 7, 10 Hz, CH_2CH_3). Anal. Calcd for $C_8H_{19}NO_2$: C, 59.59; H, 11.88; N, 8.69. Found: C, 59.43; H, 11.78; N, 8.95.

α,α-Diethoxy-*N*,*N*-dimethylbenzenemethanamine (2b) was prepared from 28.3 g (190 mmol) of *N*,*N*-dimethylbenzamide[3a] according to the procedure of Feugeas and Olschwang.[3a] The product was judged to be 92% pure by NMR. The yield of colorless oil, bp 52–53 °C (0.1 mm) [lit.[3a] bp 32 °C (10^{-5} mm)], was 20.3 g (91 mmol, 48%): IR (film) ν_{max} 2900, 1460, 1270, 1030, 770, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (t, 6 H, J = 7 Hz, CH_2CH_3), 2.09 (s, 6 H, CH_3), 3.44 and 3.58 (2 dq, 4 H, J = 7, 10 Hz, CH_2CH_3), 7.26–7.40 (m, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{21}NO_2$: C, 69.92; H, 9.48; N, 6.27. Found: C, 70.01; H, 9.37; N, 6.30.

4,5-Dihydro-2,4,4-trimethyloxazole 3-oxide (3a) was generated in deuteriochlorofrm solution according to the published procedures.[2] The crude product exhibited the following ^{13}C NMR spectral properties: ^{13}C NMR ($CDCl_3$) δ 10.27 (q, CH_3 at C-2), 23.90 (q, *gem*-dimethyl), 67.31 (s, C-4), 78.40 (t, CH_2O), 151.91 (s, C-2).

4,5-Dihydro-4,4-dimethyl-2-phenyloxazole 3-Oxide (3b). A solution of 2.95 g (20.8 mmol) of hydrochloride **1**[2] and 4.65 g (19.2 mmol based on 92% purity) of amide acetal **2b** in 8 mL of dichloromethane was stirred at 25 °C for 4 h. The solvent was evaporated, and the residue was suspended in ether. Filtration of the mixture and evaporation of solvent yielded 3.54 g of an oil, which was judged to be a 2:1 mixture of nitrone **3b** and *N*,*N*-dimethylbenzamide in 65% and 30% yields, respectively, by the integrated ratios of the nitrone *gem*-dimethyl group at δ 1.60, the amide *N*,*N*-dimethyl group at δ 2.98, and the methyl group of an internal hexamethylbenzene standard at δ 2.20 in the ^1H NMR spectrum. The oil was purified by fractional distillation through a 15-cm Vigreux column yielding 0.57 g (20% based on amide acetal **2b**) of *N*,*N*-dimethylbenzamide, bp 60–70 °C (0.1 mm), and 2.16 g (59% based on amide acetal) of nitrone **3b**, bp 113–120 °C (0.1 mm). The latter fraction, which subsequently solidified, gave a satisfactory microanalysis and was judged to be 97% pure by NMR. Recrystallization from hexane gave 1.47

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g (40% based on amide acetal) of colorless needles, mp 93–94 °C.

The ^1H NMR spectrum of nitrone **3b** in deuterium oxide showed no time dependence. In addition, evaporation of a solution of 100 mg of nitrone **3b** in 2 mL of water left 100 mg of a white solid, mp 91–93 °C. The ^1H NMR spectrum of this solid in $CDCl_3$ was identical with that of the starting nitrone. Thus, the nitrone evidently is stable to hydrolysis.

The product exhibited the following spectral properties: IR ($CHCl_3$) ν_{max} 2900, 1440, 1370, 1260, cm^{-1}; UV (EtOH) λ_{max} 231 (ϵ 12 380), 308 (9770) nm; ^1H NMR ($CDCl_3$) δ 1.60 (s, 6 H, CH_3), 4.41 (s, 2 H, CH_2O), 7.46–7.48 (m, 3 H, *m*- and *p*-C_6H_5), 8.47–8.49 (m, 2 H, *o*-C_6H_5); ^1H NMR (CD_2Cl_2) δ 1.52 (s, 6 H, CH_3), 4.39 (s, 2 H, CH_2O), 7.46–7.49 (m, 3 H, *m*- and *p*-C_6H_5), 8.43–8.46 (m, 2 H, *o*-C_6H_5); ^1H NMR (D_2O) δ 1.55 (s, 6 H, CH_3), 4.63 (s, 2 H, CH_2O), 7.58–7.72 (m, 3 H, *m*- and *p*-C_6H_5), 8.32–8.34 (m, 2 H, *o*-C_6H_5); ^{13}C NMR ($CDCl_3$) δ 23.90 (q, J = 129 Hz, *gem*-dimethyl), 69.63 (s, C-4), 76.84 (t, CH_2O), 123.39 (s, C_6H_5), 126.82 (d, J = 144 Hz, *o*- or *m*-C_6H_5), 128.35 (d, J = 141 Hz, *o*- or *m*-C_6H_5), 131.35 (d, J = 161 Hz, *p*-C_6H_5), 145.84 (s, C-2). Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.02; H, 6.93; N, 7.26.

Ethyl *N*-Methylbenzenecarboximidate *N*-Oxide (4). A solution of 2.21 g (26.4 mmol) of *N*-methylhydroxylamine hydrochloride (Aldrich Chemical Co.) and 5.90 g (24.3 mmol based on 92% purity) of amide acetal **2b** in 10 mL of dichloromethane was stirred at 25 °C for 5 h. The solvent was evaporated and the residue was suspended in ether. Filtration of the mixture and evaporation of the solvent gave 3.78 g of an oil. The oil was fractionally distilled through a 15-cm Vigreux column yielding 1.84 g (51% based on amide acetal) of *N,N*-dimethylbenzamide, bp 75–80 °C, and 1.37 g of crude nitrone **4** by NMR analysis. The crude nitrone mixture was purified further by flash chromatography on 300 g of Woelm 32–63 μm silica gel by flash chromatography apparatus with methanol as eluant. Two fractions were collected, corresponding to two different nitrone isomers (**4a** and **4b**), and each was pure by thin-layer chromatography. Evaporation of solvent yielded 0.22 g (5% based on amide acetal) of the first fraction and 0.37 g (9% based amide acetal) of the second fraction, each of which was judged to be identical 5:2 mixtures of nitrone isomers **4a**–**4b** by the integrated ratio of the *N*-methyl groups at δ 3.83 and 3.51, respectively, in the NMR spectrum. The infrared spectra of the two fractions were identical, and both fractions exhibited a satisfactory analysis. Both fractions exhibited the following spectral properties: IR (film) ν_{max} 1625, 1220, 1070, 770, 690 cm^{-1}; ^1H NMR ($CDCl_3$) **4a**, δ 1.39 (t, 3 H, J = 7 Hz, CH_2CH_3), 3.83 (s, 3 H, CH_3), 3.94 (q, 2 H, J = 7 Hz, CH_2CH_3), 7.40–8.18 (m, 5 H, C_6H_5), **4b**, δ 1.35 (t, 3 H, J = 7 Hz, CH_2CH_3), 3.51 (s, 3 H, CH_3), 4.04 (q, 2 H, J = 7 Hz, CH_2CH_3), 7.40–8.18 (m, 5 H, C_6H_5). Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.79; H, 7.32; N, 7.88.

3,4-Dihydro-2,2,5-trimethyl-2*H*-pyrrole 1-oxide (5a) was prepared from 34.20 g (0.22 mol) of 5-methyl-5-nitro-2-hexanone[17] according to the procedure of Delpierre and Lamchen.[18] The yield of colorless oil, bp 84–86 °C (2 mm) [lit.[18] bp 71–72 °C (2 mm)], was 26.01 g (0.21 mol, 95%): IR (film) ν_{max} 2880, 1590, 1220, 725 cm^{-1}; UV (EtOH) λ_{max} 230 (ϵ 9950) nm; ^1H NMR ($CDCl_3$) δ 1.40 (s, 6 H, *gem*-dimethyl), 2.03 (s, 3 H, CH_3 at C-5), 2.00 and 2.58 (2 t, 4 H, J = 7 Hz, CH_2CH_2); ^{13}C NMR ($CDCl_3$) δ 13.04 (q, J = 129 Hz, CH_3 at C-5), 25.43 (q, J = 126 Hz, *gem*-dimethyl), 29.05 (t, J = 135 Hz, CH_2CH_2), 32.21 (t, J = 133 Hz, CH_2CH_2), 73.05 (s, C-2), 140.79 (s, C-5).

3,4-Dihydro-2,2-dimethyl-5-phenyl-2*H*-pyrrole 1-oxide (5b) was prepared from 3.83 g (20.0 mmol) of 1-hydroxy-2,2-dimethyl-5-phenylpyrrolidine[19] according to the procedures of Black and Boscacci.[19] The yield of colorless prisms, mp 100–101 °C (lit.[19] mp 101–102 °C), was 2.91 g (77%): IR ($CHCl_3$) ν_{max} 2870, 1540, 1440, 1360, 1200 cm^{-1}; UV (EtOH) λ_{max} 224 (ϵ 8580), 292 (15 790) nm; ^1H NMR ($CDCl_3$) δ 1.50 (s, 6 H, *gem*-dimethyl), 2.12 and 3.05 (2 t, 4 H, J = 7 Hz, CH_2CH_2), 7.41–7.45 (m, 3 H, *m*- and *p*-C_6H_5), 8.36–8.40 (m, 2 H, *o*-C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.56 (q, J = 128 Hz, *gem*-dimethyl), 26.73 (d, J = 134 Hz, CH_2CH_2), 31.85 (d, J = 133 Hz, CH_2CH_2), 75.59 (s, C-2), 127.10 (d, J = 162 Hz, *o*- or *m*-C_6H_5), 128.24 (d, J = 160 Hz, *o*- or *m*-C_6H_5), 129.72 (s, C_6H_5), 129.80 (d, J = 161 Hz, *p*-C_6H_5), 137.32 (s, C-5). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.24; H, 7.99; N, 7.35.

4,5-Dihydro-2,4,4-trimethyloxazole (6a) was prepared according to the procedure of Allen and Ginos.[20] The yield of colorless oil, bp 112–113 °C (lit.[20] bp 112–113 °C), was 43 g (38%): ^{13}C NMR ($CDCl_3$) δ 14.00 (q, J = 129 Hz, CH_3 at C-2), 28.43 (q, J = 126 Hz, *gem*-dimethyl), 67.04 (s, C-4), 79.14 (t, J = 148 Hz, CH_2O), 162.81 (s, C-2).

4,5-Dihydro-4,4-dimethyl-2-phenyloxazole (6b) was prepared according to the procedures of Allen and Ginos.[20] The yield of colorless oil, bp 131–133 °C (15 mm) [lit.[20] bp 112–114 °C (10 mm)], was 4.67 g (53%): IR (film) ν_{max} 1640, 1350, 1060, 780, 690 cm^{-1}; UV (EtOH) λ_{max} 236 (ϵ 10 460) nm; ^1H NMR ($CDCl_3$) δ 1.40 (s, 6 H, *gem*-dimethyl), 4.12 (s, 2 H, CH_2O), 7.40–7.47 (m, 3 H, *m*- and *p*-C_6H_5), 7.93–7.96 (m, 2 H, *o*-C_6H_5); ^{13}C NMR ($CDCl_3$) δ 28.31 (q, J = 127 Hz, *gem*-dimethyl), 67.48 (s, C-4), 79.13 (t, J = 149 Hz, CH_2O), 127.94 (s, C_6H_5), 128.20 and 128.24 (2 d, J = 161 Hz, *o*- and *m*-C_6H_5), 131.16 (d, J = 161 Hz, *p*-C_6H_5), 162.19 (s, C-2).

3,3a,5,6-Tetrahydro-3a,6,6-trimethyl-3-phenyl-2*H*-oxazolo[3,2-*b*][1,2,4]oxadiazol-2-one (7a).[2] Procedure for the in Situ Generation of 2-Phenyl- and 2,4,4-Trimethoxyoxazoline *N*-Oxides. A solution of 0.31 g (1.9 mmol) of amide acetal **2a** [or 0.43 g (1.9 mmol) of amide acetal **2b** for nitrone **3b**] in 1 mL of dichloromethane was added to a suspension of 0.25 g (1.8 mmol) of hydrochloride **1** in 1 mL of dichloromethane, and the solution was stirred at 25 °C for 1 h. A 0.2-mL (1.9 mmol) aliquot of phenyl isocyanate was added dropwise at 0 °C, and the solution was stirred at 25 °C for 1 h. Purification by flash chromatography and crystallization from hexane gave 0.36 g (82% based on hydroxylamine hydrochloride **1**) of colorless prisms, mp 65–66 °C (lit.[2] mp 65–66 °C): ^{13}C NMR ($CDCl_3$) δ 19.85 (q, J = 127 Hz, CH_3), 25.12 (q, J = 129 Hz, CH_3), 26.06 (q, J = 127 Hz, CH_3), 67.78 (s, C-6), 73.01 (t, J = 147 Hz, CH_2O), 112.22 (s, C-3a), 126.01 (d, J = 163 Hz, *o*- or *m*-C_6H_5), 127.69 (d, *p*-C_6H_5), 129.17 (d, J = 161 Hz, *o*- or *m*-C_6H_5), 133.82 (s, C_6H_5), 153.63 (s, C=O).

General Procedure for Preparative Cycloadditions (7b, 8, 9, 10a,b, and 16). Solutions of 1 equiv (0.8–1.3 mmol) of nitrone and 1.1 equiv of dipolarophile in 1 mL of dichloromethane (benzene for nitrone **5b**) were stirred at 25 °C for the indicated time in hours. Adducts **8**, **9**, **15**, and **16** were purified by flash chromatography. Adducts **10a,b** were purified by evaporation of solvent and removal of impurities under reduced pressure. The weight (mg) and percent yields (based on nitrone) are given, followed by spectral data. All adducts except **7b** were obtained as colorless oils.

3,3a,5,6-Tetrahydro-6,6-dimethyl-3,3a-diphenyl-2*H*-oxazolo[3,2-*b*][1,2,4]oxadiazol-2-one (7b): time, 2 h; yield, 327 mg (100%) of white crystals; mp 196–197 °C; IR ($CHCl_3$) ν_{max} 1740, 1370, 1145, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 and 1.50 (2 s, 6 H, CH_3), 4.09 (s, 2 H, CH_2O), 7.15–7.59 (m, 10 H, C_6H_5). Anal. Calcd for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.26; H, 5.75; N, 9.14.

3-Ethoxy-2-methyl-3,4-diphenyl-1,2,4-oxadiazol-5-one (8): time, 5 h; yield, 206 mg (88%); IR (film) ν_{max} 1760, 1600, 1490, 1350, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 and 1.38 (2 t, 3 H, J = 7 Hz, OCH_2CH_3), 2.58 and 2.65 (2 s, 3 H, NCH_3), 3.72 and 4.12 (2 dq, 2 H, J = 7, 9 Hz, CH_2CH_3), 7.05–7.60 (m, 10 H, C_6H_5). Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.20; H, 6.03; N, 9.41.

Dimethyl 3-ethoxy-2,3-dihydro-2-methyl-3-phenylisoxazole-4,5-dicarboxylate (9): time, 1 h; yield, 186 mg (45%); IR (film) ν_{max} 2900, 1750, 1700, 1200, 1110, 750, 695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 and 1.35 (2 t, 3 H, J = 7 Hz, OCH_2CH_3), 2.95 and 2.97 (2 s, 3 H, NCH_3), 3.60, 3.61, 3.86, and 3.89 (4 s, 6 H, OCH_3), 3.65–3.80 (m, 2 H, OCH_2CH_3), 7.40–7.60 (m, 5 H, C_6H_5); Exact mass calcd for $C_{16}H_{19}NO_6$ m/e 321.12124, found m/e 321.12117.

Dimethyl 3a,6-dihydro-6,6-dimethyl-3a-phenyl-5*H*-oxazolo[3,2-*b*]isoxazole-2,3-dicarboxylate (10a): time, 2 h; yield, 350 mg (100%); IR (film) ν_{max} 1750, 1720, 1220, 1140, 1050, 745, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 and 1.42 (2 s, 6 H, *gem*-di-

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methyl), 3.54 and 3.94 (2 s, 6 H, OCH_3), 3.61 and 3.99 (2 d, 2 H, J = 9 Hz, CH_2O), 7.30–7.35 (m, 3 H, *m*- and *p*-C_6H_5), 7.62–7.66 (m, 2 H, *o*-C_6H_5); ^1H NMR (CD_2Cl_2) δ 0.94 and 1.39 (2 s, 6 H, *gem*-dimethyl), 3.51 and 3.90 (2 s, 6 H, OCH_3), 3.56 and 3.98 (2 d, 2 H, J = 9 Hz, CH_2O), 7.31–7.35 (m, 3 H, *m*- and *p*-C_6H_5), 7.58–7.62 (m, 2 H, *o*-C_6H_5). Anal. Calcd for $C_{17}H_{19}NO_6$: C, 61.25; H, 5.75; N, 4.20. Found: C, 61.09; H, 5.81; N, 4.15.

Methyl 3a,6-dihydro-6,6-dimethyl-2,3a-diphenyl-5*H*-oxazolo[3,2-*b*]isoxazole-3-carboxylate (10b): time, 71 h; yield, 370 mg (100%); IR (film) ν_{max} 1700, 1635, 1330, 1110, 750, 690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.03 and 1.45 (2 s, 6 H, *gem*-dimethyl), 3.43 (s, 3 H, OCH_3), 3.66 and 4.01 (2 d, 2 H, J = 9 Hz, CH_2O), 7.26–7.50 (m, 6 H, *m*- and *p*-C_6H_5), 7.68–7.78 (m, 4 H, *o*-C_6H_5); ^1H NMR (CD_2Cl_2) δ 0.98 and 1.42 (2 s, 6 H, *gem*-dimethyl), 3.39 (s, 3 H, OCH_3), 3.61 and 3.97 (2 d, 2 H, J = 9 Hz, CH_2O), 7.27–7.51 (m, 6 H, *m*- and *p*-C_6H_5), 7.65–7.74 (m, 4 H, *o*-C_6H_5); exact mass calcd for $C_{21}H_{21}NO_4$ m/e 351.14706, found m/e 351.14697. Anal. Calcd for $C_{21}H_{21}NO_4$: C, 71.78; H, 6.02; N, 3.99. Found: C, 71.38; H, 5.91; N, 3.86.

Hexahydro-6,6-dimethyl-3,3a-diphenylpyrrolo[1,2-*b*][1,2,4]oxadiazol-2-one (15): time, 12 h; yield, 257 mg (79%); IR (film) ν_{max} 1750, 1600, 1490, 1210, 965, 760, 690 cm^{-1}; ^1H NMR ($CDCl_3$) 1.31 and 1.39 (2 s, 6 H, *gem*-dimethyl), 1.99 and 2.08 (2 dd, 2 H, J = 7, 13 Hz, CH_2), 2.58 (t, 2 H, J = 7 Hz, CH_2), 7.05–7.40 (m, 10 H, C_6H_5). Anal. Calcd for $C_{19}H_{20}N_2O_2$: C, 74.00; H, 6.54; N, 9.08. Found: C, 74.06; H, 6.70; N, 8.94.

Dimethyl 3a,4,5,6-tetrahydro-6,6-dimethyl-3a-phenylpyrrolo[1,2-*b*]isoxazole-2,3-dicarboxylate (16): time, 12 h; yield, 321 mg (92%); IR (film) ν_{max} 1745, 1710, 1650, 1300, 1200, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 and 1.38, (2 s, 6 H, *gem*-dimethyl), 1.70–2.95 (m, 2 H, CH_2), 2.40–2.60 (m, 1 H, CH), 2.80–2.95 (m, 1 H, CH), 3.62 and 3.88 (2 s, 6 H, OCH_3), 7.20–7.40 (m, 3 H, *m*- and *p*-C_6H_5), 7.59–7.63 (m, 2 H, *o*-C_6H_5). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.23; H, 6.57; N, 4.14.

Dimethyl 3-Phenylisoxazole-4,5-dicarboxylate (11a). Method A. A solution of nitrone **3b** (prepared from 0.25 g (1.8 mmol) of hydrochloride **1**, 2 M in dimethylamine hydrochloride), a 0.27-mL (2.2 mmol) aliquot of dimethyl acetylenedicarboxylate, and 1 mL of dichloromethane was stirred at 25 °C for 3 h. Purification by flash chromatography and crystallization from hexane gave 0.26 g (56% based on hydroxylamine salt) of colorless acicular needles, mp 66–67 °C (lit.[21] mp 64–65 °C).

Method B. A 0.27-mL (2.2 mmol) aliquot of dimethyl acetylenedicarboxylate was added dropwise to a stirring solution of 338 mg (1.8 mmol) of nitrone **3b**, 147 mg (1.9 mmol) of (2 M) dimethylamine hydrochloride (mp 170–171 °C), 163 mg (3.6 mmol) of absolute ethanol, and 1 mL of dichloromethane-d_2 at 0 °C. The solution was stirred at 25 °C for 2 h. The crude reaction mixture was judged to contain a 93:7 mixture of isoxazole **11a** and adduct **10a** by the ratio of the peak heights of the isoxazole methyl ester groups at δ 3.88 and 4.00 and the adduct methyl ester groups at δ 3.51 and 3.90 in the proton NMR (CD_2Cl_2) spectrum. Purification by flash chromatography and crystallization from hexane gave 391 mg (85% based on nitrone **3b**) of colorless acicular needles, mp 66–67 °C: IR ($CHCl_3$) ν_{max} 1735, 1430, 1290, 1140, 1070 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91 and 4.02 (2 s, 6 H, OCH_3), 7.47–7.70 (m, 5 H, C_6H_5); ^1H NMR (CD_2Cl_2) δ 3.88 and 4.00 (2 s, 6 H, OCH_3), 7.49–7.70 (m, 5 H, C_6H_5); exact mass calcd for $C_{13}H_{11}NO_5$ m/e 261.06372, found m/e 261.06374. Anal. Calcd for $C_{13}H_{11}NO_5$: C, 59.77; H, 4.24; N, 5.36. Found: C, 59.69; H, 4.03; N, 5.37.

Methyl 3,5-Diphenylisoxazole-4-carboxylate (11b). A solution of nitrone **3b** (prepared from 0.25 g (1.8 mmol) of hydrochloride **1**, 2 M in dimethylamine hydrochloride), 0.31 g (1.9 mmol) of methyl phenylpropiolate,[2] and 1 mL of dichloromethane was stirred at 25 °C for 48 h. Purification by flash chromatography yielded 0.25 g of an oil, which was crystallized from hexane into 0.11 g (22% based on hydroxylamine salt) or colorless rectangular prisms, mp 99–100 °C (lit.[22] mp 98–99 °C): IR ($CHCl_3$) ν_{max} 1715, 1315, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.72 (s, 3 H, OCH_3), 7.47–7.93 (m, 10 H, C_6H_5). Anal. Calcd for $C_{17}H_{13}NO_3$: C, 73.11; H, 4.69; N, 5.01. Found: C, 73.09; H, 4.63; N, 5.02.

General Procedures for the Determination of Rate Constants for Cycloadditions. A. Oxazoline *N*-Oxide 3b. Separate solutions of 6.0 mg (0.03 mmol) of nitrone **3b** and 3.7 mg (0.03 mmol) of phenyl isocyanate each in 10 mL of deuteriochloroform were prepared (final concentration, 0.0015 M). A 0.5-mL aliquot of each solution was added to a 5-mm OD NMR tube, and a NMR spectrum was recorded every 60 s (T = 17 °C). The ratio of adduct **7b** to nitrone **3b** was calculated for each spectrum by division of the sum of adduct **7b** *gem*-dimethyl peak heights by the nitrone **3b** *gem*-dimethyl peak height. The slope of the ratios as a function of time was calculated by means of the least-mean-squares program on a Texas Instruments TI-55 calculator, and the rate constant was calculated by the method of Daniels and Alberty.[23] Three independent measurements of the rate constant and the average rate constant for the cycloadditions of nitrone **3b** with phenyl isocyanate are as follows: k = 6.6, 7.0, 7.4 L mol^{-1} s^{-1}; k_{av} = 7.0 (±0.4) L mol^{-1} s^{-1}.

Separate solutions of 120.0 mg (0.63 mmol) of **3b** and 89.2 mg (0.63 mmol) of DMAD each in 10 mL of deuteriochloroform were prepared, and the rate constants were determined as above: k = 1.10 × 10^{-2}, 1.16 × 10^{-2}, 1.11 × 10^{-2} L mol^{-1} s^{-1}; k_{av} = 1.12 (±0.03) × 10^{-2} L mol^{-1} s^{-1}.

B. Pyrroline *N*-Oxide 5b. Separate solutions of 37.5 mg (20.0 mmol) of **5b** and 23.6 mg (20.0 mmol) of phenyl isocyanate and 37.5 mg (20.0 mmol) of **5b** and 28.2 mg (20.0 mmol) of DMAD each in chloroform-*d* were prepared (final volume, 0.25 mL; concentration, 0.8 M). Aliquots were removed from each solution (T = 19 °C) approximately every 45 min and diluted about 50 fold with chloroform-*d*, and then the NMR spectrum was obtained. The rate constants were calculated in the same manner as above. **5b** and phenyl isocyanate: k = 9.20 × 10^{-5}, 9.28 × 10^{-5}, 9.19 × 10^{-5} L mol^{-1} s^{-1}; k_{av} = 9.22 (±0.05) × 10^{-5} L mol^{-1} s^{-1}. **5b** and DMAD: 1.66 × 10^{-4}, 1.69 × 10^{-4}, 1.51 × 10^{-4} L mol^{-1} s^{-1}; k_{av} = 1.62 (±0.09) × 10^{-4} L mol^{-1} s^{-1}.

Acknowledgment. This research was supported in part by a grant (CA 20436) from the National Institutes of Health. High-field NMR spectra were obtained with the aid of the Midwest Regional Instrumentation Facility for NMR Spectroscopy sponsored by the National Science Foundation (CHE 79-16100).

Registry No. 1, 63829-84-5; **2a**, 19429-85-7; **2b**, 19429-87-9; **3a**, 90900-23-5; **3b**, 96915-24-1; **4a**, 96915-25-2; **4b**, 96915-26-3; **5a**, 4567-18-4; **5b**, 58134-17-1; **6a**, 1772-43-6; **6b**, 19312-06-2; **7a**, 90900-25-7; **7b**, 96915-27-4; **8**, 96915-28-5; **9**, 96915-29-6; **10a**, 96915-30-9; **10b**, 96915-31-0; **11a**, 7710-44-3; **11b**, 2289-55-6; **15**, 96915-32-1; **16**, 96915-33-2; *N*,*N*-dimethylbenzamide, 611-74-5; *N*-methylhydroxylamine hydrochloride, 4229-44-1; phenyl isocyanate, 103-71-9; dimethyl acetylenedicarboxylate, 762-42-5; methyl phenylpropiolate, 4891-38-7.

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