chromatographed in a 2.54 × 50 cm Sephadex LH-20 column using methyl acetate as solvent (4.3 mL/min) and a refractive index detector. After a forecut of about 450 mL, **2a** was eluted within 90 mL followed immediately by **1a** (300 mL). The purity of **2a** isolated after solvent evaporation was 84% (^{1}H NMR, LC). Material, mp 23–27 °C, obtained by evaporation of the middle third portion of the second peak was 99.9% pure **1a** (LC). Traces of succinimide and 3-methylpyrrolin-2-one were found in intermediate fractions.

***N*-Methylpyrrolin-2-ones (1c and 2c).** This procedure was adopted from Atkinson et al.[9] *N*-Methylpyrrole (192 g, 2.37 mol) and pyridine (320 mL) were heated at 90 ± 2 °C. H_2O_2 (240 mL, 30% w/v, 2.17 mol) was added over 1.5 h with stirring at the same temperature. The reaction was not exothermic. Heating was continued for an additional 5 h and the mixture was left at 24 °C overnight. The mixture was heated again at 90 °C and a pinch of PbO_2 was added to destroy any remaining peroxide. Most of the pyridine and unreacted *N*-methylpyrrole were removed by evaporation in vacuo at 40 °C. The residue was extracted with 200 mL of $CHCl_3$, the extract was dried with Na_2SO_4, and the solvent was evaporated. Repeated fractional distillation at 40–41 °C (0.1 mm) yielded 40 g (19% yield) of light yellow liquid. The product was a 9:1 mixture of **1c** and **2c**, respectively: ^{1}H NMR (neat) **1c**, δ 7.3 (m, C4-H), 6.2 (m, C3-H), 4.1 (m, C5-H_2), 2.9 (s, CH_3); **2c**, δ 6.7 (m, C5-H), 5.3 (m, C4-H), 3.0 (m, C3-H_2), 3.0 (s, CH_3).

Enrichment of *N*-Methyl-Δ^3-pyrrolin-2-one (1c). An isomeric mixture of **1c** and **2c** (9:1 molar ratio, respectively) (2.7 g) was dissolved in 16 mL of Et_2O and made slightly cloudy with the addition of 10 mL of hexanes. The mixture was cooled over 3 h with stirring to -5 °C under N_2. The liquid was decanted off quickly and the solid was washed twice by decantation with 10 mL of 1.6:1 v/v Et_2O/hexanes at -70 °C. The solid recovered after evaporation of the solvent in vacuo was 2.2 g (81% yield) of 98% **1b** and 2% **2b**.

Acknowledgments. We wish to thank Dr. William J. Boyle, Jr., for helpful discussions and assistance in the preparation of this paper.

Registry No. 1a, 4031-15-6; **1b**, 70399-10-9; **1c**, 13950-21-5; **2a**, 27406-82-2; **2b**, 70399-11-0; **2c**, 22124-67-0; **3**, 25747-41-5; **4**, 70399-12-1; methyl 4-phthalimidocrotonoate, 54238-27-6; potassium phthalimide, 1074-82-4; methyl 4-bromocrotonoate, 1117-71-1; 4-amino-3-hydroxybutyric acid hydrochloride, 51085-21-3; 4-amino-3-hydroxybutyric acid, 352-21-6; *N*-methylpyrrole, 96-54-8.

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(11) This procedure was developed in cooperation with Louis Palmer, Separation Labs, Allied Chemical Corp., Morristown, N.J.

Alkyl Substituent Effects on Rates of Arylnitrile Oxide Cycloadditions

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Alkyl substituents may either accelerate or decelerate the rates of attack by electrophiles on alkenes. The gas-phase proton affinity of ethylene is increased as the number or size of attached alkyl groups is increased,[2] and this behavior is for the most part paralleled by rates of acid-catalyzed hydration.[3] The results reflect the cation-stabilizing effects of alkyl substituents. However, for other electrophiles such as bromine,[4] carbenes,[5] and boranes,[6] increasing the number or size of alkyl substituents causes first acceleration and then deceleration, the latter a reflection of the steric effects of alkyl substituents.

Table I. Rates of Cycloadditions of Benzonitrile Oxides to Alkylethylenes in CCl_4 (L/(mol s) × 10^{-3})

alkene			substituted BNO[a]	
R	R′	IP[11]	*p*-NO_2 (25 °C)	*p*-MeO (20 °C)
H	H	10.52		
Me	H	9.90	13.4	2.41[b]
Et	H	9.79	12.9	2.41
Pr	H	9.68	12.6	2.38
Bu	H	9.64	12.9	2.39
i-Pr	H	9.69	11.3	2.08
t-Bu	H	9.61	7.26	1.44
Me	Me	9.40	4.79	0.691

[a] BNO = Benzonitrile oxide. [b] The propene rate was measured at −12.5 °C and was found to be identical (0.090 × 10^{-3} L/(mol s)) to that of 1-butene at the same temperature.

Less is known about the influence of alkyl substituents on concerted 1,3-dipolar cycloadditions. Huisgen and co-workers have reported that the relative rates of cycloadditions of benzonitrile oxide to ethylene, propene, and 1-hexene are 1:0.32:0.31,[7] which suggests that the steric, rather than the electronic, influence of alkyl substituents is being manifested. We report here a study of the rates of cycloadditions of *p*-methoxy- and *p*-nitrobenzonitrile oxides (MBNO and NBNO, respectively) to a series of simple alkenes—propene, 1-butene, 1-pentene, 1-hexene, 3-methyl-1-butene, 3,3-dimethyl-1-butene, and isobutene. Our goal was, first, to determine the influence of the "classic" series of alkyl substituents on rates of cycloadditions of relatively electrophilic 1,3 dipoles[7,8] and, second, to determine whether increasing the electrophilicity of the nitrile oxide would cause the electron-donor influence of the alkyl substituents to be manifested. Third, we wished to have quantitative rate data to compare with theoretical treatments of 1,3-dipolar cycloaddition rates.[9,10]

Results and Discussion

The cycloadditions studied here all gave, within the experimental limits of detection (by NMR), only the 5-substituted isoxazolines:

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[7] Bast, K.; Christl, M.; Huisgen, R.; Mack, W. *Chem. Ber.* **1973**, *106*, 3313.

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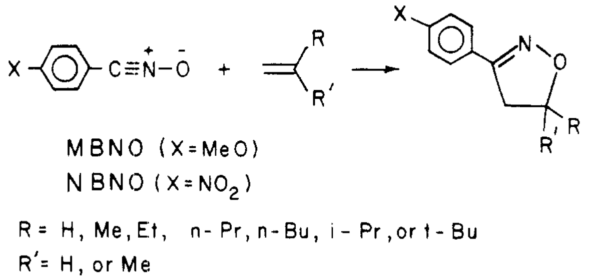


MBNO (X=MeO)
NBNO (X=NO$_2$)

R = H, Me, Et, n-Pr, n-Bu, i-Pr, or t-Bu
R′ = H, or Me

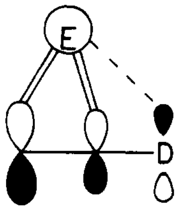
The rates of these reactions were measured by following the disappearance of the nitrile oxide band at 2290 cm^{-1} in the infrared spectrum, under conditions where the rates of dimerization of the nitrile oxides are negligible compared to the rates of cycloadditions to alkenes. The results are given in Table I, which also includes ionization potentials of the various alkenes studied here.[11]

In accord with the electrophilic nature of the nitrile oxide, NBNO reacts about 10 times faster than MBNO with all of the alkenes studied here.[12] This is compatible with the dominant interaction of the 1,3-dipole LUMO with the alkene HOMO: the nitro group should lower the LUMO energy of the nitrile oxide and increase the interaction of this orbital with the alkene HOMO, accelerating the reaction.[8,9] This nitrile oxide LUMO–alkene HOMO interaction also governs the regioselectivity of the cycloaddition, since the unsubstituted terminus of the alkene (larger HOMO coefficient) will prefer to become bonded to the carbon terminus of the nitrile oxide (larger LUMO coefficient) in the transition state.[9]

However, this frontier orbital interaction should also be increased by alkyl substituents, which lower the alkene IP or, equivalently, raise the alkene HOMO energy. Nevertheless, there is either no change, or a small decrease, in rates of reaction of arylnitrile oxide as the IP of the alkene decreases. More potent electron donors do accelerate the reaction but only feebly. For example, butyl vinyl ether reacts 2.1 times faster than ethylene with BNO at 0 °C, while styrene reacts only 1.2 times faster than ethylene with BNO, in spite of the low IP of styrene (8.48 eV).[7]

The decrease in rate of reaction upon alkylation of alkenes, like that observed for other electrophilic additions, can be classified as a steric effect. Although there is no general correlation with Taft's steric substituent parameter[13] E_s for all the substituents, good correlations are obtained for Me, Et, *i*-Pr, and *t*-Bu substituents, with $\log (k_R/k_{Me}) = 0.38 + 0.14E_s$ for MBNO and $\log (k_R/k_{Me}) = 1.13 + 0.18E_s$ for NBNO. The correlation of these substituents with the Taft equation, but not of the larger *n*-alkyl substituents, has been observed by Moss and Mamantov for dichlorocarbene cycloadditions to alkylethylenes.[14] In that case, a slope of ~1.0 was observed.[14]

Calculations performed on these and related systems[10] indicate that alkyl groups decrease the rate of reaction not only by increasing exchange, or closed-shell, repulsion between the nitrile oxide and the alkyl substituents but also by slightly decreasing charge-transfer interactions. This appears to be a general feature for electrophilic attack on electron-rich alkenes: the HOMO of a donor-substituted alkene invariably has a substituent orbital mixed in an antibonding fashion with the vinyl π orbital, and an incoming electrophile which interacts with both vinyl carbons (a "two-bond" electrophile)[15] will also experience an antibonding interaction with the substituent orbital, as shown by the dotted lines below:



This interaction will diminish the alkene HOMO–electrophile LUMO interaction and may counteract the effect of HOMO energy raising by the donor, in cases where the electrophile forms bonds at both termini of the alkene in the transition state.

"One-bond" electrophiles,[15] which interact only with the carbon remote from the substituent, should not experience this antibonding secondary orbital interaction. This, rather than the relatively small size of the hydrated proton, may account for the apparent lack of alkyl steric effects in acid-catalyzed hydration reactions.[3] We are further pursuing, on both experimental and theoretical levels, the possible ramifications of such specific steric effects.[16]

Experimental Section

Alkenes were obtained from Chemical Samples Co.[17] The nitrile oxides were prepared immediately prior to kinetic measurements from the corresponding benzohydroxamic acid chlorides by literature procedures.[18]

Kinetic Procedure. Concentrations of alkenes in stock CCl_4 solutions were determined by titration with excess bromine in acetic acid and back-titration with standard thiosulfate solution.[19] Rates were measured in a thermostated sealed cell in triplicate by removal of aliquots with a pressure-tight syringe at regular intervals and measuring the nitrile oxide absorbance at 2290 cm^{-1} in the infrared spectrum of the mixture.[20] Control experiments showed that under the conditions used for the kinetic measurements, the concentrations of solutions of alkenes were unchanged after 4 times the half-life of the reaction. The second-order rate constants were calculated graphically by using the integrated form of the second-order rate equation. Rate constants were reproducible within 2–3%.

Preparation of Adducts. The nitrile oxides, prepared as above, were mixed with a fivefold excess of the alkene in CCl_4, and the solutions were allowed to stand overnight at room temperature. Evaporation of solvent and recrystallization of the resulting adducts gave colorless crystals. All new compounds gave elemental analyses in accord with the proposed structures. The NMR spectra of the adducts had multiplets due to two methylene protons at δ 3–3.5 and, for the monosubstituted alkene adducts, a methine multiplet at δ ~5, with the appropriate coupling constants.[21] Full details of the physical properties of these compounds will be reported at a later date.

Acknowledgments. Financial support of this work by the National Science Foundation and the Italian CNR

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[11] Masclet, P.; Grosjean, D.; Mouvier, G.; Dubois, J.-E. *J. Electron Spectrosc. Rel. Phenom.* **1973**, *2*, 225. In order to compare vertical IPs, 0.16 eV has been added to the adiabatic IPs of substituted ethylenes given by Masclet et al.

[12] This is estimated from the fact that the *p*-nitro compound reacts 5–7 times faster at 20 °C than the *p*-methoxy compound does at 25 °C.

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[17] All of these were ≥99% (nominally ≥99.9%) pure except for isobutylene, which contained about 3–4% of a more reactive compound (butadiene?) which could be removed by treatment of the alkene mixture with a 0.2 molar equiv of NBNO and removal of the resulting adducts.

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[20] Beer's law is obeyed for the 2290-cm^{-1} band in the range of 0.001–0.01 M for MBNO and 0.001–0.006 M for NBNO, used in these experiments.

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(Fellowship To A.B.) is gratefully acknowledged.

Registry No. *p*-Nitrobenzonitrile oxide, 2574-03-0; *p*-methoxybenzonitrile oxide, 15500-73-9; propene, 115-07-1; 1-butene, 106-98-9; 1-pentene, 109-67-1; 1-hexene, 592-41-6; 3-methyl-1-butene, 563-45-1; 3,3-dimethyl-1-butene, 558-37-2; isobutene, 115-11-7; 5-methyl-3-(*p*-nitrophenyl)isoxazoline, 63008-35-5; 5-ethyl-3-(*p*-nitrophenyl)-isoxazoline, 70416-55-6; 3-(*p*-nitrophenyl)-5-propylisoxazoline, 70416-56-7; 5-butyl-3-(*p*-nitrophenyl)isoxazoline, 70416-57-8; 5-isopropyl-3-(*p*-nitrophenyl)isoxazoline, 70416-58-9; 5-*tert*-butyl-3-(*p*-nitrophenyl)isoxazoline, 70428-87-4; 5,5-dimethyl-3-(*p*-nitrophenyl)isoxazoline, 70416-59-0; 3-(*p*-methoxyphenyl)-5-methylisoxazoline, 63008-36-6; 5-ethyl-3-(*p*-methoxyphenyl)isoxazoline, 70416-60-3; 3-(*p*-methoxyphenyl)-5-propylisoxazoline, 70416-61-4; 5-butyl-3-(*p*-methoxyphenyl)isoxazoline, 70416-62-5; 5-isopropyl-3-(*p*-methoxyphenyl)isoxazoline, 70416-63-6; 5-*tert*-butyl-3-(*p*-methoxyphenyl)isoxazoline, 70416-64-7; 5,5-dimethyl-3-(*p*-methoxyphenyl)isoxazoline, 70428-86-3.

Cyclobutenecarboxylic Esters via Aluminum Chloride Induced [2 + 2] Cycloadditions of 2-Propynoic Esters to Cyclic Olefins

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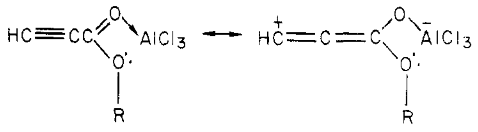
Thermal [2 + 2] cycloadditions involving unactivated olefins are quite rare.[1] Snider has demonstrated recently that 2-propynoic esters (propiolic esters)[2a,b] and also 3-butyn-2-one[2c] can be activated by Lewis acids[3] to yield [2 + 2] cycloadducts with simple alkenes. Specifically, he showed that *cis*-2-butene as well as *trans*-2-butene maintain their configuration,[2a] each giving a single cyclobutenecarboxylic ester (Scheme I).

As this subject still seems at the stage where the collection of further data is desirable, we have studied $AlCl_3$-promoted [2 + 2] cycloadditions of 2-propynoic esters (**1a,b**) to a number of cyclic alkenes (Table I). In all cases, the cycloaddition is preparatively useful as suggested,[2] proceeding over several hours or days at room temperature. The reaction with *trans*-cyclooctene is quite fast, taking a few minutes and giving adduct **5b** without discernible leakage into cis-fused **3b**. Of the two esters, the ethyl ester **1b** seems superior to the methyl ester **1a** in reacting more quickly and giving products which can be separated more easily by GC because of their reduced volatility. Mechanistically, two paths have been considered: a two-step reaction via ionic intermediate(s) with retention of olefin configuration and a concerted ${}_\pi 2_s + {}_\pi 2_a$ process.[2a] We suggest that complexed 2-propynoic ester is a species which has the character of an electron-deficient acetylene i and also a sterically accessible vinyl (allenyl) cation ii. In accord with the description as i, cyclopentadiene and norbornadiene furnish Diels–Alder and homo-Diels–Alder adducts **9a** and **8a**, respectively, at very much enhanced rates as expected. Note, however, that norbornadiene gives not only **8a** but also [2 + 2] adduct **7a**. We have checked independently that adduct **7a** is not formed at all in the *absence* of $AlCl_3$. Further, the pattern of reactivity of monoolefinic reaction partners in Table I together with that in the literature[2] parallels in many ways the one established by Ghosez[4] for cycloadditions of dichloroketene. In conclusion, complexed 2-propynoic ester seems capable of reacting as a conventional, but strongly activated, dienophile (cf. i) and also as a powerful ketene-like ${}_\pi 2_a$ component (cf. ii), depending on the reaction partner.[5]



i ii

Experimental Section

All boiling points are uncorrected. Infrared spectra (CCl_4) were recorded on Perkin-Elmer 457 and 580 infrared spectrometers. NMR spectra (CCl_4) were determined on Varian EM 360 and Bruker HX 90 spectrometers (Me_4Si internal standard). The mass spectra were obtained with a Varian CH 5 (70 eV) mass spectrometer. Preparative GC was carried out on a Varian Aerograph Autoprep Model 700 (column: 6 m, 3% QF1; carrier gas hydrogen). Microanalyses are due to Frau Jirotkova of the Institut für Organische Chemie.

Cycloadditions with 2-Propynoic Esters.[2a] General Procedure. Commercial aluminum trichloride was vigorously stirred into a solution of 2-propynoic ester in dried benzene. After 15 min, evolution of heat had subsided, and the cyclic olefin was added to the resulting clear solution which was stirred at room temperature. The progress of the reaction was monitored by pouring aliquots of the reaction solution into aqueous $NaHCO_3$/ether, shaking the solution, and examining the ether layer by GC. When the product peak no longer increased substantially, the reaction mixture was poured into aqueous $NaHCO_3$/ether with precipitation of aluminum hydroxide, and the product was extracted continuously overnight with a rotatory perforator. The organic phase was washed with water until neutral and dried ($MgSO_4$), and the solvent was evaporated.

Methyl *cis*-Bicyclo[3.2.0]hept-6-ene-6-carboxylate (2a). Methyl 2-propynoate (0.84 g, 10 mmol), cyclopentene (1.36 g, 20 mmol), and aluminum trichloride (0.67 g, 5 mmol) were allowed to react in 25 mL of dried benzene according to the general procedure. Workup after 72 h afforded 0.63 g of the crude product which was distilled (Kugelrohr) to give 0.27 g (18%) of pure **2a**: bp 120 °C (10 mm); ^{1}H NMR[6] δ 1.0–2.0 (m, 6 H, CH_2), 3.08 (m, 1 H, CH), 3.34 (m, 1 H, CH), 3.66 (s, 3 H, OMe), 6.52 (m, 1 H, HC=C); IR ($CHCl_3$) 2955, 2860, 1712, 1610, 1600, 1436, 1277, 1135 cm^{-1}; mass spectrum, *m/e* 152 (M^+). Anal. Calcd for $C_9H_{12}O_2$ (152.2): C, 71.03; H, 7.95. Found: C, 70.82; H, 7.99.

Ethyl *cis*-Bicyclo[6.2.0]dec-9-ene-9-carboxylate (3b). Following the general procedure, ethyl 2-propynoate (2.96 g, 30 mmol), *cis*-cyclooctene (6.60 g, 60 mmol), and aluminum trichloride (2.01 g, 15 mmol) were allowed to react in 45 mL of benzene (48 h). Fractional distillation (Kugelrohr) yielded **3b** (2.7 g, 43%): bp 120 °C (0.1 mm); ^{1}H NMR δ 1.27 (t, *J* = 7 Hz, 3 H, CH_3),

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(1) (a) D. Seebach in "Houben-Weyl", Vol. 4, Thieme, Stuttgart, 1971; (b) R. Huisgen, R. Grashey, and J. Sauer in "The Chemistry of Alkenes", S. Patai, Ed., Interscience, London, 1964, Chapter 11; (c) J. D. Roberts and C. M. Sharts, *Org. React.*, **12**, 1 (1962); cf. also K. Alder, unpublished work cited by M. Günzel and W. Günzel, *Angew. Chem.*, **72**, 219 (1960).

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(5) [2 + 2] cycloadditions of acetylenic esters to electron-rich olefins such as enamines proceed presumably stepwise; see D. N. Reinhoudt, J. Geevers, and W. P. Trompenaars, *Tetrahedron Lett.*, 1351 (1978), and literature cited.

(6) Cf. L. A. Paquette and G. Zon, *J. Am. Chem. Soc.*, **96**, 224 (1974).

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