by using methylene chloride–hexane to give 640 mg (68%) of 3-phenyl-5-[(phenylsulfonyl)methyl]isoxazole (**30**) as a white crystalline solid: mp 123–124 °C; IR (KBr) 3130, 2995, 2940, 1610, 1585, 1445, 1310, and 1150 cm^{-1}; NMR (CDCl$_3$, 90 MHz) δ 4.55 (s, 2 H), 6.65 (s, 1 H), and 7.35–7.85 (m, 10 H). Anal. Calcd for $C_{16}H_{13}NO_3S$: C, 64.20; H, 4.38; N, 4.68. Found: C, 64.10; H, 4.29; N, 4.59.

Acknowledgment. We gratefully acknowledge the National Cancer Institute for generous support of this work. U.C. thanks the NATO Foundation for a travel grant and the MPI for partial financial support.

Registry No. **1**, 2525-42-0; **1**-d_2, 113648-18-3; **2**, 113648-12-7; **3**, 113648-13-8; **4**, 113648-14-9; **5**, 113648-15-0; **7**, 51105-55-6; **8**, 113648-17-2; **9**, 2525-40-8; **12**, 51445-25-1; **12**-d_2, 113648-16-1; **13**, 113668-34-1; **16**, 106910-59-2; **16**-d_2, 113648-19-4; **17**, 106910-54-7; **30**, 106808-15-5; **31**, 113648-20-7; **32**, 113648-21-8; **40**, 51146-39-5; CH_2N_2, 334-88-3; PhNHN=CClPh, 15424-14-3; diazopropane, 764-02-3; benzohydroximinoyl chloride, 698-16-8.

Peracid Oxidation of 4-Isoxazolines as a Method for the Preparation of α,β-Unsaturated Carbonyl Compounds

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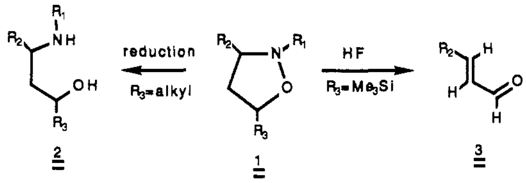
Received October 29, 1987

A study of the MCPBA peracid oxidation of a series of 4-isoxazolines has been carried out. A variety of isoxazolines were synthesized by treating nitrones with electron-deficient alkynes. An alternate approach involves dipolar cycloaddition of nitrones with activated allenes followed by a subsequent base-catalyzed isomerization of the initially formed cycloadduct. Treatment of the 5-*exo*-methyleneisoxazolidine derived from the reaction of *N*-benzylidenemethylamine *N*-oxide and (phenylsulfonyl)propadiene with LDA followed by γ-alkylation also produced substituted 4-isoxazolines. The peracid oxidation of the isoxazoline ring afforded α,β-unsaturated carbonyl compounds in excellent yield. Reductive cleavage of the sulfonyl group of some of the enones was achieved by initial protection of the carbonyl functionality by cyanosilylation using trimethylsilyl cyanide, and this was followed by aluminum-amalgam reduction. The cycloaddition–oxidation procedure provides an attractive route to synthesize α,β-unsaturated ketones since it avoids acidic or basic conditions.

The presence of a nitrogen atom within the isoxazolidine ring has made this heterocycle moiety especially attractive for the synthesis of a wide variety of alkaloids and other nitrogen-containing natural products.[1-11] Through the use of nitrone cycloaddition chemistry,[12] numerous isoxazolidines have been synthesized with excellent stereochemical control.[13] The key feature of this approach generally involves the subsequent reductive cleavage of the isoxazolidine ring to give a γ-amino alcohol, which is further manipulated into other functional groups.[14-18] Recent work by DeShong and Leginus[19] has demonstrated that nitrone cycloadditions with vinyltrimethylsilane give 5-silylisoxazolidines, which can easily be transformed into α,β-unsaturated aldehydes. This methodology is quite useful since it allows for the homologation of aldehydes by two carbons while avoiding strongly basic reaction conditions.



As part of an ongoing program aimed at the development of general methods for the construction of nitrogen-containing heterocycles,[20] we have been investigating the 1,3-dipolar cycloadditions of nitrones with allenes[21]

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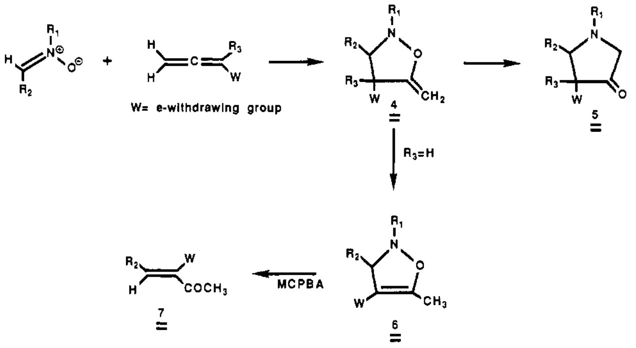
followed by their thermal rearrangement.[22] During the course of this work we had the occasion to study the MCPBA peracid oxidation of 4-isoxazolines derived from the allene cycloadducts and found that α,β-unsaturated ketones are produced in excellent yield.[23] This paper documents the results of these studies.



Results and Discussion

Isoxazolidines have been reported to undergo oxidative ring opening with hydrogen peroxide or peracids to produce nitrones or *N*-hydroxyoxazines.[24-26] The nitrones resulting from the N-oxidation reaction readily cycloadd to olefins, and Tufariello made elegant use of this fact in a synthesis of *dl*-cocaine.[25] Since there is a continuing need to use mild and versatile procedures for the synthesis of nitrones, we thought it worthwhile to probe some of the features of the N-oxidation reaction in greater detail. Toward this end we have investigated the reaction of a typical isoxazolidine (i.e., 8) with MCPBA. The major product obtained (64%) is assigned as 1,3-oxazine 11 on the basis of its spectral data (see Experimental Section). This interesting transformation can be explained by an initial N-oxidation followed by ring opening to a nitrosonium ion, which subsequently tautomerizes to nitrone 10. Cyclization of the neighboring alcohol onto the methylene carbon of the nitrone produces oxazine 11. In support of the proposed mechanism, we found that the MCPBA reaction of the closely related *tert*-butylisoxazolidines 12 and 13 produced nitrones 14 and 15 in high yield. Support for these structures was obtained by their acid-induced conversion to compounds 16–18 by loss of isobutylene.

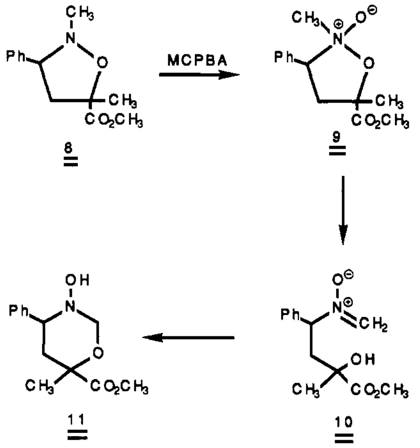
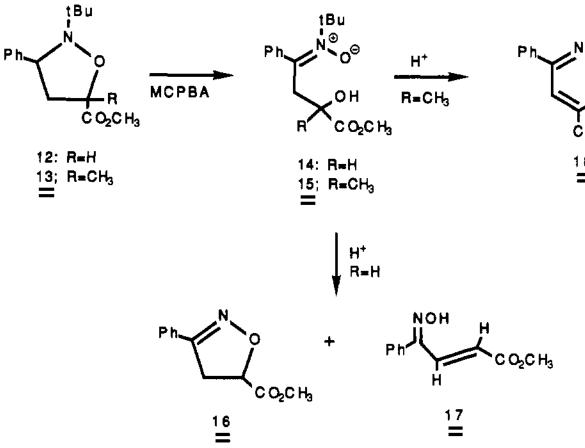
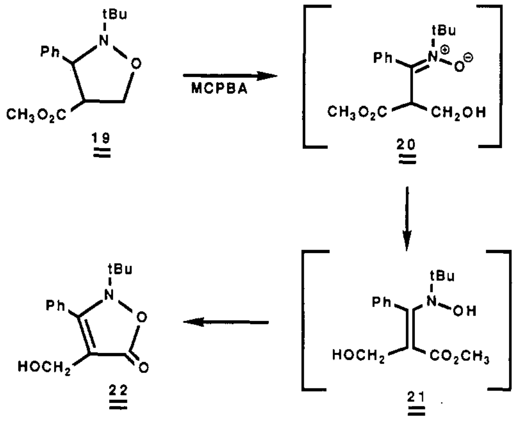


Chart I

Δ^4-ISOXAZOLINE	ENONE (%)
23 W=SO_2Ph;R_1=R_2=CH_3	24 (98%)
25 W=CN;R_1=R_2=CH_3	26 (97%)
27 W=CO_2CH_3;R_1=R_2=CH_3	28 (75%)
29 W=SO_2Ph;R_1=CH_3;R_2=n-C_3H_7	30 (98%)
31 W=SO_2Ph;R_1=CH_3;R_2=$CH_2CH_2C{\equiv}CH$	32 (96%)
38 W=R_2=CO_2CH_3;R_1=CH_3	39 (85%)
40 W=H;R_1=CH_3;R_2=CO_2CH_3	41 (98%)
43 W=H;R_1=t-C_4H_9;R_2=CO_2CH_3	41 (65%)
44 W=CO_2CH_3;R_1=CH_3;R_2=H	45 (97%)



We have also examined the MCPBA reaction of the regioisomeric 4-substituted isoxazolidine 19. Stirring a sample of 19 with *m*-chloroperbenzoic acid produced isoxazolinone 22 in 68% yield. The formation of 22 is consistent with a nitrone intermediate (i.e., 20) which tautomerizes to a transient hydroxylamine (21) followed by cyclization to the observed product.



In striking contrast to the N-oxidation reaction of isoxazolidines, the MCPBA oxidation of the 4-isoxazoline ring system produced α,β-unsaturated ketones in excellent yield. Nitrones undergo smooth cycloaddition with acti-

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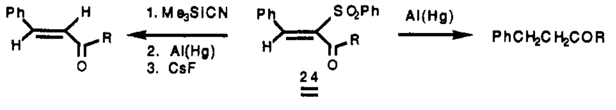
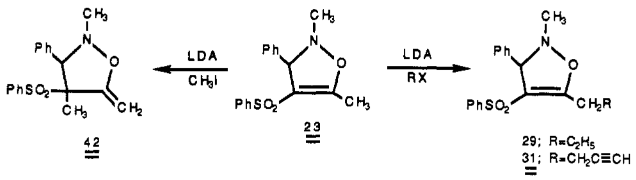
vated allenes to produce 5-methylene-substituted isoxazolidines. The regiochemistry of the cycloaddition can be rationalized in terms of a maximum overlap of the nitrone HOMO–dipolarophile LUMO orbitals. The initially formed cycloadduct can be readily isomerized to the thermodynamically more stable 4-isoxazoline by treatment with base. A variety of 4-isoxazolines can also be prepared by treating nitrones with electron-deficient alkynes. The results summarized in Chart I show that the peracid oxidation of the 4-isoxazolidine system smoothly produces α,β-unsaturated ketones. The peracid oxidation step was performed at 25 °C in methylene chloride for 12 h. In all cases, the yield of the isolated enone is excellent (see Chart I).[27]

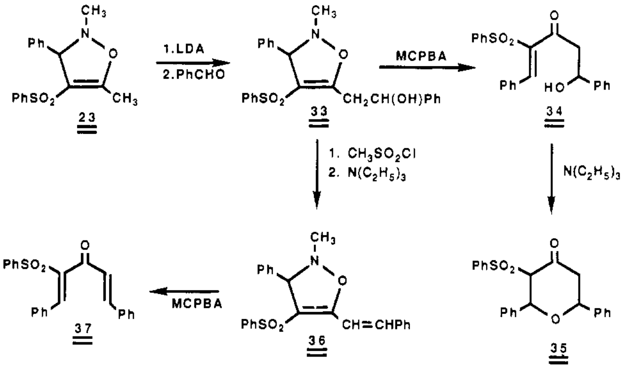
Reductive cleavage of the sulfonyl group of some of the enones was achieved by initial protection of the carbonyl functionality by cyanosilylation using trimethylsilyl cyanide followed by aluminum-amalgam reduction.[28] The overall sequence was completed by a cesium fluoride induced desilylation reaction. Desulfonylation without protection of the carbonyl group resulted in formation of the saturated ketone.[29]



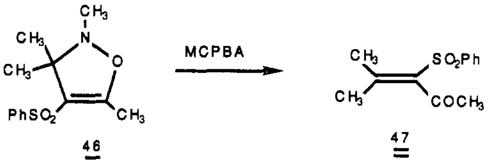
R = CH_3, C_3H_7, $CH_2CH_2C{\equiv}CH$

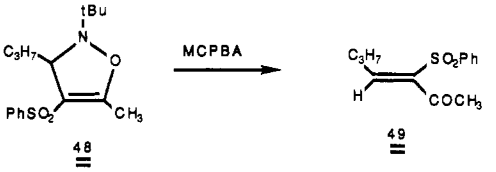
We have also studied the base-induced alkylation reaction of 2,5-dimethyl-3-phenyl-4-(phenylsulfonyl)isoxazoline (**23**). Considerable interest has recently been focused on the chemical transformations of allyl sulfones.[30] The key steps of these transformations are the generation of allyl sulfonyl carbanions and their reactions with electrophilic compounds, leading to the formation of new C–C bonds. The RSO_2 functionality is subsequently removed from the product via reduction, elimination, or substitution, affording the target molecule. The reaction of lithiated allylic sulfones with alkyl halides is a well-documented, synthetically useful process leading to α-alkylation.[31] Thus, the formation of 4-isoxazolines **29** and **31** from the reaction of **23** with LDA followed by reaction with ethyl iodide or propargyl bromide is a bit surprising. With a small electrophile such as methyl iodide, however, α-alkylation (leading to **42**) was the exclusive pathway encountered. Evidently, as the bulk of the electrophile increases, γ-alkylation becomes the major path. In fact, we have found that the reaction of **23** with a series of electrophiles (acetyl chloride, allyl bromide, trimethylsilyl chloride) produced only the γ-alkylated product in high yield. This may be a reflection of steric factors as well as the greater thermodynamic stability of the 4-isoxazoline ring system. The reaction of **23** with LDA followed by treatment of the anion with benzaldehyde also afforded a product derived from γ-attack. The resulting alcohol could readily be dehydrated to the corresponding styryl derivative. Treatment of either **33** or **36** with MCPBA produced the expected α,β-unsaturated ketones (**34** and **37**) in high yield. In the case of **34**, this material was readily converted to tetrahydro-γ-pyranone **35** upon treatment with triethylamine.



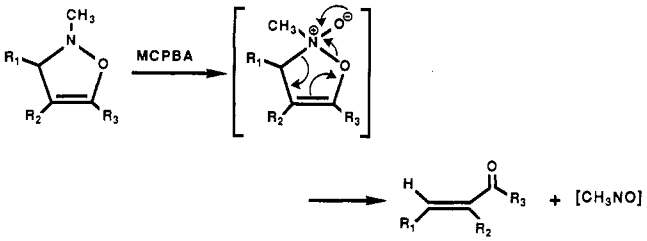


In an effort to further establish the generality and scope of the MCPBA reaction of 4-isoxazolines, we studied the peracid reaction of cycloadducts **46** and **48** which were prepared from the reaction of aliphatic nitrones with (phenylsulfonyl)-1-propyne. These compounds were smoothly converted to the expected enones in high yield. Thus, the peracid reaction of isoxazolines as a method for preparing diactivated unsaturated ketones appears to be quite general.





It has previously been suggested that peracids oxidize isoxazolidines to unstable N-oxides, which further react to generate nitrones.[24-26] We believe a similar process is involved in the peracid oxidation of the 4-isoxazoline system. The initially generated N-oxide undergoes a cheletropic extrusion of nitrosomethane in a manner similar to that encountered with cyclopent-3-enones, diazenes, and 2,5-dihydrothiophene 1,1-dioxides.[32]



We also examined the peracid oxidation of 4-isoxazoline **50**. This compound was readily prepared from the cyclic

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[27] A single enone was formed in all cases and is tentatively assigned as the thermodynamically most stable isomer.

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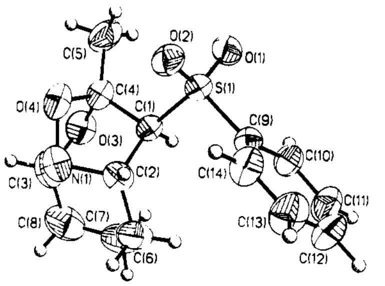
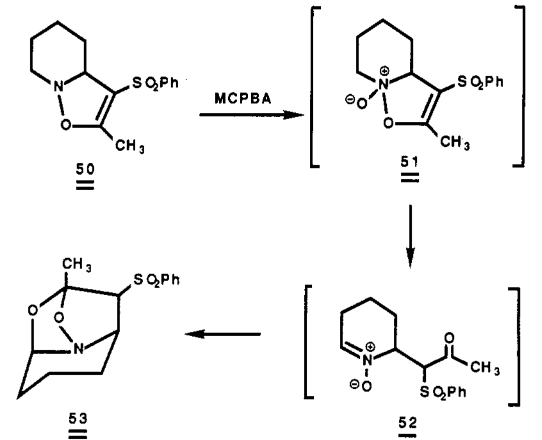


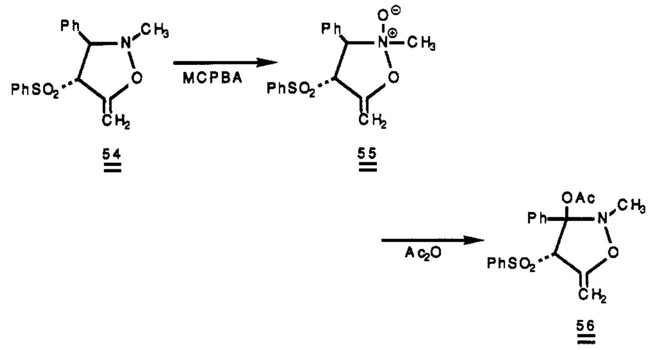
Figure 1. General view of tricyclic isoxazolidine 53.

nitrone and (phenylsulfonyl)propadiene followed by a base-induced isomerization of the initially produced dipolar cycloadduct. Reaction with MCPBA proceeded quite smoothly and gave a single product (**53**) in excellent yield. This structure assignment is based on a single-crystal X-ray structure analysis. The structure was derived by using direct methods and refined by least squares to give a R value of 0.0518 for all the data. The overall geometry of the molecule is shown in Figure 1.



The formation of **53** from **50** is a most interesting transformation and merits some comment. We believe that the initially formed N-oxide **51** undergoes a subsequent elimination to generate nitrone **52**, which exists, to a significant extent, in the enol form. Addition of the enol oxygen across the C,N-bond of the nitrone followed by conjugate addition of the resulting N-oxide onto the vinyl sulfone nicely accounts for compound **53**.

The MCPBA oxidation of N-methyl-5-methylene-3-phenyl-4-(phenylsulfonyl)isoxazolidine (**54**) was also studied. The exclusive product obtained here was isoxazolidine N-oxide **55**. The preferential N-oxidation of **54** is to be expected since MCPBA is known to selectively oxidize unsaturated tertiary amines to their corresponding N-oxides.[33] Treatment of **55** with acetic anhydride in pyridine afforded **56** by means by a Polonovski rearrangement.[34]



The preparation of α,β-unsaturated carbonyl compounds is an important process in organic synthesis since these compounds are extremely powerful synthetic intermediates.[35-38] The vast majority of enones are constructed by carbonyl addition and condensation reactions.[39] Dipolar cycloaddition strategies have recently been developed which complement the standard carbonyl addition approach. These include the cycloaddition of an olefin with a nitrile oxide followed by hydrogenolysis–hydrolysis–elimination of the resultant 2-isoxazoline.[40-42] An alternate method involves cycloaddition of a nitrone with a vinyl silane followed by protodesilylation of the resulting cycloadduct with HF.[19] In this paper we have described a conceptually different dipolar-cycloaddition approach to unsaturated ketones that involves the peracid oxidation of 4-isoxazolines. The cycloaddition–oxidation procedure provides an alternative to the previously reported cycloaddition–reduction protocol used to synthesize α,β-unsaturated ketones. The advantage of the methodology is that it avoids the acidic or basic conditions traditionally used in condensation chemistry.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were run on a Perkin-Elmer Model 283 infrared spectrometer. Proton NMR spectra were obtained on Varian EM-390 and Nicolet NMC-360 MHz spectrometers. ^{13}C NMR spectra were recorded on an IBM NB 200 SY FT spectrometer. Microanalyses were performed at Atlantic Microlabs, Atlanta, GA. Mass spectra were determined with a VG MM-7070S mass spectrometer at an ionizing voltage of 70 eV.

Peracid Oxidation of Methyl 2,5-Dimethyl-3-phenylisoxazolidine-5-carboxylate (8). To an ice-cooled solution containing 0.65 g of methyl 2,5-dimethyl-3-phenylisoxazolidine-5-carboxylate (8)[43] in 2 mL of methylene chloride was added a solution containing 0.56 g of m-chloroperbenzoic acid (85%) in 10 mL of methylene chloride. After the addition was complete, the mixture was stirred for an additional 45 min at 25 °C, then extracted with a 10% sodium carbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave behind a thick oil, which was subjected to silica gel chromatography using a 60% ethyl acetate-hexane mixture as the eluent. The major fraction isolated from the column contained 0.48 g (64%) of a white solid, mp 125–126 °C, whose structure was assigned as 6-carbomethoxy-3-hydroxy-6-methyl-4-phenyltetrahydro-1,3-oxazine (11) on the basis of its spectral data: IR (KBr) 3200, 2870, 1733, 1455, 1387, 1300, 1265, 1240, 1213, 1162, 1148, 1089, 1078, 998, 985, 965, 940, 915, 820, 795, 762, 701, and 667 cm^{-1}; NMR (CDCl$_3$, 90 MHz) δ 1.47 (s, 3 H), 2.33 (br s, 2 H), 3.78 (s, 3 H), 4.56 (br s, 2 H), 5.28 (br s, 1 H), and 7.27–7.45 (m, 5 H); MS, m/e 251 (M^+), 234, 192, 173, 159, 147, 131, 121, 105 (base), 91, and 77. Anal. Calcd for $C_{13}H_{17}NO_4$:

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(43) Huisgen, R.; Hauck, H.; Grashy, R.; Seidl, H. *Chem. Ber.* **1968**, *101*, 2568.

C, 62.14; H, 6.82; N, 5.57. Found: C, 62.08, H, 6.82; N, 5.55.

Peracid Oxidation of Methyl *N-tert*-Butyl-3-phenylisoxazolidine-5-carboxylate (12). To an ice-cooled solution containing 1.31 g of 12[20] in 10 mL of methylene chloride was added a solution containing 1.0 g of *m*-chloroperbenzoic acid (85%) in 20 mL of methylene chloride over a 15-min period. After the addition was complete, the mixture was stirred for 1 h, then extracted with a 10% sodium carbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave behind a pale yellow oil, which slowly crystallized on standing. Fractional recrystallization of the solid afforded .04 g (75%) of *N*-(3-carbomethoxy-3-hydroxy-1-phenylpropylidene)-*tert*-butylamine *N*-oxide (14): mp 100–101 °C; IR (KBr) 3180, 3020, 2970, 1735, 1550, 1430, 1380, 1360, 1290, 1240, 1210, 1000, 1050, 1020, 985, 930, 890, 850, 800, 770, 750, and 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.31 (s, 9 H), 3.17 (dd, 1 H, J = 12.6 and 4.80 Hz), 3.40 (dd, 1 H, J = 12.6 and 7.80 Hz), 3.60 (s, 3 H), 4.58 (dd, 1 H, J = 7.80 and 4.80 Hz), 6.63 (br s, 1 H), and 7.2–7.47 (m, 5 H); UV (95% ethanol) 253 nm (ϵ 9980); MS, *m/e* 164, 146, 135, 104, 77, and 57 (base). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 69.49; H, 7.58; N, 5.01. Found: C, 69.47; H, 7.31; N, 5.01.

Support for structure 14 was obtained from some acid-induced reactions. A mixture containing 206 mg of 14 and 117 mg of pyridine in 2.7 mL of benzene was cooled to 10 °C. To this mixture was added 0.07 mL of phosphorus oxychloride. After being stirred for 10 min, the mixture was allowed to warm to room temperature and was stirred for another 3.5 h. The mixture was extracted with water and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography using a 25% ethyl acetate–hexane mixture as the eluent. The major fraction contained 95 mg (63%) of a white solid, mp 73–74 °C, whose structure was assigned as methyl 3-phenyl-2-isoxazoline-5-carboxylate (16): IR (KBr) 2968, 1753, 1438, 1378, 1348, 1248, 1213, 1163, 1008, 918, 878, and 758 cm^{-1}; NMR (CCl_4, 90 MHz) δ 3.49 (d, 1 H, J = 9.0 Hz), 3.53 (d, 1 H, J = 7.50 Hz), 3.77 (s, 3 H), 5.0 (dd, 1 H, J = 9.0 and 7.50 Hz), and 7.62–7.70 (78 5 H); UV (95% ethanol) 265 nm (ϵ 13 700); MS, *m/e* 205 (M$^+$), 146, 118, 91, and 77 (base). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.42; H, 5.44; N, 6.82.

A solution containing 0.5 g of 14 and 11 mg of *p*-toluenesulfonic acid in 10 mL of benzene was heated at reflux under a nitrogen atmosphere for 13 h. The solvent was removed under reduced pressure, and the residue was subjected to silica gel chromatography using a 20% ethyl acetate–hexane mixture as the eluent. The first component isolated from the column contained 160 mg (44%) of methyl 3-phenyl-2-isoxazoline-5-carboxylate (16).[44] The second component contained 58 mg (16%) of a 1:1 mixture of the syn and anti oximes of methyl benzoylacrylate (17). The mixture exhibited the following spectral properties: IR ($CHCl_3$): 3535, 3240, 2850, 1715, 1620, and 1410 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.69 (s, 3 H), 3.73 (s, 3 H), 5.80 (d, 1 H, J = 16.0 Hz), 6.15 (d, 1 H, J = 16.5 Hz), 7.20–7.40 (m, 12 H), 7.57 (d, 1 H, J = 16.0 Hz), and 8.10 (d, 1 H, J = 16.5 Hz); MS, *m/e* 205 (M$^+$), 186 (base), 157, 146, 128, 115, and 77. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.42; H, 5.44; N, 6.82.

The structure of the isomeric oximes was verified by an independent synthesis. To a solution containing 0.75 g of methyl benzoylacrylate in 5 mL of ethanol and 5 mL of pyridine was added 0.27 g of hydroxylamine hydrochloride, and the solution was heated at reflux for 16 h. After cooling, water was added and the mixture was extracted with ether. The ether solution was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel with a 20% ether–hexane mixture as the eluent. The major fraction contained 0.4 g (49%) of a mixture of syn and anti oximes of methyl benzoylacrylate. These compounds were identical in all respects with the material obtained from the acid-catalyzed reaction of nitrone 14.

A similar peracid-induced reaction was carried out with the regioisomeric 4-carboxylate 19.[20] The crude reaction mixture was subjected to silica gel chromatography using a 60% ethyl acetate–hexane mixture as the eluent. The major fraction (68%) contained *N*-*tert*-butyl-3-phenyl-4-(hydroxymethyl)isoxazolin-5-one (22): mp 150–151 °C; IR (KBr) 3415, 3010, 1710, 1610, 1580, 1450, 1390, 1380, 1365, 1300, 1210, 190, 1090, 1020, 840, and 750 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.20 (s, 9 H), 2.56 (br s, 1 H), 4.17 (s, 1 H), and 7.82 (s, 5 H); UV (cyclohexane) 278 (ϵ 6700) and 226 nm (7800); MS, *m/e* 247 (M$^+$), 191, 174, 77, and 57 (base). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93; N, 5.66. Found: C, 67.92; H, 6.94; N, 5.64.

Peracid Oxidation of Methyl *N-tert*-Butyl-5-methyl-3-phenylisoxazolidine-5-carboxylate (13). To an ice-cooled solution containing 1.0 g of 13[45] in 10 mL of methylene chloride was added 0.73 g of *m*-chloroperbenzoic acid (85%) over a 10-min peroid. After the addition was complete, the mixture was stirred for 45 min, then extracted with a 10% sodium carbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to give 1.02 g (97%) of *N*-(3-carbomethoxy-3-hydroxy-1-phenylbutylidene)-*tert*-butylamine *N*-oxide (15) as a clear oil: IR (neat) 2990, 1745, 1480, 1445, 1370, 1310, 1195, 1115, 1048, 1018, 992, 848, 812, 768, 734, and 705 cm^{-1}; NMR (CCl_4, 90 MHz) δ 1.23 (s, 12 H), 3.07 (s, 2 H), 3.5 (s, 3 H), 6.24 (s, 1 H), and 7.3 (s, 5 H); MS, *m/e* 293 (M$^+$), 237, 178, 163, 135, 105, 77, and 57 (base). Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.78. Found: C, 65.73; H, 7.85; N, 4.55.

Support for the structure of 15 was obtained from an acid-catalyzed cyclization. A solution containing 1.02 g of 15 and 0.1 g of *p*-toluenesulfonic acid in 20 mL of benzene was heated at reflux under a nitrogen atmosphere for 11 h. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel with a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.46 g (71%) of a white solid, mp 135–136 °C, whose structure was assigned as 5-methyl-3-phenyloxazin-6-one (18) on the basis of its spectral data: IR (KBr) 1720, 1630, 1439 1325, 1208, 1062, 940, 915, 897, 780, 750, 698, 672, and 632 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.23 (d, 3 H, J = 1.5 Hz) and 7.30–7.82 (m, 6 H); UV (95% ethanol) 285 (ϵ 2190) and 240 nm (20 900); MS, *m/e* 187 (M$^+$), 157, 144, 129 (base), and 77. Anal. Calcd for $C_{11}H_9NO_2$: C, 70.58; H, 4.85; N, 7.48. Found: C, 70.64; H, 4.90; N, 7.45.

Peracid Oxidation of 2,5-Dimethyl-3-phenyl-4-(phenylsulfonyl)-4-isoxazoline (23). To an ice-cooled solution containing 315 mg of isoxazoline 23[20] in 15 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid (85%) in small portions. After the addition was complete, the solution was stirred for 2 h. The mixture was then diluted with methylene chloride and washed with a saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give 277 mg (98%) of a white crystalline solid. Recrystallization from a 10% ethyl acetate–hexane mixture gave colorless crystals of 4-phenyl-3-(phenylsulfonyl)-3-buten-2-one (24): mp 86–87 °C; IR (KBr) 1700, 1610, 1450, 1320, 1150, 1090, 990, 950, 820, 760, 730, and 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.28 (s, 3 H) and 7.2–7.9 (m, 11 H). Anal. Calcd for $C_{16}H_{14}O_3S$: C, 67.13; H, 4.90; S, 11.18. Found: C, 66.96; H, 4.97; S, 11.12.

A 400-mg sample of aluminum foil was immersed in 3 mL of a 2% mercuric chloride solution for 30 s and was then washed successively with a 95% ethanol solution followed by ether. This material was placed in a reaction flask containing a solution of 4-phenyl-3-(phenylsulfonyl)-3-buten-2-one (24) in 20 mL of 10% aqueous tetrahydrofuran. The mixture was heated at reflux for 3 h at 60 °C, cooled to room temperature, and filtered through a Celite pad. The resulting was concentrated under reduced pressure to give a pure sample of 4-phenyl-2-butanone as a colorless oil (195 mg, 92%): IR (neat) 1720, 1500, 1450, 1370, 1170, and 1020 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.05 (s, 3 H), 2.8 (m, 4 H), and 7.2 (s, 5 H).

To a solution containing 286 mg of 24 in 10 mL of methylene chloride were added 500 mg of trimethylsilyl cyanide and a catalytic amount of zinc iodide. The resulting solution was stirred at 25 °C for 2 days. Normal workup of the mixture gave a colorless oil, which was shown to be the expected cyanosilylated product as judged by its NMR spectrum ($CDCl_3$, 90 MHz): δ 0.1 (s, 9 H), 2.7 (s, 3 H), 6.1 (d, 1 H, J = 12 Hz), 6.9 (d, 1 H, J = 12 Hz), and

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(44) Christl, M.; Huisgen, R. *Chem. Ber.* **1973**, *106*, 3345.

(45) See supplementary material for a description of its preparation and spectroscopic properties.

7.4 (m, 5 H). This material was desulfonylated by stirring with 10 mmol of aluminum amalgam in 15 mL of a 2% aqueous tetrahydrofuran solution. The mixture was stirred at 0 °C for 1 h and at room temperature for 1 day. The mixture was filtered through a Celite plug and concentrated to give a yellow oil, which was purified by silica gel chromatography to give 160 mg of a yellow oil. This material was dissolved in acetonitrile and treated with 100 mg of cesium fluoride at room temperature. Normal workup of the mixture followed by silica gel purification of the crude residue gave 30 mg (83%) of 4-phenyl-3-buten-2-one as a colorless oil: IR (neat) 1680, 1610, 1500, 1450, 1250, 1200, and 1180 cm^{-1}; NMR (90 MHz) δ 2.3 (s, 3 H), 6.75 (d, 1 H, J = 16 Hz), 7.45 (m, 5 H), and 7.55 (d, 1 H, J = 16 Hz). Anal. Calcd for $C_{10}H_{10}O$: C, 82.19; H, 6.85. Found: C, 82.12; H, 7.15.

Peracid Oxidation of 2,5-Dimethyl-3-phenyl-4-cyano-4-isoxazoline (25). To a solution containing 200 mg of isoxazoline **25**[20] in 10 mL of methylene chloride was added 220 mg of *m*-chloroperbenzoic acid (85%) in small portions at room temperature. The reaction mixture was stirred at 25 °C for 20 h, diluted with methylene chloride, and washed with a saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give a white solid. Recrystallization using a 10% ethyl acetate–hexane mixture yielded 194 mg of 4-phenyl-3-cyano-3-buten-2-one (**26**) (97%): mp 80–81 °C; IR (KBr) 2210, 1700, 1600, 1370, 1250, 1200, 970, and 990 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.3 (s, 3 H), 7.15–7.3 (m, 3 H), 7.6–7.8 (m, 2 H), and 7.85 (s, 1 H). Anal. Calcd for $C_{11}H_9NO$: C, 77.19; H, 5.26; N, 8.18. Found: C, 77.14; H, 5.33; N, 8.17.

Peracid Oxidation of 2,5-Dimethyl-3-phenyl-4-carbomethoxy-4-isoxazoline (27). To a stirred solution containing 233 mg of **27**[20] in 10 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid in small portions at room temperature. The reaction mixture was stirred for 20 h, diluted with methylene chloride, washed with a saturated sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to give 150 mg (75%) of a white solid. Recrystallization from a 5% ethyl acetate–hexane mixture provided a fluffy solid, whose structure was assigned as 4-phenyl-3-carbomethoxy-3-buten-2-one (**28**): mp 89–90 °C; IR (KBr) 1730, 1700, 1600, 1430, 1310, and 1260 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.3 (s, 3 H), 3.8 (s, 3 H), and 7.2–8.1 (m, 6 H); HRMS calcd for $C_{12}H_{12}O_3$ 204.0786, found 204.0785. Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.88. Found: C, 70.49; H, 5.82.

Peracid Oxidation of 2-Methyl-3-phenyl-4-(phenylsulfonyl)-5-*n*-propyl-4-isoxazoline (29). To an ice-cooled stirred solution containing 343 mg of isoxazoline **29**[45] in 10 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid in small portions. After the addition was complete, the resulting solution was stirred for 3 h. The mixture was diluted with methylene chloride, washed with a sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to give 304 g (98%) of a white solid. Recrystallization from a 10% ethyl acetate–hexane mixture gave a pure sample of 1-phenyl-2-(phenylsulfonyl)-hex-1-en-3-one (**30**): mp 84–85 °C; IR (KBr) 1710, 1620, 1450, 1400, 1390, 1330, 1150, 1130, 1090, 960, 770, 750, and 700 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 0.80 (t, 3 H, J = 9.0 Hz), 1.5 (sextet, 2 H, J = 9.0 Hz), 2.5 (t, 2 H, J = 9.0 Hz), and 7.2–7.9 (m, 6 H). Anal. Calcd for $C_{18}H_{18}O_3S$: C, 68.79; H, 5.73; S, 10.20. Found: C, 68.71; H, 5.79; S, 10.14.

Peracid Oxidation of 2-Methyl-3-phenyl-4-(phenylsulfonyl)-5-(3-butynyl)-4-isoxazoline (31). To an ice-cooled solution containing 344 mg of isoxazoline **31**[45] was added 200 mg of *m*-chloroperbenzoic acid in small portions. After the addition was complete, the reaction mixture was stirred for 4 h. The mixture was then diluted with methylene chloride and washed with a sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give 318 mg (96%) of a white solid. Recrystallization of this material from a 5% ethyl acetate–hexane mixture gave a pure sample of 4-phenyl-3-(phenylsulfonyl)-1-propargyl-3-buten-2-one (**32**): mp 79–80 °C; IR (KBr) 3300, 2360, 1710, 1620, 1450, 1400, 1310, 1150, 1110, 1090, 770, and 750 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.95 (t, 1 H, J = 2.64 Hz), 2.45 (dt, 2 H, J = 6.85 and 2.64 Hz), 2.85 (t, 2 H, J = 6.85 Hz), and 7.25–7.90 (m, 11 H). Anal. Calcd for $C_{19}H_{16}O_3S$: C, 70.37; H, 4.93; S, 9.87. Found: C, 70.20; H, 5.02; S, 9.81.

Peracid Oxidation of 5-(2-Phenyl-2-hydroxyethyl)-2-methyl-3-phenyl-4-(phenylsulfonyl)-4-isoxazoline (33). To a solution containing 315 mg of 2-methyl-3-phenyl-4-(phenylsulfonyl)-5-methylisoxazoline (**23**)[20] in 7 mL of dry tetrahydrofuran was added 1 mL of a 1.3 M solution of *n*-butyllithium at −78 °C. The resulting red-brown solution was quenched with 106 mg of benzaldehyde. The reaction mixture was stirred at −78 °C for 30 min and was then warmed to 10 °C, and 1 mL of a saturated ammonium chloride solution was added. The solution was extracted with methylene chloride, dried over magnesium sulfate, and concentrated under reduced pressure to leave behind a brown residue, which was chromatographed on a silica gel column with a 30% ethyl acetate–hexane mixture as the eluent. The major fraction contained 335 mg (80%) of a white solid, whose structure was assigned as 5-(2-phenyl-2-hydroxyethyl)-2-methyl-3-phenyl-4-(phenylsulfonyl)-4-isoxazoline (**33**): mp 105–106 °C; IR (KBr) 3500, 1630, 1460, 1310, 1300, 1160, and 1050 cm^{-1}; NMR (90 MHz) δ 2.8 (s, 3 H), 3.2 (m, 2 H), 4.9 (s, 1 H), 5.2 (m, 1 H), and 7.0–7.5 (m, 15 H).

To an ice-cooled solution containing 230 mg of the above compound in 15 mL of methylene chloride was added 104 mg of *m*-chloroperbenzoic acid in small portions. After the addition was complete, the mixture was stirred for 2 h at 25 °C. The mixture was diluted with methylene chloride and washed with a saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and was concentrated under reduced pressure to give 200 mg (98%) of a pure sample of 1,5-diphenyl-1-hydroxy-4-(phenylsulfonyl)-4-penten-3-one (**34**) as a colorless oil: IR (neat) 3500, 1700, 1600, 1440, 1320, 1150, 1080, and 910 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.9 (dd, 1 H, J = 18, 4.5 Hz), 3.0 (dd, 1 H, J = 18, 8.5 Hz), 3.2 (d, 1 H, J = 3 Hz), 5.2 (t, 1 H, J = 4.5 Hz), and 7.2–8.0 (m, 15 H).

A methylene chloride solution of the above alcohol was mixed with 3 drops of triethylamine, and the mixture was stirred overnight at room temperature. A smooth cyclization occurred to give 200 mg (100%) of 2,6-diphenyl-3-(phenylsulfonyl)tetrahydro-γ-pyranone (**35**) as a white solid: mp 134–135 °C; IR (KBr) 1720, 1500, 1440, 1320, 1150, and 910 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.8 (dd, 1 H, J = 18, 10 Hz), 3.3 (dd, 1 H, J = 18, 5 Hz), 4.2 (d, 1 H, J = 6 Hz), 5.5 (dd, 1 H, J = 10, 5 Hz), 5.85 (d, 1 H, J = 6 Hz), and 7.2–7.9 (m, 15 H). Anal. Calcd for $C_{23}H_{20}SO_4$: C, 70.40; H, 5.14. Found: C, 70.28; H, 5.09.

Preparation and Peracid Oxidation of *N*-Methyl-3-phenyl-4-(phenylsulfonyl)-5-styrylisoxazoline (36). To a solution containing 160 mg of isoxazoline **33** in 3 mL of methylene chloride was added 50 mg of triethylamine followed by 60 mg of methanesulfonyl chloride at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 45 min. The solution was washed with a 5% hydrochloric acid solution followed by a saturated sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give 180 mg (95%) of the corresponding mesylate of **33** as a clear liquid: IR (neat) 1620, 1480, 1430, 1300, and 1180 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.8 (s, 3 H), 2.9 (s, 3 H), 3.6 (m, 2 H), 4.8 (s, 1 H), 6.0 (t, 1 H, J = 9 Hz), and 7.0–7.5 (m, 15 H).

To a solution containing 180 mg of the above compound in 5 mL of methylene chloride was added 0.5 mL of DBU at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 30 min. The mixture was diluted with methylene chloride and washed with a dilute hydrochloric acid solution followed by a 10% sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give *N*-methyl-3-phenyl-4-(phenylsulfonyl)-5-styrylisoxazoline (**36**) (98%) as a white solid: mp 120–121 °C; IR (KBr) 1630, 1600, 1440, 1320, 1180, and 1090 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.91 (s, 3 H), 5.02 (s, 1 H), and 7.1–7.6 (m, 17 H); UV (95% ethanol) 232 (ϵ 11 700) and 320 nm (21 150). Anal. Calcd for $C_{24}H_{21}NO_3S$: C, 71.46; H, 5.21; N, 3.47. Found: C, 71.49; H, 5.23; N, 3.41.

To a solution containing 403 mg of the above isoxazoline **36** in 20 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid in small portions. The resulting solution was stirred at room temperature for 5 h and was then washed with a saturated sodium bicarbonate solution. The organic layer was separated, dried over magnesium sulfate, and concentrated under reduced pressure to give 360 mg (97%) of 1,5-diphenyl-2-(phenylsulfonyl)-1,4-pentadien-3-one (**37**) as a colorless oil: IR (neat) 1640, 1600, 1500, 1450, 1320, 1200, 1150, 1100, 980, and 910 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 6.8 (d, 1 H, J = 16 Hz), 7.1–8.0 (m, 16 H), and 8.12 (s, 1 H). Anal. Calcd for $C_{23}H_{18}SO_3$: C, 73.79; H, 4.85. Found: C, 73.62; H, 4.83.

Peracid Oxidation of 2-Methyl-3-phenyl-4,5-dicarbomethoxyisoxazoline (38). To a stirred solution containing 277 mg of isoxazoline **38**[46] in 10 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid (85%) in small portions at room temperature. A slight exothermic reaction occurred, and the solution was then stirred for 20 h. The mixture was extracted with a sodium bicarbonate solution, and the organic layer was separated, dried over magnesium sulfate, and concentrated under reduced pressure to give a colorless oil, whose structure was assigned as methyl 4-phenyl-3-carbomethoxy-2-oxo-3-butenoate (**39**) (85%): IR ($CHCl_3$) 1750, 1700, 1600, 1460, 1450, 1340, 1260, 1100, 1000, and 750 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.85 (s, 3 H), 3.95 (s, 3 H), and 7.3–8.0 (m, 6 H); HRMS calcd for $C_{13}H_{12}O_5$ 248.0685, found 248.0683.

Peracid Oxidation of 2-Methyl-3-phenyl-5-carbomethoxy-4-isoxazoline (40). To a stirred solution containing 210 mg of isoxazoline **40**[47] in 5 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid (85%) in small portions at room temperature. A slight exothermic reaction occurred, after which the reaction mixture turned green. The solution was stirred for 4 h, washed with a sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to give 185 mg (98%) of a yellow solid. Recrystallization from a 5% ethyl acetate–hexane mixture gave methyl 4-phenyl-2-oxo-3-butenoate (41) as yellow crystals: mp 62–63 °C; IR (KBr) 1750, 1700, 1600, 1460, 1450, 1340, 1310, 1260, 1100, 1000, and 750 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.9 (s, 3 H), 7.25 (d, 1 H, J = 17.5 Hz), 7.35–7.60 (m, 5 H), and 7.81 (d, 1 H, J = 17.5 Hz); UV (95% ethanol) 313 (ϵ 16 700) and 227 nm (6260); MS, m/e 190 (M^+), 131 (base), 103, and 77. Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.47; H, 5.26. Found: C, 69.39; H, 5.31.

Peracid Oxidation of Methyl *N-tert*-Butyl-3-phenylisoxazoline-5-carboxylate (43). To an ice-cooled solution containing 160 mg of **43**[45] in 10 mL of methylene chloride was added dropwise a solution containing 125 mg of *m*-chloroperbenzoic acid (85%) in 5 mL of methylene chloride over a 5-min interval. After the addition was complete, the solution was stirred for another 90 min, then extracted with a 10% sodium carbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to leave behind a yellow residue, which was subjected to silica gel chromatography using a 20% ethyl acetate–hexane mixture as the eluent. The major fraction isolated from the column contained 59 mg (65%) of methyl 4-phenyl-2-oxo-3-butenoate (41).

Peracid Oxidation of 2-Methyl-3-phenyl-4-carbomethoxy-4-isoxazoline (44). To a stirred solution containing 210 mg of isoxazoline **44**[47] in 5 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid (85%) in small portions at room temperature. A slight exothermic reaction occurred, after which the mixture turned green. The solution was stirred for 3 h at 25 °C, diluted with methylene chloride, and washed with a sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give 184 mg (97%) of 3-phenyl-2-carbomethoxyacrolein (**45**) as a yellow oil: IR (CCl_4) 1760, 1700, 1640, 1610, 1450, 1230, and 1150 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 3.85 (s, 3 H), 7.35 (m, 6 H), and 8.15 (s, 1 H). Anal. Calcd for $C_{11}H_{10}O_3$: C, 69.47; H, 5.26. Found: C, 69.38; H, 5.25.

Peracid Oxidation of 2,3,3-Trimethyl-4-(phenylsulfonyl)-5-methyl-4-isoxazoline (46). To an ice-cooled stirred solution containing 267 mg of **46**[45] in 10 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid in small portions. A transient blue-green color of nitrosomethane was noticed. The reaction mixture was stirred at 0 °C for 1 h and at room temperature for 2 h. The mixture was diluted with methylene chloride, washed with a sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to give a colorless oil (98%) whose structure was assigned as 4-methyl-3-(phenylsulfonyl)-3-penten-2-one (**47**): IR ($CHCl_3$) 1700, 1630, 1450, 1340, 1200, 1150, 1100, and 920 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 1.8 (s, 3 H), 2.0 (s, 3 H), 2.5 (s, 3 H), and 7.4–7.9 (m, 5 H). Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.50; H, 5.88; S, 13.44. Found: C, 60.37; H, 5.91; S, 13.39.

Peracid Oxidation of *N-tert*-Butyl-3-*n*-propyl-4-(phenylsulfonyl)-4-isoxazoline (48). To an ice-cooled solution containing 323 mg of isoxazoline **48**[45] was added 200 mg of *m*-chloroperbenzoic acid in small portions. After the addition was complete, the mixture was stirred for 3 h. The solution was diluted with methylene chloride and washed with a sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give a clear oil, which was purified by column chromatography to give 226 mg (90%) of 3-(phenylsulfonyl)-3-hepten-2-one (**49**) as a colorless oil: IR (neat) 1700, 1620, 1450, 1370, 1320, 1160, 1090, 990, 940, and 880 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 0.95 (t, 3 H, J = 9 Hz), 1.60 (m, 2 H), 2.35 (q, 2 H, J = 9 Hz), 2.30 (s, 3 H), 7.15 (t, 1 H, J = 9 Hz), and 7.5–8.0 (m, 5 H). Anal. Calcd for $C_{13}H_{16}O_3S$: C, 61.90; H, 6.35; S, 12.70. Found: C, 61.95; H, 6.39; S, 12.60.

Peracid Oxidation of 2-Methyl-3-(phenylsulfonyl)octahydropyridino[1,2-*b*]isoxazoline (50). To a solution containing 200 mg of **50**[45] in 5 mL of methylene chloride was added 170 mg of *m*-chloroperbenzoic acid in small portions. The reaction mixture was stirred for 8 h, diluted with methylene chloride, and washed with a sodium bicarbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give 196 mg (95%) of a white solid. Recrystallization from a 5% chloroform–hexane mixture provided a pure sample of tricyclic ketal **53** as a colorless crystalline compound: mp 179–180 °C; IR (KBr) 1450, 1400, 1310, 1290, 1150, 1100, 920, and 750 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.02–1.11 (m, 1 H), 1.32–1.51 (m, 2 H), 1.58–1.83 (m, 2 H), 1.96 (s, 3 H), 1.96–2.08 (m, 1 H), 3.45–3.52 (m, 1 H), 3.83–3.95 (m, 1 H), 4.88 (s, 1 H), 7.60 (t, 2 H, J = 7.5 Hz), 7.70 (t, 1 H, J = 7.5 Hz), and 7.90 (d, 2 H, J = 7.5 Hz). Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.959; H, 5.76; N, 4.75; S, 10.85. Found: C, 57.01; H, 5.84; N, 4.72; S, 10.80.

Colorless crystals were grown from chloroform–hexane. A suitable crystal of approximately 0.42 × 0.15 × 0.20 mm was mounted on a quartz fiber with epoxy cement such that the longest crystal dimension was parallel to the fiber axis. Unit cell parameters were determined on a Syntex $P2_1$ automated diffractometer using Mo Kα radiation. Twenty-three reflections were machine centered and used in the least-squares refinement of the lattice parameters and orientation matrix. The unit cell parameters obtained were a = 8.8719 (0.0038) Å, b = 15.2002 (0.0087) Å, c = 10.7526 (0.0062) Å, α = 90.000 (0.006)°, β = 105.818 (0.039)°, γ = 90.000 (0.000)°, V = 139.513 (1.26) Å^3, d_{calcd} = 1.40 g cm^{-3}, $F(000)$ = 623.92, Z = 4, and space group $P\ 2_1/C$.

Intensity data were collected by using the ω scan technique with a mini scan rate X-29.3. A scan width of 1.0° was sufficient to collect all of the peak intensities. Check reflections, monitored after each set of 200 scans, showed no significant change during the course of data collection. Lorentz and polarization corrections were made in the usual way. No absorption correction was applied. Of the total of 2101 reflections collected with $4.0° < 2\theta < 50.0°$, 1605 were found to be unique and have $I \geq 3\sigma(I)$. The structure was solved by direct methods with the SHELXTL. In addition to locating the backbone atoms, the three hydrogen atoms necessary to specify the stereochemistry were found without fixation. Following anisotropic refinement of the skeleton atoms, all other hydrogen atoms were fixed into position. The final discrepancy index and weighted discrepancy index were R = 0.0480 and R_w = 0.0518, respectively. The final positional and thermal parameters are given in Tables 1–5 (supplementary material).

Preparation of 2-Methyl-3-phenyl-4-(phenylsulfonyl)-5-methyleneisoxazolidine *N*-Oxide (55). To an ice-cooled solution containing 316 mg of 2-methyl-3-phenyl-4-(phenylsulfonyl)-5-methyleneisoxazolidine (**54**)[20] in 5 mL of methylene chloride was added 200 mg of *m*-chloroperbenzoic acid. The reaction mixture was stirred at 0 °C for 5 h, diluted with methylene chloride, and washed with a sodium carbonate solution. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure to give a brown oil, which was subjected

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to silica gel chromatography. The *N*-oxide was separated by using a 15% ethyl acetate–hexane mixture as the eluent. Evaporation of the solvent under reduced pressure gave 265 mg (80%) of 2-methyl-3-phenyl-4-(phenylsulfonyl)-5-methyleneisoxazolidine *N*-oxide (**55**) as a white solid. Recrystallization from a 10% ethyl acetate–hexane mixture gave colorless crystals: mp 131–132 °C; IR (KBr) 1760, 1450, 1310, 1150, 760, and 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.5 (s, 3 H), 4.0 (d, 1 H, J = 6 Hz), 4.4 (d, 2 H), 4.8 (d, 1 H, J = 6 Hz), and 7.2–7.8 (m, 10 H).

A stirred solution containing 331 mg of the above *N*-oxide in 10 mL of methylene chloride was cooled to 0 °C, and to this solution was added 204 mg of acetic anhydride over a 5-min period. The mixture was allowed to warm to room temperature, and after the mixture was stirred for 5 h, 0.2 mL of pyridine was added. The organic layer was washed with water and a dilute hydrochloric acid solution, dried over magnesium sulfate, and concentrated in vacuo to give a white solid (298 mg, 80%). Recrystallization of this material from a 5% ethyl acetate–hexane mixture provided a pure sample of 2-methyl-3-acetoxy-3-phenyl-4-(phenylsulfonyl)-5-methyleneisoxazolidine (**56**): mp 154–155 °C; IR (KBr) 1790, 1660, 1450, 1370, 1310, 1290, 1180, and 1150 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 2.2 (s, 3 H), 2.3 (s, 3 H), 4.25 (d, 1 H, J = 2.5 Hz), 4.5 (d, 1 H, J = 2.5 Hz), 4.75 (s, 1 H), and 7.1–7.3 (m, 10 H). Anal. Calcd for $C_{19}H_{19}O_5NS$: C, 61.13; H, 5.09; N, 3.75; S, 8.58. Found: C, 61.06; H, 5.17; N, 3.75; S, 8.52.

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Registry No. **8**, 19345-08-5; **11**, 113549-18-1; **12**, 106745-24-8; **13**, 113549-19-2; **14**, 113549-20-5; **15**, 113549-21-6; **16**, 17647-39-1; **17** (*E* oxime), 113549-15-8; **17** (*Z* oxime), 113549-22-7; **18**, 113549-23-8; **19**, 113549-24-9; **22**, 113549-25-0; **23**, 107402-99-3; **24**, 113549-26-1; **24** (*o*–trimethylsilylcyanohydrin), 113549-16-9; **25**, 108817-75-0; **26**, 110729-87-8; **27**, 108817-72-7; **28**, 20048-05-9; **29**, 113549-27-2; **30**, 113549-28-3; **31**, 113549-29-4; **32**, 113549-30-7; **33**, 113549-31-8; **33** (mesylate), 113549-17-0; **34**, 113549-32-9; **35**, 113549-33-0; **36**, 113549-34-1; **37**, 113549-35-2; **38**, 109787-18-0; **39**, 113549-36-3; **40**, 87352-10-1; **41**, 107969-78-8; **43**, 87352-09-8; **43** (regioisomer), 87352-06-5; **44**, 109787-19-1; **45**, 113549-37-4; **46**, 113549-38-5; **46** (5-methylene isomer), 113549-42-1; **47**, 113549-39-6; **48**, 113549-40-9; **49**, 113549-41-0; **50**, 107403-02-1; **50** (5-methylene isomer), 107402-98-2; **53**, 113549-43-2; **54**, 108817-77-2; **55**, 113549-44-3; **56**, 113549-45-4; $PhCOCH{=}CHCO_2CH_3$, 14274-07-8; $Ph(CH_2)_2COCH_3$, 2550-26-7; $PhCH{=}CHCOCH_3$, 122-57-6; $PhCH{=}N(O)C_4H_9$-*t*, 3376-24-7; $CH_2{=}C(CH_3)CO_2CH_3$, 80-62-6; $HC{\equiv}CCO_2CH_3$, 922-67-8; $(CH_3)_2C(OC_2H_5)_2$, 77-76-9; $(CH_3)_2C{=}N(O)CH_3$, 72552-73-9; $PhSO_2CH{=}C{=}CH_2$, 2525-42-0; *n*–$C_3H_7CH{=}N(O)C_4H_9$-*t*, 72552-75-1; $PhSO_2C{\equiv}CCH_3$, 2525-41-9; 1-hydroxypiperidine, 4801-58-5.

Supplementary Material Available: Experimental details for the preparation of compounds **13**, **29**, **31**, **43**, **46**, **48**, and **50**, base-induced alkylations of 2,5-dimethyl-3-phenyl-4-(phenylsulfonyl)isoxazoline (**23**), and crystallographic data for **53** (Tables 1–5) (9 pages). Ordering information is given on any current masthead page.

Acylation of Pyrrole and *N*-Methylpyrrole with 1,3-Benzoxathiolium Tetrafluoroborates. A High-Yield Method for the Synthesis of Diacylpyrroles[†]

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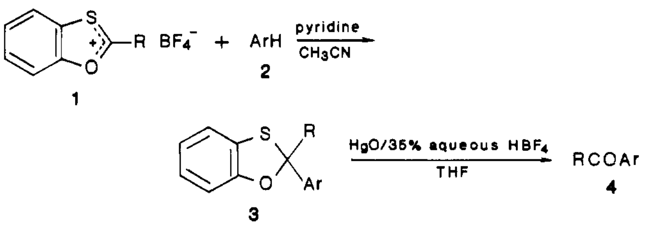
2-Substituted 1,3-benzoxathiolium tetrafluoroborates (I) were used as masked acylating agents for pyrrole and *N*-methylpyrrole. The reactions on pyrrole (II) were regiospecific, and according to the molar ratio of the reagents (I:II = 1:3 or 2.5–3:1), 2-acylpyrroles were obtained in moderate to good yields (38–82%) and 2,5-diacylpyrroles were obtained in excellent yields (in most cases, quantitative). The reactions on *N*-methylpyrrole (III) were not regioselective, and both α- and β-positions were attacked. So, depending on the molar ratio of the reagents (I:III = 1:3 or 2.5–3:1), 2- and 3-acyl-*N*-methylpyrroles (9–51% and 27–68% yields, respectively) and 2,4- and 2,5-diacyl-*N*-methylpyrroles (60–93% and 17–40%, respectively) were obtained. A very interesting feature of the new method is the possibility of introducing two identical or different acyl groups in the pyrrole ring under mild conditions. ^1H and ^{13}C NMR spectra of all the new compounds and IR spectra, recorded in the gas phase, of 2- and 3-acylpyrroles and of 2,4- and 2,5-diacylpyrroles are reported.

In previous work we have shown the synthetic effectiveness of 1,3-benzoxathiolium tetrafluoroborates **1** as masked acylating agents.[2] In particular, we have recently found that in certain cases the salts **1** can be advantageously utilized for a two-step acylation of electron-rich aromatic and heteroaromatic compounds.[3] Indeed, according to Scheme I, various 2,2-disubstituted 1,3-benzoxathioles **3** were first obtained by electrophilic aromatic substitution from reaction of **1** with **2**, under mild conditions; subsequently, hydrolysis of **3** easily yielded the acyl derivatives **4**.

Scheme I



In connection with these last investigations, we have undertaken a specific study on the acylation of pyrrole and

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[†] Part 18 in Pentaatomic Heteroaromatic Cations series. Part 17 is ref. 1. Presented in part at XVI Convegno Nazionale della Divisione di Chimica Organica della Società Chimica Italiana, Urbino, Italy, September 7–14, 1986 (Atti, p 42).

(1) Barbero, M.; Cadamuro, S.; Ceruti, M.; Degani, I.; Fochi, R.; Regondi, V. *Gazz. Chim. Ital.* **1987**, *117*, 227.

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