Synthesis of the Benzazepin-4-one Ring System via Dipolar Cycloaddition of *N*-Phenylnitrones with Activated Allenes

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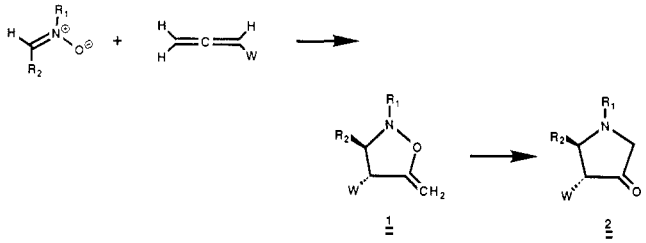
The 1,3-dipolar cycloaddition of *N*-phenyl-*C*-phenylnitrone with several allenes containing electron-withdrawing groups has been investigated. The cycloaddition proceeds in good yield to give a substituted benzazepin-4-one. The structure of the cycloadduct was established by high-field NMR spectroscopy as well as by an X-ray crystal structure. The results are consistent with a mechanism that involves dipolar cycloaddition of the nitrone across the more activated π-bond of the allene to give a transient 5-methyleneisoxazolidine. This material undergoes rapid N–O bond cleavage, and the resulting diradical intermediate cyclizes onto the ortho position of the phenyl group. The cycloaddition chemistry of 2,3-bis(phenylsulfonyl)-1-propene and ethyl 3-(phenylsulfonyl)but-3-enoate with several nitrones were also investigated. These reagents correspond to formal "allene equivalents" and can be used to prepare the unfavorable cycloadduct derived from a nitrone and the less activated π-bond of the allene. The effects of high pressure on the cycloaddition of nitrones with these "allene equivalent reagents" has also been investigated.

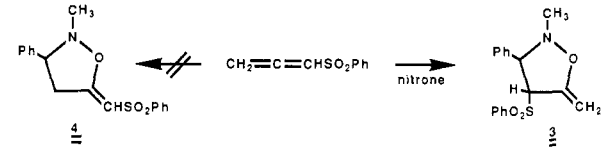
The development of procedures for efficiently constructing nitrogen-containing rings is of great importance in alkaloid synthesis.[1,2] As part of an ongoing program in the area of heterocyclic chemistry,[3] we have been investigating the 1,3-dipolar cycloaddition chemistry of nitrones with allenes[4] followed by their thermal rearrangement.[5-8] The 1,3-sigmatropic reorganization of 5-methyleneisoxazolidines attracted our attention as a particularly appealing vehicle for developing a new pyrrolidine synthesis. Toward this end we have studied the dipolar



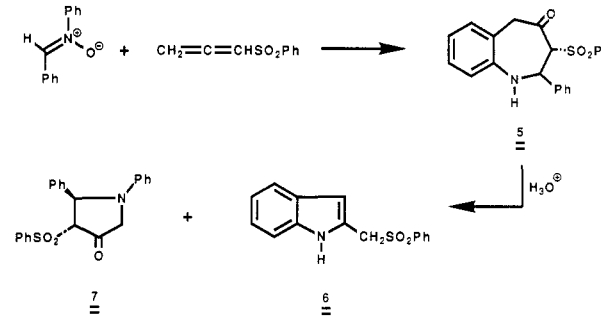
cycloaddition behavior of several activated allenes with various nitrones with the expectation that the resulting 5-methylene-substituted isoxazolidine **1** should be of some use in organic synthesis. During the course of these inquiries we had the occasion to examine the reaction of *N*-phenyl-*C*-phenylnitrone with several substituted allenes. In contrast to the results obtained with *N*-alkylnitrones, this reaction proceeded in an entirely different fashion, giving rise to the benzazepin-4-one ring system.[9] The present paper documents the results of these studies.

Results and Discussion

Allenes are an intriguing group of dipolarophiles since they contain two positions for attack.[14] On the basis of FMO theory,[15] allenes possessing electron-withdrawing substituents are expected to undergo dipolar cycloaddition across the more activated π-bond.[16] This proved to be the case in the reaction of *N*-methyl-*C*-phenylnitrone with (phenylsulfonyl)-1,2-propadiene. No detectable quantities of the regioisomeric cycloadduct **4** could be found in the crude reaction mixture.



Interestingly, the reaction of *C*-phenyl-*N*-phenylnitrone with (phenylsulfonyl)-1,2-propadiene[17] at room temperature for 6 h gave 1,2,3,5-tetrahydro-2-phenyl-3-(phenylsulfonyl)-4*H*-1-benzazepin-4-one (**5**) as the major product in 67% isolated yield. The structure of benzazepinone **5** was assigned on the basis of its characteristic spectral



(1) Glasby, J. S. *Encyclopedia of the Alkaloids*; Plenum Press: New York, 1975; Vol. 1 and 2, 1977, Vol. 3.
(2) Pinder, A. R. *The Alkaloids*; Grundon, M. F., Ed.; Chemical Society: London, 1982; Vol. 12.
(3) Padwa, A.; Kline, D. N.; Koehler, K. F.; Venkatramanan, M. D. *J. Org. Chem.* **1987**, *52*, 3909. Padwa, A.; Koehler, K. F.; Rodriguez, A. *J. Am. Chem. Soc.* **1981**, *103*, 4974. Padwa, A.; Fisera, L.; Koehler, K. F.; Rodriguez, A.; Wong, G. S. K. *J. Org. Chem.* **1984**, *49*, 282.
(4) Padwa, A.; Carter, S. P.; Chiacchio, U.; Kline, D. N. *Tetrahedron Lett.* **1986**, 2683. Padwa, A.; Tomioka, Y.; Venkatramanan, M. K. *Tetrahedron Lett.* **1987**, 755.
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(6) Tufariello, J. J.; Ali, S. A.; Klingele, H. O. *J. Org. Chem.* **1979**, *44*, 4213.
(7) LeBel, N. A.; Banucci, E. *J. Am. Chem. Soc.* **1970**, *92*, 5278.
(8) Bruche, L.; Gelmi, M. L.; Zecchi, G. *J. Org. Chem.* **1985**, *50*, 3206.
(9) This result is not totally unexpected in that there have been some related reports that show that the initially formed 5-methyleneisoxazolidine adduct can undergo a subsequent 3,3-sigmatropic rearrangement.[10-13]
(10) Tuffariello, J. J.; Ali, S. A.; Klingele, H. O. *J. Org. Chem.* **1979**, *44*, 4213.
(11) Blechert, S. *Justus Liebigs Ann. Chem.* **1985**, 673. Wilkens, J.; Kuhling, A.; Blechert, S. *Tetrahedron* **1987**, *44*, 3237.
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(13) Padwa, A.; Matzinger, M.; Tomioka, Y.; Venkatramanan, M. K. *J. Org. Chem.* **1988**, *53*, 955.
(14) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; J. Wiley, Inc.: New York, 1984.
(15) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; J. Wiley, Inc.: New York, 1976.
(16) MNDO calculations indicate that the introduction of a phenylsulfonyl group causes a significant lowering of the LUMO energy level compared with allene and the largest LUMO coefficient resides on the central carbon and the next on the carbon bearing the phenylsulfonyl group.
(17) Stirling, C. J. M. *J. Chem. Soc.* **1964**, 5856.

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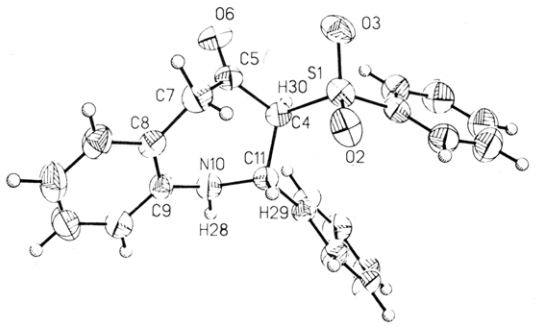
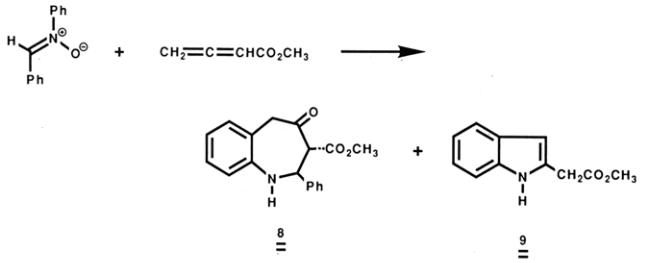


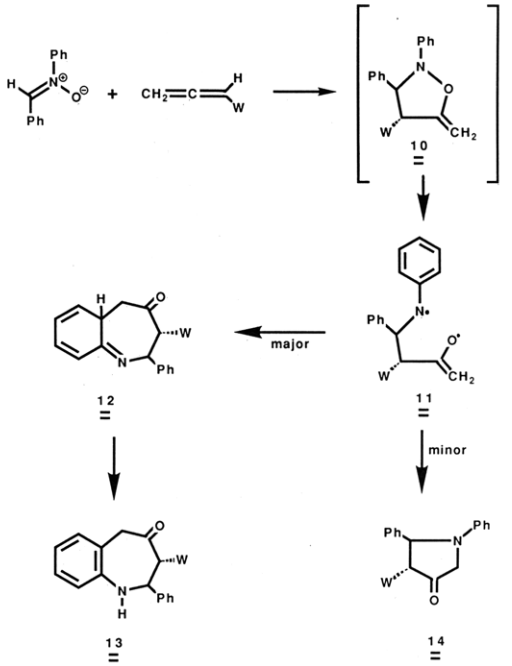
Figure 1. X-ray crystal structure of benzazepin-4-one **5**.

data (NMR ($CDCl_3$, 360 MHz) δ 3.52 (br s, 1 H), 3.70 (d, 1 H, J = 14.0 Hz), 4.62 (d, 1 H, J = 10.3 Hz), 4.93 (d, 1 H, J = 14.0 Hz), 5.30 (d, 1 H, J = 10.3 Hz), 6.48 (d, 1 H, J = 7.8 Hz), 6.85 (t, 1 H, J = 7.5 Hz), 7.03 (t, 1 H, J = 7.8 Hz), 7.09 (d, 1 H, J = 7.5 Hz), 7.23–7.36 (m, 7 H), and 7.45–7.53 (m, 3 H)). The structure of **5** was unequivocally established by an X-ray single-crystal structure analysis. The overall geometry of the molecule is shown in Figure 1. Two minor products were also isolated and identified as 2-[(phenylsulfonyl)methyl]indole (**6**) (13%) and 1,5-diphenyl-4-(phenylsulfonyl)pyrrolidin-3-one (**7**) (3%).[18] Control experiments demonstrated that benzazepinone **5** was converted to indole **6** and benzaldehyde when subjected to silica gel chromatography or by simply standing for long periods of time. More than likely this transformation proceeds via a retro-Mannich reaction followed by hydrolysis and cyclization to the indole ring.

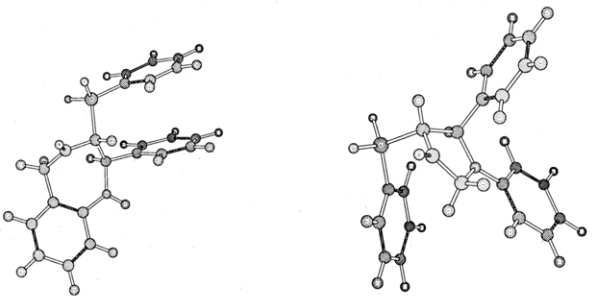
An analogous set of reactions was also observed upon treating methyl 2,3-butadienoate with *C,N*-diphenylnitrone. The major product formed was identified as benzazepinone **8** on the basis of its spectral properties (see the Experimental Section).



The formation of the benzazepin-4-one ring system can nicely be accounted for in terms of an initial 1,3-dipolar cycloaddition of the nitrone across the activated π-bond of the allene to give a transient 5-methyleneisoxazolidine. The nitrogen–oxygen bond of the resulting heterocyclic ring is expected to be readily cleaved, since such heteroatom–heteroatom bonds are known to be very weak.[19–22] The resulting diradical intermediate either cyclizes onto the ortho position of the *N*-phenyl group or, to a much lesser extent, recombines on the enolic carbon atom to give pyrrolidinone **7**. The preference for the seven-membered benzazepine ring is probably related to its greater thermodynamic stability. In support of this suggestion, molecular mechanics calculations were carried out by use of the Still–Steliou Model 2.92 program so as to calculate the



total energy of the two isomeric ring systems. We assume that the relative energy differences of the two lowest energy conformations of both heterocyclic compounds will parallel the energy differences for five- vs seven-membered ring formation in the transition state. The results obtained demonstrate that the seven-membered benzazepine ring (total energy = 28.41 kcal/mol) is lower in energy than the corresponding pyrrolidinone ring (total energy = 32.27 kcal/mol). MNDO calculations (AM1) also show that the



Benzazepinone 13 Pyrrolidinone 14

Et=28.41 kcal Et=32.27 kcal

five- and seven-membered rings differ by 16 kcal in their heat of formation.[23] Some of this energy difference is presumably involved in the transition state for product formation. We believe that the diradical mechanism more accurately describes the rearrangement of **10** to **14** than the concerted hetero-Cope rearrangement advocated by Blechert.[11]

In order to provide support for the intermediacy of the 5-methyleneisoxazolidine, we have studied the reaction of several nitrones with 2,3-bis(phenylsulfonyl)-1-propene (**15**). This reagent corresponds to a formal "allene equivalent" and permits the indirect synthesis of the unfavorable cycloadduct **4** derived by nitrone cycloaddition across the less activated π-bond of the allene. Thus, heating a solution of *C*-phenyl-*N*-methylnitrone with **15** at 80 °C for 2 days gave cycloadduct **16** in 79% yield. Treatment of this material with DBU afforded 5-methyleneisoxazolidine **4**, thereby providing an indirect synthesis of the previously unknown cycloadduct.

(18) While this work was in progress a similar set of observations was made by Zecchi and Parpani.[12]

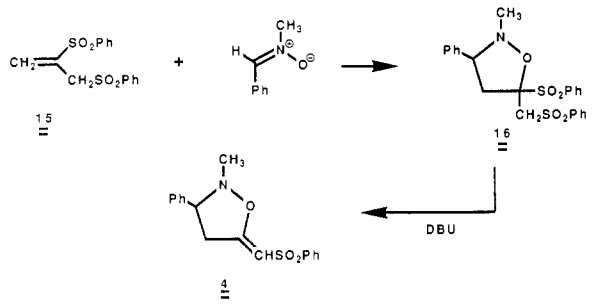
(19) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 496.

(20) Cottrell, T. I. *The Strengths of Chemical Bonds*, 2nd ed.; Butterworths: London, 1958.

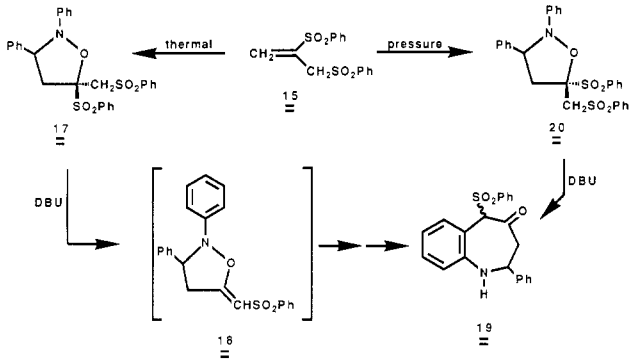
(21) Baldwin, J. E.; Pudussery, R. G.; Qureshi, A. K.; Sklarz, B. B. *J. Am. Chem. Soc.* **1968**, *90*, 5326.

(22) For a preliminary report of this work, see: Padwa, A.; Kline, D. N.; Norman, B. H. *Tetrahedron Lett.* **1988**, 265.

(23) QCPE no. 506 (Ampac) using the AM1 Hamiltonian.



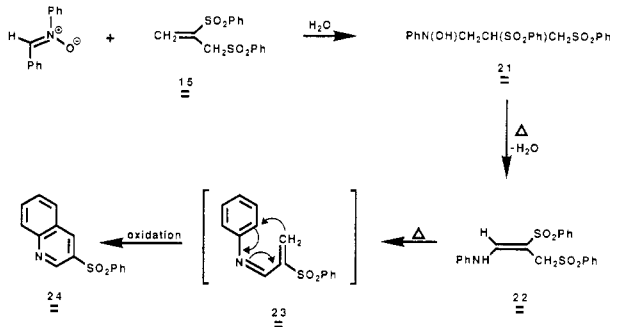
We also found that **15** undergoes clean 1,3-dipolar cycloaddition (80 °C, 4 days) with *C*-phenyl-*N*-phenylnitrone to give isoxazolidine **17** as the exclusive cycloadduct in 85% isolated yield. The stereochemical assignment of the (phenylsulfonyl)methyl group is based on NOE experiments. Treatment of cycloadduct **17** with DBU afforded a 1:2 mixture of *cis*- and *trans*-1,2,3,5-tetrahydro-2-phenyl-5-(phenylsulfonyl)-4*H*-1-benzazepin-4-one (**19**) in 87% yield. The formation of **19** from the base-induced reaction of **17** provides strong support for the intermediacy of a 5-methyleneisoxazolidine (i.e. **18**), which readily undergoes rearrangement to the benzazepinone via the diradical mechanism outlined above.



Given the long periods of time to effect the dipolar cycloaddition of **15** with the above nitrones, we turned to the use of high pressures. High pressures are known to very markedly accelerate intermolecular cycloadditions with volumes of activation and reaction typically lying in the range of −30 to −40 $cm^3\ mol^{-1}$.[24-29] Most interestingly, we have found that the cycloaddition stereochemistry is distinctly dependent upon the reaction conditions employed. When a solution of **15** and *N*-phenyl-*C*-phenylnitrone were pressurized to 5 kbar at room temperature for 36 h, a 92% yield of cycloadduct **20** was obtained. No detectable signs of the thermal cycloadduct **17** were found in the crude reaction mixture. Treatment of **20** with DBU afforded the same 1:2 mixture of diastereomeric benzazepinones (i.e. **19**) as that derived from **17**.

At first glance it would seem that one could rationalize the results by assuming that the thermolysis experiments give the thermodynamically more stable cycloadduct (i.e. **17**) while the high-pressure reaction affords the kinetic product (i.e. **20**). Molecular mechanics calculations were carried out[30] so as to determine the total energy of the two diastereomers. These calculations reveal that an energy difference of 2.5 kcal (45.78 kcal/mol vs 43.24 kcal/mol) exists between the lower energy thermal cycloadduct and the isoxazolidine derived from the high-pressure experiments. We have subjected the pressure cycloadduct **20** to the thermolysis conditions and find, however, that it does not rearrange to cycloadduct **17**. The factors controlling the stereochemical outcome in these cycloadditions are not clearly defined, and further experiments are needed to rationalize the results and to evaluate the potential of pressure as a means of influencing stereochemical control.[31] It should be noted that a somewhat related pressure-induced diastereoselectivity has recently been encountered by Tietze and co-workers in their study of the hetero Diels–Alder reaction of enamino ketones.[32]

During the course of these experiments we found that 2,3-bis(phenylsulfonyl)-1-propene reacts with phenylhydroxylamine to give structure **21**. Heating a sample of **21** in benzene at 80 °C for 60 h with a trace of *p*-toluenesulfonic acid afforded 3-(phenylsulfonyl)quinoline (**24**) in 60% yield. A reasonable mechanism to rationalize

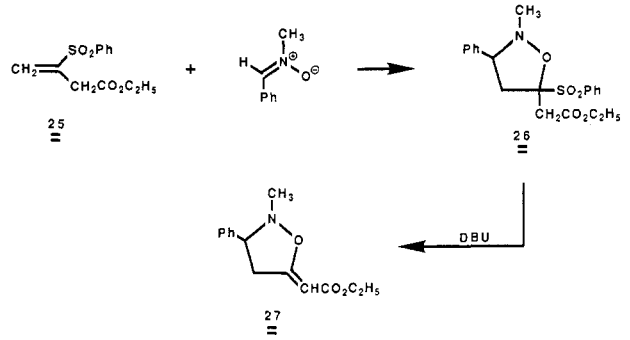


the reaction involves initial dehydration of **21** to **22** followed by a thermal elimination of phenylsulfinic acid to give aza diene **23**. This transient intermediate undergoes a 6π-electrocyclization followed by an oxidation to give quinoline **24**. In support of the above suggestion we have been able to isolate structure **23** by carrying out the thermolysis of **21** for only 30 h. Further heating of **22** gave quinoline **24** in high yield.

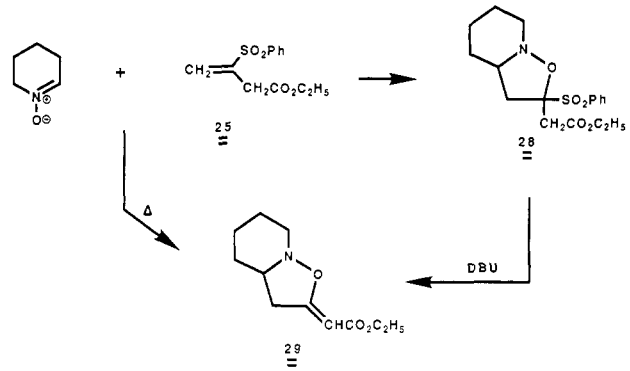
The ability of allenes to undergo bimolecular cycloaddition reactions with a variety of unsaturated π-systems has provided the synthetic chemist with a convenient route for the construction of complex ring systems.[33-39] Allenes activated with electron-deficient groups are of particular interest in cycloaddition chemistry since they can be used synthetically in a variety of ways. As a consequence of our interest in this area,[40] we sought to develop useful olefinic

(24) For a recent review on organic synthesis under high pressure, see: Matsumoto, K.; Sera, A.; Uchida, T. *Synthesis* **1985**, 1.
(25) Dicken, C. M.; DeShong, P. *J. Org. Chem.* **1982**, *47*, 2047.
(26) Dauben, W. G.; Krabbenhoft, D. *J. Am. Chem. Soc.* **1976**, *98*, 1992. Dauben, W. G.; Kessel, C. R.; Takemura, K. H. *J. Am. Chem. Soc.* **1980**, *102*, 6893.
(27) Bunce, R. A.; Schlecht, M. F.; Dauben, W. G.; Heathcock, C. W. *Tetrahedron Lett.* **1983**, 4943. Tomamoto, Y.; Maruyama, K.; Matsumoto, K. *J. Am. Chem. Soc.* **1983**, *105*, 6963.
(28) Dauben, W. G.; Bunce, R. A.; Gerdes, J. M.; Heneger, K. E.; Cunningham, A. F.; Ottoboni, T. B. *Tetrahedron Lett.* **1983**, 5709.
(29) Dauben, W. G.; Gerdes, J. M.; Bunce, R. A. *J. Org. Chem.* **1984**, *49*, 4293.
(30) We wish to thank Professor Kosta Steliou of the University of Montreal for providing a copy of the extensively rewritten Still Model program (version 2.92).
(31) The results described here complement those of DeShong and Dicken[25] who had previously found that the ratio of stereoisomeric isoxazolidines can vary as a function of pressure.
(32) We wish to thank Professor Lutz F. Tietze for providing us with a preprint of his findings, see: Tietze, L. F.; Hubsch, T.; Vo, E.; Buback, M.; Tost, W. *J. Am. Chem. Soc.* **1988**, *110*, 4065.
(33) Corey, E. J.; Bass, J. D.; Le Mathieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570.
(34) Eaton, P. E. *Tetrahedron Lett.* **1964**, 3695.
(35) Pasto, D. J. *Tetrahedron* **1984**, *40*, 2805.
(36) Heathcock, C. H.; Graham, S. L.; Pirrung, M. C.; Plavec, F.; White, C. T. *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1983; Vol. 5.
(37) Hayakawa, K.; Nishiyama, H.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 512.
(38) Gras, J. L.; Guerin, A. *Tetrahedron Lett.* **1985**, 1781.
(39) Hayakawa, K.; Yamaguchi, Y.; Kanematsu, K. *Tetrahedron Lett.* **1985**, 2689.

reagents that could be used as formal allene equivalents and allow for reaction across the less activated π-bond of the allene. Toward this end we have investigated the cycloaddition behavior of ethyl 3-(phenylsulfonyl)but-3-enoate (**25**). This material was readily prepared by the addition of sodium benzenesulfinate to ethyl 2,3-butadienoate. Heating a solution of *C*-phenyl-*N*-methylnitrone with **25** at 80 °C gave 5-methyleneisoxazolidine **27** as the exclusive product. Apparently, the initially formed 1,3-

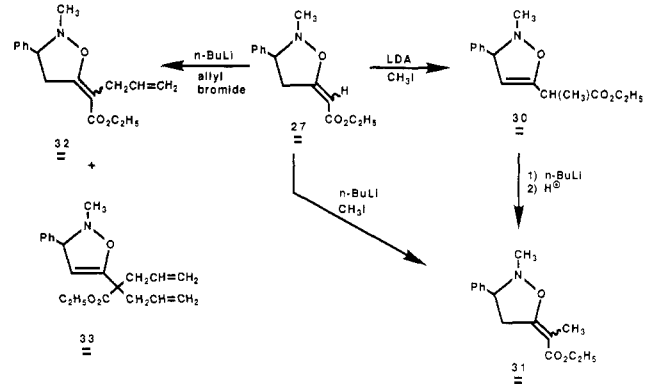


dipolar cycloadduct undergoes ready loss of phenylsulfinic acid under the thermal conditions employed for the reaction. When the cycloaddition was carried out under high pressure, it was possible to isolate the suspected cycloadduct **26**. Treatment of **26** with DBU cleanly afforded isoxazolidine **27**. A similar set of reactions were observed to occur with tetrahydropyridine *N*-oxide and (phenylsulfonyl)butenoate **25**.

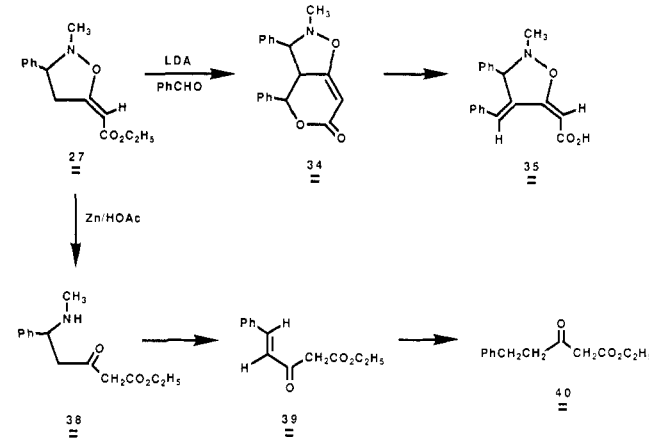


In order to obtain some information concerning the potential synthetic utility of the carboethoxy substituted 5-methyleneisoxazolidine system, we investigated its reaction with base and various electrophiles. The only product formed (94%) from this reaction (using LDA as the base) corresponded to the α-methylated product **30**. Interestingly, when **27** was treated with *n*-butyllithium followed by methylation, the major product corresponded to the isomerized 5-methyleneisoxazolidine **31**. The formation of **31** proceeds via a base-induced isomerization of **30**. This could be independently established by subjecting a sample of **30** to the strongly basic conditions used. An analogous reaction occurred with **27** and allyl bromide. When an excess of the electrophile was used, the diallylated product **33** was also formed.

We also examined the reaction of the carbanion derived from isoxazolidine **27** with benzaldehyde and found that only γ-attack had occurred. Thus, treatment of **27** with



LDA followed by reaction with excess benzaldehyde gave lactone **34**, which was readily opened to give the unsaturated carboxylic acid **35**. Reduction of **27** with zinc in acetic acid proceeded to give keto ester **38**, which subsequently eliminated methyl amine to produce **39**. This material was further reduced to ethyl 3-oxo-5-phenylpentanoate (**40**) under the experimental conditions employed.



In summary, the dipolar cycloaddition reaction of *N*-phenylnitrones with activated allenes affords the benazepin-4-one ring system in good yield. The reaction can be rationalized in terms of a cycloaddition across the more activated π-bond followed by cleavage of the N–O bond of a transient 5-methyleneisoxazolidine. The resulting diradical intermediate cyclizes onto the ortho position of the *N*-phenyl group and this is followed by a subsequent hydrogen shift. 2,3-Bis(phenylsulfonyl)-1-propene represents a useful synthetic reagent, which formally corresponds to an allene equivalent and which can be used to prepare 3-sulfonyl-substituted quinolines.

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 a Varian EM-390 and a Nicolet NMC-360 MHz spectrometer. ^{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.

Reaction of *C*,*N*-Diphenylnitrone with (Phenylsulfonyl)propadiene. A solution containing 1.30 g of *C*,*N*-diphenylnitrone and 1.18 g of (phenylsulfonyl)propadiene[17] in 150 mL of carbon tetrachloride was stirred at room temperature for 6 h. Removal of the solvent under reduced pressure and recrystallization of the solid from methylene chloride–ethyl acetate gave 1,2,3,5-tetrahydro-2-phenyl-3-(phenylsulfonyl)-4*H*-1-benzazepin-4-one[11] (**5**) in 57% yield: mp 145–146 °C; IR (KBr) 3400,

(40) Padwa, A.; Yeske, P. *J. Am. Chem. Soc.* **1988**, *110*, 1617.
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(43) LeBel, N. A.; Post, M. E.; Whang, J. J. *J. Am. Chem. Soc.* **1964**, *86*, 3759.
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3070, 3040, 2960, 2920, 1730, 1600, 1585, 1480, 1305, 1150, 1108, 760, 745, 735, and 688 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.52 (br s, 1 H), 3.70 (d, 1 H, J = 14.0 Hz), 4.62 (d, 1 H, J = 10.3 Hz), 4.93 (d, 1 H, J = 14.0 Hz), 5.30 (d, 1 H, J = 10.3 Hz), 6.48 (d, 1 H, J = 7.8 Hz), 6.85 (t, 1 H, J = 7.5 Hz), 7.03 (t, 1 H, J = 7.8 Hz), 7.09 (d, 1 H, J = 7.5 Hz), 7.23–7.36 (m, 7 H), and 7.45–7.53 (m, 3 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 47.8, 59.7, 82.9, 118.6, 121.0, 121.9, 127.6, 128.1, 128.3, 128.9, 129.2, 131.2, 133.8, 138.3, 138.9, 145.6, and 197.5; m/e 377 (M^+), 375, 220, 193, 165, 130, and 77. Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.02; H, 5.07; N, 3.71. Found: C, 69.91; H, 5.11; N, 3.70.

Colorless crystals were grown from ethyl acetate–methylene chloride. A suitable crystal of **5** approximately 0.42 × 0.31 × 0.32 mm was mounted on a quartz fiber with epoxy cement. Unit-cell parameters were determined on a Syntex P2 automated diffractometer using Mo Kα radiation. Twenty-four 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 = 9.2559 (0.0059) Å, b = 10.1972 (0.0074) Å, c = 11.4829 (0.0092) Å, α = 73.725 (0.060)°, β = 73.124 (0.053)°, γ = 63.107 (0.050)°, V = 910.78 (1.13) Å^3, d_{calcd} = 1.38 g cm^{-3}, $F(000)$ = 395.95, Z = 2, and space group $P\bar{1}$ BAR. Intensity data were collected by using the ω scan technique with a miniscan rate of 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 4794 reflections collected with 4.0° < 2θ < 50.0°, 2181 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 two hydrogens that determine the trans orientation of the substituents on the seven-membered ring 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 = 0.0435 and R_W = 0.0438, respectively. The final positional and thermal parameters are given in Tables 1–5 (supplementary material).

Chromatography of the residue on silica gel using a hexane–ethyl acetate–methanol (10:5:1) mixture as the eluent gave a number of minor products. The first minor component isolated from the column was assigned as 2-[(phenylsulfonyl)methyl]-indole[12] (**6**) (13%) on the basis of the following spectral data: mp 193–194 °C; IR (KBr) 3310, 3060, 2990, 2920, 1450, 1400, 1310, 1290, 1155, 810, 745, 715, and 690 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 4.53 (s, 2 H), 6.14 (d, 1 H, J = 1.0 Hz), 7.08 (dt, 1 H, J = 8.0 and 1.0 Hz), 7.25 (dt, 1 H, J = 7.5 and 1.0 Hz), 7.37–7.49 (m, 4 H), 7.59 (t, 1 H, J = 7.5 Hz), 7.65 (dd, 2 H, J = 8.0 and 1.0 Hz), and 8.72 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 56.2, 105.7, 111.2, 120.1, 120.6, 122.9, 124.6, 127.5, 128.2, 129.0, 134.0, 137.0, and 137.3. Anal. Calcd for $C_{15}H_{13}NO_2S$: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.28; H, 4.84; N, 5.14.

The second minor component isolated (3%) was assigned as 1,5-diphenyl-4-(phenylsulfonyl)pyrrolidin-3-one[12] (**7**): mp 105–106 °C; IR (CCl_4) 3080, 2980, 2940, 2860, 1770, 1605, 1550, 1540, 1510, 1455, 1345, 1155, 745, and 695 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.95 (d, 1 H, J = 18.8 Hz), 3.99 (d, 1 H, J = 0.8 Hz), 4.05 (d, 1 H, J = 18.8 Hz), 5.88 (d, 1 H, J = 0.8 Hz), 6.50 (d, 2 H, J = 8.0 Hz), 6.81 (t, 1 H, J = 7.5 Hz), 7.15–7.35 (m, 7 H), 7.53 (t, 2 H, J = 8.0 Hz), 7.68 (t, 1 H, J = 7.5 Hz), and 7.87 (d, 2 H, J = 7.5 Hz); MS, m/e 377 (M^+), 375, 236, 235, 234, and 77; HRMS calcd for $C_{22}H_{19}NO_3S$ 377.1086, found 377.1042.

Reaction of *C,N*-Diphenylnitrone with Methyl 2,3-Butadienoate. A solution containing 1.00 g of *C,N*-diphenylnitrone[46] and 500 mg of methyl 2,3-butadienoate[47] in 10 mL of carbon tetrachloride was stirred at room temperature for 12 h under a nitrogen atmosphere. Concentration of the solution under reduced pressure followed by silica gel chromatography of the residue using a 2% ethyl acetate–hexane mixture as the eluent gave two fractions. The first fraction contained 720 mg (60%) of a solid whose structure was assigned as 1,2,3,5-tetrahydro-2-phenyl-3-(methylcarboxyl)-4*H*-1-benzazepin-4-one (**8**) based on the following spectral data: mp 123–124 °C; IR (KBr) 3400, 3160, 2960, 1760, 1710, 1610, 1440, 1260, 1200, 1135, 960, 820, 740, and 705 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.66 (s, 1 H), 3.82 (d, 1 H, J = 14.3 Hz), 3.90 (s, 3 H), 4.10 (d, 1 H, J = 10.0 Hz), 4.25 (d, 1 H, J = 14.3 Hz), 5.05 (d, 1 H, J = 10.0 Hz), 6.64 (d, 1 H, J = 7.90 Hz), 6.92 (t, 1 H, J = 8.0 Hz), 7.10 (t, 1 H, J = 7.90 Hz), 7.16 (d, 1 H, J = 8.0 Hz), and 7.30–7.40 (m, 5 H); m/e 295 (M^+), 277, 245, 217, 203, 189, 144, 121, 105, and 89; HRMS calcd for $C_{18}H_{17}NO_3$ 295.1208, found 295.1206.

The second fraction isolated contained 70 mg (7%) of a clear oil whose structure was assigned as 2-(carbomethoxymethyl)indole (**9**) on the basis of its spectral data and by comparison with an authentic sample:[48] ^1H NMR (90 MHz, $CDCl_3$) δ 4.70 (s, 3 H), 4.79 (s, 2 H), 6.30 (s, 1 H), 7.0–7.60 (m, 4 H), and 8.60 (br s, 1 H).

Reaction of *N*-Methyl-*C*-phenylnitrone with 2,3-Bis(phenylsulfonyl)-1-propene (15). A solution containing 500 mg of *N*-methyl-*C*-phenylnitrone[49] and 1.00 g of 2,3-bis(phenylsulfonyl)-1-propene[17] (**15**) in 75 mL of benzene was heated at 80 °C for 48 h. The reaction mixture was concentrated under reduced pressure, stirred overnight in a 50% ethyl acetate–hexane mixture, and then filtered. The filtrate was concentrated under reduced pressure and then poured into 100 mL of water and extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give a colorless oil, which crystallized on standing. Recrystallization from methylene chloride–hexane gave 2-methyl-3-phenyl-5-[(phenylsulfonyl)methyl]-5-(phenylsulfonyl)-isoxazolidine (**16**) as a white solid (79%): mp 126–127 °C; IR (KBr) 3100, 3060, 2970, 2920, 2880, 1580, 1500, 1450, 1310, 1150, 770, 745, 700, and 690 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.70 (s, 3 H), 3.30 (dd, 1 H, J = 14.0 and 10.4 Hz), 3.98 (dd, 1 H, J = 14.0 and 6.9 Hz), 4.10 (d, 1 H, J = 14.6 Hz), 4.15 (d, 1 H, J = 14.6 Hz), 4.37 (dd, 1 H, J = 10.4 and 6.9 Hz), 6.93–7.00 (m, 2 H), 7.20–7.28 (m, 3 H), 7.54–7.65 (m, 4 H), 7.69 (t, 1 H, J = 7.4 Hz), 7.75 (t, 1 H, J = 7.4 Hz), 7.92 (d, 2 H, J = 7.4 Hz), and 7.99 (d, 2 H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 42.2, 43.2, 55.0, 72.6, 97.4, 127.6, 128.2, 128.4, 128.5, 128.7, 129.0, 129.3, 130.8, 131.1, 133.4, 134.0, 134.2, 134.5, 136.4, and 140.8. Anal. Calcd $C_{23}H_{23}NO_5S_2$: C, 60.39; H, 5.07; N, 3.06. Found: C, 60.32; H, 5.08; N, 3.02.

To a solution containing 3.50 g of the above compound in 150 mL of a 25% methanol–benzene mixture was added 500 mg of sodium methoxide. The reaction mixture was stirred for 15 min at room temperature and was quenched with a saturated ammonium chloride solution. The organic layer was removed under reduced pressure, and the reaction mixture was extracted with chloroform and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure followed by recrystallization of the solid from carbon tetrachloride–hexane gave 2-methyl-5-[(phenylsulfonyl)methylene]-3-phenylisoxazolidine (**4**) as white needles (95%): mp 67–68 °C; IR (KBr) 3060, 2960, 2870, 1625, 1580, 1320, 1140, 810, 782, 770, 720, and 700 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.78 (s, 3 H), 3.32 (dd, 1 H, J = 17.1 and 11.0 Hz), 3.85 (dd, 1 H, J = 11.0 and 6.1 Hz), 4.07 (dd, 1 H, J = 17.1 and 6.1 Hz), 5.75 (s, 1 H), 7.36 (s, 4 H), 7.47–7.53 (m, 3 H), 7.56 (dt, 1 H, J = 7.1 and 1.4 Hz), and 7.85 (dd, 1 H, J = 7.1 and 1.4 Hz); m/e 315 (M^+), 267, 212, and 77. Anal. Calcd for $C_{17}H_{17}NO_3S$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.76; H, 5.44; N, 4.40.

Reaction of *C,N*-Diphenylnitrone with 2,3-Bis(phenylsulfonyl)propene (15). A solution containing 810 mg of *C,N*-diphenylnitrone and 1.32 g of 2,3-bis(phenylsulfonyl)propene (**15**) in 50 mL of benzene was heated at 80 °C for 96 h under a nitrogen atmosphere. Removal of the solvent under reduced pressure followed by silica gel chromatography of the crude residue using a 10% ethyl acetate–hexane mixture as the eluent gave (*S,R*)-2,3-diphenyl-5-[(phenylsulfonyl)methyl]-5-(phenylsulfonyl)isoxazolidine (**17**) as the major product: mp 129–130 °C; IR (KBr) 3050, 2980, 2970, 2880, 1600, 1580, 1490, 1440, 1300, 1140, 800, 780, 760, 730, and 685 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.08 (dd, 1 H, J = 14.3 and 10.2 Hz), 3.92 (dd, 1 H, J = 14.3 and 7.2 Hz), 3.94 (d, 1 H, J = 14.9 Hz), 4.07 (d, 1 H, J = 14.9 Hz), 4.76 (dd, 1 H, J = 10.2 and 7.2 Hz), 6.77 (d, 2 H, J = 7.9 Hz), 6.84 (d, 2 H, J = 7.7 Hz), 7.03 (t, 1 H, J = 7.2 Hz), 7.09 (t, 2 H, J = 7.9 Hz),

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7.15–7.22 (m, 3 H), 7.35 (t, 2 H, J = 7.7 Hz), 7.53 (t, 1 H, J = 8.0 Hz), 7.60 (t, 2 H, J = 8.0 Hz), 7.75–7.81 (m, 3 H), and 8.05 (d, 2 H, J = 7.2 Hz). Irradiation of the signal at δ 4.76 corresponding to proton H_X showed an enhancement of proton H_A at 3.92. There was no enhancement in the signal of H_B at 3.08. Irradiation of the signal at δ 3.92 showed an enhancement of the doublet at 4.07, suggesting that H_A and the (phenylsulfonyl)methylene group are in a cis orientation: ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.4, 54.6, 69.9, 97.1, 120.3, 125.3, 127.2, 127.8, 128.3, 128.5, 128.8, 129.1, 129.2, 129.9, 130.0, 130.1, 131.5, 134.0, 134.5, 134.6, 137.1, 140.3 and 146.8. Anal. Calcd for $C_{28}H_{25}NO_5S_2$: C, 64.73; H, 4.85; N, 2.70. Found: C, 64.67; H, 4.86; N, 2.65.

The above cycloaddition was also carried out under high pressure. A solution containing 134 mg of *C,N*-diphenylnitrone and 220 mg of 2,3-bis(phenylsulfonyl)propene (**15**) in 9 mL of methylene chloride was seated in a 20-mL syringe and was pressurized at 48 °C for 36 h at 5 kbar. Removal of the solvent under reduced pressure followed by silica gel chromatography of the residue using a 10% ethyl acetate–hexane mixture as the eluent gave a clear oil, which crystallized on standing. Recrystallization of the solid from chloroform–hexane gave (*S,S*)-2,3-diphenyl-5-[(phenylsulfonyl)methyl]-5-(phenylsulfonyl)isoxazolidine (**20**) as the exclusive cycloadduct: mp 120–121 °C; IR (KBr) 3060, 2985, 2920, 2880, 1600, 1585, 1490, 1450, 1310, 1150, 760, 730, 705, and 690 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.45 (dd, 1 H, J = 14.3 and 6.7 Hz), 3.83 (d, 1 H, J = 15.2 Hz), 3.87 (d, 1 H, J = 15.2 Hz), 4.02 (dd, 1 H, J = 14.3 and 11.2 Hz), 4.34 (dd, 1 H, J = 11.2 and 6.7 Hz), 6.48 (d, 2 H, J = 7.7 Hz), 6.96 (t, 1 H, J = 7.2 Hz), 7.08 (t, 2 H, J = 8.0 Hz), 7.28–7.47 (m, 6 H), 7.51–7.68 (m, 5 H), 7.69 (d, 2 H, J = 7.2 Hz), and 7.91 (d, 2 H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 44.5, 55.3, 68.8, 96.7, 117.6, 123.7, 127.4, 128.1, 128.3, 128.5, 128.6, 128.7, 128.9, 129.0, 129.2, 129.3, 130.9, 133.0, 133.6, 134.8, 137.8, 140.5, and 148.7. Anal. Calcd for $C_{28}H_{25}NO_5S_2$: C, 64.73; H, 4.85; N, 2.70. Found: C, 64.62; H, 4.87; N, 2.69.

Treatment of 2,3-Diphenyl-5-[(phenylsulfonyl)methyl]-5-(phenylsulfonyl)isoxazolidine (17 or 20) with Base. A solution containing 150 mg of either **17** or **20** and 0.04 mL of 1,8-diazabicyclo[5.4.0]undec-7-ene in 20 mL of benzene was stirred at room temperature for 1 h. At the end of this time the reaction mixture was quenched with a saturated ammonium chloride solution, and the organic layer was removed under reduced pressure. The solution was poured into 100 mL of water and extracted with methylene chloride and dried over anhydrous magnesium sulfate. Removal of the solvent under reduced pressure followed by silica gel chromatography using a 10% ethyl acetate–hexane mixture as the eluent gave a 2:1 diastereomeric mixture of 1,2,3,5-tetrahydro-2-phenyl-5-(phenylsulfonyl)-4*H*-1-benzazepin-4-one (**19**) as a colorless oil (85% yield): IR (neat) 3370, 3070, 3040, 2960, 2930, 2860, 1715, 1600, 1580, 1560, 1480, 1450, 1320–1310, 1260, 1150, 800, 760, 730, 705, and 695 cm^{-1}. The major diastereomer showed the following NMR spectral properties: NMR ($CDCl_3$, 360 MHz) δ 2.92 (dd, 1 H, J = 16.2 and 4.0 Hz), 3.05 (dd, 1 H, J = 16.2 and 11.6 Hz), 3.90 (br s, 1 H), 5.05 (s, 1 H), 5.30 (dd, 1 H, 11.6 and 4.0 Hz), and 6.45–7.77 (m, 14 H). The minor diastereomer showed the following NMR spectrum: δ 2.77 (ddd, 1 H, J = 12.6, 2.6, and 1.6 Hz), 3.55 (br s, 1 H), 3.62 (dd, 1 H, J = 12.6 and 10.0 Hz), 4.25 (dd, 1 H, J = 10.0 and 2.6 Hz), 4.82 (d, 1 H, J = 1.6 Hz), and 6.45–7.77 (m, 14 H); HRMS calcd for $C_{22}H_{19}NO_3S$ 377.1086, found 377.1092.

Reaction of *C,N*-Diphenylnitrone with 2,3-Bis(phenylsulfonyl)propene (15) in the Presence of Water. A solution containing 320 mg of *C,N*-diphenylnitrone, 524 mg of 2,3-bis-(phenylsulfonyl)-1-propene (**15**), and a small amount of water in 15 mL of methylene chloride was sealed in a 20-mL syringe, and the mixture was pressurized at 48 °C for 24 h at 5 kbar. Removal of the solvent under reduced pressure followed by crystallization of the residue from methylene chloride–hexane gave 1,2-bis-(phenylsulfonyl)-3-(*N*-phenyl-*N*-hydroxylamino)propane (**21**) in 70% yield as a white crystalline solid: mp 129–130 °C; IR (KBr) 3470, 3065, 2925, 1600, 1590, 1495, 1450, 1310, 1150, 1085, 780, 735, 710, and 695 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 3.52 (dd, 1 H, J = 13.2 and 5.4 Hz), 3.64 (dd, 1 H, J = 13.2 and 9.4 Hz), 3.74 (dd, 1 H, J = 14.7 and 6.4 Hz), 3.98 (dd, 1 H, J = 14.7 and 2.8 Hz), 4.10 (dddd, 1 H, J = 9.4, 6.4, 5.4 and 2.8 Hz), 6.72 (s, 1 H), 7.05 (t, 1 H, J = 7.2 Hz), 7.13 (d, 2 H, J = 8.0 Hz), 7.25 (d, 1 H, J = 7.8 Hz), 7.32 (d, 1 H, J = 8.0 Hz), 7.57 (q, 4 H, J = 7.8 Hz), 7.70 (q, 2 H, J = 7.2 Hz), 7.83 (d, 2 H, J = 7.6 Hz), and 7.90 (d, 2 H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.4, 57.4, 58.0, 116.6, 122.9, 128.2, 128.8, 128.9, 129.6, 129.9, 130.3, 134.4, 134.6, 137.2, 138.3, and 151.7. Anal. Calcd for $C_{21}H_{21}NO_5S_2$: C, 58.46; H, 4.91; N, 3.25. Found: C, 58.56; H, 4.95; N, 3.21.

The structure of this material was unequivocally established by comparison with an independently synthesized material, which was prepared in the following fashion. A solution containing 300 mg of *N*-phenylhydroxylamine and 887 mg of 2,3-bis(phenylsulfonyl)-1-propene (**15**) in 40 mL of methylene chloride was stirred at room temperature for 16 h. Concentration of the reaction mixture under reduced pressure followed by recrystallization from methylene chloride–hexane gave 1,2-bis(phenylsulfonyl)-3-(*N*-phenyl-*N*-hydroxylamino)propane (**21**) in 89% yield as a white solid, which was identical in every detail with the sample of **21** obtained from the pressurized reaction.

Thermolysis of 1,2-Bis(phenylsulfonyl)-3-(*N*-phenyl-*N*-hydroxylamino)propane (21). A solution containing 360 mg of **21** and a catalytic amount of *p*-toluenesulfonic acid in 40 mL of benzene was heated at 80 °C for 30 h. Removal of the solvent under reduced pressure followed by silica gel chromatography of the residue using a 15% ethyl acetate–hexane mixture as the eluent gave a yellow oil which crystallized on standing. Recrystallization of the solid from methanol–chloroform–ether gave 1-(phenylamino)-2,3-bis(phenylsulfonyl)propene (**22**) in 47% yield: mp 169–170 °C; IR (KBr) 3390, 3070, 2930, 1650, 1600, 1510, 1310, 1150, 790, 760, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 4.20 (s, 2 H), 7.08 (d, 2 H, J = 7.9 Hz), 7.15 (d, 1 H, J = 7.4 Hz), 7.35 (d, 1 H, J = 7.5 Hz), 7.44 (t, 3 H, J = 7.9 Hz), 7.52 (t, 3 H, J = 7.5 Hz), 7.64 (d, 1 H, J = 7.4 Hz), 7.68 (d, 2 H, J = 7.9 Hz), 7.81 (d, 2 H, J = 7.9 Hz), 8.19 (d, 1 H, J = 13.0 Hz), and 8.83 (d, 1 H, J = 13.0 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 55.3, 77.2, 99.7, 116.4, 124.1, 127.0, 128.7, 129.1, 129.2, 129.9, 132.5, 134.5, 136.9, 140.0, 142.0, and 143.8. Anal. Calcd for $C_{21}H_{19}NO_4S_2$: C, 61.01; H, 4.63; N, 3.39. Found: C, 60.84; H, 4.69; N, 3.38.

Further heating of this material in the presence of a trace of acid resulted in a subsequent rearrangement to 3-(phenylsulfonyl)quinoline (**24**). A solution containing 310 mg of 1-(phenylamino)-2,3-bis(phenylsulfonyl)propene (**22**) and a catalytic amount of *p*-toluenesulfonic acid in 30 mL of benzene was heated at 80 °C for 30 h. Removal of the solvent under reduced pressure followed by silica gel chromatography of the residue using a 10% ethyl acetate–hexane mixture as the eluent gave a clear oil. Crystallization of this material from ethyl acetate–hexane afforded 3-(phenylsulfonyl)quinoline (**24**) in 51% yield: mp 151–152 °C; IR (KBr) 3080, 1620, 1600, 1580, 1505, 1450, 1440, 1320, 1310, 1165, 795, 760, 735, and 700 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 7.50–7.64 (m, 3 H), 7.68 (dt, 1 H, J = 7.0 and 1.0 Hz), 7.88 (t, 1 H, J = 7.0 Hz), 7.96 (dd, 1 H, J = 8.3 and 1.0 Hz), 8.04 (dd, 2 H, J = 8.3 and 1.0 Hz), 8.17 (d, 1 H, J = 8.3 Hz), 8.82 (d, 1 H, J = 2.3 Hz), and 9.26 (d, 1 H, J = 2.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 126.4, 127.8, 128.4, 129.2, 129.2, 129.6, 132.8, 133.7, 134.7, 136.9, 141.0, 147.1, and 149.4; *m/e* 269 (M^+), 176, 116, 101, and 77. Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.76; H, 4.17; N, 5.14.

Preparation of Ethyl 3-(Phenylsulfonyl)but-3-enoate (25). A solution containing 1.00 g of ethyl 2,3-butadienoate,[47] 4.40 g of sodium benzenesulfonate, and 0.54 g of glacial acetic acid in 70 mL of acetonitrile was stirred for 24 h at room temperature. To the solution was added 100 mL of chloroform and 100 mL of water. The organic layer was separated and washed twice with water, dried over magnesium sulfate, and concentrated under reduced pressure to give 2.20 g (97% yield) of a yellow oil whose structure was assigned as ethyl 3-(phenylsulfonyl)but-3-enoate (**25**) on the basis of its spectral properties: IR (neat) 3075, 2990, 1740, 1590, 1310, and 1155 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.15 (t, 3 H, J = 7.2 Hz), 3.29 (s, 2 H), 3.98 (q, 2 H, J = 7.2 Hz), 6.04 (d, 1 H, J = 0.9 Hz), 6.55 (s, 2 H), 7.54 (m, 2 H), 7.63 (m, 1 H), and 7.88 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.0, 35.3, 61.4, 128.0, 128.5, 129.4, 133.9, 138.5, 143.7 and 168.4. Anal. Calcd for $C_{12}H_{14}O_4S$: C, 56.68; H, 5.55. Found: C, 56.69; H, 5.58.

Cycloaddition Reaction of *N*-Methyl-*C*-phenylnitrone with Ethyl 3-(Phenylsulfonyl)but-3-enoate (25). A solution containing 0.75 g of **25** and 1.01 g of *N*-methyl-*C*-phenylnitrone in 10 mL of methylene chloride was placed inside a 20-mL plastic

syringe. The syringe pressurized at 6 kbar (50 °C) for 48 h. At the end of this time the yellow solution was concentrated under reduced pressure to give a 3:4 mixture of *N*-methyl-3-phenyl-5-(carbethoxymethyl)-5-(phenylsulfonyl)isoxazolidine (**26**) and *N*-methyl-3-phenyl-5-(carbethoxymethylene)isoxazolidine (**27**). The structure of **26** was assigned on the basis of its NMR spectrum: NMR ($CDCl_3$, 360 MHz) δ 1.28 (t, 3 H, J = 7.1 Hz), 2.45 (s, 3 H), 2.83 (d, 1 H, J = 15.3 Hz), 3.08 (d, 1 H, J = 15.3 Hz), 3.12 (dd, 1 H, J = 13.8 and 10.2 Hz), 3.24 (dd, 1 H, J = 13.8 and 7.2 Hz), 3.72 (dd, 1 H, J = 10.1 and 7.2 Hz), 4.18 (q, 2 H, J = 7.1 Hz), 7.26 (m, 5 H), 7.59 (m, 2 H), 7.70 (m, 1 H), and 8.05 (m, 2 H).

This mixture of compounds was dissolved in 30 mL of benzene, 1.37 g of DBU was added, and the solution was stirred for 30 min at room temperature. The bright red solution was washed three times with a saturated ammonium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The crude material was chromatographed on a silica gel column with use of a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.63 g (85% yield) of a yellow oil whose structure was assigned as *N*-methyl-3-phenyl-5-(carbethoxymethylene)isoxazolidine (**27**) on the basis of its spectral properties: IR (neat) 2980, 2880, 1710, and 1645 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.25 (t, 3 H, J = 7.1 Hz), 2.80 (s, 3 H), 3.36 (dd, 1 H, J = 17.2 and 11.4 Hz), 3.85 (dd, 1 H, J = 11.4 and 6.5 Hz), 3.98 (dd, 1 H, 17.2 and 6.5 Hz), 4.12 (q, 2 H, J = 7.1 Hz), 5.30 (s, 1 H), and 7.30–7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 43.5, 44.4, 59.6, 72.5, 87.4, 127.6, 128.7, 129.0, 136.7, 168.0, and 171.0; UV (95% ethanol) 262 nm (ϵ 13900). Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 67.85; H, 6.97; N, 5.63.

Cycloaddition Reaction of Tetrahydropyridine 1-Oxide with Ethyl 3-(Phenylsulfonyl)but-3-enoate. To a stirred solution containing 1.39 g of *N*-hydroxypiperidine in 100 mL of methylene chloride was added 7.45 g of yellow mercury(II) oxide at 25 °C. After being stirred for 20 min, 10 g of anhydrous magnesium sulfate was added, and the mixture was stirred for an additional 10 min. The green mercury salts were filtered and were then washed with an additional 150 mL of methylene chloride. The resulting solution was added dropwise to a solution containing 1.75 g of ethyl 3-(phenylsulfonyl)but-3-enoate (**25**) in 100 mL of benzene held at 50 °C, and the mixture was stirred at 50 °C for 18 h. The solution was allowed to cool to room temperature and was concentrated under reduced pressure to give a yellow oil. The crude material was subjected to silica flash chromatography with use of methylene chloride as the eluent. The major fraction contained 1.35 g (96% yield) of a clear oil, whose structure was assigned as 2-(carbethoxymethyl)-2-(phenylsulfonyl)hexahydro-2*H*-isoxazolo[2,3-*a*]pyridine (**28**) on the basis of its spectral properties: IR (neat) 2940, 2860, 1740, 1310, and 1160 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.04 (m, 2 H), 1.24 (t, 3 H, J = 7.1 Hz), 1.45–1.72 (m, 3 H), 1.83 (m, 1 H), 2.28 (m, 2 H), 2.63 (m, 1 H), 2.86 (d, 1 H, J = 14.7 Hz), 2.87 (m, 1 H), 3.03 (d, 1 H, J = 14.7 Hz), 3.20 (m, 1 H), 4.14 (q, 2 H, J = 7.1 Hz), 7.50 (m, 2 H), 7.62 (m, 1 H), and 7.92 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.3, 23.4, 24.5, 24.5, 29.0, 36.9, 39.2, 54.9, 61.2, 66.3, 97.2, 128.5, 130.9, 133.9, 135.7, and 168.4. Anal. Calcd for $C_{17}H_{23}NO_5S$: C, 57.77; H, 6.56; N, 3.96. Found: C, 57.63; H, 6.58; N, 3.92.

To a solution containing 2.00 g of the above material in 150 mL of benzene was added 2.58 g of DBU. The bright yellow solution was stirred at room temperature for 30 min and was then washed three times with a saturated ammonium chloride solution. The pale yellow solution was dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting oil was chromatographed on a silica gel column using a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 1.15 g (96%) of a clear oil whose structure was assigned as a 1:1 mixture of the *E* and *Z* isomers of 2-(carbethoxymethylene)hexahydro-2*H*-isoxazolo-[2,3-*a*]pyridine (**29**) on the basis of its spectral properties: IR (neat) 2940, 2855, 1705, 1645, and 1450 cm^{-1}; NMR ($CDCl_3$, 360 MHz) (isomer A) δ 1.18 (t, 3 H, J = 7.1 Hz), 1.45 (m, 2 H) 1.65 (m, 2 H), 1.80 (m, 1 H), 2.45 (m, 1 H), 2.60 (m, 1 H), 2.72 (m, 1 H), 3.02 (m, 1 H), 3.22 (m, 1 H), 3.58 (m, 1 H), 4.05 (q, 2 H, J = 7.1 Hz), and 5.18 (s, 1 H); (isomer B) δ 1.19 (t, 3 H, J = 7.1 Hz), 1.46 (m, 2 H), 1.65 (m, 2 H), 1.95 (m, 1 H), 2.45 (m, 1 H), 2.60 (m, 1 H), 2.72 (m, 1 H), 3.13 (m, 1 H), 3.55 (m, 1 H), 3.58 (m, 1 H), 4.06 (q, 2 H, J = 7.1 Hz), and 5.27 (s, 1 H); HRMS calcd for $C_{11}H_{17}NO_3$ 211.1208, found 211.1203.

Alkylation Studies of *N*-Methyl-3-phenyl-5-(carbethoxymethylene)isoxazolidine (27). To a solution containing 2.4 mmol of LDA in 30 mL of tetrahydrofuran at −78 °C under a nitrogen atmosphere was added 0.50 g of **27** via syringe. The resulting orange solution was stirred at −78 °C for 10 min, and then 1.79 g of HMPA was added. The solution was stirred for an additional 30 min, and then 0.34 g of methyl iodide was added. After being stirred for 30 min at −78 °C, the solution was allowed to warm to room temperature and was quenched with a saturated ammonium chloride solution. The solvent was removed under reduced pressure, and the residue was taken up in ether. The organic layer was washed three times with a saturated ammonium chloride solution and twice with water to remove the HMPA. The solution was then dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting yellow oil was chromatographed on a silica gel column with a 20% ethyl acetate–hexane mixture as the eluent to give 0.49 g (94% yield) of a clear yellow oil whose structure was assigned as *N*-methyl-3-phenyl-5-(methylcarbethoxymethyl)isoxazoline (**30**) on the basis of its spectral properties: IR (neat) 2980, 2870, 1740, 1635, 1455, 1190, and 1020 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.22 (2 t, 3 H, J = 7.2 Hz), 1.37 (d, 3 H, J = 7.2 Hz), 2.80 (s, 3 H), 3.30 (dq, 1 H, J = 7.2 and 1.0 Hz), 4.13 (2 q, 2 H, J = 7.2 Hz), 4.58 (br s, 1 H), 4.80 (m, 1 H), and 7.20–7.30 (m, 5 H); HRMS calcd for $C_{15}H_{19}NO_3$ 261.1365, found 261.1364.

A solution containing 0.50 g of **27** in 15 mL of dry tetrahydrofuran was cooled to −78 °C under a nitrogen atmosphere. To this solution was added 2.63 mL of a 1.67 M *n*-butyllithium solution in hexane. The resulting yellow solution was stirred for 10 min at −78 °C, and then 1.07 g of HMPA (3.0 equiv) was added. The solution was stirred for 10 min at −78 °C, and this was followed by the addition of 0.62 g of methyl iodide. The reaction was warmed to room temperature and was quenched with a saturated ammonium chloride solution. Evaporation of the solvent under reduced pressure left a yellow oil, which was dissolved in ether. The organic layer was washed with a saturated sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to leave behind a yellow oil. The crude material was chromatographed on silica gel using a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.48 g (92% yield) of a clear yellow oil whose structure was assigned as *N*-methyl-3-phenyl-5-(methylcarbethoxymethylene)isoxazolidine (**31**) on the basis of its spectral properties: IR (neat) 3020, 2970, 2920, 2860, 1700, 1630, 1450, 1365, 1340, 1290, and 1110 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.20 (t, 3 H, J = 7.1 Hz), 1.80 (s, 3 H), 2.75 (s, 3 H), 3.30 (m, 1 H), 3.82 (m, 1 H), 3.90 (m, 1 H), 4.15 (q, 2 H, J = 7.1 Hz), and 7.45 (m, 5 H); HRMS calcd for $C_{15}H_{19}NO_3$ 261.1365, found 261.1364.

A solution containing 200 mg of **27** in 10 mL of dry tetrahydrofuran was cooled to −78 °C under a nitrogen atmosphere. To this solution was added 0.52 mL of a 1.57 M *n*-butyllithium solution in hexane. The resulting yellow solution was stirred for 10 min at −78 °C, and then 0.44 g of HMPA (3.0 equiv) was added. The solution was stirred for 10 min at −78 °C, and this was followed by the addition of 400 mg of allyl bromide. The reaction was warmed to room temperature and was quenched with a saturated ammonium chloride solution. Evaporation of the solvent under reduced pressure left a yellow oil that was dissolved in ether. The organic layer was washed with a saturated sodium bicarbonate solution, dried over magnesium sulfate, and concentrated under reduced pressure to leave behind a yellow oil, which consisted of an inseparable 3:2 mixture of *N*-methyl-3-phenyl-5-(allylcarbethoxymethylene)isoxazolidine (**32**) and *N*-methyl-3-phenyl-5-(diallylcarbethoxymethyl)isoxazoline (**33**) as the two major products. The structures were assigned on the basis of their spectral properties: IR (neat) 3070, 2950, 2920, 1735, 1690, 1635, 1450, 1300, 1200, 1110, 1035, 915, 790, and 695 cm^{-1}; NMR ($CDCl_3$, 360 MHz) **32** δ 1.20 (t, 3 H, J = 7.1 Hz), 2.75 (s, 3 H), 3.00 (d, 2 H, J = 6.3 Hz), 3.28 (dd, J = 17.1 and 10.8 Hz), 3.78 (m, 1 H), 3.85 (dd, 1 H, J = 17.1 and 6.6 Hz), 4.07 (q, 2 H, J = 7.1 Hz), 4.89 (ddd, 1 H, J = 10.1, 3.3, and 1.3 Hz), 5.00 (ddd, 1 H, J = 17.0, 3.3, and 1.5 Hz), 5.80 (ddt, 1 H, j = 17.0 , 10.1, and 6.3 Hz), and

7.35 (m, 5 H); NMR **33** δ 1.22 (t, 3 H, J = 7.1 Hz), 2.54 (d, 4 H, J = 7.3 Hz), 2.80 (s, 3 H), 4.12 (q, 2 H, J = 7.1 Hz), 4.58 (br s, 1 H), 4.84 (d, 1 H, J = 2.5 Hz), 5.00–5.10 (m, 4 H), 5.55–5.70 (m, 2 H), and 7.20 (m, 5 H).

To a solution containing 0.57 mmol of LDA in 30 mL of tetrahydrofuran at −78 °C under a nitrogen atmosphere was added 0.14 g of **27** via syringe. The resulting orange solution was stirred at −78 °C for 10 min, and then 0.31 g of HMPA was slowly added via syringe. The solution was stirred for an additional 30 min, and then 0.12 g of benzaldehyde was added. After stirring for 30 min at −78 °C, the solution was allowed to warm to room temperature and was quenched with a saturated ammonium chloride solution. The solvent was removed under reduced pressure, and the residue was taken up in methylene chloride. The organic layer was washed with a saturated ammonium chloride solution followed by water to remove the HMPA. The solution was then dried over magnesium sulfate and concentrated under reduced pressure to give a yellow oil. This material was chromatographed on a silica gel column with use of a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.10 g (57% yield) of a yellow oil whose structure was assigned as carboxylic acid **35** on the basis of its spectral properties: IR (CCl_4) 3000 (br), 2600 (br), 1670, 1590, 1490, 1440, 1415, 1345, 1250, 1195, 1170, 1080, and 1060 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 2.78 (s, 3 H), 4.95 (s, 1 H), 5.55 (s, 1 H), 7.20–7.45 (m, 11 H), and 8.82 (s, 1 H); HRMS calcd for $C_{19}H_{17}NO_3$ 307.1208, found 307.1198. On one occasion an intermediate lactone was isolated whose structure was assigned as **34** on the basis of its NMR spectrum: NMR ($CDCl_3$, 300 MHz) δ 2.82 (s, 3 H), 3.62 (d, 1 H, J = 11.3 Hz), 3.95 (t, 1 H, J = 11.3 Hz), 5.24 (d, 1 H, J = 11.3 Hz), 5.28 (s, 1 H), and 6.95–7.15 (m, 10 H).

Zinc-Induced Reduction of *N*-Methyl-3-phenyl-5-(carbethoxymethylene)isoxazolidine (27). A solution containing 200 mg of **27** and 510 mg of activated zinc dust in 10 mL of a 50% aqueous acetic acid solution was stirred at room temperature for 36 h. The solution was filtered, and the filtrate was neutralized with sodium bicarbonate. The solution was extracted with methylene chloride, and the combined extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to leave behind a yellow oil. This material was chromatographed on a silica gel column with a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.11 g (62% yield) of a clear oil whose structure was assigned as ethyl 3-oxo-5-phenylpent-4-enoate (**39**) as a mixture of the keto and enol tautomers on the basis of its spectral properties: IR (neat) 3000, 1745, 1650, and 1605 cm^{-1}; NMR ($CDCl_3$, 300 MHz) keto tautomer δ 1.30 (t, 3 H, J = 7.1 Hz), 3.70 (s, 2 H), 4.22 (q, 2 H, J = 7.1 Hz), 6.42 (d, 1 H, J = 16.0 Hz), 6.80 (d, 1 H, J = 16.0 Hz), and 7.30–7.60 (m, 5 H); enol tautomer δ 1.27 (t, 3 H, J = 7.1 Hz), 4.20 (q, 2 H, J = 7.1 Hz), 5.15 (s, 1 H), 7.30–7.60 (m, 7 H), and 12.00 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.1, 14.2, 47.6, 60.1, 61.3, 91.8, 121.8, 125.2, 127.5, 128.4, 128.7, 128.9, 129.2, 130.8, 134.1, 135.3, 136.7, 144.5, 167.3, 169.1, 172.7, and 191.8; HMRS calcd for $C_{13}H_{14}O_3$ 218.0943, found 218.0947.

A solution containing 0.50 g of **27** and 1.57 g of activated zinc dust in 20 mL of a 50% aqueous acetic acid solution was stirred at 80 °C for 16 h and allowed to cool to room temperature. The solution was filtered, and the filtrate was neutralized with sodium bicarbonate. The solution was extracted with methylene chloride, and the combined extracts were washed with water, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to leave behind a yellow oil. This material was chromatographed on a silica gel column with use of a 20% ethyl acetate–hexane mixture as the eluent. The major fraction contained 0.13 g (30% yield) of a clear oil whose structure was assigned as ethyl 3-oxo-5-phenylpentanoate (**40**) on the basis of its spectral properties: IR (neat) 3030, 2990, 2940, 1745, 1715, 1650, 1500, 1455, 1375, 1320, 1260, 1190, 1165, and 1035 cm^{-1}; NMR ($CDCl_3$, 300 MHz) keto tautomer δ 1.15 (t, 3 H, J = 7.1 Hz), 2.80 (m, 4 H), 3.35 (s, 2 H), 4.05 (q, 2 H, J = 7.1 Hz), and 7.10–7.30 (m, 5 H); HRMS calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1095.

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Registry No. **4**, 118171-16-7; **5**, 118171-17-8; **6**, 107081-91-4; **7**, 118171-18-9; **8**, 118171-19-0; **9**, 21422-40-2; **15**, 2525-55-5; **16**, 118171-20-3; **17**, 118171-21-4; **19** isomer 1, 118171-22-5; **19** isomer 2, 118171-37-2; **20**, 118171-23-6; **21**, 118171-24-7; **22**, 117620-34-5; **24**, 117620-35-6; **25**, 118171-25-8; **26**, 118171-26-9; **27**, 118171-27-0; **28**, 118171-28-1; **29** isomer 1, 118171-29-2; **29** isomer 2, 118171-36-1; **30**, 118171-30-5; **31**, 118171-31-6; **32**, 118171-32-7; **33**, 118171-33-8; **34**, 118171-34-9; **35**, 118171-35-0; **39**, 1503-99-7; **40**, 17071-29-3; *C,N*-diphenylnitrone, 1137-96-8; (phenylsulfonyl)propadiene, 2525-42-0; methyl 2,3-butadienoate, 18913-35-4; *N*-methyl-*C*-phenylnitrone, 3376-23-6; *N*-phenylhydroxylamine, 100-65-2; ethyl 2,3-butadienoate, 14369-81-4; sodium benzenesulfonate, 515-42-4; *N*-hydroxypiperidine, 4801-58-5.

Supplementary Material Available: The final positions and thermal parameters of the X-ray analysis of benzazepinone **5** are given in Tables 1–5 (4 pages). Ordering information is given on any current masthead page.

Reactivity Patterns in the Rhodium Carbenoid Induced Tandem Cyclization–Cycloaddition Reaction

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The rhodium(II) acetate catalyzed behavior of *o*-[(propenyloxy)methyl]-α-diazoacetophenone was studied. The results obtained are consistent with a mechanism in which the key step involves intramolecular cyclization of the ketocarbenoid onto the oxygen atom of the side chain to give an oxonium ylide intermediate which undergoes either C–H insertion or a competitive 2,3-sigmatropic rearrangement. The reaction of 1-diazo-9-decene-2,5-dione with rhodium(II) acetate results in cyclization of the intermediate rhodium carbenoid to give a six-ring carbonyl ylide which readily undergoes intramolecular dipolar cycloaddition. This reaction does not occur when the keto group of the diazo compound has been replaced by an ester functionality. Similar results were also obtained with *cis*-2-benzoyl-1-(diazoacetyl)cyclopentane.

The stereoselective preparation of highly substituted oxygen heterocycles, especially structurally complex tetrahydrofurans and tetrahydropyrans, has attracted considerable attention and provides a challenging synthetic

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