(11) For a recent review, see J. Ficini, *Tetrahedron*, **32**, 1449 (1976).
(12) Y. Oikawa and O. Yonemitsu, *J. Chem. Soc., Perkin Trans. 1*, 1479 (1976).
(13) The ^{13}C NMR of the dihydroantirhine acetate was taken on a Bruker WP 80 apparatus by Dr. J. P. Genêt ($CDCl_3$): δ 172.2, 136.3, 132.4, 127.6, 121.7, 119.6, 118.1, 111.1, 107.3, 63.0, 54.5, 51.1, 46.0, 43.6, 31.6, 31.4, 28.9, 21.2, 17.4, 11.6 ppm.
(14) We thank Professor P. Potier and Dr. H. P. Husson (Gif sur Yvette) for a sample of natural antirhine.

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Benzenesulfonylnitrile Oxide: a Useful Intermediate for the Syn-Cyanohydroxylation of Alkenes

Sir:

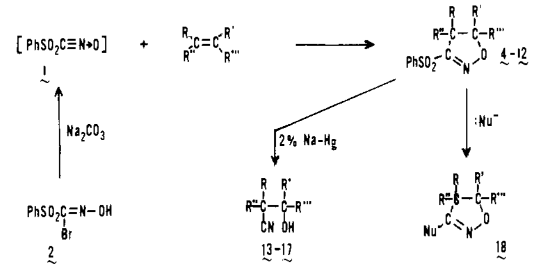
Several synthetic transformations have been reported which permit the stereospecific syn attachment of carbon and oxygen to the double bond of alkenes.[1-3] Typically, a heterodiene,[1] 1,3 dipole,[2] or ketene[3] is reacted with the alkene, followed by elaboration of the resulting cycloadduct. Nitrile oxides are among the 1,3 dipoles successfully employed for this transformation. The range of alkenes which react well with typical nitrile oxides is, however, somewhat limited owing to competition from nitrile oxide dimerization.[2a] Certain unconjugated alkenes do not work well, notably six-membered cyclic and tri- and tetrasubstituted ones.

We report here two new general synthetic procedures based on an improved version of the nitrile oxide cycloaddition process. The first of these permits the syn-cyanohydroxylation[4] of alkenes, while the second introduces an efficient indirect way to obtain 3-substituted isoxazolines. Central to both procedures is the cycloaddition of benzenesulfonylnitrile oxide (**1**) to alkenes (Scheme I). The resulting cycloadducts undergo reductive ring fragmentation to complete the syn-cyanohydroxylation process. Alternatively, nucleophilic substitution of the benzenesulfonyl group leads to a number of 3-substituted isoxazolines which would be difficult at best to prepare by direct cycloaddition.

The bromo oxime **2** has proven a convenient precursor to the nitrile oxide **1**. It is readily prepared from benzenesulfonylnitromethane (**3**)[5] in 30–40% overall yield (Scheme II).[6] Sequential bromination and O-methylation of α-nitro sulfone **3** affords an unstable nitronic ester rapidly converted in refluxing methylene chloride to bromo oxime **2**.

Slow addition (syringe pump technique) of a solution containing the bromo oxime **2** to a mixture of excess alkene and aqueous sodium carbonate[7] results in fair to excellent yields of the cycloadducts **4–12** (Table I). It is noteworthy that the normally sluggish cyclohexene reacts very well. Cycloaddition also occurs readily with 1-methylcyclohexene, an alkene not previously reported to react with nitrile oxides. The limit of this procedure is reached with tetramethylethylene;[8] reaction does occur to give a 17% yield of cycloadduct **10** but the major product, obtained in 61% yield, is dibenzenesulfonylfurazan oxide (nitrile oxide dimer).

Scheme I



Scheme II

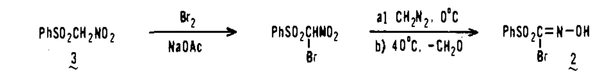
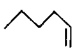
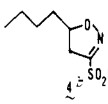
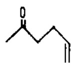
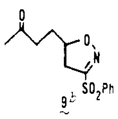
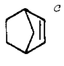
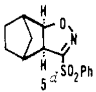
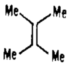
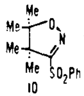
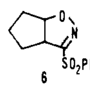
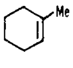
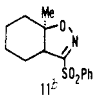
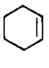
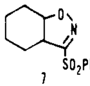
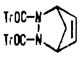
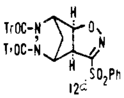
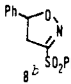


Table I. Cycloadducts Obtained from Benzenesulfonylnitrile Oxide

ALKENE	CYCLOADDUCT[a]	ALKENE	CYCLOADDUCT[a]
	 76% **4**[b]		 81% **9**[b]
 [c]	 90% **5**[d]	 [e]	 17%[f] **10**
	 81% **6**	 [e]	 59% **11**[b]
	 76% **7**	 [g-i]	 94%[j] **12**[d]
	 82% **8**[b]		

[a] Using an ~50-fold excess of alkene unless otherwise stated. Yields are based on the nitrile oxide precursor **2** and refer to pure, isolated products. [b] NMR indicated only this regioisomer. [c] A 1.5-fold excess of alkene was employed. [d] NMR indicated the exo isomer; for the endo and bridgehead H, $J \leq 2$ Hz in all cases. [e] Distilled (spinning band) to remove isomers and passed through silica gel. [f] The major product (61% yield) was dibenzenesulfonylfurazan oxide. [g] We thank Dr. K. C. Nicolaou for a research sample. [h] A 1.5-fold excess of the alkene was used. [i] TrOC = Cl_3CCH_2OCO. [j] Based on the alkene.

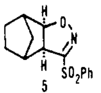
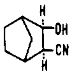
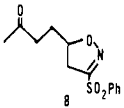
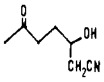
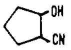
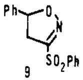
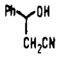
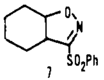
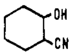
We attribute the high reactivity of benzenesulfonylnitrile oxide to synergistic electronic and steric factors. Electron-attracting substituents are known to increase the reactivity of other 1,3 dipoles[9,2f] toward alkenes and presumably this is one function of the benzenesulfonyl substituent. Also, its large size is expected to retard the dread nitrile oxide dimerization.[8]

Our syn-cyanohydroxylation process is completed by treatment of the cycloadduct with 2% sodium amalgam. The resulting expulsion of the benzenesulfonyl group with concommitant nitrogen–oxygen bond cleavage affords vicinal cyanohydrins in excellent yield[10] (Table II). For those cases where there is a stereochemical choice, only the cis isomer is obtained. Thus, the cyanohydrin **15** clearly differs in spectral and physical properties from its trans isomer obtained by treating cyclohexene oxide with potassium cyanide.

Arenesulfonyl groups are well-known one-electron acceptors.[11] Presumably the first step in fragmentation of cycloadducts **5–9** involves electron transfer from sodium amalgam to the benzenesulfonyl group. However, the conditions employed here (2% Na–Hg at 20 °C) are exceptionally mild for such a process. Consequently, the cyano group of the products is unaffected,[12] nor is the carbonyl group of cycloadduct **8** reduced during ring fragmentation.

The syn-cyanohydroxylation of cyclohexene is a typical example of the general procedure. A solution containing bromo

Table II. Vicinal Cyanohydrins Obtained by Ring Fragmentation.

CYCLOADDUCT	CYANOHYDRIN[a]		CYCLOADDUCT	CYANOHYDRIN[a]	
 5	 13	91%	 8	 16	86 %
 6	 14	94 %	 9	 17[b]	88 %
 7	 15	89 %			

[a] Employing an excess of 2% Na–Hg in wet THF at 20 °C. Yields refer to isolated products. [b] We thank Miss C. L. Gualtieri for preparing a standard sample of this compound.

Table III. Nucleophilic Substitution Products

6, n = 3
7, n = 4

18

substrate	nucleophile	product **18**	yield, %
6	LiOMe[a]	*n* = 3, Nu = OMe	82
6	KCN[b]	*n* = 3, Nu = CN	87
7	$NaBH_4$[c]	*n* = 4, Nu = H	51
7	LiOMe[a]	*n* = 4, Nu = OMe[d]	88

[a] Refluxing MeOH, 1 h. [b] Me_2SO, 40 °C, 48 h. [c] *i*-PrOH, 80 min. [d] We thank Mr. S. A. Hardinger for carrying out a preliminary investigation.

oxime **2** (1.34 g, 5.06 mmol), CH_2Cl_2 (8.0 mL), and cyclohexene (8.1 g, 99 mmol) was added dropwise over 3 h to a mixture of 1.0 M aqueous sodium carbonate (8.0 mL) and cyclohexene (8.1 g, 99 mmol). The crude product was chromatographed (silica gel, CH_2Cl_2 elution) to give dibenzenesulfonylfurazan oxide (99 mg, 11% yield) followed by pure cycloadduct **7** (1.02 g, 76% yield). A vigorously stirred THF (17 mL) solution of the cycloadduct (0,59 g, 2.23 mmol) was treated with water (0.52 mL) and 2% Na-Hg (7.37 g, 6.4 mg-atoms of Na). After 1 h, additional water (0.26 mL) and 2% Na-Hg (3.71 g) were added. Kugelrohr distillation of the crude product afforded 0.24 g (86% yield) of pure vicinal cyanohydrin **15**:[13] bp 130-40 °C at 0.1 Torr; mp 32.5-34 °C; IR (melt) 2.75-3.15 (br, OH), 4.46 μ (C≡N); NMR ($CDCl_3$) δ 3.75 (m, 1 H, C*H*OH), 3.03 (m, 1H, CHCN), 2.6 (s, 1 H, D_2O exchanges, OH), 1.3-2.2 (m, 8 H).

The carbon-nitrogen double bond of isoxazolines undergoes nucleophilic attack resulting in substitution if a suitable leaving group is attached at carbon.[14] Consequently, the reaction of cycloadducts **6** and **7** with various nucleophiles was examined in the hope that substitution would occur. Treatment with lithium methoxide, sodium cyanide, and sodium borohydride leads readily to the corresponding substitution products (Table III). These reactions, in conjunction with the cycloaddition process, constitute an alternative to direct reaction of the alkene with fulminic acid,[2b] cyanogen *N*-oxide,[15] or the as yet unknown methoxynitrile oxide. Consequently, benzenesulfonylnitrile oxide is a useful synthetic equivalent to other members of the class. This matter, as well as the broad application of benzenesulfonylnitrile oxide to synthetic problems, is under further investigation.

Acknowledgments. We thank Dr. G. H. Posner for helpful discussions. The financial support of the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

References and Notes

(1) (a) T. K. das Gupta, D. Felix, U. M. Kempe, and A. Eschenmoser, *Helv. Chim. Acta*, **55**, 2198 (1972); (b) R. R. Schmidt and R. Machat, *Angew. Chem., Int. Ed. Engl.*, **9**, 311 (1972).

(2) Ch. Grundmann and P. Grünanger, "The Nitrile Oxides", Springer-Verlag New York, New York, 1971; (b) R. Huisgen and M. Christl, *Chem. Ber.*, **106**, 3291 (1973); (c) R. Huisgen, R. Grashey, H. Hauck, and H. Seidl, *ibid.*, **101**, 2043 (1968); (d) A. Padwa, *Angew. Chem. Int. Ed. Engl.*, **15**, 123 (1976); (e) A. V. Kamernitzky, I. S. Levina, E. I. Mortikova, and B. S. El'yanov, *Tetrahedron Lett.*, 3235 (1975); (f) V. A. Tartakovskii, I. E. Chlenov, G. V. Lagodzinskaya, and S. S. Novikov, *Dokl. Akad. Nauk SSSR*, **161**, 136 (1965).

(3) (a) W. T. Brady, *Synthesis*, 415 (1971); (b) B. M. Trost, *Acc. Chem. Res.*, **7**, 85 (1974); (c) L. R. Krepski and A. Hassner, *J. Org. Chem.*, **43**, 2879 (1978).

(4) Anti-Cyanohydroxylation is a straightforward matter. The alkene is converted to its epoxide, which is in turn treated with potassium cyanide: (a) M. Mousseron, F. Winternitz, and J. Joullien, *C.R. Acad. Sci.*, **226**, 91 (1948); (b) German Offen. 1 917 658; *Chem. Abstr.*, **74**, 3330w (1971).

(5) Prepared by modification of a general procedure: J. J. Zeilstra and J. B. F. N. Engberts, *Recl. Trav. Chim. Pays-Bas*, **93**, 11 (1974). We employed NaOMe rather than KO-*t*-Bu as base; also formed in addition to α-nitro sulfone **3** was a small amount of 1,3-dibenzenesulfonyl-1,3-dinitropropane.

(6) The procedure was as follows. A solution of Br_2 (4.03 g, 25.2 mmol) in CH_2Cl_2 (100 mL) was added dropwise over 30 min to a cold (0-5 °C) mixture of α-nitro sulfone **3** (5.04 g, 25.1 mmol), NaOAc (8.43 g), and CH_2Cl_2 (100 mL). The resulting crude product was a 7:86:7 mixture of non-, mono-, and dibrominated α-nitro sulfone. Without purification this was dissolved in ether (anhydrous, 40 mL) and the solution cooled (−10 °C). Treatment with five 10-mL portions of 0.55 M ethereal CH_2N_2 over 15 min effected complete conversion to the nitronic ester (TLC). The resulting solution was *partially* stripped under reduced pressure (*Caution:* complete stripping may lead to vigorous decomposition) and the solvent replaced by CH_2Cl_2 (100 mL). Refluxing for 15 min resulted in complete destruction of the nitronic ester. The oily crude product crystallized (with difficulty) from a concentrated CH_2Cl_2–hexanes solution. Recrystallization gave 2.03 g (31% yield) of crystalline **2**: mp 101-102 °C; IR (KBr) 2.85-3.2 (br, OH), 6.21 and 6.32 (C=N and C=C), 7.24, 7.51, and 8.64 μ (sulfone).

(7) Triethylamine can be used instead but only with the more reactive alkenes.

(8) Tetramethylethylene does not react with typical nitrile oxides. It can react in low yield with mesitonitrile oxide (which dimerizes with extreme difficulty owing to the large size of the aryl substituent), but this is an isolated instance: Ch. Grundmann, H.-D. Frommeld, K. Flory, and S. K. Datta, *J. Org. Chem.*, **33**, 1464 (1968).

(9) K. J. Dignam, A. F. Hegarty, and R. L. Quain, *J. Org. Chem.*, **43**, 388 (1978).

(10) Base treatment of isoxazolines unsubstituted at the 3 position also gives cis-vicinal cyanohydrins.[2b] In some cases, decarboxylation of 3-carboxyisoxazolines will afford vicinal cyanohydrins: J. Kalvoda and H. Kaufmann, *J. Chem. Soc., Chem. Commun.*, 209 (1976).

(11) See, for example, (a) G. H. Posner and D. J. Brunelle, *Tetrahedron Lett.*, 935 (1973); (b) Y.-H. Chang and H. W. Pinnick, *J. Org. Chem.*, **43**, 373 (1978); (c) B. M. Trost, H. C. Arndt, P. E. Strege, and T. R. Verhoeven, *Tetrahedron Lett.*, 3477 (1976).

(12) Cyano groups, too, are good one-electron acceptors. See, for example, J. A. Marshall and L. J. Karas, *J. Am. Chem. Soc.*, **100**, 3615 (1978).

(13) The trans isomer of **15**, prepared by treating cyclohexene oxide with KCN, is clearly a different compound: mp 46-47 °C (lit.[4a] mp 46-47 °C); IR (melt) 2.75-3.15 (br, OH), 4.46 μ (CN); NMR ($CDCl_3$) δ 3.6 (M, 1 H, C*H*OH), 3.18 (s, 1 H, D_2O exchanges, OH), 1.2-2.5 (m, 9 H, CHCN and other ring H).

(14) P. A. Wade, *J. Org. Chem.*, **43**, 2020 (1978). (b) See also R. Bonnett, "The Chemistry of the Carbon-Nitrogen Double Bond", S. Patai, Ed., Interscience, New York, 1970, p 597.

(15) Ch. Grundmann and H.-D. Frommeld, *J. Org. Chem.*, **31**, 4235 (1966).

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Reactions of Zirconium Atoms with Alkanes: Oxidative Additions to Carbon–Hydrogen and Carbon–Carbon Bonds

Sir:

The activation of saturated hydrocarbons by molecular species has been one of the important goals of organometallic chemistry in recent years. We report here the oxidative addi-