matographed on a column of alumina (10 g of activity III) by using benzene, benzene/chloroform, and chloroform. The less polar compound **42** (46 mg) after crystallization from ethyl ether melted at 172-173 °C: IR (Nujol) ν_{max} 1730, 1240 (acetate) 1665, 925 (C=CH_2), 1375 (CCH_3), 3550 (OH) cm^{-1}; ^1H NMR δ 0.76 (3 H, s, C(4) CH_3), 2.05 (3 H, s, $COCH_3$), 4.37 (1 br s, H, C(20) H), 5.10 (1 H, br s, C(15) H), 5.20 (2 H, m, >C=CH_2). For ^{13}C NMR analysis, see Table IV. $C_{35}H_{37}NO_4$ requires C, 72.26; H, 8.97; N, 3.37; found, C, 72.29; H, 9.02; N, 3.33. The more polar fraction (51 mg) melted at 145-161 °C, and attempts to separate this mixture via column chromatography as well as by crystallization failed.

Treatment of Atisine Azomethine Acetate (46) with Glycidol. Atisine azomethine acetate (60 mg) in methanol (10 mL) was treated with glycidol (1 mL). The usual workup as described above afforded 61 mg of compound **47** as a colorless oil, which showed a single spot on TLC. The ^1H NMR spectrum of compound **47** showed the following signals: δ 0.65 and 0.88 (3 H, s, C(4) CH_3), 2.18 (3 H, s, $COCH_3$), 4.23 (1 H, br s, C(20) H), 4.95 (1 H, br s, C(15) H), 5.16 and 5.28 (each 1 H, br s, >C=CH_2). For ^{13}C NMR analysis, see Table IV.

Treatment of Ajaconine Azomethine Diacetate (48) with Glycidol. Ajaconine azomethine diacetate (50 mg) was subjected to the reaction procedure developed for the preparation of compound **42**. The crude reaction product after filtration through 5 g of silica gel gave 47 mg of compound **49** as a thick colorless oil. The ^1H NMR spectrum of compound **49** exhibited the following signals: δ 0.87 (3 H, s, C(4) CH_3), 2.03 (3 H, s, C(7) $OCOCH_3$), 2.15 (3 H, s, C(15) $OCOCH_3$), 4.13 (1 H, br s, C(20) H), 4.95 (1 H, br s, C(15) H), 5.13 and 5.33 (each 1 H, br s, >C=CH_2). For ^{13}C NMR analysis, see Table IV.

Treatment of Ajaconine Azomethine Diacetate (48) with Ethylene Oxide To Obtain 50. Ajaconine azomethine diacetate (70 mg) in absolute methanol (10 mL) was treated with ethylene oxide (2 mL) at 25 °C for 5 h. The solvent was removed in vacuo, and the residue was dissolved in chloroform and passed through a column of silica gel (10 g). The amorphous product (73 mg) was identified as 7-(α-acetoxy)atisine acetate (**50**). The ^1H NMR spectrum of compound **50** exhibited the following signals: δ 0.83 and 1.06 (3 H, s, C(4) CH_3), 2.01 (3 H, s, C(7) $OCOCH_3$), 2.12 (3 H, s, C(15) $OCOCH_3$), 4.2 (1 H, br s, C(20) H), 5.01 (2 H, br m, C=CH_2). The ^{13}C NMR spectrum (Table IV) indicated it to be a mixture of C(20) epimers.

Supplementary Material Available: Tables of atomic coordinates, bond distances, and bond angles for β-tetrahydroatisine and 22-hydroxyhomoveatchinchine acetate (11 pages). Ordering information is given on any current masthead page.

Benzenesulfonylcarbonitrile Oxide. 4. Substitution Reactions of 3-(Phenylsulfonyl)isoxazolines

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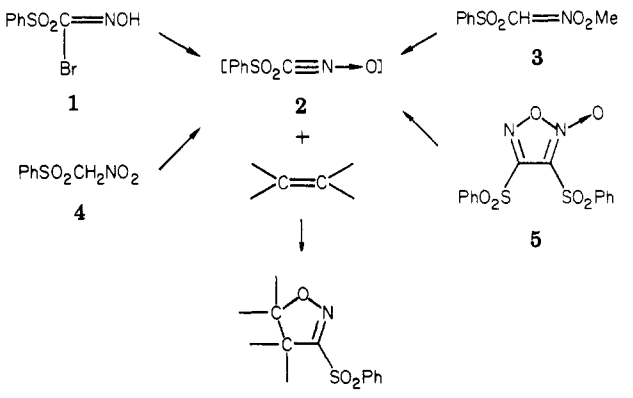
3-(Phenylsulfonyl)isoxazolines, readily obtained from alkenes by cycloaddition with benzenesulfonylcarbonitrile oxide, undergo a variety of substitution reactions. Alkyl, aryl, and acetylenic lithium reagents, cyanide, lithium or sodium alkoxides, and sodium borohydride are all useful nucleophiles. Tandem alkylations are possible with alkyllithium reagents when excess base and alkyl iodide are used. Excess base can also be used to cleave the isoxazoline ring of the initial substitution products. 3-(2-Propenyloxy)isoxazolines will undergo an aza-Claisen rearrangement on heating.

3-(Phenylsulfonyl)isoxazolines are readily prepared from alkenes by a number of routes in which the key intermediate is benzenesulfonylcarbonitrile oxide (**2**). This nitrile oxide can be generated by base[1] or silver(I)[2] treatment of bromo oxime **1**, base treatment of the methyl nitronic ester **3** of (phenylsulfonyl)nitromethane,[2] and thermolysis of furoxan **5**[3] (Scheme I). (Phenylsulfonyl)nitromethane (**4**) also gives nitrile oxide **2** under acidic conditions at elevated temperature.[4] The utility of sulfonyl isoxazolines as synthetic intermediates for the syn-cyano hydroxylation of alkenes and the preparation of certain other 3-substituted isoxazolines has previously been reported.[1,2] The present study is concerned with the use of sulfonyl isoxazolines for the general preparation of 3-substituted isoxazolines and compounds easily derived from them.

The phenylsulfonyl group attached at the 3-position of an isoxazoline is easily substituted by a variety of nucleophiles.[5] This is consistent with the general ability of

Scheme I

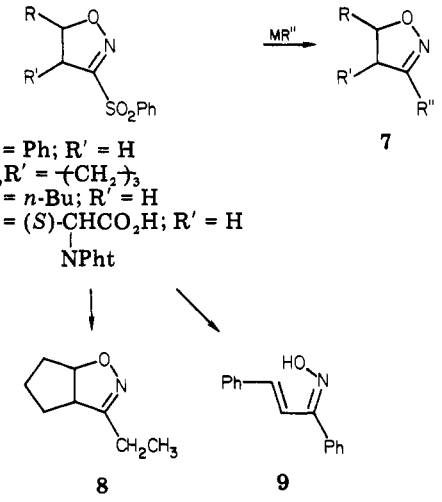


the sulfonyl function at unsaturated carbon to serve as a leaving group.[6] Alkyl-, aryl-, and alkynyllithium reagents all give clean substitution under relatively mild conditions (Scheme II). For methyl-, *n*-butyl-, *sec*-butyl-, and phe-

(1) Wade, P. A.; Hinney, H. R. *J. Am. Chem. Soc.* **1979**, *101*, 1319.
(2) Wade, P. A.; Pillay, M. K. *J. Org. Chem.* **1981**, *46*, 5425.
(3) Whitney, R. A.; Nicholas, E. S. *Tetrahedron Lett.* **1981**, 3371.
(4) Using *p*-toluenesulfonic acid at 160 °C: Wade, P. A.; Amin, N. V., studies currently in progress.
(5) For a preliminary account, see ref 1.
(6) Some examples include: (a) Farrar, W. V. *J. Chem. Soc.* **1964**, 904. (b) Smorada, R. L.; Truce, W. E. *J. Org. Chem.* **1979**, *44*, 3444. (c) Schank, K. *Tetrahedron Lett.* **1977**, 2567.

0022-3263/83/1948-1796$01.50/0

Scheme II



nyllithium, reactions can be conducted at −70 °C and are complete in 10 min, affording the products listed in Table I. Lithium phenylacetylide is slower to react and requires 0 °C but otherwise is similar in its behavior. One Grignard reagent, methylmagnesium bromide, has also been investigated and does react, although at a distinctly slower rate than any of the lithium reagents.

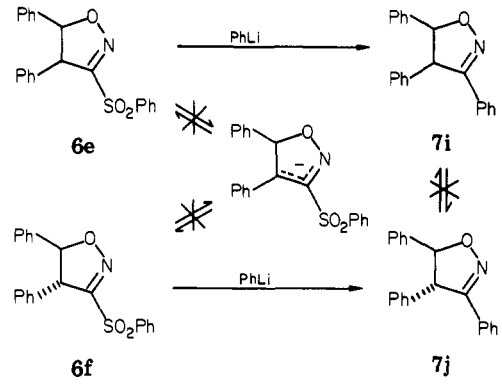
Weaker carbon nucleophiles may be employed under more vigorous conditions. For example, cyanide gives substitution in over 80% yield in the two cases examined. For the cyanide reaction, there is a significant difference in reaction rate depending on the structure of the starting isoxazoline. The 4,5-disubstituted **6b** is significantly slower than the 4-unsubstituted isoxazoline **6d**. Presumably branching at the 4-position of the ring slows down attack at the adjacent unsaturated 3-position, which is already difficult to approach owing to the relatively bulky phenylsulfonyl group.

It is possible to do tandem alkylations of 3-(phenylsulfonyl)isoxazolines. When compound **6b** was treated with excess methyllithium at −70 °C and after 10 min with excess diisopropylamine[7] followed at 1 h by methyl iodide, the 3-ethylisoxazoline (**8**) was obtained. This is consistent with prior formation of the 3-methyl derivative **7d** followed by in situ deprotonation and methylation. It has been reported[8] that alkylation reactions can occur at either the α-position of 3-alkylisoxazolines or the 4-position depending on isoxazoline structure and the nature of the base. Clearly this chemistry can be carried out in tandem with alkylation of a sulfonylisoxazoline.

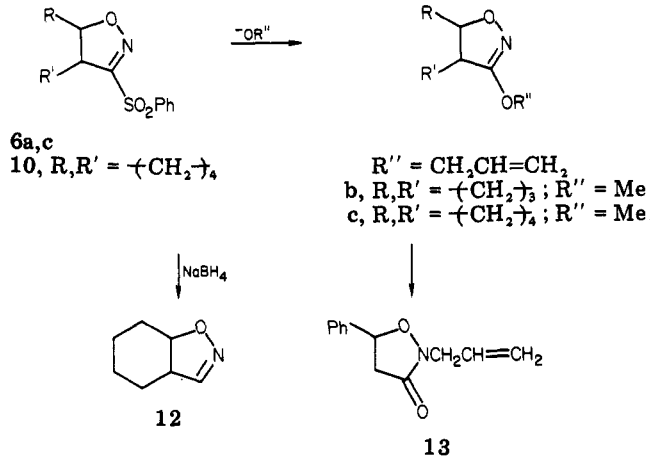
Base-induced ring-opening reactions have been reported[8] for isoxazolines, and these can be conveniently carried out subsequent to substitution of the phenylsulfonyl group. Treatment of isoxazoline **6a** with 3 equiv of phenyllithium at −70 °C followed after 15 min by diisopropylamine gave on heating to room temperature the α,β-unsaturated oxime **9**.

It is important to recognize that substitution on sulfonyl isoxazolines employing organolithium reagents is a very rapid process compared to possible competitive pathways. For example, if deprotonation at the 4-position of a sulfonyl isoxazoline (or its substitution product) occurred, this could lead to the equilibration of cis and trans 4,5-disubstituted isoxazolines (Scheme III). As a demanding test of this possibility, phenyllithium was reacted separately

Scheme III



Scheme IV



with the diastereomeric sulfonylisoxazolines **6e** and **6f** derived from (*Z*)- and (E)-stilbene. The cis diastereomer **6e** gave only the *cis*-3,4-diphenylisoxazoline (**7i**) without contamination by the trans isomer **7j**. Likewise the trans diastereomer **6f** gave *trans*-4,5-diphenylisoxazoline (**7j**), again without crossover. For both stereoisomers, then, substitution occurred much faster than deprotonation. Sulfonylisoxazolines with a 4-alkyl substituent should be even less prone to competitive deprotonation owing to a decreased acidity at the 4-position.

Treatment of sulfonylisoxazolines with alkoxides leads to the formation of 3-alkoxyisoxazolines (Scheme IV). It is necessary to carry these reactions out under somewhat more vigorous conditions, conveniently at 60–100 °C. Further transformations are also possible for these products. In the one case examined, the isolated 3-propenyloxy substitution product **11a** underwent thermal rearrangement to the *N*-propenyl compound **13**. This appears to be another example of the aza-Claisen rearrangement.[9] Refluxing toluene may be used, but isomerization is only 40% complete at 48 h under these relatively mild conditions. In refluxing dimethylaniline, reaction is complete in 15 min.

Isoxazolines are in general subject to facile ring cleavage with a number of reducing agents.[10] However, we found that it was possible by using sodium borohydride to retain the heterocyclic nucleus while replacing the sulfone group of a sulfonylisoxazoline by hydrogen. In early experiments[1]

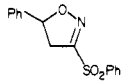
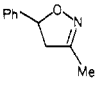
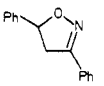
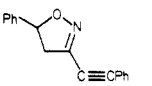
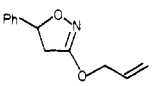
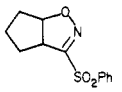
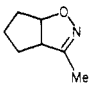
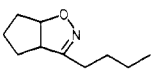
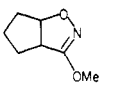
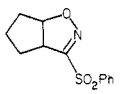
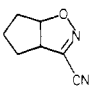
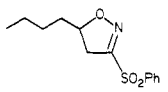
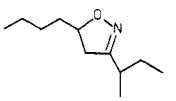
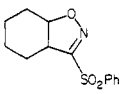
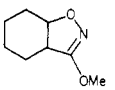
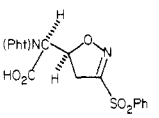
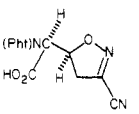
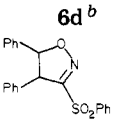
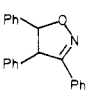
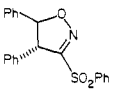
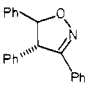
(7) Excess methyllithium by itself does not give the reaction. It is essential to form a better kinetic base, conveniently LDA.

(8) Grund, H.; Jäger, V. *Liebigs Ann. Chem.* **1980**, 80.

(9) Some examples include: (a) Padwa, A.; Cohen, L. A. *Tetrahedron Lett.* **1982**, 915. (b) Overman, L. E. *Acc. Chem. Res.* **1980**, *13*, 218 and references cited therein. (c) Knapp, S.; Patel, D. V. *Tetrahedron Lett.* **1982**, 3539.

(10) (a) Jäger, V.; Buss, V. *Liebigs Ann. Chem.* **1980**, 101. (b) Jäger, V.; Buss, V.; Schwab, W. *Ibid.* **1980**, 122. (c) Kotera, K.; Takano, Y.; Matsuura, A.; Kitahonoki, K. *Tetrahedron* **1970**, *26*, 539.

Table I. Substitution Products of Sulfonyl Isoxazolines

sulfonyl isoxazoline	nucleophile	substitution product	conditions	yield, %
	MeLi MeMgBr		−70 °C, 15 min 0–5 °C, 4 h	94 58[a]
6a		7a		
	PhLi		−70 °C, 15 min	88
		7b		
	LiC≡CPh		0–5 °C, 30 min	76
		7c		
	$NaOCH_2CH{=}CH_2$		97 °C, 30 min	78
		11a		
	MeLi		−70 °C, 15min	81
6b		7d		
	n-BuLi		−70 °C, 15 min	85
		7e		
	LiOMe		65 °C, 1 h	82
		11b		
	KCN		38–41 °C, 48 h	87
6b		7f		
	*s*-BuLi		−70 °C, 15 min	62
6c		7g		
	LiOMe		65 °C, 1 h	88
10		11c		
	$NaBH_4$		20 °C, 2 h	78
		12		
	NaCN		20 °C, 6 h	86
6d[b]		7h[b]		
	PhLi		−70 °C, 10 min	78
6e		7i		
	PhLi		−70 °C, 10 min	88
6f		7j		

[a] Unreacted sulfonyl isoxazoline was recovered in 16% yield. [b] Pht refers to the phthalyl group.

acid was employed during workup, which led to low yields of the 3-unsubstituted isoxazoline (**12**), undoubtedly due to overreduction. Without the addition of acid during workup, the yield of compound **12** was substantially improved, rising to 78%.

In summary, sulfonylisoxazolines make valuable synthetic intermediates with which to carry out a variety of transformations. It is possible to carry out cycloaddition with nitrile oxide **2** and then transform the phenylsulfonyl group of the resulting cycloadduct to alkyl, aryl, alkynyl, alkoxy, cyano, or hydrogen. Thus nitrile oxide **2** serves as a convenient general synthetic equivalent of other nitrile oxides. This is particularly useful considering the enhanced reactivity of species **2**[1,2] for tri- and tetrasubstituted alkenes and the possibility for further transformations of the resulting 3-substituted isoxazolines.

Experimental Section

General Methods. Infrared spectra were obtained on a Perkin-Elmer 457 spectrometer. ^1H NMR spectra were recorded (in $CDCl_3$ with Me_4Si as internal Standard, unless otherwise noted) on JEOL FX-90Q and Varian A-60A instruments. Gas chromatography (VPC) was performed on a Varian 1420 instrument equipped with OV-101 and SE-30 columns. Thin-layer chromatography was carried out on Analtech 0.25-mm precoated silica gel GF analytical plates with UV and I_2 development or on 1.00-mm silica gel preparative plates. Simple column chromatography was carried out on Baker Analyzed reagent silica gel, 60–200 mesh; medium pressure (30–50 psi) and flash chromatography were carried out on Merck Silica Gel 60, 230–400 mesh. Organolithium reagents and methylmagnesium bromide were purchased commercially (Aldrich). Reactions were routinely run under nitrogen and were worked up by washing the organic layer with water, drying over anhydrous sodium sulfate, and concentrating at reduced pressure.

***(S)*-*N*-Phthalylvinylglycine.** Prepared in 89% yield from (S)-vinylglycine hydrochloride[11] by the general procedure of Nefkens.[12] The crude product was purified by flash chromatography (CH_2Cl_2–CH_3COOH, 95:5): mp 86–88 °C; IR (KBr) 2400–3650 (br, CO_2H) and 1680 cm^{-1} (br, C=O); NMR δ 9.02 (s, 1 H), 7.7–8.1 (m, 4 H), 6.2–6.8 (m, 1 H), 5.37–5.65 (m, 1 H), 5.22 (d, 1 H, J = 6 Hz); $[\alpha]^{27}_D$–86.52° (*c* 2.0, MeOH).

(αS,5*S*)-4,5-Dihydro-3-(phenylsulfonyl)-α-(phthalylamino)-5-isoxazoleacetic Acid (6d). A solution containing bromo oxime **1** (8.57 g, 32.5 mmol) in THF (40 mL) was added dropwise over 2 h to a warm (50 °C) mixture of (*S*)-*N*-phthalylvinylglycine (5.01 g, 21.7 mmol), silver nitrate (10.92 g, 65 mmol), and THF (50 mL). After being stirred for an additional 10 min, silver salts were filtered off and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2 (50 mL) and the resulting solution extracted with aqueous 10% $NaHCO_3$. Acidification (6 N HCl) of the aqueous layer followed by extraction with four 100-mL portions of chloroform, drying of the combined extracts, and concentration gave a yellow solid, which was purified by medium-pressure chromatography. Elution (benzene–acetic acid, 87:13) gave products in the following order: starting alkene (1.22 g, 24% recovery), epimeric αS,5*R* cycloadduct (4.26 g, 47% yield), a mixed cycloadduct fraction (0.37 g, 4% yield), and αS,5*S* cycloadduct **6d** (2.15 g, 24% yield). The analytical sample of **6d** was recrystallized from CH_2Cl_2–CCl_4 containing 1% acetic acid: mp 198–200 °C dec; IR (KBr) 2920–3500 (br, CO_2H), 1720, 1778 (C=O), 1330, 1160 cm^{-1} (SO_2); NMR (acetone-d_6) δ 7.5–7.9 (m, 5 H), 5.55–5.87 (m, 1 H), 5.27 (d, 1 H, J = 5.7 Hz), 3.63–3.86 (m, 2 H).

Anal. Calcd for $C_{19}H_{14}N_2O_7S$: C, 55.07; H, 3.41. Found: C, 54.71; H, 3.31.

***cis*-4,5-Dihydro-4,5-diphenyl-3-(phenylsulfonyl)isoxazole (6e).** A solution containing 0.535 g (2.03 mmol) of bromo oxime **1**, *cis*-stilbene (2 mL, Aldrich 97% pure, containing 3–5% *trans*-stilbene), and methylene chloride (2 mL) was added dropwise (syringe-pump technique) over 3 h to a stirred mixture containing *cis*-stilbene (2 mL) and aqueous 1 M Na_2CO_3 (3 mL). Water was added, and the organic products were extracted with three 10-mL portions of CH_2Cl_2. The combined organic layers were washed, dried, and concentrated. The crude product was chromatographed at medium pressure. Elution (CH_2Cl_2–CCl_4, 60:40) afforded products in the following order: 83.5 mg (22% yield) of furoxan **5**, 72.5 mg (10% yield) of trans isomer **6f**, and 406.7 mg (55% yield) of cis isomer **6e**. Compound **6e** was recrystallized from benzene–hexane to obtain the analytical sample: mp 131.5–32.5 °C; IR (KBr) 1335, 1165, 1155 cm^{-1} (SO_2); NMR δ 6.6–7.9 (m, 15 H), 6.04 (d, 1 H, J = 9.5 Hz), 4.91 (d, 1 H, J = 9.5 Hz).

Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71. Found: C, 69.49; H, 4.71.

***trans*-4,5-Dihydro-4,5-diphenyl-3-(phenylsulfonyl)isoxazole (6f).** Prepared in 69% yield analagous to sulfonyl isoxazoline **6d**. The crude product was purified by column chromatography; elution came after furoxan **5** (hexane–ethyl acetate, 80:20). The analytical sample was recrystallized from hexane–benzene: mp 94–95 °C; IR (KBr) 1170 and 1330 cm^{-1} (SO_2); NMR δ 7.0–7.8 (m, 15 H), 5.67 (d, 1 H, J = 6.6 Hz), 4.66 (d, 1 H, J = 6.6 Hz).

Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71. Found: C, 69.12; H, 4.83.

Reaction of Organolithium Reagents with Sulfonyl Isoxazolines 6a–f. General Procedure. The organolithium reagent (5.25 mmol) was added dropwise over 5 min to a cold (−70 to −75 °C) solution of the sulfonylisoxazoline (3.5 mmol) in 50 mL of THF. After the solution stirred for 15 min, wet THF and then water were added. The organic products were extracted with three 50-mL portions of CH_2Cl_2. The combined organic layers were washed, dried, and concentrated. Isoxazolines **7a**, **7d**, **7e**, and **7g** were purified simply by Kugelrohr distillation; except for compound **7g** the products thus obtained were pure (>98%, VPC).

4,5-Dihydro-3-methyl-5-phenylisoxazole (7a). Prepared in 94% yield by the general procedure. Also prepared in 58% yield by using methylmagnesium bromide (6.7 equiv) at 0–5 °C for 4 h; starting material (16% recovery) remained and was separated by column chromatography (CH_2Cl_2–CH_3OH, 99:1).

4,5-Dihydro-3,5-diphenylisoxazole (7b). The crude product was recrystallized from methanol to afford pure **7b** in 81% yield. An additional 7% yield was obtained by preparative TLC (hexane–acetic acid, 99:1) of the recrystallization mother liquor: mp 74–74.5 °C (lit.[13] mp 74–75.5 °C).

4,5-Dihydro-5-phenyl-3-(2-phenylethynyl)isoxazole (7c). Prepared in 76% yield by the general procedure except that the lithium phenylacetylide (3 equiv) was added at 0–5 °C and stirring was continued for 30 min. Pure **7c** was obtained in 76% yield through column chromatography (CH_2Cl_2) followed by recrystallization from aqueous alcohol: mp 59–60 °C; IR (KBr) 2210 cm^{-1} (C≡C); NMR δ 7.3–7.6 (m, 10 H), 5.71 (dd, 1 H, J_{ax} = 11, J_{bx} = 8.8 Hz), 3.58 (dd, 1 H, J_{ax} = 11, J_{ab} = 16.9 Hz), 3.12 (dd, 1 H, J_{bx} = 8.8, J_{ab} = 16.9 Hz).

Anal. Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.88; H, 5.56; N, 5.66.

3-Butyl-3a,5,6,6a-tetrahydro-4*H*-cyclopent[*d*]isoxazole (7e). Prepared in 85% yield by the general procedure: IR (film) 1620 cm^{-1} (C=N); NMR δ 5.0–5.2 (m, 1 H), 3.5–3.7 (m, 1 H), 0.8–2.6 (m, 15 H).

Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.25. Found: C, 71.44; H, 10.20.

3-*sec*-Butyl-4,5-dihydro-5-butylisoxazole (7g). Prepared in 62% yield by the general procedure. The distilled product contained several minor impurities (92% pure, VPC) and was further purified by preparative VPC: IR (film) 1620 cm^{-1} (C=N); NMR δ 4.3–4.7 (m, 1 H), 2.3–3.1 (m, 3 H), 0.8–1.7 (m) overlapping 1.12 (d, J = 7 Hz) (17 H total).

Anal. Calcd for $C_{11}H_{21}NO$: C, 72.08; H, 11.55. Found: C, 71.68; H, 11.34.

***cis*-4,5-Dihydro-3,4,5-triphenylisoxazole (7i).** Prepared in 78% yield by the general procedure followed by recrystallization

(11) Afzali-Ardakani, A.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 4817.
(12) Nefkens, G. H. L.; Tesser, G. I.; Nivard, R. J. F. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 688.
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from aqueous alcohol: mp 164–66 °C (lit.[13] mp 166–67 °C). The crude product, obtained in quantitative yield, contained none (<2% by NMR, TLC) of the trans isomer **7j**.

***trans*-4,5-Dihydro-3,4,5-triphenylisoxazole (7j).** Prepared in 88% yield by the general procedure followed by preparative TLC (CH_2Cl_2–CCl_4, 50:50): mp 137–38 °C (lit.[13] mp 138–40 °C). The crude product contained none (<2% by NMR, TLC) of the cis isomer **7i** and no remaining starting material.

In a preliminary experiment when less care was taken, some isomerization was noted. Besides a 74% yield of (trans) **7j**, a 7% yield of (cis) **7i**, a 6% yield of (cis) **6e** (isomerized starting material), and a 7% yield of recovered starting material **6f** were isolated.

3-Ethyl-3a,5,6,6a-tetrahydro-4*H*-cyclopent[*d*]isoxazole (8). Methyl lithium (5.8 mL of a 1.35 M hexane solution; 7.77 mmol) was added dropwise to a cold (−70 °C) solution of sulfonylisoxazoline **6b** (0.653 g, 2.59 mmol) in THF (11 mL). After 15 min, diisopropylamine (0.8 mL, 6 mmol) was added and stirring in the cold continued for another 1.5 h. Methyl iodide (0.7 mL, 7.8 mmol) was added and stirring continued for 2 h. Water was added and the organic product extracted with CH_2Cl_2. The organic layer was washed, dried, and concentrated to give an oil. This was Kugelrohr distilled to afford 0.318 g (88% yield) of pure (>99%, VPC) **8**: bp 50–60 °C (0.7 mm) [lit.[8] bp 60–65 °C (0.9 mm)].

(*E*,*E*)-1,3-Diphenyl-2-propen-1-one Oxime (9). Phenyl lithium (1.96 mL of a 1.15 M hexane solution, 2.25 mmol) was added dropwise to a cold (−70 °C) solution of sulfonylisoxazoline **6a** (0.222 g, 0.77 mmol) in THF (5 mL). After 15 min, diisopropylamine (0.37 mL, 2.5 mmol) was added and the solution stirred for 2 h at −70 to −78 °C and 1 h at room temperature. Water and CH_2Cl_2 were added, and the pH was adjusted to 4 with saturated ammonium chloride. The organic layer was separated, washed, dried, and concentrated to give a solid residue. Pure **9** was obtained through preparative TLC (hexane–ethyl acetate, 80:20) followed by recrystallization (ether–hexane, 50:50) affording 0.12 g (65% yield): mp 113–115 °C (lit.[14] mp 115 °C).

3-Cyano-3a,5,6,6a-tetrahydro-4*H*-cyclopent[*d*]isoxazole (7f). A solution containing sulfonylisoxazoline **6b** (0.24 g, 0.97 mmol) and potassium cyanide (1.02 g, 15.6 mmol) in Me_2SO (10 mL) was stirred at 38–41 °C for 48 h. The resulting solution was added to water and CH_2Cl_2. The organic layer was separated, washed, dried, and concentrated at 0–5 °C. Kugelrohr distillation gave 0.11 g (87% yield) of an oil (>99% pure, VPC): IR (film) 2245 cm^{-1} (C≡N); NMR δ 5.2–5.5 (m, 1 H), 3.7–4.1 (m, 1 H), 1.2–2.3 (m, 6 H).

Anal. Calcd for $C_7H_8N_2O$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.95; H, 6.06; N, 20.43.

(α*S*,5*S*)-3-Cyano-4,5-dihydro-α-(phthalylamino)-5-isoxazoleacetic Acid (7h).[15] A solution of (α*S*,5*S*)-4,5-dihydro-3-(phenylsulfonyl)-α-(phthalylamino)-5-isoxazoleacetic acid (**6d**) (1.06 g, 2.56 mmol) and sodium cyanide (0.50 g, 10.26 mmol) in Me_2SO (10 mL) was stirred at room temperature for 6 h and then poured into 50 mL of ice water. The pH was adjusted to 3 with 6 N HCl, and the organic product was extracted with three 100-mL portions of CH_2Cl_2. The combined organic layers were dried, concentrated, and column chromatographed (ethyl acetate–acetic acid, 95:5) to remove remaining Me_2SO. A second chromatography (benzene–acetic acid, 85:15) gave 0.66 g (86% yield) of TLC-pure **7h** as a hygroscopic white solid: mp 66–69 °C; $[\alpha]^{25}D$ 136.2° (*c* 1.47, MeOH); IR (KBr) 3700–2300 (br, CO_2H), 2240 (w, C≡N), 1710 cm^{-1} (br, C=O); NMR (acetone-d_6) δ 8.32 (s, 4 H), 5.77 (dt, 1 H, J = 5.7, 9.7 Hz), 5.33 (d, 1 H, J = 5.7 Hz), 3.65 (d, 2 H, J = 9.7 Hz).

Anal. Calcd for $C_{14}H_9N_3O_5$: C, 56.19; H, 3.03. Found: C, 55.95; H, 3.34.

(14) Henrich, F. *Justus Liebigs Ann. Chem.* **1907**, *351*, 172.

(15) This compound is currently being derivatized prior to submission to the National Cancer Institute for biological evaluation.

4,5-Dihydro-5-phenyl-3-(2-propenyloxy)isoxazole (11a). A solution of sodium 2-propenyl oxide was prepared from sodium (0.322 g, 14.0 mmol) and allyl alcohol (10 mL). Sulfonylisoxazoline **6a** (0.275 g, 0.96 mmol) was added and the resulting solution refluxed for 30 min after which water and CH_2Cl_2 were added. The organic layer was separated, washed, dried, and concentrated. The crude product was purified by preparative TLC (CH_2Cl_2) followed by Kugelrohr distillation, giving 0.179 g (78% yield) of pure product: bp 80–85 °C (0.05 mm); IR (film) 1610 cm^{-1} (C=N); NMR δ 7.37 (s, 5 H), 5.2–6.3 (m, 4 H), 4.68 (dt, 1 H, J = 6, 1 Hz), 3.37 (dd, 1 H, J_{ax} = 9.7, J_{ab} = 16 Hz), 3.09 (dd, 1 H, J_{bx} = 9.3, J_{ab} = 16 Hz).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.44. Found: C, 70.96; H, 6.55.

3a,5,6,6a-Tetrahydro-3-methoxy-4*H*-cyclopent[*d*]isoxazole (11b). A solution of lithium methoxide was prepared from lithium (166 mg, 22.9 mmol) and methanol (10 mL). Sulfonylisoxazoline **6b** (0.23 g, 0.93 mmol) was added and the resulting solution refluxed for 1 h after which water and CH_2Cl_2 were added. The organic layer was separated, washed, dried, and concentrated. Kugelrohr distillation gave 0.115 g (82% yield) of pure (TLC) product: bp 45–55 °C (0.1 mm); IR (film) 1630 cm^{-1} (CN); NMR δ 4.9–5.3 (m, 1 H), 3.78 (s, 3 H), 3.3–3.7 (m, 1 H), 1.4–2.2 (m, 6 H).

Anal. Calcd for $C_7H_{11}NO_2$: C, 59.56; H, 7.85; N, 9.92. Found: C, 59.85; H, 8.00; N, 9.98.

3a,4,5,6,7,7a-Hexahydro-3-methoxy-1,2-benzisoxazole (11c). Prepared from sulfonylisoxazoline **10** in 88% yield by the same procedure as compound **11b**: bp 55–65 °C (0.1 mm); IR (film) 1610 cm^{-1} (CN); NMR δ 4.4–4.7 (m, 1 H), 3.85 (s, 3 H), 2.92 (m, 1 H), 1.2–2.1 (m, 8 H).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.45; N, 9.02. Found: C, 61.56; H, 8.75; N, 9.32.

5-Phenyl-2-(2-propenyl)isoxazolidinone (13). Isoxazoline **11a** (0.336 g, 1.65 mmol) was refluxed for 15 min in *N*,*N*-dimethylaniline (4 mL). Methylene chloride and 5% HCl were added. The organic layer was separated, washed, dried, and concentrated. The crude product was column chromatographed (CH_2Cl_2) and Kugelrohr distilled whereupon it crystallized. The pure product (0.260 g, 77% yield) was recrystallized from aqueous alcohol to provide the analytical sample: mp 47–48 °C; IR (melt) 1700 cm^{-1} (br, C=O); NMR δ 7.39 (s, 5 H), 5.3–5.7 (m, 4 H), 4.0–4.5 (m, 2 H), 2.7–3.2 (m, 2 H).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.44. Found: C, 70.77, H, 6.58.

3a,4,5,6,7,7a-Hexahydro-1,2-benzisoxazole (12). A mixture of sulfonylisoxazoline **10** (0.46 g, 1.72 mmol), sodium borohydride (0.78 g, 20.6 mmol), and 2-propanol (5 mL) was stirred for 2 h at room temperature. Water and CH_2Cl_2 were added, and the organic layer was separated, washed, dried, and concentrated (0–5 °C). Kugelrohr distillation of the crude material gave 0.168 g (78% yield) of product (>99% pure, VPC): bp 80–95 °C (4.2 mm); IR (film) 1580 cm^{-1} (weak, C=N); NMR δ 7.20 (d, 1 H, J = 1.5 Hz), 4.1–4.5 (m, 1 H), 2.8–3.3 (m, 1 H), 1.1–2.1 (m, 8 H).

Anal. Calcd for $C_7H_{11}NO$: C, 67.17; H, 8.86; N, 11.19. Found: C, 66.96; H, 9.16, N, 11.12.

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Registry No. 1, 70367-23-6; **6a**, 70367-29-2; **6b**, 70367-27-0; **6c**, 70367-25-8; **6d**, 85355-66-4; **6e**, 85355-67-5; **6f**, 85355-68-6; **7a**, 7064-06-4; **7b**, 4894-23-9; **7c**, 85355-69-7; **7d**, 20936-78-1; **7e**, 85355-70-0; **7f**, 70367-38-3; **7g**, 85355-71-1; **7h**, 85355-72-2; **7i**, 17669-25-9; **7j**, 4894-25-1; **8**, 73661-46-8; **9**, 52939-94-3; **10**, 70367-28-1; **11a**, 85355-73-3; **11b**, 70367-37-2; **11c**, 70367-40-7; **12**, 70367-39-4; **13**, 85355-74-4; (*S*)-*N*-phthalylvinylglycine, 85369-51-3; *cis*-stilbene, 645-49-8.