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Generation of Sulfur-Functionalized Nitrile Oxide, (Phenylthio)-acetonitrile Oxide, and Synthetic Applications

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The first generation of a new sulfur-functionalized nitrile oxide 1,3-dipole, (phenylthio)acetonitrile oxide, is presented. Its cycloadditions to a variety of olefins and acetylenes lead to 3-(phenylthiomethyl)-2-isoxazolines and -oxazoles, the formers being selectively deprotonated at the carbon substituted by the sulfur moiety. The resulting sulfur-stabilized carbanions react with aldehydes, esteric Michael acceptors, and alkyl halides to enable the introduction of a carbon substituent to the side chain on 3-position. Raney Ni reduction of these 2-isoxazolines gives β,β'-dihydroxy ketones and β-hydroxy ketones.

A phosphorus-functionalized nitrile oxide, (diethoxyphosphinyl)acetonitrile oxide, was first prepared in our laboratory[1] and its synthetic versatility is now gradually established.[2-4] Advantages of the phosphorus-functionalized nitrile oxide in organic synthesis are that 1) its cycloadditions to olefins or acetylenes regioselectively lead to 3-(phosphinylmethyl)-2-isoxazolines or -oxazoles bearing a variety of substituents at the 5-position, 2) these heterocycles can be converted into 3-[1-(diethoxyphosphinyl)alkyl], 3-(1-alkenyl), and 3-acyl derivatives via the phosphorus-stabilized carbanions, 3) the phosphorus moiety of the cycloadducts can survive intact on their reductive cleavage of the nitrogen–oxygen bond with Raney Ni to afford 4-hydroxy-2-oxoalkylphosphonates which undergo Horner–Emmons olefinations under mild conditions.

A sulfur-functionalized nitrile oxide, (phenylthio)-acetonitrile oxide, is an additional example for the family of α-functionalized nitrile oxides. Its synthetic applications would be characterized by its cycloadditions with olefins or acetylenes leading to 3-(phenylthio)-substituted 2-isoxazolines or isoxazoles and the generation of sulfur-stabilized carbanions followed by the subsequent reactions with electrophiles. The most characteristic advantage would be that reductive cleavage of the nitrogen–oxygen bond and elimination of the sulfur moiety can be carried out in one step.[5]

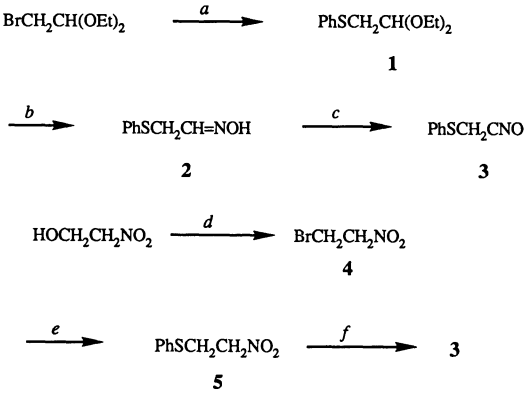
The present paper presents the first preparation of a sulfur-functionalized nitrile oxide, (phenylthio)acetonitrile oxide, and its synthetic application.

Results and Discussion

Generation of (Phenylthio)acetonitrile Oxide. Two routes were examined for the generation of (phenylthio)acetonitrile oxide (**3**). One consists of the direct oxidation of (phenylthio)acetaldehyde oxime (**2**) with sodium hypochlorite–triethylamine in dichloromethane (Scheme 1). As oxime **2** (syn:anti=4:5 by ^{1}H NNR; 91% from **1**) can be readily prepared in quantities and in a good yield from commercially available bromoacetaldehyde diethyl acetal via (phenylthio)acetaldehyde diethyl acetal (**1**, 95% based on the starting acetal), the rather low yield oxidation step of **2** into **3** is enough compensated. The nitrile oxide **3** is trapped, as soon as it is generated, in a 1,3-dipolar cycloaddition with an olefinic dipolarophile. This will be mentioned below.

The other route involves the Mukaiyama reaction[6] using 2-phenylthio-1-nitroethane (**5**). A mixture of the nitro compound **5** and phenyl isocyanate was heated in benzene in the presence of triethylamine and an olefin. The strating **5** is available from 2-nitroethanol via 1-bromo-2-nitroethane (**4**), however this preparation involves the use of rather expensive and difficult-to-handle 2-nitroethanol and the poor yield of **4**.[7]

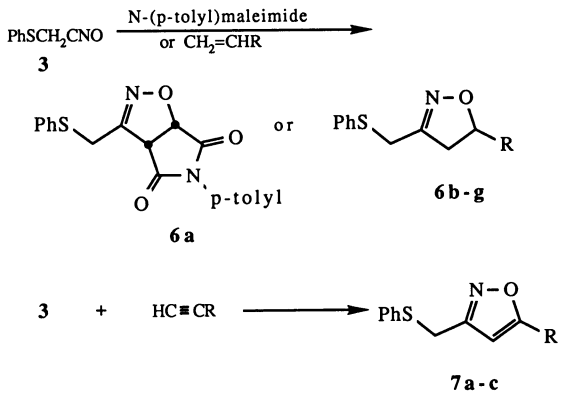
The bromination of oxime **3** with *N*-bromosuccinimide (NBS)[8] or the chlorination with *N*-chlorosuccinimide (NCS) followed by the dehydrohalogenation with triethylamine failed to generate nitrile oxide **3**.



a: NaOEt in EtOH, *b*: NH_2OH HCl in EtOH, 50 °C, *c*: NaOCl/NEt_3 in dichloromethane, *d*: PBr_3 in diethyl ether, 0 °C, *e*: PhSH/Na in THF, *f*: PhNCO/NEt_3 in benzene

Scheme 1.

Cycloadditions of (Phenylthio)acetonitrile Oxide to Olefins and Acetylenes. Efficiency in the generation of (phenylthio)acetonitrile oxide (**3**) from the above two precursors, oxime **2** and nitro compound **5**, was evaluated in the trapping reactions of **3** with olefinic dipolarophiles. An equimolar mixture of oxime **2** and *N*-(*p*-tolyl)maleimide in dichloromethane was treated with 5% aqueous sodium hypochlorite (3 equiv) and a catalytic amount of triethylamine in benzene at room temperature for 4 h. After chromatographic purification, the expected 2-isoxazoline **6a** was obtained in 65% yield based on **2** (Scheme 2 and Table 1, Entry 1).



Scheme 2.

The generation step of nitrile oxide **3** from oxime **2** was, first of all, optimized in its cycloaddition reaction with *N*-(*p*-tolyl)maleimide as a highly reactive dipolarophile. Employment of a phase-transfer catalyst (Entry 6) did not improve the yield of **6a**; replacement of aqueous hypochlorite with the sodium hypochlorite supported on Celite 545[9] failed to generate nitrile oxide **3** (Entry 7). The use of 3 equivalents of aqueous sodium hypochlorite at room temperature (Entry 5) gave the best yield of **6a** (compare with Entries 1—3 and 8—10).

Trapping experiments of nitrile oxide **3** with other olefinic dipolarophiles were performed under the conditions which gave the best yield of **6a** (Table 1, Entry 5). Nitrile oxide **3** could be regioselectively trapped with electron-deficient olefins, 1-alkenes, and electron-rich olefins to produce 5-substituted 3-(phenylthiomethyl)-2-isoxazolines **6b—g** (Scheme 2 and Table 2, Entries 2, 4, 6—8, and 10). Similar

Table 1. Generation of (Phenylthio)acetonitrile Oxide **3** from Oxime **2** and Its Trapping with *N*-(*p*-Tolyl)maleimide Leading to **6a**

Entry	NaOCl (equiv)[a]	Condition[b]	Yield/%[c]
1	1	rt, 18 h	27
2	2	0°C, 1 h→rt, 1.5 h	33
3	3	0°C, 1 h→rt, 4 h	46
4	3	0°C, 5 min→rt, 17 h	51
5	3	rt, 4 h	65
6	3[d]	rt, 4 h	61
7	3[e]	rt, 4 h	0
8	5	rt, 5 h	48
9	5	reflux, 5 h	40
10	7	0°C, 5 min→rt, 5 h	47

a) Aqueous solution was used (5%). b) To an equimolar mixture of oxime **3**, and *N*-(*p*-tolyl)maleimide in dichloromethane were added NaOCl and a catalytic amount of triethylamine. The resulting mixture was allowed to react under the conditions listed above. c) Yield of isolated **6a** based on **2**. d) A catalytic amount of tetrabutylammonium hydrogensulfate was used as a phase transfer catalyst. e) NaOCl supported on Celite 545 was used in ethyl acetate.

Table 2. Generation and Cycloaddition of (Phenylthio)acetonitrile Oxide **3**

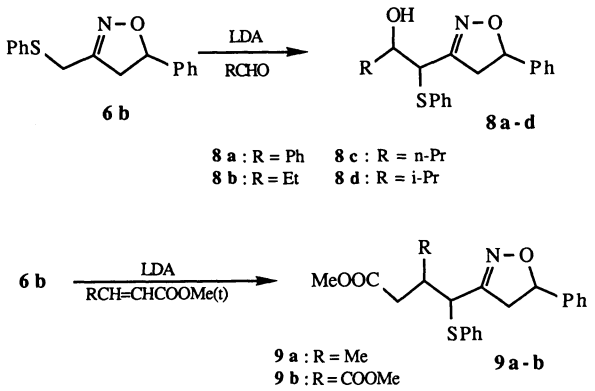
Entry	Precursor	Dipolarophile (equiv)	Condition[a]	Time/h	Product	R	Yield/%[b]
1	**2**	*N*-(*p*-Tolyl)maleimide (1)	A, rt	5	**6a**	—	65
2	**2**	Styrene (5)	A, rt	5	**6b**	Ph	52
3	**5**	Styrene (2.5)	B, rt→reflux	1→4	**6b**		90
4	**2**	Methyl acrylate (1.2)	A, rt	5	**6c**	COOMe	43
5	**5**	Methyl acrylate (2)	B, rt→reflux	1→4	**6c**		78
6	**2**	3-Buten-2-one (2)	A, rt	5	**6d**	COMe	46
7	**2**	3-Butenenitrile (1.5)	A, rt	4	**6e**	CH_2CN	22
8	**2**	1-Heptene (5)	A, rt	5	**6f**	n-C_5H_{11}	39
9	**5**	1-Heptene (2)	B, rt→reflux	1→4	**6f**		57
10	**2**	Vinyl acetate (5)	A, rt	5	**6g**	OCOMe	41
11	**2**	Methyl propiolate (2)	C, reflux	4	**7a**	COOMe	17
12	**2**	2-Propyn-1-ol (2)	C, reflux	4	**7b**	CH_2OH	21
13	**2**	3-Chloropropyne (2)	C, reflux	4	**7c**	CH_2Cl	15
14	**5**	3-Chloropropyne (2)	B, rt→reflux	1→4	**7c**		54

a) A: NaOCl (3 equiv)–NEt_3 (0.1 equiv) in dichloromethane; B: PhNCO (2 equiv)–NEt_3 (cat.) in benzene; C: NaOCl (2.5 equiv)–NEt_3 (0.25 equiv) in dichloromethane. b) Yield of isolated product based on **2** or **5**.

cycloadditions to electron-deficient acetylenes and 1-alkynes gave isoxazoles **7a—c** as single regioisomers, albeit in low yields (Scheme 2 and Table 2, Entries 11—13).

The relatively low yield formation of **6** and **7** mentioned above is apparently due to the poor efficiency in the generation step of **3** from **2** since the same nitrile oxide **3** undergoes a high-yield cycloaddition (90%) to styrene when generated by the dehydration of **5** with phenyl isocyanate (Table 2, Entry 3). In all the attempted cases the generation of **3** from **5** is much more effective than the generation from **2** (Entries 3, 5, 9, and 14).

Reactions of the Carbanions of 3-(Phenylthiomethyl)-2-isoxazolines with Electrophiles. The phenylthio functionality of 2-isoxazolines **6** would permit the selective deprotonation at the position adjacent to the sulfur moiety rather than 4-position.[10] Accordingly the styrene adduct **6b** as an example was deprotonated with lithium diisopropylamide (LDA) and the resulting anion was captured with aromatic and aliphatic aldehydes. Thus excellent yields of adducts **8a—d** were obtained as mixtures of diastereomers when the anions were treated with three equivalents of aldehydes (Scheme 3 and Table 3, Entries 1—4).



Scheme 3.

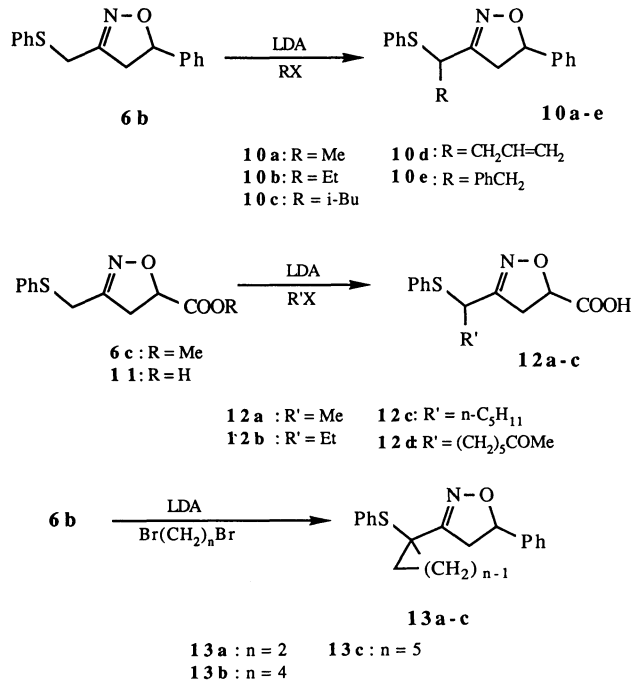
Although Michael additions of the carbanion derived from **6b** with methyl crotonate as an acceptor did not take place at −78 °C in THF, the presence of hexamethylphosphoric triamide (HMPA, 1.2 equiv) highly accelerated the addition reaction. Thus the Michael adducts **9a,b** were produced, as mixtures of diastereomers, in the reactions with methyl crotonate and dimethyl fumarate (Scheme 3 and Table 3, Entries 5,6). Use of 3-buten-2-one as a Michael acceptor led to a mixture of complex products with the 53% recovery of **6b**. Presumably the olefin acceptor underwent a base-catalyzed polymerization under the above basic conditions.

The carbanion of 2-isoxazoline **6b** was similarly alkylated at −78 °C in the presence of HMPA (Scheme 4 and Table 3). Not only alkyl iodides (Entries 7,8) but also alkyl bromides could be employed as well (Entries 9—11). Especially methylation, benzylation, and allylation were effective. On the other hand, the carbanion derived from methyl 2-isoxazoline-5-carboxylate **6c** could not be smoothly alkylated with methyl iodide, the starting **11** being partly recovered (44%). Accordingly the ester **6c** was first hydrolyzed quantitatively by aqueous lithium hydroxide in *t*-

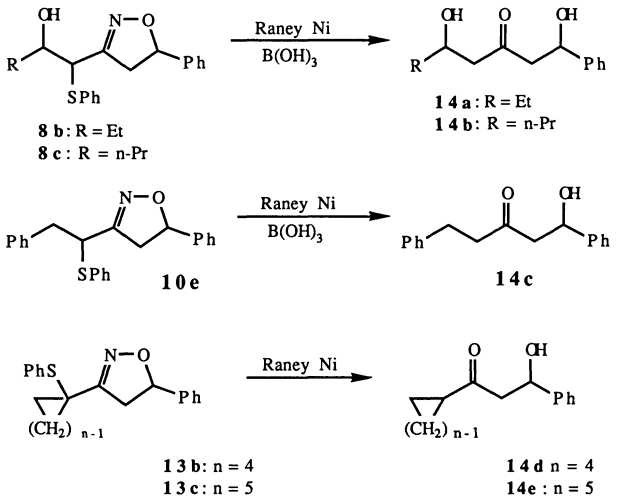
Table 3. Reactions of the Carbanions of 2-Isoxazolines **6** and **11** with Electrophiles

Entry	2-Isoxazoline	Electrophile (equiv)	Condition[a]	Time/h	Product	Yield/%[b]
1	**6b**	PhCHO (3)	A	1	**8a**	85
2	**6b**	EtCHO (3)	A	1	**8b**	86
3	**6b**	*n*-PrCHO (3)	A	1	**8c**	99
4	**6b**	*i*-PrCHO (3)	A	1	**8d**	92
5	**6b**	Methyl crotonate (1.2)	B	2	**9a**	86
6	**6b**	Dimethyl fumarate (1.2)	B	2	**9b**	45
7	**6b**	MeI (2)	B	2	**10a**	91
8	**6b**	EtI (3)	B	2	**10b**	67[c]
9	**6b**	*i*-BuBr (1.2)	C	4	**10c**	47[d]
10	**6b**	$PhCH_2Br$ (1.2)	C	2	**10d**	92
11	**6b**	CH_2=$CHCH_2Br$ (1.2)	D	2	**10e**	77
12	**11**	MeI (2)	E	3	**12a**	82
13	**11**	EtI (1.2)	E	24	**12b**	32[e]
14	**11**	*n*-$C_5H_{11}Br$ (1.5)	E	8	**12c**	49[f]
15	**11**	7-Iodo-2-heptanone ethylene acetal (1.2)	E	48	**12d**	35[g]
16	**6b**	$Br(CH_2)_2Br$ (4)	E	2	**13a**	35[h]
17	**6b**	$Br(CH_2)_4Br$ (3)	E	2	**13b**	77
18	**6b**	$Br(CH_2)_5Br$ (2)	E	2	**13c**	74

a) A—D: The carbanion of **6b** was generated by treating with LDA (1.2 equiv) in THF at −78 °C. After an electrophile was added, the reaction was continued at −78 °C in the absence (Condition A) or presence of HMPA (B: 1.2 equiv; C: 5.7 equiv; D: 11.5 equiv). E: The carbanion of **6b** or **11** was generated by treating with LDA (2.2—2.4 equiv) in THF at −78 °C. After an electrophile and HMPA (11.5 equiv) were added, the reaction was continued at −78 °C. b) Yield of isolated products. c) Recovered **6b**: 27%. d) Recovered **6b**: 40%. e) Recovered **11**: 30%. f) Recovered **11**: 34%. g) Recovered **11**: 17%. h) Recovered **6b**: 41%.



Scheme 4.



Scheme 5.

butyl alcohol and the resulting acid **11** was used for alkylation. The acid **11** was converted into the dianion with a little excess than two equivalents of LDA and then alkylations with several alkyl halides were performed to give moderate to good yields of alkylated acids **12a—d** (Entries 12—15). In the alkylation with 7-iodo-2-heptanone ethylene acetal, the dioxolane protecting group was cleaved on the usual acidic work up to give **12d**.

Alkylations of **6b** with 1,2-dibromoethane, 1,4-dibromobutane, and 1,5-dibromopentane in the presence of more than two equivalents of LDA produced 3-[1-(phenylthio)cycloalkyl]-2-isoxazolines **13a—c** (Entries 16—19).

Raney Ni Reduction of 2-Isoxazolines Leading to β-Hydroxy Ketones. It was anticipated that the sulfur moiety of 3-[1-(phenylthio)alkyl]-2-isoxazolines would be concurrently removed on the reductive cleavage of the nitrogen–oxygen bond with Raney Ni.[5] This desulfurization must be particularly important in the synthetic applications of sulfur-functionalized nitrile oxide **3** since the sulfur functionality can serve as a side chain-activating group through a sequence of deprotonation and reactions with nucleophiles.

Aldehyde adducts **8b,c** were treated with Raney Ni in aqueous ethanol in the presence of boric acid to give β,β′-dihydroxy ketones **14a,b** as mixtures of two diastereomers of desulfurized products, respectively (Scheme 5). Alkylated 2-isoxazolines **10e** and **13b,c** were similarly reduced to produce the corresponding β-hydroxy ketones **14c—e**.

Although sulfur-functionalized nitrile oxides are quite rare,[11] organic synthesis using 3-sulfinyl-2-isoxazolines has been recently reported.[5] These isoxazolines could be prepared in an optically pure form by treatment of 3-lithiomethyl-2-isoxazolines with a chiral sulfinate after separation of two diastereomers. Though the cycloadducts of our nitrile oxide **3** are synthetically equivalent to these precedents, one advantage is that a variety of functionalities can be introduced at the 5-position of 2-isoxazoline ring by use of **3**.[12]

Experimental

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz), a JEOL FX-100 (100 MHz), or a JEOL GSX-270 (270 MHz) instrument and ^{13}C NMR on a JEOL FX-100 (25.05 MHz) or a GSX-270 spectrometer (67.94 MH). Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. High-resolution mass spectra were obtained on the same instrument. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), and Silicagel 60 (Merck) were employed.

(Phenylthio)acetaldehyde Diethyl Acetal (1). To a solution of sodium ethoxide (20.4 g, 0.30 mol) in dry ethanol (90 ml) was added thiophenol (33.0 g, 0.30 mol). After the mixture was stirred at room temperature for 0.5 h, bromoacetaldehyde diethyl acetal (68.43 g, 0.33 mol) was added in a period of 1.5 h. The mixture was stirred for 22 h, poured into water (80 ml), and extracted with diethyl ether (100 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue

was subjected to vacuum distillation to give **1** (64.95 g, 95%): Colorless liquid; bp 103—104 °C/106 Pa; ^{1}H NMR ($CDCl_3$) δ=1.18 (6H, t, J=7.0 Hz, Me), 3.13 (2H, d, J=5.4 Hz, SCH_2), 3.32—3.81 (4H, m, OEt), 4.61 (1H, t, J=5.4 Hz, CH), and 7.06—7.42 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=15.24 (q, Me), 37.53 (t, SCH_2), 62.24 (t, OEt), 102.01 (d, CH), 126.24, 129.07, 129.54 (each d), and 136.72 (s); MS m/z (rel intensity, %) 226 (M^+, 5), 135 (47), 123 (58), 109 (35), 103 (59), 77 (Ph, 34), 75 (66), 65 (30), 51 (35), 47 (base peak), 45 (63), 43 (24), and 39 (21). Found: C, 63.63; H, 7.94%. Calcd for $C_{12}H_{18}O_2S$: C, 63.68, H, 8.02%.

(Phenylthio)acetaldehyde Oxime (2). To a solution of acetal **1** (10.0 g, 44.25 mmol) in ethanol (60 ml) was added aqueous hydroxylamine hydrochloride (3.38 g, 48.67 mmol in 30 ml of water). This mixture was stirred at 50 °C for 5 h and the ethanol was evaporated in vacuo. From the resulting aqueous solution products were extracted with dichloromethane (30 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel with hexane–ethyl acetate (5:1 v/v) to give oxime **2** (6.69 g, 91%) as a 4:5 mixture of syn and anti isomers: Pale yellow viscous oil; IR (neat) 3000 and 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.53 (1H, d, J=6.5 Hz, one of SCH_2), 3.75 (1H, d, J=5.8 Hz, the other of SCH_2), 6.74 (4/9H, t, J=5.8 Hz, CH (syn)), 7.08—7.50 (6H, m, Ph and CH (anti)), and 8.90 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ=26.95 (t, SCH_2 (syn)), 32.88 (t, SCH_2 (anti)), 126.72, 127.19, 129.18, 129.42, 130.77 (each d), 134.30, 135.01 (each s), 148.01, and 148.66 (each d); MS m/z (rel intensity, %) 167 (M^+, 21), 123 (49), 110 (71), 109 (base peak), 104 (21), 77 (54), 69 (50), 66 (24), 65 (86), 63 (22), 51 (91), 50 (41), 45 (85), and 39 (77). HRMS Found: m/z 167.0404. Calcd for C_8H_9NOS: M, 167.0399.

General Procedure for the Generation of Nitrile Oxide 3 from Oxime 2 and Its Cycloadditions with Olefins Leading to 6a—g. To a solution of oxime **2** (0.167 g, 1 mmol) and an olefin (1 to 5 mmol) in dichloromethane (20 ml) was added slowly an aqueous solution of soduim hypochlorite (5%, 4.47 g, 3 mmol) and triethylamine (0.01 g, 0.1 mmol). The mixture was stirred at room temperature for 4 to 5 h, poured into ice water (30 ml), and extracted with dichloromethane (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate as an eluent to give cycloadduct **6**. The ratios of hexane–ethyl acetate employed are as follows: **6a**, **6c**, **6d**: 4:1 v/v; **6b**: 20:1 v/v; **6e**: 1:1 v/v; **6f**: 10:1 v/v; **6g**: 6:1 v/v. Yields of **6**, molar amounts of the olefin used, and reaction times are summarized in Table 2.

6a: Colorless needles (ethyl acetate–hexane); mp 129—130 °C; IR (KBr) 1700 and 1570 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.34 (3H, s, Me), 3.75 (1H, d, J=14.5 Hz, one of SCH_2), 4.63 (1H, d, J=14.5 Hz, the other of SCH_2), 5.29 (1H, d, J=9.5 Hz, 4-H), 5.29 (1H, d, J=9.5 H, 5-H), and 7.00—7.44 (9H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=21.24 (q, Me), 29.30 (t, SCH_2), 54.89 (d, 4-C), 79.59 (d, 5-C), 126.07, 127.77, 128.30, 129.54, 130.13, 130.78 (each d), 133.66, 139.60 (each s), 152.01 (s, 3-C), 170.30, and 171.48 (each s, C=O); MS m/z (rel intensity, %) 352 (M^+, 81), 187 (26), 162 (22), 146 (24), 133 (56), 132 (45), 130 (24), 109 (base peak), 104 (39), 91 (51), 78 (33), 77 (58), 69 (20), 65 (68), 52 (50), 51 (50), 45 (47), and 39 (34). Found: C, 64.66; H, 4.67; N, 8.12%. Calcd for $C_{19}H_{16}N_2O_3S$: C, 64.76; H, 4.58; N, 7.95%.

6b: Yellow oil; IR (neat) 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.94 (1H, dd, J=8.3 and 17.0 Hz, one of 4-H), 3.37 (1H, dd, J=11.0 and 17.0 Hz, the other of 4-H), 3.67 (1H, d, J=14.7 Hz, one of SCH_2), 3.87 (1H, d, J=14.7 Hz, the other of SCH_2), 5.45 (1H, dd, J=8.3 and 11.0 Hz, 5-H), and 7.02—7.38 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=30.76 (t, SCH_2), 43.55 (t, 4-C), 82.32 (d, 5-C), 125.88, 127.15, 128.17, 129.24, 130.33 (each d), 134.18, 141.02 (each s), and 155.83 (s, 3-C); MS m/z (rel intensity, %) 269 (M^+, 4), 125 (74), 109 (21), 97 (35), 76 (base peak), 51 (63), and 50 (25). HRMS Found: m/z 269.0875. Calcd for $C_{16}H_{15}NOS$: M, 269.0874.

6c: Yellow oil; IR (neat) 1740 and 1585 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.28 (2H, d, J=9.0 Hz, 4-H), 3.67 (3H, s, Me of COOMe), 3.77 (2H, s, SCH_2), 4.92 (1H, t, J=9.0 Hz, 5-H), and 7.13—7.40 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=30.47 (t, SCH_2), 39.53 (t, 4-C), 52.71 (q, COOMe), 77.77 (d, 5-C), 127.36, 129.30, 130.42 (each d), 134.13 (s), 155.71 (s, 3-C), and 170.66 (s, C=O); MS m/z (rel intensity, %) 251 (M^+, 20), 123 (46), 109 (68), 77 (34), 69 (23), 65 (50), 59 (base peak), 54 (23), 51 (47), 44 (57), and 38 (36). HRMS Found: m/z 251.0617. Calcd for $C_{12}H_{13}NO_3S$: M, 251.0615.

6d: Yellow oil; IR (neat) 1720 and 580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.04 (3H, s, Me), 3.18 (1H, d, J=11.0 Hz, one of 4-H), 3.20 (1H, d, J=7.2 Hz, the other of 4-H), 3.66 (1H, d, J=16.0 Hz, one of SCH_2), 3.84 (1H, d, J=16.0 Hz, the other of SCH_2), 4.75 (1H, dd, J=11.0 and 7.2 Hz, 5-H), and 7.12—7.39 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=25.94 (q, Me), 30.47 (t, SCH_2), 37.94 (t, 4-C), 84.06 (d, 5-C), 127.42, 129.30, 130.60 (each d), 133.83 (s), 156.01 (s, 3-C), and 207.66 (s, C=O); MS m/z (rel intensity, %) 235 (M^+, 11), 123 (67), 109 (32), 77 (27), 65 (27), 51 (28), 45 (33), 43 (base peak), and 39 (20). HRMS Found: m/z 235.0665. Calcd for $C_{12}H_{13}NO_2S$: M, 235.0666.

6e: Yellow viscous oil; ^{1}H NMR ($CDCl_3$) δ=2.37 (1H, d, J=6.0 Hz, one of CH_2CN), 2.39 (1H, d, J=5.5 Hz, the other of CH_2CN), 2.84 (1H, dd, J=6.0 and 17.2 Hz, one of 4-H), 3.23 (1H, dd, J=10.0 and 17.4 Hz, the other of 4-H), 3.72 (1H, d, J=17.2 Hz, one of SCH_2), 3.86 (1H, ddd, J=6.0, 6.0, and 5.5 Hz, 5-H), and 7.14—7.43 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=23.18 (t, CH_2CN), 30.53 (t, SCH_2), 40.47 (t, 4-C), 75.54 (d, 5-C), 116.36 (s, CN), 127.54, 129.48, 130.54 (each d), 133.95 (s), and 156.12 (s, 3-C); MS m/z (rel intensity, %) 232 (M^+, base peak), 164 (21), 163 (35), 162 (25), 130 (40), 123 (44), 109 (78), 77 (30), 65 (46), 54 (38), 51 (29), 45 (37), and 39 (28). HRMS Found: m/z 232.0666. Calcd for $C_{12}H_{12}N_2OS$: M, 232.0669.

6f: Colorless needles (ethyl acetate–hexane); mp 32—33 °C; IR (KBr) 1575 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.85 (3H, t, J=6.0 Hz, Me), 1.02—1.68 (8H, m, CH_2 of n-C_5H_{11}), 2.61 (1H, dd, J=8.2 and 7.0 Hz, one of 4-H), 3.02 (1H, dd, J=10.1 and 17.0 Hz, the other of 4-H), 3.67 (1H, d, J=14.5 Hz, one of SCH_2), 3.85 (1H, d, J=14.5 Hz, the other of SCH_2), 4.28—4.65 (1H, m, 5-H), and 7.10—7.42 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=14.00 (q, Me), 22.47, 24.94, 31.00, 31.59, 35.00 (each t, CH_2 of n-C_5H_{11}), 40.41 (t, 4-C), 81.36 (d, 5-C), 127.01, 129.24, 130.07 (each d), 134.66 (s), and 155.71 (s, 3-C); MS m/z (rel intensity, %) 263 (M^+, 72), 192 (base peak), 130 (21), 123 (51), 110 (29), 109 (42), 77 (45), 64 (22), 56 (21), 55 (29), 44 (29), 40 (36), and 38 (20). Found: C, 68.35; H, 7.95; N, 5.24%. Calcd for $C_{15}H_{21}NOS$: C, 68.40; H, 8.04; N, 5.32%.

6g: Yellow oil; IR (neat) 1740 and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.96 (3H, s, Me), 2.96 (1H, dd, J=1.5 and 18.0 Hz, one of 4-H), 3.26 (1H, dd, J=6.2 and 18.0 Hz, the other of 4-H), 3.81 (2H, s, SCH_2), 6.55 (1H, dd, J=1.5 and 6.2 Hz, 5-H), and 7.14—7.43 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=20.94

(q, Me), 30.59 (t, SCH_2), 41.83 (t, 4-C), 95.83 (d, 5-C), 127.60, 129.36, 130.83 (each d), 133.83 (s), 156.89 (s, 3-C), and 169.72 (s, C=O); MS *m/z* (rel intensity, %) 251 (M^+, 43), 163 (28), 123 (29), 109 (25), 45 (22), and 43 (base peak). HRMS Found: *m/z* 251.0610. Calcd for $C_{12}H_{13}NO_3S$: M, 251.0615.

General Procedure for the Cycloadditions of Nitrile Oxide 3 Generated from Oxime 2 with Acetylenes Leading to 7a—c. To a solution of oxime **2** (0.334 g, 2 mmol) and acetylene (3 mmol to 4 mmol) in dichloromethane (15 ml) was added slowly an aqueous solution of sodium hypochlorite (5%, 7.45 g, 5 mmol) and triethylamine (0.051 g, 0.5 mmol). The mixture was stirred at 50 °C for 4 h, poured into water (15 ml), and extracted with dichloromethane (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate to give cycloadduct **7**. The ratios of hexane–ethyl acetate employed as eluents are as follows: **7a**: 50:1 v/v; **7b**: 2:1 v/v **7c**: 100:1 v/v. Yields of **7**, molar amounts of the acetylene used, and reaction times are summarized in Table 2.

7a: Colorless needles (diethyl ether–hexane); mp 39—40 °C; ^{1}H NMR ($CDCl_3$) δ=3.87 (3H, s, Me), 4.10 (2H, s, SCH_2), 6.86 (1H, s, 4-H), and 7.12—7.40 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=29.00 (t, SCH_2), 52.89 (q, Me), 109.42 (d, 4-C), 127.48, 129.19, 130.48 (each d), 134.13 (s), 157.25 (s, C=O), 160.54 (s, 3-C), and 162.42 (s, 5-C); MS *m/z* (rel intensity, %) 249 (M^+, 60), 190 (base peak), 162 (22), 144 (34), 125 (26), 123 (52), 110 (22), 109 (80), 77 (69), 65 (38), 51 (50), 45 (59), and 39 (27). Found: C, 58.05; H, 4.76; N, 5.72%. Calcd for $C_{12}H_{11}NO_3S$: C, 57.82; H, 4.45; N, 5.62%.

7b: Yellow oil; ^{1}H NMR ($CDCl_3$) δ=3.58 (1H, br s, OH), 4.00 (2H, s, SCH_2), 4.56 (2H, s, CH_2OH), 6.14 (1H, s, 4-H), and 7.06—7.36 (5H, m, Ph) ^{13}C NMR ($CDCl_3$) δ=28.91 (t, SCH_2), 56.15 (t, CH_2OH), 101.76 (d, 4-C), 127.05, 129.24, 129.98 (each d), 134.77 (s), 161.57 (s, 3-C), and 172.41 (s, 5-C); MS *m/z* (rel intensity, %) 221 (M^+, 17), 190 (39), 162 (29), 144 (26), 130 (22), 123 (64), 109 (base peak), 77 (59), 69 (35), 65 (64), 53 (25), 52 (23), 51 (77), 50 (25), 45 (88), 39 (66), and 31 (69). HRMS Found: *m/z* 221.0508. Calcd for $C_{11}H_{11}NO_2S$: M, 221.0509.

7c: Pale yellow needles (diethyl ether–hexane); mp 47—48 °C; ^{1}H NMR ($CDCl_3$) δ=4.03 (2H, s, SCH_2), 4.47 (2H, s, CH_2Cl), 6.21 (1H, s, 4-H), and 7.10—7.39 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=29.10 (t, SCH_2), 34.47 (t, CH_2Cl), 103.71 (d, 4-C), 127.29, 129.34, 130.27 (each d), 134.66 (s), 161.96 (s, 3-C), and 168.06 (s, 5-C); MS *m/z* (rel intensity, %) 241 (M^+ +2, 16), 239 (M^+, 37), 206 (20), 198 (27), 190 (33), 162 (39), 149 (26), 145 (20), 142 (28), 123 (31), 110 (21), 109 (base peak), 76 (68), 65 (37), 45 (37), 43 (25), and 39 (27). Found: C, 55.21; H, 4.34; N, 5.74%. Calcd for $C_{11}H_{10}NOSCl$: C, 55.11; H, 4.20; N, 5.84%.

General Procedure for the Cycloadditions of Nitrile Oxide 3 Generated from 2-Phenylthio-1-nitroethane 5. To a solution of the nitro compound **5** (1.5 g, 8.2 mmol) and triethylamine (0.10 g, 1.0 mmol) in dry benzene (5 ml) was added the solution of an olefin (16.4 mmol) and phenyl isocyanate (1.95 g, 6.4 mmol). The mixture was stirred at room temperature for 1 h, and then refluxed for 4 h. The insoluble material (*N,N'*-diphenylurea) was filtered off, and the filtrate was evaporated in vacuo. The residue was chromatographed over silica gel with hexane–ethyl acetate to give cycloadduct **6** or **7**. The ratios of hexane–ethyl acetate employed are as follows: **6b**, **6f**, **7c**: 20:1 v/v; **6c**: 4:1 v/v. Yields of **6** or **7**, molar amounts of the olefin or acetylene used, and reaction times are summarized in Table 2.

General Procedure for the Addition Reactions of 2-Isoxazoline 6b with Aldehydes Leading to 8a—d. To a solution of diisopropylamine (0.242 g, 2.4 mmol) in dry THF (25 ml) was added butyllithium (15% in hexane, 1.5 ml, 2.4 mol) at −78 °C under nitrogen. After 5 min, a solution of 2- isoxazoline **6b** (0.538 g, 2 mmol) in dry THF (15 ml) was added. After 0.5 h at −78 °C, an aldehyde (6 mmol) was added. The mixture was stirred at the same temperature for 1 h, poured into saturated aqueous ammonium chloride (50 ml), and extracted with dichloromethane (40 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate (10:1 v/v) as an eluent to give adduct **8**. All the adducts **8** were mixtures of more than three diastereomers (^{13}C NMR). The results are summarized in Table 3.

8a: Yellow viscous oil; IR (neat) 3400 and 1575 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.64—3.50 (2H, m, 4-H), 3.70 (1H, br s, OH), 4.20—4.44 (1H, m, SCH), 4.81—5.08 (1H, m, CHOH), 5.11—5.44 (1H, m, 5-H), and 6.82—7.42 (15H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=43.30 (t, 4-C), 55.12, 55.36 (each d, SCH), 74.01, 74.42 (each d, CHOH), 81.89 (d, 5-C), 125.89, 126.54, 126.89, 127.07, 127.89, 128.13, 128.36, 128.54, 128.65, 129.24, 132.25, 132.54, (each d), 133.30, 133.48, 140.13, 140.60, 140.77 (each s), 157.01, 157.25, and 157.36 (each s, 3-C); MS *m/z* (rel intensity, %) 269 (M^+ −PhCHO), and 105 (22). Satisfactory elemental analysis was not available because of its instability.

8b: Yellow oil; IR (neat) 3400 and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.81—1.08 (3H, m, Me), 1.40—1.80 (2H, m, CH_2), 2.80—3.64 (3H, m, 4-H and OH), 3.64—3.96 (1H, m, CHOH), 3.96—4.26 (1H, m, SCH), 5.27—5.57 (1H, m, 5-H), and 6.94—7.47 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=9.94 (q, Me), 27.59, 27.88, 28.18 (each t, CH_2), 43.00, 43.36 (each t, 4-C), 51.42, 51.77, 53.24, 53.47 (each d, SCH_2), 72.95, 73.12, 73.53, 73.65 (each d, CHOH), 125.95, 126.13, 127.71, 127.83, 128.25, 129.30, 132.07, 132.25 (each d), 133.19, 133.42, 133.71, 140.95, 141.07 (each s), 157.77, 157.89, and 158.19 (each s, 3-C); MS *m/z* (rel intensity, %) 327 (M^+, 5), 269 (base peak), and 77 (22). HRMS Found: *m/z* 327.1288. Calcd for $C_{19}H_{21}N_2OS$: M, 327.1292.

8c: Yellow oil; IR (neat) 3400 and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.91 (3H, t, *J*=7.0 Hz, Me), 2.15—2.77 (4H, m, CH_2), 2.80—3.64 (3H, m, 4-H, CHOH), 3.76—4.22 (2H, m, SCH and OH), 5.30—5.58 (1H, m, 5-H), and 6.95—7.47 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=13.88 (q, Me), 18.88 (t, CH_2), 36.71, 37.00, 37.36, (each t, CH_2), 43.12, 43.24, 43.47 (each t, 4-C), 51.89, 52.18, 53.77, 54.00 (each d, SCH), 71.42, 71.59, 72.06 (each d, CHOH), 82.01 (d, 5-C), 125.95, 127.89, 128.25, 128.77, 129.36, 132.25 (each d), 133.13, 133.54, 133.71 (each s), 140.95, 141.07 (each s), 157.30, 157.72, 157.95, and 158.06 (each s, 3-C); MS *m/z* (rel intensity, %) 341 (M^+, 7), 269 (base peak), 126 (45), 111 (31), 110 (22), 78 (27), 77 (39), 51 (22), and 43 (30). HRMS Found: *m/z* 341.1447. Calcd for $C_{20}H_{23}NO_2S$: M, 341.1448.

8d: Yellow oil; IR (neat) 3400 and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.99 (6H, d, *J*=6.8 Hz, Me), 1.77—2.08 (1H, m, CH), 2.65 (1H, br s, OH), 2.90—3.77 (3H, m, 4-H, CHOH), 4.20—4.41 (1H, m, SCH), 5.47 (1H, dd, *J*=8.2 and 10.8 Hz, 5-H), and 6.97—7.44 (10H, m, Ph); ^{13}C NMR ($CDCl_3$)

δ=16.41, 17.24, 19.41, 19.94 (each q, Me), 31.36 (d, CH), 42.94, 43.30 (each t, 4-C), 49.94, 51.95 (each d, SCH), 76.48, 77.18 (each d, CHOH), 82.06 (d, 5-C), 126.01, 127.89, 128.18, 128.77, 129.36, 132.30 (each d), 133.07, 133.30, 141.13 (each s), 157.25, and 157.83 (each s, 3-C); MS *m/z* (rel intensity, %) 341 (M^+, 5), 269 (base peak), 126 (27), 111 (23), 77 (23), and 43 (23). HRMS Found: *m/z* 341.1444. Calcd for $C_{20}H_{23}NO_2S$: M, 341.1446.

General Procedure for the Michael Additions of 2-Isoxazoline 6b Leading to 9a,b. To a solution of diisopropylamine (0.121 g, 1.2 mmol) in dry THF (10 ml) was added butyllithium (15% in hexane, 0.75 ml, 1.20 mol) at −78 °C under nitrogen. After a solution of 2-isoxazoline **6b** (0.269 g, 1 mmol) in dry THF (10 ml) was added, stirring was continued at −78 °C for 0.5 h. An α,β-unsaturated ester (1.2 mmol) and HMPA (0.215 g, 1.2 mmol) were added. The mixture was stirred at the same temperature for 2 h, poured into saturated aqueous ammonium chloride (30 ml), and extracted with dichloromethane (40 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using the following eluent to give adduct **9**: **9a**: hexane–ethyl acetate (6:1 v/v); **9b**: chloroform. All the adducts **9** were mixtures of more than two diastereomers. The results are summarized in Table 3.

9a: Yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.04—1.33 (3H, m, Me), 2.06—2.66 (3H, m, CH and CH_2), 2.72—3.81 (2H, m, 4-H), 3.51, 3.57 (3H, each s, CO_2Me), 3.94—4.18 (1H, m, SCH), 5.22—5.55 (1H, m, 5-H), and 6.80—7.46 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=18.12 (q, Me), 32.41 (t), 38.71, 39.24 (each d, SCH), 42.12 (t, 4-C), 51.36, 51.47 (each q, CO_2Me), 81.77 (d, 5-C), 125.71, 127.36, 127.89, 128.48, 129.07, 130.01, 131.71 (each d), 133.36, 133.77, 140.60, 140.95 (each s), 157.42, 157.95 (each s, 3-C), 172.25, and 172.36 (each s, C=O); MS *m/z* (rel intensity, %) 369 (M^+, base peak), 260 (67), 228 (73), 129 (23), 115 (27), 113 (30), 109 (45), 105 (25), 104 (33), 103 (30), 91 (39), 78 (20), 77 (50), 65 (29), 55 (22), 51 (22), 38 (20), and 25 (21). HRMS Found: *m/z* 369.1400. Calcd for $C_{21}H_{23}NO_3S$: M, 369.1399.

9b: Yellow oil; ^{1}H NMR ($CDCl_3$) δ=2.53—3.79 (11H, m, 4-H, CH_2, CH, and CO_2Me), 4.16—4.44 (1H, m, SCH), 5.32—5.62 (1H, m, 5-H), and 6.94—7.47 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=34.47 (t), 42.71, 43.30, 43.94, 47.94 (each d, SCH), 51.95, 52.36 (each q, CO_2Me), 82.30 (d, 5-C), 125.89, 128.30, 128.77, 129.42, 132.54, 132.83 (each d), 133.01, 140.77, 140.60 (each s), 156.18, 156.36 (each s, 3-C), 171.71, 171.89, 172.31, and 172.54 (each s, C=O); MS *m/z* (rel intensity, %) 413 (M^+, 37), 272 (29), 168 (22), 155 (21), 153 (20), 147 (28), 141 (29), 129 (23), 128 (43), 116 (20), 115 (42), 110 (21), 109 (base peak), 105 (36), 104 (49), 103 (33), 51 (43), and 40 (34). HRMS Found: *m/z* 413.1296. Calcd for $C_{22}H_{23}NO_5S$: M, 413.1296.

General Procedure for the Alkylations of 2-Isoxazoline 6b Leading to 10a—e. To a solution of diisopropylamine (0.121 g, 1.2 mmol) in dry THF (10 ml) was added butyllithium (15% in hexane, 0.75 ml, 1.2 mol) at −78 °C under nitrogen. A solution of 2-isoxazoline **6b** (0.269 g, 1 mmol) in dry THF (10 ml) was added. After stirring was continued for 0.5 h at −78 °C, an alkyl halide (1.2 to 3 mmol) and HMPA (1.2 mmol to 11.5 mmol) were added. The mixture was stirred at −78 °C for 2 h, poured into saturated aqueous ammonium chloride (30 ml), and extracted with dichloromethane (40 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate as an eluent to give **10**. The ratios of hexane–ethyl acetate employed are as follows: **10a**: 6:1 v/v; **10b**, **10c**, and **10e**: 15:1 v/v; **10d**: 10:1 v/v. These adducts **10** were all mixtures of two diastereomers. The results are summarized in Table 3.

10a: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.46, 1.47 (3H, each d, each J=7.0 Hz, Me), 2.95 (H, dd, J_{4-5}=8.5 and J=16.7 Hz, one of 4-H), 3.37 (1H, dd, J_{4-5}=11.0 and J=16.7 Hz, the other of 4-H), 4.14, 4.28 (1H, each q, J=7.0 Hz, SCH), 5.25—5.54 (1H, m, 5-H), and 6.87—7.40 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=18.12, 18.35 (each q, Me), 40.00, 40.41 (each d, SCH), 41.30, 41.94 (each t, 4-C), 81.89, 82.06 (each d, 5-C), 125.83, 127.66, 127.83, 128.01, 128.18, 128.65, 129.13, 132.07, 132.30 (each d), 133.42, 140.95, 141.24 (each s), 159.01, and 159.42 (each s, 3-C); MS *m/z* (rel intensity, %) 283 (M^+, 63), 174 (base peak), 156 (34), 131 (44), 129 (71), 128 (31), 126 (20), 115 (20), 110 (34), 109 (43), 104 (28), 103 (32), 91 (28), and 77 (27). HRMS Found: *m/z* 283.0980. Calcd for $C_{17}H_{17}NOS$: M, 283.1030.

10b: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=0.95, 1.02 (3H, each t, J=7.5 Hz, Me), 1.53—1.89 (2H, m, CH_2), 2.48—3.56 (2H, m, 4-H), 3.98, 4.08 (1H, each t, J=7.0 Hz, SCH), 5.37 (1/2H, dd, J_{5-4}=8.2 and 11.0 Hz, 5-H), 5.41 (1/2H, dd, J_{5-4}=8.0 and 11.0 Hz, 5-H), and 6.83—7.44 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=11.82, 11.94 (each q, Me), 25.18, 25.35 (each t, CH_2), 41.06, 41.59 (each t, 4-C), 46.71, 47.12 (each d, SCH), 81.59 (d, 5-H), 125.60, 127.24, 127.42, 127.83, 127.95, 128.48, 128.60, 128.95, 131.66 (each d), 133.42, 133.60, 140.95, 141.13 (each s), 157.89, and 158.30 (each s,3-C); MS *m/z* (rel intensity, %) 297 (M^+, 4), 109 (base peak), and 77 (56). HRMS Found: *m/z* 297.1180. Calcd for $C_{18}H_{19}NOS$: M, 297.1186.

10c: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=0.76—1.04 (6H, m, Me), 1.46—1.73 (3H, m, CH_2CH), 2.83 (1/2H, dd, J_{4-5}=8.5 and J=16.5 Hz, one of 4-H), 2.99 (1/2H, dd J_{4-5}=8.3 and J=16.5 Hz, one of 4-H), 3.29 (1/2H, dd, J_{4-5}=10.8 and J=16.5 Hz, the other of 4-H), 3.42 (1/2H, dd, J_{4-5}=10.8 and J=16.5 Hz, the other of 4-H), 4.20, 4.32 (1H, each t, each J=7.0 Hz, SCH_2), 5.35 (1/2H, dd, J_{5-4}=8.5 and 10.8 Hz, 5-H), 5.40 (1/2H, dd, J_{5-4}=8.3 and 10.8 Hz, 5-H), and 6.83—7.42 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=21.94, 22.41, 22.53 (each q, Me), 25.77, 25.94 (each d, *i*-Pr), 40.59, 40.77 (each t, CH_2), 41.06, 41.59 (each t, 4-C), 43.41, 43.89 (each d, SCH), 81.77, 81.89 (each d, 5-C), 125.83, 127.42, 127.60, 128.01, 128.13, 128.72, 129.13, 131.89 (each d), 133.54, 133.77, 141.01, 141.30 (each s), 158.13, and 158.71 (each s, 3-C). MS *m/z* (rel intensity, %) 325 (M^+, 22), 269 (38), 218 (27), 216 (base peak), 109 (32), 44 (43), 42 (35), and 40 (30). HRMS Found: *m/z* 325.1506. Calcd for $C_{20}H_{23}NOS$: M, 325.1499.

10d: Colorless prisms (diethyl ether); mp 110—111 °C; ^{1}H NMR ($CDCl_3$) δ=2.96 (1H, dd, J_{4-5}= 8.5 and J=17.0 Hz, one of 4-H), 3.34 (1H, dd, J_{4-5}= 10.8 and J=17.0 Hz, the other of 4-H), 3.10 (2H, d, J=8.0 Hz, CH_2), 4.41, 4.47 (1H, each t, J=8.0 Hz, SCH), 5.37 (1H, dd, J_{5-4}= 8.5 and 10.8 Hz, 5-H), and 6.84—7.38 (15H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=38.43, 38.57 (each t, CH_2), 41.80, 42.09 (each t, 4-C), 46.73, 46.87 (each d, SCH), 81.98 (d, 5-C), 125.93, 127.20, 127.73, 128.12, 128.76, 129.20, 132.23 (each d), 133.30, 137.50, 141.02 (each s), and 157.66 (s, 3-C); MS *m/z* (rel intensity, %) 359 (M^+, 7), 109 (22), 91 (base peak), 77 (39), 65 (32), 51 (22), and 39 (21). Found: C, 76.70; H, 5.83; N, 4.05%. Calcd for $C_{23}H_{21}NOS$: C, 76.85, H, 5.89; N, 3.90%.

10e: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=2.34—2.62 (2H,

m, CH_2), 2.72—3.56 (2H, m, 4-H), 4.17, 4.24 (1H, each t, J=8.0 Hz, SCH), 4.84—6.01 (4H, m, 5-H, CH_2=CH), and 6.83—7.20 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=36.24, 36.41 (each t), 41.41, 41.94 (each t, 4-C), 44.77, 45.12 (each d, SCH), 81.89, 82.01 (each d, 5-C), 118.18 (t,=CH_2), 125.83, 127.66, 127.83, 128.07, 128.65, 129.19, 132.13 (each d), 133.13 (s), 133.95 (d, =CH), 141.01, 141.13 (each s), 157.72, and 158.13 (each s, 3-C); MS m/z (rel intensity, %) 309 (M^+, 4), 129 (29), 128 (46), 115 (32), 109 (base peak), 105 (30), 104 (28), 103 (24), 91 (44), 77 (36), 76 (86), 69 (22), 65 (63), 53 (23), 51 (51), 41 (35), and 39 (49). HRMS Found: m/z 309.1179. Calcd for $C_{19}H_{19}NOS$: M, 309.1186.

Hydrolysis of 2-Isoxazoline-5-carboxylate 6c into 2-Isoxazoline-5-carboxylic Acid 11. To a solution of 2-isoxazoline **6a** (1 g, 4 mmol) in aqueous 2-methyl-2-propanol (50%, 20 ml) was added lithium hydroxide (monohydrate, 0.18 g, 4.2 mmol). The mixture was stirred at room temperature for 1 h, poured into water (20 ml), and washed with diethyl ether (20 ml). The pH of the aqueous layer was adjusted below 5 with 1 M hydrochloric acid, and the resulting water layer was extracted with dichloromethane (40 ml). The extract was dried over magnesium sulfate and evaporated in vacuo to give 2-isoxazoline-5-carboxylic acid **11** (0.92 g, 97%): Pale yellow solid; mp 72—73 °C; IR (KBr) 3000 and 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.28 (1H, d, J_{4-5}=8.5 Hz, one of 4-H), 3.29 (1H, d, J_{4-5}=9.5 Hz, the other of 4-H), 3.73 (2H, s, SCH_2), 4.92 (1H, dd, J_{5-4}=8.5 and 9.5 Hz, 5-H), 7.01—7.38 (5H, m, Ph), and 9.19 (1H, s, CO_2H); ^{13}C NMR ($CDCl_3$) δ=30.47 (t, SCH_2), 39.83 (t, 4-C), 77.30 (d, 5-C), 127.66, 129.48, 130.83 (each d), 133.83 (s), 156.54 (s, 3-C), and 174.01 (s, C=O); MS m/z (rel intensity, %) 237 (M^+, 21), 192 (28), 164 (26), 130 (38), 123 (93), 109 (base peak), 76 (49), 69 (27), 65 (61), 54 (27), 51 (59), 50 (20), 45 (96), and 39 (46). Found: C, 55.46; H, 4.72; N, 5.86%. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90%.

General Procedure for the Alkylations of 2-Isoxazoline-5-carboxylic Acid 11 Leading to 12a—c. To a solution of diisopropylamine (0.222 g, 2.2 mmol) in dry THF was added butyllithium (15% in hexane, 1.38 ml, 2.2 mmol) at −78°C under nitrogen. A solution of 2-isoxazoline **11** (0.237 g, 1 mmol) in dry THF (5 ml) was added. After 0.5 h at −78 °C, an alkyl iodide (1.2—2 mmol) and HMPA (2 ml, 11.5 mmol) were added, and the mixture was stirred for the time shown in Table 3. Saturated aqueous ammonium chloride (30 ml) was added, the mixture was acidified to pH 5 by adding 1 M hydrochloric acid, and extracted with dichloromethane (30 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane–ethyl acetate containing acetic acid as an eluent to give **12**: The ratios of hexane–ethyl acetate–acetic acid employed are as follows: **12a**: 10:10:1 v/v **12b**: 50:10:3 v/v; **12c**: 15:5:1 v/v. All the alkylated 2-isoxazoline-5-carboxylic acids **12** were mixtures of two diastereomers. The results are summarized in Table 3.

12a: Yellow viscous oil; IR (neat) 2920, 1730, and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.48 (3H, d, J=7.0 Hz, Me), 3.35 (1H, d, J_{4-5}=8,6 Hz, one of 4-H), 3.37 (1H, d, J_{4-5}=9.0 Hz, the other of 4-H), 4.15 (1H, q, J=7.0 Hz, SCH), 4.91 (1/2H, t, J_{5-4}=8.6 Hz, 5-H), 4.96 (1/2H, J_{5-4}=9.0 Hz, 5-H), 7.12—7.44 (5H, m, Ph), and 8.32 (1H, br s, CO_2H); ^{13}C NMR ($CDCl_3$) δ=17.97, 18.36 (each q, Me), 38.04 (t, 4-C), 39.84, 40.48 (each d, SCH), 77.05 (d, 5-C), 128.22, 128.41, 129.34, (each d), 132.66 (s), 160.10 (s, 3-C), 173.83, and 173.97 (each s, C=O); MS m/z (rel intensity, %) 251 (M^+, 7), 177 (28), 150 (25), 111 (base peak), 110 (55), 66 (30), 43 (30), 41 (22), 39 (29), and 32 (21), HRMS Found: m/z 251.0605. Calcd for $C_{12}H_{13}NO_3S$: M, 251.0613.

12b: Pale yellow viscous oil; IR (neat) 3000, 1730, and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.02, 1.04 (3H, each t, J=7.2 Hz, Me), 1.61—1.99 (2H, m, CH_2), 3.21—3.45 (2H, m, 4-H), 3.99 (1/2H, dd, J_{5-4}=7.0 and 10.5 Hz, 5-H), 4.98 (1/2H, dd, J_{5-4}=6.6 and 10.8 Hz, 5-H), 7.09—7.43 (5H, m, Ph), and 9.81 (1H, br s, CO_2H); ^{13}C NMR ($CDCl_3$) δ=12.00 (q, Me), 25.24, 25.65 (each t, CH_2), 37.71, 37.83, (each t, 4-C), 46.65, 47.42 (each d, SCH), 76.83, 77.01 (d, 5-C), 127.89, 128.25, 129.30, 132.07, 132.95 (each d), 133.19 (s), 159.18, 159.36 (each s, 3-C), and 174.48 (s, C=O); MS m/z (rel intensity, %) 265 (M^+, 31), 156 (34), 110 (58), 109 (39), 65 (20), and 41 (base peak). HRMS Found: m/z 265.0782. Calcd for $C_{13}H_{15}NO_3S$: M, 265.0772.

12c: Pale yellow oil; IR (neat) 3000, 1730, and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.89 (3H, t, J=7.0 Hz, Me), 1.09—1.94 (8H, m, CH_2), 3.04—3.63 (2H, m, 4-H), 3.95—4.22 (1H, m, SCH), 4.77—5.09 (1H, m, 5-H), 7.08—7.44 (5H, m, Ph), and 10.24 (1H, br s, CO_2H); ^{13}C NMR ($CDCl_3$) δ=13.94 (q, Me), 22.35, 27.00, 31.24, 31.77, 32.12 (each t, CH_2), 37.71 (t, 4-C), 44.94, 45.71 (each d, SCH), 76.83, 77.01 (each d, 5-C), 127.89, 128.25, 129.30, 132.07, 132.95 (each d), 133.24 (s, 1-C of Ph), 159.48 (s, 3-C), and 174.60 (s, C=O); MS m/z (rel intensity, %) 307 (M^+, 17), 198 (45), 135 (24), 123 (30), 110 (59), 109 (86), 91 (21), 77 (27), 65 (43), 56 (95), 52 (22), 46 (24), 42 (31), 41 (base peak), and 39 (47). HRMS Found: m/z 307.1242. Calcd for $C_{16}H_{21}NO_3S$: M, 307.1241.

Alkylation of 2-Isoxazoline-5-carboxylic Acid 11 with 7-Iodo-2-heptanone Ethylene Acetal Leading to 12d. To a solution of LDA prepared from diisopropylamine (0.355 g, 3.51 mmol) and butyllithium (15% in hexane, 2.2 ml, 3.51 mmol) in dry THF (21 ml) was added 2-isoxazoline-5-carboxylic acid **11** (0.379 g, 1.67 mmol) in dry THF (12 ml) at −78 °C under nitrogen. After 0.5 h, 7-iodo-2-heptanone ethylene acetal (0.951 g, 3.35 mmol) and HMPA (3.3 ml, 19.0 mmol) were added. The mixture was stirred at −78 °C for 48 h and poured into saturated aqueous ammonium chloride (50 ml). After acidified to pH 1 by adding diluted sulfuric acid (10%), the mixture was extracted with dichloromethane (50 ml×3). The combined dichloromethane extracts were washed with water, dried over magnesium sulfate, and evaporated in vacuo. The residue was chromatographed over silica gel with hexane–ethyl acetate–acetic acid (10:10:1 v/v) to give isoxazoline **12d** (0.202 g, 35%) and **11** (0.067 g, 17%).

12d: Pale yellow viscous oil; ^{1}H NMR ($CDCl_3$) δ=1.19—2.00 (8H, m, CH_2), 2.12 (3H, s, Me), 2.44 (2H, t, J=6.8 Hz, CH_2CO), 3.10—3.64 (2H, m, 4-H), 4.06 (1H, t, J=7.5 Hz, SCH), 4.84—5.14 (1H, m, 5-H), 7.16—7.30 (5H, m, Ph), and 8.62 (1H, s, CO_2H); MS m/z (rel intensity, %) 349 (M^+, 19), 137 (21), 123 (23), 110 (46), 109 (36), and 52 (base peak). HRMS Found: m/z 349.1321. Calcd for $C_{18}H_{23}O_4NS$: M, 349.1346.

General Procedure for the Dialkylations of 2-Isoxazoline 6b Leading to 13a—c. To a solution of diisopropylamine (0.242 g, 2.4 mmol) in dry THF (10 ml) was added butyllithium (15% in hexane, 1.5 ml, 2.4 mol) at −78 °C under nitrogen. A solution of 2-isoxazoline **6b** (0.269 g, 1 mmol) in dry THF (10 ml) was added at −78 °C. After

0.5 h, an α,ω-dibromoalkane (2 to 4 mmol) and HMPA (2 ml, 11.5 mmol) were added. The mixture was stirred at −78 °C for 2 h, poured into saturated aqueous ammonium chloride (30 ml), and extracted with dichloromethane (40 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was subjected to column chromatography over silica gel by using hexane–ethyl acetate as an eluent to give **13**. The ratios of hexane–ethyl acetate employed are as follows: **13a** and **13c**: 10:1 v/v; **13b**: 15:1 v/v. The results are summarized in Table 3.

13a: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.16—1.43, 1.45—1.69 (4H, m, CH_2CH_2), 3.06 (1H, dd, J_{4-5}=8.0 and J=17.5 Hz, one of 4-H), 3.49 (1H, dd, J_{4-5}=10.8 and J=17.5 Hz, the other of 4-H), 5.47 (1H, dd, J_{5-4}=8.0 and 10.8 Hz, 5-H), and 6.83—7.52 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=17.24, 17.63 (each t), 21.97 (s, q-C), 44.48 (t, 4-C), 82.86 (d, 5-C), 125.83, 125.98, 126.12, 127.68, 128.17, 128.76, 129.15, 129.34, 132.81 (each d), 136.18, 141.06 (each s), and 160.88 (s, 3-C); MS m/z (rel intensity, %) 295 (M^+, 89), 278 (49), 218 (47), 189 (28), 188 (72), 169 (29), 168 (64), 156 (37), 149 (22), 147 (23), 141 (27), 128 (37), 117 (24), 116 (22), 115 (60), 110 (45), 109 (base peak), 105 (39), 104 (41), 103 (29), 91 (58), 78 (31), 77 (90), 69 (23), 65 (54), 51 (50), 45 (21), 43 (39), and 39 (33). HRMS Found: m/z 295.1027. Calcd for $C_{18}H_{17}NOS$: M, 295.1030.

13b: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ=1.44—2.24 (8H, m, CH_2), 3.12 (1H, dd, J_{4-5}=8.5 and J=16.7 Hz, one of 4-H), 3.54 (1H, dd, J_{4-5}=10.8 and J=16.7 Hz, the other of 4-H), 5.51 (1H, dd, J_{5-4}=8.5 and 10.8 Hz, 5-H), and 6.94—7.38 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=23.41, 36.65, 36.88 (each t, CH_2), 43.41 (t, 4-C), 58.12 (s, q-C), 82.18 (d, 5-C), 125.77, 128.01, 128.72, 128.89, 134.60 (each d), 132.72, 141.24 (each s), and 161.25 (s, 3-C); MS m/z (rel intensity, %) 323 (M^+, 6), and 214 (base peak). HRMS Found: m/z 323.1345. Calcd for $C_{20}H_{21}NOS$: M, 323.1345.

13c: Pale yellow oil; ^{1}H NMR ($CDCl_3$) δ−1.17—2.12(10H, m, CH_2), 3.10 (1H, dd, J_{4-5}=8.5 and J=16.5 Hz, one of 4-H), 3.53 (1H, dd, J_{4-5}=11.0 and J=16.5 Hz, the other of 4-H), 5.51 (1H, dd, J_{5-4}=8.5 and 11.0 Hz, 5-H), and 7.21—7.27 (10H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=22.65, 25.47, 35.00, (each t, CH_2), 42.47 (t, 4-C), 52.53 (s, q-C), 81.77 (d, 5-C), 125.89, 128.06, 128.77, 129.18, 136.54 (each d), 130.65, 141.30 (each s), and 160.54 (s, 3-C); MS m/z (rel intensity, %) 337 (M^+, 2), 228 (78), 115 (23), 110 (22), 109 (base peak), 104 (28), 91 (36), 81 (30), 79 (28), 78 (27), 77 (57), 65 (54), 53 (21), 51 (34), 41 (33), and 39 (44). HRMS Found: m/z 337.1512. Calcd for $C_{21}H_{23}NOS$: M, 337.1491.

General Procedure for the Raney Ni Hydrogenolysis of 2-Isoxazolines 8, 10, and 13 Leading to 14. To a solution of 2-isoxazoline **8**, **10**, or **13** (0.809 mmol) in aqueous ethanol (17%, 9.8 ml) were added boric acid (0.25 g, 4.045 mmol) and Raney Ni (W-2, 0.4 ml, 0.8 ml suspension in ethanol). Air in the reaction flask was replaced with hydrogen gas by repeated (5 times) evacuation and flushing with hydrogen. The mixture was stirred under hydrogen at room temperature. Insoluble materials were removed off by filtration through Celite 545. To the filtrate was added water (100 ml) and the organic layer was extracted with dichloromethane (100 ml×3). The combined extracts were dried over magnesium sulfate and evaporated in vacuo to give **14**. Reaction times, yields of **14**, and purification methods are as follows: **14a**: 16 h, 97%, silica-gel chromatography with hexane–diethyl ether (3:2 v/v) **14b**: 13 h, 76%, silica-gel chromatography with hexane–diethyl ether (2:1 v/v); **14c**: 18.5 h, 56%, silica-gel chromatography with dichloroethane; **14d**: 14.5 h, 91%, silica-gel chromatography with hexane–diethyl ether (3:1 v/v); **14e**: 16 h, 91%, silica-gel chromatography with hexane–diethyl ether (3:1 v/v).

14a: (a 1:1 mixture of two diastereomers (by ^{13}C NMR)): Colorless viscous oil; IR (neat) 3400 and 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.95 (3H, t, J=7.0 Hz, Et), 1.27—1.68 (2H, m, Et), 2.50—3.10 (4H, m, $COCH_2$), 3.98 (2H, m, OH), 5.16 (2H, dd, J=4.0 and 9.0 Hz, CHOH), and 7.16—7.40 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=9.79 (Me), 29.52, 29.56 (Et), 49.93, 49.99, 52.11, 52.37, ($COCH_2$), 68.93, 69.16, 69.83, 69.99 (CHOH), 125.65, 127.67, 128.53, 143.02, 143.06, 211.27 (CO), and 211.44 (CO); MS m/z (rel intensity, %) 232 (M^+, 64), 149 (base peak), 107 (81), 104 (32), 83 (50), 79 (39), 77 (37), 55 (37), and 41 (25). HRMS Found: m/z 222.1255. Calcd for $C_{13}H_{18}O_3$: M, 222.1255.

14b: (a 1:1 mixture of two diastereomers (by ^{13}C NMR)): Pale yellow viscous oil; IR (neat) 3400 and 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.76—1.02 (3H, m, n-Pr), 1.12—1.70 (4H, m, n-Pr), 2.31—3.07 (4H, m, $COCH_2$), 4.00 (2H, br s, OH), 5.02—5.22 (2H, m, CHOH), and 7.12—7.40 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ=13.86 (Me), 18.48 (CH_2), 38.72 (CH_2), 50.12, 51.12, 52.06, 52.35 ($COCH_2$), 67.15, 67.33, 69.55, 69.72 (CHOH), 125.54, 127.35, 128.23, 143.21, 210.72 (CO), and 210.90 (CO); MS m/z (rel intensity, %) 236 (M^+, 16), 162 (23), 120 (64), 107 (base peak), 106 (25), 105 (85), 104 (35), 78 (45), 76 (38), 73 (20), 58 (33), 55 (34), and 42 (42). HRMS Found: m/z 236.1414. Calcd for $C_{14}H_{20}O_3$: M, 236.1411.

14c: Colorless viscous oil; IR (neat) 3440 and 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.52—3.06 (6H, m, CH_2), 3.26 (1H, br s, OH), 5.14 (1H, dd, J=5.0 and 7.5 Hz, CHOH), and 7.04—7.40 (10H, m, Ph); MS m/z (rel intensity, %) 254 (M^+, 23), 236 (53), 229 (39), 149 (20), 145 (21), 135 (23), 131 (22), 121 (44), 107 (65), 105 (80), 104 (99), 91 (base peak), 79 (56), and 77 (53). Found: C, 80.07; H, 7.12%. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13%.

14d: Pale yellow viscous oil; IR (neat) 3440 and 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.40—1.92 (8H, m, cyclopentyl), 2.65—3.03 (3H, m, $CHCOCH_2$), 3.56 (1H, br s, OH), 5.09 (1H, dd, J=5.0 and 7.0 Hz, CHOH), and 7.12—7.38 (5H, m, Ph); MS m/z (rel intensity, %) 218 (M^+, 13), 149 (33), 107 (65), 105 (23), 104 (40), 103 (22), 79 (base peak), 78 (29), 77 (98), 71 (22), 69 (69), 51 (33), 43 (25), 41 (87), and 39 (42). HRMS Found: m/z 218.1303. Calcd for $C_{14}H_{18}O_2$: M, 218.1306.

14e: Colorless viscous oil; IR (neat) 3440 and 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.04—2.00 (10H, m, cyclohexyl) 2.12—2.50 (1H, m, cyclohexyl), 2.76 (1H, dd, J=17.0 and 5.5 Hz, one of $COCH_2$), 2.92 (1H, dd, J=17.0 and 7.0 Hz, the other of $COCH_2$), 3.60 (1H, br s, OH), 5.11 (1H, dd, J=7.0 and 5.5 Hz, CHOH), and 7.18—7.40 (5H, m, Ph); MS m/z (rel intensity, %) 222 (M^+, 20), 204 (30), 120 (58), 107 (base peak), 106 (26), 105 (70), 104 (25), 79 (58), 78 (26), 77 (51), 59 (32), 58 (38), and 43 (45). HRMS Found: m/z 232.1464. Calcd for $C_{15}H_{20}O_2$: M, 232.1462.

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References

1) O. Tsuge, S. Kanemasa, and H. Suga, *Chem. Lett.*, **1986**, 183.

2) O. Tsuge, S. Kanemasa, H. Suga, and N. Nakagawa, *Bull. Chem. Soc. Jpn.*, **60**, 2463 (1987).

3) O. Tsuge, S. Kanemasa, and H. Suga, *Chem. Lett.*, **1987**, 323.

4) O. Tsuge, S. Kanemasa, N. Nakagawa, and H. Suga, *Bull. Chem. Soc. Jpn.*, **60**, 4091 (1987).

5) R. Annunziata, M. Cinquini, F. Cozzi, A. Gilardi, and A. Restelli, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 2289 and 2293.

6) T. Mukaiyama and T. Hoshino, *J. Am. Chem. Soc.*, **82**, 5339 (1960).

7) D. Ranganathan, *J. Chem. Res. (S)*, **1983**, 78.

8) The bromination-dehydrobromination route of oximes leading to nitrile oxides have been well documented (Refs. 1, 2, and references cited therein).

9) O. Tsuge, H. Watanabe, and S. Kanemasa, *Chem. Lett.*, **1984**, 1415.

10) H. Grund and V. Jäger, *Liebigs Ann. Chem.*, **1980**, 80; S. Shatzmiller, E. Shalom, R. Lidor, and E. Tartkovski, *ibid.*, **1983**, 906; W. Schwab and V. Jäger, *Angew. Chem., Int. Ed. Engl.*, **20**, 603 (1981); A. P. Kozikowski and A. K. Ghosh, *J. Org. Chem.*, **49**, 2762 (1984).

11) An arylsulfonyl-substituted methanenitrile oxide is known: P. A. Wade and J. F. Bereznak, *J. Org. Chem.*, **52**, 2973 (1987); D. Sarlo, A. Guarna, A. Brandi, and A. Goti, *Tetrahedron*, **41**, 5181 (1985); P. A. Wade and H. R. Hinney, *J. Am. Chem. Soc.*, **101**, 1319 (1979).

12) So far neither successful lithiations at the side chain of the 2-isoxazolines bearing a carbonyl-type substituent at 5-position nor smooth reactions of the resulting anions with sulfinates are known.