# Solid-Phase Combinatorial Synthesis of Polyisoxazolines: A Two-Reaction Iterative Protocol

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*Received September 10, 1996*[⊗]

Starting from a polymer-bound olefin, iterative application of nitrile oxide 1,3-dipolar cycloaddition and selenide oxidation/elimination steps were employed to deliver a polymer-bound triisoxazoline that can be liberated from the resin by transesterification. When four nitroseleno ethers (**2**−**5**) and four capping nitroalkanes (**6**−**9**) were employed, a triisoxazoline library (**V**) of 64 positional isomers was obtained by three iterative applications of these two reactions. The tactical flexibility of this strategy for preparing small polyfunctional oligomers is particularly attractive in that each subunit addition proceeds via a C−C bond-forming step.

## Introduction

The first reports of combinatorial chemistry focused on creation of peptide libraries utilizing iterative amide bond-forming protocols.[2] Thus, starting with suitably protected amino acid building blocks, large array and split-mix peptide libraries can be prepared by the iterative application of deprotection and activation/coupling steps. The resulting peptides are of utility, but their pharmaceutical applications are limited because of difficulties encountered in biodistribution[3,4] (e.g., crossing the blood−brain barrier) and *in vivo* stability (e.g., proteases in the stomach and bloodstream effectively degrade these biopolymers).[5] The combinatorial synthesis of peptoid libraries from readily available starting materials has been exploited to address these issues.[6,7] For example, the Chiron peptoid approach[6] employed iterative synthetic steps of *N*-acylation and Cα-*N*-substitution to deliver oligomers of *N*-substituted glycines.

These results, coupled with the importance of methodological developments in solid-phase[8] and combinatorial strategies,[9] the general advantages of iterative synthetic strategies,[10] the importance of C−C bond-forming reactions in organic chemistry, and our interest in small molecule library synthesis,[11] led us to explore the isoxazoline-based iterative strategy outlined in Figure 1. In addition, isoxazolines are often biological active[12] suggesting that the targeted polyisoxazolines may prove useful in addressing some of the biochemical issues mentioned above.

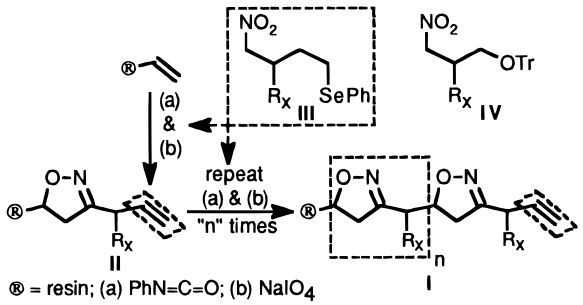


**Figure 1.** Iterative strategy for the solid-phase synthesis of polyisoxazolines.

Starting from a polymer-bound olefin, iterative application of nitrile oxide 1,3-dipolar cycloaddition[13] and selenide oxidation/elimination[14] steps were envisioned to deliver polymer-bound polyisoxazoline **I**. This strategy could be adopted to library preparations by one of three methods: (i) polyisoxazoline libraries with the same repeating unit but variable length (variable "*n*" in **I**) could be prepared, (ii) polyisoxazoline libraries of fixed length (fixed "*n*" in **I**) but incorporating variable "subunits" (i.e., prepared from various nitroseleno ethers of general structure **III**) could be prepared, and (iii) polyisoxazoline libraries of variable length and composed of variable

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1996.

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S0022-3263(96)01730-6 CCC: $12.00 

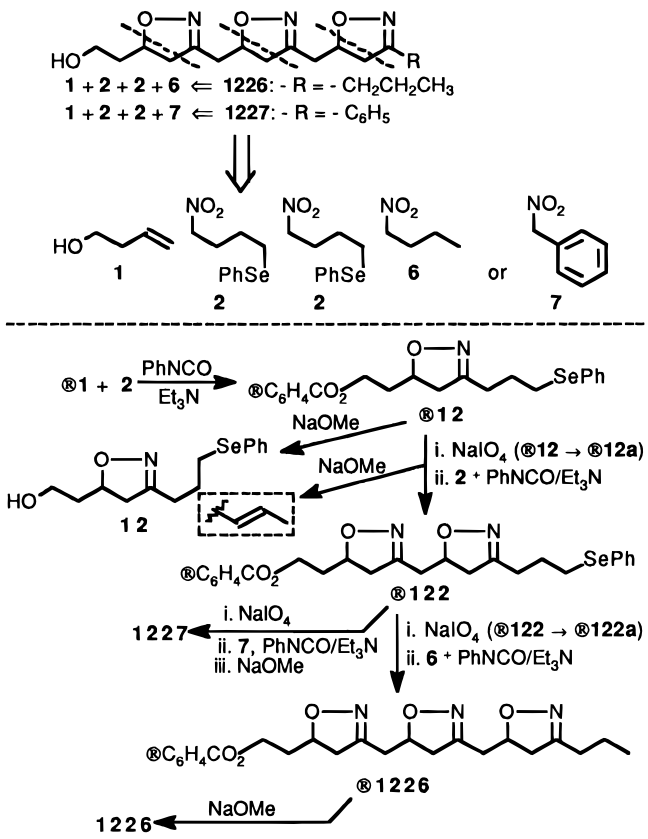
"subunits" could be prepared. In addition to this tactical flexibility, the strategy outlined in Figure 1 is appealing in that each subunit addition proceeds via a C−C-bond-forming step. Here, we report iterative application of the two-step process outlined in Figure 1 to prepare a small library of fixed length (three isoxazoline units) composed of variable subunits (four nitroseleno ethers plus four "capping" nitroalkanes).

## Results and Discussion

Our initial plan was to employ nitrotrityl ether **IV** as the generic precursor to each isoxazoline subunit. The idea was that 1,3-dipolar cycloaddition followed by trityl deprotection, $-CH_2OH \rightarrow -CHO$ oxidation, and Wittig methenylation would deliver homologated resin **II**. Moreover, condensation of the aldehyde intermediate with $(MeO)_2P(O)CHN_2$ would deliver the alkyne analog of **II**[15] and set the stage for isoxazole formation in the second iteration. However, since this approach requires four steps per iteration versus the two steps required using nitroseleno ether **III**, the former was abandoned.[16]

To validate the nitroseleno ether iterative strategy outlined in Figure 1, we set out to prepare triisoxazolines **1226** and **1227** (Scheme 1).[17] Our starting resin, polymer-bound 3-butenyl benzoate [®**1**; ® = resin (styrene/2% divinylbenzene copolymer)], was prepared from polystyrene/2%-divinylbenzene copolymer by lithiation/$CO_2$ quench,[18] $-CO_2H \rightarrow -COCl$ activation,[19] and esterification with 3-buten-1-ol in pyridine. Dehydrative 1,3-dipolar cycloaddition of 1-nitro-4-(phenylseleno)butane (**2**) with resin ®**1** was accomplished by treatment of the benzene swollen resin with phenyl isocyanate (4 equiv), triethylamine, and **2** (2 equiv) at reflux for 4 d under nitrogen. Subsequent transesterification of resin ®**12** with sodium methoxide (THF:MeOH4:1)[20] delivered isoxazoline **12** [44% yield and ≈95% crude purity (see Figure 3) from $®CO_2H$; yield based on a titrated $®CO_2H$ loading of 2.1 mequiv/g], establishing that the crucial C−C bond-forming 1,3-dipolar cycloaddition step was successful. Sodium periodate selenide to selenoxide oxidation with concomitant elimination regenerated the requisite olefin functional group. The success of this transformation was again established by NaOMe transesterification, but the product obtained proved to be the conjugated olefin (a consequence of olefin isomerization during the transesterification step as no isoxazoline products arising from the conjugated olefin were observed in subsequent iterations). Having thus established the efficacy of both the 1,3-dipolar cycloaddition step and the olefin regeneration

**Scheme 1**[a]




[a] Note: see ref 17 for a comment regarding compound numbering.

step, we applied a second iteration converting ®**12** to diisoxazoline ®**122** (again employing nitroseleno ether **2**) and a third iteration converting ®**122** to triisoxazoline ®**1226** [using nitrobutane (**6**) as a "capping" unit]. Both steps of solid-phase iterations two (®**12** → ®**122**) and three (®**122** → ®**1226**) were effected at room temperature (instead of reflux for the 1,3-dipolar cycloaddition steps as optimized in corresponding solution-phase reactions) and validated by sodium methoxide transesterification of ®**1226**, yielding the targeted "trimer" **1226**. This fully characterized triisoxazoline was obtained in 18% overall yield and ≈95% purity (see the supporting information) from $®C_6H_4CO_2H$; an average yield of 81% per step for this eight step solid-phase synthesis. In a similar fashion, "trimer" **1227** was obtained from ®**1** by two iterations with nitroseleno ether **2** and a capping iteration with nitroalkane **7** (overall yield of 17%; 80% per step).

With these results in hand, attention was turned to the construction of a library of triisoxazolines of generalized structure **V**. By employing four different nitroseleno ethers (**2**−**5**) in iterations one and two plus four different capping nitroalkanes (**6**−**9**) in iteration three, a library of 64 (4 × 4 × 4) positionally isomeric triisoxazolines would be obtained. We anticipated using mass spectrometry to verify that each[21] targeted triisoxazoline was in fact obtained in this split-mix[22] protocol. However, since numerous of these analogs would have the same

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(16) A polyisoxazole version of this approach is currently under investigation and will be reported in due course.

(17) Note: a systematic numbering system is employed where the product number is derived from the compound numbers of its component precursors. Thus, refering to Scheme 1, combinatorial components **1**, **2**, **2**, and **6** are employed to construct triisoxazoline **1226** (®**1226** when polymer-bound) by the sequence **1** → ®**1** + **2** → ®**12** + **2** → ®**122** + **6** → ®**1226** → **1226**. Solution libraries (see Table 1) are lettered A−U; when polymer-bound, these same libraries are referred to as ®A−®U. Finally, oxidative elimination of selenium from ®**12** gives olefin ®**12a**; likewise, oxidative elimination of selenium from library ®A gives library ®Aa. The symbol ® denotes the resin (styrene/2% divinyl benzene copolymer).

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(21) In a large library, it is quite probable that not all of the targets would be present [see: (a) Lowe, G. *Chem. Soc. Rev.* **1995**, *24*, 309−317. (b) Zhao, P.-L.; Zambias, R.; Bolognese, J. A.; Boulton, D.; Chapman, K. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 10212−6]. We have used mass spectrometry to verify that each targeted positional isomer is present in our library.

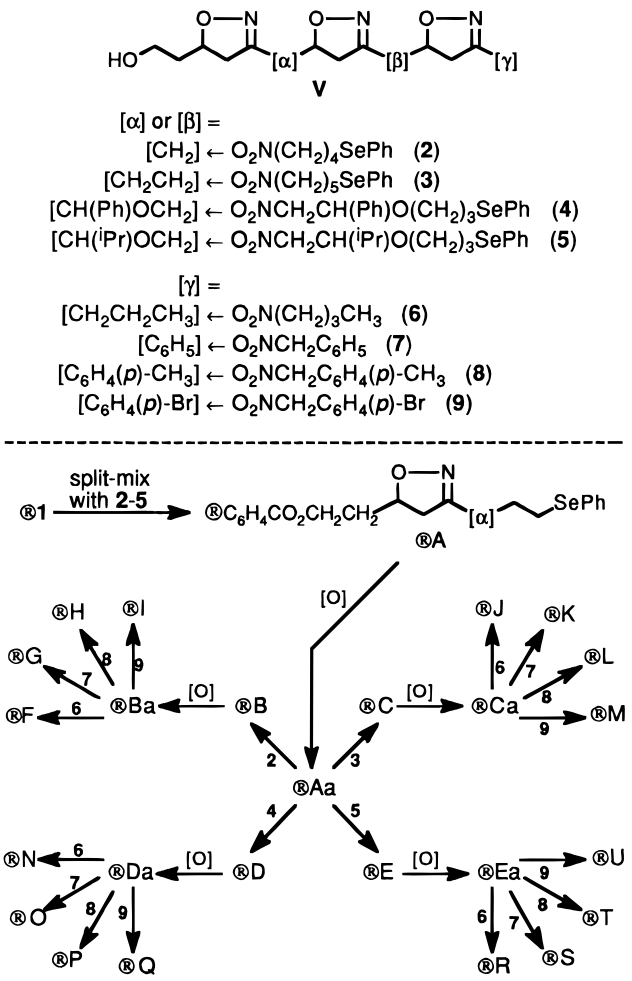


**Figure 2.** Combinatorial targets, precursors, and modified split-mix protocol.

molecular formula, we adapted the modified split-mix procedure outlined in Figure 2. Treating resin ®**1** with each of the four nitroseleno ethers **2**−**5** in separate flasks followed by admixture gave the four-component resin mixture ®A ([α] is defined in Figure 2; ®A = ®**12** + ®**13** + ®**14** + ®**15**). Phenylseleno ether to olefin conversion (®A → ®Aa) followed by performing iteration two in four flasks, again using nitroseleno ethers **2**−**5**, delivered four unique positionally isomeric mixtures designated ®B, ®C, ®D, and ®E. Submitting each of these mixtures to oxidative elimination and iteration three (required four flasks for each diisoxazoline mixture ®Ba−®Ea, one for each "capping" subunit **6**−**9**) produced a total of 16 unique positionally isomeric mixtures; for example, ®B → ®Ba and subsequent reaction with $O_2N(CH_2)_3CH_3$ (**6**) gives ®F, with $O_2NCH_2C_6H_5$ (**7**) gives ®G, with $O_2NCH_2C_6H_4(p)$-$CH_3$ (**8**) gives ®H, and with $O_2NCH_2C_6H_4$-(*p*)-Br (**9**) gives ®I.

The combinatorial players required for this modified split-mix procedure were all readily available. Nitroseleno ethers **2** and **3** were prepared from bromochlorobutane and bromochloropentane, respectively, by sequential treatment with sodium nitrite[23] (−Br → $-NO_2$), sodium iodide (−Cl → −I), and diphenyl diselenide/sodium boro-

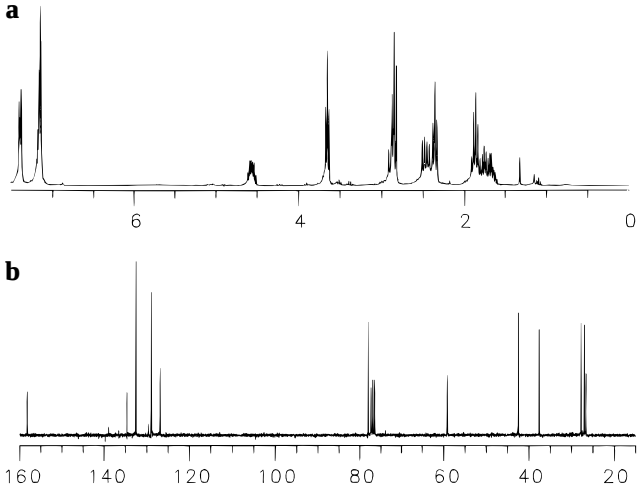


**Figure 3.** (a) $^1$H-NMR spectrum of **12.** (b) $^{13}$C-NMR spectrum of **12**.

hydride[24] (−I → −SePh). Nitroseleno ethers **4** and **5** were prepared by Michael addition of the potassium alkoxide of $HO(CH_2)_3SePh$ [in turn prepared from $HO(CH_2)_3Br$ + $(PhSe)_2/NaBH_4$] to $O_2NCH{=}CHC_6H_5$ and $O_2NCH{=}CHCH$-$(CH_3)_2$, respectively. Nitrobutane (**6**) is commercially available, and nitroalkanes **7**−**9** were prepared by treatment of the appropriate benzyl bromide with sodium nitrite.[25]

Several observations regarding this combinatorial synthesis are pertinent. For example, both the $-CH{=}CH_2$ → isoxazoline and $-CH_2CH_2SePh$ → $-CH{=}CH_2$ transformations are reliable solid-phase reactions. Figure 3 shows the crude $^1$H- and $^{13}$C-NMR spectra for **12**, the product obtained by sequential treatment of resin ®**1** with nitroseleno ether **2** + PhNCO/$Et_3N$ and sodium methoxide. These spectra, as well as the $^1$H- and $^{13}$C-NMR spectra obtained from **13** (®**1** + **3**), **14** (®**1** + **4**), and **15** (®**1** + **5**), show essentially pure monoisoxazoline product.

We find that both solution- and solid-phase 1,3-dipolar cycloaddition reactions deliver mixtures of diastereomers in iterations two and three. While this can present reaction management problems in solution, these issues are minimized in our solid-phase protocol where product diastereomers are as easily manipulated as are subunit positional isomers.

Mass spectrometry has proven to be an ideal tool for verifying the split-mix ensemble of products formed by this iterative strategy (see Table 1). Using the modified split-mix protocol outlined in Figure 2, 21 four-component libraries were obtained where library A is a monoisoxazoline mixture, libraries B−E are diisoxazoline mixtures, and libraries F−U are triisoxazoline mixtures. All of these libraries were analyzed by low-resolution $FAB^+$ mass spectrometry to verify that each targeted isoxazoline derivative was indeed present in the relevant library (our modified split-mix protocol ensured that no library contained positional isomers with identical formulas). For example, library D contains four phenylseleno-containing diisoxazolines (**124**, **134**, **144**, and **154**), and unit mass $FAB^+$ data provides clear evidence that each anticipated

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**Table 1. FAB$^+$ Mass Spectrometry Data for Combinatorial Products**

| compd | [MH]$^+$ | [MNa]$^+$ | library | compd | [MH]$^+$ | [MNa]$^+$ | library |
|---|---|---|---|---|---|---|---|
| **12** | 314 | 336 | A | **1437** | 478 | 500 | K |
| **13** | 328 | 350 | A | **1537** | 444 | 466 | K |
| **14** | 420 | 442 | A | **1238** | 386 | 408 | L |
| **15** | 386 | 408 | A | **1338** | 400 | 422 | L |
| **122** | 397 | 419 | B | **1438** | 492 | 514 | L |
| **132** | 411 | 433 | B | **1538** | 458 | 480 | L |
| **142** | 503 | 525 | B | **1239** | 450/452 | 472/474 | M |
| **152** | 469 | 491 | B | **1339** | 464/466 | 486/488 | M |
| **123** | 411 | 433 | C | **1439** | 556/558 | 578/580 | M |
| **133** | 425 | 447 | C | **1539** | 522/524 | 544/546 | M |
| **143** | 517 | 539 | C | **1246** | 430 | 452 | N |
| **153** | 483 | 505 | C | **1346** | 444 | 466 | N |
| **124** | 503 | 525 | D | **1446** | 536 | 558 | N |
| **134** | 517 | 539 | D | **1546** | 502 | 524 | N |
| **144** | 609 | 631 | D | **1247** | 464 | 486 | O |
| **154** | 575 | 597 | D | **1347** | 478 | 500 | O |
| **125** | 469 | 491 | E | **1447** | 570 | 592 | O |
| **135** | 483 | 505 | E | **1547** | 536 | 558 | O |
| **145** | 575 | 597 | E | **1248** | 478 | 500 | P |
| **155** | 541 | 563 | E | **1348** | 492 | 514 | P |
| **1226** | 324 | 346 | F | **1448** | 584 | 606 | P |
| **1326** | 338 | 360 | F | **1548** | 550 | 572 | P |
| **1426** | 430 | 452 | F | **1249** | 542/544 | 564/566 | Q |
| **1526** | 396 | 418 | F | **1349** | 556/558 | 578/580 | Q |
| **1227** | 358 | 380 | G | **1449** | 648/650 | 670/672 | Q |
| **1327** | 372 | na | G | **1549** | 614/616 | 636/638 | Q |
| **1427** | 464 | 486 | G | **1256** | 396 | 418 | R |
| **1527** | 430 | 452 | G | **1356** | 410 | na | R |
| **1228** | 372 | 394 | H | **1456** | 502 | 524 | R |
| **1328** | 386 | 408 | H | **1556** | 468 | 490 | R |
| **1428** | 478 | 500 | H | **1257** | 430 | 452 | S |
| **1528** | 444 | 466 | H | **1357** | 444 | na | S |
| **1229** | 436/438 | 458/460 | I | **1457** | 536 | 558 | S |
| **1329** | 450/452 | 472/474 | I | **1557** | 502 | 524 | S |
| **1429** | 542/544 | 564/566 | I | **1258** | 444 | 466 | T |
| **1529** | 508/510 | 530/532 | I | **1358** | 458 | 480 | T |
| **1236** | 338 | 360 | J | **1458** | 550 | 572 | T |
| **1336** | 352 | 374 | J | **1558** | 516 | 538 | T |
| **1436** | 444 | 466 | J | **1259** | 508/510 | 530/532 | U |
| **1536** | 410 | 432 | J | **1359** | 522/524 | na | U |
| **1237** | 372 | 394 | K | **1459** | 614/616 | na | U |
| **1337** | 386 | 408 | K | **1559** | 580/582 | 602/604 | U |

positional isomer is present in the mixture; selenium isotope fingerprints for both the [MH]$^+$ and the [MNa]$^+$ molecular ions in libraries B−E are particularly unequivocal. Likewise, library M contains four bromine-containing triisoxazolines (**1239**, **1339**, **1439**, and **1539**), and again, unit mass FAB$^+$ data provide definitive evidence that each anticipated positional isomer is present in the mixture. Exact mass FAB$^+$ analysis of these mixtures also proved useful. For example, HRMS FAB$^+$ data for library N gave ([triisoxazoline·H]$^+$/calculated g/mol/observed g/mol) **1246**/430.2342/430.2355, **1346**/444.2498/444.2510, **1446**/536.2761/536.2778, and **1546**/502.2917/502.2933. Electrospray mass analysis was also investigated and corroborated the FAB$^+$ data presented in Table 1.

## Summary

A tactically flexible strategy for the preparation of oligomeric isoxazolines has been reported. In addition to the subunit versatility of this approach to combinatorial synthesis, the method benefits from the fact that each subunit addition proceeds via a C−C-bond forming step. A "traceless attachment"[26] and isoxazole variants of this strategy will be reported in due course.

(26) See, for example: Plunkett, M. J.; Ellman, J. A. *J. Org. Chem.* **1995**, *60*, 6006−7.

## Experimental Section

**General Procedures.** Polystyrene/2%-divinylbenzene (200−400 mesh) was purchased from Acros Organics and used directly. Solvents were purified as follows: dimethyl sulfoxide (DMSO) and ethanol were dried over 4 Å molecular sieves; pyridine was distilled from sodium; benzene was distilled from potassium; tetrahydrofuran (THF) was distilled from sodium/benzophenone. All reactions were conducted under an inert atmosphere. Infrared spectra were determined on a Galaxy 3000 Series Mattson FTIR. $^1$H and $^{13}$C NMR spectra were measured in $CDCl_3$ at 300 and 75 MHz, respectively, and chemical shifts are reported in ppm downfield from internal tetramethylsilane. Mass spectra were obtained with a Fisons/VG ZAB-VSE double focus sector instrument with BE geometry [fast-atom bombardment (FAB); sample dissolved in $CH_2Cl_2$ or MeOH; probe tip contained NBA/Na matrix; ionization by Cs+ and accelerated to 8000 eV]. Elemental analyses were performed at the MidWest Microlab, Indianapolis, IN.

**1-Nitro-4-(phenylseleno)butane (2).** To a solution of $NaNO_2$ (6.90 g, 100.0 mmol) in DMSO (120 mL) was added 1-bromo-4-chlorobutane (8.57 g, 50.0 mmol), and the reaction was stirred at room temperature for 3 h. Water (50 mL) was added, and the resulting mixture was extracted with ether (3 × 100 mL). The combined extracts were washed with brine, dried ($Na_2SO_4$), and evaporated under atmospheric pressure at 50 °C to give 6.58 g (96%) of crude 1-chloro-4-nitrobutane as a pale yellow oil: $^1$H NMR $\delta$ 1.84−1.95 (m, 2 H), 2.15−2.24 (m, 2 H), 3.59 (t, 2 H, $J$ = 6 Hz), 4.44 (t, 2 H, $J$ = 6 Hz).

To a solution of crude 1-chloro-4-nitrobutane (6.58 g, 48 mmol) in acetone (250 mL) was added NaI (10.8 g, 71.8 mmol), and the solution was refluxed overnight. The reaction was quenched by the addition of aqueous $NaHSO_3$ (50 mL), and the resulting solution was extracted with ether (3 × 100 mL). The combined extracts were washed with brine, dried ($Na_2SO_4$), and evaporated under atmospheric pressure at 50 °C to give 4.37 g (40%) of crude 1-iodo-4-nitrobutane as a brown oil: $^1$H NMR $\delta$ 1.92 (quintet, 2 H, $J$ = 6 Hz), 2.15 (quintet, 2 H, $J$ = 6 Hz), 3.22 (t, 2 H, $J$ = 6 Hz), 4.42 (t, 2 H, $J$ = 6 Hz).

To a solution of diphenyl diselenide (3.57 g, 11 mmol) in absolute EtOH (120 mL) was added $NaBH_4$ (0.87 g, 22 mmol), and the reaction mixture was stirred at room temperature for 0.5 h. A solution of crude 1-iodo-4-nitrobutane (4.37 g, 19 mmol) in absolute EtOH (25 mL) was added to the reaction and stirring continued for 2 h at room temperature. After concentration of the solution *in vacuo*, water (100 mL) was added, and the solution was extracted with ether (3 × 100 mL). The combined extracts were washed with brine, dried ($Na_2SO_4$), and evaporated *in vacuo*. The residue was purified by silica gel chromatography (1:99 → 2:98 → 4:96 ethyl acetate/hexane) to give **2** (3.23 g, 25% from 1-bromo-4-chlorobutane) as a colorless oil: FTIR (neat) 1556 ($NO_2$), 1383 ($NO_2$) cm$^{-1}$; $^1$H NMR $\delta$ 1.74 (quintet, 2 H, $J$ = 6 Hz), 2.10 (quintet, 2 H, $J$ = 6 Hz), 2.90 (t, 2 H, $J$ = 6 Hz), 4.33 (t, 2 H, $J$ = 6 Hz), 7.22−7.29 (m, 3 H), 7.44−7.49 (m, 2 H); $^{13}$C NMR $\delta$ 26.54, 26.96, 27.02, 74.81, 127.01, 129.04, 129.44, 132.72. Anal. Calcd for $C_{10}H_{13}NO_2Se$: C, 46.52; H, 5.08; N, 5.43. Found: C, 46.53; H, 5.14; N, 5.39.

**5-Nitro-1-(phenylseleno)butane (3).** Following the procedure described for the synthesis of **2**, 1-bromo-5-chloropentane was converted to **3** (50% from 1-bromo-5-chloropentane) as a colorless oil: FTIR (neat) 1550 ($NO_2$), 1383 ($NO_2$) cm$^{-1}$; $^1$H NMR $\delta$ 1.47−1.55 (m, 2 H), 1.73 (quintet, 2 H, $J$ = 6 Hz), 1.99 (quintet, 2 H, $J$ = 6 Hz), 2.89 (t, 2 H, $J$ = 6 Hz), 4.34 (t, 2 H, $J$ = 6 Hz), 7.23−7.29 (m, 3 H), 7.46−7.49 (m, 2 H); $^{13}$C NMR $\delta$ 26.25, 26.76, 27.18, 29.29, 75.35, 126.89, 129.04, 129.96, 132.66. Anal. Calcd for $C_{11}H_{15}NO_2Se$: C, 48.54; H, 5.55; N, 5.15. Found: C, 48.61; H, 5.64; N, 5.13.

**2-Phenyl-2-[[3-(phenylseleno)propyl]oxy]nitroethane (4).** To a solution of diphenyl diselenide (26.95 g, 86 mmol) in absolute EtOH (900 mL) was slowly added $NaBH_4$ (6.53 g, 173 mmol) and the solution stirred at room temperature for 0.5 h. 3-Bromoethanol (20.0 g, 144 mmol) was added with stirring for 3 h at room temperature. After concentration *in vacuo*, water (200 mL) was added and the mixture extracted with ether (3 × 200 mL). The combined extracts were washed

with brine, dried ($Na_2SO_4$), and evaporated *in vacuo* to give crude 3-(phenylseleno)propanol quantitatively (35.92 g) as an orange oil: IR (neat) 3351 (br), 1579, 1478, 1437, 1247, 1065, 1022 $cm^{-1}$; $^1H$ NMR $\delta$ 1.85 (quintet, 2 H, $J = 7$ Hz), 2.45 (t, 1 H $J = 7$ Hz), 2.96 (t, 2 H, $J = 7$ Hz), 3.67 (q, 2 H, $J = 7$ Hz), 7.22 (m, 3 H), 7.49 (m, 2 H)]; $^{13}C$ NMR $\delta$ 23.95, 32.48, 61.79, 126.66, 128.90, 129.91, 132.33.

Potassium hydride (10.66 g, 93.0 mmol, 35 wt % KH in mineral oil) was washed with hexane (6 × 10 mL), dried in a stream of $N_2$, and suspended in dry THF (50 mL). A solution of crude 3-(phenylseleno)propanol (17.11 g, 79 mmol) in THF (50 mL) was added dropwise at room temperature. The mixture was cooled to −40 °C, and a solution of *trans-β*-nitrostyrene (6.22 g, 41.7 mmol) in THF (50 mL) was added dropwise over 15 min and stirred for an additional 0.5 h. The reaction was quenched by the addition of 1 M acetic acid (120 mL) followed by water (150 mL), the mixture separated, and the aqueous extracted with ether (3 × 200 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried ($Na_2SO_4$), and evaporated *in vacuo*. The residue was purified by silica gel chromatography (2: 98 ethyl acetate/hexane) to give **4** (5.80 g, 38% from *trans-β*-nitrostyrene) as a pale yellow oil: FTIR (neat) 1554 ($NO_2$), 1379 ($NO_2$) $cm^{-1}$; $^1H$ NMR $\delta$ 1.89 (quintet, 2 H, $J = 6$ Hz), 2.91 (t, 2 H, $J = 6$ Hz), 3.40 (dt, 1 H, $J = 6$, 12 Hz), 3.47 (dt, 1 H, $J = 6$, 12 Hz), 4.36 (dd, 1 H, $J = 3$, 12 Hz), 4.58 (dd, 1 H, $J = 9$, 12 Hz), 5.02 (dd, 1 H, $J = 3$, 9 Hz), 7.19−7.26 (m, 3 H), 7.30−7.46 (m, 7 H); $^{13}C$ NMR $\delta$ 24.02, 29.97, 68.43, 78.50, 80.29, 126.67, 126.70, 128.98, 129.01, 129.98, 132.40, 132.47, 136.30. Anal. Calcd for $C_{17}H_{19}NO_3Se$: C, 56.05; H, 5.26; N, 3.84. Found: C, 56.18; H, 5.28; N, 3.94.

**3-Methyl-2[[3-(phenylseleno)propyl]oxy]nitrobutane (5).** Nitromethane (48.8 g, 0.80 mol) and isobutyl aldehyde (28.8 g, 0.40 mol) were stirred together in a room temperature water bath. Potassium hydroxide in MeOH (1.5 mL, 3 M) was added dropwise, and the reaction was stirred for 30 min and quenched by the addition of concd $H_2SO_4$ (20 drops, to pH = 1). The layers were separated, and the organic was washed with saturated aqueous $NaHCO_3$ and brine, dried ($Na_2SO_4$), and concentrated *in vacuo* to give 1-nitro-3-methyl-2-butanol (44.0 g, 83%) as a pale yellow liquid: $^1H$ NMR $\delta$ 0.97 (d, 3 H, $J = 7$ Hz), 0.99 (d, 3 H, $J = 7$ Hz), 1.79 (octet, 1 H, $J = 7$ Hz), 2.92 (d, 2 H, $J = 6$ Hz), 4.07−4.13 (m, 1 H), 4.33−4.51 (m, 2 H); $^{13}C$ NMR $\delta$ 17.20, 18.12, 31.62, 73.30, 79.24.

1-Nitro-3-methyl-2-butanol (38.2 g, 0.29 mol) and acetic anhydride (43.97 g, 0.431 mol) were refluxed together for 5 h before quenching with aqueous $NaHCO_3$. The resulting mixture was heated for 1 h at 80 °C while $NaHCO_3$ powder was added. The layers were separated, and the aqueous was extracted with ether (3 × 75 mL). The combined organics were dried ($Na_2SO_4$) and concentrated *in vacuo* to give a light brown oil (32.76 g, 99%). The 1-nitro-3-methyl-1-butene oil was distilled to a yellow oil prior to use: $^1H$ NMR $\delta$ 1.13(s, 6 H), 1.16 (s, 6 H), 2.56−2.64 (m, 1 H), 6.95 (dd, 1 H, $J = 1$, 13 Hz), 7.25 (dd, 1 H, $J = 7$, 13 Hz); $^{13}C$ NMR $\delta$ 20.79, 28.17, 137.96, 148.33.

Following the procedure described for the synthesis of **4**, 3-methyl-1-nitro-1-butene was converted to **5**, purifying by silica gel chromatography (5:95 EtOAc/Hex) to give **5** as a colorless oil (72% from 3-methyl-1-nitro-1-butene): FTIR (neat) 1558 ($NO_2$), 1385 ($NO_2$) $cm^{-1}$; $^1H$ NMR $\delta$ 0.91 (d, 3 H, $J = 6$ Hz), 0.93 (d, $J = 6$ Hz, 3 H), 1.83−1.97 (m, 3 H), 1.92 (t, 2 H, $J = 6$ Hz), 3.51 (dt, 1 H, $J = 6$, 9 Hz), 3.61 (dt, 1 H, $J = 6$, 9 Hz), 3.82 (dt, 1 H, $J = 3$, 6 Hz), 4.34−4.43 (m, 2 H), 7.20−7.27 (m, 3 H), 7.44−7.48 (m, 2 H); $^{13}C$ NMR $\delta$ 17.62, 17.86, 24.13, 30.06, 30.33, 70.01, 77.00, 81.49, 126.70, 128.98, 130.06, 132.45. Anal. Calcd for $C_{14}H_{21}NO_3Se$: C, 50.91; H, 6.41; N, 4.24. Found: C, 50.86; H, 6.38; N, 4.17.

**Polymer-Bound Benzoic Acid.** With adaptation of the Fyles and Leznoff procedure,[18] polystyrene/2% divinylbenzene (20.0 g) was swollen in cyclohexane (200 mL) with stirring at room temperature for 0.5 h and treated sequentially with *n*-butyllithium (150 mL, 0.24 mol, 1.6 M in *n*-hexane) and TMEDA (30.8 g, 0.265 mol). The mixture was heated to 65 °C for 15 h and cooled to room temperature, the polymer allowed to settle, and the supernatant was removed via canula. The polymer was rinsed with anhydrous THF (2 × 50 mL), additional THF (200 mL) was added, and $CO_2$ was bubbled into the mixture for 5 h at room temperature. The reaction mixture was filtered, washed sequentially with THF (2 × 50 mL), water (4 × 50 mL), and EtOH (1 × 50 mL), and suspended in 20% HCl in THF (200 mL). The mixture was stirred at room temperature for 0.5 h and filtered and the polymer washed with THF/water (1:1, 2 × 50 mL), water (6 × 50 mL), EtOH (4 × 50 mL), and $Et_2O$ (4 × 50 mL). Drying under vacuum overnight gave polymer-bound benzoic acid as a light brown solid. The average acid content of the polymer was found to be 2.1 mmol $H^+$/g-polymer by acid−base titration [the resin (0.2 g) was swollen in THF/water (1/1) with excess standard aqueous NaOH and back-titrated with standard aqueous HCl]: FTIR (KBr) 1687 (shoulder at 1727) (C═O), 2500−3600 (OH) $cm^{-1}$. Anal. Calcd for $[(C_9H_8O_2{\cdot}H_2O)_{0.20} + (C_8H_8)_{0.80}]$: C, 84.50; H, 7.26. Found: C, 84.75; H, 7.07.

**Polymer-Bound Benzoyl Chloride.**[19] To a solution of polymer-bound benzoic acid (5.00 g) in $SOCl_2$ (75 mL, 1.03 mol) was added 10 drops of DMF, and the resulting mixture was refluxed for 2 h. The reaction mixture was filtered and the polymer washed (3 × 25 mL each) with $CHCl_3$, THF, and $Et_2O$ and dried under vacuum overnight to give polymer-bound benzoyl chloride as a pale yellow solid: FTIR (KBr) 1755 (C═O) $cm^{-1}$.

**Polymer-Bound 3-Butenyl Benzoate (®1).** Polymer-bound benzoyl chloride (4.98 g) was swollen in pyridine (100 mL) with stirring at room temperature for 3.5 h and treated with 3-buten-1-ol (**1**; 1.39 g, 19.2 mmol). Stirring was continued at room temperature for 7 d. The mixture was filtered, and the polymer was washed with THF (2 × 20 mL), THF/water (1:1; 2 × 20 mL), THF (3 × 20 mL), water (2 × 20 mL), THF (4 × 20 mL), and $Et_2O$ (3 × 20 mL) and dried under vacuum overnight to give ®**1** as a yellowish brown solid: FTIR (KBr) 1724 (C═O) $cm^{-1}$. Anal. Calcd for $[(C_{13}H_{14}O_2)_{0.20} + (C_8H_8)_{0.80}]$: C, 87.34; H, 7.49. Found: C, 87.75; H, 7.48.

**Polymer-Bound 2-[4,5-Dihydro-3-[3-(phenylseleno)-propyl]-5-isoxazolyl]ethyl Benzoate (®12).** Resin ®**1** (1.00 g) was swollen in benzene (15 mL) with stirring for 0.5 h. Sequential addition of **2** (997 mg, 3.86 mmol; in 5 mL of benzene), phenyl isocyanate (920 mg, 7.72 mmol), and triethylamine (10 drops) gave a mixture that was refluxed for 4 d. Upon cooling to room temperature, water (2 mL) was added and stirring continued for 1 h. The resulting mixture was filtered and the polymer washed (3 × 5 mL each) with THF, THF/water (1:1), THF, $CH_2Cl_2$, THF, and $Et_2O$. Drying under vacuum overnight gave ®**12** as a brown solid: FTIR (KBr) 1715 (C═O) $cm^{-1}$. Anal. Calcd for $[(C_{23}H_{25}NO_3Se)_{0.20} + (C_8H_8)_{0.80}]$: C, 76.90; H, 6.69; N, 1.63. Found: C, 78.03; H, 6.74; N, 1.80.

**Polymer-Bound 2-[4,5-Dihydro-3-(2-propenyl)-5-isoxazolyl]ethyl Benzoate (®12a).** Resin ®**12** (320 mg) was swollen in THF (6 mL) with stirring at room temperature for 1.5 h and treated with $NaIO_4$ (396 mg, 1.85 mmol) in a mixture of water/MeOH (2 mL/2 mL). After being refluxed for 15 h, the reaction mixture was filtered and the polymer was washed (3 × 5 mL each) with THF, THF/water (1/1), saturated aqueous $NaHCO_3$, water, THF/water (1/1), THF, $CH_2Cl_2$, THF, and $Et_2O$. Drying under vacuum overnight gave resin ®**12a** as a pale brown solid: FTIR (KBr) 1717 (C═O) $cm^{-1}$.

**Polymer-Bound 2-[4,5-Dihydro-3-[[4,5-dihydro-3-[3-(phenylseleno)propyl]-5-isoxazolyl]methyl]-5-isoxazolyl]-ethyl Benzoate (®122).** Resin ®**12a** (559 mg) was swollen in benzene (10 mL) with stirring at room temperature for 0.5 h. Sequential addition of **2** (836 mg, 3.24 mmol; in 5 mL benzene), phenyl isocyanate (771 mg, 6.47 mmol), and triethylamine (10 drops) gave a mixture that was stirred at room temperature for 4 d. The reaction mixture was quenched with water (1 mL), allowed to stir for 1 h, and filtered. The polymer was washed (3 × 3 mL each) with THF, THF/water (1:1), THF, $CH_2Cl_2$, THF, and $Et_2O$ and dried under vacuum overnight to give ®**122** as a yellowish brown solid: FTIR (KBr) 1717 (C═O) $cm^{-1}$. Anal. Calcd for $[(C_{27}H_{30}N_2O_4Se)_{0.20} + (C_8H_8)_{0.80}]$: C, 75.22; H, 6.63; N, 2.97. Found: C, 75.71; H, 6.75; N, 2.93.

**Polymer-Bound 2-[4,5-Dihydro-3-[[4,5-dihydro-3-(2-propenyl)-5-isoxazolyl]methyl]-5-isoxazolyl]ethyl Ben-**

**zoate (®122a)**. Following the procedure described for the preparation of ®**12a**, ®**122** (600 mg) gave ®**122a** as a pale yellow solid: FTIR (KBr) 1717 (C═O) $cm^{-1}$.

**Polymer-Bound 2-[4,5-Dihydro-3-[[4,5-dihydro-3-[(4,5-dihydro-3-propyl-5-isoxazolyl]methyl]-5-isoxazolyl]methyl)-5-isoxazolyl]ethyl Benzoate (®1226).** Following the procedure described for the preparation of ®**12**, ®**122a** (100 mg) and nitrobutane (60 mg, 0.58 mmol) gave ®**1226** as a pale yellow solid: FTIR (KBr) 1718 (C═O) $cm^{-1}$. Anal. Calcd for $[(C_{25}H_{31}N_3O_5Se{\cdot}H_2O)_{0.20} + (C_8H_8)_{0.80}]$: C, 77.08; H, 7.38; N, 4.73. Found: C, 77.26; H, 7.27; N, 4.27.

**4,5-Dihydro-3-[[4,5-dihydro-3-[(4,5-dihydro-3-propyl-5-isoxazolyl)methyl]-5-isoxazolyl]methyl]-5-(2-hydroxyethyl)isoxazole (1226)**. Resin ®**1226** (86 mg) was swollen in a mixture of THF/MeOH (2 mL:0.5 mL) with stirring at room temperature for 0.5 h. Sodium methoxide (72 mg, 25 wt % in MeOH, 0.33 mmol) was added, and the mixture was stirred at room temperature for 2 h. Saturated aqueous $NH_4Cl$ (1 mL) was added and stirring continued for 1 h. The resulting mixture was filtered, and the polymer was washed (3 × 2 mL each) with $CH_2Cl_2$, water, and $CH_2Cl_2$. The filtrate was separated into two layers, and the aqueous layer was extracted with $CH_2Cl_2$ (2 × 5 mL). The combined organics were dried ($Na_2SO_4$), and the solvent was removed *in vacuo* to give 22.8 mg of crude product. The crude material was purified by silica gel chromatography (EtOAc/Hex (1/1) → EtOAc) to give **1226** (7.3 mg, 18.1% from the polymer-bound acid) as a white waxy solid: FTIR (neat) 3300 (br), 2922, 1427, 1051, 870, 810 $cm^{-1}$; $^1$H NMR $\delta$ 0.97 (dt, 3 H, $J$ = 3, 6 Hz), 1.55−1.67 (m, 2 H), 1.77−2.20 (m, 3 H), 2.32 (dt, 2 H, $J$ = 3, 6 Hz), 2.64 (d, 4 H, $J$ = 6 Hz), 2.67−2.91 (m, 3 H), 3.05−3.25 (m, 3 H), 3.74−3.82 (m, 2 H), 4.71−4.88 (m, 3 H); $^{13}$C NMR $\delta$ 13.72, 13.75, 19.69, 29.55, 29.67, 33.00, 33.04, 33.09, 33.14, 33.22, 37.52, 37.57, 37.59, 42.07, 42.14, 42.22, 42.87, 42.94, 42.99, 43.34, 43.39, 59.74, 59.77, 59.83, 76.71, 76.81, 76.86, 77.16, 77.20, 77.30, 77.52, 77.60, 77.62, 77.72, 78.65, 78.67, 78.73, 155.76, 155.96, 155.98, 159.17. Anal. Calcd for $C_{16}H_{25}N_3O_4$: C, 59.43; H, 7.79; N, 12.99. Found: C, 59.39; H, 7.96; N, 12.77. The recovered polymer was washed (3 × 3 mL each) with THF and $Et_2O$ and dried under vacuum overnight to give polymer-bound methyl benzoate as a pale yellow solid: FTIR (KBr) 1722 (C═O) $cm^{-1}$.

**Library Synthesis. Polymer-Bound Monoisoxazolines (®12, ®13, ®14, ®15).** Resin ®**1** (2.1 mmol $H^+$/g polymer, 4.00 g each) was placed into four flasks and swollen in benzene (50 mL) with stirring at room temperature for 0.5 h. Sequential addition of each of the four nitro compounds [16.8 mmol: **2** (4.34 g in 20 mL benzene) to flask one; **3** (4.57 g in 20 mL benzene) to flask two; **4** (6.12 g in 20 mL benzene) to flask three; **5** (5.55 g in 20 mL benzene)], phenyl isocyanate (4.00 g, 33.6 mmol), and triethylamine (50 drops) at room temperature gave mixtures that were refluxed for 4 d. The reactions were cooled, quenched with water (20 mL), and allowed to stir for 1 h. Each mixture was filtered and the polymer washed (5 × 15 mL each) with THF, THF/water (1:1), THF, $CH_2Cl_2$, THF, and $Et_2O$, and dried under vacuum overnight to give ®**12**, ®**13**, ®**14**, and ®**15** as brown solids: FTIR (KBr) ®**12**, 1716 (C═O); ®**13**, 1714 (C═O); ®**14**, 1716 (C═O); ®**15**, 1716 (C═O) $cm^{-1}$. These resins were mixed to form library ®A.

**Monoisoxazoline 12**. Resin ®**12** (0.20 g) was suspended in THF (3 mL) and allowed to swell for 15 min. Sodium methoxide was added (0.2 mL, 25 wt % solution in MeOH), and the reaction was stirred for 2 h, quenched with $H_2O$ (1 mL), and filtered. The polymer was washed with THF/$H_2O$ (1:1, 8 × 1 mL), THF (3 × 1 mL), MeOH (3 × 1 mL), THF (6 × 1 mL), and ether (3 × 1 mL). The filtrate was concentrated *in vacuo* and extracted with ether (3 × 4 mL). The organic was washed with brine, dried ($MgSO_4$), and concentrated to give 0.065 g of **12** as a brown solid: FTIR (neat) 3419 (OH), 1579, 1478, 1438, 1065, 1022 $cm^{-1}$; $^1$H NMR $\delta$ 1.73−1.91 (m, 2 H), 1.95 (quintet, 2 H, $J$ = 7 Hz), 2.45 (br t, 3 H, $J$ = 7 Hz), 2.55 (dd, 1 H, $J$ = 8 Hz), 2.91−3.01 (m, 3 H), 3.76 (t, 2 H, $J$ = 6 Hz), 4.63−4.73 (m, 1 H), 7.24−7.27 (m, 3 H), 7.47−7.50 (m, 2 H); $^{13}$C NMR $\delta$ 26.53, 26.92, 27.67, 37.50, 42.62, 59.61, 78.09, 126.89, 128.99, 132.65, 134.73, 158.27.

**Monoisoxazolines 13−15.** As described for **12**, resins ®**13**−®**15** gave **13**−**15** as brown oils. **13**: FTIR (neat) 3437 (OH), 1579, 1478, 1438, 1073, 1023 $cm^{-1}$; $^1$H NMR $\delta$ 1.62−1.91 (m, 6 H), 2.31−2.44 (m, 3 H), 2.57 (dd, 1 H, $J$ = 8 Hz), 2.89−3.03 (m, 3 H), 3.75 (t, 2 H, $J$ = 6 Hz), 4.62−4.72 (m, 1 H), 7.21−7.28 (m, 3 H), 7.44−7.48 (m, 2 H); $^{13}$C NMR $\delta$ 26.11, 27.10, 29.36, 37.52, 42.35, 59.54, 77.77, 78.28, 126.68, 128.94, 130.02, 132.35, 158.85. **14** (≈1:1 mixture of diastereomers): FTIR (neat) 3426 (OH), 1578, 1478, 1437, 1073, 1022 $cm^{-1}$; $^1$H NMR $\delta$ 1.62−2.06 (m, 4 H), 2.22 (br s, 1 H), 2.30−2.82 (m, 2 H), 3.02 (t, 2 H, $J$ = 8 Hz), 3.54−3.76 (m, 4 H), 4.62−4.74 (m, 1 H), 5.24 (s, 1 H), 7.19−7.25 (m, 3 H), 7.26−7.43 (m, 5 H), 7.43−7.53 (m, 2 H); $^{13}$C NMR $\delta$ 24.19, 29.94, 29.97, 30.20, 37.30, 37.70, 38.01, 38.06, 59.34, 59.42, 68.08, 76.41, 76.46, 77.42, 78.71, 78.78, 125.34, 125.81, 125.94, 126.05, 126.68, 128.01, 128.48, 128.93, 129.97, 132.31, 132.34, 136.68, 137.63, 159.32, 159.50. **15** (≈1:1 mixture of diastereomers): FTIR (neat) 3433 (OH), 1579, 1478, 1438, 1266, 1095, 1023 $cm^{-1}$; $^1$H NMR $\delta$ 0.82 (d, 3 H, $J$ = 7 Hz), 1.01 (d, 3 H, $J$ = 7 Hz), 1.74−1.97 (m, 5 H), 2.52−2.71 (m, 2 H), 2.93−3.10 (m, 3 H), 3.36−3.53 (m, 2 H), 3.67 (d, 1 H, $J$ = 9 Hz), 3.77 (t, 2 H, $J$ = 6 Hz), 4.72−4.77 (m, 1 H), 7.21−7.27 (m, 3 H), 7.45−7.49 (m, 2 H); $^{13}$C NMR $\delta$ 18.25, 18.29, 19.01, 19.05, 24.22, 29.88, 30.20, 30.96, 31.00, 37.73, 38.43, 38.56, 59.41, 68.27, 78.21, 78.24, 80.65, 80.73, 126.69, 128.94, 129.91, 132.37, 132.41, 159.22. See Table 1 for FAB MS data ($m/e$ $[M + H]^+$ and $[M + Na]^+$) for these monoisoxazolines.

**Polymer-Bound Monoisoxazoline Alkene ®12a**. Resin ®**12** (4.82 g) was swollen in THF (45 mL) with stirring at room temperature for 1 h. A solution of sodium periodate (6.48 g, 30.3 mmol) in $H_2O$/MeOH (15 mL/15 mL) was added, and the mixture was heated at reflux for 14.5 h. Upon cooling, the mixture was filtered and the polymer was washed (5 × 15 mL each) with THF, THF/water (1:1), saturated aqueous $NaHCO_3$, water, THF/water (1:1), THF, $CH_2Cl_2$, THF, and $Et_2O$. The resin was dried under vacuum overnight to give ®**12a** as a brown solid: FTIR (KBr) 1716 (C═O) $cm^{-1}$.

**Polymer-Bound Monoisoxazoline Alkenes ®13a, ®14a, and ®15a.** As described for ®**12a**, ®**13** (4.70 g) and $NaIO_4$ (6.33 g, 29.6 mmol) gave ®**13a** [FTIR (KBr) 1716 (C═O) $cm^{-1}$], ®**14** (5.45 g) and $NaIO_4$ (7.34 g, 34.3 mmol) gave ®**14a** [FTIR (KBr) 1716 (C═O) $cm^{-1}$], and ®**15** (5.11 g) and $NaIO_4$ (6.89 g, 32.2 mmol) gave ®**15a** [FTIR (KBr) 1716 (C═O) $cm^{-1}$].

**Polymer-Bound Diisoxazolines ®B, ®C, ®D,** and **®E.** Resins ®**12a**, ®**13a**, ®**14a**, and ®**15a** were mixed together (3.20 g each) to give mixed resin ®Aa. This mixed resin was partitioned into four flasks (3.10 g each) and swollen in benzene (50 mL) with stirring at room temperature for 0.5 h. Nitroseleno ether **2** (5.04 g, 19.5 mmol, in 20 mL benzene) was added to flask one, nitroseleno ether **3** (5.32 g, 19.5 mmol, in 20 mL benzene) was added to flask two, nitroseleno ether **4** (7.11 g, 19.5 mmol, in 20 mL benzene) was added to flask three, and nitroseleno ether **5** (6.45 g, 19.5 mmol, in 20 mL benzene) was added to flask four. Phenyl isocyanate (4.65 g, 39.1 mmol) and triethylamine (50 drops) were added to each flask, and the mixtures were stirred at room temperature for 4 d. The reactions were quenched with water (20 mL) and allowed to stir for 1 h. Each mixture was filtered, and the polymer was washed (5 × 15 mL each) with THF, THF/water (1:1), THF, $CH_2Cl_2$, THF, and $Et_2O$ and dried under vacuum overnight to give ®**B**, ®**C**, ®**D**, and ®**E** as a brown solid: FTIR (KBr) ®**B**, 1712 (C═O); ®**C**, 1716 (C═O); ®**D**, 1716 (C═O); ®**E**, 1716 (C═O) $cm^{-1}$.

**Solution Diisoxazoline Libraries B, C, D, and E.** The procedure described for transesterification of ®**12** to liberate monoisoxazoline **12** was followed except 0.40 g of resin (®B, ®C, ®D, or ®E), THF (6 mL), NaOMe/MeOH (0.4 mL), and water (2 mL) were used, giving ≈110 mg each of solution libraries B, C, D, and E. See Table 1 for FAB MS data ($m/e$ $[M + H]^+$ and $[M + Na]^+$) for these diisoxazolines.

**Polymer-Bound Olefin ®Ba, ®Ca, ®Da, and ®Ea.** The procedure described for conversion of ®**12** to olefin ®**12a** was followed except resin ®B (3.02 g), ®C, (3.07 g) ®D (2.94 g), or ®E (2.93 g) was used in place of ®**12** to give ®Ba, ®Ca, ®Da, and ®Ea as light brown solids: FTIR (KBr) ®Ba, 1718 (C═O); ®Ca, 1716 (C═O); ®Da, 1716 (C═O); ®Ea, 1716 (C═O) $cm^{-1}$.

**Polymer-Bound Triisoxazolines ®F, ®G, ®H, and ®I.** Resin ®Ba was partitioned into four flasks (600 mg each) and swollen in benzene (15 mL) with stirring at room temperature for 1 h. To these flasks were added a nitroalkane [nitrobutane (390 mg) to flask one, phenylnitromethane[25a] (518 mg, 3.8 mmol) to flask two, (4-methylphenyl)nitromethane[25b] (571 mg) to flask three, and (4-bromophenyl)nitromethane[25b] (817 mg) to flask four], phenyl isocyanate (0.90 g, 7.6 mmol), and triethylamine (20 drops). Each mixture was stirred for 4 d at room temperature, quenched with water (3 mL), and allowed to stir for 1 h. The mixtures were filtered, and each polymer was washed (5 × 5 mL each) with THF, THF/water (1/1), THF, $CH_2Cl_2$, THF, and $Et_2O$ and dried under vacuum overnight to give ®F, ®G, ®H, and ®I as a yellow solids: FTIR (KBr) ®F, 1718 (C═O); ®G, 1718 (C═O); ®H, 1718 (C═O); ®I, 1718 (C═O) $cm^{-1}$.

**Polymer-Bound Triisoxazolines ®J, ®K, ®L, ®M, ®N, ®O, ®P, ®Q, ®R, ®S, ®T, and ®U.** The same procedure described for the conversion of ®Ba to ®F, ®G, ®H, and ®I was followed: FTIR (KBr) ®J, 1718 (C═O); ®K, 1718 (C═O); ®L, 1718 (C═O); ®M, 1718 (C═O); ®N, 1718 (C═O); ®O, 1718 (C═O); ®P, 1716 (C═O); ®Q, 1718 (C═O); ®R, 1718 (C═O); ®S, 1718 (C═O); ®T, 1718 (C═O); ®U, 1718 (C═O) $cm^{-1}$.

**Solution Triisoxazoline Libraries F−U.** The procedure described for transesterification of ®**12** to liberate monoisoxazoline **12** was followed except 0.40 g of resin (®F, ®G, ®H, ®I, ®J, ®K, ®L, ®M, ®N, ®O, ®P, ®Q, ®R, ®S, ®T, or ®U), THF (6 mL), NaOMe/MeOH (0.4 mL), and water (2 mL) were used, giving 90−230 mg each of solution libraries F, G, H, I, J, K, L, M, N, O, P, Q, R, S, T, or U. See Table 1 for FAB MS data (*m*/*e* $[M + H]^+$ and $[M + Na]^+$) for these triisoxazolines.

**Acknowledgment.** We are grateful to the National Science Foundation (Grant CHE-9406891) and Teijin Ltd. for financial support of this work.

**Supporting Information Available:** $^1H$- and $^{13}C$-NMR spectra for **122** and **1226** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO961730L