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# Solid-Phase Synthesis of 1,2-Diheterocyclic-Substituted (E)-Olefins from a Supported Selenium Resin

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A library of 1,2,3-triazoles, isoxazoles, 1,2,4-oxadiazoles, and isoxazoline-containing 1,2-di-heterocyclic-substituted compounds with three points of diversity linked by an *E* double bond were prepared. Key steps include a 1,3-dipolar cycloaddition and Porco's two-step, one-pot condensation and α-alkylation reaction of selenium resins.

## Introduction

The preparation of diverse libraries of organic compounds is an important facet of modern drug discovery programs. One of the most commonly employed methods in library production is solid-phase organic synthesis (SPOS).[1] The field of solid-phase heterocyclic chemistry has rapidly expanded because experience has shown that compounds with biological activity are often derived from heterocyclic structures. Synthesis methods that enable the rapid production of arrays of heterocycles, useful for the identification of new lead structures, are of critical importance to the pharmaceutical industry.[2]

Isoxazoles and isoxazolines represent two classes of pharmacophores that are observed in many therapeutic agents,[3] while oxadiazoles are important bioisosters for esters and amides in drug discovery with reported muscarinic agonist, 5-HT agonist, benzodiazepine receptor agonist, and antirhinoviral activities.[4] Several members of the 1,2,3-triazole family have also shown interesting biological properties, such as antiallergic, antibacterial, and anti-HIV activity.[5] Therefore, they are all interesting targets which potentially can be made via solid-phase chemistry.[6] Although the solid-phase synthesis of 1,2,3-triazoles via 1,3-dipolar cycloaddition is well developed,[6d,7] the one-pot 1,3-dipolar cycloaddition through aryl halides, alkynes, and sodium azide on the solid phase to synthesize 1,2,3-triazole is first developed. A one-pot methodology that avoids the isolation of organic azides is desirable for low molecular weight organic azides as they are unstable and difficult to handle;[8] sometimes that would be especially true for small molecules with several azide functionalities that would be of much interest for the generation of polyvalent structures. The incorporation of 1,2,3-triazoles or isoxazoles or 1,2,4-oxadiazoles and isoxazoline into a bis-ring system linked by a double bond could be useful as di-heterocyclic substituted compounds[9] have been rarely investigated.

An important aspect of the solid-phase methodology is the choice of the linker, which is crucial for the attachment and detachment of the requisite substrates to and from the resin. Many solid-phase syntheses rely on the release of carboxylic acids, esters, ethers, and amides from an ester- or amide-bound substrate. Alternative methods that allow the cleavage of resin, with access to more variable functionalities, are extremely desirable.[10,11] Since the first organoselenium resin[12] was reported in 1976, several groups have developed organoselenium resins as convenient linkers.[13,14] Recently, our research group has been interested in the application of organic selenium resins in organic synthesis.[10,15] Herein we report the preparation of a library of bis-heterocyclic-containing compounds linked by a double bond (*E*) with the advantages of straightforward operation, lack of odor, stability, and good resulting purity of the product. It is noteworthy that the polystyrene-supported selenium resins used here assist the crucial reaction of α-alkylation and selenoxide *syn*-elimination, which ensures the purity of the products and introduces a new *E* double bond into the target molecules.

## Results and Discussion

Efforts began from polystyrene-supported selenenyl bromide **1**[13] (dark-red resin, Br: 0.99 mmol/g), which was treated with $NaBH_4$ and propargyl bromide to give the corresponding white resin **2**.[10] Resin **2** reacted smoothly with aryl halides and sodium azide through a one-pot 1,3-dipolar cycloaddition[16] catalyzed by CuI and proline to furnish polystyrene-supported 1,2,3-triazolyl-substituted selenium resin **3** (FTIR: 1635 $cm^{-1}$ with disappearance of 3299 $cm^{-1}$; Scheme 1).

The α-alkylation of **3** by base treatment and addition of substituted allyl bromides was investigated. It was found that by keeping the reaction temperature at −70 °C and using 1.2 equiv of LDA, 4.0 equiv of substituted allyl bromide

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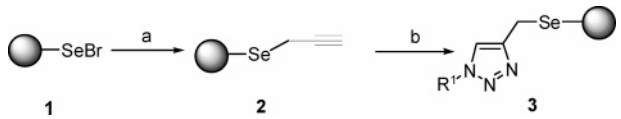
**Scheme 1**[a]




[a] Reagents and conditions: (a) $NaBH_4$, THF/DMF, 40 °C, 6 h then propargyl bromide, 3 h; (b) $NaN_3$, $R^1I$, proline, CuI, $Et_3N$, DMSO, 65 °C, 12 h.

**Table 1.** Synthesis of Triazolyl- and Isoxazolinyl-Substituted (*E*)-Olefins

| product | $R^1$ | $R^2$ | $R^3$ | yield (%)[a] | purity (%)[b] |
|---|---|---|---|---|---|
| **6a** | $C_6H_5$ | H | 4-$CH_3C_6H_4$ | 51 | 89 |
| **6b** | $C_6H_5$ | H | 4-$FC_6H_4$ | 47 | 91 |
| **6c** | $C_6H_5$ | H | 4-$BrC_6H_4$ | 58 | 92 |
| **6d** | $C_6H_5$ | H | $C_6H_5$ | 66 | 95 |
| **6e** | 4-$ClC_6H_4$ | H | 4-$CH_3C_6H_4$ | 45 | 90 |
| **6f**[c] | $C_6H_5$ | CH3 | 4-$ClC_6H_4$ | 43 | 89 |
| **6g**[c] | $C_6H_5$ | CH3 | 4-$CH_3C_6H_4$ | 49 | 90 |

[a] Yield of the crude product based on the loading of the resin **1**. [b] Determined by HPLC ($\lambda = 287$ nm). [c] 1,3-Dipolar cycloaddition step performed twice prior to cleavage.

gave the optimal results. The α-alkylated **4** then underwent another 1,3-dipolar cycloaddition to furnish the polystyrene-supported 1,2,3-triazolyl- and isoxazolinyl-substituted selenide resin **5**. It is noteworthy that in this process the sequence of adding the substrates was reversed compared to our previous work;[10] thus, hydroximoyl halide was added dropwise to a mixture of resin **4** and an excess of $Et_3N$. No product was obtained when $Et_3N$, was added dropwise. Triazolyl- and isoxazolinyl-substituted olefins **6** were obtained regioselectively through selenoxide *syn*-elimination of resin **5** (Scheme 2). Results are described in Table 1and show that triazolyl- and isoxazolinyl-substituted olefins **6** could be obtained in moderate to good yield with good levels of purity.

On the basis of our previous work,[10] polystyrene-supported isoxazolyl-substituted selenium resin **7** underwent α-alkylation and 1,3-dipolar cycloaddition smoothly, which was followed by selenoxide *syn*-elimination to obtain isoxazolyl- and isoxazolinyl-substituted olefins **10** (Scheme 3). The results are summarized in Table 2.

**Table 2.** Synthesis of Isoxazolyl- and Isoxazolinyl-Substituted Olefins

| product | $R^1$ | $R^2$ | $R^3$ | yield (%)[a] | purity (%)[b] |
|---|---|---|---|---|---|
| **10a** | 4-$ClC_6H_4$ | $C_6H_5$ | COOEt | 75 | 93 |
| **10b** | 4-$CH_3C_6H_4$ | $C_6H_5$ | COOEt | 77 | 91 |
| **10c** | 4-$CH_3C_6H_4$ | $C_6H_5$ | 4-$ClC_6H_4$ | 64 | 89 |
| **10h** | 4-$ClC_6H_4$ | $C_6H_5$ | 4-$CH_3C_6H_4$ | 66 | 94 |
| **10e** | 4-$CH_3C_6H_4$ | H | 4-$FC_6H_4$ | 61 | 90 |
| **10f** | 4-$ClC_6H_4$ | $C_6H_5$ | 4-$FC_6H_4$ | 57 | 96 |

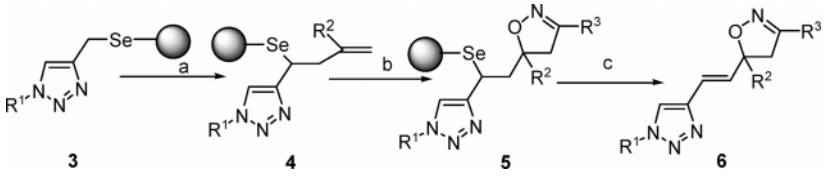
[a] Yield of the crude product based on the loading of the resin **1**. [b] Determined by HPLC. ($\lambda = 287$ nm).

The scope of the products is of upmost importance in the solid-phase organic synthesis; thus, besides 1,3-dipolar cycloadditions,[17] Porco's condensation[18] is also an important method to prepare 1,2,4-oxadiazoles. Although 1,2,4-oxadiazoles are biologically interesting compounds, their preparation on solid phase is relatively rare.[6c,19]

Thus, polystyrene-supported selenenyl bromide **1**[13] (dark-red resin, Br: 0.99 mmol/g) was treated with $NaBH_4$ and α-bromoacetic acid to give the corresponding white resin **11**[15d] almost quantitatively (Br was undetectable) while the reaction was monitored by FT-IR, which showed a strong peak for the carbonyl absorptions at 1700 $cm^{-1}$. It was also found that resin **11** reacted smoothly with amidoxime and DCC through Porco's two-step, one-pot condensation to furnish polystyrene-supported oxadiazolyl-substituted selenium resin **12** (FTIR: 1653 $cm^{-1}$ with disappearance of the band at 1700 $cm^{-1}$; Scheme 4).

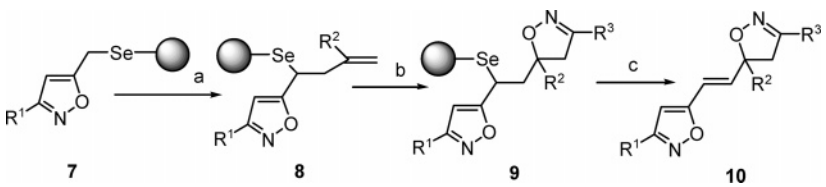
The potential α-alkylation with LDA and substituted allyl bromides was also investigated. It should be noted that during this step higher temperatures or excessive base (LDA) would result in the di-allylation of the selenide resin **12**, and thus, it was found that keeping the reaction temperature at −60 °C and 1.2 equiv of LDA, 4.0 equiv of substituted allyl bromide gave the optimal results. The α-alkylated selenium resin **13** was used in a 1,3-dipolar cycloaddition to furnish polystyrene-supported oxadiazolyl- and isoxazolinyl-substituted selenium resin **14**. Oxadiazolyl- and isoxazolinyl-substituted olefins **15** were obtained stereoselectively through selenoxide *syn*-elimination from resins **14** (Scheme 5).

**Scheme 2**[a]



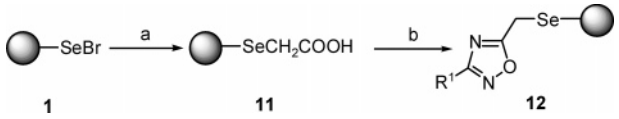

[a] Reagents and conditions: (a) LDA (1.2 equiv), THF, −70 °C, 1.5 h; substituted allyl bromide (4 equiv), THF, −70 to −50 °C, 1 h; (b) $R^3CH{=}NOH$ (4 equiv), NCS (4 equiv), $CH_2Cl_2$, $Et_3$ N, (20 equiv), rt, 12 h; (c) $H_2O_2$, THF, 0 °C, 1 h, then rt, 20 min.

**Scheme 3**[a]




[a] Reagents and conditions: (a) LDA (1.2 equiv), THF, −60 °C, 1.5 h; substituted allyl bromide (4 equiv), THF, −60 to −40 °C, 1 h; (b) $R_3CH{=}NOH$ (3 equiv), NCS (3 equiv), $CH_2Cl_2$, $Et_3$ N, (6 equiv), rt, 24 h; (c) $H_2O_2$, THF, 0 °C, 1 h, then rt, 20 min.

**Scheme 4**[a]




[a] Reagents and conditions: (a) $NaBH_4$, THF/DMF, 40 °C, 6 h then $BrCH_2COOH$, 3 h; (b) DCC, $R^1C(NH_2)$═NOH, 1,4-dioxane.

**Table 3.** Synthesis of Oxadiazolyl- and Isoxazolinyl-Substituted (*E*)-Olefins

| product | $R^1$ | $R^2$ | $R^3$ | yield (%)[a] | purity (%)[b] |
|---|---|---|---|---|---|
| **15a** | 4-$CH_3C_6H_4$ | H | 4-$ClC_6H_4$ | 64 | 93 |
| **15b** | 4-$FC_6H_4$ | $C_6H_5$ | 4-$CH_3C_6H_4$ | 51 | 90 |
| **15c** | 4-$CH_3C_6H_4$ | H | COOEt | 71 | 95 |
| **15d** | 4-$CH_3C_6H_4$ | $C_6H_5$ | COOEt | 69 | 89 |
| **15e** | 4-$CH_3C_6H_4$ | $C_6H_5$ | 4-$BrC_6H_4$ | 60 | 92 |
| **15f** | 4-$CH_3C_6H_4$ | $C_6H_5$ | 4-$ClC_6H_4$ | 59 | 90 |
| **15g** | 4-$CH_3C_6H_4$ | $C_6H_5$ | 4-$CH_3C_6H_4$ | 64 | 93 |
| **15h** | 4-$FC_6H_4$ | $C_6H_5$ | COOEt | 61 | 93 |
| **15i** | $C_6H_5$ | H | COOEt | 70 | 96 |
| **15j** | $C_6H_5$ | H | 4-$ClC_6H_4$ | 63 | 90 |
| **15k** | $C_6H_5$ | H | 4-$CH_3C_6H_4$ | 64 | 95 |
| **15l** | $C_6H_5$ | H | 4-$CH_3OC_6H_4$ | 68 | 89 |
| **15m** | 4-$ClC_6H_4$ | $C_6H_5$ | 4-$CH_3C_6H_4$ | 57 | 90 |
| **15n** | 4-$ClC_6H_4$ | H | 4-$ClC_6H_4$ | 60 | 95 |
| **15o** | 4-$ClC_6H_4$ | $C_6H_5$ | 4-$BrC_6H_4$ | 66 | 91 |
| **15p** | 4-$ClC_6H_4$ | H | COOEt | 72 | 95 |
| **15q** | 4-$ClC_6H_4$ | H | 4-$CH_3OC_6H_4$ | 65 | 91 |
| **15r** | 4-$ClC_6H_4$ | $C_6H_5$ | 4-$O_2NC_6H_4$ | 48 | 87 |
| **15s** | 4-$ClC_6H_4$ | $C_6H_5$ | COOEt | 70 | 97 |

[a] Yield of the crude product based on the loading of the resin **1**. [b] Determined by HPLC ($\lambda$ = 287 nm).

Results are described in Table 3 and show that oxadiazolyl- and isoxazolinyl-substituted olefins **15** were obtained in moderate to good yield with good purity.

It is noteworthy that in all these processes only the alkylated resins **5**, **9**, and **14** underwent selenoxide *syn*-elimination under mild cleavage conditions (Schemes 2, 3, and 5 step c). No reaction was observed for the unalkylated resins **3**, **7**, and **12** under the same conditions, which thus ensures the purity of the crude products in a "safely catch linker" type of approach.

In summary, we developed a solid-phase method to prepare libraries of 1,2,3-triazoles, isoxazoles, 1,2,4-oxadiazoles, and isoxazoline-containing di-heterocyclic-substituted compounds linked via an *E* double bond. The polystyrene-supported selenium resins used here not only facilitate the separation of the products, but also assist in the crucial reaction of α-alkylation and selenoxide *syn*-elimination, which ensures the purity of the products liberated from the resin.

## Experimental Section

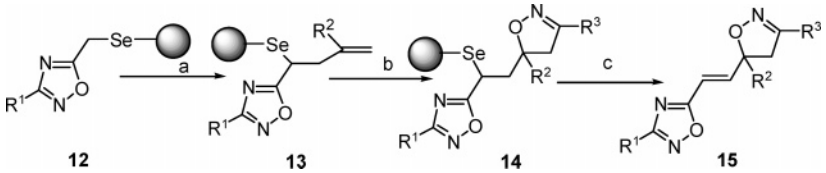
**General Methods.** Starting materials were obtained from commercial suppliers and used without further purification. THF was distilled from sodium/benzophenone immediately prior to use. Polystyrene (H 1000, 100−200 mesh, cross-linked with 1% divinylbenzene) was used for the preparation of selenenyl bromide resin (Br: 0.99 mmol/g) according to the procedure described by Nicolaou[13,14a] and was purchased from Nan-Kai University. $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra were recorded on a Bruker Avance (400 MHz) spectrometer using $CDCl_3$ as the solvent and TMS as an internal standard. Mass spectra (EI, 70 eV) were recorded on a HP5989B mass spectrometer. Infrared spectra were recorded on a Shimadzu IR-408 spectrometer. Elemental analyses were performed on a Flash EA1112 instrument. HPLC was performed on an Agilent 1100 (column, ODS 5 $\mu$m 250 × 4 mm; mobile phase, THF/MeOH/$H_2O$ = 50/20/30(V/V); flow rate, 0.8 mL/min; detector, UV 287 nm). Samples were purified by TLC for $^{13}$C NMR and microanalyses.

**Typical Procedure for the Preparation of Polystyrene-Supported Triazolyl-Substituted Selenium Resin 3.** To a suspension of the swollen polystyrene-supported propargyl selenide resin **2** (1.0 g) in DMSO (10 mL) was added $NaN_3$ (3.0 mmol), ArI (6.0 mmol), proline (0.5 mmol), CuI (0.5 mmol), and $Et_3$ N, (0.5 mmol) under nitrogen. The mixture was stirred at 65 °C for 12 h. The resin **3** was collected by filtration, washed with DMF (10 mL × 2), DMF/0.1 N HCl (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried in a vacuum.

**Typical Procedure for the Preparation of Triazolyl- and Isoxazolinyl-Substituted Olefins (Products 6a−g).** To a suspension of the swollen resin **3** (0.5 g) in anhydrous THF (15 mL), cooled to −70 °C, was added dropwise LDA (2 M in THF/hexane, 0.3 mL) under nitrogen. After stirring for 1.5 h at −70 °C, a solution of substituted allyl bromide (2 mmol) in anhydrous THF (1 mL) was added. The suspension was stirred for another 0.5 h at −70 °C, being slowly warmed to −50 °C over 0.5 h before quenching with $H_2O$ (1 mL). Resin **4** was collected by filtration, washed with THF (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried in a vacuum.

To a suspension of the swollen resin **4** (0.5 g) and 10 mmol $Et_3N$, in $CH_2Cl_2$ (15 mL) a solution of hydroximoyl halide (4.0 mmol) in $CH_2Cl_2$ (10 mL) (prepared from 4.0 mmol of aldoxime and 4.0 mmol of NCS stirring at room temperature for 3 h before use) was slowly added dropwise over 3 h. After stirring at room temperature for 12 h, resin **5** was collected by filtration and washed with THF (10 mL × 2),

**Scheme 5**[a]




[a] Reagents and conditions: (a) LDA (1.2 equiv), THF, −60 °C, 1.5 h; substituted allyl bromide (4 equiv), THF, −60 to −40 °C, 1 h; (b) $R^3CH$═NOH (8 equiv), NCS (8 equiv), $CH_2Cl_2$, $Et_3$ N, (10 equiv), rt, 24 h (c) $H_2O_2$, THF, 0 °C, 1 h, then rt, 20 min.

ether (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), benzene (10 mL × 2), MeOH (10 mL×2), and $CH_2Cl_2$ (10 mL×2). The washed resin **5** was suspended in THF (15 mL), 30% (aq) $H_2O_2$ (0.5 mL) was added, and the mixture was stirred at 0 °C for 1 h followed by 20 min at room temperature. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (15 mL × 2). The filtrate was washed with $H_2O$ (30 mL × 2), dried over $MgSO_4$, and evaporated to dryness under vacuum to obtain the crude products **6**. Further purification was via flash chromatography with *n*-hexanes−EtOAc (2:1 v/v) as the eluent for $^{13}C$ NMR and microanalyses.

**6a:** pale yellow solid, mp 136−138 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.93 (1H, s), 7.72 (2H, d, $J$ = 8.0 Hz), 7.58−7.42 (5H, m), 7.21 (2H, d, $J$ = 8.0 Hz), 6.80 (1H, d, $J$ = 16.0 Hz), 6.63 (1H, dd, $J_1$ = 6.8 Hz, $J_2$ = 16.0 Hz), 5.37−5.34 (1H, m), 3.58 (1H, dd, $J_1$ = 10.4 Hz, $J_2$ = 16.4 Hz), 3.24 (1H, dd, $J_1$ = 8.0 Hz, $J_2$ = 16.4 Hz), 2.38 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 156.4, 145.4, 140.4, 136.8, 130.0, 129.7, 129.4, 128.7, 126.6, 126.5, 120.5, 120.4, 118.7, 80.9, 40.9, 21.4; MS *m*/*z* 168 (100), 330 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3133, 2919, 2850, 1632, 1597, 1500, 1041, 905, 841, 815, 760, 690, 537. Anal. Calcd for $C_{20}H_{18}N_4O$: C, 72.71; H, 5.49; N, 16.96. Found: C, 72.60; H, 5.55; N, 16.89.

**6b:** pale yellow solid, mp 125−126 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.94 (1H, s), 7.73−7.66 (4H, m), 7.54−7.46 (3H, m), 7.10 (2H, t, $J$ = 8.6 Hz), 6.80 (1H, d, $J$ = 16.0 Hz), 6.63 (1H, dd, $J_1$ = 6.8 Hz, $J_2$ = 16.0 Hz), 5.41−5.35 (1H, m), 3.58 (1H, dd, $J_1$ = 10.6 Hz, $J_2$ = 16.4 Hz), 3.24 (1H, dd, $J_1$ = 8.0 Hz, $J_2$ = 16.4 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 163.8 ($J$ = 249.3 Hz), 155.4, 145.3, 136.8, 129.7, 128.8, 128.6 ($J$ = 8.4 Hz), 125.6 ($J$ = 3.0 Hz), 120.6, 120.4, 118.8, 115.8 ($J$ = 21.8 Hz), 107.9, 81.2, 40.8; MS *m*/*z* 168 (100), 334 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3131, 2925, 2852, 1634, 1598, 1501, 932, 823, 761, 690, 539. Anal. Calcd for $C_{19}H_{15}FN_4O$: C, 68.25; H, 4.52; N, 16.76. Found: C, 68.33; H, 4.47; N, 16.85.

**6c:** pale yellow solid, mp 166−167 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.93 (1H, s), 7.72 (2H, d, $J$ = 8.0 Hz), 7.55−7.44 (7H, m), 6.81 (1H, d, $J$ = 16.0 Hz), 6.63 (1H, dd, $J_1$ = 6.8 Hz, $J_2$ = 16.0 Hz), 5.38−5.35 (1H, m), 3.57 (1H, dd, $J_1$ = 10.4 Hz, $J_2$ = 16.4 Hz), 3.23 (1H, dd, $J_1$ = 8.0 Hz, $J_2$ = 16.4 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 155.6, 145.2, 136.8, 131.9, 129.7, 129.6, 128.8, 128.3, 128.1, 124.4, 120.7, 120.4, 118.8, 81.4, 40.6; MS *m*/*z* 394 ($M^+$, 100), 396 ($M^+$ + 2, 97); IR $\nu_{max}$ ($cm^{-1}$) 3131, 2920, 2850, 1632, 1599, 1501, 1033, 837, 758, 688. Anal. Calcd for $C_{19}H_{15}BrN_4O$: C, 57.74; H, 3.83; N, 14.17. Found: C, 57.62; H, 3.91; N, 14.22.

**6d:** pale yellow solid, mp 111−113 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.97 (1H, s), 7.75−7.69 (4H, m), 7.56−7.43 (6H, m), 6.83 (1H, d, $J$ = 16.0 Hz), 6.66 (1H, dd, $J_1$ = 6.8 Hz, $J_2$ = 16.0 Hz), 5.42−5.37 (1H, m), 3.62 (1H, dd, $J_1$ = 10.8 Hz, $J_2$ = 16.4 Hz), 3.29 (1H, dd, $J_1$ = 8.0 Hz, $J_2$ = 16.4 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 156.4, 136.8, 130.1, 130.0, 129.76, 129.73, 128.81, 128.78, 128.71, 128.68, 126.7, 120.5, 120.4, 80.9, 40.9; MS *m*/*z* 168 (100), 316 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3132, 2922, 2851, 1633, 1599, 1501, 1028, 761, 690, 540. Anal. Calcd for $C_{19}H_{16}N_4O$: C, 72.13; H, 5.10; N, 17.71. Found: C, 72.01; H, 5.18; N, 17.80.

**6e:** pale yellow solid, mp 145−146 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.90 (1H, s), 7.68 (2H, d, $J$ = 8.0 Hz), 7.58 (2H, d, $J$ = 7.6 Hz), 7.51 (2H, d, $J$ = 7.6 Hz), 7.22 (2H, d, $J$ = 7.6 Hz), 6.80 (1H, d, $J$ = 16.0 Hz), 6.62 (1H, dd, $J_1$ = 6.8 Hz, $J_2$ = 16.0 Hz), 5.37−5.33 (1H, m), 3.58 (1H, dd, $J_1$ = 11.2 Hz, $J_2$ = 16.4 Hz), 3.24 (1H, dd, $J_1$ = 7.6 Hz, $J_2$ = 16.4 Hz), 2.38 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 156.3, 145.6, 140.4, 135.3, 134.5, 130.4, 129.9, 129.4, 126.6, 126.5, 121.5, 120.2, 118.6, 80.8, 40.9, 21.4; MS *m*/*z* 203 (100), 364 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3133, 2920, 2852, 1634, 1597, 1504, 1042, 905, 841, 823. Anal. Calcd for $C_{20}H_{17}ClN_4O$: C, 65.84; H, 4.70; N, 15.36. Found: C, 65.75; H, 4.77; N, 15.28.

**6f:** pale yellow solid, mp 81−83 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.94 (1H, s), 7.73 (2H, d, $J$ = 8.0 Hz), 7.61−7.45 (5H, m), 7.39 (2H, d, $J$ = 8.0 Hz), 6.79 (2H, s), 3.41 (1H, d, $J$ = 16.4 Hz), 3.26 (1H, d, $J$ = 16.4 Hz), 1.71 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 155.3, 145.4, 136.8, 135.9, 134.3, 129.7, 128.9, 128.8, 128.3, 127.7, 120.4, 118.9, 116.8, 86.5, 46.4, 25.5; MS *m*/*z* 168 (100), 364 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3126, 2924, 2850, 1632, 1599, 1500, 1088, 905, 759, 689, 540. Anal. Calcd for $C_{20}H_{17}ClN_4O$: C, 65.84; H, 4.70; N, 15.36. Found: C, 65.99; H, 4.62; N, 15.47.

**6g:** pale yellow solid, mp 91−92 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.89 (1H, s), 7.71 (2H, d, $J$ = 8.0 Hz), 7.55−7.44 (5H, m), 7.20 (2H, d, $J$ = 8.0 Hz), 6.80 (1H, d, $J$ = 15.6 Hz), 6.74 (1H, d, $J$ = 15.6 Hz), 3.40 (1H, d, $J$ = 16.4 Hz), 3.25 (1H, d, $J$ = 16.4 Hz), 2.37 (3H, s), 1.71 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 156.3, 145.6, 140.2, 136.8, 134.6, 129.7, 129.3, 128.7, 126.9, 126.4, 120.4, 118.7, 116.8, 85.9, 46.6, 25.4, 21.4; MS *m*/*z* 168 (100), 344 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3125, 2922, 2852, 1633, 1598, 1502, 1355, 1231, 1074, 907, 758, 687, 537. Anal. Calcd for $C_{21}H_{20}N_4O$: C, 73.23; H, 5.85; N, 16.27. Found: C, 73.35; H, 5.94; N, 16.19.

**Typical Procedure for the Preparation of Isoxazolyl- and Isoxazolinyl-Substituted Olefins (Products 10a−f).** To a suspension of the swollen resin **7** (0.5 g) in anhydrous THF (15 mL), cooled to −60 °C, was added dropwise LDA (2 M in THF/hexane, 0.3 mL) under nitrogen. After stirring at −60 °C for 1.5 h, a solution of substituted allyl bromide (2 mmol) in anhydrous THF (1 mL) was added. The suspension was stirred for another 0.5 h at −60 °C, being slowly warmed to −40 °C over 0.5 h before quenching with $H_2O$ (1 mL). Resin **8** was collected by filtration, washed with THF (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried in a vacuum.

To a suspension of the swollen resin **8** (0.5 g) in $CH_2Cl_2$ (15 mL) was added a solution of hydroximoyl halide (1.5 mmol) in $CH_2Cl_2$ (10 mL) (prepared from 1.5 mmol of aldoxime and 1.5 mmol of NCS stirring at room temperature for 3 h before use). A solution of $Et_3N$ (3 mmol) in $CH_2Cl_2$ (15 mL) was slowly added dropwise in three portions every 8 h (each time 1 mmol $Et_3N$, in 5 mL of anhydrous $CH_2Cl_2$ was added). After stirring for 24 h at room temperature, Resin **9** was collected by filtration, washed with THF (10 mL × 2), ether (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), benzene (10 mL × 2), MeOH (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried in a vacuum. The washed resin **9** was suspended in THF (15

mL), 30% (aq) $H_2O_2$ (0.5 mL) was added, and the mixture was stirred for 1 h at 0 °C followed by 20 min at room temperature. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (15 mL × 2). The filtrate was washed with $H_2O$ (30 mL × 2), dried over $MgSO_4$, and evaporated to dryness under vacuum to obtain the crude products **10**. Further purification was via flash chromatography with *n*-hexanes−EtOAc (4:1 V/V) as the eluent for $^{13}C$ NMR and microanalyses.

**10a:** pale yellow solid, mp 136−138 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.69 (2H, d, $J$ = 8.4 Hz), 7.45−7.34 (7H, m), 6.80 (1H, d, $J$ = 16.0 Hz), 6.58 (1H, d, $J$ = 16.0 Hz), 6.45 (1H, s), 4.32 (2H, q, $J$ = 7.2 Hz), 3.61 (2H, d, $J$ = 3.6 Hz), 1.36 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.5, 161.8, 160.2, 151.2, 140.4, 136.7, 136.1, 129.2, 128.9, 128.5, 128.0, 127.2, 125.4, 115.9, 100.7, 92.0, 62.2, 46.2, 14.1; MS *m*/*z* 282 (100), 422 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1716, 1602, 1560, 1428, 1271, 1127, 1093, 930, 833, 767, 699. Anal. Calcd for $C_{23}H_{19}ClN_2O_4$: C, 65.33; H, 4.53; N, 6.62. Found: C, 65.37; H, 4.58; N, 6.56.

**10b:** pale yellow solid, mp 118−119 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.69 (2H, d, $J$ = 8.0 Hz), 7.49−7.38 (5H, m), 7.27 (2H, d, $J$ = 8.0 Hz), 6.83 (1H, d, $J$ = 15.6 Hz), 6.61 (1H, d, $J$ = 15.6 Hz), 6.49 (1H, s), 4.37 (2H, q, $J$ = 7.2 Hz), 3.65 (2H, s), 2.41 (3H, s), 1.39 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.1, 162.8, 160.3, 151.3, 140.6, 140.3, 136.3, 129.7, 129.0, 128.6, 126.7, 126.0, 125.6, 115.9, 101.0, 92.2, 62.4, 46.2, 21.5, 14.2; MS *m*/*z* 282 (100), 402 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2924, 1718, 1601, 1560, 1366, 1093, 928, 828, 761, 697. Anal. Calcd for $C_{24}H_{22}N_2O_4$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.71; H, 5.58; N, 7.03.

**10c:** pale yellow solid, mp 148−149 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.68 (2H, d, $J$ = 8.0 Hz), 7.63 (2H, d, $J$ = 8.0 Hz), 7.55 (2H, d, $J$ = 7.6 Hz), 7.45−7.37 (5H, m), 7.26 (2H, d, $J$ = 7.6 Hz), 6.91 (1H, d, $J$ = 16.0 Hz), 6.68 (1H, d, $J$ = 16.0 Hz), 6.48 (1H, s), 3.76 (2H, s), 2.41 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.4, 162.8, 155.4, 141.6, 140.3, 137.4, 136.4, 129.7, 129.1, 128.9, 128.3, 128.0, 127.8, 126.7, 126.1, 125.7, 115.6, 100.7, 89.8, 47.7, 21.4; MS *m*/*z* 199 (100), 440 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1723, 1671, 1591, 1542, 1410, 1333, 1258, 977, 931, 841, 751. Anal. Calcd for $C_{27}H_{21}ClN_2O_2$: C, 73.55; H, 4.80; N, 6.35. Found: C, 73.48; H, 4.73; N, 6.26.

**10d:** pale yellow solid, mp 146−147 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.71 (2H, d, $J$ = 8.4 Hz), 7.57 (2H, d, $J$ = 8.0 Hz), 7.54 (2H, d, $J$ = 8.4 Hz), 7.44−7.40 (5H, m), 7.21 (2H, d, $J$ = 8.0 Hz), 6.91 (1H, d, $J$ = 15.8 Hz), 6.68 (1H, d, $J$ = 15.8 Hz), 6.44 (1H, s), 3.75 (2H, d, $J$ = 2.2 Hz), 2.37 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.9, 161.7, 156.2, 141.5, 140.7, 138.0, 136.0, 129.4, 129.1, 128.7, 128.1, 128.0, 127.3, 126.6, 126.2, 125.6, 114.9, 100.3, 89.1, 47.8, 21.4; MS *m*/*z* 199(100), 440 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1723, 1671, 1591, 1542, 1410, 1333, 1258, 977, 931, 841, 751. Anal. Calcd for $C_{27}H_{21}ClN_2O_2$: C, 73.55; H, 4.80; N, 6.35. Found: C, 73.48; H, 4.73; N, 6.26.

**10e:** pale yellow solid, mp 172−173 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.68−7.65 (4H, m), 7.53 (2H, d, $J$ = 7.6 Hz), 7.44−7.34 (3H, m), 7.35 (2H, d, $J$ = 7.6 Hz), 7.10 (2H, t, $J$ = 8.6 Hz), 6.89 (1H, d, $J$ = 15.8 Hz), 6.66 (1H, d, $J$ = 15.8 Hz), 6.45 (1H, s), 3.74 (2H, s), 2.38 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.3, 163.9 ($J$ = 248.8 Hz), 162.7, 155.3, 141.5, 140.2, 137.4, 129.5, 128.8, 128.7 ($J$ = 8.3 Hz), 128.2, 126.6, 126.0, 125.6, 125.5 ($J$ = 3.6 Hz), 115.9 ($J$ = 21.9 Hz), 115.4, 100.6, 89.5, 47.8, 21.4; MS *m*/*z* 199 (100), 424 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1723, 1671, 1591, 1542, 1410, 1333, 1258, 977, 931, 841, 751. Anal. Calcd for $C_{27}H_{21}FN_2O_2$: C, 76.40; H, 4.99; N, 6.60. Found: C, 76.28; H, 5.03; N, 6.66.

**10f:** pale yellow solid, mp 174−176 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.72−7.70 (4H, m), 7.54 (2H, d, $J$ = 7.6 Hz), 7.44−7.33 (5H, m), 7.10 (2H, t, $J$ = 8.4 Hz), 6.90 (1H, d, $J$ = 15.8 Hz), 6.67 (1H, d, $J$ = 15.8 Hz), 6.45 (1H, s), 3.75 (2H, d, $J$ = 3.0 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 167.9, 164.0 ($J$ = 250.1 Hz), 161.8, 155.3, 141.5, 137.9, 136.1, 129.2, 128.9, 128.7 ($J$ = 9.1 Hz), 128.3, 128.0, 127.4, 125.6, 125.5 ($J$ = 3.7 Hz), 116.0 ($J$ = 22.0 Hz), 115.2, 100.4, 89.5, 47.8; MS *m*/*z* 199(100), 444 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1723, 1671, 1591, 1542, 1410, 1333, 1258, 977, 931, 841, 751. Anal. Calcd for $C_{26}H_{18}ClFN_2O_2$: C, 70.19; H, 4.08; N, 6.30. Found: C, 70.28; H, 4.03; N, 6.26.

**General Procedure for the Preparation of Polystyrene-Supported α-Selenoacetic Acids 11.** To a THF/DMF (v/v 3/1) (20 mL) swollen polystyrene-supported selenenyl bromide **1**, $NaBH_4$ (2 mmol) was added and stirred at 40 °C for 6 h. Cooled to 0 °C, bromoacetic acid (3 mmol) in THF (2 mL) was added slowly, and the mixture was stirred for another 2 h at room temperature. The resin was collected by filtration and washed successively with THF (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), 0.1 N HCl solution (10 mL), $H_2O$ (10 mL × 2), THF (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and then dried in a vacuum overnight to afford resin **11**.

**Typical Procedure for the Preparation of Polystyrene-Supported Oxadiazolyl-Substituted Selenium Resin 12.** To a suspension of the swollen polystyrene-supported α-selenoacetic acid resin **11** (1.0 g) in anhydrous 1,4-dioxane (15 mL) was added DCC (4.0 mmol) and amidoxime (2.5 mmol) under nitrogen. The mixture was stirred at 95 °C for 20 h. Resin **12** was collected by filtration, washed with hot THF (10 mL × 2) and hot EtOH (10 mL × 2), and dried in a vacuum.

**Typical Procedure for the Preparation of Oxadiazolyl- and Isoxazolinyl-Substituted Olefins (Products 15a−s).** To a suspension of the swollen resin **12** (0.5 g) in anhydrous THF (15 mL), cooled to −60 °C, was added dropwise LDA (2 M in THF/hexane, 0.3 mL) under nitrogen. After stirring for 1.5 h at −60 °C, a solution of allyl bromide (2 mmol) in anhydrous THF (1 mL) was added. The suspension was stirred for another 0.5 h at −60 °C, being slowly warmed to −40 °C over 0.5 h before quenching with $H_2O$ (1 mL). Resin **13** was collected by filtration, washed with THF (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried under vacuum.

To the suspension of the swollen resin **13** (0.5 g) in $CH_2Cl_2$ (15 mL) was added a solution of hydroximoyl halide (4.0 mmol) in $CH_2Cl_2$ (10 mL) (prepared from 4.0 mmol of aldoxime and 4.0 mmol of NCS stirring at room temperature for 3 h before use). A solution of $Et_3N$ (5 mmol) in $CH_2Cl_2$

(15 mL) was added dropwise in three portions every 8 h (each time 1.66 mmol in anhydrous $CH_2Cl_2$ (5 mL) was added). After stirring for 24 h at room temperature, resin **14** was collected by filtration, washed with THF (10 mL × 2), ether (10 mL × 2), THF/$H_2O$ (3:1) (10 mL × 2), $H_2O$ (10 mL × 2), THF (10 mL × 2), benzene (10 mL × 2), MeOH (10 mL × 2), and $CH_2Cl_2$ (10 mL × 2), and dried in a vacuum. The washed resin **14** was suspended in THF (15 mL), 30% (aq) $H_2O_2$ (0.5 mL) was added, and the mixture was stirred at 0 °C for 1 h followed by 20 min at room temperature. The mixture was filtered, and the resin was washed with $CH_2Cl_2$ (15 mL × 2). The filtrate was washed with $H_2O$ (30 mL × 2), dried over $MgSO_4$, and evaporated to dryness under vacuum to obtain the crude products **15**. Further purification was via flash chromatography with *n*-hexanes−EtOAc (4:1 v/v) as the eluent for $^{13}C$ NMR and microanalyses.

**15a:** pale yellow solid, mp 138−140 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.96 (2H, d, $J$ = 8.0 Hz), 7.61 (2H, d, $J$ = 8.4 Hz), 7.39 (2H, d, $J$ = 8.4 Hz), 7.28 (2H, d, $J$ = 8.0 Hz), 7.12 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.83 (1H, d, $J$ = 16.0 Hz), 5.47−5.44 (1H, m), 3.65 (1H, dd, $J_1$ = 10.4 Hz, $J_2$ = 16.4 Hz), 3.25 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz), 2.41 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.7, 168.7, 155.2, 141.9, 141.6, 136.5, 129.6, 129.1, 128.0, 127.4, 127.3, 123.8, 115.0, 79.6, 40.6, 21.5; MS *m*/*z* 132 (100), 365 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3032, 2918, 1671, 1615, 1546, 1353, 1091, 905, 828, 750, 509. Anal. Calcd for $C_{20}H_{16}ClN_3O_2$: C, 65.67; H, 4.41; N, 11.49. Found: C, 65.77; H, 4.36; N, 11.55.

**15b:** pale yellow solid, mp 94−95 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 8.08−8.04 (2H, m), 7.61 (2H, d, $J$ = 8.0 Hz), 7.54 (2H, d, $J$ = 8.0 Hz), 7.45−7.30 (6H, m), 7.15 (2H, t, $J$ = 8.6 Hz), 6.79 (1H, d, $J$ = 16.0 Hz), 3.77 (2H, d, $J$ = 4.0 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.2, 167.9, 164.6 ($J$ = 250.5 Hz), 15.2, 145.8, 140.5, 136.5, 129.5 ($J$ = 8.7 Hz), 129.1, 129.0, 128.5, 127.9, 127.5, 125.5, 122.9 ($J$ = 3.2 Hz), 116.0 ($J$ = 22.0 Hz), 113.1, 89.4, 47.2; MS *m*/*z* 128 (100), 445 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3028, 2924, 1662, 1596, 1410, 917, 830, 751, 695. Anal. Calcd for $C_{25}H_{17}FClN_3O_2$: C, 67.34; H, 3.84; N, 9.42. Found: C, 67.41; H, 3.91; N, 9.38.

**15c:** pale yellow solid, mp 77−78 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.97 (2H, d, $J$ = 8.0 Hz), 7.29 (2H, d, $J$ = 8.0 Hz), 7.06 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.77 (1H, d, $J$ = 16.0 Hz), 5.51−5.48 (1H, m), 4.37 (2H, q, $J$ = 7.2 Hz), 3.54 (1H, dd, $J_1$ = 11.6 Hz, $J_2$ = 17.6 Hz), 3.17 (1H, dd, $J_1$ = 7.6 Hz, $J_2$ = 17.6 Hz), 2.41 (3H, s), 1.38 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.4, 168.8, 160.1, 151.2, 141.7, 140.6, 129.6, 127.3, 123.7, 115.4, 81.5, 62.4, 39.3, 21.6, 14.1; MS *m*/*z* 132 (100), 327 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2928, 1738, 1668, 1615, 1596, 1547, 1240, 920, 827, 749, 506. Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; N, 12.84. Found: C, 62.31; H, 5.18; N, 12.90.

**15d:** pale yellow solid, mp 103−104 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.95 (2H, d, $J$ = 8.0 Hz), 7.48−7.28 (8H, m), 6.72 (1H, d, $J$ = 16.0 Hz), 4.35 (2H, q, $J$ = 7.2 Hz), 3.67 (2H, d, $J$ = 2.0 Hz), 2.41 (3H, s), 1.37 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.7, 168.8, 160.1, 151.2, 144.4, 141.6, 139.6, 129.6, 129.1, 128.8, 127.3, 125.4, 123.8, 113.6, 91.7, 62.4, 45.9, 21.5, 14.1; MS *m*/*z* 84 (100), 404 ($M^+$ + 1); IR $\nu_{max}$ ($cm^{-1}$) 3028, 2983, 1713, 1672, 1592, 1557, 1271, 936, 831, 748, 704. Anal. Calcd for $C_{23}H_{21}N_3O_4$: C, 68.47; H, 5.25; N, 10.42. Found: C, 68.56; H5.18; N, 10.51.

**15e:** pale yellow solid, mp 141−142 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.95 (2H, d, $J$ = 8.0 Hz), 7.54−7.28 (12H, m), 6.78 (1H, d, $J$ = 16.0 Hz), 3.77 (2H, d, $J$ = 2.8 Hz), 2.40 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.0, 168.7, 155.3, 145.5, 141.6, 140.5, 132.0, 129.5, 129.0, 128.5, 128.1, 128.0, 127.3, 125.6, 124.9, 123.8, 113.3, 89.5, 47.1, 21.5; MS *m*/*z* 128 (100), 485 ($M^+$), 487 ($M^+$ + 2); IR $\nu_{max}$ ($cm^{-1}$) 3025, 2977, 1661, 1595, 1555, 1360, 910, 830, 751, 697. Anal. Calcd for $C_{26}H_{20}BrN_3O_2$: C, 64.21; H, 4.14; N, 8.64. Found: C, 64.33; H, 4.07; N, 8.55.

**15f:** pale yellow solid, mp 137−179 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 7.94 (2H, d, $J$ = 8.0 Hz), 7.60 (2H, d, $J$ = 8.4 Hz), 7.54−7.33 (8H, m), 7.25 (2H, d, $J$ = 8.0 Hz), 6.78 (1H, d, $J$ = 16.0 Hz), 3.76 (2H, d, $J$ = 2.0 Hz), 2.39 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.0, 168.7, 155.3, 145.6, 141.6, 140.6, 136.5, 129.6, 129.1, 129.0, 128.5, 127.9, 127.6, 125.6, 124.9, 123.9, 113.3, 89.5, 47.1, 21.5; MS *m*/*z* 128 (100), 442 ($M^+$ + 1); IR $\nu_{max}$ ($cm^{-1}$) 3025, 1662, 1595, 1557, 1406, 1360, 1093, 910, 828, 748, 699, 553. Anal. Calcd for $C_{26}H_{20}ClN_3O_2$: C, 70.67; H, 4.56; N, 9.51. Found: C, 70.77; H, 4.67; N, 9.42.

**15g:** low point solid. $^1H$ NMR ($CDCl_3$) $\delta$ 7.94 (2H, d, $J$ = 8.0 Hz), 7.56−7.52 (4H, m), 7.43−7.33 (4H, m), 7.25 (2H, d, $J$ = 8.4 Hz), 7.19 (2H, d, $J$ = 8.0 Hz), 6.78 (1H, d, $J$ = 16.0 Hz), 3.77 (2H, s), 2.38 (3H, s), 2.34 (3H, s); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.1, 168.7, 156.1, 145.9, 141.5, 140.9, 140.8, 129.6, 129.5, 128.9, 128.3, 127.3, 126.7, 126.2, 125.6, 123.9, 113.1, 88.9, 47.4, 21.5, 21.4; MS *m*/*z* 128 (100), 421 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3025, 1662, 1595, 1557, 1409, 1366, 911, 830, 756, 698. Anal. Calcd for $C_{27}H_{23}N_3O_2$: C, 76.94; H, 5.50; N, 9.97. Found: C, 76.85; H, 5.42; N, 10.06.

**15h:** pale yellow solid, mp 92−94 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 8.08−8.05 (2H, m), 7.48−7.38 (5H, m), 7.32 (1H, d, $J$ = 16.0 Hz), 7.16 (2H, t, $J$ = 8.8 Hz), 6.72 (1H, d, $J$ = 16.0 Hz), 4.36 (2H, q, $J$ = 7.2 Hz), 3.67 (2H, d, $J$ = 3.6 Hz), 1.37 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 174.0, 167.9, 164.6 ($J$ = 250.4 Hz), 160.0, 151.1, 144.7, 139.6, 129.5 ($J$ = 9.2 Hz), 129.1, 128.8, 125.4, 122.8 ($J$ = 3.8 Hz), 116.0 ($J$ = 21.9 Hz), 113.4, 91.6, 62.4, 45.9, 14.1; MS *m*/*z* 128 (100), 407 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3025, 2983, 1721, 1660, 1601, 1547, 1410, 1270, 973, 833, 748, 698, 627. Anal. Calcd for $C_{22}H_{18}FN_3O_4$: C, 64.86; H, 4.45; N, 10.31. Found: C, 64.91; H, 4.37; N, 10.38.

**15i:** low point solid. $^1H$ NMR ($CDCl_3$) $\delta$ 8.08 (2H, d, $J$ = 7.6 Hz), 7.51−7.47 (3H, m), 7.07 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.78 (1H, d, $J$ = 16.0 Hz), 5.53−5.47 (1H, m), 4.37 (2H, q, $J$ = 7.2 Hz), 3.54 (1H, dd, $J_1$ = 11.6 Hz, $J_2$ = 17.6 Hz), 3.17 (1H, dd, $J_1$ = 7.6 Hz, $J_2$ = 17.6 Hz), 1.38 (3H, t, $J$ = 7.2 Hz); $^{13}C$ NMR ($CDCl_3$) $\delta$ 173.6, 168.7, 160.0, 151.2, 140.7, 131.3, 128.9, 127.4, 126.6, 115.4, 81.4, 62.4, 39.4, 14.1; MS *m*/*z* 119 (100), 313 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3029, 2924, 1735, 1666, 1596, 1580, 1410, 1240, 920, 827, 758, 691, 542. Anal. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.83; N, 13.41. Found: C, 61.27; H, 4.77; N, 13.47.

**15j:** pale yellow solid, mp 132−133 °C. $^1H$ NMR ($CDCl_3$) $\delta$ 8.09−8.06 (2H, m), 7.60 (2H, d, $J$ = 8.0 Hz), 7.51−7.48 (3H, m), 7.39 (2H, d, $J$ = 8.0 Hz), 7.14 (1H, dd, $J_1$ = 5.6

Hz, $J_2$ = 16.0 Hz), 6.83 (1H, d, $J$ = 16.0 Hz), 5.49−5.43 (1H, m), 3.65 (1H, dd, $J_1$ = 10.4 Hz, $J_2$ = 16.4 Hz), 3.25 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 173.9, 168.8, 155.2, 142.0, 136.5, 131.2, 131.2, 129.1, 129.9, 128.0, 127.4, 126.6, 114.9, 79.5, 40.6; MS *m*/*z* 55 (100), 351 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2924, 1670, 1595, 1549, 1360, 1093, 976, 889, 828, 732, 693. Anal. Calcd for $C_{19}H_{14}ClN_3O_2$: C, 64.87; H, 4.01; N, 11.94. Found: C, 64.95; H, 4.07; N, 11.87.

**15k:** pale yellow solid, mp 128 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.09−8.06 (2H, m), 7.56 (2H, d, $J$ = 8.0 Hz), 7.50−7.47 (3H, m), 7.22 (2H, d, $J$ = 8.0 Hz), 7.14 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.83 (1H, d, $J$ = 16.0 Hz), 5.49−5.43 (1H, m), 3.66 (1H, dd, $J_1$ = 10.8 Hz, $J_2$ = 16.4 Hz), 3.27 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz), 2.38 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.0, 168.7, 156.1, 142.4, 140.8, 131.2, 129.5, 128.8, 127.4, 126.7, 126.1, 114.7, 79.1, 40.8, 21.4; MS *m*/*z* 91(100), 331 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2920, 1668, 1548, 1445, 1360, 978, 904, 823, 735, 693, 542. Anal. Calcd for $C_{20}H_{17}N_3O_2$: C, 72.49; H, 5.17; N, 12.68. Found: C, 72.61; H, 5.11; N, 12.79.

**15l:** pale yellow solid, mp 111−112 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.09−8.06 (2H, m), 7.61 (2H, d, $J$ = 7.2 Hz), 7.50−7.47 (3H, m), 7.14 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.92 (2H, d, $J$ = 7.2 Hz), 6.83 (1H, d, $J$ = 16.0 Hz), 5.42−5.39 (1H, m), 3.84 (3H, s), 3.65 (1H, dd, $J_1$ = 10.8 Hz, $J_2$ = 16.4 Hz), 3.27 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.0, 168.7, 161.4, 155.7, 142.6, 131.2, 128.8, 128.3, 127.4, 126.7, 121.4, 114.7, 114.2, 79.1, 55.4, 40.9; MS *m*/*z* 347 (100, $M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2920, 1669, 1607, 1545, 1364, 1253, 1179, 976, 835, 733, 695. Anal. Calcd for $C_{20}H_{17}N_3O_3$: C, 69.15; H, 4.93; N, 12.10. Found: C, 69.05; H, 4.99; N, 12.01.

**15m:** low point solid. $^1$H NMR ($CDCl_3$) $\delta$ 7.99 (2H, d, $J$ = 8.4 Hz), 7.57−7.53 (4H, m), 7.44−7.35 (6H, m), 7.20 (2H, d, $J$ = 8.0 Hz), 6.78 (1H, d, $J$ = 15.8 Hz), 3.78 (2H, d, $J$ = 2.8 Hz), 2.37 (3H, s); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.5, 167.9, 156.1, 146.3, 140.9, 140.8, 137.4, 129.5, 129.2, 128.9, 128.7, 128.4, 126.7, 126.1, 125.6, 125.2, 112.9, 88.9, 47.5, 21.4; MS *m*/*z* 128 (100), 441 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3028, 2928, 1664, 1597, 1558, 1410, 1360, 911, 828, 749, 697, 554. Anal. Calcd for $C_{26}H_{20}ClN_3O_2$: C, 70.67; H, 4.56; N, 9.51. Found: C, 70.78; H, 4.47; N, 9.59.

**15n:** pale yellow solid, mp 160−161 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.02 (2H, d, $J$ = 6.8 Hz), 7.61 (2H, d, $J$ = 6.8 Hz), 7.46 (2H, d, $J$ = 6.8 Hz), 7.40 (2H, d, $J$ = 6.8 Hz), 7.14 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.83 (1H, d, $J$ = 16.0 Hz), 5.50−5.45 (1H, m), 3.66 (1H, dd, $J_1$ = 10.8 Hz, $J_2$ = 16.4 Hz), 3.25 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.1, 168.0, 155.2, 142.3, 137.4, 136.6, 129.2, 129.1, 128.7, 128.0, 127.4, 125.2, 114.8, 79.5, 40.6; MS *m*/*z* 55 (100), 385 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3028, 2925, 1671, 1615, 1546, 1403, 905, 828, 746, 510. Anal. Calcd for $C_{19}H_{13}Cl_2N_3O_2$: C, 59.08; H, 3.39; N, 10.88. Found: C, 58.97; H, 3.31; N, 10.99.

**15o:** pale yellow solid, mp 120−122 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.00 (2H, d, $J$ = 8.4 Hz), 7.53−7.35 (12H, m), 6.79 (1H, d, $J$ = 16.0 Hz), 3.78 (2H, d, $J$ = 5.2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$174.4, 167.9, 155.4, 145.9, 140.5, 137.4, 132.1, 129.2, 129.0, 128.7, 128.5, 128.1, 127.9, 125.5, 125.2, 124.9, 113.1, 89.4, 47.2; MS *m*/*z* 128 (100), 506 ($M^+$), 506 ($M^+ + 2$); IR $\nu_{max}$ ($cm^{-1}$) 3025, 2924, 1665, 1595, 1557, 918, 829, 754, 695. Anal. Calcd for $C_{25}H_{17}BrClN_3O_2$: C, 59.25; H, 3.38; N, 8.29. Found: C, 59.38; H, 3.32; N, 8.40.

**15p:** pale yellow solid, mp 98−99 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.02 (2H, d, $J$ = 8.4 Hz), 7.46 (2H, d, $J$ = 8.4 Hz), 7.07 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.78 (1H, d, $J$ = 16.0 Hz), 5.53−5.49 (1H, m), 4.37 (2H, q, $J$ = 7.2 Hz), 3.55 (1H, dd, $J_1$ = 11.6 Hz, $J_2$ = 17.6 Hz), 3.17 (1H, dd, $J_1$ = 7.6 Hz, $J_2$ = 17.6 Hz), 1.38 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 173.8, 168.0, 160.1, 151.2, 141.0, 137.5, 129.2, 128.7, 125.1, 115.2, 81.3, 62.4, 39.4, 14.1; MS *m*/*z* 199 (100), 347 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2933, 1723, 1671, 1591, 1542, 1410, 1333, 1258, 977, 931, 841, 751. Anal. Calcd for $C_{16}H_{14}ClN_3O_4$: C, 55.26; H, 4.06; N, 12.08. Found: C, 55.37; H, 4.13; N, 12.16.

**15q:** pale yellow solid, mp 148−150 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.01 (2H, d, $J$ = 8.4 Hz), 7.61 (2H, d, $J$ = 8.8 Hz), 7.45 (2H, d, $J$ = 8.4 Hz), 7.14 (1H, dd, $J_1$ = 5.6 Hz, $J_2$ = 16.0 Hz), 6.92 (2H, d, $J$ = 8.8 Hz), 6.82 (1H, d, $J$ = 16.0 Hz), 5.44−5.38 (1H, m), 3.84 (3H, s), 3.65 (1H, dd, $J_1$ = 11.2 Hz, $J_2$ = 16.4 Hz), 3.26 (1H, dd, $J_1$ = 7.2 Hz, $J_2$ = 16.4 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.2, 167.9, 161.4, 155.7, 142.9, 137.4, 129.1, 128.7, 128.4, 125.2, 121.3, 114.5, 114.2, 79.0, 55.4, 40.9; MS *m*/*z* 149 (100), 381 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2932, 1670, 1610, 1550, 1518, 1409, 1362, 1258, 1179, 1093, 973, 896, 832, 751, 540. Anal. Calcd for $C_{20}H_{16}ClN_3O_3$: C, 62.91; H, 4.22; N, 11.01. Found: C, 62.77; H, 4.17; N, 11.12.

**15r:** pale yellow solid, mp 129−130 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.27 (2H, d, $J$ = 8.6 Hz), 7.99 (2H, d, $J$ = 8.0 Hz), 7.85 (2H, d, $J$ = 8.6 Hz), 7.55−7.37 (8H, m), 6.79 (1H, d, $J$ = 16.0 Hz), 3.84 (2H, d, $J$ = 4.8 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$174.2, 167.9, 154.6, 148.7, 145.4, 140.1, 137.5, 135.0, 129.2, 129.1, 128.7, 128.6, 127.4, 125.5, 125.1, 124.1, 113.3, 90.3, 46.8; MS *m*/*z* 128 (100), 472 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 2930, 1675, 1611, 1518, 1409, 1350, 1093, 915, 824, 758, 699, 540. Anal. Calcd for $C_{19}H_{13}ClN_4O_4$: C, 57.51; H, 3.30; N, 14.12. Found: C, 57.40; H, 3.22; N, 14.01.

**15s:** pale yellow solid, mp 119−121 °C. $^1$H NMR ($CDCl_3$) $\delta$ 8.00 (2H, d, $J$ = 8.4 Hz), 7.48−7.31 (8H, m), 6.73 (1H, d, $J$ = 16.0 Hz), 4.36 (2H, q, $J$ = 7.2 Hz), 3.68 (2H, d, $J$ = 4.4 Hz), 1.37 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR ($CDCl_3$) $\delta$ 174.1, 160.0, 151.1, 144.8, 139.6, 137.4, 129.2, 129.0, 128.8, 128.7, 125.4, 125.1, 113.4, 91.6, 62.4, 45.9; MS *m*/*z* 128 (100), 423 ($M^+$); IR $\nu_{max}$ ($cm^{-1}$) 3078, 2982, 1722, 1660, 1602, 1545, 1409, 1351, 1271, 1251, 1126, 971, 933, 836, 748, 696, 616. Anal. Calcd for $C_{22}H_{18}ClN_3O_4$: C, 62.34; H, 4.28; N, 9.91. Found: C, 62.47; H, 4.37; N, 9.83.

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**Supporting Information Available.** $^1$H NMR and $^{13}$C NMR spectra of all the products and parts and HPLC spectra of **6a**, **6g**, **10a**, **10i**, **15d**, **15n**. This material is available free of charge via the Internet at http://pubs.acs.org.

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