Traceless Solid-Phase Synthesis of 3-Substituted Isoxazoles and 3-Substituted 5-Iodoisoxazolines Using Polystyrene-Supported Vinyl Selenide

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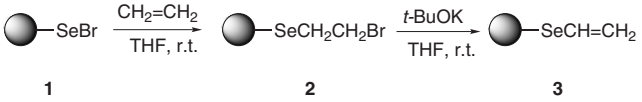
Abstract: A novel facile procedure for the traceless solid-phase synthesis of 3-substituted isoxazoles and 3-substituted 5-iodoisoxazolines in good yields and with excellent purities using polymer-supported vinyl selenide is described. The polymeric reagent can be regenerated and reused as an environmentally benign reagent.

Key words: solid-phase organic synthesis, polymer-supported vinyl selenide, isoxazole, isoxazoline

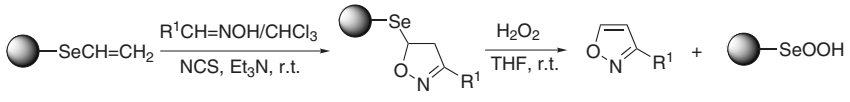
Polymer-supported reagents have attracted growing interest because they have provided attractive and practical methods for combinatorial chemistry and solid-phase organic synthesis (SPOS) in recent years.[1] Synthesis on a polymer support shows a number of advantages compared to solution chemistry. The most salient is the possibility to apply an excess of reagents and remove them without involving time-consuming separation techniques. Now, the synthesis of highly diverse organic molecule libraries using SPOS methodology is recognized as a valuable tool for the acceleration of drug discovery. Isoxazole and isoxazoline moieties, which are typically prepared by the 1,3-dipolar cycloaddition of a nitrile oxide to alkynes and alkenes, represent two classes of unique pharmacophores that are observed in many therapeutic agents and are versatile intermediates for the synthesis of complex natural products.[2] It is therefore not surprising that these compounds have been both widely studied and used, in particular in combinatorial synthesis and some methods for their preparation have been transferred to the solid-phase in recent years.[3] Since the first organoselenium resin[4] used in SPOS with the combined advantage of decreased volatility and simplification of product work-up was reported in 1976, several research groups[5] including ours[6] have developed selenium-based approaches for SPOS. More recently, we reported 3-substituted-5-iodomethyl isoxazolines, isoxazoline-containing 1,2-di-heterocyclic substituted compounds using a polystyrene-supported allyl selenide reagent.[7] In continuation of our interest in solid-phase organoselenium chemistry, we wish to describe another simple and efficient traceless solid-phase synthetic approach to 3-substituted isoxazoles and 3-substituted 5-iodoisoxazolines based on a novel polystyrene-supported vinyl selenide (Scheme 1).



1 2 3

Scheme 1

Treatment of polymer-supported β-bromoethyl selenide **2**[6e] easily prepared from polystyrene-bound selenenyl bromide **1**[5a] with *t*-BuOK in THF at room temperature afforded the vinyl selenide resin **3** (Scheme 1), which was evidenced by its FT-IR spectrum with the complete disappearance of the C–Br (572 cm^{-1}) absorption and the absence of bromine from the elemental analysis. According to the classical method, resin **3** was allowed to react with nitrile oxides generated in situ from oximes and NCS in the presence of triethylamine to form the isoxazoline resin **4**, which exhibited a weaker C=N stretching band at 1606–1620 cm^{-1}. As expected, the newly loaded resins when treated with excess 30% hydrogen peroxide at room temperature resulted in the facile oxidation of the selenide to the corresponding selenoxide. A *syn*-elimination of the selenoxide resulted in the release of 3-substituted isoxazoles **5** (Scheme 2) in good yields and with excellent purities in excess of 95% (Table 1). The residual resin **6**, polystyrene-supported phenylseleninic acid, was obtained as a by-product, whose IR data were identical to the previously reported data.[8] The polystyrene-supported phenylseleninic acid could be converted to resin **1** and recycled by treatment with potassium iodide and sodium thiosulfate[6c,9] followed by bromine.[6a] For example, 3-phe-



3 4 5 6

Scheme 2

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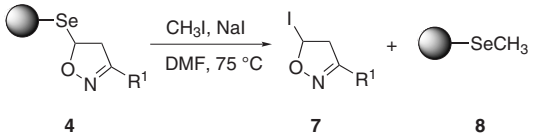
nyl isoxazole (**5a**) was obtained in 85% yield under the same reaction conditions using the recovered selenenyl bromide resin **1** (second run), and in 80% yield after being recycled for a second time (i.e. third run). It was shown that recycling the resin two to three times led to a gradual deterioration of the resin **1**.

Table 1 Yields and Purities of 3-Substituted Isoxazoles **5**

Entry	R^1	Products	Yield (%)[a]	Purity (%)[b]
1	Ph	**5a**	88	>95
2	*p*-MeC_6H_4	**5b**	87	>95
3	*p*-$NO_2C_6H_4$	**5c**	80	>95
4	*p*-ClC_6H_4	**5d**	82	>95
5	*m*-ClC_6H_4	**5e**	83	>95
6	2,6-$Cl_2C_6H_3$	**5f**	83	>95
7	*p*-FC_6H_4	**5g**	84	>95
8	2-furyl	**5h**	85	>95
9	$PhCH_2CH_2$	**5i**	84	>95
10	*n*-Pr	**5j**	78	>95

[a] Overall yields based on polymer-supported selenium bromide **1** (1.18 mmol Br/g).
[b] Determined from the ^1H NMR spectrum of the crude cleavage product.



Scheme 3

Another cleavage protocol for traceless cleavage of resin **4** employs methyl iodide and sodium iodide in DMF,[7b] and we applied this to isoxazoline resin **4** (Scheme 3). It was shown that 3-substituted 5-iodoisoxazolines **7** could be obtained in moderate to good yields with good purity (Table 2). It should be noted that the regenerated polystyrene-supported methyl selenide **8** could be easily converted into polystyrene-supported selenium bromide **1** by treatment with bromine.[5a] To show the reactivity of the regenerated polymeric reagent, the conversion of polystyrene-supported selenium bromide **1** into 3-phenyl 5-iodoisoxazoline (**7a**) was repeated four times. The purity of **7a** (Table 2, entry 7), remained almost the same as the originally prepared selenium bromide resin but with a slight decrease in yield.

In conclusion, an efficient and convenient method for the traceless solid-phase synthesis of 3-substituted isoxazoles and 3-substituted 5-iodoisoxazolines in good yields and purities employing a selenium-based traceless linker strategy has been developed. Simple work-up procedure replaces the time-consuming isolation and purification steps in the corresponding solution-phase synthesis. Moreover, the polymeric reagent can be regenerated and reused as an environmentally benign reagent.

Table 2 Yields and Purities of 3-Substituted 5-Iodoisoxazolines **7**

Entry	R^1	Products	Yield (%)[a]	Purity (%)[b]
1	Ph	**7a**	85	>95
2	*p*-MeC_6H_4	**7b**	84	>95
3	*p*-$NO_2C_6H_4$	**7c**	78	>95
4	*p*-ClC_6H_4	**7d**	82	>95
5	*n*-Pr	**7j**	80	>95
6	Ph	**7a**[c]	82	>95
7	Ph	**7a**[d]	80	>95

[a] Overall yields based on polymer-supported selenium bromide **1** (1.18 mmol Br/g).
[b] Determined by ^1H NMR spectroscopy of the crude cleavage product.
[c] With the third regenerated resin **1**.
[d] With the fourth regenerated resin **1**.

Mps were uncorrected. ^1H 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 internal standard. MS (EI, 70 eV) were recorded on a HP5989B mass spectrometer. FT-IR spectra were taken on a Perkin-Elmer SP One FT-IR spectrophotometer. Microanalyses were performed with a PE 2400 elemental analyzer. Polystyrene (H 1000, 100–200 mesh, cross-linked with 1% divinylbenzene) for the preparation of polystyrene-supported selenium bromide and other starting materials were purchased from commercial suppliers and used without further purification. DMF was distilled from CaH_2 and THF was distilled from Na/benzophenone immediately prior to use. Selenyl bromide was prepared according to a known procedure.[5a]

Polystyrene-Supported Vinyl Selenide 3

THF (10 mL) saturated with anhyd ethane was added to the polystyrene-bound selenenyl bromide **1** (1.0 g, 1.18 mmol). The deep-red coloration of the polymer disappeared instantly and the mixture was stirred at r.t. for 5 min. After removal of the solvent, the yellow resin **2** containing 1.14 mmol of Br was obtained and then swelled in THF (5 mL). A solution of *t*-BuOK (1.50 mmol) in THF (10 mL) was added under a N_2 atmosphere. The mixture was stirred at r.t. for 5 h and then filtered. The polymer was washed successively with H_2O, THF, MeOH, and CH_2Cl_2 (2 × 5 mL of each) and then dried under vacuum to afford resin **3**.

FT-IR (KBr): 3059, 2934, 1578, 1478, 1436, 1170, 1022, 736, 690, 471 cm^{-1}.

3-Substituted Isoxazoles 5; General Procedure

To a stirred solution of NCS (4 mmol) in anhyd $CHCl_3$ (5 mL) was added aldoxime (4 mmol) under a N_2 atmosphere at r.t. in one portion. Resin **3** (1.0 mmol) was added after chlorination was complete (ca. 20 min), then Et_3N (4.5 mmol) in $CHCl_3$ (2 mL) was added dropwise over ca. 10 min. The mixture was stirred at r.t. for 12 h and then filtered, the polymer was filtered and washed successively with THF, MeOH, H_2O, and CH_2Cl_2 (2 × 5 mL of each) to funish a yellow resin **4**. The washed resin **4** was pre-swollen with THF (15 mL), then treated with 30% H_2O_2 (1.0 mL, 11.6 mmol) and stirred at r.t. for 30 min. The residual resin was filtered off and washed with Et_2O (4 × 3 mL). The filtrate was treated with a sat. solution of $NaHCO_3$

and extracted with Et_2O (2 × 20 mL). The organic layer was washed with H_2O (20 mL), dried over anhyd $MgSO_4$, and concentrated to afford **5a–k**.

3-Phenylisoxazole (5a)[10]
Colorless oil.

IR (film): 3034, 2927, 1552, 1609, 1458, 1437, 1396, 1124, 1099, 1028, 946, 763 cm^{-1}.

^1H NMR: δ = 8.46 (d, *J* = 1.7 Hz, 1 H), 7.85–7.82 (m, 2 H), 7.56–7.26 (m, 3 H), 6.67 (d, *J* = 1.7 Hz, 1 H).

3-(*p*-Methylphenyl)isoxazole (5b)
Colorless solid; mp 54–55 °C (Lit.[11] 55–56 °C).

IR (KBr): 3033, 2925, 1614, 1553, 1524, 1381, 1126, 1098, 908, 824, 776, 733 cm^{-1}.

^1H NMR: δ = 8.45 (d, *J* = 1.6 Hz, 1 H), 7.75 (d, *J* = 8.1 Hz, 2 H), 7.28 (d, *J* = 8.1 Hz, 2 H), 6.66 (d, *J* = 1.6 Hz, 1 H), 2.31 (s, 3 H).

3-(*p*-Nitrophenyl)isoxazole (5c)
Pale-yellow solid; mp 170–171 °C (Lit.[10] 169–171 °C).

IR (KBr): 3006, 2961, 1612, 1587, 1554, 1522, 1464, 1385, 1290, 1225, 1177, 1126, 1098, 1028, 880, 836, 777, 609 cm^{-1}.

^1H NMR: δ = 8.66 (d, *J* = 1.8 Hz, 1 H), 8.21 (d, *J* = 8.7 Hz, 2 H), 7.34 (d, *J* = 8.6 Hz, 2 H), 6.94 (d, *J* = 1.8 Hz, 1 H).

3-(*p*-Chlorophenyl)isoxazole (5d)
Colorless solid; mp 69–70 °C (Lit.[12] 69–71 °C).

IR (KBr): 3129, 2926, 1648, 1606, 1547, 1502, 1429, 1371, 1275, 1121, 1111, 1098, 1013, 946, 886, 834, 784 cm^{-1}.

^1H NMR: δ = 8.47 (d, *J* = 1.7 Hz, 1 H), 7.77 (d, *J* = 8.7 Hz, 2 H), 7.35 (d, *J* = 8.7 Hz, 2 H), 6.64 (d, *J* = 1.7 Hz, 1 H).

3-(*m*-Chlorophenyl)isoxazole (5e)[10]
Colorless oil.

IR (film): 3129, 2926, 1645, 1602, 1546, 1502, 1429, 1370, 1276, 1121, 1112, 1097, 1015, 945, 885, 836, 784 cm^{-1}.

^1H NMR: δ = 8.12 (d, *J* = 1.8 Hz, 1 H), 7.37–7.26 (m, 4 H), 6.35 (d, *J* = 1.8 Hz, 1 H).

3-(2,6-Dichlorophenyl)isoxazole (5f)
Colorless solid; mp 59–60 °C (Lit.[10] 59–60 °C).

IR (KBr): 3132, 2926, 1645, 1605, 1547, 1500, 1429, 1373, 1276, 1124, 1112, 1095, 1016, 945, 887, 840, 784 cm^{-1}.

^1H NMR: δ = 8.55 (d, *J* = 1.9 Hz, 1 H), 7.38–7.29 (m, 3 H), 6.46 (d, *J* = 1.9 Hz, 1 H).

3-(*p*-Fluorophenyl)isoxazole (5g)
Colorless solid; mp 35–36 °C.

IR (KBr): 3030, 2929, 1607, 1557, 1520, 1494, 1434, 1379, 1236, 1159, 1125, 1098, 885, 842, 777 cm^{-1}.

^1H NMR: δ = 8.38 (d, *J* = 1.6 Hz, 1 H), 7.77 (d, *J* = 8.1 Hz, 2 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 6.66 (d, *J* = 1.6 Hz, 1 H).

^{13}C NMR: δ = 166.1, 162.2, 134.1, 128.3, 121.0, 114.7, 102.2.

EIMS: *m*/*z* (%) = 163 (M^+, 100), 108 (48.3), 107 (61.7), 95 (80.7), 75 (52.1), 57 (49.9), 43 (41.8).

Anal. Calcd for C_9H_6NFO: C, 66.26; H, 3.71; N, 8.59. Found: C, 66.22; H, 3.65; N, 8.53.

3-(2-Furyl)isoxazole (5h)
Colorless oil.

IR (film): 3128, 2958, 2927, 1616, 1556, 1514, 1459, 1438, 1387, 1365, 1125, 1014, 872, 780 cm^{-1}.

^1H NMR: δ = 8.43 (d, *J* = 1.6 Hz, 1 H), 7.57 (dd, *J* = 1.8, 0.8 Hz, 1 H), 7.28 (dd, *J* = 3.5, 0.8 Hz, 1 H), 6.62 (d, *J* = 1.6 Hz, 1 H), 6.54 (dd, *J* = 3.5, 1.8 Hz, 1 H).

^{13}C NMR: δ = 160.9, 146.9, 146.6, 135.0, 128.3, 125.5, 102.2.

EIMS: *m*/*z* (%) = 135 (M^+, 49.2), 86 (59.7), 84 (100), 78 (52.1), 52 (53.9), 51 (50.1), 43 (40.8).

Anal. Calcd for $C_7H_5NO_2$: C, 66.22; H, 3.73; N, 10.37. Found: C, 66.16; H, 3.70; N, 10.32.

3-(2-Phenylethyl)isoxazole (5i)[13]
Colorless oil.

IR (film): 3125, 2926, 1614, 1600, 1555, 1521, 1475, 1425, 1248, 1095, 1025, 1102, 909, 746 cm^{-1}.

^1H NMR: δ = 8.01 (d, *J* = 1.6 Hz, 1 H), 7.26–7.20 (m, 2 H), 7.15–7.01 (m, 3 H), 5.92 (d, *J* = 1.6 Hz, 1 H), 2.90–2.85 (m, 4 H).

3-(Propyl)isoxazole (5j)[13]
Colorless oil.

IR (film): 3120, 2925, 1604, 1475, 1425, 1248, 1096, 1025, 1105, 910, 745 cm^{-1}.

^1H NMR: δ = 8.39 (dt, *J* = 1.6, 0.6 Hz, 1 H), 6.22 (d, *J* = 1.5 Hz, 1 H), 2.65 (t, *J* = 7.0 Hz, 2 H), 2.12–1.40 (m, 2 H), 0.99 (t, *J* = 7.0 Hz, 3 H).

3-Substituted 5-Iodoisoxazolines 7; General Procedure
To a suspension of the swollen resin **4** (1.0 g) in anhyd DMF (10 mL) was added NaI (1.0 g) and CH_3I (1.0 mL) under N_2. The mixture was stirred at 75–80 °C for 24 h and then cooled to r.t. The mixture was filtered and the resin was washed with CH_2Cl_2 (10 × 3 mL). The filtrate was washed successively with a sat. solution of $NaHCO_3$ (30 mL), a sat. solution of $Na_2S_2O_3$ (30 mL), H_2O (10 × 3 mL), dried over anhyd $MgSO_4$, and concentrated to afford product **7a–e**.

3-Phenyl-5-iodoisoxazoline (7a)
Colorless oil.

IR (film): 3056, 2954, 2887, 1625, 1500, 1435, 1108, 1040, 892, 690, 540 cm^{-1}.

^1H NMR: δ = 7.65–7.63 (m, 2 H), 7.44–7.42 (m, 3 H), 5.03 (t, *J* = 7.1 Hz, 1 H), 3.50 (d, *J* = 7.1 Hz, 2 H).

^{13}C NMR: δ = 155.4, 132.2, 128.7, 128.0, 124.9, 81.2, 41.5.

EIMS: *m*/*z* (%) = 273 (M^+).

Anal. Calcd for C_9H_8INO: C, 39.59; H, 2.95; N, 5.13. Found: C, 39.66; H, 3.02; N, 5.18.

3-(*p*-Methylphenyl)-5-iodoisoxazoline (7b)
White solid; mp 84–85 °C.

IR (film): 3052, 2958, 2927, 1630, 1599, 1495, 1377, 1105, 1098, 898, 818, 691 cm^{-1}.

^1H NMR: δ = 7.57 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 4.98 (t, *J* = 7.2 Hz, 1 H), 3.50 (d, *J* = 7.2 Hz, 2 H), 2.38 (s, 3 H).

^{13}C NMR: δ = 155.8, 140.7, 129.7, 126.8, 126.5, 80.8, 41.7, 21.5.

EIMS: *m*/*z* (%) = 287 (M^+).

Anal. Calcd for $C_{10}H_{10}INO$: C, 41.84; H, 3.51; N, 4.88. Found: C, 41.92; H, 3.63; N, 4.95.

3-(*p*-Nitrophenyl)-5-iodoisoxazoline (7c)
White solid; mp 93–94 °C.

IR (film): 3052, 2960, 2930, 1632, 1600, 1495, 1106, 1098, 895, 825, 613, 543 cm^{-1}.

^1H NMR: δ = 7.67 (d, *J* = 8.4 Hz, 2 H), 7.46 (d, *J* = 8.4 Hz, 2 H), 5.01 (t, *J* = 7.4 Hz, 1 H), 3.53 (d, *J* = 7.4 Hz, 2 H).

^{13}C NMR: δ = 155.2, 136.2, 128.8, 127.8, 127.5, 80.6, 40.8.

EIMS: *m*/*z* (%) = 307 (M^+).

Anal. Calcd for C_9H_7ClINO: C, 35.15; H, 2.29; N, 4.55. Found: C, 35.18; H, 2.37; N, 4.59.

3-(*p*-Chlorophenyl)-5-iodoisoxazoline (7d)
Pale-yellow solid; mp 124–125 °C.

IR (film): 3050, 2962, 2931, 1631, 1598, 1511, 1495, 1340, 1320, 1098, 905, 828, 752, 690 cm^{-1}.

^1H NMR: δ = 8.21 (d, *J* = 8.2 Hz, 2 H), 7.81 (d, *J* = 8.2 Hz, 2 H), 4.96 (t, *J* = 7.3 Hz, 1 H), 3.51 (d, *J* = 7.3 Hz, 2 H).

^{13}C NMR: δ = 154.2, 135.2, 127.5, 126.2, 124.1, 81.8, 40.8.

EIMS: *m*/*z* (%) = 318 (M^+).

Anal. Calcd for $C_9H_7IN_2O_3$: C, 33.99; H, 2.22; N, 8.81. Found: C, 34.08; H, 2.34; N, 8.92.

3-(Propyl)-5-iodoisoxazole (7j)
Colorless oil.

IR (film): 2965, 1618, 1600, 1495, 1378, 1100, 904, 750, 690 cm^{-1}.

^1H NMR: δ = 4.98 (t, *J* = 7.1 Hz, 1 H), 3.50 (d, *J* = 7.1 Hz, 2 H), 2.65 (t, *J* = 7.0 Hz, 2 H), 2.12–1.40 (m, 2 H), 0.99 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR: δ = 155.0, 81.8, 40.8, 39.8, 20.1, 13.6.

EIMS: *m*/*z* (%) = 239 (M^+).

Anal. Calcd for $C_6H_{10}INO$: C, 30.15; H, 4.22; N, 5.86. Found: C, 30.24; H, 4.31; N, 5.94.

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References

(1) Recent reviews on SPOS: (a) Guillier, F.; Orain, D.; Bradley, M. *Chem. Rev.* **2000**, *100*, 2091. (b) Sammelson, R. E.; Kurth, M. J. *Chem. Rev.* **2001**, *101*, 137. (c) Czarnik, A. W. *Solid-phase Organic Synthesis*, Vol. 1; Wiley: New York, **2001**. (d) Nicolaou, K. C.; Hanko, R.; Hartwig, H. *Handbook of Combinatorial Chemistry*; Wiley-VCH: Weinheim, **2002**. (e) Dolle, R. E. *J. Comb. Chem.* **2002**, *4*, 369.

(2) (a) Koiowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410. (b) Baraldi, P. G.; Barco, A.; Benneti, S.; Olllini, G. P.; Simoni, D. *Synthesis* **1987**, 857. (c) Dominguez, E.; Ibeus, E.; Matrinez de Margorta, E.; Palacious, J. K.; San Marka, E. *J. Org. Chem.* **1996**, *61*, 5435. (d) Buron, C.; Kairon, L. E.; Hslu, A. *Tetrahedron Lett.* **1997**, *38*, 8027. (e) Grunanger, P.; Vitafinzi, P. *Isoxazoles in the Chemistry of Heterocylic Compounds*, Vol. 1, Part I; Taylor, E. C., Ed.; Wiley Interscience: New York, **1991**, 1–46. (f) Pruitt, J. R.; Pinto, D. J.; Estrella, M. J.; Bostrom, L. L.; Knabb, R. M.; Wong, P. C.; Wright, M. R.; Wexler, R. R. *Bioog. Med. Chem. Lett.* **2000**, *10*, 685.

(3) (a) Franzen, R. G. *J. Comb. Chem.* **2000**, *2*, 195. (b) Dörwald, F. Z. *Organic Synthesis on Solid Phase*; Wiley-VCH: Weinheim, **2002**, Chap. 15.

(4) Michels, R.; Kato, M.; Heitz, W. *Makromol. Chem.* **1976**, *177*, 2311.

(5) (a) Nicolaou, K. C.; Pastor, J.; Barluenga, S.; Winssinger, N. *Chem. Commun.* **1998**, 1947. (b) Ruhland, T.; Andersen, K.; Pedersen, H. *J. Org. Chem.* **1998**, *63*, 9204. (c) Uehlin, L.; Wirth, T. *Org. Lett.* **2001**, *3*, 2931. (d) Fujita, K.-I.; Hashimoto, S.; Oishi, A.; Taguchi, Y. *Tetrahedron Lett.* **2003**, *44*, 3793. (e) Berlin, S.; Ericsson, C.; Engman, L. *J. Org. Chem.* **2003**, *68*, 8386. (f) Cohen, R. J.; Fox, D. L.; Salvatore, R. N. *J. Org. Chem.* **2004**, *69*, 4265.

(6) (a) Huang, X.; Sheng, S.-R. *Tetrahedron Lett.* **2001**, *42*, 9035. (b) Huang, X.; Sheng, S.-R. *J. Comb. Chem.* **2003**, *5*, 273. (c) Huang, X.; Xu, W.-M. *Tetrahedron Lett.* **2002**, *43*, 5495. (d) Xu, W. M.; Tang, E.; Huang, X. *Synthesis* **2004**, 2094. (e) Sheng, S.-R.; Liu, X.-L.; Wang, X.-C.; Xin, Q.; Song, C.-S. *Synthesis* **2004**, 2833. (f) Tang, E.; Huang, X.; Xu, W. M. *Tetrahedron* **2004**, *60*, 9963.

(7) (a) Huang, X.; Xu, W. M. *Org. Lett.* **2003**, *5*, 4649. (b) Xu, W. M.; Wang, Y.-G.; Miao, M.-Z.; Huang, X. *Synthesis* **2005**, 2143. (c) Xu, W. M.; Huang, X.; Tang, E. *J. Comb. Chem.* **2005**, *7*, 726.

(8) Zundel, G. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 499.

(9) Ferranti, F.; Filippo, D. D. *J. Chem. Soc. B* **1971**, 1925.

(10) Nunno, L. D.; Scilimati, A. *Tetrahedron* **1987**, *43*, 2181.

(11) Choji, K.; Katsumi, T.; Akira, H. *Heterocycles* **1994**, *37*, 1075.

(12) Cadogan, J. I. G.; Cameron, D. K.; Gosney, I.; Tinley, E. J.; Wyse, S. J.; Amaro, A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2081.

(13) Barber, G. N.; Olofson, R. A. *J. Org. Chem.* **1978**, *43*, 3015.