‘Long-Range’ Pummerer-Type Cyclization: A Simple and Facile Synthesis of 5-Vinyl-1,3-oxazoles

Guangyu Xu,[a] Kaixiong Chen,[a] Hongwei Zhou*[b]

[a] Chemistry & Chemical Engineering College, Hunan Normal University, Changsha 410081, P. R. of China

[b] Department of Chemistry, Zhejiang University, (Campus Xixi), Hangzhou 310028, P. R. of China
Fax +86(571)88920271; E-mail: zhouhw@zju.edu.cn

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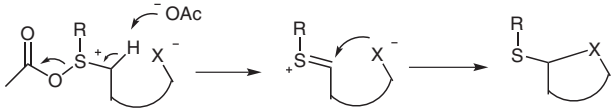
Abstract: A simple and facile Pummerer cyclization for the synthesis of substituted 5-[2-(phenylthio)vinyl]-1,3-oxazoles, which are common substructures in numerous biologically active compounds, synthetic intermediates, and pharmaceuticals, has been developed.

Key words: Pummerer reaction, cyclization, vinyl-1,3-oxazoles, heterocycles, sulfoxides

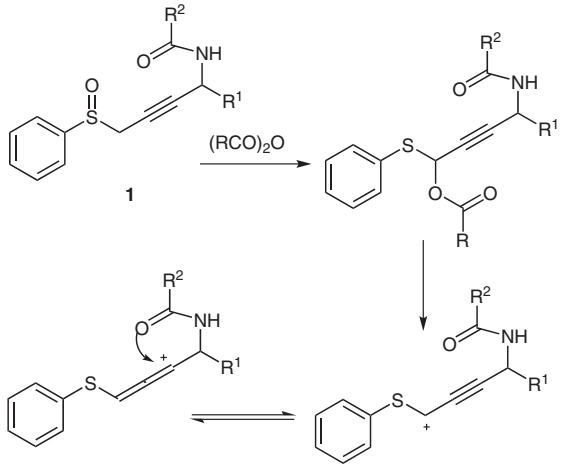
1,3-Oxazole, although not found in nature in the free state, is usually encountered as a substituted oxazole within the structures of complex natural products,[1] among which there are antitumor, antiviral, and antileukemia agents, as well as herpes simplex virus inhibitors, serine–threonine phosphatase inhibitors, antibacterials, antialgicidals, and peripheral analgesics.[2] Therefore, a large number of classical methods for the construction of oxazole ring systems have been developed;[3,4] however, the synthesis of 5-vinyl-1,3-oxazole is not well documented.[5]

The Pummerer reaction, first reported by Pummerer in 1909,[6] has been studied extensively over the past century and has received considerable attention as a synthetically useful process.[7] Generally, it involves a thionium ion intermediate, generated by the reaction of a sulfoxide with an acid anhydride, which with substitution by tethered nucleophiles provides a valuable synthetic tool for building the expected heterocycles (Scheme 1).[3a,7a,b]



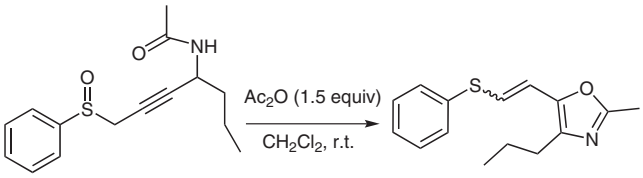
Scheme 1

N-[4-(Phenylsulfinyl)but-2-ynyl]acetamides **1**, which contain a sulfoxide and an adjacent alkynyl moiety, might undergo a ‘long-range’ Pummerer reaction. The thionium ion intermediate, produced in situ from the α-acyloxy sulfide, might give a 3-(phenylthio)allenic cation, which could be attacked intramolecularly by the oxygen of the amide to afford a cyclic derivative (Scheme 2).



Scheme 2

This proposal stimulated us to examine the cyclization of *N*-[4-(phenylsulfinyl)-1-propylbut-2-ynyl]acetamide (**1a**) under the Pummerer conditions. On the first attempt, we treated amide **1a** with acetic anhydride in dichloromethane at room temperature and obtained 2-methyl-5-[2-(phenylthio)vinyl]-4-propyl-1,3-oxazole (**2a**) in a yield of 17% with a 1:1 *E*/*Z* ratio (Scheme 3).



Scheme 3

Further screening showed that use of 1.5 equivalents of trifluoroacetic anhydride at –78 °C and then allowing the temperature of the reaction mixture to slowly warm to room temperature could give 82% yield as well as a 2:1 *E*/*Z* ratio, and that triflic anhydride, acetyl chloride, or trifluoroacetic acid gave sluggish results. Accordingly, we treated a series of *N*-[4-(phenylsulfinyl)but-2-ynyl]acetamides **1** with trifluoroacetic anhydride in dichloromethane at –78 °C, which was followed by slow warming to room temperature; the 5-[2-(phenylthio)vi-

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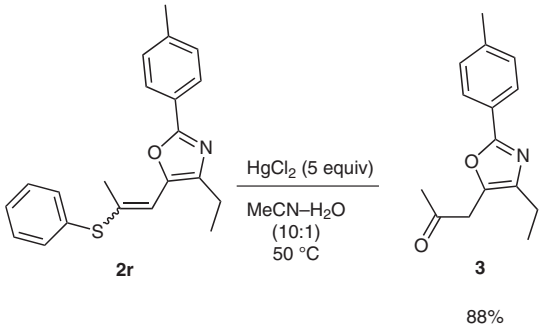
nyl]-1,3-oxazoles **2** were obtained in moderate to good yields (Table 1).

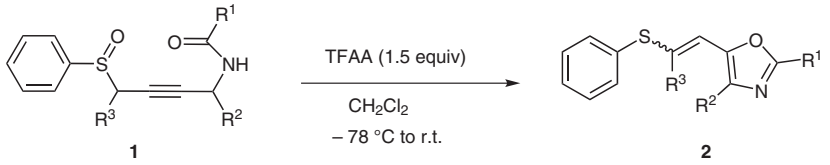
5-[2-(Phenylthio)vinyl]-1,3-oxazoles, containing a phenyl(vinyl)sulfane moiety which may react with various reagents, could be applied as useful building blocks in oxazole synthesis. We tested a mercury(II) chloride initiated hydrolysis of 4-ethyl-5-[2-(phenylthio)prop-1-enyl]-2-(4-tolyl)-1,3-oxazole (**2r**) in aqueous acetonitrile at 50 °C and obtained 1-[4-ethyl-2-(4-tolyl)-1,3-oxazol-5-yl]propan-2-one (**3**) in 88% yield (Scheme 4).



Scheme 4

In conclusion, we have developed a simple and facile Pummerer cyclization for the synthesis of substituted 5-[2-(phenylthio)vinyl]-1,3-oxazoles, which are common

Table 1 Pummerer Cyclization for the Synthesis of 5-[2-(Phenylthio)vinyl]-1,3-oxazoles **2**[a]



1 **2**

Entry	R^1	R^2	R^3	Product	*E*/*Z* ratio[b]	Yield[c] (%)
1	Me	*n*-Pr	H	**2a**	2:1	82
2	Ph	*n*-Pr	H	**2b**	1:0.9	70
3	*n*-C_5H_{11}	*n*-Pr	H	**2c**	1:0.6	52
4	Me	Et	H	**2d**	1:0.6	62
5	*n*-C_5H_{11}	Et	H	**2e**	5:1	76
6	Bn	Et	H	**2f**	3:1	63
7	*p*-Tol	Et	H	**2g**	7:1	55
8	Ph	Et	H	**2h**	3:1	57
9	*n*-C_5H_{11}	H	H	**2i**	4:1	58
10	*p*-Tol	H	H	**2j**	1:0.9	59
11	*t*-Bu	H	H	**2k**	1:1.5	80
12	*p*-Tol	*i*-Pr	H	**2l**	2:1	82
13	*n*-C_5H_{11}	*i*-Pr	H	**2m**	2:1	71
14	*n*-C_9H_{19}	*i*-Pr	H	**2n**	1:0.6	55
15	*n*-C_5H_{11}	Ph	H	**2o**	5:1	62
16	*p*-Tol	*p*-ClC_6H_4	H	**2p**	2:1	66
17	*n*-C_5H_{11}	Et	Me	**2q**	5:1[d]	78
18	*p*-Tol	Et	Me	**2r**	2.5:1[d]	58
19	Me	*p*-Tol	H	**2s**	6:1	85
20	*n*-C_5H_{11}	*p*-Tol	H	**2t**	4:1	69

[a] All reactions were run under the following conditions: amide **1** (0.5 mmol) and TFAA (0.75 mmol) in CH_2Cl_2 (3 mL) at –78 °C, followed by warming to room temperature under N_2 atmosphere for 4 h.
[b] *E*/*Z* ratio was determined from the ^1H NMR spectra.
[c] Isolated yield.
[d] *E*/*Z* ratio was determined by NOESY experiments.

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substructures in numerous biologically active compounds, synthetic intermediates, and pharmaceuticals. As a result of the simple and convenient operation, this type of reaction presented here has potential utility in organic synthesis.

All ^{1}H NMR spectra were measured in $CDCl_3$ and recorded on a Bruker Avance-400 (400 MHz) spectrometer with TMS as the internal standard. ^{13}C NMR spectra were measured in $CDCl_3$ and recorded on Bruker Avance-400 (100 MHz) spectrometer with TMS as the internal standard. Chemical shifts are expressed in ppm and *J* values are given in Hz. IR spectra were run on a Bruker vector 22 spectrometer. EIMS were determined with a HP5989B mass spectrometer. All the reactions in this paper were performed under nitrogen atmosphere.

4-Phenylthiobut-2-yn-1-ols; Typical Procedure

To a soln of EtMgBr (10 mmol) in THF (20 mL) was added prop-2-yne-1-thiol (10 mmol) dropwise under a N_2 atmosphere at r.t. for 3 h, which was followed by cooling in an ice-water bath and the addition of aldehyde (10 mmol). The reaction mixture was stirred for 5 h, then quenched with sat. NH_4Cl soln (50 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The extracts were dried (anhyd Na_2SO_4) and concentrated. Chromatography of the crude product on silica gel (EtOAc–petroleum ether, 1:10) afforded 4-phenylthiobut-2-yn-1-ols, generally in higher than 80% yield.

4-Phenylthiobut-2-yn-1-amines; Typical Procedure

To a soln of diisopropyl azodicarboxylate (DIAD, 6 mmol), Ph_3P (6 mmol), and 4-mercaptobut-2-yn-1-ol (5 mmol) in THF (10 mL) was added a soln of phthalimide (5 mmol) in THF (15 mL) at 0 °C, which was followed by warming to r.t. for 10 h. The reaction mixture was quenched with H_2O (30 mL) and extracted with Et_2O (3 × 20 mL). The extracts were dried (anhyd Na_2SO_4) and concentrated. Chromatography of the crude product on silica gel (EtOAc–petroleum ether, 1:20) afforded 2-[4-(phenylthio)but-2-ynyl]isoindoline-1,3-dione, generally in higher than 50% yield.

To a soln of 2-[4-(phenylthio)but-2-ynyl]isoindoline-1,3-dione (3 mmol) in EtOH (30 mL) was added anhyd NH_2NH_2 (1 mL), which was followed by refluxing for 5 h. The solvent was removed and the residue was extracted with Et_2O (3 × 15 mL). The combined organic phase, after concentration, gave the crude 4-phenylthiobut-2-yn-1-amines, generally in higher than 90% yield.

***N*-[4-(Phenylthio)but-2-ynyl]acetamides 1; General Procedure**

To a soln of $NaIO_4$ (1 mmol) in 20 mL of H_2O–MeOH (1:1) was added a soln of *N*-[1-(phenylthio)hept-2-yn-4-yl]acetamide (0.7 mmol) in MeOH (2 mL) at r.t. for 24 h. After evaporation of MeOH, the reaction mixture was diluted with H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were dried (anhyd Na_2SO_4) and concentrated. Silica gel chromatography of the crude product (EtOAc–petroleum ether, 1:2) afforded **1**, generally in higher than 90% yield.

5-[2-(Phenylthio)vinyl]-1,3-oxazoles 2; General Procedure

To a soln of a *N*-[4-(phenylthio)but-2-ynyl]acetamide **1** (0.5 mmol) in anhyd CH_2Cl_2 (3 mL) was added TFAA (0.75 mmol) under a N_2 atmosphere at –78 °C, which was followed by warming to r.t. for 4 h. The reaction mixture was quenched with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were dried (anhyd Na_2SO_4) and concentrated. Chromatography of the crude product on silica gel (petroleum ether) afforded the desired product **2** in 52–85% yield.

2-Methyl-5-[2-(phenylthio)vinyl]-4-propyl-1,3-oxazole (2a)

Yield: 106 mg (82%).

IR (neat): 1577, 1703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.48 (d, *J* = 7.2 Hz, 1 H), 7.42–7.41 (d, *J* = 7.2 Hz, 2 H), 7.38–7.33 (m, 3 H), 7.31–7.26 (m, 1.5 H), 6.74–6.70 (d, *J* = 14.8 Hz, 1 H), 6.49–6.45 (d, *J* = 14.8 Hz, 1 H), 6.36–6.34 (d, *J* = 11.2 Hz, 0.5 H), 6.28–6.26 (d, *J* = 11.2 Hz, 0.5 H), 2.52–2.46 (m, 3 H), 2.42 (s, 1.5 H), 2.18 (s, 3 H), 1.70–1.61 (m, 3 H), 0.96–0.89 (m, 4.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 160.3, 144.4, 144.2, 137.4, 136.0, 135.8, 134.5, 130.2, 129.9, 129.2, 129.1, 127.9, 127.2, 125.6, 122.7, 115.3, 109.8, 27.5, 27.3, 22.1, 22.0, 13.9, 13.7, 13.6, 13.6.

MS: *m*/*z* (%) = 259 (100) [M$^+$], 109 (40) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{15}H_{17}NOS$: 259.1031; found: 259.1020.

2-Phenyl-5-[2-(phenylthio)vinyl]-4-propyl-1,3-oxazole (2b)

Yield: 112 mg (70%).

IR (neat): 1550, 1582 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.15 (d, *J* = 7.4 Hz, 1.8 H), 8.05–8.02 (d, *J* = 7.4 Hz, 2 H), 7.56–7.54 (m, 1.8 H), 7.49–7.44 (m, 4.7 H), 7.44–7.40 (m, 3 H), 7.40–7.35 (m, 3.8 H), 7.33–7.27 (m, 1.9 H), 6.92–6.88 (d, *J* = 14.8 Hz, 1 H), 6.57–6.53 (d, *J* = 15.6 Hz, 1 H), 6.47–6.44 (d, *J* = 10.8 Hz, 0.9 H), 6.37–6.35 (d, *J* = 10.4 Hz, 0.9 H), 2.61–2.57 (t, *J* = 7.6 Hz, 1.8 H), 2.55–2.51 (t, *J* = 7.4 Hz, 2 H), 1.78–1.69 (m, 3.8 H), 1.01–0.95 (m, 5.7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 159.8, 144.6, 144.3, 139.9, 138.6, 136.2, 134.7, 130.6, 130.2, 130.1, 129.2, 129.2, 128.7, 128.7, 128.6, 127.4, 127.3, 127.2, 126.3, 126.3, 126.2, 125.9, 122.8, 115.7, 109.9, 28.2, 27.9, 22.4, 22.3, 13.8, 13.7.

MS: *m*/*z* (%) = 321 (100) [M$^+$], 109 (20) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{20}H_{19}NOS$: 321.1187; found: 321.1176.

2-Pentyl-5-[2-(phenylthio)vinyl]-4-propyl-1,3-oxazole (2c)

Yield: 82 mg (52%).

IR (neat): 1568, 1686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.45 (d, *J* = 7.8 Hz, 1.2 H), 7.40–7.39 (d, *J* = 7.8 Hz, 2 H), 7.34–7.31 (m, 3.2 H), 7.26–7.24 (m, 1.6 H), 6.71–6.67 (d, *J* = 15.6 Hz, 1 H), 6.48–6.44 (d, *J* = 15.6 Hz, 1 H), 6.33–6.30 (d, *J* = 11.6 Hz, 0.6 H), 6.27–6.24 (d, *J* = 11.6 Hz, 0.6 H), 2.80–2.76 (t, *J* = 7.8 Hz, 1.2 H), 2.70–2.66 (t, *J* = 7.6 Hz, 2 H), 2.48–2.44 (t, *J* = 7.8 Hz, 1.2 H), 2.42–2.39 (t, *J* = 7.4 Hz, 2 H), 1.84–1.67 (m, 3.2 H), 1.64–1.59 (m, 3.2 H), 1.38–1.31 (m, 6.4 H), 0.94–0.88 (m, 9.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 160.0, 144.2, 144.1, 137.3, 136.5, 135.7, 134.6, 130.6, 129.8, 129.5, 129.4, 127.8, 127.1, 125.3, 122.6, 115.5, 109.7, 28.8, 28.7, 28.2, 28.0, 27.6, 27.5, 27.3, 27.2, 22.6, 22.5, 22.1, 22.0, 13.9, 13.7, 13.6, 13.5.

MS: *m*/*z* (%) = 315 (100) [M$^+$], 109 (40) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{19}H_{25}NOS$: 315.1657; found: 315.1642.

4-Ethyl-2-methyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2d)

Yield: 76 mg (62%).

IR (neat): 1576, 1684 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.44 (d, *J* = 7.8 Hz, 1.2 H), 7.39–7.37 (d, *J* = 7.8 Hz, 2 H), 7.34–7.29 (m, 3.2 H), 7.24–7.21 (m, 1.6 H), 6.71–6.67 (d, *J* = 15.6 Hz, 1 H), 6.47–6.43 (d, *J* = 15.2 Hz, 1 H), 6.33–6.30 (d, *J* = 11.2 Hz, 0.6 H), 6.25–6.22 (d, *J* = 11.2 Hz, 0.6 H), 2.51–2.49 (m, 1.2 H), 2.48 (s, 1.8 H), 2.45–2.41 (m, 2 H), 2.38 (s, 3 H), 1.22–1.15 (m, 4.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.5, 160.4, 144.3, 144.2, 137.5, 136.1, 135.9, 134.6, 130.1, 129.9, 129.1, 129.0, 127.8, 127.2, 125.7, 122.8, 115.4, 109.8, 27.6, 27.5, 14.0, 13.9, 13.7, 13.6.

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MS: *m*/*z* (%) = 245 (100) [M$^+$], 109 (40) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{14}H_{15}NOS$: 245.0874; found: 245.0862.

4-Ethyl-2-pentyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2e)
Yield: 114 mg (76%).

IR (neat): 1568, 1685 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.45 (d, *J* = 7.6 Hz, 0.4 H), 7.40–7.37 (d, *J* = 7.6 Hz, 2 H), 7.34–7.29 (m, 2.4 H), 7.26–7.21 (m, 1.2 H), 6.71–6.67 (d, *J* = 15.2 Hz, 1 H), 6.49–6.45 (d, *J* = 15.2 Hz, 1 H), 6.33–6.31 (d, *J* = 10.8 Hz, 0.2 H), 6.27–6.24 (d, *J* = 10.8 Hz, 0.2 H), 2.80–2.76 (t, *J* = 7.8 Hz, 0.4 H), 2.70–2.66 (t, *J* = 7.8 Hz, 2 H), 2.54–2.43 (m, 2.4 H), 1.84–1.70 (m, 2.4 H), 1.40–1.31 (m, 4.8 H), 1.21–1.16 (m, 3.6 H), 0.90–0.86 (m, 3.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 160.0, 144.3, 144.2, 137.5, 136.6, 135.8, 134.6, 130.8, 129.9, 129.4, 129.2, 127.7, 127.4, 125.6, 122.8, 115.6, 109.8, 28.9, 28.8, 28.5, 28.4, 27.5, 27.4, 27.3, 27.1, 22.5, 22.4, 13.8, 13.7, 13.6, 13.6.

MS: *m*/*z* (%) = 301 (100) [M$^+$], 109 (20) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{18}H_{23}NOS$: 301.1500; found: 301.1508.

2-Benzyl-4-ethyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2f)
Yield: 101 mg (63%).

IR (neat): 1580, 1625 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.46 (m, 1.4 H), 7.44–7.40 (m, 2.3 H), 7.36–7.29 (m, 7.4 H), 7.29–7.24 (m, 2.7 H), 6.73–6.69 (d, *J* = 15.6 Hz, 1 H), 6.49–6.45 (d, *J* = 15.6 Hz, 1 H), 6.37–6.34 (d, *J* = 10.8 Hz, 0.35 H), 6.28–6.25 (d, *J* = 10.8 Hz, 0.35 H), 4.16 (s, 0.7 H), 4.08 (s, 2 H), 2.57–2.47 (m, 2.7 H), 1.28–1.20 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 160.9, 145.8, 145.6, 140.9, 139.8, 137.5, 136.7, 135.6, 135.5, 134.2, 133.2, 133.2, 129.7, 129.6, 129.2, 129.1, 128.8, 128.7, 128.3, 128.2, 127.1, 127.0, 126.5, 115.6, 110.1, 35.6, 35.5, 28.2, 28.1, 13.7, 13.6.

MS: *m*/*z* (%) = 321 (100) [M$^+$], 109 (20) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{20}H_{19}NOS$: 321.1187; found: 321.1178.

4-Ethyl-5-[2-(phenylthio)vinyl]-2-(4-tolyl)-1,3-oxazole (2g)
Yield: 89 mg (55%).

IR (neat): 1555, 1621 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–8.03 (d, *J* = 8.4 Hz, 0.3 H), 7.93–7.91 (d, *J* = 8.4 Hz, 2 H), 7.55–7.53 (m, 0.3 H), 7.47–7.45 (m, 2 H), 7.39–7.35 (m, 2.3 H), 7.31–7.27 (m, 1.15 H), 7.26–7.22 (m, 2.3 H), 6.89–6.85 (d, *J* = 14.8 Hz, 1 H), 6.57–6.54 (d, *J* = 15.6 Hz, 1 H), 6.45–6.43 (d, *J* = 11.2 Hz, 0.15 H), 6.37–6.34 (d, *J* = 10.4 Hz, 0.15 H), 2.67–2.54 (m, 2.3 H), 2.40 (s, 0.45 H), 2.39 (s, 3 H), 1.32–1.25 (m, 3.45 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 160.6, 144.2, 144.1, 142.8, 142.6, 142.0, 139.9, 137.2, 136.3, 135.2, 135.1, 133.1, 129.5, 129.3, 129.2, 129.0, 128.6, 128.5, 128.3, 128.2, 127.3, 127.2, 126.4, 115.5, 109.8, 28.4, 28.3, 21.5, 21.3, 13.8, 13.7.

MS: *m*/*z* (%) = 321 (100) [M$^+$], 109 (15) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{20}H_{19}NOS$: 321.1187; found: 321.1172.

4-Ethyl-2-phenyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2h)
Yield: 87 mg (57%).

IR (neat): 1580, 1625 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17–8.15 (d, *J* = 8.0 Hz, 0.7 H), 8.04–8.01 (d, *J* = 8.0 Hz, 2 H), 7.54–7.52 (m, 0.7 H), 7.48–7.39 (m, 6 H), 7.38–7.33 (m, 2.7 H), 7.30–7.26 (m, 1.35 H), 6.91–6.87 (d, *J* = 14.4 Hz, 1 H), 6.56–6.52 (d, *J* = 14.4 Hz, 1 H), 6.45–6.43 (d, *J* = 11.2 Hz, 0.35 H), 6.36–6.33 (d, *J* = 10.8 Hz, 0.35 H), 2.66–2.55 (m, 2.7 H), 1.32–1.25 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 160.4, 144.2, 144.1, 140.8, 139.8, 138.4, 138.3, 136.3, 136.1, 135.1, 134.8, 134.1, 129.8, 129.6, 129.5, 129.4, 128.8, 128.7, 128.4, 128.3, 127.8, 127.7, 126.9, 115.8, 109.9, 28.5, 28.3, 13.7, 13.6.

MS: *m*/*z* (%) = 307 (100) [M$^+$], 109 (15) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{19}H_{17}NOS$: 307.1031; found: 307.1038.

2-Pentyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2i)
Yield: 79 mg (58%).

IR (neat): 1526, 1685 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (d, *J* = 7.6 Hz, 0.25 H), 7.54–7.51 (d, *J* = 7.6 Hz, 1 H), 7.47–7.44 (m, 1.25 H), 7.39–7.35 (m, 1.25 H), 7.31–7.28 (m, 1.25 H), 7.25–7.20 (m, 2.5 H), 6.96–6.92 (d, *J* = 15.2 Hz, 1 H), 6.77–6.73 (d, *J* = 15.2 Hz, 1 H), 6.62–6.59 (d, *J* = 10.8 Hz, 0.25 H), 6.50–6.47 (d, *J* = 10.8 Hz, 0.25 H), 2.91–2.88 (t, *J* = 7.2 Hz, 0.5 H), 2.80–2.76 (t, *J* = 8.0 Hz, 2 H), 1.94–1.90 (m, 0.5 H), 1.84–1.78 (m, 2 H), 1.40–1.38 (m, 5 H), 0.95–0.91 (m, 3.75 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.1, 160.0, 142.2, 142.0, 136.8, 136.6, 135.8, 134.7, 130.5, 129.2, 129.1, 128.6, 127.6, 127.0, 125.5, 122.8, 115.6, 109.0, 28.9, 28.8, 28.5, 28.4, 27.4, 27.3, 22.5, 22.4, 13.7, 13.6.

MS: *m*/*z* (%) = 273 (100) [M$^+$], 109 (30) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{16}H_{19}NOS$: 273.1187; found: 273.1180.

5-[2-(Phenylthio)vinyl]-2-(4-tolyl)-1,3-oxazole (2j)
Yield: 86 mg (59%).

IR (neat): 1582, 1613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.98 (d, *J* = 8.0 Hz, 1.8 H), 7.92–7.90 (d, *J* = 8.0 Hz, 2 H), 7.52–7.46 (m, 4 H), 7.41–7.36 (m, 4.2 H), 7.34–7.32 (m, 2 H), 7.29–7.27 (m, 3 H), 7.26–7.23 (m, 1 H), 7.00–6.96 (d, *J* = 15.6 Hz, 1 H), 6.95 (s, 1 H), 6.58–6.56 (d, *J* = 10.8 Hz, 0.9 H), 6.49–6.47 (d, *J* = 10.8 Hz, 0.9 H), 6.44–6.40 (d, *J* = 15.2 Hz, 1 H), 2.41 (s, 3 H), 2.39 (s, 2.7 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.2, 160.4, 142.4, 142.1, 141.2, 141.0, 140.9, 139.6, 136.9, 136.2, 135.8, 135.4, 132.0, 129.2, 129.1, 129.0, 128.5, 128.4, 128.2, 128.1, 128.0, 127.8, 127.5, 126.2, 115.0, 109.1, 21.9, 21.7.

MS: *m*/*z* (%) = 293 (100) [M$^+$], 109 (20) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{18}H_{15}NOS$: 293.0874; found: 293.0882.

2-*tert*-Butyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2k)
Yield: 104 mg (80%).

IR (neat): 1557, 1583 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.43 (m, 3.4 H), 7.38–7.27 (m, 5.1 H), 7.08 (s, 1 H), 6.84–6.80 (d, *J* = 15.6 Hz, 0.7 H), 6.73 (s, 0.7 H), 6.50–6.48 (d, *J* = 10.4 Hz, 1 H), 6.41–6.39 (d, *J* = 10.8 Hz, 1 H), 6.37–6.33 (d, *J* = 15.2 Hz, 0.7 H), 1.42 (s, 9 H), 1.37 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 160.6, 142.8, 142.6, 137.8, 136.2, 135.9, 133.9, 131.6, 129.8, 129.5, 128.2, 127.4, 127.1, 125.6, 123.2, 115.8, 109.2, 34.6, 34.4, 28.6, 28.2.

MS: *m*/*z* (%) = 259 (100) [M$^+$], 109 (30) [PhS$^+$].

HRMS: *m*/*z* calcd for $C_{15}H_{17}NOS$: 259.1031; found: 259.1022.

4-Isopropyl-5-[2-(phenylthio)vinyl]-2-(4-tolyl)-1,3-oxazole (2l)
Yield: 137 mg (82%).

IR (neat): 1581, 1625 cm^{-1}.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07–8.05 (d, *J* = 8.0 Hz, 1 H), 7.97–7.95 (d, *J* = 8.0 Hz, 2 H), 7.57–7.55 (m, 1 H), 7.48–7.46 (m, 2 H), 7.40–7.36 (m, 3 H), 7.33–7.27 (m, 2.5 H), 7.25–7.23 (m, 2 H), 6.90–6.86 (d, *J* = 14.4 Hz, 1 H), 6.64–6.61 (d, *J* = 14.4 Hz, 1 H), 6.45–6.42 (d, *J* = 10.8 Hz, 0.5 H), 6.42–6.39 (d, *J* = 10.8 Hz, 0.5 H), 3.06–2.94 (m, 1.5 H), 2.41–2.39 (m, 4.5 H), 1.36–1.30 (m, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 160.0, 141.7, 141.5, 141.0, 140.8, 140.4, 139.8, 136.5, 136.1, 135.2, 135.1, 132.4, 129.6, 129.3, 129.0, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.3, 126.2, 115.3, 109.0, 33.3, 33.2, 22.2, 22.1, 21.6, 21.4.

MS: *m*/*z* (%) = 335 (100) [M^+], 109 (25) [PhS^+].

HRMS: *m*/*z* calcd for $C_{21}H_{21}NOS$: 335.1344; found: 335.1350.

4-Isopropyl-2-pentyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2m)
Yield: 112 mg (71%).

IR (neat): 1570, 1685 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.46 (m, 1 H), 7.41–7.39 (m, 2 H), 7.35–7.31 (m, 3 H), 7.30–7.22 (m, 1.5 H), 6.72–6.68 (d, *J* = 15.2 Hz, 1 H), 6.54–6.50 (d, *J* = 15.2 Hz, 1 H), 6.33–6.31 (d, *J* = 10.8 Hz, 0.5 H), 6.30–6.28 (d, *J* = 10.8 Hz, 0.5 H), 2.92–2.89 (t, *J* = 7.2 Hz, 0.5 H), 2.87–2.84 (t, *J* = 7.2 Hz, 1 H), 2.81–2.78 (t, *J* = 7.6 Hz, 1 H), 2.71–2.67 (t, *J* = 8.0 Hz, 2 H), 1.86–1.69 (m, 3 H), 1.44–1.31 (m, 6 H), 1.31–1.21 (m, 9 H), 0.95–0.84 (m, 4.5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.3, 160.2, 142.8, 142.5, 136.4, 136.0, 135.2, 134.3, 130.0, 129.5, 129.3, 128.2, 127.1, 127.0, 125.6, 122.2, 115.5, 109.1, 33.4, 33.3, 28.9, 28.8, 27.7, 27.6, 25.6, 25.4, 22.6, 22.4, 22.2, 22.0, 13.8, 13.7.

MS: *m*/*z* (%) = 315 (100) [M^+], 109 (45) [PhS^+].

HRMS: *m*/*z* calcd for $C_{19}H_{25}NOS$: 315.1657; found: 315.1668.

4-Isopropyl-2-nonyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2n)
Yield: 102 mg (55%).

IR (neat): 1570, 1686 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.48 (d, *J* = 7.2 Hz, 1.2 H), 7.43–7.41 (d, *J* = 7.2 Hz, 2 H), 7.37–7.33 (m, 3.2 H), 7.30–7.27 (m, 1.6 H), 6.73–6.69 (d, *J* = 15.6 Hz, 1 H), 6.56–6.52 (d, *J* = 15.2 Hz, 1 H), 6.35–6.33 (d, *J* = 10.8 Hz, 0.6 H), 6.32–6.29 (d, *J* = 11.2 Hz, 0.6 H), 2.94–2.85 (m, 1.6 H), 2.84–2.80 (t, *J* = 7.6 Hz, 1.2 H), 2.73–2.70 (t, *J* = 8.0 Hz, 2 H), 1.87–1.70 (m, 3.2 H), 1.44–1.22 (m, 28.8 H), 0.90–0.85 (m, 4.8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 160.4, 142.6, 142.4, 136.2, 136.0, 135.6, 134.8, 130.2, 129.8, 129.6, 128.4, 127.6, 127.5, 125.8, 122.6, 115.8, 109.2, 33.3, 33.1, 30.5, 30.3, 29.1, 29.1, 29.0, 28.9, 28.8, 28.7, 28.6, 28.2, 27.8, 27.7, 25.5, 25.4, 22.8, 22.6, 22.1, 22.0, 13.8, 13.7.

MS: *m*/*z* (%) = 371 (100) [M^+], 109 (20) [PhS^+].

HRMS: *m*/*z* calcd for $C_{23}H_{33}NOS$: 371.2283; found: 371.2288.

2-Pentyl-4-phenyl-5-[2-(phenylthio)vinyl]-1,3-oxazole (2o)
Yield: 108 mg (62%).

IR (neat): 1582, 1702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.66 (d, *J* = 7.8 Hz, 0.4 H), 7.61–7.60 (d, *J* = 7.8 Hz, 2 H), 7.53–7.49 (m, 2.4 H), 7.40–7.30 (m, 4.8 H), 7.24–7.16 (m, 2.4 H), 6.96–6.93 (d, *J* = 14.4 Hz, 1 H), 6.74–6.70 (d, *J* = 15.2 Hz, 1 H), 6.60–6.57 (d, *J* = 10.8 Hz, 0.2 H), 6.52–6.49 (d, *J* = 10.8 Hz, 0.2 H), 2.91–2.87 (t, *J* = 8.0 Hz, 0.4 H), 2.80–2.76 (t, *J* = 8.0 Hz, 2 H), 1.92–1.77 (m, 2.4 H), 1.44–1.33 (m, 4.8 H), 0.93–0.90 (m, 3.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.4, 160.2, 142.8, 142.2, 136.9, 136.6, 135.2, 134.6, 130.9, 130.3, 130.2, 130.1, 129.6, 129.4, 129.2, 129.1, 128.8, 128.6, 127.9, 127.7, 127.6, 127.0, 125.6, 122.9, 115.6, 109.1, 29.1, 28.9, 28.6, 28.4, 27.5, 27.3, 22.5, 22.4, 13.7, 13.6.

MS: *m*/*z* (%) = 349 (25) [M^+], 109 (25) [PhS^+], 77 (100) [Ph^+].

HRMS: *m*/*z* calcd for $C_{22}H_{23}NOS$: 349.1500; found: 349.1508.

4-(4-Chlorophenyl)-5-[2-(phenylthio)vinyl]-2-(4-tolyl)-1,3-oxazole (2p)
Yield: 134 mg (66%).

IR (neat): 1582, 1673 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12–8.10 (d, *J* = 7.8 Hz, 1 H), 8.00–7.97 (d, *J* = 7.8 Hz, 2 H), 7.73–7.71 (m, 1 H), 7.65–7.63 (m, 2 H), 7.59–7.57 (m, 1 H), 7.52–7.50 (m, 2 H), 7.44–7.39 (m, 6 H), 7.37–7.31 (m, 3 H), 7.28–7.27 (m, 1.5 H), 7.14–7.10 (d, *J* = 14.8 Hz, 1 H), 6.71–6.68 (d, *J* = 15.2 Hz, 1 H), 6.63 (s, 1 H), 2.44 (s, 1.5 H), 2.42 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.3, 160.5, 142.1, 142.0, 141.8, 141.2, 140.7, 139.2, 138.6, 138.3, 137.2, 137.1, 136.8, 136.1, 135.8, 135.4, 132.0, 129.2, 129.1, 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.3, 127.0, 126.0, 115.2, 109.3, 21.6, 21.5.

MS: *m*/*z* (%) = 405 (11) [M^+ + 2], 403 (20) [M^+], 109 (20) [PhS^+], 91 (100) [$MePh^+$].

HRMS: *m*/*z* calcd for $C_{24}H_{18}ClNOS$: 403.0798; found: 403.0788.

4-Ethyl-2-pentyl-5-[2-(phenylthio)prop-1-enyl]-1,3-oxazole (2q)
Yield: 123 mg (78%).

IR (neat): 1572, 1677 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.45 (m, 0.4 H), 7.42–7.40 (m, 2 H), 7.35–7.31 (m, 2.4 H), 7.29–7.27 (m, 1.2 H), 6.29 (s, 1 H), 6.24 (s, 0.2 H), 2.76–2.69 (m, 2.4 H), 2.54–2.48 (q, *J* = 8.0 Hz, 0.4 H), 2.44–2.39 (q, *J* = 7.6 Hz, 2 H), 2.23 (s, 3 H), 1.93 (s, 0.6 H), 1.79–1.70 (m, 2.4 H), 1.37–1.32 (m, 4.8 H), 1.23–1.19 (t, *J* = 7.6 Hz, 0.6 H), 1.17–1.13 (t, *J* = 7.2 Hz, 3 H), 0.92–0.84 (m, 3.6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.2, 160.1, 144.6, 144.5, 144.2, 144.0, 137.5, 136.6, 130.2, 129.3, 129.0, 128.9, 127.6, 127.2, 125.2, 122.9, 115.5, 109.3, 28.7, 28.6, 28.4, 28.3, 27.2, 27.1, 27.0, 26.9, 22.3, 22.2, 20.9, 20.7, 13.9, 13.8, 13.7, 13.6.

MS: *m*/*z* (%) = 315 (100) [M^+], 109 (15) [PhS^+].

HRMS: *m*/*z* calcd for $C_{19}H_{25}NOS$: 315.1657; found: 315.1668.

4-Ethyl-5-[2-(phenylthio)prop-1-enyl]-2-(4-tolyl)-1,3-oxazole (2r)
Yield: 97 mg (58%).

IR (neat): 1556, 1578 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00–7.97 (m, 0.8 H), 7.90–7.88 (m, 2 H), 7.56–7.52 (m, 0.8 H), 7.47–7.45 (m, 2 H), 7.39–7.31 (m, 4.2 H), 7.25–7.23 (m, 2.8 H), 6.35 (s, 1 H), 6.32 (s, 0.4 H), 2.65–2.60 (q, *J* = 7.6 Hz, 0.8 H), 2.55–2.50 (q, *J* = 7.5 Hz, 2 H), 2.39 (s, 3 H), 2.38 (s, 4.2 H), 1.98 (s, 1.2 H), 1.31–1.28 (t, *J* = 8.0 Hz, 1.2 H), 1.24–1.20 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.9, 160.7, 144.8, 144.6, 142.7, 142.3, 142.0, 141.3, 139.6, 137.0, 135.3, 135.1, 132.1, 129.5, 129.3, 129.1, 129.0, 128.8, 128.4, 128.3, 128.1, 127.4, 127.3, 126.2, 115.6, 109.2, 28.5, 28.3, 21.7, 21.6, 21.5, 21.4, 13.8, 13.7.

MS: *m*/*z* (%) = 335 (80) [M^+], 109 (20) [PhS^+], 91 (100) [$MePh^+$].

HRMS: *m*/*z* calcd for $C_{21}H_{21}NOS$: 335.1344; found: 335.1350.

2-Methyl-5-[2-(phenylthio)vinyl]-4-(4-tolyl)-1,3-oxazole (2s)
Yield: 130 mg (85%).

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IR (neat): 1582, 1709 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.51–7.46 (m, 2.4 H), 7.42–7.38 (m, 3 H), 7.37–7.34 (m, 2.3 H), 7.29–7.23 (m, 3 H), 7.17–7.13 (d, *J* = 15.2 Hz, 1 H), 6.73–6.70 (d, *J* = 10.8 Hz, 0.17 H), 6.45–6.41 (d, *J* = 15.2 Hz, 1 H), 2.80 (s, 0.5 H), 2.71 (s, 3 H), 2.39 (s, 0.5 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.8, 160.6, 144.5, 144.4, 137.8, 136.6, 135.6, 134.8, 131.9, 131.6, 130.9, 130.7, 130.6, 129.6, 129.5, 129.4, 129.2, 129.1, 128.6, 128.1, 127.6, 127.0, 125.4, 122.3, 115.6, 109.6, 21.6, 21.4, 13.9, 13.8.

MS: *m*/*z* (%) = 307 (75) [M^+], 109 (25) [PhS^+], 91 (100) [$MePh^+$].

HRMS: *m*/*z* calcd for $C_{19}H_{17}NOS$: 307.1031; found: 307.1026.

2-Pentyl-5-[2-(phenylthio)vinyl]-4-(4-tolyl)-1,3-oxazole (2t)
Yield: 125 mg (69%).

IR (neat): 1563, 1673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (d, *J* = 8.4 Hz, 0.5 H), 7.54–7.51 (d, *J* = 8.4 Hz, 2 H), 7.47–7.45 (m, 2.5 H), 7.39–7.35 (m, 2.5 H), 7.31–7.28 (m, 1.25 H), 7.26–7.20 (m, 2.5 H), 6.96–6.92 (d, *J* = 15.2 Hz, 1 H), 6.77–6.73 (d, *J* = 15.2 Hz, 1 H), 6.62–6.59 (d, *J* = 10.8 Hz, 0.25 H), 6.50–6.47 (d, *J* = 10.8 Hz, 0.25 H), 2.91–2.88 (t, *J* = 7.2 Hz, 0.5 H), 2.80–2.76 (t, *J* = 8.0 Hz, 2 H), 2.38 (s, 3 H), 2.05 (s, 0.75 H), 1.92–1.78 (m, 2.5 H), 1.45–1.35 (m, 5 H), 0.97–0.91 (m, 3.75 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.6, 160.4, 144.3, 144.2, 137.6, 136.5, 135.4, 134.3, 131.8, 131.5, 130.8, 130.6, 130.4, 129.9, 129.7, 129.6, 129.3, 129.1, 128.9, 128.4, 127.9, 127.5, 125.6, 122.2, 115.9, 109.8, 28.8, 28.6, 28.4, 28.3, 27.3, 27.1, 22.9, 22.7, 21.8, 21.7, 13.8, 13.6.

MS: *m*/*z* (%) = 363 (100) [M^+], 109 (50) [PhS^+].

HRMS: *m*/*z* calcd for $C_{23}H_{25}NOS$: 363.1657; found: 363.1650.

1-[4-Ethyl-2-(4-tolyl)-1,3-oxazol-5-yl]propan-2-one (3)
To a soln of $HgCl_2$ (1.0 mmol) in H_2O–MeCN (5 mL, 1:10) was added a soln of **2r** (0.2 mmol) in H_2O–MeCN (2 mL, 1:10) at 50 °C for 12 h. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The extracts were dried (anhyd Na_2SO_4) and concentrated. Silica gel chromatography of the crude product (EtOAc–petroleum ether, 1:20) afforded **3**.

Yield: 43 mg (88%).

IR (neat): 1563, 1673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.89 (d, *J* = 7.8 Hz, 2 H), 7.25–7.23 (d, *J* = 7.8 Hz, 2 H), 3.75 (s, 2 H), 2.57–2.52 (q, *J* = 7.3 Hz, 2 H), 2.39 (s, 3 H), 2.22 (s, 3 H), 1.28–1.25 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.3, 160.8, 140.6, 140.0, 139.2, 129.4, 126.2, 124.4, 40.1, 29.2, 21.5, 19.2, 13.7.

MS: *m*/*z* (%) = 243 (25) [M^+], 200 (100) [$M^+ - 43$].

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References

(1) (a) Lindquist, N.; Fenical, W.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 2303. (b) Cruz-Monserrate, Z.; Vervoort, H. C.; Bai, R. L.; Newman, D.; Howell, S. B.; Los, G.; Mullaney, J. T.; Williams, M. D.; Pettit, G. R.; Fenical, W.; Hamel, E. *Mol. Pharmacol.* **2003**, *63*, 1273. (c) Kobayashi, J.; Tsuda, M.; Fuse, H.; Sasaki, T.; Mikami, Y. *J. Nat. Prod.* **1997**, *60*, 150.

(2) (a) Carmeli, S.; Moore, R. E.; Patterson, G. M.; Cortbett, T. H.; Valeriote, F. A. *J. Am. Chem. Soc.* **1990**, *112*, 8195. (b) Palmer, D. C.; Venkatraman, S. *Oxazoles: Synthesis, Reactions and Spectroscopy,* In *The Chemistry of Heterocyclic Compounds, A Series of Monographs*, Part A; Palmer, D. C., Ed.; Wiley & Sons: Hoboken, **2003**. (c) Kato, Y.; Fusetani, N.; Matsunaga, S.; Hashimoto, K.; Fujita, S.; Furuya, T. *J. Am. Chem. Soc.* **1986**, *108*, 2780. (d) Pattenden, G. *J. Heterocycl. Chem.* **1992**, *29*, 607. (e) Lewis, J. R. *Nat. Prod. Rep.* **1995**, *12*, 135. (f) Anderson, B. A.; Becke, L. M.; Booher, R. N.; Flaugh, M. E.; Harnh, N. K.; Kress, D. L.; Wepsiec, J. P. *J. Org. Chem.* **1997**, *62*, 8634.

(3) (a) Kreisberg, J. D.; Magnus, P.; Shinde, S. *Tetrahedron Lett.* **2002**, *43*, 7393. (b) Yang, S.; Li, B.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 6066. (c) Liu, G.; Stahl, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 6328. (d) Thiery, E.; Chevrin, C.; Le Bras, J.; Harakat, D.; Muzart, J. *J. Org. Chem.* **2007**, *72*, 1859.

(4) (a) Wipf, P.; Lim, S. *J. Am. Chem. Soc.* **1995**, *117*, 558. (b) Wipf, P.; Miller, C. P. *J. Org. Chem.* **1993**, *58*, 3604. (c) Zhang, Z.; Tan, J.; Wang, Z. *Org. Lett.* **2008**, *10*, 173. (d) Muniz, K.; Hovelmann, C. H.; Streuff, J. *J. Am. Chem. Soc.* **2008**, *130*, 763. (e) Phillips, A. J.; Uto, Y.; Wipf, P.; Reno, M. J.; Williams, D. R. *Org. Lett.* **2000**, *2*, 1165. (f) Wipf, P.; Methot, J.-L. *Org. Lett.* **2001**, *3*, 1261. (g) Wipf, P.; Aoyama, Y.; Benedum, T. E. *Org. Lett.* **2004**, *6*, 3593.

(5) Maquestiau, A.; Flammang, R.; Ben, A.; Fouad, B. *Heterocycles* **1989**, *29*, 103.

(6) (a) Pummerer, R. *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 2282. (b) Pummerer, R. *Ber. Dtsch. Chem. Ges.* **1910**, *3*, 1401.

(7) For reviews in the past 20 years, please see: (a) Bur, S. K.; Padwa, A. *Chem. Rev.* **2004**, *104*, 2401. (b) Padwa, A.; Gunn, D. E. Jr.; Osterhout, M. H. *Synthesis* **1997**, 1353. (c) Padwa, A.; Bur, S. K.; Danca, D. M.; Ginn, J. D.; Lynch, S. M. *Synlett* **2002**, 851. (d) Padwa, A.; Danca, D. M.; Ginn, J. D.; Lynch, S. M. *J. Braz. Chem. Soc.* **2001**, *12*, 571. (e) DeLucchi, O.; Miotti, U.; Modena, G. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley & Sons: New York, **1991**, Chap. 3, 157–184. (f) Grierson, D. S.; Husson, H. P. In *Comprehensive Organic Synthesis*, Vol. 6; Trost, B. M., Ed.; Pergamon: Oxford, **1991**, 909–947. (g) Kennedy, M.; McKervey, M. A. In *Comprehensive Organic Synthesis*, Vol. 7; Trost, B. M., Ed.; Pergamon: Oxford, **1991**, 193–216. (h) Padwa, A. *Phosphorus, Sulfur Silicon Relat. Elem.* **1999**, *153*, 23. (i) Matsugi, M.; Gotanda, K.; Murata, K.; Kita, Y. *Chem. Commun.* **1997**, 1381. (j) Toy, P. H.; Reger, T. S.; Janda, K. D. *Org. Lett.* **2000**, *2*, 2209. (k) Kita, Y.; Tekeda, Y.; Matsugi, M.; Iio, K.; Gotanda, K.; Murata, K.; Akai, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1529. (l) Akai, S.; Kakiguchi, K.; Nakamura, Y.; Kuriwaki, I.; Dohi, T.; Harada, S.; Kubo, O.; Morita, N.; Kita, Y. *Angew. Chem. Int. Ed.* **2007**, *46*, 7458.

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