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# Isoquinoline-mediated *S*-vinylation and *N*-vinylation of benzo[*d*]oxazole-2-thiol and benzo[*d*]thiazole-2-thiol

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**Abstract**

An effective route to *S*-vinylated and *N*-vinylated benzo[*d*]oxazole-2(3*H*)-thiones and benzo[*d*]thiazole-2(3*H*)-thiones is described via reaction of acetylenic esters and benzo[*d*]oxazole-2-thiol and benzo[*d*]thiazole-2-thiol in the presence of 15 mol% of isoquinoline.


*Keywords:* *S*-Vinylation; *N*-Vinylation; Acetylenic esters; Benzo[*d*]oxazole-2-thiol; Benzo[*d*]thiazole-2-thiol; Isoquinoline

The development of new methods for catalytic C–N bond formation is highly challenging [1]. A variety of active metal catalyst systems have been reported for the *N*-arylation of amines, amides, azoles, and carbamates [2,3]. However, there exist fewer examples of C–N bond formation as a method of *N*-vinylation [4,5]. Reports concerning the *N*-vinylation of amides and carbamates are even less common as compared to reports of *N*-vinylation of amines [6,7]. However, research in the field of carbon–sulfur coupling reactions has lagged behind, largely because of sulfur's long-standing reputation as a catalyst poison [8,9]. Only a handful of publications describe the vinylation of thiols [10,11]. Here we report simple one-pot method for *S*-vinylation and *N*-vinylation of benzo[*d*]oxazole-2(3*H*)-thiones and benzo[*d*]thiazole-2(3*H*)-thiones in the presence of isoquinoline as a catalyst.

## 1. Experimental

Compounds **1**, **2** and **9** were obtained from Merck and were used without further purification. Mp: Electrothermal-9100 apparatus; uncorrected. IR spectra: Shimadzu IR-460 spectrometer. $^{1}H$ and $^{13}C$ NMR spectra: Bruker DRX-500 Avance instrument; in $CDCl_3$ at 500 and 125 MHz, respectively; EI-MS (70 eV): Finnigan-MAT-8430 mass spectrometer, in *m*/*z*. Elemental analyses (C, H, N) were performed with a Heraeus CHN-O-Rapid analyzer.

### *1.1. General procedure for the preparation of compounds* ***3***

To a stirred solution of **1** (0.151 g, 1 mmol) and **2** (1 mmol) in $CH_2Cl_2$ (10 mL), a solution of isoquinoline (0.25 mmol) in $CH_2Cl_2$ (2 mL) was added. The reaction mixture was stirred for 2–4 h. The solvent was removed under

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reduced pressure, and the residue was purified by flash column chromatography ($SiO_2$; hexane/AcOEt 4:1) to afford the pure title compounds. Compound **12a** is known [12].

*Dimethyl 2-(2-thioxobenzo[d]oxazol-3(2H)-yl)fumarate* (**3a**): Yellow powder, yield: 0.27 g (92%), mp: 130–132 °C. IR (KBr): 1731 (C=O), 1729 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.64 (s, 3 H, MeO), 3.85 (s, 3 H, MeO), 6.83–6.86 (m, 1 H, CH), 7.25–7.27 (m, 2 H, 2 CH), 7.33 (s, 1 H, CH), 7.37–7.39 (m, 1 H, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 52.7 (MeO), 53.6 (MeO), 109.8 (CH), 110.7 (CH), 124.6 (CH), 125.0 (CH), 130.1 (CH), 131.9 (C), 133.8 (C), 147.9 (C), 161.3 (C=O), 162.2 (C=O), 179.6 (C=S). MS (EI, 70 eV): *m/z* (%) 293 ($M^+$, 10), 262 (8), 235 (100), 207 (60), 163 (5), 150 (6), 76 (10). Anal. Calcd. for $C_{13}H_{11}NO_5S$ (293.29): C, 53.24%; H, 3.78%; N, 4.78%. Found: C, 53.23%; H, 3.75%; N, 4.80%.

*Diethyl 2-(2-thioxobenzo[d]oxazol-3(2H)-yl)fumarate* (**3b**): Yellow powder, yield: 0.28 g (86%), mp: 110–112 °C. IR (KBr): 1732 (C=O), 1729 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 1.03 (t, 3 H, Me), 1.30 (t, 3 H, Me), 4.07 (m, 2H, $OCH_2$), 4.30–4.37 (m, 2 H, $OCH_2$), 6.84–6.87 (m, 1 H, CH), 7.23–7.26 (m, 2 H, 2 CH), 7.36 (s, 1 H, CH), 7.37–7.39 (m, 1 H, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 13.6 (Me), 14.0 (Me), 61.9 ($OCH_2$), 62.8 ($OCH_2$), 109.8 (CH), 110.0 (CH), 124.5 (CH), 125.0 (CH), 130.6 (CH), 132.2 (C), 133.7 (C), 147.9 (C), 160.8 (C=O), 161.9 (C=O), 179.5 (C=S). MS (EI, 70 eV): *m/z* (%) 321 ($M^+$, 11), 276 (10), 248 (100), 220 (75), 176 (13), 150 (6), 76 (7). Anal. Calcd. for $C_{15}H_{15}NO_5S$ (321.34): C, 56.07%; H, 4.70%; N, 4.36%. Found: C, 56.11%; H, 4.75%; N, 4.40%.

*Di-tert-butyl 2-(2-thioxobenzo[d]oxazol-3(2H)-yl)fumarate* (**3c**): Yellow powder, yield: 0.31 g (82%), mp: 97–99 °C. IR (KBr): 1737 (C=O), 1728 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 1.08 (s, 9 H, $Me_3C$), 1.25 (s, 9 H, $Me_3C$), 6.84–6.87 (m, 1 H, CH), 7.25–7.28 (m, 2 H, 2 CH), 7.37 (s, 1 H, CH), 7.38–7.40 (m, 1 H, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 27.4 (*Me*$_3$C), 28.3 (*Me*$_3$C), 79.7 (O*C*Me$_3$), 80.1 (O*C*Me$_3$), 109.4 (CH), 110.9 (CH), 124.1 (CH), 125.1 (CH), 130.4 (CH), 131.7 (C), 134.0 (C), 147.7 (C), 161.2 (C=O), 162.5 (C=O), 179.9 (C=S). MS (EI, 70 eV): *m/z* (%) 377 ($M^+$, 3), 305 (11), 277 (100), 249 (55), 205 (30), 150 (9), 76 (13). Anal. Calcd. for $C_{19}H_{23}NO_5S$ (377.45): C, 60.46%; H, 6.14%; N, 3.71%. Found: C, 60.40%; H, 6.20%; N, 3.74%.

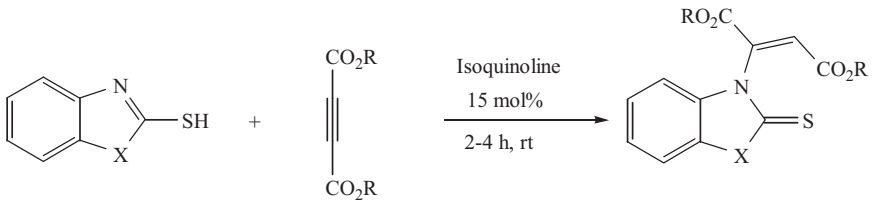
*Dimethyl 2-(2-thioxobenzo[d]thiazol-3(2H)-yl)fumarate* (**3d**): Pale yellow crystals, yield: 0.27 g (87%), mp: 124–126 °C. IR (KBr): 1731 (C=O), 1727 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.60 (s, 3 H, MeO), 3.84 (s, 3 H, MeO), 6.95 (s, 1 H, CH), 7.37 (t, 1 H, $^3J$ = 7.3, CH), 7.47 (t, 1 H, $^3J$ = 7.4, CH), 7.81 (d, 1 H, $^3J$ = 8.0, CH), 7.93 (d, 1 H, $^3J$ = 8.1, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 52.3 (MeO), 53.4 (MeO), 121.0 (CH), 122.4 (CH), 125.2 (CH), 127.0 (C), 130.7 (C), 136.2 (CH), 141.6 (C), 153.0 (CH), 164.2 (C=O), 164.8 (C=O), 179.1 (C=S). MS (EI, 70 eV): *m/z* (%) 309 ($M^+$, 14), 278 (10), 250 (100), 222 (75), 178 (10), 166 (6), 76 (9). Anal. Calcd. for $C_{13}H_{11}NO_4S_2$ (309.35): C, 50.47%; H, 3.58%; N, 4.53%. Found: C, 50.49%; H, 3.60%; N, 4.58%.

*Di-tert-butyl 2-(2-thioxobenzo[d]thiazol-3(2H)-yl)fumarate* (**3e**): Pale yellow powder, yield: 0.32 g (81%), mp: 117-119 °C. IR (KBr): 1733 (C=O), 1726 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 1.1 (s, 9 H, $Me_3C$), 1.30 (s, 9 H, $Me_3C$), 7.0 (s, 1 H, CH), 7.35 (t, 1 H, $^3J$ = 7.2, CH), 7.44 (t, 1 H, $^3J$ = 7.4, CH), 7.84 (d, 1 H, $^3J$ = 8.1, CH), 7.92 (d, 1 H, $^3J$ = 8.3, CH), $^{13}C$ NMR ($CDCl_3$): $\delta$ 27.4 (*Me*$_3$C), 28.3 (*Me*$_3$C), 79.7 (O*C*Me$_3$), 80.1 (O*C*Me$_3$), 121.2 (CH), 122.1 (CH), 125.3 (CH), 127.0 (C), 130.5 (C), 136.4 (CH), 141.3 (C), 153.2 (CH), 162.1 (C=O), 164.6 (C=O), 178.9 (C=S). MS (EI, 70 eV): *m/z* (%) 393 ($M^+$, 6), 320 (10), 292 (100), 264 (45), 220 (10), 166 (8), 76 (10). Anal. Calcd. for $C_{19}H_{23}NO_4S_2$ (393.51): C, 57.99%; H, 5.89%; N, 3.56%. Found: C, 58.22%; H, 5.95%; N, 3.64%.

*Methyl (Z)-3-(benzo[d]oxazol-2-ylthio)acrylate* (**10a**): White powder, yield: 0.10 g (44%), mp: 122–124 °C. IR (KBr): 1738 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.83 (s, 3 H, Me), 6.23 (d, 1 H, $^3J$ = 9.9, CH), 7.34–7.36 (m, 2 H, 2 CH), 7.51–7.53 (m, 1 H, CH), 7.68–7.69 (m, 1 H, CH), 8.23 (d, 1 H, $^3J$ = 9.9, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 52.0 (Me), 110.4 (CH), 119.3 (CH), 120.9 (CH), 124.9 (CH), 125.0 (CH), 139.7 (CH), 151.9 (C), 152.0 (C), 162.7 (C=N), 166.8 (C=O). MS (EI, 70 eV): *m/z* (%) 235 ($M^+$, 8), 204 (12), 176 (100), 150 (10), 76 (6). Anal. Calcd. for $C_{11}H_9NO_3S$ (235.25): C, 56.16%; H, 3.86%; N, 5.95%. Found: C, 56.20%; H, 3.90%; N, 5.99%.

*Methyl (E)-3-(benzo[d]oxazol-2-ylthio)acrylate* (**11a**): White powder, yield: 0.12 g (56%), mp: 120–122 °C. IR (KBr): 1741 (C=O) $cm^{-1}$. $^1H$ NMR ($CDCl_3$): $\delta$ 3.81 (s, 3 H, Me), 6.32 (d, 1 H, $^3J$ = 15.8, CH), 7.31–7.33 (m, 2 H, 2 CH), 7.50–7.51 (m, 1 H, CH), 7.65–7.67 (m, 1 H, CH), 8.30 (d, 1 H, $^3J$ = 15.8, CH). $^{13}C$ NMR ($CDCl_3$): $\delta$ 51.9 (Me), 110.3 (CH), 116.6 (CH), 119.0 (CH), 124.6 (CH), 124.7 (CH), 137.6 (CH), 141.6 (C), 151.2 (C), 159.3 (C=N), 164.6 (C=O). MS (EI, 70 eV): *m/z* (%) 235 ($M^+$, 8), 204 (12), 176 (100), 150 (10), 76 (6). Anal. Calcd. for $C_{11}H_9NO_3S$ (235.25): C, 56.16%; H, 3.86%; N, 5.95%. Found: C, 56.20%; H, 3.90%; N, 5.99%.

*Ethyl 4-oxo-4H-[1,3]thiazino[3,2-a]benzimidazole-2-carboxylate* (**12b**): Yellow powder, yield: 0.25 g (91%), mp: 161–163 °C. IR: 1692 (C=O) $cm^{-1}$. $^1H$ NMR (500 MHz, $CDCl_3$): $\delta$ 1.38 (t, 3H, $^3J$ = 6.9 Hz, Me), 4.37 (q, 2H, $^3J$ = 7.1 Hz, $OCH_2$), 7.19–7.20 (m, 1H, CH), 7.26–7.38 (m, 2H, 2 CH), 7.65 (d, 1H, $^3J$ = 7.8 Hz, CH), 7.93 (d, 1H, $^3J$ = 7.6 Hz, CH). $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 13.6 (Me), 61.8 ($OCH_2$), 112.3 (CH), 119.5 (CH), 121.6 (CH), 124.3




| | X |
|---|---|
| **1a** | O |
| **1b** | S |

| | R |
|---|---|
| **2a** | Me |
| **2b** | Et |
| **2c** | *t*-Bu |

| | X | R | Yilde (%) |
|---|---|---|---|
| **3a** | O | Me | 92 |
| **3b** | O | Et | 86 |
| **3c** | O | *t*-Bu | 82 |
| **3d** | S | Me | 87 |
| **3e** | S | *t*-Bu | 81 |

Scheme 1.

(CH), 125.9 (CH), 129.6 (C), 144.1 (C), 148.5 (C), 154.6 (C), 157.1 (C=O), 164.7 (C=O). MS (EI, 70 eV): *m*/*z* (%) 274 ($M^+$, 100), 229 (22), 201 (40), 174 (60), 129 (30). Anal. Calcd. for $C_{13}H_{10}N_2O_3S$ (274.30): C, 56.92%; H, 3.67%; N, 10.21%. Found: C, 56.70%; H, 3.53%; N, 10.09%.

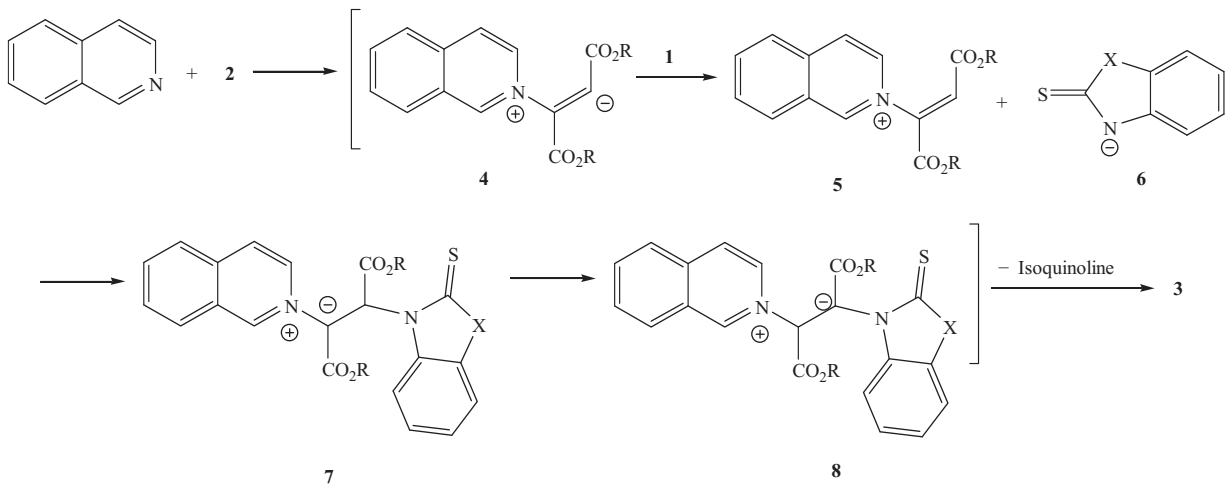
## 2. Results and discussion

The reaction of 2-mercaptobenzoxazol and 2-mercaptobenzothiazol with acetylenic esters **2** in the presence of 15 mol% of isoquinoline proceeded at r.t. in $CH_2Cl_2$ and was finished after 2–4 h. Any product other than **3** could not be detected by NMR spectroscopy. The structures of compounds **3a–e** were deducted from their IR, $^1$H NMR, and $^{13}$C NMR spectra. Thus, the $^1$H NMR spectrum of each isolated product **3a–e** exhibited a vinylic proton signal at about 6.95–7.37 ppm, which is in agreement with the (*Z*) configuration [13] for the vinyl moiety (Scheme 1).

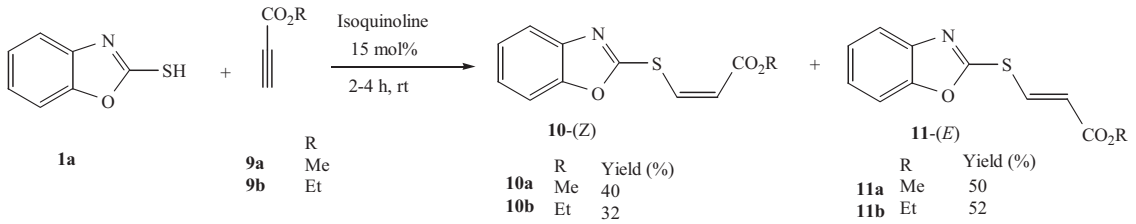
Presumably, the zwitterionic intermediate formed from the acetylenic ester and isoquinoline, is protonated by **1** to furnish intermediate **4**, which is attacked by the anion of the SH-acidic **1** in a Michael fashion to produce **7**. This intermediate is converted to **8** via a proton-shift reaction, and produces **3** by elimination of isoquinoline (Scheme 2).

Under similar conditions, the reaction of alkyl propiolates **9a** and **b** with **1a** led to alkyl 3-(benzo[*d*]oxazol-2-ylthio)acrylates **10** and **11** (Scheme 3).

To extend our knowledge of this reaction, we performed the reaction between dialkyl acetylenedicarboxylates and 2-mercaptobenzimidazol in the presence of isoquinoline. These reactions led to alkyl 4-oxo-4*H*-[1,3]thiazino[3,2-*a*]benzimidazole-2-carboxylates **12a** and **b** (Fig. 1).




Scheme 2.




Scheme 3.

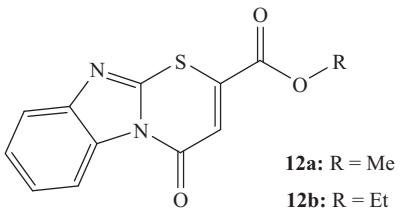



Fig. 1. Strctures of compounds **12**.

In summary, the reaction between dialkyl acetylenedicarboxylates and 2-mercaptobenzoxazole in the presence of isoquinoline as catalyst provides a simple one-pot synthesis of dialkyl (*Z*)-2-[2-thioxo-1,3-benzoxazole-3(2*H*)-yl]-2-butendioates of potential synthetic and pharmaceutical interest. In the same way, alkyl propiolates and 2-mercaptobenzoxazole led to alkyl 3-(benzo[d]oxazol-2-ylthio)acrylates.

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