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# Synthesis and Herbicidal Activity of Novel 3-Aminocarbonyl-2-oxazolidinethione Derivatives Containing a Substituted Pyridine Ring

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A series of 3-aminocarbonyl-2-oxazolidinethione derivatives containing a substituted pyridine ring were designed and synthesized. The structures of all of the title compounds were characterized by $^1$H NMR, $^{13}$C NMR, IR, and HRMS. Their agricultural bioactivities were evaluated, and some of these compounds exhibited good herbicidal activities against *Echinochloa crusgalli*, *Sorghum vulgare*, *Digitaria sanguinalis*, *Eclipta prostrasta*, *Cucumis sativus*, and *Brassica campestris*, which were associated mainly with their steric properties and lipophilicities based on the structure−activity relationship discussion.

**KEYWORDS: 2-Oxazolidinethiones; pyridine ring; herbicidal activity**

## INTRODUCTION

Weeds compete with crops for sunshine, water, nutrients, and physical space and are thus capable of greatly influencing the growth of crops and undermining both crop quality and yield. Also, many weeds are the harbor or nest of pathogens, viruses, and pests, which may result in the occurrence and spread of plant diseases and insect pests in crops. Herbicides, as the main weed control tool, play a very important role in modern agriculture.

Since the discovery of the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) by Zimerman and Hitchcock, the agrochemical industry has successfully developed a wide array of herbicides with various chemical structures and modes of action (*1*). However, an inevitable problem associated with the use of herbicides is the occurrence of herbicide-resistant weeds (*2*). For example, the widespread use of herbicides such as chlorsulfuron, atrazine, diclofop-methyl, and paraquat has caused herbicide resistance in many weeds. Therefore, it is necessary to develop efficient herbicides with novel structures and modes of action to overcome the resistance of weeds.

In the study of pharmaceuticals and agrochemicals, the introduction of pyridine into a parent compound may improve the properties and biological activities of the compounds, and many pyridyl-containing compounds are also known to possess a wide range of biological and pharmacological activities (*3*−*6*), as well as low toxicity toward mammals. On the other hand, the chemistry of 2-oxazolidinethiones has received considerable attention because their derivatives exhibit much higher potentials of biological activities, such as antithyroid (*7*, *8*), antifertility (*9*, *10*), inhibition of dopamine $\beta$-hydroxylase (*11*), antibacterial (*12*, *13*), and insecticidal activities (*14*). However, 2-oxazolidinethione derivatives used as herbicide have been rarely reported. This provides us with a chance to obtain the herbicidal lead compound with 2-oxazolidinethione containing a substituted pyridine. In this paper, we have synthesized a series of novel compounds by introducing pyridine rings with different substituted groups into 2-oxazolidinethiones, and the results of bioassay showed efficient herbicidal activities.

## MATERIALS AND METHODS

**Synthesis**. *Chemicals*. Melting points were obtained with an X-6 micro-melting point apparatus and are uncorrected. The infrared (IR) spectra were recorded on a Nicolet 20DXB FR-IR spectrometer using potassium bromide pellets or films. The $^1$H NMR spectra were measured on a Varian INOVA-400 spectrometer with chemical shifts reported as parts per million (in $CDCl_3$, TMS as internal standard). The $^{13}$C NMR spectra were measured on a Varian INOVA-400 or a Bruker AVANCE-500 spectrometer (in $CDCl_3$, TMS as internal standard). Mass spectra were measured on an HP 1100 LC-MSD spectrometer. High-resolution mass spectra (HRMS) were obtained on an HPLC-Q-T of MS (Mcrio) spectrometer. Flash chromatography was performed on silica gel. All of the solvents were of analytical grade. All chemicals or reagents were purchased from standard commercial suppliers.

*General Procedure for the Preparation of erythro-Amino Alcohol (**1**)*. To a solution of aminoketone (5.0 mmol) in MeOH (50 mL) was added $NaBH_4$ (25.0 mmol) in five portions every 10 min at 0 °C. After

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20 min of stirring, the solvent was evaporated at reduced pressure, taken up with $CH_2Cl_2$. The mixture was filtered, and the filtrate was concentrated to dryness to give the crude products **1** in the range of 90−95% yields, which were directly used in the next reaction without further purification. The *erythro*-amino alcohols **1** are ∼85% determined by HPLC.

*General Procedure for the Preparation of 2-Oxazolidinethione (**2**).* To a thick solution of *erythro*-amino alcohol **1** (5 mmol) in 20 mL of aqueous 2 M sodium carbonate was added $CS_2$ (7.5 mmol). The reaction mixture was stirred under reflux until the system became transparent. After cooling to room temperature, the reaction mixture was extracted with dichloromethane. The combined organic layers were dried over anhydrous $MgSO_4$, and then the solvent was removed under reduced pressure to afford crude products, which were recrystallized from ethanol/hexane to provide 2-oxazolidinethiones **2** in the range of 55−70% yields.

*General Procedure for the Preparation of 3-Aminocarbonyl-2-oxazolidinethione (**3**).* A 1.0 mmol amount of 2-oxazolidinethiones **2** was dissolved in 15 mL of $CHCl_3$. Several drops of DBU and 1.0 mmol of cyclohexyl or substituted phenyl isocyanate were added to the stirred solution. The reaction was stirred at 0 °C to room temperature for 0.5−2 h. Then, the solvent was evaporated under vacuum, and the residue was purified via column chromatography on silica gel by using petroleum ether and acetone as eluent to give pure *cis*-compounds **3** in the range of 50−92% yields. The *cis*-conformation was supported by the observation of a NOE cross-peak between the two conjoined H of the 2-oxazolidinethione ring.

*Data for **3a**:* yield, 68%; mp, 91.4−92.4 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3226, 2933, 1707, 1591, 1538, 1299, 1190; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.96 (d, $J$ = 6.4 Hz, 3H), 1.22−1.47 (m, 5H), 1.50−1.62 (m, 1H), 1.62−1.80 (m, 2H), 1.82−2.00 (m, 2H), 3.74−3.87 (m, 1H), 5.20−5.30 (m, 1H), 5.84 (d, $J$ = 8.0 Hz, 1H), 7.30 (dd, $J$ = 5.0 Hz, $J$ = 7.4 Hz, 1H), 7.57 (d, $J$ = 7.8 Hz, 1H), 7.79 (dd, $J$ = 7.4 Hz, $J$ = 7.8 Hz, 1H), 8.62 (d, $J$ = 5.0 Hz, 1H), 9.58 (d, $J$ = 7.2 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.92, 24.28, 24.31, 25.55, 32.45, 32.51, 49.62, 58.57, 82.78, 120.81, 123.49, 137.04, 149.57, 149.88, 153.53, 184.81; HRMS (ESI) calculated for $C_{16}H_{22}N_3O_2S$ [M + $H^+$] 320.1433, found 320.1429.

*Data for **3b**:* yield, 92%; mp, 125.9−127.8 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3208, 2929, 1700, 1590, 1540, 1294, 1194; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.01 (d, $J$ = 6.8 Hz, 3H), 1.22−1.52 (m, 5H), 1.54−1.64 (m, 1H), 1.66−1.82 (m, 2H), 1.86−2.05 (m, 2H), 3.70−3.87 (m, 1H), 5.04−5.21 (m, 1H), 5.86 (d, $J$ = 7.6 Hz, 1H), 7.42 (d, $J$ = 8.4 Hz, 1H), 7.70 (dd, $J$ = 2.4 Hz, $J$ = 8.4 Hz, 1H), 8.38 (d, $J$ = 2.4 Hz, 1H), 9.49 (d, $J$ = 6.8 Hz, 1H, −NH); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 15.34, 24.30, 24.33, 25.58, 32.44, 32.51, 49.67, 58.42, 80.43, 124.31, 127.71, 136.53, 147.46, 149.52, 152.19, 184.15; HRMS (ESI) calculated for $C_{16}H_{21}ClN_3O_2S$ [M + $H^+$] 354.1043, found 354.1032.

*Data for **3c**:* yield, 85%; mp, 124.7−125.7 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3211, 2934, 1704, 1609, 1578.18, 1539, 1287, 1254, 1200; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (d, $J$ = 6.8 Hz, 3H), 1.23−1.48 (m, 5H), 1.50−1.64 (m, 1H), 1.64−1.80 (m, 2H), 1.86−2.03 (m, 2H), 3.73−3.84 (m, 1H), 3.95 (s, 3H), 4.96−5.07 (m, 1H), 5.74 (d, $J$ = 7.6 Hz, 1H), 6.80 (d, $J$ = 8.0 Hz, 1H), 7.57 (d, $J$ = 8.0 Hz, 1H), 8.12 (s, 1H), 9.57 (d, $J$ = 6.4 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 15.19, 24.25, 24.30, 25.54, 32.44, 32.51, 49.65, 53.84, 58.74, 81.47, 111.21, 121.12, 136.84, 145.08, 149.96, 164.71, 184.93; HRMS (ESI) calculated for $C_{17}H_{24}N_3O_3S$ [M + $H^+$] 350.1538, found 350.1528.

*Data for **3d**:* yield, 80%; mp, 106.0−107.2 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3195, 2927, 1698, 1614, 1550, 1495, 1255, 1166; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.4 Hz, 3H), 1.22−1.50 (m, 5H), 1.54−1.67 (m, 1H), 1.67−1.82 (m, 2H), 1.90−2.03 (m, 2H), 3.68−3.87 (m, 1H), 4.77 (q, $J$ = 8.4 Hz, 2H), 4.79−5.10 (m, 1H), 5.76 (d, $J$ = 7.6 Hz, 1H), 6.94 (d, $J$ = 8.4 Hz, 1H), 7.65 (dd, $J$ = 2.0 Hz $J$ = 8.4 Hz, 1H), 8.13 (d, $J$ = 2.0 Hz, 1H), 9.54 (d, $J$ = 7.6 Hz, 1H, −NH); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 15.39, 24.46, 24.49, 25.73, 32.61, 32.68, 49.83, 58.79, 62.48 (q, $J$ = 35.8 Hz), 81.22, 111.37, 122.99, 123.58 (q, $J$ = 275.8 Hz), 137.48, 144.80, 149.89, 162.26, 184.70; HRMS (ESI) calculated for $C_{18}H_{23}F_3N_3O_3S$ [M + $H^+$] 418.1412, found 418.1403.

*Data for **3e**:* yield, 79%; mp, 112.6−113.5 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3188, 2933, 1679, 1611, 1558.90, 1293, 1196; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (d, $J$ = 6.8 Hz, 3H), 1.24−1.50 (m, 8H), 1.52−1.63 (m, 1H), 1.66−1.84 (m, 2H), 1.88−2.00 (m, 2H), 3.73−3.85 (m, 1H), 4.37 (q, $J$ = 7.2 Hz, 2H), 4.95−5.06 (m, 1H), 5.73 (d, $J$ = 8.0 Hz, 1H), 6.78 (d, $J$ = 8.4 Hz, 1H), 7.57 (dd, $J$ = 2.4 Hz, $J$ = 8.4 Hz, 1H), 8.10 (d, $J$ = 2.4 Hz, 1H), 9.57 (d, $J$ = 7.6 Hz, 1H, −NH); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 14.81, 15.41, 24.48, 24.51, 25.77, 32.64, 32.71, 49.82, 58.91, 62.30, 81.68, 111.31, 120.90, 136.78, 145.25, 150.01, 164.52, 184.95; HRMS (ESI) calculated for $C_{18}H_{26}N_3O_3S$ [M + $H^+$] 364.1695, found 364.1691.

*Data for **3f**:* yield, 92%; mp, 149.4−150.7 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3152, 2987, 1693, 1601, 1544, 1297, 1195; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.08 (d, $J$ = 6.4 Hz, 3H), 1.52 (t, $J$ = 7.0 Hz, 3H), 4.14 (q, $J$ = 7.0 Hz, 2H), 5.16−5.26 (m, 1H), 5.85 (d, $J$ = 7.6 Hz, 1H), 6.91 (d, $J$ = 8.0 Hz, 1H), 6.96 (t, $J$ = 7.6 Hz, 1H), 7.07 (ddd, $J$ = 1.6 Hz, $J$ = 7.6 Hz, $J$ = 8.0 Hz, 1H), 7.44 (d, $J$ = 8.4 Hz, 1H), 7.73 (dd, $J$ = 2.8 Hz, $J$ = 8.4 Hz, 1H), 8.23 (dd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, 1H), 8.41 (d, $J$ = 2.8 Hz, 1H), 11.76 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 15.10, 15.16, 58.57, 64.43, 80.47, 111.17, 119.94, 120.77, 124.47, 124.47, 126.96, 127.66, 136.64, 147.54, 147.91, 148.52, 152.46, 183.94; HRMS (ESI) calculated for $C_{18}H_{19}ClN_3O_3S$ [M + $H^+$] 392.0836, found 392.0823.

*Data for **3g**:* yield, 77%; mp, 110.6−112.0 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3106, 2978, 1704, 1602, 1541, 1296, 1193; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.12 (d, $J$ = 6.8 Hz, 3H), 1.41 (t, $J$ = 7.0 Hz, 3H), 1.52 (t, $J$ = 7.0 Hz, 3H), 4.13 (q, $J$ = 7.0 Hz, 2H), 4.38 (q, $J$ = 7.0 Hz, 2H), 5.07−5.16 (m, 1H), 5.79 (d, $J$ = 7.6 Hz, 1H), 6.79 (d, $J$ = 8.6 Hz, 1H), 6.90 (d, $J$ = 8.0 Hz, 1H), 6.96 (dd, $J$ = 6.8 Hz, $J$ = 8.0 Hz, 1H), 7.06 (dd, $J$ = 6.8 Hz, $J$ = 8.0 Hz, 1H), 7.60 (dd, $J$ = 2.4 Hz, $J$ = 8.6 Hz, 1H), 8.13 (d, $J$ = 2.4 Hz, 1H), 8.25 (d, $J$ = 8.0 Hz, 1H), 11.82 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.58, 15.10, 15.10, 58.89, 62.23, 64.43, 81.56, 111.15, 111.30, 119.97, 120.78, 120.78, 124.32, 127.15, 136.83, 145.21, 148.19, 148.56, 164.54, 184.56; HRMS (ESI) calculated for $C_{20}H_{24}N_3O_4S$ [M + $H^+$] 402.1488, found 402.1470.

*Data for **3h**:* yield, 82%; mp, 133.0−134.2 °C; IR (KBr) $\upsilon_{max}$ ($cm^{-1}$) 3191, 2934, 1704, 1580, 1539, 1295, 1190; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.97 (d, $J$ = 6.8 Hz, 3H), 1.25−1.52 (m, 5H), 1.520−1.67 (m, 1H), 1.67−1.83 (m, 2H), 1.83−2.05 (m, 2H), 3.70−3.90 (m, 1H), 5.31−5.46 (m, 1H), 5.92 (d, $J$ = 7.6 Hz, 1H), 7.38 (dd, $J$ = 4.8 Hz, $J$ = 7.8 Hz, 1H), 7.99 (d, $J$ = 7.8 Hz, 1H), 8.45 (d, $J$ = 4.8 Hz, 1H), 9.52 (d, $J$ = 7.6 Hz, 1H, −NH); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 15.38, 24.42, 24.48, 25.74, 32.59, 32.68, 49.80, 57.46, 79.94, 122.79, 128.59, 136.53, 148.36, 149.71, 150.01, 184.05; HRMS (ESI) calculated for $C_{16}H_{21}ClN_3O_2S$ [M + $H^+$] 354.1043, found 354.1053.

*Data for **3i**:* yield, 77%; oil; IR (film) $\upsilon_{max}$ ($cm^{-1}$) 3214, 2931, 1705, 1591, 1292, 1180; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.92 (d, $J$ = 6.4 Hz, 3H), 1.20−1.49 (m, 5H), 1.53−1.63 (m, 1H), 1.66−1.78 (m, 2H), 1.88−2.00 (m, 2H), 3.74−3.86 (m, 1H), 3.98 (s, 3H), 5.17−5.27 (m, 1H), 5.79 (d, $J$ = 7.6 Hz, 1H), 6.98 (dd, $J$ = 5.2 Hz, $J$ = 7.6 Hz, 1H), 7.81 (d, $J$ = 7.6 Hz, 1H), 8.18 (d, $J$ = 5.2 Hz, 1H), 9.59 (d, $J$ = 7.2 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.78, 24.24, 24.29, 25.56, 32.41, 32.51, 49.54, 53.70, 57.73, 79.45, 116.24, 116.81, 135.20, 147.10, 150.02, 159.85, 184.76; HRMS (ESI) calculated for $C_{17}H_{24}N_3O_3S$ [M + $H^+$] 350.1538, found 350.1552.

*Data for **3j**:* yield, 70%; oil; IR (film) $\upsilon_{max}$ ($cm^{-1}$) 3219, 2933, 1708, 1592, 1538, 1279, 1177; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.94 (d, $J$ = 6.4 Hz, 3H), 1.20−1.49 (m, 5H), 1.52−1.67 (m, 1H), 1.67−1.78 (m, 2H), 1.84−2.01 (m, 2H), 3.70−3.85 (m, 1H), 4.71−4.85 (m, 2H), 5.18−5.26 (m, 1H), 5.85 (d, $J$ = 7.6 Hz, 1H), 7.10 (dd, $J$ = 5.2 Hz, $J$ = 7.4 Hz, 1H), 7.88−7.93 (m, 1H), 8.18 (dd, $J$ = 1.2 Hz, $J$ = 5.2 Hz, 1H), 9.55 (d, $J$ = 7.6 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.90, 24.28, 24.33, 25.57, 32.44, 32.54, 57.82, 62.11 (q, $J$ = 35.8 Hz), 78.82, 116.55, 118.60, 120.45, 123.40 (q, $J$ = 275.8 Hz), 136.31, 146.93, 149.90, 157.40, 184.54; HRMS (ESI) calculated for $C_{18}H_{23}F_3N_3O_3S$ [M + $H^+$] 418.1412, found 418.1426.

*Data for **3k**:* yield, 69%; oil; IR (film) $\upsilon_{max}$ ($cm^{-1}$) 3213, 2931, 1706, 1589, 1538, 1292, 1176; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.94 (d, $J$ = 6.4 Hz, 3H), 1.22−1.48 (m, 8H), 1.59−1.63 (m, 1H), 1.66−1.78 (m, 2H), 1.88−2.00 (m, 2H), 3.75−3.85 (m, 1H), 4.34−4.51 (m, 2H), 5.16−5.26 (m, 1H), 5.81 (d, $J$ = 7.6 Hz, 1H), 6.95 (dd, $J$ = 4.8 Hz, $J$ = 7.6 Hz, 1H), 7.80 (d, $J$ = 7.6 Hz, 1H), 8.16 (d, $J$ = 4.8 Hz, 1H), 9.60 (d, $J$ = 7.6 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.65, 14.83,

24.24, 24.29, 25.57, 32.40, 32.51, 49.59, 57.81, 62.17, 79.51, 116.25, 116.60, 135.27, 147.06, 150.08, 159.59, 184.80; HRMS (ESI) calculated for $C_{18}H_{26}N_3O_3S$ [M + H$^+$] 364.1695, found 364.1678.

*Data for* ***3l****:* yield, 85%; mp, 151.4−152.0 °C; IR (KBr) $\upsilon_{max}$ (cm$^{-1}$) 3157, 2978, 1703, 1604, 1541, 1294, 1189; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (d, $J$ = 6.4 Hz, 3H), 1.52 (t, $J$ = 6.8 Hz, 3H), 4.14 (q, $J$ = 6.8 Hz, 2H), 5.46−5.55 (m, 1H), 5.98 (d, $J$ = 7.6 Hz, 1H), 6.91 (d, $J$ = 8.0 Hz, 1H), 6.94−7.01 (m, 1H), 7.08 (ddd, $J$ = 1.6 Hz, $J$ = 7.6 Hz, $J$ = 8.0 Hz, 1H), 7.39 (dd, $J$ = 4.8 Hz, $J$ = 8.0 Hz, 1H), 8.034 (dd, $J$ = 1.2 Hz, $J$ = 8.0 Hz, 1H), 8.26 (dd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, 1H), 8.46 (dd, $J$ = 1.2 Hz, $J$ = 4.8 Hz, 1H), 11.78 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 15.10, 15.10, 57.44, 64.42, 79.84, 111.14, 119.97, 120.82, 122.78, 124.39, 127.04, 128.47, 136.57, 147.92, 148.33, 148.51, 150.05, 183.68; HRMS (ESI) calculated for $C_{18}H_{19}ClN_3O_3S$ [M + H$^+$] 392.0836, found 392.0834.

*Data for* ***3m****:* yield, 80%; mp, 122.0−122.8 °C; IR (KBr) $\upsilon_{max}$ (cm$^{-1}$) 3189, 2931, 1696, 1600, 1557, 1293, 1198; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 0.98 (d, $J$ = 6.4 Hz, 3H), 1.25−1.48 (m, 5H), 1.54−1.62 (m, 1H), 1.67−1.78 (m, 2H), 1.90−2.00 (m, 2H), 3.73−3.84 (m, 1H), 5.08−5.18 (m, 1H), 5.76 (d, $J$ = 8.0 Hz, 1H), 7.29 (d, $J$ = 5.6 Hz, 2H), 8.70 (d, $J$ = 5.6 Hz, 2H), 9.52 (d, $J$ = 7.2 Hz, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 15.00, 24.25, 24.28, 25.51, 32.41, 32.49, 49.68, 58.21, 81.42, 120.71, 141.82, 149.74, 150.24, 184.46; HRMS (ESI) calculated for $C_{16}H_{22}N_3O_2S$ [M + H$^+$] 320.1433, found 320.1429.

*Data for* ***3n****:* yield, 75%; mp, 129.5−130.7 °C; IR (KBr) $\upsilon_{max}$ (cm$^{-1}$) 3146, 2969, 1701, 1594, 1542, 1287, 1174; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.06 (d, $J$ = 6.4 Hz, 3H), 5.19−5.27 (m, 1H), 5.84 (d, $J$ = 7.6 Hz, 1H), 7.10 (ddd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, $J$ = 8.0 Hz, 1H), 7.27−7.31 (m, 1H), 7.32 (d, $J$ = 6.0 Hz, 2H), 7.43 (dd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, 1H), 8.21 (dd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, 1H), 8.72 (d, $J$ = 6.0 Hz, 2H), 11.75 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.89, 58.46, 81.61, 120.67, 122.49, 124.68, 125.46, 127.44, 129.62, 134.29, 141.49, 148.39, 150.33, 184.19; HRMS (ESI) calculated for $C_{16}H_{15}ClN_3O_2S$ [M + H$^+$] 348.0574, found 348.0580.

*Data for* ***3o****:* yield, 90%; mp, 140.5−141.7 °C; IR (KBr) $\upsilon_{max}$ (cm$^{-1}$) 3170, 2978, 1704, 1605, 1554, 1296, 1179; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.04 (d, $J$ = 6.4 Hz, 3H), 1.52 (t, $J$ = 7.0 Hz, 3H), 4.14 (q, $J$ = 7.0 Hz, 2H) 5.19−5.28 (m, 1H), 5.81 (d, $J$ = 7.6 Hz, 1H), 6.91 (dd, $J$ = 1.2 Hz, $J$ = 8.0 Hz, 1H), 6.77 (ddd, $J$ = 1.2 Hz, $J$ = 7.6 Hz, $J$ = 8.0 Hz, 1H), 7.08 (ddd, $J$ = 1.6 Hz, $J$ = 7.6 Hz, $J$ = 8.0 Hz, 1H), 7.32 (d, $J$ = 6.0 Hz, 2H), 8.24 (dd, $J$ = 1.6 Hz, $J$ = 8.0 Hz, 1H), 8.71 (d, $J$ = 6.0 Hz, 2H), 11.78 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.91, 15.09, 58.34, 64.42, 81.45, 111.16, 119.93, 120.68, 120.75, 124.43, 127.00, 141.65, 147.96, 148.53, 150.33, 184.06; HRMS (ESI) calculated for $C_{18}H_{20}N_3O_3S$ [M + H$^+$] 358.1225, found 358.1230.

*Data for* ***3p****:* yield, 50%; mp, 136.4−137.8 °C; IR (KBr) $\upsilon_{max}$ (cm$^{-1}$) 3110, 2970, 1704, 1606, 1581, 1269, 1168; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.05 (d, $J$ = 6.4 Hz, 3H), 5.15−5.25 (m, 1H), 5.84 (d, $J$ = 7.6 Hz, 1H), 7.28−7.35 (m, 3H), 7.66 (dd, $J$ = 7.2 Hz, $J$ = 8.4 Hz, 1H), 8.12 (d, $J$ = 8.4 Hz, 1H), 8.21 (d, $J$ = 8.0 Hz, 1H), 8.73 (d, $J$ = 6.0 Hz, 2H), 12.42 (s, 1H, −NH); $^{13}$C NMR (125 MHz, $CDCl_3$) $\delta$ 14.84, 16.75, 58.68, 81.52, 120.69, 125.10, 125.58, 131.83, 134.39, 140.49, 141.49, 149.10, 150.34, 183.80; HRMS (ESI) calculated for $C_{16}H_{15}N_4O_4S$ [M + H$^+$] 359.0814, found 359.0814.

**Biological Assay.** The herbicidal activities of compounds **3** were measured with the method described as follows. Each sample was dissolved in DMF, and then the solution was diluted with emulsifier 0201 (a mixture of anionic and nonionic surfactant) containing water (0.1 g L$^{-1}$) until the required concentration was achieved. The biological tests were carried out in plastic boxes. Nineteen milliliters of 0.9% thawed water agar and a 1 mL of diluted solution were added to the plastic boxes and shaken. After the drug-containing agar was cool, the seeds of *Echinochloa crusgalli*, *Sorghum vulgare*, *Digitaria sanguinalis*, *Eclipta prostrasta*, *Cucumis sativus*, and *Brassica campestris* were sowed, and then the cultivations were kept at 24 ± 1 °C with exposure to light of 3000 lx for 7 days. The root growth inhibitory rates (percent) of compounds **3** related to the control were determined. The experiments were conducted in three replicates with 150 seeds per plant for each concentration. The results of compounds **3** demonstrating activity are listed in **Table 1**.

**Table 1.** Herbicidal Activity of Compounds **3**[a] at 100 mg L$^{-1}$

| | av growth inhibitory rate (%) against | | | | | |
|---|---|---|---|---|---|---|
| compd | *E. crus-galli* | *S. vulgare* | *D. sanguin-alis* | *E. pro-strasta* | *C. sativus* | *B. campestris* |
| **3a** | 70 | 0 | 70 | 80 | 0 | 0 |
| **3d** | 80 | 60 | 70 | 80 | 40 | 40 |
| **3f** | 90 | 70 | 80 | 90 | 90 | 90 |
| **3g** | 50 | 0 | 80 | 20 | 0 | 0 |
| **3m** | 90 | 30 | 80 | 85 | 20 | 80 |
| **3p** | 60 | 70 | 70 | 80 | 20 | 50 |

[a] Only the results of effective compounds are listed.

## RESULTS AND DISCUSSION

**Synthesis.** The title *cis*-compounds **3** were synthesized as shown in **Scheme 1**. The starting materials *erythro*-amino alcohols **1** were prepared by reduction of the corresponding aminoketones with sodium borohydride in methanol at 0 °C. The reaction of *erythro*-**1** with $CS_2$ in a basic medium led to the corresponding *cis*-2-oxazolidinethiones **2** in the range of 55−70% yields (*15*). The further reaction of intermediates **2** with cyclohexyl or substituted phenyl isocyanate could proceed readily at or below room temperature under a moisture-free condition to give target compounds **3**. The yields of compounds **3** could be decreased because isocyanates were active enough to easily form the corresponding ureas under a moisture condition. The variation of substituent $R_1$ at the pyridine ring also influenced the reaction yield, and the yield of reaction toward compounds **3** slightly decreased with the increasing electron-donating ability of $R_1$ and the increasing electron density on the pyridine ring. The structures of the title compounds were well characterized by $^1$H NMR, $^{13}$C NMR, IR, and HRMS.

**Biological Activity.** As shown in **Table 1**, compounds **3a**, **3d**, **3f**, **3g**, **3m**, and **3p** exhibited considerable inhibitory activity against both dicotyledonous and monocotyledonous weeds, and their herbicidal activities against *E. crusgalli*, *D. sanguinalis*, and *E. prostrasta* were greater than those against *S. vulgare*, *C. sativus*, and *B. campestris*. The inhibitory activity of compound **3f** against some test plants reached 90% at 100 mg L$^{-1}$. Compounds with an X group at the 2-, 3- and 4- positions of the pyridine ring possess some herbicidal activity (**3a**, **3d**, **3m**), but it was obvious that the compounds having substituents at the *ortho*-position of the X group (**3h**−**3l**) did not show any herbicidal activities.

Although we have no information about the mode of action of these compounds, it was presumed that their mode of action is possibly concerned with the photosynthesis system according to the symptoms of the yellow of *E. crusgalli's* leaf and the albinism of the weed. Further research on the modification of structure and the mode of action is in progress.

**Structure−Activity Relationship.** It is well-known that the steric property is one of the factors affecting biological activities of compounds. The dihedral angles, expressing the steric property, were calculated by using a molecular modeling program, PCMODEL 6.), of Serena Software (**Table 2**). Before all parameters of a compound were calculated, it was essential that its spatial molecular conformation be optimized with PCMODEL to acquire its most relaxed conformation. For example, for compound **3h**, the dihedral angle was indicated as the C1−C2−C3−O dihedral angle or the C1−C2−C3−C4 dihedral angle (**Figure 1**). From **Table 2**, it was found that with compounds having no substituent at the *ortho*-position of the X group (**3a**−**3g**, **3m**−**3p**), their dihedral angles are smaller

**Scheme 1.** Synthesis Route of Compounds **3**

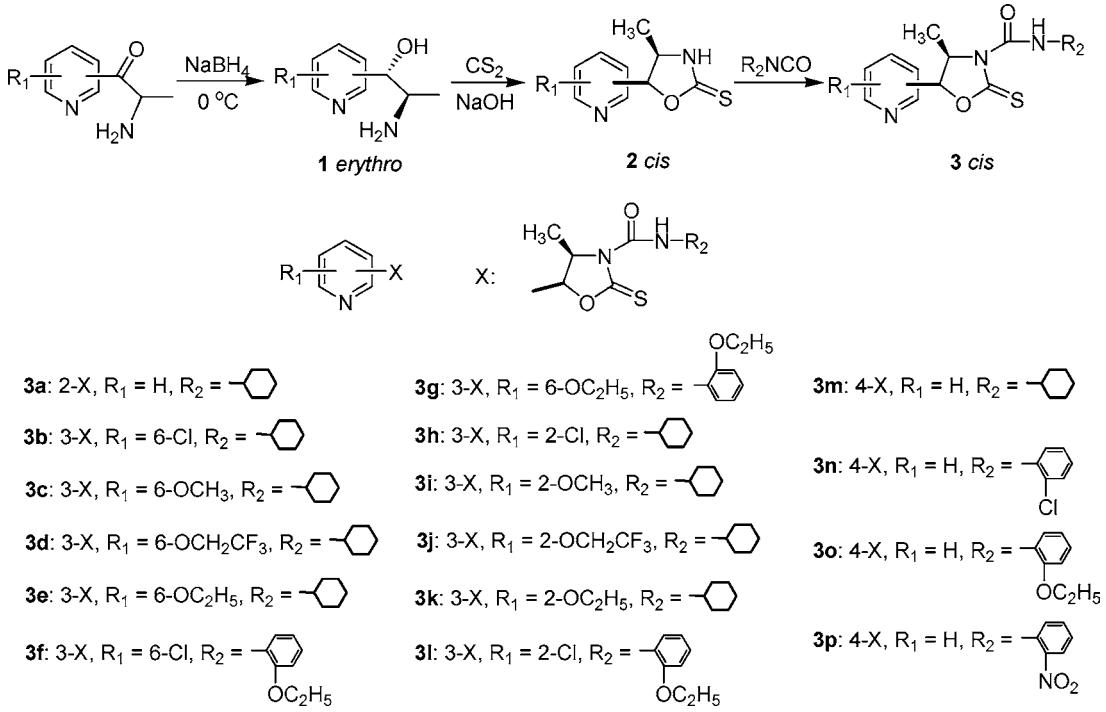


**Table 2.** Molecular Parameters Calculated by PCMODEL

| | | | | | dihedral angle (deg) | |
|---|---|---|---|---|---|---|
| compd | $V_T$ (Å$^2$) | $V_P$ (Å$^2$) | $V_N$ (Å$^2$) | $V_N/V_P$ | 1 | 2 |
| **3a** | 432.964 | 99.958 | 333.006 | 3.331 | 164.1 | −80.2 |
| **3b** | 435.943 | 103.458 | 332.485 | 3.214 | 158.5 | −85.5 |
| **3c** | 456.498 | 106.838 | 349.660 | 3.273 | 157.2 | −86.7 |
| **3d** | 513.870 | 110.889 | 402.981 | 3.634 | 161.3 | −82.6 |
| **3e** | 494.282 | 104.519 | 389.763 | 3.729 | 160.3 | −83.7 |
| **3f** | 489.117 | 112.740 | 376.377 | 3.338 | 159.0 | −84.9 |
| **3g** | 536.868 | 122.241 | 414.627 | 3.392 | 162.0 | −81.9 |
| **3h** | 439.242 | 104.876 | 334.366 | 3.188 | 164.7 | −79.4 |
| **3i** | 459.685 | 102.079 | 357.606 | 3.503 | 170.1 | −73.5 |
| **3j** | 488.141 | 101.186 | 386.955 | 3.824 | 179.5 | −63.6 |
| **3k** | 489.383 | 103.270 | 386.113 | 3.739 | 171.9 | −71.5 |
| **3l** | 484.274 | 112.071 | 372.203 | 3.321 | 166.2 | −77.9 |
| **3m** | 422.590 | 96.458 | 326.132 | 3.381 | 163.2 | −79.7 |
| **3n** | 416.631 | 105.213 | 311.418 | 2.960 | 153.3 | −91.0 |
| **3o** | 473.776 | 114.356 | 359.420 | 3.143 | 159.3 | −84.8 |
| **3p** | 417.593 | 152.643 | 264.950 | 1.736 | 159.3 | −85.0 |

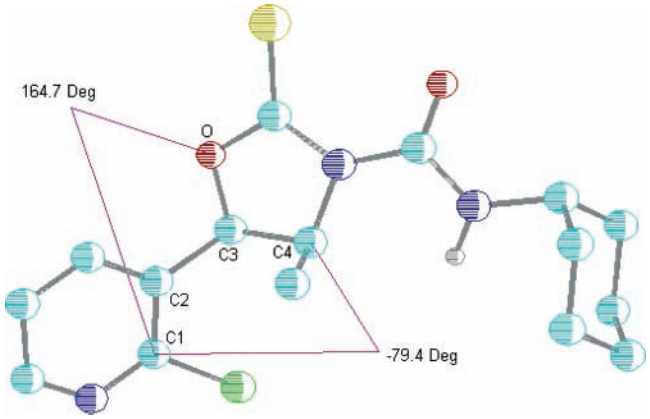


**Figure 1.** Molecular model of compound **3h** based on MMX-E of PCMODEL 6.0 software.

than 164.1° or −79.4°. Compared with H, the *ortho*-substituent of the X group is big enough to make the dihedral angle bigger than 164.7° or −79.4°. Therefore, it is a premise of compounds **3** possessing activity that the dihedral angle remains in the range from 153.3° to 164.1° or from −91.0° to −79.7°.

On the other hand, it has been proposed that a certain degree of lipophilicity is necessary for compounds with bioactivities because the strongly polar compounds would not be allowed to cross the membranes and extremely low water-soluble compounds would not be soluble enough. The molecular lipophilicity parameters $V_N/V_P$, where $V_T$, $V_N$, and $V_P$ stand for the total surface area, nonpolar surface area, and polar surface area of the water solvation shell, respectively, were also calculated (**Table 2**).

From **Table 2**, it was found that $V_N/V_P$ is a very important parameter influencing the activity, and the suitable $V_N/V_P$ value of compounds **3** with herbicidal activities should remain in the range of 3.331−3.634. Compounds **3b**, **3c**, **3e**, **3n**, and **3o** obey the dihedral angle rule but are inactive because their $V_N/V_P$ values lie outside the acceptable range. On the contrary, compound **3i** obeys the lipophilicity rule but also is inactive because its dihedral angles lie outside the acceptable range. On the basis of the above discussion, the combination of appropriate steric property and proper lipophilicity is necessary for herbicidal activity. However, nitro compound **3p** did not obey the lipophilicity rule (1.736) but is active, and this might be due to its probably different mode of action from the other non-nitro compounds.

In conclusion, we have demonstrated that the novel compounds of 3-aminocarbonyl-2-oxazolidinethione containing a substituted pyridine ring presented good herbicidal activity. It was found that the activities of such compounds against *E. crusgalli*, *S. vulgare*, *D. sanguinnalis*, *E. prostrasta*, *C. sativus*, and *B. campestris* can be strongly related to the lipophilicity together with the steric property. Future structural modification and biological evaluation should be carried out to explore the full potential of this novel class of herbicidal molecules.

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