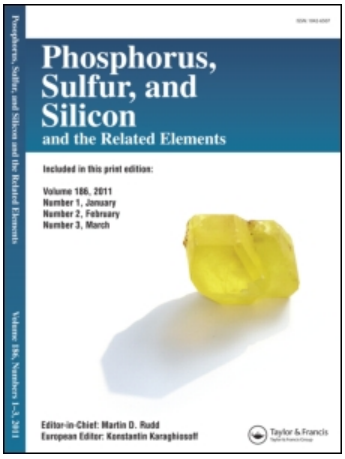

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Synthesis and Biological Activity of a Series of New Thieno[2,3-d]Pyrimidines

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SYNTHESIS AND BIOLOGICAL ACTIVITY OF A SERIES OF NEW THIENO[2,3-d]PYRIMIDINES

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Ethyl 2-amino-5-ethylthiophene-3- carboxylate 1, obtained from the reaction of butyraldehyde, ethyl cyanoacetate, sulfur, and triethylamine, reacted with benzoylisothiocyanate to give the corresponding ureido derivatives 2 in a high yield. Further reactions of the compound 2 with an aqueous-alcohol solution of potassium hydroxide and then with hydrochloric acid gave the 2-thio-thieno[2,3-d]pyrimidine-4-ones 3, which were reacted with RX to give novel compounds 4a–4i. Treating the compound 3 with dibromoalkane led to the formation of triacylic compounds 5j–5m. Their structures were clearly verified by IR, ^{1}H NMR, EI-MS spectroscopy, and elemental analysis. The results of a preliminary bioassay indicated that some compounds possess excellent inhibitory activities against the root and the stalk of* Brassica napus *(rape) and* Echinochloa crusgalli *(barnyard grass) at a dosage of 100 mg/L.

Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.

Keywords Biological activities; synthesis; thieno[2,3-d]pyrimidines

INTRODUCTION

The thieno[2,3-d]pyrimidines have been the focus of great interest over many years. This is due to the wide range of biological activities associated with this heterocyclic scaffold. Some of their derivatives have shown remarkable biological properties such as anticonvulsant, anxiolytic, antihypertensive, anti-arthritic, antimicrobial, antiviral, and antibronchitis, and and have also shown tranquilizer activity.[1–18] Although many methodologies have been developed for the synthesis of various substituted thienopyrimidines,[19–21] the synthesis and herbicidal activities of 2-substituted thio-6-ethylthieno[2,3-d]pyrimidine-4-ones have not been reported. Recently, we have become interested in the synthesis of new bioactive heterocycles such as 2-substituted thio-6-ethylthieno[2,3-d] pyrimidine-4-ones, with the aim of evaluating their biological activities. In this article, we describe a facile synthesis of 2-substituted thio-6-ethylthieno[2,3-d]pyrimidine-4-ones via the ureido

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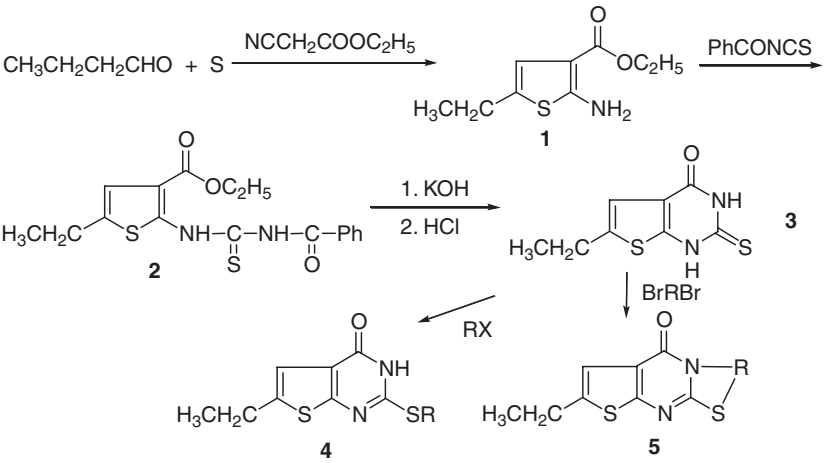
derivatives and cyclization reaction. The results of the bioassay indicated that these title compounds possess herbicidal activity against the root and the stalk of *Brassica napus* (rape) and *Echinochloa crusgalli* (barnyard grass).

RESULTS AND DISCUSSION

Synthesis

The starting material, ethyl 2-amino-5-ethylthiophene-3-carboxylate **1**, was synthesized according to the procedures in the literature.[22] Ethyl 2-amino-5-ethyl-thiophene-3-carboxylate **1**, obtained from the reaction of butyraldehyde, ethyl cyanoacetate, sulfur, and triethylamine in DMF at room temperature, reacted with benzoylisothiocyanate to give the corresponding ureido derivatives **2** with a high yield. Further reactions of the compound **2** with an aqueous alcohol solution of potassium hydrocide and then with hydrochloric acid gave the 2-thio-thieno[2,3-d]pyrimidine-4-ones **3**, which were reacted with RX to give novel compounds **4a–4i** (Table I). Treating compound **3** with dibromoalkane led to the formation of triacylic compounds **5j–5m** (Scheme 1).



Scheme 1 Synthesis of the title compounds **4a–i** and **5j-m**. **R:** **4a**, CH_3; **4b**, CH_2CH_3; **4c**, $CH_2CH_2CH_3$; **4d**, $CH_2CH_2CH_2CH_3$; **4e**, $CH(CH_3)CH_2CH_3$; **4f**, $CH_2(CH_2)_3CH_3$; **4g**, CH_2Ph; **4h**, CH_2COOH; **4i**, CH_2COOEt; **5j**, CH_2CH_2; **5k**, $CH_2CH_2CH_2$; **5l**, $CH_2(CH_2)_2CH_2$; **5m**, $CH_2(CH_2)_3CH_2$.

The molecular structures of all new compounds obtained were confirmed by ^1H NMR, IR spectra, MS, and elemental analyses.

In the ^1H NMR spectra of **4a–4i** and **5j–5m**, the proton in the thiophene moiety exhibits a singlet. The IR spectra of all compounds showed normal stretching absorption bands indicating the existence of the N–H ($\sim$3400 cm^{-1}), C=O ($\sim$1660 cm^{-1}). The EI mass spectra of compounds **4a–4i** and **5j–5m** gave the anticipated molecular ion peaks. All the fragmentation ions of **4a–4i** and **5j–5m** were consistent with their structures and can be clearly assigned.

Table I The physical data of compounds **4a–4i** and **5j–5m**

Compound	R	Formula	Color	mp (°C)	Rt (h)	Yield (%)[a]
4a	CH_3	$C_9H_{10}N_2OS_2$	Yellow	225–227	12	94
4b	CH_2CH_3	$C_{10}H_{12}N_2OS_2$	Yellow	>280	13	87
4c	$CH_2CH_2CH_3$	$C_{11}H_{14}N_2OS_2$	Yellow	>280	12	91
4d	$CH_2CH_2CH_2CH_3$	$C_{12}H_{16}N_2OS_2$	Yellow	150–153	11	78
4e	$CH(CH_3)CH_2CH_3$	$C_{12}H_{16}N_2OS_2$	Yellow	156–158	12	89
4f	$CH_2(CH_2)_3CH_3$	$C_{13}H_{18}N_2OS_2$	White	143–145	13	80
4g	CH_2Ph	$C_{15}H_{14}N_2OS_2$	White	226–228	12	82
4h	CH_2COOH	$C_{10}H_{10}N_2O_3S_2$	White	>300	12	87
4i	CH_2COOEt	$C_{12}H_{14}N_2O_3S_2$	White	>280	12	70
5j	CH_2CH_2	$C_{10}H_{10}N_2OS_2$	Yellow	81–83	13	77
5k	$CH_2CH_2CH_2$	$C_{11}H_{12}N_2OS_2$	Yellow	90–92	13	72
5l	$CH_2(CH_2)_2CH_2$	$C_{12}H_{14}N_2OS_2$	Yellow	103–105	13	68
5m	$CH_2(CH_2)_3CH_2$	$C_{13}H_{16}N_2OS_2$	Yellow	121–123	13	67

[a]Yields of isolated products based on iminophosphorane **3**.

Herbicidal Activity

The herbicidal activity of all compounds **4a–4i** and **5j–5m** against *Brassica napus* (rape) and *Echinochloa crusgalli* (barnyard grass) has been investigated at the dosage of 100 mg/L and 10 mg/L using a known procedure[23] compared with distilled water. (See the Supplemental Materials, Table S1, available online.)

EXPERIMENTAL

Melting points were measured on an electrothermal melting point apparatus and are uncorrected. Mass spectra were measured on a Finnigan Trace MS 2000 spectrometer. IR spectra were recorded on a PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H NMR spectra were recorded in DMSO-d_6 or $CDCl_3$ as solvent on a Varian Mercury 400 spectrometer, and resonances are given in ppm (δ) relative to TMS. Elementary analyses were taken on a Vario EL III elementary analysis instrument. All of the solvents and materials were reagent grade and purified as required.

Synthesis of 2-(N-Benzoylthioureido)-3-ethoxycarbonyl-5-ethylthiophene 2

To a solution of 1.99 g (0.01 mol) of ethyl 2-amino-5-ethylthiophene-3-carboxylate **1** in CH_3CN (20 mL) at 35°C, benzoylisothiocyanate 1.63 g (0.01 mol) was added with stirring. The mixture was stirred for 3 h. The precipitate was separated by filtration and washed with diethyl ether (10 mL) to obtain 3.22 g (88.9%) of compound **2**. Colorless crystals, mp 136–138°C; ^1H NMR (400 MHz, $CDCl_3$) δ: 14.74 (s, 1H, NH—CS—), 9.14 (s, 1H, NH—CO—), 7.53–7.99 (m, 5H, —Ph), 7.07 (s, 1H, C_4HS-4H), 4.47 (q, J = 5.6 Hz, 2H, COO$\underline{CH_2}CH_3$), 2.79 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.42 (t, J = 5.6 Hz, 3H, $COOCH_2\underline{CH_3}$), 1.35 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$).

Synthesis of 2-Thio-thieno[2,3-d]pyrimidine-4-ones 3

A mixture of 3.62 g (0.01 mol) of compound **2** and potassium hydroxide 1.12 g (0.02 mol) in 50% aqueous ethanol (20 mL) was boiled for 2 h. Upon cooling, the reaction mixture was acidified with a 10% aqueous hydrochloric acid solution (6 mL) to obtain a weakly acidic solution. The precipitated crystals were separated by filtration, washed with water, and dried to obtain 1.23 g (58%) of compound **3**; Colorless crystals, mp 261–263°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 6.16 (s, 1H, C_4HS-4H), 2.04 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 0.52 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$). MS (EI, m/z,%): 212 (M^+ 56.2); Anal. Calcd. (%) for $C_8H_8N_2OS_2$: C 45.26, H 3.80, N 13.20; Found C 45.33, H 4.01, N 13.41.

General Procedure for the Preparation of 2-Substituted Thio-6-ethylthieno[2,3-d]pyrimidine-4-ones 4a–4i and 5j–5m

To a solution of compound **3** (2.12 g, 0.01 mol) and potassium hydroxide (0.56 g, 0.01 mol) in 90% aqueous ethanol (90 mL) was added dropwise to RX (0.01 mol) or dibromoalkane (0.01 mol), and the mixture was boiled for 12–13 h. Upon cooling, the reaction mixture was diluted with water (50 mL). The precipitated crystals were separated by filtration, washed with water, and dried to obtain compounds **4a–4i** and **5j–5m**.

2-Methylthio-6-ethylthieno[2,3-d]pyrimidine-4-ones (4a). IR (KBr, υ/cm^{-1}): 3410 (NH), 1661 (C=O), 1554, 1323, 794; ^{1}H NMR (MeOD, 400 MHz): 7.01 (s, 1H, C_4HS-4H), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 2.70 (s, 3H, SCH_3), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, $CDCl_3$, TMS, 400 MHz): 9.2 ($S\underline{CH_3}$), 14.6 ($CH_2\underline{C}H_3$), 23.2 ($\underline{C}H_2CH_3$), 116.1 (thienyl-5C), 119.4 (pyrimidine-8C), 140.6 (thienyl-6C), 160.2 (pyrimidine-9C), 163.2 (pyrimidine-2C), 164.8 (pyrimidine-4C); MS (EI, m/z,%): 226 (M^+ 12.6); Anal. Calcd. (%) for $C_9H_{10}N_2OS_2$: C 47.76, H 4.45, N 12.38; Found C 47.52, H 4.64, N 12.47.

2-Ethylthio-6-ethylthieno[2,3-d] pyrimidine-4-ones (4b). IR (KBr, υ/cm^{-1}): 3401 (NH), 1660 (C=O), 1559, 1333, 795; ^{1}H NMR (MeOD, 400 MHz): 6.97 (s, 1H, C_4HS-4H), 3.14 (q, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_3$), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.37 (t, J = 5.6 Hz, 3H, $SCH_2\underline{CH_3}$), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, $CDCl_3$, TMS, 400 MHz): 14.9($SCH_2\underline{C}H_3$), 15.2 ($CH_2\underline{C}H_3$), 21.3 ($S\underline{C}H_2CH_3$), 23.4 ($\underline{C}H_2CH_3$), 116.1 (thienyl-5C), 120.3 (pyrimidine-8C), 140.5 (thienyl-6C), 160.2 (pyrimidine-9C), 163.6 (pyrimidine-2C), 165.2 (pyrimidine-4C); MS (EI, m/z,%): 240 (M^+ 21.9); Anal. Calcd. (%) for $C_{10}H_{12}N_2OS_2$: C 49.97, H 5.03, N 11.66; Found C 49.71, H 5.24, N 11.58.

2-n-Propylthio-6-ethylthieno[2,3-d]pyrimidine-4-ones (4c). IR (KBr, υ/cm^{-1}): 3414 (NH), 1665 (C=O), 1536, 1331, 796; ^{1}H NMR (MeOD, 400 MHz): 6.98 (s, 1H, C_4HS-4H), 3.17 (t, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_2CH_3$), 2.85 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.70 (t, J = 5.6 Hz, 2H, $SCH_2\underline{CH_2}CH_3$), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$), 0.97 (t, J = 5.6 Hz, 3H, $SCH_2CH_2\underline{CH_3}$); ^{13}C NMR ($\delta$/ppm, $CDCl_3$, TMS, 400 MHz): 13.9 ($SCH_2CH_2\underline{C}H_3$), 15.3 ($CH_2\underline{C}H_3$), 21.4 ($SCH_2\underline{C}H_2CH_3$), 23.8 ($\underline{C}H_2CH_3$), 27.8 ($S\underline{C}H_2CH_2CH_3$), 115.6 (thienyl-5C), 120.0 (pyrimidine-8C), 141.0 (thienyl-6C), 160.2 (pyrimidine-9C), 164.3 (pyrimidine-2C), 165.5 (pyrimidine-4C); MS (EI, m/z,%): 254 (M^+ 19.2); Anal. Calcd. (%) for $C_{11}H_{14}N_2OS_2$: C 51.94, H 5.55, N 11.01; Found C 51.73, H 5.62, N 11.26.

2-n-Butylthio-6-ethylthieno[2,3-d]pyrimidine-4-ones (4d). IR (KBr, υ/cm^{-1}): 3415 (NH), 1656 (C=O), 1536, 1322, 793; ^{1}H NMR (MeOD, 400 MHz): 6.99 (s, 1H, C_4HS-4H), 3.17 (t, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_2CH_2CH_3$), 2.86 (q, J = 5.6 Hz,

2H, $\underline{CH_2}CH_3$), 1.70 (m, J = 5.6 Hz, 2H, $SCH_2\underline{CH_2}CH_2CH_3$), 1.51 (m, J = 5.6 Hz, 2H, $SCH_2CH_2\underline{CH_2}CH_3$), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$), 0.98 (t, J = 5.6 Hz, 3H, $SCH_2CH_2CH_2\underline{CH_3}$); ^{13}C NMR ($\delta$/ppm, $CDCl_3$, TMS, 400 MHz): 13.6($SCH_2CH_2CH_2\underline{CH_3}$), 15.4 ($CH_2\underline{CH_3}$), 22.1 ($SCH_2CH_2\underline{CH_2}CH_3$), 23.9 ($\underline{CH_2}CH_3$), 30.4 ($S\underline{CH_2}CH_2CH_2CH_3$), 31.3 ($SCH_2\underline{CH_2}CH_2CH_3$), 116.3 (thienyl-5C), 120.5 (pyrimidine-8C), 141.2 (thienyl-6C), 160.1 (pyrimidine-9C), 164.6 (pyrimidine-2C), 165.9 (pyrimidine-4C); MS (EI, m/z,%): 268 (M^+ 26.4); Anal. Calcd. (%) for $C_{12}H_{16}N_2OS_2$: C 53.70, H 6.01, N 10.44; Found C 53.76, H 6.12, N 10.66.

2-Isobutylthio-6-ethylthieno[2,3-d]pyrimidine-4-ones (4e). IR (KBr, υ/cm^{-1}): 3413 (NH), 1641 (C=O), 1554, 1322, 795; ^{1}H NMR (MeOD, 400 MHz): 7.07 (s, 1H, C_4HS-4H), 3.96 (m, J = 5.6 Hz, 1H, $S\underline{CH}(CH_3)CH_2CH_3$), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.75 (m, J = 5.6 Hz, 1H, $SCH(CH_3)\underline{CH_2}CH_3$), 1.42 (d, J = 5.6 Hz, 3H, $SCH(\underline{CH_3})CH_2CH_3$), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$), 1.03 (t, J = 5.6 Hz, 3H, $SCH(CH_3)CH_2\underline{CH_3}$); ^{13}C NMR ($\delta$/ppm, $CDCl_3$, TMS, 400 MHz): 12.2($SCH(CH_3)_2CH_2\underline{CH_3}$), 15.2 ($CH_2\underline{CH_3}$), 17.2 ($SCH(\underline{CH_3})_2CH_2CH_3$), 23.2 ($\underline{CH_2}CH_3$), 28.6 ($SCH(CH_3)_2\underline{CH_2}CH_3$), 29.3 ($S\underline{CH}(CH_3)_2CH_2CH_3$), 115.5 (thienyl-5C), 120.2 (pyrimidine-8C), 141.0 (thienyl-6C), 159.5 (pyrimidine-9C), 164.1 (pyrimidine-2C), 165.2 (pyrimidine-4C); MS (EI, m/z,%): 268 (M^+ 20.6); Anal. Calcd. (%) for $C_{12}H_{16}N_2OS_2$: C 53.70, H 6.01, N 10.44; Found C 53.83, H 6.26, N 10.58.

2-n-Pentylthio-6-ethylthieno[2,3-d]pyrimidine-4-ones (4f). IR (KBr, υ/cm^{-1}): 3415 (NH), 1662 (C=O), 1547, 1321, 793; ^{1}H NMR (MeOD, 400 MHz): 6.97 (s, 1H, C_4HS-4H), 3.16 (t, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_2CH_2CH_2CH_3$), 2.86 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.72 (t, J = 5.6 Hz, 2H, $SCH_2\underline{CH_2}CH_2CH_2CH_3$), 1.38∼1.48 (m, J = 5.6 Hz, 2H, $SCH_2CH_2\underline{CH_2}CH_2CH_3$), 1.33 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$), 0.94 (t, J = 5.6 Hz, 3H, $SCH_2CH_2CH_2CH_2\underline{CH_3}$); ^{13}C NMR ($\delta$/ppm, $CDCl_3$, TMS, 400 MHz): 11.8($SCH_2CH_2CH_2CH_2\underline{CH_3}$), 15.5 ($CH_2\underline{CH_3}$), 22.2 ($SCH_2CH_2CH_2\ \underline{CH_2}CH_3$), 23.7 ($\underline{CH_2}CH_3$), 24.7 ($S\underline{CH_2}CH_2CH_2CH_2CH_3$), 28.4 ($SCH_2CH_2\underline{CH_2}CH_2CH_3$), 29.3 ($SCH_2\underline{CH_2}CH_2CH_2CH_3$), 115.4 (thienyl-5C), 119.6 (pyrimidine-8C), 140.6 (thienyl-6C), 159.8 (pyrimidine-9C), 164.2 (pyrimidine-2C), 166.1 (pyrimidine-4C); MS (EI, m/z,%): 282 (M^+ 14.2); Anal. Calcd. (%) for $C_{13}H_{18}N_2OS_2$: C 55.28, H 6.42, N 9.92; Found C 55.43, H 6.54, N 10.17.

2-Benzylthio-6-ethylthieno[2,3-d] pyrimidine-4-ones (4g). IR (KBr, υ/cm^{-1}): 3425 (NH), 1662 (C=O), 1526, 1322, 793; ^{1}H NMR (MeOD, 400 MHz): 7.20–7.44 (m, 5H, Ph-H), 7.00 (s, 1H, C_4HS-4H), 4.44 (s, 2H, CH_2Ph), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.35 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, DMSO, TMS, 400 MHz): 15.4 ($CH_2\underline{CH_3}$), 23.2 ($\underline{CH_2}CH_3$), 33.8 ($S\underline{CH_2}C_6H_5$), 117.6 (thienyl-5C), 117.7 (phenyl-2C), 117.9 (phenyl-6C), 120.7 (phenyl-4C), 126.6 (pyrimidine-8C), 128.2 (phenyl-3C), 128.9 (phenyl-5C), 135.8 (phenyl-1C), 139.3 (thienyl-6C), 162.9 (pyrimidine-9C), 164.4 (pyrimidine-2C), 165.8 (pyrimidine-4C); MS (EI, m/z,%): 302 (M^+ 17.9); Anal. Calcd. (%) for $C_{15}H_{14}N_2OS_2$: C 59.57, H 4.67, N 9.26; Found C 59.78, H 4.39, N 9.06.

2-Hydroxycarbonylmethylthio-6-ethyl-thieno[2,3-d]pyrimidine-4-ones (4h). IR (KBr, υ/cm^{-1}): 3441 (NH), 1678, 1638 (C=O), 1554, 1321, 791; ^{1}H NMR (MeOD, 400 MHz): 11.5 (s, 1H, COOH), 7.25 (s, 1H, C_4HS-4H), 4.23 (s, 2H, $\underline{CH_2}$COOH), 2.94 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.39 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, $CDCl_3$, TMS, 400 MHz): 15.3 ($CH_2\underline{CH_3}$), 23.5 ($\underline{CH_2}CH_3$), 30.2 ($S\underline{CH_2}$COOH), 116.4 (thienyl-5C), 120.4 (pyrimidine-8C), 141.3 (thienyl-6C), 160.3 (pyrimidine-9C), 164.4 (pyrimidine-2C), 165.8 (pyrimidine-4C), 177.6 ($SCH_2\underline{C}$OOH); MS (EI, m/z,%): 270 (M^+

25.3); Anal. Calcd. (%) for $C_{10}H_{10}N_2O_3S_2$: C 44.43, H 3.73, N 10.36; Found C 44.69, H 3.56, N 10.52.

2-Ethoxycarbonylmethylthio-6-ethyl-thieno[2,3-d]pyrimidine-4-ones (4i). IR (KBr, υ/cm^{-1}): 3445 (NH), 1675, 1624 (C=O), 1551, 1387, 777; ^{1}H NMR (MeOD, 400 MHz): 7.01 (s, 1H, C_4HS-4H), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 2.70 (s, 3H, SCH_3), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, $CDCl_3$, TMS, 400 MHz): 13.7 ($SCH_2COOCH_2\underline{C}H_3$), 15.3 ($CH_2\underline{C}H_3$), 23.7 ($\underline{C}H_2CH_3$), 28.4 ($S\underline{C}H_2COOCH_2CH_3$), 57.2 ($SCH_2COO\underline{C}H_2CH_3$), 116.1 (thienyl-5C), 120.6 (pyrimidine-8C), 141.1 (thienyl-6C), 160.5 (pyrimidine-9C), 164.2 (pyrimidine-2C), 166.3 (pyrimidine-4C), 174.4 ($SCH_2\underline{C}OOCH_2CH_3$); MS (EI, m/z,%): 298 ($M^+$ 12.4); Anal. Calcd.(%) for $C_{12}H_{14}N_2O_3S_2$: C 48.30, H 4.73, N 9.39; Found C 48.46, H 4.81, N 9.53.

6-Ethylthieno[2,3-d]thiazo[3,2-a]pyrimidine-4-ones (5j). IR (KBr, υ/cm^{-1}): 3432 (NH), 1670 (C=O), 1526, 1322, 778; ^{1}H NMR (MeOD, 400 MHz): 7.06 (s, 1H, C_4HS-4H), 4.54 (t, J = 5.6 Hz, 2H, $SCH_2\underline{CH_2}N$), 3.62 (t, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_2N$), 2.88 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 1.35 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, DMSO, TMS, 400 MHz): 15.2 ($CH_2\underline{C}H_3$), 23.1 ($\underline{C}H_2CH_3$), 26.8 ($S\underline{C}H_2CH_2N$), 48.3 ($SCH_2\underline{C}H_2N$), 117.0 (thienyl-5C), 120.1 (pyrimidine-8C), 142.8 (thienyl-6C), 155.9 (pyrimidine-9C), 160.4 (pyrimidine-2C), 162.8 (pyrimidine-4C); MS (EI, m/z,%): 238 (M^+ 17.8); Anal. Calcd. (%) for $C_{10}H_{10}N_2OS_2$: C 50.39, H 4.23, N 11.75; Found C 50.46, H 4.30, N 11.86.

6-Ethylthieno[2,3-d]thiazino[3,2-a]pyrimidine-4-ones (5k). IR (KBr, υ/cm^{-1}): 3430 (NH), 1668 (C=O), 1544, 1320, 774; ^{1}H NMR (MeOD, 400 MHz): 7.01 (s, 1H, C_4HS-4H), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 2.70 (s, 3H, SCH_3), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, DMSO, TMS, 400 MHz): 15.2 ($CH_2\underline{C}H_3$), 23.3 ($\underline{C}H_2CH_3$), 25.9 ($S\underline{C}H_2$ CH_2CH_2N), 37.2 ($SCH_2\underline{C}H_2CH_2N$), 46.8 ($SCH_2CH_2\underline{C}H_2N$), 117.3 (thienyl-5C), 120.4 (pyrimidine-8C), 142.3 (thienyl-6C), 155.7 (pyrimidine-9C), 160.1 (pyrimidine-2C), 162.9 (pyrimidine-4C); MS (EI, m/z,%): 252(M^+ 11.8); Anal. Calcd. (%) for $C_{11}H_{12}N_2OS_2$: C 52.35, H 4.79, N 11.10; Found C 52.43, H 4.54, N 11.19.

6-Ethylthieno[2,3-d]thiazepino[3,2-a]pyrimidine-4-ones (5l). IR (KBr, υ/cm^{-1}): 3433 (NH), 1672 (C=O), 1548, 1322, 791; ^{1}H NMR (MeOD, 400 MHz): 7.01 (s, 1H, C_4HS-4H), 2.84 (q, J = 5.6 Hz, 2H, $\underline{CH_2}CH_3$), 2.70 (s, 3H, SCH_3), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, DMSO, TMS, 400 MHz): 15.1 ($CH_2\underline{C}H_3$), 23.2 ($\underline{C}H_2CH_3$), 24.6 ($S\underline{C}H_2$ $CH_2CH_2CH_2N$), 34.4 ($SCH_2CH_2\underline{C}H_2CH_2N$), 36.2 ($SCH_2\underline{C}H_2CH_2CH_2N$), 45.3 ($SCH_2CH_2CH_2\underline{C}H_2N$), 117.7 (thienyl-5C), 121.2 (pyrimidine-8C), 143.1 (thienyl-6C), 156.4 (pyrimidine-9C), 161.2 (pyrimidine-2C), 163.8 (pyrimidine-4C); MS (EI, m/z,%): 266 (M^+ 14.6); Anal. Calcd. (%) for $C_{12}H_{14}N_2OS_2$: C 54.11, H 5.30, N 10.52; Found C 54.22, H 5.54, N 10.77.

6-Ethylthieno[2,3-d]thiazeoctino[3,2-a]pyrimidine-4-ones (5m). IR (KBr, υ/cm^{-1}): 3432 (NH), 1670 (C=O), 1558, 1328, 781; ^{1}H NMR (MeOD, 400 MHz): 7.09 (s, 1H, C_4HS-4H), 3.91 (t, J = 5.6 Hz, 2H, SCH_2CH_2 $CH_2CH_2\underline{CH_2}N$), 3.68 (m, J = 5.6 Hz, 2H, $SCH_2CH_2CH_2\underline{CH_2}CH_2N$), 3.60 (t, J = 5.6 Hz, 2H, $S\underline{CH_2}CH_2CH_2CH_2CH_2N$), 2.05 (m, J = 5.6 Hz, 2H, $SCH_2\underline{CH_2}CH_2CH_2CH_2N$), 1.73 (m, J = 5.6 Hz, 2H, $SCH_2CH_2\underline{CH_2}CH_2CH_2N$), 1.34 (t, J = 5.6 Hz, 3H, $CH_2\underline{CH_3}$); ^{13}C NMR (δ/ppm, DMSO, TMS, 400 MHz): 15.0 ($CH_2\underline{C}H_3$), 23.0 ($\underline{C}H_2CH_3$), 22.3 ($S\underline{C}H_2CH_2CH_2CH_2CH_2N$), 32.4 ($SCH_2CH_2\underline{C}H_2CH_2CH_2N$), 33.2 ($SCH_2CH_2CH_2\underline{C}H_2CH_2N$), 35.7 ($SCH_2\underline{C}H_2CH_2CH_2CH_2N$), 44.2 ($SCH_2CH_2CH_2CH_2$ $\underline{C}H_2N$), 116.5 (thienyl-5C), 120.2 (pyrimidine-8C), 141.5 (thienyl-6C), 154.1 (pyrimidine-9C), 160.7 (pyrimidine-2C), 162.4 (pyrimidine-4C); MS (EI, m/z,%): 280 (M^+ 18.2);

Anal. Calcd. (%) for $C_{13}H_{16}N_2OS_2$: C 55.68, H 5.75, N 9.99; Found C 55.42, H 5.64, N 9.77.

Herbicidal Testing

Herbicidal testing of the newly synthesized compounds **4a–4i** and **5j–5m** was carried out in a plant growth room. (See the Supplemental Materials.)

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