

Article

Synthesis, Herbicidal Activity, Crop Safety and Soil Degradation of Pyrimidine- and Triazine-Substituted Chlorsulfuron Derivatives

Lei Wu ¹, Yu-Cheng Gu ², Yong-Hong Li ¹, Sha Zhou ¹, Zhong-Wen Wang ^{1,*} and Zheng-Ming Li ^{1,*}

¹ State Key Laboratory of Elemento-Organic Chemistry, College of Chemistry, Nankai University, Tianjin 300071, China; wl836929871@163.com (L.W.); bioassay@nankai.edu.cn (Y.-H.L.); zhousha@nankai.edu.cn (S.Z.)

² Syngenta Jealott's Hill International Research Centre, Bracknell RG42 6EY, Berkshire, UK; yucheng.gu@syngenta.com

* Correspondence: wzwrj@nankai.edu.cn (Z.-W.W.); nkzml@vip.163.com (Z.-M.L.)

Abstract: Chlorsulfuron, a classical sulfonylurea herbicide that exhibits good safety for wheat but causes a certain degree of damage to subsequent corn in a wheat–corn rotation mode, has been suspended field application in China since 2014. Our previous study found that diethylamino-substituted chlorsulfuron derivatives accelerated the degradation rate in soil. In order to obtain sulfonylurea herbicides with good crop safety for both wheat and corn, while maintaining high herbicidal activities, a series of pyrimidine- and triazine-based diethylamino-substituted chlorsulfuron derivatives (**W102–W111**) were systematically evaluated. The structures of the synthesized compounds were confirmed with ¹H NMR, ¹³C NMR, and HRMS. The preliminary biological assay results indicate that the 4,6-disubstituted pyrimidine and triazine derivatives could maintain high herbicidal activity. It was found that the synthesized compounds could accelerate degradation rates, both in acidic and alkaline soil. Especially, in alkaline soil, the degradation rate of the target compounds accelerated more than 22-fold compared to chlorsulfuron. Moreover, most chlorsulfuron analogs exhibited good crop safety for both wheat and corn at high dosages. This study provided a reference for the further design of new sulfonylurea herbicides with high herbicidal activity, fast degradation rates, and high crop safety.

Keywords: sulfonylurea herbicides; herbicidal activity; soil degradation; crop safety; DT₅₀



Citation: Wu, L.; Gu, Y.-C.; Li, Y.-H.; Zhou, S.; Wang, Z.-W.; Li, Z.-M. Synthesis, Herbicidal Activity, Crop Safety and Soil Degradation of Pyrimidine- and Triazine-Substituted Chlorsulfuron Derivatives. *Molecules* **2022**, *27*, 2362. <https://doi.org/10.3390/molecules27072362>

Academic Editor: James Barker

Received: 21 March 2022

Accepted: 5 April 2022

Published: 6 April 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Chlorsulfuron, one of the classical sulfonylurea herbicides, was developed and marketed in the 1980s and has been widely used as a wheat-field herbicide due to its extremely efficient herbicidal activity and safety for mammals [1].

As acetolactate synthase (ALS) inhibitors, chlorsulfuron blocks the biosynthesis of three essential amino acids (valine, leucine, and isoleucine) and leads to the inhibition of weed growth [2].

China feeds 22% of the world's population with 7% of the world's cultivated area [3]. Due to the large demand of food for a growing population, a crop rotation mode has been implemented in some countries, including China [4]. With the large-scale use of sulfonylurea herbicides, some sulfonylurea herbicides show different toxicities of residues on different crop varieties because of their long degradation times and this has caused serious economic losses [5]. Chlorsulfuron, a classical sulfonylurea herbicide that exhibits good safety on wheat but seriously endangers the normal growth of subsequent corn, had its field application suspended by the Ministry of Agriculture of China in 2014 [6].

Sulfonylurea herbicides have a long residual period in alkaline soils. Walker et al. reported that the DT₅₀ of chlorsulfuron in sandy soil (at 6% soil moisture) with pH 7.1 was

54.2 days at 10 °C [7]. Thirunarayanan et al. reported that the degradation half-life (DT_{50}) of chlorsulfuron was 105.0 days in soil with pH 7.1 at 20 °C and 143.3 days at pH 8.1 [8] Fredrickson et al. reported that the DT_{50} of chlorsulfuron was 10 weeks in soil with pH 7.5 and 12.5 weeks at pH 8.0 [9]. Nicholls et al. reported that the DT_{50} of chlorsulfuron could be 18 months in soils with low microbial activity and high pH [10].

Our group has been working on the problem of the long degradation times of sulfonylurea herbicides. In our previous study, we found that the 5th substituted groups on the benzene ring in chlorsulfuron has a great influence on its degradation rate in acidic soils and concluded for the first time that electron-donating substituents could accelerate degradation rates in acidic soil (Figure 1) [11,12]. Li et al. found that 5-dialkylamino-substituted groups on the benzene ring of chlorsulfuron could greatly accelerate degradation under alkaline conditions [13–15]. However, they found that 5-dialkylamino-substituted groups on the benzene ring of chlorsulfuron could endanger the normal growth of wheat and corn through post-emergence treatment [15]. At the same time, they found that heterocyclic amines-based 5-dialkylamino-substituted chlorsulfuron derivatives could improve crop safety of wheat [14], and the crop safety of corn with diethylamino-substituted chlorsulfuron was better than that of dimethylamino-substituted chlorsulfuron through pre-emergence treatment [15].

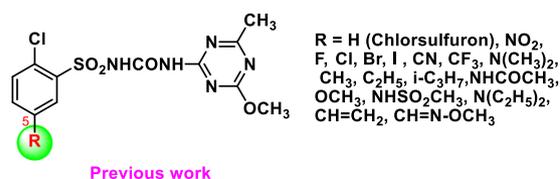


Figure 1. The 5th substituted groups on the benzene ring in chlorsulfuron.

In recent years, pyrimidine- and triazine-based heterocycles have been reported to exhibit excellent bioactivity in herbicides, especially sulfonylurea herbicides used on wheat and corn [16,17].

In order to obtain sulfonylurea herbicides with good crop safety both for wheat and corn, while maintaining their high herbicidal activities, we synthesized a series of pyrimidine- and triazine-based diethylamino-substituted chlorsulfuron derivatives (Figure 2). As multi-factor (activities, crop safety and soil degradation) relationship should be considered to explore new green sulfonylurea herbicides under different crop rotation modes, we herein systematically evaluated their herbicidal activities, crop safety for both wheat and corn, as well as soil degradation (in both acidic and alkaline soil) with chlorsulfuron as the control.

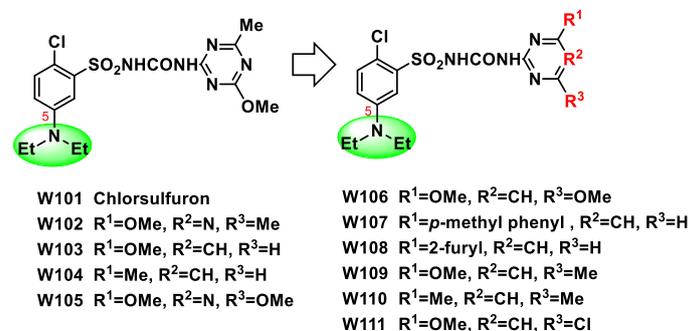


Figure 2. Design of the title compounds W.

2. Materials and Methods

2.1. Instruments and Materials

¹H and ¹³C NMR were obtained using a 400 MHz Bruker AV 400 spectrometer (Bruker Co., Fallanden, Switzerland). A Rigaku Saturn 70 CCD diffractometer (Rigaku Corpora-

tion, Tokyo, Japan) was used to obtain crystal data. Agilent 6520 Q-TOF LC/MS high-resolution mass spectrometer (HRMS) (Agilent Co., Santa Clara, CA, USA) was used to obtain the HRMS.

All reagents for high-performance liquid chromatography (HPLC) were chromatographic grade, reaction reagents were analytical grade and the water phase was double-distilled water. A TU-1810 ultraviolet-visible spectrophotometer (Persee General Analysis Co., Beijing, China) was used to detect the wavelength. HPLC data were obtained on a SHIMADZU LC-20AT (SHIMADZU Co., Kyoto, Japan), equipped with a binary pump (SHIMADZU, LC-20AT), a UV-vis detector (SHIMADZU, SPD-20A), an auto sampler (SHIMADZU, SIL-20A), a Shimadzu shim-pack VP-ODS column (5 μ m, 250 \times 4.6 mm, C18 reversed phase chromatography) connected to a Shimadzu shim-pack GVP-ODS (10 \times 4.6 mm) guard column, a column oven (SHIMADZU, CTO-20AC), and a computer (Dell) to carry out experimental data analysis. Column chromatography purification was carried out using silica gel (200–300 mesh). A SHZ-88 thermostatic oscillator (Jintan Medical Instrument Factory, Changzhou, China), Thermo Scientific Legend Mach 1.6 R centrifuge (Thermo Fisher Scientific Inc., Waltham, MA, USA) and SPX-150B-Z biochemical incubator (Boxun Industrial Co., Shanghai, China) were used in the degradation experiments.

2.2. Synthetic Method

The synthetic procedure for compounds **W102–W111** is shown in Figure 3.

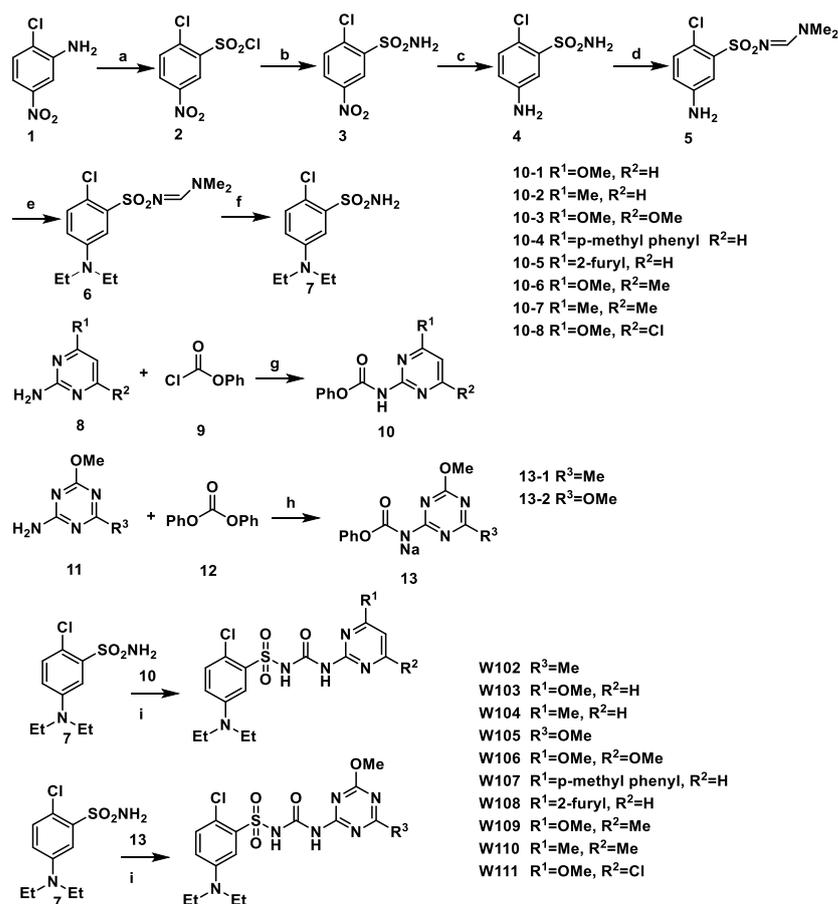


Figure 3. The synthesis of compounds **W102–W111**. Reagents and conditions: (a) H₂O, HCl, NaNO₂→H₂O, HCl, CuCl₂, NaHSO₃, −5 °C; (b) 28% NH₃ H₂O, THF, 0 °C→RT (room temperature), overnight; (c) Fe, HCl, C₂H₅OH, H₂O, reflux; (d) DMF-DMA (*N,N*-dimethylformamide dimethyl acetal), CH₂Cl₂; (e) IC₂H₅, K₂CO₃, DMF, 65 °C; (f) 80% H₂NNH₂•H₂O, C₂H₅OH; (g) KI, K₂CO₃, THF, 0 °C→RT; (h) 60% NaH, THF, 0 °C→RT; (i) DBU (1,8-diazabicyclo[5.4.0]undec-7-ene), CH₃CN.

The synthesis of intermediates 7, 10 and 13 has been reported in previous work [11,18–25].

Intermediate 8 (1.90 mmol) and 9 (2.00 mmol), KI (1.90 mmol), K₂CO₃ (3.80 mmol) and 20 mL THF were added to a 100 mL round bottom flask, and magnetically stirred overnight at 0 °C in an ice bath. The progress was monitored by TLC. After completion of the reaction, THF was removed by concentration in a vacuum, and the residue was purified through chromatography on silica gel using petroleum ether/ethyl acetate (*v/v* = 6:1) as eluent to obtain intermediate 10.

Intermediate 11 (1.90 mmol), 12 (3.80 mmol), NaH (1.90 mmol) and 20 mL THF were added to a 100 mL round bottom flask, and magnetically stirred overnight at 0 °C in ice bath. Then, 60% NaH (2.06 mmol) was slowly added to the flask. The progress was monitored by TLC. After completion of the reaction, suction filtration was implemented and solid product intermediate 13 was obtained.

Synthesis of target compound **W102–W111**.

W102 was reported in our previous research [11].

Intermediate 10 (1.90 mmol) and 12 (2.00 mmol), DBU (2.85 mmol) and 10 mL of acetonitrile were added to a 25 mL round bottom flask, and magnetically stirred overnight at room temperature. The progress was monitored by TLC. After completion of the reaction, acetone was removed by concentration in a vacuum, and the residue was purified through chromatography on silica gel using petroleum ether/ethyl acetate (*v/v* = 5:1) as eluent to obtain the target compounds **W103–W111** (**W105** was not included).

Intermediate 13 (1.90 mmol) and 12 (2.00 mmol), DBU (2.85 mmol) and 10 mL of acetonitrile were added to a 25 mL round bottom flask, and magnetically stirred overnight at room temperature. The progress was monitored by TLC. After completion of the reaction, acetone was removed by concentration in a vacuum. A total of 10 mL of water was added to the residue and the mixture was adjusted to pH 4. The resulting precipitate was obtained by filtration. The product was purified through chromatography on silica gel using petroleum ether/ethyl acetate (*v/v* = 5:1) as eluent to obtain the target compounds **W105**.

W103 White solid product with a yield of 83.2%. Melting point: 179–181 °C. ¹H NMR (400 MHz, Chloroform-*d*) δ 12.84 (s, 1H, NH), 8.30 (d, *J* = 5.1 Hz, 1H, pyrimidin-H), 7.53 (s, 1H, Ph-H), 7.22 (d, *J* = 8.9 Hz, 1H, Ph-H), 6.72 (d, *J* = 6.5 Hz, 1H, Ph-H), 6.45 (d, *J* = 5.9 Hz, 1H, pyrimidin-H), 4.01 (s, 3H, OCH₃), 3.40 (q, *J* = 13.9, 6.9 Hz, 4H, CH₂CH₃), 1.19 (t, *J* = 7.0 Hz, 6H, CH₂CH₃). ¹³C NMR (101 MHz, Chloroform-*d*) δ 170.14, 157.36, 156.43, 148.81, 146.44, 136.21, 132.10, 116.64, 115.75, 115.17, 103.24, 54.72, 44.65, 12.29. HRMS (ESI) calcd for C₁₆H₂₁ClN₅O₄S [M+H]⁺ 414.0997, found 414.0994.

W104 White solid product with a yield of 81.8%. Melting point: 144–146 °C. ¹H NMR (400 MHz, Chloroform-*d*) δ 12.98 (s, 1H, NH), 8.46 (d, *J* = 5.1 Hz, 1H, pyrimidin-H), 7.55 (s, 1H, Ph-H), 7.24 (d, *J* = 9.0 Hz, 1H, Ph-H), 6.90 (d, *J* = 5.2 Hz, 1H, Ph-H), 6.76 (d, *J* = 7.1 Hz, 1H, pyrimidin-H), 3.40 (q, *J* = 7.1 Hz, 4H, CH₂CH₃), 2.53 (s, 3H, CH₃), 1.19 (t, *J* = 7.1 Hz, 6H, CH₂CH₃). ¹³C NMR (101 MHz, Chloroform-*d*) δ 168.54, 158.30, 156.57, 149.25, 146.38, 136.48, 132.12, 116.59, 115.67, 114.84, 114.84, 44.65, 24.01, 12.27. HRMS (ESI) calcd for C₁₆H₂₁ClN₅O₃S [M+H]⁺ 398.1048, found 398.1049.

W105 White solid product with a yield of 82.2%. Melting point: 187–189 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.56 (s, 1H, NH), 11.07 (s, 1H, NH), 7.39 (d, *J* = 8.9 Hz, 1H, Ph-H), 7.30 (s, 1H, Ph-H), 6.95 (d, *J* = 9.0 Hz, 1H, Ph-H), 3.98 (s, 6H, OCH₃), 3.39 (q, *J* = 7.0 Hz, 4H, CH₂CH₃), 1.12 (t, *J* = 7.1 Hz, 6H, CH₂CH₃). ¹³C NMR (101 MHz, Chloroform-*d*) δ 172.06, 164.52, 147.83, 146.34, 135.85, 132.18, 116.89, 115.75, 115.29, 55.91, 44.75, 12.23. HRMS (ESI) calcd for C₁₆H₂₂ClN₆O₅S [M+H]⁺ 445.1055, found 445.1054.

W106 White solid product with a yield of 84.1%. Melting point: 197–200 °C. ¹H NMR (400 MHz, Chloroform-*d*) δ 12.83 (s, 1H, NH), 7.54 (s, 1H, Ph-H), 7.22 (d, *J* = 4.7 Hz, 1H, Ph-H), 6.76 (s, 1H, Ph-H), 5.79 (s, 1H, pyrimidin-H), 3.96 (s, 6H, OCH₃), 3.40 (q, *J* = 6.8 Hz, 4H, CH₂CH₃), 1.19 (t, *J* = 6.9 Hz, 6H, CH₂CH₃). ¹³C NMR (101 MHz, Chloroform-*d*) δ 171.48, 155.35, 148.52, 146.26, 136.07, 132.14, 116.76, 115.41, 85.34, 85.28, 54.90, 44.75, 12.23. HRMS (ESI) calcd for C₁₇H₂₃ClN₅O₅S [M+H]⁺ 444.1103, found 444.1102.

W107 White solid product with a yield of 82.6%. Melting point: 226–228 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 13.35 (s, 1H, NH), 10.81 (s, 1H, NH), 8.75 (d, $J = 5.4$ Hz, 1H, pyrimidin-H), 8.11 (d, $J = 8.2$ Hz, 2H, Ph-H), 7.79 (d, $J = 5.4$ Hz, 1H, pyrimidin-H), 7.39 (d, $J = 8.1$ Hz, 2H, Ph-H), 7.35 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.32 (d, $J = 3.1$ Hz, 1H, Ph-H), 6.93 (dd, $J = 9.0, 3.1$ Hz, 1H, Ph-H), 3.39 (dd, $J = 13.3, 6.3$ Hz, 4H, CH_2CH_3), 2.41 (s, 3H, CH_3), 1.12 (t, $J = 7.0$ Hz, 6H, CH_2CH_3). ^{13}C NMR (101 MHz, DMSO- d_6) δ 169.58, 164.18, 163.98, 159.27, 146.43, 141.73, 140.73, 134.67, 132.37, 129.74, 127.08, 115.67, 114.90, 111.50, 105.93, 44.37, 21.40, 12.57. HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{25}\text{ClN}_5\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 474.1361, found 474.1360.

W108 White solid product with a yield of 84.8%. Melting point: 231–233 °C. ^1H NMR (400 MHz, DMSO- d_6) δ 12.87 (s, 1H, NH), 10.78 (s, 1H, NH), 8.70 (d, $J = 4.9$ Hz, 1H, pyrimidin-H), 8.16 (s, 1H, Thio-H), 7.98 (d, $J = 3.7$ Hz, 1H, Thio-H), 7.72 (d, $J = 4.8$ Hz, 1H, Thio-H), 7.36 (d, $J = 8.9$ Hz, 1H, Ph-H), 7.32 (s, 1H, Ph-H), 6.94 (d, $J = 8.3$ Hz, 1H, Ph-H), 5.77 (s, 1H, pyrimidin-H), 3.43–3.36 (m, 4H, CH_2CH_3), 1.12 (t, $J = 6.3$ Hz, 6H, CH_2CH_3). HRMS (ESI) calcd for $\text{C}_{19}\text{H}_{21}\text{ClN}_5\text{O}_3\text{S}_2$ $[\text{M}+\text{H}]^+$ 465.0769, found 466.0768.

W109 White solid product with a yield of 80.9%. Melting point: 185–187 °C. ^1H NMR (400 MHz, Chloroform- d) δ 13.34 (s, 1H, NH), 7.57 (s, 1H, Ph-H), 7.28 (d, $J = 3.7$ Hz, 1H, Ph-H), 6.77 (d, $J = 5.8$ Hz, 1H, Ph-H), 6.31 (s, 1H, pyrimidin-H), 3.97 (s, 3H, OCH_3), 3.42 (dd, $J = 7.0$ Hz, 4H, CH_2CH_3), 2.44 (s, 3H, CH_3), 1.21 (t, $J = 7.1$ Hz, 6H, CH_2CH_3). ^{13}C NMR (101 MHz, Chloroform- d) δ 170.69, 167.79, 155.90, 148.83, 146.29, 136.36, 132.09, 116.62, 115.89, 115.21, 101.80, 54.48, 44.73, 23.46, 12.25. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{ClN}_5\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$ 428.1154, found 428.1153.

W110 White solid product with a yield of 83.5%. Melting point: 199–201 °C. ^1H NMR (400 MHz, CDCl_3) δ 13.32 (s, 1H, NH), 7.77 (s, 1H, NH), 7.54 (d, $J = 2.6$ Hz, 1H, Ph-H), 7.23 (d, $J = 8.8$ Hz, 1H, Ph-H), 6.78 (s, 1H, Ph-H), 6.73 (dd, $J = 8.8, 2.7$ Hz, 1H, pyrimidin-H), 3.41 (q, $J = 6.9$ Hz, 4H, CH_2CH_3), 2.48 (s, 6H, CH_3), 1.20 (t, $J = 7.0$ Hz, 6H, CH_2CH_3). ^{13}C NMR (101 MHz, Chloroform- d) δ 168.49, 156.31, 149.08, 146.34, 136.43, 132.05, 116.49, 115.61, 115.25, 114.92, 44.61, 23.67, 12.27. HRMS (ESI) calcd for $\text{C}_{17}\text{H}_{23}\text{ClN}_5\text{O}_3\text{S}$ $[\text{M}+\text{H}]^+$ 412.1205, found 412.1203.

W111 White solid product with a yield of 85.1%. Melting point: 209–210 °C. ^1H NMR (400 MHz, CDCl_3) δ 12.29 (s, 1H, NH), 7.54 (s, 1H, Ph-H), 7.31 (s, 1H, Ph-H), 6.78 (s, 1H, Ph-H), 6.50 (s, 1H, pyrimidin-H), 4.05 (s, 3H, CH_3), 3.40 (dd, $J = 13.7, 6.8$ Hz, 4H, CH_2CH_3), 1.19 (t, $J = 6.9$ Hz, 6H, CH_2CH_3). ^{13}C NMR (101 MHz, DMSO- d_6) δ 171.04, 160.35, 156.70, 148.24, 146.45, 136.33, 132.74, 117.59, 114.69, 114.49, 101.82, 55.68, 44.53, 12.46. HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{20}\text{Cl}_2\text{N}_5\text{O}_4\text{S}$ $[\text{M}+\text{H}]^+$ 448.0608, found 448.0609.

2.3. X-ray Diffraction

The crystal of **W110** was obtained by self-evaporation of the mixture solvent of dichloromethane and methyl tert-butyl ether ($v/v = 1:2$). It was colorless and analyzed using X-ray diffraction. Crystal data of compound **W110** can be found in the Supplementary Materials (SI).

2.4. Herbicidal Activity

The herbicidal activity test methods of the target compounds referred to the literature [26–28]. Pot trials for herbicidal activities against *Echinochloa crusgalli*, *Digitaria sanguinalis*, *Amaranthus tricolor*, and *Brassica campestris* were tested with chlorsulfuron as a positive control.

Pre-emergence treatment: An appropriate amount of culture soil (vermiculite:loam:fertilizer soil = 1:1:1) was added to a paper cup with a height of 7.5 cm. The chemicals were sprayed at the dosage of $15 \text{ g}\cdot\text{ha}^{-1}$ and $150 \text{ g}\cdot\text{ha}^{-1}$, respectively. Weed seeds were planted and water was added to adjust soil moisture. Samples were cultivated in a greenhouse at 25 ± 2 °C. Plants were watered regularly to ensure normal growth of weeds. The fresh weight of the above-ground weeds was measured after 28 days, and the inhibition rate was calculated and the herbicidal activity of the target compound was indicated by the fresh

weight inhibition percentage. The variance analysis of the data was performed using the Duncan multiple comparisons with DPS16.5 software.

Post-emergence treatment: Seeding was conducted following adjustment of the moisture and temperature, and the tested chemicals were sprayed until the weeds grew up to the one leaf and one stem stage. The fresh weight of the above-ground weeds was measured after 28 days, and the inhibition rate was calculated and the herbicidal activity of the target compound was indicated by the fresh weight inhibition percentage. The variance analysis of the data was performed using the Duncan multiple comparisons with DPS16.5 software.

2.5. Soil Degradation

The culture method was consistent with our previous reports [11–15,23]. The detailed experimental procedure can be found in the Supplementary Materials (SI). Soil degradation steps are described here briefly.

Soil was selected from Jiangxi (pH 5.46) and Hebei (pH 8.39) provinces to develop degradation studies [29]. The properties of the tested soils are listed in Table 1. HPLC analysis conditions were measured using acetonitrile, ultrapure water (pH 3.0) and chromatographically pure methanol as the mobile phase. The retention time remained between 10–20 min. Standard curves were established with an injection volume of 10 μL at 20 $^{\circ}\text{C}$ and concentration range was between 200 $\mu\text{g mL}^{-1}$ and 0.025 $\mu\text{g mL}^{-1}$. Additionally, the concentrations of the test compounds in the 100 mL conical flask were 0.5, 2, and 5 mg kg^{-1} (in acetonitrile) for 20 g of soil. Each concentration of sample was repeated 5 times. In addition, the recovery rates remained between 70 and 110% with a coefficient of variation (RSD) no more than 5%. And for cultivation of samples, the concentration of each sample was 5 mg kg^{-1} in soil. Water was added to adjust soil moisture and the samples were cultivated at 25 ± 1 $^{\circ}\text{C}$ by a biochemical incubator at 80% humidity under dark conditions. Soil samples of three replicates were collected at six different times. Finally, according to the kinetic equation $C_t = C_0 \times e^{-kt}$, DT_{50} values were calculated following the formula: $DT_{50} = \ln(2)/k$ (the analytical data for verification of recovery rates in various concentrations can be found in Supplementary Materials (SI)).

Table 1. Analytical data of soils.

Soils	Soil Texture	pH	Cation Exchange Capacity ($\text{cmol}^+ \cdot \text{kg}^{-1}$)	Organic Matter ($\text{g} \cdot \text{kg}^{-1}$)	Soil Separation (mm)/Mechanical Composition (%)								
					1–2	0.5–1	0.025–0.5	0.05–0.02	0.02–0.002	<0.002	0.25–0.05	2.0–0.05	0.05–0.002
Alkaline soils	Loam	8.39	7.30	19.4	1–2	0.5–1	0.025–0.5	0.05–0.02	0.02–0.002	<0.002	0.25–0.05	2.0–0.05	0.05–0.002
					0.795	2.46	2.33	7.90	28.6	28.2	29.7	35.3	36.5
Acidic soils	Sandy loam	5.46	14.4	8.37	0.075	0.381	0.708	12.5	17.9	10.5	57.9	59.1	30.4

2.6. Crop Safety Assay

Chlorsulfuron is a classic sulfonylurea herbicide used in wheat fields. Its residual in soil seriously affects the normal growth of following crop seedlings. Corn is one of the crops planted after wheat. In this study, wheat (Xinong 529) and corn (Xindan 66) were used as test crops, and chlorsulfuron was used as control. The culture method was consistent with previous reports [15,23,27].

Methods of plant cultivation: An appropriate amount of culture soil (vermiculite: loam: fertilizer soil = 1:1:1) was added to a paper cup with a height of 7.5 cm. Seeds were planted and water was added to adjust the soil moisture. Samples were covered with plastic wrap and cultivated in a greenhouse at 25 ± 2 $^{\circ}\text{C}$.

Pre-emergence treatment: The chemicals were sprayed at concentrations of 15 $\text{g} \cdot \text{ha}^{-1}$ and 150 $\text{g} \cdot \text{ha}^{-1}$. Seeds were planted and water was added to adjust the soil moisture. Samples were cultivated in a greenhouse at 25 ± 2 $^{\circ}\text{C}$. Plants were watered regularly to ensure the normal growth of weeds. The fresh weight of the cover crops was measured after several days (22 days for wheat and 16 days for corn).

Post-emergence treatment: The chemicals were sprayed when the wheat grew to the 4-leaf stage. For corn, the safety assay began when the corn grew to the 3-leaf stage. The fresh weight of the cover crops was measured after several days (28 days for wheat and 23 days for corn).

The fresh weight of the above-ground crops was measured after several days, and the inhibition rates of fresh weight were used to represent the safety of the crops. The variance analysis of the data was performed using the Duncan multiple comparisons with SPSS 22.0.

3. Results and Discussion

3.1. Chemistry

Compounds **W103**–**W111** were characterized by melting points, ^1H NMR, ^{13}C NMR and HRMS (all the spectra are listed in Supplementary Materials (SI)).

For pyrimidine- and triazine-substituted chlorsulfuron derivatives, the ^1H NMR spectra of compound **W103** and **W105** was taken as an example.

^1H NMR spectra of compound **W103**: The chemical shifts of NH in the sulfonylurea bridge was at δ 12.84. The chemical shift of H on pyrimidine ring was displayed at δ 8.30 and δ 6.45, while 2- CH_3O was at δ 4.01. The aromatic hydrogens presented at δ 7.53, δ 7.22 and δ 6.72, respectively. The chemical shifts of CH_3 and CH_2 on 5-amino were at δ 1.19 and δ 3.40, respectively.

^1H NMR spectra of compound **W105**: The chemical shifts of NH in the sulfonylurea bridge was at δ 12.56 and δ 11.07. The chemical shift of H was displayed at δ 3.98 (CH_3O) on the triazine ring. The aromatic hydrogens presented at δ 7.39, δ 7.30 and δ 6.95, respectively. The chemical shifts of CH_3 and CH_2 on 5-amino were at δ 1.12 and δ 3.39, respectively.

3.2. X-ray Diffraction

A suitable crystal was selected and obtained using a Rigaku Saturn 70 CCD diffractometer. The crystal was kept at 113.15 K during data collection. Using Olex2 [30], the structure was solved with the ShelXT [31] structure solution program using Intrinsic Phasing and refined with the ShelXL [31] refinement package using least squares minimization.

The crystal structure of **W110** is shown in Figure 4 (CCDC no. 2142702).

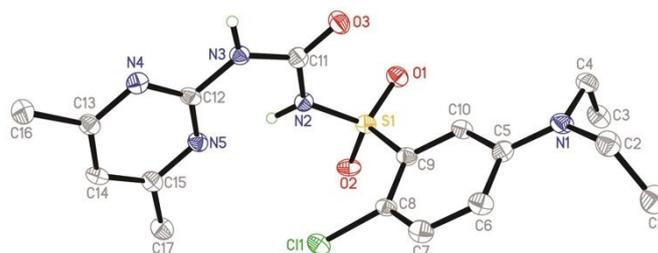


Figure 4. Crystal structure **W110**.

The sum of the angles $\text{O}(3)\text{--C}(11)\text{--N}(2)$ [$123.7(7)^\circ$], $\text{O}(3)\text{--C}(11)\text{--N}(3)$ [$121.8(7)^\circ$], and $\text{N}(2)\text{--C}(11)\text{--N}(3)$ [$114.5(6)^\circ$] was 360° , indicating the plane sp^2 hybridization state of the C(11) atom.

The bonds angles $\text{O}(1)\text{--S}(1)\text{--N}(2)$, $\text{O}(2)\text{--S}(1)\text{--C}(9)$, and $\text{N}(2)\text{--S}(1)\text{--C}(9)$ were $110.5(3)^\circ$, $109.8(3)^\circ$, and $104.0(3)^\circ$, respectively, which indicated that the state of S(1) atom was sp^3 hybridization. The bond lengths of $\text{N}(1)\text{--C}(4)$ and $\text{N}(1)\text{--C}(2)$ were 1.468(10) nm and 1.462(10) nm, respectively. The bond length of $\text{N}(1)\text{--C}(5)$ was 1.370(10) nm, which was shorter than the general C–N bonds. It was speculated that the shorter bond was caused by the transfer of π electrons to the benzene ring. The dihedral angle of the pyrimidine ring and benzene ring was $87.938(225)$, which were non-planar.

3.3. Herbicidal Activity

The herbicidal activities of title compounds against *Echinochloa crusgalli*, *Digitaria sanguinalis*, *Amaranthus tricolor*, and *Brassica campestris* were screened through pre- and post-emergence treatment at 15 g·ha⁻¹ and 150 g·ha⁻¹ with chlorsulfuron as a positive control.

As shown in Table 2, the herbicidal activities of **W103**, **W104**, **W107** and **W108** are not ideal. For pre-emergence treatment, at concentration of 150 g·ha⁻¹, the inhibition rates of **W104**, **W103**, **W107** and **W108** against *Brassica campestris* were 70.8%, 13.9%, 11.8% and 2.4%, respectively. The inhibition rates against *Echinochloa crusgalli* were 65.3%, 40.1%, 0% and 0%. It seemed that mono substituents on the 4-position of the pyrimidine ring derivatives may have decreased the herbicidal activity. The larger the volume of the mono substituent, the lower the herbicidal activity. Overall scanning of the herbicidal activities of **W106**, **W109**, **W110** and **W111** showed that they maintained high herbicidal activities compared with chlorsulfuron. At a concentration of 150 g·ha⁻¹, the inhibition rates against *Brassica campestris* were 100%, 100%, 94.2% and 100%, respectively, which were comparable to chlorsulfuron (100%) under post-emergence treatments. At a concentration of 150 g·ha⁻¹, the inhibition rates of **W106** and **W109** against *Amaranthus tricolor* surpassed chlorsulfuron under both pre- and post-emergence treatments. For post-emergence treatments, the inhibition rates of **W109**, **W110** and **W111** against *Echinochloa crusgalli* were 98.4%, 79.4% and 98.4%, respectively, which were higher than chlorsulfuron (60.2%). For compound **W105**, the inhibition rates against *Brassica campestris* and *Amaranthus tricolor* were 88.1% and 91.2%, respectively, at 150 g·ha⁻¹ through pre-emergence treatments. The inhibition rate of **W105** against *Echinochloa crusgalli* was 90.6%, which was better than chlorsulfuron (60.2%).

Table 2. Herbicidal activities of the title compounds (W) at a concentration of 15 g·ha⁻¹ and 150 g·ha⁻¹.

Compd.	Concentration (g·ha ⁻¹)	Herbicidal Activity, Inhibition Rates (%)							
		Pre-Emergence Treatment				Post-Emergence Treatment			
		<i>Brassica campestris</i>	<i>Amaranthus tricolor</i>	<i>Echinochloa crusgalli</i>	<i>Digitaria sanguinalis</i>	<i>Brassica campestris</i>	<i>Amaranthus tricolor</i>	<i>Echinochloa crusgalli</i>	<i>Digitaria sanguinalis</i>
W101 (Chlorsulfuron)	15	93.7	91.2	57.5	51.0	87.9	53.3	39.1	40.5
	150	96.9	94.1	92.1	61.3	100.0	80.8	60.2	79.7
W102	15	82.5	70.6	89.0	47.6	88.4	14.2	38.3	20.0
	150	98.7	95.9	96.8	65.1	100	98.3	59.4	82.4
W103	15	0	0	8.2	0	0.0	0	0	0
	150	13.9	52.9	40.1	20.9	37.2	28.3	28.9	0
W104	15	4.9	41.2	29.5	21.1	40.9	11.7	0	16.2
	150	70.8	70.6	65.3	42.0	97.5	61.7	33.9	48.6
W105	15	81.9	64.7	46.8	28.4	87.7	41.7	27.3	0
	150	88.1	91.2	90.9	52.1	100.0	73.3	90.6	86.5
W106	15	57.2	85.3	73.2	0	78.3	53.3	31.3	0
	150	87.5	97.1	87.4	47.8	100	90.8	76.6	79.7
W107	15	0	29.4	0	0	0.0	0	0	0
	150	11.8	64.7	0	23.5	15.8	3.3	11.6	6.7
W108	15	0	0	0	0	0	0	0	0
	150	2.4	0.0	0	14.2	16.6	9.2	10.8	0
W109	15	74.7	83.3	35.0	18.3	79.4	56.7	86.3	18.1
	150	96.3	98.3	76.1	57.4	100	100	98.4	60.1
W110	15	65.7	58.3	20.8	0	35.9	16.3	66.3	0
	150	88.4	88.3	80.5	52.5	94.2	86.5	79.4	42.6
W111	15	55.7	66.7	3.2	0	52.6	30.8	52.0	0
	150	92.6	83.3	71.0	7.0	100	66.3	98.4	61.5

Based on the data above, we found that the 4,6-disubstituted pyrimidine and triazine derivatives could maintain a high herbicidal activity.

3.4. Soil Degradation

Anderson et al. reported that chlorsulfuron had long persistence in soil with pH 5.7 and 6.1 [32]. Thirunarayanan et al. reported that the degradation half-life (DT_{50}) of chlorsulfuron was 38.1 days in soil with pH 6.2 at 20 °C [8]. Fredrickson et al. reported that the DT_{50} of chlorsulfuron in soil with pH 5.6 was 1.9 weeks and, in soil with pH 6.3, it was 2.7 weeks at 25 °C [8]. Li found that the DT_{50} of chlorsulfuron was 12.91 days in soil with pH 5.40 at 25 °C, and the DT_{50} of diethylamino-substituted chlorsulfuron was 1.60 days [11].

With chlorsulfuron as the positive control, the degradation of compounds (W) were firstly investigated in soil at pH 5.46. The kinetic parameters for acidic soil degradation are listed in Table 3.

Table 3. Kinetic parameters for acidic soil (pH 5.46) degradation.

Compound	Kinetic Equations of Soil Degradation	Correlation Coefficient (R^2)	DT_{50} (Days)
W101 (Chlorsulfuron)	$C_t = 3.8317e^{-0.0393t}$	0.9477	17.64
W102	$C_t = 3.6838e^{-0.3700t}$	0.9866	1.87
W103	$C_t = 3.4989e^{-0.3666t}$	0.9664	1.89
W104	$C_t = 3.2440e^{-0.2414t}$	0.9629	2.87
W105	$C_t = 3.2659e^{-0.2150t}$	0.9575	3.22
W106	$C_t = 3.3608e^{-0.0623t}$	0.9973	11.13
W107	$C_t = 3.5961e^{-0.0458t}$	0.9909	15.13
W109	$C_t = 3.6979e^{-0.1721t}$	0.9760	4.03
W110	$C_t = 3.4616e^{-0.1051t}$	0.9594	6.60
W111	$C_t = 3.4271e^{-0.0683t}$	0.9614	10.15

As shown in Table 3, the DT_{50} of W102–W111 were 1.87–15.13 days, while the DT_{50} of chlorsulfuron was 17.64 days in acidic soil (pH 5.46). The degradation rates of the W-series compounds were 1.17–9.43 times faster than that of chlorsulfuron.

The DT_{50} of W102 was 1.87 days, which was 9.43 times faster than that of chlorsulfuron (17.64 days). For the other compounds, the DT_{50} of W103 was 1.89 days (9.33 times faster), the DT_{50} of W104 was 2.87 days (6.15 times faster), the DT_{50} of W105 was 3.22 days (5.48 times faster), the DT_{50} of W106 was 11.13 days (1.58 times faster), the DT_{50} of W107 was 15.13 days (1.17 times faster), the DT_{50} of W109 was 4.03 days (4.38 times faster), the DT_{50} of W110 was 6.60 days (2.67 times faster), and the DT_{50} of W111 was 10.15 days (1.74 times faster).

Comparing the degradation rates with the diethylamino-substituted chlorsulfuron derivative (W102), it was found that the degradation rates can be adjusted by introducing pyrimidine and triazine heterocycles into acidic soil.

Walker et al. reported that the DT_{50} of chlorsulfuron in sandy soil (at 6% soil moisture) with pH 7.1 at 20 °C was 56.0 days [7]. Thirunarayanan et al. reported that the DT_{50} of chlorsulfuron in soil with pH 7.7 was 136.6 days at 20 °C and 231.7 days at 10 °C [8]. Fredrickson et al. reported that the DT_{50} of chlorsulfuron was 12.5 weeks at pH 8.0 in sandy loam [9]. Nicholls et al. reported that the DT_{50} of chlorsulfuron could be 18 months in soil with low microbial activity and a high pH [10]. Li reported that the DT_{50} of chlorsulfuron was 158 days at pH 8.39, and DT_{50} of diethylamino-substituted chlorsulfuron was 6.39 days [15].

Considering the slow degradation of chlorsulfuron in alkaline soil, the degradation of compounds (W) were investigated in soil with pH 8.39. The kinetic parameters for alkaline soil degradation are listed in Table 4.

As shown in Table 4, the DT_{50} of W102–W111 was 5.81–6.97 days while the DT_{50} of chlorsulfuron was 157.53 days in alkaline soil (pH 8.39). The degradation rates of the W-series compounds were 22.6–27.1 times faster than that of chlorsulfuron.

Table 4. Kinetic parameters for alkaline soil (pH 8.39) degradation.

Compound	Kinetic Equations of Soil Degradation	Correlation Coefficient (R ²)	DT ₅₀ (Days)
W101 (Chlorsulfuron)	$C_t = 4.3043e^{-0.0044t}$	0.9899	157.53
W102	$C_t = 5.1771e^{-0.1091t}$	0.9888	6.35
W103	$C_t = 4.9927e^{-0.1100t}$	0.9839	6.30
W104	$C_t = 4.6088e^{-0.1095t}$	0.9765	6.33
W105	$C_t = 5.3757e^{-0.1158t}$	0.9795	5.99
W106	$C_t = 5.0349e^{-0.1054t}$	0.9787	6.58
W109	$C_t = 5.4294e^{-0.1162t}$	0.9761	5.97
W110	$C_t = 5.5261e^{-0.1193t}$	0.9857	5.81
W111	$C_t = 4.3883e^{-0.0995t}$	0.9892	6.97

As the alkaline soil degradation results showed, the degradation rates of **W102–W111** were reduced to 5.81–6.97 days, which were accelerated by 22.6–27.1-fold as compared to chlorsulfuron (157.53 days). The DT₅₀ of **W102** was 6.35 days, which was 24.81 times faster than that of chlorsulfuron. For the other compounds, the DT₅₀ of **W103**, **W104**, **W106** and **W111** were 6.30, 6.33, 6.58 and 6.97 days, respectively. The DT₅₀ of **W105** was 5.99 days (26.3 times faster), the DT₅₀ of **W109** was 5.97 days (26.4 times faster), and the DT₅₀ of **W110** was 5.81 days (27.1 times faster). The degradation rates of the synthesized compounds were accelerated dramatically compared with chlorsulfuron.

Considering the degradation rates of compounds (W) in soil with pH 5.46 and pH 8.39, we could find that introduction of the pyrimidine and triazine heterocycles into the 5-diethylamino substituted chlorsulfuron could accelerate the degradation rate in soil. Moreover, the heterocyclic amine is not the key factor affecting its degradation in alkaline soil.

3.5. Crop Safety

The crop safety of the target compounds is shown in Table 5 (for wheat) and Table 6 (for corn).

As the data show, crop safety was evaluated at 30 and 60 g·ha⁻¹ with chlorsulfuron as the control. The inhibition rates, presented in Tables 5 and 6, indicate that most compounds were safe for wheat and corn.

Chlorsulfuron is a popular sulfonylurea herbicide applied to wheat fields, but it causes a certain degree of damage to corn [7,33]. In 2018, Li found that diethylamino-substituted chlorsulfuron could cause a certain degree of damage to wheat (Jima 22) [14]. Li also found that diethylamino-substituted chlorsulfuron derivative was less safe for wheat (Xinong 529) and corn (Xindan 66) through post-emergence treatments [15].

In this research, a series of pyrimidine- and triazine-based diethylamino-substituted chlorsulfuron derivatives were tested using a crop safety assay for wheat (Xinong 529) and corn (Xindan 66).

The inhibition rates of compounds (W) indicated that most compounds were safe for wheat. At 60 g·ha⁻¹, the inhibition rate of **W102** was 23.3% under pre-emergence treatment. Compounds **W103–W111** improved the safety of diethylamino-substituted chlorsulfuron derivatives for pre-emergence treatment on wheat. It was found that the inhibition rates of **W103**, **W105**, **W106** and **W107** were 0% under pre and post emergence treatments. They indeed exhibited good crop safety compared with chlorsulfuron (6.3% and 0%). For other compounds, the inhibition rates of **W104** and **W111** were 1.2% and 0%, 0% and 12.1%, respectively.

In the case of corn, chlorsulfuron exhibited a certain degree of damage to the corn. At 60 g·ha⁻¹, the inhibition rates of chlorsulfuron was 46.7% under pre-emergence treatment. The inhibition rates of **W102**, **W109** and **W110** were 36.6%, 59.7% and 47.5%, respectively; they exhibited poor safety for corn. While the inhibition rates of **W107** and **W111** decreased to 1.8% and 19.2%, respectively. Moreover, for **W103**, **W104**, **W105** and **W106**, the inhibition rates were all 0%, which surpassed chlorsulfuron (46.7%).

Table 5. Crop safety of target compounds on wheat.

Compound	Concentration (g·ha ⁻¹)	Wheat (Xinong 529)							
		Pre. (22 Days after Treatment)			Post. (28 Days after Treatment)				
		Fresh Weight g/10 Strains	Analysis of Variance ^a		Inhibition (%)	Fresh Weight g/10 Strains	Analysis of Variance ^a		Inhibition (%)
			5%	1%			5%	1%	
	0	2.879	ab	AB	-	3.168	c	B	-
W101 (Chlorsulfuron)	30	3.043	a	A	0	3.287	a	A	0
	60	2.697	abcd	ABC	6.3	3.287	ab	AB	0
W102	30	2.340	de	CD	18.7	3.182	ab	AB	0
	60	2.207	e	D	23.3	3.236	ab	AB	0
W103	30	2.942	ab	AB	0	3.427	ab	AB	0
	60	3.070	a	A	0	3.843	abc	AB	0
W104	30	2.927	ab	AB	0	3.530	abc	AB	0
	60	2.843	abc	AB	1.2	3.443	abc	AB	0
W105	30	2.924	ab	AB	0	3.447	abc	AB	0
	60	2.931	ab	AB	0	3.423	abc	AB	0
W106	30	2.969	ab	AB	0	3.287	abc	AB	0
	60	2.917	ab	AB	0	3.575	abc	AB	0
W107	30	2.950	ab	AB	0	3.244	abc	AB	0
	60	3.080	a	A	0	3.283	abc	AB	0
W109	30	2.747	a	AB	4.6	2.703	bcd	BC	14.7
	60	2.544	ab	AB	11.6	2.674	cd	BC	15.6
W110	30	2.607	ab	AB	9.4	3.082	abc	AB	2.7
	60	2.557	ab	AB	11.2	2.996	abc	AB	5.4
W111	30	2.915	a	A	0	3.105	abc	AB	2.0
	60	2.890	a	A	0	2.784	bc	BC	12.1

^a Among the averages, the same letter indicates that there was no significant difference, and different letters indicate that there was a significant difference.

Table 6. Crop safety of target compounds on corn.

Compound	Concentration (g·ha ⁻¹)	Corn (Xindan 66)							
		Pre. (16 Days after Treatment)				Post. (23 Days after Treatment)			
		Fresh Weight g/5 Strains	Analysis of Variance ^a		Inhibition (%)	Fresh Weight g/5 Strains	Analysis of Variance ^a		Inhibition (%)
			5%	1%			5%	1%	
W101 (Chlorsulfuron)	0	6.312	abc	ABCD	-	8.073	a	A	-
	30	4.043	cdef	BCDE	35.9	7.932	a	A	1.7
	60	3.361	ef	DE	46.7	7.370	a	A	8.7
W102	30	4.060	cdef	BCDE	35.7	7.146	a	A	11.5
	60	4.000	cdef	BCDE	36.6	7.109	a	A	11.9
W103	30	7.080	ab	ABC	0	8.419	a	A	0
	60	6.716	ab	ABCD	0	8.433	a	A	0
W104	30	7.622	a	A	0	8.493	a	A	0
	60	6.787	ab	ABC	0	8.644	a	A	0
W105	30	6.437	abc	ABCD	0	8.329	a	A	0
	60	7.222	ab	AB	0	7.764	a	A	3.8
W106	30	7.109	ab	ABC	0	8.138	a	A	0
	60	6.360	abc	ABCD	0	7.454	a	A	7.7
W107	30	6.902	ab	ABC	0	8.389	a	A	0
	60	6.200	abcd	ABCD	1.8	8.377	a	A	0
W109	30	3.524	cd	BCD	44.2	7.871	a	A	2.5
	60	2.547	de	DE	59.7	7.514	a	A	6.9
W110	30	3.521	cd	BCD	44.2	7.132	a	A	11.7
	60	3.314	cde	BCD	47.5	7.013	a	A	13.1
W111	30	5.671	ab	A	10.2	8.095	a	A	0
	60	5.102	ab	AB	19.2	8.077	a	A	0

^a Among the averages, the same letter indicates that there was no significant difference, and different letters indicate that there was a significant difference.

It was found that such pyrimidine- and triazine-derived sulfonylureas could exhibit good crop safety on wheat and improve crop safety on corn.

Based on the above results, we believe that compounds such as **W105** and **W106** are potential green sulfonylurea herbicides for wheat and corn.

4. Conclusions

In order to explore sulfonylurea herbicides with high herbicidal activities, controllable degradation, and good crop safety, a series of chlorsulfuron derivatives were designed and synthesized by introducing pyrimidine and triazine heterocycles.

Pot trials for herbicidal activities indicated that the 4,6-disubstituted pyrimidine and triazine derivatives could maintain high herbicidal activity, while 4-monosubstituted derivatives exhibited poor herbicidal activities. It was found that pyrimidine- and triazine-substituted chlorsulfuron derivatives could accelerate degradation rates, both in acidic and alkaline soil. Especially, in alkaline soil, the degradation rate of the target compounds accelerated more than 22-fold compared to chlorsulfuron. Additionally, heterocyclic amine is not the key factor affecting its degradation in alkaline soil. Moreover, the W-series compounds exhibited good crop safety for wheat and could improve crop safety for corn. In combination with structures, herbicidal activities, crop safety, as well as soil degradation (in both acidic and alkaline soil), it could be concluded that compounds such as **W105** and **W106** could be potentially employed as sulfonylurea herbicides on wheat and corn. Compounds such as **W111** are potential green sulfonylurea herbicides for pre-emergence treatment for wheat and corn. Further research will be continued to discover new sulfonylurea herbicides to meet the needs of crop rotation modes.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/molecules27072362/s1>. SI: SI1-Melting points, ¹H-NMR, ¹³C-NMR and HRMS of **W103–W111**; SI2-Crystal data of compound **W110** (CCDC number 2142702); SI3-Soil degradation assay; SI4-Report of soil analysis in English.pdf; SI5-Report of soil analysis in Chinese.pdf [35–37].

Author Contributions: Conceptualization, L.W.; data curation, L.W.; formal analysis, L.W.; funding acquisition, Y.-C.G.; investigation, L.W., Y.-H.L. and Z.-M.L.; methodology, Y.-H.L.; project administration, Z.-W.W. and Z.-M.L.; supervision, S.Z.; writing—original draft, L.W.; writing—review and editing Z.-W.W., Y.-C.G. and S.Z. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the National Key Research and Development Program of China, Nankai University (2021YFD1700103), and a Syngenta PhD Scholarship.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are contained within the article and the Supplementary Materials.

Conflicts of Interest: The authors declare no conflict of interest.

Sample Availability: Not applicable.

References

1. Levitt, G. Discovery of the Sulfonylurea Herbicides. In *Synthesis and Chemistry of Agrochemicals II*; ACS: Washington, DC, USA, 1991; Volume 443, pp. 16–31.
2. Brown, H.M.J. Mode of Action, Crop Selectivity, and Soil Relations of the Sulfonylurea Herbicides. *Pest. Manag. Sci.* **2010**, *29*, 263–281. [[CrossRef](#)]
3. Luo, Y.F. The Impact of Grain's Land-Scaled Management on Land Productivity—Based on the Perspective of Mechanization and Quality of Hired Labors. Master's Thesis, Nanjing Agricultural University, Nanjing, China, 2017. (In Chinese)
4. Yang, L. Analysis of China's Grain Supply and Demand Balance. Master's Thesis, Shandong University of Technology, Zibo, China, 2009. (In Chinese)
5. Yang, Q.; Xue, S.; Zhu, R.; Han, S.; Yang, C. Conservation Tillage Techniques for Two Crops within One Year in North China. *Trans. Chin. Soc. Agric. Eng.* **2007**, *23*, 32–39.

6. Ministry of Agriculture of the People's Republic of China. *Bulletin of the Ministry of Agriculture of the People's Republic of China, Announcement No. 2032*; Ministry of Agriculture: Beijing, China, 2014.
7. Walker, A.; Brown, P.A. Measurement and Prediction of Chlorsulfuron Persistence in Soil. *Bull. Environ. Contam. Toxicol.* **1983**, *30*, 365–372. [[CrossRef](#)] [[PubMed](#)]
8. Thirunarayanan, K.; Zimdahl, R.; Smika, D. Chlorsulfuron Adsorption and Degradation in Soil. *Weed Sci.* **1985**, *33*, 558–563. [[CrossRef](#)]
9. Fredrickson, D.; Shea, P. Effect of Soil pH on Degradation, Movement, and Plant Uptake of Chlorsulfuron. *Weed Sci.* **1986**, *34*, 328–332. [[CrossRef](#)]
10. Nicholls, P.H.; Evans, A.A.; Walker, A. The Behavior of Chlorsulfuron and Metsulfuron in Soils in Relation to Incidents of Injury to Sugar Beet. In *Proceedings of the Brighton Crop Protection Conference—Weeds*, Brighton, UK, 16–19 November 1987; Volume 2, pp. 549–556.
11. Hua, X.W.; Zhou, S.; Chen, M.G.; Wei, W.; Liu, M.; Lei, K.; Zhou, S.; Li, Y.H.; Wang, B.L.; Li, Z.M. Controllable Effect of Structural Modification of Sulfonylurea Herbicides on Soil Degradation. *Chin. J. Chem.* **2016**, *34*, 1135–1142. [[CrossRef](#)]
12. Hua, X.W.; Chen, M.G.; Zhou, S.; Zhang, D.K.; Liu, M.; Zhou, S.; Liu, J.B.; Lei, K.; Song, H.B.; Li, Y.H.; et al. Research on Controllable Degradation of Sulfonylurea Herbicides. *RSC Adv.* **2016**, *6*, 23038–23047. [[CrossRef](#)]
13. Zhou, S.; Hua, X.W.; Wei, W.; Chen, M.G.; Gu, Y.C.; Zhou, S.; Song, H.B.; Li, Z.M. Research on Controllable Alkaline Soil Degradation of 5-Substituted Chlorsulfuron. *Chin. Chem. Lett.* **2018**, *29*, 945–948. [[CrossRef](#)]
14. Zhou, S. The Research on Novel RyR Insecticides and Sulfonylurea Herbicides with Controllable Degradation. Ph.D. Thesis, Nankai University, Tianjin, China, 2018. (In Chinese).
15. Wu, L.; Gu, Y.-C.; Li, Y.-H.; Meng, F.-F.; Zhou, S.; Li, Z.-M. Degradation of 5-DialkylaminoSubstituted Chlorsulfuron Derivatives in Alkaline Soil. *Molecules* **2022**, *27*, 1486. [[CrossRef](#)]
16. Ma, H.J.; Li, Y.H.; Zhao, Q.F.; Zhang, T.; Xie, R.L.; Mei, X.D.; Ning, J. Synthesis and herbicidal activity of novel N-(2,2,2)-trifluoroethylpyrazole derivatives. *J. Agric. Food Chem.* **2010**, *58*, 4356–4360. [[CrossRef](#)]
17. Ohno, R.; Watanabe, A.; Matsukawa, T.; Ueda, T.; Hirai, K. Synthesis and Herbicidal Activity of New Pyrazole-4-carboxamide Derivatives. *J. Pestic. Sci.* **2004**, *29*, 96–104. [[CrossRef](#)]
18. Pan, L.; Jiang, Y.; Liu, Z.; Liu, X.H.; Liu, Z.; Wang, G.; Li, Z.M.; Wang, D. Synthesis and evaluation of novel monosubstituted sulfonylurea derivatives as antituberculosis agents. *Eur. J. Med. Chem.* **2012**, *50*, 18–26. [[CrossRef](#)] [[PubMed](#)]
19. Zhang, D.K.; Hua, X.W.; Liu, M.; Wu, C.C.; Wei, W.; Liu, Y.; Chen, M.G.; Zhou, S.; Li, Y.H.; Li, Z.M. Design, synthesis and herbicidal activity of novel sulfonylureas containing triazole and oxadiazole moieties. *Chem. Res. Chin. Univ.* **2016**, *32*, 607–614. [[CrossRef](#)]
20. Wu, Z.X.; Liao, D.H.; Pi, H.J.; Li, C.; Wang, M.J.; Yang, F.; Shi, W.J. Synthesis of Oxasulfuron. *Agrochemicals* **2008**, *47*, 794–796.
21. Yasuo, I.; Kazunari, O.; Tatsuo, N.; Harutoshi, Y. Sulfonylurea Compound and Herbicidal Use. US5017212A, 21 May 1991.
22. Wang, J.G.; Li, Y.H. A Class of Sulfonylurea Compounds and Preparation Method Thereof Use in Herbicides. CN110642791A, 3 January 2020.
23. Meng, F.F.; Wu, L.; Gu, Y.C.; Zhou, S.; Li, Y.H.; Chen, M.G.; Zhou, S.; Zhao, Y.Y.; Ma, Y.; Li, Z.M. Research on the Controllable Degradation of N-methylamido and Dialkylamino Substituted at the 5th Position of the Benzene Ring in Chlorsulfuron in Acidic Soil. *RSC Adv.* **2020**, *10*, 17870–17880. [[CrossRef](#)]
24. Yoichi, K.; Hideo, A. Process for the Preparation of Phenyl (1,3,5-triazin-2-yl) Carbamates. EP1209153A2, 29 May 2002.
25. Chen, W. Design, Synthesis and Biological Evaluation of Novel Sulfonylureas. Ph.D. Thesis, NanKai University, TianJin, China, 2015. (In Chinese)
26. Wang, B.L.; Duggleby, R.G.; Li, Z.M.; Wang, J.G.; Li, Y.H.; Wang, S.H.; Song, H.B. Synthesis, crystal structure and herbicidal activity of mimics of intermediates of the KARI reaction. *Pest Manag. Sci.* **2005**, *61*, 407–412. [[CrossRef](#)]
27. Zhou, S.; Meng, F.F.; Hua, X.W.; Li, Y.H.; Liu, B.; Wang, B.L.; Chen, J.; Chen, A.L.; Li, Z.M. Research on Controllable Degradation of Novel Sulfonylurea Herbicides in Acidic and Alkaline Soils. *J. Agric. Food Chem.* **2020**, *68*, 3017–3025. [[CrossRef](#)]
28. Teaney, S.R.; Armstrong, L.; Bentley, K.; Cotterman, D.; Leep, D.; Liang, P.H.; Powley, C.; Summers, J.; Cranwell, S.; Lichtner, F.; et al. DPX-KE459 A new sulfonylurea for postemergence grass and broadleaf weed control in cereals. *Brighton Crop Prot. Conf. Weeds* **1995**, *1*, 49.
29. *Chinese National Standard GB/T 31270.1-2014*; Test Guidelines on Environmental Safety Assessment for Chemical Pesticides—Part 1: Transformation in Soils. The Institute for the Control of Agrochemicals under the Ministry of Agriculture: Beijing, China, 2014.
30. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. OLEX2: A complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339–341. [[CrossRef](#)]
31. Sheldrick, G.M. SHELXT—Integrated space-group and crystal-structure determination. *Acta Cryst.* **2015**, *A71*, 3–8. [[CrossRef](#)]
32. Sheldrick, G.M. SHELXT—Integrated space-group and crystal-structure determination. *Acta Cryst.* **2015**, *C71*, 3–8.
33. Anderson, R.L.; Barrett, M.R. Residual phytotoxicity of chlorsulfuron in two soils. *J. Environ. Qual.* **1985**, *14*, 111–114. [[CrossRef](#)]
34. Rubin, B.; Casida, J.E. R-25788 Effects on Chlorsulfuron Injury and Acetohydroxyacid Synthase Activity. *Weed Sci.* **1985**, *33*, 462–468. [[CrossRef](#)]
35. *Chinese National Standard GB/T 16631-2008*; General rules for high performance liquid chromatography. National Chemical Standardization Technical Committee: Beijing, China, 2008.

36. *Chinese Agricultural Industry Standard NY/T 788-2004*; Guideline on pesticide residue trials. Ministry of Agriculture, Pesticide Testing Center: Beijing, China, 2004.
37. *Chinese Agricultural Industry Standard NY/T 788-2018*; Guideline on pesticide residue trials. Ministry of Agriculture, Pesticide Testing Center: Beijing, China, 2018.