Chinese Chemical Letters xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Communication

Research on controllable alkaline soil degradation of 5-substituted chlorsulfuron

Shaa Zhou[a], Xuewen Hua[b], Wei Wei[a], Minggui Chen[a], Yucheng Gu[c], Sha Zhou[a],
Haibin Song[a], Zhengming Li[a,*]

[a] *State Key Laboratory of Elemento-Organic Chemistry, Collaborative Innovation Centre of Chemical Science and Engineering (Tianjin), College of Chemistry, Nankai University, Tianjin 300071, China*
[b] *College of Agriculture, Liaocheng University, Liaocheng 252000, China*
[c] *Syngenta Jealott's Hill International Research Centre, RG42 6EY, United Kingdom, UK*

ARTICLE INFO

Article history:
Received 16 June 2017
Received in revised form 12 September 2017
Accepted 21 September 2017
Available online xxx

Keywords:
Chlorsulfuron Sulfonylurea herbicides
Soil degradation
Alkaline soil
DT_{50}

ABSTRACT

Sulfonylurea (SU) has become one class of the most important herbicides worldwide due to their ultra-low application rate and mammalian toxicity. Recently application licenses of 3 classical SU herbicides chlorsulfuron, metsulfuron-methyl and ethametsulfuron were suspended due to their undesirable long persistence which is incompatible with the particular rotation planting system in China. Our previous study has discovered that electron-donating groups, especially dimethylamino and diethylamino substituents, on the 5th position of the benzene ring in chlorsulfuron, greatly accelerated its degradation rate in an acidic soil (pH 5.41). Owing to the natural slower degradation of SUs in alkaline soil, dimethylamino and diethylamino substituted chlorsulfuron **Ia** and **Ib** were further studied in an alkaline soil (pH 8.46) with chlorsulfuron as a control. The experimental data indicated that the half-life of degradation (DT_{50}) of **Ia** was 3.36 days while **Ib** was 6.25 days which amounted to 30 and 15 folds faster than chlorsulfuron (DT_{50} 84.53 days), respectively. The research confirmed that our newly-designed structures **Ia** and **Ib** can hasten their degradation rate in alkaline soil as well as in acidic soil. This structural modification of the classical SU provided an opportunity to control the degradation rate to reduce their impact on relevant environment and ecology.

Chlorsulfuron (Fig. 1) was firstly reported by G. Levitt as it effectively controls a large number of weed species among cereal crops at ultra-low application rate in both pre- and post-emergence treatment [1]. The invention of chlorsulfuron has led further efforts to develop a new class of important sulfonylurea herbicides whose target enzyme is AHAS (acetohydroxyacid synthase) or ALS (acetolactate synthase) that it exists only in plants and microbes, not in mammals [2–4].

In consideration of the particular crop rotation systems (2-3 successive crops/same plot/same year) in many regions of China and the long persistence behavior which is detrimental to sensitive following rotation crops including wheat, corn, paddy, cotton and bean [5–8], the Ministry of Agriculture of China suspended the field application of 3 classical SUs chlorsulfuron, metsulfuron-methyl and ethametsulfuron since 2014 [9]. In view of the environment protection and sustainable development, the ban has attracted our attention to undertake a green chemical approach to solve this problem. Soil pH is one of the most important factors influencing the degradation rate of sulfonylurea herbicides in soils due to their acidic nature [10–13]. Thirunarayanan *et al.* reported that DT_{50} of chlorsufuron was 88.5 days in pH 6.2 soil and 144 days in pH 8.1 soil [14]. Wiese *et al.* measured persistence of chlorsulfuron in field study in Pullman clay loam under a 3-year winter wheat-sorghum-fallow crop rotation pattern with an application of 34 g/ha on growing wheat. After a lengthy period of 25 months in soil pH >7.5, the residue of chlorsulfuron injured the newly planted sorghum [15]. Previous studies demonstrated that soil degradation of sulfonylurea herbicides is pH-dependent and has strong negative correlation with pH [16–19].

Our previous research firstly discovered that electron-donating groups on the 5th position of the benzene ring of SU structures, such as dimethylamino and diethylamino substituents accelerated their degradation rate than their parent structure chlorsulfuron in acidic soil (pH 5.41) while the herbicidal activities were retained

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* Corresponding author.
E-mail address: nkzml@vip.163.com (Z. Li).

https://doi.org/10.1016/j.cclet.2017.09.046
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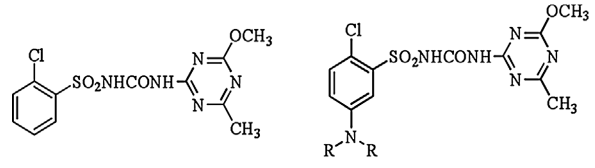

Chlorsulfuron

Ia: R=CH$_3$; **Ib**: R=C$_2$H$_5$

Fig. 1. Structures of Chlorsulfuron and 5- substituted compounds **Ia** and **Ib**.

[20,21] (Table 1). In order to further examine the degradation behavior of these new structures in high pH soil, an alkaline soil (pH 8.46) was selected according to the Chinese National Standard GB/T 31270.1-2014 from Cangzhou, Hebei Province [22]. The dimethylamino and diethylamino substituted compounds **Ia** and **Ib** (Fig. 1) were taken as the tested samples and chlorsulfuron as a control.

The synthesis procedures of dimethylamino and diethylamino substituted compounds **Ia** and **Ib** have been reported by our previous researches [20,21]. The crystal structure of compound **Ia** was diffracted by the following procedures. A colorless crystal of **Ia** was obtained by self-evaporation in the mixture solvent of dichloromethane and *n*-hexane. The crystal was analyzed by X-ray diffraction with dimensions of 0.20 mm × 0.18 mm × 0.12 mm. The data was collected on a Rigaku Saturn 724 CCD diffractometer equipped with a graphite monochromated Mo *Kα* radiation (λ = 0.71073 Å) at 113(2) K with θ_{max} = 27.59°. The molecular formula is $C_{14}H_{17}ClN_6O_4S$, and the formula weight is 400.85 g/mol. The crystal was a triclinic system, space group P-1, with cell parameters existed as α = 7.920(4) Å, b = 8.661(4) Å, c = 13.968(6) Å; α = 101.766(9)°, β = 93.734(6)°, γ = 107.614(13)°; cell ratio as α/b = 0.9144, b/c = 0.6201, c/α = 1.7636; calculated density was 1.503 g/cm^3; V = 885.73(70) Å^3; Z = 2 and linear absorption coefficient was 0.368 mm^{-1}. A total 11448 integrated reflections were collected, and 4022 were independent with R_{int} = 0.0558 and completeness of data was 97.5%. The structure was elucidated by direct methods with the program of SHELXS-97 [23]. Full-matrix least-squares refinement which was based on F^2 gave final values of R = 0.0412, wR = 0.1187 using the weight of $1/[\sigma^2(F_o{}^2) + (0.0843P)^2 + 0.0029P]$. Hydrogen atoms were located by a fixed value of isotropic displacement parameter. The data was corrected for absorption with multi-scan, T_{min} = 0.9301, T_{max} = 0.9572.

The crystal structure of **Ia** was showed in Fig. 2 (CCDC number. 1546964). From the data, the bond length of N(1)-C(5), N(2)-C(9), N(3)-C(9) were 1.361(2) nm, 1.375(2) nm and 1.384(2) nm respectively, which were shorter than general C-N bond that they may be caused by the transfer of π electrons. The sum angles of O(3)-C(9)-N(2) 123.31(16)°, O(3)-C(9)-N(3) 120.92(15)° and N(2)-C(9)-N(3) 115.77(15)° was 360°, indicating the plane sp^2 hybridization state of C(9) atom. The bond angles of O(1)-S(1)-C(1), O(2)-S(1)-C(1), N(2)-S(1)-C(1) were 108.05(8)°, 110.69(8)° and 104.36(8)° respectively which indicated state of the S(1) atom was sp^3 hybridization. The torsion angle of O(3)-C(9)-N(2)-H(2) was 169.806(1510)° while the O(3)-C(9)-N(3)-H(3) showed as 0.331(1237)°. The benzene ring and the triazine ring were non-planar for their dihedral angle being 79.676(48)°. The conformation of dimethylamino group was nearly located on the plane of the benzene ring and their dihedral angle was 3.473(110)°. From Fig. 2, two kinds of H-bonds could also be found: N(2)-H(2)···N(6) and N(3)-H(3)···O(3), it could be explained as the reason of the torsion angles of O(3)-C(9)-N(2)-H(2) and O(3)-C(9)-N(3)-H(3).

The surflex-dock method [24] was applied to study the binding mode of our newly-designed **Ia** with the target AHAS (ALS) for its high herbicidal activity. **Ia** was manually docked into the active site of yeast AHAS using the SYBYL 6.9 software package referring to the crystal complex of chlorimuron-ethyl and yeast AHAS [25] which was retrieved from the RCSB Protein Data Bank (PDB code: 1N0H).

The molecular docking study of **Ia** was illustrated in Fig. 3. The conformation of aromatic ring and triazine ring connected to the sulfonyl urea bridge were approximately mutual vertical (Fig. 3a) which was similar to the binding structure of AHAS and chlorimuron-ethyl that the heterocyclic part blocks the substrate access channel through intramolecular interactions (H-bonds and π-π stacking) [4]. H-bonds interaction between the urea-triazine moiety of **Ia** and the guanidine group of B/Arg 380 was showed in yellow dashed lines. There was a π-π stacking interaction between the triazine moiety of **Ia** and the indole part of B/Trp 586 (Fig. 3b).

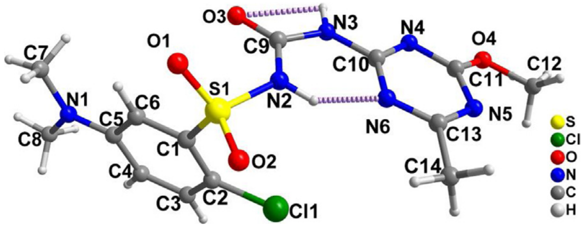

Fig. 2. Crystal structure of **Ia**.

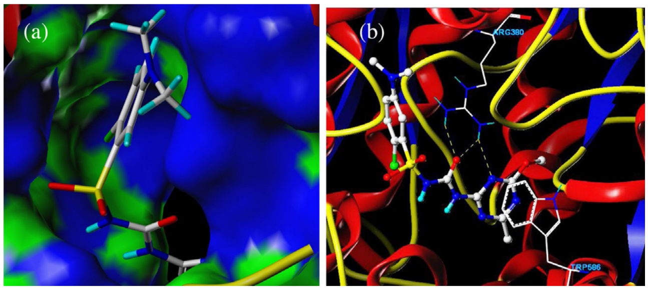

Fig. 3. Binding mode of **Ia** to yeast AHAS.

Table 1
The herbicidal activity of dimethylamino and diethylamino substituted compounds **Ia** and **Ib**.

Compd.	Concentration (a.i. g/ha)	Herbicidal activity (%)							
		Brassica campestris		*Amaranthus tricolor*		*Echinochloa crusgalli*		*Digitaria sanguinalis*	
		Pre	Post	Pre	Post	Pre	Post	Pre	Post
Ia	30	93.7	100	69.7	100	38.3	69.8	38.8	16.7
	150	100	100	98.5	100	92.6	88.3	91.3	38.3
Ib	30	97.9	100	63.9	93.0	81.8	100	10.5	93.9
	150	98.6	100	76.4	100	88.6	100	40.8	99.5
Chlorsulfuron	30	96.5	100	79.2	100	82.4	80.3	0	43.9
	150	97.2	100	91.7	100	86.4	100	21.4	73.5

Please cite this article in press as: S. Zhou, et al., Research on controllable alkaline soil degradation of 5-substituted chlorsulfuron, Chin. Chem. Lett. (2017), https://doi.org/10.1016/j.cclet.2017.09.046