Synthesis and Herbicidal Activity of Novel Sulfonylureas Containing 1,2,4-Triazolinone Moiety

LIU Zhuo, PAN Li, LI Yong-hong, WANG Su-hua and LI Zheng-ming*

State Key Laboratory of Elemento-Organic Chemistry, Institute of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P. R. China

Abstract A series of new sulfonylureas incorporating 1,2,4-triazolinone moiety was synthesized, which were further bio-assayed for the herbicidal activity against four herbs, representative of monocotyledons and dicotyledons. Some of them exhibited high potency to inhibit the growth of dicotyledons(*Bassica napus* and *Amaranthus retroflexus*) in the pot experiment. Compounds **9**a and **9**b also displayed an excellent herbicidal activity against *Bassica napus* at a concentration of 15 g/hectare, which were comparable with commercial triasulfuron.

Keywords Sulfonylurea herbicide; Acetohydroxyacid synthetase(AHAS); 1,2,4-Triazolinone derivative; Protox; Herbicidal activity

1 Introduction

Since DuPont discovered the first triazolinone herbicide azafenidin in 1977, some reports have been disclosed other novel triazolinones to improve their ecofriendly characteristics[1]. Based on the structural optimization of *N*-phenylphthalimide and oxadiazolinone herbicides(Fig.1), these triazolinone derivatives have been explored, and the mode of their action has been proposed as protoporphyrinogen(Protox) inhibitor. They exhibit herbicidal activity in the presence of light and inhibit the synthesis of Protox in chlorophyll organisms to cause cell membrane damage, accompanied with the leaves being dried-up[2,3].

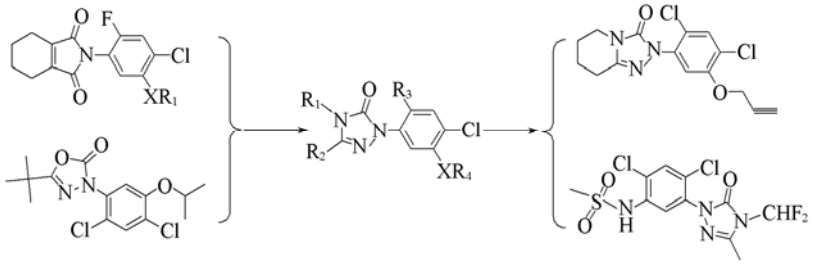

Fig.1 Development of triazolinone herbicides

Up to date, some commercial products, including amicarbazone, propoxycarbazone, sulfentrazone, azafenidin and carfentrazone-ethyl(Fig.2) have been shown to exhibit potent inhibitory activity against weeds tolerant of sulfonylurea herbicides[4,5]. Meanwhile, further studies on the replacement of benzene ring with heterocyclic rings in propoxycarbazone indicate that some triazolinone derivatives show significant herbicidal activity against *Alopecurus aequalis*, amaranth, polygonum, chickweed, bristlegrass, *Matricaria chamomilla L.* and *Veronica persica*[4—8].

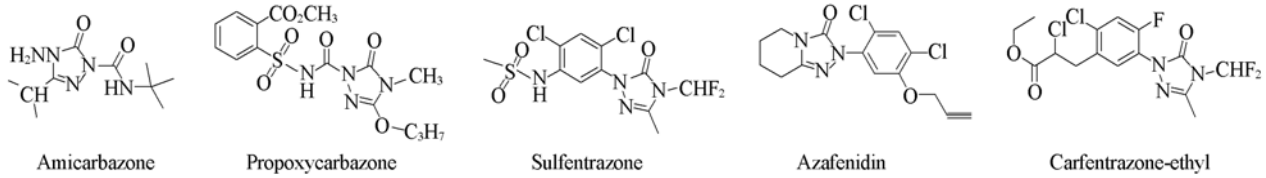

Fig.2 Commercial and developing triazolinone herbicides

Acetohydroxyacid synthase(AHAS, EC 2.2.1.6, also referred as acetolactate synthase, ALS) is an enzyme that catalyzes the first step in the biosynthesis pathway of the branched-chain amino acids(BCAA), which exist in plants, algae, fungi and bacteria, but not in animals. Thus, the enzymes of the BCAA biosynthetic pathway are potential targets in the

*Corresponding author. E-mail: nkzml@vip.163.com

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development of ecological safe herbicides, fungicides and antimicrobial compounds. Specific plant AHAS inhibitors, such as sulfonylureas, have been considered to be the milestone of hyper-active herbicides[6]. Since then sulfonylurea researches have followed Levitt's guidelines, which mentioned that the sulfonylureas comprise a central sulfonylurea bridge with an *o*-substituted aromatic ring attached to the sulfur atom and a heterocyclic ring attached to the nitrogen atom[7,8].

Previous studies found 5-substituted benzene sulfonylurea derivatives not only showed shorter residual life but also remained their effective inhibition[9].

Some commercial sulfonylurea herbicides with triazine ring, such as chlorsulfuron, triasulfuron and cinosulfuron(Fig.3) display potent efficacies in the field of wheat and rice[10]. Therefore, it is of interest to modify the structure of triasulfuron in which the triazine ring is replaced by 1,2,4-triazolinone and halogen(Cl or Br) group is attached to C_5-substituted benzenesulfonyl moiety for the evaluation of their herbicidal activities.

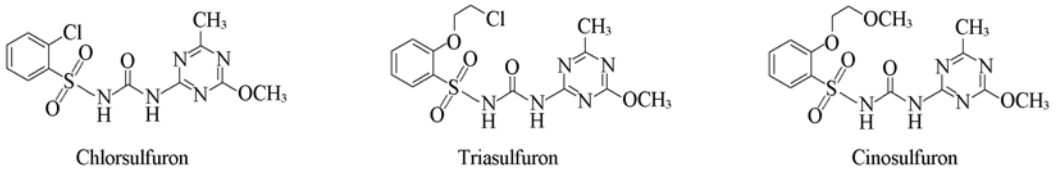


Fig.3 Commercial sulfonylurea herbicides

2 Experimental

2.1 Reagents and Instruments

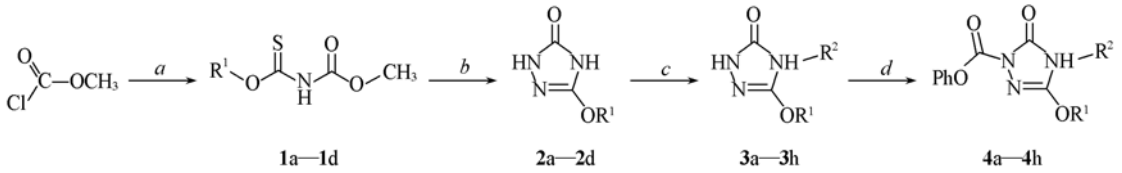
All the applied reagents were of analytical or chemical standard purity. The solvents and liquid reagents were dried by standard methods and distilled prior to utilization. ^{1}H NMR spectra were recorded at 400 MHz on a Bruker AV 400 spectrometer(Bruker Co., Switzerland) in $CDCl_3$ or DMSO-d_6 solution with tetramethylsilane(TMS) as the internal standard. Elemental analyses were performed on a Yanaco MT-3 CHN elemental analyzer. High-resolution mass spectrometry(HRMS) data were obtained on a high resolution Varian 7.0T Fourier transform ion cyclotron resonance-mass spectrometer (FTICR-MS). The melting points were determined on an X-4 binocular microscope melting point apparatus(Beijing Tech Instruments Co., Beijing, China) and were uncorrected.

2.2 Syntheses of Title Compounds

The general synthetic procedures for compounds **4**a—**4**h and **9**a—**9**t are illustrated in Scheme 1 and Scheme 2, respectively.

2.2.1 General Synthetic Procedure for Phenyl 3-Alkoxy-4-alkyl-5-oxo-4,5-dihydro-1,2,4-triazole-1-carboxylate(4a—4h)

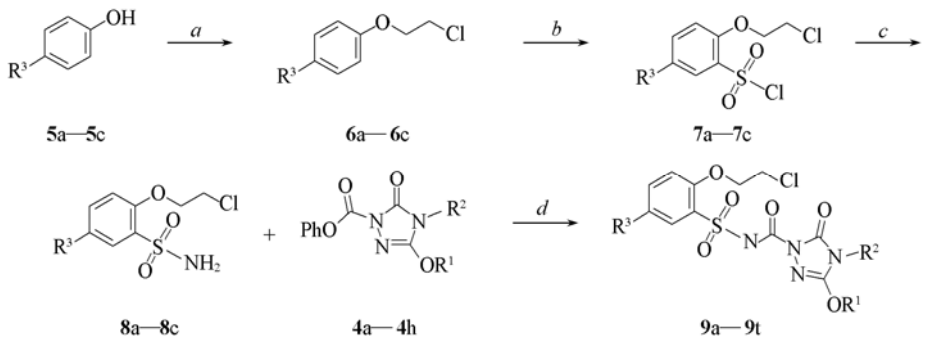
As indicated in Scheme 1, 3-alkoxy-4-alkyl-1*H*-1,2,4-triazol-5(4*H*)-one derivatives(**3**a—**3**h) were synthesized *via*



4a: R^1=Me, R^2=Me; **4**b: R^1=Et, R^2=Me; **4**c: R^1=*n*-Pr, R^2=Me; **4**d: R^1=*i*-Pr, R^2=Me; **4**e: R^1=Me, R^2=Et; **4**f: R^1=Et, R^2=Et; **4**g: R^1=*n*-Pr, R^2=Et; **4**h: R^1=*i*-Pr, R^2=Et

Scheme 1 Syntheses of compounds 4a—4h

Reagent and conditions: *a*. KSCN, pyridine, ethyl acetate, 50—60 °C, R^1OH; *b*. $NH_2NH_2{\cdot}H_2O$, KOH(aq.), triethylamine(TEA), CH_3OH, r. t.; *c*. KOH(aq.), $(CH_3)_2SO_4$(R^2=CH_3), reflux, 4 h; KOH(aq.), $(C_2H_5)_2SO_4$(R^2=C_2H_5), reflux, 4 h; *d*. ClCOOPh, K_2CO_3, acetone, r. t., 2 h.



8a: R^3=Cl; **8**b: R^3=Br; **8**c: R^3=OCH_2CH_2Cl

Scheme 2 Syntheses of compounds 9a—9t

Reagents and conditions: *a*. 1,2-dichloroethane, NaOH(aq.), Bu_4NCl, 80 °C; *b*. chlorosulfonic acid, 120 °C; *c*. ammonia(aq.), r. t., overnight; *d*. 1,8-diazabicyclo[5.4.0]undec-7-ene(DBU), CH_3CN, r. t., overnight.

three steps[11].

Each of compounds **3**a—**3**h(0.1 mol), potassium carbonate(16.6 g, 0.12 mol) and 150 mL of acetone were placed into a flask. Phenyl chloroformate(15.7 g, 0.1 mol) was added to this mixture within 20—30 min. After stirring at room temperature for 2 h, the suspension was filtered. The precipitate was washed with a sodium carbonate solution(10%, mass fraction), a hydrochloric acid solution(5%, mass fraction) and water.

The crude products **4**a—**4**h were obtained as a yellow solid, which were used in the next step without further purification.

*2.2.2 General Synthetic Procedure for 4-(2-Chloroethoxy)-1-substituted Benzene(**6**a—**6**c)*

To a stirred 1, 2-dichloroethane(216.12 g, 2.18 mol) was added dropwise a solution of 4-substituted phenol(**5**a—**5**c, 0.12 mol), Bu_4NCl(1.68 g, 0.006 mol) and 300 mL of a sodium hydroxide solution(5%, mass fraction). The reaction was heated at 80 °C for 10 h with mechanically stirring. After the reaction was completed, the solution was cooled and then the organic layer was washed with a sodium hydroxide solution(5%, mass fraction) and brine and dried with anhydrous Na_2SO_4. The solvent was removed *in vacuo* to give the crude product **6**a—**6**c. Other compounds were synthesized *via* the same procedure as above.

*2.2.3 General Synthetic Procedure for 2-(2-Chloroethoxy)-5-substituted Sulfon Amide(**8**a—**8**c)*

To chlorosulphonic acid(14.96 g, 8.45 mL, 25.0 mmol) was added compound **6**(21.4 mmol) in small portions at 5—10 °C. The reaction mixture was stirred at 120 °C for 4 h and then poured into ice with vigorous stirring. After stirring for 10 min, the gray precipitate was filtered and pressed into dryness. The solid was dried overnight in a desiccator under vacuum to give compound **7**. Compounds **7**b and **7**c were synthesized *via* the same procedure as above.

*2.2.4 General Synthetic Procedure for Title Compounds(**9**a—**9**t)*

To a suspension of each of compound **4**a—**4**h(2 mmol) and each of compound **8**a—**8**c(2 mmol) in 15 mL of acetonitrile was added 2 mmol of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at room temperature. The reaction mixture was stirred overnight and then the solvent was removed by distillation. The residue was poured into water to adjust pH to 1—2 with 20% hydrochloric acid. The aqueous phase was extracted with dichloromethane and the organic layer was dried over anhydrous Na_2SO_4. After the solvent was removed *in vacuo*, the yellow sticky residue was obtained, which was purified *via* column chromatography. The physico-chemical data of the title compounds **9**a—**9**t are shown in Table 1.

Table 1 Physico-chemical data of compounds 9a—9t*

Compd.	R_1	R_2	R_3	Appearance	m.p./ °C	Yield(%)
9a	CH_3	CH_3	Cl	White solid	138—140	73
9b	C_2H_5	CH_3	Cl	White solid	127—129	66
9c	*n*-C_3H_7	CH_3	Cl	White solid	119—121	56
9d	*i*-C_3H_7	CH_3	Cl	White solid	158—160	76
9e	CH_3	C_2H_5	Cl	White solid	158—160	60
9f	C_2H_5	C_2H_5	Cl	White solid	119—121	68
9g	*n*-C_3H_7	C_2H_5	Cl	White solid	136—138	63
9h	*i*-C_3H_7	C_2H_5	Cl	White solid	142—144	59
9i	CH_3	CH_3	Br	White solid	156—158	59
9j	C_2H_5	CH_3	Br	White solid	138—140	62
9k	*n*-C_3H_7	CH_3	Br	White solid	131—133	60
9l	*i*-C_3H_7	CH_3	Br	White solid	164—166	68
9m	CH_3	C_2H_5	Br	White solid	148—150	72
9n	C_2H_5	C_2H_5	Br	White solid	119—121	58
9o	*n*-C_3H_7	C_2H_5	Br	White solid	140—141	66
9p	*i*-C_3H_7	C_2H_5	Br	White solid	147—149	63
9q	CH_3	CH_3	OCH_2, CH_2Cl	Light yellow oil	NT	66
9r	C_2H_5	CH_3	OCH_2, CH_2Cl	Light yellow oil	NT	71
9s	*n*-C_3H_7	CH_3	OCH_2, CH_2Cl	Yellow oil	NT	75
9t	*i*-C_3H_7	CH_3	OCH_2, CH_2Cl	Yellow oil	NT	64

* NT=not tested.

Compound **9**a: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 3.18(s, 3H, CH_3), 3.88—3.91(t, 2H, J=5.7 Hz, $OCH_2C\mathbf{H}_2Cl$), 4.06(s, 3H, OCH_3), 4.32—4.34(t, 2H, J=5.7 Hz, $OC\mathbf{H}_2CH_2Cl$), 6.92—6.94 (d, 1H, J=8.8 Hz, ArH), 7.51—7.53(dd, 1H, J=1.6, 1.6 Hz, ArH), 8.11—8.12(d, 1H, J=1.6 Hz, ArH), 10.67(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{13}H_{14}Cl_2N_4O_6S$: C 36.72, H 3.32, N 13.18; found: C 36.45, H 3.44, N 12.93.

Compound **9**b: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 1.40—1.44 (t, 3H, J=7.1 Hz, $OCH_2C\mathbf{H}_3$), 3.18(s, 3H, CH_3), 3.88—3.90(t, 2H, J=5.8 Hz, $OCH_2C\mathbf{H}_2Cl$), 4.31—4.34(t, 2H, J=5.8 Hz, $OC\mathbf{H}_2CH_2Cl$), 4.41—4.46(q, 2H, J=7.1 Hz, $OC\mathbf{H}_2CH_3$), 6.92—6.94(d, 1H, J=8.9 Hz, ArH), 7.50—7.53(dd, 1H, J=2.6, 2.6 Hz, ArH), 8.11—8.12(d, 1H, J=2.6 Hz, ArH), 10.70(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{14}H_{16}Cl_2N_4O_6S$: C 38.28, H 3.67, N 12.75; found: C 38.41, H 3.84, N 12.88.

Compound **9**c: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 0.97—1.00 (t, 3H, J=7.4 Hz, $OCH_2CH_2C\mathbf{H}_3$), 1.76—1.85(m, 2H, $OCH_2C\mathbf{H}_2CH_3$), 3.18(s, 3H, CH_3), 3.88—3.91(t, 2H, J=5.8 Hz, $OCH_2C\mathbf{H}_2Cl$), 4.31—4.34(m, 4H, O $C\mathbf{H}_2H_2Cl$, $OC\mathbf{H}_2CH_2CH_3$),

6.92—6.94(d, 1H, *J*=8.9 Hz, ArH), 7.50—7.53(dd, 1H, *J*=2.5, 2.5 Hz, ArH), 8.11—8.12(d, 1H, *J*=2.5 Hz, ArH), 10.70(br, s, 1H, SO_2NHCO). Matrix assisted laser desorption ionization-Fourier transform ion cyclotron resonance-mass spectra (MALDI-FTICR-MS) for $C_{15}H_{18}Cl_2N_4O_6S$ (positive ion), *m*/*z*: found 475.0220$[M+Na]^+$, calcd. 475.0222$[M+Na]^+$.

Compound **9**d: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.39—1.40 [d, 6H, *J*=6.1 Hz, $OCH(CH_3)_2$], 3.16(s, 3H, CH_3), 3.89—3.92(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.32—4.35(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 5.13—5.19[m, 1H, $OCH(CH_3)_2$], 6.93—6.95(d, 1H, *J*=8.8 Hz, ArH), 7.51—7.53(dd, 1H, *J*=2.6, 2.6 Hz, ArH), 8.11—8.12(d, 1H, *J*=2.6 Hz, ArH), 10.73(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{15}H_{18}Cl_2N_4O_6S$(positive ion), *m*/*z*: found 475.0215$[M+Na]^+$, calcd. 475.0222$[M+Na]^+$.

Compound **9**e: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.26—1.30 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 3.63—3.69(q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.88—3.90(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.06(s, 3H, OCH_3), 4.32—4.35(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 6.92—6.94(d, 1H, *J*=8.8 Hz, ArH), 7.50—7.53(dd, 1H, *J*=2.6, 2.6 Hz, ArH), 8.11—8.12(d, 1H, *J*=2.6 Hz, ArH), 10.71(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{14}H_{16}Cl_2N_4O_6S$ (positive ion), *m*/*z*: found 461.0057$[M+Na]^+$, calcd. 461.0066 $[M+Na]^+$.

Compound **9**f: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.26—1.30 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.40—1.43(t, 3H, *J*=7.1 Hz, OCH_2CH_3), 3.63—3.68(q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.87—3.90(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.32—4.34(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.41—4.46(q, 2H, *J*=7.1 Hz, OCH_2CH_3), 6.92—6.94(d, 1H, *J*=8.8 Hz, ArH), 7.50—7.52(dd, 1H, *J*=2.6, 2.6 Hz, ArH), 8.11—8.12(d, 1H, *J*=2.6 Hz, ArH), 10.73(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{15}H_{18}Cl_2N_4O_6S$: C 39.74, H 4.00, N 12.36; found: C 39.65, H 4.13, N 12.29.

Compound **9**g: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 0.97—1.00 (t, 3H, *J*=7.4 Hz, $OCH_2CH_2CH_3$), 1.27—1.30(t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.76—1.85(m, 2H, $OCH_2CH_2CH_3$), 3.64—3.69 (q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.88—3.91(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.32—4.35(m, 4H, OCH_2CH_2Cl, $OCH_2CH_2CH_3$), 6.92—6.94(d, 1H, *J*=8.9 Hz, ArH), 7.50—7.53 (dd, 1H, *J*=2.5, 2.5 Hz, ArH), 8.12—8.13(d, 1H, *J*=2.5 Hz, ArH), 10.73(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{16}H_{20}Cl_2N_4O_6S$: C 41.12, H 4.31, N 11.99; found: C 41.08, H 4.26, N 11.91.

Compound **9**h: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.24—1.29 (t, 3H, *J*=9.6 Hz, CH_2CH_3), 1.38—1.40[d, 6H, *J*=8.2 Hz, $OCH(CH_3)_2$], 3.60—3.67(q, 2H, *J*=9.6 Hz, CH_2CH_3), 3.87—3.91(t, 2H, *J*=7.8 Hz, OCH_2CH_2Cl), 4.31—4.35(t, 2H, *J*=7.8 Hz, OCH_2CH_2Cl), 5.10—5.20[m, 1H, $OCH(CH_3)_2$], 6.91—6.94(d, 1H, *J*=11.8 Hz, ArH), 7.50—7.53(dd, 1H, *J*=3.5, 3.5 Hz, ArH), 8.11—8.12(d, 1H, *J*=3.5 Hz, ArH), 10.75(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{16}H_{20}Cl_2N_4O_6S$: C 41.12, H 4.31, N 11.99; found: C 41.08, H 4.23, N 12.09.

Compound **9**i: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 3.18(s, 3H, CH_3), 3.88—3.91(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.06(s, 3H, OCH_3), 4.31—4.34(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 6.86—6.89 (d, 1H, *J*=8.8 Hz, ArH), 7.65—7.67(dd, 1H, *J*=2.5, 2.5 Hz, ArH), 8.25—8.26(d, 1H, *J*=2.5 Hz, ArH), 10.67(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{13}H_{14}BrClN_4O_6S$: C 33.24, H 3.00, N 11.93; found: C 33.30 H 3.16, N 11.71.

Compound **9**j: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.41—1.44 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 3.18(s, 3H, CH_3), 3.88—3.91(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.31—4.34(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.41—4.47(t, 2H, *J*=7.1 Hz, OCH_2CH_3), 6.86—6.88(d, 1H, *J*=8.8 Hz, ArH), 7.65—7.67(dd, 1H, *J*=2.5, 2.5 Hz, ArH), 8.25—8.26(d, 1H, *J*=2.5 Hz, ArH), 10.69(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{14}H_{16}BrClN_4O_6S$ (positive ion), *m*/*z*: found 506.9534$[M+Na]^+$, calcd. 506.9540$[M+Na]^+$.

Compound **9**k: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 0.97—1.00(t, 3H, *J*=7.4 Hz, $OCH_2CH_2CH_3$), 1.76—1.85(m, 2H, $OCH_2CH_2CH_3$), 3.19(s, 3H, CH_3), 3.88—3.91(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.31—4.35(m, 4H, OCH_2CH_2Cl, $OCH_2CH_2CH_3$), 6.86—6.88(d, 1H, *J*=8.8 Hz, ArH), 7.64—7.67 (dd, 1H, *J*=2.4, 2.4 Hz, ArH), 8.25—8.26(d, 1H, *J*=2.4 Hz, ArH), 10.69(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{15}H_{18}BrClN_4O_6S$: C 36.20, H 3.64, N 11.26; found: C 36.15 H 3.53, N 11.40.

Compound **9**l: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.38—1.40 [d, 6H, *J*=6.2 Hz, $OCH(CH_3)_2$], 3.16(s, 3H, CH_3), 3.88—3.91(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.31—4.34(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 5.11—5.20[m, 1H, $OCH(CH_3)_2$], 6.86—6.88(d, 1H, *J*=8.8 Hz, ArH), 7.64—7.67(dd, 1H, *J*=2.5, 2.5 Hz, ArH), 8.25—8.26(d, 1H, *J*=2.5 Hz, ArH), 10.72(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{15}H_{18}BrClN_4O_6S$(positive ion), *m*/*z*: found 520.9693$[M+Na]^+$, calcd. 520.9696$[M+Na]^+$.

Compound **9**m: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.26—1.30(t, 3H, *J*=7.2 Hz, CH_2CH_3), 3.63—3.69(q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.87—3.90(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.06(s, 3H, OCH_3), 4.31—4.34(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 6.86—6.88(d, 1H, *J*=8.9 Hz, ArH), 7.64—7.67(dd, 1H, *J*=2.4, 2.4 Hz, ArH), 8.24—8.25(d, 1H, *J*=2.4 Hz, ArH), 10.71(br, s, 1H, SO_2NHCO). Elemental anal.(%) calcd. for $C_{14}H_{16}BrClN_4O_6S$: C 34.76, H 3.33, N 11.58; found: C 34.68, H 3.55, N 11.49.

Compound **9**n: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 1.26—1.30 (t, 3H, *J*=7.2 Hz, CH_2CH_3), 1.40—1.43(t, 3H, *J*=7.1 Hz, OCH_2CH_3), 3.63—3.68(q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.87—3.90(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.31—4.34(t, 2H, *J*=5.8 Hz, OCH_2CH_2Cl), 4.41—4.46(q, 2H, *J*=7.1 Hz, OCH_2CH_3), 6.86—6.88(d, 1H, *J*=8.8 Hz, ArH), 7.64—7.67(dd, 1H, *J*=2.4, 2.4 Hz, ArH), 8.24—8.25(d, 1H, *J*=2.4 Hz, ArH), 10.74(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{15}H_{18}BrClN_4O_6S$(positive ion), *m*/*z*: found 520.9697$[M+Na]^+$, calcd. 520.9696$[M+Na]^+$.

Compound **9**o: ^{1}H NMR(400 MHz, $CDCl_3$), *δ*: 0.97—1.00(t, 3H, *J*=7.4 Hz, $OCH_2CH_2CH_3$), 1.27—1.30(t, 3H, *J*= 7.2 Hz, CH_2CH_3), 1.76—1.85(m, 2H, $OCH_2CH_2CH_3$), 3.64—3.69 (q, 2H, *J*=7.2 Hz, CH_2CH_3), 3.87—3.90(t, 2H, *J*=5.7 Hz, OCH_2CH_2Cl), 4.32—4.35(m, 4H, OCH_2CH_2Cl, $OCH_2CH_2CH_3$), 6.86—6.88(d, 1H, *J*=8.8 Hz, ArH), 7.64—7.67 (dd, 1H, *J*=2.1, 2.1 Hz, ArH), 8.25—8.26(d, 1H, *J*=2.1 Hz, ArH), 10.72(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{16}H_{20}BrClN_4O_6S$(positive ion), *m*/*z*: found 534.9848$[M+Na]^+$, calcd. 534.9853$[M+Na]^+$.

Compound **9**p: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 1.25—1.28 (t, 3H, J=7.2 Hz, $CH_2C\mathbf{H}_3$), 1.38—1.39[d, 6H, J=6.2 Hz, $OCH(C\mathbf{H}_3)_2$], 3.61—3.66(q, 2H, J=7.2 Hz, $C\mathbf{H}_2CH_3$), 3.88—3.91(t, 2H, J=5.8 Hz, $OCH_2C\mathbf{H}_2Cl$), 4.31—4.34(t, 2H, J=5.8 Hz, $OC\mathbf{H}_2CH_2Cl$), 5.11—5.21[m, 1H, $OC\mathbf{H}(CH_3)_2$], 6.86—6.88(d, 1H, J=8.8 Hz, ArH), 7.64—7.67(dd, 1H, J=2.5, 2.5 Hz, ArH), 8.25—8.26(d, 1H, J=2.5 Hz, ArH), 10.77(br, s, 1H, SO_2NHCO). MALDI-FTICR-MS for $C_{16}H_{20}BrClN_4O_6S$ (positive ion), m/z: found 534.9848$[M+Na]^+$, calcd. 534.9853 $[M+Na]^+$.

Compound **9**q: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 3.18(s, 3H, CH_3), 3.79—3.82(t, 2H, J=5.6 Hz, 5-$OCH_2C\mathbf{H}_2Cl$), 3.87—3.90 (t, 2H, J=5.8 Hz, 2-$OCH_2C\mathbf{H}_2Cl$), 4.06(s, 3H, OCH_3), 4.24—4.27(t, 2H, J=5.6 Hz, 5-$OC\mathbf{H}_2CH_2Cl$), 4.29—4.32(t, 2H, J=5.8 Hz, 2-$OC\mathbf{H}_2CH_2Cl$), 6.94—6.97(d, 1H, J=9.0 Hz, ArH), 7.15—7.18(dd, 1H, J=3.1, 3.1 Hz, ArH), 7.63—7.64(d, 1H, J=3.1 Hz, ArH), 10.67(br, s, 1H, SO_2NHCO). High resolution Fourier transform-mass spectra(HRFTMS) for $C_{15}H_{18}Cl_2N_4O_7S$ (negative ion), m/z: found 467.0205$[M-H]^-$, calcd. 467.0195 $[M-H]^-$.

Compound **9**r: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 1.40—1.43 (t, 3H, J=7.1 Hz, $OCH_2C\mathbf{H}_3$), 3.17(s, 3H, CH_3), 3.78—3.81(t, 2H, J=5.6 Hz, 5-$OCH_2C\mathbf{H}_2Cl$), 3.86—3.89(t, 2H, J=5.8 Hz, 2-$OCH_2C\mathbf{H}_2Cl$), 4.23—4.26(t, 2H, J=5.6 Hz, 5-$OC\mathbf{H}_2CH_2Cl$), 4.29—4.32(t, 2H, J=5.8 Hz, 2-$OC\mathbf{H}_2CH_2Cl$), 4.40—4.46(q, 2H, J=7.1 Hz, $OC\mathbf{H}_2CH_3$), 6.94—6.96(d, 1H, J=9.0 Hz, ArH), 7.14—7.18(dd, 1H, J=3.1, 3.1 Hz, ArH), 7.62—7.63(d, 1H, J=3.1 Hz, ArH), 10.68(br, s, 1H, SO_2NHCO). HRFTMS for $C_{16}H_{20}Cl_2N_4O_7S$(negative ion), m/z: found 481.0360$[M-H]^-$, calcd. 481.0352$[M-H]^-$.

Compound **9**s: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 0.96—1.00 (t, 3H, J=7.4 Hz, $OCH_2CH_2C\mathbf{H}_3$), 1.75—1.84(m, 2H, $OCH_2C\mathbf{H}_2CH_3$), 3.18(s, 3H, CH_3), 3.78—3.81(t, 2H, J=5.6 Hz, 5-$OCH_2C\mathbf{H}_2Cl$), 3.86—3.89(t, 2H, J=5.8 Hz, 2-$OCH_2C\mathbf{H}_2Cl$), 4.23—4.26(t, 2H, J=5.6 Hz, 5-$OC\mathbf{H}_2CH_2Cl$), 4.28—4.34(m, 4H, 2-$OC\mathbf{H}_2CH_2Cl$, $OC\mathbf{H}_2CH_2CH_3$), 6.94—6.96(d, 1H, J=9.0 Hz, ArH), 7.14—7.17(dd, 1H, J=3.1, 3.1 Hz, ArH), 7.62—7.63 (d, 1H, J=3.1 Hz, ArH), 10.68(br, s, 1H, SO_2NHCO). HRFTMS for $C_{17}H_{22}Cl_2N_4O_7S$(negative ion), m/z: found 495.0512$[M-H]^-$, calcd. 495.0508$[M-H]^-$.

Compound **9**t: ^{1}H NMR(400 MHz, $CDCl_3$), δ: 1.37—1.39 [d, 6H, J=6.2 Hz, $OCH(C\mathbf{H}_3)_2$], 3.15(s, 3H, CH_3), 3.78—3.81(t, 2H, J=5.6 Hz, 5-$OCH_2C\mathbf{H}_2Cl$), 3.86—3.89(t, 2H, J=5.8 Hz, 2-$OCH_2C\mathbf{H}_2Cl$), 4.23—4.26(t, 2H, J=5.6 Hz, 5-$OC\mathbf{H}_2CH_2Cl$), 4.29—4.32(t, 2H, J=5.8 Hz, 2-$OC\mathbf{H}_2CH_2Cl$), 5.12—5.18[m, 1H, $OC\mathbf{H}(CH_3)_2$], 6.94—6.97(d, 1H, J=9.1 Hz, ArH), 7.15—7.18(dd, 1H, J=3.1, 3.1 Hz, ArH), 7.62—7.63(d, 1H, J=3.1 Hz, ArH), 10.71(br, s, 1H, SO_2NHCO). HRFTMS for $C_{17}H_{22}Cl_2N_4O_7S$(negative ion), m/z: found 495.0505$[M-H]^-$, calcd. 495.0508[M–H].

3 Results and Discussion

3.1 Preparation

All the title compounds listed in Table 1 were prepared as illustrated in Scheme 2. 1,2,4-Triazolinone derivatives **4**a—**4**h were prepared from the starting materials KSCN and methyl carbonochloridate as in the literature[11]. In order to optimize the yield and treat the reaction mixture conveniently，ethyl acetate was introduced as solvent instead of methyl isobutyl ketone. Compounds **5**a—**5**c reacted respectively with the appropriate amounts of 1,2-dichloroethane in the presence of alkali at 80 °C to give the corresponding compounds **6**a—**6**c, which were converted to compounds **7**a—**7**c by the reaction of compounds **6**a—**6**c with chlorosulfonic acid at 120 °C. The treatment of compounds **7**a—**7**c with ammonia(aq.) at room temperature gave the intermediate sulfonamides **8**a—**8**c. The reaction of each of compounds **4**a—**4**h with each of sulfonamides **8**a—**8**c in the presence of DBU in CH_3CN at room temperature gave the target compounds **9**a—**9**t. All the title compounds were identified with ^{1}H NMR, HRFTMS and elemental analysis.

3.2 Biological Assay

The herbicidal activities of 20 title compounds were tested and evaluated against the growth of four weeds, representative of monocotyledonous and dicotyledonous plants, through the pot experiment, in which soil treatment and foliage spray were adopted. After the tested plants emerged for 20 d, the damage to the plants or the negative effect on the tested plants was recorded(Table 2).

These novel compounds showed better herbicidal activities against dicotyledonous plants than against monocotyledonous plants. In most cases, the effect of soil treatment was greater than that of foliage spray. When the concentration of the inhibitor was reduced to 15 g/hectare, some of the target compounds still showed satisfactory herbicidal activities(Table 3). In order to investigate whether the variation of substituent groups at the 3-position and 4-position of 1,2,4-triazolinone ring has effect on the herbicidal activity of the title compounds, alkoxy group and alkyl group(methyl and ethyl group) were introduced at 3-position and 4-position of 1,2,4-triazolinone ring, respectively. It was significantly observed that the methyl group at the 4-position in the 1,2,4-triazolinone ring is beneficial for the satisfactory herbicidal activity in comparison with the ethyl group at that position. Thus, this indicates that the variation of substituent groups at 4-position in the 1,2,4-triazolinone moiety absolutely impacted the herbicidal activity of the title compounds.

Our further experiment was to set methyl group at the 4-position, the methoxy(**9**a, **9**i, **9**q), ethoxy(**9**b, **9**j, **9**r) and isopropoxy(**9**d, **9**l, **9**t) at the 3-position in the 1,2,4-triazolinone ring respectively in order to evaluate whether the substituent group at the 3-position impacted the herbicidal activity against four kinds of weeds. The herbicidal activities of compounds **9**a—**9**d against dicotyledonous plants decreased successively, which is similar to those of compounds **9**i—**9**l and **9**q—**9**t.

In another set of experiments, chloro group(**9**a—**9**h) was replaced with bromo group(**9**i—**9**p) at 5-position in 2-(2-chloroethoxy) benzenesulfonyl moiety. The herbicidal activities of compounds **9**a—**9**h against monocotyledonous and dicotyledonous plants were comparable to those of compounds **9**i—**9**p. It was speculated that the variation of halogen group in

the benzenesulfonyl moiety of the title compounds exerted no effect on the herbicidal activity. Compounds **9**a and **9**b also displayed excellent herbicidal activity against *Bassica napus* at a concentration of 15 g/hectare, which is comparable with that of commercial triasulfuron.

Table 2 Herbicidal activities(%) of target compounds 9a—9t in the pot experiment(375 g/hectare)*

Compd.	*Brassica napus*		*Amaranthus retroflexus*		*Echinochloa crusgalli*		*Digitaria adscendens*	
	Soil treatment	Foliage spray	Soil treatment	Foliage spray	Soil treatment	Foliage spray	Soil treatment	Foliage spray
9a	99.6	100.0	98.3	92.2	85.2	89.9	66.9	80.6
9b	95.4	100.0	93.1	79.0	99.8	100.0	80.5	77.8
9c	86.9	97.6	82.8	25.4	14.1	25.8	0.0	8.3
9d	70.1	89.6	64.7	42.5	0.0	41.5	0.0	34.7
9e	46.1	5.0	55.6	35.8	43.4	15.0	8.8	5.0
9f	71.2	41.8	86.9	54.3	51.4	53.5	10.0	0.0
9g	0.0	10.0	35.3	14.5	0.0	8.2	0.0	0.0
9h	10.5	19.5	18.5	48.4	0.0	0.0	10.0	0.0
9i	100.0	100.0	99.3	53.5	99.0	85.5	65.9	81.5
9j	99.0	100.0	99.3	89.5	100.0	87.8	56.1	84.7
9k	100.0	81.4	72.9	20.0	20.0	0.0	24.9	75.0
9l	98.0	75.9	18.0	15.0	7.6	0.0	5.0	67.9
9m	64.9	24.8	44.7	62.9	0.9	15.0	0.0	51.9
9n	52.3	5.6	67.5	25.0	5.3	10.0	10.0	23.8
9o	34.2	10.0	5.0	0.0	0.0	10.0	0.0	18.1
9p	54.1	15.0	33.2	5.0	0.0	0.0	5.0	49.2
9q	99.6	73.6	95.2	20.2	61.6	90.4	8.0	10.0
9r	98.3	67.5	89.9	18.8	74.6	100.0	28.5	3.9
9s	48.9	26.5	29.0	58.9	4.1	0.0	0.0	4.9
9t	26.6	12.4	30.6	21.5	19.4	0.0	0.0	0.0
Triasulfuron	100.0	100.0	100.0	99.6	NT	96.9	NT	NT

* NT=not tested.

Table 3 Herbicidal activities(%) of target compounds 9a, 9b, 9i, 9j, 9q and 9r in the pot experiment (120, 60, 30, 15 g/hectare)*

Dosages/ (g·hectare^{-1})	Compd.	*Brassica napus*		*Amaranthus retroflexus*		*Echinochloa crusgalli*		*Digitaria adscendens*	
		Soil treatment	Foliage spray	Soil treatment	Foliage spray	Soil treatment	Foliage spray	Soil treatment	Foliage spray
120	**9**a	100.0	100.0	98.9	36.8	39.5	92.0	NT	21.1
	9b	100.0	100.0	97.8	31.4	77.5	100.0	74.7	27.6
	9i	97.8	47.1	99.2	NT	35.8	36.8	NT	0.0
	9j	98.6	42.0	97.1	4.8	44.3	48.1	NT	4.6
	9q	89.6	43.5	46.0	10.5	41.7	32.8	5.0	0.0
	9r	62.7	52.2	58.1	17.4	4.5	25.6	0.0	0.0
60	**9**a	100.0	100.0	97.8	31.4	21.6	69.8	NT	17.1
	9b	97.8	100.0	88.3	17.2	44.1	100.0	73.9	5.7
	9i	52.7	24.6	29.7	NT	16.2	10.3	NT	0.0
	9j	95.3	35.3	65.7	0.0	14.1	21.5	NT	0.0
	9q	72.0	29.1	42.3	2.6	15.9	12.7	0.0	0.0
	9r	45.6	32.4	31.5	4.0	0.0	0.0	0.0	0.0
30	**9**a	86.0	90.3	78.8	18.6	7.8	66.0	NT	0.0
	9b	88.6	100.0	38.7	4.4	13.0	81.5	64.9	0.0
	9i	37.9	14.8	24.8	NT	0.0	5.8	NT	0.0
	9j	65.0	34.3	35.4	0.0	0.0	19.1	NT	0.0
	9q	29.4	18.7	5.0	0.0	4.5	8.0	0.0	0.0
	9r	19.7	16.7	5.0	0.0	0.0	0.0	0.0	0.0
15	**9**a	53.1	89.5	47.6	4.4	0.0	47.5	NT	0.0
	9b	63.8	100.0	36.5	0.0	0.9	41.4	52.7	0.0
	9i	38.3	9.7	17.4	NT	0.0	0.0	NT	0.0
	9j	45.8	19.7	12.1	0.0	0.0	8.2	NT	0.0
	9q	20.4	0.0	0.0	0.0	0.0	6.0	0.0	0.0
	9r	12.4	13.7	0.0	0.0	0.0	0.0	0.0	0.0
15	Triasulfuron	100	100.0	100	83.6	NT	46.9	NT	NT

* NT=not tested.

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