

New benzenesulfonylurea derivatives possessing β -hydroxyalkyl subgroup: Synthesis and herbicidal activity

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Abstract : New benzenesulfonylurea derivatives possessing β -hydroxyalkyl subgroup were synthesized and found to have interesting herbicidal activity in greenhouse screening. (Received August 30, 2001; accepted September 19, 2001)

Key words : benzenesulfonylurea derivatives, β -hydroxyalkyl subgroup, ALS (acetolactate synthase).

ALS (acetolactate synthase), which is the first common enzyme of branched chain amino acid biosynthesis in plants, has been widely utilized as the target enzyme for the development of new herbicides (Schloss, 1994). ALS inhibiting herbicides have several advantages such as low application rates, broad weed control spectra, good crop selectivities and favorable toxicological and environmental properties over classical ones. Up to now, a number of sulfonylurea herbicides, which consist of one major class of ALS inhibiting herbicides, have been commercialized and being developed (Brown *et al.*, 1995; Bryant and Bite, 2000) since the discovery of sulfonylurea structure in 1970's.

Recently, we have published papers concerning new benzenesulfonylurea derivatives possessing α -hydroxyalkyl subgroup as an ortho substituent (Hwang *et al.*, 1999; Ko *et al.*, 1999; Hwang *et al.*, 2000). We thought that hydroxy functional group might play an important role for the herbicidal activity. During our continuing research program for the development of new herbicides we have reasoned that benzenesulfonylurea derivatives possessing β -hydroxyalkyl subgroup might also show interesting herbicidal activity. In this paper we want to describe the synthesis and herbicidal activity of new benzenesulfonylurea derivatives possessing β -hydroxyalkyl subgroup at ortho position.

Synthesis of new benzenesulfonylurea derivatives possessing β -hydroxyalkyl subgroup could be carried out via two different synthetic pathways (Scheme 1, 2).

As shown in Scheme 1, N-t-butyl-2-methylbenzene sulfonamide **1** was lithiated at a 2-methyl position with n-BuLi employing carbanion chemistry, and reacted with an electrophile (acetaldehyde or ethyl

fluoroacetate). The resulting β -hydroxyalkylsulfonamide **2** (carbonyl compound was reduced with NaBH₄ before acylation) was treated with Ac₂O to provide β -acetyloxyalkyl N-t-butylbenzenesulfonamide **3**, which was treated with trifluoroacetic acid to give primary sulfonamide **4**. Sulfonamide **4** was coupled with carbamate employing conventional method (Gee and Hay, 1994) to afford sulfonylurea, which was deacylated with LiOH to give benzenesulfonylurea **5**.

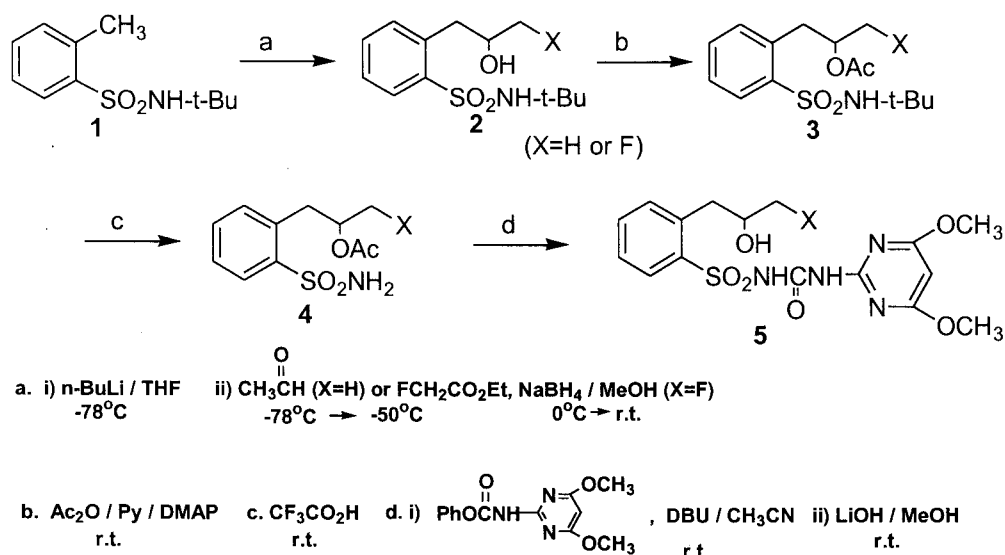
For the synthesis of benzenesulfonylurea derivatives possessing α -halo- β -hydroxyalkyl subgroup, we followed another synthetic route. (Scheme 2)

N-t-butylbenzenesulfonamide **6** was lithiated with n-BuLi, and followed by addition of electrophile. The resulting ketosulfonamide was reduced with NaBH₄ to give sulfonamide **7**, which was halogenated with halogenating agent (NCS or DAST) to afford the corresponding chloro or fluorosulfonamide **8**. Chloro or fluorosulfonamide **8** was debenzylated with H₂/Pd and acylated with Ac₂O, and followed by the reaction with trifluoroacetic acid to provide primary sulfonamide **9**. Sulfonamide **9** was coupled with carbamate, and the acetyl group was removed with LiOH to give benzenesulfonylurea **10**. The structures of new benzenesulfonylurea **5a~b**, **10a~f** were assigned by ¹H NMR spectroscopy.

The herbicidal activities of new sulfonylurea derivatives **5a~b**, **10a~f** were examined in the pot test under greenhouse conditions. Upland screening results of new benzenesulfonylureas are summarized in Table 1.

In a comparison of compounds **5a** and **5b** having alkyl substituent, compound **5b** with fluorine atom has better herbicidal activity against grass and broadleaf weeds in upland condition than compound **5a** possessing no fluorine atom. Furthermore, compound

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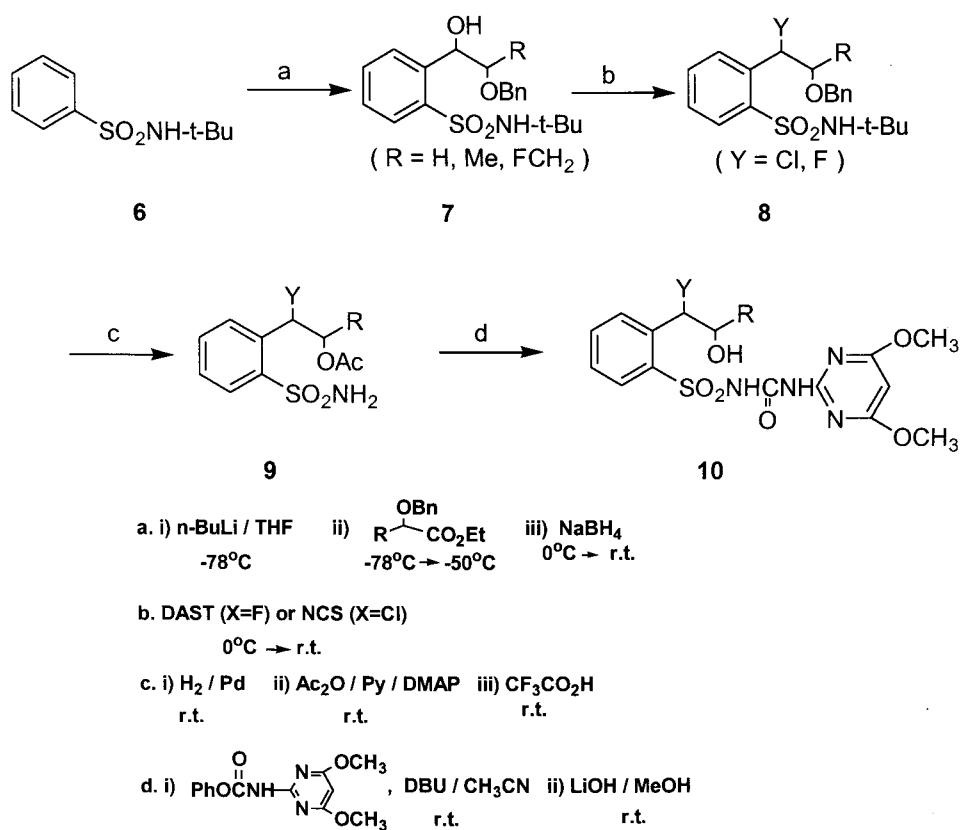


(Scheme 1)

5b has good tolerance to wheat and it also shows superior herbicidal activity to compounds **10a**~**f** having alkyl substituent with an α -halogen (chlorine or fluorine) under post-emergent upland condition.

Table 2 shows paddy screening results of new analogs. In this test, the most promising compound **5b**

in upland screening showed no selectivity to the rice in spite of a high level of herbicidal activity against several weeds in submerged paddy condition. Most of compounds except **10f** have poor selectivity to the rice. Compound **10f** exhibited good tolerance to the rice and good to excellent herbicidal activity to several



(Scheme 2)

Table 1. Herbicidal activities of compounds 5a ~ b, 10a ~ f under post-emergent upland condition

Compound	X	Y	R	Rate (g/ha)	TRZAW	ECHCG	DIGSA	PANDI	XANSI
5a	H	-	-	50	-	100	85	90	90
5b	F	-	-	100	40	100	100	100	100
10a ^{a)}	-	Cl	Me	25	0	100	100	90	100
				100	40	95	70	95	100
10b ^{b)}	-	Cl	Me	25	0	90	50	80	85
				100	40	95	60	80	95
10c	-	F	H	25	10	85	40	60	75
				100	60	100	60	80	100
10d ^{c)}	-	F	Me	25	30	80	20	60	60
				100	50	90	20	60	80
10e ^{d)}	-	F	Et	25	30	80	0	60	70
				2000	-	100	40	70	100
10f ^{d)}	-	F	CH ₂ F	250	20	95	40	80	90
				63	0	80	40	40	70

TRZAW : *Triticum aestivum* L. (Wheat), ECHCG : *Echinochloa crus-galli* P. Beauv (Barnyardgrass), DIGSA : *Digitaria sanguinalis* (L) Scop. (Large crabgrass), PANDI : *Panicum dichotomiflorum* Michx. (Fall panicum), XANSI : *Xanthium strumarium* L., (Cockbur)

^{a)}Nonpolar isomer at N-t-butyl-2-(α -chloro- β -hydroxypropyl)benzenesulfonamide stage.

^{b)}Polar isomer at N-t-butyl-2-(α -chloro- β -hydroxypropyl)benzenesulfonamide stage.

^{c)}Mixture of diastereomers.

^{d)}Nonpolar isomer at N-t-butyl-2-(α -fluoro- β -hydroxypropyl)benzenesulfonamide stage.

0 : no effect, 100 : complete kill.

Table 2 Herbicidal activities of new benzenesulfonylurea derivatives under paddy submerged condition

Compound	Rate(g/ha)	ORYSA (3leaf)	ECHOR	SCPJU	MOOVA	CYPSE	SAGPY
5a	12	80	95	100	95	100	90
	3	20	60	90	30	100	90
5b	12	80	85	95	100	100	100
	3	50	40	70	90	90	90
10a	25	80	90	95	90	95	95
	6	70	70	95	70	95	90
10b	25	70	90	100	90	100	95
	6	60	60	80	70	90	95
10c	6	60	100	70	90	100	100
	1.5	50	80	50	80	100	100
10d	6	40	90	90	95	100	80
	1.5	20	70	90	90	100	80
10e	25	40	80	100	90	100	90
	6	0	50	100	50	80	90
10f	8	30	80	90	100	100	80
	2	0	60	80	100	100	80

ORYSA : *Oryza sativa* L. (Rice), ECHOR : *Echinochloa crus-galli* var. *oryzicola* (Barnyardgrass), SCPJU: *Scirpus juncooides* Roxb. (Bulrush), MOOVA : *Monochoria vaginalis* Presl. (Monochoria), CYPSE : *Cyperus serotinus* Rottb. (Flat-sedge), SAGPY: *Sagittaria pygmaea* Miq. (Arrow head)

0 : no effect, 100 : complete kill

annual and perennial weeds below 10 g/ha application rate.

In conclusion, a series of benzenesulfonylurea derivatives possessing a β -hydroxyalkyl subgroup represented a new class of sulfonylurea herbicide with interesting herbicidal activity. In upland condition, compound **5b** was found to have a potential as a postemergent wheat herbicide candidate.

In paddy condition, however, further research to improve herbicidal efficacy against some trouble paddy weeds such as barnyardgrass, bulrush, and arrow head is needed for rice herbicide candidate.

Spectral Data for Compounds **5a** ~ **b**, **10a** ~ **f**

- 5a** : ^1H NMR(200 MHz, CDCl_3) δ 1.24(d, 3H, J=6Hz), 3.18-3.50(m, 3H), 3.96(s, 6H), 5.20-5.30(m, 1H), 5.80(s, 1H), 7.10-7.62(m, 4H), 8.22-8.24(m, 1H)
- 5b** : ^1H NMR(200 MHz, CDCl_3) δ 3.30(d, 2H, J=7Hz), 3.96(s, 6H), 4.20-4.60(m, 3H), 5.80(s, 1H), 7.06-7.62(m, 4H), 8.22-8.24(m, 1H)
- 10a** : ^1H NMR(500 MHz, CDCl_3) δ 1.20(d, 3H, J=7Hz), 2.48(d, 1H, J=5Hz), 3.97(s, 6H), 4.24-4.28(m, 1H), 5.81(s, 1H), 5.93(d, 1H, J=6Hz), 7.16(s, 1H), 7.54-8.28(m, 4H), 12.91(s, 1H)
- 10b** : ^1H NMR(500 MHz, CDCl_3) δ 1.40(d, 1H, J=6Hz), 2.22(d, 1H, J=7Hz), 3.97(s, 6H), 4.18-4.22(m, 1H), 5.80(s, 1H), 5.98(d, 1H, J=7Hz), 7.05(s, 1H), 7.17-8.26(m, 4H), 12.88(s, 1H)
- 10c** : ^1H NMR(500 MHz, CDCl_3) δ 3.95(s, 6H), 4.34-4.51(m, 2H), 5.78(s, 1H), 6.69(ddd, 1H, $J_1=46\text{Hz}$, $J_2=7\text{Hz}$, $J_3=2\text{Hz}$), 7.18(s, 1H), 7.54-7.75(m, 3H), 8.21(d, 1H, J=8Hz), 12.84(s, 1H)
- 10d** : (Mixture of diastereoisomers X and Y) : ^1H NMR(500 MHz, CDCl_3) δ 1.27(d, 1Hx, J=6Hz), 1.42-1.43(m, 1Hy), 2.01-2.11(m, 1Hy), 2.16-2.26(m, 1Hx), 3.93(s, 6Hx + 6Hy), 4.05-4.15(m, 1Hx + 1Hy), 5.78(s, 1Hx + 1Hy), 6.33(dd, 1Hy, $J_1=47\text{Hz}$, $J_2=4\text{Hz}$), 6.34(dd, 1Hx, $J_1=47\text{Hz}$, $J_2=5\text{Hz}$), 7.17(s, 1Hx + 1Hy), 7.52-7.72(m, 3Hx + 3Hy), 8.20(d, 1Hy, J=8Hz), 8.22(d, 1Hx, J=8Hz), 12.83(s, 1Hx + 1Hy)
- 10e** : ^1H NMR(500 MHz, CDCl_3) δ 1.00(t, 3H, J=7.5Hz), 1.70-1.80(m, 1H), 2.15-2.25(m, 1H), 3.75-3.85(m, 1H), 3.94(s, 6H), 5.77(s, 1H), 6.34(dd, 1H, $J_1=47\text{Hz}$, $J_2=6\text{Hz}$), 7.15(s, 1H), 7.53-7.73(m, 3H), 8.21(d, 1H, J=8Hz), 12.81(s, 1H)
- 10f** : ^1H NMR(500 MHz, CDCl_3) δ 3.93(s, 6H), 4.53-4.56(m, 1H), 4.60(dd, 2H, $J_1=46\text{Hz}$, $J_2=5\text{Hz}$), 5.78(s, 1H), 6.58(dd, 1H, $J_1=46\text{Hz}$, $J_2=2\text{Hz}$), 7.18(s, 1H), 7.55-7.80(m, 3H), 8.16(d, 1H, J=8Hz), 12.82(s, 1H)

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β -Hydroxyalkyl subgroup을 갖는 새로운 벤젠술폰닐우레아 유도체 : 합성과 생리활성

고영관*, 장해성, 류재욱, 우재춘, 구동완, 황인택, 김대황 (한국화학연구원, 대전, 유성 사서함 107, 305-606)

요약 : β -Hydroxyalkyl subgroup을 갖는 새로운 벤젠술폰닐우레아 유도체들을 합성하여 제초활성을 온실에서 시험하였다. 그중 화합물 **5b**는 처리약량 25 g/ha의 발조건 발아후 처리에서 밀에 대한 좋은 선택성을 가지면서 여러 잡초들을 잘 방제하였다. 논조건에서는 화합물 **10f**가 10 g/ha이하의 처리약량에서 벼선택성을 가지며 비교적 좋은 제초활성을 나타내었다.

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