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〈Note〉

Synthesis and herbicidal activity of new benzenesulfonylurea derivatives possessing bicyclic ketal subgroup

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Abstract : New benzenesulfonylurea derivatives possessing bicyclic ketal subgroup were synthesized and shown to have interesting herbicidal activities under upland greenhouse screening. (Received March 5, 2002; accepted March 20, 2002)

Key words : benzenesulfonylurea derivatives, bicyclic ketal subgroup, ALS (acetolactate synthase).

Recently, a group of sulfonylurea herbicides, which act through the inhibition of ALS (acetolactate synthase) enzyme absent in human being and animal, has become a good example of environmentally friendly pesticides. The main reason for that lies in their innovative properties such as extremely low application rates and the favorable toxicological profiles (Brown and Cotterman, 1994). Thus, since the first commercial sulfonylurea chlorosulfuron a number of sulfonylurea herbicides including modified compounds such as sulfonyltriazinones have been commercialized and are still under development (Brown *et. al.*, 1995 ; Bryant and Bite, 2001).

From the analysis of the structures of commercial sulfonylurea herbicides it is concluded that the introduction of noble subgroup into aromatic backbone of sulfonylurea is a general strategy for the development of new sulfonylurea having characteristic herbicidal activity. Until now, various functional groups such as chloride, carboxylic ester, carboxamide, alkyl sulfone and haloalkyl moiety were employed (Gee and Hay, 1994).

Previously, we have published several papers concerning new benzenesulfonylurea derivatives possessing novel subgroups (Hwang *et. al.*, 1999; Hwang *et. al.*, 2000; Ko *et. al.*, 1998; Ko *et. al.*, 1999; Ko *et. al.*, 2001).

As a continuing research program for the development of new herbicide herein we want to describe the synthesis of new benzenesulfonylurea derivatives possessing bicyclic ketal subgroup at ortho position. We thought bicyclic ketal group might be a noble subgroup since there are many biologically active natural products including bicyclic ketal skeleton (Elliott *et. al.*, 1976; Kinzer *et. al.*,1969; Silverstein *et. al.*, 1968).

Sulfonylurea derivatives possessing bicyclic ketal moiety could be easily synthesized from 2-bromo phenyl methoxymethyl sulfide employing the literature procedure (Kim *et. al.*, 1992).

2-Bromophenyl methoxymethyl sulfide **1** was treated with n-BuLi employing carbanion chemistry, and reacted with an electrophile **2** which could be prepared from the reaction of solketal sodium salt with ethyl bromoacetate or ethyl 2-bromopropionate. The resulting carbonyl compound **3** could be cyclized by addition of p-toluenesulfonic acid in dichloromethane at room temperature to afford bicyclic ketal sulfide **4**, which could be transformed into bicyclic ketal sulfonamide **5** by chlorination with chlorine followed by amination with aqueous ammonia. Sulfonamide **5** was coupled with various carbamates employing conventional method to give the corresponding benzenesulfonylurea derivatives **6a~k**. The structures of new benzenesulfonylurea derivatives were assigned by ^{1}H NMR spectroscopy. The herbicidal activities of new sulfonylurea analogs **6a~k** were examined in the pot test under upland greenhouse conditions. Table 1 summarizes the primary upland screening results at 100 g/ha application rate.

Among the compounds synthesized, **6b** and **6i,** which have the same triazine ring, were selected as the candidates for further test under post emergent greenhouse condition from the consideration of both the tolerance toward crop and the herbicidal activities toward weeds. Compounds **6c**, **6f** and **6j** have the comparable herbicidal activities with the above candidates. However, their crop selectivities were poor.

In advanced experiment, thifensulfuron methyl was

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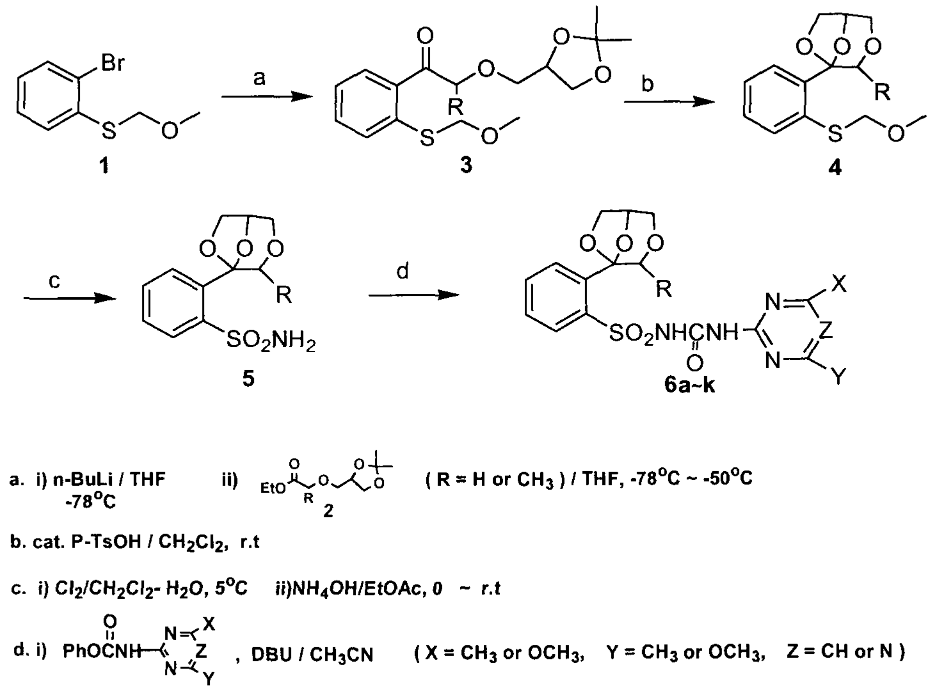

(Scheme 1)

used as reference compound for the comparison of biological properties. Table 2 shows the results. Compound **6b** exhibits better tolerance toward wheat and slightly weaker herbicidal activity than the thifensulfuron methyl. However, compound **6i** was inferior to compound **6b** and thifensulfuron methyl in terms of wheat selectivity and herbicidal activity.

In conclusion, we have synthesized several benzenesulfonylurea derivatives possessing bicyclic ketal subgroup and found that bicyclic ketal moiety subgroup could be employed as a potential subgroup for a new class of sulfonylurea herbicide having interesting herbicidal activity.

Table 1. Herbicidal activities of compound 6a~k under post-emergent upland condition at 100 g/ha application rate

Compound	R	X	Y	Z	TRZAW	GLXMX	DACGL	AMAVI	DIGSA	RUMJA	AESIN
6a	H	CH_3	CH_3	CH	65	100	100	70	65	70	90
6b	H	CH_3	OCH_3	N	0	100	90	100	40	100	100
6c	H	CH_3	OCH_3	CH	90	100	100	100	65	100	100
6d	H	Cl	OCH_3	CH	25	60	100	100	25	80	60
6e	H	OCH_3	OCH_3	N	0	100	60	100	0	100	100
6f	H	Cl	CH_3	CH	90	100	100	100	85	90	90
6g	CH_3	OCH_3	OCH_3	N	0	90	60	100	40	100	90
6h	CH_3	Cl	OCH_3	N	0	90	40	70	0	75	80
6i	CH_3	CH_3	OCH_3	N	15	85	90	100	65	95	90
6j	CH_3	CH_3	OCH_3	CH	70	90	100	100	100	90	80
6k	CH_3	Cl	OCH_3	CH	10	10	100	100	50	100	20

TRZAW, *Triticum acstivum* L. (Wheat); GLXMX, *Glycin max* (L.) Merr. (Soybean); DACGL, *Dactylis glomerata* L. (Orchardgrass); AMAVI, *Amaranthus viridis* L. (Amaranth), DIGSA, *Digitaria sanguinalis* (L.) Scop. (Crabgrass); RUMJA, *Rumex japonicus* Houtt. (Rumex); AESIN, *Aeschynimene indica* L. (Indian jointvetch).

0 : no effect, 100 : complete kill according to visual rating.

Table 2. Advanced post-emergent upland screening data for 6b, 6i and thifensulfuron methyl

Compound	Rate (g/ha)	TRZAW	ALOAE	RUMJA	BRANA	CAGHE	CHEAL	STEAU
	100	0	100	100	100	100	100	100
6b	25	0	90	80	100	90	100	100
	6	0	70	70	100	60	70	90
	100	40	90	90	100	100	100	100
6i	25	10	70	80	100	40	70	100
	6	0	10	50	80	10	70	90
	100	30	100	100	100	100	100	100
thifensulfuron methyl	25	0	100	90	90	100	100	100
	6	0	70	90	80	100	90	90

TRZAW, *Triticum aestivum* L. (Wheat); ALOAE, *Alopecurus amurensis* Komarov/Ohwi (Foxtail); RUMJA, *Rumex japonicus* Houtt. (Rumex); BRANA, *Brassica napus* L. (Rape); CAGHE; *Calystegia hederacea* Wall. (Bindweed), CHEAL, *Chenopodium album* L. (Pigweed); STEAU, *Stellaria alsine* grimm (Starwart).
0 : no effect, 100 : complete kill according to visual rating.

Spectral Data for Compounds 6a~k

6a : ^{1}H NMR(200 MHz, $CDCl_3$) δ2.49(s, 6H), 3.65-4.50(m, 7H), 6.75(s, 1H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H)

6b : ^{1}H NMR(200 MHz, $CDCl_3$) δ2.55(s, 3H), 3.60-4.80(m, 7H), 4.04(s, 3H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H)

6c : ^{1}H NMR(200 MHz, $CDCl_3$) δ2.45(s, 3H), 3.65-4.50(m, 7H), 4.00(s, 3H), 6.29(s, 1H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H)

6d : ^{1}H NMR(200 MHz, $CDCl_3$) δ3.65-4.55(m, 7H), 4.05(s, 3H), 6.48(s, 1H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H), 11.85(br s, 1H)

6e : ^{1}H NMR(200 MHz, $CDCl_3$) δ3.65-4.60(m, 7H), 4.07(s, 6H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H), 12.02(br s, 1H)

6f : ^{1}H NMR(200 MHz, $CDCl_3$) δ2.55(s, 3H), 3.65-4.60(m, 7H), 6.94(s, 1H), 7.30-7.95(m, 4H), 8.45-8.55(m, 1H), 11.85(br s, 1H)

6g : ^{1}H NMR(200 MHz, $CDCl_3$) δ0.90(d, 3H J=6.4Hz), 3.65-4.80(m, 6H), 4.04(s, 6H), 7.25-7.95(m, 4H), 8.45-8.55(m, 1H), 11.99(br s, 1H)

6h : ^{1}H NMR(200 MHz, $CDCl_3$) δ0.90(d, 3H J=6.4Hz), 3.65-4.80(m, 6H), 4.04(s, 6H), 7.30-7.95(m, 4H), 8.45-8.55(m, 1H), 11.95(br s, 1H)

6i : ^{1}H NMR(200 MHz, $CDCl_3$) δ0.90(d, 3H J=6.4Hz), 2.55(s, 3H), 3.65-4.80(m, 6H), 4.04(s, 3H), 7.30-7.95(m, 4H), 8.45-8.55(m, 1H), 12.05(br s, 1H)

6j : ^{1}H NMR(200 MHz, $CDCl_3$) δ0.90(d, 3H J=6.4Hz), 2.43(s, 3H), 3.65-4.80(m, 6H), 3.94(s, 3H), 6.28(s, 1H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H)

6k : ^{1}H NMR(200 MHz, $CDCl_3$) δ0.89(d, 3H J=6.4Hz), 3.65-4.80(m, 6H), 3.97(s, 3H), 6.47(s, 1H), 7.20-7.95(m, 4H), 8.45-8.55(m, 1H)

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Bicyclic ketal subgroup을 갖는 새로운 벤젠술포닐우레아 유도체의 합성과 제초활성

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요약 : Bicyclic ketal subgroup을 갖는 새로운 벤젠술포닐우레아 유도체들을 합성하여 제초활성을 온실에서 시험하였다. 그중에서 화합물 **6b**는 표준물질 thifensulfuron methyl과 비교 실험한 결과 처리약량 6～100 g/ha의 밭조건 발아후 처리에서 밀에 대해서 보다 좋은 선택성을 나타내었으며 밭잡초들에 대한 제초활성은 비슷하거나 약간 떨어지는 결과를 나타내었다.

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