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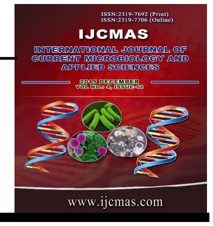

**Original Research Article**

# S-Benzyl Isothiouronium salts of some Sulfonylureas as potential herbicides

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**Keywords**

Isothiouronium Salts, Sulfonylureas, Herbicidal activity

**A B S T R A C T**

S-Benzyl isothiouronium salt of carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester (I) together with a series of S-benzyl isothiouronium salts of N- substituted-N'- 3,4- dichlorophenyl sulfonylurea (IIa-p) were prepared. Structure confirmation was based on element analysis and infrared spectroscopy. The herbicidal activity of the prepared compounds was evaluatedagainst *Echinoocloa crus – galli*L. Beauv (barnyard grass). The introduction of the functional isothiouronium group $[C_6H_5CH_2SC(NH_2)_2]^+$into the piperidyl- N- substituted- N'- 3,4- dichlorophenyl sulfonylurea relatively raised the herbicidal activity, but the trend was lowering of the herbicidal activity of the prepared isothiouronium salts which will be discussed in detail later.

## Introduction

Isothiouronium salts constitute a class of compounds containing a di-coordinated sulfur cation (Reid, 1963). Isothiouronium salts or pseudothiouronium salts are helpful in characterization of carboxylic acids and sulfonic acids and also in preparation of isothioureas, thiols (Dancke et al., 1970)guanidines (Brand and Brand, 1942) and also sulfonyl chlorides (Follcers et al., 1941). On the other hand, isothiouronium salts have been recognized to have diverse biological activities. Thus, S-[(3-oxopyridazin-2-yl] isothiouronium halides were reported as antihypertensive agents.(Hiroshi et al., 1987). Uracil-5-isothiouronium chlorideprotects against the leucopenic effect of different anticancer agents without interfering the anticancer effect (Spasskaya et al., 1968; Dauvarote and Zidermane, 1969). The ethylene bis-isothiouronium salt $[(NH_2)_2S(CH_2)_2SC(NH_2)_2]^{++}$ $M^{--}$of some carboxylic acids, glycine, sulfanilamide, sulfadiazine and folic acid furnished a series having antibacterial and antifungal activity (Badawi et al., 1988).The fungicidal activity of isothiouronium salts of some dichlorobenzene sulfonanilides was dependent on the type of the positive ion, that is S-benzyl-isothiouronium derivatives were more active than the corresponding S-alkyl-isothiouronium derivatives (El-Dib et al., 1990). Polyoxyethyleneisothiouronium salts of the type $[C_6H_5CH_2SC(NH_2)_2]_2^{++}$ $[(OCH_2CH_2)_nO]^{--}$showed a decrease in their insecticidal activity as the number of polyoxyethylene units increased probably due to lowering in penetration of the insecticide as its molecular weight increases (Salama et al., 1993).However, the fungicidal activity of the six isomers of isothiouronium salts of dodecylbenzene sulfonic acid is related to their surface properties in particular surface tension and critical micelle concentration (Salama et al., 1993). In the present work, it was aimed to prepare the S-Benzyl isothiouronium salt of carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester(I) and a series of the corresponding sulfonylurea (IIa-p) as candidate herbicides.

## Materials and Methods

Melting points were uncorrected and were measured on Gallenkamp melting point apparatus. IR spectra were recorded on Perkin Elmer 1430 instrument using potassium bromide wafer technique.

### Preparation of S-Benzyl Isothiouronium Salts of Carbamic Acid 3,4-Dichlorophenyl Sulfonyl Methyl (I) Ester and N- Substituted- N'- 3,4-Dichlorophenyl Sulfonylurea(IIa-p)

Carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester (0.01 mole)or the appropriate N- substituted- N'- 3,4- dichlorophenyl sulfonylurea (0.01 mole) was dissolved in1% aqueous sodium hydroxide solution (the equivalent amount). Addition of few drops of 0.1 N hydrochloric acidin presence of phenolphthalein till faintly basic, then filtration. The filtrate was gradually added while cooling and vigorously stirring to5% aqueous solution of S-Benzyl isothiouronium chloride (0.01 mole). The solid product was filtered off and thoroughly washed with distilled water till neutral, then dried. Recrystallization from the proper solvent gave the required S-Benzyl isothiouronium salts of carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester(I) and N- substituted- N'- 3,4- dichlorophenyl sulfonylurea (IIa-p) (Table 1).

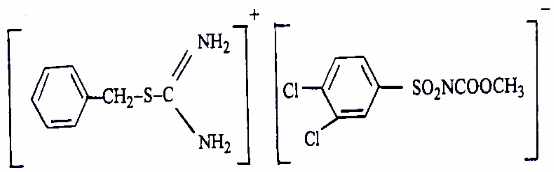
### Herbicidal and Phytocidal Activities (Zemanek, 1963)

A hot solution of the tested compound in ethanol was mixed with a calculated amount of a hot solution of Agar so that concentration of 2, 4 and 6ppm were obtained. The hot solutions, thus obtained, were poured in test tubes (15 x 1.5cm) up to 10cm height and allowed to solidify. The grains of barnyard grass or rice were soaked for 16hrs, then water was drained and the grains were kept for 20 hrs. at 27- 28°C. Homogenous germinating grains with rootlet length 0.3 - 0.5cm were collected and one geminating grain of barnyard grass or rice was inserted on the top of agar in each test tube. The tubes were incubated at 27- 28°C for 12hrs.every day under artificial illumination. Three replicates were made for each treatment. Observations, which were taken after 21 days, were based on the length of shoot and root systems above and below the agar surface. The formation of the secondary roots was also considered.

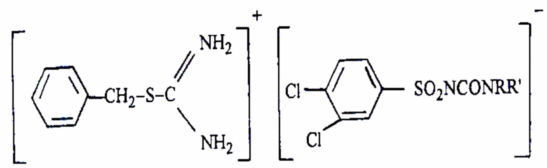
## Results and Discussion

lsothiuronium salts have been reported as herbicides (Mel'nikov et al., 1981). Thus, it wasseen that combination of an isothiuronium moiety together with a sulfonylurea moiety in one molecule may increase the herbicidal activity. Accordingly, S-Benzyl isothiouronium salts of carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester (I) and N- substituted- N'- 3,4-

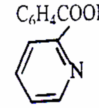
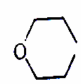
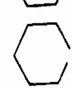
dichlorophenyl sulfonylurea (IIa-p)were developed through the interaction of S-benzyl isothiuroniurn chloride with carbamic acid 3,4-dichlorophenyl sulfonyl methyl ester or the correspondingN-substituted- N'- 3,4- dichlorophenyl sulfonylurea(Salama et al., 2007) (Table 1).



I



II

| | R | R' | | R | R' |
|---|---|---|---|---|---|
| IIa : | H | $CH(CH_3)_2$ | IIi : | H | $C_6H_4OH$-o |
| b : | H | $(CH_2)_3CH_3$ | j : | H | $C_6H_4OH$-m |
| c : | H | $CH_2CH(CH_3)_2$ | k : | H | $C_6H_4OH$-p |
| d : | H | $CH_2C_6H_5$ | l : | H | $C_6H_4CH_3$-p |
| e : | H | $C_6H_5$ | m : | H | $C_6H_4COOH$-p |
| f : | H | $C_6H_4Cl$-m | n : | H |  |
| g : | H | $C_6H_4Cl$-p | o : |  | |
| h : | H | 2, 4-$C_6H_3Cl_2$ | p : |  | |

Regarding the preparation of S-bensylisothiuronium salts of sulfonylureas (IIa-p) the reaction was repeated twice once with equimolar ratio of reactants and another once with a ratio l: 2 (sulfonylurea: S-benzyl isothiuroniurn chloride). Both reactions gave the same product with no depression in mixed melting points and no change in I.R. spectra, i.e. one NH in the sulfonylurea bridge was only reactive. This was the more acidic >NH present between the >$SO_2$ and >C=0. Elemental analysis and infrared data were in accordance with the proposed structures (I &IIa-p). lnfrared spectra of these compounds (Table 1) showed two absorption bands at wavelengths 3085-3350 $cm^{-1}$ in the >NH stretching region, also there was a band near l600 $cm^{-1}$ indicative for the >C=O group. Two absorption bands were observed in the range 2800-2975 $cm^{-1}$ characteristic for the symmetric and asymmetric modes of >$CH_2$ group. In addition, a band at 665- 734 $cm^{-1}$ assigned for >C-S group appeared in the I.R. spectra**.**

The compounds described in the present investigation were screened fortheir herbicidal activity against *Echinoocloa crus-galli* L. Beauv (Barnyardgrass). In addition, it was necessary to examine the phytotoxicity of theprepared compounds against *Oryzasativa* L. (rice).In general, the herbicidal study (Table 2) showed that the highestefficacy was recorded for the isothiouromium salt (IIp) which bears aheterocyclic moiety (piperidinyl) in its side chain.Meanwhile, compounds (IIn,IIo) showed moderate efficacies. However,isothiuroniurn salts (I& IIa-p) have low-moderate herbicidal activities. Change of the parent compoundcarbamicacid

3, 4-dichlorophenyl sulfonyl methyl esterto the isothiuroniurn salt (I) lowered theherbicidal activity. Thus,the mean shoot length reduction was 40.07% and the mean root length reduction was 54.21% as previously reported by Salama et al. (2007), while in the present study the corresponding figures were respectively 32.56 and 38.31% (Table 2).The isothiuroniurn salt (I) was relatively more toxic to the root system as compared to the shoot system.

**Table.1** Physical and IR Data of Compounds I&IIa-p

| Comp. | Crystalliz. | m.p. °C | Yield % | IR ($cm^{-1}$) | | | |
|---|---|---|---|---|---|---|---|
| | | | | >C= O | >NH | >$CH_2$ | >C−S |
| I | aq.ethanol | 136-8 | 69.4 | 1694 | 3222, 3322 | 2900, 2975 | 720 |
| IIa | aq.ethanol | 127-31 | 52.4 | 1664 | 3326, 3337 | 2913, 2965 | 716 |
| IIb | aq.ethanol | 126- 7 | 71.3 | 1620 | 3344,3352 | 2760, 2920 | 683 |
| IIc | aq.ethanol | 118-21 | 57.0 | 1616 | 3176, 3244 | 2900, 2956 | 710 |
| IId | aq.ethanol | 125-7 | 61.5 | 1655 | 3174, 3348 | 2815, 3000 | 734 |
| IIe | aq.ethanol | 81-3 | 67.5 | 1660 | 3170, 3340 | 2800, 3010 | 730 |
| IIf | aq.ethanol | 64-7 | 52.2 | 1665 | 3244, 3300 | 2739, 3075 | 728 |
| IIg | aq.ethanol | 97-102 | 97.0 | 1730 | 3173, 3315 | 2740, 2828 | 700 |
| IIh | aq.ethanol | 86-94 | 20.4 | 1644 | 3156, 3329 | 2900, 2956 | 725 |
| IIi | aq.ethanol | 221-6 | 50.2 | 1670 | 3090, 3290 | 2850, 2900 | 670 |
| IIj | aq.ethanol | 69-71 | 68.5 | 1625 | 3230, 3320 | 2865, 2965 | 711 |
| IIk | aq.ethanol | 85-8 | 54.8 | 1653 | 3108, 3311 | 2890, 2934 | 681 |
| IIl | aq.ethanol | 99-104 | 54.7 | 1675 | 3288, 3350 | 2836, 2890 | 694 |
| IIm | aq.ethanol | 156-9 | 14.0 | 1650 | 3285, 3350 | 2845, 22895 | 685 |
| IIn | aq.ethanol | 100-2 | 27.0 | 1631 | 3238, 3326 | 2826, 2905 | 734 |
| IIo | aq.ethanol | 142-4 | 13.4 | 1667 | 3085, 3304 | 2852, 2931 | 710 |
| IIp | aq.ethanol | 102-7 | 67.0 | 1688 | 3217, 3304 | 2826, 2934 | 666 |

**Table.2** Effect of Isothiouronium Salts (I&IIa-p) on Barnyard Grass and Rice

| Comp. | Conc. ppm | Average length of barnyard grass(cm) | | | | | | Average length ofrice (cm) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Shoot leng. | Redu-ction % | Mean reduc-tion % | Root leng. | Redu-ction % | Mean reduc-tion % | Shoot leng. | Redu-ction % | Mean reduc-tion % | Root leng. | Redu-ction % | Mean reduc-tion % |
| Control | - | 10.40 | - | - | 14.93 | - | - | 11.83 | - | - | 13.53 | - | - |
| | 2 | 7.70 | 25.96 | | 9.97 | 33.22 | | 8.40 | 28.99 | | 11.03 | 18.48 | |
| I | 4 | 7.07 | 32.02 | 32.56 | 9.13 | 38.85 | 38.31 | 7.73 | 34.66 | 32.49 | 10.07 | 25.57 | 27.08 |
| | 6 | 6.27 | 39.71 | | 8.53 | 42.87 | | 7.83 | 33.81 | | 8.50 | 37.18 | |
| | 2 | 9.50 | 8.65 | | 12.20 | 18.29 | | 12.17 | -- | | 13.83 | -- | |
| IIa | 4 | 8.77 | 15.67 | 17.72 | 11.47 | 23.17 | 24.11 | 8.70 | 26.46 | 20.46 | 11.40 | 15.74 | 15.50 |
| | 6 | 7.40 | 28.85 | | 10.32 | 30.88 | | 7.70 | 34.91 | | 9.37 | 30.75 | |
| | 2 | 9.60 | 7.69 | | 13.00 | 12.93 | | 11.43 | 3.38 | | 11.60 | 14.26 | |
| b | 4 | 8.93 | 14.13 | 12.63 | 12.10 | 18.96 | 20.01 | 9.10 | 23.08 | 19.25 | 9.83 | 27.35 | 20.60 |
| | 6 | 8.73 | 16.06 | | 10.73 | 28.13 | | 8.13 | 31.28 | | 10.80 | 20.18 | |
| | 2 | 8.37 | 19.52 | | 11.93 | 20.09 | | 11.33 | 4.23 | | 11.80 | 12.79 | |
| c | 4 | 7.67 | 26.25 | 26.06 | 11.33 | 24.11 | 26.19 | 9.77 | 17.41 | 14.99 | 10.60 | 21.66 | 23.56 |
| | 6 | 7.03 | 32.40 | | 9.80 | 34.36 | | 9.07 | 23.33 | | 8.63 | 36.22 | |
| | 2 | 8.27 | 20.48 | | 11.13 | 25.45 | | 10.77 | 8.96 | | 9.93 | 26.61 | |
| d | 4 | 7.53 | 27.60 | 25.96 | 9.43 | 36.84 | 34.90 | 10.30 | 12.93 | 14.06 | 9.47 | 30.01 | 29.47 |
| | 6 | 7.30 | 29.81 | | 8.60 | 42.40 | | 9.43 | 20.29 | | 9.23 | 31.78 | |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 2 | 11.33 | -- | | 15.93 | -- | | 12.30 | -- | | 11.37 | 15.96 | |
| e | 4 | 9.80 | 5.77 | 4.07 | 14.67 | 1.74 | 3.84 | 11.50 | 2.79 | 7.97 | 10.87 | 19.66 | 22.22 |
| | 6 | 9.73 | 6.44 | | 13.47 | 9.78 | | 9.33 | 21.13 | | 9.33 | 31.04 | |
| | 2 | 9.30 | 10.58 | | 13.10 | 12.26 | | 11.83 | - | | 12.43 | 8.13 | |
| f | 4 | 7.73 | 25.67 | 20.64 | 11.47 | 23.17 | 19.31 | 10.40 | 12.09 | 15.95 | 10.40 | 23.13 | 17.88 |
| | 6 | 7.73 | 25.67 | | 11.57 | 22.51 | | 7.60 | 35.76 | | 10.50 | 23.39 | |
| | 2 | 10.00 | 3.85 | | 13.47 | 9.78 | | 12.03 | -- | | 13.87 | -- | |
| g | 4 | 9.47 | 8.94 | 12.18 | 11.90 | 20.29 | 16.94 | 10.50 | 11.24 | 10.40 | 11.30 | 16.48 | 17.07 |
| | 6 | 7.93 | 23.75 | | 11.83 | 20.76 | | 9.47 | 19.95 | | 8.83 | 34.74 | |
| | 2 | 9.27 | 10.87 | | 11.83 | 20.76 | | 12.10 | -- | | 13.80 | -- | |
| h | 4 | 8.27 | 20.48 | 17.28 | 10,53 | 29.47 | 27.01 | 9.47 | 19.95 | 17.64 | 12.53 | 7.39 | 10.49 |
| | 6 | 8.27 | 20.48 | | 10.33 | 30.81 | | 7.93 | 32.97 | | 10.27 | 24.09 | |
| | 2 | 10.73 | -- | | 16.23 | -- | | 12.37 | -- | | 13.87 | -- | |
| i | 4 | 10.63 | -- | 4.17 | 15.33 | -- | 3.42 | 11.63 | 1.69 | 7.13 | 12.97 | 4.14 | 7.93 |
| | 6 | 9.10 | 12.50 | | 13.40 | 10.25 | | 9.50 | 19.70 | | 10.87 | 19.66 | |
| | 2 | 10.00 | 3.85 | | 13.70 | 8.24 | | 9.73 | 17.75 | | 10.40 | 23.13 | |
| **j** | 4 | 8.33 | 19.90 | 16.96 | 13.63 | 8.71 | 12.04 | 8.13 | 31.28 | 28.54 | 8.40 | 37.92 | 32.57 |
| | 6 | 7.57 | 27.21 | | 12.07 | 19.16 | | 7.50 | 36.60 | | 8.57 | 36.66 | |
| | 2 | 8.00 | 23.08 | | 13.57 | 9.11 | | 9.37 | 20.79 | | 19.90 | 19.44 | |
| **k** | 4 | 7.47 | 28.17 | 29.58 | 13.53 | 9.38 | 12.33 | 8.27 | 30.09 | 29.16 | 9.90 | 26.83 | 27.15 |
| | 6 | 6.50 | 37.50 | | 12.17 | 18.49 | | 7.50 | 36.60 | | 8.77 | 35.18 | |
| | 2 | 9.07 | 12.88 | 19.58 | 12.83 | 14.07 | | 11.90 | -- | | 13.90 | -- | |
| **l** | 4 | 8.23 | 20.87 | | 12.63 | 15.41 | 17.86 | 10.30 | 12.93 | 12.09 | 10.80 | 20.18 | 16.48 |
| | 6 | 7.80 | 25.00 | | 11.33 | 24.11 | | 9.07 | 23.33 | | 9.57 | 29.27 | |
| | 2 | 10.63 | - | | 14.07 | 5.76 | | 12.17 | -- | | 12.20 | 9.83 | |
| **m** | 4 | 9.30 | 10.58 | 7.37 | 13.33 | 10.72 | 10.92 | 9.60 | 18.85 | 16.99 | 11.03 | 18.48 | 19.19 |
| | 6 | 9.20 | 11.54 | | 12.50 | 16.28 | | 8.03 | 32.12 | | 9.57 | 29.27 | |
| | 2 | 8.10 | 22.12 | | 10.73 | 28.13 | | 7.77 | 34.32 | | 9.67 | 28.53 | |
| **n** | 4 | 6.10 | 41.35 | 34.07 | 9.88 | 33.82 | 33.29 | 7.87 | 33.47 | 40.63 | 9.37\ | 30.75 | 33.14 |
| | 6 | 6.37 | 38.75 | | 9.27 | 37.91 | | 5.43 | 54.10 | | 8.10 | 40.13 | |
| | 2 | 8.80 | 15.38 | | 11.57 | 22.51 | | 9.90 | 16.31 | | 11.07 | 18.18 | |
| **o** | 4 | 6.23 | 40.10 | 33.65 | 10.13 | 32.15 | 32.35 | 8.77 | 25.87 | 27.67 | 9.27 | 31.49 | 29.44 |
| | 6 | 5.67 | 45.48 | | 8.60 | 42.40 | | 7.00 | 40.83 | | 8.30 | 38.65 | |
| | 2 | 5.73 | 44.90 | | 10.60 | 29.00 | | 8.67 | 26.71 | | 9.87 | 27.05 | |
| **p** | 4 | 6.37 | 38.75 | 41.67 | 8.60 | 42.40 | 42.11 | 7.23 | 38.88 | 36.12 | 8.47 | 37.40 | 36.09 |
| | 6 | 6.10 | 41.35 | | 6.73 | 54.92 | | 6.77 | 42.77 | | 7.60 | 43.83 | |

L.S.D. compound 1.030 0.99 1.288 1.148
at concentration 0.416 0.396 0.495 0.475
0.05 interaction 1.802 1.723 2.099 1.999

The herbicidal activity of the isothiuroniurn salt (I) was higher than that of the correspondingisothiuroniurn salts (IIa-m) and vice versa for the isothiouronium salts (IIn-p)that is when a heterocyclic moiety was introduced in the isothiuroniurn salt the herbicidai eficacy became higher.The data (Tables 2) indicated that isothiuronium salts (IIa-p) were variably toxic to the root system system of barnyard grass when compared to the its shoot system. The phenomenon of concentration quenching (i.e. decrease of biological activity of a given compound with increase of its concentration) early reported by Aldrien(1968) was also observed by Salama et al. (2007) in a study concerning the herbicidal activity of some isothiouronium salts of sulfonylureas. Here, theisothiuronium salts (IIa-p) (Table 2) have no concentration quenching.In general,the present study revealed that the phytotoxicity of the isothiuronium salts (IIa-p) were higher when regarding the root system in relation to the shoot systemof rice.

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