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Synthesis and Herbicidal Activity of Novel Sulfonylureas Containing Thiadiazol Moiety

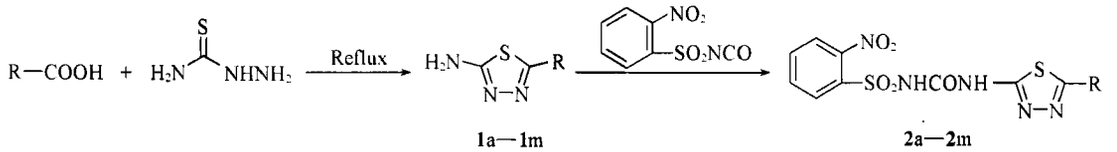
GUO Wan-cheng, LIU Xing-hai, LI Yong-hong, WANG Su-hua and LI Zheng-ming*
Institute of Elemento-Organic Chemistry, State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, P. R. China

Abstract Thirteen novel sulfonylureas containing thiadiazole moiety were synthesized in a two-step reaction. Their structures were determined using IR, ^{1}H NMR, HRFTMS, and elemental analysis. Herbicidal activities of these compounds were determined in the green house bio-assay. The results show that four compounds among them exhibit some activity toward four tested herbs.

Keywords Sulfonylurea; Synthesis; Herbicidal activity

1 Introduction

Since the synthesis and application of chlorsulfuron, a sulfonylurea herbicide, for the control of weed in 1982, various novel sulfonylurea herbicides, such as nicosulfuron, primisulfuron, foramsulfuron *etc.*[1—3], have been rapidly commercialized worldwide. Many scientists have devoted their large efforts to this field becasue of their high activity at low application rates(in the range of 2 to 75 g/ha) and low mammal toxicity. Considering that 2,5-disubstituted-1,3,4-thiadiazole derivatives have biological activity[4—6], a novel series of sulfonylureas containing 1,3,4-thiadiazole moiety was designed and synthesized as potential herbicidal agents(Scheme 1). Herbicidal activity of these compounds was tested in the green house on four types of herbs. The results show that four compounds among them exhibit some activity against barnyardgrass.



1a—1m 2a—2m

Scheme 1 Synthesis route of compounds 2a—2m

R=H, Me, Et, *n*-propyl, cyclopropyl, phenyl, 2-methylphenyl, 2-chlorophenyl, 2-fluorophenyl, 3-methylphenyl, 4-methylphenyl, furyl, pyridyl.

2 Experimental

2.1 Reagents and Instruments

Melting points were measured using Yanaco MP-500 micromelting point apparatus. Infrared spectra were recorded on a Bruker Equinox55 spectrophotometer with KBr pellets. ^{1}H NMR spectra were recorded on a Bruker AC-P500 instrument(300 MHz) with tetramethylsilane as internal standard and DMSO-d_6 as solvent. Elemental analyses were performed using Yanaco MT-3CHN elemental analyzer. HRFTMS were performed using FT-ICR 7.0-T mass spectrometer.

2.2 Syntheses of Title Compounds

2.2.1 General Procedure for the Synthesis of Compounds 1a—1d

As the method shown in ref. [7], a mixture of thiosemicarbazide(2.73 g, 30 mmol), carboxylic acid(30 mmol), and hydrochloric acid(15.21 g, 75 mmol) was refluxed for 3 h. Having been cooled, the reaction mixture was neutralized to pH 8—9 with aqueous sodium hydroxide. The products 1a—1d were obtained by filtration and recrystallization from water.

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

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2.2.2 General Procedure for the Synthesis of Compounds 1e—1m

As the method shown in ref. [8], a mixture of thiosemicarbazide(2.73 g, 30 mmol), substituted benzoic acid(50 mmol), and phosphorus oxychloride(12.42 g, 81 mmol) was refluxed for 0.5 h at 75 °C. After the mixture was cooled to room temperature, 30 mL of water was added to it and the mixture was refluxed for 4 h at 110 °C. Then the reaction mixture was neutralized to pH 8 with aqueous sodium hydroxide. The products **1e**—**1m** were obtained by filtration and recrystallization from alcohol.

2.2.3 General Procedure for the Synthesis of Compounds 2a—2m

As the method shown in ref. [9], to a stirred suspension of 2-amino-5-substituted thiadiazole (3 mmol) in 12 mL of anhydrous acetonitrile at room temperature, 2-nitrobenzenesulfonyl isocyanate (0.68 g, 3 mmol) was added. The mixture was stirred for 12—20 h. Then the products **2a**—**2m** were separated by filtration, washed with acetonitrile, and recrystallized from acetonitrile.

2.3 Data for Title Compounds

2.3.1 1-(2-Nitrobenzensulfonyl)-3-([1,3,4]thiadiazol-2-yl)-urea(2a)

Yield 92.4%; m. p. 244—246 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 7.86—7.90(m, 2H, benzo-H), 7.93—7.97(m, 1H, benzo-H), 8.18—8.23(m, 1H, benzo-H), 8.97(s, 1H, Het-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3376, 3277(N—H), 1712(C=O), 1365 and 1160 (S=O); HRFTMS (*m/z*): 327.9821 (M^-−H for $C_9H_6N_5O_5S_2$, 327.9816).

2.3.2 1-(2-Nitrobenzensulfonyl)-3-(5-methyl-[1,3,4]thiadiazol-2-yl)-urea(2b)

Yield 94.5%; m. p. 254—256 °C; ^{1}H NMR (300 MHz, DMSO-d_6), δ: 2.50(s, 3H, CH_3), 7.86—7.89(m, 2H, benzo-H), 7.93—7.97(m, 1H, benzo-H), 8.20—8.23(m, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3375, 3262(N—H), 1702(C=O), 1363 and 1157(S=O); HRFTMS(*m/z*): 341.9970(M^-−H for $C_{10}H_8N_5O_5S_2$, 341.9972); elemental anal.(%) calcd. for $C_{10}H_9N_5O_5S_2$: C 34.98, H 2.64, N 20.40; found: C 35.06, H 2.65, N 20.21.

2.3.3 1-(2-Nitrobenzensulfonyl)-3-(5-ethyl-[1,3,4]thiadiazol-2-yl)-urea(2c)

Yield 79.6%; m. p. 272—274 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 1.22(t, J=7.5 Hz, 3H, CH_3), 2.86(q, J=7.5 Hz, 2H, CH_2), 7.84—7.90(m, 2H, benzo-H), 7.93—7.97(m, 1H, benzo-H), 8.18—8.23(m, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3223, 3129(N—H), 1728(C=O), 1361 and 1162(S=O); HRFTMS(*m/z*): 356.0127(M^-−H for $C_{11}H_{10}N_5O_5S_2$, 356.0129); elemental anal.(%) calcd. for $C_{11}H_{11}N_5O_5S_2$: C 36.97, H 3.10, N 19.60; found: C 36.78, H 3.20, N 19.45.

2.3.4 1-(2-Nitrobenzensulfonyl)-3-(5-propyl-[1,3,4]thiadiazol-2-yl)-urea(2d)

Yield 75.2%; m. p. 233—235 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 0.89(t, J=7.5 Hz, 3H, CH_3), 1.64(m, J=7.5 Hz, 2H, CH_2), 2.80(t, J=7.2 Hz, 2H, CH_2), 7.73—7.78(m, 3H, benzo-H), 8.10—8.13(m, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3375, 3262(N—H), 1717(C=O), 1363 and 1150(S=O); HRFTMS(*m/z*): 370.0281(M^-−H for $C_{12}H_{12}N_5O_5S_2$, 370.0285).

2.3.5 1-(2-nitrobenzensulfonyl)-3-(5-cyclopropyl-[1,3,4]thiadiazol-2-yl)-urea(2e)

Yield 49.1%; m. p. 237—239 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 0.82—0.86(m, 2H, cyclopropyl-H), 1.02—1.05(m, 2H, cyclopropyl-H), 2.19—2.26(m, 1H, CH), 7.65—7.75(m, 3H, benzo-H), 8.07(d, J=7.6 Hz, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3376, 3267(N—H), 1702(C=O), 1365 and 1162(S=O); HRFTMS(*m/z*): 368.0140(M^-−H for $C_{12}H_{10}N_5O_5S_2$, 368.0129).

2.3.6 1-(2-Nitrobenzensulfonyl)-3-(5-phenyl-[1,3,4]thiadiazol-2-yl)-urea(2f)

Yield 55.5%; m. p. 147—149 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 7.48—7.51(m, 4H, benzo-H), 7.54—7.58(m, 1H, benzo-H), 7.84—7.86(m, 2H, benzo-H), 7.91—7.93(m, 1H, benzo-H), 8.19—8.22 (m, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3441, 3231 (N—H), 1725(C=O), 1358 and 1155(S=O); HRFTMS(*m/z*): 404.0121(M^-−H for $C_{15}H_{10}N_5O_5S_2$, 404.0129); elemental anal.(%) calcd. for $C_{15}H_{11}N_5O_5S_2$: C 44.44, H 2.73, N 17.27; found: C 44.60, H 2.78, N 17.30.

2.3.7 1-(2-Nitrobenzensulfonyl)-3-(5-[2-chlorophenyl]-[1,3,4]thiadiazol-2-yl)-urea(2g)

Yield 32.8%; m. p. 195—197 °C; ^{1}H NMR(300 MHz, DMSO-d_6), δ: 7.43—7.50(m, 3H, benzo-H), 7.57—7.61(m, 1H, benzo-H), 7.69—7.77(m, 2H, benzo-H), 7.95—8.00(m, 1H, benzo-H), 8.09—8.11 (m, 1H, benzo-H); IR(KBr), $\tilde{\nu}$/cm^{-1}: 3311, 3205 (N—H), 1724(C=O), 1363 and 1164(S=O); HRFTMS(*m/z*): 437.9740(M^-−H for $C_{15}H_9ClN_5O_5S_2$, 437.9739); elemental anal.(%) calcd. for