An unusual reaction of phenacylsulfonylacetic acid methyl ester and styrylsulfonylacetic acid methyl ester with hydrazine hydrate

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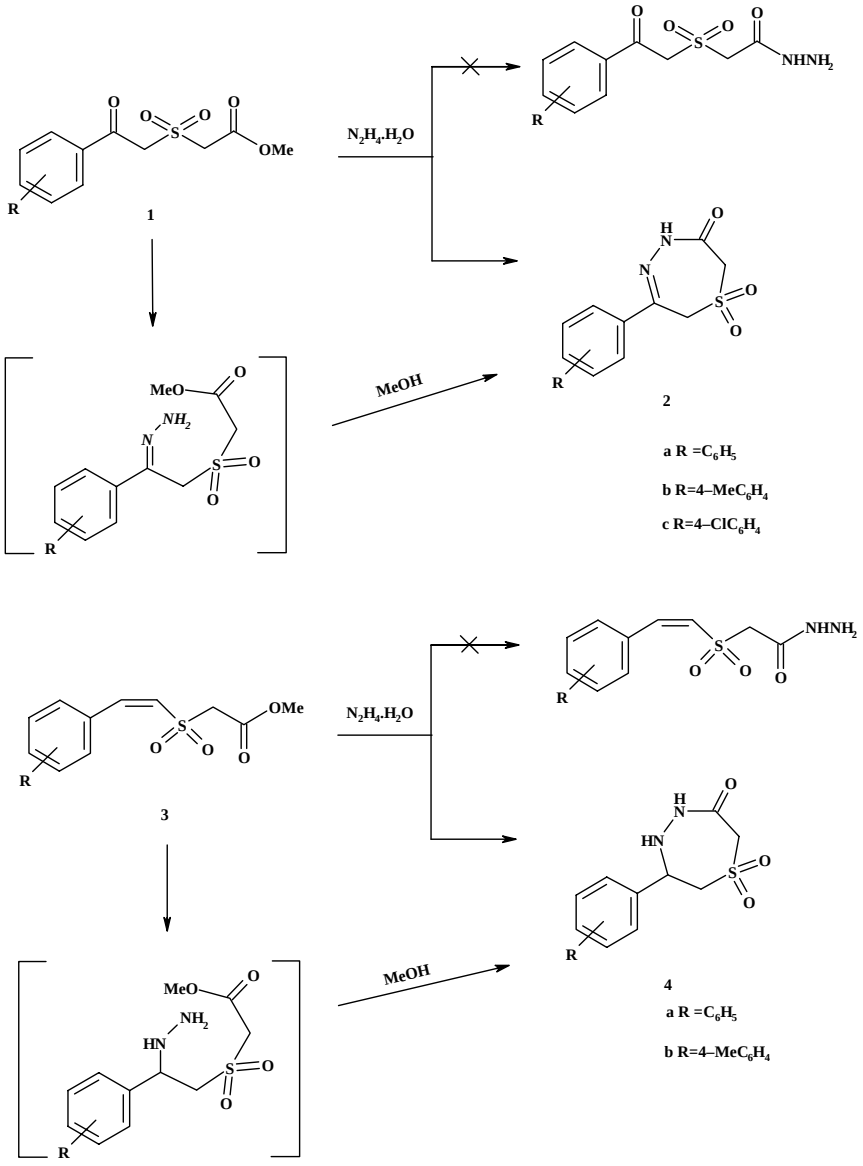
The reaction of phenacylsulfonylacetic acid methyl ester and styrylsulfonylacetic acid methyl ester with hydrazine hydrate gives unusual products, 1,1-dioxo-6-phenyl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one and 1,1-dioxo-6-phenyl-1λ^6-[1,4,5]thiadiazepan-3-one instead of the expected acid hydrazide.

Keywords: phenacylsulfonylacetic acid methyl ester, styrylsulfonylacetic acid methyl ester, hydrazine hydrate, cycloaddition, cyclocondensation.

Nitrogen containing five membered heterocycles have considerable interest due to their wide range of pharmacological importance. In fact, pyrrole, pyrazole and isoxazole derivatives possess anti-inflammatory activity.[1] For the last one and half decades we have been actively involved in the synthesis of five membered heterocycles with two heteroatoms *viz*., pyrazolines and isoxazolines.[2] In addition, recently we have reported five membered heterocycles having three heteroatoms *viz*., triazoles, oxadiazoles and thiadiazoles *via* a common route from phenylsulfonyl and benzylsulfonylacetic acids .[3] Our successful results in these areas suggested further synthetic studies using phenacylsulfonylacetic acid and styrylsulfonylacetic acid.



Scheme 1

* Correspondence.

Earlier it was reported the formation of 1,4,5- thiadiazepines from (phenacylthio)acetic acid derivatives by esterification followed by oxidation and treatment with hydrazine hydrate.[4]

When the methyl ester of phenacylsulfonylacetic acid (**1**) is made to react with hydrazine hydrate instead of the expected acid hydrazide, a cyclic product (**2**) is obtained (Scheme 1). The ^{1}H NMR spectrum of this compound showed signals at δ_H 4.25 and 4.89 for C_2–H and C_7–H and a broad singlet at δ_H 10.65 for NH which disappeared on deuteration. The IR spectrum of this compound displayed bands in the regions 1650 (C=O), 1321,1129 (SO_2), 1540 (C=N) and 3258 cm^{-1} (NH). The ^{13}C NMR spectrum of this compound showed signals at δ_C 67.2, 166.3, 154.8 and 61.2 for C-2, C-3, C-6 and C-7. Based on this, the structure of the cyclic compound is predicted as 1, 1-dioxo-6-phenyl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2a**). Besides a molecular ion peak is observed at *m/z* 238, which is in agreement with its chemical composition. It seems that the initially formed hydrazone undergoes intramolecular cyclocondensation to **2a**. In order to confirm the methodology, the reaction was repeated with 4-methyl and 4-chlorophenacylsulfonylacetic acids where 1,1-dioxo-6-p-tolyl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2b**) and 1,1-dioxo-6-(4-chlorophenyl)-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2c**) were obtained. The structures of these compounds are confirmed by spectral parameters.

Similarly, when the methyl ester of styrylsulfonylacetic acid (**3**) is condensed with hydrazine hydrate, a cyclic adduct 1, 1-dioxo-6-phenyl -1λ^6-[1,4,5]thiadiazepan-3-one (**4a**) is obtained. The ^{1}H NMR spectra of this compound displayed a singlet and two multiplets at δ_H 4.35, 4.17–4.22 and 3.84-3.89 for C_2–H, C_6–H and C_7–H, respectively. A broad singlet was observed at δ_H 10.58 for NH which disappeared on deuteration. The ^{13}C NMR spectrum of this compound displayed signals at δ_C 60.6, 165.7, 58.9 and 66.8 for C-2, C-3, C-6 and C-7. The mass spectrum of **4a** showed $M^{+\cdot}$ peak at *m/z* 240, which confirms its chemical composition. In this reaction also it is presumed that the initially formed Michael addition product undergoes intramolecular cyclocondensation to **4a**. When the same reaction is repeated with 4-methylstyrylsulfonylacetic acid, 1,1-dioxo-6-p-tolyl-1λ^6-[1,4,5] thiadiazepan-3-one (**4b**) is obtained whose structure is confirmed by spectral parameters.

Experimental

The purity of the compounds was checked by thin layer chromatography over silica gel [Silica gel-G, hexane-ethyl acetate (3:1)]. IR spectra were run as KBr pellets using Perkin-Elmer 993 infrared spectrometer and NMR spectra were recorded in $CDCl_3$-DMSO using a 300 MHz Perkin-Elmer Instrument. The mass spectra were recorded on a krates MS-80 double focusing mass spectrometer. The starting substrates, phenacylsulfonylacetic acid methyl ester[5] and styrylsulfonylacetic acid methyl ester[6] were prepared by standard procedures.

General procedure for the synthesis of 1,1-dioxo-6-aryl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2a**–**c**): A mixture of **1** (0.2 mmol), hydrazine hydrate (0.4 mmol) and methanol (15 ml) was refluxed for 10 h. It was cooled and the solid separated was filtered, dried and recrystallised from methanol.

1,1-Dioxo-6-phenyl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2a**): Yield 64%, m.p. 301–303 ^{0}C (Found: C, 50.50; H, 4.27; N, 11.82. Calc. for $C_{10}H_{10}N_2O_3S$: C, 50.41; H, 4.23; N, 11.76 %). ν_{max} /cm^{-1} 1129, 1321(SO_2); 1540 (C=N); 1650 (C=O); 3258 (NH). δ_H (DMSO) 4.25 (s, 2H, C_2–H), 4.89 (s, 2H, C_7–H), 7.22–7.63 (m, 5H, aromatic H); 10.65 (bs, 1H, NH). δ_c 67.2 (C-2), 166.3 (C-3), 154.8 (C-6), 61.2 (C-7).

1,1-Dioxo-6-p-tolyl-1,2,4,7-tetrahydro-1λ^6-[1,4,5]thiadiazepin-3-one (**2b**): Yield 62%, m.p. 293–295 ^{0}C (Found: C, 52.46; H, 4.85; N, 11.20. Calc. for $C_{11}H_{12}N_2O_3S$: C, 52.37; H, 4.79; N, 11.10 %). ν_{max} /cm^{-1} 1141,1294 (SO_2); 1535 (C=N); 1648 (C=O); 3200 (NH). δ_H (DMSO) 2.36 (s, 3H, Ar–CH_3), 4.28 (s, 2H, C_2–H), 4.86 (s, 2H, C_7–H), 6.98-7.60 (m, 4H, aromatic H), 10.68 (bs, 1H, NH). δ_c 64.5 (C-2), 164.2 (C-3), 152.4 (C-6), 59.2 (C-7).

*1,1-Dioxo-6-(4-chlorophenyl)–1,2,4,7-tetrahydro-1λ^6-[1,4,5] thiadiazepin-3-one (**2c**):* Yield 66%, m.p. 304–307^{0}C (Found: C, 44.12; H, 3.31; N, 10.35. Calc. for $C_{10}H_9ClN_2O_3S$: C, 44.04; H, 3.33; N, 10.27 %). ν_{max} /cm^{-1} 1124, 1296 (SO_2), 1538 (C=N), 1635 (C=O), 3320 (NH). δ_H (DMSO) 4.29 (s, 2H, C_2–H), 4.94 (s, 2H, C_7–H), 7.52–7.94 (m, 4H, aromatic H), 10.88 (bs, 1H, NH). δ_c 68.5(C-2), 168.4 (C-3), 155.6 (C-6), 63.1 (C-7).

General procedure for the synthesis of 1,1-dioxo-6-aryl-1λ^6-[1,4,5]thiadiazepan-3-one (**4a** & **4b**): A mixture of **3** (0.25 mmol) and hydrazine hydrate (0.5 mmol) in methanol (15 ml) was refluxed for 10 h. It was cooled and the solid separated was filtered and dried.

1,1-Dioxo-6-phenyl-1λ^6-[1,4,5]thiadiazepan-3-one (**4a**): Yield 76% , m.p. 210–212 ^{0}C. (Found: C, 50.08; H, 5.08; N, 11.60. Calc. for $C_{10}H_{12}N_2O_3S$: C, 49.99; H, 5.03; N, 11.66 %). ν_{max} /cm^{-1} 1129,1322 (SO_2); 1638 (C=O); 3304 (NH). δ_H (DMSO) 3.84–3.89 (m, 2H, C_7–H), 4.17–4.22 (m, 1H, C_6–H), 4.35 (s, 2H, C_2–H), 10.58 (bs, 2H, NH). δ_c 60.6 (C-2), 165.7 (C-3), 58.9 (C-6), 66.8 (C-7).

1,1-Dioxo-6-p-tolyl-1λ^6-[1,4,5] thiadiazepan-3-one (**4b**): Yield 79% , m.p. 225–227 ^{0}C. (Found: C, 51.83; H, 5.52; N, 12.00. Calc. for $C_{11}H_{14}N_2O_3S$: C, 51.95; H, 5.55; N, 11.02 %). ν_{max} /cm^{-1} 1125, 1320 (SO_2); 1640 (C=O); 3310 (NH). δ_H (DMSO) 2.34 (s, 3H, Ar–CH_3), 3.71–3.75 (m, 2H, C_7–H), 4.15–4.19 (m, 1H, C_6–H), 4.32 (s, 2H, C_2–H), 10.52 (bs, 2H, NH). δ_c 58.7 (C-2), 164.6 (C-3), 56.5 (C-6), 64.2 (C-7).

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