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Rapid Communication

A rapid one-pot synthesis of 5-substituted-2-mercapto-1,3,4-thiadiazoles using microwaves

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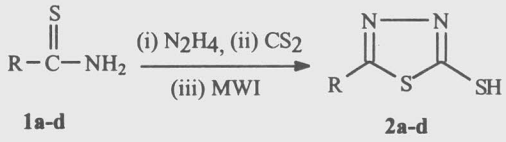
A rapid one-pot synthesis is described for 5-substituted-2-mercapto-1,3,4-thiadiozoles **2a-d** under microwave irradiation starting from thioamides **1a-d**.

In recent times there has been much interest in the development of microwave assisted technique in the synthesis of heterocycles.[1] In view of the utility of microwave irradiation[2] and the biological importance[3] of 5-substituted-2-mercapto-1,3,4-thiadiazoles, it was thought worthwhile to develop a convenient method for the synthesis of the title compounds. One of the title compounds 5-methyl-2-mercapto-1,3,4-thiadiazole is a side-chain at C-3 position of the antibiotic Cefazolin sodium.[4] 5-Substituted-2-mercapto-1,3,4-thiadia-zoles have been synthesised earlier from esters,[1f-g] orthoesters, and thioacid esters,[5-8] in low yields via multistep and lengthy procedures which involve difficult work-ups. We report herein one-pot, rapid synthesis of the title compounds **2** from thioamides **1** in high yields using microwave irradiation (cf. **Scheme I**).



1a-d **2a-d**

Scheme I

Thioamides **1** were treated with hydrazine hydrate followed by CS_2 solution in the cold. The reaction mixture was then irradiated in a microwave oven to yield the title compounds **2**. This was evidenced by the disappearance of the IR absorption band in the region 3250-3400 due to. NH_2 and the appearance of a band at 2550-2650 cm^{-1} due to SH group. The ^1H NMR showed signal for SH proton appeared at δ 12.7-13.1 and the peak for the NH_2 protons was absent. This is the first report on one-pot rapid synthesis of the title compounds **2** where microwave technique has been utilized. The analytical and spectral data of the products **2a-d** are given in Table I.

Table I — Analytical and spectral data of compounds **2a-d**

Compd	R	m..p..(°C) (lit)	Reaction period (min)	Yield (%)	$M^{+\cdot}$ observed (expected)	^1H NMR (DMSO-d_6 + $CDCl_3$) δ , ppm
2a	CH_3	185-87 (186-87)[9]	1.0	88	132 (132)	2.7 (s, 3H, CH3), 12.7 (s, 1H, SH)
2b	C_6H_5	216-17 (215-17)[10]	1.5	86	194 (194)	7.4-7.7 (m, 5H, Ar-H), 12.9 (s, 1H, SH)
2c	4-C_5H_4N[a]	218-20	1.5	79	194 (195)	7.7 (d, 2H, 3′-CH & 5′-CH), 8.75(d, 2H, 2′-CH and 6′-CH), 13.0 (s, 1H, SH)
2d	3-C_5H_4N[b]	80-82	2.0	81	195 (195)	7.55 (t, 1H, 5′-CH), 8.20 (d, 1H, 4′-CH) , 8.75 (d, 1H, 6′-CH), 9.10 (s, 1H, 2′-CH), 13.1 (s, 1H, SH)

[a] Anal. Calcd for $C_7H_5N_3S_2$: C, 43.07; H, 2.56; N, 21.53. Found : C, 43.20; H, 2.48; N, 21.55%.
[b] Anal. Calcd for $C_7H_5N_3S_2$: C, 43.07; H, 2.56; N, 21.53. Found : C, 42..95; H, 2.51; N, 21.45%.

Experimental Section

General procedure for preparation of 5-substituted-2-mercapto-1,3,4-thiadiazoles 2a-d : The substituted thioamide **1** (0.02 mole) was dissolved in 10 mL DMF in an Erlenmeyer flask (100 mL) and hydrazine hydrate (0.02 mole) added to it slowly with stirring followed by the dropwise addition of CS_2 (0.021 mole) maintaining the temperature of the reaction mixture at 0-5 °C. Thereafter, the reaction mixture was subjected to microwave irradiation (MWI) at 450 watts. TLC was run after every half a min. to check the progress of the reaction. On completion of the reaction, the reaction mixture was poured over crushed ice and treated with HCl to bring down the *p*H to 5. The solid obtained was collected and washed with water. It was dried and recrystallised from acetone.

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