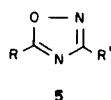


Table II
Substituted 1,2,4-Oxadiazoles



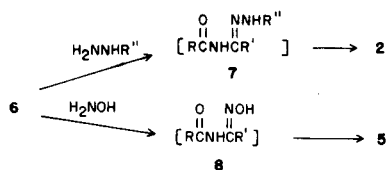
Compound	R	R'	Yield, %	Mp, °C	Formula
5a	3,5-(CH ₃ O) ₂ C ₆ H ₃	H	90	108-109 [a]	C ₁₀ H ₁₀ N ₂ O ₃
5b	3,5-(CH ₃ O) ₂ C ₆ H ₃	CH ₃	93	90-91 [b]	C ₁₁ H ₁₂ N ₂ O ₃
5c	<i>p</i> -ClC ₆ H ₄	CH ₃	96	92-94	C ₉ H ₇ ClN ₂ O
5d	<i>p</i> -ClC ₆ H ₄	C ₆ H ₅	94	122-124 [c]	C ₁₄ H ₉ ClN ₂ O
5e	<i>p</i> -CF ₃ C ₆ H ₄	C ₆ H ₅	94	100-102	C ₁₅ H ₉ F ₃ N ₂ O
5f	<i>p</i> -CF ₃ C ₆ H ₄	<i>p</i> -(CH ₃ O)C ₆ H ₄	91	125-127	C ₁₆ H ₁₁ F ₃ N ₂ O ₂
5g	<i>p</i> -CF ₃ C ₆ H ₄	<i>p</i> -ClC ₆ H ₄	93	127-129	C ₁₅ H ₈ ClF ₃ N ₂ O

[a] Lit mp 108-109° [6]. [b] Lit mp 90-91° [6]. [c] Lit mp 124-125° [12].

Table III
Analytical Data of All New Compounds Reported

Compound	C		H		N		F		Cl or Br	
	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
2e	66.8	66.7	4.49	4.50	15.6	15.8	—	—	13.1	12.8
2f	47.9	47.6	3.29	3.22	15.2	15.2	20.7	21.1	12.9	12.6
2g	62.3	62.2	3.48	3.42	14.5	14.5	19.7	19.7	—	—
2h	63.4	63.4	3.99	4.08	13.9	14.0	18.8	18.9	—	—
2i	69.0	68.9	3.86	3.91	11.5	11.5	15.6	15.7	—	—
2j	56.8	56.6	2.95	2.90	9.46	9.23	12.8	12.8	18.0	17.9
2k	66.8	66.8	4.08	4.14	10.6	10.6	14.4	14.2	—	—
2l	50.3	50.2	2.48	2.34	10.4	10.1	28.1	28.0	8.74	8.71
5c	55.4	55.3	3.63	3.60	14.4	14.4	—	—	18.2	18.3
5e	62.1	62.1	3.12	3.21	9.65	9.56	19.6	19.8	—	—
5f	60.0	60.0	3.46	3.45	8.75	8.70	17.8	17.4	—	—
5g	55.5	55.2	2.48	2.35	8.63	8.50	17.6	17.6	10.9	10.9

amine **6** with hydrazines and hydroxylamine to the intermediates **7** and **8** occurred spontaneously at room temperature with evolution of hydrogen sulfide and disappearance of the yellow or orange color from the monothiodiacylamine **6**. The cyclization of the intermediates **7** and **8** was effected at a higher temperature, for instance, 90°. Twenty 1,2,4-triazoles **2** and 1,2,4-oxadiazoles **5** have been synthesized and are tabulated in Table I and II.



The structures of 1,2,4-triazoles **2** and 1,2,4-oxadiazoles **5** synthesized in this report were all supported by nmr, ir, and elemental analysis data. The structures of 1,2,4-triazoles **2b** and **2c** have been previously determined by single-crystal x-ray analyses [6].

The overlap of the carbon 2*p*-orbitals and sulphur 3*p*-orbitals of the C=S group is less efficient than the 2*p*-overlap of the C=O link, owing to the different spatial symmetry of 2*p*- and 3*p*-orbitals. In addition, the interaction of the lone pair of the nitrogen with the C=S group results in a polarization towards a more stable singly-bonded form, *e.g.* C⁺-S⁻, the dipole being stabilized by delocalization of the positive charge within the remainder of the molecule. Therefore, a regiospecific reaction of monothiodiacylamines **6** with hydrazines or hydroxylamine is expected. The numerous reactions of thioamide and its derivatives with hydrazines and hydroxylamine reported in the literature [10] are supporting evidence for this reaction.

The present method provides a regiospecific synthesis of 3,5-diaryl-1,2,4-triazoles **2g-2m** and 3,5-diaryl-1,2,4-oxadiazoles **5d-5g** which are not available from the previous method [6]. Since every conceivable monothiodiacylamine can be prepared from the reported methods [8,9], the present method does provide a practical synthesis of 1,2,4-triazoles and 1,2,4-oxadiazoles.

EXPERIMENTAL

All melting points were taken on a Mel-Temp apparatus. Samples for elemental analyses were dried over phosphorus pentoxide under high vacuum for 1-24 hours. The nmr spectra were determined with a Varian Model HA-100 spectrometer; chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Monothiodiacylamines **6** were synthesized by reported methods [8,9].

N-(Phenylthioxomethyl)-4-(trifluoromethyl)benzamide (**6a**) [9].

To a stirred solution of 62.6 g (0.30 mole) of *p*-trifluoromethylbenzoyl chloride in 250 ml of acetone was added a solution of 41.1 g (0.30 mole) of thiobenzamide and 23.7 g (0.30 mole) of pyridine in 250 ml of acetone. During the addition, the reaction mixture turned red and pyridine hydrochloride precipitated. After the addition was completed, the reaction mixture was heated to boiling for 15 minutes and then poured into 2000 ml of ice water to give 73.1 g of an orange product. Recrystallization from a chloroform/methanol mixture gave 28.4 g (31%) of **6a** as orange crystals, mp 127-129°; nmr (deuteriochloroform): δ 7.2-8.5 (m, 9H), 10.03 (bs, 1H).

Anal. Calcd. for $C_{15}H_{10}F_3NOS$: C, 58.2; H, 3.26; F, 18.4; N, 4.53; S, 10.4. Found: C, 58.0; H, 3.22; F, 18.7; N, 4.09; S, 10.4.

1-(4-Bromophenyl)-3-phenyl-5-[4-(trifluoromethyl)phenyl]-1*H*-1,2,4-triazole (**2j**). Typical Procedure for **2a-m**.

A mixture of 3.09 g (0.010 mole) of *N*-(phenylthioxomethyl)-4-trifluoromethylbenzamide (**6a**), 2.69 g (0.012 mole) of 4-bromophenylhydrazine hydrochloride, 0.984 g (0.012 mole) of sodium acetate, 15 ml of acetic acid and 15 ml of *p*-dioxane was stirred at 90° for 40 minutes. The volatile materials were removed under reduced pressure. The residue was triturated with water and then recrystallized from ethanol to give 3.91 g of **2j** as tan crystals, mp 192-194°; nmr (deuteriochloroform): δ 7.1-7.8 (m, 11H), 8.15 (m, 2H).

3-Phenyl-5-(4-trifluoromethylphenyl)-1,2,4-oxadiazole (**5e**). Typical Procedure for **5a-g**.

A mixture of 3.09 g (0.010 mole) of *N*-(phenylthioxomethyl)-4-trifluoromethylbenzamide **6a**, 0.834 g (0.012 mole) of hydroxylamine hydrochloride, 0.984 g (0.012 mole) of sodium acetate, 15 ml of acetic acid and 15 ml of *p*-dioxane was stirred at 90° for 40 minutes. After being cooled down to room temperature, the mixture was poured into 150 ml of water. The resulting mixture deposited 2.73 g (94%) of **5e** as colorless crystals,

mp 100-102°; nmr (deuteriochloroform): δ 7.57 (m, 3H), 7.88 (d, $J = 9$ Hz, 2H), 8.25 (m, 2H), 8.40 (d, $J = 9$ Hz, 2H).

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REFERENCES AND NOTES

- [1] This is a continuation of our work published in reference [8]. After the completion of this work, the regiospecific reaction of monothiodiacylamines with hydrazines and hydroxylamine has been recently reported: L. L. Whitfield and E. P. Papadopoulos, *J. Heterocyclic Chem.*, **18**, 1197 (1981). Since our reactions were carried out under different conditions and a different set of 1,2,4-triazoles and 1,2,4-oxadiazoles was made with consistently high yields, we think it is worthwhile to publish our results.
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