5-(THIAZOL-4-YL)-1,2,4-TRIAZOLES

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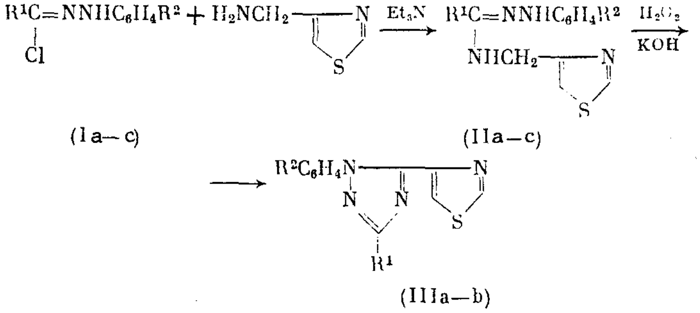
By reaction of arylhydrazones of benzoyl chloride with 4-aminomethylthiazole in the presence of triethylamine, the corresponding amidrazones were obtained, which upon oxidation gave 5-(thiazol-4-yl)-1,2,4-triazoles with fungicidal and bactericidal activity.

Triazoles with a heterocyclic substituent in position 4, for example a benzimidazole, furan, or other group, are widely used as antihelmintosic and systemic fungicides [1]. With the goal of obtaining new biologically active compounds we synthesized for the first time (5-thiazol-4-yl)-1,2,4-triazoles by the following scheme:



R^1 = Ph (a, b), CH_3 (c); R^2 = 4-NO_2 (a, c), H (b).

Amidrazones (IIa-c) are easily ozidized compounds and therefore are converted into thiazolyltriazole (III) without additional purification. Thiazolyltriazoles (III) have fungicidal and bactericidal activity which is lower than the activity of a known preparation [2-(thiazol-4-yl)-benzimidazole].

EXPERIMENTAL

PMR Spectra were taken on a Varian T-60 instrument (60 MHz) with TMS as internal standard.

1-(4-Nitrophenyl)-3-phenyl-5-(thiazol-4-yl)-1,2,4-triazole (IIIa). To a mixture of 0.6 g (0.053 mole) of 4-aminomethylthiazole and 0.9 ml of triethylamine (0.065 mole) in 20 ml of acetonitrile a solution of 1.45 g (0.053 mole) of hydrazone (Ia) in acetonitrile was added. The mixture was kept for 1 day at 20-25°C. The precipitated salts were filtered. Most of the solvent was removed and the thick residue was poured into water. The precipitated deposit of amidrazone (IIa) was separated and dissolved in 5 ml of acetonitrile to which 5 ml of 30% H_2O_2 and several drops of concentrated KOH was added. The precipitate was filtered, washed with water, and recrystallized from ethanol. There was obtained 0.7 g (38%) of triazole (IIIa), mp 214-214.5°C. IR spectrum (ν, cm^{-1}): 1510, 1530, 1600 (Ar), 3085, 3125 (=C—H). PMR spectrum ($DMSO-d_6$, δ, ppm, J, Hz): 8.46 d (2H) and 7.92 d (2H, $C_6H_4NO_2$-4; $^3J_{HH}$ = 9.0); 7.60 m (3H) and 8.20 m (2H, Ph); 8.62 d (1H, 5-H, $^4J_{HH}$ = 2.0); 9.25 d (1H, 2-H, $^4J_{HH}$ = 2.0). UV spectrum {λ, nm (log ε), ethanol}: 250 (4.48); 3.09 (4.02). Found, %: C 58.56; H 3.16; N 19.95; S 9.05. $C_{17}H_{11}N_5O_2S$. Calculated, %: C 58.45; H 3.15; N 20.05; S 9.16.

1,3-Diphenyl-5-(thiazol-4-yl)-1,2,4-triazole (IIIb) was obtained by analogously to triazole (IIIa) from hydrazone (Ib). The precipitate obtained after oxidation of amidrazone

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(IIb) was chromatographed on a column (silica gel, ether—petroleum ether as eluent). 1,3,5-Triphenylformazan (7%) and triazole (IIIb) were isolated. The latter one was recrystallized from a mixture of petroleum ether—benzene (3:1). The yield was 60%, mp 133-134°C. PMR spectrum ($CDCl_3$, δ, ppm): 8.66 d (1H, 2-H, $^4J_{HH}$ = 2.0); 7.77 d (1H, 5-H, $^4J_{HH}$ = 2.0); 8.10 m (2H) and 7.30 m (8H, 2Ph). Found, %: C 67.18; H 3.88; N 18.03; S 10.67. $C_{17}H_{12}N_4S$. Calculated, %: C 67.10; H 3.94; N 18.42; S 10.52.

1-(4-Nitrophenyl)-3-methyl-5-(thiazol-4-yl)-1,2,4-triazole (IIIc) was obtained analogously to (IIIa) by oxidation of amidrazone (IIc) (synthesized in methanol and extracted with ether from aqueous solution). The yield was 55%, mp 201-202°C. PMR spectrum ($CDCl_3$, δ, ppm, J, Hz): 8.68 d (1H, 2-H, $^4J_{HH}$ = 2.0); 8.05 d (1H, 5-H, $^4J_{HH}$ = 2.0); 8.23 d (2H) and 7.57 d (2H, $C_6H_4NO_2$-4, $^3J_{HH}$ = 9.0); 2.50 s (3H, CH_3). Found, %: C 49.85; H 3.02; N 24.75; S 11.45. $C_{12}H_9N_5O_2S$. Calculated, %: C 50.17; H 3.14; N 24.39; S 11.15.

LITERATURE CITED

1. J. V. Metzger (ed.), Thiazole and Its Derivatives, No. 1, Intersc. Publ. (1979), p. 2.

SYNTHESIS OF 2H-IMIDAZOLE 1-OXIDES AND STABLE NITROXYL RADICALS BASED ON THEM

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2H-Imidazole 1-oxides containing an aldonitrone group in the heterocyclic ring are obtained by the condensation of hydroximinomethyl ketones with ketones and ammonium acetate. Their oxidation with lead dioxide in methanol gives stable nitroxyl radicals — 5,5-dimethoxy-3-imidazoline-1-oxyls.

It has previously been shown that cyclic aldonitrones, which are capable of capturing short-lived radicals, can undergo oxidative methoxylation, giving stable nitroxyl radicals

TABLE 1. Preparation of Compounds (IIa-p)

Compound	Amount of the reagent (mole) per mole of (I)			T, °C	Time, h	Yield, %
	ketone	NH_4OAc	AcOH			
(IIa)	13	6	0	56	8	35
(IIa)	13	6	12	56	3	90
(IIa)	13	6	12	20	20	95
(IIb)	5	6	12	60	5	60
(IIc)	3,5	6	12	70	4	70
(IId)	8	18	12	90	3	50
(IIe)	4	6	12	90	4	40
(IIf)	5	6	12	90	4	75
(IIg)	7,5	6	12	60	0,5	90
(IIh)	3	6	24	70	30	50
(IIi)	5	6	12	90	5	65
(IIj)	5	6	12	90	5	50
(IIk)	5	6	12	90	5	50
(IIℓ)	26	8	15	56	1	55
(IIm)	18	3,5	7	20	75	60
(IIn)	1,7	3,5	22	60	20	7
(IIo)	1	8	52	60	30	35
(IIp)	24	3,7	0	56	2	60
(IIp)	13	4	0	20	36	50

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