Selenium Heterocycles. XLIII [1]. Syntheses of 3,5-Diaryl-1,2,4-thiadiazoles and 3,5-Diaryl-1,2,4-selenadiazoles

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Starting from readily available α-arylsulfonyl-α-bromoacetophenones **2** a series of 3,5-diaryl-1,2,4-thiadiazoles and 3,5-diaryl-1,2,4-selenadiazoles were prepared in moderate yield. Reaction of compounds **2** with thiourea or selenourea gave 2-amino-5-arylsulfonyl-4-phenylthiazole or selenazole in good yield.

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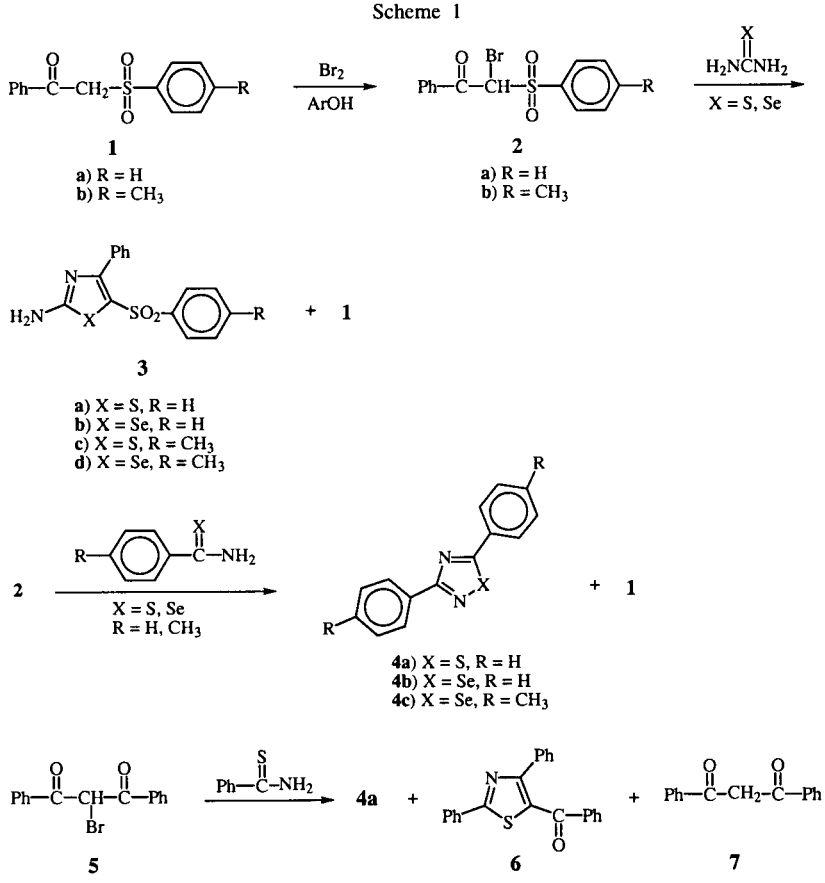
In view of potential biological activity of the thiazoles [2] and in continuation of our research program on the chemistry of selenium heterocycles [1], it was thought worthwhile to prepare the title compounds as possible effective drugs against tropical diseases [3]. 2-Amino-4-phenyl-5-arylsulfonylthiazoles or selenazoles **3**, (X = S, Se) were prepared by the reaction of α-bromoketones **2** [4] with thiourea or selenourea, respectively. Reaction of compound **2** with thiobenzamide or selenobenzamide did not give the expected thiazoles or selenazoles, instead the compounds **4** were obtained [5] (Scheme 1).

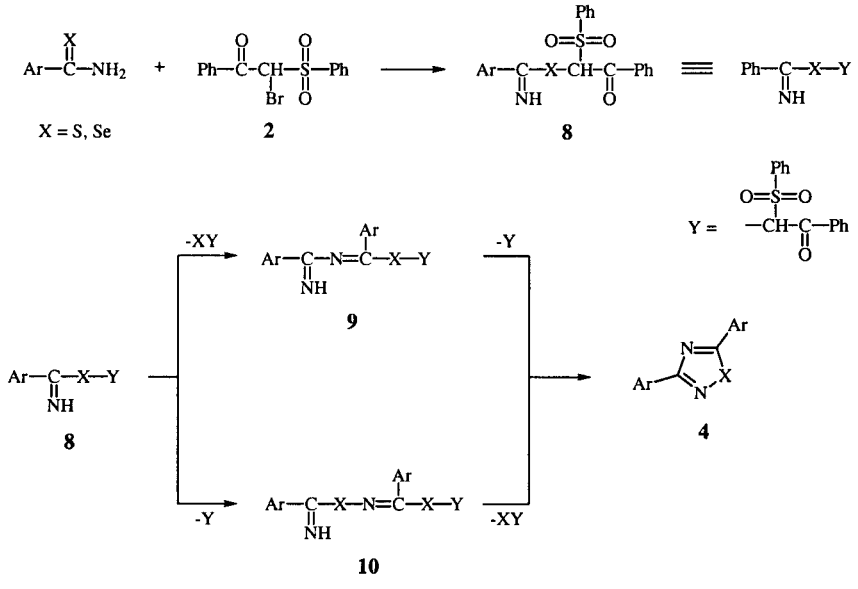
Compound **4** is a known oxidation product of thiobenzamide [6], with hydrogen peroxide [7], nitrous acid [8], iodine [9], bromine [10], or other oxidizing agents [11, 12]. This compound also can be prepared by treatment of thiobenzamide with phosphorus pentachloride [13], pyrolysis of several compounds with thiobenzamide and thioacetamide [14], from thioamide, dimethyl sulfoxide and haloiminium salts [15], by photochemical rearrangement of oxadiazoles with sulfur nucleophiles [16] or treatment of aryl aminosulfine (thioacetamide *S*-oxide) with either triethyloxonium tetrafluoroborate or thionyl chloride [17].

A possible mechanism for the formation of compound **4** is shown in Scheme 2. Reaction of thio or selenobenzamide with α-haloketones gave compound **8** condensation of two moles of **8** could provide either compounds **9** or **10** which then cyclize to the desired compounds **4**.

Scheme 1



Scheme 2



A similar mechanism has been suggested for the reaction of arylsulfine with either triethyloxonium tetrafluoroborate or thionyl chloride [17].

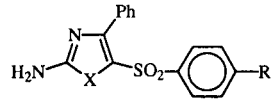
Reaction of α-bromodiketone **5** with thiobenzamide afforded expected thiazole **6** in addition to the desired thiadiazole **4a**.

The physical constants of all compounds prepared are summarized in Tables 1 and 2.

EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. The ir spectra were obtained using a Perkin Elmer Model 781 spectrograph (potassium bromide, disks). The ^{1}H-nmr spectra were recorded on a Bruker FT-80 spectrometer and chemical shifts (δ) are in ppm relative to internal tetramethylsilane. Mass spectra

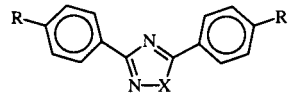
Table 1



Compound	R	X	Yield (%)	Mp, °C [a]	Formula	Calcd. C%	Found C%	Calcd. H%	Found H%	Calcd. N%	Found N%
3a	H	S	41	190-191	$C_{15}H_{12}N_2O_2S_2$	56.96	56.91	3.80	3.73	8.86	8.84
3b	H	Se	23	230-232	$C_{15}H_{12}N_2O_2SSe$	49.59	49.48	3.31	3.22	7.71	7.65
3c	CH_3	S	43	151-152	$C_{16}H_{14}N_2O_2S_2$	58.18	58.27	4.24	4.30	8.48	8.51
3d	CH_3	Se	26	198-199	$C_{16}H_{14}N_2O_2SSe$	50.93	50.89	3.71	3.72	7.43	7.46

[a] All compounds were crystallized from ethanol/water.

Table 2



Compound	R	X	Yield (%)	Mp, °C [a]	Formula	Calcd. C%	Found C%	Calcd. H%	Found H%	Calcd. N%	Found N%
4a	H	S	46	90	$C_{14}H_{10}N_2S$	70.59	70.53	4.20	4.23	11.76	11.71
4b	H	Se	44	81	$C_{14}H_{10}N_2Se$	58.95	58.89	3.51	3.41	9.82	9.78
4c	CH_3	Se	47	115-116 [b]	$C_{15}H_{12}N_2Se$	60.20	60.18	4.01	4.04	9.36	9.39

[a] All compounds were crystallized from ethanol; [b] Ref 18, mp 116°.

were obtained using a Finnigan TSQ 70 Mass spectrophotometer at 70 eV.

2-Amino-4-phenyl-5-phenylsulfonylselenazole (**3b**).

A stirring solution of α-bromo-α-phenylsulfonylacetophenone (2.7 g, 7 mmoles) [4] and selenaurea (1.2 g, 14 mmoles) in dry ethanol (100 ml) was refluxed for 1 hour. The solvent was removed and the residue was neutralized with 5% ammonia and extracted with chloroform. The solvent was evaporated and the residue was purified by preparative tlc on silica gel using chloroform-methanol (97:3) as the eluent. The desired compound was crystallized from ethanol/water to give 0.58 g (23%) of **3b**, mp 230-232°; ir (potassium bromide): ν 3400, 3260 (NH_2) 1620 (C=N), 1510, 1470 (aromatic) and 1150, 1310 cm^{-1} (SO_2); ms: m/z (%) 364 (M^+ +1, 6), 196 (20), 181 (10), 105 (100), 91 (13) 89 (12) 77 (56).

Anal. Calcd. for $C_{15}H_{12}N_2O_2SSe$: C, 49.59; H, 3.31; N, 7.71, Found: C, 49.48; H, 3.22; N, 7.65.

Other 2-amino-4-phenyl-5-arylsulfonylthiazoles (or selenazole) were prepared similarly (Table 1).

3,5-Diphenyl-1,2,4-selenadiazole (**4b**).

To a stirring solution of selenobenzamide (1.1 g, 6 mmoles) in dry acetone (20 ml) at 0° was added dropwise a solution of α-bromo-α-phenylsulfonylacetophenone (1.02 g, 3 mmoles) in 15 ml of dry acetone. After the addition was complete the mixture was stirred at room temperature for 30 minutes. The solvent was removed and the residue was treated with saturated aqueous sodium bicarbonate and extracted with chloroform. The solvent was evaporated and the residue was crystallized from ethanol to give 376 mg (44%) of **4b**, mp 80-81° (ref 18, mp 85°); ^{1}H-nmr (deuteriochloroform): 8.37 (m, 2H, aromatic), 7.95 (m, 2H, aromatic) and 7.42 ppm (m, 6H, aromatic); ms: m/z (%) 285 (M^+, 42), 182 (100), 77 (11).

Anal. Calcd. for $C_{14}H_{10}N_2Se$: C, 58.95; H, 3.51; N, 9.82. Found: C, 58.89; H, 3.41; N, 9.78.

Compounds **4a**, **4c** and **6** were prepared similarly (Table 2).

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