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FUNCTIONALIZED 1,2,5-SELENADIAZOLE DERIVATIVES (***)

Riassunto — *Derivati funzionalizzati dell'1,2,5-selenadiazolo.* Vengono studiate reazioni di ossidazione di derivati dell'1,2,5-selenadiazolo che salvando il sistema eterococlico consentono trasformazioni in catena laterale con formazione di prodotti funzionalizzati. Vengono così preparati alcoli, aldeide, acido e alcuni loro derivati, nonché prodotti con aumentato numero di ossidazione dell'atomo di selenio quali 1,1-dibromuri e idrossinitrati.

Abstract — Oxidations of 1,2,5-selenadiazoles which allow side transformations and afford functionalized derivatives by saving the cyclic structure are reported. Alcohols, aldehyde, acid, and several of their derivatives as well as products with higher selenium oxidation number like 1,1-dibromides and hydroxynitrates are prepared.

Key words — 1,2,5-selenadiazoles, 1,1-dibromo-1,2,5-selenadiazoles, 1,2,5-selenadiazole-1-hydroxynitrates.

Introduction

Previous studies (Bertini et Al., 1974) indicated that both 1,2,5-selena- and -thiadiazole systems are fairly resistant to oxidative or electrophilic attacks and rather prone to reductive or nucleophilic cleavage, with the observation that towards various reagents, as well as heating and sunlight, the selenium compounds are generally less stable than the corresponding sulphur derivatives, in agreement with an heterocyclic ring less-stabilized by resonance.

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The present paper deals with the chemical behaviour of 1,2,5-selenadiazoles towards oxidizing agents with special attention to reactions which by saving the cyclic structure allow side transformations and afford functionalized derivatives.

Several comparisons with 1,2,5-thiadiazoles are performed and some unexpected behaviour differences between the two classes of compounds are evidenced.

Results and discussion

The reactivity of 3-methyl-1,2,5-selenadiazole (**1**) and 3,4-dimethyl-1,2,5-selenadiazole (**2**) was tested towards several oxidizing agents under different conditions.

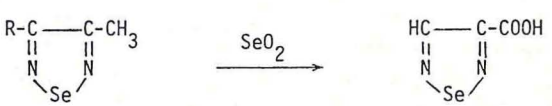
Potassium permanganate, potassium dichromate, chromic anhydride, and peracetic acid failed in giving controlled oxidation in side chain or oxide formation at the selenium atom with retention of the ring, the substrate being generally degraded down to selenites.

The N-bromosuccinimide destroyed the ring with no formation of bromomethyl derivatives in contrast with known reactions of the 3-methyl-1,2,5-thiadiazole (De Munno et Al., 1979).

The bromine, as well as silver oxide and sodium nitrate, gave addition reactions at the selenium atom (see later).

The selenium dioxide yielded the 1,2,5-selenadiazole-3-carboxylic acid (**3**) from both **1** (43% yields) and **2** (18% yields) by heating the reagents in sealed tube without solvent (see experimental section).

Scheme 1



1: R = H; **2**: R = CH_3 **3**

The reaction between selenium dioxide and **2** did not afford expected products like 1,2,5-selenadiazole-3,4-dicarboxylic acid or 3-methyl-1,2,5-selenadiazole-4-carboxylic acid probably owing to

their low stability under the reaction conditions. The same 1,2,5-selenadiazole-3-carboxylic acid was found to decompose into 1,2,5-selenadiazole and carbon dioxide by heating at 170 °C under atmospheric pressure.

As far as thiadiazoles are concerned, in opposition to the behaviour of selenium isologs, any attempt of controlled oxidation at the benzylic position of 3-methyl-1,2,5-thiadiazole was unsuccessful.

The preparation of compound **3** was also carried out by cyclization of 2,3-diaminopropanoic acid hydrobromide as an extention of the general synthesis of 1,2,5-selenadiazoles described by one of us (BERTINI, 1967) to functionalized derivatives. The usual cyclizing agents, selenium dioxide or selenium monochloride, failed, but a new procedure was set up which with selenium tetrachloride afforded the expected product in 44% yields, offering further proof of its molecular structure.

From the carboxylic acid **3** several other acyl derivatives were prepared with conventional reactions. Compound **3** was quantitatively transformed into 1,2,5-selenadiazole-3-methylcarboxylate (**4**) by reacting with diazomethane. It was also transformed into 3-chlorocarbonyl-1,2,5-selenadiazole (**5**) by the action of thionyl chloride or oxalyl chloride. Such an acyl chloride with ammonia yielded 1,2,5-selenadiazole-3-carboxamide (**6**). The prepared acyl derivatives are not always very stable, in fact the chloride slowly loses elemental selenium at room temperature, nevertheless their stability increases in the following order: chloride, amide, acid, ester.

Some reactivity comparisons between acyl function and heterocyclic system, carried out with strong nucleophilic and reducing agents which can open the ring by a known mechanism (BERTINI et Al., 1974), indicated the selenium atom as the center of preferred attack in the first step of the ring cleavage. The 1,2,5-selenadiazole-3-methylcarboxylate with $LiAlH_4$ yielded hydrogen selenide and no reduction products of the ester function. The 3-chlorocarbonyl-1,2,5-selenadiazole with diethyl cadmium afforded diethyl selenide and no acyl substitution products, in contrast with the known behaviour towards the same reagent of the analogous thiadiazole (GILL, 1964), confirming that selenium atom in the 1,2,5-selenadiazole system is definitely more electrophilic than sulphur in the isologous ring.

The higher reactivity of selenium in respect to acyl group towards nucleophilic and reductive agents attenuate the synthetic potentialities of acyl derivatives for the production of less-oxidated functions such as the aldehydic and alcoholic ones.

For this we dealt with the preparation of 3-hydroxymethyl-1,2,5-selenadiazole (**7**) from 2,3-diaminopropanol. The diaminoalcohol was THP protected and submitted to the usual cyclization with SeO_2, but also in this case SeO_2 resulted rather poorly (13% yields). Such inadequacy of SeO_2 was confirmed by having it react with 3-methoxy-1,2-propanediamine; in fact 3-methoxymethyl-1,2,5-selenadiazole (**8**) was obtained in 4.5% yields only.

A definite improvement in the cyclization was attained by using ditosylseleniumdiimide (SHARPLESS et Al., 1976) as cyclizing agent. With such a reagent the THP derivative of 2,3-diaminopropanol gave the corresponding 1,2,5-selenadiazole compound in 27% yields at room temperature. Such a result was confirmed by a similar cyclization of the THP-derivative of 3,4-diaminobutanol which yielded the corresponding THP-derivative of 3-(2'-hydroxyethyl)-1,2,5-selenadiazole (**9**) in 28% yields.

3-Hydroxymethyl-1,2,5-selenadiazole (**7**) resulted suitable for the preparation of more-oxidated derivatives like aldehyde or acid. A satisfactory oxidation of **7** to 3-formyl-1,2,5-selenadiazole (**10**) was achieved with trifluorocetic anhydride and dimethylsulphoxide (OMURA et Al., 1976). The formyl derivative was oxidated in its turn to 1,2,5-selenadiazole-3-carboxylic acid by silver oxide.

Compoud **7** failed in giving hydroxyl group substitution reaction with phosphor trichloride or pentachloride or with thionyl or oxalyl chloride, but it might yield the corresponding 3-chloromethyl-1,2,5-selenadiazole (**11**) through its transformation into the tosylderivative and nucleophilic substitution of the tosyl group by lithium chloride.

Further investigations into the reactivity of the benzylic position of the selenadiazole ring confirmed its proneness to S_N2 substitutions and its indifference towards S_N1 ones, in agreement with an electron withdrawing effect of the ring, which destabilises the carbonium ion.

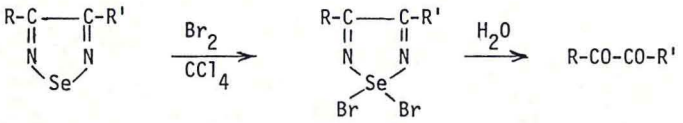
Compound **11** with NaI in acetone at room temperature was transformed into the corresponding iodide faster than benzylchloride does. On the other hand a clear mixture of 3-chloromethyl-

1,2,5-selenadiazole and diluted aqueous silver nitrate did not precipitate silver chloride.

Furthermore, compound **11** reacted with triphenylphosphine to give the corresponding phosphonium salt which was profitably transformed into the corresponding phosphorane by a phase transfer catalysis reaction with saturated aqueous KOH and methylene chloride mixture. The phosphorane gave the expected 3-(β-styryl)-1,2,5-selenadiazole (**12**) by reacting with benzaldehyde.

When compounds **1** and **2** were treated with aqueous bromine they promptly reacted to give in good yields respectively methylglyoxal and dimethylglyoxal besides ammonia, selenites and bromides. Nevertheless, the same 1,2,5-selenadiazoles by treatment with bromine under anhydrous conditions gave red-orange crystalline adducts very sensitive to humidity, which by reacting with water or damp solvents again yielded the mentioned glyoxal derivatives and inorganic products (Scheme 2).

Scheme 2



R = R' = H ; R = R' = CH_3 ; R = H, R' = CH_3

Analogous adduct formation or hydrolytic destruction was also observed with the unsubstituted 1,2,5-selenadiazole, but in general it resulted strongly dependent on substituents. In fact the heterocyclic ring of ester **4** or 3,4-diphenyl-1,2,5-selenadiazole or 3-phenyl-1,2,5-selenadiazole resulted stable towards bromine either in presence or absence of water, even if the phenyl derivatives underwent bromination at the phenyl group (De Munno et Al., 1978).

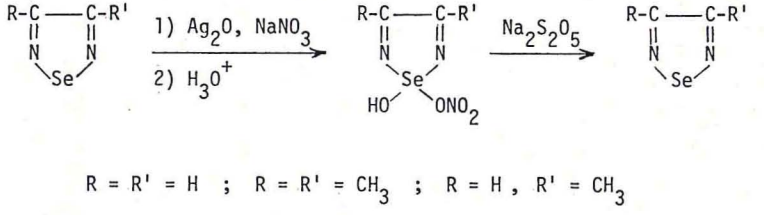
On the basis of elemental analysis, infrared spectra, and analogies with the reaction of the same 1,2,5-selenadiazoles with silver oxide and sodium nitrate (see later) the prepared red-orange adducts were assumed to have the structure of 1,1-dibromo-1,2,5-selenadiazoles. Therefore bromine is an interesting oxidizer, at least for unstabilised 1,2,5-selenadiazoles, for enhancement of the

selenium oxidation number from +2 to+4 and for convenient transformations of such derivatives into 1,2-dicarbonyl compounds.

To confirm the proneness towards oxidations at the selenium atom of 1,2,5-selenadiazoles sometimes observed with bromine, the same products tested with bromine were treated at room temperature with an aqueous mixture of silver oxide and sodium nitrate. In perfect agreement with the previous finding, the unsubstituted 1,2,5-selenadiazole and compounds **1** and **2,** which reacted with bromine, yielded stable crystalline derivatives, while 3,4-diphenyl-1,2,5-selenadiazole, 3-phenyl-1,2,5-selenadiazole and ester **4** remained unchanged.

The crystalline derivatives resulted to be hydroxynitrates. They are rather strong acids, which consume an equivalent of base per mole, they oxidize two equivalents of iodide to iodine, they rapidly decompose under I.R. running between KBr windows, they regenerate the starting selenadiazole by reacting with sodium methabisulphite (Scheme 3).

Scheme 3



R = R' = H ; R = R' = CH_3 ; R = H , R' = CH_3

Experimental section

Melting points were determined with a Kofler apparatus unless otherwise indicated and are uncorrected. I.r. spectra were recorded with a Perkin-Elmer 337 spectrophotometer, ^{1}H-n.m.r. spectra with a Jeol PS 100 instrument operating at 100 MHz (Me_4Si as internal standard), and u.v. spectra with a Hilgher-Watts Uvispek H700 apparatus. Mass spectral data were determined with a Varian MAT CH7 spectrometer operating at 70 eV, the values are referred to the selenium isotope 80.

1,2,5-*Selenadiazole-3-carboxylic acid* (**3**). - *Method A. By oxida-*

tion of 3-methyl-1,2,5-selenadiazole (**1**). Compound **1** (500 mg, 3.40 mmol) and SeO_2 (566 mg, 5.10 mmol) were heated at 150 °C for 2 h 45' in a Pyrex vial, sealed under vacuum. The reaction mixture was washed with light petroleum (b.p. 40-60 °C) (3x10 ml), then it was treated with 2 ml of 6N HCl and exhaustively extracted with ether. After drying over anhydrous sodium sulphate, removal of the solvent and crystallization from ethanol, the extracts afforded 261 mg (1,47 mmol) of **3**. (Yields 43%). m.p. under nitrogen atmosphere in sealed capillary 198-199 °C with decomposition. Found: C, 20.54; H, 1.31; N, 15.64. $C_3H_2N_2O_2Se$ requires C, 20.36; H, 1.14; N, 15.82%. λ_{max} (H_2O) 295 nm (log ε 3.86); λ_{max} (0.1N NaOH) 295 nm (log ε 3.85); λ_{max} (3M H_2SO_4) 298 nm (log ε 3.83). ν_{MAX} (KBr) 3100-2500 (OH), 1680 (C=O), 920 (OH), 750, 495, 440 cm^{-1} (ring). δ (D_2O, 3-trimethylsylilpropanoic acid-d_4 sodium salt as internal reference) 9.1 (s, ring proton). m/z 178 (M^+, 82%). pK_a = 2.6 ± 0.1 (measurements were carried out by potentiometric titrations at 25 °C of aqueous solutions about O.O1M in the examined acid and 0.05M in KCl, with a Orion Research 601 A pH-meter. The electrode was standardized with phthalate (pH = 4.01) and phosphate (pH = 6.81) buffers).

Compound **3** decomposes into 1,2,5-selenadiazole and carbon dioxide by heating at 170 °C under atmospheric pressure.

Method B. By oxidation of 3,4-dimethyl-1,2,5-selenadiazole (**2**). The oxidation of compound **2** was carried out with SeO_2 as described for compound **1**, but with the reagents molar ratio 1:3 and 1 h heating at 140 °C. Yields of **3** after crystallization, 18%.

Method C. From 2,3-diaminopropanoic acid hydrobromide. Selenium tetrachloride (2.23 g, 10.10 mmol), dissolved in 5 ml of freshly distilled DMF was treated under stirring in about 2 minutes with 938 mg (5.07 mmol) of 2,3-diaminopropanoic acid hydrobromide. After 40 minutes stirring at room temperature the mixture was added with 20 ml of water, filtered to remove the elemental selenium, basified with aqueous KOH and evaporated to dryness at 50-60 °C under reduced pressure. The residue, treated with concentrated HCl, was extracted with ether. The extracts, dried over anhydrous sodium sulphate. afforded, by removal of the solvent, 391 mg (2.21 mmol) of **3** (yields 44%) which was crystallized from ethanol after treatment with active charcoal.

1,2,5-*Selenadiazole-3-methylcarboxylate* (**4**). Compound **3** was quantitatively transformed into **4** with diazomethane by usual pro-

cedure. The crude product was purified by crystallization from methanol after treatment with active charcoal. m.p. 112-113 °C. Found: C, 25.30; H, 2.09; N, 14.47. $C_4H_4N_2O_2Se$ requires C, 25.15; H, 2.11; N, 14.66%. ν_{max} (KBr) 1700 (C=0), 766, 518, 437 cm^{-1} (ring): δ (CCl_4) 9.70 (s, 1H, ring proton), 3.95 (s, 3H, methyl).

3-*Chlorocarbonyl*-1,2,5-*selenadiazole* (**5**). Compound **3** (140 mg, 0.79 mmol) was refluxed with 2.8 ml (30.36 mmol) of oxalyl chloride up to disappearance of the bands of compound **3** from the i.r. spectrum of the reaction mixture. The mixture after evaporation to dryness and sublimation at 60 °C/0.03 Torr afforded 81 mg (0.41 mmol) of **5** (yields 52%). m.p. in sealed capillary 114-115 °C. Found: C, 18.20; H, 0.48; Cl. 18.32; N, 14.30. C_3HClN_2OSe requires C, 18.43; H, 0.52; C1, 18.14; N, 14.33%. ν_{max} (KBr) 1720 (C=0), 810 (C-C1), 755, 480, 440 cm^{-1} (ring). m/z 196 (M^+, 25%, referred to chlorine isotope 35). Analogous chlorination carried out with thionyl chloride in place of oxalyl chloride gave 48.3% yields.

1,2,5-*Selenadiazole*-3-*carboxamide* (**6**). A solution of 154 mg (0.789 mmol) of compound **5** in 12 ml of anhydrous ethanol was treated at 0 °C for 20 minutes with a stream of ammonia anhydrified by distillation over sodium. After one day staying at room temperature the mixture was distilled at reduced pressure and the solid residue was sublimed at 95 °C/0.03 Torr to give **6** (112 mg, 0.636 mmol). m.p. 200-201 °C. Found: C, 20.16; H, 2.00; N, 23.76. $C_3H_3N_3OSe$ requires C, 20.47; H, 1.72; N, 23.87%. ν_{max} (KBr) 3480, 3150 (N-H), 1670 (C=0), 1600 (N-H), 750, 480, 435 cm^{-1} (ring). m/z 177 (M^+; 39%).

3-*Hydroxymethyl*-1,2,5-*selenadiazole* (**7**). *Method A: With ditosylseleniumdiimide.* A suspension of ditosylseleniumdiimide (Sharpless et Al., 1976) (11 mmol) in 45 ml of methylene chloride distilled over P_2O_5, was treated under stirring in nitrogen atmosphere with 958 mg (5.50 mmol) of tetrahydropyranyl derivative of the 2,3-diaminopropanol prepared according to Okamoto et Al. (1974) from 2,3-dibromopropanol. After 0.5 h stirring at room temperature the mixture was poured into a solution of 2.5 g of NaOH and 1 g of Na_2SO_3 in 25 ml of water, then it was extracted with methylene chloride (3 x 10 ml), dried over anhydrous sodium sulphate and distilled up to the removal of the solvent, then the residue was extracted with boiling light petroleum (b.p. 40-60 °C) (4 x 25 ml). The removal of the solvent afforded the crude product which by column chromatography on 34 g of Brockman's alumina with

light petroleum (b.p. 40-60 °C) - benzene (80:20) as eluant yielded 368 mg (1.49 mmol) of the oily tetrahydropyranyl derivative of **7** (yields 27%). ν_{max} (film) 1115, 1070, 1060, 1030 (THP), 725, 435 cm^{-1} (ring); δ (CCl_4) 9.15 (s, 1H, ring proton), 4.77 (q, 2H), 4.68 (m, 1H), 3.63 (m, 2H), 1.65 (m, 6H).

The THP derivative of **7** (594 mg; 2.40 mmol) dissolved in 6 ml of methanol, treated with 6ml of 2N HC1, heated at 45 °C for 1 hour, alkalinized with KOH, extracted with ether and dried over anhydrous magnesium sulphate. after removal of the solvent yielded 375 mg (2.30 mmol) of **7**. After crystallization from ether at —30 °C m.p. 43-45 °C. Found: C, 22.41; H, 2.43; N, 17.31. $C_3H_4N_2OSe$ requires C, 22.10; H, 2.47; N, 17.18%. ν_{max} (KBr) 3350 (OH), 1055 (C-O), 737, 440 cm^{-1} (ring); δ (CCl_4) 9.10 (s, 1H, ring proton), 4.85 (s, 2H, CH_2), 2.53 (s broad, 1H, OH); m/z 164 (M^+, 14%).

Method B. With SeO_2. A mixture of SeO_2 (1.225 g; 11.04 mmol), DMF (18 ml) and triethylamine (0.52 ml; 3.68 mmol) heated at 100 °C was treated by drops with a solution of 642 mg (3.68 mmol) of THP-derivative of 2,3-diaminopropanol in 5 ml of DMF. After 30 minutes stirring at 100-110 °C the reaction mixture was treated with an equal volume of water, extracted with ether (6 x 25 ml), dried over anhydrous sodium sulphate and distilled at reduced pressure up to the removal of the solvents. By extraction with boiling light petroleum (b.p. 40-60 °C) and column chromatography as described above, the residue yielded 120 mg (0.49 mmol) of the THP-derivative of **7** (yields 13%).

3-*Methoxymethyl*-1,2,5-*selenadiazole* (**8**). A solution of 10 g (43.1 mmol) of 2,3-dibromo-1-methoxypropane in 75 ml of DMSO was treated under stirring with 8.38 g (128.9 mmol) of sodium azide and heated at 70 °C for 22 hours. The mixture was diluted with an equal volume of water, extracted with n-pentane (8 x 20 ml) and dried over anhydrous sodium sulphate. The removal of the solvent yielded 6.06 g (38.8 mmol) of 2,3-diazido-1-methoxypropane which were dissolved in 30 ml of anhydrous THF and added dropwise in 30 minutes to a suspension of 7.30 g of $LiAlH_4$ in 100 ml of THF. After 12 hours reflux the mixture was ice cooled and treated with 8 ml of water then with 8 ml of 15% sodium hydroxide. Filtration and THF washing (5 x 20 ml) of the solid afforded a solution which after drying over KOH pellets and distillation of the residue at reduced pressure yielded 1.81 g (17.4 mmol) of 3-methoxy-1,2-propanediamine (SCHREYER, 1951). b.p. 72-

74 °C/20 Torr. A suspension of SeO_2 (2.578 g; 23.23 mmol) in 19 ml of DMF was treated in 5 minutes under stirring at 135 °C with a solution of 0.803 g (7.71 mmol) of 3-methoxy-1,2-propanediamine in 5 ml of DMF. After a further 25 minutes stirring at 140 °C the mixture was treated with 35 ml of water and distilled in a 25 ml fraction, which was acidified with H_2SO_4 and distilled from a 12 theoretical plates column. The first fraction (10 ml) was saturated with ammonium sulphate and extracted with 30 ml of ether in small portions. After drying over anhydrous sodium sulphate and removal of the solvent the extracts yielded by distillation 62 mg (0.35 mmol) of **8**. Found: C, 27.36; H, 3.25; N, 15.70. $C_4H_6N_2OSe$ requires C, 27.13; H, 3.42; N, 15.82%. ν_{max} (film) 1100 (C-O), 720, 435 cm^{-1} (ring); δ (CCl_4) 9.24 (s, 1H, ring proton), 4.65 (s, 2H, CH_2), 3.42 (s, 3H, CH_3); m/z 178 (M^+, 7%).

3-(2'-*Hydroxyethyl*)-1,2,5-*selenadiazole* (**9**). The 3,4-dibromo-1-butanol was THP protected, then it was transformed into the THP derivative of 3,4-diamino-1-butanol which in turn was cyclized with ditosylseleniumdiimide, operating as descibed for the preparation of **7**, method A (cyclization yields 28.4%). The removal of the THP protection as described for **7** yielded the oily **9** which was purified by column chromatography on Brockman's alumina with light petroleum (b.p. 40-60 °C) - chloroform (1:1) as eluant. Found: C, 27.23; H, 3.40; N, 15.76. $C_4H_6N_2OSe$ requires C, 27.13; H, 3.42; N, 15.82%. ν_{max} (film) 3350 (OH), 1045 (C-O), 735, 440 cm^{-1} (ring); δ ($CDCl_3$) 9.27 (1H, s, ring proton), 4.14 (2H, t, CH_2), 3.27 (2H, t, CH_2), 2.7 (1H, s broad, OH).

3-*Formyl*-1,2,5-*selenadiazole* (**10**). At —60 °C under nitrogen atmosphere a stirred solution of DMSO (396 mg, 5.07 mmol) in 4 ml of anhydrous methylene chloride was treated with trifluoroacetic anhydride (805 mg; 3.83 mmol), then after 10 minutes with a solution of 377 mg (2.31 mmol) of **7** in 2.5 ml of methylene chloride, and finally after further 30 minutes with 0.9 ml (6.5 mmol) of triethylamine. The cooling bath was removed and the mixture was treated with 6 ml of 1.3N HCl then it was extracted with methylene chloride (3 x 5 ml) and dried over anhydrous sodium sulphate. The removal of the solvent at reduced pressure yielded 354 mg (2.20 mmol) of solid **10**. The product was purified by low temperature (—60 °C) crystallization from ether then from acetone. m.p. 78-80 °C. ν_{max} (KBr) 2847 (CHO), 1700 (C=O), 725, 521, 438 cm^{-1}

(ring); δ ($CDCl_3$) 10.19 (1H, s, formyl proton), 9.82 (1H, s, ring proton).

The crystallized product may be stored at —30 °C without decomposition. The oxidation of **10** with silver oxide in ethanol-water gave the acid **3** in 80% yields. *Phenylhydrazone* of **10** m.p. 147-149 °C (from ethanol). Found: C, 42.97; H, 3.15; N, 22.03. $C_9H_8N_4Se$ requires C, 43.04; H, 3.21; N, 22.31%.

3-*Hydroxymethyl*-1,2,5-*selenadiazole tosylate* (**11**). Compound **7** (154 mg; 0.94 mmol) in 0.5 ml of anhydrous pyridine was added to a solution of 4-methylbenzenesulphonylchloride (237 mg; 1.24 mmol) in 0.5 ml of pyridine at —12 °C and stirred at the same temperature for 35 minutes. The mixture, hydrolysed with 2.5 ml of 5N H_2SO_4, extracted with ether and dried over anhydrous magnesium sulphate, yielded by removal of the solvent 170 mg (0.54 mmol) of **11** which was crystallized from ether at —30 °C. m.p. 82 °C. Found: C, 37.63; H, 2.99; N, 8.56. $C_{10}H_{10}N_2O_3SSe$ requires C, 37.86; H, 3.18; N, 8.83%. ν_{max} (KBr) 1355, 1165 (SO_2), 490, 428 cm^{-1} (ring).

3-*Chloromethyl*-1,2,5-*selenadiazole* (**12**). Compound **11** (294 mg; 0.93 mmol), 2 ml of DMF and 200 mg (4.72 mmol) of lithium chloride were sealed under nitrogen in a Pyrex vial and heated for 12 hours at 90 °C. The reaction mixture, added with water up to dissolution of the salts, extracted with 30 ml of n-pentane in small portions and dried over anhydrous magnesium sulphate yielded by removal of the solvent 131 mg (0.72 mmol) of **12** which after purification by preparative layer chromatography on Merck $PF_{254 \div 366}$ silica gel, (thickness 1.5 mm; eluant benzene - methanol 97:3) appeared as a colourless oil. Found: C, 19.80; H, 1.72; N, 15.39. $C_3H_3ClN_2Se$ requires C, 19.85; H, 1.67; N, 15.44%. ν_{max} (film) 722, 438 cm^{-1} (ring); m/z 182 (M^+, 64%, referred to chlorine isotope 35).

Reactivities of **12** and benzyl chloride towards sodium iodide were compared in the following manner: 0.03 mmol of each substance was treated at room temperature with 0.5 ml of 1.1M solution of NaI in acetone. Turbidity of NaCl appeared after 16 seconds for compound **12** and after 55 seconds for benzyl chloride.

3-(*β-Styryl*)-1,2,5-*selenadiazole* (**13**). Compound **12** (215 mg; 1.18 mmol) and triphenylphosphine (505 mg; 1.93 mmol) in 10 ml of benzene were refluxed up to disappearance of **12** (26 hours) by TLC control. The solid phosphonium salt was filtered, washed

three times with benzene, dried at reduced pressure (220 mg; 0.50 mmol) and used without further purification. A mixture of 2.5 ml of saturated aqueous KOH containing solid pellets of the solute, 5 ml of methylene chloride and 155 mg (0.35 mmol) of the phosphonium salt was shaked for 1 minute, then the yellow phosphorane in the organic phase was separated with the help of further extractions with methylene chloride (2 x 5 ml) and added under stirring to 100 mg (0.94 mmol) of benzaldehyde. The mixture was refluxed for 30 minutes in nitrogen atmosphere, then treated with two drops of water and evaporated at reduced pressure. The crude product by preparative layer chromatography on Merck $PF_{254 \div 366}$ silica gel (thickness 1.5 mm; eluant benzene) yielded 50 mg (0.21 mmol) of **13** which was further purified by crystallization from ether at —30 °C. m.p. 95.5-96.5 °C. Found: C, 51.36; H, 3.65; N, 12.08. $C_{10}H_8N_2Se$ requires C, 51.08; H, 3.43; N, 11.91%. ν_{max} (KBr) 955 (olefin), 495, 430 cm^{-1} (ring); δ (CCl_4, Me_4Si as external standard) 9.91 (1H, s, ring proton), 8.64-8.21 (7H, m); m/z 236 (M^+, 71%).

General procedure for the preparation of 1,1-*dibromo*-1,2,5-*selenadiazoles.* A stirred solution of the selenadiazole derivative (1 mmol) in anhydrous CCl_4 (5 ml) was treated under nitrogen atmosphere with 6 mmol of bromine in 2 ml of CCl_4. After 4 hours stirring at room temperature, the obtained red-orange crystals were filtered, washed with anhydrous CCl_4 and used without further purification owing to their high sensitivity towards humidity and the not availability of adequate dry-box (yields between 75 and 90%). The obtained products decompose without melt in sealed capillary, while they don't show definite decomposition points.

1,1-*Dibromo*-1,2,5-*selenadiazole.* Found: C, 8.56; H, 0.84; Br, 54.02, N, 9.26. $C_2H_2Br_2N_2Se$ requires C, 8.20; H, 0.69; Br, 54.58; N, 9.57%. ν_{max} (nujol) 710, 570, 399 cm^{-1} (ring).

1,1-*Dibromo*-3-*methyl*-1,2,5-*selenadiazole.* Found: C, 11.63; H, 1.37; Br, 51.86; N, 8.96. $C_3H_4Br_2N_2Se$ requires C, 11.74; H, 1.31; Br, 52.08; N, 9.13%. ν_{max} (nujol) 708, 563, 405 cm^{-1} (ring).

1,1-*Dibromo*-3,4-*dimethyl*-1,2,5-*selenadiazole.* Found: C, 14.82; H, 2.13; Br, 49.08; N, 8.73. $C_4H_6Br_2N_2Se$ requires C, 14.97; H, 1.88; Br, 49.80; N, 8.73%.

The above reported 1,1-dibromo-1,2,5-selenadiazoles, treated with water yielded ammonia, selenites, bromides and glyoxal or

methylglyoxal or diacetyl respectively. The same decomposition products were obtained by treating under stirring at room temperature 1,2,5-selenadiazole or its monomethyl or dimethyl derivatives with aqueous bromine up to persistent brown colour. Quantitative determination of diacetyl by nickeldiacetyldioxime precipitation (SCHMALFUSS et Al., 1935) afforded 85% yields.

General procedure for the preparation of 1,2,5-*selenadiazolehydroxynitrates.* A mixture of freshly precipitated and washed silver oxide (6 mmol), water (2.5 ml), sodium nitrate (20 mmol) and 1,2,5-selenadiazole derivative (3 mmol) was stirred for 3 hours at room temperature, then it was acidified with concentrated HCl and exhaustively extracted with ether. The extracts, after drying over anhydrous sodium sulphate, removal of the solvent and sublimation of the solid residue at 50 °C/0.03 Torr, gave the hydroxynitrate (yields between 60 and 70%). The obtained hydroxynitrates were titrated either with KOH in presence of phenolphthaleine or with thiosulphate after treatment with excess of KI.

1,2,5-*Selenadiazole hydroxynitrate.* m.p. 79 °C (sealed capillary). Found: C, 11.06; H, 1.27; N, 19.51; Se, 37.40. $C_2H_3N_3O_4Se$ requires C, 11.33; H, 1.43; N, 19.82; Se, 37.24%. Equivalent weight from acidimetric titration 211; equivalent weight from iodometric titration 105; δ ($CDCl_3$) 12.87 (1H, s broad, OH), 9.42 (2H, s, J ^{77}Se-^1H 26.1 Hz, ring protons).

3-*Methyl*-1,2,5-*selenadiazole hydroxynitrate.* m.p. 102-103 °C (sealed capillary). Found: C, 15.80; H, 2.06; N, 18.61; Se, 34.78. $C_3H_5N_3O_4Se$ requires C, 15.94; H, 2.23; N, 18.59; Se, 34.93%. Equivalent weight from acidimetric titration 224; equivalent weight from iodometric titration 111; molecular weight by osmometry (CH_2Cl_2) 225; δ ($CDCl_3$) 11.41 (1H, s broad, OH), 9.15 (1H, s, ring proton), 2.69 (3H, s, Me).

3,4-*Dimethyl*-1,2,5-*selenadiazole hydroxynitrate.* m.p. 109-110 °C (sealed capillary). Found: C, 21.09; H, 3.16; N, 17.23; Se, 32.56. $C_4H_7N_3O_4Se$ requires C, 20.01; H, 2.94; N, 17.50; Se, 32.89%. Equivalent weight from acidimetric titration 243; equivalent weight from iodometric titration 119; δ ($CDCl_3$) 9.49 (1H, s broad, OH), 2.59 (6H, s, Me).

The prepared hydroxynitrates regenerate the starting 1,2,5-selenadiazole derivatives by treatment with 1M aqueous solution of $Na_2S_2O_5$ at room temperature.

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