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RESEARCHES ON 2, 1, 3-THIA- AND SELENADIAZOLE

XLI. Chloromethylation of Benzo-2, 1, 3-Selenadiazole and its 4- and 5-Methyl Derivatives*

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Depending on the reaction conditions, benzo-2, 1, 3-selenadiazole (I), dichlorodimethyl ether and aluminum chloride react to give a complex IV, or else 4-chloromethyl- (V) or 4, 7-di (chloromethyl) benzo-2, 1, 3-selenadiazole (VI). 5- (II) and 4-methylbenzo-2, 1, 3-selenadiazole (III) are chloromethylated by dichlorodimethyl ether in the presence of chlorosulfonic acid. Compound II is converted mainly into 5-methyl-4-chloromethylbenzo-2, 1, 3-selenadiazole (VII) or a mixture of three possible isomers VII, VIII, and IX, depending on the amount of base or pseudo-base in the reaction mixture. III gives mainly 4-methyl-7-chloromethylbenzo-2, 1, 3-selenadiazole (X), independent of the presence of base. The structures of the chloromethylation products are shown by reductive splitting to o-diamides, and chromatography of the latter in the presence of reference spots. The high reactivity of the chlorine in the chloromethyl group made it possible to obtain new derivatives by replacing it with a hydroxyl, cyano, or thiocyano group.

It was previously shown [2-4], that chloromethylation of benzo-2, 1, 3-thiadiazole and its 4- and 5-methyl derivatives does not take place under conditions described for aromatic and heterocyclic compounds. Reaction could be effected under special conditions.

The present paper states the results of research on the chloromethylation of benzo-2, 1, 3-selenadiazole (I) and its 5- and 4-methyl derivatives (II and III). Compound I does not undergo the reaction under known conditions [5-8], and it proceeds with difficulty under the conditions which we found for the thio analog. Prolonged heating (70-75° C) of compound I with dichlorodimethyl ether in the presence of chlorosulfonic acid led to the isolation of the starting material I; at a higher temperature, I is decomposed with separation of selenium. When the reaction is carried out in the presence of anhydrous aluminum chloride, then, depending on the reaction conditions, either the complex IV** is formed, or else 4-chloromethyl- (V) or 4, 7-di (chloromethyl) benzo-2, 1, 3-selenadiazole (VI).

Compounds II and III are likewise not chloromethylated under known conditions [5-8]. These compounds are chloromethylated when heated (70-75° C) with dichlorodimethyl ether for a long time in the presence of chlorosulfonic acid. Under those conditions, II reacts with dichlorodimethyl ether, prepared according to [9], to give mainly 5-methyl-4-chloromethylbenzo-2, 1, 3-selenadiazole (VII)*** whose structure is proved by reductive scission, followed by thin-layer chromatography on aluminum oxide using reference spots, of the resultant 1, 2-dimethyl-3, 4-diaminobenzene.

Use of dichlorodimethyl ether prepared by the method of [10], gives a mixture of three theoretically possible isomers VII, VIII, and IX, melting points 135-150° C. This is shown by the results of chromatographing the mixture of o-diaminoxylenes formed by reductive scission of the chloromethylation product.

Under the same conditions 4-methylbenzo-2, 1, 3-selenadiazole (III) gives, with dichlorodimethyl ether prepared by the method of [9] or [10], mainly 4-methyl-7-chloromethylbenzo-2, 1, 3-selenadiazole (X). Its structure is proved by reductive scission and comparison of the 1, 4-dimethyl-2, 3-diaminobenzene formed with an authentic specimen.

The chlorine of compounds VII and X is highly reactive. Under ordinary conditions, it reacts with potassium carbonate, cyanide, and thiocyanate, to give 5-methyl-4-hydroxymethyl- (XI), 5-methyl-4-cyanomethyl- (XII), 5-methyl-4-thiocyanatomethyl- (XIII), 4-methyl-7-hydroxymethyl- (XIV), 4-methyl-7-cyanomethyl- (XV), and 4-methyl-7-thiocyanatomethylbenzo-2, 1, 3-selenadiazole (XVI) (see table).

*For Part XL see [1].

** According to the analytical data.

*** Along with small amounts of 5-methyl-6-chloromethyl- (VIII) and 5-methyl-7-chloromethylbenzo-2, 1, 3-selenadiazole (IX).

Experimental

Starting materials. The dichloromethyl ether prepared by the methods of [9] and [10], differed in paraform content [4]. Benzo-2, 1, 3-selenadiazole (I), 5-methyl- and 4-methylbenzo-2, 1, 3-selenadiazoles II and III were prepared as described in [11]. See also [12] regarding III.

Syntheses Based on Chloromethylated Selenadiazole Derivatives

Reaction product	Starting materials	M_p°C	Formula	N, % Found	N, % Calc.
5-Methyl-4-hydroxymethylbenzo-2, 1, 3-selanadiazole (XI)	VII, Potassium carbonate, water	125—126***	$C_8H_8N_2OSe$	12.24 12.35	12.33
4-Methyl-7-hydroxymethylbenzo-2, 1, 3-selenadiazole (XIV)	X, Potassium carbonate, water	142—143***		12.56 12.54	
5-Methyl-4-cyanomethylbenzo-2, 1, 3-selenadiazole (XII)	VII, KCN aqueous EtOH	174—176****	$C_9H_7N_3Se$	17.74 17.84	17.80
4-Methyl-7-cyanomethylbenzo-2, 1, 3-selenadiazole (XV)	X, KCN, aqueous EtOH*	175****		17.68 17.97	
5-Methyl-4-thiocyanatomethylbenzo-2, 1, 3-selenadiazole (XIII)	VII, KCNS, aqueous Me_2CO**	128—129****	$C_9H_7N_3SSe$	16.14 15.90	15.66
4-Methyl-7-thicvanatomethylbenzo-2, 1, 3-selenadiazole (XVI)	X, KCNS, aqueous Me_2CO**	105****		15.93 15.97	

*Boiled till solid completely dissolved.

**Boiled for 2 hr, poured into water.

***Ex water.

****Ex EtOH.

4-Chloromethylbenzo-2, 1, 3-selenadiazole (V). 7.3 g (0.04 mole) I was added in portions to a solution of 10.7 g (0.08 mole) anhydrous aluminum chloride in 6.7 ml (0.08 mole) dichlorodimethyl ether [10], the mixture heated at 100° for 4 hr with stirring, cooled, treated with a large volume of water, and filtered. The solid was boiled for some minutes with 50 ml EtOH, and filtered off hot. The filtrate was evaporated, the dry residue treated a few times with acetone, and the acetone removed to give a pale yellow compound mp 132.5–133.5° C (ex EtOH). Found: Cl 15.42, 15.37; N 12.35, 12.34%. Calculated for $C_7H_5ClN_2Se$: Cl 15.32; N 12.10%.

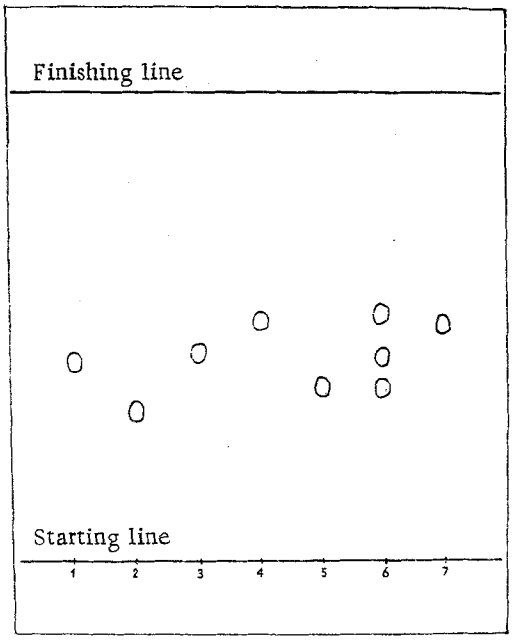
4, 7-Di (chloromethyl) benzo-2, 1, 3-selenadiazole (VI). 8 g (0.044 mole) I was added in portions to a solution of 16 g (0.12 mole) anhydrous aluminum chloride and 8.2 ml dichlorodimethyl ether [9], the mixture stirred and held for 4 hr at 85–90°C, cooled and treated with a large amount of water. The solid which had separated after a few hours was filtered off, washed with water, boiled for a few minutes with 50 ml EtOH, and recrystallized a few times from aqueous EtOH, to give yellowish needles mp 163–164°C. Found: Cl 24.89, 24.94; N 10.20, 10.37%. Calculated for $C_8H_6Cl_2N2Se$: Cl 25.33; N 10.00%.

5-Methyl-4-chloromethylbenzo-2, 1, 3-selenadiazole (VII). 3 ml dichlorodimethyl ether, prepared as described in [9], was added to a solution of 2.9 g (0.015 mole) 5-methylbenzo-2, 1, 3-selenadiazole (II) in 25 ml chlorosulfonic acid, and the mixture stirred and held at 70–75° for 6-8 hr, then left overnight and poured onto ice. The crystals which separated were filtered off, and washed with water. Recrystallized from EtOH they formed white needles mp 159–160°C. Found: Cl 14.02, 14.45; N 10.91, 11.32%. Calculated for $C_8H_7ClN_2Se$: Cl 14.45; N 11.41%.

4-Methyl-7-chloromethylbenzo-2, 1, 3-selenadiazole (X). This was prepared similarly, mp 148–149° C.* Found: Cl 14.06, 14.26; N 11.71, 11.34%. Calculated for $C_8H_7ClN_2Se$: Cl 14.45; N 11.41%.

*Sometimes the reaction product had mp 159–160°C, but then its mixed mp with the compound mp 148–194° C was undepressed.

Benzo-2, 1, 3-selenadiazole-aluminum chloride complex (IV). 2 g (0.015 mole) anhydrous $AlCl_3$ was added to a solution of 2 g (0.011 mole) compound I in 3 ml dry dichlorodimethyl ether. The mixture was refluxed for 5 min, cooled, and poured onto ice. The bright-yellow precipitate was filtered off and washed with water. Found: Cl 21.11, 21.42%. Calculated for $C_{12}H_8N_4Se_2 \cdot AlCl_3$: Cl 21.30%. Compound IV was decomposed by heating with EtOH or AcOH, when the starting compound I was isolated.



1) 2,3-Diaminotoluene (R_f 0.41); 2) 3, 4-diaminotoluene (R_f 0.31); 3) 1, 2-dimethyl-3, 4-diaminobenzene (R_f 0.43); 4) 1, 4-dimethyl-2, 3-diaminobenzene (R_f 0.50); 5) 1,2-dimethyl-4,5-diaminobenzene (R_f 0.36); 6) Residue from reductive scission of the product of chloromethylating 5-methylbenzo-2,1,3-selenadiazole with dichlorodimethyl ether prepared according to [10]; 7) Residue from reductive scission of the product of chloromethylating 4-methylbenzo-2, 1, 3-selenadiazole.

A typical reductive scission run on the chloromethylation products and identification of the o-diamines formed. $SnCl_2$ was added in portions to a suspension of the chloromethyl derivative in HCl (d 1.19). The mixture was heated and stirred for 3 hr on a water bath, cooled, the precipitate filtered off, the filtrate made acid until the precipitate which first formed dissolved completely, and then extracted with benzene. The extract was dried over K_2CO_3, the solvent distilled off, and the residue chromatographed by thin-layer chromatography, using an unsecured thin layer of aluminum oxide (Brockman activity II), solvent system CCl_4-Et_2O (10:1). The visualizer was iodine vapor (figure).

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