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

XLII. Action of Chlorine on Nitro Derivatives of Benzo-2,1,3-thiadiazole*

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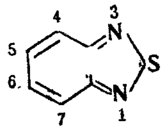
Action of chlorine in the presence of iron on molten 4-nitrobenzo-2,1,3-thiadiazole gives mainly 4,5,6,7-tetrachlorobenzo-2,1,3-thiadiazole, with a little 4, 7-dichlorobenzo-2,1,3-thiadiazole (VI). The tetrachloro compound is also found by the action of chlorine in the presence of iron on 4-nitro-5-chlorobenzo-2,1,3-thiadiazole. The action of chlorine in the presence of iron on 5-nitrobenzo-2,1,3-thiadiazole gives 5-nitro-7-chlorobenzo-2, 1, 3-thiadiazole. The structures of the reaction products are proved by retrosynthesis and thin-layer chromatography.

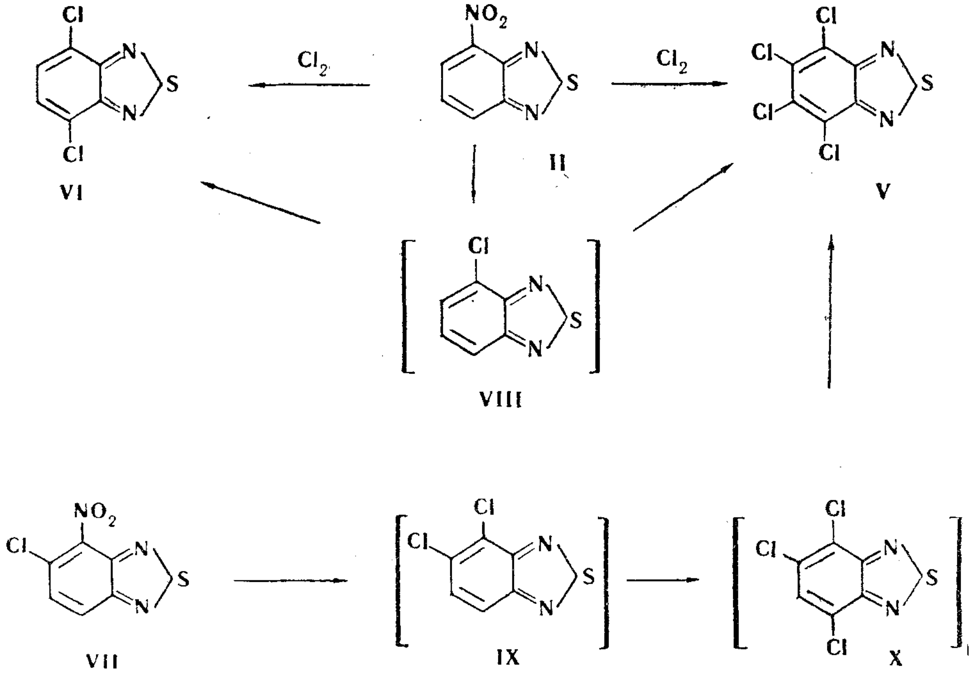
4-(II) and 5-nitrobenzo-2,1,3-thiadiazole (III), like benzene nitro derivatives, are nitrated under drastic conditions, e.g., by heating with nitrating mixture or sodium nitrate in concentrated sulfuric acid. In that way, it is possible to introduce a second nitro group into compound II or III [18]. It was of interest to investigate the behavior of nitro derivatives of benzo-2,1,3-thiadiazole (I) towards chlorine.



I

When chlorine was passed into molten II or III at 150° C, the starting materials were recovered. Under such conditions, reaction takes place only in the presence of activated iron.

When the reaction is carried out with compound II, the main product is 4,5,6,7-tetrachlorobenzo-2,1,3-thiadiazole (V); another product is 4, 7-dichlorobenzo-2,1,3-thiadiazole (VI). In addition, a small amount of substance A, melting point 165° C, is isolated, which proves to be a mixture of the starting compound II and dichloride VI. The tetrachloride V is also obtained by the action of chlorine on 5-chloro-4-nitrobenzo-2, 1, 3-thiadiazole (VII). Evidently with



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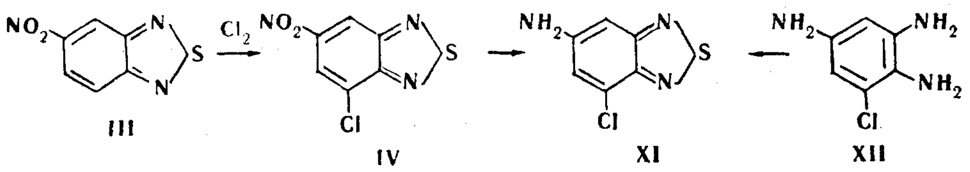
* For Part XLI see [1].

compound II reaction involves intermediate formation of 4-chlorobenzo-2, 1, 3-thiadiazole (VIII), which is further subsequently converted to dichloride VI and tetrachloride V. Similarly, when chlorine reacts with compound VII, the first product is probably 4, 5-dichlorobenzo-2, 1, 3-thiadiazole (IX), from which are subsequently formed 4, 5, 7-trichloro-(X) and 4, 5, 6, 7-tetrachlorobenzo-2, 1, 3-thiadiazole (V).* Replacement of the nitro group by chlorine involves electrophilic substitution, since the reaction is effected under conditions typical of that type of substitution (in the presence of iron catalyst).** As would be expected, compound III is converted into 5-nitro-7-chlorobenzo-2, 1, 3-thiadiazole (IV). Here, the nitro group and thiadiazole ring exert their orientating effects simultaneously.



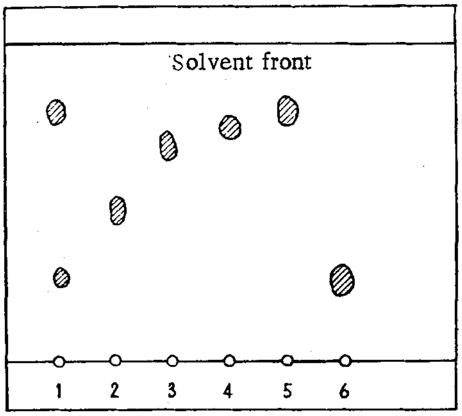
The structure of compound IV is shown by its reduction to 5-amino-7-chlorobenzo-2, 1, 3-thiadiazole (XI) and comparison of the latter with the compound obtained by reacting thionylaniline with 2, 3, 5-triaminochlorobenzene dihydrochloride (XII), synthesized as described in [10, 11]. The structures of the dichloro compound VI tetrachloro compound V were established by retrosynthesis as described in [12] and [13] respectively.

Experimental

Starting materials. 4-Nitrobenzo-2, 1, 3-thiadiazole (II) was prepared as described in [14, 15]. 5-Nitro- (III), 5-chloro- (XIII), and 5, 6-dichlorobenzo-2, 1, 3-thiadiazole (XIV) were prepared as described in [16]. 4, 5-Dichlorobenzo-2, 1, 3-thiadiazole (XV) was prepared as described in [12]. 4-Nitro-5-chloro- (VII) and 4-nitro-5, 7-dichlorobenzo-2, 1, 3-thiadiazole (XVI) were prepared as described in [17]. 4, 5-Dichloro-7-nitrobenzo-2, 1, 3-thiadiazole (XVII) was prepared as described in [18]. 4, 5-Dichloro-1, 2-dinitro-(XVIII) and 4, 5-dichloro-1, 2-diaminobenzene(XIX) were prepared as described in [19, 20].

Action of chlorine on 4-nitrobenzo-2, 1, 3-thiadiazole (II). Chlorine was passed for 4 hr into a mixture of 5 g II and 1 g activated Fe at 120° C. The products were cooled, treated with boiling EtOH and filtered hot. On cooling, the filtrate gave 3.5 g colorless crystals mp 152° C, mixed mp with authentic 4, 5, 6, 7-tetrachloro-2, 1, 3-thiadiazole (V) prepared as described in [13], undepressed. Found: Cl 51.67, 51.69; S 11.56, 11.67; N 9.55, 9.90%. Calculated for $C_6Cl_4N_2S$: Cl 51.82; S 11.68; N 10.22%.

The ethanolic filtrate was diluted with water, and the solid which separated fractionally crystallized from CCl_4. Two products were obtained. One, mp 181° C, was identical with 4, 7-dichloro-2, 1, 3-thiadiazole (VI) prepared as described in [12]. The other, A, gave analytical results corresponding to a nitrochlorobenzo-2, 1, 3-thiadiazole, but its melting point was not that of any of the three possible isomers. Found: Cl 28.40; 28.33; S 12.48, 12.45; N 17.69, 17.42%. Calculated for $C_6HCl_2N_3O_2S$: Cl 28.40; S 12.80; N 16.80%.



Chromatograms on plates. 1) Substance A mp 165°C (R_f 0.24 and R_f 0.73); 2) 4-nitro-5, 6-dichlorobenzo-2, 1, 3-thiadiazole (R_f 0.374); 3) 4-nitro-5, 7-dichloro-2, 1, 3-thiadiazole (R_f 0.545); 4) 4-nitro-6, 7-dichlorobenzo-2, 1, 3-thiadiazole (R_f 0.61); 5) 4, 7-dichlorobenzo-2, 1, 3-thiadiazole (R_f 0.73); 6) 4-nitrobenzo-2, 1, 3-thiadiazole (R_f 0.24).

This product was thin-layer chromatographed using an unfixed aluminum oxide (Brockman II activity) layer on glass plates 12 × 9 cm, and the solvent system CCl_4-$CHCl_3$(2:2). Iodine vapor was the visualizer. The chromatograms showed that the product mp 165° C was a mixture of starting material II with dichloro compound VI.

Action of chlorine on 4-nitro-5-chlorobenzo-2, 1, 3-thiadiazole (VII). Chlorine was passed for 1 hr 30 min into a

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*Experimental checking of this view will be the subject of a subsequent paper.

** The literature contains statements about replacement of the nitro group in nitro derivatives of aromatic compounds by chlorine [2-9]. However, the results could not be compared with those of the present paper, as the experiments were carried out under different conditions.

mixture of 1.2 g VII and 0.2 g activated Fe at 150° C. Treatment with boiling EtOH gave the tetrachloro compound V, mp 152° C, undepressed mixed mp with the similar compound prepared as described in [13].

5-Nitro-7-chlorobenzo-2, 1, 3-thiadiazole (IV). Chlorine was passed for 3 hr into a mixture of 2 g III and 1 g activated Fe at 150° C. 2.5 g substance was obtained which, after recrystallizing from EtOH had mp 118–119° C. Found: Cl 16.95, 16.84; N 19.08, 19.18%. Calculated for $C_6H_2ClN_2O_2S$: Cl 16.49; N 19.49%.

5-Amino-7-chlorobenzo-2, 1, 3-thiadiazole (XI). a) A mixture of 2 g Fe filings, 25 ml water, 0.5 ml glacial AcOH, and 1.5 g IV was refluxed for 20 min, cooled, the reaction products extracted with ether, the ether evaporated, and the residue recrystallized from aqueous EtOH, to give yellow needles, mp 156–157°C, undepressed mixed mp with the analogous compound prepared by reacting 2, 3, 5-triaminochlorobenzene (XII) dihydrochloride with thionylaniline. Found: N 21.85, 21.95; S 17.46, 17.30%. Calculated for $C_6H_4ClN_3S$: N 22.64; S 17.25%.

b) A mixture of 1.5 g XII, 15 ml pyridine, and 2 ml thionylaniline was heated for 30 min on a boiling water-bath, cooled, acidified with 4% HCl, and the precipitate recrystallized from water, to give yellow needles mp 157° C, mixed mp with the compound prepared as described in (a) undepressed.

Amide from the amine XI and phthalic acid. A mixture of 0.5 g amine XI, 0.5 g phthalic anhydride, and 30 ml $CHCl_3$ was heated for 2 hr on a boiling water-bath, the solvent evaporated off, and the residue recrystallized from aqueous EtOH, mp 210° C. Found: N 13.07, 12.93; S 9.40, 9.02%. Calculated for $C_{14}H_8ClN_3O_3S$: N 12.60; S 9.60%.

4-Nitro-5, 6-dichlorobenzo-2, 1, 3-thiadiazole (XX). 0.5 g XIV was dissolved in 10 ml H_2SO_4 (d 1.84), the solution cooled to 0–2° C, and a mixture of 2 ml HNO_3 (d 1.4) and 4 ml H_2SO_4 (d 1.84) added dropwise. After keeping at 20° C for half an hour, the products were poured into water, the precipitate filtered off, and washed with water. Yield 0.6 g material, which after recrystallizing from dilute AcOH had mp 100–101° C. Found: Cl 27.88, 27.93; N 17.16, 17.38; S 13.38, 13.37%. Calculated for $C_6HCl_2N_3O_2S$: Cl 28.40; N 16.80; S 12.80%.

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