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

XLIII. Chlorination and Chloromethylation*

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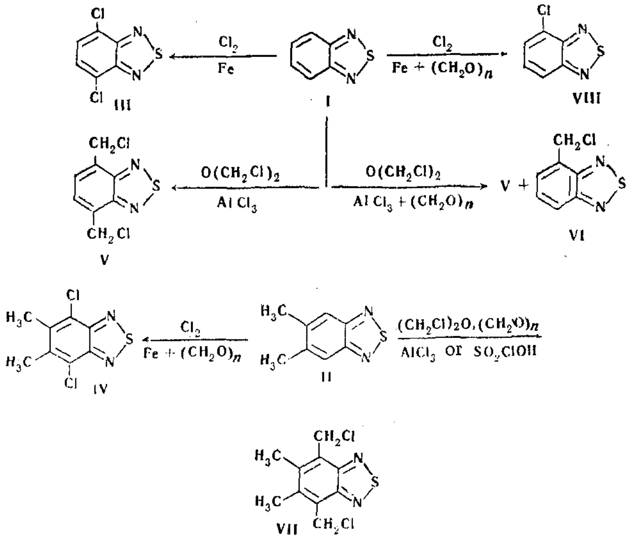
Chlorination of benzo-2, 1, 3-thiadiazole (I) in the presence of iron and paraform gives only 4-chlorobenzo-2, 1, 3-thiazole. Chlorination of 5, 6-dimethylbenzo-2, 1, 3-thiadiazole (II) under exactly the same conditions gives only 5, 6-dimethyl-4, 7-dichlorobenzo-2, 1, 2-thiadiazole. Similarly chloromethylation of II in the presence of paraform gives only 5, 6-dimethly-4, 7-di(chloromethyl)benzo-2, 1, 3-thiadiazole. Chlorination and chloromethylation of I proceed through the intermediate formation of monosubstituted compounds which change into disubstituted ones.

It is known [2, 3] that chlorination of benzo-2, 1, 3-thiadiazole (I) and its 5, 6-dimethyl derivative (II) with chlorine in the presence of iron gives mainly the 4,7-dichloro substitution products III and IV respectively.

It was previously shown [4] that chloromethylation of I with dichlorodimethyl ether in the presence of anhydrous aluminum chloride also gives mainly 4, 7-di(chloromethyl)benzo-2, 1, 3-thiadiazole (V). Bases and pseudo-bases (paraform, urotropine, dimethylformamide) have a retarding effect on chloromethylation. When the reaction is run in the presence of these latter the products comprise besides V, 4-chloromethyl-2, 1, 3-thiadiazole (VI), or else, if enough base is added, there is no reaction.

In the present work it is established that chloromethylation of compound II with dichlorodimethyl ether in the presence of chlorosulfonic acid or anhydrous aluminum chloride gives mainly 4,7-di(chloromethyl)-5,6-dimethylbenzo-2,1,3-thiadiazole (VII), yield 75%. This reaction is unaffected by the presence of a base.



It should be mentioned that bromination of I or II with excess bromine also gives mainly 4,7-dibromo compounds [2,3]. Nitration [5] and sulfonation [4] of I are also found to give mainly 4,7-disubstitution products. It is quite probable that formation of the 4,7-disubstitution products in electrophilic substitution reactions of I and its derivatives takes place by the same mechanism, involving intermediate formation of mono-substitution products. To test this hypothesis, a study was made of the chlorination of I and II in the presence of iron and paraform, using thin-layer chromatography. The chlorination products (Fig. 1) and their reductive scission products (Fig. 2) were chromatographed.

Chlorination in the presence of paraform gives only 4-chlorobenz-2,1,3-thiadiazole (VIII), a considerable amount of the starting I remaining unchanged. Attempts to raise the yield of VIII by varying the amount of paraform used were unsucessful. Decrease in the amount of paraform led to formation of the 4,7-dichloro derivative and VIII, while increasing it, slowed down the reaction.

Chlorination of II under similar conditions gave only IV, whether paraform was present or not. No 5,6-dimethyl-4-chlorobenzo-2,1,3-thiadiazole was found. This introduction of two methyl groups at positions 5 and 6 in benzo-2,1,3-thiadiazole arises because the electron-donating substance (paraform) does not slow down chlorination and chloromethylation. Possibly this is due to Cl^+ and CH_2^+Cl ions attacking not only the most nucleophilic position 4 (7) of molecules I and II, but the bases too. The latter are obviously more powerfully nucelophilic than position 7 in the 4-monosubstitution products. With 5,6-dimethylbenzo-2,1,3-thiadiazole (II) under the influence of the electron-donating effect of the methyl groups positions 4 and 7 become more nucelophilic than the bases (paraform), and therefore primarily suffer electrophilic attack. This also explains 4,7-dichloro compounds and 4,7-di(chloromethyl) compounds being the main products of chlorination and chloromethylation, respectively, of II. Obviously the ease of converting 4-monosubstituted compounds to 4,7-disubstituted ones is conditioned by the feeble inductive effect, and the considerable conjugation effect of chlorine or the chloromethyl group in the monosubstituted compounds.

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*For Part XLII see [1].

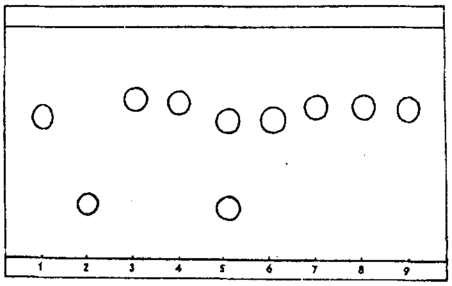

Fig. 1 Chromatography of the chlorination products of I and II: 1) I, R_f 0.59; 2) 4-chlorobenzo-2,1,3-thiadiazole, R_f 0.22; 3) 4,7-dichlorobenzo-2,1,3-thiadiazole, R_f 0.67; 4) product of chlorinating I in the presence of Fe, R_f 0.67; 5) product of chlorinating I in the presence of Fe and paraform, R_f 0.22; 0.59; 6) II, R_f 0.60; 7) product of chlorinating II in the presence of Fe, R_f 0.65; 8) product of chlorinating II in the presence of Fe and paraform, R_f 0.65; 9) 4,7-dichloro-5,6-dimethylbenzo-2,1,3-thiadiazole, R_f 0.65.

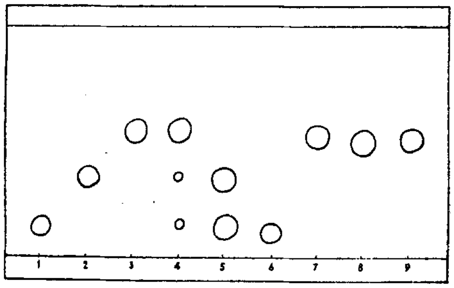

Fig. 2 Chromatography of the reductive scission products of I and II: 1) o-phenylenediamine R_f 0.12; 2—3-chloro-1,2-phenylenediamine, R_f 0.33; 3) 1,4-dichloro-2,3-phenylenediamine R_f 0.53; 4) reductive scission product after chlorinating I in the presence of Fe, R_f 0.12, 0.33, 0.53; 5) reductive scission product after chlorinating I in the presence of Fe and paraform, R_f 0.12, 0.33; 6) 1,4-dimethyl-2,3-phenylenediamine, R_f 0.09; 7) product of reductive scission after chlorinating II in the presence of Fe, R_f 0.50; 8) product of reductive scission after chlorinating II in the presence of Fe and paraform, R_f 0.50; 9) 3,6-dichloro-4,5-dimethyl-1,2-phenylenediamine, R_f 0.50.

EXPERIMENTAL

The starting materials were prepared by known methods. Benzo-2, 1, 3-thiadiazole (I) was prepared as described in [6], 5, 6-dimethybenzo-2, 1, 3-thiadiazole (II) as described in [7], and the dichlorodimethyl ether as described in [4].

4, 7-Di(chloromethyl)-5, 6-dimethylbenzo-2, 1, 3-thiadiazole (IV). 10 g II, 12.5 ml dichlorodimethyl ether, and 60 ml chlorosulfonic acid (or 30 g anhydrous $AlCl_3$) were heated together at 70–74° for 6 hr, the products cooled and poured onto ice. The precipitate was filtered off, and washed with water. Yield 12 g (75.5%), white needless, mp 169–171° (ex EtOH). Found: Cl 27.01; 26.53; S 12.18; 12.18%. Calculated for $C_{10}H_{10}Cl_2N_2S$: Cl 27.2; S 12.26%.

Typical experiments on chlorinating and subjecting the chlorination products to reductive scission. a) 0.3 g powdered Fe and 0.1 g paraform* were added to a melt (100°) of I and dry chlorine passed in for 30 min, with good stirring. 25 ml conc. HCl was then added to the products, followed by 5 g $SnCl_2$, and the mixture heated and stirred on a water-bath for 1 hr. The products were cooled, poured into excess of 25% NaOH solution, and the whole extracted with benzene. Removal of the solvent left diamines, which were subjected to TLC on alumina (Brockman activity grade II), using CCl_4-EtOH 10:1, iodine vapor being the visualizer (Fig. 2).

b) 0.1 g Fe powder and 0.1 g paraform* were added to melt (100°) of 0.82 g II, and dry chlorine passed in, with good stirring, till constant weight was reached (0.34 g). The reaction products were reduced, and chromatographed as above, using the CCl_4-$CHCl_3$ (3:1) system (Fig. 1).

REFERENCES

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*The experiment without paraform was carried out similarly.