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

XLV. Nitration of 4-Hydroxy-and 4-Ethoxybenzo-2,1,3-Thiadiazole*

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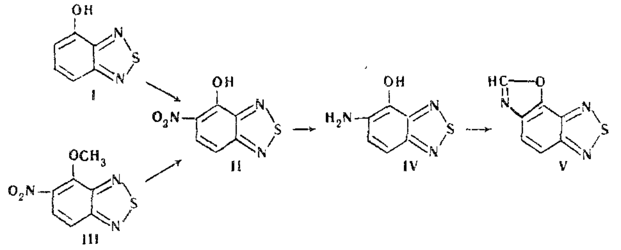
Nitration of 4-hydroxybenzo-2,1,3-thiadiazole under conditions generally used for phenols, gave a high yield of 4-hydroxy-5-nitrobenzo-2,1,3-thiadiazole. The latter is readily reduced to 4-hydroxy-5-aminobenzo-2,1,3-thiadiazole which on treatment with orthoformic ester gives oxazolo [5,4-e]benzo-2,1,3-thiadiazole. 4-Ethoxybenzo-2,1,3-thiadiazole is nitrated under similar conditions, giving a high yield of a mixture of equal quantities of 4-ethoxy-5-nitro- and 4-ethoxy-7-nitrobenzo-2,1,3-thiadiazole.

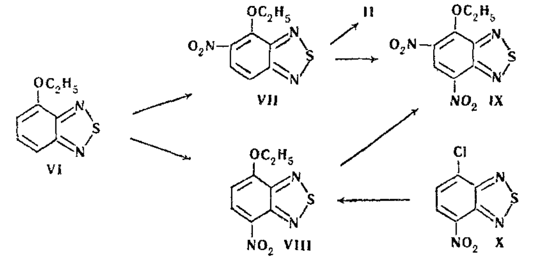
It was previously shown [2] that nitration of 4-hydroxybenzo-2,1,3-thiadiazole (I) using a mixture of sulfuric (d 1.84) and nitric (d 1.4) acids gives a 95% yield of mononitro derivative, assumed to have the structure 4-hydroxy-7-nitrobenzo-2,1,3-thiadiazole.

The present paper established that this mononitro derivative is 4-hydroxy-5-nitrobenzo-2,1,3-thiadiazole (II). This is proved by its identification with the 4-hydroxy-5-nitrobenzo-2,1,3-thiadiazole (II) obtained by hydrolyzing 4-methoxy-5-nitrobenzo-2,1,3-thiadiazole (III) with 48% hydrobromic acid [3], as well as by reducing mononitro derivative II to the corresponding amine (IV), and converting the latter, by orthoformic ester, to oxazolo [5,4-e] benzo-2,1,3-thiadiazole (V).



Thus when 4-hydroxybenzo-2,1,3-thiadiazole (I) is nitrated under conditions usually used with phenols, the hydrogen at position 5 is replaced to give 4-hydroxy-5-nitrobenzo-2,1,3-thiadiazole (II). These results, as well as the results of nitrosating I [4] show that under the experimental conditions, maximum electron density in 4-hydroxybenzo-2,1,3-thiadiazole occurs at the carbon atom at position 5.

Nitration of 4-ethoxybenzo-2,1,3-thiadiazole (VI) gives a mixture of equal amounts of 4-ethoxy-5-nitro- (VII) and 4-ethoxy-7-nitrobenz-2,1,3-thiadiazole (VIII). The structure of VII is shown by its conversion to II and 4-ethoxy-5,7-dinitrobenzo-2,1,3-thiadiazole (IX) of known structure [4]. The structure of VIII is established by its synthesis [3,5] from 4-chloro-7-nitrobenzo-2,1,3-thiadiazole [10] (X) and sodium ethoxide, and conversion to IX.



It is interesting to compare the nitration of I with the corresponding results for nitration of 4-methyl- (XI), 4-methoxy- (XII), and 4-ethoxybenzo-2,1,3-thiadiazole (VI). Nitration of XI gives a 97% yield of isomeric 4-methyl-5-nitro- (XIII) and 4-methyl-7-nitrobenzo-2,1,3-thiadiazole (XIV) in the proportions 35 and 65% respectively [6,7]. Nitration of XII or VI gives a high yield of a mixture of equal amounts of isomeric 4-methoxy-5-nitro- (III) and 4-methoxy-7-nitro- (XV), or 4-ethoxy-5-nitro- (VII) and 4-ethoxy-7-nitrobenzo-2,1,3-thiadiazole (VIII), respectively. Nitration of I gives a high yield of II only, which is to be regarded as a manifestation of the nature of the substituent on the orientation found when nitrating benzo-2,1,3-thiadiazole derivatives. The given data can be explained in terms of increased nucleophilicity in the order $CH_3 < OCH_3$ $(OC_2H_5) < OH$ [8].

EXPERIMENTAL

4-Hydroxy-5-nitrobenzo-2,1,3-thiadiazole (II) a) Prepared by nitrating 4-hydroxybenzo-2,1,3-thiadiazole [9] in the way described in [2]. The yield was raised from 86.1 to 94.5% by extracting compound II from the filtrate with $CHCl_3$.

b) A mixture of 1.2 g (about 0.0057 mole) III [7] and 20 ml 48% HBr was refluxed for 2 hr, the products cooled, the precipitate filtered off, washed with water, and dried. Yield 0.85 g (70.6%), mp 189–190° (ex EtOH) [3], undepressed mixed up with the compound prepared by method a.

c) A mixture of 0.5 g VII and 10 ml 48% HBr was reacted as described in b above. Yield 0.26 g (59.4%), mp 190° (ex EtOH), undepressed mixed mp with the compound prepared by methods a and b above.

4-Methoxy-5-nitrobenzo-2,1,3-thiadiazole (III). Isolated from the mixture of III and XV, formed on nitrating XII, yield 40%, mp 93° (ex EtOH) [7].

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*For Part XLIV see [1].

Oxazolo[5,4-e]benzo-2,1,3-thiadiazole (V). A mixture of 0.5 g (0.003 mole) IV [4] and 5 ml orthoformic ester was refluxed for 3 hr, the products evaporated to dryness, treated with 10% NaOH, filtered, the solid washed with water and dried. Yield 0.43 g (81.12%) material soluble in organic solvents. White needles mp 176–177° (ex water). Found: N 23.70; 23.73; S 18.14; 17.96%. Calculated for $C_7H_3N_3OS$: N 23.73; S 18.08%.

4-Ethoxy-5-nitro- (VII) and 4-ethoxy-7-nitrobenzo-2,1,3-thiadiazole (VIII). A mixture of 1 g (about 0.0055 mole) VI, 10 ml concentrated H_2SO_4 and 0.5 g $NaNO_3$ was stirred for 30 min at 18–20°, and the products then poured onto ice. The solid was filtered off, washed with water until neutral to Congo Red, then dried. Yield 1.12 (89.6%) of a mixture of equal quantities of VII and VIII, mp 104–109°, separated by steam distillation. VIII formed pale yellow needles mp 153–154° (ex EtOH), not distilling over with steam, undepressed mixed mp on mixing the same compound prepared from 4-chloro-7-nitrobenzo-2,1,3-thiadiazole (X) [5]. Found: N 18.35; 18.32; S 14.22; 14.03%. Calculated for $C_8H_7N_3O_3S$: N 18.68; S 14.22%. VII formed pale yellow crystals mp 70–71° (ex aqueous EtOH), volatile in steam, much more soluble in EtOH than the p-isomer. Found: N 18.82; 18.70; S 14.45; 14.54%. Calculated for $C_8H_7N_3O_3S$: N 18.68; S 14.22%.

4-Ethoxy-5,7-dinitrobenzo-2,1,3-thiadiazole (IX). a) A mixture of 0.5 g (about 0.0023 mole), 0.5 g $NaNO_3$, and 5 ml H_2SO_4 (d 1.84) was stirred for 30 min at 18–20°, then poured onto ice. The solid was filtered off, washed with water until neutral to Congo Red, then dried. Yield 0.62 g (82.6%), mp 122–123° (ex EtOH), undepressed mixed mp with the same compound previously prepared [4].

b) A mixture of 0.5 g VII or VIII, 5 ml H_2SO_4 (d 1.84) and 0.25 g $NaNO_3$ was stirred for 30 min at 18–20°, and the products worked up as described under a. Yield 0.54 g (90%), mp 122–123° (ex EtOH), undepressed mixed mp with the compound prepared by method b.

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