INVESTIGATIONS IN THE 1,2,4-TRIAZOLE SERIES

IX. Synthesis of Some Substituted 1-Phenyl-1,2,4-triazoles*

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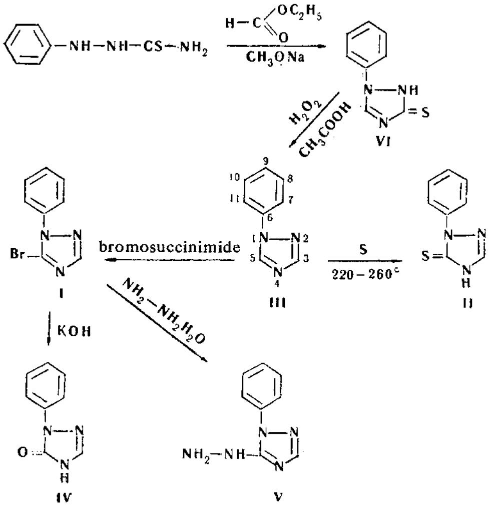
To select a method for the synthesis of the previously difficulty accessible 5-bromo-1-phenyl-1,2,4-triazole (I) and 1-phenyl-1,2,4-triazoline-5-thione (II), a MO LCAO calculation has been carried out in Huckel's approximation of the energies of the radical, electrophilic, and nucleophilic localization on the various carbon atoms of 1-phenyl-1,2,4-triazole (III). In accordance with this calculation, the required compounds have been obtained in good yields by reactions taking place by a radical mechanism: I by bromination with bromosuccinimide and II by the direct thionation of III. The high reactivity of the bromine atom in position 5 has been noted.

In a continuation of work on the synthesis of phenylated derivatives of 1,2,4-triazole and a study of their properties [1], the preparation of 1-phenyl-1,2,4-triazoles substituted in position 5 was planned in order to compare their properties with those of isomeric phenyltriazoles. As the key compounds for further syntheses we selected 5-bromo-1-phenyl-1,2,4-triazole (I) and 1-phenyl-1,2,4-triazoline-5-thione (II).



Such compounds of triazole with a vicinal arrangement of the phenyl and functional groups have been little studied and are difficulty accessible. Bromine derivatives of I have not been described in the literature. It was proposed to effect their synthesis by the direct bromination of 1-phenyl-1,2,4-triazole. In order to select a method of directed synthesis and to elucidate the most probable position of entry of the bromine, a MO LCAO calculation in Hückel's approximation of the energies of the radical, electrophilic, and nucleophilic localization on the various carbon atoms of 1-phenyl-1,2,4-triazole, was carried out. The parameters suggested by B. Pullman [2,3] were used in the calculation. The inductive effect of the nitrogen atom and all the overlap intervals were not taken into account. The solution of the secular determinant was obtained on a Ural-2 electronic computer.

As this calculation showed (see table), the synthesis of 5-substituted 1-phenyl-1,2,4-triazoles can be effected by either the radical or the nucleophilic attack of position 5. The low energy of radical localization shows the ease and, probably, the unambiguous occurrence of radical reactions at this position, which determined the choice of the method of synthesis (see scheme above).

The bromination of 1-phenyl-1,2,4-triazole (III) was carried out with N-bromosuccinimide, the radical mechanism of the action of which is regarded as established [4]. By this method we obtain the desired bromide in excellent yield. Its structure was confirmed by hydrolysis to 1-phenyl-1,2,4-triazolin-5-one (IV). The bromide proved to be a fairly reactive compound Thus, the bromine is replaced by hydroxy and hydrazine groups.

Having established the experimental possiblity of introducing substituents in position 5 by a direct reaction taking place by a radical mechanism, it could be expected that direct thionation would lead to the second planned product—1-phenyl-1,2,4-triazoline-5-thione (II). In actual fact, when 1-phenyl-1,2,4-triazole was fused with elementary sulfur at 220°–260° C the thione II, previously obtained by an inconvenient method [5] was formed in good yield

The 1-phenyl-1,2,4-triazole required for the syntheses described above was obtained by the oxidation of 1-phenyl-1,2,4-triazoline-3-thione (VI). The latter was obtained by the method of Pesson et al. [6], with some modifications introduced by us.

EXPERIMENTAL

1-Phenyl-1,2,4-triazoline-3-thione (VI). A solution of 6.9 g (0.3 g-at) of metallic sodium in 250 ml of anhydrous methanol and 50.1 g (0.3 mole) of 1-phenyl-3-thiosemicarbazide with mp 200° C (obtained by Koshkin's method [7]) was heated until a solution had been formed, after which 25 ml of anhydrous ethyl formate was added. The mixture was boiled for 8 hr, another 12 ml of the ester was added, and boiling was continued for 7 hr. The method and the ester were distilled off under vacuum, a solution of the residue in 300 ml of water was boiled in the presence of activated carbon and filtered, and, after cooling, the filtrate was acidified with dilute hydrochloric acid. The 1-phenyl-1,2,4-triazoline-3-thione that deposited was filtered off, dried, and crystallized from a large amount of water (1 : 100). Yield 44 g (83%), mp 188°–189° C. According to the literature [8], mp 189°

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*For part VIII, see [1].

C. A mixture with an authentic sample gave no depression of the melting point.

1-Phenyl-1, 2, 4-triazole (III). With heating, 17.7 g (0.1 mole) of 1-phenyl-1, 2, 4-triazoline-3-thione (VI) was dissolved in 250 ml of glacial acetic acid and then the solution was heated to the boil and 60 ml of 30% hydrogen peroxide was added dropwise. After this, the solution was evaporated to dryness on the water bath. The residue was dissolved in 100 ml of water and neutralized with 10% sodium carbonate solution, and the oil separating out on the bottom was extracted with chloroform (2 × 100 ml). The chloroform solution was dried over calcined sodium sulfate for 10–15 hr, the chloroform was driven off, and the oil was distilled, a fraction boiling at 264°–266° C being collected which solidified in the receiver to form long colorless needles. Yield 14.1 (97.2%), mp 46° C. According to the literature [9], mp 46°–47° C. Found, %: N 28.85. Calculated for $C_8H_7N_3$, %: N 28.95.

5-Bromo-1-phenyl-1, 2, 4-triazole (I). A mixture of 2.9 g (0.02 mole) of 1-phenyl-1, 2, 4-triazole and 7.12 g (0.04 mole) of N-bromosuccinimide in 100 ml of chloroform was boiled for 15 hr. After the end of the reaction, the solvent was distilled off, the residue was shaken with 50 ml of hot water (40°–60° C), and the light brown insoluble residue was crystallized from a small amount of ethanol. Yield 4.2 g (93.8%), colorless plates, mp 89°–90° C. Found, %: C 43.30; H 2.82; N 18.71. Calculated for $C_8H_7N_3Br$, %: C 42.88; H 2.70; N 18.75.

1-Phenyl-1, 2, 4-triazolin-5-one (IV). 0.31 g (1.4 mM) of 5-bromo-1-phenyl-1, 2, 4-triazole (I) was boiled with 3 ml of 10% caustic soda until it had dissolved completely. After the reaction mixture had cooled, it was acidified with dilute hydrochloric acid. The 1-phenyl-1, 2, 4-triazolin-5-one that separated out was filtered off and crystallized from water. Yield 0.2 g (90.1%), mp 181°–182° C. According to the literature [10], mp 182°–183° C. Found, %: N 26.11. Calculated for $C_8H_7N_3O$, %: N 26.07.

5-Hydrazino-1-phenyl-1, 2, 4-triazole (V). 0.35 g (1.6 mM) of 5-bromo-1-phenyl-1, 2, 4-triazole was boiled with 2 ml of hydrazine hydrate for 1 hr. The colorless crystals that deposited on cooling were filtered off and recrystallized from water. Yield 0.27 g (94.0%), mp 146° C. Found, %: C 54.48; H 5.18; N 40.22. Calculated for $C_8H_9N_5$, %: C 54.84; H 5.18; N 39.98.

1-Phenyl-1, 2, 4-triazoline-5-thione (II). 2.2 g (15 mM) of 1-phenyl-1, 2, 4-triazole was ground with 1.1 g of elemental sulfur and the mixture was heated in a flask immersed in Wood's alloy at 220°–260° C for 30 min. The content of the flask were poured into a dish, ground to a powder, and treated with 15 ml of 2 N caustic soda solution. The solution of the sodium salt of the thione was filtered, boiled in the presence of activated carbon, filtered again, and, after cooling, acidified with dilute hydrochloric acid. Fine colorless leaflets separated out. Yield 2.1 g (79%), mp 178°–178.5° C. According to the literature [5], mp 178° C. Found, %: N 23.87. Calculated for $C_8H_7N_3S$, %: N 23.72.

Localization Energies of 1-Phenyl-1, 2, 4-triazole (III)

Number of the carbon atom	Localization energy in β units for		
	nucleophilic attack	electrophilic attack	radical attack
3	2.253	2.397	2.325
5	2.051	2.439	2.245
7(11)	2.524	2.359	2.442
8(10)	2.542	2.542	2.542
9	2.560	2.394	2.477

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