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The Reactions of 4-Aminothiazolium Salts with Amines

Akiko Chinone, Mineo Maruyama, and Masaki Ohta

Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo

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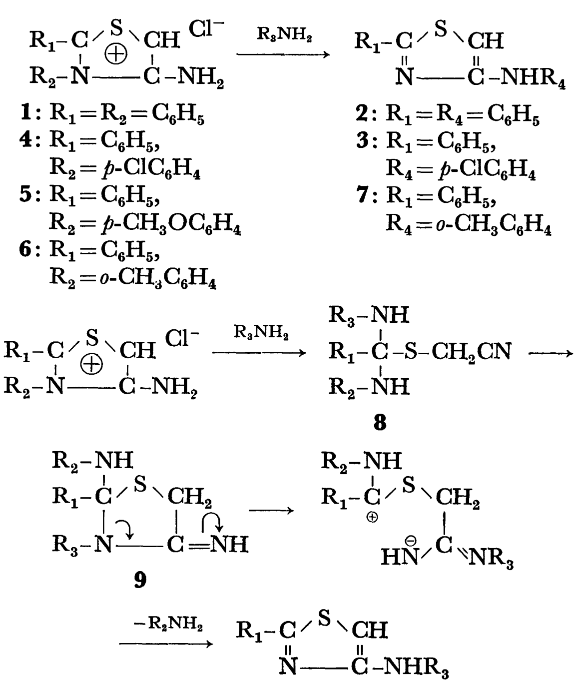
In our previous papaer,[1] we reported that 4-amino-2,3-diphenylthiazolium chloride (**1**) reacted to give 4-anilino-2-phenylthiazole (**2**) in the presence of aniline. In this report, we wish to describe the further detail of the reactions of 4-amino-2,3-diarylthiazolium chlorides with amines.

A benzene solution of **1** was heated with excess amount of *p*-chloroaniline at 50°C for 6 hr and neutralized with hydrochloric acid to give **2** and 4-*p*-chloroanilino-2-phenylthiazole (**3**). The structure of **3** was determined by elementary analysis and spectral data. The IR spectrum of **3** showed absorption peaks at 3330 cm^{-1} due to an NH stretching vibration and at 1530 cm^{-1} due to a thiazole ring. As in the UV spectrum of **2**, **3** showed characteristic absorption peaks at 278 mμ (ε 34000) and 360 mμ (ε 4600), which are suggestive of an aromatic heterocyclic system. In the NMR spectrum, **3** showed a peak at τ 3.64 which was attributed to 5-proton. When a toluene solution of **1** was heated with excess amount of *p*-chloroaniline at 100°C for 3 hr, **3** was obtained exclusively. In the presence of excess amount of aniline and *p*-chloroaniline (1: 1) or aniline and *p*-anisidine (1: 1) at room temperature, **1** afforded **2**. Expecting that the reaction of 4-amino-3-*p*-chlorophenylthiazolium chloride (**4**) with aniline may proceed *via* the same intermediate as that of the reaction of **1** with *p*-chloronailine, we examined the reaction of **4** with aniline. Treatment of **4** with aniline followed by neutralization with hydrochloric acid afforded **3** at room temperature. The products from the reaction of **4** with aniline were dependent on reaction temperature as in the case of the reaction of **1** with *p*-chloroaniline. The reaction of **4** with aniline was carried out at 50°C to give **2** and **3**, and at 100°C **2** was obtained exclusively. Treatment of **4** with *p*-chloroaniline at 50°C gave **3**, which was not obtained by treating *S*-cyanomethylisothiobenz-*p*-chloroanilide with *p*-chloroaniline in benzene at 50°C. The consideration that the substituent at 2-phenyl group may effect the course of the reaction led us to examine the reaction of 2-*p*-methoxy derivative **5** with amines. Compound **5** was treated with aniline at room temperature to give **2**, and treatment of **5** with *p*-chloroaniline, *p*-anisidine or *o*-toluidine afforded intractable oil. Treatment of 2-*o*-tolyl derivative **6** with aniline afforded **2**, and with *o*-toluidine, the corresponding thiazole **7** was obtained only as the picrate. Compound **6** was treated with *p*-chloroaniline at 50°C to give **3**. Compound **3** was not converted to **2** in the presence of amine at 100°C, and *vice versa*.

These results indicated that the reaction mechanism previously postulated,[1] in which amine used was not involved in a final product, required revision for the reaction of **5** and **6** even at room temperature. But we could not show the reasonable reaction mechanism and intermediate conclusively which was commonly involved. In the presence of equimolar amount of *p*-chloroaniline in toluene, DMSO or pyridine at 100°C, **1** afforded **2** instead of **3**. The reaction may probably proceed as shown below. It seems plausible that amine interchange occurs at the step **8**→**9** preferentially at 100°C, and consequently, the reaction may be controlled by the concentration of the amine.



1: $R_1=R_2=C_6H_5$
4: $R_1=C_6H_5$, $R_2=p\text{-}ClC_6H_4$
5: $R_1=C_6H_5$, $R_2=p\text{-}CH_3OC_6H_4$
6: $R_1=C_6H_5$, $R_2=o\text{-}CH_3C_6H_4$

2: $R_1=R_4=C_6H_5$
3: $R_1=C_6H_5$, $R_4=p\text{-}ClC_6H_4$
7: $R_1=C_6H_5$, $R_4=o\text{-}CH_3C_6H_4$

Experimental

The Reaction of 4 with Aniline. Compound **4** (0.6 g) was dissolved in 6 g of aniline and heated at 50°C for 6 hr. After cooling, the reaction mixture was neutralized with 10% hydrochloric acid under cooling with ice-water. Precipitates were collected by filtration and filtrate was treated as shown below. Precipitates were recrystallized from ethanol to give **2**; yield 0.4 g (80%). From the filtrate, **3** was precipitated out on standing for 3 days, which was recrystallized from ethanol to give needles with a mp of 104—105°C; yield 0.1 g (20%).

Found: C, 62.55; H, 3.95; N, 9.93; S, 11.19%. Calcd for $C_{15}H_{11}N_2SCl$: C, 62.83; H, 3.84; N, 9.81; S, 11.17%. IR: 3330, 1595, 1530, 820, 770, and 695 cm^{-1}. λ_{max}^{EtOH}mμ (ε) 278 (34000) and 360 (4600). NMR: τ ($CDCl_3$) 3.64 (1H) and 2.0—2.9 (10H).

The Reaction of 4 with p-*Chloroaniline.* A mixture of **4** (1 g), *p*-chloroaniline (10 g) and benzene (15 m*l*) was heated at 50°C for 14 hr. After cooling the reaction mixture was neutralized with 10% hydrochloric acid and extracted

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[1] S. Sato and M. Ohta, This Bulletin, **41**, 2801 (1968).

with ether. Ether layer was washed with water, dried over sodium sulfate and concentrated to give **3**, which was treated as shown above.

*The Reaction of **6** with* o-*Toluidine.* In 10 g of *o*-toluidine **6** (1 g) was heated at 50°C for 12 hr. The reaction mixture was treated as mentioned above to give **7**, which was converted to the picrate. The picrate was recrystallized from ethanol to give prisms with a mp of 105—106°C; yield 0.2 g (10%).

Found: C, 53.47; H, 3.36; N, 14.40; S, 6.51%. Calcd for $C_{22}H_{17}O_7N_5S$: C, 53.33; H, 3.46; N, 14.14; S, 6.47%. IR: 3350, 1600, 1570, and 1535 cm^{-1}.