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Chemistry

N-DEACETYLATION OF SOME AROMATIC AMIDES

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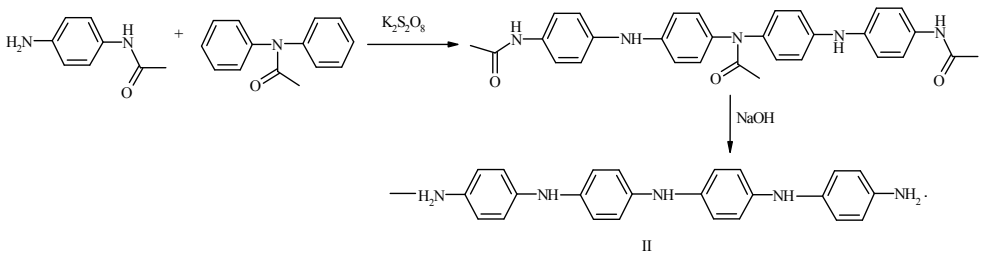
N-deacetylation of the amide groups of 4,4'-diamino-*N*-acetyldiphenylamine, 4,4'-di(p-acetaminoanilino)-*N*-acetyldiphenylamine and 4,4'-dinitro-*N*-acetyldiphenylamine were carried out. Reactions were proceeded under reflux, correspondingly by 4*N* alkaline mixture of methanol / dioxane and concentrated hydrochloric acid. The structures of obtained compounds were confirmed by NMR spectroscopy.

Keywords: 4,4'-diaminodiphenylamine hydrochloride, 4,4'-di(p-aminoanilino)diphenylamine, 4,4'-dinitro-*N*-acetyldiphenylamine, *N*-deacetylation, oligomer.

Introduction. It is well known that aromatic amines have a special place for the synthesizing of new conjugated conducting polymers and oligomers, and there is a lot of studies dedicated to the polymerization of various aromatic amines [1, 2]. Obtaining the corresponding oligomers helps to understand the structure and some properties of the processes in polymers [3]. Some anticorrosion and electroactive compounds, especially, aniline trimmer were obtained by using 4,4'-diaminodiphenylamine (compound II) [4]. Due to its unique properties, polyaniline is considered one of the most studied conducting polymer and is used in a lot of applications [5–9]. The most important oxidation state of polyaniline is the emeraldine base form. The emeraldine oxidation state of polyaniline has three benzene rings for every quinoid ring [3]. 4,4'-Di(p-aminoanilino)diphenylamine (compound IV), which is considered as NH_2/NH_2 capped aniline tetramer, represents an important model compound for polyaniline, because it is the shortest oligomer that can represent the polyaniline oxidation states [3]. A simple method based on of oxidative condensation was worked out for the synthesis of compound (IV) and can be illustrated by (Scheme 1) [10].



II

Scheme 1.

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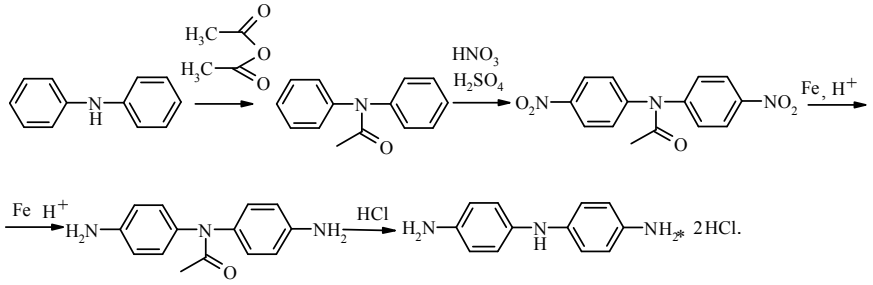
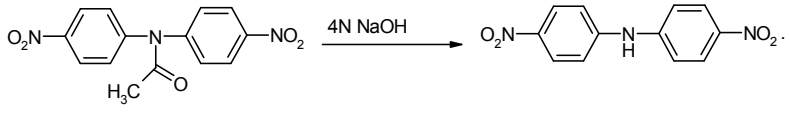
Then hydrolysis was carried out under classical vigorous reaction conditions and for a long reaction times using refluxing in 5*N* NaOH/H_2O solution. Aiming to reduce the reaction time and find mild conditions for removing the acetic group protection in case of secondary aromatic amides alkaline hydrolysis in dioxane/methanol medium and, for comparison, acidic hydrolysis in were investigated.

Results and Discussion. In general, amides are exceptionally stable to acid and basic hydrolysis and classically they are hydrolyzed under vigorous reaction conditions and long reaction times by heating in the presence of mineral acids or concentrated solutions of alkali hydroxides (10–40%), which can sometimes cause undesirable side reactions and low yield [11, 12]. Different mild and rapid reaction procedures were worked out for the alkaline hydrolysis in non aqueous reaction conditions. Based on these data we considered to use the same protocol for the hydrolysis of 4,4'-di(p-acetaminoanilino)-*N*-acetyldiphenylamine (Ac-IV). As we noticed previously, the secondary amide in Ac-IV was more difficult to be cleaved than the primary, 4,4'-diamino-*N*-acetyldiphenylamine (Ac-II) was synthesized first, as a model compound to work out more convenient method for removing protecting groups. Ac-II was synthesized by known methods from diphenylamine [13] (Scheme 2).



Scheme 2.

And then hydrolysis was carried out by appropriate method. Alkaline hydrolysis of Ac-II was carried out by 4*N* methanol solution of sodium hydroxide in dioxane similar to literature [12]. As it was mentioned [12], changing the traditional protic solvents, used in hydrolysis reactions, to less polar aprotic solvents, that do not stabilize the reactants, seems to be a good modification, since the relatively unsolvated hydroxide acts as a stronger nucleophile, but as it found out in case of hydrolysis of Ac-II using of dioxane as a solvent has only very low impact on the reaction: it did not process at room temperature and even after 30 *h* of refluxing. It is noteworthy to mention that the applied protocol works efficiently with initial 4,4'-dinitro substituted compound. Probably due to electron acceptor nitro groups the *N*-deacetylation reaction proceeds during 2 *h* under stirring at room temperature.



Scheme 3.

But, because of capped electron donor amino groups *N*-deacetylation of Ac-II does not proceed by 4*N* alkaline solution of methanol/dioxane. Comparatively, *N*-deacetylations of Ac-II and Ac-IV were carried out by concentrated hydrochloric acid under reflux. *N*-deacetylation of Ac-II proceeded during 1.5 *h*, while for Ac-IV it took 11 *h*. The structures of obtained compounds were confirmed by NMR spectroscopy (Fig. 1).

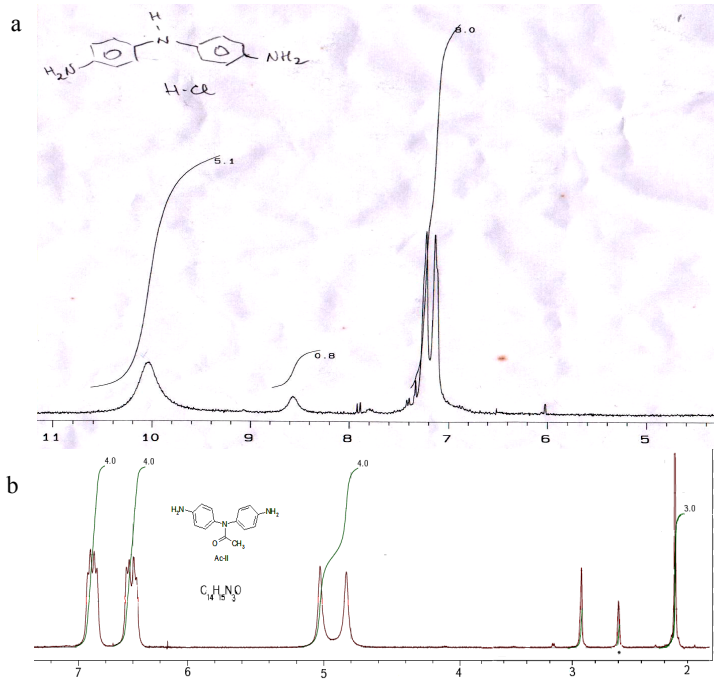


Fig. 1. ^{1}H NMR spectra ($(CD_3)_2SO$, δ, *ppm*) of compounds II (a) and Ac-II (b).

^{1}H NMR spectrum ($(CD_3)_2SO$, δ, *ppm*) (Fig. 1, a) of the compound II featured the following signals: NH_2 protons with acidic protons δ = 10.4–9.6 *ppm* with 6H (the intensity of one proton 5.1/6 = 0.85), NH proton δ = 8.5 *ppm* with 1H (the intensity of one proton 0.8/1 = 0.8), protons of aromatic group at δ = 7.4–6.8 *ppm* with 8H (the intensity of one proton 8/8 = 1).

^{1}H NMR spectrum of the compound Ac-II featured the following signals (Fig. 1, b): NH_2 protons at δ = 5.2–4.8 *ppm* with 4H (the intensity of one proton 4/4 = 1), protons of aromatic group at δ = 7.0–6.4 *ppm* with 8H (the intensity of one proton 8/8 = 1), protons of CH_3 group at δ = 2.2–2.0 *ppm* with 3H (the intensity of one proton 3/3 = 1). To improve the synthesis methods of compound IV, compound Ac-IV was obtained by known method [13] (Scheme 2), by the oxidative condensation of p-aminoacetanilide with *N*-acetyldiphenylamine.

N-deacetylation of all amide groups of compound Ac-IV proceeded after 30 *h* reflux by alkaline, while it took 11 *h* by concentrated hydrochloric acid.

^{1}H NMR spectrum of the compound IV (Fig. 2) featured the following signals: NH_2 protons δ = 5.8–5.0 *ppm* with 4H (the intensity of one proton 2/4 = 0.5), protons of aromatic and NH groups at δ = 8.4–6.4 *ppm* with 19H (the intensity of one proton 9.8/19 = 0.51).

Data show that *N*-deacetylation of compounds Ac-II and Ac-IV does not proceed as fast as it is mentioned [11, 12] for aromatic amides. Compare to alkaline hydrolysis the acidic has some advantages:

1) the *N*-deacetylation reaction takes 1.5–11.0 *h* instead of 30–33;

2) it excludes the side reactions that can appear due to amino groups.

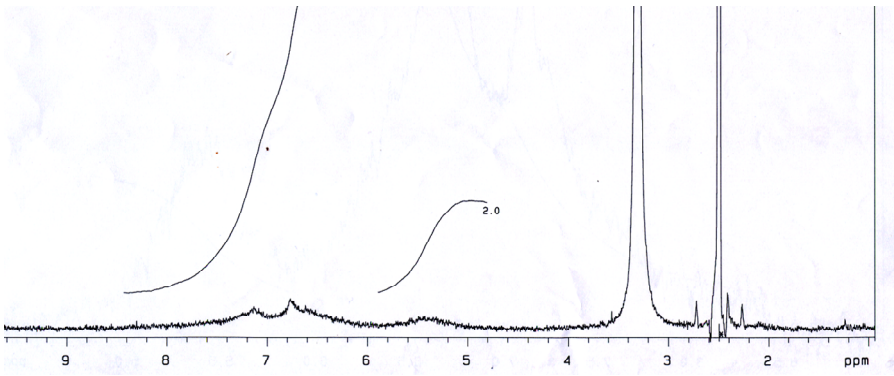


Fig. 2. ^{1}H NMR spectra ($(CD_3)_2SO$, δ, *ppm*) of compound IV.

Experimental Part. ^{1}H NMR spectra were obtained in deuterated dimethylsulfoxide using Mercury 300 Varian NMR spectrometer. Compounds Ac-II and Ac-IV were synthesized by known methods [10, 13]. All compounds were purified by recrystallization. The vacuum (0.2 *kPa*) desiccator with P_2O_5 was used for drying the obtained compounds.

Synthesis of 4,4'-diaminodiphenylamine Hydrochloride. The mixture of 0.201 *g* (0.834 *mmol*) of 4,4'-diamino-*N*-acetyldiphenylamine, 5 *mL* of methanol and 0.78 *mL* of 37% HCl was stirred under reflux for 1.5 *h*. Then to get rid of the acid the reaction mixture was evaporated at 90°*C*, until neutral. The product was washed by diethyl ether and dried in vacuum to constant weight. The yield is 0.17 *g* (m.p. >290°*C*).

Synthesis of 4,4'-di(p-aminoanilino)diphenylamine. The mixture of 0.03235 *g* (0.064 *mmol*) of 4,4'-di(p-aminoanilino)-*N*-acetyldiphenylamine, 1.2 *mL* of methanol and 0.6 *mL* of 37% HCl was stirred under reflux for 11 *h*. Then the reaction mixture was treated by 10% of sodium carbonate aqueous solution until pH 9, it was stirred at 0–5°*C* for 4 *h*. The precipitation was filtered and washed by water until neutral. The product was dried in vacuum to constant weight. The yield is 0.02 *g* (m.p. >290°*C*).

N-deacetylation of 4,4'-dinitro-N-acetyldiphenylamine. The mixture of 9 *g* (2.99 *mmol*) of 4,4'-dinitro-*N*-acetyldiphenylamine (m.p. 160–161°*C*), 340 *mL* of dioxane and 38 *mL* of methanol solution of 4.1 *N* NaOH (15.19 *mmol*) was stirred under reflux for 2 *h* at room temperature. Then 400 *mL* of water was added to the reaction mixture. The precipitation was filtered and washed by water until neutral. The product was dried under vacuum to constant weight. The yield is 7.72 *g* (m.p. 208°*C*).

Conclusion. Probably, because of capped electron donor amino groups *N*-deacetylation of compound Ac-II does not proceed by 4*N* alkaline solution of methanol/dioxane, even after 30 *h* reflux. *N*-deacetylation of all amide groups of compound Ac-IV proceeded after 30 *h* reflux, while it took 11 *h* by concentrated

hydrochloric acid. It was found out that dioxane did not have any important influence on the rate of the hydrolysis of compounds Ac-II and Ac-IV.

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