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Study of Liquid-Phase Dehydration of *d,l*-1-(4-Aminophenyl)ethanol in the Presence of Acid Catalysts

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Abstract—Thermal acid-catalyzed liquid-phase dehydration of 1-(4-aminophenyl)ethanol at 250–260°C and 30–100 mm Hg was studied. In the presence of $KHSO_4$ a 2:1 mixture of 1-amino-4-ethylbenzene with 4-aminostyrene is formed, the use of $KHSO_4/KH_2PO_4$ causes the formation of polymers, and the use of H_3BO_3 ($\leq$ 0.26 wt %) in a mixture with $KHSO_4$ allows the preparation of pure 4-aminostyrene. The structure of the reaction products was confirmed by NMR spectroscopy and by authentic synthesis.

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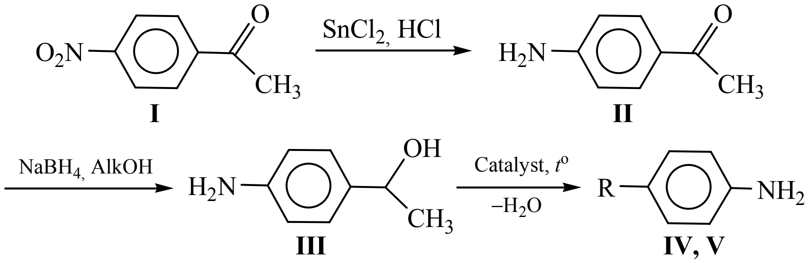
The thermal dehydration of phenylmethylcarbinols substituted in the aromatic ring is used widely for the synthesis of various styrene derivatives. Usually this process is carried out in the melt at high temperature and mainly $KHSO_4$ is used as a catalyst of the reaction [1, 2]. Another way of carrying out the reaction is the gas phase dehydration of 1-phenylethanol derivatives over activated Al_2O_3 at 250–310°C [3]. However, the publications regarding the thermal dehydration of aminophenylmethylcarbinols in the melt are scarse. For example, a transformation was described of 1-(3,4-diaminophenyl)ethanol at 280–320°C and in the presence of KOH at 180–230°C leading to the formation of either *o*-phenylenediamine, or of a mixture of 1,2-diamino-4-ethylbenzene with 3,4-diaminostyrene [4]. Thus, actually the problem of synthesis of vinylaromatic amines by liquid phase dehydration of the appropriate alcohol has not been studied.

In the literature there are no data concerning the synthesis of 4-aminostyrene from 1-(4-aminophenyl) ethanol by liquid-phase dehydration.

A purpose of this work is the study of thermal dehydration of 1-(4-aminophenyl)ethanol in the melt in the presence of acidic catalysts.



R = Et (**IV**), $CH=CH_2$ (**V**).

The *p*-aminoacetophenone was synthesized in 75–79% yield by the modified method [5]. Further reduction of the *p*-aminoacetophenone to *d,l*-1-(4-aminophenyl)ethanol was carried out in the medium of anhydrous ethanol or methanol, with the yield 90% and 83–88%, respectively.

Dehydration of *d,l*-1-(4-aminophenyl)ethanol was performed at 250–260°C at the pressure of 100–30 mm Hg, in the presence of hydroquinone (0.50–1.02 wt %). H_3BO_3, $KHSO_4$ and a mixture of the latter with KH_2PO_4 or H_3BO_3 were used as catalysts. The choice of the catalysts was defined by the variation in the acidic properties; in addition, KH_2PO_4 and H_3BO_3 are antipyrenes, which means that they inhibit free-radical processes already at this temperature.

At performing the reaction in the presence of $KHSO_4$ a mixture containing 1-amino-4-ethylbenzene (**V**) with a small amount of *p*-aminostyrene (**IV**) is formed. The variation in amount of $KHSO_4$ in the range 1–4 wt % does not affect significantly the reaction rate and the product composition and yield. The duration of the synthesis in this case is 1–2 h, which is determined by the efficiency of distilling off the reaction products and the sorption properties of the reaction mixture.

From the spectral data (Fig. 1) follows that the ratio of products **IV** and **V** is about 2 : 1. In the strong field intense signals are observed of the protons of methylene and methyl groups with the characteristic splitting into the quartet and triplet, belonging to the ethyl group in compound **V**. Broad signal of the amine **V** NH_2 group partially overlaps one of the doublets belonging to the *cis*-H at the styrene **IV** double bond, and the signal of the vicinal H is partially eclipsed by the signals of protons located at positions 2 and 6 of the aromatic ring of 1-amino-4-ethylbenzene.

Use of a mixture of KH_2PO_4 (1.8 wt %) with $KHSO_4$ (2.0 wt %) reduces the duration of the reaction to a few minutes and suppresses the oxidation processes. In this case the main product is a resin, while 4-aminostyrene is formed with the yield less than 1%, without an admixture of amine **V**. When a mixture of H_3BO_3 (0.2–0.26 wt %) with $KHSO_4$ (1.02 wt %) was used as a catalyst for dehydration, the contribution of the oxidation processes is also low, and tarring is insignificant. Distillation of the reaction products occurs at 255°C at the pressure of 30 mm Hg, simultaneously with the initial amino alcohol **III**, which prevails in the distillate.

^1H NMR analysis of the distillate showed no trace of 1-amino-4-ethylbenzene. The signals of groups CH_3 and CH in the side chain of the aminoalcohol **III** are,

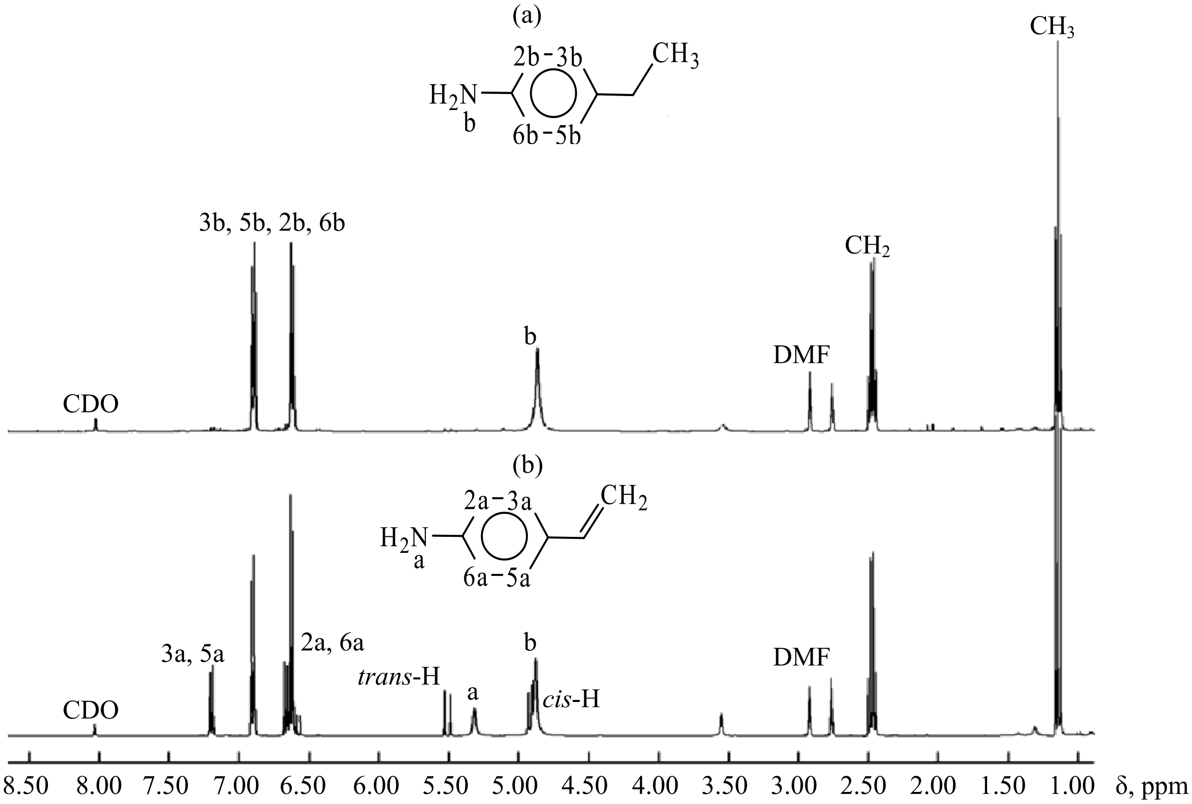


Fig. 1. ^1H NMR spectra in DMF-d_7: (a) sample of 1-amino-4-ethylbenzene and (b) the reaction product.

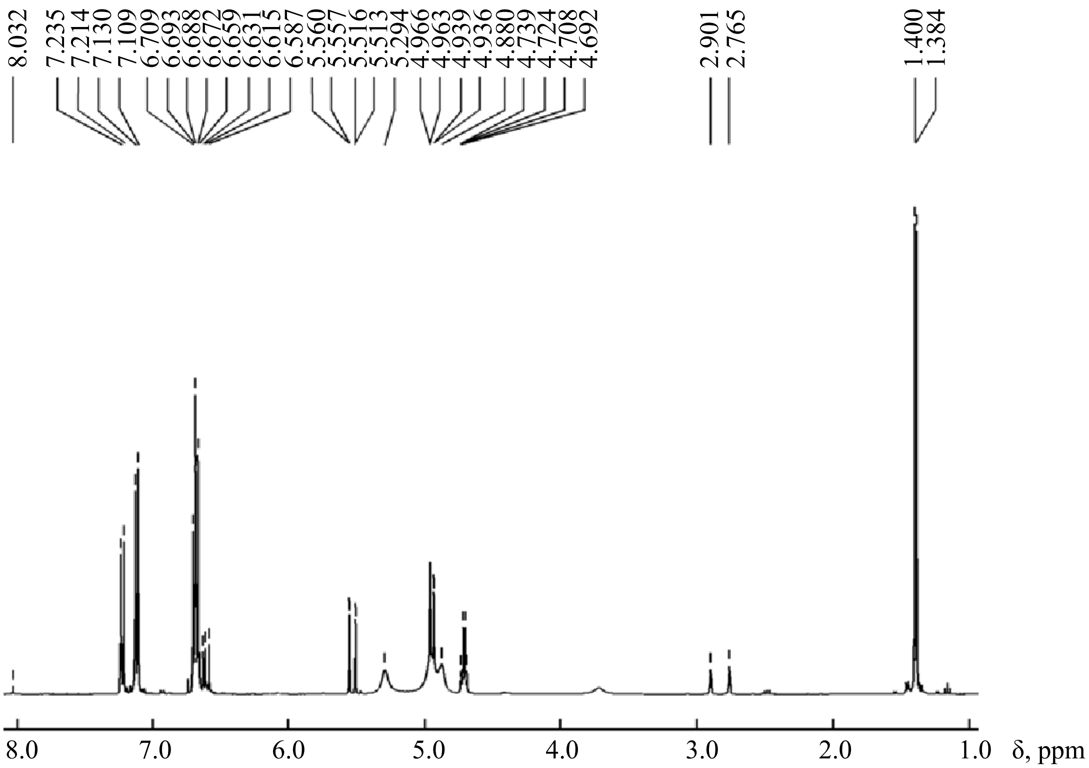


Fig. 2. ^{1}H NMR spectrum in DMF-d_7 of a mixture of compounds **III** and **IV**.

respectively, a doublet at 1.4 ppm and a quadruplet at 4.7 ppm. The signals of the protons in positions 2 and 6 of the aromatic ring overlap with those of 4-aminostyrene and with the signals of vicinal proton at the double bond in the region of 6.5–6.8 ppm.

The amine isolated from the mixture also was characterized spectrally and identified as 4-amino-styrene, as evidences ^{1}H NMR spectrum (Fig. 3).

In the region of 4.9–5.6 ppm there are doublets of the *cis*- and *trans*-protons at the double bond, with splitting of 10.9 Hz and 17.6 Hz, respectively, as well as a broad signal of the amino group. The signals of the protons of aromatic ring and vicinal protons of the vinyl group fall to the range of 6.5–7.2 ppm.

Use of H_3BO_3 as a catalyst has an inhibitory effect on the free-radical oxidation processes that result in the formation of 1-amino-4-ethylbenzene at the dehydration of 1-(4-aminophenyl)ethanol, but a significant increase in the content of H_3BO_3 in the reaction mixture from 0.2 wt % to 2.0 wt % leads to tarring which becomes the main process. Removal of 4-amino-styrene from the reaction zone becomes rather slow, which leads to a decrease in the yield and appearance of the associated impurity product, 1-amino-4-ethylbenzene.

Thus, at the liquid-phase thermal dehydration of *d,l*-1-(4-aminophenyl)ethanol, the product composition is influenced greatly by the additives. Use of H_3BO_3 in the amount no more than 0.2–0.26 wt % determines the reaction direction toward the formation of 4-aminostyrene, especially at a joint application with the catalysts of dehydration such as anhydrous $KHSO_4$ and K_2SO_4. A necessary condition for this is the rapid removal of the resulting 4-aminostyrene from the reaction zone, that is possible at the distilling it simultaneously with the parent 1-(4-aminophenyl)ethanol.

EXPERIMENTAL

We used 99.6% *p*-nitroacetophenone, mp 80°C. The removal of water from methanol and ethanol was achieved at the prolonged boiling with excess CaH_2 followed by distillation. Diethyl ether was preliminary treated for removing peroxides and distilled. Potassium hydroxide of “chemically pure” grade was used in the form of plates. We used anhydrous $KHSO_4$ prepared preliminary from solutions of KOH and H_2SO_4 combined in the molar ratio 1:1.5, with subsequent extraction of H_2SO_4 with boiling ethanol. The NMR spectra of the synthesized compounds were taken from

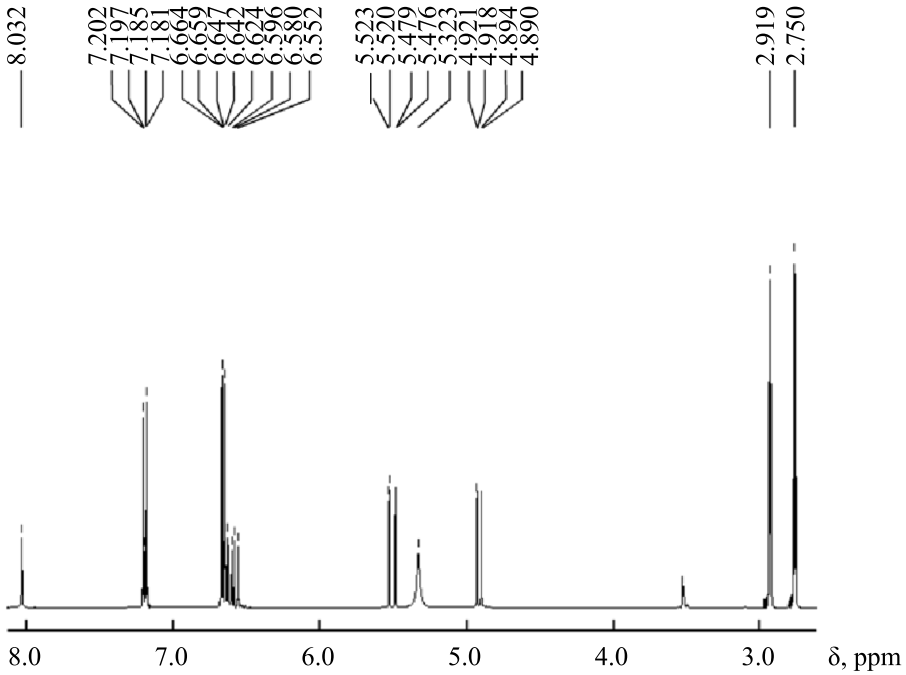


Fig. 3. ^{1}H NMR spectrum of 4-aminostyrene in DMF-d_7.

the solutions in DMF-d_7 (^{1}H NMR spectrum: δ, ppm: 8.032 (CDO); ^{13}C NMR spectrum: δ, ppm: 29.784, 34.888, 162.397) on a Bruker AVANCE II 400 spectrometer (^{1}H, 400.1 MHz, ^{13}C, 100.6 MHz) . TLC was carried out on Silufol UV 254 plates (eluent ethanol, developer I_2).

Synthesis of 4-aminoacetophenone. The synthesis was carried out by reduction of 4-methoxy-3-nitro-acetophenone using a modified method [5]. 24.93 g (0.1510 mol) of 4-nitroacetophenone was added in one portion to the heated to 50°C suspension of 130.91 g (0.6308 mol of $SnCl_2$) $SnCl_2{\cdot}H_2O$ in 131 ml of 37.2% HCl containing 50 ml of ethanol. 19.78 g of crude product was isolated and recrystallized from benzene. Yield 15.91 g (78.5%), yellow crystalline solid, mp 105–105.5ºC. TLC: R_f 0.62–0.65.

Synthesis of *d,l*-1-(4-aminophenyl)ethanol. To a solution of 6.60 g (0.0488 mol) of 4-aminoacetophenone in 100 ml of anhydrous ethanol heated to 40°C was added in small portions 9.23 g (2.2425 mol) of $NaBH_4$. The thickened reaction mixture was diluted with 80 ml of anhydrous ethanol. After adding the whole amount of $NaBH_4$, to the reaction mixture was added 20 ml of ethanol, the mixture was stirred. When the gas evolution ceased, 5 ml of water was added to precipitate a white mineral substance. The solution was decanted from the precipitate, 200 ml of chloroform, 100 ml of benzene and 145 ml of water were added, and after shaking and phase separation the organic layer was isolated and the aqueous layer was extracted twice with chloroform, by 50 ml portions, then with benzene, twice by 50 ml portions. The precipitate was dissolved in 50 ml of water, the solution was extracted with 50 ml of chloroform, all organic extracts were combined, and the solvents were removed in vacuo on a rotary evaporator. The residual yellow liquid was left for crystallization, the next day the crystalline mass was ground and dried. Yield of *d,l*-1-(4-aminophenyl) ethanol 6.0 g (90%), light-yellow crystalline solid, mp 60–60.5ºC (racemic), mp 68.5–69°C (non-equilibrium mixture of enantiomers). *d,l*-(4-Aminophenyl)ethanol is soluble in Et_2O, and is easily soluble in $CHCl_3$, EtOH, MeOH, and H_2O; insoluble in C_6H_6 and petroleum ether. TLC: R_f 0.54. ^{1}H NMR spectrum, δ, ppm: 1.336, 1.352 d (3H, CH_3, J 6.4 Hz), 4.641, 4.657, 4.673, 4.689 q (CH), 4.846 (OH), 6.632, 6.637, 6.648, 6.653 d (2H, 2,6-Ar), 7.065, 7.070, 7.081, 7.085, 7.086 d (2H, 3,5-Ar). ^{13}C NMR spectrum, δ, ppm: 25.748 (CH_3), 88.988 (CH), 114.021 (2,6-Ar), 128.481 (3,5-Ar), 135.441 (4-Ar), 148.032 (C-NH_2, 1-Ar).

Dehydration of *d,l*-1-(4-aminophenyl) ethanol. *a.* Powdered mixture of 11.55 g (0.0842 mol) of 1-(4-aminophenyl)ethanol, 0.115 g (1 wt %) of hydroquinone, and 0.115 g (1 wt %) of $KHSO_4$ was heated in the apparatus for distillation to 250–255ºC at a residual pressure of 100–80 mm Hg. The distillate was collected over 1.5 h at gradual lowering the pressure to 30 mm Hg at the end of the reaction. 4.10 g of distillate was obtained which was subjected to steam-distillation, the products were extracted with diethyl ether, the extract was dried for 5 minutes over KOH, then ether was removed in a vacuum on a rotary evaporator. Yield of a mixture of **IV** and **V** was 0.48 g. Transparent liquid, easily oxidized in air. ^{1}H NMR spectrum, δ, ppm: 1.110, 1.129, 1.148 t (3H, CH_3), 2.434, 2.453, 2.472, 2.491 q (2H, CH_2), 4.873 s (2H, NH_2, **V**), 4.898, 4.901, 4.925, 4.929 d.d (*cis*-H, *J* 10.9 Hz), 5.310 s (2H, NH_2, **IV**), 5.481, 5.485, 5.525, 5.529 d.d (*trans*-H, *J* 17.6 Hz), 6.558, 6.585 (*vic*-H), 6.611, 6.616, 6.627, 6.632 d (2H, 2,6-Ar, **V**), 6.652, 6.657, 6.669, 6.673 d (2H, 2,6-Ar, *J* 8.5 Hz, **IV**), 6.889, 6.894, 6.905, 6.910 d (2H, 3,5-Ar, **V**), 7.184, 7.189, 7.201, 7.206 d (2H, 3,5-Ar, *J* 8.4 Hz, **IV**).

b. To a mixture of 9.8 g (0.0714 mol) of *d,l*-1-(4-aminophenyl)ethanol, 0.10 g (1.02 wt %) of $KHSO_4$ and 0.10 g (1.02 wt %) of hydroquinone heated to 65–70°C was added 0.025 g (0.255 wt %) of H_3BO_3, the reaction mixture was heated to 255°C, then the pressure in the system was lowered to 100 mm Hg and after 10 min to 30 mm Hg, and then the distillation started. The distillate weight was 4.96 g. The residue was subjected to steam-distillation, the distillates were combined and again subjected to steam-distillation. Then 4-aminostyrene was extracted with diethyl ether, the extract was dried for 5 minutes over KOH, the solution was decanted from drying agent, and the solvent was removed in a vacuum on a rotary evaporator. Yield: 0.15 g (1.8%), clear liquid colorizing in air. ^{1}H NMR spectrum, δ, ppm: 4.890, 4.894, 4.918, 4.921 d.d (*cis*-H, *J* 10.9 Hz), 5.323 s (2H, NH_2), 5.476, 5.479, 5.520, 5.523 d.d (*trans*-H, *J* 17.6 Hz), 6.552, 6.580, 6.596, 6.624 m (*vic*-H), 6.642, 6.647, 6.659, 6.664 (2H, 2,6-Ar), 7.181, 7.185, 7.197, 7.202 (2H, 3, 5-Ar).

c. Finely ground mixture of 10.85 g (0.0791 mol) of *d,l*-1-(4-aminophenyl)ethanol, 0.0543 g (0.5 wt.%) of hydroquinone, and 0.211 g (2.0 wt.%) of H_3 BO_3 was heated to 245ºC at a pressure of 80 mm Hg. The mixture began to boil, and along with the increase in the bath temperature to 255ºC a small amount of distillate was obtained. The product was isolated and purified as described above. Yield: 0.05 g, colored liquid. According to the ^{1}H NMR spectroscopy, a substance consisted mostly of 4-aminostyrene containing admixture of 1-amino-4-ethylbenzene.

d. A mixture of 8.33 g (0.06 mol) of *d,l*-1-(4-aminophenyl)ethanol, 0.05 g (0.6 wt %) of hydroquinone, 0.167 g of $KHSO_4$ (2.0 wt.%), and 0.150 g of KH_2PO_4 (1.8 wt.%) was treated as described in the method *b*. Yield 0.05 g (0.7%) of 4-aminostyrene.

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