ISSN 1070-3632, Russian Journal of General Chemistry, 2013, Vol. 83, No. 10, pp. 1859–1863. © Pleiades Publishing, Ltd., 2013.
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Preparation of 4-Nitrostyrene

A. L. Shultsev

Institute of Macromolecular Compounds, Russian Academy of Sciences,
Bol'shoi pr. Vasil'evskogo ostrova 31, St. Petersburg, 199004 Russia
e-mail: shultsev@list.ru

Received March 12, 2013

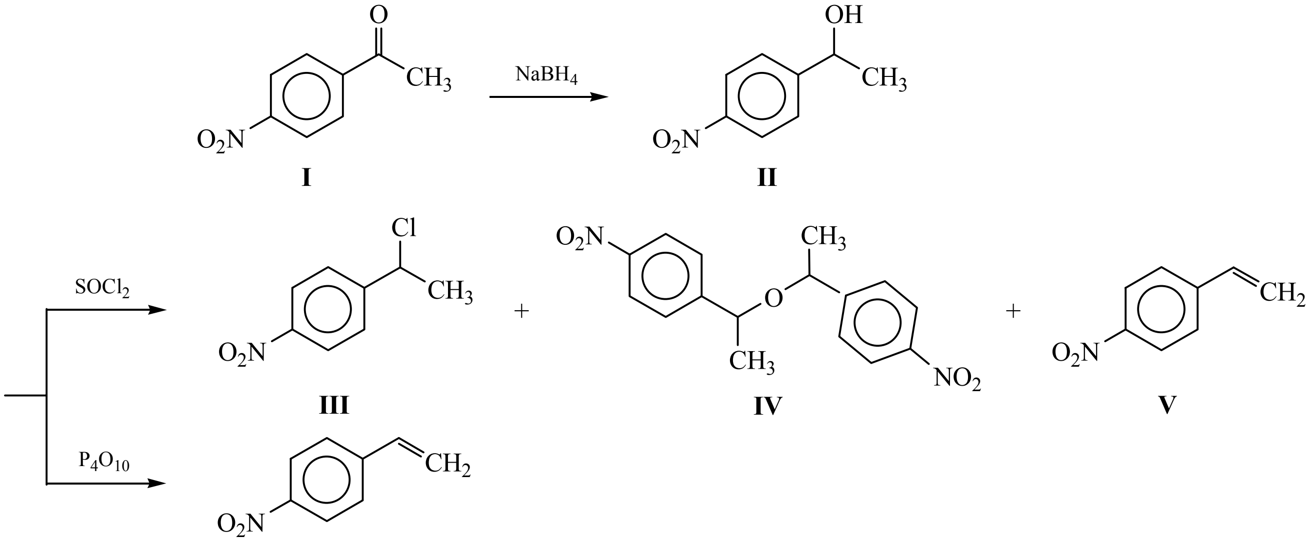
Abstract—The interaction of *D,L*-1-(4-nitrophenyl)ethanol with $SOCl_2$ and P_4O_{10} has been studied. In the reaction of *D,L*-1-(4-nitrophenyl)ethanol with $SOCl_2$ a mixture of 1-(4-nitrophenyl)-1-chloroethane, 1,1'-bis-(4-nitrophenyl)diethyl ether, and 4-nitrostyrene (yield 21%) has been formed. The direction of reaction of *D,L*-1-(4-nitrophenyl)ethanol with P_4O_{10} in toluene has been affected significantly by the order of reagents addition and the solution concentration. 4-Nitrostyrene has been obtained in the only case: the addition of P_4O_{10} to a diluted solution of *D,L*-1-(4-nitrophenyl)ethanol and subsequent refluxing. Also the procedure of 4-nitrostyrene preparation via the cleavage of 2-(4-nitrophenyl)ethyl nitrate with alkoxy anion in the alcoholic solution has been upgraded.

DOI: 10.1134/S1070363213100101

Nowadays several methods of 4-nitrostyrene preparation are known, for instance, decarboxylation of 4-nitrocinnamic acid in the presence of quinoline and copper powder at 160–165°C [1, 2] dehydrohalogenation of β-(4-nitrophenyl)ethyl bromide in the presence of triethanolamine [3], and the interaction of 2-(4-nitrophenyl)ethyl nitrate with alkaline reagents [5, 6]. However, the latter method has remained imperfect, being time-, energy-, and materials-consuming and giving only a crude product that requires purification. Other procedures to prepare 4-nitrostyrene have not been described so far. Therefore, development of new synthetic pathways to this compound as well as improvement of the existing procedures is an important task.

This work aimed at a study of *D,L*-1-(4-nitrophenyl)ethanol interaction with thionyl chloride and phosphorus(V) oxide and at an upgrading of the known method of 4-nitrostyrene preparation via the treatment of 2-(4-nitrophenyl)ethyl nitrate with alkoxy anion.

The starting 4-nitroacetophenone was reduced in ethanol or methanol, avoiding heating above 30°C;



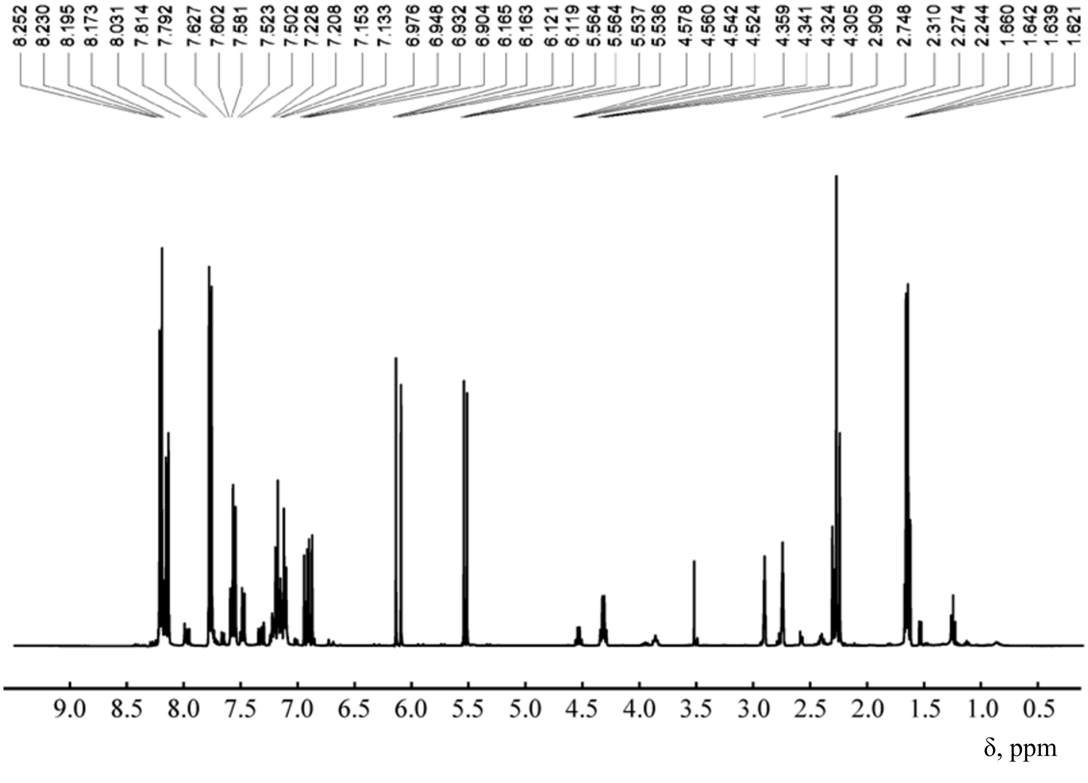
that gave nitroalcohol **II** in 93.8–100% yield without amine impurities. Further treatment of **II** with $SOCl_2$ gave a mixture of products **III**–**V**, the corresponding chloro derivative being the major one. After elimination of most part of minor 1,1'-bis-(4-nitrophenyl)-diethyl ether, we obtained a mixture containing about 21% of 4-nitrostyrene (^{1}H NMR).

In [4] 3-nitrostyrene was obtained with low yield via dehydration of 1-(3-nitrophenyl)ethanol with phosphorus(V) oxide in benzene solution. The amount of consumed P_4O_{10} and the reaction duration were not reported; the described procedures implied a set of technology cycles. In this work, the dehydration of *p*-isomer of nitroalcohol **II** was performed in toluene solution, thus the reaction temperature could be increased, whereas the reaction duration was shortened. In the case of P_4O_{10} addition to the diluted solution of 1-(4-nitrophenyl)ethanol and subsequent refluxing the dehydration became the major reaction pathway. After isolation of organic part and steam discillation of major part of starting nitroalcohol with admixture of 4-nitrostyrene, a mixture of products was obtained containing 60–70 mol % of 4-nitrostyrene. For the reaction to proceed smoothly, the solvent should be anhydrous.

From the ^{1}H NMR spectrum (see the Figure), the major component of the products mixture was 4-nitrostyrene. To the CH_2= protons corresponds the doublet of doublets at δ = 5.536–5.564 ppm, the vicinal proton at the double bond appeared as quartet at δ of 6.904–6.948 ppm., whereas the aromatic protons at the 2, 6 and 3, 5 appeared at doublets at 7.79, 7.81 ppm (J = 8.83 Hz) and 8.23, 8.25 ppm (J = 8.73 Hz), respectively.

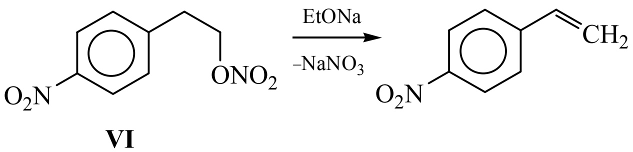
When the reagents were mixed without solvent, their interaction was faster, in particular, after a short induction period the exothermic decomposition of the reaction products occurred. If a certain amount of solvent with high boiling point was added to the mixture prior to the start of the uncontrolled reaction, it allowed for efficient heat exchange, and the process was fast but safe. Within 15–20 min of such reaction a mixture of products was obtained, however, containing only minor amount of 4-nitrostyrene. Its subsequent treatment with phosphorus(V) oxide under reflux during 5.5 h gave a solid complex compound, decomposition of it with water gave a mixture lacking 4-nitrostyrene.

As was discussed above, the method of 4-nitrostyrene production via nucleophilic cleavage of 2-



^{1}H NMR spectrum of the residue after volatile compounds after steam discillation.

(4-nitrophenyl)ethyl nitrate [6] was not perfect. The drawbacks of the method were as follows. The heterogeneous nature of the process slowed it down, additionally the reaction should be performed at 10–12°C (under cooling). The unreasonably slow addition of EtONa solution (during 1.5 h) and the long stirring after EtONa introduction (45 min) led to the total reaction time of 2 h 15 min. Furthermore, the decomposition of excessive EtONa in the reaction mixture was performed by treatment with CH_3COOH, the latter being added to the anhydrous mixture till pH 6; that resulted in the presence of acetic acid and sodium acetate in the crude product. Note that the salt could not be removed by filtration since it is dissolved and remained in the product after solvent evaporation. Then, the described procedure did not imply the removal of the residual amounts of the side product $NaNO_3$ after removal of its major part, that additionally decreased the yield. The losses were no less than 7.9–17% of the potential yield. Finally, the target product isolation by drying from the anhydrous mass led to considerable losses of 4-nitrostyrene and was time- and material-consuming.



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Thus, the discussed method could only give technical product, vacuum discillation of which gave the target compound in 81% yield.

After having significantly changed the procedure, we were able to prepare pure (^{1}H NMR) 4-nitrostyrene from 2-(4-nitrophenyl)ethyl nitrate. The yield of 4-nitrostyrene reached 100% and the yield of sifficiently pure by-product, alkali metal nitrate, was of 97.9–100%; the process duration was reduced to a minimum.

EXPERIMENTAL

The following chemicals were used: 4-nitroacetophenone (99.6%, mp 80°C), $NaBH_4$ (glanules, chemically pure grade or B grade according to TU 1-92-162-90), $CHCl_3$ (chemically pure grade, TU 6-09-4263-76). 2-(4-Nitrophenyl)ethyl nitrate was prepared as described in [7]. Diethyl ether was purified. Acetone was distilled, the fraction with bp of 56.3°C (760 mm Hg) was used. Anhydrous toluene was obtained by refluxing over Na, then it was treated with P_4O_{10} prior to use.

NMR spectra [δ, ppm: 8.031 (CDO) DMF-d_7; 7.283 $CDCl_3$] were registered using Bruker AVANCE II 400 spectrometer [^{1}H (400.1 MHz), ^{13}C (100.6 MHz)].

Preparation of *D,L*-1-(4-nitrophenyl)ethanol. In a 500 ml 2-neck flask equiped with a condenser a solution of 7.45 g (0.0451 mol) of 4-nitroacetophenone in 100 ml of methanol was prepared; then 2.0 g (0.0529 mol) of $NaBH_4$ was added to it at 20–30°C during 45 min, in small portions, at stirring. After 1 h, after the gas evolution stopped, the obtained mixtire was evaporated at a rotary evaporator to half of the initial volume, and then 50 ml of H_2O was added (temporary opacification was observed). The clear solution was extracted with chloroform (70 and 2×30 ml) and then with 20 ml of benzene. The solvent was evacuated from the combined extracts with rotary evaporator. Yield 7.07 g (93.8%), colored liquid.

D,L-1-(4-Nitrophenyl)ethanol was purified by discillation at 137.5–138°C (1–1.5 mm Hg). The product was a clear green-yellow fluid. ^{1}H NMR spectrum, δ, ppm: 1.44 d (3H, CH_3, J 6.5 Hz), 4.97–5.03 m (1H, CH, J 6.5 Hz), 5.58 d (1H, OH, J 4.3 Hz), 7.72 d (2H, 2,6-Ar, J 8.9 Hz), 8.25 d (2H, 3,5-Ar, J 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 26.40 (CH_3), 69.18 (CH), 124.37 (3,5-Ar), 127.58 (2,6-Ar), 147.72 (4-Ar), 156.65 (1-Ar).

Treatment of *D,L*-1-(4-nitrophenyl)ethanol with thionyl chloride. 3.28 g (0.0276 mol) of $SOCl_2$ was added to 3.87 g (0.0232 mol) of *D,L*-1-(4-nitrophenyl)-ethanol. After the initial vigorous reaction slowed down, the reaction mixture was heated at 70–85°C till gas evolution almost stopped, then 1.64 g (0.0138 mol) of $SOCl_2$ was added, the gas evolution stopped at this point, and the mixture became dark. The volatile components were removed in a vacuum, 4.44 g of dark liquid (partially crystallizing at cooling) was obtained. To thus obtained suspension, 25 ml of acetone was added, the precipitate was filtered off, washed with acetone, and dried in air. 0.06 g of 1,1'-bis-(4-nitrophenyl)diethyl ether was thus obtained. Then, the solvent was evaporated from the filtrate in a vacuum at heating, 4.0 g of colored liquid was obtained. After its keeping at –21°C, the precipitate was formed, it was filtered off, washed several times with acetone, and dried in air; 0.01 g of 1,1'-bis-(4-nitrophenyl)diethyl ether was thus obtained. Acetone was then evaporated from the filtrate at heating in ar vacuum, from the obtained colored liquid the precipitate of 1,1'-bis-(4-nitrophenyl)diethyl ether was formed after keeping at

23°C. The precipitate was filtered off, washed with small amount of acetone, and dried (0.04 g). The combined yield of 1,1'-bis-(4-nitrophenyl)diethyl ether was 0.11 g (3.7%), white crystalline compound, soluble in $CHCl_3$, sparingly soluble in $(CH_3)_2CO$ and DMF, and insoluble in H_2O. Found, %: C 59.34; H 5.26; N 8.63. $C_{16}H_{16}N_2O_5$. Calculated, %: C 60.75; H 5.10; N 8.86. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 d (6H, CH_3, *J* 6.5 Hz), 4.35 q (2H, CH, *J* 6.5 Hz), 7.48 d (4H, 2,6-Ar, *J* 8.5 Hz), 8.26 d (4H, 3,5-Ar, *J* 8.8 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 24.47 (CH_3), 74.86 (CH), 124.05 (3,5-Ar), 126.90 (2,6-Ar), 147.60 (4-Ar), 151.107 (1-Ar). ^{13}C NMR spectrum (DMF-d_7), δ_C, ppm: 24.09 (CH_3), 74.95 (CH), 124.05 (3,5-Ar), 127.63 (2,6-Ar), 147.63 (4-Ar), 152.35 (1-Ar).

The filtrate was vacuum-evaporated. 3.26 g of liquid was obtained of the following molar composition (^1H NMR): 21.0 (**V**), 72.8 (**III**), 6.2 (**IV**). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.87 d [3H, CH_3 (**III**), *J* 6.9 Hz], 5.15 q [1H, CH, (**III**) *J* 6.8 Hz], 7.61 d [2H, 2,6-Ar (**III**), *J* 8.6 Hz], 8.22 d [2H, 3,5-Ar (**III**), *J* 8.9 Hz], 5.52 d. d (1H, *cis*-H, *J* 10.9 Hz), 5.95 d. d (1H, *trans*-H, *J* 17.6 Hz), 6.80 q (1H, *vic*-H, *J* 10.9 hz), 7.55 d [2H, 2,6-Ar (**V**), *J* 8.6 Hz], 8.19 d [2H, 3,5-Ar (**V**), *J* 8.9 Hz].

Treatment of *D,L*-1-(4-nitrophenyl)ethanol with P_4O_{10}. *a*. 50.0 g (0.1761 mol) of P_4O_{10} was added to 21.53 g (0.1289 mol) of *D,L*-1-(4-nitrophenyl)ehtanol, the compounds were mixed, and 50 ml of anhydrous toluene was added. The obtained dense mass was crushed, 30 ml of anhydrous toluene was then added, and the mixture was vigorously stirred. After 5 min from the reaction start, the mixture was refluxed during 10 min at stirring, and then maintained during 6 min. Then, the mixture was heated up to boiling, cooled down, and decanted. The solid residue in the flask was twice extracted with 40 ml of toluene. The extracts were combined, and the solvent was evaporated in a vacuum. The solid residue was decomposed with water, the obtained emulsion was extracted with toluene, and the solvent was evaporated in a vacuum. The liquid residues were combined, water was added, and toluene admixture was distilled off with water. The residue was extracted with diethyl ether, the extract was dried over Na_2SO_4, and ether was evaporated in a vacuum. 24.18 g of brown liquid was obtained, not crystallizible at –21°C; it contained admixture of 4-nitrostyrene. 200 ml of anhydrous toluene and 80 g (0.2817 mol) of P_4O_{10} were then added to the liquid, and the mixture was refluxed during 5.5 h. The colorless solution was decanted from dark precipitate, and the obtained solid complex was decomposed with water. The so obtained emulsion was extracted with toluene, the solutions were combined and treated as described above. After removal of the volatile compounds, 23.58 g of non-crystallizible brown liquid was obtained, it contained traces of 4-nitrostyrene.

b. A mixture of 23.64 g (0.1416 mol) of *D,L*-1-(4-nitrophenyl)ethanol, 500 ml of anhydrous toluene, and 40.0 g (0.1409 mol) of P_4O_{10} was refluxed during 25 min, then the heating was stopped, and the solution was decanted. The precipitate was washed with 50 ml of anhydrous toluene, the extract was combined with the solution, and 60.0 g (0.2113 mol) of P_4O_{10} was added; at that point the yellowish color changed to orange-browm. The mixture was then refluxed during 1.5 h. The formed precipitate was decomposed by water; the solution was extracted with 55 ml of chloroform, then with 20 ml of benzene, and finally with 75 ml of chloroform. After the reaction was finished, the toluene solution was decanted, the precipitate was twice extracted with 100 ml of boiling toluene. All the extracts and organic solutions were combined, and the solvent was evaporated in a vacuum. The liquid residue was steam distilled; thus, 1 l of the distillate was obtained, then it was extracted with diethyl ether. After ether was evaporated in a vacuum, 2.17 g of *D,L*-1-(4-nitrophenyl)ethanol was obtained with admixture of 4-nitrostyrene. The distillation residue was extracted with diethyl ether, the extract was dried over $CaCl_2$, and the solvent was evaporated in a vacuum. 23.32 g of dark-orange liquid was obtained, crystallizing under cooling. 4-Nitrostyrene was isolated from it via fractional distillation in a vacuum. Yield 15.27 g (64.6%).

Preparation of 4-nitrostyrene from 2-(4-nitrophenyl)ethyl nitrate [8]. Solution of EtONa was prepared from 1.15 g of Na and 45 ml of anhydrous ethanol. That solution was added dropwise under stirring at 22–25°C to a solution of 10.608 g (0.050 mol) of 2-(4-nitrophenyl)ethyl nitrate in 160 ml of anhydrous ethanol. 4/5 of the EtONa solution was added within 20 minutes, the rest was added in portions; after addition of a portion, pH went up to 8; each next portion was added when pH was back at 7. After addition of all EtONa, the mixture was kept for 0.5 h at cooling, and then its pH (8–8.5) was adjusted to 6 by adding concentrated HCl dropwise. The precipitate was filtered off, washed with ethanol, and dried in air. Thus 3.83 g of $NaNO_3$ was obtained. Ethanol was evacuated from the filtrate at rotary evaporator. The residue (orange liquid containing inorganic precipitate) was dissolved in diethyl ether, $NaNO_3$ was filtered off, the precipitate was washed with diethyl ether and combined with the major part after drying. Ether was evacuated from the filtrate at rotary evaporator at 50°C, and then by keeping at the residual pressure of 3 mm Hg. Yield 7.45 g (100%) of 4-nitrostyrene in the form of yellow liquid crystallizing at cooling. ^1H NMR spectrum, δ, ppm: 5.57 d. d (1H, *cis*-H, *J* 10.9 Hz), 6.16 d. d (1H, *trans*-H, *J* 17.7 Hz), 6.95 q (1H, *vic*-H, *J* 10.9 Hz), 7.83 d (2H, 2,6-Ar, *J* 8.8 Hz), 8.26 d (2H, 3,5-Ar, *J* 8.9 Hz).

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