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Catalytic Liquid-Phase Reduction of Aromatic Nitro Compounds Containing Highly Reactive Functional Groups

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Abstract—Improved procedures have been proposed for fast and selective hydrogenation of aromatic nitro compounds with the goal of obtaining practically important amines.

We have studied the effects of catalyst nature, solvent, temperature, reactant concentration, and various additives on the hydrogenation of aromatic nitro compounds containing highly reactive functional groups and fragments, namely chlorine atom, cyano, hydroxy, ether, ester, and carbonyl groups, amide and sulfamide bonds, and pyrazolone ring. The goal of the study was to find conditions ensuring high selectivity of the process. The subjects for study were nitroarenes which are used as starting compounds in the synthesis of practically important aromatic amines: 2-(3-amino-4-chlorobenzoyl)benzoic acid (**I**), 3-(3-aminobenzamido)-1-(2,4,6-trichlorophenyl)-4,5-dihydropyrazol-5-one (**II**), 1-(2,4,6-trichlorophenyl)-3-(2-chloro-5-aminoanilino)-4,5-dihydropyrazol-5-one (**III**), ethyl (4-aminobenzoyl)cyanoacetate (**IV**), *N*-(3-amino-4-chlorophenyl)-4-(2,4-di-*tert*-pentylphenoxy)butanamide (**V**), *N*-[4-(2,4-di-*tert*-pentylphenoxy)butyl]-4-(4-aminophenoxy)-1-hydroxy-2-naphthalenecarboxamide (**VI**), *N*-[3,5-bis(methoxycarbonyl)phenyl]-3-amino-4-chlorobenzenesulfonamide (**VII**), *N*-(3-amino-4-chlorophenyl)-4,4-dimethyl-3-oxopentanamide (**VIII**), and *N*-(3-amino-4-chlorophenyl)-1-hydroxy-2-naphthalenecarboxamide (**IX**). Amino compounds **I**–**IX** are intermediate products in the synthesis of anthraquinone dyes (amino acid **I**) and materials for color photography (**II**–**IX**). They are usually prepared by reduction of the corresponding nitro compounds with iron, iron and tin salts in acid medium [1, 2], or molecular hydrogen over Raney nickel in the liquid phase [3]. However, this catalyst does not ensure high selectivity in the reduction of halogen-containing nitro compounds: As a rule, the process is accompanied by hydrodehalogenation, so that addition of appropriate inhibitors is necessary.

The nitro and amino compounds under study were divided into two groups. The first of these includes carboxylic and CH acids which are soluble in aqueous solutions of salts and alkalies, and the second group included compounds soluble in organic solvents.

We have examined the reduction of 2-(4-chloro-3-nitrobenzoyl)benzoic acid in a 5% aqueous solution of sodium hydroxide in the presence of Raney nickel, 0.8% Pd/Al_2O_3, and 0.5% Pt/Al_2O_3. The degree of hydrodehalogenation was 46, 3, and 0.4%, respectively, the conversion of the nitroarene being complete. Therefore, the platinum catalyst was selected for further studies. We have found that hydrogenation in an aqueous solution of sodium carbonate is more advantageos: The resulting amine is formed in a larger yield and with higher purity, the rate of the process increases, and the activity of the catalyst is retained throughout 3–4 series against one series in aqueous alkali. Increase in the concentration of sodium carbonate from 5 to 20% accelerates the hydrogenation process, presumably due to enhanced adsorption of the initial nitro compound from more basic medium. As a result, we proposed an improved procedure for synthesizing the target amino compound [4, 5], which ensures high rate of the process and its selectivity (Table 1).

In the reduction of 3-(3-nitrobenzamido)-1-(2,4,6-trichlorophenyl)-4,5-dihydropyrazol-5-one and 1-(2,4,6-trichlorophenyl)-3-(2-chloro-5-nitroanilino)-4,5-dihydropyrazol-5-one we tried as solvents aqueous solutions of ammonia, sodium carbonate, and sodium hydroxide with various concentrations. In the synthesis of compound **II** the best results were obtained using 0.5% Pt/Al_2O_3 as catalyst in aqueous sodium carbonate. Raising the concentration of Na_2CO_3 from 10 to 20% increases the rate of hydrogenation by a factor of 1.8–2.2. The hydrogenation of 1-(2,4,6-trichlorophenyl)-3-(2-chloro-5-nitroanilino)-4,5-dihydropyrazol-5-one in aqueous ammonia and aqueous

Table 1. Synthesis of amino compounds in aqueous solutions of sodium carbonate and sodium hydroxide in the presence of 0.5% Pt/Al_2O_3 as catalyst

Product no.	Solvent	Reaction conditions[a]	Yield, %
I	Na_2CO_3 (10–20%)–H_2O	60–80°C, p_{H_2} = 2–4 MPa, c_0 = 0.8–1.0 M, γ = 2–4	96–98
II	Na_2CO_3 (10–20%)–H_2O	60–80°C, p_{H_2} = 1–3 MPa, c_0 = 0.3–0.6 M, γ = 3–5	97–99
III	NaOH (3%)–H_2O	80°C, p_{H_2} = 2–3 MPa, c_0 = 0.1–0.2 M, γ = 7	87–91
IV	Na_2CO_3 (5–8%)–H_2O	20–35°C, p_{H_2} = 0.5–2 MPa, c_0 = 0.4–0.8 M, γ = 3–7	98–99

[a] c_0 is the concentration of initial nitroarene; γ is the concentration of the catalyst (wt % relative to nitroarene).

sodium carbonate was very slow because of the poor solubility of nitro and amino compounds. The reaction rate increases in going to aqueous sodium hydroxide. The concentration of alkali strongly affects the yield and purity of the product. In 7% aqueous sodium hydroxide the complete conversion of the nitro compound was attained in 0.5 h, and the hydrogenation product contained 78–80% of the main substance. In 3% aqueous NaOH the yeild of the target product was 87–91% (Table 1), and its purity was 98–99%. Our results indicate that the selectivity of the process is determined mainly by the nature of the catalyst. The hydrogenation over 0.8% Pd/C was accompanied by partial hydrodehalogenation (8–10%); in the presence of 2% Pd/Al_2O_3 complete reductive dehalogenation was observed (according to the ^1H NMR data). We thus proposed new procedures for the synthesis of amines **II** [6] and **III**. The optimal conditions are given in Table 1.

The hydrogenation of ethyl (4-nitrobenzoyl)cyanoacetate can be accompanied by reduction of the cyano group. When the reaction was performed over Raney nickel in alcoholic ammonia above 35°C, the yield of the target product was as low as 60%. In the presence of platinum catalyst in 10% aqueous sodium hydroxide no hydrogen absorption was observed. Presumably, in this case decomposition of the initial nitro compound occurs to give lower cyano derivatives which inhibit the hydrogenation process. The reaction was fast in aqueous sodium carbonate at a molar ratio of the nitro compound and Na_2CO_3 of 1 : 1.0–1.5. Raising the sodium carbonate concentration reduces the reaction rate, and complete conversion of the substrate is inattainable. The optimal conditions for the synthesis of ester **IV** [7] are given in Table 1; they ensure 98–99% yield of the product.

As noted above, the second group of substrates includes nitro compounds which are soluble in alcohols, aromatic hydrocarbons, and aprotic solvents. The hydrogenation of *N*-(4-chloro-3-nitropheny)-4-(2,4-di-*tert*-pentylphenoxy)butanamide was carried out in toluene and 2-propanol over 0.5% Pt/Al_2O_3 at 80–110°C and hydrogen pressure 2–4 MPa; the reaction time was 4–5 h. The reaction rate in toluene was 1.3–1.5 times higher than in 2-propanol. By adding aliphatic amines (triethylamine, 2-aminoethanol, etc.) we succeeded in reducing the temperature, and the target amine was obtained in 93–95% yield in 1.5–2 h (Table 2).

N-[4-(2,4-Di-*tert*-pentylphenoxy)butyl]-1-hydroxy-4-(4-nitrophenoxy)-2-naphthalenecarboxamide was hydrogenated over 2% Pd/Al_2O_3, 3% Pt/C, and 0.5% Pt/Al_2O_3. The reduction rate in toluene and 2-propanol was high in the presence of the first two catalysts. However, the process was accompanied by hydrogenation of the ether moiety. The mass spectra of the products contained the molecular ion peak of amine **VI** (*m*/*z* 582) and its fragmentation products and also the molecular ion peak of *N*-[4-(2,4-di-*tert*-pentylphenoxy)butyl]-1-hydroxy-2-naphthalenecarboxamide (*m*/*z* 475). No by-products were detected when the hydrogenation was performed over 0.5% Pt/Al_2O_3, but the reaction time was 5–7 h. Addition of an aliphatic amine (2–4 wt % of the nitro compound) increases the reaction rate 2–2.5-fold. The conditions are given in Table 2.

We examined the effect of the solvent nature on the reduction of *N*-[3,5-bis(methoxycarbonyl)phenyl]-4-chloro-3-nitrobenzenesulfonamide with molecular hydrogen in the presence of 0.5% Pt/Al_2O_3. The reaction in aliphatic alcohols gave mixtures of the target amine and the corresponding arylhydroxylamine whose yield attained ~43–46%. With dimethylformamide as solvent, the reaction was slow, and it stopped when 2/3 of the theoretical amount of hydrogen was absorbed. The corresponding arylhydroxylamine was isolated in 88–92% yield. This fact may be explained by the low rate of decomposition of arylhydroxylamine in alcohols and DMF. The rate of hydrogenation was satisfactory in a 10% aqueous

Table 2. Synthesis of amino compounds in organic solvents in the presence of 0.5% Pt/Al_2O_3 as catalyst

Product no.	Solvent	Reaction conditions[a]	Yield, %
V	Toluene, *i*-PrOH, amine (2–4%)	60–90°C, p_{H_2} = 2–4 MPa, c_0 = 0.3–0.5 M, γ = 3–7	93–95
VI	Toluene, *i*-PrOH, amine (2–4%)	80–90°C, p_{H_2} = 2–3 MPa, c_0 = 0.4–0.5 M, γ = 7–10	90–92
VII	Acetic acid	90–100°C, p_{H_2} = 2–3 MPa, c_0 = 0.03–0.05 M, γ = 3–7	94–96
VIII	Toluene, *i*-PrOH	80–90°C, p_{H_2} = 4 MPa, c_0 = 0.2–0.4 M, γ = 10	89–95
IX	DMF	80–90°C, p_{H_2} = 3–4 MPa, c_0 = 0.3–0.5 M, γ = 5–7	93–95

[a] c_0 is the concentration of initial nitroarene; γ is the concentration of the catalyst (wt % relative to nitroarene).

Table 3. Melting points, IR spectra, and elemental analyses of amines **I–IX**

Comp. no.	mp, °C	IR spectrum, ν, cm^{-1}	Found, %				Formula	Calculated, %			
			C	H	Cl	N		C	H	Cl	N
I	169–171	1555, 1718, 2510, 3430	60.90	3.53	12.69	5.23	$C_{14}H_{10}ClNO_3$	60.98	3.63	12.89	5.08
II	286–287	1679, 3301, 3472	48.17	2.67	26.89	13.95	$C_{16}H_{11}Cl_3N_2O_4$	48.29	2.77	26.79	14.08
III	237–238	1563, 1648, 3295, 3300, 3500	44.80	2.40	35.00	13.62	$C_{15}H_{10}Cl_4N_4O$	44.54	2.48	35.14	13.86
IV	141–142	1245, 1532, 1676, 1748, 2229, 3410	59.81	5.59	–	12.55	$C_{11}H_{12}N_2O_3$	60.04	5.45	–	12.73
V	113–114	1650, 3294, 3485	70.34	8.30	8.15	6.21	$C_{26}H_{37}ClN_2O_2$	70.18	8.32	7.99	6.30
VI	129–130	1018, 1198, 1279, 1700, 3280, 3478, 3608	76.20	7.68	–	4.69	$C_{37}H_{46}N_2O_4$	76.28	7.90	–	4.81
VII[a]	223–225	1247, 1570, 1738, 3401	48.10	3.67	8.84	6.91	$C_{16}H_{15}ClN_2O_6S$	48.18	3.76	8.91	7.03
VIII	108–110	1565, 1716, 3305, 3499	57.96	6.26	13.06	10.34	$C_{13}H_{17}ClN_2O_2$	58.08	6.33	13.22	10.42
IX	209–211	1209, 1602, 3487, 3612	65.17	4.06	11.15	8.82	$C_{17}H_{13}ClN_2O_2$	65.28	4.16	11.36	8.96

[a] Found S, %: 8.05; calculated S, %: 8.03.

solution of sodium carbonate, but the process was accompanied by hydrolysis of the ester moiety. As a result, *N*-(3,5-dicarboxyphenyl)-3-amino-4-chlorobenzenesulfonamide was obtained in quantitative yield. The target amine was isolated in 94–96% yield when the reaction was carried out in acetic acid (Table 2). In this case neither accumulation of arylhydroxylamine nor elimination of the halogen atom was observed.

The high rate and selectivity of hydrogenation of *N*-(4-chloro-3-nitrophenyl)-4,4-dimethyl-3-oxopentanamide were observed in toluene and 2-propanol in the presence of 0.5% Pt/Al_2O_3 as catalyst. The yield of amine **VIII** was 89–91% (Table 2); it contained ~99% of the main substance, according to the potentiometric titration data. Amine **IX** and the corresponding nitro compound are sparingly soluble in aqueous alkalies, aliphatic alcohols, and aromatic hydrocarbons and are readily soluble in DMF. The reduction in DMF was not accompanied by dehalogenation, and its rate was sufficiently high (Table 2).

The melting points, IR spectra, and elemental analyses of amines **I**–**IX** are given in Table 3.

EXPERIMENTAL

The IR spectra were recorded in the region 400–4000 cm^{-1} on a Specord M-80 spectrometer in mineral oil. The elemental compositions were determined on a CHN-1 analyzer. The platinum and palladium catalysts were prepared by impregnating appropriate supporting material with solutions of chloroplatinic acid or palladium(II) chloride, following the procedure described in [8]. The hydrodehalogenation products were quantitated indirectly, by analysis for chloride ion [9]. Arylhydroxylamines were determined by potentiometric titration with a solution of sodium nitrite according to [10].

Synthesis of amines I–IX. The reactions were carried out in a 200-cm^3 Vishnevskii high-pressure reactor equipped with a jacket. The reaction mixtures were stirred at 2800 rpm, and the hydrogen pressure was 0.5–4 MPa. The volume of the reaction mixture was 100 cm^3. The pressure inside the reactor was maintained constant with the aid of a set of receivers. The reactions were continued until hydrogen was no longer absorbed; its volume was measured using a calibrated burette. When the reaction was complete, the mixture was cooled, the catalyst was separated by filtration, the filtrate was acidified with 50% acetic acid to pH 4–5, and the precipitate was filtered off and dried (amines **I**–**IV**). In the other cases, the filtrate was evaporated, and the residue was poured into hexane (compounds **V** and **VI**) or water (**VII**–**IX**).

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