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ScienceDirect

Resource-Efficient Technologies 2 (2016) 215–224

www.elsevier.com/locate/reffit

Review article

Resource-efficient technology to produce 4-aminodiphenylamine

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Received 6 July 2016; received in revised form 25 October 2016; accepted 27 October 2016

Abstract

A critical analysis of the existing and emerging methods for preparation of 4-aminodiphenylamine has been conducted. It is noted that, in economic and environmental terms, the promising methods are based on condensation of aniline with nitrobenzene in an alkaline medium, followed by hydrogenation of the resulting intermediates. Using the above method for industrial production of 4-ADPA will help eliminate principal shortcomings inherent in the existing industrial methods: reduce unit operations of the process, use more accessible, inexpensive raw materials, increase product yield, eliminate formation of carcinogenic substances, significantly decrease the formation of waste products and, most importantly, decrease the volume of waste water. The most promising methods for industrial production are recent discoveries that use heterogeneous catalysts during condensation of aniline with nitrobenzene, e.g., zeolite ZSM-5 treated with tetramethylammonium hydroxide or highly basic anions which considerably simplify production technology and process control, lower costs and comply with strict environmental requirements.

Keywords: 4-Aminodiphenylamine; 4-Nitrodiphenylamine; 4-Nitrosodiphenylamine; Aniline; Nitrobenzene; Condensation reaction

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1. Introduction

4-Aminodiphenylamine (4-ADPA) is an intermediate product in the preparation of its alkylated derivatives that were used as antiozonants, antioxidants and stabilizers for monomers and various polymeric materials [1].

Currently, 4-ADPA is obtained based on technologies differing in the feedstocks, the registration of individual process stages, etc. Given the scope of production of 4-ADPA as well as its practical importance for the production of amine stabilizers, this paper includes a brief analysis of the existing methods for its preparation and attempts to identify promising methods which are most appropriate for practical implementation in production.

Depending on the feedstock choice, there are several methods for preparation of 4-ADPA (see Fig. 1).

- The reaction of aniline with *p*-nitrochlorobenzene followed by reduction of 4-nitrodiphenylamine (4-NO_2DPA) (see Fig. 1, method 1) [2]. During condensation stage, a variety of compounds of transition metals, preferably Cu [2] complex compounds, are proposed as catalysts. In recent years, researchers paid close attention to the Buchwald–Hartwig amination, wherein the reaction of aryl halides with amines forms a new C—N bond catalysed by Pd complexes [3,4]. The hydrogenation stage is carried out in the liquid phase in the presence of 0.1–0.3% mass (wt.) of catalyst (Ni, Co, Ru, Pd, Pt) at 50–100 °C and at elevated pressure.
- The reaction of aniline or formanilide with *p*-nitrochlorobenzene (method 2) in the presence of K_2CO_3 and metallic Cu, Al, Mg, Zn [5]. Using *p*-nitrochlorobenzene as a raw material during the condensation stage results in the formation of waste products containing transition metal chlorides and HCl and, hence, leads to additional costs for recycling of the same.
- Reduction of 4-nitrosodiphenylamine (4-NODPA) (method 3) in solution phase with Pd, Pt, Ni, Re, Rh, Ru catalysts at 50–75 °C and pressure of 7–35 bar [6].
- Reduction of 4-anilinazobenzole (method 4) [7]. This method does not ensure high yields or good product quality: technical 4-ADPA yield does not exceed 45–80%, and the insoluble residue content reaches 20%. Alternatively, 4-ADPA can be produced from diphenylamine, which includes stages of nitrosation, rearrangement, azo coupling and hydrogenation (method 5) [8]. The main disadvantage of

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http://dx.doi.org/10.1016/j.reffit.2016.10.011

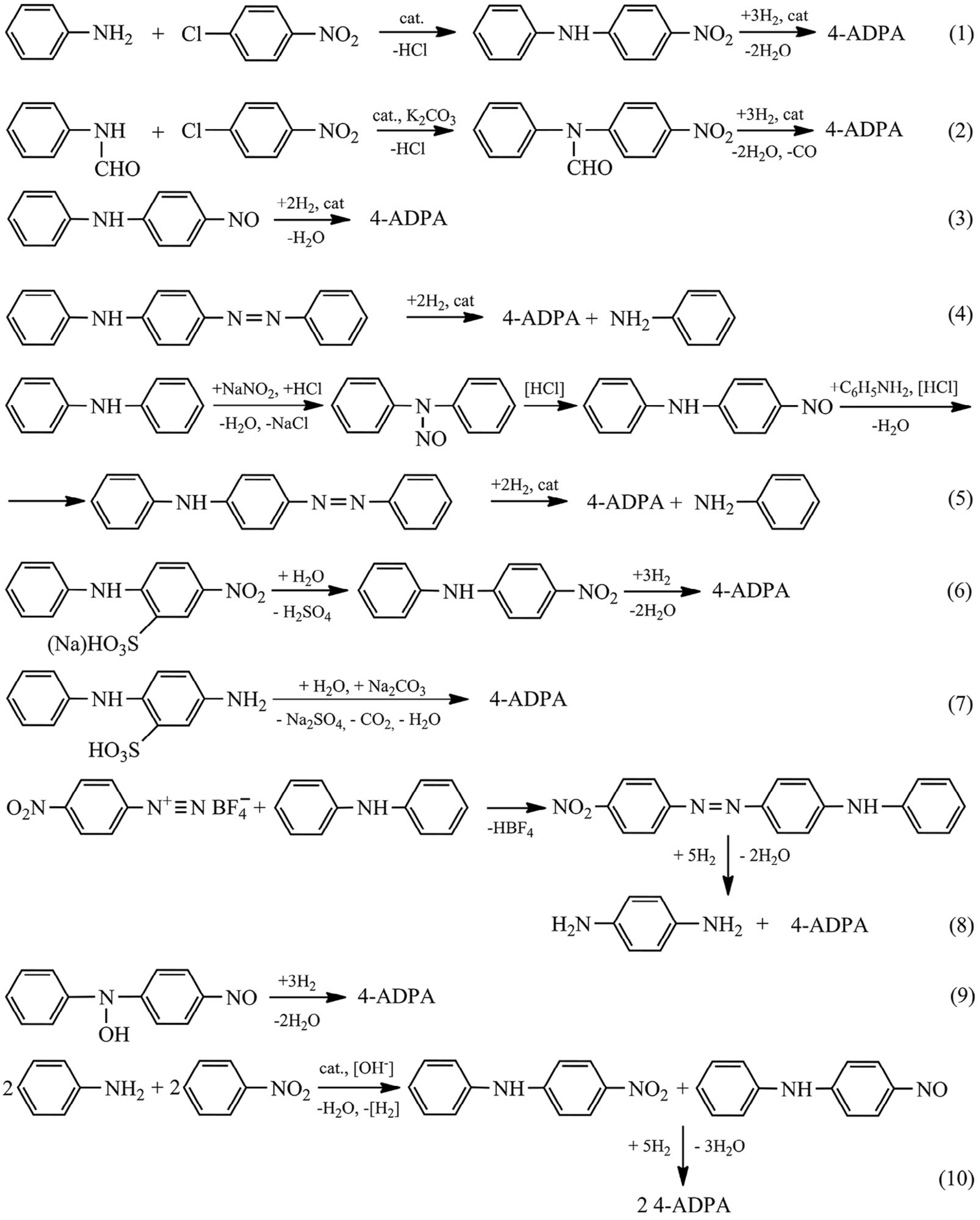

Fig. 1. Methods of preparation of 4-ADPA.

the latter method is its multiple stages and a significant amount of waste water produced.

- Hydrolysis of 4-nitrodiphenylamine-2′-sulphonic acid followed by reduction of 4-NO_2DPA (method 6) or hydrolysis of 4-aminodiphenylamine-2′-sulphonic acid (method 7) [9]. The main disadvantage of such a method is the formation of large amounts of acidic waste water and the use of expensive raw materials.
- Azo coupling of 4-nitrophenyldiazonium with 4-diphenylamine, followed by hydrogenation of the formed azo compounds (method 8) [10]. This method is not economically feasible because it requires expensive starting reagents and organic solvents.
- Hydrogenation of *p*-nitrosophenylhydroxylamine (method 9) [11]. This method is rather simple to carry out but requires specific raw materials.

The industrial synthesis of 4-ADPA used in several countries based on chemical reduction of 4-NODPA with sulphur compounds is not profitable due to the high cost of nitroso compounds, multi-stage production, and heavy use of environmentally hazardous reducing agents. Technical 4-ADPA obtained by reduction of 4-NODPA with sulphides contains the unwanted and difficult to remove sulphur compounds. The impurities are a mixture of inorganic sulphur compounds (sulphides) and free sulphur, although some organic substances, e.g. aryl mercaptans, may be present as well [9]. These sulphur impurities prevent 4-ADPA from being used in a number of industrial processes.

The need to improve the technology of production of rubber chemical stabilizers is due partly to the demands of the industry associated with intensification of polymer processing and higher performance standards for the materials and products made therefrom. This need is also motivated by the tightening of chemical hygiene requirements, changes in the raw materials base of synthetic stabilizers, and changing market conditions. Development of the production of amine-derived stabilizers depends on the price and availability of raw materials. Therefore, there is a tendency to transition from the naphthyl- and diphenylamine-based stabilizers to the derivatives of aniline, the cheapest aromatic amine.

Currently, scientists and engineers are actively developing new methods for producing 4-ADPA by the aniline and nitrobenzene (NB) reaction in an alkaline medium to produce mixtures of salts, 4-NO_2DPA and 4-NODPA. Hydrogenation of the latter leads to the formation of 4-ADPA (method 10). This general method was first described by Stern and associates in 1992 [12,13].

2. The use of raw materials in the preparation of 4-aminodiphenylamine

As an indicator characterizing the environmental and economic efficiency of a particular technology the index of raw material use ($\boldsymbol{I}_{RMU}$) can be employed, where $\boldsymbol{I}_{RMU}$ is the ratio of the mass of the desired product (kg) to the mass of the raw materials expended in its production (kg). There is a theoretical $\boldsymbol{I}_{RMU,\ t}$ and practical $\boldsymbol{I}_{RMU,\ pr}$. $\boldsymbol{I}_{RMU,\ pr}$ takes into account the consumption of raw materials and auxiliary materials of the actual production and $\boldsymbol{I}_{RMU,\ t}$ takes into account the consumption of raw materials by the reaction stoichiometry. The value of $\boldsymbol{I}_{RMU,\ pr}$ reflects the amount of production waste which has to be disposed of during production of 1 kg of the desired product. Table 1 provides values of $\boldsymbol{I}_{RMU,\ t}$ and $\boldsymbol{I}_{RMU,\ pr}$ for the methods described above.

As evidenced from Table 1, methods 3, 9 and 10 have the highest values of $\boldsymbol{I}_{RMU,\ t}$ and $\boldsymbol{I}_{RMU,\ pr}$. The main product formed by the main reaction and subject to disposal in methods 3, 9 and 10 is water, a non-toxic material, easy to clean from impurities. However, expensive and not readily available feedstock used in methods 3 and 9 makes such methods uncompetitive compared to method 10, which allows large capacity and uses inexpensive intermediates for organic synthesis. Thus, to date, the most resource-efficient and environmentally safe technology for preparing 4-ADPA is the technology based on using aniline and NB as a feedstock.

Table 1
Values of $\boldsymbol{I}_{RMU,\ t}$ and $\boldsymbol{I}_{RMU,\ pr}$ in various methods for preparation of 4-ADPA.

Method	$\boldsymbol{I}_{RMU,\ t}$	Yield, %	$\boldsymbol{I}_{RMU,\ pr}$[a]	References
1	0.717	79–91	0.57–0.65	[2]
		97	0.70	[3]
		90–97	0.65–0.7	[4]
2	0.647	90–94	0.58–0.61	[5]
3	0.911	65–99	0.59–0.90	[6]
4	0.664	45–80	0.30–0.53	[7]
5	0.661	88	0.58	[8]
6	0.579	85–90	0.49–0.52	[9]
7	0.474	94	0.45	[9]
8	0.442	76	0.34	[10]
9	0.836	97.5	0.82	[11]
10	0.836	93–96	0.78–0.80	[12]

[a] $\boldsymbol{I}_{RMU,\ pr} = \boldsymbol{I}_{RMU,\ t} \cdot$Yield (%)/100.

3. Methods of production of 4-aminodiphenylamine and aniline from nitrobenzene

Monsanto Company (US) provided methods for preparing 4-ADPA intermediates by reaction of aniline with NB in the presence of bases in aprotic solvents, with a controlled amount of a protic solvent [14,15]. As bases, they used alkali hydroxides, alkoxides, hydrides and quaternary ammonium hydroxides with alkyl- and aryl substituents as well as alkyl-substituted diammonium hydroxides. It was demonstrated that a high yield of the reaction products and a highly-selective process could only be achieved using quaternary ammonium hydroxides (preferably tetramethylammonium hydroxide, TMAH). As solvents, they used aniline, NB, dimethylsulphoxide, dimethylformamide, *N*-methylpyrrolidone, pyridine, toluene, hexane, ethylene glycol dimethyl ether, diisopropylethylamine and mixtures thereof.

Studies have shown that the presence of a protic solvent (water) in the reaction system has a great influence. The optimum amount of water should not exceed 4 vol.%; otherwise, the NB conversion decreases and the by-product output (azobenzene and phenazine) increases. To control the water content in the reaction system they used azeotropic distillation of water with aniline under reduced pressure and desiccants. Anhydrous sodium sulphate or calcium chloride, anhydrous bases, molecular sieves, and so forth were considered as desiccants. Adding desiccants increased the NB conversion and the output of intermediates but, in some cases, they also increased the output of azobenzene and phenazine. The effect of the aniline/NB ratio has been studied. It was demonstrated that the higher the ratio, the greater yield of 4-NODPA, compared to 4-NO_2DPA, and the lower the yield of azobenzene. The catalytic hydrogenation was carried out in an aniline medium with the addition of water, using a hydrogenation catalyst from the group of Pt/C, Ni/SiO_2, Ni/$Al_2O_3 \cdot SiO_2$ or Raney nickel.

The disadvantage of using quaternary ammonium hydroxides is their low stability in concentrated form and their low thermal stability at temperatures above 70 °C. Therefore, in each cycle, there is a serious technical problem in isolating and recycling quaternary ammonium bases for the next production cycle. It leads to accumulation, in the reaction mixture, of decomposition products of the catalyst and to decreased activity of the catalyst system.

In the U.S. patent [16], the reaction of aniline with NB was carried out in the presence of water (25–80 mass (wt.) %). After adding NB, the reaction was maintained for 4 hours with continuous distillation of the azeotropic mixture of aniline and water. After hydrogenation, toluene was added, and filtration of the catalyst took place followed by separation of the organic and aqueous phases. The aqueous phase may be returned to the reaction as it contains up to 99.7% TMAH. Since in Ref. [16] the repeated cycles of coupling and hydrogenation reactions are not described, the reactivity of the recovered base is actually unknown. The main disadvantages of this method are as follows: large quantities of aromatic solvent are involved; the need for regeneration of the solvent and catalyst solution; the lengthy process duration (about 11 hours); low yields of 4-ADPA, 92% based on the loaded NB.

The researchers of Flexsys America, L.P. (USA), suggested a more cost-effective approach which provides for recirculation of the base, aniline, and hydrogenation catalyst by adjusting the amount of water relative to the amount of the base (to ensure optimum molar ratio of the loaded water to the loaded base) [17]. It was established that if, by the end of the condensation reaction, too little water is left, it leads to decomposition of the base. The minimum amount of water relative to base, as required for protection of the base, depends on the nature of the base used, since TMAH and the related compounds, e.g., carbonates, are distinguished by high heat resistance. On the other hand, too little water left at the end of the reaction decreases the yield of the desired condensation products, indicating that the molar ratio of water to base is an important parameter of the process and requires appropriate controls. It should be noted that the use of a co-catalyst (e.g., activated charcoal) in the process of hydrogenation of the condensation products helps hydrogenate azobenzene to aniline, which may be further separated and returned to the cycle.

The associates of Sinorgchem Co., Ltd. (China) [18–22] proposed a principal flow chart (see Fig. 2) which includes five process stages as follows: (1) condensation of aniline with NB; (2) hydrogenation of the condensation products; (3) the stage of separating a complex base catalyst and hydrogenation catalyst from the products of hydrogenation; (4) hydrogenation stage of hydrogenation solvent and aniline; (5) purification stage of crude (technical) 4-ADPA.

In the condensation reaction, which lasts from 3.5 to 6 hours, the molar ratio of NB to aniline may vary from 1:1 to 1:15. The temperature of the Sinorgchem reaction is 50–90 °C. As the main catalyst, they use a mixture of TMAH, alkali metal hydroxide, and tetraalkylammonium salt. The effect of water content on the process of condensation is decreased by using tetraalkylammonium salts. The condensation is carried out in a film type reactor in which the yield and selectivity have higher values than in a continuous stirred reactor. The only disadvantage of this method is the use of thermally unstable quaternary ammonium compounds as components of a complex base catalyst of the condensation stage. (Over)heating the reaction mixture above 80 °C leads to a significant acceleration of catalyst decomposition, formation of by-products, and decreased selectivity of the condensation and hydrogenation processes.

In the patent [23], at the stage of condensation of aniline with NB, it is suggested to use a mixture which contains a strong organic base and the oxidizing agent hydrogen peroxide, in the amount of 0.01–0.6 mol per mole of NB. Hydrogen peroxide is added to accelerate the transition (oxidation) of a Meisenheimer complex to 4-NO_2DPA and 4-NODPA. Additionally, the presence of peroxide results in decreased yields of azobenzene, which helps return aniline to recycling without a tedious purification procedure.

In the previous work [24], preparation of intermediates for the synthesis of 4-ADPA was carried out in the presence of a mixture which contains a strong base and a phase transfer catalyst selected from the group of compounds defined by the formula $\left[(R_4)_e - Y(Z)_d - (R_1R_2R_3N^+)\right]_c X_b^{-a}$, where R_1, R_2, R_3 = any alkyl group with a straight or branched chain from C_1 to C_{20}; $(R_4)_e$ – hydrogen, for $e = 0$, and $R_1R_2R_3N^+$, for $e = 1$ or 2; Y = alkyl, aryl, alkylaryl or benzyl and substituted derivatives thereof; Z = substituent selected from the group consisting of hydroxyl, halo, and other heteroatoms; X = the anionic moiety in the form of fluoride, chloride, hydroxide, sulphate, etc., where a = valence of the anionic moiety (1, 2 or 3), b and c are integers with a value of 1, 2 or 3; d = a whole number with a

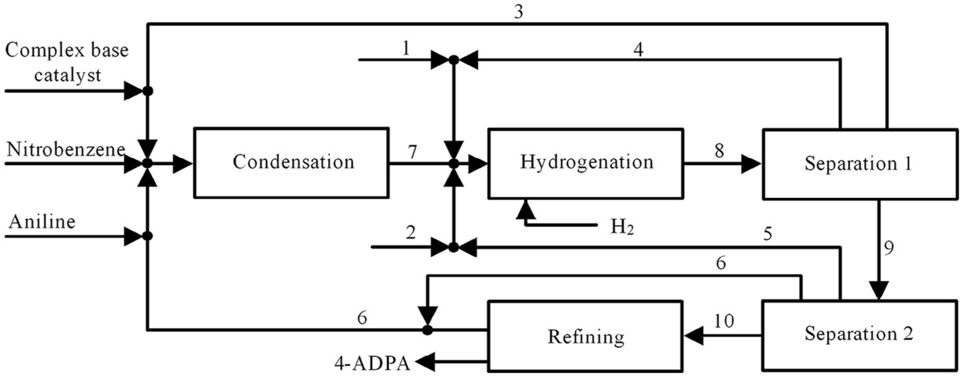

Fig. 2. Flow chart of the process for obtaining 4-ADPA. 1. Powdery hydrogenation catalyst; 2. Solvent for the hydrogenation step; 3. Recycle complex base catalyst; 4. Recycle partially-restored powdered hydrogenation catalyst; 5. Recycle solvent from the hydrogenation stage; 6. Return aniline; 7. Reaction mixture after the condensation stage; 8. Reaction mixture after the hydrogenation stage; 9. Aqueous phase obtained by evaporation during concentration and organic phase; 10. Crude 4-ADPA.

value from 0 to 4. In these cases, the strong base and phase transfer catalyst may be the same or different.

In the patents [25,26], the inventors describe a method for obtaining intermediates 4-NO_2DPA and/or 4-NODPA (and/or their salts) by reaction of aniline with NB (the aniline to NB ratio varied from 6.4:1 to 9.4:1) in a liquid medium at a temperature of 50–130 °C. Additionally, the process was conducted under atmospheric or reduced pressure, under an inert gas atmosphere or in the presence of atmospheric oxygen. As a reaction system, they used a solution of salts of zwitterions with hydroxides of the general formula $OH^{-}\left[\left(R_1R_2R_3N^{+}\right)-CHR_4-\left(CH_2\right)_x-Y^{-}\right]Z^{+}$, where preferably R_1, R_2, R_3 = methyl, R_4 = hydrogen, $x = 0$, Y = COO^{-}, Z^{+} represents a cation of potassium and/or a cation of tetraalkylammonium with the number of carbon atoms in the alkyl chain from 1 to 4. According to the authors, the proposed reaction system is technically more easily accessible and more stable than quaternary ammonium and alkyl diammonium hydroxides, and there is a possibility for its regeneration. At the same time, the reaction of aniline with NB is selective with respect to 4-NO_2DPA and/or 4-NODPA, with a high yield of the prepared 4-ADPA. Notably, high yields of the intermediate products (93–94% per introduced NB) could be obtained in the event of azeotropic distillation of water from the reaction zone.

In Russia, studies also continue in this field [27–29]. For example, in patent [27], work was conducted to reduce flow times of the basic stages of the process by at least 6 hours and to improve the yield of 4-ADPA from 92 to 94% by distillation of aniline and use of a solvent, a mixture of water with toluene, during the hydrogenation stage.

The use of tetramethylammonium chloride instead of the expensive and thermally unstable TMAH reduces the cost of raw materials [28]. Additionally, it reduces consumption of the hydrogenation catalyst, based on platinum, and the catalytic hydrogenation time was shortened from 4 to 2 hours.

A complete removal of TMAH from the reaction mixture immediately after the condensation reaction allows for catalytic hydrogenation of the mixture of 4-NO_2DPA and 4-NODPA at a temperature above 80 °C. This helps increase the degree of conversion during hydrogenation to 100% as well as reduce the duration of the process [29].

Condensation of the tetramethylammonium salt of anilide anion, with formula C_6H_5NHM (where M = tetramethylammonium cation), with NB in the aniline medium by removing water and producing a mixture of tetramethylammonium salts, 4-NO_2DPA and 4-NODPA, is carried out at a temperature of 67–75 °C and a pressure of 26.6 kPa [30]. The tetramethylammonium anilide is prepared by stirring aniline, tetramethylammonium chloride, KOH, water, and subsequent filtration from excess KCl. Once the condensation is complete, TMAH is removed from the reaction mixture, and the remaining mixture of 4-NO_2DPA and 4-NODPA is catalytically hydrogenated to 4-ADPA. The media for hydrogenation are aniline, toluene, and water. Using solution of the tetramethylammonium salt of anilide anion helps increase the 4-ADPA yield and reduce process costs.

Of special note is a combined single-stage process for preparation of ADPA, where NB is loaded into the reaction zone under hydrogen pressure in the presence of a strong organic base (TMAH) and hydrogenation catalyst [31]. Thus, during the first stage, in the reactor, NB is hydrogenated to aniline, then the formed aniline is condensed with NB in the presence of a base, and the intermediates are further hydrogenated to 4-ADPA. The process is carried out at temperatures of 80−90 °C, pressures of 400−3000 kPa, and the NB to base ratio of less than 1. When a molar ratio of TMAH to NB was greater than 1, the selectivity of the reaction shifted towards the formation of azoxybenzene, aniline, and diphenylhydrazine.

4. The mechanism of condensation reaction of nitrobenzene with aniline

Condensation of aniline with NB serves as an example of nucleophilic aromatic substitution of hydrogen, or NASH. Stern et al. [13], upon the research of NB with aniline-d5 reaction, have proposed a mechanism of condensation of NB with aniline in strongly basic media. In anhydrous, highly polar solvents, a very active nucleophile, anilide anion **P1**, is generated from aniline by deprotonation with tetraalkylammonium hydroxide (TMA-OH). The attack of anilide ion on the NB molecule mostly happens in the *para*-position and leads to the formation of anionic *p*-σ-complex **P2** (see Fig. 3). The attack of anilide-ion in the *ortho*-position of NB leads to the formation of phenazine. The authors suppose that further transformations of **P2** are connected with the oxidation–reduction process of hydride ion abstraction with two possible mechanisms: the intermolecular mechanism of elimination and transfer of hydride from σ-complex **P2** to the nitro group of another molecule, forming water and salt 4-NO_2DPA **P3**. The corresponding intramolecular mechanism transfers hydride to the nitro group of NB and leads to the formation of water and salt 4-NODPA **P4**.

Participation of the nitro group of the initial nitroarene, or its σ-complex, in hydrogen oxidative substitution was marked by the reaction of acetanilide with NB [32] and the reaction of benzamide acetanilide with NB [33]. The peculiarity of these reactions is the absence of external oxidant. Either the initial reagent, i.e. nitrobenzene, or a nitro group of the σ-complex **P2** can (and must) participate in the oxidation–reduction process required for hydride ion abstraction from the σ-complex.

The results of modelling the condensation reaction of aniline with NB in the presence of TMAH by the PM6 method [34] revealed that the catalyst had been actively involved in the process by activating the reactants (**P1**) and intermediates (**P2**) while stabilizing the end products (**P3**, **P4**). The mechanism of its action is as follows: tetramethylammonium cation can form ionic or ion-dipole complexes with the reactants and impact their charge distribution, thereby governing their reactivity. As a result of calculations, the rate determining step for condensation of aniline with NB in the presence of TMAH is the hydride transfer from **P2** to the acceptor, NB or 4-NO_2DPA. The most probable path is the intermolecular transfer mechanism which has a lower activation energy (E_a = 98–121 kJ/mol),

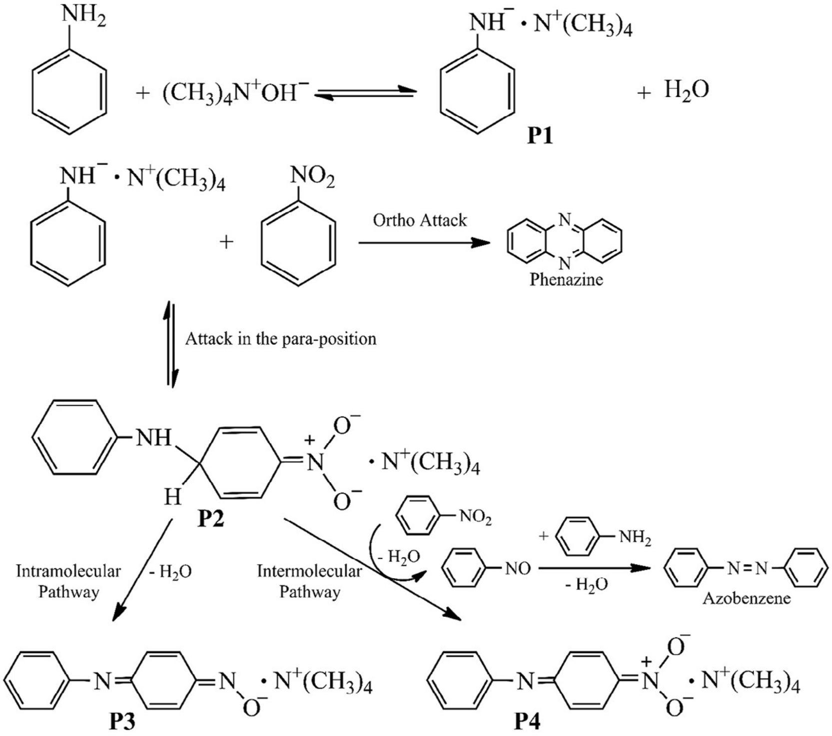

Fig. 3. The mechanism of condensation of nitrobenzene with aniline.

compared with the intramolecular transfer mechanism ($E_a = 270–330$ kJ/mol). However, the intermolecular reaction is dependent on the concentration of other acceptor molecules (e.g., NB concentration) while the rate of intramolecular reaction is fixed, all else being equal.

5. Homogeneous catalysts of the stage of condensation of aniline with nitrobenzene

The activity of various quaternary ammonium bases as catalysts for the condensation reaction of aniline with NB was evaluated (see Table 2) in the previous work [35].

The effectiveness of quaternary ammonium bases as catalysts of nucleophilic aromatic substitution for hydrogen is supported by the fact that the reaction of NB with aniline, in the presence of KOH only, is very slow and has low selectivity for desired products (5.2%).

As evidenced from Table 2, the most complete conversion of NB is achieved by using TMAH, tetrapropylammonium hydroxide, and benzyltrimethylammonium hydroxide as catalysts. It should be noted that the most active phase transfer catalyst of the group, tetrabutylammonium hydroxide, proved ineffective in this process. The selectivity of the process for target products 4-NO_2DPA and 4-NODPA decreases in the series: bis-(dibutylethyl) hexametylendiamine hydroxide (97.3%), benzyltrimethylammonium hydroxide (87.1%), tetrapropylammonium hydroxide (82.1%), tetrabutylammonium hydroxide (79.7%), TMAH (77.0%) under the reaction conditions used.

The catalyst systems based on quaternary ammonium halides and related salts in combination with and alkali metal hydroxide, the thermal and chemical resistance of which are higher than the respective ammonium hydroxides, have found wide application. Patent [36] presents testing results of the

Table 2
The activity and selectivity of various quaternary ammonium bases as catalysts for the condensation reaction of aniline with NB.

Catalyst	Conversion NB, %	Yield, %			
		4-NODPA	4-NO_2DPA	Azobenzene	Phenazine and other
Tetramethylammonium hydroxide	100	43.0	34.0	12.1	10.9
Tetrapropylammonium hydroxide	100	63.8	18.3	17.5	0.4
Benzyltrimethylammonium hydroxide	100	74.7	12.4	11.7	1.2
Tetrabutylammonium hydroxide	77.5	52.1	9.7	3.4	12.3
Bis-(dibutylethyl)hexamethylene diammonium hydroxide	85.3	76.0	7.0	1.1	1.2
(Hydroxyethyl)trimethylammonium (Choline) hydroxide	83.6	33.0	9.6	40.2	0.9
KOH only, no phase transfer catalyst added [36]	19.6	1.2	4.0	3.3	11.1

Table 3
Activity and selectivity of various catalytic systems in the reaction of aniline with NB (temperature – 60 °C; duration – 1 hour; ratio NB:aniline:KOH:catalyst = 1:6:3:1).

Catalyst	Conversion NB, %	Yield, %			
		4-NODPA	4-NO_2DPA	Azobenzene	Phenazine and other
Tetramethylammonium fluoride	100	42.4	27.2	27.4	3.0
Tetramethylammonium hydroxide	100	38.4	29.6	30.4	1.6
Tetramethylammonium acetate	100	25.9	43.1	30.6	0.4
Tetramethylammonium chloride	98.8	24.3	37.1	30.8	6.6
Tetramethylammonium carbonate	97.6	46.6	24.6	23.7	2.7
Methyltributylammonium chloride	81.7	23.5	30.6	22.2	5.4
Tetramethylammonium formate	74.9	29	23.8	21	1.1
Tricaprylylmethylammonium chloride	67	19.1	21.3	19.6	7.0
Benzyltrimethylammonium hydroxide	52.5	39.6	6.2	5.5	1.2
Tetramethylammonium nitrate	61.3	12	27.4	19.6	2.3
Tetrabutylammonium chloride	42.6	8.2	23.8	9.3	1.3
Tetramethylammonium bromide	36.5	11.3	12.2	6.7	6.3
Tetrabutylammonium bromide	34.1	8.3	14.2	5.8	5.8
Cetyltrimethylammonium bromide	36.2	7	19.3	8.7	1.2
Tetramethylammonium iodide	27.8	2.4	8	5.8	11.6
Tetrabutylphosphonium bromide	25.6	1.6	5.1	9.4	9.5

process of condensation of aniline with NB in alkaline medium in the presence of catalysts which are various salts of tetraalkylammonium ion: chlorides, fluorides, bromides, iodides, acetates, carbonates, etc. The experimental results are presented in Table 3.

The results demonstrated in Table 3 show that chloride, fluoride, hydroxide, carbonate, tetramethylammonium formate and acetate, methyltributylammonium chloride and benzyltrimethylammonium hydroxide, all in combination with KOH, are most effective as catalysts for condensation of aniline with NB. Others, such as tetrabutylammonium chloride and tetramethylammonium nitrate, are moderately active and no tetraalkylammonium iodides and bromides examined were effective in the condensation process. It should be noted that, in tetramethylammonium salts, there is a tendency of decreased conversion, yield and selectivity in the series fluoride > chloride > bromide > iodide. This trend indicates that the mechanism of action of quaternary ammonium bases (and salts) in the condensation reaction of aniline with NB is different from the mechanism of action of interphase or phase transfer catalysts.

More accurate information on the catalytic activity of various catalysts can be obtained from the kinetics of the process. In such work [37], the inventors studied the kinetics of the condensation of aniline with NB and defined the observed relative activity of various catalysts $(C_2H_5)_4NCl/NaOH$ (1.02) ≈ $(CH_3)_4NCl/NaOH$ (1.00) > $(C_3H_7)_4NCl/NaOH$ (0.72) > $(C_4H_9)_4NCl/NaOH$ (0.37). The resulting range of activity for various catalyst systems clearly points to the fact that positively charged quaternary ammonium groups participate in the rate-determining step of the condensation process. Moreover, the catalytic activity of quaternary ammonium compounds is determined primarily by geometrical dimensions of the cation $N(R)_4^+$. The experimental value of the observed activation energy of condensation is $E_{obs} = 71.0$ kJ/mol, which is in fairly good agreement with the calculated activation energy for the intermolecular mechanism of hydride ion transfer involving NB, $E_a = 98.0$ kJ/mol [34].

As noted above, the thermal instability of quaternary ammonium bases imposes severe restrictions on the conditions of the condensation stage. The decomposition of quaternary ammonium bases during condensation and typical requirement for extracting the base (or extracting the product from the base) affects the technical and economic parameters of the process of preparing 4-ADPA and largely determines the economic feasibility of industrial applications.

The associates of NOCIL LIMITED (India) [38] have conducted studies to determine the conditions of aniline/NB condensation and the regeneration temperature, pressure and duration for a homogeneous catalyst in which virtually no decomposition of TMAH was observed. Temperature, pressure and duration of the process, the initial molar ratio of TMAH/NB, H_2O/TMAH, together with the design of the reactor, affect the rate of decomposition of TMAH. In the reaction mixture, TMAH may be in a “free” or “bound” state, where bound ions form ion pairs with salts **P3** and **P4** (see Fig. 3), the relative amount of which depends on the degree of NB conversion. It was found that TMAH begins to decompose visibly if the H_2O/“free” TMAH ratio in the reaction mass, in the condensation stage, is less than 3.5:1 (or the molar ratio of water to the total amount of TMAH is less than 0.3:1). The authors of the patent [38] defined optimal conditions for conducting the stage of condensation of aniline with NB as follows:

- the temperature in the reaction zone is 60–75 °C
- residual pressure in the reaction zone is 0.7–7.0 kPa
- the initial molar ratio of aniline to NB is 6–10:1
- the initial molar ratio of the total TMAH to NB is 0.85–1.00:1
- the molar ratio of water to the total amount of TMAH in the reaction mass is not less than 0.3:1
- the molar ratio of water to the amount of “free” TMAH in the reaction mass is not less than 3.5:1
- the reaction is run continuously in a cascade of reactors, the first of which is a mixing reactor (or a cascade of several mixing reactors), and the last – the displacement reactor

Using a continuous mixing reactor at the initial stage of condensation makes it possible to maintain optimal process conditions by changing (a) the feed rate of the starting materials and the catalyst solution, and (b) the temperature and pressure in the reaction zone to control the concentrations of the reactants and reaction products. The use of a displacement reactor at the final stage of condensation helps control the degree of NB conversion. The results of experiments carried out under the above conditions show that the observed decomposition of TMAH is less than 1% and nearly 50% less phenazine than usual is formed.

Conducting the condensation reaction by a continuous method in a mixing reactor leads to the fact that reactants are fed into the reaction mixture which contains the reaction products, 4-NO_2DPA and 4-NODPA. As discussed above, the most likely mechanism is the intermolecular hydride-ion transfer from **P2**, involving NB or 4-NO_2DPA. Therefore, the presence of 4-NO_2 DPA in the reaction mixture leads to competition between NB and 4-NO_2 DPA for the transfer of a hydride ion and, consequently, leads to an increase in 4-NODPA/4-NO_2DPA ratio and decrease of azobenzene formation. This diminution in azobenzene formation should increase the consumption index of raw materials $\boldsymbol{I}_{RMU,\,t}$ and, accordingly, improve the technical, economic and environmental performance of the method of 4-ADPA production.

6. Heterogeneous catalysts of the stage of condensation of aniline with nitrobenzene

To decrease TMAH consumption and to improve the technical and economic performance of the process, in the patent [39], the inventors use zeolite ZSM-5 treated with TMAH as a catalyst for the reaction of aniline with NB. TMAH content in the catalyst is approximately 25% by mass. The process is carried out with the ratio of aniline to nitrobenzene greater than or equal to 5:1, nitrobenzene to base 1.05:1, at a temperature of approximately 70–75 °C. Using this heterogeneous catalyst helped reduce the formation of by-products azobenzene and phenazine (the selectivity for 4-NO_2DPA and 4-NODPA is close to 100%), and decreased degradation of TMAH by its application to the zeolite. The process may be conducted in two stages (the first stage – obtaining intermediates, the second – hydrogenation of the said intermediates) or in a single stage. The reaction scheme of a single-stage process for preparing 4-ADPA using a catalyst containing, in addition to TMAH and ZSM-5 zeolite, a palladium hydrogenation component, is provided in Fig. 4.

The two-stage process is preferred over the single-stage process, as it allows maintenance of optimum parameters separately for condensation (temperature 60–75 °C, residual pressure of 0.5–9.5 kPa) and hydrogenation (temperature 60–120 °C, excess pressure of 0.1–3.0 MPa).

The use of ZSM-5 zeolite treated with TMAH significantly decreases decomposition of the latter at high temperature and helps carry out the process at a wide range of operating temperatures. Additionally, using a heterogeneous catalyst eliminates the process stages of separation and regeneration of the organic base, which reduces the cost of the resulting 4-ADPA.

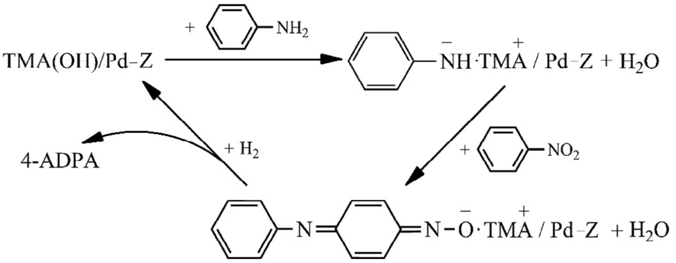

Fig. 4. Reaction scheme of a one-stage process for preparing 4-ADPA with catalyst TMA (OH)/Pd-Z (Pd-Z-Pd applied to ZSM-5).

Bochkarev and associates [40] developed a method of producing 4-ADPA and intermediate products of its synthesis by reacting aniline and NB in the presence of a catalyst containing a quaternary ammonium group to produce 4-NO_2DPA and 4-NODPA as intermediates. Subsequent hydrogenation of the intermediates of the reaction in the presence of a catalyst and a solvent, which is lower alcohol or water, produces 4-ADPA. The catalyst characterizes the method: at the stage of reacting of aniline with nitrobenzene, they use a highly basic anion exchange resin in the OH-form, containing a quaternary ammonium group $\sim N(CH_3)_3^+$, and the reaction is carried out in the presence of inorganic base.

The use of a polymeric catalyst eliminates the process step or unit operation of separating catalyst from the reaction mixture and removes strict temperature and concentration limits at the subsequent stages of producing 4-ADPA. Such a method helps lower the cost of raw materials by using a heterogeneous catalyst and reduces the energy consumption for separation of the reaction products. The known, highly porous strong base anion exchange resins may thus be used as condensation catalysts without having to synthesize a heterogeneous catalyst.

To determine the effectiveness of anion exchange resins as catalysts, the inventors conducted comparative kinetic studies of the condensation process using highly basic anion exchangers AB-17-8 and Dowex Marathon MSA in the OH-form, and an existing catalyst system $(CH_3)_4NCl$/NaOH [37,41]. It was demonstrated that at the same concentration of active quaternary ammonium groups, the activity of the catalysts decreases in the following series: a macroporous anion exchanger Dowex Marathon MSA (1.11) > $(CH_3)_4NCl$/NaOH (1.00) > gel anion exchanger AB-17-8 (0.91). With a low molar ratio of catalyst/NB (0.5–0.8), the activity of AB-17-8 and Dowex Marathon MSA is essentially the same. With further increase in the molar ratio of catalyst/NB concentration, the dependence of the observed rate constant is seen to have a maximum: for AB-17-8, with the molar ratio of catalyst/NB = 1; for Dowex Marathon MSA, with the molar ratio of catalyst/NB ≈ 2.

This fact can be explained as follows: On the one hand, the catalyst activates a molecule of aniline which must accelerate the condensation process. On the other hand, the condensation products, 4-NO_2DPA and 4-NODPA, as anions, can be adsorbed at the active sites of the catalyst and an increase in the amount of catalyst (above the equimolar with respect to NB) should decrease the concentration of the adsorbed products of

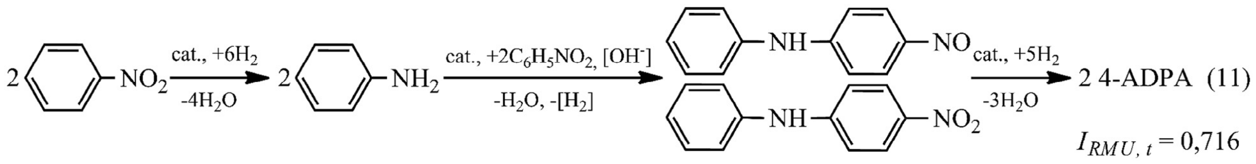

Fig. 5. A method of obtaining 4-ADPA from nitrobenzene.

the reaction and, accordingly, the diffusion rates of the reaction products from the catalyst surface into the solution. For the macroporous anion exchange resin Dowex Marathon MSA such factor is less significant than for a gel anion-exchange resin AB-17-8. Therefore, the rate of condensation of aniline with NB using highly basic anion exchangers as catalyst is controlled by both kinetic and internal diffusion factors. The analysis of experimental data demonstrates that, when using anion exchangers, the process is controlled by internal diffusion of the product, with the molar ratio of catalyst/nitrobenzene > 1 for AB-17-8, and the molar ratio of catalyst/nitrobenzene > 2 for Dowex Marathon MSA. In practical implementation of the process of condensation of aniline with NB, it is recommended to use molar ratio of catalyst/nitrobenzene = 1.

Given the advantages of using heterogeneous catalysts, we can propose the following method of producing 4-ADPA from cheap NB (see Fig. 5, $\boldsymbol{I}_{RMU,t} = 0.719$, among the highest indices in the reviewed methods). The flowchart of this process is provided in Fig. 6.

The hydrogenation stage of NB to aniline is a well-developed industrial process. The said stage may be carried out at the following conditions: temperature 60–150 °C; pressure 0.1–3.0 MPa; NB conversion degree 0.52–0.60; catalyst Pd, Pt, Ni, etc., in various media. Reaction conditions of the condensation stage are as follows: temperature 60–75 °C; residual pressure 0.7–7.0 kPa; conversion degree of NB 0.95–0.99; catalyst TMA(OH)/ZSM-5 or highly basic anion exchanger Dowex Marathon MSA (or Tulsion A-74 MP, Purolite A500 [40]). As a reaction unit at this stage, a cascade of 2 reactors with a fixed catalyst bed can be used. The first device is a reactor with recirculation of the reaction mixture; the second is a displacement reactor. Both reactors are operated under vacuum with distillation of the aniline–water mixture. Reaction conditions of the hydrogenation stage are as follows: temperature 60–150 °C; pressure 0.1–3.0 MPa; conversion degree of NB 0.98–1.00; catalysts Pd, Pt, Ni, etc., in various media.

7. Conclusions

The reaction of aniline with nitrobenzene in the presence of strong bases and condensation catalysts has commercial value since it eliminates the need for halogenated aromatic compounds which cause environmental problems in the production of substituted aromatic amines. Using the methods of Section 6 in particular for the industrial production of 4-ADPA will eliminate in the most modern way some of the disadvantages inherent in the existing industrial methods. These methods will reduce unit operations of the process, employ more accessible and inexpensive raw materials, improve the yield, eliminate the formation of carcinogenic substances, significantly decrease the formation of waste products and, most importantly, eliminate vast amounts of wastewater associated with many versions of this chemistry.

The most promising methods for industrial production are the ones that use heterogeneous catalyst during the stage of condensation of aniline with NB, e.g., zeolite ZSM-5 treated with TMAH, or highly basic anion exchangers, which considerably simplify the production technology and process control, lower costs and comply with strict environmental requirements. Highly basic anion-exchange resins containing quaternary ammonium groups (Dowex Marathon MSA et al.), by their catalytic activity in the reaction of aniline with NB, are only slightly inferior to the known catalytic system $(CH_3)_4NCl$/NaOH. However, when selecting the reaction conditions and hardware design, it must be taken into account that the rate of condensation of aniline with NB, using a heterogeneous catalyst, is controlled by kinetic factors including diffusion.

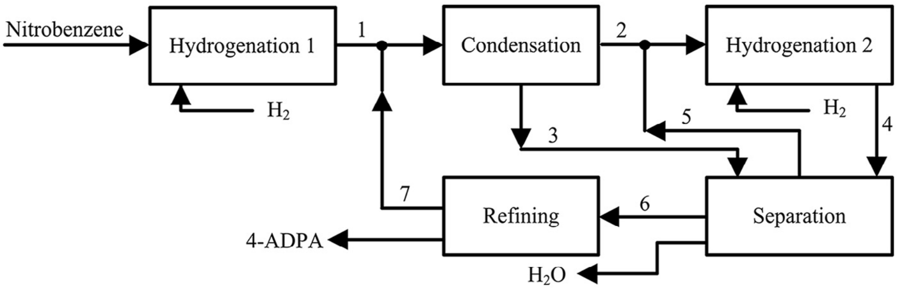

Fig. 6. Flow chart of the 4-ADPA preparation from nitrobenzene. 1 – reaction mixture after hydrogenation of nitrobenzene; 2 – reaction mixture after condensation; 3 – distilled water with aniline at the condensation stage; 4 – reaction mixture after hydrogenation of condensation products; 5 – circulating water to the hydrogenation stage; 6 – organic products from the separation stage; 7 – returnable aniline.

Acknowledgement

The authors are thankful to all staff of Tomsk Polytechnic University for discussion of this work and their assistance in the preparation of this manuscript.

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